(19)中华人民共和国国家知识产权局

(12)发明专利

(10)授权公告号 CN 105209450 B
(45)授权公告日 2017.10.20

(21)申请号 201480027669.8

(22)申请日 2014.03.13

(65)同一申请的已公布的文献号
申请公布号 CN 105209450 A

(43)申请公布日 2015.12.30

(30)优先权数据
61/784,020 2013.03.14 US

(85)PCT国际申请进入国家阶段日
2015.11.13

(86)PCT国际申请的申请数据
PCT/US2014/025674 2014.03.13

(87)PCT国际申请的公布数据
WO2014/160031 EN 2014.10.02

(73)专利权人 美国陶氏益农公司
地址 美国印第安纳州

(72)发明人 L·G·费希尔 E·W·鲍姆
G·D·克劳斯 C·迪米西斯
B·洛尔斯巴赫 J·佩特库斯
T·C·斯帕克斯 G·T·惠特克
A·L·沃德 R·罗斯 Y·郝
N·C·詹彼得罗

(74)专利代理机构 北京坤瑞律师事务所 11494
代理人 吴培善

(51)Int.Cl.
C07D 401/00(2006.01)
A61K 31/4196(2006.01)
A01N 43/647(2006.01)
A01P 7/00(2006.01)
A01P 9/00(2006.01)
A01P 19/00(2006.01)

(56)对比文件
US 2013/0019348 A1,2013.01.17,
US 2012/0053216 A1,2012.03.01,
CN 101998963 A,2011.03.30,
CN 102548411 A,2012.07.04,

审查员 张旋

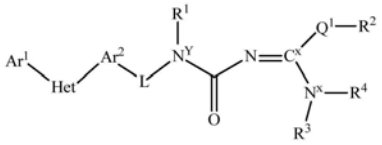
权利要求书1页 说明书538页

(54)发明名称

具有一定农药效用的分子和中间体、组合物及其相关方法

(57)摘要

本申请涉及具有抵抗门线虫，节肢动物，和/或软体动物中害虫的农药效用的分子的领域，制备该分子的方法和用于该方法的中间体，含有该分子的组合物，和使用该分子抵抗该害虫的方法。这些分子可以例如，作为杀线虫剂，杀螨剂，杀昆虫剂，杀螨剂，和/或杀软体动物剂使用。该文件披露具有下式的分子(“式一”)。



CN 105209450 B

1.一种分子,其为选自说明书表P-I、表P-II、表2A和表2C中所列的分子。

2.权利要求1的分子,其中所述分子为选自说明书表2A、表2B和表2C中所列的分子。

3.防治害虫的方法,包括:施用权利要求1的分子至所在地,从而防治害虫,其量足以防治该害虫。

具有一定农药效用的分子和中间体、组合物及其相关方法

技术领域

[0001] 本申请涉及具有抵抗门线虫，节肢动物，和软体动物中害虫的农药效用的分子的领域，制备该分子的方法和用于该方法的中间体，含有该分子的组合物，和使用该分子抵抗该害虫的方法。这些分子可以例如，作为杀线虫剂，杀螨剂，杀昆虫剂，杀螨剂，和杀软体动物剂使用。

背景技术

[0002] “许多最危险的人类疾病由昆虫媒介传播”(Rivero，A.等人，InsectControl of Vector-Borne Diseases:When is Insect Resistance a Problem?Public Library of Science Pathogens，6(8)(2010))。在历史上，从1600年代初到1900年代初，媒介传播的疾病(尤其例如疟疾、登革热、黄热病、瘟疫和虱传斑疹伤寒)，相比于所有其他原因的组合，引起更多的人类疾病和死亡(Gubler D.，Resurgent Vector-Borne Diseases as a Global Health Problem，Emerging Infectious Diseases，Vol.4，No.3，July-September(1998))。目前，媒介传播的疾病对约17％的全球寄生和感染性疾病负责。估计每年全世界约2.5亿人患有疟疾和约800，000人死亡，85％的那些死者都是五岁以下的孩子。每年还出现250，000至500，000例的登革出血热(Matthews，G.，Integrated Vector Management:controlling vectors of malaria and other insect vector borne diseases(2011))。媒介控制在预防和控制感染性疾病方面起到关键作用。但是，杀昆虫剂抗性，包括对多种杀昆虫剂的抗性，已经出现在作为人类疾病主要载体的所有的昆虫种类中(Rivero，A.等人)。

[0003] 每年，昆虫、植物病原体和杂草破坏大于40％的所有潜在的食品生产。尽管施用农药和使用广泛的非化学控制，例如作物轮作和生物控制，但这样的损失仍然发生。如果能保存这种食品中的仅一些食品，就会将其用于供养世界范围内大于三十亿营养不良的人(Pimental，D.，PestControl in World Agriculture，Agricultural Sciences-Vol.II(2009))。

[0004] 植物寄生线虫是最普遍的害虫，并且经常是最具潜在危险的和成本最高的。估计归因于线虫的损失为在发达国家的约9％至在不发达国家的约15％。但是，在美国，35个州对多种作物的调查表明，线虫类引起的损失高达25％(Nicol，J.等人，Current Nematode Threats to World Agriculture，Genomic and Molecular Genetics of Plant-Nematode Interactions(Eds.Jones，J.等人)，Chapter 2，(2011))。

[0005] 值得注意的是，腹足类(蛞蝓和螺蛳)是比昆虫或线虫经济重要性小的害虫，但在某些区域内，腹足类可以大幅降低产量，严重影响所收获产品的质量，以及传播给人类、动物和植物疾病。尽管仅有几十种腹足动物是严重区域性害虫，但少数种类在世界范围内是重要的害虫。特别是腹足类影响各种农业和园艺作物，例如可耕种的作物、田园作物和纤维作物；蔬菜；灌木和树果；草本植物；和观赏植物(Speiser，B.，Molluscicides，Encyclopedia of Pest Management(2002))。

[0006] 白蚁对各种私人和公共结构以及农业和林业资源造成损害。2003年，估计白蚁每

年造成超过200亿美元的损失(Su,N.Y.,Overview of the global distribution andControl of the Formosan subterranean termite,Sociobiology 2003,41,177-192)。

[0007] 因此,由于许多原因,包括上述原因,存在新的农药的需要。

[0008] 定义

[0009] 在定义中给出的实例通常是非穷举性的且不能被解释为对本申请公开的发明进行限制。应该理解的是,取代基应该符合化学键合规则及就与其连接的特定分子而言符合立体化学相容性限制。

[0010] “烯基”表示由碳和氢组成的非环状的不饱和的(至少一个碳-碳双键)支链或非支链的取代基,例如乙烯基、烯丙基、丁烯基、戊烯基和己烯基。

[0011] “烯基氧基”表示还包含碳-氧单键的烯基,例如烯丙基氧基、丁烯基氧基、戊烯基氧基、己烯基氧基。

[0012] “烷氧基”表示还包含碳-氧单键的烷基,例如甲氧基、乙氧基、丙氧基、异丙氧基、丁氧基、异丁氧基,和叔丁氧基。

[0013] “烷基”表示由碳和氢组成的非环状的饱和的支链或非支链的取代基,例如甲基、乙基、正丙基、异丙基、丁基和叔丁基。

[0014] “炔基”表示由碳和氢组成的非环状的不饱和的(至少一个碳-碳叁键)支链或非支链的取代基,例如乙炔基、炔丙基、丁炔基和戊炔基。

[0015] “炔基氧基”表示还包含碳-氧单键的炔基,例如戊炔基氧基、己炔基氧基、庚炔基氧基和辛炔基氧基。

[0016] “芳基”表示由氢和碳组成的环状的芳族的取代基,例如苯基、萘基和联苯基。

[0017] “环烯基”表示由碳和氢组成的单环或多环的不饱和的(至少一个碳-碳双键)取代基,例如环丁烯基、环戊烯基、环己烯基、降冰片烯基、二环[2.2.2]辛烯基、四氢萘基、六氢萘基和八氢萘基。

[0018] “环烯基氧基”表示还包含碳-氧单键的环烯基,例如环丁烯基氧基、环戊烯基氧基、降冰片烯基氧基和二环[2.2.2]辛烯基氧基。

[0019] “环烷基”表示由碳和氢组成的单环或多环的饱和的取代基,例如环丙基、环丁基、环戊基、降冰片基、二环[2.2.2]辛基和十氢萘基。

[0020] “环烷氧基”表示还包含碳-氧单键的环烷基,例如环丙基氧基、环丁基氧基、环戊基氧基、降冰片基氧基和二环[2.2.2]辛基氧基。

[0021] “卤素”表示氟、氯、溴和碘。

[0022] “卤代烷氧基”表示还包含一个至最大可能数目的相同或不同的卤素的烷氧基,例如氟甲氧基、三氟甲氧基、2,2-二氟丙氧基、氯甲氧基、三氯甲氧基、1,1,2,2-四氟乙氧基,和五氟乙氧基。

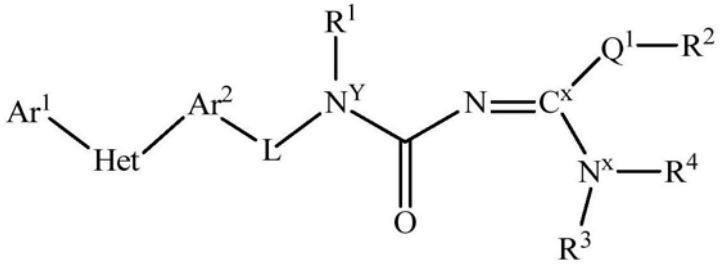
[0023] “卤代烷基”表示还包含一个至最大可能数目的相同或不同的卤素的烷基,例如氟甲基、三氟甲基、2,2-二氟丙基、氯甲基、三氯甲基和1,1,2,2-四氟乙基。

[0024] “杂环基”表示环状取代基,其可为完全饱和、部分不饱和或完全不饱和的,其中所述环状结构含有至少一个碳和至少一个杂原子,其中所述杂原子为氮、硫或氧。芳族杂环基的实例包括但不限于苯并呋喃基、苯并异噻唑基、苯并异噁唑基、苯并噁唑基、苯并噻吩基、

苯并噻唑基、噌啉基(cinnolinyl)、呋喃基、吲唑基、吲哚基、咪唑基、异吲哚基、异喹啉基、异噻唑基、异噁唑基、噁二唑基、噁唑啉基、噁唑基、酞嗪基、吡嗪基、吡唑啉基、吡唑基、哒嗪基、吡啶基、嘧啶基、吡咯基、喹唑啉基、喹啉基、喹喔啉基、四唑基、噻唑啉基、噻唑基、噻吩基、三嗪基，和三唑基。完全饱和杂环基的实例包括但不限于哌嗪基、哌啶基、吗啉基、吡咯烷基、四氢呋喃基和四氢吡喃基。部分不饱和杂环基的实例包括但不限于1,2,3,4-四氢喹啉基、4,5-二氢-噁唑基、4,5-二氢-1H-吡唑基、4,5-二氢-异噁唑基，和2,3-二氢-[1,3,4]-噁二唑基。

具体实施方式

[0025] 该文件披露具有下式的分子(“式一”)

[0026] 

式一

[0027] 其中：

[0028] (A)Ar^1选自

[0029] (1)苯基，哒嗪基，吡啶基，嘧啶基，或

[0030] (2)取代苯基，取代哒嗪基，取代吡啶基，或取代嘧啶基，

[0031] 其中所述取代苯基，取代哒嗪基，取代吡啶基，和取代嘧啶基具有一个或多个取代基，所述一个或多个取代基独立地选自H，F，Cl，Br，I，CN，NO_2，C_1-C_6烷基，C_1-C_6卤代烷基，C_3-C_6环烷基，C_3-C_6卤代环烷基，C_3-C_6环烷氧基，C_3-C_6卤代环烷氧基，C_1-C_6烷氧基，C_1-C_6卤代烷氧基，C_2-C_6烯基，C_2-C_6炔基，S(=O)$_n$(C_1-C_6烷基)，S(=O)$_n$(C_1-C_6卤代烷基)，OSO_2(C_1-C_6烷基)，OSO_2(C_1-C_6卤代烷基)，C(=O)NR^xR^y，(C_1-C_6烷基)NR^xR^y，C(=O)(C_1-C_6烷基)，C(=O)O(C_1-C_6烷基)，C(=O)(C_1-C_6卤代烷基)，C(=O)O(C_1-C_6卤代烷基)，C(=O)(C_3-C_6环烷基)，C(=O)O(C_3-C_6环烷基)，C(=O)(C_2-C_6烯基)，C(=O)O(C_2-C_6烯基)，(C_1-C_6烷基)O(C_1-C_6烷基)，(C_1-C_6烷基)S(C_1-C_6烷基)，C(=O)(C_1-C_6烷基)C(=O)O(C_1-C_6烷基)，苯基，苯氧基，取代苯基和取代苯氧基

[0032] 其中该取代苯基和取代苯氧基具有一个或多个取代基，所述一个或多个取代基独立地选自H，F，Cl，Br，I，CN，NO_2，C_1-C_6烷基，C_1-C_6卤代烷基，C_3-C_6环烷基，C_3-C_6卤代环烷基，C_3-C_6环烷氧基，C_3-C_6卤代环烷氧基，C_1-C_6烷氧基，C_1-C_6卤代烷氧基，C_2-C_6烯基，C_2-C_6炔基，S(=O)$_n$(C_1-C_6烷基)，S(=O)$_n$(C_1-C_6卤代烷基)，OSO_2(C_1-C_6烷基)，OSO_2(C_1-C_6卤代烷基)，C(=O)NR^xR^y，(C_1-C_6烷基)NR^xR^y，C(=O)(C_1-C_6烷基)，C(=O)O(C_1-C_6烷基)，C(=O)(C_1-C_6卤代烷基)，C(=O)O(C_1-C_6卤代烷基)，C(=O)(C_3-C_6环烷基)，C(=O)O(C_3-C_6环烷基)，C(=O)(C_2-C_6烯基)，C(=O)O(C_2-C_6烯基)，(C_1-C_6烷基)O(C_1-C_6烷基)，(C_1-C_6烷基)S(C_1-C_6烷基)，C(=O)(C_1-C_6烷基)C(=O)O(C_1-C_6烷基)，苯基，和苯氧基；

[0033] (B)Het为5元或6元，饱和或不饱和的杂环，含有一个或多个杂原子，所述一个或多

个杂原子独立地选自氮,硫或氧,并且其中Ar^1和Ar^2彼此不是邻位(但可以为间位或对位,例如,对于五元环它们是1,3,对于6元环它们是1,3或1,4),并且其中所述杂环也可以取代有一个或多个取代基,所述一个或多个取代基独立地选自H,F,Cl,Br,I,CN,NO_2,氧代,C_1-C_6烷基,C_1-C_6卤代烷基,C_3-C_6环烷基,C_3-C_6卤代环烷基,C_3-C_6环烷氧基,C_3-C_6卤代环烷氧基,C_1-C_6烷氧基,C_1-C_6卤代烷氧基,C_2-C_6烯基,C_2-C_6炔基,S(=O)$_n$(C_1-C_6烷基),S(=O)$_n$(C_1-C_6卤代烷基),OSO_2(C_1-C_6烷基),OSO_2(C_1-C_6卤代烷基),C(=O)NR^xR^y,(C_1-C_6烷基)NR^xR^y,C(=O)(C_1-C_6烷基),C(=O)O(C_1-C_6烷基),C(=O)(C_1-C_6卤代烷基),C(=O)O(C_1-C_6卤代烷基),C(=O)(C_3-C_6环烷基),C(=O)O(C_3-C_6环烷基),C(=O)(C_2-C_6烯基),C(=O)O(C_2-C_6烯基),(C_1-C_6烷基)O(C_1-C_6烷基),(C_1-C_6烷基)S(C_1-C_6烷基),C(=O)(C_1-C_6烷基)C(=O)O(C_1-C_6烷基),苯基,苯氧基,取代苯基和取代苯氧基

[0034] 其中该取代苯基和取代苯氧基具有一个或多个取代基,所述一个或多个取代基独立地选自H,F,Cl,Br,I,CN,NO_2,C_1-C_6烷基,C_1-C_6卤代烷基,C_3-C_6环烷基,C_3-C_6卤代环烷基,C_3-C_6环烷氧基,C_3-C_6卤代环烷氧基,C_1-C_6烷氧基,C_1-C_6卤代烷氧基,C_2-C_6烯基,C_2-C_6炔基,S(=O)$_n$(C_1-C_6烷基),S(=O)$_n$(C_1-C_6卤代烷基),OSO_2(C_1-C_6烷基),OSO_2(C_1-C_6卤代烷基),C(=O)H,C(=O)NR^xR^y,(C_1-C_6烷基)NR^xR^y,C(=O)(C_1-C_6烷基),C(=O)O(C_1-C_6烷基),C(=O)(C_1-C_6卤代烷基),C(=O)O(C_1-C_6卤代烷基),C(=O)(C_3-C_6环烷基),C(=O)O(C_3-C_6环烷基),C(=O)(C_2-C_6烯基),C(=O)O(C_2-C_6烯基),(C_1-C_6烷基)O(C_1-C_6烷基),(C_1-C_6烷基)S(C_1-C_6烷基),苯基,和苯氧基;

[0035] (C)Ar^2选自

[0036] (1)苯基,哒嗪基,吡啶基,嘧啶基,或

[0037] (2)取代苯基,取代哒嗪基,取代吡啶基,或取代嘧啶基,

[0038] 其中所述取代苯基,取代哒嗪基,取代吡啶基,和取代嘧啶基具有一个或多个取代基,所述一个或多个取代基独立地选自H,F,Cl,Br,I,CN,NO_2,C_1-C_6烷基,C_1-C_6卤代烷基,C_3-C_6环烷基,C_3-C_6卤代环烷基,C_3-C_6环烷氧基,C_3-C_6卤代环烷氧基,C_1-C_6烷氧基,C_1-C_6卤代烷氧基,C_2-C_6烯基,C_2-C_6炔基,S(=O)$_n$(C_1-C_6烷基),S(=O)$_n$(C_1-C_6卤代烷基),OSO_2(C_1-C_6烷基),OSO_2(C_1-C_6卤代烷基),C(=O)NR^xR^y,(C_1-C_6烷基)NR^xR^y,C(=O)(C_1-C_6烷基),C(=O)O(C_1-C_6烷基),C(=O)(C_1-C_6卤代烷基),C(=O)O(C_1-C_6卤代烷基),C(=O)(C_3-C_6环烷基),C(=O)O(C_3-C_6环烷基),C(=O)(C_2-C_6烯基),C(=O)O(C_2-C_6烯基),(C_1-C_6烷基)O(C_1-C_6烷基),(C_1-C_6烷基)S(C_1-C_6烷基),C(=O)(C_1-C_6烷基)C(=O)O(C_1-C_6烷基),苯基,苯氧基,取代苯基和取代苯氧基

[0039] 其中该取代苯基和取代苯氧基具有一个或多个取代基,所述一个或多个取代基独立地选自H,F,Cl,Br,I,CN,NO_2,C_1-C_6烷基,C_1-C_6卤代烷基,C_3-C_6环烷基,C_3-C_6卤代环烷基,C_3-C_6环烷氧基,C_3-C_6卤代环烷氧基,C_1-C_6烷氧基,C_1-C_6卤代烷氧基,C_2-C_6烯基,C_2-C_6炔基,S(=O)$_n$(C_1-C_6烷基),S(=O)$_n$(C_1-C_6卤代烷基),OSO_2(C_1-C_6烷基),OSO_2(C_1-C_6卤代烷基),C(=O)H,C(=O)NR^xR^y,(C_1-C_6烷基)NR^xR^y,C(=O)(C_1-C_6烷基),C(=O)O(C_1-C_6烷基),C(=O)(C_1-C_6卤代烷基),C(=O)O(C_1-C_6卤代烷基),C(=O)(C_3-C_6环烷基),C(=O)O(C_3-C_6环烷基),C(=O)(C_1-C_6卤代烷基),C(=O)(C_2-C_6烯基),C(=O)O(C_2-C_6烯基),(C_1-C_6烷基)O(C_1-C_6烷基),(C_1-C_6烷基)S(C_1-C_6烷基),C(=O)(C_1-C_6烷基)C(=O)O(C_1-C_6烷基),苯基,和苯氧基;

[0040] (D)R^1选自H,C_1-C_6烷基,C_3-C_6环烷基,C_2-C_6烯基,C_2-C_6炔基,S(=O)$_n$(C_1-C_6烷基),C

(=O)NR^xR^y,(C_1-C_6烷基)NR^xR^y,C(=O)O(C_1-C_6烷基),C(=O)(C_3-C_6环烷基),C(=O)O(C_3-C_6环烷基),C(=O)(C_2-C_6烯基),C(=O)O(C_2-C_6烯基),(C_1-C_6烷基)O(C_1-C_6烷基),(C_1-C_6烷基)OC(=O)(C_1-C_6烷基),(C_1-C_6烷基)S(C_1-C_6烷基),和(C_1-C_6烷基)OC(=O)O(C_1-C_6烷基),

[0041] 其中每个烷基,环烷基,环烷氧基,烷氧基,烯基,和炔基任选地取代有一个或多个取代基,所述一个或多个取代基独立地选自F,Cl,Br,I,CN,NO_2,氧代,C_1-C_6烷基,C_1-C_6卤代烷基,C_3-C_6环烷基,C_3-C_6卤代环烷基,C_3-C_6环烷氧基,C_3-C_6卤代环烷氧基,C_1-C_6烷氧基,C_1-C_6卤代烷氧基,S(=O)$_n$(C_1-C_6烷基),S(=O)$_n$(C_1-C_6卤代烷基),OSO_2(C_1-C_6烷基),OSO_2(C_1-C_6卤代烷基),C(=O)NR^xR^y,(C_1-C_6烷基)NR^xR^y,C(=O)(C_1-C_6烷基),C(=O)O(C_1-C_6烷基),C(=O)(C_1-C_6卤代烷基),C(=O)O(C_1-C_6卤代烷基),C(=O)(C_3-C_6环烷基),C(=O)O(C_3-C_6环烷基),C(=O)(C_2-C_6烯基),C(=O)O(C_2-C_6烯基),(C_1-C_6烷基)O(C_1-C_6烷基),(C_1-C_6烷基)S(C_1-C_6烷基),C(=O)(C_1-C_6烷基)C(=O)O(C_1-C_6烷基),苯基,和苯氧基;

[0042] (E)R^2选自(J),H,C_1-C_6烷基,C_3-C_6环烷基,C_2-C_6烯基,C_2-C_6炔基,C(=O)(C_1-C_6烷基),(C_1-C_6烷基)O(C_1-C_6烷基),(C_1-C_6烷基)S(C_1-C_6烷基),C_1-C_6烷基苯基,C_1-C_6烷基-O-苯基,C(=O)(Het-1),(Het-1),(C_1-C_6烷基)-(Het-1),C_1-C_6烷基-O-C(=O)C_1-C_6烷基,C_1-C_6烷基-O-C(=O)(C_1-C_6烷基),C_1-C_6烷基-O-C(=O)OC_1-C_6烷基,C_1-C_6烷基-O-C(=O)NR^xR^y,C_1-C_6烷基C(=O)N(R^x)C_1-C_6烷基-(Het-1),C_1-C_6烷基C(=O)(Het-1),C_1-C_6烷基C(=O)N(R^x)C_1-C_6烷基(N(R^x)(R^y))(C(=O)OH),C_1-C_6烷基C(=O)N(R^x)C_1-C_6烷基N(R^x)(R^y),C_1-C_6烷基C(=O)N(R^x)C_1-C_6烷基N(R^x)C(=O)-O-C_1-C_6烷基,C_1-C_6烷基C(=O)N(R^x)C_1-C_6烷基(N(R^x)C(=O)-O-C_1-C_6烷基)(C(=O)OH),C_1-C_6烷基C(=O)(Het-1)C(=O)-O-C_1-C_6烷基,C_1-C_6烷基-O-C(=O)-O-C_1-C_6烷基,C_1-C_6烷基-O-C(=O)C_1-C_6烷基,C_1-C_6烷基-O-C(=O)C_3-C_6环烷基,C_1-C_6烷基-O-C(=O)(Het-1),C_1-C_6烷基-O-C(=O)C_1-C_6烷基-N(R^x)C(=O)-O-C_1-C_6烷基,C_1-C_6烷基-NR^xR^y,(C_1-C_6烷基)S-(Het-1)或C_1-C_6烷基-O-(Het-1),

[0043] 其中每个烷基,环烷基,烯基,炔基,苯基,和(Het-1)任选地取代有一个或多个取代基,所述一个或多个取代基独立地选自F,Cl,Br,I,CN,NO_2,NR^xR^y,C_1-C_6烷基,C_1-C_6卤代烷基,C_3-C_6环烷基,C_3-C_6卤代环烷基,C_3-C_6环烷氧基,C_3-C_6卤代环烷氧基,C_1-C_6烷氧基,C_1-C_6卤代烷氧基,C_2-C_6烯基,C_3-C_6环烯基,C_2-C_6炔基,S(=O)$_n$(C_1-C_6烷基),S(=O)$_n$(C_1-C_6卤代烷基),OSO_2(C_1-C_6烷基),OSO_2(C_1-C_6卤代烷基),C(=O)H,C(=O)OH,C(=O)NR^xR^y,(C_1-C_6烷基)NR^xR^y,C(=O)(C_1-C_6烷基),C(=O)O(C_1-C_6烷基),C(=O)(C_1-C_6卤代烷基),C(=O)O(C_1-C_6卤代烷基),C(=O)(C_3-C_6环烷基),C(=O)O(C_3-C_6环烷基),C(=O)(C_2-C_6烯基),C(=O)O(C_2-C_6烯基),(C_1-C_6烷基)O(C_1-C_6烷基),(C_1-C_6烷基)S(C_1-C_6烷基),C(=O)(C_1-C_6烷基)C(=O)O(C_1-C_6烷基),苯基,苯氧基,Si(C_1-C_6烷基)$_3$,S(=O)$_n$$NR^xR^y$,或(Het-1);

[0044] (F)R^3选自苯基,C_1-C_6烷基苯基,C_1-C_6烷基-O-苯基,C_2-C_6烯基-O-苯基,(Het-1),C_1-C_6烷基(Het-1),或C_1-C_6烷基-O-(Het-1),

[0045] 其中每个烷基,环烷基,烯基,炔基,苯基,和(Het-1)任选地取代有一个或多个取代基,所述一个或多个取代基独立地选自F,Cl,Br,I,CN,NO_2,NR^xR^y,C_1-C_6烷基,C_3-C_6环烷基,C_3-C_6卤代环烷基,C_3-C_6环烷氧基,C_3-C_6卤代环烷氧基,C_1-C_6烷氧基,C_1-C_6卤代烷氧基,C_2-C_6烯基,C_3-C_6环烯基,C_2-C_6炔基,S(=O)$_n$(C_1-C_6烷基),S(=O)$_n$(C_1-C_6卤代烷基),OSO_2(C_1-C_6烷基),OSO_2(C_1-C_6卤代烷基),C(=O)H,C(=O)NR^xR^y,(C_1-C_6烷基)NR^xR^y,C(=O)(C_1-C_6烷基),C(=O)O(C_1-C_6烷基),C(=O)(C_1-C_6卤代烷基),C(=O)O(C_1-C_6卤代烷基),C(=O)(C_3-C_6

环烷基)，C(=O)O(C_3-C_6环烷基)，C(=O)(C_2-C_6烯基)，C(=O)O(C_2-C_6烯基)，O(C_1-C_6烷基)，S(C_1-C_6烷基)，C(=O)(C_1-C_6烷基)C(=O)O(C_1-C_6烷基)，苯基，苯氧基，和(Het-1)；

[0046] (G)R^4选自(J)，H，或C_1-C_6烷基；

[0047] (H)Q^1选自O或S，

[0048] (I)R^x和R^y独立地选自H，C_1-C_6烷基，C_1-C_6卤代烷基，C_3-C_6环烷基，C_3-C_6卤代环烷基，C_2-C_6烯基，C_2-C_6炔基，S(=O)$_n$(C_1-C_6烷基)，S(=O)$_n$(C_1-C_6卤代烷基)，OSO_2(C_1-C_6烷基)，OSO_2(C_1-C_6卤代烷基)，C(=O)H，C(=O)(C_1-C_6烷基)，C(=O)O(C_1-C_6烷基)，C(=O)(C_1-C_6卤代烷基)，C(=O)O(C_1-C_6卤代烷基)，C(=O)(C_3-C_6环烷基)，C(=O)O(C_3-C_6环烷基)，C(=O)(C_2-C_6烯基)，C(=O)O(C_2-C_6烯基)，(C_1-C_6烷基)O(C_1-C_6烷基)，(C_1-C_6烷基)S(C_1-C_6烷基)，C(=O)(C_1-C_6烷基)C(=O)O(C_1-C_6烷基)，和苯基，

[0049] 其中每个烷基，环烷基，环烷氧基，烷氧基，烯基，炔基，苯基，苯氧基，和(Het-1)，任选地取代有一个或多个取代基，所述一个或多个取代基独立地选自F，Cl，Br，I，CN，NO_2，OH，氧代，C_1-C_6烷基，C_1-C_6卤代烷基，C_3-C_6环烷基，C_3-C_6卤代环烷基，C_3-C_6环烷氧基，C_3-C_6卤代环烷氧基，C_1-C_6烷氧基，C_1-C_6卤代烷氧基，C_2-C_6烯基，C_3-C_6环烯基，C_2-C_6炔基，S(=O)$_n$(C_1-C_6烷基)，S(=O)$_n$(C_1-C_6卤代烷基)，OSO_2(C_1-C_6烷基)，OSO_2(C_1-C_6卤代烷基)，C(=O)H，C(=O)OH，C(=O)(C_1-C_6烷基)，C(=O)O(C_1-C_6烷基)，C(=O)(C_1-C_6卤代烷基)，C(=O)O(C_1-C_6卤代烷基)，C(=O)(C_3-C_6环烷基)，C(=O)O(C_3-C_6环烷基)，C(=O)(C_2-C_6烯基)，C(=O)O(C_2-C_6烯基)，(C_1-C_6烷基)O(C_1-C_6烷基)，(C_1-C_6烷基)S(C_1-C_6烷基)，C(=O)(C_1-C_6烷基)C(=O)O(C_1-C_6烷基)，苯基，卤代苯基，苯氧基，和(Het-1)，

[0050] 或R^x和R^y可任选地一起形成5元至7元饱和或不饱和环状基团，所述环状基团可以含有一个或多个杂原子，所述一个或多个杂原子选自氮，硫和氧，并且其中所述环状基团可以取代有如下基团：F，Cl，Br，I，CN，氧代，硫代，C_1-C_6烷基，C_1-C_6卤代烷基，C_3-C_6环烷基，C_3-C_6卤代环烷基，C_3-C_6环烷氧基，C_3-C_6卤代环烷氧基，C_1-C_6烷氧基，C_1-C_6卤代烷氧基，C_2-C_6烯基，C_3-C_6环烯基，C_2-C_6炔基，S(=O)$_n$(C_1-C_6烷基)，S(=O)$_n$(C_1-C_6卤代烷基)，OSO_2(C_1-C_6烷基)，OSO_2(C_1-C_6卤代烷基)，C(=O)(C_1-C_6烷基)，C(=O)O(C_1-C_6烷基)，C(=O)(C_1-C_6卤代烷基)，C(=O)O(C_1-C_6卤代烷基)，C(=O)(C_3-C_6环烷基)，C(=O)O(C_3-C_6环烷基)，C(=O)(C_2-C_6烯基)，C(=O)O(C_2-C_6烯基)，(C_1-C_6烷基)O(C_1-C_6烷基)，(C_1-C_6烷基)S(C_1-C_6烷基)，C(=O)(C_1-C_6烷基)C(=O)O(C_1-C_6烷基)，苯基，取代苯基，苯氧基，和(Het-1)；

[0051] (J)R^2和R^4可以为1元至4元饱和或不饱和的烃基链，所述烃基链可以含有一个或多个杂原子，所述一个或多个杂原子选自氮，硫和氧，所述烃基链与C^x(Q^1)(N^x)一起形成环状结构，其中所述烃基链可以任选地取代有一个或多个取代基，所述一个或多个取代基独立地选自R^5，R^6，和R^7，其中每个R^5，R^6，和R^7选自H，F，Cl，Br，I，CN，OH，C_1-C_6烷基，氧代，硫代，C_1-C_6卤代烷基，C_3-C_6环烷基，C_3-C_6卤代环烷基，C_3-C_6环烷氧基，C_3-C_6卤代环烷氧基，C_1-C_6烷氧基，C_1-C_6卤代烷氧基，C_2-C_6烯基，C_3-C_6环烯基，C_2-C_6炔基，S(=O)$_n$(C_1-C_6烷基)，S(=O)$_n$(C_1-C_6卤代烷基)，OSO_2(C_1-C_6烷基)，OSO_2(C_1-C_6卤代烷基)，C(=O)(C_1-C_6烷基)，C(=O)O(C_1-C_6烷基)，C(=O)(C_1-C_6卤代烷基)，C(=O)O(C_1-C_6卤代烷基)，C(=O)(C_3-C_6环烷基)，C(=O)O(C_3-C_6环烷基)，C(=O)(C_2-C_6烯基)，C(=O)O(C_2-C_6烯基)，(C_1-C_6烷基)O(C_1-C_6烷基)，(C_1-C_6烷基)S(C_1-C_6烷基)，C(=O)(C_1-C_6烷基)C(=O)O(C_1-C_6烷基)，苯基，取代苯基，苯氧基，或(Het-1)；

[0052] (K)(Het-1)为5元或6元，饱和或不饱和的杂环，含有一个或多个杂原子，所述一个或多个杂原子独立地选自氮，硫或氧，其中所述杂环也可以取代有一个或多个取代基，所述一个或多个取代基独立地选自H，F，Cl，Br，I，CN，NO_2，氧代，C_1-C_6烷基，C_1-C_6卤代烷基，C_3-C_6环烷基，C_3-C_6卤代环烷基，C_3-C_6环烷氧基，C_3-C_6卤代环烷氧基，C_1-C_6烷氧基，C_1-C_6卤代烷氧基，C_2-C_6烯基，C_2-C_6炔基，S(=O)$_n$(C_1-C_6烷基)，S(=O)$_n$(C_1-C_6卤代烷基)，OSO_2(C_1-C_6烷基)，OSO_2(C_1-C_6卤代烷基)，C(=O)NR^xR^y，(C_1-C_6烷基)NR^xR^y，C(=O)(C_1-C_6烷基)，C(=O)O(C_1-C_6烷基)，C(=O)(C_1-C_6卤代烷基)，C(=O)O(C_1-C_6卤代烷基)，C(=O)(C_3-C_6环烷基)，C(=O)O(C_3-C_6环烷基)，C(=O)(C_2-C_6烯基)，C(=O)O(C_2-C_6烯基)，(C_1-C_6烷基)O(C_1-C_6烷基)，(C_1-C_6烷基)S(C_1-C_6烷基)，C(=O)(C_1-C_6烷基)C(=O)O(C_1-C_6烷基)，苯基，苯氧基，取代苯基和取代苯氧基，

[0053] 其中该取代苯基和取代苯氧基具有一个或多个取代基，所述一个或多个取代基独立地选自H，F，Cl，Br，I，CN，NO_2，C_1-C_6烷基，C_1-C_6卤代烷基，C_3-C_6环烷基，C_3-C_6卤代环烷基，C_3-C_6环烷氧基，C_3-C_6卤代环烷氧基，C_1-C_6烷氧基，C_1-C_6卤代烷氧基，C_2-C_6烯基，C_2-C_6炔基，S(=O)$_n$(C_1-C_6烷基)，S(=O)$_n$(C_1-C_6卤代烷基)，OSO_2(C_1-C_6烷基)，OSO_2(C_1-C_6卤代烷基)，C(=O)H，C(=O)NR^xR^y，(C_1-C_6烷基)NR^xR^y，C(=O)(C_1-C_6烷基)，C(=O)O(C_1-C_6烷基)，C(=O)(C_1-C_6卤代烷基)，C(=O)O(C_1-C_6卤代烷基)，C(=O)(C_3-C_6环烷基)，C(=O)O(C_3-C_6环烷基)，C(=O)(C_2-C_6烯基)，C(=O)O(C_2-C_6烯基)，(C_1-C_6烷基)O(C_1-C_6烷基)，(C_1-C_6烷基)S(C_1-C_6烷基)，苯基，和苯氧基；

[0054] (L)L为连接基团，所述连接基团选自

[0055] (1)饱和或不饱和，取代或未取代，直链(C_1-C_4)烃基连接基团，或

[0056] (2)饱和或不饱和，取代或未取代，环状(C_3-C_8)烃基连接基团，

[0057] 其中所述连接基团各自连接Ar^2至N^Y和

[0058] 其中所述取代直链(C_1-C_4)烃基连接基团和取代环状(C_3-C_8)烃基连接基团具有一个或多个取代基，所述一个或多个取代基独立地选自R^8，R^9，R^{10}，R^{11}，和R^{12}，其中每个R^8，R^9，R^{10}，R^{11}，和R^{12}选自F，Cl，Br，I，CN，氧代，C_1-C_6烷基，C_2-C_6烯基，C_2-C_6卤代烯基，C_2-C_6炔基，C_1-C_6卤代烷基，C_3-C_6环烷基，C_3-C_6环烯基，C_3-C_6卤代环烷基，或苯基；和

[0059] (M)n各自独立地为0，1，或2。

[0060] 在另一个实施方式中，Ar^1为取代苯基。该实施方式可以与其他实施方式中的Het，Ar^2，R^1，R^2，R^3，R^4，Q^1，R^2和R^4烃基链，和/或L组合使用。

[0061] 在另一个实施方式中，Ar^1为具有一个或多个取代基的取代苯基，所述一个或多个取代基选自C_1-C_6卤代烷基和C_1-C_6卤代烷氧基。该实施方式可以与其他实施方式中的Het，Ar^2，R^1，R^2，R^3，R^4，Q^1，R^2和R^4烃基链，和/或L组合使用。

[0062] 在另一个实施方式中，Ar^1为具有一个或多个取代基的取代苯基，所述一个或多个取代基选自CF_3，OCF_3，和OC_2F_5。该实施方式可以与其他实施方式中的Het，Ar^2，R^1，R^2，R^3，R^4，Q^1，R^2和R^4烃基链，和/或L组合使用。

[0063] 在另一个实施方式中，Het选自苯并呋喃基，苯并异噻唑基，苯并异噁唑基，苯并噁唑基，苯并噻吩基，苯并噻唑基，噌啉基，呋喃基，吲唑基，吲哚基，咪唑基，异吲哚基，异喹啉基，异噻唑基，异噁唑基，噁二唑基，噁唑啉基，噁唑基，酞嗪基，吡嗪基，吡唑啉基，吡唑基，哒嗪基，吡啶基，嘧啶基，吡咯基，喹唑啉基，喹啉基，喹喔啉基，四唑基，噻唑啉基，噻唑基，

噻吩基，三嗪基，三唑基，哌嗪基，哌啶基，吗啉基，吡咯烷基，四氢呋喃基，四氢吡喃基，1,2,3,4-四氢-喹啉基，4,5-二氢-噁唑基，4,5-二氢-1H-吡唑基，4,5-二氢-异噁唑基，和2,3-二氢-[1,3,4]-噁二唑基。

[0064] 在另一个实施方式中，Het为三唑基。该实施方式可以与其他实施方式中的Ar^1，Ar^2，R^1，R^2，R^3，R^4，Q^1，R^2和R^4烃基链，和/或L组合使用。

[0065] 在另一个实施方式中，Het为1,2,4-三唑基。该实施方式可以与其他实施方式中的Ar^1，Ar^2，R^1，R^2，R^3，R^4，Q^1，R^2和R^4烃基链，和/或L组合使用。

[0066] 在另一个实施方式中，Het为噁二唑基。该实施方式可以与其他实施方式中的组合使用Ar^1，Ar^2，R^1，R^2，R^3，R^4，Q^1，R^2和R^4烃基链，和/或L。

[0067] 在另一个实施方式中，Het为1,3,4噁二唑基。该实施方式可以与其他实施方式中的Ar^1，Ar^2，R^1，R^2，R^3，R^4，Q^1，R^2和R^4烃基链，和/或L组合使用。

[0068] 在另一个实施方式中，Het为吡唑基。该实施方式可以与其他实施方式中的Ar^1，Ar^2，R^1，R^2，R^3，R^4，Q^1，R^2和R^4烃基链，和/或L组合使用。

[0069] 在另一个实施方式中，Ar^2为苯基。该实施方式可以与其他实施方式中的Ar^1，Het，R^1，R^2，R^3，R^4，Q^1，R^2和R^4烃基链，和/或L组合使用。

[0070] 在另一个实施方式中，Ar^2为取代苯基。该实施方式可以与其他实施方式中的Ar^1，Het，R^1，R^2，R^3，R^4，Q^1，R^2和R^4烃基链，和/或L组合使用。

[0071] 在另一个实施方式中，Ar^2为具有一个或多个取代基的取代苯基，所述一个或多个取代基选自C_1-C_6烷基。该实施方式可以与其他实施方式中的Ar^1，Het，R^1，R^2，R^3，R^4，Q^1，R^2和R^4烃基链，和/或L组合使用。

[0072] 在另一个实施方式中，Ar^2为具有一个或多个取代基的取代苯基，其中所述取代基为CH_3。该实施方式可以与其他实施方式中的Ar^1，Het，R^1，R^2，R^3，R^4，Q^1，R^2和R^4烃基链，和/或L组合使用。

[0073] 在另一个实施方式中，R^1为H。该实施方式可以与其他实施方式中的Ar^1，Het，Ar^2，R^2，R^3，R^4，Q^1，R^2和R^4烃基链，和/或L组合使用。

[0074] 在另一个实施方式中，R^2为(J)，H，C_1-C_6烷基，C_1-C_6烷基-O-C(=O)C_1-C_6烷基，C_1-C_6烷基-O-C(=O)N(R^xR^y)，或(C_1-C_6烷基)S-(Het-1)。该实施方式可以与其他实施方式中的Ar^1，Het，Ar^2，R^1，R^3，R^4，Q^1，R^2和R^4烃基链，和/或L组合使用。

[0075] 在另一个实施方式中，R^2为(J)，H，CH_3，C_1-C_6烷基，$CH_2OC(=O)CH(CH_3)_2$，$CH_2OC(=O)N(H)(C(=O)OCH_2Ph)$，或$CH_2S$(3,4,5-三甲氧基-2-四氢吡喃)。该实施方式可以与其他实施方式中的Ar^1，Het，Ar^2，R^1，R^3，R^4，Q^1，R^2和R^4烃基链，和/或L组合使用。

[0076] 在另一个实施方式中，R^3为取代苯基。该实施方式可以与其他实施方式中的Ar^1，Het，Ar^2，R^1，R^2，R^4，Q^1，R^2和R^4烃基链，和/或L组合使用。

[0077] 在另一个实施方式中，R^3为取代苯基，其中所述取代苯基具有一个或多个取代基，所述一个或多个取代基选自F，Cl，C_1-C_6烷基，C_3-C_6环烷基，C_1-C_6烷氧基，和苯基。该实施方式可以与其他实施方式中的Ar^1，Het，Ar^2，R^1，R^2，R^4，Q^1，R^2和R^4烃基链，和/或L组合使用。

[0078] 在另一个实施方式中，R^3为取代苯基，其中所述取代苯基具有一个或多个取代基，所述一个或多个取代基选自F，CH_3，2-$CH(CH_3)_2$，$CH(CH_3)(C_2H_5)$，OCH_3，和苯基。该实施方式可以与其他实施方式中的Ar^1，Het，Ar^2，R^1，R^2，R^4，Q^1，R^2和R^4烃基链，和/或L组合使用。

[0079] 在另一个实施方式中，R^3为取代苯基，其中所述取代苯基具有大于一种的取代基和至少一对所述取代基彼此不是邻位。该实施方式可以与其他实施方式中的Ar^1，Het，Ar^2，R^1，R^2，R^4，Q^1，R^2和R^4烃基链，和/或L组合使用。

[0080] 在另一个实施方式中，R^3为C_1-C_6烷基苯基。该实施方式可以与其他实施方式中的Ar^1，Het，Ar^2，R^1，R^2，R^4，Q^1，R^2和R^4烃基链，和/或L组合使用。

[0081] 在另一个实施方式中，R^3为(Het-1)。该实施方式可以与其他实施方式中的Ar^1，Het，Ar^2，R^1，R^2，R^4，Q^1，R^2和R^4烃基链，和/或L组合使用。

[0082] 在另一个实施方式中，R^4为H。该实施方式可以与其他实施方式中的Ar^1，Het，Ar^2，R^1，R^2，R^3，Q^1，R^2和R^4烃基链，和/或L组合使用。

[0083] 在另一个实施方式中，$Q^1$is O。该实施方式可以与其他实施方式中的Ar^1，Het，Ar^2，R^1，R^2，R^3，R^4，R^2和R^4烃基链，和/或L组合使用。

[0084] 在另一个实施方式中，R^2和R^4为烃基链，其中所述烃基链取代有氧代或C_1-C_6烷基。该实施方式可以与其他实施方式中的Ar^1，Het，Ar^2，R^1，R^2，R^3，R^4，Q^1，和/或L组合使用。

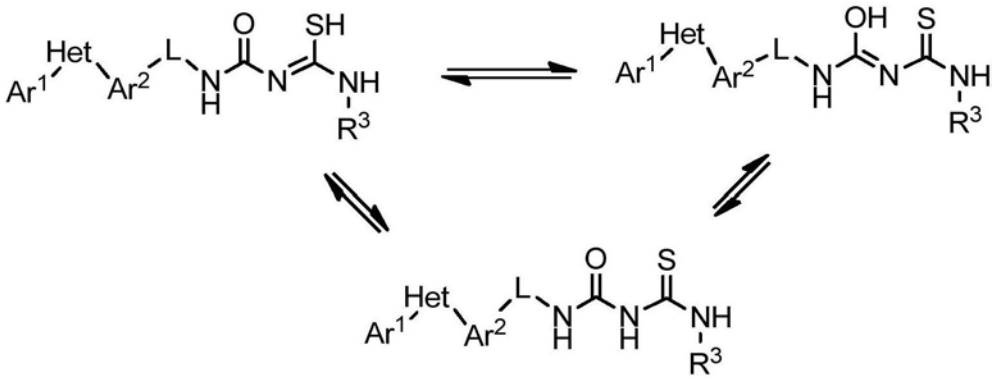
[0085] 在另一个实施方式中，R^2和R^4为烃基链，其中所述烃基链为$CH_2C(=O)$，$C(C(OH)(CH_3)_2)C(=O)$，C(环丙基)C(=O)，$C(CH_3)_2C(=O)$，CFHC(=O)，CBrHC(=O)，$CH(CH_3)C(=O)$，CH_2CH_2，$CH_2C(OH)(CH_3)$，$CH_2CH_2CH_2$，$CH_2CH_2C(=O)$，$CH_2CH(CH_3)CH_2$，$N(CH_3)C(=O)$，$N(CH_2CH_3)C(=O)$，$CH=C(CH_3)$，或$CH_2CH(CH_3)$。该实施方式可以与其他实施方式中的Ar^1，Het，Ar^2，R^1，R^2，R^3，R^4，Q^1，和/或L组合使用。

[0086] 在另一个实施方式中，L为CH_2，CH_2CH_2，$CH_2CH(CH_3)$，$CH_2C(CH_3)_2$，$CH_2CH(CH_2CH_3)$，$CH=CH$，$CH(CH_3)CH_2$，$C(CH_3)_2CH_2$，$CHBrCH_2$，CH_2C(环丙基)，$CH(CH_2CH_3)CH_2$，$C(CH_3)=CH$，$CH_2CH_2CH_2$，$CH(CH_3)CH(CH_3)$，$CH_2CH_2CH_2CH_2$，$C\equiv CCH_2CH_2$，环丙基，或环己基。该实施方式可以与其他实施方式中的Ar^1，Het，Ar^2，R^1，R^2，R^3，R^4，Q^1，和/或R^2和R^4烃基链组合使用。

[0087] 许多所述式一分子可以以两种或更多种互变异构体形式描述，例如当R^1，R^2，或R^4为H时(参见例如，下面的“方案TAU”)。为简化所述方案起见，所有分子描述为作为单一互变异构体存在。任何和所有替换的互变异构体均包括在该式一的范围内，并且不应断定分子是否存在所绘出的互变异构体形式。

[0088] “方案TAU”

[0089]



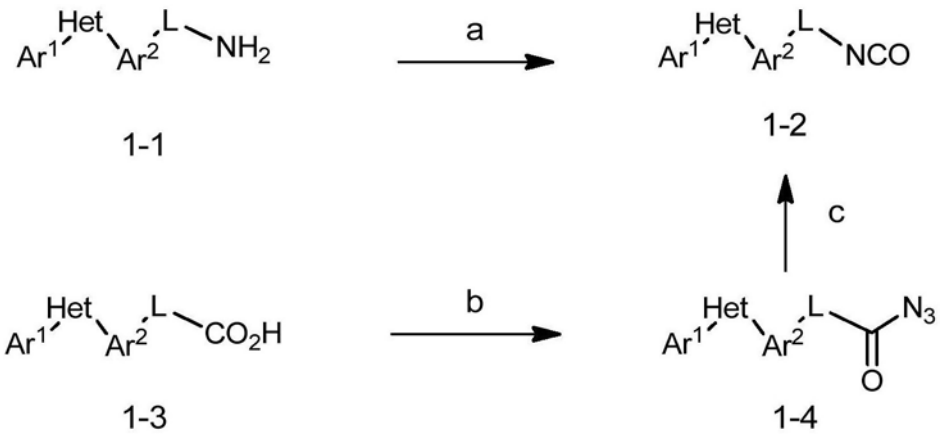
[0090] 所述式一分子通常会具有约400道尔顿至约1200道尔顿的分子量。但是，通常优选分子量为约300道尔顿至约1000道尔顿，甚至更普遍优选分子量为约400道尔顿至约750道尔顿。

[0091] 制备硫代缩二脲

[0092] 本文披露的硫代缩二脲由相应的异氰酸酯，Ar^1-Het-Ar^2-L-NCO(1-2)制备。通常，制备硫代缩二脲时，这些异氰酸酯不进行分离，相反从适宜的前体原位生成并且直接使用。一种该适宜的前体是胺(1-1)，所述胺(1-1)可通过如下转化成异氰酸酯：使用几种常用试剂中的一种，例如光气、双光气、三光气或羰基二咪唑(方案1，步骤a)，在混合溶剂体系例如二氯甲烷与水或乙醚与水中，在碱例如碳酸氢钠或三乙胺的存在下，在温度为约-10℃至约50℃。

[0093] 方案1

[0094]

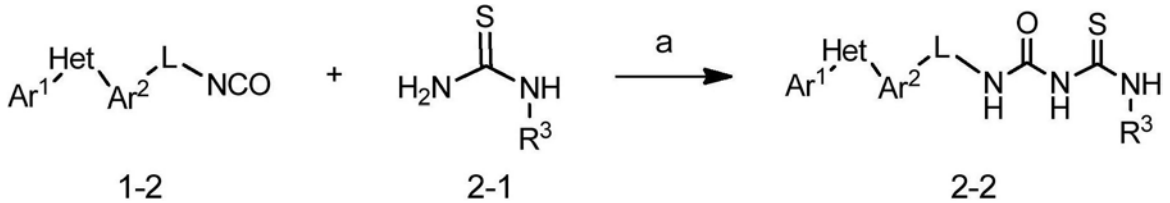


[0095] 可选择地，异氰酸酯可以经由酰基叠氮化物Ar^1-Het-Ar^2-L-C(O)N_3(1-4)的库尔修斯(Curtius)重排生成，酰基叠氮化物Ar^1-Het-Ar^2-L-C(O)N_3(1-4)，反过来由相应羧酸前体Ar^1-Het-Ar^2-L-CO_2H(1-3)制备。酰基叠氮化物的形成(方案1，步骤b)通过如下发生：将酸在胺碱例如三乙胺的存在下用氯甲酸乙酯和叠氮化钠处理，或将酸在胺碱例如三乙胺的存在下用叠氮化磷酸二苯酯处理。然后使酰基叠氮化物进行库尔修斯重排(其可能需要热诱导)，导致相应的异氰酸酯(1-3)。取决于特定酰基叠氮化物的性质，该重排可以在环境温度自发地发生，或可以需要在适宜的溶剂例如甲苯或乙腈或醚类溶剂例如二氧六环或四氢呋喃中从约40℃加热至约100℃。虽然芳基乙酸的叠氮化物是已知的，但由于其反应性，它们常常不分离为纯固体。因此，酰基叠氮化物中间体不总是充分表征，但可以仅直接加热而不表征，从而生成异氰酸酯。

[0096] 异氰酸酯，Ar^1-Het-Ar^2-L-NCO(1-2)，可在约0.1至约2当量的无机碱例如碳酸铯或氢化钠存在下用N-芳基硫脲(2-1)直接处理，导致形成硫代缩二脲(2-2，方案2)。反应可如下进行：在温度为约0℃至约100℃，优选为约20℃至约80℃，在非质子溶剂或溶剂混合物中，所述非质子溶剂或溶剂混合物选自乙腈，丙酮，甲苯，四氢呋喃，1,2-二氯乙烷，二氯甲烷，或其混合物，但优选使用乙腈。

[0097] 方案2

[0098]

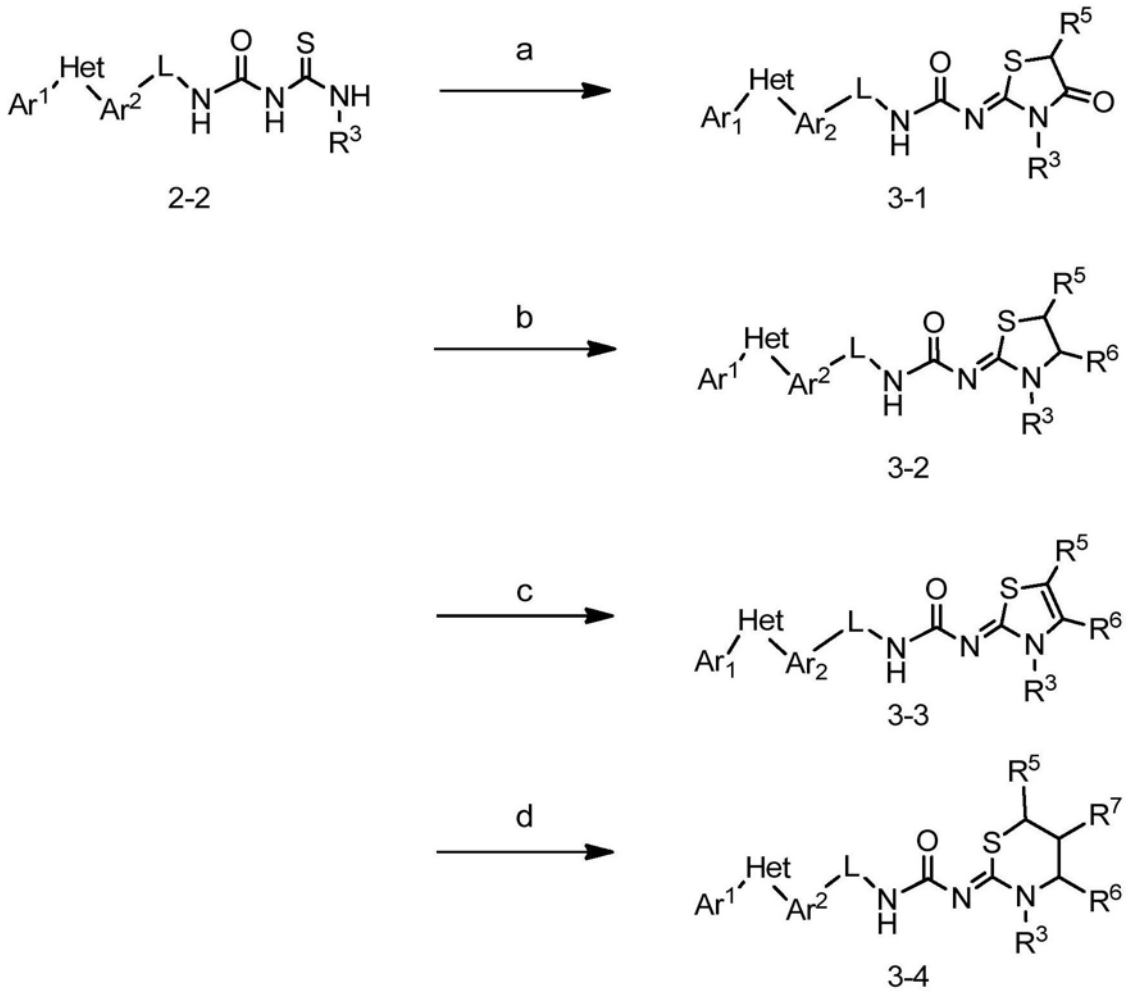


[0099] 原位生成的硫代缩二脲(2-2)可直接转化成各种环化类似物而不纯化(方案3)，或

它们可在环化之前从反应介质分离。环化可通过如下实现：用α-卤代酯例如溴乙酸甲酯处理，形成未取代或由R^5一取代或二取代的2-亚氨基-1,3-噻唑啉-4-酮(3-1，步骤a)；用邻二卤代物例如1-溴-2-氯乙烷或1,2-二氯乙烷处理，形成未取代或由R^5或R^6一取代的2-亚氨基-1,3-噻唑啉(3-2，步骤b)；用α-卤代酮例如氯丙酮处理，形成未取代有R^5或R^6的2-亚氨基-1,3-噻唑(3-3，步骤c)；或用1,3-二卤代丙烷例如1-溴-3-氯-丙烷处理，形成未取代或由R^5或R^6一取代或未取代或由R^7一取代或二取代的2-亚氨基-1,3-噻嗪烷(3-4，步骤d)。步骤a中，优选在质子溶剂例如乙醇或甲醇中，在温度范围为约20℃至约70℃，使用乙酸钠。步骤b中，优选在溶剂例如乙腈或(优选)2-丁酮中，在温度为约0℃至约80℃，使用无机碱例如碳酸钾。

[0100] 方案3

[0101]



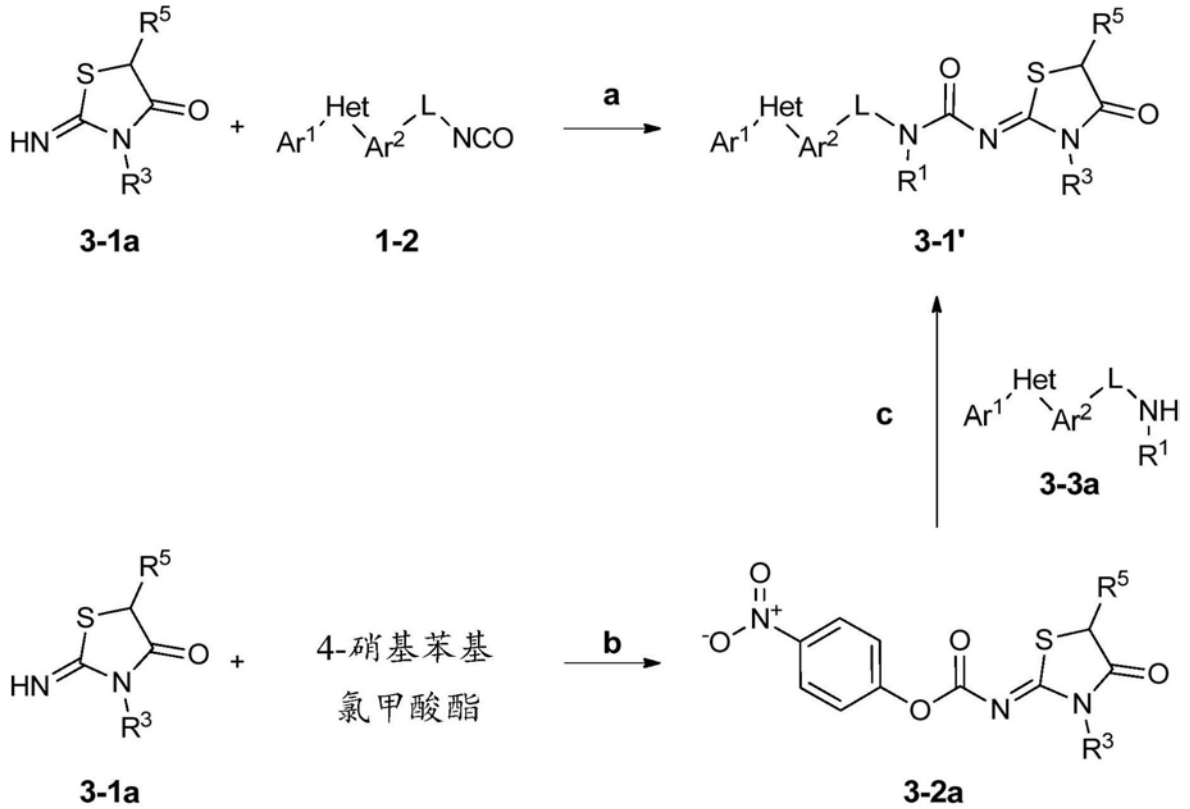
[0102] 制备具有一般结构3-1'的类似物的替代方法(方案3)描述于方案3a中。中间体2-亚氨基噻唑烷-4-酮(3-1a，步骤a)，在约0.1至约2当量的无机碱例如碳酸铯或氢化钠的存在下与异氰酸酯(1-2)直接反应，形成环化的硫代缩二脲(3-1')。反应可如下进行：在温度为约0℃至约100℃，优选为约20℃至约80℃，在非质子溶剂或溶剂混合物中，所述非质子溶剂或溶剂混合物选自乙腈，丙酮，甲苯，四氢呋喃，1,2-二氯乙烷，二氯甲烷，或其混合物，但优选使用乙腈。

[0103] 可选择地，2-亚氨基噻唑烷-2-酮(3-1a)可以与4-硝基苯基氯甲酸酯反应(步骤

b)，形成4-硝基苯基氨基甲酸酯中间体(3-2a)。该反应如下进行：用等摩尔量的亚胺和氯甲酸酯，在极性非质子溶剂例如四氢呋喃或二氧六环中，和在约0.1至约2当量的无机碱例如碳酸铯或碳酸钾的存在下，优选在室温。中间体(3-2a)可以通过从无机盐过滤和蒸发溶剂分离，或可在步骤C中直接使用。步骤c中，3-2a用烷基伯胺Ar_1-Het-Ar_2-L-NHR^1(其中R^1为H或烷基)处理，可以生成环化的硫代缩二脲(3-1')。步骤c也可以在无机碱例如碳酸铯或碳酸钾(约0.1至约2当量，优选约1至约1.2当量)的存在下进行；其也最常规地在室温进行，尽管其可以在温度为约0℃至约100℃进行。

[0104] 方案3a

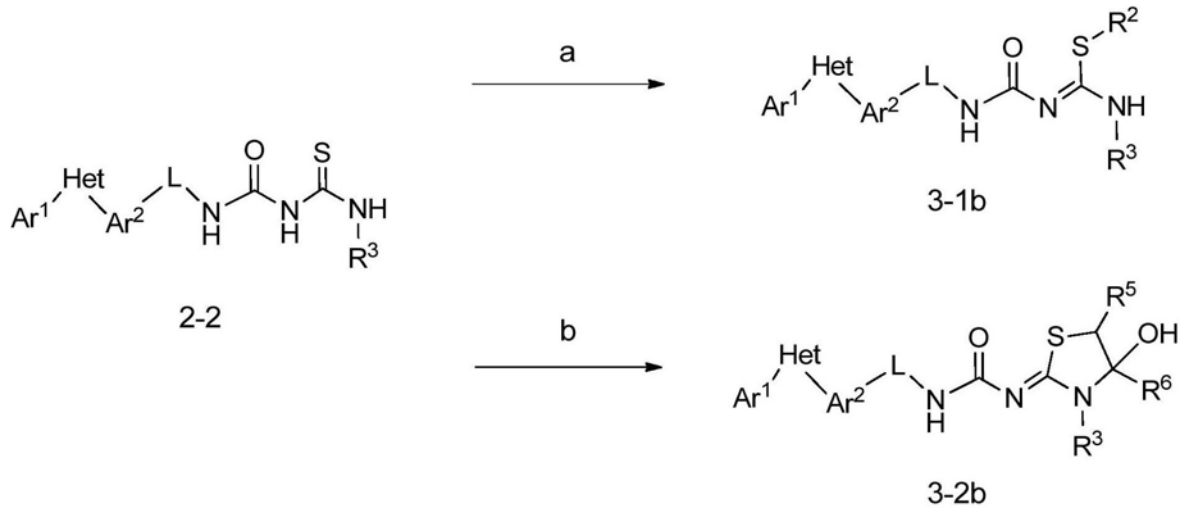
[0105]



[0106] 硫代缩二脲(2-2)也可如方案3b中所述转化成新的S-烷基化的类似物。例如，硫代缩二脲2-2与烷基碘、在质子溶剂例如乙醇中和在碱例如乙酸钠的存在下、在温度为约0℃至约60℃的反应(步骤a)，导致形成S-R^2取代产物(3-1b)。采用方案3、步骤c中所述反应条件的变化，小心控制反应条件，确保温度不超过20℃。在这些条件下，可以分离4-羟基-2-亚氨基噻唑烷(3-2b，步骤b)。

[0107] 方案3b

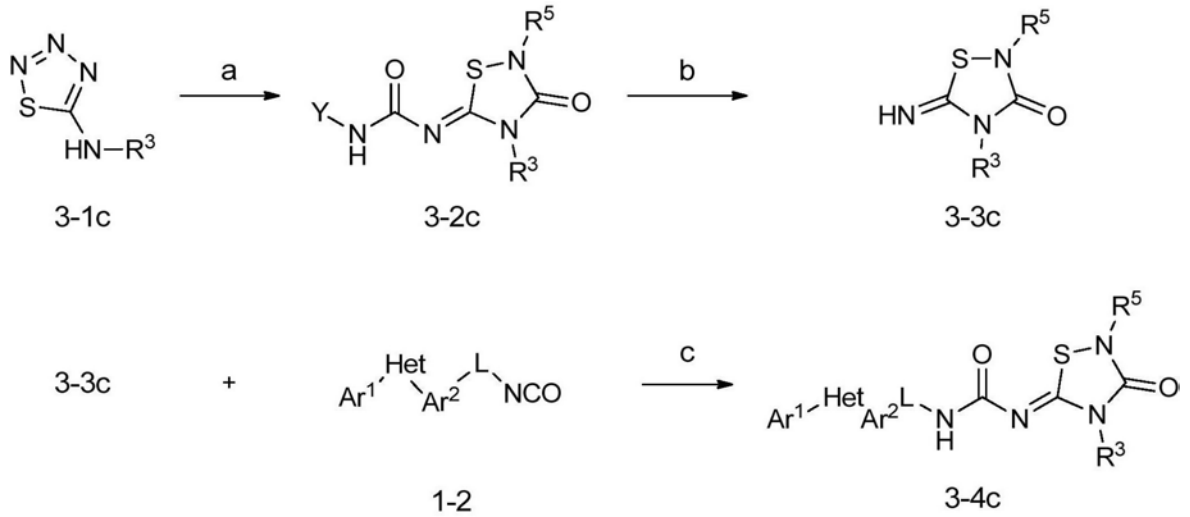
[0108]



[0109] 可以如方案3c中所述构成式1类似物，其中R^2和R^4进行环化，形成2-(R^5)-4-(R^3)-5-亚氨基-1,2,4-噻二唑烷-3-酮(3-4c)。由Kaugers等人所述的研究之后(J.Org.Chem 1992,57,1671)，将由相应的N^3-芳基缩氨基硫脲通过氧化与亚硝酸钠在一个步骤中制备的N-芳氨基1,2,3,4-噻三唑(3-1c)，用异氰酸烷基酯处理，形成3-2c。3-2c与碱例如甲醇钠在甲醇中在室温(步骤b)的处理导致脲键断裂，并且形成2-(R^5)-4-(R^3)--5-亚氨基-1,2,4-噻二唑烷-3-酮(3-3c)。然后可以将该亚胺用异氰酸酯在等同于方案3a、步骤a中所述那些的条件下处理，形成3-4c。

[0110] 方案3c

[0111]

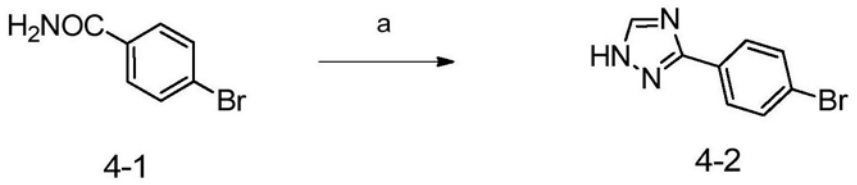


[0112] 制备三芳基中间体

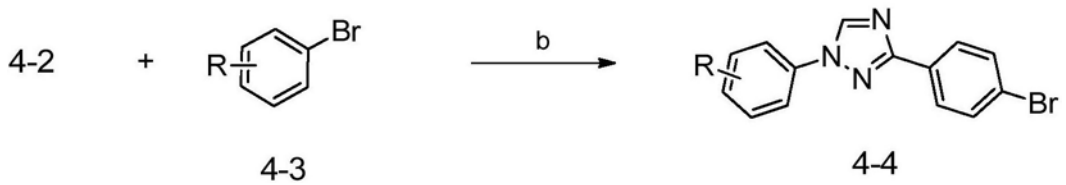
[0113] 式一分子可通过如下制备：制得三芳基中间体Ar^1-Het-Ar^2，然后将其连接至适宜的中间体，形成所需要的化合物。多种多样的三芳基中间体可用于制备式一分子，条件是该三芳基中间体在Ar^2上含有适宜的官能团，所需官能团的剩余部分可连接至Ar^2。适宜的官能团包括氨基，异氰酸酯，羧基，或卤素(优选溴或碘)。这些三芳基中间体可通过化学文献中已经描述过的方法制备，所述化学文献包括Crouse等人的WO2009102736(将整个公开内容在此引入以作参考)。

[0114] 制备式一分子时用作前体的三芳醛可根据Crouse等人的US2012/0202688A1中所述的工序制备。上述的一些工序需要使用卤代芳基中间体Ar^1-Het-Ph-Br，其为新的中间体。这些可以如方案4中所述制备。3-(4-溴苯基)-1,2,4-三唑(4-2，步骤a)由4-溴苯甲酰胺(4-1)在前面所述条件下在两个步骤中制备(Crouse等人的WO2009102736)。然后可将该三唑在碳酸铯或磷酸钾的存在下，在极性非质子溶剂例如二甲基甲酰胺中，偶联至芳基卤(R＝C_1-C_6卤代烷氧基)例如4-三氟甲氧基苯基溴苯。该反应为通过铜盐例如碘化亚铜(I)和螯合剂例如8-羟基喹啉(两者均以约0.05至约0.25当量存在)，在温度范围为约80℃至约140℃催化，形成1-芳基-3-(4-溴苯基)三唑(4-4，步骤b)。

[0115] 方案4



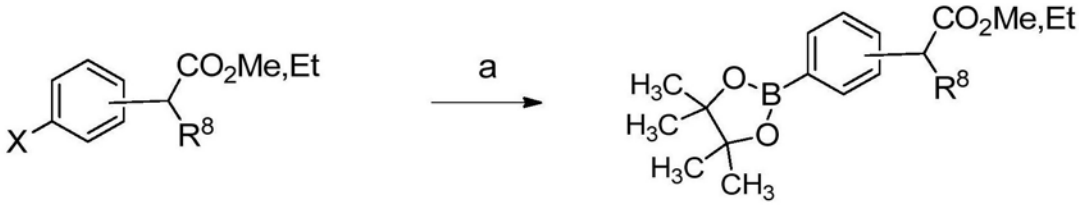
[0116]



[0117] 制备1个原子连接的中间体

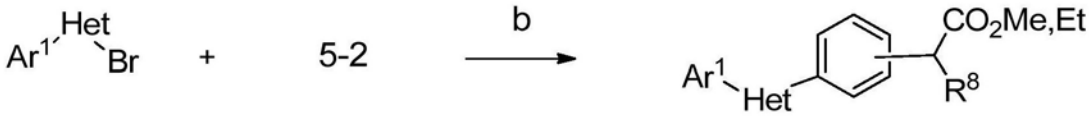
[0118] 其中L为一个碳的连接基团的式一分子，可分别由方案5和方案6中所述的酸或胺中间体制备。酸前体Ar^1-Het-Ar^2-L-CO_2H(未取代或由R^8一取代或二取代)可如方案5中所示制备。硼酸酯(5-2，步骤a)可使用Miyaura条件由卤代苯基酯(5-1)制备。硼酸酯与溴代杂环(5-3，步骤b)的偶联可使用钯催化剂和膦配体，在碱例如碳酸氢钠、磷酸钾或氟化铯的存在下，在适宜的溶剂体系例如二氧六环/水中，在温度为约50℃至约120℃实现，形成三芳基酯中间体(5-4，步骤c)。钯催化剂中，尽管可以使用其他公知钯催化剂，但优选四(三苯基膦)钯(0)。酯的皂化可以通过如下实现：使用强碱例如氢氧化钠或氢氧化锂，在甲醇或乙醇中，存在或不存在四氢呋喃/水，提供所需要的羧酸(5-5，步骤c)。

[0119] 方案5

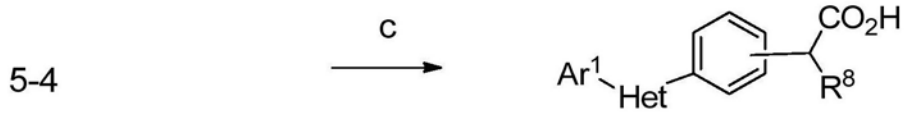


5-1 5-2

[0120]



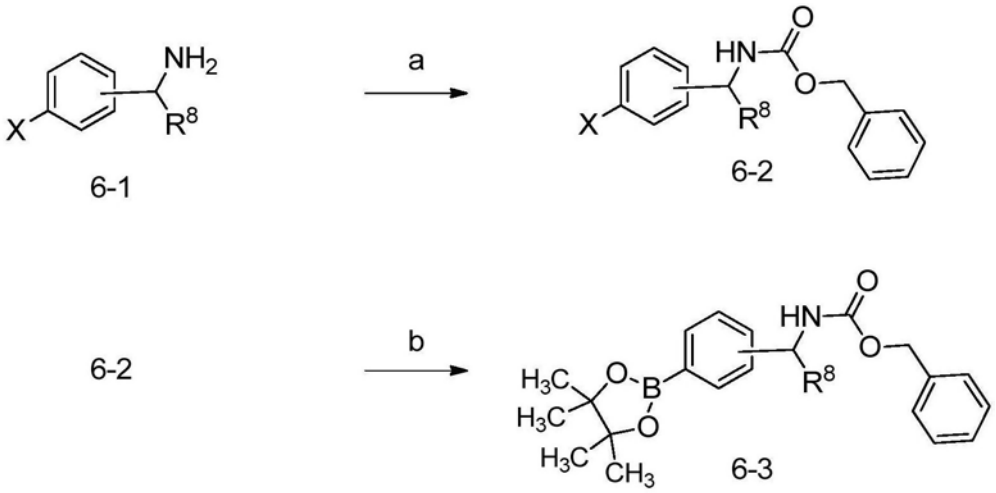
5-3 5-4



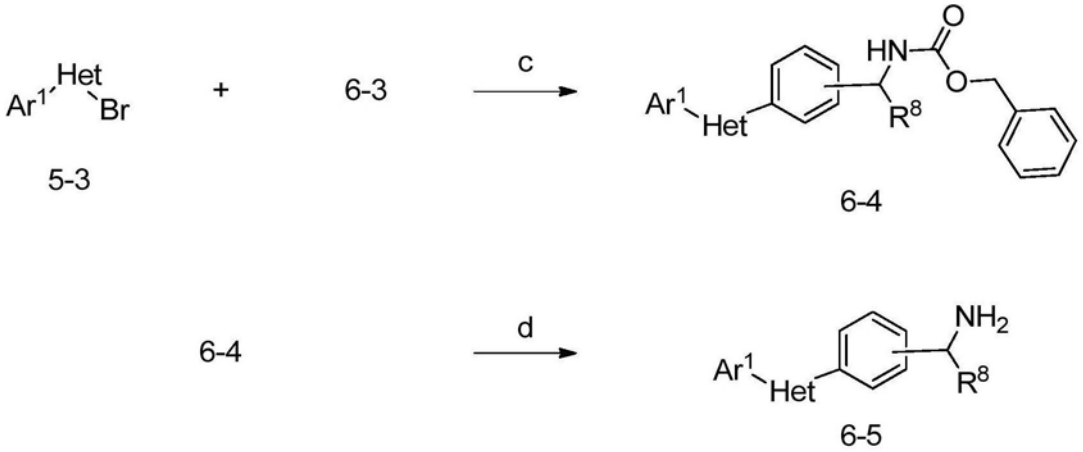
5-5

[0121] 胺前体Ar^1-Het-Ar^2-L-NH_2(未取代或由R^8一取代或二取代),可如方案6中所示制备。卤代苄基胺(6-1)可以在碱例如三乙胺的存在下、在非质子溶剂例如二氯甲烷中、在约-10℃至约10℃使用氯甲酸苄酯进行保护,提供N-羧基苄基(Cbz)保护的苄基胺(6-2,步骤a)。可选择地,在使用上述类似于Cbz的条件的步骤中,可以采用其他N-保护基团例如叔丁氧基羰基(BOC)或9-芴甲基羰基(Fmoc)。Cbz保护的硼酸酯6-3可使用Miyaura条件制备(步骤b)。硼酸酯与溴代杂环(5-3)的偶联可使用钯催化剂和膦配体,在碱例如碳酸氢钠、磷酸钾或氟化铯的存在下,在适宜的溶剂体系例如二氧六环/水中,在温度为约50℃至约120℃实现,形成N-保护的氨基烷基苯基中间体(6-4,步骤c)。Cbz基团的脱保护可在酸性条件下,用强酸例如溴化氢,随后用碱例如碳酸氢钠或氢氧化钠游离碱化实现,提供游离胺前体Ar^1-Het-Ar^2-L-NH_2(6-5,步骤d)。类似方法会适用于其中L为大于1个碳的化合物。

[0122] 方案6



[0123]



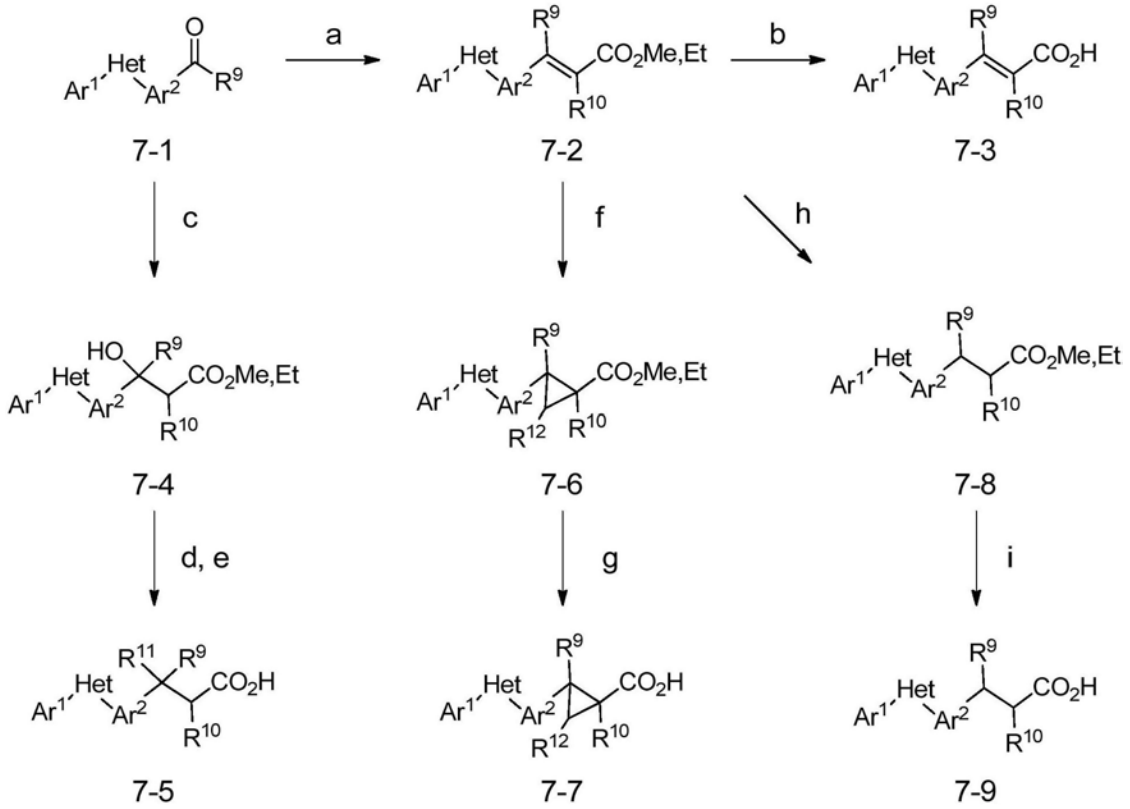
[0124] 制备乙基连接的中间体

[0125] 其中L为两个原子基团的化合物的制备描述于方案7至方案9中。醛(7-1,R^9=H)(描述于US 2012/0202688A1中)与试剂例如二乙基膦酰乙酸乙酯(ethyl diethylphosphonoacetate)或维蒂希(Wittig)试剂例如2-(三苯基膦)丙酸乙基酯(ethyl 2-(triphenylphosphoranylidene)propanoate)或α-取代乙酸酯例如2-氟乙酸乙酯或2-氰基乙酸乙酯的缩合(在适宜的碱例如氢化钠或正丁基锂的存在下,在非质子溶剂例如四氢呋喃或乙醚中,在温度为约-78℃至约20℃),可用于制备未取代或由R^9和R^{10}一取代的丙烯酸酯(7-2,步骤a)。所得酯的皂化可以通过使用强碱例如氢氧化钠在甲醇或乙醇中,存在或不存在四氢呋喃/水实现,提供乙烯基羧酸(7-3,步骤b)。在一些情况下,醛(7-1,R^9=H)的部分缩合可以导致分离醇中间体(7-4,步骤c),特别是当R^{10}吸电子时。该醇与亲核试剂例如Deoxo-Fluor®的取代(步骤d)、随后如上所述的皂化(步骤e),可生成另外由R^{11}取代的高度取代乙基羧酸(7-5),其中R^{11}为如上R^8所定义。当优选饱和连接基时,使用硫叶立德(sulfurylides)例如由三甲基碘化锍原位形成的那些,在无机碱例如氢化钠的存在下在极性非质子溶剂例如二甲亚砜或四氢呋喃中,丙烯酸酯(7-2)可转化为相应未取代或由R^{12}一取代或二取代的环丙烷(7-6,步骤f)。类似的丙烯酸酯(7-2)可使用氢气和钯催化剂还原为母烷烃(parent alkane)(7-8,步骤h)。环丙烷和烷烃两者可分别在上述碱性条件下水解,生成游离羧酸7-7(步骤g)和7-9(步骤i)。

[0126] 以类似方式，酮(7-1，R^9＝烷基)(描述于WO 2011017504 A1中)与二乙基膦酰乙酸乙酯或维蒂希试剂例如2-(三苯基膦)丙酸乙基酯或α-取代烷基酯例如2-氟乙酸乙酯或2-氰基乙酸乙酯在上述类似条件下的缩合，可以生成α-烷基丙烯酸酯7-2或醇7-4。随后对于R^9＝H的如上所述的处理7-2或7-4可以导致相应的不饱和(7-3)或饱和(7-5，7-7，7-9)羧酸。

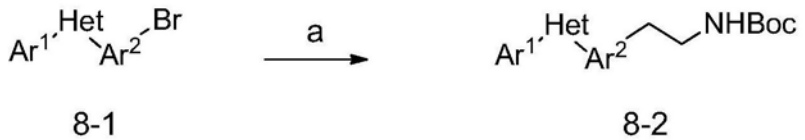
[0127] 方案7

[0128]

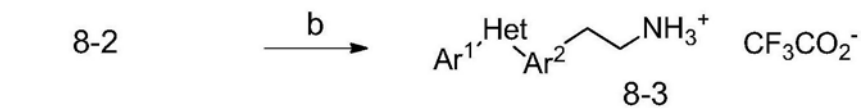


[0129] 可选择地，其中L为2个碳的连接基团的化合物也可以如方案8中所示制备。使用首先由Molander等人Org.Lett.，2007，9(2)，pp 203-206描述的条件，溴化物Ar^1-Het-Ar^2-Br(8-1，步骤a)与(2-((叔丁氧基羰基)氨基)乙基)三氟硼酸钾在钯催化剂例如乙酸钯(II)和碱例如碳酸铯的存在下，在温度为约80℃至约120℃的偶联，导致形成相应的2-(叔丁氧基羰基)氨基)乙基衍生物8-2。将该材料用约1至约5当量的酸例如三氟乙酸或氯化氢、在非质子溶剂例如二氯甲烷或二氧六环中、在温度为约0℃至约50℃的进一步处理，导致叔丁氧基羰基基团的断裂和形成胺Ar^1-Het-Ar^2-L-NH_2的三氟乙酸盐(8-3，步骤b)。

[0130] 方案8



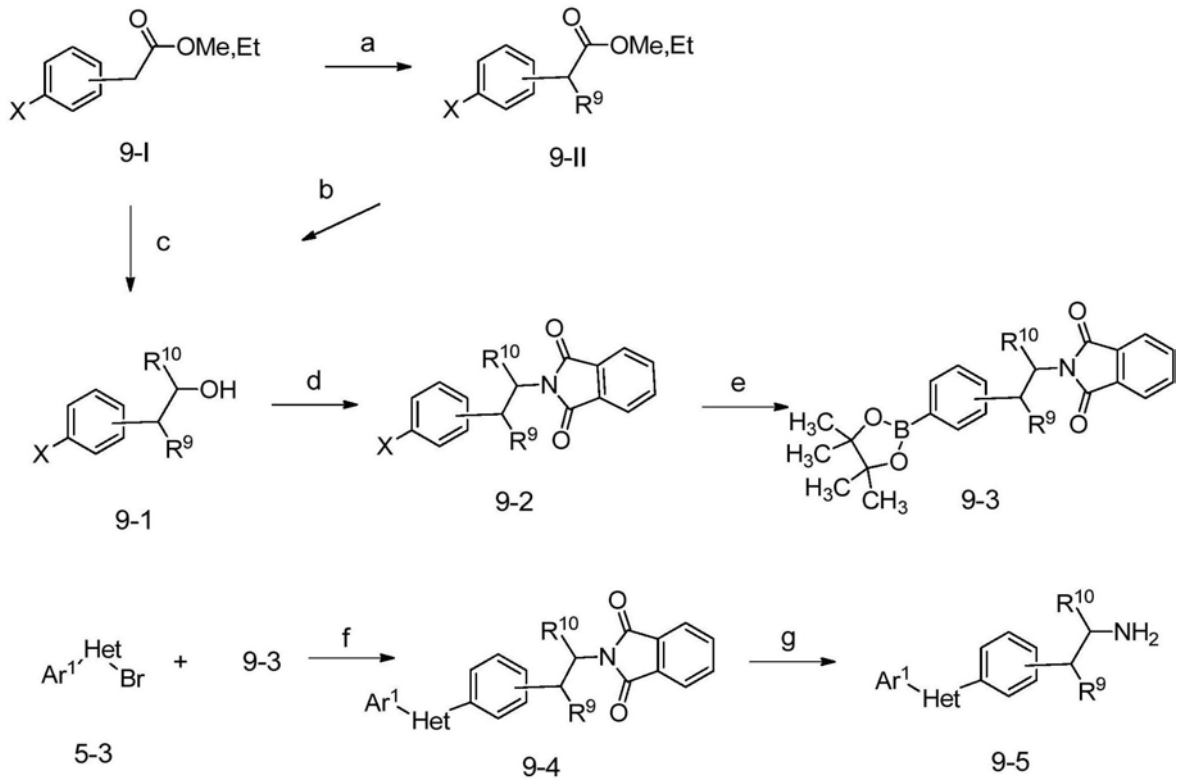
[0131]



[0132] 氨基烷基前体Ar^1-Het-Ar^2-L-NH_2(其中L为2个碳原子)(由R^9一取代或二取代,其中R^9为如上面所定义;和未取代或由R^{10}一取代,其中R^{10}为如上面所定义),可如方案9中所示制备。卤代苯基甲醇9-1(其中X可选自Cl、Br或I,在R^9和R^{10}未取代)在商业上可得。在R^9一取代或二取代的甲醇9-1可由相应的卤代苯基乙酸酯(9-I,步骤a)以与由Shin等人Bioorg.Med.Chem.Lett.,2008,18,pp 4424-442描述的类似方式制备,随后用金属氢化物例如氢化铝锂、在醚类溶剂例如四氢呋喃或乙醚中、在约0℃或低于约0℃的温度还原。9-I和9-II两者可以进一步由R^{10}一取代(步骤b或步骤c),用金属氢化物例如二异丁基氢化铝还原为相应的醛,并且进一步用格氏试剂以与由Brimble等人Org.Lett.,2012,14(23),pp 5820-5823描述的类似方式处理。甲醇9-1可用邻苯二甲酰亚胺在Mitsunobu条件下处理,生成N-苯二甲酰亚氨基中间体9-2(步骤d)。卤代物在Miyaura条件下可转化成硼酸酯(boronic ester),形成硼酸酯(boronate esters)(9-3,步骤e)。硼酸酯与溴代杂环的偶联可使用钯催化剂(该四(三苯基膦)钯(0)),在碱例如碳酸氢钠的存在下,在适宜的溶剂体系例如二氧六环/水中,在温度为约50℃至约120℃实现,提供N-苯二甲酰亚氨基中间体9-4(步骤f)。脱保护使用肼和甲醇或其他适宜的溶剂,可提供胺9-5(步骤g)。

[0133] 方案9

[0134]

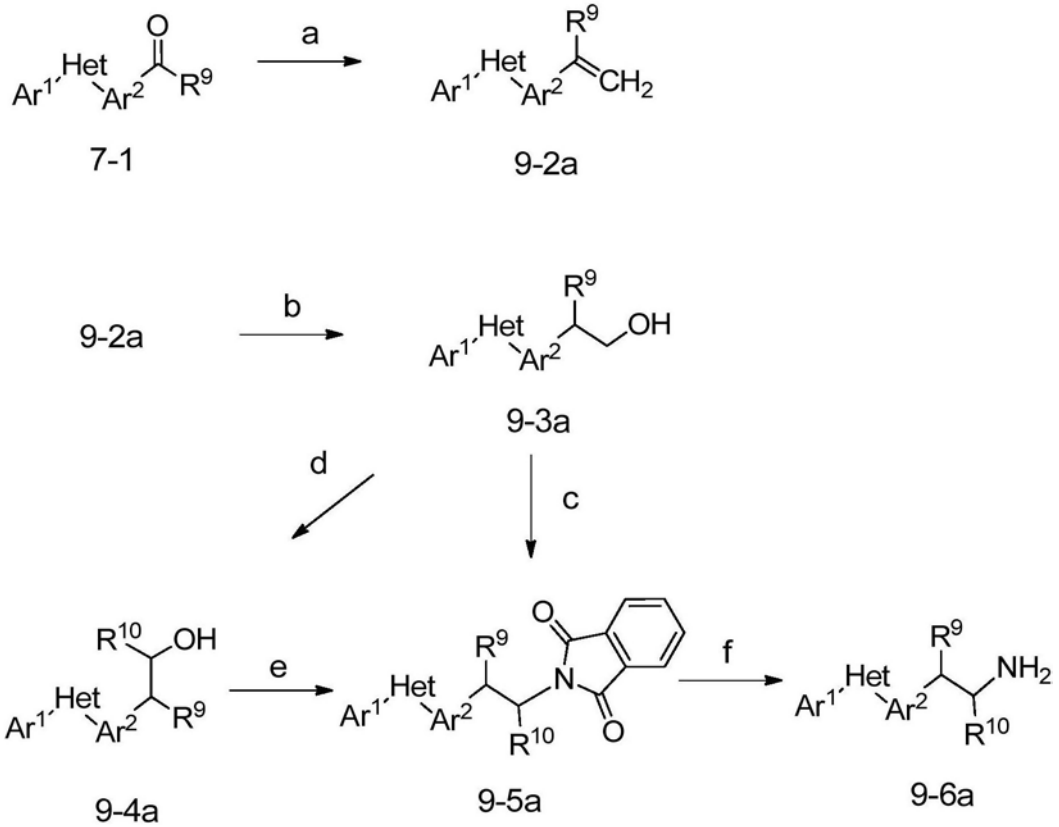


[0135] 可选择地,其中L为2个原子连接基团的化合物也可以如方案9a中所示制备。醛(7-1,R^9=H,步骤a)的烯化可以用亚甲基三苯基膦烷实现,所述亚甲基三苯基膦烷可由三苯基甲基碘化磷在碱例如氢化钠或1,8-二氮杂双环十一碳-7-烯的存在下在非质子溶剂例如四氢呋喃或二氯甲烷中在温度为约-78℃至约40℃制备。该物质(9-2a)用硼氢化试剂例如9-硼杂双环[3.3.1]壬烷在非质子溶剂例如四氢呋喃中进一步处理、随后用氧化剂氧化例如过氧化氢,可生成乙醇9-3a(步骤b)。甲醇9-3a可用邻苯二甲酰亚胺在Mitsunobu条件下处

理，生成N-苯二甲酰亚氨基中间体9-5a(步骤c)，其中R^{10}＝H。使用肼和甲醇或其他适宜的溶剂脱保护可提供胺9-6a(步骤f)。另外，9-3a可以进一步由R^{10}一取代(步骤d)，其中R^{10}为如上面所定义，其在Swern条件下随后加入格氏试剂氧化为相应的醛，例如上述(方案9)。甲醇9-4a可进一步用邻苯二甲酰亚胺在Mitsunobu条件下处理，生成N-苯二甲酰亚氨基中间体9-5a(步骤e)。使用肼和甲醇或其他适宜的溶剂脱保护可提供胺9-6a(步骤f)。

[0136] 方案9a

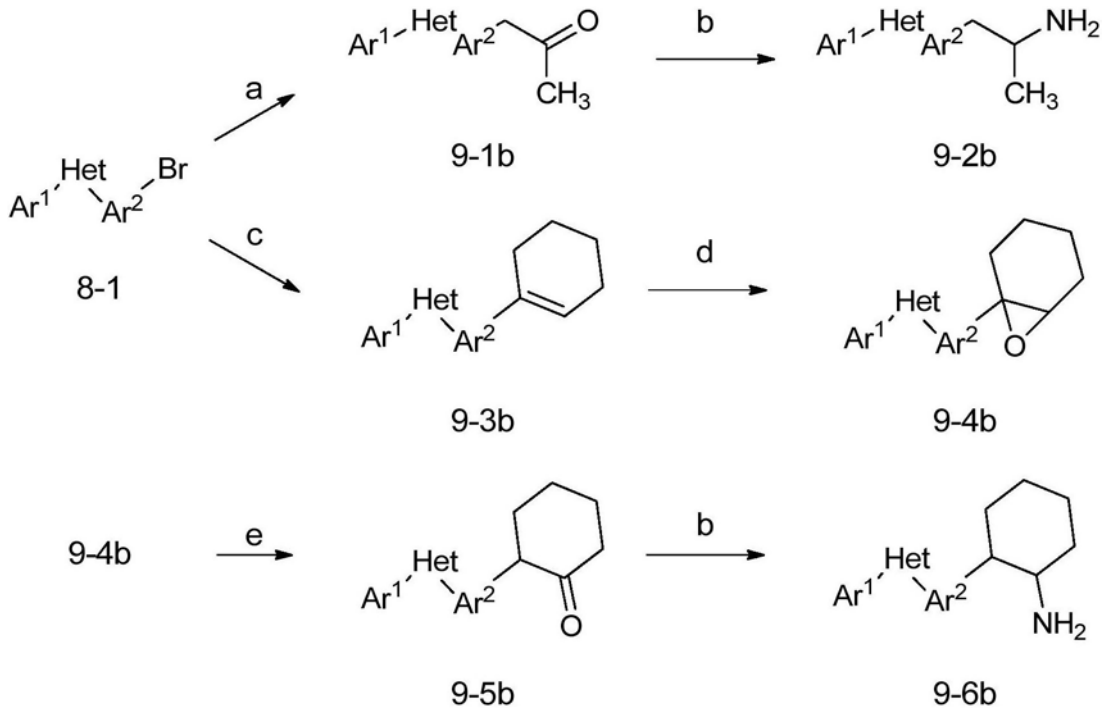
[0137]



[0138] 方案9b概述了构造其中连接基团L为两个原子连接基团的类似物的替代路线。2,4-戊烷-2,4-二酮与8-1的铜催化的芳基化(JACS，2010，132，8273.)，可以提供取代丙酮中间体9-1b(步骤a)。使用本领域技术人员知晓的各种条件的任一种进行还原胺化(步骤b)，可以生成胺9-2b，其可以使用前面方案2中所述条件转化成目标分子。当连接基团含有手性中心时，例如在中间体9-2b的情况下，这些中间体可以借助于手性柱，或由手性酸例如(+)和(-)酒石酸制备的盐的分步结晶，分离成它们的纯异构体形式。

[0139] 方案9b

[0140]



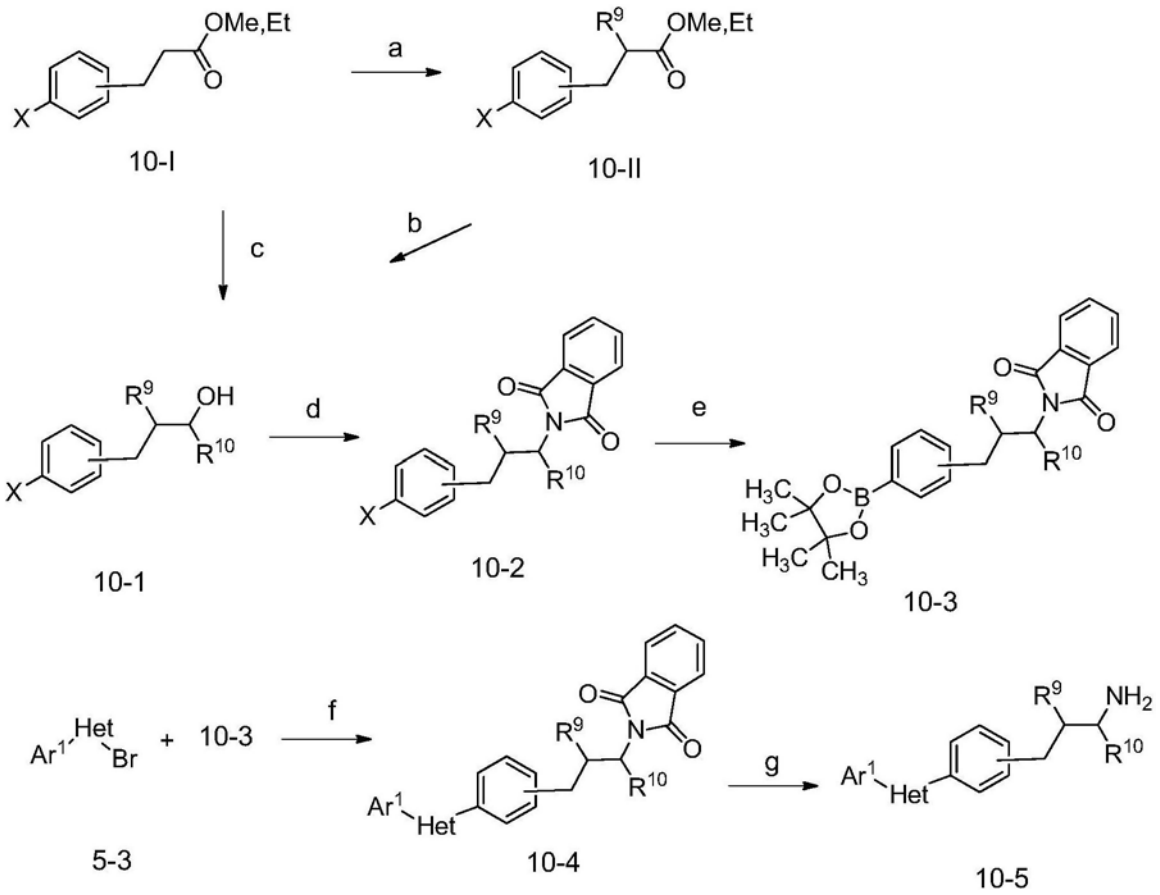
[0141] 从溴化物8-1开始，也可以实现其中乙基连接基团为6元环一部分的类似物的构造。8-1与2-环己-1-烯基-4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷(方案9b，步骤c)在标准Suzuki偶联条件下的偶联可导致烯烃9-3b。使用标准试剂例如间氯过氧苯甲酸的环氧化反应(步骤d)，随后进行使用三氯化铟的酸催化重排(J.Org.Chem.1998,63(23),8212.)，可以生成酮9-5b。使用上述条件可实现还原胺化并且转化成目标分子。

[0142] 制备丙基连接的中间体

[0143] 制备其中L为三个原子的基团的化合物描述于方案10和11中。氨基烷基前体Ar^1-Het-Ar^2-L-NH_2(其中L为3个碳原子，由R^9一取代或二取代，其中R^9为如上面所定义；和未取代或由R^{10}一取代，其中R^{10}为如上面所定义)，可如方案10中所示制备。卤代苯基甲醇10-1(其中X为Br和R^9和R^{10}为H)商业可得。在R^9一取代或二取代的甲醇10-1可由相应的卤代苯基乙酸酯(10-I，步骤a)以与由Shin等人Bioorg.Med.Chem.Lett.,2008,18,pp4424-4427描述的类似方式制备，随后用金属氢化物例如氢化铝锂在醚类溶剂例如四氢呋喃中在约0℃或低于约0℃的温度进行还原。10-I和10-II两者可以进一步由R^{10}一取代(步骤b或步骤c)，其用金属氢化物例如二异丁基氢化铝还原为相应的醛，进一步用格氏试剂例如甲基溴化镁以与由Brimble等人Org.Lett.,2012,14(23),pp 5820-5823描述的类似方式处理；甲醇10-1可用邻苯二甲酰亚胺在Mitsunobu条件下处理，生成N-苯二甲酰亚氨基中间体10-2(步骤d)。

[0144] 方案10

[0145]

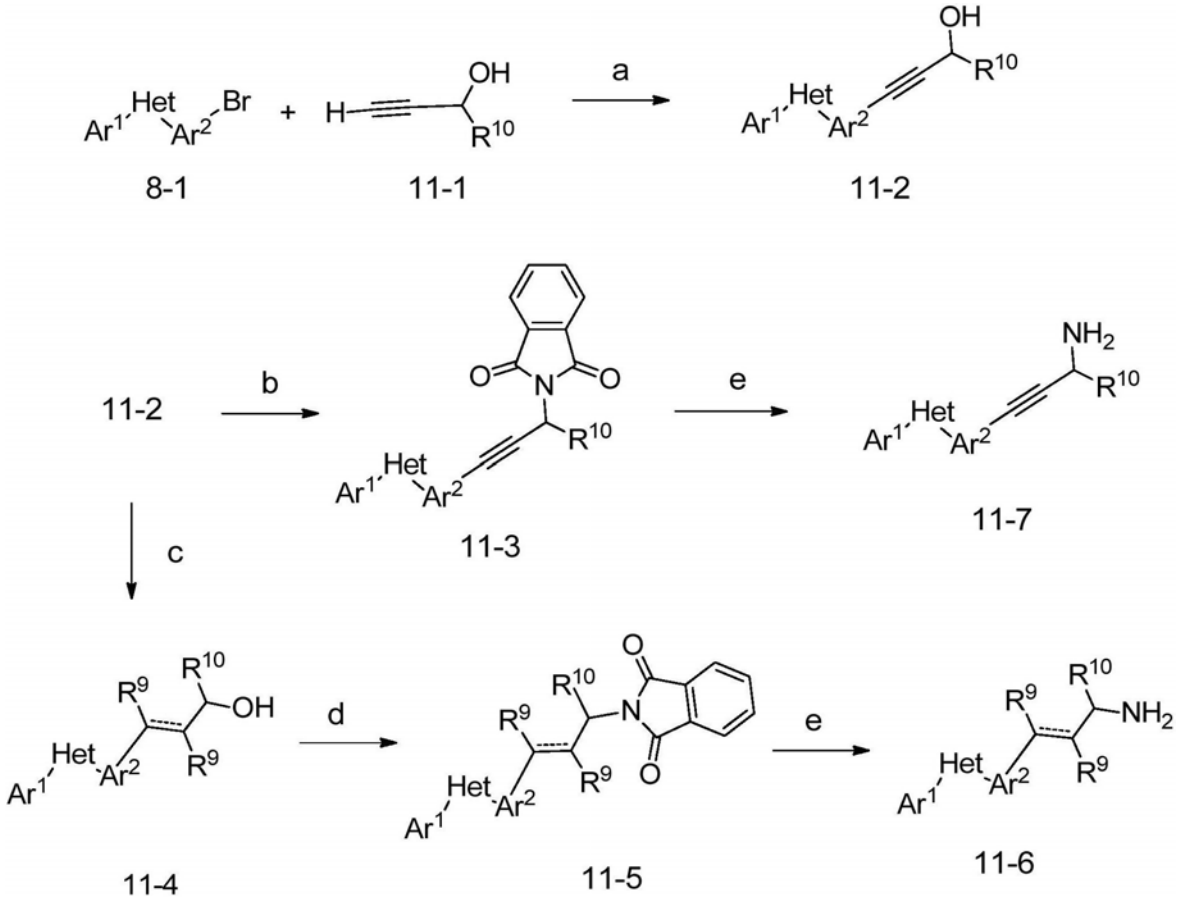


[0146] 卤代物可在Miyaura条件下转化成硼酸酯(boronic ester),形成硼酸酯(boronate esters)(10-3,步骤e)。硼酸酯与溴代杂环的偶联可使用钯催化剂(该四(三苯基膦)钯(0)),在碱例如碳酸氢钠的存在下,在适宜的溶剂体系例如二氧六环/水中,在温度为约50℃至约120℃实现,提供N-苯二甲酰亚氨基中间体10-4(步骤f)。使用肼和甲醇或其他适宜的溶剂的脱保护可提供胺10-5(步骤g)。

[0147] 可选择地,其中L为3个原子连接基团的化合物也可以如方案11中所示制备。溴化物Ar^1-Het-Ar^2-Br(8-1)可与适宜的未取代或由R^{10}一取代的炔醇(11-1,步骤a),其中R^{10}为如上面所定义;在钯催化剂例如(二(三苯基膦)合二氯化钯(II)、碘化亚铜(I)和碱例如三乙胺的存在下,在温度为约50℃至约120℃偶联,生成相应炔醇衍生物11-2。所得甲醇11-2可用邻苯二甲酰亚胺在Mitsunobu条件下处理,生成N-苯二甲酰亚氨基中间体11-3(步骤b),其可使用肼和甲醇或其他适宜的溶剂转化为胺(11-7,步骤e)。甲醇11-2可使用过渡金属催化剂例如钯在氢的气氛下还原,提供在R^{10}未取代的烯基或完全饱和的烷基甲醇11-4。另外,甲醇11-2可用金属氢化物例如氢化铝锂处理,提供(E)-烯基甲醇11-4。同样,甲醇11-2可以用保护基团例如叔丁基二苯基硅烷保护,并且用加氢金属化试剂例如施瓦茨试剂处理,随后用例如单质碘或NBS进行亲电子试剂淬灭。可选择地,甲醇11-2可以用金属转移试剂例如频哪醇基二硼(pinacol diboron)处理进一步用于过渡金属催化的偶联反应,例如Suzuki或Negishi,制备由R^9一取代或二取代的甲醇11-4,其中R^9为如上面所定义(步骤c)。脱保护之后,所得甲醇11-4可用邻苯二甲酰亚胺在Mitsunobu条件下处理,生成N-苯二甲酰亚氨基中间体11-5(步骤d),其可使用肼和甲醇或其他适宜的溶剂转化为胺(11-6,步骤e)。

[0148] 方案11

[0149]

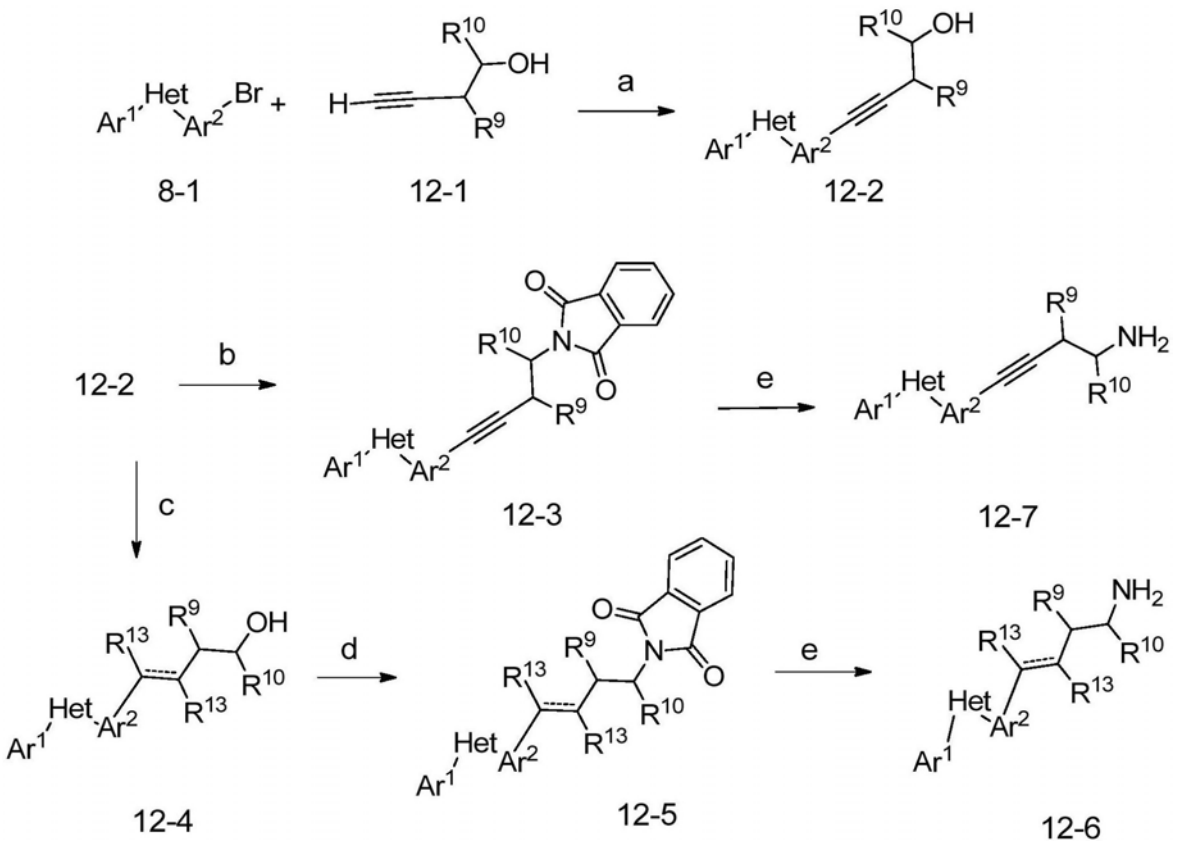


[0150] 制备丁基连接的中间体

[0151] 其中L为4个原子连接基团的化合物可以如方案12中所示制备。溴化物Ar^1-Het-Ar^2-Br(8-1)可与适宜的炔醇(12-1,步骤a)(未取代或由R^{10}一取代,其中R^{10}为如上面所定义;由R^9一取代或二取代,其中R^9为如上面所定义)在钯催化剂例如(二(三苯基膦)合二氯化钯、碘化亚铜(I)和碱例如三乙胺的存在下,在温度为约50℃至约120℃偶联,生成相应炔醇衍生物12-2。所得甲醇12-2可用邻苯二甲酰亚胺在Mitsunobu条件下处理(步骤b),生成N-苯二甲酰亚氨基中间体12-3,所述中间体12-3可使用肼和甲醇或其他适宜的溶剂转化为胺(12-7,步骤e)。甲醇12-2可使用过渡金属催化剂例如钯在氢的气氛下进行还原,提供在R^{13}未取代的烯基或完全饱和的烷基甲醇12-4(步骤c)。另外,甲醇12-2可用金属氢化物例如氢化铝锂处理,提供(E)-烯基甲醇12-4(步骤c)。同样,甲醇12-2可以用保护基团例如叔丁基二苯基硅烷保护,并且用加氢金属化试剂例如施瓦茨试剂处理,随后用例如单质碘或NBS进行亲电子试剂淬灭。可选择地,甲醇12-2可以用金属转移试剂例如频哪醇基二硼(pinacol diboron)处理,进一步用于过渡金属催化的偶联反应,例如Suzuki或Negishi,制备由R^{13}一取代或二取代的甲醇12-4,其中R^{13}为如上所定义R^8(步骤c)。

[0152] 方案12

[0153]



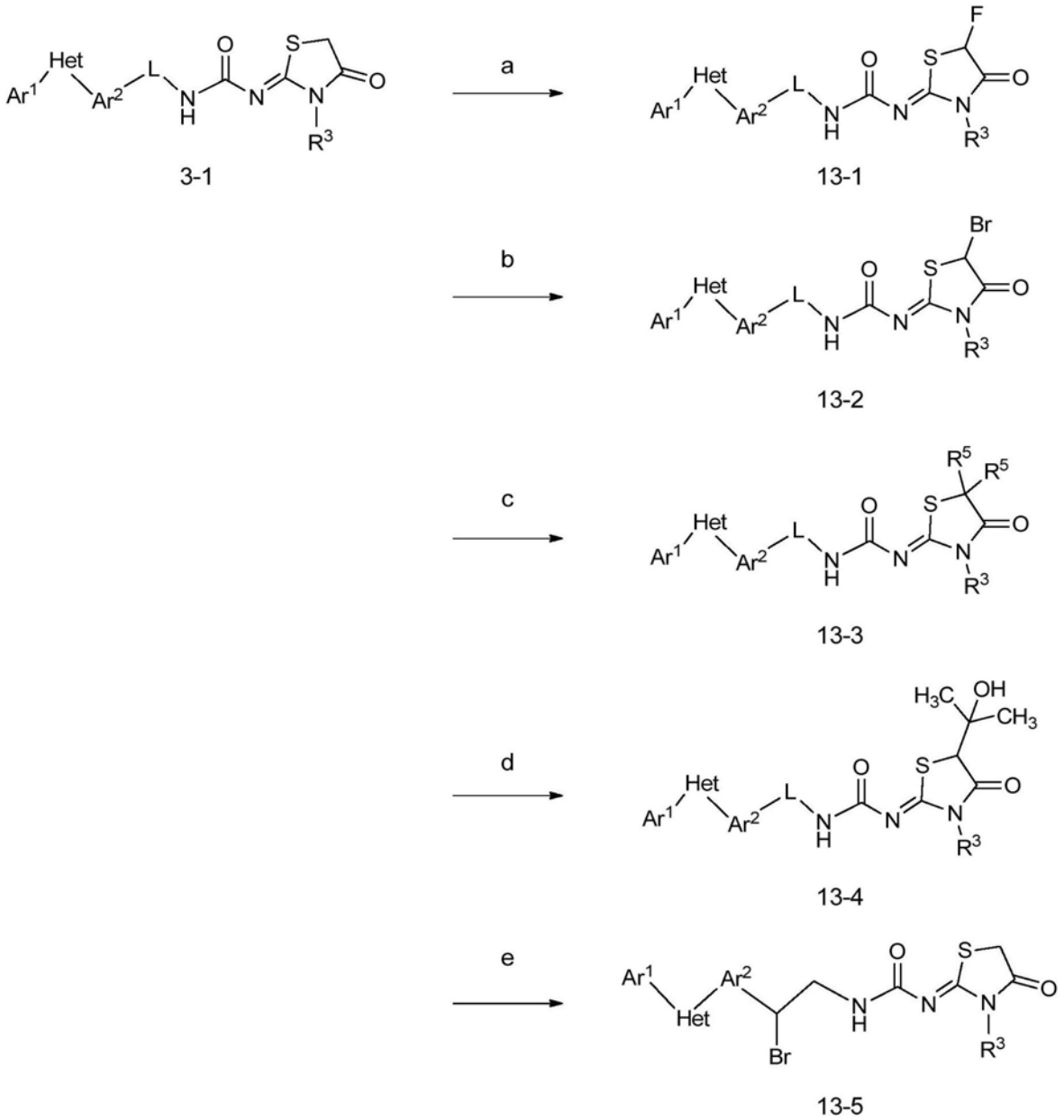
[0154] 脱保护之后,所得甲醇12-4可用邻苯二甲酰亚胺在Mitsunobu条件下处理(步骤d),生成N-苯二甲酰亚氨基中间体12-5,所述中间体12-5可使用肼和甲醇或其他适宜的溶剂转化为胺(12-6,步骤e)。

[0155] 制备取代硫代缩二脲

[0156] 2-亚氨基-1,3-噻唑啉-4-酮(3-1)可以使用各种条件进一步官能化。当用Selectfluor®和9-芴酮在无水乙腈中处理时(JACS.2013,135,17494.),具有式3-1的分子可以转化成单氟类似物(13-1)。

[0157] 方案13

[0158]



[0159] 用分子溴在非质子溶剂中例如二氯甲烷在约0℃至约30℃处理(步骤b)可以导致噻唑啉酮环上的单溴化(13-2)。使用至少2当量的烷基化试剂R^5-I和强碱例如氢化钠或二异丙基氨基锂、在极性非质子溶剂例如二甲基甲酰胺或四氢呋喃中的烷基化(步骤c),可以导致双烷基化产物(13-3)。用酮或醛和无机碱例如碳酸钾或碳酸铯处理,可以导致形成甲醇(13-4)。对于其中L为-CH_2CH_2-基团的式3-1化合物的类似物,使用N-溴代琥珀酰亚胺和自由基引发剂例如偶氮二异丁腈在四氯化碳中在约30℃至约77℃的自由基溴化,可以导致其中溴并入乙基连接基团中的单溴代产物(13-5)。

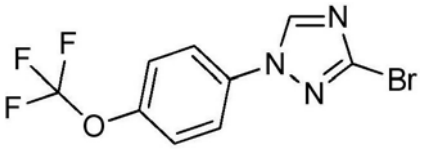
[0160] 实施例

[0161] 这些实施例用于说明的目的,而不解释为限制本申请至仅这些实施例中披露的实施方式。

[0162] 使用从商业来源得到的起始原料、试剂和溶剂而不进一步纯化。无水溶剂购自来自Aldrich的Sure/Seal™,按接收的原样使用。熔点通过来自Stanford Research Systems

的Thomas Hoover Unimelt毛细管熔点设备或OptiMelt自动熔点系统得到，未进行校正。使用“室温”的实施例在室内气候调节的实验室内在温度范围为约20℃至约24℃进行。分子给出其已知名称，所述名称根据ISIS Draw、ChemDraw或ACD Name Pro内的命名程序进行命名。如果该程序不能命名分子，则分子使用常规命名规则命名。除非另外指明，^{1}H NMR光谱数据按ppm(δ)计并且在300、400或600MHz记录，^{13}C NMR光谱数据按ppm(δ)计并且在75、100或150MHz记录。

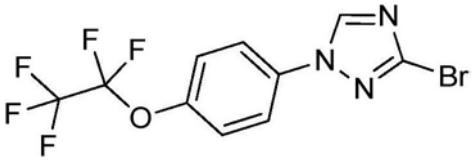
[0163] 实施例1：制备3-溴-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C1)

[0164] 

[0165] 向100mL装配有搅拌棒的圆底烧瓶，加入为固体的碘化亚铜(I)(0.397g，2.08mmol)，3-溴-1H-1,2,4-三唑(4.62g，31.2mmol)，和碳酸铯(6.79g，20.83mmol)。将这些固体用无水二甲亚砜(34.7mL)稀释。然后加入作为液体的1-碘-4-(三氟甲氧基)苯(1.65mL，10.4mmol)。将烧瓶放置在氮气气氛下，并且将悬浮液加热至内部温度为100℃保持20小时。使得反应混合物冷却至室温并且通过Celite®垫过滤，用过量的乙酸乙酯(200mL)洗涤。将滤液倒入盐水溶液(200mL)中，分层。将水相用另外的乙酸乙酯(2×100mL)提取。将合并的有机层经无水硫酸镁干燥，过滤，浓缩。将所得残留物经使用10-50%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化，提供为白色固体的标题化合物(1.80g，54%)：^{1}H NMR(400MHz，DMSO-d_6)δ9.35(s，1H)，7.97(d，J＝8.9Hz，2H)，7.60(d，J＝8.4Hz，2H)；^{19}F NMR(376MHz，DMSO-d_6)δ-57.06；ESIMS m/z 308，310([M+H]$^{+}$)。

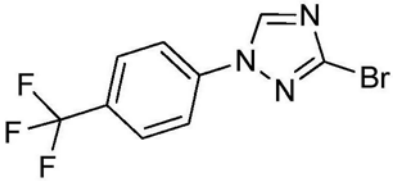
[0166] 下面的化合物根据实施例1中的步骤制备。

[0167] 制备3-溴-1-(4-(全氟乙氧基)苯基)-1H-1,2,4-三唑(C1a)

[0168] 

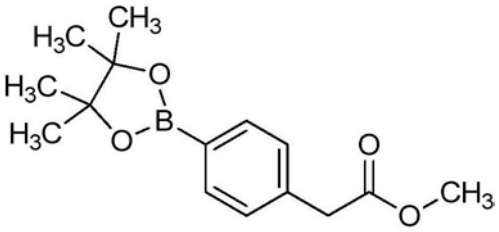
[0169] 标题化合物如实施例1中所述使用1-碘-4-全氟乙氧基苯制备，并且分离为白色固体(1.60g，31%)：mp 72-74℃；^{1}H NMR(400MHz，$CDCl_3$)δ8.44(s，1H)，7.75-7.68(m，2H)，7.42-7.36(m，2H)；^{19}F NMR(376MHz，$CDCl_3$)δ-85.94，-87.92；ESIMS m/z 357，359([M+H]$^{+}$)。

[0170] 制备3-溴-1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑(C1b)

[0171] 

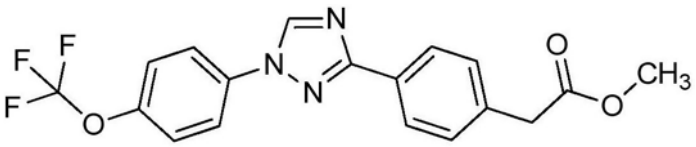
[0172] 标题化合物如实施例1中所述使用1-碘-4-三氟甲基苯制备，并且分离为白色固体(2.32g，31%)：mp 104-105℃；^{1}H NMR(400MHz，$CDCl_3$)δ8.52(s，1H)，7.81(s，4H)；^{19}F NMR(376MHz，$CDCl_3$)δ-62.64；ESIMS m/z 292，294([M+H]$^{+}$)。

[0173] 实施例2：制备2-(4-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苯基)乙酸甲酯(C2)

[0174] 

[0175] 向200mL装配有搅拌棒的圆底烧瓶，加入为固体的[1,1′-双(二苯基膦基)二茂铁]二氯化钯(II)(0.799g，1.09mmol)，4,4,4’,4’,5,5,5’,5’-八甲基-2,2’-双(1,3,2-二氧杂硼杂环戊烷)(6.65g，26.2mmol)，和乙酸钾(4.28g，43.7mmol)。将这些固体用二氧六环(100mL)稀释。将烧瓶密封、抽吸并且用氮气氛吹扫。然后加入甲基2-(4-溴苯基)乙酸酯(5.00g，21.8mmol)。然后将反应混合物温热至内部温度为70℃保持6小时。使得反应混合物冷却至室温，并且倒入盐水溶液中，分层。将水相用乙酸乙酯提取(3×125mL)。将合并的有机层经无水硫酸镁干燥，过滤，浓缩。将所得残留物经使用0-30％乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化，提供为澄清液体的标题化合物(4.93g，70％)：^{1}H NMR(400MHz，DMSO-d_6)δ7.68-7.58(m，2H)，7.35-7.23(m，2H)，3.71(s，2H)，3.61(s，3H)，1.29(s，12H)；^{13}C NMR(101MHz，DMSO-d_6)δ171.29，137.72，134.45，128.86，83.56，82.79，51.68，40.23，24.62；EIMS m/z 276([M]$^{+}$)。

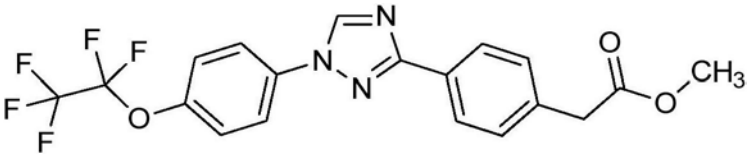
[0176] 实施例3：制备2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酸甲酯(C3)

[0177] 

[0178] 向200mL装配有磁搅拌棒的圆底烧瓶，加入3-溴-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C1)(3.45g，11.2mmol)，和2-(4-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苯基)乙酸甲基酯(C2)(3.71g，13.4mmol)。将这些试剂用二氧六环(45.0mL)和水(11.3mL)稀释，所得溶液用氮气吹扫10分钟。加入为固体的四氟硼酸三叔丁基膦(0.325g，1.12mmol)，乙酸钯(II)(0.126g，0.560mmol)和氟化铯(3.40g，22.4mmol)。将烧瓶密封并且放置在氮气氛下。将反应混合物加热至内部温度为60℃。使得反应混合物冷却至室温，并且倒入盐水溶液中，分层。将水相用乙酸乙酯提取(3×100mL)。将合并的有机层经无水硫酸镁干燥，过滤，浓缩。将所得残留物经使用0-10％乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化，提供为灰白色固体的标题化合物(3.45g，82％)：^{1}H NMR(400MHz，DMSO-d_6)δ9.41(s，1H)，8.11-8.04(m，4H)，7.63(ddt，J＝7.9，2.1，1.1Hz，2H)，7.48-7.36(m，2H)，3.77(s，2H)，3.64(s，3H)；^{19}F NMR(376MHz，DMSO-d_6)δ-57.02；ESIMS m/z 378([M+H]$^{+}$)。

[0179] 下面的化合物根据实施例3中的步骤制备。

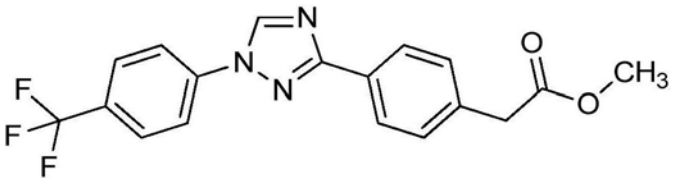
[0180] 制备2-(4-(1-(4-(全氟乙氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酸甲酯(C4)

[0181] 

[0182] 标题化合物如实施例3中所述使用3-溴-1-(4-(全氟乙氧基)苯基)-1H-1,2,4-三

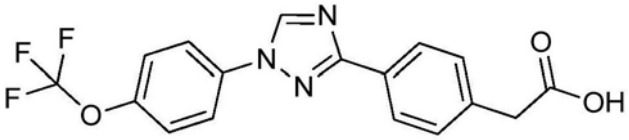
唑(C1a)和甲基2-(4-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苯基)乙酸酯(C2)制备，并且分离为白色固体(3.57g，59%)：^{1}H NMR(400MHz，DMSO-d_6)δ9.42(s，1H)，8.18-8.04(m，4H)，7.68-7.58(m，2H)，7.48-7.38(m，2H)，3.78(s，2H)，3.65(s，3H)；^{19}F NMR(376MHz，DMSO-d_6)δ-85.20(d，J＝2.9Hz)，-86.93；ESIMS m/z 428([M+H]$^{+}$)。

[0183] 制备甲基2-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酸酯(C5)

[0184] 

[0185] 标题化合物如实施例3中所述使用3-溴-1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑(C1b)和2-(4-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苯基)乙酸甲基酯(C2)制备，并且分离为白色固体(2.3g，81%)：^{1}H NMR(400MHz，DMSO-d_6)δ9.53(s，1H)，8.23-8.16(m，2H)，8.08(d，J＝8.2Hz，2H)，8.03-7.96(m，2H)，7.49-7.38(m，2H)，3.78(s，2H)，3.65(s，3H)；^{19}F NMR(376MHz，DMSO-d_6)δ-60.82；ESIMS m/z 362([M+H]$^{+}$)。

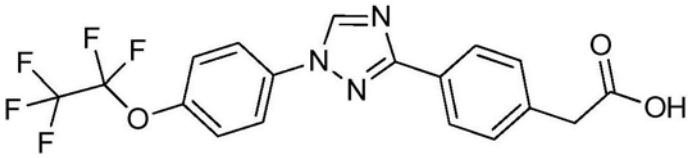
[0186] 实施例4：制备2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酸(C6)

[0187] 

[0188] 向100mL装配有磁搅拌棒的圆底烧瓶，加入为固体的2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酸甲酯(C3)(3.45g，9.14mmol)和氢氧化锂·一水合物(1.15g，27.4mmol)。将这些固体用四氢呋喃(24mL)，甲醇(24mL)，和水(12mL)稀释。将反应在室温搅拌2小时。然后将反应混合物浓缩至干燥。然后将所得固体用水稀释，并且将所得悬浮液调节至pH 2.9。将随后的沉淀物用乙酸乙酯(5×100mL)提取。将合并的有机提取物经无水硫酸镁干燥，过滤，浓缩，提供为白色固体的标题化合物(3.27g，96%)：^{1}H NMR(400MHz，DMSO-d_6)δ12.41(s，1H)，9.40(s，1H)，8.15-8.03(m，4H)，7.63(dq，J＝7.9，1.0Hz，2H)，7.49-7.36(m，2H)，3.66(s，2H)；^{19}F NMR(376MHz，DMSO-d_6)δ-56.98；ESIMS m/z 364([M+H]$^{+}$)。

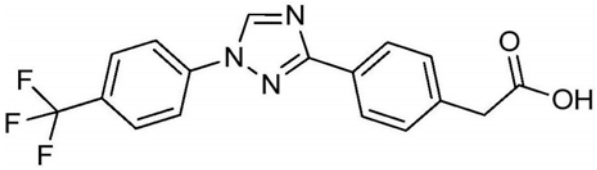
[0189] 下面的化合物根据实施例4中的步骤制备。

[0190] 制备2-(4-(1-(4-(全氟乙氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酸(C7)

[0191] 

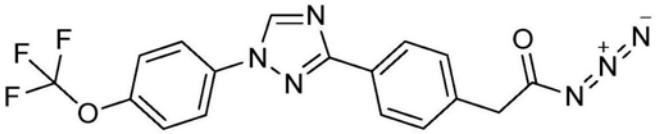
[0192] 标题化合物中所述实施例4使用2-(4-(1-(4-(全氟乙氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酸甲酯(C4)制备，并且分离为白色固体(3.4g，94%)：^{1}H NMR(400MHz，DMSO-d_6)δ12.41(s，1H)，9.41(s，1H)，8.15-8.02(m，4H)，7.67-7.58(m，2H)，7.47-7.37(m，2H)，3.66(s，2H)；^{19}F NMR(376MHz，DMSO-d_6)δ-85.20，-86.92；ESIMS m/z 414([M+H]$^{+}$)。

[0193] 制备2-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酸(C8)

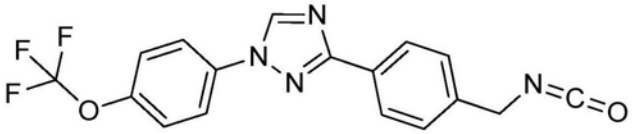
[0194] 

[0195] 标题化合物中所述实施例4用2-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酸甲基酯(C5)制备,并且分离为白色固体(0.378g,98%):^{1}H NMR(400MHz,DMSO-d_6)δ12.42(s,1H),9.53(s,1H),8.25-8.16(m,2H),8.11-8.04(m,2H),7.99(d,J=8.6Hz,2H),7.47-7.39(m,2H),3.66(s,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-60.79;ESIMS m/z 348([M+H]$^{+}$)。

[0196] 实施例5:制备(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酰基叠氮化物/2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)甲基异氰酸酯(C9)



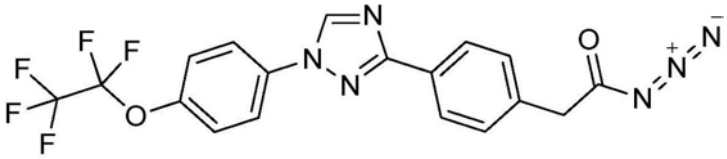
[0197]



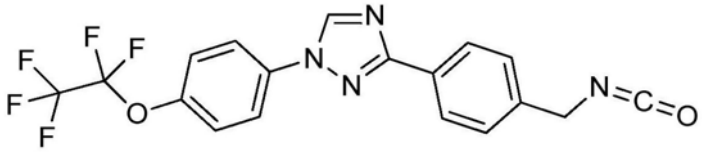
[0198] 在100mL装配有磁搅拌棒的圆底烧瓶中,将2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酸(C6)(2.00g,5.51mmol)用甲苯(37mL)稀释。然后加入三乙胺(0.767mL,5.51mmol)和叠氮磷酸二苯酯(1.19mL,5.51mmol)。使得反应在室温搅拌2.5小时。然后将反应混合物倒入水中并且用乙酸乙酯(3×50mL)提取。将合并的有机层经无水硫酸镁干燥,过滤,浓缩。将所得残留物经使用0-10%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化,提供为灰白色固体的标题化合物(0.800g,37%):^{1}H NMR(400MHz,DMSO-d_6)δ9.41(d,J=5.9Hz,1H),8.21-7.99(m,4H),7.69-7.57(m,2H),7.57-7.38(m,2H),4.70(s,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.99(d,J=4.1Hz);ESIMS m/z 361([M+H]$^{+}$)(氨基甲酸甲酯)。

[0199] 下面的化合物根据实施例5中的步骤制备。物理性质表明,经分离的产物经常是酰基叠氮化物和重排的异氰酸酯的混合物。

[0200] 制备2-(4-(1-(4-(全氟乙氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酰基叠氮化物/2-(4-(1-(4-(全氟乙氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)甲基异氰酸酯(C10)



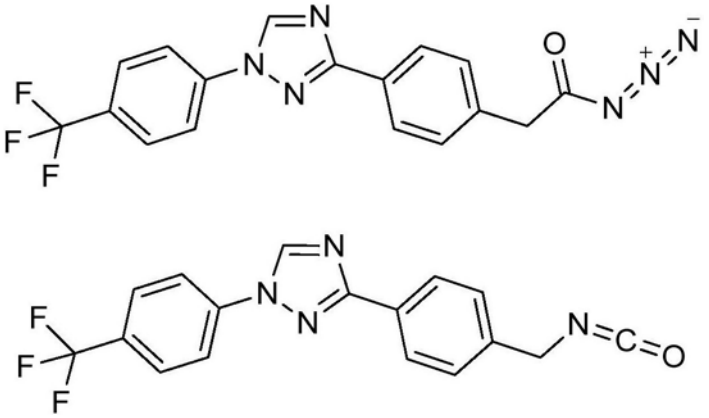
[0201]



[0202] 标题化合物如实施例5中所述使用2-(4-(1-(4-(全氟乙氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酸(C7)制备,并且分离为白色固体(1.45g,46%):^{1}H NMR(400MHz,DMSO-d_6)δ9.46-9.32(m,1H),8.19-7.97(m,4H),7.68-7.36(m,4H),4.70(s,1H),4.34(d,J=6.1Hz,1H);^{19}F NMR(376MHz,DMSO-d_6)δ-85.23(d,J=9.8Hz),-86.95(d,J=8.0Hz);ESIMS m/z 442([M+H]$^{+}$)(氨基甲酸甲酯)。

[0203] 制备2-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酰基叠氮化物/2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)甲基异氰酸酯(C11)

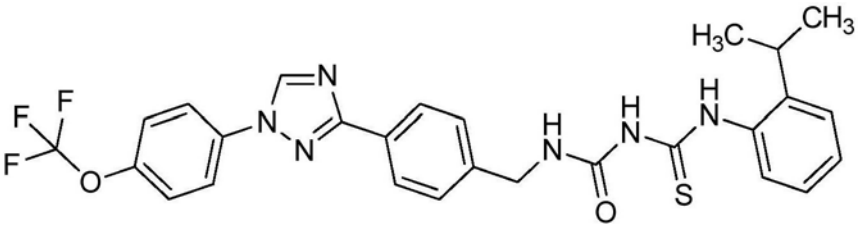
[0204]



[0205] 标题化合物如实施例5中所述用2-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酸(C8)制备,并且分离为白色固体(0.082g,25%):^{1}H NMR(400MHz,DMSO-d_6)δ9.55(s,1H),8.27-8.06(m,4H),7.99(d,J=8.5Hz,2H),7.56-7.49(m,1H),7.44(dd,J=8.4,6.9Hz,1H),4.71(s,1H),3.87(s,1H);^{19}F NMR(376MHz,DMSO-d_6)δ-60.80(d,J=2.9Hz);ESIMS m/z 345([M+H]$^{+}$)。

[0206] 实施例6:制备N-[2-(丙烷-2-基)苯基]-N'-(4-{1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基}苄基)硫代缩二脲(dicarbonimidothioic diamide)(F14)

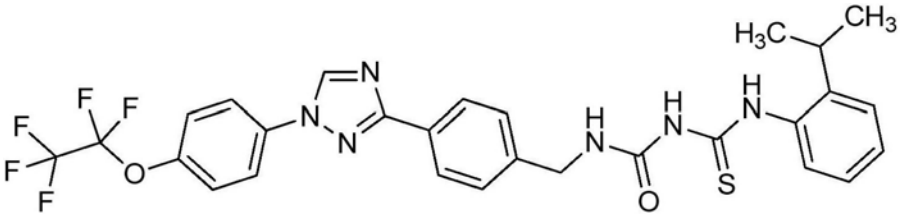
[0207]



[0208] 在20mL装配有磁搅拌棒的小瓶中,将(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酰基叠氮化物/2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)甲基异氰酸酯(C9)(0.200g,0.515mmol)悬浮在乙腈(3.3mL)中。将小瓶盖住并且将悬浮液在80℃加热3小时。将悬浮液冷却至室温,装入为固体的1-(2-异丙基苯基)硫脲(0.110g,0.567mmol)和碳酸铯(0.201g,0.618mmol)。将该悬浮液在室温搅拌18小时。反应混合物通过烧结玻璃漏斗(glass-fritted funnel)过滤。将滤液浓缩,将所得残留物经由使用5-100%乙腈/水作为洗脱剂的反相快速柱色谱(C_{18}柱)纯化,提供为浅黄色固体的标题化合物(0.104g,36%)。

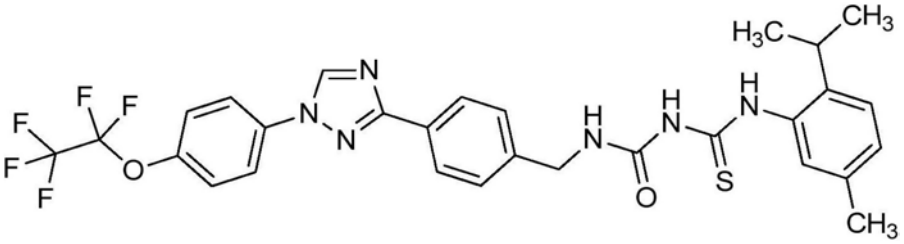
[0209] 下面的化合物根据实施例6中的步骤制备。

[0210] 制备N-(4-{1-[4-(全氟乙氧基)苯基]-1H-1,2,4-三唑-3-基}苄基)-N'-[2-(丙烷-2-基)苯基]硫代缩二脲(F15)

[0211] 

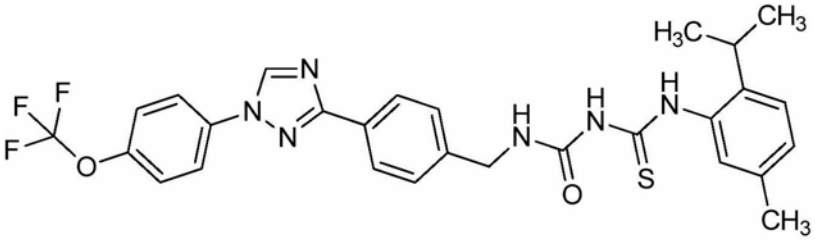
[0212] 标题化合物如实施例6中所述使用2-(4-(1-(4-(全氟乙氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酰基叠氮化物/2-(4-(1-(4-(全氟乙氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)甲基异氰酸酯(C10)和1-(2-异丙基苯基)硫脲制备,并且分离为黄色固体(0.102g,36%)。

[0213] 制备N-[5-甲基-2-(丙烷-2-基)苯基]-N'-(4-{1-[4-(全氟乙氧基)苯基]-1H-1,2,4-三唑-3-基}苄基)硫代缩二脲(F16)

[0214] 

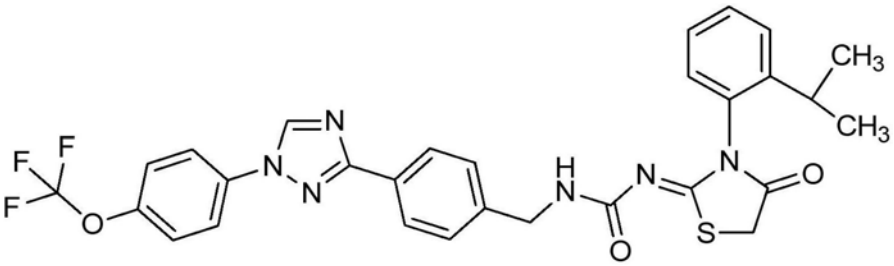
[0215] 标题化合物如实施例6中所述使用2-(4-(1-(4-(全氟乙氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酰基叠氮化物/2-(4-(1-(4-(全氟乙氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)甲基异氰酸酯(C10)和1-(2-异丙基-5-甲基苯基)硫脲制备,并且分离为黄色固体(0.130g,44%)。

[0216] 制备N-[5-甲基-2-(丙烷-2-基)苯基]-N'-(4-{1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基}苄基)硫代缩二脲(F35)

[0217] 

[0218] 标题化合物如实施例6中所述使用(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酰基叠氮化物/2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)甲基异氰酸酯(C9)和1-(2-异丙基-5-甲基苯基)硫脲制备,并且分离为黄色固体(0.043g,15%)。

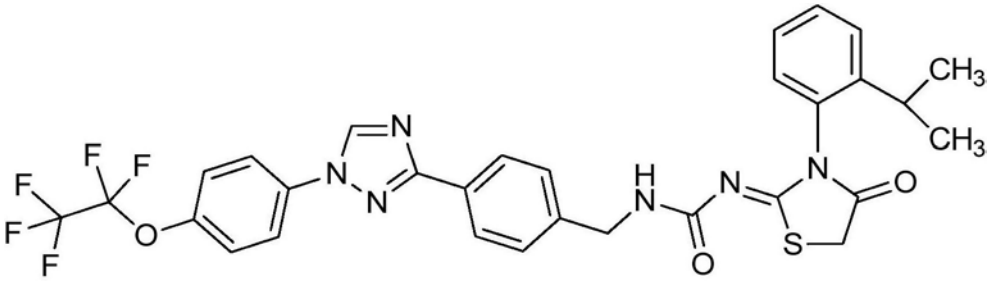
[0219] 实施例7:制备(Z)-1-(3-(2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)脲(F17)

[0220] 

[0221] 在50mL装配有磁搅拌棒的圆底烧瓶中，N-[2-(丙烷-2-基)苯基]-N'-(4-{1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基}苄基)硫代缩二脲(F14)(0.067g，0.12mmol)和乙酸钠(0.012g，0.15mmol)用乙腈(1.2mL)稀释，然后加入2-溴乙酸甲酯(0.013mL，0.13mmol)。烧瓶安装有回流冷凝器并且将反应混合物在70℃加热。4小时之后，加入另外等份的2-溴乙酸甲酯(0.013mL，0.13mmol)，使得反应加热另外的18小时。加入另外等份的2-溴乙酸甲酯(0.013mL，0.13mmol)和乙酸钠(0.012g，0.15mmol)，使得反应加热另外的4小时。反应混合物冷却，用水稀释，并且用乙酸乙酯提取(50mL)。将有机层经无水硫酸镁干燥，过滤，浓缩。将所得残留物经由使用5-100%乙腈/水作为洗脱剂的反相快速柱(C_{18}柱)色谱纯化，提供为白色固体的标题化合物(0.036g，49%)。

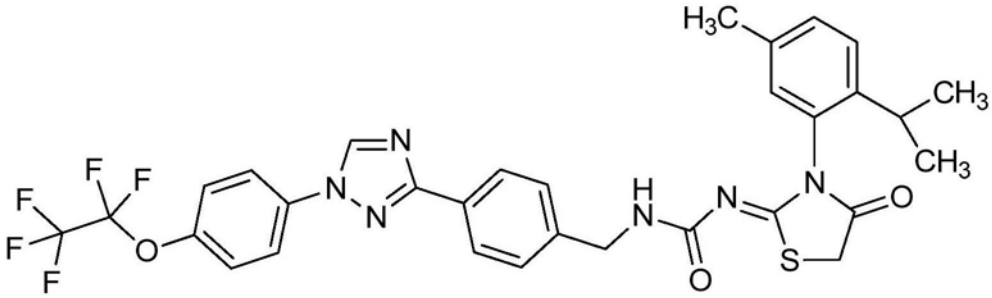
[0222] 下面的化合物根据实施例7中的步骤制备。

[0223] 制备(Z)-1-(3-(2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(全氟乙氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)脲(F18)

[0224] 

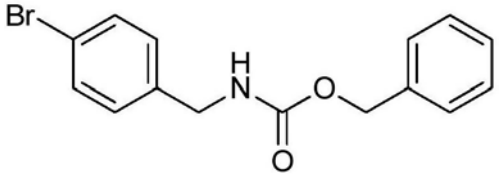
[0225] 标题化合物如实施例7中所述使用N-(4-{1-[4-(全氟乙氧基)苯基]-1H-1,2,4-三唑-3-基}苄基)-N'-[2-(丙烷-2-基)苯基]硫代缩二脲(F15)制备，并且分离为灰白色固体(0.043g，47%)。

[0226] 制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(全氟乙氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)脲(F19)

[0227] 

[0228] 标题化合物如实施例7中所述使用N-[5-甲基-2-(丙烷-2-基)苯基]-N'-(4-{1-[4-(全氟乙氧基)苯基]-1H-1,2,4-三唑-3-基}苄基)硫代缩二脲(F16)制备，并且分离为白色固体(0.056g，46%)。

[0229] 实施例8：制备4-溴苄基氨基甲酸苄酯(C12)

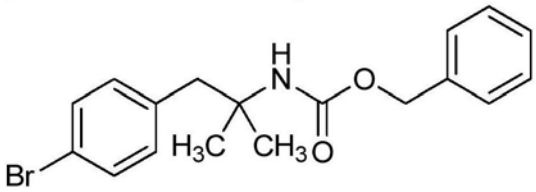
[0230] 

[0231] 在500mL装配有磁搅拌棒的圆底烧瓶中，将(4-溴苯基)甲基氯化铵(10.0g，

44.9mmol)和氢氧化钠(4.00g,100mmol)溶解在四氢呋喃(80mL)和水(80mL)中。将溶液在冰水浴中冷却,逐滴加入氯甲酸苄酯(7.06mL,49.4mmol)。使得反应搅拌1小时。将反应混合物倒入盐水溶液中并且用乙酸乙酯(2×200mL)提取。将合并的有机层经无水硫酸镁干燥,干燥,浓缩,提供为白色固体的标题化合物(14.8g,102%):^{1}H NMR(400MHz,DMSO-d_6)δ7.92(t,J=6.0Hz,1H),7.64-7.53(m,2H),7.47-7.33(m,5H),7.32-7.20(m,2H),5.10(s,2H),4.23(d,J=6.2Hz,2H);^{13}C NMR(101MHz,DMSO-d_6)δ156.33,139.20,137.05,131.10,129.22,128.33,127.72,119.77,65.42,43.19;ESIMS m/z 320,322([M+H]$^{+}$)。

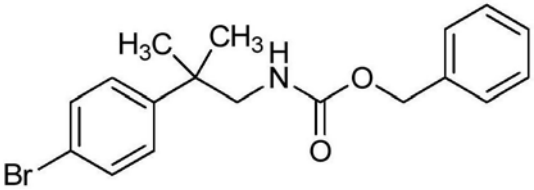
[0232] 下面的化合物根据实施例8中的步骤制备。

[0233] 制备(1-(4-溴苯基)-2-甲基丙烷-2-基)氨基甲酸苄酯(CB1)

[0234] 

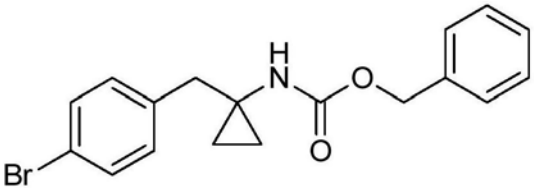
[0235] 标题化合物如实施例8中所述使用1-(4-溴苯基)-2-甲基丙烷-2-胺制备,并且分离为灰白色固体(6.67g,81%):mp 82-86℃;^{1}H NMR(400MHz,$CDCl_3$)δ7.43-7.27(m,7H),6.90(d,J=8.3Hz,2H),5.09(s,2H),4.47(s,1H),2.94(s,2H),1.27(s,6H);^{13}C NMR(101MHz,$CDCl_3$)δ150.02,136.77,132.13,131.02,130.49,128.54,128.23,128.15,120.32,69.73,66.09,53.02,27.41;ESIMS m/z 363([M+H]$^{+}$)。

[0236] 制备(2-(4-溴苯基)-2-甲基丙基)氨基甲酸苄酯(CB2)

[0237] 

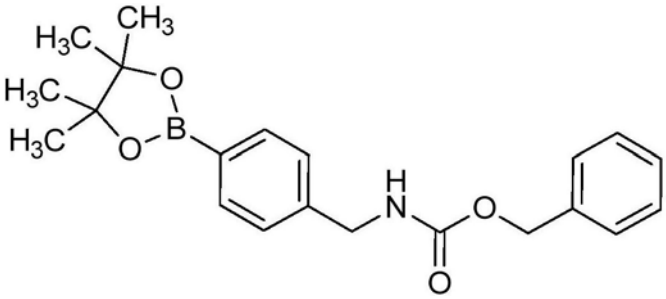
[0238] 标题化合物如实施例8中所述使用2-(4-溴苯基)-2-甲基丙烷-1-胺制备,并且分离为褐色油(7.83g,95%):^{1}H NMR(400MHz,$CDCl_3$)δ7.47-7.40(m,2H),7.40-7.27(m,5H),7.20(d,J=8.6Hz,2H),5.05(s,2H),4.48(t,J=6.1Hz,1H),3.38(d,J=6.3Hz,2H),1.30(s,6H);^{13}C NMR(101MHz,$CDCl_3$)δ156.51,145.44,136.42,131.54,128.53,128.17,128.13,127.87,120.27,66.77,52.39,38.86,26.36;ESIMS m/z 363([M+H]$^{+}$)。

[0239] 制备(1-(4-溴苄基)环丙基)氨基甲酸苄酯(CB3)

[0240] 

[0241] 标题化合物如实施例8中所述使用1-(4-溴苄基)环丙胺(Ukrorgsyntez Ltd)制备,并且分离为浅黄色固体(3.33g,81%):mp 84-86℃;^{1}H NMR(400MHz,$CDCl_3$)δ7.51-7.28(m,7H),5.08(s,2H),2.82(s,2H),0.85-0.69(m,4H)(NH未观测);^{13}C NMR(101MHz,$CDCl_3$)δ155.85,136.52,131.43,131.07,128.73,128.57,128.51,128.14,120.39,66.47,40.93,34.36,13.54;ESIMS m/z362([M+2]$^{+}$)。

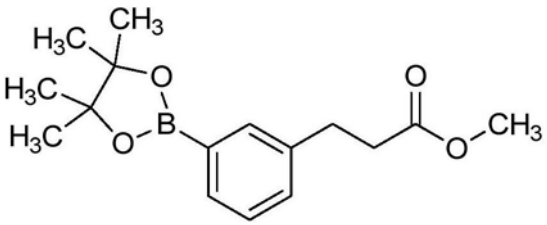
[0242] 实施例9：制备4-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苄基氨基甲酸苄酯(C13)

[0243] 

[0244] 在500mL装配有磁搅拌棒的圆底烧瓶中，将4-溴苄基氨基甲酸苄酯(C12)(14.3g，44.7mmol)，4,4,4',4',5,5,5',5'-八甲基-2,2'-双(1,3,2-二氧杂硼杂环戊烷)(12.5g，49.1mmol)，和乙酸钾(8.77g，89.0mmol)用二氧六环(170mL)稀释。将悬浮液用氮气吹扫10分钟。加入为固体的[1,1′-双(二苯基膦基)二茂铁]二氯化钯(II)(1.63g，2.23mmol)。将烧瓶放置在氮气气氛下，并且将反应混合物温热至内部温度为70℃保持18小时。将反应混合物冷却至室温，倒入盐水溶液中并且用乙酸乙酯(3×250mL)提取。将合并的有机层经无水硫酸镁干燥，过滤，浓缩。将所得残留物经使用0-10%乙酸乙酯/B(其中B＝1:1二氯甲烷:己烷)作为洗脱剂的快速柱色谱纯化，提供为橙色固体的标题化合物(11.8g，69%)：^{1}H NMR(400MHz，DMSO-d_6)δ7.87(t，J＝6.2Hz，1H)，7.71-7.60(m，2H)，7.43-7.24(m，7H)，5.06(s，2H)，4.24(d，J＝6.2Hz，2H)，1.29(s，12H)；^{13}C NMR(101MHz，DMSO-d_6)δ156.35，143.18，137.12，134.45，128.31，127.69，126.38，83.51，66.32，65.37，64.89，43.83，24.62；ESIMS m/z 368($[M+H]^+$)。

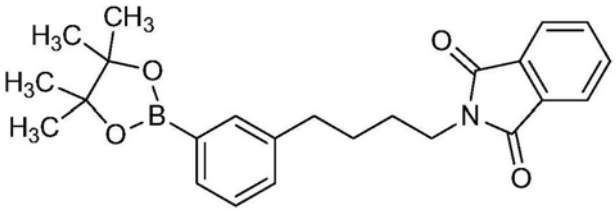
[0245] 下面的化合物根据实施例9中的步骤制备。

[0246] 制备3-(3-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苯基)丙酸甲酯(C13a)

[0247] 

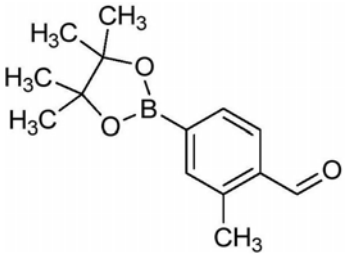
[0248] 标题化合物如实施例9中所述使用3-(3-溴苯基)丙酸甲酯制备，并且分离为褐色固体(9.18g，75%)：^{1}H NMR(400MHz，DMSO-d_6)δ7.56-7.47(m，2H)，7.35(dt，J＝7.7，1.7Hz，1H)，7.33-7.23(m，1H)，3.57(s，3H)，2.86(t，J＝7.6Hz，2H)，2.62(t，J＝7.6Hz，2H)，1.29(s，12H)；^{13}C NMR(101MHz，DMSO-d_6)δ172.57，139.91，134.28，132.18，131.32，127.86，83.54，51.20，34.88，30.10，24.63；EIMS m/z 290。

[0249] 制备2-(4-(3-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苯基)丁基)异吲哚啉-1,3-二酮(C13b)

[0250] 

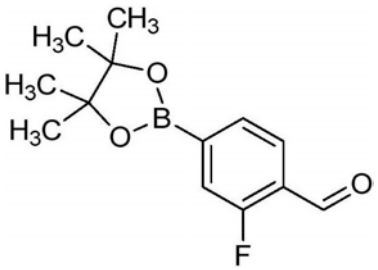
[0251] 标题化合物如实施例9中所述使用2-(4-(3-溴苯基)丁基)异吲哚啉-1,3-二酮(C57a)制备,并且分离为褐色固体(5.50g,62%):^{1}H NMR(400MHz,DMSO-d_6)δ7.90-7.78(m,4H),7.54-7.42(m,2H),7.33-7.23(m,2H),3.59(t,J=6.5Hz,2H),2.60(t,J=7.2Hz,2H),1.70-1.48(m,4H),1.28(s,12H);^{13}C NMR(101MHz,DMSO-d_6)δ167.90,141.32,134.33,131.83,131.56,131.40,127.76,122.93,83.50,37.17,34.52,28.49,27.67,24.64;ESIMS m/z 406([M+H]$^{+}$)。

[0252] 制备2-甲基-4-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苯甲醛(CB4)

[0253] 

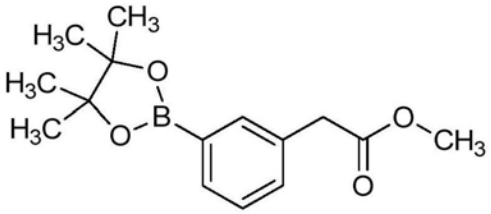
[0254] 标题化合物如实施例9中所述使用4-溴-2-甲基苯甲醛制备,并且分离为澄清的无色油(0.623g,50%):^{1}H NMR(400MHz,$CDCl_3$)δ10.31(s,1H),7.78(d,J=0.8Hz,2H),7.70(s,1H),2.67(s,3H),1.36(s,12H);^{13}C NMR(101MHz,$CDCl_3$)δ193.08,139.40,138.02,135.89,132.45,130.86,84.28,24.87,19.37;IR(薄膜)cm^{-1} 2978,2927,2728,1700,1355,1194。

[0255] 制备2-氟-4-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苯甲醛(CB5)

[0256] 

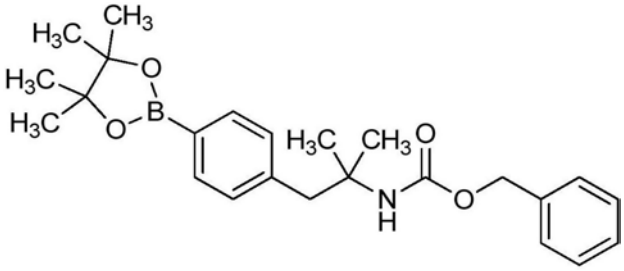
[0257] 标题化合物如实施例9中所述使用4-溴-2-氟苯甲醛制备,并且分离为白色固体(4.1g,67%):^{1}H NMR(400MHz,$CDCl_3$)δ10.40(d,J=0.8Hz,1H),7.84(dd,J=7.6,6.7Hz,1H),7.67(dt,J=7.6,0.8Hz,1H),7.58(dd,J=10.7,0.9Hz,1H),1.36(s,12H);^{19}F NMR(376MHz,$CDCl_3$)δ-123.56。

[0258] 制备2-(3-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苯基)乙酸甲酯(CB6)

[0259] 

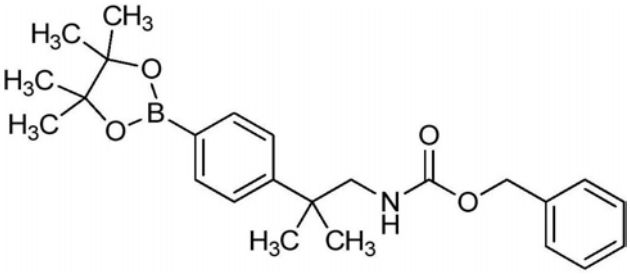
[0260] 标题化合物如实施例9中所述使用2-(3-溴苯基)乙酸甲酯制备，并且分离为白色固体(14.68g，97%，80%纯度)：^{1}H NMR(400MHz，DMSO-d_6)δ7.58(dt，J＝8.4，1.7Hz，2H)，7.44-7.28(m，2H)，3.71(s，2H)，3.62(s，3H)，1.30(s，12H)；ESIMS m/z 276([M]$^+$)。

[0261] 制备(2-甲基-1-(4-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苯基)丙烷-2-基)氨基甲酸苄酯(CB7)

[0262] 

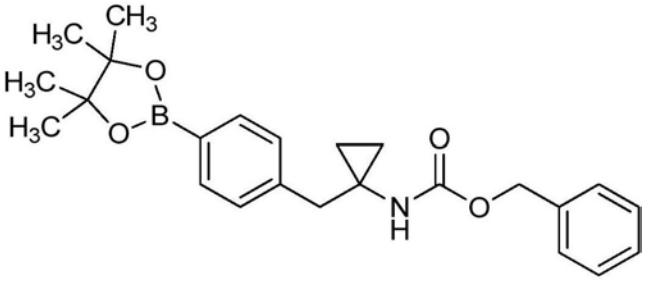
[0263] 标题化合物如实施例9中所述使用(1-(4-溴苯基)-2-甲基丙烷-2-基)氨基甲酸苄酯(CB1)制备，并且分离为澄清的油(6.12g，80%)：^{1}H NMR(400MHz，$CDCl_3$)δ7.69(d，J＝7.9Hz，2H)，7.38(d，J＝5.6Hz，5H)，7.10(d，J＝7.9Hz，2H)，5.09(s，2H)，4.51(s，1H)，3.00(s，2H)，1.34(s，12H)，1.29(s，6H)；^{13}C NMR(101MHz，$CDCl_3$)δ152.73，141.11，136.77，134.45，129.95，128.52，128.10，128.06，83.71，66.09，54.47，53.21，27.43，24.88；ESIMS m/z410([M+H]$^+$)。

[0264] 制备(2-甲基-2-(4-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苯基)丙基)氨基甲酸苄酯(CB8)

[0265] 

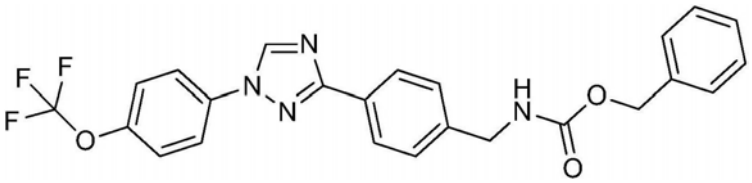
[0266] 标题化合物如实施例9中所述使用(2-(4-溴苯基)-2-甲基丙基)氨基甲酸苄酯(CB2)制备，并且分离为浅黄色油(8.47g，95%)：^{1}H NMR(400MHz，$CDCl_3$)δ7.81-7.73(m，2H)，7.32(dtd，J＝14.5，7.4，6.8，2.7Hz，7H)，5.04(s，2H)，4.50-4.37(m，1H)，3.41(d，J＝6.3Hz，2H)，1.34(s，12H)，1.33(s，6H)；^{13}C NMR(101MHz，$CDCl_3$)δ156.56，149.64，136.52，135.07，131.54，128.48，128.06，127.87，125.34，83.77，66.66，52.46，39.15，26.36，24.86；ESIMS m/z 410([M+H]$^+$)。

[0267] 制备(1-(4-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苄基)环丙基)氨基甲酸苄酯(CB9)

[0268] 

[0269] 标题化合物如实施例9中所述使用(1-(4-溴苄基)环丙基)氨基甲酸苄酯(CB3)制备，并且使用乙酸乙酯/己烷作为洗脱剂纯化；分离为白色固体(2.53g，67%)：mp 102-104℃；^{1}H NMR(400MHz，$CDCl_3$)δ7.79-7.63(m，2H)，7.51-7.28(m，5H)，7.16(d，J＝7.5Hz，2H)，5.08(s，2H)，4.90(s，1H)，2.89(s，2H)，1.34(s，12H)，0.80(s，4H)；ESIMS m/z 408([M+H]$^+$)。

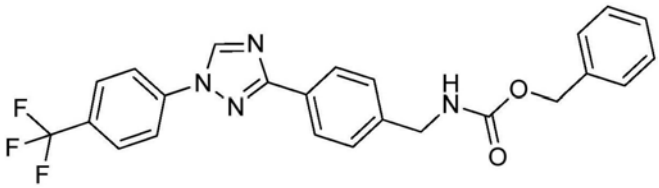
[0270] 实施例10：制备4-(1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑-3-基)苄基氨基甲酸苄酯(C14)

[0271] 

[0272] 在50mL装配有磁搅拌棒的圆底烧瓶中，装入为固体的3-溴-1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑(C1)(1.0g，3.3mmol)，4-(4，4，5，5-四甲基-1，3，2-二氧杂硼杂环戊烷-2-基)氨基甲酸苄酯(C13)(1.3g，3.6mmol)，(二(三苯基膦)合二氯化钯(II)(0.120g，0.171mmol)，和磷酸钾(1.38g，6.49mmol)。将烧瓶密封并且放置在氮气氛下。加入二氧六环(17.3mL)和水(4.3mL)。将反应温热至内部温度为65℃保持18小时。反应混合物冷却至室温，倒入盐水溶液中并且用乙酸乙酯提取(3×75mL)。将合并的有机层经无水硫酸镁干燥，过滤，浓缩。将所得残留物经使用0-50%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化，提供为白色固体的标题化合物(0.850g，56%)：^{1}H NMR(400MHz，DMSO-d_6)δ9.40(s，1H)，8.17-8.00(m，4H)，7.91(t，J＝6.2Hz，1H)，7.72-7.59(m，2H)，7.46-7.12(m，7H)，5.07(s，2H)，4.29(d，J＝6.1Hz，2H)；^{19}F NMR(376MHz，DMSO-d_6)δ-56.96；ESIMS m/z 469([M+H]$^+$)。

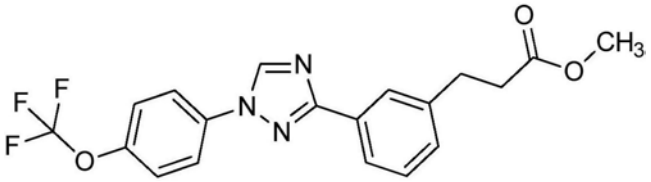
[0273] 下面的化合物根据实施例10中的步骤制备。

[0274] 制备4-(1-(4-(三氟甲基)苯基)-1H-1，2，4-三唑-3-基)苄基氨基甲酸苄酯(C15)

[0275] 

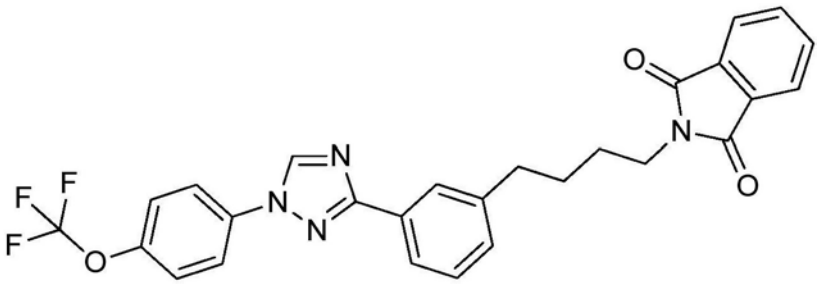
[0276] 标题化合物如实施例10中所述使用3-溴-1-(4-(三氟甲基)苯基)-1H-1，2，4-三唑(C1b)，4-(4，4，5，5-四甲基-1，3，2-二氧杂硼杂环戊烷-2-基)苄基氨基甲酸苄酯(C13)，四氟硼酸三叔丁基膦，乙酸钯(II)，和氟化铯制备，并且分离为白色固体(0.846g，36%)：^{1}H NMR(400MHz，DMSO-d_6)δ9.53(s，1H)，8.28-8.14(m，2H)，8.16-8.04(m，2H)，8.04-7.95(m，2H)，7.92(t，J＝6.2Hz，1H)，7.49-7.13(m，7H)，5.07(s，2H)，4.29(d，J＝6.2Hz，2H)；^{19}F NMR(376MHz，DMSO-d_6)δ-60.79；ESIMS m/z 453([M+H]$^+$)。

[0277] 制备3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑-3-基)苯基)丙酸甲酯(CA1)

[0278] 

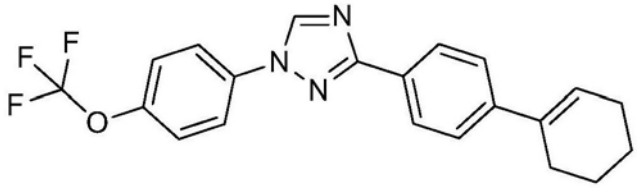
[0279] 标题化合物如实施例10中所述使用3-溴-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C1),3-(3-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苯基)丙酸甲酯(C13a),和[1,1′-双(二叔丁基膦)二茂铁]二氯化钯(II)在80℃制备,并且分离为深橙色固体(9.86g,91%):^{1}H NMR(400MHz,DMSO-d_6)δ9.40(s,1H),8.12-8.03(m,2H),8.01-7.91(m,2H),7.66-7.58(m,2H),7.49-7.40(m,1H),7.34(dt,J=7.8,1.6Hz,1H),3.59(s,3H),2.95(t,J=7.5Hz,2H),2.70(t,J=7.6Hz,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-57.01;ESIMS m/z 392([M+H]$^{+}$)。

[0280] 制备2-(4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)异吲哚啉-1,3-二酮(CA2)

[0281] 

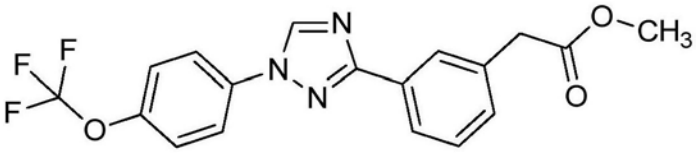
[0282] 标题化合物如实施例10中所述使用3-溴-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C1),2-(4-(3-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苯基)丁基)异吲哚啉-1,3-二酮(C13b),和[1,1′-双(二叔丁基膦)二茂铁]二氯化钯(II)在75℃制备,并且分离为深橙色固体(5.48g,82%):^{1}H NMR(400MHz,DMSO-d_6)δ9.39(s,1H),8.13-8.04(m,2H),7.96-7.89(m,2H),7.88-7.77(m,4H),7.67-7.57(m,2H),7.45-7.38(m,1H),7.31(dt,J=7.7,1.5Hz,1H),3.69-3.53(m,2H),2.70(t,J=6.8Hz,2H),1.64(dq,J=6.6,3.1Hz,4H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 507([M+H]$^{+}$)。

[0283] 制备3-(2',3',4',5'-四氢-[1,1'-联苯]-4-基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(CB10)

[0284] 

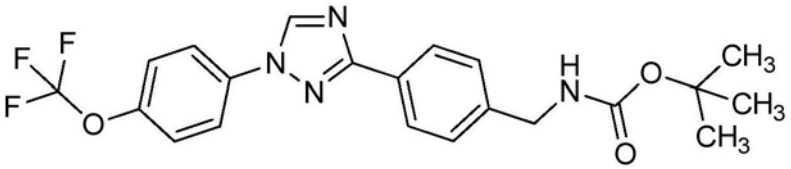
[0285] 标题化合物如实施例10中所述使用3-(4-溴苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C52)用四(三苯基膦)钯(0)作为催化剂,碳酸钠作为碱并且加热至100℃保持3小时制备;分离为橙色固体(2.18g,57%,79%纯度):^{1}H NMR(400MHz,$CDCl_3$)δ8.56(s,1H),8.15-8.06(m,2H),7.80(dd,J=9.0,2.3Hz,2H),7.50(d,J=8.4Hz,2H),7.39(ddd,J=8.0,2.5,1.3Hz,2H),6.28-6.21(m,1H),2.46(ddt,J=6.3,4.1,2.0Hz,2H),2.24(dtd,J=6.3,3.8,1.8Hz,2H),1.85-1.75(m,2H),1.71-1.63(m,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-58.03;ESIMS m/z 386([M+H]$^{+}$)。

[0286] 制备2-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酸甲酯(CB11)

[0287] 

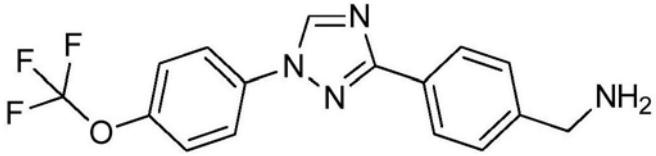
[0288] 标题化合物如实施例10中所述使用2-(3-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苯基)乙酸甲基酯(CB6)使用[1,1′-双(二叔丁基膦)二茂铁]二氯化钯(II)作为催化剂,碳酸钠作为碱并且加热至75℃保持30小时制备;分离为粉红色固体(4.96g,72%):^{1}H NMR(400MHz,DMSO-d_6)δ9.41(s,1H),8.12-8.05(m,2H),8.05-7.98(m,2H),7.61(ddt,J=7.9,2.0,1.0Hz,2H),7.47(td,J=7.6,0.6Hz,1H),7.38(ddd,J=7.6,2.0,1.2Hz,1H),3.81(s,2H),3.64(s,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-57.06;ESIMS m/z 378([M+H]$^{+}$)。

[0289] 实施例10a:制备4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基氨基甲酸叔丁基酯(C15a)

[0290] 

[0291] 在20mL小瓶中,将(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酰基叠氮化物/2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)甲基异氰酸酯(C9)(0.205g,0.528mmol)用叔丁醇(10.0mL,105mmol)稀释。将溶液加热至80℃过夜。将反应混合物冷却并且倒入盐水溶液中,用乙酸乙酯(4×)提取。将合并的有机物经硫酸镁干燥,过滤,浓缩。将所得残留物通过使用0-40%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供为白色固体的标题化合物(0.0890g,39%):^{1}H NMR(400MHz,DMSO-d_6)δ9.40(s,1H),8.15-8.01(m,4H),7.63(dp,J=7.9,1.0Hz,2H),7.47(t,J=6.1Hz,1H),7.42-7.35(m,2H),4.20(d,J=6.2Hz,2H),1.41(s,9H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 435([M+H]$^{+}$)。

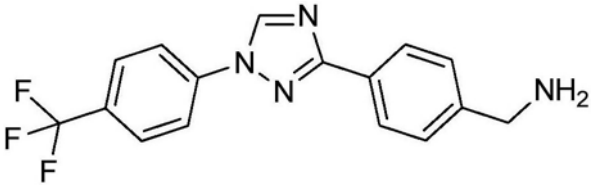
[0292] 实施例11:制备(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)甲烷胺(C16)

[0293] 

[0294] 在200mL装配有磁搅拌棒的圆底烧瓶中,将4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基氨基甲酸苄酯(C14)(0.850g,1.82mmol)用溴化氢在乙酸中的溶液(33wt%,15.0mL,1.82mmol)稀释。使得悬浮液搅拌1小时。加入乙醚(150mL),并且将反应混合物搅拌另外的30分钟。将所得沉淀物经由过滤收集并且用含水氢氧化钠处理。将所得悬浮液用乙酸乙酯(3×75mL)提取。将合并的有机层经无水硫酸镁干燥,干燥,浓缩,提供为白色固体的标题化合物(0.448g,74%):^{1}H NMR(400MHz,DMSO-d_6)δ9.39(s,1H),8.07(dd,J=10.6,8.6Hz,4H),7.69-7.56(m,2H),7.48(d,J=8.2Hz,2H),3.79(s,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.98;ESMIS m/z 318([M+H]$^{+}$)(-NH_2)。

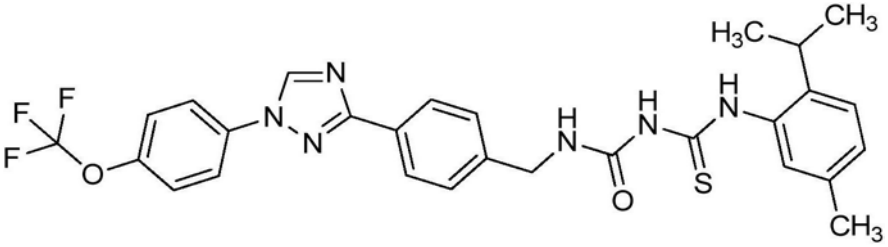
[0295] 下面的化合物根据实施例11中的步骤制备。

[0296] 制备(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)甲烷胺(CA3)

[0297] 

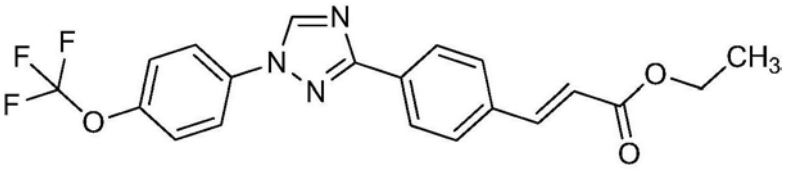
[0298] 标题化合物如实施例11中所述由4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苄基氨基甲酸苄酯(C15)制备,并且分离为褐色固体(4.67g,79%):^{1}H NMR(400MHz,DMSO-d_6)δ9.52(s,1H),8.21(d,J=8.3Hz,2H),8.09(d,J=7.9Hz,2H),8.00(d,J=8.4Hz,2H),7.51(d,J=7.9Hz,2H),3.82(s,2H)。

[0299] 实施例12:制备N-[5-甲基-2-(丙烷-2-基)苯基]-N'-(4-{1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基}苄基)硫代缩二脲(F35)

[0300] 

[0301] 在200mL装配有磁搅拌棒的圆底烧瓶中,(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)甲烷胺(C16)(0.448g,1.34mmol)用四氢呋喃(9.0mL)稀释。向悬浮液加入三光气(0.398g,1.34mmol)和三乙胺(0.374mL,2.68mmol)。将所得悬浮液在室温搅拌1小时。甲醇猝灭的等份试样的UPLC分析显示出氨基甲酸甲酯和异氰酸酯的混合物。向反应混合物加入1-(2-异丙基-5-甲基苯基)硫脲(0.279g,1.34mmol)和碳酸铯(0.480g,1.47mmol)。使得反应混合物在室温搅拌18小时。加入另外部分的1-(2-异丙基-5-甲基苯基)硫脲(0.279g,1.34mmol)和碳酸铯(0.480g,1.47mmol),并且将反应混合物温热至内部温度为60℃保持1小时。将反应混合物倒入水中并且用乙酸乙酯(3×75mL)提取。将合并的有机层经无水硫酸镁干燥,过滤,浓缩。将所得残留物通过使用5-100%乙腈/水作为洗脱剂的反相快速柱(C_{18}柱)色谱、随后使用0-100%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化,给出为白色固体的标题化合物(0.007g,0.9%)。

[0302] 实施例13:制备(E)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烯酸乙酯(C17)

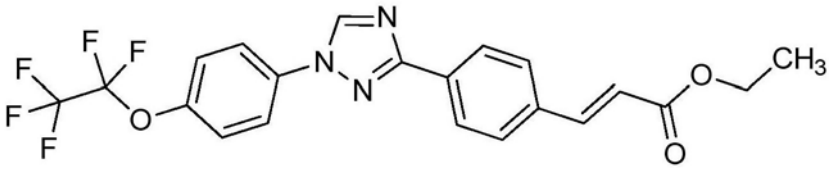
[0303] 

[0304] 向烘干的2L装配有搅拌棒的三颈圆底烧瓶,加入预先称入25-mL小瓶中的作为固体的氢化钠(60%油浸,7.20g,180mmol)。将其用无水四氢呋喃(1L)在氮气下稀释,并且将溶液在冰浴中搅拌。2-(二乙氧基磷酰基)乙酸乙酯(30.0mL,151mmol)经20分钟分批逐滴加入,并且将反应在0℃搅拌另外的2小时。将固体部分的4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯甲醛(50.0.g,150mmol)经20分钟加入,反应混合物变成橙色。搅拌30分钟之后,将冰浴除去,并且将反应经1小时温热至室温。将反应在缓慢加入饱和氯化铵水溶

液(500mL)猝灭，使得在室温静置过夜。将两相反应混合物用水稀释，并且用1:1乙酸乙酯/己烷(3×)提取。将合并的有机层经无水硫酸钠干燥，干燥，浓缩，提供为橙色固体的标题化合物(61.4g，100%)：mp135-137℃；^{1}H NMR(400MHz，$CDCl_3$)δ8.59(s，1H)，8.22(d，J＝8.4Hz，2H)，7.85-7.77(m，2H)，7.73(d，J＝16.0Hz，1H)，7.64(d，J＝8.3Hz，2H)，7.40(d，J＝8.3Hz，2H)，6.51(d，J＝16.0Hz，1H)，4.29(q，J＝7.1Hz，2H)，1.35(t，J＝7.1Hz，3H)；^{19}F NMR(376MHz，$CDCl_3$)δ-58.02；ESIMS m/z 404([M+H]$^{+}$)。

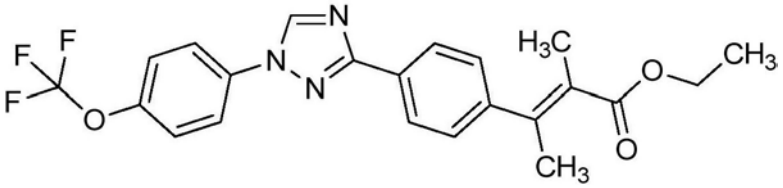
[0305] 下面的化合物根据实施例13中的步骤制备。

[0306] 制备(E)-3-(4-(1-(4-(全氟乙氧基)苯基)-1H-1，2，4-三唑-3-基)苯基)丙烯酸乙酯(C18)

[0307] 

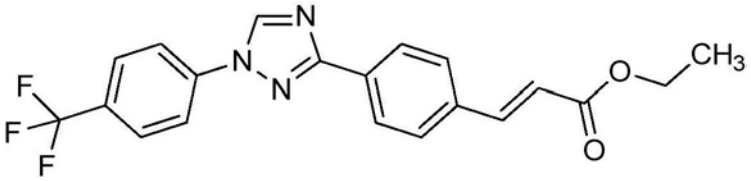
[0308] 标题化合物如实施例13中所述由4-(1-(4-(全氟乙氧基)苯基)-1H-1，2，4-三唑-3-基)苯甲醛制备，并且分离为白色固体(2.08g，100%)：mp 149-153℃；^{1}H NMR(400MHz，$CDCl_3$)δ8.59(s，1H)，8.32-8.16(m，2H)，7.89-7.77(m，2H)，7.73(d，J＝16.0Hz，1H)，7.68-7.58(m，2H)，7.47-7.35(m，2H)，6.51(d，J＝16.0Hz，1H)，4.29(q，J＝7.1Hz，2H)，1.35(t，J＝7.1Hz，3H)；^{19}F NMR(376MHz，$CDCl_3$)δ-85.89，-87.85，-87.86；ESIMS m/z 454([M+H]$^{+}$)。

[0309] 制备(E)-2-甲基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑-3-基)苯基)丁-2-烯酸乙酯(CA4)

[0310] 

[0311] 标题化合物如实施例13中所述由1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑-3-基)苯基)乙酮(C25)和2-(二乙氧基磷酰基)丙酸乙酯制备，并且分离为浅黄色固体(0.480g，27%)：mp 68-70℃；^{1}H NMR(400MHz，$CDCl_3$)δ8.58(s，1H)，8.22-8.13(m，2H)，7.86-7.77(m，2H)，7.40(dt，J＝8.0，1.0Hz，2H)，7.31-7.25(m，2H)，4.28(q，J＝7.1Hz，2H)，2.29(q，J＝1.5Hz，3H)，1.80(q，J＝1.5Hz，3H)，1.36(t，J＝7.1Hz，3H)；^{19}F NMR(376MHz，$CDCl_3$)δ-58.03；^{13}C NMR(101MHz，$CDCl_3$)δ169.91，163.24，148.37，144.86，144.66，141.54，135.56，129.10，127.77，126.57，125.32，122.42，121.18，60.45，22.94，17.45，14.32；ESIMS m/z 432([M+H]$^{+}$)。

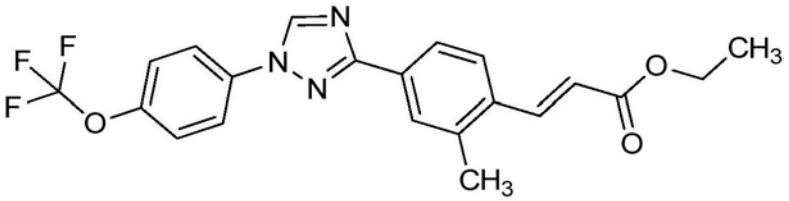
[0312] 制备(E)-3-(4-(1-(4-(三氟甲基)苯基)-1H-1，2，4-三唑-3-基)苯基)丙烯酸乙酯(CA5)

[0313] 

[0314] 标题化合物如实施例13中所述由4-(1-(4-(三氟甲基)苯基)-1H-1，2，4-三唑-3-

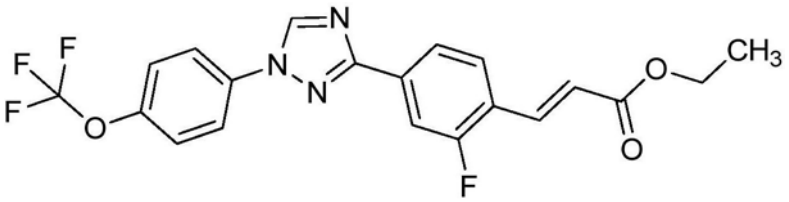
基)苯甲醛制备,并且分离为浅黄色固体(4.02g,100%):mp 135-140℃;^{1}H NMR(400MHz,$CDCl_3$)δ8.67(s,1H),8.23(d,J=8.3Hz,2H),7.95-7.88(m,2H),7.81(dt,J=8.3,0.7Hz,2H),7.73(d,J=16.0Hz,1H),7.69-7.56(m,2H),6.51(d,J=16.0Hz,1H),4.29(q,J=7.1Hz,2H),1.41-1.31(m,3H);^{19}F NMR(376MHz,$CDCl_3$)δ-62.50;ESIMS m/z 388([M+H]$^{+}$)。

[0315] 制备(E)-3-(2-甲基-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烯酸乙酯(CB12)

[0316] 

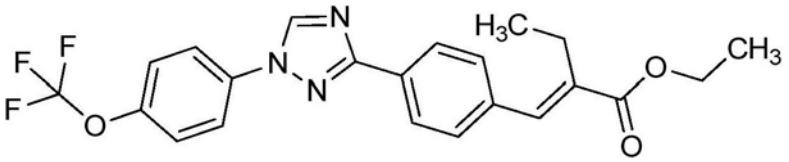
[0317] 标题化合物如实施例13中所述由2-甲基-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯甲醛(CB35)制备,并且分离为白色固体(1.16g,98%):mp 157-160℃;^{1}H NMR(400MHz,$CDCl_3$)δ8.58(s,1H),8.10-7.96(m,3H),7.84-7.76(m,2H),7.68(d,J=8.1Hz,1H),7.40(dt,J=8.1,1.0Hz,2H),6.44(d,J=15.9Hz,1H),4.29(q,J=7.1Hz,2H),2.53(s,3H),1.36(t,J=7.1Hz,3H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.02;ESIMS m/z 418([M+H]$^{+}$)。

[0318] 制备(E)-3-(2-氟-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烯酸乙酯(CB13)

[0319] 

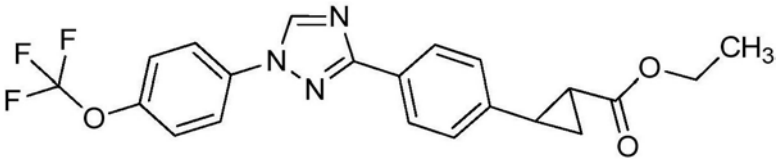
[0320] 标题化合物如实施例13中所述由2-氟-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯甲醛(CB36)制备,并且分离为淡橙色固体(1.1g,92%):^{1}H NMR(400MHz,$CDCl_3$)δ8.58(s,1H),8.03-7.91(m,2H),7.80(d,J=9.0Hz,2H),7.65(t,J=7.8Hz,1H),7.40(dt,J=8.1,1.0Hz,2H),6.63(s,1H),6.59(s,1H),4.29(q,J=7.1Hz,2H),1.35(t,J=7.1Hz,3H);ESIMS m/z 422([M+H]$^{+}$)。

[0321] 制备(E/Z)-2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯亚甲基)丁酸乙酯(CB14)

[0322] 

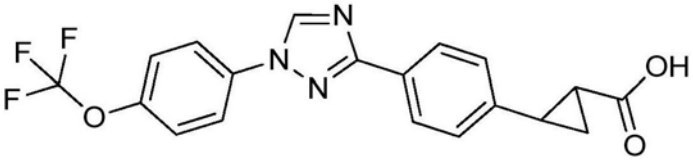
[0323] 标题化合物如实施例13中所述由4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯甲醛和乙基2-(二乙氧基磷酰基)丁酸酯制备;分离为作为E和Z同分异构体混合物的黄色固体(4.36g,102%):^{1}H NMR(400MHz,$CDCl_3$)δ8.66-8.53(m,1H),8.29-8.10(m,2H),7.86-7.66(m,3H),7.58-7.48(m,2H),7.44-7.31(m,2H),4.23(dq,J=53.7,7.1Hz,2H),2.70-2.42(m,2H),1.42-1.09(m,6H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.02;ESIMS m/z 432([M+H]$^{+}$)。

[0324] 实施例14:制备2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)环丙烷甲酸乙酯(C19)

[0325] 

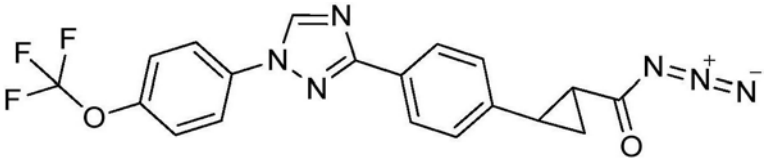
[0326] 向烘干的圆底烧瓶,加入氢化钠(60%油浸,0.380g,9.50mmol)和无水二甲亚砜(30mL)。气体放出,将溶液在室温搅拌15分钟。加入三甲基氧化锍碘化物(2.10g,9.54mmol),将烧瓶颈部用无水二甲亚砜(5mL)冲洗,将反应搅拌15分钟。向反应加入为固体的(E)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烯酸乙酯(C17)(3.22g,7.98mmol)。将反应在室温搅拌30分钟,然后用水猝灭,并且用1:1乙酸乙酯/己烷(2×)提取。将合并的有机层用水(3×)洗涤,经无水硫酸钠干燥,干燥,浓缩,提供为黄色油的标题化合物(1.50g,41%):^{1}H NMR(400MHz,$CDCl_3$)δ8.55(s,1H),8.10(d,J=8.4Hz,2H),7.80(d,J=9.1Hz,2H),7.39(dd,J=6.6,5.9Hz,2H),7.20(d,J=8.3Hz,2H),4.19(dt,J=14.0,7.0Hz,2H),2.64-2.52(m,2H),1.97(ddd,J=8.5,5.3,4.2Hz,1H),1.71-1.61(m,1H),1.42-1.32(m,1H),1.29(t,J=7.1Hz,3H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 418([M+H]$^{+}$)。

[0327] 实施例15:制备2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)环丙烷甲酸(C20)

[0328] 

[0329] 向在甲醇(24mL)中的2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)-环丙烷-甲酸乙酯(C19)(1.50g,3.59mmol)加入氢氧化钠(2N,7.20mL,14.4mmol),在室温搅拌4小时。反应用氯化氢(2N)酸化,将甲醇在真空下蒸发掉。将水溶液用乙酸乙酯(2×)提取,经无水硫酸钠干燥,干燥,浓缩,提供为黄色油的标题化合物(1.62g,98%):^{1}H NMR(400MHz,$CDCl_3$)δ8.58(s,1H),8.13-8.08(m,2H),7.83-7.77(m,3H),7.40(t,J=5.9Hz,4H),7.22(d,J=8.3Hz,2H),2.65(ddd,J=6.7,5.3,2.8Hz,2H),2.03-1.95(m,1H),1.76-1.66(m,2H),1.47(ddd,J=8.4,6.6,4.7Hz,2H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 390([M+H]$^{+}$)。

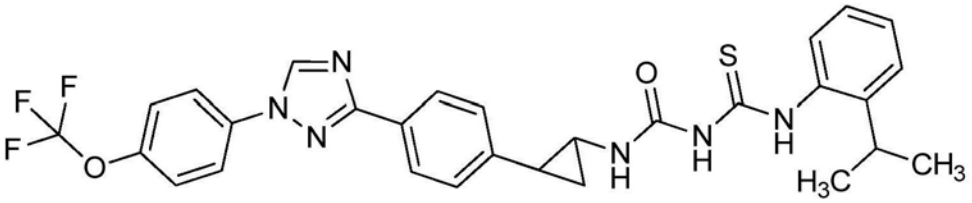
[0330] 实施例16:制备2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)环丙烷羰基叠氮化物(C21)

[0331] 

[0332] 向在甲苯(30mL)中的2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)-环丙烷甲酸(C20)(2.49g,6.40mmol)加入三乙胺(2.20mL,16.0mmol),随后叠氮磷酸二苯酯(1.70mL,8.00mmol)。将黄色溶液在室温搅拌过夜。将反应用水和饱和碳酸氢钠溶液猝

灭，用1:1乙酸乙酯/己烷(2×)提取，经无水硫酸钠干燥，并且过滤。将粗制化合物吸附到硅胶上，并且通过使用0-100%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化，提供为黄色油的标题化合物(1.94g，73%)：^{1}H NMR(400MHz，$CDCl_3$)δ8.56(s，1H)，8.16-8.03(m，2H)，7.83-7.72(m，2H)，7.44-7.34(m，2H)，7.20(d，J=8.2Hz，2H)，2.70(ddd，J=9.3，6.8，4.1Hz，1H)，1.98(ddd，J=8.4，5.3，4.1Hz，1H)，1.78(dt，J=9.4，5.0Hz，1H)，1.53(ddd，J=8.3，6.8，4.7Hz，1H)；^{19}F NMR(376MHz，$CDCl_3$)δ-58.03。

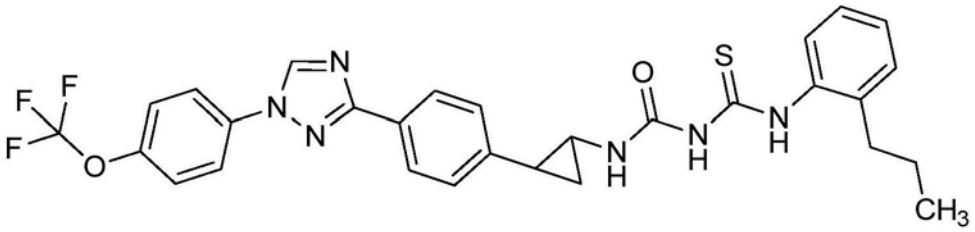
[0333] 实施例17：制备N-[2-(丙烷-2-基)苯基]-N'-，2-(4-{1-[4-(三氟甲氧基)苯基]-1H-1，2，4-三唑-3-基}苯基)环丙基]硫代缩二脲(F22)

[0334] 

[0335] 将(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑-3-基)苯基)环丙烷羰基叠氮化物(C21)(0.250g，0.600mmol)在1，2-二氯乙烷(3mL)中的溶液在80℃加热3小时。反应冷却，加入2-(异丙基苯基)硫脲(0.129g，0.660mmol)和碳酸铯(0.443g，1.36mmol)。将反应混合物在室温搅拌过夜，然后用乙酸乙酯稀释，用水洗涤。将有机层经无水硫酸钠干燥，过滤，浓缩。将粗制化合物装到具有二氯甲烷的Celite®柱体上，并且通过使用0-40%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化，提供为白色固体的标题化合物(0.108g，31%)。

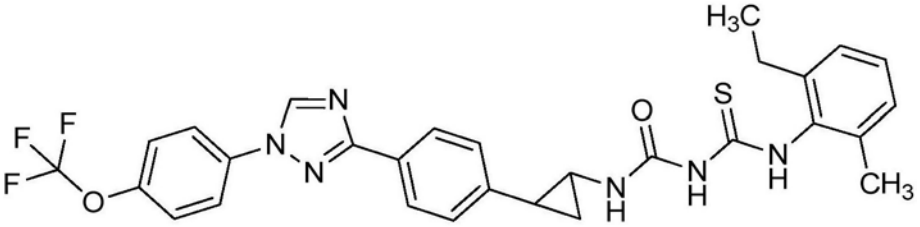
[0336] 下面的化合物根据实施例17中的步骤制备。

[0337] 制备N-(2-丙基苯基)-N'-[(2-(4-{1-[4-(三氟甲氧基)苯基]-1H-1，2，4-三唑-3-基}苯基)环丙基]硫代缩二脲(F23)

[0338] 

[0339] 标题化合物如实施例17中所述使用(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑-3-基)苯基)环丙烷羰基叠氮化物(C21)和1-(2-丙基苯基)硫脲制备，并且分离为灰白色固体(0.059g，18%)。

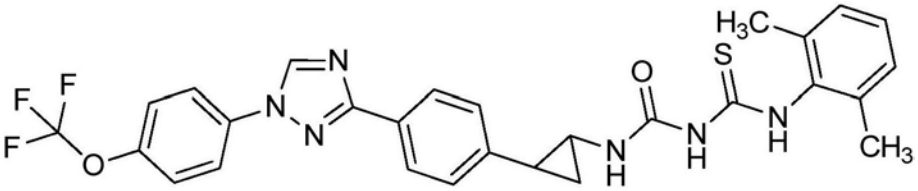
[0340] 制备N-(2-乙基-6-甲基苯基)-N'-[2-(4-{1-[4-(三氟甲氧基)苯基]-1H-1，2，4-三唑-3-基}苯基)环丙基]硫代缩二脲(F24)

[0341] 

[0342] 标题化合物如实施例17中所述使用(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1，2，4-

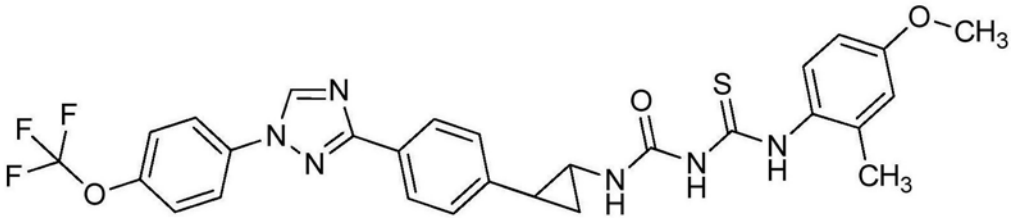
三唑-3-基)苯基)环丙烷羰基叠氮化物(C21)和1-(2-乙基-6-甲基苯基)硫脲(CA39)制备，并且分离为白色固体(0.105g,33%)。

[0343] 制备N-(2,6-二甲基苯基)-N'-[(2-(4-{1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基}苯基)环丙基]硫代缩二脲(F25)

[0344] 

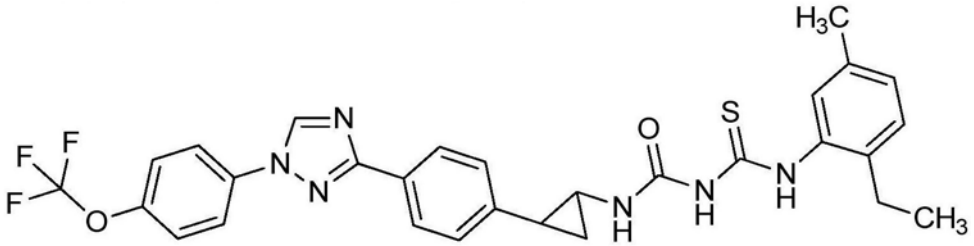
[0345] 标题化合物如实施例17中所述使用(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)环丙烷羰基叠氮化物(C21)和1-(2,6-二甲基苯基)硫脲制备，并且分离为白色固体(0.105g,29%)。

[0346] 制备N-(4-甲氧基-2-甲基苯基)-N'-[(2-(4-{1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基}苯基)环丙基]硫代缩二脲(F26)

[0347] 

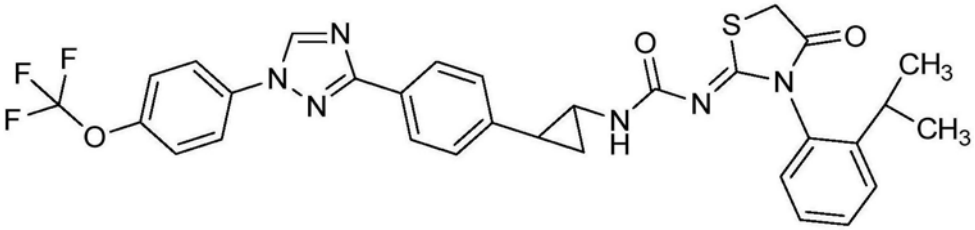
[0348] 标题化合物如实施例17中所述使用(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)环丙烷羰基叠氮化物(C21)和1-(4-甲氧基-2-甲基苯基)硫脲制备，并且分离为白油性固体(0.009g,3%)。

[0349] 制备N-(2-乙基-5-甲基苯基)-N'-[2-(4-{1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基}苯基)环丙基]硫代缩二脲(F27)

[0350] 

[0351] 标题化合物如实施例17中所述使用(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)环丙烷羰基叠氮化物(C21)和1-(2-乙基-5-甲基苯基)硫脲(CA41)制备，并且分离为灰白色固体(0.069g,22%)。

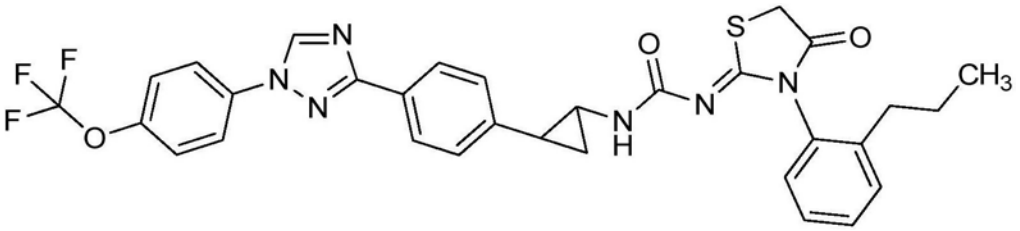
[0352] 实施例18:制备(Z)-1-(3-(2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)环丙基)脲(F29)

[0353] 

[0354] 将N-[2-(丙烷-2-基)苯基]-N'-,2-(4-{1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基}苯基)环丙基]硫代缩二脲(F22)(0.082g,0.14mmol),2-溴乙酸甲酯(0.020mL,0.21mmol),和乙酸钠(0.027g,0.33mmol)在乙醇(1.8mL)中的溶液在65℃加热过夜。反应冷却,装到Celite®柱体上,并且通过使用0-40%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供为灰白色固体的标题化合物(0.061g,68%)。

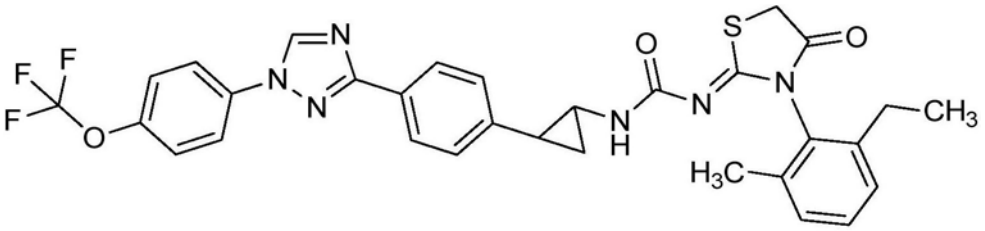
[0355] 下面的化合物根据实施例18中的步骤制备。

[0356] 制备(Z)-1-(4-氧代-3-(2-丙基苯基)噻唑烷-2-亚基)-3-(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)环丙基)脲(F30)

[0357] 

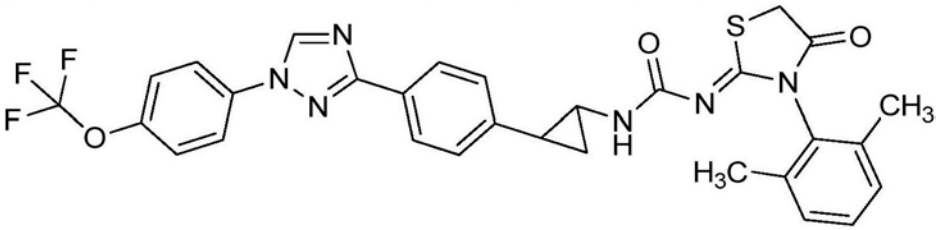
[0358] 标题化合物如实施例18中所述由N-(2-丙基苯基)-N'-[(2-(4-{1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基}苯基)环丙基]硫代缩二脲(F23)制备,并且分离为灰白色油性固体(0.026g,68%)。

[0359] 制备(Z)-1-(3-(2-乙基-6-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)环丙基)脲(F31)

[0360] 

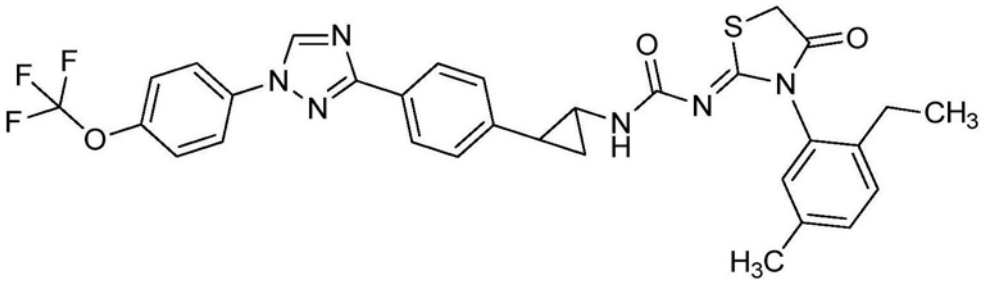
[0361] 标题化合物如实施例18中所述由N-(2-乙基-6-甲基苯基)-N'-[2-(4-{1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基}苯基)环丙基]硫代缩二脲(F24)制备,并且分离为油(0.006g,8%)。

[0362] 制备(Z)-1-(3-(2,6-二甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)环丙基)脲(F32)

[0363] 

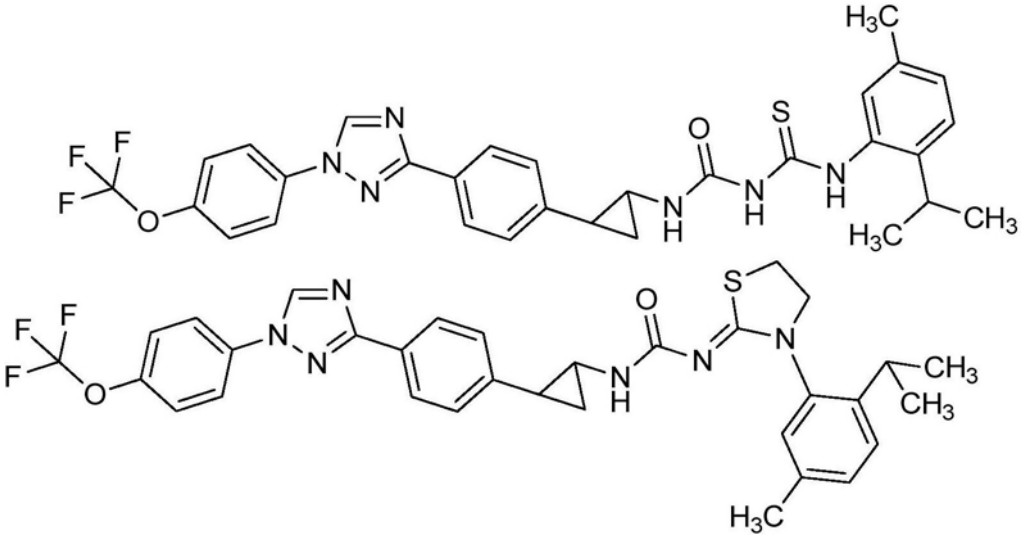
[0364] 标题化合物如实施例18中所述由N-(2,6-二甲基苯基)-N'-[(2-(4-{1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基}苯基)环丙基]硫代缩二脲(F25)制备,并且分离为油(0.006g,7%)。

[0365] 制备(Z)-1-(3-(2-乙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)环丙基)脲(F33)

[0366] 

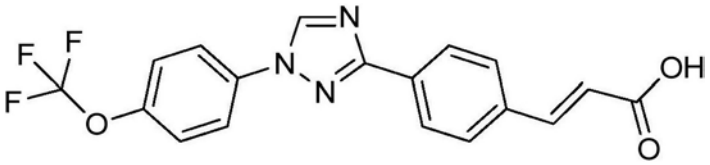
[0367] 标题化合物如实施例18中所述由N-(2-乙基-5-甲基苯基)-N'-[2-(4-{1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基}苯基)环丙基]硫代缩二脲(F27)制备,并且分离为黄色固体(0.035g,71%)。

[0368] 实施例19:制备N-[5-甲基-2-(丙烷-2-基)苯基]-N'-[2-(4-{1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基}苯基)环丙基]硫代缩二脲(F28)和(Z)-1-(3-(2-异丙基-5-甲基苯基)噻唑烷-2-亚基)-3-(2-(4-(1-(4-(三氟甲氧基)-苯基)-1H-1,2,4-三唑-3-基)苯基)环丙基)脲(F34)

[0369] 

[0370] 将(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)环丙烷羰基叠氮化物(C21)(0.210g,0.510mmol)在1,2-二氯乙烷(2.5mL)中的溶液在80℃加热3小时。反应冷却至室温,加入1-(2-异丙基-5-甲基苯基)硫脲(0.127g,0.610mmol)和碳酸铯(0.345g,1.06mmol)。将反应混合物在室温搅拌过夜。将反应混合物用乙酸乙酯稀释和用水洗涤。将水层用乙酸乙酯(2×)提取,将有机层经无水硫酸钠干燥,过滤,浓缩。将粗制物质装到具有二氯甲烷的Celite®柱体上,并且通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供为白色固体的标题化合物(F28)(0.025g,8%)和为黄色油的标题化合物(F34)(0.028g,8%)。

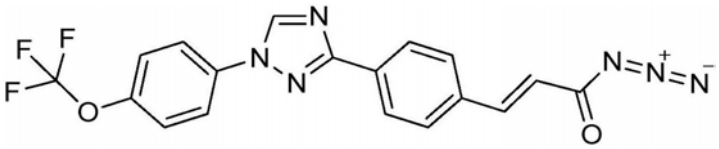
[0371] 实施例20:制备(E)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烯酸(C22)

[0372] 

[0373] 向在甲醇(25mL)中的(E)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-

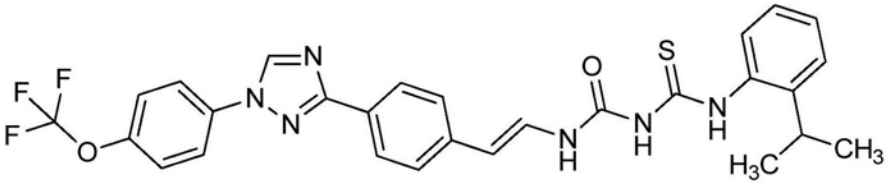
基)苯基)丙烯酸乙酯(C17)(1.95g,4.83mmol),加入氢氧化钠(2N,10mL,20.0mmol),将溶液在室温搅拌过夜。将甲醇在减压下蒸发掉,将试剂用乙腈稀释,加入另外的氢氧化钠(2N,20mL,40.0mmol)。将反应在室温搅拌5小时,然后用氯化氢(2N)酸化。将白色沉淀物真空过滤,提供为白色固体的标题化合物(1.72g,94%):mp 239-241℃;^{1}H NMR(400MHz,DMSO-d_6)δ 12.48(s,1H),9.44(s,1H),8.14(d,J=8.4Hz,2H),8.12-8.05(m,2H),7.85(d,J=8.4Hz,2H),7.69-7.59(m,3H),6.61(d,J=16.0Hz,1H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 376([M+H]$^{+}$)。

[0374] 实施例21:制备(E)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烯酰基叠氮化物(C23)

[0375] 

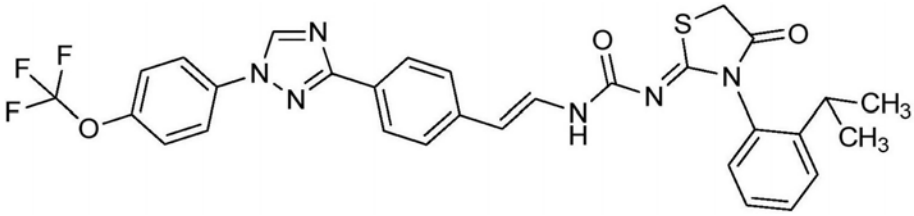
[0376] 向在异丙醇(15.3mL)中的(E)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烯酸(C22)(1.72g,4.59mmol)加入叠氮磷酸二苯酯(1.3mL,6.03mmol)和三乙胺(0.96mL,6.89mmol),并且在室温搅拌6小时。将白色沉淀物过滤,用异丙醇冲洗,并且干燥,提供为白色固体的标题化合物(1.46g,78%):mp 106℃(dec);^{1}H NMR(400MHz,$CDCl_3$)δ 8.59(s,1H),8.24(d,J=8.4Hz,2H),7.86-7.73(m,3H),7.66(d,J=8.3Hz,2H),7.40(d,J=8.3Hz,2H),6.52(t,J=14.6Hz,1H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.02;ESIMS m/z 401([M+H]$^{+}$)。

[0377] 实施例22:制备N-[2-(丙烷-2-基)苯基]-N'-[(E)-2-(4-{1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基}苯基)乙烯基]硫代缩二脲(F11)

[0378] 

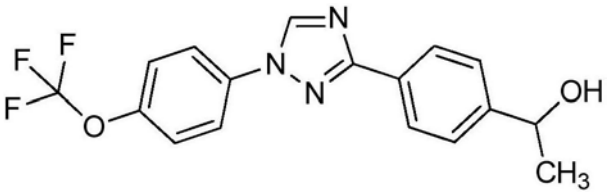
[0379] 将在无水乙腈(2.2mL)中的(E)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烯酰基叠氮化物(C23)(0.175g,0.440mmol)在80℃加热2小时。反应冷却,加入1-(2-异丙基苯基)硫脲(0.110g,0.570mmol)和碳酸铯(0.214g,0.660mmol)。将反应混合物在室温搅拌过夜,然后用乙酸乙酯稀释和用水洗涤。将有机层经无水硫酸钠干燥,过滤,浓缩。将粗制物质装到Celite®柱体上,并且通过使用0-40%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供为黄色固体的标题化合物(0.0800g,32%)。

[0380] 实施例23:制备(Z)-1-(3-(2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-((E)-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙烯基)脲(F12)

[0381] 

[0382] 向在乙醇(0.86mL)中的N-[2-(丙烷-2-基)苯基]-N'-[(E)-2-(4-{1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基}苯基)乙烯基]硫代缩二脲(F11)(0.056g,0.099mmol)和乙酸钠(0.020g,0.24mmol),加入2-溴乙酸甲酯(0.012mL,0.12mmol),将溶液在65℃加热2小时。将反应混合物直接装到Celite®柱体上,并且通过使用0-50%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供为橙色固体的标题化合物(0.052g,84%)。

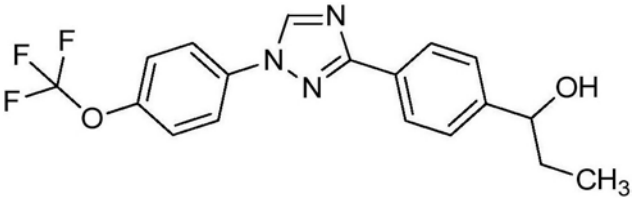
[0383] 实施例24:制备1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙醇(C24)

[0384] 

[0385] 向在干冰/丙酮浴的无水四氢呋喃(102mL)中的4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯甲醛(8.49g,25.5mmol),加入甲基溴化镁(1M,在丁醚中,25.5mL,25.5mmol)。然后将溶液温热至室温,并且搅拌过夜。反应用氯化氢(2N,10mL)酸化,直至pH 2,用水稀释,并且用乙酸乙酯(2×)提取。将有机层经无水硫酸钠干燥,干燥,浓缩,提供为橙色液体的标题化合物(8.80g,94%):^{1}H NMR(400MHz,$CDCl_3$)δ8.55(s,1H),8.27-8.11(m,2H),7.90-7.68(m,2H),7.49(d,J=8.1Hz,2H),7.39(d,J=8.3Hz,2H),4.98(q,J=6.5Hz,1H),1.54(d,J=6.5Hz,3H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 350([M+H]$^{+}$)。

