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(56)对比文件
Wen-Ting Zhang等.Iodine-Catalyzed Synthesis of Fused Polycyclic Heterocycles Containing Pyrazoloquinoline via PovarovReaction.《Polycyclic Aromatic Compounds》.2015,第1-11页.

Ming-Yue Yin等.Synthesis of 7-aryl-9-methyl-3h- pyrazolo[4,3-f]quinoline derivatives catalysed by iodine.《JOURNAL OF CHEMICAL RESEARCH》.2011,第513-515页.

Wei Wang等.Iodine-catalysed synthesis of thiopyrano[3,4-c]quinoline derivatives via imino-Diels-Alder reaction.《JOURNAL OF CHEMICAL RESEARCH》.2012,第318-321页.

审查员 常傲

权利要求书1页 说明书107页

(54)发明名称

激酶网络抑制剂及其用途

(57)摘要

本发明总体上涉及作为双重激酶-脱甲基酶抑制剂的化合物,用于治疗由激酶和/或组蛋白脱甲基酶介导的疾病,例如炎症、癌症、病毒和细菌感染、神经和免疫疾病。用于治疗这些疾病的药物组合物和方法也在本发明的范围内。

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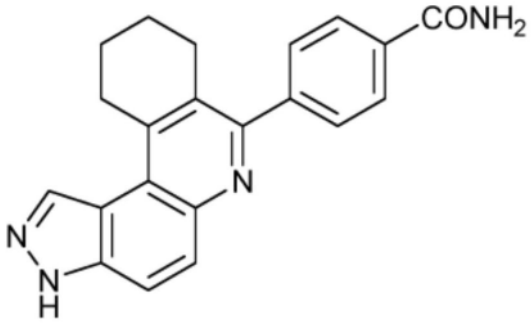
1.一种化合物或其药学上可接受的盐,所述化合物具有如下结构式:



。

2.一种药物组合物,包含一种或多种如权利要求1所述的化合物或其药学上可接受的盐,以及一种或多种稀释剂、赋形剂或载体;或一种或多种权利要求1所述的化合物的纳米颗粒,以及一种或多种稀释剂、赋形剂或载体。

3.根据权利要求1所述的化合物,其中所述化合物为组蛋白脱甲基酶抑制剂。

4.根据权利要求1所述的化合物,其中所述化合物为激酶抑制剂。

5.根据权利要求4所述的化合物,其中,所述激酶选自FLT3、MNK1/2、JAK1/2/3、Limk1/2、各种CDK、Haspin、ROCK1/2、TOPK、LRRK2、GSK3a/3b、RSK1-4、ERK、P70S6K、AKT、PI3K、p38、PKC、PKA、FGFR1-4、VEGFR1-3、ALK、AXL、LIMK1/2、Aurora A/B、ABL1、AKT、CSF1R、CSNK1D、DCAMKL1、CSNK1G2、EPHA2、ERBB2、IKK-alpha、IKK-β、JNK1/2/3、MARK3、MEK1/2、MET、MLK1、PAK1/2/4、PDGFRa/b、PIM1/2/3、PLK1/2/3/4、PRKCE、PRKX、RET、TAOK2、TRKA/B/C、ULK2和受体相互作用蛋白激酶4(RIPK4)。

激酶网络抑制剂及其用途

[0001] 相关申请的交叉引用

[0002] 本美国专利申请涉及并要求于2017年3月29日提交的美国临时申请序列号62/478,069和于2018年1月12日提交的美国临时申请序列号62/616,643的优先权权益，通过引用将其全部内容并入本文。

技术领域

[0003] 本发明总体上涉及作为激酶抑制剂的化合物以及治疗由激酶介导的疾病的方法，所述疾病例如炎症、癌症、病毒和细菌感染、神经和免疫疾病。

背景技术

[0004] 本节介绍可帮助促进更好理解本公开的几个方面。因此，应从这些角度来阅读这些陈述，并且不应将这些陈述理解为对现有技术或非现有技术的承认。

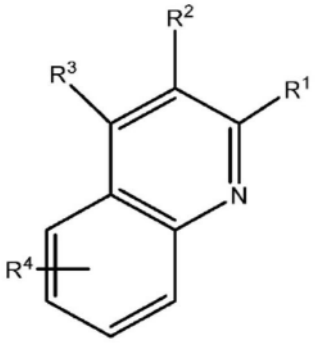
[0005] 细胞包含500多种调节各种过程的激酶，例如调节细胞周期、生长、移行、免疫反应[1]。几种失调的激酶(即已获得功能获得性突变或过表达的激酶)可驱动癌症扩散[1]。癌症驱动激酶的小分子抑制剂(例如BCR-ABL1融合蛋白，FLT3-ITD，突变或过表达的ALK、EGFR、PDGFR、Kit、VEGFR、B-Raf、BTK、PI3Kδ、ErbB2)已见临床成功[2]。最近，人们已努力针对其他激酶，例如细胞周期激酶(CDK)或靶向组蛋白、细胞骨架或对细胞重要的其他过程的激酶，以阻止癌症的生长。大多数进入临床的激酶抑制剂起初都是起作用的，但是随着时间的流逝会出现耐药克隆而导致药物无效[3]。各种机制解释了癌细胞对激酶抑制剂的耐药性。例如，拷贝数倍增，其他激酶突变(例如在FLT3-ITD激酶的酪氨酸激酶域中产生的二级突变)或其他激酶途径和/或下游靶标的激活可以绕过特定激酶靶标的抑制作用[4]。抑制癌症驱动激酶以及下游靶标(激酶和非激酶靶标，例如组蛋白脱甲基酶)的激酶抑制剂和/或与驱动激酶协同作用的激酶可能会增强药效，并降低对该激酶抑制剂产生耐药性的可能性[5]。然而，这种多药效团的挑战是避免可导致毒性的混杂结合。

[0006] 激酶抑制剂也已被证明可有效治疗免疫疾病(例如JAK激酶[6])、高血压和勃起功能障碍(ROCK1/2激酶[7])和青光眼(ROCK和LIMK激酶[8])。其他激酶靶标(如LRRK2)也已显示对CNS相关疾病很重要，如阿尔茨海默氏病或帕金森氏病[9]。特有的化学支架可调节以选择性抑制疾病相关激酶或抑制位于特定途径或网络中的一组激酶，其可以促进多种疾病状态的治疗。

发明内容

[0007] 本发明总体上涉及抑制激酶和/或组蛋白脱甲基酶网络的化合物，作为治疗由激酶介导的疾病的有用化合物，所述疾病例如炎症、癌症、病毒和细菌感染、神经和免疫疾病。用于治疗这些疾病的药物组合物和方法在本发明的范围内。

[0008] 在一些说明性的实施方案中，本发明涉及一种具有以下结构式的化合物或其药学上可接受的盐，

[0009] 

(I),

[0010] 其中，

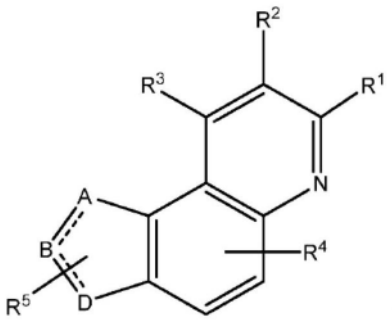
[0011] R^1为氨基、羟基及其衍生物、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、酰基、芳基、杂芳基、芳基烷基、芳基烯基或芳基炔基，其中的每个被任选取代；

[0012] R^2和R^3各自独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基，其中的每个被任选取代；或

[0013] R^2和R^3与连接的碳一起形成任选取代的环部分或杂环部分；以及

[0014] R^4代表四个取代基，每个取代基独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基，其中的每个被任选取代；或所述四个取代基中的任何两个相邻的取代基与连接的碳一起形成任选取代的环部分或杂环部分。

[0015] 在一些说明性的实施方案中，本发明涉及一种具有如下结构式的化合物或其药学上可接受的盐，

[0016] 

(II),

[0017] 其中，n＝1～5；A与B之间的键、B与D之间的键可为双键或单键，但不能同时为双键；A、B和D独立地表示C、O、N和S，其中A、B和D中的至少一个是杂原子；

[0018] R^1为氨基、羟基及其衍生物、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、酰基、芳基、杂芳基、芳基烷基、芳基烯基或芳基炔基，其中的每个被任选取代；

[0019] R^2和R^3各自独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳

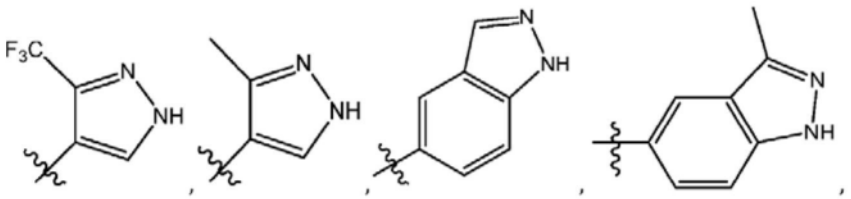
基烯基和芳基炔基，其中的每个被任选取代；或

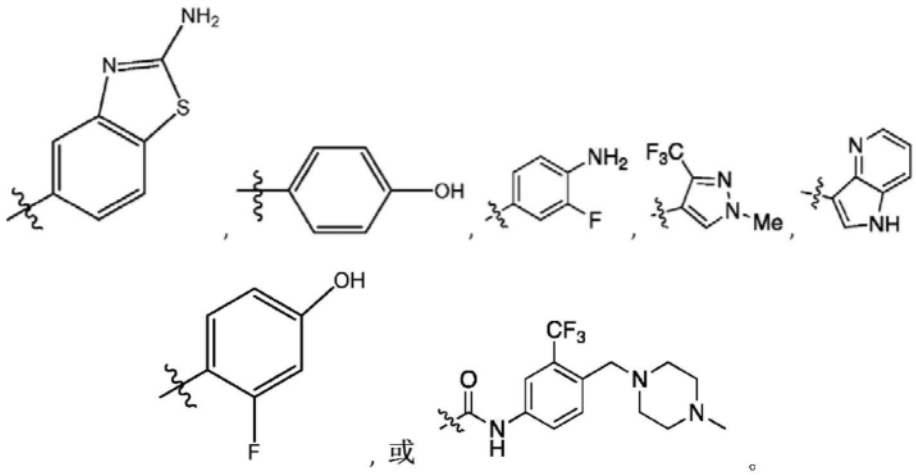
[0020] R^2和R^3与连接的碳一起形成任选取代的环部分或杂环部分；

[0021] R^4代表两个取代基，每个取代基独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基，其中的每个被任选取代；或所述两个取代基与连接的碳一起形成任选取代的环部分或杂环部分；以及

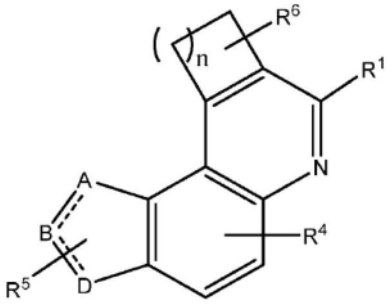
[0022] 根据A、B和D的元素，R^5代表两个或三个取代基，每个取代基独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基，其中的每个被任选取代。

[0023] 在一些说明性的实施方案中，本发明涉及一种具有结构式(II)的化合物，其中R^1为

[0024] 

[0025] 

[0026] 在一些说明性的实施方案中，本发明涉及一种具有结构式(III)的化合物或其药学上可接受的盐，

[0027] 

[0028] 其中n＝1～5；A与B之间的键、B与D之间的键可为双键或单键，但不能同时为双键；

A、B和D独立地表示C、O、N和S，其中A、B和D中的至少一个是杂原子；

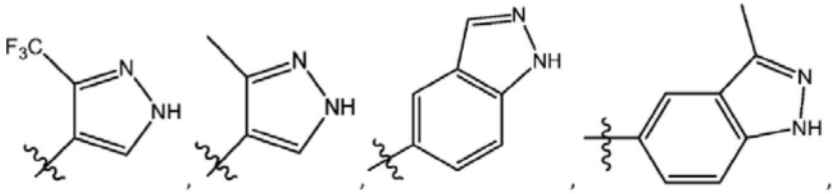
[0029] R^1为氨基、羟基及其衍生物、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、酰基、芳基、杂芳基、芳基烷基、芳基烯基或芳基炔基，其中的每个被任选取代；

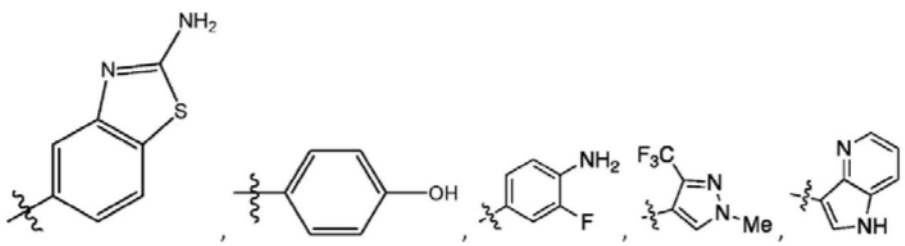
[0030] R^4代表两个取代基，每个取代基独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基，其中的每个被任选取代；或所述两个取代基与连接的碳一起形成任选取代的环部分或杂环部分；

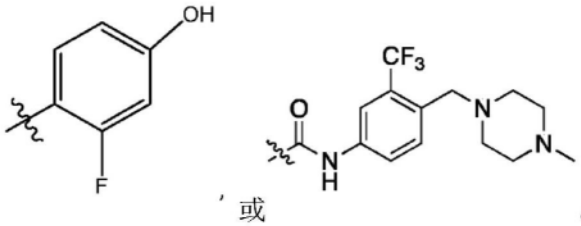
[0031] 根据A、B和D的元素，R^5代表两个或三个取代基，每个取代基独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基，其中的每个被任选取代；以及

[0032] 根据n的值，R^6代表2至6个取代基，每个取代基独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基，其中的每个被任选取代。

[0033] 在一些说明性的实施方案中，本发明涉及一种具有结构式(III)的化合物，其中R^1为：

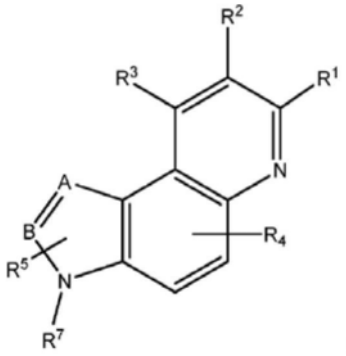
[0034] 

[0035] 



或 。

[0036] 在一些说明性的实施方案中，本发明涉及一种具有结构式(IV)的化合物或其药学上可接受的盐，

[0037] 

(IV),

[0038] 其中＝1～5；

[0039] R^1为氨基、羟基及其衍生物、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、酰基、芳基、杂芳基、芳基烷基、芳基烯基或芳基炔基，其中的每个被任选取代；

[0040] R^2和R^3各自独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基，其中的每个被任选取代；或R^2和R^3与连接的碳一起形成任选取代的环部分或杂环部分；

[0041] R^4代表两个取代基，每个取代基独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基，其中的每个被任选取代；或所述两个取代基与连接的碳一起形成任选取代的环部分或杂环部分；

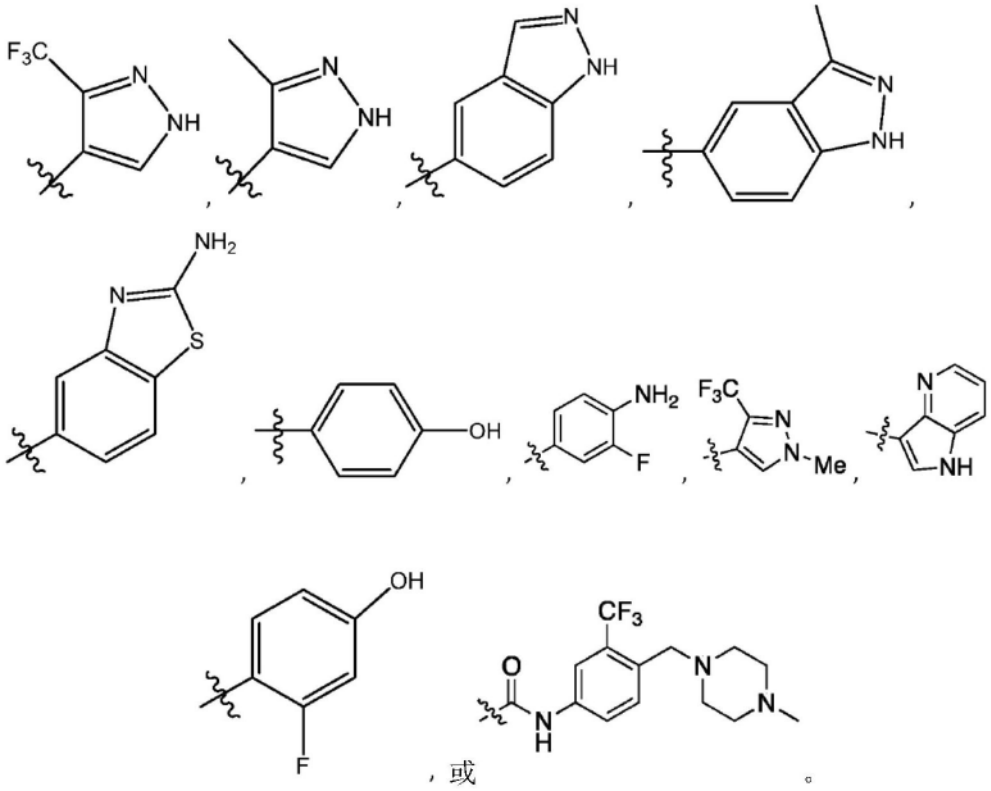
[0042] 根据以下限定的A和B的元素，R^5代表一个或两个取代基，每个取代基独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基，其中的每个被任选取代；

[0043] A和B独立地代表CR^8、N或NR^9，其中R^8和R^9独立地代表氢、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、酰基、芳基、杂芳基、芳基烷基、芳基烯基或芳基炔基，其中的每个被任选取代；

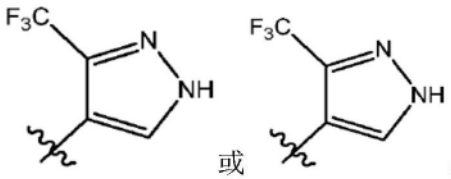
[0044] 根据n的值，R^6代表2至6个取代基，每个取代基独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基，其中的每个被任选取代；以及

[0045] R^7为烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、酰基、芳基、杂芳基、芳基烷基、芳基烯基或芳基炔基，其中的每个被任选取代。

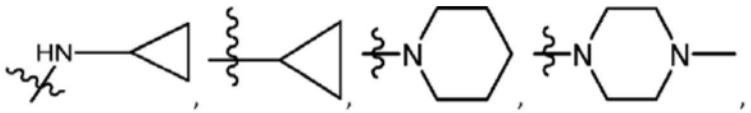
[0046] 在一些说明性的实施方案中，本发明涉及一种具有结构式(IV)的化合物，其中R^1为

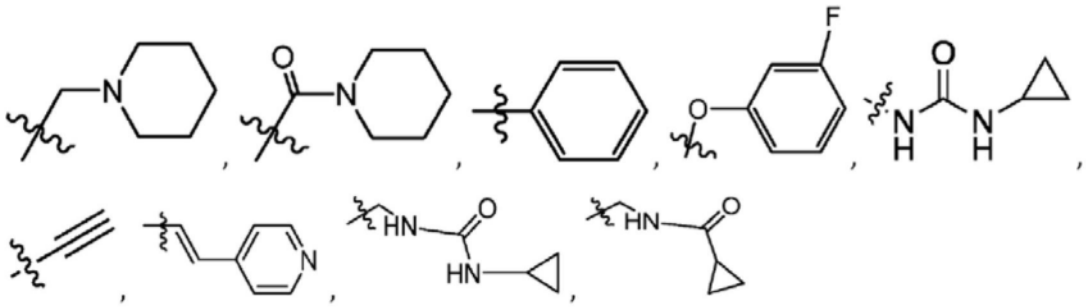
[0047] 

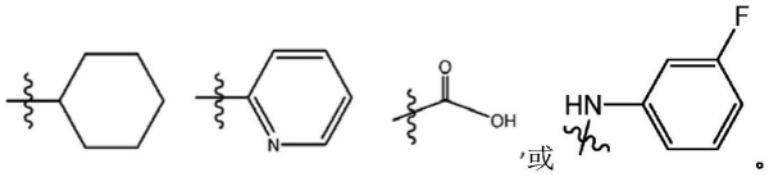
[0048] 在一些说明性的实施方案中，本发明涉及一种具有结构式(IV)的化合物，其中R^1为

[0049]  A为碳(C)；B为氮(N)；R^5、R^6和R^7均代表氢，R^4代表两个取代基，每个取代基独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基，其中的每个被任选取代；或所述两个取代基与连接的碳一起形成任选取代的环部分或杂环部分。

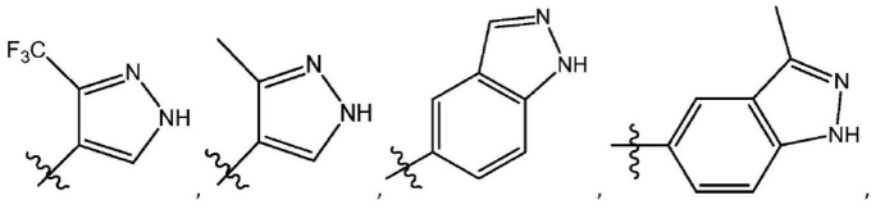
[0050] 在一些说明性的实施方案中，本发明涉及一种具有结构式(IV)的化合物，其中R^3为

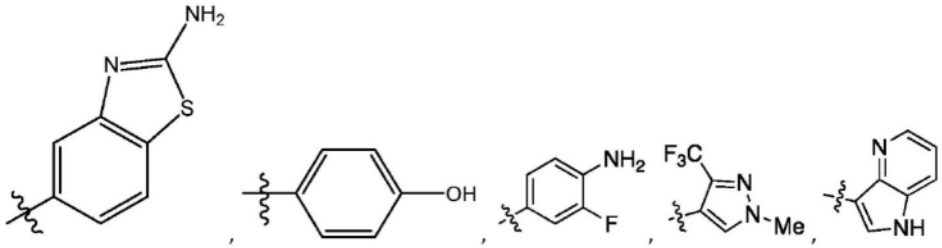


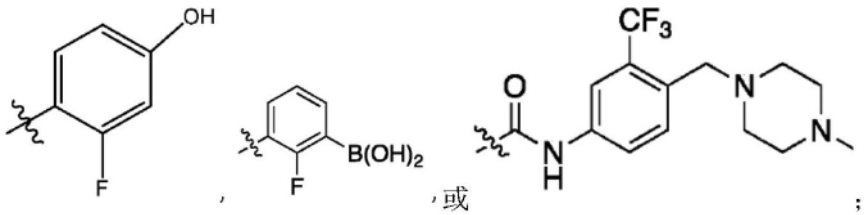
[0051] 

[0052] 

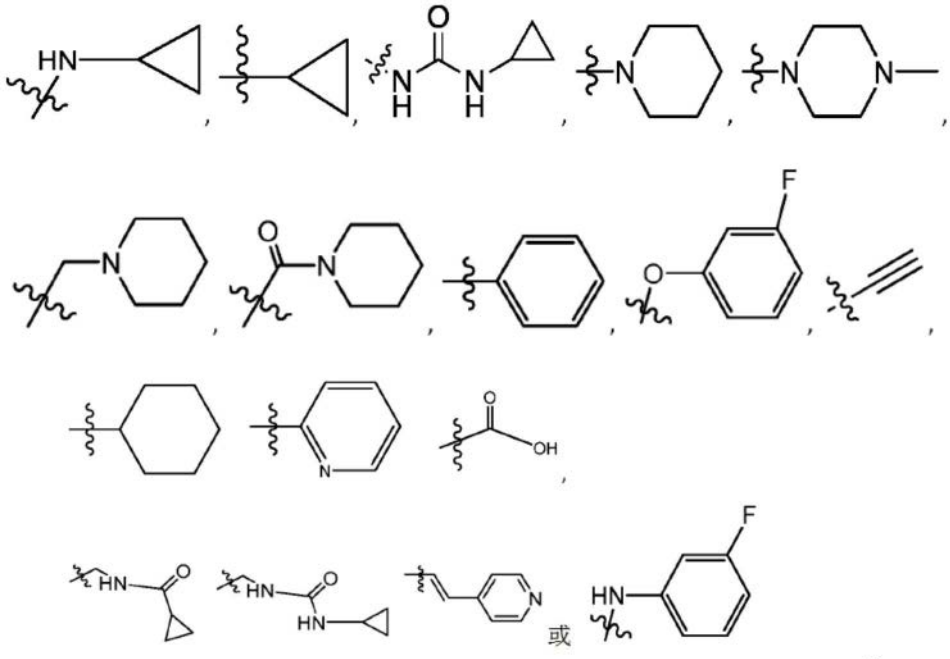
[0053] 在一些说明性的实施方案中，本发明涉及一种具有结构式(IV)的化合物，其中R^1为



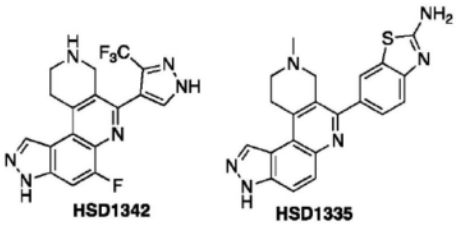
[0054] 

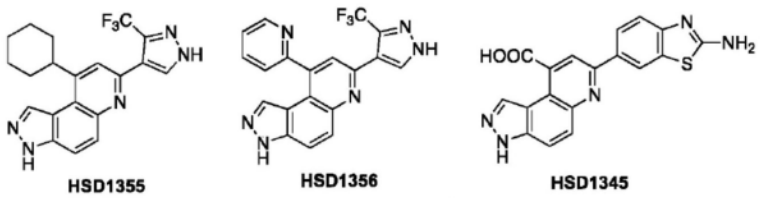
[0055]  以及R^3为

；

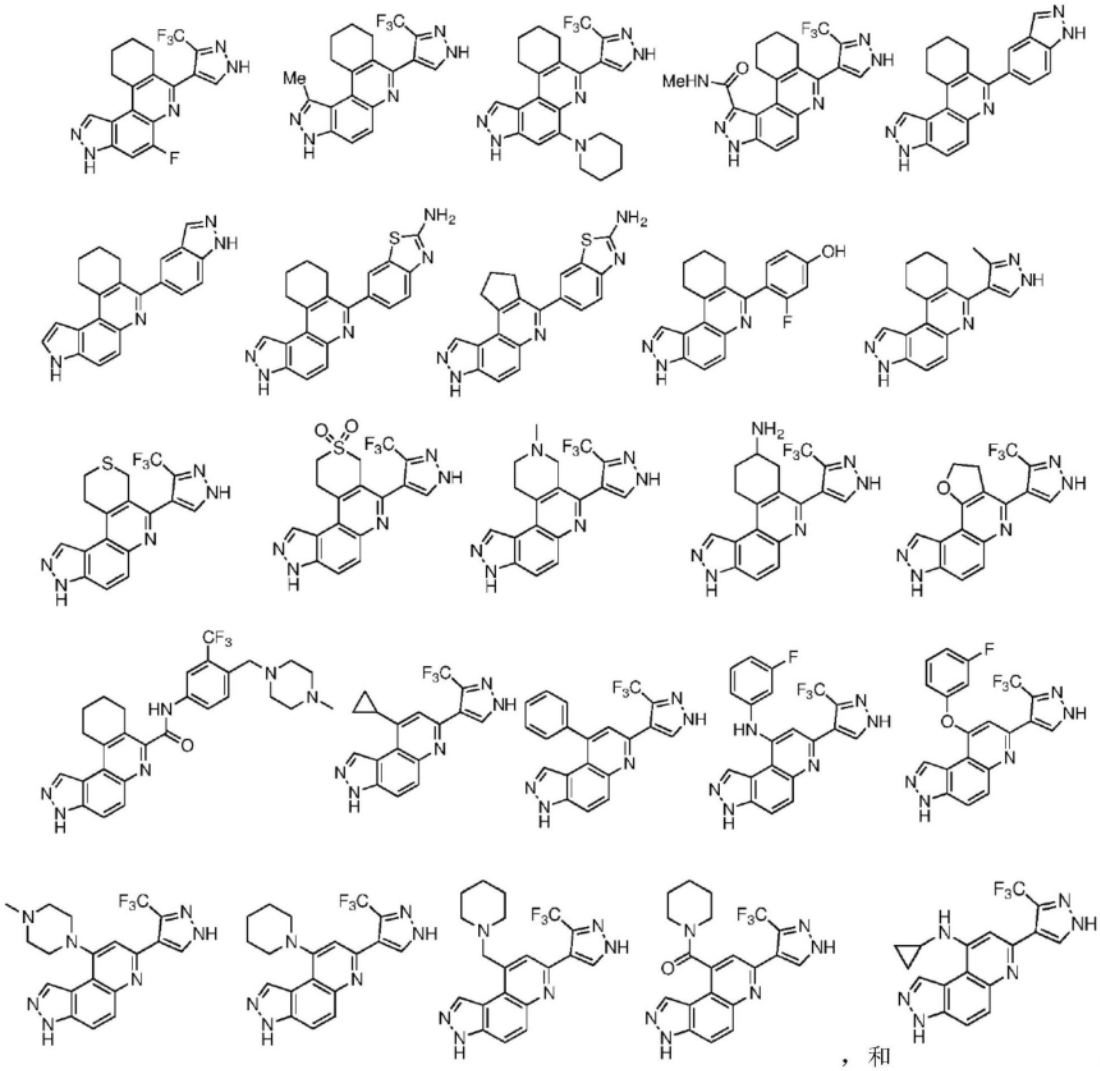
[0056] 

[0057] 在一些说明性的实施方案中,本发明涉及一种具有结构式(I)的化合物,其中所述化合物为





[0058]



[0059] 在一些说明性的实施方案中,本发明涉及药物组合物,其包含一种或多种如本文公开的化合物或其药学上可接受的盐,以及一种或多种稀释剂、赋形剂或载体。

[0060] 在一些说明性的实施方案中,本发明涉及一种激酶抑制剂,其中,所述激酶选自下组:FLT3、MNK1/2、JAK1/2/3、Limk1/2、各种CDKs、Haspin、ROCK1/2、TOPK、LRRK2、GSK3a/3b、RSK1-4、ERK、P70S6K、AKT、PI3K、p38、PKC、PKA、FGFR1-4、VEGFR1-3、ALK、AXL、LIMK1/2、Aurora A/B、ABL1、AKT、CSF1R、CSNK1D、DCAMKL1、CSNK1G2、EPHA2、ERBB2、IKK-α、IKK-β、

JNK1/2/3、MARK3、MEK1/2、MET、MLK1、PAK1/2/4、PDGFRa/b、PIM1/2/3、PLK1/2/3/4、PRKCE、PRKX、RET、TAOK2、TRKA/B/C、ULK2和受体相互作用蛋白激酶4(RIPK4)。

[0061] 在一些说明性的实施方案中,本发明涉及一种用于治疗由激酶和/或组蛋白脱甲基酶介导的疾病的方法,所述疾病包括炎症、癌症、病毒和细菌感染、胃肠道疾病、眼病、神经疾病、心血管疾病和免疫疾病,所述方法包括以下步骤:将治疗有效量的一种或多种如本文公开的化合物、以及一种或多种载体、稀释剂或赋形剂给予需要从所述癌症中缓解的患者。

[0062] 在一些说明性的实施方案中,本发明涉及一种用于治疗由激酶和组蛋白脱甲基酶介导的疾病的方法,所述疾病包括炎症、癌症、病毒和细菌感染、胃肠道疾病、眼病、神经疾病、心血管疾病和免疫疾病,所述方法包括以下步骤:将治疗有效量的如本文公开的化合物与一种或多种具有相同或不同作用的其他化合物以及一种或多种载体、稀释剂或赋形剂组合给予需要从所述癌症中缓解的患者。

[0063] 参考以下具体实施方式和权利要求,将更好地理解本发明的这些和其他特征、方面和优点。

具体实施方式

[0064] 尽管本文的说明书示出和详细描述了本公开的构思,但是说明书中的结果应视为示例性的,在性质上不具有限制性。应当理解的是,仅示出和描述了示例性实施例,并且希望保护落入本公开的精神内的所有改变和修改。

[0065] 本发明总体涉及作为激酶抑制剂的化合物,其可用于治疗由激酶介导的疾病,例如炎症、癌症、病毒和细菌感染、神经和免疫疾病。用于治疗这些疾病的药物组合物和方法在本发明的范围内。

[0066] 如本文所使用,以下术语和短语应具有如下所述含义。除非另有定义,否则本文使用的所有技术和科学术语具有与本领域普通技术人员的通常理解的相同的含义。

[0067] 本发明中,术语“约”可允许值或范围一定程度的可变性,例如,在所声称的数值或范围的限度的10%以内、5%以内或1%以内。本公开中,术语“基本上”可允许值或范围一定程度的可变性,例如,在所声称的数值或范围的限度的90%以内、95%、99%、99.5%、99.9%、99.99%或至少约99.999%以内或更高。

[0068] 在本文中,除非上下文另外明确指出,否则术语“一(a/an)”或“所述(the)”用于包括一个或多个。除非另有说明,否则术语“或”用于表示非排他性的“或”。另外,应当理解的是,本文中采用且没有另外定义的措词或术语仅是出于描述的目的,而不是限制性的。节标题的任何使用均旨在帮助阅读文本,而不应理解为限制性的。此外,与节标题相关的信息可出现在该特定节之内或之外。此外,本文中引用的所有出版物、专利和专利文件通过全文引用并入本文,如同通过引用单独地并入。当本文与通过引用方式并入的那些文本之间用法不一致时,应将所并入的参考文献中的用法视为对本文本的补充;对于矛盾的不一致之处,以本文本中的用法为准。

[0069] 如本文所用,术语“取代”是指官能团中包含的一个或多个氢原子被一个或多个非氢原子替代。本文所用的术语“官能团”或“取代基”是指可被分子取代或已被分子取代的基团。取代基或官能团的实例包括但不限于卤素(例如,F、Cl、Br和I);诸如以下基团中的氧原

子:羟基、烷氧基、芳氧基、芳烷氧基、氧代(羰基)基、羧酸、羧酸盐和羧酸酯的羧基;诸如以下基团中的硫原子:硫醇基、烷基和芳基硫基、亚砜基、磺酸基、磺酰基和磺酰胺基;诸如以下基团中的氮原子:胺、叠氮化物、羟胺、氰基、硝基、N-氧化物、酰肼和烯胺;和其他各种基团中的杂原子。

[0070] 本文所用的术语"烷基"是指具有1至约20个碳原子(C_1-C_{20})、1至12个碳(C_1-C_{12})、1至8个碳原子(C_1-C_8)的取代或未取代的直链和支链烷基和环烷基,或在一些实施方案中,具有1-6个碳原子(C_1-C_6)。直链烷基的实例包括具有1至8个碳原子的烷基,例如甲基、乙基、正丙基、正丁基、正戊基、正己基、正庚基和正辛基。支链烷基的实例包括但不限于异丙基、异丁基、仲丁基、叔丁基、新戊基、异戊基和2,2-二甲基丙基。如本文所用,术语"烷基"涵盖正烷基、异烷基和反异烷基以及其他支链形式的烷基。代表性的取代的烷基可被本文列出的任何基团例如氨基、羟基、氰基、羧基、硝基、巯基、烷氧基和卤素取代一次或多次。

[0071] 本文所用的术语"烯基"是指具有2至20个碳原子(C_2-C_{20})、2至12个碳(C_2-C_{12})、2至8个碳原子(C_2-C_8)和至少一个碳-碳双键的取代或未取代的直链和支链二价烯基和环烯基,或在一些实施方案中,具有2-4个碳原子(C_2-C_4)和至少一个碳-碳双键。直链烯基的实例包括具有2至8个碳原子的直链烯基,例如-CH=CH-、-CH=CHCH$_2$-等。支链烯基的实例包括但不限于-CH=C(CH$_3$)-等。

[0072] 炔基是在碳原子上包含开放的连接点的片段,如果从炔烃分子中除去与三键键合的碳原子相连的氢原子,则会形成开放的连接点。本文所用的术语"羟烷基"是指被至少一个羟基(-OH)取代的本文所定义的烷基。

[0073] 本文所用的术语"环烷基"是指取代或未取代的环状烷基,例如但不限于环丙基、环丁基、环戊基、环己基、环庚基和环辛基。在一些实施方案中,环烷基可具有3至约8-12个环成员,而在其他实施方案中,环碳原子数的范围为3至4、5、6或7。在一些实施方案中,环烷基可具有3至6个碳原子(C_3-C_6)。环烷基还包括多环环烷基,例如但不限于降冰片基、金刚烷基、冰片基、脱氧苯基(camphenly)、异脱氧苯基(isocamphenyl)和蒈烯基(carenyl groups),以及稠合环,诸如但不限于十氢化萘基等。

[0074] 本文使用的术语"酰基"是指含有羰基部分的基团,其中该基团通过羰基碳原子键合。羰基碳原子还与另一个碳原子键合,该另一个碳原子可以是取代或未取代的烷基、芳基、芳烷基环烷基,环烷基烷基、杂环基、杂环基烷基、杂芳基、杂芳基烷基等的一部分。在其中羰基碳原子与氢键合的特殊情况下,该基团是"甲酰基",术语"酰基"如本文所定义。酰基可包括0至约12-40、6-10、1-5或2-5个与羰基键合的额外碳原子。丙烯酰基是酰基的实例。在本文含义内酰基也可包括杂原子。烟酰基(吡啶基-3-羰基)是本文含义内的酰基的实例。其他实例包括乙酰基、苯甲酰基、苯乙酰基、吡啶基乙酰基、肉桂酰基和丙烯酰基等。当包含与羰基碳原子键合的碳原子的基团包含卤素时,该基团被称为"卤代酰基"。实例是三氟乙酰基。

[0075] 本文所用的术语"芳基"是指在环中不包含杂原子的取代或未取代的环状芳族烃。因此,芳基包括但不限于苯基、奥基(azulenyl)、庚烯基(heptalenyl)、联苯基(biphenyl)、茚并烯基(indacenyl)、芴基(fluorenyl)、菲基(phenanthrenyl)、三联苯基(triphenylenyl)、芘基(pyrenyl)、萘并烯基(naphthacenyl)、草基(chrysenyl)、二联苯基(biphenylenyl)、蒽基(anthracenyl)和萘基。在一些实施方案中,在芳基基团的环部分中

包含约6至约14个碳(C_6-C_{14})或6至10个碳原子(C_6-C_{10})。如本文所定义,芳基可以是未取代的或取代的。代表性的取代的芳基基团可以被单取代或多取代,例如但不限于2-、3-、4-、5-或6-取代的苯基或2-8取代的萘基,它们可以被如本文所列的那些碳或非碳基团取代。

[0076] 本文所用的术语"芳烷基(aralkyl)"和"芳基烷基(arylalkyl)"是指本文所定义的烷基,其中烷基的氢或碳键被与本文所定义的芳基键合的键取代。代表性的芳烷基包括苄基和苯乙基,以及稠合的(环烷基芳基)烷基,例如4-乙基-茚满基。芳烯基是本文定义的烯基,其中烷基的氢或碳键被与本文定义的芳基键合的键取代。

[0077] 本文使用的术语"杂环基"是指含有3个或更多个环成员的取代或未取代的芳族和非芳族环化合物,其中一个或多个是杂原子,例如但不限于B、N、O和S。因此,杂环基可以是环杂烷基或杂芳基,或者如果是多环的,则可以是它们的任何组合。在一些实施方案中,杂环基包括3至约20个环成员,而其他此类基团具有3至约15个环成员。在一些实施方案中,杂环基包括包含3至8个碳原子(C_3-C_8)、3至6个碳原子(C_3-C_6)或6至8个碳原子(C_6-C_8)的杂环基。

[0078] 杂芳基环是杂环基的一个具体实例。短语"杂环基"包括稠环,稠环包括那些包括稠合的芳族和非芳族基团的环。代表性的杂环基包括但不限于吡咯烷基、氮杂环丁烷基(azetidinyl)、哌啶基(piperidynyl)、哌嗪基(piperazinyl)、吗啉基(morpholinyl)、吡喃基(chromanyl)、吲哚基(indolinonyl)、异吲哚基(isoindolinonyl)、呋喃基(furanyl)、吡咯烷基(pyrrolidinyl)、吡啶基(pyridinyl)、吡嗪基(pyrazinyl)、嘧啶基(pyrimidinyl)、三嗪基(triazinyl)、噻吩基(thiophenyl)、四氢呋喃基(tetrahydrofuranyl)、吡咯基(pyrrolyl)、恶唑基(oxazolyl)、恶二唑基(oxadiazolyl)、咪唑基(imidazolyl)、三唑基(triazyolyl)、四唑基(tetrazolyl)、苯并恶唑啉基(benzoxazolinyl)、苯并噻唑啉基(benzthiazolinyl)和苯并咪唑啉基(benzimidazolinyl)。

[0079] 本文所用的术语"杂环基烷基"是指本文所定义的烷基,其中本文所定义的烷基的氢或碳键被如本文所定义的杂环基的键取代。代表性的杂环基烷基包括但不限于呋喃-2-基甲基、呋喃-3-基甲基、吡啶-3-基甲基、四氢呋喃-2-基甲基和吲哚-2-基丙基。

[0080] 本文所用的术语"杂芳基烷基"是指本文所定义的烷基,其中烷基的氢或碳键被与本文所定义的杂芳基键合的键取代。

[0081] 本文所用的术语"烷氧基"是指氧原子与烷基连接,包括与如本文所定义的环烷基连接。直链烷氧基的实例包括但不限于甲氧基、乙氧基、丙氧基、丁氧基、戊氧基、己氧基等。支链烷氧基的实例包括但不限于异丙氧基、仲丁氧基、叔丁氧基、异戊氧基、异己基氧基等。环状烷氧基的实例包括但不限于环丙氧基、环丁氧基、环戊氧基、环己氧基等。烷氧基可进一步包含双键或三键,并且还可包含杂原子。例如,烯丙氧基是本文含义内的烷氧基。在本文的含义中,甲氧基乙氧基也是烷氧基,在亚甲二氧基结构中的两个相邻原子被其取代的情况下,亚甲二氧基也是。

[0082] 本文所用的术语"胺"是指具有例如式$N(基团)_3$的伯、仲和叔胺,其中每个基团可以独立地为H或非H,例如烷基、芳基等。胺包括但不限于$R\text{-}NH_2$,例如,烷基胺、芳基胺、烷基芳基胺;R_2NH,其中每个R独立地选择,例如二烷基胺、二芳基胺、芳烷基胺、杂环基胺等;R_3N,其中每个R独立地选择,例如三烷基胺、二烷基芳基胺、烷基二芳基胺、三芳基胺等。术语"胺"还包括本文所用的铵离子。

[0083] 本文所用的术语“氨基”是指-NH_2、-NHR、-NR_2、-NR_3^+形式的取代基，其中每个R独立地选择，以及每个取代基的质子化形式，但-NR_3^+不能被质子化。因此，可以将任何被氨基取代的化合物视为胺。本文含义内的“氨基”可以是伯、仲、叔或季氨基。“烷基氨基”包括单烷基氨基、二烷基氨基和三烷基氨基。

[0084] 除非另有说明，否则本文所用的术语“卤代”、“卤素”或“卤化”基团本身可作为取代基或作为另一取代基的一部分，是指氟、氯、溴或碘原子。

[0085] 如本文所用，术语“卤代烷基”包括单卤代烷基，其中所有卤原子可相同或不同的聚卤代烷基，以及其中所有氢原子均被卤素原子例如氟取代的全卤代烷基。卤代烷基的实例包括三氟甲基、1,1-二氯乙基、1,2-二氯乙基、1,3-二溴-3,3-二氟丙基、全氟丁基、-$CF(CH_3)_2$等。

[0086] 本文所用的术语“任选地取代(optionally substituted)”或“任选取代(optional substitutents)”是指所讨论的基团未被取代或被一个或多个指定的取代基取代。当所讨论的基团被多个取代基取代时，这些取代基可以相同或不同。当使用术语“独立地”，“独立地是”和“独立地选自”时，所讨论的基团可以相同或不同。本文定义的某些术语可在结构中出现多次，并且一旦出现，每个术语应独立定义。

[0087] 本文所述的化合物可以包含一个或多个手性中心，或者可以另外以多种立体异构体的形式存在。应当理解，在一个实施方案中，本文所述的本发明不限于任何特定的立体化学要求，而是包括它们的化合物、组合物、方法、用途和药物可以是光学纯的，或者可以是包括以下各种立体异构体的任意混合物：对映异构体的外消旋和其他合物、非对映异构体的其他混合物等。还应理解，此类立体异构体的混合物可包括处于一个或多个手性中心的单一的立体化学构型，同时包括处于一个或多个其他手性中心的立体化学构型的混合物。

[0088] 类似地，本文所述的化合物可包括几何中心，例如顺式、反式、E和Z双键。应当理解，在另一个实施方案中，本文所述的本发明不限于任何特定的几何异构体要求，而是包括它们的化合物、组合物、方法、用途和药物可以是纯的，或者可以是各种几何异构体的任意混合物。还应理解，此类几何异构体的混合物可包括处于一个或多个双键的单一构型，同时包括处于一个或多个其他双键的几何形状的混合物。

[0089] 如本文所用，术语“盐”和“药学上可接受的盐”是指所公开化合物的衍生物，其中母体化合物通过制备其酸式盐或碱式盐而被修饰。药学上可接受的盐的实例包括但不限于碱性基团如胺的无机酸盐或有机酸盐；以及酸性基团如羧酸的碱金属盐或有机盐。药学上可接受的盐包括例如由无毒无机酸或有机酸形成的母体化合物的常规无毒盐或季铵盐。例如，这种常规无毒盐包括衍生自无机酸例如盐酸、氢溴酸、硫酸、氨基磺酸、磷酸和硝酸的那些无毒盐；由有机酸如乙酸、丙酸、琥珀酸、乙醇酸、硬脂酸、乳酸、苹果酸、酒石酸、柠檬酸、抗坏血酸、巴莫酸、马来酸、羟基马来酸、苯乙酸、谷氨酸、苯甲酸、水杨酸、磺胺酸、2-乙酰氧基苯甲酸、富马酸、甲苯磺酸、甲磺酸、乙烷二磺酸、草酸和羟乙磺酸等制备的盐。

[0090] 药学上可接受的盐可以通过常规化学方法从含有碱性或酸性部分的母体化合物合成。在某些情况下，可以通过使游离酸或碱形式的这些化合物与化学计算量的适当的碱或酸在水或有机溶剂中或在两者的混合物中反应来制备此类盐。通常，非水介质如乙醚、乙酸乙酯、乙醇、异丙醇或乙腈是优选的。合适的盐的列表可见于雷明登氏药学全书(Remington’s Pharmaceutical Sciences)，第17版，Mack出版公司，宾夕法尼亚州伊斯顿，

1985年,其公开内容通过引用结合到本文中。

[0091] 术语“溶剂化物(solvate)”是指还包括通过非共价分子间力结合的化学计量或非化学计量量的溶剂的化合物或其盐。当溶剂是水时,溶剂化物是水合物。

[0092] 术语“前药”是指化合物的衍生物,其可以在生物条件下(体外或体内)水解、氧化或以其他方式反应以提供活性化合物,特别是本发明化合物。前药的实例包括但不限于本发明化合物的衍生物和代谢物,其包括可生物水解的部分,例如可生物水解的酰胺、可生物水解的酯、可生物水解的氨基甲酸酯、可生物水解的碳酸盐、可生物水解的脲酸酯和可生物水解的磷酸盐类似物。具有羧基官能团的化合物的特定前药是羧酸的低级烷基酯。通过酯化分子上存在的任何羧酸部分,方便形成羧酸酯。前药通常可以使用众所周知的方法来制备,例如汉堡药物化学和药物发现(Burger’s Medicinal Chemistry and Drug Discovery)第6版(Donald J.Abraham编辑,2001,Wiley)和原药的设计和应用(Design and Application of Prodrugs)(H.Bundgaard编辑,1985,哈伍德学术出版社(Harwood Academic Publishers GmbH))中记载的方法。

[0093] 此外,在前述和以下每个实施方案中,应理解,结构式不仅包括并代表化合物的所有药学上可接受的盐,而且还包括化合物结构式或其盐的任何和所有水合物和/或溶剂化物。应当理解,某些官能团,例如羟基、氨基和类似基团形成各种物理形式的具有水和/或各种溶剂的络合物和/或配位化合物。因此,以上结构式应理解为包括并代表那些各种水合物和/或溶剂化物。在前述和以下实施方案的每一个中,还应理解,该结构式包括并代表每种可能的异构体,例如单独和以任何和所有可能的混合物形式的立体异构体和几何异构体。在前述和以下实施方案的每一个中,还应理解,结构式包括并代表任何和所有结晶形式、部分结晶形式以及非结晶和/或无定形形式的化合物。

[0094] 术语“药学上可接受的载体”是本领域公认的,并且是指药学上可接受的材料、组合物或媒介物,例如液体或固体填充剂、稀释剂、赋形剂、溶剂或胶囊材料,其参与或运输任何主题组合物或其组分。每个载体在与主题组合物及其组分相容且对患者无害的意义上必须是“可接受的”。可以用作药学上可接受的载体的材料的一些实例包括:(1)糖,例如乳糖、葡萄糖和蔗糖;(2)淀粉,例如玉米淀粉和马铃薯淀粉;(3)纤维素及其衍生物,例如羧甲基纤维素钠、乙基纤维素和醋酸纤维素;(4)黄芪粉;(5)麦芽;(6)明胶;(7)滑石;(8)赋形剂,例如可可脂和栓剂蜡;(九)油,例如花生油、棉籽油、红花油、芝麻油、橄榄油、玉米油和大豆油;(10)二醇,例如丙二醇;(11)多元醇,例如甘油、山梨糖醇、甘露糖醇和聚乙二醇;(12)酯,例如油酸乙酯和月桂酸乙酯;(13)琼脂;(14)缓冲剂,例如氢氧化镁和氢氧化铝;(15)海藻酸;(16)无热原水;(17)等渗盐水;(18)林格溶液;(19)乙醇;(20)磷酸盐缓冲溶液;(21)药物制剂中使用的其他无毒相容性物质。

[0095] 本文所用术语“给药”包括将本文所述的化合物和组合物给予患者的所有方式,包括但不限于口服(po)、静脉内(iv)、肌内(im)、皮下(sc)、经皮、吸入、颊、眼、舌下、阴道、直肠等。本文所述的化合物和组合物可以以单位剂型和/或含有常规无毒的药学上可接受的载体、佐剂和赋形剂的制剂给药。

[0096] 口服给药的说明性形式包括片剂、胶囊剂、酏剂、糖浆剂等。肠胃外给药的示例性途径包括静脉内、动脉内、腹膜内、硬膜外、尿道内、胸骨内、肌内和皮下以及任何其他本领域公认的肠胃外给药途径。

[0097] 肠胃外给药的说明性手段包括针头(包括微针)注射器、无针注射器和输液技术，以及本领域公认的任何其他肠胃外给药手段。肠胃外制剂通常是水溶液，其可以包含赋形剂例如盐、碳水化合物和缓冲剂(优选pH范围为约3至约9)，但是对于某些应用，它们可以更合适地配制成无菌无水溶液或制成可与合适的媒介物例如无菌无热原水一起使用的干燥形式。在无菌条件下例如通过冻干制备肠胃外制剂可以使用本领域技术人员众所周知的标准制药技术容易地完成。化合物的肠胃外给药说明性地以盐溶液形式或将化合物掺入脂质体中进行。在化合物本身不具有足够的溶解度而不能溶解的情况下，可以使用诸如乙醇的增溶剂。

[0098] 所要求保护的组合的每种化合物的剂量取决于几个因素，包括：给药方法、待治疗的病症、病症的严重程度、是否要治疗或预防该病症以及被治疗的人年龄、体重和健康状况。另外，关于特定患者的药物基因组学(基因型对治疗药物的药代动力学、药效动力学或功效谱的影响)信息可影响所用剂量。

[0099] 应该理解的是，在本文所述的方法中，可以通过任何合适的方式同时、并行、顺序、分别或以单一药物制剂的形式给予共同给药或组合给药的各个组分。当共同给药的化合物或组合物以不同剂型给予时，每种化合物每天给予的剂量数可相同或不同。化合物或组合物可通过相同或不同的给药途径来给药。化合物或组合物可以根据同时或交替方案在治疗过程中的相同或不同时间以分开或单一形式同时给药。

[0100] 在本文所用术语“治疗有效量”指的是引起由研究者、兽医、医生或其他临床医生所寻找的组织系统、动物或人的生物或医学反应的活性化合物或药剂的量，所述生物或医学反应包括减轻所治疗疾病或病症的症状。一方面，治疗有效量是可以以适用于任何医学治疗的合理的利益/风险比治疗或减轻疾病或疾病症状的量。然而，应理解，本文所述的化合物和组合物的每日总用量可由主治医师在合理的医学判断范围内决定。任何特定患者的具体治疗有效剂量水平将取决于多种因素，包括所治疗的疾病和疾病的严重程度；所用特定化合物的活性；使用的具体组合物；患者的年龄、体重、总体健康状况、性别和饮食；给药时间、给药途径和所用特定化合物的排泄率；治疗的持续时间；与所用特定化合物组合或同时使用的药物；以及研究人员、兽医、医生或其他普通技术人员众所周知的因素。

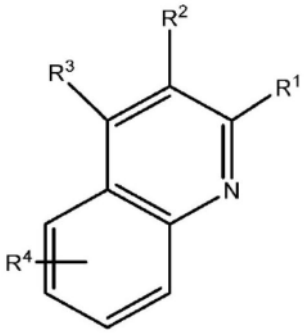
[0101] 根据给药途径，本文考虑了宽范围的允许剂量，包括落入约1μg/kg至约1g/kg范围内的剂量。剂量可以是单一的或分开的，并且可以根据以下多种方案来给药，包括q.d.(一天一次)、b.i.d.(一天两次)、t.i.d.(一天3次)、甚至每隔一天一次、每周一次、每月一次、每季度一次等。在这些情况的每一种中，应理解，本文所述的治疗有效量对应于给药实例，或替代地对应于由给药方案确定的每日、每周、每月或每季度的总剂量。

[0102] 除了本文所述的示例性剂量和给药方案外，应理解，主治医生或医师可以使用已知技术和/或方法和/或通过观察在类似情况下获得的结果来确定本文所述化合物的任何一种或混合物的有效量。主治医生或医师在确定有效量或剂量时，会考虑许多因素，这些因素包括但不限于哺乳动物的物种，包括人类、其大小、年龄和总体健康状况、所涉及的特定疾病或病症、疾病或病症的介入或严重程度、患者的反应、所用的特定化合物、所用的给药方式、所用制剂的生物利用度特征、所选择的剂量方案、并用药物的使用以及其他相关情况。

[0103] 术语“患者”包括人类和非人类动物，例如伴侣动物(狗和猫等)和家畜。家畜是为

食物生产而饲养的动物。待治疗的患者优选是哺乳动物，特别是人类。

[0104] 在一些说明性的实施方案中，本发明涉及具有以下结构式的化合物或其药学上可接受的盐，

[0105]  其中，

(I),

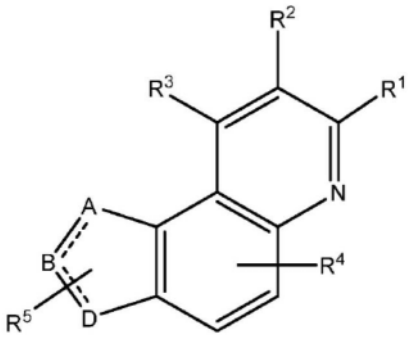
[0106] R^1为氨基、羟基及其衍生物、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、酰基、芳基、杂芳基、芳基烷基、芳基烯基或芳基炔基，其中的每个被任选取代；

[0107] R^2和R^3各自独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基，其中的每个被任选取代；或

[0108] R^2和R^3与连接的碳一起形成任选取代的环部分或杂环部分；以及

[0109] R^4代表四个取代基，每个取代基独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基，其中的每个被任选取代；或所述四个取代基中的任何两个相邻的取代基与连接的碳一起形成任选取代的环部分或杂环部分。

[0110] 在一些说明性的实施方案中，本发明涉及一种具有如下结构式的化合物或其药学上可接受的盐，

[0111] 

(II),

[0112] 其中，n＝1～5；A与B之间的键、B与D之间的键可为双键或单键，但不能同时为双键；A、B和D独立地表示C、O、N和S，其中A、B和D中的至少一个是杂原子；

[0113] R^1为氨基、羟基及其衍生物、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、酰基、芳基、杂芳基、芳基烷基、芳基烯基或芳基炔基，其中的每个被任选取代；

[0114] R^2和R^3各自独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯

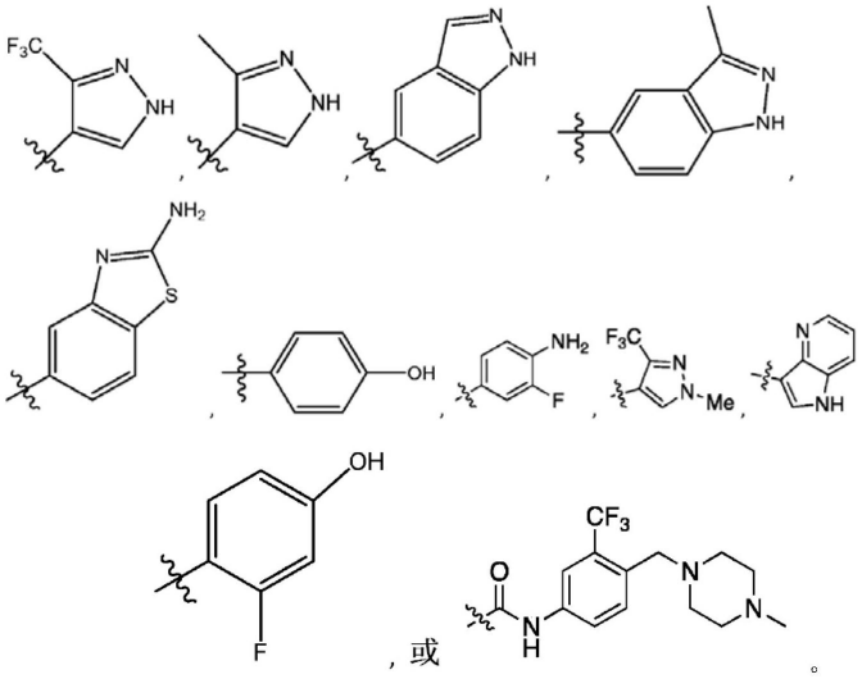
基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基，其中的每个被任选取代；或

[0115] R^2和R^3与连接的碳一起形成任选取代的环部分或杂环部分；

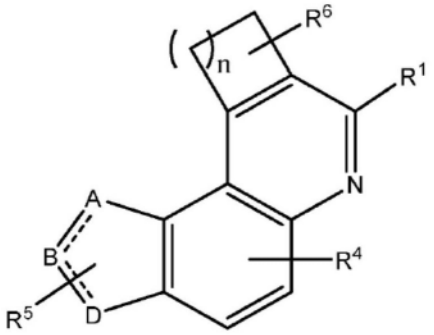
[0116] R^4代表两个取代基，每个取代基独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基，其中的每个被任选取代；或所述两个取代基与连接的碳一起形成任选取代的环部分或杂环部分；以及

[0117] 根据A、B和D的元素，R^5代表两个或三个取代基，每个取代基独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基，其中的每个被任选取代。

[0118] 在一些说明性的实施方案中，本发明涉及一种具有结构式(II)的化合物，其中R^1为

[0119] 

[0120] 在一些说明性的实施方案中，本发明涉及一种具有结构式(III)的化合物或其药学上可接受的盐，

[0121] 

(III),

[0122] 其中n＝1～5;A与B之间的键、B与D之间的键可为双键或单键,但不能同时为双键;A、B和D独立地表示C、O、N和S,其中A、B和D中的至少一个是杂原子;

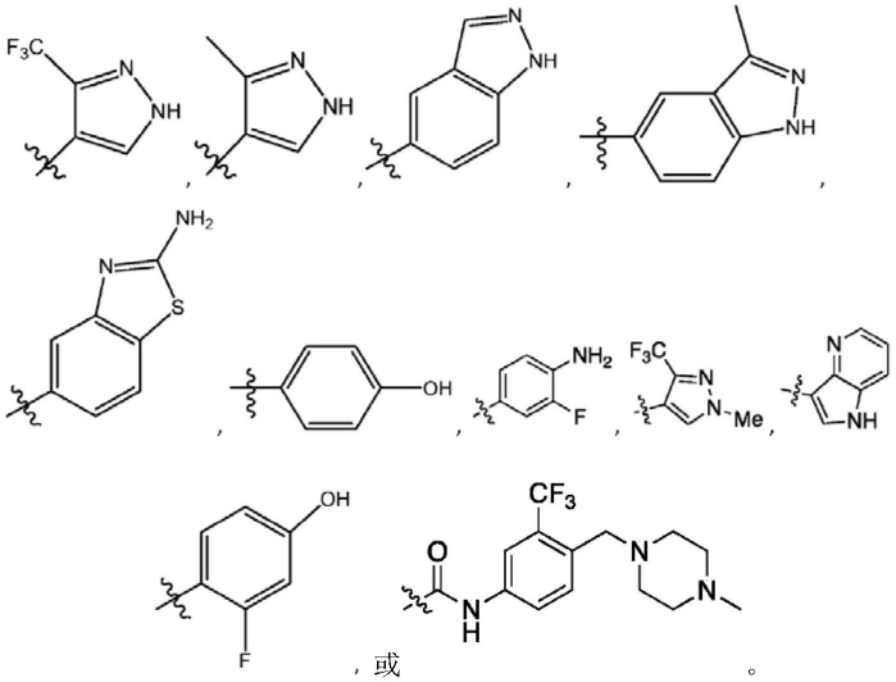
[0123] R^1为氨基、羟基及其衍生物、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、酰基、芳基、杂芳基、芳基烷基、芳基烯基或芳基炔基,其中的每个被任选取代;

[0124] R^4代表两个取代基,每个取代基独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基,其中的每个被任选取代;或所述两个取代基与连接的碳一起形成任选取代的环部分或杂环部分;

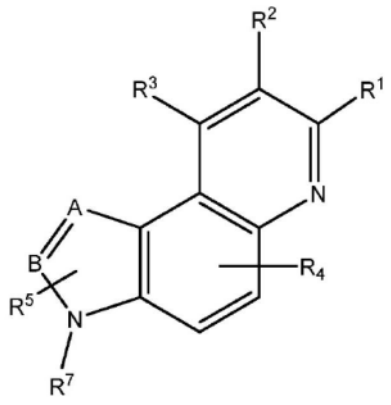
[0125] 根据A、B和D的元素,R^5代表两个或三个取代基,每个取代基独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基,其中的每个被任选取代;以及

[0126] 根据n的值,R^6代表2至6个取代基,每个取代基独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基,其中的每个被任选取代。

[0127] 在一些说明性的实施方案中,本发明涉及一种具有结构式(III)的化合物,其中R^1为

[0128] 

[0129] 在一些说明性的实施方案中，本发明涉及一种具有结构式(IV)的化合物或其药学上可接受的盐，

[0130] 

(IV)，

[0131] 其中＝1～5；

[0132] R^1为氨基、羟基及其衍生物、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、酰基、芳基、杂芳基、芳基烷基、芳基烯基或芳基炔基，其中的每个被任选取代；

[0133] R^2和R^3各自独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基，其中的每个被任选取代；或R^2和R^3与连接的碳一起形成任选取代的环部分或杂环部分；

[0134] R^4代表两个取代基，每个取代基独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基，其中的每个被任选取代；或所述两个取代基与

连接的碳一起形成任选取代的环部分或杂环部分；

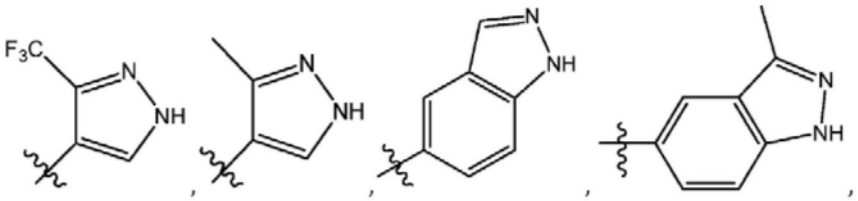
[0135] 根据以下限定的A和B的元素，R^5代表一个或两个取代基，每个取代基独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基，其中的每个被任选取代；

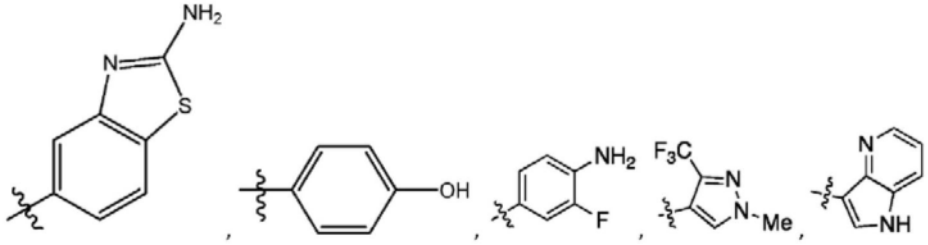
[0136] A和B独立地代表CR^8、N或NR^9，其中R^8和R^9独立地代表氢、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、酰基、芳基、杂芳基、芳基烷基、芳基烯基或芳基炔基，其中的每个被任选取代；

