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Chengjian Tan等. Alkaloids from

Oxytropis ochrocephala and

antiproliferative activity of sophoridine
derivatives against cancer cell lines.

《Bioorganic & Medicinal Chemistry
Letters》. 2015, 第26卷第1496-1497页.

审查员 王瑞

(54) 发明名称

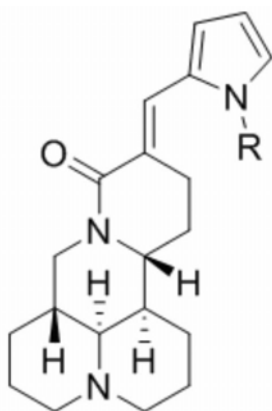
槐定碱吡咯、吲哚类衍生物及其制备方法与
应用

(57) 摘要

一种槐定碱吡咯、吲哚类衍生物, 本发明公
开了该类化合物的化学结构, 还公开了该类化合
物的制备方法。本通过在体外抗肿瘤活性研究说
明该类化合物具有发展前景的抗肿瘤药物, 给广
大的癌症患者提供多一种治疗的可能。

权利要求书4页 说明书43页 附图2页

1. 一种槐定碱吡咯、吲哚类衍生物,其特征在于,所述化合物具有以下结构:
通式I:

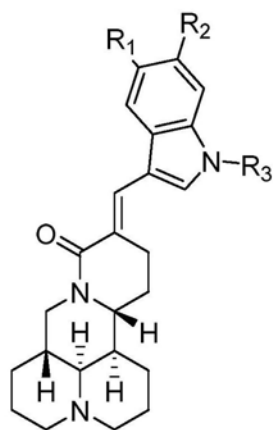


LMY-02~21

LMY-02:R=Bn
LMY-03:R=2-MeBn
LMY-04:R=3-MeBn
LMY-05:R=4-MeBn
LMY-06:R=3,5-di-MeBn
LMY-07:R=4-tBuBn
LMY-08:R=3,5-di-tBuBn
LMY-09:R=4-FBn
LMY-10:R=2-ClBn
LMY-11:R=3-ClBn

LMY-12:R=4-ClBn
LMY-13:R=2-BrBn
LMY-14:R=4-BrBn
LMY-15:R=3-OMeBn
LMY-16:R=4-OMeBn
LMY-17:R=3,5-di-OMeBn
LMY-18:R=2-Br-5-OMeBn
LMY-19:R=Naphthalenylmethyl
LMY-20:R=4-OCF₃Bn
LMY-21:R=4-BnOBn

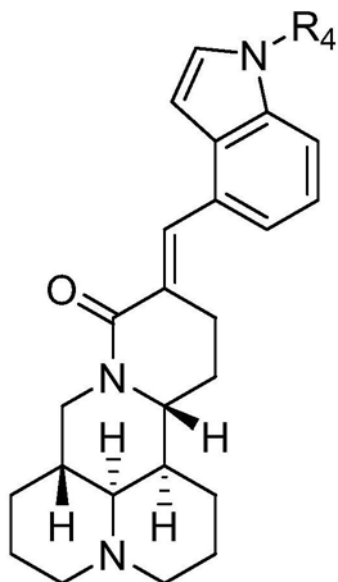
通式 II:



LMY-22~62

- | | |
|---|--|
| LMY-22: R ₁ , R ₂ =H, R ₃ =Bn | LMY-43: R ₁ =Me, R ₂ =H, R ₃ =4-BnOBn |
| LMY-23: R ₁ , R ₂ =H, R ₃ =2-MeBn | LMY-44: R ₁ =OMe, R ₂ =H, R ₃ =3-BrBn |
| LMY-24: R ₁ , R ₂ =H, R ₃ =3-MeBn | LMY-45: R ₁ =OMe, R ₂ =H, R ₃ =4-BnOBn |
| LMY-25: R ₁ , R ₂ =H, R ₃ =4-MeBn | LMY-46: R ₁ =Br, R ₂ =H, R ₃ =3-BrBn |
| LMY-26: R ₁ , R ₂ =H, R ₃ =3,5-di-MeBn | LMY-47: R ₁ =Br, R ₂ =H, R ₃ =4-BnOBn |
| LMY-27: R ₁ , R ₂ =H, R ₃ =4-tBuBn | LMY-48: R ₁ =H, R ₂ =Cl, R ₃ =3-BrBn |
| LMY-28: R ₁ , R ₂ =H, R ₃ =3,5-di-tBuBn | LMY-49: R ₁ =H, R ₂ =Cl, R ₃ =4-BnOBn |
| LMY-29: R ₁ , R ₂ =H, R ₃ =2-ClBn | LMY-50: R ₁ =H, R ₂ =OMe, R ₃ =3-BrBn |
| LMY-30: R ₁ , R ₂ =H, R ₃ =4-ClBn | LMY-51: R ₁ , R ₂ =H, R ₃ =4-(4-MeBnO)Bn |
| LMY-31: R ₁ , R ₂ =H, R ₃ =2,6-di-ClBn | LMY-52: R ₁ , R ₂ =H, R ₃ =4-(4-tBuBnO)Bn |
| LMY-32: R ₁ , R ₂ =H, R ₃ =2-BrBn | LMY-53: R ₁ , R ₂ =H, R ₃ =4-(4-FBnO)Bn |
| LMY-33: R ₁ , R ₂ =H, R ₃ =3-BrBn | LMY-54: R ₁ , R ₂ =H, R ₃ =4-(4-ClBnO)Bn |
| LMY-34: R ₁ , R ₂ =H, R ₃ =4-BrBn | LMY-55: R ₁ , R ₂ =H, R ₃ =4-(4-BrBnO)Bn |
| LMY-35: R ₁ , R ₂ =H, R ₃ =3-OMeBn | LMY-56: R ₁ , R ₂ =H, R ₃ =4-(4-OCF ₃ BnO)Bn |
| LMY-36: R ₁ , R ₂ =H, R ₃ =4-OMeBn | LMY-57: R ₁ =OMe, R ₂ =H, R ₃ =4-(4-MeBnO)Bn |
| LMY-37: R ₁ , R ₂ =H, R ₃ =3,5-di-OMeBn | LMY-58: R ₁ =OMe, R ₂ =H, R ₃ =4-(4-tBuBnO)Bn |
| LMY-38: R ₁ , R ₂ =H, R ₃ =2-Br-5-OMeBn | LMY-59: R ₁ =OMe, R ₂ =H, R ₃ =4-(4-FBnO)Bn |
| LMY-39: R ₁ , R ₂ =H, R ₃ =Naphthalenylmethyl | LMY-60: R ₁ =OMe, R ₂ =H, R ₃ =4-(4-ClBnO)Bn |
| LMY-40: R ₁ , R ₂ =H, R ₃ =4-OCF ₃ Bn | LMY-61: R ₁ =OMe, R ₂ =H, R ₃ =4-(4-BrBnO)Bn |
| LMY-41: R ₁ , R ₂ =H, R ₃ =4-BnOBn | LMY-62: R ₁ =OMe, R ₂ =H, R ₃ =4-(4-OCF ₃ BnO)Bn |
| LMY-42: R ₁ =Me, R ₂ =H, R ₃ =3-BrBn | |

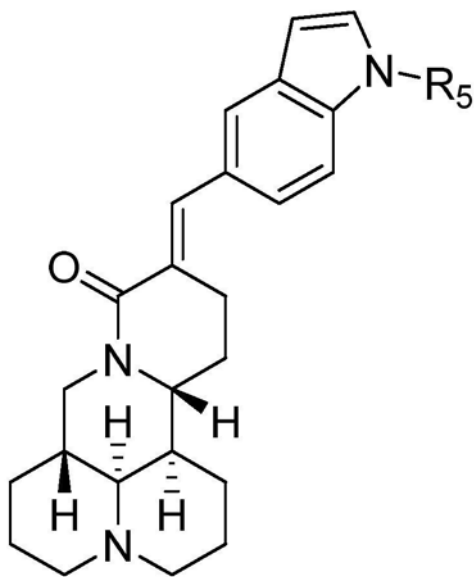
通式 III:



LMY-63~64

LMY-63: $R_4 = 3\text{-BrBn}$ LMY-64: $R_4 = 4\text{-BnOBn}$

通式IV:



LMY-65~66

LMY-65: $R_5 = 3\text{-BrBn}$ LMY-66: $R_5 = 4\text{-BnOBn}$

2. 根据权利要求1所述的吡咯类槐定碱衍生物LMY-01~LMY-21的制备方法, 其特征在于, 以槐定碱为起始原料, 经过氢化钠使槐定碱内酰胺 α 位上的氢离去, 形成了 α -碳负离子,