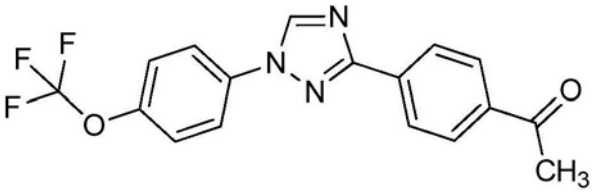
[0386] 下面的化合物根据实施例24中的步骤制备。

[0387] 制备1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-醇(CA6)

[0388] 

[0389] 标题化合物中所述实施例24由4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯甲醛和溴化乙基镁制备,并且分离为黄色油(5.00g,100%):^{1}H NMR(400MHz,$CDCl_3$)δ8.56(s,1H),8.20-8.12(m,2H),7.85-7.76(m,2H),7.50-7.44(m,2H),7.39(dq,J=8.0,1.0Hz,2H),4.68(t,J=6.5Hz,1H),1.93-1.75(m,2H),1.59(s,1H),0.95(t,J=7.4Hz,3H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 364([M+H]$^{+}$)。

[0390] 实施例25:制备1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酮(C25)

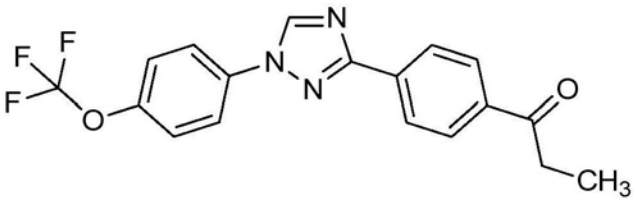
[0391] 

[0392] 向在二氯甲烷(168mL)和二甲亚砜(84mL)中的1-(4-(1-(4-(三氟甲氧基)苯基)-

1H-1,2,4-三唑-3-基)苯基)乙醇(C24)(8.80g,25.2mmol),加入三乙胺(17mL),并且在冰浴中搅拌。分两批加入吡啶·三氧化硫(16.0g,101mmol)。将反应经3小时温热至室温,用二氯甲烷稀释,并且用水洗涤。将水层用二氯甲烷提取另外一个时间。将合并的二氯甲烷层用水洗涤,经无水硫酸钠干燥,过滤,并且吸附到硅胶上。通过使用0-100%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化,提供为白色固体的标题化合物(6.71g,73%):mp140-141.5℃;^{1}H NMR(400MHz,$CDCl_3$)δ8.61(s,1H),8.33-8.27(m,2H),8.11-8.05(m,2H),7.85-7.78(m,2H),7.41(dd,J=9.0,0.8Hz,2H),2.66(s,3H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.01;ESIMS m/z 348([M+H]$^{+}$)。

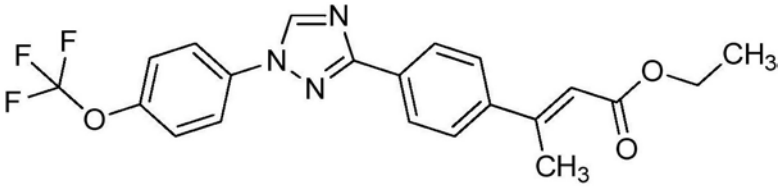
[0393] 下面的化合物根据实施例25中的步骤制备。

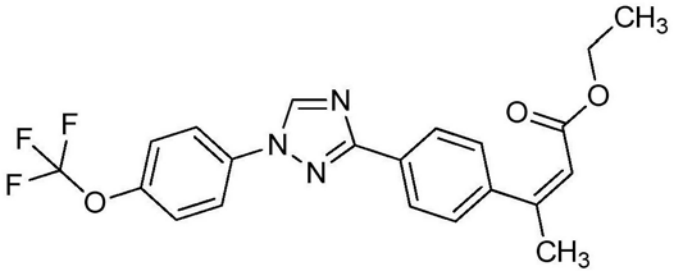
[0394] 制备1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-酮(CA7)

[0395] 

[0396] 标题化合物由1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-醇(CA6)制备,并且分离为白色固体(4.1g,63%,75%纯度):^{1}H NMR(400MHz,$CDCl_3$)δ8.60(s,1H),8.32-8.25(m,2H),8.11-8.05(m,2H),7.82(dd,J=8.9,1.9Hz,2H),7.41(dt,J=8.1,1.0Hz,2H),3.06(q,J=7.2Hz,2H),1.26(t,J=7.2Hz,3H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.02;ESIMS m/z362([M+H]$^{+}$)。

[0397] 实施例26:制备(E)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁-2-烯酸乙基酯(C26)和(Z)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁-2-烯酸乙基酯(C27)

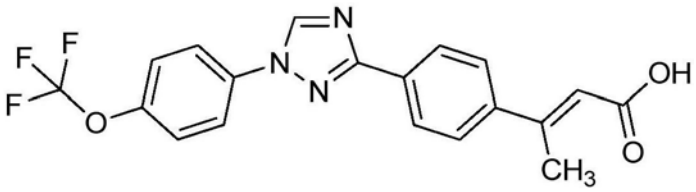


[0398] 

[0399] 向烘干的圆底烧瓶加入氢化钠(60%的油悬浮液,0.880g,1.53mmol)和无水四氢呋喃(36mL),将溶液在氮气下在冰浴中搅拌。逐滴加入2-(二乙氧基磷酰基)乙酸乙酯(3.4mL,17.3mmol),并且在冰浴中搅拌30分钟。1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酮(C25)(5.00g,14.4mmol)以固体部分加入至溶液,其中溶液变为黄色。将反应温热至室温过夜,用饱和氯化铵水溶液猝灭,并且用乙醚(2×)提取。将有机层经

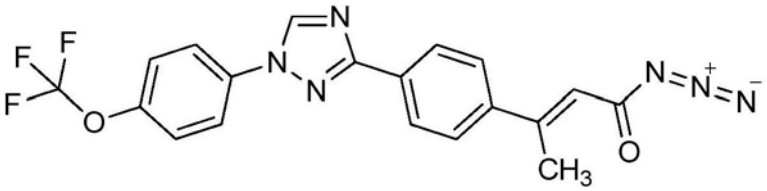
无水硫酸钠干燥，过滤，浓缩。将粗制物质装到具有二氯甲烷的Celite®柱体上，将柱体在真空烘箱中干燥。通过使用0-100％乙腈/水作为洗脱剂的反相快速柱色谱纯化，提供为白色固体的标题化合物(C26)(4.06g，67％)：mp 109-110.5℃；^{1}H NMR(400MHz，$CDCl_3$)δ8.58(s，1H)，8.28-8.16(m，2H)，7.88-7.77(m，2H)，7.66-7.55(m，2H)，7.45-7.34(m，2H)，6.22(d，J＝1.3Hz，1H)，4.24(q，J＝7.1Hz，2H)，2.62(d，J＝1.3Hz，3H)，1.33(t，J＝7.1Hz，3H)；^{19}F NMR(376MHz，$CDCl_3$)δ-58.02；ESIMS m/z 418([M+H]$^+$)，和为白色固体的标题化合物(C27)(1.08g，18％)：mp 83-86℃；^{1}H NMR(400MHz，$CDCl_3$)δ8.57(s，1H)，8.22-8.15(m，2H)，7.86-7.76(m，2H)，7.39(dd，J＝9.0，0.8Hz，2H)，7.36-7.31(m，2H)，5.95(d，J＝1.4Hz，1H)，4.02(q，J＝7.1Hz，2H)，2.22(d，J＝1.4Hz，3H)，1.09(t，J＝7.1Hz，3H)；^{19}F NMR(376MHz，$CDCl_3$)δ-58.03；ESIMS m/z 418([M+H]$^+$)。

[0400] 实施例27：制备(E)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑-3-基)苯基)丁-2-烯酸(C28)

[0401] 

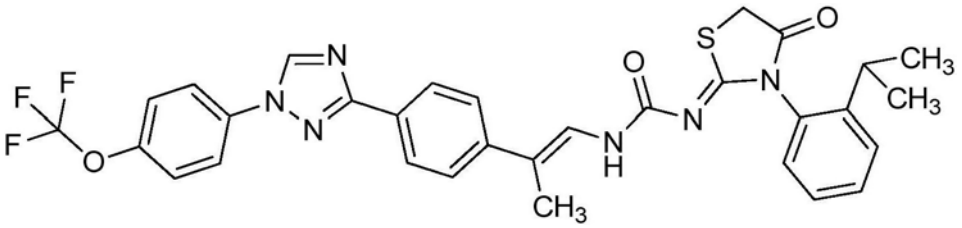
[0402] 向在甲醇(10mL)中的(E)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑-3-基)苯基)丁-2-烯酸乙基酯(C26)(1.30g，3.10mmol)，加入氢氧化钠(2N，12.3mL，24.6mmol)，并且在室温搅拌过夜。加入另外的氢氧化钠(2N)，并且将反应加热至50℃保持3天。反应用氯化氢(2N)酸化，将白色沉淀物通过真空过滤收集，提供为白色固体的标题化合物(1.16g，95％)：mp 234-238℃；^{1}H NMR(400MHz，DMSO-d_6)δ12.32(s，1H)，9.43(s，1H)，8.14(d，J＝8.6Hz，2H)，8.09(d，J＝9.1Hz，2H)，7.73(d，J＝8.6Hz，2H)，7.68-7.53(m，2H)，6.22(d，J＝1.3Hz，1H)，2.54(d，J＝1.3Hz，3H)；^{19}F NMR(376MHz，DMSO-d_6)δ-56.96；ESIMS m/z 390([M+H]$^+$)。

[0403] 实施例28：制备(E)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑-3-基)苯基)丁-2-烯酰基叠氮化物(C29)

[0404] 

[0405] 向在异丙醇(9.8mL)中的(E)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑-3-基)苯基)丁-2-烯酸(C28)(1.14g，2.93mmol)，加入三乙胺(0.53mL，3.81mmol)和叠氮磷酸二苯酯(0.68mL，3.23mmol)。将反应在室温搅拌过夜。将白色沉淀物真空过滤并且在真空烘箱中干燥，提供为白色固体的标题化合物(0.978g，80％)：^{1}H NMR(400MHz，$CDCl_3$)δ8.59(s，1H)，8.25-8.19(m，2H)，7.85-7.78(m，2H)，7.65-7.58(m，2H)，7.44-7.37(m，2H)，6.16(d，J＝1.3Hz，1H)，2.68(d，J＝1.2Hz，3H)；^{19}F NMR(376MHz，$CDCl_3$)δ-58.02；ESIMS m/z387([M+H]$^+$)(异氰酸酯)。

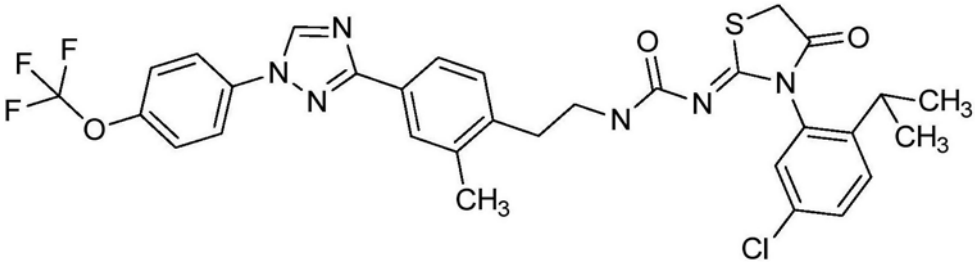
[0406] 实施例29：制备(Z)-1-(3-(2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-((E)-2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑-3-基)苯基)丙-1-烯-1-基)脲(F13)

[0407] 

[0408] 将在乙腈(3.4mL)中的(E)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁-2-烯酰基叠氮化物(C29)(0.28g,0.68mmol)在80℃加热3小时。反应冷却,加入1-(2-异丙基苯基)硫脲(0.14g,0.74mmol)和碳酸铯(0.28g,0.86mmol)。将反应在室温搅拌过夜,用乙酸乙酯稀释和用水洗涤。将有机层经无水硫酸钠干燥,干燥,浓缩,提供橙色泡沫。向粗制物质(0.39g)加入乙酸钠(0.082g,1.0mmol),乙醇(3.4mL),和2-溴乙酸甲酯(0.10mL,1.0mmol)。将反应混合物在65℃加热3小时。反应冷却,用乙酸乙酯稀释,并且用水洗涤。将有机层经无水硫酸钠干燥,过滤,浓缩。将粗制化合物装到具有二氯甲烷的Celite®柱体上,并且通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供为橙色粘性胶的标题化合物(0.16g,37%)。

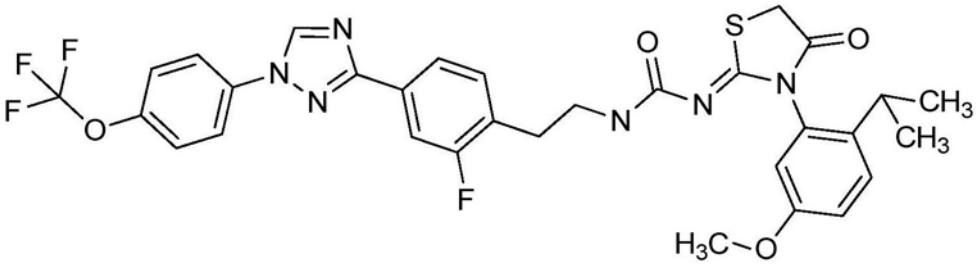
[0409] 下面的化合物根据实施例29中的步骤制备。

[0410] 制备(Z)-1-(3-(5-氯-2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(2-甲基-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB7)

[0411] 

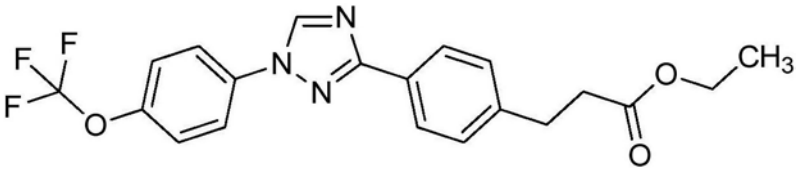
[0412] 标题化合物如实施例29中所述制备:使用3-(2-甲基-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物(CB20)和1-(5-氯-2-异丙基苯基)硫脲(CB32),并且加入2-溴乙酸甲酯之后加热至温度为60℃;经由反相色谱纯化,并且分离为粉红色固体(0.033g,17%)。

[0413] 制备(Z)-1-(2-氟-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)-3-(3-(2-异丙基-5-甲氧基苯基)-4-氧代噻唑烷-2-亚基)脲(FB9)

[0414] 

[0415] 标题化合物如实施例29中所述制备:使用3-(2-氟-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物(CB21)和1-(5-氯-2-异丙基苯基)硫脲(CB32)并且当加入2-溴乙酸甲酯时加热至温度为60℃;经由反相色谱纯化,并且分离为粉红色固体(0.023g,11%)。

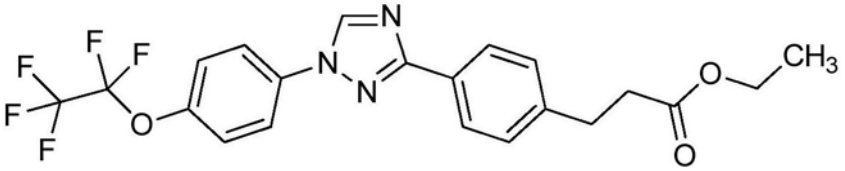
[0416] 实施例30：制备3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸乙基酯(C30)

[0417] 

[0418] 将(E)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烯酸乙酯(C17)(1.08g,2.68mmol)和钯碳(10%,0.285g,0.270mmol)在乙酸乙酯(10.7mL)中的混合物在室温搅拌。将反应烧瓶在真空下抽吸，反填充氮气，在真空下再次抽吸，然后反填充氢气球(～1atm)。将反应在室温搅拌过夜，然后通过Celite®垫过滤并且浓缩，提供为灰色油(在室温静置时固化为蜡)的标题化合物(0.999g,87%)：^{1}H NMR(400MHz,$CDCl_3$)δ8.56(s,1H),8.14-8.07(m,2H),7.80(d,J=9.1Hz,2H),7.42-7.36(m,2H),7.32(d,J=8.4Hz,2H),4.14(q,J=7.1Hz,2H),3.02(t,J=7.8Hz,2H),2.67(t,J=7.8Hz,2H),1.24(t,J=7.1Hz,3H)；^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 406([M+H]$^{+}$)。

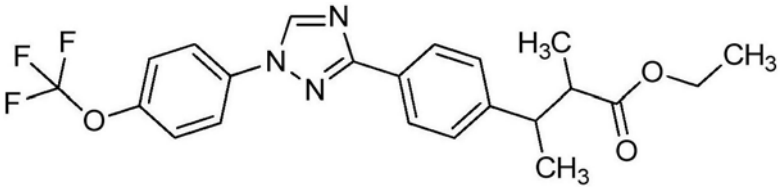
[0419] 下面的化合物根据实施例30中的步骤制备。

[0420] 制备3-(4-(1-(4-(全氟乙氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸乙酯(C31)

[0421] 

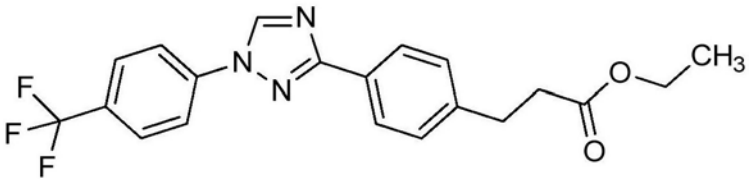
[0422] 标题化合物由(E)-3-(4-(1-(4-(全氟乙氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烯酸乙酯(C18)制备，并且分离为灰白色的松软固体(2.00g,97%)：mp109-110.5℃；^{1}H NMR(400MHz,$CDCl_3$)δ8.56(d,J=1.3Hz,1H),8.14-8.08(m,2H),7.84-7.77(m,2H),7.42-7.36(m,2H),7.35-7.29(m,2H),4.14(q,J=7.2Hz,2H),3.02(t,J=7.8Hz,2H),2.67(dd,J=8.3,7.2Hz,2H),1.24(t,J=7.1Hz,3H)；^{19}F NMR(376MHz,$CDCl_3$)δ-85.90,-87.85;ESIMS m/z 456([M+H]$^{+}$)。

[0423] 制备2-甲基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁酸乙酯(CA8)

[0424] 

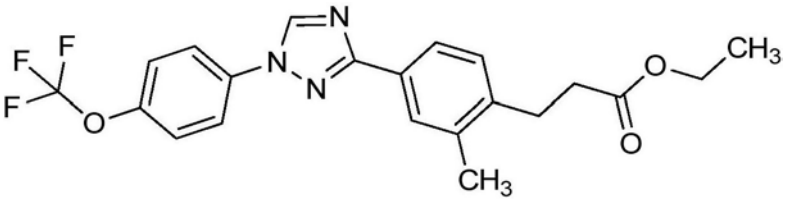
[0425] 标题化合物由(E)-2-甲基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁-2-烯酸乙基酯(CA4)制备，并且分离为黄色油(0.495g,100%)：^{1}H NMR(400MHz,$CDCl_3$)δ8.55(s,1H),8.12-8.05(m,2H),7.83-7.73(m,2H),7.38(dq,J=8.0,1.1Hz,2H),7.34-7.29(m,2H),3.94(q,J=7.1Hz,2H),3.11(dq,J=8.8,7.1Hz,1H),2.69(dd,J=8.6,6.9Hz,1H),1.31(d,J=7.1Hz,3H),1.21(d,J=6.9Hz,3H),1.04(t,J=7.1Hz,3H)；^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 434([M+H]$^{+}$)。

[0426] 制备3-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸乙酯(CA9)

[0427] 

[0428] 标题化合物由(E)-3-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烯酸乙基酯(CA5)制备,并且分离为白色固体(3.88g,96%):mp 81-84℃;^{1}H NMR(400MHz,$CDCl_3$)δ8.64(s,1H),8.12(d,J=8.2Hz,2H),7.91(dt,J=8.2,0.8Hz,2H),7.83-7.74(m,2H),7.33(dd,J=8.0,0.7Hz,2H),4.14(q,J=7.1Hz,2H),3.02(t,J=7.8Hz,2H),2.67(dd,J=8.3,7.2Hz,2H),1.35(td,J=7.1,0.6Hz,3H);^{19}F NMR(376MHz,$CDCl_3$)δ-62.50;ESIMS m/z 390([M+H]$^+$)。

[0429] 制备3-(2-甲基-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸乙酯(CB15)

[0430] 

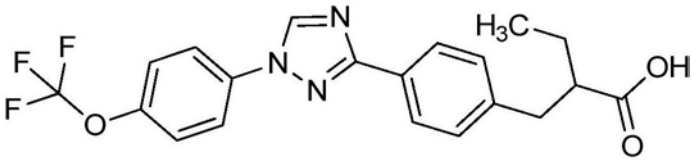
[0431] 标题化合物由(E)-3-(2-甲基-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烯酸乙基酯(CB12)制备,并且分离为灰色固体(1.14g,98%):mp109-111℃;^{1}H NMR(400MHz,$CDCl_3$)δ8.55(s,1H),7.99(d,J=1.8Hz,1H),7.95(ddd,J=7.8,2.0,0.7Hz,1H),7.83-7.77(m,2H),7.38(dq,J=7.9,1.0Hz,2H),7.26(s,1H),4.15(q,J=7.1Hz,2H),3.00(dd,J=8.9,7.0Hz,2H),2.69-2.55(m,2H),2.41(s,3H),1.26(t,J=7.1Hz,3H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 420([M+H]$^+$)。

[0432] 制备3-(2-氟-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸乙酯(CB16)

[0433] 

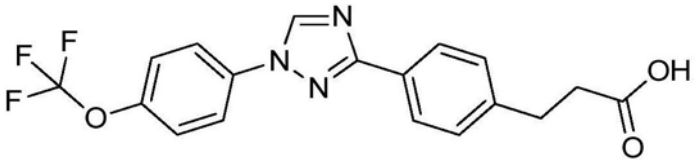
[0434] 标题化合物由(E)-3-(2-氟-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烯酸乙基酯(CB13)使用碳负载氢氧化钯和乙醇作为溶剂制备;分离为褐色固体(0.871g,67%,85%纯度):^{1}H NMR(400MHz,$CDCl_3$)δ8.56(s,1H),7.92-7.82(m,2H),7.79(d,J=9.0Hz,2H),7.43-7.36(m,2H),7.32(t,J=7.8Hz,1H),4.14(q,J=7.1Hz,2H),3.03(t,J=7.7Hz,2H),2.67(dd,J=8.2,7.2Hz,2H),1.24(t,J=7.1Hz,3H)。;^{19}F NMR(376MHz,$CDCl_3$)δ(376MHz,$CDCl_3$)δ-58.03,-117.98;ESIMS m/z 423([M]$^+$)。

[0435] 制备2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)丁酸(CB17)

[0436] 

[0437] 标题化合物由(E/Z)-2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯亚甲基)丁酸乙酯(CB14)制备,并且分离为褐色固体(1.15g,28%):mp149-150℃;^{1}H NMR(400MHz,$CDCl_3$)δ8.58(s,1H),8.13-8.02(m,2H),7.82-7.74(m,2H),7.38(dq,J=8.9,0.9Hz,2H),7.35-7.28(m,2H),3.04(dd,J=13.7,8.3Hz,1H),2.85(dd,J=13.8,6.6Hz,1H),2.75-2.61(m,1H),1.77-1.60(m,2H),1.00(t,J=7.4Hz,3H)(OH未观测);^{19}F NMR(376MHz,$CDCl_3$)δ(376MHz,$CDCl_3$)δ-58.03,-117.98;ESIMS m/z 406([M+H]$^{+}$)。

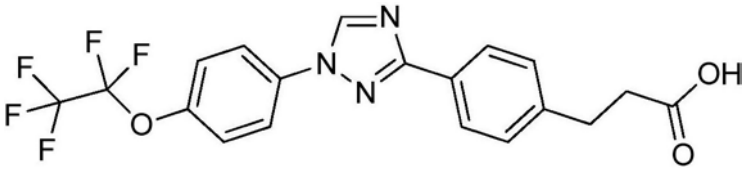
[0438] 实施例31:制备3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸(C32)

[0439] 

[0440] 向在甲醇(60mL)中的3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸乙酯(C30)(0.975g,2.41mmol),加入氢氧化钠(2N,12.0mL,24.1mmol),将溶液在室温搅拌过夜。将甲醇在真空下浓缩,将残留物用氯化氢(2N)酸化。将白色沉淀物真空过滤并且干燥,提供为白色固体的标题化合物(0.945g,99%):mp 145℃(dec);^{1}H NMR(400MHz,DMSO-d_6)δ9.39(s,1H),8.04(dd,J=21.4,8.7Hz,4H),7.62(d,J=8.3Hz,2H),7.38(d,J=8.4Hz,2H),2.89(t,J=7.6Hz,2H),2.59(t,J=7.6Hz,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.98;ESIMS m/z 378([M+H]$^{+}$)。

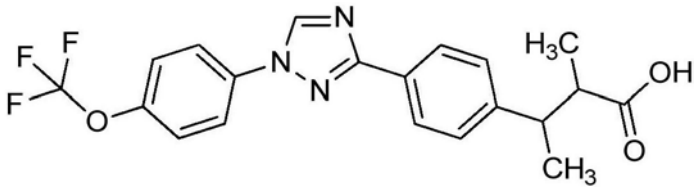
[0441] 下面的化合物根据实施例31中的步骤制备。

[0442] 制备3-(4-(1-(4-(全氟乙氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸(C33)

[0443] 

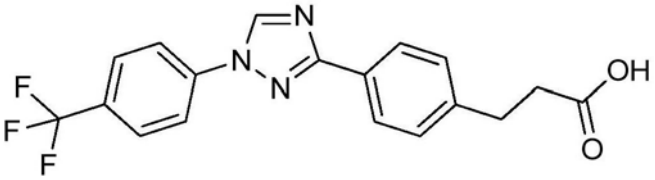
[0444] 标题化合物由3-(4-(1-(4-(全氟乙氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸乙酯(C31)制备,并且分离为白色固体(2.25g,100%):mp 142-144℃;^{1}H NMR(400MHz,DMSO-d_6)δ9.40(s,1H),8.05(dd,J=24.5,8.6Hz,4H),7.62(d,J=8.9Hz,2H),7.38(d,J=8.3Hz,2H),2.89(t,J=7.6Hz,2H),2.59(t,J=7.6Hz,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-74.86,-85.19,-86.92;ESIMS m/z 428([M+H]$^{+}$)。

[0445] 制备2-甲基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁酸(CA10)

[0446] 

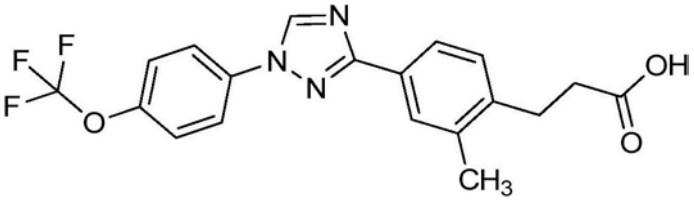
[0447] 标题化合物由2-甲基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁酸乙酯(CA8)制备,并且分离为黄色油(0.370g,33%):^{1}H NMR(400MHz,$CDCl_3$)δ8.57(d,J=4.0Hz,1H),8.15-8.03(m,2H),7.83-7.73(m,2H),7.40-7.27(m,4H),3.18(p,J=7.2Hz,1H),2.76(dq,J=8.3,7.0Hz,1H),1.35-1.29(m,3H),1.23(d,J=6.9Hz,3H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 406([M+H]$^+$)。

[0448] 制备3-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸(CA11)

[0449] 

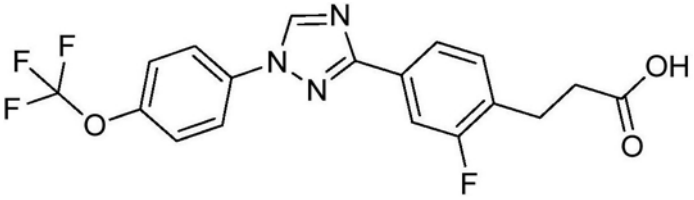
[0450] 标题化合物由3-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸乙酯(CA9)制备,并且分离为白色固体(2.85g,79%):mp 155-157℃;^{1}H NMR(400MHz,DMSO-d_6)δ12.17(s,1H),9.52(s,1H),8.26-8.12(m,2H),8.12-7.86(m,3H),7.39(d,J=8.2Hz,2H),2.89(t,J=7.6Hz,2H),2.59(t,J=7.6Hz,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-60.79;ESIMS m/z362([M+H]$^+$)。

[0451] 制备3-(2-甲基-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸(CB18)

[0452] 

[0453] 标题化合物由3-(2-甲基-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸乙酯(CB15)制备,并且分离为白色固体(1.039g,96%):^{1}H NMR(400MHz,CD_3OD)δ9.13(s,1H),8.06-7.99(m,2H),7.94(d,J=1.8Hz,1H),7.89(dd,J=7.8,1.9Hz,1H),7.54-7.46(m,2H),7.30(d,J=7.9Hz,1H),2.99(t,J=7.9Hz,2H),2.61(dd,J=8.5,7.2Hz,2H),2.42(s,3H);^{19}F NMR(376MHz,CD_3OD)δ-59.68;ESIMS m/z 391([M]$^+$)。

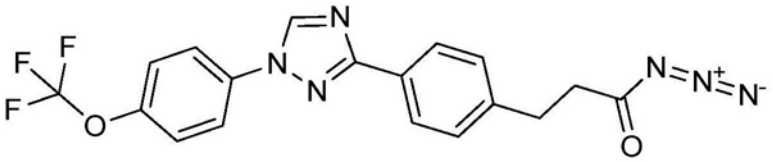
[0454] 制备3-(2-氟-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸(CB19)

[0455] 

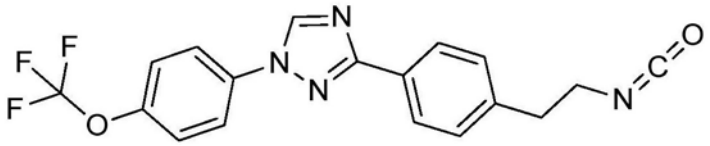
[0456] 粗制的标题化合物由3-(2-氟-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸乙酯(CB16)制备,并且分离为白色固体并且使用而不进一步纯化:^{1}H NMR(400MHz,$CDCl_3$)δ9.14(s,1H),8.01(d,J=9.0Hz,2H),7.93-7.83(m,1H),7.80(dd,J=11.4,1.6Hz,1H),7.49(d,J=8.6Hz,2H),7.41(t,J=7.8Hz,1H),3.00(t,J=7.7Hz,2H),2.64(t,J=7.6Hz,2H);^{19}F NMR(376MHz,$CDCl_3$)δ-55.72,-116.16;ESIMS m/z 395([M]$^+$)。

[0457] 实施例32:制备3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙

酰基叠氮化物(34)和3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)



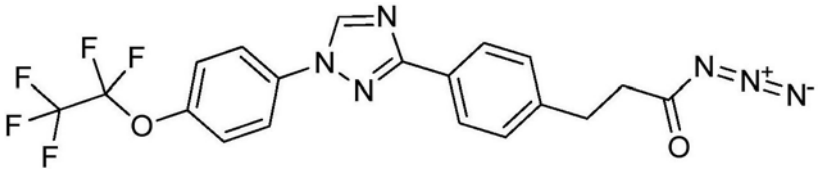
[0458]



[0459] 向在无水甲苯(12mL)中的3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸(C32)(0.70g,1.9mmol),加入三乙胺(0.26mL,1.9mmol)和叠氮磷酸二苯酯(0.40mL,1.9mmol)。将反应混合物在室温搅拌2小时,将其直接装在Celite®柱体上,并且通过使用0-100%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化,提供为白色固体的标题化合物(0.37g,50%)。^{1}H NMR与酰基叠氮化物(34)和重排的异氰酸酯(34a)的混合物一致:^{1}H NMR(400MHz,$CDCl_3$)δ8.56(两个单线谱,总计=1H),8.20-8.07(m,2H),7.80(m,2H),7.44-7.27(m,4H),3.59(t,J=6.9Hz,1H),3.00(t,J=7.2Hz,2H),2.72(d,J=7.2Hz,1H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 403([M+H]$^{+}$)(酰基叠氮化物)。

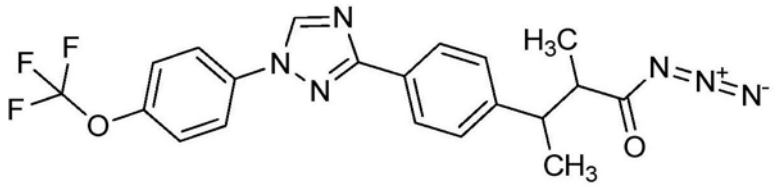
[0460] 下面的化合物根据实施例32中的步骤制备。

[0461] 制备3-(4-(1-(4-(全氟乙氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物(C35)

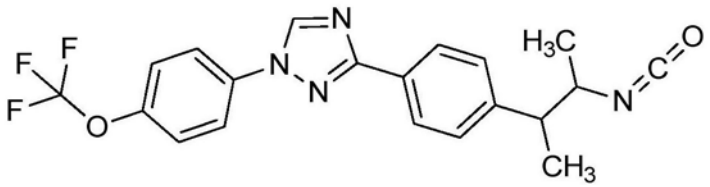
[0462] 

[0463] 标题化合物由3-(4-(1-(4-(全氟乙氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸(C33)制备,并且分离为白色固体(0.416g,57%):mp 68℃(dec.):^{1}H NMR与酰基叠氮化物和重排的异氰酸酯的混合物一致:^{1}H NMR(400MHz,$CDCl_3$)δ8.64-8.53(m,1H),8.23-8.06(m,2H),7.85-7.75(m,2H),7.39(m,2H),7.36-7.28(m,2H),3.59(t,J=6.8Hz,1H),3.00(t,J=7.3Hz,2H),2.70(d,J=7.2Hz,1H);^{19}F NMR(376MHz,$CDCl_3$)δ-85.90,-87.85;ESIMS m/z 453([M+H]$^{+}$)。

[0464] 制备2-甲基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁酰基叠氮化物/3-(4-(3-异氰酸酯基丁烷-2-基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C35a)

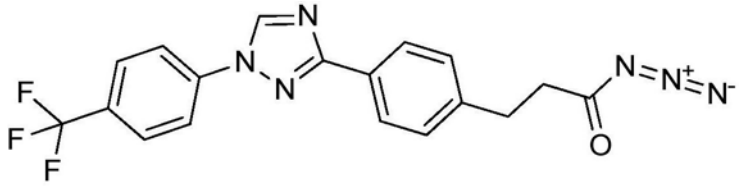


[0465]

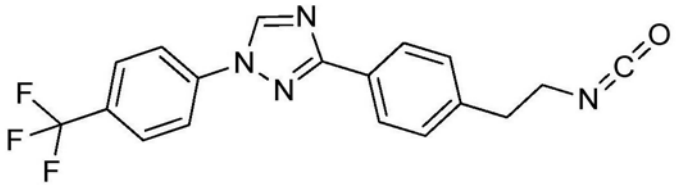


[0466] 目标化合物由2-甲基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁酸(CA10)制备,并且分离为澄清的油(3:1叠氮化物:异氰酸酯,0.246g,67%):^{1}H NMR(400MHz,$CDCl_3$)δ8.56(s,1H),8.20-8.10(m,2H),7.83-7.73(m,2H),7.42-7.28(m,4H),3.77(m,1H),2.86(m,1H),1.39(two d,J=7.0Hz,3H),1.25(two d,J=6.5Hz,3H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 431([M+H]$^{+}$)。

[0467] 制备3-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物/3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑(C35b)

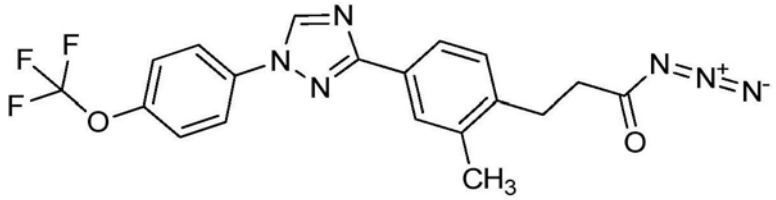


[0468]



[0469] 目标化合物由3-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸(CA11)制备,并且分离为澄清的油(混合物叠氮化物:异氰酸酯,0.595g,57%):^{1}H NMR(400MHz,$CDCl_3$)δ8.65(d,J=2.8Hz,1H),8.21-8.10(m,2H),7.91(m,2H),7.80(m,2H),7.38-7.29(m,2H),3.59(t,J=6.9Hz,1H),3.00(t,J=7.2Hz,2H),2.72(d,J=7.2Hz,1H);^{19}F NMR(376MHz,$CDCl_3$)δ-62.49。

[0470] 制备3-(2-甲基-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物(CB20)

[0471] 

[0472] 标题化合物由3-(2-甲基-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸(CB18)使用乙腈作为共溶剂制备,并且分离为白色固体(0.636g,57%):^{1}H NMR

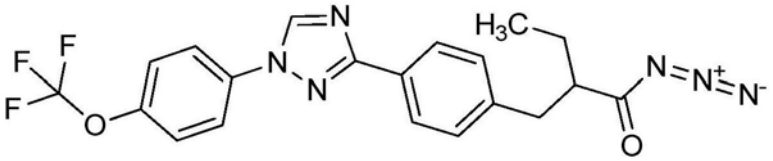
(400MHz,$CDCl_3$)δ8.55(s,1H),8.00(d,J=1.8Hz,1H),7.98-7.94(m,1H),7.84-7.75(m,2H),7.39(ddt,J=7.9,2.0,1.0Hz,2H),7.24(d,J=7.9Hz,1H),3.06-2.90(m,2H),2.75-2.59(m,2H),2.41(s,3H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.04;ESIMS m/z 389([M+H]-N_2^+)。

[0473] 制备3-(2-氟-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物(CB21)

[0474] 

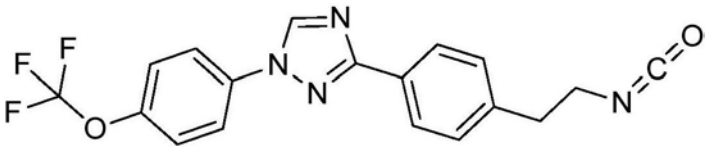
[0475] 标题化合物由3-(2-氟-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸(CB19)使用乙腈作为共溶剂制备,并且分离为白色固体(0.084g,29%):^{1}H NMR(400MHz,$CDCl_3$)δ8.56(s,1H),7.94-7.83(m,2H),7.83-7.75(m,2H),7.39(ddd,J=7.7,1.9,0.9Hz,2H),7.35-7.29(m,1H),3.10-2.96(m,2H),2.81-2.66(m,2H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03,-117.86.

[0476] 制备2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)丁酰基叠氮化物(CB22)

[0477] 

[0478] 标题化合物由2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)丁酸(CB17)制备,并且分离为澄清的油(0.512g,56%):^{1}H NMR(400MHz,$CDCl_3$)δ8.56(s,1H),8.20-8.10(m,2H),7.84-7.74(m,2H),7.39(dt,J=8.0,1.0Hz,2H),7.36-7.29(m,2H),3.68(tdd,J=8.3,5.3,4.4Hz,1H),2.98-2.77(m,2H),1.76-1.64(m,1H),1.61-1.51(m,1H),1.05(t,J=7.4Hz,3H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03,-117.86;ESIMS m/z 431([M+H]$^+$)。

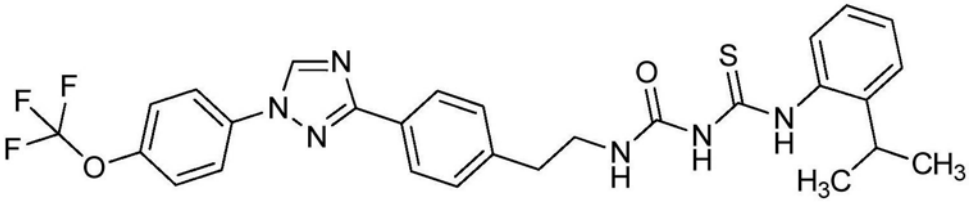
[0479] 实施例32a:制备3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)

[0480] 

[0481] 1L三颈圆底烧瓶装配有机械搅拌器,热电偶,和冷凝器。加入四氢呋喃(120mL)。将其冷却至-3℃之后,加入氯甲酸乙酯(3.16mL,33.2mmol)和三乙胺(4.64mL,33.2mmol)。分批加入3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸(C32)(11.4g,30.2mmol),保持反应温度低于0℃。反应混合物迅速变成白色悬浮液。LC-MS显示1小时之后没有起始原料剩余。缓慢加入叠氮化钠(2.16g,33.2mmol)在水(44mL)中的溶液,保持反应温度低于-2℃。将反应混合物在-2℃搅拌2小时。在0℃搅拌的同时,非常缓慢地向反应混合物加入冷水(200mL)。加入之后,将其在0℃搅拌30分钟。将其冷却的同时过滤所形成的白色固体。将固体在氮气流下在室温真空干燥48小时,提供为褐色固体的异氰酸酯(10.5g,

86%)：^{1}H NMR(400MHz，$CDCl_3$)δ8.56(s，1H)，8.20-8.11(m，2H)，7.85-7.76(m，2H)，7.47-7.30(m，4H)，3.59(t，J＝6.9Hz，2H)，2.97(t，J＝6.9Hz，2H)；^{19}F NMR(376MHz，$CDCl_3$)δ-58.02；ESIMS m/z 375.2([M+H]$^{+}$)。

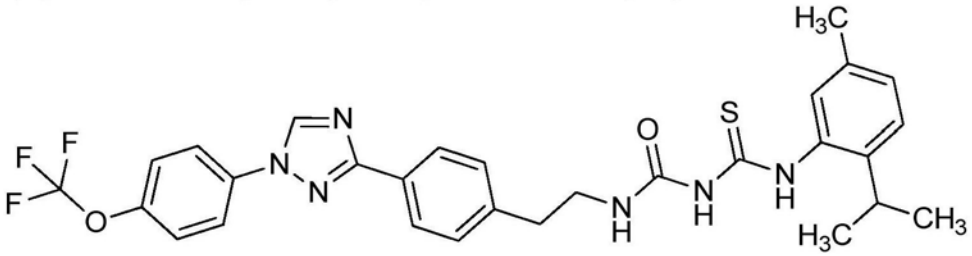
[0482] 实施例33：制备N-[2-异丙基苯基]-N'-[2-(4-{1-[4-(三氟甲氧基)苯基]-1H-1，2，4-三唑-3-基}苯基)乙基]硫代缩二脲(F2)

[0483] 

[0484] 将在乙腈(2.3mL)中的3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑-3-基)苯基)丙酰基叠氮化物(C34)(0.19g，0.46mmol)在80℃加热2小时。将反应混合物冷却，加入1-(2-异丙基苯基)硫脲(0.11g，0.55mmol)和碳酸铯(0.20g，0.60mmol)。将反应在室温搅拌4小时，然后用水猝灭并且用乙酸乙酯(2×)提取。将有机层经无水硫酸钠干燥，过滤，浓缩，并且装到具有二氯甲烷的Celite®柱体上。通过使用0-100%乙酸乙酯/B(其中B＝1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化，提供为白色粉末的标题化合物(0.097g，36%)。

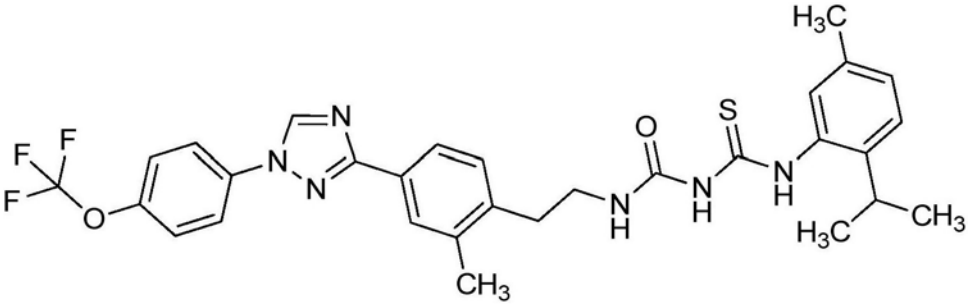
[0485] 下面的化合物根据实施例33中的步骤制备。

[0486] 制备N-[5-甲基-2-异丙基苯基]-N'-[2-(4-{1-[4-(三氟甲氧基)-苯基]-1H-1，2，4-三唑-3-基}苯基)乙基]硫代缩二脲(F3)

[0487] 

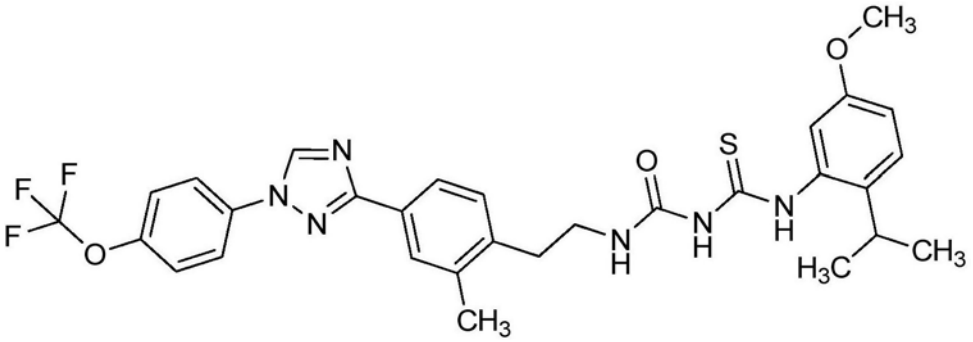
[0488] 标题化合物由3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑-3-基)苯基)丙酰基叠氮化物(C34)和1-(2-异丙基-5-甲基苯基)硫脲制备，并且分离为白色固体(0.158g，43%)。

[0489] 制备1-[(2-异丙基-5-甲基-苯基)氨基硫代甲酰基]-3-[2-[2-甲基-4-[1-[4-(三氟甲氧基)苯基]-1H-1，2，4-三唑-3-基]苯基]乙基]脲(FB1)

[0490] 

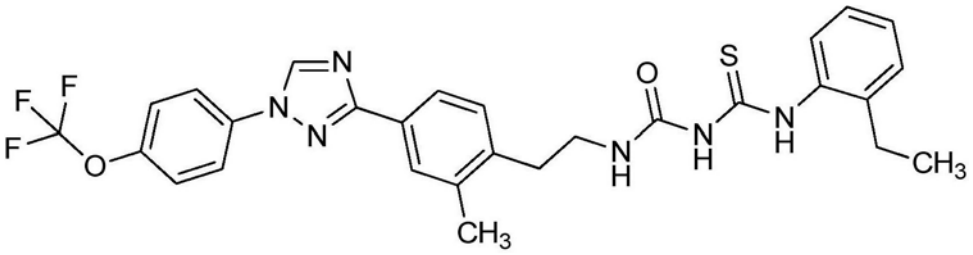
[0491] 标题化合物由3-(2-甲基-4-(1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑-3-基)苯基)丙酰基叠氮化物(CB20)和1-(2-异丙基-5-甲基苯基)硫脲制备，并且在不纯化的情况下分离为白色固体(0.180g，79%，88%纯度)。

[0492] 制备1-[(2-异丙基-5-甲氧基-苯基)氨基硫代甲酰基]-3-[2-[2-甲基-4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(FB2)

[0493] 

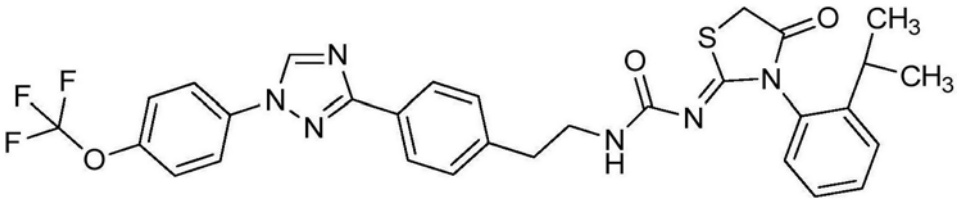
[0494] 标题化合物由3-(2-甲基-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物(CB20)和1-(2-异丙基-5-甲氧基苯基)硫脲(CA40)制备,并且在不纯化的情况下分离为黄色固体(0.165g,75%)。

[0495] 制备1-[(2-乙基苯基)氨基硫代甲酰基]-3-[2-[2-甲基-4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(FB5)

[0496] 

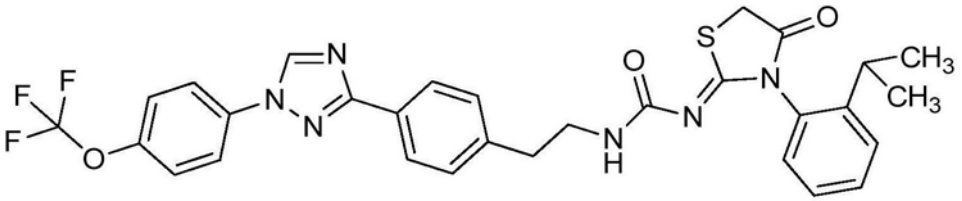
[0497] 标题化合物由3-(2-甲基-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物(CB20)和1-(2-乙基苯基)硫脲制备,并且在不纯化的情况下分离为黄色固体(0.144g,83%)。

[0498] 实施例34:制备(Z)-1-(3-(2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(F1),方法A

[0499] 

[0500] 向在乙醇(0.5mL)中的N-[2-异丙基苯基]-N'-[2-(4-{1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基}苯基)乙基]硫代缩二脲(F2)(0.030g,0.053mmol)和乙酸钠(0.016g,0.20mmol),加入2-溴乙酸甲酯(0.01mL,0.10mmol),并且将溶液在65℃加热1.5小时。反应冷却,将其直接装在Celite®柱体上。通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供为澄清的油的标题化合物(0.016g,49%)。

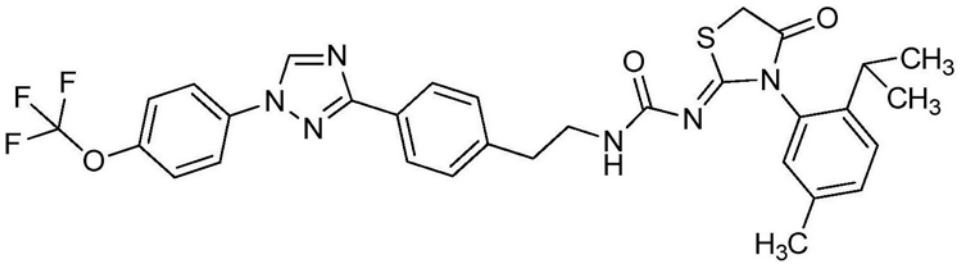
[0501] 实施例35:制备(Z)-1-(3-(2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(F1),方法B

[0502] 

[0503] 将在乙腈(2.9mL)中的3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物(C34)(0.24g,0.59mmol)在80℃加热2小时。反应冷却,加入碳酸铯(0.29g,0.88mmol)和1-(2-异丙基苯基)硫脲(0.14g,0.70mmol)。将反应在室温搅拌过夜。LC/MS显示,完全形成硫代缩二脲。将反应混合物用乙醇(2.9mL)和乙酸钠(0.19g,2.4mmol)稀释,加入2-溴乙酸甲酯(0.12mL,1.2mmol)。将溶液在65℃加热2小时。将反应混合物用乙酸乙酯稀释和用水洗涤。将有机层经无水硫酸钠干燥,过滤,浓缩,并且装到具有二氯甲烷的Celite®柱体上。通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供为褐色油的标题化合物(0.22g,62%)。

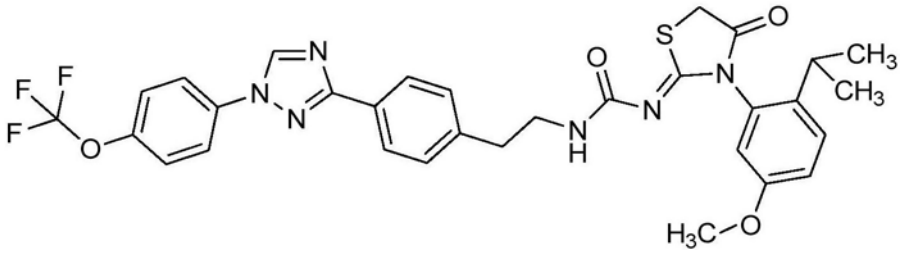
[0504] 下面的化合物根据实施例34或35中的步骤制备。

[0505] 制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(F5)

[0506] 

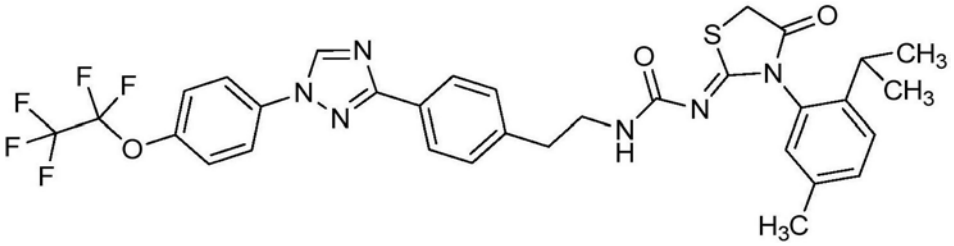
[0507] 标题化合物如实施例34中所述使用N-[5-甲基-2-异丙基苯基]-N'-[2-(4-{1-[4-(三氟甲氧基)-苯基]-1H-1,2,4-三唑-3-基}苯基)乙基]硫代缩二脲(F3)和1-(2-异丙基-5-甲基苯基)硫脲制备,并且分离为淡粉色固体(0.114g,29%)。

[0508] 制备(Z)-1-(3-(2-异丙基-5-甲氧基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(F6)

[0509] 

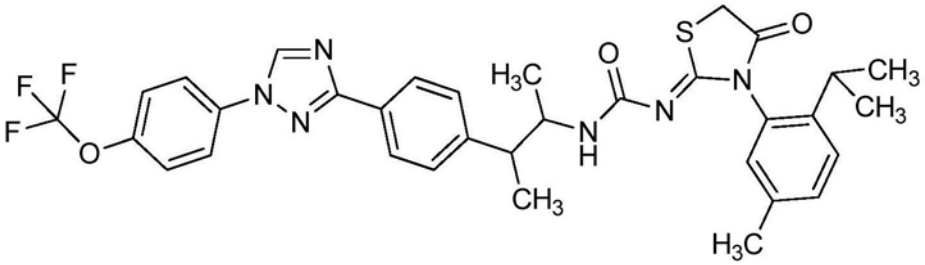
[0510] 标题化合物如实施例35中所述使用3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物(C34)和1-(2-异丙基-5-甲氧基苯基)硫脲(CA40)制备,并且分离为橙色固体(0.075g,35%)。

[0511] 制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(全氟乙氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(F9)

[0512] 

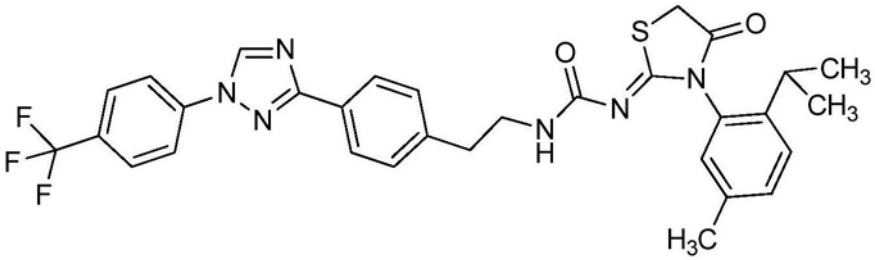
[0513] 标题化合物如实施例35中所述使用1-(2-异丙基-5-甲基苯基)硫脲和3-(4-(1-(4-(全氟乙氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)-丙酰基叠氮化物(C35)制备,并且分离为褐色胶(0.146g,43%)。

[0514] 制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-2-基)脲(P66,P353)

[0515] 

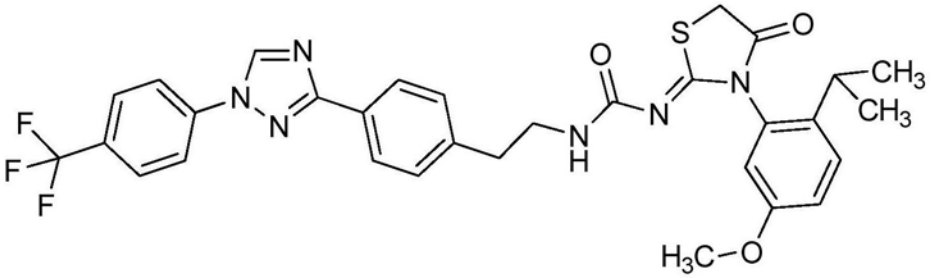
[0516] 标题化合物如实施例35中所述使用1-(2-异丙基-5-甲基苯基)硫脲和2-甲基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁酰基叠氮化物/3-(4-(3-异氰酸酯基丁烷-2-基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C35a)制备,并且分离为灰白色粉末(0.146g,39%)。

[0517] 制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P52)

[0518] 

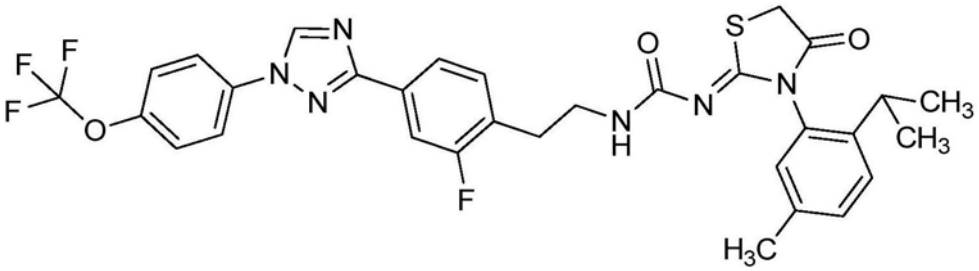
[0519] 标题化合物如实施例35中所述使用3-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物/3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑(C35b)和1-(2-异丙基-5-甲基苯基)硫脲制备,并且分离为褐色玻璃状泡沫(0.132g,46%)。

[0520] 制备(Z)-1-(3-(2-异丙基-5-甲氧基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P53)

[0521] 

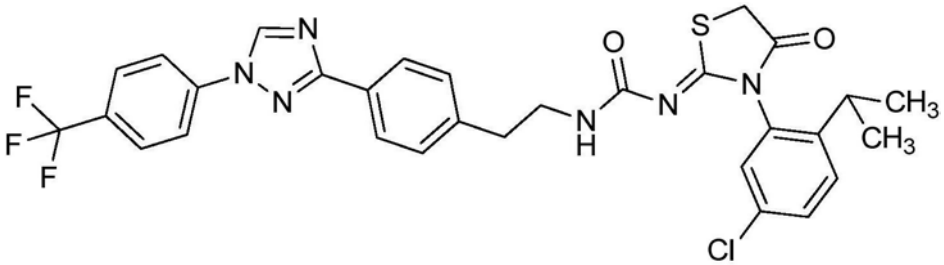
[0522] 标题化合物如实施例35中所述使用3-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物/3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑(C35b)和1-(2-异丙基-5-甲氧基苯基)硫脲(CA40)制备,并且分离为褐色泡沫(0.040g,30%)。

[0523] 制备(Z)-1-(2-氟-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)-3-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)脲(FB8)

[0524] 

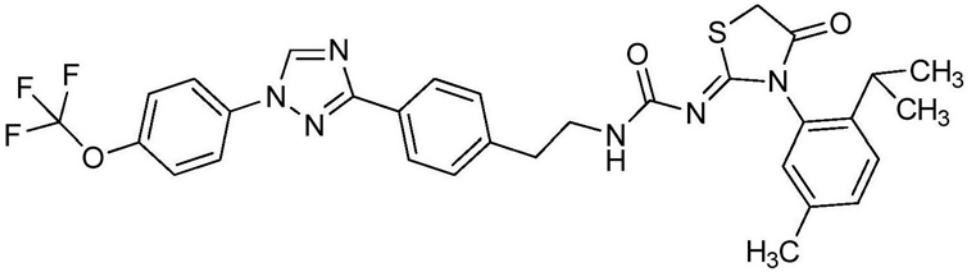
[0525] 标题化合物如实施例35中所述使用3-(2-氟-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物(CB21)和1-(2-异丙基-5-甲基苯基)硫脲在温度为60℃制备,随后用反相色谱分离为橙色油(0.028g,13%)。

[0526] 制备(Z)-1-(3-(5-氯-2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB50)

[0527] 

[0528] 标题化合物如实施例35中所述使用3-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物/3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑(C35b)和1-(5-氯-2-异丙基苯基)硫脲(CB32)在温度为60℃制备;分离为澄清的油(0.019g,12%)。

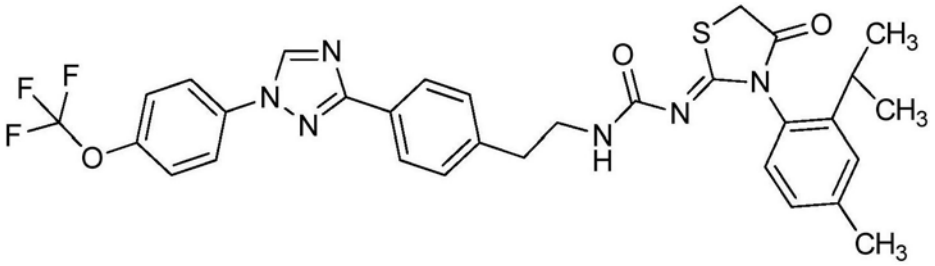
[0529] 实施例35a:制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(F5)

[0530] 

[0531] 向250mL圆底烧瓶加入乙腈(100mL)。一批加入3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(34a)(11.0g,29.4mmol)。将1-(2-异丙基-5-甲基苯基)硫脲(6.73g,32.3mmol)和碳酸铯(9.57g,29.4mmol)加入至上述溶液中。将反应混合物在室温在氮气下搅拌过夜。将乙醇(100mL)加入至混合物。然后加入2-溴乙酸甲酯(8.99g,58.8mmol)和乙酸钠(9.64g,118mmol)。将反应混合物在60℃搅拌2小时,形成橙色悬浮液。将反应混合物冷却并且通过滤纸过滤,并且将固体用乙酸乙酯(2×100mL)洗涤。将橙色滤液浓缩。固体残留物通过使用10-20%二氯甲烷/B(其中B=1:1乙酸乙酯/丙酮)作为洗脱剂的快速柱色谱纯化,提供为略带橙色的泡沫的标题化合物(8.60g,45%)。

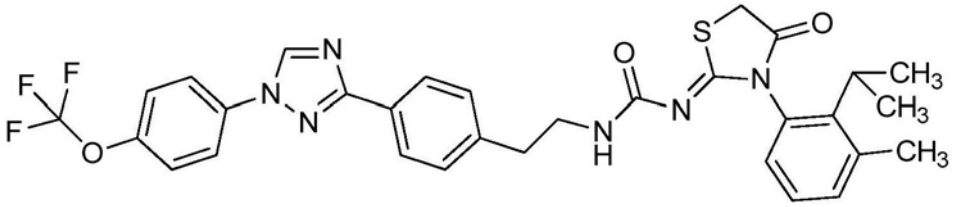
[0532] 下面的化合物根据实施例35a中的步骤制备。

[0533] 制备(Z)-1-(3-(2-异丙基-4-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P26)

[0534] 

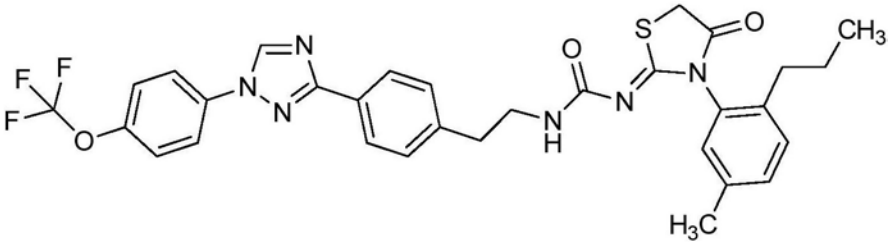
[0535] 标题化合物由1-(2-异丙基-4-甲基苯基)硫脲和3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)制备,并且分离为褐色油(0.121g,47%)。

[0536] 制备(Z)-1-(3-(2-异丙基-3-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P27)

[0537] 

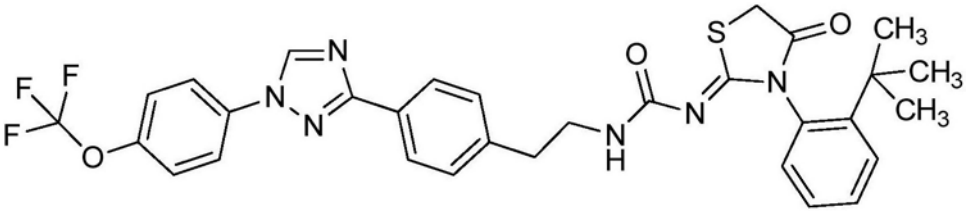
[0538] 标题化合物由1-(2-异丙基-3-甲基苯基)硫脲和3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)制备,并且分离为黄色油(0.075g,31%)。

[0539] 制备(Z)-1-(3-(5-甲基-2-丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P29)

[0540] 

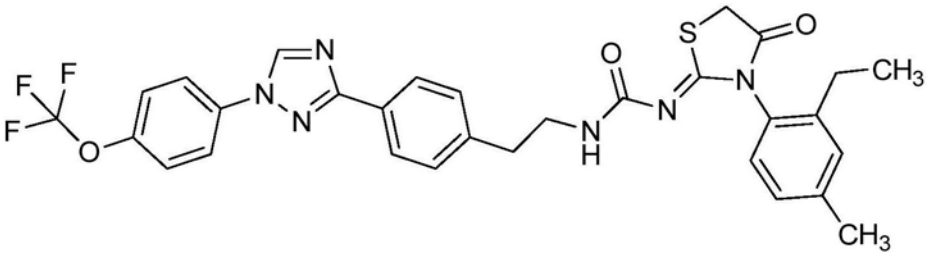
[0541] 标题化合物由1-(5-甲基-2-丙基苯基)硫脲(CA38)和3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)制备,并且分离为淡粉色固体(0.113g,43%)。

[0542] 制备(Z)-1-(3-(2-(叔丁基)苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P30)

[0543] 

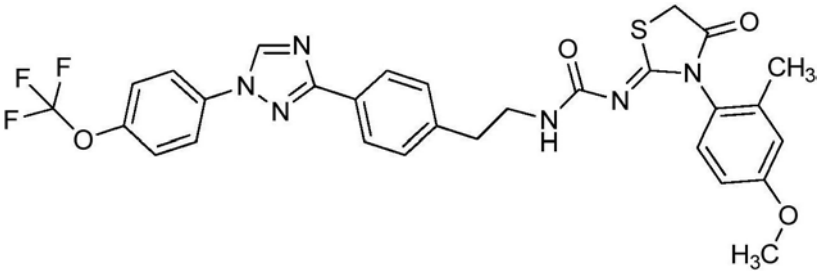
[0544] 标题化合物由1-(2-(叔丁基)苯基)硫脲和3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)制备,并且分离为粉红色固体(0.076g,31%)。

[0545] 制备(Z)-1-(3-(2-乙基-4-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P31)

[0546] 

[0547] 标题化合物由1-(2-乙基-4-甲基苯基)硫脲(CA42)和3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)制备,并且分离为粉红色固体(0.114g,47%)。

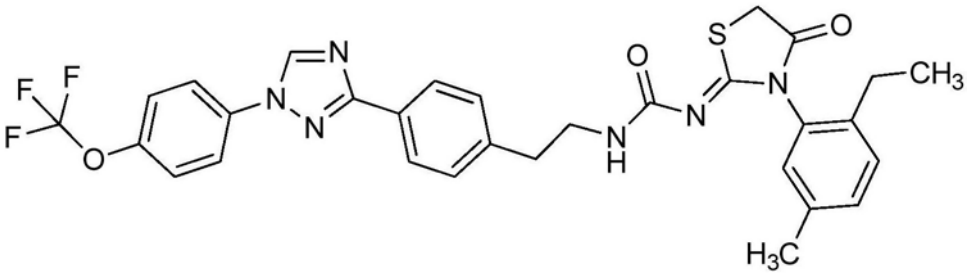
[0548] 制备(Z)-1-(3-(4-甲氧基-2-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P44)

[0549] 

[0550] 标题化合物如实施例35中所述使用1-(4-甲氧基-2-甲基苯基)硫脲和3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)制备,并且分离为

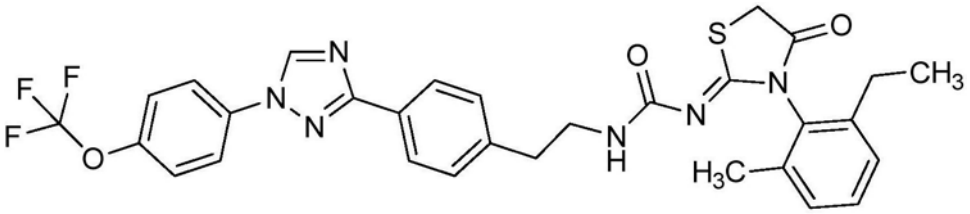
黄色固体(0.120g,49%)。

[0551] 制备(Z)-1-(3-(2-乙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P49)

[0552] 

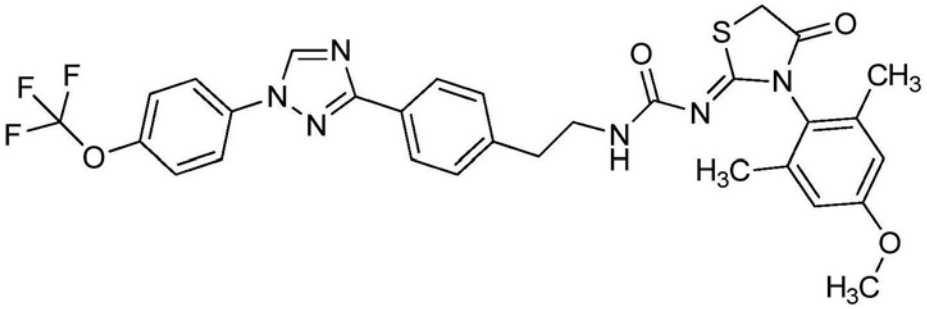
[0553] 标题化合物由1-(2-乙基-5-甲基苯基)硫脲(CA41)和3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)制备,并且分离为粉红色固体(0.099g,43%)。

[0554] 制备(Z)-1-(3-(2-乙基-6-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P50)

[0555] 

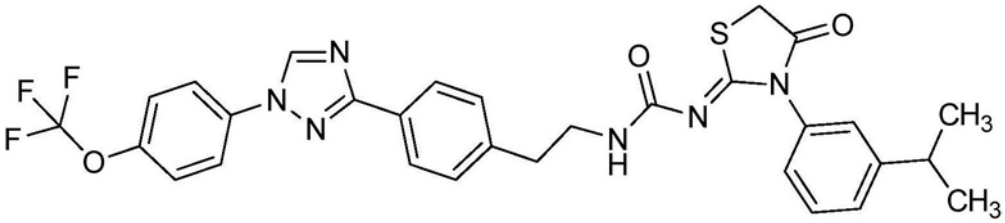
[0556] 标题化合物由1-(2-乙基-6-甲基苯基)硫脲(CA39)和3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)制备,并且分离为灰白色固体(0.076g,33%)。

[0557] 制备(Z)-1-(3-(4-甲氧基-2,6-二甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P47)

[0558] 

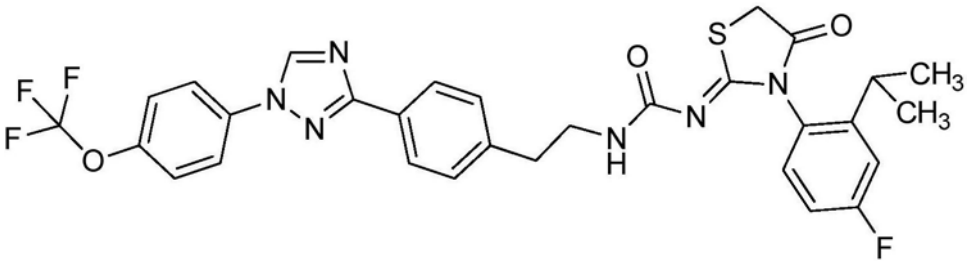
[0559] 标题化合物由1-(4-甲氧基-2,6-二甲基苯基)硫脲和3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)制备,并且分离为黄色油(0.055g,23%)。

[0560] 制备(Z)-1-(3-(3-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P51)

[0561] 

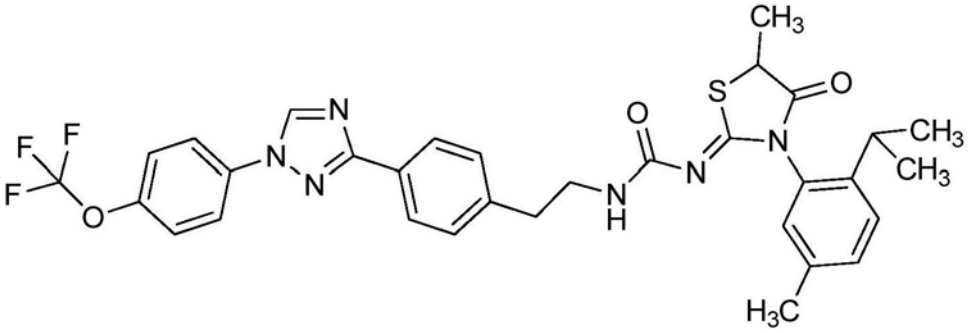
[0562] 标题化合物由1-(3-异丙基苯基)硫脲和3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)制备,并且分离为深褐色油(0.094g,37%)。

[0563] 制备(Z)-1-(3-(4-氟-2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P28)

[0564] 

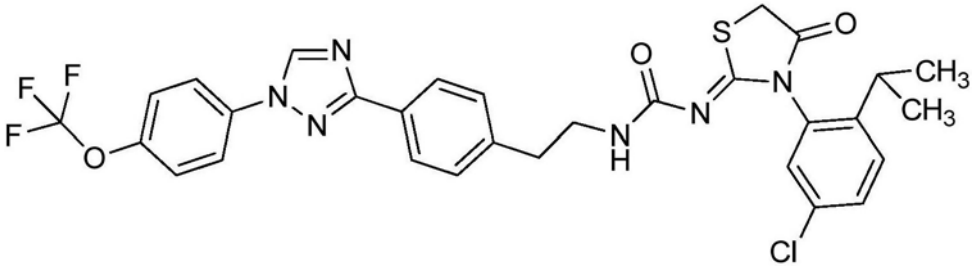
[0565] 标题化合物由1-(4-氟-2-异丙基苯基)硫脲和3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)制备,并且分离为褐色泡沫(0.151g,37%)。

[0566] 制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-5-甲基-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P57)

[0567] 

[0568] 标题化合物由1-(2-异丙基-5-甲基苯基)硫脲,3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a),和2-溴丙酸甲酯制备,并且分离为澄清的粘性油(0.192g,49%)。

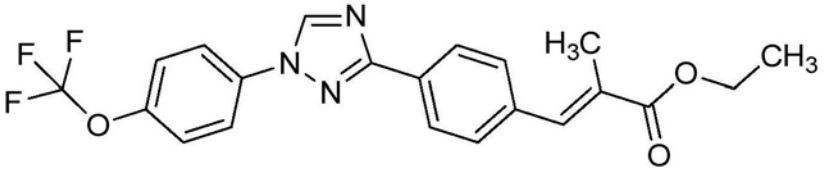
[0569] 制备(Z)-1-(3-(5-氯-2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB40)

[0570] 

[0571] 标题化合物由1-(5-氯-2-异丙基苯基)硫脲(CB32)和3-(4-(2-异氰酸酯基乙基)

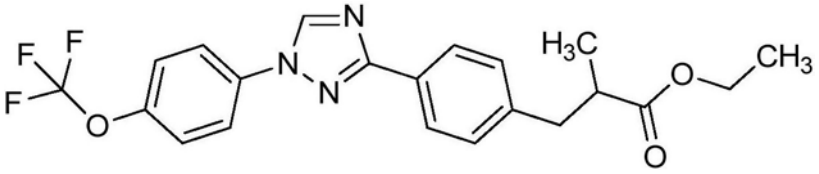
苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)制备,并且分离为褐色玻璃状泡沫(0.173g,48%)。

[0572] 实施例36:制备(E)-2-甲基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烯酸乙基酯(C36)

[0573] 

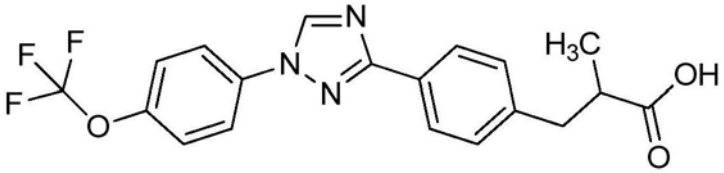
[0574] 将在无水甲苯(30mL)中的4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯甲醛(7.56g,22.7mmol)和2-(三苯基膦烯)丙酸乙酯(9.87g,27.2mmol)在110℃加热16小时。然后加入另外的2-(三苯基膦烯)丙酸乙酯(2.40g,6.06mmol),并且将反应在110℃加热4小时。反应冷却,在真空下浓缩,并且将其装到硅胶上。通过使用0-100%乙酸乙酯/己烷作为洗脱剂的快速柱色谱、随后使用0-100%乙腈/水作为洗脱剂的反相快速柱色谱纯化,提供为白色固体的标题化合物(5.92g,62%):mp 126-127.5℃;^{1}H NMR(400MHz,$CDCl_3$)δ8.58(s,1H),8.27-8.17(m,2H),7.84-7.78(m,2H),7.73(s,1H),7.52(d,J=8.2Hz,2H),7.40(d,J=8.3Hz,2H),4.29(q,J=7.1Hz,2H),2.17(d,J=1.5Hz,3H),1.37(t,J=7.1Hz,3H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.02;ESIMS m/z 418([M+H]$^+$)。

[0575] 实施例37:制备2-甲基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸乙基酯(C37)

[0576] 

[0577] 将含有在乙酸乙酯(10mL)中的(E)-2-甲基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烯酸乙基酯(C36)(0.96g,2.3mmol)和钯碳(10wt%,0.24g,0.23mmol)的烧瓶在真空下抽吸,填充氮气,在真空下抽吸,然后放置在氢气球下(~1atm)。在室温搅拌20小时之后,将反应通过Celite®垫过滤并且浓缩,提供为白色固体的标题化合物(1.0g,100%):mp 73-75℃;^{1}H NMR(400MHz,$CDCl_3$)δ8.56(s,1H),8.14-8.07(m,2H),7.86-7.76(m,2H),7.39(d,J=8.3Hz,2H),7.29(d,J=8.3Hz,2H),4.10(q,J=7.1Hz,2H),3.22-2.99(m,1H),2.75(dq,J=13.3,7.5Hz,2H),1.24-1.15(m,6H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 420([M+H]$^+$)。

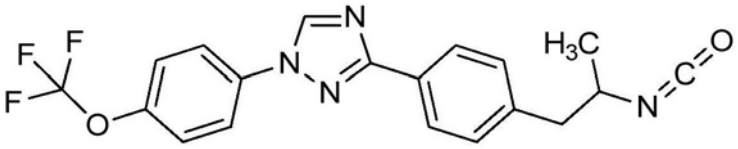
[0578] 实施例38:制备2-甲基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸(C38)

[0579] 

[0580] 向在甲醇(7.8mL)中的2-甲基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸乙酯(C37)(0.986g,2.35mmol),加入氢氧化钠(2N,5.9mL,11.8mmol),将溶

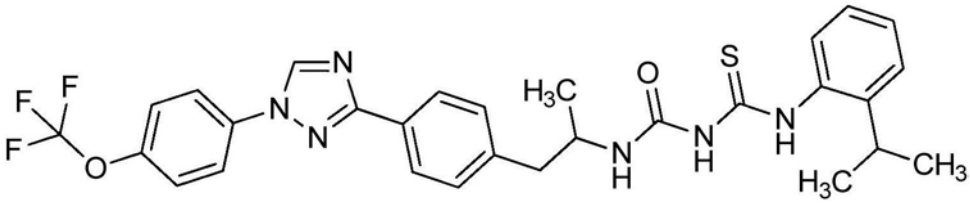
液在室温搅拌4小时。反应用氯化氢(2N)酸化，将白色沉淀物真空过滤，提供为白色固体的标题化合物(0.865g，93%)：mp142-144℃；^{1}H NMR(400MHz，DMSO-d_6)δ12.19(s，1H)，9.39(s，1H)，8.14-7.95(m，4H)，7.71-7.55(m，2H)，7.42-7.27(m，2H)，3.04-2.89(m，1H)，2.75-2.62(m，2H)，1.07(d，J＝6.2Hz，3H)。^{19}F NMR(376MHz，丙酮-D_6)δ-58.03；ESIMS m/z 392([M+H]$^+$)。

[0581] 实施例39：制备3-(4-(2-异氰酸酯基丙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C39)

[0582] 

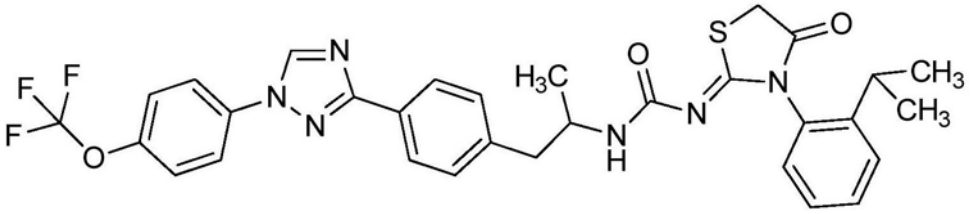
[0583] 向在甲苯(21.6mL)中的2-甲基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)-丙酸(0.84g，2.2mmol)，加入三乙胺(0.33mL，2.4mmol)和叠氮磷酸二苯酯(0.47mL，2.2mmol)，将溶液在室温搅拌2小时。将反应混合物用乙酸乙酯和水稀释，分层。将有机层经无水硫酸钠干燥，过滤，浓缩。将粗制物质装到Celite®柱体上，并且通过使用0-100%乙酸乙酯/B(其中B＝1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化，提供为白色固体的标题化合物(0.53g，58%)：^{1}H NMR(400MHz，$CDCl_3$)δ8.56(s，1H)，8.21-8.11(m，2H)，7.88-7.77(m，2H)，7.39(d，J＝8.3Hz，2H)，7.32(d，J＝8.4Hz，2H)，3.94-3.80(m，1H)，2.87(d，J＝6.8Hz，2H)，1.35(d，J＝6.5Hz，3H)；^{19}F NMR(376MHz，$CDCl_3$)δ-58.03；ESIMS m/z 389([M+H]$^+$)。

[0584] 实施例40：制备N-[2-(丙烷-2-基)苯基]-N'-[1-(4-{1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基}苯基)丙烷-2-基]硫代缩二脲(F4)

[0585] 

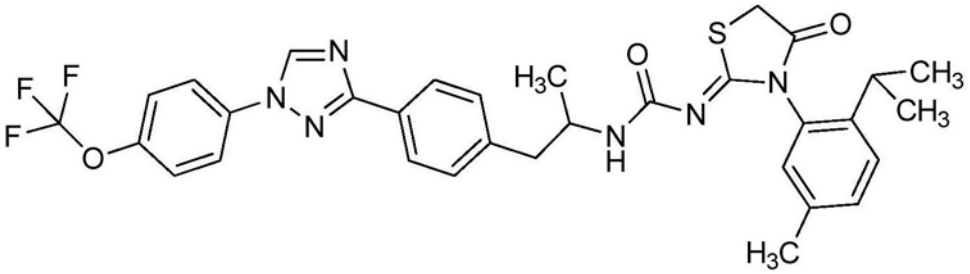
[0586] 将在乙腈(2.1mL)中的3-(4-(2-异氰酸酯基丙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C39)(0.17g，0.41mmol)在80℃加热2小时，确保完全转化为异氰酸酯。将反应冷却，加入1-(2-异丙基苯基)硫脲(0.83g，0.43mmol)和碳酸铯(0.17g，0.53mmol)，并且在室温搅拌过夜。将反应混合物用乙酸乙酯稀释和用水洗涤。将水层用乙酸乙酯提取，将合并的有机层经无水硫酸钠干燥，干燥，浓缩，提供为白色固体的标题化合物(0.25g，95%)。

[0587] 实施例41：制备(Z)-1-(3-(2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-基)脲(F7)

[0588] 

[0589] 向在乙醇(2.3mL)中的N-[2-(丙烷-2-基)苯基]-N'-[1-(4-{1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基}苯基)丙烷-2-基]硫代缩二脲(F4)(0.20g,0.34mmol)和乙酸钠(0.056g,0.68mmol),加入2-溴乙酸甲酯(0.05mL,0.51mmol),将反应在65℃加热2小时。反应冷却,用水稀释,并且用乙酸乙酯(2×)提取。将有机层经无水硫酸钠干燥,过滤,浓缩。将粗制物质装到具有二氯甲烷的硅胶柱体上,并且通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供为白色固体的标题化合物(0.070g,33%)。

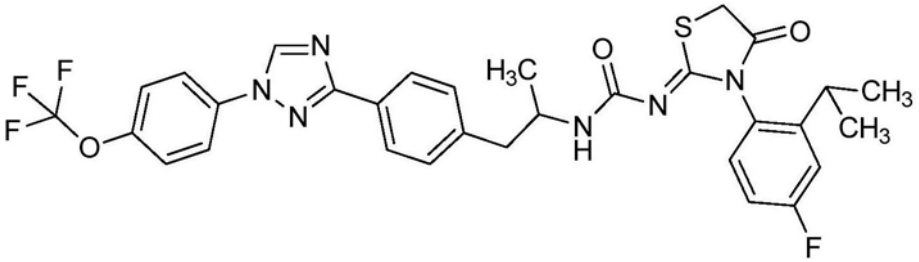
[0590] 实施例42:制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-基)脲(F8)

[0591] 

[0592] 将在乙腈(2mL)中的3-(4-(2-异氰酸酯基丙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C39)(0.17g,0.41mmol)在加热80℃2小时,确保完全转化为异氰酸酯。将反应冷却,加入1-(2-异丙基-5-甲基苯基)硫脲(0.095g,0.46mmol)和碳酸铯(0.20g,0.60mmol)。将反应在室温搅拌3天。将反应用乙醇(2.5mL)稀释,加入乙酸钠(0.064g,0.78mmol)和2-溴乙酸甲酯(0.05mL,0.53mmol)。将反应在65℃加热2.5小时。反应混合物用乙酸乙酯稀释和用水洗涤。将水层用乙酸乙酯提取另外的时间。将合并的有机层经无水硫酸钠干燥,过滤,浓缩。将粗制物质装到Celite®柱体上,并且通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供为灰白色固体的标题化合物(0.054g,20%)。

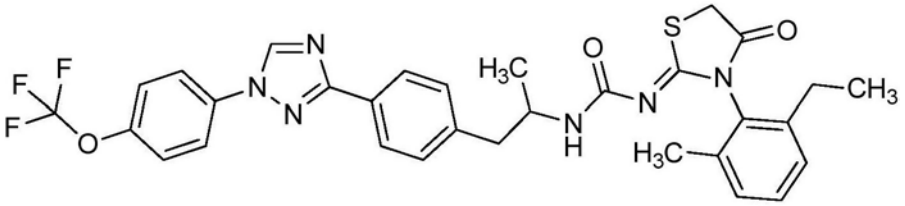
[0593] 下面的化合物根据实施例42中的步骤制备。

[0594] 制备(Z)-1-(3-(4-氟-2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-基)脲(P33)

[0595] 

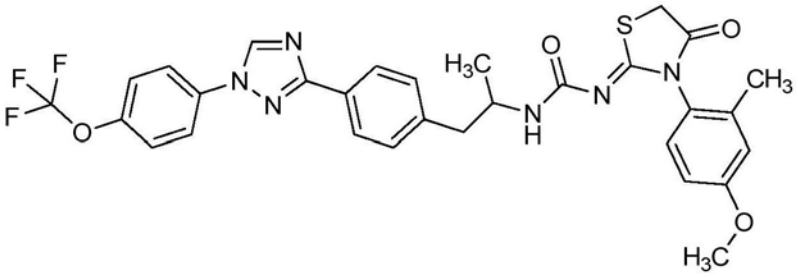
[0596] 标题化合物由2-甲基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物(C39)和1-(4-氟-2-异丙基苯基)硫脲制备,并且分离为褐色固体(0.183g,60%)。

[0597] 制备(Z)-1-(3-(2-乙基-6-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-基)脲(P42)

[0598] 

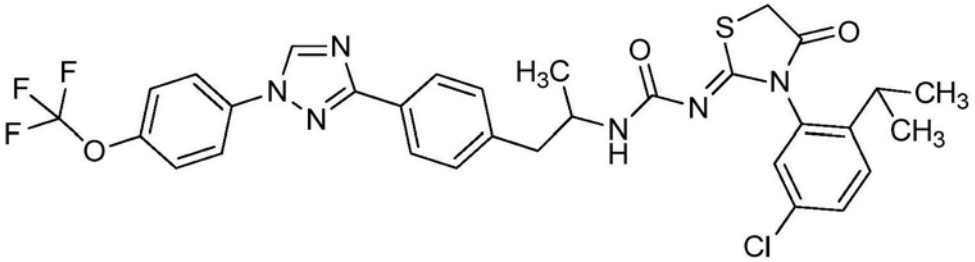
[0599] 标题化合物由2-甲基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物(C39)和1-(2-乙基-6-甲基苯基)硫脲(CA39)制备,并且分离为灰白色固体(0.117g,39%)。

[0600] 制备(Z)-1-(3-(4-甲氧基-2-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-基)脲(P45)

[0601] 

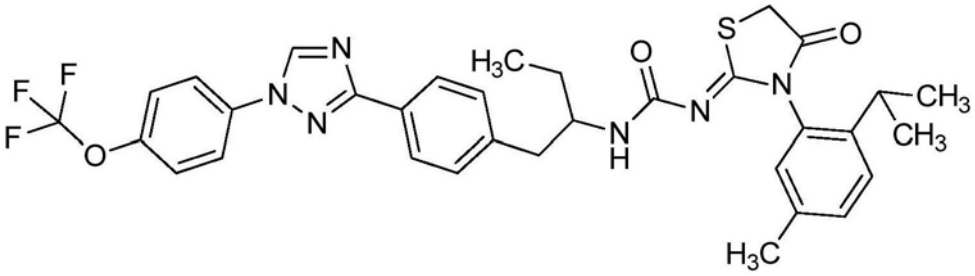
[0602] 标题化合物由2-甲基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物(C39)和1-(4-甲氧基-2-甲基苯基)硫脲制备,并且分离为褐色固体(0.224g,65%)。

[0603] 制备(Z)-1-(3-(5-氯-2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-基)脲(FB42)

[0604] 

[0605] 标题化合物由2-甲基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物(C39)和1-(5-氯-2-异丙基苯基)硫脲(CB32)制备,并且分离为褐色油(0.110g,46%)。

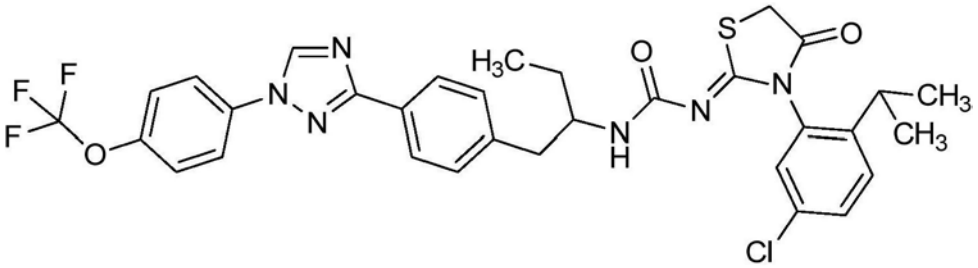
[0606] 制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-2-基)脲(FB43)12412827

[0607] 

[0608] 标题化合物由2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)丁酰基叠氮化物(CB22)和1-(2-异丙基-5-甲基苯基)硫脲制备,并且分离为桃色玻璃状泡沫

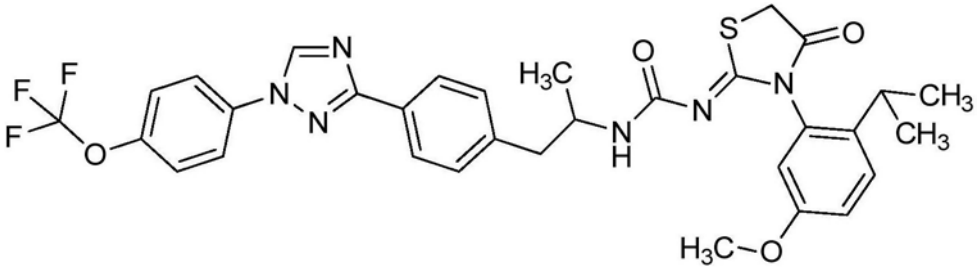
(0.122g,53%)。

[0609] 制备(Z)-1-(3-(5-氯-2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-2-基)脲(FB44)

[0610] 

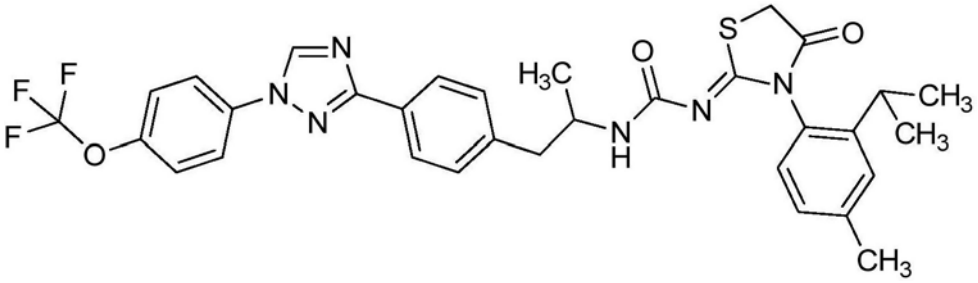
[0611] 标题化合物由2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)丁酰基叠氮化物(CB22)和1-(5-氯-2-异丙基苯基)硫脲(CB32)制备,并且分离为褐色玻璃状泡沫(0.132g,60%)。

[0612] 制备(Z)-1-(3-(2-异丙基-5-甲氧基苯基)-4-氧代噻唑烷-2-亚基)-3-(1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-基)脲(FB47)

[0613] 

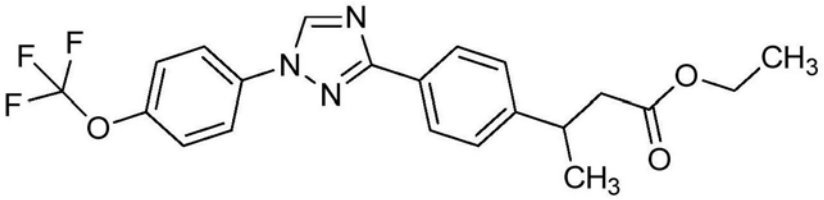
[0614] 标题化合物由2-甲基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物(C39)和1-(2-异丙基-5-甲氧基苯基)硫脲(CA40)制备,并且分离为褐色油(0.146g,42%)。

[0615] 制备(Z)-1-(3-(2-异丙基-4-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-基)脲(FB48)

[0616] 

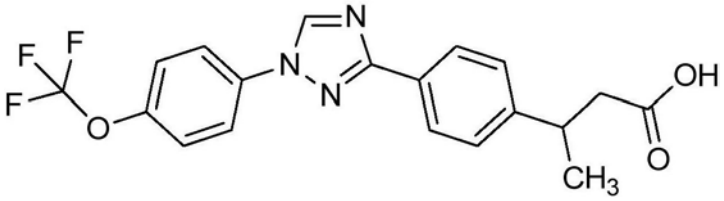
[0617] 标题化合物由2-甲基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物(C39)和1-(2-异丙基-4-甲基苯基)硫脲制备,并且分离为褐色油(0.130g,47%)。

[0618] 实施例43:制备3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁酸乙基酯(C40)

[0619] 

[0620] 将含有(E)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁-2-烯酸乙基酯(C26)(1.80g,4.31mmol)和钯碳(10wt%,0.46g,0.43mmol)在中乙酸乙酯(14.5mL)的烧瓶抽吸和反填充氮气,然后抽吸和放置在氢气球下(～1atm)。将反应在室温搅拌过夜,然后通过Celite®过滤并且浓缩,提供为褐色液体的标题化合物(1.79g,98%):^{1}H NMR(400MHz,$CDCl_3$)δ8.55(s,1H),8.17-8.07(m,2H),7.87-7.75(m,2H),7.38(d,J=9.1Hz,2H),7.36-7.31(m,2H),4.08(qd,J=7.1,0.8Hz,2H),3.35(dd,J=14.6,7.2Hz,1H),2.62(qd,J=15.1,7.6Hz,2H),1.34(d,J=7.0Hz,3H),1.19(t,J=7.1Hz,3H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 420([M+H]$^{+}$)。

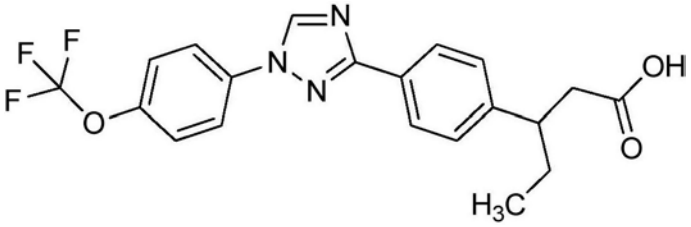
[0621] 实施例44:制备3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁酸(C41)

[0622] 

[0623] 向在甲醇(14mL)中的3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁酸乙酯(C40)(1.78g,4.24mmol),加入氢氧化钠(2N,12.7mL,25.4mmol),在室温搅拌4小时。反应用氯化氢(2N)酸化,将甲醇在真空下浓缩掉。将水溶液用乙酸乙酯(3×)提取。将有机层经无水硫酸钠干燥,干燥,浓缩,提供为澄清胶的标题化合物(0.470g,28%):^{1}H NMR(400MHz,DMSO-d_6)δ9.38(s,1H),8.11-8.05(m,2H),8.02(d,J=8.3Hz,2H),7.62(d,J=8.3Hz,2H),7.41(d,J=8.3Hz,2H),3.21(dd,J=14.4,7.1Hz,1H),2.56(d,J=7.4Hz,2H),1.26(d,J=7.0Hz,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 392([M+H]$^{+}$)。

[0624] 下面的化合物根据实施例44中的步骤制备。

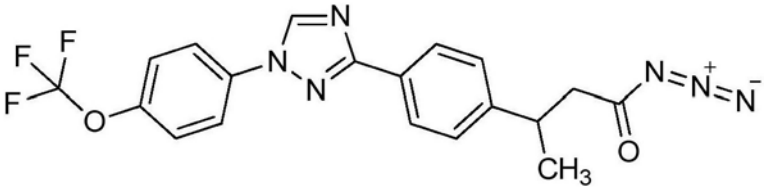
[0625] 制备3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)戊酸(CA12)

[0626] 

[0627] 标题化合物由3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)戊酸乙酯(CA48)制备,并且分离为白色固体(0.927g,36%):^{1}H NMR(400MHz,DMSO-d_6)δ12.05(s,1H),9.39(s,1H),8.17-7.94(m,4H),7.73-7.51(m,2H),7.46-7.25(m,2H),2.96(ddd,J=14.7,8.7,6.0Hz,1H),2.64(dd,J=15.5,6.6Hz,1H),2.55-2.49(m,1H),1.79-1.49(m,2H),0.74(t,J=7.3Hz,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.99;ESIMS m/z 406([M+H]$^{+}$)。

[0628] 实施例45:制备3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁

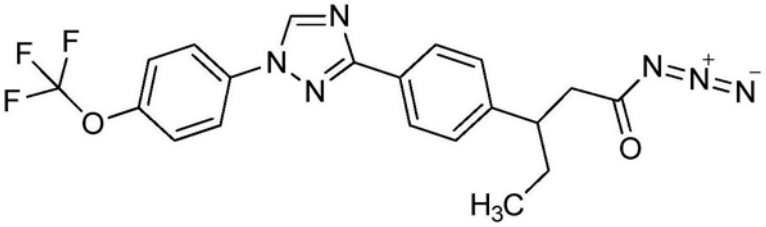
酰基叠氮化物(C42)

[0629] 

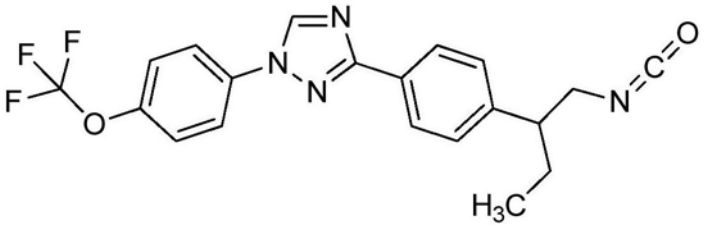
[0630] 向在甲苯(18mL)中的3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁酸(C41)(1.77g,4.52mmol),加入三乙胺(0.82mL,5.88mol)和叠氮磷酸二苯酯(1.05mL,4.98mmol),将溶液在室温搅拌3小时。将反应混合物用乙酸乙酯稀释和用水洗涤。将水层用乙酸乙酯提取。将有机层经无水硫酸钠干燥,过滤,浓缩。将粗制物质装到Celite®柱体上,并且通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供为澄清的油的标题化合物(0.223g,12%收率):^{1}H NMR与羰基叠氮化物和异氰酸酯的混合物一致。^{1}H NMR(400MHz,$CDCl_3$)δ8.56(s,1H),8.28-8.03(m,2H),7.88-7.66(m,2H),7.48-7.30(m,4H),3.60-3.40(m,2H),3.08(q,J=6.9Hz,1H),2.81-2.49(m,1H),1.37(dd,J=10.4,7.0Hz,3H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 417($[M+H]^+$)。

[0631] 下面的化合物根据实施例45中的步骤制备。

[0632] 制备3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)戊酰基叠氮化物/3-(4-(1-异氰酸酯基丁烷-2-基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C42a)

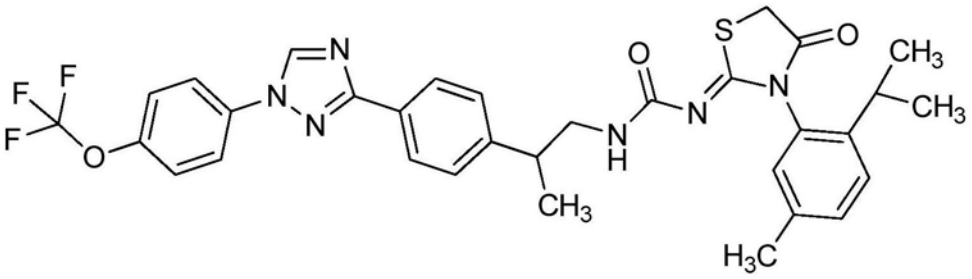


[0633]



[0634] 标题化合物由3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)戊酸(CA12)制备,提供叠氮化物和异氰酸酯的混合物(0.723g,72%):^{1}H NMR(400MHz,$CDCl_3$)δ8.56(two s,1H),8.20-8.15(m,2H),7.85-7.74(m,2H),7.39(dt,J=9.0,1.0Hz,2H),7.34-7.29(m,2H),3.62-3.38(m,2H),2.77-2.59(m,1H),1.93-1.59(m,2H),0.94-0.83(m,3H)。

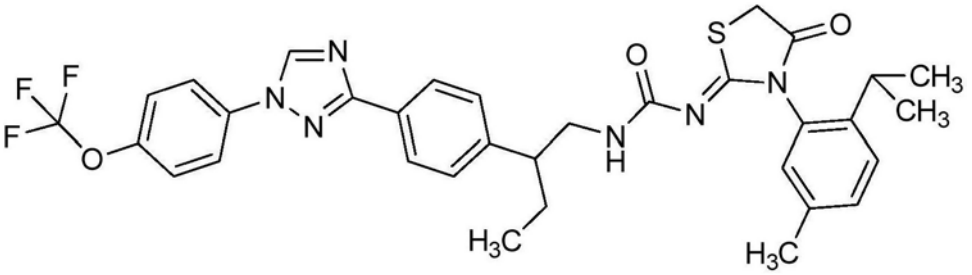
[0635] 实施例46:制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(F10)

[0636] 

[0637] 将在乙腈(2.6mL)中的3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁酰基叠氮化物(C42)(0.22g,0.52mmol)在80℃加热2小时。反应冷却,加入1-(2-异丙基-5-甲基苯基)硫脲(0.12g,0.57mmol)和碳酸铯(0.20g,0.61mmol)。将反应在室温搅拌18小时。加入乙酸钠(0.093g,1.1mmol),2-溴乙酸甲酯(0.07mL,0.78mmol)和乙醇(2.6mL),并且将反应混合物在65℃加热3小时。反应冷却,用乙酸乙酯稀释,并且用水洗涤。将水层再用乙酸乙酯提取一次。将合并的有机层经无水硫酸钠干燥,过滤,浓缩。将粗制物质装到Celite®柱体上,并且通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供为橙色固体的标题化合物(0.12g,35%)。

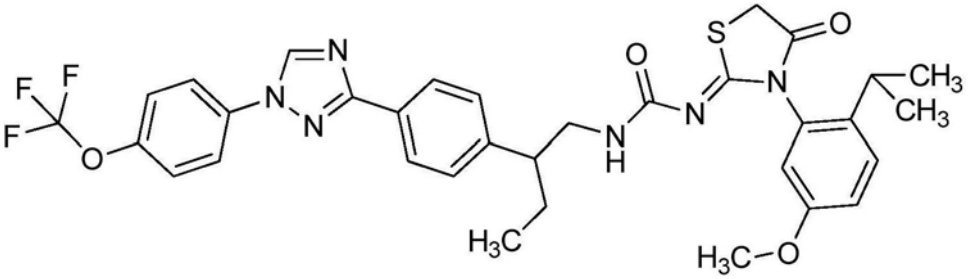
[0638] 下面的化合物根据实施例46中的步骤制备。

[0639] 制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P364)

[0640] 

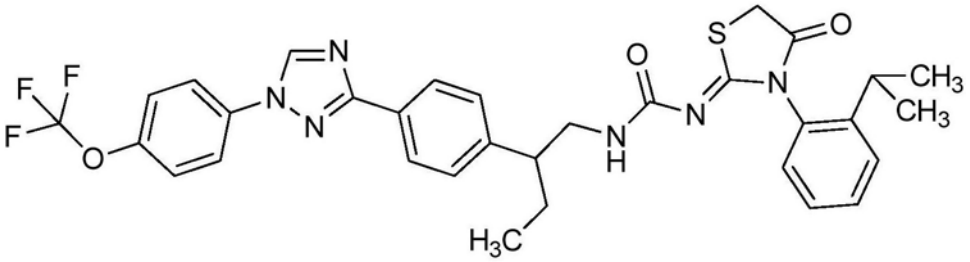
[0641] 标题化合物由3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)戊酰基叠氮化物/3-(4-(1-异氰酸酯基丁烷-2-基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C42a)和1-(2-异丙基-5-甲基苯基)硫脲制备,并且分离为粉红色固体(0.110g,43%)。

[0642] 制备(Z)-1-(3-(2-异丙基-5-甲氧基苯基)-4-氧代噻唑烷-2-亚基)-3-(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P683)

[0643] 

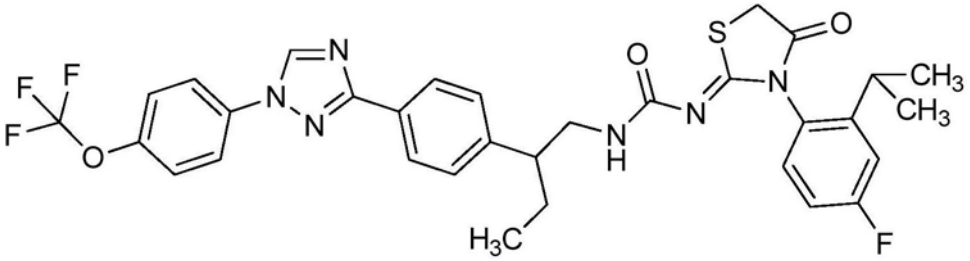
[0644] 标题化合物由3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)戊酰基叠氮化物/3-(4-(1-异氰酸酯基丁烷-2-基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C42a)和1-(2-异丙基-5-甲氧基苯基)硫脲(CA40)制备,并且分离为褐色泡沫(0.091g,47%)。

[0645] 制备(Z)-1-(3-(2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P209)

[0646] 

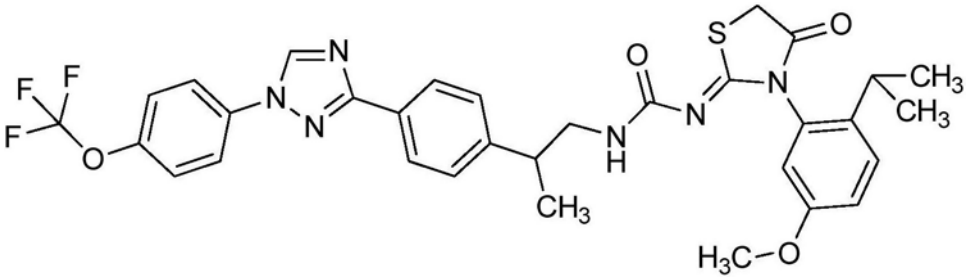
[0647] 标题化合物由3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)戊酰基叠氮化物/3-(4-(1-异氰酸酯基丁烷-2-基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C42a)和1-(2-异丙基苯基)硫脲制备,并且分离为褐色泡沫(0.041g,30%)。

[0648] 制备(Z)-1-(3-(4-氟-2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P1163)

[0649] 

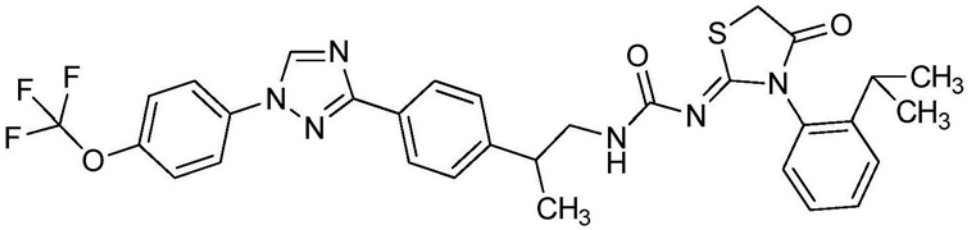
[0650] 标题化合物由3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)戊酰基叠氮化物/3-(4-(1-异氰酸酯基丁烷-2-基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C42a)和1-(4-氟-2-异丙基苯基)硫脲制备,并且分离为褐色泡沫(0.072g,30%)。

[0651] 制备(Z)-1-(3-(2-异丙基-5-甲氧基苯基)-4-氧代噻唑烷-2-亚基)-3-(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(P679)

[0652] 

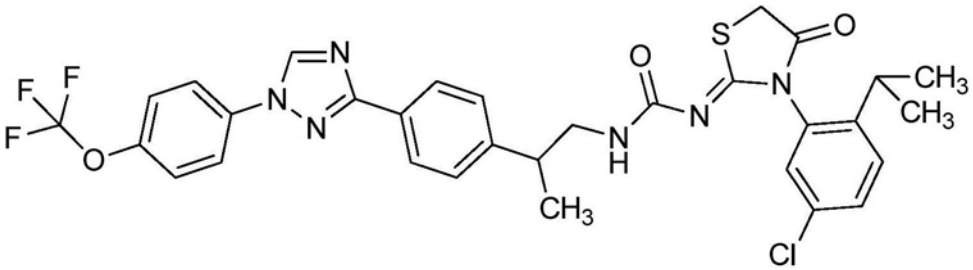
[0653] 标题化合物如实施例46中所述使用3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁酰基叠氮化物(C42)和1-(2-异丙基-5-甲氧基苯基)硫脲(CA40)制备,并且分离为褐色固体(0.118g,54%)。

[0654] 制备(Z)-1-(3-(2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(P205)

[0655] 

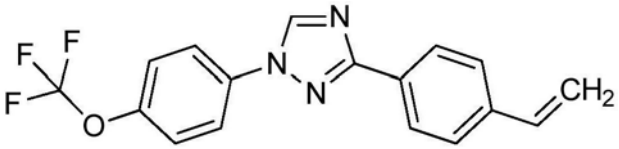
[0656] 标题化合物由3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁酰基叠氮化物(C42)和1-(2-异丙基苯基)硫脲制备,并且分离为褐色固体(0.105g,43%)。

[0657] 制备(Z)-1-(3-(5-氯-2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(FB49)

[0658] 

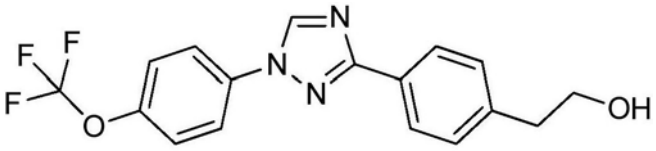
[0659] 标题化合物由3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁酰基叠氮化物(C42)和1-(5-氯-2-异丙基苯基)硫脲(CB32)制备,并且分离为褐色油(0.055g,22%)。

[0660] 实施例47:制备1-(4-(三氟甲氧基)苯基)-3-(4-乙烯基苯基)-1H-1,2,4-三唑(C43)

[0661] 

[0662] 将甲基三苯基溴化鏻(32.2g,90.0mmol)和1,8-二氮杂双环十一碳-7-烯(14.9mL,99.0mmol)溶解在四氢呋喃(260mL)中,回流30分钟。加入4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯甲醛(15.0g,45.0mmol),将反应在65℃加热5小时。溶液冷却,并且在室温搅拌过夜。将反应混合物倒入水中,并且用已烷提取。将有机层经无水硫酸钠干燥,过滤,浓缩。将粗制化合物通过使用0-70%乙酸乙酯/已烷作为洗脱剂的快速柱色谱纯化,提供为白色固体的标题化合物(10.4g,67%):^{1}H NMR(400MHz,$CDCl_3$)δ8.57(s,1H),8.16(d,J=8.3Hz,2H),7.80(d,J=9.0Hz,2H),7.58-7.47(m,2H),7.39(d,J=9.1Hz,2H),6.77(dd,J=17.6,10.9Hz,1H),5.84(dd,J=17.6,0.8Hz,1H),5.32(dd,J=10.9,0.8Hz,1H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.02;ESIMS m/z 332([M+H]$^{+}$)。

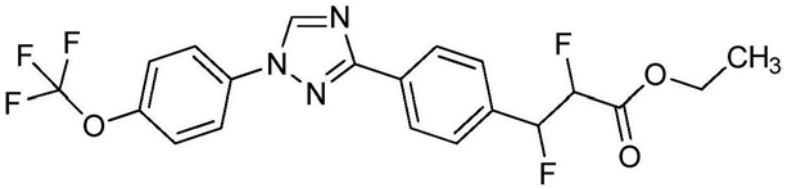
[0663] 实施例48:制备2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙醇(C44)

[0664] 

[0665] 向在四氢呋喃(50mL)中的1-(4-(三氟甲氧基)苯基)-3-(4-乙烯基苯基)-1H-1,2,

4-三唑(C43)(2.0g,6.0mmol),加入9-硼杂双环[3.3.1]壬烷(24mL,12.1mmol),将反应在室温搅拌4.5小时。加入氢氧化钠(3N,4.0mL,12.0mmol),随后过氧化氢(30%wt,1.5mL,15.1mmol)。将浅绿色溶液在室温搅拌过夜。将反应混合物用水稀释并且用乙酸乙酯提取。将有机层经无水硫酸钠干燥,干燥,浓缩,给出浅绿色油。将粗制化合物通过使用0-50%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化,提供为白色固体的标题化合物(1.5g,69%):mp 85-98℃;^{1}H NMR(400MHz,DMSO-d_6)δ9.37(s,1H),8.06(d,J=9.0Hz,2H),8.01(d,J=8.1Hz,2H),7.61(dd,J=9.2,1.0Hz,2H),7.41-7.30(m,2H),4.69(t,J=5.2Hz,1H),3.65(td,J=7.0,5.1Hz,2H),2.79(t,J=6.9Hz,2H);^{13}C NMR(101MHz,DMSO-d_6)δ162.18,147.08,143.70,141.45,135.72,129.39,128.23,127.93,125.96,122.57,121.10,61.90,61.90;^{19}F NMR(376MHz,DMSO-d_6)δ-56.98;ESIMS m/z 349([M+H]$^{+}$)。

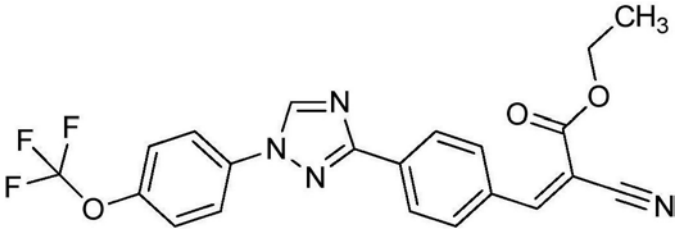
[0666] 实施例49:制备2,3-二氟-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸乙酯(C45)

[0667] 

[0668] 步骤1.将氢化钠(60%油浸,0.48g,12mmol)加入至干燥、烘干的圆底烧瓶,并且放置在氮气下。加入乙醚(9mL),随后无水乙醇(0.05mL),并且将反应在冰浴中冷却。逐滴加入2-氟乙酸乙酯(0.87mL,9.0mmol)。将反应在冰浴中搅拌15分钟(停止放气)。加入4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯甲醛(2.2g,6.5mmol)的固体部分。溶液缓慢变色至金黄色。将冰浴在1小时之后除去并且温热至室温,搅拌另外2小时直到将反应用饱和氯化铵水溶液猝灭,用乙醚稀释,在室温搅拌3天。将两相溶液用盐水稀释并且用乙酸乙酯(2×)提取。将有机层为经无水硫酸钠干燥的有机物,干燥,浓缩,给出橙色液体。将粗制物质通过使用0-100%乙腈/水作为洗脱剂的反相快速柱色谱纯化,提供作为粗制化合物的中间体2-氟-3-羟基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸乙酯(0.11g)。

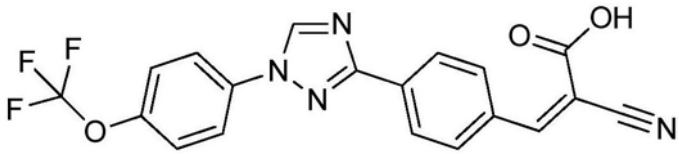
[0669] 步骤2.在0℃向在二氯甲烷(1.7mL)中的粗制的2-氟-3-羟基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸乙酯(0.11g,0.26mmol)加入Deoxo-fluor®(0.05mL,0.28mmol),搅拌30分钟。将反应混合物装到Celite®柱体上,并且通过使用0-60%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化,提供为黄色油的标题化合物(0.054g,47%):^{1}H NMR(400MHz,$CDCl_3$)δ8.58(d,J=1.9Hz,1H),8.32-8.14(m,2H),7.87-7.73(m,2H),7.50(d,J=8.1Hz,2H),7.39(d,J=8.6Hz,2H),6.11-5.76(m,1H),5.52-4.90(m,1H),4.27(dqd,J=23.6,7.1,2.1Hz,2H),1.27(dt,J=19.4,7.1Hz,3H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.04,-187.64,-187.68,-192.41,-192.44,-202.56,-202.60,-204.97,-205.00;ESIMS m/z 442([M+H]$^{+}$)。

[0670] 实施例50:制备(Z)-2-氰基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烯酸乙酯(C46)

[0671] 

[0672] 向在乙醇(11.5mL)中的4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯甲醛(3.0g,9.0mmol)加入2-氰基乙酸乙酯(0.95mL,8.9mmol)和吡咯烷(0.97mL,12mmol)。立即形成黄色沉淀物,加入另外的乙醇(10mL)。将反应在室温搅拌18小时,然后在Celite®上浓缩。通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供为白色固体的标题化合物(2.1g,50%):^{1}H NMR(400MHz,$CDCl_3$)δ8.61(s,1H),8.36-8.31(m,2H),8.29(s,1H),8.12(d,J=8.4Hz,2H),7.85-7.79(m,2H),7.41(d,J=8.3Hz,2H),4.41(q,J=7.1Hz,2H),1.42(t,J=7.1Hz,3H);^{13}C NMR(101MHz,$CDCl_3$)δ162.46,162.24,154.18,141.89,135.36,134.76,132.41,131.53,127.22,122.47,121.33,115.51,103.28,62.82,14.19;ESIMS m/z 429([M+H]$^{+}$)。

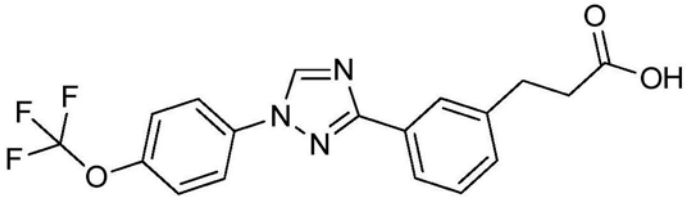
[0673] 实施例51:制备(Z)-2-氰基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烯酸(C47)

[0674] 

[0675] 向在四氢呋喃/甲醇/水(3:2:1,42mL)中的(Z)-2-氰基-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烯酸乙酯(C46)(2.5g,5.8mmol),加入氢氧化锂(2.5mL,7.5mmol),在室温搅拌18小时。将反应混合物在真空下浓缩,在冰浴中冷却,用氯化氢(2N)酸化。将沉淀物过滤,用冷水洗涤,提供为褐色固体的标题化合物(2.2g,82%):^{1}H NMR(400MHz,DMSO-d_6)δ9.49(s,1H),8.39(s,1H),8.28(d,J=8.5Hz,2H),8.18(d,J=8.5Hz,2H),8.13-8.08(m,2H),7.64(d,J=8.4Hz,2H);ESIMS m/z 401([M+H]$^{+}$)。

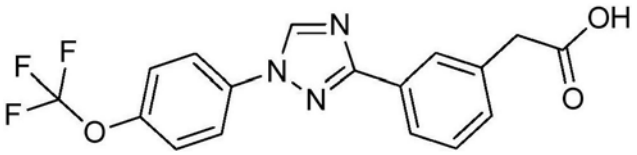
[0676] 下面的化合物根据实施例51中的步骤制备。

[0677] 制备3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸(CA13)

[0678] 

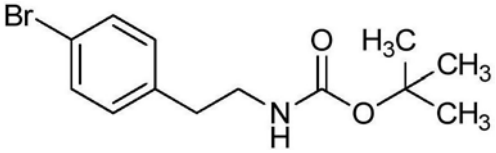
[0679] 标题化合物由3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸甲酯(CA1)制备,并且分离为褐色固体(9.09g,94%):^{1}H NMR(400MHz,DMSO-d_6)δ9.41(s,1H),8.13-8.04(m,2H),7.98(t,J=1.7Hz,1H),7.94(dt,J=7.7,1.4Hz,1H),7.62(d,J=8.8Hz,2H),7.43(t,J=7.6Hz,1H),7.35(dt,J=7.7,1.4Hz,1H),2.93(t,J=7.5Hz,2H),2.61(t,J=7.5Hz,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.99;ESIMS m/z 378([M+H]$^{+}$),376([M-H]$^{-}$)。

[0680] 制备2-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酸(CB23)

[0681] 

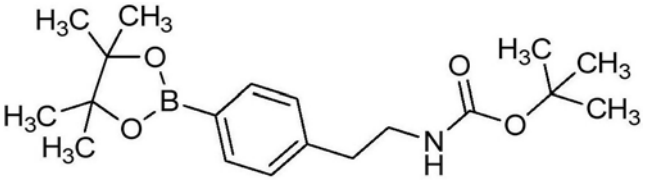
[0682] 标题化合物由2-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酸甲酯(CB11)制备,并且分离为浅褐色固体(4.28g,88%):^{1}H NMR(400MHz,DMSO-d_6)δ12.40(s,1H),9.42(s,1H),8.13-8.06(m,2H),8.06-7.96(m,2H),7.63(dq,J=8.0,1.0Hz,2H),7.47(td,J=7.6,0.6Hz,1H),7.38(dt,J=7.7,1.5Hz,1H),3.70(s,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 364([M+H]$^{+}$),362([M-H]$^{-}$)。

[0683] 实施例52:制备4-溴苯乙基氨基甲酸叔丁酯(C48)

[0684] 

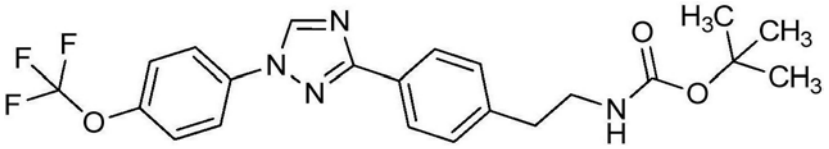
[0685] 向4-二甲基氨基吡啶(0.19g,1.5mmol)和二碳酸二叔丁酯(2.6g,12mmol)在二氯甲烷(40mL)中的搅拌溶液,加入4-溴苯乙基胺(1.6mL,10mmol),在室温继续搅拌48小时。将反应混合物直接吸附到硅胶上,并且通过使用0-40%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化,提供为白色固体的标题化合物(0.68g,22%):mp 58-59℃;^{1}H NMR(400MHz,$CDCl_3$)δ7.42(d,J=8.3Hz,2H),7.07(d,J=8.3Hz,2H),4.51(s,1H),3.43-3.27(m,2H),2.75(t,J=7.0Hz,2H),1.43(s,9H);^{13}C NMR(101MHz,$CDCl_3$)δ155.79,137.97,131.62,130.55,120.25,77.21,41.58,35.65,28.39;EIMS m/z 301([M]$^{+}$)。

[0686] 实施例53:制备4-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苯乙基氨基甲酸叔丁酯(C49)

[0687] 

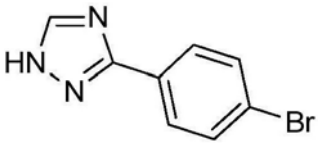
[0688] 将4-溴苯乙基氨基甲酸叔丁酯(C48)(0.68g,2.3mmol),双(频哪醇合)二硼(0.89g,3.5mmol),乙酸钾(0.69g,7.0mmol),[1,1′-双(二苯基膦基)二茂铁]二氯化钯(II)(0.10g,0.14mmol),和1,1′-双(二苯基膦基)二茂铁(0.075g,0.14mmol)在无水二氧六环(7mL)中的混合物在80℃加热18小时。反应冷却,用乙酸乙酯稀释,并且用水洗涤。将水层用乙酸乙酯提取。将合并的有机层经无水硫酸钠干燥,过滤,浓缩。将粗制化合物吸附到硅胶上,并且通过使用0-60%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化,提供为澄清的油的标题化合物(0.86g,104%):^{1}H NMR(400MHz,$CDCl_3$)δ7.75(d,J=7.9Hz,2H),7.23-7.17(m,2H),4.51(s,1H),3.46-3.28(m,2H),2.81(t,J=7.1Hz,2H),1.43(s,9H),1.34(s,12H);ESIMS m/z 348([M+H]$^{+}$)。

[0689] 实施例54:制备4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基氨基甲酸叔丁基酯(C50)

[0690] 

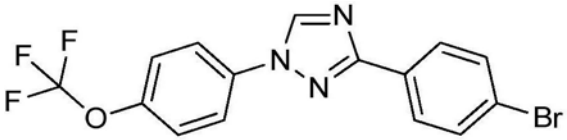
[0691] 将在20mL小瓶中的3-溴-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C1)(0.55g,1.8mmol),4-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苯乙基氨基甲酸叔丁酯(C49)(0.63g,1.8mmol),四(三苯基膦)钯(0)(0.21g,0.18mmol),和碳酸氢钠(0.33g,3.9mmol)在二氧六环/水(16mL,3:1)中的混合物盖住,并且在140℃于Biotage Initiator®微波反应器中加热30分钟,在容器侧有外部红外传感器温度监测。将反应混合物用乙酸乙酯稀释和用水洗涤。将水层用乙酸乙酯(2×)提取,和将合并的有机层经无水硫酸钠干燥,过滤,浓缩。将粗制物质装到Celite®柱体上,并且通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供为白色固体的标题化合物(0.48g,60%):mp 149-151℃;^{1}H NMR(400MHz,$CDCl_3$)δ8.56(s,1H),8.13(d,J=8.1Hz,2H),7.84-7.76(m,2H),7.42-7.35(m,2H),7.31(d,J=7.9Hz,2H),4.55(s,1H),3.51-3.34(m,2H),2.87(t,J=7.0Hz,2H),1.44(s,9H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 449([M+H]$^+$)。

[0692] 实施例55:制备3-(4-溴苯基)-1H-1,2,4-三唑(C51)

[0693] 

[0694] 将4-溴苯甲酰胺(28.0g,0.140mol)悬浮在1,1-二甲氧基-N,N-二甲基甲胺(50mL,420mmol)中,将溶液搅拌并且加热至90℃保持2小时。然后将溶液冷却至环境温度,加入乙醚(150mL)。将溶液冷却至0℃过夜,过滤,给出作为无色固体的(E)-4-溴-N-((二甲基氨基)亚甲基)苯甲酰胺(25.6g)。然后将该物质溶解在乙酸(50mL)中,将肼(3.50g,110mmol)缓慢加入(放热)至搅拌的溶液,固化。将混合物加热至90℃,增加搅拌棒。将固体经8小时缓慢溶解,然后冷却至环境温度,将溶液用水(35mL)稀释。将所得白色固体过滤并且在真空中干燥,提供作为无色固体的标题化合物(19.8g,88%):^{1}H NMR(400MHz,DMSO-d_6)δ13.91(s,1H),8.51(s,1H),8.01-7.93(m,2H),7.73-7.67(m,2H;ESIMS m/z 224,226([M+H]$^+$)。

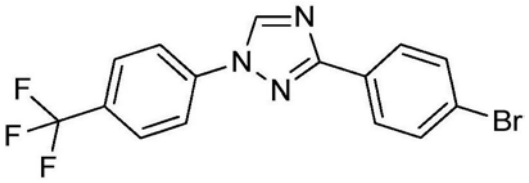
[0695] 实施例56:制备3-(4-溴苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C52)

[0696] 

[0697] 向1-碘-4-(三氟甲氧基)苯(15.0g,52.0mmol)在二甲基甲酰胺(90mL)和水(10mL)中的溶液,加入3-(4-溴苯基)-1H-1,2,4-三唑(C51)(11.0g,49.0mmol),碳酸铯(34.0g,104mmol),碘化亚铜(I)(2.80g,14.7mmol),和8-羟基喹啉(2.20g,15.0mmol),将溶液在140℃加热8小时。将冷却的溶液从固体层倾泻,用氢氧化铵(1N,100mL)溶液稀释,并且用乙醚(2×100mL)提取。将合并的有机层干燥并且浓缩,将褐色固体通过使用20%乙酸乙酯/己烷作为洗脱剂的短硅胶柱洗脱,给出为浅褐色固体的标题化合物(9.50g,50%):mp 111-113℃;^{1}H NMR(400MHz,$CDCl_3$)δ8.56(s,1H),8.07(d,J=8.6Hz,2H),7.79(d,J=8.8Hz,2H),

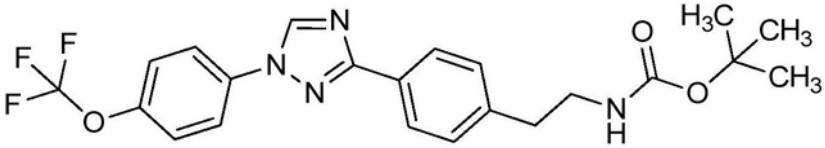
7.62(d,J=8.6Hz,2H),7.39(d,J=8.8Hz,2H);ESIMS m/z 384([M+H]$^+$)。

[0698] 制备3-(4-溴苯基)-1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑(C53)

[0699] 

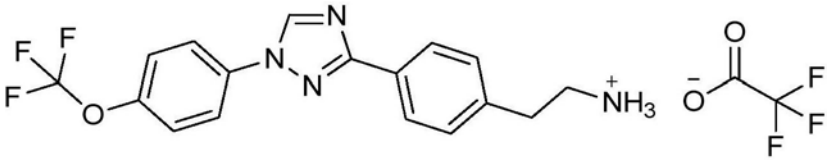
[0700] 标题化合物中所述实施例56使用1-碘-4-(三氟甲基)苯制备,提供为白色固体的标题化合物(3.21g,64%):^{1}H NMR(400MHz,$CDCl_3$)δ8.67(s,1H),8.06(d,J=8.6Hz,2H),7.89(d,J=8.5Hz,2H),7.78(d,J=8.5Hz,2H),7.59(d,J=8.6Hz,2H);ESIMS m/z 368,370([M+H]$^+$)。

[0701] 实施例57:制备4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基氨基甲酸叔丁基酯(C50)

[0702] 

[0703] 向3-(4-溴苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C52)(0.13g,0.32mmol)在甲苯(4mL)和水(1mL)中的溶液,加入(2-((叔丁氧基羰基)氨基)乙基)三氟硼酸钾(0.082g,0.33mmol),乙酸钯(II)(0.027g,0.027mmol),碳酸铯(0.33g,1.0mmol),和二环己基(2',6'-二异丙氧基-[1,1'-联苯]-2-yl)膦(0.016g,0.034mmol),将溶液在氮气下搅拌并且加热至95℃保持8小时。然后将溶液冷却,用乙醚(5mL)稀释,将其吸附至硅胶前置柱上。使用0-50%乙酸乙酯/己烷作为洗脱剂的快速柱色谱,提供为浅褐色固体的标题化合物(0.095g,63%):mp 149-153℃;^{1}H NMR(400MHz,$CDCl_3$)δ8.56(s,1H),8.18-8.10(m,2H),7.84-7.77(m,2H),7.43-7.35(m,2H),7.31(d,J=8.2Hz,2H),4.58(d,J=8.1Hz,1H),3.49-3.34(m,1H),2.87(t,J=7.0Hz,1H),1.44(s,9H);ESIMS m/z 449([M+H]$^+$)。

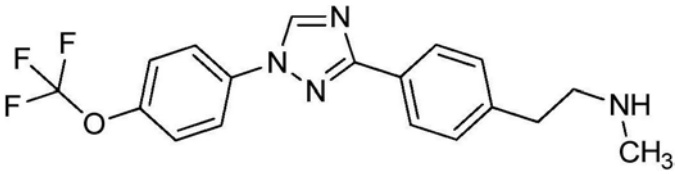
[0704] 实施例58:制备2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙烷胺(C55)

[0705] 

[0706] 向4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基氨基甲酸叔丁酯(C50)(0.35g,0.77mmol)在二氯甲烷(2.6mL)中的经搅拌和冷却(0℃)的溶液,加入三氟乙酸(0.060mL,0.78mmol),使得溶液缓慢温热至环境温度。18小时之后,加入另外量的三氟乙酸(0.060mL,0.78mmol)。24小时之后,加入三分之一等份的三氟乙酸(0.060mL,0.78mmol)。另外的24小时之后,将溶液浓缩,给出为褐色固体的标题化合物(0.325g,88%):^{1}H NMR(400MHz,DMSO-d_6)δ9.41(s,1H),8.08(dd,J=8.8,2.6Hz,4H),7.87(s,2H),7.63(d,J=8.3Hz,2H),7.43(d,J=8.3Hz,2H),3.17-3.06(m,2H),2.99-2.89(m,2H);ESIMS m/z 349([M+H]+)。

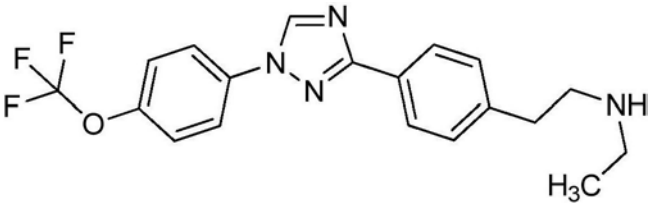
[0707] 下面的化合物根据实施例58中的步骤制备。

[0708] 制备N-甲基-2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙烷胺(CB24)

[0709] 

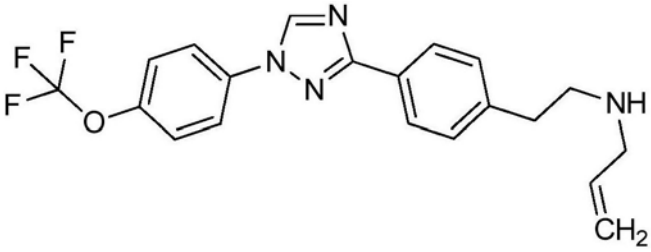
[0710] 标题化合物由制备甲基(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)氨基甲酸叔丁基酯(CB63),用碳酸氢钠溶液中和,并且用过量的三氟乙酸分离为黄色蜡状固体(5.73g,111%):^{1}H NMR(400MHz,$CDCl_3$)δ8.53(s,1H),8.12(d,J=8.2Hz,2H),7.77(d,J=9.0Hz,2H),7.37(dd,J=9.0,1.0Hz,2H),7.31(d,J=8.2Hz,2H),3.23-3.12(m,2H),3.05(dd,J=9.4,6.3Hz,2H),2.67(s,3H),1.29-1.22(m,1H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.04,-75.71;ESIMS m/z 363([M+H]$^{+}$)。

[0711] 制备N-乙基-2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙烷胺(CB25)

[0712] 

[0713] 标题化合物由乙基(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)氨基甲酸叔丁基酯(CB64)制备,用碳酸氢钠溶液中和,并且分离为橙色固体(0.167g,98%,80%纯度):^{1}H NMR(400MHz,$CDCl_3$)δ8.54(s,1H),8.17-8.06(m,2H),7.87-7.63(m,2H),7.37(dt,J=8.0,1.0Hz,2H),7.34-7.28(m,2H),3.21(s,2H),3.14-2.97(m,4H),1.84(s,1H),0.87(ddd,J=12.0,8.9,6.6Hz,3H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.04;ESIMS m/z 377([M+H]$^{+}$)。

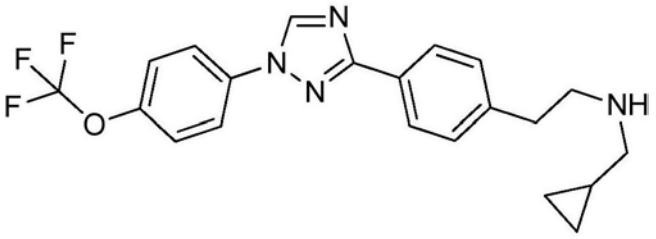
[0714] 制备N-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)丙-2-烯-1-胺(CB26)

[0715] 

[0716] 标题化合物由烯丙基(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)氨基甲酸叔丁基酯(CB65)制备,用碳酸氢钠溶液中和,并且分离为黄色固体(0.124g,90%):mp 110-120℃;^{1}H NMR(400MHz,$CDCl_3$)δ8.54(s,1H),8.14-8.07(m,2H),7.81-7.73(m,2H),7.42-7.34(m,2H),7.34-7.28(m,2H),5.92(ddt,J=16.9,10.2,6.6Hz,1H),5.43-5.22(m,2H),3.49(dt,J=6.6,1.2Hz,2H),3.19-2.92(m,5H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.04;ESIMS m/z 389([M+H]$^{+}$)。

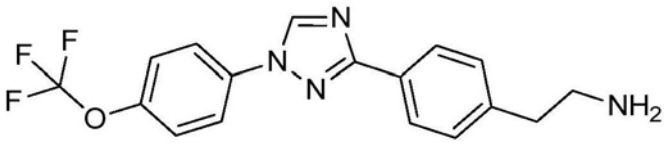
[0717] 制备N-(环丙基甲基)-2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯

基)乙烷胺(CB27)

[0718] 

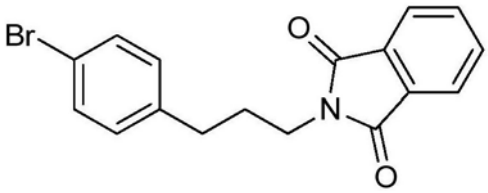
[0719] 标题化合物由(环丙基甲基)(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)氨基甲酸叔丁酯(CB66)制备,用碳酸氢钠溶液中和,并且分离为白色固体(0.125g,100%):mp 162-166℃;^{1}H NMR(400MHz,$CDCl_3$)δ8.54(s,1H),8.15-8.09(m,2H),7.81-7.75(m,2H),7.38(dq,J=8.9,0.9Hz,2H),7.34-7.29(m,2H),3.22(dd,J=10.2,6.0Hz,2H),3.09(dd,J=10.0,6.1Hz,2H),2.84(d,J=7.3Hz,2H),1.11(ddd,J=12.7,8.1,4.8Hz,1H),0.86(dd,J=12.8,5.8Hz,1H),0.69-0.58(m,2H),0.37-0.29(m,2H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 403([M+H]$^{+}$)。

[0720] 实施例58a:制备2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙烷胺(CA51)

[0721] 

[0722] 向4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基氨基甲酸叔丁酯(C50)(0.10g,0.22mmol)在二氯甲烷(1.6mL)中经搅拌和冷却(0℃)的溶液,加入三氟乙酸(0.19mL,0.25mmol),使得溶液缓慢温热至环境温度,并且搅拌过夜。将反应混合物浓缩,取入己烷中,浓缩直到得到固体。将固体溶解在二氯甲烷中,并且用饱和碳酸氢钠洗涤。将水层用二氯甲烷(2×)提取。将合并的有机层用饱和的碳酸氢钠洗涤。将有机层经硫酸镁干燥,过滤,和浓缩,给出为白色固体的标题化合物(0.075g,97%):^{1}H NMR(400MHz,$CDCl_3$)δ8.56(s,1H),8.18-8.07(m,2H),7.83-7.74(m,2H),7.41-7.29(m,4H),3.02(t,J=6.8Hz,2H),2.81(t,J=6.8Hz,2H),1.45-1.29(m,2H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.04。

[0723] 实施例59:制备2-(3-(4-溴苯基)丙基)异吲哚啉-1,3-二酮(C56)

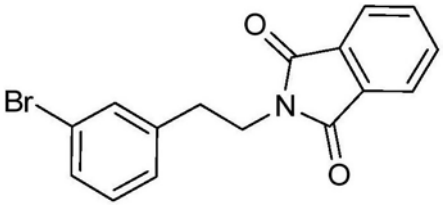
[0724] 

[0725] 向在装配有搅拌棒、氮气和添加漏斗并且在冰水浴中冷却的500mL圆底烧瓶中的3-(4-溴苯基)丙烷-1-醇(4.70g,21.9mmol),异吲哚啉-1,3-二酮(3.54g,24.0mmol)和三苯基膦(6.88g,26.2mmol),加入偶氮二甲酸二异丙酯(5.10mL,26.2mmol)。使得反应在周末温热至室温。将反应混合物吸附到Celite®上。通过使用5-20%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化,提供固体,所述固体在50℃的真空中干燥过夜,提供为白色固体的标题化合物(6.51g,87%):mp 88-90℃;^{1}H NMR(400MHz,$CDCl_3$)δ7.86-7.79(m,2H),7.71(dd,J=5.5,3.0Hz,2H),7.38-7.32(m,2H),7.11-7.04(m,2H),3.73(t,J=7.1Hz,2H),2.68-2.59

(m,2H),2.07-1.96(m,2H);ESIMS m/z 346[(M+2)$^+$]。

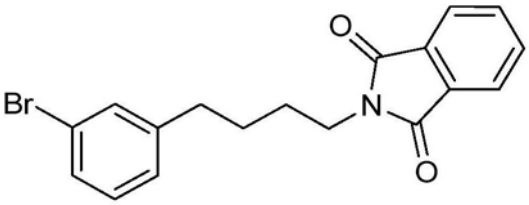
[0726] 下面的化合物根据实施例59中的步骤制备。

[0727] 制备2-(3-溴苯乙基)异吲哚啉-1,3-二酮(C57)

[0728] 

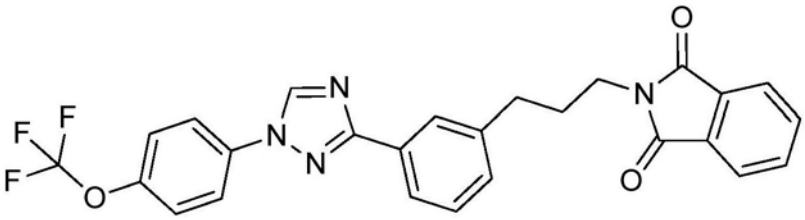
[0729] 标题化合物由2-(3-溴苯基)乙醇制备,提供为白色固体的标题化合物(3.92g,81%):mp 100-104℃;^{1}H NMR(400MHz,$CDCl_3$)δ7.88-7.81(m,2H),7.76-7.69(m,2H),7.43-7.39(m,1H),7.35(dt,J=7.4,1.8Hz,1H),7.22-7.13(m,2H),3.94-3.87(m,2H),2.99-2.92(m,2H);ESIMS m/z 332([M+2]$^+$)。

[0730] 制备2-(4-(3-溴苯基)丁基)异吲哚啉-1,3-二酮(C57a)

[0731] 

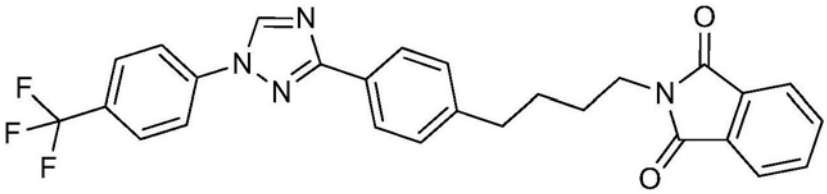
[0732] 标题化合物由4-(3-溴苯基)丁烷-1-醇(C86)制备,提供为白色固体的标题化合物(7.68g,62%):^{1}H NMR(400MHz,DMSO-d_6)δ7.91-7.78(m,4H),7.40(t,J=1.9Hz,1H),7.35(dt,J=7.2,2.0Hz,1H),7.28-7.15(m,2H),3.59(t,J=6.5Hz,2H),2.59(t,J=7.1Hz,2H),1.72-1.45(m,4H);^{13}C NMR(101MHz,DMSO-d_6)δ167.92,144.86,134.30,131.57,131.00,130.34,128.57,127.41,122.94,121.55,37.10,34.08,28.08,27.50;EIMS m/z 357,359。

[0733] 制备2-(3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)异吲哚啉-1,3-二酮(CA14)

[0734] 

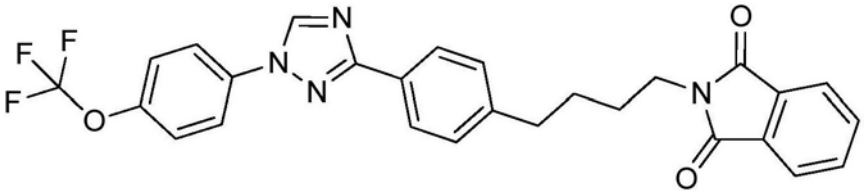
[0735] 标题化合物由3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-醇(CA45)制备,并且分离为浅黄色固体(4.49g,81%):^{1}H NMR(400MHz,DMSO-d_6)δ9.39(s,1H),8.18-8.02(m,2H),7.96(t,J=1.7Hz,1H),7.89(dt,J=7.7,1.5Hz,1H),7.87-7.76(m,4H),7.62(d,J=8.5Hz,2H),7.40(t,J=7.6Hz,1H),7.34(dt,J=7.7,1.5Hz,1H),3.65(t,J=7.0Hz,2H),2.73(t,J=7.7Hz,2H),1.97(p,J=7.5Hz,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.98;ESIMS m/z 493([M+H]$^+$)。

[0736] 制备2-(4-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)异吲哚啉-1,3-二酮(CA15)

[0737] 

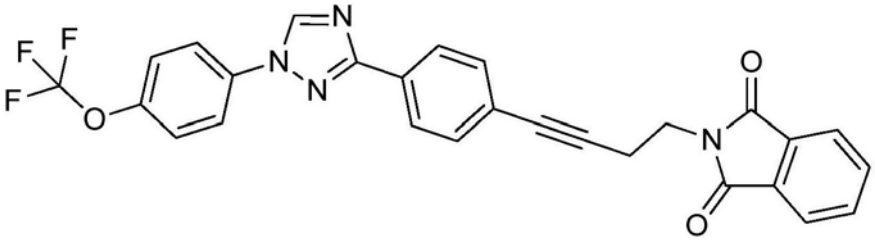
[0738] 标题化合物由4-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-醇(CA24)制备,进一步通过用乙醚/己烷研制纯化,分离为白色固体(0.372g,76%):^{1}H NMR(400MHz,$CDCl_3$)δ8.64(s,1H),8.15-8.06(m,2H),7.94-7.87(m,2H),7.87-7.81(m,2H),7.81-7.77(m,2H),7.71(dd,J=5.5,3.0Hz,2H),7.29(d,J=8.2Hz,2H),3.73(t,J=6.7Hz,2H),2.73(t,J=7.1Hz,2H),1.82-1.65(m,4H);^{19}F NMR(376MHz,$CDCl_3$)δ-62.48;ESIMS m/z 491([M+H]$^{+}$)。

[0739] 制备2-(4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)异吲哚啉-1,3-二酮(CA16)

[0740] 

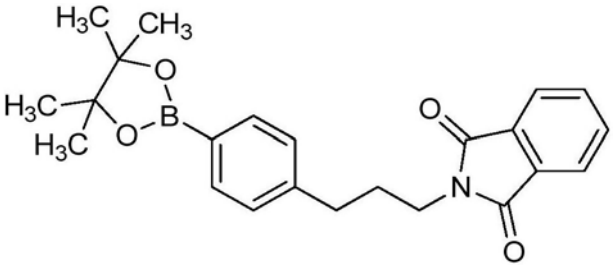
[0741] 标题化合物由4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-醇(CA25)制备,并且分离为白色固体(2.39g,59%):^{1}H NMR(400MHz,$CDCl_3$)δ8.55(s,1H),8.12-8.06(m,2H),7.84(dd,J=5.4,3.0Hz,2H),7.83-7.77(m,2H),7.75-7.66(m,2H),7.38(dd,J=9.2,1.0Hz,2H),7.29(d,J=8.2Hz,2H),3.73(t,J=6.7Hz,2H),2.72(t,J=7.1Hz,2H),1.85-1.61(m,4H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 507([M+H]$^{+}$)。

[0742] 制备2-(4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁-3-炔-1-基)异吲哚啉-1,3-二酮(CA17)

[0743] 

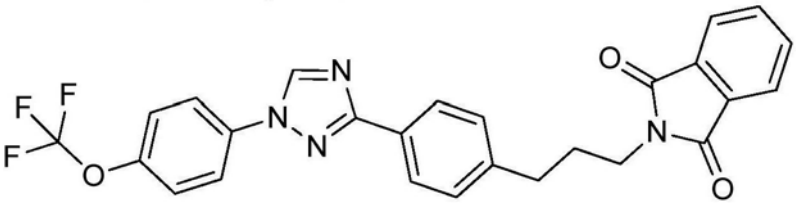
[0744] 标题化合物由4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁-3-炔-1-醇(CA23)制备,并且分离为白色固体(0.393g,74%):^{1}H NMR(400MHz,$CDCl_3$)δ8.56(s,1H),8.09(d,J=8.3Hz,2H),7.88(dd,J=5.5,3.1Hz,2H),7.79(d,J=8.9Hz,2H),7.73(dd,J=5.5,3.0Hz,2H),7.43(d,J=8.3Hz,2H),7.39(d,J=8.6Hz,2H),4.00(t,J=7.0Hz,2H),2.86(t,J=7.0Hz,2H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.02;ESIMS m/z 503([M+H]$^{+}$)。

[0745] 实施例60:制备2-(3-(4-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苯基)丙基)异吲哚啉-1,3-二酮(C58)

[0746] 

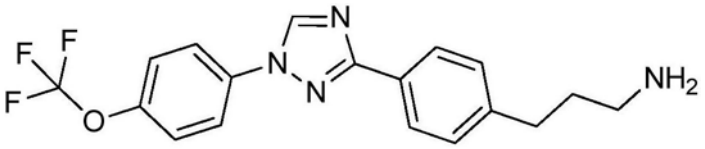
[0747] 向在装配有搅拌棒和氮气的200mL圆底烧瓶中的2-(3-(4-溴苯基)丙基)异吲哚啉-1,3-二酮(C56)(6.46g,18.8mmol),4,4,4',4',5,5,5',5'-八甲基-2,2'-双(1,3,2-二氧杂硼杂环戊烷)(7.15g,28.2mmol),[1,1′-双(二苯基膦基)二茂铁]二氯化钯(II)(0.831g,1.13mmol),和1,1′-双(二苯基膦基)二茂铁(0.624g,1.13mmol),加入乙酸钾(II)(5.53g,56.3mmol),随后二氧六环(56.9mL)。将反应混合物抽吸并且用氮气吹扫。将反应加热至80℃过夜。反应冷却。将反应混合物用乙酸乙酯稀释和用水洗涤。将水层用乙酸乙酯提取。将合并的有机层用盐水洗涤,经硫酸钠干燥,过滤,浓缩。通过使用5-20%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化,提供为黄色油的标题化合物(7.41g,101%):^{1}H NMR(400MHz,$CDCl_3$)δ7.82(dd,J=5.4,3.0Hz,2H),7.72-7.67(m,4H),7.23-7.17(m,2H),3.74(t,J=7.2Hz,2H),2.75-2.65(m,2H),2.08-1.97(m,2H),1.33(s,12H);^{13}C NMR(101MHz,$CDCl_3$)δ168.38,144.40,134.93,133.84,132.09,127.73,123.17,83.62,60.40,37.81,33.42,29.71,24.85;ESIMS m/z 392($[M+H]^+$)。

[0748] 实施例61:制备2-(3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)异吲哚啉-1,3-二酮(C59)

[0749] 

[0750] 向在10-20mL装配有搅拌棒的微波瓶(microwave vial)中的3-溴-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C1)(0.50g,1.6mmol),2-(3-(4-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苯基)丙基)异吲哚啉-1,3-二酮(C58)(0.64g,1.6mmol),碳酸氢钠(0.27g,3.3mmol),和四(三苯基膦)钯(0)(0.19g,0.16mmol),加入二氧六环(12mL)和水(4.1mL)。将反应盖住,在140℃于Biotage Initiator®微波反应器中加热30分钟,在容器侧有外部红外传感器温度监测。将混合物用乙酸乙酯稀释和用水洗涤。将水层用乙酸乙酯提取。将合并的有机层用盐水洗涤,经硫酸钠干燥,过滤,浓缩。通过使用0-30%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供固体,其在室内真空干燥过夜。得到为白色固体的标题化合物(0.42g,53%):mp 145-148℃;^{1}H NMR(400MHz,$CDCl_3$)δ8.54(d,J=0.8Hz,1H),8.08(d,J=8.1Hz,2H),7.84(ddd,J=5.5,3.0,0.8Hz,2H),7.82-7.77(m,2H),7.69(ddd,J=5.5,3.0,0.8Hz,2H),7.38(dt,J=9.0,1.0Hz,2H),7.31(d,J=8.0Hz,2H),3.78(t,J=7.2Hz,2H),2.79-2.71(m,2H),2.08(p,J=7.5Hz,2H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 493($[M+H]^+$)。

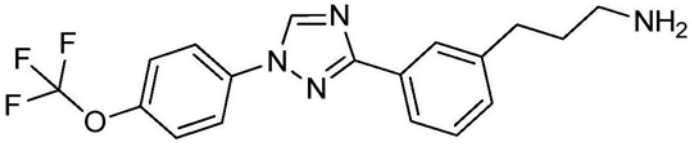
[0751] 实施例62:制备3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-胺(C60)

[0752] 

[0753] 向在25mL装配有搅拌棒、Vigreux柱和氮气的小瓶中的2-(3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)异吲哚啉-1,3-二酮(C59)(0.373g,0.758mmol),加入甲醇(7.58mL),随后单水合肼(0.110mL,2.27mmol)。将反应加热至50℃直到由LCMS确定反应完全。反应混合物冷却至室温和用二氯甲烷稀释。分层,将水层用二氯甲烷(2×)提取。将有机层用氢氧化钠(1N,4×)洗涤,灌注经过相分离器并且浓缩。将所得固体在50℃的真空中干燥72小时,提供为灰白色固体的标题化合物(0.262g,95%):^{1}H NMR(400MHz,DMSO-d_6)δ9.38(s,1H),8.10-8.04(m,2H),8.04-7.98(m,2H),7.66-7.59(m,2H),7.35(d,J=8.1Hz,2H),2.69-2.63(m,2H),2.56(t,J=6.9Hz,2H),1.74-1.59(m,2H),(NH_2未观测);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 363([M+H]$^{+}$)。

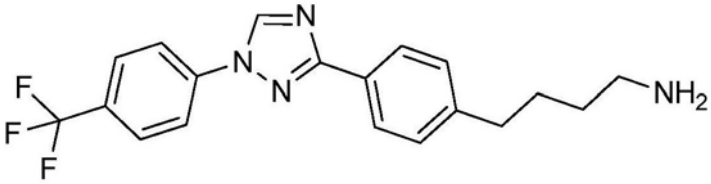
[0754] 下面的化合物根据实施例62中的步骤制备。

[0755] 制备3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-胺(CA18)

[0756] 

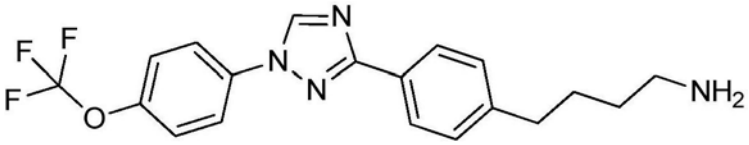
[0757] 标题化合物如实施例62中所述使用2-(3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)异吲哚啉-1,3-二酮(CA14)制备,并且分离为澄清的油(3.49g,100%):^{1}H NMR(400MHz,DMSO-d_6)δ9.40(s,1H),8.12-8.04(m,2H),8.00-7.88(m,2H),7.61(d,J=8.6Hz,2H),7.42(t,J=7.6Hz,1H),7.31(dt,J=7.7,1.5Hz,1H),2.71(q,J=9.0,7.9Hz,2H),2.57(t,J=6.8Hz,2H),1.74-1.62(m,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-57.01;ESIMS m/z 364([M+H]$^{+}$)。

[0758] 制备4-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA19)

[0759] 

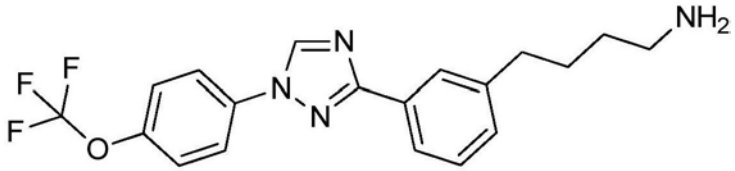
[0760] 标题化合物如实施例62中所述使用2-(4-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)异吲哚啉-1,3-二酮(CA15)制备,进一步用SCX柱纯化,并且分离为黄色固体(0.215g,79%):^{1}H NMR(400MHz,$CDCl_3$)δ8.64(s,1H),8.11(d,J=8.2Hz,2H),7.91(d,J=8.4Hz,2H),7.79(d,J=8.5Hz,2H),7.30(d,J=8.1Hz,2H),2.70(t,J=7.6Hz,2H),1.82-1.65(m,6H),1.54(d,J=8.1Hz,2H);^{19}F NMR(376MHz,$CDCl_3$)δ-62.48;ESIMS m/z 361([M+H]$^{+}$)。

[0761] 制备4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA20)

[0762] 

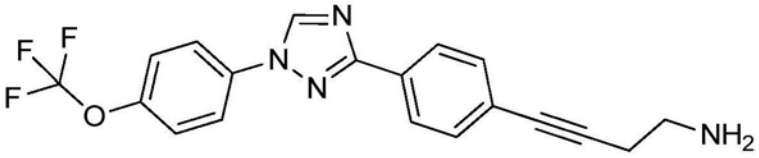
[0763] 标题化合物如实施例62中所述使用2-(4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)异吲哚啉-1,3-二酮(CA16)制备,并且分离为白色固体(1.76g,99%):^{1}H NMR(400MHz,$CDCl_3$)δ8.55(s,1H),8.10(d,J=8.2Hz,2H),7.84-7.77(m,2H),7.38(dt,J=8.1,1.0Hz,2H),7.33-7.27(m,2H),2.78-2.65(m,4H),1.76-1.64(m,2H),1.58-1.45(m,2H),1.08(bs,2H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 377([M+H]$^+$)。

[0764] 制备4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA21)

[0765] 

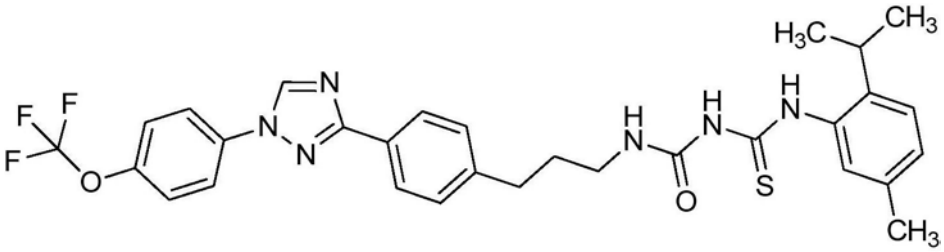
[0766] 标题化合物如实施例62中所述使用2-(4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)异吲哚啉-1,3-二酮(CA2)制备,并且分离为浅褐色残留物(1.94g,47%):^{1}H NMR(400MHz,DMSO-d_6)δ9.40(s,1H),8.13-8.05(m,2H),7.98-7.89(m,2H),7.67-7.56(m,2H),7.43(t,J=7.6Hz,1H),7.31(dt,J=7.8,1.5Hz,1H),2.67(t,J=7.7Hz,2H),2.57(t,J=6.9Hz,2H),1.64(tt,J=9.2,6.8Hz,2H),1.40(p,J=7.1Hz,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.98;ESIMS m/z 378([M+H]$^+$)。

[0767] 制备4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁-3-炔-1-胺(CA22)

[0768] 

[0769] 标题化合物如实施例62中所述使用2-(4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁-3-炔-1-基)异吲哚啉-1,3-二酮(CA17)制备,进一步使用SCX柱纯化,并且分离为黄色固体(0.304g,104%):^{1}H NMR(400MHz,$CDCl_3$)δ8.56(s,1H),8.16-8.09(m,2H),7.84-7.76(m,2H),7.56-7.48(m,2H),7.44-7.34(m,2H),2.95(t,J=6.3Hz,2H),2.59(t,J=6.3Hz,2H),(NH_2未观测);^{19}F NMR(376MHz,$CDCl_3$)δ-58.02;ESIMS m/z 373([M+H]$^+$)。

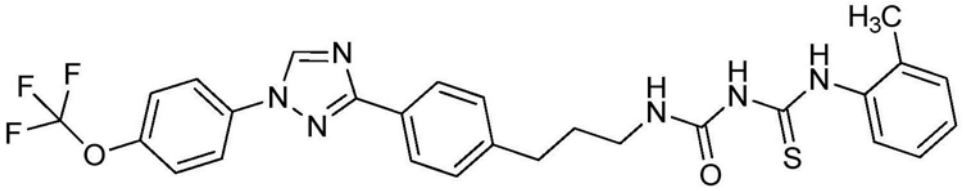
[0770] 实施例63:制备1-[(2-异丙基-5-甲基-苯基)氨基硫代甲酰基]-3-[3-[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丙基]脲(F21)

[0771] 

[0772] 向在25mL装配有搅拌棒和氮气的小瓶中的3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-胺(C60)(0.231g,0.639mmol),加入二氯甲烷(4.3mL),水(2.1mL),和碳酸氢钠(0.161g,1.92mmol)。一批加入三光气(0.0760g,0.255mmol),将反应剧烈搅拌直到通过LCMS观察到起始原料转化。将反应混合物用二氯甲烷稀释,灌注通过相分离器并且浓缩。将所得固体悬浮在100mL装配有搅拌棒和氮气的圆底烧瓶的乙腈(6.0mL)中。向其加入碳酸铯(0.229g,0.702mmol)和1-(2-异丙基-5-甲基苯基)硫脲(0.133g,0.639mmol)。将反应在室温搅拌过夜。将混合物用乙酸乙酯稀释和用水洗涤。将水层用乙酸乙酯提取。将合并的有机层经硫酸钠干燥,过滤,浓缩。通过使用0-30%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供混合的级分。将级分合并,通过使用0-30%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱再纯化,将所得固体在50℃的真空中干燥过夜,提供为白色固体的标题化合物(0.145g,38%)。

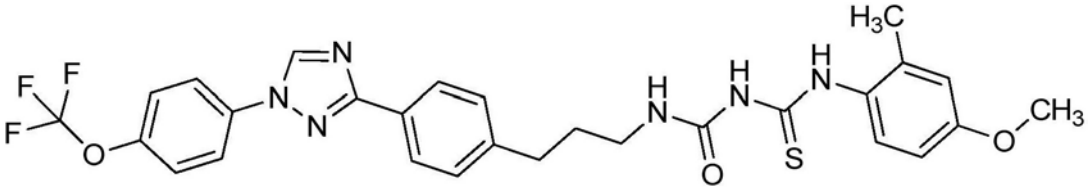
[0773] 下面的化合物根据实施例63中的步骤制备。

[0774] 制备1-(邻甲苯基氨基硫代甲酰基)-3-[3-[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丙基]脲(PC92)

[0775] 

[0776] 标题化合物如实施例63中所述使用3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-胺(C60)和1-(邻甲苯基)硫脲制备。使用乙酸钠替代碳酸氢钠。标题化合物分离为白色固体(0.061g,21%):^{1}H NMR(400MHz,DMSO-d_6)δ12.02(s,1H),10.06(s,1H),9.39(s,1H),8.14-7.99(m,3H),7.63(dt,J=7.3,1.3Hz,3H),7.45-7.35(m,2H),7.33-7.14(m,4H),7.09(t,J=5.6Hz,1H),3.17(q,J=6.6Hz,2H),2.70(t,J=7.6Hz,2H),2.21(s,3H),1.92-1.74(m,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 555([M+H]$^{+}$),553([M-H]$^{-}$)。

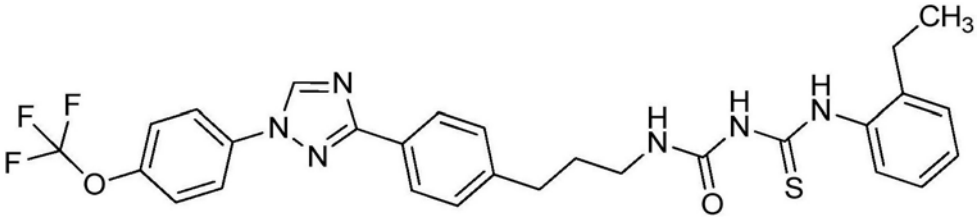
[0777] 制备1-[(4-甲氧基-2-甲基-苯基)氨基硫代甲酰基]-3-[3-[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丙基]脲(PC105)

[0778] 

[0779] 标题化合物如实施例63中所述使用3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-胺(C60)和1-(4-甲氧基-2-甲基苯基)硫脲制备。使用乙酸钠替代碳酸氢钠。标题化合物分离为白色固体(0.119g,38%):^{1}H NMR(400MHz,DMSO-d_6)δ11.79(s,1H),10.00(s,1H),9.39(s,1H),8.16-7.98(m,4H),7.70-7.57(m,2H),7.38(dd,J=8.4,1.9Hz,3H),7.08(t,J=5.7Hz,1H),6.84(d,J=2.9Hz,1H),6.77(dd,J=8.7,3.0Hz,1H),3.75(s,3H),3.16(q,J=6.5Hz,2H),2.70(dd,J=8.5,6.7Hz,2H),2.17(s,3H),1.81(p,J=7.2Hz,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 585([M+H]$^{+}$),583([M-H]$^{-}$)。

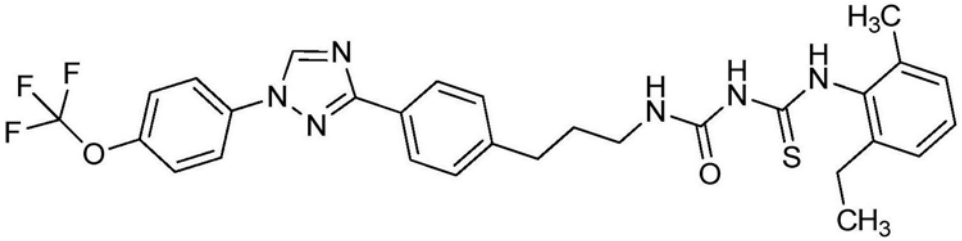
[0780] 制备1-[(2-乙基苯基)氨基硫代甲酰基]-3-[3-[4-[1-[4-(三氟甲氧基)苯基]-

1H-1,2,4-三唑-3-基]苯基]丙基]脲(PC93)

[0781] 

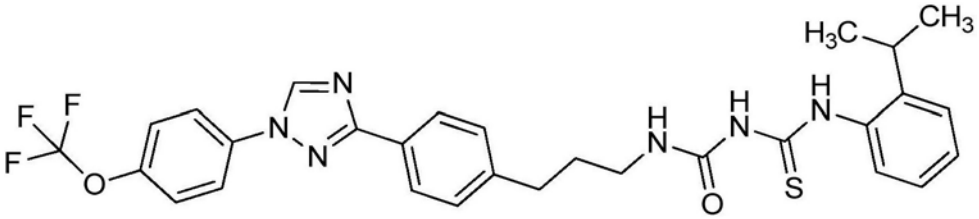
[0782] 标题化合物如实施例63中所述使用3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-胺(C60)和1-(2-乙基苯基)硫脲制备。使用乙酸钠替代碳酸氢钠。标题化合物分离为白色固体(0.112g,37%):^{1}H NMR(400MHz,DMSO-d_6)δ12.04(s,1H),10.07(s,1H),9.39(s,1H),8.16-7.98(m,4H),7.66-7.59(m,2H),7.59-7.52(m,1H),7.43-7.35(m,2H),7.31-7.19(m,3H),7.10(t,J=5.6Hz,1H),3.17(q,J=6.5Hz,2H),2.70(t,J=7.6Hz,2H),2.55(q,J=7.6Hz,2H),1.91-1.71(m,2H),1.17-1.11(m,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 569([M+H]$^+$),567([M-H]$^-$)。

[0783] 制备1-[(2-乙基-6-甲基-苯基)氨基硫代甲酰基]-3-[3-[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丙基]脲(PC101)

[0784] 

[0785] 标题化合物如实施例63中所述使用3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-胺(C60)和1-(2-乙基-6-甲基苯基)硫脲(CA39)制备。使用乙酸钠替代碳酸氢钠。标题化合物分离为白色固体(0.146g,47%):^{1}H NMR(400MHz,DMSO-d_6)δ11.59(s,1H),10.07(s,1H),9.39(s,1H),8.14-8.00(m,4H),7.68-7.59(m,2H),7.45-7.33(m,2H),7.23-7.02(m,4H),3.17(q,J=6.6Hz,2H),2.70(t,J=7.6Hz,2H),2.51(p,J=1.9Hz,2H),2.18(s,3H),1.90-1.73(m,2H),1.12(t,J=7.5Hz,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 583([M+H]$^+$),581([M-H]$^-$)。

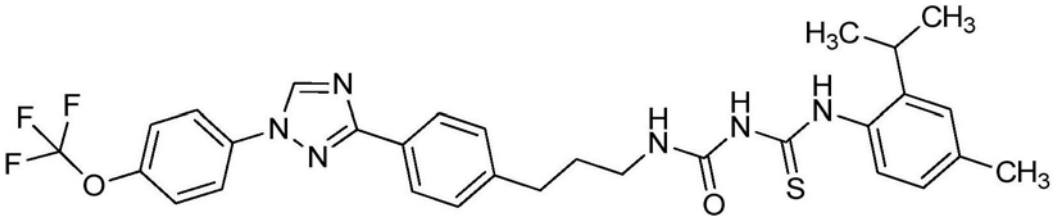
[0786] 制备1-[(2-异丙基苯基)氨基硫代甲酰基]-3-[3-[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丙基]脲(PC94)

[0787] 

[0788] 标题化合物如实施例63中所述使用3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-胺(C60)和1-(2-异丙基苯基)硫脲制备。使用乙酸钠替代碳酸氢钠。标题化合物分离为白色固体(0.161g,31%):^{1}H NMR(400MHz,DMSO-d_6)δ11.97(s,1H),10.08(s,1H),9.39(s,1H),8.13-7.99(m,4H),7.68-7.58(m,2H),7.49-7.31(m,4H),7.24(dtd,J=24.9,7.4,1.6Hz,2H),7.09(t,J=5.4Hz,1H),3.17(q,J=6.5Hz,2H),3.01(p,J=

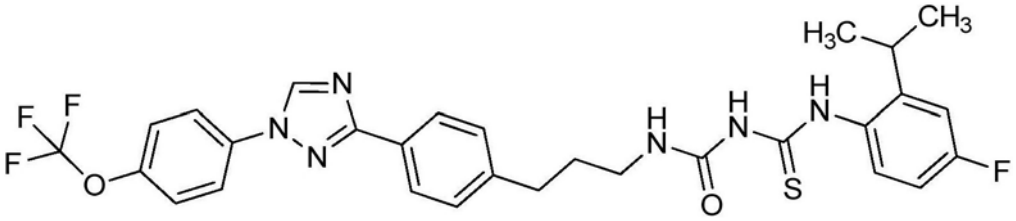
6.8Hz,1H),2.70(t,J=7.7Hz,2H),1.82(p,J=7.3Hz,2H),1.17(d,J=6.9Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 583([M+H]$^+$),581([M-H]$^-$)。

[0789] 制备1-[(2-异丙基-4-甲基-苯基)氨基硫代甲酰基]-3-[3-[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丙基]脲(PC102)

[0790] 

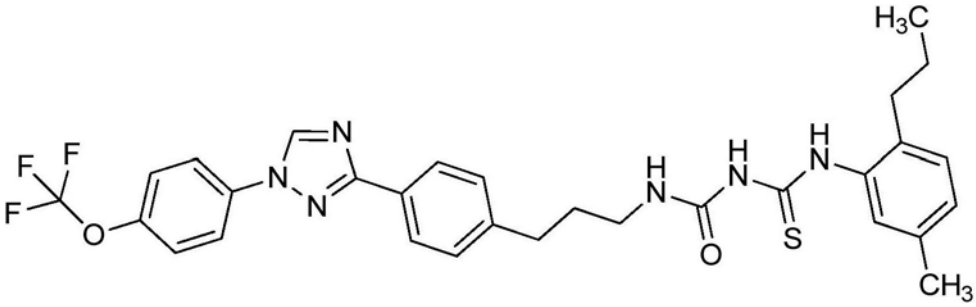
[0791] 标题化合物如实施例63中所述使用3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-胺(C60)和1-(2-异丙基-4-甲基苯基)硫脲制备。使用乙酸钠替代碳酸氢钠。标题化合物分离为白色固体(0.101g,32%):^{1}H NMR(400MHz,DMSO-d_6)δ11.87(s,1H),10.04(s,1H),9.39(s,1H),8.14-7.99(m,4H),7.71-7.55(m,2H),7.46-7.33(m,2H),7.26(d,J=8.0Hz,1H),7.14(d,J=2.0Hz,1H),7.08(t,J=5.6Hz,1H),7.04-6.95(m,1H),3.17(d,J=5.2Hz,2H),2.96(p,J=6.8Hz,1H),2.70(dd,J=8.6,6.6Hz,2H),2.31(s,3H),1.81(p,J=7.3Hz,2H),1.16(d,J=6.9Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 597([M+H]$^+$),595([M-H]$^-$)。

[0792] 制备1-[(4-氟-2-异丙基-苯基)氨基硫代甲酰基]-3-[3-[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丙基]脲(PC103)

[0793] 

[0794] 标题化合物如实施例63中所述使用3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-胺(C60)和1-(4-氟-2-异丙基苯基)硫脲制备。使用乙酸钠替代碳酸氢钠。标题化合物分离为白色固体(0.116g,36%):^{1}H NMR(400MHz,DMSO-d_6)δ11.85(s,1H),10.11(s,1H),9.39(s,1H),8.15-7.97(m,4H),7.63(dd,J=8.7,1.5Hz,2H),7.39(dd,J=8.5,5.7Hz,3H),7.16(dd,J=10.4,3.0Hz,1H),7.12-6.97(m,2H),3.26-3.11(m,2H),3.05-2.89(m,1H),2.70(dd,J=8.6,6.7Hz,2H),1.92-1.71(m,2H),1.16(d,J=6.8Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97,-114.39;ESIMS m/z 601([M+H]$^+$),599([M-H]$^-$)。

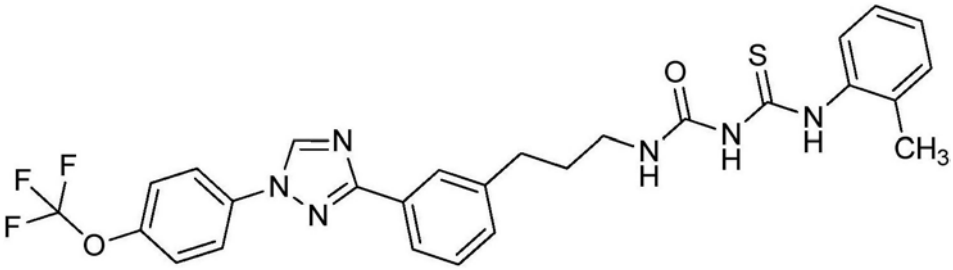
[0795] 制备1-[(5-甲基-2-丙基-苯基)氨基硫代甲酰基]-3-[3-[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丙基]脲(PC99)

[0796] 

[0797] 标题化合物如实施例63中所述使用3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-胺(C60)和1-(5-甲基-2-丙基苯基)硫脲(CA38)制备。使用乙酸钠替代碳酸氢钠。标题化合物分离为白色固体(0.111g,35%):^{1}H NMR(400MHz,DMSO-d_6)δ 12.01(s,1H),10.04(s,1H),9.39(s,1H),8.14-7.98(m,4H),7.62(d,J=8.6Hz,2H),7.45-7.33(m,3H),7.14(d,J=7.8Hz,1H),7.09(t,J=5.7Hz,1H),7.05-6.98(m,1H),3.17(q,J=6.5Hz,2H),2.70(t,J=7.6Hz,2H),2.49-2.41(m,2H),2.27(s,3H),1.81(dt,J=13.7,6.7Hz,2H),1.50(q,J=7.4Hz,2H),0.86(t,J=7.3Hz,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 597([M+H]$^{+}$),595([M-H]$^{-}$)。

[0798] 制备1-(邻甲苯基氨基硫代甲酰基)-3-[3-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丙基]脲(PC118)

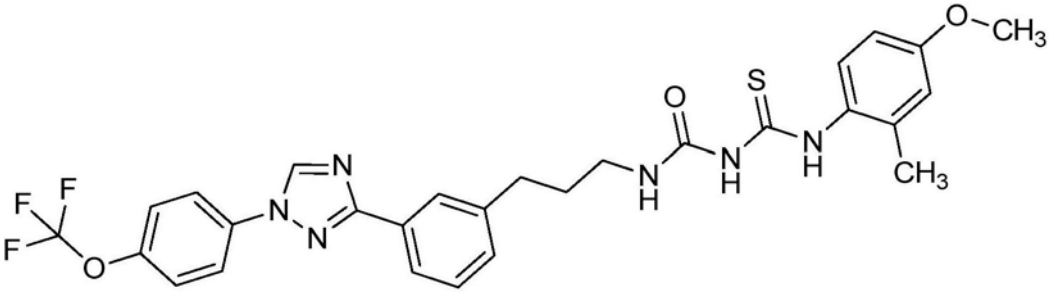
[0799]



[0800] 标题化合物如实施例63中所述使用3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-胺(CA18)和1-(邻甲苯基)硫脲制备。使用乙酸钠替代碳酸氢钠。标题化合物分离为白色固体(0.075g,24%):^{1}H NMR(400MHz,DMSO-d_6)δ12.03(s,1H),10.05(s,1H),9.40(s,1H),8.12-8.04(m,2H),8.01-7.92(m,2H),7.68-7.57(m,3H),7.46(t,J=7.6Hz,1H),7.36(dt,J=7.7,1.4Hz,1H),7.29-7.24(m,1H),7.24-7.13(m,2H),7.10(t,J=5.7Hz,1H),3.18(q,J=6.5Hz,2H),2.73(t,J=7.6Hz,2H),2.20(s,3H),1.93-1.74(m,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 555([M+H]$^{+}$),553([M-H]$^{-}$)。

[0801] 制备1-[(4-甲氧基-2-甲基-苯基)氨基硫代甲酰基]-3-[3-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丙基]脲(PC131)

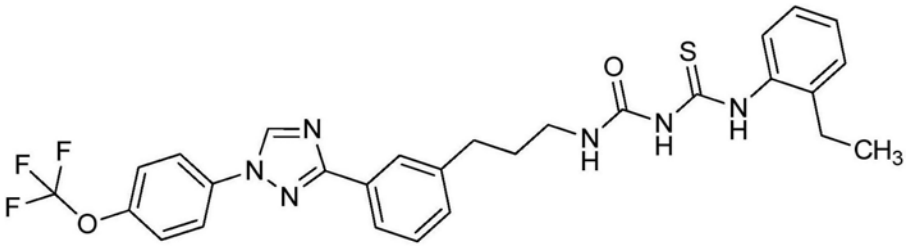
[0802]



[0803] 标题化合物如实施例63中所述使用3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-胺(CA18)和1-(4-甲氧基-2-甲基苯基)硫脲制备。使用乙酸钠替代碳酸氢钠。标题化合物分离为白色固体(0.103g,31%):^{1}H NMR(400MHz,DMSO-d_6)δ11.80(s,1H),10.00(s,1H),9.40(s,1H),8.13-8.04(m,2H),8.02-7.92(m,2H),7.67-7.57(m,2H),7.46(t,J=7.6Hz,1H),7.42-7.30(m,2H),7.08(t,J=5.6Hz,1H),6.83(d,J=2.9Hz,1H),6.76(dd,J=8.7,2.9Hz,1H),3.74(s,3H),3.17(q,J=6.5Hz,2H),2.73(t,J=7.6Hz,2H),2.16(s,3H),1.93-1.72(m,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 585([M+H]$^{+}$),583([M-H]$^{-}$)。

[0804] 制备1-[(2-乙基苯基)氨基硫代甲酰基]-3-[3-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丙基]脲(PC119)

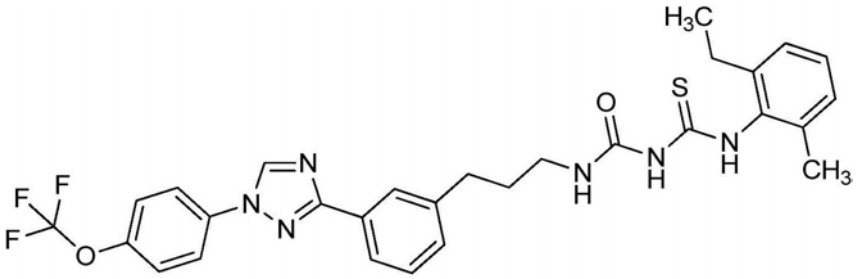
[0805]



[0806] 标题化合物如实施例63中所述使用3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-胺(CA18)和1-(2-乙基苯基)硫脲制备。使用乙酸钠替代碳酸氢钠。标题化合物分离为白色固体(0.175g,55%):^{1}H NMR(400MHz,DMSO-d_6)δ12.04(s,1H),10.07(s,1H),9.40(s,1H),8.13-8.04(m,2H),8.02-7.93(m,2H),7.65-7.59(m,2H),7.55(dt,J=6.5,3.7Hz,1H),7.46(t,J=7.6Hz,1H),7.36(dt,J=7.7,1.4Hz,1H),7.31-7.24(m,1H),7.21(dd,J=5.8,3.5Hz,2H),7.15-7.06(m,1H),3.18(q,J=6.5Hz,2H),2.73(t,J=7.6Hz,2H),2.55(t,J=7.5Hz,2H),1.90-1.74(m,2H),1.12(t,J=7.5Hz,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.98;ESIMS m/z 569([M+H]$^{+}$),567([M-H]$^{-}$)。

[0807] 制备1-[(2-乙基-6-甲基-苯基)氨基硫代甲酰基]-3-[3-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丙基]脲(PC127)

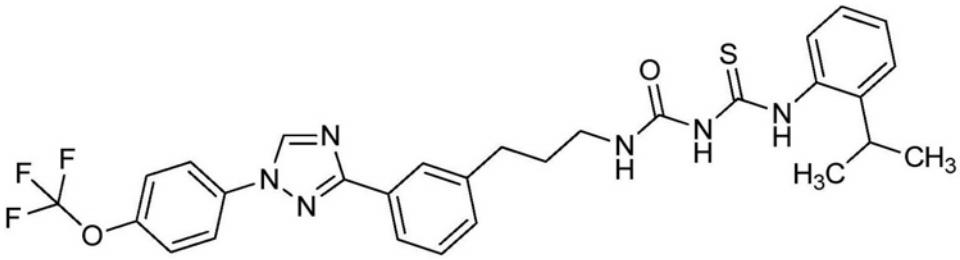
[0808]



[0809] 标题化合物如实施例63中所述使用3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-胺(CA18)和1-(2-乙基-6-甲基苯基)硫脲(CA39)制备。使用乙酸钠替代碳酸氢钠。标题化合物分离为白色固体(0.154g,47%):^{1}H NMR(400MHz,DMSO-d_6)δ11.59(s,1H),10.07(s,1H),9.41(s,1H),8.13-8.05(m,2H),8.03-7.92(m,2H),7.62(dt,J=7.8,1.1Hz,2H),7.46(t,J=7.6Hz,1H),7.36(dt,J=7.7,1.5Hz,1H),7.21-7.14(m,1H),7.14-7.04(m,3H),3.18(q,J=6.6Hz,2H),2.83-2.67(m,2H),2.48(d,J=2.6Hz,2H),2.17(s,3H),1.92-1.76(m,2H),1.11(t,J=7.6Hz,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 583([M+H]$^{+}$),581([M-H]$^{-}$)。

[0810] 制备1-[(2-异丙基苯基)氨基硫代甲酰基]-3-[3-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丙基]脲(PC120)

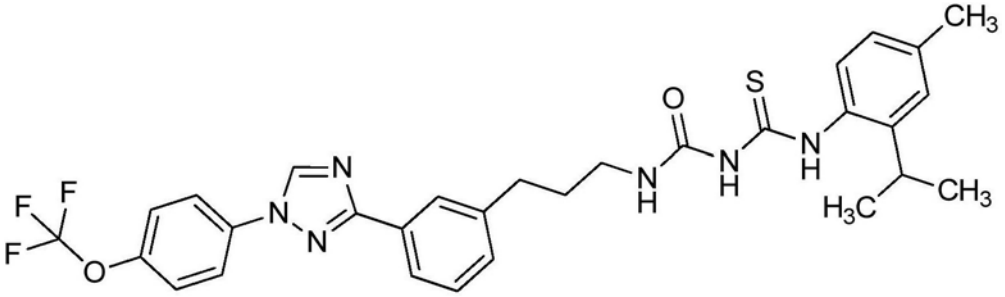
[0811]



[0812] 标题化合物如实施例63中所述使用3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-胺(CA18)和1-(2-异丙基苯基)硫脲制备。使用乙酸钠替代碳酸氢钠。标题化合物分离为白色固体(0.131g,40%):^{1}H NMR(400MHz,DMSO-d_6)δ11.97(s,1H),10.07(s,1H),9.41(s,1H),8.13-8.04(m,2H),8.01-7.93(m,2H),7.62(ddd,J=7.9,2.0,1.0Hz,2H),7.46(t,J=7.6Hz,1H),7.41(dd,J=7.8,1.5Hz,1H),7.39-7.32(m,2H),7.27(td,J=7.5,1.5Hz,1H),7.20(td,J=7.5,1.7Hz,1H),7.11(t,J=5.6Hz,1H),3.18(q,J=6.5Hz,2H),3.00(hept,J=6.8Hz,1H),2.73(t,J=7.7Hz,2H),1.93-1.75(m,2H),1.16(d,J=6.9Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 583([M+H]$^{+}$),581([M-H]$^{-}$)。

[0813] 制备1-[(2-异丙基-4-甲基-苯基)氨基硫代甲酰基]-3-[3-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丙基]脲(PC128)

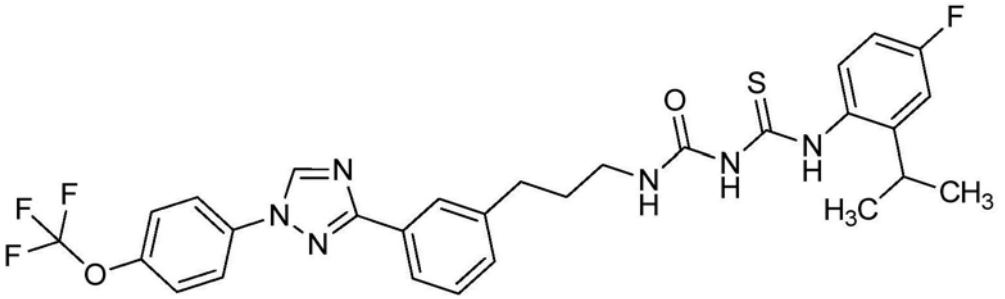
[0814]



[0815] 标题化合物如实施例63中所述使用3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-胺(CA18)和1-(2-异丙基-4-甲基苯基)硫脲制备。使用乙酸钠替代碳酸氢钠。标题化合物分离为白色固体(0.123g,37%):^{1}H NMR(400MHz,DMSO-d_6)δ11.87(s,1H),10.04(s,1H),9.41(s,1H),8.12-8.04(m,2H),8.02-7.91(m,2H),7.61(ddd,J=7.9,2.0,1.0Hz,2H),7.46(t,J=7.6Hz,1H),7.36(dt,J=7.7,1.4Hz,1H),7.26(d,J=8.0Hz,1H),7.13(d,J=1.9Hz,1H),7.09(t,J=5.6Hz,1H),7.04-6.97(m,1H),3.17(q,J=6.5Hz,2H),2.95(hept,J=7.0Hz,1H),2.82-2.64(m,2H),2.30(s,3H),1.91-1.77(m,2H),1.14(d,J=6.8Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 597([M+H]$^{+}$),595([M-H]$^{-}$)。

[0816] 制备1-[(4-氟-2-异丙基-苯基)氨基硫代甲酰基]-3-[3-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丙基]脲(PC129)

[0817]

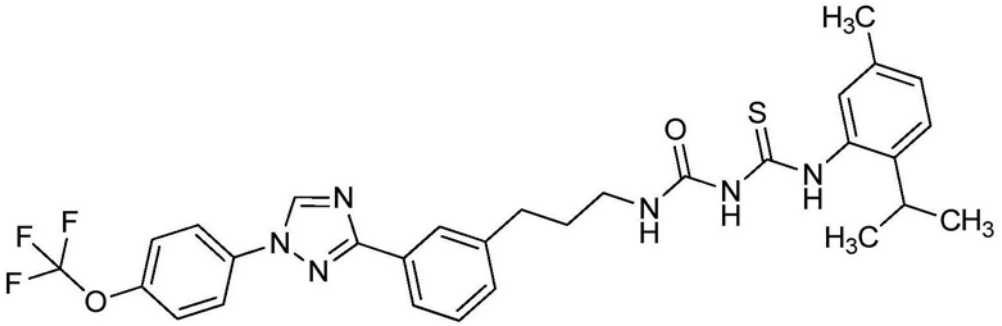


[0818] 标题化合物如实施例63中所述使用3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-胺(CA18)和1-(4-氟-2-异丙基苯基)硫脲制备。使用乙酸钠替代碳酸氢钠。标题化合物分离为白色固体(0.140g,41%):^{1}H NMR(400MHz,DMSO-d_6)δ11.85(s,1H),10.11(s,1H),9.41(s,1H),8.13-8.04(m,2H),8.02-7.92(m,2H),7.61(dq,J=7.8,1.0Hz,2H),7.46(t,J=7.6Hz,1H),7.43-7.31(m,2H),7.15(dd,J=10.4,3.0Hz,1H),7.10

(t,J=5.6Hz,1H),7.03(td,J=8.5,3.0Hz,1H),3.26-3.10(m,2H),2.97(pd,J=6.9,1.6Hz,1H),2.73(dd,J=8.5,6.7Hz,2H),1.90-1.76(m,2H),1.15(d,J=6.8Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97,-114.41;ESIMS m/z 601([M+H]$^+$),599([M-H]$^-$)。

[0819] 制备1-[(2-异丙基-5-甲基-苯基)氨基硫代甲酰基]-3-[3-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丙基]脲(PC124)

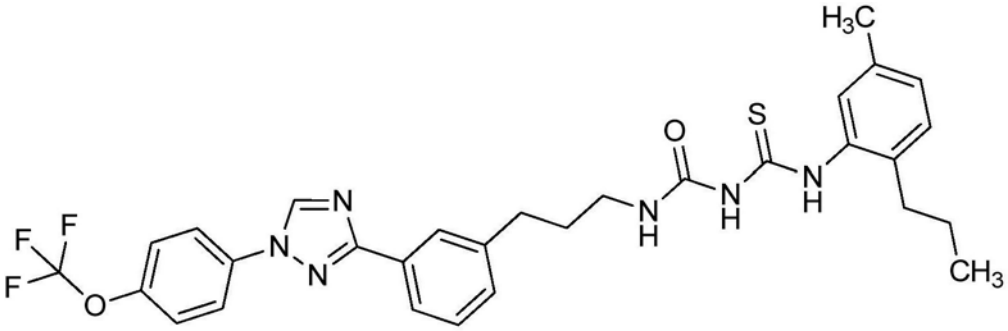
[0820]



[0821] 标题化合物如实施例63中所述使用3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-胺(CA18)和1-(2-异丙基-5-甲基苯基)硫脲制备。使用乙酸钠替代碳酸氢钠。标题化合物分离为白色固体(0.118g,35%):^{1}H NMR(400MHz,DMSO-d_6)δ11.91(s,1H),10.05(s,1H),9.40(s,1H),8.13-8.04(m,2H),8.03-7.93(m,2H),7.61(d,J=8.6Hz,2H),7.46(t,J=7.6Hz,1H),7.36(dt,J=7.8,1.4Hz,1H),7.21(dd,J=4.9,3.0Hz,2H),7.15-7.03(m,2H),3.18(q,J=6.5Hz,2H),2.95(hept,J=6.7Hz,1H),2.73(t,J=7.7Hz,2H),2.25(s,3H),1.90-1.76(m,2H),1.13(d,J=6.8Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.98;ESIMS m/z 597([M+H]$^+$),595([M-H]$^-$)。

[0822] 制备1-[(5-甲基-2-丙基-苯基)氨基硫代甲酰基]-3-[3-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丙基]脲(PC125)

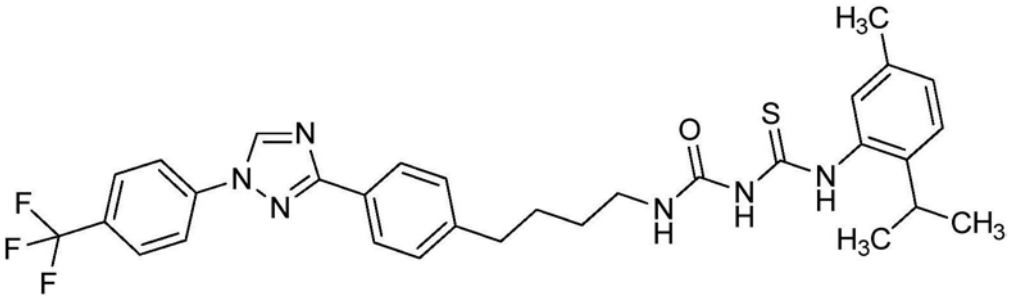
[0823]



[0824] 标题化合物如实施例63中所述使用3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-胺(CA18)和1-(5-甲基-2-丙基苯基)硫脲(CA38)制备。使用乙酸钠替代碳酸氢钠。标题化合物分离为白色固体(0.134g,40%):^{1}H NMR(400MHz,DMSO-d_6)δ12.01(s,1H),10.04(s,1H),9.40(s,1H),8.14-8.04(m,2H),8.03-7.92(m,2H),7.68-7.57(m,2H),7.45(t,J=7.6Hz,1H),7.42-7.32(m,2H),7.11(t,J=7.1Hz,2H),7.01(ddd,J=7.9,1.7,0.8Hz,1H),3.18(q,J=6.5Hz,2H),2.73(dd,J=8.7,6.6Hz,2H),2.45(dd,J=8.6,6.6Hz,2H),2.26(s,3H),1.91-1.75(m,2H),1.55-1.41(m,2H),0.84(t,J=7.3Hz,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.98;ESIMS m/z 597([M+H]$^+$),595([M-H]$^-$)。

[0825] 制备1-[(2-异丙基-5-甲基-苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC159)

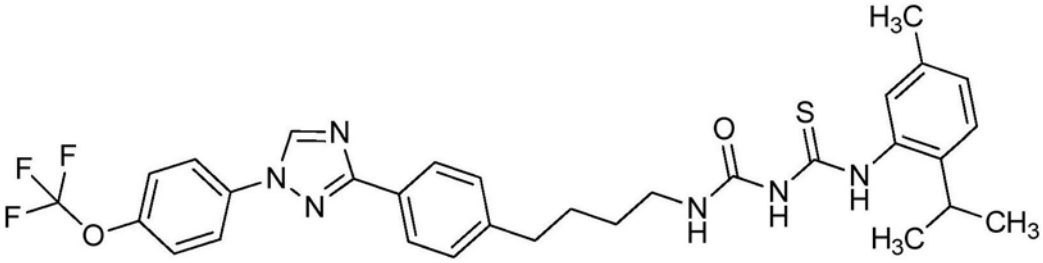
[0826]



[0827] 标题化合物如实施例63中所述使用4-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA19)和1-(2-异丙基-5-甲基苯基)硫脲制备,并且分离为白色固体(0.101g,37%):^{1}H NMR(400MHz,$CDCl_3$)δ11.86(bs,1H),9.77(bs,1H),8.65(s,1H),8.19-8.03(m,2H),7.91(d,J=8.4Hz,2H),7.85-7.72(m,2H),7.40-7.20(m,5H),5.68(bs,1H),3.29(d,J=17.5Hz,2H),3.13-2.94(m,1H),2.69(t,J=7.5Hz,2H),2.32(s,3H),1.69(s,2H),1.56(s,2H),1.21(d,J=6.9Hz,6H);^{19}F NMR(376MHz,$CDCl_3$)δ-62.48;ESIMS m/z 595($[M+H]^+$)。

[0828] 制备1-[(2-异丙基-5-甲基-苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC150)

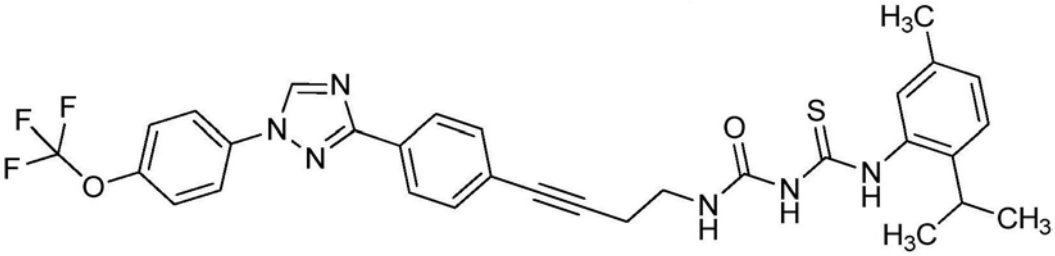
[0829]



[0830] 标题化合物如实施例63中所述使用4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA20)和1-(2-异丙基-5-甲基苯基)硫脲制备,并且分离为白色固体(0.153g,38%):^{1}H NMR(400MHz,DMSO-d_6)δ11.91(s,1H),10.01(s,1H),9.38(s,1H),8.11-8.00(m,4H),7.67-7.59(m,2H),7.37(d,J=8.2Hz,2H),7.22(d,J=8.1Hz,2H),7.12-7.05(m,1H),7.05-6.98(m,1H),3.17(q,J=6.5Hz,2H),2.94(hept,J=6.7Hz,1H),2.75-2.64(m,2H),2.25(s,3H),1.73-1.59(m,2H),1.58-1.43(m,2H),1.13(d,J=6.9Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 611($[M+H]^+$)。

[0831] 制备1-[(2-异丙基-5-甲基-苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁-3-炔]脲(PC160)

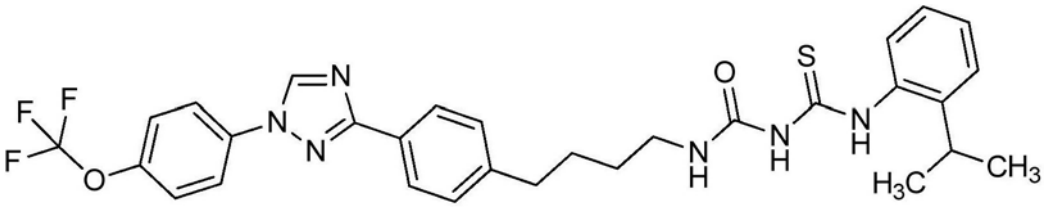
[0832]



[0833] 标题化合物如实施例63中所述使用4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁-3-炔-1-胺(CA22)和1-(2-异丙基-5-甲基苯基)硫脲制备,并且分离为白色固体(0.183g,39%):^{1}H NMR(400MHz,DMSO-d_6)δ11.90(s,1H),10.27(s,1H),9.43(s,

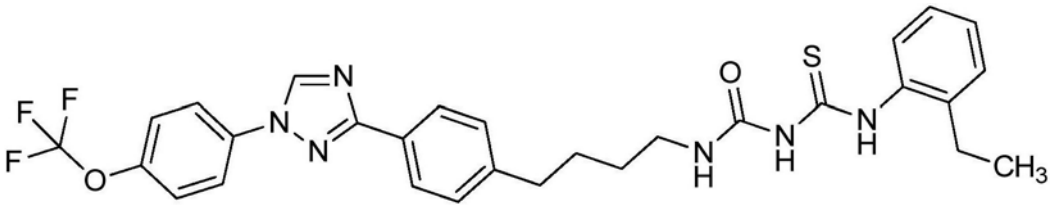
1H),8.09(m,4H),7.66-7.60(m,2H),7.60-7.55(m,2H),7.25-7.18(m,3H),7.09(d,J=7.7Hz,1H),3.40(q,J=6.4Hz,2H),2.96(hept,J=6.7Hz,1H),2.68(t,J=6.6Hz,2H),2.26(s,3H),1.14(d,J=6.8Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 607([M+H]$^+$)。

[0834] 制备1-[(2-异丙基苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC146)

[0835] 

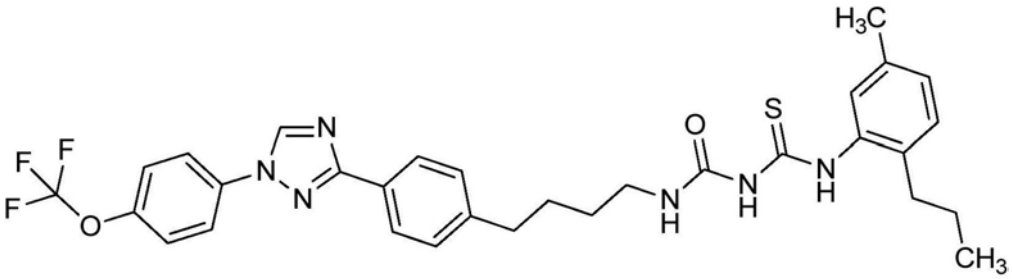
[0836] 标题化合物如实施例63中所述使用4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA20)和1-(2-异丙基苯基)硫脲制备,并且分离为白色固体(0.091g,38%):^{1}H NMR(300MHz,DMSO-d_6)δ11.95(s,1H),10.02(s,1H),9.37(s,1H),8.10-7.97(m,4H),7.61(d,J=8.6Hz,2H),7.44-7.29(m,4H),7.29-7.14(m,2H),7.01(s,1H),3.23-3.11(m,2H),3.04-2.90(m,1H),2.67(t,J=7.4Hz,2H),1.71-1.56(m,2H),1.56-1.42(m,2H),1.14(d,J=6.9Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 597([M+H]$^+$)。

[0837] 制备1-[(2-乙基苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC145)

[0838] 

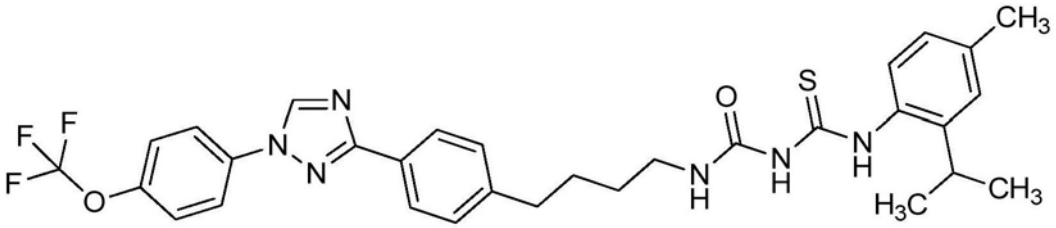
[0839] 标题化合物如实施例63中所述使用4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA20)和1-(2-乙基苯基)硫脲制备,并且分离为白色固体(0.111g,48%):^{1}H NMR(300MHz,DMSO-d_6)δ12.01(s,1H),10.01(s,1H),9.37(s,1H),8.09-7.98(m,4H),7.61(d,J=8.6Hz,2H),7.53(dd,J=5.6,3.7Hz,1H),7.35(d,J=8.1Hz,2H),7.30-7.23(m,1H),7.19(dd,J=5.8,3.5Hz,2H),7.01(s,1H),3.22-3.11(m,2H),2.73-2.63(m,2H),2.52(d,J=7.6Hz,2H),1.63(m,2H),1.49(m,2H),1.15-1.04(m,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 583([M+H]$^+$)。

[0840] 制备1-[(5-甲基-2-丙基-苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC151)

[0841] 

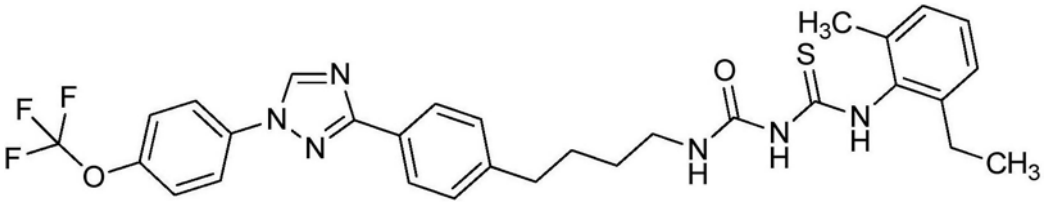
[0842] 标题化合物如实施例63中所述使用4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA20)和1-(5-甲基-2-丙基苯基)硫脲(CA38)制备,并且分离为白色固体(0.110g,45%):^{1}H NMR(300MHz,DMSO-d_6)δ11.98(s,1H),9.97(s,1H),9.36(s,1H),8.03(m,4H),7.60(d,J=8.7Hz,2H),7.35(m,3H),7.11(d,J=7.8Hz,1H),7.05-6.92(m,2H),3.16(q,J=6.3Hz,2H),2.66(t,J=7.5Hz,2H),2.42(t,J=7.6Hz,2H),2.24(s,3H),1.72-1.56(m,2H),1.56-1.38(m,4H),0.82(t,J=7.3Hz,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 611([M+H]$^{+}$)。

[0843] 制备1-[(2-异丙基-4-甲基-苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC154)

[0844] 

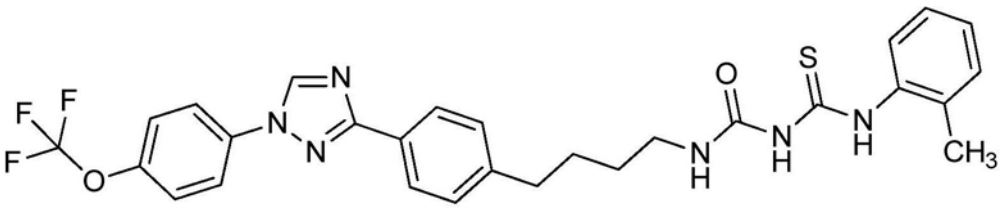
[0845] 标题化合物如实施例63中所述使用4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA20)和1-(2-异丙基-4-甲基苯基)硫脲制备,并且分离为白色固体(0.100g,41%):^{1}H NMR(300MHz,DMSO-d_6)δ11.84(s,1H),9.97(s,1H),9.36(s,1H),8.11-7.96(m,4H),7.60(d,J=8.5Hz,2H),7.35(d,J=8.0Hz,2H),7.23(d,J=8.0Hz,1H),7.11(s,1H),6.98(d,J=8.0Hz,2H),3.15(q,J=6.3Hz,2H),3.00-2.83(m,1H),2.66(t,J=7.6Hz,2H),2.28(s,3H),1.72-1.55(m,2H),1.55-1.42(m,2H),1.12(d,J=6.8Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 611([M+H]$^{+}$)。

[0846] 制备1-[(2-乙基-6-甲基-苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC153)

[0847] 

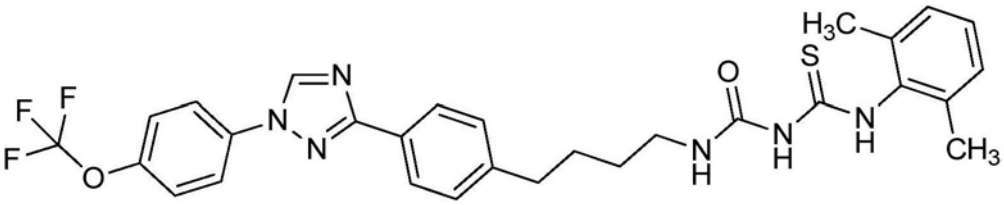
[0848] 标题化合物如实施例63中所述使用4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA20)和1-(2-乙基-6-甲基苯基)硫脲(CA39)制备,并且分离为白色固体(0.141g,59%):^{1}H NMR(400MHz,DMSO-d_6)δ11.59(s,1H),10.00(s,1H),9.37(s,1H),8.12-7.98(m,4H),7.66-7.54(m,2H),7.37(d,J=8.2Hz,2H),7.24-7.13(m,1H),7.11(d,J=2.9Hz,2H),7.00(d,J=5.7Hz,1H),3.18(q,J=6.5Hz,2H),2.75-2.61(m,2H),2.49-2.44(m,2H),2.16(s,3H),1.65(q,J=7.7Hz,2H),1.52(q,J=7.3Hz,2H),1.11(t,J=7.6Hz,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 597([M+H]$^{+}$)。

[0849] 制备1-(邻甲苯基氨基硫代甲酰基)-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC144)

[0850] 

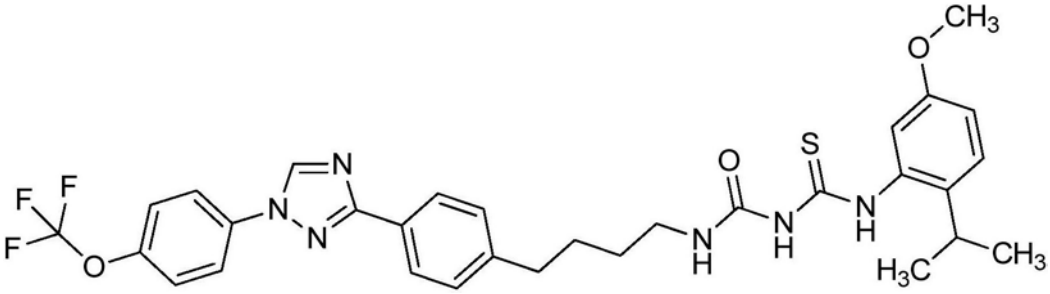
[0851] 标题化合物如实施例63中所述使用4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA20)和1-(邻甲苯基)硫脲制备,并且分离为白色固体(0.097g,43%):^{1}H NMR(400MHz,DMSO-d_6)δ12.01(s,1H),9.98(s,1H),9.37(s,1H),8.14-7.90(m,4H),7.66-7.54(m,3H),7.37(d,J=8.1Hz,2H),7.31-7.23(m,1H),7.23-7.14(m,2H),7.02(s,1H),3.23-3.12(m,2H),2.68(t,J=7.5Hz,2H),2.20(s,3H),1.70-1.59(m,2H),1.57-1.44(m,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 569([M+H]$^{+}$)。

[0852] 制备1-[(2,6-二甲基苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC152)

[0853] 

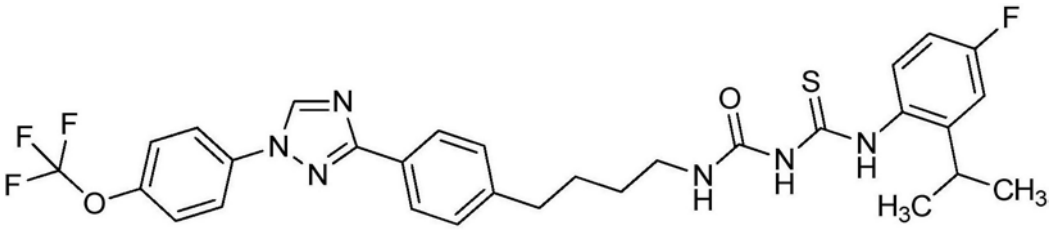
[0854] 标题化合物如实施例63中所述使用4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA20)和1-(2,6-二甲基苯基)硫脲制备,并且分离为白色固体(0.122g,53%):^{1}H NMR(400MHz,DMSO-d_6)δ11.53(s,1H),9.98(s,1H),9.37(s,1H),8.11-8.00(m,4H),7.66-7.58(m,2H),7.37(d,J=8.1Hz,2H),7.09(q,J=5.2Hz,3H),6.99(t,J=5.7Hz,1H),3.18(q,J=6.5Hz,2H),2.69(t,J=7.6Hz,2H),2.15(s,6H),1.66(p,J=7.5Hz,2H),1.51(p,J=6.9Hz,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 583([M+H]$^{+}$)。

[0855] 制备1-[(2-异丙基-5-甲氧基-苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC156)

[0856] 

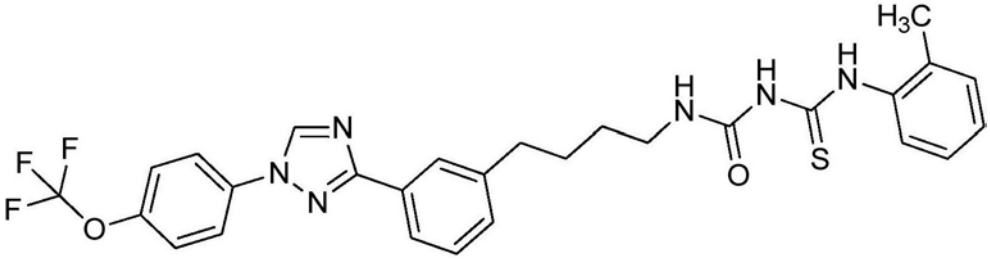
[0857] 标题化合物如实施例63中所述使用4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA20)和1-(2-异丙基-5-甲氧基苯基)硫脲(CA40)制备,并且分离为白色固体(0.114g,46%):^{1}H NMR(400MHz,DMSO-d_6)δ12.01(s,1H),10.01(s,1H),9.36(s,1H),8.13-7.97(m,4H),7.68-7.56(m,2H),7.37(d,J=8.1Hz,2H),7.23(d,J=8.7Hz,1H),7.11(d,J=2.7Hz,1H),7.01(d,J=5.9Hz,1H),6.84(dd,J=8.6,2.8Hz,1H),3.71(s,3H),3.18(q,J=6.5Hz,2H),2.92(hept,J=6.9Hz,1H),2.68(t,J=7.6Hz,2H),1.65(p,J=7.6Hz,2H),1.51(q,J=7.2Hz,2H),1.13(d,J=6.8Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 627([M+H]$^{+}$)。