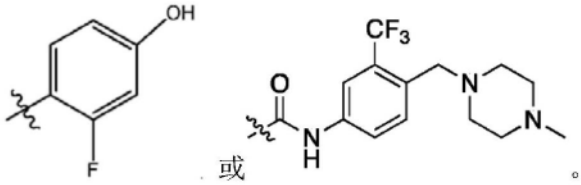
[0137] 根据n的值，R^6代表2至6个取代基，每个取代基独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基，其中的每个被任选取代；以及

[0138] R^7为烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、酰基、芳基、杂芳基、芳基烷基、芳基烯基或芳基炔基，其中的每个被任选取代。

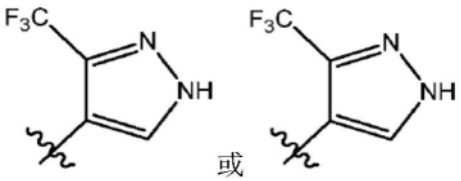
[0139] 在一些说明性的实施方案中，本发明涉及一种具有结构式(IV)的化合物，其中R^1为

[0140] 

[0141] 



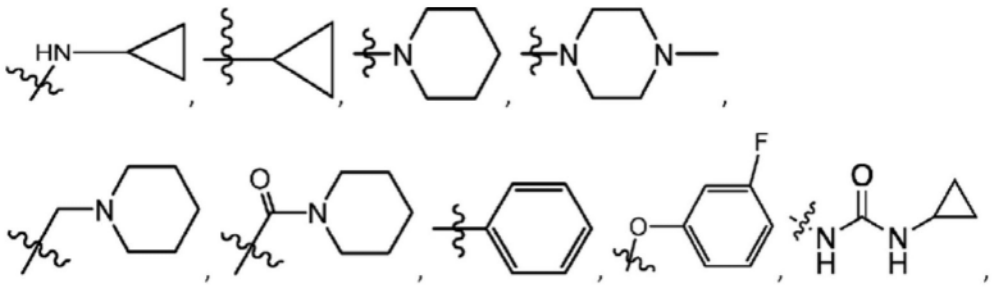
[0142] 在一些说明性的实施方案中，本发明涉及一种具有结构式(IV)的化合物，其中R^1为

[0143] 

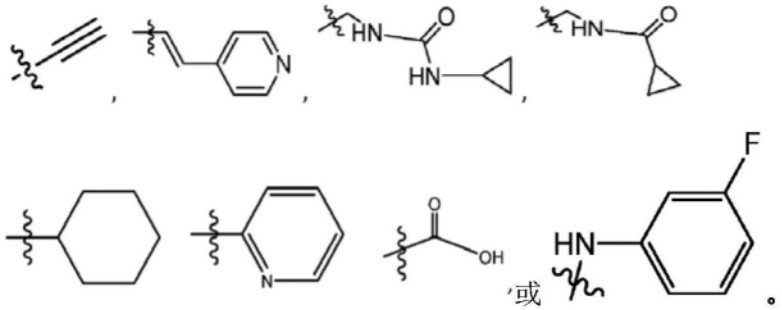
A为碳(C)；B为氮(N)；R^5、R^6和R^7均代表氢，R^4代

表两个取代基，每个取代基独立地选自氢、氘、卤素、叠氮基、氰基、硝基、羟基、氨基、巯基、羧基、酯基、酰胺基及其衍生物、以及酰基、磺基、磺酰基、磷酸基、磷酰基、烷基、烯基、炔基、杂烷基、杂烯基、杂炔基、杂环基、环烷基、环烯基、环杂烷基、环杂烯基、芳基、杂芳基、芳基烷基、芳基烯基和芳基炔基，其中的每个被任选取代；或所述两个取代基与连接的碳一起形成任选取代的环部分或杂环部分。

[0144] 在一些说明性的实施方案中，本发明涉及一种具有结构式(IV)的化合物，其中R^3为



[0145]

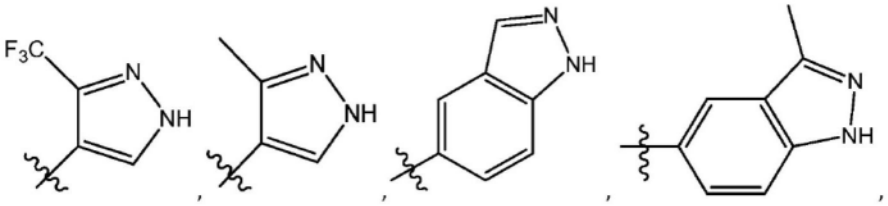


或

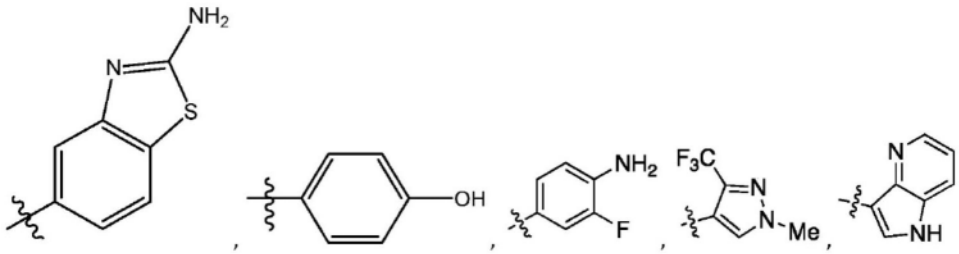
。

[0146] 在一些说明性的实施方案中，本发明涉及一种具有结构式(IV)的化合物，其中R^1为

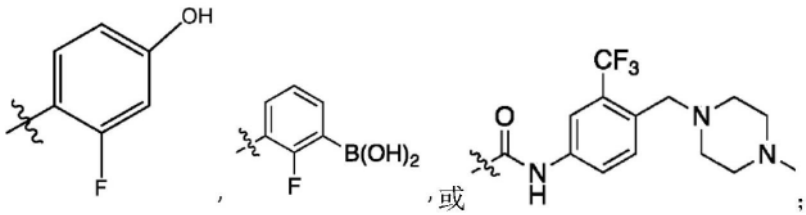
[0147]



[0148]

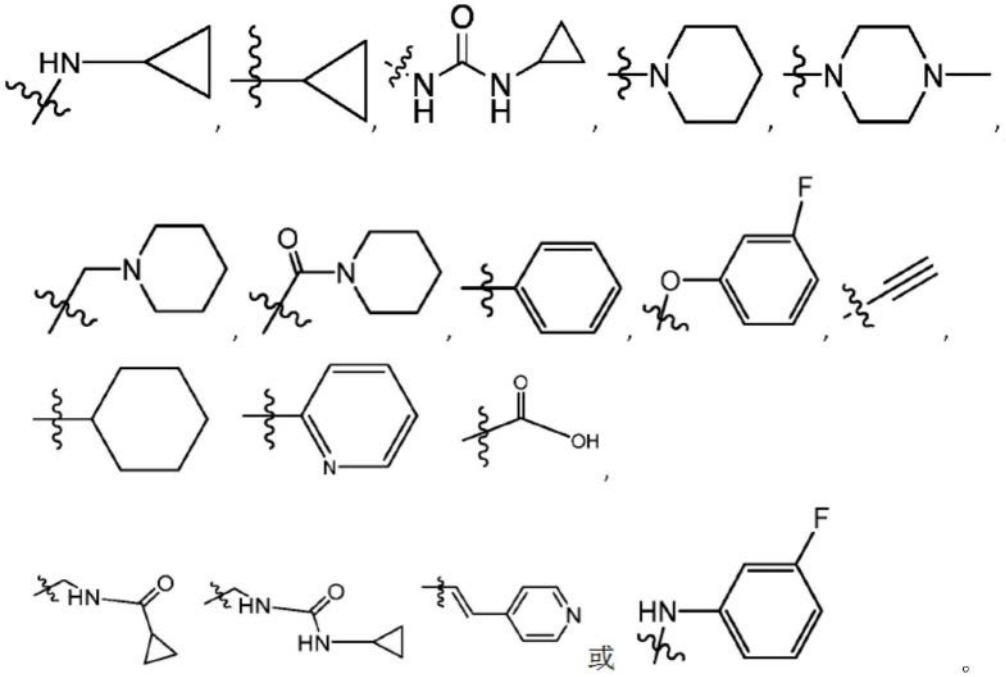


[0149]

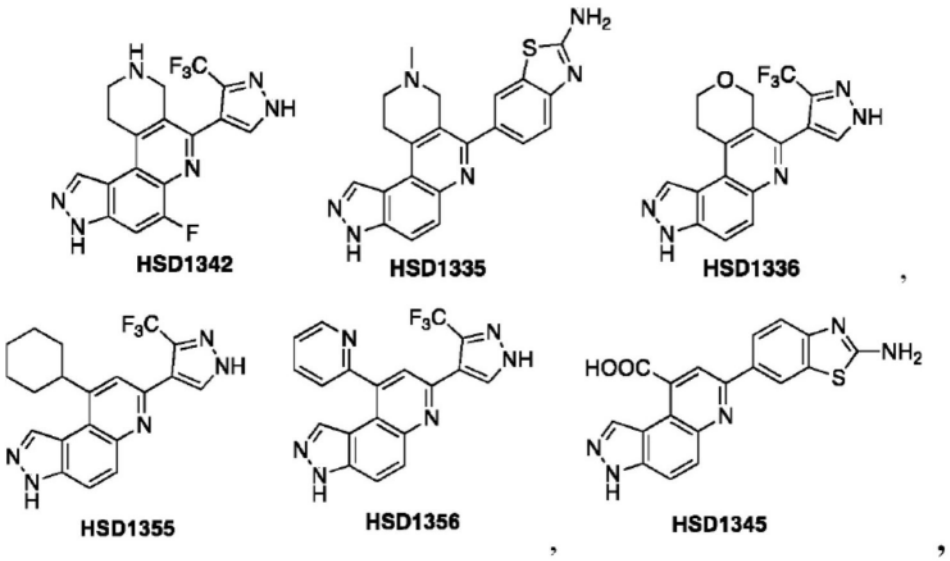


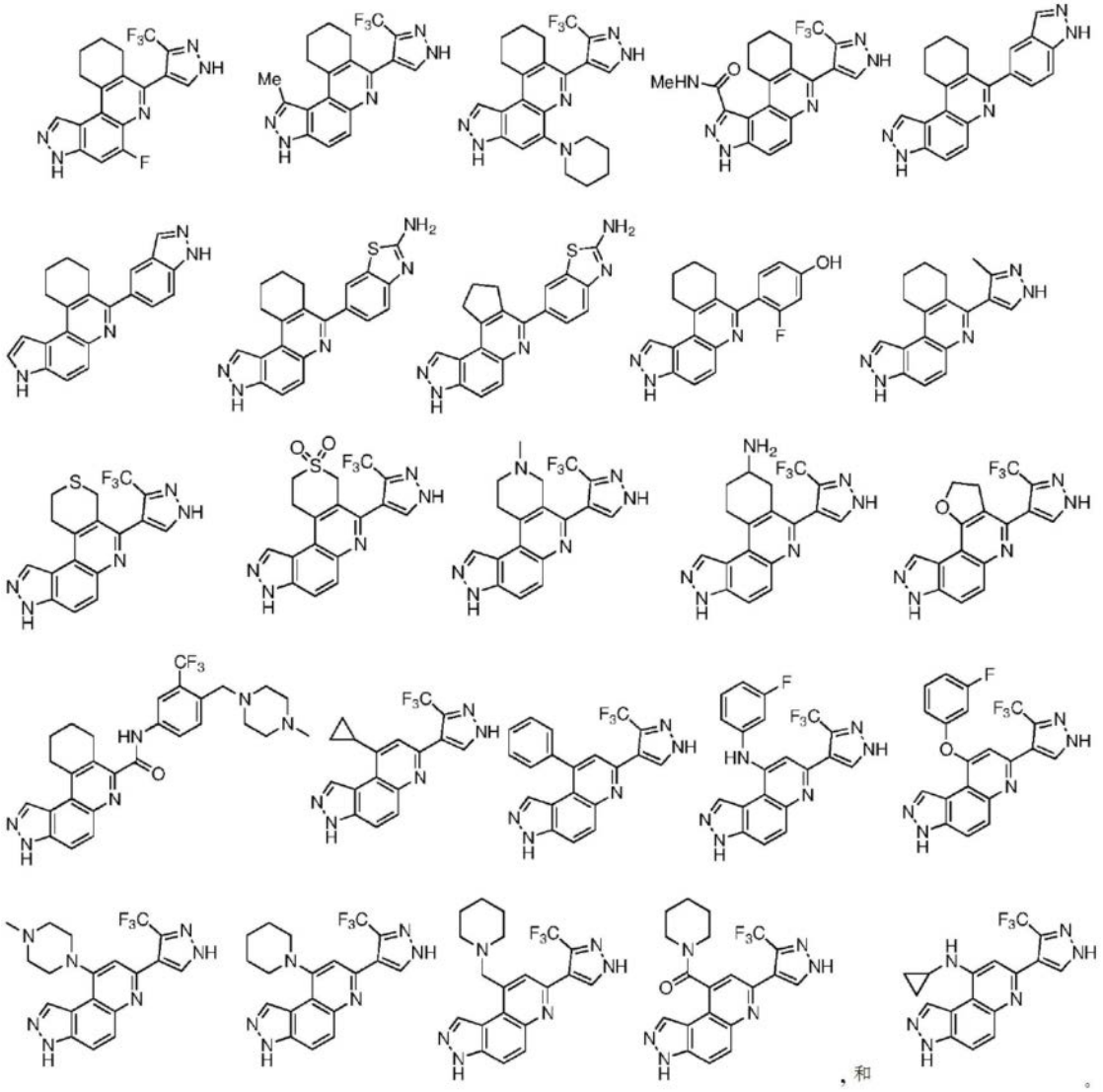
以及R^3为

；

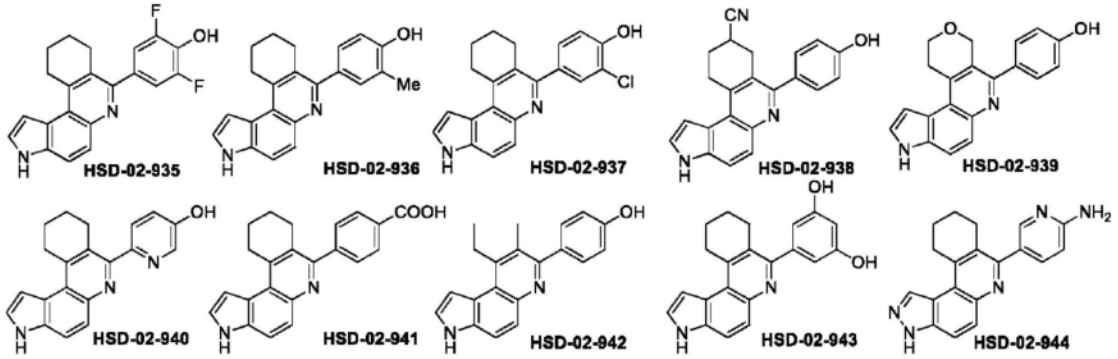
[0150] 

[0151] 在一些说明性的实施方案中,本发明涉及一种具有结构式(I)的化合物,其中所述化合物为

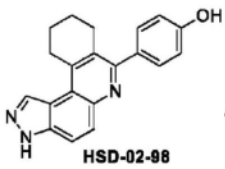
[0152] 

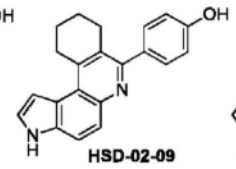
[0153] 

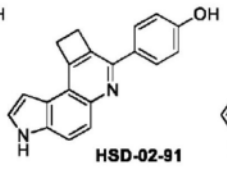
[0154] 在一些说明性的实施方案中,本发明涉及一种具有结构式(I)的化合物,其中所述化合物为

[0155] 

[0156]


HSD-02-98


HSD-02-09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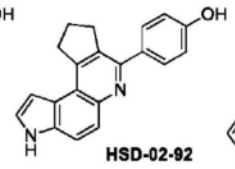
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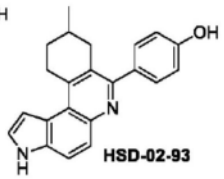
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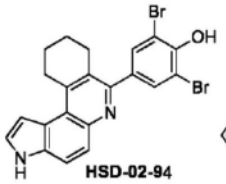
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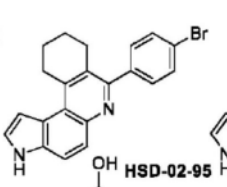
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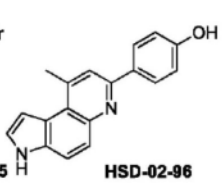
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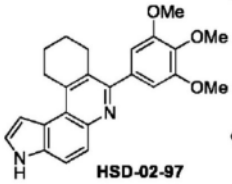
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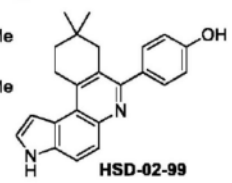
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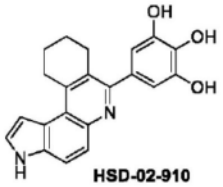
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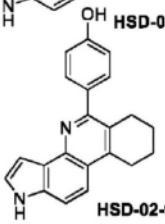
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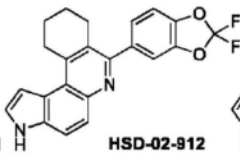
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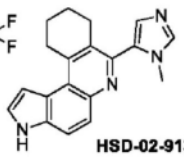
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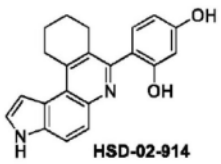
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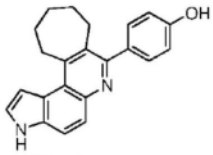
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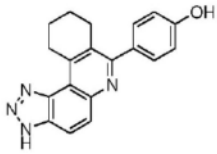
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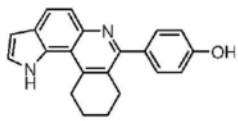
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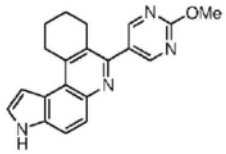
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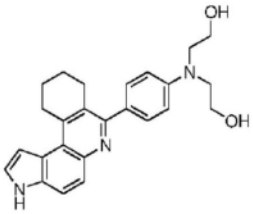
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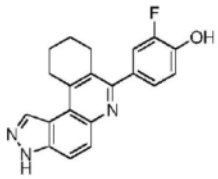
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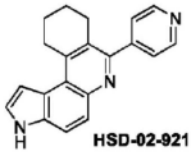
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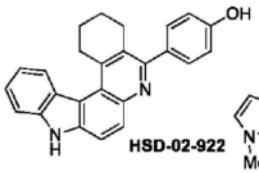
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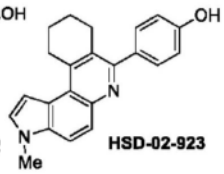
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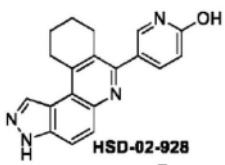
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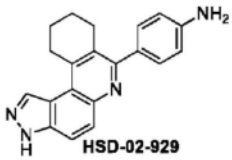
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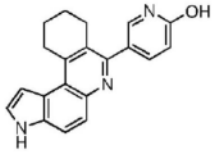
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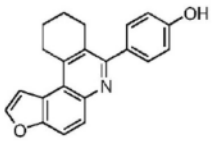
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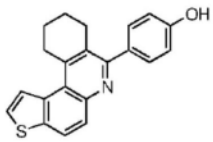
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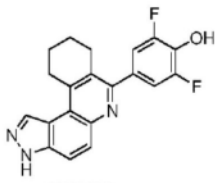
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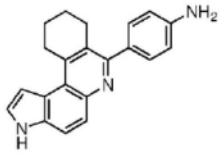
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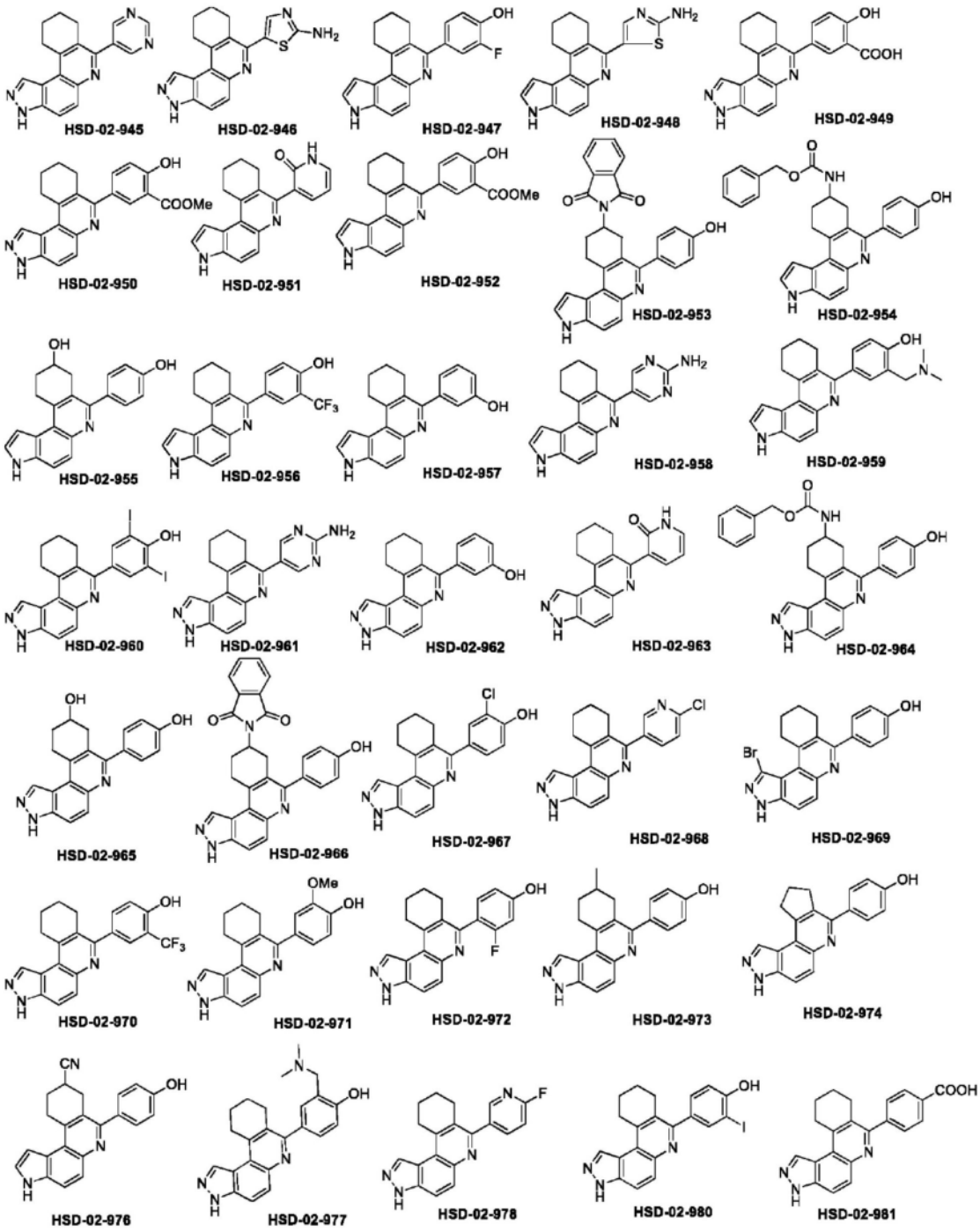
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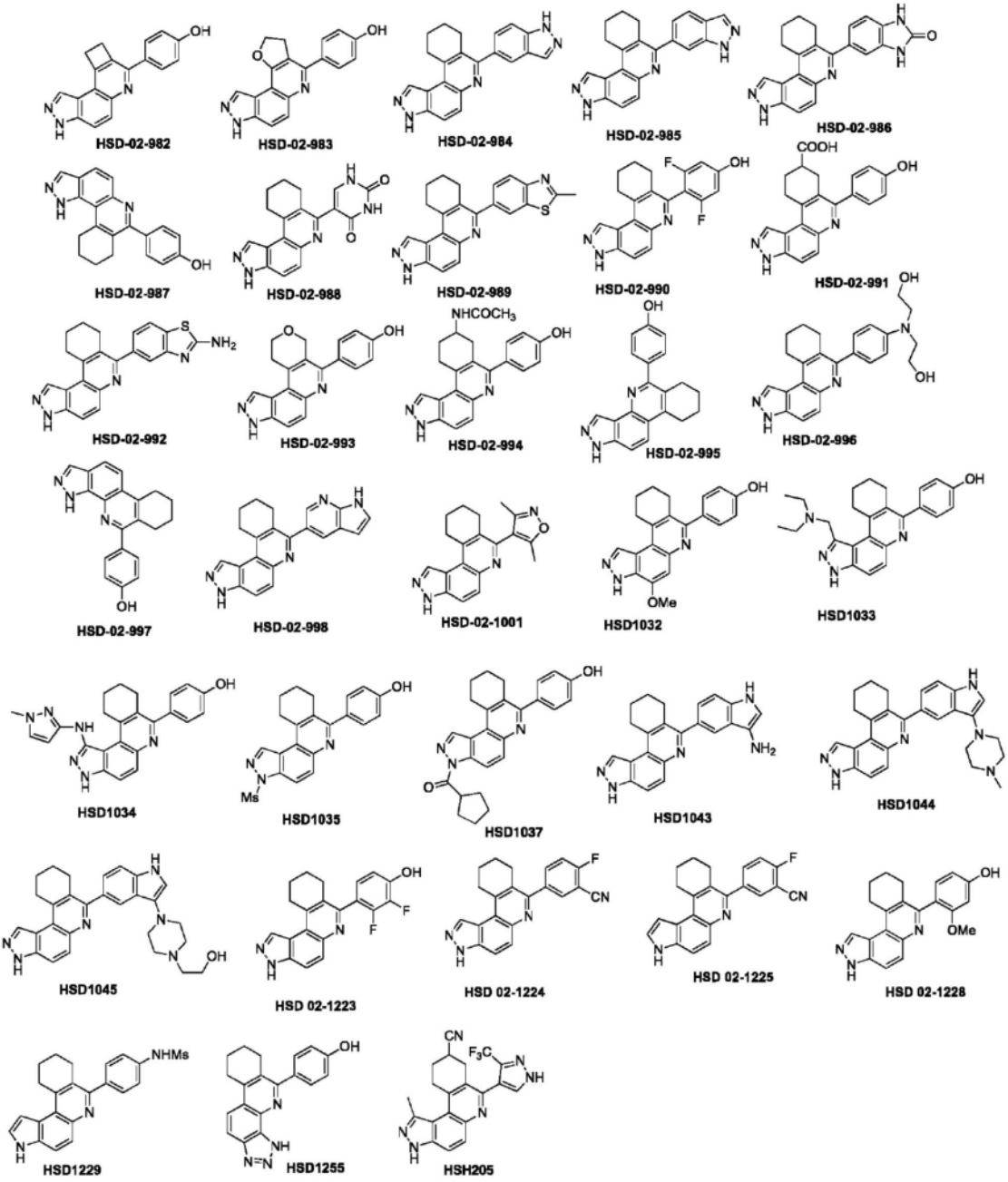
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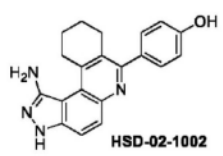
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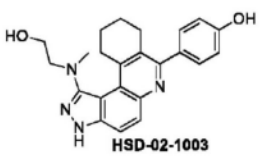
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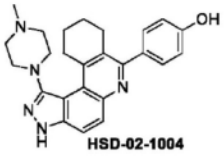
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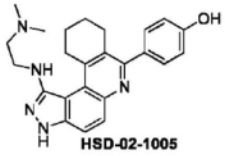
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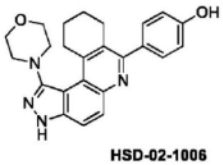
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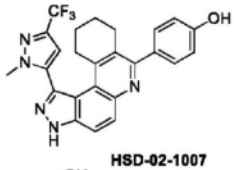
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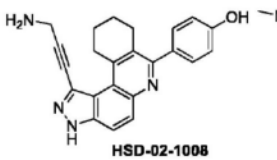
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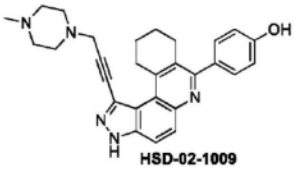
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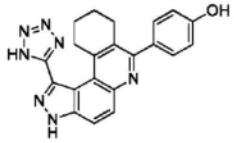
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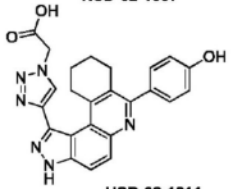
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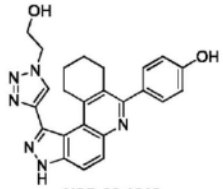
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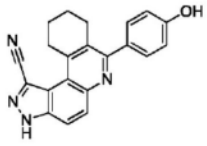
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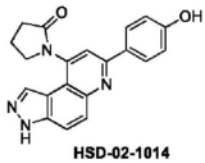
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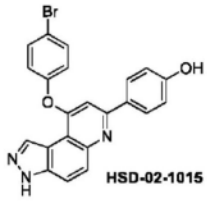
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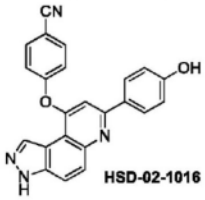
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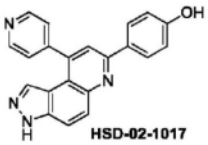
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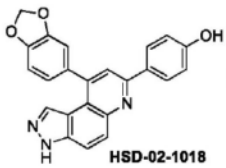
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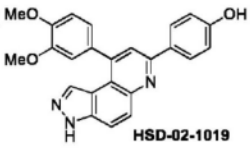
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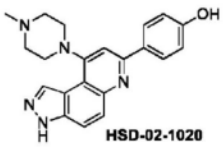
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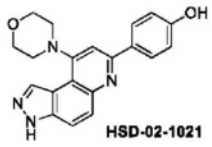
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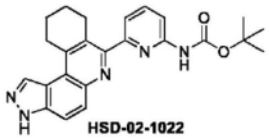
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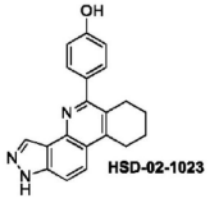
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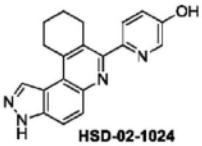
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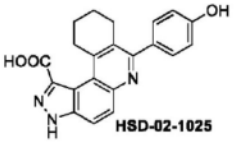
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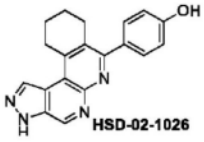
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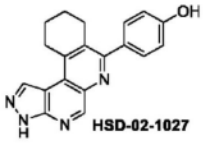
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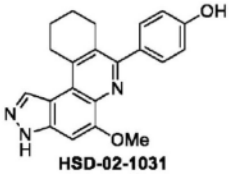
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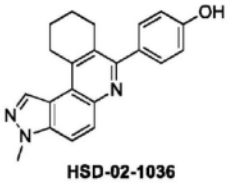
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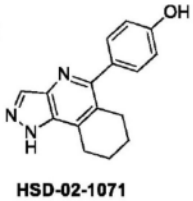
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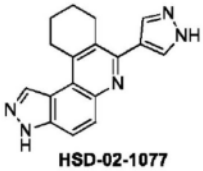
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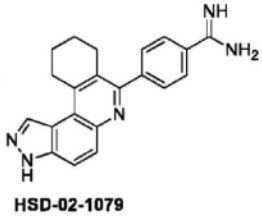
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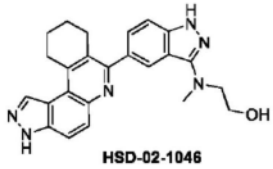
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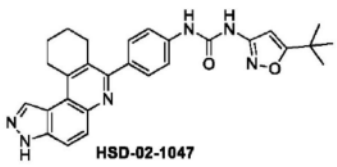
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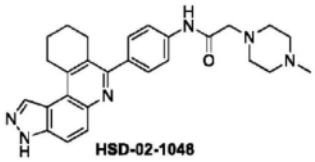
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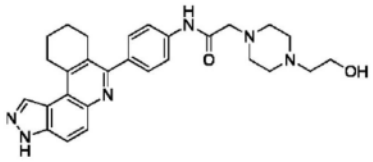
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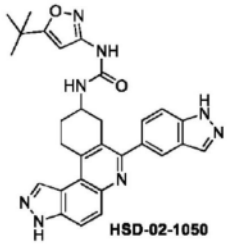
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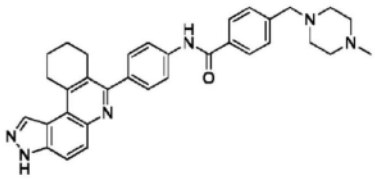
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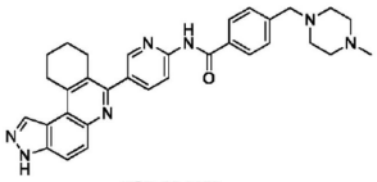
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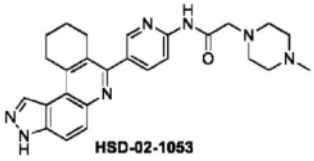
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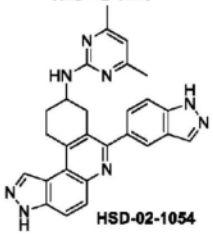
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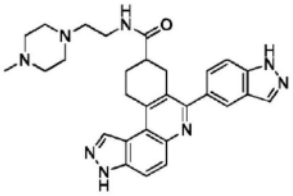
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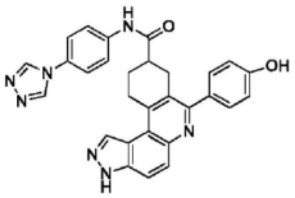
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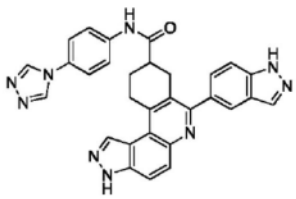
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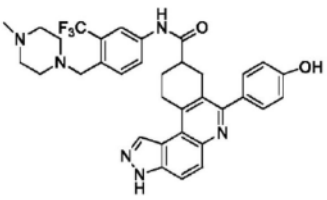
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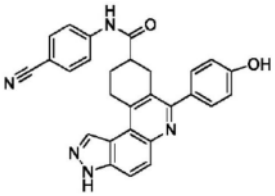
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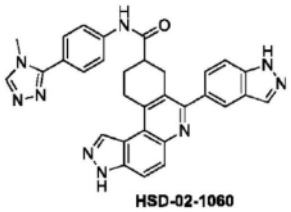
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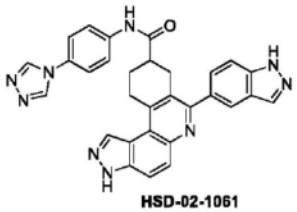
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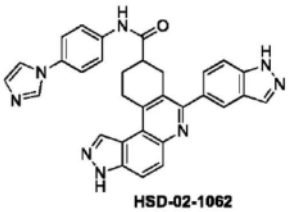
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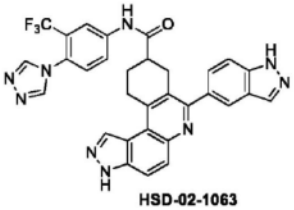
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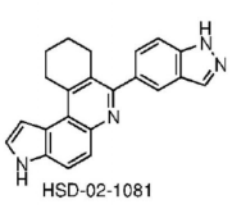
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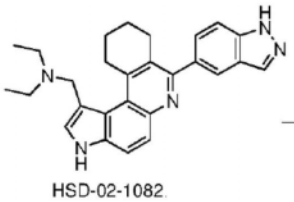
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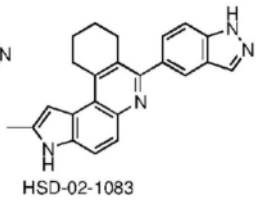
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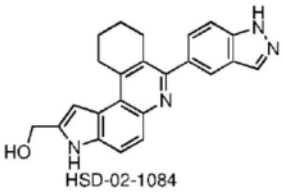
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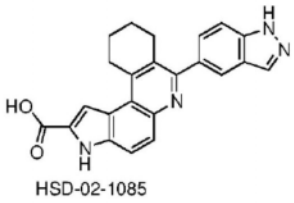
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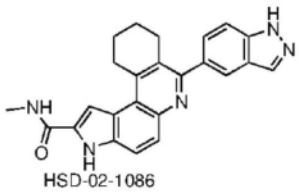
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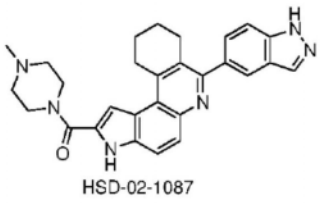
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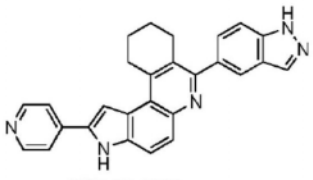
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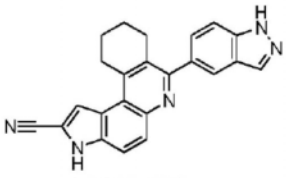
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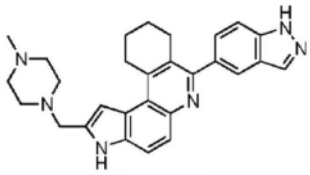
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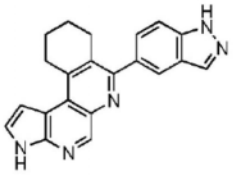
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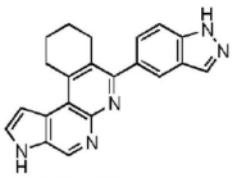
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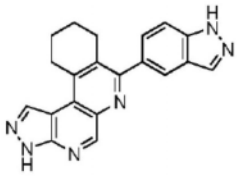
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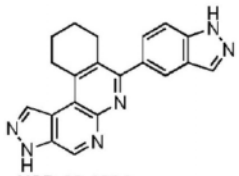
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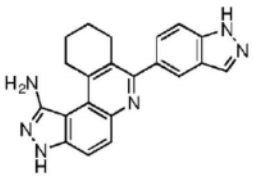
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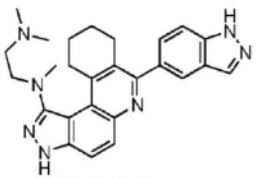
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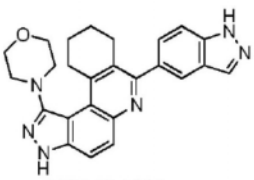
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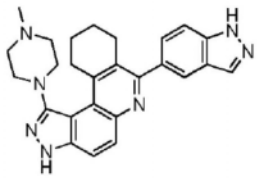
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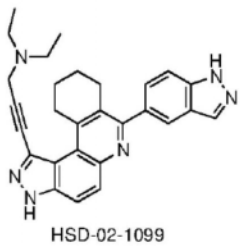
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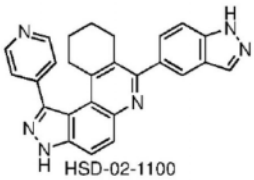
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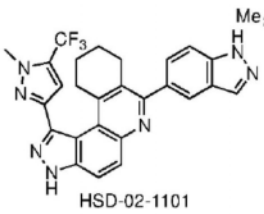
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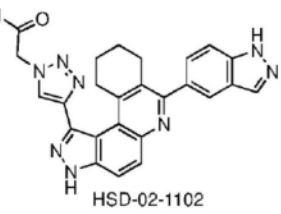
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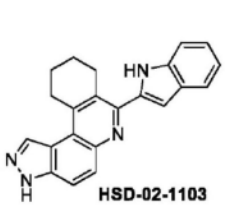
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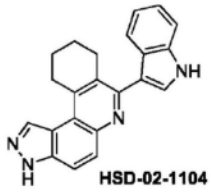
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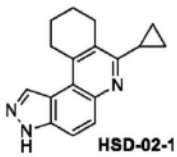
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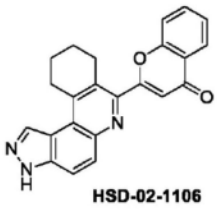
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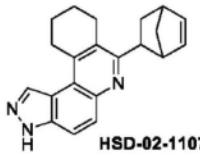
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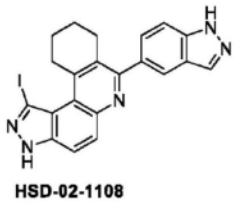
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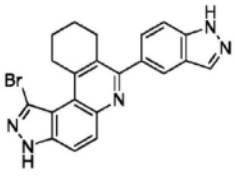
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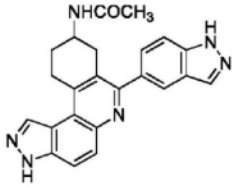
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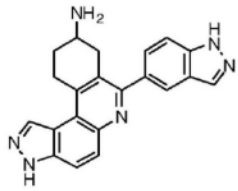
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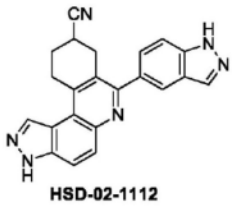
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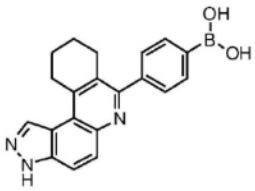
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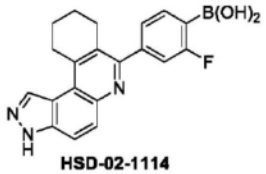
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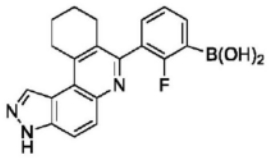
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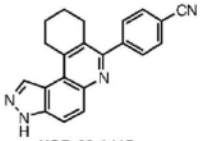
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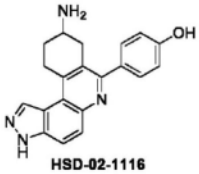
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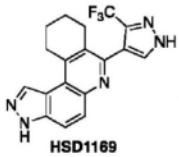
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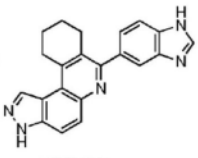
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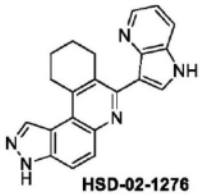
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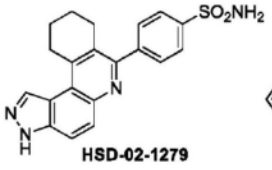
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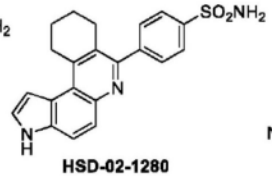
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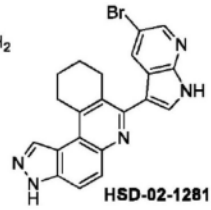
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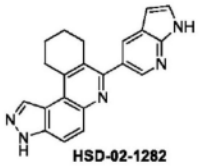
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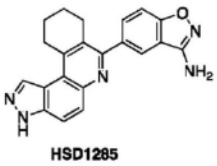
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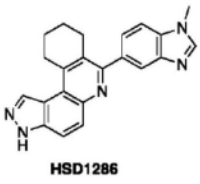
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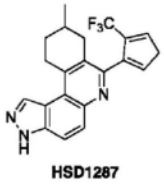
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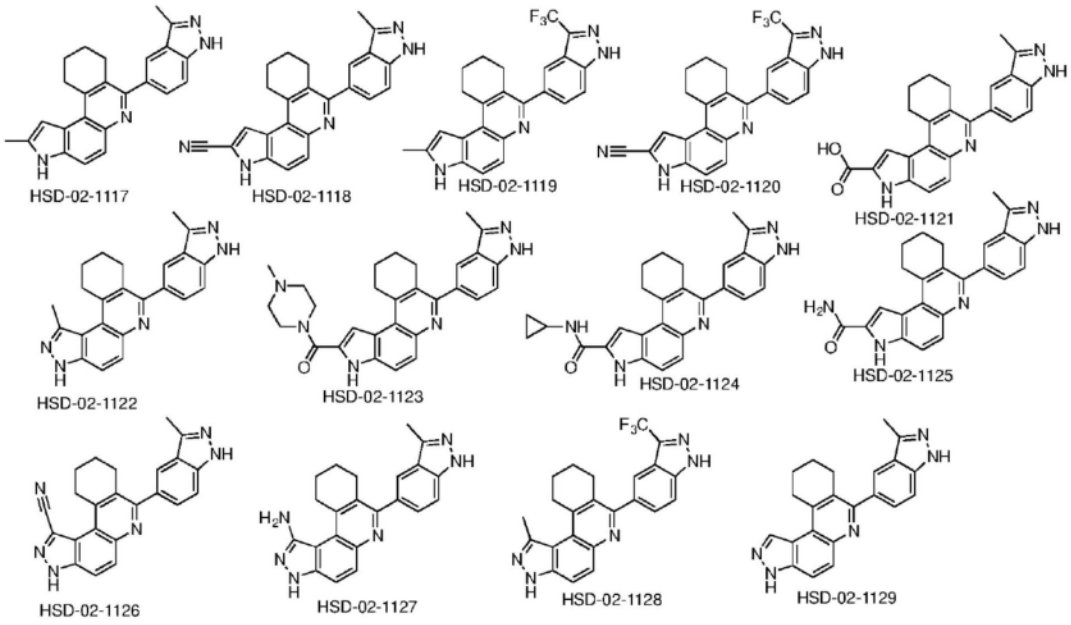
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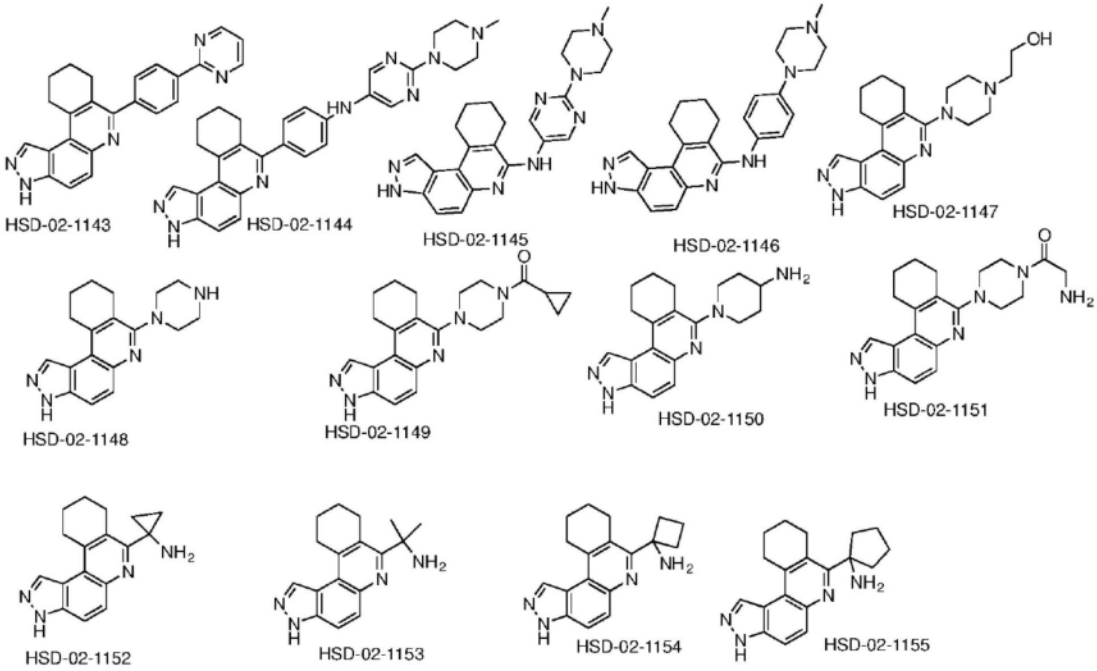
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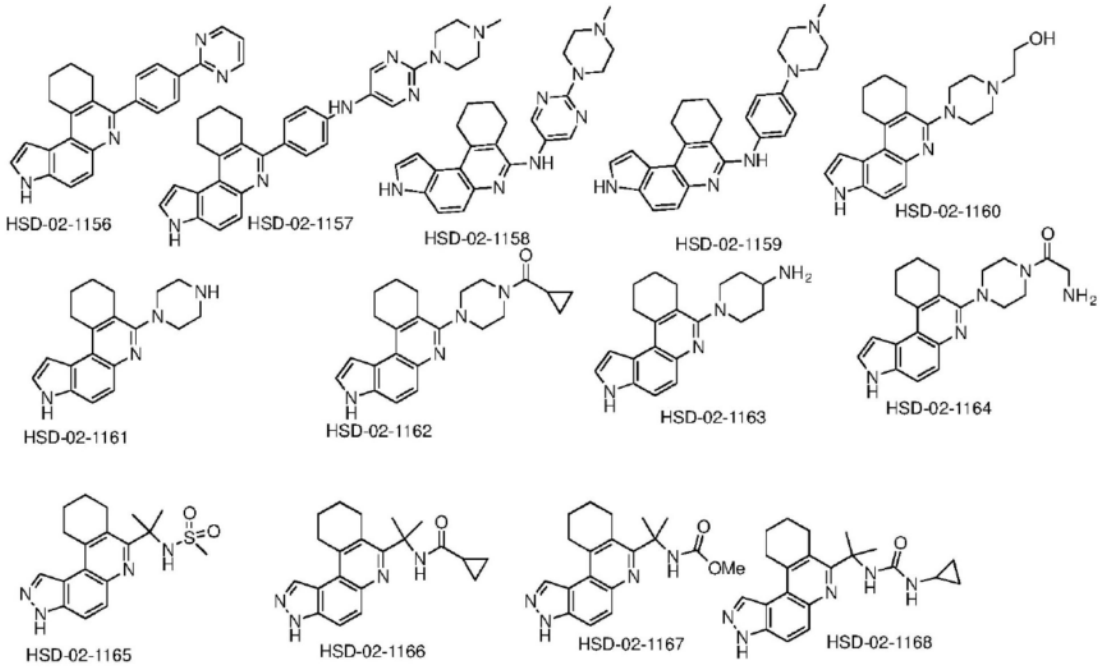
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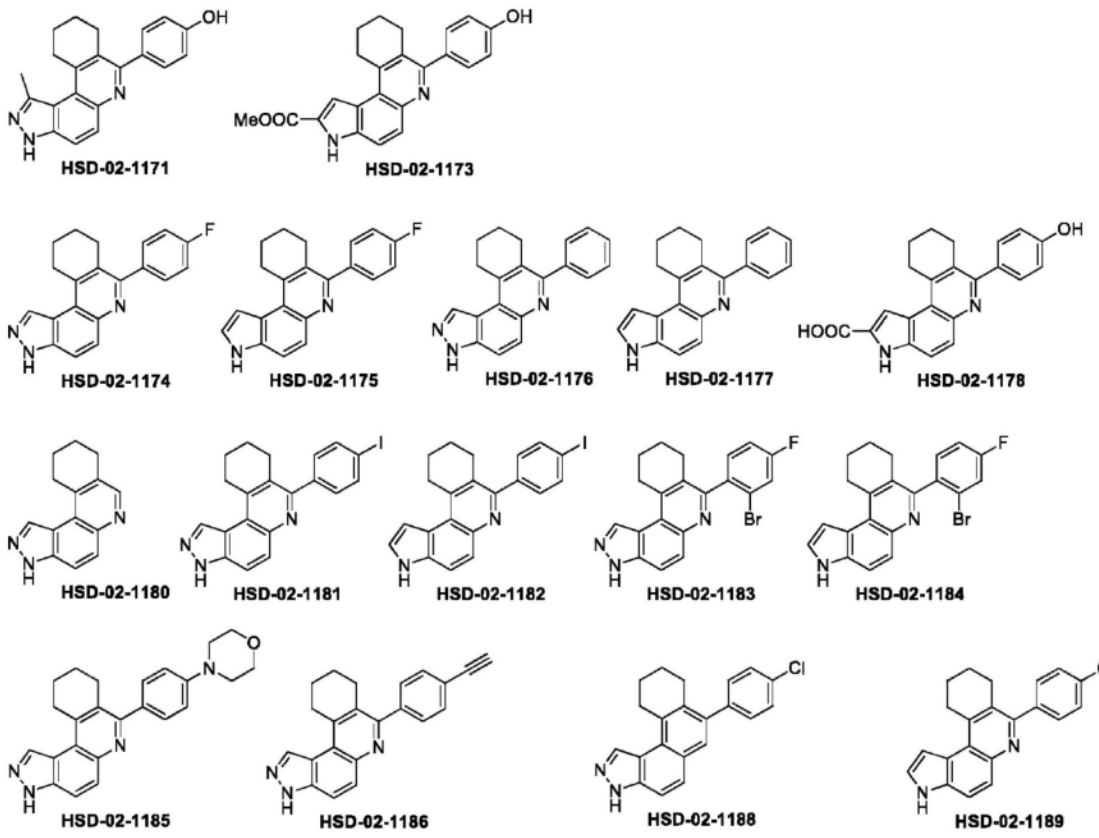
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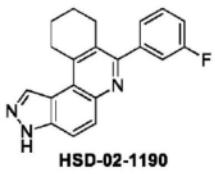
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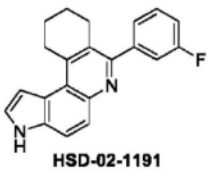
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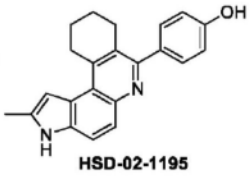
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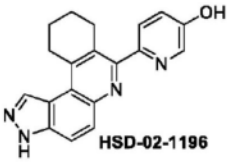
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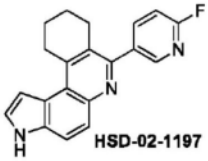
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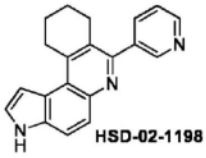
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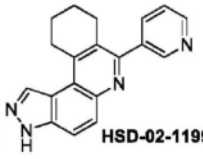
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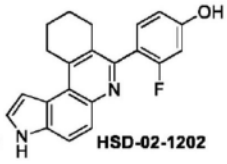
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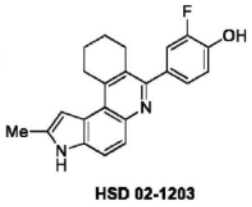
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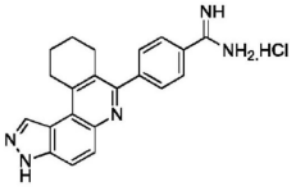
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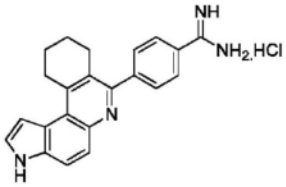
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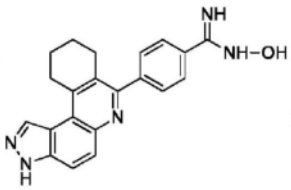
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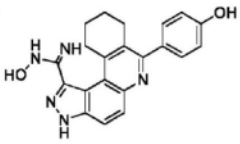
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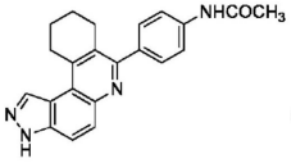
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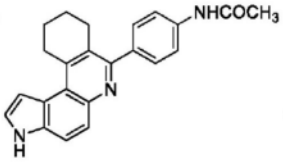
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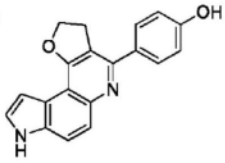
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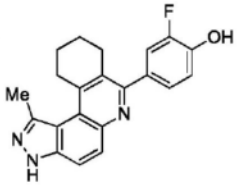
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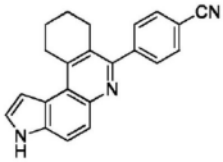
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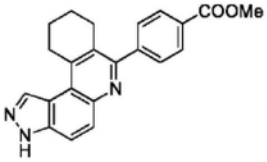
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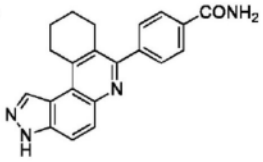
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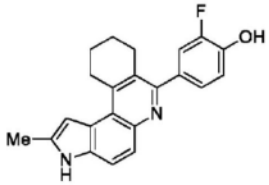
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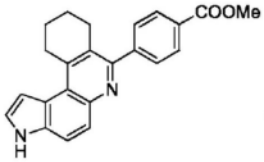
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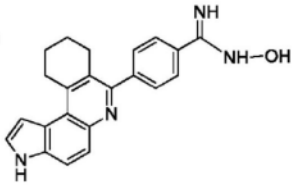
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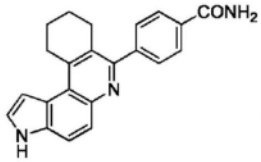
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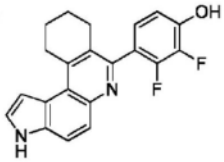
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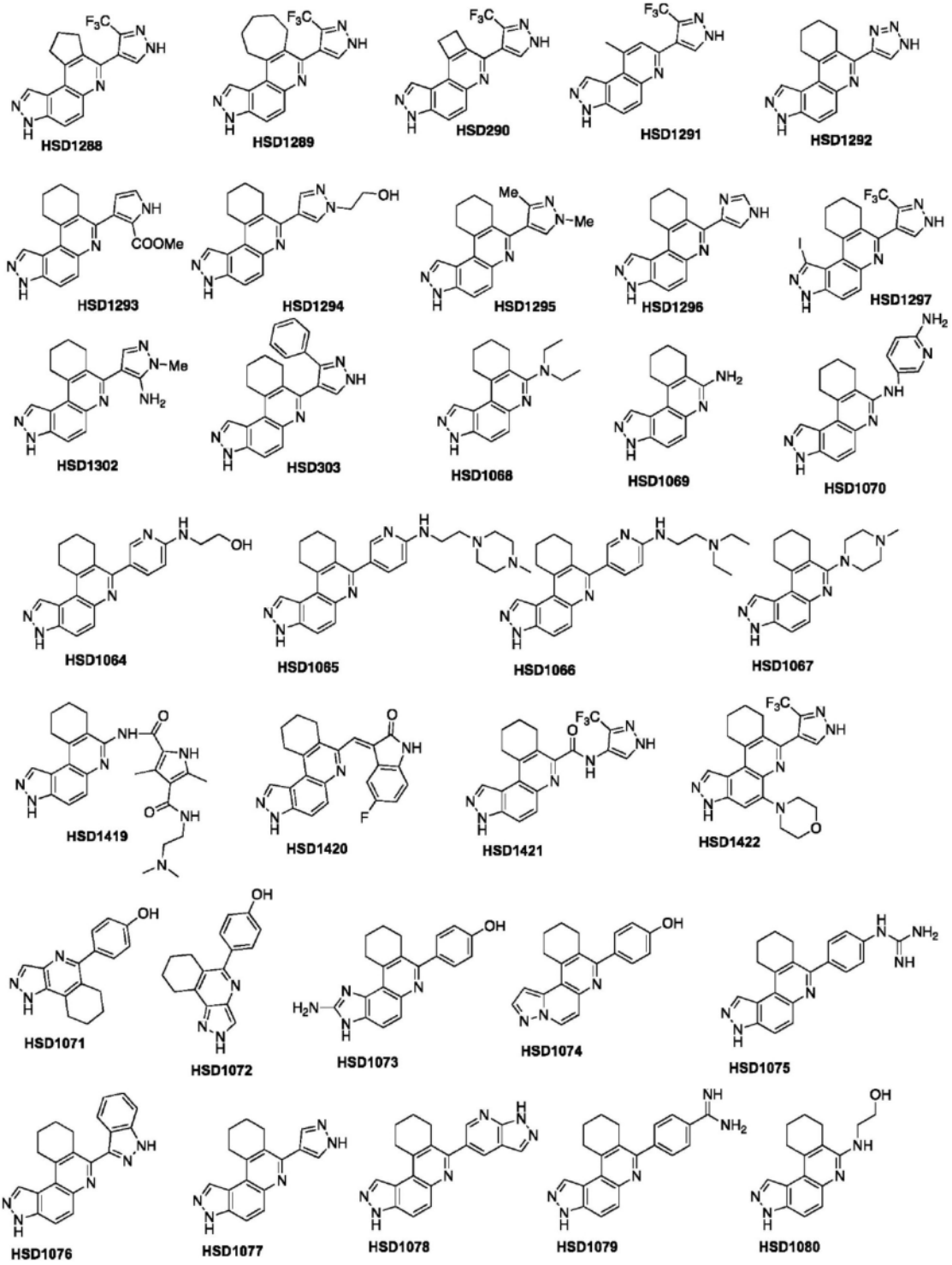
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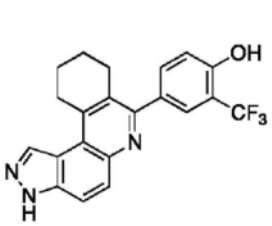
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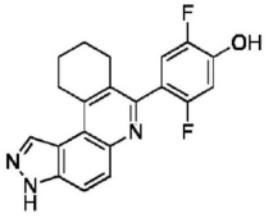
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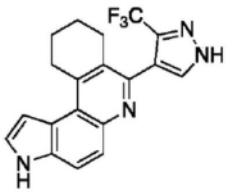
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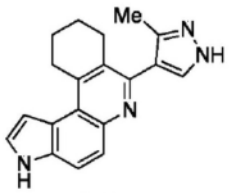
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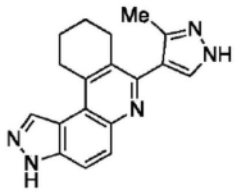
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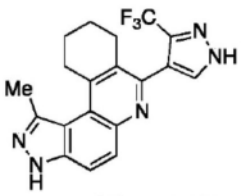
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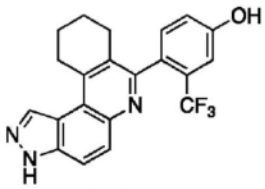
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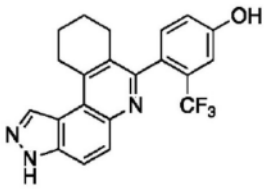
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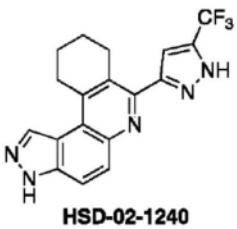
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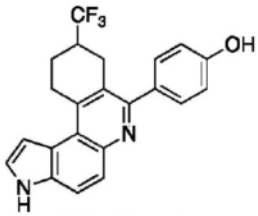
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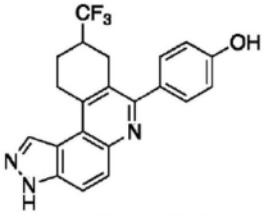
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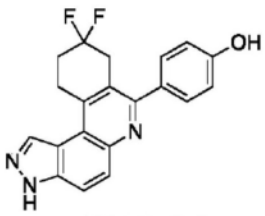
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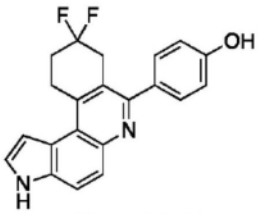
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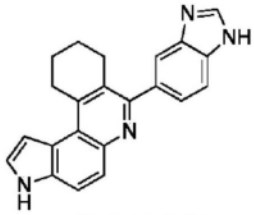
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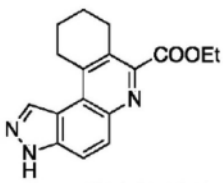
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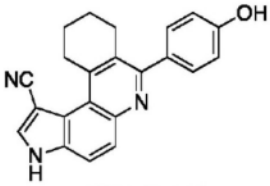
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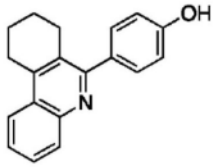
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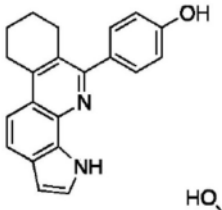
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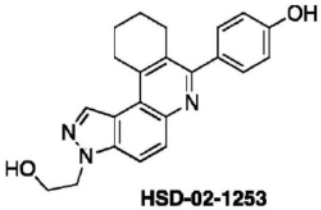
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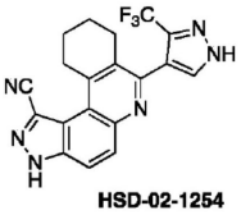
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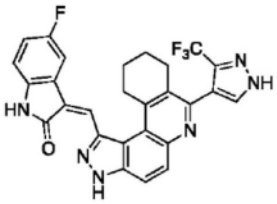
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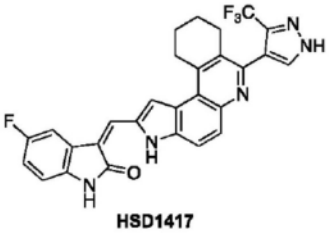
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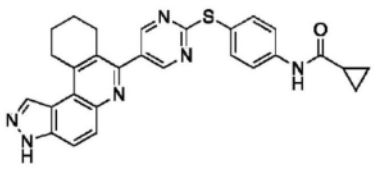
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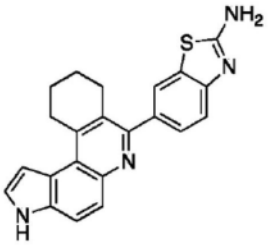
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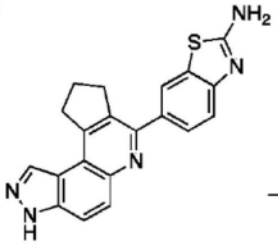
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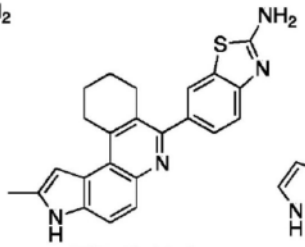
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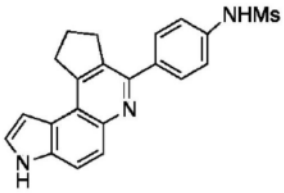
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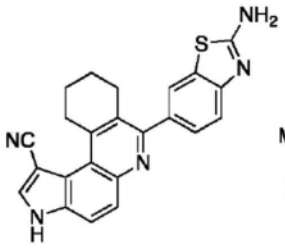
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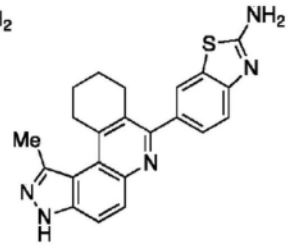
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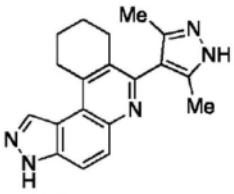
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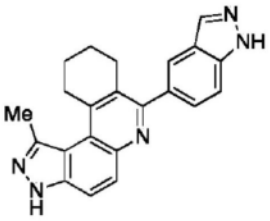
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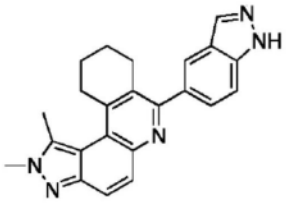
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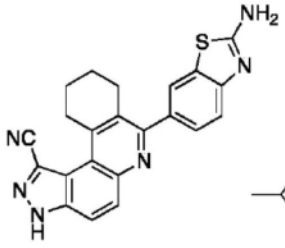
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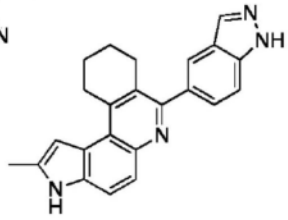
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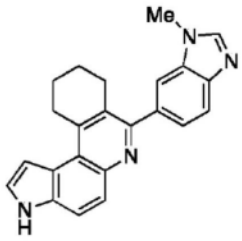
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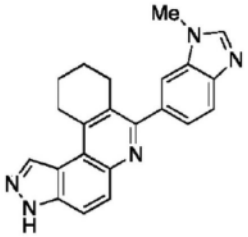
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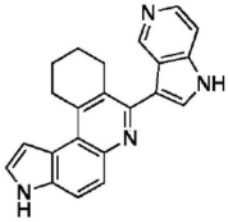
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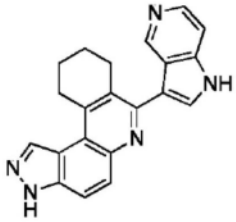
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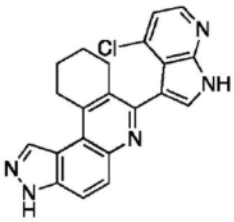
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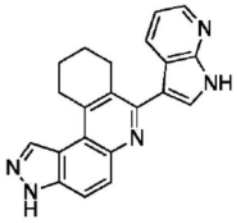
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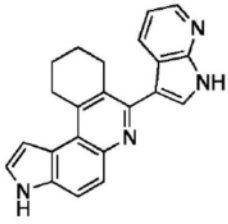
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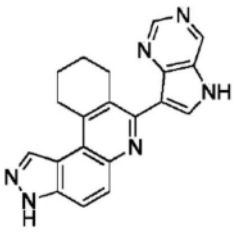
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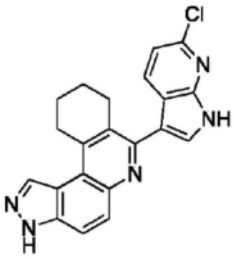
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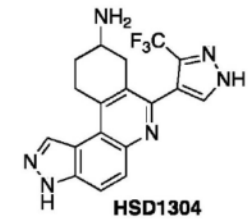
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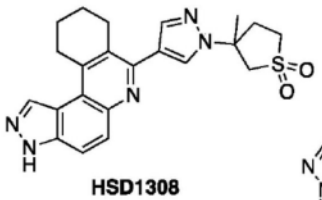
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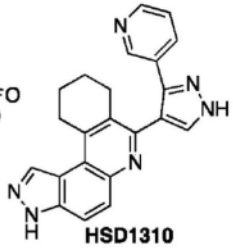
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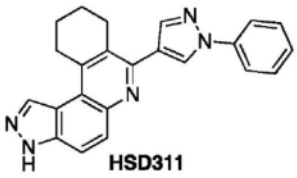
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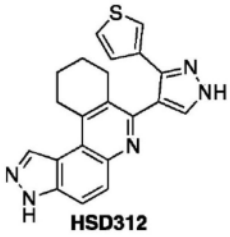
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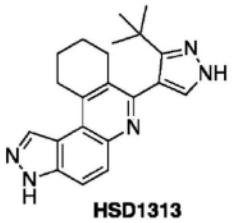
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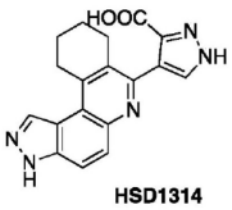
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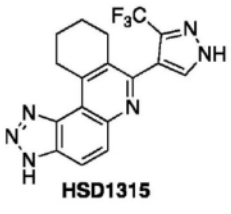
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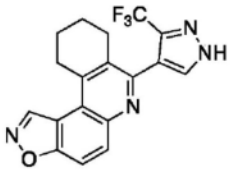
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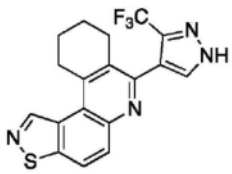
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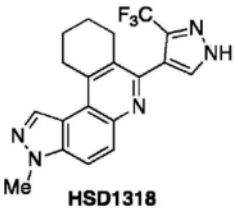
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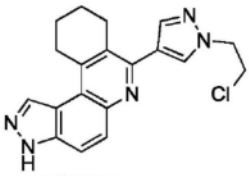
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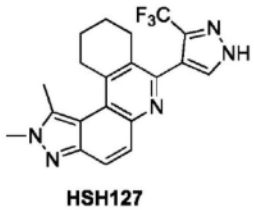
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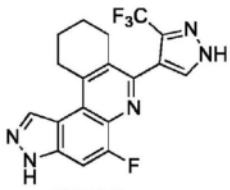
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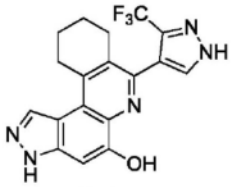
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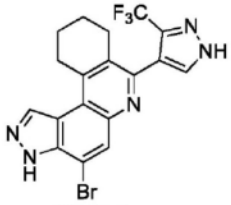
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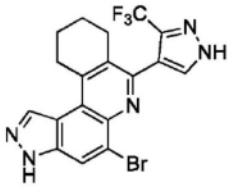
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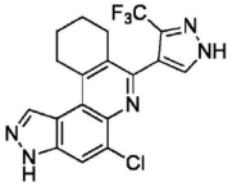
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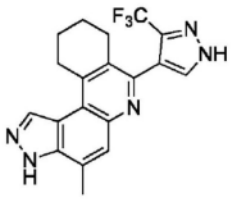
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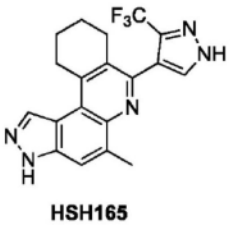
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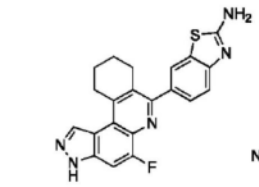
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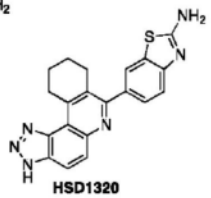
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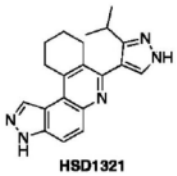
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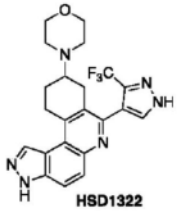
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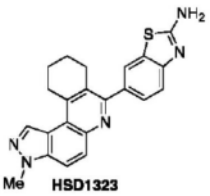
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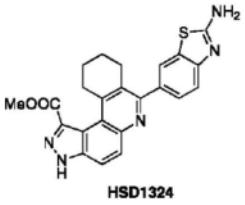
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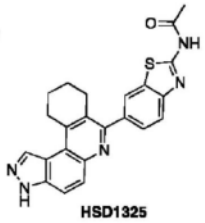
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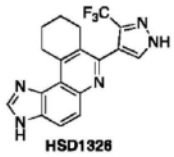
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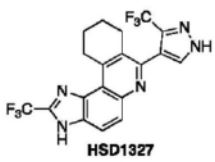
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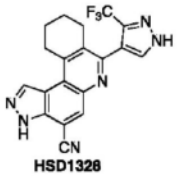
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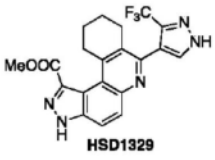
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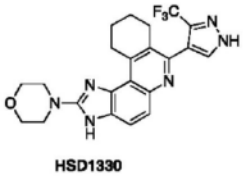
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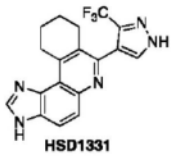
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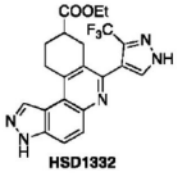
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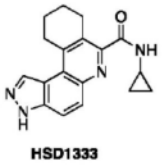
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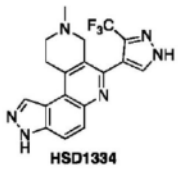
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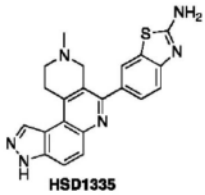
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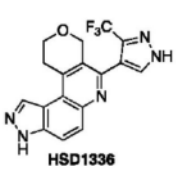
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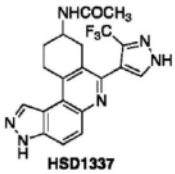
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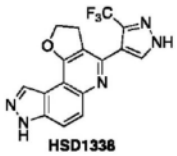
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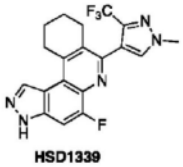
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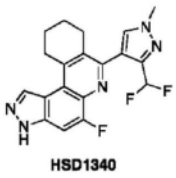
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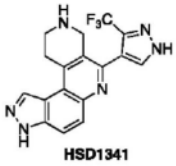
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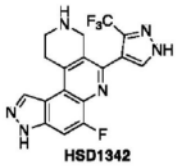
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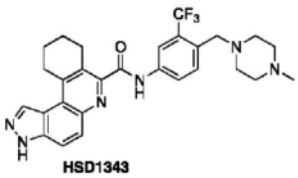
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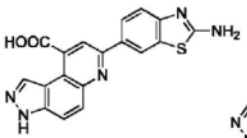
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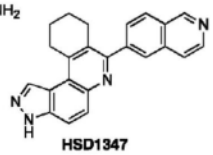
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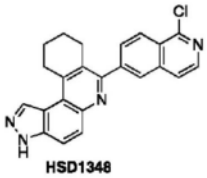
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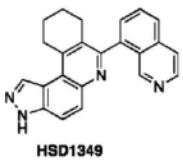
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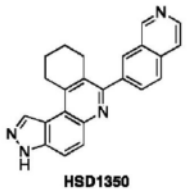
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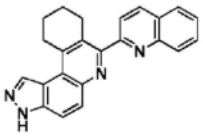
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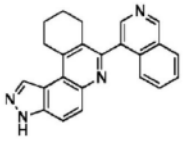
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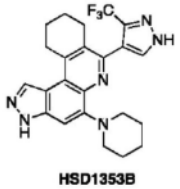
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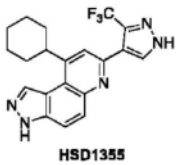
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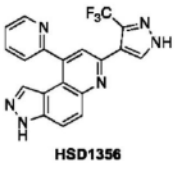
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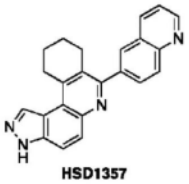
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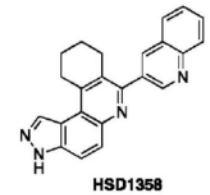
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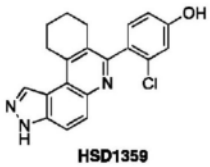
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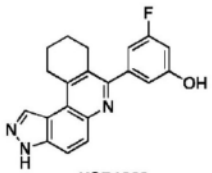
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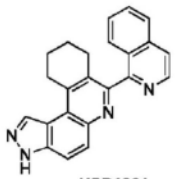
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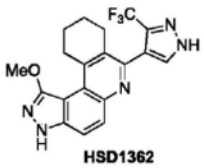
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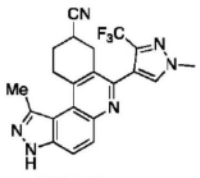
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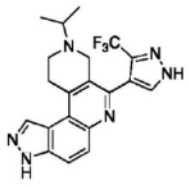
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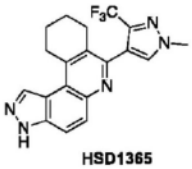
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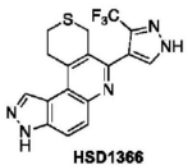
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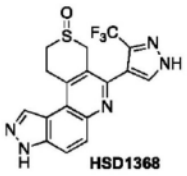
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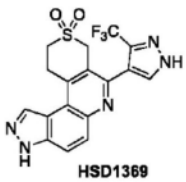
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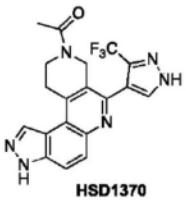
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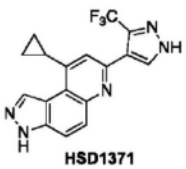
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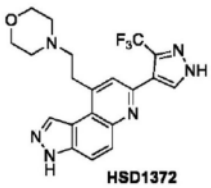
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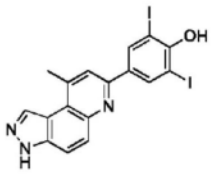
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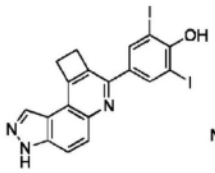
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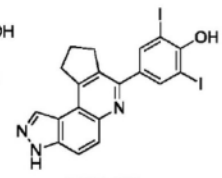
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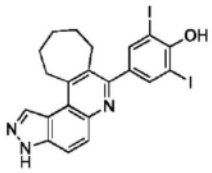
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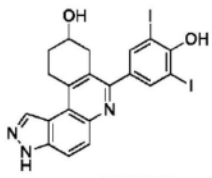
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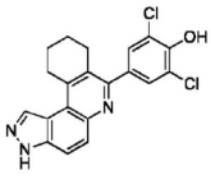
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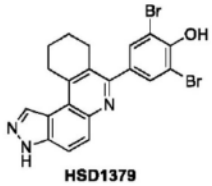
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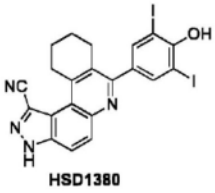
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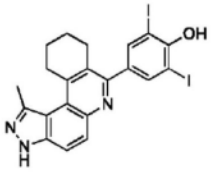
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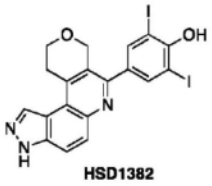
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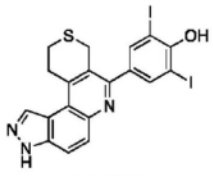
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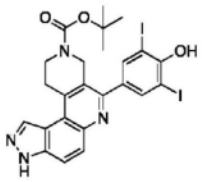
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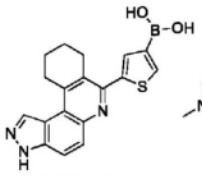
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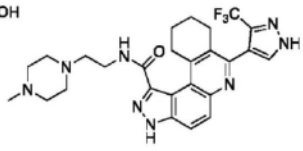
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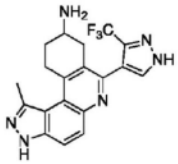
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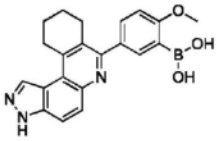
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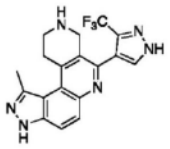
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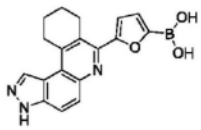
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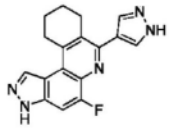
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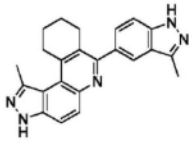
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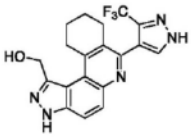
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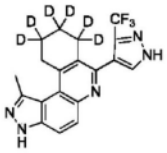
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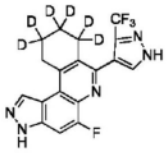
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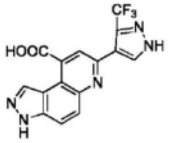
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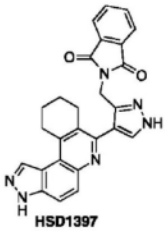
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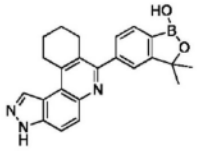
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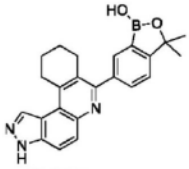
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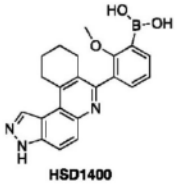
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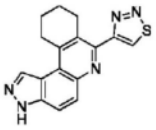
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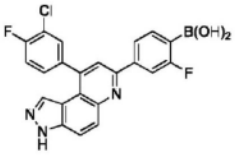
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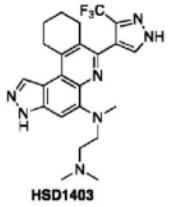
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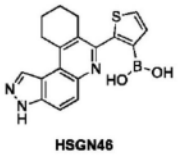
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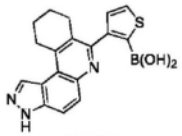
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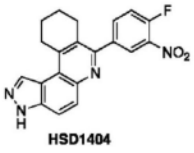
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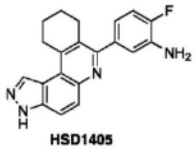
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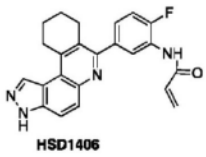
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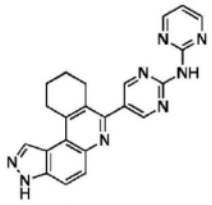
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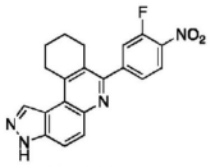
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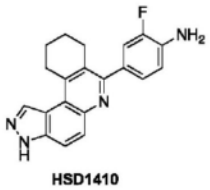
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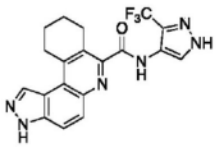
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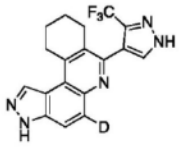
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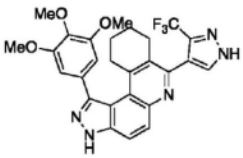
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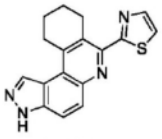
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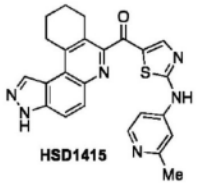
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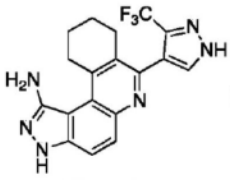
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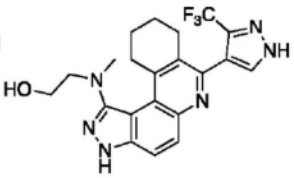
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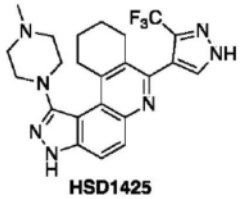
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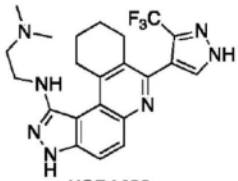
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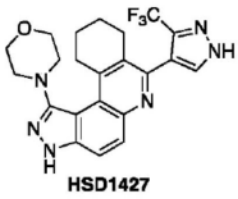
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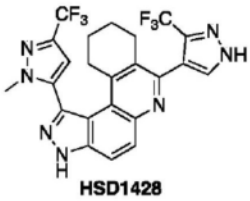
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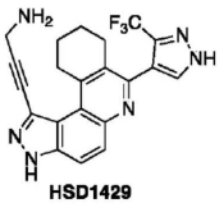
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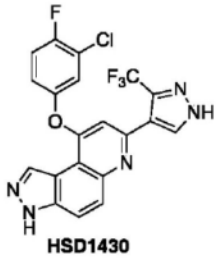
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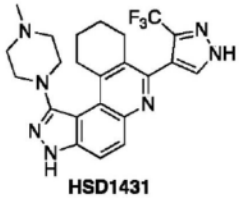
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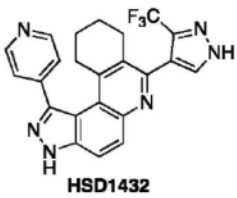
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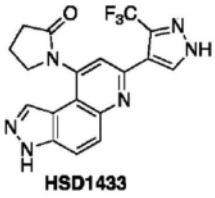
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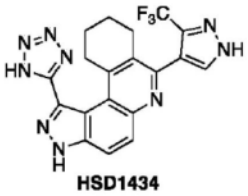
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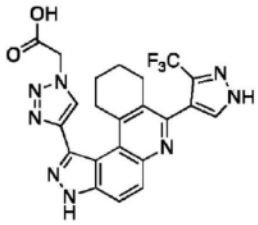
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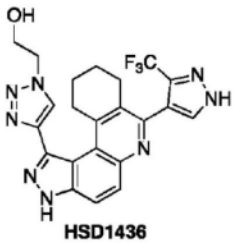
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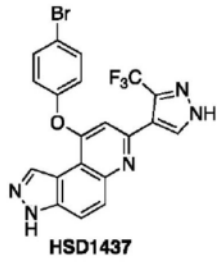
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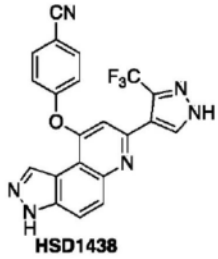
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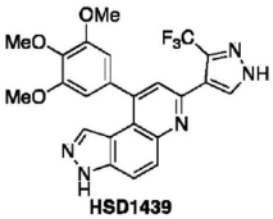
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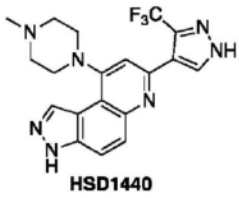
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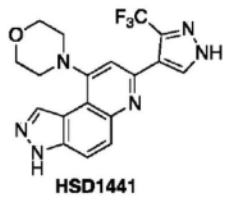
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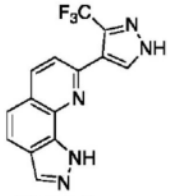
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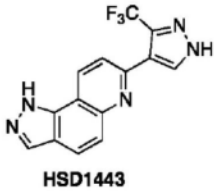
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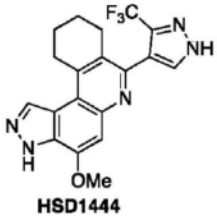
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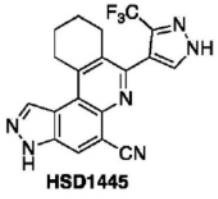
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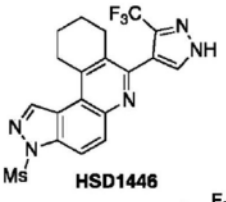
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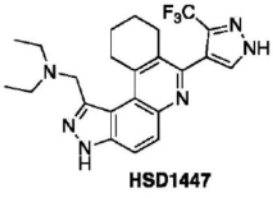
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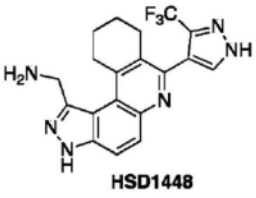
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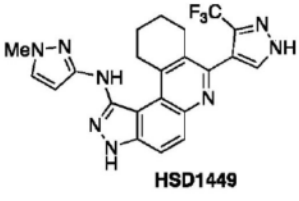
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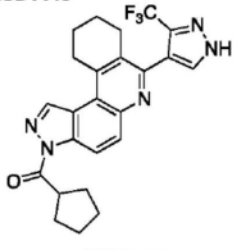
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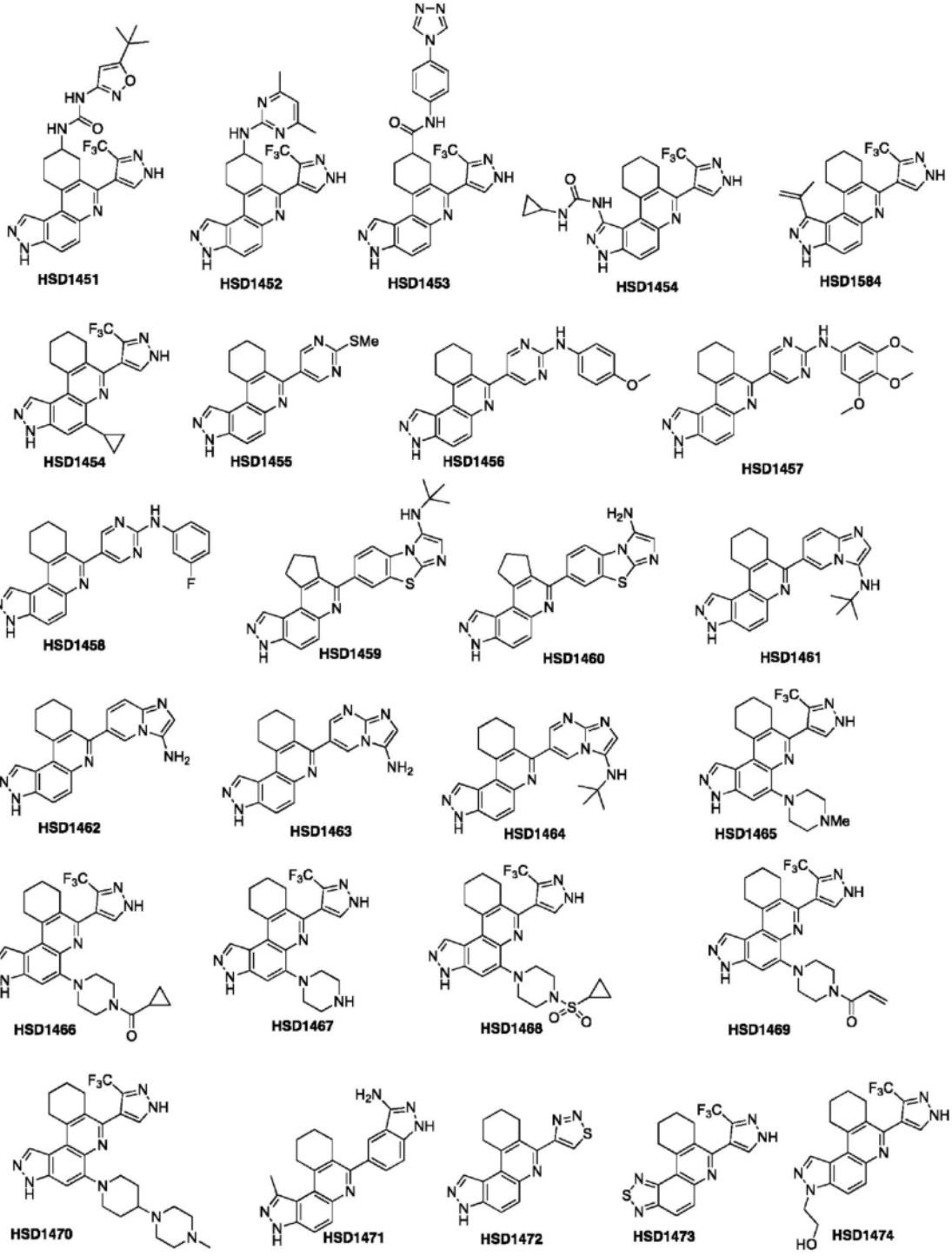
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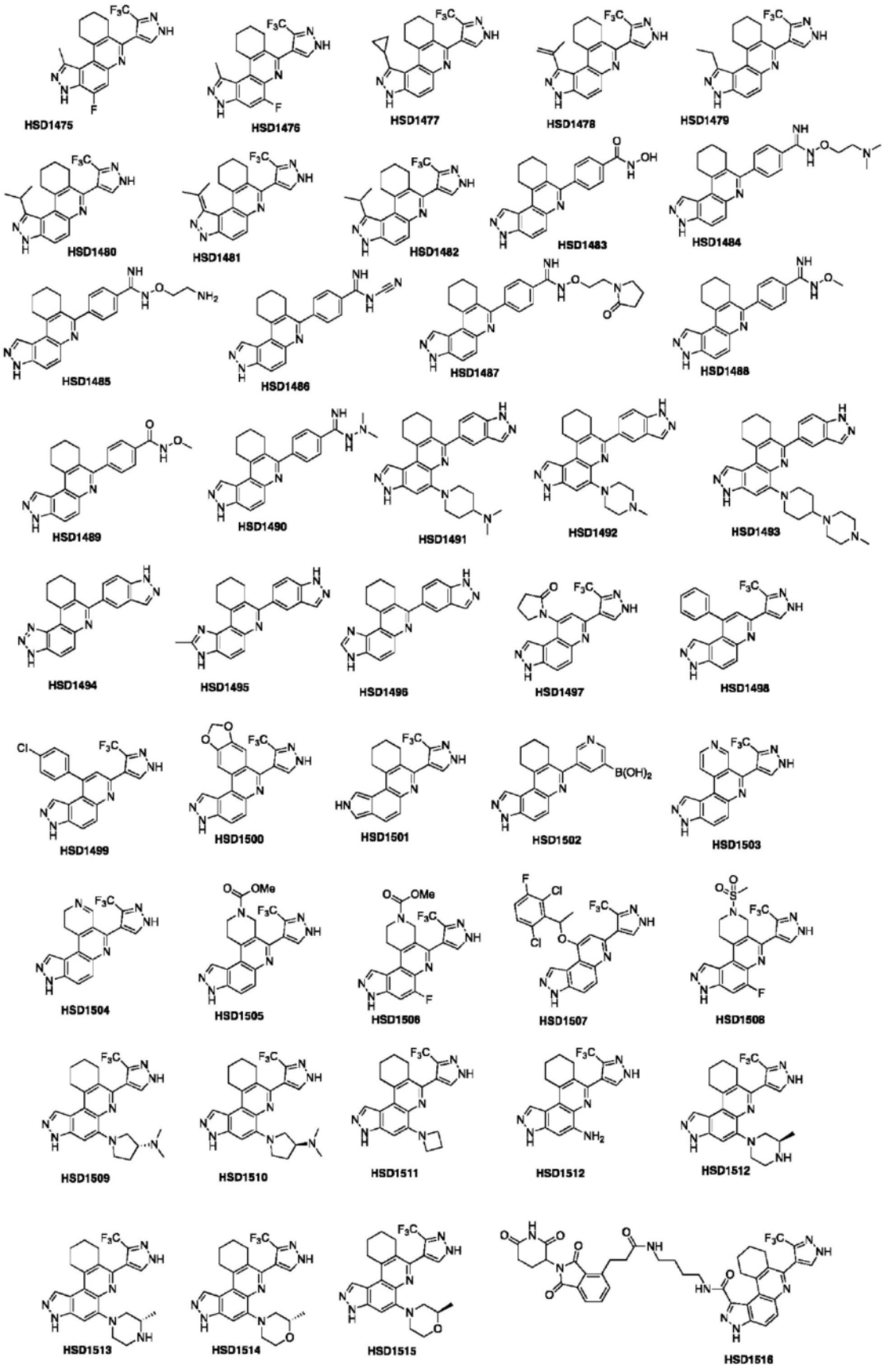
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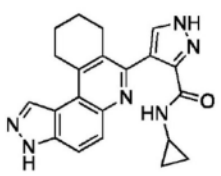
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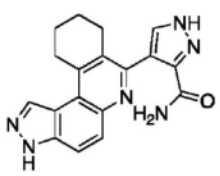
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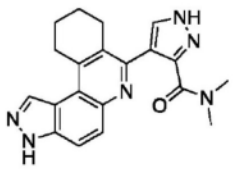
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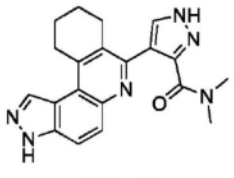
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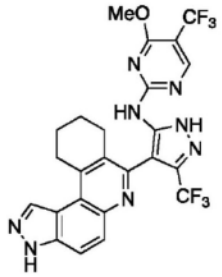
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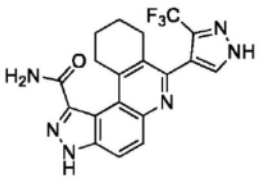
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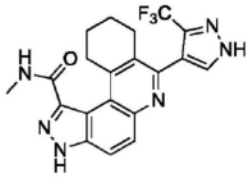
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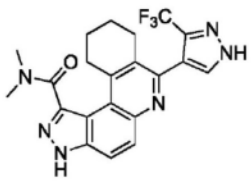
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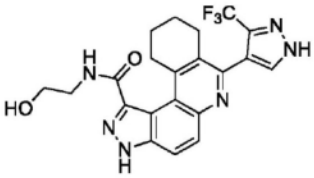
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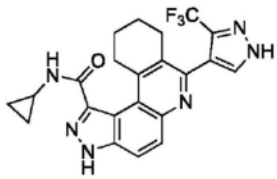
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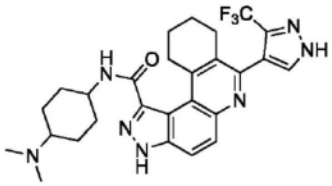
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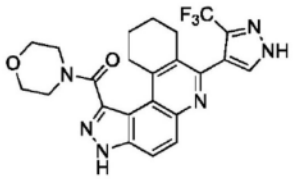
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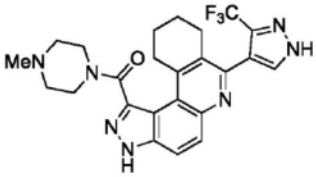
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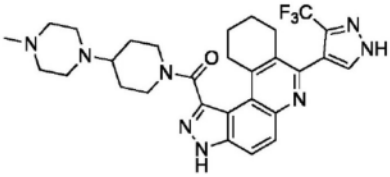
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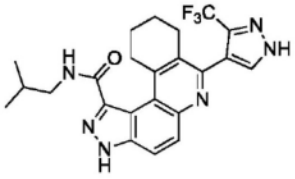
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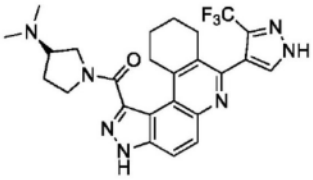
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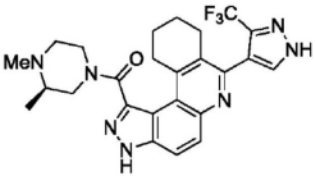
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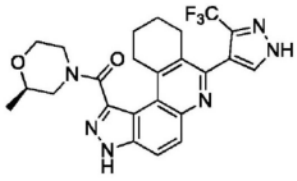
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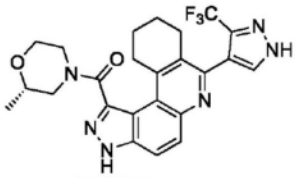
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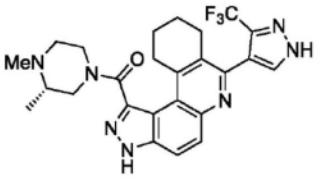
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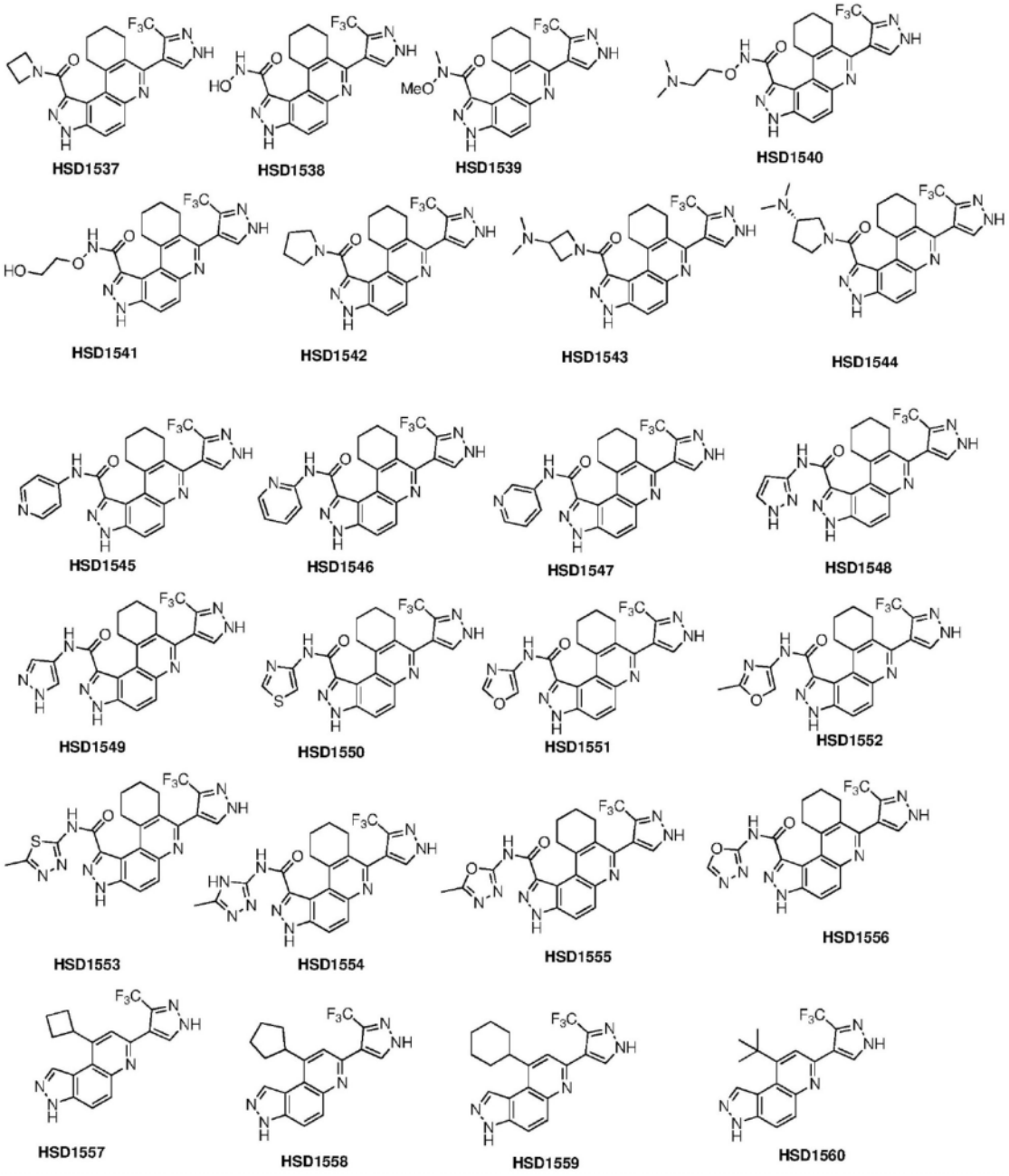
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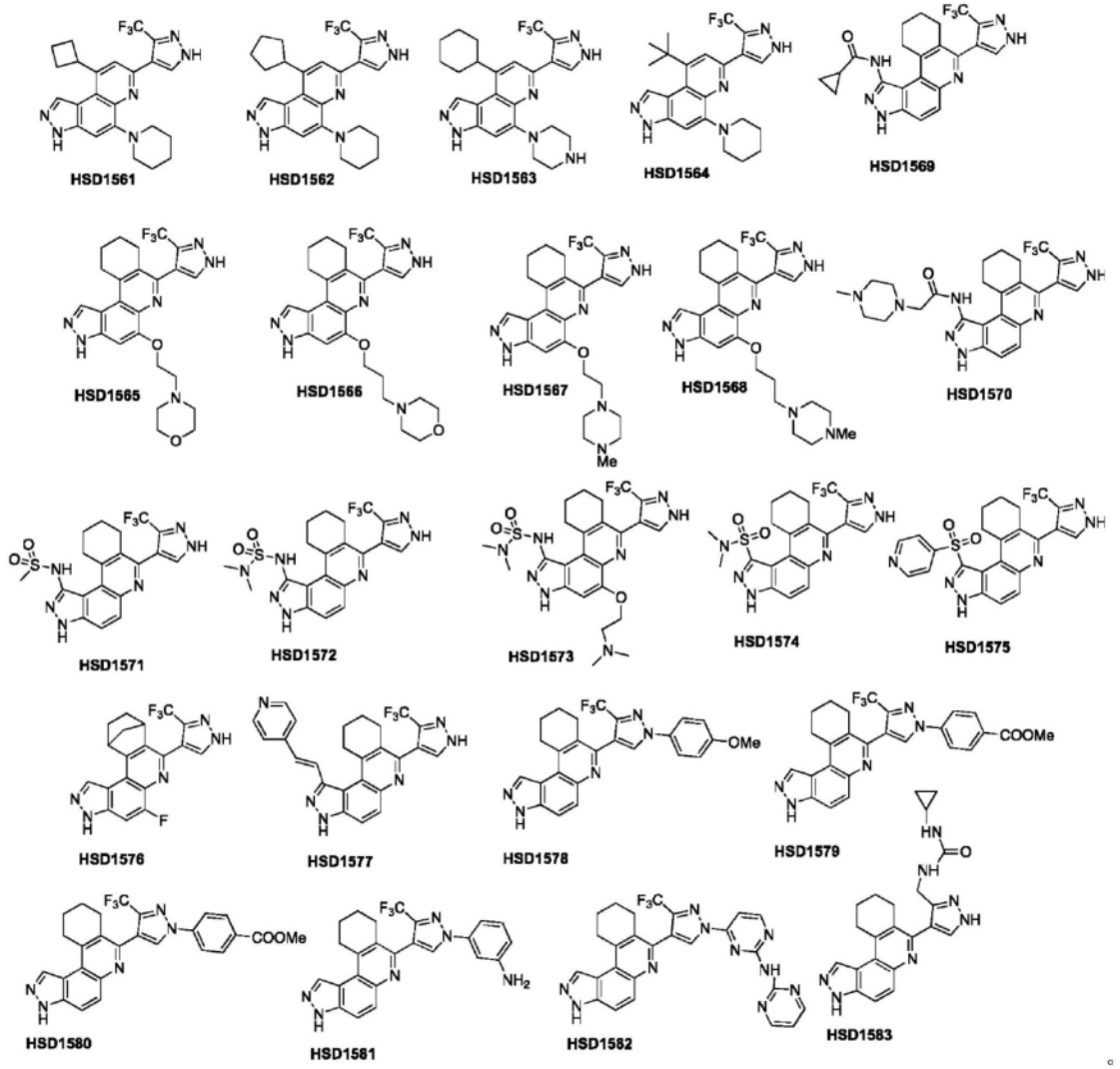
HSD1560