再与N-取代吡咯甲醛类化合物进行羟醛缩合反应即得；

所述N-取代吡咯甲醛类化合物包括N-甲基-2-吡咯甲醛、N-苄基-2-吡咯甲醛、N-(2-甲基苄基)-2-吡咯甲醛、N-(3-甲基苄基)-2-吡咯甲醛、N-(4-甲基苄基)-2-吡咯甲醛、N-(3,5-二甲基苄基)-2-吡咯甲醛、N-(4-叔丁基苄基)-2-吡咯甲醛、N-(3,5-二叔丁基苄基)-2-吡咯甲醛、N-(4-氟苄基)-2-吡咯甲醛、N-(2-氯苄基)-2-吡咯甲醛、N-(3-氯苄基)-2-吡咯甲醛、N-(4-氯苄基)-2-吡咯甲醛、N-(2-溴苄基)-2-吡咯甲醛、N-(4-溴苄基)-2-吡咯甲醛、N-(3-甲氧基苄基)-2-吡咯甲醛、N-(4-甲氧基苄基)-2-吡咯甲醛、N-(3,5-二甲氧基苄基)-2-吡咯甲醛、N-(2-溴-5-甲氧基苄基)-2-吡咯甲醛、N-(2-萘基亚甲基)-2-吡咯甲醛、N-(4-三氟甲氧基苄基)-2-吡咯甲醛和N-(4-苄氧基苄基)-2-吡咯甲醛。

3. 根据权利要求1所述的吡咯类槐定碱衍生物LMY-22~LMY-66的制备方法，其特征在于，以槐定碱为起始原料，经过氢化钠使槐定碱内酰胺 α 位上的氢离去，形成了 α -碳负离子，再与N-取代吡咯甲醛类化合物进行羟醛缩合反应即得；

所述N-取代吡咯甲醛类化合物N-(苄基)-3-吡咯甲醛、N-(2-甲基苄基)-3-吡咯甲醛、N-(3-甲基苄基)-3-吡咯甲醛、N-(4-甲基苄基)-3-吡咯甲醛、N-(3,5-二甲基苄基)-3-吡咯甲醛、N-(4-叔丁基苄基)-3-吡咯甲醛、N-(3,5-二叔丁基苄基)-3-吡咯甲醛、N-(2-氯苄基)-3-吡咯甲醛、N-(4-氯苄基)-3-吡咯甲醛、N-(2,6-二氯苄基)-3-吡咯甲醛、N-(2-溴苄基)-3-吡咯甲醛、N-(3-溴苄基)-3-吡咯甲醛、N-(4-溴苄基)-3-吡咯甲醛、N-(3-甲氧基苄基)-3-吡咯甲醛、N-(4-甲氧基苄基)-3-吡咯甲醛、N-(3,5-二甲氧基苄基)-3-吡咯甲醛、N-(2-溴-5-甲氧基苄基)-3-吡咯甲醛、N-(2-萘基亚甲基)-3-吡咯甲醛、N-(4-三氟甲氧基苄基)-3-吡咯甲醛、N-(4-苄氧基苄基)-3-吡咯甲醛、5-甲基-N-(3-溴苄基)-3-吡咯甲醛、5-甲基-N-(4-苄氧基苄基)-3-吡咯甲醛、5-甲氧基-N-(3-溴苄基)-3-吡咯甲醛、5-甲氧基-N-(4-苄氧基苄基)-3-吡咯甲醛、5-溴-N-(3-溴苄基)-3-吡咯甲醛、5-溴-N-(4-苄氧基苄基)-3-吡咯甲醛、6-氯-N-(3-溴苄基)-3-吡咯甲醛、6-氯-N-(4-苄氧基苄基)-3-吡咯甲醛、6-甲氧基-N-(3-溴苄基)-3-吡咯甲醛、N-(4-(4-甲基苄氧基)苄基)-3-吡咯甲醛、N-(4-(4-叔丁基苄氧基)苄基)-3-吡咯甲醛、N-(4-(4-氟苄氧基)苄基)-3-吡咯甲醛、N-(4-(4-氯苄氧基)苄基)-3-吡咯甲醛、N-(4-(4-溴苄氧基)苄基)-3-吡咯甲醛、N-(4-(4-三氟甲氧基苄氧基)苄基)-3-吡咯甲醛、5-甲氧基-N-(4-(4-甲基苄氧基)苄基)-3-吡咯甲醛、5-甲氧基-N-(4-(4-叔丁基苄氧基)苄基)-3-吡咯甲醛、5-甲氧基-N-(4-(4-氟苄氧基)苄基)-3-吡咯甲醛、5-甲氧基-N-(4-(4-氯苄氧基)苄基)-3-吡咯甲醛、5-甲氧基-N-(4-(4-溴苄氧基)苄基)-3-吡咯甲醛、5-甲氧基-N-(4-(4-三氟甲氧基苄氧基)苄基)-3-吡咯甲醛、N-(3-溴苄基)-4-吡咯甲醛、N-(4-苄氧基苄基)-4-吡咯甲醛、N-(3-溴苄基)-5-吡咯甲醛和N-(4-苄氧基苄基)-5-吡咯甲醛。

4. 根据权利要求1所述的吡咯类和吡咯类槐定碱衍生物在制备抗癌药物方面的应用。

槐定碱吡咯、吲哚类衍生物及其制备方法与应用

技术领域

[0001] 本发明涉及制药技术领域,具体涉及一类新的槐定碱吡咯、吲哚类衍生物,以及制备方法和这些化合物在制备抗肿瘤药物中的应用。

背景技术

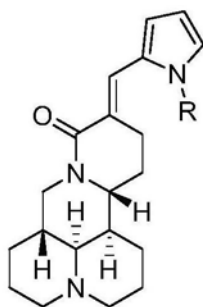
[0002] 研究发现槐定碱作为从豆科槐属植物苦豆子中提取分离的单体生物碱,具有抗肿瘤、抗心律失常、抗炎抑菌、体外抑精和免疫抑制等作用。临床上槐定碱对恶性滋养细胞肿瘤有显著疗效,对恶性淋巴瘤和消化道肿瘤也有一定疗效,是一种高效低毒的抗癌生物碱。随着研究的深入,吡咯,吲哚类药物的抗肿瘤活性也日益引起了人们的重视。未见兼具槐定碱的抗肿瘤活性和吡咯、吲哚类药物的抗肿瘤活性的相关药物。

发明内容

[0003] 本发明要解决的技术问题是提供一种用于制备抗肿瘤药物的槐定碱衍生物及其制备方法。

[0004] 本发明所述的槐定碱吡咯、吲哚类衍生物,其结构如下:

[0005] 通式I:

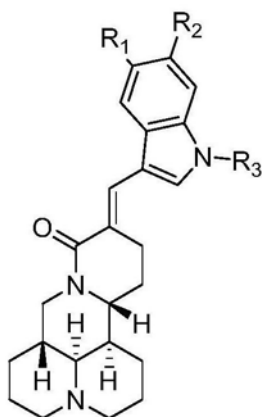


LMY-01~21

- | | |
|-----------------------|--------------------------------|
| LMY-01:R=Me | LMY-12:R=4-ClBn |
| LMY-02:R=Bn | LMY-13:R=2-BrBn |
| LMY-03:R=2-MeBn | LMY-14:R=4-BrBn |
| LMY-04:R=3-MeBn | LMY-15:R=3-OMeBn |
| LMY-05:R=4-MeBn | LMY-16:R=4-OMeBn |
| LMY-06:R=3,5-di-MeBn | LMY-17:R=3,5-di-OMeBn |
| LMY-07:R=4-tBuBn | LMY-18:R=2-Br-5-OMeBn |
| LMY-08:R=3,5-di-tBuBn | LMY-19:R=Naphthalenylmethyl |
| LMY-09:R=4-FBn | LMY-20:R=4-OCF ₃ Bn |
| LMY-10:R=2-ClBn | LMY-21:R=4-BnOBn |
| LMY-11:R=3-ClBn | |

[0008] 通式II:

[0009]



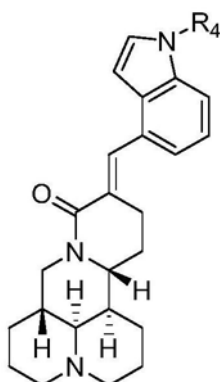
LMY-22~62

[0010]