[0858] 制备1-[(4-氟-2-异丙基-苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC155)

[0859] 

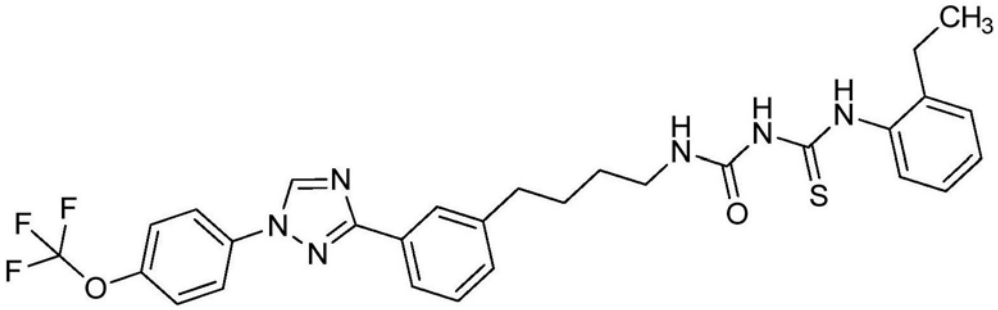
[0860] 标题化合物如实施例63中所述使用4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA20)和1-(4-氟-2-异丙基苯基)硫脲制备,并且分离为白色固体(0.089g,36%):^{1}H NMR(400MHz,DMSO-d_6)δ11.85(s,1H),10.04(s,1H),9.37(s,1H),8.11-7.99(m,4H),7.61(d,J=8.8Hz,2H),7.44-7.31(m,3H),7.14(dd,J=10.4,2.9Hz,1H),7.09-6.96(m,2H),3.18(q,J=6.5Hz,2H),3.03-2.90(m,1H),2.68(t,J=7.5Hz,2H),1.70-1.58(m,2H),1.56-1.44(m,2H),1.15(d,J=6.8Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97,-114.40;ESIMS m/z 615([M+H]$^{+}$)。

[0861] 制备1-(邻甲苯基氨基硫代甲酰基)-3-[4-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC170)

[0862] 

[0863] 标题化合物如实施例63中所述使用4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA21)和1-(邻甲苯基)硫脲制备,并且分离为白色固体(0.102g,35%):^{1}H NMR(400MHz,DMSO-d_6)δ12.03(s,1H),10.01(s,1H),9.39(s,1H),8.11-8.05(m,2H),7.98(t,J=1.7Hz,1H),7.94(dt,J=7.7,1.4Hz,1H),7.67-7.57(m,3H),7.44(t,J=7.6Hz,1H),7.34(dt,J=7.7,1.5Hz,1H),7.28-7.23(m,1H),7.23-7.13(m,2H),7.03(t,J=5.7Hz,1H),3.19(q,J=6.5Hz,2H),2.72(t,J=7.6Hz,2H),2.19(s,3H),1.74-1.60(m,2H),1.52(p,J=6.9Hz,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 569([M+H]$^{+}$)。

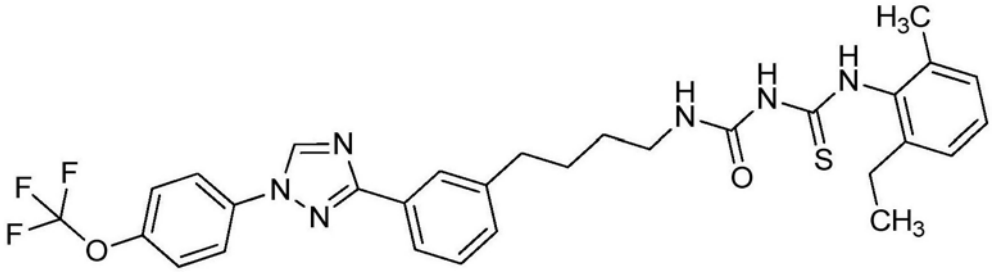
[0864] 制备1-[(2-乙基苯基)氨基硫代甲酰基]-3-[4-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC171)

[0865] 

[0866] 标题化合物如实施例63中所述使用4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA21)和1-(2-乙基苯基)硫脲制备,并且分离为白色固体(0.113g,38%):^{1}H NMR(400MHz,DMSO-d_6)δ12.05(s,1H),10.04(s,1H),9.41(s,1H),8.13-8.06(m,2H),8.00(d,J=1.7Hz,1H),7.96(dt,J=7.7,1.4Hz,1H),7.69-7.60(m,2H),7.56(dd,J=5.6,3.6Hz,1H),7.46(t,J=7.6Hz,1H),7.36(dt,J=7.7,1.5Hz,1H),7.31-7.26(m,1H),7.26-7.19(m,2H),7.05(t,J=5.6Hz,1H),3.21(q,J=6.5Hz,2H),2.74(t,J=7.6Hz,2H),2.59-2.53(m,2H),1.69(tt,J=9.0,6.6Hz,2H),1.54(p,J=6.9Hz,2H),1.12(t,J=7.5Hz,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 583([M+H]$^+$)。

[0867] 制备1-[(2-乙基-6-甲基-苯基)氨基硫代甲酰基]-3-[4-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC179)

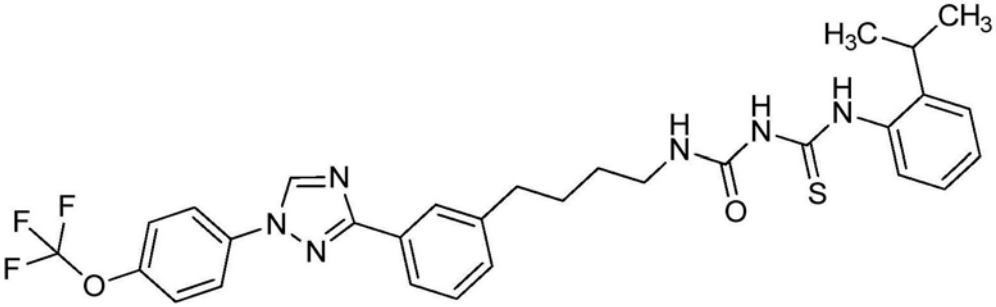
[0868]



[0869] 标题化合物如实施例63中所述使用4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA21)和1-(2-乙基-6-甲基苯基)硫脲(CA39)制备,并且分离为白色固体(0.143g,47%):^{1}H NMR(400MHz,DMSO-d_6)δ11.62(s,1H),10.04(s,1H),9.40(s,1H),8.12-8.06(m,2H),8.00(t,J=1.6Hz,1H),7.96(dt,J=7.7,1.4Hz,1H),7.64(ddt,J=7.8,1.9,0.9Hz,2H),7.46(t,J=7.6Hz,1H),7.36(dt,J=7.7,1.4Hz,1H),7.22-7.15(m,1H),7.10(dq,J=6.3,1.8Hz,2H),7.02(t,J=5.7Hz,1H),3.21(q,J=6.5Hz,2H),2.74(t,J=7.6Hz,2H),2.48(td,J=7.5,1.9Hz,2H),2.17(s,3H),1.69(p,J=7.6Hz,2H),1.62-1.48(m,2H),1.11(t,J=7.6Hz,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 597([M+H]$^+$)。

[0870] 制备1-[(2-异丙基苯基)氨基硫代甲酰基]-3-[4-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC172)

[0871]

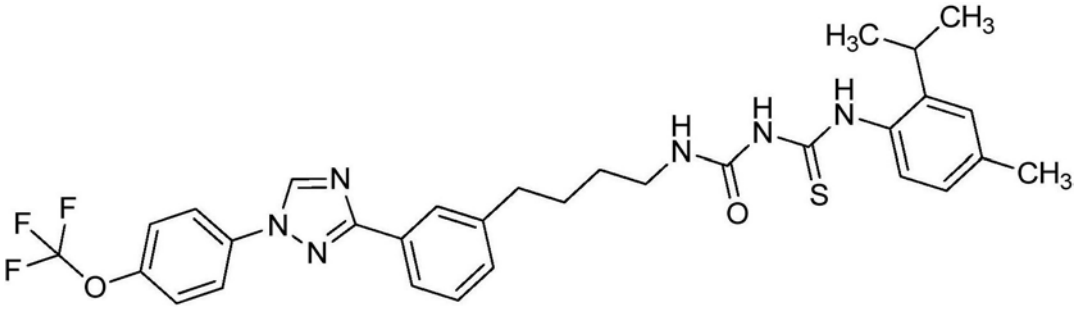


[0872] 标题化合物如实施例63中所述使用4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA21)和1-(2-异丙基苯基)硫脲制备,并且分离为白色固体(0.072g,24%):^{1}H NMR(400MHz,DMSO-d_6)δ11.99(s,1H),10.05(s,1H),9.41(s,1H),8.13-8.07(m,2H),8.00(t,J=1.7Hz,1H),7.96(dt,J=7.8,1.4Hz,1H),7.64(dq,J=7.7,1.0Hz,2H),7.46(t,J=7.6Hz,1H),7.42(dd,J=7.9,1.5Hz,1H),7.36(ddd,J=7.8,3.3,1.6Hz,

2H),7.28(td,J=7.5,1.5Hz,1H),7.21(td,J=7.5,1.7Hz,1H),7.05(t,J=5.7Hz,1H),3.21(q,J=6.4Hz,2H),3.00(p,J=6.9Hz,1H),2.74(t,J=7.6Hz,2H),1.69(p,J=7.8Hz,2H),1.54(p,J=7.0Hz,2H),1.16(d,J=6.8Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 597([M+H]$^+$)。

[0873] 制备1-[(2-异丙基-4-甲基-苯基)氨基硫代甲酰基]-3-[4-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC180)

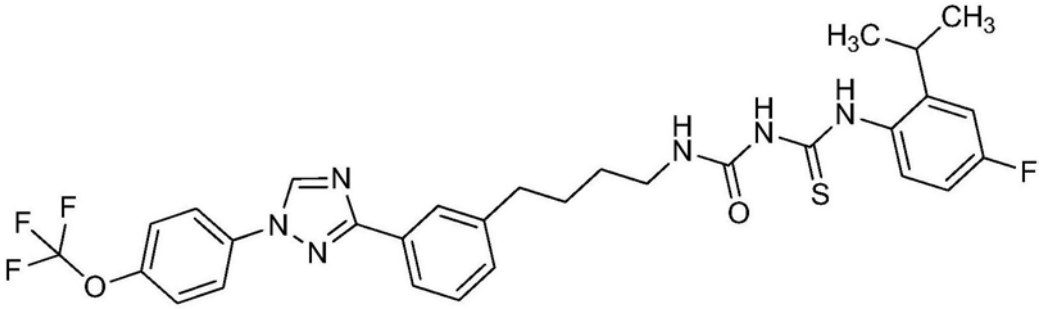
[0874]



[0875] 标题化合物如实施例63中所述使用4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA21)和1-(2-异丙基-4-甲基苯基)硫脲制备,并且分离为白色固体(0.139g,45%):^{1}H NMR(400MHz,DMSO-d_6)δ11.89(s,1H),10.01(s,1H),9.40(s,1H),8.13-8.07(m,2H),8.00(d,J=1.7Hz,1H),7.96(dt,J=7.7,1.4Hz,1H),7.64(dq,J=7.8,1.0Hz,2H),7.46(t,J=7.6Hz,1H),7.36(dt,J=7.7,1.4Hz,1H),7.26(d,J=8.0Hz,1H),7.15(dd,J=2.0,0.9Hz,1H),7.07-6.97(m,2H),3.20(q,J=6.5Hz,2H),2.95(p,J=6.9Hz,1H),2.74(t,J=7.6Hz,2H),2.32(s,3H),1.68(p,J=7.3Hz,2H),1.61-1.47(m,2H),1.15(d,J=6.8Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 611([M+H]$^+$)。

[0876] 制备1-[(4-氟-2-异丙基-苯基)氨基硫代甲酰基]-3-[4-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC181)

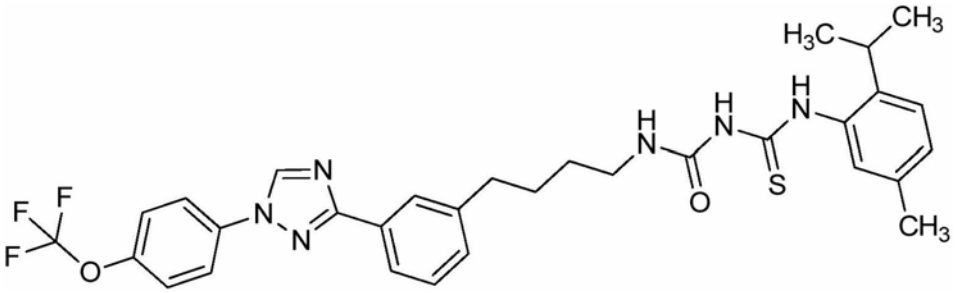
[0877]



[0878] 标题化合物如实施例63中所述使用4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA21)和1-(4-氟-2-异丙基苯基)硫脲制备,并且分离为白色固体(0.114g,36%):^{1}H NMR(400MHz,DMSO-d_6)δ11.87(s,1H),10.09(s,1H),9.41(s,1H),8.13-8.07(m,2H),8.00(t,J=1.6Hz,1H),7.96(dt,J=7.7,1.4Hz,1H),7.69-7.61(m,2H),7.46(t,J=7.6Hz,1H),7.43-7.33(m,2H),7.16(dd,J=10.4,3.0Hz,1H),7.05(td,J=8.3,2.9Hz,2H),3.20(q,J=6.5Hz,2H),3.05-2.90(m,1H),2.74(t,J=7.6Hz,2H),1.76-1.62(m,2H),1.61-1.48(m,2H),1.15(d,J=6.8Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96,-114.42;ESIMS m/z 615([M+H]$^+$)。

[0879] 制备1-[(2-异丙基-5-甲基-苯基)氨基硫代甲酰基]-3-[4-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC176)

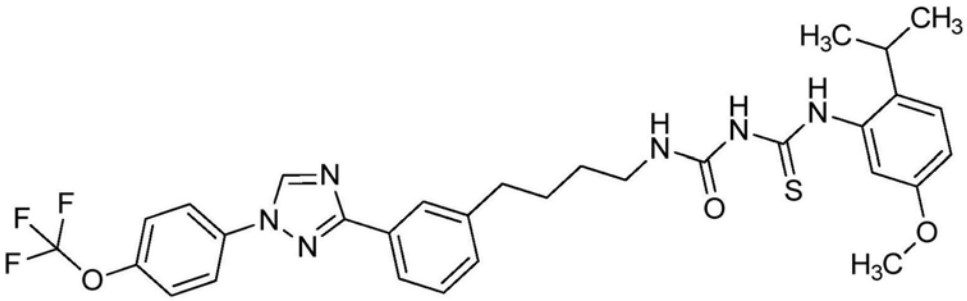
[0880]



[0881] 标题化合物如实施例63中所述使用4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA21)和1-(2-异丙基-5-甲基苯基)硫脲制备,并且分离为白色固体(0.119g,38%):^{1}H NMR(400MHz,DMSO-d_6)δ11.93(s,1H),10.03(s,1H),9.41(s,1H),8.13-8.07(m,2H),8.00(t,J=1.7Hz,1H),7.96(dt,J=7.6,1.4Hz,1H),7.68-7.61(m,2H),7.46(t,J=7.6Hz,1H),7.36(dt,J=7.6,1.5Hz,1H),7.23(d,J=8.0Hz,2H),7.13-7.07(m,1H),7.04(t,J=5.5Hz,1H),3.20(q,J=6.5Hz,2H),2.95(p,J=6.9Hz,1H),2.74(t,J=7.6Hz,2H),2.27(s,3H),1.78-1.62(m,2H),1.61-1.46(m,2H),1.14(d,J=6.8Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 611([M+H]$^+$)。

[0882] 制备1-[(2-异丙基-5-甲氧基-苯基)氨基硫代甲酰基]-3-[4-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC182)

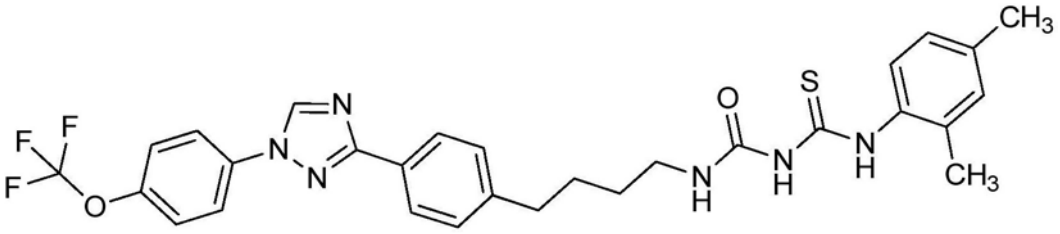
[0883]



[0884] 标题化合物如实施例63中所述使用4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA21)和1-(2-异丙基-5-甲氧基苯基)硫脲(CA40)制备,并且分离为白色固体(0.141g,44%):^{1}H NMR(400MHz,DMSO-d_6)δ12.02(s,1H),10.03(s,1H),9.39(s,1H),8.12-8.04(m,2H),7.98(t,J=1.6Hz,1H),7.94(dt,J=7.7,1.4Hz,1H),7.62(ddd,J=7.7,1.9,1.0Hz,2H),7.45(t,J=7.6Hz,1H),7.34(dt,J=7.7,1.5Hz,1H),7.23(d,J=8.7Hz,1H),7.10(d,J=2.7Hz,1H),7.03(t,J=5.6Hz,1H),6.84(dd,J=8.7,2.8Hz,1H),3.71(s,3H),3.18(q,J=6.4Hz,2H),2.91(p,J=6.8Hz,1H),2.72(t,J=7.6Hz,2H),1.67(p,J=7.7Hz,2H),1.52(p,J=6.9Hz,2H),1.12(d,J=6.8Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 627([M+H]$^+$)。

[0885] 制备1-[(2,4-二甲基苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(FB16)

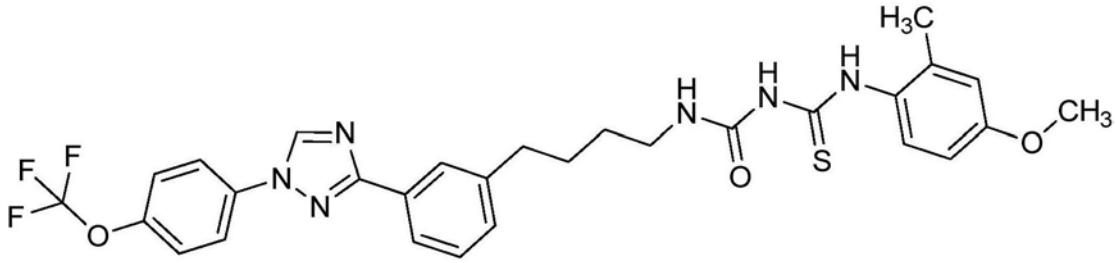
[0886]



[0887] 标题化合物如实施例63中所述使用4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA20)和1-(2,4-二甲基苯基)硫脲制备,并且分离为白色固体(0.106g,46%)。

[0888] 制备1-[(4-甲氧基-2-甲基-苯基)氨基硫代甲酰基]-3-[4-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(FB36)

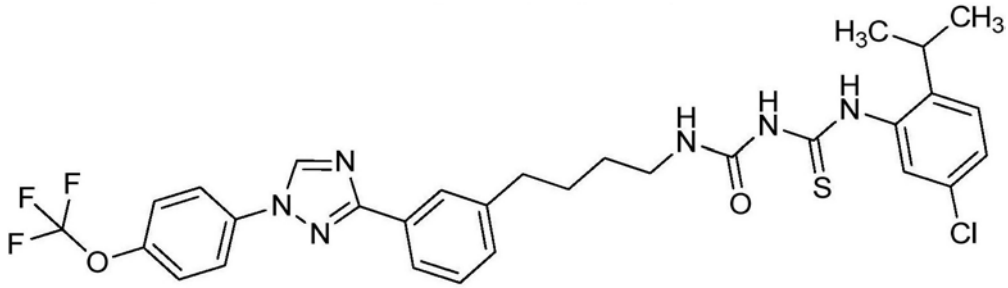
[0889]



[0890] 标题化合物如实施例63中所述使用4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA21)和1-(4-甲氧基-2-甲基苯基)硫脲制备,并且分离为白色固体(0.082g,27%)。

[0891] 制备1-[(5-氯-2-异丙基-苯基)氨基硫代甲酰基]-3-[4-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(FB37)

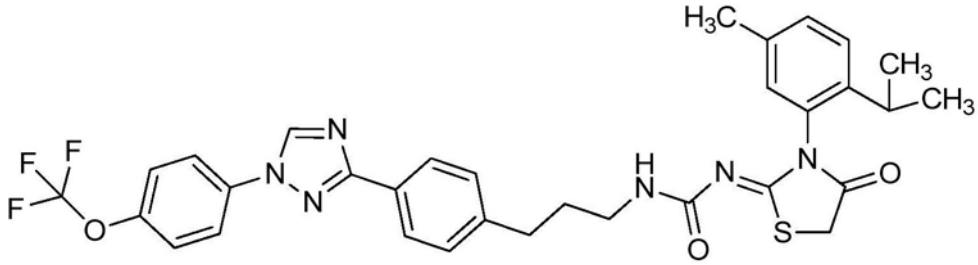
[0892]



[0893] 标题化合物如实施例63中所述使用4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-胺(CA21)和1-(5-氯-2-异丙基苯基)硫脲(CB32)制备,并且分离为白色固体(0.098g,31%)。

[0894] 实施例64:制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(F20)

[0895]



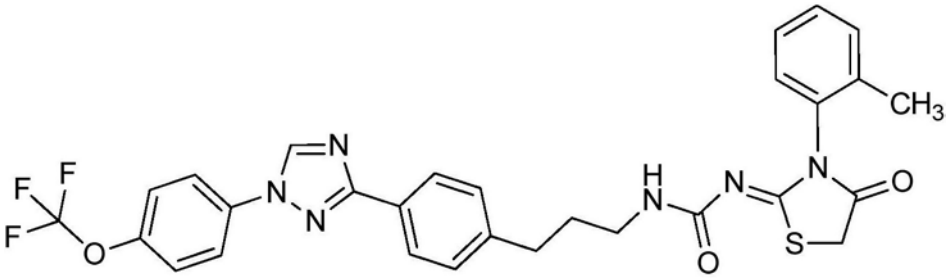
[0896] 向在25mL装配有搅拌棒和Vigreux柱的小瓶中的1-[(2-异丙基-5-甲基-苯基)氨基硫代甲酰基]-3-[3-[4-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丙基]脲(F21)(0.110g,0.184mmol),加入乙酸钠(0.0600g,0.735mmol),乙醇(2mL)和溴乙酸甲酯(0.0250mL,0.276mmol)。将反应加热至70℃过夜。反应冷却和用二氯甲烷稀释。分层,将水层用二氯甲烷提取。将有机层灌注经过相分离器并且浓缩。通过使用0-30%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供固体在50℃的真空中干燥过

夜，提供为白色固体的标题化合物(0.0791g，68%)。

[0897] 下面的化合物根据实施例64中的步骤制备。

[0898] 制备(Z)-1-(4-氧代-3-(邻甲苯基)噻唑烷-2-亚基)-3-(3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(P92)

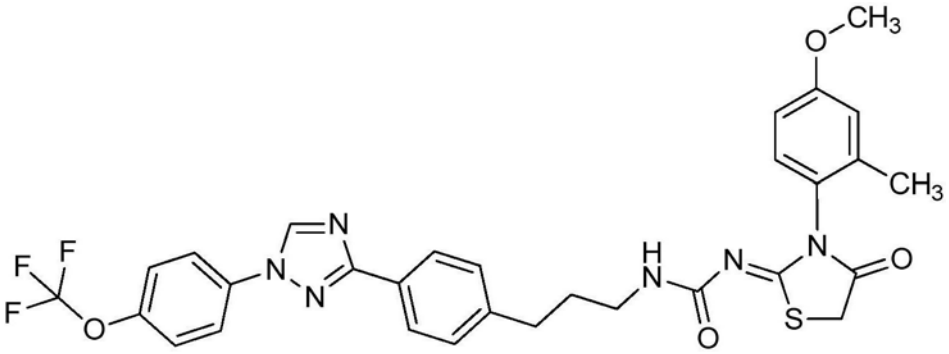
[0899]



[0900] 标题化合物如实施例64中所述使用1-(邻甲苯基氨基硫代甲酰基)-3-[3-[4-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丙基]脲(PC92)制备，并且分离为浅黄色固体(0.036g，72%)。

[0901] 制备(Z)-1-(3-(4-甲氧基-2-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(P105)

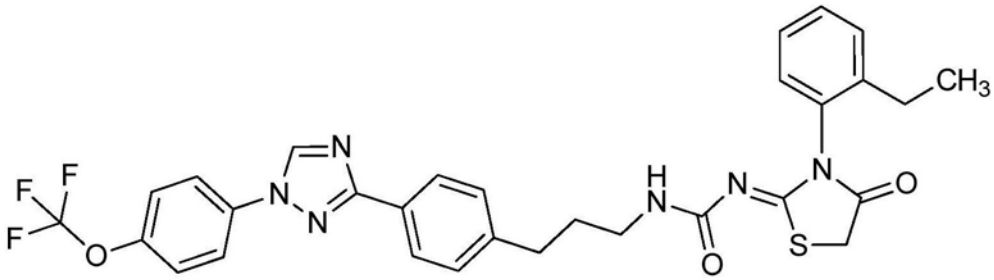
[0902]



[0903] 标题化合物如实施例64中所述使用1-[(4-甲氧基-2-甲基-苯基)氨基硫代甲酰基]-3-[3-[4-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丙基]脲(PC105)制备，并且分离为浅黄色固体(0.085g，75%)。

[0904] 制备(Z)-1-(3-(2-乙基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(P93，P510)

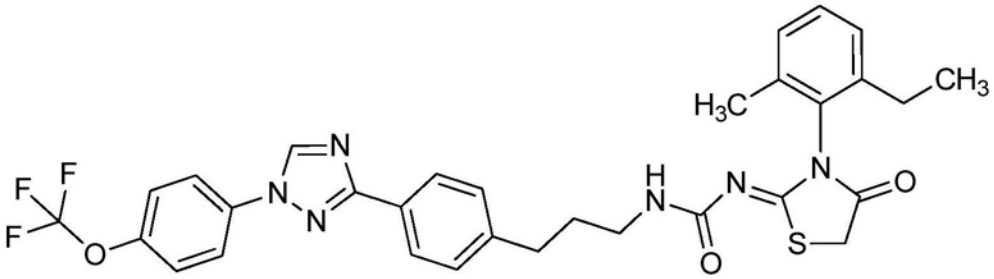
[0905]



[0906] 标题化合物如实施例64中所述使用1-[(2-乙基苯基)氨基硫代甲酰基]-3-[3-[4-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丙基]脲(PC93)制备，并且分离为浅黄色固体(0.057g，54%)。

[0907] 制备(Z)-1-(3-(2-乙基-6-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(P101)

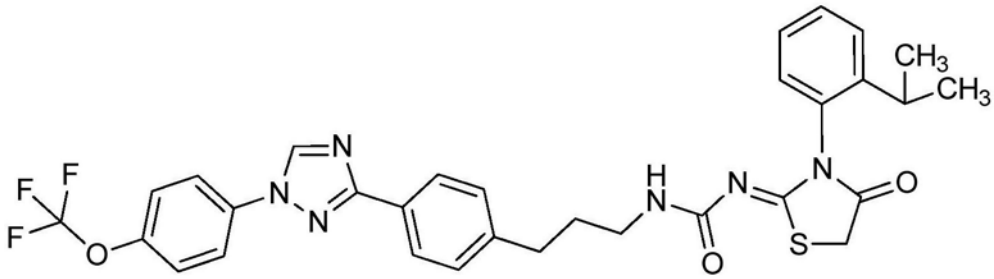
[0908]



[0909] 标题化合物如实施例64中所述使用1-[(2-乙基-6-甲基-苯基)氨基硫代甲酰基]-3-[3-[4-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丙基]脲(PC101)制备,并且分离为浅黄色固体(0.059g,41%)。

[0910] 制备(Z)-1-(3-(2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(P94,P197)

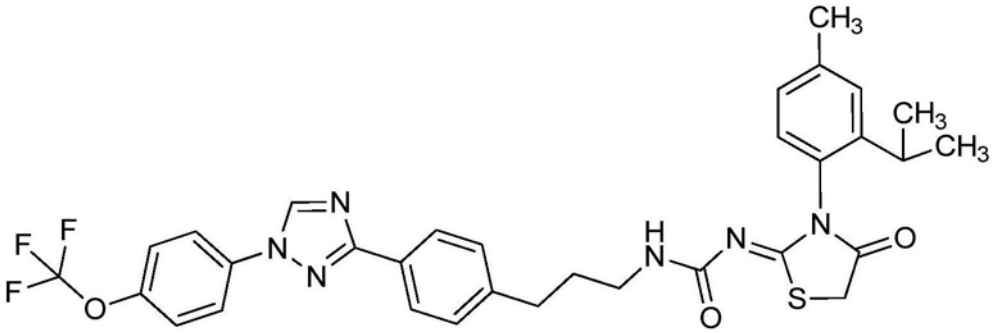
[0911]



[0912] 标题化合物如实施例64中所述使用1-[(2-异丙基苯基)氨基硫代甲酰基]-3-[3-[4-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丙基]脲(PC94)制备,并且分离为浅黄色固体(0.071g,80%)。

[0913] 制备(Z)-1-(3-(2-异丙基-4-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(P102)

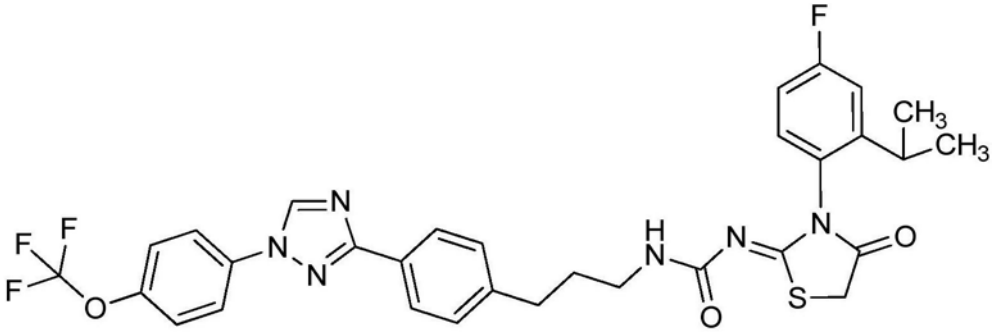
[0914]



[0915] 标题化合物如实施例64中所述使用1-[(2-异丙基-4-甲基-苯基)氨基硫代甲酰基]-3-[3-[4-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丙基]脲(PC102)制备,并且分离为浅黄色固体(0.070g,75%)。

[0916] 制备(Z)-1-(3-(4-氟-2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(P103,P1150)

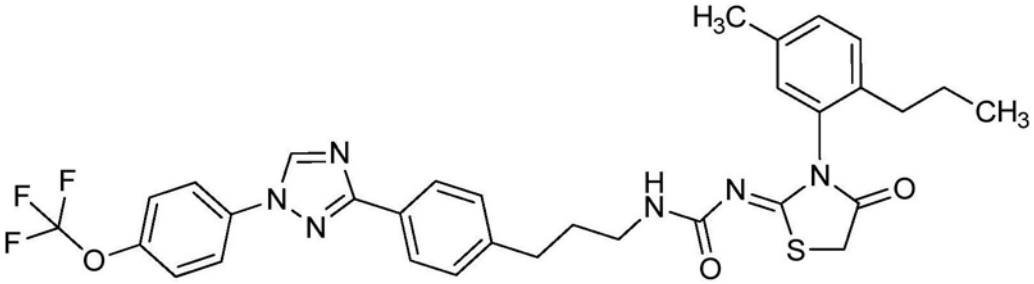
[0917]



[0918] 标题化合物如实施例64中所述使用1-[(4-氟-2-异丙基-苯基)氨基硫代甲酰基]-3-[3-[4-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丙基]脲(PC103)制备,并且分离为浅黄色固体(0.084g,77%)。

[0919] 制备(Z)-1-(3-(5-甲基-2-丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(P99,P830)

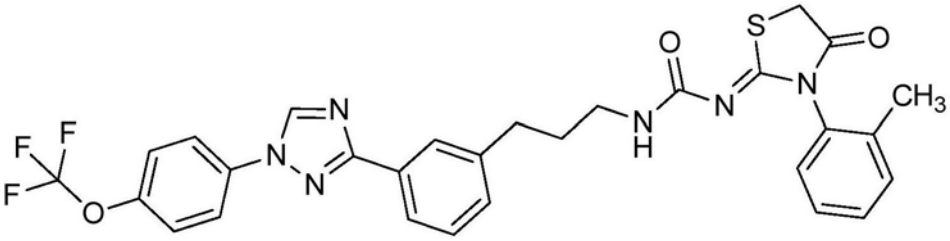
[0920]



[0921] 标题化合物如实施例64中所述使用1-[(5-甲基-2-丙基-苯基)氨基硫代甲酰基]-3-[3-[4-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丙基]脲(PC99)制备,并且分离为浅黄色固体(0.075g,72%)。

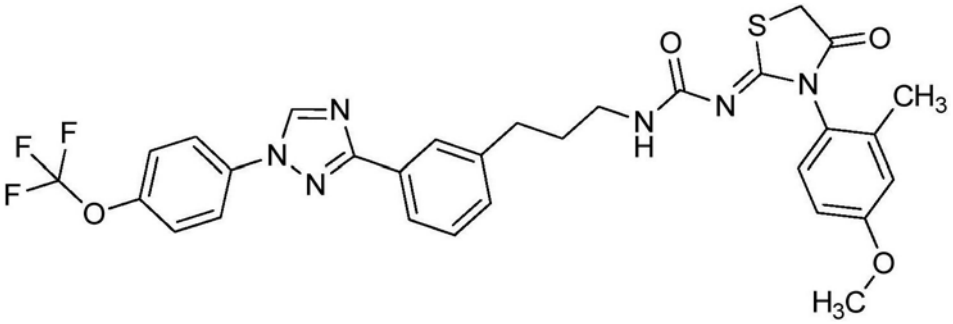
[0922] 制备(Z)-1-(4-氧代-3-(邻甲苯基)噻唑烷-2-亚基)-3-(3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(P118)

[0923]



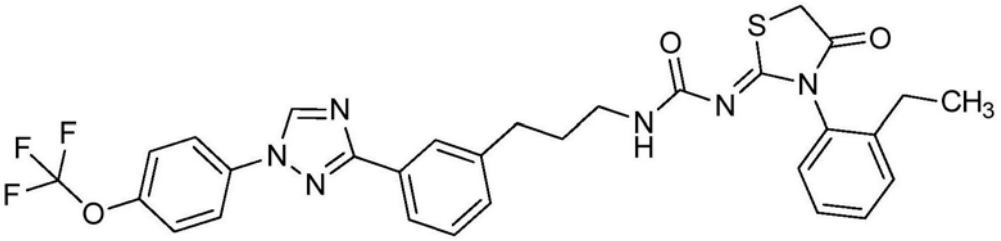
[0924] 标题化合物如实施例64中所述使用1-(邻甲苯基氨基硫代甲酰基)-3-[3-[3-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丙基]脲(PC118)制备,并且分离为灰白色固体(0.051g,80%)。

[0925] 制备(Z)-1-(3-(4-甲氧基-2-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(P131)

[0926] 

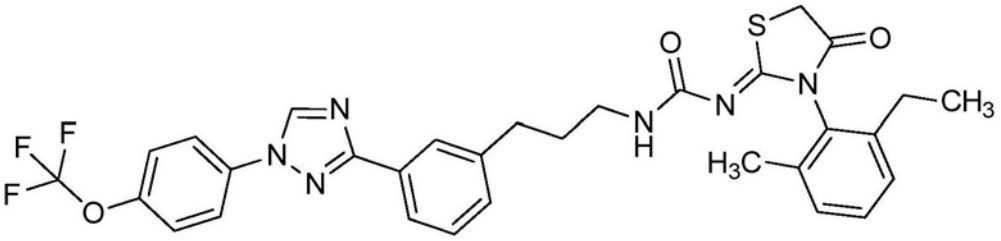
[0927] 标题化合物如实施例64中所述使用1-[(4-甲氧基-2-甲基-苯基)氨基硫代甲酰基]-3-[3-[3-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丙基]脲(PC131)制备，并且分离为灰白色固体(0.074g,89%)。

[0928] 制备(Z)-1-(3-(2-乙基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(P119)

[0929] 

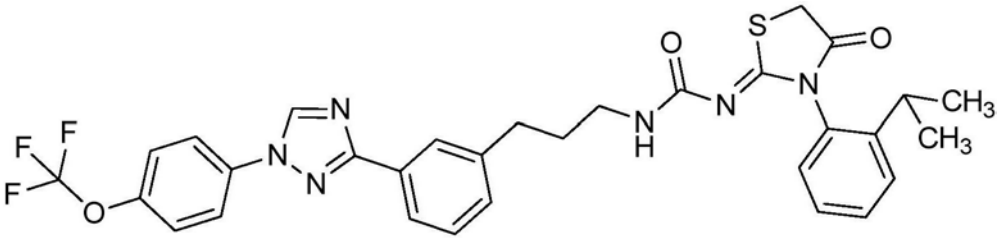
[0930] 标题化合物如实施例64中所述使用1-[(2-乙基苯基)氨基硫代甲酰基]-3-[3-[3-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丙基]脲(PC119)制备，并且分离为灰白色固体(0.071g,83%)。

[0931] 制备(Z)-1-(3-(2-乙基-6-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(P127)

[0932] 

[0933] 标题化合物如实施例64中所述使用1-[(2-乙基-6-甲基-苯基)氨基硫代甲酰基]-3-[3-[3-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丙基]脲(PC127)制备，并且分离为灰白色固体(0.061g,43%)。

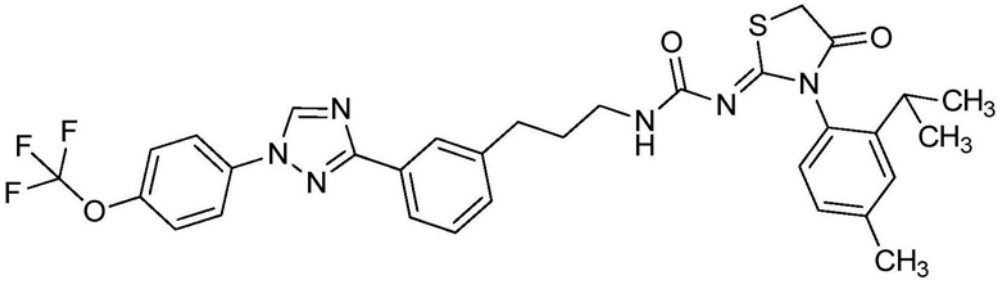
[0934] 制备(Z)-1-(3-(2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(P120)

[0935] 

[0936] 标题化合物如实施例64中所述使用1-[(2-异丙基苯基)氨基硫代甲酰基]-3-[3-

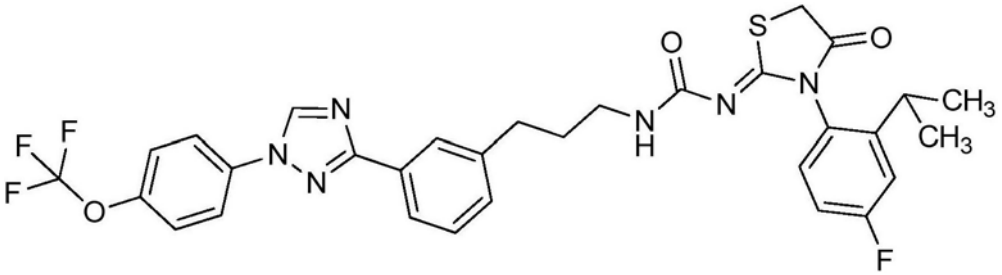
[3-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丙基]脲(PC120)制备,并且分离为灰白色固体(0.091g,80%)。

[0937] 制备(Z)-1-(3-(2-异丙基-4-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(P128)

[0938] 

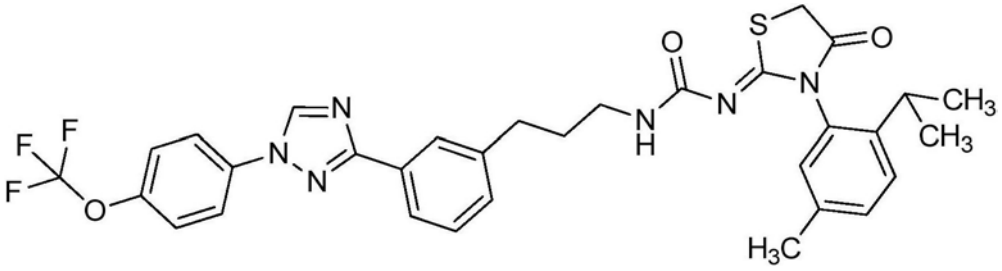
[0939] 标题化合物如实施例64中所述使用1-[(2-异丙基-4-甲基-苯基)氨基硫代甲酰基]-3-[3-[3-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丙基]脲(PC128)制备,并且分离为灰白色固体(0.091g,84%)。

[0940] 制备(Z)-1-(3-(4-氟-2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(P129)

[0941] 

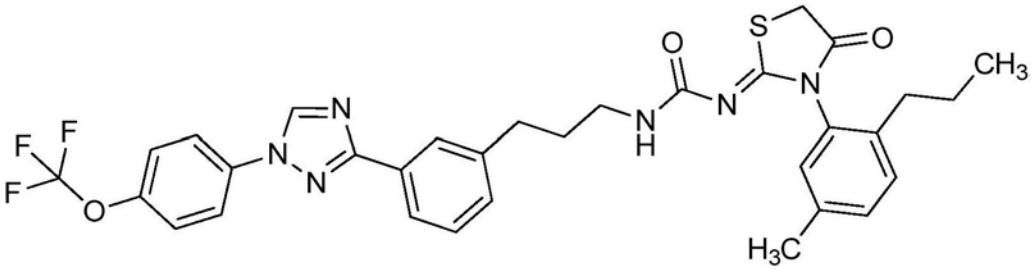
[0942] 标题化合物如实施例64中所述使用1-[(4-氟-2-异丙基-苯基)氨基硫代甲酰基]-3-[3-[3-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丙基]脲(PC129)制备,并且分离为灰白色固体(0.095g,81%)。

[0943] 制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(P124)

[0944] 

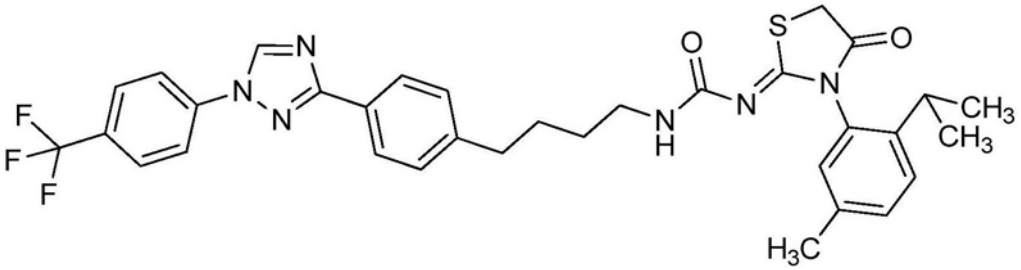
[0945] 标题化合物如实施例64中所述使用1-[(2-异丙基-5-甲基-苯基)氨基硫代甲酰基]-3-[3-[3-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丙基]脲(PC124)制备,并且分离为灰白色固体(0.077g,80%)。

[0946] 制备(Z)-1-(3-(5-甲基-2-丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(P125)

[0947] 

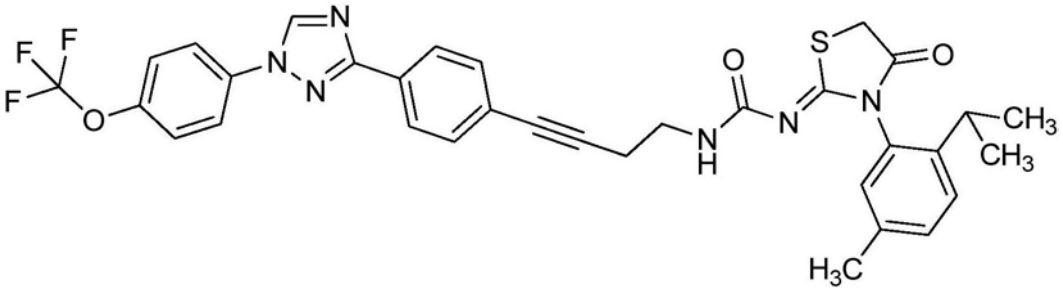
[0948] 标题化合物如实施例64中所述使用1-[(5-甲基-2-丙基-苯基)氨基硫代甲酰基]-3-[3-[3-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丙基]脲(PC125)制备,并且分离为灰白色固体(0.097g,86%)。

[0949] 制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P159)

[0950] 

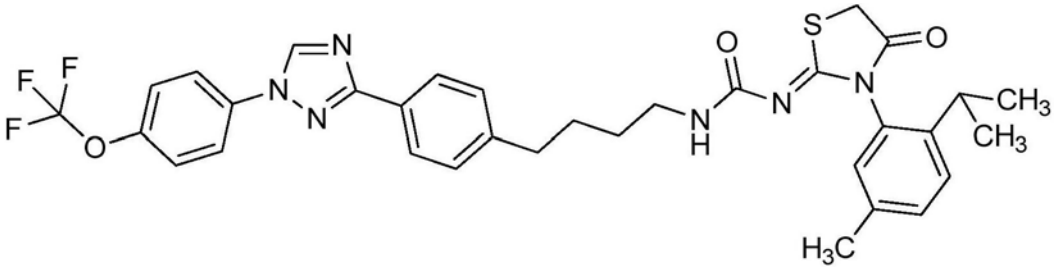
[0951] 标题化合物如实施例64中所述使用1-[(2-异丙基-5-甲基-苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲基)苯基]-1,2,4-三唑-3-基]苯基]丁基]脲(PC159)制备,并且分离为白色固体(0.063g,70%)。

[0952] 制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁-3-炔-1-基)脲(P160)

[0953] 

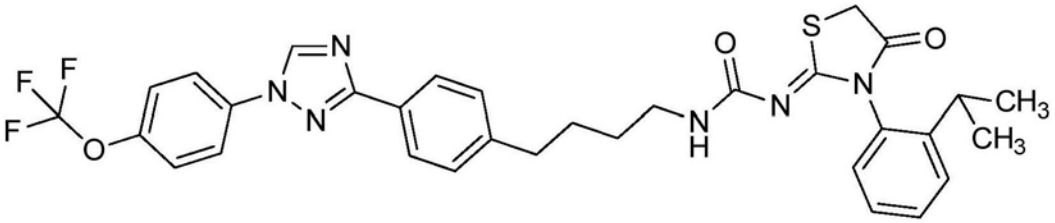
[0954] 标题化合物如实施例64中所述使用1-[(2-异丙基-5-甲基-苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丁-3-炔]脲(PC160)制备,并且分离为黄色固体(0.122g,74%)。

[0955] 制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P150,P363)

[0956] 

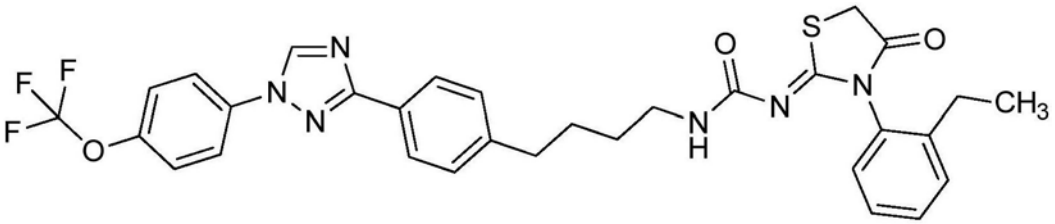
[0957] 标题化合物如实施例64中所述使用1-[(2-异丙基-5-甲基-苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丁基]脲(PC150)制备，并且分离为白色固体(0.068g,78%)。

[0958] 制备(Z)-1-(3-(2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P146,P208)

[0959] 

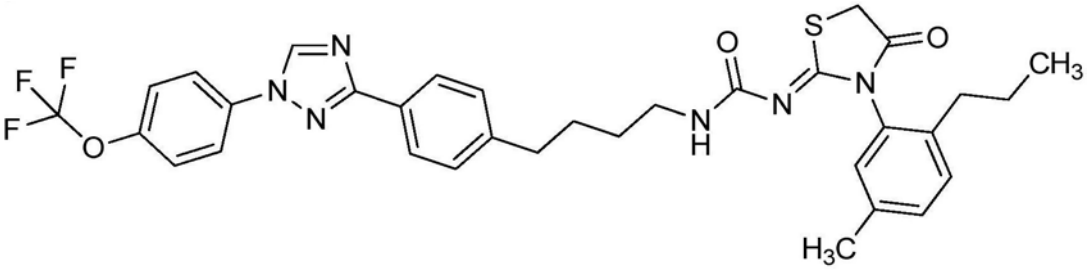
[0960] 标题化合物如实施例64中所述使用1-[(2-异丙基苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丁基]脲(PC146)制备，分离为白色固体(0.063g,80%)。

[0961] 制备(Z)-1-(3-(2-乙基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P145,P522)

[0962] 

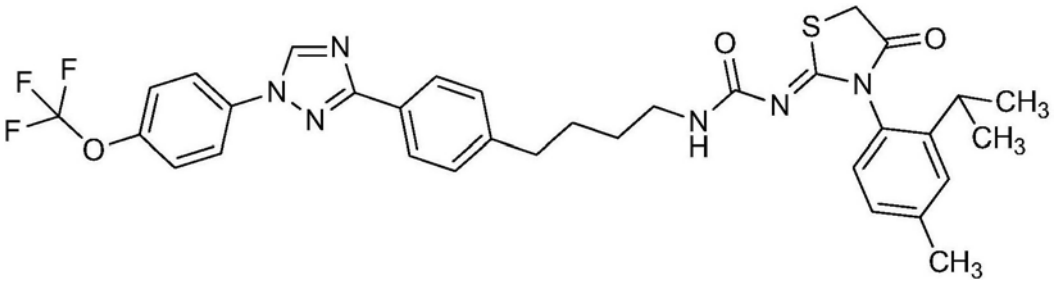
[0963] 标题化合物如实施例64中所述使用1-[(2-乙基苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丁基]脲(PC145)制备，并且分离为白色固体(0.084g,83%)。

[0964] 制备(Z)-1-(3-(5-甲基-2-丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P151,P842)

[0965] 

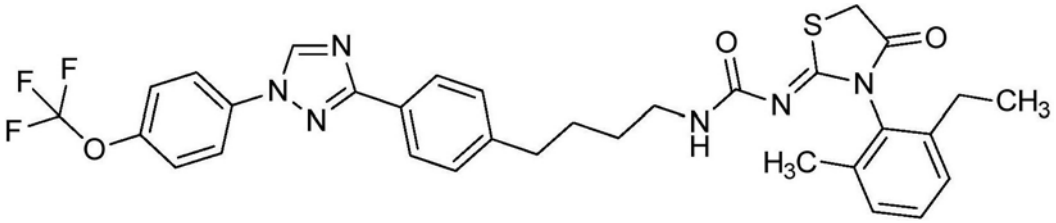
[0966] 标题化合物如实施例64中所述使用1-[(5-甲基-2-丙基-苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丁基]脲(PC151)制备，并且分离为白色固体(0.081g,81%)。

[0967] 制备(Z)-1-(3-(2-异丙基-4-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P154)

[0968] 

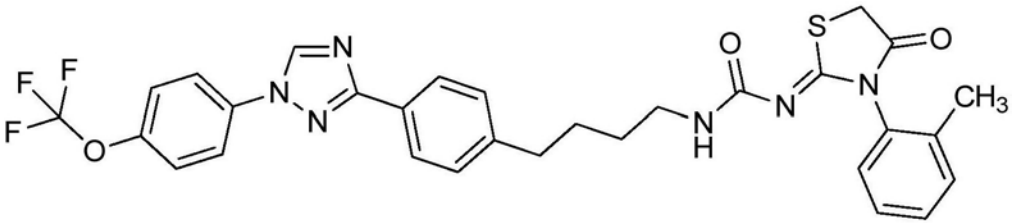
[0969] 标题化合物如实施例64中所述使用1-[(2-异丙基-4-甲基-苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丁基]脲(PC154)制备，并且分离为白色固体(0.070g，82%)。

[0970] 制备(Z)-1-(3-(2-乙基-6-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P153)

[0971] 

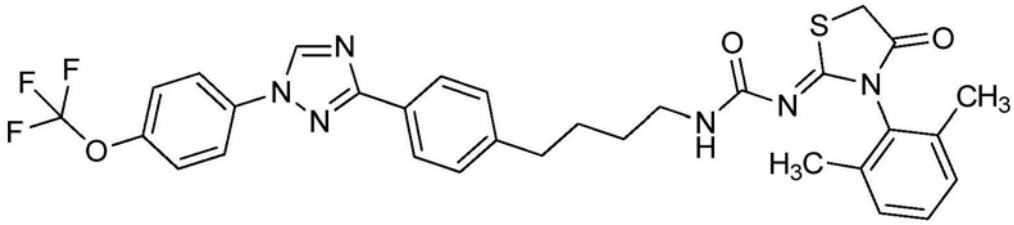
[0972] 标题化合物如实施例64中所述使用1-[(2-乙基-6-甲基-苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丁基]脲(PC153)制备，并且分离为白色泡沫(0.059g，52%)。

[0973] 制备(Z)-1-(4-氧代-3-(邻甲苯基)噻唑烷-2-亚基)-3-(4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P144)

[0974] 

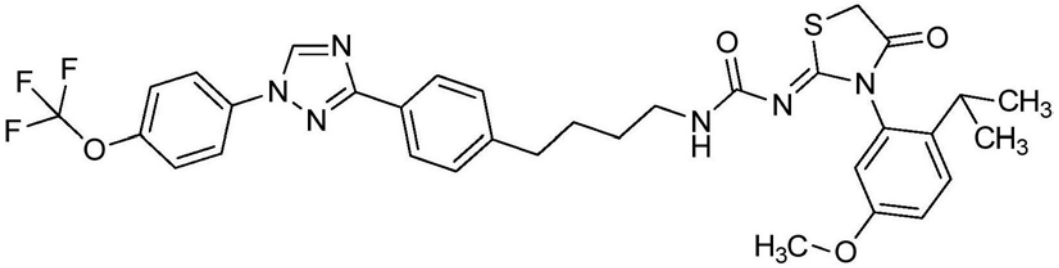
[0975] 标题化合物如实施例64中所述使用1-(邻甲苯基氨基硫代甲酰基)-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丁基]脲(PC144)制备，并且分离为白色泡沫(0.070g，76%)。

[0976] 制备(Z)-1-(3-(2,6-二甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P152，P1481)

[0977] 

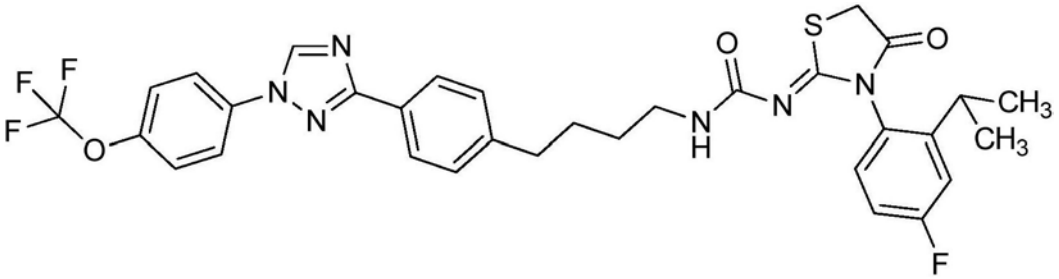
[0978] 标题化合物如实施例64中所述使用1-[(2,6-二甲基苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丁基]脲(PC152)制备，并且分离为白色固体(0.078g，72%)。

[0979] 制备(Z)-1-(3-(2-异丙基-5-甲氧基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P156,P682)

[0980] 

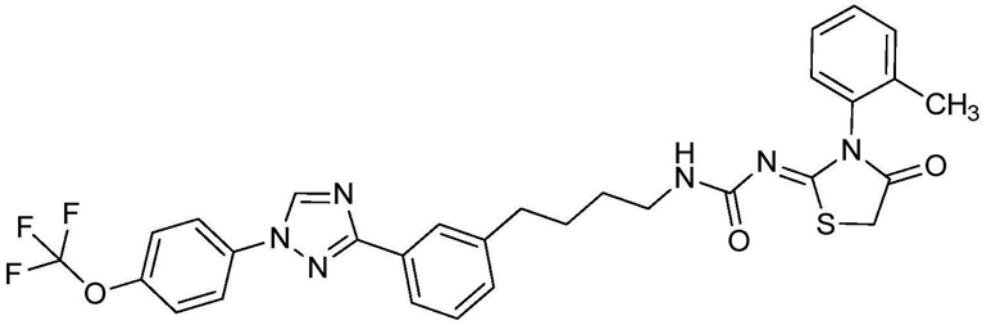
[0981] 标题化合物如实施例64中所述使用1-[(2-异丙基-5-甲氧基-苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丁基]脲(PC156)制备，并且分离为白色固体(0.089g,82%)。

[0982] 制备(Z)-1-(3-(4-氟-2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P155,P1162)

[0983] 

[0984] 标题化合物如实施例64中所述使用1-[(4-氟-2-异丙基-苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1,2,4-三唑-3-基]苯基]丁基]脲(PC155)制备，并且分离为白色泡沫(0.075g,88%)。

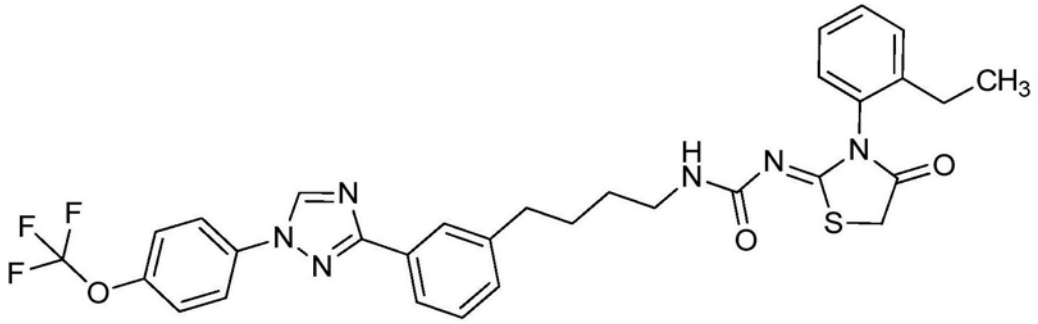
[0985] 制备(Z)-1-(4-氧代-3-(邻甲苯基)噻唑烷-2-亚基)-3-(4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P170)

[0986] 

[0987] 标题化合物如实施例64中所述使用1-(邻甲苯基氨基硫代甲酰基)-3-[4-[3-[1-[4-(三氟甲氧基)苯基])-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC170)制备，并且分离为白色固体(0.061g,72%)。

[0988] 制备(Z)-1-(3-(2-乙基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P171)

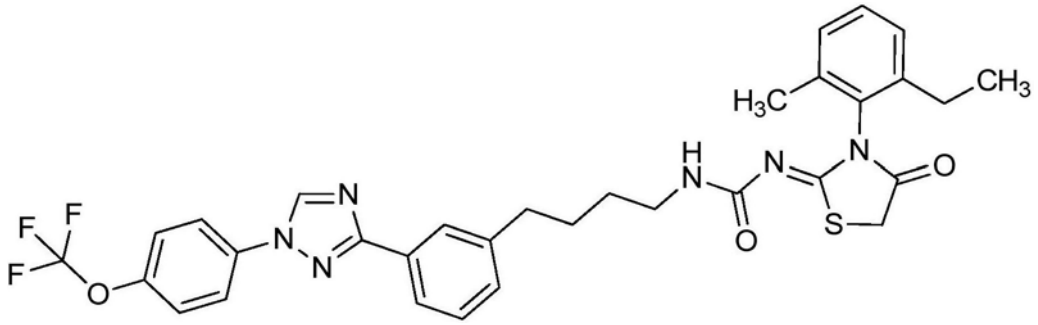
[0989]



[0990] 标题化合物如实施例64中所述使用1-[(2-乙基苯基)氨基硫代甲酰基]-3-[4-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC171)制备,并且分离为白色固体(0.078g,77%)。

[0991] 制备(Z)-1-(3-(2-乙基-6-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P179)

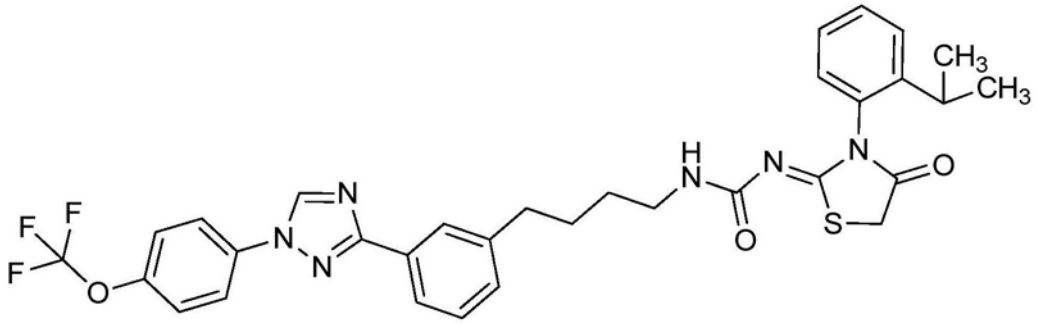
[0992]



[0993] 标题化合物如实施例64中所述使用1-[(2-乙基-6-甲基-苯基)氨基硫代甲酰基]-3-[4-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC179)制备,并且分离为白色固体(0.048g,37%)。

[0994] 制备(Z)-1-(3-(2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P172)

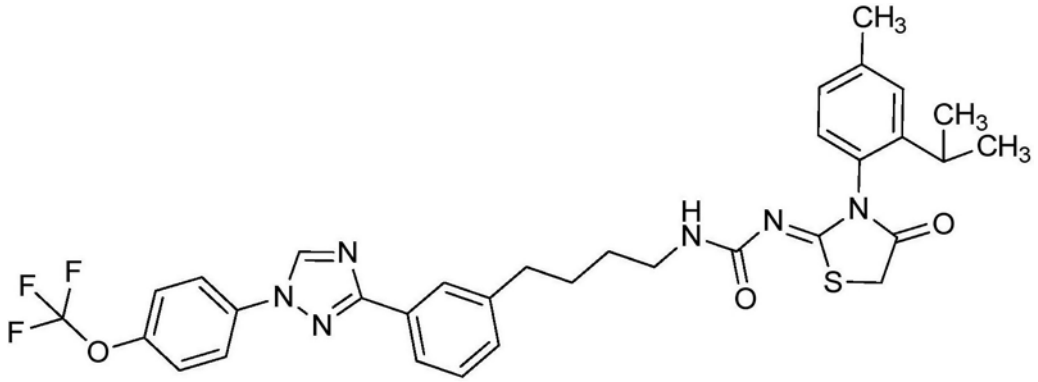
[0995]



[0996] 制备标题化合物如实施例64中所述使用1-[(2-异丙基苯基)氨基硫代甲酰基]-3-[4-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC172),并且分离为白色固体(0.048g,80%)。

[0997] 制备(Z)-1-(3-(2-异丙基-4-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P180)

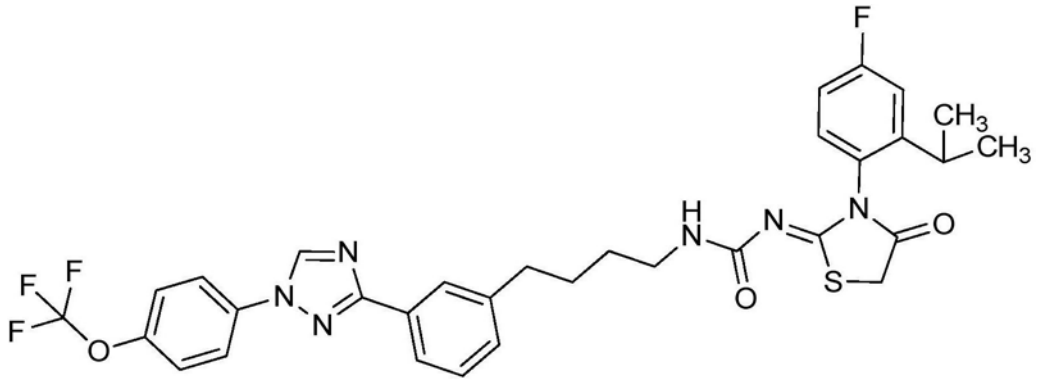
[0998]



[0999] 标题化合物如实施例64中所述使用1-[(2-异丙基-4-甲基-苯基)氨基硫代甲酰基]-3-[4-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC180)制备,并且分离为白色固体(0.086g,66%)。

[1000] 制备(Z)-1-(3-(4-氟-2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P181)

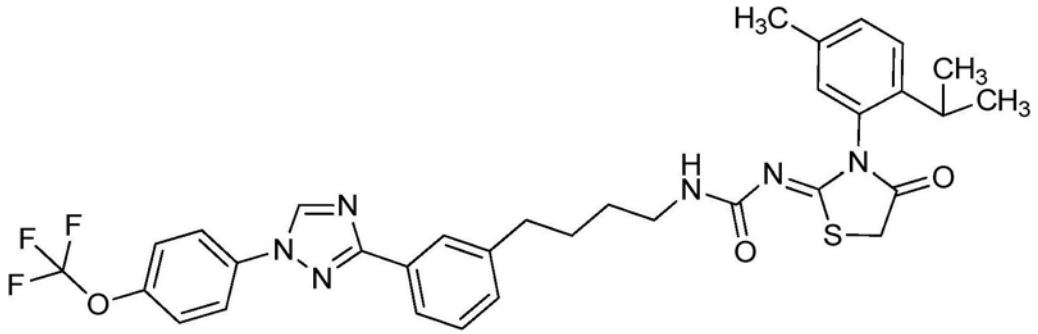
[1001]



[1002] 标题化合物如实施例64中所述使用1-[(4-氟-2-异丙基-苯基)氨基硫代甲酰基]-3-[4-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC181)制备,并且分离为白色固体(0.058g,57%)。

[1003] 制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P176)

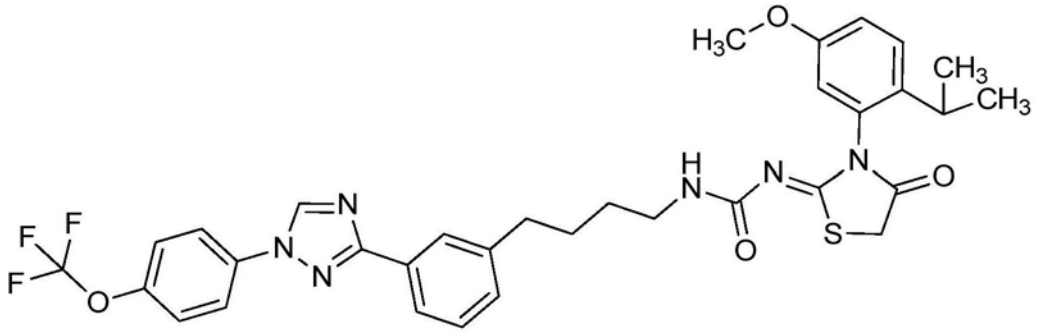
[1004]



[1005] 标题化合物如实施例64中所述使用1-[(2-异丙基-5-甲基-苯基)氨基硫代甲酰基]-3-[4-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC176)制备,并且分离为白色固体(0.076g,74%)。

[1006] 制备(Z)-1-(3-(2-异丙基-5-甲氧基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(P182)

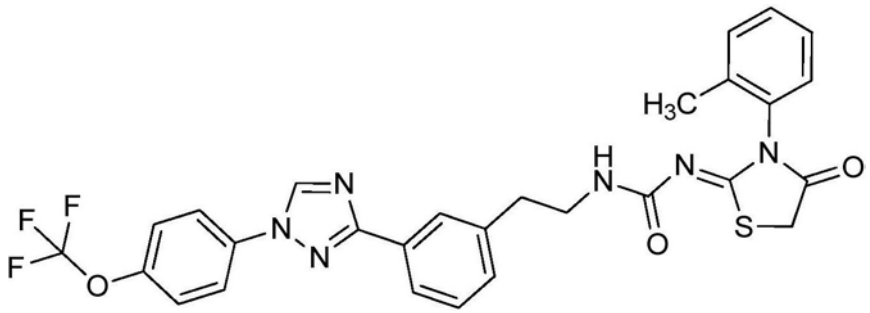
[1007]



[1008] 标题化合物如实施例64中所述使用1-[(2-异丙基-5-甲氧基-苯基)氨基硫代甲酰基]-3-[4-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(PC182)制备,并且分离为白色固体(0.064g,58%)。

[1009] 制备(Z)-1-(4-氧代-3-(邻甲苯基)噻唑烷-2-亚基)-3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P74)

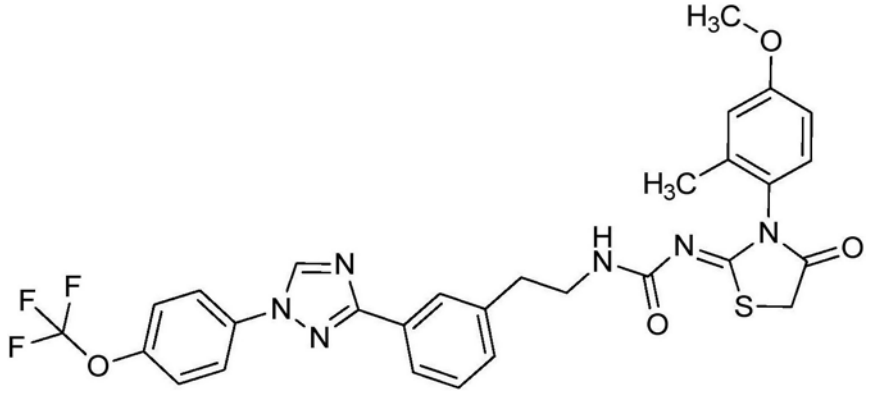
[1010]



[1011] 标题化合物如实施例64中所述使用1-(邻甲苯基氨基硫代甲酰基)-3-[2-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(PC74)制备,并且分离为白色固体(0.076g,77%)。

[1012] 制备(Z)-1-(3-(4-甲氧基-2-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P87)

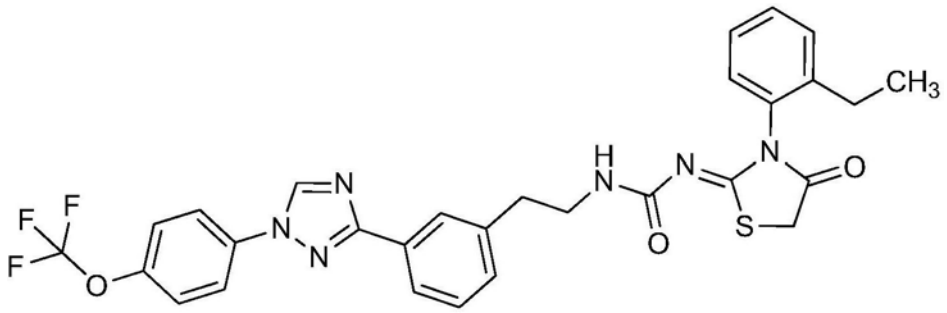
[1013]



[1014] 标题化合物如实施例64中所述使用1-[(4-甲氧基-2-甲基-苯基)氨基硫代甲酰基]-3-[2-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(PC87)制备,并且分离为白色固体(0.079g,84%)。

[1015] 制备(Z)-1-(3-(2-乙基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P75)

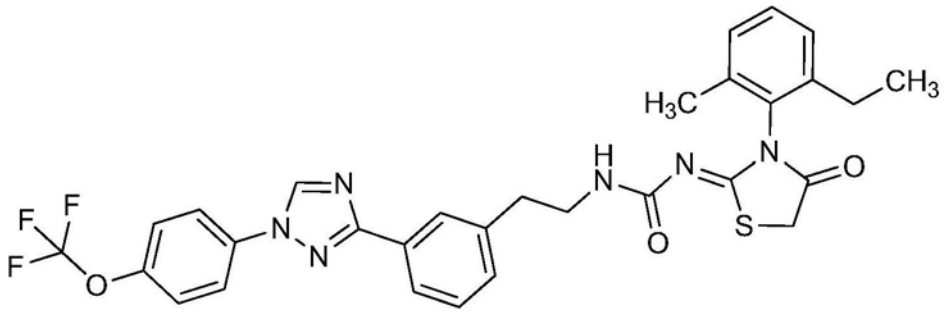
[1016]



[1017] 标题化合物如实施例64中所述使用1-[(2-乙基苯基)氨基硫代甲酰基]-3-[2-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(PC75)制备,并且分离为白色固体(0.071g,73%)。

[1018] 制备(Z)-1-(3-(2-乙基-6-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P83)

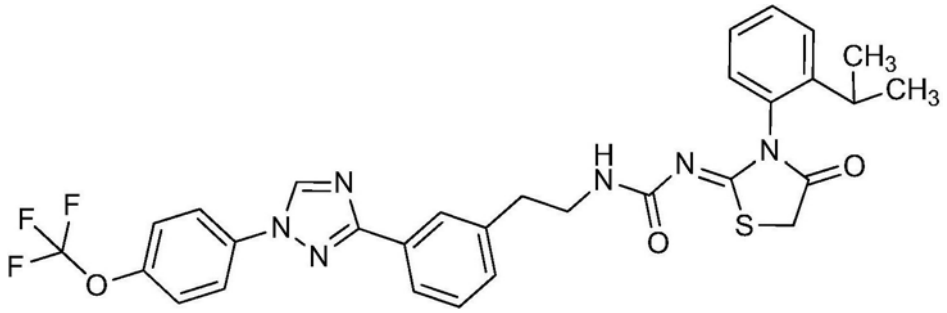
[1019]



[1020] 标题化合物如实施例64中所述使用1-[(2-乙基-6-甲基-苯基)氨基硫代甲酰基]-3-[2-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(PC83)制备,并且分离为白色固体(0.042g,34%)。

[1021] 制备(Z)-1-(3-(2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P76)

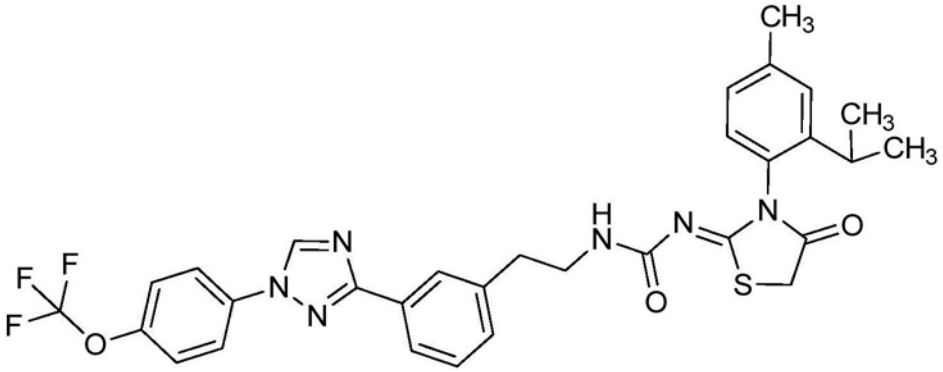
[1022]



[1023] 标题化合物如实施例64中所述使用1-[(2-异丙基苯基)氨基硫代甲酰基]-3-[2-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(PC76)制备,并且分离为白色固体(0.026g,72%)。

[1024] 制备(Z)-1-(3-(2-异丙基-4-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P84)

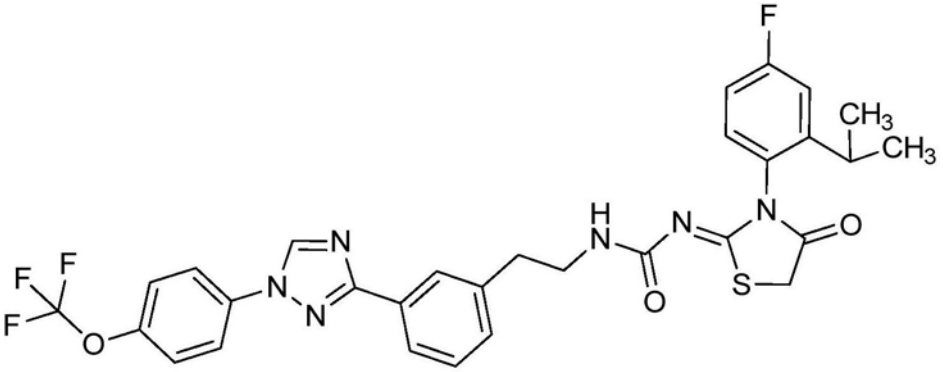
[1025]



[1026] 标题化合物如实施例64中所述使用1-[(2-异丙基-4-甲基-苯基)氨基硫代甲酰基]-3-[2-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(PC84)制备,并且分离为白色固体(0.056g,77%)。

[1027] 制备(Z)-1-(3-(4-氟-2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P85)

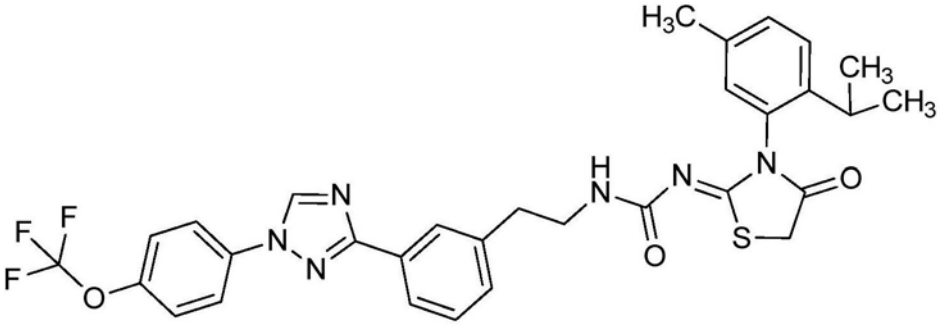
[1028]



[1029] 标题化合物如实施例64中所述使用1-[(4-氟-2-异丙基-苯基)氨基硫代甲酰基]-3-[2-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(PC85)制备,并且分离为白色固体(0.063g,77%)。

[1030] 制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P81)

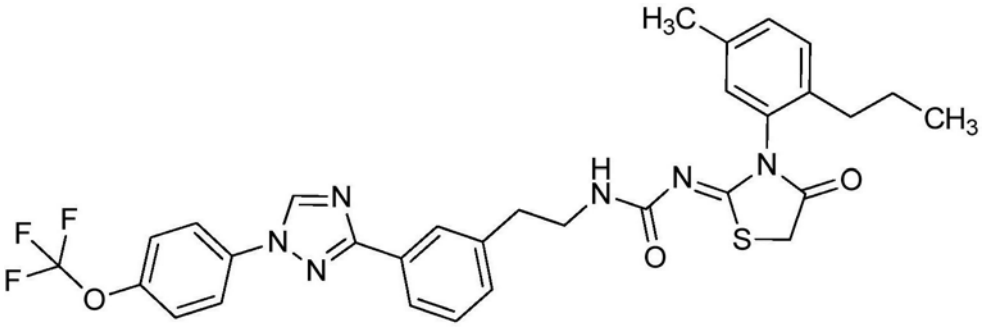
[1031]



[1032] 标题化合物如实施例64中所述使用1-[(2-异丙基-5-甲基-苯基)氨基硫代甲酰基]-3-[2-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(PC81)制备,并且分离为黄色固体(0.014g,68%)。

[1033] 制备(Z)-1-(3-(5-甲基-2-丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P80)

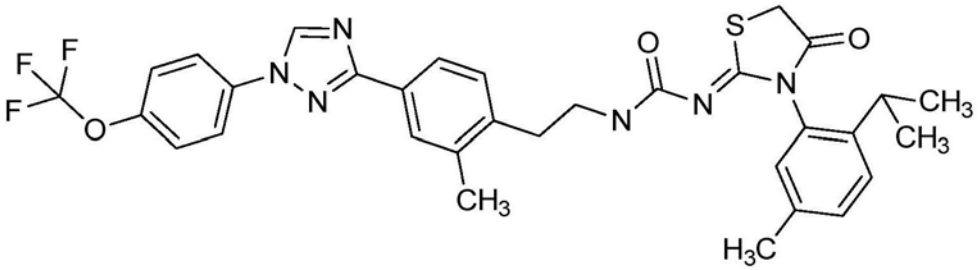
[1034]



[1035] 标题化合物如实施例64中所述使用1-[(5-甲基-2-丙基-苯基)氨基硫代甲酰基]-3-[2-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(PC80)制备,并且分离为白色固体(0.076g,74%)。

[1036] 制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(2-甲基-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB3)

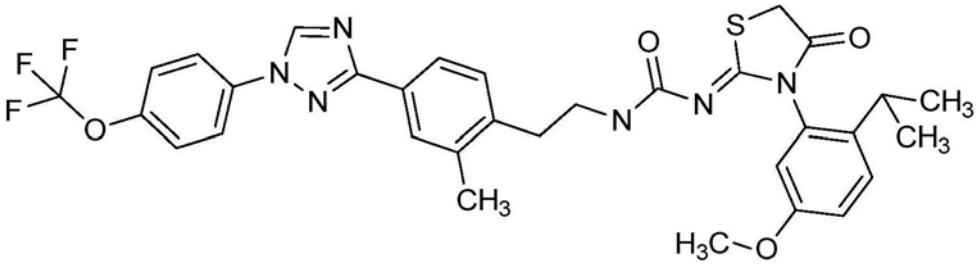
[1037]



[1038] 标题化合物如实施例64中所述使用1-[(2-异丙基-5-甲基-苯基)氨基硫代甲酰基]-3-[2-[2-甲基-4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(FB1)在温度为60℃制备,随后进行反相色谱;分离为黄色蜡(0.016g,10%)。

[1039] 制备(Z)-1-(3-(2-异丙基-5-甲氧基苯基)-4-氧代噻唑烷-2-亚基)-3-(2-甲基-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB4)

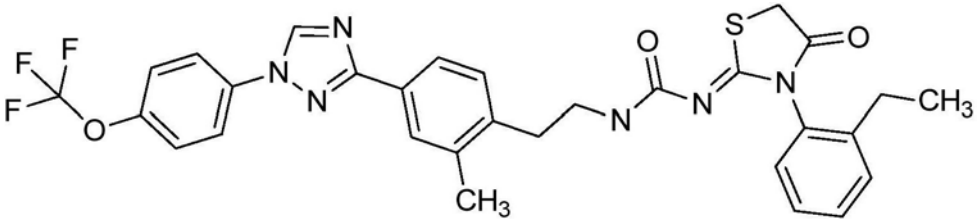
[1040]



[1041] 标题化合物如实施例64中所述使用1-[(2-异丙基-5-甲氧基-苯基)氨基硫代甲酰基]-3-[2-[2-甲基-4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(FB2)在温度为60℃制备,随后进行反相色谱,分离为浅黄色固体(0.034g,19%)。

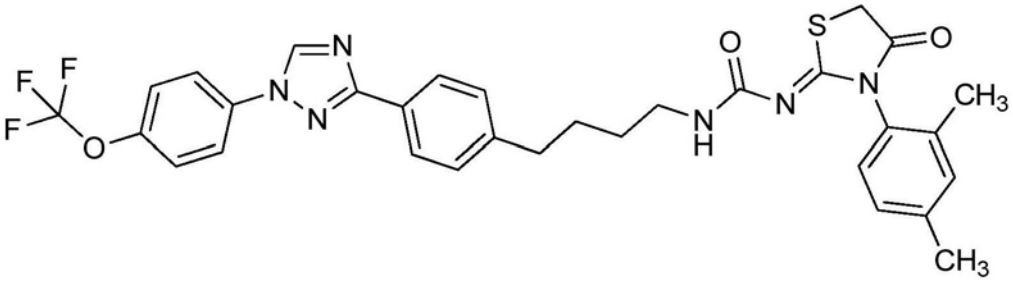
[1042] 制备(Z)-1-(3-(2-乙基苯基)-4-氧代噻唑烷-2-亚基)-3-(2-甲基-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB6)

[1043]



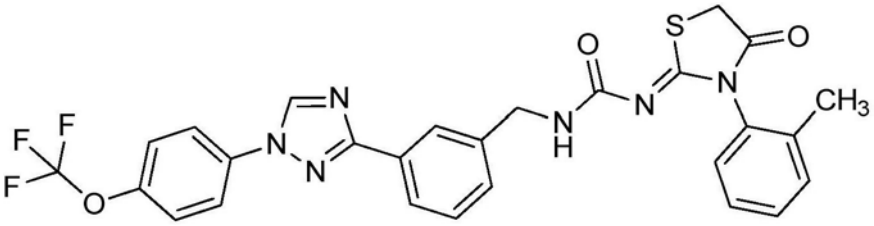
[1044] 标题化合物如实施例64中所述使用1-[(2-乙基苯基)氨基硫代甲酰基]-3-[2-[2-甲基-4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(FB5)在温度为60℃制备,随后进行反相色谱;分离为粉红色固体(0.010g,7%)。

[1045] 制备(Z)-1-(3-(2,4-二甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(FB17)

[1046] 

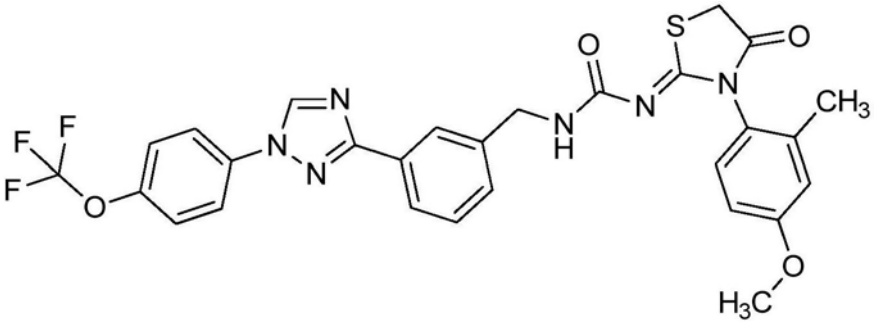
[1047] 标题化合物如实施例64中所述使用1-[(2,4-二甲基苯基)氨基硫代甲酰基]-3-[4-[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(FB16)制备,并且分离为白色泡沫(0.078g,83%)。

[1048] 制备(Z)-1-(4-氧代-3-(邻甲苯基)噻唑烷-2-亚基)-3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)脲(FB27)

[1049] 

[1050] 制备标题化合物如实施例64中所述使用1-(邻甲苯基氨基硫代甲酰基)-3-[[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(FB18),并且分离为灰白色固体(0.090g,68%)。

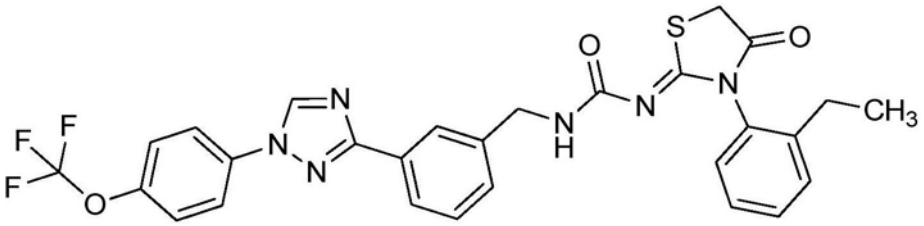
[1051] 制备(Z)-1-(3-(4-甲氧基-2-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)脲(FB28)

[1052] 

[1053] 标题化合物如实施例64中所述使用1-[(4-甲氧基-2-甲基-苯基)氨基硫代甲酰基]-3-[[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(FB19)制备,并且分离为淡橙色固体(0.042g,88%)。

[1054] 制备(Z)-1-(3-(2-乙基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)脲(FB29)

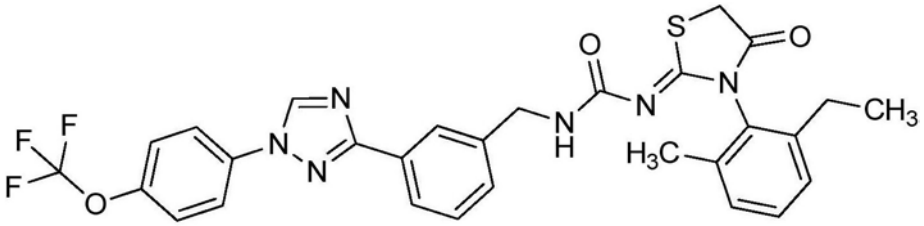
[1055]



[1056] 标题化合物如实施例64中所述使用1-[(2-乙基苯基)氨基硫代甲酰基]-3-[[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(FB20)制备,并且分离为白色固体(0.078g,57%)。

[1057] 制备(Z)-1-(3-(2-乙基-6-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)脲(FB30)

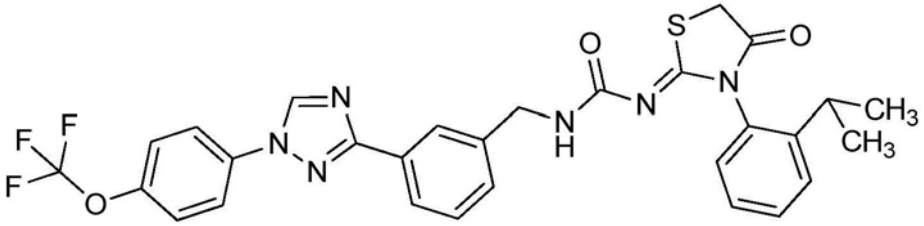
[1058]



[1059] 标题化合物如实施例64中所述使用1-[(2-乙基-6-甲基-苯基)氨基硫代甲酰基]-3-[[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(FA21)制备,并且分离为白色固体(0.035g,17%)。

[1060] 制备(Z)-1-(3-(2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)脲(FB31)

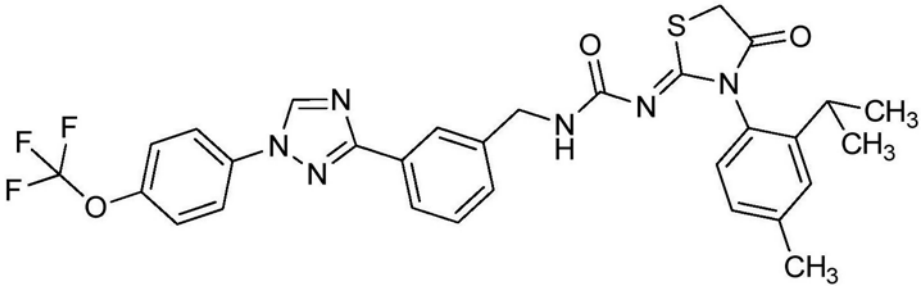
[1061]



[1062] 标题化合物如实施例64中所述使用1-[(2-异丙基苯基)氨基硫代甲酰基]-3-[[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(FA22)制备,并且分离为浅黄色固体(0.115g,57%)。

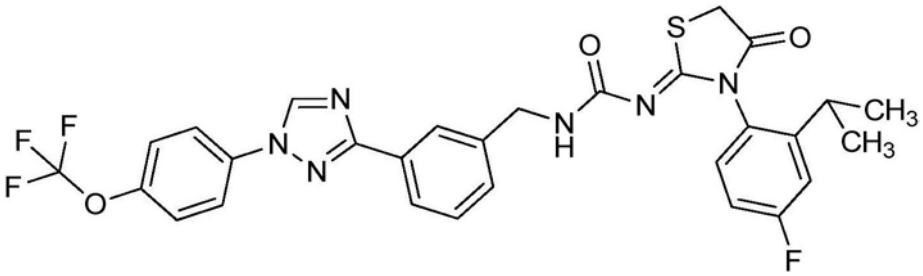
[1063] 制备(Z)-1-(3-(2-异丙基-4-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)脲(FB32)

[1064]



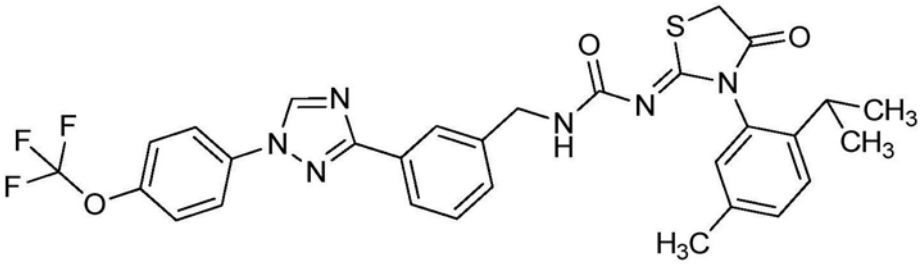
[1065] 标题化合物如实施例64中所述使用1-[(2-异丙基-4-甲基-苯基)氨基硫代甲酰基]-3-[[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(FB23)制备,并且分离为淡橙色固体(0.144g,70%)。

[1066] 制备(Z)-1-(3-(4-氟-2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)脲(FB33)

[1067] 

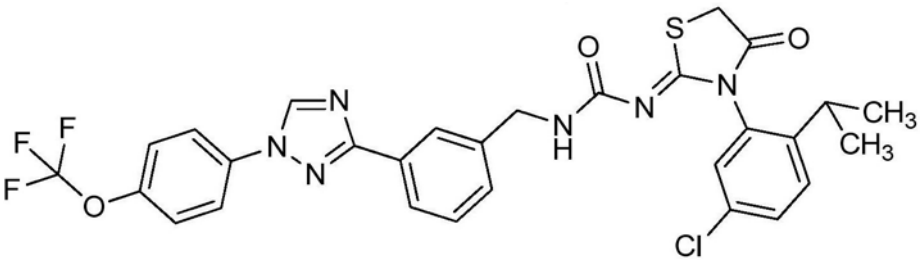
[1068] 标题化合物如实施例64中所述使用1-[(4-氟-2-异丙基-苯基)氨基硫代甲酰基]-3-[[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(FB24)制备,并且分离为灰白色固体(0.097g,44%)。

[1069] 制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)脲(FB34)

[1070] 

[1071] 标题化合物如实施例64中所述使用1-[(2-异丙基-5-甲基-苯基)氨基硫代甲酰基]-3-[[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(FB25)制备,并且分离为灰白色固体(0.091g,56%)。

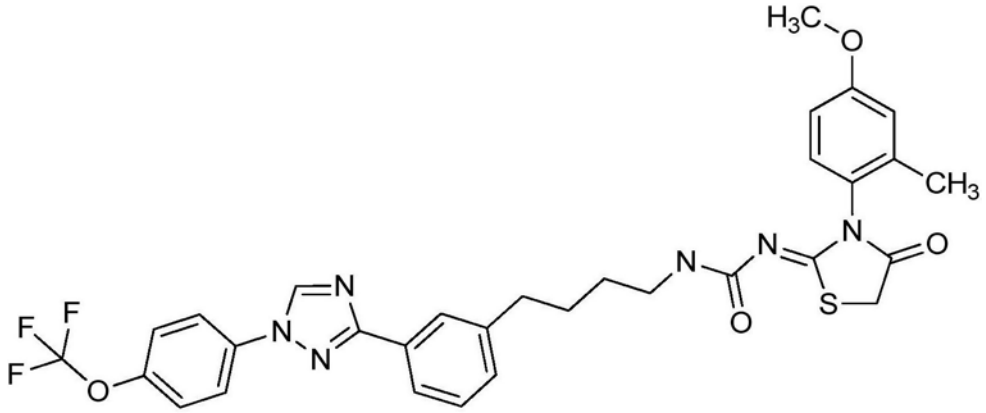
[1072] 制备(Z)-1-(3-(5-氯-2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)脲(FB35)

[1073] 

[1074] 标题化合物如实施例64中所述使用1-[(5-氯-2-异丙基-苯基)氨基硫代甲酰基]-3-[[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(FB26)制备,并且分离为浅黄色固体(0.095g,62%)。

[1075] 制备(Z)-1-(3-(4-甲氧基-2-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(FB38)

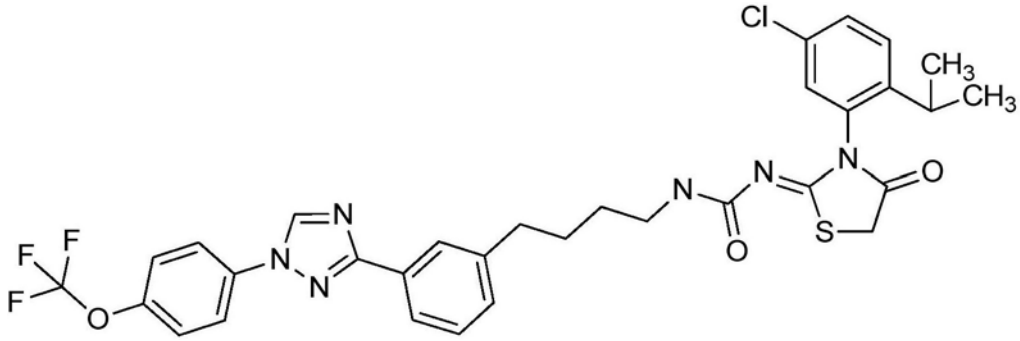
[1076]



[1077] 标题化合物如实施例64中所述使用1-[(4-甲氧基-2-甲基-苯基)氨基硫代甲酰基]-3-[4-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(FB36)制备,并且分离为白色固体(0.048g,67%)。

[1078] 制备(Z)-1-(3-(5-氯-2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁基)脲(FB39)

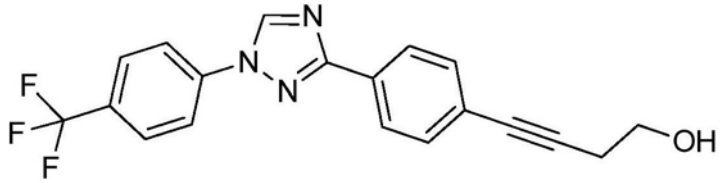
[1079]



[1080] 标题化合物如实施例64中所述使用1-[(5-氯-2-异丙基-苯基)氨基硫代甲酰基]-3-[4-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]丁基]脲(FB37)制备,并且分离为白色固体(0.060g,58%)。

[1081] 实施例65:制备4-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁-3-炔-1-醇(C61)

[1082]

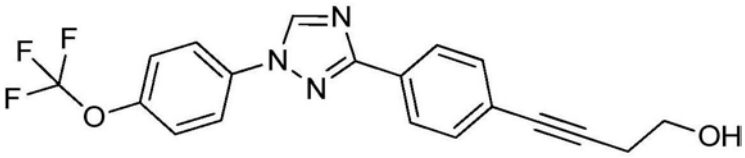


[1083] 向在25mL装配有搅拌棒和用隔片盖住的小瓶中3-(4-溴苯基)-1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑(C53)(0.50g,1.4mmol),加入双(三苯基膦)氯化钯(II)(0.019g,0.027mmol),碘化亚铜(I)(0.0026g,0.014mmol)和三乙胺(8.5mL),随后丁-3-炔-1-醇(0.12mL,1.6mmol)。将反应加热至60℃过夜。将反应停止,冷却至室温。将反应混合物用50%乙酸乙酯/水处理。将水层用乙酸乙酯提取。将合并的有机层用水洗涤。将有机层经硫酸钠干燥,过滤,浓缩。通过使用0-50%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供固体,其在50℃的真空中干燥过夜,提供为褐色固体的标题化合物。将其与起始的丁炔醇(8%)混合基于^{1}H NMR计算(0.38g,71%):^{1}H NMR(400MHz,$CDCl_3$)δ 8.66(s,1H),8.20-8.11(m,2H),7.94-7.88(m,2H),7.83-7.76(m,2H),7.56-7.50(m,2H),

3.85(q,J=6.3Hz,2H),2.74(t,J=6.2Hz,2H),1.83(t,J=6.3Hz,1H);^{19}F NMR(376MHz,$CDCl_3$)δ-62.51;ESIMS m/z 358([M+H]$^+$)。

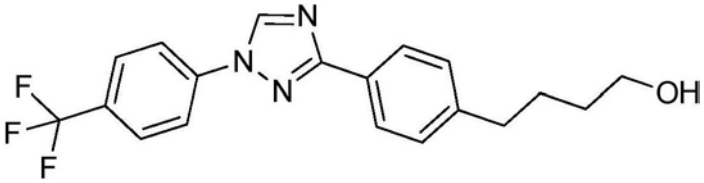
[1084] 下面的化合物根据实施例65中的步骤制备。

[1085] 制备4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁-3-炔-1-醇(CA23)

[1086] 

[1087] 标题化合物中所述实施例65使用3-(4-溴苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C52)制备,进一步通过用研制乙醚/己烷纯化,并且分离为白色固体(5.46g,66%):^{1}H NMR(400MHz,$CDCl_3$)δ8.57(s,1H),8.19-8.08(m,2H),7.84-7.76(m,2H),7.57-7.49(m,2H),7.39(dq,J=8.8,0.9Hz,2H),3.85(q,J=6.3Hz,2H),2.73(t,J=6.3Hz,2H),1.83(t,J=6.3Hz,1H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.02;ESIMS m/z 374([M+H]$^+$)。

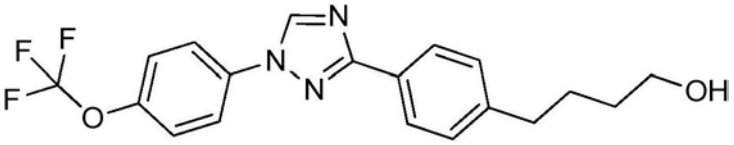
[1088] 实施例66:制备4-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-醇(CA24)

[1089] 

[1090] 向在100mL装配有搅拌棒和隔片的圆底烧瓶中的4-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁-3-炔-1-醇(C61)(0.376g,0.967mmol),加入乙酸乙酯(9.67mL)、随后钯碳(0.103g,0.0970mmol)。将反应混合物真空抽吸并且用氢气(球)(2×)吹扫,并且在室温搅拌过夜。将反应混合物通过Celite®过滤,用乙酸乙酯洗涤并且浓缩,提供为白色固体的标题化合物(0.363g,104%):^{1}H NMR(400MHz,$CDCl_3$)δ8.65(s,1H),8.15-8.08(m,2H),7.94-7.88(m,2H),7.80(dd,J=8.2,1.1Hz,2H),7.34-7.28(m,2H),3.74-3.66(m,2H),3.66-3.60(m,1H),2.72(t,J=7.6Hz,2H),1.81-1.71(m,2H),1.69-1.60(m,2H);^{19}F NMR(376MHz,$CDCl_3$)δ-62.48;ESIMS m/z 362([M+H]$^+$)。

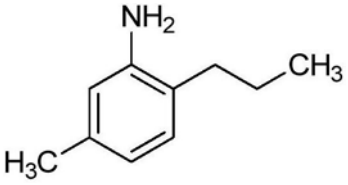
[1091] 下面的化合物根据实施例66中的步骤制备。

[1092] 制备4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁烷-1-醇(CA25)

[1093] 

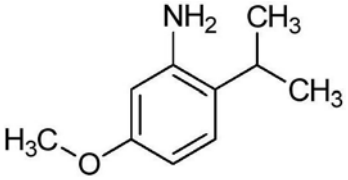
[1094] 标题化合物如实施例66中所述使用4-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丁-3-炔-1-醇(CA23)制备,并且分离为白色固体(3.03g,100%):^{1}H NMR(400MHz,$CDCl_3$)δ8.55(s,1H),8.10(d,J=8.2Hz,2H),7.86-7.76(m,2H),7.39(dq,J=9.0,0.9Hz,2H),7.33-7.27(m,2H),3.73-3.59(m,3H),2.72(t,J=7.6Hz,2H),1.82-1.70(m,2H),1.70-1.59(m,2H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 378([M+H]$^+$)。

[1095] 制备5-甲基-2-丙基苯胺(CA26)

[1096] 

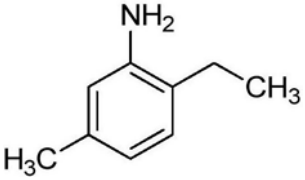
[1097] 标题化合物如实施例66中所述使用1-烯丙基-4-甲基-2-硝基苯(CA30)制备,并且分离为黄色油(1.39g,93%):^{1}H NMR(400MHz,$CDCl_3$)δ6.92(d,J=7.6Hz,1H),6.55(d,J=7.6Hz,1H),6.51(s,1H),3.55(s,2H),2.47-2.37(m,2H),2.24(s,3H),1.69-1.53(m,2H),0.99(t,J=7.3Hz,3H);^{13}C NMR(101MHz,$CDCl_3$)δ143.91,136.52,129.46,123.83,119.49,116.29,33.05,22.10,21.05,14.19;EIMS m/z 149([M]$^{+}$)。

[1098] 制备2-异丙基-5-甲氧基苯胺(CA27)

[1099] 

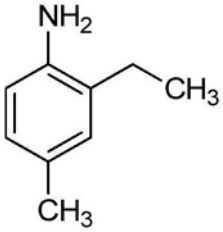
[1100] 标题化合物如实施例66中所述使用4-甲氧基-2-硝基-1-(丙-1-烯-2-基)苯(CA43)制备,并且分离为黄色油(2.23g,95%):^{1}H NMR(400MHz,$CDCl_3$)δ7.03(d,J=8.4Hz,1H),6.35(dd,J=8.5,2.6Hz,1H),6.25(d,J=2.6Hz,1H),3.75(s,3H),3.65(s,2H),2.83(p,J=6.8Hz,1H),1.24(d,J=6.8Hz,6H);EIMS m/z 165([M]$^{+}$)。

[1101] 制备2-乙基-5-甲基苯胺(CA28)

[1102] 

[1103] 标题化合物如实施例66中所述使用4-甲基-2-硝基-1-乙烯基苯(CA31)制备,并且分离为黄色油(0.926g,88%):^{1}H NMR(400MHz,$CDCl_3$)δ6.95(d,J=7.6Hz,1H),6.57(d,J=7.6Hz,1H),6.52(s,1H),3.56(s,2H),2.48(q,J=7.5Hz,2H),2.25(s,3H),1.23(t,J=7.6Hz,3H);^{13}C NMR(101MHz,$CDCl_3$)δ143.80,136.48,128.32,125.22,119.59,116.15,23.67,21.03,13.24;EIMS m/z 135([M]$^{+}$)。

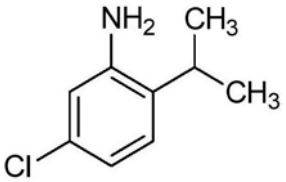
[1104] 制备2-乙基-4-甲基苯胺(CA29)

[1105] 

[1106] 标题化合物如实施例66中所述使用5-甲基-2-硝基-1-乙烯基苯(CA32)制备,并且分离为褐色油(1.07g,88%):^{1}H NMR(400MHz,$CDCl_3$)δ6.88(s,1H),6.86-6.82(m,1H),6.60(d,J=7.9Hz,1H),3.55(s,2H),2.50(q,J=7.5Hz,2H),2.24(s,3H),1.24(t,J=7.5Hz,3H);^{13}C NMR(101MHz,$CDCl_3$)δ141.35,129.09,128.25,128.01,127.19,115.56,24.05,

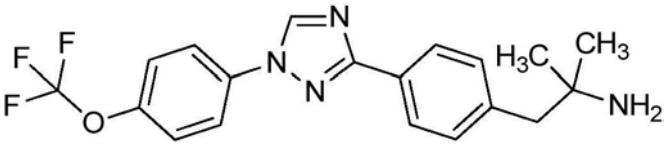
20.55,13.17;EIMS m/z 135([M]$^+$)。

[1107] 制备5-氯-2-异丙基苯胺(CB27)

[1108] 

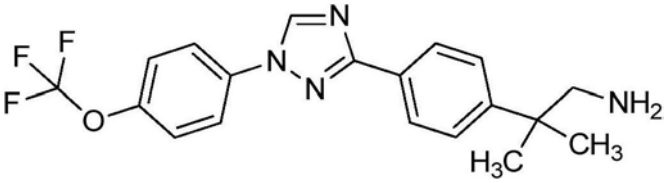
[1109] 标题化合物如实施例66中所述使用4-氯-2-硝基-1-(丙-1-烯-2-基)苯(CB33)制备,并且分离为褐色油(1.82g,84%):^{1}H NMR(400MHz,$CDCl_3$)δ7.38-7.31(m,1H),7.22-7.16(m,1H),7.07(d,J=8.1Hz,1H),6.83-6.77(m,2H),2.90(p,J=6.8Hz,1H),1.25(d,J=6.8Hz,6H);^{13}C NMR(101MHz,$CDCl_3$)δ126.91,126.83,126.51,121.34,120.07,116.37,27.44,22.34;EIMS m/z 169([M]$^+$)。

[1110] 制备2-甲基-1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-胺(CB28)

[1111] 

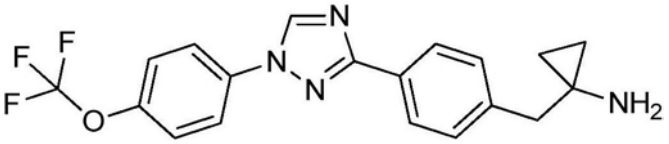
[1112] 标题化合物如实施例66中所述使用(2-甲基-1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-基)氨基甲酸苄酯(CB67)和甲醇作为溶剂制备;分离为黄色胶(0.775g,92%):^{1}H NMR(400MHz,$CDCl_3$)δ8.57(s,1H),8.13(d,J=8.2Hz,2H),7.81(d,J=9.0Hz,2H),7.39(dd,J=9.1,1.0Hz,2H),7.31(d,J=8.2Hz,2H),2.74(s,2H),2.05(s,2H),1.16(s,6H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 377([M+H]$^+$)。

[1113] 制备2-甲基-2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-胺(CB29)

[1114] 

[1115] 标题化合物如实施例66中所述使用(2-甲基-2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)氨基甲酸苄基酯(CB68)和甲醇作为溶剂制备;分离为澄清的油(0.427g,80%):^{1}H NMR(400MHz,$CDCl_3$)δ8.57(s,1H),8.15(d,J=8.4Hz,2H),7.84-7.77(m,2H),7.49-7.42(m,2H),7.39(dt,J=7.9,1.0Hz,2H),2.85(s,2H),1.78(s,2H),1.36(s,6H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 377([M+H]$^+$)。

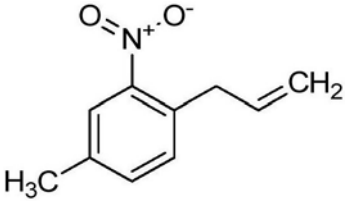
[1116] 制备1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)环丙胺(CB30)

[1117] 

[1118] 标题化合物如实施例66中所述使用(1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)环丙基)氨基甲酸苄基酯(CB69)制备,并且分离为褐色油(0.392g,95%)

:^{1}H NMR(400MHz,$CDCl_3$)δ8.60-8.49(m,1H),8.19-8.06(m,2H),7.84-7.72(m,2H),7.44-7.29(m,4H),3.49(s,2H),2.17(s,3H),0.73-0.59(m,4H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 375([M+H]$^{+}$)。

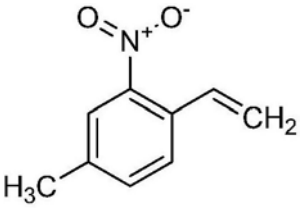
[1119] 实施例67:制备1-烯丙基-4-甲基-2-硝基苯(CA30)

[1120] 

[1121] 向在两个25-mL反应瓶中的1-氯-4-甲基-2-硝基苯(2.00g,11.7mmol),烯丙基三丁基锡烷(5.79g,17.5mmol)和双(三苯基膦)氯化钯(II)(0.818g,1.17mmol),加入1,2-二氯乙烷(20mL)。将瓶盖住,在120℃于BiotageInitiator®微波反应器中加热45分钟,在容器侧有外部红外传感器温度监测。将反应混合物装到Celite®柱体上。将粗制物质通过使用0-50%乙酸乙酯/己烷作为洗脱剂的快速柱色谱、随后使用0-100%乙腈/水作为洗脱剂的反相快速柱色谱纯化。将合并的乙腈/水级分浓缩,用乙酸乙酯提取,经硫酸钠干燥,过滤,浓缩,并且在真空烘箱中干燥,提供为黄色油的标题化合物(1.76g,84%):^{1}H NMR(400MHz,$CDCl_3$)δ7.73(d,J=0.9Hz,1H),7.34(dd,J=7.8,1.2Hz,1H),7.24(d,J=7.8Hz,1H),5.96(ddt,J=16.6,10.1,6.4Hz,1H),5.08(ddq,J=18.5,17.0,1.5Hz,2H),3.64(d,J=6.4Hz,2H),2.40(s,3H);^{13}C NMR(101MHz,$CDCl_3$)δ149.09,137.62,135.35,133.81,131.81,131.72,124.94,116.81,36.62,20.72;EIMS m/z 176([M]$^{+}$)。

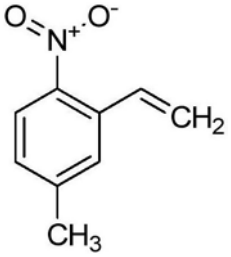
[1122] 下面的化合物根据实施例67中的步骤制备。

[1123] 制备4-甲基-2-硝基-1-乙烯基苯(CA31)

[1124] 

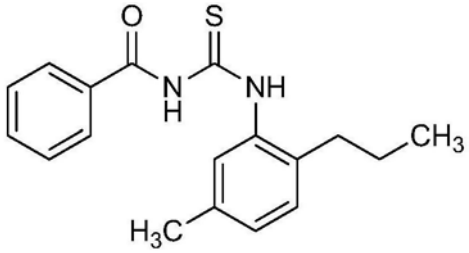
[1125] 标题化合物如实施例67中所述使用1-氯-4-甲基-2-硝基苯和三丁基(乙烯基)锡烷制备,进一步通过快速柱色谱和反相色谱纯化,并且分离为黄色油(1.26g,65%):^{1}H NMR(400MHz,$CDCl_3$)δ7.73(d,J=0.8Hz,1H),7.52(d,J=8.0Hz,1H),7.46-7.35(m,1H),7.13(dd,J=17.3,11.0Hz,1H),5.71(dd,J=17.3,0.9Hz,1H),5.43(dd,J=11.0,0.9Hz,1H),2.42(s,3H);^{13}C NMR(101MHz,$CDCl_3$)δ147.71,138.91,133.92,132.31,130.52,128.22,124.63,118.10,20.88;EIMS m/z 163([M]$^{+}$)。

[1126] 制备5-甲基-2-硝基-1-乙烯基苯(CA32)

[1127] 

[1128] 标题化合物如实施例67中所述使用1-氯-4-甲基-2-硝基苯和三丁基(乙烯基)锡烷制备，进一步通过快速柱色谱和反相色谱纯化，并且分离为黄色油(1.46g，75%)：^{1}H NMR(400MHz，$CDCl_3$)δ7.88(d，J＝8.3Hz，1H)，7.40(d，J＝1.2Hz，1H)，7.21(ddd，J＝11.0，9.9，8.2Hz，2H)，5.71(dd，J＝17.3，1.0Hz，1H)，5.46(dd，J＝11.0，1.0Hz，1H)，2.44(s，3H)；^{13}C NMR(101MHz，$CDCl_3$)δ145.56，144.31，133.64，133.05，129.08，128.98，124.68，118.52，21.49；EIMS m/z 163([M]$^{+}$)。

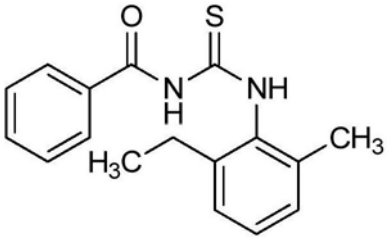
[1129] 实施例68：制备N-((5-甲基-2-丙基苯基)氨基硫代甲酰基)苯甲酰胺(CA33)

[1130] 

[1131] 向5-甲基-2-丙基苯胺(CA26)(1.38g，9.22mmol)和苯甲酰基异硫氰酸酯(1.24mL，9.22mmol)，加入丙酮(13mL)。将反应在60℃加热4h。反应冷却并且浓缩。将所得油在真空炉中干燥过夜，提供为褐色油的标题化合物(3.26g，100%)：^{1}H NMR(400MHz，$CDCl_3$)δ12.20(s，1H)，9.15(s，1H)，7.92(dt，J＝8.5，1.7Hz，2H)，7.71-7.60(m，1H)，7.55(m，3H)，7.18(d，J＝7.8Hz，1H)，7.09(dd，J＝7.8，1.1Hz，1H)，2.66-2.55(m，2H)，2.36(s，3H)，1.72-1.57(m，2H)，0.97(t，J＝7.3Hz，3H)；^{13}C NMR(101MHz，$CDCl_3$)δ179.64，166.90，136.22，135.72，134.57，133.74，131.68，129.79，129.22，128.64，127.55，127.24，33.28，23.58，21.01，13.98；ESIMS m/z 313([M+H]$^{+}$)。

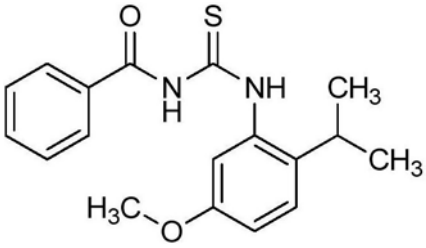
[1132] 下面的化合物根据实施例68中的步骤制备。

[1133] 制备N-((2-乙基-6-甲基苯基)氨基硫代甲酰基)苯甲酰胺(CA34)

[1134] 

[1135] 标题化合物如实施例68中所述使用2-乙基-6-甲基苯胺制备，并且分离为黄色油(6.41g，100%)：^{1}H NMR(400MHz，$CDCl_3$)δ11.88(s，1H)，9.21(s，1H)，8.02-7.85(m，2H)，7.73-7.63(m，1H)，7.62-7.50(m，2H)，7.29-7.23(m，1H)，7.20-7.14(m，2H)，2.75-2.57(m，2H)，2.33(s，3H)，1.25(t，J＝7.6Hz，3H)；ESIMS m/z 299([M+H]$^{+}$)。

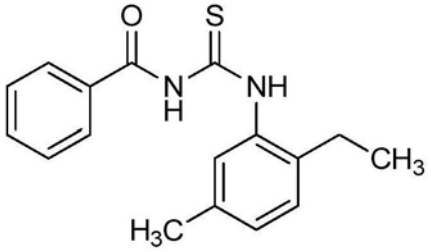
[1136] 制备N-((2-异丙基-5-甲氧基苯基)氨基硫代甲酰基)苯甲酰胺(CA35)

[1137] 

[1138] 标题化合物如实施例68中所述使用2-异丙基-5-甲氧基苯胺(CA27)制备，并且分

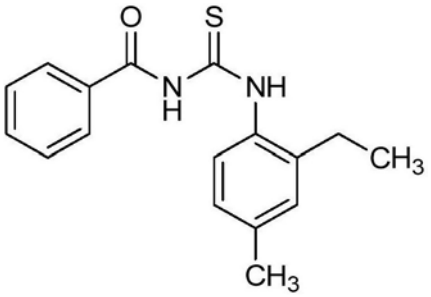
离为黄色油(4.63g,100%):^{1}H NMR(400MHz,$CDCl_3$)δ12.23(s,1H),9.13(s,1H),7.98-7.82(m,2H),7.74-7.61(m,1H),7.61-7.51(m,2H),7.32-7.26(m,2H),6.89(dd,J=8.7,2.7Hz,1H),3.81(s,3H),3.10(p,J=6.9Hz,1H),1.26(d,J=6.8Hz,6H);ESIMS m/z 329([M+H]$^+$)。

[1139] 制备N-((2-乙基-5-甲基苯基)氨基硫代甲酰基)苯甲酰胺(CA36)

[1140] 

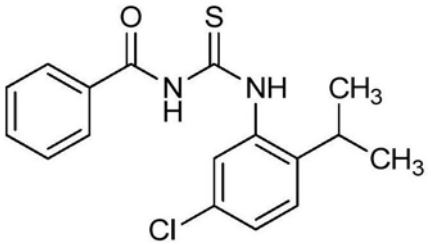
[1141] 标题化合物如实施例68中所述使用2-乙基-5-甲基苯胺(CA28)制备,并且分离为橙色固体(2.10g,97%):mp 105-107℃;^{1}H NMR(400MHz,$CDCl_3$)δ12.18(s,1H),9.14(s,1H),7.92(dt,J=8.6,1.7Hz,2H),7.73-7.60(m,1H),7.59-7.53(m,2H),7.50(s,1H),7.21(d,J=7.8Hz,1H),7.11(dd,J=7.8,1.1Hz,1H),2.71-2.59(m,2H),2.37(s,3H),1.24(t,J=7.6Hz,3H);^{13}C NMR(101MHz,$CDCl_3$)δ179.72,166.94,136.22,136.13,135.53,133.75,131.65,129.23,128.88,128.86,127.53,127.23,24.26,20.98,14.56;ESIMS m/z 299([M+H]$^+$)。

[1142] 制备N-((2-乙基-4-甲基苯基)氨基硫代甲酰基)苯甲酰胺(CA37)

[1143] 

[1144] 标题化合物如实施例68中所述使用2-乙基-4-甲基苯胺(CA29)制备,并且分离为橙色固体(2.46g,100%):mp 103℃(dec.);^{1}H NMR(400MHz,$CDCl_3$)δ12.16(s,1H),9.18(s,1H),7.95-7.86(m,2H),7.68-7.60(m,1H),7.60-7.51(m,4H),7.15-7.05(m,2H),2.66(q,J=7.6Hz,2H),2.37(s,3H),1.25(t,J=7.6Hz,3H);^{13}C NMR(101MHz,$CDCl_3$)δ179.89,166.97,138.94,137.88,133.75,133.20,131.67,129.77,129.23,127.55,127.15,126.71,24.63,21.27,14.52;ESIMS m/z 299([M+H]$^+$)。

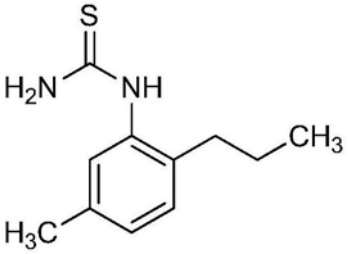
[1145] 制备N-((5-氯-2-异丙基苯基)氨基硫代甲酰基)苯甲酰胺(CB31)

[1146] 

[1147] 标题化合物如实施例68中所述使用5-氯-2-异丙基苯胺(CB27)制备,随后通过快速柱色谱纯化,并且分离为浅黄色固体(16.3g,98%):^{1}H NMR(400MHz,DMSO-d_6)δ12.32(s,1H),11.76(s,1H),8.07-7.95(m,2H),7.72-7.63(m,1H),7.60-7.50(m,3H),7.42(d,J=

8.5Hz,1H),7.37(dd,J=8.5,2.2Hz,1H),3.08(hept,J=6.9Hz,1H),1.19(d,J=6.8Hz,6H);^{13}C NMR(101MHz,DMSO)δ181.12,168.37,142.95,137.03,133.18,131.93,129.67,128.75,128.40,127.61,127.55,127.52,27.63,22.84;ESIMS m/z 333([M+H]$^{+}$)。

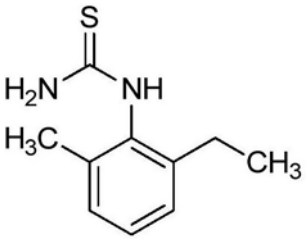
[1148] 实施例69:制备1-(5-甲基-2-丙基苯基)硫脲(CA38)

[1149] 

[1150] 向在甲醇(80mL)中的N-((5-甲基-2-丙基苯基)氨基硫代甲酰基)苯甲酰胺(C72)(3.21g,10.3mmol),加入氢氧化钠(2N,10.3mL,20.5mmol),在50℃加热2小时,然后在周末在室温搅拌。将反应混合物浓缩,用水稀释,用二氯甲烷提取,通过相分离器过滤,浓缩,并且在真空烘箱中干燥,提供为褐色固体的标题化合物(1.80g,83%):mp 143-145℃;^{1}H NMR(400MHz,$CDCl_3$)δ7.84(s,1H),7.20(d,J=7.8Hz,1H),7.12(dd,J=7.8,1.2Hz,1H),7.04(s,1H),5.99(d,J=254.5Hz,2H),2.57(d,J=7.5Hz,2H),2.33(s,3H),1.59(dq,J=14.8,7.4Hz,2H),0.95(t,J=7.3Hz,3H);^{13}C NMR(101MHz,$CDCl_3$)δ181.96,137.53,136.74,134.00,130.69,129.72,127.85,32.90,23.66,20.80,13.93;ESIMS m/z 209([M+H]$^{+}$)。

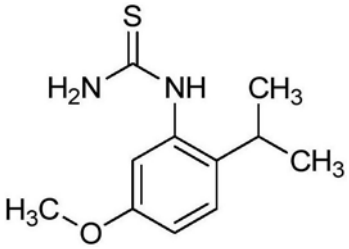
[1151] 下面的化合物根据实施例69中的步骤制备。

[1152] 制备1-(2-乙基-6-甲基苯基)硫脲(CA39)

[1153] 

[1154] 标题化合物中所述实施例69使用N-((2-乙基-6-甲基苯基)氨基硫代甲酰基)苯甲酰胺(CA34)制备,进一步通过用水研磨纯化,并且分离为白色固体(3.46g,83%):^{1}H NMR(400MHz,$CDCl_3$)δ7.63(s,1H),7.25(d,J=7.9Hz,1H),7.22-7.11(m,2H),6.13(bs,1H),5.33(bs,1H),2.77-2.55(m,2H),2.31(s,3H),1.21(t,J=7.6Hz,3H);ESIMS m/z 195([M+H]$^{+}$)。

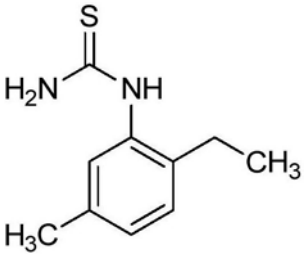
[1155] 制备1-(2-异丙基-5-甲氧基苯基)硫脲(CA40)

[1156] 

[1157] 标题化合物中所述实施例69使用N-((2-异丙基-5-甲氧基苯基)氨基硫代甲酰基)苯甲酰胺(CA35)制备,并且分离为橙色固体(2.65g,83%):mp134-139℃;^{1}H NMR(400MHz,$CDCl_3$)δ7.60(s,1H),7.30(d,J=8.7Hz,1H),6.93(dd,J=8.7,2.7Hz,1H),6.75(d,J=

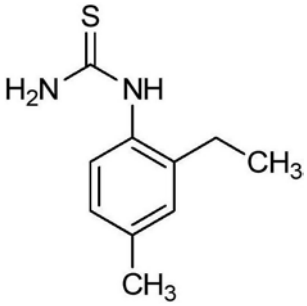
2.7Hz,1H),5.88(s,2H),3.79(s,3H),3.10(p,J=6.9Hz,1H),1.19(d,J=6.9Hz,6H);ESIMS m/z 225([M+H]$^+$)。

[1158] 制备1-(2-乙基-5-甲基苯基)硫脲(CA41)

[1159] 

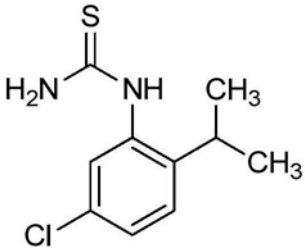
[1160] 标题化合物中所述实施例69使用N-((2-乙基-5-甲基苯基)氨基硫代甲酰基)苯甲酰胺(CA36)制备,并且分离为淡橙色固体(1.26g,94%):mp 143-147℃;^{1}H NMR(400MHz,$CDCl_3$)δ7.48(s,1H),7.23(d,J=7.8Hz,1H),7.14(d,J=8.0Hz,1H),7.04(s,1H),5.86(s,2H),2.61(q,J=7.5Hz,2H),2.33(s,3H),1.19(t,J=7.6Hz,3H);^{13}C NMR(101MHz,$CDCl_3$)δ182.13,138.27,137.53,133.74,129.95,129.93,127.84,24.00,20.79,14.77;ESIMS m/z 195([M+H]$^+$)。

[1161] 制备1-(2-乙基-4-甲基苯基)硫脲(CA42)

[1162] 

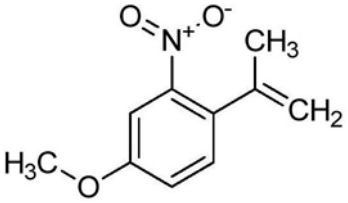
[1163] 制备标题化合物中所述实施例69使用N-((2-乙基-4-甲基苯基)氨基硫代甲酰基)苯甲酰胺(CA37),并且分离为褐色固体(1.40g,86%):mp 153-155℃;^{1}H NMR(400MHz,$CDCl_3$)δ7.60(s,1H),7.14(d,J=0.5Hz,1H),7.08(dt,J=8.1,4.8Hz,2H),5.85(d,J=184.3Hz,2H),2.62(q,J=7.6Hz,2H),2.35(s,3H),1.20(t,J=7.6Hz,3H);^{13}C NMR(101MHz,$CDCl_3$)δ182.32,141.33,139.33,131.29,130.75,128.15,127.36,24.36,21.18,14.74;ESIMS m/z 195([M+H]$^+$)。

[1164] 制备1-(5-氯-2-异丙基苯基)硫脲(CB32)

[1165] 

[1166] 标题化合物中所述实施例69使用N-((5-氯-2-异丙基苯基)氨基硫代甲酰基)苯甲酰胺(CB31)制备,并且分离为褐色粘性胶(1.38g,93%):^{1}H NMR(400MHz,$CDCl_3$)δ7.96(s,1H),7.34(d,J=1.4Hz,2H),7.24(t,J=1.3Hz,1H),5.97(s,2H),3.27-3.10(m,1H),1.21(d,J=6.8Hz,6H);ESIMS m/z 229([M+H]$^+$)。

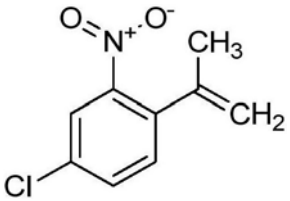
[1167] 实施例70:制备4-甲氧基-2-硝基-1-(丙-1-烯-2-基)苯(CA43)

[1168] 

[1169] 向1-氯-4-甲氧基-2-硝基苯(5.03g,26.8mmol),4,4,5,5-四甲基-2-(丙-1-烯-2-基)-1,3,2-二氧杂硼杂环戊烷(5.41g,32.2mmol),双(三苯基膦)氯化钯(II)(1.50g,2.15mmol),和碳酸钠(3.41g,32.2mmol),加入二氧六环/水(4:1,100mL:25mL)。将反应在80℃加热5小时。反应冷却至室温过夜。反应混合物用水稀释,用乙酸乙酯(3×)提取,经硫酸钠干燥,过滤,浓缩。通过使用0-5%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化,随后在真空烘箱中干燥,提供为橙色油的标题化合物(2.74g,53%):^{1}H NMR(400MHz,$CDCl_3$)δ7.37(d,J=2.7Hz,1H),7.23(d,J=8.6Hz,1H),7.08(dd,J=8.5,2.6Hz,1H),5.24-4.75(m,2H),3.86(s,3H),2.19-1.88(m,3H);^{13}C NMR(101MHz,$CDCl_3$)δ158.79,148.61,142.53,131.41,131.32,119.24,115.20,108.64,55.84,23.38;EIMS m/z 193([M]$^{+}$)。

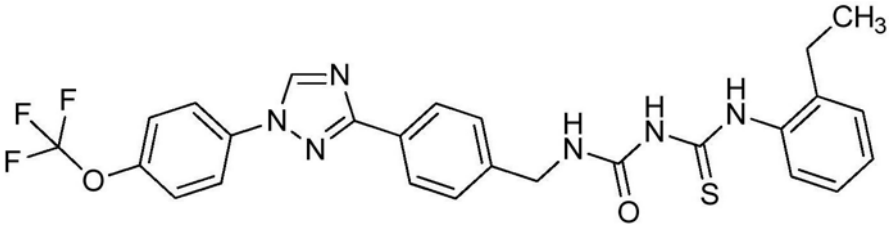
[1170] 下面的化合物根据实施例70中的步骤制备。

[1171] 制备4-氯-2-硝基-1-(丙-1-烯-2-基)苯(CB33)

[1172] 

[1173] 标题化合物中所述实施例70使用1-溴-4-氯-2-硝基苯加热过夜制备,并且分离为淡橙色液体(10.73g,84%):^{1}H NMR(400MHz,DMSO-d_6)δ8.04(d,J=2.2Hz,1H),7.76(dd,J=8.3,2.2Hz,1H),7.52(d,J=8.3Hz,1H),5.24(p,J=1.5Hz,1H),4.95(p,J=1.0Hz,1H),2.07(dd,J=1.5,0.9Hz,3H);^{13}C NMR(101MHz,DMSO)δ148.37,140.83,136.10,132.62,132.45,131.63,123.50,115.98,22.60;EIMS m/z 197([M]$^{+}$)。

[1174] 实施例71:制备1-[(2-乙基苯基)氨基硫代甲酰基]-3-[[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(PC2)

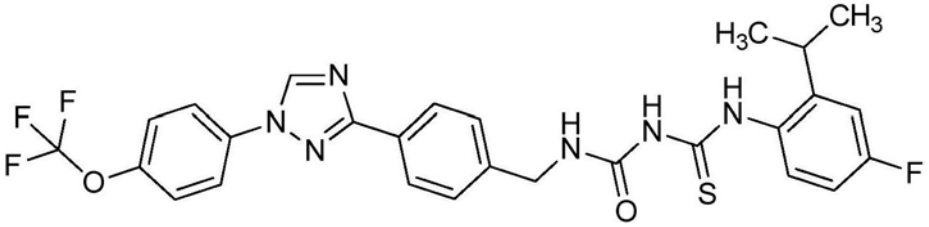
[1175] 

[1176] 将(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)甲烷胺(C16)(0.300g,0.897mmol)在二氯甲烷(4.0mL)中的微细悬浮液,以缓慢逐滴的方式加入到双(三氯甲基)碳酸酯(0.107g,0.359mmol)和乙酸钠(0.221g,2.69mmol)在二氯甲烷(4.0mL)和水(2.0mL)的两相溶液中。使反应搅拌30分钟。使反应通过相分离器,用另外的二氯甲烷洗涤,将有机层浓缩。将所得残留物用乙腈(4.0mL)稀释,加入为固体的1-(2-乙基苯基)硫脲(0.178g,0.987mmol)和碳酸铯(0.351g,1.08mmol)。使得反应在室温搅拌过夜。反应混合物

用二氯甲烷与水稀释，通过相分离器。将有机层浓缩到Celite上，并且通过使用20-100％乙腈/水作为洗脱剂的反相快速柱色谱(C_{18})纯化，提供为白色固体的标题化合物(0.100g，16％)(由～20％的二聚脲污染)：^{1}H NMR(400MHz，DMSO-d_6)δ11.99(s，1H)，10.24(s，1H)，9.41(s，1H)，9.40(d，J＝1.0Hz，1H)，8.18-8.03(m，6H)，7.63(dddd，J＝9.2，4.3，2.0，1.0Hz，3H)，7.54(ddd，J＝12.1，7.0，4.8Hz，2H)，7.50-7.38(m，3H)，7.35-7.26(m，1H)，7.26-7.20(m，2H)，4.44(d，J＝5.8Hz，2H)，2.56(q，J＝7.6Hz，2H)，1.14(t，J＝7.6Hz，3H)；^{19}F NMR(376MHz，DMSO-d_6)δ-56.96；ESIMS m/z 541([M+H]$^{+}$)，539([M-H]$^{-}$)

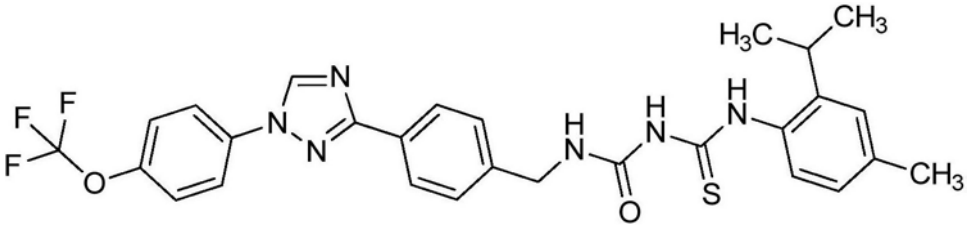
[1177] 下面的化合物根据实施例71中的步骤制备。

[1178] 制备1-[(4-氟-2-异丙基-苯基)氨基硫代甲酰基]-3-[[4-[1-[4-(三氟甲氧基)苯基]-1H-1，2，4-三唑-3-基]苯基]甲基]脲(PC3)

[1179] 

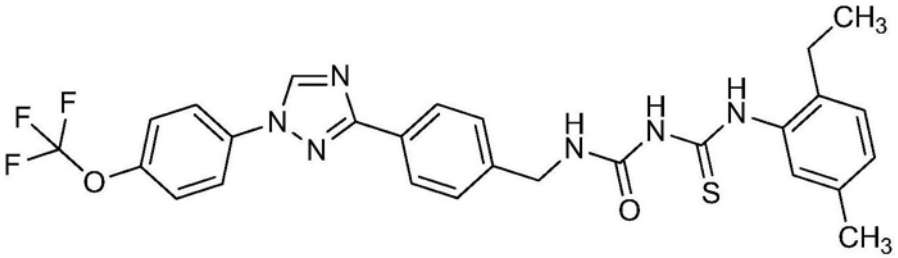
[1180] 标题化合物中所述实施例71使用(4-(1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑-3-基)苯基)甲烷胺(C16)和1-(4-氟-2-异丙基苯基)硫脲制备，并且分离为白色固体(0.157g，30％)：^{1}H NMR(400MHz，DMSO-d_6)δ11.81(s，1H)，10.26(s，1H)，9.41(s，1H)，8.15-8.03(m，4H)，7.63(ddt，J＝7.8，1.9，0.9Hz，2H)，7.58-7.44(m，3H)，7.39(dd，J＝8.8，5.6Hz，1H)，7.17(dd，J＝10.3，3.0Hz，1H)，7.05(td，J＝8.5，3.0Hz，1H)，4.44(d，J＝5.8Hz，2H)，3.05-2.93(m，1H)，1.16(d，J＝6.8Hz，6H)；^{19}F NMR(376MHz，DMSO-d_6)δ-56.96，-114.33；ESIMS m/z 573([M+H]$^{+}$)，571([M-H]$^{-}$)。

[1181] 制备1-[(2-异丙基-4-甲基-苯基)氨基硫代甲酰基]-3-[[4-[1-[4-(三氟甲氧基)苯基]-1H-1，2，4-三唑-3-基]苯基]甲基]脲(PC5)

[1182] 

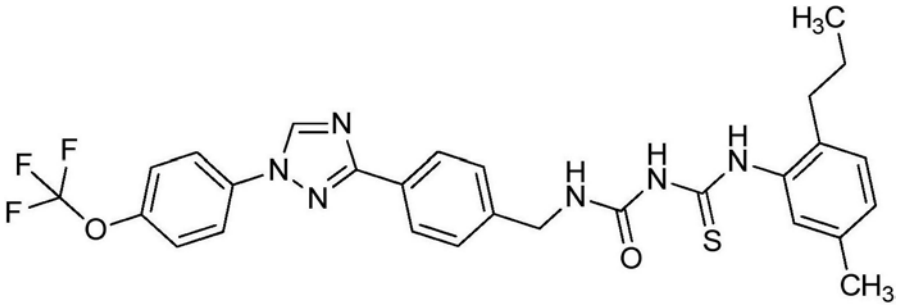
[1183] 标题化合物中所述实施例71使用(4-(1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑-3-基)苯基)甲烷胺(C16)和1-(2-异丙基-4-甲基苯基)硫脲制备，并且分离为白色固体(0.110g，21％)：^{1}H NMR(400MHz，DMSO-d_6)δ11.83(s，1H)，10.21(s，1H)，9.41(s，1H)，8.17-8.05(m，4H)，7.63(dq，J＝8.9，0.9Hz，2H)，7.56-7.44(m，3H)，7.26(d，J＝8.0Hz，1H)，7.15(d，J＝2.0Hz，1H)，7.06-6.98(m，1H)，4.44(d，J＝5.8Hz，2H)，2.97(hept，J＝6.7Hz，1H)，2.31(s，3H)，1.16(d，J＝6.8Hz，6H)；^{19}F NMR(376MHz，DMSO-d_6)δ-56.96；ESIMS m/z 569([M+H]$^{+}$)，567([M-H]$^{-}$)。

[1184] 制备1-[(2-乙基-5-甲基-苯基)氨基硫代甲酰基]-3-[[4-[1-[4-(三氟甲氧基)苯基]-1H-1，2，4-三唑-3-基]苯基]甲基]脲(PC7)

[1185] 

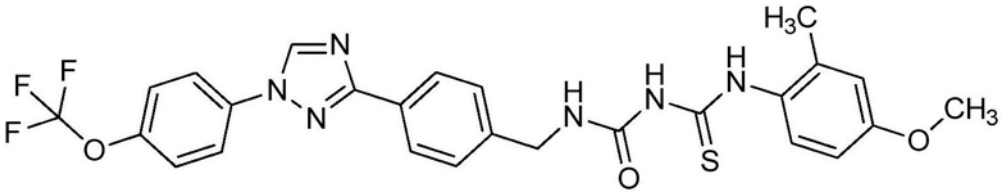
[1186] 标题化合物中所述实施例71使用(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)甲烷胺(C16)和1-(2-乙基-5-甲基苯基)硫脲(CA41)制备,并且分离为灰白色固体(0.092g,18%):^{1}H NMR(400MHz,DMSO-d_6)δ11.94(s,1H),10.22(s,1H),9.41(d,J=0.8Hz,1H),8.18-8.04(m,4H),7.63(d,J=8.7Hz,2H),7.57-7.44(m,3H),7.39-7.31(m,1H),7.17(d,J=7.7Hz,1H),7.04(dd,J=8.0,1.7Hz,1H),4.44(d,J=5.8Hz,2H),2.51(dt,J=3.6,1.9Hz,2H),2.27(s,3H),1.14-1.08(m,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 555([M+H]$^{+}$),553([M-H]$^{-}$)。

[1187] 制备1-[(5-甲基-2-丙基-苯基)氨基硫代甲酰基]-3-[[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(PC8)

[1188] 

[1189] 标题化合物中所述实施例71使用(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)甲烷胺(C16)和1-(5-甲基-2-丙基苯基)硫脲(CA38)制备,并且分离为灰白色固体(0.079g,15%):^{1}H NMR(400MHz,DMSO-d_6)δ11.98(s,1H),10.22(s,1H),9.41(s,1H),8.14-8.06(m,4H),7.69-7.61(m,2H),7.56-7.44(m,3H),7.39(s,1H),7.14(d,J=7.7Hz,1H),7.08-6.99(m,1H),4.44(d,J=5.8Hz,2H),2.49-2.43(m,2H),2.27(s,3H),1.50(h,J=7.3Hz,2H),0.86(t,J=7.3Hz,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 569([M+H]$^{+}$),567([M-H]$^{-}$)。

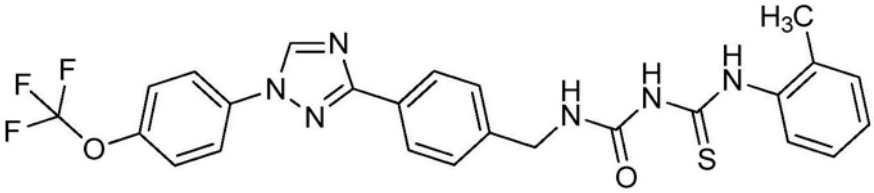
[1190] 制备1-[(4-甲氧基-2-甲基-苯基)氨基硫代甲酰基]-3-[[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(PC6)

[1191] 

[1192] 标题化合物中所述实施例71使用(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)甲烷胺(C16)和1-(4-甲氧基-2-甲基苯基)硫脲制备,并且分离为白色固体(0.076g,15%):^{1}H NMR(400MHz,DMSO-d_6)δ11.76(s,1H),10.18(s,1H),9.41(s,1H),8.11-8.04(m,5H),7.69-7.58(m,3H),7.58-7.35(m,5H),6.90-6.82(m,1H),6.77(dd,J=8.7,

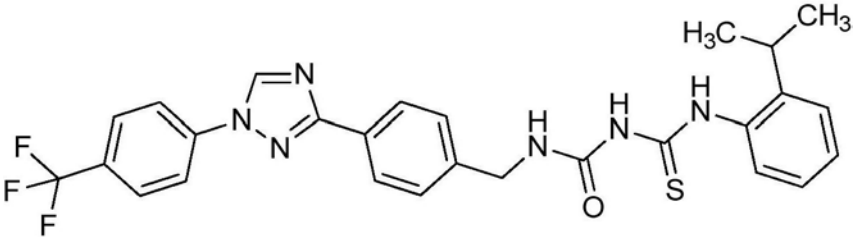
2.9Hz,1H),4.43(d,J=5.8Hz,2H),3.75(s,3H),2.18(s,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESMIS m/z 557([M+H]$^+$),555([M-H]$^-$)。

[1193] 制备1-(邻甲苯基氨基硫代甲酰基)-3-[[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(PC1)

[1194] 

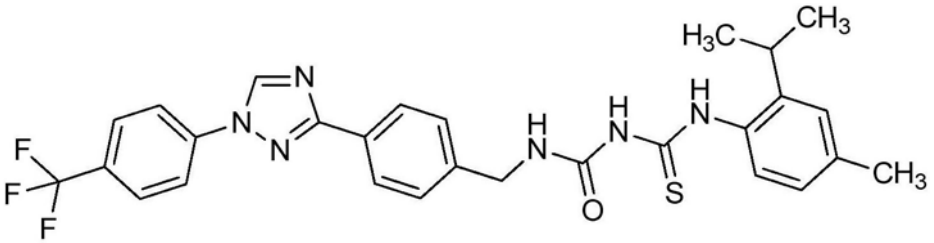
[1195] 标题化合物中所述实施例71使用(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)甲烷胺(C16)和1-(邻甲苯基)硫脲制备,并且分离为白色固体(0.116g,24%):^{1}H NMR(400MHz,DMSO-d_6)δ12.00(s,1H),10.22(s,1H),9.41(s,1H),8.18-8.06(m,4H),7.64(dp,J=7.8,0.9Hz,3H),7.55(t,J=5.9Hz,1H),7.52-7.46(m,2H),7.32-7.28(m,1H),7.27-7.17(m,2H),4.46(d,J=5.8Hz,2H),2.25(s,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 527([M+H]$^+$),525([M-H]$^-$)。

[1196] 制备1-[(2-异丙基苯基)氨基硫代甲酰基]-3-[[4-[1-[4-(三氟甲基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(PC14)

[1197] 

[1198] 标题化合物中所述实施例71使用(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)甲烷胺(CA3)和1-(2-异丙基苯基)硫脲制备,并且分离为白色固体(0.088g,17%):^{1}H NMR(400MHz,DMSO-d_6)δ11.94(s,1H),10.24(s,1H),9.55(s,1H),8.22(d,J=8.5Hz,2H),8.19-8.13(m,2H),8.01(d,J=8.4Hz,2H),7.56(t,J=5.9Hz,1H),7.53-7.48(m,2H),7.45(dd,J=7.8,1.5Hz,1H),7.38(dd,J=7.7,1.6Hz,1H),7.30(td,J=7.5,1.5Hz,1H),7.24(td,J=7.6,1.7Hz,1H),4.47(d,J=5.8Hz,2H),3.05(hept,J=7.0Hz,1H),1.20(d,J=6.8Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-60.79;ESIMS m/z 539([M+H]$^+$),537([M-H]$^-$)。

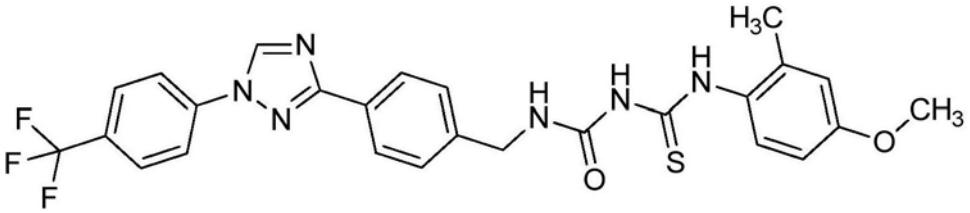
[1199] 制备1-[(2-异丙基-4-甲基-苯基)氨基硫代甲酰基]-3-[[4-[1-[4-(三氟甲基)苯基]-1,2,4-三唑-3-基]苯基]甲基]脲(PC15)

[1200] 

[1201] 标题化合物中所述实施例71使用(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)甲烷胺(CA3)和1-(2-异丙基-4-甲基苯基)硫脲制备,并且分离为白色固体

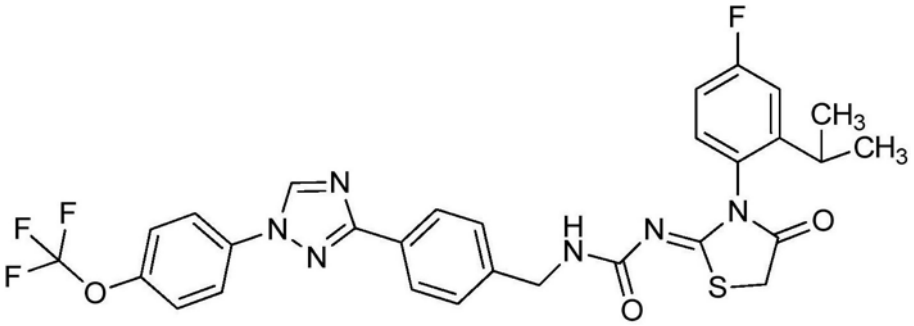
(0.073g,14%):^{1}H NMR(400MHz,DMSO-d_6)δ11.84(s,1H),10.21(s,1H),9.55(s,1H),8.22(d,J=8.4Hz,2H),8.19-8.12(m,2H),8.01(d,J=8.5Hz,2H),7.54(t,J=6.0Hz,1H),7.52-7.47(m,2H),7.29(d,J=8.0Hz,1H),7.17(d,J=2.0Hz,1H),7.07-7.01(m,1H),4.47(d,J=5.8Hz,2H),3.00(hept,J=6.9Hz,1H),2.33(s,3H),1.19(d,J=6.8Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-60.79;ESIMS m/z 553([M+H]$^{+}$),551([M-H]$^{-}$)。

[1202] 制备1-[(4-甲氧基-2-甲基-苯基)氨基硫代甲酰基]-3-[[4-[1-[4-(三氟甲基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(PC16)

[1203] 

[1204] 标题化合物中所述实施例71使用(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苯基)甲烷胺(CA3)和1-(4-甲氧基-2-甲基苯基)硫脲制备,并且分离为白色固体(0.033g,6%):^{1}H NMR(400MHz,DMSO-d_6)δ10.17(s,1H),9.53(s,1H),9.18(s,1H),8.22(d,J=8.4Hz,2H),8.15-8.06(m,2H),8.01(d,J=8.5Hz,2H),7.37(d,J=8.3Hz,2H),7.12(d,J=8.6Hz,1H),7.07(t,J=6.0Hz,1H),6.92(d,J=2.9Hz,1H),6.88(dd,J=8.6,2.9Hz,1H),4.29(dd,J=5.9,2.9Hz,2H),3.82(s,3H),2.11(s,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-60.79;ESIMS m/z 541([M+H]$^{+}$),539([M-H]$^{-}$)。

[1205] 实施例72:制备(Z)-1-(3-(4-氟-2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)脲(P3,P1172)

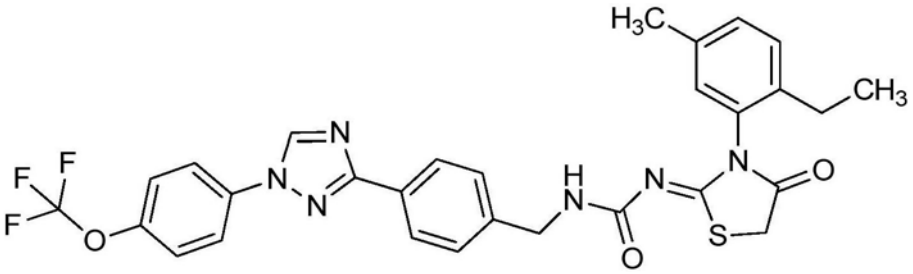
[1206] 

[1207] 向20mL小瓶加入1-[(4-氟-2-异丙基-苯基)氨基硫代甲酰基]-3-[[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(PC3)(0.092g,0.16mmol),乙酸钠(0.040g,0.48mmol),2-溴乙酸甲酯(0.084mL,0.80mmol)和乙腈(2.0mL)。将小瓶密封,并且将反应在65℃加热过夜。将反应混合物用盐水溶液和二氯甲烷稀释,通过相分离器。将有机层浓缩,将所得残留物通过使用10-80%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化,提供为白色固体的标题化合物(0.058g,58%)。

[1208] 下面的化合物根据实施例72中的步骤制备。

[1209] 制备(Z)-1-(3-(2-乙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)脲(P7)

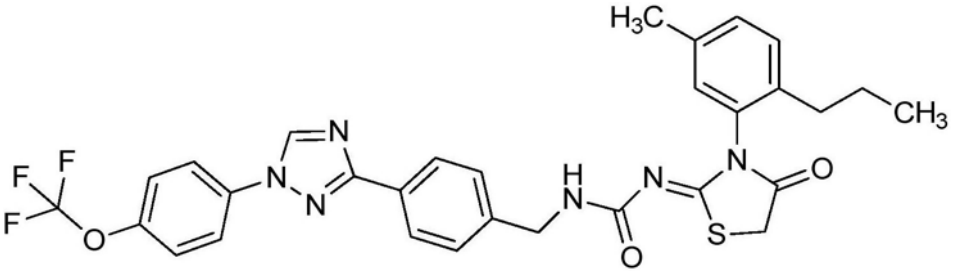
[1210]



[1211] 标题化合物如实施例72中所述使用1-[(2-乙基-5-甲基-苯基)氨基硫代甲酰基]-3-[[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(PC7)制备,并且分离为灰白色固体(0.034g,44%)。

[1212] 制备(Z)-1-(3-(5-甲基-2-丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)脲(P8,P852)

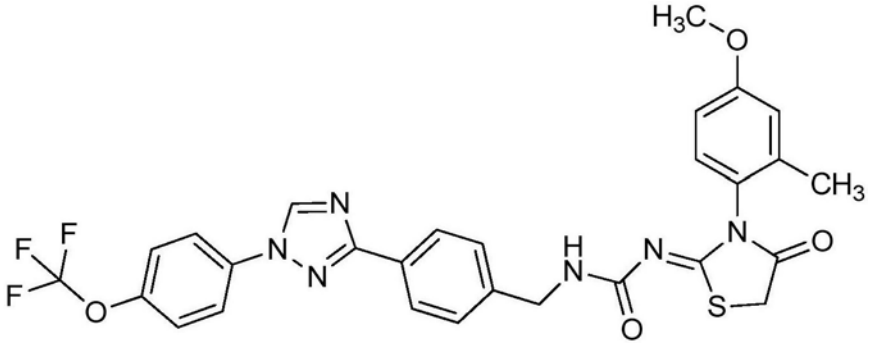
[1213]



[1214] 制备标题化合物如实施例72中所述使用1-[(5-甲基-2-丙基-苯基)氨基硫代甲酰基]-3-[[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(PC8),并且分离为灰白色固体(0.018g,25%)。

[1215] 制备(Z)-1-(3-(4-甲氧基-2-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)脲(P6)

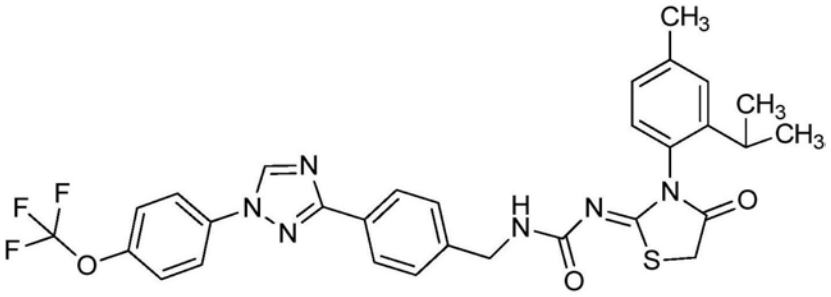
[1216]



[1217] 标题化合物如实施例72中所述使用1-[(4-甲氧基-2-甲基-苯基)氨基硫代甲酰基]-3-[[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(PC6)制备,并且分离为灰白色固体(0.041g,46%)。

[1218] 制备(Z)-1-(3-(2-异丙基-4-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)脲(P5)

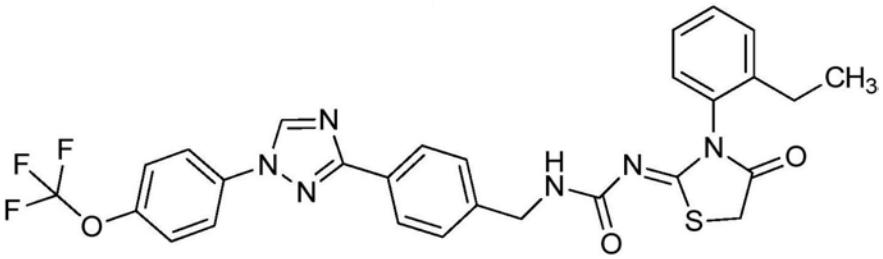
[1219]



[1220] 标题化合物如实施例72中所述使用1-[(2-异丙基-4-甲基-苯基)氨基硫代甲酰基]-3-[[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(PC5)制备,并且分离为灰白色固体(0.012g,25%)。

[1221] 制备(Z)-1-(3-(2-乙基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)脲(P2,P532)

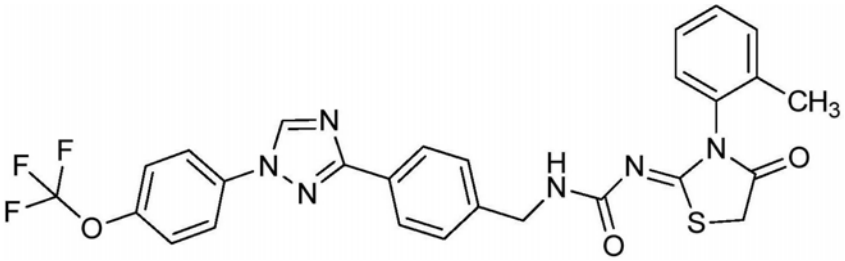
[1222]



[1223] 标题化合物如实施例72中所述使用1-[(2-乙基苯基)氨基硫代甲酰基]-3-[[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(PC2)制备,并且分离为白色固体(0.031g,28%)。

[1224] 制备(Z)-1-(4-氧代-3-(邻甲苯基)噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)脲(P1)

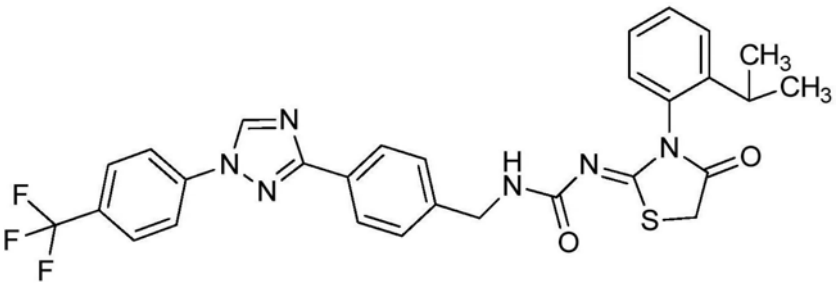
[1225]



[1226] 标题化合物如实施例72中所述使用1-(邻甲苯基氨基硫代甲酰基)-3-[[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(PC1)和乙醇作为溶剂制备,并且分离为白色固体(0.086g,79%)。

[1227] 制备(Z)-1-(3-(2-异丙基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苄基)脲(P14)

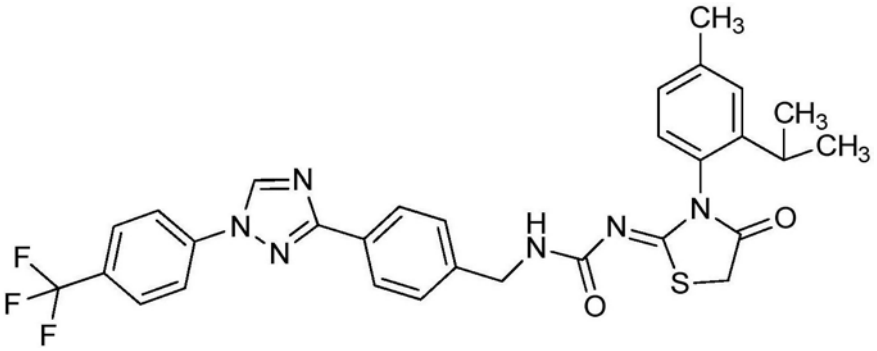
[1228]



[1229] 标题化合物如实施例72中所述使用1-[(2-异丙基苯基)氨基硫代甲酰基]-3-[[4-[1-[4-(三氟甲基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(PC14)和乙醇作为溶剂制备,并且分离为白色固体(0.055g,69%)。

[1230] 制备(Z)-1-(3-(2-异丙基-4-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲基)苯基)-1H-1,2,4-三唑-3-基)苄基)脲(P15)

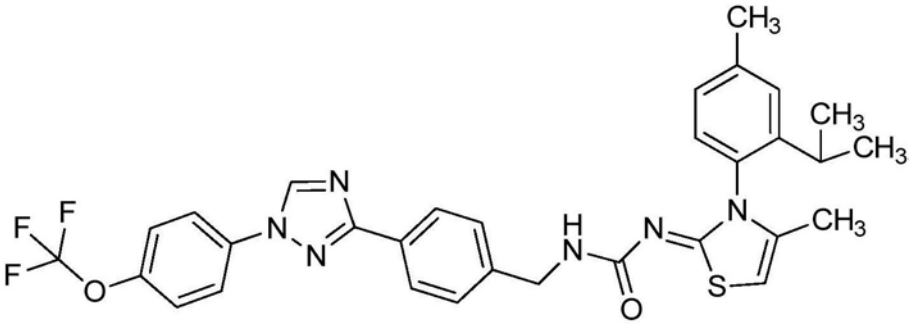
[1231]



[1232] 标题化合物如实施例72中所述使用1-[(2-异丙基-4-甲基-苯基)氨基硫代甲酰基]-3-[[4-[1-[4-(三氟甲基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(PC15)和乙醇作为溶剂制备,并且分离为白色固体(0.049g,80%)。

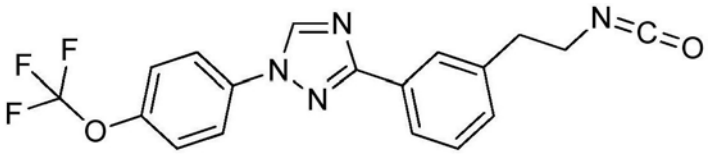
[1233] 实施例73:制备(Z)-1-(3-(2-异丙基-4-甲基苯基)-4-甲基噻唑-2(3H)-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)脲(P20)

[1234]



[1235] 向20mL小瓶加入1-[(2-异丙基-4-甲基-苯基)氨基硫代甲酰基]-3-[[4-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(PC5)(0.044g,0.077mmol),乙酸钠(0.019g,0.23mmol),1-氯丙烷-2-酮(0.0092mL,0.12mmol)和乙腈(1.5mL)。将小瓶密封,在65℃加热过夜。将反应混合物用盐水溶液和二氯甲烷稀释,通过相分离器。将有机层浓缩,将所得残留物通过使用10-80%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化,提供为灰白色固体的标题化合物(0.010g,21%):^{1}H NMR(400MHz,DMSO-d_6)δ9.38(s,1H),8.14-8.01(m,4H),7.70(s,1H),7.62(dq,J=7.7,1.0Hz,2H),7.45-7.35(m,2H),7.34-7.27(m,1H),7.15(t,J=1.3Hz,2H),6.66(q,J=0.9Hz,1H),4.47-4.28(m,2H),2.73-2.62(m,1H),2.39(s,3H),2.10(d,J=1.1Hz,3H),1.10(d,J=6.8Hz,3H),1.00(d,J=6.8Hz,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 607([M+H]$^{+}$)。

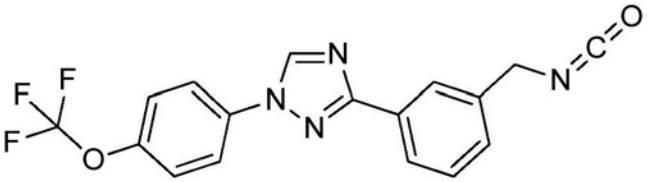
[1236] 实施例74:制备3-(3-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(CA44)

[1237] 

[1238] 向在200mL圆底烧瓶中的3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸(CA13)(3.0g,8.0mmol)和三乙胺(1.1mL,8.0mmol)于甲苯(80mL)中的悬浮液,加入叠氮磷酸二苯酯(1.7mL,8.0mmol)。将反应混合物在室温搅拌2小时。将反应混合物浓缩到Celite®上。通过使用0-50%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化,提供浅黄色油(1.8g),将其储存过夜。所述油(通过^{1}H NMR确定为酰基叠氮化物和异氰酸酯的混合物)随着时间流逝而固化,将其在真空下储存另外一个晚上。将所得固体溶解在1,2-二氯乙烷(50mL)1,2-二氯乙烷中,在60℃加热3小时。将溶剂浓缩,给出标题化合物(1.8g,59%):^{1}H NMR(400MHz,DMSO-d_6)δ9.41(s,1H),8.13-8.06(m,2H),8.06-7.98(m,2H),7.63(dq,J=7.9,1.0Hz,2H),7.49(td,J=7.6,0.6Hz,1H),7.41(dt,J=7.7,1.3Hz,1H),3.66(t,J=6.6Hz,2H),2.99(t,J=6.7Hz,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97.

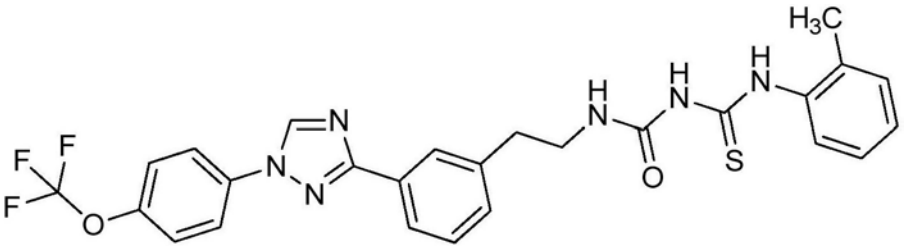
[1239] 下面的化合物根据实施例74中的步骤制备。

[1240] 制备3-(3-(异氰酸酯基甲基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(CB34)

[1241] 

[1242] 标题化合物中所述实施例74使用2-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙酸(CB23)制备,并且分离为白色固体(2.41g,48%,85%纯度):^{1}H NMR(400MHz,DMSO-d_6)δ9.43(s,1H),8.17-8.03(m,4H),7.65-7.44(m,4H),4.73(s,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-57.00;ESIMS m/z 361([M+H]$^{+}$)。

[1243] 实施例75:制备1-(邻甲苯基氨基硫代甲酰基)-3-[2-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(PC74)

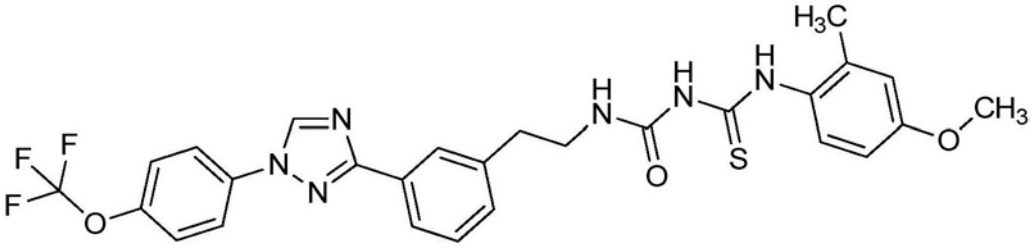
[1244] 

[1245] 向20mL的小瓶,装入为固体的1-(邻甲苯基)硫脲(0.096g,0.58mmol)和碳酸铯(0.22g,0.68mmol)。然后加入在乙腈(4.0mL)中的3-(3-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(CA44)(0.20g,0.52mmol)。使得反应在室温搅拌过夜。将反应混合物用二氯甲烷稀释并且通过相分离器过滤。将滤液通过使用0-50%乙酸乙酯/己烷作为洗脱剂的快速柱色谱、随后使用10-50%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供为白色固体的标题化合物(0.11g,37%):^{1}H NMR(400MHz,DMSO-d_6)δ12.01(s,1H),10.12(s,1H),9.42(s,1H),8.13-8.05(m,2H),8.04-7.96

(m,2H),7.66-7.54(m,3H),7.54-7.46(m,1H),7.39(dt,J=7.7,1.5Hz,1H),7.29-7.24(m,1H),7.24-7.14(m,2H),7.03(t,J=5.6Hz,1H),3.46(q,J=6.6Hz,2H),2.96-2.84(m,2H),2.20(s,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 541([M+H]$^+$),539([M-H]$^-$)。

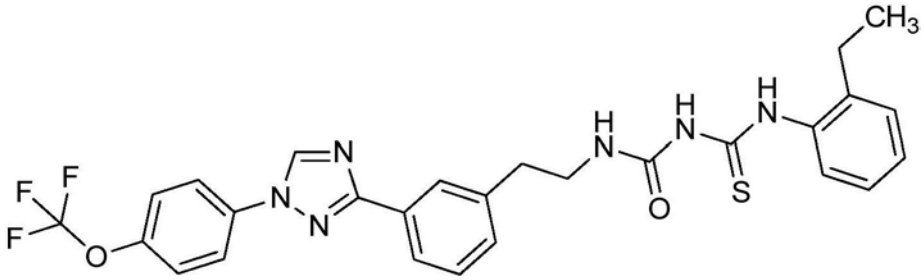
[1246] 下面的化合物根据实施例75中的步骤制备。

[1247] 制备1-[(4-甲氧基-2-甲基-苯基)氨基硫代甲酰基]-3-[2-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(PC87)

[1248] 

[1249] 标题化合物如实施例75中所述使用3-(3-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(CA44)和1-(4-甲氧基-2-甲基苯基)硫脲制备,分离为白色固体(0.105g,34%):^{1}H NMR(400MHz,DMSO-d_6)δ11.78(s,1H),10.07(s,1H),9.42(s,1H),8.13-8.05(m,2H),8.04-7.96(m,2H),7.66-7.57(m,2H),7.53-7.45(m,1H),7.42-7.32(m,2H),7.01(t,J=5.7Hz,1H),6.85-6.81(m,1H),6.76(dd,J=8.7,2.9Hz,1H),3.74(s,3H),3.45(q,J=6.6Hz,2H),2.89(t,J=6.9Hz,2H),2.15(s,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 517([M+H]$^+$),569[(M-H)$^+$]。

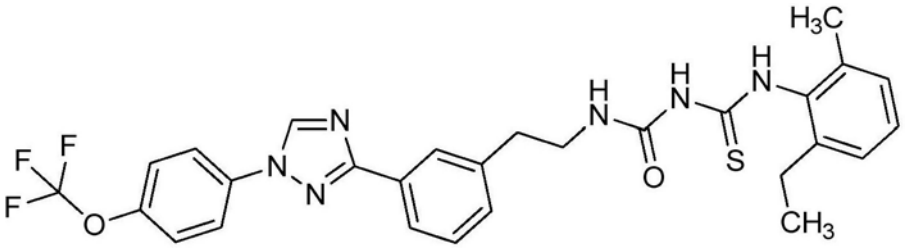
[1250] 制备1-[(2-乙基苯基)氨基硫代甲酰基]-3-[2-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(PC75)

[1251] 

[1252] 标题化合物如实施例75中所述使用3-(3-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(CA44)和1-(2-乙基苯基)硫脲制备,分离为白色固体(0.104g,35%):^{1}H NMR(400MHz,DMSO-d_6)δ12.01(s,1H),10.13(s,1H),9.42(s,1H),8.15-8.05(m,2H),8.05-7.96(m,2H),7.67-7.57(m,2H),7.56-7.45(m,2H),7.39(dt,J=7.7,1.4Hz,1H),7.33-7.25(m,1H),7.25-7.17(m,2H),7.09-6.96(m,1H),3.47(q,J=6.5Hz,2H),2.89(t,J=6.9Hz,2H),2.58-2.51(m,2H),1.11(t,J=7.5Hz,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 555([M+H]$^+$),553([M-H]$^-$)。

[1253] 制备1-[(2-乙基-6-甲基-苯基)氨基硫代甲酰基]-3-[2-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(PC83)

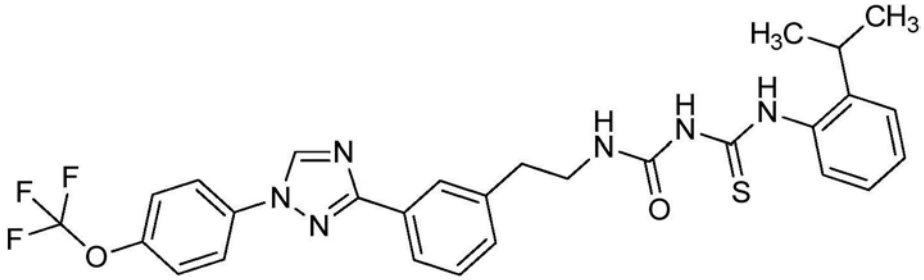
[1254]



[1255] 标题化合物如实施例75中所述使用3-(3-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(CA44)和1-(2-乙基-6-甲基苯基)硫脲(CA39)制备,分离为白色固体(0.137g,45%):^{1}H NMR(400MHz,DMSO-d_6)δ11.58(s,1H),10.13(s,1H),9.42(s,1H),8.16-8.05(m,2H),8.05-7.96(m,2H),7.62(ddd,J=7.9,2.0,1.0Hz,2H),7.49(t,J=7.6Hz,1H),7.39(dt,J=7.7,1.4Hz,1H),7.21-7.12(m,1H),7.13-7.05(m,2H),7.00(t,J=5.7Hz,1H),3.47(q,J=6.7Hz,2H),2.90(t,J=6.9Hz,2H),2.47(dd,J=7.6,2.9Hz,2H),2.14(s,3H),1.14-1.08(m,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 569([M+H]$^{+}$),567([M-H]$^{-}$)。

[1256] 制备1-[(2-异丙基苯基)氨基硫代甲酰基]-3-[2-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(PC76)

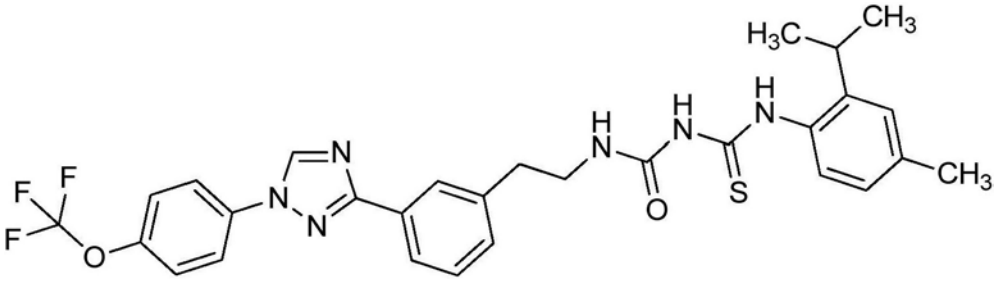
[1257]



[1258] 标题化合物如实施例75中所述使用3-(3-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(CA44)和1-(2-异丙基苯基)硫脲制备,分离为白色固体(0.033g,11%):^{1}H NMR(400MHz,DMSO-d_6)δ11.95(s,1H),10.14(s,1H),9.42(s,1H),8.14-8.05(m,2H),8.05-7.94(m,2H),7.68-7.57(m,2H),7.49(t,J=7.6Hz,1H),7.39(dq,J=7.8,1.5Hz,2H),7.34(dd,J=7.8,1.6Hz,1H),7.26(td,J=7.5,1.5Hz,1H),7.20(td,J=7.5,1.6Hz,1H),7.03(t,J=5.7Hz,1H),3.47(q,J=6.6Hz,2H),2.98(p,J=6.9Hz,1H),2.89(t,J=6.9Hz,2H),1.15(d,J=6.8Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 569([M+H]$^{+}$),567([M-H]$^{-}$)。

[1259] 制备1-[(2-异丙基-4-甲基-苯基)氨基硫代甲酰基]-3-[2-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(PC84)

[1260]

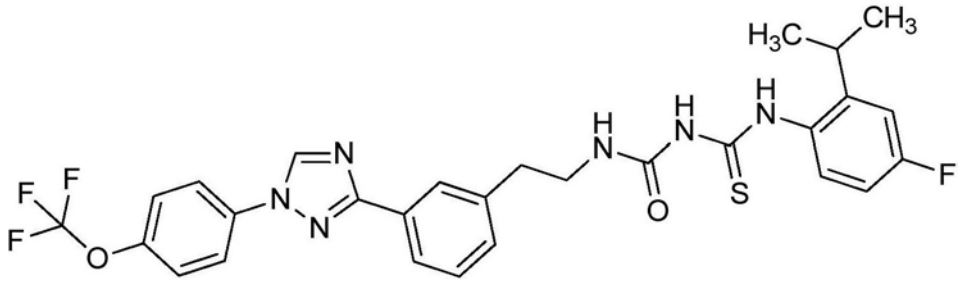


[1261] 标题化合物如实施例75中所述使用3-(3-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟

甲氧基)苯基)-1H-1,2,4-三唑(CA44)和1-(2-异丙基-4-甲基苯基)硫脲制备,分离为白色固体(0.077g,25%):^{1}H NMR(400MHz,DMSO-d_6)δ11.85(s,1H),10.10(s,1H),9.42(s,1H),8.15-8.05(m,2H),8.04-7.96(m,2H),7.61(ddd,J=7.9,2.0,1.0Hz,2H),7.49(t,J=7.6Hz,1H),7.39(dt,J=7.7,1.4Hz,1H),7.23(d,J=8.0Hz,1H),7.16-7.11(m,1H),7.05-6.96(m,2H),3.46(q,J=6.7Hz,2H),2.91(dt,J=17.9,6.9Hz,3H),2.30(s,3H),1.14(d,J=6.8Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 583([M+H]$^{+}$),581([M-H]$^{-}$)。

[1262] 制备1-[(4-氟-2-异丙基-苯基)氨基硫代甲酰基]-3-[2-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(PC85)

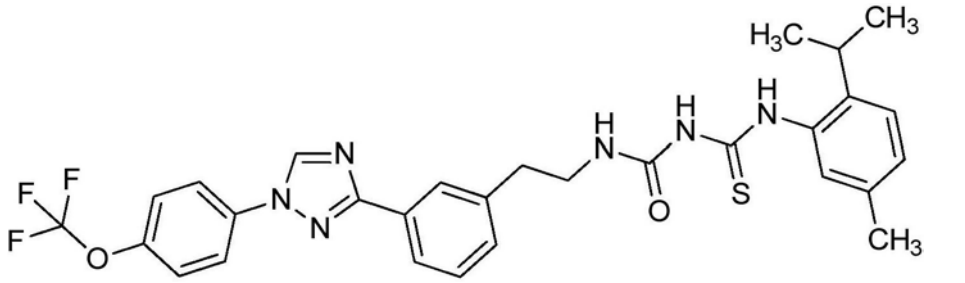
[1263]



[1264] 标题化合物如实施例75中所述使用3-(3-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(CA44)和1-(4-氟-2-异丙基苯基)硫脲制备,分离为白色固体(0.085g,27%):^{1}H NMR(400MHz,DMSO-d_6)δ11.83(s,1H),10.17(s,1H),9.42(s,1H),8.14-8.05(m,2H),8.05-7.95(m,2H),7.68-7.58(m,2H),7.49(t,J=7.6Hz,1H),7.43-7.31(m,2H),7.15(dd,J=10.3,3.0Hz,1H),7.03(td,J=8.3,2.9Hz,2H),3.47(q,J=6.6Hz,2H),3.01-2.82(m,3H),1.14(d,J=6.8Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97,-114.40;ESIMS m/z 587([M+H]$^{+}$),585([M-H]$^{-}$)。

[1265] 制备1-[(2-异丙基-5-甲基-苯基)氨基硫代甲酰基]-3-[2-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(PC81)

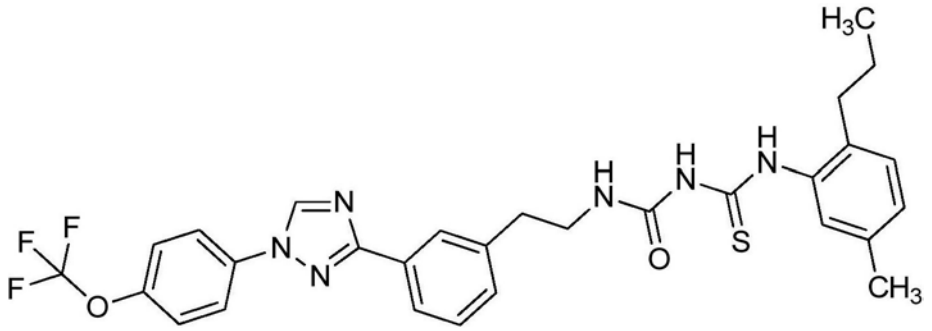
[1266]



[1267] 标题化合物如实施例75中所述使用3-(3-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(CA44)和1-(2-异丙基-5-甲基苯基)硫脲制备,分离为灰白色固体(0.019g,6%):^{1}H NMR(400MHz,DMSO-d_6)δ11.89(s,1H),10.12(s,1H),9.42(s,1H),8.14-8.05(m,2H),8.05-7.96(m,2H),7.62(ddd,J=7.8,1.9,0.9Hz,2H),7.49(t,J=7.6Hz,1H),7.39(dt,J=7.7,1.5Hz,1H),7.24-7.17(m,2H),7.12-7.05(m,1H),7.02(t,J=5.8Hz,1H),3.52-3.42(m,2H),2.91(dt,J=14.1,6.9Hz,3H),2.25(s,3H),1.13(d,J=6.8Hz,6H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 583([M+H]$^{+}$),581([M-H]$^{-}$)。

[1268] 制备1-[(5-甲基-2-丙基-苯基)氨基硫代甲酰基]-3-[2-[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]乙基]脲(PC80)

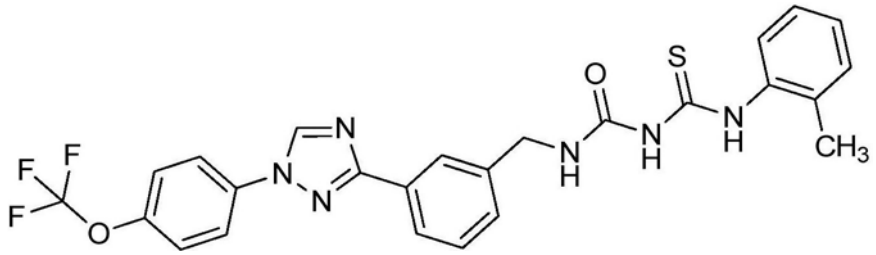
[1269]



[1270] 标题化合物如实施例75中所述使用3-(3-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(CA44)和1-(5-甲基-2-丙基苯基)硫脲(CA38)制备,分离为白色固体(0.107g,34%):^{1}H NMR(400MHz,DMSO-d_6)δ11.99(s,1H),10.09(s,1H),9.42(s,1H),8.14-8.05(m,2H),8.05-7.95(m,2H),7.61(dd,J=8.6,1.3Hz,2H),7.49(t,J=7.6Hz,1H),7.44-7.34(m,2H),7.13(d,J=7.8Hz,1H),7.07-6.97(m,2H),3.46(q,J=6.5Hz,2H),2.89(t,J=6.9Hz,2H),2.48-2.39(m,2H),2.26(s,3H),1.54-1.42(m,2H),0.84(t,J=7.3Hz,3H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.96;ESIMS m/z 583([M+H]$^{+}$),581([M-H]$^{-}$)。

[1271] 制备1-(邻甲苯基氨基硫代甲酰基)-3-[[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(FB18)

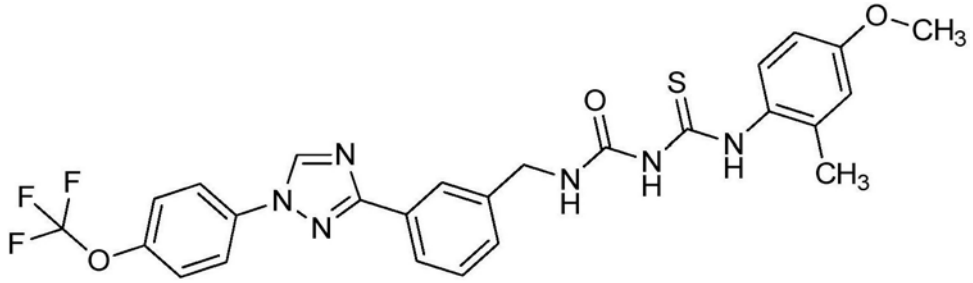
[1272]



[1273] 制备标题化合物如实施例75中所述使用3-(3-(异氰酸酯基甲基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(CB34)和1-(邻甲苯基)硫脲,并且分离为灰白色固体(0.148g,37%)。

[1274] 制备1-[(4-甲氧基-2-甲基-苯基)氨基硫代甲酰基]-3-[[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(FB19)

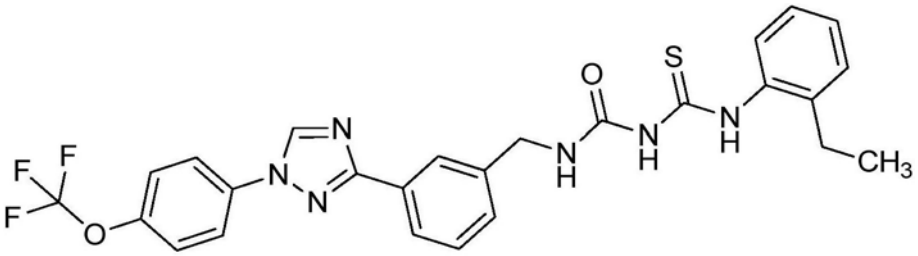
[1275]



[1276] 标题化合物如实施例75中所述使用3-(3-(异氰酸酯基甲基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(CB34)和1-(4-甲氧基-2-甲基苯基)硫脲制备,并且分离为灰白色固体(0.212g,50%)。

[1277] 制备1-[(2-乙基苯基)氨基硫代甲酰基]-3-[[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(FB20)

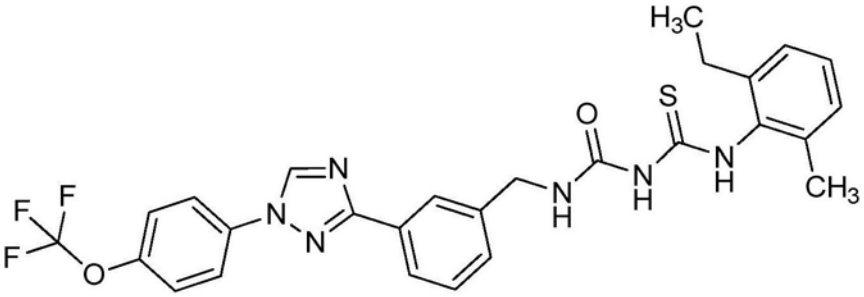
[1278]



[1279] 标题化合物如实施例75中所述使用3-(3-(异氰酸酯基甲基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(CB34)和1-(2-乙基苯基)硫脲制备,并且分离为灰白色固体(0.152g,37%)。

[1280] 制备1-[(2-乙基-6-甲基-苯基)氨基硫代甲酰基]-3-[[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(FB21)

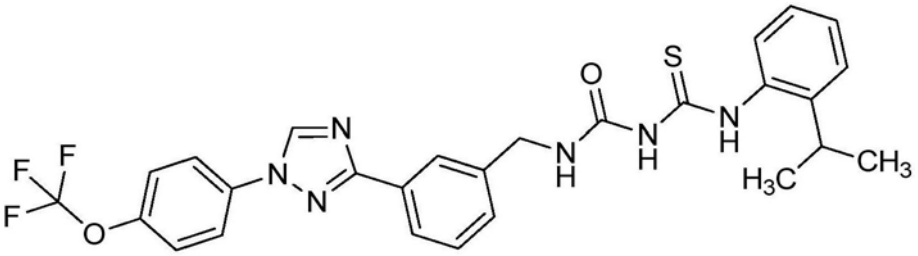
[1281]



[1282] 标题化合物如实施例75中所述使用3-(3-(异氰酸酯基甲基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(CB34)和1-(2-乙基-6-甲基苯基)硫脲(CA39)制备,并且分离为灰白色固体(0.212g,50%)。

[1283] 制备1-[(2-异丙基苯基)氨基硫代甲酰基]-3-[[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(FB22)

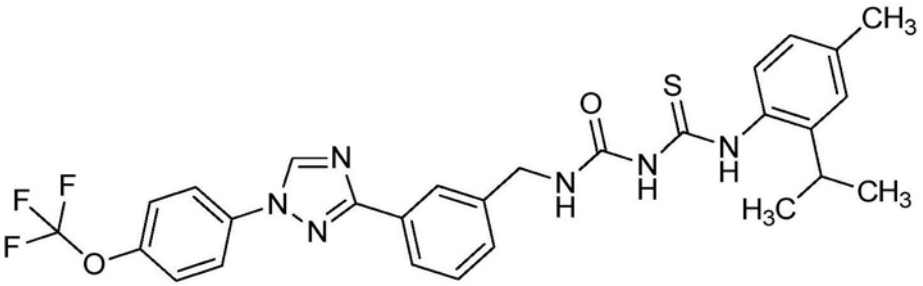
[1284]



[1285] 标题化合物如实施例75中所述使用3-(3-(异氰酸酯基甲基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(CB34)和1-(2-异丙基苯基)硫脲制备,并且分离为灰白色固体(0.213g,47%)。

[1286] 制备1-[(2-异丙基-4-甲基-苯基)氨基硫代甲酰基]-3-[[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(FB23)

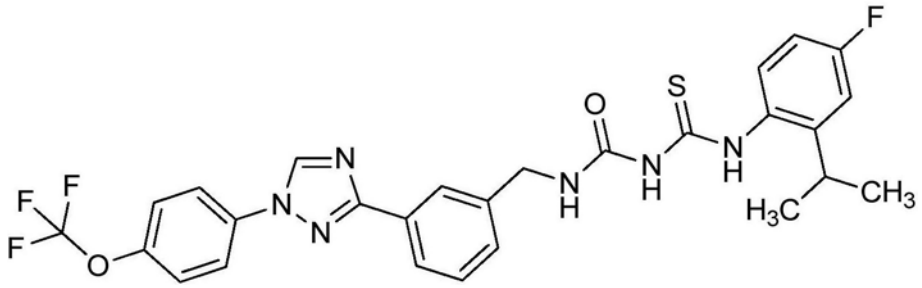
[1287]



[1288] 标题化合物如实施例75中所述使用3-(3-(异氰酸酯基甲基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(CB34)和1-(2-异丙基-4-甲基苯基)硫脲制备,并且分离为灰白色固体(0.216g,50%)。

[1289] 制备1-[(4-氟-2-异丙基-苯基)氨基硫代甲酰基]-3-[[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(FB24)

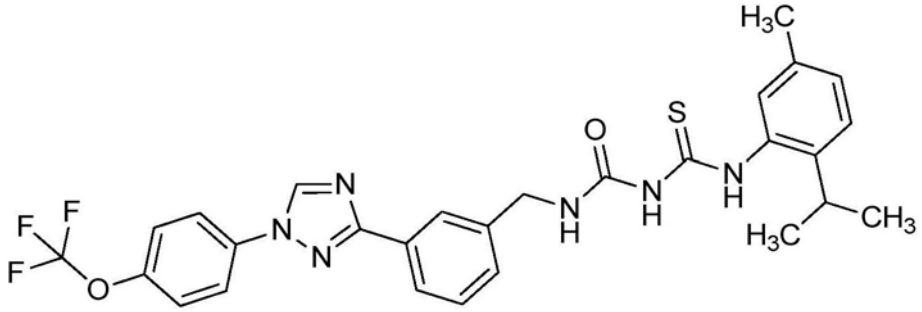
[1290]



[1291] 标题化合物如实施例75中所述使用3-(3-(异氰酸酯基甲基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(CB34)和1-(4-氟-2-异丙基苯基)硫脲制备,并且分离为灰白色固体(0.242g,56%)。

[1292] 制备1-[(2-异丙基-5-甲基-苯基)氨基硫代甲酰基]-3-[[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(FB25)

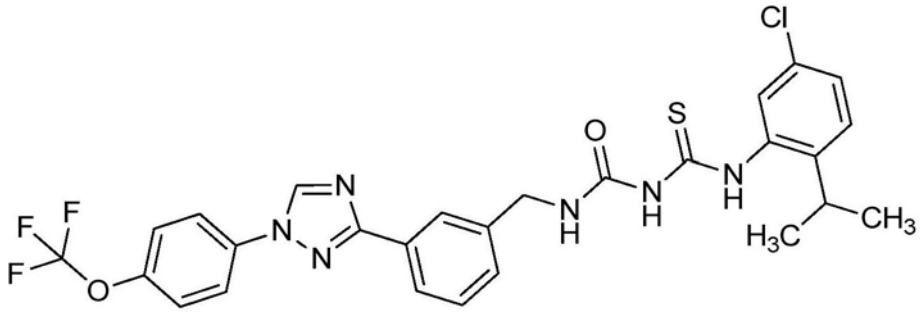
[1293]



[1294] 标题化合物如实施例75中所述使用3-(3-(异氰酸酯基甲基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(CB34)和1-(2-异丙基-5-甲基苯基)硫脲制备,并且分离为灰白色固体(0.181g,42%)。

[1295] 制备1-[(5-氯-2-异丙基-苯基)氨基硫代甲酰基]-3-[[3-[1-[4-(三氟甲氧基)苯基]-1H-1,2,4-三唑-3-基]苯基]甲基]脲(FB26)

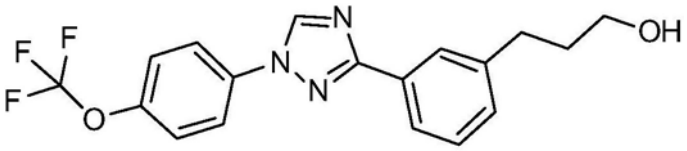
[1296]



[1297] 标题化合物如实施例75中所述使用3-(3-(异氰酸酯基甲基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(CB34)和1-(5-氯-2-异丙基苯基)硫脲(CB32)制备,并且分离为灰白色固体(0.170g,38%)。

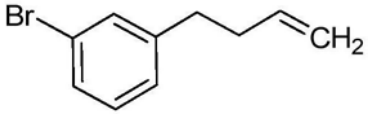
[1298] 实施例76:制备3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙

烷-1-醇(CA45)

[1299] 

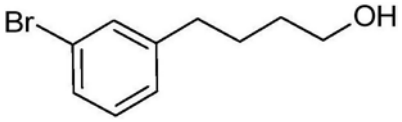
[1300] 在500mL圆底烧瓶中,将3-(3-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酸(CA13)(5.68g,15.1mmol)溶解在四氢呋喃(151mL)中。将反应在冰水浴中冷却,并且放置在惰性气氛下。逐滴加入氢化铝(III)锂(2.0M,在四氢呋喃中,15.8mL,31.6mmol)。使得反应逐渐温热至室温,并且搅拌过夜。将反应在冰浴中冷却,将水(1.2mL)逐滴加入,猝灭过量的氢化铝(III)锂,使得反应混合物搅拌1小时。然后氢氧化钠(15wt%,1.2mL)逐滴加入。使得反应搅拌1小时。然后水(3.6mL)加入。将所得沉淀物经由过滤除去。将滤液浓缩,给出黄色固体(5.20g)。将所述固体通过使用0-60%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化,提供为白色固体的标题化合物(4.01g,72%):^{1}H NMR(400MHz,DMSO-d_6)δ9.40(s,1H),8.18-8.04(m,2H),7.99-7.89(m,2H),7.68-7.57(m,2H),7.43(t,J=7.6Hz,1H),7.32(dt,J=7.7,1.5Hz,1H),4.51(t,J=5.2Hz,1H),3.45(td,J=6.4,5.1Hz,2H),2.71(dd,J=8.8,6.7Hz,2H),1.87-1.70(m,2H);^{19}F NMR(376MHz,DMSO-d_6)δ-56.97;ESIMS m/z 364([M+H]$^{+}$)。

[1301] 实施例77:制备1-溴-3-(丁-3-烯-1-基)苯(CA46)

[1302] 

[1303] 向1-溴-3-(溴甲基)苯(10.0g,40.0mmol)在四氢呋喃(50mL)中的溶液,在惰性气氛下加入烯丙基溴化镁(1.0M,在乙醚中,40.0mL,40.0mmol)。使得反应回流过夜。将反应用硫酸(2M,45mL)猝灭。所得两相溶液为相分离的溶液。将水层用乙醚(2×50mL)提取。将合并的有机层经硫酸镁干燥,过滤,浓缩。将所得残留物通过使用100%己烷作为洗脱剂的快速柱色谱纯化,提供为澄清液体的标题化合物(7.51g,71%,~80%纯度):^{1}H NMR(400MHz,DMSO-d_6)δ7.42(ddd,J=2.1,1.4,0.7Hz,1H),7.37(dt,J=7.1,2.1Hz,1H),7.28-7.18(m,2H),5.81(ddt,J=16.9,10.2,6.5Hz,1H),5.09-4.90(m,2H),2.67(dd,J=8.6,6.8Hz,2H),2.32(tdt,J=7.7,6.5,1.5Hz,2H);13C NMR(101MHz,DMSO-d_6)δ144.35,137.61,131.05,130.28,128.62,127.44,121.53,115.37,34.59,33.91;EIMS m/z 210([M]$^{+}$)。

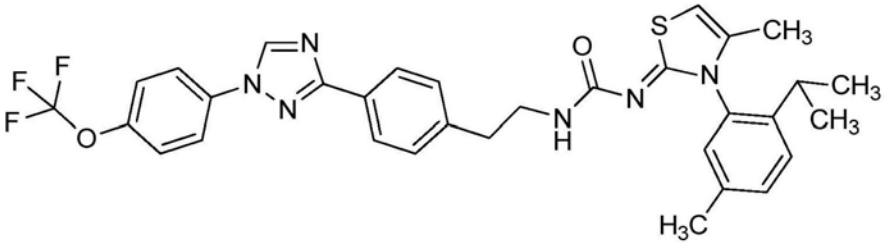
[1304] 实施例78:制备4-(3-溴苯基)丁烷-1-醇(CA47)

[1305] 

[1306] 向1-溴-3-(丁-3-烯-1-基)苯(CA46)(7.51g,35.6mmol)在己烷(80mL)中的溶液,加入(1S,5S)-9-硼杂双环[3.3.1]壬烷(0.5M,在四氢呋喃中,74.7mL,37.4mmol)。使得反应在室温搅拌过夜。向所得澄清溶液逐滴加入氢氧化钠(6.0M,5.93mL,35.6mmol)。将反应放置在冰水浴中,加入过氧化氢(13.8mL,135mmol)。然后将所得混合物加热至内部温度为50℃,过夜。反应混合物冷却至室温。将两相溶液相分离,并且将有机层用亚硫酸氢钠和盐水溶液洗涤。使合并的水层经饱和的碳酸钠呈碱性,并且用乙醚(2×100mL)提取。将合并的有

机物经硫酸镁干燥，过滤，浓缩。将液体装到二氧化硅上，并且通过使用0-40％乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化，提供为澄清液体的标题化合物(7.50g，90％)：^{1}H NMR (400MHz，DMSO-d_6) δ7.40(t，J＝1.9Hz，1H)，7.37(dt，J＝7.6，1.8Hz，1H)，7.28-7.17(m，2H)，4.39(t，J＝5.2Hz，1H)，3.40(td，J＝6.5，5.2Hz，2H)，2.57(t，J＝7.6Hz，2H)，1.65-1.51(m，2H)，1.49-1.35(m，2H)；EIMS m/z 228([M]$^+$)。

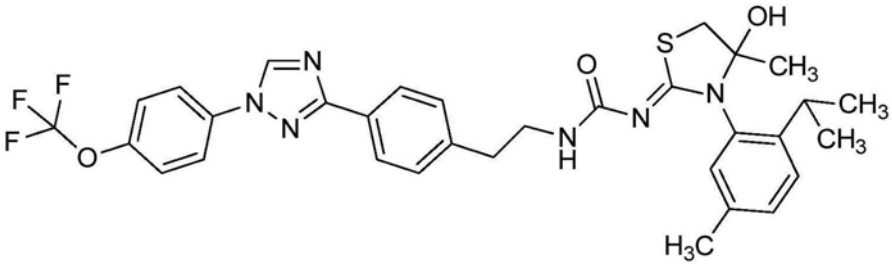
[1307] 实施例79：制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-甲基噻唑-2(3H)-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑-3-基)苯乙基)脲(P65)

[1308] 

[1309] 向在丁酮(4mL)中的N-[5-甲基-2-异丙基苯基]-N'-[2-(4-{1-[4-(三氟甲氧基)-苯基]-1H-1，2，4-三唑-3-基}苯基)乙基]硫代缩二脲(F3)(0.23g，0.40mmol)，加入三乙胺(0.060mL，0.43mmol)和氯丙酮(0.035mL，0.44mmol)，并且在加热80℃过夜。反应冷却，用水稀释，用二氯甲烷(2×)提取，并且通过相分离器过滤。将有机层浓缩，装到具有二氯甲烷的柱体Celite®上。通过使用0-100％乙酸乙酯/B(其中B＝1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化，随后在真空烘箱中干燥，提供为橙色固体的标题化合物(0.085g，34％)。

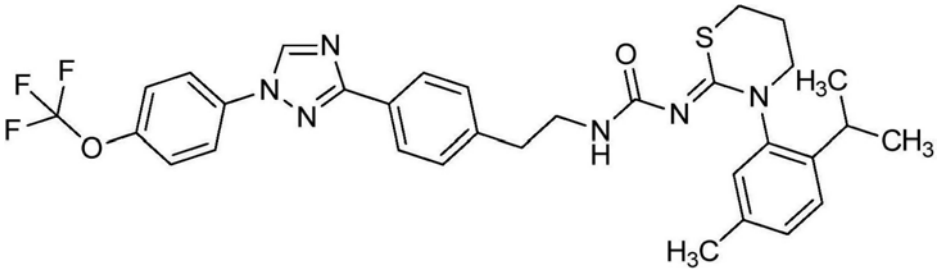
[1310] 下面的化合物根据实施例79中的步骤制备。

[1311] 制备(Z)-1-(4-羟基-3-(2-异丙基-5-甲基苯基)-4-甲基噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑-3-基)苯乙基)脲(FB67)

[1312] 

[1313] 标题化合物中所述实施例79使用N-[5-甲基-2-异丙基苯基]-N'-[2-(4-{1-[4-(三氟甲氧基)-苯基]-1H-1，2，4-三唑-3-基}苯基)乙基]硫代缩二脲(F3)和乙酸钠作为碱在室温制备；通过使用0-100％乙腈/水作为洗脱剂的反相快速柱色谱纯化，并且分离为澄清的油(0.036g，33％)。

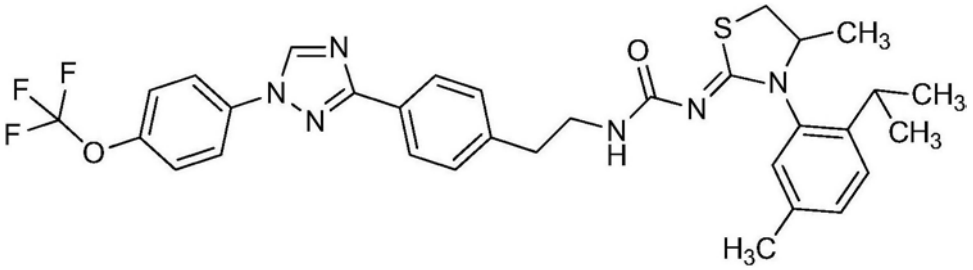
[1314] 实施例80：制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-1，3-噻嗪烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑-3-基)苯乙基)脲(P59)

[1315] 

[1316] 向在丁酮(3.1mL)中的N-[5-甲基-2-异丙基苯基]-N'-[2-(4-{1-[4-(三氟甲氧基)-苯基]-1H-1,2,4-三唑-3-基}苯基)乙基]硫代缩二脲(F3)(181mg,0.31mmol)和碳酸钾(0.064g,0.47mmol),加入1-溴-3-氯丙烷(0.050mL,0.47mmol)。将反应在加热60℃过夜。将反应混合物冷却,用水稀释,用二氯甲烷(2×)提取,并且通过相分离器过滤。将有机层浓缩并且装到具有二氯甲烷的Celite®柱体上。通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱,随后使用0-100%乙腈/水作为洗脱剂的反相快速柱色谱纯化,并且在真空烘箱中干燥,提供为白色固体的标题化合物(0.032g,16%)。

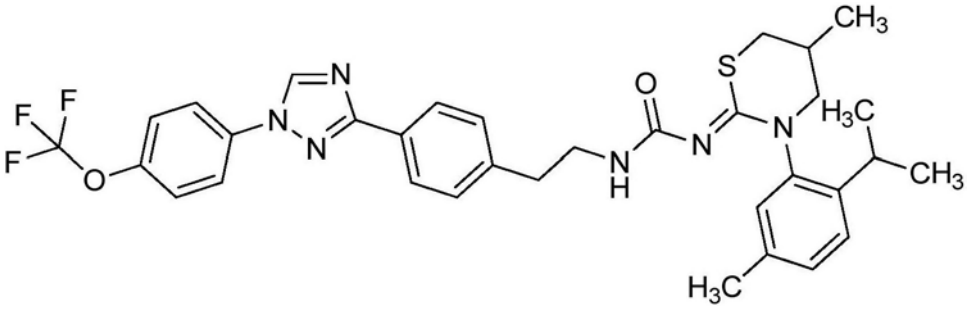
[1317] 下面的化合物根据实施例80中的步骤制备。

[1318] 制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-甲基噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P58)

[1319] 

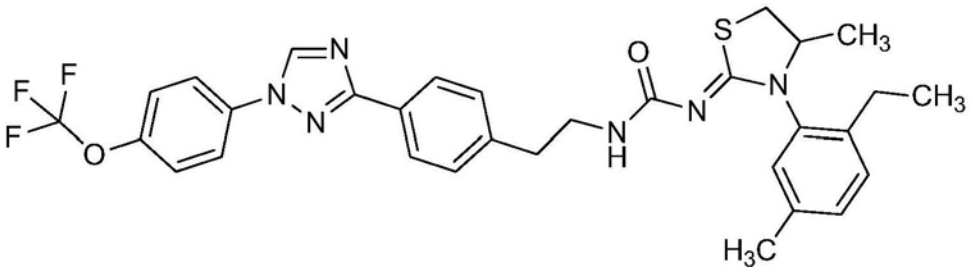
[1320] 标题化合物如实施例80中所述使用N-[5-甲基-2-异丙基苯基]-N'-[2-(4-{1-[4-(三氟甲氧基)-苯基]-1H-1,2,4-三唑-3-基}苯基)乙基]硫代缩二脲(F3)和1,2-二溴丙烷在80℃制备,并且分离为黄色油(0.050g,26%)。

[1321] 制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-5-甲基-1,3-噻嗪烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(P64)

[1322] 

[1323] 标题化合物如实施例80中所述使用N-[5-甲基-2-异丙基苯基]-N'-[2-(4-{1-[4-(三氟甲氧基)-苯基]-1H-1,2,4-三唑-3-基}苯基)乙基]硫代缩二脲(F3)和1-溴-3-氯-2-甲基丙烷制备,并且分离为白色固体(0.061g,14%)。

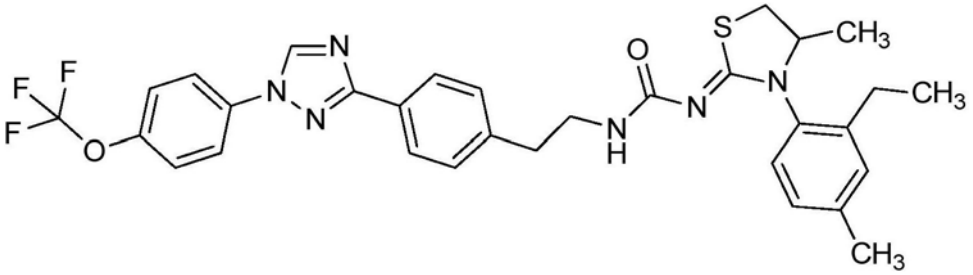
[1324] 实施例80a:制备(Z)-1-(3-(2-乙基-5-甲基苯基)-4-甲基噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB55)

[1325] 

[1326] 将在乙腈(1.9mL)中的3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)(0.16g,0.42mmol),1-(2-乙基-5-甲基苯基)硫脲(CA41)(0.081g,0.42mmol),和碳酸铯(0.13g,0.39mmol)在室温搅拌3小时。反应用丁酮(2mL)稀释,加入碳酸钾(0.12g,0.83mmol)和1,2-二溴丙烷(0.090mL,0.83mmol)。将反应加热至60℃保持6小时。将反应用水稀释,并且用二氯甲烷(2×)提取,将有机层通过相分离器过滤并且浓缩。通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供为黄色油的标题化合物(0.034g,13%)。

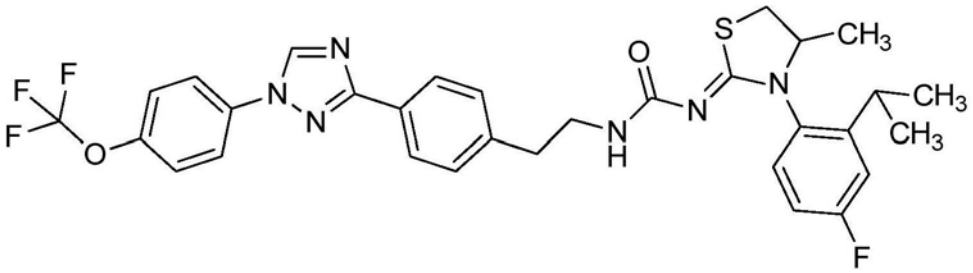
[1327] 下面的化合物根据实施例80a中的步骤制备。

[1328] 制备(Z)-1-(3-(2-乙基-4-甲基苯基)-4-甲基噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB56)

[1329] 

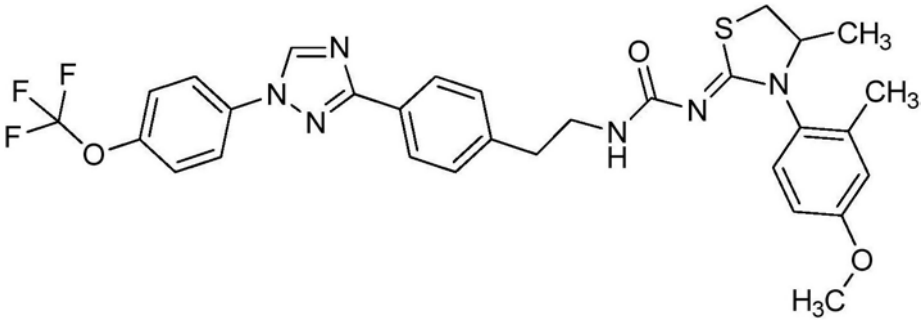
[1330] 标题化合物如实施例80a中所述使用3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)和1-(2-乙基-4-甲基苯基)硫脲(CA42)制备,分离为黄色油(0.040g,16%)。

[1331] 制备(Z)-1-(3-(4-氟-2-异丙基苯基)-4-甲基噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB57)

[1332] 

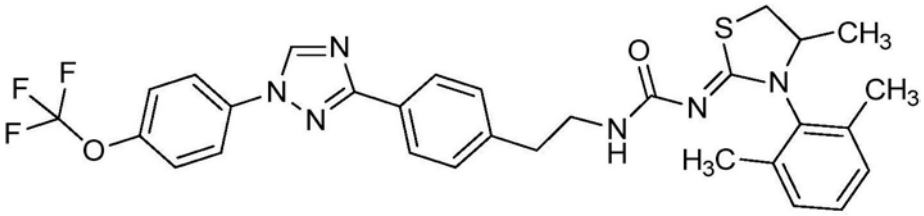
[1333] 标题化合物如实施例80a中所述使用3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)和1-(4-氟-2-异丙基苯基)硫脲制备,并且分离为黄色油(0.056g,22%)。

[1334] 制备(Z)-1-(3-(4-甲氧基-2-甲基苯基)-4-甲基噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB58)

[1335] 

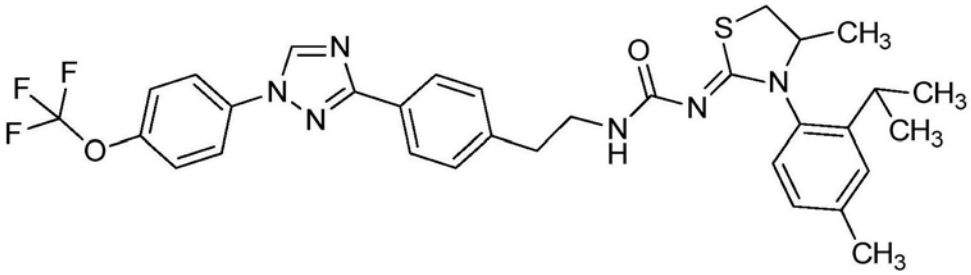
[1336] 标题化合物如实施例80a中所述使用3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)和1-(4-甲氧基-2-甲基苯基)硫脲制备,并且分离为黄色油(0.054g,21%)。

[1337] 制备(Z)-1-(3-(2,6-二甲基苯基)-4-甲基噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB59)

[1338] 

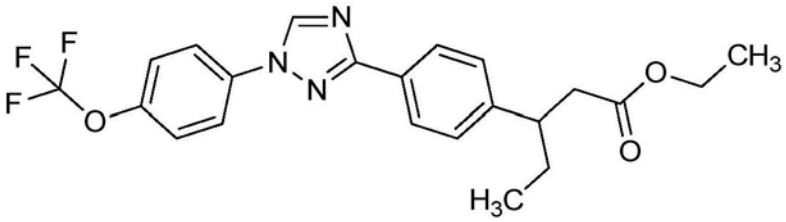
[1339] 标题化合物如实施例80a中所述使用3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)和1-(2,6-二甲基苯基)硫脲制备,并且分离为澄清的油(0.044g,18%)。

[1340] 制备(Z)-1-(3-(2-异丙基-4-甲基苯基)-4-甲基噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB60)

[1341] 

[1342] 标题化合物如实施例80a中所述使用3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)和1-(2-异丙基-4-甲基苯基)硫脲制备,并且分离为黄色泡沫(0.047g,17%)。

[1343] 实施例81:制备3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)戊酸乙基酯(CA48)

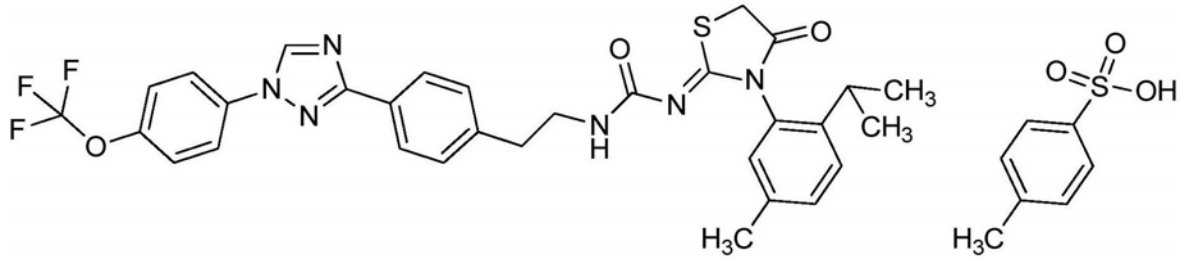
[1344] 

[1345] 将氢化钠(60%油浸,0.32g,7.9mmol)称入烘干的三颈圆底烧瓶中。将烧瓶放置在氮气下,加入四氢呋喃(44mL)。将经搅拌的混合物放置在冰浴中。加入膦酰基乙酸三乙酯(1.4mL,6.9mmol),将混合物搅拌2小时。加入为固体的1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-酮(CA7)(2.4g,6.5mmol)并且温热至室温过夜。将反应用水稀释并且用乙酸乙酯提取/己烷(1:1,2×)。将有机层经硫酸钠干燥,干燥,浓缩。向粗制的残留物加入钯碳(10wt%,0.70g,0.66mmol)并且溶解在乙酸乙酯(20mL)中。将反应在氢气球下搅拌过夜。将反应混合物通过Celite®过滤并且浓缩,给出为褐色油的标题化合物(2.7g,90%):^{1}H NMR(400MHz,$CDCl_3$)δ8.55(d,J=0.6Hz,1H),8.11(dd,J=8.1,6.0Hz,2H),

7.83-7.76(m,2H),7.38(dq,J=7.9,1.0Hz,2H),7.35-7.27(m,2H),4.24-4.14(m,1H),4.04(qd,J=7.1,1.6Hz,1H),3.13-2.99(m,1H),2.74-2.55(m,2H),1.79-1.61(m,2H),1.38-1.24(m,3H),1.06(dt,J=72.0,7.2Hz,3H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 434([M+H]$^+$)。

[1346] 实施例82:制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲的对甲苯磺酸盐(F5A)

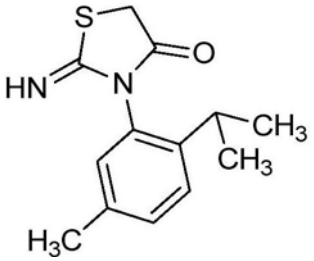
[1347]



[1348] 向250mL圆底烧瓶中的(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(F5)(4.82g,7.46mmol),加入异丙醇(50mL)。将悬浮液温热至50℃,搅拌20分钟。加入丙酮(50mL)。将4-甲基苯磺酸一水合物(1.42g,7.46mmol)溶解在丙酮(20mL)中,并且以逐滴的方式加入上述溶液中。将所得澄清淡褐色溶液在50℃浓缩。将所得残留物在50℃的真空中干燥过夜。将褐色泡沫转移至500mL圆底烧瓶并且溶解在丙酮(200mL)中。将混合物加热回流15小时。将溶液浓缩,提供为深灰色泡沫的标题化合物(5.90g,95%)。

[1349] 实施例83:制备2-亚氨基-3-(2-异丙基-5-甲基苯基)噻唑烷-4-酮(CA49)

[1350]



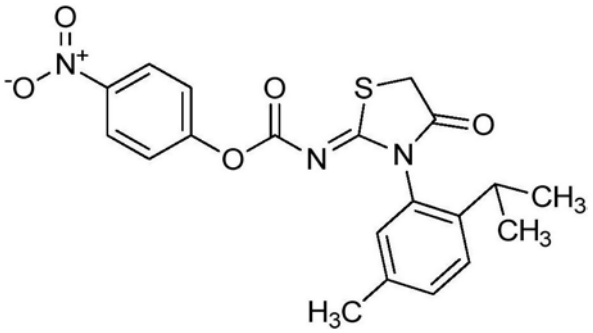
[1351] 方法A.向在乙醇(8.0mL)中的(1-(2-异丙基-5-甲基苯基)硫脲(0.20g,0.96mmol),加入溴乙酸甲酯(0.17mL,1.9mmol)和乙酸钠(0.23g,2.8mmol)。将反应在室温搅拌过夜。将溶液倒到水上并且用乙酸乙酯(3×)提取,将有机物干燥并且浓缩,给出作为红色固体的标题化合物(0.24g,93%):^{1}H NMR(400MHz,$CDCl_3$)δ7.21(d,J=7.9Hz,1H),7.07(dd,J=8.3,1.8Hz,1H),6.85(d,J=1.6Hz,1H),3.85(d,J=0.9Hz,2H),3.03(p,J=6.9Hz,1H),2.31(t,J=0.7Hz,4H),1.15(d,J=6.9Hz,6H);ESIMS m/z 248([M]$^+$)。

[1352] 方法B,步骤1.将2-异丙基-5-甲基苯胺(286g,1.91mol)和碳酸氢钠(270g,3.22mol)在搅拌时在氮气气氛下装到圆底烧瓶中,并且冷却至0-5℃。将2-二氯乙酰氯(218g,1.93mol)在0-5℃经1小时的时间逐滴加入。将反应在0-5℃搅拌1小时。反应完成之后,加入净化水(2.86L)并且在25-30℃搅拌15分钟。然后分层。将有机层用水(2×2.86L)和盐水(1.43L)洗涤。将水层合并并且用乙酸乙酯(1.43L)提取。将有机层用硫酸钠干燥,干燥,在50-55℃在真空下(500-600mm Hg)浓缩至体积的2/5。加入己烷(2.86L),并且将混合物在25-30℃搅拌1小时。将固体过滤,用己烷(1.43L)洗涤,并且在45-50℃在真空下(500-

600mm Hg)干燥,给出为灰白色固体的2-氯-N-(2-异丙基-5-甲基苯基)乙酰胺(270g,66%):mp 97-99℃;^{1}H NMR(300MHz,$CDCl_3$)δ8.27(s,1H),7.60(s,1H),7.20(d,J=7.95Hz,1H),7.04(d,J=7.89Hz,1H),4.25(s,2H),2.99(q,J=6.78Hz,1H),2.34(s,3H),1.26(d,J=6.84Hz,6H);^{13}C NMR(100MHz,$CDCl_3$)δ164.07,137.28,136.33,132.95,127.35,125.62,124.46,43.21,27.86,22.98,21.00;ESIMS m/z 226([M+H]$^+$)。

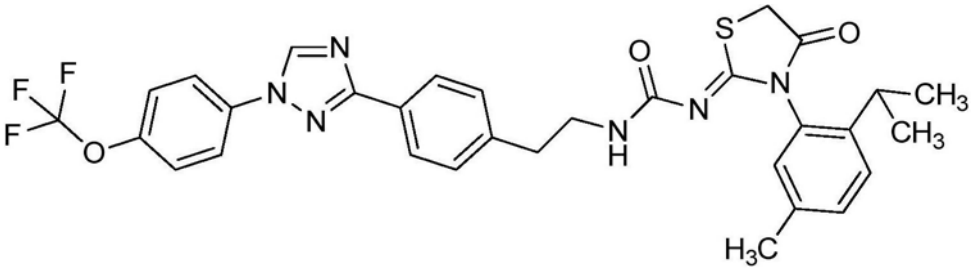
[1353] 步骤2.将2-氯-N-(2-异丙基-5-甲基苯基)乙酰胺(290g,1.28mol)和丙酮(1.60L)在搅拌时在氮气气氛下装到圆底烧瓶中。将硫氰酸钾(250g,2.57mol)在保持温度15-20℃经时间30分钟分批加入。将反应在15-20℃搅拌10分钟,之后温度缓慢升到53-55℃,并且保持在53-55℃3小时。然后将反应冷却至20-25℃,加入碳酸铯(20.9g,0.0641mol),并且将反应混合物在20-25℃搅拌30分钟。完成之后,将反应混合物通过Celite®过滤,用丙酮(1.45L)洗涤,收集滤液。将滤液在40-45℃在真空下(500-600mm Hg)浓缩,提供浆料。将浆料溶解在乙酸乙酯(2.90L)中,用水(2×2.90L)和盐水(1.45L)洗涤。将有机层用硫酸钠干燥,干燥,在50-55℃在真空下(500-600mm Hg)浓缩,提供为深褐色浆料的标题化合物(345g,99%)。

[1354] 实施例84:制备(Z)-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)氨基甲酸4-硝基苯基酯(CA50)

[1355] 

[1356] 圆底烧瓶装有溶解在乙腈(13mL)中的2-亚氨基-3-(2-异丙基-5-甲基苯基)噻唑烷-4-酮(CA49)(1.30g,5.23mmol),氯甲酸4-硝基苯基酯(1.06g,5.23mmol)和碳酸铯(1.71g,5.23mmol)。将反应混合物在室温搅拌1.5小时。将反应用二氯甲烷稀释并且吸附到硅胶上。通过使用0-100%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化,提供为深红色固体的标题化合物(1.88g,86%):^{1}H NMR(400MHz,$CDCl_3$)δ8.31-8.18(m,2H),7.39-7.27(m,4H),6.92-6.83(m,1H),4.14-4.00(m,2H),2.61(p,J=6.9Hz,1H),2.36(d,J=0.7Hz,3H),1.30-1.10(m,6H);ESIMS m/z 414([M+H]$^+$)。

[1357] 实施例85:制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(F5)

[1358] 

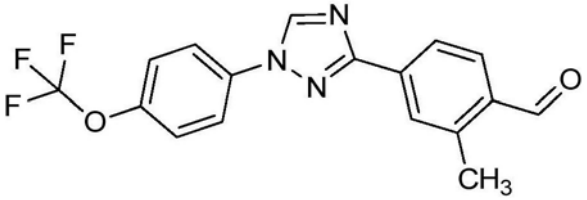
[1359] 方法A.在氮气下向在无水乙腈中的2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-

三唑-3-基)苯基)乙烷胺(CA51)(0.030g,0.086mmol)和碳酸铯(0.028g,0.086mmol)逐滴加入(Z)-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)氨基甲酸4-硝基苯基酯(CA50)(0.039g,0.095mmol)。将反应混合物在室温搅拌3小时。将粗制的混合物真空浓缩。通过使用10-60%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化,提供为橙色泡沫的标题化合物(0.036g,67%)。

[1360] 方法B.向3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)(3.00g,8.01mmol)在甲苯(20.0mL)中的溶液,加入碳酸铯(0.261g,0.801mmol)。向其加入在乙腈(20.0mL)中的2-亚氨基-3-(2-异丙基-5-甲基苯基)噻唑烷-4-酮(CA49)(1.99g,8.01mmol)。将反应在室温搅拌3.5小时,之后将反应混合物浓缩。加入丙酮(200mL),将固体过滤。将滤液浓缩,提供红色固体。将红色固体溶解在丙酮中,加入己烷直到形成沉淀物。将固体过滤,浓缩滤液。通过使用0-20%丙酮/二氯甲烷作为洗脱剂的快速柱色谱纯化,提供为灰白色固体的标题化合物(3.10g,62%)。

[1361] 方法C.将3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)(432g,1.15mol)和乙腈(1.51L)在搅拌时在氮气气氛下装到圆底烧瓶中。在25-30℃加入2-亚氨基-3-(2-异丙基-5-甲基苯基)噻唑烷-4-酮(CA49)(320g,1.29mol)在乙腈(1.43L)中的溶液。将反应在25-30℃搅拌20小时。反应完成之后,将反应混合物过滤,用乙腈(2.16L)、庚烷(464mL)洗涤,并且在50-55℃在真空下(500-600mm Hg)干燥,给出为灰白色固体的标题化合物(540g,75%)。

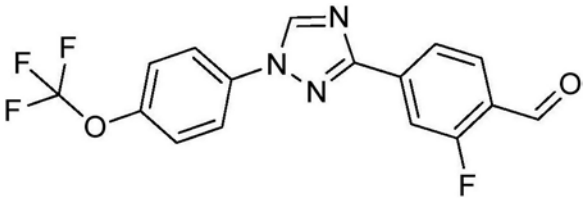
[1362] 实施例86:制备2-甲基-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯甲醛(CB35)

[1363] 

[1364] 将3-溴-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C1)(0.30g,1.0mmol),2-甲基-4-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苯甲醛(CB4)(0.25g,1.0mmol),碳酸氢钠(0.25g,2.9mmol),四(三苯基膦)钯(0)(0.17g,0.15mmol),dioxane(3.9mL),和水(0.97mL)在0.5-2.0mL的小瓶中盖住和在140℃的Biotage Initiator®微波反应器中加热30分钟,在容器侧有外部红外传感器温度监测。反应混合物用乙酸乙酯稀释和用水洗涤。将水层用乙酸乙酯提取。将有机层灌注经过相分离器并且浓缩。通过使用0-20%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供为白色固体的标题化合物(0.19g,57%):^{1}H NMR(400MHz,$CDCl_3$)δ10.33(s,1H),8.61(s,1H),8.19(dd,J=8.0,1.6Hz,1H),8.13(t,J=1.1Hz,1H),7.92(d,J=8.0Hz,1H),7.86-7.78(m,2H),7.45-7.37(m,2H),2.77(s,3H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.01;ESIMS m/z 348($[M+H]^+$)

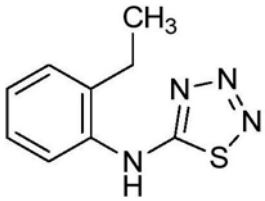
[1365] 下面的化合物根据实施例86中的步骤制备。

[1366] 制备2-氟-4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯甲醛(CB36)

[1367] 

[1368] 标题化合物如实施例86中所述使用3-溴-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C1)和2-氟-4-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苯甲醛(CB5)制备,并且分离为白色固体(0.569g,47%):^{1}H NMR(400MHz,$CDCl_3$)δ10.42(d,J=0.7Hz,1H),8.61(s,1H),8.12(ddd,J=8.1,1.5,0.8Hz,1H),8.05-7.95(m,1H),7.81(d,J=9.0Hz,2H),7.70(d,J=9.0Hz,1H),7.45-7.39(m,2H);ESIMS m/z 352([M+H]$^+$)。

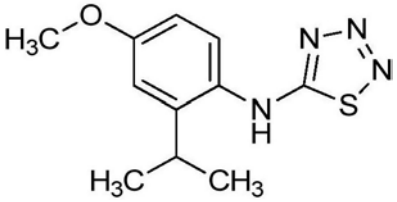
[1369] 实施例87:制备N-(2-乙基苯基)-1,2,3,4-噻三唑-5-胺(CB37)

[1370] 

[1371] 向N-(2-乙基苯基)氨基硫脲(0.500g,2.56mmol)和乙酸(2.00mL,17.5mmol)的经搅拌和冷却的混合物,加入在水(1mL)中的亚硝酸钠(0.177g,2.56mmol)。混合物在加入时变黄,将反应搅拌1小时。将固体过滤,得到为橙色固体的标题化合物(0.389g,73%):^{1}H NMR(400MHz,$CDCl_3$)δ9.02(s,1H),7.42-7.28(m,4H),2.76(q,J=7.5Hz,2H),1.25(t,J=7.5Hz,3H);^{13}C NMR(101MHz,$CDCl_3$)δ138.69,137.90,130.38,128.28,128.14,121.60,24.73,14.79;ESIMS m/z 179([M+H]-N_2^+)。

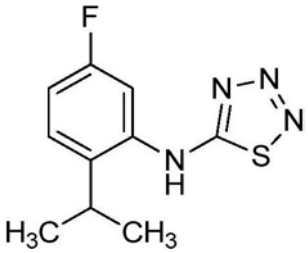
[1372] 下面的化合物根据实施例87中的步骤制备。

[1373] 制备N-(2-异丙基-4-甲氧基苯基)-1,2,3,4-噻三唑-5-胺(CB38)

[1374] 

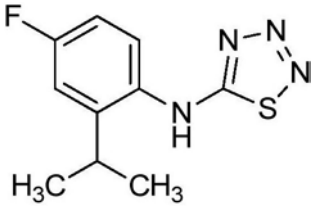
[1375] 标题化合物如实施例87中所述使用N-(2-异丙基-4-甲氧基苯基)氨基硫脲(CB53)制备,并且分离为橙色固体(0.531g,67%):^{1}H NMR(400MHz,$CDCl_3$)δ8.51(s,1H),7.28(d,J=8.7Hz,1H),6.91(d,J=2.9Hz,1H),6.80(dd,J=8.7,2.9Hz,1H),3.85(s,3H),3.17(dq,J=13.7,6.9Hz,1H),1.22(d,J=6.9Hz,6H);^{13}C NMR(101MHz,$CDCl_3$)δ160.18,146.49,131.57,128.24,126.34,113.46,112.61,55.95,28.88,23.81.