[0178] 

[0179] 在一些说明性的实施方案中，本发明涉及药物组合物，其包含一种或多种如本文公开的化合物或其药学上可接受的盐，以及一种或多种稀释剂、赋形剂或载体。

[0180] 在一些说明性的实施方案中，本发明涉及一种激酶抑制剂，其中，所述激酶选自FLT3、MNK1/2、JAK1/2/3、Limk1/2、各种CDK、Haspin、ROCK1/2、TOPK、LRRK2、GSK3a/3b、RSK1-4、ERK、P70S6K、AKT、PI3K、p38、PKC、PKA、FGFR1-4、VEGFR1-3、ALK、AXL、LIMK1/2、Aurora A/B、ABL1、AKT、CSF1R、CSNK1D、DCAMKL1、CSNK1G2、EPHA2、ERBB2、IKK-alpha、IKK-β、JNK1/2/3、MARK3、MEK1/2、MET、MLK1、PAK1/2/4、PDGFRa/b、PIM1/2/3、PLK1/2/3/4、PRKCE、PRKX、RET、TAOK2、TRKA/B/C、ULK2和受体相互作用蛋白激酶4(RIPK4)。

[0181] 在一些说明性的实施方案中，本发明涉及一种用于治疗由激酶和/或组蛋白脱甲基酶介导的疾病的方法，所述疾病包括炎症、癌症、病毒和细菌感染、胃肠道疾病、眼病、神经疾病、心血管疾病和免疫疾病，所述方法包括以下步骤：将治疗有效量的一种或多种如本文公开的化合物、以及一种或多种载体、稀释剂或赋形剂给予需要从所述癌症中缓解的患者。

[0182] 在一些说明性的实施方案中，本发明涉及一种用于治疗由激酶和组蛋白脱甲基酶介导的疾病的方法，所述疾病包括炎症、癌症、病毒和细菌感染、胃肠道疾病、眼病、神经疾病、心血管疾病和免疫疾病，所述方法包括以下步骤：将治疗有效量的如本文公开的化合物

与一种或多种具有相同或不同作用的其他化合物以及一种或多种载体、稀释剂或赋形剂组合给予需要从所述癌症中缓解的患者。

[0183] 在一些其他说明性实施方案中，本发明涉及一种药物偶联物，其为小分子或生物偶联物，包含一种或多种本文公开的化合物，其中所述偶联物赋予细胞类型靶向或组织类型靶向，或该偶联物靶向另一途径，所述另一途径协同所述化合物的作用。

[0184] 在一些说明性的实施方案中，本发明涉及一种药物偶联物，其为小分子或生物偶联物，包含一种或多种本文公开的化合物，其中所述偶联物赋予水溶性或低清除率。

[0185] 在一些说明性的实施方案中，本发明涉及一种药物偶联物，其包含一种或多种本文公开的化合物，以及通过系统帮助靶蛋白降解的部分，所述系统包括但不限于泛素连接酶/蛋白酶体降解系统。

[0186] 在一些说明性的实施方案中，本发明涉及一种药物组合物，其包含纳米粒子形式的一种或多种本文公开的化合物，以及一种或多种稀释剂、赋形剂或载体。

[0187] 在一些说明性的实施方案中，本发明涉及一种前药，其包含一种或多种本文公开的化合物，其中所述前药部分在特定位置被去除，所述特定位置例如胃肠道中或血液中或组织中或癌症特异性的位置。

[0188] 在一些说明性的实施方案中，本发明涉及本文公开的化合物的类似物，其中特定的代谢热点被例如氘或氟的基团修饰。

[0189] 另外，本文中应理解，本文所述的化合物可与其他化合物组合使用，所述其他化合物被施用以治疗癌症的其他症状，例如被施用以减轻疼痛、恶心、呕吐等的化合物。

[0190] 以下非限制性示例性实施例包括在本文中以进一步说明本发明。这些示例性实施例并非旨在且不应以任何方式解释为限制本发明的范围。还应理解，本文考虑了这些示例性实施方案的多种变化。

[0191] 实验部分和表征：

[0192] 多组分反应的通用程序：[10]

[0193] 方法A：将胺(1mmol)和醛(1mmol)在3mL无水乙醇中的混合物回流2小时，然后向反应混合物中加入环酮或乙醛(2.1mmol)。加入催化计量的浓盐酸，使反应继续回流6-12小时。将反应混合物浓缩并溶解在DCM(50mL)中，用盐水溶液(20mL X 2)洗涤。将有机层干燥(Na_2SO_4)，减压浓缩，并通过硅胶色谱法纯化(二氯甲烷:甲醇(99:01至80:20))，得到所需的环化化合物。

[0194] 方法B：将胺(1mmol)和醛(1mmol)在3mL乙腈中的混合物回流2小时。将反应混合物冷却至室温，然后添加烯烃(2mmol)和$Y(OTf)_3$(30mol％)。反应继续回流过夜。浓缩反应混合物，并通过硅胶色谱法纯化，用二氯甲烷:甲醇(99:01)洗脱，得到所需的环化化合物。

[0195] 方法C：将胺(1mmol)、醛(1mmol)和环酮(2mmol)在6mL四氢呋喃中在碘(10mol％)存在下的混合物回流6-12h。反应完成后，将反应混合物浓缩并通过硅胶色谱法纯化：乙酸乙酯:己烷(80:20)或二氯甲烷:甲醇(99:01)，得到所需的环化化合物。(注意：有时产品可能会沉淀出来，将其过滤，用无水乙醇洗涤并通过柱色谱法进一步纯化)。

[0196] 激酶测定：HotSpot激酶筛选测定(反应生物学)用于测量激酶/抑制剂相互作用。将激酶和底物在含有20mM HEPES pH 7.5、10mM $MgCl_2$、1mM EGTA、0.02％Brij35、0.02mg/mL BSA、0.1mM Na_3VO_4、2mM DTT和1％DMSO的缓冲液中混合。然后将单剂量化合物(500nM)添

加到每种反应混合物中。孵育20分钟后，在室温下以100μM的最终总浓度添加ATP(西格玛(Sigma))和[γ-^{33}P]ATP(珀金埃尔默(Perkin Elmer))，然后在室温下放置2小时，然后在P81离子交换纤维素色谱纸(Whatman,Inc.)上点样。滤纸用0.75％磷酸洗涤以除去未结合的ATP。使用Prism 5(GraphPad)，针对每个激酶/抑制剂对计算包含激酶反应物的媒介物(DMSO)的剩余激酶活性百分比。

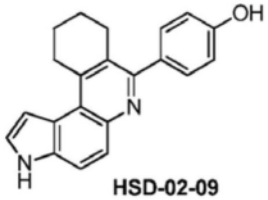
[0197] LSD1分析：

[0198] LSD1检测试剂盒用于测量纯化的LSD1酶的LSD1活性。在96孔板中添加LSD1缓冲液、10uM组蛋白H3(1-21)K4me2肽和测试化合物或DMSO对照。用LSD1酶引发反应。在室温下孵育30分钟后，加入过氧化物酶和Ampiex Red试剂，并在5分钟后使用酶标仪测量荧光(λex＝530±13nm，λem＝590±18nm)。抑制百分比计算为抑制剂存在下的荧光强度除以DMSO对照乘以100％。

[0199] IC50增殖测定

[0200] 在处理之前的下午，将细胞系和原代细胞接种到96孔板中。大约18小时后，将化合物在二甲亚砜(DMSO)中进行半连续稀释，然后在生长培养基中稀释，然后添加到细胞中。在添加阿尔玛蓝(Alamar Blue)(美国加利福尼亚州卡尔斯巴德的生命技术公司(Life Technologies,Carlsbad,CA))之前，将板孵育72小时。在37℃下再孵育4小时后，使用Bio-Tek Synergy HT平板读数器(美国福蒙特州威努斯基的宝特公司(Bio-Tek,Winooski,VT))读取平板。使用GraphPad Prism软件(Graphpad,美国加利福尼亚州拉荷亚(La Jolla,CA))对数据进行分析并进行绘图。

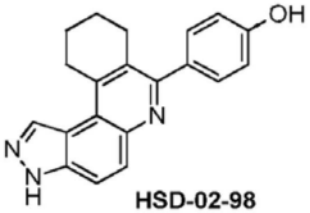
[0201] 4-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯酚

[0202] 

HSD-02-09

黄色固体 (195 mg, 62%)。 ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.35 (s, 1H), 8.20 (d, J = 9.0 Hz, 1H), 8.02 (d, J = 9.0 Hz, 1H), 7.79 (s, 1H), 7.58 (d, J = 8.2 Hz, 2H), 7.31 (s, 1H), 7.05 (d, J = 8.2 Hz, 2H), 3.56 (d, J = 6.6 Hz, 2H), 2.80 (t, J = 6.3 Hz, 2H), 2.02 (d, J = 8.4 Hz, 2H), 1.87 - 1.61 (m, 2H). ^{13}C NMR (126 MHz, DMSo-d_6) δ 160.28, 150.26, 133.77, 131.92, 129.82, 127.07, 123.08, 121.33, 119.87, 115.98, 106.80, 31.35, 28.22, 22.01, 21.65; $C_{21}H_{19}N_2O$ [M + H]$^+$的HRMS(ESI)m/z计算值315.1497，实测值315.1499。

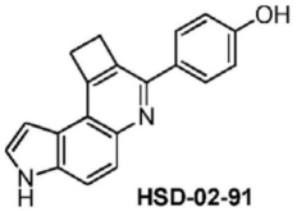
[0203] 4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0204] 

HSD-02-98

方法 A: 灰白色固体(189 mg, 60%)。 ^{1}H NMR (500 MHz, DMSO- d_6) δ 10.46 (s, 1H), 8.67 (s, 1H), 8.16 (d, J = 9.5 Hz, 1H), 7.60 (d, J = 8.1 Hz, 2H), 7.06 (d, J = 5Hz, 1H), 3.31 (s, 1H), 2.80 (s, 1H), 2.00 (s, 1H), 1.74 (s, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 160.40, 152.79, 151.09, 134.91, 132.09, 131.87, 122.67, 122.43, 119.96, 115.95, 114.66, 30.85, 28.21, 21.72, 21.66; $C_{20}H_{18}N_{3O}$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 316.1449, 实测值 316.1458。

[0205] 4-(8,9-二氢-3H-环丁[c]吡咯并[3,2-f]喹啉-7-基)苯酚

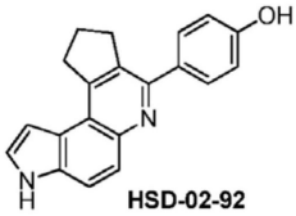
[0206] 

HSD-02-91

方法 C: 黄色固体 (166 mg, 58%)。 ^{1}H NMR (500 MHz, 甲醇- d_4) δ 8.12 (d, J = 9.1 Hz, 1H), 8.00 (d, J = 8.5 Hz, 2H), 7.97 (d, J = 9.2 Hz, 2H), 7.65 (d, J = 3.0 Hz, 1H), 7.14 - 7.04 (m, 2H), 3.92 (t, J = 3.7 Hz, 2H), 3.85 (t, J =3.8 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 161.86, 154.45, 143.71, 135.70, 134.66, 132.88, 131.33, 127.84, 123.68, 120.93, 119.32, 118.50, 116.87, 109.93, 103.31, 31.49. $C_{19}H_{15}N_2O$ [M + H]$^+$的 HRMS (ESI) m/z 计算值

287.1184,实测值287.1184。

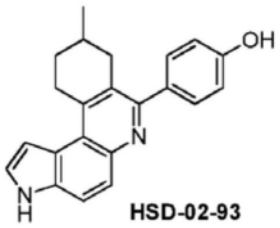
[0207] 4-(3,8,9,10-四氢环戊[c]吡咯并[3,2-f]喹啉-7-基)苯酚

[0208] 

HSD-02-92

方法A: 黄色固体 (181 mg, 60%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 8.18 (dd, J = 9.0, 0.9 Hz, 1H), 7.92 (d, J = 9.0 Hz, 1H), 7.79 - 7.72 (m, 2H), 7.70 (d, J = 3.1 Hz, 1H), 7.27 (dd, J = 3.1, 0.9 Hz, 1H), 7.11 - 7.04 (m, 2H), 3.92 - 3.79 (m, 2H), 3.37 (t, J = 7.6 Hz, 2H), 2.49 (p, J = 7.7 Hz, 2H); ^{13}C NMR (126 MHz, 甲醇-d_4) δ 160.89, 146.91, 136.04, 135.25, 133.22, 130.80, 126.63, 122.44, 121.08, 120.85, 120.21, 115.78, 112.16, 104.20, 35.16,31.66,24.38;$C_{20}H_{17}N_{20}$[M+H]$^+$的HRMS(ESI)m/z计算值301.1340,实测值301.340。

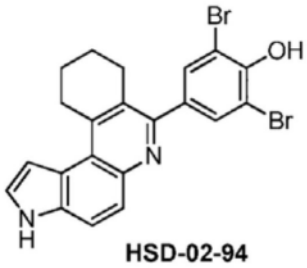
[0209] 4-(9-甲基-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯酚

[0210] 

HSD-02-93

方法A: 黄色固体 (236 mg, 72%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 8.17 (d, J = 8.9 Hz, 1H), 7.84 (d, J = 8.8 Hz, 1H), 7.71 (d, J = 3.1 Hz, 1H), 7.55 (d, J = 8.6 Hz, 2H), 7.40 (d, J = 3.2 Hz, 1H), 7.07 (d, J = 8.6 Hz, 2H), 3.86 (ddd, J = 19.3, 5.9, 2.4 Hz, 1H), 3.69 - 3.50 (m, 1H), 2.89 (ddd J, = 16.7, 4.5, 2.0 Hz, 1H), 2.62 (dd, J= 16.9,10.6 Hz, 1H), 2.30 (ddt, J = 13.0, 7.0, 2.4 Hz, 1H), 1.98 - 1.83 (m, 1H), 1.71 (dtd, J =12.9, 10.9, 5.8 Hz, 1H), 1.14 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, 甲醇-d_4) δ 160.12, 154.73, 150.23, 133.79, 130.78, 129.45,126.06,123.12,122.70,120.75,120.16,115.52,112.48,106.36,36.01,31.36, 29.62,27.78,20.23;$C_{22}H_{21}N_2O$[M+H]$^+$的HRMS(ESI)m/z计算值329.1653,实测值329.1653。

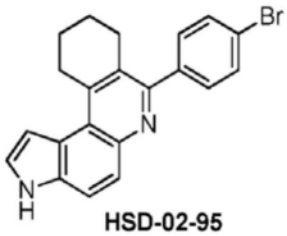
[0211] 2,6-二溴-4-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯酚

[0212] 

HSD-02-94

方法A: 黄色固体 (277 mg, 59%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 11.80 (s, 1H), 10.10 (s, 1H), 7.80 (d, J= 8.9 Hz, 0H), 7.73 (s, 1H), 7.64 (d, J = 8.9 Hz, 0H), 7.51 (t, J = 2.7 Hz, 0H), 7.13 (t, J = 2.5 Hz, 1H), 3.37 (t, J = 6.5 Hz, 1H), 2.79 (t, J = 6.1 Hz, 1H), 2.03 - 1.89 (m, 1H), 1.74 (dq, J = 6.3, 3.2 Hz, 1H); ^{13}C NMR (126 MHz, DMSO) δ 152.61, 150.86, 142.79, 135.62, 133.32, 127.69, 124.22, 123.48, 122.70, 120.25, 116.95, 116.65, 111.87, 106.37, 30.09, 28.90, 22.72, 22.48; $C_{21}H_{17}Br_2N_2O$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 470.9707, 实测值 470.9705。

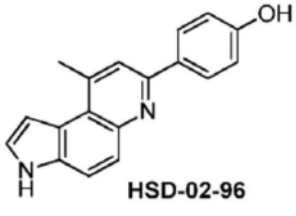
[0213] 7-(4-溴苯基)-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶

[0214] 

HSD-02-95

方法A: 灰白色固体 (207 mg, 55%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 7.80 (dd, J = 8.9, 0.9 Hz, 1H), 7.70 (d, J = 8.9 Hz, 1H), 7.66 (d, J = 8.4 Hz, 2H), 7.44 - 7.40 (m, 3H), 7.20 (dd, J = 3.3, 0.9 Hz, 1H), 3.53 - 3.45 (m, 2H), 2.74 (t, J = 6.2 Hz, 2H), 2.13 - 2.01 (m, 2H), 1.87 - 1.76 (m, 2H); ^{13}C NMR (126 MHz, 甲醇-d_4) δ 154.80, 143.92, 142.60, 140.03, 133.30, 131.01, 130.67, 127.22, 122.92, 122.85, 121.94, 121.71, 120.23, 116.08, 105.79, 29.93, 28.51, 22.43, 22.09; $C_{21}H_{18}BrN_2$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值377.0653,实测值377.0653。

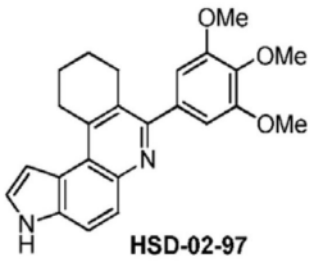
[0215] 4-(9-甲基-3H-吡咯并[3,2-f]喹啉-7-基)苯酚

[0216] 

HSD-02-96

方法A: 黄色固体 (173 mg, 63%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 10.57 (s, 1H), 8.24 (d, J = 6.4 Hz, 3H), 8.09 (d, J = 8.8 Hz, 1H), 7.80 (s, OH), 7.28 (s, 1H), 7.07 (d, J = 8.8 Hz, 1H), 3.14 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.75, 149.00, 133.54, 131.40, 127.61, 122.28, 121.80, 121.28, 120.94, 116.69, 105.84, 24.33; $C_{18}H_{15}N_2O$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 275.1184, 实测值 275.1192。

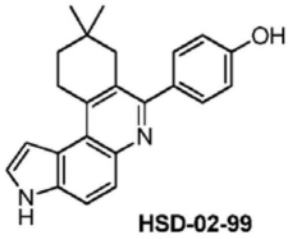
[0217] 7-(3,4,5-三甲氧苯基)-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶

[0218] 

HSD-02-97

方法A: 白色结晶固体 (213 mg, 55%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.18 (dd, J = 8.9, 0.8 Hz, 1H), 7.85 (d, J = 8.9 Hz, 1H), 7.71 (d, J = 3.1 Hz, 1H), 7.38 (dd, J = 3.2, 0.9 Hz, 1H), 7.01 (s, 2H), 3.92 (s, 6H), 3.88 (s, 3H), 3.67 (t, J = 6.6 Hz, 3H), 2.93 (t, J = 6.2 Hz, 2H), 2.22 - 2.11 (m, 3H), 1.92 (ddd, J = 9.1, 7.4, 4.5 Hz, 2H). ^{13}C NMR (126 MHz, 甲醇-d_4) δ 154.94, 153.66, 149.75, 139.80, 133.79, 133.67, 129.57, 127.67, 126.01, 123.58, 120.83, 120.04, 112.80, 106.71, 106.41, 59.88, 55.66, 31.23, 27.71, 21.56, 21.24; $C_{24}H_{25}N_2O_3$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 389.1865, 实测值389.1861。

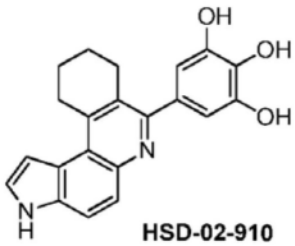
[0219] 4-(9,9-二甲基-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯酚

[0220] 

HSD-02-99

方法A: 白色结晶固体 (188 mg, 53%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 7.79 (d, J = 8.9 Hz, 1H), 7.71 (d, J = 8.9 Hz, 1H), 7.43 (d, J = 3.1 Hz, 1H), 7.32 (d, J = 8.1 Hz, 2H), 7.21 (d, J = 3.1 Hz, 1H), 6.92 (d, J = 8.1 Hz, 2H), 3.50 (t, J = 6.8 Hz, 2H), 2.56 (s, 2H), 1.80 (t, J = 6.7 Hz, 2H), 0.97 (s, 6H); ^{13}C NMR (126 MHz, 甲醇-d_4) δ 157.35, 156.02, 143.16, 141.88, 133.19, 131.52, 130.07, 126.84, 122.96, 122.26, 121.28, 120.30, 116.11, 114.60, 105.73, 48.11, 48.05, 47.94, 47.77, 47.60, 47.43, 47.26, 47.09, 42.06, 34.69,28.29,27.71,26.60;$C_{23}H_{23}N_2O$[M+H]$^+$的HRMS(ESI)m/z计算值343.1810,实测值343.1808。

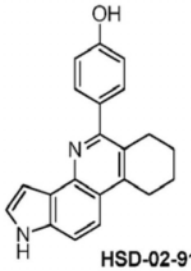
[0221] 5-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯-1,2,3-三醇

[0222] 

HSD-02-910

方法A: 黄色固体 (246 mg, 71%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 9.52 (s, 2H), 9.01 (s, 1H), 8.17 (d, J = 8.9 Hz, 1H), 7.95 (d, J = 8.9 Hz, 1H), 7.78 (s, 1H), 7.27 (s, 1H), 6.65 (s, 2H), 3.50 (t, J = 6.4 Hz, 2H), 2.80 (t, J = 6.2 Hz, 2H), 2.03 - 1.98 (m, 2H), 1.83 - 1.73 (m, 2H). ^{13}C NMR (126 MHz, DMSCO-d_6) δ 154.17, 150.35, 146.76, 136.24, 133.69, 129.63, 127.03, 122.96, 122.04, 121.27, 119.85, 113.64, 109.26, 109.26, 106.74, 31.31, 28.26, 21.99, 21.58; $C_{21}H_{19}N_2O_3$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 347.1395,实测值347.1390。