- | | |
|--|--|
| LMY-22: $R_1, R_2 = H, R_3 = Bn$ | LMY-43: $R_1 = Me, R_2 = H, R_3 = 4-BnOBn$ |
| LMY-23: $R_1, R_2 = H, R_3 = 2-MeBn$ | LMY-44: $R_1 = OMe, R_2 = H, R_3 = 3-BrBn$ |
| LMY-24: $R_1, R_2 = H, R_3 = 3-MeBn$ | LMY-45: $R_1 = OMe, R_2 = H, R_3 = 4-BnOBn$ |
| LMY-25: $R_1, R_2 = H, R_3 = 4-MeBn$ | LMY-46: $R_1 = Br, R_2 = H, R_3 = 3-BrBn$ |
| LMY-26: $R_1, R_2 = H, R_3 = 3,5-di-MeBn$ | LMY-47: $R_1 = Br, R_2 = H, R_3 = 4-BnOBn$ |
| LMY-27: $R_1, R_2 = H, R_3 = 4-tBuBn$ | LMY-48: $R_1 = H, R_2 = Cl, R_3 = 3-BrBn$ |
| LMY-28: $R_1, R_2 = H, R_3 = 3,5-di-tBuBn$ | LMY-49: $R_1 = H, R_2 = Cl, R_3 = 4-BnOBn$ |
| LMY-29: $R_1, R_2 = H, R_3 = 2-ClBn$ | LMY-50: $R_1 = H, R_2 = OMe, R_3 = 3-BrBn$ |
| LMY-30: $R_1, R_2 = H, R_3 = 4-ClBn$ | LMY-51: $R_1, R_2 = H, R_3 = 4-(4-MeBnO)Bn$ |
| LMY-31: $R_1, R_2 = H, R_3 = 2,6-di-ClBn$ | LMY-52: $R_1, R_2 = H, R_3 = 4-(4-tBuBnO)Bn$ |
| LMY-32: $R_1, R_2 = H, R_3 = 2-BrBn$ | LMY-53: $R_1, R_2 = H, R_3 = 4-(4-FBnO)Bn$ |
| LMY-33: $R_1, R_2 = H, R_3 = 3-BrBn$ | LMY-54: $R_1, R_2 = H, R_3 = 4-(4-ClBnO)Bn$ |
| LMY-34: $R_1, R_2 = H, R_3 = 4-BrBn$ | LMY-55: $R_1, R_2 = H, R_3 = 4-(4-BrBnO)Bn$ |
| LMY-35: $R_1, R_2 = H, R_3 = 3-OMeBn$ | LMY-56: $R_1, R_2 = H, R_3 = 4-(4-OCF_3BnO)Bn$ |
| LMY-36: $R_1, R_2 = H, R_3 = 4-OMeBn$ | LMY-57: $R_1 = OMe, R_2 = H, R_3 = 4-(4-MeBnO)Bn$ |
| LMY-37: $R_1, R_2 = H, R_3 = 3,5-di-OMeBn$ | LMY-58: $R_1 = OMe, R_2 = H, R_3 = 4-(4-tBuBnO)Bn$ |
| LMY-38: $R_1, R_2 = H, R_3 = 2-Br-5-OMeBn$ | LMY-59: $R_1 = OMe, R_2 = H, R_3 = 4-(4-FBnO)Bn$ |
| LMY-39: $R_1, R_2 = H, R_3 = Naphthalenylmethyl$ | LMY-60: $R_1 = OMe, R_2 = H, R_3 = 4-(4-ClBnO)Bn$ |
| LMY-40: $R_1, R_2 = H, R_3 = 4-OCF_3Bn$ | LMY-61: $R_1 = OMe, R_2 = H, R_3 = 4-(4-BrBnO)Bn$ |
| LMY-41: $R_1, R_2 = H, R_3 = 4-BnOBn$ | LMY-62: $R_1 = OMe, R_2 = H, R_3 = 4-(4-OCF_3BnO)Bn$ |
| LMY-42: $R_1 = Me, R_2 = H, R_3 = 3-BrBn$ | |

[0011] 通式 III:

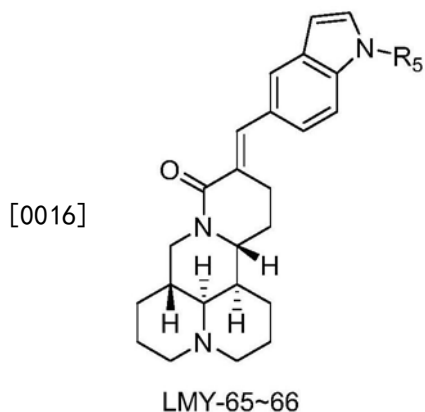
[0012]



LMY-63~64

[0013] LMY-63: $R_4 = 3-BrBn$ [0014] LMY-64: $R_4 = 4-BnOBn$

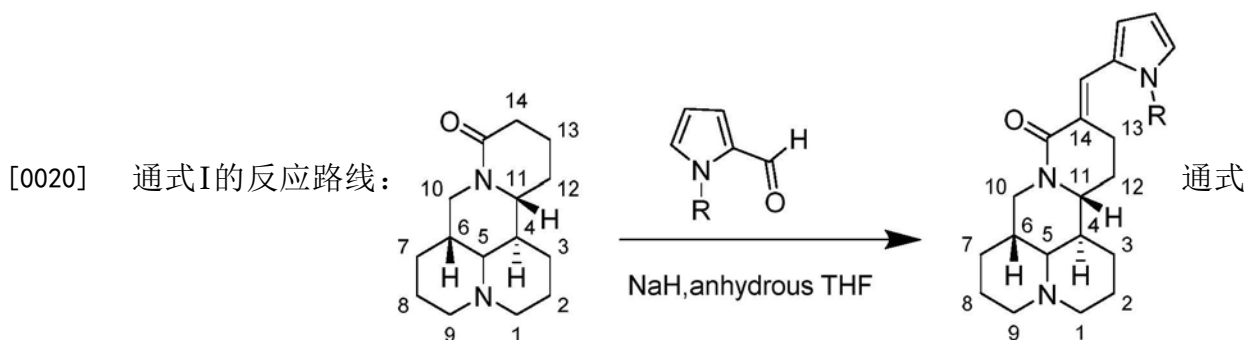
[0015] 通式IV:



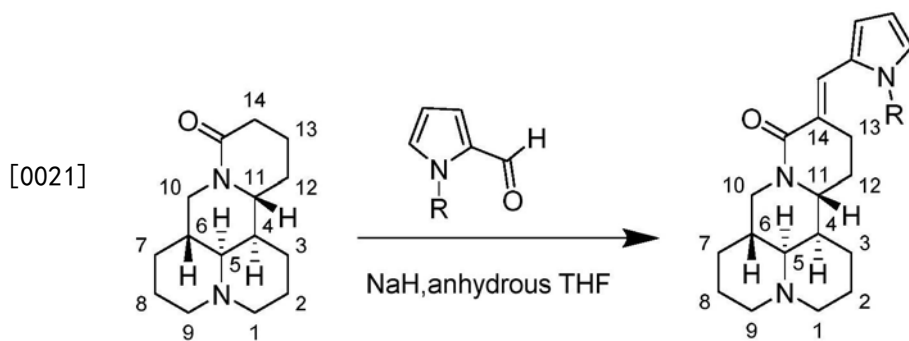
[0017] LMY-65: $R_5 = 3\text{-BrBn}$

[0018] LMY-66: $R_5 = 4\text{-BnOBn}$ 。

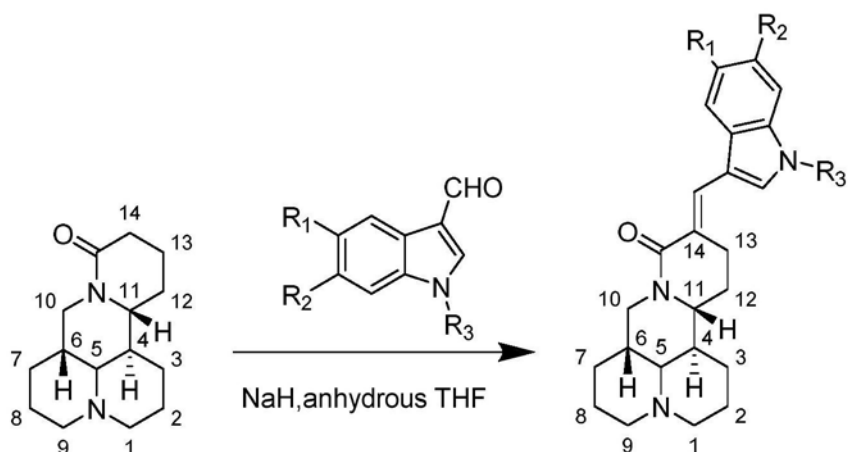
[0019] 本发明还提供了上述化合物的制备方法,该方法采用如下反应路线:



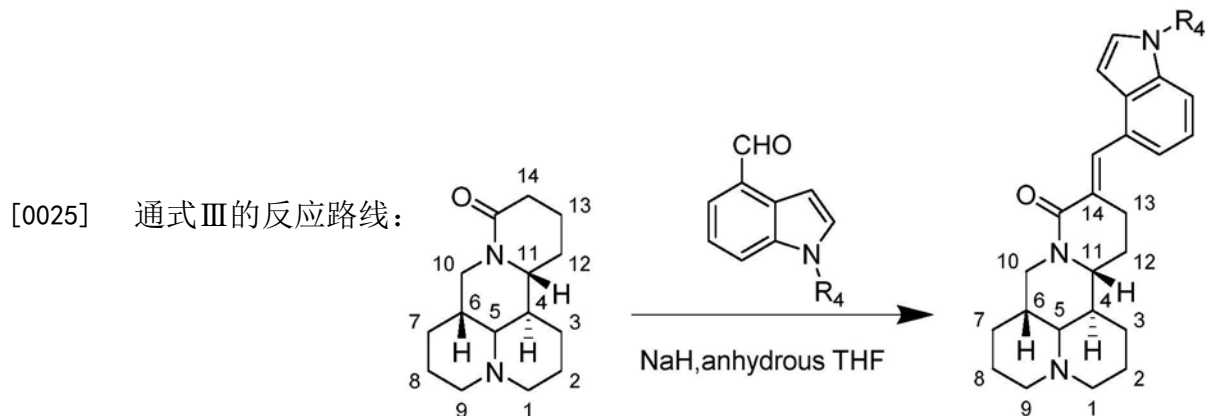
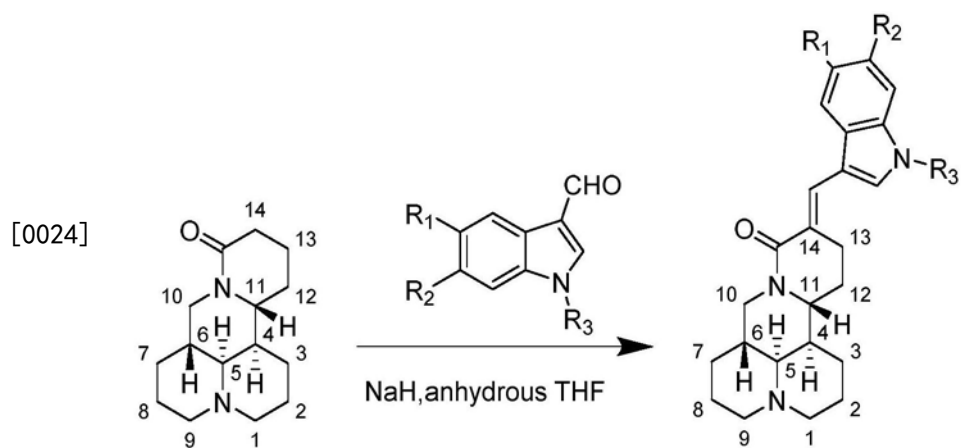
I的反应路线更加具体如下:



[0022] 通式 II 的反应路线:

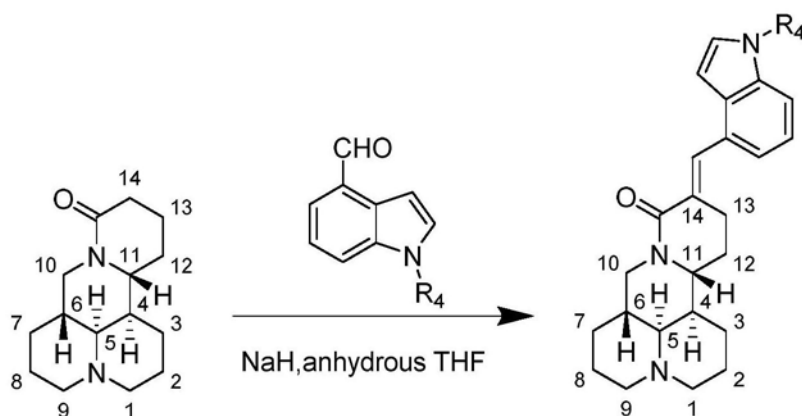


[0023] 通式 II 的反应路线更加具体如下：

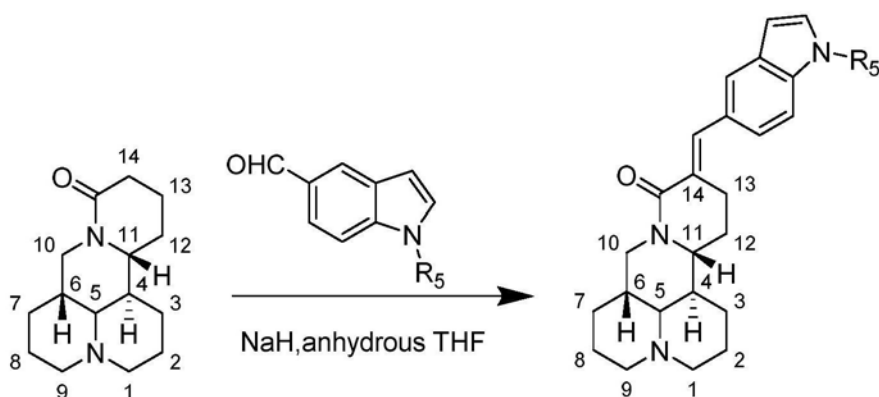


[0026] 通式 III 的反应路线更加具体如下：

[0027]

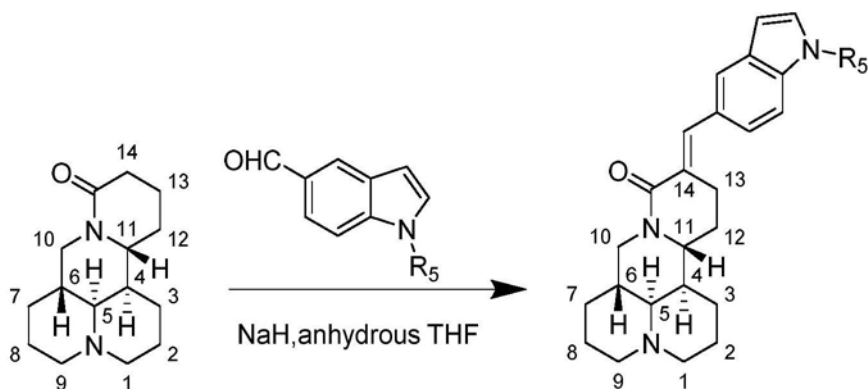


[0028] 通式IV的反应路线:



[0029] 通式IV的反应路线更加具体如下:

[0030]



[0031] 本发明在于提供了一种有发展前景的抗肿瘤药物,给广大的癌症患者提供多一种治疗的可能。

附图说明

[0032] 图1为CNE2细胞在不同浓度的LMY-45药物处理24h后细胞凋亡实验结果。

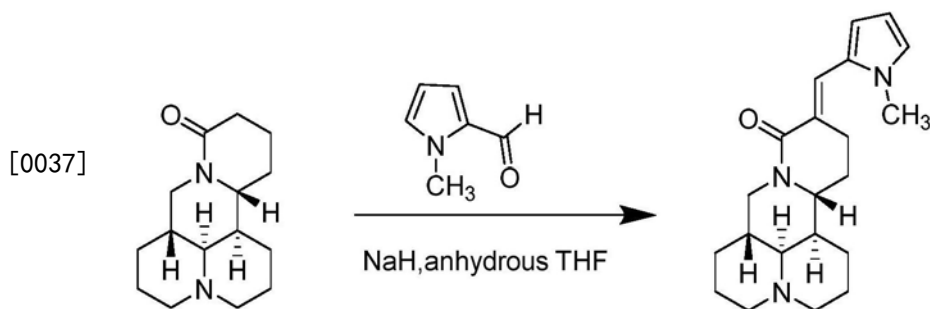
[0033] 图2为SMMC-7721细胞在不同浓度的LMY-45药物处理24h后细胞凋亡实验结果。

具体实施方式

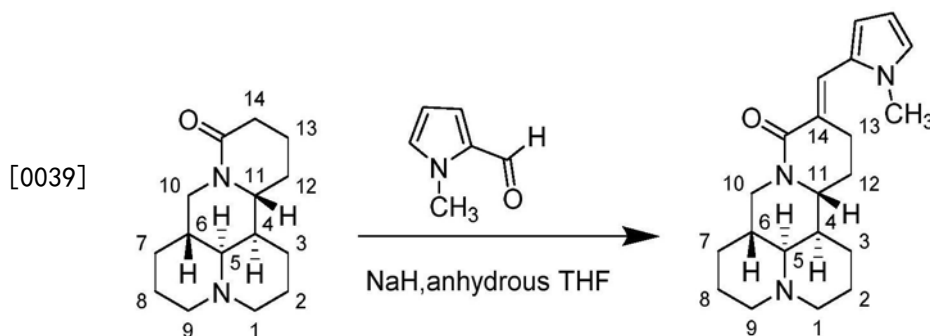
[0034] 下面通过实施例对本发明的技术方案作进一步阐述。

[0035] 实施例1

[0036] (1) LMY-01的制备:



[0038] LMY-01的制备更加具体的如下：



[0040] 具体制备LMY-01的实验方法：

[0041] 于100mL圆底烧瓶中分别加入2.4g (100mmol) 氢化钠, 50mL无水四氢呋喃, 搅拌均匀, 加入1.24g (5mmol) 槐定碱, 缓慢升温至85℃加入0.654g (6mmol) N-甲基-2-吡咯甲醛, 反应36h至终点(TLC检测)。冷却至室温, 逐滴加入3N的盐酸中和过量的氢化钠。二氯甲烷萃取(40mLx3), 合并有机相, 无水Na₂SO₄干燥, 减压抽滤、浓缩滤液后经硅胶柱层析(V_{二氯甲烷}:V_{甲醇} = 50:1)纯化, 得0.389g浅棕色固体粉末LMY-01: 14-(N-甲基-2-吡咯甲烯基)槐定碱: 收率23%;