[1376] 制备N-(5-氟-2-异丙基苯基)-1,2,3,4-噻三唑-5-胺(CB39)

[1377] 

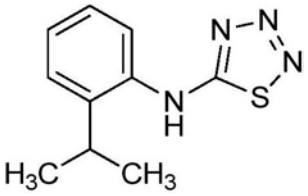
[1378] 制备标题化合物如实施例87中所述使用N-(5-氟-2-异丙基苯基)氨基硫脲，并且分离为红色固体(0.520g，64%)：^{1}H NMR(400MHz，$CDCl_3$)δ7.37(dd，J＝8.7，6.2Hz，1H)，7.13(dd，J＝9.3，2.6Hz，1H)，7.04(ddd，J＝8.7，7.9，2.7Hz，1H)，3.19(dt，J＝13.7，6.9Hz，2H)，1.24(d，J＝6.8Hz，6H)；^{19}F NMR(376MHz，$CDCl_3$)δ-113.32；ESIMS m/z 237([M-H]$^-$)。

[1379] 制备N-(4-氟-2-异丙基苯基)-1，2，3，4-噻三唑-5-胺(CB40)

[1380] 

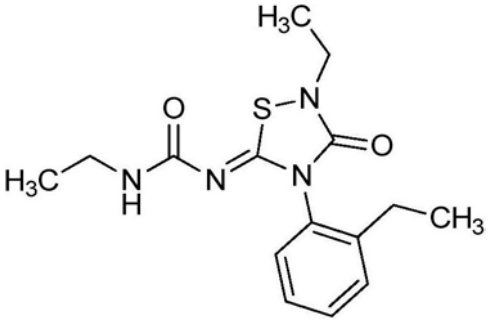
[1381] 标题化合物如实施例87中所述使用N-(4-氟-2-异丙基苯基)氨基硫脲制备，并且分离为红色固体(0.520g，64%)：^{1}H NMR(400MHz，$CDCl_3$)δ(400MHz，$CDCl_3$)δ8.63(s，1H)，7.35(dd，J＝8.7，5.2Hz，1H)，7.11(dd，J＝9.8，3.0Hz，1H)，7.00(ddd，J＝8.7，7.5，2.9Hz，1H)，3.20(pd，J＝6.8，1.7Hz，1H)，1.23(d，J＝6.8Hz，6H)；^{19}F NMR(376MHz，$CDCl_3$)δ-111.20；ESIMS m/z 238([M]$^+$)。

[1382] 制备N-(2-异丙基苯基)-1，2，3，4-噻三唑-5-胺(CB41)

[1383] 

[1384] 标题化合物如实施例87中所述使用N-(2-异丙基苯基)氨基硫脲制备，并且分离为芥末黄的固体(0.574g，71%)：^{1}H NMR(400MHz，$CDCl_3$)δ8.63(s，1H)，7.44-7.39(m，1H)，7.39-7.34(m，2H)，7.34-7.29(m，1H)，3.21(p，J＝6.7Hz，1H)，1.26(d，J＝6.9Hz，6H)；^{13}C NMR(101MHz，$CDCl_3$)δ179.95，143.24，138.10，128.78，128.17，127.56，122.85，28.54，23.73。

[1385] 实施例88：制备(Z)-1-乙基-3-(2-乙基-4-(2-乙基苯基)-3-氧代-1，2，4-噻二唑烷-5-亚基)脲(CB42)

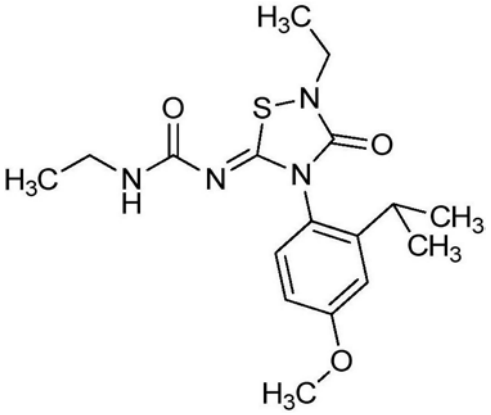
[1386] 

[1387] 将N-(2-乙基苯基)-1，2，3，4-噻三唑-5-胺(CB37)(0.350g，1.70mmol)溶解在四氢呋喃(5mL)中。加入异氰酸乙酯(0.121mL，1.53mmol)和三乙胺(5滴)。将反应在室温搅拌过夜。将溶液浓缩，给出为橙色油的标题化合物(0.484g，89%)：^{1}H NMR(400MHz，$CDCl_3$)δ7.48-7.36(m，2H)，7.36-7.29(m，1H)，7.19(dd，J＝7.8，1.4Hz，1H)，5.54-5.43(m，1H)，3.68(q，J＝7.2Hz，2H)，3.26(qdd，J＝7.3，5.9，4.8Hz，2H)，2.51(qd，J＝7.6，2.9Hz，2H)，1.33(t，J＝

7.2Hz,3H),1.18(t,J=7.6Hz,3H),1.12(t,J=7.3Hz,3H);ESIMS m/z 320([M]$^+$)。

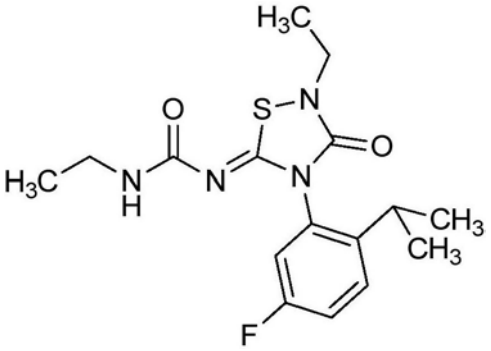
[1388] 下面的化合物根据实施例88中的步骤制备。

[1389] 制备(Z)-1-乙基-3-(2-乙基-4-(2-异丙基-4-甲氧基苯基)-3-氧代-1,2,4-噻二唑烷-5-亚基)脲(CB43)

[1390] 

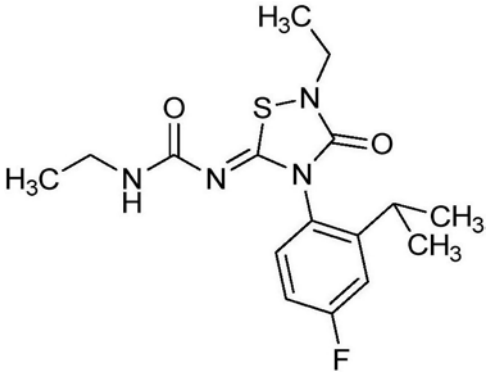
[1391] 标题化合物如实施例88中所述使用N-(2-异丙基-4-甲氧基苯基)-1,2,3,4-噻三唑-5-胺(CB38)制备,并且分离为深褐色油(0.693g,82%):^{1}H NMR(400MHz,$CDCl_3$)δ7.10(d,J=8.7Hz,1H),6.94(d,J=2.8Hz,1H),6.83(dd,J=8.7,2.8Hz,1H),5.48(t,J=5.8Hz,1H),3.84(s,3H),3.67(q,J=7.3Hz,2H),3.08(q,J=7.3Hz,2H),2.70(p,J=6.9Hz,1H),1.34(dt,J=10.0,7.3Hz,3H),1.18(t,J=6.9Hz,6H),1.12(t,J=7.3Hz,3H);^{13}C NMR(101MHz,$CDCl_3$)δ167.43,165.14,161.07,148.57,144.62,129.93,126.14,113.06,112.28,55.82,46.36,39.68,36.02,29.31,24.01,15.31,14.56;ESIMS m/z 364([M]$^+$)。

[1392] 制备(Z)-1-乙基-3-(2-乙基-4-(5-氟-2-异丙基苯基)-3-氧代-1,2,4-噻二唑烷-5-亚基)脲(CB44)

[1393] 

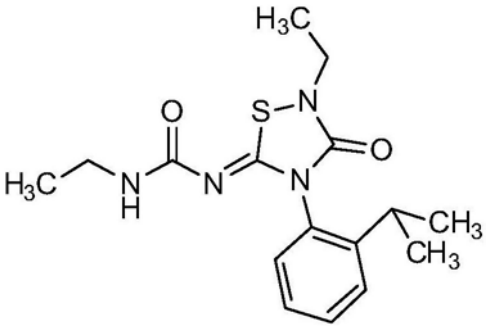
[1394] 标题化合物如实施例88中所述使用N-(5-氟-2-异丙基苯基)-1,2,3,4-噻三唑-5-胺(CB39)制备,并且分离为深褐色油(0.316g,37%):^{1}H NMR(400MHz,$CDCl_3$)δ7.41(dd,J=8.8,6.0Hz,1H),7.21-7.13(m,1H),6.92(dd,J=8.7,2.7Hz,1H),5.46(d,J=6.8Hz,1H),3.75-3.56(m,2H),3.36-3.15(m,2H),2.72(p,J=6.8Hz,1H),1.34(t,J=7.2Hz,3H),1.18(dd,J=10.9,6.9Hz,6H),1.13(t,J=7.3Hz,3H);^{19}F NMR(376MHz,$CDCl_3$)δ-115.44;ESIMS m/z 352([M]$^+$)。

[1395] 制备(Z)-1-乙基-3-(2-乙基-4-(4-氟-2-异丙基苯基)-3-氧代-1,2,4-噻二唑烷-5-亚基)脲(CB45)

[1396] 

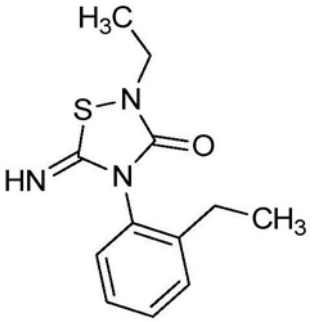
[1397] 标题化合物如实施例88中所述使用N-(4-氟-2-异丙基苯基)-1,2,3,4-噻三唑-5-胺(CB40)制备,并且分离为红色油(0.340g,44%):^{1}H NMR(400MHz,$CDCl_3$)δ7.18-7.08(m,2H),7.00(ddd,J=8.7,7.6,2.9Hz,1H),5.46(t,J=5.8Hz,1H),3.67(q,J=7.2Hz,2H),3.36-3.17(m,2H),2.72(td,J=6.8,1.8Hz,1H),1.33(t,J=7.3Hz,3H),1.22-1.07(m,9H);^{19}F NMR(376MHz,$CDCl_3$)δ-111.31;ESIMS m/z 352([M]$^{+}$)。

[1398] 制备(Z)-1-乙基-3-(2-乙基-4-(2-异丙基苯基)-3-氧代-1,2,4-噻二唑烷-5-亚基)脲(CB46)

[1399] 

[1400] 标题化合物如实施例88中所述使用N-(2-异丙基苯基)-1,2,3,4-噻三唑-5-胺(CB41)制备,并且分离为红色油(0.788g,87%):^{1}H NMR(400MHz,$CDCl_3$)δ7.48-7.44(m,2H),7.34-7.28(m,1H),7.19-7.15(m,1H),3.68(q,J=7.2Hz,2H),3.34-3.19(m,3H),2.75(p,J=6.9Hz,1H),1.34(t,J=7.2Hz,3H),1.20(dd,J=7.8,6.8Hz,6H),1.12(t,J=7.3Hz,3H);^{13}C NMR(101MHz,$CDCl_3$)δ167.07,165.09,152.63,147.13,133.37,130.65,128.95,127.37,127.30,46.36,39.67,36.01,29.08,24.07,15.32,14.56;ESIMS m/z 334([M]$^{+}$)。

[1401] 实施例89:制备2-乙基-4-(2-乙基苯基)-5-亚氨基-1,2,4-噻二唑烷-3-酮(CB47)

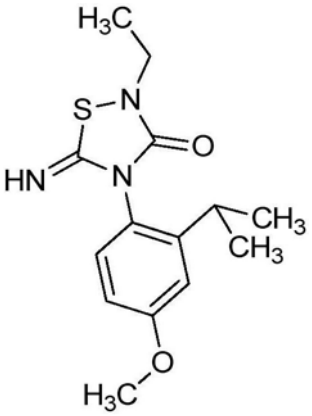
[1402] 

[1403] 将(Z)-1-乙基-3-(2-乙基-4-(2-乙基苯基)-3-氧代-1,2,4-噻二唑烷-5-亚基)脲(CB42)(0.484g,1.51mmol)溶解在甲醇(150mL)中。缓慢加入氢氧化钠(3.36g,84.0mmol),将反应在室温搅拌。4小时之后,将溶液浓缩至体积的1/2,倒至水上,并且用乙酸乙酯提取。

将有机物干燥并且浓缩，给出为橙色固体的标题化合物(0.249g，65%)：^{1}H NMR(400MHz，$CDCl_3$)δ7.35-7.32(m，2H)，7.30(dd，J＝5.4，1.5Hz，1H)，7.25-7.20(m，1H)，3.65(q，J＝7.2Hz，2H)，3.39-3.19(m，1H)，2.73(q，J＝7.6Hz，2H)，1.26-1.13(m，6H)；^{13}C NMR(101MHz，$CDCl_3$)δ173.32，165.49，141.20，135.74，130.42，129.31，127.67，126.01，39.50，24.79，15.22，14.93；ESIMS m/z 250([M]$^{+}$)。

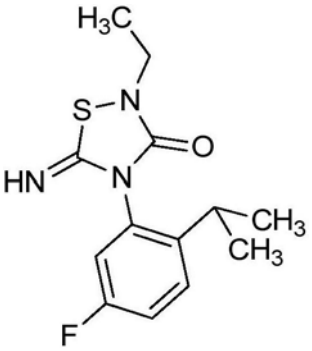
[1404] 下面的化合物根据实施例89中的步骤制备。

[1405] 制备2-乙基-5-亚氨基-4-(2-异丙基-4-甲氧基苯基)-1，2，4-噻二唑烷-3-酮(CB48)

[1406] 

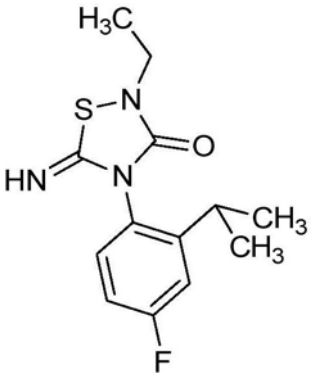
[1407] 标题化合物如实施例89中所述使用(Z)-1-乙基-3-(2-乙基-4-(2-异丙基-4-甲氧基苯基)-3-氧代-1，2，4-噻二唑烷-5-亚基)脲(CB43)制备，并且分离为红色油(0.442g，63%)：^{1}H NMR(400MHz，$CDCl_3$)δ7.22(d，J＝8.6Hz，1H)，6.90(d，J＝2.9Hz，1H)，6.74(dd，J＝8.7，2.9Hz，1H)，3.83(s，3H)，3.68-3.57(m，2H)，3.24-3.13(m，2H)，1.20(dd，J＝8.5，7.1Hz，9H)；^{13}C NMR(101MHz，$CDCl_3$)δ165.84，160.88，148.76，129.20，126.94，126.13，113.50，112.05，55.90，39.44，28.90，23.87，15.23；ESIMS m/z 293([M]$^{+}$)。

[1408] 制备2-乙基-4-(5-氟-2-异丙基苯基)-5-亚氨基-1，2，4-噻二唑烷-3-酮(CB49)

[1409] 

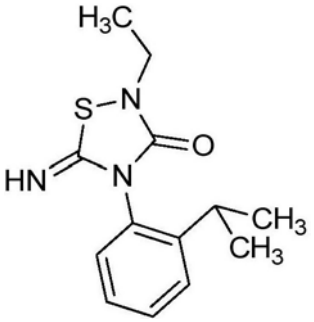
[1410] 标题化合物如实施例89中所述使用(Z)-1-乙基-3-(2-乙基-4-(5-氟-2-异丙基苯基)-3-氧代-1，2，4-噻二唑烷-5-亚基)脲(CB44)制备，并且分离为红色固体(0.145g，56%)：^{1}H NMR(400MHz，$CDCl_3$)δ7.38-7.28(m，1H)，7.06-6.94(m，2H)，3.64(q，J＝7.1Hz，H)，3.18(p，J＝6.8Hz，1H)，1.30-1.05(m，10H)；^{19}F NMR(376MHz，$CDCl_3$)δ-115.44；ESIMS m/z 281([M]$^{+}$)。

[1411] 制备2-乙基-4-(4-氟-2-异丙基苯基)-5-亚氨基-1，2，4-噻二唑烷-3-酮(CB50)

[1412] 

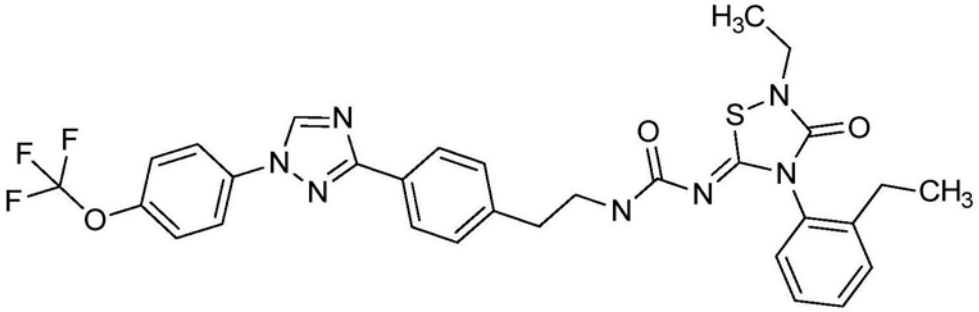
[1413] 标题化合物如实施例89中所述使用(Z)-1-乙基-3-(2-乙基-4-(4-氟-2-异丙基苯基)-3-氧代-1,2,4-噻二唑烷-5-亚基)脲(CB45)制备,并且分离为黄色油(0.110g,38%):^{1}H NMR(400MHz,$CDCl_3$)δ7.32-7.25(m,1H),7.08(dd,J=9.9,2.9Hz,1H),6.92(ddd,J=8.7,7.6,2.9Hz,1H),3.75-3.57(m,3H),3.32-3.13(m,1H),1.23(d,J=6.9Hz,6H),1.19(t,J=7.2Hz,3H);^{19}F NMR(376MHz,$CDCl_3$)δ-110.83;ESIMS m/z 281([M]$^{+}$)。

[1414] 制备2-乙基-5-亚氨基-4-(2-异丙基苯基)-1,2,4-噻二唑烷-3-酮(CB51)

[1415] 

[1416] 标题化合物如实施例89中所述使用(Z)-1-乙基-3-(2-乙基-4-(2-异丙基苯基)-3-氧代-1,2,4-噻二唑烷-5-亚基)脲(CB46)制备,并且分离为红色油(0.421g,65%):^{1}H NMR(400MHz,$CDCl_3$)δ7.42-7.34(m,2H),7.31-7.27(m,1H),7.22(dd,J=9.2,6.5Hz,1H),4.06(s,1H),3.65(d,J=8.5Hz,2H),3.34-3.13(m,1H),1.21(m,9H);ESIMS m/z 263([M]$^{+}$)。

[1417] 实施例90:制备(Z)-1-(2-乙基-4-(2-乙基苯基)-3-氧代-1,2,4-噻二唑烷-5-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB10)

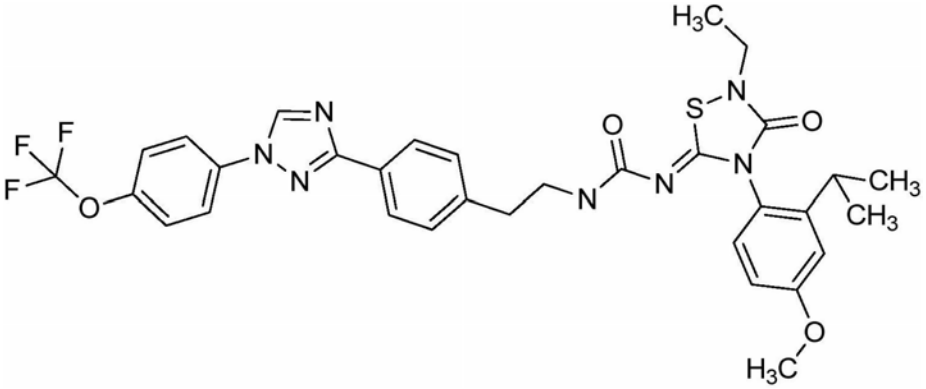
[1418] 

[1419] 将3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物(C34)(0.100g,0.249mmol)在乙腈(4mL)中的溶液在70℃加热2小时。反应冷却至室温,然后将2-乙基-4-(2-乙基苯基)-5-亚氨基-1,2,4-噻二唑烷-3-酮(CB47)(0.0660g,0.265mmol)加入到四氢呋喃和三乙胺(3滴)中。将反应搅拌过夜。将溶液稀释在乙酸乙酯中,用水洗涤。

将有机物提取，干燥，浓缩。通过使用0-90％乙腈/水(0.1％乙酸)作为洗脱剂的反相制备型HPLC纯化，提供为白色固体的标题化合物(0.045g，26％)。

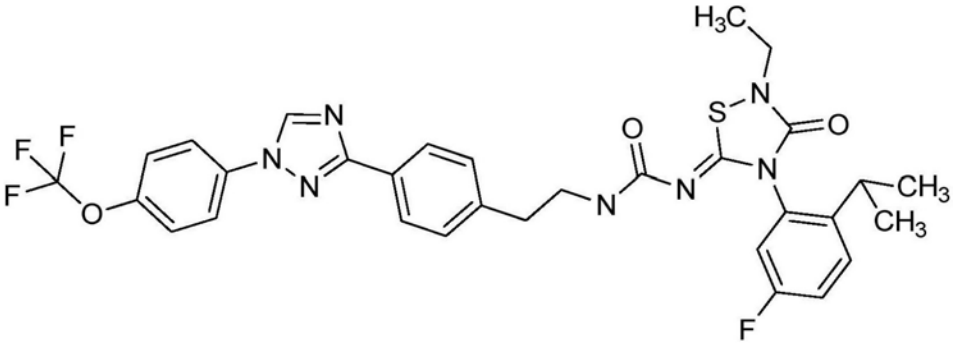
[1420] 下面的化合物根据实施例90中的步骤制备。

[1421] 制备(Z)-1-(2-乙基-4-(2-异丙基-4-甲氧基苯基)-3-氧代-1,2,4-噻二唑烷-5-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB11)

[1422] 

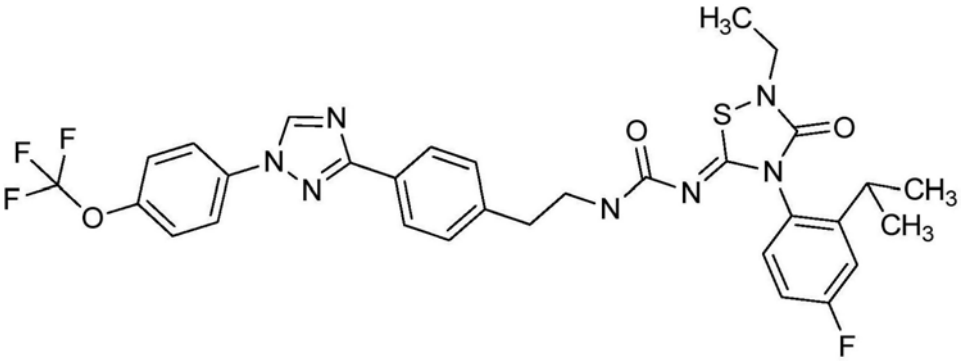
[1423] 标题化合物如实施例90中所述使用3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物(C34)和2-乙基-5-亚氨基-4-(2-异丙基-4-甲氧基苯基)-1,2,4-噻二唑烷-3-酮(CB48)制备，并且分离为黄色固体(0.016g，7％)。

[1424] 制备(Z)-1-(2-乙基-4-(5-氟-2-异丙基苯基)-3-氧代-1,2,4-噻二唑烷-5-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB12)

[1425] 

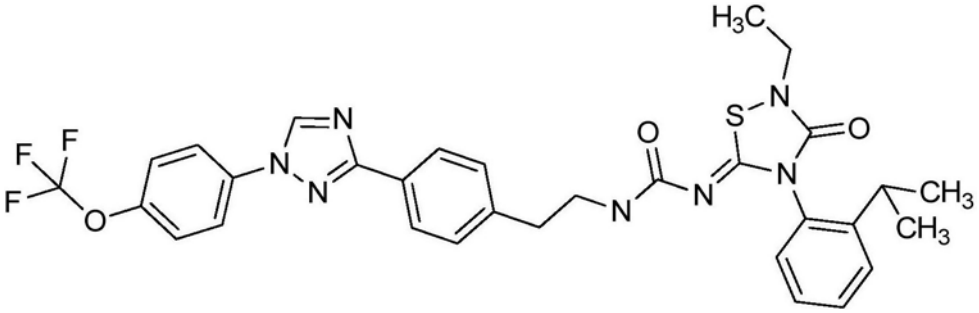
[1426] 标题化合物如实施例90中所述使用3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物(C34)和2-乙基-4-(5-氟-2-异丙基苯基)-5-亚氨基-1,2,4-噻二唑烷-3-酮(CB49)制备，并且分离为黄色油(0.068g，40％)。

[1427] 制备(Z)-1-(2-乙基-4-(4-氟-2-异丙基苯基)-3-氧代-1,2,4-噻二唑烷-5-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB13)

[1428] 

[1429] 标题化合物如实施例90中所述使用3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物(C34)和2-乙基-4-(4-氟-2-异丙基苯基)-5-亚氨基-1,2,4-噻二唑烷-3-酮(CB50)制备,并且分离为黄色油(0.018g,14%)。

[1430] 制备(Z)-1-(2-乙基-4-(2-异丙基苯基)-3-氧代-1,2,4-噻二唑烷-5-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB14)

[1431] 

[1432] 标题化合物如实施例90中所述使用3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙酰基叠氮化物(C34)和2-乙基-5-亚氨基-4-(2-异丙基苯基)-1,2,4-噻二唑烷-3-酮(CB51)制备,并且分离为黄色固体(0.047g,23%)。

[1433] 实施例91:制备N-(2-乙基-4-甲氧基苯基)氨基硫脲(CB52)

[1434] 

[1435] 步骤1.向2-乙基-4-甲氧基苯胺(4.5g,30mmol)和三乙胺(6.0g,60mmol)在二氯甲烷(31mL)中的溶液,在0℃经1小时的时间逐滴加入硫光气(3.4g,30mmol)。完成之后,将反应混合物倒入冰水(100mL)中,并且用乙酸乙酯(3×200mL)提取,用冰水(2×100mL)、随后盐水(2×50mL)洗涤。有机相经硫酸钠干燥,过滤,在减压下蒸发。通过使用0-10%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化,提供为黄色油的2-乙基-1-异硫氰酸根合-4-甲氧基苯(4.9g,25mmol),将其立即用于下一步骤上。

[1436] 步骤2.向2-乙基-1-异硫氰酸根合-4-甲氧基苯(4.9g,25mmol)在乙醇(22mL)中的溶液,缓慢加入肼·一水合物(1.3g,28mmol)。将反应混合物在室温搅拌18小时。将反应混合物在减压下蒸发,用乙酸乙酯稀释(250mL)用水(2×50mL)、随后盐水(2×50mL)洗涤。有机相经硫酸钠干燥,过滤,在减压下蒸发。通过使用0-40%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化,提供为白色固体的标题化合物(4.9g,86%):mp 113-115℃;^{1}H NMR (400MHz,DMSO-d_6)δ9.19(s,1H),8.89(s,1H),7.20-7.19(m,1H),6.77-6.71(m,2H),4.71(bs,2H),3.74(s,3H),2.52-2.47(m,2H),1.13-1.08(m,3H);ESIMS m/z 224([M-H]$^-$)。

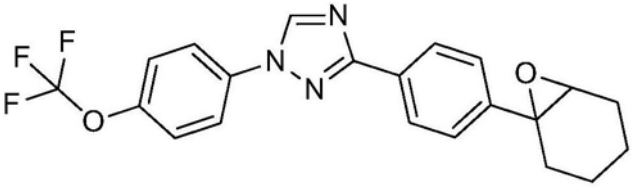
[1437] 下面的化合物根据实施例91中的步骤制备。

[1438] 制备N-(2-异丙基-4-甲氧基苯基)氨基硫脲(CB53)

[1439] 

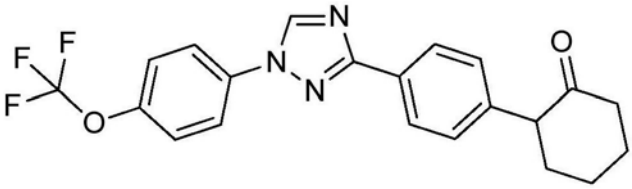
[1440] 标题化合物如实施例88中所述使用2-异丙基-4-甲氧基苯胺制备，并且分离为白色固体(9.5g)：mp 153-156℃；^{1}H NMR(400MHz，DMSO-d_6)δ9.18(s，1H)，8.96(s，1H)，7.12-7.10(m，1H)，6.78-6.78(m，2H)，4.71(bs，2H)，3.17(s，3H)，3.05-3.00(m，1H)，1.14(d，J＝6.6Hz，6H)；ESIMS m/z 238([M-H]$^-$)。

[1441] 实施例92：制备3-(4-(7-氧杂双环[4.1.0]庚烷-1-基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑(CB54)

[1442] 

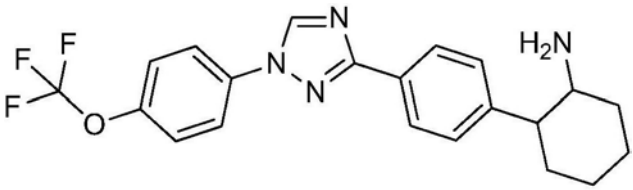
[1443] 向3-(2'，3'，4'，5'-四氢-[1，1'-联苯]-4-基)-1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑(CB10)(3.11g，8.07mmol)在乙醚(60mL)中的溶液，在0℃缓慢加入间氯过氧苯甲酸(70％；2.79g，11.3mmol)。将反应搅拌，使得逐渐温热至室温，然后继续搅拌18小时。将溶液在乙醚中稀释，用洗涤碳酸氢钠，用乙醚提取，用水洗涤，再次用乙醚提取。将有机物干燥，干燥，浓缩，提供为白色固体的标题化合物(2.5g，77％)(将其使用而不进一步纯化)：^{1}H NMR(400MHz，$CDCl_3$)δ8.58(s，1H)，8.20-8.11(m，2H)，7.84-7.77(m，2H)，7.52-7.46(m，2H)，7.39(dt，J＝8.0，1.0Hz，2H)，3.12(dd，J＝3.1，1.7Hz，1H)，2.34(ddd，J＝14.9，8.5，5.3Hz，1H)，2.09-1.95(m，2H)，1.74-1.45(m，4H)，1.42-1.28(m，1H)；^{19}F NMR(376MHz，$CDCl_3$)δ-58.03；ESIMS m/z 402([M+H]$^+$)。

[1444] 实施例93：制备2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑-3-基)苯基)环己酮(CB55)

[1445] 

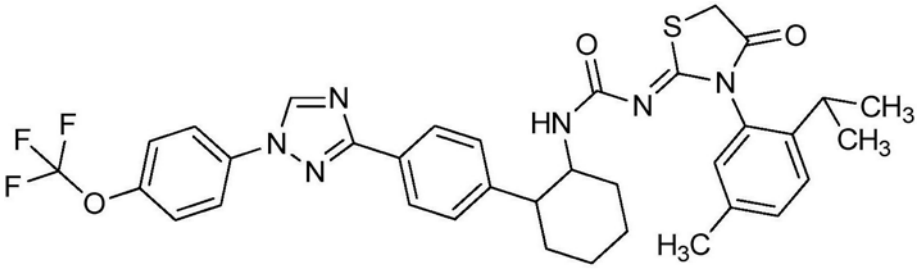
[1446] 向100mL烧瓶中的氯化铟(1.259g，5.69mmol)在15mL干燥的THF中经搅拌的溶液，加入3-(4-(7-氧杂双环[4.1.0]庚烷-1-基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1，2，4-三唑(CB54)(1.14g，2.85mmol)在干燥的四氢呋喃(10mL)中的溶液。在氮气下继续搅拌24小时，然后将溶液用乙醚(50mL)稀释和用水洗涤，干燥，并且真空浓缩。通过使用0-60％乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化，提供为白色固体的标题化合物(0.566g，35％)：^{1}H NMR(400MHz，$CDCl_3$)δ^{1}H NMR(400MHz，$CDCl_3$)δ8.54(s，1H)，8.16(dd，J＝8.6，2.1Hz，2H)，7.83-7.72(m，2H)，7.43-7.33(m，2H)，7.30-7.21(m，2H)，3.68(dd，J＝12.2，5.4Hz，1H)，2.61-2.41(m，2H)，2.37-2.24(m，1H)，2.23-1.92(m，3H)，1.85-1.60(m，2H)；^{19}F NMR(376MHz，$CDCl_3$)δ-58.03；ESIMS m/z 402([M+H]$^+$)。

[1447] 实施例94:制备2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)环己胺(CB56)

[1448] 

[1449] 向干燥的烧瓶加入2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)环己酮(CB55)(0.98g,2.4mmol)在干燥甲醇(30mL)中的溶液。将烧瓶抽吸/反填充氮气,加入乙酸铵(2.6g,34mmol),随后氰基硼氢化钠(0.18g,2.9mmol)。将反应在室温搅拌过夜。将溶液用水猝灭并且用乙酸乙酯提取。将有机物干燥,干燥,浓缩,提供为白色固体的标题化合物(0.42g,34%):^{1}H NMR表明存在2种不分离的同分异构体。^{1}H NMR(400MHz,DMSO-d_6)δ 9.41(two s,1H),8.14-8.03(m,4H),7.66-7.60(m,2H),7.53-7.40(m,2H),3.47-3.16(br s,2H),3.29(td,J=11.0,3.8Hz,1H),2.59(td,J=11.6,11.1,3.7Hz,1H),2.17-2.04(m,1H),1.86-1.68(m,3H),1.68-1.30(m,4H);ESIMS m/z 402([M]$^+$)。

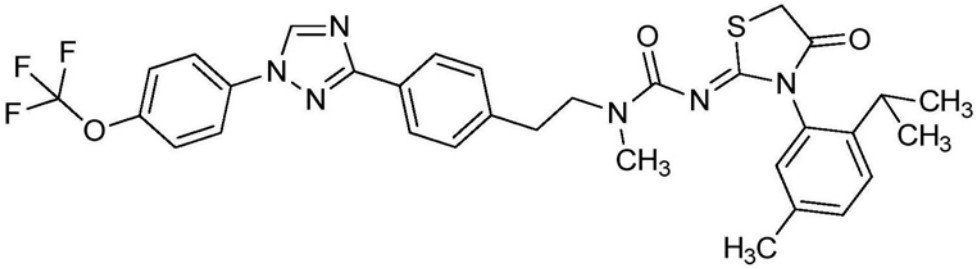
[1450] 实施例95:制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)环己基)脲(FB15)

[1451] 

[1452] 将2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)环己胺(CB56)(0.200g,0.497mmol)和(Z)-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)氨基甲酸4-硝基苯基酯(CA50)(0.205g,0.497mmol)溶解在小瓶的乙腈(10mL)中。加入碳酸铯(0.162g,0.497mmol),将反应在室温搅拌25小时。将溶液吸附到二氧化硅上。通过使用0-100%乙腈/水作为洗脱剂的反相快速柱色谱纯化,提供作为红色油的标题化合物(0.020g,6%)。

[1453] 下面的化合物根据实施例95中的步骤制备。

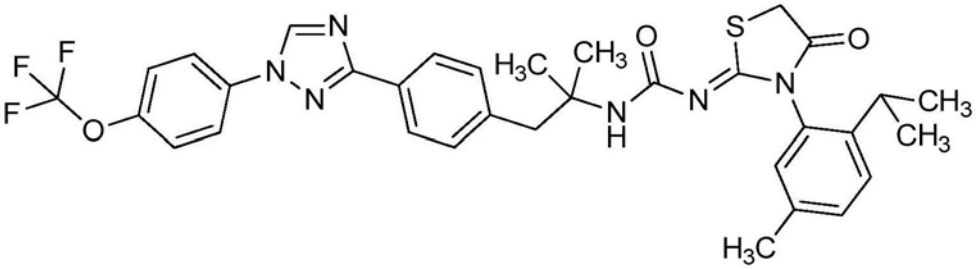
[1454] 制备(Z)-3-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-1-甲基-1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB51)

[1455] 

[1456] 标题化合物如实施例95中所述使用N-甲基-2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙烷胺(CB24)和(Z)-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-

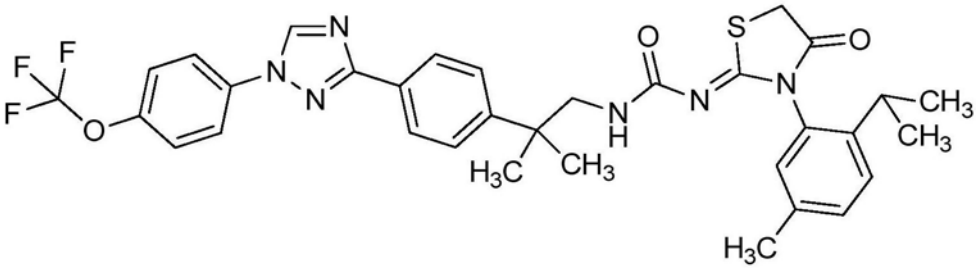
2-亚基)氨基甲酸4-硝基苯基酯(CA50)制备,通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,并且分离为淡橙色泡沫(0.160g,63%)。

[1457] 制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(2-甲基-1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-基)脲(FB52)

[1458] 

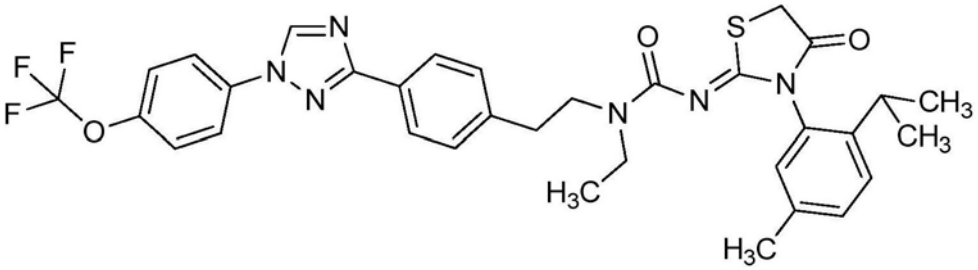
[1459] 标题化合物如实施例95中所述使用2-甲基-1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-胺(CB28)和(Z)-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)氨基甲酸4-硝基苯基酯(CA50)制备,通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,并且分离为褐色油(0.018g,9%)。

[1460] 制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(2-甲基-2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)脲(FB53)

[1461] 

[1462] 标题化合物如实施例95中所述使用2-甲基-2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-1-胺(CB29)和(Z)-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)氨基甲酸4-硝基苯基酯(CA50)制备,通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,并且分离为褐色玻璃状泡沫(0.084g,46%)。

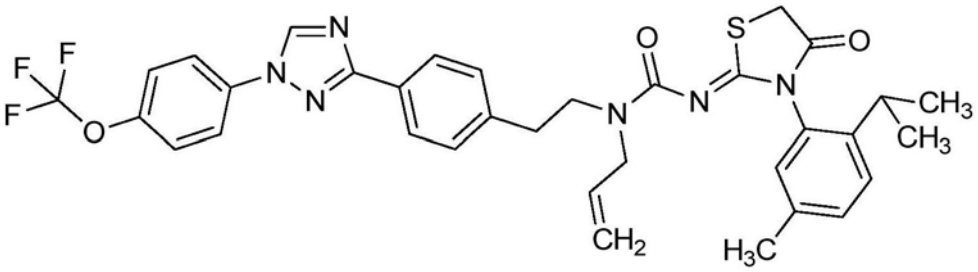
[1463] 制备(Z)-1-乙基-3-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB54)

[1464] 

[1465] 标题化合物如实施例95中所述使用N-乙基-2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙烷胺(CB25)和(Z)-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)氨基甲酸4-硝基苯基酯(CA50)制备,通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,并且分离为红色固体(0.075g,56%)。

[1466] 制备(Z)-1-烯丙基-3-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB61)

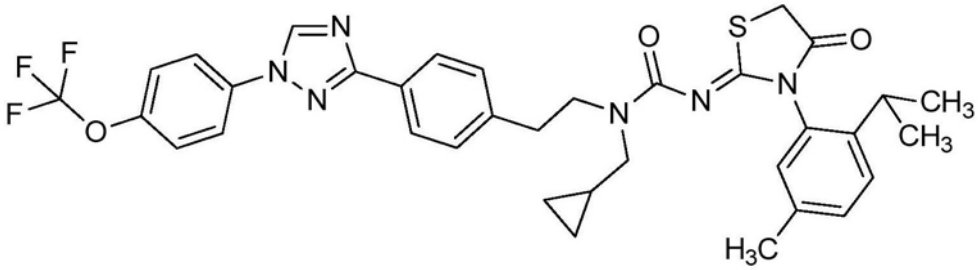
[1467]



[1468] 标题化合物如实施例95中所述使用N-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)丙-2-烯-1-胺(CB26)和(Z)-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)氨基甲酸4-硝基苯基酯(CA50)制备,通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,并且分离为褐色油(0.040g,43%)。

[1469] 制备(Z)-1-(环丙基甲基)-3-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB62)

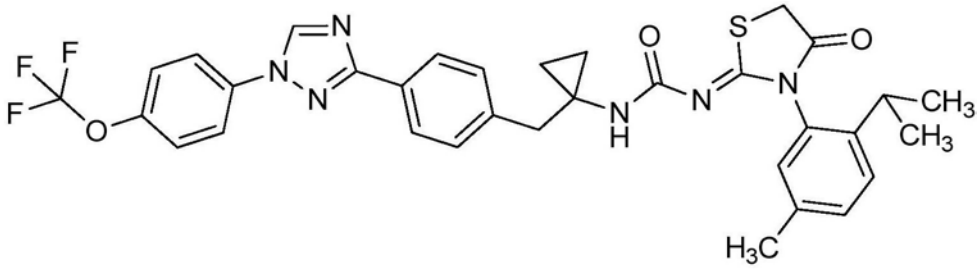
[1470]



[1471] 标题化合物如实施例95中所述使用N-(环丙基甲基)-2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙烷胺(CB27)和(Z)-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)氨基甲酸4-硝基苯基酯(CA50)制备,通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,并且分离为橙红色油(0.127g,60%)。

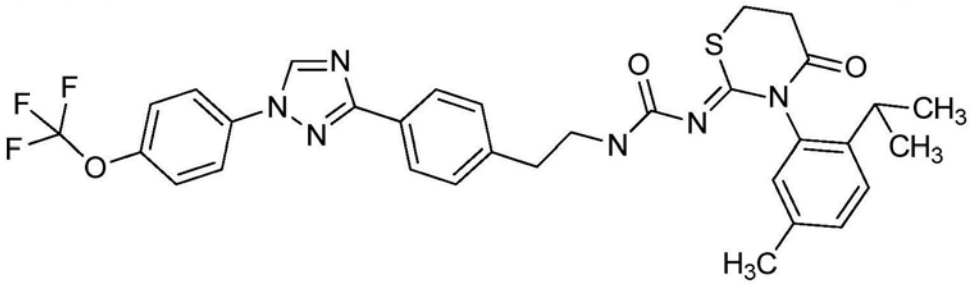
[1472] 制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)环丙基)脲(FB63)

[1473]



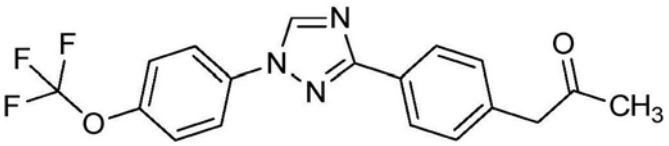
[1474] 标题化合物如实施例95中所述使用1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)环丙胺(CB30)和(Z)-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)氨基甲酸4-硝基苯基酯(CA50)制备,通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,并且分离为红色油(0.104g,37%)。

[1475] 实施例96:制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代-1,3-噻嗪烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB41)

[1476] 

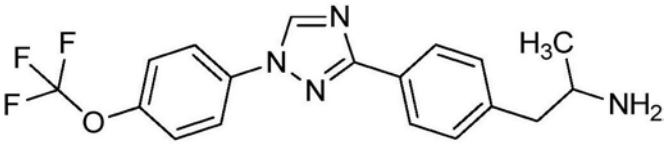
[1477] 将在乙腈(2.3mL)中的3-(4-(2-异氰酸酯基乙基)苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C34a)(0.18g,0.47mmol),1-(2-异丙基-5-甲基苯基)硫脲(0.10g,0.50mmol),和碳酸铯(0.21g,0.63mmol)在室温搅拌过夜。将反应混合物用乙酸乙酯稀释和用水洗涤。将有机层经硫酸钠干燥,过滤,浓缩。将粗制物质溶解在丁酮(2.3mL)中,随后加入丙烯酰氯(0.045mL,0.55mmol)。将反应在40℃加热4小时。反应冷却并且浓缩。通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,随后在真空烘箱中干燥,提供为黄色油的标题化合物(0.13g,44%)。

[1478] 实施例97:制备1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-酮(CB57)

[1479] 

[1480] 将3-(4-溴苯基)-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C52)(11g,29mmol),碘化亚铜(I)(0.55g,2.9mmol),磷酸钾(18g,86mmol),和戊烷-2,4-二酮(8.9mL,86mmol)溶解在500mL圆底烧瓶的二甲亚砜(120mL)中。将反应在110℃加热19小时。将溶液冷却至室温,然后用氯化氢(2N)猝灭。将过量的碱通过重力过滤除去,将滤液用乙酸乙酯提取。将有机物用水洗涤,提取,干燥,浓缩。通过快速柱色谱使用0-30%乙酸乙酯/己烷纯化,提供作为纯橙色固体的标题化合物(3.7g,35%):^{1}H NMR(400MHz,$CDCl_3$)δ8.56(s,1H),8.17(d,J=8.2Hz,2H),7.80(d,J=9.0Hz,2H),7.39(dt,J=8.1,1.0Hz,2H),7.33(dd,J=8.1,0.6Hz,2H),3.76(s,2H),2.19(s,3H);ESIMS m/z 361([M]$^+$)。

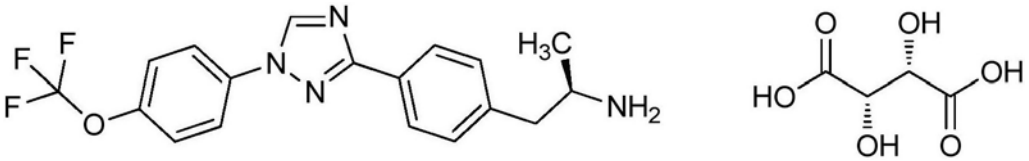
[1481] 实施例98:制备1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-胺(CB58)

[1482] 

[1483] 将1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-酮(CB57)(1.0g,2.8mmol)和乙酸铵(1.7g,22mmol)合并在干燥甲醇(22mL)中,室温搅拌,同时将氰基硼氢化钠(0.17g,2.7mmol)以3等份经30分钟加入。将反应搅拌过夜。将反应浓缩,在碳酸钾溶液和乙醚之间分离。分层,干燥,过滤,浓缩。通过使用0-100%乙腈/水作为洗脱剂的反相快速柱(C18)色谱纯化,提供为褐色固体的标题化合物(1.0g,38%):mp 140-160℃;^{1}H NMR(400MHz,$CDOD_3$)d 9.13(s,1H),8.09(d,J=8.0Hz,2H),8.00(d,J=9.0Hz,2H),7.52 7.43(m,2H),7.35(d,J=8.0Hz,2H),3.40-3.33(m,1H),2.86(t,J=6.7Hz,1H),2.77(dd,J

＝13.3,7.3Hz,1H),1.18(d,J＝6.2Hz,3H)(NH_2未观测);ESIMS m/z 363([M+H]$^+$)。

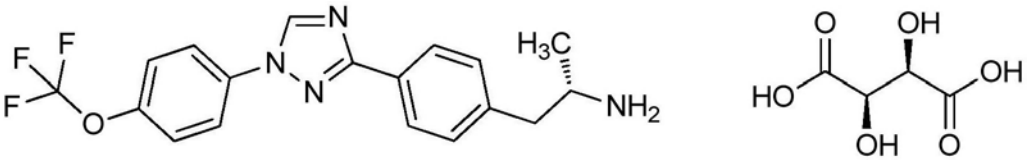
[1484] 实施例99:制备(R)-1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-胺(2S,3S)-2,3-二羟基琥珀酸酯(CB59)

[1485] 

[1486] 向在甲醇(10mL)中的1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-胺(CB58)(0.60g,1.7mmol),加入(2S,3S)-2,3-二羟基琥珀酸(0.25g,1.7mmol)。将所得固体过滤,风干过夜:mp 182-185℃。将固体重新溶解在甲醇(10mL)中,加热回流(～65℃)。将溶液冷却至室温,静置过夜。经所形成的白色固体过滤,风干,给出为白色固体的标题化合物(0.40g,46%):mp 191-194℃;^{1}H NMR(400MHz,$CDOD_3$)d 9.16(s,1H),8.15(d,J＝8.2Hz,2H),8.02(d,J＝9.1Hz,2H),7.50(dd,J＝9.2,1.0Hz,2H),7.41(d,J＝8.2Hz,2H),4.40(s,2H),3.59(dt,J＝8.1,6.2Hz,1H),3.07(dd,J＝13.6,6.1Hz,1H),2.88(dd,J＝13.6,8.3Hz,1H),1.29(d,J＝6.5Hz,3H)(OH和NH_2未观测)。

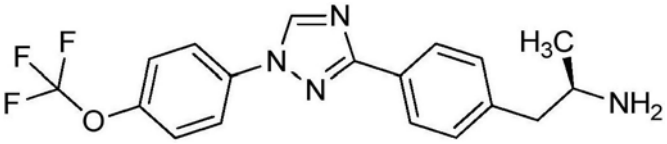
[1487] 下面的化合物根据实施例99中的步骤制备。

[1488] 制备(S)-1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-胺(2R,3R)-2,3-二羟基琥珀酸酯(CB60)

[1489] 

[1490] 标题化合物如实施例99中所述使用1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-胺(CB58)和(2R,3R)-2,3-二羟基琥珀酸制备,并且分离为白色固体(0.70g,49%):mp 187-191℃;^{1}H NMR ^{1}H NMR(400MHz,DMSO-d_6)d 9.40(s,1H),8.08(dd,J＝8.6,3.6Hz,4H),7.63(dt,J＝8.1,1.0Hz,2H),7.49 7.32(m,2H),3.81(s,2H),3.47(dt,J＝8.5,6.2Hz,1H),3.01(dd,J＝13.4,5.5Hz,1H),2.74(dd,J＝13.4,8.7Hz,1H),1.13(d,J＝6.4Hz,3H)(OH和NH_2未观测)。

[1491] 实施例100:制备(R)-1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-胺(CB61)

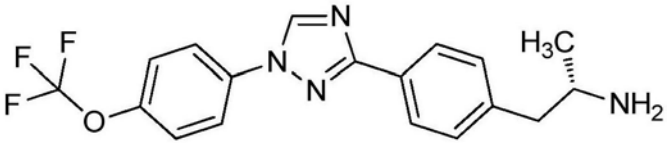
[1492] 

[1493] 将(R)-1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-胺(2S,3S)-2,3-二羟基琥珀酸酯(CB59)(0.35g,0.68mmol)在甲醇(20mL)和SCX硅胶(2g)中成为浆状。将溶液搅拌3小时,过滤,用甲醇(20mL)洗涤。将化合物从SCX硅胶使用氢氧化铵(5%,在MeOH中,25mL)洗脱。将滤液浓缩,提供为白色固体的标题化合物(0.22g,87%):mp 84-88℃;^{1}H NMR(400MHz,$CDCl_3$)d 8.56(s,1H),8.13(d,J＝8.2Hz,2H),7.80(d,J＝9.0Hz,2H),7.447.35(m,2H),7.31(d,J＝8.1Hz,2H),3.293.15(m,1H),2.78(dd,J＝13.2,5.4Hz,

1H),2.60(dd,J=13.2,8.0Hz,1H),1.49(s,2H),1.15(d,J=6.3Hz,3H)。

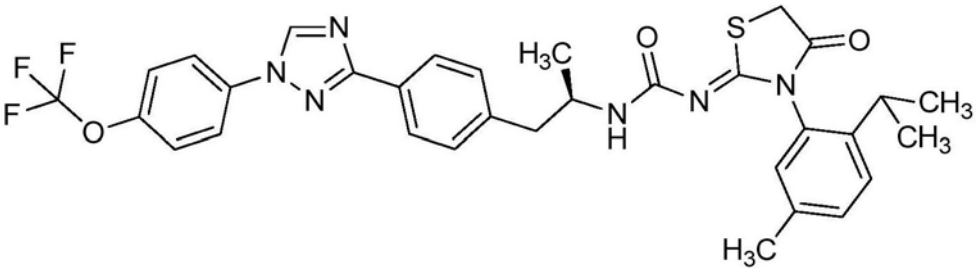
[1494] 下面的化合物根据实施例100中的步骤制备。

[1495] 制备(S)-1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-胺(CB62)

[1496] 

[1497] 标题化合物如实施例100中所述使用(S)-1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-胺(2R,3R)-2,3-二羟基琥珀酸酯(CB60)制备,并且分离为白色固体(0.40g,94%):mp 84-86℃;^{1}H NMR(400MHz,$CDCl_3$)d 8.56(s,1H),8.13(d,J=8.2Hz,2H),7.80(d,J=9.0Hz,2H),7.447.35(m,2H),7.357.28(m,2H),3.293.16(m,1H),2.78(dd,J=13.2,5.3Hz,1H),2.60(dd,J=13.2,8.0Hz,1H),1.15(d,J=6.3Hz,3H)($N\underline{H}_2$未观测)。

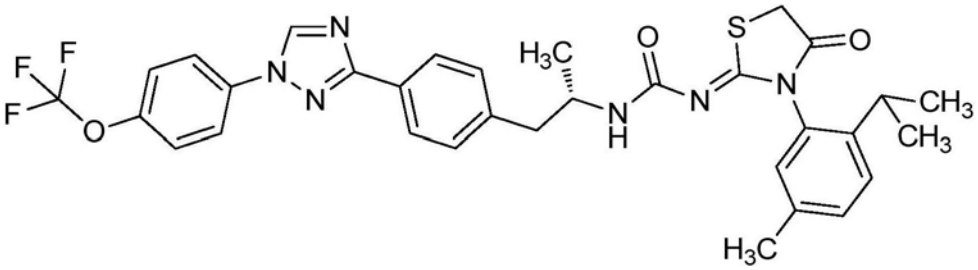
[1498] 实施例101:制备(R,Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-基)脲(FB45)

[1499] 

[1500] 向在冰浴的二氯甲烷/水(2:1,3.1mL)中的(R)-1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-胺(CB61)(0.12g,0.32mmol)和碳酸氢钠(0.10g,1.2mmol),加入三光气(0.052g,0.18mmol)。将反应用几滴水猝灭,用二氯甲烷稀释。将反应混合物通过相分离器过滤,浓缩。将残留物溶解在乙腈(2mL)中,以单个批次加入1-(2-异丙基-5-甲基苯基)硫脲(0.069g,0.33mmol)和碳酸铯(0.14g,0.42mmol)。将反应在室温搅拌过夜。加入另外部分的1-(2-异丙基-5-甲基苯基)硫脲(0.070g,0.33mmol)和碳酸铯(0.070g,0.21mmol),将反应搅拌过夜。加入乙醇(4mL),2-溴乙酸甲酯(0.10mL,0.96mmol),和乙酸钠(0.079g,0.96mmol),将反应在60℃加热6小时。反应冷却,并且在周末在室温搅拌。将反应用水稀释并且用乙酸乙酯(2×)提取。将有机层用硫酸钠干燥,过滤,浓缩。通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供为黄色油的标题化合物(0.039g,19%)。

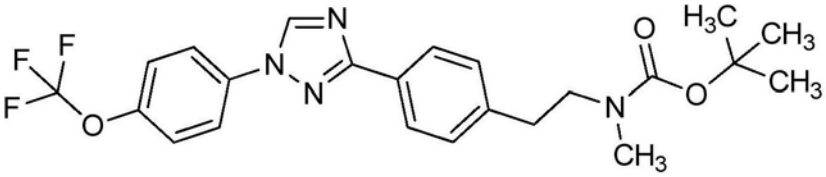
[1501] 下面的化合物根据实施例101中的步骤制备。

[1502] 制备(S,Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-基)脲(FB46)

[1503] 

[1504] 标题化合物如实施例101中所述使用(S)-1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-胺(CB62)和1-(2-异丙基-5-甲基苯基)硫脲制备，并且分离为灰白色泡沫(0.045g，24%)。

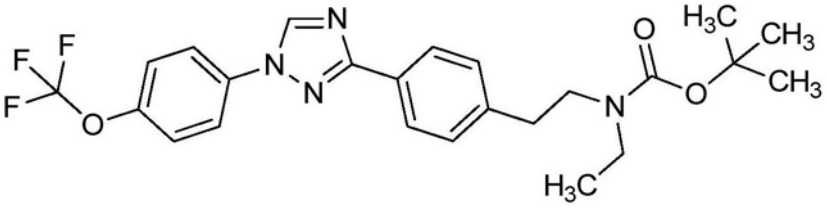
[1505] 实施例102：制备甲基(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)氨基甲酸叔丁基酯(CB63)

[1506] 

[1507] 向在无水二甲基甲酰胺(0.023mL)中的4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基氨基甲酸叔丁基酯(C50)(0.021g，0.047mmol)在0℃，加入氢化钠(60%油悬浮液，0.012g，0.30mmol)，在冰浴中搅拌5分钟。加入碘代甲烷(0.013g，0.094mmol)，黄色溶液立即变成白色。10分钟之后，将反应用水猝灭，并且用二氯甲烷提取。将有机层浓缩，提供为黄色油的标题化合物(0.022g，97%)：^{1}H NMR(400MHz，$CDCl_3$)δ8.56(s，1H)，8.12(d，J＝8.2Hz，2H)，7.80(d，J＝9.0Hz，2H)，7.39(dt，J＝8.0，1.0Hz，2H)，7.37-7.20(m，2H)，3.47(s，2H)，2.86(s，2H)，1.57(s，3H)，1.44(d，J＝13.7Hz，9H)；^{19}F NMR(376MHz，$CDCl_3$)δ-58.03；ESIMS m/z 463([M+H]$^{+}$)。

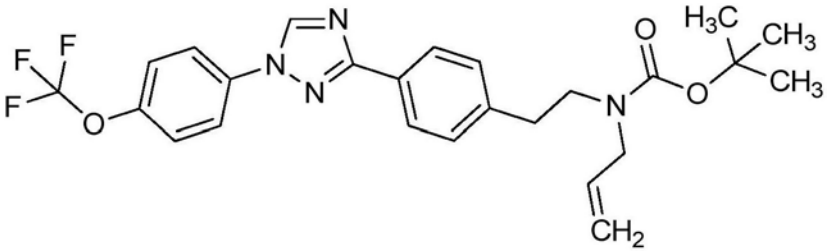
[1508] 下面的化合物根据实施例102中的步骤制备。

[1509] 制备乙基(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)氨基甲酸叔丁基酯(CB64)

[1510] 

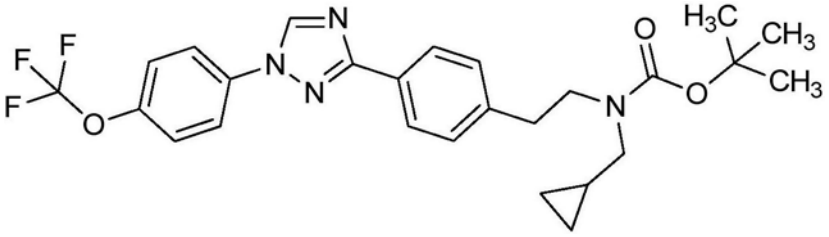
[1511] 标题化合物如实施例102中所述使用4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基氨基甲酸叔丁酯(C50)和碘代乙烷制备，并且分离为黄色油(0.175g，100%)：^{1}H NMR(400MHz，$CDCl_3$)δ8.56(s，1H)，8.16-8.06(m，2H)，7.89-7.73(m，2H)，7.45-7.36(m，2H)，7.31(s，2H)，3.42(s，2H)，3.23(t，J＝35.4Hz，2H)，2.96-2.84(m，2H)，1.47(s，9H)，1.08(s，3H)；^{19}F NMR(376MHz，$CDCl_3$)δ-58.03；ESIMS m/z 477([M+H]$^{+}$)。

[1512] 制备烯丙基(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)氨基甲酸叔丁酯(CB65)

[1513] 

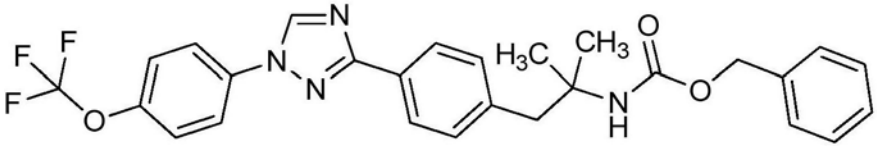
[1514] 标题化合物如实施例102中所述使用4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基氨基甲酸叔丁基酯(C50)和烯丙基溴制备,并且分离为黄色油(0.144g,99%):^{1}H NMR(400MHz,$CDCl_3$)δ8.56(s,1H),8.15-8.08(m,2H),7.85-7.76(m,2H),7.39(dq,J=7.8,1.0Hz,2H),7.30(s,2H),5.76(s,1H),5.12(s,2H),3.76(d,J=45.8Hz,2H),3.42(s,2H),2.89(d,J=0.7Hz,2H),1.47(s,9H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 489([M+H]$^+$)。

[1515] 制备(环丙基甲基)(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)氨基甲酸叔丁酯(CB66)

[1516] 

[1517] 标题化合物如实施例102中所述使用4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基氨基甲酸叔丁酯(C50)和环丙基甲基溴制备,并且分离为澄清的油(0.155g,96%):^{1}H NMR(400MHz,$CDCl_3$)δ8.56(s,1H),8.16-8.07(m,2H),7.84-7.77(m,2H),7.39(dq,J=8.0,0.9Hz,2H),7.31(s,2H),3.50(t,J=7.6Hz,2H),3.17-2.86(m,4H),1.48(s,9H),0.87(ddd,J=11.2,9.0,6.7Hz,1H),0.49(d,J=8.0Hz,2H),0.21(s,2H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 503([M+H]$^+$)。

[1518] 实施例103:制备(2-甲基-1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙烷-2-基)氨基甲酸苄酯(CB67)

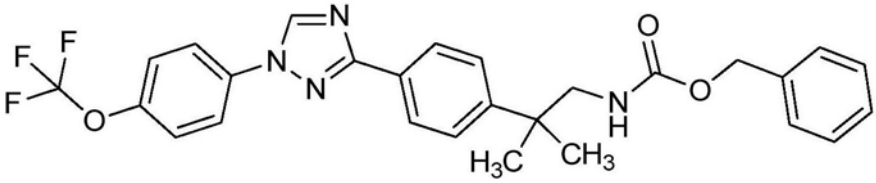
[1519] 

[1520] 将在二氧六环/水(4:1,90mL)中的3-溴-1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑(C1)(4.28g,13.9mmol),(2-甲基-1-(4-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苯基)丙烷-2-基)氨基甲酸苄基酯(CB7)(6.12g,15.0mmol),四氟硼酸三叔丁基鏻(0.390g,1.40mmol),乙酸钯(II)(0.150g,0.680mmol),和氟化铯(4.34g,28.6mmol)的混合物在70℃加热过夜。反应冷却,用盐水稀释,并且用乙酸乙酯(2×)提取。将有机层经硫酸钠干燥,过滤,浓缩。通过使用0-100%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化,提供为澄清的油的标题化合物(1.16g,15%):^{1}H NMR(400MHz,$CDCl_3$)δ8.57(s,1H),8.06(d,J=8.2Hz,2H),7.81(d,J=9.0Hz,2H),7.44-7.32(m,7H),7.19(d,J=8.2Hz,2H),5.12(s,2H),4.56(s,1H),3.05(s,2H),1.33(s,6H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.02;ESIMS m/z 511([M

+H]$^+$)。

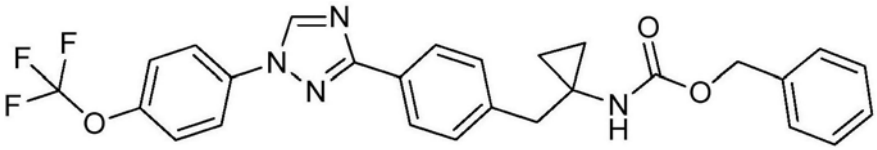
[1521] 下面的化合物根据实施例103中的步骤制备。

[1522] 制备(2-甲基-2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)丙基)氨基甲酸苄酯(CB68)

[1523] 

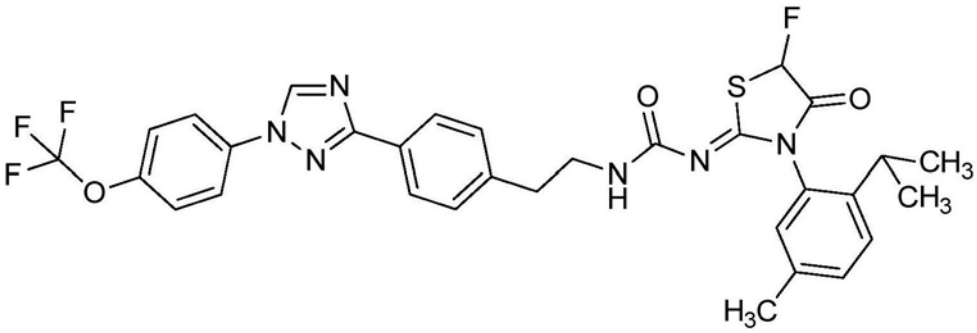
[1524] 标题化合物如实施例103中所述使用(2-甲基-2-(4-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苯基)丙基)氨基甲酸苄酯(CB8)制备,并且分离为澄清的油(0.045g,24%):^{1}H NMR(400MHz,$CDCl_3$)δ8.57(s,1H),8.18-8.10(m,2H),7.84-7.75(m,2H),7.49-7.42(m,2H),7.39(dq,J=9.0,0.9Hz,2H),7.31(q,J=6.8,6.4Hz,5H),5.06(s,2H),4.52(s,1H),3.45(d,J=6.3Hz,2H),1.38(s,6H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 511([M+H]$^+$)。

[1525] 制备(1-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苄基)环丙基)氨基甲酸苄酯(CB69)

[1526] 

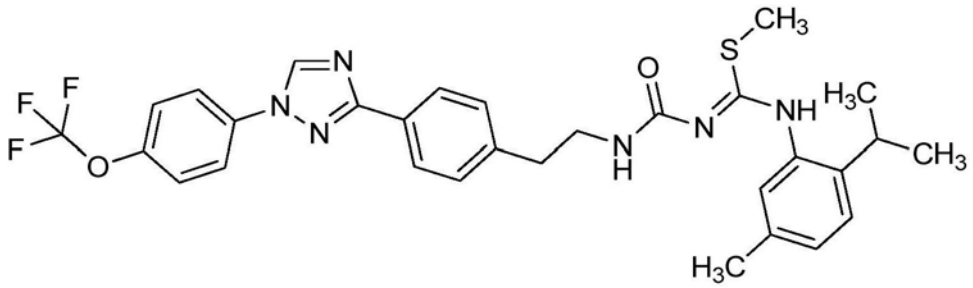
[1527] 标题化合物如实施例103中所述使用(1-(4-(4,4,5,5-四甲基-1,3,2-二氧杂硼杂环戊烷-2-基)苄基)环丙基)氨基甲酸苄酯(CB9)制备,并且分离为褐色固体(2.19g,68%):mp 156-158℃;^{1}H NMR(400MHz,$CDCl_3$)δ8.56(s,1H),8.10(d,J=8.1Hz,2H),7.84-7.73(m,2H),7.42-7.30(m,6H),7.26-7.25(m,3H),5.10(s,2H),4.96(s,1H),2.94(s,2H),0.85(s,4H);^{19}F NMR(376MHz,$CDCl_3$)δ-58.03;ESIMS m/z 509([M+H]$^+$)。

[1528] 实施例104:制备(Z)-1-(5-氟-3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB64)

[1529] 

[1530] 向在无水乙腈(0.80mL)中的(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(F5)(0.050g,0.080mmol)和2-芴酮(0.0080g,0.044mmol),加入Selectfluor®(0.062g,0.18mmol)。将反应在室温搅拌过夜。通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供为黄色油的标题化合物(0.033g,63%)。

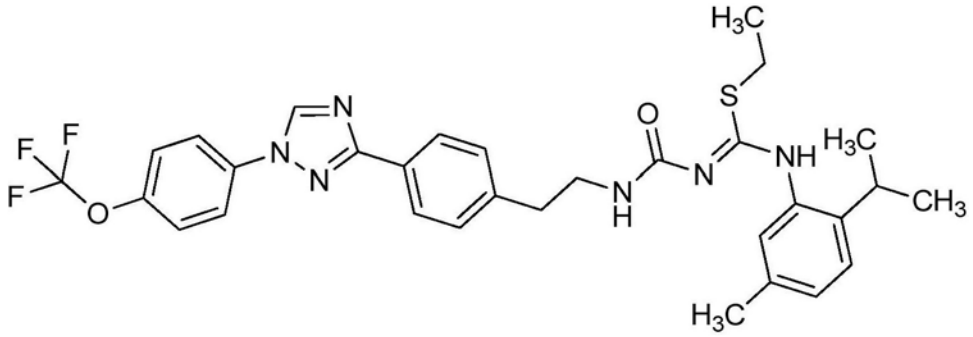
[1531] 实施例105:制备(Z)-甲基N-(2-异丙基-5-甲基苯基)-N'-((4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)氨基甲酰基)异硫脲(carbamimidothioate)(FB65)

[1532] 

[1533] 向在乙醇(1mL)中的N-[5-甲基-2-异丙基苯基]-N'-[2-(4-{1-[4-(三氟甲氧基)-苯基]-1H-1,2,4-三唑-3-基}苯基)乙基]硫代缩二脲(F3)(0.15g,0.26mmol)和乙酸钠(0.053g,0.65mmol),加入碘代甲烷(0.020mL,0.32mmol)。将反应在室温搅拌过夜。反应混合物用水稀释,将水倾泻掉,留下白色固体,将其在真空下干燥3小时。通过使用0-100%乙酸乙酯/B(其中B=1:1二氯甲烷/己烷)作为洗脱剂的快速柱色谱纯化,提供为澄清的油的标题化合物(0.081g,49%)。

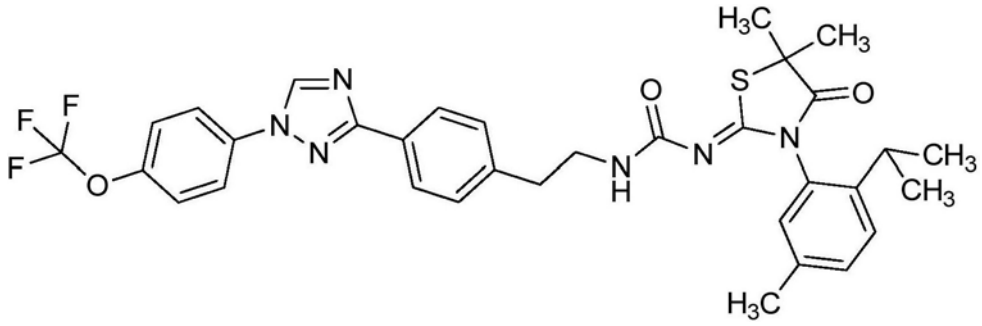
[1534] 下面的化合物根据实施例105中的步骤制备。

[1535] 制备(Z)-乙基N-(2-异丙基-5-甲基苯基)-N'-((4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)氨基甲酰基)异硫脲(FB66)

[1536] 

[1537] 标题化合物如实施例105中所述制备使用N-[5-甲基-2-异丙基苯基]-N'-[2-(4-{1-[4-(三氟甲氧基)-苯基]-1H-1,2,4-三唑-3-基}苯基)乙基]硫代缩二脲(F3)和碘代乙烷,通过使用0-100%乙腈/水作为洗脱剂的反相快速柱色谱纯化,并且分离为澄清的油(0.050g,43%)。

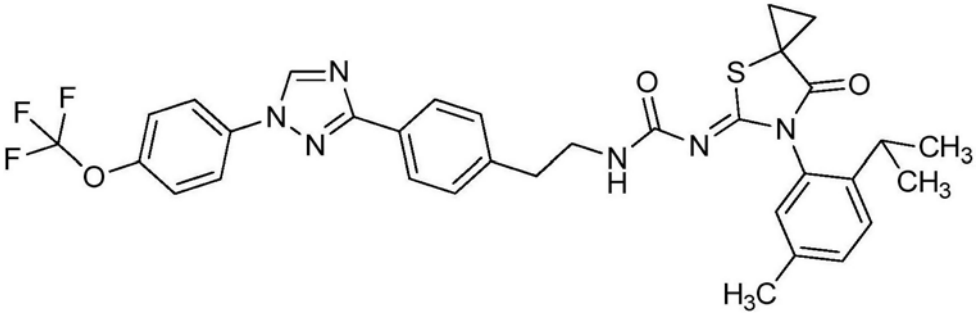
[1538] 实施例106:制备(Z)-1-(3-(2-异丙基-5-甲基苯基)-5,5-二甲基-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB68)

[1539] 

[1540] 向装配有磁搅拌器的干燥的2打兰的小瓶，加入(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(F5)(0.10g，0.16mmol)和无水二甲基甲酰胺(0.5mL)。向该溶液加入氢化钠(60%油悬浮液，0.0064g，0.16mmol)，随后碘代甲烷(0.022g，0.16mmol)。将反应在室温搅拌过夜。通过使用0-100%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化，提供为浅黄色泡沫的标题化合物(0.054g，52%)。

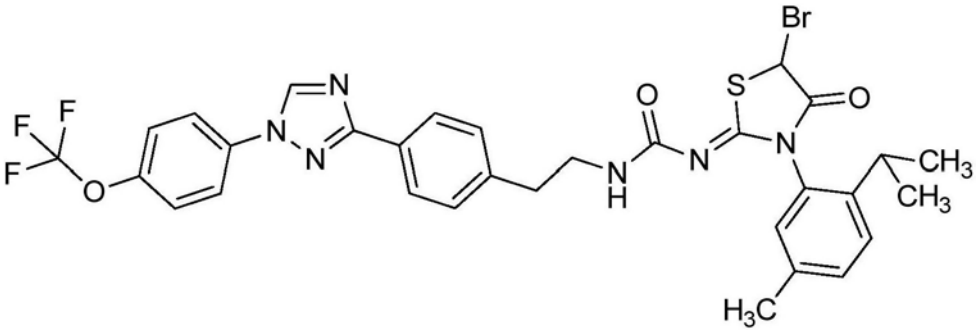
[1541] 下面的化合物根据实施例106中的步骤制备。

[1542] 制备(Z)-1-(6-(2-异丙基-5-甲基苯基)-7-氧代-4-硫杂-6-氮杂螺[2.4]庚烷-5-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB69)

[1543] 

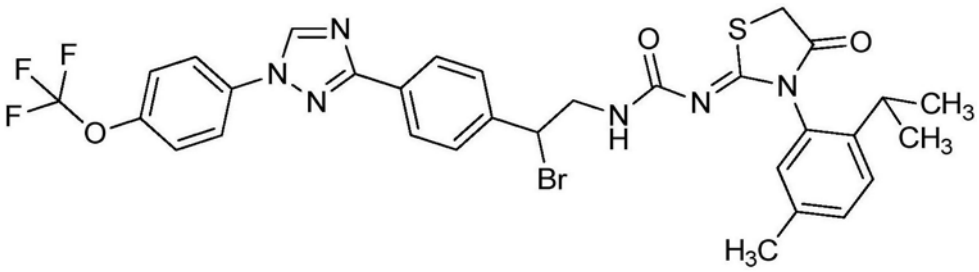
[1544] 标题化合物如实施例106中所述使用N-[5-甲基-2-异丙基苯基]-N'-[2-(4-{1-[4-(三氟甲氧基)-苯基]-1H-1,2,4-三唑-3-基}苯基)乙基]硫代缩二脲(F3)和1,2-二溴乙烷制备，并且分离为白色泡沫(0.023g，22%)。

[1545] 实施例107：制备(Z)-1-(5-溴-3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB70)

[1546] 

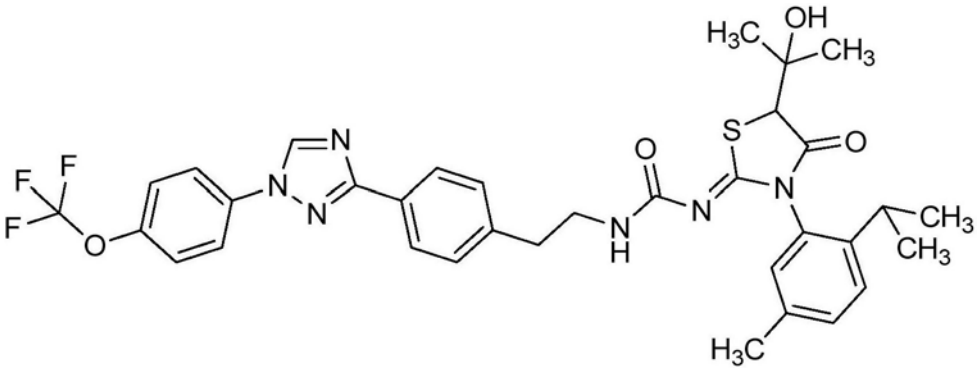
[1547] 向装配有磁搅拌器的干燥的2打兰的小瓶，加入(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(F5)(0.20g，0.32mmol)和无水二氯甲烷(0.5mL)。向该溶液加入溴(0.033mL，0.64mmol)。将反应在室温搅拌过夜。通过使用0-100%乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化，提供为澄清无色油的标题化合物(0.041g，18%)。

[1548] 实施例108：制备(Z)-1-(2-溴-2-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯基)乙基)-3-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)脲(FB71)

[1549] 

[1550] 向装配有磁搅拌器和回流冷凝器的干燥的圆底烧瓶(20mL)，加入(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(F5)(0.20g，0.32mmol)，四氯化碳(1mL)，N-溴代琥珀酰亚胺(0.057g，0.32mmol)，和偶氮二异丁腈(0.0053g，0.032mmol)。将反应加热回流2小时。反应冷却。通过使用0-100％乙酸乙酯/己烷作为洗脱剂的快速柱色谱纯化，提供为黄色油的标题化合物(0.049g，21％)。

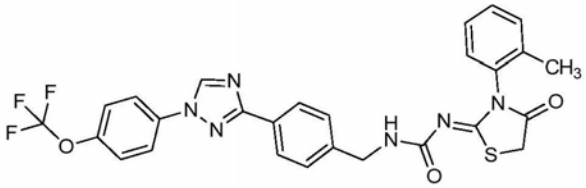
[1551] 实施例109:制备(Z)-1-(5-(2-羟基丙烷-2-基)-3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(FB72)

[1552] 

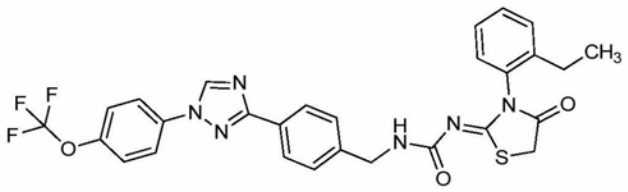
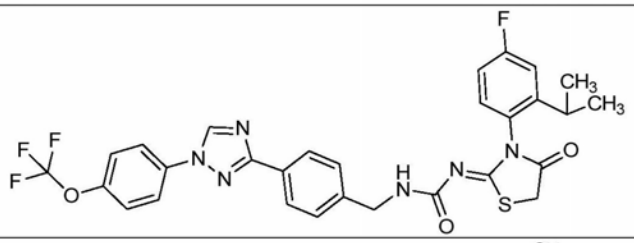
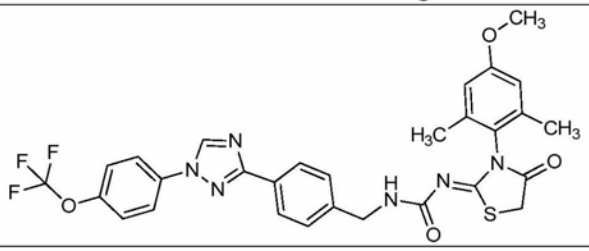
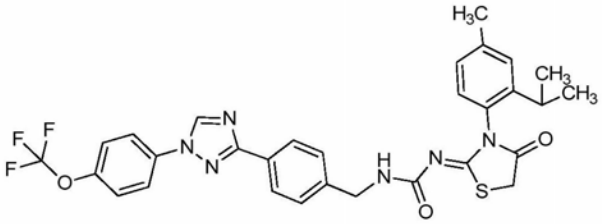
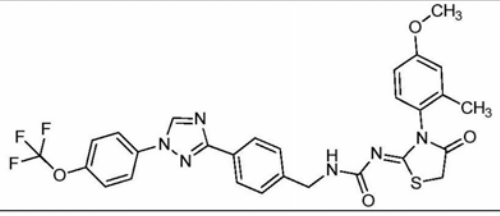
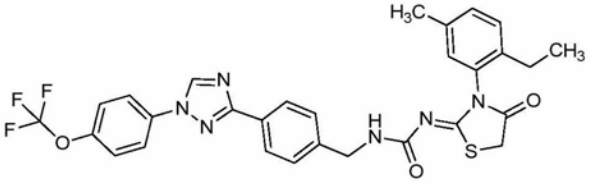
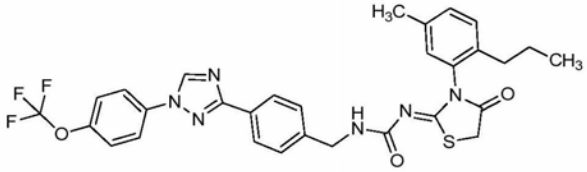
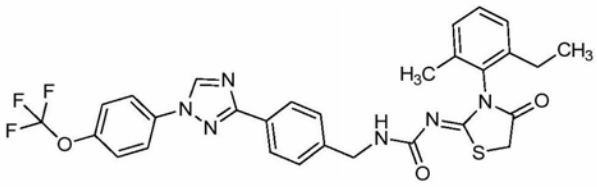
[1553] 向在丙酮(30mL)中的(Z)-1-(3-(2-异丙基-5-甲基苯基)-4-氧代噻唑烷-2-亚基)-3-(4-(1-(4-(三氟甲氧基)苯基)-1H-1,2,4-三唑-3-基)苯乙基)脲(F5)(0.40g，0.64mmol)，加入饱和碳酸氢钠溶液(3mL)。将反应加热回流12小时，冷却，浓缩。将反应混合物在乙酸乙酯和水之间分离。将有机层干燥并且浓缩。通过使用100-40％A/B(其中A＝1:1二氯甲烷/己烷和B＝3:1乙酸乙酯/丙酮)作为洗脱剂的快速柱色谱纯化，提供为白色固体的标题化合物(0.095g，19％)。

[1554] 使用本文披露的步骤，可以制备下列预知的具有根据式一的结构的分子(表P-I)。

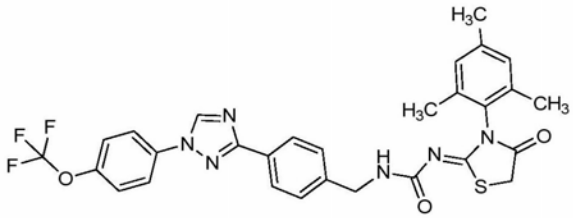
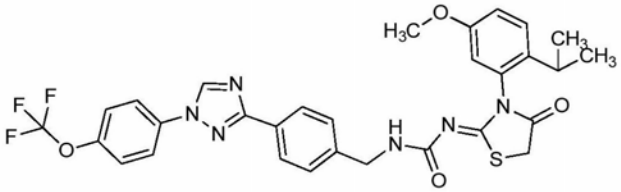
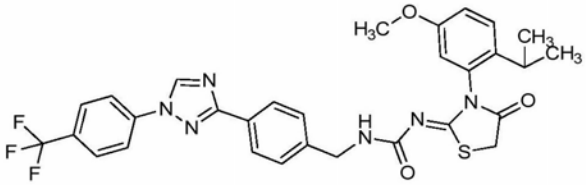
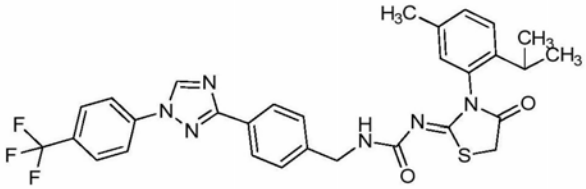
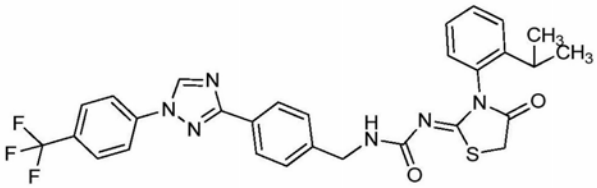
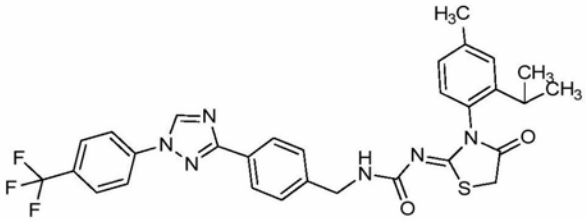
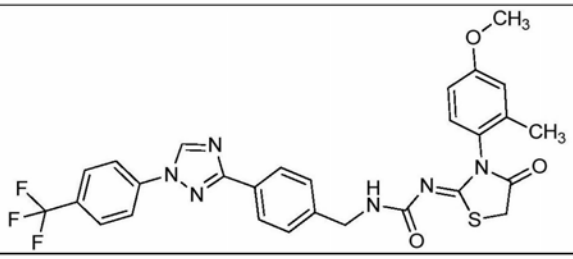
[1555]

表 P-Ⅰ	
P1	

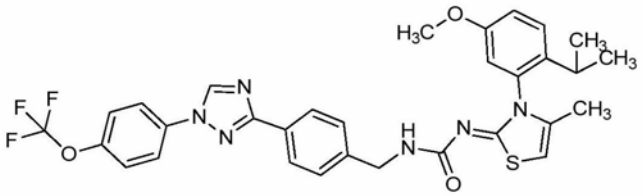
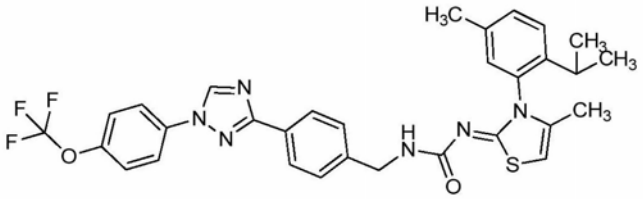
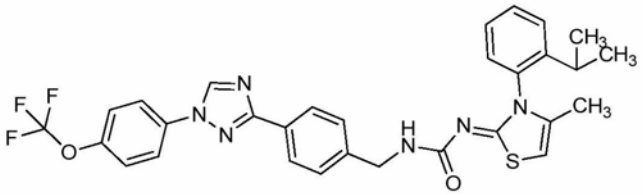
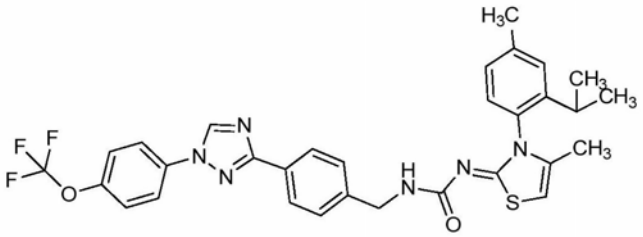
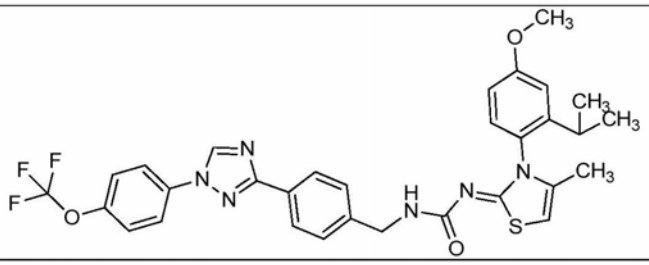
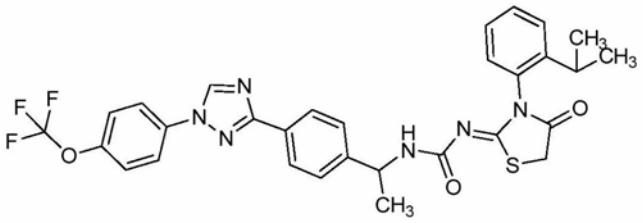
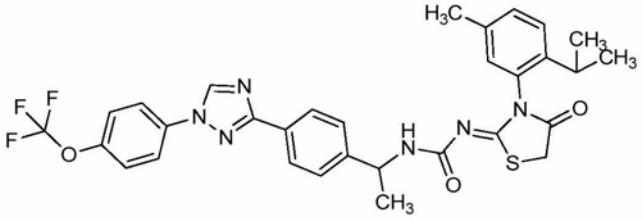
[1556]

P2	
P3	
P4	
P5	
P6	
P7	
P8	
P9	

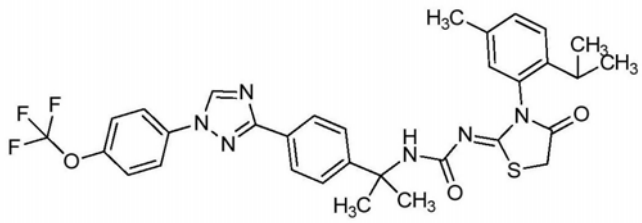
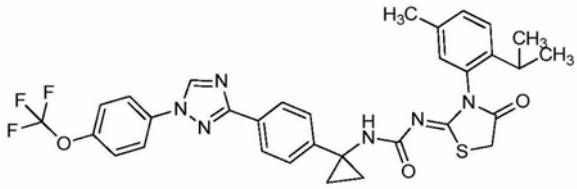
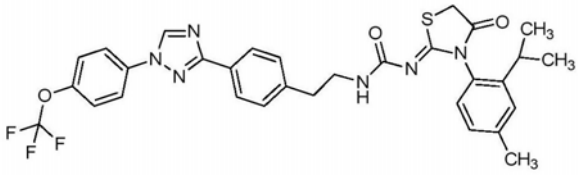
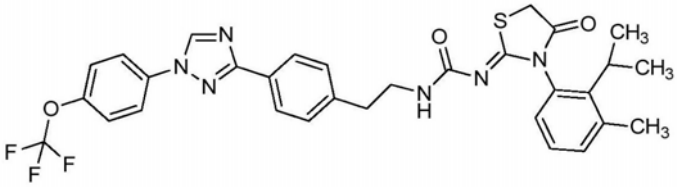
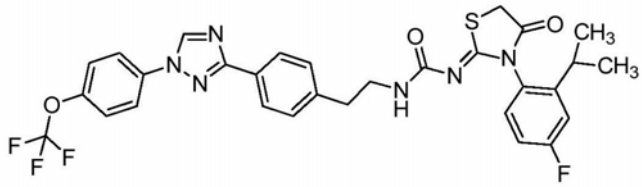
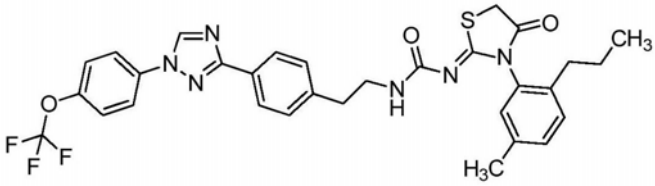
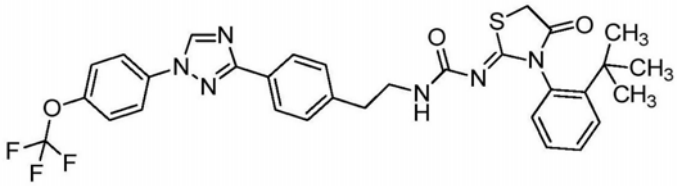
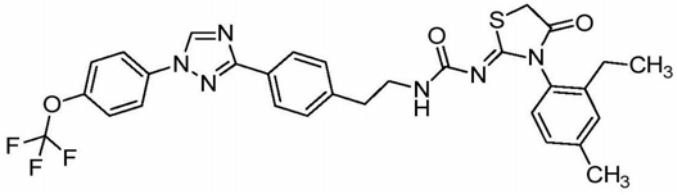
[1557]

P10	
P11	
P12	
P13	
P14	
P15	
P16	

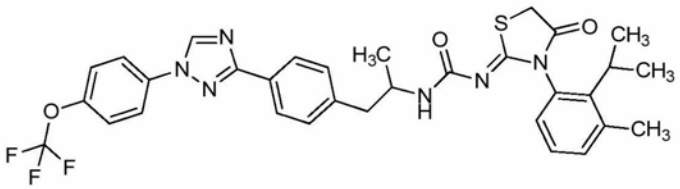
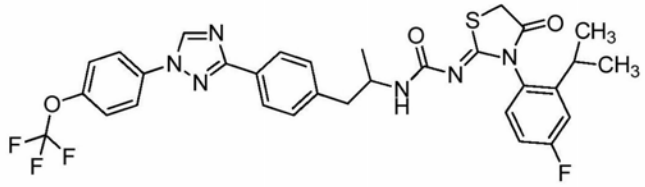
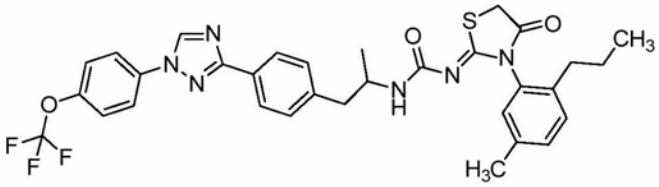
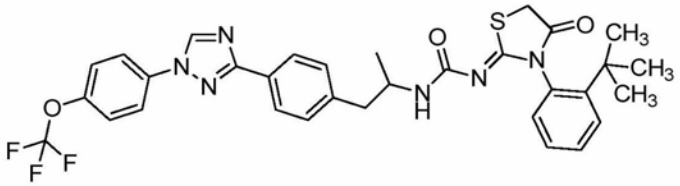
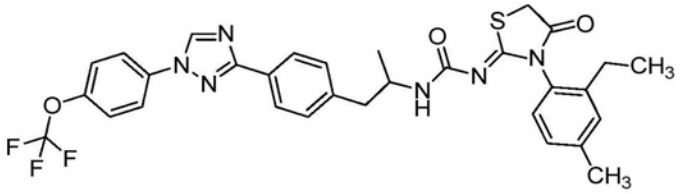
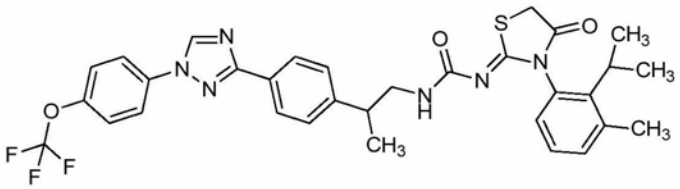
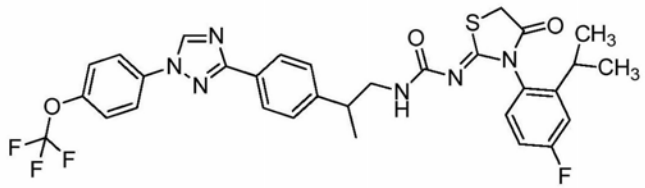
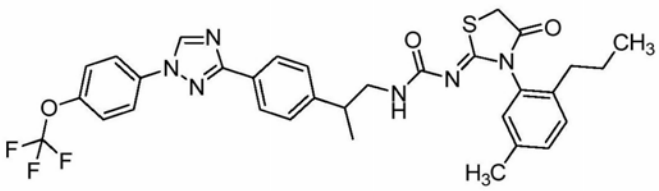
[1558]

P17	
P18	
P19	
P20	
P21	
P22	
P23	

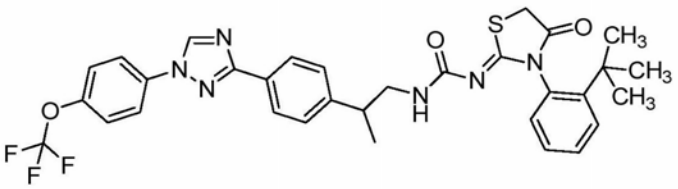
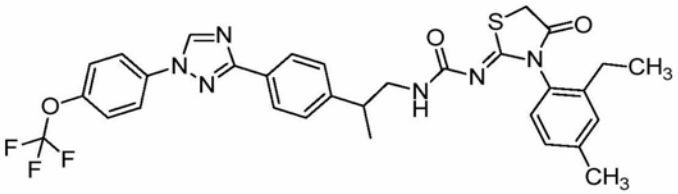
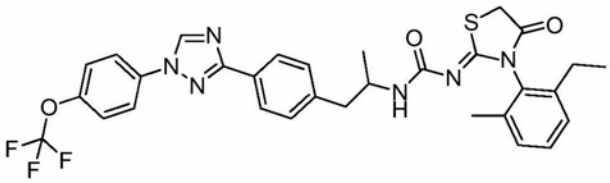
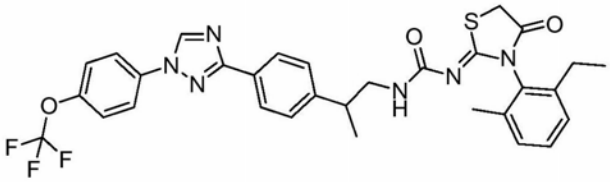
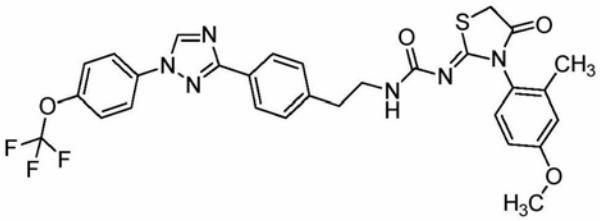
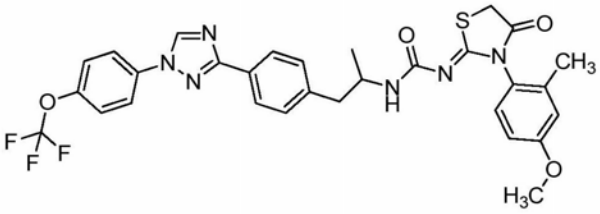
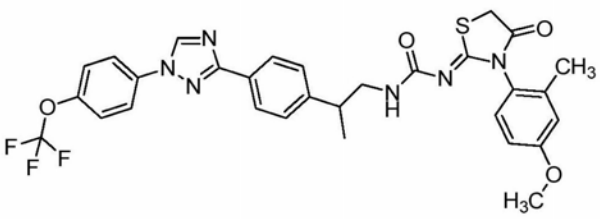
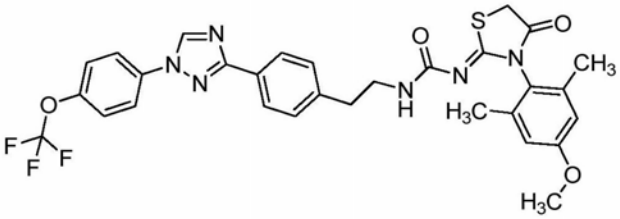
[1559]

P24	
P25	
P26	
P27	
P28	
P29	
P30	
P31	

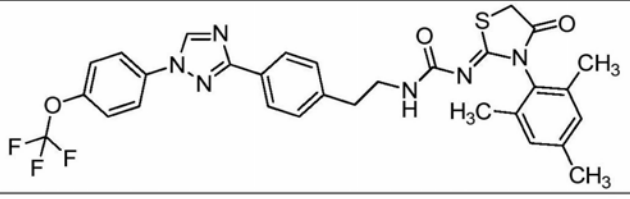
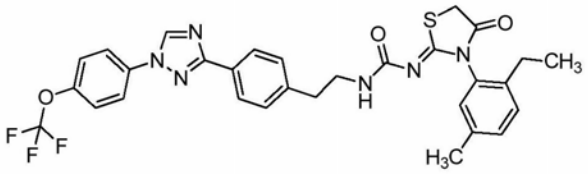
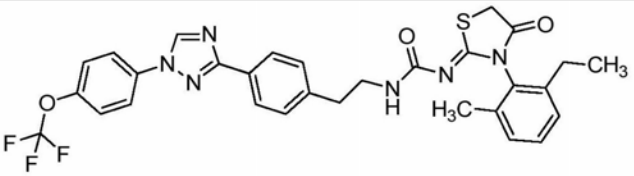
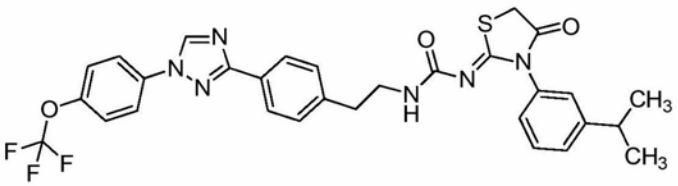
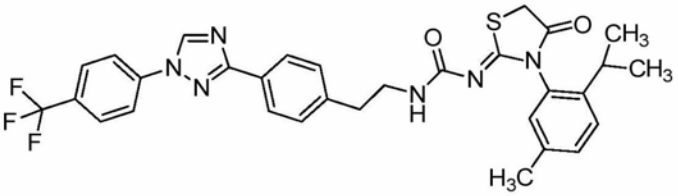
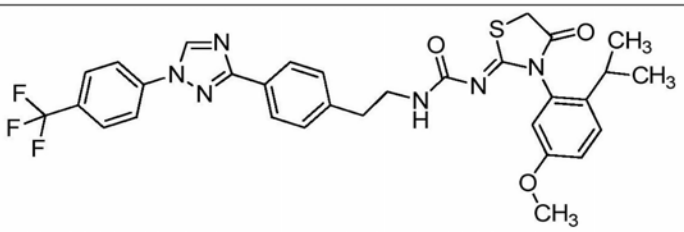
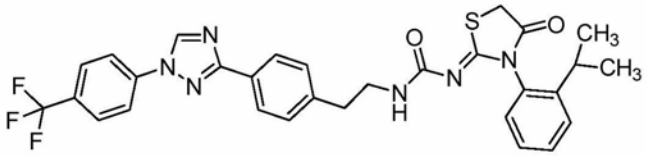
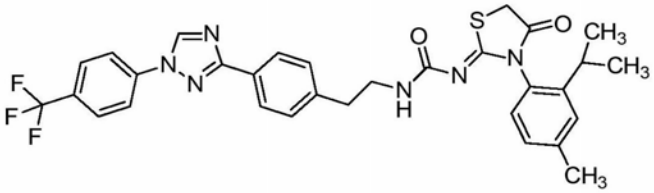
[1560]

P32	
P33	
P34	
P35	
P36	
P37	
P38	
P39	

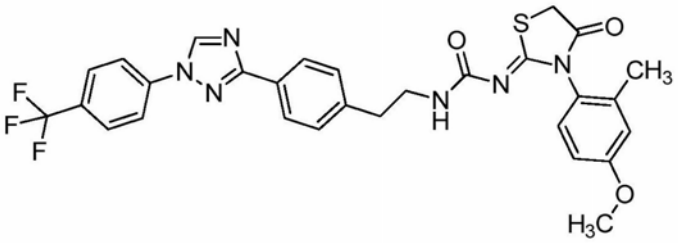
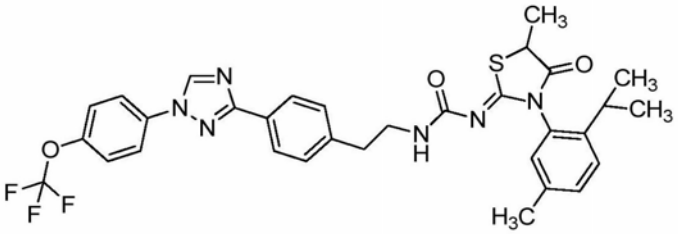
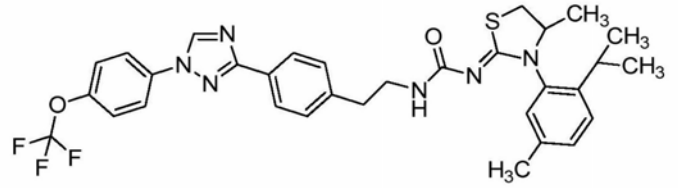
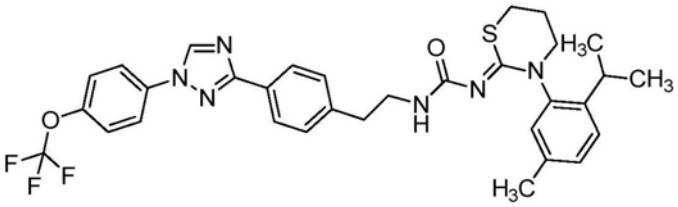
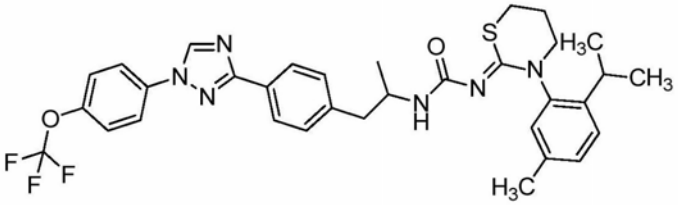
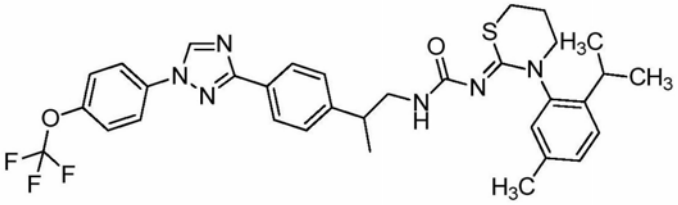
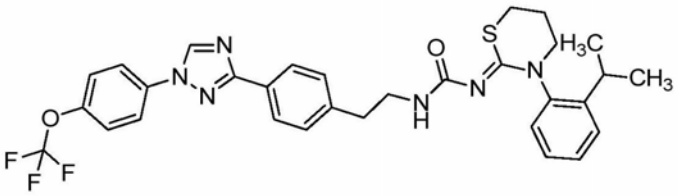
[1561]

P40	
P41	
P42	
P43	
P44	
P45	
P46	
P47	

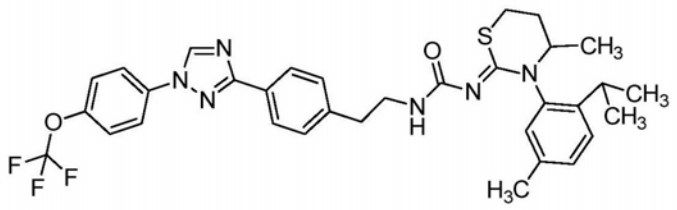
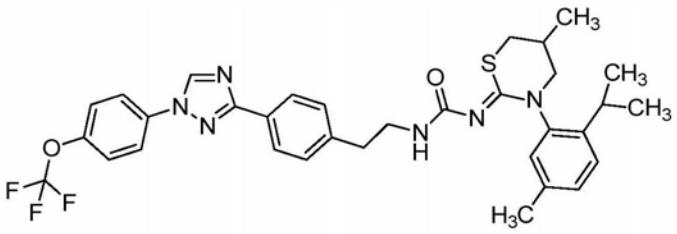
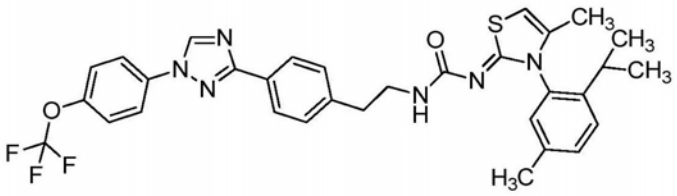
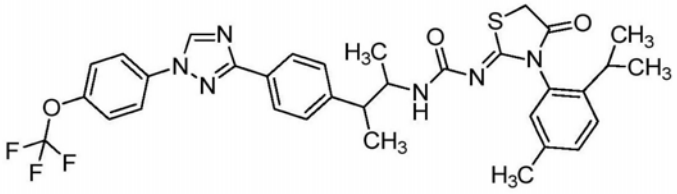
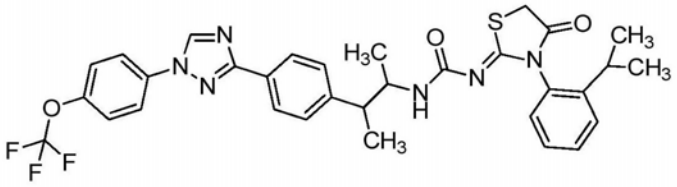
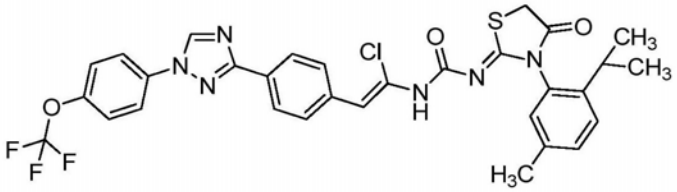
[1562]

P48	
P49	
P50	
P51	
P52	
P53	
P54	
P55	

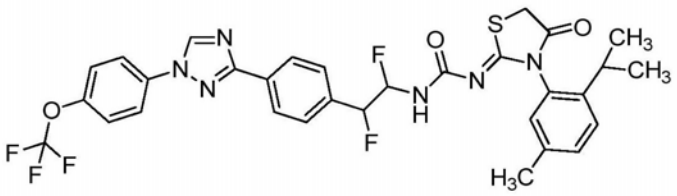
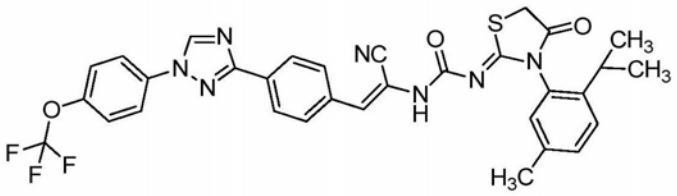
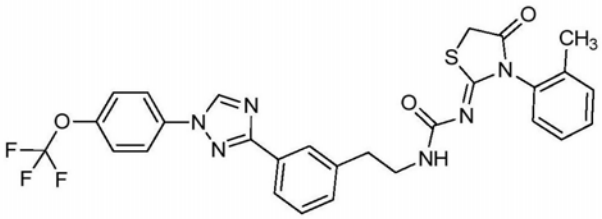
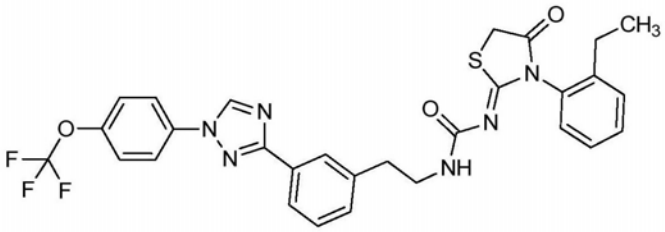
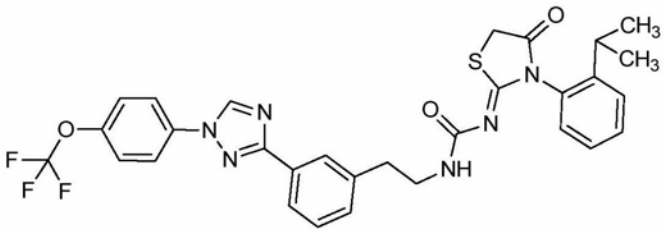
[1563]

P56	
P57	
P58	
P59	
P60	
P61	
P62	

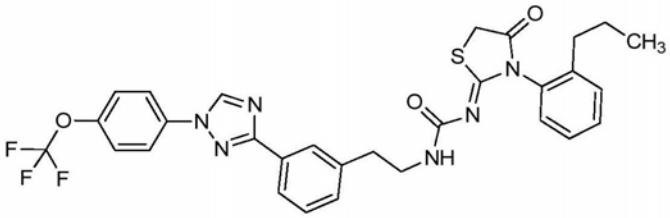
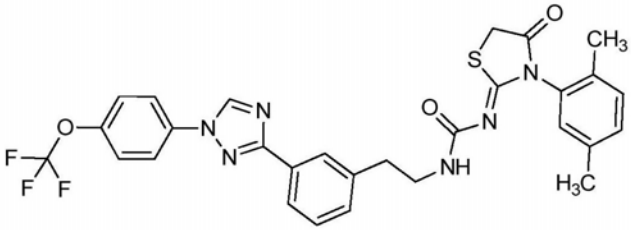
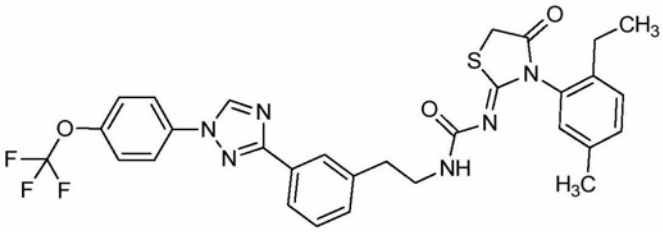
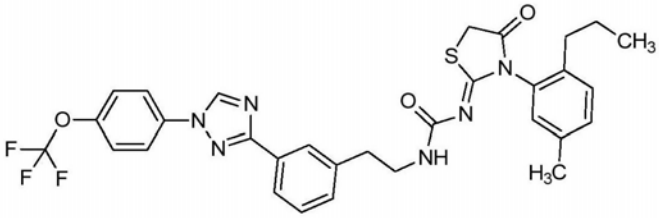
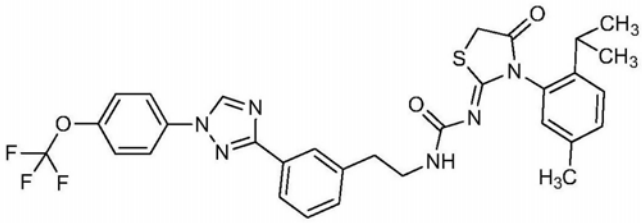
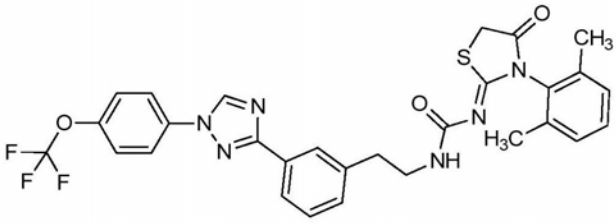
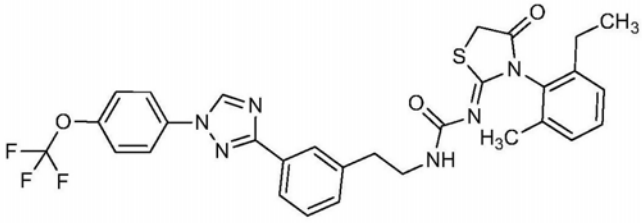
[1564]

P63	
P64	
P65	
P66	
P67	
P68	
P69	

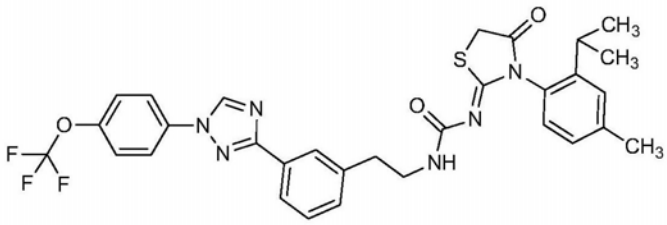
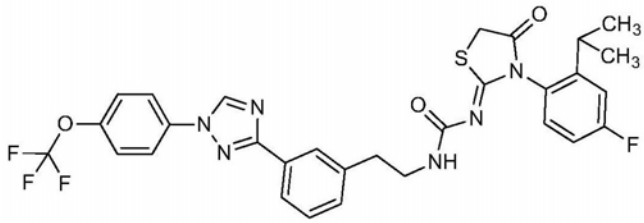
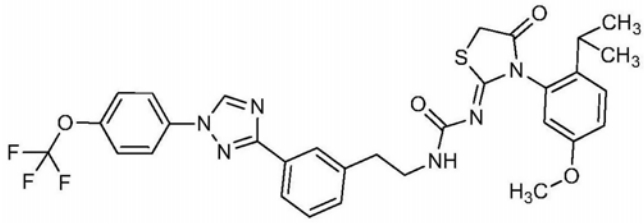
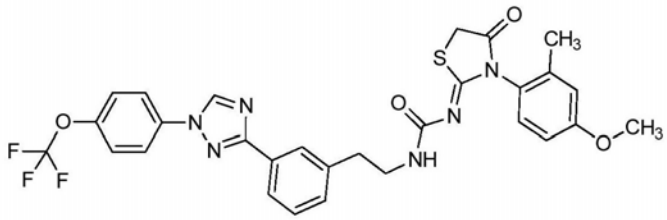
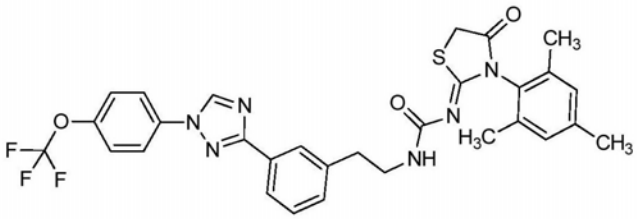
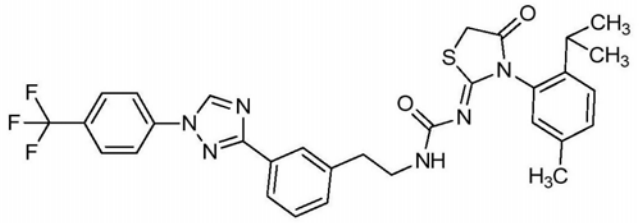
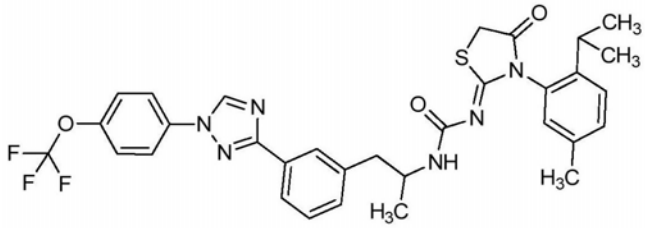
[1565]

P70	
P71	
P72	
P73	
P74	
P75	
P76	

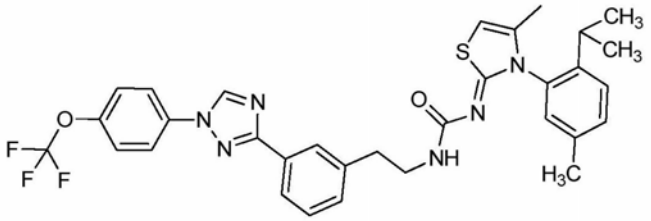
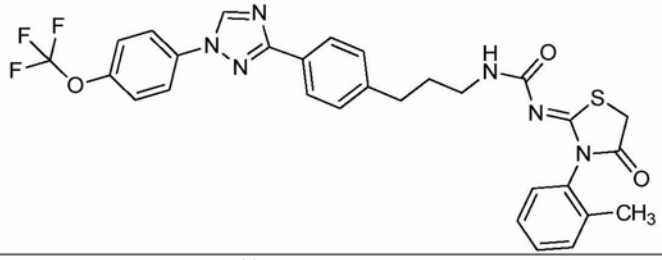
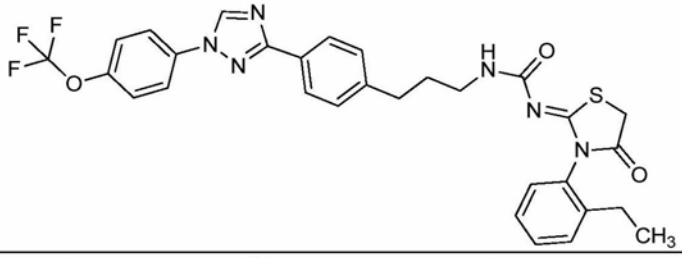
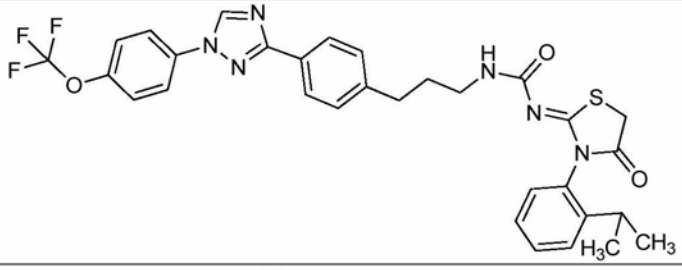
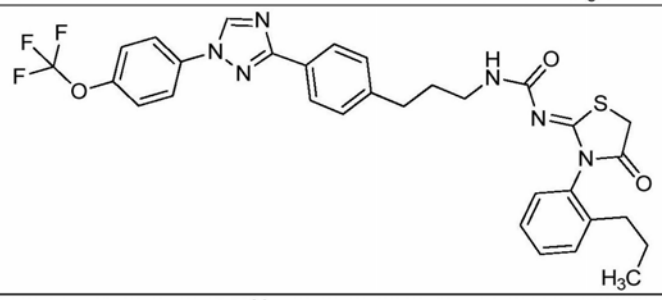
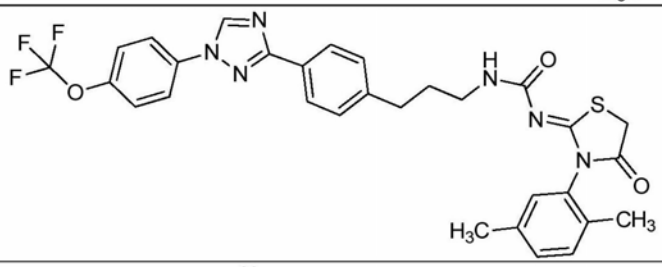
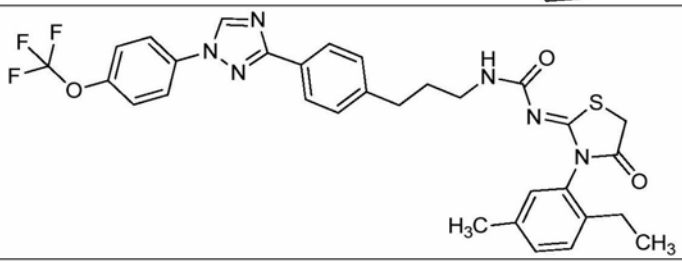
[1566]

P77	
P78	
P79	
P80	
P81	
P82	
P83	

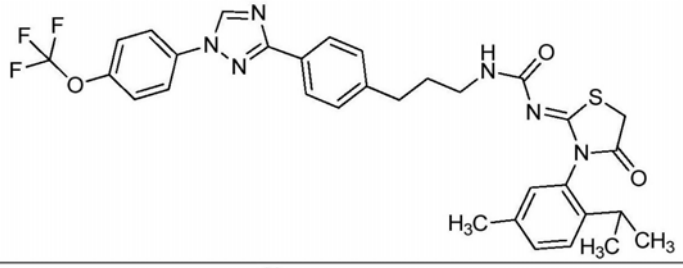
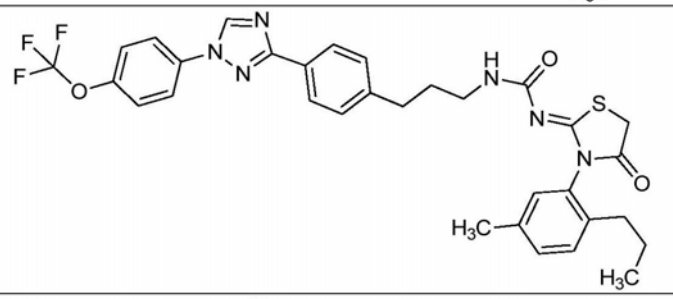
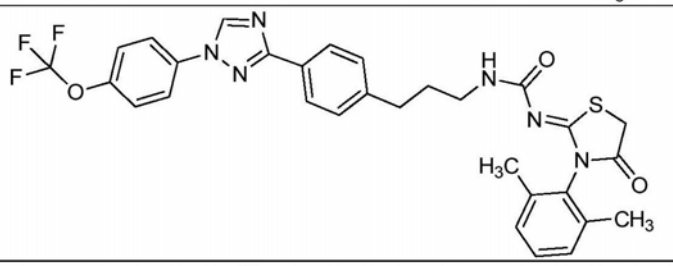
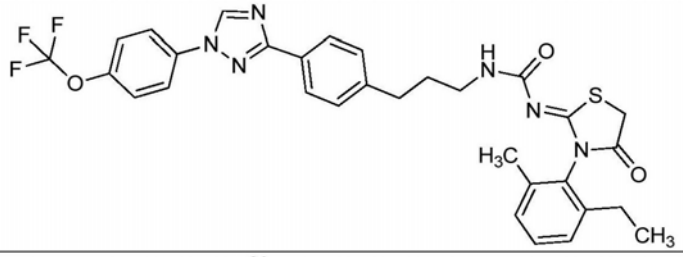
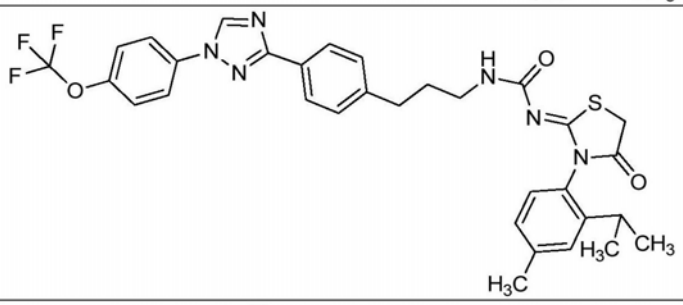
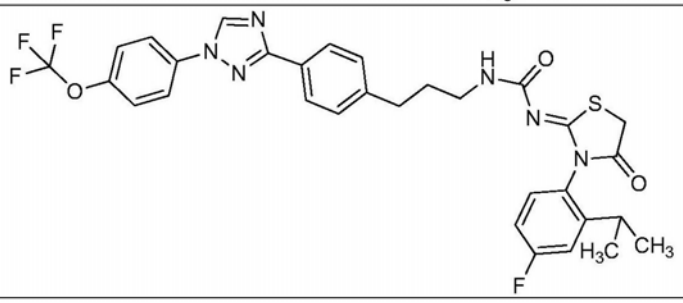
[1567]

P84	
P85	
P86	
P87	
P88	
P89	
P90	

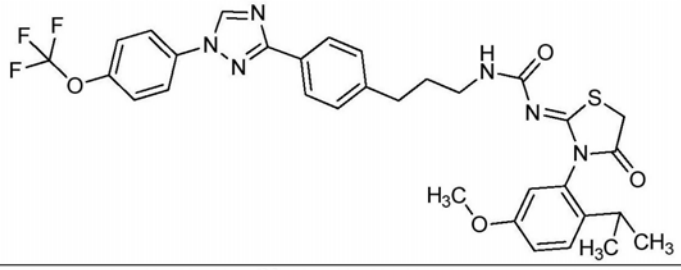
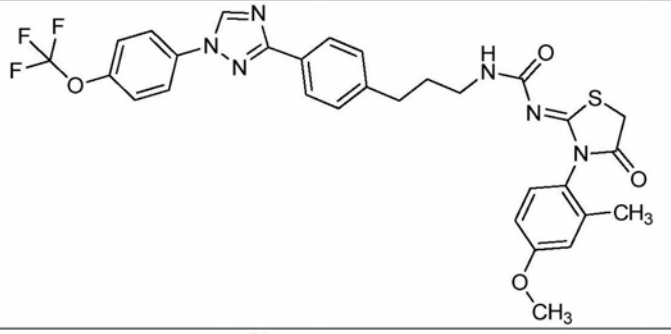
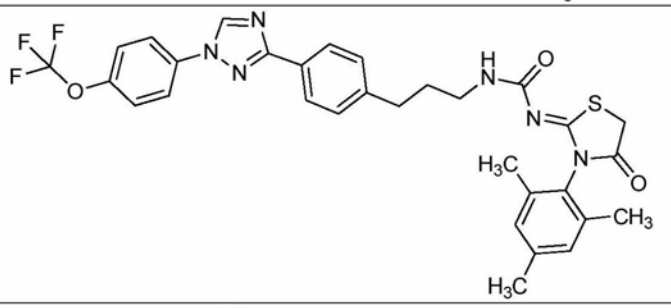
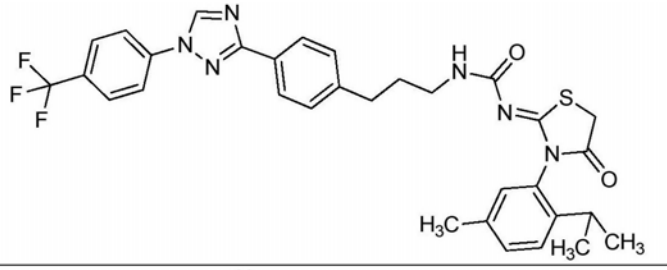
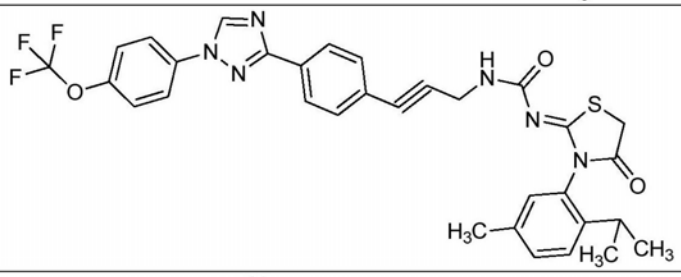
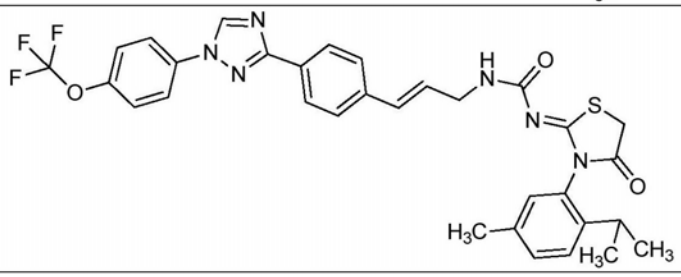
[1568]

P91	
P92	
P93	
P94	
P95	
P96	
P97	

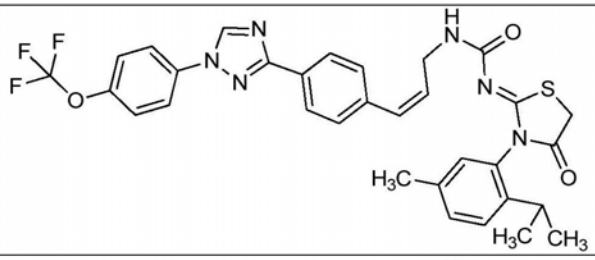
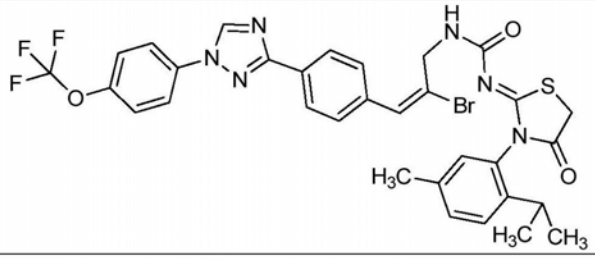
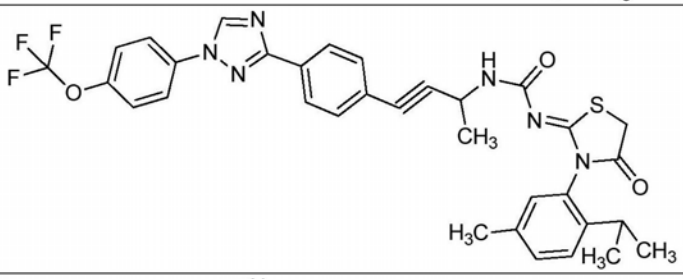
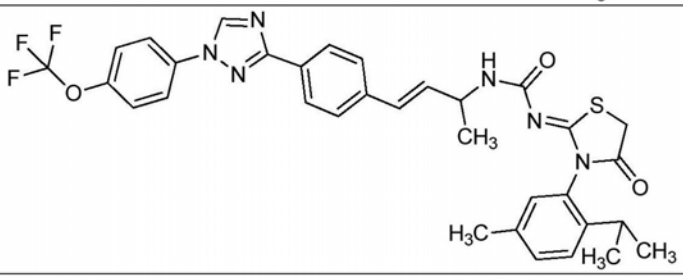
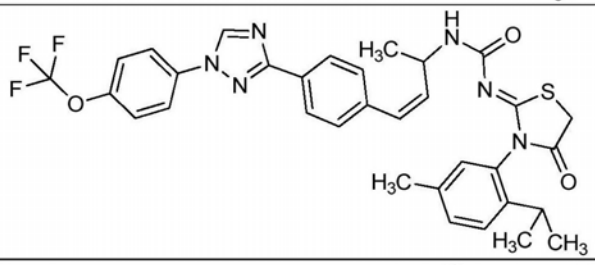
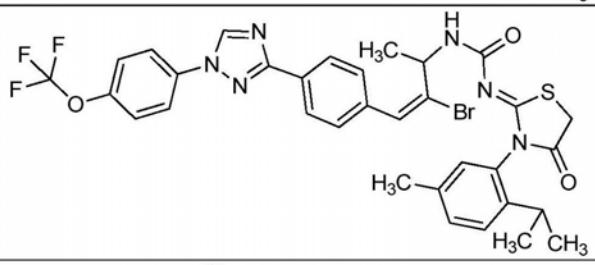
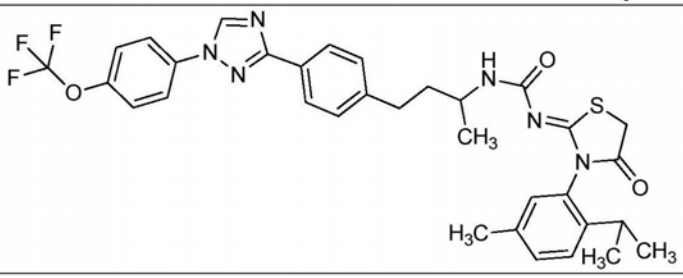
[1569]

P98	
P99	
P100	
P101	
P102	
P103	

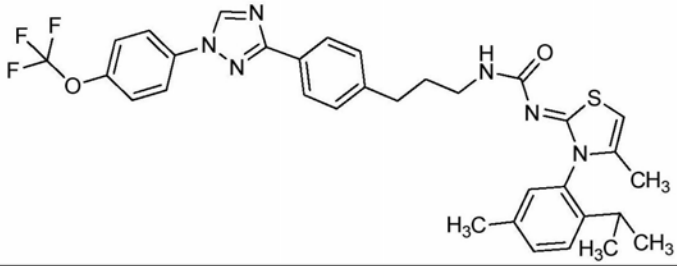
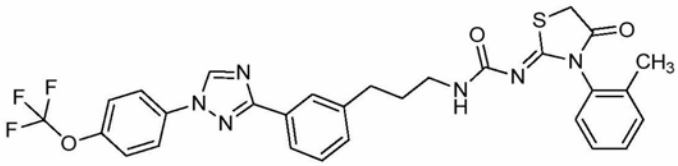
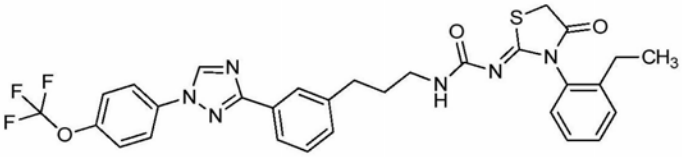
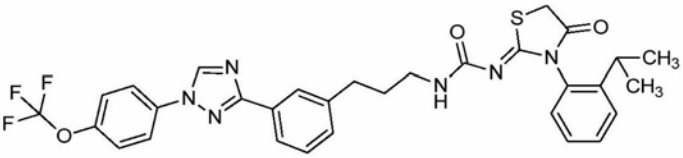
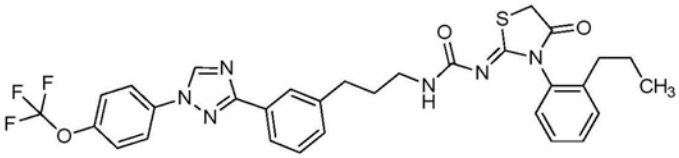
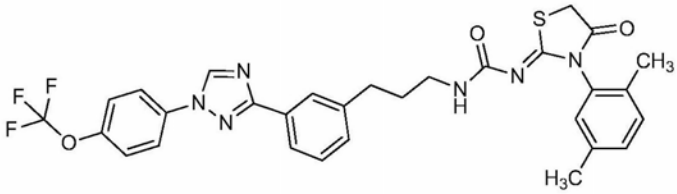
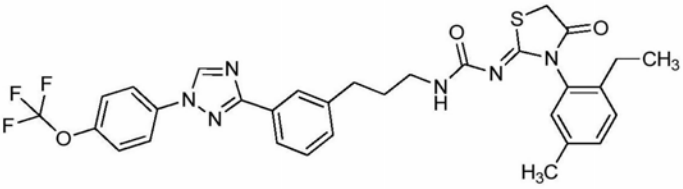
[1570]

P104	
P105	
P106	
P107	
P108	
P109	

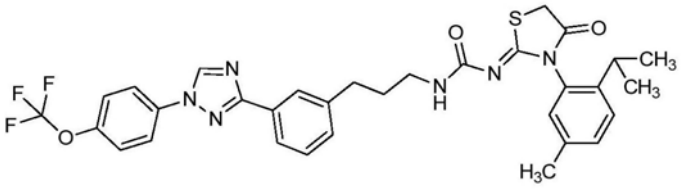
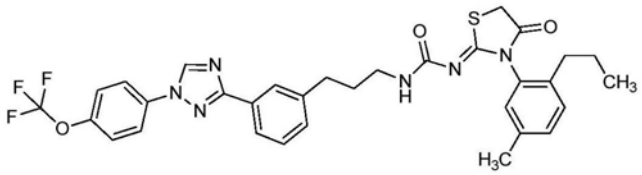
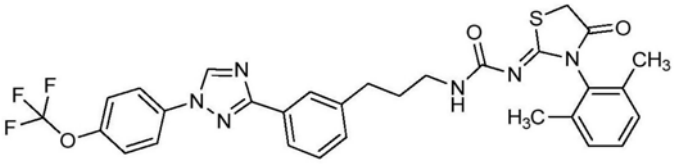
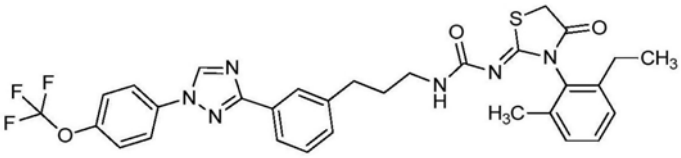
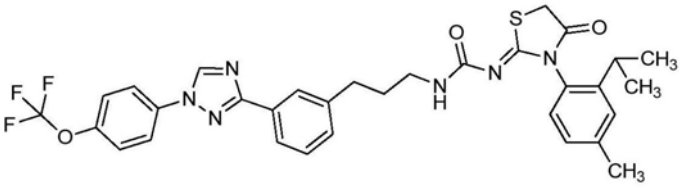
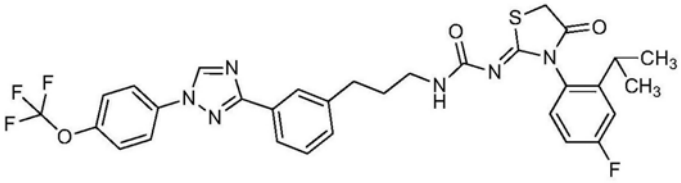
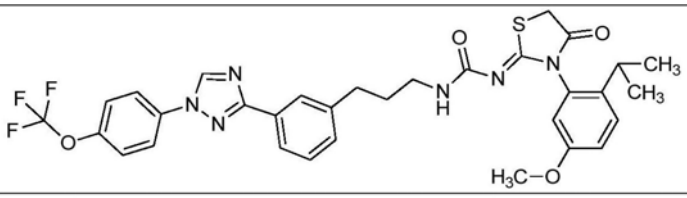
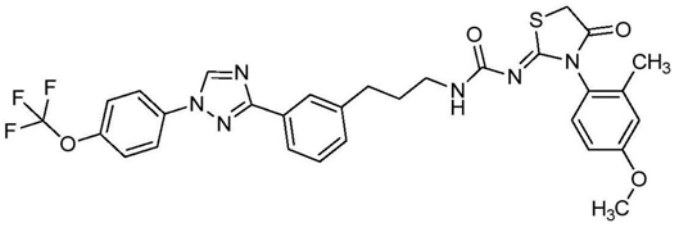
[1571]

P110	
P111	
P112	
P113	
P114	
P115	
P116	

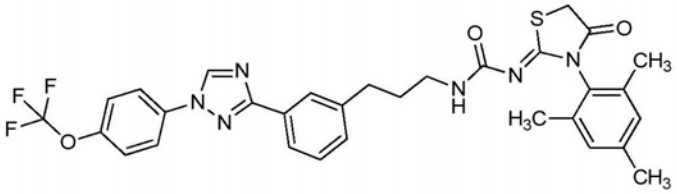
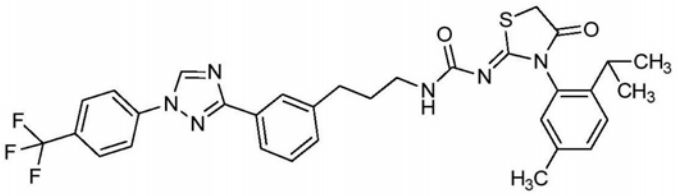
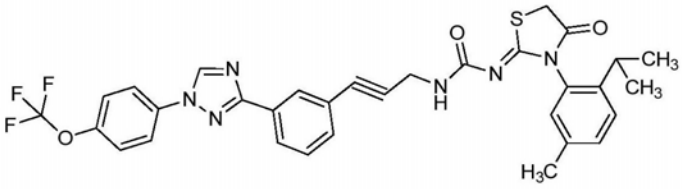
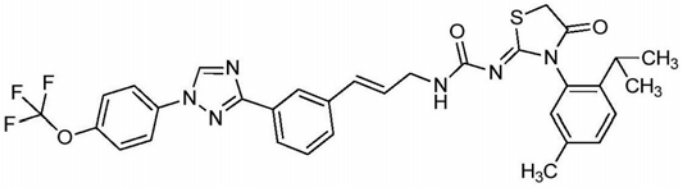
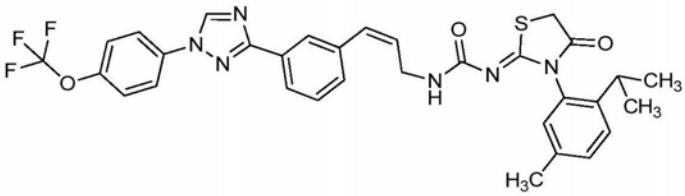
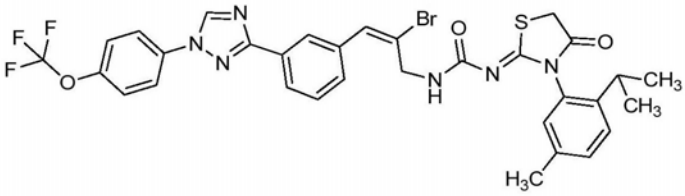
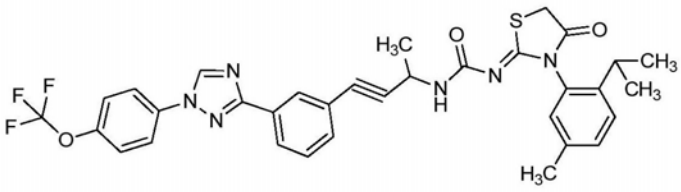
[1572]

P117	
P118	
P119	
P120	
P121	
P122	
P123	

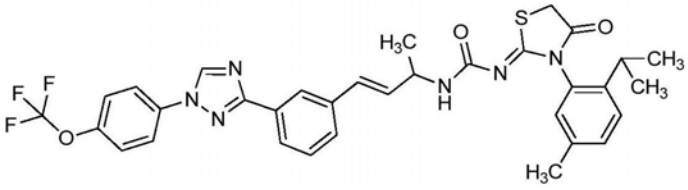
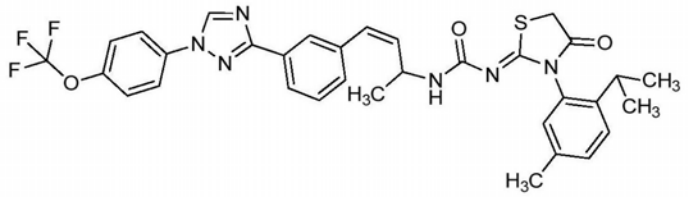
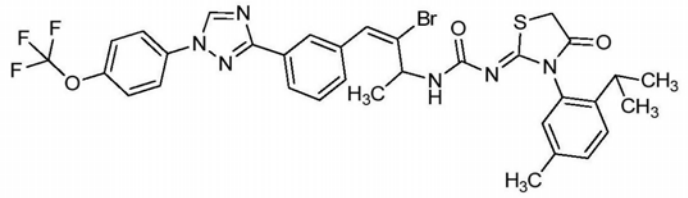
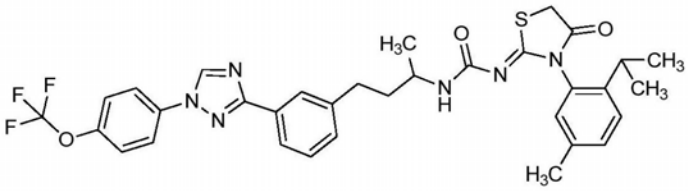
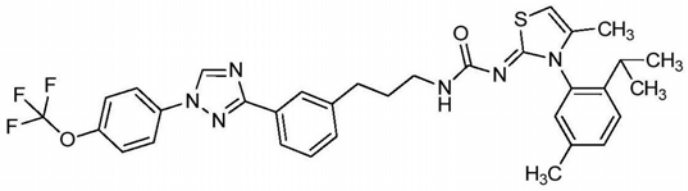
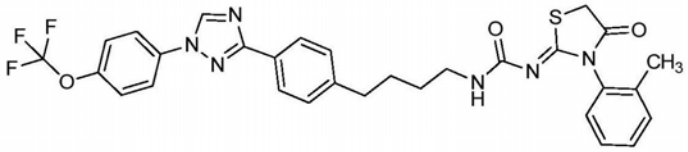
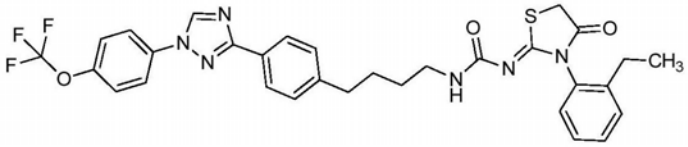
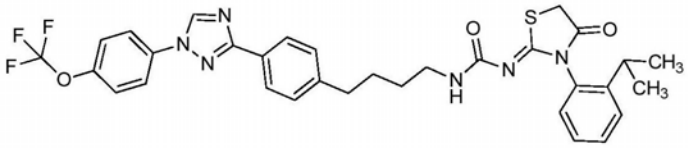
[1573]

P124	
P125	
P126	
P127	
P128	
P129	
P130	
P131	

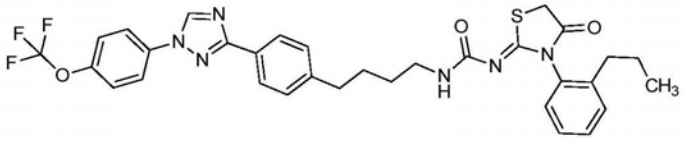
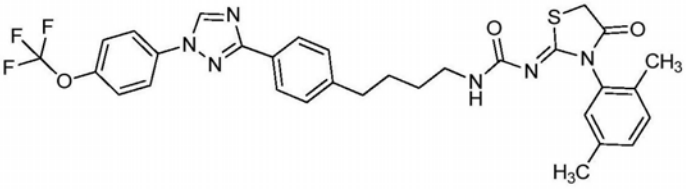
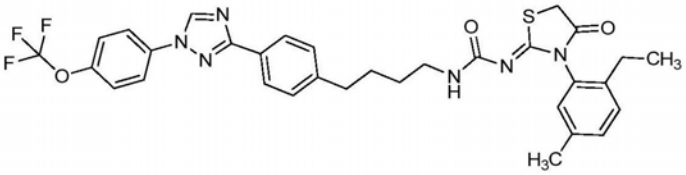
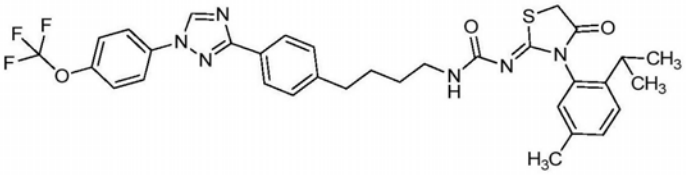
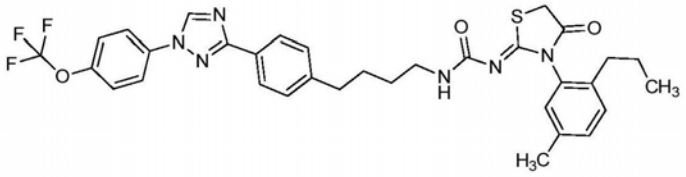
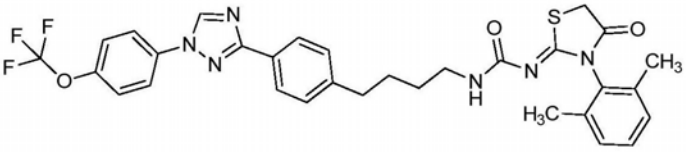
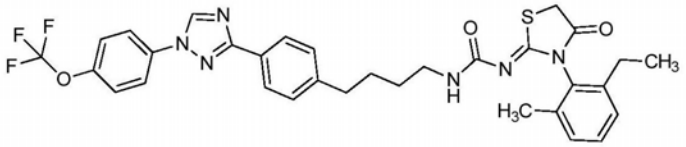
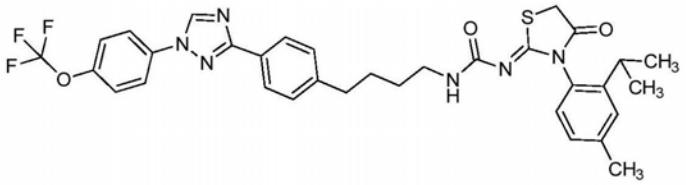
[1574]

P132	
P133	
P134	
P135	
P136	
P137	
P138	

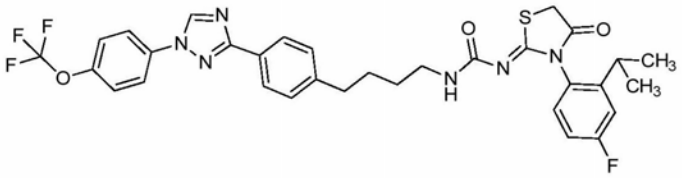
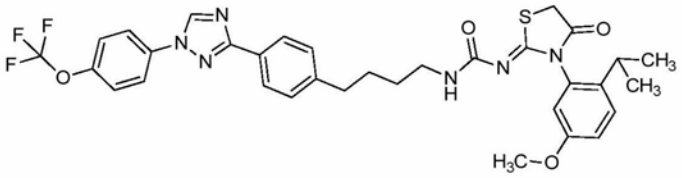
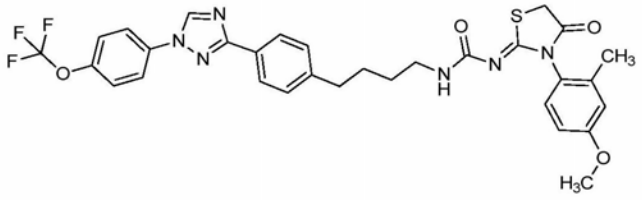
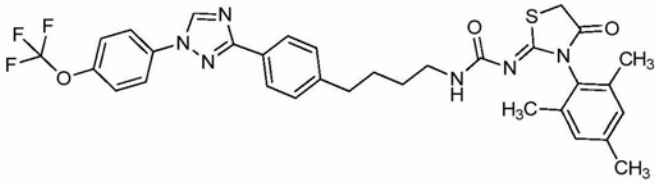
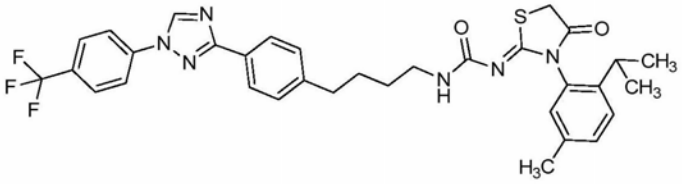
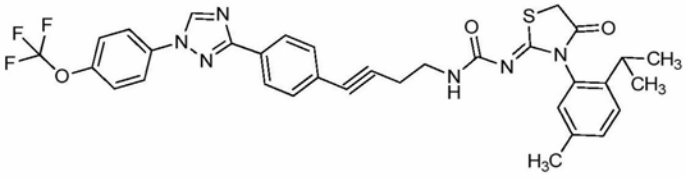
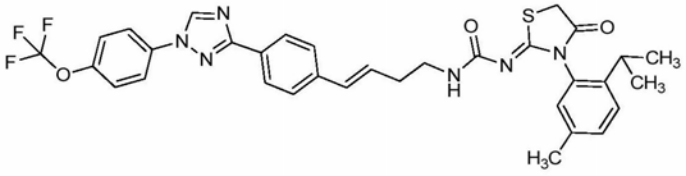
[1575]

P139	
P140	
P141	
P142	
P143	
P144	
P145	
P146	

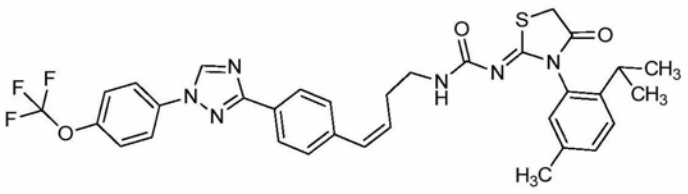
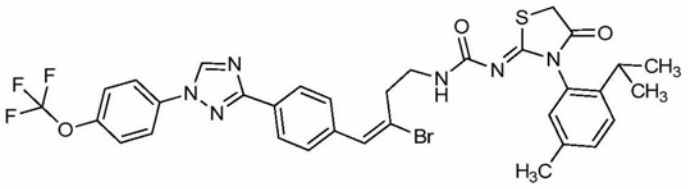
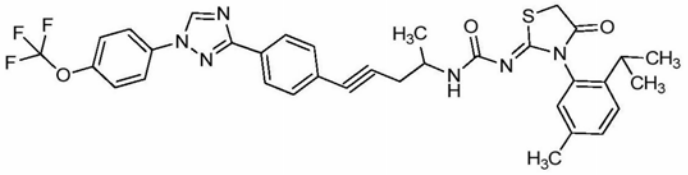
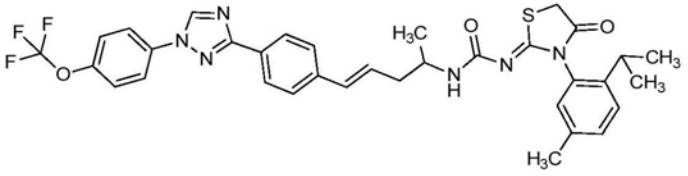
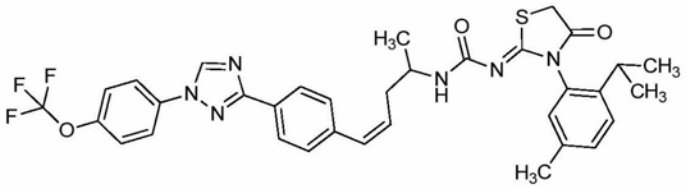
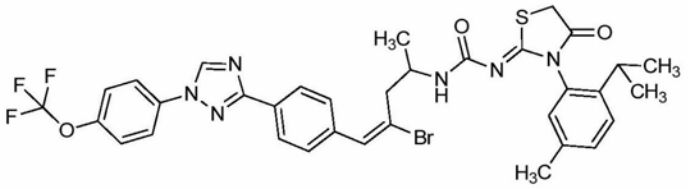
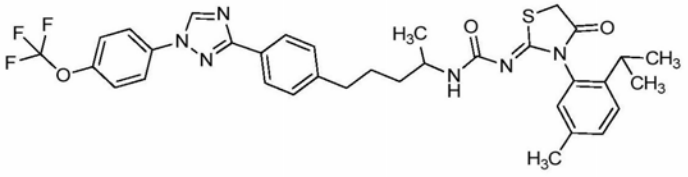
[1576]

P147	
P148	
P149	
P150	
P151	
P152	
P153	
P154	

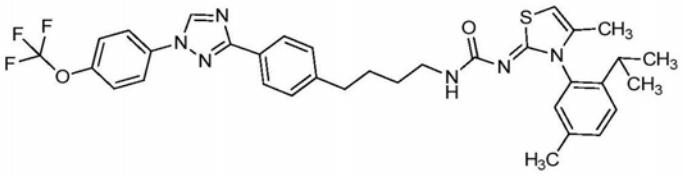
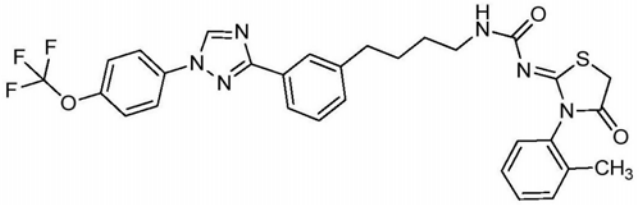
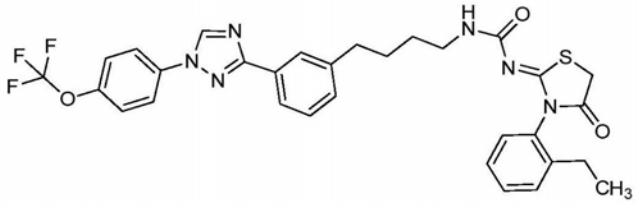
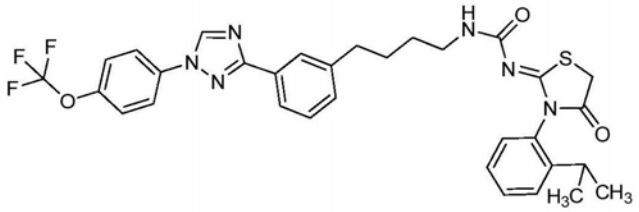
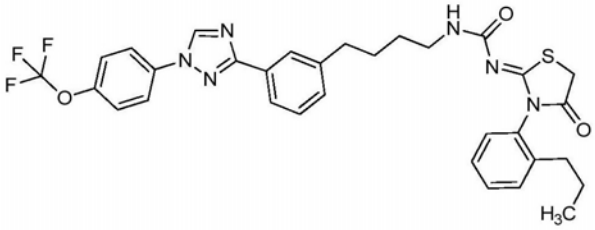
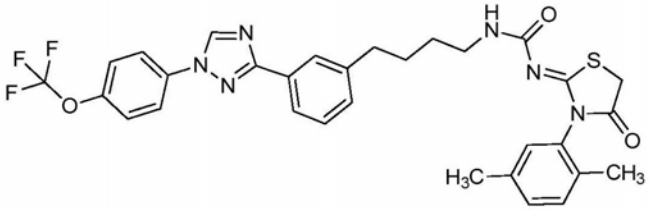
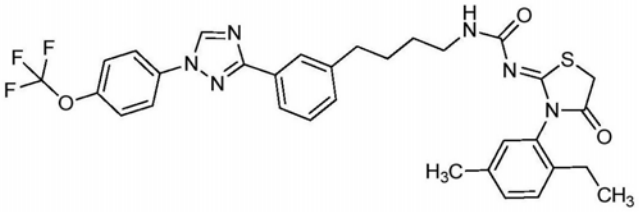
[1577]

P155	
P156	
P157	
P158	
P159	
P160	
P161	

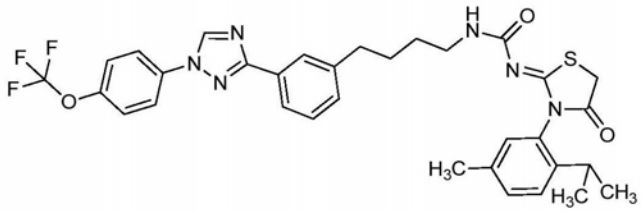
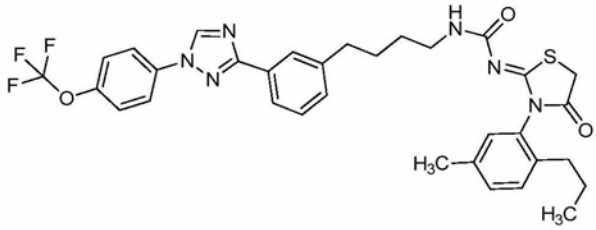
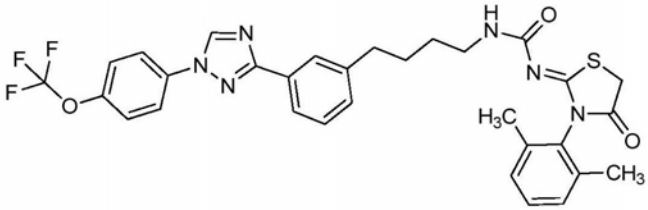
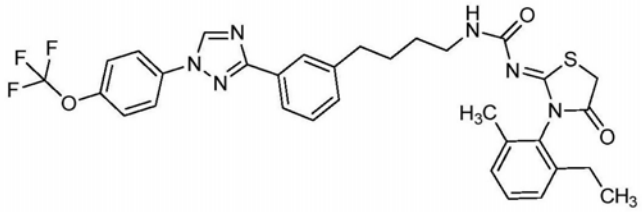
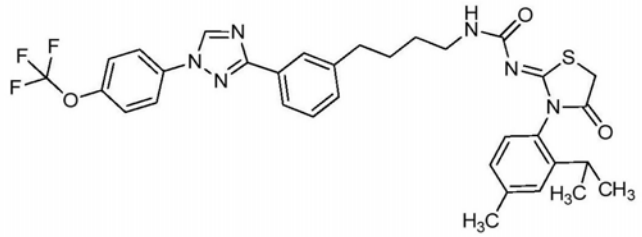
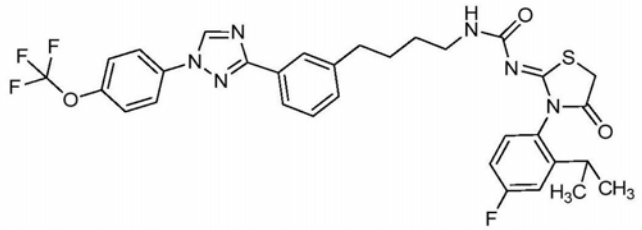
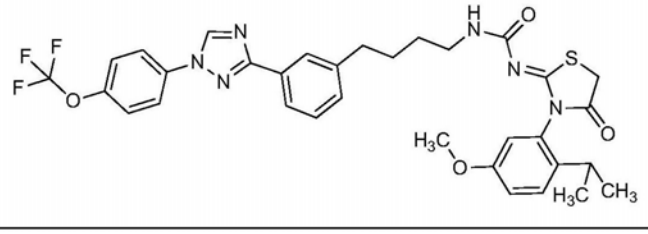
[1578]

P162	
P163	
P164	
P165	
P166	
P167	
P168	

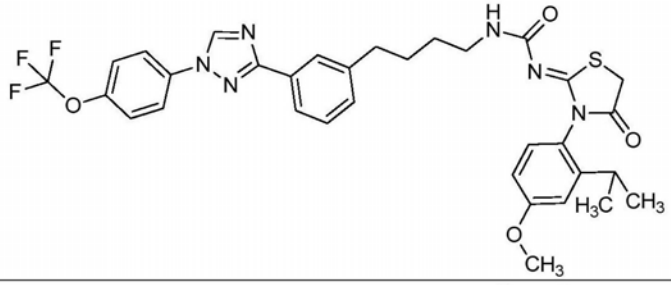
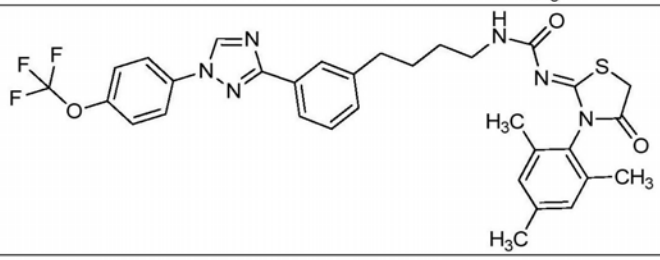
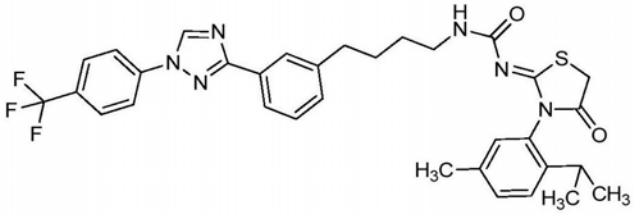
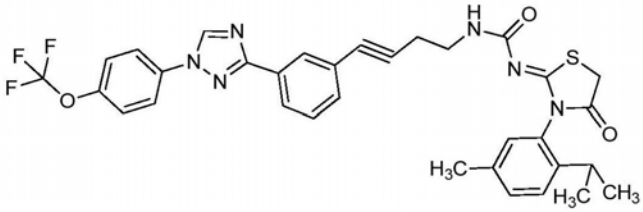
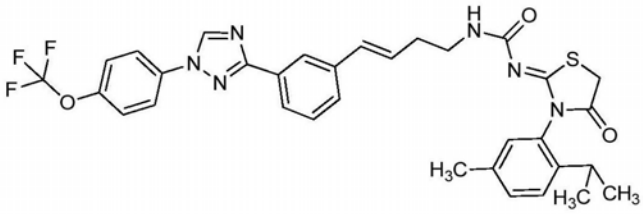
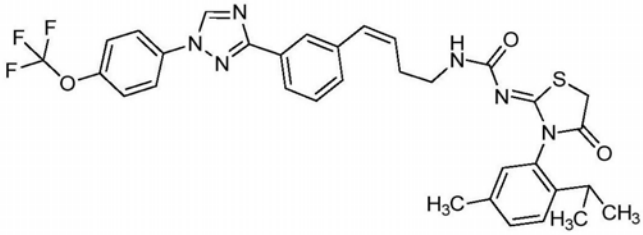
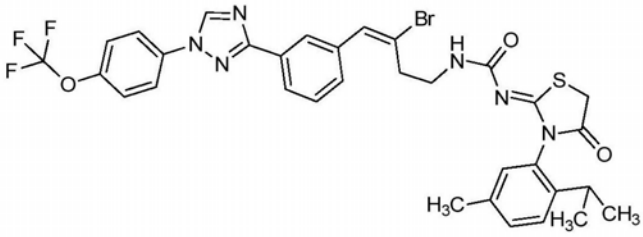
[1579]

P169	
P170	
P171	
P172	
P173	
P174	
P175	

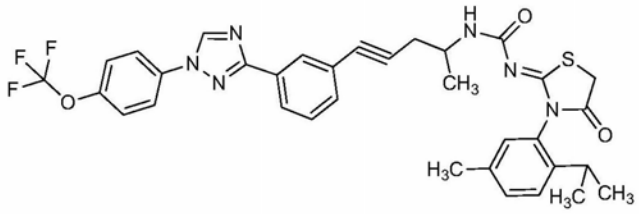
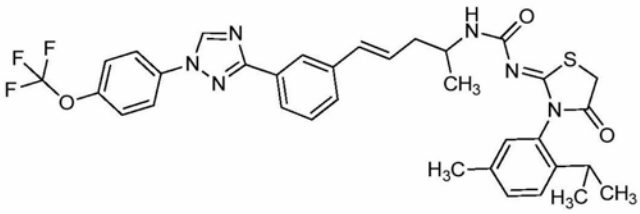
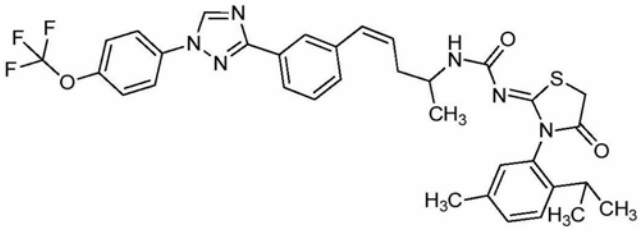
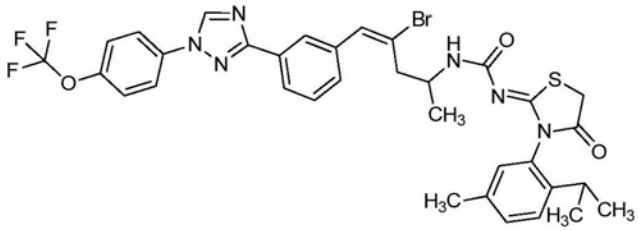
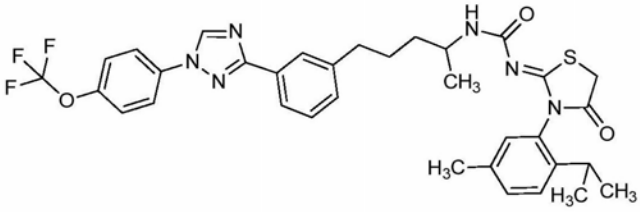
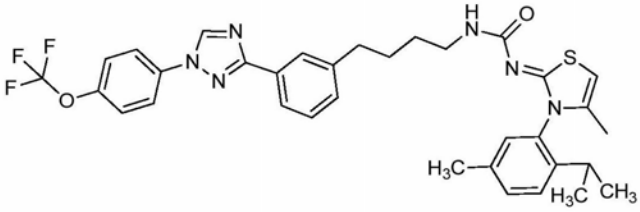
[1580]

P176	
P177	
P178	
P179	
P180	
P181	
P182	

[1581]

P183	
P184	
P185	
P186	
P187	
P188	
P189	

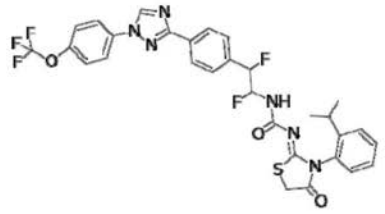
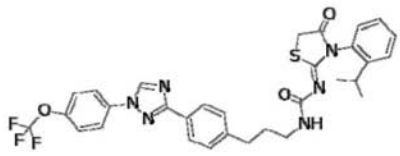
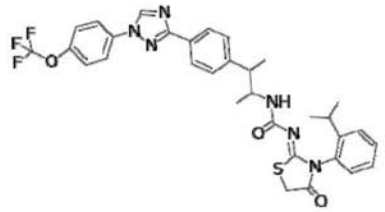
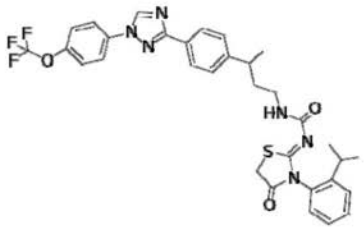
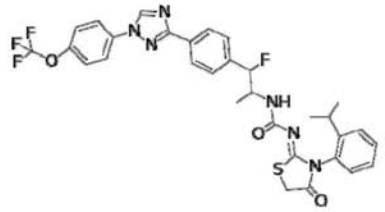
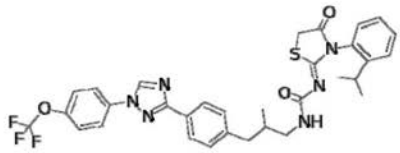
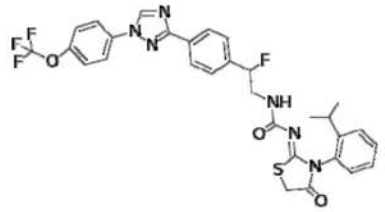
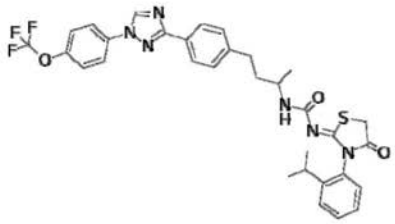
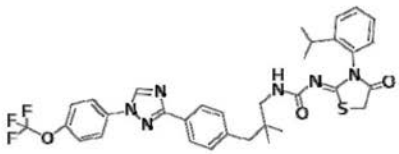
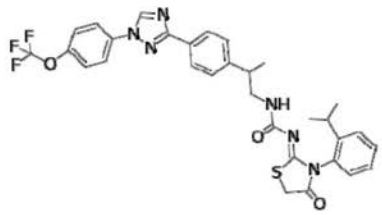
[1582]

190	
P191	
P192	
P193	
P194	
P195	

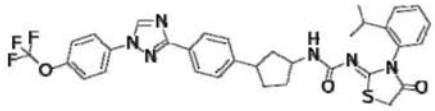
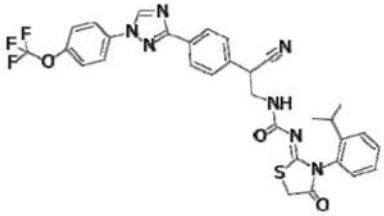
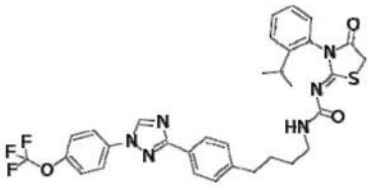
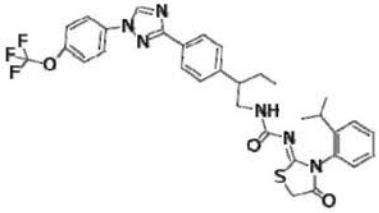
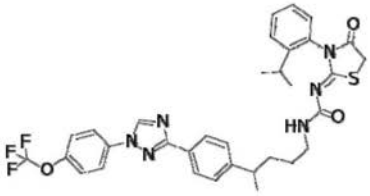
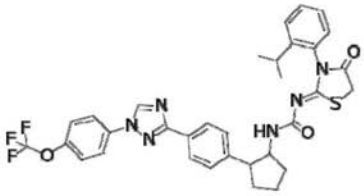
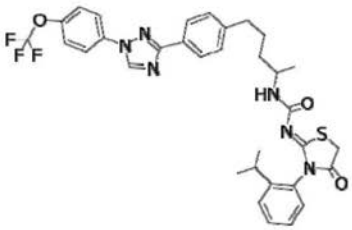
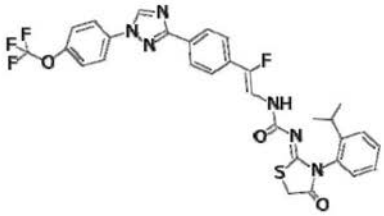
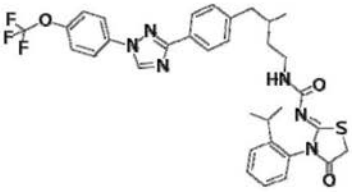
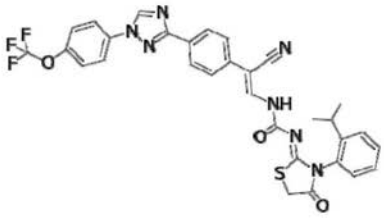
[1583] 另外，使用本文披露的步骤，可以制备下列预料到的具有根据式一的结构的分子(表P-Ⅱ)。

[1584] P-Ⅱ

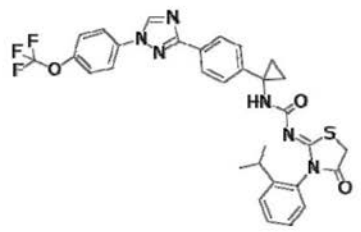
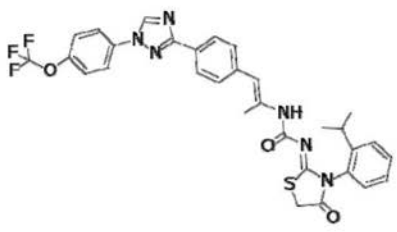
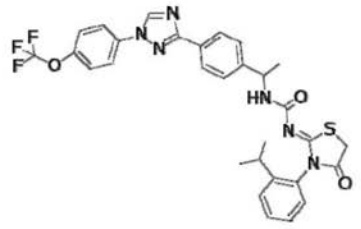
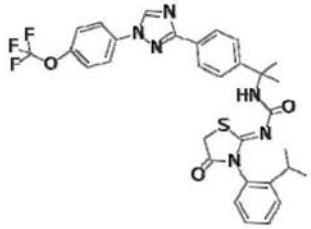
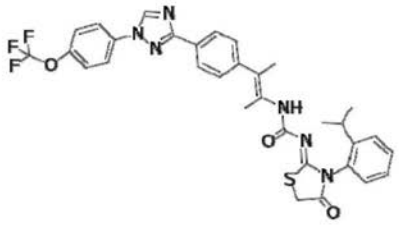
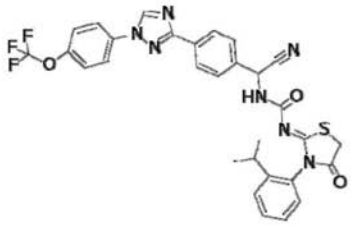
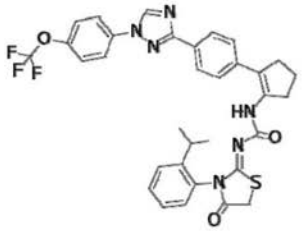
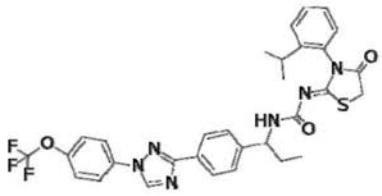
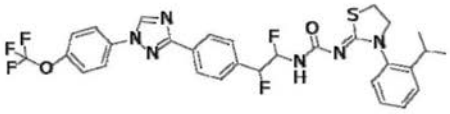
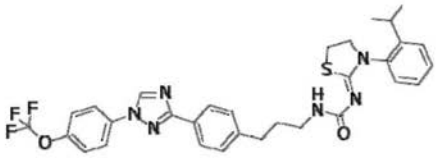
[1585]

 P196	 P197
 P198	 P199
 P200	 P201
 P202	 P203
 P204	 P205

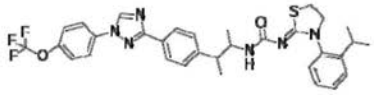
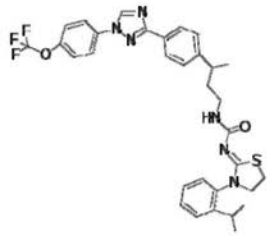
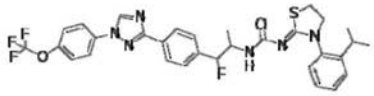
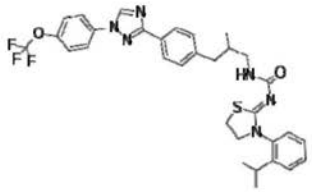
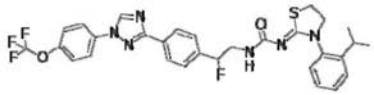
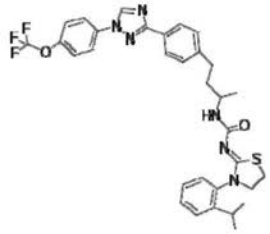
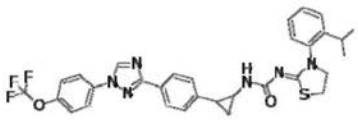
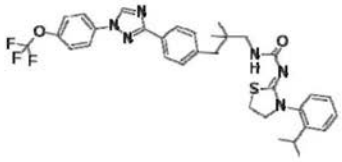
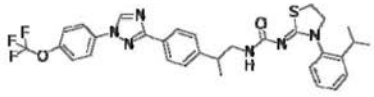
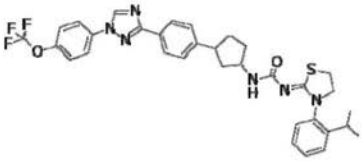
[1586]

 P206	 P207
 P208	 P209
 P210	 P211
 P212	 P213
 P214	 P215

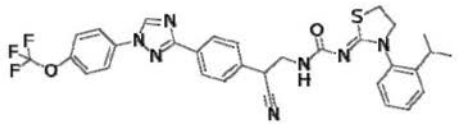
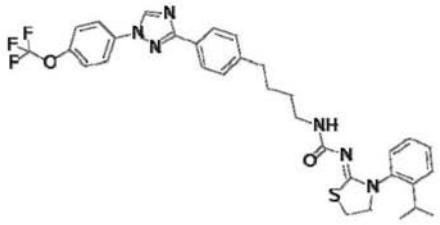
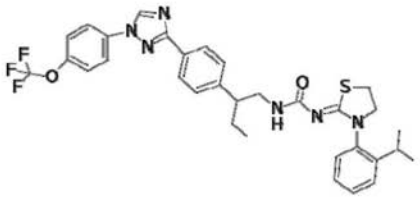
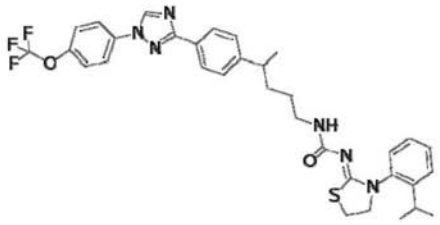
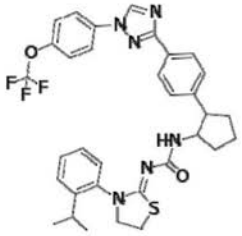
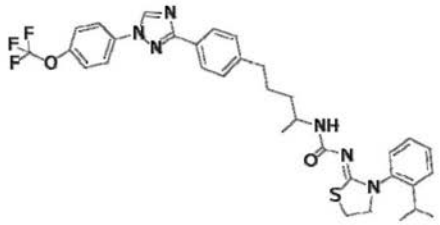
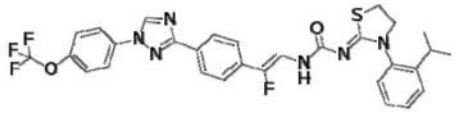
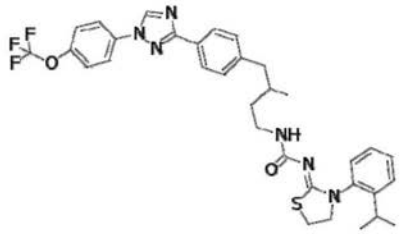
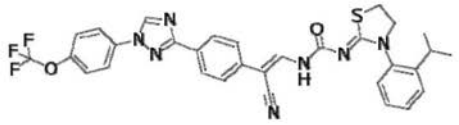
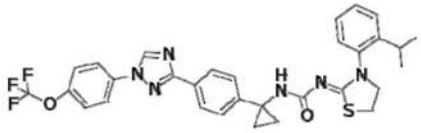
[1587]

 P216	 P217
 P218	 P219
 P220	 P221
 P222	 P223
 P224	 P225

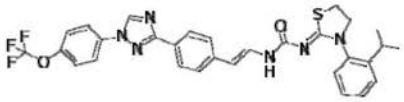
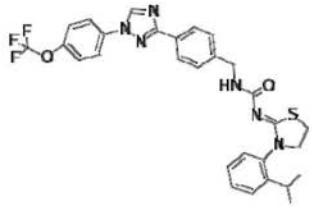
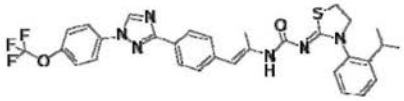
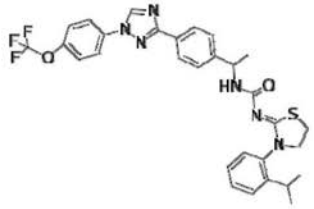
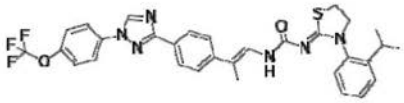
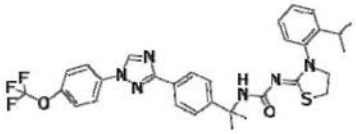
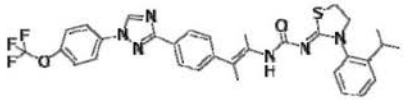
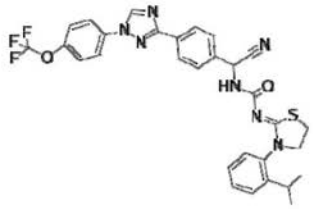
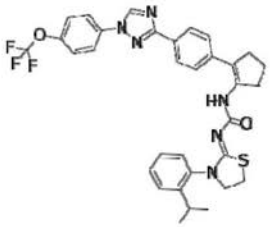
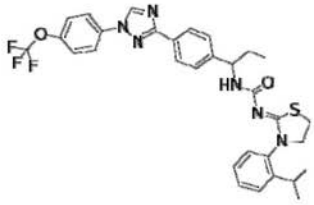
[1588]

 P226	 P227
 P228	 P229
 P230	 P231
 P232	 P233
 P234	 P235

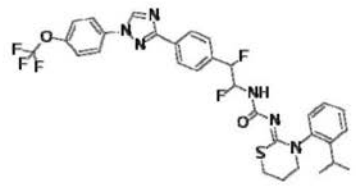
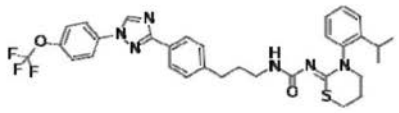
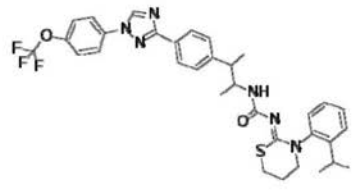
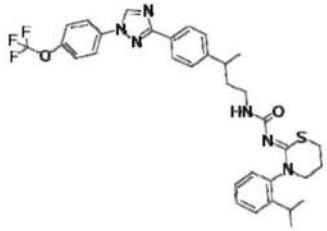
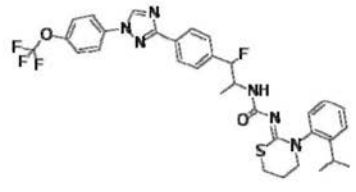
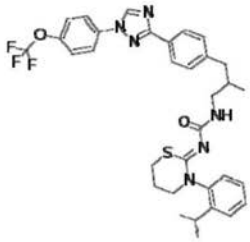
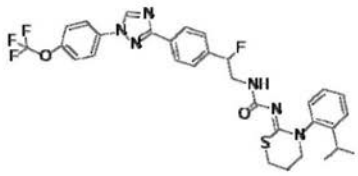
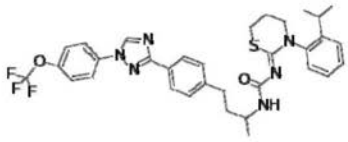
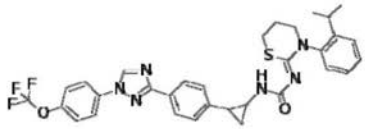
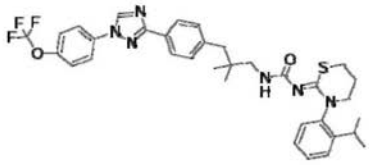
[1589]

 P236	 P237
 P238	 P239
 P240	 P241
 P242	 P243
 P244	 P245

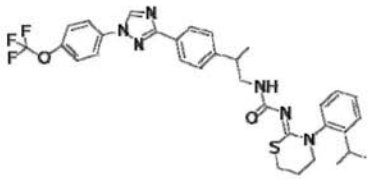
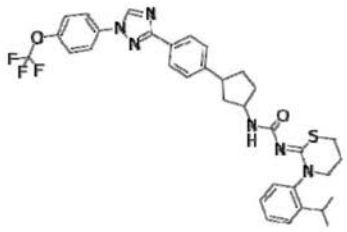
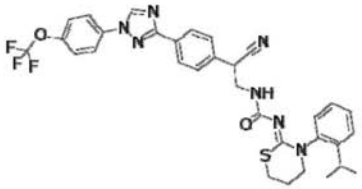
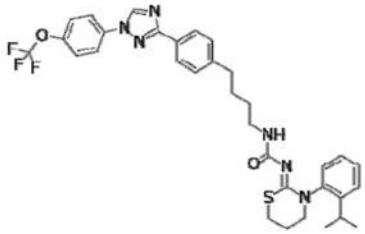
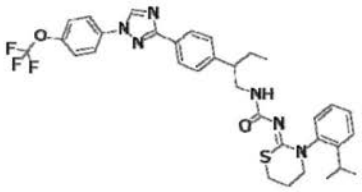
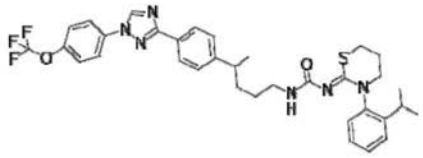
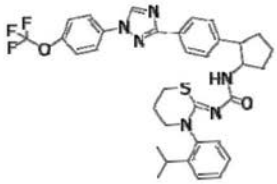
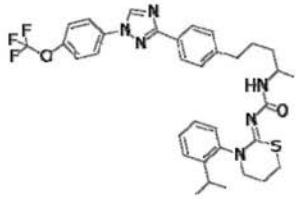
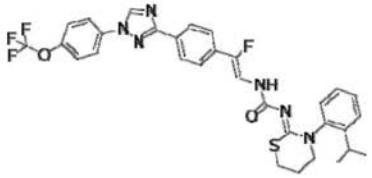
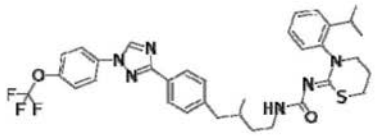
[1590]

 P246	 P247
 P248	 P249
 P250	 P251
 P252	 P253
 P254	 P255

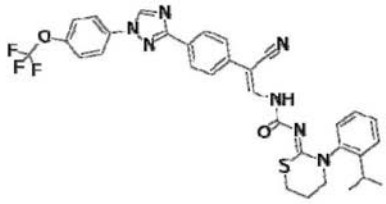
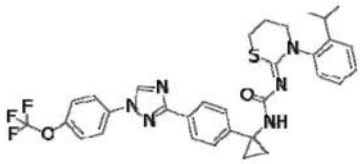
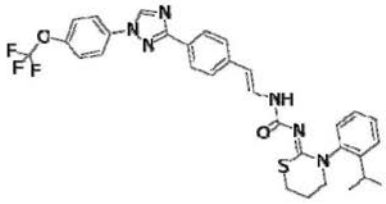
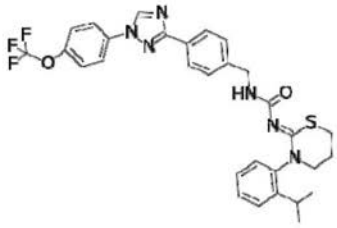
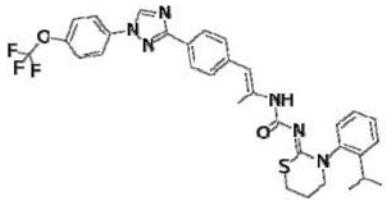
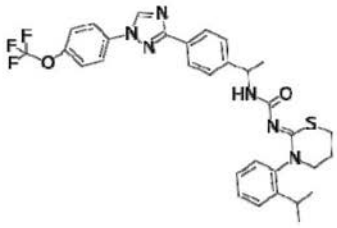
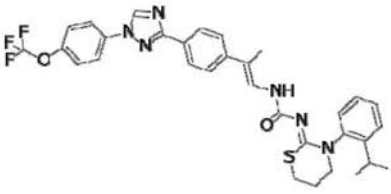
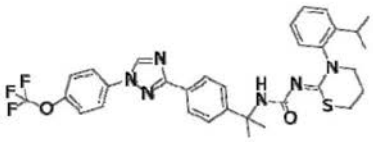
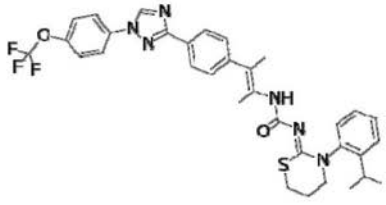
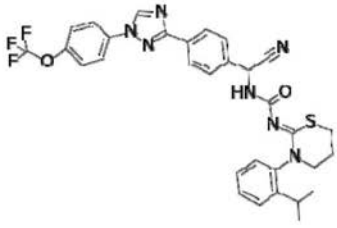
[1591]

 P256	 P257
 P258	 P259
 P260	 P261
 P262	 P263
 P264	 P265

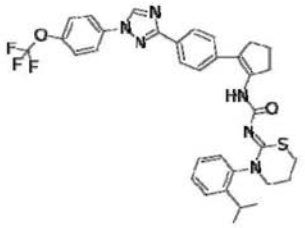
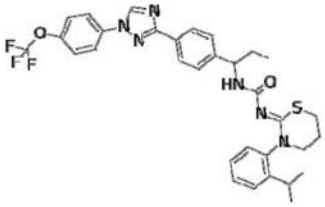
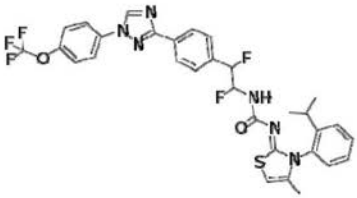
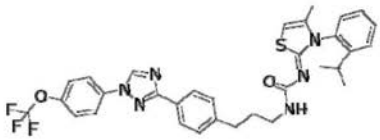
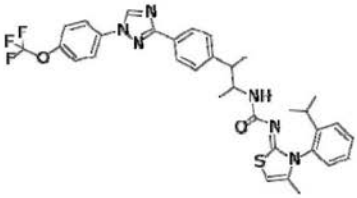
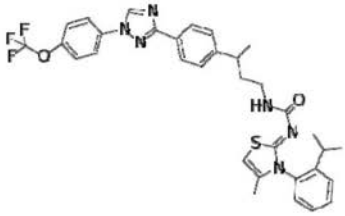
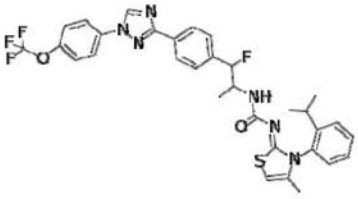
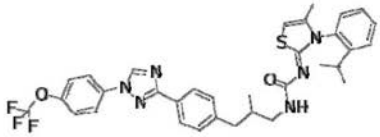
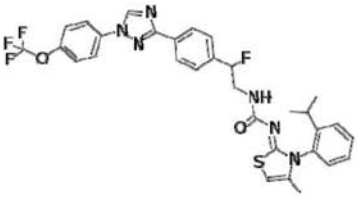
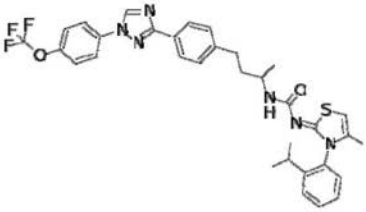
[1592]

 P266	 P267
 P268	 P269
 P270	 P271
 P272	 P273
 P274	 P275

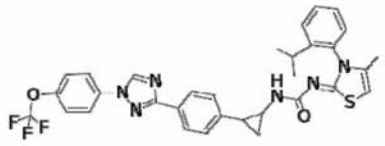
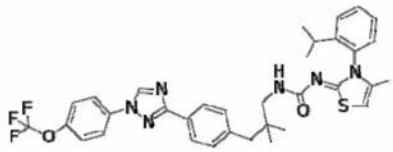
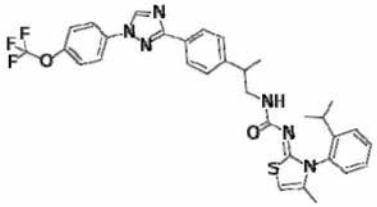
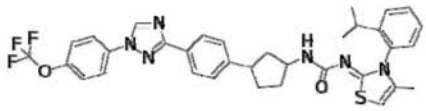
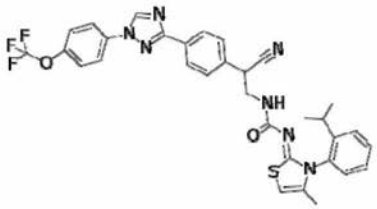
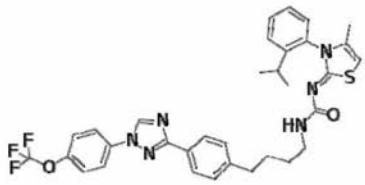
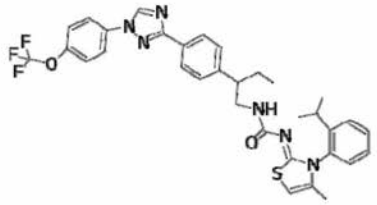
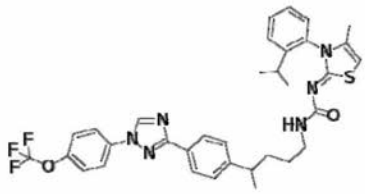
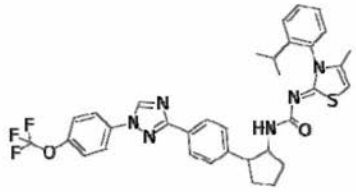
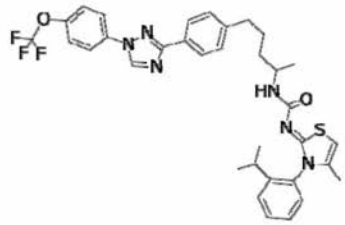
[1593]

 P276	 P277
 P278	 P279
 P280	 P281
 P282	 P283
 P284	 P285

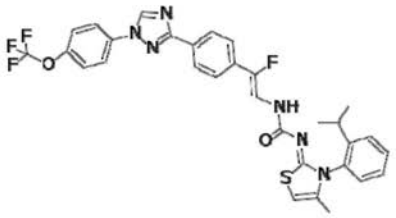
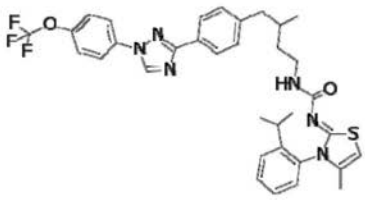
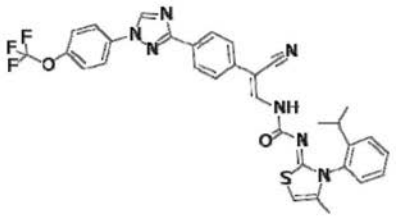
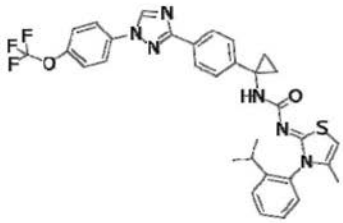
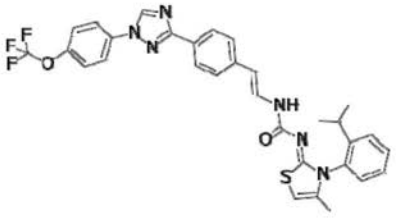
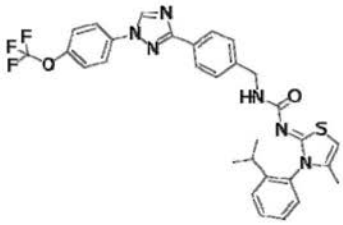
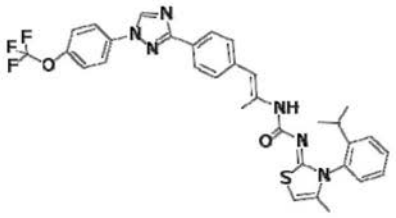
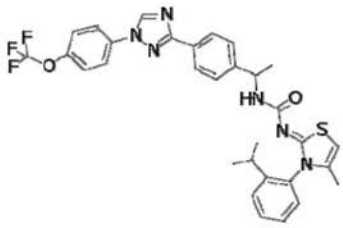
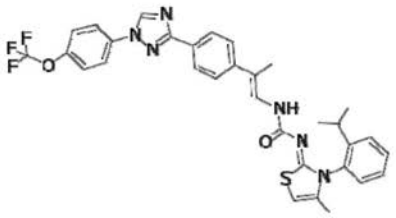
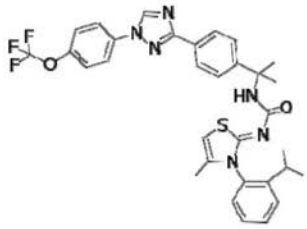
[1594]