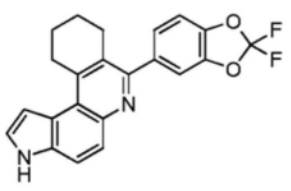
[0223] 4-(6,7,8,9-四氢-1H-吡咯并[2,3-c]菲啶-5-基)苯酚

[0224] 

HSD-02-911

方法A: 黄色固体 (163 mg, 52%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.05 - 7.92 (m, 2H), 7.58 - 7.52 (m, 3H), 7.48 (d, J = 3.2 Hz, 1H), 7.07 (d, J = 8.3 Hz, 2H), 3.51 (t, J = 6.5 Hz, 2H), 2.82 (d, J = 6.4 Hz, 2H), 2.06 (dd, J = 7.7, 4.3 Hz, 2H), 1.92 - 1.77 (m, 2H). ^{13}C NMR (126 MHz, 甲醇-d_4) δ 160.10, 155.63, 152.51, 137.17, 131.84, 130.93, 128.03, 125.79, 122.79, 122.70, 116.47, 116.22, 115.74, 115.44, 101.89, 27.60, 27.36, 21.68, 21.30; $C_{21}H_{19}N_2O$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 315.1497, 实测值 315.1495。

[0225] 7-(2,2-二氟苯并[d][1,3]二恶唑-5-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

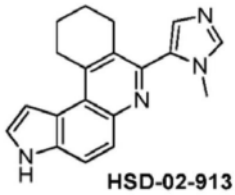
[0226] 

ND-02-912

方法A: 灰白色固体 (57 mg, 15%)^{1}H NMR (500 MHz, 甲醇- d_4) δ 7.78 (dd, J = 9.0, 3.6 Hz, 1H), 7.68 (dd, J = 9.1 =, 3.6 Hz, 1H), 7.36 (dt, J = 40.7, 3.0 Hz, 2H), 7.32 - 7.20 (m, 2H), 7.15 (d, J = 3.5 Hz, 1H), 3.42 (q, J = 5.7 Hz, 2H), 2.69 (q, J = 5.4 Hz, 2H), 2.05 - 1.94 (m, 2H), 1.82 - 1.69 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 154.25, 144.03, 143.32, 143.22, 142.52, 137.40, 133.29, 131.73, 127.27, 124.87, 122.96, 122.87, 121.94, 120.19, 116.15, 110.39, 108.94, 105.81, 29.90, 28.49, 22.35, 22.03; HRMS (ESI) m/z 计算值

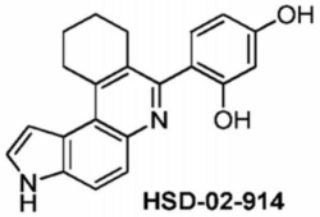
$C_{21}H_{16}F_2N_3O_2[M+H]^+$380.1211,实测值380.1216。

[0227] 7-(1-甲基-1H-咪唑-5-基)-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶

[0228] 
HSD-02-913

方法A:灰白色固体(151 mg,50%)。^{1}H NMR(500 MHz,甲醇-d_4)δ 7.79(d,J = 7.9 Hz,2H),7.66(d,J = 8.9 Hz,IH),7.40(d J,= 3.1 Hz,1H),7.18(s,1H),7.12(d,J = 3.1 Hz,1H),3.60(s,3H),3.38(t,J = 6.5 Hz,2H),2.75(t,J = 6.3 Hz,2H),2.00 - 1.94(m,2H),1.81(q,J = 6.0,5.6 Hz,2H). ^{13}C NMR(126 MHz,甲醇-d_4)δ 144.67,144.01,142.83,138.47,133.43,130.97,129.25,128.07,122.97,122.14,120.11,116.34,105.94,31.45,29.82,27.83,22.28,21.90;HRMS(ESI)m/z计算值$C_{19}H_{19}N_4[M+H]^+$303.1609,实测值303.1599。

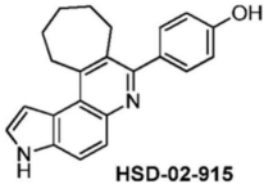
[0229] 4-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯-1,3-二醇

[0230] 
HSD-02-914

方法A:黄色固体(142 mg,43%)。^{1}H NMR(500 MHz,甲醇-d_4)δ 7.77(dd,J = 8.9,0.8 Hz,1H),7.68(d,J = 8.9 Hz,1H),7.42(d,J = 3.1 Hz,1H),7.19(dd,J = 3.2,0.9 Hz,1H),7.09(d,J = 8.9 Hz,1H),6.46 - 6.42(m,2H),3.49(t,J = 6.5 Hz,2H),2.80(t,J = 6.3 = Hz,2H),2.09 - 2.02(m,2H),1.87 - 1.78(m,2H). ^{13}C NMR(126 MHz,甲醇-d_4)δ 158.65,156.16,154.02,143.81,141.57,133.18,130.73,129.43,122.78,122.59,121.13,120.30,118.60,115.81,106.34,105.68,102.35,29.99,27.42,22.52,22.05;$C_{21}H_{19}N_2O_2[M+H]^+$的HRMS(ESI)m/z计算值331.1446,实测值331.1440。

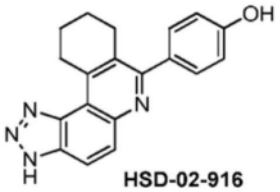
[0231] 4-(3,8,9,10,11,12-六氢环庚基[c]吡咯并[3,2-f]喹啉-7-基)苯酚

[0232] 方法A:灰白色固体(187mg,57%)。^{1}H NMR(500MHz,DMSO-d_6)δ11.67(s,1H),9.52(s,1H),7.72(s,1H),7.56(d,J=8.9Hz,1H),7.45(d,J=2.8Hz,1H),7.29(d,J=8.1Hz,2H),7.07(d,J=3.1Hz,1H),6.85

[0233] 
HSD-02-915

(s,2H),3.55(dd,J = 6.8,3.3 Hz,2H),3.08 - 2.96(m,2H),1.88(dq,J = 16.5,4.5 Hz,4H),1.63(p,J = 5.1 Hz,2H). ^{13}C NMR(126 MHz,DMSO-d_6)δ 157.25,157.11,154.98,148.20,144.09,133.98,133.26,133.10,132.98,130.91,124.12,123.99,123.82,121.64,120.00,116.78,116.72,115.09,115.00,105.09,31.64,30.68,30.11,27.75,25.12;$C_{22}H_{21}N_2O$ $[M+H]^+$的HRMS(ESI)m/z计算值329.1653,实测值329.1652。

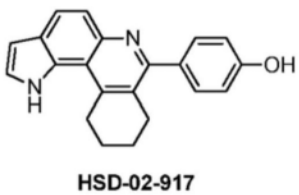
[0234] 4-(8,9,10,11-四氢-3H-[1,2,3]三唑[4,5-a]菲啶-7-基)苯酚

[0235] 
HSD-02-916

方法A:灰白色固体(237 mg,75%)。^{1}H NMR(500 MHz,DMSO-d_6)δ 9.73(s,1H),8.04(d,J = 9.1 Hz,1H),7.89(d,J = 9.1 Hz,1H),7.44(d,J = 8.3 Hz,2H),6.89(d,J = 8.4 Hz,2H),3.67(s,2H),2.81(s,1H),2.03 - 1.88(m,2H),1.82 - 1.59(m,2H); ^{13}C NMR(126 MHz,DMSO)δ 158.08,143.69,131.01,130.34,118.90,115.25,30.03,28.96,26.90,24.76. $C_{19}H_{17}N_4O$ $[M+H]^+$的

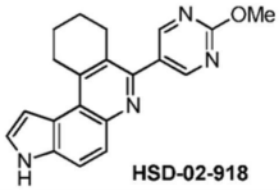
[0236] HRMS(ESI)m/z计算值317.1402,实测值317.1408。

[0237] 4-(2,3,4,8-四氢-1H-吡咯并[3,2-b]菲啶-5-基)苯酚

[0238] 
HSD-02-917

方法A:灰白色固体(185 mg,59%)。^{1}H NMR(500 MHz,甲醇-d_4)δ 7.87(d,J = 8.7 Hz,1H),7.62(d,J = 8.7 Hz,1H),7.43(d,J = 3.1 Hz,1H),7.34(d,J = 8.5 Hz,1H),6.92(d,J = 8.5 Hz,2H),6.70(d,J = 3.1 Hz,1H),3.50(t,J 6.5 Hz,2H),2.78(t,J = 6.3 Hz,2H),2.13 - 2.05(m,2H),1.86 - 1.80(m,2H); ^{13}C NMR(126 MHz,MeOD)δ 157.34,156.57,143.27,141.29,131.70,130.00,128.49,127.57,125.52,124.19,123.50,119.83,117.04,114.57,102.65,29.32,28.61,22.41,22.04;$C_{21}H_{19}N_2O[M+H]^+$的HRMS(ESI)m/z计算值315.1497,实测值315.1495。

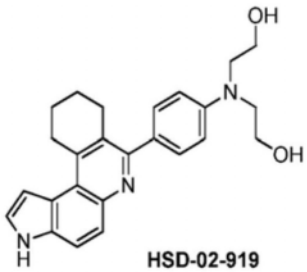
[0239] 4-(2,3,4,8-四氢-1H-吡咯并[3,2-b]菲啶-5-基)苯酚

[0240] 

HSD-02-918

方法A: 灰白色固体 (178 mg, 54%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 11.81 (s, 1H), 8.85 (s, 2H), 7.81 (d, J = 8.8 Hz, 1H), 7.66 (d, J = 8.8 Hz, 1H), 7.51 (t, J = 2.8 Hz, 1H), 7.13 (t, J = 2.5 Hz, 1H), 3.99 (s, 3H), 3.37 (t, J = 6.5 Hz, 2H), 2.84 (t, J = 6.2 Hz, 2H), 1.99 - 1.91 (m, 2H), 1.75 (dd, J = 7.5, 4.3 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 164.77, 159.82, 149.96, 143.68, 142.81, 133.37,129.18,127.97,124.12,124.09,122.80,120.25,116.84,106.43,55.22,29.96, 28.70,22.75,22.49;$C_{20}H_{19}N_4O$[M+H]$^+$的HRMS(ESI)m/z计算值331.1558,实测值331.1553。

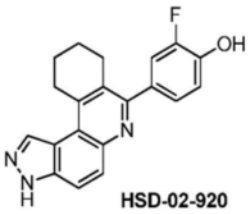
[0241] 2,2'-((4-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯基)氮杂二基)二乙醇

[0242] 

HSD-02-919

方法A: 黄色固体 (209 mg, 70%)。^{1}H NMR (500 MHz, 甲醇-d_6) δ 8.00 (d, J = 8.9 Hz, 1H), 7.77 (d, J = 8.9 Hz, 1H), 7.59 (d, J = 3.1 Hz, 1H), 7.48 - 7.43 (m, 2H), 7.28 (d, J = 3.2 Hz, 1H), 6.95 (d, J = 8.9 Hz, 2H), 3.79 (t, J = 6.0 Hz, 4H), 3.65 (t, J = 6.0 Hz, 4H), 2·90 (t, J = 6.2 Hz, 2H), 2.12 - 2.06 (m, 2H), 1.84 (td, J = 6.2, 3.2 Hz, 2H); ^{13}C NMR (126 MHz, MeOD) δ 152.36, 151.09, 149.41, 136.32, 133.50, 130.36, 129.04, 124.91, 122.68, 121.37, 120.18, 118.91, 115.34, 111.33, 106.08, 58.85, 53.41, 30.85, 28.37, 21.94, 21.66; $C_{25}H_{28}N_3O_2$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 402.2181, 实测值402.2179。

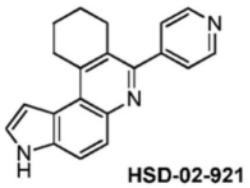
[0243] 2-氟-4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0244] 

HSD-02-920

方法A: 灰白色固体 (207 mg, 62%)。^{1}H NMR (500 MHz, DMSO- de) δ 10.81 (s, 1H), 8.83 (s, 1H), 8.26 (d, J = 9.2 Hz, 1H), 8.21 (d, J = 9.2 Hz, 1H), 7.66 (dd, J = 11.8, 2.2 Hz, 1H), 7.42 (dd, J = 8.4, 2.1 Hz, 1H), 7.26 (t, J = 8.6 Hz, 1H), 3.49 (t, J = 6.4 Hz, 2H), 2.83 (t, J = 6.2 Hz, 2H), 2.07 - 2.00 (m, 2H), 1.85 - 1.76 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 151.89, 149.96, 147.88, 135.32, 132.02, 127.33,123.16,120.36,118.65,118.49,118.29,114.87,30.92,28.11,21.80,21.69; $C_{20}H_{17}FN_3O$[M+H]$^+$的HRMS(ESI)m/z计算值334.1355,实测值334.1352。

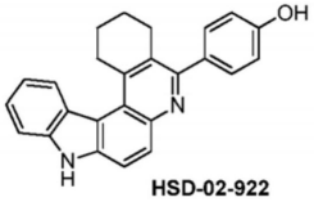
[0245] 7-(吡啶-4-基)-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶

[0246] 

HSD-02-921

方法A: 灰白色固体 (183 mg, 61%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 11.81 (s, 1H), 8.67 (dt, J = 4.4, 1.5 Hz, 2H), 7.81 (d, J = 8.8 Hz, 1H), 7.65 (d, J = 8.9 Hz, 1H), 7.60 - 7.55 (m, 2H), 7.54 - 7.48 (m, 1H), 7.14 (s, 1H), 3.40 (t, J = 6.6 Hz, 2H), 2.77 (t, J = 6.1 Hz, 2H), 2.01 - 1.94 (m, 2H), 1.75 (q, J = 5.9 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 153.34, 149.84, 149.10, 143.44, 142.78, 133.41, 127.19, 124.49, 124.16, 124.08, 122.90, 120.26, 116.87, 106.42, 29.94, 28.67,22.76,22.39;$C_{20}H_{18}N_3$[M+H]$^+$的HRMS(ESI)m/z计算值300.1500,实测值300.1508。

[0247] 4-(2,3,4,9-四氢-1H-吲哚并[3,2-a]菲啶-5-基)苯酚

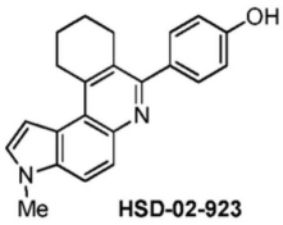
[0248] 

HSD-02-922

方法A: 棕色固体 (175 mg, 48%)。^{1}H NMR (500 MHz, DMSO- d6) δ 8.52 (d, J = 8.5 Hz, 1H), 8.25 (dd, J = 8.0, 3.7 Hz, 2H), 7.73 (dd, J = 8.5, 4.1 Hz, 1H), 7.58 (ddd, J = 8.3, 5.4, 2.6 Hz, 2H), 7.51 (td, J = 7.7, 2.5 Hz, 1H), 7.33 (t, J = 7.7 Hz, 1H), 7.09 - 7.00 (m, 2H), 3.86 (t, J = 6.0 Hz, 2H), 2.89 (t, J = 6.7 Hz, 2H), 1.91 (p, J = 6.6 Hz, 2H), 1.81 (q, , J = 6.3 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 159.66, 151.29, 145.82, 140.03, 139.23,132.51,131.70,130.16,128.83,125.54,125.33,125.13,123.01,120.08,116.30,

115.84,113.14,112.73,110.76,33.12,26.84,21.64,21.36;$C_{25}H_{21}N_2O[M+H]^+$的HRMS(ESI)m/z计算值365.1653,实测值365.1647。

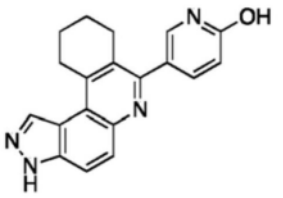
[0249] 4-(3-甲基-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯酚

[0250] 

HSD-02-923

方法A: 黄色固体 (246 mg, 75%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.23 (d, J = 9.0 Hz, 1H), 7.89 (d, J = 9.1 Hz, 1H), 7.66 (d, J =3.1 Hz, 1H), 7.54 (d, J = 8.5 Hz, 2H), 7.35 (d, J = 3.1 Hz, 1H), 7.06 (d, J = 8.4 Hz, 2H), 4.08 (s, 3H), 3.65 (t, J = 6.4 Hz, 2H), 2.92 (t, J = 6.2 Hz, 2H), 2.14 (dq, J = 8.6, 5.9, 4.6 Hz, 2H), 1.94 - 1.85 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 160.06, 154.70, 150.64, 134.12, 133.70, 130.78, 130.35, 129.85, 123.15, 122.88, 120.71, 118.64,115.50,112.77,105.58,32.40,31.23,27.96,21.60,21.28;$C_{22}H_{21}N_2O[M+H]^+$的HRMS(ESI)m/z计算值329.1653,实测值329.1645。

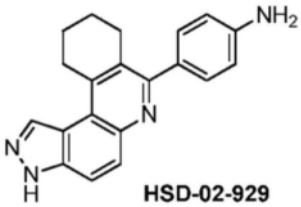
[0251] 5-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)吡啶-2-醇

[0252] 

HSD-02-928

方法A: 灰白色固体 (158 mg, 50%)。H NMR (500 MHz, DMSO- d_6) δ 11.86 (s, 1H), 8.53 (s, 1H), 7.83 (d, J = 9.0 Hz, 1H), 7.80 - 7.73 (m, 2H), 7.65 (d, J = 2.6 Hz, 1H), 6.42 (d, J = 9.4 Hz, 1H), 3.25 (t, J = 6.6 Hz, 2H), 2.84 (t, J = 6.1 Hz, 2H), 2.01 - 1.92 (m, 2H), 1.80 - 1.68 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 162.21, 152.68, 143.74, 142.84, 142.59, 136.37, 129.51, 129.43, 121.76, 119.38, 118.73, 116.21, 29.69, 28.78, 22.59, 22.54; $C_{19}H_{17}N_4O[M+H]^+$的HRMS(ESI)m/z计算值317.1402,实测值317.1403。

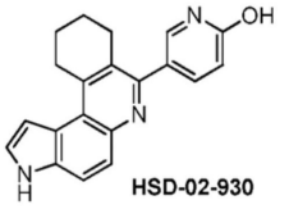
[0253] 4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯胺

[0254] 

HSD-02-929

方法A: 橙色固体 (192 mg, 61%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.73 (s, 1H), 8.16 (t, J = 11.5 Hz, 2H), 7.45 (d, J = 8.5 Hz, 2H), 6.79 (d, J = 8.3 Hz, 2H), 3.46 (s, 2H), 2.98 - 2.78 (m, 2H), 2.09 - 1.92 (m, 2H), 1.82 - 1.63 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 162.75, 154.28, 150.08, 138.83, 136.20, 131.25, 130.62, 129.84, 124.50, 121.76, 115.68, 114.96, 113.80, 111.38, 30.33, 28.84, 22.22; $C_{20}H_{19}N_4$ $[M + H]^+$ 的 HRMS (ESI) m/z计算值315.1609,实测值315.1619。

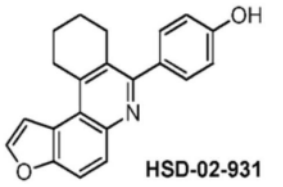
[0255] 5-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)吡啶-2-醇

[0256] 

HSD-02-930

方法A: 灰白色固体 (170 mg, 54%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 10.47 (s, 1H), 8.47 (d, J = 2.1 Hz, 1H), 8.36 (q, J = 9.2 Hz, 2H), 7.79 (d, J = 2.2 Hz, 1H), 7.66 - 7.56 (m, 2H), 7.10 - 6.98 (m, 2H), 3.56 (t, J = 6.4 Hz, 2H), 2.82 (t, J = 6.2 Hz, 2H), 2.00 (dq, J = 8.7, 5.8, 4.5 Hz, 2H), 1.85 - 1.65 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 160.63, 153.59, 153.01, 148.23, 132.05, 131.37, 122.86, 121.34, 119.47, 116.00, 110.37, 30.67, 28.32, 21.74, 21.57; $C_{20}H_{18}N_3O[M+H]^+$的HRMS(ESI)m/z计算值316.1449,实测值316.1455。

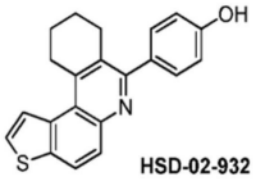
[0257] 4-(8,9,10,11-四氢呋喃并[3,2-a]菲啶-7-基)苯酚

[0258] 

HSD-02-931

方法A: 灰白色固体 (218 mg, 69%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 8.47 (d, J = 2.1 Hz, 1H), 8.36 (q, J = 9.2 Hz, 2H), 7.79 (d, J = 2.2 Hz, 1H), 7.61 (d, J = 8.6 Hz, 2H), 7.06 (d, J = 8.6 Hz, 2H), 3.56 (t, J = 6.4 Hz, 15 2H), 2.82 (t, J = 6.2 Hz, 2H), 2.00 (dq, J = 8.7, 5.8, 4.5 Hz, 2H), 1.86 - 1.65 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 160.63, 153.59, 153.01, 148.23, 132.05, 131.37,122.86,121.34,119.47,116.00,110.37,30.67,28.32,21.74,21.57;$C_{21}H_{18}NO_2[M+H]^+$的HRMS(ESI)m/z计算值316.1337,实测值316.1343。

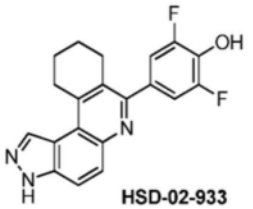
[0259] 4-(8,9,10,11-四氢噻吩并[3,2-a]菲啶-7-基)苯酚

[0260] 

HSD-02-932

方法 A: 灰白色固体 (245 mg, 74%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 9.96 (s, 1H), 8.36 (d, J = 8.9 Hz, 1H), 8.32 (d, J = 5.6 Hz, 1H), 8.08 (d, J = 5.5 Hz, 1H), 7.97 (d, J = 8.9 Hz, 1H), 7.46 (d, J = 8.5 Hz, 2H), 6.94 (d, J = 8.5 Hz, 2H), 3.49 (q, J = 6.5 Hz, 2H), 2.80 (t, J = 6.2 Hz, 2H), 1.94 (dp, J = 6.6, 4.6, 2.8 Hz, 2H), 1.79 - 1.65 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 158.82, 139.74, 133.74, 131.22,130.02,128.68,127.46,125.78,123.88,115.49,31.70,29.13,22.58,21.88; $C_{21}H_{18}NOS[M+H]^+$的HRMS(ESI)m/z计算值332.1109,实测值332.1118。

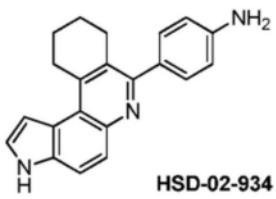
[0261] 2,6-二氟-4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0262] 

HSD-02-933

方法 A: 灰白色固体 (221 mg, 63%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 8.76 (s, 1H), 8.22 (s, 2H), 7.66 - 7.43 (m, 2H), 3.43 (t, J = 6.4 Hz, 2H), 2.83 (t, J = 6.1 Hz, 2H), 2.19 - 1.94 (m, 2H), 1.88 - 1.50 (m, 2H). ^{13}C NMR (126 MHz, DMSO) δ 153.27, 151.34, 151.28, 136.31, 131.82, 123.22, 114.73, 114.52, 30.79, 27.97, 21.80, 21.69; $C_{20}H_{16}F_2N_3O$ $[M+H]^+$ 的 HRMS (ESI) m/z 计算值 352.1261, 实测值 352.1260。

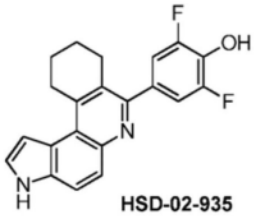
[0263] 4-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯胺

[0264] 

HSD-02-934

方法 A: 明黄色固体 (194 mg, 62%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.09 (d, J = 8.9 Hz, 1H), 7.93 (d, J = 8.8 Hz, 1H), 7.72 (s, 1H), 7.40 (d, J = 8.2 Hz, 2H), 7.26 (s, 1H), 6.75 (d, J = 8.3 Hz, 2H), 5.79 (s, 2H),3.51 (t, J = 6.5 Hz, 2H), 3.32 (s, 2H), 2.85 (t, J = 6.2 Hz, 2H), 2.09 - 1.95 (m, 2H), 1.81 - 1.68 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 151.31, 133.58, 133.58, 131.48, 129.37, 129.33, 127.94, 126.34, 122.49, 120.03, 118.73, 113.57, 106.60, 31.13,28.60,22.25,21.94;$C_{21}H_{20}N_3[M+H]^+$的HRMS(ESI)m/z计算值314.1657,实测值314.1651。

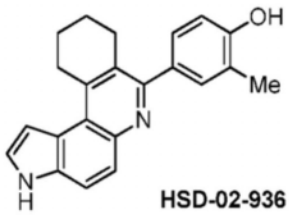
[0265] 2,6-二氟-4-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯酚

[0266] 

HSD-02-935

方法 A: 方法 A: 黄色固体 (161 mg, 46%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 12.43 (s, 1H), 10.91 (s, 1H), 8.13 (d, J = 9.0 Hz, 1H), 7.95 (d, J = 8.9 Hz, 1H), 7.73 (s, 1H), 7.50 (d, J = 7.2 Hz, 2H), 7.28 (s, 1H), 3.52 (t, J = 6.5 Hz, 2H), 2.81 (t, J = 6.1 Hz, 2H), 2.03 - 1.99 (m, 2H), 1.78 (dd, J = 6.2, 2.7 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 153.28, 153.22, 151.35, 151.29, 148.78, 135.89, 133.70, 132.12, 129.36, 126.45, 123.30, 120.58, 119.86, 114.37, 106.78, 31.05, 28.08, 22.12, 21.76; $C_{21}H_{17}F_2N_2O$ [M+H]$^+$的HRMS(ESI)m/z计算值351.1308,实测值351.1302。

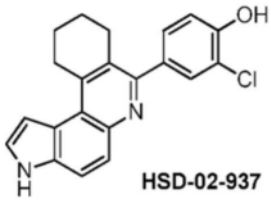
[0267] 2-甲基-4-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯酚

[0268] 

HSD-02-936

方法 A: 黄色固体 (260 mg, 79%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 10.31 (s, 1H), 8.19 (d, J = 9.0 Hz, 1H), 8.03 (d, J = 9.0 Hz, 1H), 7.78 (t, J = 2.9 Hz, 1H), 7.47 (t, J = 1.5 Hz, 1H), 7.41 (dd, J = 8.3, 2.4 Hz, 1H), 7.29 (d, J = 2.5 Hz, 1H), 7.10 (d, J = 8.3 Hz, 1H), 3.54 (t, J = 6.4 Hz, 2H), 2.82 (t, J = 6.2 Hz, 2H), 2.06 - 1.97 (m, 2H), 1.78 (qd, J = 6.2, 3.0 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 158.45, 154.02, 150.34, 133.74, 132.54, 129.76, 129.19,127.02,124.97,122.99,122.46,121.27,119.85,115.10,113.79,106.76,31.34, 28.25,22.01,21.65,16.42;$C_{22}H_{21}N_2O[M+H]^+$的HRMS(ESI)m/z计算值329.1653,实测值329.1645。

[0269] 2-氯-4-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯酚

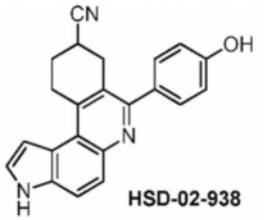
[0270] 

HSD-02-937

方法A：黄色固体 (226 mg, 65%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 11.74 (s, 1H), 7.77 (dd, J = 8.9, 0.7 Hz, 1H), 7.62 (d, J = 8.8 Hz, 1H), 7.50 (d, J = 2.1 Hz, 1H), 7.48 (t, J = 2.6 Hz, 1H), 7.34 (dd, J = 8.3, 2.1 Hz, 1H), 7.13 - 7.10 (m, 1H), 7.04 (d, J = 8.3 Hz, 1H), 3.37 (d, J = 6.6 Hz, 2H), 2.78 (t, J = 6.1 Hz, 2H), 1.97 (pd, J = 6.1, 2.6 Hz, 2H), 1.77 - 1.68 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ

[0271] 154.51,153.28,143.38,142.36,133.59,133.20,130.91,129.36,127.54,124.08,123.92,122.39,120.33,119.60,116.47,116.41,106.27,29.99,29.17,22.87,22.60；$C_{21}H_{18}ClN_2O[M+H]^+$的HRMS(ESI)m/z计算值349.1107,实测值349.1112。

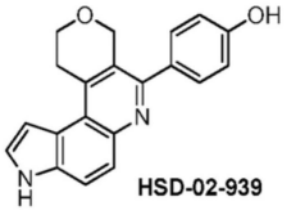
[0272] 7-(4-羟基苯基)-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-9-腈

[0273] 

HSD-02-938

方法A：黄色固体 (190 mg, 56%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 10.46 (s, 1H), 8.21 (d, J = 8.9 Hz, 1H), 8.05 (d, J = 9.0 Hz, 1H), 7.81 (s, 1H), 7.62 (d, J = 8.6 Hz, 2H), 7.29 (s, 1H), 7.08 (d, J = 8.6 Hz, 2H), 3.63 (q, J = 5.8 Hz, 2H), 3.40 - 3.36 (m, OH), 3.17 (qd, J = 16.6, 6.4 Hz, 2H), 2.42 - 2.35 (m, 1H), 2.32 - 2.24 (m, 1H); ^{13}C NMR (126 MHz, DMSO) δ 160.52, 151.84, 150.21, 134.27, 133.81, 132.07, 127.33, 126.12, 122.49, 122.38, 122.15, 121.66, 119.70, 116.10, 114.00,106.64,30.73,29.32,24.59,23.97；$C_{22}H_{18}N_3O[M+H]^+$的HRMS(ESI)m/z计算值340.1449,实测值340.1445。

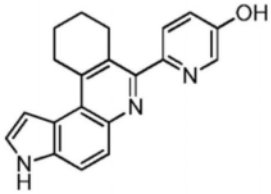
[0274] 4-(1,2,4,9-四氢吡喃并[3,4-c]吡咯并[3,2-f]喹啉-5-基)苯酚

[0275] 

HSD-02-939

方法A：黄色固体 (193 mg, 61%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 10.36 (s, 1H), 8.22 (d, J = 9.0 Hz, 1H), 8.03 (d, J = 9.0 Hz, 1H), 7.81 (t, J = 2.9 Hz, 1H), 7.59 (d, J = 8.5 Hz, 2H), 7.30 (t, 7= 2.4 Hz, 1H), 7.03 (d, J = 8.5 Hz, 2H), 4.17 (t, J = 5.7 Hz, 2H), 3.61 (t, 7= 5.8 Hz, 2H), 3.42 (s, 2H); ^{13}C NMR (126 MHz, DMSO) δ 159.90, 149.19, 133.51, 132.49, 131.49, 130.87, 127.07, 126.51, 122.13, 120.36, 119.93, 116.30, 115.93, 115.62, 105.92, 66.43, 64.15, 29.76；$C_{20}H_{17}N_2O_2[M+H]^+$的HRMS(ESI)m/z计算值317.1290,实测值317.1290。

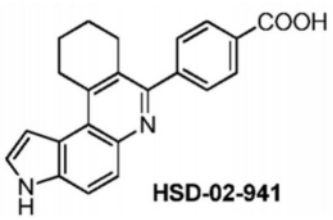
[0276] 6-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)吡啶-3-醇

[0277] 

ND-02-940

方法A：黄色固体 (98 mg, 31%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 11.74 (s, 1H), 10.03 (s, 1H), 8.18 (d, J = 2.8 Hz, 1H), 7.77 (d, J = 8.9 Hz, 1H), 7.64 (dd, J = 12.0, 8.7 Hz, 2H), 7.49 (t, J = 2.8 Hz, 1H), 7.29 (dd, J = 8.5, 2.9 Hz, 1H), 7.12 (d, J = 2.5 Hz, 1H), 3.40 - 3.35 (m, 2H), 2.95 (t, J = 6.3 Hz 2H), 1.96 - 1.92 (M, 2H), 1.78 - 1.69 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 153.80, 153.32, 151.06, 142.98, 142.40, 136.29, 133.31, 128.21, 125.55, 124.11, 123.92, 123.07, 122.67, 120.36, 116.37, 106.28, 30.10, 28.50, 22.89, 22.51; $C_{20}H_{18}N_3O[M+H]^+$的HRMS(ESI)m/z计算值316.1450,实测值316.1453。

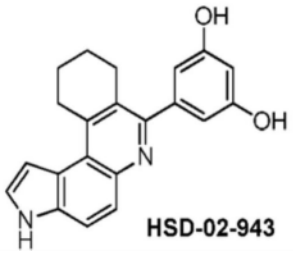
[0278] 4-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯甲酸

[0279] 

HSD-02-941

方法A：黄色固体 (212 mg, 62%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 8.17 (d, J = 8.1 Hz, 2H), 7.87 (d, J = 8.9 Hz, 1H), 7.73 (d, J = 8.9 Hz, 1H), 7.62 (d, J = 8.1 Hz, 2H), 7.49 (d, J = 3.1 Hz, 1H), 7.24 (d, J = 3.2 Hz, 1H), 3.53 (t, J = 6.5 Hz, 2H), 2.76 (t, J = 6.2 Hz, 2H), 2.11 - 2.04 (m, 2H), 1.88 - 1.79 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 153.85, 146.36, 142.90, 140.67, 133.41, 132.50, 129.30, 128.80, 127.65, 123.56, 123.12, 120.18, 119.96,117.15,105.96,47.93,30.20,28.28,22.22,21.85；$C_{22}H_{19}N_2O_2[M+H]^+$的HRMS(ESI)m/z计算值343.1446,实测值343.1438。

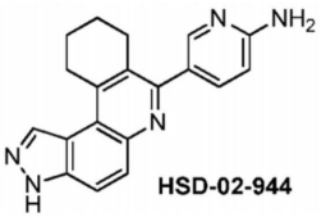
[0280] 5-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯-1,3-二醇

[0281] 

HSD-02-943

方法A: 黄色固体 (231 mg, 70%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 9.96 (s, 2H), 8.20 (d, J = 8.9 Hz, 1H), 7.96 (d J, = 9.0 Hz, 1H), 7.80 (s, 1H), 7.31 (d, J = 2.4 Hz, 1H), 6.59 - 6.47 (m, 3H), 3.54 (t, J = 6.5 Hz, 2H), 2.77 (t, J = 6.2 Hz, 2H), 2.05 - 1.97 (m, 2H), 1.82 - 1.77 (m, 2H). ^{13}C NMR (126 MHz, DMSO) δ 159.29, 154.49, 149.99, 133.76, 129.45, 127.13, 123.34, 121.54, 119.85, 113.69, 107.84, 106.82, 104.94, 40.48, 40.31, 40.14, 39.98, 39.81, 39.64, 39.48, 31.31, 27.91, 21.94, 21.44; $C_{21}H_{19}N_2O_2$ [M + H]$^+$的 HRMS (ESI)m/z计算值331.1446,实测值331.1450。

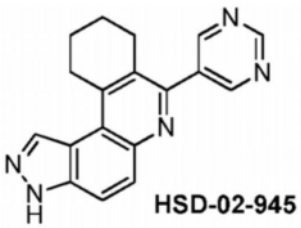
[0282] 5-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)吡啶-2-胺

[0283] 

HSD-02-944

方法A: 黄色固体 (205 mg, 65%)。^{1}H NMR (500 MHz, 甲醇-d_4) 5 8.51 (s, 1H), 8.16 (d, J = 2.1 Hz, 1H), 8.14 (dd, J = 9.0, 2.2 Hz, 1H), 7.88 (d, J = 9.1 Hz, 1H), 7.83 (d, J = 9.2 Hz, 1H), 7.09 (d, J = 9.0 Hz, 1H), 3.26 (t, J = 6.6 Hz, 2H), 2.87 (t, J = 6.1 Hz, 2H), 2.06 (ddt, J = 9.2, 6.5, 3.2 Hz, 2H), 1.86 (dp, J= 9.3, 3.1 Hz, 2H); ^{13}C NMR (126 MHz, MeOD) δ 155.32, 150.42, 145.84, 143.67, 143.48, 141.93, 138.13, 130.19, 126.90, 123.86, 122.70,119.27,115.60,111.95,29.80,28.11,21.86,21.86;$C_{19}H_{18}N_5$[M+H]$^+$的HRMS(ESI) m/z计算值316.1562,实测值316.1555.

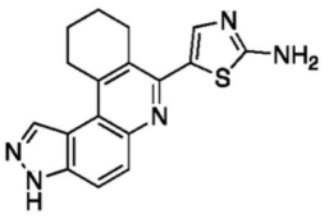
[0284] 7-(嘧啶-5-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0285] 

HSD-02-945

方法A: 黄色固体 (144 mg, 48%)。^{1}H NMR (500 MHz, DMSO-d_6) δ ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.26 (s, 1H), 9.07 (s, 2H), 8.55 (s, 1H), 7.89 (d, J =9.0 Hz, 1H), 7.84 (d, J = 11.9 Hz, 2H), 3.31 (s, 4H), 2.84 (t, J = 6.1 Hz, 2H), 2.03 - 1.94 (m, 2H), 1.80 - 1.71 (m, 2H);^{13}C NMR (126 MHz, DMSO) δ 158.00, 157.25, 150.89, 143.91, 142.97, 138.83, 136.49, 134.77, 129.84, 129.50, 122.42, 116.25, 114.94, 29.62, 28.44, 22.43, 22.38; $C_{19}H_{17}N_4$ [M + H]$^+$的HRMS(ESI)m/z计算值301.1453,实测值301.1457。

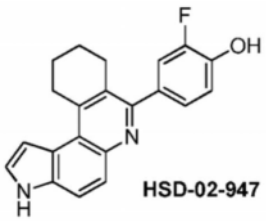
[0286] 5-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)噻唑-2-胺

[0287] 

HSD-02-946

方法A: 黄色固体 (166 mg, 52%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.50 (s, 1H), 7.79 (d, J = 9.1 Hz, 1H), 7.66 (d, J = 9.4 Hz, 1H), 7.51 (s, 1H), 7.23 (s, 2H), 3.28 - 3.22 (m, 2H), 2.96 (t, J = 6.2 Hz, 2H), 1.99 - 1.93 (m, 2H), 1.90 - 1.82 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 170.46, 148.47, 143.26, 142.39, 140.03, 138.39, 136.08, 129.21, 128.99, 128.03, 120.39, 116.44, 114.43, 29.95, 28.90, 22.52, 22.24; $C_{17}H_{16}N_5S$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 322.1126, 实测值 322.1127。

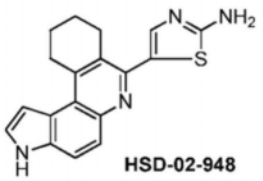
[0288] 2-氟-4-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯酚

[0289] 

HSD-02-947

方法A: 黄色固体 (196 mg, 59%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 11.75 (s, 2H), 7.85 - 7.71 (m, 2H), 7.67 - 7.56 (m, 2H), 7.48 (t, J = 2.8 Hz, 1H), 7.10 (t, J = 2.4 Hz, 1H), 6.40 (d, J = 9.4 Hz, 1H), 3.35 (t, J = 6.6 Hz, 2H), 2.84 (t, J = 6.1 Hz, 2H), 1.97 (td, J = 8.6, 7.2, 4.5 Hz, 2H), 1.75 (tq, J = 8.5, 5.4, 3.9 Hz, 2H). ^{13}C NMR (126 MHz, DMSO) δ 162.16, 151.74, 143.46, 142.97, 142.51, 136.05, 133.19, 127.71, 123.97, 122.39, 120.28, 119.30, 116.56, 106.27, 30.00, 28.90, 22.83, 22.63; $C_{21}H_{18}FN_2O$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 333.1405, 实测值333.1403。

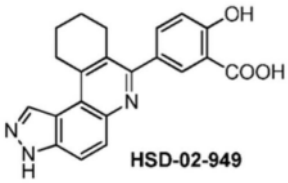
[0290] 5-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)噻唑-2-胺

[0291] 

HSD-02-948

方法 A: 黄色固体 (112 mg, 35%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 12.21 (s, 1H), 8.12 (d, J = 9.0 Hz, 1H), 8.04 - 7.94 (m, 1H), 7.56 - 7.50 (m, 2H), 6.96 (s, 1H), 5.98 (t, J = 2.4 Hz, 1H), 3.29 (t, J = 6.4 Hz, 2H), 2.84 (s, 2H), 1.96 - 1.88 (m, 2H), 1.83 (q, J = 6.0, 5.3 Hz, 2H); $C_{18}H_{17}N_4S$ $[M + H]^+$ 的 HRMS (ESI) m/z 计算值 321.1174, 实测值 321.1177。

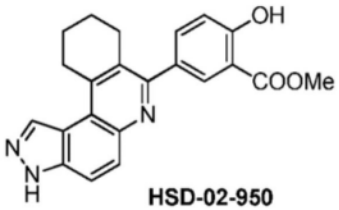
[0292] 2-羟基-5-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯甲酸

[0293] 

HSD-02-949

方法 A: 黄色固体 (187 mg, 52%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 10.10 (s, 1H), 8.67 (s, 1H), 8.09 (d, J = 9.8 Hz, 4H), 3.38 - 3.31 (m, 2H), 2.78 (t, J = 6.2 Hz, 2H), 2.06 - 1.93 (m, 2H), 1.83 - 1.72 (m, 2H); $C_{21}H_{18}N_3O_3$ $[M + H]^+$的 HRMS (ESI) m/z 计算值 360.1348, 实测值 360.1351。

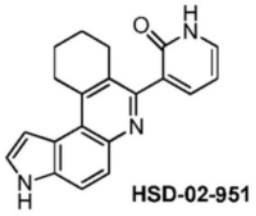
[0294] 2-羟基-5-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯甲酸甲酯

[0295] 

HSD-02-950

方法 A: 白色固体 (208 mg, 56%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 10.93 (s, 1H), 8.73 (s, 1H), 8.20 - 8.12 (m, 2H), 8.09 (d, J = 2.3 Hz, 1H), 7.87 (dd, J = 8.6, 2.4 Hz, 1H), 7.24 (d, J = 8.6 Hz, 1H), 3.89 (S, 3H) 3.40 (td, J = 6.9, 4.0 Hz, 2H), 2.78 (t, J = 6.1 Hz, 2H), 2.06 - 1.91 (m, 2H), 1.77 (tt, J = 8.9, 5.5 Hz, 2H). ^{13}C NMR (126 MHz, DMSO) δ 168.54, 168.54, 168.32, 161.15, 151.10, 150.72, 136.76, 132.49, 132.29, 131.52, 124.82,122.96,121.86,118.10,117.86,115.02,114.60,53.03,30.66,28.23,21.85, 21.79;$C_{22}H_{20}N_3O_3$[M+H]$^+$的HRMS(ESI)m/z计算值374.1505,实测值374.1508。

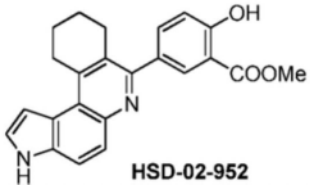
[0296] 3-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)吡啶-2(1H)-酮

[0297] 

HSD-02-951

方法 A: 黄色固体 (204 mg, 65%)。黄色固体 (217 mg, 70%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 11.76 (s, 1H), 7.80 - 7.72 (m, 2H), 7.64 - 7.58 (m, 2H), 7.48 (t, J = 2.7 Hz, 1H), 7.10 (t, J = 2.3 Hz, 1H), 6.41 (d, J = 9.4 Hz, 1H), 3.36 (d, J = 6.6 = Hz, 2H), 2.84 (t, J = 6.2 Hz, 2H), 2.02 - 1.94 (m, 2H), 1.75 (dp, J = 9.3, 3.4, 2.9 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 162.19, 151.74, 143.47, 142.98, 142.52, 136.07, 133.20, 127.72, 123.98, 122.40, 120.30, 119.29, 116.56, 106.28, 30.01,28.91,22.83,22.63;$C_{20}H_{18}N_3O$[M+H]$^+$的HRMS(ESI)m/z计算值316.1450,实测值316.1459。

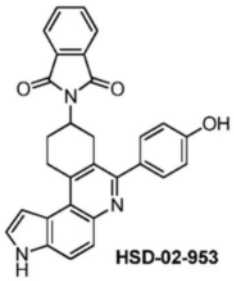
[0298] 2-羟基-5-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯甲酸甲酯

[0299] 

HSD-02-952

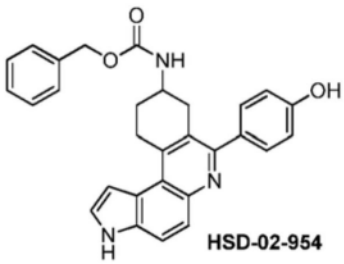
方法 A: 白色固体 (189 mg, 51%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.01 (d, J = 2.3 Hz, 1H), 7.79 (d, J = 8.9 Hz, 1H), 7.71 (d, J = 8.8 Hz, 1H), 7.66 (dt, J = 8.5, 2.1 Hz, 1H), 7.43 (d, J = 3.1 Hz, 1H), 7.20 (d, J = 3.2 Hz, 1H), 7.09 (dd, J = 8.3, 2.4 Hz, 1H), 3.96 (s, 3H), 3.49 (t, J = 6.5 Hz, 2H), 2.77 (t, J = 6.2 Hz, 2H), 2.11 - 2.03 (m, 2H), 1.83 (dp, 9.4, 3.0 Hz, 2H); ^{13}C NMR (126MHz,MeOD)δ170.24,161.08,154.60,143.93,142.64,136.22,133.26,132.11,130.33, 127.42,122.82,121.91,120.24,116.86,116.03,111.93,105.77,51.58,48.10,29.95, 28.67,22.45,22.16;$C_{23}H_{21}N_2O_3$[M+H]$^+$的HRMS(ESI)m/z计算值373.1552,实测值373.1557。

[0300] 2-(7-(4-羟基苯基)-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-9-基)异吲哚啉-1,3-二酮12.11

[0301] 

方法 A: 黄色固体 (197 mg, 43%)。 ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.85 (s, 1H), 7.81 (tt, J = 4.4, 1.9 Hz, 5H), 7.64 (d, J = 8.9 Hz, 1H), 7.50 (d, J = 3.1 Hz, 1H), 7.37 - 7.29 (m, 2H), 7.12 (d, J = 3 J.3 = Hz, 1H), 6.85 - 6.78 (m, 2H), 4.44 - 4.33 (m, 1H), 3.78 - 3.69 (m, 1H), 3.69 - 3.57 (m, 1H), 3.54 - 3.44 (m, 1H), 2.89 - 2.81 (m, 1H), 2.79 - 2.68 (m, 1H), 2.34 - 2.26 (m, 1H); ^{13}C NMR (126 MHz, DMSO) δ 168.40, 157.71, 155.84, 143.60, 141.02, 134.77, 133.23, 132.00, 130.64, 125.66, 124.08, 123.99, 123.38, 121.75, 120.41, 116.72, 115.24, 106.26, 47.58, 32.31, 30.31, 26.40; $C_{29}H_{22}N_3O_3$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 460.1661, 实测值460.1665。

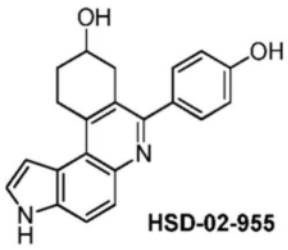
[0302] 苄基(7-(4-羟基苯基)-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-9-基)氨基甲酸酯

[0303] 

方法 A: 黄色固体 (240 mg, 52%)。 ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.46 (s, 1H), 8.20 (d, J = 9.0 Hz, 1H), 8.07 (d, J = 8.9 Hz, 1H), 7.78 (d, J = 3.0 Hz, 1H), 7.55 (d, J = 8.4 Hz, 2H), 7.37 - 7.19 (m, 6H), 7.08 (s, 1H), 4.97 (d, J = 3.2 Hz, 2H), 3.84 (t, J = 7.4 Hz, 1H), 3.69 (dt, J = 19.6, 5.6 Hz, 1H), 3.56 (dt, 7 = 19.2, 7.4 Hz, 1H), 3.01 (dd, J = 16.9, 4.6 Hz, 1H), 2.81 (dd, J = 16.6, 8.4 Hz, 1H), 2.31 - 2.18 (m, 1H), 2.06 - 1.95 (m, 1H). ^{13}C NMR (126 MHz, DMSO) δ 160.39, 156.05, 153.02, 150.33,

[0304] 137.46,133.91,133.75,131.95,128.79,128.27,127.75,127.12,122.61,122.34,121.41,119.89,116.02,113.72,106.77,65.77,45.47,33.92,29.80,27.29; $C_{29}H_{26}N_3O_3$[M+H]$^+$的HRMS(ESI)m/z计算值4,64.1974实测值464.1970。

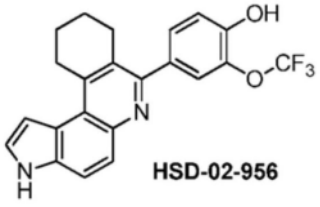
[0305] 7-(4-羟基苯基)-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-9-醇

[0306] 

方法 A: 黄色固体 (172 mg, 52%)。 ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.43 (s, 1H), 8.19 (d, J = 8.9 Hz, 1H), 8.04 (d, J = 8.9 Hz, 1H), 7.78 (t, J = 2.9 Hz, 1H), 7.65 - 7.51 (m, 2H), 7.29 (t, J = 2.4 Hz, 1H), 7.12 - 7.00 (m, 2H), 4.05 (tt, J = 7.0, 3.1 Hz, 1H), 3.70 - 3.60 (m, 1H), 3.52 (dt, J = 19.2, 6.8 Hz, 1H), 2.99 (dd, J = 16.6, 4.1 Hz, 1H), 2.75 (dd, J = 16.6, 6.7 Hz, 1H), 2.19 - 2.09 (m, 1H), 1.99 (dq, J = 13.9, 7.0 Hz, 1H). ^{13}C NMR (126 MHz, DMSO) δ 160.37, 153.53, 150.30, 133.89, 133.72, 132.01, 127.94, 127.08, 122.53, 121.38,

119.84,115.99,113.73,106.74,63.25,36.67,29.46,29.03;$C_{21}H_{19}N_2O_2$[M+H]$^+$的HRMS(ESI)m/z计算值331.1447,实测值331.1452。

[0307] 4-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)-2-(三氟甲基)苯酚

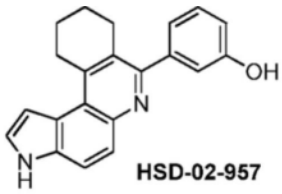
[0308] 

方法 A: 灰白色固体 (242 mg, 61%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 11.16 (s, 1H), 8.22 (d, J = 8.9 Hz, 1H), 8.01 (d, J = 9.0 Hz, 1H), 7.86 - 7.75 (m, 2H), 7.60 (dd, J = 8.4, 2.2 Hz, 1H), 7.41 - 7.29 (m, 2H), 3.57 (t, J = 6.4 Hz, 2H), 2.79 (t, J = 6.2 Hz, 2H), 2.09 - 1.97 (m, 2H), 1.83 - 1.76 (m, 2H). ^{13}C NMR (126 MHz, DMSO) δ 152.73, 148.65, 136.08, 134.20, 133.76, 130.85, 129.77, 126.94, 125.54, 123.93 (q, J = 257 Hz), 123.31,

121.29,119.80,118.25,114.31,106.81,,31.29,28.01,21.96,21.63;$C_{22}H_{18}F_3N_2O$[M+H]$^+$的HRMS(ESI)m/z计算值399.1320,实测值399.1321。

[0309] 3-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯酚

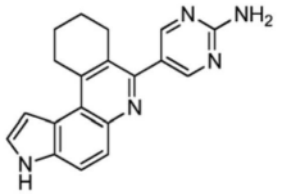
[0310] 方法A:黄色固体(188mg,60%)。^{1}H NMR(500MHz,DMSO-d_6)δ10.28(s,1H),8.17(d,J=8.9Hz,1H),7.97(d,J=8.9Hz,1H),7.77(t,J=2.9Hz,1H),7.43(t,J=7.9Hz,1H),7.27-

[0311] 

HSD-02-957

7.16 (m, 2H), 7.09 (td, J = 5.2, 2.2 Hz, 2H), 3.45 (t, J = 6.5 Hz, 2H), 2.73 (t, J = 6.2 Hz, 2H), 2.03 - 1.95 (m, 2H), 1.81 - 1.72 (m, 2H). ^{13}C NMR (126 MHz, DMSO) δ 158.18, 154.01, 149.81, 133.69, 130.40, 129.35, 126.95, 123.26, 121.30, 120.36, 119.72, 118.04, 116.76, 113.98, 106.74, 31.22, 27.99, 21.92, 21.47; $C_{21}H_{19}N_2O$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 315.1497, 实测值 315.1499。

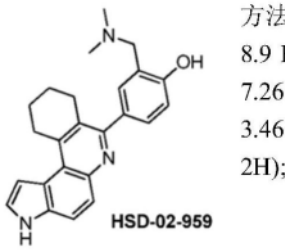
[0312] 5-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)嘧啶-2-胺

[0313] 

ND-02-958

方法 A: 浅黄色固体 (185 mg, 59%)。 ^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.07 (dd, J = 2.4, 0.9 Hz, 1H), 7.77 (dd, J = 8.9, 0.9 Hz, 1H), 7.69 (d, J = 8.9 Hz, 1H), 7.63 (dd, J = 8.5, 2.4 Hz, 1H), 7.40 (d, J = 3.1 Hz, 1H), 7.14 (dd, J = 3.2, 0.9 Hz, 1H), 6.70 (dd, J = 8.5, 0.8 Hz, 1H), 3.42 (t, J = 6.4 Hz, 2H), 2.78 (t, J = 6.2 Hz, 2H), 2.05 - 1.96 (m, 2H), 1.83 - 1.75 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 163.22, 158.63, 158.15, 152.27, 144.04, 142.51, 134.14, 129.66, 129.58, 123.56, 123.39, 121.80, 116.22, 29.69, 28.81, 22.63, 22.56; $C_{19}H_{18}N_5$[M+H]$^+$的HRMS(ESI)m/z计算值316.1562,实测值316.1565。

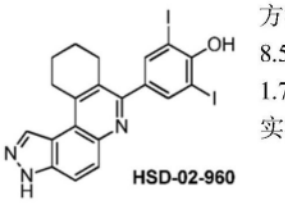
[0314] 2-((二甲氨基)甲基)-4-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯酚

[0315] 

HSD-02-959

方法 A: 浅黄色固体 (170 mg, 46%)。 ^{1}H NMR (500 MHz, 甲醇- d_4) δ 7.77 (d, J = 8.9 Hz, 1H), 7.69 (d, J = 9.0 Hz, 1H), 7.41 (s, 1H), 7.33 (dd, J = 8.2, 2.2 Hz, 1H), 7.26 (d, J = 2.2 Hz, 1H), 7.19 - 7.15 (m, 1H), 6.92 (d, J = 8.2 Hz, 1H), 3.88 (s, 2H), 3.46 (t, J = 6.5 Hz, 2H), 2.75 (t, J = 6.2 Hz, 2H), 2.05 - 2.01 (m, 2H), 1.82 - 1.76 (m, 2H); $C_{24}H_{26}N_3O$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 372.2076, 实测值 372.2082。

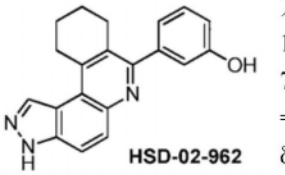
[0316] 2,6-二碘-4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0317] 

HSD-02-960

方法 A: 黄色固体 (272 mg, 48%)。 ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.79 (s, 1H), 8.57 (s, 1H), 7.94 (s, 2H), 7.92 - 7.78 (m, 3H), 3.29 (s, 2H), 2.03 - 1.95 (m, 2H), 1.78 - 1.70 (m, 2H); $C_{20}H_{16}I_2N_3O$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 567.9383, 实测值 567.9388。

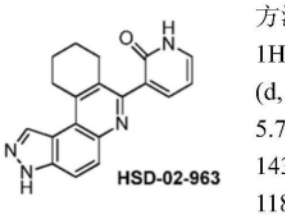
[0318] 3-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0319] 

HSD-02-962

方法 A: 白色固体 (195 mg, 62%)。 ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.18 (s, 1H), 8.72 (s, 1H), 8.13 (dd, J = 37.4, 8.8 Hz, 2H), 7.42 (t, J = 7.9 Hz, 1H), 7.17 - 7.03 (m, 3H), 3.37 (q, J = 8 J.2 =, 6.3 Hz, 2H), 2.75 (t, J = 6.2 Hz, 2H), 2.00 (p, J = 6.5, 6.1 Hz, 2H), 1.76 (dd, J = 11.3, 5.9 Hz, 2H). ^{13}C NMR (126 MHz, DMSO) δ 158.08, 152.26, 151.41, 135.68, 134.33, 131.45, 130.29, 123.05, 120.90, 120.40, 117.83,116.79,114.86,30.73,28.07,21.77,21.59;$C_{19}H_{18}N_5$[M+H]$^+$的HRMS(ESI)m/z计算值316.1562,实测值316.1555。

[0320] 3-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)吡啶-2(1H)-酮

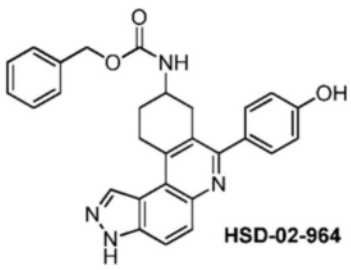
[0321] 

HSD-02-963

方法 A: 灰白色固体 (214 mg, 67%)。 ^{1}H NMR (500 MHz, DMSO- d_6) δ 8.53 (s, 1H), 7.83 (d, J = J9. =0 Hz, 1H), 7.81 - 7.73 (m, 2H), 7.65 (d, J = 2.7 Hz, 1H), 6.42 (d, J = 9.4 Hz, 1H), 3.25 (t, J = 6.5 Hz, 2H), 2.84 (t, J = 6.0 Hz, 2H), 1.97 (dq, 8.4, 5.7 Hz, 2H), 1.78 - 1.69 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 162.24, 152.74, 143.82, 142.86, 142.53, 140.86, 139.70, 136.38, 134.04, 129.50, 121.76, 119.36, 118.81, 116.19, 115.37, 29.69, 28.79, 22.61, 22.55; $C_{19}H_{17}N_4O$ [M + H]$^+$的 HRMS

(ESI)m/z计算值317.1402,实测值317.1411。

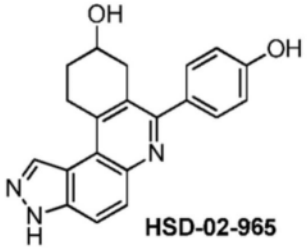
[0322] 苄基(7-(4-羟基苯基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-9-基)氨基甲酸酯

[0323] 

HSD-02-964

方法A: 灰白色固体 (241 mg, 52%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.66 (d, J = 9.1 Hz, 1H), 8.08 (dd, J = 9.2, 6.3 Hz, 1H), 7.93 (dd, J = 9.3, 5.3 Hz, 1H), 7.50 (d, J = 8.2 Hz, 2H), 7.29 - 7.20 (m, 5H), 7.02 (d, J = 8.2 Hz, 2H), 5.01 (s, 2H), 3.97 - 3.84 (m, 1H), 3.67 - 3.56 (m, 1H), 3.54 - 3.41 (m, 1H), 3.18 - 3.08 (m, 1H), 2.95 - 2.82 (m, 1H), 2.42 - 2.29 (m, 1H), 2.11 - 2.01 (m, 1H). ^{13}C NMR (126 MHz, MeOD) δ 161.72, 159.87, 156.89, 152.70, 150.63, 139.58, 136.84, 136.35, 130.82, 129.46, 128.03, 127.56, 127.34, 123.73, 122.33, 120.83, 119.33,118.00,115.47,114.97,66.04,48.13,48.08,47.96,47.79,47.62,47.45,47.28,47.11,45.66,33.71,29.28,26.87;$C_{28}H_{25}N_4O_3$[M+H]$^+$的HRMS(ESI)m/z计算值465.1927,实测值465.1927。

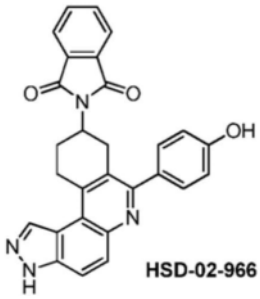
[0324] 7-(4-羟基苯基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-9-醇

[0325] 

HSD-02-965

方法A: 灰白色固体 (211 mg, 64%)。 ^{1}H NMR (500 MHz, DMSO- d_6) δ 9.87 (s, 1H), 8.57 (s, 1H), 7.97 - 7.80 (m, 2H), 7.45 (d, J = 8.1 Hz, 2H), 6.93 (d, J = 8.1 Hz, 2H), 4.92 (s, 1H), 3.95 (tt, J = 7.8, 3.3 Hz, 1H), 3.41 (dt, J = 20.7, 4.7 Hz, 1H), 3.27 (p, J = 7.1 Hz, 1H), 2.96 (dd, J = 16.6, 4.2 Hz, 1H), 2.74 (dd, J = 16.5, 7.4 Hz, 1H), 2.13 (dt, J = 13.1, 6.2 Hz, 1H), 1.90 (dq, J = 15.0, 7.8 Hz, 1H).^{13}C NMR (126 MHz, DMSO) δ 158.44, 155.40, 144.50, 141.23, 138.96, 136.06, 131.24, 129.27, 128.15, 126.83, 121.32, 115.90, 115.38,64.42,37.63,30.18,28.16;$C_{20}H_{18}N_3O_2$[M+H]$^+$的HRMS(ESI)m/z计算值332.1399,实测值332.1402。

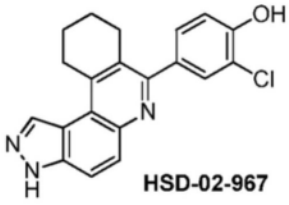
[0326] 2-(7-(4-羟基苯基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-9-基)异吲哚啉-1,3-二酮

[0327] 

HSD-02-966

方法A: 灰白色固体 (239 mg, 52%)。 ^{1}H NMR (500 MHz, DMSO- d_6) δ 9.56 (s, 1H), 8.57 (s, 1H), 7.89 - 7.84 (m, 2H), 7.83 - 7.78 (m, 4H), 7.36 (d, J = 8.6 Hz, 1H), 6.82 (d, J = 8.6 Hz, 1H), 4.45 - 4.33 (m, 1H), 3.73 - 3.59 (m, 2H), 3.53 - 3.39 (m, 1H), 2.92 - 2.85 (m, 1H), 2.82 - 2.69 (m, 1H), 2.36 - 2.26 (m, 1H); ^{13}C NMR (126 MHz, DMSO) δ 168.38, 157.66, 156.88, 143.84, 141.13, 138.66, 136.38, 134.76, 132.01, 131.67, 130.75, 129.58, 127.50, 123.38, 121.10, 116.54, 115.25, 114.60, 47.46, 32.19, 31.15, 26.15; $C_{28}H_{21}N_4O_3$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 461.1614, 实测值 461.1619。

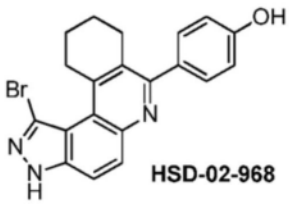
[0328] 2-氯-4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0329] 

HSD-02-967

方法A: 灰白色固体 (191 mg, 55%)。 ^{1}H NMR (500 MHz, DMSO- d_6) δ 11.20 (s, 1H), 8.74 (s, 1H), 8.25 - 8.12 (m, 2H), 7.80 (d, J = 2.1 Hz, 1H), 7.56 (dd, J = 8.4, 2.2 Hz, 1H), 7.30 (d, J = 8 J.4 = Hz, 1H), 3.40 (d, J = 6.7 Hz, 2H), 2.81 (t, J = 6.1 Hz, 2H), 2.07 - 1.98 (m, 2H), 1.81 - 1.75 (m, 2H). ^{13}C NMR (126 MHz, DMSO) δ 155.92, 152.58, 149.60, 135.00, 131.94, 131.83, 130.50, 123.67, 122.81, 120.32, 120.19, 116.98, 114.53, 30.78, 28.06, 21.65,21.61;$C_{20}H_{17}ClN_3O$[M+H]$^+$的HRMS(ESI)m/z计算值350.1060,实测值350.1066。

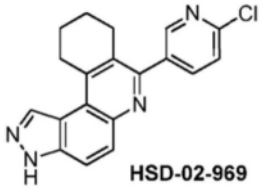
[0330] 4-(1-溴-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0331] 

HSD-02-968

方法A：黄色固体 (110 mg, 28%)。灰白色固体 (153 mg, 39%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.18 (d, J = 9.1 Hz, 1H), 8.06 (d, J = 9.2 Hz, 1H), 7.57 (d, J = 8.3 Hz, 2H), 7.07 (d, J = 8.3 Hz, 2H), 3.99 (s, 2H), 2.97 (s, 2H), 1.97 (t, J = 3.5 Hz, 4H). ^{13}C NMR (126 MHz, MeOD) δ 160.37, 155.96, 151.79, 141.59, 135.37, 132.94, 130.83, 123.46, 121.93, 120.38, 119.36, 115.60, 114.56,36.01,27.02,20.91,20.80.^{13}C NMR(126MHz,MeOD)δ160.37,155.96,154.60,151.79,141.55,135.37,132.94,130.83,127.59,123.46,121.93,120.38,119.25,115.60,114.56,36.01,27.02,20.91,20.80;$C_{20}H_{17}BrN_3O$[M+H]$^+$的HRMS(ESI)m/z计算值394.0555,实测值394.0556。