[0042] ¹H NMR (600MHz, Chloroform-d) δ7.67 (s, 1H), 6.73 (dd, J=2.6, 1.6Hz, 1H), 6.38 (dd, J=4.0, 1.5Hz, 1H), 6.23-6.17 (m, 1H), 3.70 (s, 3H), 3.59 (dd, J=13.6, 5.1Hz, 1H), 3.52-3.46 (m, 1H), 3.30 (t, J=13.7, 11.7 Hz, 1H), 2.96-2.88 (m, 2H), 2.87-2.78 (m, 1H), 2.63-2.55 (m, 1H), 2.25-2.14 (m, 2H), 2.14-2.02 (m, 1H), 2.01-1.83 (m, 3H), 1.78-1.68 (m, 1H), 1.62 (d, J=13.7, 2.6Hz, 1H), 1.59-1.49 (m, 5H), 1.35-1.25 (m, 1H), 1.18-1.07 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ165.17, 129.55, 125.61, 124.69, 122.45, 112.36, 108.39, 63.53, 56.06, 55.19, 50.66, 50.05, 47.98, 39.84, 32.08, 30.04, 26.86, 24.00, 23.94, 21.61, 21.60. HRMS m/z (ESI⁺) calcd. for C₂₁H₃₀N₃O [M+H⁺] 340.2389, found 340.3095. Mp: 104.0℃~104.7℃

[0043] 参考化合物LMY-01的实验方法制备化合物LMY-02~LMY-21, 化合物LMY-02~LMY-21结构鉴定数据如下：

[0044] 化合物LMY-02: 14-(N-苄基-2-吡咯甲烯基)槐定碱: 棕色固体粉末, 收率42%;

[0045] ¹H NMR (600MHz, Chloroform-d) δ7.68 (d, J=1.8Hz, 1H), 7.34-7.29 (m, 2H), 7.29-7.24 (m, 1H), 7.13-7.07 (m, 2H), 6.83 (dd, J=2.7, 1.6Hz, 1H), 6.44 (d, J=3.9, 1.5Hz, 1H), 6.31-6.27 (m, 1H), 5.22 (s, 2H), 3.59 (dd, J=13.6, 5.1Hz, 1H), 3.52-3.46 (m, 1H), 3.30 (t, J=13.7, 11.7Hz, 1H), 2.96-2.88 (m, 2H), 2.87-2.78 (m, 1H), 2.63-2.55 (m, 1H), 2.25-2.14 (m, 2H), 2.14-2.02 (m, 1H), 2.01-1.83 (m, 3H), 1.78-1.68 (m, 1H), 1.62 (d, J=13.7, 2.6Hz,

1H), 1.59-1.49 (m, 5H), 1.35-1.25 (m, 1H), 1.18-1.07 (m, 1H). ^{13}C NMR (151 MHz, CDCl_3) δ 165.26, 137.66, 129.24, 128.77 (2), 127.57, 126.77 (2), 125.64, 124.25, 122.03, 112.78, 109.02, 63.49, 56.04, 55.19, 50.71, 50.61, 47.93, 39.81, 32.02, 29.99, 26.87, 24.00, 23.84, 21.60, 21.54. HRMS m/z (ESI^+) calcd. for $\text{C}_{27}\text{H}_{34}\text{N}_3\text{O}$ [$\text{M}+\text{H}^+$] 416.2702, found 416.2813. Mp: 144.1°C ~ 145.2°C

[0046] 化合物 LMY-03: 14-[N-(2-甲基苄基)-2-吡咯甲烯基]槐定碱: 淡黄色固体粉末, 收率 38%;

[0047] ^1H NMR (600MHz, Chloroform- d) δ 7.63 (s, 1H), 7.18 (d, $J=4.2\text{Hz}$, 2H), 7.14-7.09 (m, 1H), 6.69-6.67 (m, 1H), 6.65 (d, $J=7.6\text{Hz}$, 1H), 6.46 (d, $J=3.9, 1.5\text{Hz}$, 1H), 6.28 (t, $J=3.3\text{Hz}$, 1H), 5.17 (s, 2H), 3.58 (dd, $J=13.6, 5.0\text{Hz}$, 1H), 3.51-3.46 (m, 1H), 3.28 (t, $J=13.6, 11.7\text{Hz}$, 1H), 2.97-2.86 (m, 2H), 2.82-2.77 (m, 1H), 2.63-2.58 (m, 1H), 2.32 (s, 3H), 2.23-2.08 (m, 3H), 2.01-1.82 (m, 5H), 1.75-1.67 (m, 1H), 1.64-1.51 (m, 5H), 1.16-1.05 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.28, 135.59, 135.38, 130.29, 129.42, 127.64, 126.98, 126.40, 125.72, 124.06, 121.88, 112.67, 108.95, 63.56, 56.07, 55.19, 50.69, 48.66, 48.00, 39.86, 32.12, 30.06, 26.91, 24.06, 23.99, 21.63 (2), 19.00. HRMS m/z (ESI^+) calcd. for $\text{C}_{28}\text{H}_{36}\text{N}_3\text{O}$ [$\text{M}+\text{H}^+$] 430.2858, found 430.3067. Mp: 164.2°C ~ 165.0°C

[0048] 化合物 LMY-04: 14-[N-(3-甲基苄基)-2-吡咯甲烯基]槐定碱: 白色固体粉末, 收率 47%;

[0049] ^1H NMR (600MHz, Chloroform- d) δ 7.68 (d, $J=1.8\text{Hz}$, 1H), 7.20 (t, $J=7.6\text{Hz}$, 1H), 7.07 (d, $J=7.6\text{Hz}$, 1H), 6.92 (s, 1H), 6.89 (d, $J=7.8\text{Hz}$, 1H), 6.83-6.79 (m, 1H), 6.43 (d, 1H), 6.28 (t, $J=3.2\text{Hz}$, 1H), 5.18 (s, 2H), 3.59 (dd, $J=13.6, 5.0\text{Hz}$, 1H), 3.51-3.45 (m, 1H), 3.30 (t, $J=13.6, 11.7\text{Hz}$, 1H), 2.96-2.86 (m, 2H), 2.83-2.75 (m, 1H), 2.63-2.55 (m, 1H), 2.31 (s, 3H), 2.22-2.07 (m, 3H), 2.01-1.82 (m, 4H), 1.76-1.67 (m, 1H), 1.64-1.51 (m, 5H), 1.38-1.23 (m, 1H), 1.16-1.06 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.27, 138.39, 137.57, 129.26, 128.66, 128.35, 127.47, 125.70, 124.21, 123.89, 122.06, 112.68, 108.93, 63.57, 56.07, 55.19, 50.68, 50.68, 47.99, 39.87, 32.11, 30.07, 26.90, 24.03, 23.99, 21.63 (2), 21.44. HRMS m/z (ESI^+) calcd. for $\text{C}_{28}\text{H}_{36}\text{N}_3\text{O}$ [$\text{M}+\text{H}^+$] 430.2858, found 430.2728. Mp: 157.9°C ~ 158.9°C

[0050] 化合物 LMY-05: 14-[N-(4-甲基苄基)-2-吡咯甲烯基]槐定碱: 白色固体粉末, 收率 54%;

[0051] ^1H NMR (600MHz, Chloroform- d) δ 7.69 (s, 1H), 7.11 (d, $J=7.8\text{Hz}$, 2H), 7.01 (d, $J=7.9\text{Hz}$, 2H), 6.81 (t, $J=2.0\text{Hz}$, 1H), 6.42 (d, $J=3.9, 1.5\text{Hz}$, 1H), 6.27 (t, $J=3.3\text{Hz}$, 1H), 5.17 (s, 2H), 3.59 (dd, $J=13.6, 5.0\text{Hz}$, 1H), 3.51-3.42 (m, 1H), 3.29 (t, $J=13.6, 11.7\text{Hz}$, 1H), 2.94-2.85 (m, 2H), 2.82-2.75 (m, 1H), 2.60-2.54 (m, 1H), 2.31 (s, 3H), 2.21-2.06 (m, 3H), 1.99 (t, $J=10.8, 9.0\text{Hz}$, 1H), 1.97-1.81 (m, 3H), 1.76-1.66 (m, 1H), 1.64-1.47 (m, 5H), 1.32-1.25 (m, 1H), 1.16-1.06 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.30, 137.20, 134.60, 129.44 (2), 129.19, 126.83 (2), 125.49, 124.19, 122.10, 112.74, 108.91, 63.57, 56.07, 55.18, 50.68, 50.53, 48.00, 39.86, 32.12, 30.07, 26.87, 24.01, 23.99, 21.63 (2), 21.09. HRMS m/z (ESI^+) calcd. for $\text{C}_{28}\text{H}_{36}\text{N}_3\text{O}$ [$\text{M}+\text{H}^+$] 430.2858, found 430.2813. Mp: 116.6

℃~120.0℃

[0052] 化合物LMY-06:14-[N-(3,5-二甲基苄基)-2-吡咯甲烯基]槐定碱:浅棕色固体粉末,收率40%;