 P286	 P287
 P288	 P289
 P290	 P291
 P292	 P293
 P294	 P295

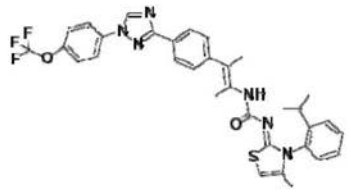
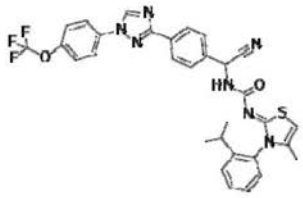
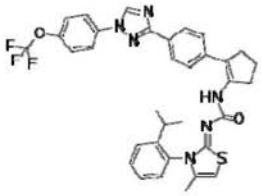
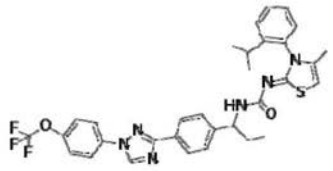
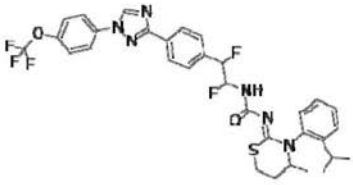
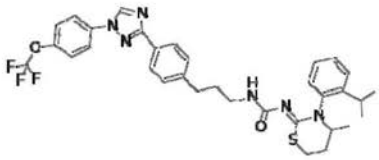
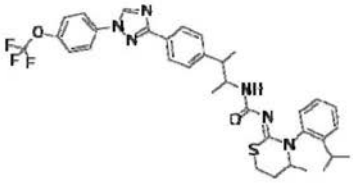
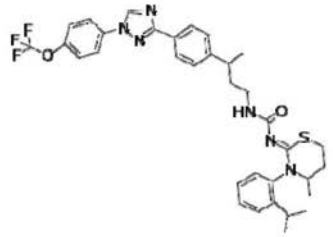
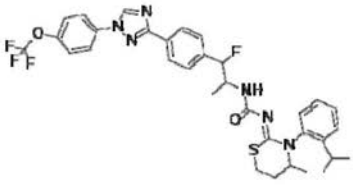
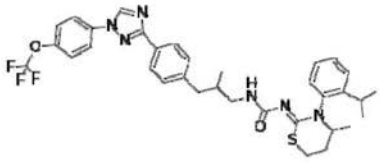
[1595]

 P296	 P297
 P298	 P299
 P300	 P301
 P302	 P303
 P304	 P305

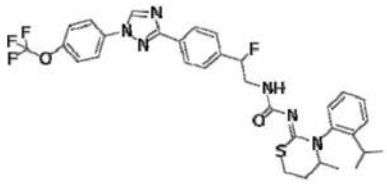
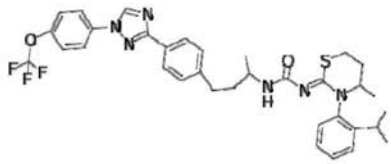
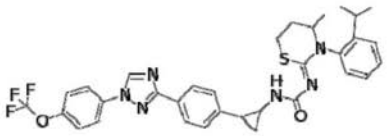
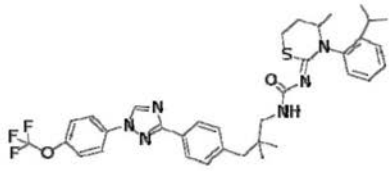
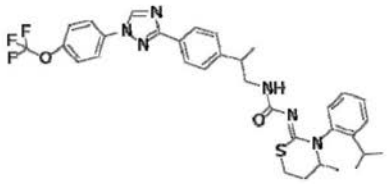
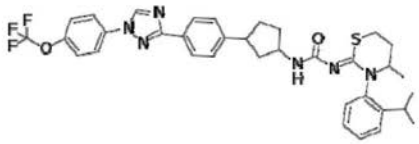
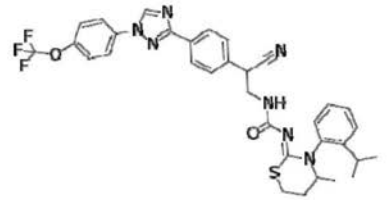
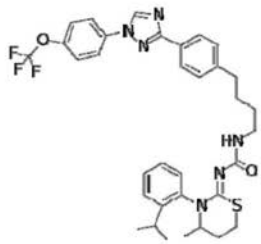
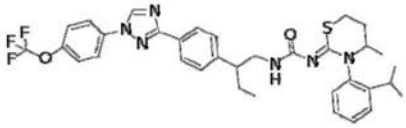
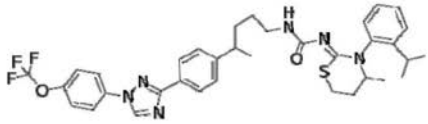
[1596]

 P306	 P307
 P308	 P309
 P310	 P311
 P312	 P313
 P314	 P315

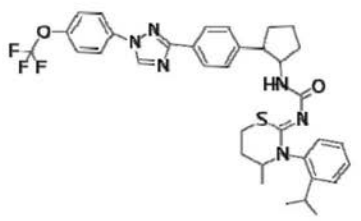
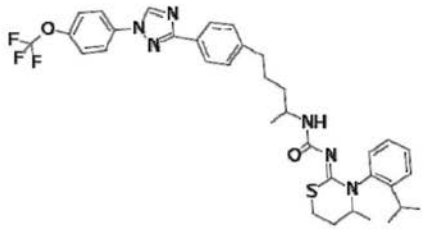
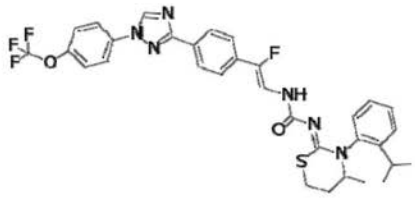
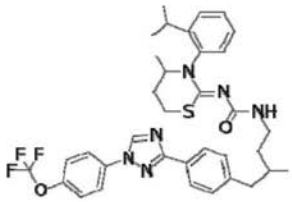
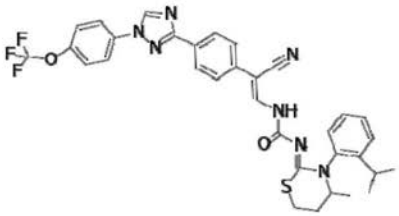
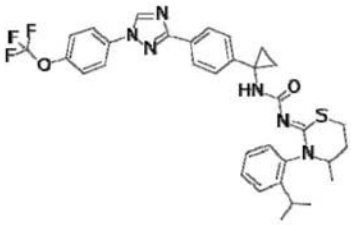
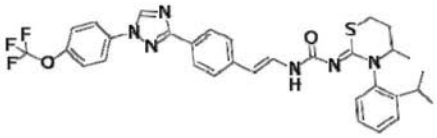
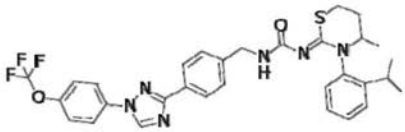
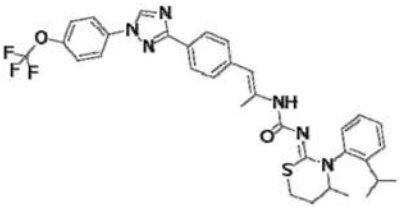
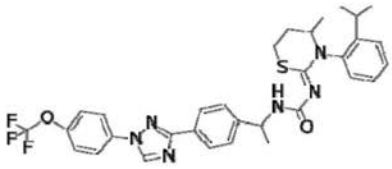
[1597]

 P316	 P317
 P318	 P319
 P320	 P321
 P322	 P323
 P324	 P325

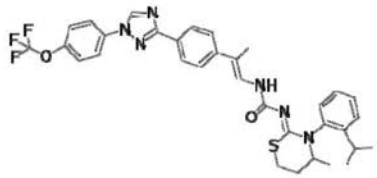
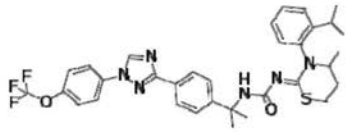
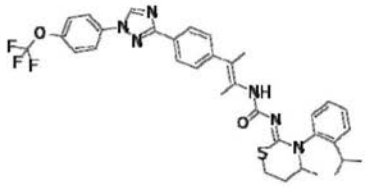
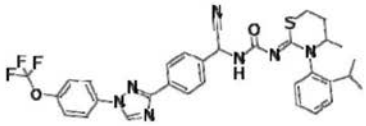
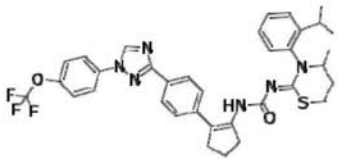
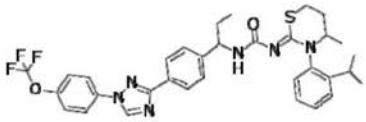
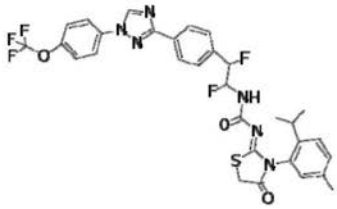
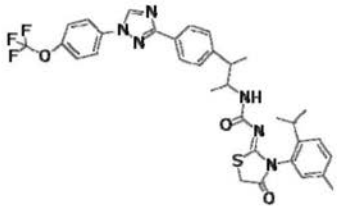
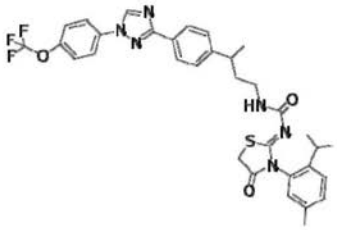
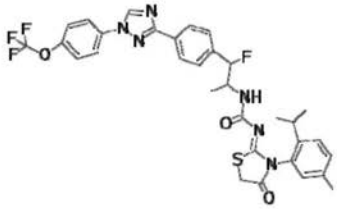
[1598]

 P326	 P327
 P328	 P329
 P330	 P331
 P332	 P333
 P334	 P335

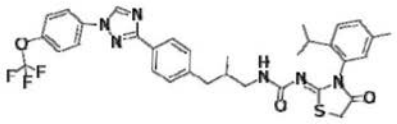
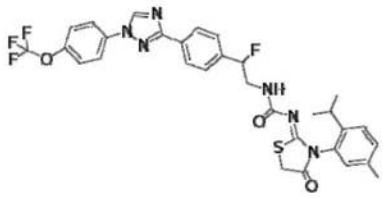
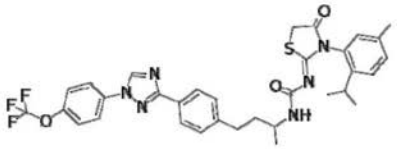
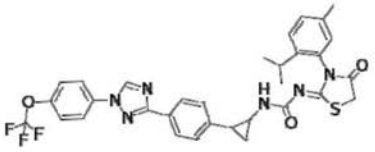
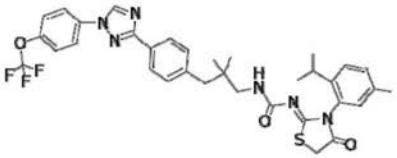
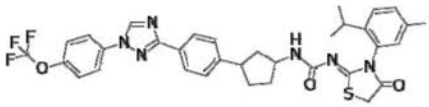
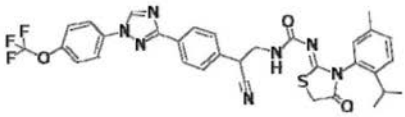
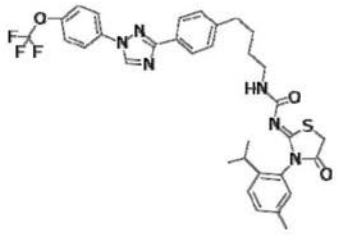
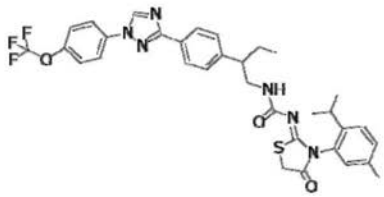
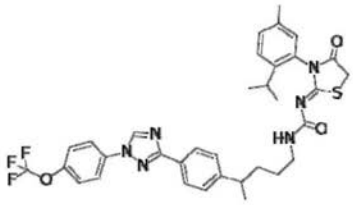
[1599]

 P336	 P337
 P338	 P339
 P340	 P341
 P342	 P343
 P344	 P345

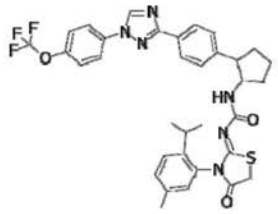
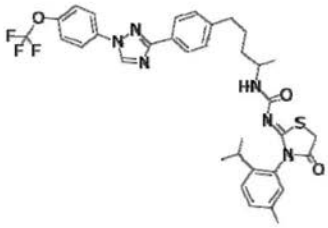
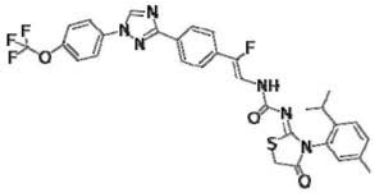
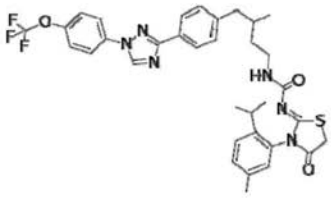
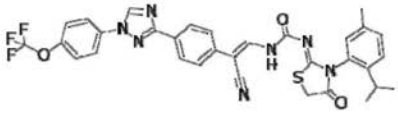
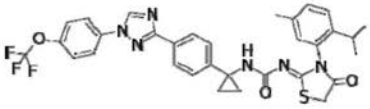
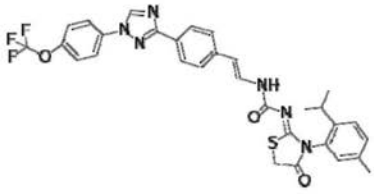
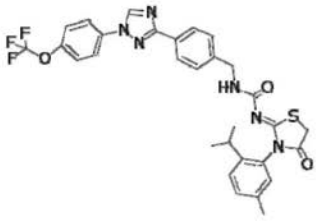
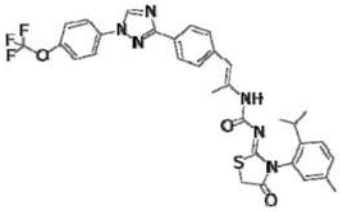
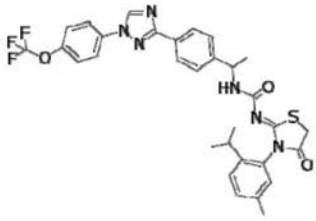
[1600]

 P346	 P347
 P348	 P349
 P350	 P351
 P352	 P353
 P354	 P355

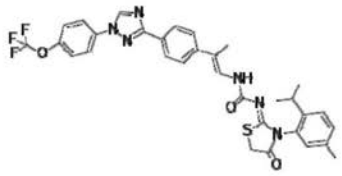
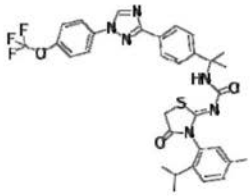
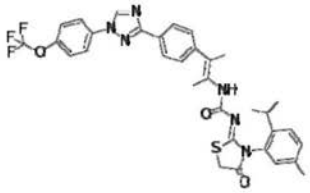
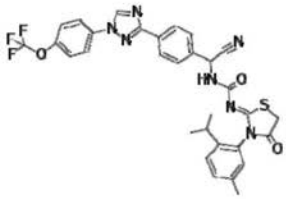
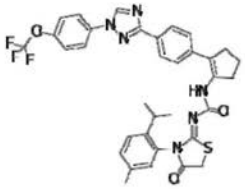
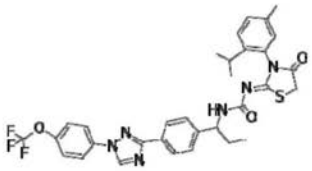
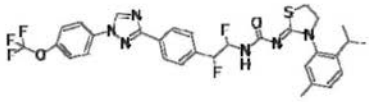
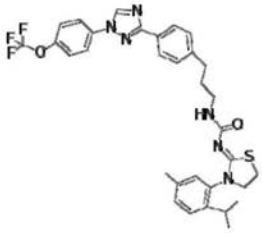
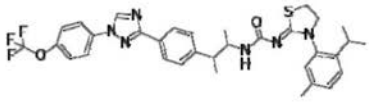
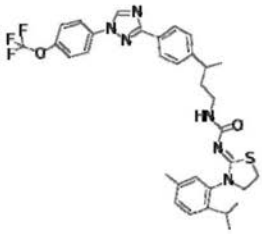
[1601]

 P356	 P357
 P358	 P359
 P360	 P361
 P362	 P363
 P364	 P365

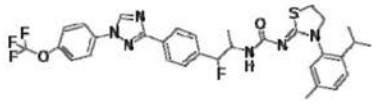
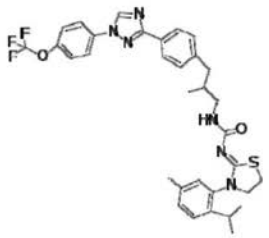
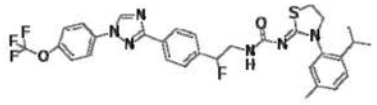
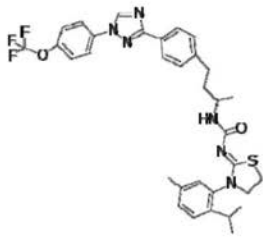
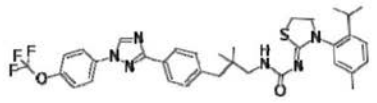
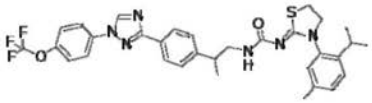
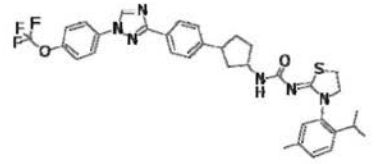
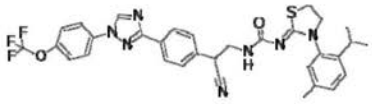
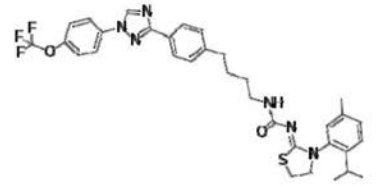
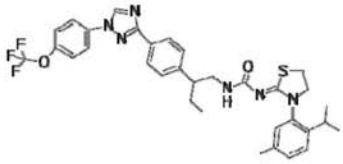
[1602]

 P366	 P367
 P368	 P369
 P370	 P371
 P372	 P373
 P374	 P375

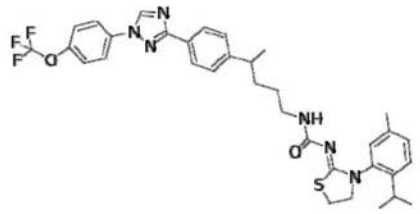
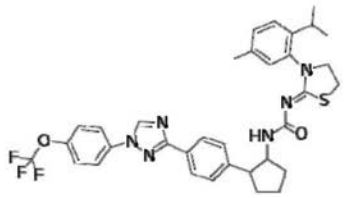
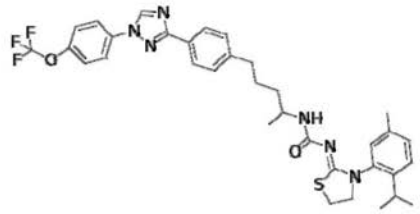
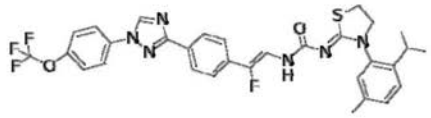
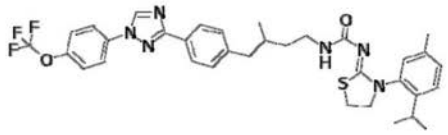
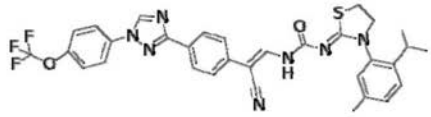
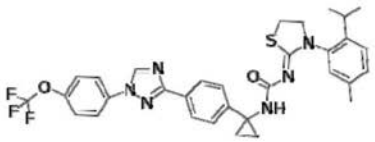
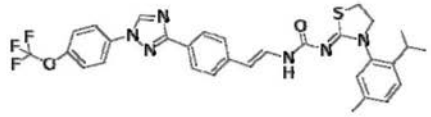
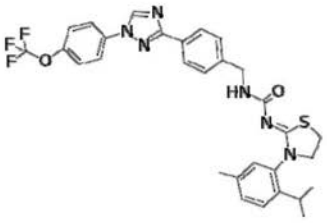
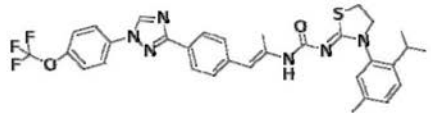
[1603]

 P376	 P377
 P378	 P379
 P380	 P381
 P382	 P383
 P384	 P385

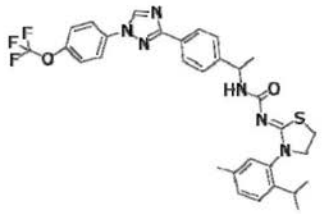
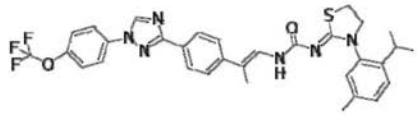
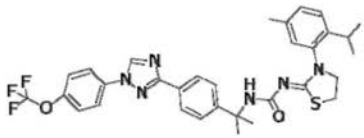
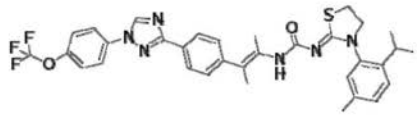
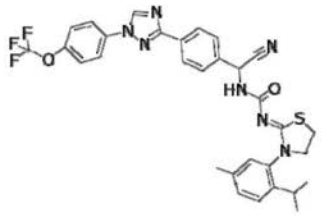
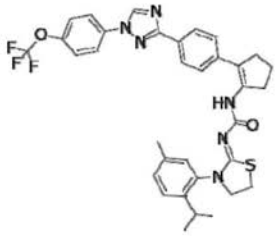
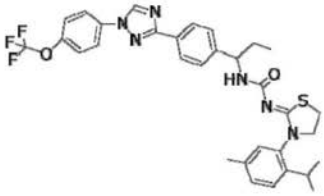
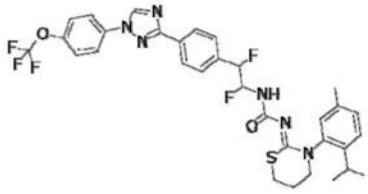
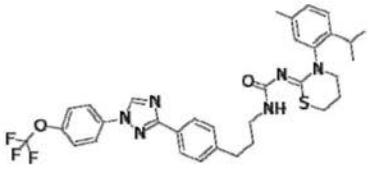
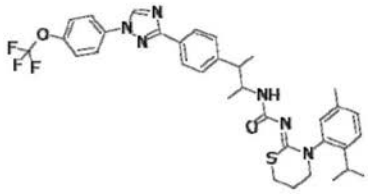
[1604]

 P386	 P387
 P388	 P389
 P390	 P391
 P392	 P393
 P394	 P395

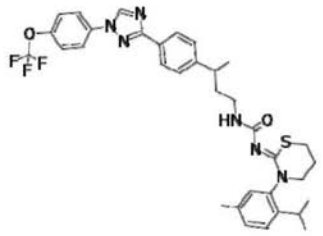
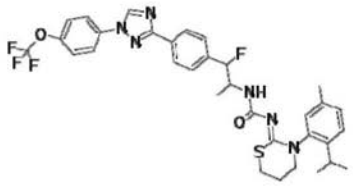
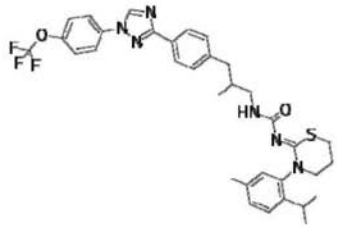
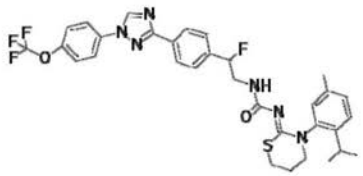
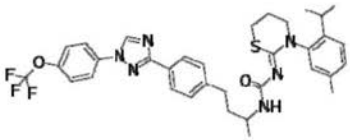
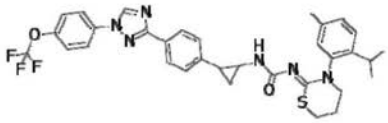
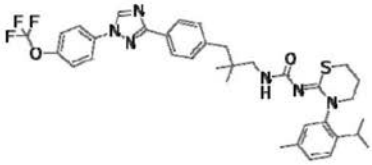
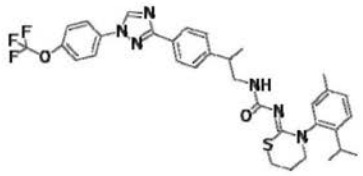
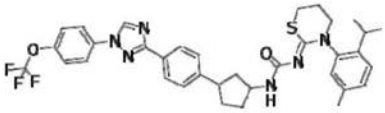
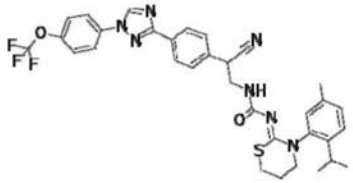
[1605]

 P396	 P397
 P398	 P399
 P400	 P401
 P402	 P403
 P404	 P405

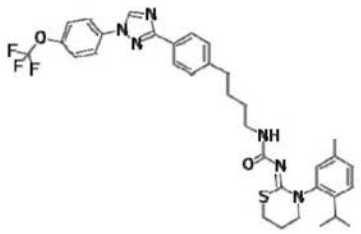
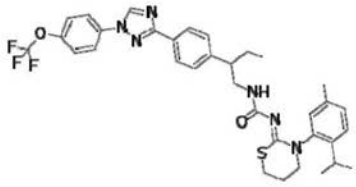
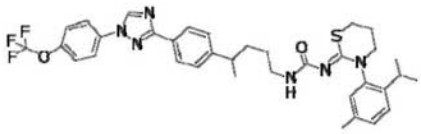
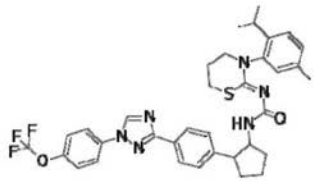
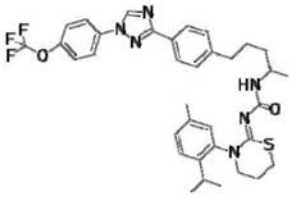
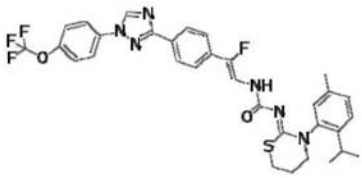
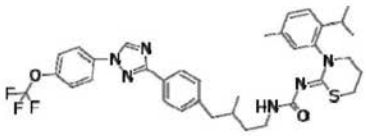
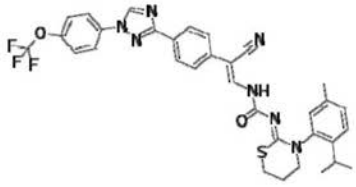
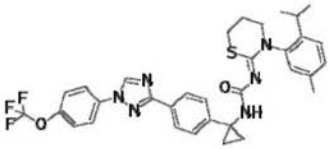
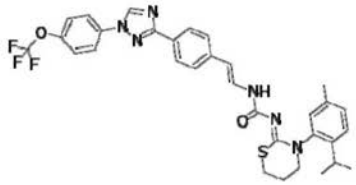
[1606]

 P406	 P407
 P408	 P409
 P410	 P411
 P412	 P413
 P414	 P415

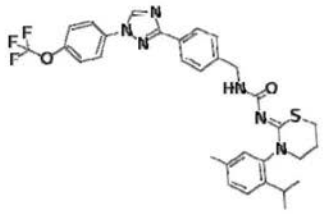
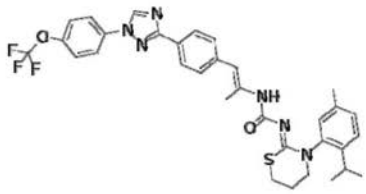
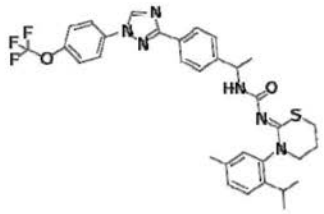
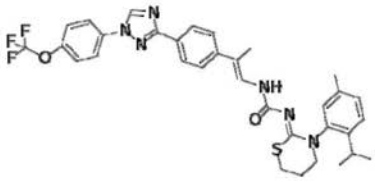
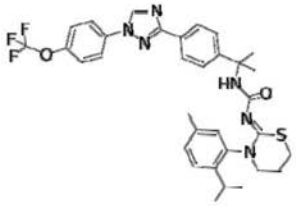
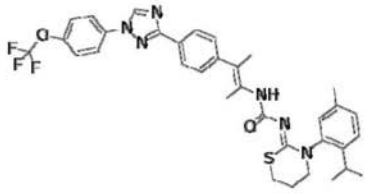
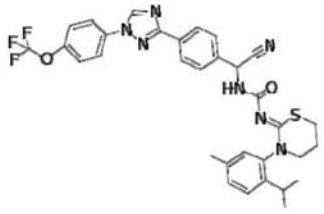
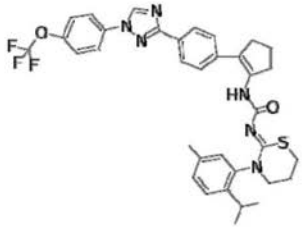
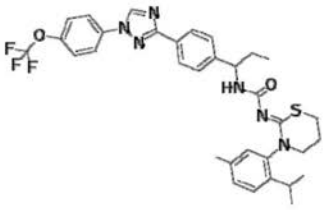
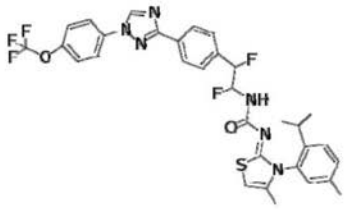
[1607]

 P416	 P417
 P418	 P419
 P420	 P421
 P422	 P423
 P424	 P425

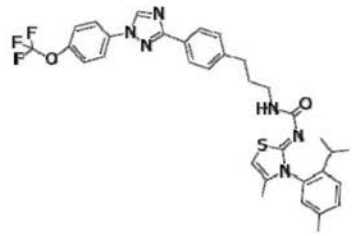
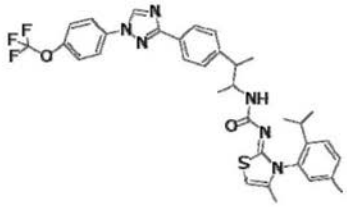
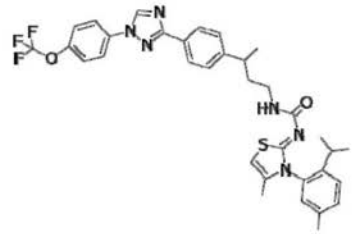
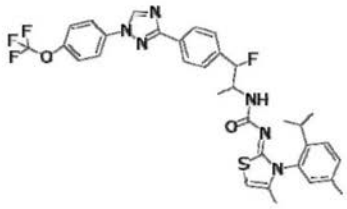
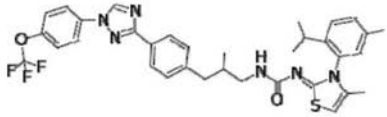
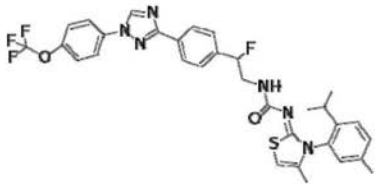
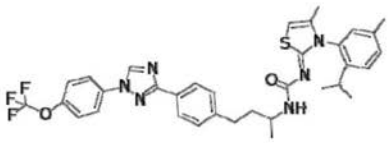
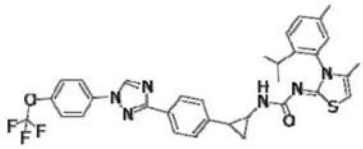
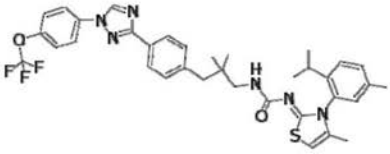
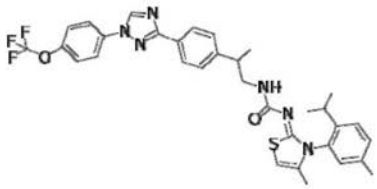
[1608]

 P426	 P427
 P428	 P429
 P430	 P431
 P432	 P433
 P434	 P435

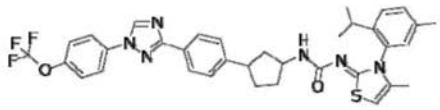
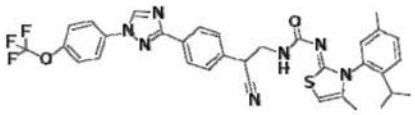
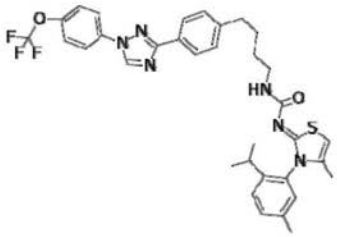
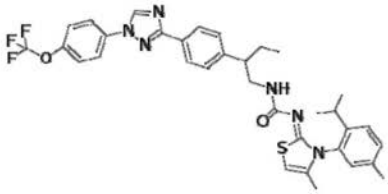
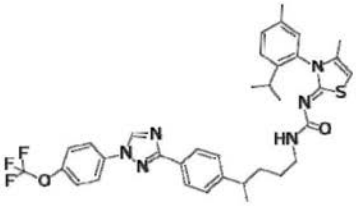
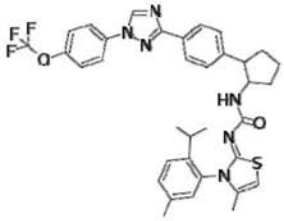
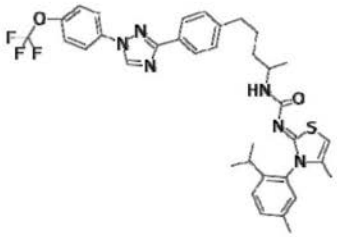
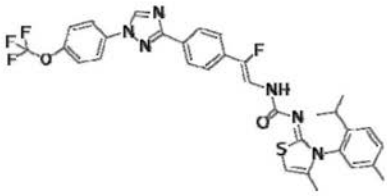
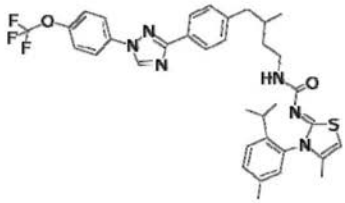
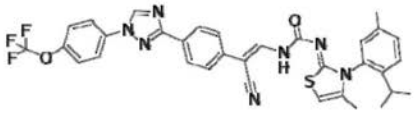
[1609]

 P436	 P437
 P438	 P439
 P440	 P441
 P442	 P443
 P444	 P445

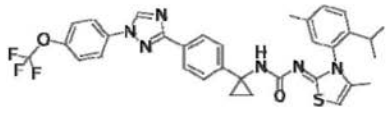
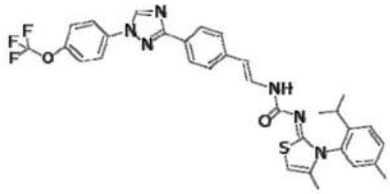
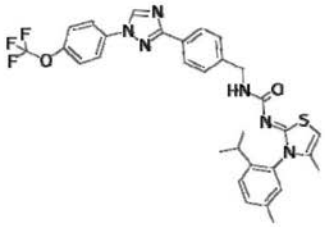
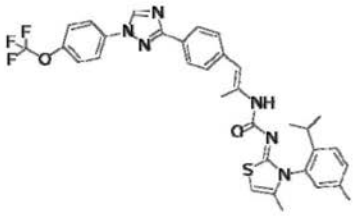
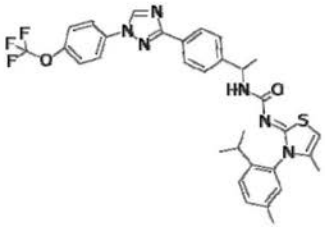
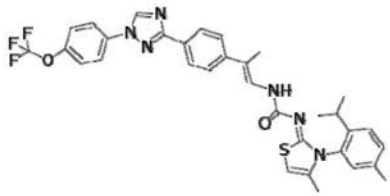
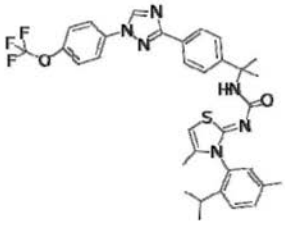
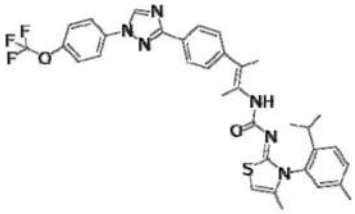
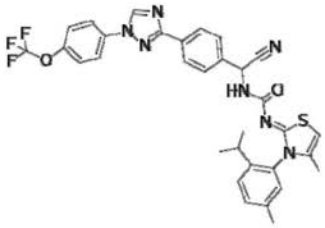
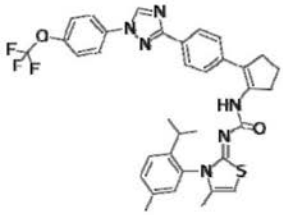
[1610]

 P446	 P447
 P448	 P449
 P450	 P451
 P452	 P453
 P454	 P455

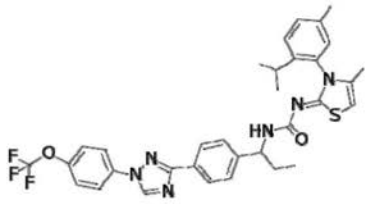
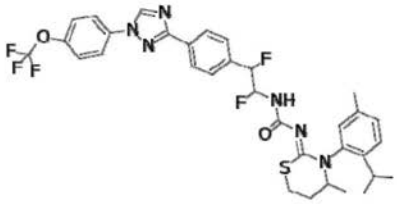
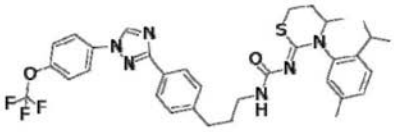
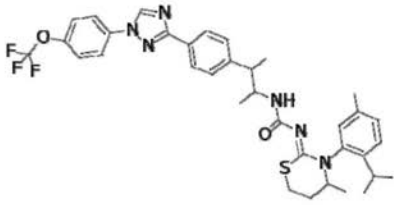
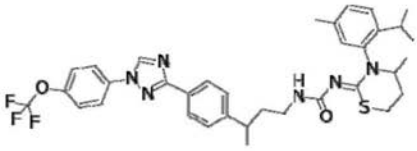
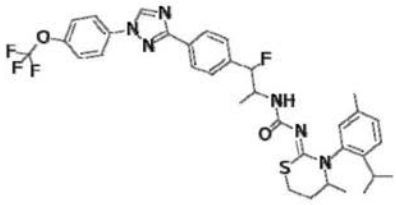
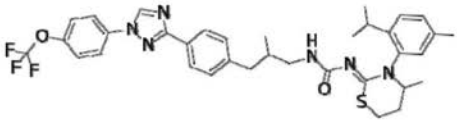
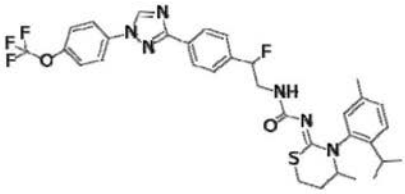
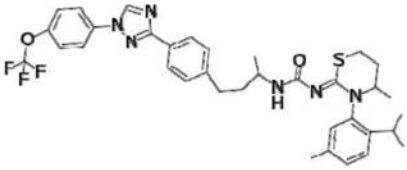
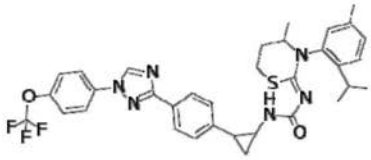
[1611]

 P456	 P457
 P458	 P459
 P460	 P461
 P462	 P463
 P464	 P465

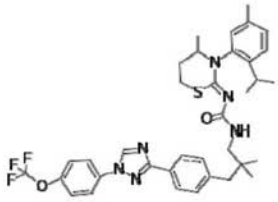
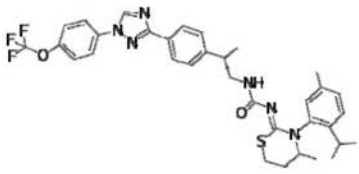
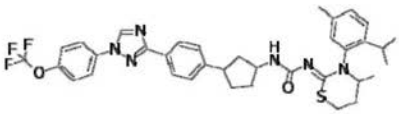
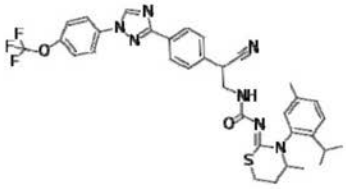
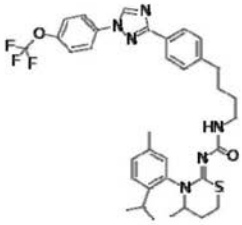
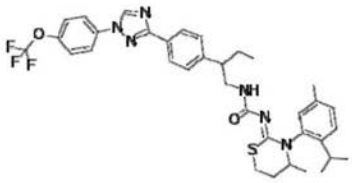
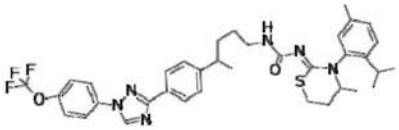
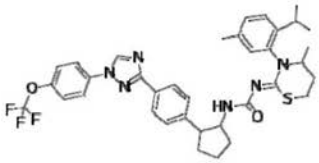
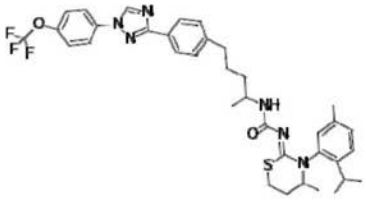
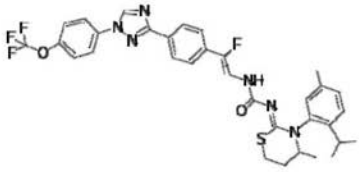
[1612]

 P466	 P467
 P468	 P469
 P470	 P471
 P472	 P473
 P474	 P475

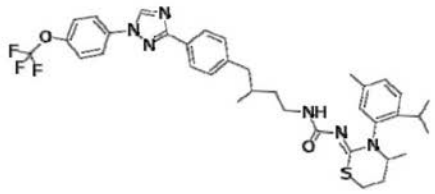
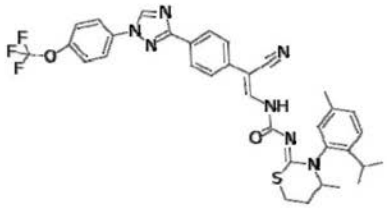
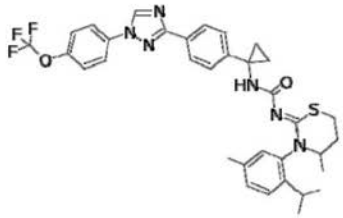
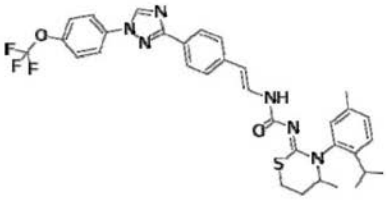
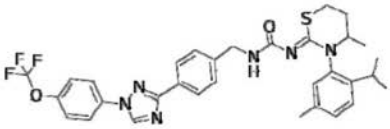
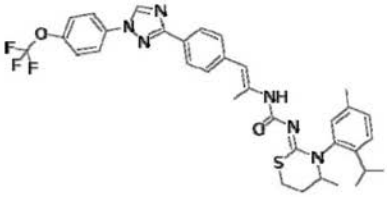
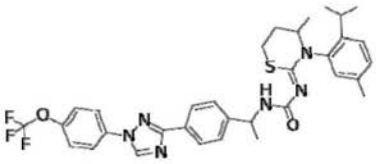
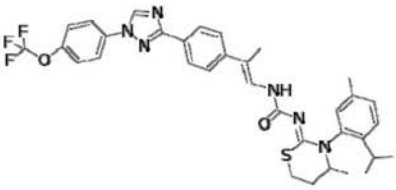
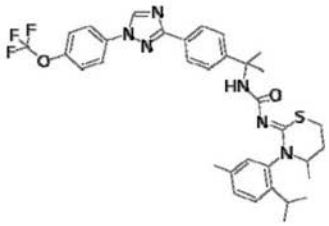
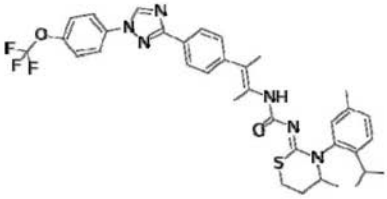
[1613]

 P476	 P477
 P478	 P479
 P480	 P481
 P482	 P483
 P484	 P485

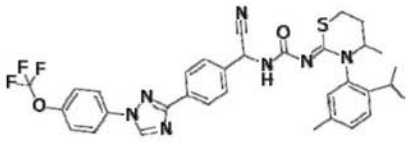
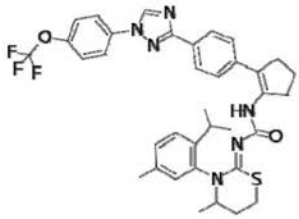
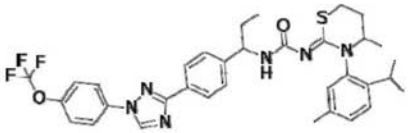
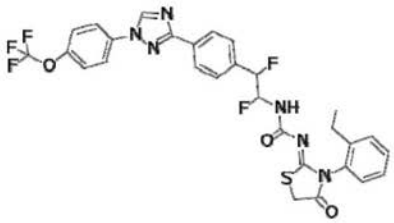
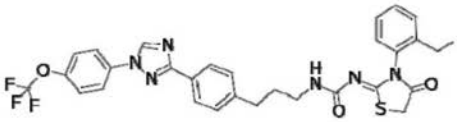
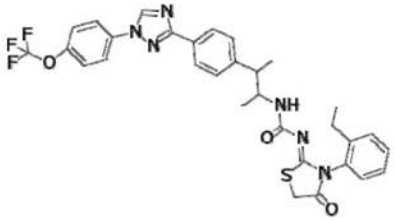
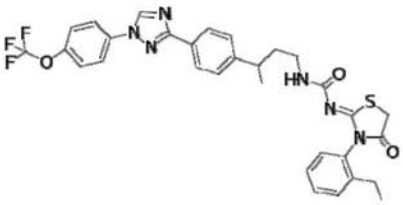
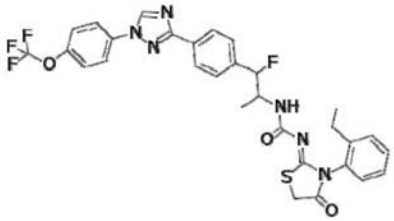
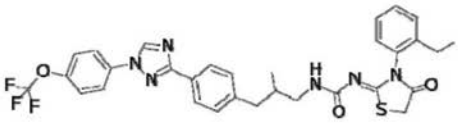
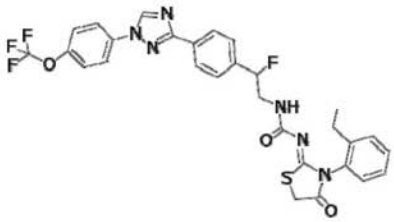
[1614]

 P486	 P487
 P488	 P489
 P490	 P491
 P492	 P493
 P494	 P495

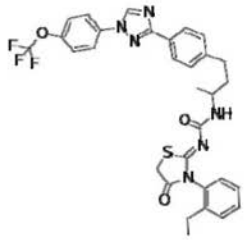
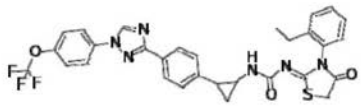
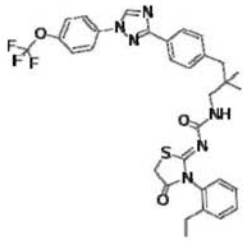
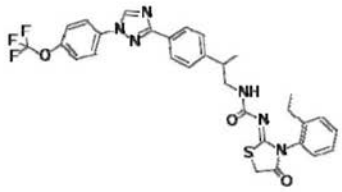
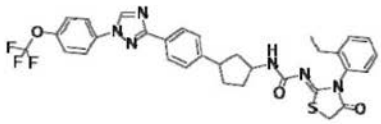
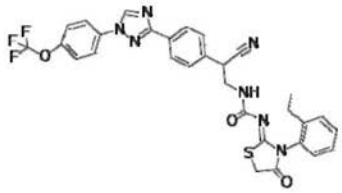
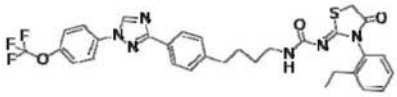
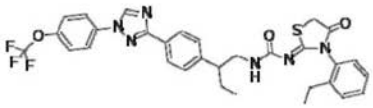
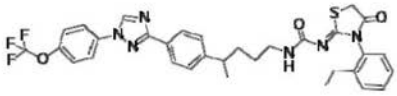
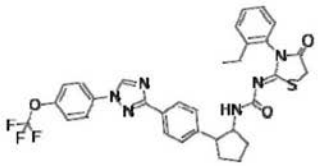
[1615]

 P496	 P497
 P498	 P499
 P500	 P501
 P502	 P503
 P504	 P505

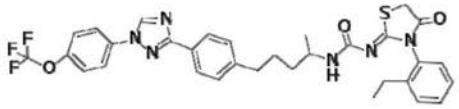
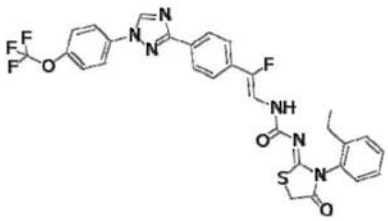
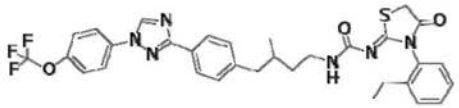
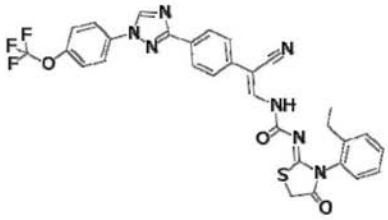
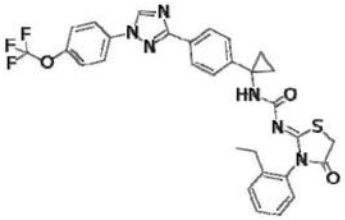
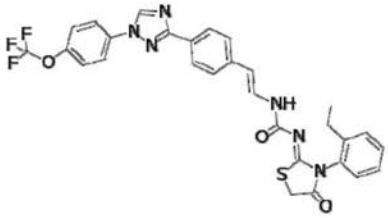
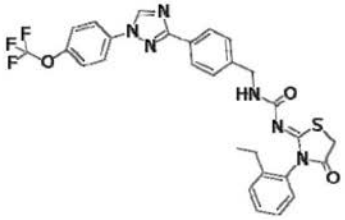
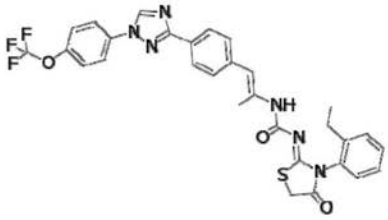
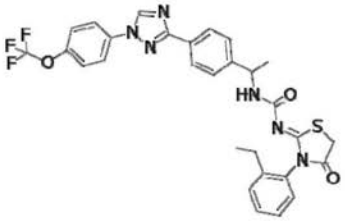
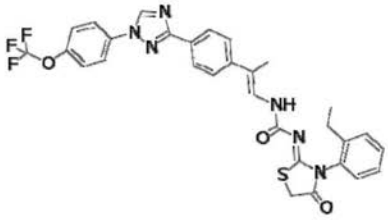
[1616]

 P506	 P507
 P508	 P509
 P510	 P511
 P512	 P513
 P514	 P515

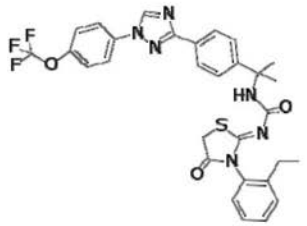
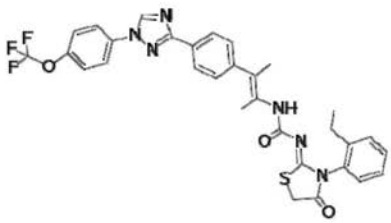
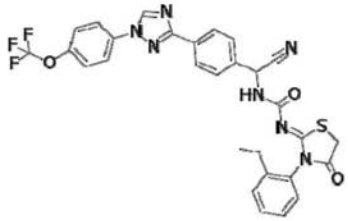
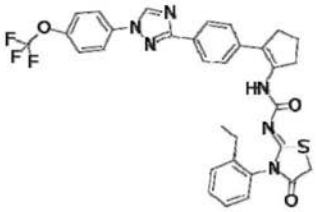
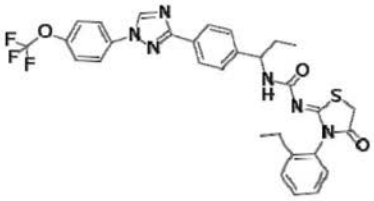
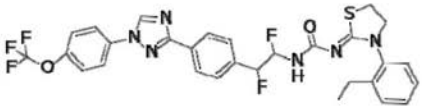
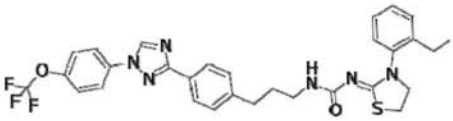
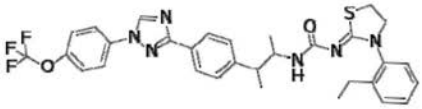
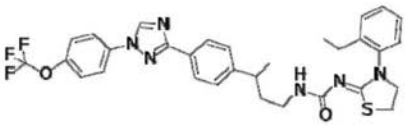
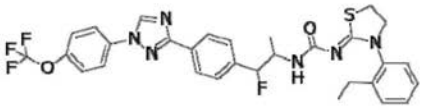
[1617]

 P516	 P517
 P518	 P519
 P520	 P521
 P522	 P523
 P524	 P525

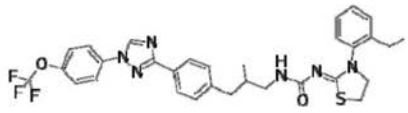
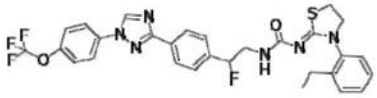
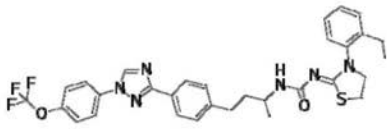
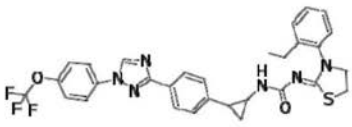
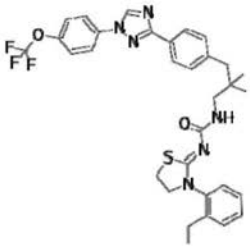
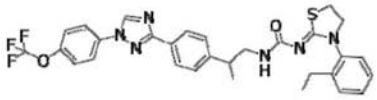
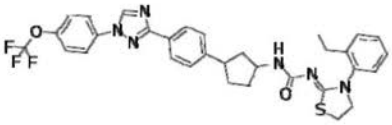
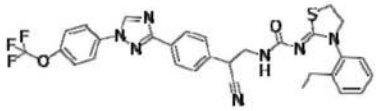
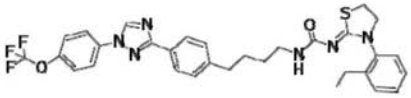
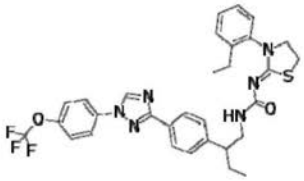
[1618]

 P526	 P527
 P528	 P529
 P530	 P531
 P532	 P533
 P534	 P535

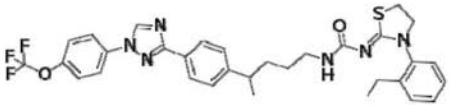
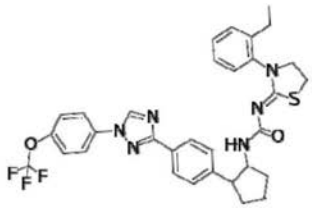
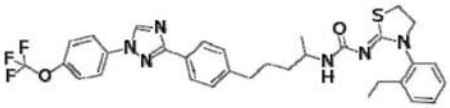
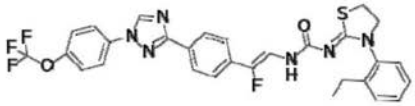
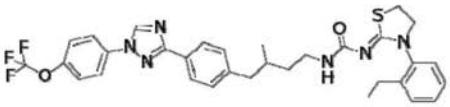
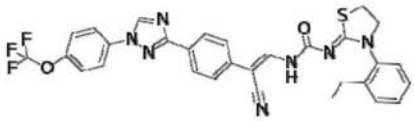
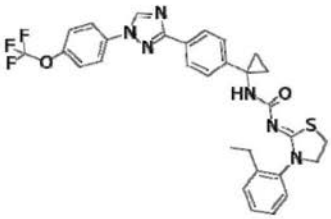
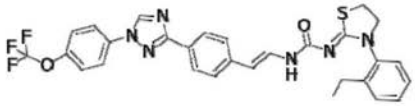
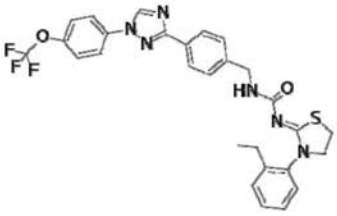
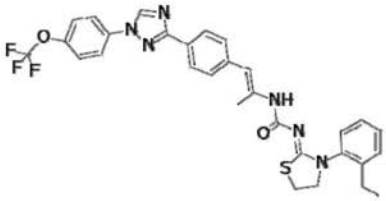
[1619]

 P536	 P537
 P538	 P539
 P540	 P541
 P542	 P543
 P544	 P545

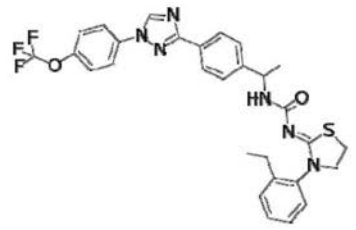
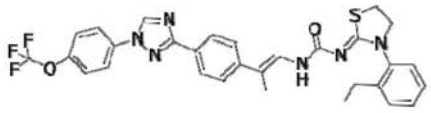
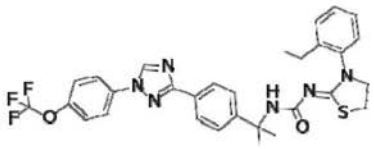
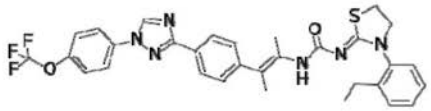
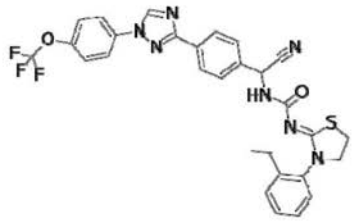
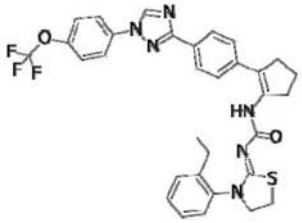
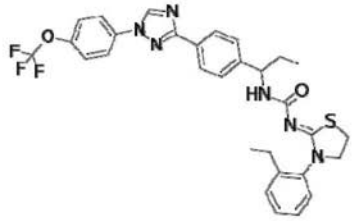
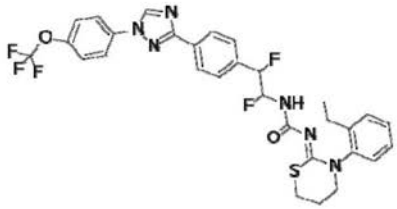
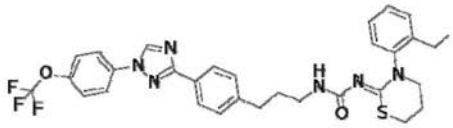
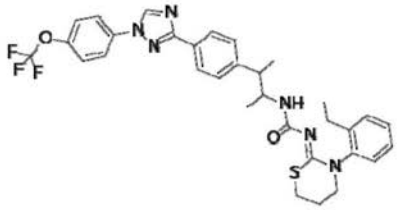
[1620]

 P546	 P547
 P548	 P549
 P550	 P551
 P552	 P553
 P554	 P555

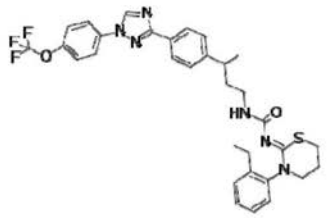
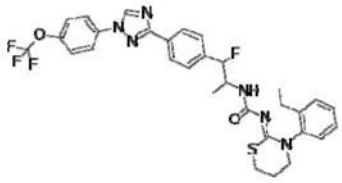
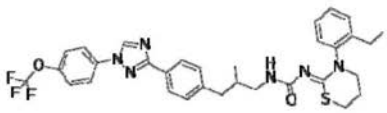
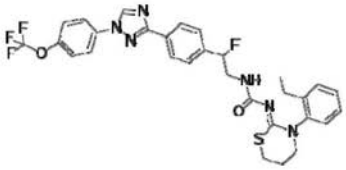
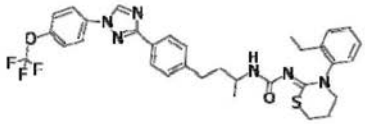
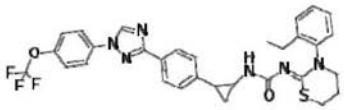
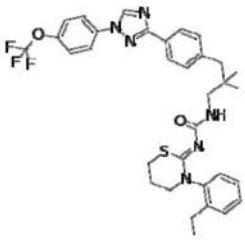
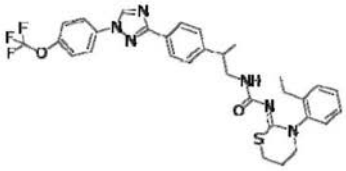
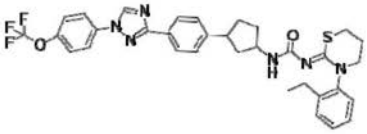
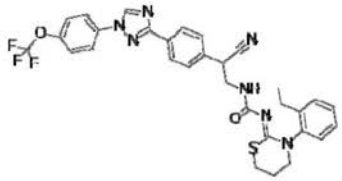
[1621]

 P556	 P557
 P558	 P559
 P560	 P561
 P562	 P563
 P564	 P565

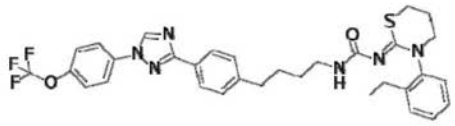
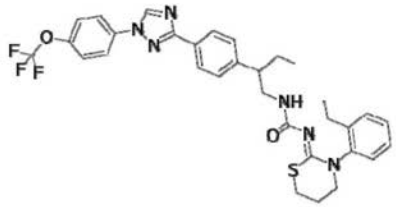
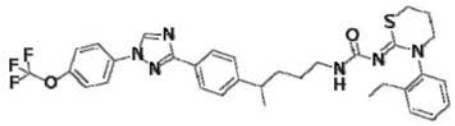
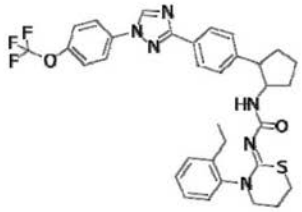
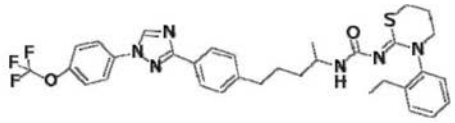
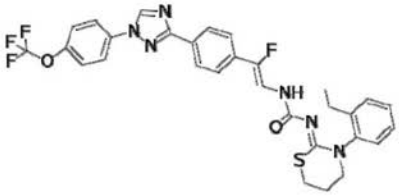
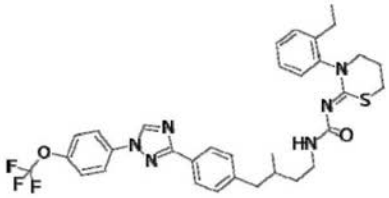
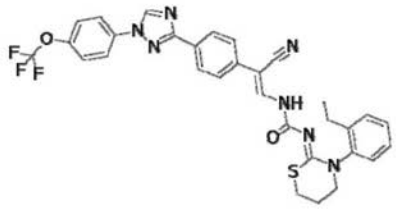
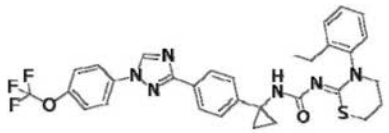
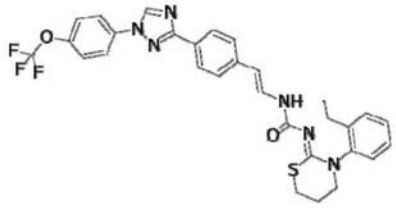
[1622]

 P566	 P567
 P568	 P569
 P570	 P571
 P572	 P573
 P574	 P575

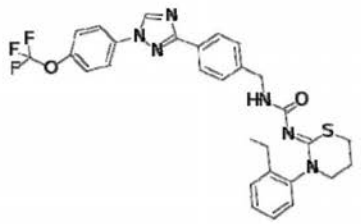
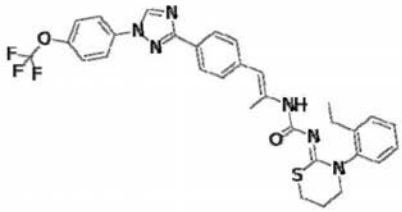
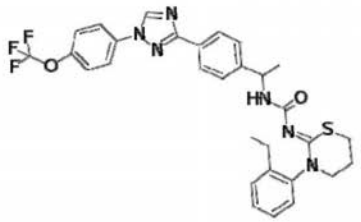
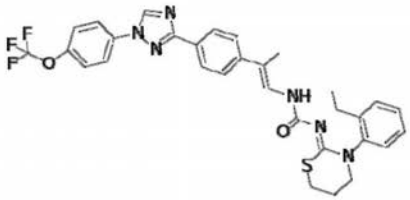
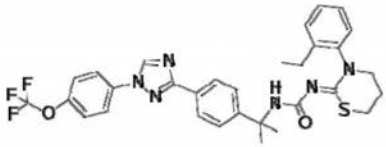
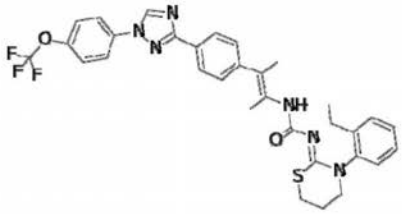
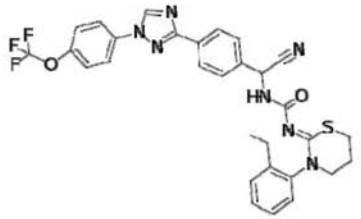
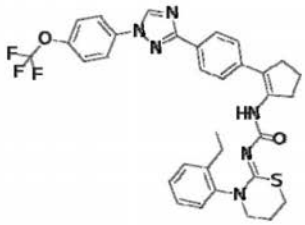
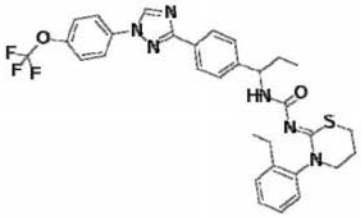
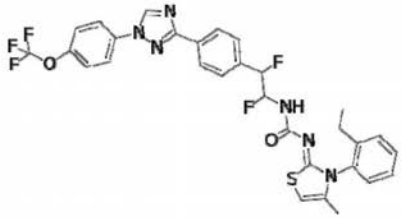
[1623]

 P576	 P577
 P578	 P579
 P580	 P581
 P582	 P583
 P584	 P585

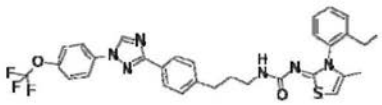
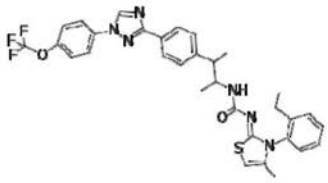
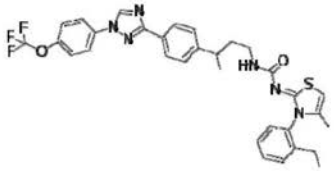
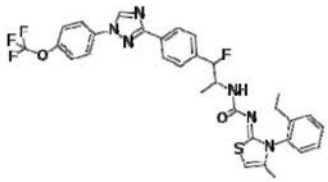
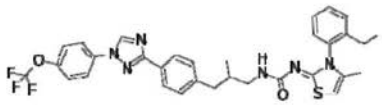
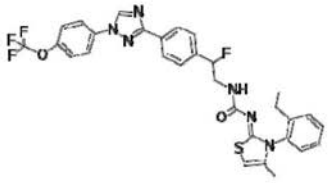
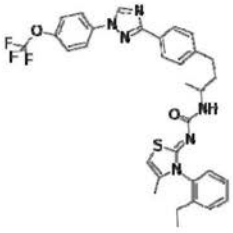
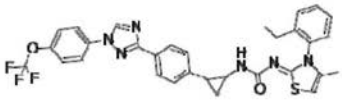
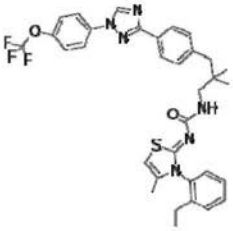
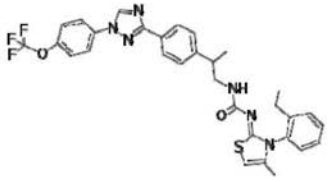
[1624]

 P586	 P587
 P588	 P589
 P590	 P591
 P592	 P593
 P594	 P595

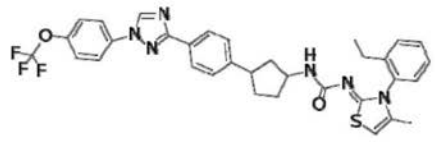
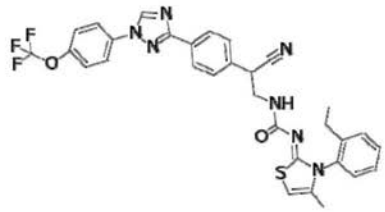
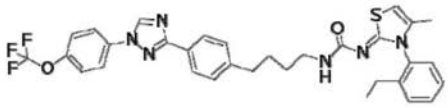
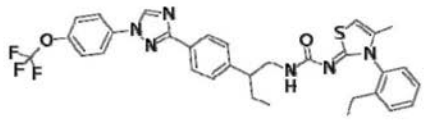
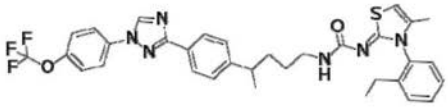
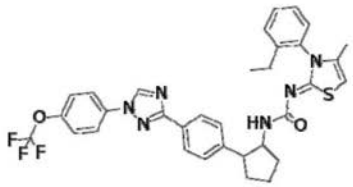
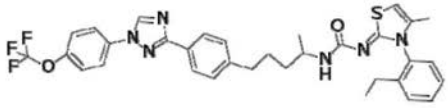
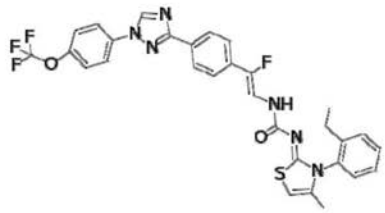
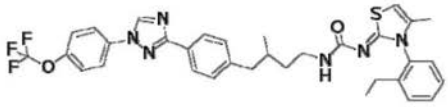
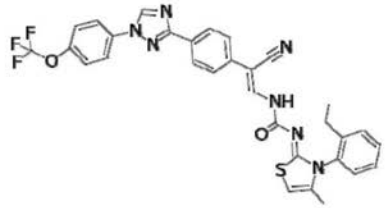
[1625]

 P596	 P597
 P598	 P599
 P600	 P601
 P602	 P603
 P604	 P605

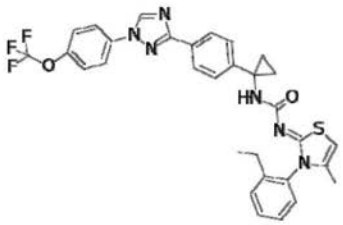
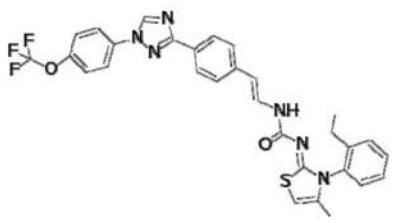
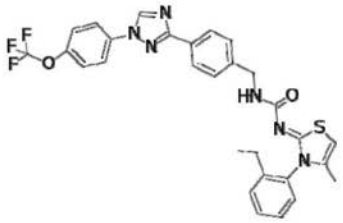
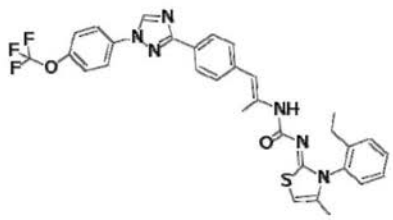
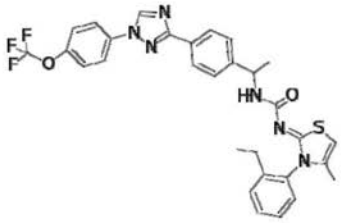
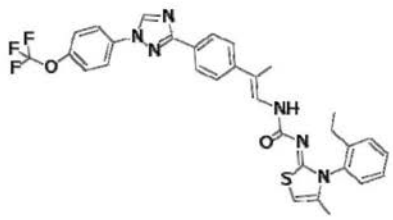
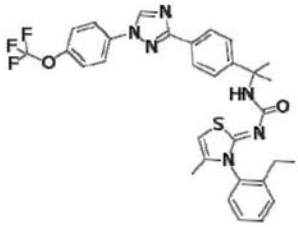
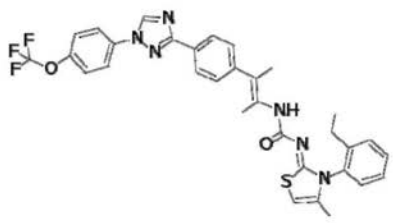
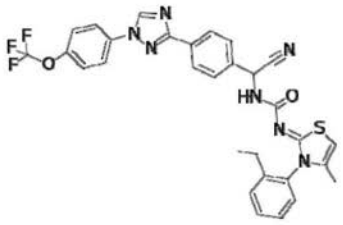
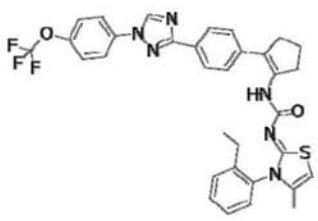
[1626]

 P606	 P607
 P608	 P609
 P610	 P611
 P612	 P613
 P614	 P615

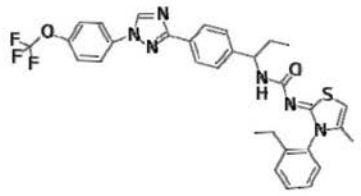
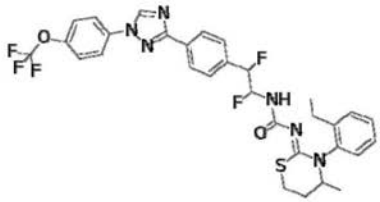
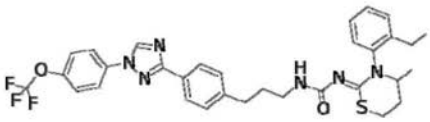
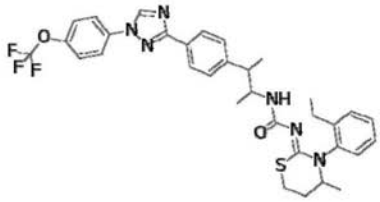
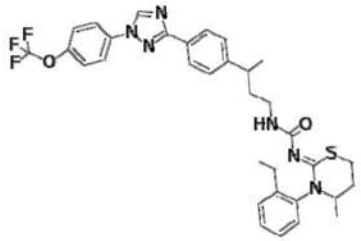
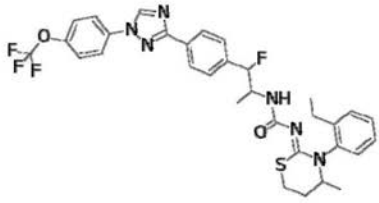
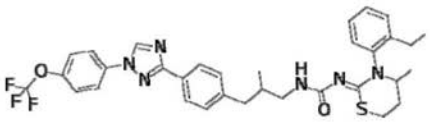
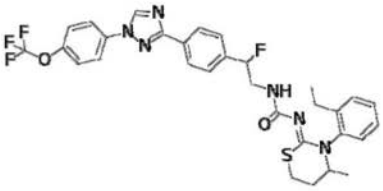
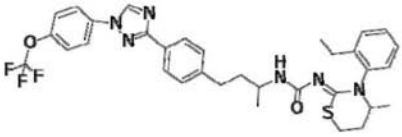
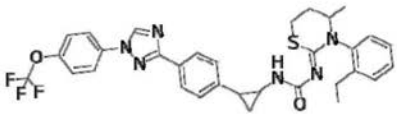
[1627]

 P616	 P617
 P618	 P619
 P620	 P621
 P622	 P623
 P624	 P625

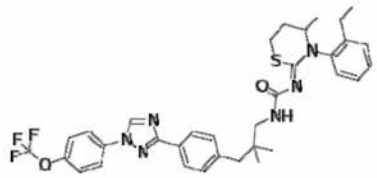
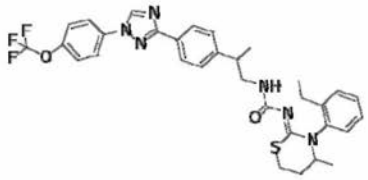
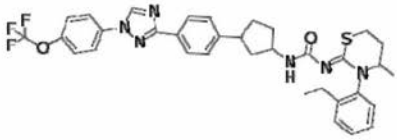
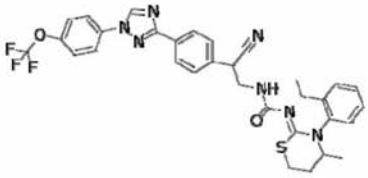
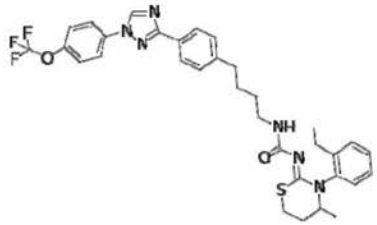
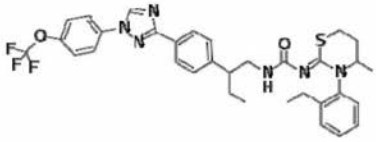
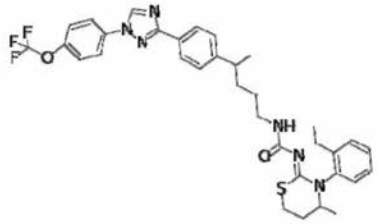
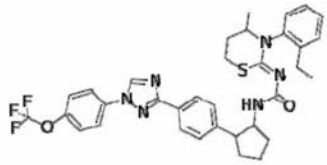
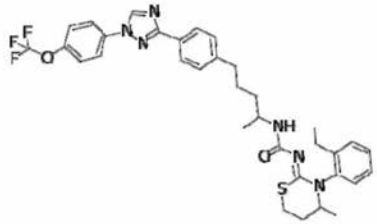
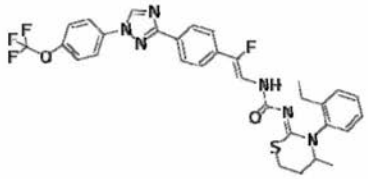
[1628]

 P626	 P627
 P628	 P629
 P630	 P631
 P632	 P633
 P634	 P635

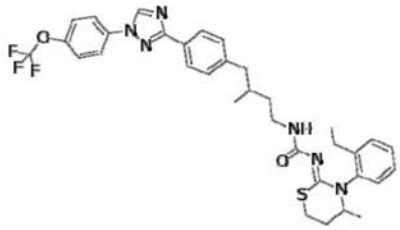
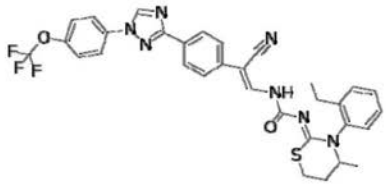
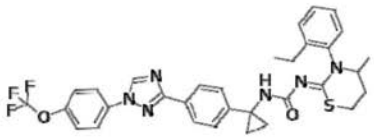
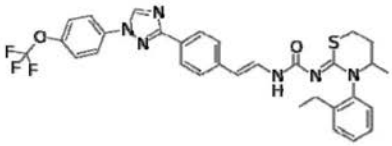
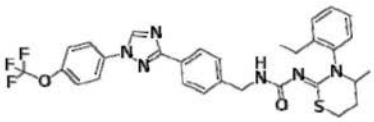
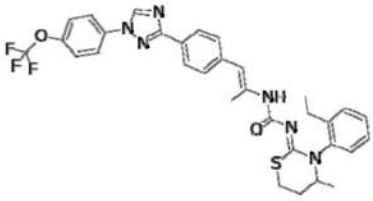
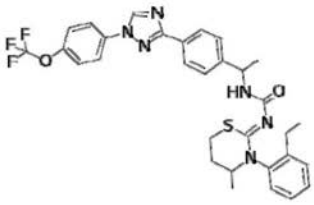
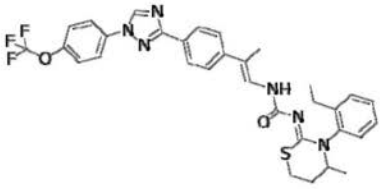
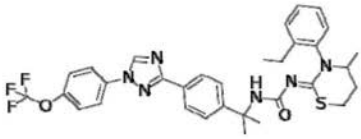
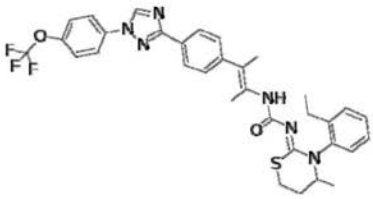
[1629]

 P636	 P637
 P638	 P639
 P640	 P641
 P642	 P643
 P644	 P645

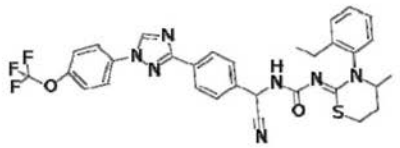
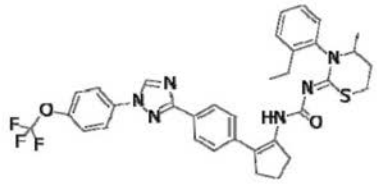
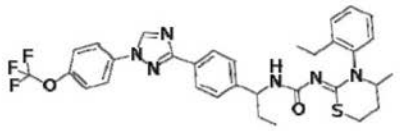
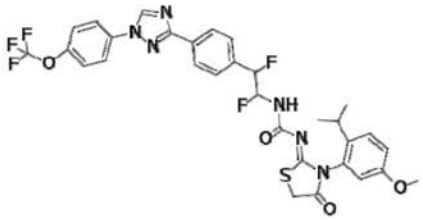
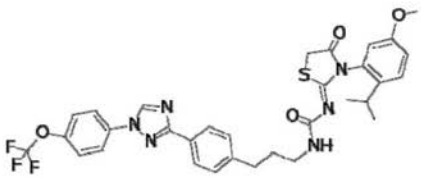
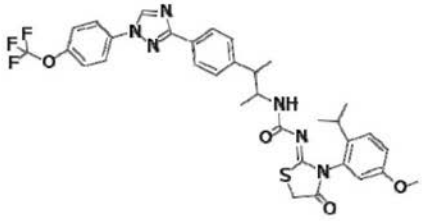
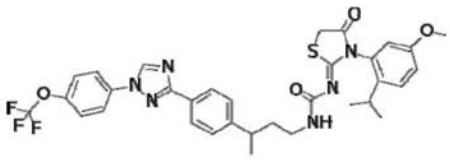
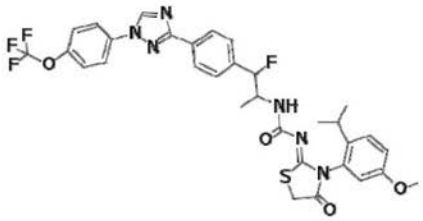
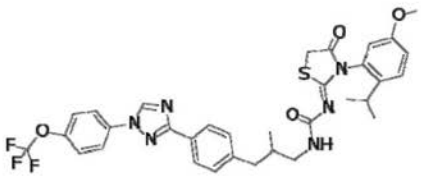
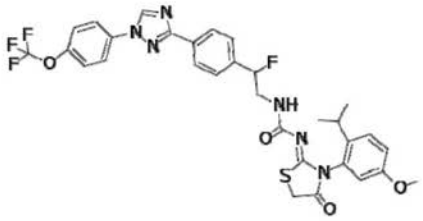
[1630]

 P646	 P647
 P648	 P649
 P650	 P651
 P652	 P653
 P654	 P655

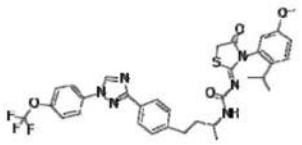
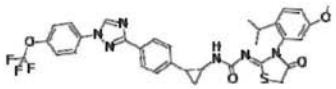
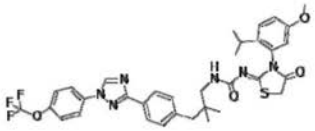
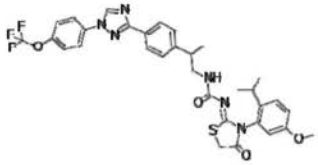
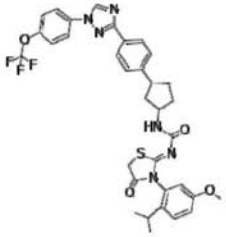
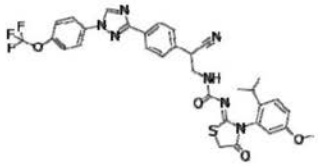
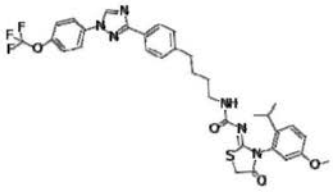
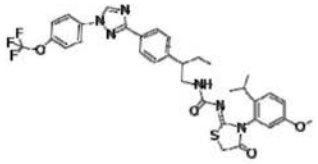
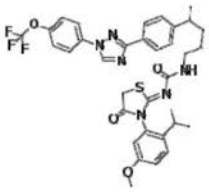
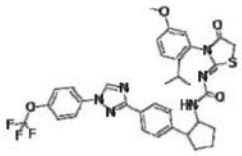
[1631]

 P656	 P657
 P658	 P659
 P660	 P661
 P662	 P663
 P664	 P665

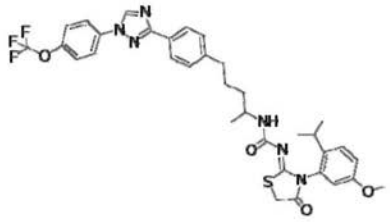
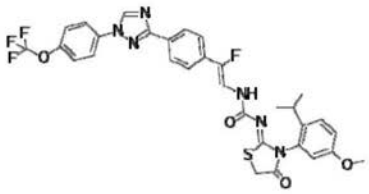
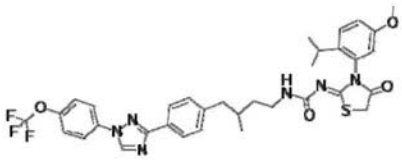
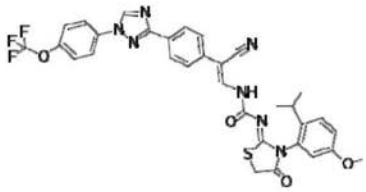
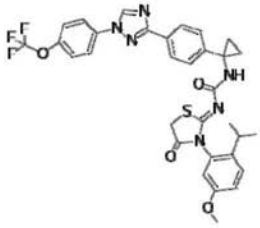
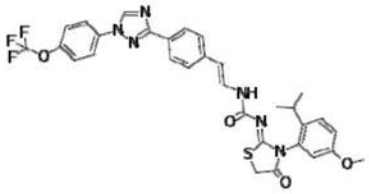
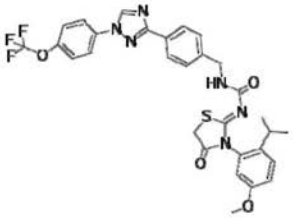
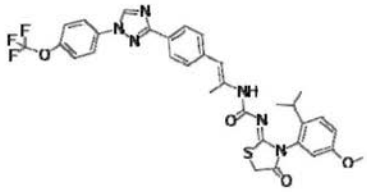
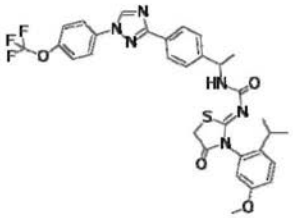
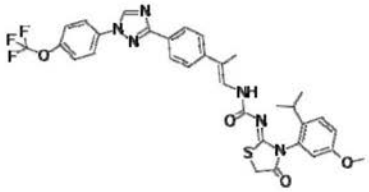
[1632]

 P666	 P667
 P668	 P669
 P670	 P671
 P672	 P673
 P674	 P675

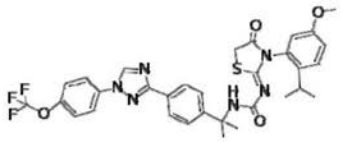
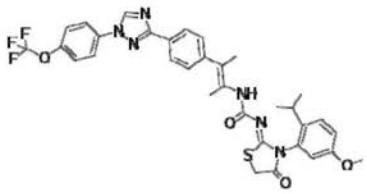
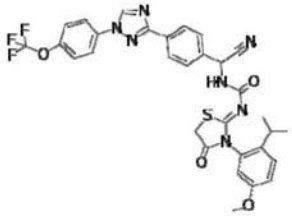
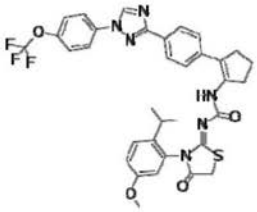
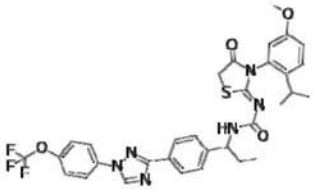
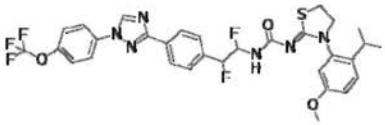
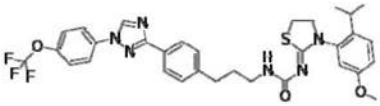
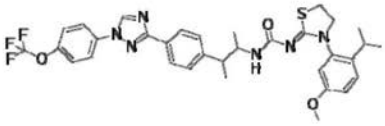
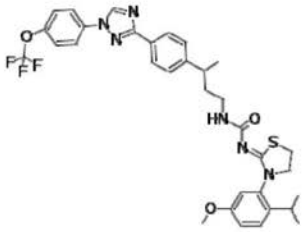
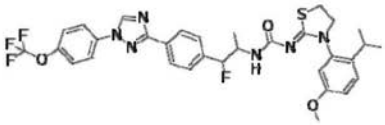
[1633]

 P676	 P677
 P678	 P679
 P680	 P681
 P682	 P683
 P684	 P685

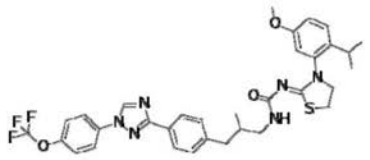
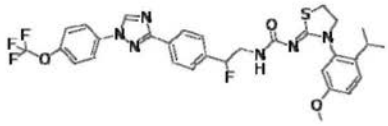
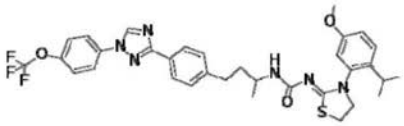
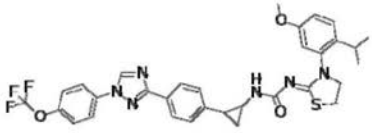
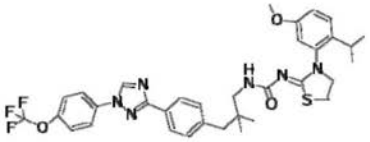
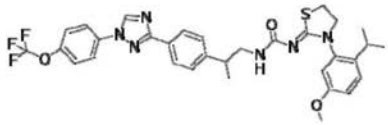
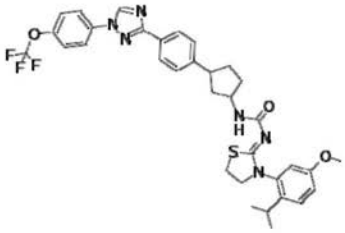
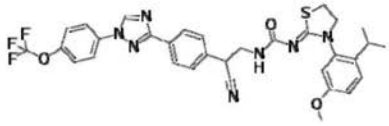
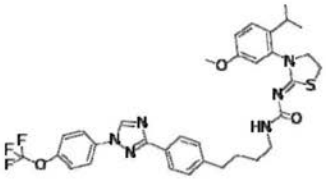
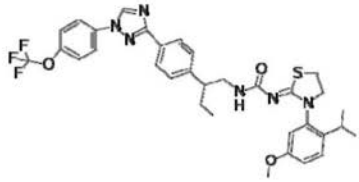
[1634]

 P686	 P687
 P688	 P689
 P690	 P691
 P692	 P693
 P694	 P695

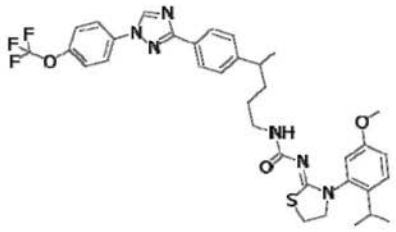
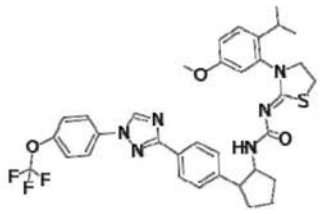
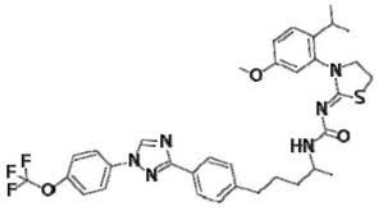
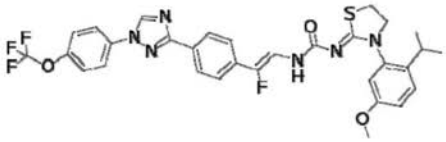
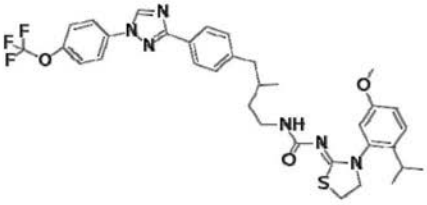
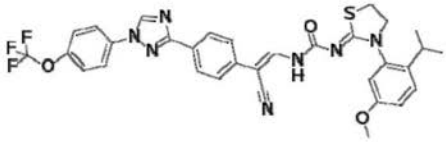
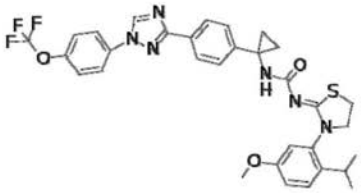
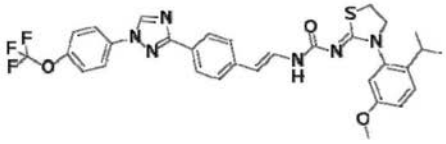
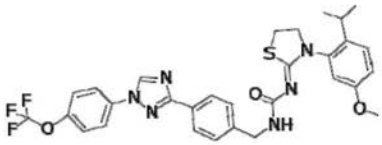
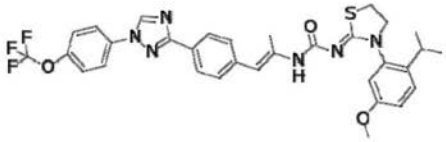
[1635]

 P696	 P697
 P698	 P699
 P700	 P701
 P702	 P703
 P704	 P705

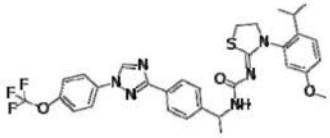
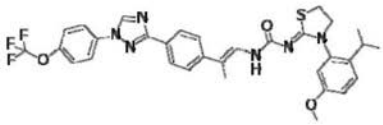
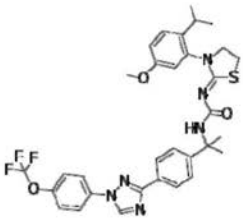
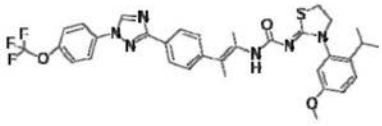
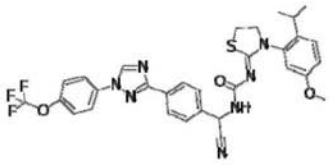
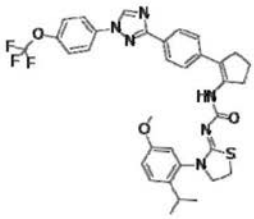
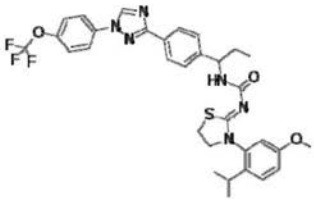
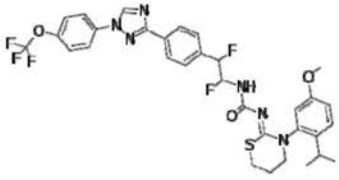
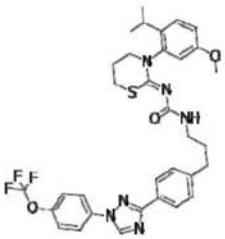
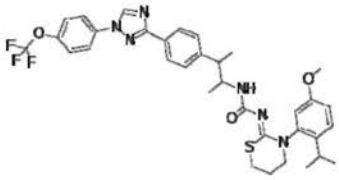
[1636]

 P706	 P707
 P708	 P709
 P710	 P711
 P712	 P713
 P714	 P715

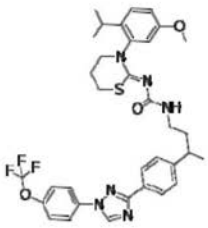
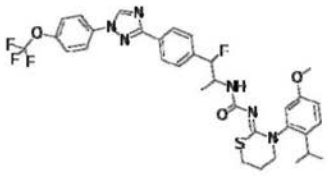
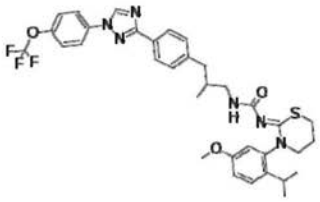
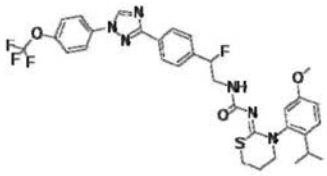
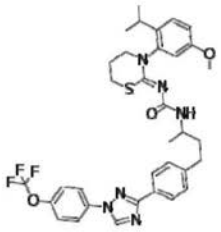
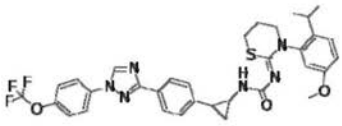
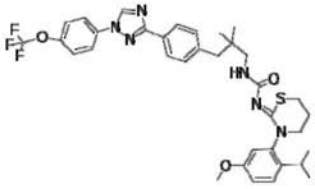
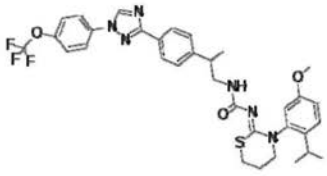
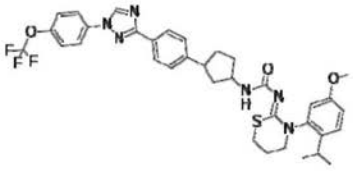
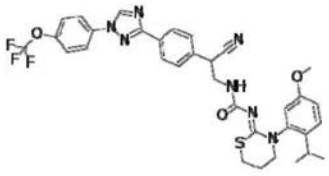
[1637]

 P716	 P717
 P718	 P719
 P720	 P721
 P722	 P723
 P724	 P725

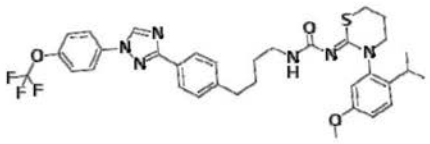
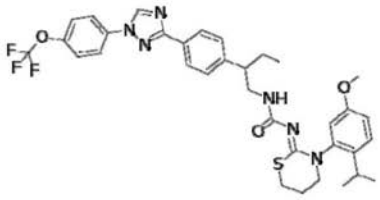
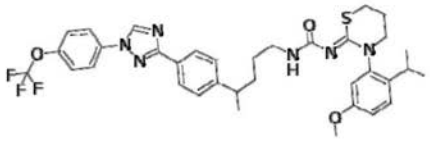
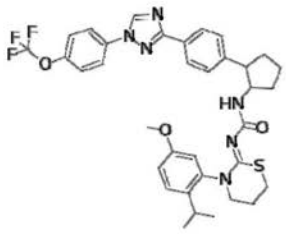
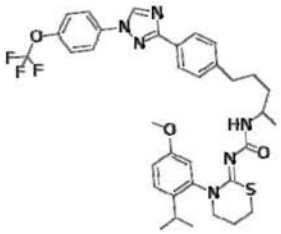
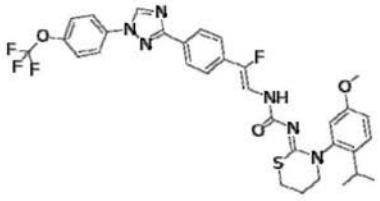
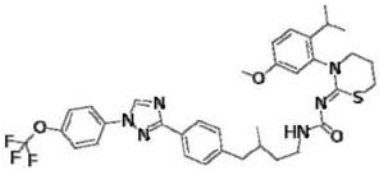
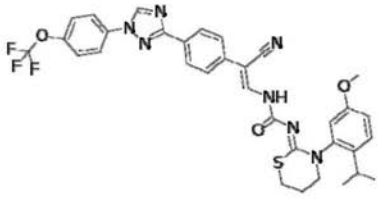
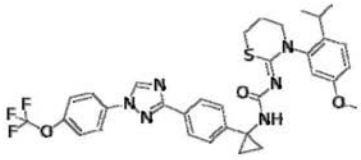
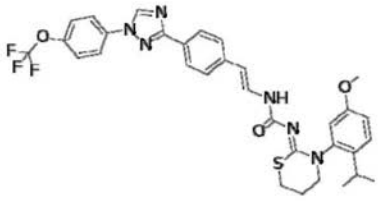
[1638]

 P726	 P727
 P728	 P729
 P730	 P731
 P732	 P733
 P734	 P735

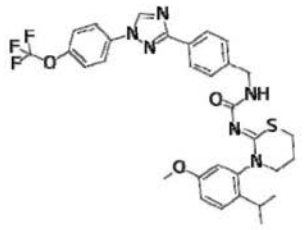
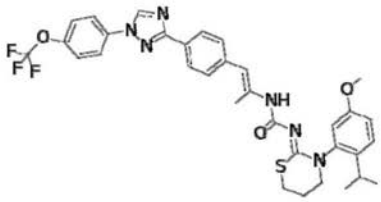
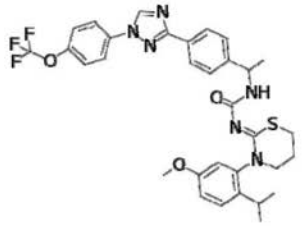
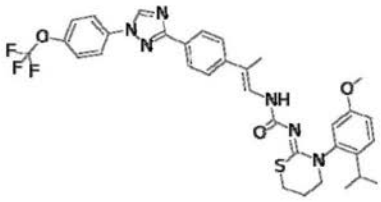
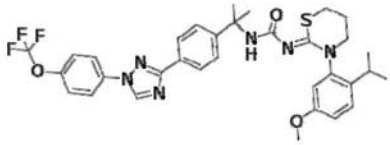
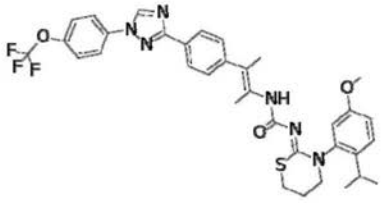
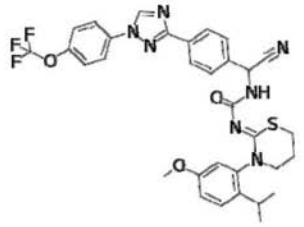
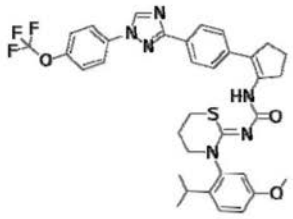
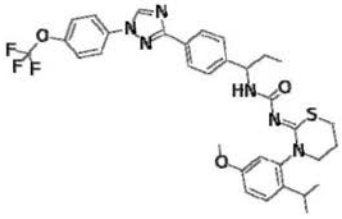
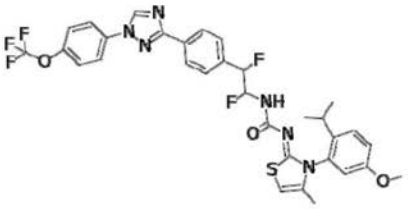
[1639]

 P736	 P737
 P738	 P739
 P740	 P741
 P742	 P743
 P744	 P745

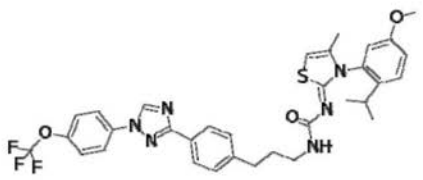
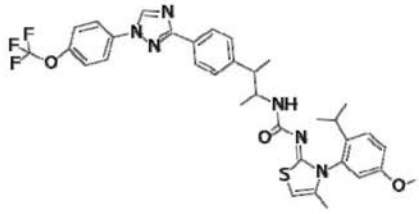
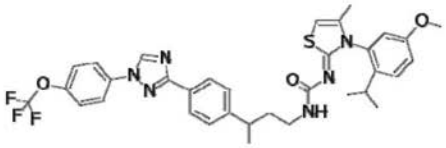
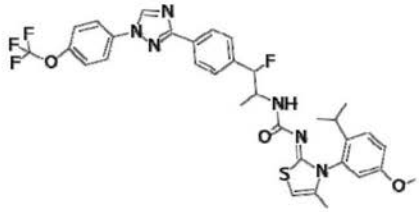
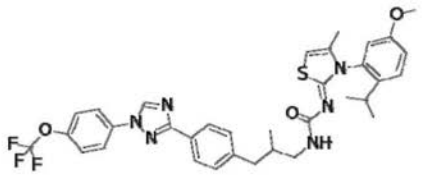
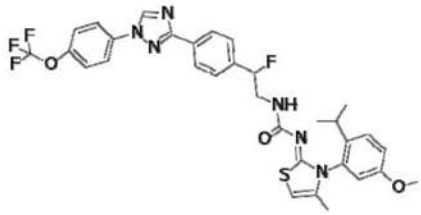
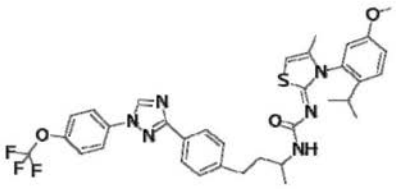
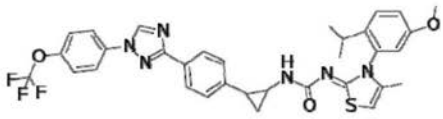
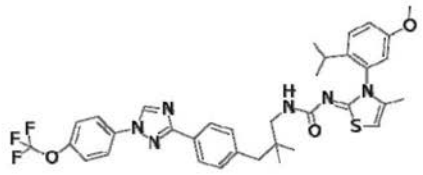
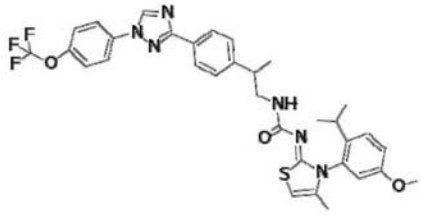
[1640]

 P746	 P747
 P748	 P749
 P750	 P751
 P752	 P753
 P754	 P755

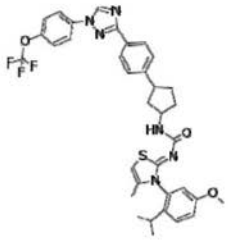
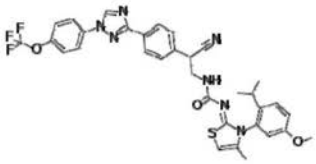
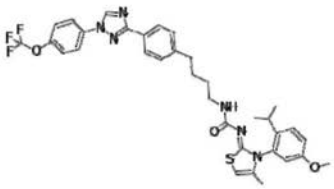
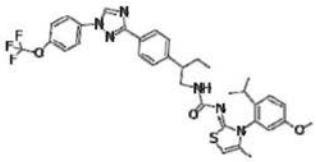
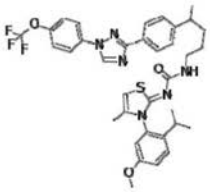
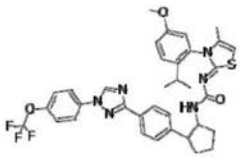
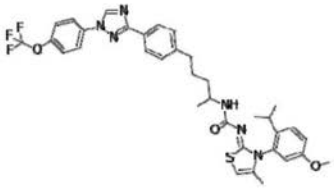
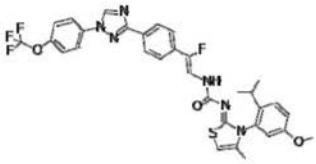
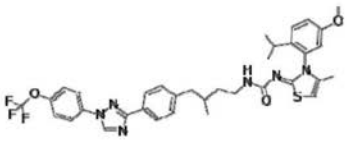
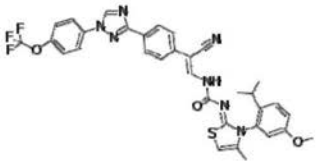
[1641]

 P756	 P757
 P758	 P759
 P760	 P761
 P762	 P763
 P764	 P765

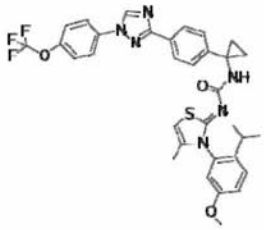
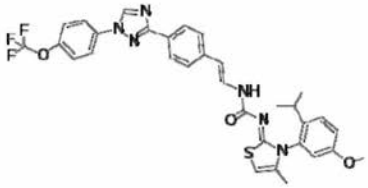
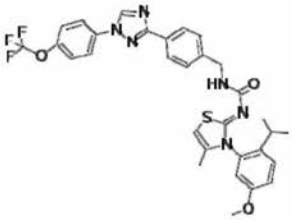
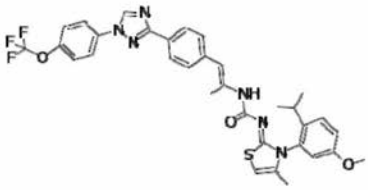
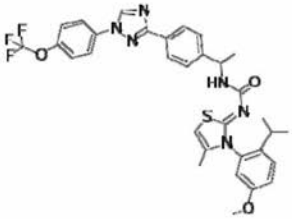
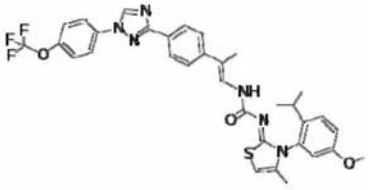
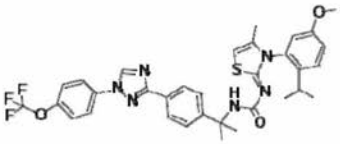
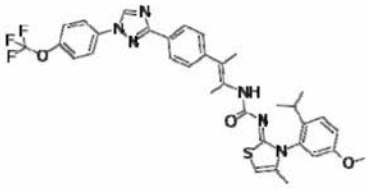
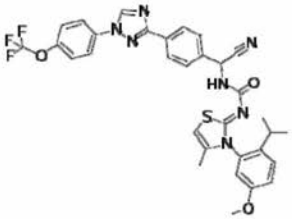
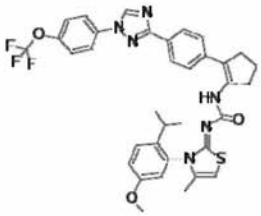
[1642]

 P766	 P767
 P768	 P769
 P770	 P771
 P772	 P773
 P774	 P775

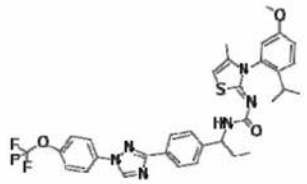
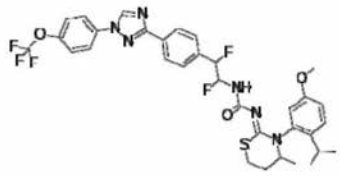
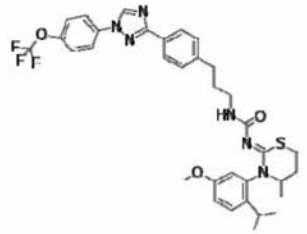
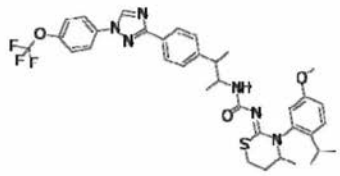
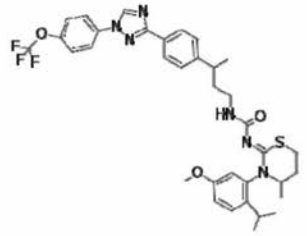
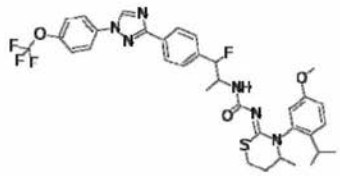
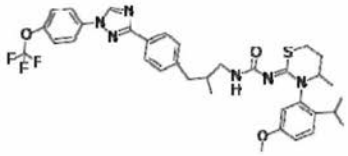
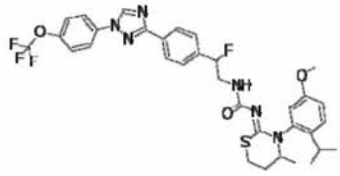
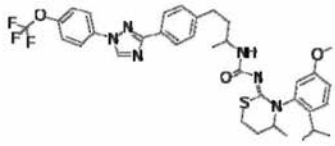
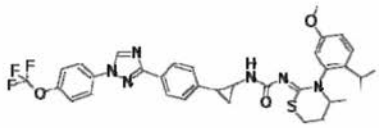
[1643]

 P776	 P777
 P778	 P779
 P780	 P781
 P782	 P783
 P784	 P785

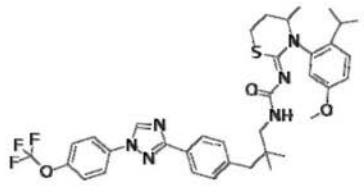
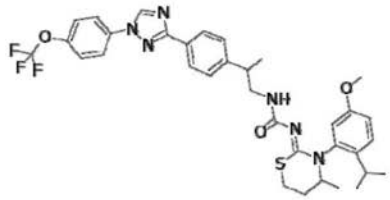
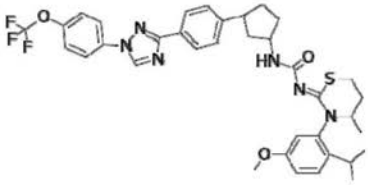
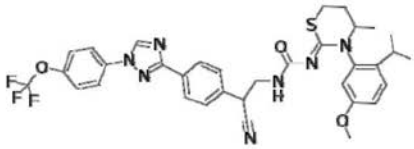
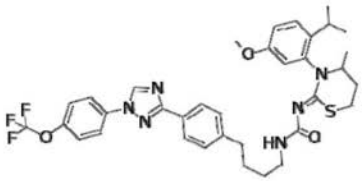
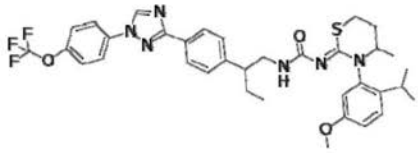
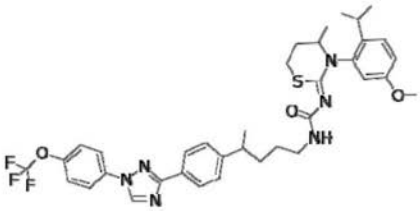
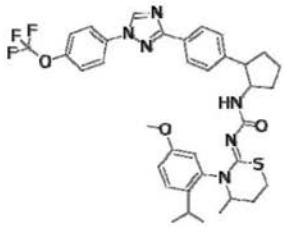
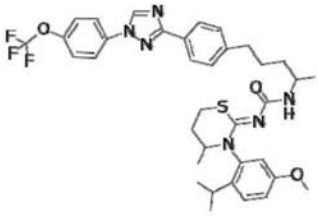
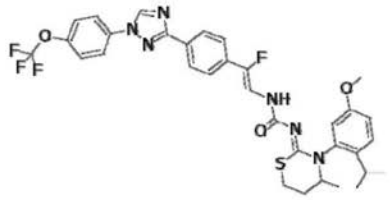
[1644]

 P786	 P787
 P788	 P789
 P790	 P791
 P792	 P793
 P794	 P795

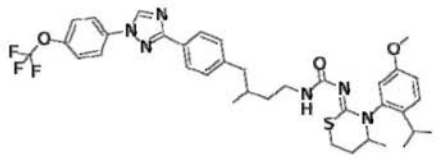
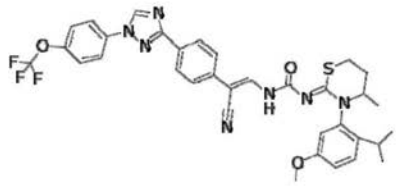
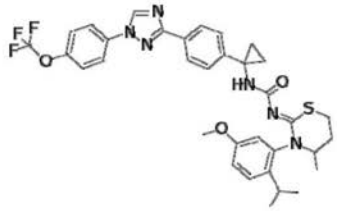
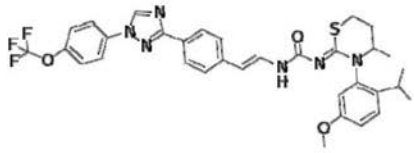
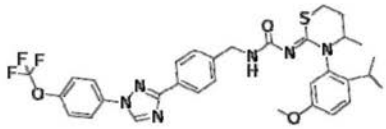
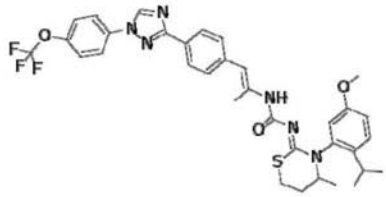
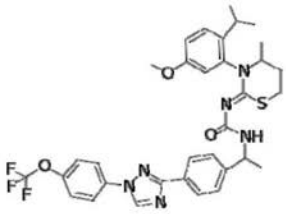
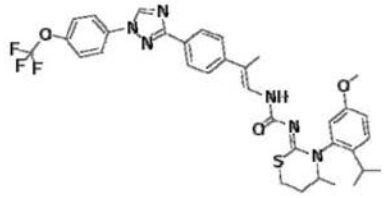
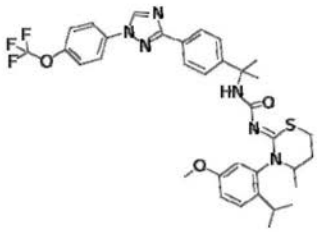
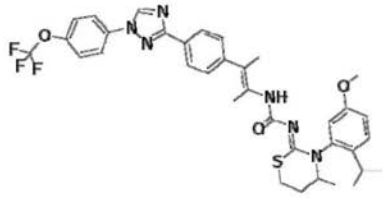
[1645]

 P796	 P797
 P798	 P799
 P800	 P801
 P802	 P803
 P804	 P805

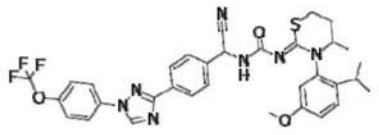
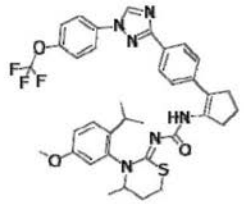
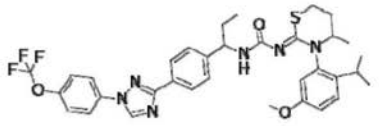
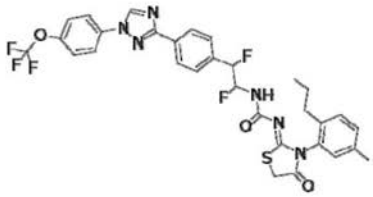
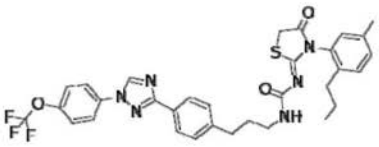
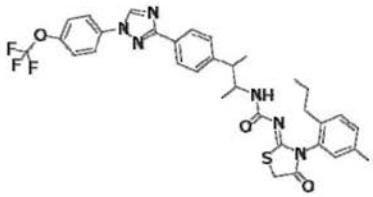
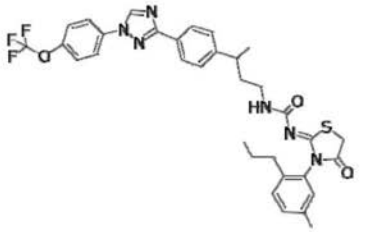
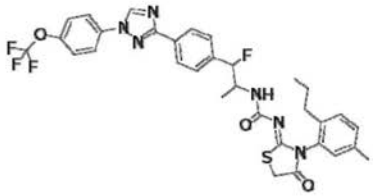
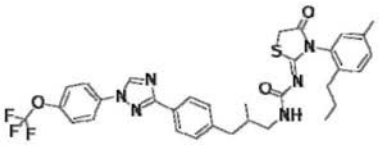
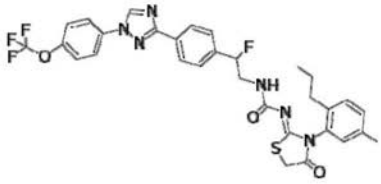
[1646]

 P806	 P807
 P808	 P809
 P810	 P811
 P812	 P813
 P814	 P815

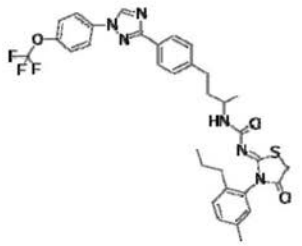
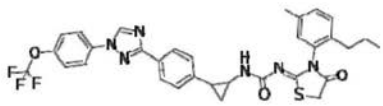
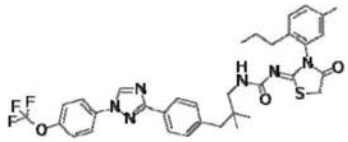
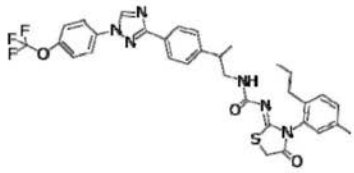
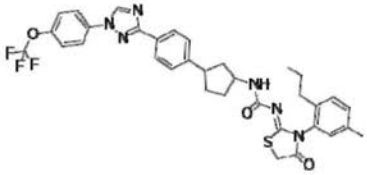
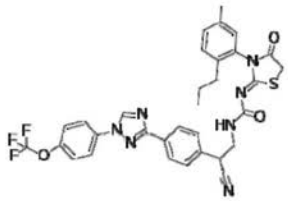
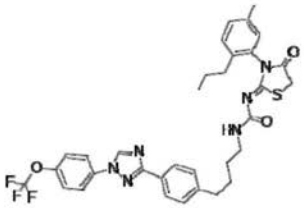
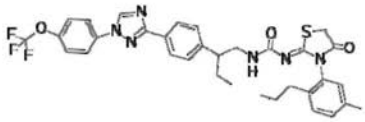
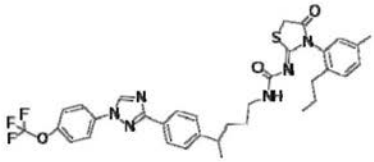
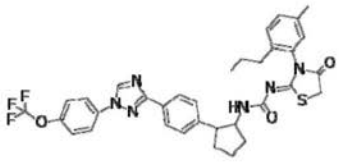
[1647]

 P816	 P817
 P818	 P819
 P820	 P821
 P822	 P823
 P824	 P825

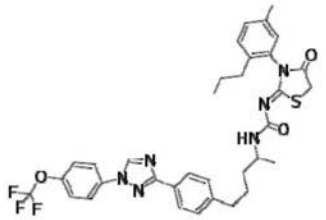
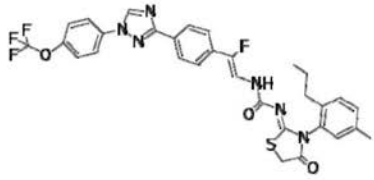
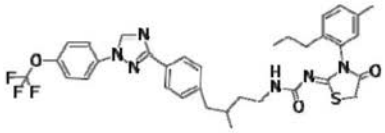
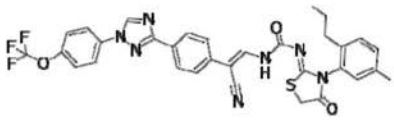
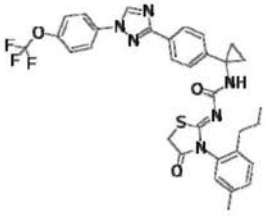
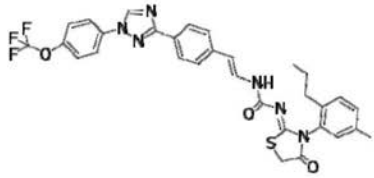
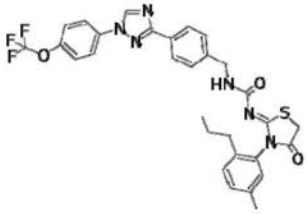
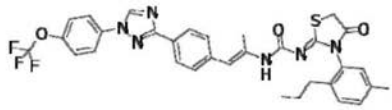
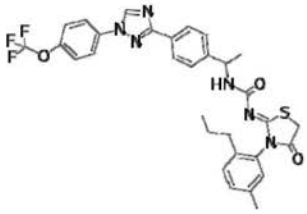
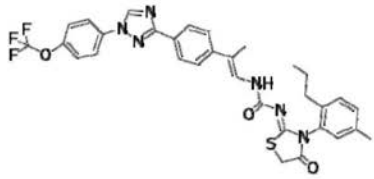
[1648]

 P826	 P827
 P828	 P829
 P830	 P831
 P832	 P833
 P834	 P835

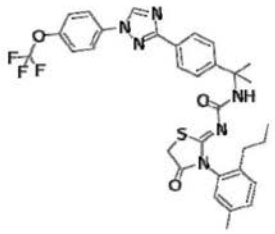
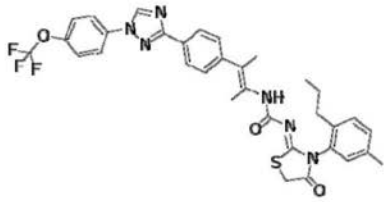
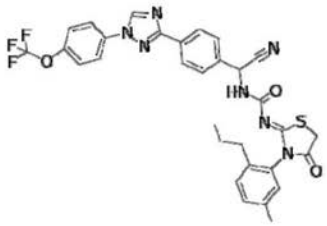
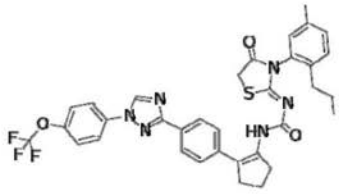
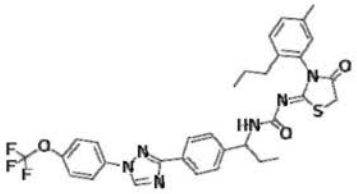
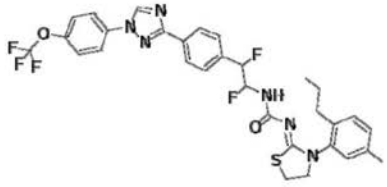
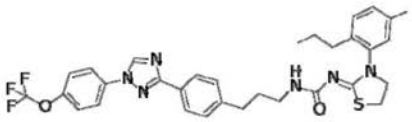
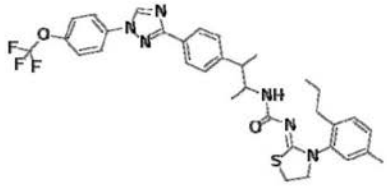
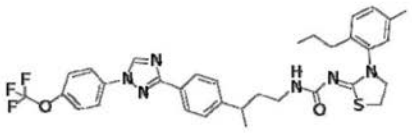
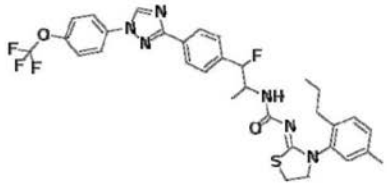
[1649]

 P836	 P837
 P838	 P839
 P840	 P841
 P842	 P843
 P844	 P845

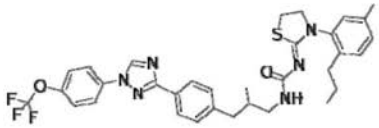
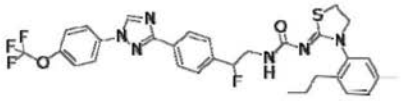
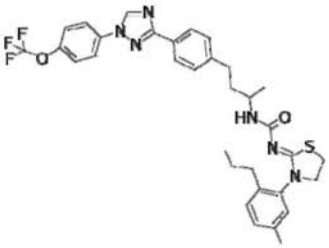
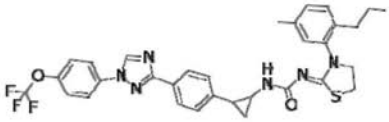
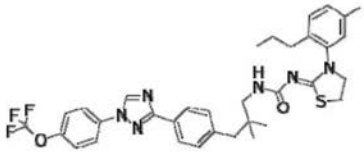
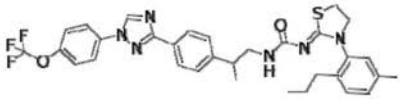
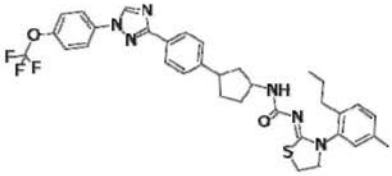
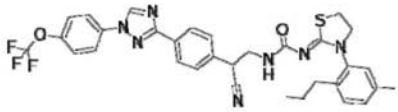
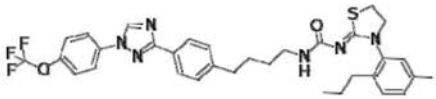
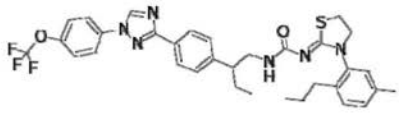
[1650]

 P846	 P847
 P848	 P849
 P850	 P851
 P852	 P853
 P854	 P855

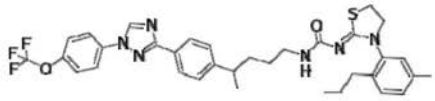
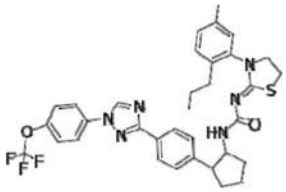
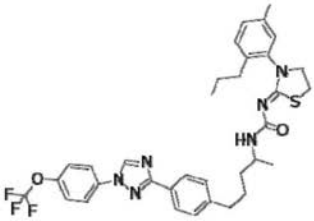
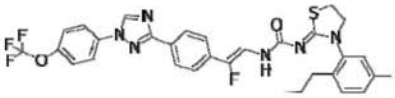
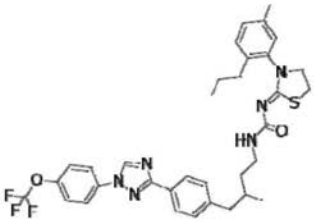
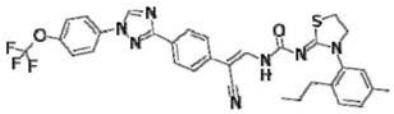
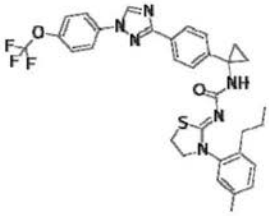
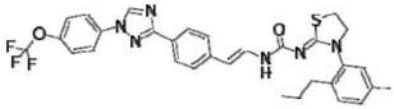
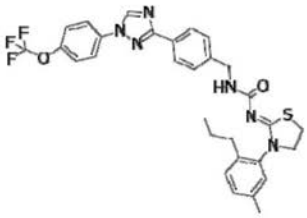
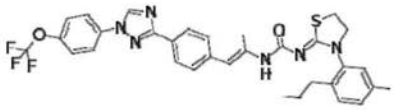
[1651]

 P856	 P857
 P858	 P859
 P860	 P861
 P862	 P863
 P864	 P865

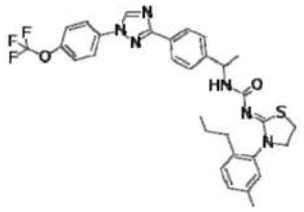
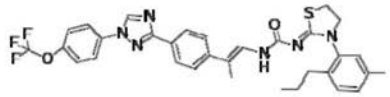
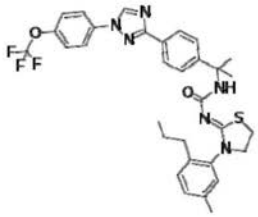
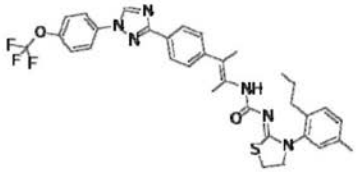
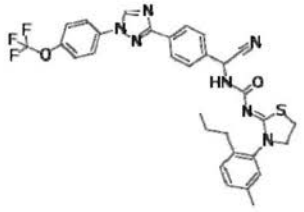
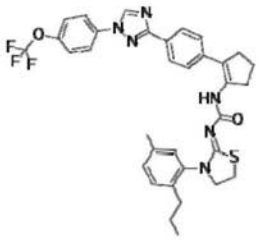
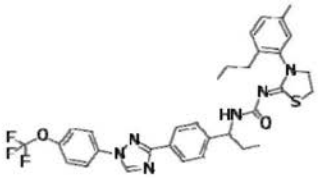
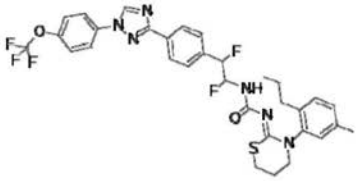
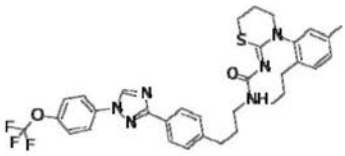
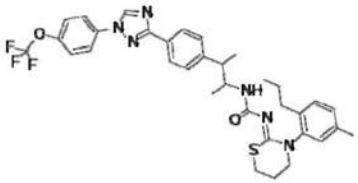
[1652]

 P866	 P867
 P868	 P869
 P870	 P871
 P872	 P873
 P874	 P875

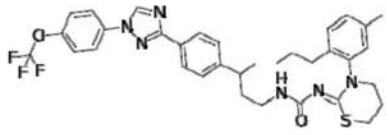
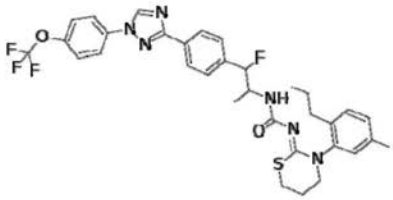
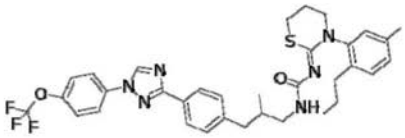
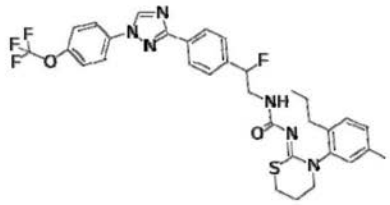
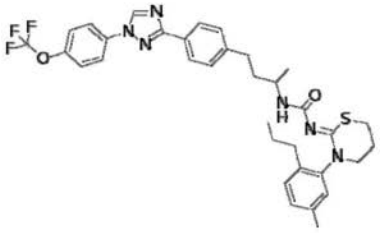
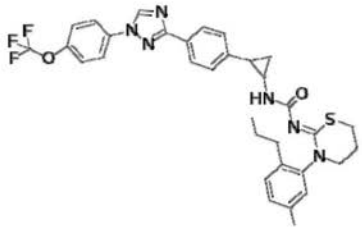
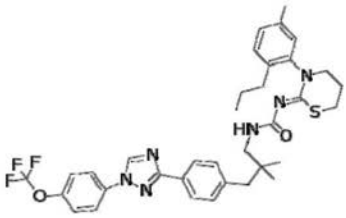
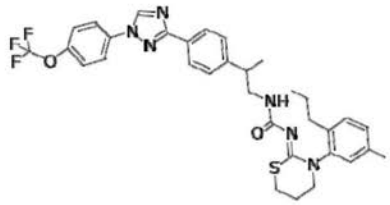
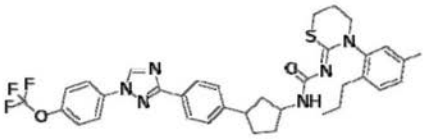
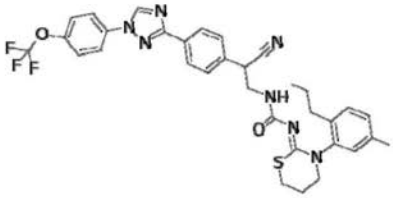
[1653]

 P876	 P877
 P878	 P879
 P880	 P881
 P882	 P883
 P884	 P885

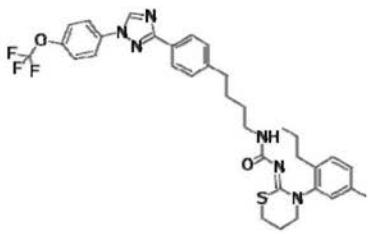
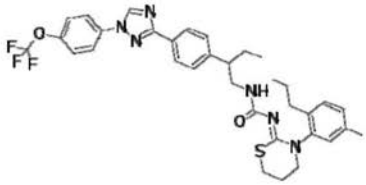
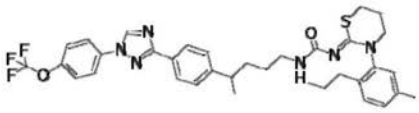
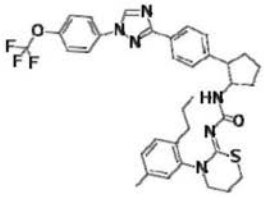
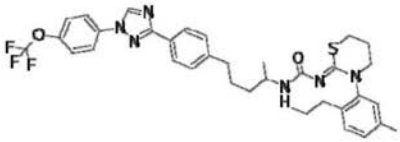
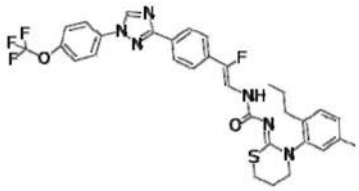
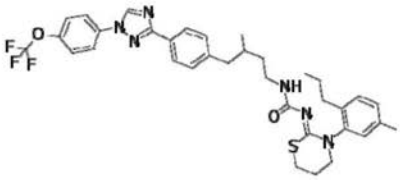
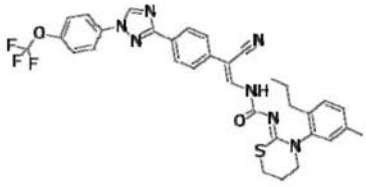
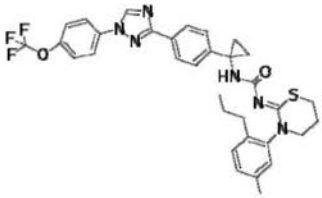
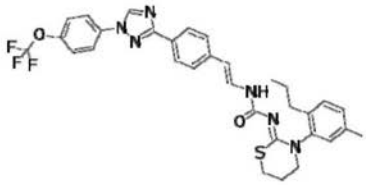
[1654]

 P886	 P887
 P888	 P889
 P890	 P891
 P892	 P893
 P894	 P895

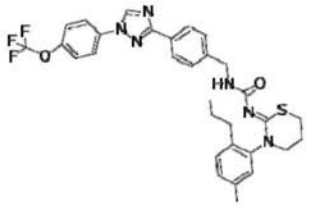
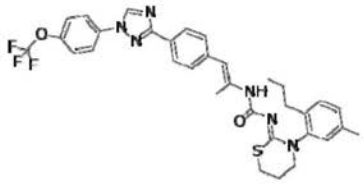
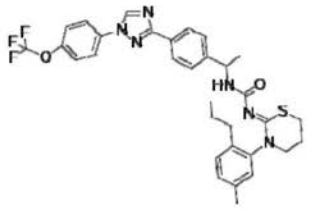
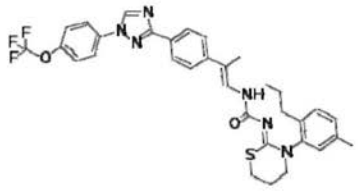
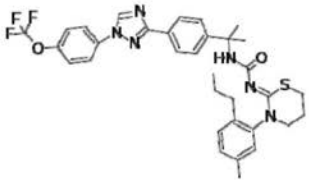
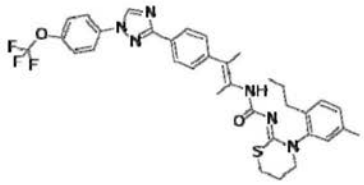
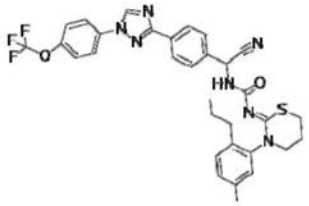
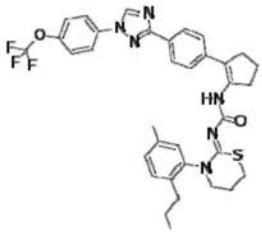
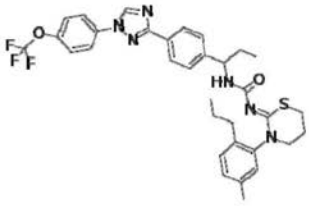
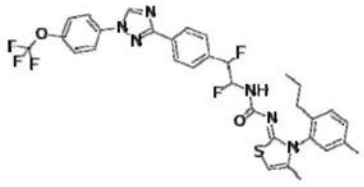
[1655]

 P896	 P897
 P898	 P899
 P900	 P901
 P902	 P903
 P904	 P905

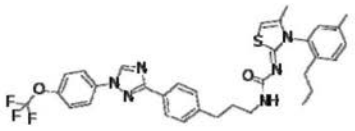
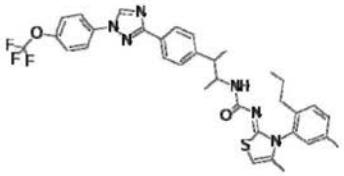
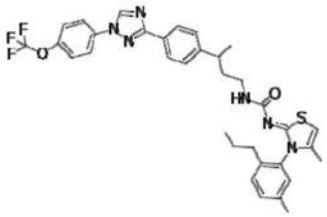
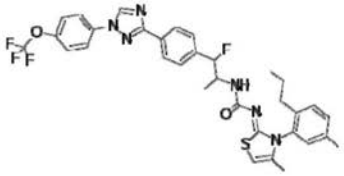
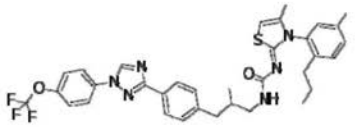
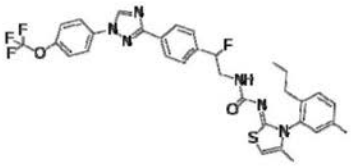
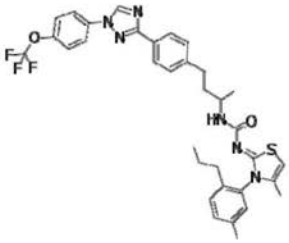
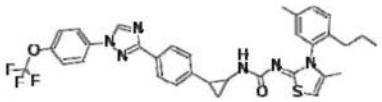
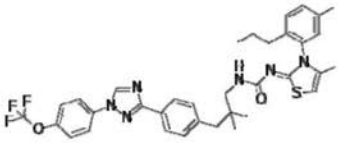
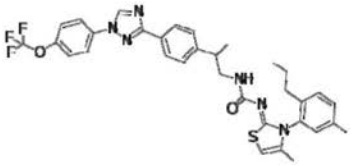
[1656]

 P906	 P907
 P908	 P909
 P910	 P911
 P912	 P913
 P914	 P915

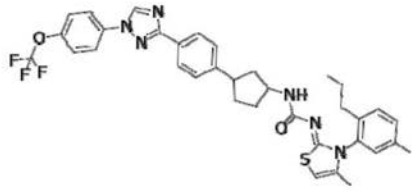
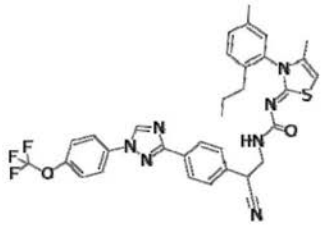
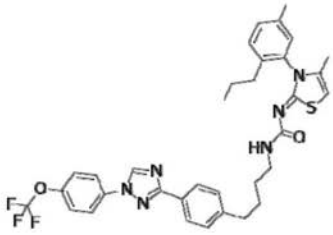
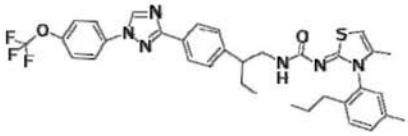
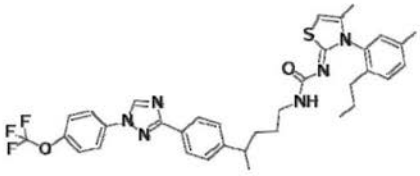
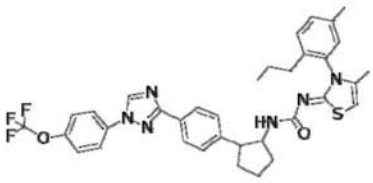
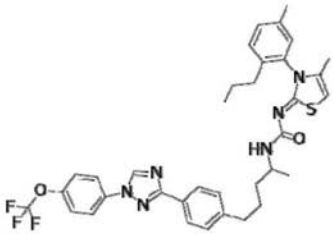
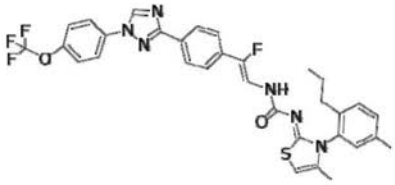
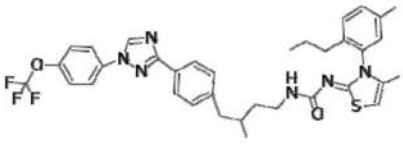
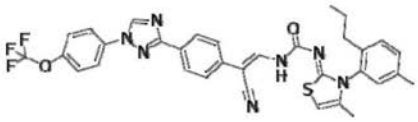
[1657]

 P916	 P917
 P918	 P919
 P920	 P921
 P922	 P923
 P924	 P925

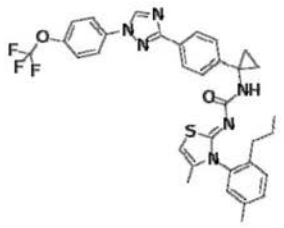
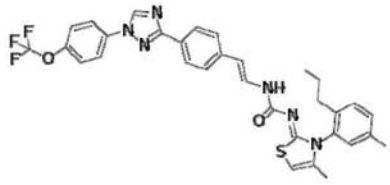
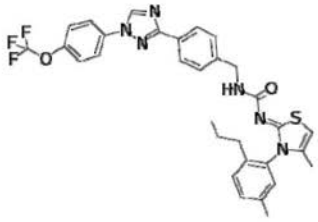
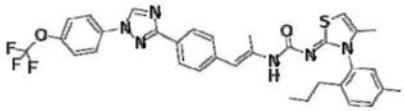
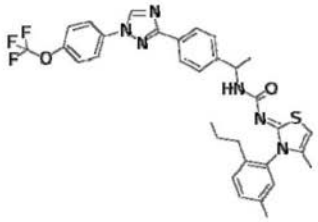
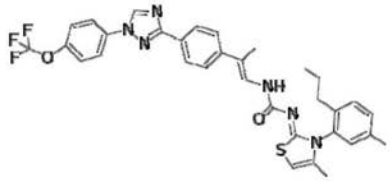
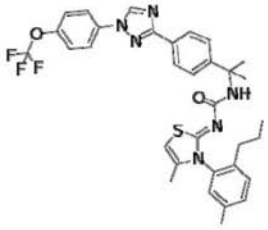
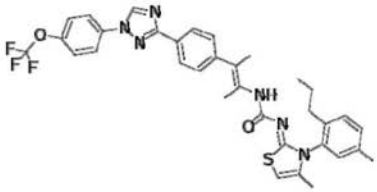
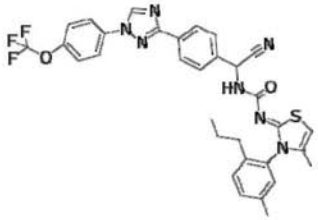
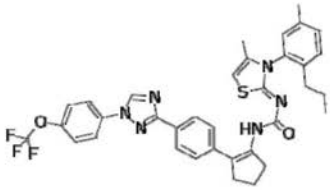
[1658]

 P926	 P927
 P928	 P929
 P930	 P931
 P932	 P933
 P934	 P935

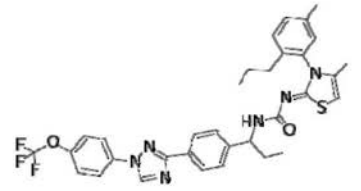
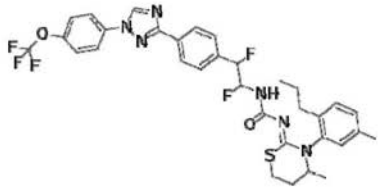
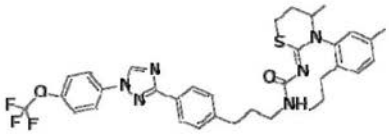
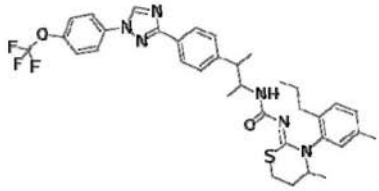
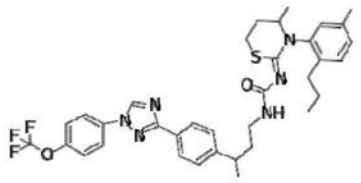
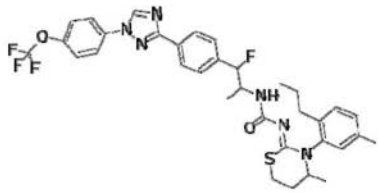
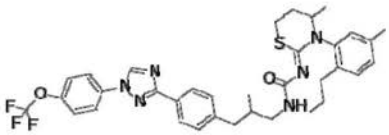
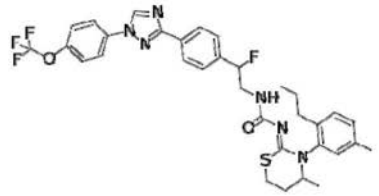
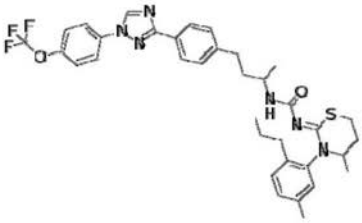
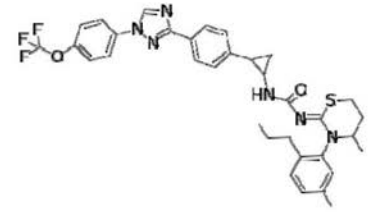
[1659]

 P936	 P937
 P938	 P939
 P940	 P941
 P942	 P943
 P944	 P945

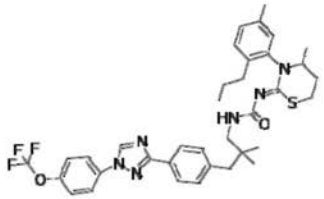
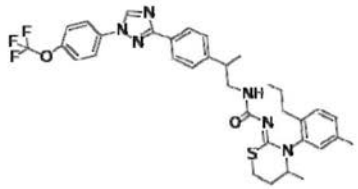
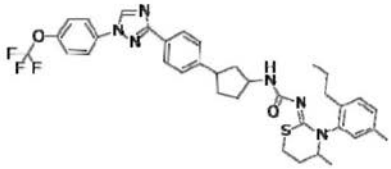
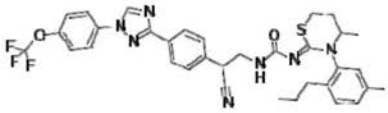
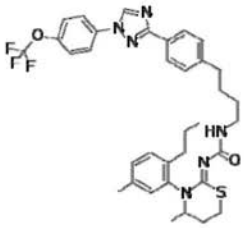
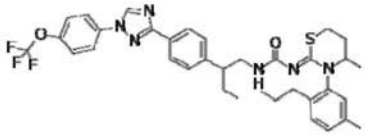
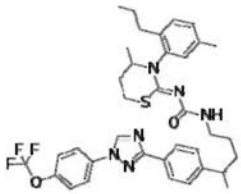
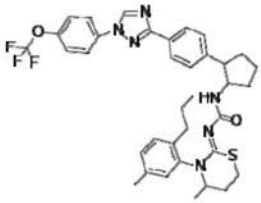
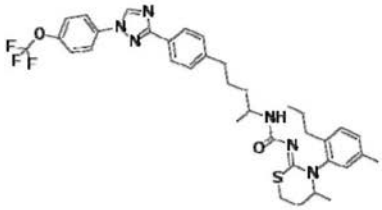
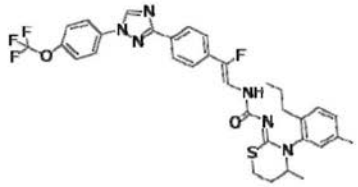
[1660]

 P946	 P947
 P948	 P949
 P950	 P951
 P952	 P953
 P954	 P955

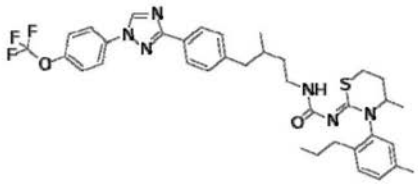
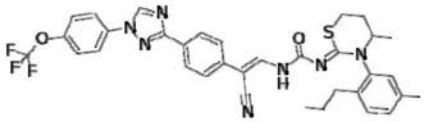
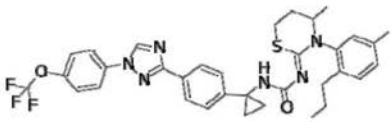
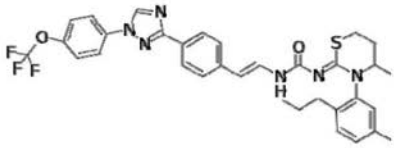
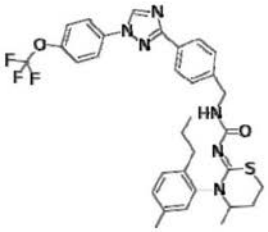
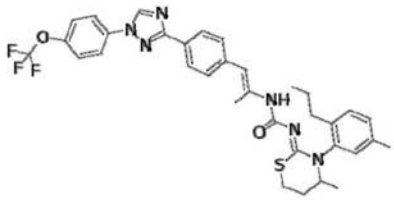
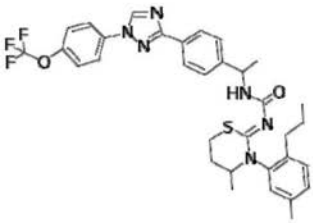
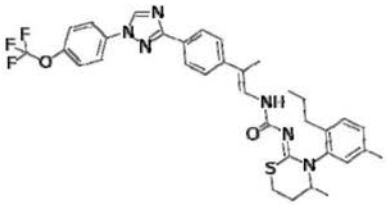
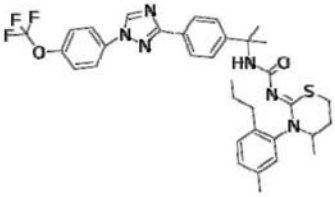
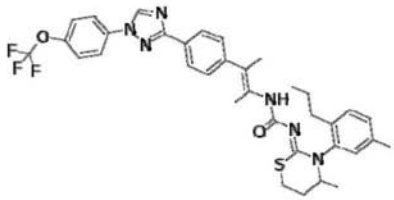
[1661]

 P956	 P957
 P958	 P959
 P960	 P961
 P962	 P963
 P964	 P965

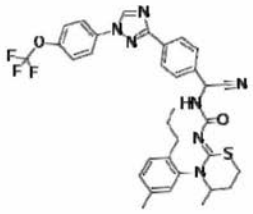
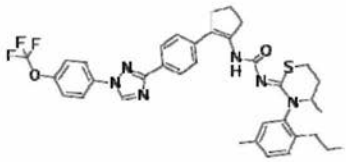
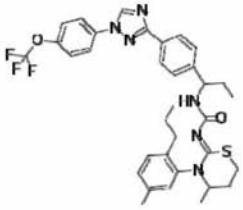
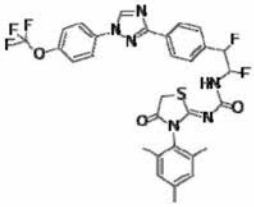
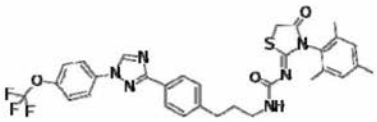
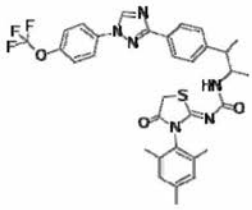
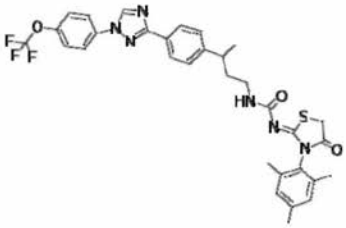
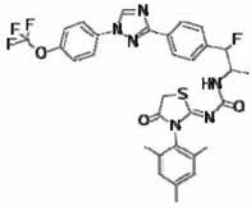
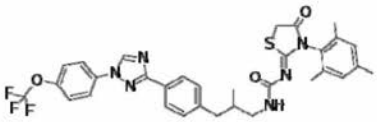
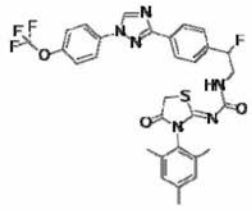
[1662]

 P966	 P967
 P968	 P969
 P970	 P971
 P972	 P973
 P974	 P975

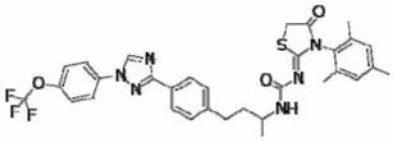
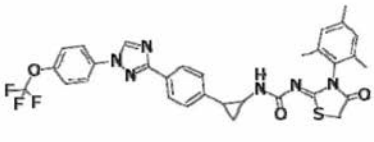
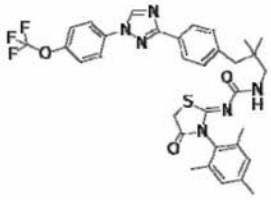
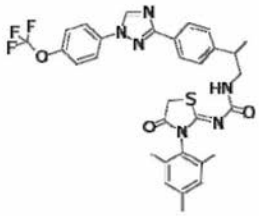
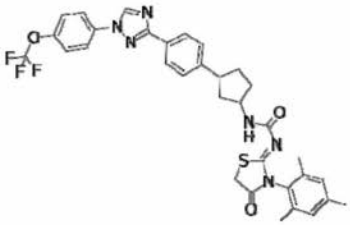
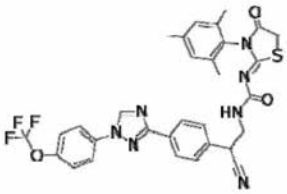
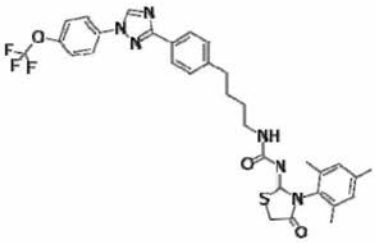
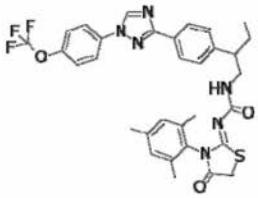
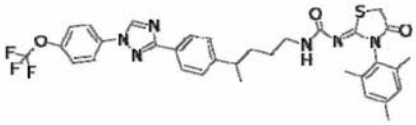
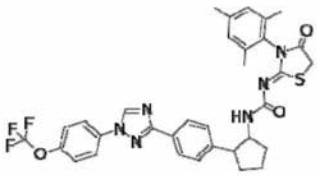
[1663]

 P976	 P977
 P978	 P979
 P980	 P981
 P982	 P983
 P984	 P985

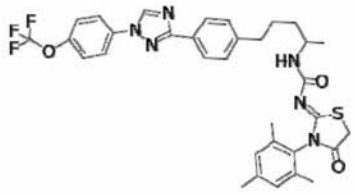
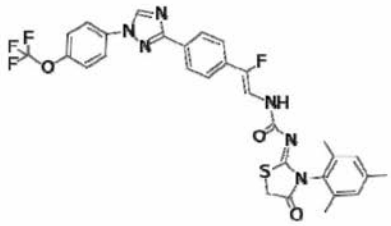
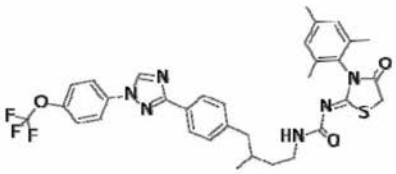
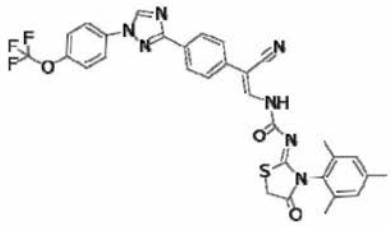
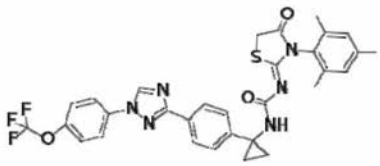
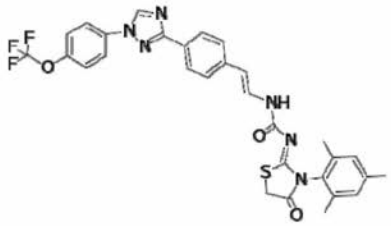
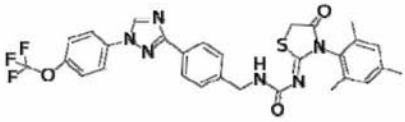
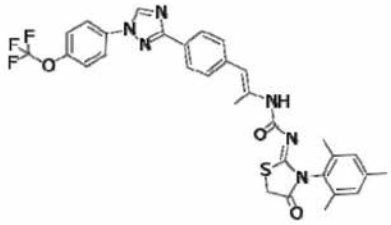
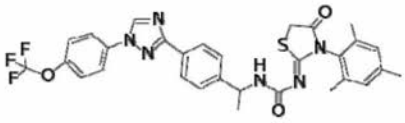
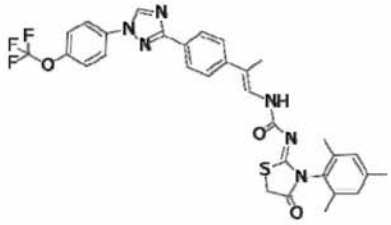
[1664]

 P986	 P987
 P988	 P989
 P990	 P991
 P992	 P993
 P994	 P995

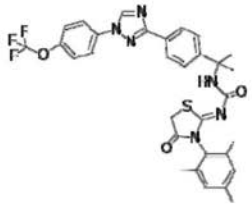
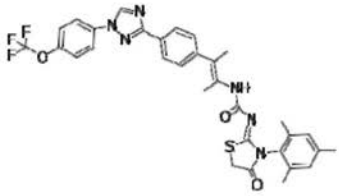
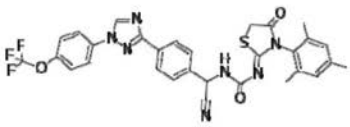
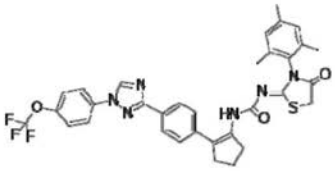
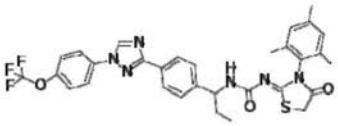
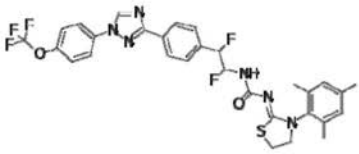
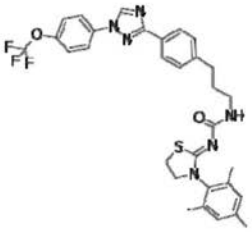
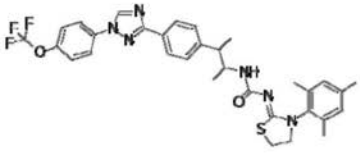
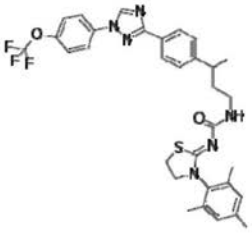
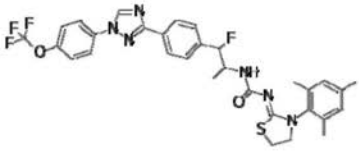
[1665]

 P996	 P997
 P998	 P999
 P1000	 P1001
 P1002	 P1003
 P1004	 P1005

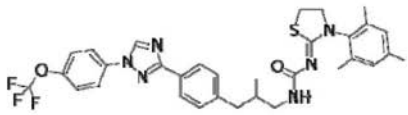
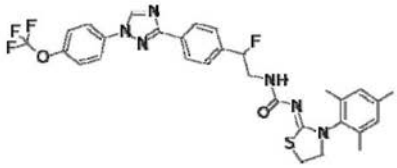
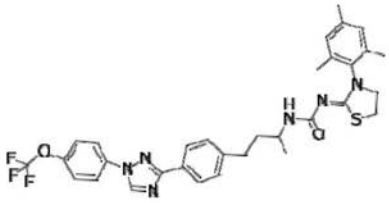
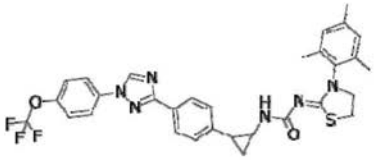
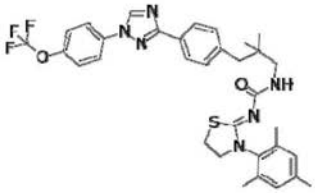
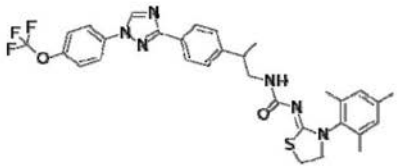
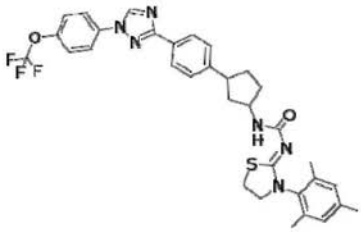
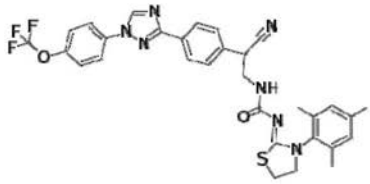
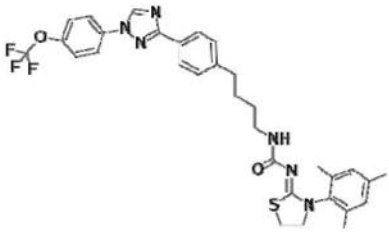
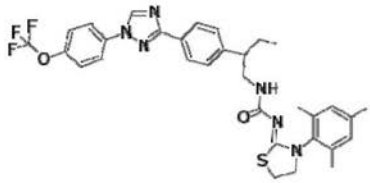
[1666]

 P1006	 P1007
 P1008	 P1009
 P1010	 P1011
 P1012	 P1013
 P1014	 P1015

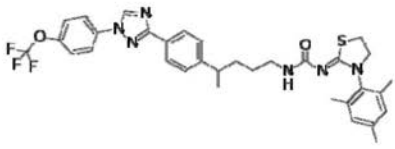
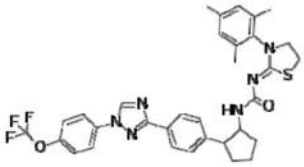
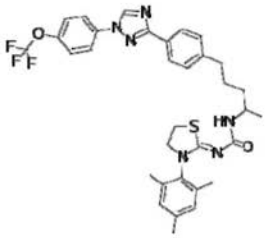
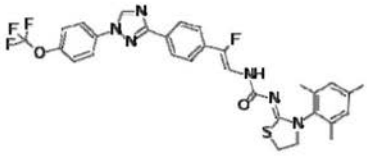
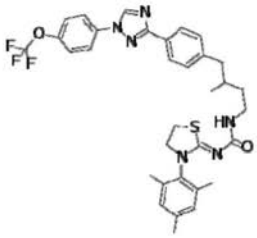
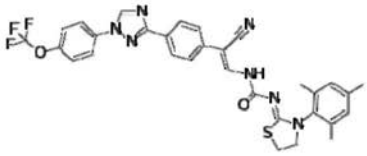
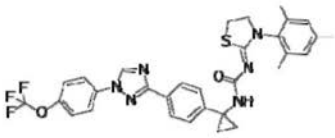
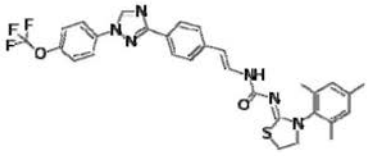
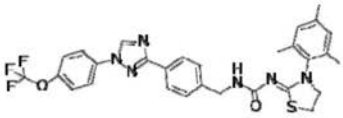
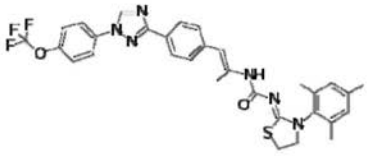
[1667]

 P1016	 P1017
 P1018	 P1019
 P1020	 P1021
 P1022	 P1023
 P1024	 P1025

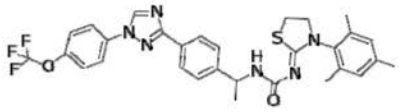
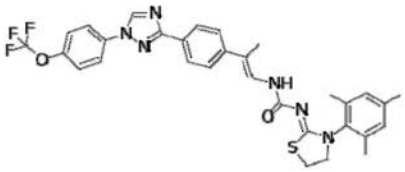
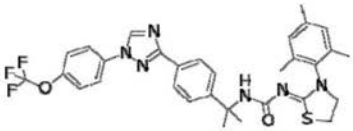
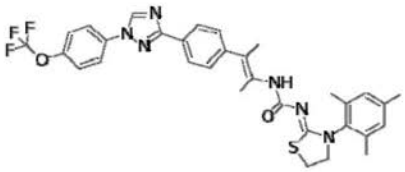
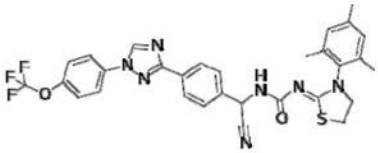
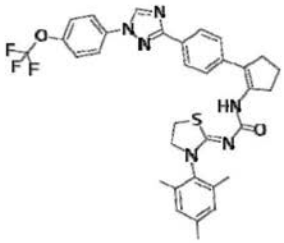
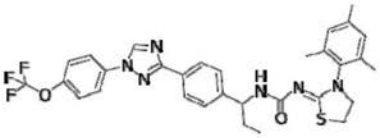
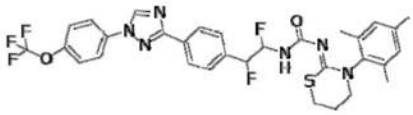
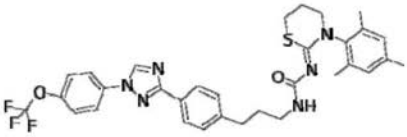
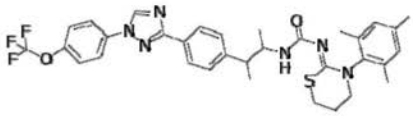
[1668]

 P1026	 P1027
 P1028	 P1029
 P1030	 P1031
 P1032	 P1033
 P1034	 P1035

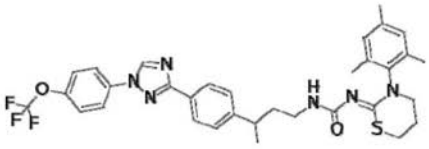
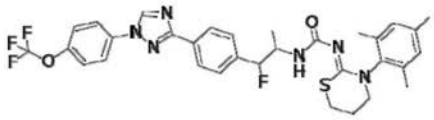
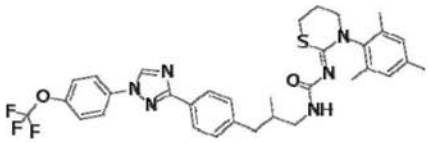
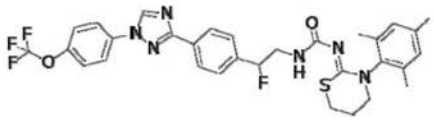
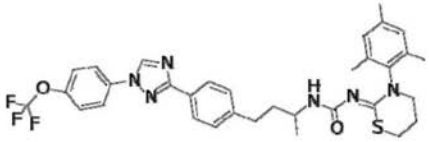
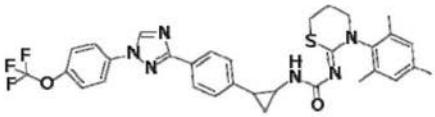
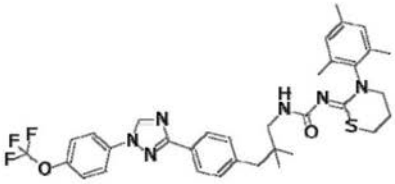
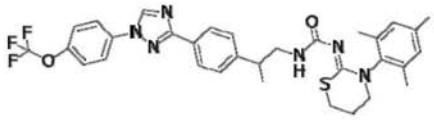
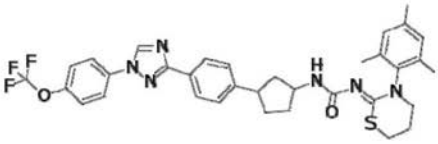
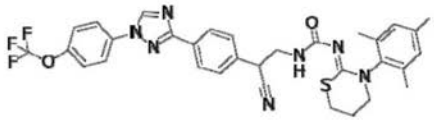
[1669]

 P1036	 P1037
 P1038	 P1039
 P1040	 P1041
 P1042	 P1043
 P1044	 P1045

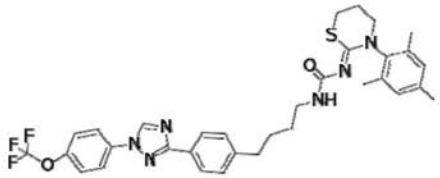
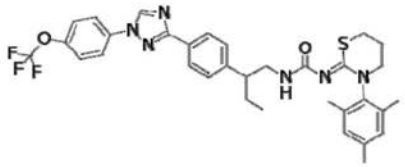
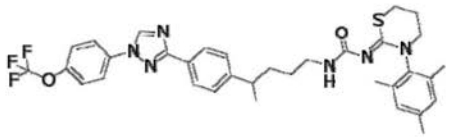
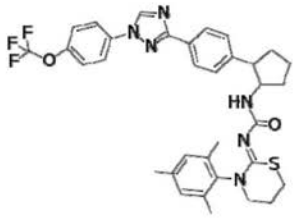
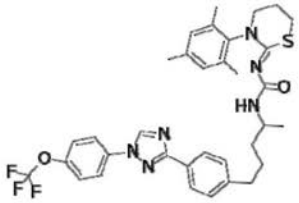
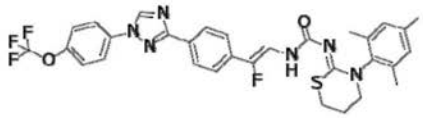
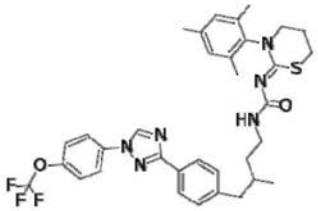
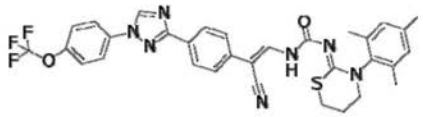
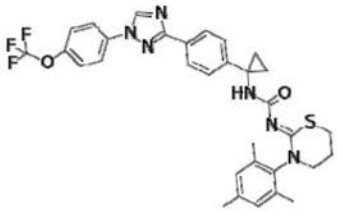
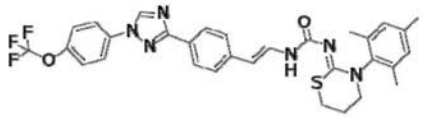
[1670]

 P1046	 P1047
 P1048	 P1049
 P1050	 P1051
 P1052	 P1053
 P1054	 P1055

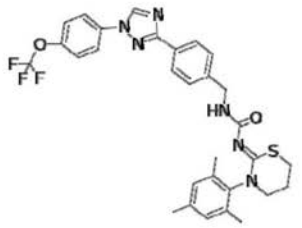
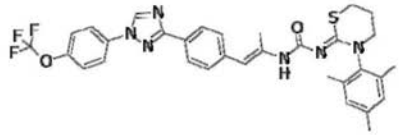
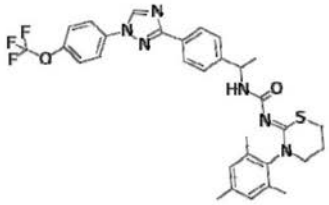
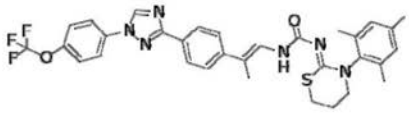
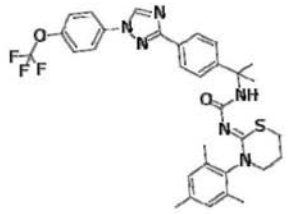
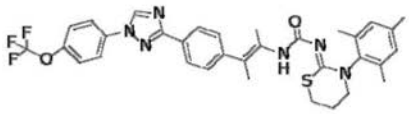
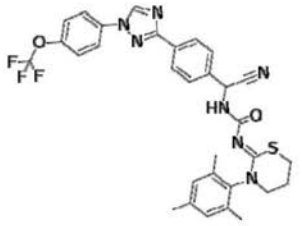
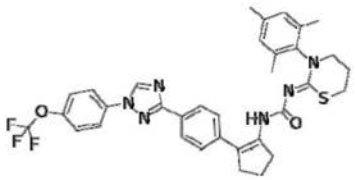
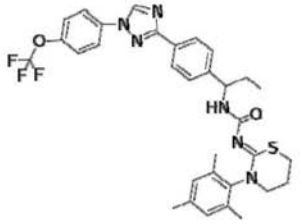
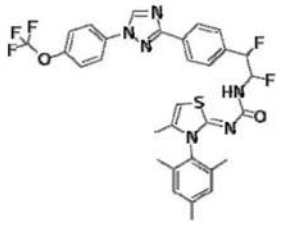
[1671]

 P1056	 P1057
 P1058	 P1059
 P1060	 P1061
 P1062	 P1063
 P1064	 P1065

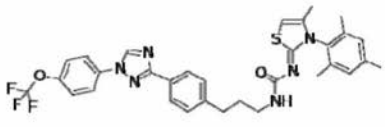
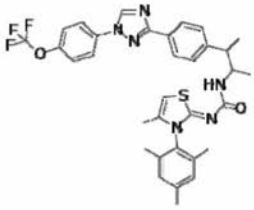
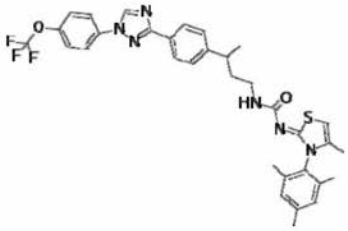
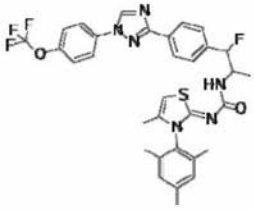
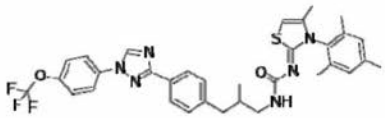
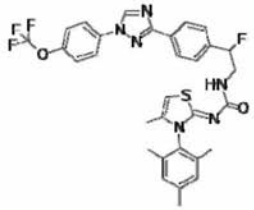
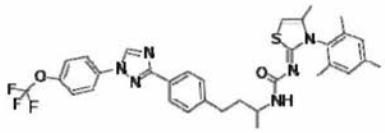
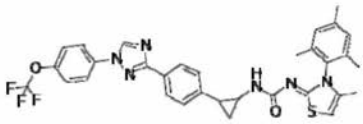
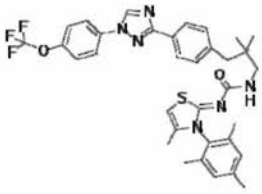
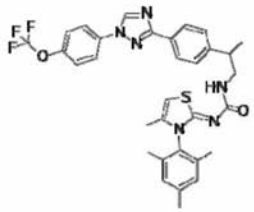
[1672]

 P1066	 P1067
 P1068	 P1069
 P1070	 P1071
 P1072	 P1073
 P1074	 P1075

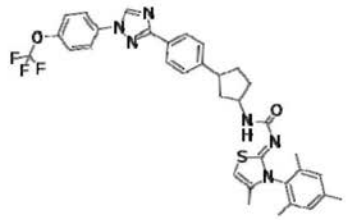
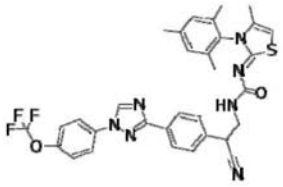
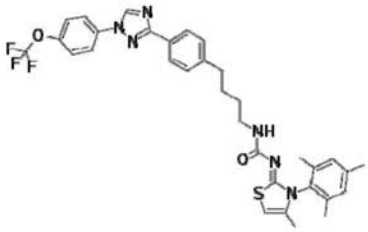
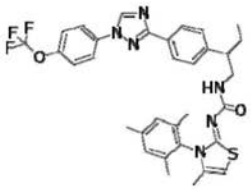
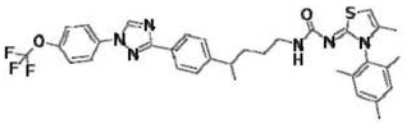
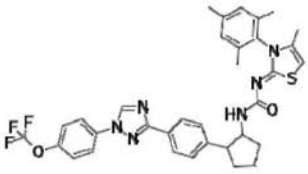
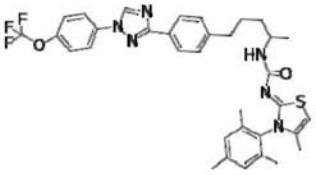
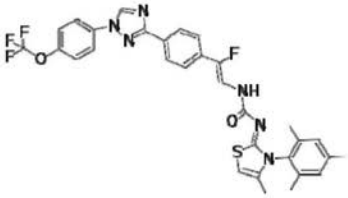
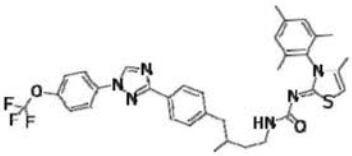
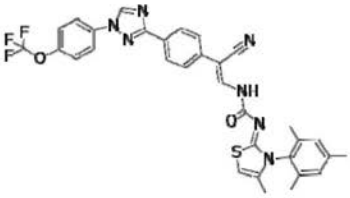
[1673]

 P1076	 P1077
 P1078	 P1079
 P1080	 P1081
 P1082	 P1083
 P1084	 P1085

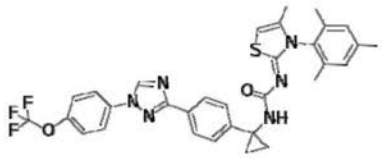
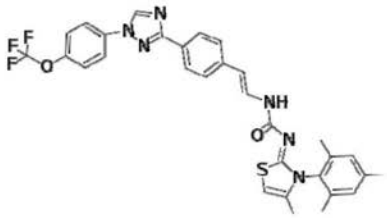
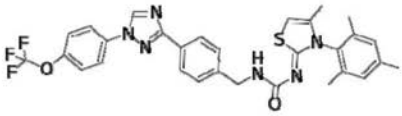
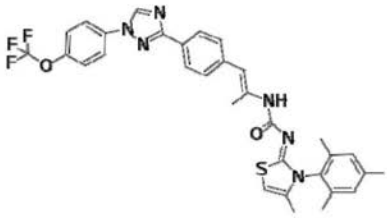
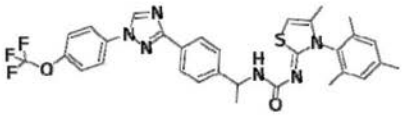
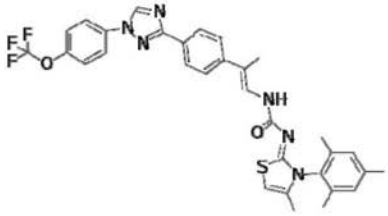
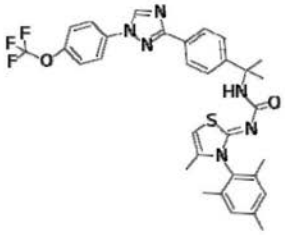
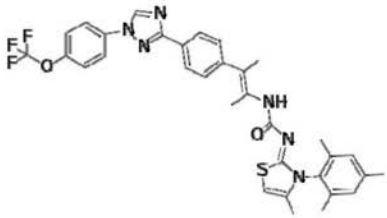
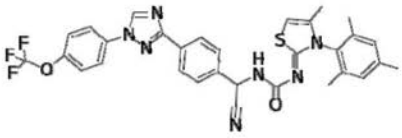
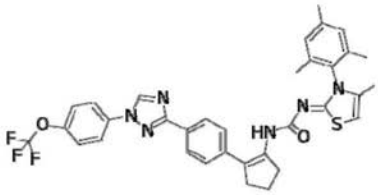
[1674]

 P1086	 P1087
 P1088	 P1089
 P1090	 P1091
 P1092	 P1093
 P1094	 P1095

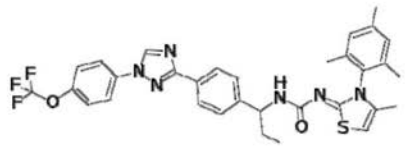
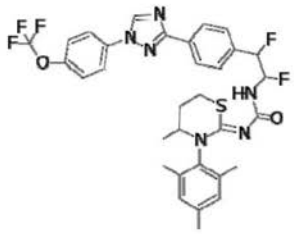
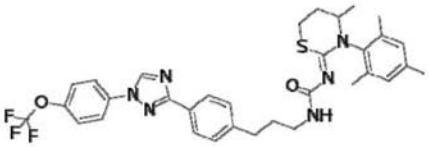
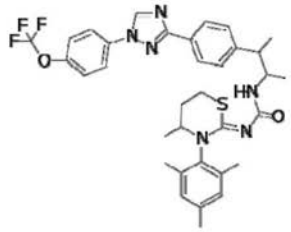
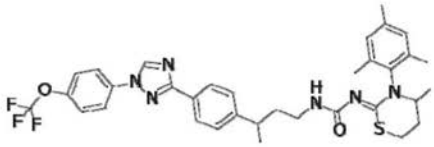
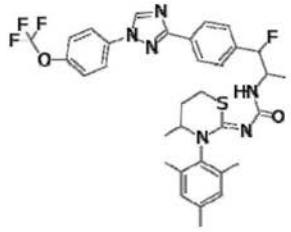
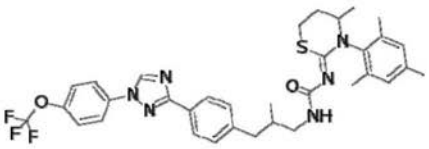
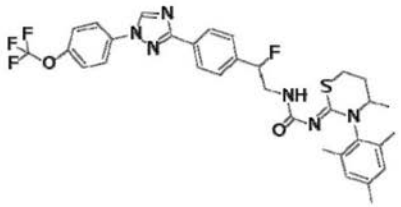
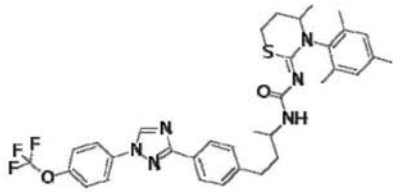
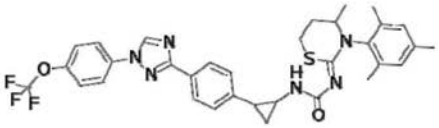
[1675]

 P1096	 P1097
 P1098	 P1099
 P1100	 P1101
 P1102	 P1103
 P1104	 P1105

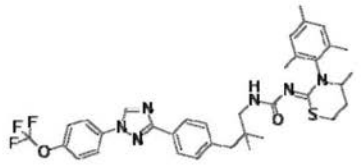
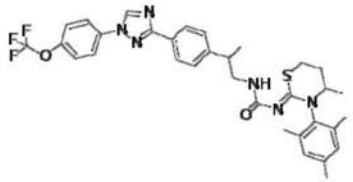
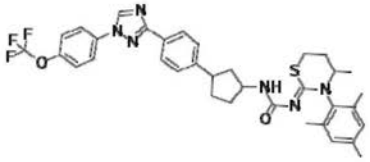
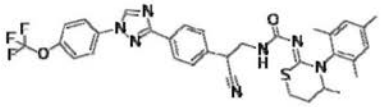
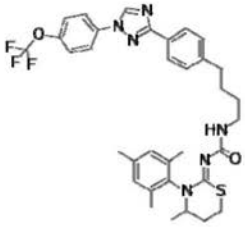
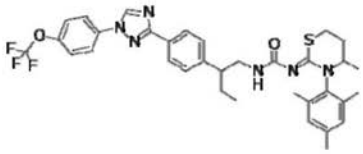
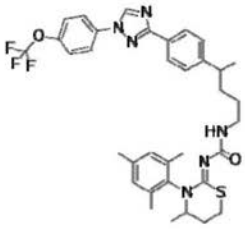
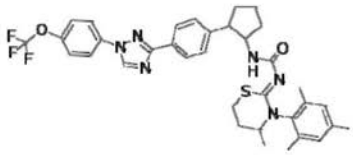
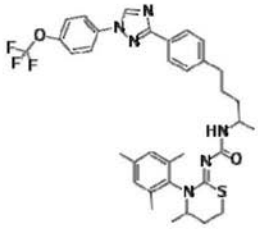
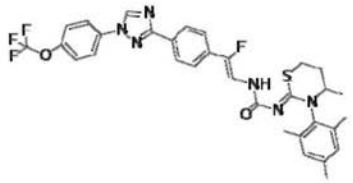
[1676]

 P1106	 P1107
 P1108	 P1109
 P1110	 P1111
 P1112	 P1113
 P1114	 P1115

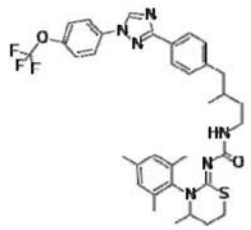
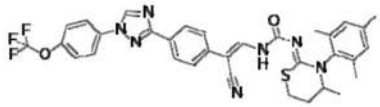
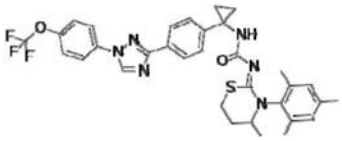
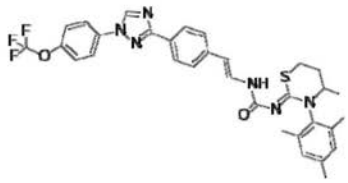
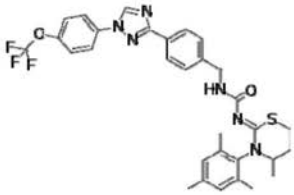
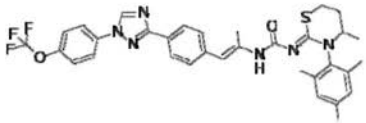
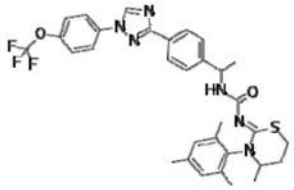
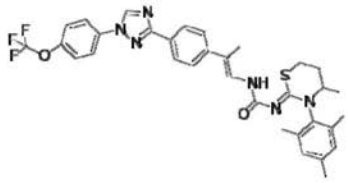
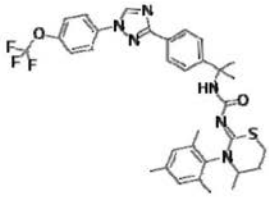
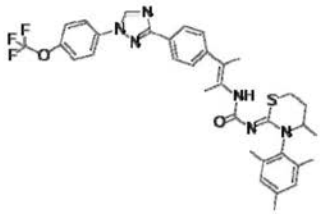
[1677]

 P1116	 P1117
 P1118	 P1119
 P1120	 P1121
 P1122	 P1123
 P1124	 P1125

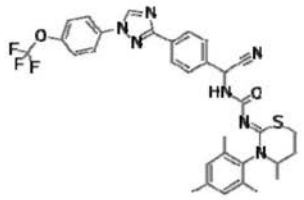
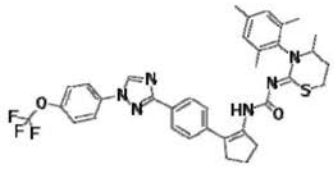
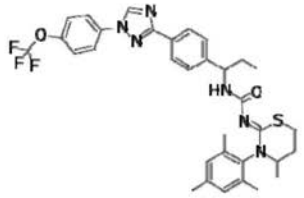
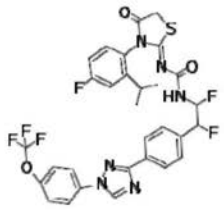
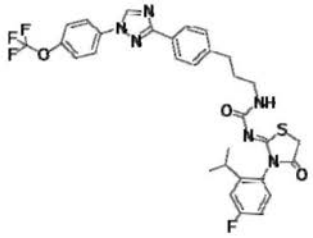
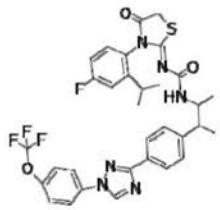
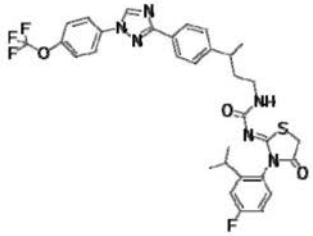
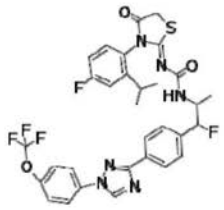
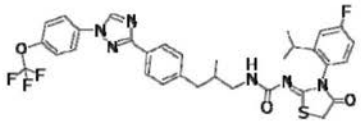
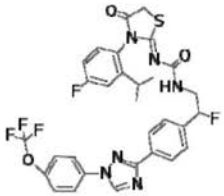
[1678]

 P1126	 P1127
 P1128	 P1129
 P1130	 P1131
 P1132	 P1133
 P1134	 P1135

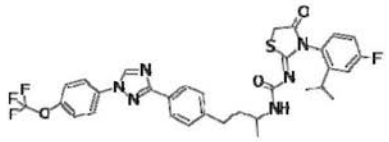
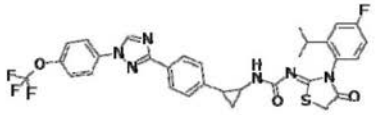
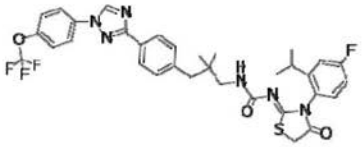
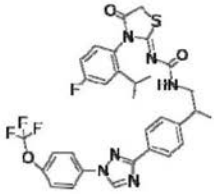
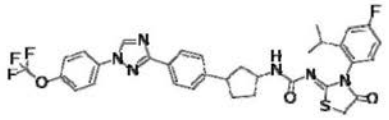
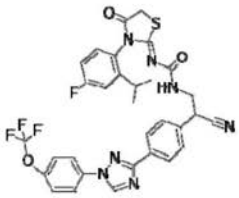
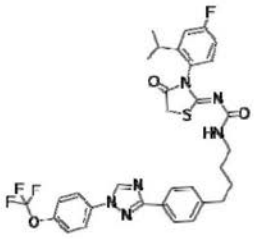
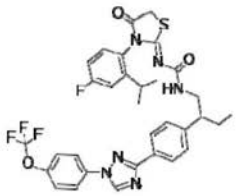
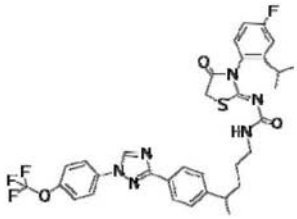
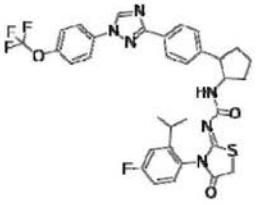
[1679]

 P1136	 P1137
 P1138	 P1139
 P1140	 P1141
 P1142	 P1143
 P1144	 P1145

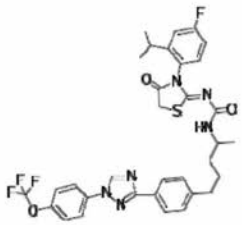
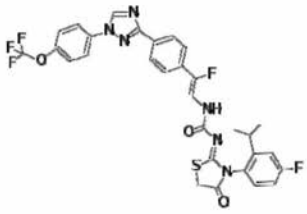
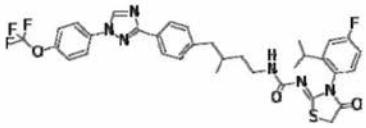
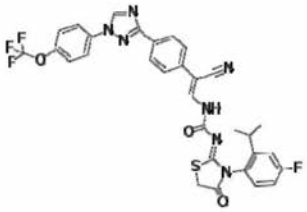
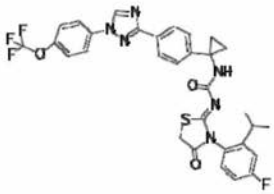
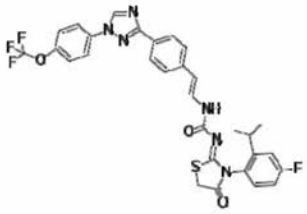
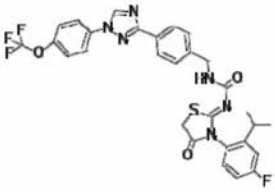
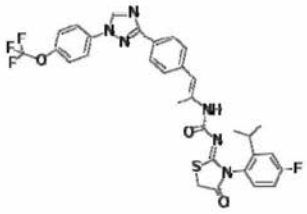
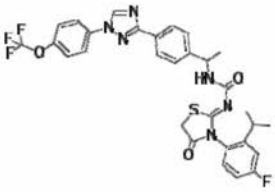
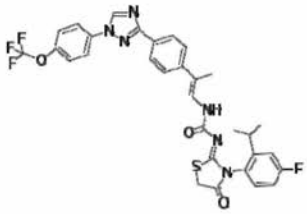
[1680]

 P1146	 P1147
 P1148	 P1149
 P1150	 P1151
 P1152	 P1153
 P1154	 P1155

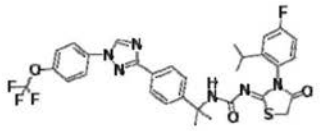
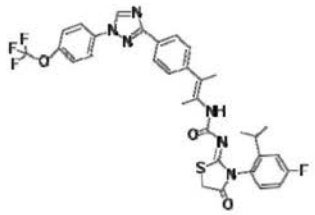
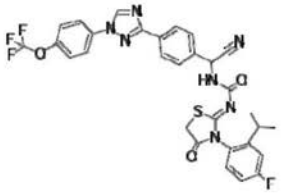
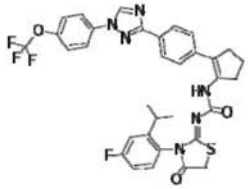
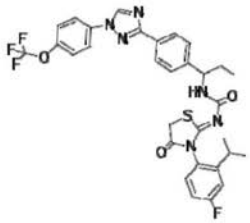
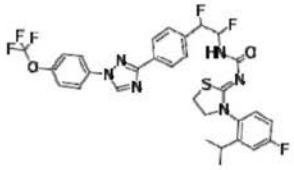
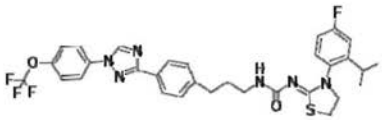
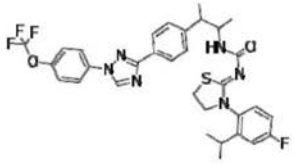
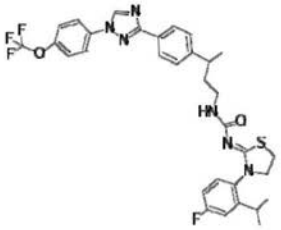
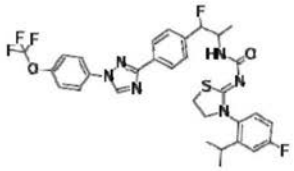
[1681]

 P1156	 P1157
 P1158	 P1159
 P1160	 P1161
 P1162	 P1163
 P1164	 P1165

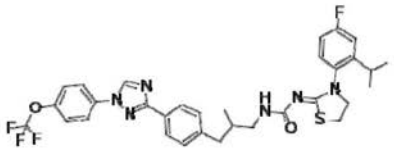
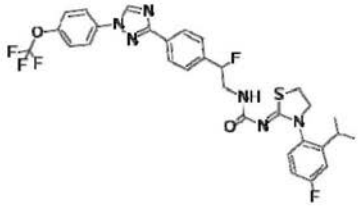
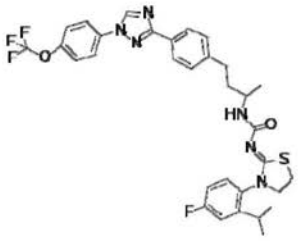
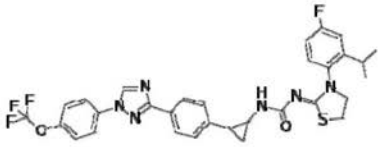
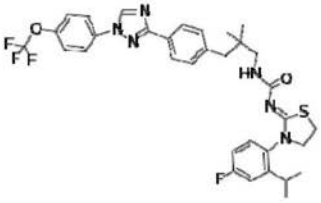
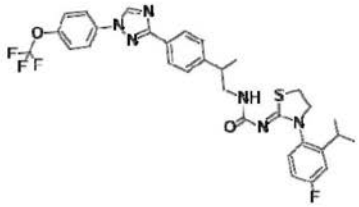
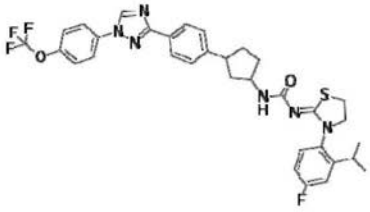
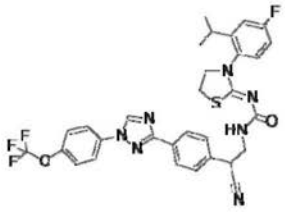
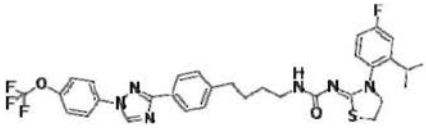
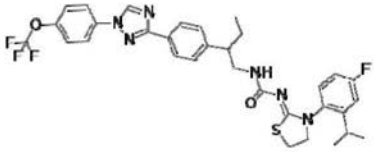
[1682]

 P1166	 P1167
 P1168	 P1169
 P1170	 P1171
 P1172	 P1173
 P1174	 P1175

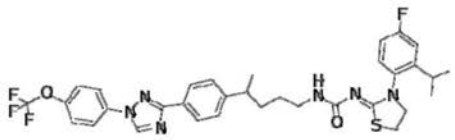
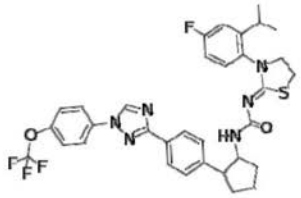
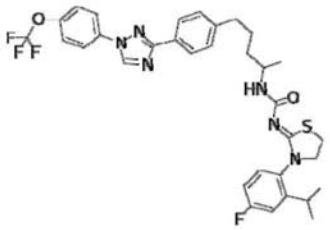
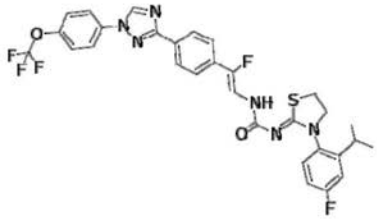
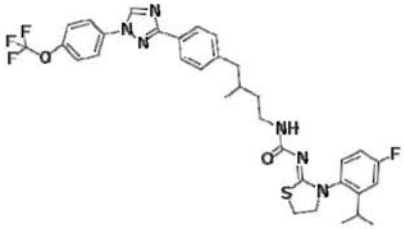
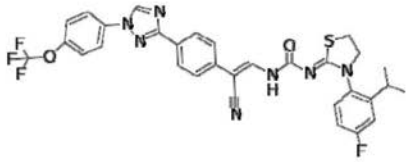
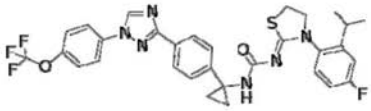
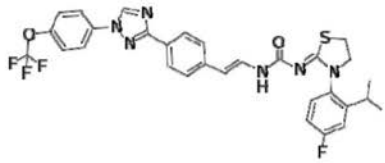
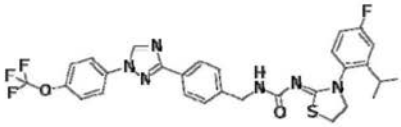
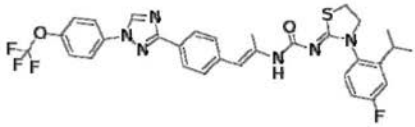
[1683]

 P1176	 P1177
 P1178	 P1179
 P1180	 P1181
 P1182	 P1183
 P1184	 P1185

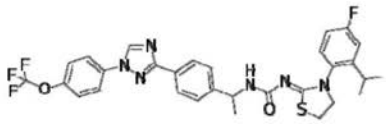
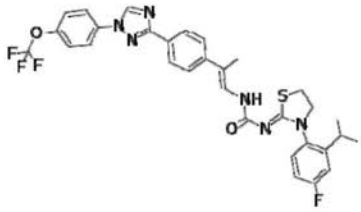
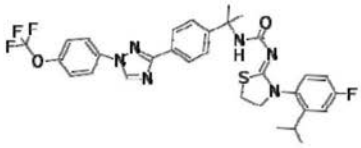
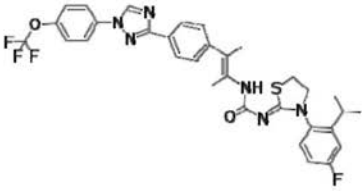
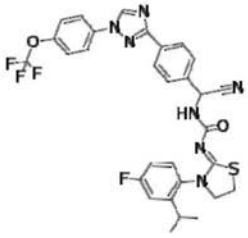
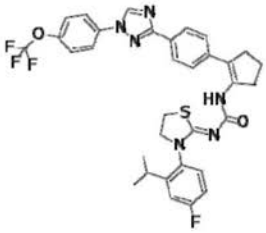
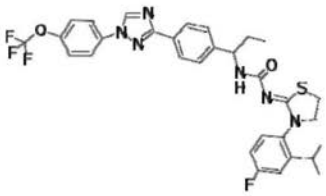
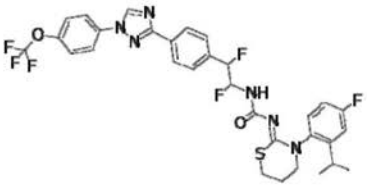
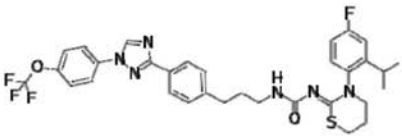
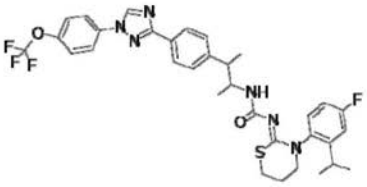
[1684]

 P1186	 P1187
 P1188	 P1189
 P1190	 P1191
 P1192	 P1193
 P1194	 P1195

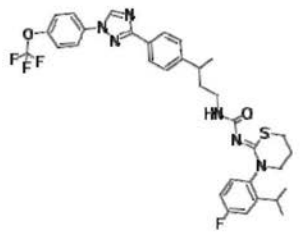
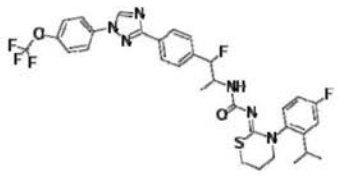
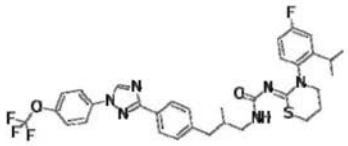
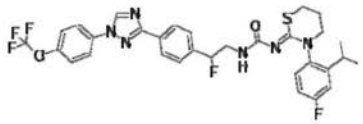
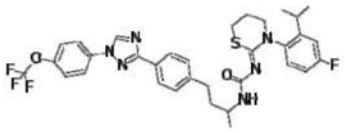
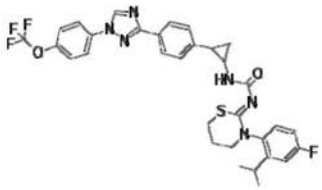
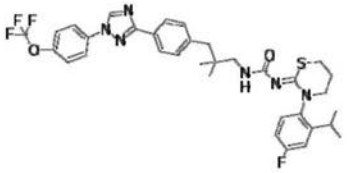
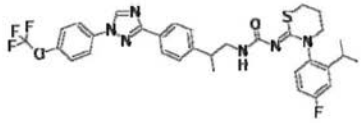
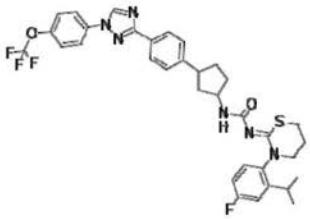
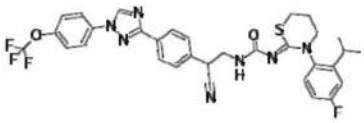
[1685]

 P1196	 P1197
 P1198	 P1199
 P1200	 P1201
 P1202	 P1203
 P1204	 P1205

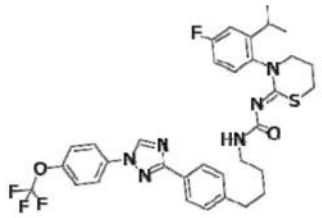
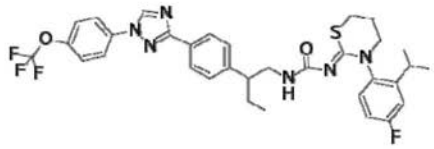
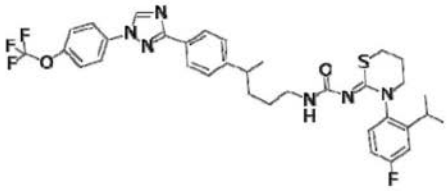
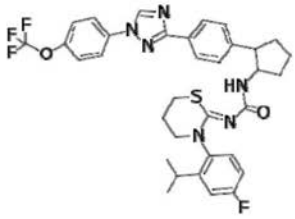
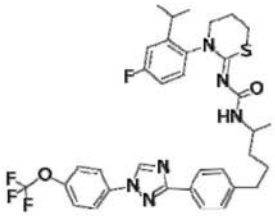
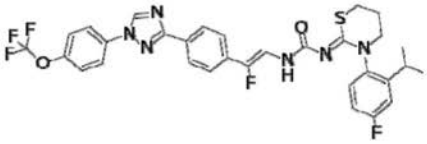
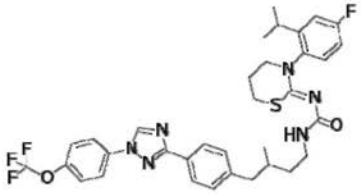
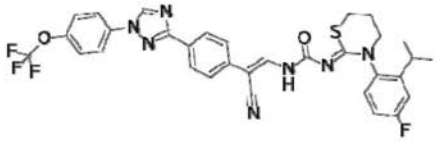
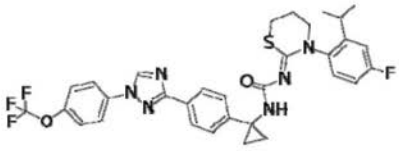
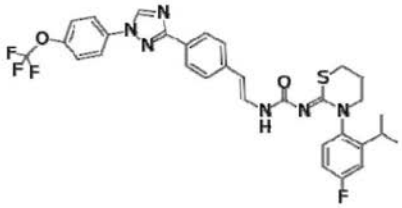
[1686]

 P1206	 P1207
 P1208	 P1209
 P1210	 P1211
 P1212	 P1213
 P1214	 P1215

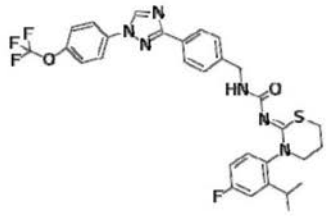
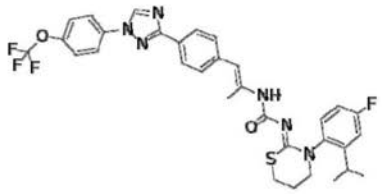
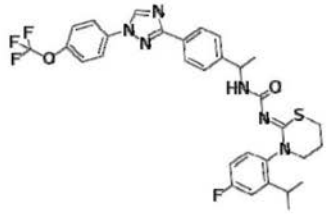
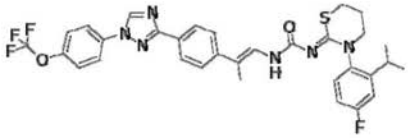
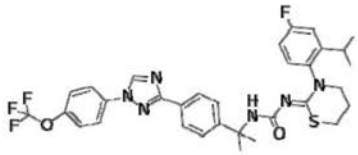
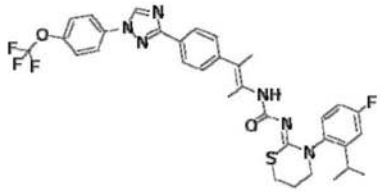
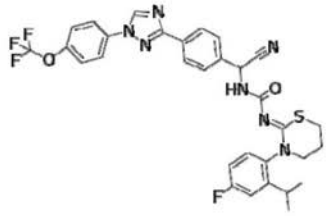
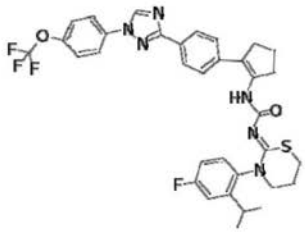
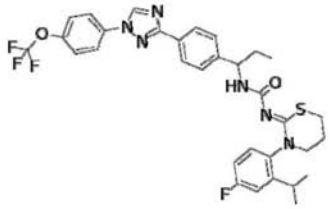
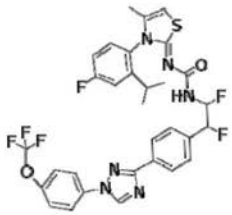
[1687]