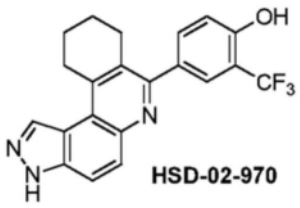
[0332] 7-(6-氯吡啶-3-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0333] 

HSD-02-969

方法A：白色固体 (210 mg, 63%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.69 (d, J = 2.4 Hz, 1H), 8.64 (s, 1H), 8.17 (dd, J = 8 J.2, 2.5 Hz, 1H), 8.02 - 7.91 (m, 2H), 7.70 (d, J = 8.2 Hz, 1H), 3.33 (t, J = 6.6 Hz, 2H), 2.78 (t, J = 6.2 Hz, 2H), 2.02 - 1.97 (m, 2H), 1.80 - 1.73 (m, 2H); $C_{19}H_{16}ClN_4$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 335.1063, 实测值 335.1063。

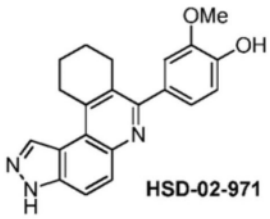
[0334] 4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)-2-(三氟甲基)苯酚

[0335] 

HSD-02-970

方法A：白色固体 (233 mg, 61%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 10.77 (s, 1H), 8.52 (s, 1H), 7.82 (d, J = 2.2 Hz, 2H), 7.72 - 7.64 (m, 2H), 7.12 (d, J = 8.3 Hz, 1H), 3.32 - 3.25 (m, 2H), 2.78 (t, J = 6.1 Hz, 2H), 2.02 - 1.92 (m, 2H), 1.77 - 1.67 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 155.93, 155.43, 143.63, 142.52, 138.66, 136.33, 134.92, 131.78, 129.60, 129.39, 127.78, 127.73, 125.63(q, J = 273.42 Hz), 121.78, 116.87, 116.43, 115.61(q, J＝30.24Hz),114.39,29.69,29.00,22.55;$C_{21}H_{17}F_3N_3O$[M+H]$^+$的HRMS(ESI)m/z计算值384.1324,实测值384.1329。

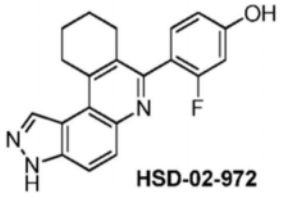
[0336] 2-甲氧基-4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0337] 

HSD-02-971

方法A：白色固体 (231 mg, 67%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 9.57 (s, 1H), 8.63 (s, 1H), 8.03 (s, 2H), 7.24 (d, J = 2.1 Hz, 1H), 7.08 (dd, 8.0, 2.0 Hz, 1H), 6.98 (d, J = 8.0 Hz, 1H), 3.83 (s, 3H), 3.35 (s, 2H), 2.82 (t, J = 6.2 Hz, 2H), 2.04 - 1.98 (m, 2H), 1.79 - 1.71 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 148.62, 147.81, 138.57, 135.55, 131.11, 126.48, 123.12, 122.31, 115.71, 114.34, 56.35, 30.47, 28.55, 22.05; $C_{21}H_{20}N_3O_2$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 346.1556,实测值346.1562。

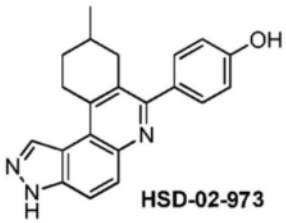
[0338] 3-氟-4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0339] 

HSD-02-972

方法A：白色固体 (186 mg, 56%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.57 (s, 1H), 7.84 (dd, J = 9.0, 0.9 Hz, 1H), 7.79 (d, J = 9.1 Hz, 1H), 7.22 (t, J = 8.6 Hz, 1H), 6.72 (dd, J = 8.3, 2.3 Hz, 1H), 6.66 (dd, J = 11.8, 2.3 Hz, 1H), 3.30 (t, J = 6.6 Hz, 2H), 2.61 (t, J = 6.0 Hz, 2H), 2.00 - 1.91 (m, 2H), 1.79 - 1.69 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 161.25 (J = 245.11 Hz), 159.59, 159.50, 152.73, 143.80, 142.04, 132.20, 132.16, 130.53, 129.53, 122.03, 119.48, 119.35,116.25,112.08,102.89,102.70,29.48,27.50,22.64,22.24;$C_{20}H_{17}FN_3O$[M+H]$^+$的HRMS(ESI)m/z计算值334.1356,实测值334.1360。

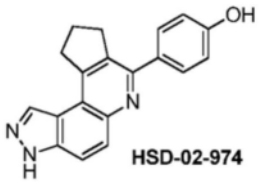
[0340] 4-(9-甲基-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0341] 

HSD-02-973

方法A: 灰白色固体 (223 mg, 68%)。 ^{1}H NMR (500 MHz, 甲醇 d_4) δ 8.81 (s, 1H), 8.22 (d, J = 9.3 Hz, 1H), 8.02 (d, J = 9.3 Hz, 1H), 7.58 (d d, J = 8.5, 1.9 Hz, 2H), 7.07 (dd, J = 8.6, 1.9 Hz, 2H), 3.75 - 3.68 (m, 1H), 3.56 (dt, j = 18.6, 8.3 Hz, 1H), 2.91 (dt, J = 17.3, 2.7 Hz, 1H), 2.65 (dd, J = 17.1, 10.6 Hz, 1H), 2.38 - 2.21 (m, 1H), 1.99 - 1.85 (m, 1H), 1.79 - 1.64 (m, 1H), 1.14 (dd, J = 6.5, 1.8 Hz, 3H); ^{13}C NMR (126 MHz, MeOD) δ 160.23, 153.67, 151.60, 134.75,132.00,130.90,124.14,123.00,123.00,122.62,121.61,119.36,119.08,116.55, 115.54,115.03,35.98,30.99,29.34,27.83,20.20;$C_{21}H_{20}N_3O$[M+H]$^+$的HRMS(ESI)m/z计算值330.1606,实测值330.1609。

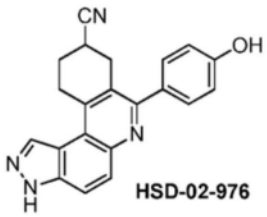
[0342] 4-(3,8,9,10-四氢环戊[c]吡唑并[4,3-f]喹啉-7-基)苯酚

[0343] 

HSD-02-974

方法A: 灰白色固体 (168 mg, 56%)。 ^{1}H NMR (500 MHz, DMSO- d_6) δ 8.42 (s, 1H), 7.85 (d, J = 9.2 Hz, 1H), 7.81 (dd, J = 9.1, 0.9 Hz, 1H), 7.74 (d, J = 8.6 Hz, 2H), 6.89 (d, J = 8.6 Hz, 2H), 3.41 (t, J = 7.6 Hz, 2H), 3.21 (t, J = 7.4 Hz, 2H), 2.21 (p, J = 7.6 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 158.20, 152.26, 149.32, 144.91, 135.59, 131.44, 130.38, 129.22, 118.73, 116.70, 115.46, 33.48, 33.40, 24.97; $O_{19}H_{16}N_3O$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 302.1293, 实测值302.1295。

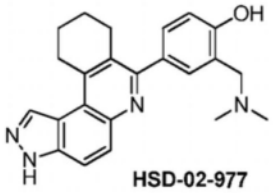
[0344] 7-(4-羟基苯基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-9-腈

[0345] 

HSD-02-976

方法A: 黄色固体 (207 mg, 61%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 10.41 (s, 1H), 8.76 (s, 1H), 8.21 (d, J = 9.2 Hz, 1H), 8.17 (d, J = 9.2 Hz, 1H), 7.62 (d, J = 8.2 Hz, 2H), 7.07 (d, J = 8.2 Hz, 2H), 3.58 - 3.48 (m, 2H), 3.45 - 3.36 (m, 1H), 3.28 - 3.12 (m, 2H), 2.43 - 2.34 (m, 1H), 2.34 2.24 (m, 1H). ^{13}C NMR (126 MHz, DMSO) δ 157.87, 156.56, 144.05, 140.61, 138.62, 136.16, 131.33, 130.95, 129.54, 125.63, 122.86, 120.97, 116.21, 115.29, 114.74, 31.73, 27.64, 25.08,24.57;$C_{21}H_{17}N_4O$[M+H]$^+$的HRMS(ESI)m/z计算值341.1402,实测值341.1410。

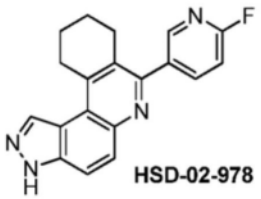
[0346] 2-((二甲氨基)甲基)-4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0347] 

HSD-02-977

方法A: 黄色固体 (148 mg, 40%)。 ^{1}H NMR (500 MHz, 甲醇- d_4) δ 8.63 (s, 1H), 7.92 (s, 2H), 7.61 - 7.55 (m, 2H), 7.12 (d, J = 8.1 Hz, 1H), 4.42 (s, 2H), 3.43 (d, J = 6.2 Hz, 2H), 2.93 (s, 6H), 2.85 (t, J = 6.2 Hz, 2H), 2.13-208 (m,2H), 1.91 - 1.82 (m,2H); $C_{23}H_{25}N_4O$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 373.2028, 实测值 373.2033。

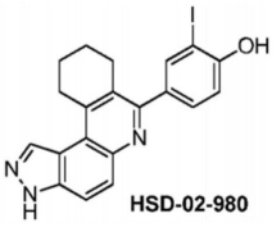
[0348] 7-(6-氟代吡啶-3-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0349] 

HSD-02-978

方法A: 浅黄色固体 (181 mg, 57%)。 ^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.51 (s, 1H), 8.40 (d, J = 2.4 Hz, 1H), 8.16 (td, J = 8.0, 2.5 Hz, 1H), 7.83 (s, 2H), 7.22 (dd, J = 8.4, 2.4 Hz, 1H), 3.27 (t, J = 6.6 Hz, 2H), 2.76 (t, J = 6.2 Hz, 2H), 2.09 - 2.02 (m, 2H), 1.86 - 1.78 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 164.30, 162.39, 152.26, 147.56, 147.45, 144.47, 142.82, 142.68, 142.61, 133.99, 129.83, 127.94, 122.52, 115.69, 108.96, 108.67, 29.58, 28.25, 21.91, 21.87; $C_{19}H_{16}FN_4$[M+H]$^+$的HRMS(ESI)m/z计算值319.1359,实测值319.1366。

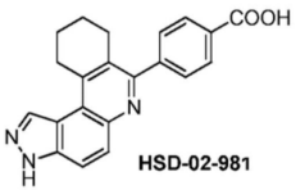
[0350] 2-碘-4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0351] 

HSD-02-980

方法A：白色固体 (198 mg, 45%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.87 (s, 1H), 8.28 (d, J = 9.2 Hz, 1H), 8.11 (d, J = 2.2 Hz, 1H), 8.06 (d, J = 9.2 Hz, 1H), 7.60 (dd, J = 8.4, 2.2 Hz, 1H), 7.10 (d, J = 8.4 Hz, 1H), 3.65 (t, J = 6.4 Hz, 2H), 2.95 (t, J = 6.2 Hz, 2H), 2.31 - 2.09 (m, 2H), 2.03 - 1.69 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 159.64, 154.77, 153.68, 149.57, 140.11, 134.50, 132.47, 130.75, 129.17, 123.97, 123.61, 118.95, 114.86, 114.28, 109.63, 83.68, 30.98, 27.82,21.28,21.20;$C_{20}H_{17}IN_3O$[M+H]的HRMS(ESI)m/z计算值442.0416,实测值442.0416。

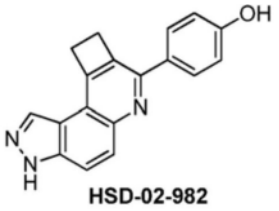
[0352] 4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯甲酸

[0353] 

HSD-02-981

方法A：黄色固体 (172 mg, 50%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 8.62 (s, 1H), 8.12 - 8.08 (m, 2H), 8.02 (d, J = 9.1 Hz, 1H), 7.95 (d, J = 9.1 Hz, 1H), 7.80 - 7.73 (m, 2H), 3.29 (t, J = 6.5 Hz, 2H), 2.75 2.68 (m, 2H), 2.00 - 1.94 (m, 2H), 1.76 - 1.66 (m, 2H). ^{13}C NMR (126 MHz, DMSO) δ 167.42, 152.75, 148.00, 140.96, 139.42, 135.00, 131.73, 130.39, 130.19, 129.66, 129.59, 124.86,122.74,118.09,115.38,30.20,28.32,22.04,21.92;$C_{21}H_{18}N_3O_2$[M+H]$^+$的HRMS(ESI)m/z计算值344.1399,实测值344.1401。

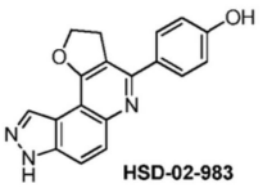
[0354] 4-(8,9-二氢-3H-环丁[c]吡唑并[4,3-f]喹啉-7-基)苯酚

[0355] 

HSD-02-982

方法A：灰白色固体 (152 mg, 53%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 9.80 (s, 1H), 8.32 (s, 1H), 8.01 (dd, J = 8.6, 1.4 Hz, 2H), 7.82 (d, J = 9.5 Hz, 1H), 7.78 (d, J = 9.1 Hz, 1H), 6.91 (dd, J = 8.6, 1.4 Hz, 2H), 3.73 - 3.64 (m, 2H), 3.62 - 3.54 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 159.12, 149.75, 148.04, 144.97, 137.96, 136.56, 134.42, 130.02, 129.03, 128.87, 116.88, 116.11, 115.24, 114.32, 32.33, 30.24; $C_{18}H_{14}N_3O$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值288.1137,实测值288.1139。

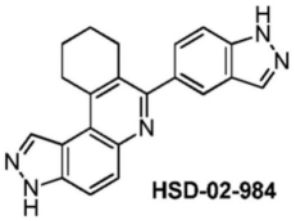
[0356] 4-(3,8-二氢-2H-呋喃并[3,2-c]吡唑并[4,3-f]喹啉-4-基)苯酚

[0357] 

HSD-02-983

方法B：灰白色固体 (127 mg, 42%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.72 (s, 1H), 8.61 (s, 1H), 7.90 (d, J = 9.2 Hz, 1H), 7.84 (d, J = 9.2 = Hz, 1H), 7.40 (d, J = 8.5 Hz, 2H), 6.94 (d, J = 8.5 Hz, 2H), 3.74 (t, J = 7.0 Hz, 2H), 3.10 (t, J = 7.0 Hz, 2H); $C_{18}H_{14}N_3O_2$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 304.1086, 实测值 304.1087。

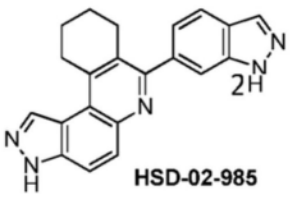
[0358] 7-(1H-吲唑-5-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0359] 

HSD-02-984

方法A：灰白色固体 (224 mg, 65%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 8.56 (s, 1H), 8.12 (s, 1H), 7.92 (s, 1H), 7.83 (d, J = 5.8 Hz, 2H), 7.61 (d, J = 8.6 Hz, 1H), 7.55 (d, J = 8.6 Hz, 1H), 3.32 - 3.26 (m, 2H), 2.78 (t, 6.1 Hz, 2H), 2.01 - 1.92 (m, 2H), 1.74 - 1.65 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 157.30, 143.71, 142.28, 139.80, 138.66, 136.27, 134.45, 133.55, 129.66, 129.54, 128.17, 123.07, 121.71, 121.43, 116.44, 114.31, 109.93, 29.69, 29.22, 22.64, 22.59; $C_{21}H_{18}N_5$[M+H]$^+$的HRMS(ESI)m/z计算值340.1562,实测值340.1565。

[0360] 7-(1H-吲唑-6-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

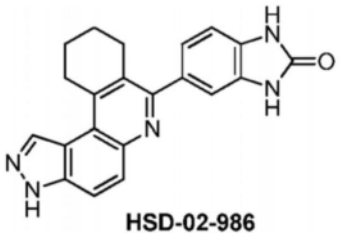
[0361] 

HSD-02-985

方法A：灰白色固体 (176 mg, 52%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 8.52 (s, dH), 7.87 - 7.77 (m, 2H), 7.61 (d, J = 1.6 = Hz, 1H), 7.48 (d, J = 8.2 Hz, 1H), 7.38 (dd, J = 8.2, 1.7 Hz, 1H), 3.27 (d, J = 7.7 Hz, 2H), 2.75 (t, J = 6.0 Hz, 2H), 1.97 (qd, J = 6.5, 4.2, 2.9 Hz, 2H), 1.79 - 1.67 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 155.27, 143.48, 142.61, 138.71, 138.01, 136.36, 133.74,131.74,129.55,129.36,125.92,122.00,116.36,114.53,111.49,110.02,29.64,

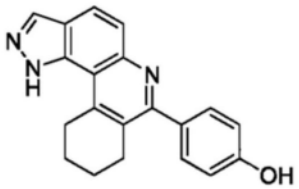
28.80,22.52,22.44;$C_{21}H_{18}N_5$[M+H]$^+$的HRMS(ESI)m/z计算值340.1562,实测值340.1565。

[0362] 5-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)-1H-苯并[d]咪唑-2(3H)-酮

[0363] 
HSD-02-986

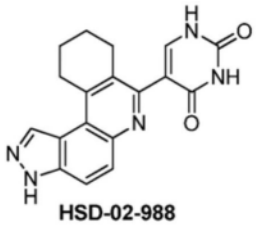
方法A: 灰白色固体 (178 mg, 50%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.55 (s, 1H), 7.84 (d, J = 9.1 Hz, 1H), 7.78 (d, J = 9.1 Hz, 1H), 7.16 - 7.09 (m, 2H), 7.00 (d, J = 7.8 Hz, 1H), 3.28 (t, J = 6.5 Hz, 2H), 2.77 (t, J = 6.1 Hz, 2H), 2.00 - 1.95 (m, 2H), 1.73 - 1.66 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 157.16, 156.09, 143.72, 142.21, 139.73, 134.99, 133.77, 130.00, 129.94, 129.53, 129.35, 122.16, 121.65, 116.30, 115.27, 109.89, 108.18,29.70,29.28,22.65,22.62;$C_{22}H_{17}N_4O_2$[M+H]$^+$的HRMS(ESI)m/z计算值369.1352,实测值369.1352。

[0364] 4-(8,9,10,11-四氢-1H-吡唑并[3,4-a]菲啶-7-基)苯酚

[0365] 
HSD-02-987

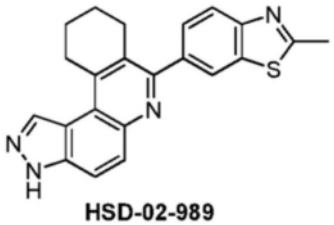
方法A: 灰白色固体 (126 mg, 40%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 9.63 (s, 1H), 8.14 (s, 1H), 7.77 (d, J = 8.9 Hz, 1H), 7.58 (d, J = 9.0 Hz, 1H), 7.43 (d, J = 8.5 Hz, 2H), 6.88 (d, J = 8.6 Hz, 2H), 3.17 (t, J = 6.6 Hz, 2H), 2.73 (t, J = 6.1 Hz, 2H), 1.88 (qd, J = 7.8, 6.4, 4.5 Hz, 2H), 1.73 - 1.63 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 158.72, 157.79, 142.88, 138.02, 134.71, 134.54, 131.87, 130.95, 129.09, 124.62, 121.76, 119.80, 116.13, 115.13, 28.93,26.48,22.74,22.32;$C_{20}H_{18}N_3O$[M+H]$^+$的HRMS(ESI)m/z计算值316.1449,实测值316.1458。

[0366] 5-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)嘧啶-2,4(1H,3H)-二酮

[0367] 
HSD-02-988

方法A: 灰白色固体 (173 mg, 52%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.77 (s, 1H), 8.18 - 8.10 (m, 1H), 8.02 - 7.85 (m, 1H), 7.74 - 7.17 (m, 2H), 3.60 - 3.48 (m, 2H), 3.02 - 2.89 (m, 2H), 2.20 - 2.09 (m, 1H), 2.04 - 1.90 (m, 1H); $C_{18}H_{16}N_5O_2$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 334.1304, 实测值 334.1305。

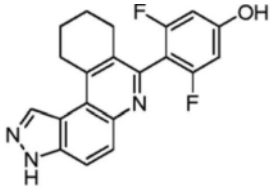
[0368] 2-甲基-6-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯并[d]噻唑e

[0369] 
HSD-02-989

方法A: 灰白色固体 (207 mg, 56%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 8.59 (s, 1H), 8.22 (d, J = 1.6 Hz, 1H), 7.97 (d, J = 8.3 Hz, 1H), 7.86 (dd, J = 9.0, 0.9 Hz, 1H), 7.82 (d, J = 9.1 Hz, 1H), 7.65 (dd, J = 8.3, 1.7 Hz, 1H), 3.36 - 3.33 (m, 3H), 2.83 (S, 3H), 2.81 - 2.78 (m, 2H), 2.04-1.98 (m, 2H), 1.78 - 1.70 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 168.24, 156.38, 152.90, 143.77, 142.53, 137.87, 135.52, 129.61, 129.48, 127.80, 122.99, 121.99, 121.67, 118.44, 116.26, 29.71, 29.02, 22.62, 22.54,20.33;$C_{22}H_{19}N_4S$[M+H]$^+$的HRMS(ESI)m/z计算值371.1330,实测值371.1333。

[0370] 3,5-二氟-4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

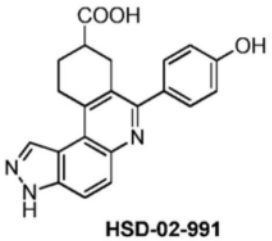
[0371] 方法A:白色固体(168mg,48%)。^{1}H NMR(500MHz,DMSO-d_6)δ8.52(s,

[0372] 
HSD-02-990

1H), 7.84 (d, J = 9.0 Hz, 1H), 7.80 (d, J = 9.5 Hz, 1H), 7.61 (d, J = 1.6 Hz, 1H), 7.48 (d, J = 8.2 Hz, 1H), 7.38 (dd, J = 8 J.2, 1.7 Hz, 1H), 3.27 (d, J = 7.7 Hz, 2H), 2.75 (t, J = 6.0 Hz, 2H), 1.99 - 1.92 (m, 2H), 1.76 - 1.65 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 155.27, 143.48, 142.96, 142.76, 142.61, 138.71, 138.01, 136.36, 133.74, 131.74, 129.55, 129.36, 125.92, 122.00, 116.36, 114.53, 111.49, 110.02, 29.64, 28.80, 22.52, 22.44; $C_{20}H_{16}FN_3O$ [M + H]$^+$的 HRMS

(ESI)m/z计算值352.1261,实测值352.1266。

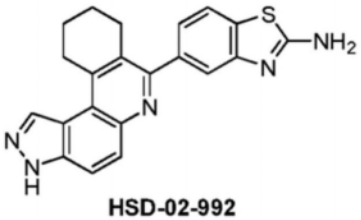
[0373] 7-(4-羟基苯基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-9-羧酸

[0374] 

HSD-02-991

方法A: 灰白色固体 (180 mg, 50%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 8.56 (s, 1H), 7.83 (d, J = 9.1 Hz, 1H), 7.78 (d, J = 9.1 Hz, 1H), 7.38 (d, J = 8.5 Hz, 2H), 6.87 (d, J = 8.5 Hz, 2H), 3.48 - 3.39 (m, 1H), 3.36 - 3.23 (m, H), 3.05 - 2.97 (m, 1H), 2.95 - 2.87 (m, 1H), 2.62 - 2.56 (m, 1H), 2.38 - 2.30 (m, 1H), 2.01 - 1.91 (m, 1H); ^{13}C NMR (126 MHz, DMSO) δ 177.11, 157.71, 156.96, 143.77, 141.52, 131.87, 130.83, 129.55, 128.25, 121.22, 116.27, 115.19, 31.66, 29.18, 25.49; $C_{21}H_{18}N_3O_3$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 360.1348, 实测值360.1351。

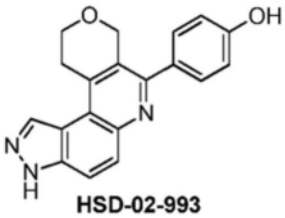
[0375] 5-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯并[d]噻唑-2-胺

[0376] 

HSD-02-992

方法A: 浅黄色固体 (137 mg, 37%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.55 (s, 1H), 7.88 - 7.78 (m, 3H), 7.55 (s, 2H), 7.45 - 7.36 (m, 2H), 3.32 (s, 2H), 2.82 (t, J = 6.1 Hz, 2H), 1.99 (qq, J = 5.2, 2.7 Hz, 2H), 1.74 (dp, J = 9.1, 3.2, 2.8 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 167.61, 156.90, 152.94, 143.53, 142.39, 138.63, 136.32, 133.93, 131.17, 129.60, 127.25, 122.13, 121.64, 117.32, 116.50, 114.34, 29.75, 29.18,22.66,22.62;$C_{21}H_{18}N_5S$[M+H]的HRMS(ESI)m/z计算值372.1283,实测值372.1285。

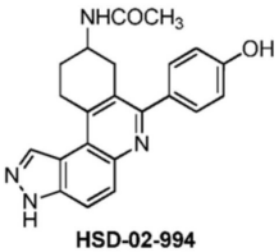
[0377] 4-(3,8,10,11-四氢吡喃并[3,4-c]吡唑并[4,3-f]喹啉-7-基)苯酚

[0378] 

HSD-02-993

方法A: 灰白色固体 (206 mg, 65%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 9.69 (s, 1H), 8.52 (s, 1H), 7.85 (q, J = 9.2 Hz, 2H), 7.40 (d, J = 8.5 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 4.77 (s, 2H), 4.11 (t, J = 5.9 Hz, 2H), 3.34 (d, J = 6.8 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 158.09, 153.88, 144.20, 139.12, 138.55, 135.81, 130.66, 130.59, 129.53, 127.54, 120.80, 116.34, 115.40, 114.82, 67.17, 64.45, 28.70; $C_{19}H_{16}N_3O_2$ [M + H]$^+$的 HRMS (ESI) m/z 计算值318.1243,实测值318.1244。

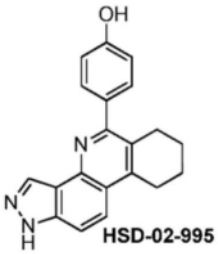
[0379] N-(7-(4-羟基苯基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-9-基)乙酰胺

[0380] 

HSD-02-994

方法A: 浅棕色固体 (220 mg, 59%)。1H NMR (500 MHz, DMSO-d_6) δ 8.57 (s, 1H), 7.97 (d, J = 7.2 Hz, 1H), 7.84 (dd, J = 9.0, 0.9 Hz, 1H), 7.79 (d, J = 9.1 Hz, 1H), 7.40 - 7.35 (m, 2H), 6.89 - 6.80 (m, 2H), 3.96 - 3.88 (m, 1H), 3.52 - 3.46 (m, 1H), 3.34 - 3.29 (m, 1H), 2.98 - 2.90 (m, 1H), 2.75 (dd, J = 16.6, 9.0 Hz, 1H), 2.24 - 2.16 (m, 1H), 1.95 - 1.83 (m, 1H), 1.77 (s, 3H); ^{13}C NMR (126 MHz, DMSO) δ 169.29, 157.68, 157.02, 143.86, 141.35, 131.82, 130.82, 129.56, 127.39, 121.15, 116.35, 115.20, 44.69, 35.05, 28.48, 28.02, 23.15; $C_{22}H_{21}N_4O_2$[M+H]$^+$的HRMS(ESI)m/z计算值373.1665,实测值373.1670。

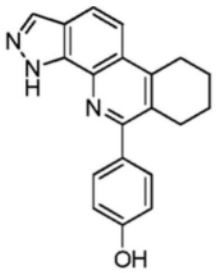
[0381] 4-(6,7,8,9-四氢-1H-吡唑并[3,4-c]菲啶-5-基)苯酚

[0382] 

HSD-02-995

方法A: 浅棕色固体 (132 mg, 42%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.90 (s, 1H), 8.28 (dd, J = 11.6, 5.5 Hz, 2H), 8.05 (t, J = 8.7 Hz, 2H), 7.62 - 7.54 (m, 2H), 7.11 - 7.05 (m, 2H), 3.57 (t, J = 6.4 Hz, 2H), 2.88 (t, J = 6.2 Hz, 2H), 2.14 - 2.05 (m, 2H), 1.93 - 1.85 (m, 2H);^{13}C NMR (126 MHz, MeOD) δ 160.37, 156.23, 153.72, 132.09, 130.99, 130.27, 123.52, 122.38, 122.21, 115.50, 111.83, 27.76, 27.47, 21.48, 21.18; $C_{20}H_{18}N_3O$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 316.1449, 实测值 316.1456。

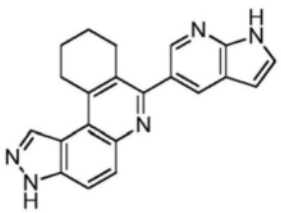
[0383] 4-(6,7,8,9-四氢-3H-吡唑并[4,3-c]菲啶-5-基)苯酚

[0384] 

HSD-02-997

方法 A: 浅黄色固体 (161 mg, 51%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.49 (s, 1H), 8.11 (d, J = 9.2 Hz, 1H), 7.89 (d, J = 9.2 Hz, 1H), 7.65 - 7.56 (m, 2H), 7.12 - 7.03 (m, 2H), 3.53 (t, J = 6.5 Hz, 2H), 2.92 (t, J = 6.3 Hz, 2H), 2.14 - 2.05 (m, 2H), 1.95 - 1.83 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 162.75, 159.17, 154.29, 147.97, 140.25, 139.21, 136.17, 134.68, 130.81, 128.84, 127.83, 124.74, 122.97, 122.65, 122.32, 115.57, 110.49, 110.49, 30.27, 28.70, 22.16, 22.08; $C_{20}H_{18}N_3O$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 316.1449, 实测值 316.1459。

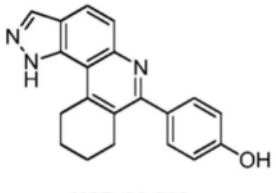
[0385] 7-(1H-吡咯并[2,3-b]吡啶-5-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0386] 

HSD-02-998

方法 A: 灰白色固体 (203 mg, 60%)。 ^{1}H NMR (500 MHz, DMSO- d_6) δ 12.09 (s, 1H), 8.78 (s, 1H), 8.54 (d, J = 2.1 Hz, 1H), 8.37 (d, J = 2.1 Hz, 1H), 8.17 (q, J = 9.2 Hz, 2H), 7.65 (t, J = 3.0 Hz, 1H), 6.61 (dd, J = 3.5, 1.8 Hz, 1H), 3.51 - 3.44 (m, 2H), 2.86 (t, J = 6 J.2 = Hz, 2H), 2.09 - 2.01 (m, 2H), 1.86 - 1.73 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 151.20, 149.00, 143.45, 136.93, 132.02, 130.20, 128.42, 122.92, 122.10, 119.30, 115.16, 115.08, 101.14, 30.71, 28.46, 21.95, 21.88; $C_{21}H_{18}N_5$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 340.1562, 实测值340.1569。

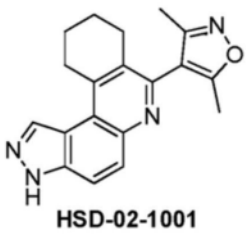
[0387] 4-(8,9,10,11-四氢-1H-吡唑并[3,4-a]菲啶-7-基)苯酚

[0388] 

HSD-02-999

方法 A: 灰白色固体 (182 mg, 58%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 8.31 (s, 1H), 7.87 (d, J = 8.9 Hz, 1H), 7.51 (d, J = 8. J9 Hz, 1H), 7.39 (d, J = 8.5 Hz, 2H), 6.85 (d, J = 8.5 Hz, 2H), 3.50 (t, J = 6 J.6 Hz, 2H), 2.79 (t, J = 6.1 Hz, 2H), 1.97 - 1.92 (m, 2H), 1.77 - 1.70 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 158.40, 157.95, 146.70, 142.55, 131.73, 130.87, 128.50, 124.50, 122.19, 119.87, 116.93, 115.17, 29.97, 29.12, 22.56; $C_{20}H_{18}N_3O$ [M + H]$^+$的 HRMS (ESI)m/z计算值316.1449,实测值316.1458。

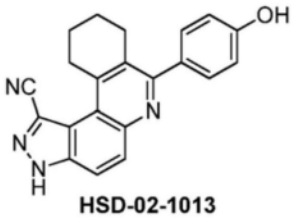
[0389] 3,5-二甲基-4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)异恶唑

[0390] 

HSD-02-1001

方法 A: 白色固体 (229 mg, 72%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 8.92 (s, 1H), 8.35 (d, J = 9.3 Hz, 1H), 8.06 (dd, J = 9.2, 2.4 Hz, 1H), 3.71 - 3.64 (m, 2H), 2.86 - 2.77 (m, 2H), 2.45 (s, 3H), 2.25 - 2.20 (m, 5H), 2.06 - 1.98 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 170.18, 158.64, 155.86, 140.72, 140.00, 135.64, 134.42, 134.28, 124.70, 121.79, 118.93, 114.70, 108.54, 30.94, 26.68, 21.17, 20.88, 10.39, 8.99; $C_{19}H_{19}N_4O$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 319.1559, 实测值 319.1563。

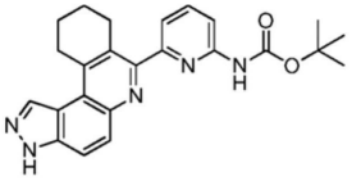
[0391] 7-(4-羟基苯基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-1-腈

[0392] 

HSD-02-1013

方法 A: 白色固体 (210 mg, 61%)。^{1}H NMR (500 MHz, 甲醇-d_6) δ 8.32 (d, J = 9.3 Hz, 1H), 8.20 (d, J= 9.2 Hz, 1H), 7.62 (d, J = 8.6 Hz, 2H), 7.09 (d, J = 8.5 Hz, 2H), 3.91 (t, J = 6.3 Hz, 2H), 3.00 (t, J = 6.3 Hz, 2H), 2.24 - 2.09 (m, 2H), 2.01 - 1.90 (m, 2H). ^{13}C NMR (126 MHz, MeOD) δ 160.62, 155.55, 153.29, 139.97, 135.54, 133.16, 130.98, 122.63, 121.71, 121.08, 119.18, 115.88, 115.65, 115.28, 33.30, 27.88, 20.92, 20.63; $C_{21}H_{21}N_4O$ [M + H]$^+$ 的 HRMS(ESI)m/z计算值345.1715,实测值345.1720。

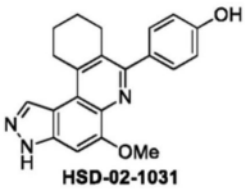
[0393] 叔丁基(6-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)吡啶-2-基)氨基甲酸酯

[0394] 

HSD-02-1022

方法A：白色固体 (270 mg, 65%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.79 (s, 1H), 8.23 (d, J = 9.3 Hz, 1H), 8.12 - 8.05 (m, 3H), 7.65 (dd, J = 5.7, 2.6 Hz, 1H), 3.53 (d, J = 6.0 Hz, 2H), 3.08 (t, J = 6.1 Hz, 2H), 2.21 - 2.14 (m, 2H), 1.99 - 1.91 (m, 2H), 1.58 (s, 9H); ^{13}C NMR (126 MHz, MeOD) δ 154.62, 153.09, 153.05, 147.37, 146.93, 140.49, 139.57, 134.87, 134.39, 132.10, 124.03, 120.98, 119.75, 119.68, 114.62, 114.29,80.98,30.97,27.41,27.15,21.16,21.06。

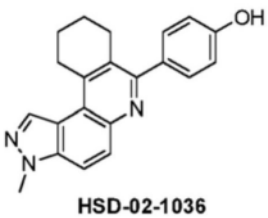
[0395] 4-(5-甲氧基-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0396] 

HSD-02-1031

方法A：白色固体 (145 mg, 42%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 10.16 (s, 1H), 8.60 (s, 1H), 7.53 - 7.39 (m, 3H), 7.03 - 6.92 (m, 2H), 4.05 (s, 3H), 3.37 (t, J = 6.5 Hz, 2H), 2.75 (t, J = 6.2 Hz, 2H), 1.99 (pd, J = 6.4, 4.3, 2.6 Hz, 2H), 1.75 (dq, J = 6.0, 2.9, 2.5 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 159.52, 152.70, 150.67,150.36,140.21,132.48,131.68,130.23,125.17,123.07,121.30,115.56,109.83, 96.56,56.90,30.79,28.48,21.93,21.80；$C_{21}H_{20}N_3O_2$[M+H]$^+$的HRMS(ESI)m/z计算值346.1556,实测值346.1559。

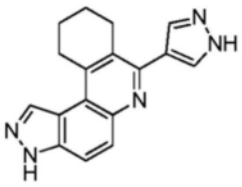
[0397] 4-(3-甲基-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0398] 

HSD-02-1036

方法A：灰白色固体 (208 mg, 63%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.74 (s, 1H), 8.34 (d, J = 9.2 Hz, 1H), 8.11 (d, J = 9.3 Hz, 1H), 7.63 - 7.56 (m, 2H), 7.10 - 7.03 (m, 2H), 4.30 (s, 3H), 3.64 (t, J = 6.4 Hz, 2H), 2.96 (t, J = 6.2 Hz, 2H), 2.23 - 2.14 (m, 2H), 1.98 - 1.88 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 160.36, 154.36, 151.77, 138.31, 134.95, 134.11, 132.57, 130.94, 123.00, 122.30, 118.94, 118.25, 116.10, 115.57, 35.20, 30.96, 27.98, 21.33, 21.26。

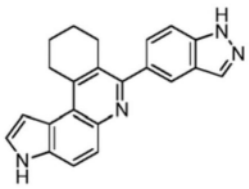
[0399] 7-(1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0400] 

HSD-02-1077

方法A：白色固体 (220 mg, 76%)。^{1}H NMR (500 MHz, DMSO-d6) δ 8.52 (s, 1H), 8.14 (s, 2H), 7.79 (d, J = 5.4 Hz, 2H), 3.28 (d, J = 6.7 Hz, 2H), 2.99 (t, J = 6.1 Hz, 2H), 1.98 (ddt, J = 9.0, 6.4, 3.2 Hz, 2H), 1.84 (dp, J = 9.2, 3.4, 2.9 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 149.72, 143.79, 142.11, 138.53, 136.11, 129.61, 128.83, 121.65, 121.03, 116.45, 114.22, 29.85, 28.67, 22.64, 22.48; $C_7H_{16}N_5$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 290.1406, 实测值 290.1406。

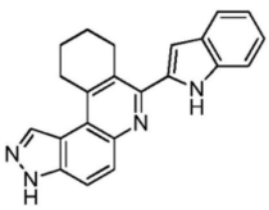
[0401] 7-(1H-吲唑-5-基)-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶

[0402] 

HSD-02-1081

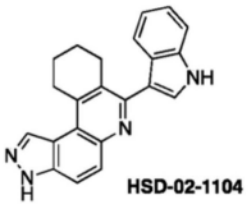
方法A：白色固体 (173 mg, 51%)。^{1}H NMR (500 MHz, DMSO-d6) δ 11.76 (s, 1H), 8.12 (s, 1H), 7.91 (s, 1H), 7.80 (d, J = 8.8 Hz, 1H), 7.66 (d, J = 8.8 Hz, 1H), 7.61 (d, J = 8.5 Hz, 1H), 7.54 (dd, J = 8.5, 1.5 Hz, 1H), 7.48 (t, J = 2.8 Hz, 1H), 7.11 (t, J = 2.6 Hz, 1H), 3.37 (d, J = 6.9 Hz, 2H), 2.77 (t, J = 6.2 Hz, 2H), 1.99 - 1.91 (m, 2H), 1.73 - 1.64 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 156.34, 143.43, 142.27, 139.73, 134.40, 134.08, 133.20, 128.24, 127.74, 124.12, 123.87, 123.10, 122.38,121.28,120.41,116.42,109.84,106.27,30.01,29.35,22.91,22.62；$C_{22}H_{19}N_4$[M+H]$^+$的HRMS(ESI)m/z计算值339.1610,实测值339.1618。

[0403] 7-(1H-吲哚-2-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0404] 
HSD-02-1103

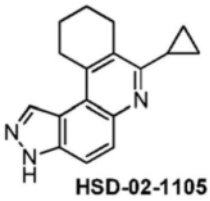
方法 A: 黄色固体 (264 mg, 78%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 12.12 (s, 1H), 8.76 (s, 1H), 8.38 - 8.08 (m, 2H), 7.70 (d, J = 8.0 Hz, 1H), 7.57 (dd, J = 8.2, 1.0 Hz, 1H), 7.30 - 7.21 (m, 2H), 7.09 (td, J = 7. J4, = 6.9, 1.0 Hz, 1H), 3.45 (t, J = 6.4 Hz, 2H), 3.18 - 3.15 (m, 2H), 2.11 - 1.99 (m, 2H), 1.92 - 1.81 (m, 2H);^{13}C NMR (126 MHz, DMSO) δ 143.78, 137.55, 134.89, 131.22, 130.49, 128.14, 124.23, 122.63, 121.72, 120.53, 119.45, 115.27, 112.54, 108.05, 30.84, 28.26, 21.91, 21.86, 21.86; $C_{22}H_{19}N_4$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 339.1610, 实测值339.1618。

[0405] 7-(1H-吲哚-3-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0406] 
HSD-02-1104

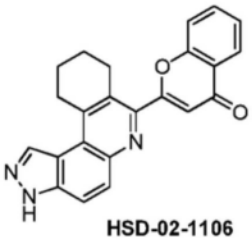
方法 A: 白色固体 (183 mg, 54%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.72 (s, 1H), 8.14 (d, J = 8.7 Hz, 1H), 8.04 - 7.93 (m, 2H), 7.61 - 7.52 (m, 2H), 7.30 - 7.16 (m, 2H), 3.49 (t, J = 6.2 Hz, 2H), 2.99 (t, J = 6.1 Hz, 2H), 2.22 - 2.10 (m, 2H), 1.87 (q, J = 5.7 Hz, 2H); ^{13}C NMR (126 MHz, MeOD) δ 152.83, 147.51, 136.55, 135.07, 132.76, 128.62, 125.73, 122.77, 122.39, 120.99, 119.61, 118.86, 115.08, 112.11, 107.22, 30.80, 27.71, 21.46, 21.29; $C_{22}H_{19}N_4$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值339.1610,实测值339.1618。

[0407] 7-环丙基-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0408] 
HSD-02-1105

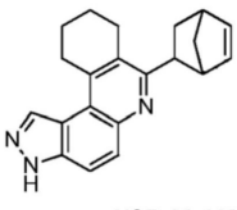
方法 A: 灰白色固体 (181 mg, 69%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.45 (s, 1H), 7.73 (d, J = 9.0 Hz, 1H), 7.64 (d, J = 9.1 Hz, 1H), 3.18 (q, J = 5.3, 4.6 Hz, 2H), 2.94 (t, J = 6.2 Hz, 2H), 2.21 (tt, J = 8.1, 4.9 Hz, 1H), 1.96 - 1.88 (m, 2H), 1.86 - 1.81 (m, 2H), 1.10 - 0.99 (m, 2H), 0.97 - 0.87 (m, 2H) ; ^{13}C NMR (126 MHz, DMSO) δ 157.71, 143.33, 140.97, 138.28, 135.75, 129.57, 129.38, 120.82, 116.55, 113.67, 29.49, 26.38, 22.40, 22.37, 13.67, 9.14; $C_{17}H_{18}N_3$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 264.1501, 实测值264.1509。

[0409] 2-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)-4H-苯并吡喃-4-酮

[0410] 
HSD-02-1106

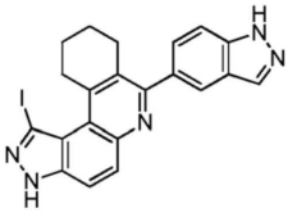
方法 A: 灰白色固体 (92 mg, 25%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.88 (s, 1H), 8.85 (s, 1H), 8.26 (d, J = 9.2 Hz, 1H), 8.23 (d, J = 9.2 Hz, 1H), 8.17 (dd, J = 8.0, 1.7 Hz, 1H), 7.95 (dt, J = 8.7, 7.1 Hz, 1H), 7.85 - 7.83 (d, J = 8.2 Hz, 1H), 7.62 (t, J = 8.0 Hz 1H), 3.52 (t, J = 6.4 Hz, 2H), 2.87 (t, J = 6.3 Hz, 2H), 2.08 -1.98 (m, 2H), 1.82 (dp J = 9.8, 3.9, 3.1 Hz, 2H); $C_{23}H_{18}N_3O_2$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 368.1399, 实测值 368.1400。

[0411] 7-(双环[2.2.1]庚-5-烯-2-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0412] 
HSD-02-1107

方法 A: 灰白色固体 (110 mg, 34%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 8.82 (s, 1H), 8.34 (d, J = 9.3 Hz, 1H), 8.23 (d, J = 9.2 Hz, 1H), 6.71 (dd, J = 5.8, 3.2 Hz, 1H), 6.44 - 6.36 (m, 1H), 5.68 (dd, J = 5.7, 2.9 Hz, 1H), 4.34 - 4.28 (m, 1H), 3.64 - 3.59 (m, 2H), 3.43 (s, 1H), 3.24 (d, J = 4.8 Hz, 2H), 2.42 (ddd, J = 12.9, 9.3, 3.6 Hz, 1H), 2.24 - 2.16 (m, 1H), 2.14 - 2.03 (m, 4H), 1.76 (d, J = 8.4 Hz, 1H), 1.74 - 1.66 (m, 2H); $C_{21}H_{22}N_3$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 316.1814, 实测值 316.1819。

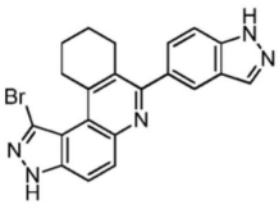
[0413] 7-(1H-吲唑-5-基)-1-碘-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0414] 

HSD-02-1108

方法 A: 黄色固体 (302 mg, 65%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.13 (s, 1H), 7.94 (t, J = 1.1 Hz, 1H), 7.79 (d, J = 9.1 Hz, 1H), 7.76 (d, J = 9.0 Hz, 1H), 7.62 (d, J = 8.6 Hz, 1H), 7.55 (dd, J = 8.6, 1.6 Hz, 1H), 3.70 (t, J = 5.9 Hz, 2H), 2.82 (t, J = 6.3 Hz, 2H), 1.76 - 1.72 (m, 4H); ^{13}C NMR (126 MHz, DMSO) δ 157.35, 144.29, 143.76, 141.32, 139.91, 134.39, 133.08, 130.70, 129.56, 129.31, 128.08, 123.10, 121.70, 121.50, 120.04, 114.80, 110.12, 37.07, 27.57, 22.22, 22.04; $C_{21}H_{17}IN_5$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 466.0529,实测值466.0535。

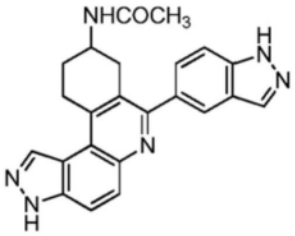
[0415] 1-溴-7-(1H-吲唑-5-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0416] 

HSD-02-1109

方法 A: 灰白色固体 (234 mg, 56%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 8.13 (d, J = 1.0 Hz, 1H), 7.94 - 7.92 (m, 1H), 7.83 - 7.76 (m, 2H), 7.62 (dt, J = 8.6, 1.0 Hz, 1H), 7.54 (dd, J = 8.6, 1.6 Hz, 1H), 3.60 (t, J = 5.9 Hz, 2H), 2.81 (t, J = 6.2 Hz, 2H), 1.79 - 1.70 (m, 4H); ^{13}C NMR (126 MHz, DMSO) δ 157.76, 144.25, 143.42, 141.60, 139.90, 134.39, 133.10, 131.25, 129.53, 128.02, 123.10, 121.51, 121.45, 115.33, 114.67, 110.13, 34.34, 27.88, 22.29, 22.10; $C_{19}H_{18}N_5$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 316.1562, 实测值 316.1555。

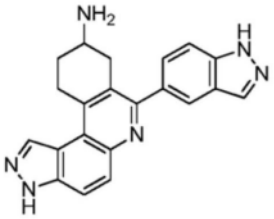
[0417] N-(7-(1H-吲唑-5-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-9-基)乙酰胺

[0418] 

HSD-02-1110

方法 A: 灰白色固体 (277 mg, 70%)。 ^{1}H NMR (500 MHz, DMSO- d6) δ 8.71 (s, 1H), 8.23 (s, 1H), 8.09 (q, J = 7.1, 5.1 Hz, 4H), 7.74 (d, J = 8.6 Hz, 1H), 7.63 (dd, J = 8.6, 1.6 Hz, 1H), 4.04 - 3.93 (m, 1H), 3.57 (dt, J = 18.7, 5.5 Hz, 1H), 3.45 (dt, J = 17.9, 7.4 Hz, 1H), 2.96 (dd, J = 16.8, 4.7 Hz, 1H), 2.80 (dd, J = 16.7, 8.7 Hz, 1H), 2.27 - 2.18 (m, 1H), 2.04 - 1.91 (m, 1H), 1.75 (s, 3H); ^{13}C NMR (126 MHz, DMSO) δ 169.40, 153.72, 140.39, 138.50, 134.76, 129.36, 127.67, 122.94, 122.22, 115.46, 110.75, 44.11, 34.25, 29.21, 27.36, 23.11; $C_{23}H_{21}N_6O$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 397.1777, 实测值397.1778。

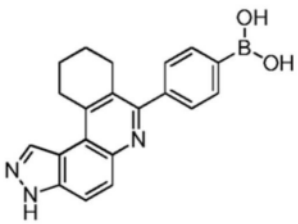
[0419] 7-(1H-吲唑-5-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-9-胺

[0420] 

HSD-02-1111

方法 A: 浅黄色固体 (227 mg, 64%)。 ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.80 (s, 1H), 8.60 - 8.51 (m, 3H), 8.27 (s, 1H), 8.24 (s, 2H), 8.16 (s, 1H), 7.80 (d, J = 8.5 Hz, 1H), 7.65 (dd, J = 8.6, 1.6 Hz, 1H), 3.74 - 3.65 (m, 1H), 3.54 (q, J = 9.8, 9.2 Hz, 2H), 3.15 - 3.09 (m, 2H), 2.55 - 2.51 (m, 1H), 2.20 - 2.10 (m, 1H); ^{13}C NMR (126 MHz, DMSO) δ 157.40, 143.77, 141.82, 139.88, 139.65, 135.14, 134.42, 133.51, 133.35, 129.58, 128.37, 128.18, 123.04, 121.43, 121.35, 116.32, 115.26, 110.08, 46.76, 38.61, 31.48, 29.03; $C_{21}H_{19}N_6$ [M + H]$^+$的 HRMS (ESI) m/z计算值355.1671,实测值355.1673。

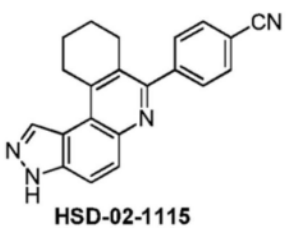
[0421] (4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯基)硼酸

[0422] 

HSD-02-1113

方法 A: 灰白色固体 (151 mg, 44%)。 ^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.84 (s, 1H), 8.25 (dd, J = 9.3, 3.1 Hz, 1H), 8.04 (dd, J = 9.2, 3.2 Hz, 2H), 7.95 (s, 1H), 7.68 (d, J = 7.5 Hz, 2H), 3.67 - 3.59 (m, 2H), 2.96 - 2.85 (m, 2H), 2.24 - 2.13 (m, 2H), 1.95 - 1.89 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 154.13, 151.37, 135.10, 134.26, 134.02, 133.60, 132.07, 128.01, 123.67, 119.63, 114.91, 30.85, 27.73, 21.31, 21.16; $C_{20}H_{19}BN_3O_2$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 344.1570, 实测值 344.1577。

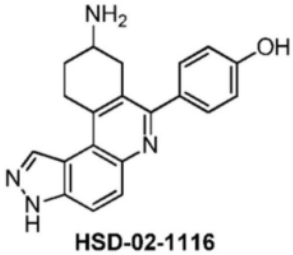
[0423] 4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯甲腈

[0424] 

HSD-02-1115

方法A: 灰白色固体 (182 mg, 56%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 8.78 (s, 1H), 8.20 (t, J = 7.4 Hz, 2H), 8.10 (d, J = 8.1 Hz, 2H), 7.94 (d, J = 8.2 Hz, 2H), 3.48 - 3.44 (m, 2H), 2.73 (t, J = 6.2 Hz, 2H), 2.07 - 1.97 (m, 2H), 1.84 - 1.72 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 150.26, 140.30, 138.64, 136.93, 135.01, 132.87, 131.23, 130.97, 123.45, 122.31, 119.99, 118.89, 115.01, 113.13, 30.63, 28.01, 21.85, 21.68; $C_{21}H_{17}N_4$ [M + H]$^+$的 HRMS (ESI) m/z计算值325.1453,实测值325.1455。

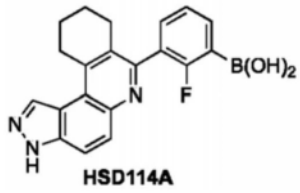
[0425] 4-(9-氨基-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0426] 

HSD-02-1116

方法A: 灰白色固体 (205 mg, 62%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.60 - 8.56 (m, 1H), 7.89 (d, J = 9.2 Hz, 1H), 7.83 (dd, J = 9.2, 0.9 Hz, 1H), 7.37 (d, J = 8.6 Hz, 1H), 6.92 (d, J = 8.6 Hz, 1H), 3.62 - 3.55 (m, 1H), 3.45 - 3.35 (m, 1H), 3.14 - 3.08 (m, 1H), 3.03 - 2.98 (m, 1H), 2.74 - 2.66 (m, 1H), 2.37 - 2.29 (m, 1H), 1.89 - 1.78 (m, 1H).^{13}C NMR (126 MHz, MeOD) δ 157.83, 157.59, 143.24, 142.36, 139.52, 134.57, 131.18, 130.07, 128.37, 128.06, 121.39, 116.01, 114.78, 114.55, 46.29, 37.35, 30.57, 28.84; $C_{20}H_{19}N_4O$ [M + H]$^+$ 的 HRMS(ESI)m/z计算值331.1559,实测值331.1561。

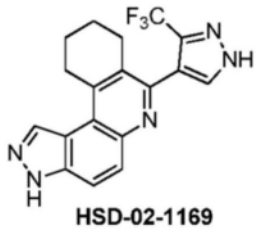
[0427] (2-氟-3-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯基)硼酸

[0428] 

HSD114A

方法A: 灰白色固体 (163mg, 45%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.77 (s, 1H), 8.10 (s, 1H), 7.94 (d, J = 7.3 Hz, 1H), 7.77 - 7.55 (m, 2H), 7.52 - 7.34 (m, 1H), 3.52 (s, 2H), 2.77 (s, 2H), 2.13 (s, 2H), 1.91 (s, 2H); ^{13}C NMR (126 MHz, MeOD) δ 150.62, 147.92, 138.23, 136.61, 132.21, 132.13, 131.10, 124.78, 124.63, 123.70, 122.50, 122.02, 115.93, 115.76, 30.40, 26.98, 21.61, 21.26。

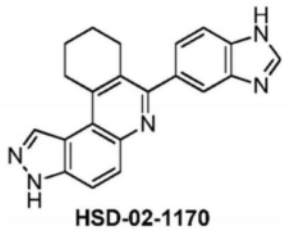
[0429] 7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0430] 

HSD-02-1169

方法A: 灰白色固体 (161 mg, 45%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.55 (s, 1H), 8.22 (s, 1H), 7.85 (d, J = 9.1 Hz, 1H), 7.77 (d, J = 9.1 Hz, 1H), 3.26 (t, J = 6.4 Hz, 2H), 2.68 (t, J = 6.2 Hz, 2H), 1.98 - 1.86 (m, 2H), 1.80 - 1.69 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 148.52, 143.61, 141.99, 139.65, 139.37(q, 35.28Hz), 135.14, 131.28, 130.36, 129.53, 123.56(q, J = 269.64Hz), 121.99, 119.73, 116.21, 115.24, 29.48, 28.17, 22.51, 22.29; $C_{18}H_{15}F_3N_5$ [M + H]$^+$的 HRMS(ESI)m/z计算值358.1280,实测值358.1286。

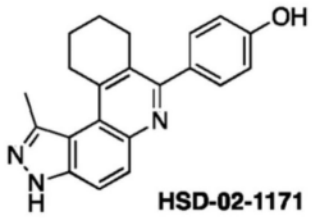
[0431] 7-(1H-苯并[d]咪唑-5-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0432] 

HSD-02-1170

方法A: 灰白色固体 (238 mg, 70%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 8.58 (s, 1H), 8.28 (s, 1H), 7.85 (d, J = 9.0, 0.8 Hz, 1H), 7.81 (d, J = 9.1 Hz, 1H), 7.74 (s, 1H), 7.66 (d, J = 8.3 Hz, 1H), 7.38 (dd, J = 8.2, 1.6 Hz, 1H), 3.33 (t, J = 6.6 Hz, 2H), 2.80 (t, J = 6.1 Hz, 2H), 2.00 (td, J = 9.0, 7.4, 4.6 Hz, 2H), 1.72 (ddt, J = 9.2, 6.3, 3.8 Hz, 2H). ^{13}C NMR (126 MHz, DMSO) δ 157.66, 143.73, 143.21, 142.24, 135.19, 129.71, 129.58, 123.77, 121.72, 116.34, 29.72, 29.29, 22.67, 22.62; $C_{21}H_{18}N_5$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 340.1562, 实测值340.1570。

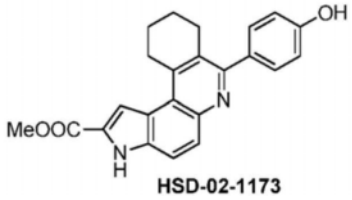
[0433] 4-(1-甲基-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0434] 

HSD-02-1171

方法A：灰白色固体 (132 mg, 40%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 10.37 (s, 1H), 8.24 - 8.03 (m, 2H), 7.56 (d, J = 8.6 Hz, 2H), 7.04 (d, J = 8.6 Hz, 2H), 3.62 (t, J = 5.9 Hz, 2H), 2.94 (s, 3H), 2.81 (t, J = 6.2 Hz, 2H), 1.93 - 1.73 (m, 4H); ^{13}C NMR (126 MHz, DMSO) δ 163.50, 160.27, 153.31, 150.55, 135.81, 135.11, 131.86, 131.49, 125.28, 122.45, 119.96, 116.00, 112.81, 32.79, 27.62, 21.69, 21.32; $C_{21}H_{20}N_3O$ [M + H]$^+$的 HRMS (ESI)m/z计算值330.1606,实测值330.1606。

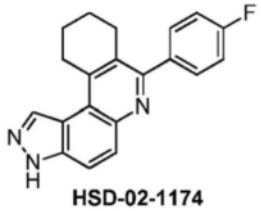
[0435] 7-(4-羟基苯基)-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-2-羧酸甲酯

[0436] 

HSD-02-1173

方法A：黄色固体 (146 mg, 39%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 9.79 (s, 1H), 7.83 (t, J = 7.1 Hz, 2H), 7.71 (d, J = 2.3 Hz, 1H), 7.42 (dd, J = 8.6, 2.3 Hz, 2H), 6.90 (dd, J = 8.4, 2.2 Hz, 2H), 3.35 - 3.32 (m, 8H), 2.77 (t, J = 6.1 Hz, 2H), 2.02 - 1.92 (m, 2H), 1.78 - 1.65 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 161.47, 158.28, 155.16, 135.67, 131.12, 129.38,126.63,122.76,119.77,118.05,115.31,112.07,30.25,29.02,22.48,22.24; $C_{23}H_{23}N_2O_3$[M+H]$^+$的HRMS(ESI)m/z计算值375.1709,实测值375.1711。

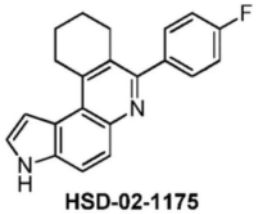
[0437] 7-(4-氟苯基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0438] 

HSD-02-1174

方法A：灰白色固体 (190 mg, 59%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.80 (s, 1H), 8.24 (d, J = 9.1 Hz, 1H), 8.20 (d, J = 9.2 Hz, 1H), 7.85 - 7.77 (m, 2H), 7.52 - 7.44 (m, 2H), 3.47 (t, J = 6.4 Hz, 2H), 2.76 (t, J = 6.2 Hz, 2H), 2.07 - 1.98 (m, 2H), 1.83 - 1.71 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 164.66, 162.69, 150.54, 132.78, 132.71, 131.76, 129.72, 123.29, 121.12, 116.26, 116.08, 114.93, 111.46,101.25,30.79,28.10,21.80,21.67; $C_{20}H_{21}FN_3$[M+H]$^{+1}$的HRMS(ESI)m/z计算值322.1720,实测值322.1724。

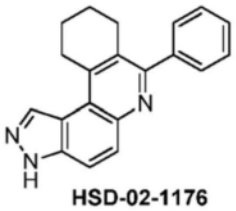
[0439] 7-(4-氟苯基)-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶

[0440] 

HSD-02-1175

方法A：灰白色固体 (144 mg, 45%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 11.76 (s, 1H), 7.78 (dd, J = 8.9, 0.8 Hz, 1H), 7.63 (d, J = 8.8 Hz, 1H), 7.61 - 7.54 (m, 2H), 7.49 (t, J = 2.8 Hz, 1H), 7.32 - 7.24 (m, 2H), 7.12 (ddd, J = 3.1, 2.0, 0.9 Hz, 1H), 3.38 (t, J = 6.5 Hz, 2H), 2.74 (t, J = 6.1 Hz, 2H), 2.01 - 1.92 (m, 2H), 1.72 (ddd, J = 9.0, 7.1, 4.1 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 163.08, 161.14, 154.88, 143.35, 142.44, 138.19, 133.25, 131.61, 131.54, 127.45, 124.06, 123.98, 122.53,120.32,116.56,115.24,115.07,106.29,29.96,29.06,22.84,22.53; $C_{21}H_{22}FN_2$[M+H]+的HRMS(ESI)m/z计算值321.1767,实测值321.1768。

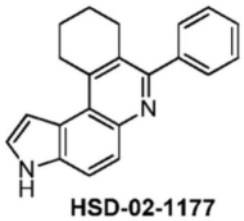
[0441] 7-苯基-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶

[0442] 

HSD-02-1176

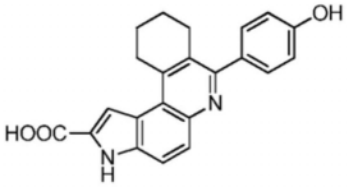
方法A：灰白色固体 (235 mg, 78%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.56 (s, 1H), 7.84 (dd, J = 9.1, 0.9 Hz, 1H), 7.80 (d, J = 9.1 Hz, 1H), 7.54 - 7.51 (m, 2H), 7.48 - 7.44 (m, 2H), 7.44 - 7.39 (m, 1H), 3.29 (t, J = 6.5 Hz, 2H), 2.74 (t, J = 6.1 Hz, 2H), 2.02 - 1.91 (m, 2H), 1.77 - 1.64 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 156.89, 143.73, 142.34, 141.33, 139.70, 135.12, 129.62, 129.45, 129.22, 128.39, 128.15, 121.89, 116.26, 115.24, 29.64, 28.95, 22.59, 22.49; $C_{20}H_{18}N_3$ [M + H]$^+$的 HRMS(ESI)m/z计算值300.1501,实测值300.1501。

[0443] 7-苯基-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶

[0444] 
HSD-02-1177

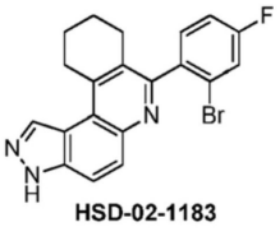
方法A：黄色固体 (180 mg, 60%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.19 (d, J = 8.9 Hz, 1H), 7.84 (d, J = 8.9 Hz, 1H), 7.72 (d, J = 3.2 Hz, 1H), 7.69 (s, 5H), 7.42 (d, J = 3.1 Hz, 1H), 3.71 (t, J = 6.5 Hz, 2H), 2.87 (t, J = 6.3 Hz, 2H), 2.16 (p, J = 6.3 Hz, 3H), 1.92 (p, J = 6.1 Hz, 2H). ^{13}C NMR (126 MHz, MeOD) δ 154.99, 150.08, 133.99, 133.82, 132.55, 130.58, 129.45, 128.93, 128.81, 126.02, 123.68, 120.84, 120.09, 112.92, 106.45, 31.23, 27.74, 21.57, 21.19; $C_{21}H_{21}N_2$ $[M+H]^+$的HRMS(ESI)m/z计算值301.1705,实测值301.1713。