[0053] ^1H NMR (600MHz, Chloroform-d) δ 7.69 (s, 1H), 6.89 (s, 1H), 6.79 (t, J=2.1Hz, 1H), 6.71 (s, 2H), 6.43 (d, J=3.8Hz, 1H), 6.28 (t, J=3.3Hz, 1H), 5.14 (s, 2H), 3.60 (dd, J=13.6, 5.1Hz, 1H), 3.52-3.47 (m, 1H), 3.31 (t, J=12.7Hz, 1H), 2.97-2.88 (m, 2H), 2.86-2.78 (m, 1H), 2.65-2.56 (m, 1H), 2.27 (s, 6H), 2.25-2.08 (m, 2H), 2.04 (t, J=10.0Hz, 1H), 2.00-1.83 (m, 2H), 1.78-1.68 (m, 1H), 1.66-1.50 (m, 5H), 1.33-1.23 (m, 3H), 1.17-1.07 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.29, 138.28 (2), 137.47, 129.27, 129.25, 125.73, 124.64 (2), 124.18, 122.14, 112.60, 108.84, 63.50, 56.03, 55.21, 50.61, 50.54, 47.96, 39.86, 32.03, 30.05, 26.93, 24.05, 23.89, 21.63, 21.59, 21.31 (2). HRMS m/z (ESI $^+$) calcd. for $\text{C}_{29}\text{H}_{38}\text{N}_3\text{O}$ [M+H $^+$] 444.3015, found 444.2972. Mp: 116.5℃~117.8℃

[0054] 化合物LMY-07:14-[N-(4-叔丁基苄基)-2-吡咯甲烯基]槐定碱:白色固体粉末,收率37%;

[0055] ^1H NMR (600MHz, Chloroform-d) δ 7.71 (s, 1H), 7.35-7.31 (m, 2H), 7.08-7.02 (m, 2H), 6.84-6.80 (m, 1H), 6.44-6.41 (m, 1H), 6.30-6.26 (m, 1H), 5.18 (s, 2H), 3.60 (dd, J=13.6, 5.0Hz, 1H), 3.51-3.46 (m, 1H), 3.31 (t, J=13.6, 11.7Hz, 1H), 2.95-2.87 (m, 2H), 2.83-2.77 (m, 1H), 2.63-2.56 (m, 1H), 2.23-2.07 (m, 3H), 2.01 (t, J=10.8, 9.0Hz, 1H), 1.98-1.83 (m, 3H), 1.71 (m, J=12.9, 4.1Hz, 1H), 1.64-1.49 (m, 5H), 1.31-1.27 (m, 10H), 1.16-1.07 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.29, 150.42, 134.61, 129.22, 126.55 (2), 125.68 (2), 125.64, 124.17, 122.08, 112.67, 108.93, 63.59, 56.08, 55.20, 50.69, 50.34, 48.00, 39.87, 34.49, 32.12, 31.33 (3), 30.08, 26.91, 24.04, 24.00, 21.64 (2). HRMS m/z (ESI $^+$) calcd. for $\text{C}_{31}\text{H}_{42}\text{N}_3\text{O}$ [M+H $^+$] 472.3328, found 472.3179. Mp: 75.5℃~81.3℃

[0056] 化合物LMY-08:14-[N-(3,5-二叔丁基苄基)-2-吡咯甲烯基]槐定碱:白色固体粉末,收率41%;

[0057] ^1H NMR (600MHz, Chloroform-d) δ 7.72 (s, 1H), 7.36-7.24 (m, 2H), 6.88 (d, J=1.8Hz, 2H), 6.78 (t, J=2.1Hz, 1H), 6.42 (d, J=3.7Hz, 1H), 6.27 (t, J=3.3Hz, 1H), 5.21 (s, 2H), 3.60 (dd, J=13.6, 5.0Hz, 1H), 3.52-3.46 (m, 1H), 3.31 (t, J=12.7Hz, 1H), 2.98-2.87 (m, 2H), 2.85-2.77 (m, 1H), 2.65-2.57 (m, 1H), 2.25-2.00 (m, 3H), 1.99-1.82 (m, 3H), 1.79-1.69 (m, 1H), 1.66-1.47 (m, 5H), 1.37-1.31 (m, 1H), 1.28 (s, 18H), 1.16-1.06 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.30, 151.06 (2), 136.69, 129.33, 125.78, 124.08, 122.38, 121.42, 121.16 (2), 112.62, 108.78, 63.53, 56.05, 55.21, 51.01, 50.63, 47.96, 39.89, 34.76 (2), 32.04, 31.39 (6), 30.05, 27.01, 24.02, 23.91, 21.60 (2). HRMS m/z (ESI $^+$) calcd. for $\text{C}_{35}\text{H}_{50}\text{N}_3\text{O}$ [M+H $^+$] 528.3954, found 528.3778. Mp: 162.5℃~162.7℃

[0058] 化合物LMY-09:14-[N-(4-氟苄基)-2-吡咯甲烯基]槐定碱:白色固体粉末,收率36%;

[0059] ^1H NMR (600MHz, Chloroform-d) δ 7.64 (s, 1H), 7.08-7.03 (m, 2H), 7.00-6.95 (m, 2H), 6.83-6.78 (m, 1H), 6.42 (dd, J=3.9, 1.6Hz, 1H), 6.27 (t, J=3.2Hz, 1H), 5.16 (s, 2H), 3.57 (dd, J=13.6, 5.0Hz, 1H), 3.50-3.44 (m, 1H), 3.28 (t, J=13.6, 11.7Hz, 1H), 2.93-

2.84 (m, 2H), 2.82-2.74 (m, 1H), 2.61-2.53 (m, 1H), 2.21-2.04 (m, 3H), 1.98 (t, J=10.8, 9.0Hz, 1H), 1.94-1.81 (m, 3H), 1.75-1.65 (m, 1H), 1.63-1.47 (m, 5H), 1.33-1.23 (m, 1H), 1.14-1.04 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.15, 162.17 (d, J=245.9Hz), 133.46 (d, J=3.2Hz), 129.11, 128.45, 128.40, 125.80, 124.09, 121.76, 115.73, 115.59, 112.89, 109.16, 63.55, 56.06, 55.17, 50.67, 50.06, 47.99, 39.84, 32.11, 30.05, 26.85, 23.98 (2), 21.63 (2). HRMS m/z (ESI^+) calcd. for $\text{C}_{27}\text{H}_{33}\text{FN}_3\text{O}$ $[\text{M}+\text{H}^+]$ 434.2608, found 434.2544. Mp: 143.9°C~145.4°C

[0060] 化合物 LMY-10:14-[N-(2-氯苄基)-2-吡咯甲烯基]槐定碱:深棕色固体粉末,收率 36%;

[0061] ^1H NMR (600MHz, Chloroform- d) δ 7.56 (s, 1H), 7.35 (d, J=7.9, 1.3Hz, 1H), 7.20-7.15 (m, 1H), 7.14-7.09 (m, 1H), 6.78 (d, J=2.7, 1.5Hz, 1H), 6.54 (d, J=7.7, 1.6Hz, 1H), 6.44 (d, J=3.9, 1.5Hz, 1H), 6.32-6.28 (m, 1H), 5.28 (s, 2H), 3.55 (dd, J=13.7, 5.1Hz, 1H), 3.49-3.44 (m, 1H), 3.26 (t, J=13.7, 11.7Hz, 1H), 2.96-2.84 (m, 2H), 2.82-2.74 (m, 1H), 2.64-2.54 (m, 1H), 2.21-2.06 (m, 3H), 1.99 (t, J=10.9, 9.0Hz, 1H), 1.94-1.79 (m, 3H), 1.75-1.64 (m, 1H), 1.62-1.47 (m, 5H), 1.32-1.28 (m, 1H), 1.13-1.04 (m, 1H). ^{13}C NMR (151 MHz, CDCl_3) δ 165.06, 135.55, 132.15, 129.40, 129.36, 128.75, 127.75, 127.24, 126.25, 124.32, 121.61, 112.84, 109.36, 63.49, 56.04, 55.17, 50.63, 48.31, 47.94, 39.85, 32.03, 30.05, 26.92, 24.09, 23.93, 22.65, 21.62. HRMS m/z (ESI^+) calcd. for $\text{C}_{27}\text{H}_{33}\text{ClN}_3\text{O}$ $[\text{M}+\text{H}^+]$ 450.2312, found 450.2339. Mp: 129.4°C~130.6°C

[0062] 化合物 LMY-11:14-[N-(3-氯苄基)-2-吡咯甲烯基]槐定碱:白色固体粉末,收率 39%;