 P1216	 P1217
 P1218	 P1219
 P1220	 P1221
 P1222	 P1223
 P1224	 P1225

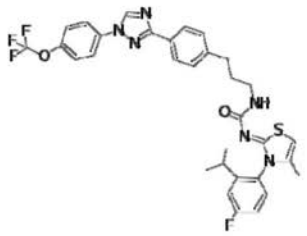
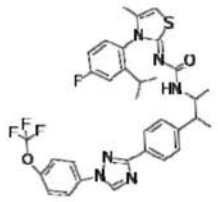
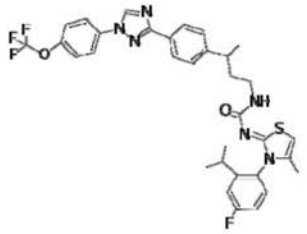
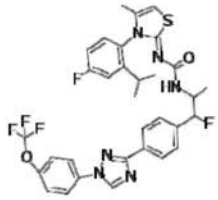
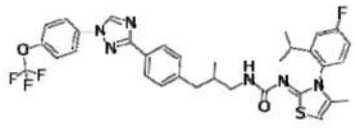
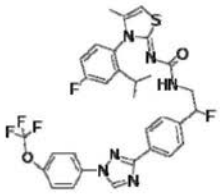
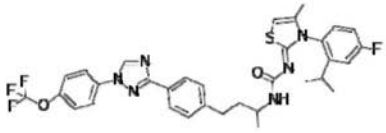
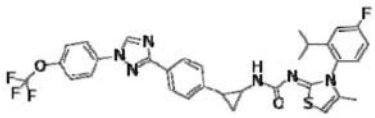
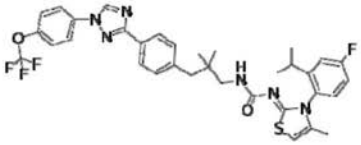
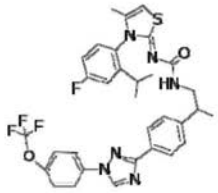
[1688]

 P1226	 P1227
 P1228	 P1229
 P1230	 P1231
 P1232	 P1233
 P1234	 P1235

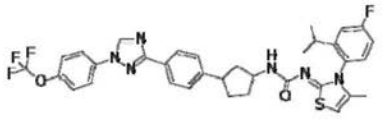
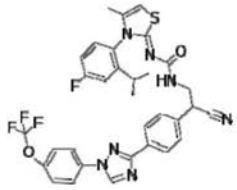
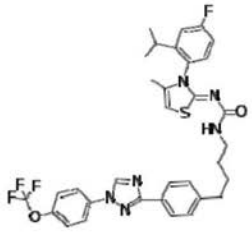
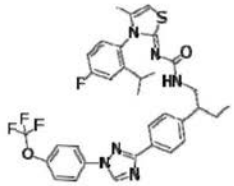
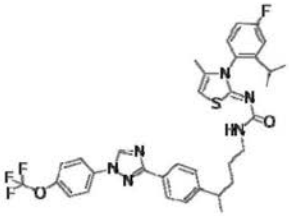
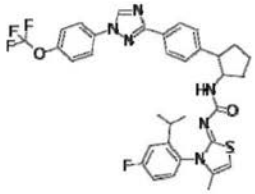
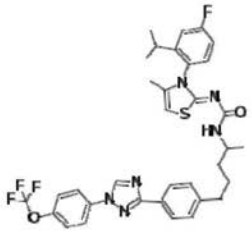
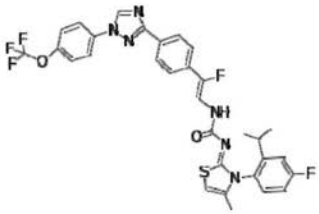
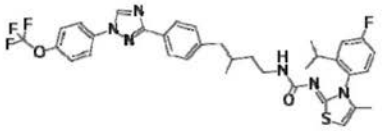
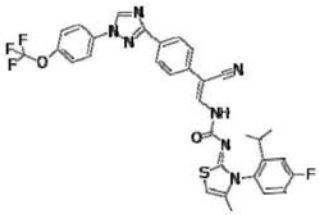
[1689]

 P1236	 P1237
 P1238	 P1239
 P1240	 P1241
 P1242	 P1243
 P1244	 P1245

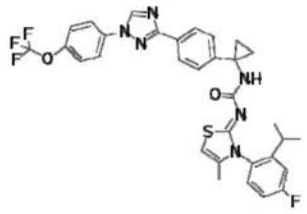
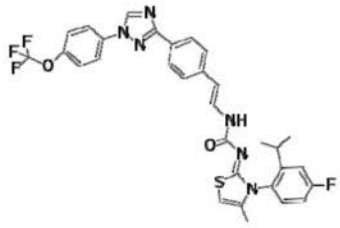
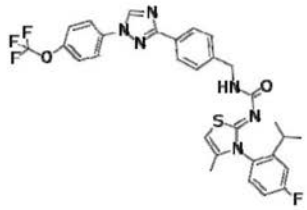
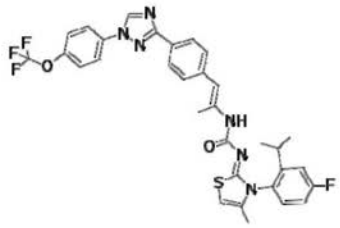
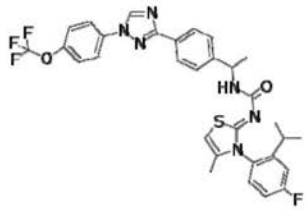
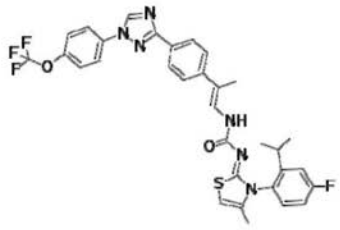
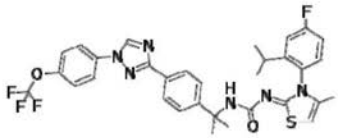
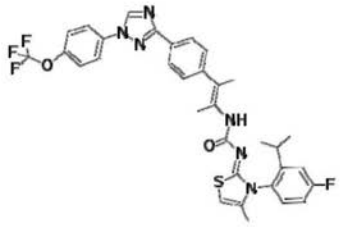
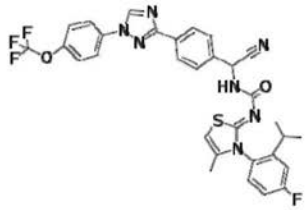
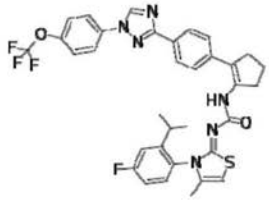
[1690]

 P1246	 P1247
 P1248	 P1249
 P1250	 P1251
 P1252	 P1253
 P1254	 P1255

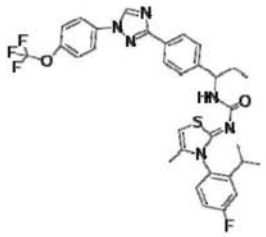
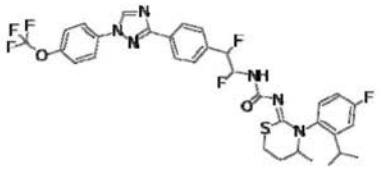
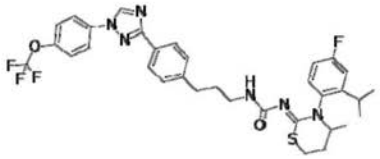
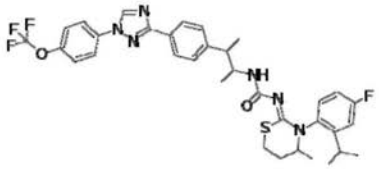
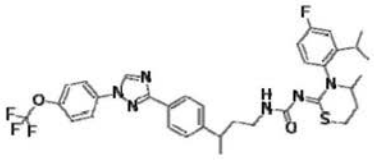
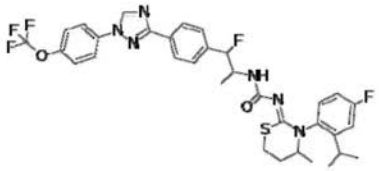
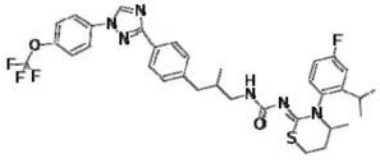
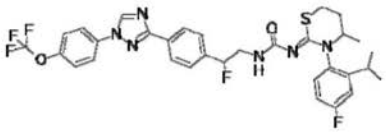
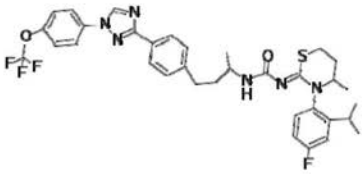
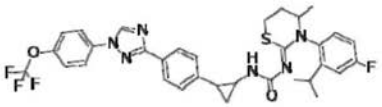
[1691]

 P1256	 P1257
 P1258	 P1259
 P1260	 P1261
 P1262	 P1263
 P1264	 P1265

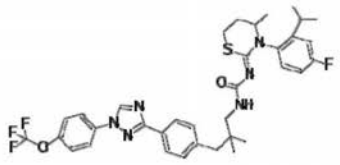
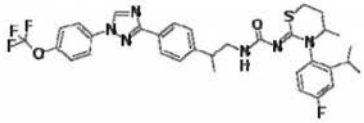
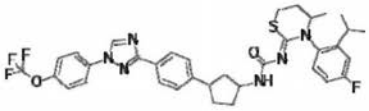
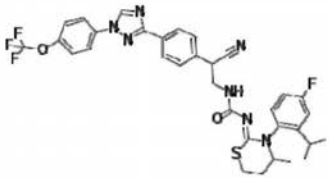
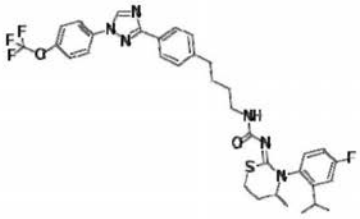
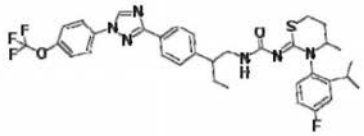
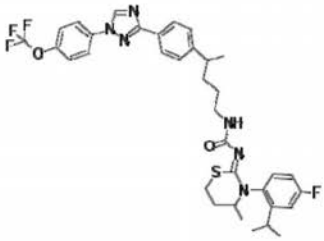
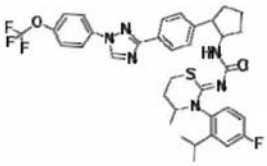
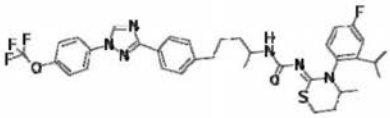
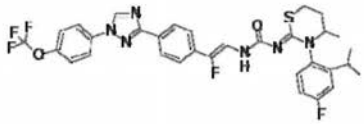
[1692]

 P1266	 P1267
 P1268	 P1269
 P1270	 P1271
 P1272	 P1273
 P1274	 P1275

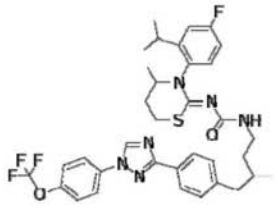
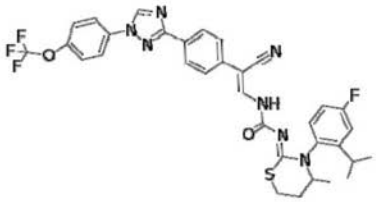
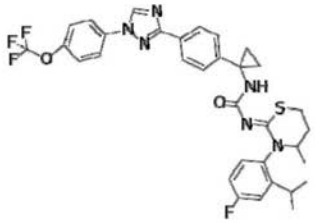
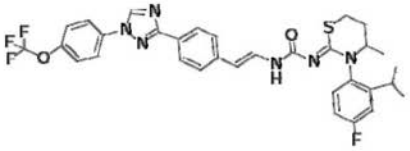
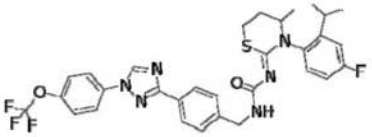
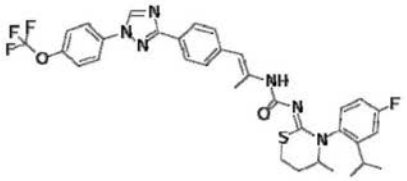
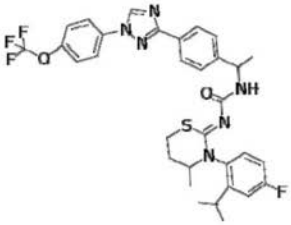
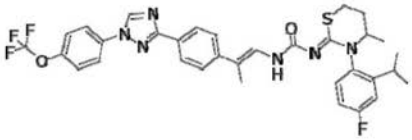
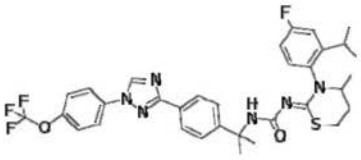
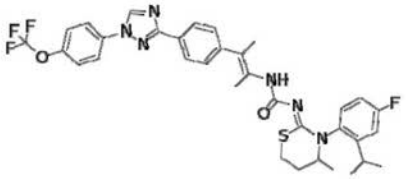
[1693]

 P1276	 P1277
 P1278	 P1279
 P1280	 P1281
 P1282	 P1283
 P1284	 P1285

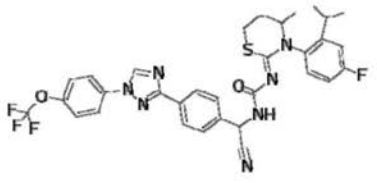
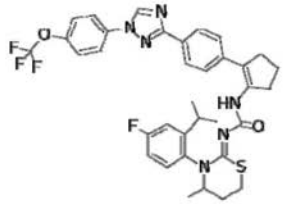
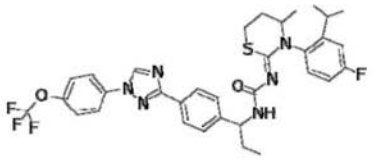
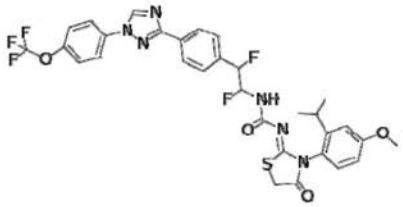
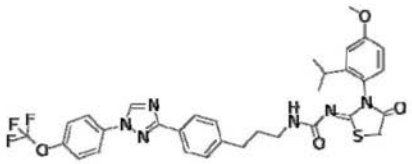
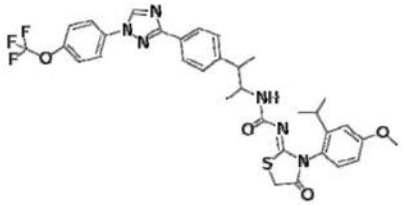
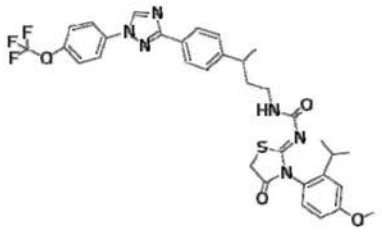
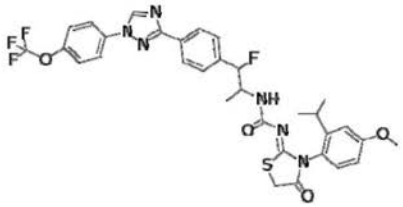
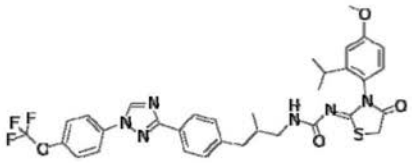
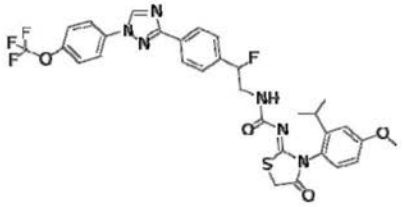
[1694]

 P1286	 P1287
 P1288	 P1289
 P1290	 P1291
 P1292	 P1293
 P1294	 P1295

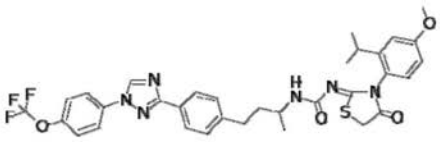
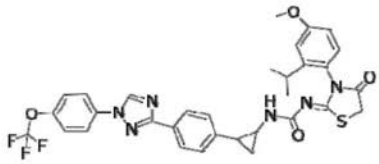
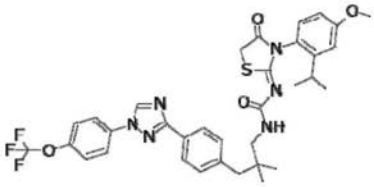
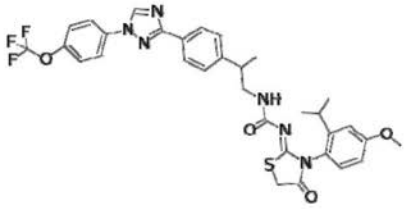
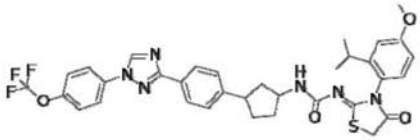
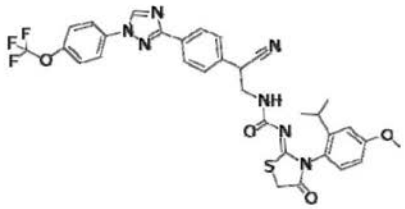
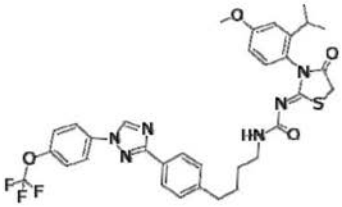
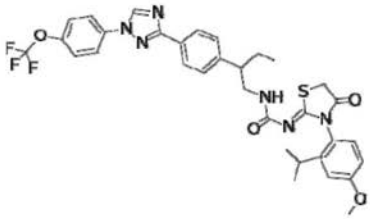
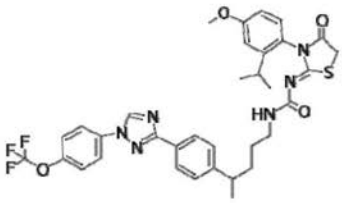
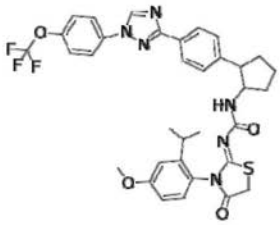
[1695]

 P1296	 P1297
 P1298	 P1299
 P1300	 P1301
 P1302	 P1303
 P1304	 P1305

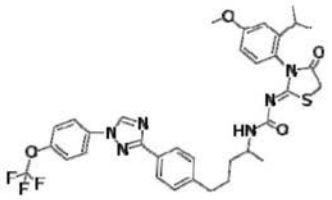
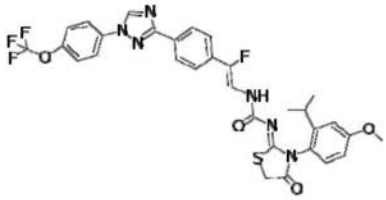
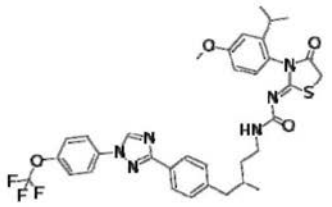
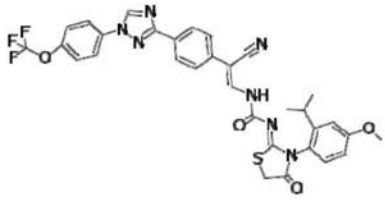
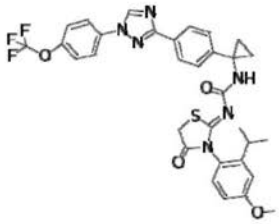
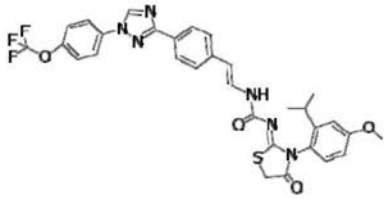
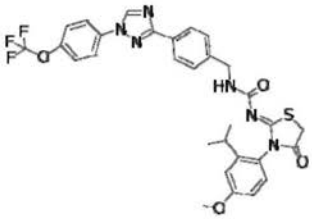
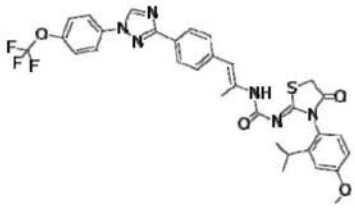
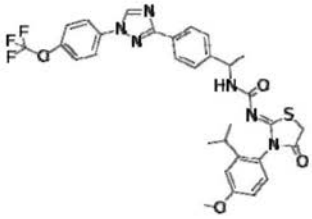
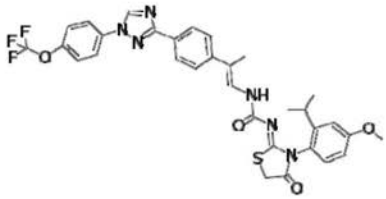
[1696]

 P1306	 P1307
 P1308	 P1309
 P1310	 P1311
 P1312	 P1313
 P1314	 P1315

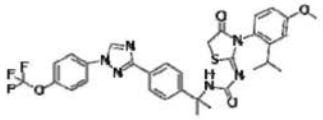
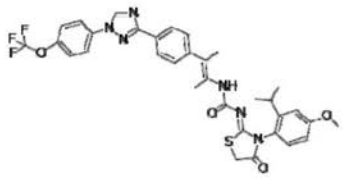
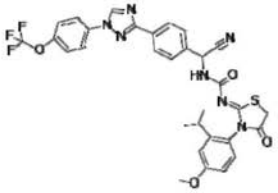
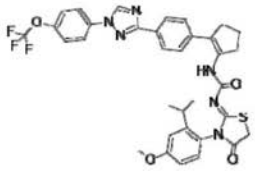
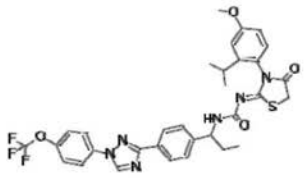
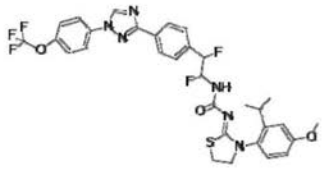
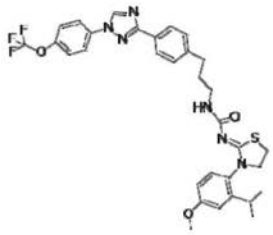
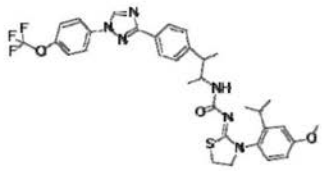
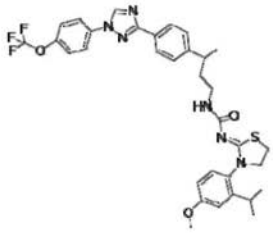
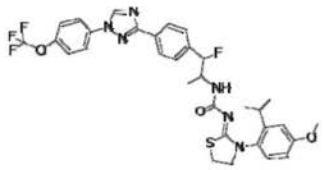
[1697]

 P1316	 P1317
 P1318	 P1319
 P1320	 P1321
 P1322	 P1323
 P1324	 P1325

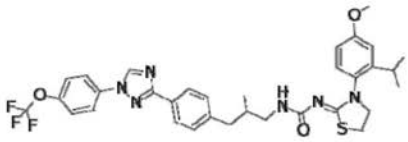
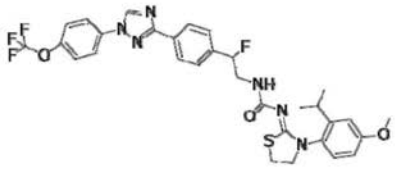
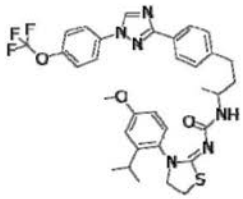
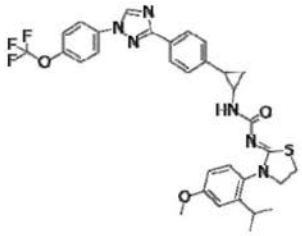
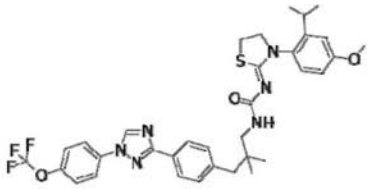
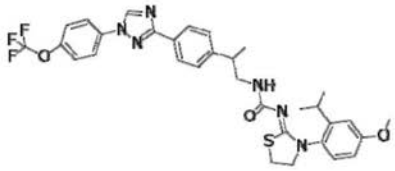
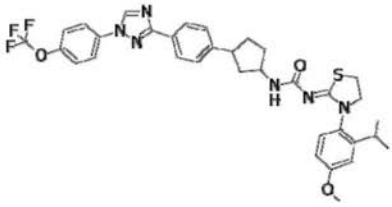
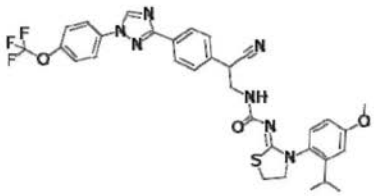
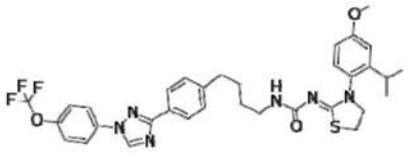
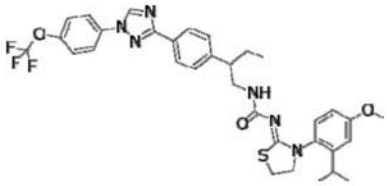
[1698]

 P1326	 P1327
 P1328	 P1329
 P1330	 P1331
 P1332	 P1333
 P1334	 P1335

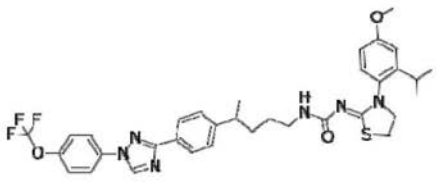
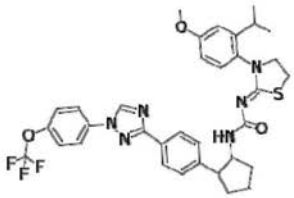
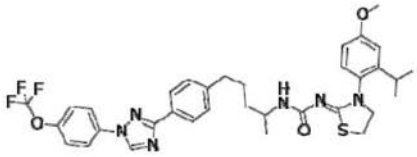
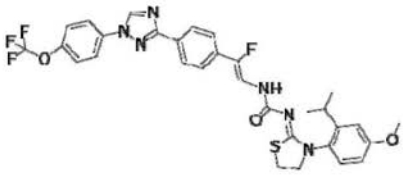
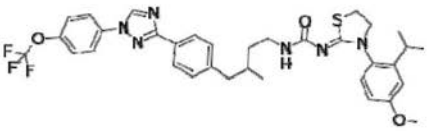
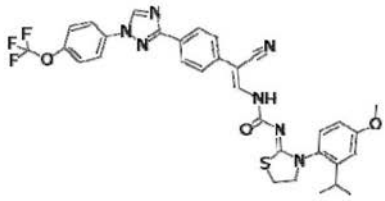
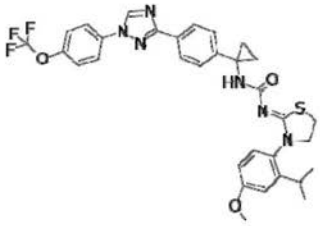
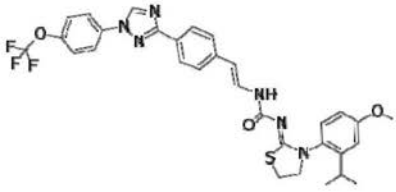
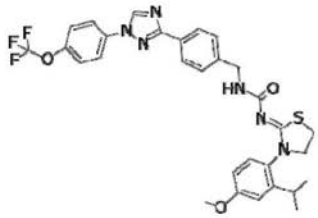
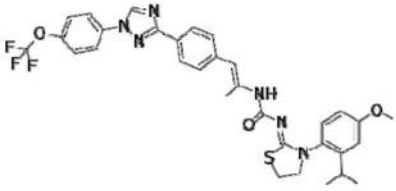
[1699]

 P1336	 P1337
 P1338	 P1339
 P1340	 P1341
 P1342	 P1343
 P1344	 P1345

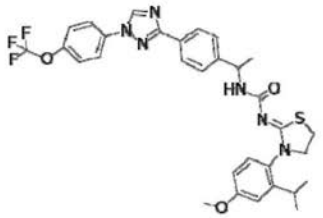
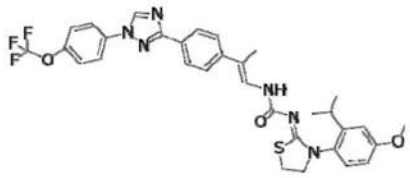
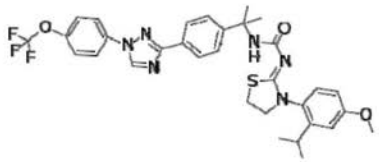
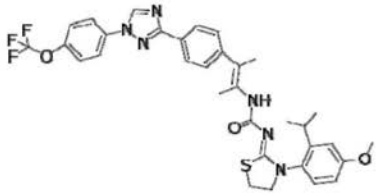
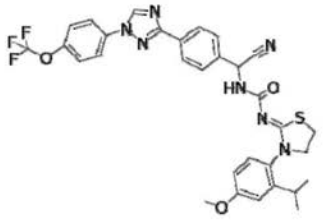
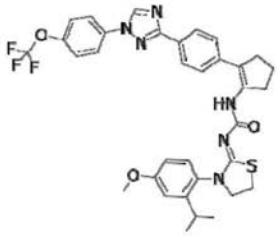
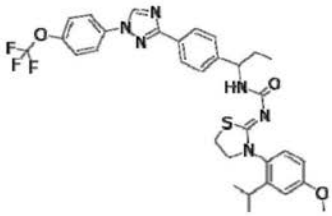
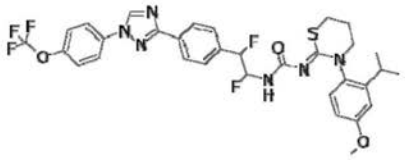
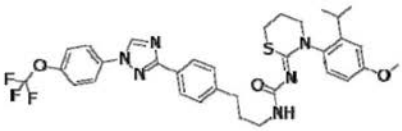
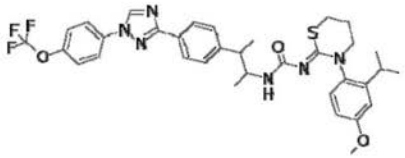
[1700]

 P1346	 P1347
 P1348	 P1349
 P1350	 P1351
 P1352	 P1353
 P1354	 P1355

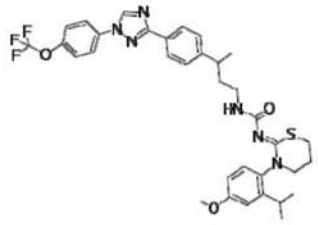
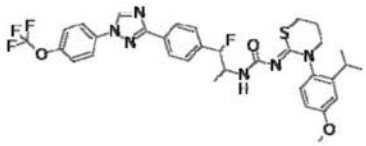
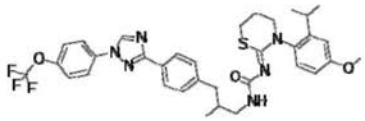
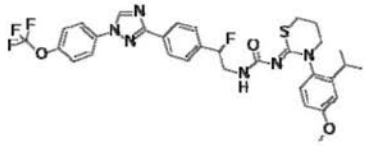
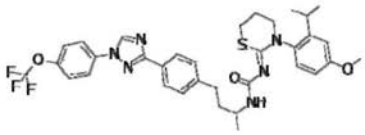
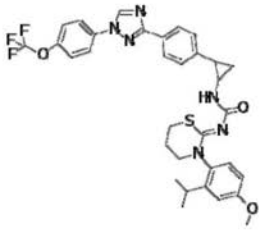
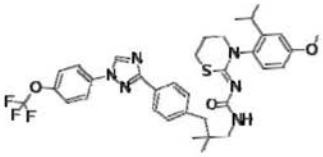
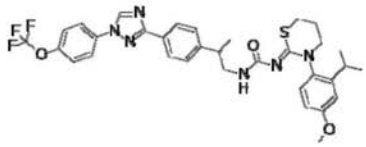
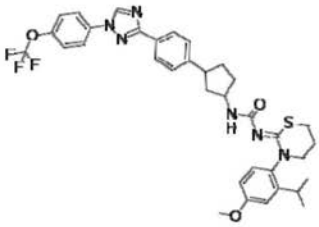
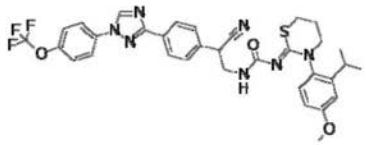
[1701]

 P1356	 P1357
 P1358	 P1359
 P1360	 P1361
 P1362	 P1363
 P1364	 P1365

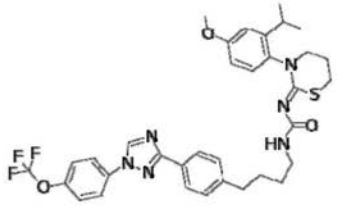
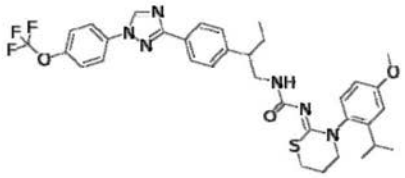
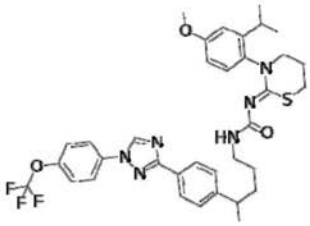
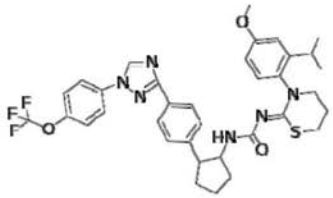
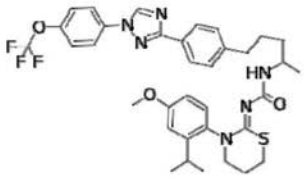
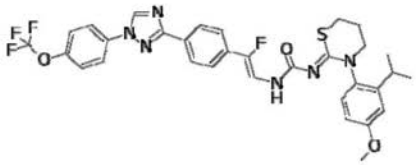
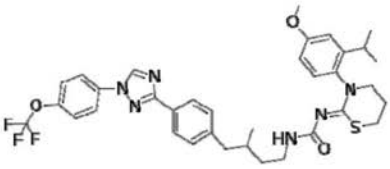
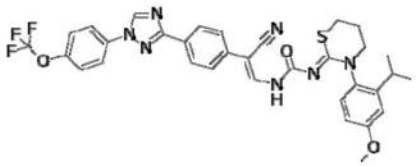
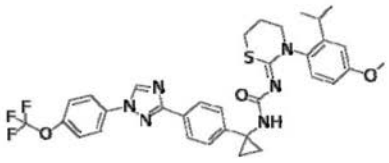
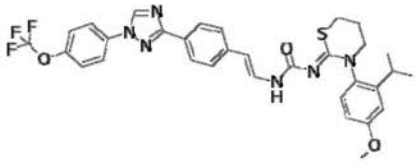
[1702]

 P1366	 P1367
 P1368	 P1369
 P1370	 P1371
 P1372	 P1373
 P1374	 P1375

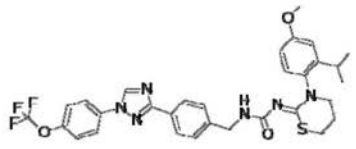
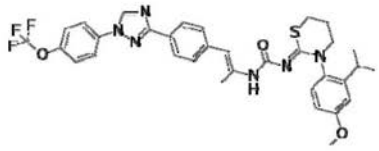
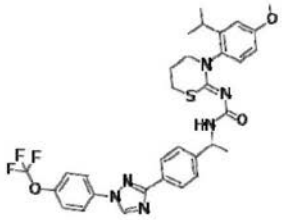
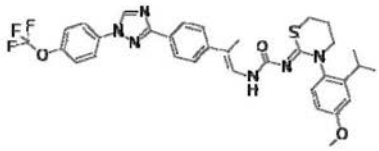
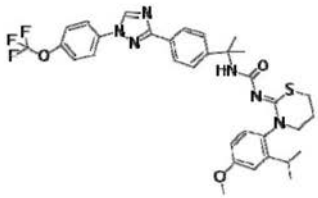
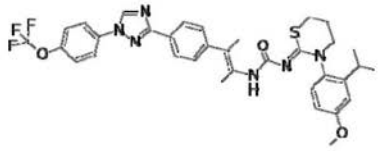
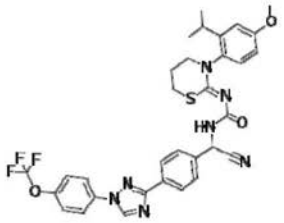
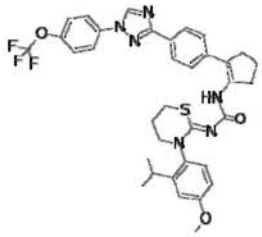
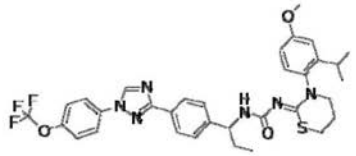
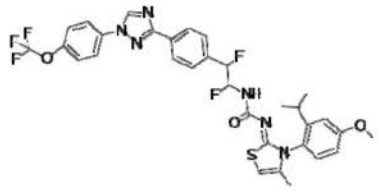
[1703]

 P1376	 P1377
 P1378	 P1379
 P1380	 P1381
 P1382	 P1383
 P1384	 P1385

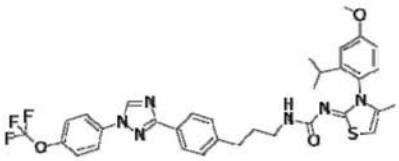
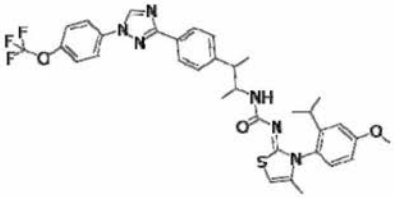
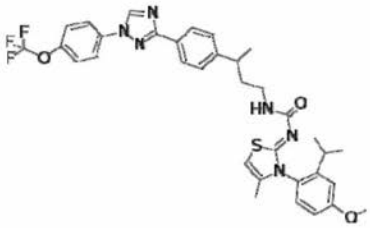
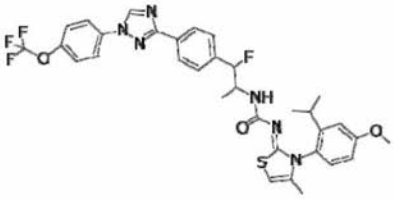
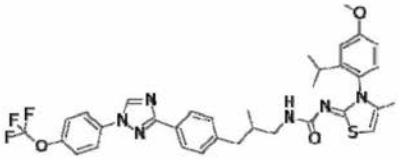
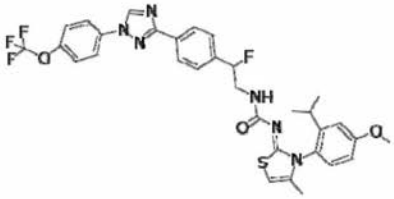
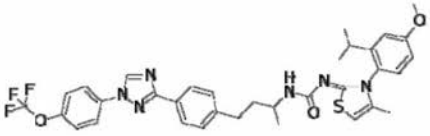
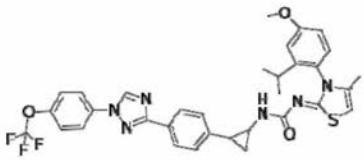
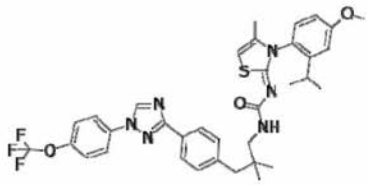
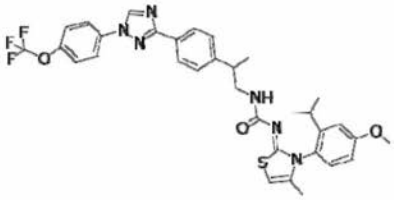
[1704]

 P1386	 P1387
 P1388	 P1389
 P1390	 P1391
 P1392	 P1393
 P1394	 P1395

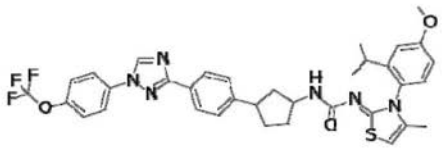
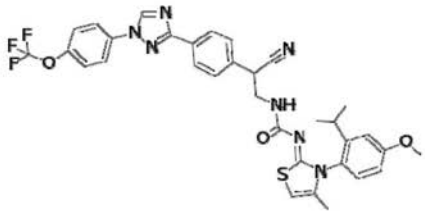
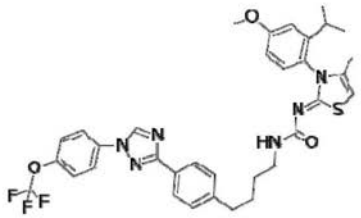
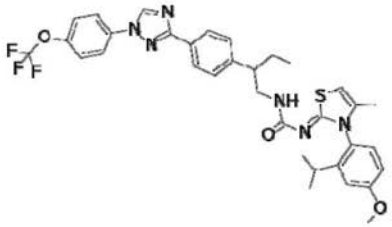
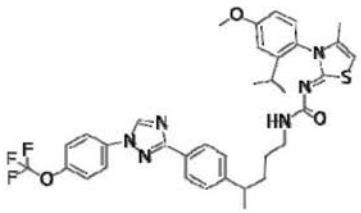
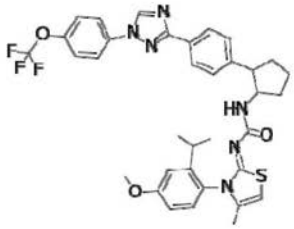
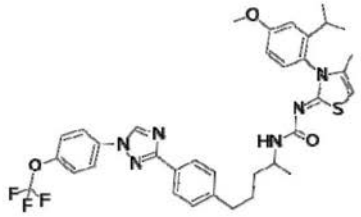
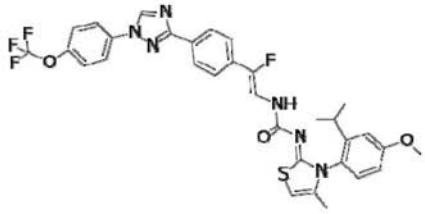
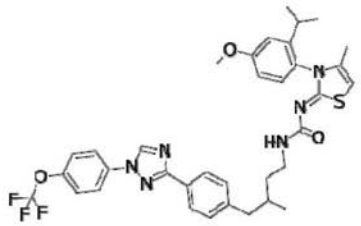
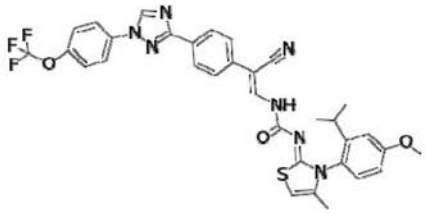
[1705]

 P1396	 P1397
 P1398	 P1399
 P1400	 P1401
 P1402	 P1403
 P1404	 P1405

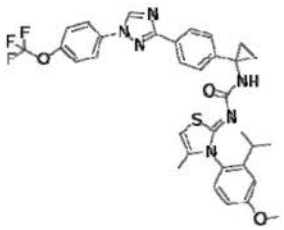
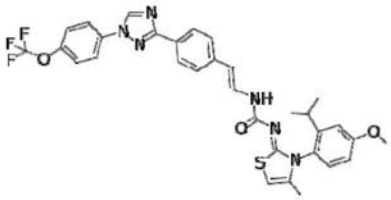
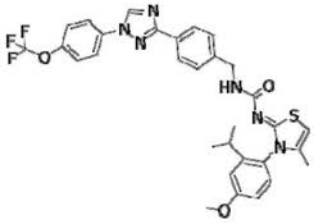
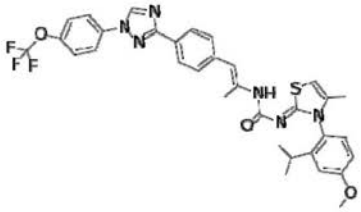
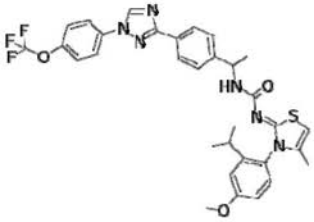
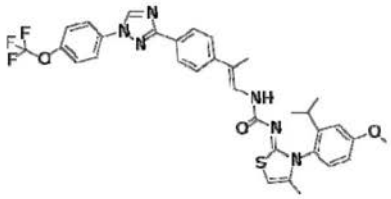
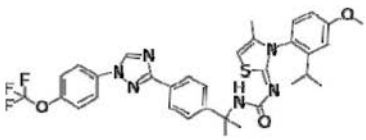
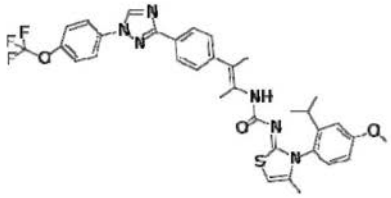
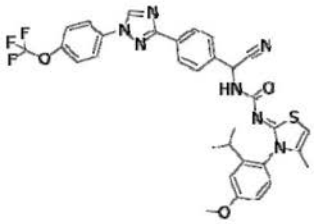
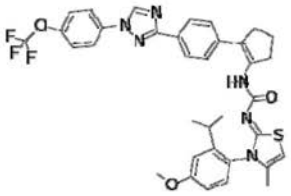
[1706]

 P1406	 P1407
 P1408	 P1409
 P1410	 P1411
 P1412	 P1413
 P1414	 P1415

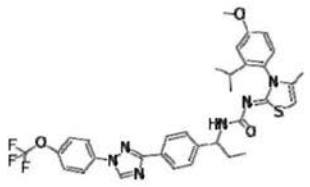
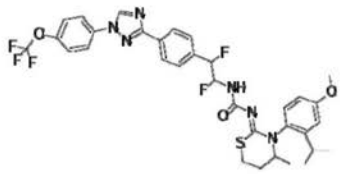
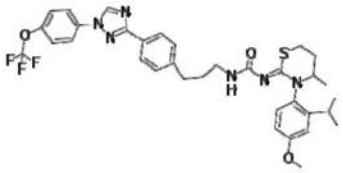
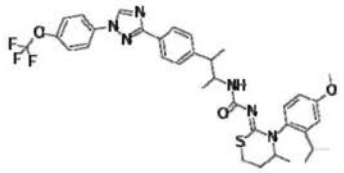
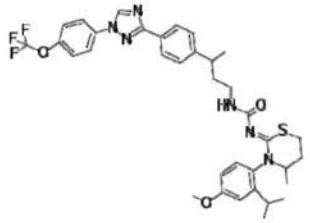
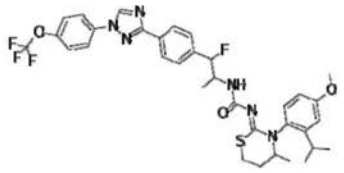
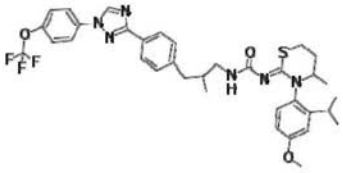
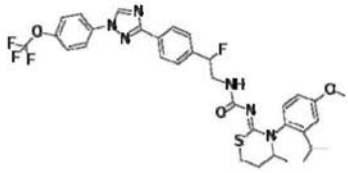
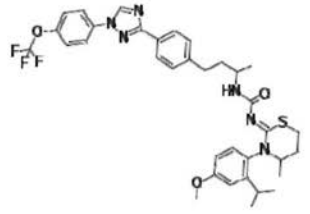
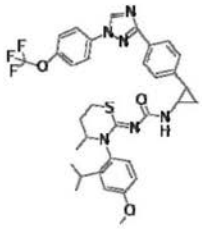
[1707]

 P1416	 P1417
 P1418	 P1419
 P1420	 P1421
 P1422	 P1423
 P1424	 P1425

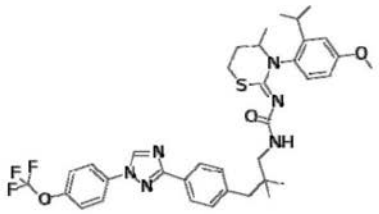
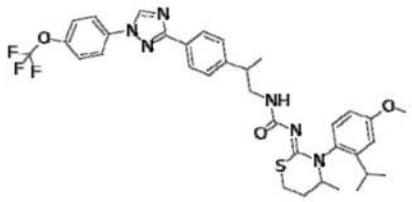
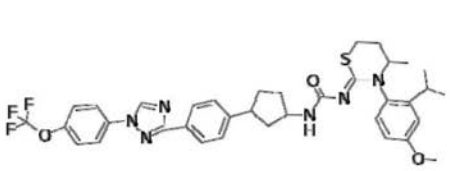
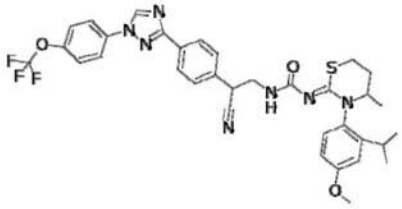
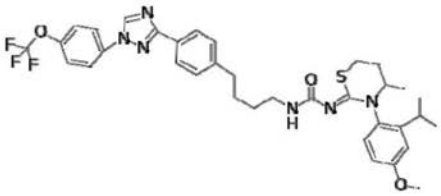
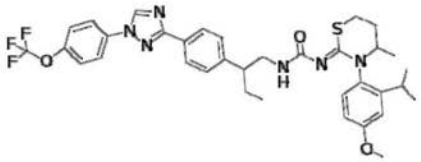
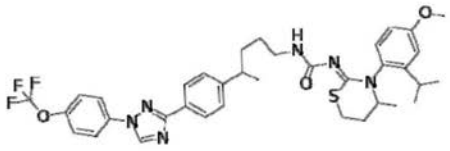
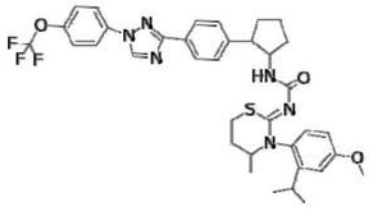
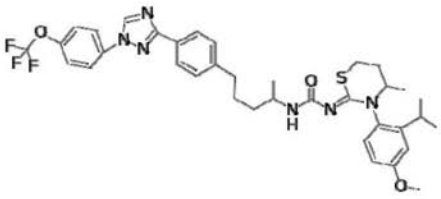
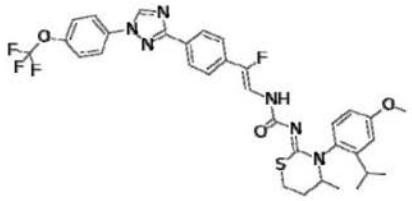
[1708]

 P1426	 P1427
 P1428	 P1429
 P1430	 P1431
 P1432	 P1433
 P1434	 P1435

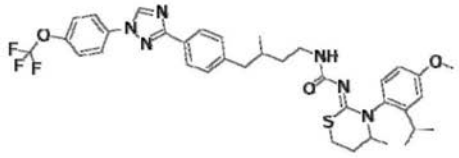
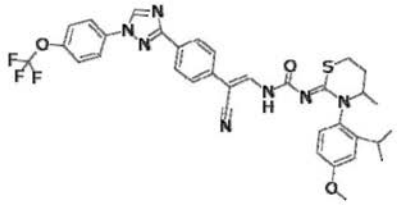
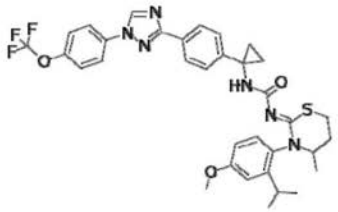
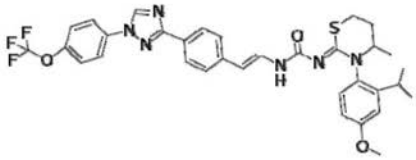
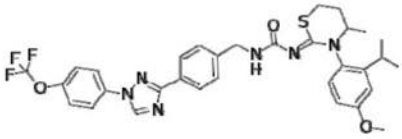
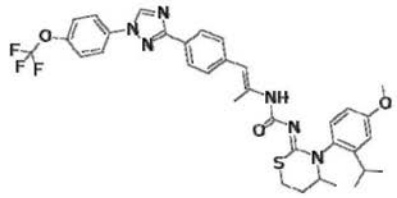
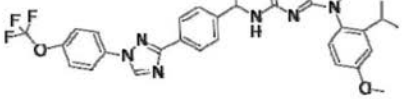
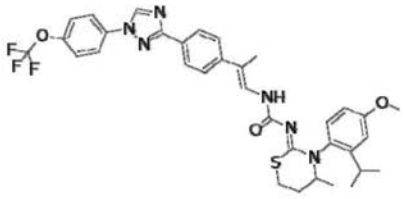
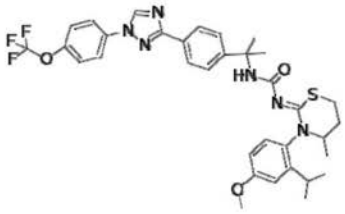
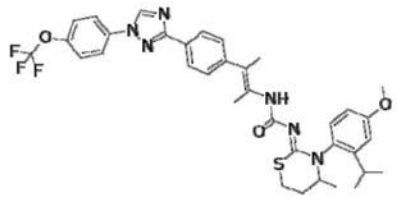
[1709]

 P1436	 P1437
 P1438	 P1439
 P1440	 P1441
 P1442	 P1443
 P1444	 P1445

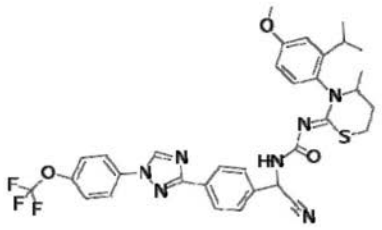
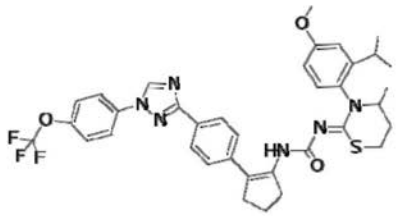
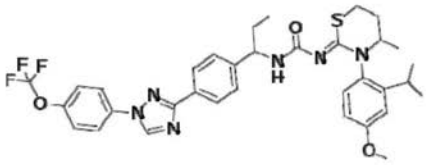
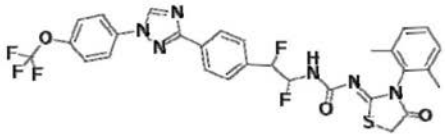
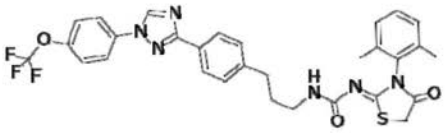
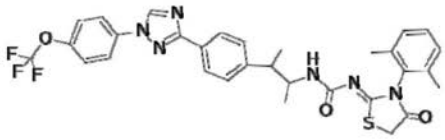
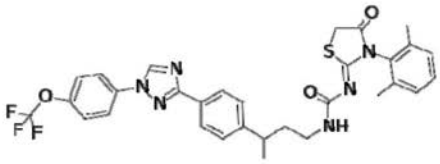
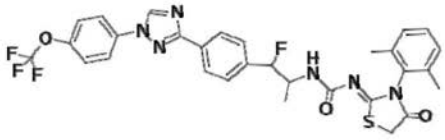
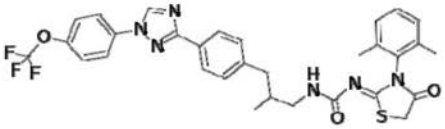
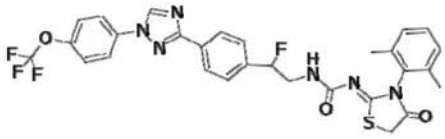
[1710]

 P1446	 P1447
 P1448	 P1449
 P1450	 P1451
 P1452	 P1453
 P1454	 P1455

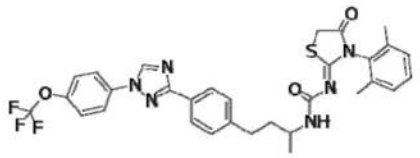
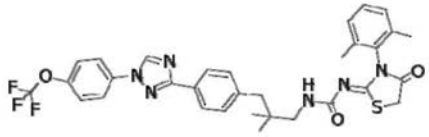
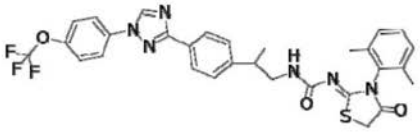
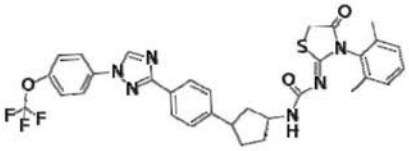
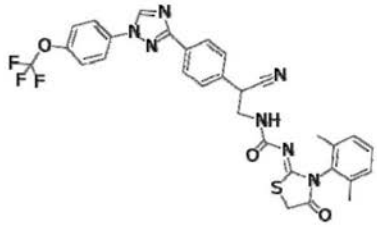
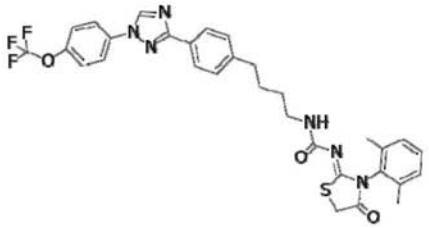
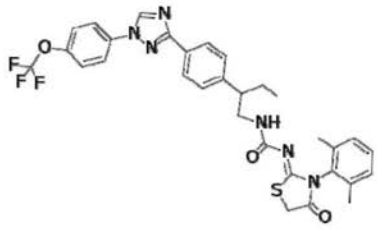
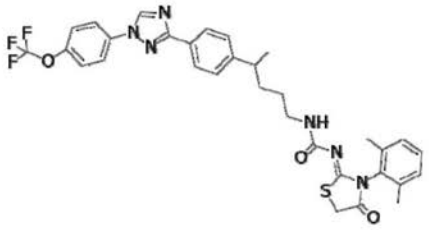
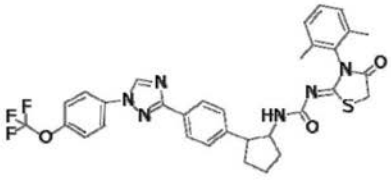
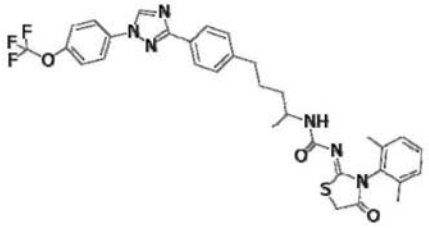
[1711]

 P1456	 P1457
 P1458	 P1459
 P1460	 P1461
 P1462	 P1463
 P1464	 P1465

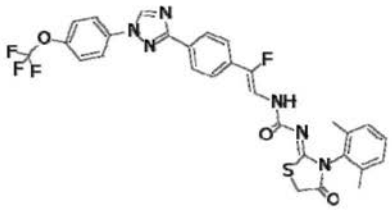
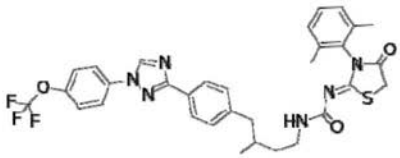
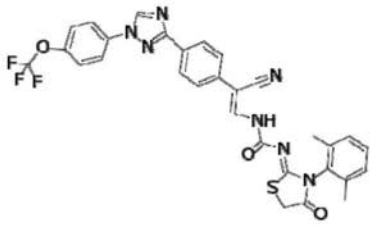
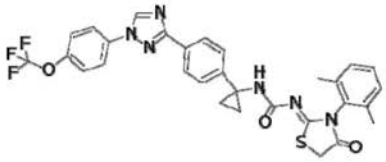
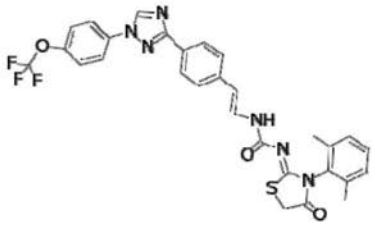
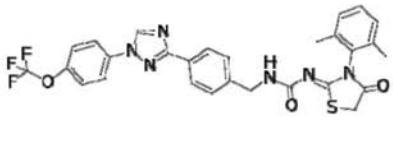
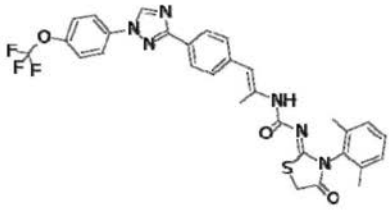
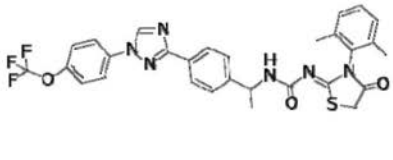
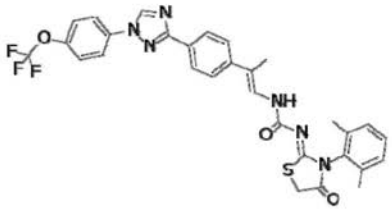
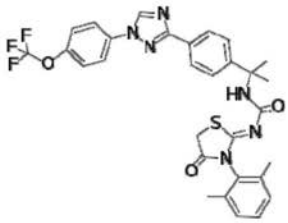
[1712]

 P1466	 P1467
 P1468	 P1469
 P1470	 P1471
 P1472	 P1473
 P1474	 P1475

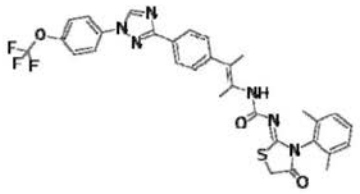
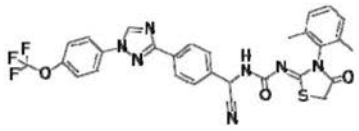
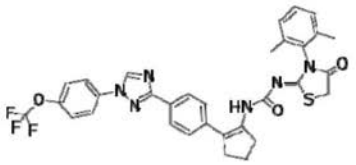
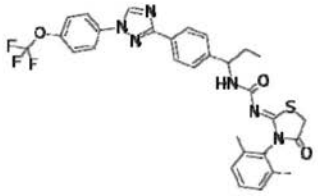
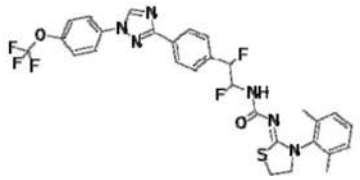
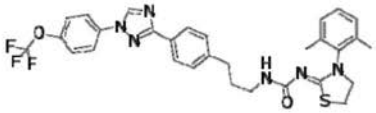
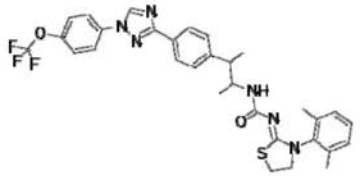
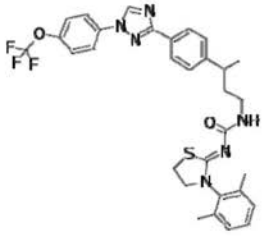
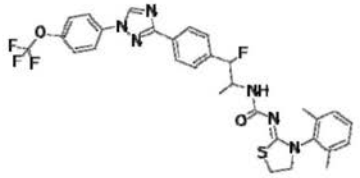
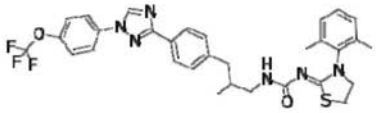
[1713]

 P1476	 P1477
 P1478	 P1479
 P1480	 P1481
 P1482	 P1483
 P1484	 P1485

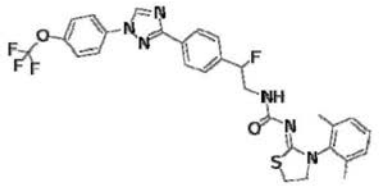
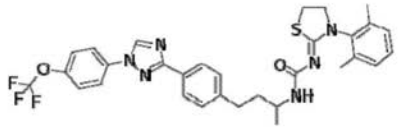
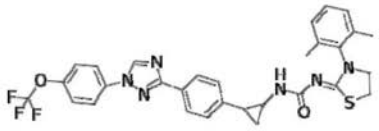
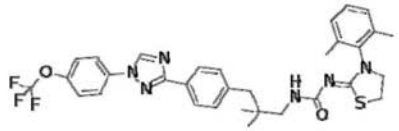
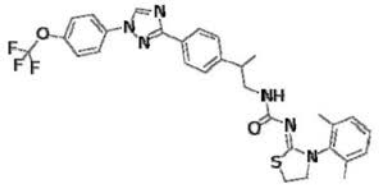
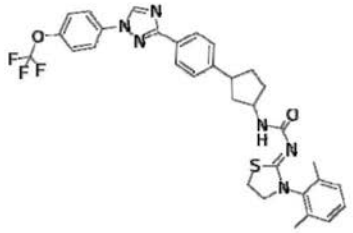
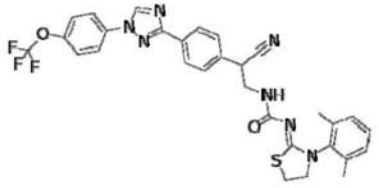
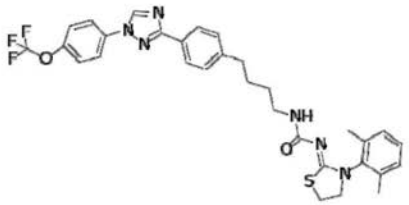
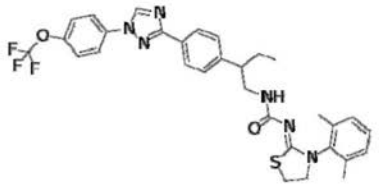
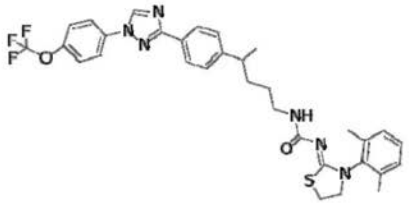
[1714]

 P1486	 P1487
 P1488	 P1489
 P1490	 P1491
 P1492	 P1493
 P1494	 P1495

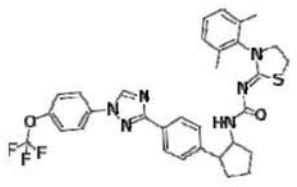
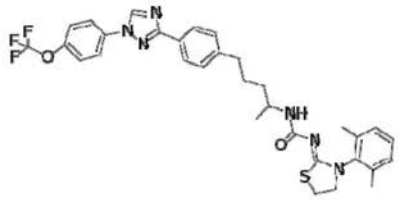
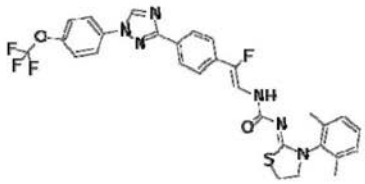
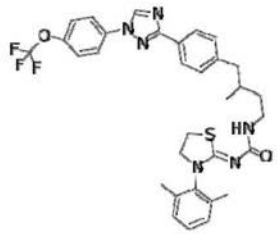
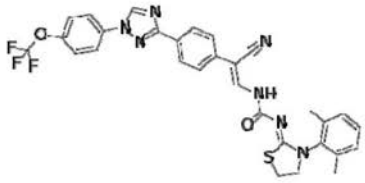
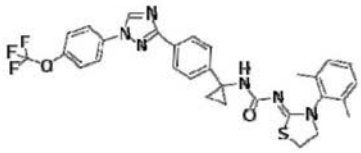
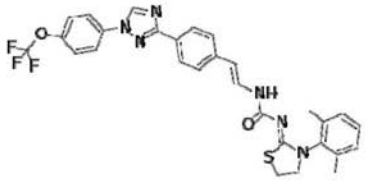
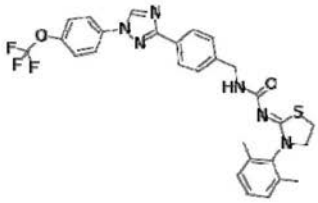
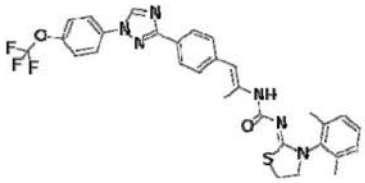
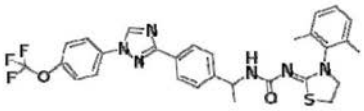
[1715]

 P1496	 P1497
 P1498	 P1499
 P1500	 P1501
 P1502	 P1503
 P1504	 P1505

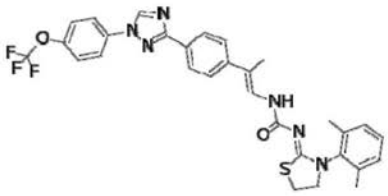
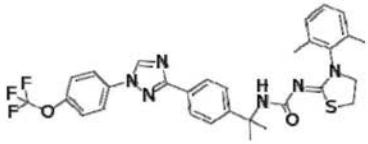
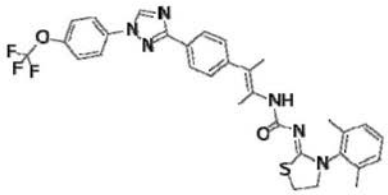
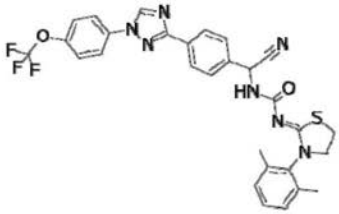
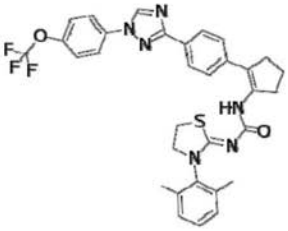
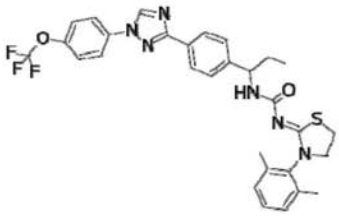
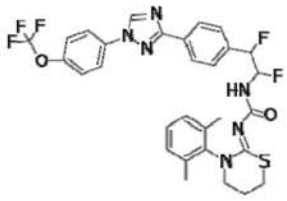
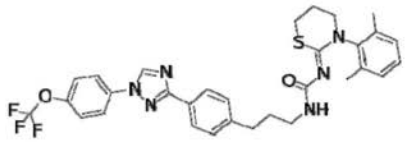
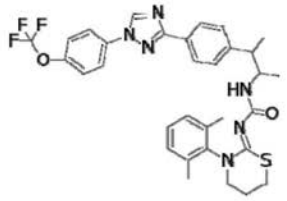
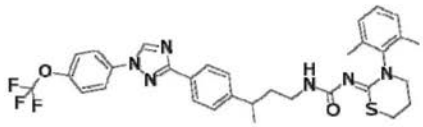
[1716]

 P1506	 P1507
 P1508	 P1509
 P1510	 P1511
 P1512	 P1513
 P1514	 P1515

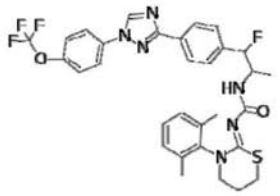
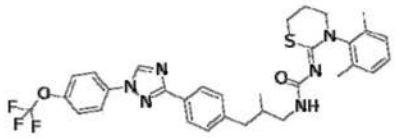
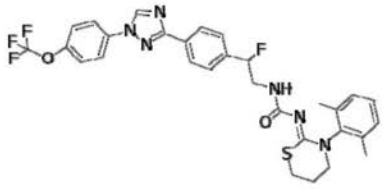
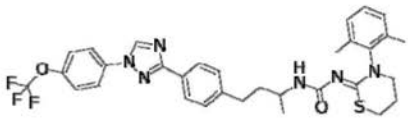
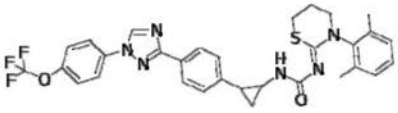
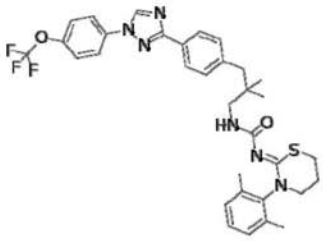
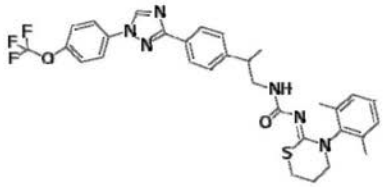
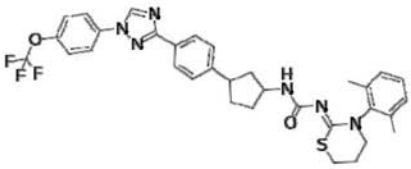
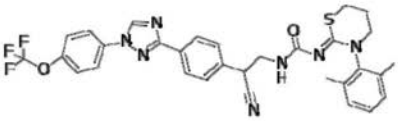
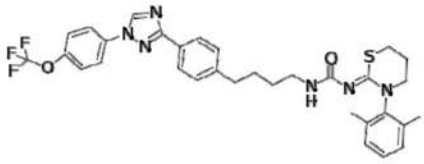
[1717]

 P1516	 P1517
 P1518	 P1519
 P1520	 P1521
 P1522	 P1523
 P1524	 P1525

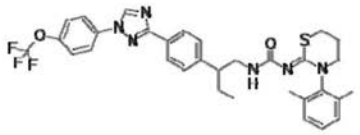
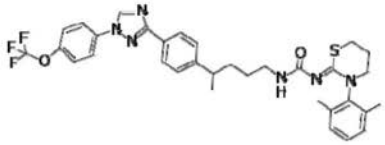
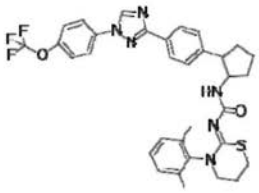
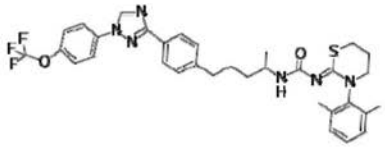
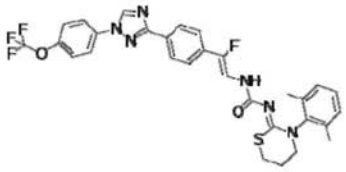
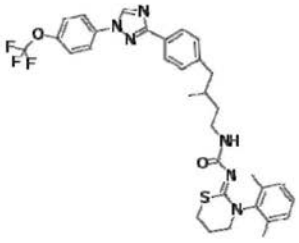
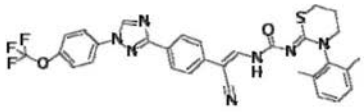
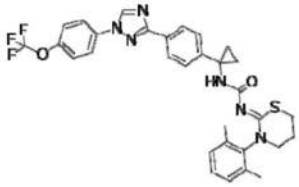
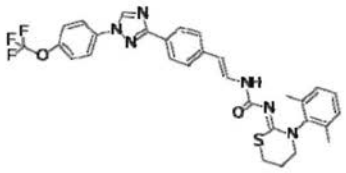
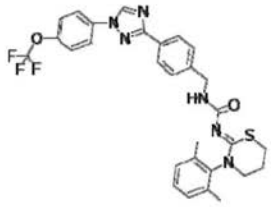
[1718]

 P1526	 P1527
 P1528	 P1529
 P1530	 P1531
 P1532	 P1533
 P1534	 P1535

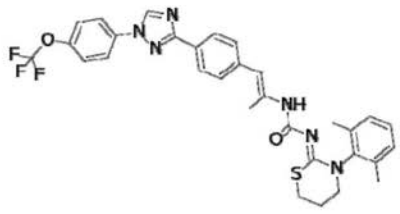
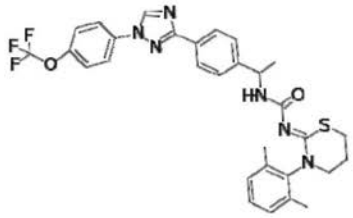
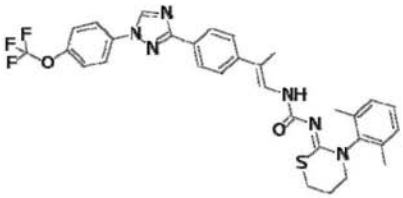
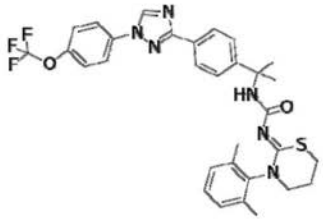
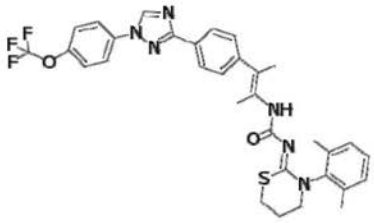
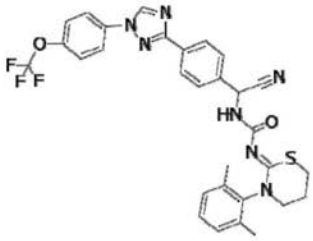
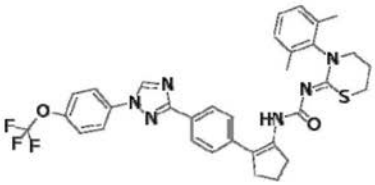
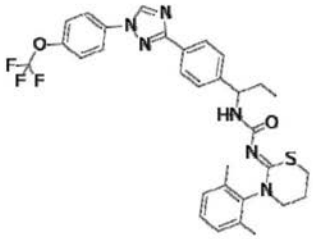
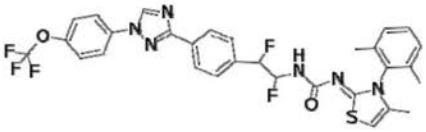
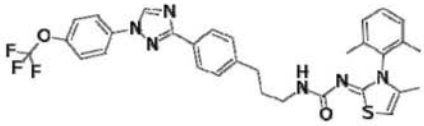
[1719]

 P1536	 P1537
 P1538	 P1539
 P1540	 P1541
 P1542	 P1543
 P1544	 P1545

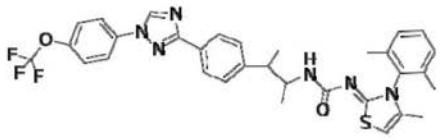
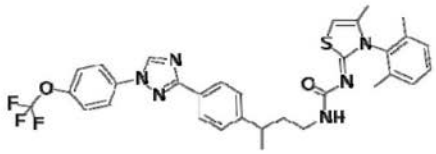
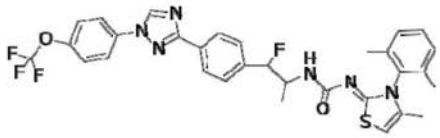
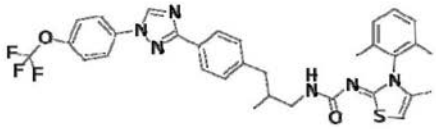
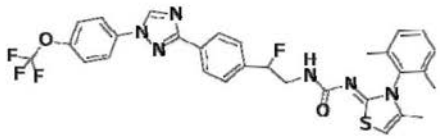
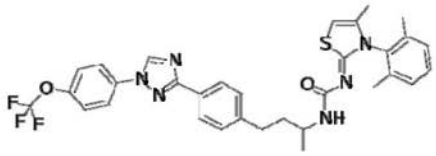
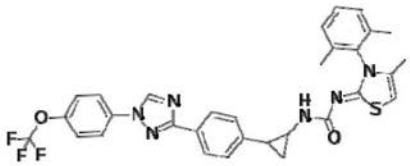
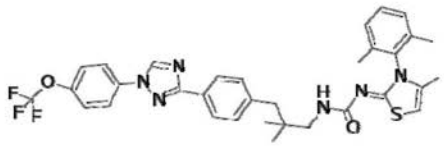
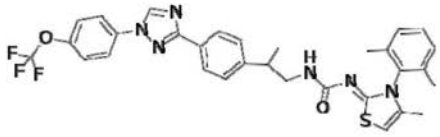
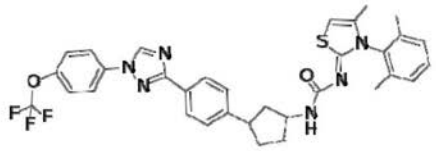
[1720]

 P1546	 P1547
 P1548	 P1549
 P1550	 P1551
 P1552	 P1553
 P1554	 P1555

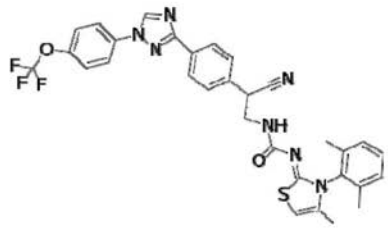
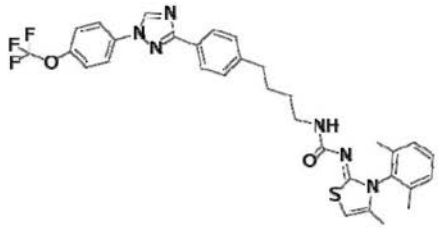
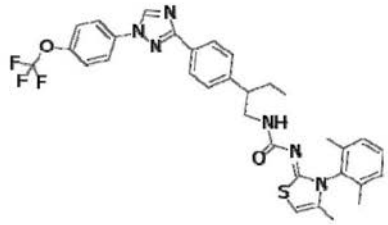
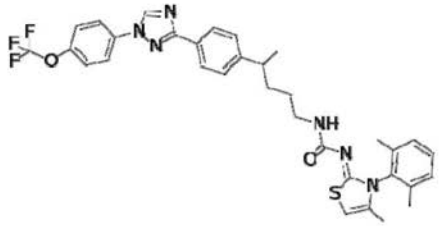
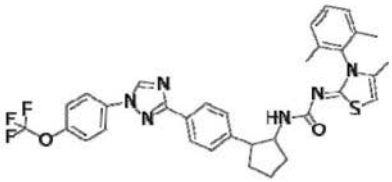
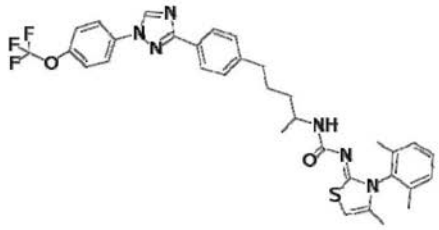
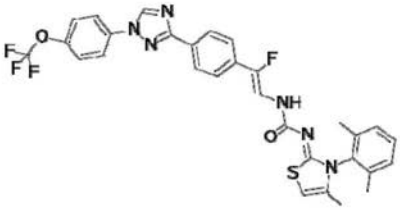
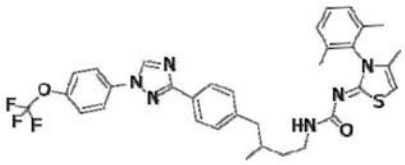
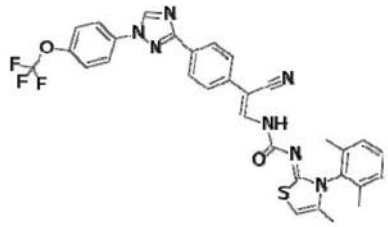
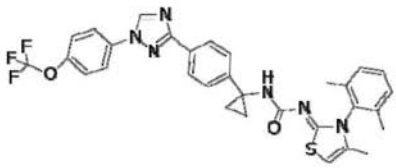
[1721]

 P1556	 P1557
 P1558	 P1559
 P1560	 P1561
 P1562	 P1563
 P1564	 P1565

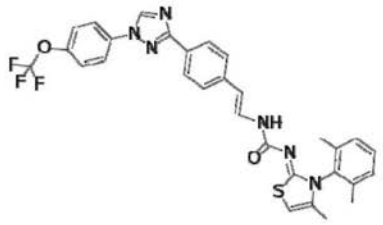
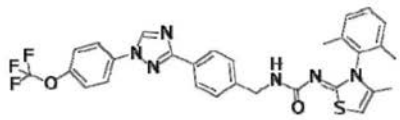
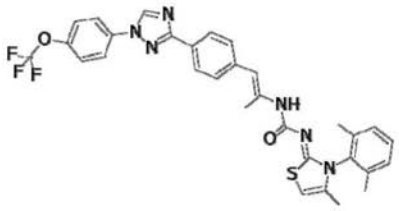
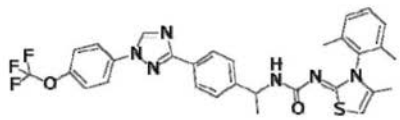
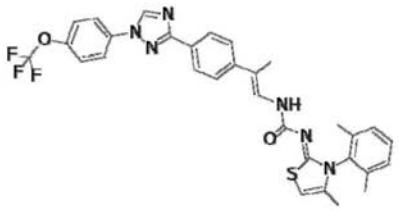
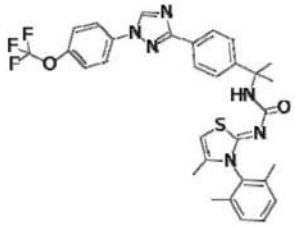
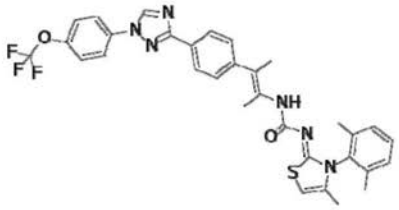
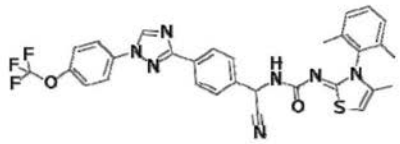
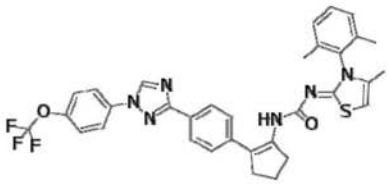
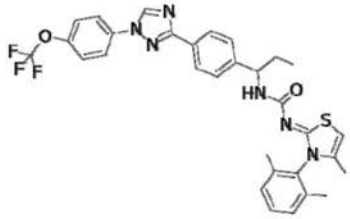
[1722]

 P1566	 P1567
 P1568	 P1569
 P1570	 P1571
 P1572	 P1573
 P1574	 P1575

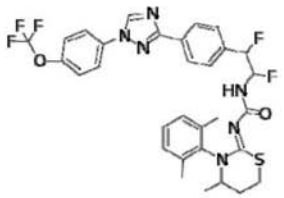
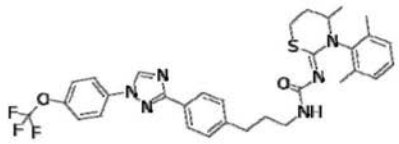
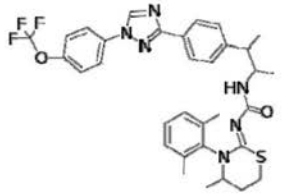
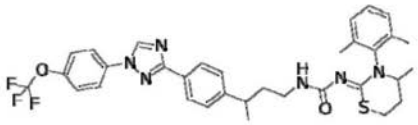
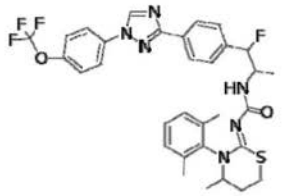
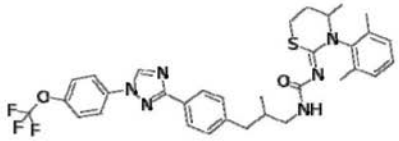
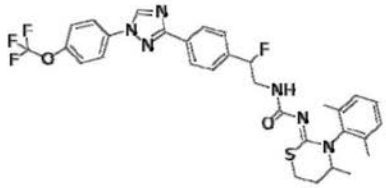
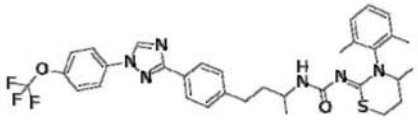
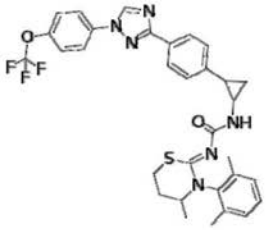
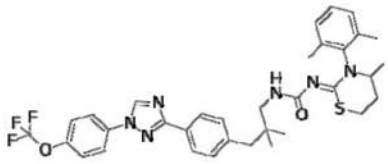
[1723]

 P1576	 P1577
 P1578	 P1579
 P1580	 P1581
 P1582	 P1583
 P1584	 P1585

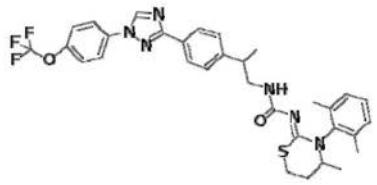
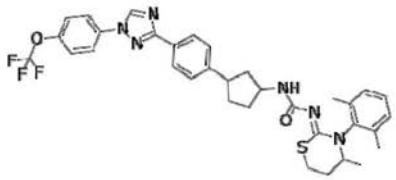
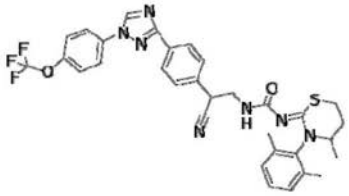
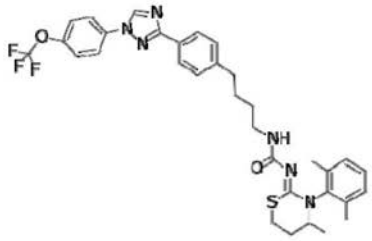
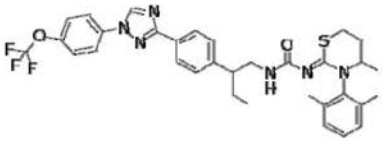
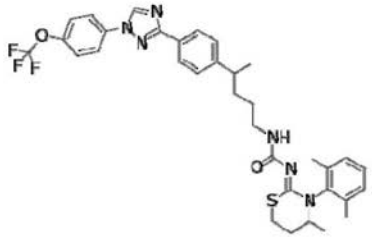
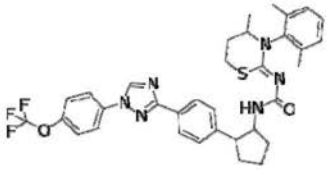
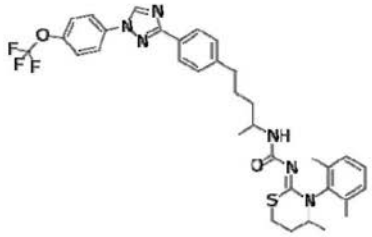
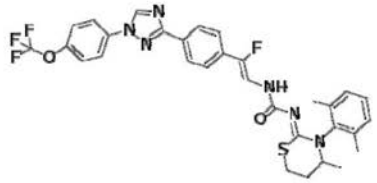
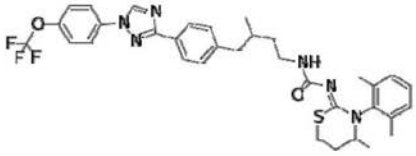
[1724]

 P1586	 P1587
 P1588	 P1589
 P1590	 P1591
 P1592	 P1593
 P1594	 P1595

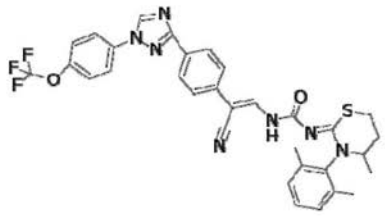
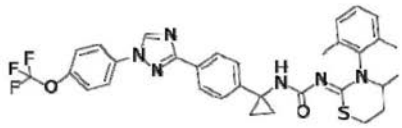
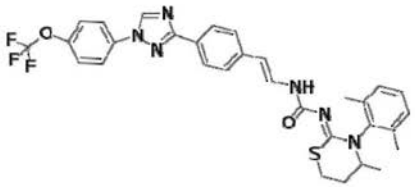
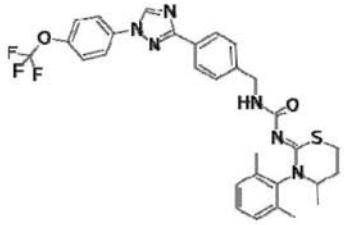
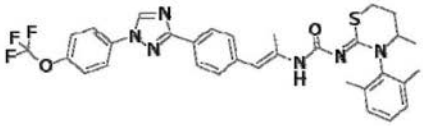
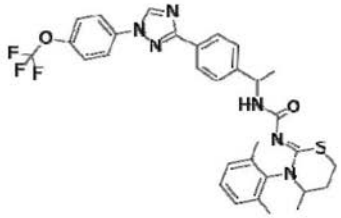
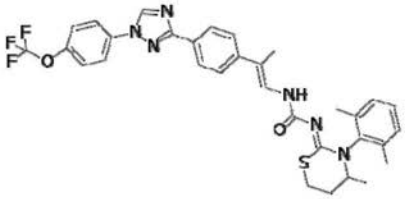
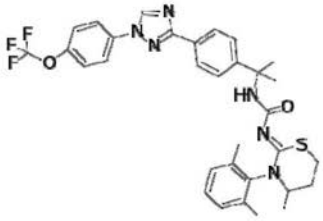
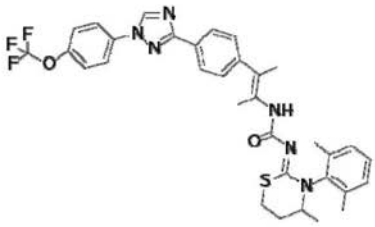
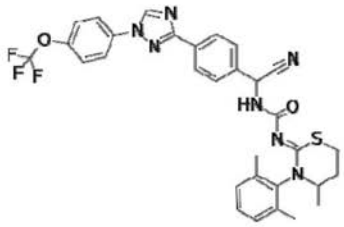
[1725]

 P1596	 P1597
 P1598	 P1599
 P1600	 P1601
 P1602	 P1603
 P1604	 P1605

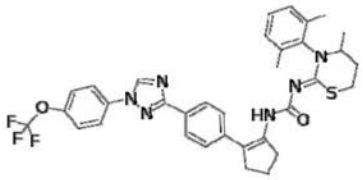
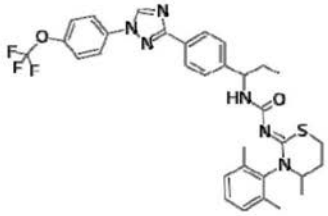
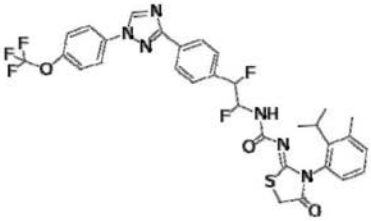
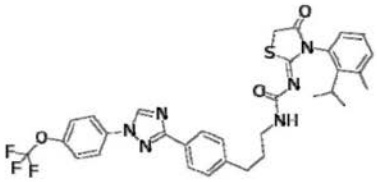
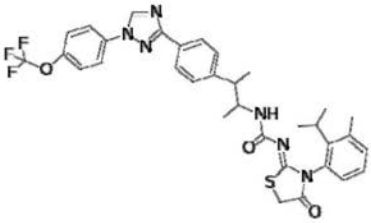
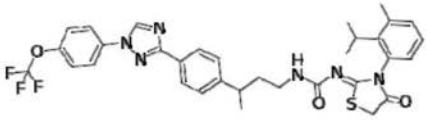
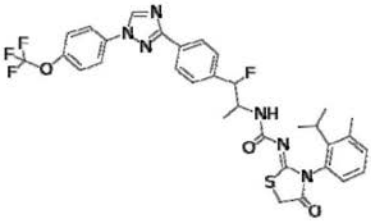
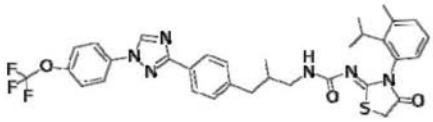
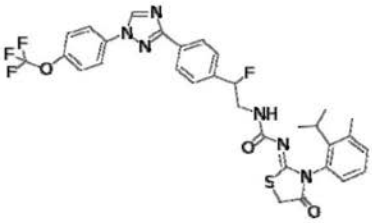
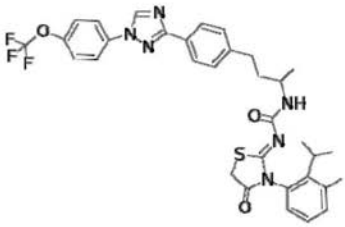
[1726]

 P1606	 P1607
 P1608	 P1609
 P1610	 P1611
 P1612	 P1613
 P1614	 P1615

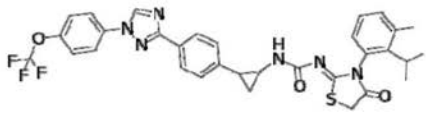
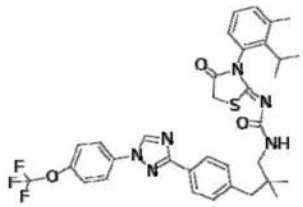
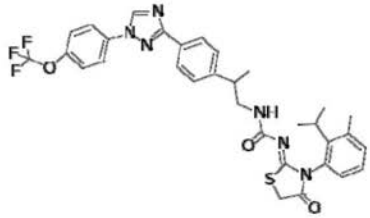
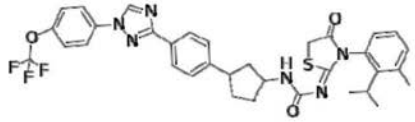
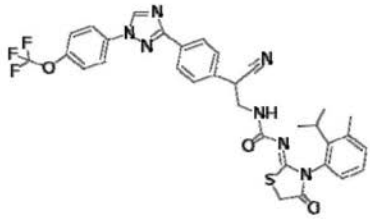
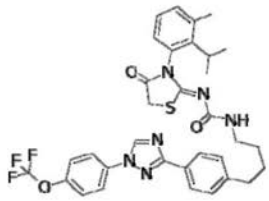
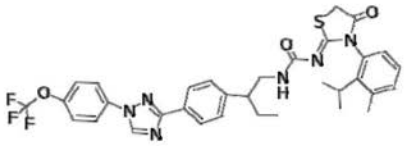
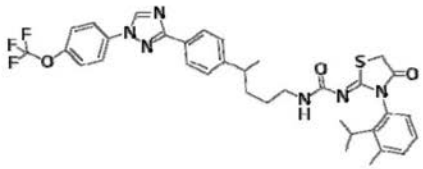
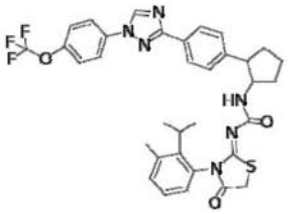
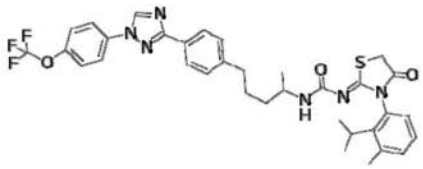
[1727]

 P1616	 P1617
 P1618	 P1619
 P1620	 P1621
 P1622	 P1623
 P1624	 P1625

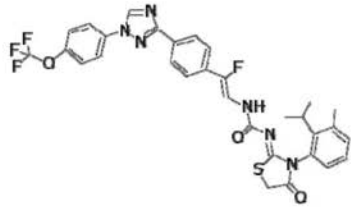
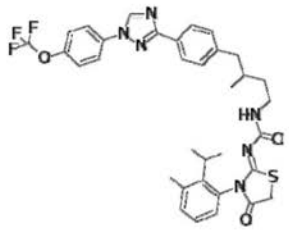
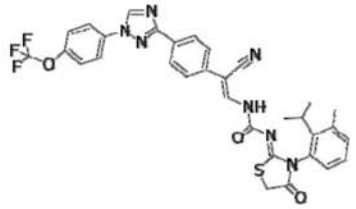
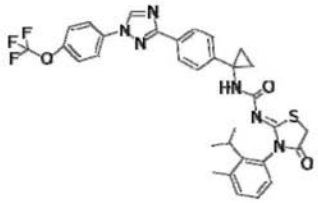
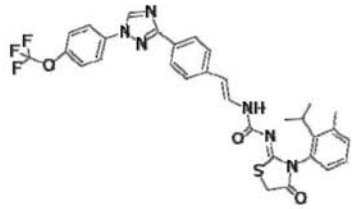
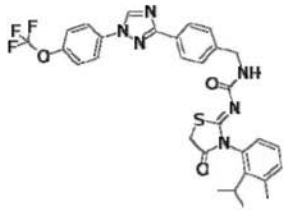
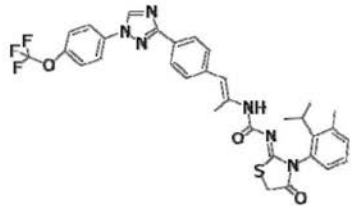
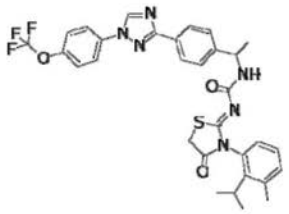
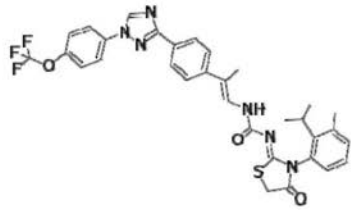
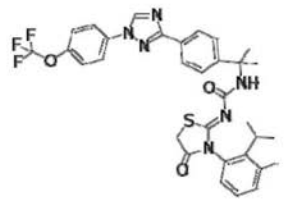
[1728]

 P1626	 P1627
 P1628	 P1629
 P1630	 P1631
 P1632	 P1633
 P1634	 P1635

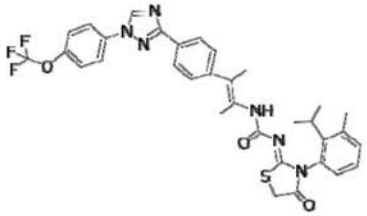
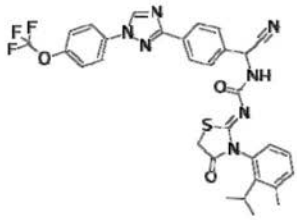
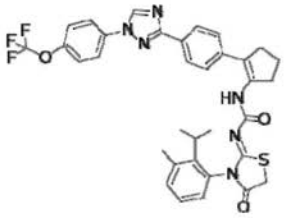
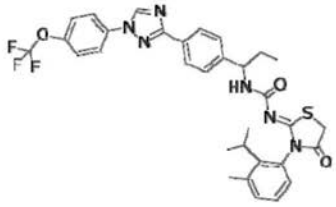
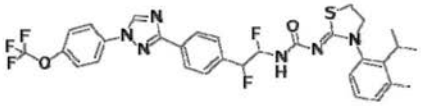
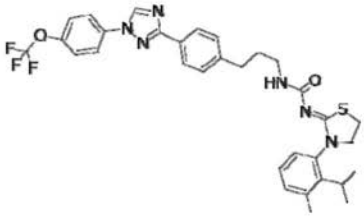
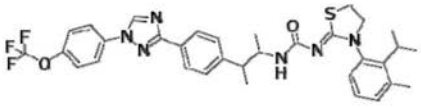
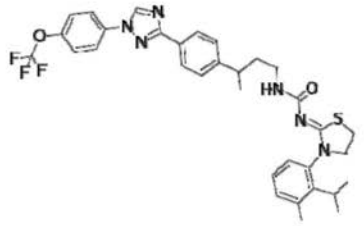
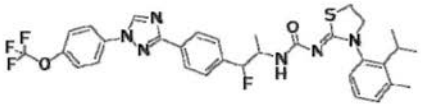
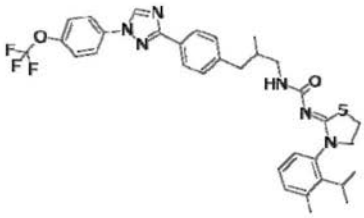
[1729]

 P1636	 P1637
 P1638	 P1639
 P1640	 P1641
 P1642	 P1643
 P1644	 P1645

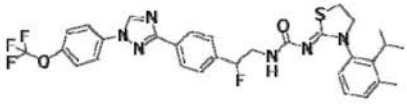
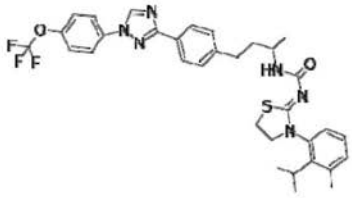
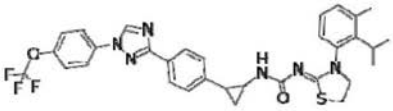
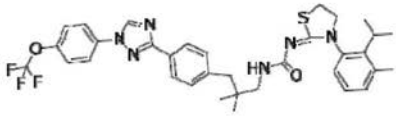
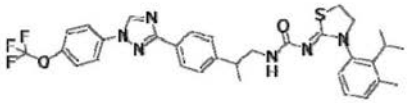
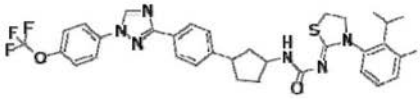
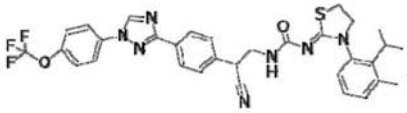
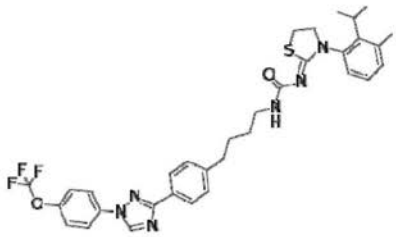
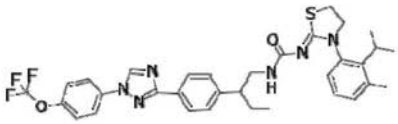
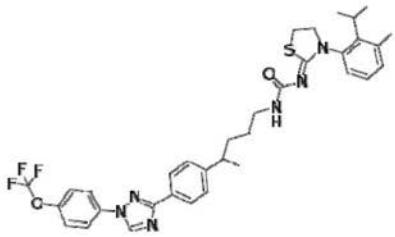
[1730]

 P1646	 P1647
 P1648	 P1649
 P1650	 P1651
 P1652	 P1653
 P1654	 P1655

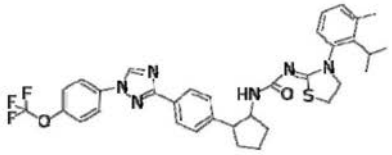
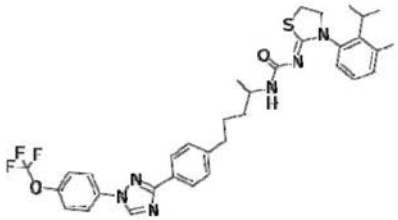
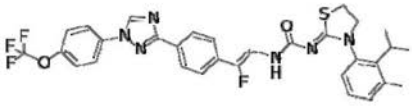
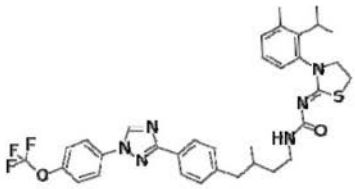
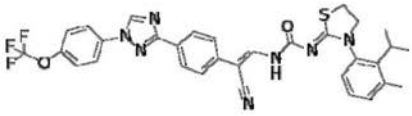
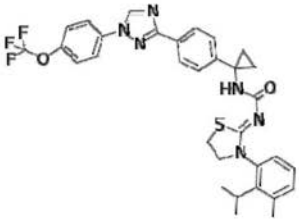
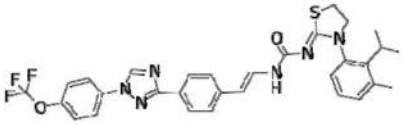
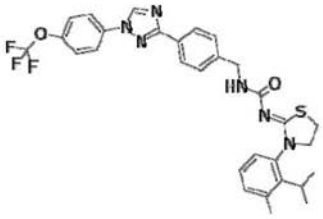
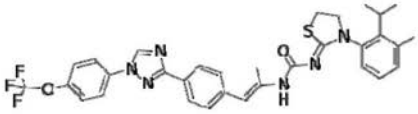
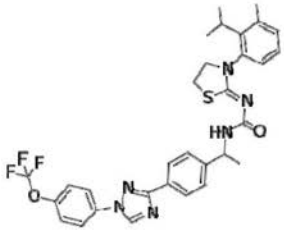
[1731]

 P1656	 P1657
 P1658	 P1659
 P1660	 P1661
 P1662	 P1663
 P1664	 P1665

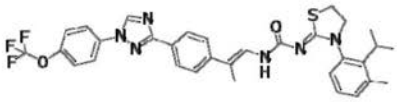
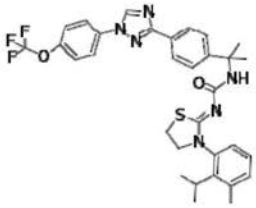
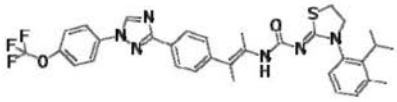
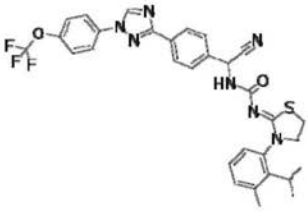
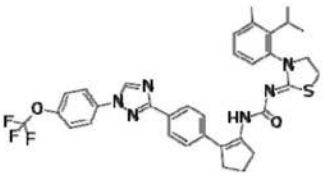
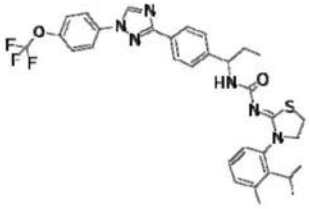
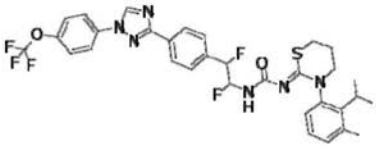
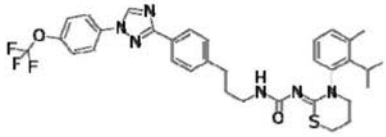
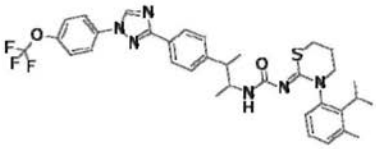
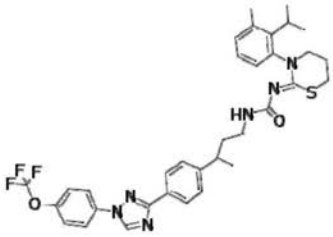
[1732]

 P1666	 P1667
 P1668	 P1669
 P1670	 P1671
 P1672	 P1673
 P1674	 P1675

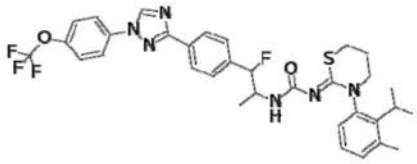
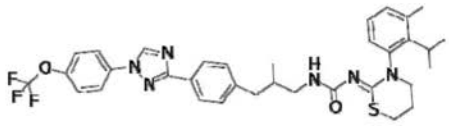
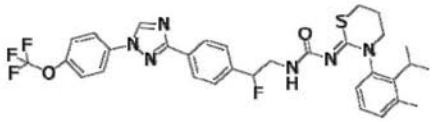
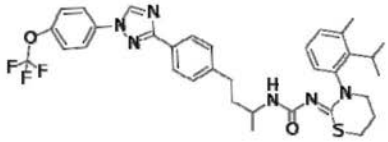
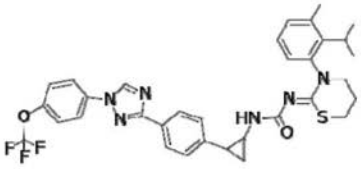
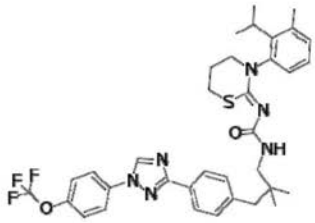
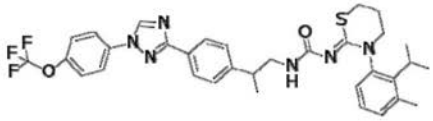
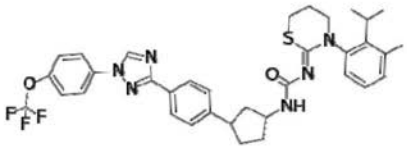
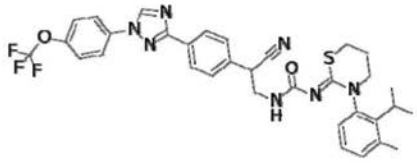
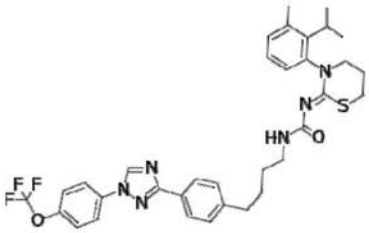
[1733]

 P1676	 P1677
 P1678	 P1679
 P1680	 P1681
 P1682	 P1683
 P1684	 P1685

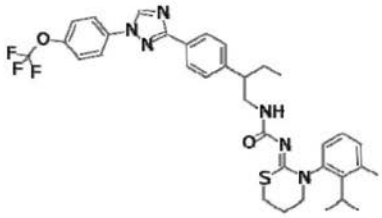
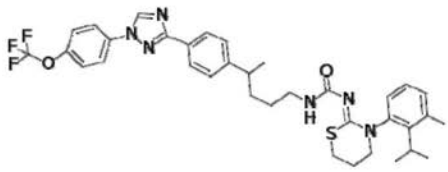
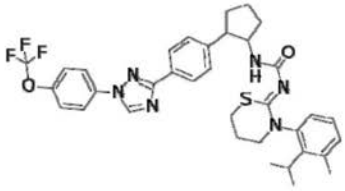
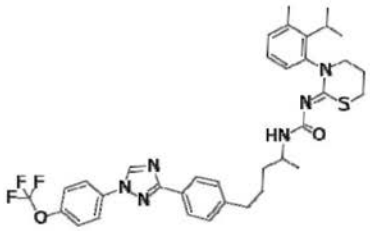
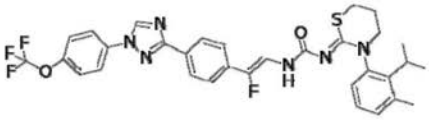
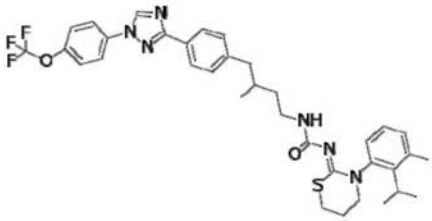
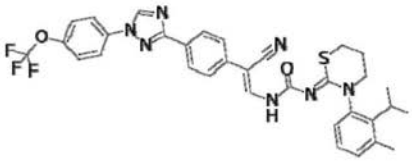
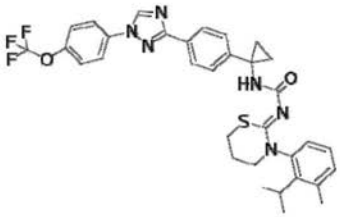
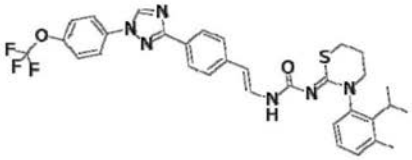
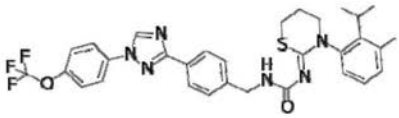
[1734]

 P1686	 P1687
 P1688	 P1689
 P1690	 P1691
 P1692	 P1693
 P1694	 P1695

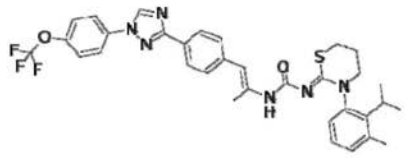
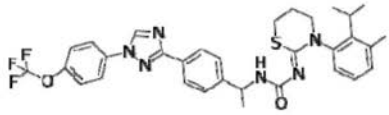
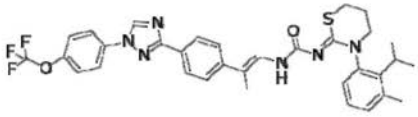
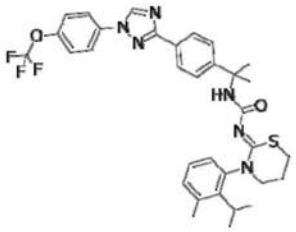
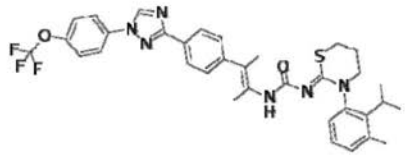
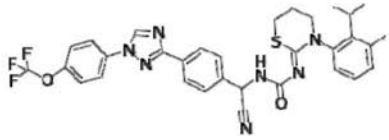
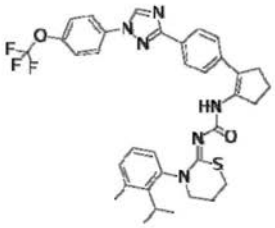
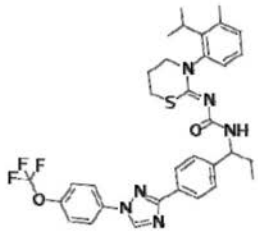
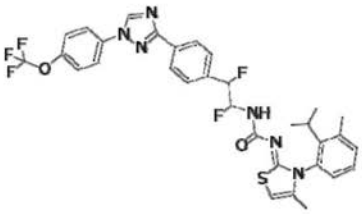
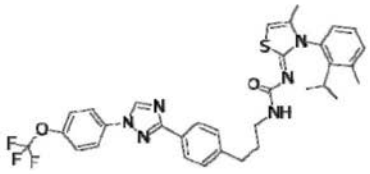
[1735]

 P1696	 P1697
 P1698	 P1699
 P1700	 P1701
 P1702	 P1703
 P1704	 P1705

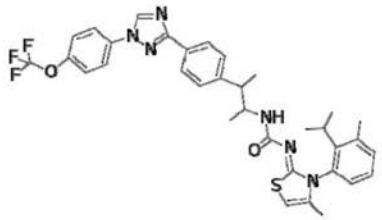
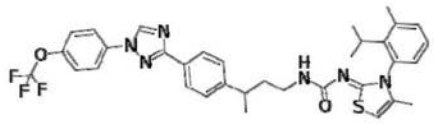
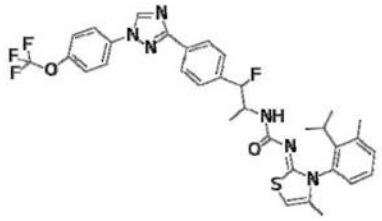
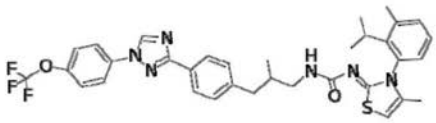
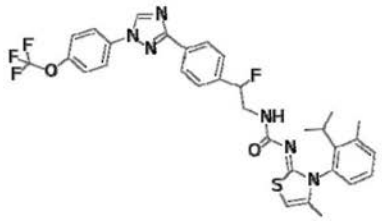
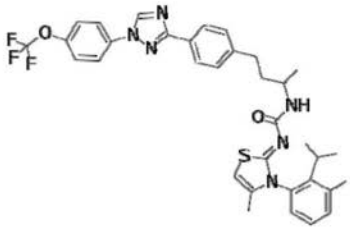
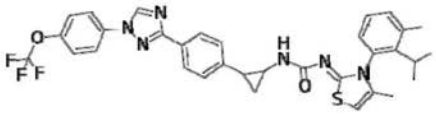
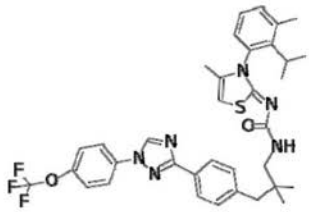
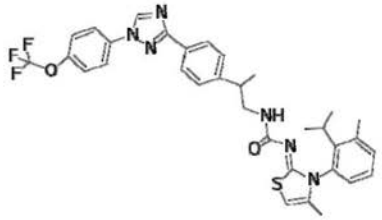
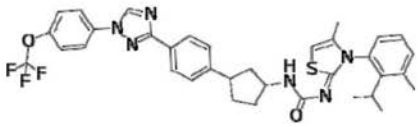
[1736]

 P1706	 P1707
 P1708	 P1709
 P1710	 P1711
 P1712	 P1713
 P1714	 P1715

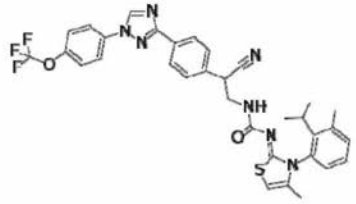
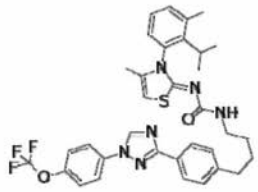
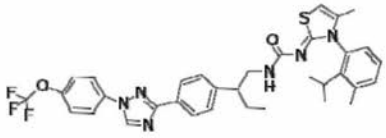
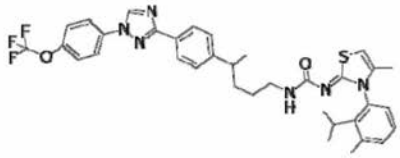
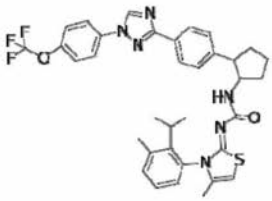
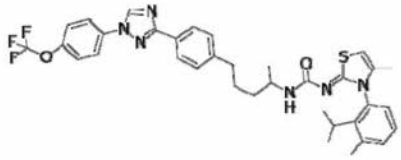
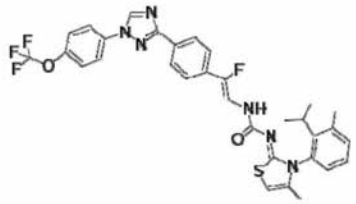
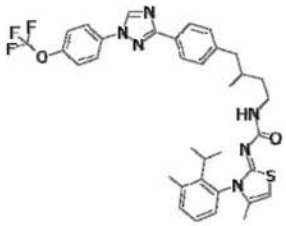
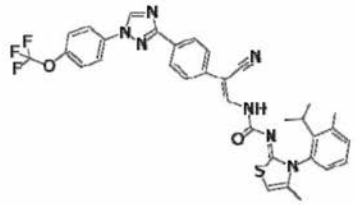
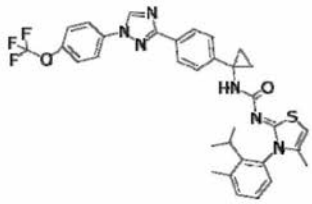
[1737]

 P1716	 P1717
 P1718	 P1719
 P1720	 P1721
 P1722	 P1723
 P1724	 P1725

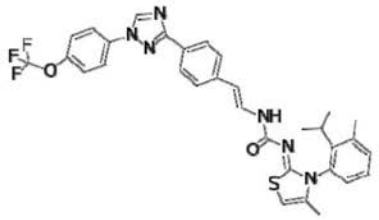
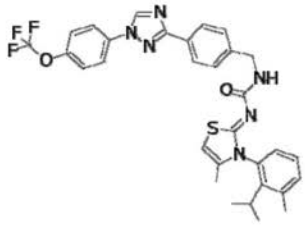
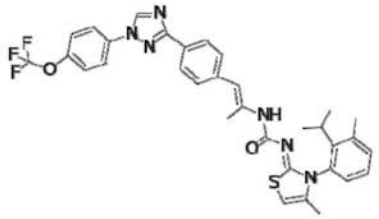
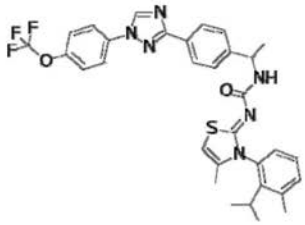
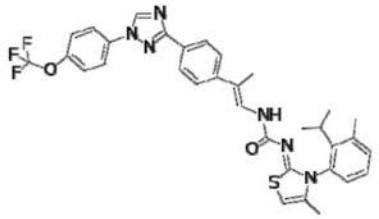
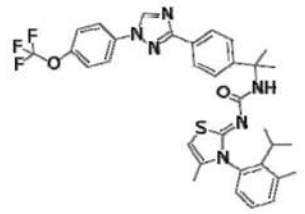
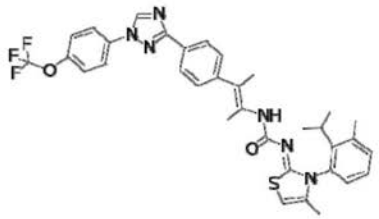
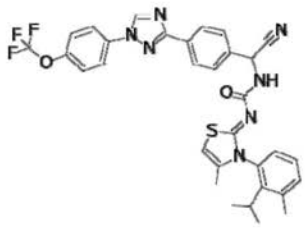
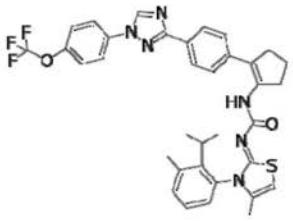
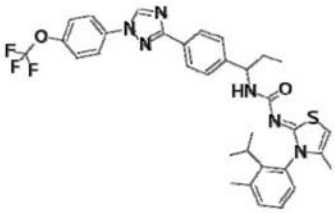
[1738]

 P1726	 P1727
 P1728	 P1729
 P1730	 P1731
 P1732	 P1733
 P1734	 P1735

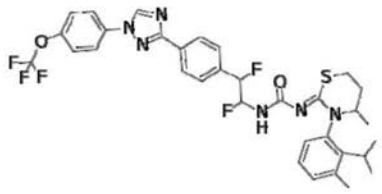
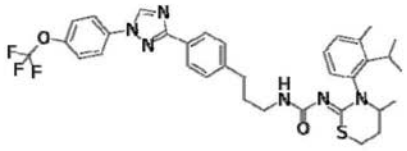
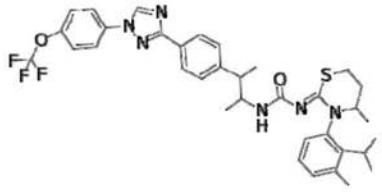
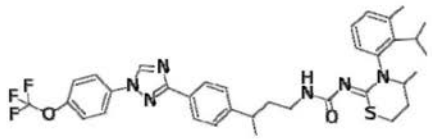
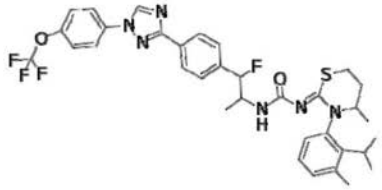
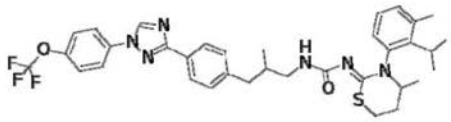
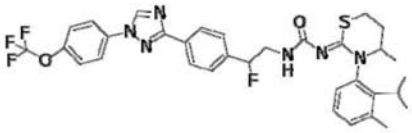
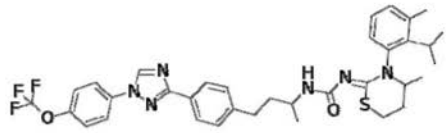
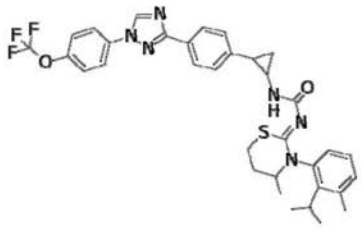
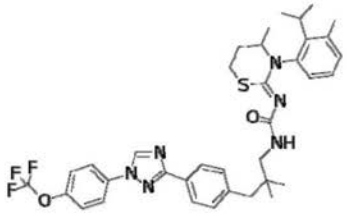
[1739]

 P1736	 P1737
 P1738	 P1739
 P1740	 P1741
 P1742	 P1743
 P1744	 P1745

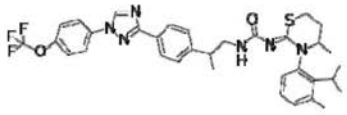
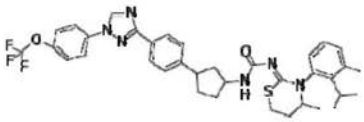
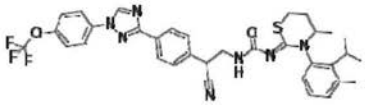
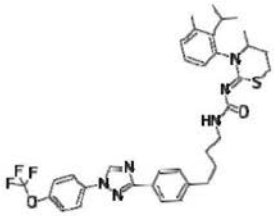
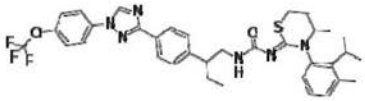
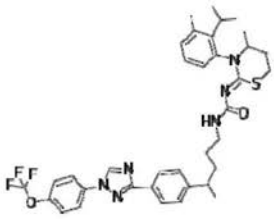
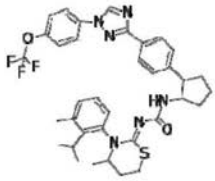
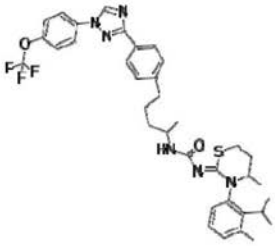
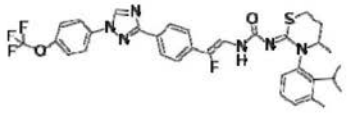
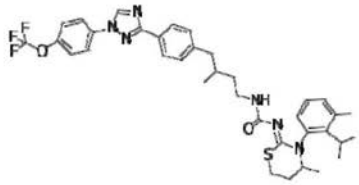
[1740]

 P1746	 P1747
 P1748	 P1749
 P1750	 P1751
 P1752	 P1753
 P1754	 P1755

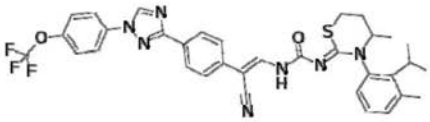
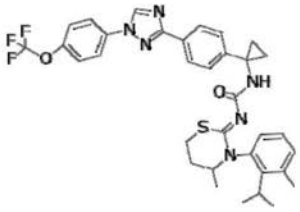
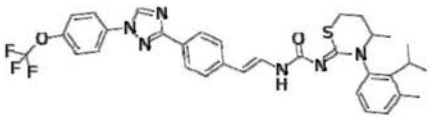
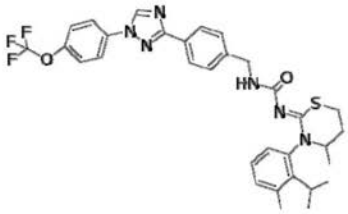
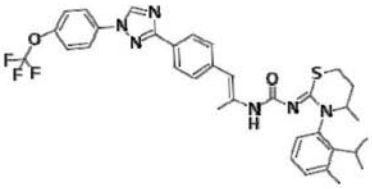
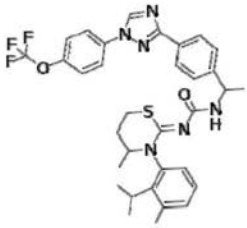
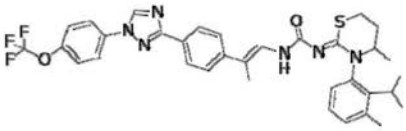
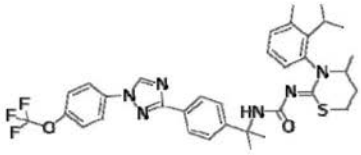
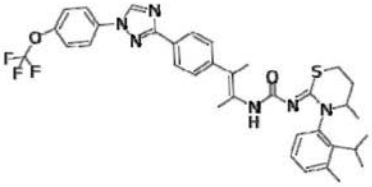
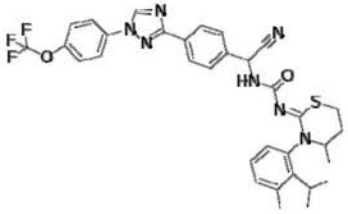
[1741]

 P1756	 P1757
 P1758	 P1759
 P1760	 P1761
 P1762	 P1763
 P1764	 P1765

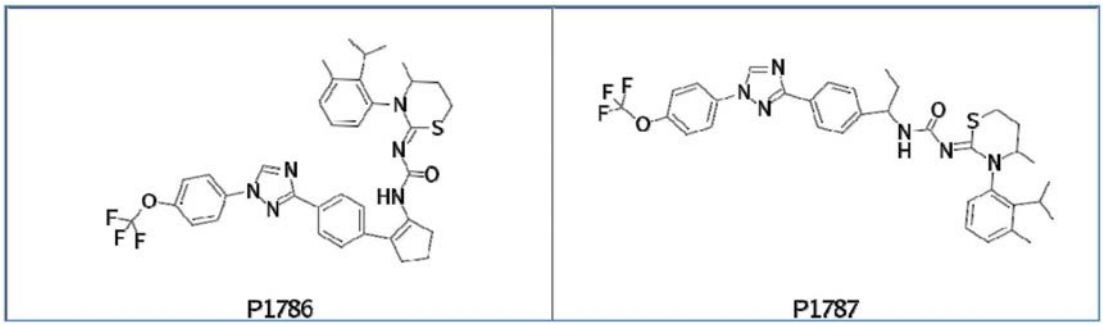
[1742]

 P1766	 P1767
 P1768	 P1769
 P1770	 P1771
 P1772	 P1773
 P1774	 P1775

[1743]

 P1776	 P1777
 P1778	 P1779
 P1780	 P1781
 P1782	 P1783
 P1784	 P1785

[1744]



[1745] 实施例A:甜菜夜蛾(Beet Armyworm,“BAW”)(Spodoptera exigua)和甘蓝银纹夜蛾(Cabbage Looper,“CL”)(Trichoplusia ni)的生物测定

[1746] BAW具有很少有效的寄生虫、疾病或捕食者来降低其种群。BAW侵害许多杂草、树木、草、豆科植物和大田作物。在不同地方,尤其对于以下植物引起的经济方面担忧:芦笋、棉花、玉米、大豆、烟草、苜蓿,甜菜,辣椒,西红柿,土豆,洋葱,豌豆,向日葵,和柑橘。甘蓝银纹夜蛾(Cabbage Looper)为夜蛾科蛾子的成员。它遍及全世界。它攻击以下植物:甘蓝,菜花,青菜花,抱子甘蓝,西红柿,黄瓜,马铃薯,饲用甘蓝,芜菁,芥菜,辣椒,茄子,西瓜,甜瓜,南瓜,棱瓜,豌豆,豆类,羽衣甘蓝,莴苣,菠菜,芹菜,欧芹,甜菜,豌豆,苜蓿,大豆,和棉花。该物种由于极大消耗叶子对植物有非常大的破坏性。但是,在甘蓝的情况下,它们不仅以包装叶为食,而且可以钻入显影头中。幼虫每天消耗的植物物质为其重量的三倍。其进食地点的标志是大量累积的粘性的湿粪物质。

[1747] 因此,由于上述因素,防治这些害虫是重要的。此外,防治这些害虫(BAW和CL)(其为已知的咀嚼害虫)的分子,用于防治咀嚼植物的其他害虫。

[1748] 使用以下实施例中所述的步骤,测试抵抗BAW和CEW的本申请披露的某些分子。在报告结果时,使用“BAW&CL评级表”(参见表部分)。

[1749] 对BAW进行的生物测定

[1750] 对BAW进行的生物测定使用128-孔饲料托盘测定进行。将一至五只第二龄期的BAW幼虫放置在饲料托盘的每一个孔(3mL)中,所述饲料托盘已经预先填充有1mL人工饲料,已向该饲料(向八个孔的每个孔中)中施加了50μg/cm^2试验化合物(溶解在50μL的90:10丙酮-水混合物中),然后使得干燥。用澄清的自粘型盖子将所述托盘盖住并在25℃、14:10光照-避光条件保持五至七天。记录每一个孔中的幼虫的死亡率百分比;然后将八个孔中的活性进行平均。结果在标题为“表ABC:生物学研究结果”的表中示出(参见表部分)。

[1751] 对CL中的甘蓝银纹夜蛾(Cabbage Looper)进行的生物测定

[1752] 对CL的生物测定使用128-孔饲料托盘测定进行。将一至五只第二龄期的CL幼虫放置在饲料托盘的每一个孔(3mL)中,然后使得干燥,所述饲料托盘已经预先填充有1mL人工饲料,已向该饲料(向八个孔的每个孔中)中施加了50μg/cm^2试验化合物(溶解在50μL的90:10丙酮-水混合物中)。用澄清的自粘型盖子将所述托盘盖住并在25℃、14:10光照-避光条件保持五至七天。记录每一个孔中的幼虫的死亡率百分比;然后将八个孔中的活性进行平均。结果在标题为“表ABC:生物学研究结果”的表中示出(参见表部分)。

[1753] 实施例B:对桃蚜(Green Peach Aphid,“GPA”)(Myzus persicae)进行的生物测定。

[1754] GPA是桃树的最重要的蚜虫害虫,导致减少的生长、叶子的干皱和各种组织的死

亡。它也是危险的，因为它充当植物病毒运输的传病媒介，例如马铃薯Y病毒和马铃薯卷叶病毒(对于龙葵/马铃薯家族茄科的成员)，和各种花叶病病毒(对于许多其它粮食作物)。GPA攻击尤其诸如以下的植物：青菜花，牛蒡，甘蓝，胡萝卜，菜花，萝卜(daikon)，茄子，菜豆，莴苣，澳大利亚坚果，番木瓜，胡椒，蕃薯，番茄，水田芥菜，和西葫芦等。GPA也攻击许多观赏作物，如康乃馨、菊花、开花白菜(flowering white cabbage)、猩猩木和玫瑰。GPA已经形成了对许多杀虫剂的耐药性。因此，由于上述因素，防治该害虫是重要的。此外，防治该害虫(GPA)(其已知为刺吸式口器害虫)的分子，用于防治刺吸植物的其他害虫。

[1755] 使用以下实施例中所述的步骤，测试抵抗的本申请披露的某些分子。在报告结果时，使用“GPA评级表”(参见表部分)。

[1756] 将在3英寸罐(pot)中生长的卷心菜幼苗(具有2-3片小的(3-5cm)真叶(true leaf))用作试验底物。用20-50个桃蚜(无翅成虫和若虫阶段)对所述幼苗进行侵害1天，然后进行化学施用。每种处理使用具有各株幼苗的四个罐。将试验化合物(2mg)溶于2mL丙酮/甲醇(1:1)溶剂中，形成浓度为1000ppm试验化合物的储备溶液。储备溶液用0.025％吐温20在水中的溶液稀释5倍以得到浓度为200ppm的试验化合物溶液。使用手持抽吸器型喷雾器将溶液喷雾到卷心菜叶子的两面直到形成径流(runoff)。对照植物(溶剂检测)用仅含20体积％丙酮/甲醇(1:1)溶剂的稀释剂喷雾。将经处理的植物在保育室中在约25℃和环境相对湿度(RH)的条件下保持三天，然后评级。评价通过在显微镜下计数每株植物上的活蚜虫数目来进行。百分比防治通过使用Abbott校正公式(W.S.Abbott,“A Method of Computing the Effectiveness of an Insecticide”J.Econ.Entomol.18(1925),pp.265-267)如下测量。

[1757] 经校正的百分比防治＝100*(X-Y)/X

[1758] 其中

[1759] X＝溶剂检测植物上的活蚜虫数目，以及

[1760] Y＝经处理的植物上的活蚜虫数目

[1761] 结果显示在标题为“表ABC:生物数据”的表中(参见表部分)。

[1762] 实施例C:对黄热病蚊(黄热病Mosquito,“YFM”)(Aedes aegypti)的生物测定。

[1763] YFM倾向于在白天叮食人，最常发现于有人居住的地方或其附近。YFM是传播几种疾病的传病媒介。它是可传播登革热和黄热病病毒的蚊子。黄热病是第二最危险的蚊子传播的疾病，仅次于疟疾。黄热病是一种急性病毒性出血性疾病，未经治疗的受严重影响的人中高达50％会死于黄热病。每年全世界估计有200,000例的黄热病，导致30,000例死亡。登革热是一种严重的病毒性疾病；有时称作"登革热"或"痛心热(break-heart fever)"，由于其可产生剧烈疼痛。登革热每年杀死约20,000个人。因此，由于上述因素，防治该害虫是重要的。此外，防治该害虫(YFM)(已知为刺吸式口器害虫)的分子，用于防治导致人类和动物痛苦的其他害虫。

[1764] 使用以下段落中所述的步骤，测试抵抗YFM的本申请披露的某些分子。在报告结果时，使用“YFM评级表”(参见表部分)。

[1765] 使用含有溶解在100μL二甲亚砜(DMSO)(等同于4000ppm溶液)中的400μg分子的主板(master plate)。主板的组装分子在每个池中含有15μL。向该皿的每个池，加入135μL 90:10水:丙酮的混合物。机器人(Biomek®NXP Laboratory Automation Workstation)进

行程序化分配，从主板吸取15μL到空的96-池浅板（“子”板）中。每个主板创建6个reps（“子”板）。然后将所创建的子板立即用YFM幼虫侵袭。

[1766] 在板待处理之前的这些天里，将蚊卵放置在含有肝粉的微孔水中，开始孵化（4g成为400mL）。使用机器人创建子板之后，将子板用220μL肝粉/蚊幼虫混合物（约1日龄幼虫）侵袭。板由蚊幼虫侵袭之后，将非蒸发性的盖用于盖住板，减少干燥。将板在室温保持3天，然后评级。3天之后，观察每个池，基于死亡率进行评分。

[1767] 结果显示在标题为“表ABC：生物学研究结果”的表中（参见表部分）。

[1768] 农业上可接受的酸加成盐、盐衍生物、溶剂化物、酯衍生物、多晶型物、同位素和放射线核素

[1769] 式一的分子可配制为农业上可接受的酸加成盐。通过非限制性实例，胺官能团可与以下酸形成盐：盐酸、氢溴酸、硫酸、磷酸、乙酸、苯甲酸、柠檬酸、丙二酸、水杨酸、苹果酸、富马酸、草酸、琥珀酸、酒石酸、乳酸、葡糖酸、抗坏血酸、马来酸、天冬氨酸、苯磺酸、甲磺酸、乙磺酸、羟基甲磺酸和羟基乙磺酸。另外，通过非限制性实例，酸官能团可形成盐，包括从碱金属或碱土金属得到的那些盐和从氨和胺得到的那些盐。优选的阳离子的实例包括钠阳离子、钾阳离子和镁阳离子。

[1770] 式一的分子可配制为盐衍生物。通过非限制性实例，盐衍生物可通过使游离碱与足量的所需要的酸接触，从而得到盐来制备。游离碱可如下重新得到：将所述盐用适宜的稀碱水溶液诸如稀氢氧化钠水溶液、稀碳酸钾水溶液、稀氨水溶液和稀碳酸氢钠水溶液处理。作为实例，在许多情况下，杀虫剂诸如2,4-D通过将其转化为其二甲胺盐来变得更具水溶性。

[1771] 式一的分子可配制为与溶剂分子形成稳定的复合物，使得所述复合物在除去非复合的溶剂之后保持完整。这些复合物通常称为“溶剂化物”。但是，特别需要与作为溶剂的水形成稳定的水合物。

[1772] 可使式一的分子配制为酯衍生物。然后，这些酯衍生物可按与本申请中披露的分子的施用方式相同的方式施用。

[1773] 可使式一的分子配制为各种结晶多晶型物。多晶型现象在开发农药中是重要的，这是因为相同分子的不同结晶多晶型物或结构可具有非常不同的物理性质和生物性能。

[1774] 可使式一的分子用不同的同位素制备。特别重要的是具有^{2}H（也称为氘）代替^{1}H的分子。

[1775] 可使式一的分子用不同的放射性核素制备。特别重要的是具有^{14}C的分子。

[1776] 立体异构体

[1777] 式一的分子可按一种或多种立体异构体的形式存在。因此，某些分子可制备为外消旋混合物。本领域技术人员应该理解的是，一种立体异构体可能比其它立体异构体更具活性。单一立体异构体可如下得到：已知的选择性的合成方法、使用拆分起始原料的常规合成方法或常规的拆分方法。本申请中披露的某些分子可作为两种或者更多种异构体存在。各种异构体包括几何异构体、非对映异构体，和对映异构体。因此，本申请中披露的分子包括几何异构体、外消旋混合物、单一立体异构体，和光学活性混合物。本领域技术人员应该理解的是，一种异构体可比其它异构体更有活性。为清楚起见，本申请中披露的结构仅以一种几何形式描绘，但是意在代表分子的所有几何形式。

[1778] 组合

[1779] 在另一个实施方式中,式一分子可以与各自具有式一分子的作用模式("MoA")相同、类似或不同的作用模式的一种或多种化合物组合使用(例如,在组合的混合物中,或同时或顺序施用)。作用模式包括,例如以下:乙酰胆碱酯酶抑制剂(Acetylcholinesterase (AChE) inhibitors);GABA门控氯化物通道拮抗剂(GABA-gatedChlorideChannel antagonists);钠通道调节剂(SodiumChannel modulators);烟碱性乙酰胆碱(nAChR)激动剂(Nicotinic acetylcholine(nAChR)agonists);烟碱性乙酰胆碱受体(nAChR)别构激活剂(Nicotinic acetylcholine receptor(nAChR)allosteric activators);氯化物通道激活剂(ChlorideChannel activators);保幼激素仿制品(Juvenile hormone mimics);杂性非特异(多位点)抑制剂(Miscellaneous non-specific(multi-site)inhibitors);选择性同翅目取食阻滞剂(Selective homopteran feeding blockers);螨生长抑制剂(Mite growth inhibitors);昆虫中肠膜微生物紊乱剂(Microbial disruptors of insect midgut membranes);线粒体ATP合成酶抑制剂(Inhibitors of mitochondrial ATP synthase);经由破坏质子梯度引起氧化磷酸化的解偶联剂(Uncouplers of oxidative phosphorylation via disruption of the proton gradient);烟碱性乙酰胆碱受体(nAChR)通道阻滞剂(Nicotinic acetylcholine receptor(nAChR)channel blockers);甲壳素生物合成抑制剂,0型(Inhibitors ofChitin biosynthesis,type 0);甲壳素生物合成抑制剂,1型(Inhibitors ofChitin biosynthesis,type 1);蜕皮干扰剂,双翅目昆虫(Moulting disruptor,Dipteran);昆虫蜕皮激素受体激动剂(Ecdysone receptor agonists);章鱼胺受体激动剂(Octopamine receptor agonists);线粒体复合物III电子传递抑制剂(Mitochondrial complex III electron transport inhibitors);线粒体复合物I电子传递抑制剂(Mitochondrial complex I electron transport inhibitors);电压依赖性钠通道阻滞剂(Voltage-dependent sodiumChannel blockers);乙酰辅酶A羧化酶抑制剂(Inhibitors of acetylCoACarboxylase);线粒体复合物IV电子传递抑制剂(Mitochondrial complex IV electron transport inhibitors);线粒体复合物II电子传递抑制剂(Mitochondrial complex II electron transport inhibitors);和兰尼碱受体调节剂(Ryanodine receptor modulators).

[1780] 在另一个实施方式中,式一分子可以与具有杀螨,杀藻,杀卵,杀细菌,杀真菌,除草,杀昆虫,杀软体动物,杀线虫,杀鼠,和/或杀病毒性质的一种或多种化合物组合使用(例如,在组合的混合物中,或同时或顺序施用)。

[1781] 在另一个实施方式中,式一分子可以与一种或多种化合物组合使用(例如,在组合的混合物中,或同时或顺序施用),所述一种或多种化合物作为抗饲育剂(antifeedants),驱鸟剂(bird repellents),化学绝育剂(chemosterilants),除草剂安全剂(herbicide safeners),昆虫引诱剂(insect attractants),昆虫驱避剂(insect repellents),哺乳动物驱避剂(mammal repellents),交配扰乱剂(mating disrupters),植物活化剂(plant activators),植物生长调节剂(plant growth regulators),和/或协同剂。

[1782] 在另一个实施方式中,式一分子可以与一种或多种下面的化合物组合使用(例如,在组合的混合物中,或同时或顺序施用):(3-乙氧基丙基)溴化汞((3-ethoxypropyl) mercury bromide),1,2-二氯丙烷(1,2-dichloropropane),1,3-二氯丙烯(1,3-

dichloropropene),1-甲基环丙烯(1-methylcyclopropene),1-萘酚(1-naphthol),2-(辛基硫基)乙醇(2-(octylthio)ethanol),2,3,5-三-碘苯甲酸(2,3,5-tri-iodobenzoic acid),草芽平(2,3,6-TBA),草芽平-二甲铵(2,3,6-TBA-dimethylammonium),草芽平-锂(2,3,6-TBA-lithium),草芽平-钾(2,3,6-TBA-potassium),草芽平-钠(2,3,6-TBA-sodium),2,4,5-涕(2,4,5-T),2,4,5-涕-2-丁氧基丙基(2,4,5-T-2-butoxypropyl),2,4,5-涕-2-乙基己基(2,4,5-T-2-ethylhexyl),2,4,5-涕-3-丁氧基丙基(2,4,5-T-3-butoxypropyl),2,4,5-涕丁酸(2,4,5-TB),2,4,5-涕-丁氧甲酯(2,4,5-T-butometyl),2,4,5-涕-丁氧乙酯(2,4,5-T-butotyl),2,4,5-涕-丁基(2,4,5-T-butyl),2,4,5-涕-异丁基(2,4,5-T-isobutyl),2,4,5-涕-异辛酯(2,4,5-T-isoctyl),2,4,5-涕-异丙基(2,4,5-T-isopropyl),2,4,5-涕-甲基(2,4,5-T-methyl),2,4,5-涕-戊基(2,4,5-T-pentyl),2,4,5-涕-钠(2,4,5-T-sodium),2,4,5-涕-三乙铵(2,4,5-T-triethylammonium),2,4,5-涕-三乙醇胺(2,4,5-T-trolamine),2,4-滴(2,4-D),2,4-滴-2-丁氧基丙基(2,4-D-2-butoxypropyl),2,4-滴-2-乙基己基(2,4-D-2-ethylhexyl),2,4-滴-3-丁氧基丙基(2,4-D-3-butoxypropyl),2,4-滴-铵(2,4-D-ammonium),2,4-滴丁酸(2,4-DB),2,4-滴丁酸-丁基(2,4-DB-butyl),2,4-滴丁酸-二甲铵(2,4-DB-dimethylammonium),2,4-滴丁酸-异辛酯(2,4-DB-isoctyl),2,4-滴丁酸-钾(2,4-DB-potassium),2,4-滴丁酸-钠(2,4-DB-sodium),2,4-滴-丁氧乙酯(2,4-D-butotyl),2,4-滴-丁基(2,4-D-butyl),2,4-滴-二乙铵(2,4-D-diethylammonium),2,4-滴-二甲铵(2,4-D-dimethylammonium),2,4-滴-二醇胺(2,4-D-diolamine),2,4-滴-十二烷基铵(2,4-D-dodecylammonium),赛信(2,4-DEB),伐草磷(2,4-DEP),2,4-滴-乙基(2,4-D-ethyl),2,4-滴-庚基铵(2,4-D-heptylammonium),2,4-滴-异丁基(2,4-D-isobutyl),2,4-滴-异辛酯(2,4-D-isoctyl),2,4-滴-异丙基(2,4-D-isopropyl),2,4-滴-异丙基铵(2,4-D-isopropylammonium),2,4-滴-锂(2,4-D-lithium),2,4-滴-甲基庚基酯(2,4-D-meptyl),2,4-滴-甲基(2,4-D-methyl),2,4-滴-辛基(2,4-D-octyl),2,4-滴-戊基(2,4-D-pentyl),2,4-滴-钾(2,4-D-potassium),2,4-滴-丙基(2,4-D-propyl),2,4-滴-钠(2,4-D-sodium),2,4-滴-糖草酯(2,4-D-tefuryl),2,4-滴-十四烷基铵(2,4-D-tetradecylammonium),2,4-滴-三乙铵(2,4-D-triethylammonium),2,4-滴-三(2-羟基丙基)铵(2,4-D-tris(2-hydroxypropyl)ammonium),2,4-滴-三乙醇胺(2,4-D-trolamine),2iP,2-甲氧基乙基氯化汞(2-methoxyethylmercury chloride),2-苯基苯酚(2-phenylphenol),3,4-滴胺(3,4-DA),3,4-滴丁酸(3,4-DB),3,4-滴丙酸(3,4-DP),4-氨基吡啶(4-aminopyridine),对氯苯氧乙酸(4-CPA),对氯苯氧乙酸-二乙醇胺(4-CPA-diolamine),对氯苯氧乙酸-钾(4-CPA-potassium),对氯苯氧乙酸-钠(4-CPA-sodium),氯苯氧丁酸(4-CPB),氯苯氧丙酸(4-CPP),4-羟基苯乙醇(4-hydroxyphenethyl alcohol),8-羟基硫酸喹啉(8-hydroxyquinoline sulfate),8-phenylmercurioxyquinoline,阿维菌素(abamectin),诱抗素(abscisic acid),ACC,乙酰甲胺磷(acephate),灭螨醌(acequinocyl),啶虫脒(acetamiprid),家蝇磷(acethion),乙草胺(acetochlor),乙酯磷(acetophos),acetoprole,活化酯(acibenzolar),活化酯-S-甲基(acibenzolar-S-methyl),三氟羧草醚(acifluorfen),三氟羧草醚-甲基(acifluorfen-methyl),三氟羧草醚-钠(acifluorfen-sodium),苯草醚(aclonifen),acrep,氟丙菊酯(acrinathrin),丙烯醛(acrolein),丙烯腈(acrylonitrile),八九十混酸(acypetacs),八九十混酸铜

(acypetacs-copper),八九十混酸锌(acypetacs-zinc),afidopyropen,甲草胺(alachlor),棉铃威(alanycarb),丙硫多菌灵(albendazole),涕灭威(aldicarb),aldimorph,涕灭砜威(aldoxycarb),艾氏剂(aldrin),烯丙菊酯(allethrin),大蒜素(allicin),二丙烯草胺(allidochlor),阿洛氨菌素(allosamidin),禾草灭(alloxydim),禾草灭-钠(alloxydim-sodium),烯丙醇(allyl alcohol),除害威(allyxycarb),五氯戊酮酸(alorac),顺式氯氰菊酯(alpha-cypermethrin),α-硫丹(alpha-endosulfan),辛唑嘧菌胺(ametoctradin),特津酮(ametridione),莠灭净(ametryn),特草嗪酮(amibuzin),氨唑草酮(amicarbazone),拌种灵(amicarthiazol),赛硫磷(amidithion),amidoflumet,酰嘧磺隆(amidosulfuron),灭害威(aminocarb),环丙嘧啶酸(aminocyclopyrachlor),环丙嘧啶酸-甲基(aminocyclopyrachlor-methyl),环丙嘧啶酸-钾(aminocyclopyrachlor-potassium),氯氨基吡啶酸(aminopyralid),氯氨基吡啶酸-钾(aminopyralid-potassium),氯氨基吡啶酸-三(2-羟基丙基)铵(aminopyralid-tris(2-hydroxypropyl) ammonium),甲基胺草磷(amiprofos-methyl),胺草磷(amiprophos),吲唑磺菌胺(amisulbrom),胺吸磷(amiton),胺吸磷草酸盐(amiton oxalate),双甲脒(amitraz),杀草强(amitrole),氨基磺酸铵(ammonium sulfamate),α-萘乙酸铵(ammoniumα-naphthaleneacetate),代森铵(amobam),1-氨基丙基磷酸(ampropylfos),新烟碱(anabasine),新烟碱硫酸盐(anabasine sulfate),环丙嘧啶醇(ancymidol),敌菌灵(anilazine),莎稗磷(anilofos),疏草隆(anisuron),蒽醌(anthraquinone),安妥(antu),唑磷嗪(apholate),杀螨特(aramite),三氧化二砷(arsenous oxide),福美砷(asomate),阿司匹林(aspirin),磺草灵(asulam),磺草灵-钾(asulam-potassium),磺草灵-钠(asulam-sodium),艾噻达松(athidathion),阿特拉通(atraton),莠去津(atrazine),金色制酶素(aureofungin),aviglycine,aviglycine hydrochloride,氧环唑(azaconazole),印楝素(azadirachtin),唑啶草酮(azafenidin),甲基吡噁磷(azamethiphos),四唑嘧磺隆(azimsulfuron),益棉磷(azinphos-ethyl),保棉磷(azinphos-methyl),叠氮净(aziprotryne),氧化辅美双(azithiram),偶氮苯(azobenzene),三唑锡(azocyclotin),偶氮磷(azothoate),嘧菌酯(azoxystrobin),bachmedesh,燕麦灵(barban),六氟硅酸钡(barium hexafluorosilicate),多硫化钡(barium polysulfide),熏虫菊(barthrin),BCPC,氟丁酰草胺(beflubutamid),苯霜灵(benalaxyl),苯霜灵-M(benalaxyl-M),草除灵(benazolin),草除灵-二甲铵(benazolin-dimethylammonium),草除灵-乙基(benazolin-ethyl),草除灵-钾(benazolin-potassium),bencarbazone,benclothiaz,噁虫威(bendiocarb),乙丁氟灵(benfluralin),丙硫克百威(benfuracarb),呋草黄(benfuresate),麦锈灵(benodanil),苯菌灵(benomyl),解草嗪(benoxacor),苯噁磷(benoxafos),醌肟腙(benquinox),苄嘧磺隆脱甲基酸(bensulfuron),苄嘧磺隆(bensulfuron-methyl),地散磷(bensulide),杀虫磺(bensultap),丙唑草隆(bentaluron),灭草松(bentazone),灭草松-钠(bentazone-sodium),苯噻菌胺(benthiavalicarb),苯噻菌胺-异丙基(benthiavalicarb-isopropyl),苯噻硫氰(benthiazole),苯草灭(bentranil),胺酸杀(benzadox),胺酸杀-铵(benzadox-ammonium),苯扎氯铵(benzalkonium Chloride),苄烯酸(benzamacril),苄烯酸(benzamacril-isobutyl),苯杂吗(benzamorf),双苯嘧草酮(benzfendizone),苄草胺

(benzipram)，苯并双环酮(benzobicyclon)，吡草酮(benzofenap)，氟磺胺草(benzofluor)，苯基异羟肟酸(benzohydroxamic acid)，苯并烯氟菌唑(benzovindiflupyr)，苯螨特(benzoximate)，新燕灵(benzoylprop)，新燕灵-乙基(benzoylprop-ethyl)，苯噻隆(benzthiazuron)，苯甲酸苄酯(benzyl benzoate)，苄基腺嘌呤(benzyladenine)，小檗碱(berberine)，盐酸小檗碱(berberine Chloride)，β-氟氯氰菊酯(beta-cyfluthrin)，β-氯氰菊酯(beta-cypermethrin)，bethoxazin，氟吡草酮(bicyclopyrone)，联苯肼酯(bifenazate)，甲羧除草醚(bifenox)，联苯菊酯(bifenthrin)，吡氟菌酯(bifujunzhi)，双丙氨酰膦(bilanafos)，双丙氨酰膦-钠(bilanafos-sodium)，乐杀螨(binapacryl)，病氰硝(bingqingxiao)，生物烯丙菊酯(bioallethrin)，bioethanomethrin，生物氯菊酯(biopermethrin)，生物苄呋菊酯(bioresmethrin)，联苯(biphenyl)，bisazir，叶枯唑(bismerthiazol)，双草醚(bispyribac)，双草醚-钠(bispyribac-sodium)，双三氟虫脲(bistrifluron)，联苯三唑醇(bitertanol)，硫氯酚(bithionol)，bixafen，灰瘟素(blasticidin-S)，硼砂(borax)，波尔多液(Bordeaux mixture)，硼酸(boric acid)，啶酰菌胺(boscalid)，芸苔素内酯(brassinolide)，乙基芸苔素内酯(brassinolide-ethyl)，小蠹性信息素(brevicomin)，溴鼠灵(brodifacoum)，溴灭菊酯(brofenvalerate)，溴氟菊酯(brofluthrinate)，除草定(bromacil)，除草定-锂(bromacil-lithium)，除草定-钠(bromacil-sodium)，溴敌隆(bromadiolone)，溴鼠胺(bromethalin)，溴苄呋菊酯(bromethrin)，溴苯烯磷(bromfenvinfos)，溴乙酰胺(bromoacetamide)，糠草腈(bromobonil)，溴丁酰草胺(bromobutide)，溴烯杀(bromocyclen)，溴-滴滴涕(bromo-DDT)，溴酚肟(bromofenoxim)，溴硫磷(bromophos)，溴硫磷-乙基(bromophos-ethyl)，溴螨酯(bromopropylate)，溴菌腈(bromothalonil)，溴苯腈(bromoxynil)，丁酰溴苯腈(bromoxynil butyrate)，庚酰溴苯腈(bromoxynil heptanoate)，辛酰溴苯腈(bromoxynil octanoate)，溴苯腈-钾(bromoxynil-potassium)，溴莠敏(brompyrazon)，糠菌唑(bromuconazole)，溴硝醇(bronopol)，增效特(bucarpolate)，合杀威(bufencarb)，特克草(buminafos)，乙嘧酚磺酸酯(bupirimate)，噻嗪酮(buprofezin)，勃垦第混合液(Burgundy mixture)，白消安(busulfan)，畜虫威(butacarb)，丁草胺(butachlor)，氟丙嘧草酯(butafenacil)，抑草磷(butamifos)，特嘧硫磷(butathiofos)，丁烯草胺(butenachlor)，苄烯菊酯(butethrin)，特咪唑草(buthidazole)，丁硫啶(buthiobate)，丁噻隆(buthiuron)，丁酮威(butocarboxim)，丁酯膦(butonate)，避蚊酮(butopyronoxyl)，丁酮砜威(butoxycarboxim)，仲丁灵(butralin)，丁苯草酮(butroxydim)，炔草隆(buturon)，丁胺(butylamine)，丁酸盐(butylate)，二甲胂酸(cacodylic acid)，硫线磷(cadusafos)，唑草胺(cafenstrole)，砷酸钙(calcium arsenate)，氯酸钙(calcium chlorate)，氰氨化钙(calcium cyanamide)，石硫合剂(calcium polysulfide)，敌敌钙(calvinphos)，克草胺酯(cambendichlor)，毒杀芬(camphechlor)，樟脑(camphor)，敌菌丹(captafol)，克菌丹(captan)，吗菌威(carbamorph)，氯灭杀威(carbanolate)，甲萘威(carbaryl)，卡巴草灵(carbasulam)，多菌灵(carbendazim)，多菌灵苯磺酸盐(carbendazim benzenesulfonate)，多菌灵亚硫酸盐(carbendazim sulfite)，双酰草胺(carbetamide)，克百威(carbofuran)，二硫化碳(carbon disulfide)，四氯化碳(carbon tetrachloride)，

三硫磷(carbophenothion),丁硫克百威(carbosulfan),特噁唑威(carboxazole),环二混剂(carboxide),萎锈灵(carboxin),唑草酮(carfentrazone),唑草酮-乙基(carfentrazone-ethyl),环丙酰菌胺(carpropamid),杀螟丹(cartap),杀螟丹盐酸盐(cartap hydrochloride),香芹酚(carvacrol),香芹酮(carvone),草立死(CDEA),叶枯炔(cellocidin),CEPC,ceralure,菌杀特(Cheshunt mixture),灭螨猛(chinomethionat),聚氨基葡糖(chitosan),灭瘟唑(chlobenthiazone),甲氧除草醚(chlomethoxyfen),氯醛糖(chloralose),草灭畏(chloramben),草灭畏-铵(chloramben-ammonium),草灭畏-二醇胺(chloramben-diolamine),草灭畏-甲基(chloramben-methyl),草灭畏-甲基铵(chloramben-methylammonium),草灭畏-钠(chloramben-sodium),氯胺磷(chloramine phosphorus),氯霉素(chloramphenicol),双胺灵(chloraniformethan),四氯对醌(chloranil),丁酰草胺(chloranocryl),氯虫苯甲酰胺(chlorantraniliprole),炔禾灵(chlorazifop),炔禾灵(chlorazifop-propargyl),可乐津(chlorazine),杀螨醚(chlorbenside),灭幼脲(chlorbenzuron),冰片丹(chlorbicyclen),氯溴隆(chlorbromuron),氯炔灵(chlorbufam),氯丹(chlordane),开蓬(chlordecone),杀虫脒(chlordimeform),杀虫脒盐酸盐(chlordimeform hydrochloride),氯烯炔菊酯(chlorempenthrin),氯氧磷(chlorethoxyfos),乙氧苯隆(chloreturon),伐草克(chlorfenac),伐草克-铵(chlorfenac-ammonium),伐草克-钠(chlorfenac-sodium),虫螨腈(chlorfenapyr),苯咪唑菌(chlorfenazole),杀螨醇(chlorfenethol),燕麦酯(chlorfenprop),杀螨酯(chlorfenson),敌螨特(chlorfensulphide),毒虫畏(chlorfenvinphos),氟啶脲(chlorfluazuron),氟嘧杀(chlorflurazole),氯芴酸(chlorfluren),chlorfluren-methyl,整形醇(chlorflurenol),整形醇-甲基(chlorflurenol-methyl),氯草敏(chloridazon),氯嘧磺隆(chlorimuron),氯嘧磺隆(chlorimuron-ethyl),氯甲硫磷(chlormephos),矮壮素(chlormequat),矮壮素(chlormequat Chloride),氯乙灵(chlornidine),草枯醚(chlornitrofen),乙酯杀螨醇(chlorobenzilate),二硝萘(chlorodinitronaphthalenes),氯仿(chloroform),伊托明(chloromebuform),灭虫脲(chloromethiuron),氯苯甲醚(chloroneb),氯鼠酮(chlorophacinone),氯敌鼠钠盐(chlorophacinone-sodium),氯化苦(chloropicrin),三氯丙酸(chloropon),丙酯杀螨醇(chloropropylate),百菌清(chlorothalonil),氯麦隆(chlorotoluron),枯草隆(chloroxuron),羟敌草腈(chloroxynil),三丁氯苄膦(chlorphonium),氯化三丁氯苄膦(chlorphonium Chloride),氯辛硫磷(chlorphoxim),chlorprazophos,草败死(chlorprocarb),氯苯胺灵(chlorpropham),毒死蜱(chlorpyrifos),甲基毒死蜱(chlorpyrifos-methyl),四氯喹噁啉(chlorquinox),氯磺隆(chlorsulfuron),氯酞酸(chlorthal),氯酞酸-二甲基(chlorthal-dimethyl),氯酞酸-甲基(chlorthal-monomethyl),氯硫酰草胺(chlorthiamid),虫螨磷(chlorthiophos),乙菌利(chlozolinate),氯化胆碱(choline Chloride),环虫酰肼(chromafenozide),瓜叶菊素I(cinerin I),瓜叶菊素II(cinerin II),瓜叶菊素(cinerins),吲哚酮草酯(cinidon-ethyl),环庚草醚(cinmethylin),醚磺隆(cinosulfuron),ciobutide,咯草隆(cisanilide),左旋反灭虫菊酯(cismethrin),clacyfos,烯草酮(clethodim),咪菌酮(climbazole),碘氯啶酯(cliodinate),clodinafop,炔草酯(clodinafop-propargyl),除

线威(cloethocarb),clofencet,clofencet-potassium,四螨嗪(clofentezine),氯贝酸(clofibric acid),clofop,clofop-isobutyl,异噁草酮(clomazone),稗草胺(clomeprop),调果酸(cloprop),环丁烯草酮(cloproxydim),二氯吡啶酸(clopyralid),二氯吡啶酸-甲基(clopyralid-methyl),二氯吡啶酸-醇胺(clopyralid-olamine),二氯吡啶酸-钾(clopyralid-potassium),二氯吡啶酸-三(2-羟基丙基)铵(clopyralid-tris(2-hydroxypropyl)ammonium),cloquintocet,解草酯(cloquintocet-mexyl),cloransulam,cloransulam-methyl,氯氰碘柳胺(closantel),噻虫胺(clothianidin),克霉唑(clotrimazole),座果酸(cloxyfonac),座果酸-钠(cloxyfonac-sodium),CMA,codlelure,噻唑硫磷(colophonate),乙酸铜(copper acetate),乙酰亚砷酸铜(copper acetoarsenite),砷酸铜(copper arsenate),碱式碳酸铜(copper Carbonate,basic),氢氧化铜(copper hydroxide),环烷羧酸铜(copper naphthenate),油酸铜(copper oleate),氯氧化铜(copper oxychloride),硅酸铜(copper silicate),硫酸铜(copper sulfate),铜锌铬酸盐(copper zinc Chromate),氯灭鼠灵(coumachlor),克鼠灵(coumafuryl),蝇毒磷(coumaphos),杀鼠醚(coumatetralyl),畜虫磷(coumithoate),coumoxystrobin,coumoxystrobin,害扑威(CPMC),氯胺叉草(CPMF),氯丙灵(CPPC),醚草敏(credazine),甲酚(cresol),鼠立死(crimidine),克罗米通(crotamiton),巴毒磷(crotoxyphos),育畜磷(crufomate),氟铝酸钠(cryolite),诱蝇酮(cue-lure),cufraneb,苄草隆(cumyluron),cuprobam,氧化亚铜(cuprous oxide),莪术醇(curcumenol),氰胺(cyanamide),氰草净(cyanatryn),氰草津(cyanazine),苯腈膦(cyanofenphos),杀螟腈(cyanophos),果虫磷(cyanthoate),cyantraniliprole,氰霜唑(cyazofamid),cybutryne,环菌胺(cyclafuramid),cyclanilide,环虫菊酯(cyclethrin),环草敌(cycloate),放线菌酮(cycloheximide),环螨酯(cycloprate),乙氰菊酯(cycloprothrin),cyclopyrimorate,环丙嘧磺隆(cyclosulfamuron),噻草酮(cycloxydim),环莠隆(cycluron),cyenopyrafen,环氟菌胺(cyflufenamid),丁氟螨酯(cyflumetofen),氟氯氰菊酯(cyfluthrin),cyhalofop,cyhalofop-butyl,氯氟氰菊酯(cyhalothrin),三环锡(cyhexatin),cymiazole,cymiazole hydrochloride,霜脲氰(cymoxanil),解草胺腈(cyometrinil),氰菌灵(cypendazole),氯氰菊酯(cypermethrin),牧草快(cyperquat),氯化牧草快(cyperquat Chloride),苯醚氰菊酯(cyphenothrin),环丙津(cyprazine),三环塞草胺(cyprazole),环丙唑醇(cyproconazole),嘧菌环胺(cyprodinil),酯菌胺(cyprofuram),环酰草胺(cypromid),cyprosulfamide,灭蝇胺(cyromazine),畜蜱磷(cythioate),香草隆(daimuron),茅草枯(dalapon),茅草枯-钙(dalapon-calcium),茅草枯-镁(dalapon-magnesium),茅草枯-钠(dalapon-sodium),丁酰肼(daminozide),哒幼酮(dayoutong),棉隆(dazomet),棉隆-钠(dazomet-sodium),二溴氯丙烷(DBCP),d-樟脑(d-camphor),二氯异丙醚(DCIP),增产胺(DCPTA),滴滴涕(DDT),咪菌威(debacarb),癸磷锡(decafentin),decarbofuran,脱氢乙酸(dehydroacetic acid),异丁草胺(delachlor),溴氰菊酯(deltamethrin),田乐磷(demephion),田乐磷-O(demephion-O),田乐磷-S(demephion-S),内吸磷(demeton),甲基内吸磷(demeton-methyl),内吸磷-O(demeton-O),内吸磷-O-甲基(demeton-O-methyl),内吸磷-S(demeton-S),内吸磷-S-甲基(demeton-S-methyl),砜吸磷(demeton-S-methylsulphon),甜菜安(desmedipham),敌草净(desmetryn),右旋反式氯炔

丙菊酯(d-fanshiluquebingjuzhi),丁醚脲(diafenthiuron),氯亚胺硫磷(dialifos),燕麦敌(di-allate),除线特(diamidafos),硅藻土(diatomaceous earth),二嗪磷(diazinon),邻苯甲二酸二丁酯(dibutyl phthalate),琥珀酸二丁酯(dibutyl succinate),麦草畏(dicamba),麦草畏-二甘醇胺(dicamba-diglycolamine),麦草畏-二甲铵(dicamba-dimethylammonium),麦草畏-二醇胺(dicamba-diolamine),麦草畏-异丙基铵(dicamba-isopropylammonium),麦草畏-甲基(dicamba-methyl),麦草畏-醇胺(dicamba-olamine),麦草畏-钾(dicamba-potassium),麦草畏-钠(dicamba-sodium),麦草畏-三乙醇胺(dicamba-trolamine),异氯磷(dicapthon),敌草腈(dichlobenil),除线磷(dichlofenthion),苯氟磺胺(dichlofluanid),二氯萘醌(dichlone),氯全隆(dichloralurea),除幼脲(dichlorbenzuron),dichlorflurenol,dichlorflurenol-methyl,苄胺灵(dichlormate),烯丙酰草胺(dichlormid),双氯酚(dichlorophen),2,4-滴丙酸(dichlorophen),2,4-滴丙酸-2-乙基己基(dichlorprop-2-ethylhexyl),2,4-滴丙酸-丁氧基乙酯(dichlorprop-butotyl),2,4-滴丙酸-二甲铵(dichlorprop-dimethylammonium),2,4-滴丙酸-乙铵(dichlorprop-ethylammonium),2,4-滴丙酸-异辛酯(dichlorprop-isoctyl),2,4-滴丙酸-甲基(dichlorprop-methyl),精2,4-滴丙酸(dichlorprop-P),精2,4-滴丙酸-2-乙基己基(dichlorprop-P-2-ethylhexyl),精2,4-滴丙酸-二甲铵(dichlorprop-P-dimethylammonium),2,4-滴丙酸-钾(dichlorprop-potassium),精2,4-滴丙酸-钾(dichlorprop-P-potassium),精2,4-滴丙酸-钠(dichlorprop-P-sodium),2,4-滴丙酸-钠(dichlorprop-sodium),敌敌畏(dichlorvos),菌核利(dichlozoline),苄氯三唑醇(diclobutrazol),双氯氰菌胺(diclocymet),氯甲草(diclofop),氯甲草(diclofop-methyl),哒菌清(diclomezine),哒菌清-钠(diclomezine-sodium),氯硝胺(dicloran),唑嘧磺胺(diclosulam),三氯杀螨醇(dicofol),双香豆素(dicoumarol),dicresyl,百治磷(dicrotophos),环虫腈(dicyclanil),dicyclonon,狄氏剂(dieldrin),除螨灵(dienochlor),二乙除草双(diethamquat),二氯化二乙除草双(diethamquat dichloride),乙酰甲草胺(diethatyl),乙酰甲草胺(diethatyl-ethyl),乙霉威(diethofencarb),dietholate,焦碳酸二乙酯(diethyl pyrocarbonate),避蚊胺(diethyltoluamide),鼠得克(difenacoum),苯醚甲环唑(difenoconazole),氟苯戊烯酸(difenopenten),氟苯戊烯酸(difenopenten-ethyl),枯莠隆(difenoxuron),野燕枯(difenzoquat),野燕枯甲硫酸盐(difenzoquat metilsulfate),噻鼠灵(difethialone),氟螨嗪(diflovidazin),除虫脲(diflubenzuron),吡氟酰草胺(diflufenican),二氟吡隆(diflufenzopyr),二氟吡隆-钠(diflufenzopyr-sodium),氟嘧菌胺(diflumetorim),调呋酸(dikegulac),调呋酸-钠(dikegulac-sodium),二羟丙茶碱(dilor),dimatif,四氟甲醚菊酯(dimefluthrin),甲氟磷(dimefox),噁唑隆(dimefuron),哌草丹(dimepiperate),菌核净(dimetachlone),地麦威(dimetan),混灭威(dimethacarb),二甲草胺(dimethachlor),戊草津(dimethametryn),二甲吩草胺(dimethenamid),精二甲吩草胺(dimethenamid-P),噻节因(dimethipin),二甲嘧酚(dimethirimol)),乐果(dimethoate),烯酰吗啉(dimethomorph),苄菊酯(dimethrin),驱蚊灵(dimethyl Carbate),避蚊酯(dimethyl phthalate),甲基毒虫畏(dimethylvinphos),敌蝇威(dimetilan),敌灭生(dimexano),敌米达松(dimidazon),醚菌胺(dimoxystrobin),消螨酚(dinex),dinex-

diclexine,啶菌噁唑(dingjunezuo),烯唑醇(diniconazole),R-烯唑醇(diniconazole-M),氨氟灵(dinitramine),消螨通(dinobuton),敌螨普(dinocap),敌螨普-4(dinocap-4),敌螨普-6(dinocap-6),二硝酯(dinocton),地乐特(dinofenate),硝戊酯(dinopenton),丙硝酚(dinoprop),戊硝酚(dinosam),地乐酚(dinoseb),地乐酚乙酸盐(dinoseb acetate),地乐酚-铵(dinoseb-ammonium),地乐酚-二醇胺(dinoseb-diolamine),地乐酚-钠(dinoseb-sodium),地乐酚-三乙醇胺(dinoseb-trolamine),硝辛酯(dinosulfon),dinotefuran,特乐酚(dinoterb),特乐酚乙酸盐(dinoterb acetate),硝丁酯(dinoterbon),苯虫醚(diofenolan),蔬果磷(dioxabenzofos),二氧威(dioxacarb),敌噁磷(dioxathion),敌鼠(diphacinone),敌鼠-钠(diphacinone-sodium),双苯酰草胺(diphenamid),二苯砜(diphenyl sulfone),二苯胺(diphenylamine),地乐灵(dipropalin),异丙净(dipropetryn),双硫氧吡啶(dipyrithione),敌草快(diquat),二溴化敌草快(diquat dibromide),disparlure,2,4-滴硫钠(disul),双硫仑(disulfiram),乙拌磷(disulfoton),2,4-滴硫钠(disul-sodium),灭菌磷(ditalimfos),二氰蒽醌(dithianon),噻喃磷(dithicrofos),二硫醚(dithioether),氟硫草定(dithiopyr),敌草隆(diuron),d-柠檬烯(d-limonene),草特磷(DMPA),二硝甲酚(DNOC),二硝甲酚-铵(DNOC-ammonium),二硝甲酚-钾(DNOC-potassium),二硝甲酚-钠(DNOC-sodium),十二环吗啉(dodemorph),十二环吗啉乙酸盐(dodemorph acetate),十二环吗啉苯甲酸盐(dodemorph benzoate),多地辛(dodicin),多地辛盐酸盐(dodicin hydrochloride),多地辛-钠(dodicin-sodium),多果定(dodine),苯氧炔螨(dofenapyn),dominicalure,多拉克汀(doramectin),肼菌酮(drazoxolon),甲胂钠(DSMA),毒氟磷(dufulin),EBEP,稻瘟净(EBP),促蜕皮甾酮(ecdysterone),敌瘟磷(edifenphos),草止津(eglinazine),草止津(eglinazine-ethyl),甲氨基阿维菌素(emamectin),甲氨基阿维菌素苯甲酸盐(emamectin benzoate),多杀威(EMPC),右旋烯炔菊酯(empenthrin),硫丹(endosulfan),茵多酸(endothal),茵多酸-二铵(endothal-diammonium),茵多酸-二钾(endothal-dipotassium),茵多酸-二钠(endothal-disodium),因毒磷(endothion),异狄氏剂(endrin),烯肟菌酯(enestroburin),enoxastrobin,苯硫磷(EPN),丙酰芸苔素内酯(epocholeone),保幼醚(epofenonane),氟环唑(epoxiconazole),爱普瑞菌素(eprinomectin),磺唑草(epronaz),茵草敌(EPTC),抑草蓬(erbon),麦角沉钙醇(ergocalciferol),二氯己酰草胺(erlujixiancaoan),S-反丙烯除虫菊(esdépallé thrine),S-氰戊菊酯(esfenvalerate),戊草丹(esprocarb),乙烯硅(etacelasil),乙环唑(etaconazole),etaphos,代森硫(etem),噻唑菌胺(ethaboxam),克草胺(ethachlor),乙丁烯氟灵(ethalfluralin),胺苯磺隆(ethametsulfuron),胺苯磺隆(ethametsulfuron-methyl),杀草胺(ethaprochlor),乙烯利(ethephon),磺噻隆(ethidimuron),乙硫苯威(ethiofencarb),硫草敌(ethiolate),乙硫磷(ethion),乙嗪草酮(ethiozin),乙虫腈(ethiprole),乙嘧酚(ethirimol),益硫磷(ethoate-methyl),乙氧呋草黄(ethofumesate),驱蚊醇(ethohexadiol),灭线磷(ethoprophos),氯氟草醚(ethoxyfen),氯氟草醚-乙基(ethoxyfen-ethyl),乙氧喹啉(ethoxyquin),乙氧嘧磺隆(ethoxysulfuron),吲熟酯(ethychlozate),甲酸乙酯(ethyl formate),α-萘乙酸乙酯(ethylα-naphthaleneacetate),乙滴滴滴(ethyl-DDD),乙烯(ethylene),二溴乙烯

(ethylene dibromide),二氯乙烯(ethylene dichloride),氧化乙烯(ethylene oxide),乙蒜素(ethylicin),2,3-二羟基丙基硫醇化乙基汞(ethylmercury 2,3-dihydroxypropyl mercaptide),乙酸乙基汞(ethylmercuryacetate),溴化乙基汞(ethylmercury bromide),氯化乙基汞(ethylmercuryChloride),磷酸乙基汞(ethylmercury phosphate),硝草酚(etinofen),乙胺草醚(etnipromid),乙氧苯草胺(etobenzanid),醚菊酯(etofenprox),乙螨唑(etoxazole),土菌灵(etridiazole),乙嘧硫磷(etrimfos),丁香酚(eugenol),草必散(EXD),噁唑菌酮(famoxadone),伐灭磷(famphur),咪唑菌酮(fenamidone),敌磺钠(fenaminosulf),fenaminstrobin,苯线磷(fenamiphos),咪菌腈(fenapanil),氯苯嘧啶醇(fenarimol),酰苯磺威(fenasulam),抗螨唑(fenazaflor),喹螨醚(fenazaquin),腈苯唑(fenbuconazole),苯丁锡(fenbutatin oxide),解草唑(fenchlorazole),解草唑-乙基(fenchlorazole-ethyl),皮蝇磷(fenchlorphos),解草啶(fenclorim),乙苯威(fenethacarb),五氟苯菊酯(fenfluthrin),甲呋酰胺(fenfuram),环酰菌胺(fenhexamid),种衣酯(fenitropan),杀螟硫磷(fenitrothion),酚菌酮(fenjuntong),仲丁威(fenobucarb),2,4,5-涕丙酸(fenoprop),2,4,5-涕丙酸-3-丁氧基丙基(fenoprop-3-butoxypropyl),2,4,5-涕丙酸-丁氧基丙酯(fenoprop-butometyl),2,4,5-涕丙酸-丁氧基乙酯(fenoprop-butotyl),2,4,5-涕丙酸-丁基(fenoprop-butyl),2,4,5-涕丙酸-异辛酯(fenoprop-isoctyl),2,4,5-涕丙酸-甲基(fenoprop-methyl),2,4,5-涕丙酸-钾(fenoprop-potassium),苯硫威(fenothiocarb),fenoxacrim,稻瘟酰胺(fenoxanil),噁唑禾草灵(fenoxaprop),噁唑禾草灵-乙基(fenoxaprop-ethyl),精噁唑禾草灵(fenoxaprop-P),精噁唑禾草灵-乙基(fenoxaprop-P-ethyl),异噁苯砜(fenoxasulfone),双氧威(fenoxycarb),拌种咯(fenpiclonil),吡氯氰菊酯(fenpirithrin),甲氰菊酯(fenpropathrin),苯锈啶(fenpropidin),丁苯吗啉(fenpropimorph),fenpyrazamine,唑螨酯(fenpyroximate),哒嗪酮酸(fenridazon),苯哒嗪(fenridazon-potassium),fenridazon-propyl,芬螨酯(fenson),丰索磷(fensulfothion),氯苯氧乙醇(fenteracol),噻唑禾草灵(fenthiaprop),噻唑禾草灵-乙基(fenthiaprop-ethyl),倍硫磷(fenthion),倍硫磷-乙基(fenthion-ethyl),三苯锡(fentin),三苯乙酸锡(fentin acetate),三苯氯化锡(fentin chloride),三苯氢氧化锡(fentin hydroxide),四唑草胺(fentrazamide),氟硝二苯胺(fentrifanil),非草隆(fenuron),非草隆TCA(fenuron TCA),氰戊菊酯(fenvalerate),福美铁(ferbam),嘧菌腙(ferimzone),硫酸亚铁(ferrous sulfate),氟虫腈(fipronil),麦草氟(flamprop),麦草氟异丙酯(flamprop-isopropyl),强麦草氟(flamprop-M),麦草氟甲酯(flamprop-methyl),强麦草氟异丙酯(flamprop-M-isopropyl),强麦草氟甲酯(flamprop-M-methyl),啶嘧磺隆(flazasulfuron),氟鼠灵(flocoumafen),flometoquin,氟啶虫酰胺(flonicamid),双氟磷草胺(florasulam),嘧螨酯(fluacrypyrim),吡氟禾草灵(fluazifop),吡氟禾草灵-丁基(fluazifop-butyl),吡氟禾草灵-甲基(fluazifop-methyl),精吡氟禾草灵(fluazifop-P),精吡氟禾草灵-丁基(fluazifop-P-butyl),氟啶胺(fluazinam),异丙吡草酯(fluazolate),啶蜱脲(fluazuron),氟苯虫酰胺(flubendiamide),噻唑螨(flubenzimine),氟酮磺隆(flucarbazone),氟酮磺隆-钠(flucarbazone-sodium),氟吡磺隆(flucetosulfuron),氯乙氟灵(fluchloralin),氟氯双苯隆(flucofuron),氟环脲(flucycloxuron),氟氰戊菊酯

(flucythrinate),咯菌腈(fludioxonil),联氟螨(fluenetil),fluensulfone,氟噻草胺(flufenacet),flufenerim,氟苯吡草(flufenican),氟虫脲(flufenoxuron),flufenoxystrobin,氟丙苄醚(flufenprox),氟哒嗪草酯(flufenpyr),氟哒嗪草酯-乙基(flufenpyr-ethyl),flufiprole,氟氯苯菊酯(flumethrin),氟酰菌胺(flumetover),氟节胺(flumetralin),唑嘧磺草胺(flumetsulam),三氟噁嗪(flumezin),氟烯草酸(flumiclorac),氟烯草酸-戊基(flumiclorac-pentyl),丙炔氟草胺(flumioxazin),炔草胺(flumipropyn),氟吗啡(flumorph),氟草隆(fluometuron),氟吡菌胺(fluopicolide),氟吡菌酰胺(fluopyram),氟杀螨(fluorbenside),增糖胺(fluoridamid),氟乙酰胺(fluoroacetamide),三氟硝草醚(fluorodifen),乙羧氟草醚(fluoroglycofen),乙羧氟草醚-乙基(fluoroglycofen-ethyl),氟酰亚胺(fluoroimide),唑啶草(fluoromidine),氟除草醚(fluoronitrofen),氟苯隆(fluothiuron),三氟苯唑(fluotrimazole),氟嘧菌酯(fluoxastrobin),氟胺草唑(flupoxam),flupropacil,氟鼠啶(flupropadine),四氟丙酸(flupropanate),四氟丙酸-钠(flupropanate-sodium),flupyradifurone,氟啶嘧磺隆脱甲基酸(flupyrsulfuron),氟啶嘧磺隆(flupyrsulfuron-methyl),氟啶嘧磺隆钠(flupyrsulfuron-methyl-sodium),氟喹唑(fluquinconazole),解草胺(flurazole),芴丁酯(flurenol),芴丁酯-丁基(flurenol-butyl),芴丁酯-甲基(flurenol-methyl),氟啶草酮(fluridone),氟咯草酮(flurochloridone),氯氟吡氧乙酸(fluroxypyr),氯氟吡氧乙酸-丁氧基丙酯(fluroxypyr-butometyl),氯氟吡氧乙酸-甲基庚基酯(fluroxypyr-meptyl),呋嘧醇(flurprimidol),氟磺酰胺(flursulamid),呋草酮(flurtamone),氟硅唑(flusilazole),磺菌胺(flusulfamide),达草氟(fluthiacet),达草氟-甲基(fluthiacet-methyl),氟噻亚菌胺(flutianil),氟酰胺(flutolanil),粉唑醇(flutriafol),氟胺氰菊酯(fluvalinate),氟苯吡菌胺(fluxapyroxad),氟草肟(fluxofenim),灭菌丹(folpet),氟磺胺草醚(fomesafen),氟磺胺草醚-钠(fomesafen-sodium),地虫硫膦(fonofos),甲酰胺磺隆(foramsulfuron),氯吡脲(forchlorfenuron),甲醛,伐虫脒(formetanate),伐虫脒盐酸盐(formetanate hydrochloride),安硫磷(formothion),胺甲威(formparanate),胺甲威盐酸盐(formparanate hydrochloride),杀木膦(fosamine),杀木膦-铵(fosamine-ammonium),三乙膦酸(fosetyl),三乙膦酸铝(fosetyl-aluminium),丁苯硫磷(fosmethilan),甲基毒死蜱(fospirate),噻唑膦(fosthiazate),丁硫环磷(fosthietan),frontalin,麦穗宁(fuberidazole),氟草净(fucaojing),氟草醚(fucaomi),氟萘禾草灵(funaihecaoling),呋苯硫脲(fuphenthiourea),多效缩醛(furalane),呋霜灵(furalaxyl),炔呋菊酯(furamethrin),福拉比(furametpyr),呋线威(furathiocarb),二甲呋酰胺(furcarbanil),呋菌唑(furconazole),呋醚唑(furconazole-cis),糠醛菊酯(furethrin),糠醛(furfural),解草噁唑(furilazole),拌种胺(furmecyclox),呋甲硫菌灵(furophanate),呋氧草醚(furyloxyfen),精高效氯氟氰菊酯(gamma-cyhalothrin),γ-六六六(gamma-HCH),格螨酯(genit),赤霉酸(gibberellic acid),赤霉素(gibberellins),甘氟(gliftor),草铵膦(glufosinate),草铵膦-铵(glufosinate-ammonium),精草铵膦(glufosinate-P),精草铵膦-铵(glufosinate-P-ammonium),精草铵膦-钠(glufosinate-P-sodium),果绿啶(glyodin),乙二肟(glyoxime),草甘膦(glyphosate),草甘膦-二铵(glyphosate-diammonium),草甘膦-二甲铵(glyphosate-

dimethylammonium)，草甘膦-异丙基铵(glyphosate-isopropylammonium)，草甘膦-一铵(glyphosate-monoammonium)，草甘膦-钾(glyphosate-potassium)，草甘膦-倍半钠(glyphosate-sesquisodium)，草甘膦-三甲基硫盐(glyphosate-trimesium)，增甘膦(glyphosine)，信铃酯(gossyplure)，诱杀烯混剂(grandlure)，灰黄霉素(griseofulvin)，双胍辛胺(guazatine)，双胍辛乙酸盐(guazatine acetates)，丙烯酸喹啉酯(halacrinate)，halauxifen，halauxifen-methyl，苄螨醚(halfenprox)，特丁苯酰肼(halofenozide)，氟硝磺酰胺(halosafen)，氯吡嘧磺隆脱甲基酸(halosulfuron)，氯吡嘧磺隆(halosulfuron-methyl)，卤草定(haloxydine)，氟吡禾灵(haloxyfop)，氟吡乙禾灵(haloxyfop-etotyl)，氟吡甲禾灵(haloxyfop-methyl)，精氟吡禾灵(haloxyfop-P)，精氟吡乙禾灵(haloxyfop-P-etotyl)，精氟吡甲禾灵(haloxyfop-P-methyl)，氟吡禾灵-钠(haloxyfop-sodium)，六六六(HCH)，六甲密胺(hemel)，六甲磷酰胺(hempa)，狄氏剂(HEOD)，七氯(heptachlor)，heptafluthrin，庚虫磷(heptenophos)，增产肟(heptopargil)，herbimycin，速杀硫磷(heterophos)，六氯丙酮(hexachloroacetone)，六氯苯(hexachlorobenzene)，六氯丁二烯(hexachlorobutadiene)，六氯酚(hexachlorophene)，己唑醇(hexaconazole)，氟铃脲(hexaflumuron)，六氟胂酸盐(hexaflurate)，红蚧诱烯(hexalure)，hexamide，环嗪酮(hexazinone)，环己硫磷(hexylthiofos)，噻螨酮(hexythiazox)，艾氏剂(HHDN)，氯乙亚磺酸(holosulf)，环草肟(huancaiwo)，磺草膦(huangcaoling)，环菌唑(huanjunzuo)，氟蚁腙(hydramethylnon)，萘磺汞(hydrargaphen)，熟石灰(hydrated lime)，氰化氢(hydrogenCyanide)，烯虫乙酯(hydroprene)，噁霉灵(hymexazol)，喹啉威(hyquincarb)，吲哚乙酸(IAA)，吲哚丁酸(IBA)，icaridin，抑霉唑(imazalil)，抑霉唑硝酸盐(imazalil nitrate)，抑霉唑硫酸盐(imazalil sulfate)，咪草酯(imazamethabenz)，咪草酯-甲基(imazamethabenz-methyl)，甲氧咪草烟(imazamox)，甲氧咪草烟-铵(imazamox-ammonium)，甲咪唑烟酸(imazapic)，甲咪唑烟酸-铵(imazapic-ammonium)，咪唑烟酸(imazapyr)，咪唑烟酸-异丙基铵(imazapyr-isopropylammonium)，咪唑喹啉酸(imazaquin)，咪唑喹啉酸-铵(imazaquin-ammonium)，咪唑喹啉酸-甲基(imazaquin-methyl)，咪唑喹啉酸-钠(imazaquin-sodium)，咪唑乙烟酸(imazethapyr)，咪唑乙烟酸-铵(imazethapyr-ammonium)，唑吡嘧磺隆(imazosulfuron)，亚胺唑(imibenconazole)，新烟碱类(imicyafos)，吡虫啉(imidacloprid)，氯噻啉(imidaclothiz)，双胍辛胺(iminoctadine)，双胍辛胺三乙酸盐(iminoctadine triacetate)，双胍辛胺三烷苯磺酸盐(iminoctadine trialbesilate)，炔咪菊酯(imiprothrin)，抗倒胺(inabenfide)，茚草酮(indanofan)，indaziflam，茚虫威(indoxacarb)，苯稻瘟净(inezin)，碘草腈(iodobonil)，iodocarb，碘甲烷，碘甲磺隆脱甲基酸(iodosulfuron)，碘甲磺隆(iodosulfuron-methyl)，碘甲磺隆-钠(iodosulfuron-methyl-sodium)，iofensulfuron，iofensulfuron-sodium，碘苯腈(ioxynil)，辛酰碘苯腈(ioxynil octanoate)，碘苯腈-锂(ioxynil-lithium)，碘苯腈-钠(ioxynil-sodium)，抑草津(ipazine)，种菌唑(ipconazole)，卤苯胺唑(ipfencarbazone)，异稻瘟净(iprobenfos)，异菌脲(iprodione)，缬霉威(iprovalicarb)，丙草定(iprymidam)，齿小蠹二烯醇(ipsdienol)，齿小蠹烯醇(ipsenol)，丰丙磷(IPSP)，isamidofos，氯唑磷(isazofos)，碳氯灵(isobenzan)，丁咪酰胺(isocarbamid)，水胺硫磷(isocarbophos)，异草定(isocil)，异

艾氏剂(isodrin),异柳磷(isofenphos),异柳磷-甲基(isofenphos-methyl),isofetamid,异索威(isolan),丁嗪草酮(isomethiozin),异草完隆(isonoruron),氮草草(isopolinate),异丙威(isoprocarb),异丙乐灵(isopropalin),稻瘟灵(isoprothiolane),异丙隆(isoproturon),吡唑萘菌胺(isopyrazam),苯嘧丙醇(isopyrimol),异拌磷(isothioate),异噻菌胺(isotianil),异噁隆(isouron),异酰菌酮(isovaledione),异噁酰草胺(isoxaben),异噁氯草酮(isoxachlortole),双苯噁唑酸(isoxadifen),isoxadifen-ethyl,异噁氟草酮(isoxaflutole),异噁草醚(isoxapyrifop),噁唑磷(isoxathion),齐墩螨素(ivermectin),浸种磷(izopamfos),japonilure,喃烯菊酯(japothrins),茉酮菊素I(jasmolin I),茉酮菊素II(jasmolin II),茉莉酸(jasmonic acid),甲磺虫腙(jiahuangchongzong),甲基增效磷(jiajizengxiaolin),甲香菌酯(jiaxiangjunzhi),解草烷(jiecaowan),解草烯(jiecaoxi),碘硫磷(jodfenphos),保幼激素I(juvenile hormone I),保幼激素II(juvenile hormone II),保幼激素III(juvenile hormone III),噻恩菊酯(kadethrin),特胺灵(karbutilate),karetazan,karetazan-potassium,春雷霉素(kasugamycin),春雷霉素盐酸盐(kasugamycin hydrochloride),克菌磷(kejunlin),克来范(kelevan),ketospiradox,ketospiradox-potassium,糖氨基嘌呤(kinetin),烯虫炔酯(kinoprene),苯氧菌酯(kresoxim-methyl),喹草烯(kuicaoxi),乳氟禾草灵(lactofen),高效氯氟氰菊酯(lambda-cyhalothrin),latilure,砷酸铅(lead arsenate),环草定(lenacil),lepimectin,溴苯膦(leptophos),林丹(lindane),lineatin,利谷隆(linuron),啶虫磷(lirimfos),litlure,looplure,虱螨脲(lufenuron),氯啶菌酯(lvdingjunzhi),氯酰草膦(lvxiancaolin),噻唑磷(lythidathion),甲基肼酸(MAA),马拉硫磷(malathion),马来酸酰肼(maleic hydrazide),苄丙二腈(malonoben),糊精-麦芽糖复合剂(maltodextrin),甲肼一铵(MAMA),代森锰铜(mancopper),代森锰锌(mancozeb),双炔酰菌胺(mandipropamid),代森锰(maneb),苦参碱(matrine),叠氮磷(mazidox),2甲4氯(MCPA),2甲4氯-2-乙基己基(MCPA-2-ethylhexyl),2甲4氯-丁氧基乙酯(MCPA-butotyl),2甲4氯-丁基(MCPA-butyl),2甲4氯-二甲铵(MCPA-dimethylammonium),2甲4氯-二醇胺(MCPA-diolamine),2甲4氯-乙基(MCPA-ethyl),2甲4氯-异丁基(MCPA-isobutyl),2甲4氯-异辛酯(MCPA-isoctyl),2甲4氯-异丙基(MCPA-isopropyl),2甲4氯-甲基(MCPA-methyl),2甲4氯-醇胺(MCPA-olamine),2甲4氯-钾(MCPA-potassium),2甲4氯-钠(MCPA-sodium),2甲4氯乙硫酯(MCPA-thioethyl),2甲4氯-三乙醇胺(MCPA-trolamine),2甲4氯丁酸(MCPB),2甲4氯丁酸-乙基(MCPB-ethyl),2甲4氯丁酸-甲基(MCPB-METHYL),2甲4氯丁酸-钠(MCPB-sodium),邻酰胺(mebenil),灭蚜磷(mecarbam),苯并威(mecarbinzid),四甲磷(mecarphon),2甲4氯丙酸(mecoprop),2甲4氯丙酸-2-乙基己基(mecoprop-2-ethylhexyl),2甲4氯丙酸-二甲铵(mecoprop-dimethylammonium),2甲4氯丙酸-二醇胺(mecoprop-diolamine),mecoprop-ethadyl,2甲4氯丙酸-异辛酯(mecoprop-isoctyl),2甲4氯丙酸-甲基(mecoprop-methyl),精2甲4氯丙酸(mecoprop-P),精2甲4氯丙酸-2-乙基己基(mecoprop-P-2-ethylhexyl),精2甲4氯丙酸-二甲铵(mecoprop-P-dimethylammonium),精2甲4氯丙酸-异丁基(mecoprop-P-isobutyl),2甲4氯丙酸-钾(mecoprop-potassium),精2甲4氯丙酸-钾(mecoprop-P-potassium),2甲4氯丙酸-钠(mecoprop-sodium),2甲4氯丙

酸-三乙醇胺(mecoprop-trolamine),杀螨脒(medimeform),丁硝酚(medinoterb),丁硝酚乙酸盐(medinoterb acetate),诱杀酯(medlure),苯噻酰草胺(mefenacet),吡咯二酸(mefenpyr),吡咯二酸二乙酯(mefenpyr-diethyl),氟磺酰草胺(mefluidide),氟磺酰草胺-二醇胺(mefluidide-diolamine),氟磺酰草胺-钾(mefluidide-potassium),megatomoic acid,灭蚜硫磷(menazon),嘧菌胺(mepanipyrim),meperfluthrin,mephenate,地胺磷(mephosfolan),甲哌鎓(mepiquat),缩节胺(mepiquat chloride),mepiquat pentaborate,灭锈胺(mepronil),二硝巴豆酸酯(meptyldinocap),氯化汞(mercuric chloride),氧化汞(mercuric oxide),氯化亚汞(mercurous chloride),脱叶亚磷(merphos),灭莠津(mesoprazine),甲磺胺磺隆脱甲基酸(mesosulfuron),甲磺胺磺隆(mesosulfuron-methyl),硝磺草酮(mesotrione),灭芥(mesulfen),甲亚砜磷(mesulfenfos),氰氟虫腙(metaflumizone),甲霜灵(metalaxyl),精甲霜灵(metalaxyl-M),四聚乙醛(metaldehyde),威百亩(metam),威百亩-铵(metam-ammonium),噁唑酰草胺(metamifop),苯嗪草酮(metamitron),威百亩-钾(metam-potassium),威百亩-钠(metam-sodium),吡唑草胺(metazachlor),双醚氯吡嘧磺隆(metazosulfuron),间氯敌菌酮(metazoxolon),叶菌唑(metconazole),米替哌(metepa),氟哒草(metflurazon),甲基苯噻隆(methabenzthiazuron),虫螨畏(methacrifos),氟烯硝草(methalpropalin),甲胺磷(methamidophos),磺菌威(methasulfocarb),灭草唑(methazole),呋菌胺(methfuroxam),杀扑磷(methidathion),甲硫苯威(methiobencarb),甲硫威(methiocarb),甲硫嘧磺隆(methiopyrisulfuron),甲硫涕巴(methiotepa),噁噻草醚(methiozolin),灭草恒(methiuron),丁烯胺磷(methocrotophos),醚草通(methometon),灭多威(methomyl),烯虫酯(methoprene),盖草津(methoprotryne),喹啉羧酯(methoquin-butyl),甲醚菊酯(methothrin),甲氧滴滴涕(methoxychlor),甲氧虫酰肼(methoxyfenozide),苯草酮(methoxyphenone),甲基不育特(methyl apholate),甲基溴,甲基丁香酚(methyl eugenol),甲基碘,异硫氰酸甲酯(methyl isothiocyanate),甲基乙酯磷(methylacetophos),甲基氯仿(methylchloroform),甲基杀草隆(methyldymron),二氯甲烷,苯甲酸甲汞(methylmercury benzoate),氰胍甲汞(methylmercury dicyandiamide),甲基五氯苯酚汞(methylmercury pentachlorophenoxide),甲基新癸酰胺(methylneodecanamide),代森联(metiram),吡喃隆(metobenzuron),溴谷隆(metobromuron),甲氧苄氟菊酯(metofluthrin),异丙甲草胺(metolachlor),速灭威(metolcarb),苯氧菌胺(metominostrobin),磺草唑胺(metosulam),噁虫酮(metoxadiazone),甲氧隆(metoxuron),苯菌酮(metrafenone),嗪草酮(metribuzin),噻菌胺(metsulfovax),甲磺隆脱甲基酸(metsulfuron),甲磺隆(metsulfuron-methyl),速灭磷(mevinphos),兹克威(mexacarbate),灭鼠安(mieshuan),米尔螨素(milbemectin),米尔贝肟(milbemycin oxime),代森环(milneb),丙胺氟磷(mipafox),灭蚁灵(mirex),MNAF,蘑菇醇(moguchun),禾草敌(molinate),molosultap,庚酰草胺(monalide),特噁唑隆(monisouron),一氯乙酸(monochloroacetic acid),久效磷(monocrotophos),绿谷隆(monolinuron),单嘧磺隆(monosulfuron),单嘧磺酯(monosulfuron-ester),灭草隆(monuron),灭草隆TCA(monuron TCA),伐草快(morfamquat),二氯化伐草快(morfamquat dichloride),吗啉胍(moroxydine),盐酸吗啉胍(moroxydine hydrochloride),茂硫磷

(morphothion),morzid,莫西克丁(moxidectin),甲胂一钠(MSMA),诱虫烯(muscalure),腈菌唑(myclobutanil),甲菌利(myclozolin),N-(乙基汞)-对甲苯磺苯胺(N-(ethylmercury)-p-toluenesulphonanilide),代森钠(nabam),萘肽磷(naftalofos),二溴磷(naled),萘,萘乙酰胺,萘二甲酸酐(naphthalic anhydride),萘氧乙酸(naphthoxyacetic acids),萘丙胺(naproanilide),敌草胺(napropamide),萘草胺(naptalam),萘草胺-钠(naptalam-sodium),那他霉素(natamycin),草不隆(neburon),杀螺胺(niclosamide),杀螺胺-醇胺(niclosamide-olamine),烟嘧磺隆(nicosulfuron),尼古丁(nicotine),氟蚁灵(nifluridide),吡氯草胺(nipyraclofen),烯啶虫胺(nitenpyram),硝虫噻嗪(nithiazine),甲磺乐灵(nitralin),三氯甲基吡啶(nitrapyrin),戊氰威(nitrilacarb),除草醚(nitrofen),三氟甲草醚(nitrofluorfen),硫氰散(nitrostyrene),酞菌酯(nitrothal-isopropyl),鼠特灵(norbormide),氟草敏(norflurazon),原烟碱(nornicotine),草完隆(noruron),氟酰脲(novaluron),多氟脲(noviflumuron),氟苯嘧啶醇(nuarimol),OCH,八氯二丙醚(octachlorodipropyl ether),辛噻酮(octhilinone),呋酰胺(ofurace),氧乐果(omethoate),坪草丹(orbencarb),贺康彼(orfralure),邻二氯苯,嘧苯胺磺隆(orthosulfamuron),oryctalure,肟醚菌胺(orysastrobin),氨磺乐灵(oryzalin),蛇床子素(osthol),非乐康(ostramone),解草腈(oxabetrinil),丙炔噁草酮(oxadiargyl),噁草酮(oxadiazon),噁霜灵(oxadixyl),草氨酸盐(oxamate),杀线威(oxamyl),噁杀草敏(oxapyrazon),oxapyrazon-dimolamine,噁杀草敏-钠(oxapyrazon-sodium),环氧嘧磺隆(oxasulfuron),oxathiapiprolin,氯噁嗪草(oxaziclomefone),喹啉铜(oxine-copper),喹菌酮(oxolinic acid),噁咪唑(oxpoconazole),噁咪唑富马酸盐(oxpoconazole fumarate),氧化萎锈灵(oxycarboxin),亚砜磷(oxydemeton-methyl),异亚砜磷(oxydeprofos),砜拌磷(oxydisulfoton),乙氧呋草醚(oxyfluorfen),烟花苦参碱(oxymatrine),土霉素(oxytetracycline),土霉素盐酸盐(oxytetracycline hydrochloride),多效唑(paclobutrazol),哌虫啶(paichongding),对二氯苯,对伏隆(parafluron),百草枯(paraquat),百草枯二氯化物(paraquat dichloride),百草枯二甲硫酸盐(paraquat dimetilsulfate),对硫磷(parathion),甲基对硫磷(parathion-methyl),氯苯吡啶(parinol),克草敌(pebulate),稻瘟酯(pefurazoate),壬酸(pelargonic acid),戊菌唑(penconazole),戊菌隆(pencycuron),二甲戊灵(pendimethalin),戊苯吡菌胺(penflufen),氟幼脲(penfluron),五氟磺草胺(penoxsulam),五氯苯酚,pentachlorophenyl laurate,甲氯酰草胺(pentanochlor),吡噻菌胺(penthiopyrad),戊烯氰氯菊酯(pentmethrin),戊噁唑草(pentoxazone),氟草磺胺(perfluidone),氯菊酯(permethrin),烯草胺(pethoxamid),氰烯菌酯(phenamacril),叶枯净(phenazine oxide),棉胺宁(phenisopham),芬硫磷(phenkapton),甜菜宁(phenmedipham),甜菜宁-乙基(phenmedipham-ethyl),酰草隆(phenobenzuron),苯醚菊酯(phenothrin),苯螨醚(phenproxide),稻丰散(phenthoate),苯基汞脲(phenylmercuriurea),苯基乙酸汞(phenylmercury acetate),苯基氯化汞(phenylmercury chloride),邻苯二酚的苯基汞衍生物(phenylmercury derivative of pyrocatechol),苯基硝酸汞(phenylmercury nitrate),苯基水杨酸汞(phenylmercury salicylate),甲拌磷(phorate),毒鼠磷(phosacetim),伏杀硫磷(phosalone),氯瘟磷

(phosdiphen),硫环磷(phosfolan),硫环磷-甲基(phosfolan-methyl),甘氨硫磷(phosglycin),亚胺硫磷(phosmet),对氯硫磷(phosnichlor),磷胺(phosphamidon),磷化氢(phosphine),乙丙磷威(phosphocarb),磷,三磷锡(phostin),辛硫磷(phoxim),辛硫磷-甲基(phoxim-methyl),四氯苯酞(phthalide),氨氯吡啶酸(picloram),氨氯吡啶酸-2-乙基己基(picloram-2-ethylhexyl),氨氯吡啶酸-异辛酯(picloram-isoctyl),氨氯吡啶酸-甲基(picloram-methyl),氨氯吡啶酸-醇胺(picloram-olamine),氨氯吡啶酸-钾(picloram-potassium),氨氯吡啶酸-三乙铵(picloram-triethylammonium),氨氯吡啶酸-三(2-羟基丙基)铵(picloram-tris(2-hydroxypropyl)ammonium),氟吡酰草胺(picolinafen),啶氧菌酯(picoxystrobin),鼠完(pindone),鼠完-钠(pindone-sodium),唑啉草酯(pinoxaden),哌丙灵(piperalin),胡椒基丁醚(piperonyl butoxide),增效环(piperonylCyclonene),哌草磷(piperophos),哌壮素(piproctanyl),菊壮素(piproctanyl bromide),增效醛(piprotal),甲胺嘧磷(pirimetaphos),抗蚜威(pirimicarb),嘧啶氧磷(pirimioxyphos),嘧啶磷(pirimiphos-ethyl),甲基嘧啶磷(pirimiphos-methyl),三氯杀虫酯(plifenate),代森福美锌(polycarbamate),多抗霉素(polyoxins),保粒霉素(polyoxorim),保粒霉素-锌(polyoxorim-zinc),多噻烷(polythialan),亚砷酸钾(potassium arsenite),叠氮化钾,氰酸钾,赤霉酸钾,环烷酸钾(potassium naphthenate),多硫化钾(potassium polysulfide),硫氰酸钾,α-萘乙酸钾,pp'-滴滴涕,右旋炔丙菊酯(prallethrin),早熟素I(precocene I),早熟素II(precocene II),早熟素III(precocene III),丙草胺(pretilachlor),酰胺嘧啶啉(primidophos),氟嘧磺隆脱甲基酸(primisulfuron),氟嘧磺隆(primisulfuron-methyl),烯丙苯噻唑(probenazole),咪鲜胺(prochloraz),咪鲜胺-锰(prochloraz-manganese),灭螨醇(proclonol),环氰津(procyazine),腐霉利(procymidone),氨氟乐灵(prodiamine),丙溴磷(profenofos),氟唑草胺(profluazol),环丙氟灵(profluralin),profluthrin,环苯草酮(profoxydim),甘扑津(proglinazine),甘扑津-乙基(proglinazine-ethyl),调环酸(prohexadione),调环酸-钙(prohexadione-calcium),prohydrojasmon,蜱虱威(promacyl),猛杀威(promecarb),扑灭通(prometon),扑草净(prometryn),灭鼠肼(promurit),毒草胺(propachlor),普罗帕脒(propamidine),普罗帕脒二盐酸盐(propamidine dihydrochloride),霜霉威(propamocarb),霜霉威盐酸盐(propamocarb hydrochloride),敌稗(propanil),丙虫磷(propaphos),噁草酸(propaquizafop),快螨特(propargite),甲呋炔菊酯(proparthrin),扑灭津(propazine),胺丙畏(propetamphos),苯胺灵(propham),丙环唑(propiconazole),丙森锌(propineb),异丙草胺(propisochlor),残杀威(propoxur),丙苯磺隆(propoxycarbazone),丙苯磺隆-钠(propoxycarbazone-sodium),增效酯(propyl isome),嗪咪唑嘧磺隆(propyrisulfuron),炔苯酰草胺(propyzamide),丙氧喹啉(proquinazid),补骨内酯(prosuler),唑啉草酯磺亚胺草(prosulfalin),苄草丹(prosulfocarb),氟磺隆(prosulfuron),乙噻唑磷(prothidathion),硫菌威(prothiocarb),硫菌威盐酸盐(prothiocarb hydrochloride),丙硫菌唑(prothioconazole),丙硫磷(prothiofos),发硫磷(prothoate),protrifenbute,扑灭生(proxan),扑灭生-钠(proxan-sodium),丙炔草胺(prynachlor),比达农(pydanon),pyflubumide,吡蚜酮(pymetrozine),吡喃灵(pyracarbolid),吡唑硫磷(pyraclofos),双

唑草腈(pyraclonil),吡唑醚菌酯(pyraclostrobin),吡草醚(pyraflufen),吡草醚-乙基(pyraflufen-ethyl),嘧啶威(pyrafluprole),嘧啶威(pyramat),唑胺菌酯(pyrametostrobin),唑菌酯(pyraoxystrobin),pyrasulfotole,吡唑特(pyrazolynate),吡菌磷(pyrazophos),吡嘧磺隆脱乙基酸(pyrazosulfuron),吡嘧磺隆(pyrazosulfuron-ethyl),吡硫磷(pyrazothion),苄草唑(pyrazoxyfen),反灭虫菊(pyresmethrin),除虫菊酯I(pyrethrin I),除虫菊酯II(pyrethrin II),除虫菊酯(pyrethrins),异丙酯草醚(pyribambenz-isopropyl),丙酯草醚(pyribambenz-propyl),吡菌苯威(pyribencarb),嘧啶肟草醚(pyribenzoxim),稗草丹(pyributicarb),氯草定(pyriclor),哒螨灵(pyridaben),pyridafol,啶虫丙醚(pyridalyl),哒嗪硫磷(pyridaphenthion),哒草特(pyridate),啶菌腈(pyridinitril),啶斑肟(pyrifenox),pyrifluquinazon,环酯草醚(pyriftalid),嘧霉胺(pyrimethanil),嘧螨醚(pyrimidifen),嘧草醚(pyriminobac),嘧草醚-甲基(pyriminobac-methyl),pyriminostrobin,pyrimisulfan,嘧啶磷(pyrimitate),灭鼠优(pyrinuron),甲氧苯啶菌(pyriofenone),吡啶醇(pyriprole),吡啶醇(pyripropanol),吡丙醚(pyriproxyfen),pyrisoxazole,嘧草硫醚(pyrithiobac),嘧草硫醚-钠(pyrithiobac-sodium),吡唑威(pyrolan),咯喹酮(pyroquilon),pyroxasulfone,啶磺草胺(pyroxsulam),氯甲氧吡啶(pyroxychlor),氯吡呋醚(pyroxyfur),苦木(quassia),喹烯酮(quinacetol),喹烯酮硫酸盐(quinacetol sulfate),喹硫磷(quinalphos),喹硫磷-甲基(quinalphos-methyl),醌菌腙(quinazamid),二氯喹啉酸(quinclorac),氯苯喹唑(quinconazole),氯甲喹啉酸(quinmerac),灭藻醌(quinoclamine),氯藻胺(quinonamid),喹塞昂(quinothion),喹氧灵(quinoxyfen),喹硫磷(quintiofos),五氯硝基苯(quintozene),喹禾灵(quizalofop),喹禾灵-乙基(quizalofop-ethyl),精喹禾灵(quizalofop-P),精喹禾灵-乙基(quizalofop-P-ethyl),喹禾糠酯(quizalofop-P-tefuryl),驱蚊酯(quwenzhi),驱蝇啶(quyingding),吡咪唑(rabenzazole),碘醚柳胺(rafoxanide),rebemide,rescalure,苄呋菊酯(resmethrin),硫氰苯乙胺(rhodethanil),闹羊花素-III(rhodojaponin-III),利巴韦林(ribavirin),砜嘧磺隆(rimsulfuron),鱼藤酮(rotenone),鱼泥汀(ryania),苯嘧磺草胺(saflufenacil),噻菌茂(saijunmao),赛森酮(saisentong),水杨酰苯胺(salicylanilide),血根碱(sanguinarine),茴蒿素(santonin),八甲磷(schradan),红海葱苷(scilliroside),另丁津(sebuthylazine),密草通(secbumeton),环丙吡菌胺(sedaxane),赛拉菌素(selamectin),单甲脒(semiamitraz),氯化单甲脒(semiamitraz chloride),增效菊(sesamex),芝麻啉(sesamolin),烯禾啶(sethoxydim),双甲胺草磷(shuangjiaancaolin),环草隆(siduron),诱虫环(siglure),灭虫硅醚(silafluofen),毒鼠硅(silatrane),硅胶,硅噻菌胺(silthiofam),西玛津(simazine),硅氟唑(simeconazole),西玛通(simeton),西草净(simetryn),杀雄啉(sintofen),SMA,精异丙甲草胺(S-metolachlor),亚砷酸钠,叠氮化钠,氯酸钠,氟化钠,氟乙酸钠,六氟硅酸钠,环烷酸钠(sodium naphthenate),邻苯基苯酚钠(sodium orthophenylphenoxide),五氯酚钠(sodium pentachlorophenoxide),多硫化钠(sodium polysulfide),硫氰酸钠,α-萘乙酸钠,苏硫磷(sophamide),乙基多杀菌素(spinetoram),艾克敌(spinosad),螺螨酯(spirodiclofen),螺甲螨酯(spiromesifen),螺虫乙酯(spirotetramat),螺噁茂胺(spiroxamine),链霉素(streptomycin),链霉素倍半硫