[0445] 7-(4-羟基苯基)-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-2-羧酸

[0446] 
HSD-02-1178

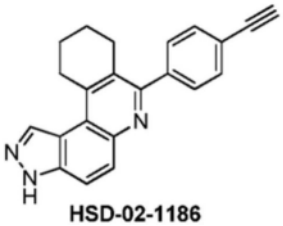
方法A：黄色固体 (220 mg, 61%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 10.44 (s, 1H), 8.29 - 7.84 (m, 2H), 7.77 - 7.44 (m, 3H), 7.06 (d, J = 8.2 Hz, 2H), 3.56 - 3.32 (m, 2H), 2.94 - 2.62 (m, 2H), 2.14 - 1.89 (m, 2H), 1.75 - 1.55 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 162.48, 160.31, 153.04, 150.98, 135.29, 131.99, 130.84, 129.33, 123.31, 122.54, 121.26, 121.09, 119.04, 117.85, 115.91, 111.63, 31.11, 28.30, 21.81, 21.55; $C_{22}H_{21}N_2O_3$[M+H]$^+$的HRMS(ESI)m/z计算值361.1552,实测值361.1552。

[0447] 7-(2-溴-4-氟苯基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0448] 
HSD-02-1183

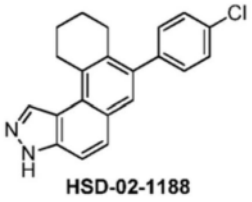
方法A：灰白色固体 (163 mg, 41%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.56 (s, 1H), 7.84 (s, 2H), 7.55 (dd, J = 8.5, 2.6 Hz, 1H), 7.42 (dd, J = 8.5, 5.9 Hz, 1H), 7.29 (td, J = 8.4, 2.6 Hz, 1H), 3.36 - 3.29 (m, 1H), 2.66 - 2.44 (m, 2H), 2.06 - 1.98 (m, 2H), 1.89 - 1.79 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 163.31(J = 250.74 Hz), 155.51, 143.71, 142.87, 137.54, 135.92, 131.53, 131.46, 130.07, 128.21, 122.77, 122.69, 122.62, 119.51, 119.32, 114.72, 114.55, 29.42, 27.22, 22.02, 21.75; $C_{20}H_{18}BrFN_3$ $[M+H]^+$的 HRMS (ESI) m/z计算值398.0668,实测值398.0673。

[0449] 7-(4-乙炔基苯基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0450] 
HSD-02-1186

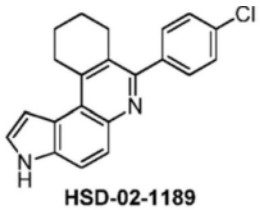
方法A：灰白色固体 (160 mg, 49%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 8.54 (d, J = 1.0 Hz, 1H), 7.88 - 7.84 (m, 1H), 7.79 (d, J = 9.1 Hz, 1H), 7.64 (t, J = 1.7 Hz, 1H), 7.58 (dt, J = 7.6, 1.5 Hz, 1H), 7.54 (dt, J = 7.7, 1.4 Hz, 1H), 7.47 (t, J = 7.7 Hz, 1H), 4.21 (s, 1H), 3.25 (t, J = 6.6 Hz, 2H), 2.73 (t, J = 6.2 Hz, 2H), 1.99 - 1.92 (m, 2H), 1.70 (tdd, J = 9.0, 5.6, 2.8 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 155.63, 143.76, 142.49, 141.73, 139.83, 135.09, 132.65, 131.45,130.16,129.47,129.13,128.86,122.07,121.97,116.19,115.47,83.85,81.41, 29.63,28.83,22.52,22.45;$C_{22}H_{20}N_3$[M+H]$^+$的HRMS(ESI)m/z计算值326.1657,实测值326.1659。

[0451] 7-(4-氯苯基)-8,9,10,11-四氢-3H-萘并[1,2-e]吲唑

[0452] 
HSD-02-1188

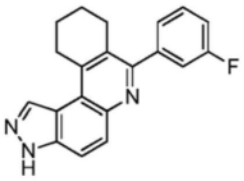
方法A：灰白色固体 (171 mg, 51%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.54 (s, 1H), 7.85 (d, J = 9.1 Hz, 1H), 7.81 (d, J = 9.1 Hz, 1H), 7.61 - 7.55 (m, 2H), 7.55 - 7.47 (m, 2H), 3.30 (t, J = 6.5 Hz, 2H), 2.74 (t, J = 6.1 Hz, 2H), 2.01 - 1.91 (m, 2H), 1.76 - 1.66 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 155.62, 143.60, 143.11, 142.56, 140.08, 138.71, 136.38, 134.90, 133.05, 131.42, 129.61, 129.49, 129.30, 128.62, 128.43, 121.95, 116.41, 114.51, 29.67, 28.86, 22.54, 22.47; $C_{20}H_{19}ClN_3$[M+H]$^+$的HRMS(ESI)m/z计算值336.1268,实测值336.1271。

[0453] 7-(4-氯苯基)-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶

[0454] 
HSD-02-1189

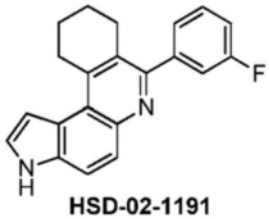
方法 A: 灰白色固体 (180 mg, 54%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 7.75 (d, J = 45.8 Hz, 2H), 7.46 (d, J = 32.4 Hz, 5H), 7.20 (s, 1H), 3.50 (s, 2H), 2.74 (s, 2H), 2.06 (s, 2H), 1.83 (s, 2H); ^{13}C NMR (126 MHz, MeOD) δ 154.78, 143.91, 142.58, 139.60, 133.67, 133.29, 130.38, 127.99, 127.27, 122.84, 121.93, 120.21, 116.07, 105.77, 29.93, 28.51, 22.42, 22.09; $C_{21}H_{20}ClN_2$ $[M+H]^+$的 HRMS (ESI) m/z 计算值 335.1315, 实测值 335.1322。

[0455] 7-(3-氟苯基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0456] 
HSD-02-1190

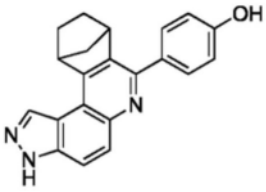
方法 A: 灰白色固体 (195 mg, 61%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.56 (s, 1H), 7.85 (dd, J = 9.1, 0.9 Hz, 1H), 7.79 (d, J = 9.1 Hz, 1H), 7.50 (td, J = 8.0, 6.1 Hz, 1H), 7.42 - 7.36 (m, 2H), 7.30 - 7.22 (m, 1H), 3.27 (t, J = 6.5 Hz, 2H), 2.75 (t, J = 6.1 Hz, 2H), 2.01 - 1.92 (m, 2H), 1.78 - 1.66 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 163.27, 161.33, 155.43, 143.69, 143.64, 142.56, 130.42, 130.36, 129.58, 129.19, 125.72, 122.10, 116.43, 116.26, 116.19, 115.11, 114.94, 29.63, 28.75, 22.52,22.43;$C_{20}H_{19}FN_3$[M+H]$^+$的HRMS(ESI)m/z计算值320.1563,实测值320.1569。

[0457] 7-(3-氟苯基)-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶

[0458] 
HSD-02-1191

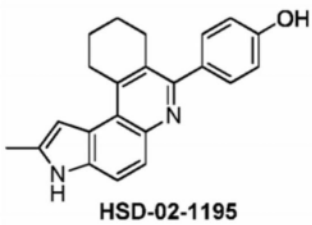
方法 A: 灰白色固体 (160 mg, 50%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 7.78 (ddd, J = 8.9, 2.1, 0.8 Hz, 1H), 7.69 (dd, J = 8.9, 3.8 Hz, 1H), 7.55 - 7.42 (m, 2H), 7.41 (dd, J = 3.1, 1.2 Hz, 1H), 7.29 (dt, J = 7.6, 1.2 Hz, 1H), 7.26 - 7.16 (m, 1H), 7.17 (dd, J = 3.2, 1.0 Hz, 1H), 3.50 - 3.41 (m, 2H), 2.71 (t, J = 6.3 Hz, 2H), 2.07 - 1.96 (m, 2H), 1.82 - 1.72 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 163.57(J = 245.70 Hz), 154.58, 143.91, 143.32, 142.54, 133.29, 130.38, 129.74, 129.68, 127.97, 127.14, 124.73, 122.96, 122.84, 121.97, 120.21, 116.09, 115.71, 115.54,114.41,114.24,105.80,29.89,28.41,22.39,22.03;$C_{21}H_{20}FN_2$[M+H]$^+$的HRMS(ESI)m/z计算值319.1611,实测值319.1618。

[0459] 4-(8,9,10,11-四氢-3H-8,11-甲基吡唑并[4,3-a]菲啶-7-基)苯酚1193

[0460] 
HSD1193

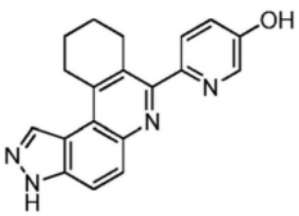
方法 C: 灰白色固体 (82 mg, 25%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 8.64 (s, 1H), 7.97 - 7.90 (m, 1H), 7.80 (d, J = 9.2 Hz, 1H), 7.62 (d, J = 8.4 Hz, 2H), 6.97 (d, J = 8.4 Hz, 2H), 4.34 (s, 1H), 3.76 (s, 1H), 2.33 - 2.18 (m, 2H), 1.93 (d, J = 9.4 Hz, 1H), 1.77 (d, J = 9.0 Hz, 1H), 1.44 - 1.31 (m, 2H). ^{13}C NMR (126 MHz, MeOD) δ 157.96, 153.18, 150.46, 144.56, 139.98, 138.03, 134.29, 130.56, 130.03, 128.51, 116.16, 114.92, 113.81, 49.47, 43.72, 42.28, 26.38, 24.64. $C_{21}H_{18}N_3O$[M+H]$^+$的HRMS(ESI)m/z计算值328.1450,实测值328.1450。

[0461] 4-(2-甲基-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯酚

[0462] 
HSD-02-1195

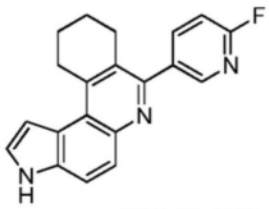
方法 A: 灰白色固体 (135 mg, 41%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 7.66 (d, J = 8.9 Hz, 1H), 7.61 (d, J = 8.9 Hz, 1H), 7.34 - 7.29 (m, 2H), 6.93 - 6.88 (m, 2H), 6.85 (s, 1H), 3.42 (t, J = 6.6 Hz, 2H), 2.73 (t, J = 6.3 Hz, 2H), 2.53 (s, 3H), 2.06 - 1.97 (m, 2H), 1.83 - 1.73 (m, 2H); ^{3}C NMR (126 MHz, MeOD) δ 157.11, 155.96, 143.48, 142.28, 133.63, 133.06, 132.20, 129.97, 127.27, 122.10, 121.13, 120.58, 115.11, 114.50, 103.96, 29.91, 28.69, 22.53, 22.23, 12.07; $C_{22}H_{23}N_2O$ $[M+H]^+$的 HRMS (ESI) m/z 计算值331.1810,实测值331.1813。

[0463] 6-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)吡啶-3-醇

[0464] 
HSD-02-1196

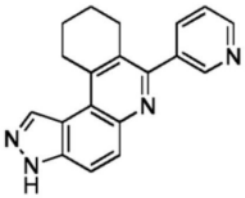
方法 A: 灰白色固体 (124 mg, 39%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 8.57 (s, 1H), 8.22 (d, J = 2.8 Hz, 1H), 7.90 (d, J = 9.8 Hz, 1H), 7.83 (d, J = 9.0 Hz, 1H), 7·55 (d, J = 8.4 Hz, 1H), 7·41 (dd, J = 8.5, 2.8 Hz, 1H), 3.38 (s, 2H), 2.82 (t, J = 6.2 Hz, 2H), 2.12 - 2.04 (m, 2H), 1.89 - 1.80 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 154.85, 154.08, 149.15, 143.75, 142.80, 138.71, 136.11, 135.86, 130.19, 128.51, 125.23, 123.37, 122.48, 116.10, 113.81, 29.62, 27.62, 22.09, 21.91; $C_{19}H_{17}N_4O$ [M + H]$^+$的HRMS (ESI) m/z计算值317.1402,实测值317.1397。

[0465] 7-(6-氟代吡啶-3-基)-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶

[0466] 
HSD-02-1197

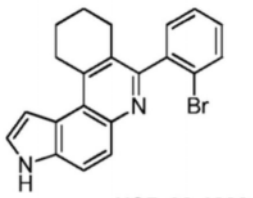
方法 A: 灰白色固体 (201 mg, 61%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 8.31 (d, J = 2.4 Hz, 1H), 8.04 (td, J = 8.0, 2.5 Hz, 1H), 7.78 (d, J = 8.9 Hz, 1H), 7.68 (d, J = 8.9 Hz, 1H), 7.40 (d, J = 3.1 Hz, 1H), 7.17 (dd, J = 8.4, 2.3 Hz, 1H), 7.12 (d, J = 3.1 Hz, 1H), 3.36 (t, J = 6.5 Hz, 2H), 2.66 (t, J = 6.2 Hz, 2H), 1.95 (ddt, J = 12.5, 9.1, 4.6 Hz, 2H), 1.79 - 1.71 (m, 2H). ^{13}C NMR (126 MHz, MeOD) δ 164.07, 162.16, 151.30, 147.35, 147.24, 144.14, 142.80, 142.65, 142.58, 134.95, 134.91, 133.32, 127.42, 123.11, 122.96, 122.05, 120.13, 116.37,116.32,108.83,108.54,105.95,105.90,29.82,28.39,22.24,21.95;$C_{20}H_{19}FN_3$[M+H]$^+$的HRMS(ESI)m/z计算值320.1563,实测值320.1566。

[0467] 7-(吡啶-3-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0468] 
HSD1199

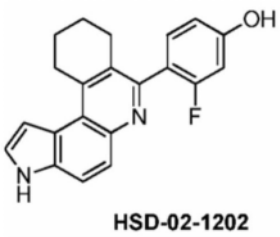
方法 A: 灰白色固体 (135 mg, 45%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 9.06 (s, 2H), 8.73 (s, 1H), 8.42 (d, J = 7.3 Hz, 1H), 8.11 (d, J = 8.4 Hz, 1H), 7.96 (d, J = 8.8 Hz, 2H), 3.55 - 3.46 (m, 2H), 2.95 - 2.81 (m, 2H), 2.20 - 2.08 (m, 2H), 1.99 - 1.84 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 150.86, 148.85, 148.27, 147.36, 140.15, 138.36, 131.44, 123.81, 122.94, 119.15, 115.51, 30.47, 27.89, 21.51, 21.42; $C_{19}H_{17}N_4$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 301.1453, 实测值 301.1453。

[0469] 7-(2-溴苯基)-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶

[0470] 
HSD-02-1200

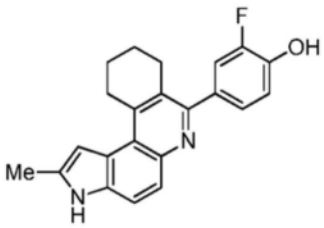
方法 A: 灰白色固体 (223 mg, 59%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 7.81 (dd, J = 8.9, 0.8 Hz, 1H), 7.73 (dd, J =8.5, 1.2 Hz, 1H), 7.69 (d, J = 8.9 Hz, 1H), 7.51 (td, J =7.5, 1.2 Hz, 1H), 7.44 (d, J = 3.1 Hz, 1H), 7.40 - 7.36 (m, 2H), 7.21 (dd, J = 3.2, 0.9 Hz, 1H), 3.50 (td, J = 6.4, 1.4 Hz, 2H), 2.57 (ddt, J = 68.3, 17.0, 6.3 Hz, 2H), 2.08 - 1.98 (m, 2H), 1.92 - 1.78 (m, 2H). ^{13}C NMR (126 MHz, MeOD) δ 155.07, 143.75, 142.37, 141.72, 133.32, 132.31, 130.23, 130.19, 129.54, 129.50, 127.66, 127.44, 123.14, 122.89, 122.52, 121.82, 120.27, 116.01, 105.69, 29.80, 27.36,22.39,21.88;$C_{21}H_{20}BrN_2$[M+H]$^+$的HRMS(ESI)m/z计算值379.0810,实测值379.0817。

[0471] 3-氟-4-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯酚

[0472] 
HSD-02-1202

方法 A: 灰白色固体 (184 mg, 55%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 11.65 (s, 1H), 9.02 (d, J = 8.9 Hz, 1H), 8.80 (d, J = 9.0 Hz, 1H), 8.60 (s, 1H), 8.34 (t, J = 8.5 Hz, 1H), 8.13 (s, 1H), 7.72 (d, J = 8.1 Hz, 2H), 4.37 (s, 2H), 3.52 (d, J = 6.3 Hz, 2H), 2.93 - 2.78 (m, 2H), 2.61 (s, 2H). ^{13}C NMR (126 MHz, MeOD) δ 163.03, 162.14, 160.18, 134.61, 133.62, 131.43, 127.83, 124.37, 122.33, 120.67, 113.54, 107.72, 104.37, 104.18, 31.98, 28.02, 22.84, 22.19; $C_{21}H_{20}FN_2O$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 335.1560, 实测值 335.1566。

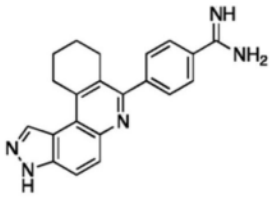
[0473] 2-氟-4-(2-甲基-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯酚

[0474] 

HSD 02-1203

方法 A: 灰白色固体 (164 mg, 47%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 7.66 (d, J = 8.9 Hz, IH), 7.61 (d, J = 8.9 Hz, 1H), 7.20 (dd, J = 11.8, 2.0 Hz, 1H), 7.13 - 7.08 (m, 1H), 7.05 - 7.00 (m, 1H), 6.84 (s, 1H), 3.39 (t, J = 6.5 Hz, 2H), 2.72 (t, J = 6.2 Hz, 2H), 2.52 (s, 3H), 2.04 - 1.94 (m, 2H), 1.82 " 1.70 (m, 2H); ^{13}C NMR (126 MHZ, MeOD) δ 154.57, 152.03, 150.11, 144.90, 143.84, 142.21, 133.78, 133.12, 132.62, 127.08, 125.12, 122.26, 121.10, 120.50, 117.06, 116.55, 116.40, 115.35, 104.03, 29.91, 28.58, 22.44, 22.15, 12.08; $C_{22}H_{22}FN_2O$ [M + H]$^+$法人 HRMS (ESI) m/z 计算值349.1716,实测值349.1720。

[0475] 4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苄脒盐酸盐

[0476] 

HSD-02-1204

方法 A: 灰白色固体 (172 mg, 50%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 9.69 (s, 2H), 9.47 (s, 2H), 8.71 (s, 1H), 8.16 - 8.06 (m, 4H), 7.94 (d, J = 8.0 Hz, 2H), 3.42 - 3.33 (m, 2H), 2.76 (t, J = 6.2 Hz, 2H), 2.07 - 1.97 (m, 2H), 1.81 - 1.65 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 165.63, 151.52, 140.26, 134.84, 130.64, 130.34, 129.16, 128.63, 123.10, 115.22, 30.40, 28.25, 21.97, 21.83; $C_{21}H_{22}N_5$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 344.1875, 实测值 344.1879。

[0477] N-羟基-4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯甲脒

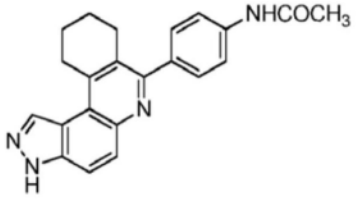
[0478]

HSD-02-1115 HSD-02-1207

[0479] 在DMSO(3mL)的$NH_2OH.H_2O$(1.5当量)溶液中,在0℃下缓慢加入KOtBut(3当量),并将悬浮液搅拌30分钟。向混合物中加入4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苄腈(0.5mmol),并在室温下继续反应4小时。反应完成后,向反应混合物中加入冷水,过滤得到的沉淀物,用水洗涤并干燥。用乙醇重结晶固体,得到所需产物。

[0480] 灰白色固体(162mg,90%)。^{1}H NMR(500MHz,DMSO-d_6)δ9.71(s,1H),8.56(s,1H),7.88-7.82(m,2H),7.79-7.76(m,2H),7.59-7.54(m,2H),5.89(s,2H),2.79(t,J=6.1Hz,2H),2.00(ddt,J=9.3,6.5,3.1Hz,2H),1.74(tt,J=8.6,5.4Hz,2H);^{13}C NMR(126MHz,DMSO)δ156.48,151.11,145.66,143.64,142.45,141.74,138.70,136.39,133.15,129.67,129.32,125.43,121.88,116.46,114.44,29.69,28.96,22.60,22.52;$C_{21}H_{22}N_5O$[M+H]$^+$的HRMS(ESI)m/z计算值360.1824,实测值360.1827。

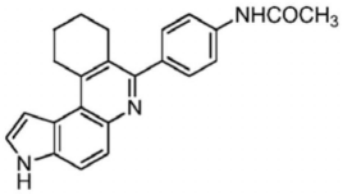
[0481] N-(4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯基)乙酰胺

[0482] 

HSD 02-1209

方法 A: 灰白色固体 (201 mg, 51%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 10.08 (s, 1H), 8.50 (s, 1H), 7.81 (s, 2H), 7.70 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.5 Hz, 2H), 3.24 (t, J = 6.0 Hz, 2H), 2.75 (t, J = 6.1 Hz, 2H), 2.08 (s, 3H), 1.96 - 1.89 (m, 2H), 1.67 (tt, 7 = 8.3, 5.4 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 168.87, 156.52, 143.62, 142.22, 139.37, 138.62, 136.27, 135.92, 129.99, 129.62, 129.35, 121.66, 118.79, 116.48, 114.22, 29.63, 29.05, 24.54, 22.59, 22.54; $C_{22}H_{23}N_4O$[M+H]$^+$的HRMS(ESI)m/z计算值359.1872,实测值359.1875。

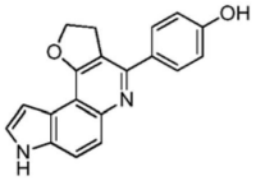
[0483] 4-(3,8-二氢-2H-呋喃并[3,2-c]吡咯并[3,2-f]喹啉-4-基)苯酚

[0484] 

HSD 02-1210

方法 A: 灰白色固体 (171 mg, 48%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 11.74 (t, J = 2.4 Hz, 1H), 10.05 (s, 1H), 7.78 (d, J = 8.8 Hz, 1H), 7.68 (d, J = 8.3 Hz, 2H), 7.63 (d, J = 8.8 Hz, 1H), 7.51 - 7.46 (m, 3H), 7.10 (d, J = 2.8 Hz, 1H), 3.38 - 3.35 (m, 2H), 2.77 (t, J = 6.2 Hz, 2H), 2.08 (s, 3H), 1.99 - 1.92 (m, 2H), 1.71 (ddt, J = 12.3, 9.5, 4.4 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 168.82, 155.57, 143.41, 142.25, 139.16, 136.45, 133.19, 129.95, 127.55, 124.10, 123.88, 122.36, 120.37, 118.76,116.42,106.27,29.98,29.18,24.55,22.90,22.61;$C_{23}H_{24}N_3O[M+H]^+$的HRMS(ESI)m/z计算值358.1919,实测值358.1922。

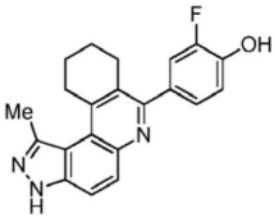
[0485] 4-(3,8-二氢-2H-呋喃并[3,2-c]吡咯并[3,2-f]喹啉-4-基)苯酚

[0486] 

HSD 02-1211

方法 B: 灰白色固体 (76 mg, 25%)。 ^{1}H NMR (500 MHz, 甲醇- d_4) δ 8.62 (s, 1H), 7.77 (d, J = 9.0 Hz, 1H), 7.67 (d, J = 9.0 Hz, 1H), 7.42 - 7.32 (m, 3H), 7.11 (d, J = 3.0 Hz, 1H), 6.96 - 6.89 (m, 2H), 3.71 (t, J =7.1 Hz, 2H), 3.07 (t, J = 7.1 Hz, 2H); ^{13}C NMR (126 MHz, MeOD) δ 157.38, 156.71, 133.00, 132.35, 131.76, 130.10, 129.51, 123.71, 122.39, 121.62, 120.57, 116.48, 114.65, 106.36, 100.91, 61.71, 35.83; $C_{19}H_{17}N_2O_2$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 305.1290, 实测值305.1299。

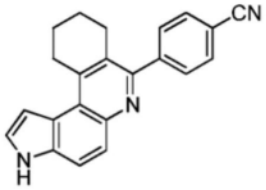
[0487] 2-氟-4-(1-甲基-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0488] 

HSD 02-1213

方法 A: 灰白色固体 (157 mg, 45%)。 ^{1}H NMR (500 MHz, 甲醇-d_4) δ 7.76 (s, 1H), 7.71 (d, J = 8.6 Hz, 1H), 7.21 (d, J = 11.7 Hz, 1H), 7.12 (d, J = 8.4 Hz, 1H), 7.04 (t, J = 8.5 Hz, 1H), 3.51 - 3.40 (m, 2H), 2.89 (s, 3H), 2.84 - 2.76 (m, 2H), 1.92 - 1.80 (m, 4H); C NMR (126 MHz, MeOD) δ 157.03, 155.85, 152.11, 150.19, 144.98, 143.53, 132.05, 128.98, 128.70, 125.04, 123.95, 117.20, 116.48, 116.32, 113.04, 31.86, 27.70, 22.03, 21.87; $C_{21}H_{21}FN_3O$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 350.1669, 实测值 350.1677。

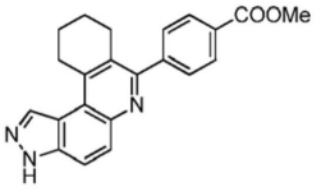
[0489] 4-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯甲腈

[0490] 

HSD 02-1214

方法 A: 灰白色固体 (195 mg, 60%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 11.80 (s, 1H), 7.92 (d, J = 8.5 Hz, 1H), 7.81 (dd, J = 8.9, 0.8 Hz, 1H), 7.75 (d, J = 8.9 Hz, 2H), 7.64 (d, J = 8.9 Hz, 1H), 7.51 (t, J = 2 J.8 = Hz, 1H), 7.15 - 7.11 (m, 1H), 3.38 (t, J = 6.1 Hz, 2H), 2.73 (t, J = 6.1 Hz, 2H), 2.00 - 1.93 (m, 3H), 1.76 - 1.68 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 154.08, 146.45, 143.42, 142.77, 133.40, 132.39, 130.61, 127.28, 124.14, 124.07, 122.82, 120.26, 119.41, 116.85, 110.74, 106.41, 29.95, 28.81, 22.76, 22.41; $C_{22}H_{20}N_3[M+H]^+$的HRMS(ESI)m/z计算值326.1657,实测值326.1662。

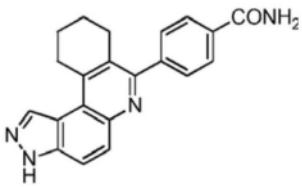
[0491] 4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯甲酸甲酯

[0492] 

HSD 02-1215

方法 A: 灰白色固体 (198 mg, 55%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.69 (s, 1H), 8.14 (dd, J = 10.7, 7.0 Hz, 4H), 7.87 (d, J = 7.6 Hz, 2H), 3.90 (s, 3H), 3.35 (d, J = 6.2 Hz, 2H), 2.73 (t, J = 5. J8 Hz, 2H), 2.06 - 1.96 (m, 2H), 1.75 (d, J = 7.1 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 166.53, 155.59, 145.92, 143.71, 142.57, 138.77, 136.40, 130.03, 129.92, 129.65, 129.55, 129.25, 129.09, 122.12, 116.33, 114.56, 52.63, 29.59, 28.75, 22.48, 22.38; $C_{22}H_{22}N_3O_2$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 360.1712, 实测值360.1718。

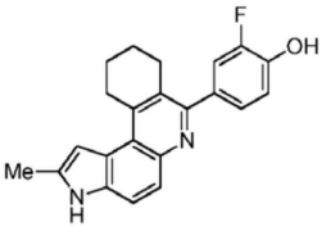
[0493] 4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯甲酰胺

[0494] 

HSD 02-1217

方法A: 灰白色固体 (172 mg, 50%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.60 (s, 1H), 8.05 (s, 1H), 7.97 (d, J = 8.0 Hz, 2H), 7.86 (d, J = 9.1 Hz, 1H), 7.81 (d, J = 9.1 Hz, 1H), 7.63 (d, J = 8.0 Hz, 2H), 7.41 (s, 1H), 3.39 - 3.34 (m, 2H), 2.77 (t, J = 6.1 Hz, 2H), 2.04 - 1.98 (m, 2H), 1.79 - 1.69 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 168.13, 156.17, 144.02, 143.77, 142.55, 133.95, 129.63, 129.40, 129.29, 127.64, 122.07, 116.23, 29.68, 28.86, 22.58, 22.49; $C_{21}H_{21}N_4O$ $[M+H]^+$ 的 HRMS (ESI) m/z 计算值 345.1715, 实测值 345.1719。

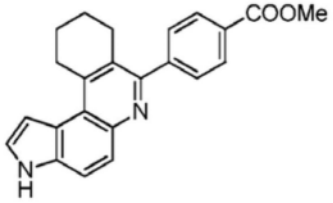
[0495] 4-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯甲酸甲酯

[0496] 

HSD 02-1218

方法A: 灰白色固体 (105 mg, 30%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 7.68 (dd, J = 8.9, 0.8 Hz, 1H), 7.62 (d, J = 8.9 Hz, 1H), 7.22 (dd, J = 11.8, 2.0 Hz, 1H), 7.13 (ddd, J = 8.2, 2.1, 0.9 Hz, 1H), 7.03 (dt, J = 8.9, 8.2 Hz, 1H), 6.87 (s, 1H), 3.48 - 3.40 (m, 2H), 2.76 (t, J = 6.2 Hz, 2H), 2.54 (s, 3H), 2.07 - 1.99 (m, 2H), 1.86 - 1.75 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 154.38, 152.03 (J = 241.92 Hz), 144.97, 144.23, 141.91, 133.92, 133.16, 132.30, 127.16, 125.13, 122.28, 121.10, 120.18, 117.07, 116.57, 116.41, 115.50, 104.05, 29.98, 28.55, 22.44, 22.14, 12.07; $C_{22}H_{22}FN_2O$ $[M+H]^+$的HRMS(ESI)m/z计算值349.1716,实测值349.1717。

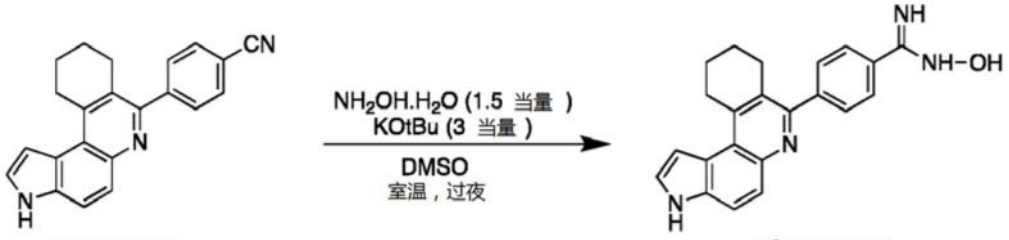
[0497] 4-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯甲酸甲酯

[0498] 

HSD 02-1219

方法A: 灰白色固体 (179 mg, 50%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 12.38 (s, 1H), 8.13 (d, J = 8.0 Hz, 2H), 8.08 (d, J = 8.7 Hz, 1H), 7.92 (d, J = 8.9 Hz, 1H), 7.82 (d, J = 8.0 Hz, 2H), 7.69 (t, J = 2.7 Hz, 1H), 7.25 - 7.22 (m, 1H), 3.90 (s, 3H), 3.48 (t, J = 6.5 Hz, 2H), 2.72 (t, J = 6.2 Hz, 2H), 2.06 - 1.94 (m, 2H), 1.85 - 1.67 (m, 3H); ^{13}C NMR (126 MHz, DMSO) δ 166.31, 150.76, 140.46, 137.32, 133.66, 130.77, 130.49, 130.13, 129.56, 129.56, 129.45, 128.64, 126.02, 123.33, 119.96, 117.68, 106.71,52.90,30.82,28.26,22.22,21.82;$C_{23}H_{23}N_2O_2$[M+H]$^+$的HRMS(ESI)m/z计算值359.1760,实测值359.1767。

[0499] N-羟基-4-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯甲脒

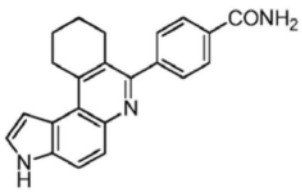
[0500] 

HSD-02-1214 HSD-02-1220

[0501] 按照1207的一般步骤进行合成。灰白色固体(163mg,91%);^{1}H NMR(500MHz,DMSO-d_6)δ11.76(d,J=2.3Hz,1H),9.69(s,1H),7.78(t,J=8.9Hz,3H),7.63(d,J=8.8Hz,1H),7.56-7.52(m,2H),7.49(t,J=2.8Hz,1H),7.13(d,J=2.5Hz,1H),5.86(s,2H),3.39(t,J=6.5Hz,3H),2.77(t,J=6.2Hz,2H),2.01-1.92(m,2H),1.79-1.69(m,2H).^{3}C NMR(126MHz,DMSO)δ155.44,151.17,143.41,142.38,142.28,133.25,132.92,129.31,127.45,125.38,124.12,123.98,122.52,120.34,116.54,106.31,29.97,29.08,22.87,22.54;$C_{22}H_{23}N_4O$[M+

H]$^+$的HRMS(ESI)m/z计算值359.1872,实测值359.1872。

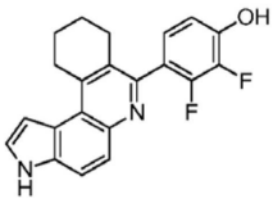
[0502] 4-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯甲酰胺

[0503] 

HSD 02-1221

方法A: 灰白色固体 (147 mg, 43%); ^{1}H NMR (500 MHz, DMSO- d_6) δ 11.77 (t, J = 2.3 Hz, 1H), 8.05 (s, 1H), 7.97 (d, J = 8.3 Hz, 2H), 7.79 (d, J = 8.9 Hz, 1H), 7.64 (d, J = 8.9 Hz, 1H), 7.61 (d, J = 8.2 Hz, 2H), 7.50 (t, J = 2.8 Hz, 1H), 7.41 (s, 1H), 7.13 (t, J = 2.5 Hz, 1H), 3.39 (t, J = 6.5 Hz, 2H), 2.75 (t, J = 6.1 Hz, 2H), 1.98 (q, J = 4.3, 3.0 Hz, 3H), 1.73 (ddt, J = 9.4, 6.5, 2.8 Hz, 2H). ^{13}C NMR (126 MHz, DMSO) δ 168.20, 155.18, 144.56, 143.40, 142.47, 133.73, 133.30, 129.39, 127.59, 127.40, 124.11, 124.02, 122.62, 120.33,116.62,106.34,29.97,28.98,22.84,22.50;$C_{22}H_{22}N_3O$[M+H]$^+$的HRMS(ESI)m/z计算值344.1763,实测值344.1769。

[0504] 2,3-二氟-4-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯酚

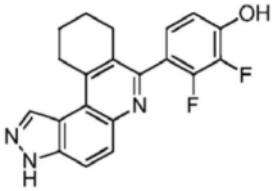
[0505] 

HSD 02-1222

方法A: 黄色固体 (166 mg, 47%)。 ^{1}H NMR (500 MHz, DMSO- d_6) δ 11.40 (s, 1H), 8.23 (d, J = 8.9 Hz, 1H), 8.05 (d, J = 8.9 Hz, 1H), 7.80 (t, J = 2.9 Hz, 1H), 7.41 - 7.34 (m, 1H), 7.31 (t, J = 2.4 Hz, 1H), 7.15 (t, J = 8.2 Hz, 1H), 3.55 (t, J = 6.4 Hz, 2H), 2.72 (s, 2H), 2.13 - 1.96 (m, 2H), 1.81 (dd, J = 7.8, 4.1 Hz, 2H). ^{13}C NMR (126 MHz, DMSO) δ 149.88, 147.97, 147.88, 143.40, 141.12, 141.01, 139.18, 139.07, 134.54, 133.83, 130.60, 127.12, 126.30, 123.79, 121.80, 119.78, 113.94, 111.57, 106.98, 31.22, 27.17, 21.96, 21.33;

$C_{21}H_{19}F_2N_2O$[M+H]$^+$的HRMS(ESI)m/z计算值353.1465,实测值353.1468。

[0506] 2,3-二氟-4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

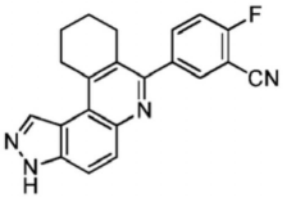
[0507] 

HSD 02-1223

方法A: 灰白色固体 (177 mg, 50%)。 ^{1}H NMR (500 MHz, DMSO- d_6) δ 10.56 (s, 1H), 8.56 (s, 1H), 7.92 - 7.76 (m, 2H), 7.05 (td, J = 8.2, 2.0 Hz, 1H), 6.90 (td, J = 8.3, 1.6 Hz, 1H), 3.32 (d, J = 7.6 Hz, 2H), 2.62 (t, J = 6.1 Hz, 2H), 1.96 (dt, J = 11.1, 5.9 Hz, 2H), 1.75 (p, J = 5. J8 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 151.48, 149.77, 147.83, 147.75, 147.03, 143.67, 142.40, 141.06, 140.95, 139.02, 138.74, 136.40, 130.47, 129.50, 125.40, 122.18, 120.81, 120.70, 116.39, 114.56, 113.32, 29.50, 27.48, 22.58, 22.19;

$C_{20}H_{16}F_2N_3O$[M+H]$^+$的HRMS(ESI)m/z计算值352.1261,实测值352.1256。

[0508] 2-氟-5-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯甲腈

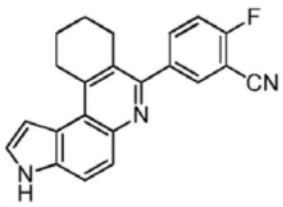
[0509] 

HSD 02-1224

方法A: 灰白色固体 (169 mg, 49%)。 ^{1}H NMR (500 MHz, DMSO- d_6) δ 8.52 (s, 1H), 8.14 (dd, J = 6.3, 2.3 Hz, 1H), 8.01 - 7.95 (m, 1H), 7.85 (d, J = 9.0 Hz, 1H), 7.81 (d, J = 9.3 Hz, 1H), 7.61 (t, J = 9.0 Hz, 1H), 3.26 (d, J = 6.7 Hz, 2H), 2.75 (t, J = 6.1 Hz, 2H), 2.03 - 1.92 (m, 2H), 1.79 - 1.68 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 163.50 (J =257.04 Hz), 153.77, 143.56, 142.81, 138.70, 137.36, 137.29, 136.44, 134.73, 129.49, 122.20, 116.85, 116.69, 116.30, 114.70, 114.42, 100.43, 100.31, 29.62, 28.60, 22.47, 22.40;

$C_{21}H_{18}F N_4$[M+H]$^+$的HRMS(ESI)m/z计算值345.1515,实测值345.1519。

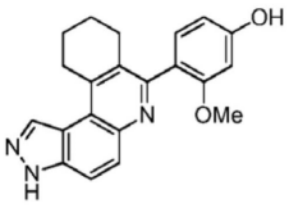
[0510] 2-氟-5-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯甲腈

[0511] 

HSD 02-1225

方法A：灰白色固体 (131 mg, 38%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 8.09 (dd, J = 6.1, 2.3 Hz, 1H), 8.04 (d, J = 9.0 Hz, 1H), 8.00 (ddd, J = 8.7, 5.1, 2.3 Hz, 1H), 7.78 (d, J = 9.0 Hz, 1H), 7.63 - 7.58 (m, 2H), 7.35 - 7.32 (m, 1H), 3.62 (t, 2H), 2.80 (t, J = 6.2 Hz, 2H), 2.13 - 2.09 (m, 2H), 1.93 - 1.87 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 164.50, 162.42, 149.33, 138.09, 136.46, 134.57, 133.67, 128.43, 124.75, 123.69, 120.09, 119.05, 117.10, 116.70, 116.53, 112.81, 106.28, 101.63, 30.66, 27.94, 21.86, 21.54; $C_{22}H_{19}FN_3$ [M + H]$^+$的HRMS(ESI)m/z计算值344.1563,实测值344.1565。

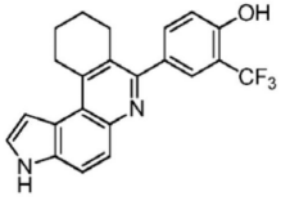
[0512] 3-甲氧基-4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0513] 

HSD 02-1228

方法A：灰白色固体 (87 mg, 25%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 9.59 (s, 1H), 8.53 (s, 1H), 7.84 - 7.74 (m, 2H), 6.97 (d, J = 8.1 Hz, 1H), 6.50 (d, J = 2.2 Hz, 1H), 6.45 (dd, J = 8.1, 2.2 Hz, 1H), 3.63 (s, 3H), 3.34 - 3.31 (m, 1H), 3.29 - 3.20 (m, 1H), 2.72 - 2.62 (m, 1H), 2.47 - 2.38 (m, 1H), 2.02 - 1.87 (m, 2H), 1.83 - 1.62 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 159.02, 157.89, 155.92, 143.53, 141.09, 138.58, 136.19, 131.12, 129.60, 121.67, 121.44, 116.57,113.84,107.41,99.24,55.49,29.45,27.19,22.74,22.27;$C_{21}H_{22}N_3O_2$[M+H]$^+$的HRMS(ESI)m/z计算值348.1712,实测值348.1717。

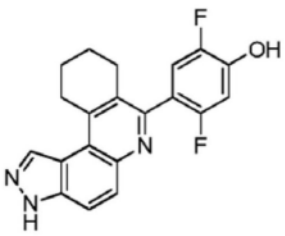
[0514] 4-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)-2-(三氟甲基)苯酚

[0515] 

HSD 02-1232

方法A：黄色固体 (219 mg, 57%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 11.75 (s, 1H), 10.73 (s, 1H), 7.78 (d, J = 8.9 Hz, 1H), 7.67 (dq, J = 3.7, 2.2 Hz, 2H), 7.63 (d, J = 8.8 Hz, 1H), 7.49 (t, J = 2.8 Hz, 1H), 7.14 - 7.08 (m, 2H), 3.37 (t, J = 6.6 Hz, 3H), 2.77 (t, J = 6.1 Hz, 2H), 2.03 - 1.93 (m, 2H), 1.78 - 1.68 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 155.74, 154.41, 143.42, 142.51, 134.89, 133.22, 132.30, 127.65, 127.50, 125.67(q, J = 273.42 Hz), 124.05, 123.95, 122.46, 120.32, 116.82, 116.55, 115.52, 115.28, 106.29, 29.99, 29.12, 22.83, 22.58;$C_{22}H_{20}F_3N_2O$[M+H]$^+$的HRMS(ESI)m/z计算值385.1528,实测值385.1530。

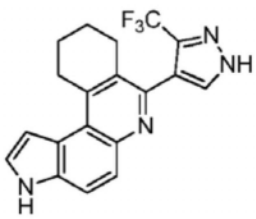
[0516] 2,5-二氟-4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0517] 

HSD 02-1233

方法A：灰白色固体 (159 mg, 45%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 8.57 (s, 1H), 7.86 (q, J = 9.1 Hz, 2H), 7.15 (dd, J = 10 J.8, 6.7 Hz, 1H), 6.81 (dd, J = 10.5, 7.1 Hz, 1H), 3.38 (s, 2H), 2.73 (s, 2H), 2.08 (p, J = 6.1 Hz, 2H), 1.86 (d, J = 9.8 Hz, 2H); ^{13}C NMR (126 MHz, MeOD) δ 156.74 (J = 239.16 Hz), 151.59, 148.92 (J = 238.14 Hz), 146.61, 143.45, 143.06, 138.67, 135.89, 130.94, 128.32, 122.39, 118.20, 116.93, 116.06, 113.85, 104.69, 29.48, 27.05, 22.11, 21.80; $C_{20}H_{218}F_2N_3O$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 354.1418, 实测值 354.1421。

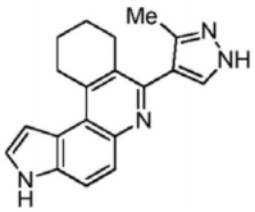
[0518] 7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶

[0519] 

HSD 02-1234

方法A：灰白色固体 (135 mg, 38%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 7.92 (s, 1H), 7.79 (d, J = 9.0 Hz, 1H), 7.71 - 7.65 (m, 1H), 7.45 - 7.40 (m, 1H), 7.18 (d, J = 3.2 Hz, 1H), 3.46 (t, J = 6.4 Hz, 2H), 2.65 (t, J = 6.3 Hz, 2H), 2.01 (dP, J = 9.8, 3.3 Hz, 2H), 1.85 (qd, J = 6.5, 3.2 Hz, 2H); ^{13}C NMR (126 MHz, MeOD) δ 146.73, 143.44, 142.52, 133.34, 130.08, 129.00, 123.12, 122.85, 121.93, 120.17, 119.38, 116.04, 105.77, 29.74, 27.88, 22.38, 21.90; $C_{19}H_{16}F_3N_4$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 357.1327, 实测值 357.1327。

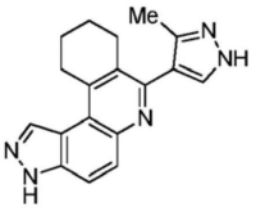
[0520] 7-(3-甲基-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶

[0521] 

HSD 02-1235

方法 A: 灰白色固体 (181 mg, 60%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.15 (d, J = 8.9 Hz, 1H), 8.09 - 8.02 (m, 1H), 7.74 (t, J = 2.9 Hz, 1H), 7.23 (t, 2.4 Hz, 1H), 3.46 (t, J = 6.4 Hz, 2H), 2.80 (t, J = 6.3 Hz, 2H), 2.30 (s, 3H), 2.03 - 1.94 (m, 2H), 1.84 - 1.74 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 144.36, 134.42, 133.65, 130.53, 126.80, 122.88, 120.88, 119.84, 113.93, 110.98, 106.60, 31.17, 27.69, 22.00, 21.57, 19.02; $C_{19}H_{19}N_4$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 303.1610, 实测值 303.1611。

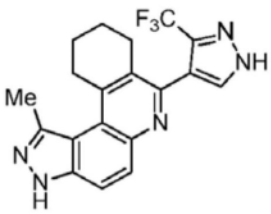
[0522] 1-甲基-7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0523] 

HSD 02-1236

方法 A: 灰白色固体 (179 mg, 59%)。 ^{1}H NMR (500 MHz, DMSO- d_6) δ 8.53 (s, 1H), 7.84 - 7.74 (m, 3H), 3.33 (s, 3H), 2.85 (t, J = 6.1 Hz, 2H), 2.33 (s, 2H), 2.00 - 1.97 (m, 2H), 1.81 - 1.77 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 151.10, 143.71, 141.83, 138.63, 136.21, 130.12,129.59, 121.02, 118.17, 116.48, 114.04, 29.70, 28.62, 22.63; $C_{18}H_{18}N_5$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 304.1562, 实测值 304.1565。

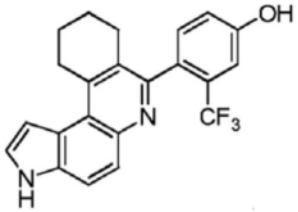
[0524] 1-甲基-7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0525] 

HSD 02-1237

方法 A: 灰白色固体 (150 mg, 42%)。^{1}H NMR (500 MHz, 甲醇 eh) δ 8.38 (d, J = 0.9 Hz, 1H), 8.19 (d, J = 9.2 Hz, 1H), 7.88 (d, J = 9.2 Hz, 1H), 3.84 - 3.71 (m, 2H), 3.04 (s, 3H), 2.83 - 2.80 (m, 2H), 2.00 - 1.98 (m, 4H); ^{13}C NMR (126 MHz, MeOD) δ 155.05, 144.54, 141.22, 140.08(q = 38 Hz), 135.79, 133.55, 132.43, 126.71, 124.45(q, J = 270 Hz), 123.66,120.18, 118.65, 112.60, 109.60, 33.05, 26.90, 21.14, 20.63, 17.53; $C_{18}H_{15}F_3N_5$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 358.1280, 实测值 358.1288。

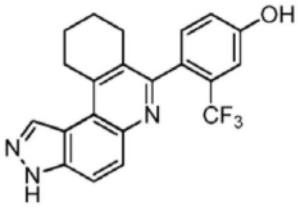
[0526] 4-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)-3-(三氟甲基)苯酚

[0527] 

HSD 02-1238

方法 A: 黄色固体 (154 mg, 40%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 7.78 (d, J = 9.0 Hz, 1H), 7.66 (d, J = 8.9 Hz, 1H), 7.40 (d, J = 3.0 Hz, 1H), 7.23 - 7.18 (m, 2H), 7.16 (d, J = 2.8 Hz, 1H), 7.11 (dd, J = 8.3, 2.3 Hz, 1H), 3.43 (t, J = 6.6 Hz, 2H), 2.57 - 2.41 (m, 2H), 2.07 - 1.87 (m, 2H), 1.83 - 1.68 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 157.58, 153.68, 143.62, 141.79, 133.27, 132.02, 129.99, 129.72, 129.38 (J = 30.24 Hz), 128.34, 122.95(J = 262.08 Hz), 122.88, 121.56, 118.37, 116.02, 114.80, 112.68, 105.70, 29.74, 27.85, 22.40, 21.83; $C_{22}H_{20}F_3N_2O$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 385.1528, 实测值385.1530。

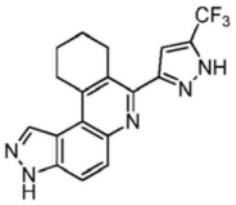
[0528] 4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)-3-(三氟甲基)苯酚

[0529] 

HSD 02-1239

方法 A: 灰白色固体 (142 mg, 36%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 10.24 (s, 1H), 8.55 (s, 1H), 7.84 (d, J = 9.0 Hz, 1H), 7.77 (d, J = 8.8 Hz, 1H), 7.24 (d, J = 8.3 Hz, 1H), 7.19 (d, J = 2.5 Hz, 1H), 7.11 (dd, J = 8.3, 2.5 Hz, 1H), 3.44 - 3.24 (m, 2H), 2.57 - 2.50 (m, 1H), 2.34 (dt, J = 17.0, 5.6 Hz, 1H), 2.00 - 1.83 (m, 2H), 1.82 - 1.62 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 157.55, 155.48, 143.04, 141.85, 138.71, 136.25, 132.68, 130.30, 129.99, 129.54, 128.57(q, J = 30.24 Hz), 125.45(q, J = 274.68 Hz), 122.04, 119.30,116.44,114.27,113.02,112.98,29.41,28.15,22.58,22.19;$C_{21}H_{19}F_3N_3O$[M+H]$^+$的HRMS(ESI)m/z计算值386.1480,实测值386.1488。

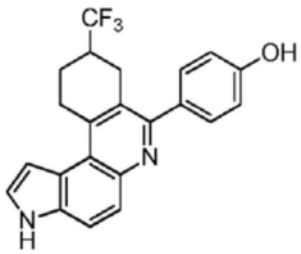
[0530] 7-(5-(三氟甲基)-1H-吡唑-3-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0531] 

HSD 02-1240

方法 A: 灰白色固体 (150 mg, 42%)。^{1}H NMR (500 MHz, OMSO-d_6) 6 8.56 (s, 1H), 7.91 (d, J = 8.7 Hz, 2H), 7.17 (s, 1H), 3.33 - 3.28 (m, 3H), 3.00 (t, J = 6.2 Hz, 2H), 2.02 - 1.95 (m, 2H), 1.88 - 1.80 (m, 2H);^{13}C NMR (126 MHz, DMSO) δ 144.59, 143.32, 142.97, 142.16, (J = 36.83 Hz), 138.87, 136.55, 129.44, 125.49 (J = 270.51 Hz), 122.50, 116.27, 115.12, 104.88, 29.83, 27.83, 22.26, 22.22; $C_{18}H_{15}F_3N_5$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 358.1280, 实测值 358.1289。

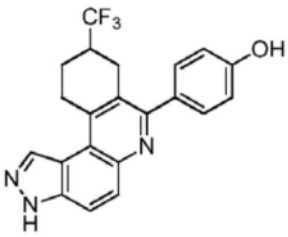
[0532] 4-(9-(三氟甲基)-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯酚

[0533] 

HSD 02-1241

方法 A: 灰白色固体 (157mg, 41%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 11.93 (s, 1H), 9.74 (s, 1H), 7.84 (d, J = 8.8 Hz, 1H), 7.67 (s, 1H), 7.60 - 7.50 (m, 1H), 7.39 (d, J = 8.0 Hz, 2H), 7.21 - 7.07 (m, 1H), 6.99 - 6.83 (m, 2H), 3.65 (dd, J = 18.1, 5.8 Hz, 1H), 3.01 - 2.93 (m, 1H), 2.89 - 2.81 (m, 1H), 2.78 - 2.65 (m, 1H), 2.43 - 2.31 (m, 1H), 1.92 - 1.77 (m, 1H); ^{13}C NMR (126 MHz, DMSO) δ 157.87, 155.35, 133.27, 131.96, 130.83, 129.75, 127.53, 124.57, 124.44, 121.71, 120.23, 117.24, 115.32, 106.11, 37.63 (q=26.6 Hz), 29.04, 27.78, 21.66; $C_{22}H_{20}F_3N_2O$ [M + H]$^+$的 HRMS(ESI)m/z计算值385.1528,实测值385.1532。

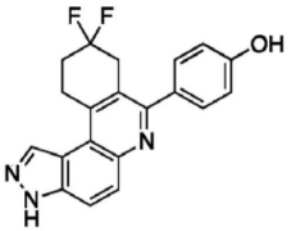
[0534] 4-(9-(三氟甲基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0535] 

HSD 02-1242

方法 A: 灰白色固体 (165 mg, 43%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 10.27 (s, 1H), 8.60 (s, 1H), 8.11 - 7.90 (m, 2H), 7.57 (d, J = 8.2 Hz, 2H), 7.03 (d, J = 8.3 Hz, 2H), 3.54 - 3.43 (m, 1H), 3.40 - 3.28 (m, 1H), 3.10 - 2.97 (m, 1H), 2.90 - 2.82 (m, 1H), 2.79 - 2.68 (m, 1H), 2.39 - 2.30 (m, 1H), 1.94 - 1.79 (m, 1H); ^{13}C NMR (126 MHz, DMSO) δ 159.74, 152.87, 148.17, 137.78, 131.71, 129.43(q, J = 278.46 Hz), 127.87, 122.81, 121.71, 115.86, 115.01, 37.62(q, J = 26.46 Hz), 29.44, 27.22, 20.90; $C_{21}H_{19}F_3N_3O$ [M + H]$^+$的 HRMS (ESI)m/z计算值386.1480,实测值386.1484。

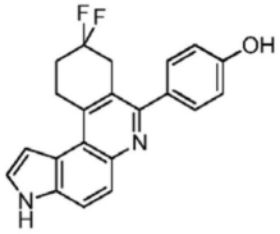
[0536] 4-(9,9-二氟-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯酚

[0537] 

HSD-02-1243

方法 A: 灰白色固体 (152 mg, 43%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 9.71 (s, 1H), 8.59 (s, 1H), 7.90 (d, J = 9.1 Hz, 1H), 7.87 - 7.81 (m, 1H), 7.41 (d, J = 8.5 Hz, 2H), 6.89 (d, J = 8.5 Hz, 2H), 3.63 - 3.55 (m, 2H), 3.41 - 3.36 (m, 2H), 2.55 - 2.50 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 157.94, 156.62, 144.16, 139.61, 138.71, 136.27, 131.03, 130.86, 129.49, 125.65, 124.54, 123.75, 121.86, 120.55, 116.30, 115.37, 115.11, 37.18 (J = 26.46 Hz), 29.37 (J = 23.94 Hz), 28.01; $C_{20}H_{18}F_2N_3O$ [M + H]$^+$的 HRMS (ESI) m/z计算值354.1418,实测值354.1421。

[0538] 4-(9,9-二氟-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯酚

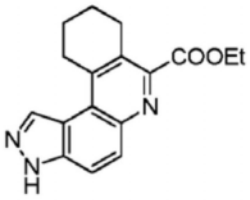
[0539] 

HSD 02-1244

方法A: 灰白色固体 (180 mg, 49%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 11.84 (s, 1H), 7.84 (d, J = 8.8 Hz, 1H), 7.67 (d, J = 8.8 Hz, 1H), 7.53 (d, J = 3.0 Hz, 1H), 7.39 (d, J = 8.1 Hz, 2H), 7.13 (d, J = 3.1 Hz, 1H), 6.88 (d, J = 8.1 Hz, 2H), 3.63 (t, J = 7.1 Hz, 2H), 3.33 (t, J = 14.5 Hz, 2H), 2.48 - 2.38 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 157.78, 155.53, 143.87, 139.53, 133.29, 131.52, 130.80, 125.76, 124.38, 123.95, 123.87, 122.78, 121.98, 121.20, 120.23, 117.15, 115.32, 106.13, 37.50(J =26.46 Hz), 29.55(J =23.94 Hz), 28.22; $C_{21}H_{19}F_2N_2O$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 353.1465, 实测值

353.1470。

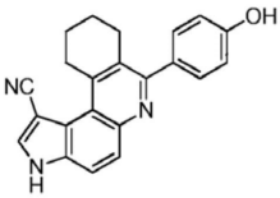
[0540] 8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-羧酸乙酯

[0541] 

HSD 02-1246

方法 A: 灰白色固体 (151 mg, 51%)。 ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.58 (s, 1H), 7.90 (d, J =9.1 Hz, 1H), 7.85 (d, J =9.1 Hz, 1H), 4.38 (q, J = 7.1 Hz, 2H), 2.94 (t, J = 6.3 Hz, 2H), 1.98 (tt, J = 7.7, 6.0, 4.6 Hz, 2H), 1.84 (dd, J = 7.6, 3.9 Hz, 2H), 1.34 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 167.34, 148.23, 143.50, 142.89, 139.08, 136.66, 129.37, 128.75, 123.47, 116.23, 115.28, 61.64, 29.54, 26.54, 22.29, 21.87, 14.60; $C_{17}H_{20}N_3O_2$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 298.1556, 实测值 298.1562。

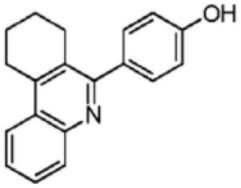
[0542] 7-(4-羟基苯基)-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-1-腈

[0543] 

HSD 02-1247

方法A: 黄色固体 (140 mg, 41%)。方法A: 灰白色固体 (182 mg, 56%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.36 (s, 1H), 8.70 (d, J = 3.1 Hz, 1H), 8.27 (d, J = 8.9 Hz, 1H), 8.19 (d, J = 9.1 Hz, 1H), 7.59 (d, J = 8.0 Hz, 2H), 7.04 (d, J = 8.1 Hz, 2H), 3.77 (t, J = 6.3 Hz, 2H), 2.84 (t, J = 6.3 Hz, 2H), 1.99 - 1.91 (m, 2H), 1.87 - 1.77 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 160.39, 153.97, 152.19, 138.86, 135.26, 135.01, 131.92, 130.79, 123.33, 122.29, 121.56, 119.23, 117.69, 117.36, 115.99, 89.30, 33.48, 27.99, 21.34, 21.30; $C_{22}H_{20}N_3O$ [M+H]$^+$的HRMS(ESI)m/z计算值342.1606,实测值342.1611。

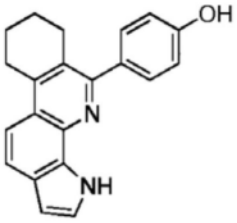
[0544] 4-(7,8,9,10-四氢菲啶-6-基)苯酚

[0545] 

HSD 02-1248

方法 A: 灰白色固体 (75 mg, 20%)。 ^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.42 (d, J = 8.5 Hz, 1H), 8.16 (d, J = 8.5 Hz, 1H), 8.04 (t, J = 7.7 Hz, 1H), 7.92 (t, J = 7.8 Hz, 1H), 7.60 (d, J = 8.2 Hz, 2H), 7.07 (d, J = 8.3 Hz, 2H), 3.52 (t, J = 6.5 Hz, 2H), 2.90 (t, J = 6.2 Hz, 2H), 2.12 - 2.06 (m, 2H), 1.95 - 1.84 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 160.77, 156.16, 155.60, 135.74, 132.96, 131.15, 130.92, 129.04, 127.05, 124.04, 122.18, 120.19, 115.59, 27.66, 26.87, 21.56, 20.93; $C_{19}H_{20}NO$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 378.1545, 实测值 378.1546。

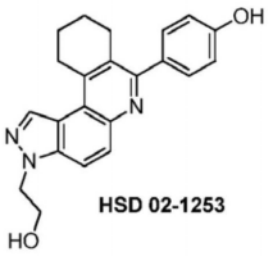
[0546] 4-(6,7,8,9-四氢-3H-吡咯并[3,2-c]菲啶-5-基)苯酚

[0547] 

HSD-02-1252

方法 A: 浅黄色固体 (119 mg, 38%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 7.73 (d, J = 8.8 Hz, 1H), 7.58 (d, J = 8.8 Hz, 1H), 7.39 - 7.32 (m, 3H), 6.96 - 6.89 (m, 2H), 6.62 (d, J = 3.0 Hz, 1H), 3.24 (tt, J = 6.6, 1.2 Hz, 2H), 2.72 (t, J = 6.3 Hz, 2H), 1.95 (td, J = 6.5, 3.0 Hz, 2H), 1.82 - 1.73 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 157.94, 157.43, 143.79, 134.49, 131.77, 130.32, 129.91, 126.79, 126.36, 123.54, 122.78, 120.97, 114.65, 113.55, 102.78, 28.24, 26.19, 22.54, 22.16; $C_{21}H_{19}N_2O$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 315.1497, 实测值 315.1498。

[0548] 4-(3-(2-羟乙基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0549] 

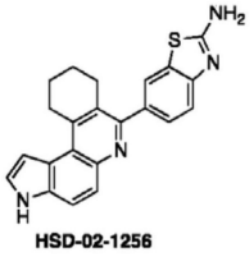
HSD 02-1253

方法 A: 灰白色固体 (177 mg, 49%)。 ^{1}H NMR (500 MHz, DMSO-J_6) δ 9.59 (s, 1H), 8.51 (s, 1H), 7.96 (d, J = 9.1 Hz, 1H), 7.81 (d, J = 9.1 Hz, 1H), 7.39 (d, J = 8.5 Hz, 2H), 6.86 - 6.82 (m, 2H), 4.55 (t, J = 5.6 Hz, 2H), 3.88 - 3.82 (m, 2H), 3.32 - 3.27 (m, 2H), 2.79 (t, J = 6.2 Hz, 2H), 2.01 - 1.96 (m, 2H), 1.77 - 1.70 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 157.58, 157.01, 143.57, 142.09, 138.61, 135.29, 131.97, 130.89, 129.53, 129.38, 121.31, 117.15, 115.09, 114.17, 60.84, 51.76, 29.69, 29.23, 22.64; $C_{12}H_{24}N_3O_2$ [M + H]$^+$的 HRMS (ESI) m/z 计算值362.1869,实测值362.1871。

[0550] 7-(3-(δ8.26(s,1H),7.95(d,J＝9.1Hz,1H),7.86(d,J＝9.1Hz,1H),3.55(t,J＝

6.3Hz,2H),2.72(t,J＝6.3Hz,2H),1.95-1.86(m,2H),1.84-1.77(m,2H);^{13}C NMR(126MHz,DMSO)δ150.24,144.55,143.03,140.24,139.34,131.66,131.35,130.73,125.49(J＝2704.68Hz),121.28,121.28,119.78,119.14,117.84,116.46,114.90,31.80,28.11,21.99;$C_{19}H_{14}F_3N_6$[M+H]$^+$的HRMS(ESI)m/z计算值383.1232,实测值383.1238。

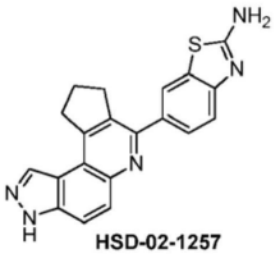
[0551] 6-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯并[d]噻唑-2-胺

[0552] 

HSD-02-1256

方法 A: 浅黄色固体 (115 mg, 31%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 7.83 (t, J = 1.2 Hz, 1H), 7.77 (dd, J = 8.8, 0.8 Hz, 1H), 7.62 (d, J = 8.7 Hz, 1H), 7.52 (s, 2H), 7.49 (t, J = 2.8 Hz, 1H), 7.42 - 7.36 (m, 2H), 7.15 - 7.09 (m, 1H), 3.38 (t, J = 6.5 Hz, 2H), 2.80 (t, J = 6.1 Hz, 2H), 2.01 - 1.93 (m, 2H), 1.78 - 1.68 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 167.48, 155.93, 152.75, 143.42, 142.23, 134.61, 133.18, 131.13, 127.69, 127.23, 124.12, 123.91, 122.33, 122.08, 120.39, 117.29, 116.41, 106.26, 30.02, 29.30, 22.94, 22.64; $C_{22}H_{19}N_4S$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 371.1330, 实测值 371.1339。