[0063] ^1H NMR (600MHz, Chloroform- d) δ 7.60 (d, J=1.8Hz, 1H), 7.31-7.20 (m, 2H), 7.03-6.94 (m, 2H), 6.83-6.79 (m, 1H), 6.46-6.41 (m, 1H), 6.31 (t, J=3.3Hz, 1H), 5.19 (s, 2H), 3.58 (dd, J=13.6, 5.1Hz, 1H), 3.51-3.46 (m, 1H), 3.28 (t, J=13.6, 11.8Hz, 1H), 2.94-2.86 (m, 2H), 2.83-2.76 (m, 1H), 2.63-2.54 (m, 1H), 2.25-2.07 (m, 3H), 2.01 (t, J=10.9, 9.0Hz, 1H), 1.96-1.81 (m, 3H), 1.77-1.66 (m, 1H), 1.65-1.49 (m, 5H), 1.36-1.24 (m, 1H), 1.15-1.05 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.13, 139.85, 134.71, 130.05, 129.18, 127.81, 126.64, 126.18, 124.75, 124.17, 121.64, 112.96, 109.37, 63.53, 56.06, 55.19, 50.66, 50.05, 47.98, 39.84, 32.08, 30.04, 26.86, 24.00, 23.94, 21.61, 21.60. HRMS m/z (ESI^+) calcd. for $\text{C}_{27}\text{H}_{33}\text{ClN}_3\text{O}$ $[\text{M}+\text{H}^+]$ 450.2312, found 450.2252. Mp: 162.3°C~162.7°C

[0064] 化合物 LMY-12:14-[N-(4-氯苄基)-2-吡咯甲烯基]槐定碱:淡黄色固体粉末,收率 42%;

[0065] ^1H NMR (600MHz, Chloroform- d) δ 7.60 (s, 1H), 7.25 (dd, J=8.5, 2.4Hz, 2H), 7.00 (dd, J=8.5, 2.0Hz, 2H), 6.83-6.77 (m, 1H), 6.46-6.39 (m, 1H), 6.32-6.24 (m, 1H), 5.16 (s, 2H), 3.57 (dd, J=13.6, 5.1, 1.8Hz, 1H), 3.49-3.43 (m, 1H), 3.27 (t, J=13.6, 11.7, 1.8Hz, 1H), 2.93-2.82 (m, 2H), 2.80-2.72 (m, 1H), 2.64-2.22 (m, 2H), 2.23-2.05 (m, 3H), 1.98-1.79 (m, 4H), 1.73-1.64 (m, 1H), 1.63-1.44 (m, 5H), 1.14-1.04 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.12, 136.27, 133.36, 129.12, 128.93 (2), 128.04 (2), 125.87, 124.16, 121.67, 112.94, 109.25, 63.53, 56.06, 55.16, 50.67, 50.09, 47.99, 39.84, 32.10, 30.05, 26.83,

23.98 (2), 21.62 (2). HRMS m/z (ESI⁺) calcd. for C₂₇H₃₃ClN₃O [M+H⁺] 450.2312, found 450.2252. Mp: 164.9°C ~ 166.0°C

[0066] 化合物 LMY-13: 14-[N-(2-溴苄基)-2-吡咯甲烯基]槐定碱: 黄色固体粉末, 收率 43%;

[0067] ¹H NMR (600MHz, Chloroform-d) δ 7.59-7.53 (m, 2H), 7.18 (t, J=7.5, 1.3Hz, 1H), 7.14-7.09 (m, 1H), 6.79 (dd, J=2.7, 1.6Hz, 1H), 6.50 (d, J=7.7, 1.6Hz, 1H), 6.46 (d, J=3.9, 1.5Hz, 1H), 6.35-6.30 (m, 1H), 5.26 (s, 2H), 3.56 (dd, J=13.7, 5.1Hz, 1H), 3.50-3.45 (m, 1H), 3.27 (t, J=13.7, 11.7Hz, 1H), 2.98-2.85 (m, 2H), 2.83-2.75 (m, 1H), 2.65-2.56 (m, 1H), 2.23-2.07 (m, 3H), 2.00 (t, J=10.9, 9.0Hz, 1H), 1.95-1.81 (m, 3H), 1.76-1.66 (m, 1H), 1.63-1.48 (m, 5H), 1.34-1.25 (m, 1H), 1.15-1.04 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ 165.09, 137.14, 132.64, 129.43, 129.02, 127.87, 127.81, 126.33, 124.28, 121.99, 121.61, 112.85, 109.40, 63.49, 56.05, 55.19, 50.80, 50.63, 47.95, 39.86, 32.03, 30.05, 26.93, 24.11, 23.92, 21.64, 21.62. HRMS m/z (ESI⁺) calcd. for C₂₇H₃₃BrN₃O [M+H⁺] 494.1807, found 494.1755. Mp: 122.4°C ~ 129.3°C

[0068] 化合物 LMY-14: 14-[N-(4-溴苄基)-2-吡咯甲烯基]槐定碱: 淡黄色固体粉末, 收率 45%;

[0069] ¹H NMR (600MHz, Chloroform-d) δ 7.60 (s, 1H), 7.44-7.37 (m, 2H), 6.94 (d, J=8.2Hz, 2H), 6.80 (dd, J=2.6, 1.5Hz, 1H), 6.42 (d, J=4.5Hz, 1H), 6.28 (t, J=3.3Hz, 1H), 5.15 (s, 2H), 3.57 (dd, J=13.6, 5.0Hz, 1H), 3.50-3.43 (m, 1H), 3.27 (t, J=13.6, 11.8Hz, 1H), 2.91-2.83 (m, 2H), 2.82-2.73 (m, 1H), 2.59-2.49 (m, 1H), 2.47-2.24 (m, 1H), 2.19-2.04 (m, 3H), 2.04-1.94 (m, 1H), 1.93-1.77 (m, 3H), 1.76-1.64 (m, 1H), 1.61-1.47 (m, 5H), 1.15-1.04 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ 165.11, 136.79, 131.88 (2), 129.13, 128.37 (2), 125.91, 124.16, 121.65, 121.50, 112.94, 109.27, 63.54, 56.06, 55.16, 50.68, 50.15, 47.99, 39.84, 32.11, 30.05, 26.84, 23.99 (2), 21.62 (2). HRMS m/z (ESI⁺) calcd. for C₂₇H₃₃BrN₃O [M+H⁺] 494.1807, found 494.2028. Mp: 165.4°C ~ 165.5°C

[0070] 化合物 LMY-15: 14-[N-(3-甲氧基苄基)-2-吡咯甲烯基]槐定碱: 黄色固体粉末, 收率 38%;

[0071] ¹H NMR (600MHz, Chloroform-d) δ 7.66 (s, 1H), 7.22 (t, J=7.9Hz, 1H), 6.86-6.76 (m, 2H), 6.68 (d, J=7.6Hz, 1H), 6.60 (s, 1H), 6.43 (d, J=3.9Hz, 1H), 6.28 (t, J=3.2Hz, 1H), 5.19 (s, 2H), 3.75 (s, 3H), 3.58 (dd, J=13.6, 5.0Hz, 1H), 3.50-3.45 (m, 1H), 3.28 (t, J=13.6, 11.7Hz, 1H), 2.97-2.84 (m, 2H), 2.82-2.74 (m, 1H), 2.62-2.54 (m, 1H), 2.29-2.04 (m, 3H), 2.02-1.82 (m, 5H), 1.75-1.66 (m, 1H), 1.64-1.47 (m, 5H), 1.14-1.04 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ 165.25, 159.92, 139.29, 129.79, 129.25, 125.71, 124.27, 122.00, 119.02, 113.02, 112.78, 112.35, 109.04, 63.56, 56.07, 55.18, 55.16, 50.68, 50.60, 47.99, 39.85, 32.11, 30.07, 26.88, 24.02, 23.98, 21.63 (2). HRMS m/z (ESI⁺) calcd. for C₂₈H₃₆N₃O₂ [M+H⁺] 446.2808, found 446.2746. Mp: 85.4°C ~ 86.1°C

[0072] 化合物 LMY-16: 14-[N-(4-甲氧基苄基)-2-吡咯甲烯基]槐定碱: 棕色固体粉末, 收率 48%;

[0073] ¹H NMR (600MHz, Chloroform-d) δ 7.70 (s, 1H), 7.06 (d, 2H), 6.85-6.78 (m, 3H),

6.41 (d, $J=3.9, 1.7\text{Hz}$, 1H), 6.29-6.22 (m, 1H), 5.13 (d, $J=2.6\text{Hz}$, 2H), 3.76 (s, 3H), 3.61-3.56 (dd, 1H), 3.50-3.44 (m, 1H), 3.29 (t, $J=13.7, 11.7\text{Hz}$, 1H), 2.93-2.84 (m, 2H), 2.81-2.75 (m, 1H), 2.62-2.52 (m, 1H), 2.20-2.05 (m, 3H), 2.01-1.81 (m, 5H), 1.75-1.65 (m, 1H), 1.62-1.50 (m, 5H), 1.15-1.04 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.28, 159.02, 129.67, 129.11, 128.26 (2), 125.45, 124.06, 122.07, 114.16 (2), 112.76, 108.88, 63.58, 56.07, 55.24, 55.18, 50.69, 50.26, 48.01, 39.85, 32.12, 30.07, 26.87, 24.00 (2), 21.64, 21.63. HRMS m/z (ESI^+) calcd. for $\text{C}_{28}\text{H}_{36}\text{N}_3\text{O}_2$ [$\text{M}+\text{H}^+$] 446.2808, found 446.2832. Mp: $73.6^\circ\text{C} \sim 74.1^\circ\text{C}$