酸盐(streptomycin sesquisulfate),马钱子碱(strychnine),食菌甲诱醇(sulcatol),磺苯醚隆(sulcofuron),磺苯醚隆-钠(sulcofuron-sodium),磺草酮(sulcotrione),菜草畏(sulfallate),甲磺草胺(sulfentrazone),舒非仑(sulfiram),氟虫胺(sulfluramid),甲嘧磺隆脱甲基酸(sulfometuron),甲嘧磺隆(sulfometuron-methyl),磺酰磺隆(sulfosulfuron),治螟磷(sulfotep),sulfoxaflor,亚砜,硫肟醚(sulfoxime),硫,硫酸,硫酰氟,吖庚磺酯(sulglycapin),硫丙磷(sulprofos),戊苯砜(sultropen),灭草灵(swep),τ-氟胺氰菊酯(tau-fluvalinate),稗草烯(tavron),噻螨威(tazimcarb),三氯乙酸(TCA),三氯乙酸-铵(TCA-ammonium),三氯乙酸-钙(TCA-calcium),TCA-ethadyl,三氯乙酸-镁(TCA-magnesium),三氯乙酸-钠(TCA-sodium),滴滴滴(TDE),戊唑醇(tebuconazole),虫酰肼(tebufenozide),吡螨胺(tebufenpyrad),异丁乙氧喹啉(tebufloquin),嘧丙磷(tebupirimfos),牧草胺(tebutam),丁噻隆(tebuthiuron),叶枯酞(tecloftalam),四氯硝基苯(tecnazene),福美双联(tecoram),氟苯脲(teflubenzuron),七氟菊酯(tefluthrin),tefuryltrione,tembotrione,双硫磷(temephos),替哌,特普(TEPP),吡喃草酮(tepraloxydim),环戊烯丙菊酯(terallethrin),特草定(terbacil),特草灵(terbucarb),特丁草胺(terbuchlor),特丁硫酸(terbufos),甲氧去草净(terbumeton),特丁津(terbuthylazine),特丁净(terbutryn),四环唑(tetcyclacis),四氯乙烷(tetrachloroethane),杀虫畏(tetrachlorvinphos),四氟醚唑(tetraconazole),三氯杀螨砜(tetradifon),氟氧隆(tetrafluron),胺菊酯(tetramethrin),tetramethylfluthrin,羟化四甲胺(tetramine),杀螨霉素(tetranactin),杀螨好(tetrasul),硫酸亚铊(thallium sulfate),噻吩草胺(thenylchlor),θ-氯氰菊酯(theta-cypermethrin),噻菌灵(thiabendazole),噻虫啉(thiacloprid),氟噻亚菌胺(thiadifluor),噻虫嗪(thiamethoxam),噻丙腈(thiapronil),赛唑隆(thiazafluron),噻唑烟酸(thiazopyr),噻氯磷(thicrofos),噻菌腈(thicyofen),噻二唑胺(thidiazimin),噻苯隆(thidiazuron),thiencarbazone,thiencarbazone-methyl,噻吩磺隆脱甲基酸(thifensulfuron),噻吩磺隆(thifensulfuron-methyl),噻呋酰胺(thifluzamide),禾草丹(thiobencarb),抗虫威(thiocarboxime),硫氯苯亚胺(thiochlorfenphim),杀虫环(thiocyclam),杀虫环盐酸盐(thiocyclam hydrochloride),杀虫环草酸盐(thiocyclam oxalate),噻二唑-铜,硫双威(thiodicarb),久效威(thiofanox),硫氟肟醚(thiofluoximate),硫代六甲磷(thiohempa),硫柳汞(thiomersal),甲基乙拌磷(thiometon),虫线磷(thionazin),硫菌灵(thiophanate),甲基硫菌灵(thiophanate-methyl),克杀螨(thioquinox),灭鼠特(thiosemicarbazide),杀虫双(thiosultap),杀虫双-二铵(thiosultap-diammonium),杀虫双-二钠(thiosultap-disodium),杀虫单(thiosultap-monosodium),噻替派(thiotepa),福美双(thiram),敌贝特(thuringiensin),噻酰菌胺(tiadinil),调节安(tiaojiean),仲草丹(tiocarbazil),嘧草胺(tioclorim),硫氰苯甲酰胺(tioxymid),环线威(tirpate),甲基立枯磷(tolclofos-methyl),唑虫酰胺(tolfenpyrad),tolprocarb,甲苯氟磺胺(tolylfluanid),甲苯基乙酸汞(tolylmercury acetate),topramezone,三甲苯草酮(tralkoxydim),溴氯氰菊酯(tralocythrin),四溴菊酯(tralomethrin),tralopyril,四氟苯菊酯(transfluthrin),反氯菊酯(transpermethrin),曲他胺(tretamine),三十烷醇(triacontanol),三唑酮

(triadimefon),三唑醇(triadimenol),triafamone,野麦畏(tri-allate),威菌磷(triamiphos),抑芽唑(triapenthenol),苯螨噻(triarathene),嘧菌醇(triarimol),醚苯磺隆(triasulfuron),唑蚜威(triazamate),丁基三唑(triazbutil),三嗪氟草胺(triaziflam),三唑磷(triazophos),咪唑嗪(triazoxide),苯磺隆脱甲基酸(tribenuron),苯磺隆(tribenuron-methyl),脱叶磷(tribufos),三丁基氧化锡(tributyltin oxide),杀草畏(tricamba),水杨菌胺(trichlamide),敌百虫(trichlorfon),异皮蝇磷(trichlormetaphos-3),毒壤膦(trichloronat),绿草定(triclopyr),绿草定-丁氧基乙酯(triclopyr-butotyl),绿草定-乙基(triclopyr-ethyl),triclopyricarb,绿草定-三乙铵(triclopyr-triethylammonium),三环唑(tricyclazole),石蜡油(tridemorph),灭草环(tridiphane),草达津(trietazine),杀螺吗啉(trifenmorph),氯苯乙丙磷(trifenofos),肟菌酯(trifloxystrobin),三氟啶磺隆(trifloxysulfuron),三氟啶磺隆-钠(trifloxysulfuron-sodium),氟菌唑(triflumizole),杀铃脲(triflumuron),氟乐灵(trifluralin),氟胺磺隆脱甲基酸(triflusulfuron),氟胺磺隆(triflusulfuron-methyl),三氟苯氧丙酸(trifop),三氟苯氧丙酸-甲基(trifop-methyl),三氟禾草肟(trifopsime),嗪氨灵(triforine),三羟基三嗪(trihydroxytriazine),诱蝇羧酯(trimedlure),混杀威(trimethacarb),三甲隆(trimeturon),挺立(trinexapac),抗倒酯(trinexapac-ethyl),烯虫硫酯(triprene),茚草酮(tripropindan),雷公藤甲素(triptolide),草达克(tritac),灭菌唑(triticonazole),三氟甲磺隆(tritosulfuron),trunc-call,烯效唑(uniconazole),精烯效唑(uniconazole-P),福美甲砷(urbacide),乌瑞替派(uredepa),氰戊菊酯(valerate),有效霉素(validamycin),valifenalate,杀鼠酮(valone),蚜灭磷(vamidothion),抑霉胺(vangard),氟吡唑虫(vaniliprole),灭草敌(vernolate),乙烯菌核利(vinclozolin),杀鼠灵(warfarin),杀鼠灵-钾(warfarin-potassium),杀鼠灵-钠(warfarin-sodium),硝虫硫磷(xiaochongliulin),辛菌胺(xinjunan),烯肟菌胺(xiwojunan),灭除威(XMC),二甲苯草胺(xylachlor),二甲苯酚(xylenols),灭杀威(xylylcarb),抑食肼(yishijing),氰菌胺(zarilamid),玉米素(zeatin),增效胺(zengxiaoan),ζ-氯氰菊酯(zeta-cypermethrin),环烷酸锌,磷化锌(zinc phosphide),噻唑锌(zinc thiazole),代森锌(zineb),福美锌(ziram),zolaprofos,苯酰菌胺(zoxamide),唑嘧磺隆(zuomihuanglong),α-氯乙醇(α-chlorohydrin),α-蜕皮素(α-ecdysone),α-multistriatin,和α-萘乙酸。对于更多信息请参见http://www.alanwood.net/pesticides/index.html的“Compendium of PesticideCommon Names”。也可参见“The Pesticide Manual”15th Edition,edited by C D S Tomlin,copyright 2009by BritishCrop ProductionCouncil,或其先前或更新的版本。

[1783] 在另一个实施方式中,式一分子也可以与一种或多种生物农药组合使用(例如在组合的混合物中,或同时或顺序施用)。术语“生物农药”用于以与化学农药类似的方式施用的微生物虫害生物防治药物(microbial biological pest control agents)。通常这些为细菌防治药物,但是也有真菌防治药物的实例,包括木霉菌(Trichoderma spp.)和白粉寄生孢(Ampelomyces quisqualis)(用于葡萄霜霉病(grape powdery mildew)的防治药物)。枯草杆菌(Bacillus subtilis)用于防治植物病原体。杂草和啮齿动物也已用微生物药物

来防治。一种熟知的杀昆虫剂实例为苏芸金杆菌(Bacillus thuringiensis),为鳞翅目、鞘翅目和双翅目的细菌性疾病。由于其对其它生物几乎不具有作用,因此认为其相比于合成农药更为环境友善的。生物学杀昆虫剂包括根据下述的产物:昆虫病原真菌(例如绿僵菌(Metarhizium anisopliae));昆虫病原线虫(例如芜菁夜蛾斯氏线虫(Steinernema feltiae));和昆虫病原病毒(例如苹果蠢蛾颗粒体病毒(Cydia pomonella granulovirus))。

[1784] 昆虫病原生物的其它实例包括但不限于杆状病毒、细菌和其它原核生物、真菌、原生动物和Microsproridia。生物学衍生的杀昆虫剂包括但不限于藤酮、藜芦定及微生物毒素;昆虫耐受或抵抗的植物种类;及经重组体DNA技术修饰的生物,从而得到杀虫剂或向经遗传修饰的生物体传达昆虫耐受性质。在一个实施方式中,式一的分子可与一种或多种生物农药在种子处理和土壤改良的区域内使用。The Manual of Biocontrol Agents给出了对可用生物学杀昆虫剂(及其它基于生物学的防治)产物的综述。Copping L.G.(ed.)(2004).The Manual of Biocontrol Agents(formerly the Biopesticide Manual)3rd Edition。British Crop Production Council(BCPC),Farnham,Surrey UK。

[1785] 在另一个实施方式中,上述可能的组合可以使用以不同的重量比使用。例如,双组分混合物中,式一分子与另一化合物的重量比,可为约100:1至约1:100;在另一实例中,重量比可为约50:1至约1:50;在另一实例中,重量比可为约20:1至约1至20;在另一实例中,重量比可为约10:1至约1:10;在另一实例中,重量比可为约5:1至1:5;在另一实例中,重量比可为约3:1至约1:3;和在最后一个实例中,重量比可为约1:1。但是,优选地,优选重量比小于约10:1至约1:10。也优选有时使用三组分或四组分混合物,其包含一种或多种的式一分子和一种或多种来自上述可能组合的其他化合物。

[1786] 制剂

[1787] 农药几乎不适于以其纯形式来施用。通常需要加入其它物质,从而使农药可按所需要的浓度和适宜的形式来使用,由此易于施用、处理、运输、储存和使农药活性最大化。因此,将农药配制成例如诱饵(bait)、浓缩乳液、粉剂(dust)、乳油(emulsifiable concentrate)、熏蒸剂(fumigant)、凝胶、颗粒、微囊形式(microencapsulation)、种子处理形式(seed treatment)、混悬浓缩物、混悬乳液(suspoemulsion)、片剂、水溶性液体、水可分散颗粒或干燥可流动物(dry flowable)、可润湿粉末和超低体积溶液。有关制剂类型的进一步信息请参阅“Catalogue of Pesticide Formulation Types and International Coding System”Technical Monograph n°2,5th Edition by CropLife International(2002)。

[1788] 农药最通常以由所述农药的浓缩制剂制备的含水混悬液或乳液的形式来施用。这样的水溶性制剂、水可混悬制剂或可乳化制剂为固体(通常已知为可润湿粉末或水可分散颗粒)或液体(通常已知为乳油或含水混悬液)。可润湿粉末(其可以被压制以形成水可分散颗粒)包含农药、载体和表面活性剂的充分混合物。农药的浓度通常为约10wt%至约90wt%。所述载体通常选自硅镁土(attapulgite clay)、蒙脱土(montmorillonite clay)、硅藻土(diatomaceous earth)或精制硅酸盐(purified silicate)。有效的表面活性剂(占可润湿粉末的约0.5%至约10%)选自磺酸化的木质素、浓缩的萘磺酸盐、萘磺酸盐、烷基苯磺酸盐、烷基硫酸盐和非离子表面活性剂(例如烷基酚的氧化乙烯加成物)。

[1789] 农药的乳油包含溶于载体(所述载体为水可混合溶剂或水不可混合有机溶剂和乳化剂的混合物)中的适宜浓度的农药(例如每升液体约50至约500克)。有用的有机溶剂包括芳族溶剂(特别是二甲苯)和石油馏分(特别是石油的高沸点萘部分和烯烃部分例如重芳族石脑油)。也可使用其它有机溶剂,例如萜类溶剂(包括松香衍生物)、脂肪族酮(例如环己酮)和复杂的醇(例如2-乙氧基乙醇)。用于乳油的适宜乳化剂选自常见的阴离子表面活性剂和非离子表面活性剂。

[1790] 含水混悬液包括水不溶性农药分散在含水载体中的混悬液,其浓度为约5wt%至约50wt%。混悬液如下制备:精细研磨所述农药且将其剧烈混合到载体中,所述载体包含水和表面活性剂。也可加入像无机盐和合成胶或天然胶那样的成分,以增加含水载体的密度和粘度。通常最有效的是通过在设备例如砂磨机、球磨机或活塞式匀化器中制备含水混合物并对其进行匀化来同时研磨和混合农药。

[1791] 农药也可按颗粒组合物的形式来施用,所述颗粒组合物特别可用于施用到土壤中。颗粒组合物通常含有分散在载体中的约0.5wt%至约10wt%的所述农药,所述载体包含粘土或相似的物质。上述组合物通常如下制备:将所述农药溶于适宜的溶剂中且将其施用到颗粒载体上,所述颗粒载体已被预先制成适宜的粒度(范围为约0.5至约3mm)。上述组合物也可如下制备:将所述载体和化合物制成面团状或糊状,然后压碎并干燥,从而得到所需颗粒粒度。

[1792] 含有农药的粉剂如下制备:对粉末状的农药与适宜的粉尘状农用载体(例如高岭粘土、研碎的火山石等)进行充分混合。粉剂可适宜地含有约1%至约10%农药。它们可用于拌种或与粉尘鼓风机一起用于叶面施用。

[1793] 同样可行的是施用溶液形式的农药(在广泛用于农业化学的适宜有机溶剂(通常为石油例如喷雾油)中)。

[1794] 农药也可按气溶胶组合物的形式来施用。在这样的组合物中,将农药溶解或分散在载体中,所述载体为可产生压力的推进剂混合物。将所述气溶胶组合物包装在容器中,通过雾化阀使所述混合物从所述容器中分散出来。

[1795] 当将农药与食物或引诱剂混合或与食物和引诱剂混合时,形成了农药诱饵。当害虫吃掉诱饵时,它们也消耗了农药。诱饵可呈颗粒、凝胶、可流动粉末、液体或固体的形式。它们可用在害虫藏身处。

[1796] 熏蒸剂是具有相对高蒸汽压的农药,因此可按气体形式存在,其以足够的浓度杀死土壤或密封空间中的害虫。熏蒸剂的毒性与其浓度和暴露时间成比例。它们的特征在于具有良好的扩散能力并通过渗透到害虫的呼吸系统中或通过害虫的表皮被吸收来发挥作用。施用熏蒸剂以便在气密房间或气密建筑物中或在专门腔室中对防气片下的储藏产品害虫(stored product pest)进行防治。

[1797] 可通过将农药粒子或小滴混悬在各种类型的塑料聚合物中来对农药进行微囊化。通过改变聚合物的化学性质或通过改变处理中的因素,可形成各种大小、各种溶解度、各种壁厚度和各种渗透度的微囊。这些因素控制其中活性成分的释放速度,而释放速度又影响产品的残留性能、作用速度和气味。

[1798] 通过将农药溶于使农药保持为溶液形式的溶剂中来制备油溶液浓缩物。农药的油溶液由于溶剂本身具有杀虫作用和体被蜡质覆盖物的溶解增加了农药的摄取速度而通常

提供比其它制剂更快的击倒及杀死害虫作用。油溶液的其它优点包括更好的贮藏稳定性、更好的裂缝渗透性和更好的油腻表面粘附性。

[1799] 另一个实施方式是水包油型乳剂，其中所述乳剂包含油性小球，所述油性小球各自提供有层状液晶包衣并分散在水相中，其中每个油性小球包含至少一种具有农业活性的化合物并各自包衣有单层的层或几层的层，所述层包含(1)至少一种非离子性亲脂性表面活性剂、(2)至少一种非离子性亲水性表面活性剂和(3)至少一种离子性表面活性剂，其中所述小球具有小于800纳米的平均粒径。有关该实施方式的进一步信息披露于美国专利公开文本20070027034(公开日期为2007年2月1日且专利申请序列号为11/495,228)中。为了易于使用，将该实施方式称作“OIWE”。

[1800] 进一步信息请参阅“Insect Pest Management”2nd Edition by D.Dent, copyright CAB International(2000)。另外，更多详细信息请参阅“Handbook of Pest Control-The Behavior,Life History,and Control of Household Pests”by Arnold Mallis,9th Edition,copyright 2004by GIE Media Inc。

[1801] 其它制剂组分

[1802] 一般地，当式一中披露的分子在制剂中使用时，所述制剂也可含有其它组分。这些组分包括但不限于(这是非穷举性且非相互排斥性的列举)润湿剂、展布剂、粘着剂、渗透剂、缓冲剂、隔离剂(sequestering agent)、防飘移剂、相容剂、消泡剂、清洁剂和乳化剂。接下来描述了几种组分。

[1803] 润湿剂是这样的物质，当将其加到液体中时，所述物质通过降低液体和液体在其上展布的表面之间的界面张力来增加液体的展布或渗透能力。润湿剂在农用化学制剂中发挥两种主要功能：在处理和制造期间增加粉末在水中的润湿速率从而制备在可溶性液体中的浓缩物或混悬浓缩物；和在将产品与水在喷雾罐中混合期间降低可润湿粉末的润湿时间并改善水向水可分散颗粒中的渗透。用于可润湿粉末、混悬浓缩物和水可分散颗粒制剂中的润湿剂的实例为：月桂基硫酸钠；二辛基磺基琥珀酸钠；烷基酚乙氧基化物；和脂肪醇乙氧基化物。

[1804] 分散剂是这样的物质，其吸附到粒子的表面上并有助于保持粒子的分散状态及防止粒子重新聚集。将分散剂加到农用化学制剂中以有助于制造期间的分散和混悬且有助于确保粒子在喷雾罐中重新分散到水中。它们广泛用于可润湿粉末、混悬浓缩物和水可分散颗粒中。用作分散剂的表面活性剂具有牢固吸附到粒子表面上的能力并提供对抗粒子重新聚集的荷电屏障或立体屏障。最常用的表面活性剂是阴离子型表面活性剂、非离子型表面活性剂或这两种类型的混合物。对于可润湿粉末制剂而言，最常见的分散剂为木质素磺酸钠。对于混悬浓缩物而言，使用聚电解质如萘磺酸钠甲醛缩合物来得到非常好的吸附和稳定作用。也使用三苯乙烯基苯酚乙氧基化物磷酸酯。非离子型表面活性剂(如烷基芳基氧化乙烯缩合物和EO-PO嵌段共聚物)有时与阴离子型表面活性剂组合起来作为用于混悬浓缩物的分散剂。近年来，已开发了新类型的分子量非常高的聚合物表面活性剂作为分散剂。这些分散剂具有非常长的疏水性“骨架”和形成“梳”状表面活性剂的“齿”的很多个氧化乙烯链。这些高分子量聚合物可为混悬浓缩物提供非常好的长期稳定性，这是因为疏水性骨架具有固定到粒子表面上的多个锚点。用于农用化学制剂中的分散剂的实例为：木质素磺酸钠；萘磺酸钠甲醛缩合物；三苯乙烯基苯酚乙氧基化物磷酸酯；脂肪醇乙氧基化物；烷基乙

氧基化物;EO-PO嵌段共聚物;和接枝共聚物。

[1805] 乳化剂是使一种液相的小滴于另一种液相中的混悬液稳定的物质。在没有乳化剂的情况下,两种液体会分离成两个不可混合的液相。最常用的乳化剂共混物含有具有12个或更多个氧化乙烯单元的烷基酚或脂肪醇及十二烷基苯磺酸的油溶性钙盐。范围为8至18的亲水亲油平衡("HLB")值通常将提供良好的稳定乳剂。乳剂稳定性有时可通过加入少量EO-PO嵌段共聚物表面活性剂来改善。

[1806] 增溶剂是在浓度超过临界胶束浓度时在水中形成胶束的表面活性剂。然后,胶束能够在胶束的疏水部分内溶解或增溶水不溶性物质。通常用于增溶的表面活性剂类型是非离子型表面活性剂:去水山梨糖醇单油酸酯、去水山梨糖醇单油酸酯乙氧基化物和油酸甲酯。

[1807] 表面活性剂有时单独使用,或有时与其它添加剂(如作为喷雾罐混合物辅料的矿物油或植物油)一起使用以改善农药对靶标的生物性能。用于生物增强的表面活性剂类型通常取决于农药的性质和作用模式。但是,它们通常是非离子型的,例如:烷基乙氧基化物;线性脂肪醇乙氧基化物;脂肪族胺乙氧基化物。

[1808] 农业制剂中的载体或稀释剂是加到农药中以得到所需强度产品的物质。载体通常是具有高吸收能力的物质,而稀释剂通常是具有低吸收能力的物质。载体和稀释剂用在粉剂制剂、可润湿粉末制剂、颗粒制剂和水可分散颗粒制剂中。

[1809] 有机溶剂主要用在乳油制剂、水包油乳剂、混悬乳剂和超低容量制剂中及以较小的程度用在颗粒制剂中。有时使用溶剂的混合物。第一主要组的溶剂是脂肪族石蜡基油,如煤油或精炼石蜡。第二主要组(及最常见)的溶剂包括芳族溶剂,如二甲苯和C_9和C_{10}芳族溶剂中分子量较高的馏分。氯代烃可用作共溶剂以当将制剂乳化到水中时防止农药的结晶。有时醇类用作共溶剂以增加溶剂能力。其它溶剂可包括植物油、种子油及植物油和种子油的酯。

[1810] 增稠剂或胶凝剂主要用在混悬浓缩物制剂、乳剂制剂和混悬乳剂制剂中以改变液体的流变学或流动性并防止经分散的颗粒或小滴发生分离或沉降。增稠剂、胶凝剂和抗沉降剂通常分为两类,即水不溶性粒子和水溶性聚合物。使用粘土和硅石来产生混悬浓缩物制剂是可能的。这些类型的物质的实例包括但不限于蒙脱石、膨润土、硅酸镁铝和活性白土(attapulgite)。水溶性多糖已用作增稠-胶凝剂多年。最常用的多糖的类型为种子和海藻的天然提取物或为纤维素的合成衍生物。这些类型的物质的实例包括但不限于瓜尔胶、豆角胶(locust beangum)、角叉菜胶(carrageenam)、藻酸盐、甲基纤维素、羧甲基纤维素钠(SCMC)、羟乙基纤维素(HEC)。其它类型的抗沉降剂基于变性淀粉、聚丙烯酸酯、聚乙烯醇和聚氧化乙烯。另一种良好的抗沉降剂为黄原胶。

[1811] 微生物可引起所配制产品的酸败。因此防腐剂用于消除或减小微生物的作用。这些试剂的实例包括但不限于:丙酸及其钠盐;山梨酸及其钠盐或钾盐;苯甲酸及其钠盐;对羟基苯甲酸钠盐;对羟基苯甲酸甲酯;和1,2-苯并异噻唑啉-3-酮(BIT)。

[1812] 表面活性剂的存在通常导致水基制剂当生产和通过喷雾罐施用时在混合操作期间起泡。为了减小起泡倾向,通常在生产阶段或在装入瓶中前加入消泡剂。一般而言,有两种类型的消泡剂即硅氧烷和非硅氧烷。硅氧烷通常为聚二甲基硅氧烷的水性乳剂,而非硅氧烷消泡剂为水不溶性油如辛醇和壬醇。在这两种情况下,消泡剂的功能都是从空气-水界

面中置换表面活性剂。

[1813] “绿色”试剂(例如辅料、表面活性剂、溶剂)可降低作物保护制剂的整体环境覆盖面积。绿色试剂为生物可降解的且通常由天然和/或可持续来源例如植物和动物来源衍生。具体实例为:植物油、种子油及植物油和种子油的酯,及烷氧基化烷基多聚葡萄糖苷。

[1814] 进一步信息参见“Chemistry and Technology of Agrochemical Formulations” edited by D.A.Knowles,copyright 1998by Kluwer Academic Publishers。还参见“Insecticides in Agriculture and Environment-Retrospects and Prospects”by A.S.Perry,I.Yamamoto,I.Ishaaya,and R.Perry,copyright 1998by Springer-Verlag。

[1815] 害虫

[1816] 一般来说,式一的分子可用于防治害虫,例如蚂蚁(ant)、蚜虫(aphid)、甲虫(beetle)、蠹虫(bristletail)、蟑螂(cockroache)、蟋蟀(cricket)、蠼螋(earwig)、蚤(flea)、蝇(fly)、蚱蜢(grasshopper)、叶蝉(leafhopper)、虱(lice)、蝗虫(locust)、螨(mite)、蛾(moth)、线虫(nematode)、蚧(scale)、综合纲(Symphylan)、白蚁(termite)、蓟马(thrip)、蜱(tick)、黄蜂(wasp)和粉虱(whitefly)。

[1817] 在另一个实施方式中,式一的分子可用于防治线虫门(Phyla Nematoda)和/或节肢动物门(Arthropoda)的害虫。

[1818] 在另一个实施方式中,式一的分子可用于防治有螯肢亚门(Subphyla Chelicerata)、多足纲(Myriapoda)和/或六足纲(Hexapoda)的害虫。

[1819] 在另一个实施方式中,式一的分子可用于防治蛛形纲(Arachnida)、综合纲(Symphyla)和/或昆虫纲(Insecta)的害虫。

[1820] 在另一个实施方式中,式一的分子可用于防治虱目(Order Anoplura)的害虫。具体种类的非穷举性列举包括但不限于吸血虱属种(Haematopinus spp.)、甲胁虱属(Hoplopleura spp.)、长颚虱属(Linognathus spp.)、虱属(Pediculus spp.)和鳞虱属(Polyplax spp.)。具体种类的非穷举性列举包括但不限于驴血虱(Haematopinus asini)、猪血虱(Haematopinus suis)、毛虱(Linognathus setosus)、绵羊颚虱(Linognathus ovillus)、头虱(Pediculus humanus capitis)、体虱(Pediculus humanus humanus)和阴虱(Pthirus pubis)。

[1821] 在另一个实施方式中,式一的分子可用于防治鞘翅目(Order Coleoptera)的害虫。具体种类的非穷举性列举包括但不限于豆象属种(Acanthoscelides spp.)、叩头虫属种(Agriotes spp.)、花象属种(Anthonomus spp.)、梨象属种(Apion spp.)、金龟属种(Apogonia spp.)、守瓜属种(Aulacophora spp.)、豆象属种(Bruchus spp.)、天牛属种(Cerosterna spp.)、Cerotoma spp.、龟象属种(Ceutorhynchus spp.)、跳甲属种(Chaetocnema spp.)、Colaspis spp.、Ctenicera spp.、象虫属种(Curculio spp.)、圆头犀金龟属种(Cyclocephala spp.)、叶甲属种(Diabrotica spp.)、叶象属种(Hypera spp.)、齿小蠹属种(Ips spp.)、粉蠹属种(Lyctus spp.)、Megascelis spp.、Meligethes spp.、鸟喙象属种(Otiorhynchus spp.)、玫瑰短喙象属种(Pantomorus spp.)、食叶鳃金龟属种(Phyllophaga spp.)、黄条跳甲属种(Phyllotreta spp.)、根鳃金龟属种(Rhizotrogus spp.)、Rhynchites spp.、隐颈象属种(Rhynchophorus spp.)、小蠹属种(Scolytus spp.)、Sphenophorus spp.、米象属种(Sitophilus spp.)和拟谷盗属种

(Tribolium spp.)。具体种类的非穷举性列举包括但不限于菜豆象(Acanthoscelides obtectus)、白蜡窄吉丁(Agrilus planipennis)、光肩星天牛(Anoplophora glabripennis)、棉铃象虫(Anthonomus grandis)、黑绒金龟(Ataenius spretulus)、Atomaria linearis、甜菜象(Bothynoderes punctiventris)、豌豆象(Bruchus pisorum)、四纹豆象(Callosobruchus maculatus)、黄斑露尾甲(Carpophilus hemipterus)、甜菜龟甲(Cassida vittata)、Cerotoma trifurcata、白菜籽龟象(Ceutorhynchus assimilis)、芫菁龟象(Ceutorhynchus napi)、Conoderus scalaris、Conoderus stigmosus、李象(Conotrachelus nenuphar)、Cotinis nitida、石刁柏负泥虫(Crioceris asparagi)、锈赤扁谷盗(Cryptolestes ferrugineus)、长角扁谷盗(Cryptolestes pusillus)、土耳其扁谷盗(Cryptolestes turcicus)、Cylindrocopturus adspersus、芒果剪叶象(Deporaus marginatus)、火腿皮蠹(Dermestes lardarius)、白腹皮蠹(Dermestes maculatus)、墨西哥豆瓢虫(Epilachna varivestis)、蛀茎象甲(Faustinus cubae)、苍白根颈象(Hylobius pales)、紫苜蓿叶象(Hypera postica)、咖啡果小蠹(Hypothenemus hampei)、烟草甲(Lasioderma serricorne)、马铃薯甲虫(Leptinotarsa decemlineata)、Liogenys fuscus、Liogenys suturalis、稻水象甲(Lissorhoptrus oryzophilus)、Maecolaspis joliveti、玉米叩甲(Melanotus communis)、油菜花露尾甲(Meligethes aeneus)、五月金龟子(Melolontha melolontha)、Oberea brevis、线性筒天牛(Oberea Linearis)、椰蛀犀金龟(Oryctes rhinoceros)、贸易锯谷盗(Oryzaephilus mercator)、锯谷盗(Oryzaephilus surinamensis)、黑角负泥虫(Oulema melanopus)、水稻负泥虫(Oulema oryzae)、Phyllophaga cuyabana、日本弧丽金龟(Popillia japonica)、大谷蠹(Prostephanus truncatus)、谷蠹(Rhyzopertha dominica)、条纹根瘤象甲(Sitona lineatus)、谷象(Sitophilus granarius)、米象(Sitophilus oryzae)、玉米象(Sitophilus zeamais)、药材甲(Stegobium paniceum)、赤拟谷盗(Tribolium castaneum)、杂拟谷盗(Tribolium confusum)、花斑皮蠹(Trogoderma variabile)和Zabrus tenebrioides。

[1822] 在另一个实施方式中,式一的分子可用于防治革翅目(Order Dermaptera)的害虫。

[1823] 在另一个实施方式中,式一的分子可用于防治蜚蠊目(Order Blattaria)的害虫。具体种类的非穷举性列举包括但不限于德国小蠊(Blattella germanica)、东方蜚蠊(Blatta orientalis)、宾夕法尼亚木蠊(Parcoblatta pennsylvanica)、美洲大蠊(Periplaneta americana)、澳洲大蠊(Periplaneta australasiae)、褐色大蠊(Periplaneta brunnea)、烟色大蠊(Periplaneta fuliginosa)、蔗绿蜚蠊(Pycnoscelus surinamensis)和长须蜚蠊(Supella longipalpa)。

[1824] 在另一个实施方式中,式一的分子可用于防治双翅目(Order Diptera)的害虫。具体种类的非穷举性列举包括但不限于伊蚊属种(Aedes spp.)、潜蝇属种(Agromyza spp.)、按实蝇属种(Anastrepha spp.)、疟蚊属种(Anopheles spp.)、果实蝇属种(Bactrocera spp.)、小条实蝇属种(Ceratitis spp.)、斑虻属种(Chrysops spp.)、锥蝇属种(Cochliomyia spp.)、瘿蚊属种(Contarinia spp.)、库蚊属种(Culex spp.)、叶瘿蚊属种(Dasineura spp.)、地种蝇属种(Delia spp.)、果蝇属种(Drosophila spp.)、厕蝇属种

(Fannia spp.)、黑蝇属种(Hylemyia spp.)、斑潜蝇属种(Liriomyza spp.)、蝇属种(Musca spp.)、Phorbia spp.,牛虻属种(Tabanus spp.)和大蚊属种(Tipula spp.)。具体种类的非穷举性列举包括但不限于紫苜蓿潜蝇(Agromyza frontella)、加勒比按实蝇(Anastrepha suspensa)、墨西哥按实蝇(Anastrepha ludens)、西印度按实蝇(Anastrepha obliqa)、瓜实蝇(Bactrocera cucurbitae)、桔小实蝇(Bactrocera dorsalis)、入侵实蝇(Bactrocera invadens)、桃实蝇(Bactrocera zonata)、地中海小条实蝇(Ceratitis capitata)、油菜叶瘿蚊(Dasineura brassicae)、灰地种蝇(Delia platura)、黄腹厕蝇(Fannia canicularis)、灰腹厕蝇(Fannia scalaris)、肠胃蝇(Gasterophilus intestinalis)、Gracillia perseae、扰血蝇(Haematobia irritans)、纹皮蝇(Hypoderma lineatum)、菜潜蝇(Liriomyza brassicae)、绵羊虱蝇(Melophagus ovinus)、秋家蝇(Musca autumnalis)、家蝇(Musca domestica)、羊狂蝇(Oestrus ovis)、欧洲麦秆蝇(Oscinella frit)、甜菜泉蝇(Pegomya betae)、胡萝卜茎蝇(Psila rosae)、樱桃果蝇(Rhagoletis cerasi)、苹果实蝇(Rhagoletis pomonella)、蓝橘绕实蝇(Rhagoletis mendax)、麦红吸浆虫(Sitodiplosis mosellana)和厩螫蝇(Stomoxys calcitrans)。

[1825] 在另一个实施方式中,式一的分子可用于防治半翅目(Order Hemiptera)的害虫。具体种类的非穷举性列举包括但不限于球蚜属种(Adelges spp.)、白轮盾蚧属种(Aulacaspis spp.)、沫蝉属种(Aphrophora spp.)、蚜虫属种(Aphis spp.)、粉虱属种(Bemisia spp.)、蜡蚧属种(Ceroplastes spp.)、雪盾蚧属种(Chionaspis spp.)、圆盾蚧属种(Chrysomphalus spp.)、软蜡蚧属种(Coccus spp.)、绿小叶蝉属种(Empoasca spp.)、蛎盾蚧属种(Lepidosaphes spp.)、蝽属种(Lagynotomus spp.)、草盲蝽属种(Lygus spp.)、长管蚜属种(Macrosiphum spp.)、黑尾叶蝉属种(Nephotettix spp.)、稻绿蝽属种(Nezara spp.)、沫蝉属种(Philaenus spp.)、植盲蝽属种(Phytocoris spp.)、Piezodorus spp.、臀纹粉蚧属种(Planococcus spp.)、粉蚧属种(Pseudococcus spp.)、Rhopalosiphum spp.、珠蜡蚧属种(Saissetia spp.)、彩斑蚜属种(Therioaphis spp.)、Toumeyella spp.、声蚜属种(Toxoptera spp.)、Trialeurodes spp.、锥蝽属种(Triatoma spp.)和尖盾蚧属种(Unaspis spp.)。具体种类的非穷举性列举包括但不限于拟绿蝽(Acrosternum hilare)、苜蓿豌豆蚜(Acyrthosiphon pisum)、Aleyrodes proletella、螺旋粉虱(Aleurodicus dispersus)、丝绒粉虱(Aleurothrixus floccosus)、Amrasca biguttula biguttula、红圆蚧(Aonidiella aurantii)、棉蚜(Aphis gossypii)、大豆蚜(Aphis glycines)、苹果蚜(Aphis pomi)、马铃薯长须蚜(Aulacorthum solani)、银叶粉虱(Bemisia argentifolii)、甘薯粉虱(Bemisia tabaci)、美洲谷长蝽(Blissus leucopterus)、天门冬小管蚜(Brachycorynella asparagi)、Brevennia rehi、甘蓝蚜(Brevicoryne brassicae)、马铃薯俊盲蝽(Calocoris norvegicus)、红蜡蚧(Ceroplastes rubens)、热带臭虫(Cimex hemipterus)、温带臭虫(Cimex lectularius)、Dagbertus fasciatus、Dichelops furcatus、麦双尾蚜(Diuraphis noxia)、柑桔木虱(Diaphorina citri)、车前圆尾蚜(Dysaphis plantaginea)、美棉红蝽(Dysdercus suturellus)、Edessa meditabunda、苹果绵蚜(Eriosoma lanigerum)、欧扁盾蝽(Eurygaster maura)、Euschistus heros、褐美洲蝽(Euschistus servus)、安氏角盲蝽(Helopeltis antonii)、茶角盲蝽(Helopeltis theivora)、吹棉蚧(Icerya purchasi)、芒果黄线叶蝉(Idioscopus

nitidulus)、灰飞虱(Laodelphax striatellus)、大稻缘蝽(Leptocorisa oratorius)、异稻缘蝽(Leptocorisa varicornis)、豆荚草盲蝽(Lygus hesperus)、木槿曼粉蚧(Maconellicoccus hirsutus)、大戟长管蚜(Macrosiphum euphorbiae)、麦长管蚜(Macrosiphum granarium)、蔷薇长管蚜(Macrosiphum rosae)、Macrosteles quadrilineatus、Mahanarva frimbiolata、麦无网蚜(Metopolophium dirhodum)、Mictis longicornis、桃蚜(Myzus persicae)、黑尾叶蝉(Nephotettix cinctipes)、Neurocolpus longirostris、稻绿蝽(Nezara viridula)、褐飞虱(Nilaparvata lugens)、糠片盾蚧(Parlatoria pergandii)、黑片盾蚧(Parlatoria ziziphi)、玉米花翅飞虱(Peregrinus maidis)、葡萄根瘤蚜(Phylloxera vitifoliae)、去杉球蚧(Physokermes piceae)、Phytocoris californicus、Phytocoris relativus、Piezodorus guildinii、四线盲蝽(Poecilocapsus lineatus)、Psallus vaccinicola、Pseudacysta perseae、菠萝洁粉蚧(Pseudococcus brevipes)、梨园盾蚧(Quadraspidiotus perniciosus)、玉米蚜(Rhopalosiphum maidis)、禾谷缢管蚜(Rhopalosiphum padi)、榄珠蜡蚧(Saissetia oleae)、Scaptocoris castanea、蚜麦二叉蚜(Schizaphis graminum)、麦长管蚜(Sitobion avenae)、白背飞虱(Sogatella furcifera)、温室粉虱(Trialeurodes vaporariorum)、结翅粉虱(Trialeurodes abutiloneus)、矢尖蚧(Unaspis yanonensis)和Zulia entrerriana。

[1826] 在另一个实施方式中,式一的分子可用于防治膜翅目(Order Hymenoptera)的害虫。具体种类的非穷举性列举包括但不限于切叶蚁属种(Acromyrmex spp.)、叶蚁属种(Atta spp.)、黑蚁属种(Camponotus spp.)、松叶蜂属种(Diprion spp.)、蚁属种(Formica spp.)、厨蚁属种(Monomorium spp.)、新松叶蜂属种(Neodiprion spp.)、收获蚁属种(Pogonomyrmex spp.)、马蜂属种(Polistes spp.)、火蚁属种(Solenopsis spp.)、黄胡蜂属种(Vespula spp.)和木蜂属种(Xylocopa spp.)。具体种类的非穷举性列举包括但不限于新疆菜叶蜂(Athalia rosae)、Atta texana、阿根廷蚁(Iridomyrmex humilis)、小黑蚁(Monomorium minimum)、厨蚁(Monomorium pharaonis)、红火蚁(Solenopsis invicta)、热带火蚁(Solenopsis geminata)、Solenopsis molesta、黑火蚁(Solenopsis richtery)、南方火蚁(Solenopsis xyloni)和臭家蚁(Tapinoma sessile)。

[1827] 在另一个实施方式中,式一的分子可用于防治等翅目(Order Isoptera)的害虫。具体种类的非穷举性列举包括但不限于乳白蚁属种(Coptotermes spp.)、角白蚁属种(Cornitermes spp.)、砂白蚁属种(Cryptotermes spp.)、异白蚁属种(Heterotermes spp.)、木白蚁属种(Kalotermes spp.)、楹白蚁属种(Incisitermes spp.)、大白蚁属种(Macrotermes spp.)、缘木白蚁属种(Marginitermes spp.)、锯白蚁属种(Microcerotermes spp.)、原角白蚁属种(Procornitermes spp.)、散白蚁属种(Reticulitermes spp.)、长鼻白蚁属种(Schedorhinotermes spp.)和古白蚁属种(Zootermopsis spp.)。具体种类的非穷举性列举包括但不限于曲颚白蚁(Coptotermes curvignathus)、新西兰乳白蚁(Coptotermes frenchii)、台湾乳白蚁(Coptotermes formosanus)、金黄异白蚁(Heterotermes aureus)、稻麦小白蚁(Microtermes obesi)、Reticulitermes banyulensis、Reticulitermes grassei、黄肢散白蚁(Reticulitermes flavipes)、美小黄散白蚁(Reticulitermes hageni)、西方散白蚁(Reticulitermes

hesperus)、桑特散白蚁(Reticulitermes santonensis)、栖北散白蚁(Reticulitermes speratus)、美黑胫散白蚁(Reticulitermes tibialis)和美小黑散白蚁(Reticulitermes virginicus)。

[1828] 在另一个实施方式中,式一的分子可用于防治鳞翅目(Order Lepidoptera)的害虫。具体种类的非穷举性列举包括但不限于褐带卷蛾属种(Adoxophyes spp.)、Agrotis spp.、卷蛾属种(Argyrotaenia spp.)、Cacoecia spp.、细蛾属种(Caloptilia spp.)、禾草螟属种(Chilo spp.)、夜蛾属种(Chrysodeixis spp.)、豆粉蝶属种(Colias spp.)、草螟属种(Crambus spp.)、绢野螟属种(Diaphania spp.)、螟属种(Diatraea spp.)、金刚钻属种(Earias spp.)、粉斑螟属种(Ephestia spp.)、Epimecis spp.、Feltia spp.、角剑夜蛾属种(Gortyna spp.)、青虫属种(Helicoverpa spp.)、实夜蛾属种(Heliothis spp.)、Indarbela spp.、Lithocolletis spp.、Loxagrotis spp.、天幕毛虫属种(Malacosoma spp.)、Peridroma spp.、细蛾属种(Phyllonorycter spp.)、Pseudaletia spp.、蛀茎夜蛾属种(Sesamia spp.)、灰翅夜蛾属种(Spodoptera spp.)、兴透翅蛾属种(Synanthedon spp.)和巢蛾属种(Yponomeuta spp.)。具体种类的非穷举性列举包括但不限于飞扬阿夜蛾(Achaea janata)、棉褐带卷蛾(Adoxophyes orana)、小地蚕(Agrotis ipsilon)、棉叶波纹夜蛾(Alabama argillacea)、Amorbia cuneana、脐橙螟(Amyelois transitella)、Anacamptodes defectaria、桃枝麦蛾(Anarsia lineatella)、黄麻桥夜蛾(Anomis sabulifera)、梨豆夜蛾(Anticarsia gemmatalis)、果树卷叶蛾(Archips argyrospila)、玫瑰卷叶蛾(Archips rosana)、桔带卷蛾(Argyrotaenia citrana)、伽马叉纹夜蛾(Autographa gamma)、Bonagota cranaodes、籼弄蝶(Borbo cinnara)、Bucculatrix thurberiella、Capua reticulana、桃蛀果蛾(Carposina niponensis)、芒果横线尾夜蛾(Chlumetia transversa)、玫瑰色卷蛾(Choristoneura rosaceana)、稻纵卷叶螟(Cnaphalocrocis medinalis)、荔枝细蛾(Conopomorpha cramerella)、芳香木蠹蛾(Cossus cossus)、Cydia caryana、李小食心虫(Cydia funebrana)、梨小食心虫(Cydia molesta)、Cydia nigricana、苹果小卷蛾(Cydia pomonella)、Darna diducta、小蔗螟(Diatraea saccharalis)、西南玉米杆草螟(Diatraea graniosella)、埃及金刚钻(Earias insulata)、翠纹金刚钻(Earias vitella)、Ecdytolopha aurantianum、南美玉米苗斑螟(Elasmopalpus lignosellus)、粉斑螟(Ephestia cautella)、烟草粉斑螟(Ephestia elutella)、地中海粉螟(Ephestia kuehniella)、夜小卷蛾(Epinotia aporema)、淡棕苹果蛾(Epiphyas postvittana)、香蕉弄蝶(Erionota thrax)、女贞细卷蛾(Eupoecilia ambiguella)、Euxoa auxiliaris、东方蛀果蛾(Grapholita molesta)、三纹螟蛾(Hedylepta indicata)、棉铃虫(Helicoverpa armigera)、谷实夜蛾(Helicoverpa zea)、烟芽夜蛾(Heliothis virescens)、菜心野螟(Hellula undalis)、番茄蠹蛾(Keiferia lycopersicella)、茄白翅野螟(Leucinodes orbonalis)、咖啡潜叶蛾(Perileucoptera coffeella)、旋纹潜蛾(Leucoptera malifoliella)、葡萄小卷叶蛾(Lobesia botrana)、Loxagrotis albicosta、舞毒蛾(Lymantria dispar)、桃潜蛾(Lyonetia clerkella)、Mahasena corbetti、甘蓝夜蛾(Mamestra brassicae)、豆荚野螟(Maruca testulalis)、袋蛾(Metisa plana)、Mythimna unipuncta、Neoleucinodes elegantalis、三点水螟(Nymphula depunctalis)、秋尺蛾(Operophtera brumata)、玉米螟(Ostrinia

nubilalis)、Oxydia vesulia、Pandemis cerasana、苹褐卷蛾(Pandemis heparana)、非洲达摩凤蝶(Papilio demodocus)、红铃麦蛾(Pectinophora gossypiella)、杂色地老虎(Peridroma saucia)、咖啡潜叶蛾(Perileucoptera coffeella)、马铃薯块茎蛾(Phthorimaea operculella)、柑桔叶潜蛾(Phyllocnisitis citrella)、菜粉蝶(Pieris rapae)、苜蓿绿夜蛾(Plathypena scabra)、印度谷斑蛾(Plodia interpunctella)、菜蛾(Plutella xylostella)、Polychrosis viteana、桔果巢蛾(Prays endocarpa)、油橄榄巢蛾(Prays oleae)、Pseudaletia unipuncta、大豆夜蛾(Pseudoplusia includens)、尺蠖(Rachiplusia nu)、三化螟(Scirpophaga incertulas)、稻蛀茎夜蛾(Sesamia inferens)、粉茎螟(Sesamia nonagrioides)、铜斑褐刺蛾(Setora nitens)、麦蛾(Sitotroga cerealella)、葡萄长须卷蛾(Sparganothis pilleriana)、甜菜夜蛾(Spodoptera exigua)、草地贪夜蛾(Spodoptera fugiperda)、南部灰翅夜蛾(Spodoptera eridania)、Thecla basilides、衣蛾(Tineola bisselliella)、粉斑夜蛾(Trichoplusia ni)、番茄斑潜蝇(Tuta absoluta)、咖啡豹蠹蛾(Zeuzera coffeae)和梨豹蠹蛾(Zeuzera pyrina)。

[1829] 在另一个实施方式中,式一的分子可用于防治食毛目(Order Mallophaga)的害虫。具体种类的非穷举性列举包括但不限于Anaticola spp.、Bovicola spp.、Chelopistes spp.、Goniodes spp.、Menacanthus spp.和Trichodectes spp.。具体种类的非穷举性列举包括但不限于Bovicola bovis、Bovicola caprae、绵羊虱(Bovicola ovis)、Chelopistes meleagridis、Goniodes dissimilis、Goniodes gigas、火鸡短角鸟虱(Menacanthus stramineus)、鸡羽虱(Menopon gallinea)和犬啮毛虱(Trichodectes canis)。

[1830] 在另一个实施方式中,式一的分子可用于防治直翅目(Order Orthoptera)的害虫。具体种类的非穷举性列举包括但不限于蚱蜢属种(Melanoplus spp.)和Pterophylla spp.。具体种类的非穷举性列举包括但不限于黑斑阿纳螽(Anabrus simplex)、非洲蝼蛄(Gryllotalpa africana)、Gryllotalpa australis、Gryllotalpa brachyptera、蝼蛄(Gryllotalpa hexadactyla)、东亚飞蝗(Locusta migratoria)、纲翅细刺螽(Microcentrum retinerve)、沙漠蝗(Schistocerca gregaria)和叉尾斯奎螽(Scudderia furcata)。

[1831] 在另一个实施方式中,式一的分子可用于防治蚤目(Order Siphonaptera)的害虫。具体种类的非穷举性列举包括但不限于鸡角叶蚤(Ceratophyllus gallinae)、Ceratophyllus niger、犬栉头蚤(Ctenocephalides canis)、猫栉头蚤(Ctenocephalides felis)和人蚤(Pulex irritans)。

[1832] 在另一个实施方式中,式一的分子可用于防治缨翅目(Order Thysanoptera)的害虫。具体种类的非穷举性列举包括但不限于Caliothrips spp.、Frankliniella spp.、硬蓟马属种(Scirtothrips spp.)和蓟马属种(Thrips spp.)。具体种类的非穷举性列举包括但不限于烟褐蓟马(Frankliniella fusca)、西花蓟马(Frankliniella occidentalis)、Frankliniella schultzei、威廉期花蓟马(Frankliniella williamsi)、温室蓟马(Heliothrips haemorrhaidalis)、Rhipiphorothrips cruentatus、桔硬蓟马(Scirtothrips citri)、茶黄蓟马(Scirtothrips dorsalis)和Taeniothrips rhopalantennalis、黄胸蓟马(Thrips hawaiiensis)、豆黄蓟马(Thrips nigropilosus)、东方蓟马(Thrips orientalis)和Thrips tabaci。

[1833] 在另一个实施方式中，式一的分子可用于防治缨尾目(Order Thysanura)的害虫。具体种类的非穷举性列举包括但不限于衣鱼属种(Lepisma spp.)和小灶衣鱼属种(Thermobia spp.)。

[1834] 在另一个实施方式中，式一的分子可用于防治螨目(Order Acarina)的害虫。具体种类的非穷举性列举包括但不限于粉螨属种(Acarus spp.)、刺皮瘿螨属种(Aculops spp.)、牛蜱属种(Boophilus spp.)、脂螨属种(Demodex spp.)、革蜱属种(Dermacentor spp.)、上瘿螨属种(Epitimerus spp.)、瘿螨属种(Eriophyes spp.)、硬蜱属种(Ixodes spp.)、小爪螨属种(Oligonychus spp.)、全爪螨属种(Panonychus spp.)、根螨属种(Rhizoglyphus spp.)和叶螨属种(Tetranychus spp.)。具体种类的非穷举性列举包括但不限于氏蜂跗腺螨(Acarapis woodi)、粗脚粉螨(Acarus siro)、Aceria mangiferae、番茄刺皮瘿螨(Aculops lycopersici)、Aculus pelekassi、斯氏刺瘿螨(Aculus schlechtendali)、Amblyomma americanum、卵形短须螨(Brevipalpus obovatus)、紫红短须螨(Brevipalpus phoenicis)、美洲狗蜱(Dermacentor variabilis)、屋尘螨(Dermatophagoides pteronyssinus)、鹅耳枥始叶螨(Eotetranychus carpini)、猫耳螨(Notoedres cati)、咖啡小爪螨(Oligonychus coffeae)、冬青小爪螨(Oligonychus ilicus)、柑桔全爪螨(Panonychus citri)、苹果全爪螨(Panonychus ulmi)、桔皱叶刺瘿螨(Phyllocoptruta oleivora)、食跗线螨属种(Polyphagotarsonemun latus)、血红扇头蜱(Rhipicephalus sanguineus)、疥螨(Sarcoptes scabiei)、鳄梨顶冠瘿螨(Tegolophus perseaflorae)、二点叶螨(Tetranychus urticae)和狄氏瓦螨(Varroa destructor)。

[1835] 在另一个实施方式中，式一的分子可用于防治综合纲(Order Symphyla)的害虫。具体种类的非穷举性列举包括但不限于白松虫(Scutigerella immaculata)。

[1836] 在另一个实施方式中，式一的分子可用于防治线虫门(Phylum Nematoda)的害虫。具体种类的非穷举性列举包括但不限于滑刃线虫属种(Aphelenchoides spp.)、刺线虫属种(Belonolaimus spp.)、小环线虫属种(Criconemella spp.)、茎线虫属种(Ditylenchus spp.)、棘皮线虫属种(Heterodera spp.)、潜根线虫属种(Hirschmanniella spp.)、纽带线虫属种(Hoplolaimus spp.)、根结线虫属种(Meloidogyne spp.)、短体线虫属种(Pratylenchus spp.)和穿孔线虫属种(Radopholus spp.)。具体种类的非穷举性列举包括但不限于犬恶丝虫(Dirofilaria immitis)、玉米胞囊线虫(Heterodera zeae)、南方根结线虫(Meloidogyne incognita)、Meloidogyne javanica、旋盘尾丝虫(Onchocerca volvulus)、Radopholus similis和香蕉肾状线虫(Rotylenchus reniformis)。

[1837] 更详细的信息请参阅“HANDBOOK OF PEST CONTROL-THE BEHAVIOR,LIFE HISTORY,AND CONTROL OF HOUSEHOLD PESTS”by Arnold Mallis,9th Edition,copyright 2004by GIE Media Inc.。

[1838] 施用

[1839] 防治门线虫，节肢动物，和/或软体动物中的害虫通常是指所在地中的害虫数、害虫活性或两者都得到减少。当在以下情况下时可发生该防治：

[1840] (a)从所在地驱逐害虫总体；

[1841] (b)使所在地中或所在地周围的害虫丧失能力；或

[1842] (c)区域中或区域周围的害虫被灭绝。

[1843] 当然，可发生这些结果的组合。通常，害虫数、害虫活性或两者都被令人满意地减少大于50％，优选减少大于90％，最优选大于98％。大体上，所述所在地不在人类体内或人体上；因此，所述所在地通常为非-人类所在地。

[1844] 在另一个实施方式中，式一分子施用到的所在地可以是占据(或可能被害虫占据或被害虫爬过)的任何所在地，例如所述所在地可为：

[1845] (a)作物、树木、水果、谷物、饲料类植物、藤本植物、草地和/或观赏植物的生长位置；

[1846] (b)家畜的居住地；

[1847] (c)建筑物的内或外表面(例如谷物贮存地)；

[1848] (d)建筑物中使用的建筑材料(例如浸渍木)；和

[1849] (e)建筑物周围的土壤。

[1850] 使用式一分子的具体作物区域包括苹果、玉米、向日葵、棉花、大豆、芸苔、小麦、稻谷、高粱、大麦、燕麦、马铃薯、柑橘、苜蓿、莴苣、草莓、番茄、胡椒、十字花科植物(crucifer)、梨、烟草、杏仁(almond)、甜菜、大豆(bean)和其它有价值作物的生长地或它们种子的待种植区域。还有利的是当栽培各种植物时将硫酸铝与式一分子一起使用。

[1851] 在另一个实施方式中，式一分子通常的使用量为约0.0001克每公顷至约5000克每公顷以提供防治。在另一个实施方式中，优选式一分子的使用量为约0.001克每公顷至约500克每公顷。在另一个实施方式中，更优选式一分子的使用量为约0.01克每公顷至约50克每公顷。

[1852] 式一分子可用在同时或顺序施用的混合物中，所述化合物单独或与其它化合物一起增强植物活力(例如，长出更好的根系、更好地经受应激生长条件)。所述其它化合物为例如调节植物乙烯受体的化合物，最著名的为1-甲基环丙烯(也称作1-MCP)。此外，该分子可以在害虫活性低时(例如植物开始生长之前)使用，制备有价值的农产品。该时间包括当害虫压力通常低时的早期播种季节。

[1853] 可将式一分子施用到植物的叶子和果实部分以防治害虫。所述分子会与所述害虫直接接触或当所述害虫吃食含有所述农药的叶子、果实或吸食树液(extracting sap)时会摄入所述农药。也可将式一分子施用到土壤，并且当以该方式施用时，可防治以根和茎为食的害虫。所述根可吸收分子，将其向上运送到植物的叶部分，从而防治地上咀嚼和以树液为食的害虫。

[1854] 一般而言，就诱饵而言，将诱饵置于例如白蚁可与诱饵发生接触和/或白蚁可被吸引到所述诱饵的场所。也可将诱饵施用到例如蚂蚁、白蚁、蟑螂和苍蝇可与诱饵发生接触和/或蚂蚁、白蚁、蟑螂和苍蝇可被吸引到所述诱饵的场所的建筑物表面(水平表面、垂直表面或倾斜表面)。诱饵可包含式一分子。

[1855] 可将式一分子包封在囊的内部或可将其放置在囊的表面上。所述囊的大小可在纳米级尺寸(直径为约100-900纳米)至微米级尺寸(直径为约10-900微米)范围内变化。

[1856] 由于某些害虫的卵具有抗一些农药的独特能力，因此可能需要重复施用式一分子以防治新出现的幼虫。

[1857] 农药在植物中的内吸性移动可用于通过将式一分子施用(例如通过喷洒区域)到所述植物的不同部位而对所述植物的另一个部位进行害虫防治。例如，防治食叶昆虫可以

通过滴注灌溉施用或沟槽施用、通过用例如种植前或种植后土壤浇灌处理土壤、或者通过种植前处理植物种子来实现。

[1858] 种子处理可以应用于所有类型的种子，包括可生长成遗传修饰为表达特定属性的植物的那些种子。代表性的实例包括表达对无脊椎害虫有毒的蛋白质(例如苏芸金杆菌(Bacillus thuringiensis))或其它杀虫毒素的那些种子、表达除草剂抵抗性的那些种子(例如“转基因(Roundup Ready)”种子)、或具有“叠加”外源基因的那些种子(所述“叠加”外源基因表达杀虫毒素、除草剂抵抗性、营养提高特性、抗旱或任何其它有益特性)。此外，用式一分子进行的所述种子处理可进一步增强植物更好经受应激生长条件的能力。这导致更健康、更旺盛的植物，由此可在收获时得到更高的产量。一般而言，每100,000粒种子约1克至约500克式一分子预期提供良好益处，每100,000粒种子约10克至约100克的量的式一分子预期提供更好益处，每100,000粒种子25克至约75克的量的式一分子预期提供甚至更高益处。

[1859] 应该显而易见的是，式一分子可用在遗传修饰为表达特定属性例如苏芸金杆菌(Bacillus thuringiensis)或其它杀虫毒素的植物上或用在所述植物中或用在所述植物周围，或用在表达除草剂抵抗性的那些植物上或用在所述植物中或用在所述植物周围，或用在具有“叠加”外源基因(所述“叠加”外源基因表达杀虫毒素、除草剂抵抗性、营养提高特性或任何其它有益特性)的植物上或用在所述植物中或用在所述植物周围。

[1860] 式一分子可用于在兽医学方面或在非-人动物饲养领域防治内寄生物和外寄生物。式一分子按已知的方式来施用，如以例如片剂、胶囊剂、饮用剂、颗粒剂的形式来口服给药，以例如浸蘸、喷雾、倾倒、点样和撒粉的形式来进行皮肤施用，以及以例如注射剂的形式来进行肠胃外给药。

[1861] 式一分子也可有利地用于家畜(例如牛、羊、猪、鸡和鹅)饲养。它们也可有利地用在宠物(例如马、狗和猫)中。所防治的具体害虫会是烦扰所述动物的蚤和蜱。将适宜的制剂与饮用水或饲料一起口服给予所述动物。适宜的剂量和制剂取决于物种。

[1862] 式一分子也可用于在上面所列动物中防治寄生虫，特别是肠部寄生虫。

[1863] 式一分子也可用在用于人体保健的治疗方法中。所述方法包括但不限于以诸如片剂、胶囊剂、饮用剂、颗粒剂的形式口服给药和通过皮肤施用。

[1864] 世界范围内的害虫已迁移到新的环境(对于所述害虫来说)，之后在所述新的环境中变成新的入侵物种。式一分子也可用在所述新的入侵物种上，从而在所述新的环境中对它们进行防治。

[1865] 式一分子也可用在植物例如作物的生长区域(例如，种植前、种植中、收获前)中，并且所述区域存在可商业上破坏所述植物的低水平(甚至无实际存在)害虫。在所述区域使用所述分子是为了有益于在所述区域生长的所述植物。所述益处可包括但不限于提高植物的健康、提高植物的收率(例如，增加有价值成分的生物量和/或增加有价值成分的含量)、增强植物活力(例如，促进植物生长和/或使叶子更绿)、提高植物质量(例如，提高一些成分的含量或组成)和增强所述植物对非生物应激和/或生物应激的耐受。

[1866] 在农药可被使用或商业销售前，所述农药经历各种政府当局(当地、地区、州、国家、国际)的漫长评价过程。大量数据要求由管理当局来规定，并且必须通过数据生成来寻址，以及由产品登记人或由代表产品登记人的第三方来提交(通常使用与万维网连接的计

算机)。然后这些政府当局评价所述数据,并且若作出安全性的决定,则将产品登记许可提供给潜在的使用者或销售者。之后,在产品登记被授权和支持的地方,所述使用者或销售者可使用或销售所述农药。

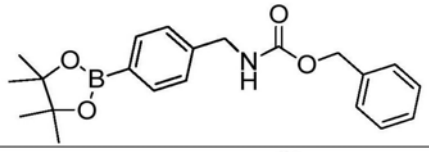
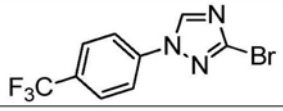
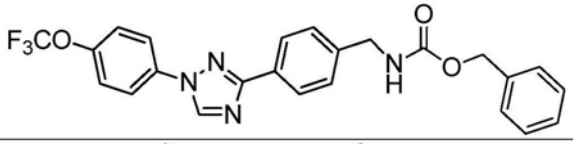
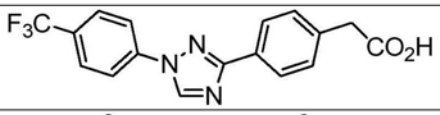
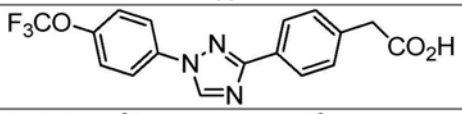
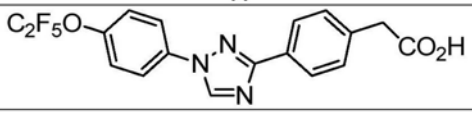
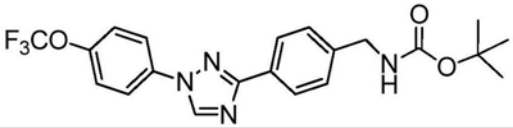
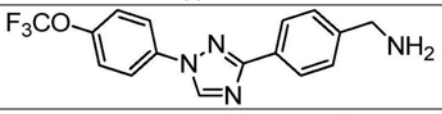
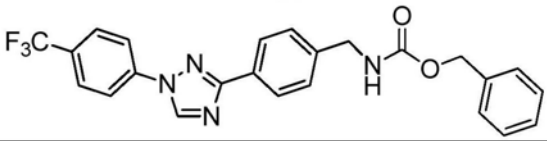
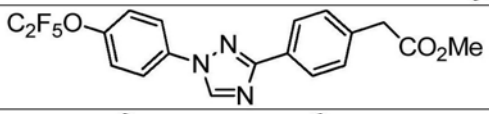
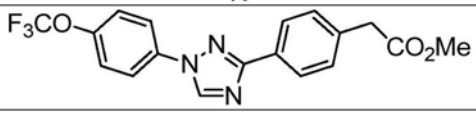
[1867] 可对根据式一分子进行试验以确定其抗害虫效力。此外,可进行作用模式研究以确定所述分子是否具有不同于其它农药的作用模式。之后,可将由此获取的该数据发放(例如通过互联网)给第三方。

[1868] 本申请中的标题仅是为了方便,而决不是用于解释本申请中的任何部分。

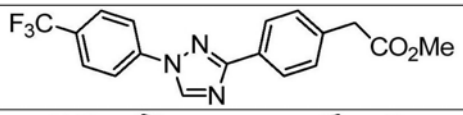
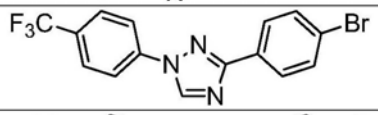
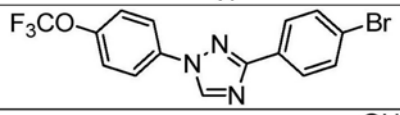
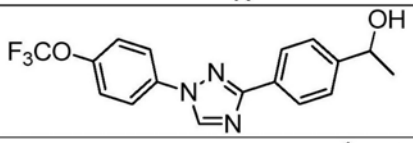
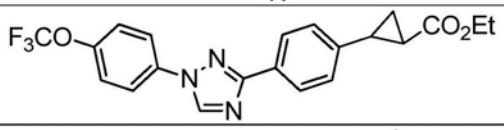
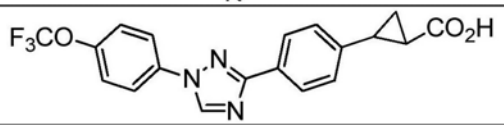
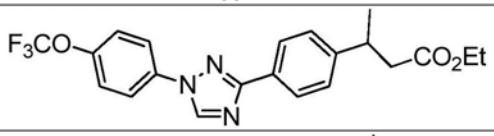
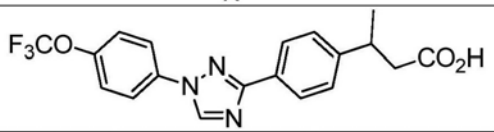
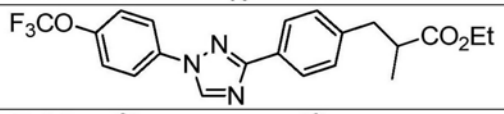
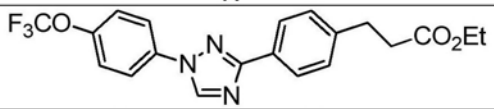
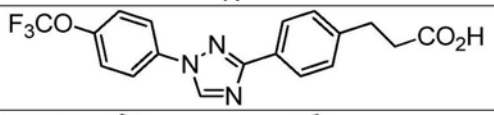
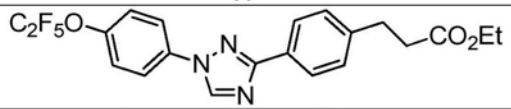
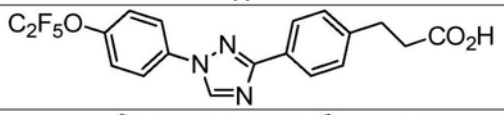
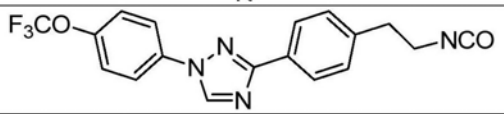
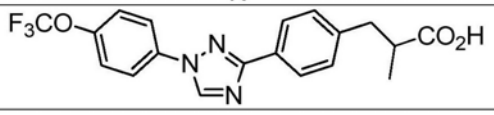
[1869] 表部分

[1870] 表1:中间体的结构

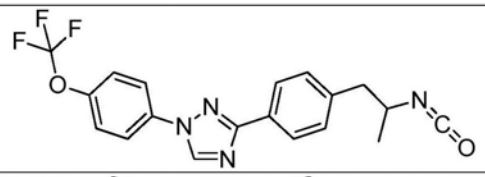
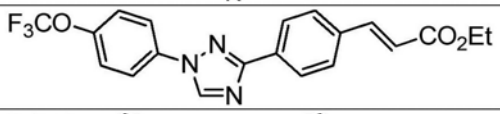
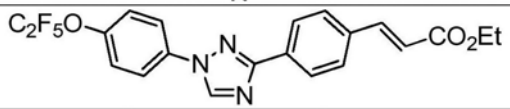
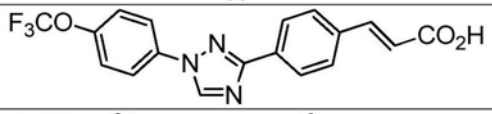
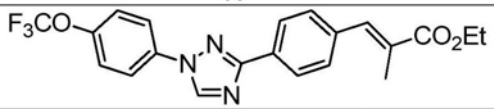
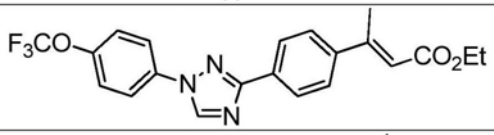
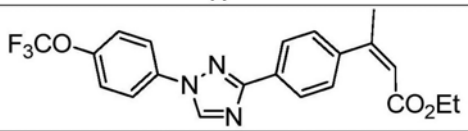
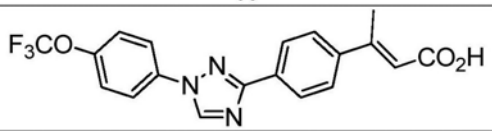
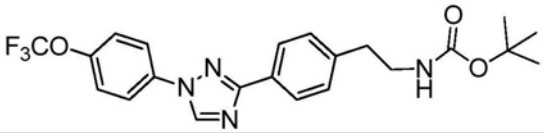
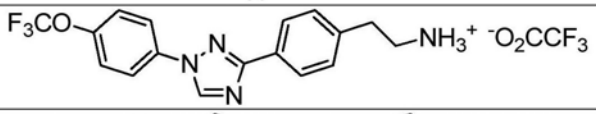
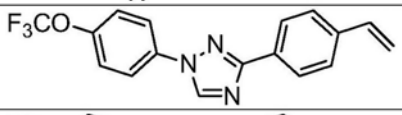
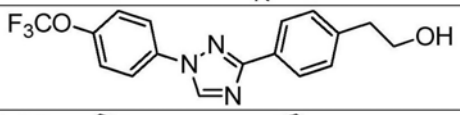
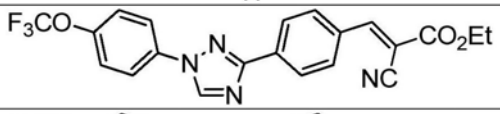
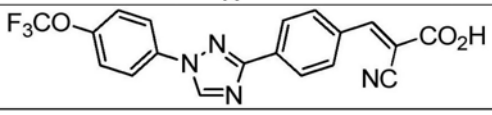
[1871]

编号	制备	结构
C13	实施例 9	
C1b	实施例 1	
C14	实施例 10	
C8	实施例 4	
C6	实施例 4	
C7	实施例 4	
C15a	实施例 10a	
C16	实施例 11	
C15	实施例 10	
C4	实施例 3	
C3	实施例 3	

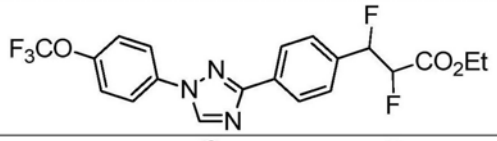
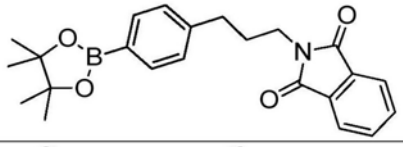
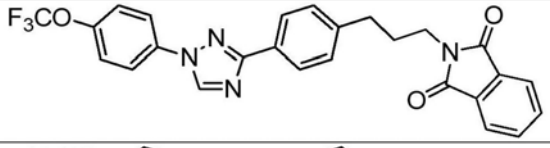
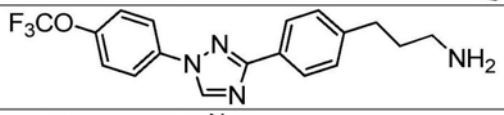
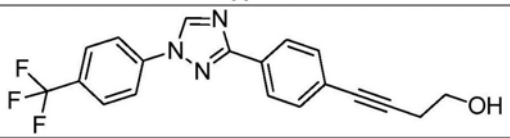
[1872]

C5	实施例 3	
C53	实施例 56	
C52	实施例 56	
C24	实施例 24	
C19	实施例 14	
C20	实施例 15	
C40	实施例 43	
C41	实施例 44	
C37	实施例 37	
C30	实施例 30	
C32	实施例 31	
C31	实施例 30	
C33	实施例 31	
C34a	实施例 32a	
C38	实施例 38	

[1873]

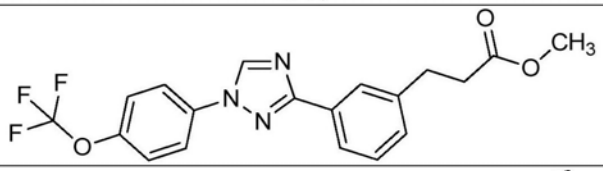
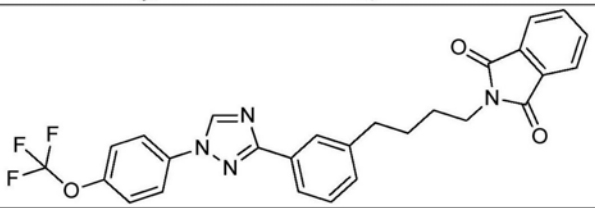
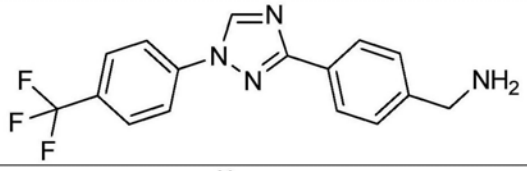
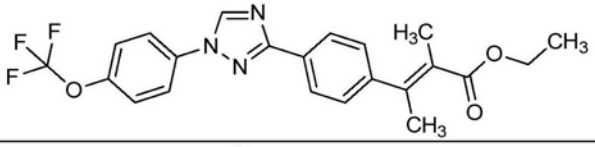
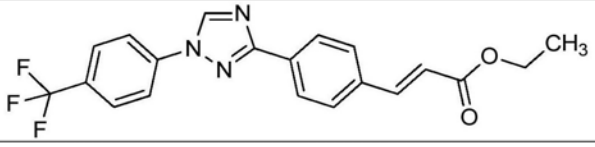
C39	实施例 39	
C17	实施例 13	
C18	实施例 13	
C22	实施例 20	
C36	实施例 36	
C26	实施例 26	
C27	实施例 26	
C28	实施例 27	
C50	实施例 54	
C55	实施例 58	
C43	实施例 47	
C44	实施例 48	
C46	实施例 50	
C47	实施例 51	

[1874]

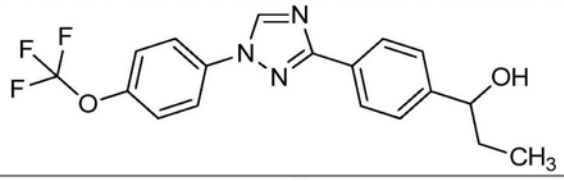
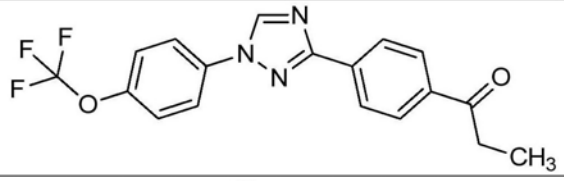
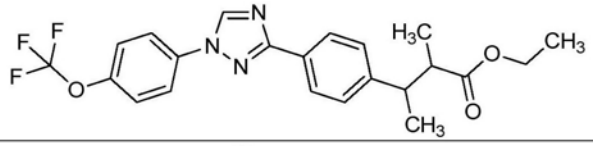
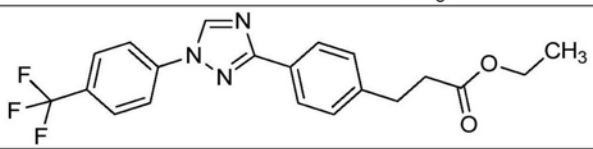
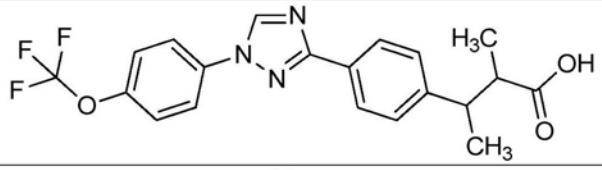
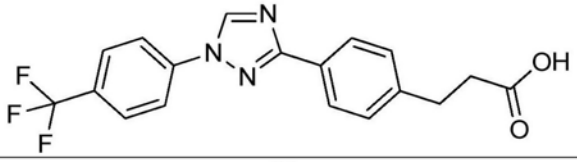
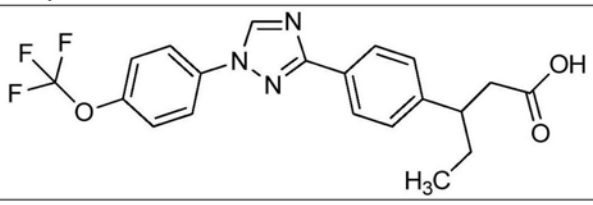
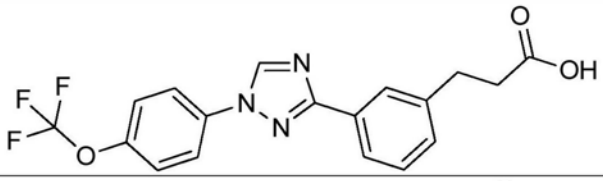
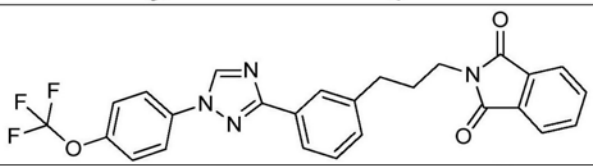
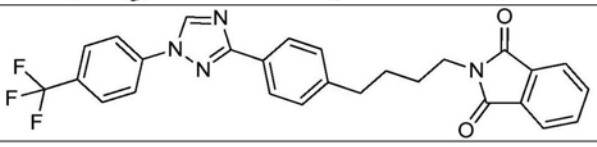
C45	实施例 49	
C58	实施例 60	
C59	实施例 61	
C60	实施例 62	
C61	实施例 65	

[1875] 表1A:中间体的结构(CA)

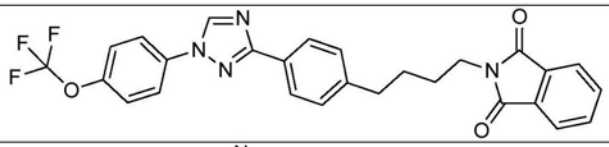
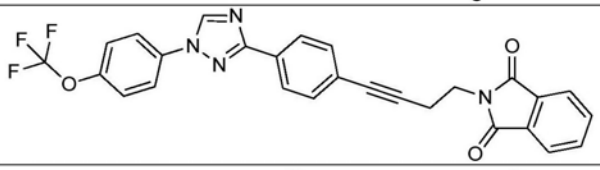
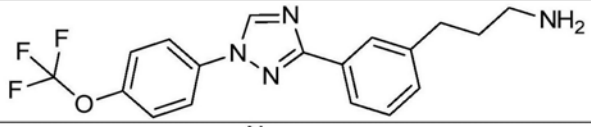
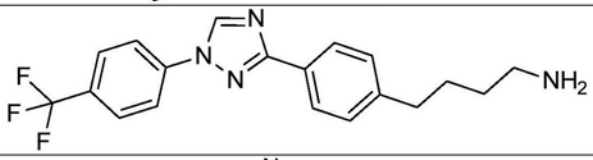
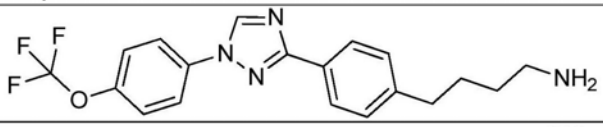
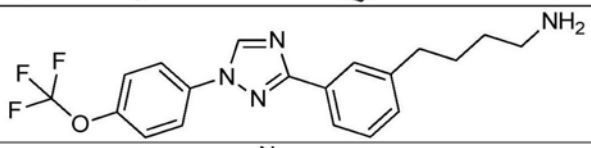
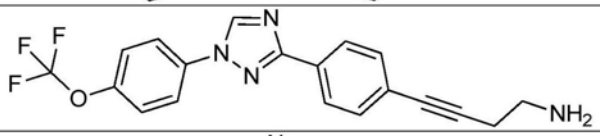
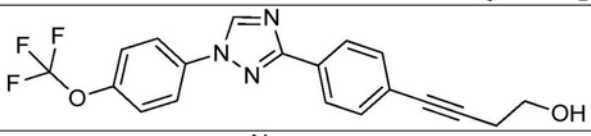
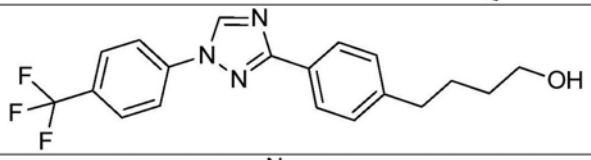
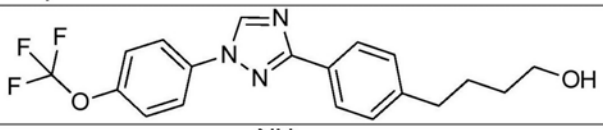
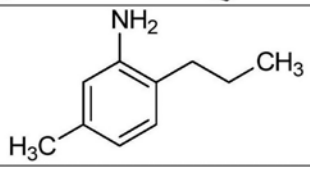
[1876]

编号	制备	结构
CA1	实施例 10	
CA2	实施例 10	
CA3	实施例 11	
CA4	实施例 13	
CA5	实施例 13	

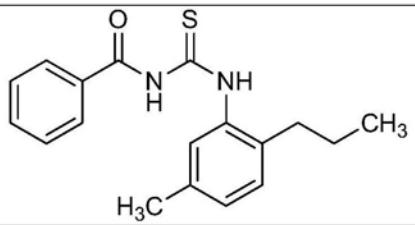
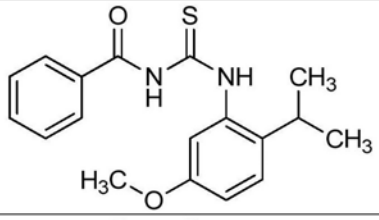
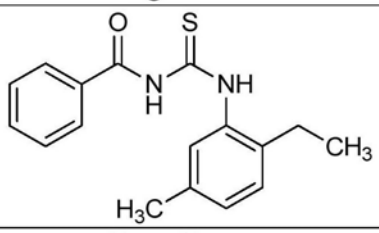
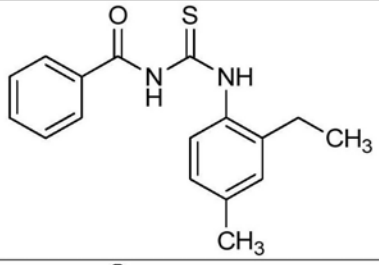
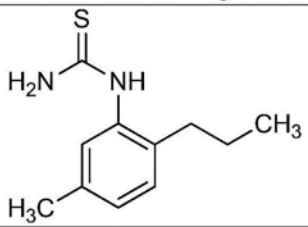
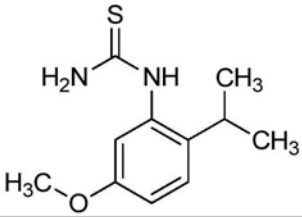
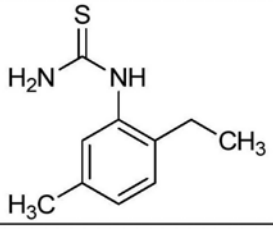
[1877]

CA6	实施例 24	
CA7	实施例 25	
CA8	实施例 30	
CA9	实施例 30	
CA10	实施例 31	
CA11	实施例 31	
CA12	实施例 44	
CA13	实施例 51	
CA14	实施例 59	
CA15	实施例 59	

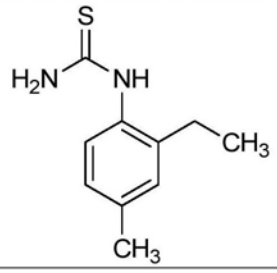
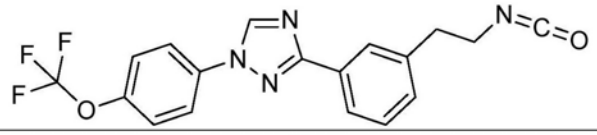
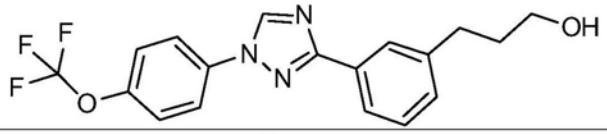
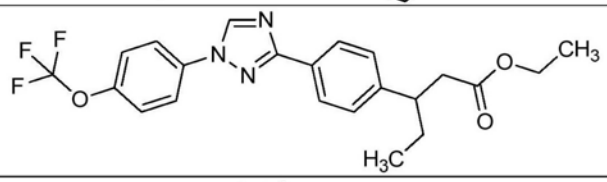
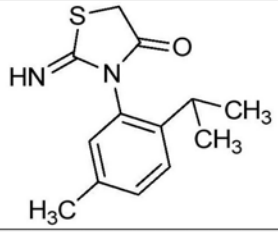
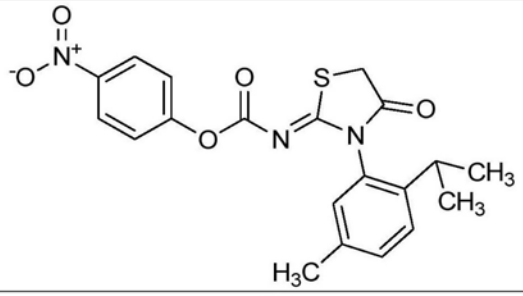
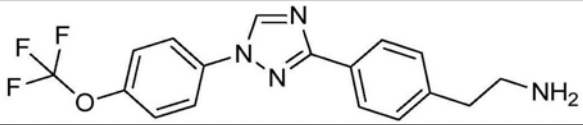
[1878]

CA16	**实施例 59**	
CA17	**实施例 59**	
CA18	**实施例 62**	
CA19	**实施例 62**	
CA20	**实施例 62**	
CA21	**实施例 62**	
CA22	**实施例 62**	
CA23	**实施例 65**	
CA24	**实施例 66**	
CA25	**实施例 66**	
CA26	**实施例 66**	

[1879]

CA33	**实施例 68**	
CA35	**实施例 68**	
CA36	**实施例 68**	
CA37	**实施例 68**	
CA38	**实施例 69**	
CA40	**实施例 69**	
CA41	**实施例 69**	

[1880]

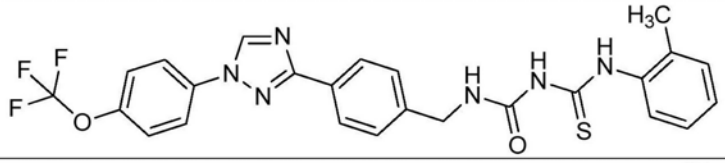
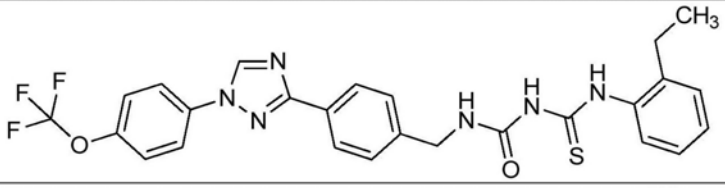
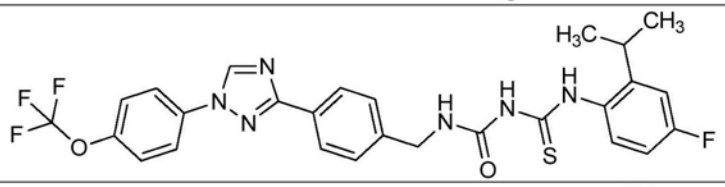
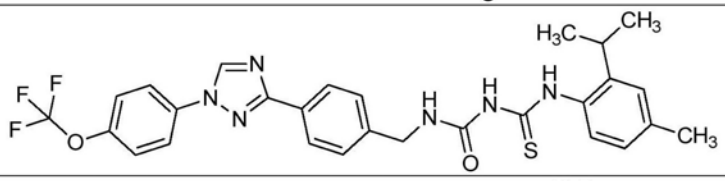
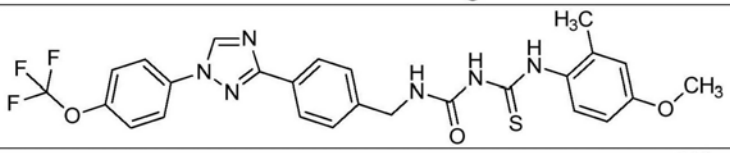
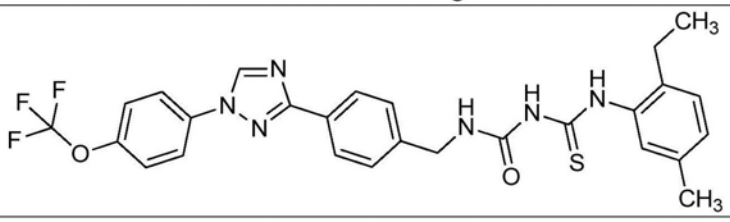
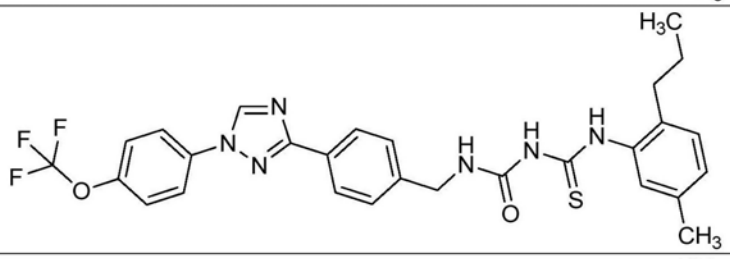
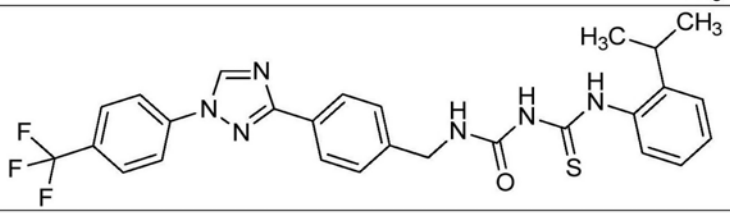
CA42	实施例 69	
CA44	实施例 74	
CA45	实施例 76	
CA48	实施例 81	
CA49	实施例 83	
CA50	实施例 84	
CA51	实施例 58a	

[1881] 表1B:中间体的结构(PC)

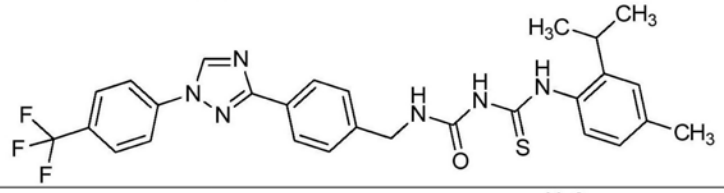
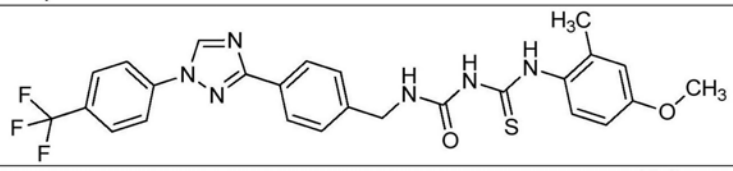
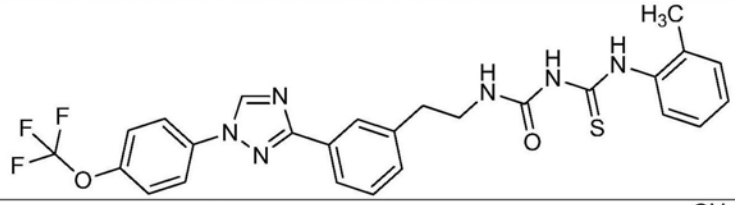
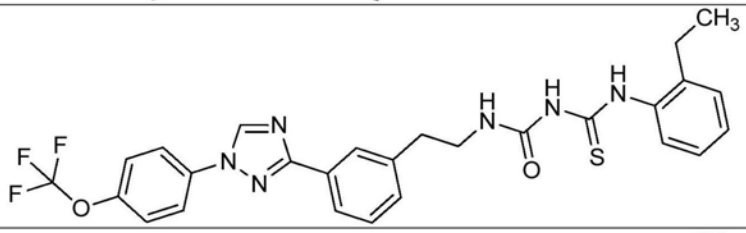
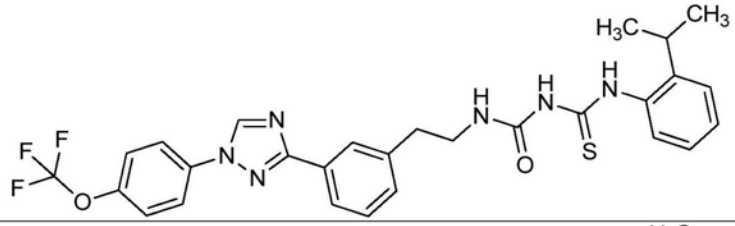
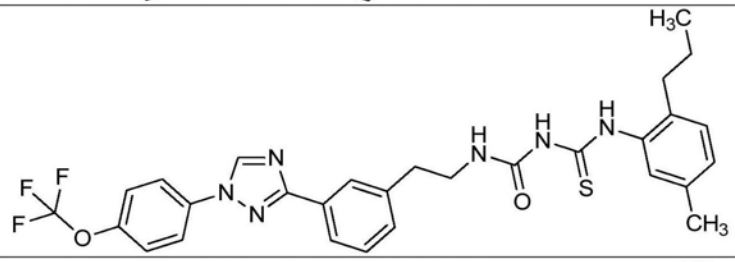
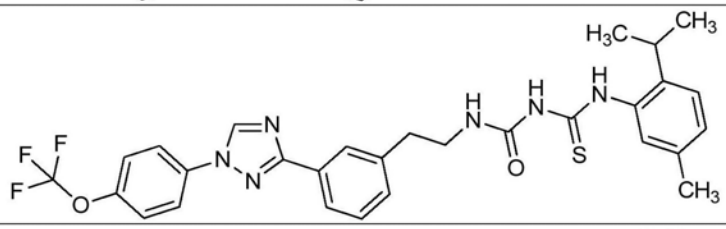
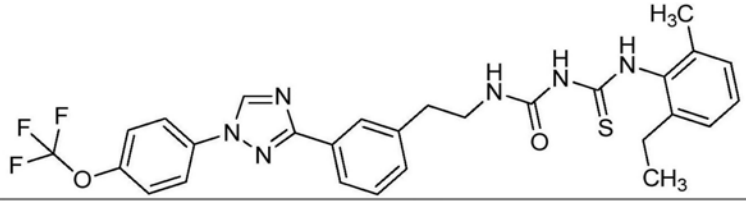
[1882]

编号	制备	结构

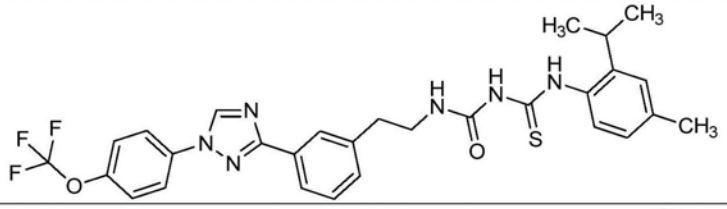
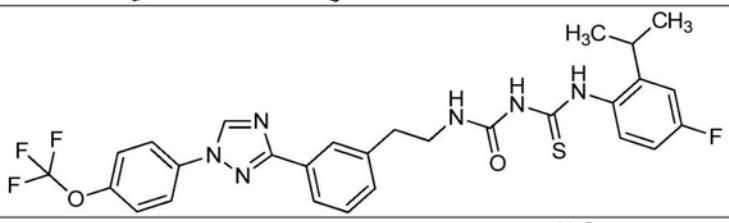
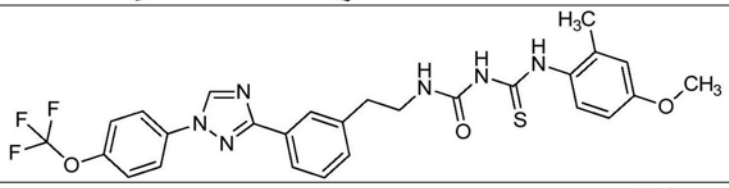
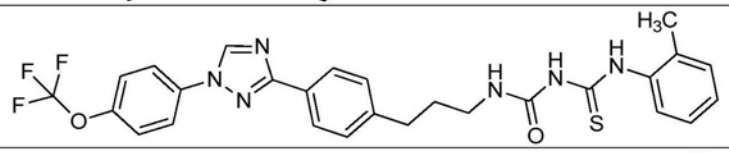
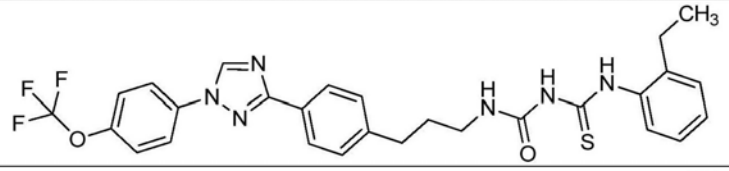
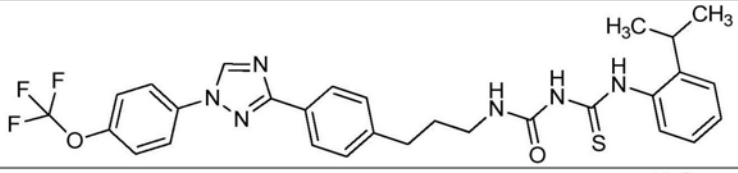
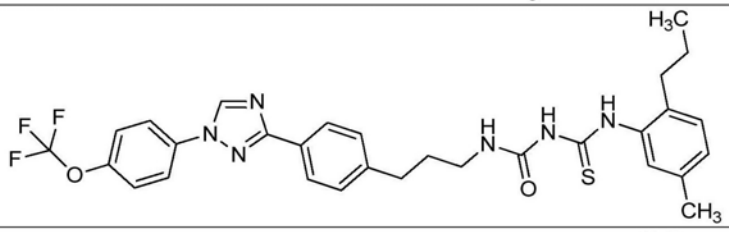
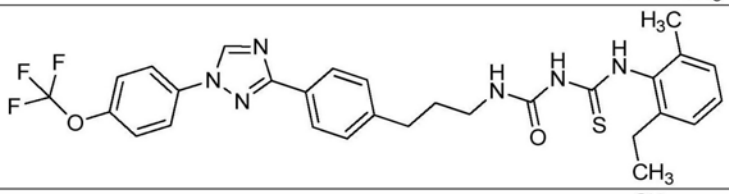
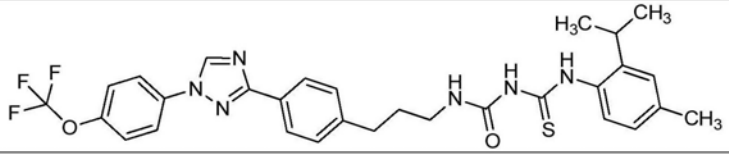
[1883]

PC1	**实施例 71**	
PC2	**实施例 71**	
PC3	**实施例 71**	
PC5	**实施例 71**	
PC6	**实施例 71**	
PC7	**实施例 71**	
PC8	**实施例 71**	
PC14	**实施例 71**	

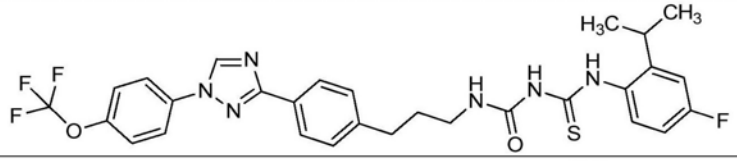
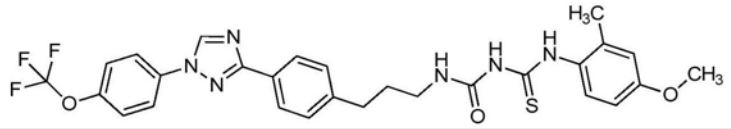
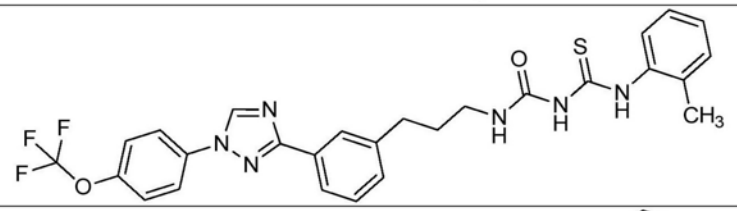
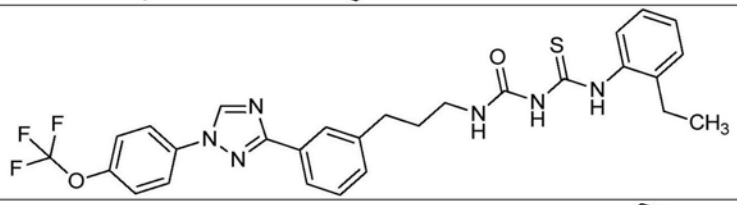
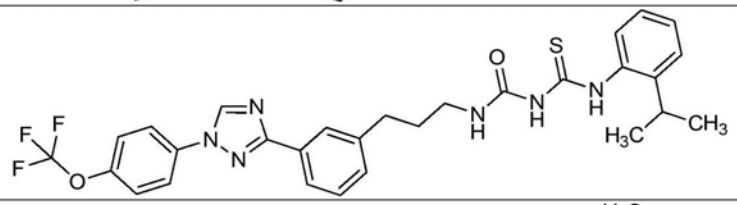
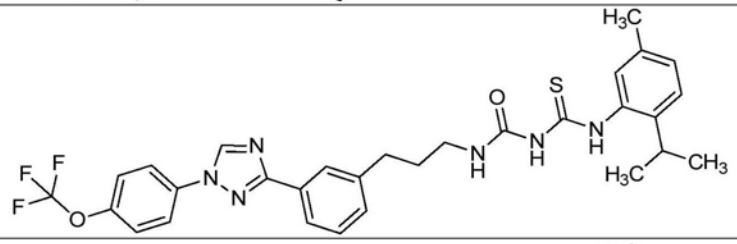
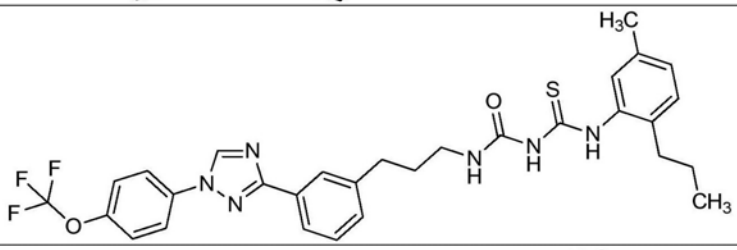
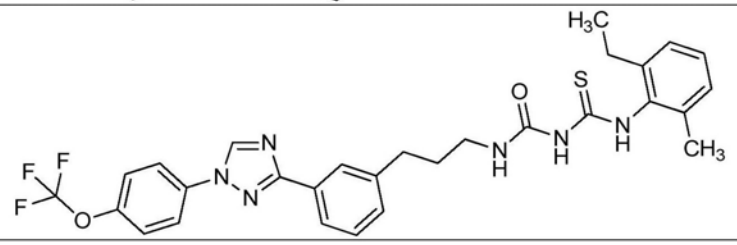
[1884]

PC15	**实施例 71**	
PC16	**实施例 71**	
PC74	**实施例 75**	
PC75	**实施例 75**	
PC76	**实施例 75**	
PC80	**实施例 75**	
PC81	**实施例 75**	
PC83	**实施例 75**	

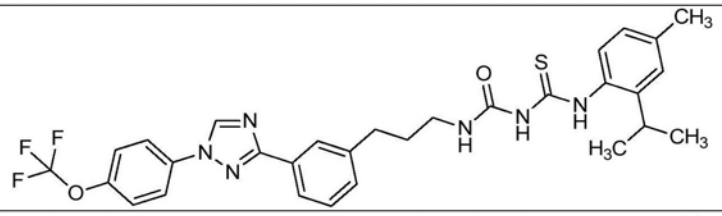
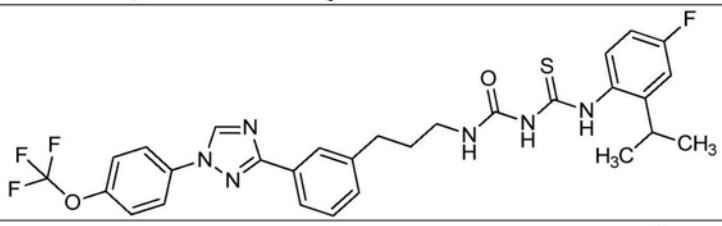
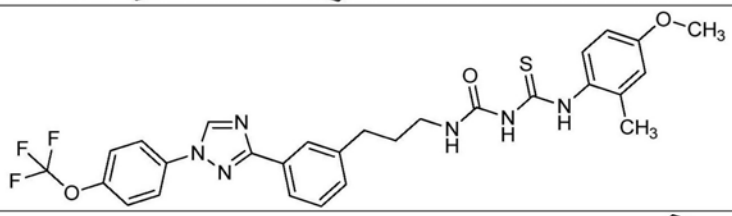
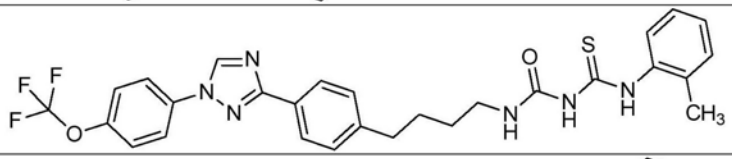
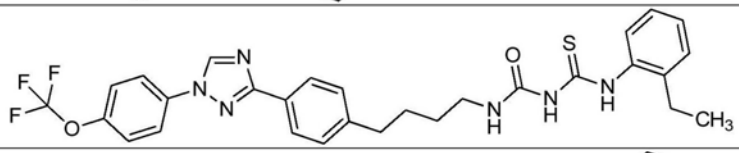
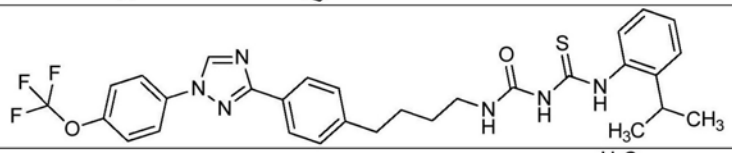
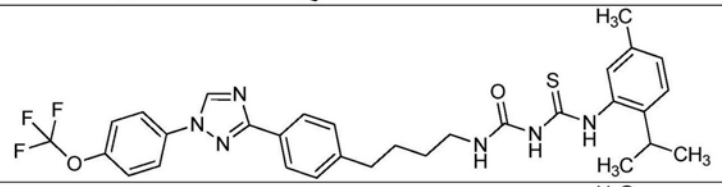
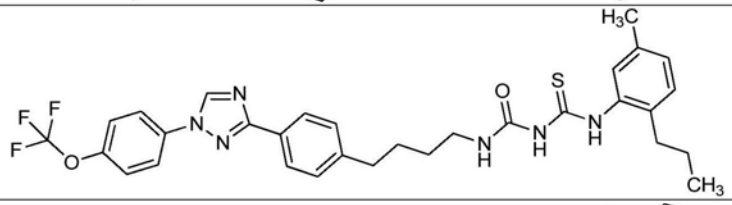
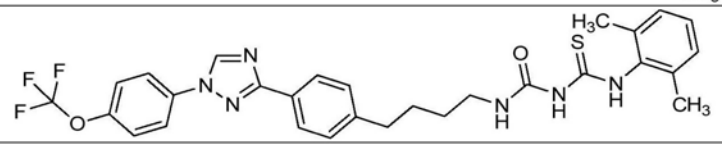
[1885]

PC84	实施例 75	
PC85	实施例 75	
PC87	实施例 75	
PC92	实施例 63	
PC93	实施例 63	
PC94	实施例 63	
PC99	实施例 63	
PC101	实施例 63	
PC102	实施例 63	

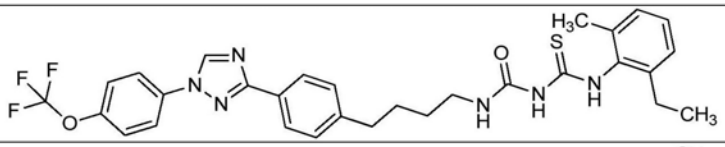
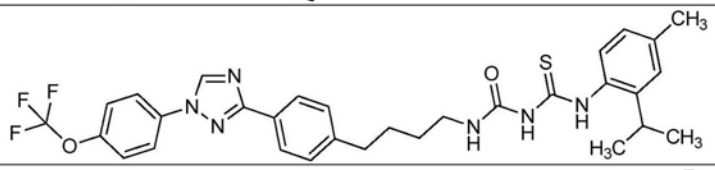
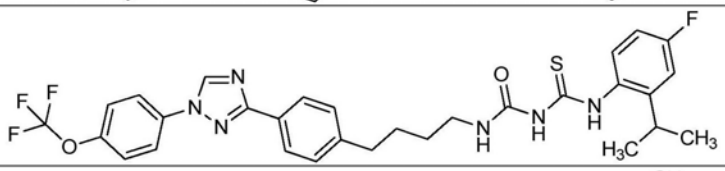
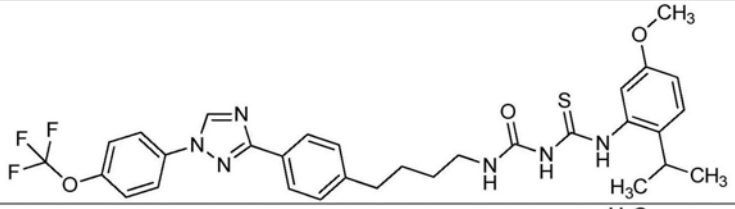
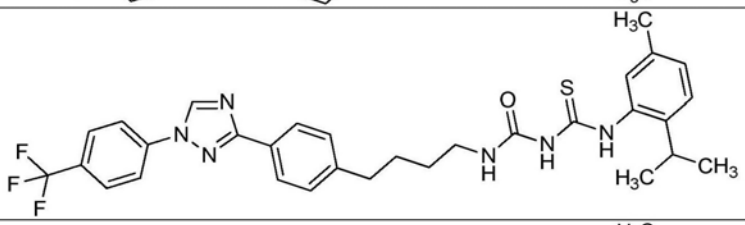
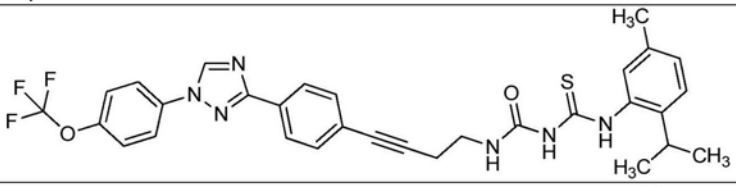
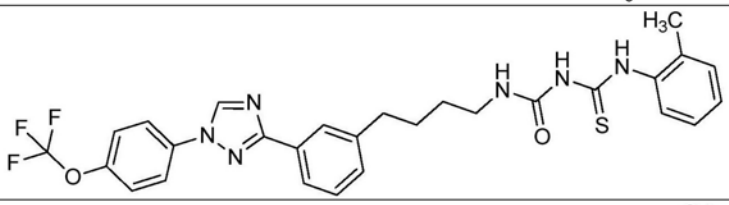
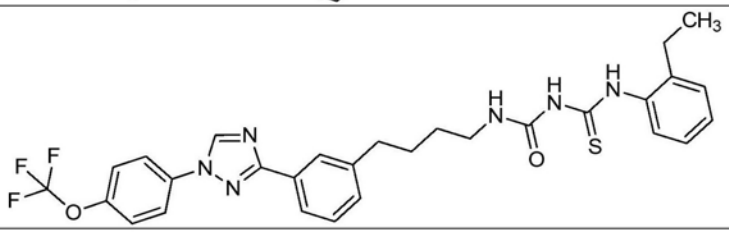
[1886]

PC103	实施例 63	
PC105	实施例 63	
PC118	实施例 63	
PC119	实施例 63	
PC120	实施例 63	
PC124	实施例 63	
PC125	实施例 63	
PC127	实施例 63	

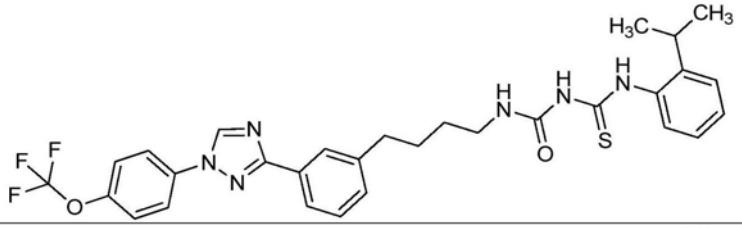
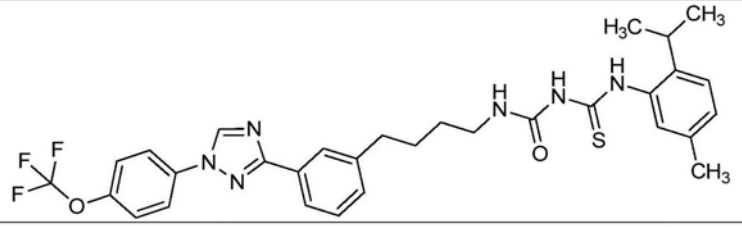
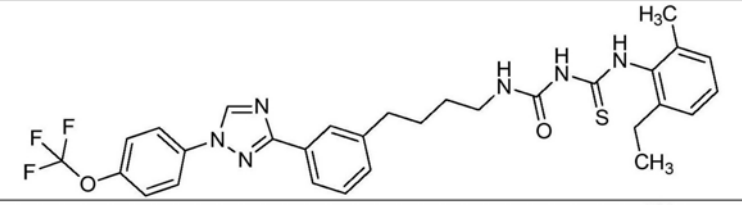
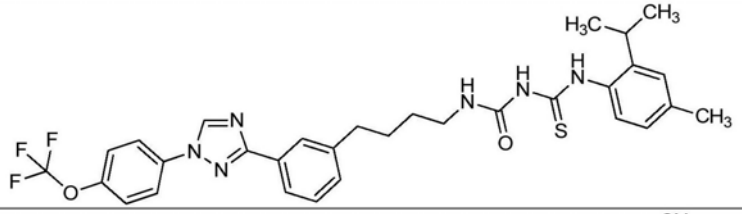
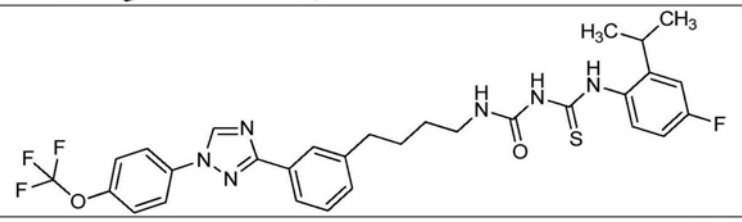
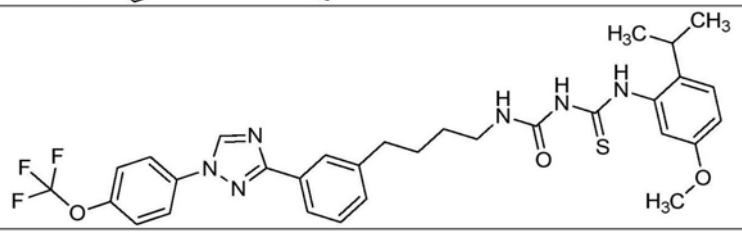
[1887]

PC128	实施例 63	
PC129	实施例 63	
PC131	实施例 63	
PC144	实施例 63	
PC145	实施例 63	
PC146	实施例 63	
PC150	实施例 63	
PC151	实施例 63	
PC152	实施例 63	

[1888]

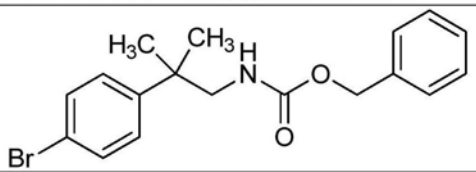
PC153	实施例 63	
PC154	实施例 63	
PC155	实施例 63	
PC156	实施例 63	
PC159	实施例 63	
PC160	实施例 63	
PC170	实施例 63	
PC171	实施例 63	

[1889]

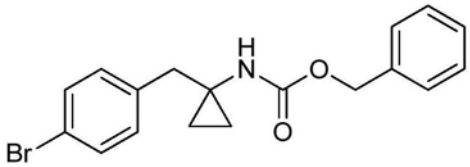
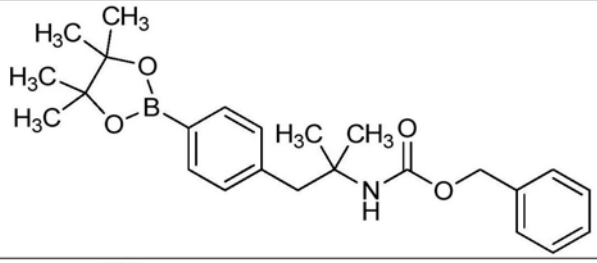
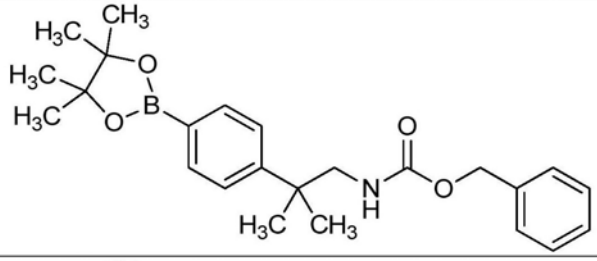
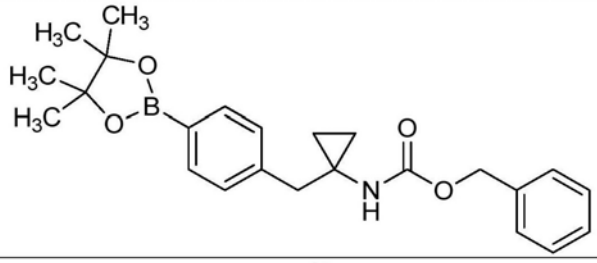
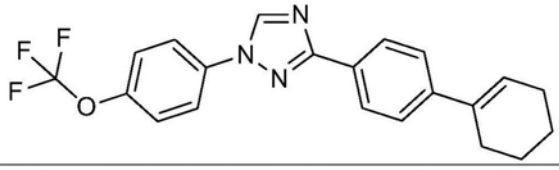
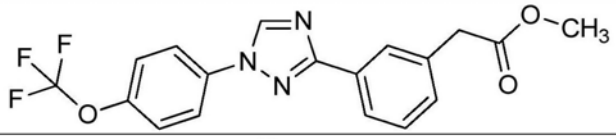
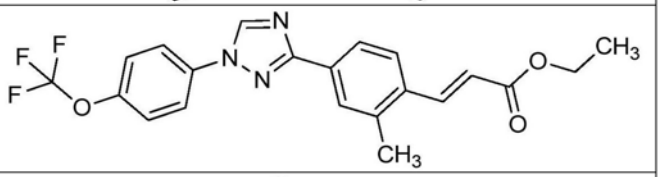
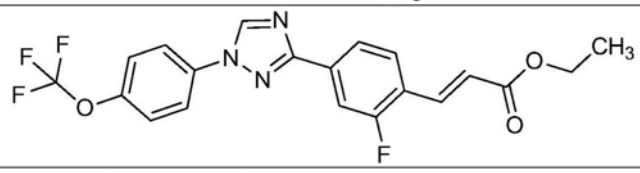
PC172	实施例 63	
PC176	实施例 63	
PC179	实施例 63	
PC180	实施例 63	
PC181	实施例 63	
PC182	实施例 63	

[1890] 表1C:中间体的结构(CB)

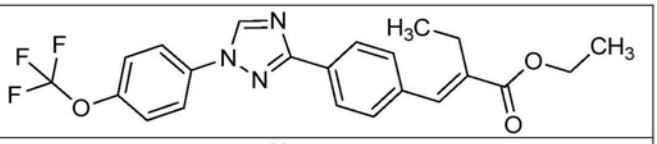
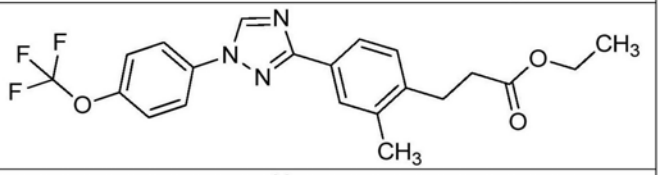
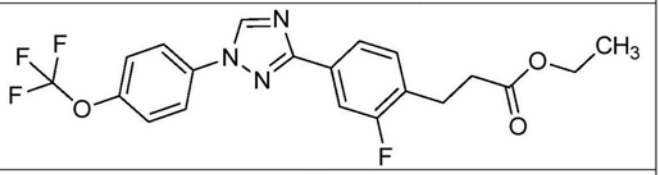
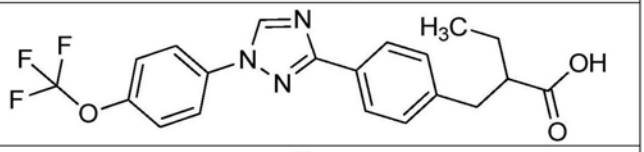
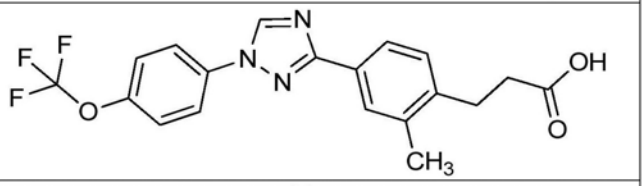
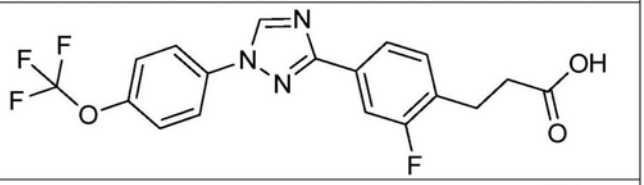
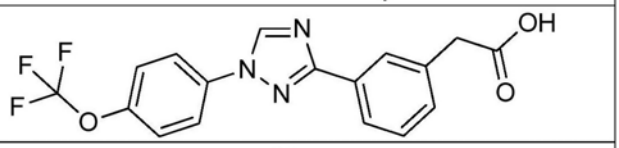
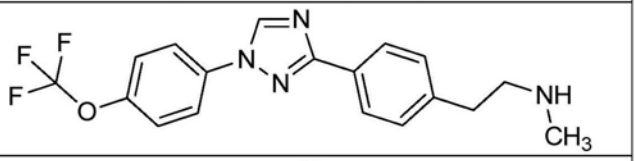
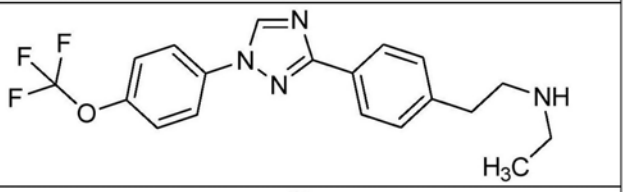
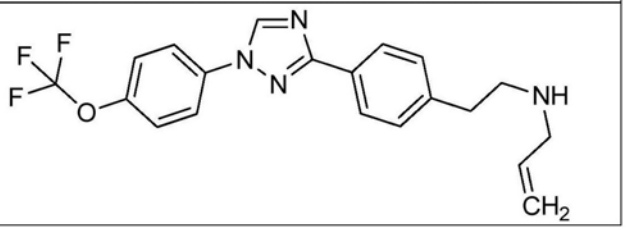
[1891]

编号	制备	结构
CB2	实施例 8	

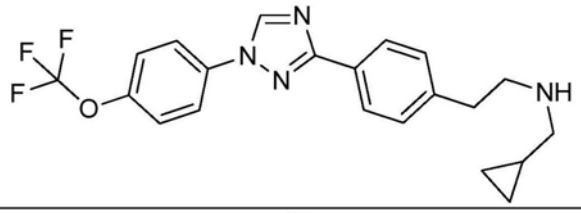
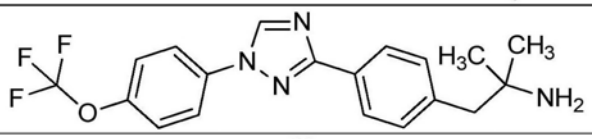
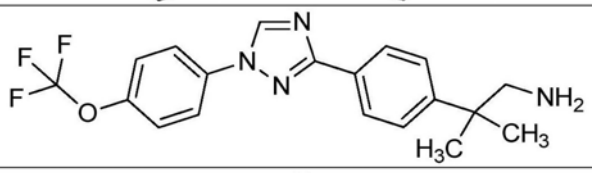
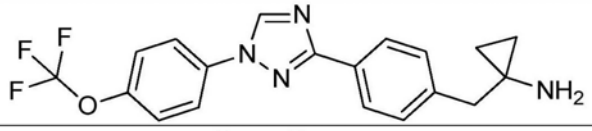
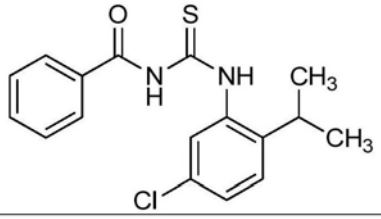
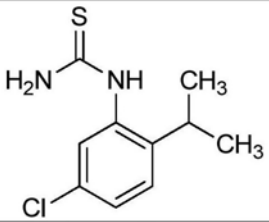
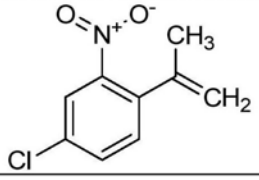
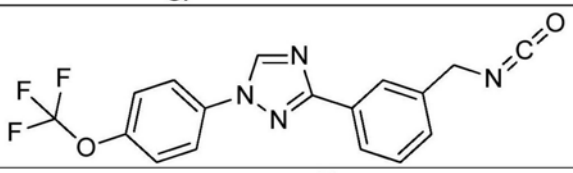
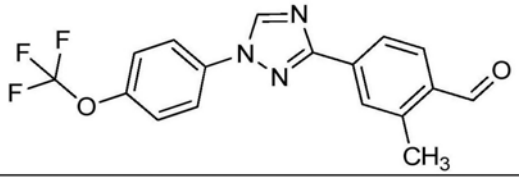
[1892]

CB3	**实施例 8**	
CB7	**实施例 9**	
CB8	**实施例 9**	
CB9	**实施例 9**	
CB10	**实施例 10**	
CB11	**实施例 10**	
CB12	**实施例 13**	
CB13	**实施例 13**	

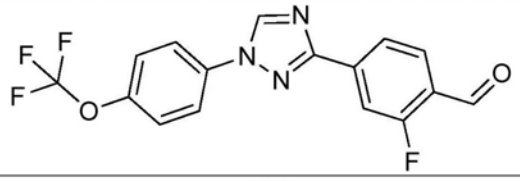
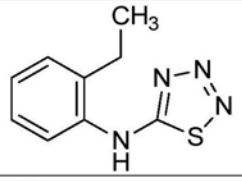
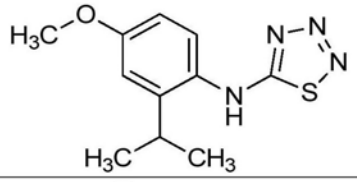
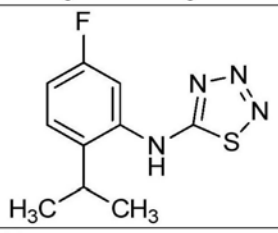
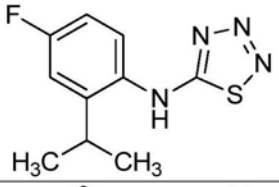
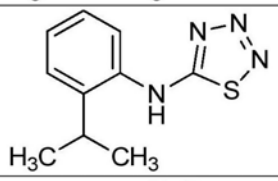
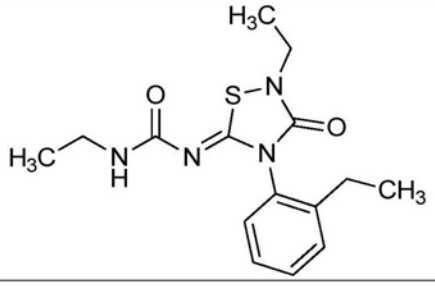
[1893]

CB14	**实施例 13**	
CB15	**实施例 30**	
CB16	**实施例 30**	
CB17	**实施例 30**	
CB18	**实施例 31**	
CB19	**实施例 31**	
CB23	**实施例 51**	
CB24	**实施例 58**	
CB25	**实施例 58**	
CB26	**实施例 58**	

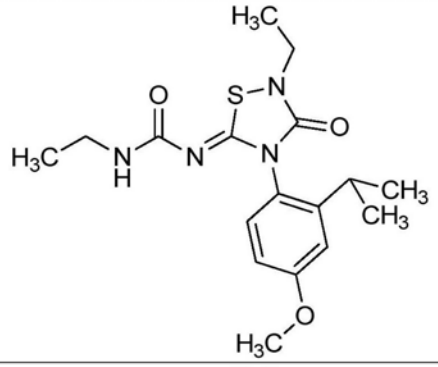
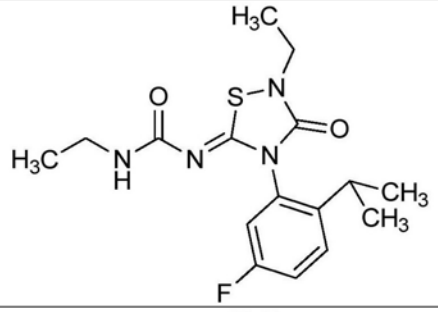
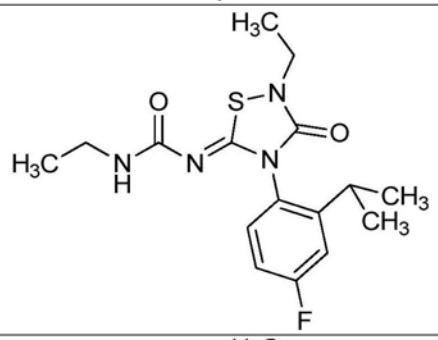
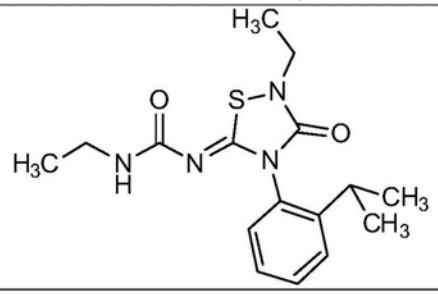
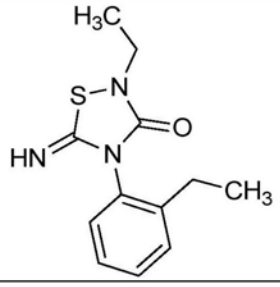
[1894]

CB27	**实施例 58**	
CB28	**实施例 66**	
CB29	**实施例 66**	
CB30	**实施例 66**	
CB31	**实施例 68**	
CB32	**实施例 69**	
CB33	**实施例 70**	
CB34	**实施例 74**	
CB35	**实施例 86**	

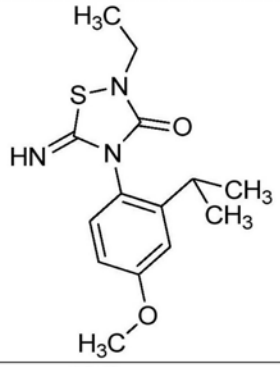
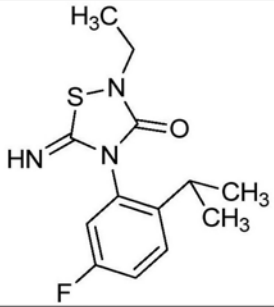
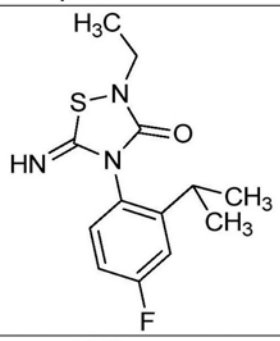
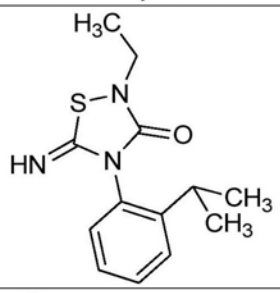
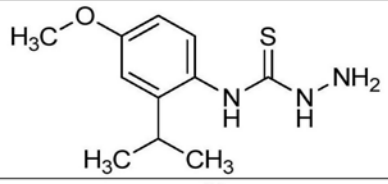
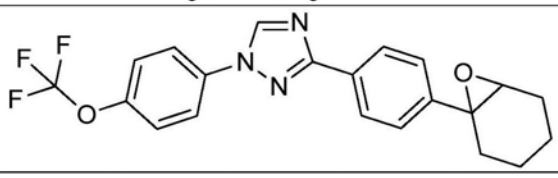
[1895]

CB36	**实施例 86**	
CB37	**实施例 87**	
CB38	**实施例 87**	
CB39	**实施例 87**	
CB40	**实施例 87**	
CB41	**实施例 87**	
CB42	**实施例 88**	

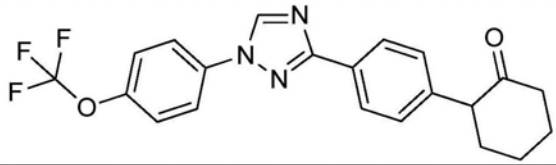
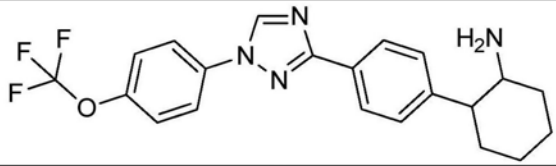
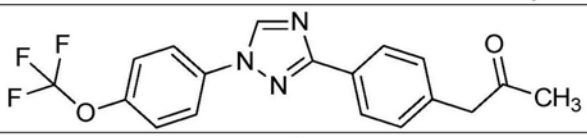
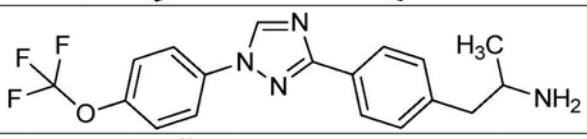
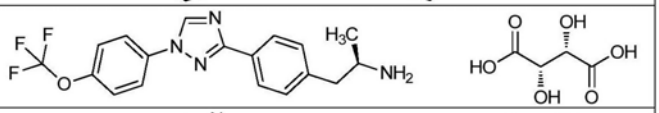
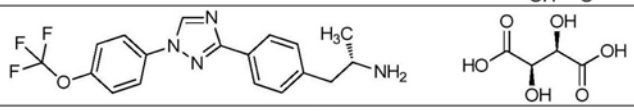
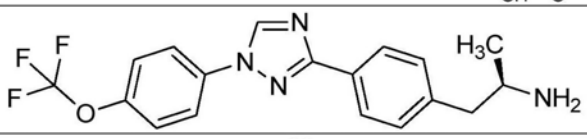
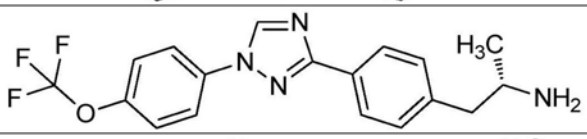
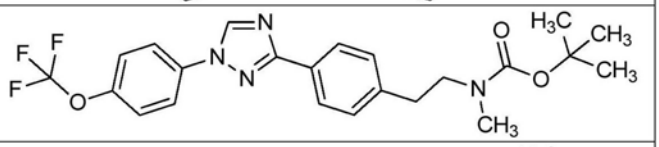
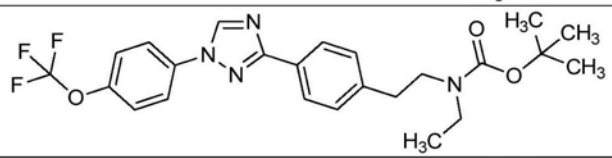
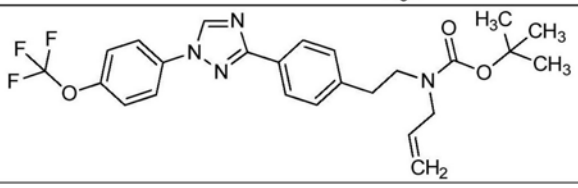
[1896]

CB43	**实施例 88**	
CB44	**实施例 88**	
CB45	**实施例 88**	
CB46	**实施例 88**	
CB47	**实施例 89**	

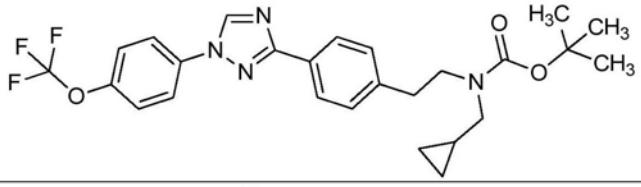
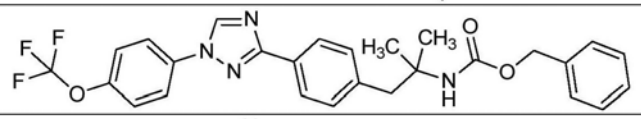
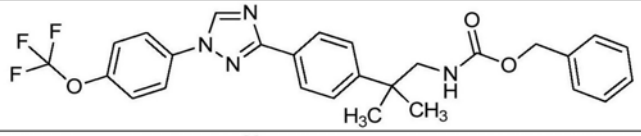
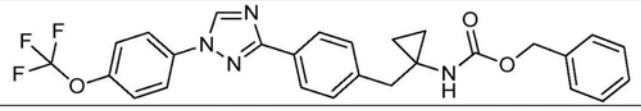
[1897]

CB48	**实施例 89**	
CB49	**实施例 89**	
CB50	**实施例 89**	
CB51	**实施例 89**	
CB53	**实施例 91**	
CB54	**实施例 92**	

[1898]

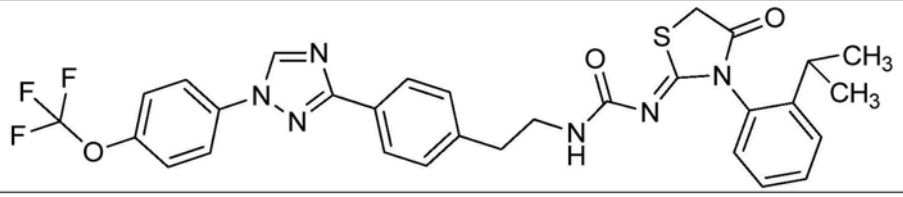
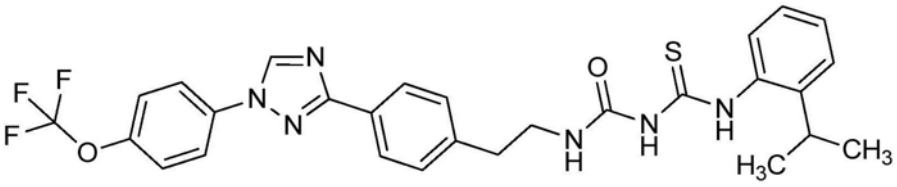
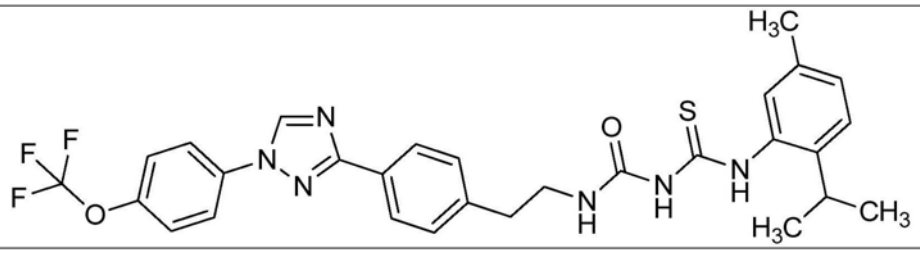
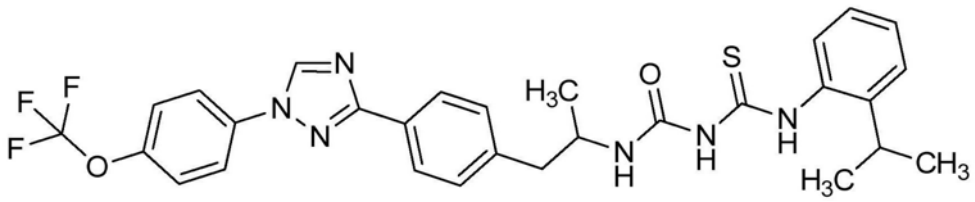
CB55	实施例 93	
CB56	实施例 94	
CB57	实施例 97	
CB58	实施例 98	
CB59	实施例 99	
CB60	实施例 99	
CB61	实施例 100	
CB62	实施例 100	
CB63	实施例 102	
CB64	实施例 102	
CB65	实施例 102	

[1899]

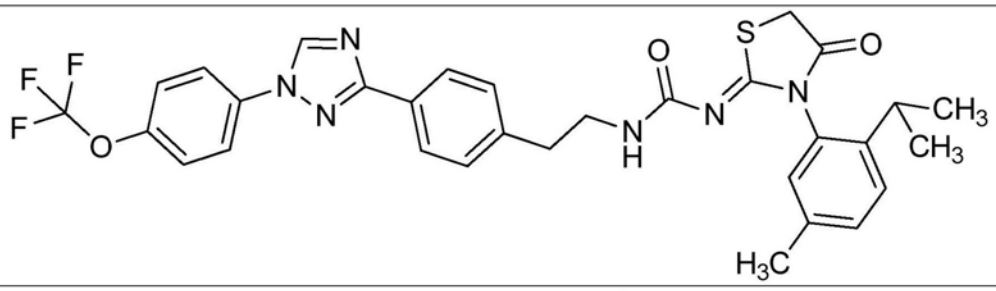
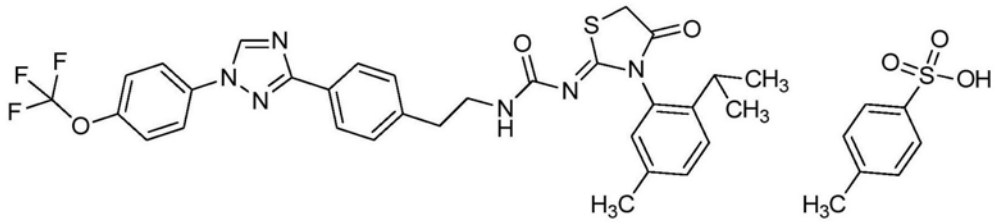
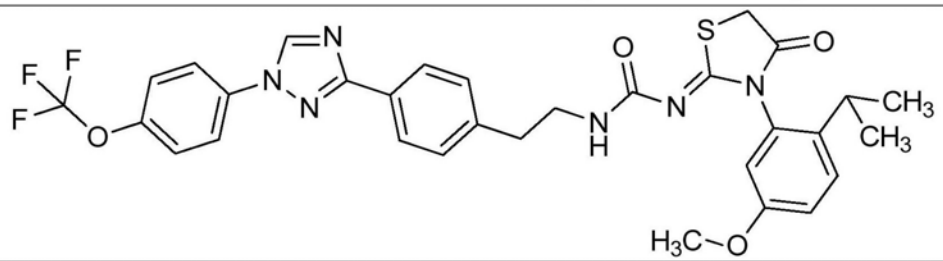
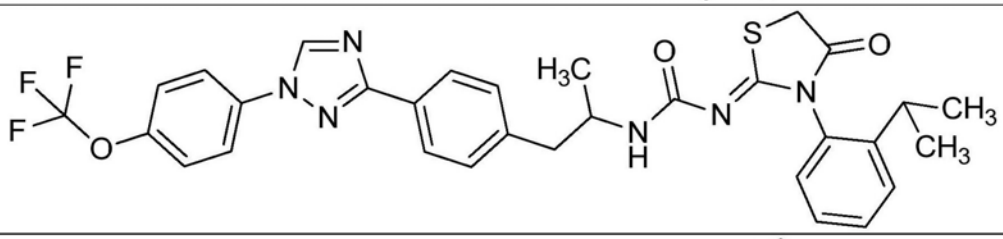
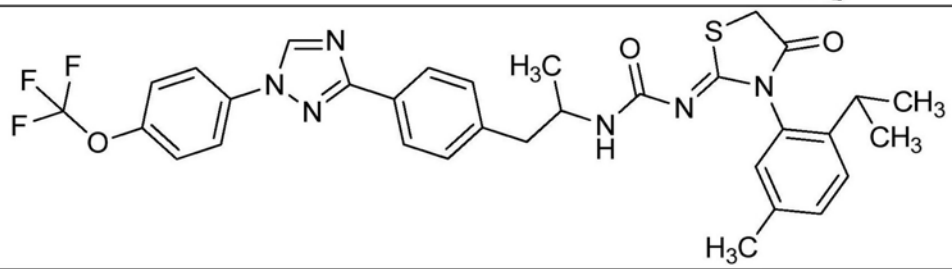
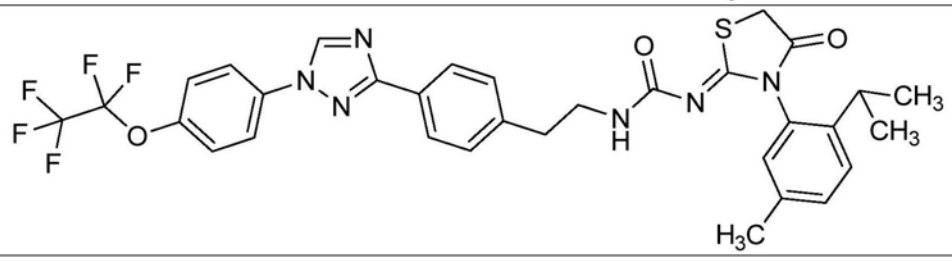
CB66	实施例 102	
CB67	实施例 103	
CB68	实施例 103	
CB69	实施例 103	

[1900] 表2A:式一分子的结构

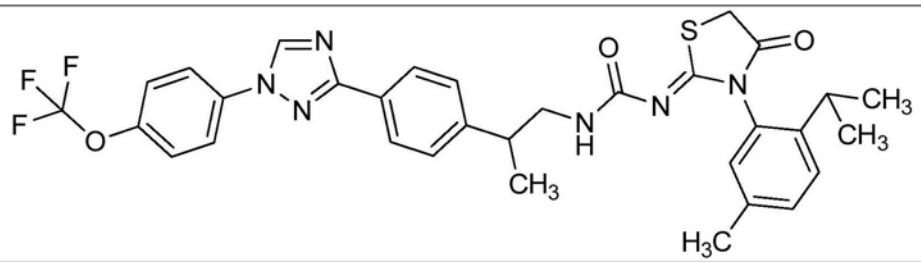
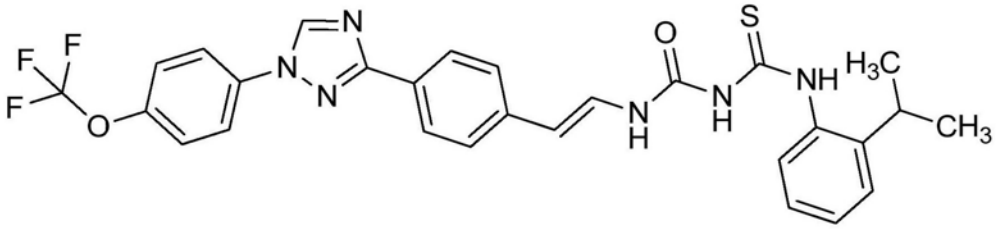
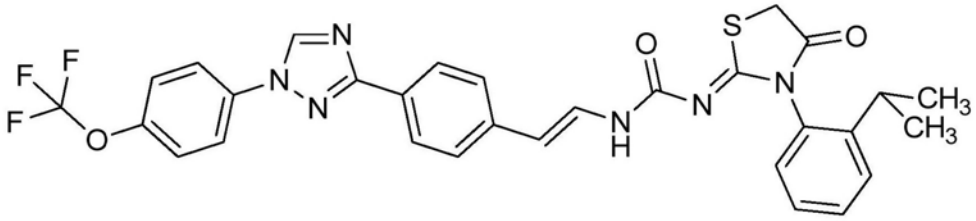
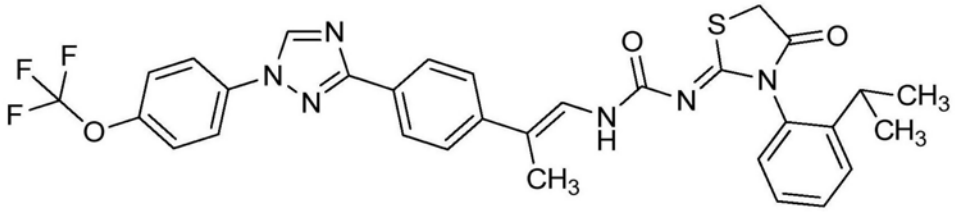
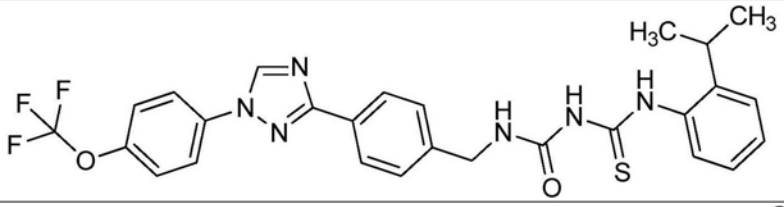
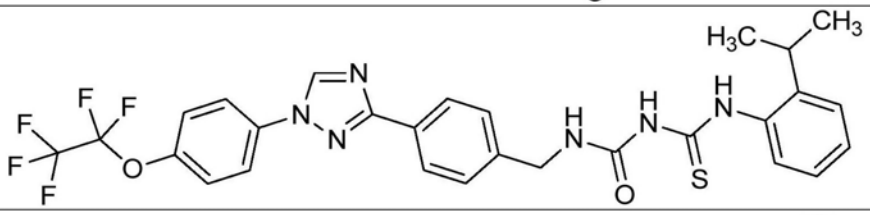
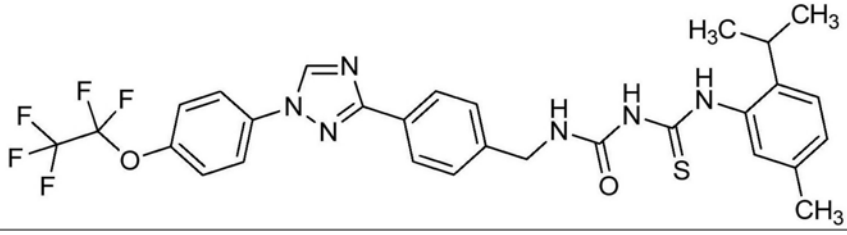
[1901]

编号	结构
F1	
F2	
F3	
F4	

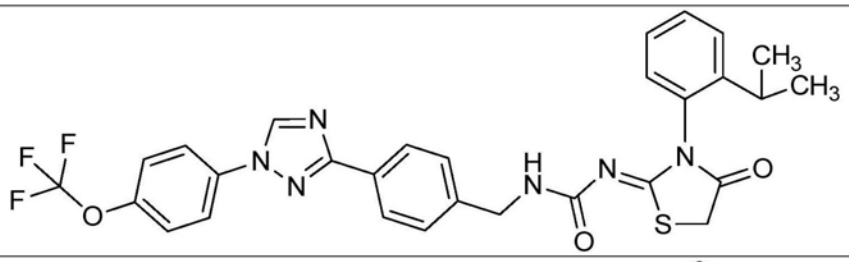
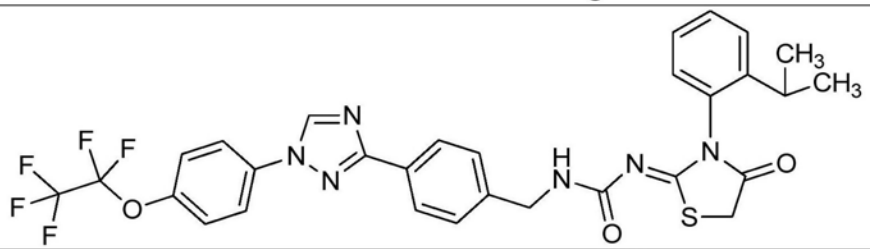
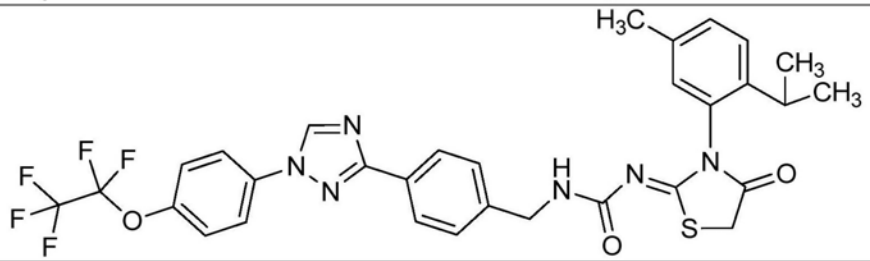
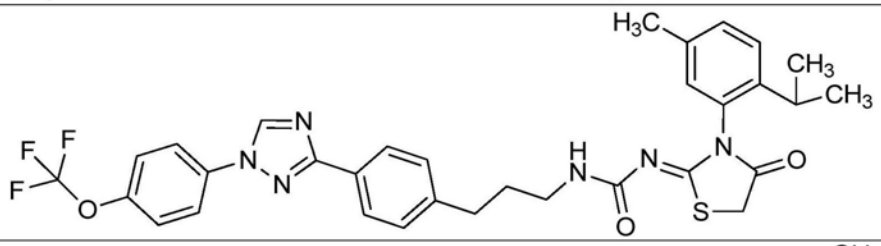
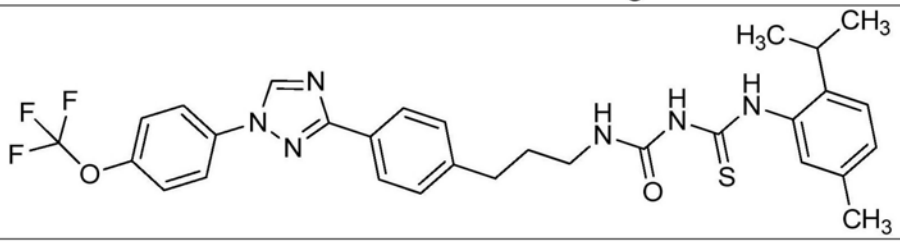
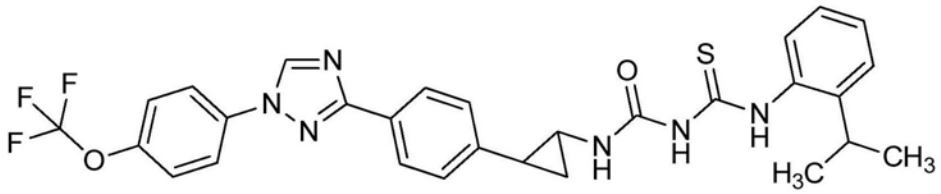
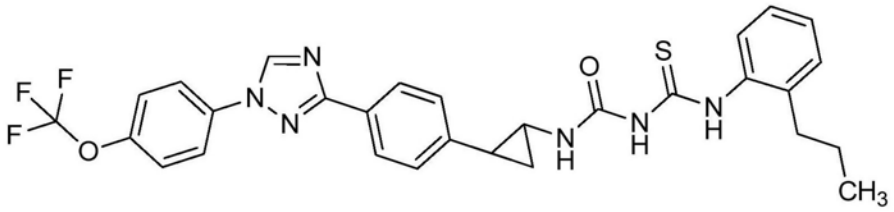
[1902]

F5	
F5A	
F6	
F7	
F8	
F9	

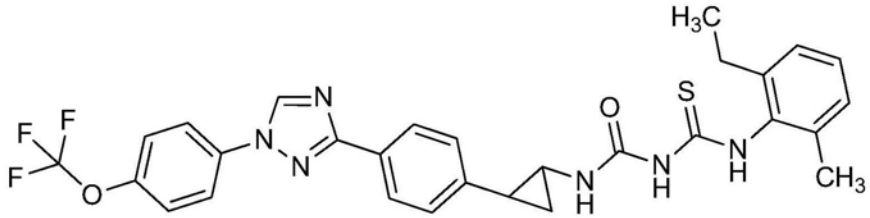
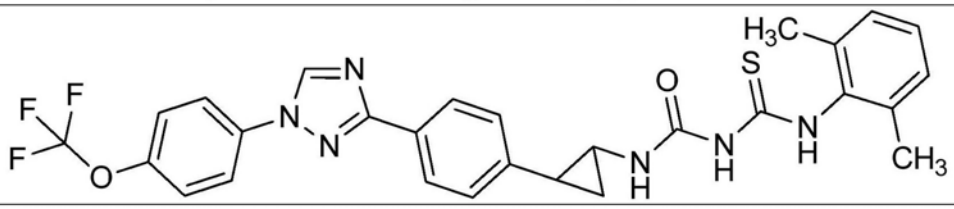
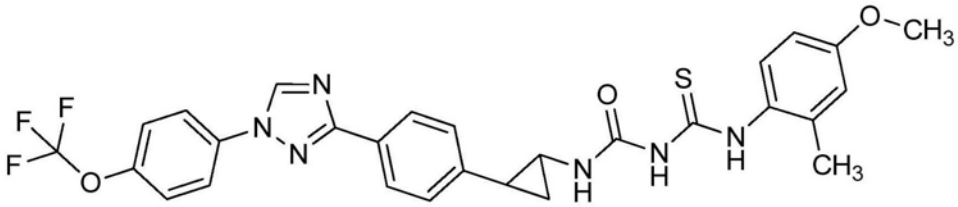
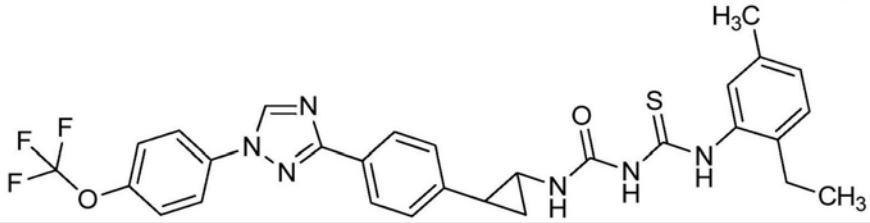
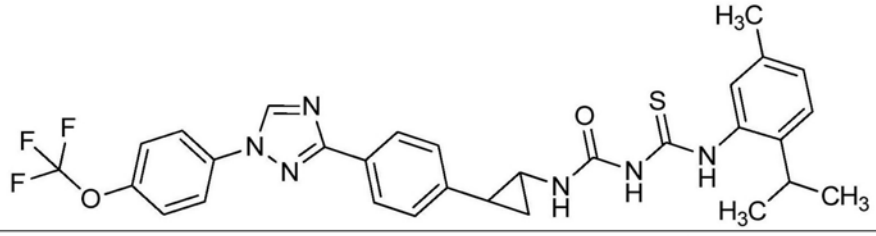
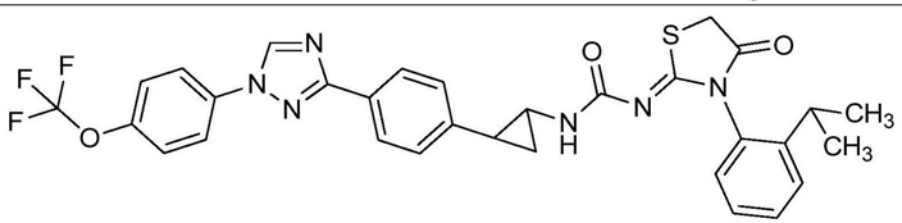
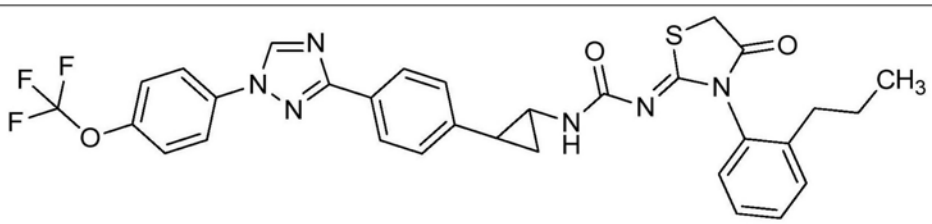
[1903]

F10	
F11	
F12	
F13	
F14	
F15	
F16	

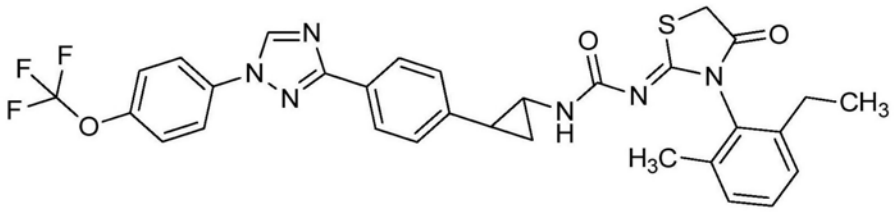
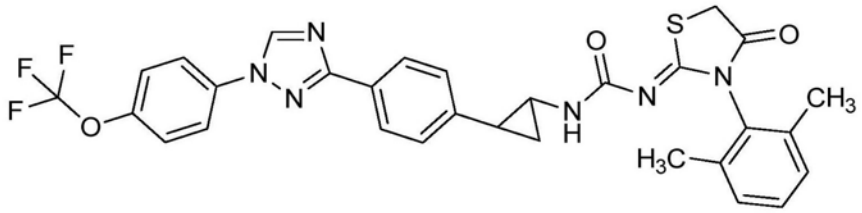
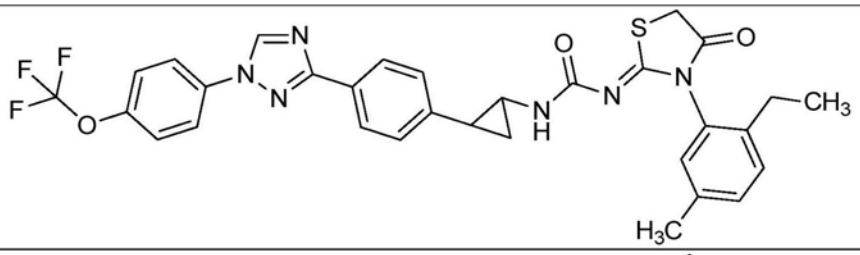
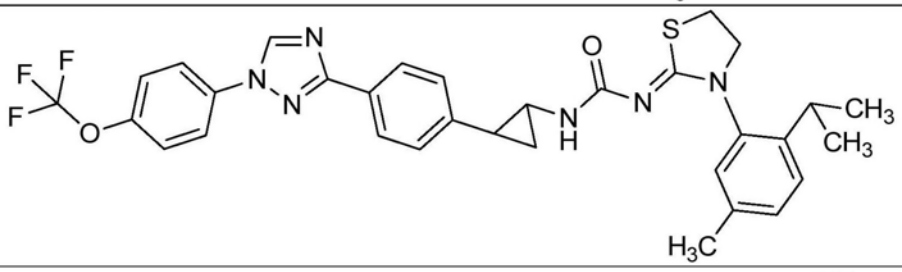
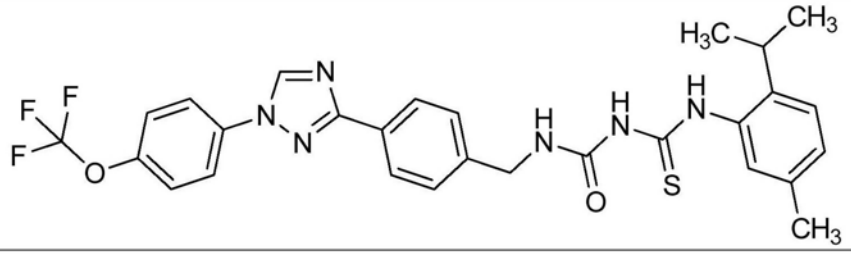
[1904]

F17	
F18	
F19	
F20	
F21	
F22	
F23	

[1905]

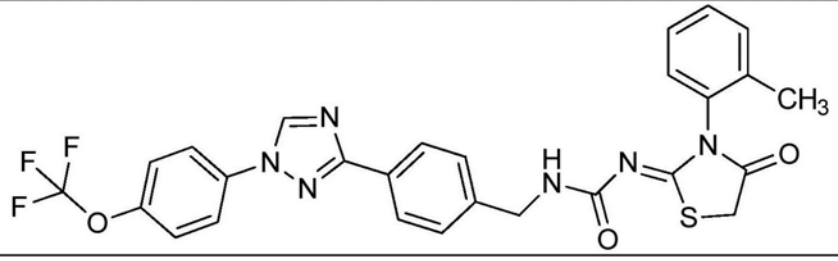
F24	
F25	
F26	
F27	
F28	
F29	
F30	

[1906]

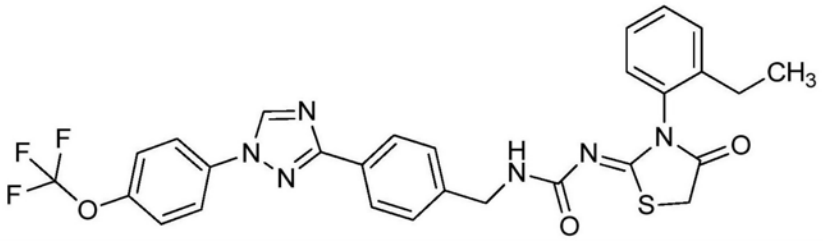
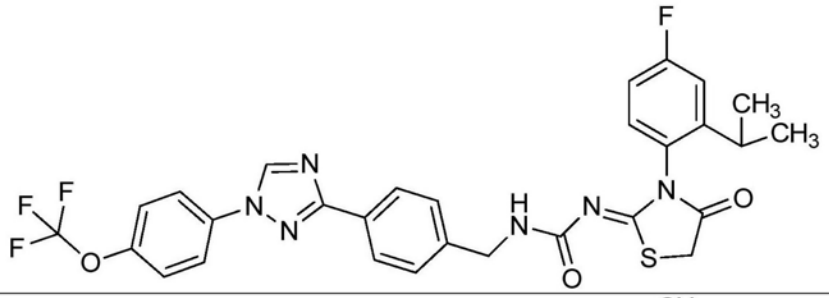
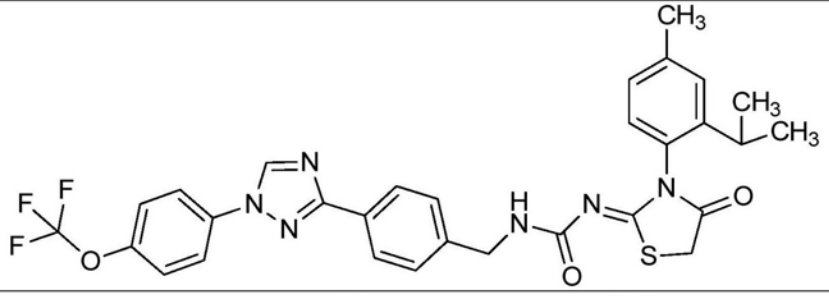
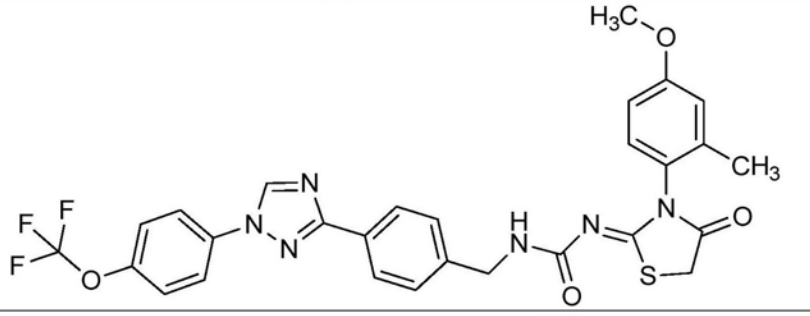
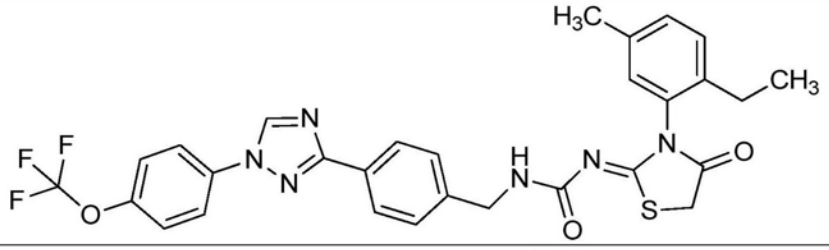
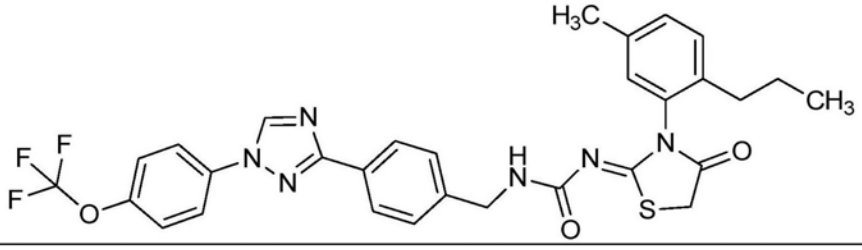
F31	
F32	
F33	
F34	
F35	

[1907] 表2B:对于式一分子的来自表P-I和P-Ⅱ的示例性预知结构(P)

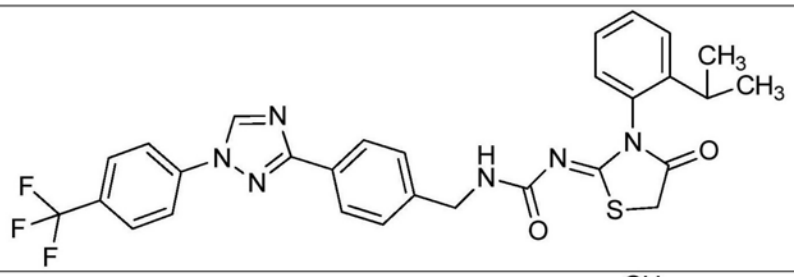
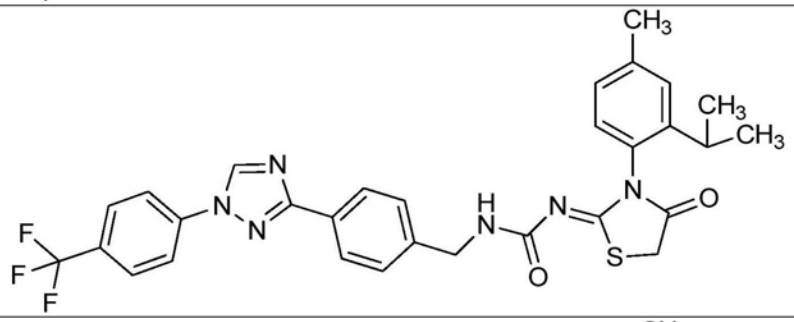
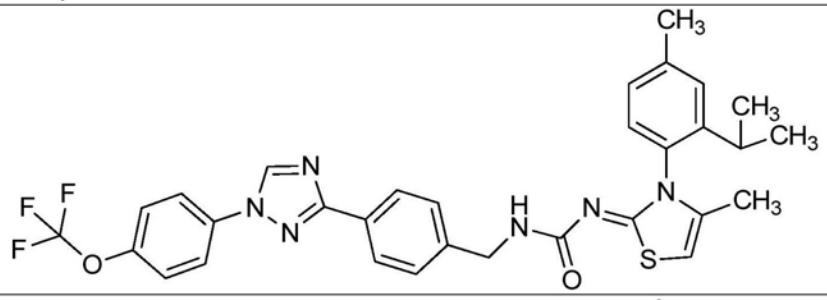
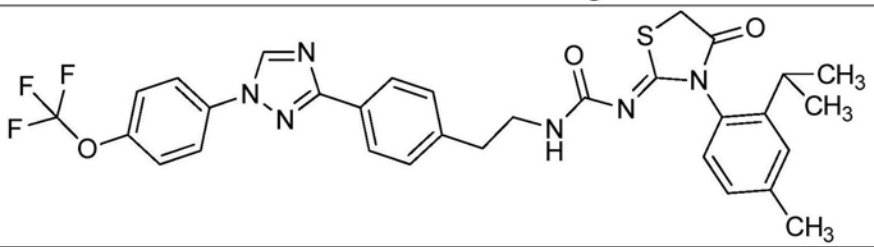
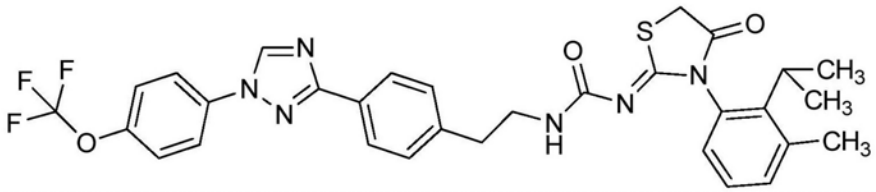
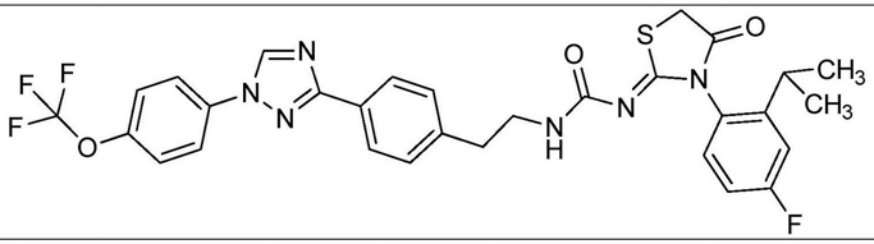
[1908]

编号	结构
P1	

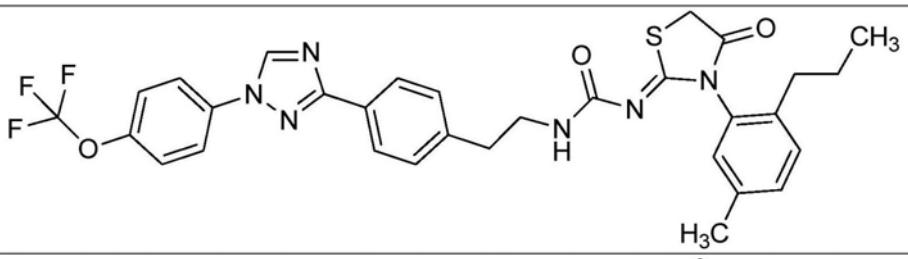
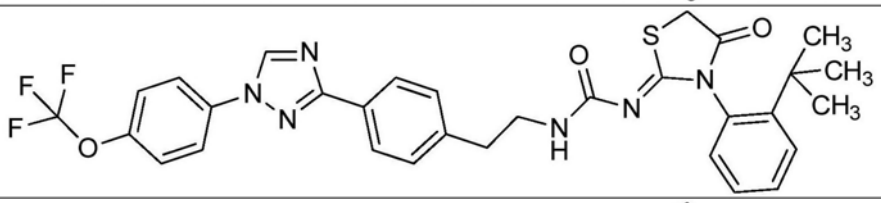
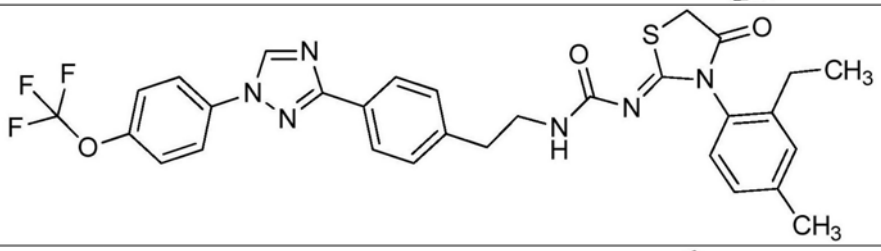
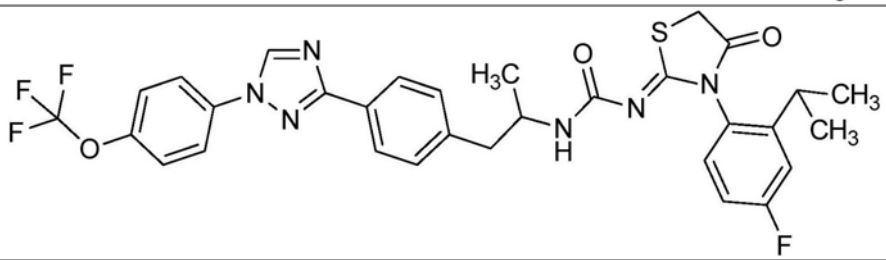
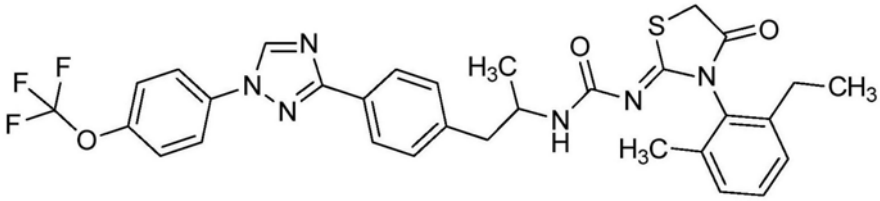
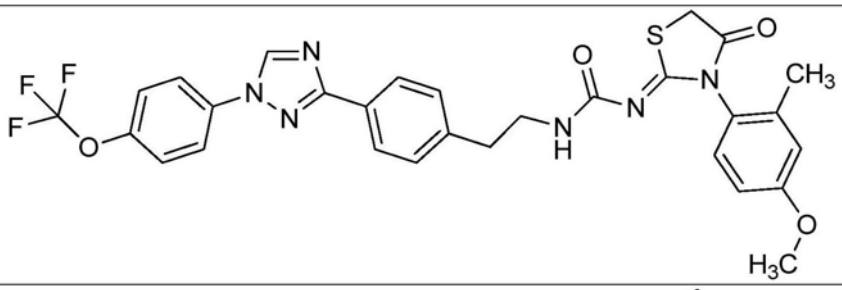
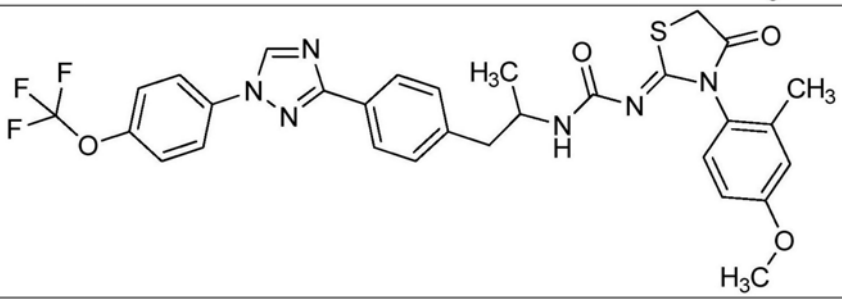
[1909]

P2，P532	
P3，P1172	
P5	
P6	
P7	
P8，P852	

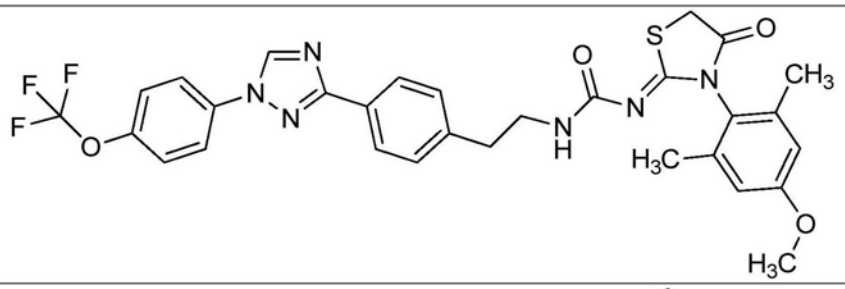
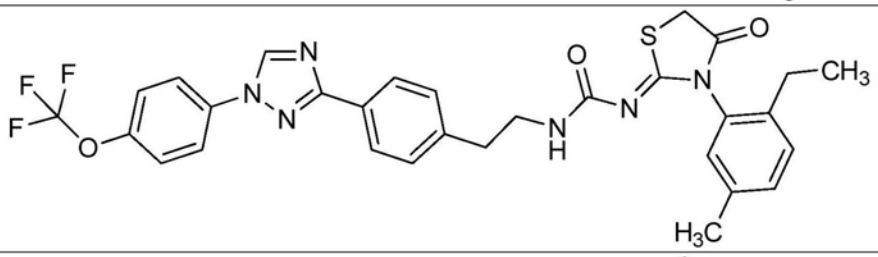
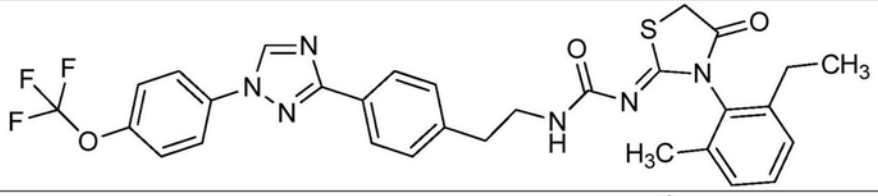
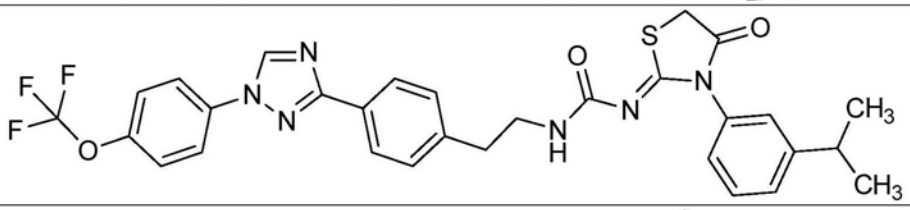
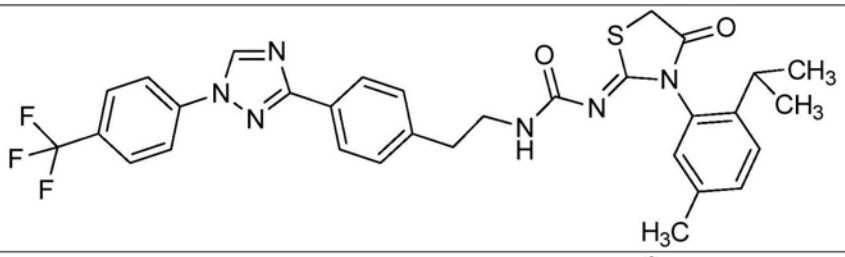
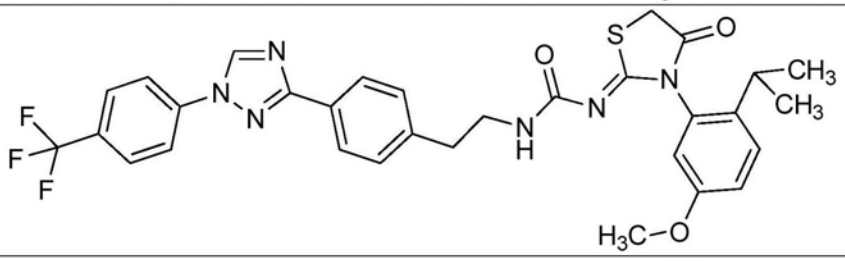
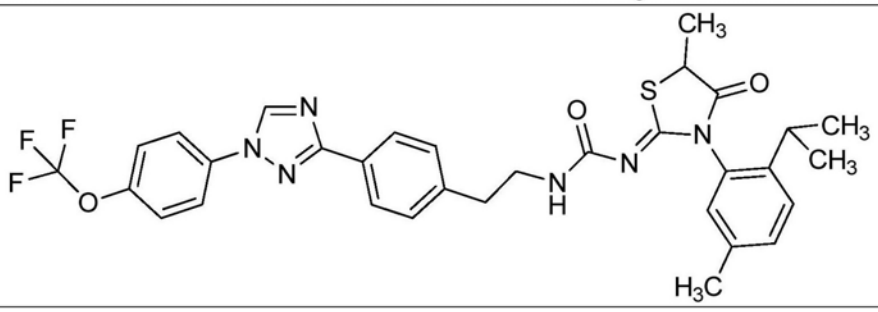
[1910]

P14	
P15	
P20	
P26	
P27	
P28	

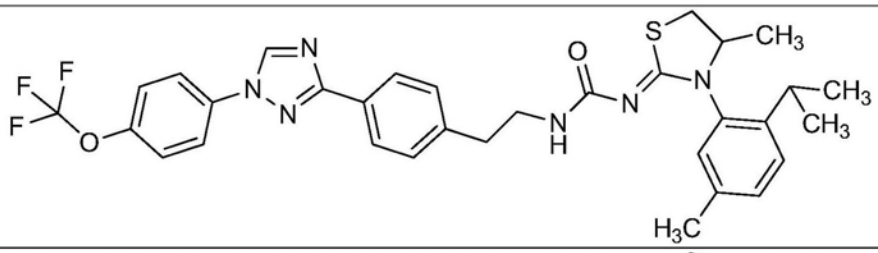
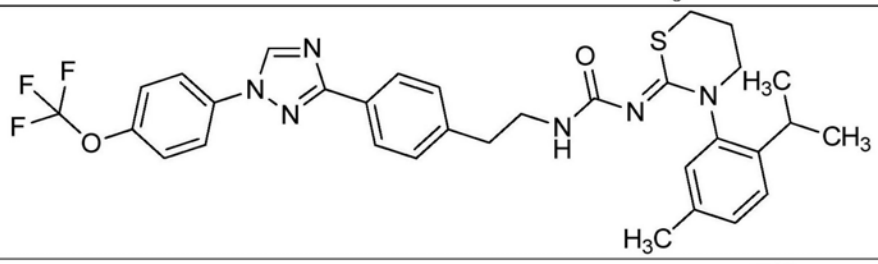
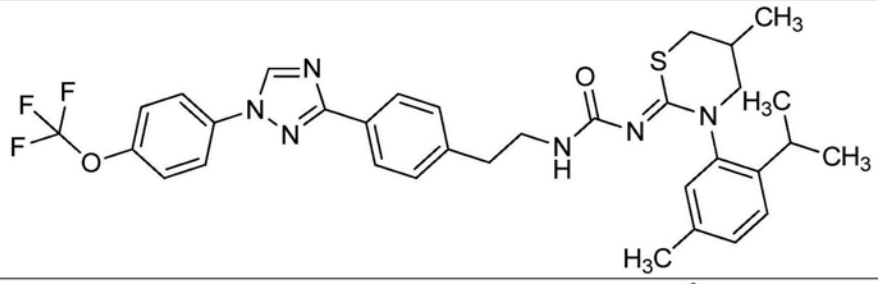
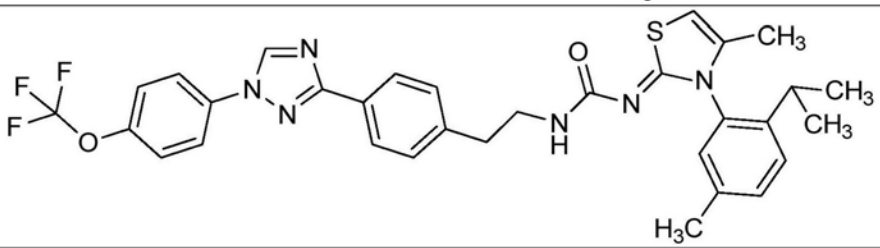
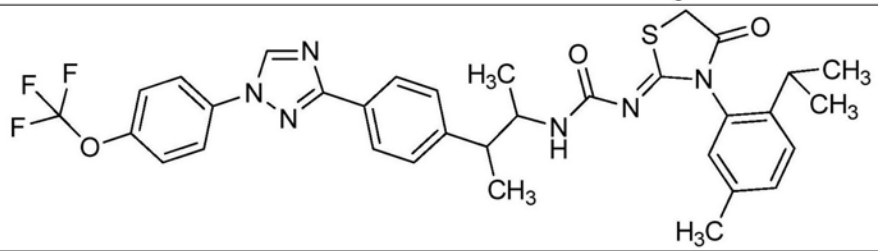
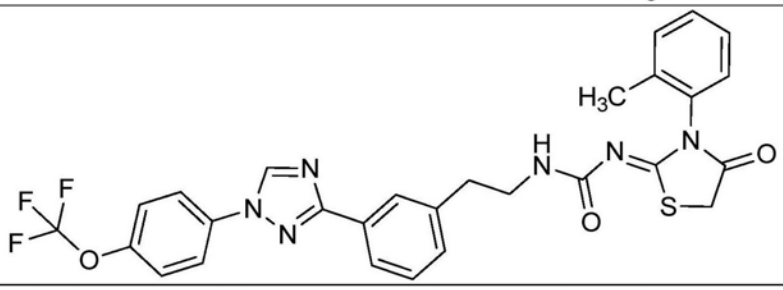
[1911]

P29	
P30	
P31	
P33	
P42	
P44	
P45	

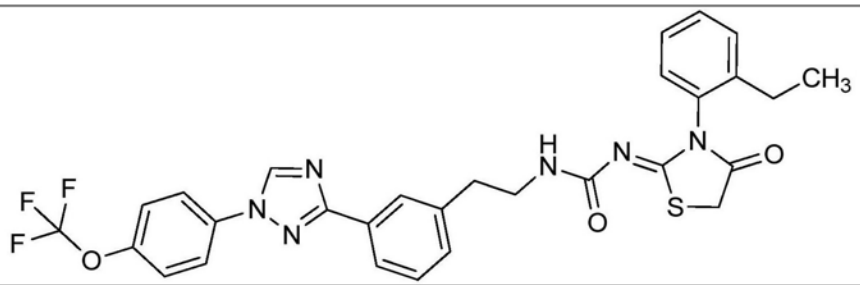
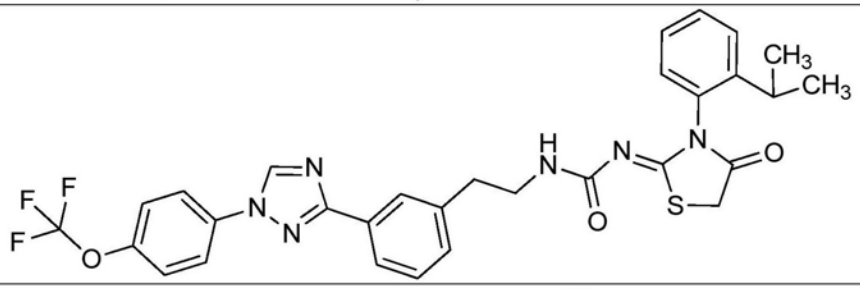
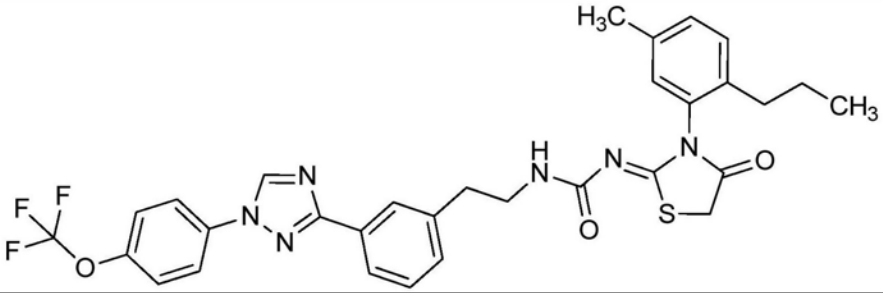
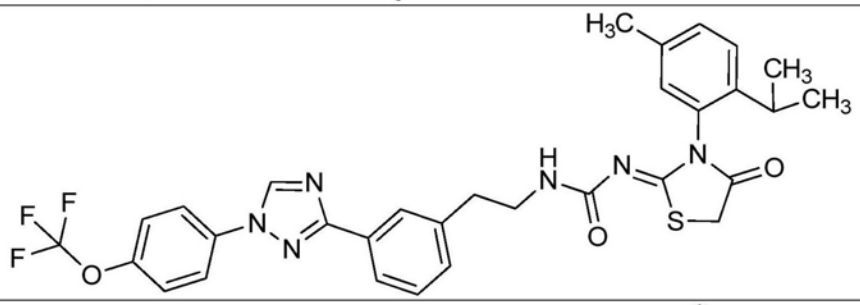
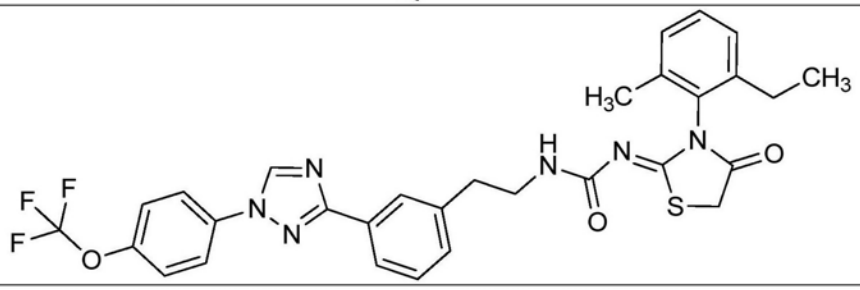
[1912]

P47	
P49	
P50	
P51	
P52	
P53	
P57	

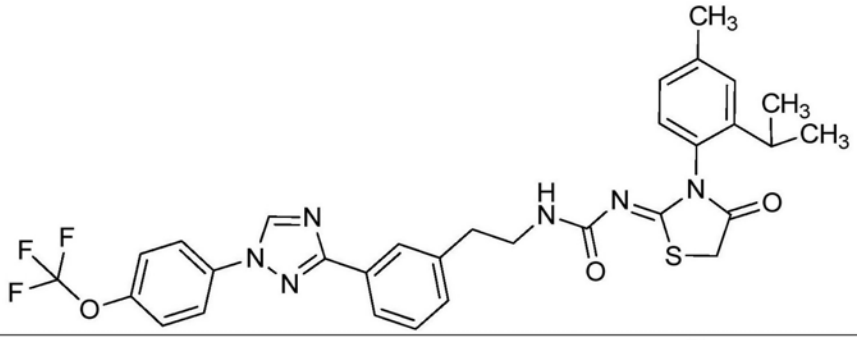
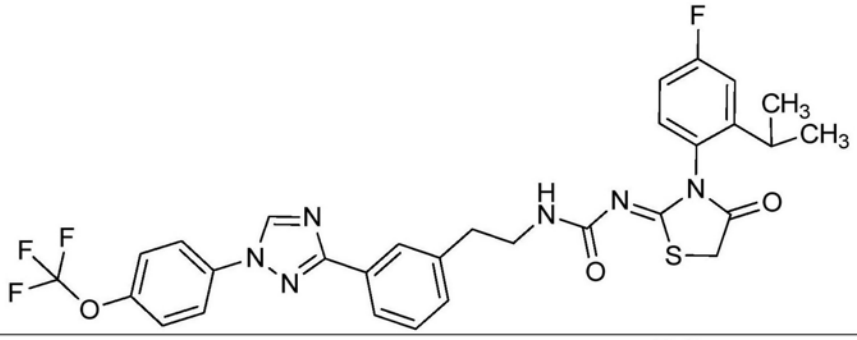
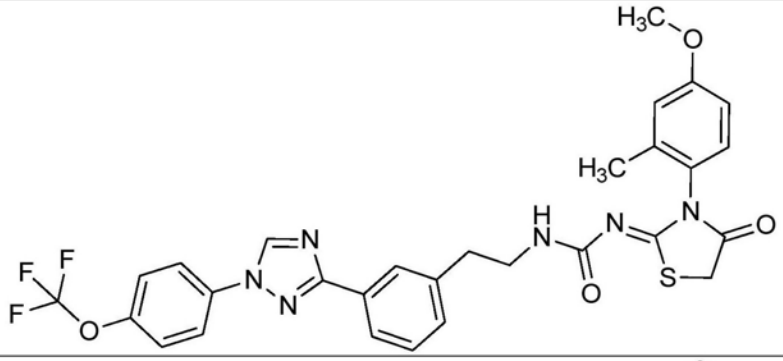
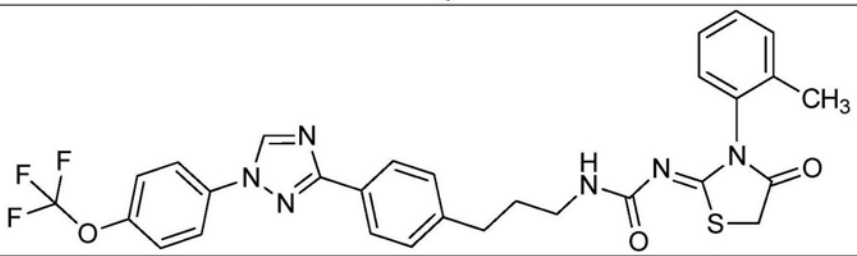
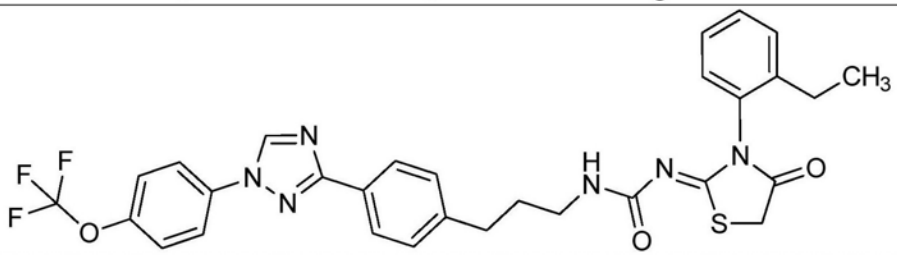
[1913]

P58	
P59	
P64	
P65	
P66，P353	
P74	

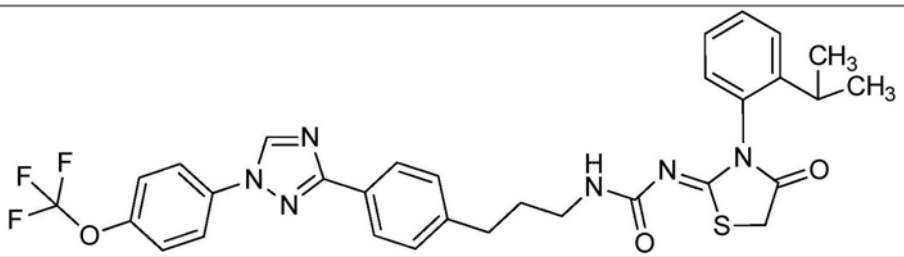
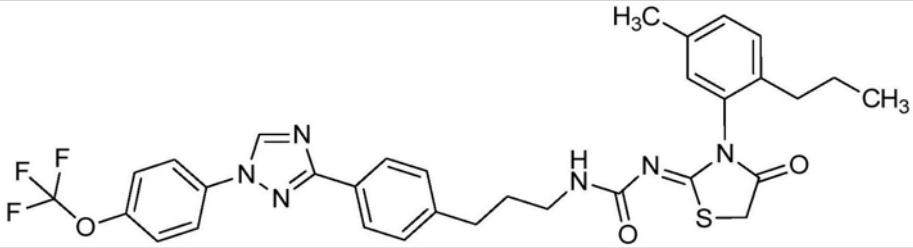
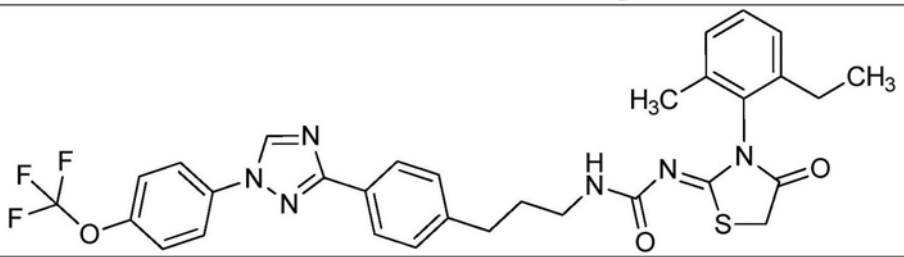
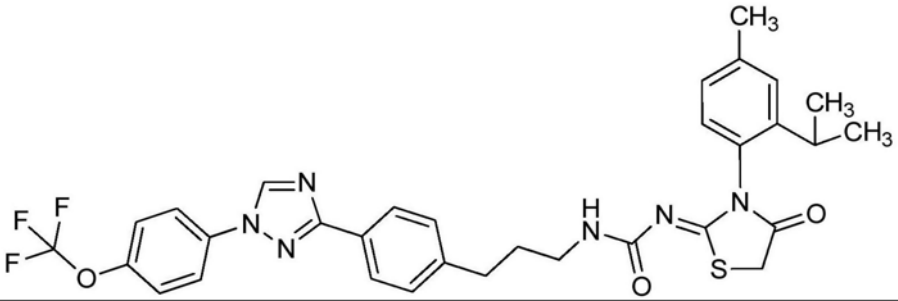
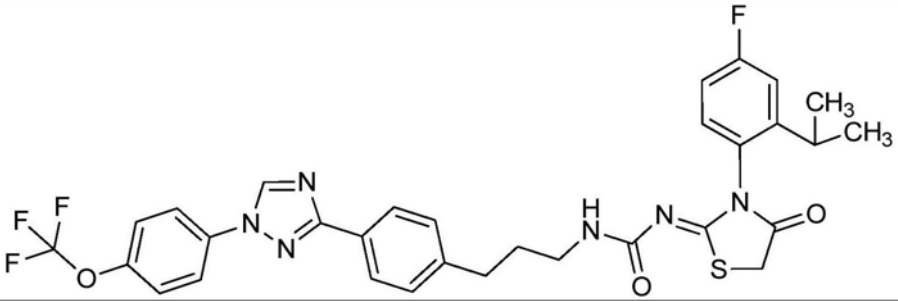
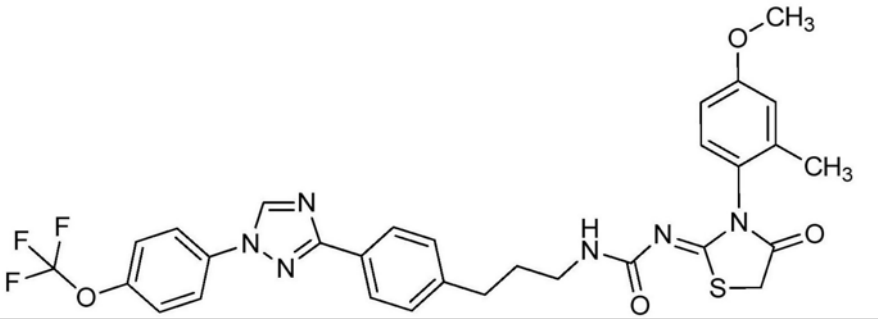
[1914]

P75	
P76	
P80	
P81	
P83	

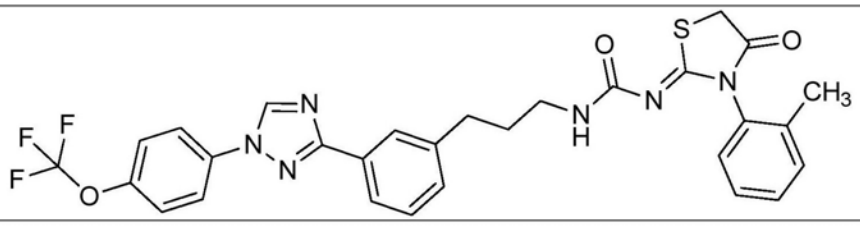
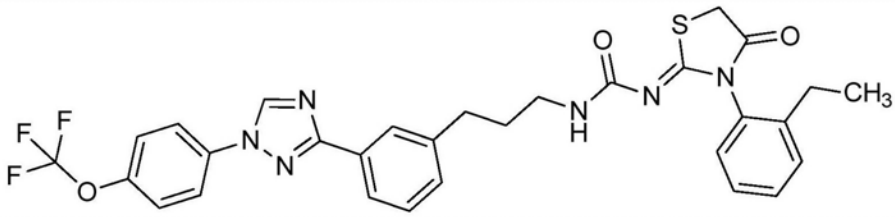
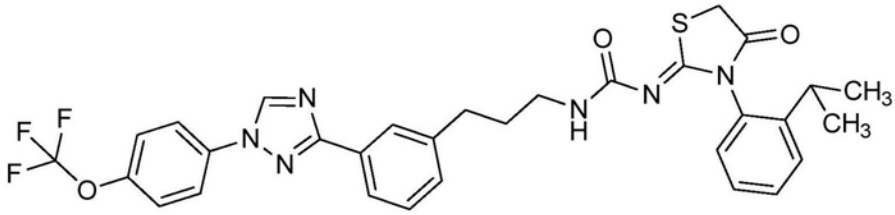
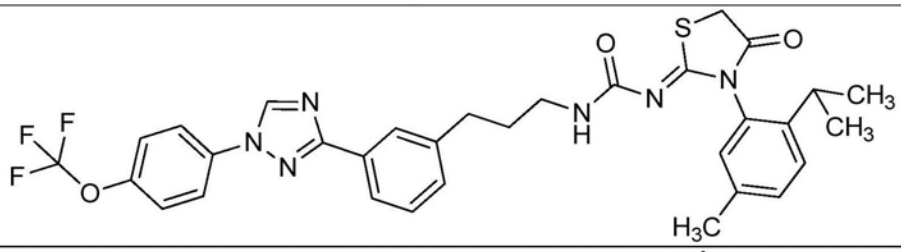
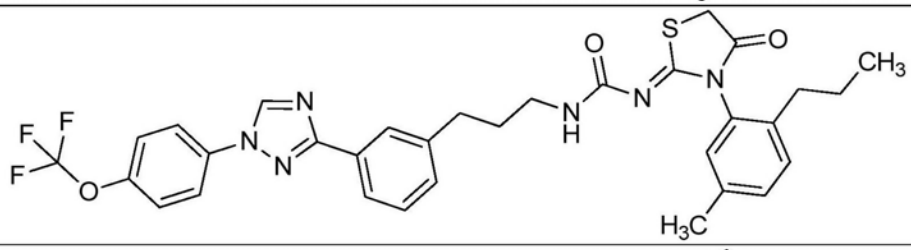
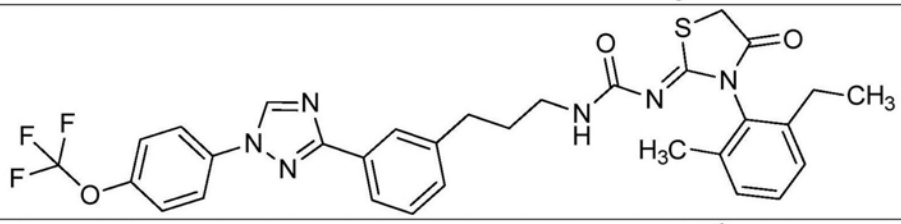
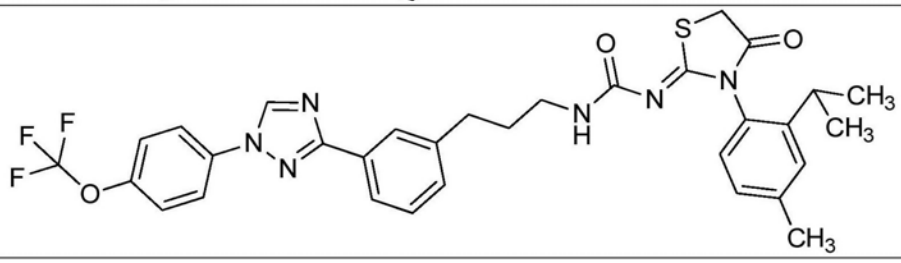
[1915]

P84	
P85	
P87	
P92	
P93，P510	

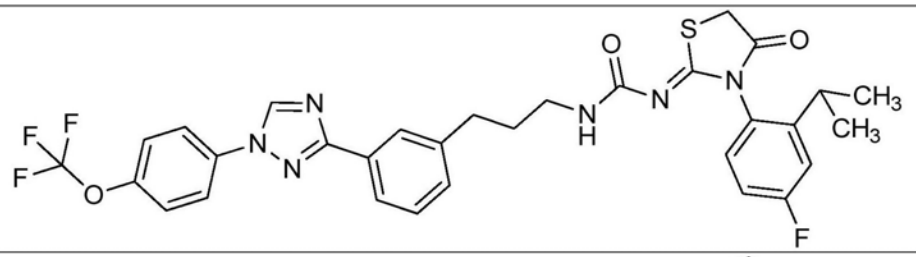
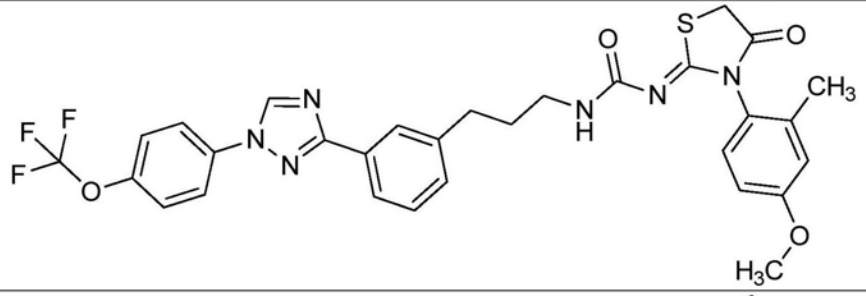
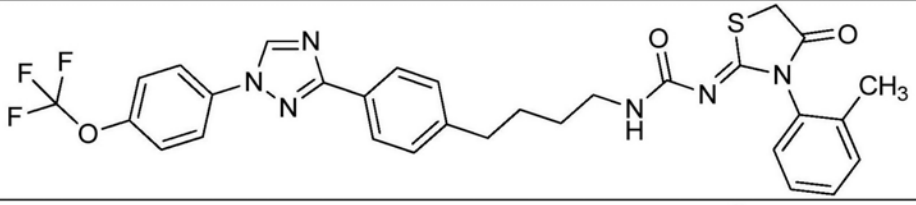
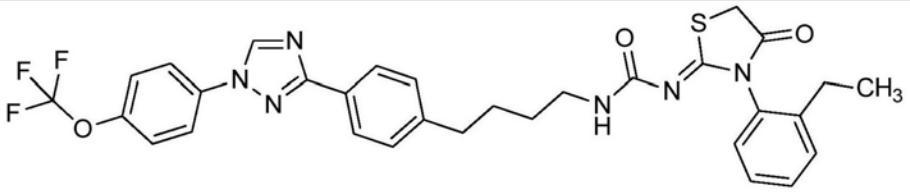
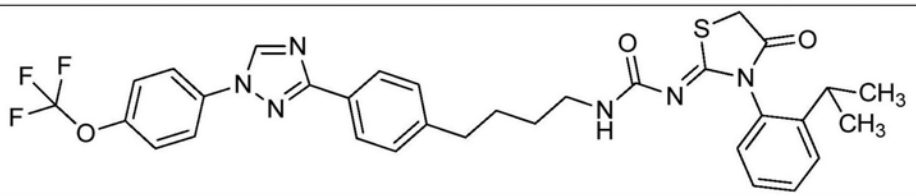
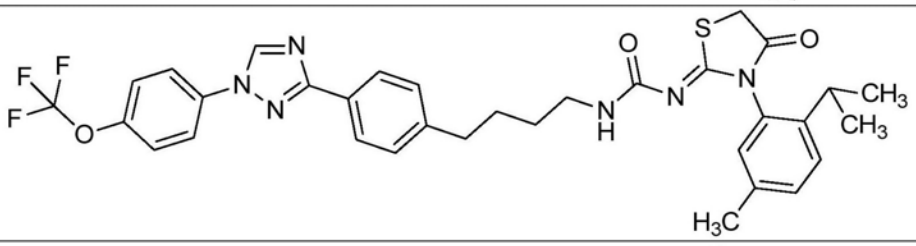
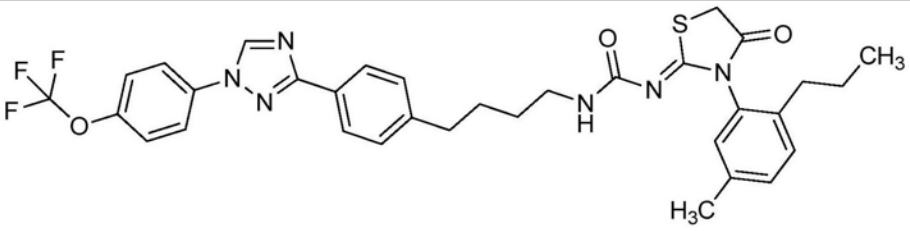
[1916]