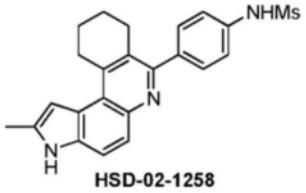
[0553] 6-(3,8,9,10-四氢环戊[c]吡唑并[4,3-f]喹啉-7-基)苯并[d]噻唑-2-胺

[0554] 

HSD-02-1257

方法 A: 黄色固体 (118 mg, 33%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.44 (s, 1H), 8.20 (d, J =1.8 Hz, 1H), 7.90 (d, J = 9.2 Hz, 1H), 7.84 (d, J = 9.0 Hz, 1H), 7.77 (dd, J =8.3, 1.9 Hz, 1H), 7.60 (s, 2H), 7.43 (d, J =8.3 Hz, 1H), 3.48 (t, J = 7.5 Hz, 2H), 3.29 (t, J = 7.6 Hz, 2H), 2.25 (p, J = 7.5 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 167.94, 153.47, 152.28, 149.49, 144.86, 138.15, 135.97, 135.08, 133.41, 131.62, 129.24, 126.75, 121.54, 118.85, 117.60, 116.83, 114.58, 33.57, 33.43, 25.01; $C_{20}H_{16}N_5S$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 358.1126, 实测值358.1128。

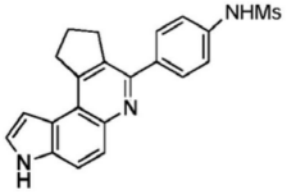
[0555] N-(4-(2-甲基-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯基)甲烷磺酰胺

[0556] 

HSD-02-1258

方法 A: 浅黄色固体 (205 mg, 50%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 7.24 (d, J = 8.9 Hz, 1H), 6.92 (d, J = 8.9 Hz, 1H), 6.86 (d, J = 8.3 Hz, 2H), 6.70 (d, J = 8.3 Hz, 2H), 6.28 (s, 1H), 2.86 - 2.78 (m, 2H), 2.29 (s, 3H), 2.11 - 2.02 (m, 2H), 1.81 (s, 2H), 1.39 - 1.28 (m, 2H), 1.14 - 1.04 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 154.13, 148.50, 140.10, 136.74, 132.90, 129.61, 128.08, 126.79, 122.08, 120.26, 119.11, 118.09, 110.65, 104.05, 37.63,30.40,26.94,20.76,20.43,11.29;HRMS(ESI)m/z计算值$C_{23}H_{28}N_3O_2S$[M+H]$^+$ 410.1902,实测值410.1907。

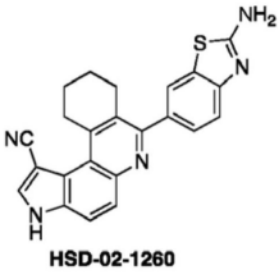
[0557] N-(4-(3,8,9,10-四氢环戊[c]吡咯并[3,2-f]喹啉-7-基)苯基)甲烷磺酰胺

[0558] 

HSD-02-1259

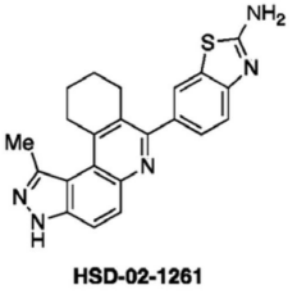
方法 A: 灰白色固体 (179 mg, 47%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 11.69 (t, J = 2.3 Hz, 1H), 9.91 (s, 1H), 7.89 - 7.84 (m, 2H), 7.77 (dd, J = 8.9, 0.8 Hz, 1H), 7.70 (d, J = 8.9 Hz, 1H), 7.48 (t, J = 2.7 Hz, 1H), 7.37 - 7.29 (m, 2H), 7.01 - 6.96 (m, 1H), 3.50 (t, J = 7.5 Hz, 2H), 3.24 (t, J = 7.5 Hz, 2H), 3.05 (s, 3H), 2.24 (p, J = 7.6 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 150.60, 149.35,144.61,138.77,136.41,134.23,132.57,129.96,124.46,123.67,120.85,120.10,119.48,116.78,104.29,33.87,33.12,25.08;$C_{21}H_{22}N_3O_2S$[M+H]$^+$的HRMS(ESI)m/z计算值380.1433,实测值380.1440。

[0559] 7-(2-氨基苯并[d]噻唑-6-基)-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-1-腈

[0560] 
HSD-02-1260

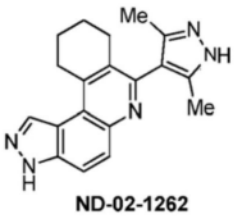
方法 A: 浅黄色固体 (119 mg, 30%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 9.19 (s, 2H), 8.69 (d, J = 3.1 Hz, 1H), 8.29 - 8.20 (m, 3H), 7.71 (dd, J = 8.3, 1.8 Hz, 1H), 7.66 (d, J = 8.3 Hz, 1H), 3.75 (t, J = 6.3 Hz, 2H), 2.83 (t, J = 6.4 Hz, 2H), 2.02 - 1.91 (m, 2H), 1.86 - 1.72 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 169.71, 154.01, 151.40, 138.84, 135.50, 135.06, 130.71, 128.82, 128.33, 126.00, 124.16, 123.58, 121.67, 119.22, 117.85, 117.28, 116.11, 114.43, 89.32, 33.49, 27.97, 21.30; $C_{23}H_{18}N_5S$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 396.1283, 实测值 396.1288。

[0561] 6-(1-甲基-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯并[d]噻唑-2-胺

[0562] 
HSD-02-1261

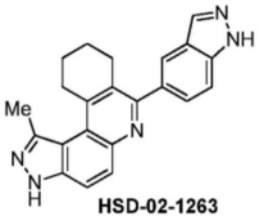
方法 A: 灰白色固体 (116 mg, 30%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 7.77 (d, J = 9.1 Hz, 1H), 7.75 - 7.68 (m, 2H), 7.53 - 7.47 (m, 1H), 7.38 (dd, J = 8.2, 1.8 Hz, 1H), 3.52 - 3.42 (m, 2H), 2.90 (s, 3H), 2.81 (q, J = 4.3, 3.1 Hz, 2H), 1.89 - 1.82 (m, 4H); ^{13}C NMR (126 MHz, MeOD) δ 169.08, 156.70, 151.68, 143.60, 143.42, 143.25, 141.25, 133.99, 130.75, 128.98, 128.59, 126.61, 123.95, 121.19, 116.95, 115.76, 113.89, 31.88, 27.83, 22.07, 21.90, 17.96; $C_{22}H_{20}N_5S$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 386.1439, 实测值 386.1447。

[0563] 7-(3,5-二甲基-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0564] 
ND-02-1262

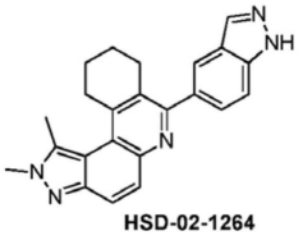
方法 A: 灰白色固体 (193 mg, 60%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.58 - 8.53 (m, 1H), 7.82 (dd, J = 9.1, 0.9 Hz, 1H), 7.76 (d, J = 9.0 Hz, 1H), 3.30 (t, J = 6.5 Hz, 2H), 2.56 (t, J = 6.2 Hz, 2H), 2.00 (s, 9H), 1.76 (qd, J = 8.6, 7.2, 4.1 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 151.69, 144.07, 141.77, 139.31, 135.31, 131.30, 129.63, 121.60, 117.69, 116.32, 114.93, 29.51, 27.72, 22.74, 22.45; $C_{19}H_{24}N_5$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 322.2032, 实测值 322.2036。

[0565] 7-(1H-吲唑-5-基)-1-甲基-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0566] 
HSD-02-1263

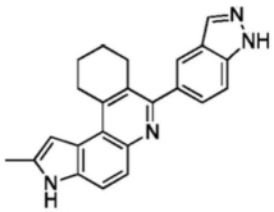
方法 A: 灰白色固体 (161 mg, 45%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 8.20 (s, 1H), 8.05 (s, 1H), 7.97 (d, J = 8.9 Hz, 1H), 7.91 (d, J = 9.2 Hz, 1H), 7.71 (d, J = 8.6 Hz, 1H), 7.59 (dd, J = 8.6, 1.6 Hz, 1H), 3.51 (q, J = 7.4, 6.5 Hz, 2H), 2.93 - 2.87 (m, 2H), 2.79 (t, J = 6.2 Hz, 2H), 1.88 - 1.73 (m, 4H); ^{13}C NMR (126 MHz, DMSO) ^{13}C NMR (126 MHz, DMSO) δ 153.72, 148.28, 140.25, 139.38, 136.90, 134.68, 130.29, 127.67, 124.60, 123.00, 122.54, 114.31, 110.60, 32.28, 27.98, 22.08, 21.72; $C_{22}H_{24}N_5$[M+H]$^+$的HRMS(ESI)m/z计算值358.2032,实测值358.2033。

[0567] 7-(1H-吲唑-5-基)-1,2-二甲基-8,9,10,11-四氢-2H-吡唑并[4,3-a]菲啶

[0568] 
HSD-02-1264

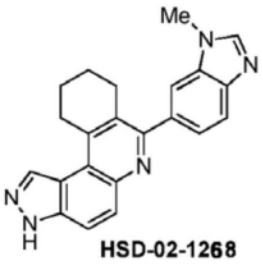
方法 A: 灰白色固体 (159 mg, 43%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 8.12 (s, 1H), 7.93 (dd, J = 1.6, 0.8 Hz, 1H), 7.75 (d, J = 9.0 Hz, 1H), 7.60 (dt, J = 8.6, 1.0 Hz, 1H), 7.55 (dd, J = 8.6, 1.6 Hz, 1H), 7.38 (d, J = 9.0 Hz, 1H), 4.10 (s, 3H), 3.61 (t, J = 6.6 Hz, 3H), 2.79 (t, J = 6.2 Hz, 2H), 2.63 (s, 3H), 1.94 - 1.89 (m, 2H), 1.75 - 1.65 (m, 3H); ^{13}C NMR (126 MHz, DMSO) δ 158.06, 147.33, 144.38, 143.84, 139.78, 134.44, 133.66, 132.84, 128.49, 128.17, 123.76, 123.05, 121.87, 121.40, 118.85, 118.33, 109.89, 37.78, 30.37, 29.10, 22.71, 22.60, 9.69; $C_{23}H_{24}N_5$[M+H]$^+$的HRMS(ESI)m/z计算值370.2032,实测值370.2039。

[0569] 7-(1H-吲唑-5-基)-2-甲基-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶

[0570] 
HSD-02-1266

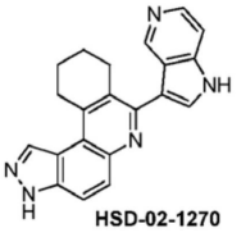
方法 A: 灰白色固体 (146 mg, 41%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.13 (s, 1H), 7.89 (t, J = 1.1 Hz, 1H), 7.69 (d, J = 8.9 Hz, 1H), 7.67 - 7.62 (m, 2H), 7.52 (dd, J = 8.5, 1.5 Hz, 1H), 6.89 (s, 1H), 3.46 (t, J = 6.5 Hz, 2H), 2.74 (t, J = 6.2 Hz, 2H), 2.54 (s, 3H), 2.07 - 1.98 (m, 3H), 1.85 - 1.75 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 156.00, 143.82, 142.24, 139.73, 133.98, 133.79, 133.15, 127.95, 127.34, 122.81, 122.28, 121.16, 120.90, 120.51, 115.34, 109.38, 104.02, 29.95, 28.71, 22.50, 22.19, 12.08; $C_{23}H_{25}N_4$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 357.2079,实测值357.2079。

[0571] 7-(1H-吲唑-5-基)-1-甲基-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0572] 
HSD-02-1268

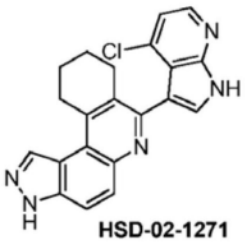
方法 A: 灰白色固体 (163 mg, 46%)。^{1}H NMR (500 MHz, MeOD -d_4) δ 9.51 (s, 1H), 8.8 (s, 1H), 8.33 - 8.31 (m, 2H), 8.24 (d, J = 8.5 Hz, 1H), 8.13 (d, J = 9.5 Hz, 1H), 8.00 (d, J = 7.7 Hz, 1H), 4.25 (s, 3H), 3.69 (t, J = 6.2 Hz, 1H), 2.91 (t, J = 5.9 Hz, 2H), 2.24 - 2.19 (m, 2H), 1.97 - 1.92 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 156.46, 155.04, 149.36, 143.88, 134.90, 134.50, 133.73, 132.46, 132.17, 129.92, 127.08, 124.13, 121.16, 119.24, 116.83, 114.80, 113.44, 32.47, 30.98, 27.74, 21.22, 21.10 ; $C_{22}H_{20}N_5$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 354.1719,实测值354.1722。

[0573] 7-(1H-吡咯并[3,2-c]吡啶-3-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0574] 
HSD-02-1270

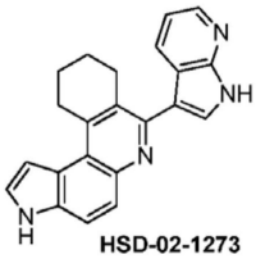
方法 A: 灰白色固体 (129 mg, 38%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 11.82 (s, 1H), 9.49 (d, J = 1.8 Hz, 1H), 8.57 (s, 1H), 8.23 (dd, J = 5.7, 2.2 Hz, 1H), 7.93 (d, J = 2.1 Hz, 1H), 7.89 - 7.82 (m, 2H), 7.44 (dd, J = 5.9, 1.8 Hz, 1H), 3.33 (s, 17H), 3.07 (t, J = 6.2 Hz, 2H), 2.04 (dtt, J = 12.3, 6.4, 2.2 Hz, 2H), 1.89 - 1.78 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 151.34, 145.38, 143.85, 142.15, 140.91, 139.91, 129.62, 129.54, 128.05, 124.66, 120.76, 116.46, 115.21, 107.29, 29.95, 28.95, 22.80, 22.62; $C_{21}H_{18}N_5$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 340.1562,实测值340.1566。

[0575] 7-(4-氯-1H-吡咯并[2,3-6]吡啶-3-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0576] 
HSD-02-1271

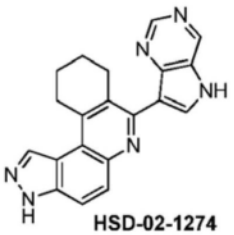
方法 A: 灰白色固体 (180 mg, 48%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 8.61 (s, 1H), 8.19 (d, J = 5.5 Hz, 1H), 7.87 (q, J = 9.3 Hz, 2H), 7.61 (s, 1H), 7.14 (d, J = 5.1 Hz, 1H), 3.40 (s, 3H), 2.75 - 2.66 (m, 2H), 2.06 (p, J = 6.3, 5.7 Hz, 2H), 1.89 - 1.80 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 151.51, 148.69, 143.14, 142.97, 142.52, 136.07, 135.88, 132.62, 128.15, 126.03, 122.42, 117.52, 116.46, 116.07, 113.67, 29.52, 28.07, 22.18, 21.86; $C_{21}H_{17}ClN_5$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 374.1172, 实测值 374.1176。

[0577] 7-(1H-吡咯并[2,3-b]吡啶-3-基)-8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶

[0578] 
HSD-02-1273

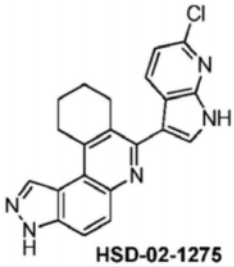
方法 A: 灰白色固体 (142 mg, 42%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 11.92 (s, 1H), 11.72 (s, 1H), 8.57 (dd, J = 7.9, 1.7 Hz, 1H), 8.27 (dd, J = 4.7, 1.7 Hz, 1H), 7.90 (s, 1H), 7.77 (d, J = 8.8 Hz, 1H), 7.68 (d, J = 8.9 Hz, 1H), 7.47 (t, J = 2.4 Hz, 1H), 7.18 - 7.12 (m, 1H), 7.11 (d, J = 3.0 Hz, 1H), 3.40 (t, J = 6.5 Hz, 2H), 3.05 (t, J = 6.1 Hz, 2H), 2.05 - 1.97 (m, 2H), 1.81 (ddt, J = 9.3, 6.3, 2.8 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 150.58, 148.89, 143.52, 143.39, 142.01, 133.07, 130.54, 127.92, 127.10, 124.02, 123.76, 121.43, 120.44, 120.16, 116.48, 116.27,114.39,106.19,30.22,28.95,22.89,22.82;$C_{22}H_{19}N_4$[M+H]$^+$的HRMS(ESI)m/z计算值 339.1610,实测值339.1615。

[0579] 7-(5H-吡咯并[3,2-d]嘧啶-7-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0580] 
HSD-02-1274

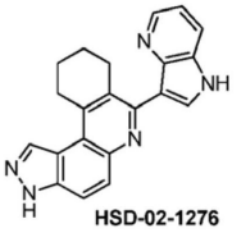
方法A: 灰白色固体 (171 mg, 50%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 9.72 (s, 1H), 8.83 (s, 1H), 8.55 (s, 1H), 8.07 (s, 1H), 7.93 (d, 9.2 J = Hz, 1H), 7.89 - 7.83 (m, 1H), 3.39 - 3.33 (m, 2H), 3.11 (t, J = 6.1 Hz, 2H), 2.08 - 2.01 (m, 2H), 1.91 - 1.81 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 151.93, 151.87, 150.53, 143.67, 142.83, 142.42, 138.64, 136.29, 129.63, 129.46, 128.35, 120.83, 118.56, 116.50, 114.42, 29.99, 28.80, 22.74, 22.53; $C_{20}H_{17}N_6$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 341.1515, 实测值 341.1517。

[0581] 7-(6-氯-1H-吡咯并[2,3-b]吡啶-3-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0582] 
HSD-02-1275

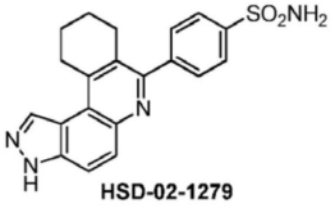
方法A: 灰白色固体 (183 mg, 49%)。 ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.82 (s, 1H), 9.50 (d, J = 1.1 Hz, 1H), 8.55 (s, 1H), 8.23 (d, J = 5.6 Hz, 1H), 7.96 - 7.78 (m, 3H), 7.44 (dd, J = 5.6, 1.1 Hz, 1H), 3.35 (s, 2H), 3.07 (t, J = 6.1 Hz, 2H), 2.04 (tdd, J = 9.2, 5.5, 2.2 Hz, 2H), 1.84 (qd, J = 8.8, 7.3, 4.1 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 151.36, 145.39, 143.74, 142.15, 140.92, 139.90, 138.58, 136.23, 129.62, 128.04, 127.85, 124.65, 120.72, 116.59, 115.20, 114.23, 107.27, 29.96, 28.95, 22.80, 22.62; $C_{21}H_{17}ClN_5$ [M + H]$^+$ HRMS (ESI) m/z 计算值 374.1172,实测值374.1178。

[0583] 7-(1H-吡咯并[3,2-b]吡啶-3-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0584] 
HSD-02-1276

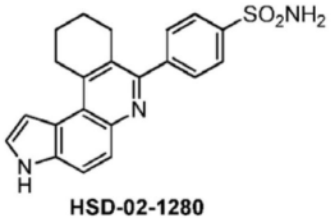
方法A: 灰白色固体 (153 mg, 45%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 11.60 (d, J = 3.1 Hz, 1H), 8.56 (s, 1H), 8.32 (dq, J = 4.3, 1.8 Hz, 1H), 7.88 - 7.77 (m, 4H), 7.17 - 7.10 (m, 1H), 3.38 - 3.33 (m, 2H), 2.94 (t, J = 6.1 Hz, 2H), 2.03 - 1.93 (m, 2H), 1.77 - 1.65 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 152.37, 144.53, 143.65, 142.86, 141.35, 138.56, 136.22, 131.63, 129.70, 129.50, 128.91, 121.53, 119.42, 117.39, 116.76, 116.64, 113.84, 29.65, 27.96, 22.77, 22.43; $C_{21}H_{18}N_5$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 340.1562, 实测值 340.1567。

[0585] 4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯磺酰胺

[0586] 
HSD-02-1279

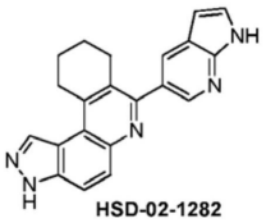
方法A: 灰白色固体 (197 mg, 52%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.59 (s, 1H), 7.93 (d, J = 8.4 Hz, 2H), 7.87 (dd, J = 9.1, 0.9 Hz, 1H), 7.80 (d, J = 9.1 Hz, 1H), 7.75 (d, J = 8.5 Hz, 2H), 3.32 (t, J = 6.5 Hz, 2H), 2.76 (t, J = 6.1 Hz, 2H), 2.03 - 1.95 (m, 2H), 1.78 - 1.69 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 155.52, 144.57, 143.84, 143.78, 142.71, 139.77, 135.26, 130.10, 129.57, 129.20, 125.83, 122.19, 116.19, 115.57,31.16,29.66,28.81,22.54,22.43;$C_{20}H_{19}N_4O_2S$[M+H]$^+$的HRMS(ESI)m/z计算值379.1229,实测值379.1234。

[0587] 4-(8,9,10,11-四氢-3H-吡咯并[3,2-a]菲啶-7-基)苯磺酰胺

[0588] 
HSD-02-1280

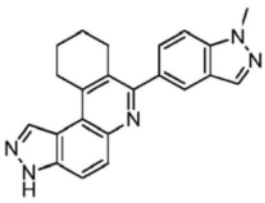
方法A: 灰白色固体 (162 mg, 43%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 11.80 (s, 1H), 7.91 (d, J = 8.4 Hz, 2H), 7.80 (d, J = 8.9 Hz, 1H), 7.73 (d, J = 8.4 Hz, 2H), 7.63 (d, J = 8.8 Hz, 1H), 7.51 (d, J = 3.1 Hz, 1H), 7.39 (s, 2H), 7.14 (d, J = 3.1 Hz, 1H), 3.40 (t, J = 6.5 Hz, 2H), 2.75 (t, J = 6.2 Hz, 2H), 2.03 - 1.97 (m, 2H), 1.74 (qd, J = 8.8, 7.3, 4.2 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 154.57, 145.05, 143.70, 143.40, 142.65,133.35,130.06,127.32,125.76,124.09,122.72,120.30,116.75,106.36,29.96, 28.94,22.81,22.46;$C_{21}H_{20}N_3O_2S$[M+H]$^+$的HRMS(ESI)m/z计算值378.1276,实测值378.1279。

[0589] 7-(1H-吡咯并[2,3-b]吡啶-5-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0590] 
HSD-02-1282

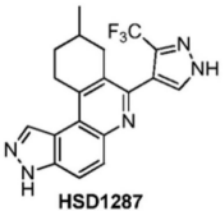
方法A: 灰白色固体 (143 mg, 42%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 11.76 (d, J = 2.2 Hz, 1H), 8.56 (s, 1H), 8.41 (d, J = 2.1 Hz, 1H), 8.15 (d, J = 2.0 Hz, 1H), 7.85 (s, 2H), 7.53 (dd, J = 3.4, 2.5 Hz, 1H), 6.51 (dd, J = 3.4, 1.8 Hz, 1H), 3.33 - 3.29 (m, 2H), 2.83 (t, J = 6.1 Hz, 2H), 2.04 - 1.95 (m, 2H), 1.79 - 1.68 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 155.77, 148.32, 143.79, 142.36, 138.66, 136.36, 129.95, 129.71, 129.03, 128.96, 127.21, 121.73, 119.22, 116.50, 114.34, 100.67,29.73,29.23,22.62;$C_{21}H_{18}N_5$[M+H]$^+$的HRMS(ESI)m/z计算值340.1562,实测值340.1565。

[0591] 7-(1-甲基-1H-吲唑-5-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0592] 
HSD1286

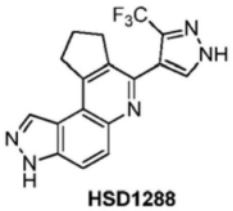
方法A: 灰白色固体 (164 mg, 46%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 9.13 (s, 1H), 8.84 (s, 1H), 8.26 (d, J = 9.2 Hz, 1H), 8.21 (s, 1H), 8.13 - 8.06 (m, 2H), 7.89 (dd, J = 8.5, 1.4 Hz, 1H), 3.63 (t, J = 6.4 Hz, 2H), 2.91 (t, J = 6.1 Hz, 2H), 2.32 - 2.11 (m, 2H), 2.05 - 1.81 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 153.92, 150.61, 144.58, 135.63, 135.49, 134.39, 132.24, 129.30, 126.03, 123.77, 119.99, 117.90, 114.89, 112.48, 31.75, 30.86, 27.89, 21.33, 21.22; $C_{22}H_{20}N_5$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 354.1719, 实测值 354.1721。

[0593] 9-甲基-7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0594] 
HSD1287

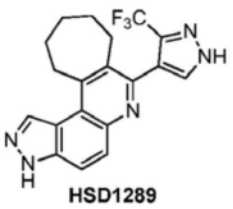
方法A: 灰白色固体 (178 mg, 48%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.60 (s, 1H), 7.97 (d, J = 1.1 Hz, 1H), 7.86 (s, 2H), 3.56 - 3.48 (m, 1H), 3.39 - 3.32 (m, 2H), 2.77 - 2.70 (m, 1H), 2.38 - 2.28 (m, 1H), 2.27 - 2.18 (m, 1H), 1.97 - 1.85 (m, 1H), 1.66 - 1.53 (m, 1H), 1.09 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, MeOD) δ 148.72, 143.06, 142.82, 139.74(J = 28.98 Hz) 134.66, 131.35, 131.12, 131.01, 128.37, 123.01, 122.23, 120.84 (J = 269.64 Hz), 115.93, 114.67, 36.13, 30.14, 29.44, 28.15, 20.47; $C_{18}H_{18}N_5$[M+H]$^+$的HRMS(ESI)m/z计算值304.1562,实测值304.1565。

[0595] 7-(3-(三氟甲基)-1H-吡唑-4-基)-3,8,9,10-四氢环戊[c]吡唑并[4,3-f]喹啉

[0596] 
HSD1288

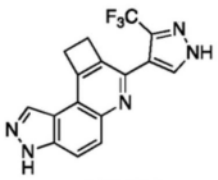
方法A: 灰白色固体 (185 mg, 54%)。^{1}H NMR (500 MHz, MeOD) δ 8.76 (s, 1H), 8.44 (s, 1H), 8.33 (d, J = 9.3 Hz, 1H), 8.05 (d, J = 9.3 Hz, 1H), 3.86 (t, J = 7.7 Hz, 2H), 3.21 (t, J = 7.7 Hz, 2H), 2.57- 2.53 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 160.67, 141.10, 140.00, 138.86, 136.50, 133.37, 132.59, 122.32(q, J = 269.64 Hz), 121.78, 121.15, 118.59, 115.19, 110.20, 35.03, 30.90, 23.82; $C_{17}H_{13}F_3N_5$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 334.1123, 实测值 334.1121。

[0597] 7-(3-(三氟甲基)-1H-吡唑-4-基)-3,8,9,10,11,12-六氢环庚基[c]吡唑并[4,3-f]喹啉

[0598] 
HSD1289

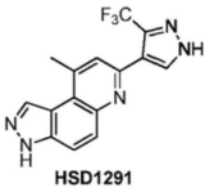
方法A: 灰白色固体 (185 mg, 50%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 8.98 - 8.87 (m, 1H), 8.37 - 8.27 (m, 2H), 7.99 (d, J = 9.2 Hz, 1H), 3.86 (d, J = 5.3 Hz, 2H), 3.17 - 3.04 (m, 2H), 2.05 (p, J = 2.7 Hz, 4H), 1.78 - 1.65 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 160.75, 140.27, 136.43, 133.66, 132.53, 123.83, 122.46, 122.13, 121.07, 120.17(q, J = 269.64 Hz), 118.79, 114.94, 114.65, 110.56, 110.56, 32.30, 30.64, 29.52, 25.85, 23.75; $C_{19}H_{17}F_3N_5$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 372.1436,实测值372.1438。

[0599] 7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9-二氢-3H-环丁[c]吡唑并[4,3-f]喹啉

[0600] 
HSD1290

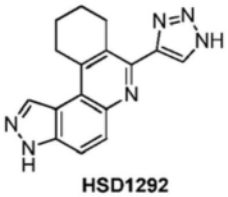
方法A:灰白色固体 (49 mg, 15%)。1H NMR (500 MHz, MeOD) δ 8.69 (d, J = 0.9 Hz, 1H), 8.53 (d, J = 0.9 Hz, 1H), 8.32 (dd, J = 9.4, 1.0 Hz, 1H), 8.11 (d, J = 9.4 Hz, 1H), 4.01 - 3.93 (m, 2H), 3.72 (t, J = 4 J.0 = Hz, 2H). ^{13}C NMR (126 MHz, MeOD) δ 161.67, 140.75, 139.64, 137.73, 136.67, 133.55, 133.12, 122.29 (q, J = 268.38 Hz), 121.46, 119.65, 119.42, 113.74, 108.80, 30.70, 29.72; $C_{16}H_{11}F_3N_5$ [M + H]$^+$的HRMS(ESI)m/z计算值330.0967,实测值330.0970。

[0601] 9-甲基-7-(3-(三氟甲基)-1H-吡唑-4-基)-3H-吡唑并[4,3-f]喹啉

[0602] 
HSD1291

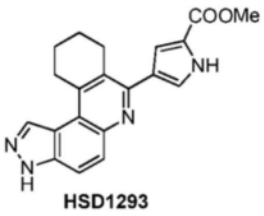
方法A: 灰白色固体 (136 mg, 43%)。 ^{1}H NMR (500 MHz, MeOD) δ 8.51 (s, 1H), 8.29 - 8.21 (m, 1H), 7.91 - 7.81 (m, 2H), 7.62 (s, 1H), 2.89 (s, 3H);^{13}C NMR (126 MHz, MeOD) δ 147.45, 145.74, 144.37, 139.03, 138.40, 135.27, 130.97, 128.87, 125.13(J = 269.64 Hz), 122.50, 121.51, 120.86, 116.35, 114.74, 21.45; $C_{15}H_{11}F_3N_5$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 318.0967, 实测值 318.0971。

[0603] 7-(1H-1,2,3-三唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0604] 
HSD1292

方法A: 灰白色固体 (159 mg, 55%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.57 (s, 1H), 8.31 (d, J = 1.9 Hz, 1H), 7.87 (d, J = 9.2 Hz, 1H), 7.82 (dd, J = 9.1, 1.9 Hz, 1H), 3.30 (d, J = 6.6 Hz, 2H), 3.12 (d, J = 6.4 = Hz, 2H), 2.05 - 1.94 (m, 2H), 1.84 (dtd, J = 10.1, 6.9, 6.3, 3.3 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 146.46, 143.65, 142.93, 131.52, 129.80, 129.48, 122.18, 116.16, 115.49, 29.87, 28.27, 22.37; $C_{16}H_{15}N_6$ [M + H]$^{+生}$物 HRMS (ESI) m/z 计算值 291.1358, 实测值 291.1360。

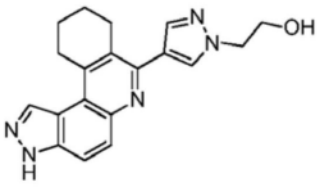
[0605] 3-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)-1H-吡咯-2-羧酸甲酯

[0606] 
HSD1293

方法A: 灰白色固体 (142 mg, 41%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 12.20 (s, 1H), 8.50 (s, 1H), 7.52 (s, 1H), 7.34 (s, 1H), 3.80 (s, 3H), 3.32 - 3.24 (m, 2H), 3.01 (t, J = 6.1 Hz, 2H), 2.03 - 1.91 (m, 2H), 1.88 - 1.74 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 161.40, 150.78, 143.78, 142.06, 138.38, 136.17, 136.16, 129.69, 129.00, 125.75, 125.46, 122.08, 121.04, 116.53, 114.14, 51.67, 29.86, 28.94, 22.68, 22.50; $C_{20}H_{19}N_4O_2$ [M + H]$^+$的 HRMS (ESI) m/z 计算值

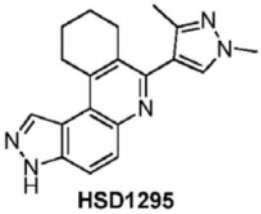
[0607] 347.1508,实测值347.1513。

[0608] 2-(4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)-1H-吡唑-1-基)乙-1-醇

[0609] 
HSD1294

方法A: 灰白色固体 (126 mg, 38%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.51 (s, 1H), 8.12 (s, 1H), 7.99 (s, 1H), 7.87 (d, J = 9.2 Hz, 1H), 7.79 (d, J = 9.0 Hz, 1H), 4.34 (t, J = 5.4 Hz, 2H), 3.97 (t, J = 5.4 Hz, 2H), 3.35 - 3.32 (m, 2H), 3.00 (t, J = 6.2 Hz, 2H), 2.10 - 2.03 (m, 2H), 1.95 - 1.86 (m, 2H). ^{13}C NMR (126 MHz, MeOD) δ 149.36, 143.28, 143.07, 139.58, 138.49, 135.72, 131.37, 129.45, 128.70, 121.71, 121.43, 116.16, 113.49, 60.48,54.17,29.73,28.38,22.12,22.03;$C_{19}H_{20}N_5O$[M+H]$^+$的HRMS(ESI)m/z计算值334.1668,实测值334.1675。

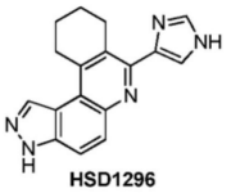
[0610] 7-(1,3-二甲基-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0611] 
HSD1295

方法A: 灰白色固体 (180 mg, 57%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.53 (s, 1H), 7.92 (s, 1H), 7.81 (d, J = 9.0 Hz, 1H), 7.76 (d, J = 9.1 Hz, 1H), 3.82 (s, 3H), 3.27 (t, J = 6.5 Hz, 3H), 2.81 (t, J = 6.2 Hz, 2H), 2.26 (s, 3H) 2.01 - 1.88 (m, 2H), 1.82 - 1.67 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 150.70, 147.24, 143.71, 141.82, 139.32, 135.07, 131.72, 129.87, 129.57, 121.05, 118.85, 116.35, 114.88, 38.70, 29.70, 28.60, 22.60, 13.53; $C_{19}H_{20}N_5$ [M + H]$^+$的 HRMS (ESI) m/z 计算

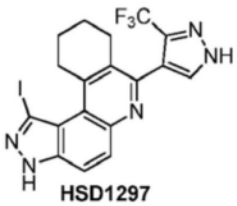
值318.1719,实测值318.1725。

[0612] 7-(1H-咪唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0613] 
HSD1296

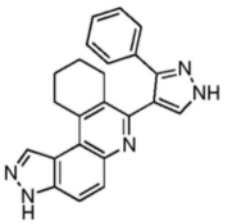
方法A: 灰白色固体 (168 mg, 58%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.62 - 8.53 (m, 2H), 7.93 - 7.82 (m, 3H), 3.36 - 3.23 (m, 2H), 3.09 - 2.97 (m, 2H), 2.02 - 1.94 (m, 2H), 1.90 - 1.78 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 144.79, 143.75, 142.88, 138.70, 136.05, 132.80, 131.40, 129.06, 128.65, 122.65, 121.92, 116.12, 115.25, 29.94, 27.98, 22.22; $C_{17}H_{16}N_5$ [M + H]$^+$的 HRMS (ESI) m/z 计算值290.1406,实测值290.1415。

[0614] 1-碘-7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0615] 
HSD1297

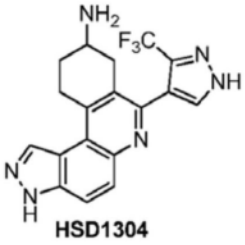
方法A: 灰白色固体 (145 mg, 30%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.90 (s, 1H), 8.35 (s, 1H), 8.33 (d, J = 9.1 Hz, 1H), 8.00 (d, J = 9.2 Hz, 1H), 3.67 (t, J = 6.4 Hz, 2H), 2.81 (t, J = 6.2 Hz, 2H), 2.18 (qd, J = 7.8, 6.3, 4.5 Hz, 2H), 2.04 - 1.90 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 154.90, 142.03, 140.54, 139.83, 134.96, 134.44, 134.02, 132.40, 124.40, 122.30 (J = 269.64 Hz), 121.60, 118.81, 114.76, 109.91, 30.80, 27.22, 21.20, 20.87; $C_{17}H_{16}N_5$ [M +H]$^+$的 HRMS (ESI) m/z 计算值484.0246,实测值484.0252。

[0616] 7-(3-苯基-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0617] 
HSD1303

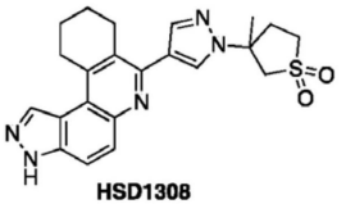
方法A: 灰白色固体 (168 mg, 45%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.81 (s, 1H), 8.27 (d, J = 9.1 Hz, 2H), 8.17 (d, J = 9.2 Hz, 1H), 7.35 - 7.22 (m, 5H), 3.51 - 3.43 (m, 2H), 2.55 - 2.49 (m, 0H), 1.95 - 1.82 (m, 2H), 1.72 - 1.61 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 145.52, 135.52, 132.94, 129.41, 128.96, 128.85, 128.19, 126.99, 123.39, 120.03, 114.91, 109.66, 30.80, 27.32, 21.75, 21.27; $C_{23}H_{20}N_5$ [M + H]+ 的 HRMS (ESI) m/z 计算值 366.1719, 实测值 366.1726。

[0618] 7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-9-胺

[0619] 
HSD1304

方法A: 灰白色固体 (137 mg, 37%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.57 (d, J = 7.7 Hz, 1H), 8.03 - 8.00 (m, 1H), 7.87 - 7.83 (m, 2H), 3.92 - 3.82 (m, 1H), 3.65 - 3.53 (m, 1H), 3.49 - 3.38 (m, 1H), 2.81 - 2.65 (m, 2H), 225 - 2.17 (m, 1H), 2.08 - 1.96 (m, 1H); ^{13}C NMR (126 MHz, MeOD) δ 148.28, 143.27, 142.44, 142.22, 139.73, 134.64, 130.59, 129.31, 128.37, 122.83(q, J = 269.64 Hz), 122.00, 118.74, 115.86, 115.82, 114.97, 46.06, 36.25, 30.30, 28.58; C18H16F_3N_6 [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 373.1389, 实测值373.1393。

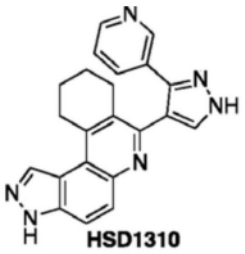
[0620] 3-甲基-3-(4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)-1H-吡唑-1-基)四氢噻吩1,1-二氧化物

[0621] 
HSD1308

方法A: 灰白色固体 (126 mg, 30%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.54 - 8.48 (m, 1H), 8.47 (s, 1H), 8.08 (s, 1H), 7.81 (s, 2H), 4.22 (dd, J = 14.1, 1.7 Hz, 1H), 3.59 (d, J = 14.1 Hz, 1H), 3.42 (ddd, J = 12.7, 7.7, 4.6 Hz, 1H), 3.29 (d, J = 6.5 Hz, 2H), 3.19 (ddd, J = 13.1, 9.6, 7.5 Hz, 1H), 3.15 - 3.07 (m, 1H), 2.55 (ddd, J = 13.9, 9.6, 7.7 Hz, 1H), 1.98 (ddt, J = 12.1, 6.1, 3.3 Hz, 2H), 1.84 (qd, J = 9.1, 7.4, 4.0 Hz, 2H), 1.75 (s,

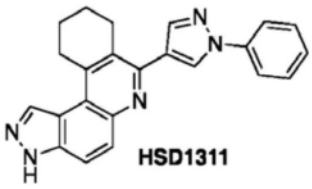
3H);^{13}C NMR(126MHz,DMSO)δ149.12,143.66,142.26,140.19,138.52,136.20,129.53,129.02,128.80,123.04,121.18,116.52,114.29,65.32,61.46,51.53,35.09,29.87,28.53,27.91,22.63,22.50。

[0622] 7-(3-(吡啶-3-基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0623] 
HSD1310

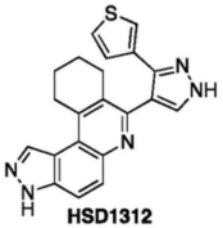
方法A: 灰白色固体 (172 mg, 47%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.56 (d, J = 1.0 Hz, 1H), 8.49 (dd, J = 2.2, 0.9 Hz, 1H), 8.36 (dd, J = 4.7, 1.7 Hz, 1H), 7.98 (s, 1H), 7.83 (dd, J = 9.0, 0.9 Hz, 1H), 7.72 (d, J = 8.0, 2.3, 1.7 Hz, 1H), 7.68 (d, J = 9.0 Hz, 1H), 7.25 (ddd, J = 8.0, 4.8, 0.9 Hz, 1H), 3.29 (t, J = 6.5 Hz, 2H), 2.58 (t, J = 6.2 Hz, 2H), 1.89 (ddt, J = 9.2, 6.4, 4.2 Hz, 2H), 1.73 - 1.64 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 150.81, 148.62, 147.71, 143.91, 143.51, 142.22, 140.11, 135.03, 134.04, 133.41, 130.51, 129.58, 129.11, 123.91, 121.95, 119.13,116.29,115.55,29.57,28.27,22.59,22.35;$C_{22}H_{19}N_6$[M+H]$^+$的HRMS(ESI)m/z计算值367.1671,实测值367.1675。

[0624] 7-(1-苯基-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0625] 
HSD1311

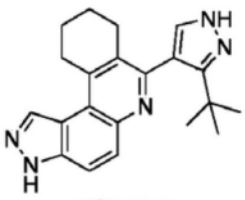
方法A: 灰白色固体 (186 mg, 51 %)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.55 (s, 1H), 7.95 (s, 1H), 7.88 - 7.73 (m, 2H), 7.37 - 7.23 (m, 1H), 6.79 (s, 1H)' 6·63 (s, 1H), 331 (t, J = 64 Hz, 2H), 2·58 (t, J = 6.1 Hz, 2H), 1.94 - 1.85 (m, 2H), 1.74 - 1.65 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 150.93, 143.68, 142.18, 138.73, 136.97, 136.67, 136.31, 131.22, 130.28, 129.55, 127.67, 125.20, 123.94, 122.00, 118.02, 116.54, 114.31, 29.56, 28.10,22.55,22.32;$C_{23}H_{20}N_5$[M+H]$^+$的HRMS(ESI)m/z计算值366.1719,实测值366.1720。

[0626] 7-(3-(噻吩-3-基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0627] 
HSD1312

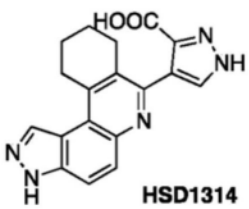
方法A: 灰白色固体 (177 mg, 46%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.89 (d, J = 1.8 Hz, 1H), 8.55 (s, 1H), 8.29 (d, J = 1.7 Hz, 1H), 7.95 (d, J = 8.2 Hz, 2H), 7.83 (s, 2H), 7.57 - 7.46 (m, 2H), 7.39 - 7.28 (m, 1H), 3.29 (d, J = 6.5 Hz, 2H), 3.07 (t, J = 6.2 Hz, 2H), 2.03 - 1.94 (m, 2H), 1.86 (tt, J = 9.6, 5.4 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 148.63, 143.82, 142.45, 142.18, 141.18, 140.01, 139.07, 130.03, 129.57, 129.19, 127.95, 126.90, 124.53, 121.44, 119.01, 118.46, 116.29, 29.86, 28.53, 22.57, 22.45; $C_{21}H_{18}N_5S$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 372.1283, 实测值372.1286。

[0628] 7-(3-(叔丁基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0629] 
HSD1313

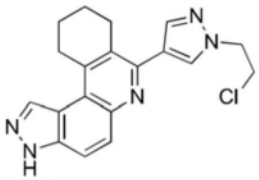
方法A: 灰白色固体 (176 mg, 51%)。^{1}H NMR (500 MHz, MeOD) δ 8.55 (s, 1H), 7.88 - 7.79 (m, 2H), 7.53 (s, 1H), 3.37 - 3.31 (m, 2H), 2.67 (t, J = 6.2 Hz, 2H), 2.08 - 1.97 (m, 2H), 1.90 - 1.81 (m, 2H).; ^{13}C NMR (126 MHz, MeOD) δ 152.31, 143.08, 142.67, 138.68, 135.79, 131.90, 128.29, 122.19, 116.70, 116.13, 113.68, 32.29, 32.24, 29.44, 29.30, 28.47, 22.15, 21.89; $C_{21}H_{24}N_5$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 346.2032, 实测值 346.2021。

[0630] 4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)-1H-吡唑-3-羧酸

[0631] 
HSD1314

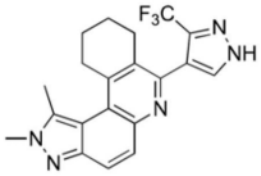
方法A: 灰白色固体 (167 mg, 50%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.62 (s, 1H), 8.25 (s, 1H), 7.99 (d, J = 9.1 Hz, 1H), 7.76 (d, J = 9.4 Hz, 1H), 3.30 (t, J = 6.5 Hz, 2H), 2.93 - 2.78 (m, 2H), 2.03 - 1.91 (m, 2H), 1.83 - 1.74 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 162.03, 148.76, 145.57, 139.73, 137.07, 136.25, 131.58, 128.69, 123.61, 122.18, 121.89, 116.71, 115.13, 30.40, 28.34, 21.77. $C_{18}H_{16}N_5O_2$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 334.1304, 实测值 334.1308。

[0632] 7-(1-(2-氯乙基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0633] 
HSH124

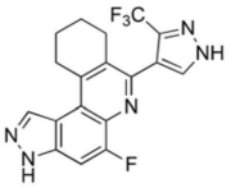
方法 A: 灰白色固体 收率: (26 mg, 28 %)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.83 (s, 1H), 8.55 (d, J = 0.8 Hz, 1H), 8.29 - 8.20 (m, 2H), 8.12 (d, J = 9.2 Hz, 1H), 4.68 (t, J = 5.6 Hz, 2H), 4.11 - 4.04 (m, 2H), 3.62 (t, J = 6.4 Hz, 2H), 3.13 (t, J = 6.2 Hz, 2H), 2.25 - 2.15 (m, 2H), 2.07 - 1.97 (m, 2H);^{13}C NMR (126 MHz, 甲醇-d_4) δ 154.27, 143.82, 140.54, 134.63, 133.72, 131.88, 122.97, 118.99, 114.92, 112.57, 53.74, 42.44, 31.04, 27.80, 21.23。

[0634] 2,3-二甲基-7-(3-(三氟甲基)-1H-吡唑-4-基)-3,6,8,9,10,11-六氢化-2H-吡唑并[3,4-a]菲啶

[0635] 
HSH127

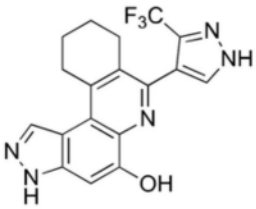
方法 A 灰白色固体, 收率: (40 mg, 20%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.33 (s, 1H), 8.27 (d, J = 9.0 Hz, 1H), 7.53 (d, J = 9.0 Hz, 1H), 4.27 (s, 3H), 3.95 (t, J = 6.4 Hz, 2H), 2.79 - 2.76(m, 5H), 2.13 - 2.05 (m, 2H), 1.98 - 1.86 (m, 2H); ^{13}C NMR (126 MHz, 甲醇-d_4) δ 156.81, 142.12, 141.73, 138.79, 135.59, 132.97, 132.27, 129.07, 122.32 (q, J = 268), 121.35, 119.06, 111.69, 110.05, 36.88, 31.69, 27.09, 21.21, 20.94, 8.19。

[0636] 5-氟-7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0637] 
HSH156

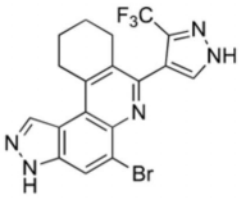
方法 A 白色固体, 收率: (94 mg, 25%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.60 (s, 1H), 8.25 (s, 1H), 7.69 (d, J = 9.9 Hz, 1H), 3.29 (t, J = 6.4 Hz, 2H), 2.71 (t, J = 6.2 Hz, 2H), 1.95 (dt, J = 12.3, 4.6 Hz, 2H), 1.87 - 1.71 (m, 2H); ^{13}C NMR (126 MHz, DMSO-J_6) δ 158.10, 156.09, 148.56, 142.63, 134.68, 134.59, 131.84, 131.42, 123.43 (q, J = 268), 122.90, 119.33, 112.71, 29.54, 28.19, 22.40, 22.13. $C_{18}H_{14}F_4N_5$ $[M+H]^+$ 的 HRMS (ESI) m/z 计算值 376.1185, 实测值 376.1185。

[0638] 7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-5-醇

[0639] 
HSH158

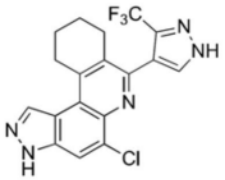
方法 A 灰白色固体, 收率: (21 mg, 11%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 9.05 (s, 1H), 8.35 (t, J = 1.0 Hz, 1H), 8.19 (s, 1H), 3.63 (t, J = 6.4 Hz, 2H), 2.79 (t, J = 6.2 Hz, 2H), 2.24 - 2.14 (m, 2H), 2.06 - 1.90 (m, 2H); ^{13}C NMR (126 MHz, 甲醇-d_4) δ 154.95, 142.50, 139.83, 135.25, 134.31, 133.85, 132.44, 123.87, 122.28 (q, J =269.64), 120.97, 115.06, 109.89, 30.71, 27.27, 21.14, 20.80。

[0640] 5-溴-7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0641] 
HSH162

方法 A 灰白色固体, 收率: (10 mg, 2%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.61 (s, 1H), 8.29 (s, 2H), 3.32 - 3.28 (m, 2H), 2.75 (t, J = 6.2 Hz, 2H), 1.96 (m, 2H), 1.78 (m, 2H); ^{13}C NMR (126 MHz, DMSO- d_6) δ 148.91, 143.00, 139.74, 139.73, 139.70, 131.56, 131.54, 131.51, 124.67, 123.42, 122.68, 121.27 (q, J =270.9 Hz), 119.30, 55.37, 29.71, 28.24, 22.49, 22.17。

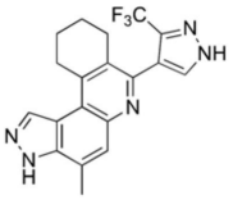
[0642] 5-氯-7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0643] 

HSH163

方法 A 灰白色固体, 收率: (12 mg, 5%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.62 (s, 1H), 8.29 (s, 1H), 8.09 (s, 1H), 3.31- 3.26 (m, 2H), 2.75 (t, J = 6.2 Hz, 2H), 2.06 - 1.87 (m, 2H), 1.82 - 1.67 (m, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 148.69, 143.00, 139.26, 132.77, 131.55, 131.55, 129.57, 123.42 (q, J = 269), 122.85, 119.37, 119.36, 115.32, 29.72, 28.23, 22.48, 22.16。

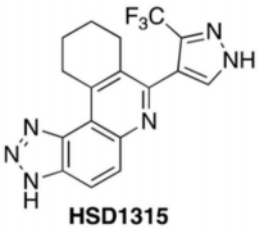
[0644] 4-甲基-7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0645] 

HSH164

方法 A 灰白色固体, 收率: (20 mg, 5%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.55 (s, 1H), 8.20 (s, 1H), 7.56 (s, 1H), 3.32 - 3.30 (m, 2H), 2.68 (t, J = 6.2 Hz, 2H), 2.63 (s, 3H), 1.96 (m, 2H), 1.77 (m, 2H);^{13}C NMR (126 MHz, DMSO-d_6) δ 148.32, 144.01, 141.68, 139.48, 136.72, 131.12, 129.51, 128.11, 124.44, 123.55 (q, J = 269), 121.41, 119.83, 116.19, 29.44, 28.13, 22.61, 22.41, 17.46。

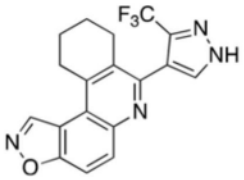
[0646] 7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-[1,2,3]三唑[4,5-a]菲啶

[0647] 

HSD1315

方法 A 灰白色固体, 收率: (72 mg, 20%)。 ^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.40 (d, J = 9.2 Hz, 1H), 8.33 (s, 1H), 8.05 (d, J = 9.2 Hz, 1H), 4.01 (t, J = 6.4 Hz, 2H), 2.82 (t, J = 6.3 Hz, 2H), 2.13 (dp, J = 9.3, 3.1 Hz, 2H), 2.02 - 1.93 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 154.39, 145.35, 140.07, 139.75, 138.56, 137.77, 134.33, 132.14, 122.37(q, J = 269.6 Hz), 121.20, 120.95, 116.39, 111.31, 30.87, 27.26, 21.12, 21.07; HRMS (ESI) m/z 计算值 $C_{17}H_{14}F_3N_6$ [M + H]$^+$ 359.1232, 实测值 359.1239。

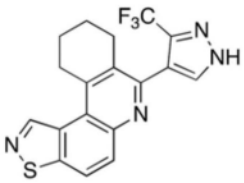
[0648] 7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢异恶唑并[4,5-a]菲啶

[0649] 

HSD1316

方法 A: 灰白色固体 (126 mg, 35%)。 ^{1}H NMR (500 MHz, 甲醇- d_4) δ 9.70 - 9.59 (m, 1H), 8.34 - 8.22 (m, 3H), 3.62 (t, J = 6.4 Hz, 2H), 2.79 (t, J = 6.3 Hz, 2H), 2.19 - 2.08 (m, 2H), 2.00 - 1.86 (m, 2H). $C_{18}H_{14}F_3N_4O$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 359.1120, 实测值 359.1122。

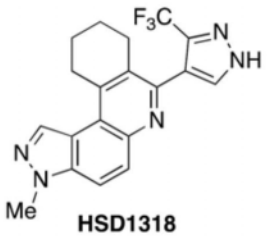
[0650] 7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢异噻唑并[4,5-a]菲啶

[0651] 

HSD1317

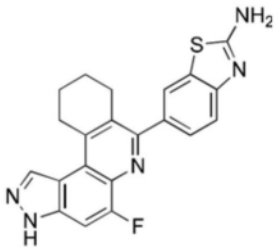
方法 A: 灰白色固体 (120 mg, 32%)。 ^{1}H NMR (500 MHz, 甲醇- d_4) δ 9.94 (s, 1H), 8.78 (d, J = 8.9 Hz, 1H), 8.41 (s, 1H), 8.21 (d, J = 8.9 Hz, 1H), 3.85 (t, J = 6.1 Hz, 2H), 2.87 (t, J = 6.1 Hz, 2H), 2.24 - 2.13 (m, 2H), 2.00 (td, J = 11.2, 9.5, 5.6 Hz, 2H); ^{13}C NMR (126 MHz, MeOD) δ 156.17, 155.87, 155.79, 145.11, 140.04, 139.75, 136.42, 135.01, 132.65, 129.80, 125.95, 125.43, 121.58, 120.19, 118.46, 109.79, 32.51, 27.76, 21.37, 20.63; $C_{18}H_{14}F_3N_4S$ [M + H]$^+$的 HRMS (ESI) m/z计算值375.0891,实测值375.0899。

[0652] 3-甲基-7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0653] 
HSD1318

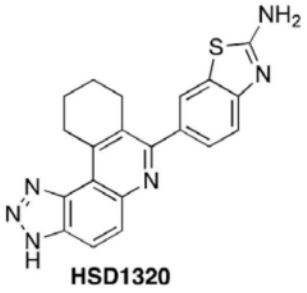
方法A: 灰白色固体 (148 mg, 40%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 8.77 (d, J = 0.9 Hz, 1H), 8.42 (dd, J = 9.3, 0.9 Hz, 1H), 8.38 (d, J = 0.9 Hz, 1H), 8.07 (d, J = 9.3 Hz, 1H), 4.32 (s, 3H), 3.68 (t, J = 6.3 Hz, 2H), 2.82 (t, J = 6.2 Hz, 2H), 2.22 - 2.12 (m, 2H), 2.05 - 1.92 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 155.03, 142.35, 140.13 (q, J = 37.8 Hz), 138.47, 135.21, 134.39, 134.19, 132.52, 124.04, 122.33 (q, J = 269.6 Hz), 119.30, 118.65, 115.97, 109.85, 35.32, 30.84, 27.26, 21.19, 20.86; $C_{19}H_{17}F_3N_5$ [M + H]$^+$ 的 HRMS (ESI)m/z计算值372.1436,实测值372.1438。

[0654] 6-(5-氟-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯并[d]噻唑-2-胺

[0655] 
HSD1319

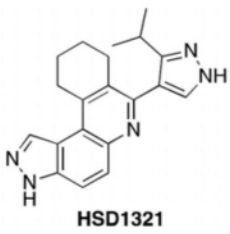
方法A: 灰白色固体 (148 mg, 38%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 8.56 (s, 1H), 7.91 - 7.84 (m, 1H), 7.70 (d, J = 9.8 Hz, IH), 7.57 (d, J = 2.4 Hz, 2H), 7.45 - 7.38 (m, 2H), 3.36 - 3.32 (m, 2H), 2.84 (t, J = 6.1 Hz, 2H), 2.04 - 1.97 (m, 2H), 1.79 - 1.71 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 167.68, 158.36(d, J = 253.26 Hz), 157.08, 153.14, 142.83, 136.79, 136.49, 134.35, 133.64, 131.24, 131.14, 127.29, 122.53, 122.22, 117.37, 113.06, 98.20, 29.80, 29.24, 22.52, 22.44; $C_{21}H_{17}FN_5S$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 390.1189, 实测值 390.1195。

[0656] 6-(8,9,10,11-四氢-3H-[1,2,3]三唑[4,5-a]菲啶-7-基)苯并[d]噻唑-2-胺

[0657] 
HSD1320

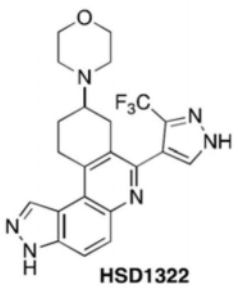
方法A: 灰白色固体 (112 mg, 30%)。^{1}H NMR (500 MHz, DMSO d_6) δ 8.03 (d, J = 9.1 Hz, 1H), 7.92 - 7.88 (m, 2H), 7.57 (s, 2H), 7.44 (dd, J = 8.2, 1.7 Hz, 1H), 7.40 (d, J = 8.2 Hz, 1H), 3.69 (t, J = 6.5 Hz, 2H), 2.85 (t, J = 6.2 Hz, 2H), 2.02 - 1.98 (m, 2H), 1.79 - 1.73 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 167.75, 158.87, 153.15, 145.33, 143.19, 139.18, 133.64, 131.24, 130.36, 130.18, 127.24, 122.15, 118.50, 117.37, 116.27, 29.93, 29.07, 22.66, 22.39. $C_{20}H_{17}N_6S$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 373.1235, 实测值 373.1237。

[0658] 7-(3-异丙基-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0659] 
HSD1321

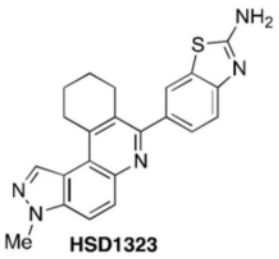
方法A: 灰白色固体 (136 mg, 41%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.82 (s, 1H), 8.23 (d, J = 14.6 Hz, 2H), 7.97 (s, 1H), 3.49 (t, J = 6.2 Hz, 2H), 3.02 (dd, J = 14.1, 7.3 Hz, 1H), 2.84 - 2.66 (m, 2H), 2.20 - 1.96 (m, 2H), 1.91 - 1.76 (m, 2H), 1.26 - 1.08 (m, 6H). $C_{20}H_{22}N_5$ [M + H]$^+$ 的HRMS (ESI) m/z 计算值 332.1875, 实测值 332.1875。

[0660] 4-(7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-9-基)吗啉

[0661] 
HSD1322

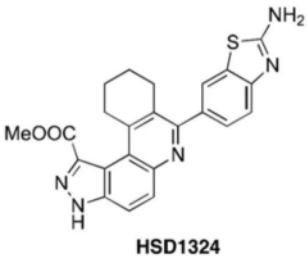
方法A: 灰白色固体 (110 mg, 25%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 8.64 (s, 1H), 8.13 (s, 1H), 7.95 (d, J = 9.2 Hz, 1H), 7.90 (d, J = 9.2 Hz, 1H), 4.17 - 3.37 (m, 11H), 3.29 - 3.19 (m, 1H), 3.19 - 3.08 (m, 1H), 2.85 2.70 (m, 1H), 2.14 (qd, J = 12.1, 5.8 Hz, 1H). $C_{22}H_{22}F_3N_6O$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 443.1807, 实测值 443.1809。

[0662] 6-(3-甲基-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯并[d]噻唑-2-胺

[0663] 
HSD1323

方法 A: 灰白色固体 (138 mg, 36%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 8.50 (d, J = 0.9 Hz, 1H), 8.02 - 7.95 (m, 1H), 7.91 - 7.85 (m, 2H), 7.63 (s, 2H), 7.46 - 7.36 (m, 2H), 4.17 (s, 3H), 3.31 (t, J = 6.5 Hz, 2H), 2.82 (t, J = 6.1 Hz, 2H), 2.01 - 1.95 (m, 2H), 1.83 - 1.66 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 167.75, 156.84, 152.94, 143.09, 142.79, 138.18, 135.06, 133.62, 131.17, 129.90, 129.18, 127.28, 122.20, 121.53, 117.29, 117.17, 114.03, 36.31, 29.76, 29.17, 22.58, 22.54. $C_{22}H_{20}N_5S$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 386.1439, 实测值 386.1442。

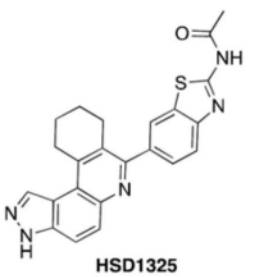
[0664] 7-(2-氨基苯并[d]噻唑-6-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-1-羧酸甲酯

[0665] 
HSD1324

方法 A: 灰白色固体 (120 mg, 28%); ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.55 (s, 1H), 8.15 (s, 1H), 8.08 (d, J = 1.9 Hz, 1H), 7.59 (dt, 7 = 8.3, 1.9 Hz, 1H), 7.56 (dd, J = 8.2, 1.8 Hz, 1H), 3.99 (s, 3H), 3.21 - 3.11 (m, 2H), 2.91 - 2.77 (m, 2H), 1.87 - 1.68 (m, 4H); ^{13}C NMR (126 MHz, DMSO) δ 169.32, 166.59, 153.43, 150.43, 140.96, 140.33, 138.84, 131.42, 129.03, 128.38, 125.04, 123.58, 122.59, 118.02, 116.40, 111.98, 53.45, 30.28, 27.43, 21.69, 21.65. $C_{23}H_{20}N_5O_2S$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 430.1338, 实测值 430.1348。

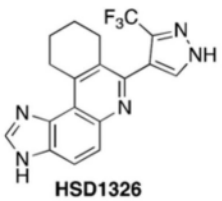
[0666] N-(6-(8,9,10,11-T四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯并[d]噻唑-2-基)乙酰胺

[0667] 将化合物HSD992(93mg,0.25mmol)溶解在DMF(2mL)和三乙胺(2当量)的混合物中,然后加入乙酰氯(30mg,1.5mmol)。之后,在室温下继续过夜反应。反应完成后,用乙酸乙酯(2X 20mL)萃取反应混合物,并用盐水溶液洗涤,并通过快速柱色谱法用二氯甲烷:甲醇(90:10)纯化粗产物,得到所需产物,为黄色固体(73mg,70%)。

[0668] 
HSD1325

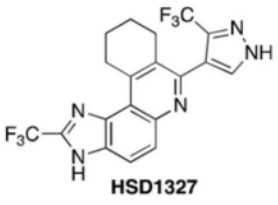
^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.76 (s, 1H), 8.38 (d, J = 9.3 Hz, 1H), 8.31 - 8.24 (m, 1H), 8.20 (d, J = 9.3 Hz, 1H), 7.88 - 7.84 (m, 1H), 7.76 (d, J = 8.4 Hz, 1H), 4.32 (s, 3H), 3.67 (t, J = 6.3 Hz, 2H), 2.95 (t, J = 6.1 Hz, 2H), 2.26 - 2.18 (m, 2H), 1.99 - 1.87 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 170.98, 155.22, 149.49, 141.56, 138.36, 135.15, 134.18, 132.65, 129.29, 127.49, 125.42, 124.19, 123.58, 118.90, 118.87, 115.92, 114.54, 35.36, 31.10, 27.83, 21.22, 21.15; $C_{23}H_{20}N_5O_2S$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 414.1389, 实测值 414.1388。

[0669] 7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-咪唑并[4,5-a]菲啶

[0670] 
HSD1326

方法 A: 灰白色固体 (75 mg, 21%)。 ^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.30 (s, 1H), 7.99 (d, J = 1.2 Hz, 1H), 7.93 (d, J = 9.0 Hz, 1H), 7.83 (d, J = 8.9 Hz, 1H), 3.68 (d, J = 6.7 Hz, 2H), 2.68 (t, J = 6.3 Hz, 2H), 2.08 - 1.98 (m, 2H), 1.91 - 1.83 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 149.00, 145.68, 143.27, 142.66, 140.11, 130.25, 130.05, 124.01, 122.80 (q, J = 270.51 Hz), 118.99, 118.30, 115.91, 112.78, 94.71, 29.26, 27.75, 22.04, 21.86. $C_{18}H_{15}F_3N_5$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 358.1280, 实测值358.1286。

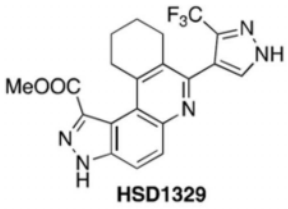
[0671] 2-(三氟甲基)-7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-咪唑并[4,5-a]菲啶

[0672] 

HSD1327

方法A: 灰白色固体 (106 mg, 25%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 7.99 (s, 1H), 7.90 (d, J = 9.1 Hz, 1H), 7.85 (d, J = 9.1 Hz, 1H), 3.91 - 3.75 (m, 2H), 2.68 (t, J = 6.3 Hz, 2H), 2.07 - 1.92 (m, 2H), 1.94 - 1.77 (m, 2H). ^{13}C NMR (126 MHz, MeOD) δ 149.46, 144.26, 143.57, 140.04, 139.76, 137.30, 131.82, 130.86, 130.17, 126.46, 124.94(q, J = 269.64 Hz), 120.67, 120.32(q, J = 268.64 Hz), 118.93, 114.85, 29.42, 27.82, 21.99, 21.94. $C_{19}H_{14}F_6N_5$ [M + H]$^+$的HRMS(ESI)m/z计算值426.1153,实测值426.1155。

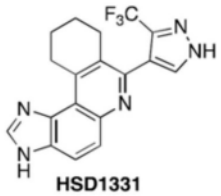
[0673] 7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-1-甲酸甲酯

[0674] 

HSD1329

方法A: 灰白色固体 (83 mg, 20%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.36 - 8.34 (m, 1H), 8.33 (d, J = 9.2 Hz, 1H), 8.07 (d, J = 9.2 Hz, 1H), 4.09 (s, 3H), 3.41 (t, J = 6.0 Hz, 2H), 2.83 (t, J = 6.5 Hz, 2H), 2.04 - 1.96 (m, 2H), 1.94 - 1.87 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 165.69, 155.80, 143.04, 140.76, 140.09, 139.80, 136.05, 134.16, 132.40, 124.22, 122.30 (268.38), 120.37, 111.65, 115.75, 109.90, 52.41, 31.10, 26.62, 21.03, 20.75; $C_{20}H_{17}F_3N_5O_2$ [M +H]$^+$的HRMS(ESI)m/z计算值416.1334,实测值416.1343。

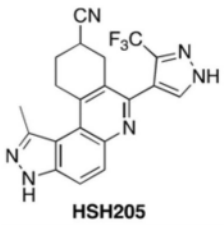
[0675] 7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-9-腈

[0676] 

HSD1331

方法A: 灰白色固体 (100 mg, 26%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.78 (s, 1H), 8.39 (s, 1H), 8.13 (d, J = 9.5, 4.5 Hz, 1H), 7.97 (d, J = 9.2, 4.4 Hz, 1H), 3.61 - 3.50 (m, 2H), 3.48 - 3.36 (m, 1H), 3.12 - 2.95 (m, 2H), 2.37 - 2.22 (m, 2H). $C_{19}H_{14}F_3N_6$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 383.1232, 实测值 383.1237。

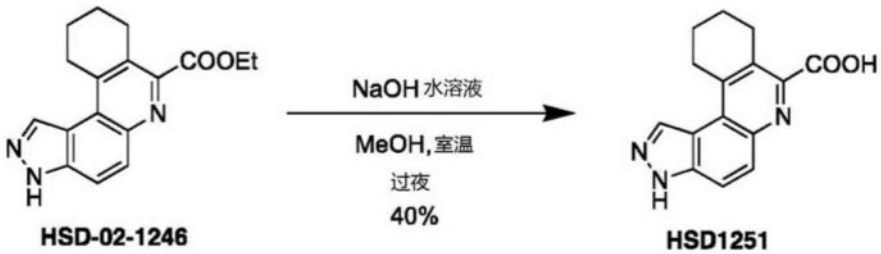
[0677] 1-甲基-7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-9-腈

[0678] 

HSH205

方法A: 灰白色固体 (59 mg, 15%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 8.37 (d, J = 1.0 Hz, 1H), 8.21 (d, J = 9.2 = Hz, 1H), 7.89 (d, J = 9.2 Hz, 1H), 3.94 (t, J = 6.6 Hz, 2H), 3.49 - 3.42 (m, 1H), 3.20 (dd, J = 17.3, 5.9 Hz, 1H), 3.09 (d, J = 7.5 Hz, 1H), 3.06 (s, 3H), 2.39 (m, J = 12.6, 6.0, 3.4 Hz, 1H), 2.21 (m, J = 13.3, 8.5, 6.5 Hz, 1H); ^{13}C NMR (126 MHz, 甲醇-d_4) δ 151.72, 141.79, 137.08, 132.47, 129.46, 126.34, 123.81, 123.71, 123.64, 122.20 (q, J = 270), 112.62, 109.78, 109.78, 30.62, 30.56,29.87,24.22,23.60,23.54,17.53。

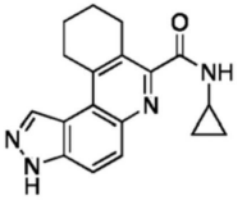
[0679] 8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-羧酸(HSD1251)

[0680] 

HSD-02-1246 HSD1251

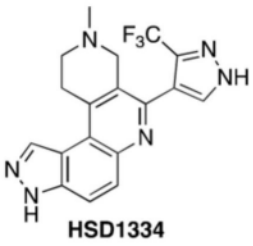
[0681] 灰白色固体(40%)。^{1}H NMR(500MHz,DMSO-d_6)δ8.60(s,1H),7.90(d,J=9.0Hz,1H),7.83(d,J=9.5Hz,1H),3.32-3.26(m,11H),3.06-2.96(m,2H),2.03-1.92(m,2H),1.87-1.75(m,2H)。

[0682] N-环丙基-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-羧酸胺

[0683] 
HSD1333

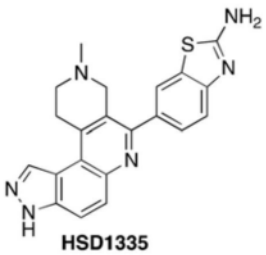
向 HSD1251（50mg，0.18mmol）的 DMF（2.5mL）溶液中加入环丙胺（0.19mmol）、HOBt（0.18mmol）、EDCl·HCl（0.18mmol）和 DIPEA（0.39mmol）。在室温下继续反应 12 小时，并通过 TLC 监测。完成后，用乙酸乙酯萃取反应混合物，并用盐水溶液洗涤，并经 Na_2SO_4 干燥。通过快速色谱法纯化粗产物，得到期所需产物，为白色固体（70％收率，39mg）。NMR (500 MHz, DMSO-d_6) δ 8.59 - 8.53 (m, 2H), 7.91 - 7.82 (m, 2H), 3.05 - 2.97 (m, 2H), 2.92 - 2.82 (m, 1H), 2.02 - 1.92 (m, 2H), 1.85 - 1.74 (m, 2H), 0.77 - 0.66 (m, 2H), 0.62 - 0.54(m,2H)；^{13}C NMR(126MHz,DMSO)δ169.02,150.75,143.04,142.46,138.96,136.49,129.42,129.13,123.13,116.31,114.78,29.62,26.70,23.08,22.44,22.07,6.21.$C_{18}H_{19}N_4O$ $[M+H]^+$的HRMS(ESI)m/z计算值307.1559,实测值307.1565。

[0684] 9-甲基-7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吲唑并[5,4-c][2,7]萘啶

[0685] 
HSD1334

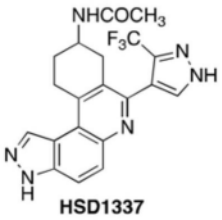
方法 A: 灰白色固体 (96 mg, 26%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.19 (s, 1H), 8.05 - 7.98 (m, 1H), 7.26 (d, 7 = 8.9 Hz, 1H), 6.81 (d, J = 8.9 Hz, 1H), 6.49 - 6.40 (m, 1H), 4.26 (d, J = 11.1 Hz, 1H), 3.66 - 3.51 (m, 1H), 3.06 - 2.89 (m, 2H), 2.65 - 2.53 (m, 1H), 2.32 (s, 3H), 1.96 (t, J = 10.9 Hz, 1H); ^{13}C NMR (126 MHz, MeOD) δ 139.53, 136.09, 131.98, 131.66, 129.91, 123.14(q, J = 269.6 Hz), 119.98, 118.88, 117.25, 110.66, 107.76, 55.06, 54.96, 51.22, 44.41, 40.51。

[0686] 6-(9-甲基-8,9,10,11-四氢-3H-吲唑并[5,4-c][2,7]萘啶-7-基)苯并[d]噻唑-2-胺

[0687] 
HSD1335

方法 A: 灰白色固体 (81 mg, 21%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 7.74 (d, J = 1.7 Hz, 1H), 7.45 (s, 2H), 7.32 (d, 8 J.1 = Hz, 1H), 7.26 (dd, J = 8.2, 1.8 Hz, 1H), 7.19 (d, J = 8.8 Hz, 1H), 6.79 (d, J = 8.9 Hz, 1H), 6.33 (d, J = 4.8 Hz, 1H), 5.95 (s, 1H), 3.94 (d, J = 11.0 Hz, 1H), 3.46 - 3.40 (m, 2H), 2.80 - 2.71 (m, 2H), 2.25 - 2.17 (m, 1H), 2.12 (s, 3H), 1.77 (t, J = 10.6 Hz, 1H); ^{13}C NMR (126 MHz, DMSO) δ 167.11, 153.11, 140.29, 135.76, 134.70, 132.26, 132.06, 131.56, 125.86, 120.50, 119.90, 118.66, 118.03, 117.84, 111.01, 107.40, 61.27, 55.89, 46.15。

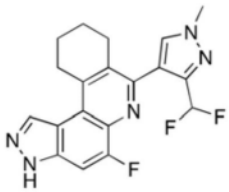
[0688] N-(7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-9-基)乙酰胺

[0689] 
HSD1337

方法 A: 灰白色固体 (137 mg, 33%)。^{1}H NMR (500 MHz, 甲醇- d_4) δ 8.56 (s, 1H), 8.02 (s, 1H), 7.86 (s, 2H), 4.25 - 4.09 (m, 1H), 3.63 - 3.55 (m, 1H), 3.50 - 3.42 (m, 2H), 3.02 - 2.92 (m, 1H), 2.71 - 2.59 (m, 1H), 2.40 - 2.30 (m, 1H), 1.98 - 1.90 (m, 4H); ^{13}C NMR (126 MHz, DMSO) δ 169.42, 153.60, 148.04, 140.41, 138.26, 134.78, 129.37, 127.68, 122.95, 122.23, 115.48, 110.76, 44.12, 34.25, 29.21, 27.37, 23.11. $C_{20}H_{18}F_3N_6O$ $[M+H]^+$ 的 HRMS (ESI) m/z 计算值 415.1494, 实测值 415.1498。

[0690] 7-(3-(二氟甲基)-1-甲基-1H-吡唑-4-基)-5-氟-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0691] 方法A:灰白色固体(37mg,10％)。^{1}H NMR(500MHz,DMSO-d_6)δ8.50(s,1H),

[0692] 

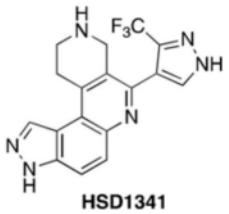
HSD1340

8.27 (s, 1H), 7.69 - 7.62 (m, 1H), 7.49 (t, J = 54.7 Hz, 1H), 3.97 (s, 3H), 3.32 - 3.24 (m, 2H), 2.94 - 2.83 (m, 2H), 2.02 - 1.92 (m, 2H), 1.85 - 1.73 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 158.06, 156.05, 148.40, 144.52, 144.34, 144.16, 143.02, 136.82, 136.43, 134.20, 132.97, 131.01, 122.11, 119.91, 113.31, 112.93, 111.45, 109.58, 98.48, 98.29, 31.15, 29.80, 28.54, 22.27。

[0693] 7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吲唑并[5,4-c][2,7]萘啶

[0694] 在本实例中,采用方法A,将4-氧杂哌啶-1-甲酸叔丁酯用作环酮,由于反应中存在HCl,Boc-基团可以原位脱保护,过滤并用乙醇洗涤反应混合物,从中沉淀出所需的化合物。

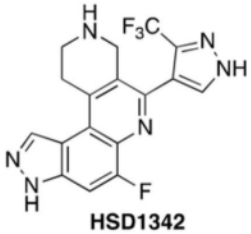
[0695] 方法A:灰白色固体(100mg,28%)。^{1}H NMR(500MHz,DMSO-d_6)δ9.70(s,

[0696] 

HSD1341

2H), 8.60 (s, 1H), 8.34 (s, 1H), 7.97 (dd, J = 9.2, 3.7 Hz, 1H), 7.84 (d, J = 9.1 Hz, 1H), 4.37 - 4.31 (m, 2H), 3.70 - 3.62 (m, 2H), 3.61 - 3.53 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 146.11, 144.36, 139.64 (q, J 36.54 Hz), 138.90, 138.14, 135.96, 131.61, 129.36, 123.35(q, J = 270.9 Hz), 122.70, 120.58, 117.94, 115.98, 43.23, 25.91; $C_{17}H_{14}F_3N_6$ $[M+H]^+$ 359.1232, 实测值 359.1233。

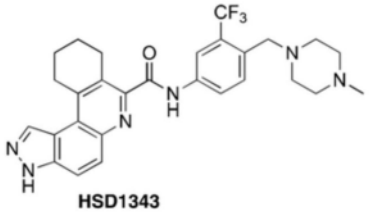
[0697] 5-氟-7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吲唑并[5,4-c][2,7]萘啶

[0698] 

HSD1342

方法 A: 与 HSD1341 中相同的环酮: 灰白色固体 (60 mg, 16%)。 ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.60 (s, 1H), 8.28 (s, 1H), 7.71 (d, J = 10.0 Hz, 1H), 3.85 (s, 2H), 3.24 (q, J = 5.1, 4.2 Hz, 2H), 3.16 (t, J = 4.4 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 158.12(d, J = 253.26 Hz), 146.55, 141.41, 139.52, 139.23, 138.48, 134.96, 131.48, 123.42(q, J = 269.64 Hz), 122.86, 118.58, 112.68, 99.76, 97.55, 55.01, 47.19, 42.89; $C_{17}H_{13}F_4N_6$ $[M+H]^+$ 的 HRMS (ESI) m/z 计算值 377.1138, 实测值 377.1138。

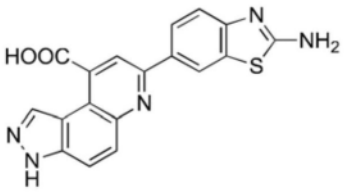
[0699] N-(4-((4-甲基哌嗪-1-基)甲基)-3-(三氟甲基)苯基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-羧酸胺

[0700] 

HSD1343

向 HSD1251（50mg，0.18mmol）的 DMF（2.5mL）溶液中加入 4-((4-甲基哌嗪-1-基)甲基)-3-(三氟甲基)苯胺（0.19mmol）、HATU（0.18mmol）和 DIPEA（0.39 mmol)。在室温下继续反应 12 小时，并通过 TLC 监测。完成后，用乙酸乙酯萃取反应混合物，并用盐水溶液洗涤，并经 Na_2SO_4 干燥。 通过快速色谱纯化粗产物，得到所需产物，为灰白色固体（50％收率，47mg)。^{1}H NMR (500 MHz,DMSO-d_6) δ10.93(s,1H),8.63(s,1H),8.29(d,J＝2.2Hz,1H),8.05(dd,J＝8.5,2.3Hz,1H),7.98-7.89(m,2H),7.71(d,J＝8.5Hz,1H),3.56(s,2H),3.34-3.30(m,2H),3.13(t,J＝6.2Hz,2H),2.37(s,8H),2.14(s,3H),1.99(ddt,J＝8.9,6.3,2.9Hz,2H),1.87-1.79(m,2H);^{13}C NMR(126MHz,DMSO)δ166.54,149.19,143.71,142.60,138.52,132.53,131.81,129.74,129.42,128.11(q,J＝28.9Hz),125.91(q,J＝274.6Hz),123.78,123.53,117.19,117.14,116.03,57.94,55.22,53.19,46.22,29.73,26.89,22.37,22.07;$C_{28}H_{30}F_3N_6O$[M+H]$^+$的HRMS(ESI)m/z计算值523.2433,实测值523.2433。

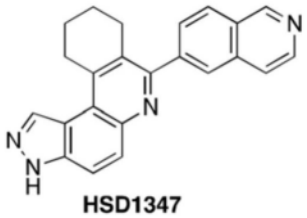
[0701] 7-(2-氨基苯并[d]噻唑-6-基)-3H-吡唑并[4,3-f]喹啉-9-羧酸

[0702] 

HSD1345

方法A: 棕色固体 (126 mg, 35%)。^{1}H NMR (500 MHz, DMSO d_6) δ 8.70 (d, J = 1.8 Hz, 1H), 8.48 - 8.35 (m, 3H), 8.32 (s, 1H), 8.25 (dd, J = 8.5, 1.9 Hz, 1H), 8.00 (d, J = 9.2 Hz, 1H), 7.96 (d, J = 9.1 Hz, 1H), 7.51 (d, J = 8.5 Hz, 1H); ^{13}C NMR (126 MHz, DMSO) δ 170.36, 169.08, 153.15, 146.62, 138.70, 132.42, 129.93, 129.24, 125.78, 120.77, 117.16, 117.04, 115.21。

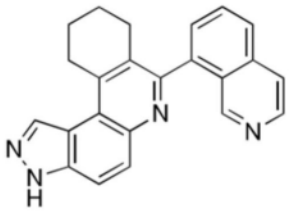
[0703] 7-(异喹啉-6-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0704] 

HSD1347

方法A: 灰白色固体 (178 mg, 51%)。^{1}H NMR (500 MHz, DMSO- de) δ 9.34 (s, 1H), 8.65 - 8.45 (m, 2H), 8.23 - 8.08 (m, 2H), 7.94 - 7.75 (m, 4H), 3.36 - 3.01 (m, 2H), 2.84 - 2.64 (m, 2H), 2.03 - 1.80 (m, 2H), 1.74 - 1.50 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 155.87, 152.56, 143.58, 143.17, 142.64, 138.79, 136.42, 135.77, 135.39, 129.57, 129.30, 127.89, 127.63, 127.02, 124.06, 122.13, 121.09, 116.40, 114.60, 29.61, 28.83, 22.51, 22.40。

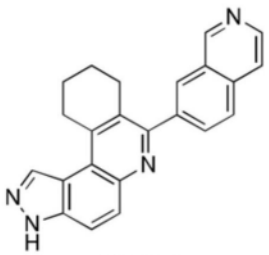
[0705] 7-(异喹啉-8-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0706] 

HSD1349

方法A: 棕色固体 (140 mg, 40%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.67 (d, J = 1.0 Hz, 1H), 8.61 (s, 1H), 8.46 (d, J = 5.8 Hz, 1H), 8.07 (dt, J = 8.4, 1.1 Hz, 1H), 7.95 - 7.90 (m, 2H), 7.86 (s, 2H), 7.70 (dd, J = 7.0, = 1.1 Hz, 1H), 3.45 - 3.36 (m, 2H), 2.71 - 2.57 (m, 1H), 2.42 - 2.30 (m, 1H), 2.08 - 2.02 (m, 2H), 1.84 - 1.71 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 154.18, 149.50, 144.02, 143.31, 141.71, 138.68, 136.43, 130.58, 130.53, 128.48, 128.34, 126.97, 126.93, 122.66, 121.40, 115.96, 29.52, 27.69, 22.02, 21.75。

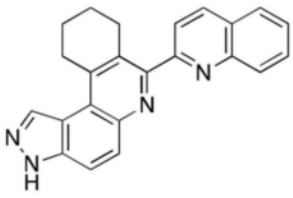
[0707] 7-(异喹啉-7-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0708] 

HSD1350

方法A: 灰白色固体 (105 mg, 30%)。 ^{1}H NMR (500 MHz,甲醇- d_4) δ 9.33 (d, J = 1.4 Hz, 1H), 8.61 (s, 1H), 8.50 (dd, J = 5.9, 1.4 Hz, 1H), 8.29 (s, 1H), 8.09 (d, J = 8.4 Hz, 1H), 7.98 (dt, J = 8.4, 1.6 Hz, 1H), 7.93 - 7.85 (m, 2H), 3.47 - 3.37 (m, 2H), 2.84 (t, J = 6.2 Hz, 2H), 2.17 - 2.08 (m, 2H), 1.89 - 1.82 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 156.08, 152.22, 143.84, 143.20, 141.99, 140.04, 138.79, 136.00, 135.65, 132.00, 129.69, 128.57, 128.47, 127.97, 126.35, 122.41, 120.88, 113.80, 29.64, 28.49, 22.13, 22.04。

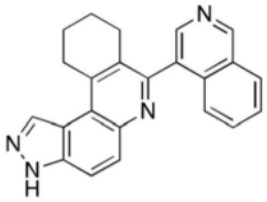
[0709] 7-(喹啉-2-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0710] 

HSD1351

方法A: 灰白色固体 (150 mg, 43%)。 ^{1}H NMR (500 MHz, DMSO- d_6) δ 8.61 (s, 1H), 8.50 (d, J = 8.5 Hz, 1H), 8.09 - 8.03 (m, 2H), 8.00 (d, J = 8.4 Hz, 1H), 7.89 (s, 2H), 7.80 (ddd, J = 8.3, 6.8, 1.5 Hz, 1H), 7.69 7.62 (m, 1H), 3.38 (d, J = 6.6 Hz, 2H), 3.09 (t, J = 6.2 Hz, 2H), 2.02 (dp, J = 9.3, 3.2 Hz, 2H), 1.82 - 1.71 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 159.31, 154.53, 146.93, 143.32, 143.03, 138.94, 136.97, 136.58, 130.38, 130.26, 129.68, 129.51, 128.37, 127.38, 122.95, 122.49, 116.48, 114.65, 29.86, 28.31, 22.54, 22.43;$C_{23}H_{19}N_4[M+H]^+$的HRMS(ESI)m/z计算值351.1610,实测值351.1608。

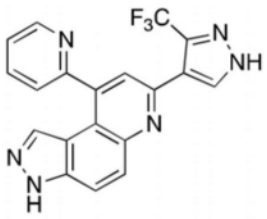
[0711] 7-(异喹啉-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0712] 

HSD1352

方法 A: 灰白色固体 (262 mg, 75%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 9.41 (d, J = 0.9 Hz, 1H), 8.61 (s, 1H), 8.50 (s, 1H), 8.28 - 8.14 (m, 1H), 7.94 - 7.80 (m, 2H), 7.73 - 7.62 (m, 2H), 7.38 - 7.31 (m, 1H), 3.44 - 3.35 (m, 2H), 2.64 - 2.54 (m, 1H), 2.40 - 2.27 (m, 1H), 2.00 - 1.95 (m, 3H), 1.77 - 1.65 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 153.43, 152.80, 143.82, 142.90, 142.62, 138.81, 136.47, 134.12, 132.07, 131.60, 130.70, 129.60, 128.54, 128.33, 128.02, 124.62, 122.35, 116.52, 114.67, 29.59, 27.87, 22.50, 22.16. $C_{23}H_{19}N_4$ [M + H]$^+$ 的 HRMS(ESI)m/z计算值351.1610,实测值351.1611。

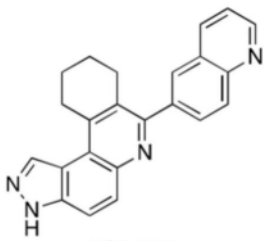
[0713] 9-(吡啶-2-基)-7-(3-(三氟甲基)-1H-吡唑-4-基)-3H-吡唑并[4,3-f]喹啉

[0714] 

HSD1356

方法 C: 灰白色固体 (160 mg, 42%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.80 (ddt, J = 5.0, 1.7, 0.7 Hz, 1H), 8.37 (s, 1H), 8.14 (td, J = 7.7, 1.7 Hz, 1H), 8.01 (d, J = 9.2 Hz, 1H), 7.92 (dd, J = 9.3, 0.9 Hz, 1H), 7.82 - 7.65 (m, 3H), 6.69 (s, 1H); ^{13}C NMR (126 MHz, MeOD) δ 157.76, 157.73, 149.27, 147.72, 146.52, 145.30, 139.22(q, J = 36.54 Hz), 138.53, 131.12, 129.05, 129.02, 124.48, 124.45, 124.33, 123.02 (q, J = 268.38 Hz), 121.14, 120.71, 119.57, 115.74。

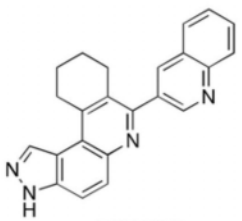
[0715] 7-(喹啉-6-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0716] 

HSD1357

方法 A: 灰白色固体 (192 mg, 55%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 9.01 (dd, J = 4.6, 1.7 Hz, 1H), 8.62 (s, 1H), 8.13 (d, J = 8.5 Hz, 1H), 7.90 (d, J = 9.1 Hz, 1H), 7.82 (d, J = 8.8 Hz, 1H), 7.77 (t, J = 7.6 Hz, 1H), 7.59 - 7.52 (m, 1H), 7.49 (t, J = 7.6 Hz, 1H), 7.34 (d, J = 8.3 Hz, 1H), 3.49 - 3.36 (m,2H), 2.61 - 2.54 (m,2H), 2.39 - 2.23 (m, 1H), 2.02 - 1.87 (m,2H), 1.77 - 1.60 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 153.87, 150.73, 148.39, 146.91, 143.65, 142.78, 138.83, 136.48, 130.02, 129.95, 129.78, 129.52, 127.55, 126.67, 125.91, 122.43,121.73,116.49,114.82,29.57,27.63,22.47,22.06$C_{23}H_{19}N_4$[M+H]$^+$的HRMS(ESI)m/z计算值351.1610,实测值351.1611。

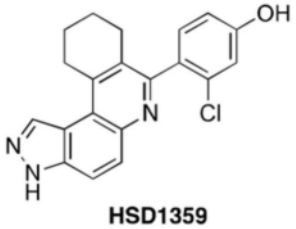
[0717] 7-(喹啉-3-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0718] 

HSD1358

方法 A: 灰白色固体 (162 mg, 46%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 9.14 (s, 1H), 8.61 - 8.60 (m, 2H), 8.10(t, J = 7.25 Hz, 2H), 7.89 (s, 2H), 7.83 (t, J = 6.95 Hz, 1H), 7.68 (d, J = 7.8 Hz, 1H), 3.39 (t, J = 5.65 Hz, 2H), 2.92 (t, J = 5.75 Hz, 2H), 2.06 - 2.02 (m, 2H), 2.07 - 1.98 (m, 2H), 1.78 - 1.77 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 153.88, 151.60, 147.28, 143.90, 142.87, 138.80, 136.53, 136.17, 134.00, 130.35, 129.97, 129.70, 129.19, 128.96, 127.45, 122.16, 116.44, 114.74, 29.75, 28.86, 22.58; $C_{23}H_{19}N_4$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 351.1610, 实测值351.1613。

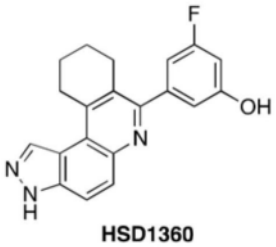
[0719] 3-氯-4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0720] 

HSD1359

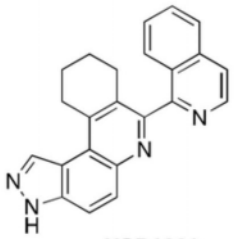
方法 A: 灰白色固体 (178 mg, 51%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.55 (s, 1H), 7.88 - 7.76 (m, 2H), 7.18 (d, J = 8.3 Hz, 1H), 6.97 (d, J = 2.4 Hz, 1H), 6.88 (dd, J = 8.3, 2.4 Hz, 1H), 3.39 - 3.31 (m, 2H), 2.67 (dt, J = 17.3, 6.3 Hz, 1H), 2.54 (dt, J = 17.2, 6.2 Hz, 1H), 2.07 - 1.98 (m, 2H), 1.91 - 1.74 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 158.50, 155.40, 143.33, 142.83, 138.70, 135.81, 132.99, 130.85, 130.10, 128.23, 122.36, 116.12, 115.69, 114.11, 113.67, 29.44, 27.16, 22.10, 21.82. $C_{20}H_{17}ClN_3O$ [M + H]$^+$的 HRMS (ESI) m/z计算值350.1060,实测值350.1063。

[0721] 3-氟-5-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0722] 
HSD1360

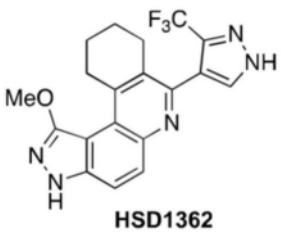
方法 A: 灰白色固体 (117 mg, 35%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.59 (s, 1H), 7.91 - 7.82 (m, 2H), 7.20 (d, J = 8.3 Hz, 1H), 6.98 (d, J = 2.4 Hz, 1H), 6.89 (dd, J = 8.3, 2.4 Hz, 1H), 3.48 - 3.35 (m, 2H), 2.70 (dt, J = 17.3, 6.3 Hz, 1H), 2.57 (dt, J = 17.2, 6.2 Hz, 1H), 2.10 - 2.03 (m, 2H), 1.92 - 1.82 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 158.52, 155.48, 143.37, 142.83, 135.85, 132.99, 130.91, 130.84, 130.11, 128.26, 122.39, 116.16, 115.69, 114.11, 113.71, 29.48, 27.18, 22.13, 21.84。

[0723] 7-(异喹啉-1-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0724] 
HSD1361

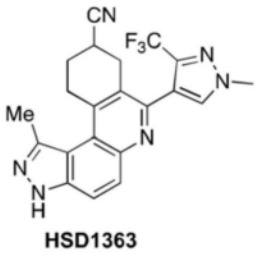
方法 A: 灰白色固体 (172 mg, 49%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.67 (s, 1H), 8.59 (dd, J = 5.9, 1.3 Hz, 1H), 8.07 (d, J = 8.3 Hz, 1H), 7.98 (d, J = 5.8 Hz, 1H), 7.90 (s, 2H), 7.81 (ddd, J = 8.3, 6.7, 1.4 Hz, 1H), 7.62 - 7.55 (m, 1H), 7.52 (d, J = 8.4 Hz, 1H), 3.49 (d, J = 8.1 Hz, 2H), 2.54 (s, 2H), 2.13 - 2.05 (m, 2H), 1.87 - 1.76 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 158.92, 153.77, 144.17, 140.73, 136.98, 131.02, 130.39, 128.41, 128.05, 127.21, 126.99, 126.27, 123.01, 121.47, 29.53, 26.71, 22.03, 21.60. $C_{23}H_{19}N_4$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 351.1610,实测值351.1606。

[0725] 1-甲氧基-7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0726] 
HSD1362

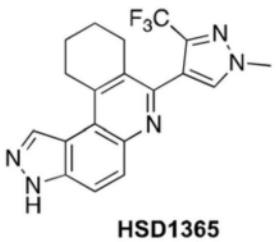
方法 A: 灰白色固体 (163 mg, 42%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.22 (s, 1H), 7.92 (d, J = 9.2 Hz, 1H), 7.86 (d, J = 9.2 Hz, 1H), 4.15 (d, J = 1.1 Hz, 3H), 3.79 (t, J = 6.1 Hz, 2H), 2.73 (t, J = 6.2 Hz, 2H), 2.01 - 1.83 (m, 4H); ^{13}C NMR (126 MHz, MeOD) δ 158.09, 154.86, 141.34, 135.93, 132.97, 131.61, 125.26, 123.06, 118.25, 118.16, 101.38, 56.07, 31.36, 27.62, 21.62, 21.18. $C_{19}H_{17}F_3N_5O$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 388.1385, 实测值 388.1390。

[0727] 1-甲基-7-(1-甲基-3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-9-腈

[0728] 
HSD1363

方法 A: 灰白色固体 (54mg , 13%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 7.96 (s, 1H), 7.85 - 7.75 (m, 2H), 4.07 (s, 3H), 3.74 - 3.64 (m, 2H), 3.14 - 3.07 (m, 1H), 3.03 - 2.96 (m, 1H), 2.33 - 2.25 (m, 1H), 2.13 - 2.04 (m, 1H); ^{13}C NMR (126 MHz, MeOD) δ 147.28, 143.95, 143.52, 141.31, 141.20, 139.12, 132.56, 128.83, 126.48, 123.95, 122.46 (q, J = 269.64 Hz), 121.58, 118.93, 114.92, 114.10, 38.46, 30.48, 29.49, 25.02, 24.24. $C_{21}H_{18}F_3N_6$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 411.1545 实测值 411.1548。

[0729] 7-(1-甲基-3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

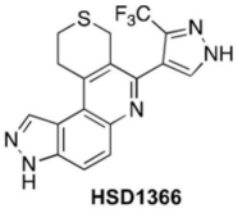
[0730] 
HSD1365

方法 A: 灰白色固体 (112 mg, 30%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.58 - 8.53 (m, 1H), 8.20 - 8.13 (m, 1H), 7.88 - 7.80 (m, 1H), 7.80 - 7.73 (m, 1H), 4.03 - 3.96 (m, 3H), 3.28 - 3.14 (m, 2H), 2.69 (t, J = 6.6 Hz, 2H), 2.01 - 1.93 (m, 2H), 1.81 - 1.75 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 148.11, 143.48, 142.15, 138.76, 138.47, 136.40, 133.48, 130.33, 129.58, 123.20 (q, J = 270.9 Hz), 121.98, 120.45, 116.40, 114.51, 29.54, 28.23, 22.57, 22.30. $C_{19}H_{17}F_3N_5$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 372.1436, 实测值 372.1444。

[0731] 7-(3-(三氟甲基)-1H-吡唑-4-基)-3,8,10,11-四氢吡唑并[4,3-f]硫基吡喃并

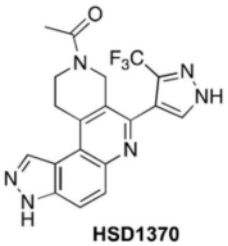
[3,4-c]喹诺酮

[0732] 方法A:Gray solid(124mg,33%)。^{1}H NMR(500MHz,DMSO-d_6)δ8.78(s,1H),

[0733] 
HSD1366

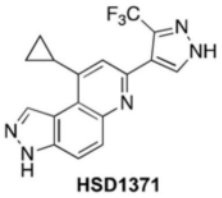
8.44 (s, 1H), 8.15 (d, J = 9.1 Hz, 1H), 8.02 (d, J = 9.2 Hz, 1H), 3.80 (s, 2H), 3.69 (t, J =6.1 Hz, 2H), 3.17 (t, J = 6.0 Hz, 2H). $C_{17}H_{13}F_3N_5S$ $[M+H]^+$ 发的 HRMS (ESI) m/z 计算值 376.0844, 实测值 376.0840。

[0734] 1-(7-(3-(三氟甲基)-1H-吡唑-4-基)-3,8,10,11-四氢-9H-吲唑并[5,4-c][2,7]萘啶-9-基)乙-1-酮

[0735] 
HSD1370

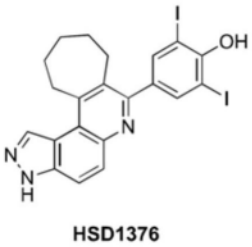
方法 C: 灰白色固体 (60 mg, 15%)。 ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.76 (d, J = 27.3 Hz, 1H), 8.45 (d, J = 10.1 Hz, 1H), 8.13 (d, J = 9.1 Hz, 1H), 7.90 (d, J= 9.1 Hz, 1H), 4.61 (s, 2H), 3.93 (t, J = 5.8 Hz, 2H), 3.64 (d, J = 6.0 Hz, 2H), 3.49 (d, J = 6.1 Hz, 1H), 2.16 (s, 2H), 1.99 (s, 1H); ^{13}C NMR (126 MHz, DMSO) δ 169.21, 140.24, 139.55, 139.27, 134.78, 132.70, 131.88, 128.81, 123.06, 122.63, 120.92, 115.44, 67.49, 42.57, 42.23, 30.01, 25.60. $C_{19}H_{16}F_3N_6O$ $[M+H]^+$的 HRMS (ESI) m/z 计算值 401.1338, 实测值 401.1328。

[0736] 9-环丙基-7-(3-(三氟甲基)-1H-吡唑-4-基)-3H-吡唑并[4,3-f]喹诺酮

[0737] 
HSD1371

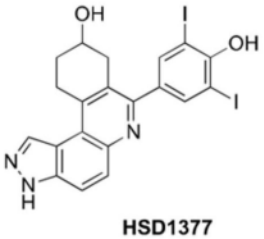
方法 A: 灰白色固体 (124 mg, 36%)。 ^{1}H NMR (500 MHz, DMSO-J_6) δ 8.80 (s, 1H), 8.66 (s, 1H), 7.91 (dd, J = 9.1, 2.8 Hz, 1H), 7.80 (d, J = 9.1 Hz, 1H), 7.62 (d, J = 2.8 Hz, 1H), 2.69 - 2.53 (m, 1H), 1.28 (dq, J = 9.3, 4.0, 3.2 Hz, 2H), 0.94 (dt, J = 5.2, 2.4 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 148.26, 147.74, 145.97, 145.51, 138.44, 131.97, 129.51, 123.71, 122.38, 121.62, 121.41, 118.34, 116.44, 115.57, 16.42, 7.59。

[0738] 4-(3,8,9,10,11,12-六氢环庚基[c]吡唑并[4,3-f]喹啉-7-基)-2,6-二碘苯酚

[0739] 
HSD1376

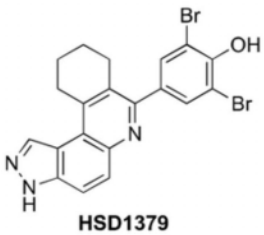
方法 A: 黄色固体 (203 mg, 35%)。 ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.92 (s, 1H), 8.72 (d, J =17.9 Hz, 1H), 8.00 (d, J = 9.1 Hz, 1H), 7.93 - 7.84 (m, 3H), 3.61 - 3.52 (m, 2H), 3.04 - 2.96 (m, 2H), 1.97 - 1.81 (m, 4H), 1.70 - 1.59 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 156.48, 150.93, 145.52, 141.82, 140.39, 137.85, 136.37, 133.12, 128.72, 121.97, 115.53, 87.03, 31.53, 31.18, 30.00, 26.90, 24.65. $C_{21}H_{18}I_2N_3O$ $[M+H]^+$ 的 HRMS (ESI) m/z 计算值 581.9539, 实测值 581.9544。

[0740] 7-(4-羟基-3,5-二碘苯基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-9-醇

[0741] 
HSD1377

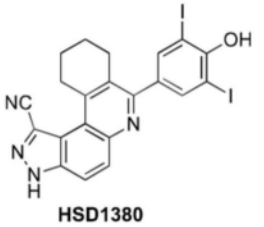
方法 A: 黄色固体 (175 mg, 30%)。 ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.20 (s, 1H), 8.80 (s, 1H), 8.22 (d, J = 9.3 Hz, 1H), 8.16 (d, J = 9.1 Hz, 1H), 8.12 (s, 2H), 4.07 (dq, J = 10.8, 6.9, 4.9 Hz, 1H), 3.56 (dt, J = 19.1, $_6$ 2 Hz, 1H), 3.50 - 3.46 (m, 1H), 2.99 (dd, J = 16.5, 4.1 Hz, 1H), 2.75 (dd, J = 16.5, 6.7 Hz, 1H), 2.20 - 2.09 (m, 1H), 2.07 - 1.96 (m, 1H); ^{13}C NMR (126 MHz, DMSO) δ 157.81, 154.46, 148.61, 140.62, 136.28, 135.37, 130.03, 122.73, 114.93, 87.09, 63.37, 36.50, 29.26, 28.51. $C_{20}H_{16}I_2N_3O_2$ $[M+H]^+$ 的 HRMS (ESI) m/z 计算值 583.9332, 实测值583.9336。

[0742] 2,6-二溴-4-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0743] 
HSD1379

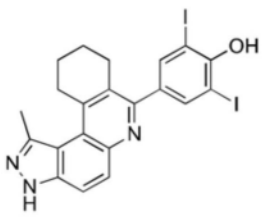
方法A：灰白色固体 (113 mg, 24%)。^{1}H NMR (500 MHz, DMSO- d_6) δ 10.25 (s, 1H), 8.58 (s, 1H), 7.92 (d, J = 9.1 Hz, 1H), 7.85 (d, J = 9.1Hz, 1H), 7.79 (s, 2H), 3.29 (d, J = 6.6 Hz, 2H), 2.80 (t, J = 6.1 Hz, 2H), 2.03 - 1.93 (m, 2H), 1.79 - 1.67 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 152.73, 151.40, 144.73, 142.09, 136.53, 133.76, 133.49, 129.93, 127.88, 122.31, 115.95, 111.95, 29.92, 28.66, 22.34. $C_{20}H_{16}Br_2N_3O$ $[M + H]^+$ 的 HRMS (ESI) m/z 计算值 471.9660, 实测值 471.9645。

[0744] 7-(4-羟基-3,5-二碘苯基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-1-腈

[0745] 
HSD1380

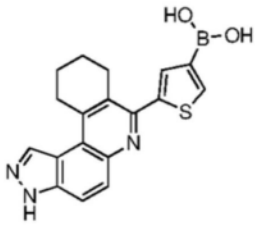
方法A：黄色固体 (224 mg, 38%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 9.77 (s, 1H), 7.93 (s, 2H), 7.86 - 7.77 (m, 2H), 3.40 (t, J = 6.5 Hz, 2H), 2.77 (t, J = 6.2 Hz, 2H), 1.90 (ddt, J = 9.2, 6.5, 3.0 Hz, 2H), 1.75 (ddt, J = 9.2, 6.4, 3.0 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 155.88, 155.23, 144.40, 143.50, 140.00, 139.78, 136.45, 131.67, 129.81, 121.16, 120.30, 117.66, 116.23, 114.52, 86.91, 31.76, 28.66, 22.03, 21.81. $C_{22}H_{15}I_2N_3O$ $[M + H]^+$ 的 HRMS (ESI) m/z 计算值 590.9304, 实测值590.9325。

[0746] 2,6-二碘-4-(1-甲基-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯酚

[0747] 
HSD1381

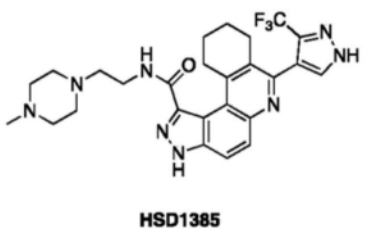
方法A：黄色固体 (244 mg, 42%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 10.08 (s, 1H), 8.04 (d, J = 9.6 Hz, 3H), 7.95 (d, J = 8.9 Hz, 1H), 3.61 - 3.50 (m, 2H), 2.92 (s, 3H), 2.82 - 2.71 (m, 2H), 1.87 - 1.74 (m, 4H). ^{13}C NMR (126 MHz, DMSO) δ 157.30, 140.34, 130.74, 125.25, 87.10, 32.52, 27.67, 21.87, 21.55. $C_{21}H_{18}I_2N_3O$ $[M + H]^+$ 的 HRMS (ESI) m/z 计算值 581.9539 实测值 581.9534。

[0748] (5-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)噻吩-3-基)硼酸

[0749] 
HSH-2-52

方法A：灰白色固体 (157, 45%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.54 (s, 1H), 8.08 (s, 2H), 8.05 (s, 1H), 7.91 (d, J = 6.8 Hz, 1H), 7.84 (d, J = 9.1 Hz, 1H), 7.78 (d, J = 9.0 Hz, 1H), 3.11 (t, J = 6.1 Hz, 2H), 2.46 (s, 2H), 2.06 - 1.98 (m, 2H), 1.88 (qd, J = 8.6, 7.1, 3.9 Hz, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 149.49, 145.18, 143.33, 143.01, 138.66, 137.70, 136.36, 133.33, 129.32, 128.70, 121.48, 116.41, 114.79, 30.05, 29.29, 22.62, 22.38。

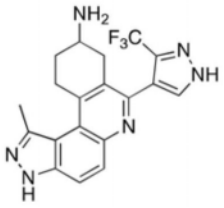
[0750] N-(2-(4-甲基哌嗪-1-基)乙基)-7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-1-羧酸胺

[0751] 
HSD1385

浅黄色固体。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.29 (s, 1H), 8.25 (d, J = 9.2 Hz, 1H), 8.03 (d, J = 9.2 Hz, 1H), 3.75 (t, J = 6.4 Hz, 2H), 3.58 (t, J = 6.0 Hz, 2H), 3.41 (s, 4H), 3.19 - 3.05 (m, 4H), 3.01 - 2.96 (m, 2H), 2.91 (s, 3H), 2.81 (t, J = 6.5 Hz, 2H), 2.01 - 1.92 (m, 2H), 1.92 - 1.87 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 167.01, 154.73, 144.30, 143.47, 140.67, 136.64, 133.59, 132.09, 124.38, 122.36 (q, J = 268.38

[0752] Hz),121.24,119.27,111.50,110.90,55.67,52.74,49.61,42.13,36.36,30.49,26.83,21.20,20.97.$C_{26}H_{30}F_3N_8O$[M+H]$^+$的HRMS(ESI)m/z计算值527.2495,实测值527.2495。

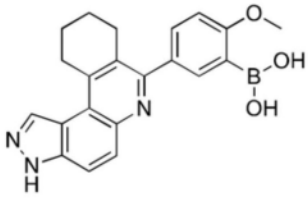
[0753] 1-甲基-7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-9-胺

[0754] 

HSD1386

方法A: 灰白色固体 (89 mg, 23%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.55 (s, 2H), 8.44 (s, 1H), 8.10 (d, J = 9.1 Hz, 1H), 8.02 (d, J = 9.3 Hz, 1H), 3.82 - 3.71 (m, 2H), 3.68 - 3.59 (m, 1H), 3.14 - 3.04 (m, 1H), 2.94 (s, 3H), 2.90 - 2.79 (m, 1H), 2.42 - 2.28 (m, 1H), 1.91 - 1.78 (m, 1H); ^{13}C NMR (126 MHz, DMSO) δ 144.18, 140.74, 139.47, 139.18, 138.89, 132.95, 129.06, 125.24, 122.97 (q, J = 269.64 Hz), 113.03, 45.50, 31.39, 30.49, 26.00, 18.97. $C_{19}H_{18}F_3N_6$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 387.1545, 实测值 387.1540。

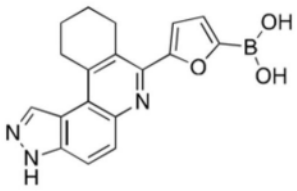
[0755] (2-甲氧基-5-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯基)硼酸

[0756] 

HSD1387

方法A: 白色固体 (166 mg, 48%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.57 - 8.51 (m, 1H), 7.83 (s, 2H), 7.76 (d, J = 6 J.0 = Hz, 3H), 7.60 (dd, J= 8.5, = 2.4 Hz, 1H), 7.06 (d, J = 8.5 Hz, 1H), 3.87 (s, 3H), 3.36 - 3.32 (m, 2H), 2.78 (t, J = 6.1 Hz, 2H), 2.05 - 1.95 (m, 2H), 1.78 - 1.69 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 163.59, 156.90, 143.67, 142.28, 138.64, 136.72, 136.33, 133.31, 132.83, 129.70, 129.44, 121.61, 116.55, 114.27, 110.23, 55.95, 29.73, 29.20, 22.67, 22.62. HRMS (ESI) m/z 计算值 $C_{21}H_{21}BN_3O_3$ [M + H]$^+$ 374.1676, 实测值 374.1671。

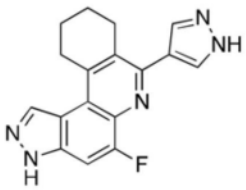
[0757] (5-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)呋喃-2-基)硼酸

[0758] 

HSD1389

方法A: 黄色固体 (133 mg, 40%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.64 - 8.60 (m, 1H), 8.02 - 7.94 (m, 2H), 7.31- 7,21 (m, 1H), 6.79 (m,1H), 3.35 - 3.34 (m, 2H), 3.07 - 3.03 (m, 2H), 2.00 (s, 2H), 1.86 (s, 2H); ^{13}C NMR (126 MHz, DMSO) δ 154.27, 145.25, 129.18, 122.17, 116.19, 112.66, 30.33, 28.05, 22.07. $C_{18}H_{17}BN_3O_3$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 334.1363, 实测值 334.1363。

[0759] 5-氟-7-(1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

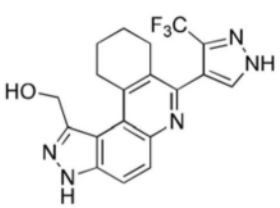
[0760] 

HSD1390

方法A: 灰白色固体 (64 mg, 21%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.81 (s, 1H), 8.29 (s, 2H), 8.00 (d, J = 10.3 Hz, 1H), 3.57 (t, J = 6.4 Hz, 2H), 3.09 (t, J =6.2 Hz, 2H), 2.20 - 2.10 (m, 2H), 2.03 - 1.82 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 153.31, 146.28, 135.79, 133.97, 133.51, 126.93, 123.44, 112.98, 111.93, 103.01, 30.97, 27.96, 21.18. $C_{17}H_{15}FN_5$[M + H]$^+$的 HRMS (ESI) m/z 计算值 308.1311, 实测值 308.1312。

[0761] (7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-1-基)甲醇

[0762] 将化合物HSD1329(100mg)溶于无水THF中,并在氩气下使用干冰丙酮冷却。冷却之后,滴加LAH(1摩尔的在THF中的溶液,1当量),并在室温下继续搅拌过夜。通过在冷却条件下缓慢加入水和THF混合物来淬灭反应。过滤反应混合物,并通过快速柱色谱纯化。

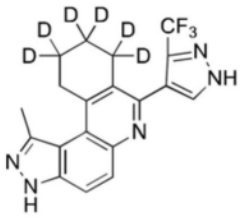
[0763] 

HSD1392

白色固体 (75 mg, 80%)。 1H NMR (500 MHz, 甲醇-d4) δ 7.98 (s, 1H), 7·79 (d, J = 8.4 Hz, 2H), 5.24 (s, 2H), 3.70 (s, 2H), 2.71 (t, J = 5.8 Hz, 2H), 2.00 - 1.84 (m, 4H); ^{13}C NMR (126 MHz, MeOD) δ 148.12, 144.28, 143.66, 139.73, 133.60, 130.48, 130.17, 128.88, 124.42, 118.85, 114.15, 60.41, 29.11, 27.68, 22.06, 21.83. $C_{19}H_{17}F_3N_5O$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 388.1385, 实测值 388.1380。

[0764] 1-甲基-7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-8,8,9,9,10,10,-d_6

[0765] 使用相同的方法A，采用氘化(D_8)环己酮作为酮。

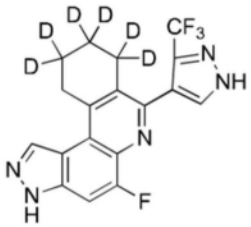
[0766] 

HSD1394

方法A：灰白色固体 (68 mg, 18%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.20 (s, 1H), 7.72 (d, J = 8.9 Hz, 1H), 7.68 (d, J = 8.7 Hz, 1H), 3.40 - 3.37 (m, 2H), 2.89 (s, 3H); $C_{19}H_{11}D_6F_3N_5$ [M + H]$^+$ 的 HRMS (ESI) m/z 计算值 378.1813，实测值 378.1804。

[0767] 5-氟-7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-8,8,9,9,10,10,-d_6

[0768] 使用相同的方法A，采用氘化(D_8)环己酮作为酮。

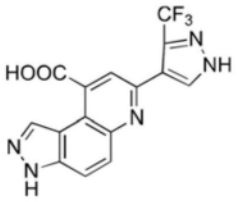
[0769] 

HSD1395

方法A：灰白色固体 (76 mg, 20%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.80 (s, 1H), 8.24 (s, 1H), 7.96 (d, J = 9.9 Hz, 1H), 3.53 (s, 2H); ^{13}C NMR (126 MHz, MeOD) δ 154.06 (q, J = 255.78 Hz), 144.99, 140.18, 139.89, 139.23, 134.60, 134.02, 131.99, 128.78, 124.39, 122.45(q, J = 269.64 Hz), 118.14, 112.31, 111.91, 102.86, 30.30, 26.74, 20.13, 16.82. $C_{18}H_8D_6F_4N_5$ [M + H]$^+$ 的HRMS (ESI) m/z 计算值 382.1562 实测值 382.1556。

[0770] 7-(3-(三氟甲基)-1H-吡唑-4-基)-3H-吡唑并[4,3-f]喹啉-9-羧酸

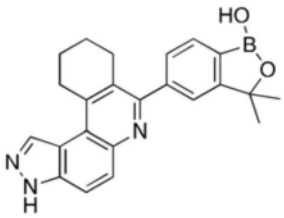
[0771] 丙酮酸作为酮的底物。

[0772] 

HSD1396

方法A：浅黄色固体 (100 mg, 29%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.69 (s, 1H), 8.32 (s, 1H), 7.96 - 7.87 (m, 2H), 7.82 (s, 1H); ^{13}C NMR (126 MHz, MeOD) δ 173.72, 147.71, 146.35, 143.54, 139.55, 138.93, 134.30, 131.27, 128.76, 122.98 (q, J = 269.64 Hz), 120.75, 118.19, 117.21, 116.10, 115.45。

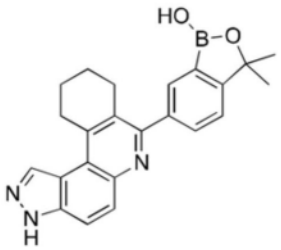
[0773] 3,3-二甲基-5-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯并[c][1,2]氧杂硼杂环戊-1(3H)-醇

[0774] 

HSD1398

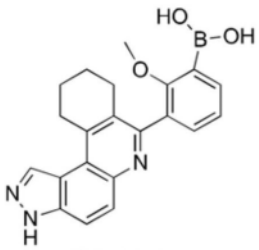
方法A：灰白色固体 (54 mg, 14%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 7.83 (d, J =9.1 Hz, 1H), 7.77 (d, J =9.1 Hz, 1H), 7.73 - 7.68 (m, 1H), 7.47 (t, J = 1.1 Hz, 1H), 7.41 (dd, J = 7.4, 1.4 Hz, 1H), 3.24 (t, J = 6.5 Hz, 2H), 2.69 (t, J = 6.2 Hz, 2H), 2.05 - 1.94 (m, 2H), 1.79 - 1.71 (m, 2H), 1.56 (s, 6H); ^{13}C NMR (126 MHz, MeOD) δ 162.29, 157.20, 143.50, 143.12, 129.88, 129.44, 128.35, 127.81, 122.15, 120.98, 119.24, 119.15, 115.90, 110.35, 98.72, 84.23, 29.51, 29.30, 28.40, 28.29, 22.07, 21.97; $C_{23}H_{23}BN_3O_2$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 384.1883 实测值 384.1882。

[0775] 3,3-二甲基-6-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯并[c][1,2]氧杂硼杂环戊-1(3H)-醇

[0776] 
HSD1399

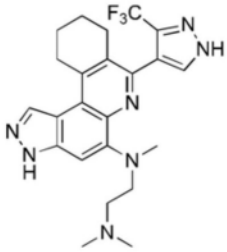
方法A: 灰白色固体 (62 mg, 16%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.62 (s, 1H), 7.88 (dd, J = 17.5, 9.0 Hz, 2H), 7.79 - 7.68 (m, 1H), 7.65 - 7.59 (m, 1H), 7.55 - 7.46 (m, 1H), 3.53 - 3.40 (m, 2H), 2.93 - 2.72 (m, 2H), 2.11 (dt, J = 11.5, 6.6 Hz, 2H), 1.94 - 1.76 (m, 2H), 1.60 (s, 6H); ^{13}C NMR (126 MHz, MeOD) δ 162.13, 157.52, 154.20, 143.64, 139.57, 138.67, 131.57, 130.39, 129.75, 128.47, 122.21, 120.28, 113.77, 84.16, 29.64, 28.56, 28.27, 22.16, 22.05. $C_{23}H_{23}BN_3O_2$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 384.1883 实测值 384.1880。

[0777] (2-甲氧基-3-(8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-7-基)苯基)硼酸

[0778] 
HSD1400

方法A: 灰白色固体 (41 mg, 11%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.58 (s, 1H), 7.89 (d, J = 9.2 Hz, 1H), 7.83 (d, J = 9.1 Hz, 1H), 7.42 (d, J =7.3 Hz, 1H), 7.32 (d, J = 7.4 Hz, 1H), 7.24 (t, J = 7.4 Hz, 1H), 3.48 (s, 3H), 3.44-3.35 (m, 2H), 2.82 (dd, J = 15.9, 7.2 Hz, 1H), 2.51 (dt, J = 17.3, 5.9 Hz, 1H), 2.09 - 2.00 (m, 2H), 1.89 - 1.82 (m, 1H), 1.81 - 1.76 (m, 1H); ^{13}C NMR (126 MHz, MeOD) δ 159.79, 155.68, 142.96, 133.21, 132.37, 131.13, 130.91, 128.28, 124.23, 123.00, 122.24, 60.00, 29.48, 27.03, 22.16, 21.79. $C_{21}H_{21}BN_3O_3$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 374.1676, 实测值 374.1670。

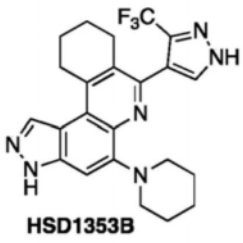
[0779] (7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶-5-基)乙烷-1,2-二胺

[0780] 
HSD1403

将 N^1, N^1, N^2, 三甲基乙烷-1,2-二胺（0.5mL）加入溶于 DMSO（1 mL）的化合物 HSH-1-156（50 mg，0.13 mmol）和粉状 K_2CO_3（2 当量）的混合物中。将反应混合物在压力管中于 200℃下加热 24 小时。反应完成后，通过硅胶快速色谱法使用二氯甲烷：甲醇（80：20）作为溶剂体系纯化反应。

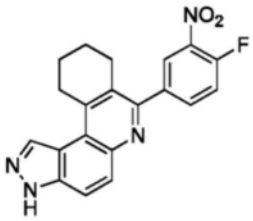
黄色固体 (8 mg, 13%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.51 (s, 1H), 8.07 (s, 1H), 7.45 (s, 1H), 3.52 (t, J = 6.4 Hz, 2H), 3.37 (t, J = 6.4 Hz, 2H), 3.21 - 3.16 (m, 2H), 2.98 (s, 3H), 2.66 (t, J = 6.6 Hz, 2H), 2.43 (s, 6H), 2.10 - 2.04 (m, 2H), 1.92 - 1.84 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 148.52, 146.67, 143.98, 139.58, 138.84, 131.49,131.11,123.95,122.86,120.72,119.24,112.05,56.25,52.86,44.02,43.71, 39.62,29.85,27.71,22.14,21.75;$C_{23}H_{24}F_3N_7$[M+H]$^+$的HRMS(ESI)m/z计算值458.2280,实测值458.2276。

[0781] 5-(哌啶-1-基)-7-(3-(三氟甲基)-1H-吡唑-4-基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0782] 
HSD1353B

方法A: 灰白色固体 (66 mg, 15%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.39 (s, 1H), 8.15 (s, 1H), 7.12 (s, 1H), 3.24 (d, J = 6.4 Hz, 2H), 3.17 (t, J = 5.2 Hz, 4H), 2.62 (t, J = 6.2 Hz, 2H), 1.93 (tt, J = 7.6, 5.2, 4.3 Hz, 2H), 1.80 - 1.72 (m, 2H), 1.64 (t, J = 5.8 Hz, 4H), 1.53 (q, J = 6.1 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 150.46, 146.47, 142.38, 139.11, 136.28, 131.34, 130.26, 123.57 (q, J = 263.34 Hz), 123.19, 120.16, 120.08, 111.84, 53.57, 31.18, 29.81, 28.19, 26.16, 24.64, 22.68, 22.29; $C_{23}H_{24}F_3N_6$ [M + H]$^+$的 HRMS (ESI) m/z 计算值 441.2015, 实测值 441.2012。

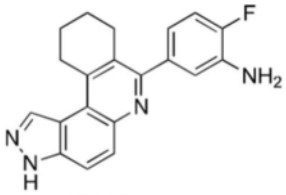
[0783] 7-(4-氟-3-硝基苯基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0784] 
HSD1404

方法 A: 黄色固体 (145 mg, 40%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.63 (s, 1H), 8.31 (dd, J = 1.2, 2.2 Hz, 1H), 7.96 (ddd, J = 8.6, 4.3, 2.3 Hz, 1H), 7.93 - 7.87 (m, 2H), 7.58 (dd, J = 11.0, 8.6 Hz, 1H), 3.44 (d, J = 7.2 Hz, 3H), 2.84 (t, J = 6.2 Hz, 2H), 2.18 - 2.08 (m, 2H), 1.94 - 1.83 (m, 2H); ^{13}C NMR (126 MHz MeOD) δ 153.80, 144.17, 137.50, 137.15, 136.31, 129.49, 128.62, 128.52, 126.50, 125.92, 122.66, 118.07, 117.90, 29.65, 28.38, 22.02。

[0785] 2-氟-5-(8,9,10,11-四氢-3H-萘并[1,2-e]吲唑-7-基)苯胺

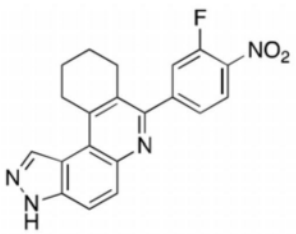
[0786] 将化合物HSD1404(100mg)溶于5mL THF中,并用氩气吹扫15分钟。之后,添加钯(10%负载于碳上,20mol%),并且使用氢气气球进行氢化反应6小时。完成后,通过烧结漏斗过滤反应混合物,浓缩并通过快速柱色谱法纯化。

[0787] 
HSD1405

浅黄色固体 (83 mg, 90%)。^{1}H NMR (500 MHz, 甲醇-d_4) δ 8.55 (s, 1H), 7.90 - 7.78 (m, 2H), 7.07 (dd, J = 11.3, 8.2 Hz, 1H), 6.96 (dd, J = 8.6, 2.1 Hz, 1H), 6.74 (ddd, J = 8.2, 4.3, 2.1 Hz, 1H), 3.34 (d, J = 7.9 Hz, 3H), 2.77 (t, J = 6.2 Hz, 2H), 2.06 (td, J = 8.6, 7.2, 4.6 Hz, 2H), 1.88 - 1.78 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 157.17, 153.73, 152.53 (d, J = 239.4 Hz)143.38, 136.87, 135.81, 135.63, 135.52, 129.70, 128.38, 122.05, 117.94, 117.38, 116.11,

[0788] 114.39,114.24,113.58,29.59,28.41,22.17,22.06.$C_{21}H_{19}FN_3[M+H]^+$的HRMS(ESI) m/z计算值332.1563,实测值332.1560。

[0789] 7-(3-氟-4-硝基苯基)-8,9,10,11-四氢-3H-吡唑并[4,3-a]菲啶

[0790] 
HSD1409

方法 A: 黄色固体 (145 mg, 40%)。^{1}H NMR (500 MHz, DMSO-d_6) δ 8.57 (s, 1H), 8.26 (t, J = 8.2 Hz), 7.89 - 7.81 (m, 3H), 7.66 (dd, J = 8.4, 1.4 Hz, 1H), 3.32 (s, 2H), 2.81 (t, J = 5.8 Hz, 2H), 2.01 - 2.79 (m, 2H), 1.76 - 1.74 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 155.83, 153.75, 153.45, 149.27, 149.20, 143.60, 143.07, 139.01, 136.56, 129.52, 126.51, 122.60, 119.60, 119.43, 116.28, 114.94, 29.66, 228.50, 22.45, 22.33。

[0791] 本领域技术人员将认识到,可以对上述特定实施方式进行多种修改。实施方式不应限于所描述的特定限制。也可以是其他实施方式。

[0792] 尽管已经在附图和前面的描述中详细示出和描述了本发明,但是其应被认为是示例性的,而不是限制性的,应理解,仅示出和描述了某些实施例,并且落入本发明的精神范围内的所有的改变和修改均在保护范围内。

[0793] 本发明的方法和组合物的范围由所附权利要求书限定。然而,必须理解,可以在不脱离本发明的精神或范围的情况下以不同于具体解释和说明的方式来实践本公开。本领域技术人员应当理解,在不脱离所附权利要求书所限定的精神和范围的情况下,可以在实践权利要求书时采用本文所述实施例的各种替代方案。

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