P94，P197	
P99，P830	
P101	
P102	
P103，P1150	
P105	

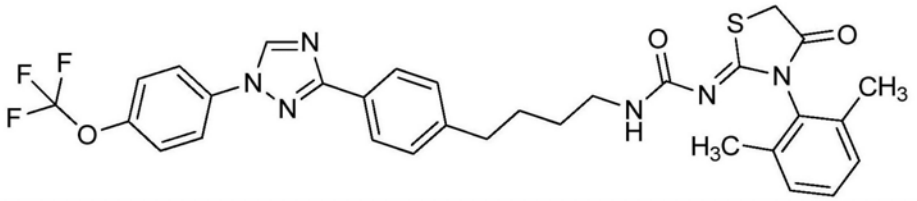
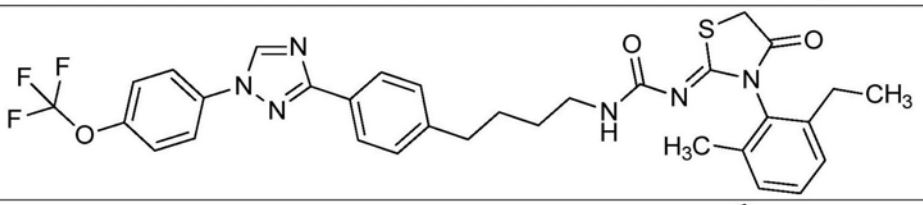
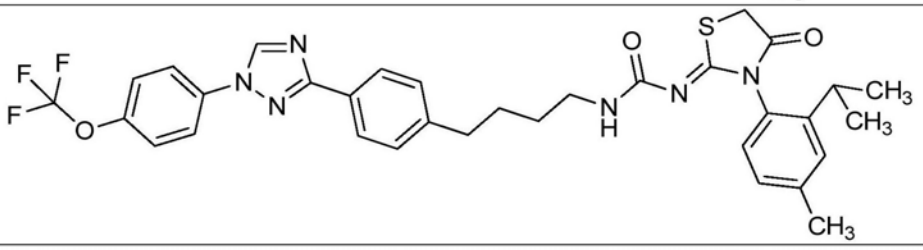
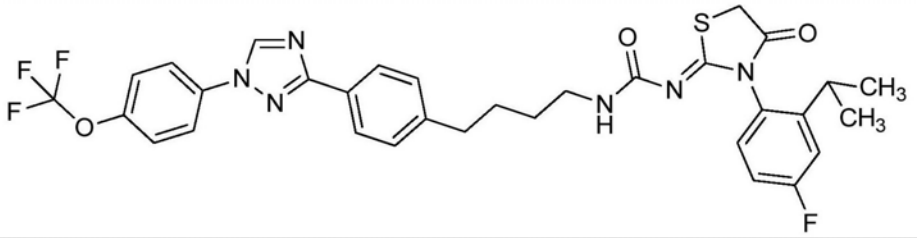
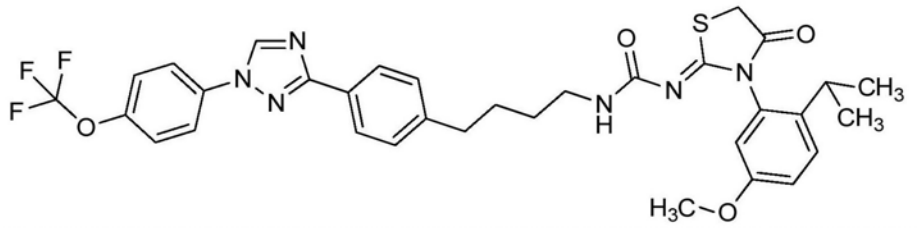
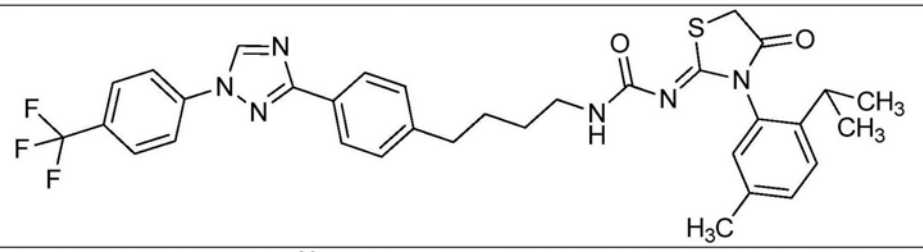
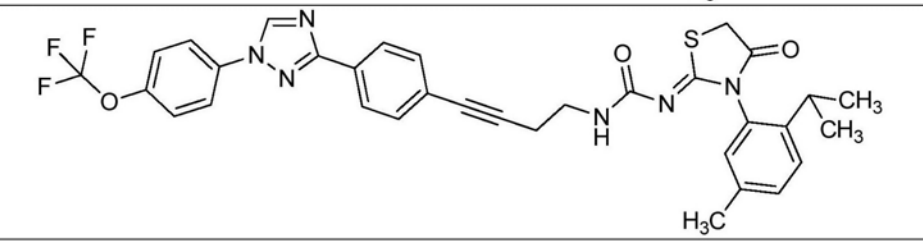
[1917]

P118	
P119	
P120	
P124	
P125	
P127	
P128	

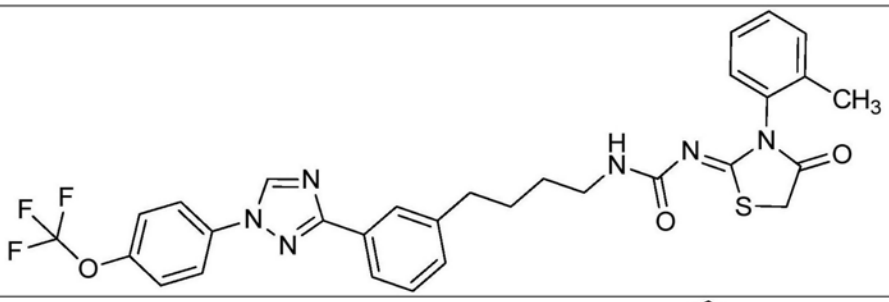
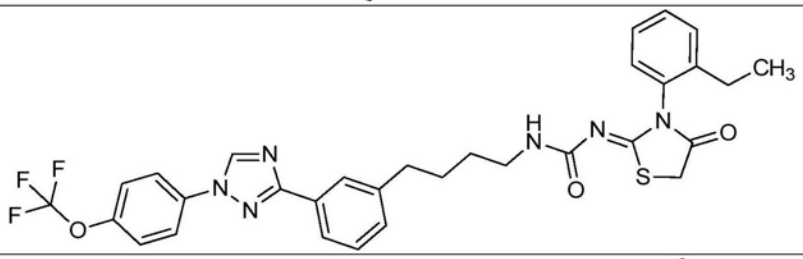
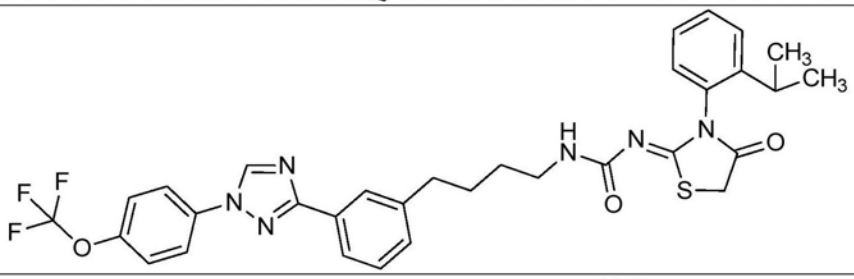
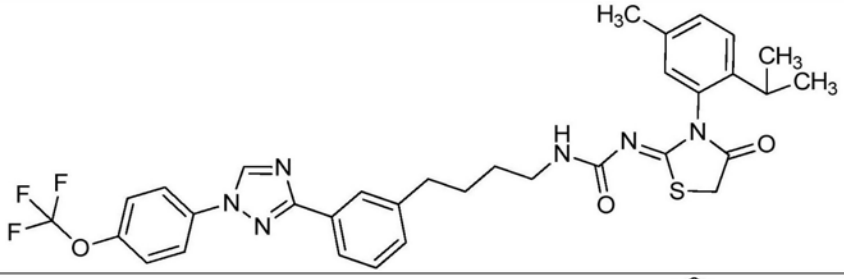
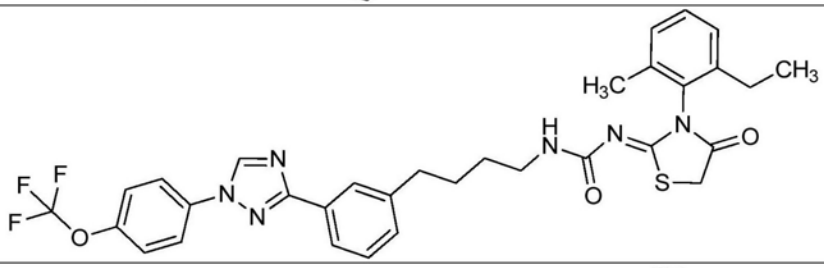
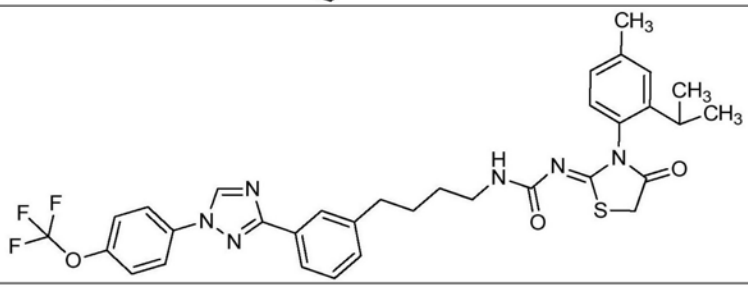
[1918]

P129	
P131	
P144	
P145, P522	
P146, P208	
P150, P363	
P151, P842	

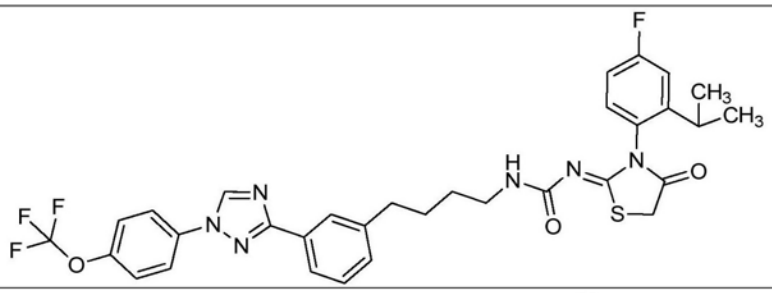
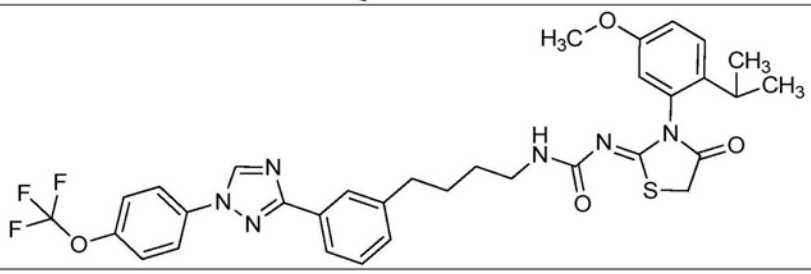
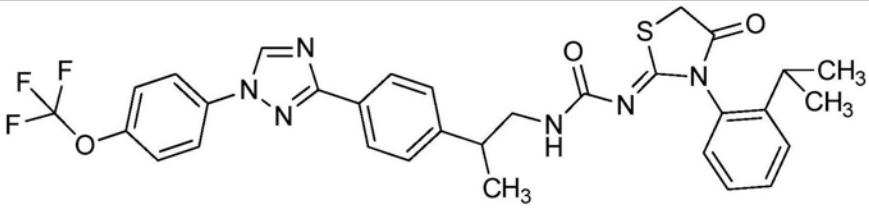
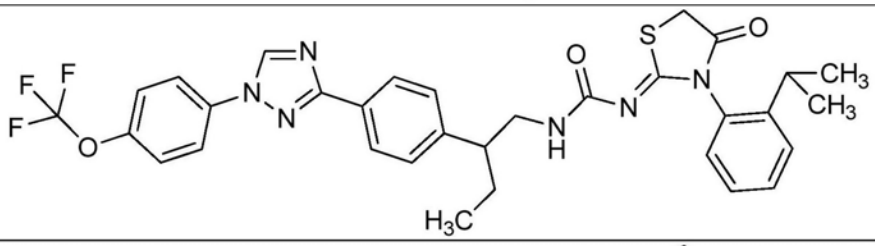
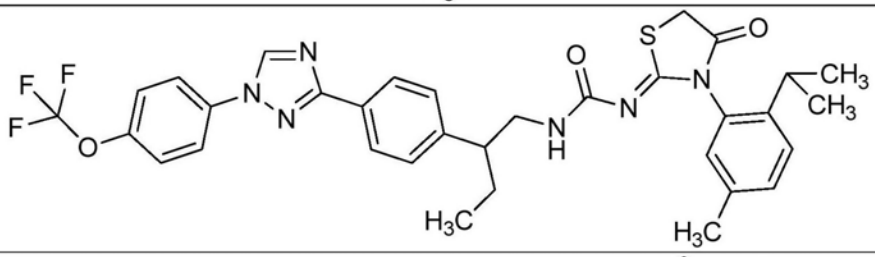
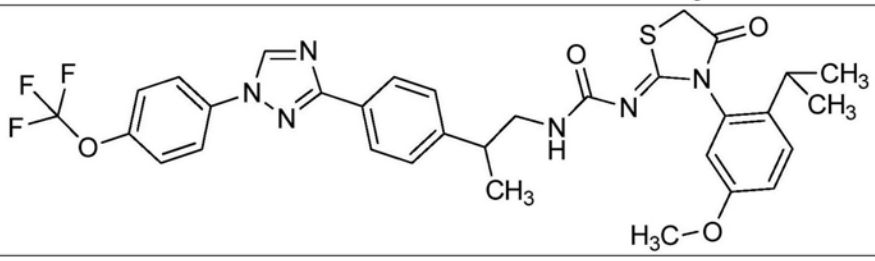
[1919]

P152，P1481	
P153	
P154	
P155，P1162	
P156，P682	
P159	
P160	

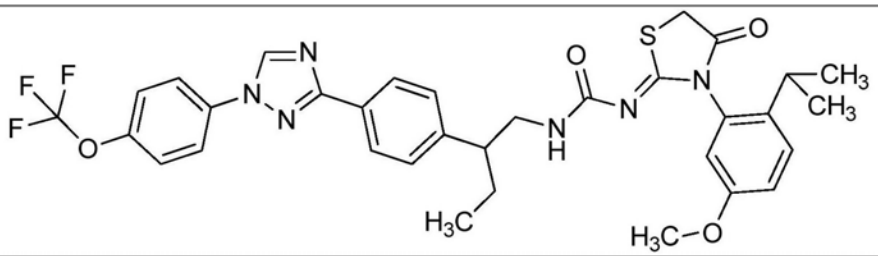
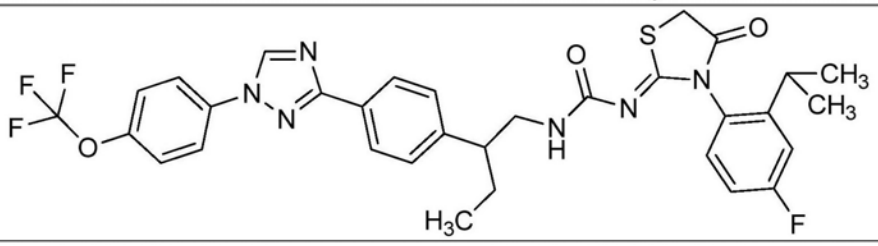
[1920]

P170	
P171	
P172	
P176	
P179	
P180	

[1921]

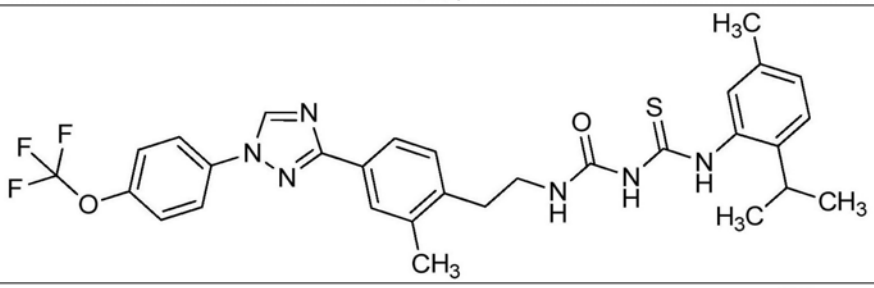
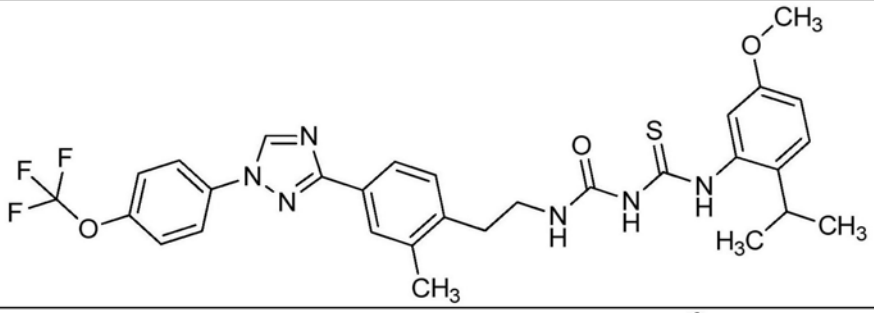
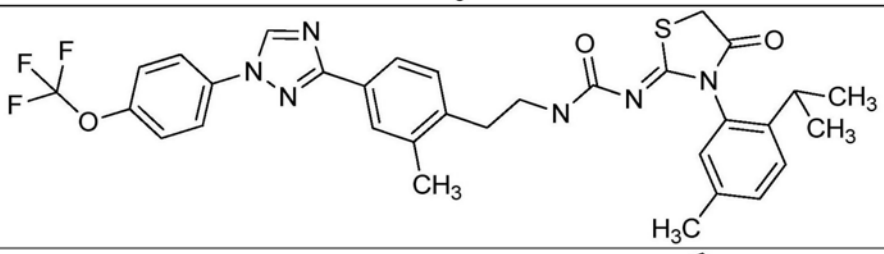
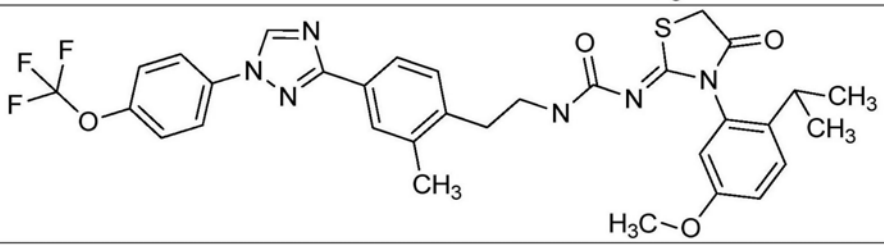
P181	
P182	
P205	
P209	
P364	
P679	

[1922]

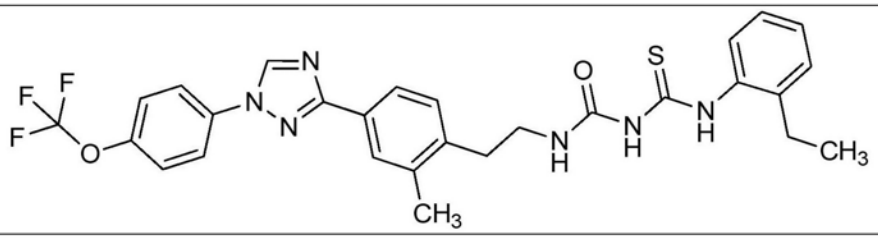
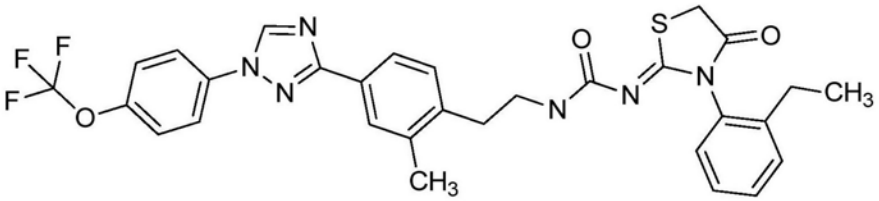
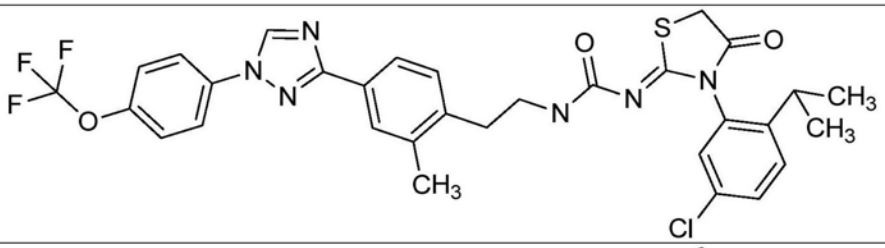
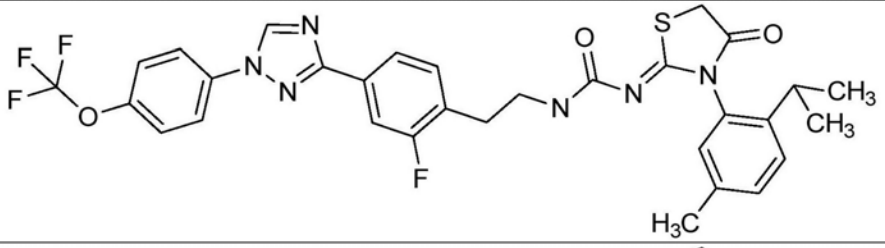
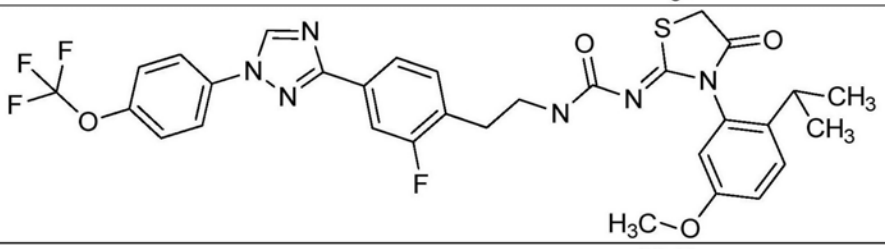
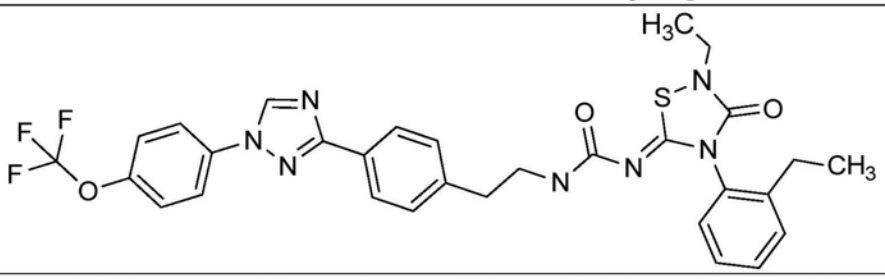
P683	
P1163	

[1923] 表2C:式一的另外的示例性分子(FB)

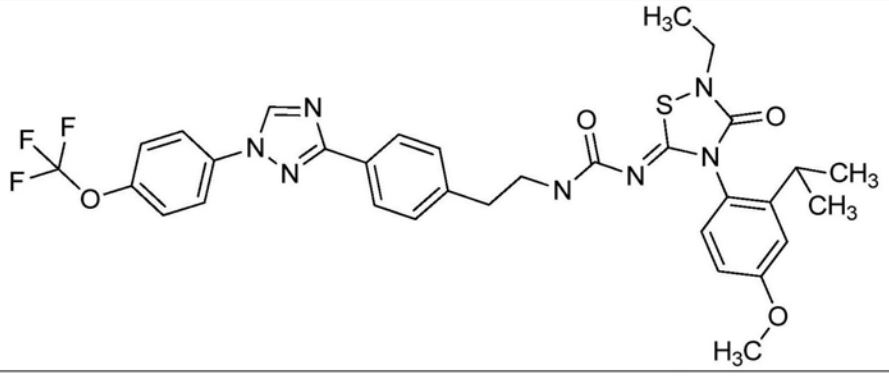
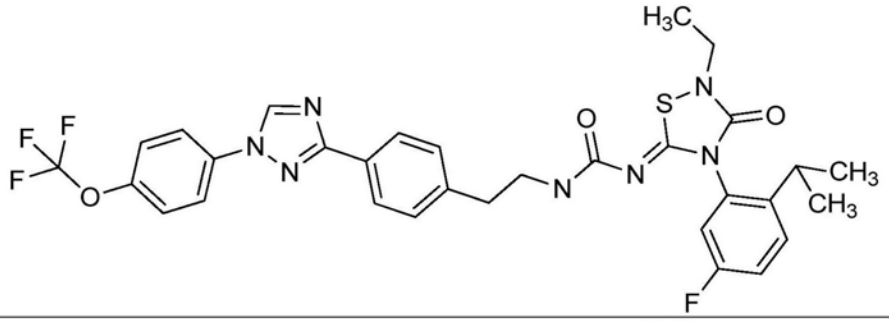
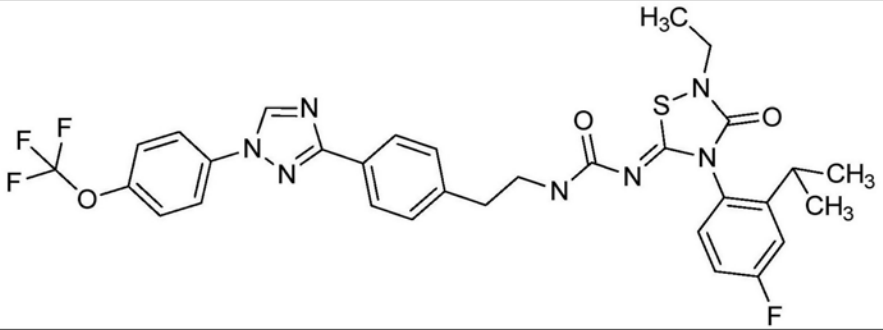
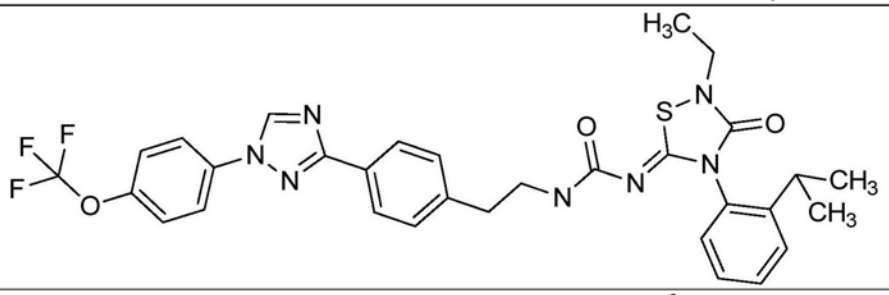
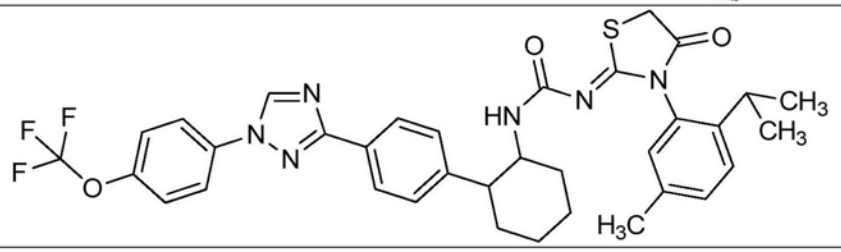
[1924]

编号	结构
FB1	
FB2	
FB3	
FB4	

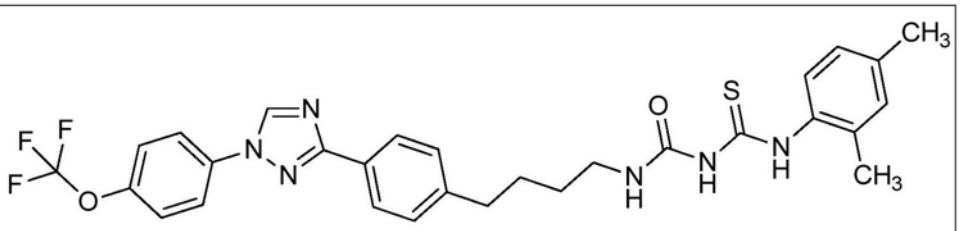
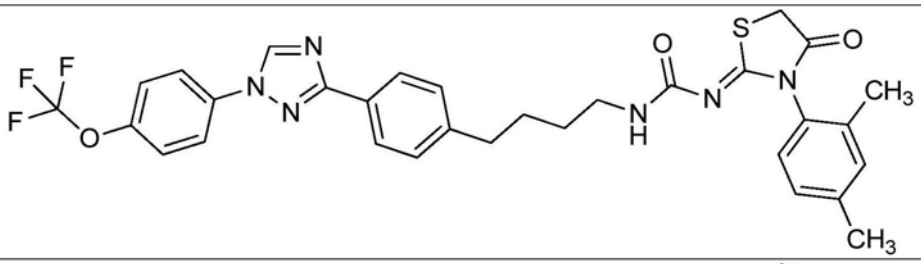
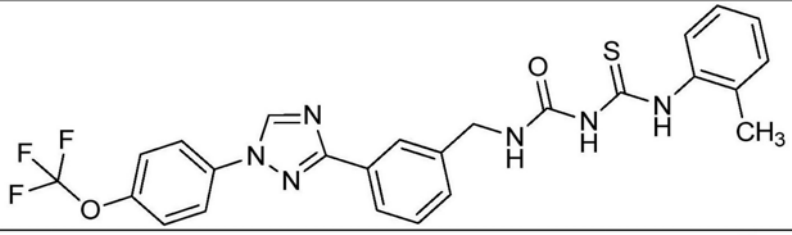
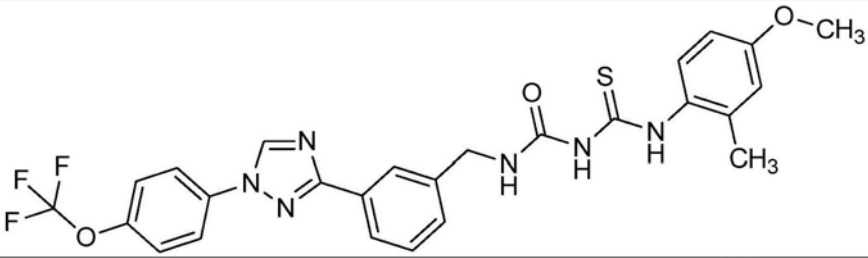
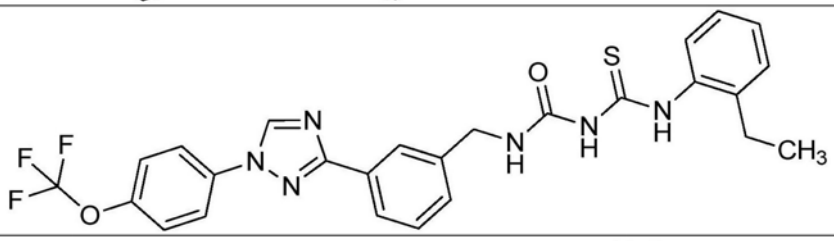
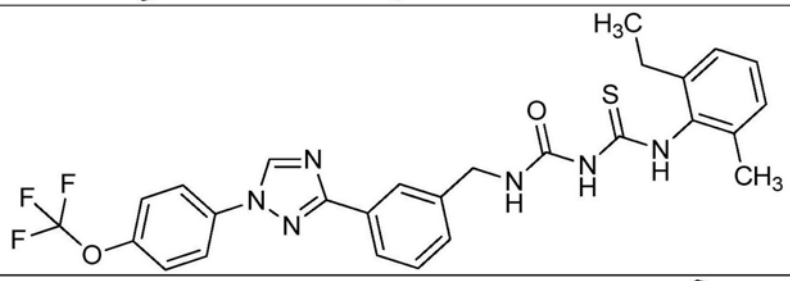
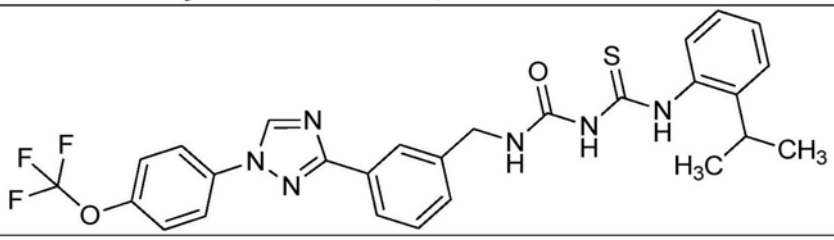
[1925]

FB5	
FB6	
FB7	
FB8	
FB9	
FB10	

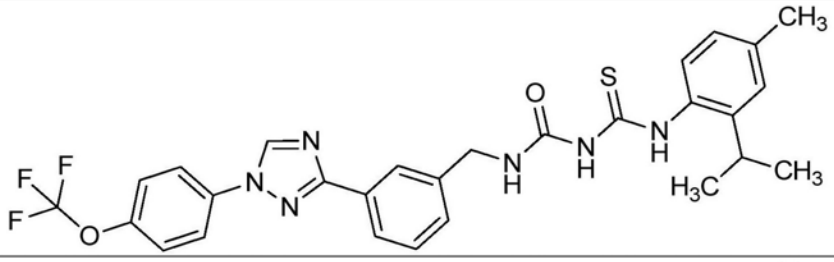
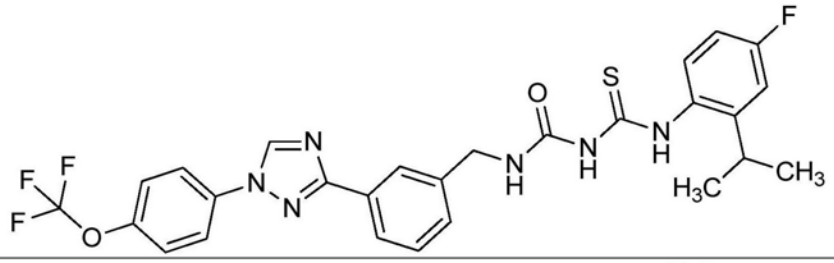
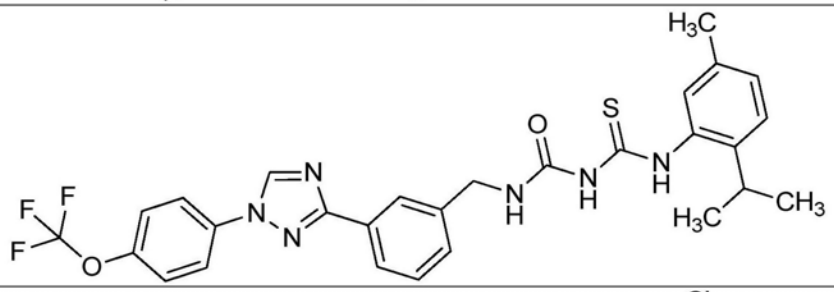
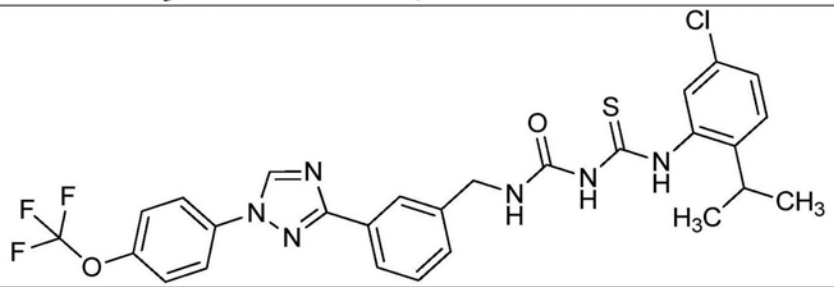
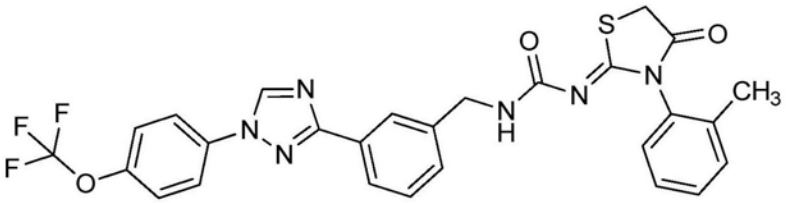
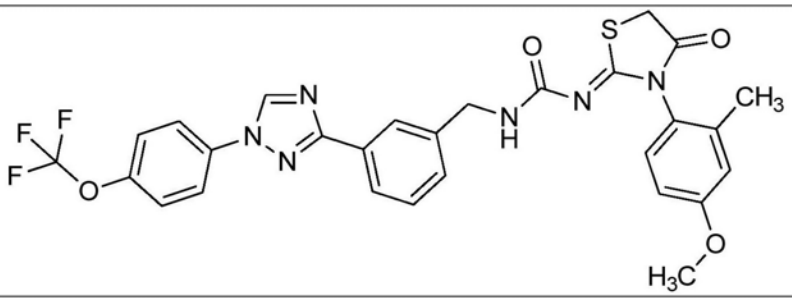
[1926]

FB11	
FB12	
FB13	
FB14	
FB15	

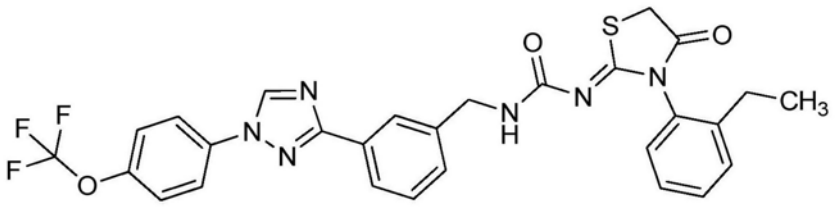
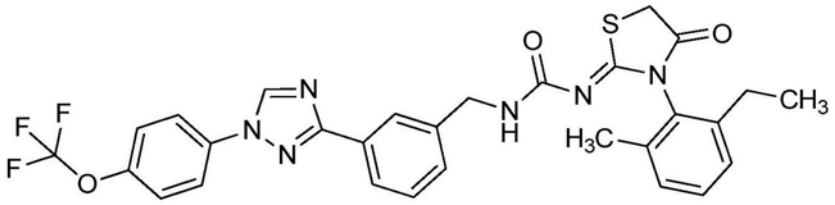
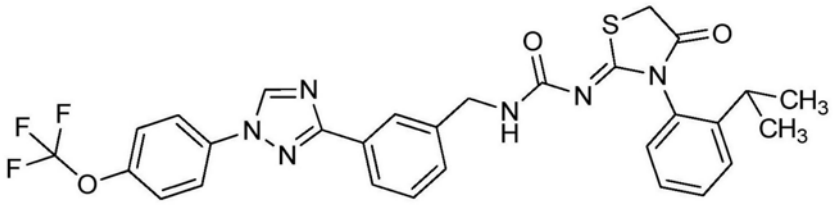
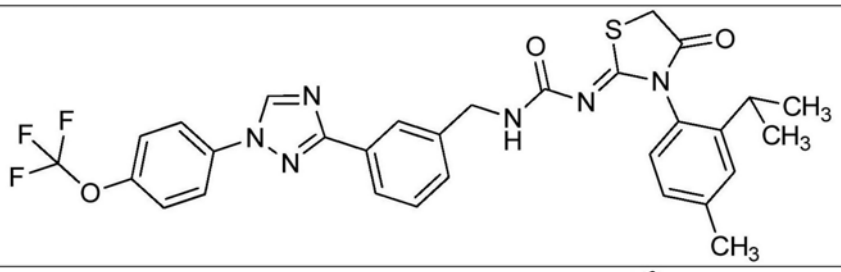
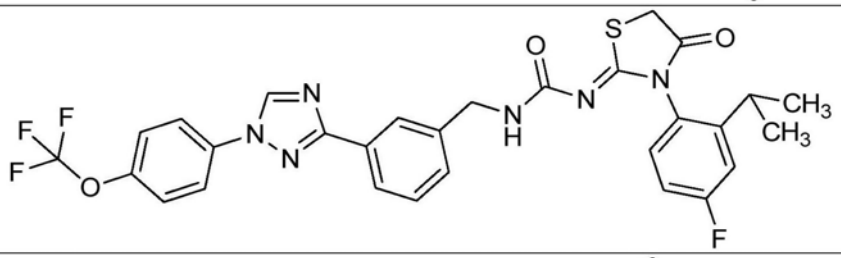
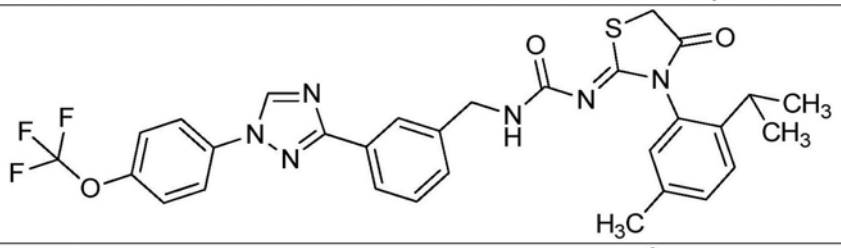
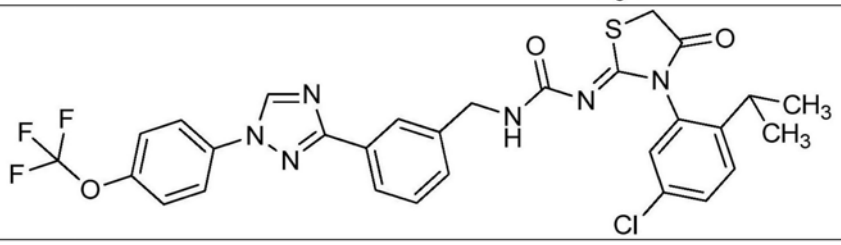
[1927]

FB16	
FB17	
FB18	
FB19	
FB20	
FB21	
FB22	

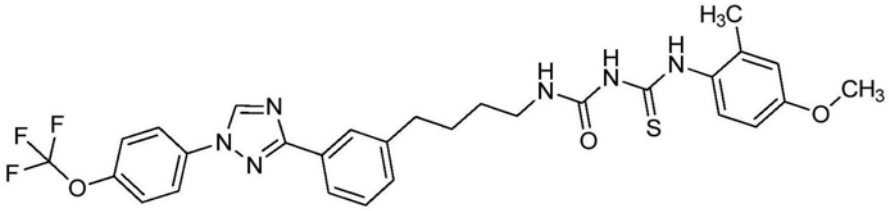
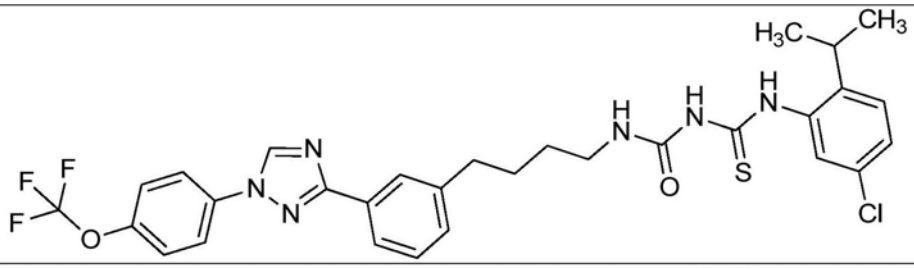
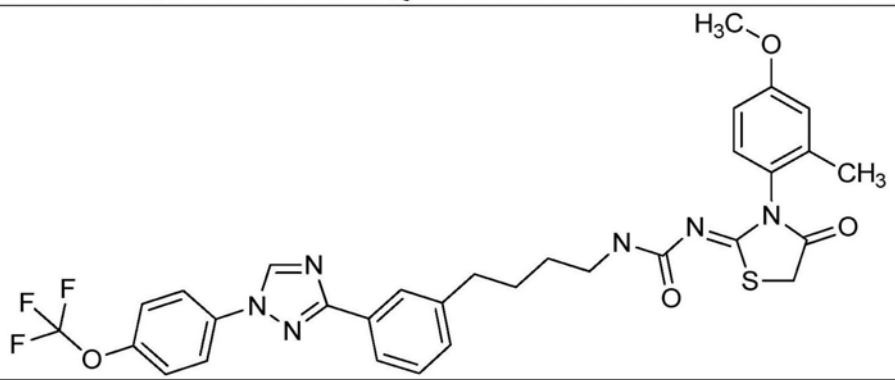
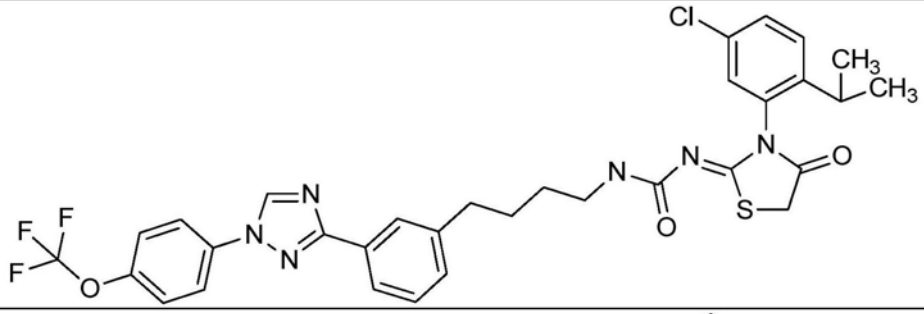
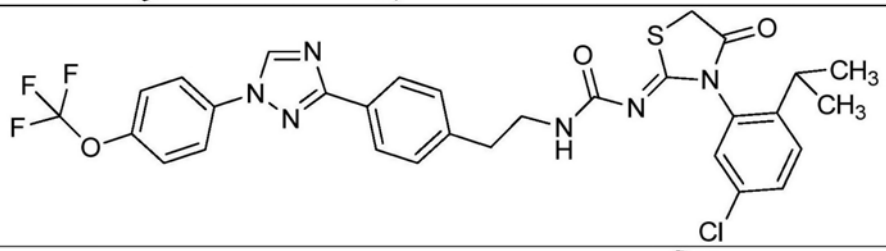
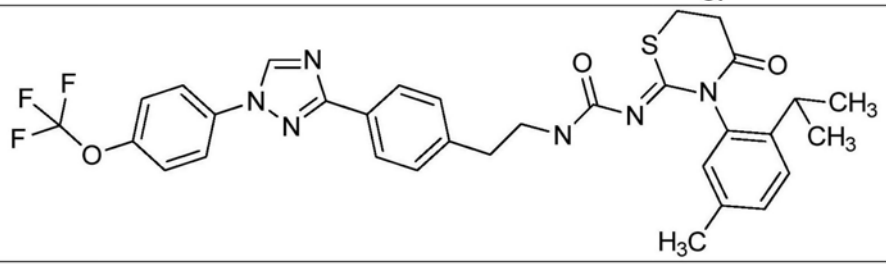
[1928]

FB23	
FB24	
FB25	
FB26	
FB27	
FB28	

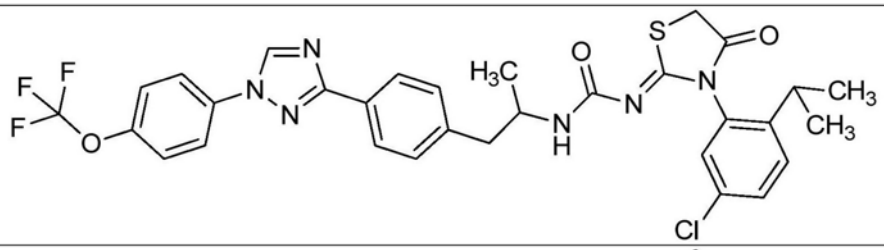
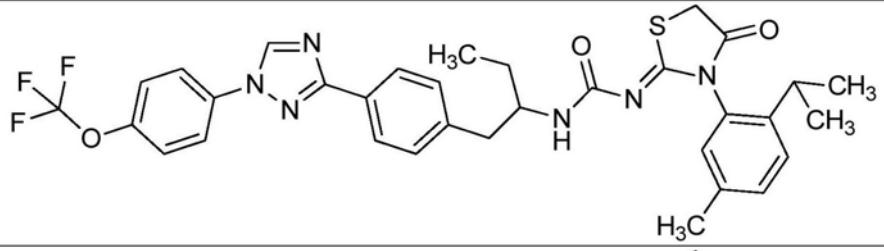
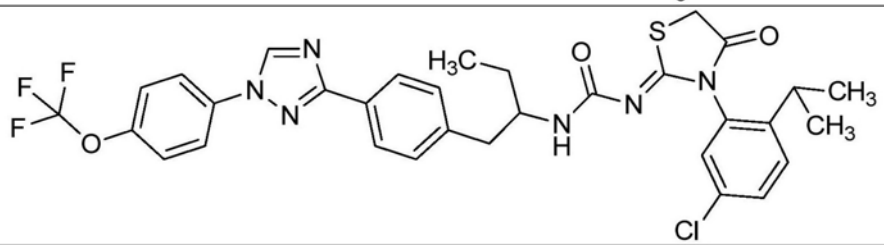
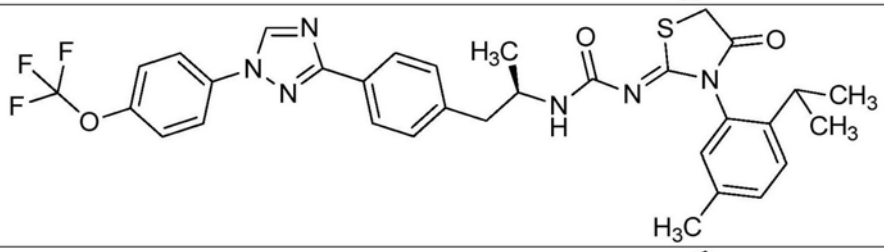
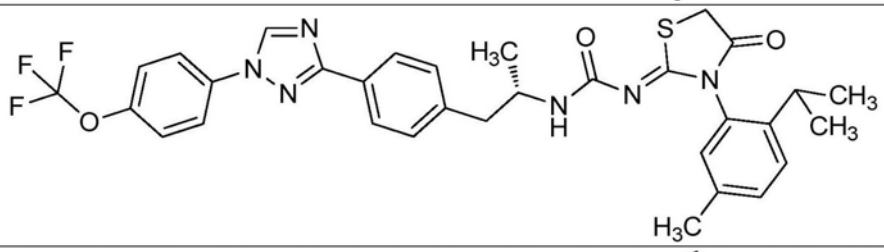
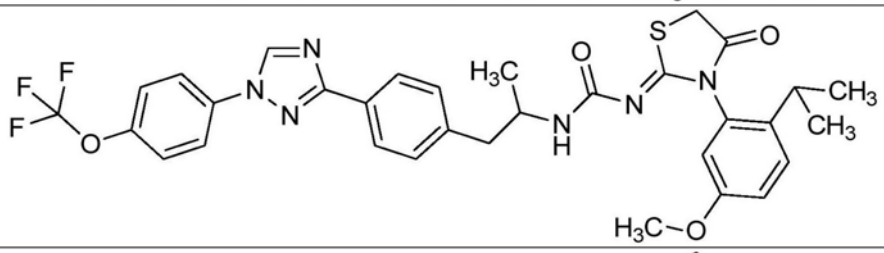
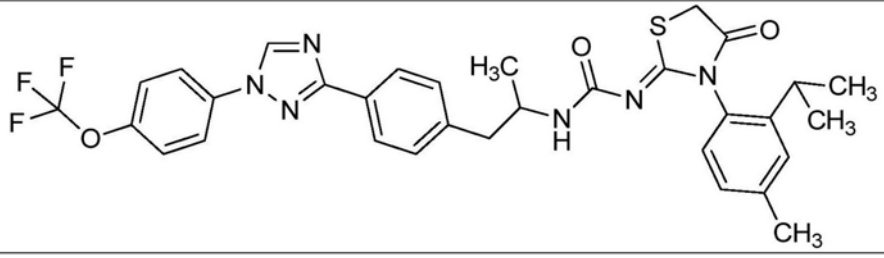
[1929]

FB29	
FB30	
FB31	
FB32	
FB33	
FB34	
FB35	

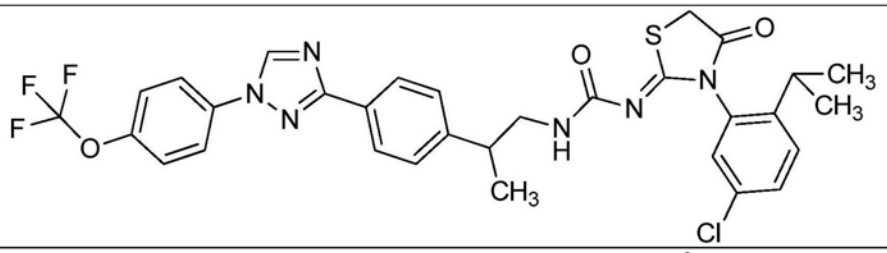
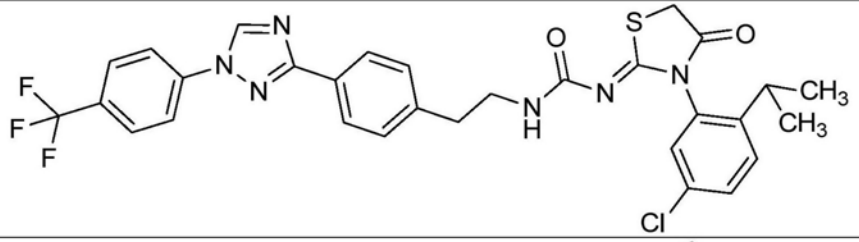
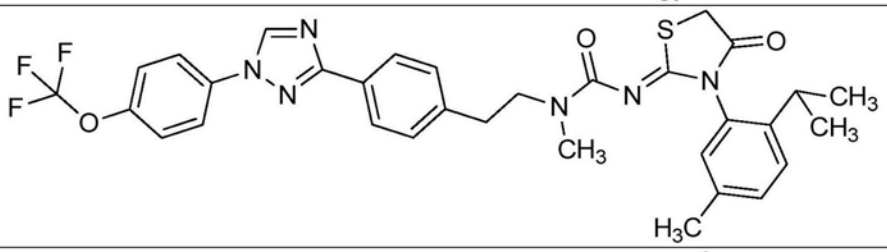
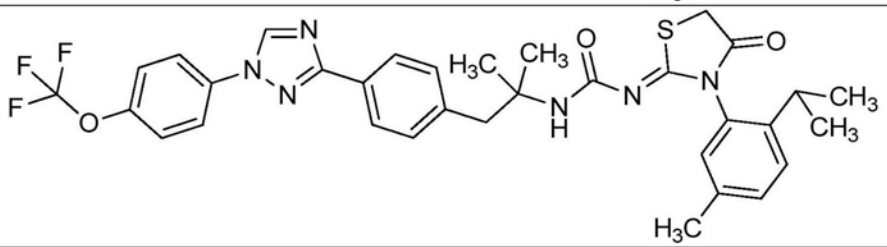
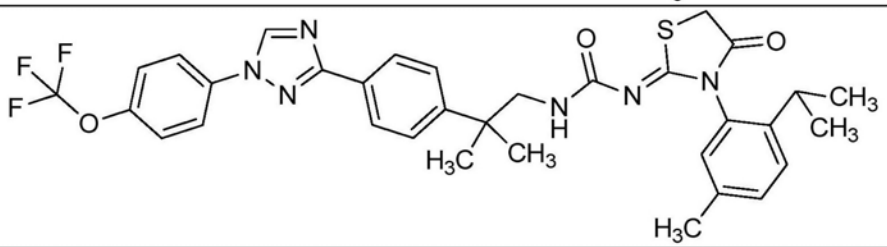
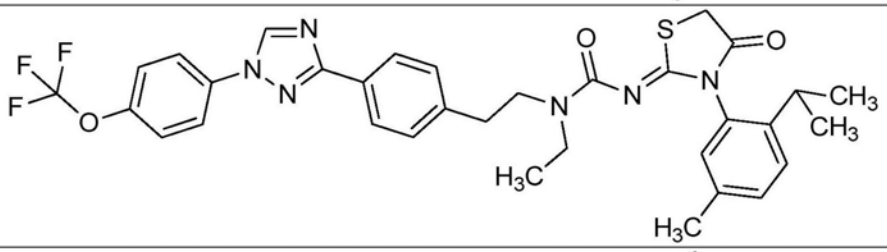
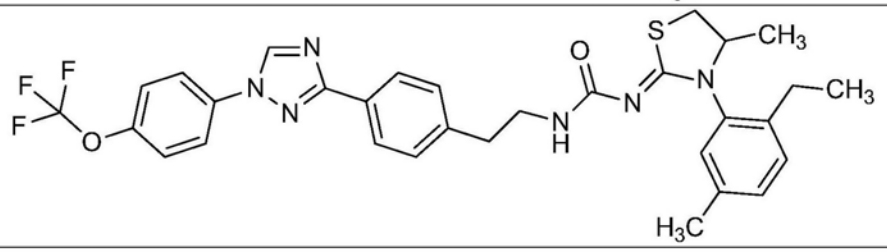
[1930]

FB36	
FB37	
FB38	
FB39	
FB40	
FB41	

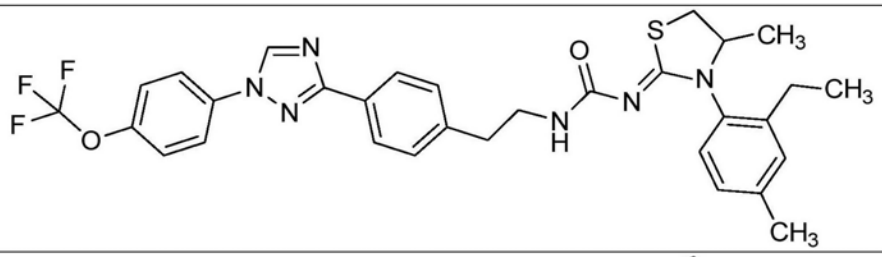
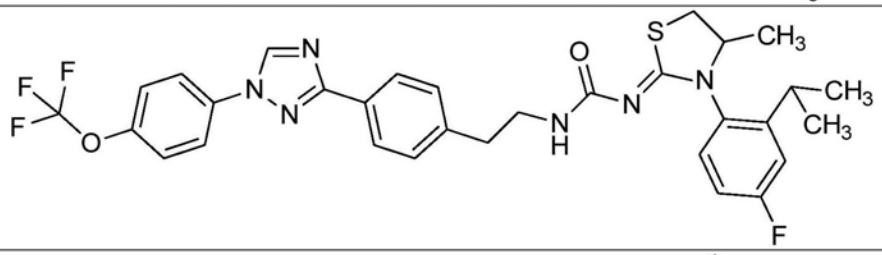
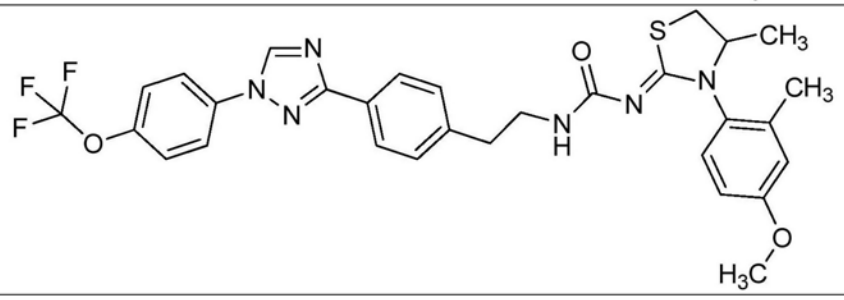
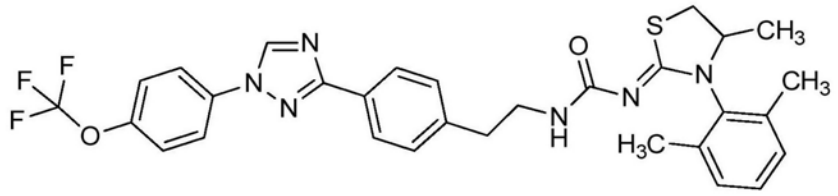
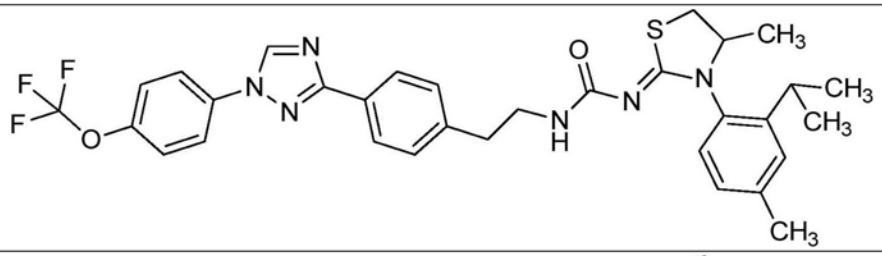
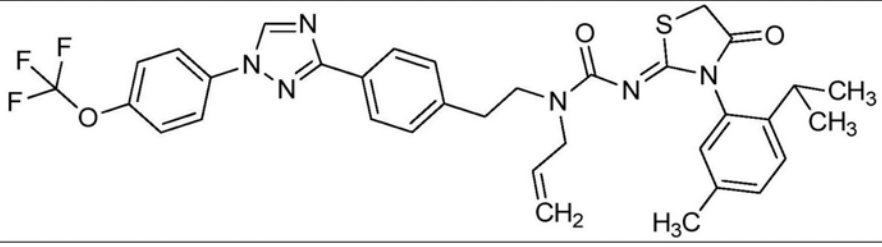
[1931]

FB42	
FB43	
FB44	
FB45	
FB46	
FB47	
FB48	

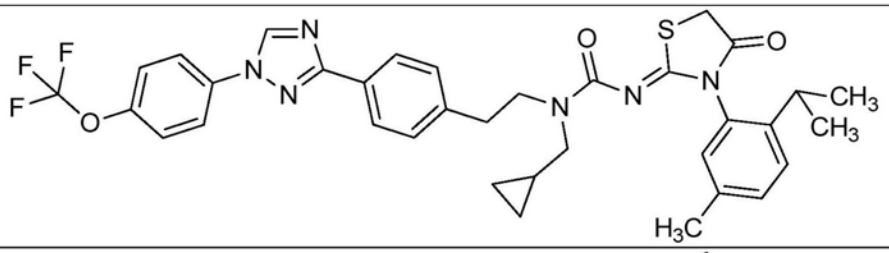
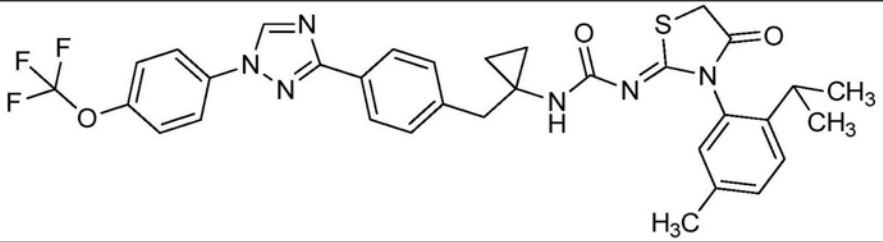
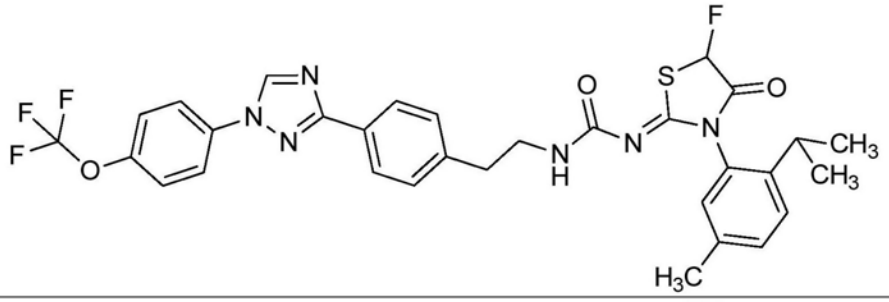
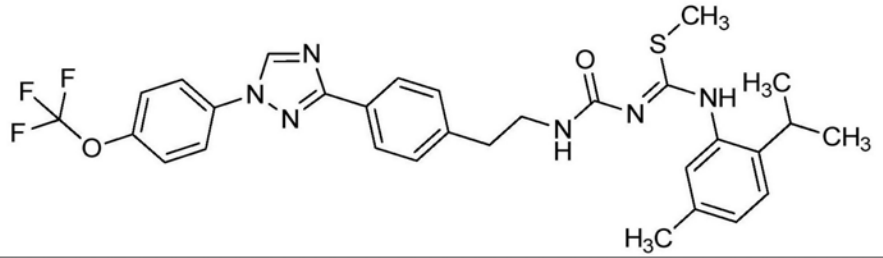
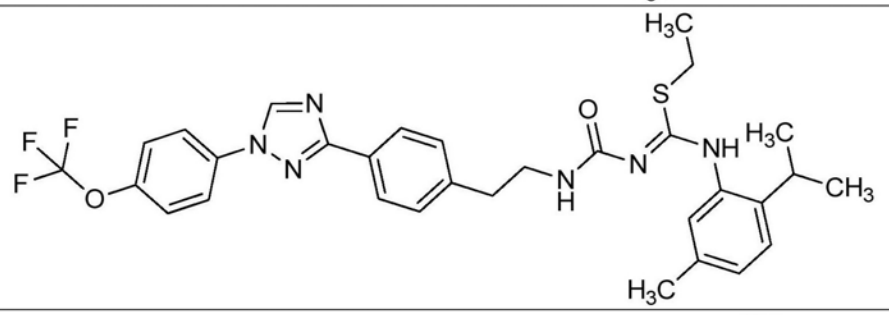
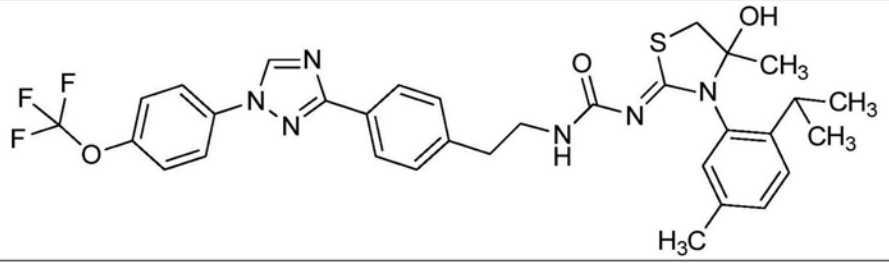
[1932]

FB49	
FB50	
FB51	
FB52	
FB53	
FB54	
FB55	

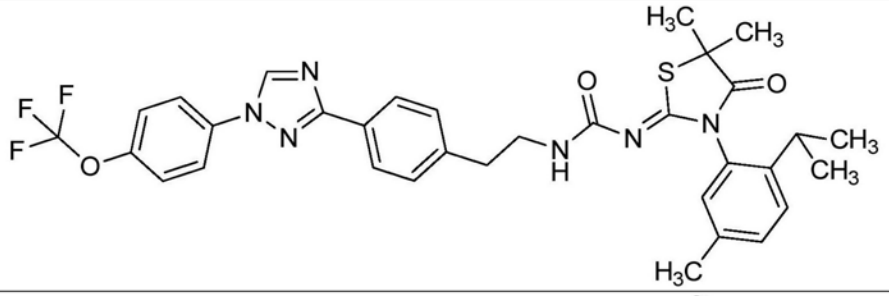
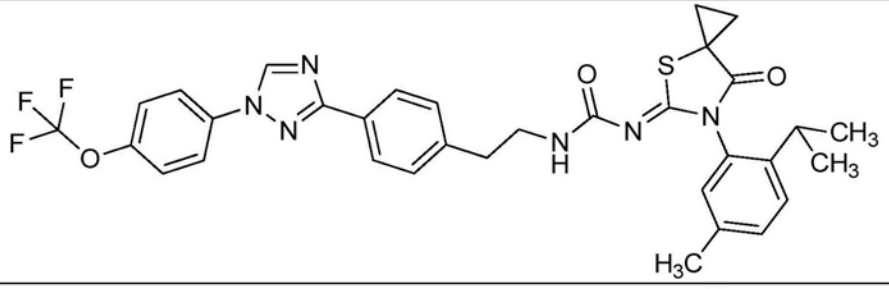
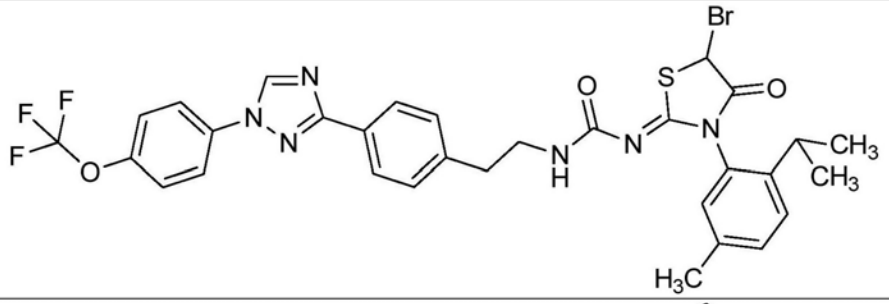
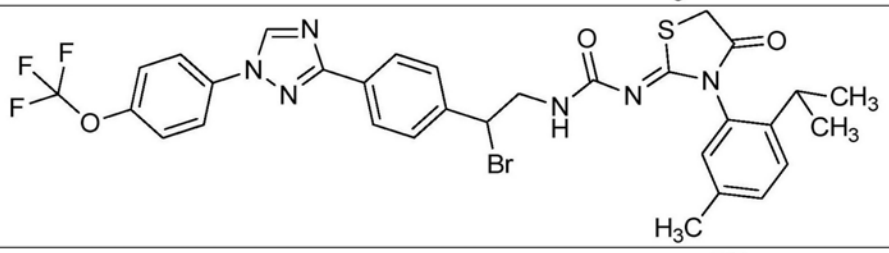
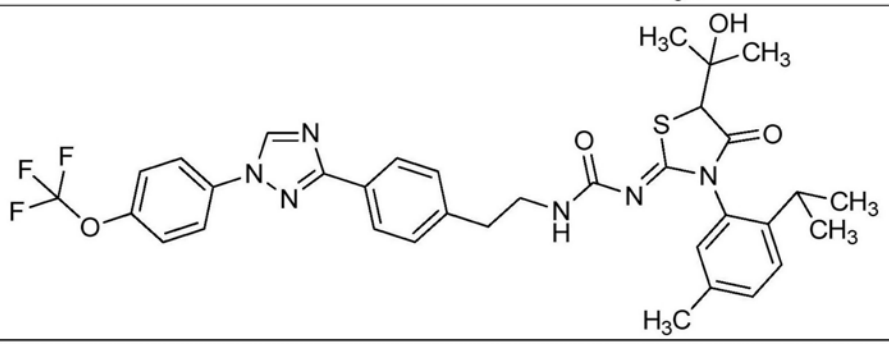
[1933]

FB56	
FB57	
FB58	
FB59	
FB60	
FB61	

[1934]

FB62	
FB63	
FB64	
FB65	
FB66	
FB67	

[1935]

FB68	
FB69	
FB70	
FB71	
FB72	

[1936] 表3a：对于表2a中的化合物的分析数据。

[1937]

编号	外观	Mp(°C)	ESIMS *m/z*	^{1}H NMR(δ)[a]	^{13}C NMR 或 ^{19}F NMR(δ)

[1938]

F1	澄清的油		609([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.55(s，1H)，8.08(d，J = 8.2 Hz，2H)，7.79(d，J = 9.0 Hz，2H)，7.43(dd，J = 3.4，2.1 Hz，2H)，7.39(d，J = 8.3 Hz，2H)，7.31- 7.24(m，3H)，7.03(d，J = 7.6 Hz，1H)，5.51(t，J = 6.1 Hz，1H)，3.93(d，J = 1.4 Hz，2H)，3.63-3.39(m，2H)，2.86(t，J = 7.0 Hz，2H)，2.68(dt，J = 13.7，6.9 Hz，1H)，1.17(dd，J = 6.8，4.7 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02
F2	白色粉末	150 – 153	569([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 10.12(s，1H)，9.40(s，1H)，8.08(dt，J = 4.3，2.7 Hz，3H)，7.63(d，J = 8.3 Hz，2H)，7.46- 7.14(m，6H)，7.00(s，1H)，3.52- 3.39(m，2H)，2.98(dd，J = 13.7，6.8 Hz，1H)，2.86(t，J = 6.9 Hz，2H)，1.15(d，J = 6.8 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-52.21
F3	白色固体	133 – 136，148 – 149	582([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 11.82(s，1H)，9.75(s，1H)，8.56(s，1H)，8.17- 8.08(m，2H)，7.84-7.74(m，2H)，7.38(dq，J = 8.0，0.9 Hz，2H)，7.30(d，J = 7.9 Hz，2H)，7.26- 7.07(m，3H)，5.75(s，1H)，3.52(d，J = 7.2 Hz，2H)，3.12-2.97(m，1H)，2.90(d，J = 7.5 Hz，2H)，2.33(s，3H)，1.22(d，J = 6.8 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02

[1939]

F4	白色固体	88 °C(dec)	583([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 11.90(s，1H)，9.96(s，1H)，8.55(s，1H)，8.12(d，J = 8.2 Hz，2H)，7.79(d，J = 9.0 Hz，2H)，7.42- 7.33(m，5H)，7.30(d，J = 8.2 Hz，2H)，7.23(dd，J = 12.0，5.8 Hz，1H)，5.81(s，1H)，4.19- 4.13(m，1H)，3.13(ddd，J = 27.5，13.7，6.9 Hz，1H)，2.94(dd，J = 13.4，6.0 Hz，1H)，2.74(dd，J = 13.3，7.6 Hz，1H)，1.32- 1.16(m，9H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
F5	淡粉色固体	102 °C(dec)	623([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.55(s，1H)，8.11- 8.05(m，2H)，7.84- 7.76(m，2H)，7.44- 7.36(m，2H)，7.31(d，J = 8.0 Hz，1H)，7.27- 7.25(m，3H)，6.85(d，J = 0.8 Hz，1H)，5.51(t，J = 6.1 Hz，1H)，3.92(d，J = 1.7 Hz，2H)，3.68- 3.38(m，2H)，2.87(t，J = 7.1 Hz，2H)，2.73- 2.52(m，1H)，2.33(s，3H)，1.15(dd，J = 6.9，2.4 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02

[1940]

F5A		60- 70		^{1}H NMR(400 MHz，DMSO-d_6)δ 9.39(s，1H)，8.13 – 8.03(m，2H)，8.03 – 7.96(m，2H)，7.69 – 7.57(m，3H)，7.50(d，J = 7.8 Hz，2H)，7.39 – 7.27(m，3H)，7.22(dd，J = 8.0，1.9 Hz，1H)，7.13(d，J = 7.8 Hz，2H)，6.98(dd，J = 1.7，0.9 Hz，1H)，4.11(d，J = 17.9 Hz，1H)，4.00(d，J = 17.9 Hz，1H)，3.27(q，J = 6.8 Hz，2H)，2.77(t，J = 7.3 Hz，2H)，2.61(p，J = 6.8 Hz，1H)，2.30(s，3H)，2.28(s，3H)，1.11(d，J = 6.8 Hz，3H)，1.09 – 1.04(m，3H)(SO_3H 未观测)	
F6	橙色固体	110 – 118 °C	639([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(d，J = 3.6 Hz，1H)，8.12- 8.05(m，2H)，7.84- 7.76(m，2H)，7.39(d，J = 8.3 Hz，2H)，7.32(d，J = 8.8 Hz，1H)，7.29- 7.25(m，2H)，6.99(dd，J = 8.7，2.7 Hz，1H)，6.56(d，J = 2.7 Hz，1H)，5.52(t，J = 5.9 Hz，1H)，3.93(d，J = 1.6 Hz，2H)，3.77(s，3H)，3.67-3.38(m，2H)，2.87(t，J = 7.1 Hz，2H)，2.60(dt，J = 13.7，6.9 Hz，1H)，1.20(dt，J = 13.0，6.8 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02

[1941]

F7	白色固体	114 °C(dec)	623([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.55(d，J = 1.0 Hz，1H)，8.12- 8.03(m，2H)，7.85- 7.75(m，2H)，7.50- 7.43(m，2H)，7.43- 7.37(m，2H)，7.35- 7.30(m，1H)，7.29- 7.22(m，2H)，7.09- 7.01(m，1H)，5.35(dd，J = 15.3，8.4 Hz，1H)，4.14(dd，J = 14.6，7.5 Hz，1H)，3.92(t，J = 1.8 Hz，2H)，2.93(ddd，J = 46.3，13.4，5.6 Hz，1H)，2.83- 2.59(m，2H)，1.17(ddd，J = 6.6，3.7，2.7 Hz，6H)，1.14- 1.03(m，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02
F8	白色灰色固体	114 °C(dec)	637([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(s，1H)，8.12- 8.02(m，2H)，7.84- 7.74(m，2H)，7.39(d，J = 8.6 Hz，2H)，7.36- 7.31(m，1H)，7.28(d，J = 7.4 Hz，2H)，7.24(d，J = 8.1 Hz，1H)，6.87(d，J = 12.4 Hz，1H)，5.36(dd，J = 14.8，8.4 Hz，1H)，3.95- 3.87(m，2H)，3.00(dd，J = 13.6，5.5 Hz，1H)，2.87(dd，J = 13.4，5.6 Hz，1H)，2.76(dd，J = 13.4，7.1 Hz，1H)，2.71- 2.57(m，1H)，2.35(d，J = 7.9 Hz，3H)，1.19- 1.05(m，9H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03

[1942]

F9	褐色胶		673([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(s，1H)，8.08(d，J = 8.1 Hz，2H)，7.85-7.77(m，2H)，7.43- 7.37(m，2H)，7.31(d，J = 8.0 Hz，1H)，7.28-7.22(m，3H)，6.86- 6.83(m，1H)，5.52(t，J = 6.2 Hz，1H)，3.92(d，J = 1.7 Hz，2H)，3.52(ddt，J = 35.7，13.7，6.7 Hz，2H)，2.87(t，J = 7.1 Hz，2H)，2.63(p，J = 7.0 Hz，1H)，2.33(s，3H)，1.15(dd，J = 6.9，2.2 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-85.89，-87.85
F10	橙色固体	113 °C(dec)	637([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.55(s，1H)，8.08(dd，J = 8.1，5.9 Hz，2H)，7.84- 7.76(m，2H)，7.39(dddd，J = 7.9，3.0，2.1，1.2 Hz，2H)，7.31-7.20(m，4H)，6.83(ddd，J = 6.6，1.8，0.9 Hz，1H)，5.42(t，J = 4.0 Hz，1H)，3.90(s，2H)，3.66- 3.18(m，2H)，3.02(p，J = 7.2 Hz，1H)，2.60(dq，J = 14.1，7.0 Hz，1H)，2.34- 2.26(m，3H)，1.27(d，J = 7.2 Hz，3H)，1.17-1.07(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03

[1943]

F11	黄色固体	178 – 182 °C	567([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 11.74(s，1H)，10.27(s，1H)，9.40(s，2H)，8.18- 7.91(m，4H)，7.59(dd，J = 24.9，8.4 Hz，4H)，7.41(ddd，J = 9.4，7.9，4.1 Hz，3H)，7.27(dtd，J = 25.3，7.4，1.5 Hz，2H)，6.25(d，J = 14.6 Hz，1H)，3.04(dt，J = 13.7，6.8 Hz，1H)，1.19(d，J = 6.9 Hz，6H)	^{19}F NMR(376 MHz，DMSO-d_6)δ-56.96
F12	橙色固体	128 °C(dec)	607([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.54(s，1H)，8.09(d，J = 8.4 Hz，2H)，7.81-7.76(m，2H)，7.52- 7.47(m，2H)，7.48- 7.41(m，1H)，7.41- 7.35(m，5H)，7.34(s，1H)，7.10- 7.05(m，1H)，6.03(d，J = 14.6 Hz，1H)，3.98(d，J = 2.4 Hz，2H)，2.69(dt，J = 13.7，6.8 Hz，1H)，1.22- 1.18(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02
F13	橙色胶		621([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(d，J = 1.4 Hz，1H)，8.16- 8.06(m，2H)，7.87- 7.74(m，2H)，7.53- 7.45(m，3H)，7.42- 7.30(m，3H)，7.26-7.21(m，2H)，7.14- 7.01(m，2H)，3.98(d，J = 2.2 Hz，2H)，2.77-2.60(m，1H)，1.98(d，J = 1.3 Hz，3H)，1.21(dd，J = 6.9，5.1 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02

[1944]

F14	黄色固体		ESIMS *m/z* 555([M+H]$^+$)，553([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 11.95(s，1H)，10.26(s，1H)，9.43(s，1H)，8.21- 8.06(m，4H)，7.65(ddd，*J* = 7.9，2.0，1.0 Hz，2H)，7.55(t，*J* = 5.9 Hz，1H)，7.53- 7.47(m，2H)，7.44(dd，*J* = 7.7，1.5 Hz，1H)，7.38(dd，*J* = 7.7，1.6 Hz，1H)，7.30(td，*J* = 7.5，1.6 Hz，1H)，7.23(td，*J* = 7.5，1.7 Hz，1H)，4.46(d，*J* = 5.8 Hz，2H)，3.04(hept，*J* = 6.8 Hz，1H)，1.20(d，*J* = 6.8 Hz，6H)。	^{19}F NMR(376 MHz，DMSO-d_6)δ-56.96.
F15	黄色固体		ESIMS *m/z* 605([M+H]$^+$)，603([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 11.93(s，1H)，10.25(s，1H)，9.42(s，1H)，8.33- 8.02(m，4H)，7.68-7.56(m，2H)，7.60- 7.05(m，7H)，4.45(d，*J* = 5.8 Hz，2H)，3.02(hept，*J* = 7.1 Hz，1H)，1.18(d，*J* = 6.8 Hz，6H)。	^{19}F NMR(376 MHz，DMSO-d_6)δ-85.19，-86.91.
F16	黄色固体		ESIMS *m/z* 619([M+H]$^+$)，617 [M-H)$^-$]	^{1}H NMR(400 MHz，DMSO-d_6)δ 11.89(s，1H)，10.25(s，1H)，9.44(s，1H)，8.17- 8.08(m，4H)，7.73-7.61(m，2H)，7.60- 7.40(m，3H)，7.33- 7.18(m，2H)，7.17- 7.05(m，1H)，4.46(d，*J* = 5.8 Hz，2H)，2.99(hept，*J* = 6.6 Hz，1H)，2.29(s，3H)，1.17(d，*J* = 6.8 Hz，6H)。	^{19}F NMR(376 MHz，DMSO-d_6)δ-85.19，-86.91.

[1945]

F17	白色固体		ESIMS *m/z* 595([M+H]$^+$)，593([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.41(d，*J* = 3.4 Hz，1H)，8.18(t，*J* = 6.3 Hz，1H)，8.11- 8.02(m，4H)，7.68- 7.61(m，2H)，7.53- 7.42(m，2H)，7.40- 7.27(m，3H)，7.23(dd，*J* = 7.9，1.4 Hz，1H)，4.37- 4.00(m，4H)，2.71(p，*J* = 6.8 Hz，1H)，1.16(dd，*J* = 27.4，6.8 Hz，6H)。	^{19}F NMR(376 MHz，DMSO-d_6)δ-56.96 .
F18	灰白色固体		ESIMS *m/z* 645([M+H]$^+$)，643([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(d，*J* = 3.0 Hz，1H)，8.16(t，*J* = 6.3 Hz，1H)，8.13- 7.99(m，4H)，7.69- 7.58(m，2H)，7.58- 7.39(m，2H)，7.40- 7.06(m，4H)，4.40- 3.94(m，4H)，2.70(p，*J* = 6.8 Hz，1H)，1.22- 1.08(m，6H)。	^{19}F NMR(376 MHz，DMSO-d_6)δ-85.19，-86.92.
F19	白色固体		ESIMS *m/z* 659([M+H]$^+$)，657([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(s，1H)，8.18(t，*J* = 6.3 Hz，1H)，8.15- 7.98(m，4H)，7.68- 7.57(m，2H)，7.51- 7.19(m，4H)，7.05- 6.96(m，1H)，4.42- 3.92(m，4H)，2.64(p，*J* = 6.9 Hz，1H)，2.29(s，3H)，1.28- 0.96(m，6H)。	^{19}F NMR(376 MHz，DMSO-d_6)δ-85.21(d，*J* = 9.4 Hz)，-86.93(d，*J* = 7.3 Hz)。

[1946]

F20	白色固体	124-128	ESIMS *m/z* 637([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.55(s，1H)，8.11- 8.05(m，2H)，7.83-7.76(m，2H)，7.42- 7.35(m，2H)，7.33(d，*J* = 8.0 Hz，1H)，7.26(s，3H)，6.87- 6.83(m，1H)，5.48(t，*J* = 6.1 Hz，1H)，3.98- 3.84(m，2H)，3.37-3.18(m，2H)，2.74- 2.57(m，3H)，2.35(s，3H)，1.86(dt，*J* = 14.8，7.3 Hz，2H)，1.16(dd，*J* = 6.9，2.7 Hz，6H)。	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03.
F21	白色固体	97(dec.)	ESIMS *m/z* 597([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 11.91(s，1H)，10.05(s，1H)，9.39(s，1H)，8.11- 8.01(m，4H)，7.67-7.56(m，2H)，7.39(d，*J* = 8.3 Hz，2H)，7.22(d，*J* = 7.9 Hz，2H)，7.08(d，*J* = 8.0 Hz，2H)，3.16(q，*J* = 6.5 Hz，2H)，2.95(p，*J* = 6.9 Hz，1H)，2.74-2.66(m，2H)，2.26(s，3H)，1.88-1.76(m，2H)，1.14(d，*J* = 6.8 Hz，6H)。	^{19}F NMR(376 MHz，DMSO-d_6)δ-56.96.
F22	白色固体	197 – 198 °C	581([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 11.87(s，1H)，10.02(s，1H)，9.38(s，1H)，8.09- 8.04(m，2H)，8.01(d，*J* = 8.4 Hz，2H)，7.62(d，*J* = 8.3 Hz，2H)，7.41- 7.18(m，7H)，2.99(dd，*J* = 13.7，6.8 Hz，1H)，2.90(s，1H)，2.16(s，1H)，1.36- 1.22(m，3H)，1.17(d，*J* = 7.3 Hz，6H)	^{19}F NMR(376 MHz，DMSO-d_6)δ-57.00

[1947]

F23	灰白色固体	185 – 190 °C	581([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 11.98(s，1H)，10.01(s，1H)，9.38(s，1H)，8.11- 8.03(m，2H)，8.01(d，J = 8.4 Hz，2H)，7.67- 7.52(m，3H)，7.39(s，1H)，7.35- 7.15(m，5H)，2.88(s，1H)，2.53- 2.50(m，2H)，2.15(d，J = 6.4 Hz，1H)，1.59- 1.45(m，2H)，1.39- 1.21(m，2H)，0.88(t，J = 7.3 Hz，3H)	^{19}F NMR(376 MHz，DMSO-d_6)δ-56.97
F24	白色固体	127 °C(dec)	581([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 11.51(s，1H)，10.01(s，1H)，9.38(s，1H)，8.10- 8.03(m，2H)，8.01(d，J = 8.1 Hz，2H)，7.61(d，J = 8.5 Hz，2H)，7.36(s，1H)，7.29(dd，J = 8.3，1.3 Hz，2H)，7.22- 7.02(m，3H)，2.90(d，J = 3.3 Hz，1H)，2.53- 2.45(m，2H)，2.17(d，J = 6.1 Hz，4H)，1.35- 1.18(m，2H)，1.12(q，J = 7.5 Hz，3H)	^{19}F NMR(376 MHz，DMSO-d_6)δ-56.97
F25	白色固体	127 °C(dec)	567([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 11.46(s，1H)，10.00(s，1H)，9.38(s，1H)，8.11- 8.04(m，2H)，8.01(d，J = 8.4 Hz，2H)，7.61(d，J = 8.3 Hz，2H)，7.35(s，1H)，7.30(d，J = 8.4 Hz，2H)，7.16- 7.03(m，3H)，2.89(d，J = 3.1 Hz，1H)，2.51(s，1H)，2.16(d，J = 7.2 Hz，6H)，1.34- 1.23(m，2H)	^{19}F NMR(376 MHz，DMSO-d_6)δ-56.97

[1948]

F26	白色油状固体		583([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 11.70(s，1H)，9.95(s，1H)，9.38(s，1H)，8.11-8.05(m，2H)，8.01(d，J = 8.4 Hz，2H)，7.62(d，J = 8.3 Hz，2H)，7.32(dd，J = 23.5，8.5 Hz，4H)，6.91-6.69(m，2H)，3.74(s，3H)，2.87(s，1H)，2.16(s，4H)，1.34-1.18(m，2H)	^{19}F NMR(376 MHz，DMSO-d_6)δ-56.98
F27	灰白色固体	111－121 °C	581([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 11.92(s，1H)，10.23(s，1H)，8.60(s，1H)，8.13-8.01(m，2H)，7.78(d，J = 9.0 Hz，2H)，7.37(d，J = 8.7 Hz，3H)，7.26(s，1H)，7.19(d，J = 7.9 Hz，3H)，7.11(d，J = 7.6 Hz，1H)，2.86(s，1H)，2.69-2.53(m，2H)，2.34(s，4H)，1.21(t，J = 7.6 Hz，5H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02
F28	白色固体	181-184 °C	595([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 11.70(d，J = 130.0 Hz，1H)，10.03(d，J = 115.9 Hz，1H)，8.58(s，1H)，8.09(d，J = 8.1 Hz，2H)，7.79(d，J = 9.0 Hz，2H)，7.38(d，J = 8.4 Hz，3H)，7.27-7.25(m，1H)，7.18(dd，J = 21.1，8.0 Hz，4H)，3.07(dt，J = 13.9，6.8 Hz，1H)，2.87(s，1H)，2.34(s，3H)，2.18(s，1H)，1.28-1.19(m，8H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03

[1949]

F29	白灰色固体	116 °C(dec)	621([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.54(s，1H)，8.07(d，J = 8.3 Hz，2H)，7.79(d，J = 9.0 Hz，2H)，7.48- 7.43(m，2H)，7.38(d，J = 8.4 Hz，2H)，7.35- 7.28(m，1H)，7.23- 7.17(m，2H)，7.05(dd，J = 7.5，2.7 Hz，1H)，5.69(dd，J = 7.1，2.9 Hz，1H)，3.94(d，J = 2.3 Hz，2H)，2.98- 2.90(m，1H)，2.74- 2.63(m，1H)，2.13- 2.03(m，1H)，1.33- 1.22(m，2H)，1.22- 1.16(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.04
F30	白灰色油状固体		621([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.54(s，1H)，8.08(d，J = 8.3 Hz，2H)，7.79(d，J = 9.0 Hz，2H)，7.46- 7.30(m，5H)，7.21(dd，J = 8.3，2.7 Hz，2H)，7.07(d，J = 7.8 Hz，1H)，5.69(s，1H)，3.93(d，J = 2.6 Hz，2H)，2.93(s，1H)，2.40(dd，J = 8.7，6.9 Hz，2H)，2.09(d，J = 9.7 Hz，1H)，1.64- 1.56(m，2H)，1.36- 1.13(m，2H)，0.93(td，J = 7.3，1.8 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.04

[1950]

F31	澄清的油		621([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.54(s，1H)，8.07(d，J = 8.3 Hz，2H)，7.79(d，J = 9.0 Hz，2H)，7.41- 7.29(m，3H)，7.20(dd，J = 13.3，7.9 Hz，4H)，5.72(s，1H)，3.95(s，2H)，2.94(dd，J = 7.4，4.1 Hz，1H)，2.43(q，J = 7.7 Hz，2H)，2.16- 2.06(m，4H)，1.31-1.22(m，2H)，1.17(td，J = 7.6，2.4 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
F32	澄清的油		607([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.54(s，1H)，8.08(d，J = 8.3 Hz，2H)，7.82-7.76(m，2H)，7.38(d，J = 8.4 Hz，2H)，7.28(d，J = 7.8 Hz，1H)，7.19(dd，J = 17.5，7.9 Hz，4H)，5.71(s，1H)，3.95(s，2H)，2.94(td，J = 7.6，3.3 Hz，1H)，2.13(d，J = 1.3 Hz，6H)，2.12- 2.06(m，1H)，1.32-1.17(m，2H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.04

[1951]

F33	黄色固体	124 °C(dec)	621([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.54(s，1H)，8.08(d，J = 8.3 Hz，2H)，7.79(d，J = 9.0 Hz，2H)，7.38(d，J = 8.3 Hz，2H)，7.28(d，J = 7.9 Hz，1H)，7.25-7.16(m，2H)，6.89(s，1H)，5.71(s，1H)，3.92(d，J = 2.0 Hz，2H)，2.94(dd，J = 7.2，3.6 Hz，1H)，2.47-2.38(m，2H)，2.36(d，J = 2.3 Hz，3H)，2.10(ddd，J = 9.6，6.4，3.4 Hz，1H)，1.33- 1.19(m，2H)，1.16(td，J = 7.6，2.7 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
F34	黄色油		621([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.53(s，1H)，8.04(d，J = 8.1 Hz，2H)，7.78(d，J = 8.9 Hz，3H)，7.37(d，J = 8.5 Hz，4H)，7.19(dd，J = 12.6，7.2 Hz，2H)，6.91(s，1H)，5.42(d，J = 11.2 Hz，1H)，3.95- 3.82(m，1H)，3.76(ddd，J = 10.3，7.5，5.5 Hz，1H)，3.26(dd，J = 15.0，7.2 Hz，2H)，2.96- 2.81(m，2H)，2.37- 2.30(m，3H)，2.05-1.96(m，1H)，1.29- 1.05(m，8H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02

[1952]

F35	黄色固体		ESIMS *m/z* 569([M+H]$^+$)，567([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 11.89(s，1H)，10.25(s，1H)，9.43(s，1H)，8.19- 8.05(m，4H)，7.72-7.60(m，2H)，7.59- 7.46(m，3H)，7.29- 7.21(m，2H)，7.11(dd，J = 8.2，1.7 Hz，1H)，4.46(d，J = 5.8 Hz，2H)，2.99(p，J = 6.9 Hz，1H)，2.29(s，3H)，1.17(d，J = 6.9 Hz，6H)	^{19}F NMR(376 MHz，DMSO-d_6)δ-56.96

[1953] [a]除非另外指明，否则所有^{1}H NMR数据在$CDCl_3$中于400MHz测量。

[1954] 表3b：对于表2b中的化合物的分析数据。

[1955]

编号	外观	Mp(°C)	ESIMS *m/z*	^{1}H NMR(δ)[a]	^{13}C NMR 或 ^{19}F NMR(δ)
P1	白色固体		ESIMS *m/z* 567([M+H]$^{+}$), 565([M-H]$^{-}$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.39(s，1H)，8.17(t，*J* = 6.3 Hz，1H)，8.11 – 8.00(m，4H)，7.67 – 7.58(m，2H)，7.40 – 7.28(m，5H)，7.28 – 7.23(m，1H)，4.25(qd，*J* = 15.4，6.3 Hz，2H)，4.17 – 3.98(m，2H)，2.10(s，3H)	^{19}F NMR(376 MHz，DMSO-d_6)δ-56.97

[1956]

P2，P532	白色固体		ESIMS *m/z* 581([M+H]$^+$)，579([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.38(s，1H)，8.15(t，*J* = 6.3 Hz，1H)，8.07 – 8.05(m，2H)，8.03(d，*J* = 8.2 Hz，2H)，7.64 – 7.60(m，3H)，7.41 – 7.39(m，2H)，7.36 – 7.33(m，2H)，7.23(dt，*J* = 7.9，0.9 Hz，1H)，4.30 – 4.18(m，2H)，4.17 – 3.99(m，2H)，2.41(q，*J* = 7.6 Hz，2H)，1.11(t，*J* = 7.6 Hz，3H)	^{19}F NMR(376 MHz，DMSO-d_6)δ-56.97
P3，P1172	灰白色固体		ESIMS *m/z* 613([M+H]$^+$)，611([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.39(s，1H)，8.17(t，*J* = 6.3 Hz，1H)，8.13 – 7.99(m，5H)，7.62(d，*J* = 8.6 Hz，2H)，7.40 – 7.27(m，3H)，7.16(td，*J* = 8.4，2.9 Hz，1H)，4.25(dd，*J* = 10.6，6.3 Hz，2H)，4.19 – 3.95(m，2H)，2.75 – 2.61(m，1H)，1.20 – 1.08(m，6H)	^{19}F NMR(376 MHz，DMSO-d_6)δ-56.97(d，*J* = 3.4 Hz)，-112.07(d，*J* = 3.6 Hz)
P5	灰白色固体		ESIMS *m/z* 609([M+H]$^+$)，607([M-H]$^-$)	8.55(s，1H)，8.11(d，*J* = 8.3 Hz，2H)，7.79(d，*J* = 9.0 Hz，2H)，7.40 – 7.32(m，4H)，7.22(d，*J* = 2.0 Hz，1H)，7.12 – 7.08(m，1H)，6.94(d，*J* = 8.0 Hz，1H)，5.83(t，*J* = 6.1 Hz，1H)，4.47(t，*J* = 6.5 Hz，2H)，3.93(d，*J* = 1.8 Hz，2H)，2.65(p，*J* = 6.9 Hz，1H)，2.38(s，3H)，1.17(d，*J* = 6.8 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02

[1957]

P6	灰白色固体		ESIMS *m/z* 597([M+H]$^+$), 595([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.39(s，1H)，8.17(t，*J* = 6.3 Hz，1H)，8.13 – 7.99(m，4H)，7.70 – 7.56(m，2H)，7.41 – 7.31(m，2H)，7.15(d，*J* = 8.7 Hz，1H)，6.93(d，*J* = 2.8 Hz，1H)，6.86(dd，*J* = 8.7，2.9 Hz，1H)，4.25(qd，*J* = 15.4，6.3 Hz，2H)，4.16 – 3.94(m，2H)，3.78(s，3H)，2.05(s，3H)。	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.96
P7	灰白色固体		ESIMS *m/z* 595([M+H]$^+$), 593([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.39(s，1H)，8.19(t，*J* = 6.3 Hz，1H)，8.13 – 7.95(m，4H)，7.63(d，*J* = 8.5 Hz，2H)，7.38 – 7.17(m，4H)，7.04(d，*J* = 1.9 Hz，1H)，4.24(dd，*J* = 13.7，6.3 Hz，2H)，4.13(d，*J* = 18.1 Hz，1H)，4.07(d，*J* = 17.9 Hz，1H)，3.39(q，*J* = 7.0 Hz，2H)，2.32(s，3H)，1.10 – 1.08(m，3H)。	^{19}F NMR(376 MHz，$CDCl_3$)δ-52.22
P8，P852	灰白色固体		ESIMS *m/z* 609([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.45(s，1H)，8.23(t，*J* = 6.3 Hz，1H)，8.18 – 8.05(m，4H)，7.68(d，*J* = 8.7 Hz，2H)，7.44 – 7.38(m，2H)，7.37 – 7.23(m，2H)，7.10(d，*J* = 1.8 Hz，1H)，4.30(t，*J* = 6.7 Hz，2H)，4.23 – 4.02(m，2H)，3.50- 3.42(m，2H)，2.37(s，3H)，1.63 – 1.47(m，2H)，1.15(t，*J* = 7.0 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-52.21

[1958]

P14	白色固体		ESIMS *m/z* 579([M+H]$^+$), 577([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.52(s，1H)，8.18(dd，*J* = 7.2，4.5 Hz，3H)，8.08 – 8.02(m，2H)，8.02 – 7.94(m，2H)，7.58 – 7.40(m，2H)，7.39 – 7.27(m，3H)，7.21(dd，*J* = 7.9，1.4 Hz，1H)，4.32 – 4.18(m，2H)，4.18 – 3.98(m，2H)，2.70(p，*J* = 6.8 Hz，1H)，1.20 – 1.08(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-60.80
P15	淡黄色固体		ESMIS *m/z* 593([M+H]$^+$), 591([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.52(s，1H)，8.20(d，*J* = 8.4 Hz，2H)，8.15(t，*J* = 6.3 Hz，1H)，8.11 – 8.04(m，2H)，8.00(d，*J* = 8.5 Hz，2H)，7.40 – 7.33(m，2H)，7.33 – 7.27(m，1H)，7.15 – 7.03(m，2H)，4.34 – 4.20(m，2H)，4.18 – 3.97(m，2H)，2.66(p，*J* = 6.8 Hz，1H)，2.37(s，3H)，1.11(dt，*J* = 7.0，3.6 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-60.80
P20	灰白色固体		ESIMS *m/z* 607([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.38(s，1H)，8.14 – 8.01(m，4H)，7.70(s，1H)，7.62(dq，*J* = 7.7，1.0 Hz，2H)，7.45 – 7.35(m，2H)，7.34 – 7.27(m，1H)，7.15(t，*J* = 1.3 Hz，2H)，6.66(q，*J* = 0.9 Hz，1H)，4.47 – 4.28(m，2H)，2.73 – 2.62(m，1H)，2.39(s，3H)，2.10(d，*J* = 1.1 Hz，3H)，1.10(d，*J* = 6.8 Hz，3H)，1.00(d，*J* = 6.8 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.96

[1959]

P26	褐色油		ESIMS *m/z* 623([M+H]$^+$)	8.55(s，1H)，8.08(d，*J* = 8.2 Hz，2H)，7.83- 7.75(m，2H)，7.44-7.35(m，2H)，7.28- 7.25(m，2H)，7.23- 7.18(m，1H)，7.09(ddd，*J* = 8.0，2.0，0.8 Hz，1H)，6.91(d，*J* = 8.0 Hz，1H)，5.51(t，*J* = 6.2 Hz，1H)，3.91(d，*J* = 1.5 Hz，2H)，3.52(ddt，*J* = 30.1，13.6，6.7 Hz，2H)，2.86(t，*J* = 7.1 Hz，2H)，2.63(p，*J* = 6.8 Hz，1H)，2.38(s，3H)，1.16(dd，*J* = 6.9，4.5 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
P27	黄色油		ESIMS *m/z* 623([M+H]$^+$)	8.55(s，1H)，8.11- 8.05(m，2H)，7.84-7.72(m，2H)，7.43- 7.35(m，2H)，7.27- 7.25(m，1H)，7.25(s，1H)，7.24-7.14(m，2H)，6.84(dd，*J* = 7.3，2.0 Hz，1H)，5.51(t，*J* = 6.1 Hz，1H)，3.91(d，*J* = 1.5 Hz，2H)，3.52(dp，*J* = 25.1，6.7 Hz，2H)，2.95(dq，*J* = 15.6，7.6 Hz，1H)，2.87(td，*J* = 7.0，2.1 Hz，2H)，2.47(s，3H)，1.25(d，*J* = 7.2 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03

[1960]

P28	褐色泡沫状固体		ESIMS *m/z* 627([M+H]$^+$)	8.55(s，1H)，8.11- 8.05(m，2H)，7.83- 7.74(m，2H)，7.39(dd，*J* = 9.1，1.0 Hz，2H)，7.29- 7.24(m，2H)，7.09(dd，*J* = 9.9，2.6 Hz，1H)，7.06- 6.93(m，2H)，5.48(t，*J* = 6.2 Hz，1H)，3.92(d，*J* = 1.7 Hz，2H)，3.53(dp，*J* = 25.1，6.7 Hz，2H)，2.87(t，*J* = 7.0 Hz，2H)，2.64(pd，*J* = 6.9，1.9 Hz，1H)，1.15(t，*J* = 6.9 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02，-110.68
P29	淡粉色固体		ESIMS *m/z* 623([M+H]$^+$)	8.55(s，1H)，8.12- 8.04(m，2H)，7.83- 7.75(m，2H)，7.43- 7.35(m，2H)，7.30- 7.26(m，2H)，7.25- 7.17(m，2H)，6.90- 6.83(m，1H)，5.52(t，*J* = 6.2 Hz，1H)，3.91(d，*J* = 2.4 Hz，2H)，3.62- 3.43(m，2H)，2.88(t，*J* = 7.1 Hz，2H)，2.43- 2.23(m，5H)，1.60- 1.48(m，2H)，0.90(t，*J* = 7.3 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
P30	粉红色固体		ESIMS *m/z* 623([M+H]$^+$)	8.55(s，1H)，8.11- 8.04(m，2H)，7.83- 7.77(m，2H)，7.59(dd，*J* = 8.2，1.5 Hz，1H)，7.44- 7.36(m，3H)，7.30(dd，*J* = 7.7，1.5 Hz，1H)，7.27- 7.25(m，3H)，6.89(dd，*J* = 7.8，1.5 Hz，1H)，3.87(s，2H)，3.51(dh，*J* = 27.3，6.9 Hz，2H)，2.87(td，*J* = 7.0，2.8 Hz，2H)，1.31(s，9H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03

[1961]

P31	灰白色固体		ESIMS *m/z* 609([M+H]$^+$)	8.55(s，1H)，8.09(d，*J* = 8.2 Hz，2H)，7.80(d，*J* = 9.0 Hz，2H)，7.43-7.35(m，2H)，7.28(s，2H)，7.17(d，*J* = 2.0 Hz，1H)，7.11(dd，*J* = 8.0，2.0 Hz，1H)，6.94(d，*J* = 7.9 Hz，1H)，5.51(t，*J* = 6.2 Hz，1H)，3.91(d，*J* = 1.5 Hz，2H)，3.52(qd，*J* = 7.0，2.6 Hz，2H)，2.87(t，*J* = 7.1 Hz，2H)，2.50- 2.32(m，5H)，1.15(t，*J* = 7.6 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
P33	褐色固体	105(dec.)	ESIMS *m/z* 641([M+H]$^+$)	8.56(d，*J* = 0.6 Hz，1H)，8.08(dd，*J* = 10.1，8.2 Hz，2H)，7.84- 7.76(m，2H)，7.43- 7.37(m，2H)，7.30-7.27(m，1H)，7.25- 7.22(m，1H)，7.11(dd，*J* = 9.8，2.6 Hz，1H)，7.02(dddd，*J* = 11.3，7.3，6.0，2.9 Hz，2H)，5.31(dd，*J* = 11.9，8.5 Hz，1H)，4.23- 4.10(m，1H)，3.91(t，*J* = 1.8 Hz，2H)，3.06- 2.59(m，3H)，1.22-1.05(m，9H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03，-110.63，-110.66，-110.66

[1962]

P42	灰白色固体		ESIMS *m/z* 623([M+H]$^+$)	8.56(s，1H)，8.13- 8.03(m，2H)，7.83-7.75(m，2H)，7.42- 7.27(m，6H)，7.25- 7.13(m，1H)，5.42- 5.29(m，1H)，3.93(d，*J* = 0.9 Hz，2H)，3.04-2.83(m，1H)，2.70(td，*J* = 13.5，7.8 Hz，2H)，2.42(q，*J* = 7.9 Hz，2H)，2.12(d，*J* = 5.3 Hz，3H)，1.16(td，*J* = 7.6，2.1 Hz，3H)，1.10(dd，*J* = 6.7，2.6 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
P44	黄色固体		ESIMS *m/z* 611([M+H]$^+$)	8.55(s，1H)，8.15- 8.04(m，2H)，7.86-7.74(m，2H)，7.39(d，*J* = 8.4 Hz，2H)，7.28(d，*J* = 8.2 Hz，2H)，7.00(d，*J* = 8.2 Hz，1H)，6.82(d，*J* = 8.6 Hz，2H)，5.52(t，*J* = 6.2 Hz，1H)，3.91(s，2H)，3.80(s，3H)，3.53(q，*J* = 6.9 Hz，2H)，2.88(t，*J* = 7.2 Hz，2H)，2.11(s，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
P45	褐色固体		ESIMS *m/z* 625([M+H]$^+$)	8.56(d，*J* = 0.6 Hz，1H)，8.12-8.05(m，2H)，7.80(d，*J* = 9.0 Hz，2H)，7.44- 7.35(m，2H)，7.30-7.27(m，2H)，7.02(dd，*J* = 9.1，7.1 Hz，1H)，6.84(qd，*J* = 5.5，4.6，1.8 Hz，2H)，5.38(dd，*J* = 8.4，5.7 Hz，1H)，3.96- 3.84(m，3H)，3.82(d，*J* = 0.7 Hz，3H)，2.98(ddd，*J* = 13.3，9.9，5.4 Hz，1H)，2.69(td，*J* = 13.9，7.9 Hz，1H)，2.12(d，*J* = 3.0 Hz，3H)，1.10(dd，*J* = 6.7，1.1 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03

[1963]

P47	黄色油		ESIMS *m/z* 625([M+H]$^+$)	8.55(s，1H)，8.09(d，*J* = 8.2 Hz，2H)，7.79(d，*J* = 9.0 Hz，2H)，7.39(ddt，*J* = 7.7，1.9，1.0 Hz，2H)，7.30- 7.26(m，2H)，6.67(s，2H)，5.56(t，*J* = 6.2 Hz，1H)，3.92(s，2H)，3.78(s，3H)，3.59- 3.40(m，2H)，2.88(t，*J* = 7.2 Hz，2H)，2.08(s，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02
P49	粉红色固体		ESIMS *m/z* 609([M+H]$^+$)	8.55(s，1H)，8.14- 8.04(m，2H)，7.83-7.74(m，2H)，7.39(dd，*J* = 8.9，1.0 Hz，2H)，7.28- 7.24(m，3H)，7.23-7.18(m，1H)，6.88(s，1H)，5.52(t，*J* = 6.1 Hz，1H)，3.91(d，*J* = 1.6 Hz，2H)，3.52(p，*J* = 6.8 Hz，2H)，2.88(t，*J* = 7.1 Hz，2H)，2.48- 2.35(m，2H)，2.34(s，3H)，1.14(t，*J* = 7.6 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
P50	灰白色固体		ESIMS *m/z* 609([M+H]$^+$)	8.55(s，1H)，8.09(d，*J* = 8.2 Hz，2H)，7.80(d，*J* = 9.0 Hz，2H)，7.46-7.34(m，2H)，7.33- 7.26(m，3H)，7.17(dd，*J* = 15.0，7.5 Hz，2H)，5.51(t，*J* = 6.0 Hz，1H)，3.94(s，2H)，3.52(dp，*J* = 13.4，6.6 Hz，2H)，2.87(t，*J* = 7.2 Hz，2H)，2.41(qd，*J* = 7.6，2.6 Hz，2H)，2.11(s，3H)，1.15(t，*J* = 7.6 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03

[1964]

P51	深褐色油		ESIMS *m/z* 609([M+H]$^+$)	8.55(s，1H)，8.17- 8.05(m，2H)，7.85- 7.71(m，2H)，7.44- 7.34(m，3H)，7.32- 7.27(m，3H)，7.10- 6.96(m，2H)，5.52(t，*J* = 6.2 Hz，1H)，3.90(s，2H)，3.60- 3.44(m，2H)，2.91(dt，*J* = 23.2，7.0 Hz，3H)，1.25(d，*J* = 6.9 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02
P52	褐色玻璃状泡沫		ESIMS *m/z* 607([M+H]$^+$)	8.64(s，1H)，8.09(d，*J* = 8.2 Hz，2H)，7.95- 7.86(m，2H)，7.84- 7.75(m，2H)，7.32- 7.22(m，4H)，6.85(dd，*J* = 1.8，0.9 Hz，1H)，5.51(t，*J* = 6.2 Hz，1H)，3.92(d，*J* = 1.8 Hz，2H)，3.52(ddt，*J* = 35.1，13.6，6.7 Hz，2H)，2.87(t，*J* = 7.1 Hz，2H)，2.62(dq，*J* = 14.3，7.2 Hz，1H)，2.33(d，*J* = 0.7 Hz，3H)，1.15(dd，*J* = 6.9，2.3 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-62.49
P53	褐色泡沫		ESIMS *m/z* 623([M+H]$^+$)	8.65(s，1H)，8.14- 8.05(m，2H)，7.95- 7.86(m，2H)，7.84- 7.75(m，2H)，7.34- 7.27(m，3H)，6.99(dd，*J* = 8.7，2.7 Hz，1H)，6.56(d，*J* = 2.7 Hz，1H)，5.53(t，*J* = 6.2 Hz，1H)，3.93(d，*J* = 1.7 Hz，2H)，3.77(s，3H)，3.53(ddt，*J* = 29.0，13.7，6.7 Hz，2H)，2.88(t，*J* = 7.1 Hz，2H)，2.60(p，*J* = 6.9 Hz，1H)，1.20- 1.06(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-62.49

[1965]

P57	澄清的粘性油		ESIMS *m/z* 637([M+H]$^+$)	8.55(s，1H)，8.11- 8.05(m，2H)，7.83- 7.76(m，2H)，7.41- 7.34(m，2H)，7.33- 7.21(m，4H)，6.90- 6.77(m，1H)，5.51(t，*J* = 6.2 Hz，1H)，4.10- 4.03(m，1H)，3.64- 3.39(m，2H)，2.87(t，*J* = 7.1 Hz，2H)，2.73- 2.51(m，1H)，2.33(q，*J* = 0.7 Hz，3H)，1.73(dd，*J* = 7.3，4.5 Hz，3H)，1.14(ddd，*J* = 7.1，4.5，2.9 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02
P58	黄色油		ESIMS *m/z* 623([M+H]$^+$)	8.54(d，*J* = 1.2 Hz，1H)，8.06(d，*J* = 8.2 Hz，2H)，7.83- 7.73(m，2H)，7.42- 7.34(m，2H)，7.25(dt，*J* = 8.0，2.1 Hz，3H)，7.19- 7.09(m，1H)，6.87- 6.77(m，1H)，5.18(dt，*J* = 25.9，6.2 Hz，1H)，4.24- 3.93(m，1H)，3.64- 3.26(m，3H)，3.05- 2.63(m，4H)，2.31(d，*J* = 8.5 Hz，3H)，1.26- 1.11(m，9H)	

[1966]

P59	白色固体		ESIMS *m/z* 623([M+H]$^+$)	8.53(d，*J* = 13.4 Hz，1H)，8.13-8.02(m，2H)，7.83- 7.73(m，2H)，7.42- 7.27(m，2H)，7.26- 7.17(m，4H)，7.01(dd，*J* = 59.3，7.4 Hz，1H)，6.86(d，*J* = 1.3 Hz，1H)，4.92(t，*J* = 6.1 Hz，1H)，3.78- 3.63(m，1H)，3.49(td，*J* = 14.1，13.0，6.9 Hz，2H)，3.32(dq，*J* = 13.4，7.0 Hz，1H)，3.07(q，*J* = 6.0 Hz，2H)，2.99-2.73(m，3H)，2.50- 2.26(m，4H)，1.16(dd，*J* = 8.2，6.9 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
P64	白色固体		ESIMS *m/z* 637([M+H]$^+$)	8.55(d，*J* = 1.8 Hz，1H)，8.14(dd，*J* = 8.2，5.4 Hz，1H)，8.06(d，*J* = 8.1 Hz，1H)，7.85- 7.75(m，2H)，7.39(d，*J* = 8.5 Hz，2H)，7.34- 7.25(m，3H)，7.20(dd，*J* = 8.0，3.5 Hz，1H)，7.12-6.81(m，2H)，4.92(d，*J* = 6.4 Hz，1H)，3.71- 3.16(m，5H)，3.08-2.76(m，5H)，2.67- 2.37(m，2H)，2.30(s，3H)，1.22- 1.08(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03

[1967]

P65	橙色固体		ESIMS *m/z* 621([M+H]$^+$)	8.57(s，1H)，8.15- 8.08(m，2H)，7.81(d，*J* = 9.0 Hz，2H)，7.43-7.29(m，5H)，7.23(d，*J* = 1.8 Hz，2H)，7.02- 6.94(m，1H)，6.27(d，*J* = 1.2 Hz，1H)，3.76- 3.62(m，2H)，2.98(q，*J* = 6.5 Hz，2H)，2.80(p，*J* = 6.9 Hz，1H)，2.31(s，3H)，2.21(d，*J* = 1.1 Hz，3H)，1.11(dd，*J* = 19.2，6.9 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
P66，P353	灰白色粉末	122(dec.)	ESIMS *m/z* 651([M+H]$^+$)	8.57- 8.52(m，1H)，8.13- 8.02(m，2H)，7.84- 7.76(m，2H)，7.43-7.36(m，2H)，7.35- 7.29(m，2H)，7.26(s，2H)，6.85(dd，*J* = 15.7，1.8 Hz，1H)，5.25(dd，*J* = 23.9，9.0 Hz，1H)，4.21- 4.03(m，1H)，3.98-3.85(m，2H)，3.08- 2.75(m，1H)，2.63(ddq，*J* = 28.1，14.0，7.0 Hz，1H)，2.39- 2.29(m，3H)，1.36-0.89(m，12H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
P74	白色固体		ESIMS *m/z* 581([M+H]$^+$)，579([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.41(s，1H)，8.13 – 8.06(m，2H)，7.98 – 7.89(m，2H)，7.72 – 7.59(m，3H)，7.43(t，*J* = 7.6 Hz，1H)，7.37 – 7.25(m，4H)，7.21(dt，*J* = 7.5，1.1 Hz，1H)，4.15 – 3.96(m，2H)，3.28(dt，*J* = 8.3，6.6 Hz，2H)，2.86 – 2.74(m，2H)，2.04(s，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.96

[1968]

P75	白色固体		ESIMS *m/z* 595([M+H]$^+$), 593([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.41(s，1H)，8.16 – 8.04(m，2H)，7.99 – 7.87(m，2H)，7.74 – 7.59(m，3H)，7.48 – 7.33(m，3H)，7.34 – 7.24(m，2H)，7.22 – 7.16(m，1H)，4.18 – 3.94(m，2H)，3.27(td，*J* = 7.8，7.2，3.9 Hz，2H)，2.84 – 2.76(m，2H)，2.35(q，*J* = 7.6 Hz，2H)，1.04(t，*J* = 7.6 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.96
P76	白色固体		ESIMS *m/z* 609([M+H]$^+$), 607([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.41(s，1H)，8.14 – 8.04(m，2H)，7.96 – 7.88(m，2H)，7.68 – 7.58(m，3H)，7.47 – 7.37(m，3H)，7.32 – 7.23(m，2H)，7.16(dd，*J* = 7.9，1.3 Hz，1H)，4.16 – 3.94(m，2H)，3.27(q，*J* = 6.9 Hz，2H)，2.84 – 2.75(m，2H)，2.63(p，*J* = 6.8 Hz，1H)，1.10 – 1.03(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.96

[1969]

P80	白色固体		ESIMS *m/z* 623([M+H]$^+$), 621([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.41(s，1H)，8.13 – 8.05(m，2H)，7.98 – 7.89(m，2H)，7.69 – 7.58(m，3H)，7.42(t，*J* = 7.6 Hz，1H)，7.28(dt，*J* = 7.7，1.4 Hz，1H)，7.22(d，*J* = 7.9 Hz，1H)，7.19 – 7.13(m，1H)，7.02 – 6.95(m，1H)，4.15 – 3.93(m，2H)，3.28(dt，*J* = 10.3，7.3 Hz，2H)，2.80(t，*J* = 7.4 Hz，2H)，2.30 – 2.20(m，5H)，1.51 – 1.33(m，2H)，0.79(t，*J* = 7.3 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.97
P81	黄色固体		ESIMS *m/z* 623([M+H]$^+$), 621([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.41(s，1H)，8.12 – 8.05(m，2H)，7.96 – 7.89(m，2H)，7.69 – 7.59(m，3H)，7.41(t，*J* = 7.7 Hz，1H)，7.33 – 7.25(m，2H)，7.23 – 7.18(m，1H)，6.96(dd，*J* = 1.8，0.9 Hz，1H)，4.15 – 3.94(m，2H)，3.27(q，*J* = 6.9 Hz，2H)，2.86 – 2.73(m，2H)，2.63 – 2.53(m，1H)，2.25(s，3H)，1.04(dd，*J* = 6.9，4.8 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.96

[1970]

P83	白色固体		ESIMS *m/z* 609([M+H]$^+$), 607([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.41(s，1H)，8.13 – 8.06(m，2H)，7.97 – 7.88(m，2H)，7.72 – 7.59(m，3H)，7.41(t，*J* = 7.6 Hz，1H)，7.31 – 7.24(m，2H)，7.20 – 7.11(m，2H)，4.15(d，*J* = 1.7 Hz，2H)，3.27(dt，*J* = 8.1，6.2 Hz，2H)，2.84 – 2.75(m，2H)，2.32(q，*J* = 7.6 Hz，2H)，1.99(d，*J* = 0.8 Hz，3H)，1.03(t，*J* = 7.6 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.97
P84	白色固体		ESIMS *m/z* 623([M+H]$^+$), 621([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.41(s，1H)，8.14 – 8.04(m，2H)，7.97 – 7.88(m，2H)，7.68 – 7.59(m，3H)，7.41(t，*J* = 7.6 Hz，1H)，7.27(dt，*J* = 7.7，1.5 Hz，1H)，7.22(d，*J* = 1.8 Hz，1H)，7.09 – 6.99(m，2H)，4.13 – 3.94(m，2H)，3.32 – 3.23(m，2H)，2.85 – 2.75(m，2H)，2.58(p，*J* = 6.8 Hz，1H)，2.32(s，3H)，1.05(dd，*J* = 6.9，3.6 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.97

[1971]

P85	白色固体		ESIMS *m/z* 627([M+H]$^+$), 625([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.41(s，1H)，8.15 – 8.03(m，2H)，7.97 – 7.87(m，2H)，7.69 – 7.58(m，3H)，7.41(t，*J* = 7.6 Hz，1H)，7.32 – 7.22(m，3H)，7.12(td，*J* = 8.4，2.9 Hz，1H)，4.15 – 3.93(m，2H)，3.32 – 3.23(m，2H)，2.85 – 2.76(m，2H)，2.61(tt，*J* = 7.6，3.8 Hz，1H)，1.09 – 1.02(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.97，-112.11
P87	白色固体		ESIMS *m/z* 611([M+H]$^+$), 609([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.41(s，1H)，8.17 – 8.02(m，2H)，7.99 – 7.88(m，2H)，7.71 – 7.57(m，3H)，7.47 – 7.39(m，1H)，7.29(dt，*J* = 7.7，1.4 Hz，1H)，7.10(d，*J* = 8.6 Hz，1H)，6.90 – 6.86(m，1H)，6.83(ddd，*J* = 8.7，2.8，0.7 Hz，1H)，4.13 – 3.92(m，2H)，3.76(s，3H)，3.28(td，*J* = 8.1，7.1，4.4 Hz，2H)，2.86 – 2.76(m，2H)，1.99(s，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.97
P92	淡黄色固体		ESIMS *m/z* 595([M+H]$^+$), 593([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.38(s，1H)，8.13 – 8.04(m，2H)，8.04 – 7.97(m，2H)，7.68 – 7.57(m，3H)，7.41 – 7.27(m，5H)，7.27 – 7.16(m，1H)，4.16 – 3.95(m，2H)，3.10 – 2.95(m，2H)，2.60(t，*J* = 7.7 Hz，2H)，2.08(s，3H)，1.72(p，*J* = 7.1 Hz，2H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.96

[1972]

P93	淡黄色固体		ESIMS *m/z* 609([M+H]$^+$), 607([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.38(s，1H)，8.11 – 8.04(m，2H)，8.04 – 7.97(m，2H)，7.66 – 7.58(m，3H)，7.45 – 7.37(m，2H)，7.37 – 7.27(m，3H)，7.22(dt，*J* = 7.9，1.0 Hz，1H)，4.17 – 3.95(m，2H)，3.04(dp，*J* = 16.0，6.4 Hz，2H)，2.59(t，*J* = 7.7 Hz，2H)，2.39(q，*J* = 7.6 Hz，2H)，1.82 – 1.64(m，2H)，1.10(td，*J* = 7.3，1.9 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.97
P94	黄色固体		ESIMS *m/z* 623([M+H]$^+$), 621([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.38(s，1H)，8.12 – 8.04(m，2H)，8.04 – 7.97(m，2H)，7.67 – 7.57(m，3H)，7.51 – 7.39(m，2H)，7.35 – 7.26(m，3H)，7.19(dd，*J* = 7.8，1.4 Hz，1H)，4.22 – 3.93(m，2H)，3.04(p，*J* = 6.7 Hz，2H)，2.68(p，*J* = 6.8 Hz，1H)，2.59(dd，*J* = 8.6，6.8 Hz，2H)，1.81 – 1.62(m，2H)，1.18 – 1.06(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.97

[1973]

P99	淡黄色固体		ESIMS *m/z* 637([M+H]$^+$), 635([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.38(s，1H)，8.13 – 8.04(m，2H)，8.04 – 7.97(m，2H)，7.68 – 7.57(m，3H)，7.39 – 7.29(m，2H)，7.25(d，*J* = 7.9 Hz，1H)，7.22 – 7.15(m，1H)，7.06 – 6.98(m，1H)，4.20 – 3.93(m，2H)，3.04(p，*J* = 6.8 Hz，2H)，2.59(dd，*J* = 8.6，6.7 Hz，2H)，2.28(d，*J* = 10.1 Hz，5H)，1.72(p，*J* = 7.2 Hz，2H)，1.48(qd，*J* = 7.4，1.9 Hz，2H)，0.84(t，*J* = 7.3 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.97
P101	淡黄色固体		ESIMS *m/z* 623([M+H]$^+$), 621([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.38(s，1H)，8.14 – 8.04(m，2H)，8.04 – 7.98(m，2H)，7.71 – 7.59(m，3H)，7.38 – 7.27(m，3H)，7.25 – 7.17(m，2H)，4.16(d，*J* = 1.0 Hz，2H)，3.04(q，*J* = 6.6 Hz，2H)，2.60(t，*J* = 7.7 Hz，2H)，2.36(q，*J* = 7.6 Hz，2H)，2.05(s，3H)，1.73(t，*J* = 7.4 Hz，2H)，1.09(t，*J* = 7.6 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.96

[1974]

P102	黄色固体		ESIMS *m/z* 637([M+H]$^+$), 635([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.38(s，1H)，8.13 – 8.04(m，2H)，8.04 – 7.96(m，2H)，7.67 – 7.57(m，3H)，7.37 – 7.29(m，2H)，7.27(d，*J* = 1.9 Hz，1H)，7.13 – 7.01(m，2H)，4.17 – 3.91(m，2H)，3.04(p，*J* = 6.7 Hz，2H)，2.60(dt，*J* = 15.4，7.4 Hz，3H)，2.34(s，3H)，1.72(p，*J* = 7.1 Hz，2H)，1.16 – 1.06(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.97
P103	淡黄色固体		ESIMS *m/z* 641([M+H]$^+$), 639([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.38(s，1H)，8.15 – 8.04(m，2H)，8.04 – 7.98(m，2H)，7.71 – 7.59(m，3H)，7.37 – 7.25(m，4H)，7.15(td，*J* = 8.4，2.9 Hz，1H)，4.18 – 3.92(m，2H)，3.04(dq，*J* = 13.2，6.6 Hz，2H)，2.75 – 2.54(m，3H)，1.72(p，*J* = 7.1 Hz，2H)，1.13 – 1.05(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.97，-112.12
P105	淡黄色固体		ESIMS *m/z* 625([M+H]$^+$), 623([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.38(s，1H)，8.14 – 8.04(m，2H)，8.04 – 7.96(m，2H)，7.71 – 7.55(m，3H)，7.38 – 7.29(m，2H)，7.13(d，*J* = 8.6 Hz，1H)，6.92(d，*J* = 2.9 Hz，1H)，6.85(dd，*J* = 8.6，2.9 Hz，1H)，4.12 – 3.93(m，2H)，3.78(s，3H)，3.16 – 2.93(m，2H)，2.60(t，*J* = 7.6 Hz，2H)，2.04(s，3H)，1.80 – 1.63(m，2H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.97

[1975]

P118	灰白色固体		ESIMS *m/z* 595([M+H]$^+$), 593([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(s，1H)，8.13 – 8.04(m，2H)，7.92(dd，*J* = 7.1，1.4 Hz，2H)，7.68 – 7.58(m，3H)，7.46 – 7.39(m，1H)，7.39 – 7.27(m，4H)，7.27 – 7.20(m，1H)，4.17 – 3.94(m，2H)，3.16 – 2.96(m，2H)，2.63(t，*J* = 7.7 Hz，2H)，2.09(s，3H)，1.74(p，*J* = 7.3 Hz，2H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.96
P119	灰白色固体		ESIMS *m/z* 609([M+H]$^+$), 607([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(s，1H)，8.14 – 8.04(m，2H)，7.92(dd，*J* = 6.3，1.4 Hz，2H)，7.68 – 7.56(m，3H)，7.47 – 7.37(m，3H)，7.37 – 7.26(m，2H)，7.22(d，*J* = 7.8 Hz，1H)，4.21 – 3.92(m，2H)，3.16 – 2.96(m，2H)，2.62(t，*J* = 7.7 Hz，2H)，2.40(q，*J* = 7.6 Hz，2H)，1.74(p，*J* = 7.1 Hz，2H)，1.10(t，*J* = 7.3，2.7 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.97

[1976]

P120	灰白色固体		ESIMS *m/z* 623([M+H]$^+$), 621([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(s，1H)，8.16 – 8.04(m，2H)，7.92(tt，*J* = 3.1，1.4 Hz，2H)，7.69 – 7.58(m，3H)，7.48(dd，*J* = 7.9，1.6 Hz，1H)，7.46 – 7.38(m，2H)，7.30(td，*J* = 7.5，1.6 Hz，2H)，7.20(dd，*J* = 7.8，1.4 Hz，1H)，4.21 – 3.93(m，2H)，3.06(qd，*J* = 6.8，3.5 Hz，2H)，2.65(dt，*J* = 26.1，7.3 Hz，3H)，1.73(p，*J* = 7.3 Hz，2H)，1.09(dt，*J* = 7.0，3.6 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.97
P124	灰白色固体		ESIMS *m/z* 637([M+H]$^+$), 635([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(s，1H)，8.14 – 8.02(m，2H)，7.92(tt，*J* = 3.1，1.4 Hz，2H)，7.70 – 7.56(m，3H)，7.42(t，*J* = 7.8 Hz，1H)，7.35(d，*J* = 8.0 Hz，1H)，7.29(dt，*J* = 7.8，1.5 Hz，1H)，7.23(dd，*J* = 8.1，1.9 Hz，1H)，6.99(dd，*J* = 1.9，0.9 Hz，1H)，4.20 – 3.92(m，2H)，3.06(qd，*J* = 6.9，3.3 Hz，2H)，2.71 – 2.54(m，3H)，2.29(s，3H)，1.85 – 1.62(m，2H)，1.16 – 1.03(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.97

[1977]

P125	白灰色固体		ESIMS *m/z* 637([M+H]$^+$), 635([M-H]$^-$)	^{1}H NMR(400 MHz, DMSO-d_6)δ 9.40(s, 1H), 8.15 – 8.03(m, 2H), 7.92(dt, *J* = 5.8, 1.6 Hz, 2H), 7.69 – 7.57(m, 3H), 7.42(dd, *J* = 8.3, 7.6 Hz, 1H), 7.30(dt, *J* = 7.6, 1.5 Hz, 1H), 7.25(d, *J* = 7.9 Hz, 1H), 7.19(ddd, *J* = 7.8, 1.9, 0.8 Hz, 1H), 7.02(dd, *J* = 1.8, 0.9 Hz, 1H), 4.20 – 3.89(m, 2H), 3.06(ddd, *J* = 12.1, 6.9, 4.9 Hz, 2H), 2.62(t, *J* = 7.7 Hz, 2H), 2.29(d, *J* = 2.9 Hz, 5H), 1.74(p, *J* = 7.3 Hz, 2H), 1.57 – 1.39(m, 2H), 0.84(t, *J* = 7.3 Hz, 3H)	^{19}F NMR(376 MHz, $CDCl_3$)δ-56.97
P127	白灰色固体		ESIMS *m/z* 623([M+H]$^+$), 621([M-H]$^-$)	^{1}H NMR(400 MHz, DMSO-d_6)δ 9.40(s, 1H), 8.12 – 8.05(m, 2H), 7.96 – 7.89(m, 2H), 7.71 – 7.58(m, 3H), 7.41(dd, *J* = 8.6, 7.3 Hz, 1H), 7.30(t, *J* = 7.5 Hz, 2H), 7.25 – 7.17(m, 2H), 4.15(d, *J* = 1.0 Hz, 2H), 3.06(q, *J* = 6.7 Hz, 2H), 2.63(t, *J* = 7.7 Hz, 2H), 2.36(q, *J* = 7.5 Hz, 2H), 2.05(s, 3H), 1.82 – 1.65(m, 2H), 1.09(t, *J* = 7.3, 3.2 Hz, 3H)	^{19}F NMR(376 MHz, $CDCl_3$)δ-56.97

[1978]

P128	灰白色固体		ESIMS *m/z* 637([M+H]$^+$), 635([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(s，1H)，8.14 – 8.04(m，2H)，7.92(dp，*J* = 5.2，1.6 Hz，2H)，7.69 – 7.56(m，3H)，7.42(t，*J* = 7.9 Hz，1H)，7.33 – 7.23(m，2H)，7.14 – 7.01(m，2H)，4.17 – 3.92(m，2H)，3.05(qd，*J* = 6.9，3.5 Hz，2H)，2.68 – 2.56(m，3H)，2.34(s，3H)，1.80 – 1.65(m，2H)，1.16 – 1.08(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.97
P129	灰白色固体		ESIMS *m/z* 641([M+H]$^+$), 639([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(s，1H)，8.15 – 8.04(m，2H)，7.92(tt，*J* = 3.1，1.4 Hz，2H)，7.69 – 7.58(m，3H)，7.42(t，*J* = 7.8 Hz，1H)，7.37 – 7.25(m，3H)，7.15(ddd，*J* = 8.7，8.1，2.9 Hz，1H)，4.18 – 3.91(m，2H)，3.06(qd，*J* = 6.9，3.4 Hz，2H)，2.73 – 2.56(m，3H)，1.83 – 1.64(m，2H)，1.17 – 1.05(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.97，-112.13

[1979]

P131	白灰色固体		ESIMS *m/z* 625([M+H]$^+$), 623([M-H]$^-$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(s，1H)，8.13 – 8.05(m，2H)，7.93(dd，*J* = 7.3，1.4 Hz，2H)，7.69 – 7.58(m，3H)，7.42(td，*J* = 7.4，1.0 Hz，1H)，7.30(dt，*J* = 7.6，1.5 Hz，1H)，7.13(d，*J* = 8.6 Hz，1H)，6.92(dd，*J* = 2.8，0.8 Hz，1H)，6.86(ddd，*J* = 8.7，3.0，0.7 Hz，1H)，4.16 – 3.91(m，2H)，3.39(q，*J* = 7.0 Hz，1H)，3.34(s，2H)，3.16 – 2.96(m，2H)，2.64(dd，*J* = 8.7，6.7 Hz，2H)，2.04(s，3H)，1.74(p，*J* = 7.3 Hz，2H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.97
P144	白色泡沫		ESIMS *m/z* 609([M+H]$^+$)	8.54(s，1H)，8.08(d，*J* = 8.1 Hz，2H)，7.85- 7.75(m，2H)，7.42-7.36(m，3H)，7.36- 7.28(m，3H)，7.26(s，1H)，7.13- 7.07(m，1H)，5.39(s，1H)，4.00- 3.82(m，2H)，3.25(qd，*J* = 6.9，4.2 Hz，2H)，2.67(t，*J* = 7.5 Hz，2H)，2.15(s，3H)，1.77-1.61(m，2H)，1.52(d，*J* = 0.5 Hz，2H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02

[1980]

P145	白色固体	82-88	ESIMS *m/z* 623([M+H]$^+$)	8.54(s，1H)，8.08(d，*J* = 8.2 Hz，2H)，7.83- 7.76(m，2H)，7.47- 7.35(m，5H)，7.32(td，*J* = 7.4，2.0 Hz，1H)，7.24(s，1H)，7.07(dd，*J* = 7.8，1.3 Hz，1H)，5.39(t，*J* = 6.1 Hz，1H)，3.98- 3.81(m，2H)，3.36- 3.09(m，*J* = 6.8 Hz，2H)，2.66(t，*J* = 7.5 Hz，2H)，2.45(qd，*J* = 7.6，1.8 Hz，2H)，1.75- 1.61(m，2H)，1.52(s，2H)，1.17(t，*J* = 7.6 Hz，3H)	
P146	白色固体	89-92	ESIMS *m/z* 637([M+H]$^+$)	8.54(s，1H)，8.11- 8.05(m，2H)，7.84- 7.76(m，2H)，7.47- 7.42(m，2H)，7.38(dt，*J* = 8.0，1.0 Hz，2H)，7.30(ddd，*J* = 7.9，5.6，3.2 Hz，1H)，7.25- 7.22(m，2H)，7.07- 7.01(m，1H)，5.38(t，*J* = 6.0 Hz，1H)，4.04- 3.81(m，2H)，3.33- 3.16(m，2H)，2.67(dt，*J* = 10.3，7.2 Hz，3H)，1.73- 1.60(m，2H)，1.60- 1.46(m，2H)，1.17(dd，*J* = 6.9，3.2 Hz，6H)	

[1981]

P150	白色固体	100-105	ESIMS *m/z* 651([M+H]$^+$)	8.55(s，1H)，8.11- 8.05(m，2H)，7.83-7.76(m，2H)，7.39(dd，*J* = 9.0，0.9 Hz，2H)，7.33(d，*J* = 8.0 Hz，1H)，7.26(s，3H)，6.86(dd，*J* = 1.9，0.9 Hz，1H)，5.43(t，*J* = 6.1 Hz，1H)，4.02-3.82(m，2H)，3.34- 3.16(m，*J* = 6.6 Hz，2H)，2.65(dt，*J* = 10.6，7.1 Hz，3H)，2.35(s，3H)，1.75- 1.60(m，2H)，1.60- 1.47(m，2H)，1.21- 1.07(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
P151	白色固体	78-82	ESIMS *m/z* 651([M+H]$^+$)	8.54(s，1H)，8.12- 8.05(m，2H)，7.84-7.75(m，2H)，7.41- 7.35(m，2H)，7.24(d，*J* = 3.8 Hz，3H)，7.22-7.17(m，1H)，6.90- 6.85(m，1H)，5.41(t，*J* = 6.1 Hz，1H)，3.97- 3.80(m，2H)，3.36- 3.13(m，2H)，2.67(t，*J* = 7.5 Hz，2H)，2.42- 2.23(m，5H)，1.75- 1.61(m，2H)，1.61- 1.48(m，4H)，0.89(t，*J* = 7.3 Hz，3H)	
P152	白色固体		ESIMS *m/z* 623([M+H]$^+$)	8.54(s，1H)，8.08(d，*J* = 8.1 Hz，2H)，7.84- 7.76(m，2H)，7.42-7.34(m，1H)，7.26(s，4H)，7.20-7.12(m，2H)，5.40(s，1H)，3.92(s，2H)，3.25(q，*J* = 6.8 Hz，2H)，2.67(t，*J* = 7.5 Hz，2H)，2.12(d，*J* = 0.7 Hz，6H)，1.66(q，*J* = 7.7 Hz，2H)，1.52(s，2H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02

[1982]

P153	白色泡沫		ESIMS *m/z* 637([M+H]$^+$)	8.54(s，1H)，8.12- 8.05(m，2H)，7.84- 7.74(m，2H)，7.43- 7.36(m，2H)，7.32(t，*J* = 7.6 Hz，1H)，7.24(s，1H)，7.18(dd，*J* = 15.3，7.6 Hz，3H)，5.40(s，1H)，3.92(s，2H)，3.25(q，*J* = 6.7 Hz，2H)，2.67(t，*J* = 7.5 Hz，2H)，2.42(dt，*J* = 8.9，7.4 Hz，2H)，2.11(s，3H)，1.66(p，*J* = 7.4 Hz，2H)，1.59- 1.47(m，2H)，1.16(t，*J* = 7.6 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02
P154	白色固体	101-108	ESIMS *m/z* 651([M+H]$^+$)	8.54(s，1H)，8.12- 8.04(m，2H)，7.84- 7.75(m，2H)，7.43- 7.35(m，2H)，7.25- 7.21(m，3H)，7.11(ddd，*J* = 8.1，2.0，0.8 Hz，1H)，6.92(d，*J* = 8.0 Hz，1H)，5.40(t，*J* = 6.1 Hz，1H)，3.97- 3.79(m，2H)，3.37- 3.16(m，2H)，2.65(q，*J* = 7.1 Hz，2H)，2.40(s，3H)，1.73- 1.59(m，2H)，1.52(s，3H)，1.16(dd，*J* = 6.9，2.7 Hz，6H)	
P155	白色固体		ESIMS *m/z* 655([M+H]$^+$)	8.55(s，1H)，8.12- 8.05(m，2H)，7.84- 7.75(m，2H)，7.44- 7.35(m，2H)，7.30- 7.21(m，2H)，7.11(dd，*J* = 9.9，2.6 Hz，1H)，7.08- 6.94(m，2H)，5.40(t，*J* = 6.1 Hz，1H)，4.00- 3.81(m，2H)，3.37- 3.16(m，2H)，2.67(t，*J* = 7.3 Hz，3H)，1.65(q，*J* = 7.8 Hz，2H)，1.55(s，2H)，1.16(dd，*J* = 6.9，5.1 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03，-110.71

[1983]

P156	白色固体		ESIMS *m/z* 667([M+H]$^+$)	8.55(s，1H)，8.12- 8.04(m，2H)，7.85-7.71(m，2H)，7.42- 7.36(m，1H)，7.34(d，*J* = 8.7 Hz，1H)，7.26(s，3H)，7.01(dd，*J* = 8.7，2.7 Hz，1H)，6.57(d，*J* = 2.7 Hz，1H)，5.44(t，*J* = 6.1 Hz，1H)，3.98- 3.85(m，2H)，3.79(s，3H)，3.26(hept，*J* = 6.7 Hz，2H)，2.66(t，*J* = 7.5 Hz，2H)，2.63-2.56(m，1H)，1.65(q，*J* = 7.6 Hz，2H)，1.56(s，2H)，1.14(dd，*J* = 6.9，4.4 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
P159	白色固体.	110-117	ESIMS *m/z* 635([M+H]$^+$)	8.64(s，1H)，8.09(d，*J* = 8.2 Hz，2H)，7.94- 7.88(m，2H)，7.83-7.76(m，2H)，7.33(d，*J* = 8.0 Hz，1H)，7.28- 7.23(m，3H)，6.89-6.83(m，1H)，5.44(t，*J* = 6.1 Hz，1H)，4.00- 3.80(m，2H)，3.41-3.15(m，2H)，2.77- 2.53(m，3H)，2.44- 2.28(m，3H)，1.71- 1.61(m，2H)，1.59- 1.50(m，2H)，1.15(d，*J* = 6.9 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-62.48

[1984]

P160	黄色固体	107-113	ESIMS *m/z* 647([M+H]$^+$)	8.57(s，1H)，8.13- 8.08(m，2H)，7.83-7.77(m，2H)，7.47- 7.42(m，2H)，7.39(dt，*J* = 8.0，1.0 Hz，2H)，7.33(d，*J* = 8.0 Hz，1H)，7.26(s，1H)，6.89-6.85(m，1H)，5.78(t，*J* = 6.2 Hz，1H)，4.01- 3.82(m，2H)，3.47(qd，*J* = 6.6，3.2 Hz，2H)，2.64(dq，*J* = 10.9，6.4 Hz，3H)，2.34(s，3H)，1.21- 1.09(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02
P170	白色固体		ESIMS *m/z* 609([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(s，1H)，8.13 – 8.05(m，2H)，7.92(dt，*J* = 6.5，1.5 Hz，2H)，7.68 – 7.60(m，2H)，7.57(t，*J* = 5.9 Hz，1H)，7.46 – 7.37(m，1H)，7.37 – 7.25(m，4H)，7.25 – 7.17(m，1H)，4.13 – 3.92(m，2H)，3.04(dp，*J* = 19.5，6.5 Hz，2H)，2.65(t，*J* = 7.6 Hz，2H)，2.06(s，3H)，1.64 – 1.50(m，2H)，1.50 – 1.37(m，2H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.96

[1985]

P171	白色固体		ESIMS *m/z* 623([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(s，1H)，8.13 – 8.05(m，2H)，7.92(ddt，*J* = 5.2，2.9，1.7 Hz，2H)，7.68 – 7.60(m，2H)，7.56(t，*J* = 5.9 Hz，1H)，7.46 – 7.35(m，3H)，7.34 – 7.25(m，2H)，7.20(dt，*J* = 7.8，0.9 Hz，1H)，4.15 – 3.93(m，2H)，3.03(dp，*J* = 16.6，6.5 Hz，2H)，2.64(t，*J* = 7.6 Hz，2H)，2.37(q，*J* = 7.6 Hz，2H)，1.54(q，*J* = 7.7 Hz，2H)，1.49 – 1.37(m，2H)，1.07(t，*J* = 7.6 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.96
P172	白色固体		ESIMS *m/z* 637([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(s，1H)，8.13 – 8.04(m，2H)，7.91(tt，*J* = 3.2，1.5 Hz，2H)，7.63(ddt，*J* = 7.9，1.9，1.0 Hz，2H)，7.55(t，*J* = 5.8 Hz，1H)，7.47 – 7.37(m，3H)，7.32 – 7.24(m，2H)，7.17(dd，*J* = 7.9，1.4 Hz，1H)，4.14 – 3.93(m，2H)，3.03(qd，*J* = 6.8，2.3 Hz，2H)，2.64(td，*J* = 7.3，4.2 Hz，3H)，1.63 – 1.48(m，2H)，1.49 – 1.37(m，2H)，1.13 – 1.05(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.96

[1986]

P176	白色固体		ESIMS *m/z* 651([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(s，1H)，8.14 – 8.04(m，2H)，7.92(dt，J = 3.9，1.7 Hz，2H)，7.67 – 7.60(m，2H)，7.57(t，J = 5.9 Hz，1H)，7.41(t，J = 7.8 Hz，1H)，7.36 – 7.26(m，2H)，7.21(dd，J = 8.2，1.8 Hz，1H)，7.00 – 6.95(m，1H)，4.12 – 3.92(m，2H)，3.03(q，J = 7.4，7.0 Hz，2H)，2.61(dt，J = 17.5，7.2 Hz，3H)，2.26(s，3H)，1.66 – 1.49(m，2H)，1.49 – 1.37(m，2H)，1.10 – 1.01(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.97
P179	白色固体		ESIMS *m/z* 637([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(s，1H)，8.13 – 8.05(m，2H)，7.97 – 7.87(m，2H)，7.68 – 7.55(m，3H)，7.41(dd，J = 8.2，7.6 Hz，1H)，7.28(ddd，J = 7.4，4.4，2.8 Hz，2H)，7.22 – 7.14(m，2H)，4.14(d，J = 1.0 Hz，2H)，3.03(q，J = 6.6 Hz，2H)，2.64(t，J = 7.5 Hz，2H)，2.34(q，J = 7.5 Hz，2H)，2.02(s，3H)，1.62 – 1.49(m，2H)，1.50 – 1.37(m，2H)，1.08 – 1.02(m，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.96

[1987]

P180	白色固体		ESIMS *m/z* 651([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(s，1H)，8.13 – 8.06(m，2H)，7.92(dp，*J* = 5.1，1.6 Hz，2H)，7.68 – 7.60(m，2H)，7.55(t，*J* = 5.9 Hz，1H)，7.45 – 7.37(m，1H)，7.28(dt，*J* = 7.7，1.5 Hz，1H)，7.26 – 7.20(m，1H)，7.09 – 7.00(m，2H)，4.13 – 3.91(m，2H)，3.10 – 2.96(m，2H)，2.61(dt，*J* = 16.9，7.1 Hz，3H)，2.32(s，3H)，1.63 – 1.48(m，2H)，1.48 – 1.37(m，2H)，1.11 – 1.02(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.97
P181	白色固体		ESIMS *m/z* 655([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(s，1H)，8.12 – 8.05(m，2H)，7.96 – 7.89(m，2H)，7.63(dp，*J* = 7.7，0.9 Hz，2H)，7.56(t，*J* = 5.9 Hz，1H)，7.46 – 7.37(m，1H)，7.33 – 7.23(m，3H)，7.12(td，*J* = 8.4，2.9 Hz，1H)，4.14 – 3.91(m，2H)，3.11 – 2.96(m，2H)，2.72 – 2.56(m，3H)，1.55(dq，*J* = 12.1，7.7，6.9 Hz，2H)，1.44(q，*J* = 7.6，7.2 Hz，2H)，1.12 – 1.03(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.96，-112.17

[1988]

P182	白色固体		ESIMS *m/z* 667([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(s，1H)，8.13 – 8.05(m，2H)，7.92(dt，*J* = 4.0，1.8 Hz，2H)，7.60(dd，*J* = 21.0，7.3 Hz，3H)，7.41(t，*J* = 7.9 Hz，1H)，7.36 – 7.25(m，2H)，6.98(dd，*J* = 8.7，2.8 Hz，1H)，6.80(d，*J* = 2.7 Hz，1H)，4.13 – 3.89(m，2H)，3.71(s，3H)，3.03(q，*J* = 7.5，6.8 Hz，2H)，2.60(dt，*J* = 28.9，7.1 Hz，3H)，1.65 – 1.49(m，2H)，1.43(dq，*J* = 13.4，7.0 Hz，2H)，1.05(dd，*J* = 16.4，6.8 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-56.96
P205	褐色固体		ESIMS *m/z* 623([M+H]$^+$)	8.55(s，1H)，8.13- 8.03(m，2H)，7.85- 7.75(m，2H)，7.47- 7.35(m，4H)，7.30- 7.23(m，3H)，7.01(ddt，*J* = 7.6，6.7，0.7 Hz，1H)，5.39(s，1H)，3.97- 3.87(m，2H)，3.65- 2.94(m，3H)，2.74- 2.56(m，1H)，1.28(dd，*J* = 6.9，1.5 Hz，3H)，1.21- 1.07(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
P209	褐色泡沫		ESIMS *m/z* 637([M+H]$^+$)	8.55(s，1H)，8.11- 8.04(m，2H)，7.83- 7.74(m，2H)，7.43- 7.35(m，4H)，7.29- 7.18(m，3H)，7.00(tt，*J* = 8.1，1.1 Hz，1H)，5.32(d，*J* = 16.6 Hz，1H)，3.94- 3.85(m，2H)，3.79- 3.54(m，1H)，3.27(dddd，*J* = 53.3，13.9，9.0，5.2 Hz，1H)，2.82- 2.56(m，2H)，1.82- 1.56(m，2H)，1.19- 1.02(m，6H)，0.86- 0.74(m，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02

[1989]

P364	粉红色固体		ESIMS *m/z* 651([M+H]$^+$)	8.56(s，1H)，8.08(dd，*J* = 8.2，6.4 Hz，2H)，7.84- 7.76(m，2H)，7.39(dq，*J* = 7.7，1.1 Hz，2H)，7.26(s，4H)，6.81(d，*J* = 7.6 Hz，1H)，5.35(d，*J* = 5.7 Hz，1H)，3.94- 3.84(m，2H)，3.67(ddt，*J* = 49.5，13.1，6.5 Hz，1H)，3.39- 3.15(m，1H)，2.80- 2.53(m，2H)，2.30(dt，*J* = 4.4，0.7 Hz，3H)，1.80- 1.56(m，2H)，1.10(ddd，*J* = 18.9，10.4，6.8 Hz，6H)，0.81(t，*J* = 7.3 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02
P679	褐色固体		ESIMS *m/z* 653([M+H]$^+$)	8.55(s，1H)，8.13- 8.03(m，2H)，7.86- 7.72(m，2H)，7.39(ddd，*J* = 8.0，1.8，0.9 Hz，2H)，7.32- 7.26(m，3H)，6.97(ddd，*J* = 8.8，4.4，2.7 Hz，1H)，6.53(dd，*J* = 6.4，2.7 Hz，1H)，5.49- 5.28(m，1H)，3.91(t，*J* = 1.4 Hz，2H)，3.75(d，*J* = 3.1 Hz，3H)，3.69- 3.20(m，2H)，3.02(dt，*J* = 13.9，6.9 Hz，1H)，2.57(h，*J* = 7.0 Hz，1H)，1.29(dd，*J* = 7.1，1.5 Hz，3H)，1.16- 1.04(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03

[1990]

P683	褐色泡沫		ESIMS *m/z* 667([M+H]$^+$)	8.55(s，1H)，8.13- 8.02(m，2H)，7.83- 7.76(m，2H)，7.42- 7.34(m，2H)，7.31- 7.19(m，3H)，6.95(ddd，*J* = 8.5，5.4，2.7 Hz，1H)，6.52(dd，*J* = 7.9，2.7 Hz，1H)，5.38(s，1H)，3.90(t，*J* = 1.6 Hz，2H)，3.79- 3.57(m，4H)，3.28(dddd，*J* = 52.9，13.9，9.0，5.2 Hz，1H)，2.81- 2.47(m，2H)，1.81- 1.55(m，2H)，1.15- 1.00(m，6H)，0.81(t，*J* = 7.3 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02
P1163	褐色泡沫		ESIMS *m/z* 655([M+H]$^+$)	8.56(s，1H)，8.12- 8.05(m，2H)，7.84- 7.77(m，2H)，7.43- 7.36(m，2H)，7.26- 7.18(m，2H)，7.05(ddd，*J* = 9.9，4.8，2.5 Hz，1H)，7.01- 6.89(m，2H)，5.29(t，*J* = 6.2 Hz，1H)，3.95- 3.85(m，2H)，3.81- 3.57(m，1H)，3.27(dddd，*J* = 46.1，13.9，9.1，5.1 Hz，1H)，2.81- 2.50(m，2H)，1.67(ddd，*J* = 56.8，15.2，8.0 Hz，2H)，1.18- 0.97(m，6H)，0.82(t，*J* = 7.3 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02，-110.70，-110.72

[1991] [a]除非另外指明，否则所有^{1}H NMR数据在$CDCl_3$中于400MHz测量。

[1992] 表3c：对于表2c中的化合物的分析数据

[1993]

编号	**外观**	**Mp (°C)**	**ESIMS** *m/z*	^{1}H NMR**(δ)**[a]	^{13}**C NMR** 或 ^{19}F NMR(δ)

[1994]

FB1	白色固体		ESIMS *m/z* 596 $[M]^+$	^{1}H NMR(400 MHz，$CDCl_3$)δ 11.84(s，1H)，9.72(s，1H)，8.54(s，1H)，7.99(s，1H)，7.95(d，*J* = 8.8 Hz，2H)，7.82- 7.74(m，4H)，7.37(ddd，*J* = 9.0，2.1，1.0 Hz，4H)，3.45-3.31(m，2H)，3.09(dt，*J* = 22.4，6.8 Hz，1H)，2.91(t，*J* = 7.3 Hz，2H)，2.42(s，3H)，2.32(d，*J* = 0.8 Hz，3H)，1.26- 1.18(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
FB2	黄色固体		ESIMS *m/z* 612 $[M]^+$	^{1}H NMR(400 MHz，$CDCl_3$)δ 11.97(s，1H)，10.39- 9.51(m，2H)，8.54(s，1H)，7.99-7.90(m，3H)，7.81- 7.75(m，3H)，7.37(ddd，*J* = 7.8，2.1，1.0 Hz，3H)，7.24(s，1H)，3.77(s，3H)，3.36(q，*J* = 6.7 Hz，2H)，3.04(p，*J* = 6.7 Hz，1H)，2.90(t，*J* = 7.3 Hz，2H)，2.41(s，3H)，1.23(t，*J* = 6.6 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
FB3	黄色蜡		ESIMS *m/z* 636 $[M]^+$	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.55(s，1H)，7.96(d，*J* = 1.8 Hz，1H)，7.93- 7.88(m，1H)，7.80(d，*J* = 9.0 Hz，2H)，7.41- 7.36(m，3H)，7.31(d，*J* = 8.0 Hz，1H)，7.19(d，*J* = 7.9 Hz，1H)，6.85(d，*J* = 1.8 Hz，1H)，5.56(t，*J* = 6.3 Hz，1H)，3.92(d，*J* = 2.2 Hz，2H)，3.58-3.36(m，2H)，2.87(t，*J* = 7.2 Hz，2H)，2.64(p，*J* = 6.8 Hz，1H)，2.38(s，3H)，2.36- 2.31(m，3H)，1.16(d，*J* = 6.9 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03

[1995]

FB4	淡黄色固体		ESIMS *m/z* 652 $[M]^+$	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.54(s，1H)，7.99- 7.95(m，1H)，7.90(ddd，*J* = 7.7，2.0，0.7 Hz，1H)，7.79(d，*J* = 9.0 Hz，2H)，7.38(dt，*J* = 8.0，1.0 Hz，2H)，7.32(d，*J* = 8.8 Hz，1H)，7.19(d，*J* = 7.9 Hz，1H)，6.99(dd，*J* = 8.7，2.7 Hz，1H)，6.56(d，*J* = 2.7 Hz，1H)，5.57(t，*J* = 6.3 Hz，1H)，3.93(d，*J* = 2.0 Hz，2H)，3.77(s，3H)，3.48(dp，*J* = 25.0，6.9 Hz，2H)，2.87(t，*J* = 7.2 Hz，2H)，2.61(p，*J* = 6.8 Hz，1H)，2.38(s，3H)，1.14(dd，*J* = 6.9，3.5 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
FB5	黄色固体		ESIMS *m/z* 568 $[M]^+$	^{1}H NMR(400 MHz，$CDCl_3$)δ 11.99(s，1H)，10.16(s，1H)，8.53(d，*J* = 2.6 Hz，1H)，7.95(ddd，*J* = 14.0，7.1，1.7 Hz，2H)，7.80-7.73(m，2H)，7.40- 7.32(m，5H)，7.25-7.15(m，3H)，3.50(q，*J* = 6.8 Hz，1H)，3.37(dd，*J* = 7.5，5.7 Hz，1H)，2.95- 2.86(m，1H)，2.83(t，*J* = 6.9 Hz，1H)，2.65(q，*J* = 7.5 Hz，2H)，2.40(s，3H)，1.27- 1.16(m，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03

[1996]

FB6	粉红色固体		ESIMS *m/z* 608 $[M]^+$	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.55(s，1H)，7.99- 7.95(m，1H)，7.94- 7.88(m，1H)，7.83- 7.75(m，2H)，7.43- 7.35(m，4H)，7.33- 7.28(m，1H)，7.20(d，*J* = 7.9 Hz，1H)，7.07(dd，*J* = 7.8，1.3 Hz，1H)，5.55(t，*J* = 6.2 Hz，1H)，3.93(d，*J* = 1.6 Hz，2H)，3.47(ddd，*J* = 11.0，7.0，3.4 Hz，2H)，2.92- 2.83(m,2H)，2.51- 2.41(m，2H)，2.38(s，3H)，1.18(t，*J* = 7.6 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
FB7	粉红色固体		ESIMS *m/z* 658 $[M]^+$	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.54(d，*J* = 3.2 Hz，1H)，8.00- 7.89(m，2H)，7.82- 7.74(m，2H)，7.41- 7.34(m，4H)，7.21(dd，*J* = 14.3，7.9 Hz，1H)，7.06(d，*J* = 2.1 Hz，1H)，5.54(t，*J* = 6.3 Hz，1H)，3.93(d，*J* = 1.9 Hz，2H)，3.59- 3.35(m，2H)，2.94- 2.83(m，3H)，2.39(d，*J* = 10.8 Hz，3H)，1.15(t，*J* =6.6 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
FB8	橙色油		ESIMS *m/z* 640 $[M]^+$	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.55(s，1H)，7.92- 7.82(m，3H)，7.79(dd，*J* = 9.1，1.3 Hz，3H)，7.42- 7.37(m，2H)，7.33- 7.28(m，1H)，6.89 – 6.78(m，1H)，5.54(t，*J* = 6.2 Hz，1H)，3.92(d，*J* = 1.7 Hz，2H)，3.04(t，*J* = 7.7 Hz，2H)，2.91(t，*J* = 7.0 Hz，2H)，2.73- 2.61(m，1H)，2.33(t，J= 0.7 Hz，3H)，1.15(dt，*J* = 6.8，0.9 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02，-117.98

[1997]

FB9	粉红色固体		ESIMS *m/z* 656 $[M]^+$	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.55(s，1H)，7.89- 7.82(m，2H)，7.79(d，*J* = 9.1 Hz，2H)，7.43-7.37(m，4H)，7.32(d，*J* = 8.8 Hz，1H)，6.99(dd，*J* = 8.7，2.7 Hz，1H)，6.56(d，*J* = 2.7 Hz，1H)，3.92(d，J= 1.6 Hz，2H)，3.77(s，3H)，3.52(ddt，*J* = 30.6，13.9，6.7 Hz，2H)，2.91(t，*J* = 7.0 Hz，2H)，2.60(p，*J* =6.7 Hz，1H)，1.14(dd，*J* = 6.9，4.7 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02，-117.96

[1998]	FB10	白色固体		ESIMS *m/z* 624([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.39(s，1H)，8.10- 7.99(m，5H)，7.66- 7.57(m，2H)，7.43-7.39(m，2H)，7.39- 7.32(m，2H)，7.32-7.22(m，2H)，4.06- 3.62(m，2H)，3.09-2.90(m，4H)，2.24(qd，J = 7.5，2.1 Hz，2H)，0.98(dt，J = 14.4，7.3 Hz，6H)	^{13}C **NMR**(101 MHz，DMSO-d_6) δ 165.51，164.05，162.06，151.48，147.08，143.76，141.37，139.84，135.72，134.04，129.59，129.44，129.22，129.06，129.01，128.46，126.92，126.15，122.60，121.11，44.12，34.76，33.99，23.50，14.51，13.81

[1999]	FB11	黄色固体		ESIMS *m/z* 668([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(s，1H)，8.13(d，*J* = 8.2 Hz，2H)，7.80(d，*J* = 9.0 Hz，2H)，7.42- 7.32(m，4H)，7.05(d，*J* = 8.7 Hz，1H)，6.91(d，*J* = 2.8 Hz，1H)，6.80(dd，*J* = 8.6，2.8 Hz，1H)，5.48(t，*J* = 5.8 Hz，1H)，4.05- 3.82(m，2H)，3.82(s，3H)，3.34- 3.18(m，2H)，3.09(td，*J* = 7.2，2.3 Hz, 2H)，2.66- 2.50(m，1H)，1.16- 1.02(m，9H)	^{13}C NMR(101 MHz，$CDCl_3$)δ 167.30，165.12，163.79，161.04，152.95，148.80，148.55，141.92，139.76, 136.06，129.92，129.70，129.36，127.30，126.04，122.85，121.61，113.01，112.25，100.44，55.80，45.46, 36.03，35.27，29.26，23.98，23.89，15.29

[2000]

FB12	黄色油		ESIMS *m/z* 655 $[M]^+$	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(s，1H)，8.14(d，*J* = 8.2 Hz，2H)，7.80(d，*J* = 9.0 Hz，2H)，7.41- 7.32(m，5H)，7.14(td，*J* = 8.3，2.7 Hz，1H)，6.85(dd，*J* = 8.7，2.7 Hz，1H)，5.52(t，*J* = 5.8 Hz，1H)，4.04- 3.76(m，2H)，3.38- 3.18(m，2H)，3.09(td，*J* = 7.2，2.9 Hz，2H)，2.58(p，*J* = 6.8 Hz，1H)，1.16-1.06(m，9H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02，-115.49

[2001]	FB13	黄色油		ESIMS *m/z* 656([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(s，1H)，8.13(d，*J* = 8.2 Hz，2H)，7.84- 7.72(m，2H)，7.42-7.31(m，4H)，7.16- 7.03(m，2H)，6.96(ddd，*J* = 8.7，7.6，2.9 Hz，1H)，5.47(t，*J* = 5.9 Hz，1H)，4.04-3.76(m，2H)，3.35-3.17(m，2H)，3.09(td，*J* = 7.2，2.5 Hz，2H)，2.66- 2.49(m，1H)，1.19- 0.99(m，9H)	(101 MHz，$CDCl_3$)δ 166.98，164.98，163.74，162.68，152.58，149.93，148.79，141.93，139.63，136.04，130.80，130.71，129.70，129.40，127.30，122.85，121.61，114.63，114.36，114.13，45.42，36.06，35.24，29.37，23.86，23.74，15.28

[2002]	FB14	黄色固体		ESIMS *m/z* 638([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(s，1H)，8.17- 8.10(m，2H)，7.86- 7.72(m，2H)，7.46- 7.33(m，7H)，7.17- 7.05(m，1H)，5.47(t，*J* = 5.8 Hz，1H)，4.06- 3.75(m，2H)，3.34- 3.16(m，2H)，3.10(td, *J* = 7.2，2.3 Hz，2H)，2.64(p，*J* = 6.9 Hz，1H)，1.20- 1.06(m，10H)	^{13}C NMR(101 MHz，$CDCl_3$)δ 166.95，165.08，163.79，152.72，148.79，147.10，141.93，139.74，136.07，133.27，130.62，129.71，129.38，128.93，127.32，127.26，122.86，121.62，119.57，77.80，45.46，36.03，35.29，29.03，24.04，23.95，15.29

[2003]

	FB15	红色油		ESIMS *m/z* 677([M+H]$^+$)	1:1 的非对映异构体的混合物 ^{1}H NMR(600 MHz，$CDCl_3$)δ 8.60(d，*J* = 11.3 Hz，1H)，8.15- 8.04(m，2H)，7.89- 7.78(m, 2H)，7.44(dd，*J* = 8.7，5.9 Hz，2H)，7.35- 7.31(m，2H)，7.30- 7.26(m，2H)，6.87- 6.73(m，1H)，5.30(dd，*J* = 37.0，8.8 Hz，1H)，3.92- 3.81(m，2H)，3.54(q，*J* = 7.0 Hz，1H)，2.62(td，*J* = 14.0，7.2 Hz，1H)，2.41- 2.26(m，4H)，2.02- 1.80(m，3H)，1.77- 1.45(m，3H)，1.34- 1.10(m，6H)，0.90(dd，*J* = 155.3, 6.8 Hz，2H)	^{13}C **NMR**(151 MHz，$CDCl_3$)δ 173.06，168.38，163.84，161.44，148.68，145.96，143.44，141.77，136.97, 135.96，132.82，131.29，129.14，128.89，128.64，128.19，127.07，126.78，122.74，121.46，53.43，50.50, 36.05，34.39，33.22，28.56，26.41，25.58，24.18，

[2004]

FB16	白色固体		ESIMS *m/z* 583([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 11.91(s，1H)，9.95(s，1H)，9.37(s，1H)，8.11- 7.94(m，4H)，7.66- 7.56(m，2H)，7.44(d，*J* = 8.0 Hz，1H)，7.36(d，*J* = 8.1 Hz，2H)，7.06(d，*J* = 1.9 Hz，1H)，7.00(d，*J* = 8.0 Hz，2H)，3.17(q，*J* = 6.5 Hz，2H)，2.68(t，*J* = 7.5 Hz，2H)，2.26(s，3H)，2.15(s，3H)，1.64(q，*J* = 7.6 Hz，2H)，1.51(q，*J* = 7.2 Hz，2H)	^{19}F NMR(376 MHz，DMSO-d_6) δ-56.97
FB17	白色泡沫		ESIMS *m/z* 623([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.54(s，1H)，8.11- 8.06(m，2H)，7.83- 7.76(m，2H)，7.38(dd，*J* = 9.1，1.0 Hz，1H)，7.26(s，3H)，7.14(dd，*J* = 1.5，0.8 Hz，1H)，7.13- 7.08(m，1H)，6.97(d，*J* = 8.0 Hz，1H)，5.41(t，*J* = 6.1 Hz，1H)，3.97- 3.77(m，2H)，3.25(qd，*J* = 6.9，4.1 Hz，2H)，2.67(t，*J* = 7.5 Hz，2H)，2.36(s，3H)，2.10(s，3H)，1.73- 1.61(m，2H)，1.60- 1.45(m，2H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02
FB18	灰白色固体		ESIMS *m/z* 527([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 11.98(s，1H)，10.24(s，1H)，9.43(s，1H)，8.16- 7.97(m，4H)，7.69- 7.59(m，3H)，7.59- 7.50(m，2H)，7.44(dt，*J* = 7.6，1.5 Hz，1H)，7.31- 7.25(m，1H)，7.20(pd，*J* = 7.5，1.9 Hz，2H)，4.47(d，*J* = 5.9 Hz，2H)，2.22(s，3H)	^{19}F NMR(376 MHz，DMSO-d_6) δ-56.96

[2005]

FB19	灰白色固体		ESIMS *m/z* 557([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 11.76(s，1H)，10.19(s，1H)，9.43(s，1H)，8.13- 8.06(m，3H)，8.03(dt，*J* = 7.7，1.4 Hz，1H)，7.68-7.60(m，2H)，7.58- 7.49(m，2H)，7.44(dt，*J* = 7.7，1.5 Hz，1H)，7.38(d，*J* = 8.7 Hz，1H)，6.84(d，*J* = 2.9 Hz，1H)，6.77(dd，*J* = 8.7，2.9 Hz，1H)，4.46(d，*J* = 5.8 Hz，2H)，3.75(s，3H)，2.17(s，3H)	^{19}F NMR(376 MHz，DMSO-d_6) δ-56.95
FB20	灰白色固体		ESIMS *m/z* 541([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 12.01(s，1H)，10.27(s，1H)，9.45(s，1H)，8.15- 8.08(m，3H)，8.06(dt，*J* = 7.8，1.4 Hz，1H)，7.65(ddd，*J* = 7.9，2.0，1.0 Hz，2H)，7.62- 7.52(m，3H)，7.46(dt，*J* = 7.8，1.5 Hz，1H)，7.33-7.27(m，1H)，7.27- 7.20(m，2H)，4.49(d，*J* = 5.8 Hz，2H)，2.57(q，*J* = 7.6 Hz，2H)，1.14(t，*J* = 7.5 Hz，3H)	^{19}F NMR(376 MHz，DMSO-d_6) δ-56.96
FB21	灰白色固体		ESIMS *m/z* 555([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 11.59(s，1H)，10.25(s，1H)，9.45(s，1H)，8.15- 8.08(m，3H)，8.06(dt，*J* = 7.7，1.4 Hz，1H)，7.69-7.62(m，2H)，7.59- 7.52(m，2H)，7.46(dt，*J* = 7.7，1.4 Hz，1H)，7.19(dd，*J* = 8.0，6.9 Hz，1H)，7.15- 7.09(m，2H)，4.49(d，*J* = 5.8 Hz，2H)，2.56- 2.48(m，2H)，2.20(s，3H)，1.13(t，*J* = 7.6 Hz，3H)	^{19}F NMR(376 MHz，DMSO-d_6) δ-56.97

[2006]

FB22	灰白色固体		ESIMS *m/z* 555([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 11.95(s，1H)，10.28(s，1H)，9.45(s，1H)，8.16- 8.08(m，3H)，7.68- 7.62(m，2H)，7.61- 7.51(m，2H)，7.50- 7.40(m，3H)，7.37(dd，*J* = 7.8，1.6 Hz，1H)，7.29(td，*J* = 7.5，1.5 Hz，1H)，7.23(td，*J* = 7.5，1.7 Hz，1H)，4.49(d，*J* = 5.8 Hz，2H)，3.03(hept，*J* = 6.5 Hz，1H)，1.18(d，*J* = 6.8 Hz，6H)	^{19}F NMR(376 MHz，DMSO-d_6) δ-56.96
FB23	灰白色固体		ESIMS *m/z* 569([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 11.85(s，1H)，10.36- 10.12(m，1H)，9.45(s，1H)，8.16- 8.08(m，3H)，8.06(dt，*J* = 7.7，1.4 Hz，1H)，7.69- 7.62(m，2H)，7.61- 7.52(m，2H)，7.46(dt，*J* = 7.7，1.5 Hz，1H)，7.28(d，*J* = 8.0 Hz，1H)，7.19- 7.14(m，1H)，7.08- 6.99(m，1H)，4.48(d，*J* = 5.8 Hz，2H)，2.98(p，*J* = 6.9 Hz，1H)，2.33(s，3H)，1.17(d，*J* = 6.8 Hz，6H)	^{19}F NMR(376 MHz，DMSO-d_6) δ-56.96
FB24	灰白色固体		ESIMS *m/z* 573([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 11.83(s，1H)，10.31(s，1H)，9.45(s，1H)，8.16- 8.08(m，3H)，8.06(dt，*J* = 7.6，1.5 Hz，1H)，7.69- 7.63(m，2H)，7.60- 7.52(m，2H)，7.46(dt，*J* = 7.7，1.5 Hz，1H)，7.41(dd，*J* = 8.8，5.6 Hz，1H)，7.18(dd，*J* = 10.4，3.0 Hz，1H)，7.06(td，*J* = 8.5，3.0 Hz，1H)，4.49(d，*J* = 5.8 Hz，2H)，3.00(pd，*J* = 6.8，1.6 Hz，1H)，1.17(d，*J* = 6.8 Hz，6H)	^{19}F NMR(376 MHz，DMSO-d_6) δ-56.97，-114.35

[2007]

FB25	灰白色固体		ESIMS *m/z* 569([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 11.90(s，1H)，10.25(s，1H)，9.45(s，1H)，8.15- 8.08(m，3H)，8.06(dt，*J* = 7.8，1.6 Hz，1H)，7.69-7.62(m，2H)，7.56(dt，*J* = 11.3，6.7 Hz，2H)，7.46(dt，*J* = 7.8，1.5 Hz，1H)，7.24(d，*J* = 8.1 Hz，2H)，7.14- 7.07(m，1H)，4.49(d，*J* = 5.8 Hz，2H)，2.98(p，*J* = 6.9 Hz，1H)，2.28(s，3H)，1.15(d，*J* = 6.8 Hz，6H)	^{19}F NMR(376 MHz，DMSO-d_6) δ-56.96
FB26	灰白色固体		ESIMS *m/z* 589([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 12.02(s，1H)，10.37(s，1H)，9.45(s，1H)，8.15- 8.08(m，3H)，8.06(dt，*J* = 7.7，1.5 Hz，1H)，7.70-7.62(m，2H)，7.62- 7.52(m，3H)，7.46(dt，*J* = 7.8，1.4 Hz，1H)，7.42- 7.31(m，2H)，4.49(d，*J* = 5.8 Hz，2H)，3.01(p，*J* = 6.8 Hz，1H)，1.17(d，*J* = 6.8 Hz，6H)	^{19}F NMR(376 MHz，DMSO-d_6) δ-56.96
FB27	灰白色固体		ESIMS *m/z* 567([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(s，1H)，8.22(t，*J* = 6.3 Hz，1H)，8.13- 8.03(m，2H)，8.01- 7.93(m，2H)，7.63(dq，*J* = 7.9，1.0 Hz，2H)，7.45(t，*J* = 7.6 Hz，1H)，7.40- 7.28(m，4H)，7.28- 7.21(m，1H)，4.35- 4.19(m，2H)，4.17- 3.96(m，2H)，2.10(s，3H)	^{19}F NMR(376 MHz，DMSO-d_6) δ-56.96

[2008]

FB28	淡橙色固体		ESIMS *m/z* 597([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(s，1H)，8.22(t，*J* = 6.3 Hz，1H)，8.11- 8.03(m，2H)，8.02- 7.93(m，2H)，7.69- 7.59(m，2H)，7.45(t，*J* = 7.6 Hz，1H)，7.33(dt，*J* = 7.7，1.5 Hz，1H)，7.15(d，*J* = 8.7 Hz，1H)，6.92(d，*J* = 2.8 Hz，1H)，6.86(dd，*J* = 8.7，2.9 Hz，1H)，4.35- 4.19(m，2H)，4.15- 3.93(m，2H)，3.78(s，3H)，2.05(s，3H)	^{19}F NMR(376 MHz，DMSO-d_6) δ-56.96
FB29	白色固体		ESIMS *m/z* 581([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(s，1H)，8.22(t，*J* = 6.3 Hz，1H)，8.12- 8.03(m，2H)，8.01- 7.93(m，2H)，7.68- 7.59(m，2H)，7.48- 7.38(m，3H)，7.37- 7.28(m，2H)，7.24(dt，*J* = 7.8，1.0 Hz，1H)，4.36- 4.18(m，2H)，4.18- 3.95(m，2H)，2.40(q，*J* = 7.6 Hz，2H)，1.10(td，*J* = 7.3，1.6 Hz，3H)	^{19}F NMR(376 MHz，DMSO-d_6) δ-56.96
FB30	白色固体		ESIMS *m/z* 595([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(s，1H)，8.25(t，*J* = 6.3 Hz，1H)，8.15- 8.02(m，2H)，8.01- 7.94(m，2H)，7.63(ddd，*J* = 7.9，2.1，1.0 Hz，2H)，7.49- 7.42(m，1H)，7.37- 7.27(m，2H)，7.26- 7.15(m，2H)，4.26(d，*J* = 6.3 Hz，2H)，4.18(d，*J* = 1.2 Hz，2H)，2.37(q，*J* = 7.5 Hz，2H)，2.06(s，3H)，1.12- 1.07(m，3H)	^{19}F NMR(376 MHz，DMSO-d_6) δ-56.96

[2009]

FB31	淡黄色固体		ESIMS *m/z* 595([M+H]$^+$)	^{1}H NMR(400 MHz, DMSO-d_6)δ 9.40(s, 1H), 8.22(t, *J* = 6.3 Hz, 1H), 8.13- 8.02(m, 2H), 8.00- 7.92(m, 2H), 7.70- 7.57(m, 2H), 7.53- 7.39(m, 3H), 7.37- 7.26(m, 2H), 7.21(dd, *J* = 7.8, 1.4 Hz, 1H), 4.35- 4.19(m, 2H), 4.18- 3.96(m, 2H), 2.68(h, *J* = 7.0 Hz, 1H), 1.13- 1.04(m, 6H)	^{19}F NMR(376 MHz, DMSO-d_6) δ-56.97
FB32	淡橙色固体		ESIMS *m/z* 609([M+H]$^+$)	^{1}H NMR(400 MHz, DMSO-d_6)δ 9.40(s, 1H), 8.21(t, *J* = 6.3 Hz, 1H), 8.11- 8.02(m, 2H), 8.01- 7.91(m, 2H), 7.67- 7.59(m, 2H), 7.44(td, *J* = 7.5, 0.9 Hz, 1H), 7.31(dt, *J* = 7.7, 1.4 Hz, 1H), 7.29- 7.24(m, 1H), 7.16- 7.02(m, 2H), 4.35- 4.18(m, 2H), 4.18- 3.93(m, 2H), 2.63(p, *J* = 6.8 Hz, 1H), 2.34(s, 3H), 1.12- 1.02(m, 6H)	^{19}F NMR(376 MHz, DMSO-d_6) δ-56.97
FB33	灰白色固体		ESIMS *m/z* 613([M+H]$^+$)	^{1}H NMR(400 MHz, DMSO-d_6)δ 9.40(s, 1H), 8.22(t, *J* = 6.3 Hz, 1H), 8.12- 8.02(m, 2H), 7.96(dd, *J* = 7.4, 1.4 Hz, 2H), 7.69- 7.59(m, 2H), 7.44(td, *J* = 7.4, 1.0 Hz, 1H), 7.37- 7.28(m, 3H), 7.15(td, *J* = 8.4, 2.9 Hz, 1H), 4.37- 4.19(m, 2H), 4.19- 3.93(m, 2H), 2.67(tt, *J* = 7.4, 5.7 Hz, 1H), 1.16- 1.03(m, 6H)	^{19}F NMR(376 MHz, DMSO-d_6) δ-56.96, -112.09

[2010]

FB34	灰白色固体		ESIMS *m/z* 609([M+H]$^+$)	^{1}H NMR(400 MHz, DMSO-d_6)δ 9.40(s, 1H), 8.24(t, *J* = 6.3 Hz, 1H), 8.13- 8.03(m, 2H), 7.96(dt, *J* = 9.2, 1.5 Hz, 2H), 7.69- 7.58(m, 2H), 7.44(t, *J* = 7.6 Hz, 1H), 7.40- 7.27(m, 2H), 7.28- 7.20(m, 1H), 7.01(dd, *J* = 1.7, 0.9 Hz, 1H), 4.35- 4.19(m, 2H), 4.18- 3.94(m, 2H), 2.63(p, *J* = 6.8 Hz, 1H), 2.28(s, 3H), 1.12- 1.03(m, 6H)	^{19}F NMR(376 MHz, DMSO-d_6) δ-56.98
FB35	淡黄色固体		ESIMS *m/z* 629([M+H]$^+$)	^{1}H NMR(400 MHz, DMSO-d_6)δ 9.40(s, 1H), 8.27(t, *J* = 6.3 Hz, 1H), 8.11- 8.03(m, 2H), 8.01- 7.92(m, 2H), 7.69- 7.58(m, 2H), 7.57- 7.47(m, 2H), 7.47- 7.39(m, 2H), 7.32(dt, *J* = 7.7, 1.5 Hz, 1H), 4.41- 4.20(m, 2H), 4.19- 3.88(m, 2H), 2.69(p, *J* = 6.8 Hz, 1H), 1.17- 1.05(m, 6H)	^{19}F NMR(376 MHz, DMSO-d_6) δ-56.97
FB36	白色固体		ESIMS *m/z* 599([M+H]$^+$)	^{1}H NMR(400 MHz, DMSO-d_6)δ 11.80(s, 1H), 9.96(s, 1H), 9.39(s, 1H), 8.13- 8.04(m, 2H), 7.98(t, *J* = 1.6 Hz, 1H), 7.94(dt, *J* = 7.7, 1.4 Hz, 1H), 7.62(dq, *J* = 9.1, 1.0 Hz, 2H), 7.44(t, *J* = 7.6 Hz, 1H), 7.40- 7.31(m, 2H), 7.01(t, *J* = 5.6 Hz, 1H), 6.82(d, *J* = 2.9 Hz, 1H), 6.75(dd, *J* = 8.7, 2.9 Hz, 1H), 3.74(s, 3H), 3.18(q, *J* = 6.4 Hz, 2H), 2.72(t, *J* = 7.6 Hz, 2H), 2.14(s, 3H), 1.65(q, *J* = 7.6 Hz, 2H), 1.52(p, *J* = 6.9 Hz, 2H)	^{19}F NMR(376 MHz, DMSO-d_6) δ-56.96

[2011]

FB37	白色固体		ESIMS *m/z* 631([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 12.08(s，1H)，10.15(s，1H)，9.41(s，1H)，8.13- 8.07(m，2H)，8.00(t，*J* = 1.7 Hz，1H)，7.96(dt，*J* = 7.7，1.4 Hz，1H)，7.64(dq，*J* = 7.9，1.0 Hz，2H)，7.59(d，*J* = 2.2 Hz，1H)，7.46(t，*J* = 7.6 Hz，1H)，7.41- 7.30(m，3H)，7.05(t，*J* = 5.7 Hz，1H)，3.21(q，*J* = 6.5 Hz，2H)，2.98(p，*J* = 6.8 Hz，1H)，2.74(t，*J* = 7.6 Hz，2H)，1.68(q，*J* = 7.6 Hz，2H)，1.54(p，*J* = 6.9 Hz，2H)，1.15(d，*J* = 6.8 Hz，6H)	^{19}F NMR(376 MHz，DMSO-d_6) δ-56.96
FB38	白色固体		ESIMS *m/z* 639([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(s，1H)，8.13- 8.04(m，2H)，7.92(dt，*J* = 6.6，1.5 Hz，2H)，7.63(dp，*J* = 7.9，1.0 Hz，2H)，7.56(t，*J* = 5.9 Hz，1H)，7.46- 7.37(m，1H)，7.30(dt，*J* = 7.7，1.5 Hz，1H)，7.11(d，*J* = 8.6 Hz，1H)，6.89(dd，*J* = 2.9，0.8 Hz，1H)，6.83(ddd，*J* = 8.7，2.9，0.7 Hz，1H)，4.11- 3.90(m，2H)，3.76(s，3H)，3.03(dh，*J* = 19.9，6.5 Hz，2H)，2.65(t，*J* = 7.6 Hz，2H)，2.02(s，3H)，1.64- 1.50(m，2H)，1.50- 1.37(m，2H)	^{19}F NMR(376 MHz，DMSO-d_6) δ-56.96
FB39	白色固体		ESIMS *m/z* 671([M+H]$^+$)	^{1}H NMR(400 MHz，DMSO-d_6)δ 9.40(s，1H)，8.13- 8.04(m，2H)，7.92(ddt，*J* = 3.8，2.9，1.4 Hz，2H)，7.67- 7.57(m，3H)，7.53- 7.45(m，2H)，7.45- 7.37(m，2H)，7.28(dt，*J* = 7.7，1.5 Hz，1H)，4.14- 3.87(m，2H)，3.04(qd，*J* = 6.9，2.9 Hz，2H)，2.73- 2.56(m，3H)，1.55(dq，*J* = 8.9，7.2 Hz，2H)，1.49- 1.37(m，2H)，1.11- 1.02(m，6H)	^{19}F NMR(376 MHz，DMSO-d_6) δ-56.97

[2012]

FB40	褐色玻璃状泡沫		ESIMS *m/z* 671([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.54(s，1H)，8.12- 8.03(m，2H)，7.84- 7.74(m，2H)，7.39(ddt，*J* = 6.9，2.8，1.7 Hz，3H)，7.34(d，*J* = 8.5 Hz，1H)，7.27(s，2H)，7.05(d，*J* = 2.1 Hz，1H)，5.47(t，*J* = 6.1 Hz，1H)，3.92(d，*J* = 1.5 Hz，2H)，3.53(dp，*J* = 26.7，6.7 Hz，2H)，2.88(t，*J* = 6.6 Hz，2H)，2.64(p，*J* = 6.9 Hz，1H)，1.14(dd，*J* = 8.8，6.9 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02
FB41	黄色油		ESIMS *m/z* 637([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(s，1H)，8.08(d，*J* = 8.2 Hz，2H)，7.82- 7.79(m，3H)，7.39(dt，*J* = 8.1，1.0 Hz，3H)，7.24(d，*J* = 3.7 Hz，2H)，7.16(dd，*J* = 8.0，1.8 Hz，1H)，6.76(dd，*J* = 1.8，0.9 Hz，1H)，5.18(t，*J* = 6.2 Hz，1H)，3.46(ddt，*J* = 36.9，13.6，6.7 Hz，2H)，3.19- 3.10(m，3H)，3.04- 2.89(m，1H)，2.85(t，*J* = 7.0 Hz，2H)，2.62(p，*J* = 7.0 Hz，1H)，2.30(t，*J* = 0.7 Hz，3H)，1.12(dd，*J* = 6.9，4.6 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
FB42	褐色油		ESIMS *m/z* 658([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(s，1H)，8.08(dd，*J* = 15.7，8.2 Hz，2H)，7.80(d，*J* = 9.0 Hz，2H)，7.44- 7.34(m，4H)，7.29(d，*J* = 8.2 Hz，1H)，7.26- 7.21(m，1H)，7.08(dd，*J* = 13.8，2.1 Hz，1H)，5.34(dd，*J* = 15.4，8.5 Hz，1H)，3.96- 3.84(m，2H)，3.01(dd，*J* = 13.4，5.6 Hz，1H)，2.87(dd，*J* = 13.5，5.8 Hz，1H)，2.77(dd，*J* = 13.5，7.0 Hz，1H)，2.71- 2.57(m，1H)，1.20- 1.06(m，9H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03

[2013]

FB43	桃色玻璃状泡沫		ESIMS *m/z* 431([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(s，1H)，8.20- 8.10(m，2H)，7.84- 7.74(m，2H)，7.39(dt，*J* = 8.0，1.0 Hz，2H)，7.36- 7.29(m，2H)，3.68(tdd，*J* = 8.3，5.3，4.4 Hz，1H)，2.98- 2.77(m，2H)，1.76- 1.64(m，1H)，1.61- 1.51(m，1H)，1.05(t，*J* = 7.4 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
FB44	褐色玻璃状泡沫	90(dec.)	ESIMS *m/z* 672([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(s，1H)，8.07(dd，*J* = 18.4，8.2 Hz，2H)，7.84- 7.75(m，2H)，7.43- 7.34(m，4H)，7.31- 7.27(m，1H)，7.25- 7.19(m，1H)，7.08(dd，*J* = 12.4，2.1 Hz，1H)，5.26(t，*J* = 9.2 Hz，1H)，4.02- 3.93(m，1H)，3.91(dd，*J* = 3.7，1.1 Hz，2H)，2.96- 2.73(m，2H)，2.63(h，*J* = 6.8 Hz，1H)，1.42- 1.28(m，2H)，1.20- 1.09(m，6H)，0.90(dt，*J* = 24.3，7.4 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02
FB45	黄色油		ESIMS *m/z* 637([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.55(d，*J* = 0.8 Hz，1H)，8.11- 8.02(m，2H)，7.84- 7.75(m，2H)，7.43- 7.35(m，2H)，7.33(dd，*J* = 8.2，1.1 Hz，1H)，7.30- 7.21(m，3H)，6.87(ddd，*J* = 12.7，1.8，0.9 Hz，1H)，5.39(dd，*J* = 16.1，8.5 Hz，1H)，4.20- 4.11(m，1H)，3.91(dd，*J* = 2.5，1.8 Hz，2H)，3.02- 2.85(m，1H)，2.81- 2.58(m，2H)，2.35(d，*J* = 7.6 Hz，3H)，1.15(ddd，*J* = 6.9，4.3，1.5 Hz，6H)，1.09(t，*J* = 6.6 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02

[2014]

FB46	灰白色泡沫		ESIMS *m/z* 637([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.55(d，*J* = 0.6 Hz，1H)，8.13- 8.02(m，2H)，7.84- 7.75(m，2H)，7.43- 7.36(m，2H)，7.36- 7.31(m，1H)，7.30- 7.21(m，3H)，6.90- 6.84(m，1H)，5.37(dd，*J* = 15.4，8.4 Hz，1H)，4.20- 4.11(m，1H)，3.98- 3.84(m，2H)，2.94(ddd，*J* = 51.6，13.4，5.5 Hz，1H)，2.76(dd，*J* = 13.5，7.1 Hz，1H)，2.70- 2.58(m，1H)，2.35(d，*J* = 7.9 Hz，3H)，1.17- 1.14(m，6H)，1.09(t，*J* = 6.8 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02
FB47	褐色油		ESIMS *m/z* 637([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(d，*J* = 0.8 Hz，1H)，8.07(dd，*J* = 11.2，8.2 Hz，2H)，7.85- 7.77(m，2H)，7.43- 7.36(m，2H)，7.34(d，*J* = 8.8 Hz，1H)，7.31- 7.27(m，1H)，7.26- 7.21(m，1H)，7.02(dt，*J* = 8.8，3.1 Hz，1H)，6.58(dd，*J* = 11.5，2.7 Hz，1H)，5.37(dd，*J* = 14.6，8.5 Hz，1H)，4.12(m，2H)，3.96- 3.88(m，2H)，3.79(d，*J* = 5.1 Hz，2H)，3.05- 2.55(m，3H)，1.18- 1.10(m，9H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
FB48	褐色油		ESIMS *m/z* 637([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(d，*J* = 0.9 Hz，1H)，8.07(dd，*J* = 10.2，8.2 Hz，2H)，7.84- 7.77(m，2H)，7.43- 7.36(m，2H)，7.28(dd，*J* = 7.4，1.4 Hz，1H)，7.26- 7.22(m，2H)，7.17- 7.07(m，1H)，6.94(dd，*J* = 11.5，8.0 Hz，1H)，5.36(dd，*J* = 14.4，8.4 Hz，1H)，4.22- 4.10(m，1H)，3.91(t，*J* = 1.8 Hz，2H)，3.05- 2.60(m，3H)，2.40(d，*J* = 2.5 Hz，3H)，1.21- 1.05(m，9H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03

[2015]

FB49	褐色油		ESIMS *m/z* 658([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(s，1H)，8.09(ddd，*J* = 9.2，5.5，3.8 Hz，2H)，7.80(d，*J* = 9.0 Hz，2H)，7.38(ddt，*J* = 8.7，6.8，2.6 Hz，3H)，7.32(dd，*J* = 8.5，4.3 Hz，1H)，7.29(d，*J* = 7.7 Hz，2H)，7.03(dd，*J* = 6.6，2.1 Hz，1H)，5.39(s，1H)，3.91(d，*J* = 2.1 Hz，2H)，3.65- 3.22(m，2H)，3.02(d，*J* = 10.0 Hz，1H)，2.62(tt，*J* = 14.6，7.6 Hz，1H)，1.32- 1.27(m，3H)，1.20- 1.04(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
FB50	澄清的油		ESIMS *m/z* 628([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.68- 8.61(m，1H)，8.15- 8.04(m，2H)，7.95- 7.85(m，2H)，7.85- 7.77(m，2H)，7.45- 7.37(m，1H)，7.35(d，*J* = 8.5 Hz，1H)，7.31- 7.27(m，2H)，7.06(d，*J* = 2.1 Hz，1H)，5.52(t，*J* = 6.2 Hz，1H)，3.93(d，*J* = 1.6 Hz，2H)，3.53(ddt，*J* = 25.1，13.6，6.7 Hz，2H)，2.88(t，*J* = 6.9 Hz，2H)，2.71- 2.57(m，1H)，1.20- 1.07(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-62.49
FB51	淡橙色泡沫	99(dec.)	ESIMS *m/z* 637([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(d，*J* = 8.0 Hz，1H)，8.00(d，*J* = 8.1 Hz，2H)，7.82(d，*J* = 8.9 Hz，2H)，7.46- 7.36(m，3H)，7.31(dd，*J* = 8.2，6.4 Hz，1H)，6.93(d，*J* = 1.1 Hz，1H)，6.75(d，*J* = 8.2 Hz，2H)，3.93(d，*J* = 5.1 Hz，2H)，3.63- 3.34(m，1H)，3.20(ddd，*J* = 13.5，9.2，6.6 Hz，1H)，2.99(s，3H)，2.77- 2.68(m，1H)，2.63- 2.51(m，2H)，2.35(d，*J* = 0.7 Hz，3H)，1.21- 1.12(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02

[2016]

FB52	褐色油		ESIMS *m/z* 651([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(d，*J* = 4.5 Hz，1H)，8.12- 8.02(m，2H)，7.83- 7.75(m，2H)，7.43- 7.35(m，2H)，7.30(d，*J* = 8.1 Hz，2H)，7.20(d，*J* = 8.1 Hz，2H)，6.87(d，*J* = 1.3 Hz，1H)，5.21(s，1H)，3.95(d，*J* = 2.6 Hz，2H)，3.28- 2.96(m，2H)，2.66(p，*J* = 6.8 Hz，1H)，2.32(s，3H)，1.25(d，*J* = 5.1 Hz，6H)，1.14(ddd，*J* = 10.9，6.9，4.7 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
FB53	褐色玻璃状泡沫		ESIMS *m/z* 651([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(s，1H)，8.09(d，*J* = 8.4 Hz，2H)，7.80(d，*J* = 9.0 Hz，2H)，7.44- 7.35(m，4H)，7.28(d，*J* = 8.1 Hz，1H)，7.24- 7.19(m，1H)，6.86- 6.77(m，1H)，5.27(s，1H)，3.89(d，*J* = 0.9 Hz，2H)，3.56(dd，*J* = 13.7，7.2 Hz，1H)，3.41(dd，*J* = 13.7，5.9 Hz，1H)，2.59(p，*J* = 6.9 Hz，1H)，2.31(d，*J* = 0.7 Hz，3H)，1.35(d，*J* = 2.5 Hz，6H)，1.11(dd，*J* = 11.5，6.9 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
FB54	红色固体	95(dec.)	ESIMS *m/z* 651([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(d，*J* = 8.6 Hz，1H)，8.04(dd，*J* = 40.0，8.1 Hz，2H)，7.85- 7.76(m，2H)，7.44- 7.35(m，3H)，7.35- 7.28(m，1H)，7.25- 7.19(m，1H)，6.98- 6.84(m，1H)，6.70(d，*J* = 8.2 Hz，1H)，3.93(dd，*J* = 5.9，4.2 Hz，2H)，3.61- 2.45(m，7H)，2.40- 2.25(m，3H)，1.32- 1.07(m，9H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02

[2017]

FB55	黄色油		ESIMS *m/z* 609([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.55(d，*J* = 0.7 Hz，1H)，8.15- 8.04(m，2H)，7.84- 7.74(m，2H)，7.38(d，*J* = 8.6 Hz，2H)，7.28(d，*J* = 2.3 Hz，1H)，7.25- 7.01(m，3H)，6.91- 6.78(m，1H)，5.28- 5.13(m，1H)，4.25- 3.89(m，1H)，3.62- 3.28(m，2H)，3.04- 2.73(m，3H)，2.70- 2.37(m，3H)，2.32(d，*J* = 7.6 Hz，3H)，1.29- 1.13(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
FB56	黄色油		ESIMS *m/z* 609([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.59- 8.47(m，1H)，8.13- 8.01(m，2H)，7.80(dd，*J* = 9.8，3.0 Hz，2H)，7.46- 7.34(m，3H)，7.28(d，*J* = 1.7 Hz，2H)，7.13(s，1H)，7.08- 6.99(m，1H)，6.92(dd，*J* = 16.0，8.0 Hz，1H)，5.18(d，*J* = 6.4 Hz，1H)，4.26- 3.92(m，1H)，3.59- 3.27(m，2H)，3.02- 2.76(m，3H)，2.62- 2.38(m，2H)，2.37- 2.26(m，3H)，1.37- 1.08(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
FB57	黄色油		ESIMS *m/z* 627([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.57- 8.52(m，1H)，8.14- 8.02(m，2H)，7.84- 7.75(m，2H)，7.44- 7.34(m，2H)，7.27- 7.22(m，2H)，7.15- 6.78(m，4H)，5.13(d，*J* = 19.1 Hz，1H)，4.41- 4.16(m，1H)，3.62- 3.28(m，2H)，3.20- 2.73(m，4H)，1.32- 1.10(m，9H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03，-112.99

[2018]

FB58	黄色油		ESIMS *m/z* 611([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.58- 8.48(m，1H)，8.16- 8.00(m，2H)，7.87- 7.67(m，2H)，7.43- 7.17(m，6H)，7.08- 6.90(m，1H)，6.83- 6.69(m，1H)，5.21(s，1H)，4.25- 3.92(m，1H)，3.77(d，*J* = 14.8 Hz，3H)，3.64- 3.27(m，2H)，3.06- 2.75(m，3H)，2.24- 2.10(m，3H)，1.28- 1.11(m，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
FB59	澄清的油		ESIMS *m/z* 595([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.55(dd，*J* = 4.6，1.1 Hz，1H)，8.12- 8.04(m，2H)，7.87- 7.70(m，2H)，7.46- 7.34(m，3H)，7.28(d，*J* = 7.9 Hz，2H)，7.22- 7.02(m，3H)，5.20(t，*J* = 6.1 Hz，1H)，4.22- 4.11(m，1H)，3.55- 3.31(m，3H)，2.95(dd，*J* = 11.0，8.4 Hz，1H)，2.87- 2.80(m，1H)，2.18(d，*J* = 12.6 Hz，6H)，1.16(d，*J* = 6.3 Hz，3H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
FB60	黄色泡沫		ESIMS *m/z* 623([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.58- 8.53(m，1H)，8.13- 8.01(m，2H)，7.84- 7.75(m，2H)，7.39(dd，*J* = 9.1，3.2 Hz，2H)，7.28- 7.23(m，3H)，7.18- 7.12(m，1H)，7.02(dt，*J* = 8.1，2.2 Hz，1H)，6.89(dd，*J* = 14.0，8.0 Hz，1H)，5.24- 5.08(m，1H)，4.24- 3.91(m，1H)，3.63- 3.29(m，3H)，3.04- 2.74(m，3H)，2.35(d，*J* = 4.0 Hz，3H)，1.34- 1.06(m，9H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03

[2019]

FB61	褐色油		ESIMS *m/z* 663([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(d，*J* = 7.7 Hz，1H)，8.11- 7.95(m，2H)，7.85- 7.75(m，2H)，7.40(td，*J* = 4.3，1.2 Hz，3H)，7.32- 7.21(m，2H)，6.98- 6.82(m，1H)，6.73- 6.65(m，1H)，5.87- 5.38(m，1H)，5.15(ddd，*J* = 13.8，3.7，1.6 Hz，1H)，4.99- 4.67(m，1H)，4.03- 3.96(m，1H)，3.94(d，*J* = 5.4 Hz，2H)，3.64- 3.47(m，1H)，3.36- 3.12(m，2H)，2.98- 2.63(m，2H)，2.59- 2.51(m，1H)，2.38- 2.29(m，3H)，1.22- 1.09(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02
FB62	橙红色油		ESIMS *m/z* 677([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(d，*J* = 8.5 Hz，1H)，8.13- 7.94(m，2H)，7.85- 7.75(m，2H)，7.44- 7.22(m，5H)，6.97- 6.80(m，1H)，6.71- 6.63(m，1H)，3.94(dd，*J* = 6.0，4.4 Hz，2H)，3.78- 3.47(m，1H)，3.42- 3.17(m，3H)，3.03- 2.87(m，1H)，2.81- 2.55(m，2H)，2.33(t，*J* = 1.1 Hz，3H)，1.22- 1.08(m，6H)，1.09- 0.94(m，1H)，0.62- 0.44(m，2H)，0.31- 0.17(m，2H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02
FB63	红色油		ESIMS *m/z* 649([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(d，*J* = 2.1 Hz，1H)，8.19- 8.00(m，2H)，7.83- 7.75(m，2H)，7.44- 7.34(m，3H)，7.28(s，1H)，7.26- 7.16(m，2H)，6.89(s，1H)，5.63(s，1H)，3.93(d，*J* = 2.5 Hz，2H)，3.19(d，*J* = 13.9 Hz，1H)，2.75(d，*J* = 13.9 Hz，1H)，2.61(dd，*J* = 13.8，7.0 Hz，1H)，2.30(s，3H)，1.13(dd，*J* = 13.3，6.8 Hz，6H)，0.97- 0.64(m，4H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03

[2020]

FB64	黄色油		ESIMS *m/z* 641([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(s，1H)，8.13- 8.05(m，2H)，7.85- 7.74(m，2H)，7.44- 7.35(m，2H)，7.32(dd，*J* = 8.1，4.9 Hz，1H)，7.29- 7.25(m，3H)，6.92- 6.81(m，1H)，6.31(dd，*J* = 55.6，11.8 Hz，1H)，5.62(s，1H)，3.54(ddt，*J* = 32.1，13.7，6.7 Hz，2H)，2.88(t，*J* = 7.0 Hz，2H)，2.73- 2.48(m，1H)，2.37- 2.30(m，3H)，1.15(ddd，*J* = 9.6，6.8，2.8 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03，-159.92，-160.90
FB65	澄清的油		ESIMS *m/z* 597([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(d，*J* = 7.8 Hz，1H)，8.21- 8.01(m，2H)，7.80(dd，*J* = 10.0，3.1 Hz，2H)，7.46- 7.35(m，3H)，7.30(d，*J* = 8.1 Hz，1H)，7.22(d，*J* = 7.9 Hz，1H)，7.13(d，*J* = 8.0 Hz，1H)，7.05(s，1H)，5.40(d，*J* = 6.2 Hz，1H)，3.59(p，*J* = 7.1 Hz，2H)，3.14(dt，*J* = 13.5，6.7 Hz，1H)，2.95(q，*J* = 6.3，5.5 Hz，2H)，2.46- 2.22(m，6H)，1.16(dd，*J* = 35.5，6.9 Hz，6H)	
FB66	澄清的油		ESIMS *m/z* 611([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 11.53(s，1H)，8.64 – 8.52(m，1H)，8.24 – 7.97(m，2H)，7.86 – 7.73(m，4H)，7.49 – 7.18(m，4H)，7.17 – 6.97(m，1H)，5.40(t，*J* = 6.1 Hz，1H)，3.71 – 3.46(m，2H)，3.28 – 2.78(m，5H)，2.29(d，*J* = 18.6 Hz，3H)，2.17(d，*J* = 2.5 Hz，3H)，1.42 – 1.12(m，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02

[2021]

FB67	澄清的油		ESIMS *m/z* 639([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 10.16(t，*J* = 5.6 Hz，1H)，8.55(d，*J* = 2.6 Hz，1H)，8.06(dd，*J* = 8.3，2.0 Hz，2H)，7.85- 7.74(m，2H)，7.39(dq，*J* = 8.0，1.1 Hz，2H)，7.30(d，*J* = 8.2 Hz，2H)，7.13(d，*J* = 7.8 Hz，1H)，6.65-6.55(m，1H)，5.21(t，*J* = 6.1 Hz，1H)，3.59(tt，*J* = 12.6，6.7 Hz，2H)，3.32- 2.99(m，2H)，2.99- 2.76(m，3H)，2.27(d，*J* = 0.8 Hz，2H)，2.17(s，3H)，1.88- 1.84(m，2H)，1.11(dd，*J* = 6.9，3.2 Hz，6H)	
FB68	浅黄色泡沫		ESIMS *m/z* 651([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.55(s，1H)，8.08(d，*J* = 8.2 Hz，2H)，7.83 – 7.76(m，3H)，7.44 – 7.38(m，2H)，7.33 – 7.20(m，3H)，6.85(dd，*J* = 1.9，0.9 Hz，1H)，5.54(t，*J* = 6.2 Hz，1H)，3.51(ddt，*J* = 35.0，13.7，6.7 Hz，2H)，2.86(t，*J* = 7.1 Hz，2H)，2.64(hept，*J* = 6.9 Hz，1H)，2.33(s，3H)，1.73(d，*J* = 2.3 Hz，6H)，1.14(dd，*J* = 11.2，6.8 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
FB69	白色泡沫		ESIMS *m/z* 649([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.55(s，1H)，8.13 – 8.02(m，2H)，7.84 – 7.73(m，2H)，7.42 – 7.35(m，2H)，7.33 – 7.20(m，4H)，6.89(dd，*J* = 1.9，0.9 Hz，1H)，5.57(t，*J* = 6.2 Hz，1H)，3.68 – 3.34(m，2H)，2.86(t，*J* = 7.1 Hz，2H)，2.67(hept，*J* = 6.9 Hz，1H)，2.32(s，3H)，1.77(q，*J* = 4.4 Hz，2H)，1.50 – 1.39(m，2H)，1.15(dd，*J* = 10.5，6.8 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.02

[2022]

FB70	澄清的无色油		ESIMS *m/z* 701([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.55(s，1H)，8.13 – 8.01(m，2H)，7.88 – 7.71(m，2H)，7.45 – 7.35(m，2H)，7.32(d，*J* = 8.1 Hz，1H)，7.29 – 7.22(m，3H)，6.87(dd，*J* = 1.9，0.9 Hz，1H)，5.65(t，*J* = 6.2 Hz，1H)，3.69 – 3.37(m，2H)，2.92 – 2.75(m，3H)，2.33(s，3H)，1.18(dd，*J* = 6.9，5.0 Hz，6H)	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.03
FB71	黄色油		ESIMS *m/z* 701([M+H]$^+$)	^{1}H NMR(400 MHz，$CDCl_3$)δ 8.56(d，*J* = 1.1 Hz，1H)，8.21 – 8.10(m，2H)，7.84 – 7.75(m，2H)，7.48(dd，*J* = 8.3，6.1 Hz，2H)，7.44 – 7.36(m，2H)，7.35 – 7.29(m，1H)，7.29 – 7.22(m，1H)，6.85(t，*J* = 2.0 Hz，1H)，5.86(dt，*J* = 25.1，6.3 Hz，1H)，5.12(ddd，*J* = 14.0，8.2，6.1 Hz，1H)，4.04 – 3.74(m，4H)，2.61(ddq，*J* = 13.6，10.1，6.4 Hz，1H)，2.33(s，3H)，1.20 – 1.05(m，6H)。	^{19}F NMR(376 MHz，$CDCl_3$)δ-58.01
FB72	白色固体	180-185		^{1}H NMR(400 MHz，$CDCl_3$)δ 8.55(s，1H)，8.08(dd，*J* = 8.2，1.0 Hz，2H)，7.85 – 7.74(m，2H)，7.45 – 7.35(m，2H)，7.33 – 7.20(m，4H)，6.87 – 6.80(m，1H)，5.54(t，***J*** = 5.9 Hz，1H)，4.13(d，*J* = 6.5 Hz，1H)，3.70(d，*J* = 1.1 Hz，1H)，3.65 – 3.53(m，1H)，3.53 – 3.40(m，1H)，2.87(t，*J* = 7.0 Hz，2H)，2.68 – 2.54(m，1H)，2.33(s，3H)，1.49 – 1.38(m，6H)，1.14(td，*J* = 6.7，4.2 Hz，6H)	

[2023] [a]除非另外指明，否则所有^{1}H NMR数据在$CDCl_3$中于400MHz测量。

[2024]

BAW 和 CL 评级表	
防治%(或死亡率)	**评级**
50-100	A
大于 0 –小于 50	B
未测试	C
在此生物测定中未注意到活性	D

[2025]

GPA & YFM 评级表	
防治%(或死亡率)	**评级**
80-100	A
大于 0 –小于 80	B
未测试	C
在此生物测定中未注意到活性	D

[2026] 表ABC:生物学研究结果(F)

[2027]

编号	昆虫种类			
	BAW	CL	GPA	YFM
F1	A	A	D	C
F2	A	A	B	A
F3	A	A	B	C
F4	A	A	C	C
F5	A	A	A	A
F5A	A	A	C	C
F6	A	A	B	A
F7	A	A	B	A
F8	A	A	D	C
F9	A	A	D	A
F10	A	A	B	A
F11	A	A	D	C

[2028]

F12	A	A	D	C
F13	A	A	D	C
F14	A	A	D	A
F15	A	A	C	C
F16	A	A	C	C
F17	A	A	C	C
F18	A	A	C	C
F19	A	A	C	C
F20	A	A	C	A
F21	A	A	D	A
F22	A	A	D	C
F23	A	A	D	C
F24	A	A	D	C
F25	A	A	D	C
F26	A	A	C	C
F27	A	A	D	C
F28	A	A	D	C
F29	A	A	D	A
F30	A	A	D	C
F31	A	A	D	C
F32	A	A	D	C
F33	A	A	D	C
F34	A	A	D	C
F35	A	C	C	C

[2029] 表ABC(P)：生物学研究结果

[2030]

编号	昆虫种类			
	BAW	CL	GPA	YFM
P1	A	A	C	C
P2，P532	A	A	C	C

[2031]

P3，P1172	A	A	C	C
P5	A	A	C	C
P6	A	A	C	C
P7	A	A	C	C
P8，P852	A	A	C	C
P14	A	A	C	C
P15	A	A	C	C
P20	C	A	C	C
P26	A	A	C	A
P27	A	A	C	A
P28	A	A	D	A
P29	A	A	C	A
P30	A	A	C	A
P31	A	A	C	A
P33	A	A	C	A
P42	A	A	C	A
P44	A	A	D	A
P45	A	A	C	A
P47	A	A	C	A
P49	A	A	C	A
P50	A	A	C	A
P51	A	A	B	A
P52	A	A	D	A
P53	A	A	C	A
P57	A	A	C	A
P58	A	A	C	C
P59	A	A	C	C
P64	A	A	C	C
P65	A	A	C	A
P66，P353	A	A	C	A

[2032]

P74	A	A	C	C
P75	A	A	C	C
P76	A	A	C	C
P80	A	A	C	C
P81	C	A	C	C
P83	A	A	C	C
P84	A	A	C	C
P85	A	A	C	C
P87	A	A	C	C
P92	A	A	C	C
P93，P510	A	A	C	C
P94，P197	A	A	C	C
P99，P830	A	A	C	C
P101	B	A	C	D
P102	A	A	C	C
P103，P1150	A	A	C	C
P105	A	A	C	C
P118	A	A	C	C
P119	A	A	C	C
P120	A	A	C	C
P124	A	A	C	C
P125	A	A	C	C
P127	A	A	C	C
P128	A	A	C	C
P129	A	A	C	C
P131	A	A	C	C
P144	A	A	C	A
P145，P522	A	A	D	A
P146，P208	A	A	C	A
P150，P363	A	A	B	A

[2033]

P151，P842	A	A	C	A
P152，P1481	D	A	C	A
P153	D	A	C	D
P154	A	A	C	B
P155，P1162	A	A	C	A
P156，P682	A	A	C	A
P159	A	A	B	A
P160	A	A	C	B
P170	D	A	C	C
P171	A	A	C	C
P172	A	A	C	C
P176	A	A	C	C
P179	D	D	C	C
P180	D	A	C	C
P181	A	A	C	C
P182	A	A	C	C
P205	A	A	C	A
P209	A	C	C	A
P364	A	A	C	C
P679	A	A	C	A
P683	A	C	C	A
P1163	A	C	C	D

[2034] 表ABC(PC)：生物学研究结果

[2035]

编号	昆虫种类			
	BAW	CL	GPA	YFM
PC1	A	A	C	C
PC2	C	C	C	C
PC3	A	A	C	C
PC5	A	A	C	C

[2036]

PC6	C	C	C	C
PC7	A	A	C	C
PC8	A	A	C	C
PC14	C	C	C	C
PC15	A	A	C	C
PC16	C	C	C	C
PC74	A	A	C	C
PC75	D	C	C	C
PC76	C	C	C	C
PC80	C	C	C	C
PC81	C	C	C	C
PC83	A	A	C	C
PC84	C	C	C	C
PC85	C	C	C	C
PC87	D	A	C	C
PC92	A	A	C	C
PC93	A	A	C	C
PC94	A	A	C	C
PC99	A	D	C	C
PC101	A	A	C	C
PC102	A	D	C	C
PC103	B	D	C	C
PC105	D	D	C	C
PC118	D	C	C	C
PC119	A	A	C	C
PC120	A	A	C	C
PC124	A	A	C	C
PC125	A	A	C	C
PC127	A	A	C	C
PC128	A	A	C	C

[2037]

PC129	A	A	C	C
PC131	A	A	C	C
PC144	A	A	C	C
PC145	A	A	C	C
PC146	A	A	C	C
PC150	A	A	C	C
PC151	A	A	C	C
PC152	A	A	C	C
PC153	D	A	D	B
PC154	A	A	C	C
PC155	A	A	C	C
PC156	A	A	C	C
PC159	A	A	C	C
PC160	A	A	C	D
PC170	B	A	C	C
PC171	B	A	C	C
PC172	A	A	C	C
PC176	B	A	C	C
PC179	B	A	C	C
PC180	B	D	C	C
PC181	B	D	C	C
PC182	D	A	C	C

[2038] 表ABC(FB):生物学研究结果

[2039]

编号	昆虫种类			
	BAW	CL	GPA	YFM
FB1	A	A	C	C
FB2	A	A	C	C
FB3	A	A	C	C
FB4	A	A	C	C

[2040]

FB5	A	A	C	C
FB6	A	A	C	C
FB7	A	A	C	C
FB8	A	A	C	C
FB9	A	A	C	C
FB10	A	A	C	C
FB11	B	A	C	C
FB12	A	A	C	C
FB13	B	A	C	C
FB14	A	A	C	C
FB15	A	A	C	C
FB16	D	A	C	C
FB17	A	A	C	A
FB18	A	A	C	C
FB19	A	A	C	C
FB20	A	A	C	C
FB21	A	A	C	C
FB22	A	A	C	C
FB23	A	A	C	C
FB24	A	A	C	C
FB25	A	A	C	C
FB26	A	A	C	C
FB27	A	A	C	C
FB28	A	A	C	C
FB29	A	A	C	C
FB30	A	A	C	C
FB31	A	A	C	C
FB32	A	A	C	C
FB33	A	A	C	C
FB34	A	A	C	C

[2041]

FB35	A	A	C	C
FB36	B	A	C	C
FB37	B	B	C	C
FB38	B	A	C	C
FB39	A	A	C	C
FB40	A	A	C	A
FB41	A	A	C	A
FB42	A	A	C	A
FB43	A	A	B	A
FB44	A	A	B	A
FB45	A	A	C	C
FB46	A	A	C	C
FB47	A	A	C	A
FB48	A	A	C	A
FB49	A	A	C	A
FB50	A	A	C	C
FB51	A	A	C	A
FB52	A	A	C	C
FB53	A	A	C	B
FB54	A	A	C	A
FB55	A	A	C	C
FB56	A	A	C	A
FB57	A	A	C	A
FB58	A	A	C	A
FB59	A	A	C	A
FB60	A	A	C	A
FB61	A	A	C	A
FB62	A	A	C	A
FB63	A	A	C	A
FB64	A	A	C	C

[2042]

FB65	A	A	C	A
FB66	A	A	C	C
FB67	A	A	C	A
FB68	A	A	C	C
FB69	A	A	C	C
FB70	A	A	C	A
FB71	A	A	C	A
FB72	A	A	C	C