[0074] 化合物 LMY-17:14-[N-(3,5-二甲氧基苄基)-2-吡咯甲烯基]槐定碱:黄色固体粉末, 收率45%;

[0075] ^1H NMR (600MHz, Chloroform- d) δ 7.65 (s, 1H), 6.80 (dd, $J=2.7, 1.5\text{Hz}$, 1H), 6.41 (dd, $J=3.9, 1.5\text{Hz}$, 1H), 6.32 (t, $J=2.3\text{Hz}$, 1H), 6.26 (t, $J=3.8, 2.7\text{Hz}$, 1H), 6.20 (d, $J=2.2\text{Hz}$, 2H), 5.13 (s, 2H), 3.72 (s, 6H), 3.57 (dd, $J=13.6, 5.0\text{Hz}$, 1H), 3.50-3.44 (m, 1H), 3.27 (t, $J=13.6, 11.7\text{Hz}$, 1H), 2.92-2.85 (m, 2H), 2.80-2.75 (m, 1H), 2.61-2.53 (m, 1H), 2.21-2.05 (m, 3H), 1.99-1.80 (m, 4H), 1.75-1.64 (m, 1H), 1.61-1.49 (m, 5H), 1.34-1.23 (m, 1H), 1.13-1.03 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.20, 161.06 (2), 140.10, 129.26, 125.75, 124.29, 121.98, 112.78, 109.04, 104.70 (2), 99.44, 63.56, 56.06, 55.26 (2), 55.17, 50.67, 50.64, 47.97, 39.85, 32.11, 30.07, 26.89, 24.03, 23.99, 21.63, 21.62. HRMS m/z (ESI^+) calcd. for $\text{C}_{29}\text{H}_{38}\text{N}_3\text{O}_3$ [$\text{M}+\text{H}^+$] 476.2913, found 476.2926. Mp: $76.8^\circ\text{C} \sim 77.4^\circ\text{C}$

[0076] 化合物 LMY-18:14-[N-(2-溴-5-甲氧基苄基)-2-吡咯甲烯基]槐定碱:黄色固体粉末, 收率52%;

[0077] ^1H NMR (600MHz, Chloroform- d) δ 7.54 (s, 1H), 7.43 (d, $J=8.7\text{Hz}$, 1H), 6.79 (s, 1H), 6.70-6.64 (m, 1H), 6.45 (s, 1H), 6.31 (t, $J=3.2\text{Hz}$, 1H), 6.03 (d, $J=3.0\text{Hz}$, 1H), 5.20 (s, 2H), 3.62 (s, 3H), 3.56 (dd, $J=13.7, 5.1\text{Hz}$, 1H), 3.51-3.45 (m, 1H), 3.27 (t, $J=13.7, 11.7\text{Hz}$, 1H), 2.97-2.85 (m, 2H), 2.83-2.76 (m, 1H), 2.64-2.56 (m, 1H), 2.23-2.07 (m, 3H), 2.05-1.98 (m, 1H), 1.96-1.81 (m, 3H), 1.76-1.66 (m, 1H), 1.63-1.48 (m, 5H), 1.33-1.23 (m, 1H), 1.15-1.04 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.08, 159.42, 138.20, 133.20, 129.36, 126.33, 124.30, 121.67, 114.39, 113.87, 112.94, 112.22, 109.46, 63.47, 56.03, 55.26, 55.19, 50.84, 50.62, 47.94, 39.85, 32.01, 30.04, 26.92, 24.10, 23.89, 21.63, 21.60. HRMS m/z (ESI^+) calcd. for $\text{C}_{28}\text{H}_{35}\text{BrN}_3\text{O}_2$ [$\text{M}+\text{H}^+$] 524.1913, found 524.1910. Mp: $141.3^\circ\text{C} \sim 141.5^\circ\text{C}$

[0078] 化合物 LMY-19:14-[N-(2-萘基亚甲基)-2-吡咯甲烯基]槐定碱:白色固体粉末, 收率41%;

[0079] ^1H NMR (600MHz, Chloroform- d) δ 7.82-7.71 (m, 4H), 7.52-7.47 (m, 1H), 7.48-7.40 (m, 2H), 7.24 (d, $J=8.5, 2.3\text{Hz}$, 1H), 6.86 (s, 1H), 6.46 (s, 1H), 6.31 (d, $J=3.1\text{Hz}$, 1H), 5.35 (s, 2H), 3.55 (dd, $J=13.6, 4.2\text{Hz}$, 1H), 3.47-3.41 (m, 1H), 3.26 (t, $J=13.9, 11.8, 3.2\text{Hz}$, 1H), 2.94-2.82 (m, 2H), 2.81-2.72 (m, 1H), 2.61-2.53 (m, 1H), 2.19-2.01 (m, 3H), 1.92-1.76 (m, 4H), 1.74-1.64 (m, 1H), 1.58 (d, $J=15.2\text{Hz}$, 1H), 1.55-1.42 (m, 4H), 1.32-1.24 (m, 1H), 1.12-1.02 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.19, 135.19, 133.39, 132.82,

129.31, 128.60, 127.96, 127.65, 126.19, 125.94, 125.82, 125.62, 124.80, 124.32, 121.98, 112.84, 109.12, 63.53, 56.06, 55.19, 50.66, 50.05, 47.98, 39.84, 32.08, 30.04, 26.86, 24.00, 23.94, 21.61, 21.60. HRMS m/z (ESI⁺) calcd. for C₃₁H₃₆N₃O [M+H⁺] 466.2858, found 466.2900. Mp: 170.6°C ~ 171.2°C

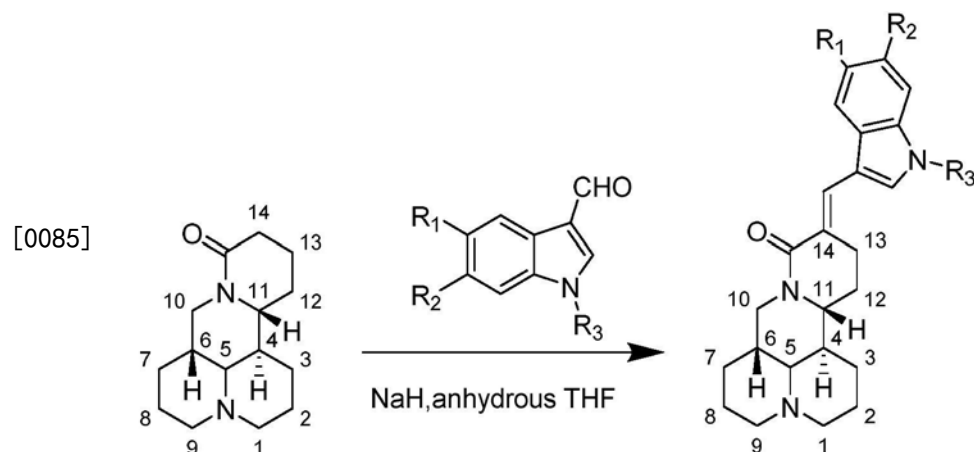
[0080] 化合物 LMY-20: 14-[N-(4-三氟甲氧基苄基)-2-吡咯甲烯基]槐定碱: 白色固体粉末, 收率 40%;

[0081] ¹H NMR (600MHz, Chloroform-d) δ 7.63 (d, J=1.8Hz, 1H), 7.20-7.13 (m, 2H), 7.10 (d, J=8.7Hz, 2H), 6.83 (dd, J=2.7, 1.6Hz, 1H), 6.44 (dd, J=4.0, 1.5Hz, 1H), 6.31 (dd, J=3.8, 2.7Hz, 1H), 5.22 (s, 2H), 3.59 (dd, J=13.6, 5.0Hz, 1H), 3.51-3.46 (m, 1H), 3.29 (t, J=13.6, 11.7Hz, 1H), 2.94-2.85 (m, 2H), 2.84-2.76 (m, 1H), 2.63-2.53 (m, 1H), 2.22-2.07 (m, 3H), 2.00 (dd, J=10.8, 9.0Hz, 1H), 1.98-1.82 (m, 4H), 1.76-1.66 (m, 1H), 1.65-1.47 (m, 5H), 1.17-1.06 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ 164.84, 148.53, 136.52, 129.17, 128.01 (2), 126.69, 124.02, 122.13, 121.23 (2), 120.41 (d, J=257.0Hz), 112.86, 109.30, 63.79, 57.30, 57.26, 52.67, 49.93, 43.16, 41.92, 35.78, 27.80, 26.53, 24.86, 23.40, 21.23, 20.84. HRMS m/z (ESI⁺) calcd. for C₂₈H₃₃F₃N₃O₂ [M+H⁺] 500.2525, found 500.2707. Mp: 186.4°C ~ 187.3°C

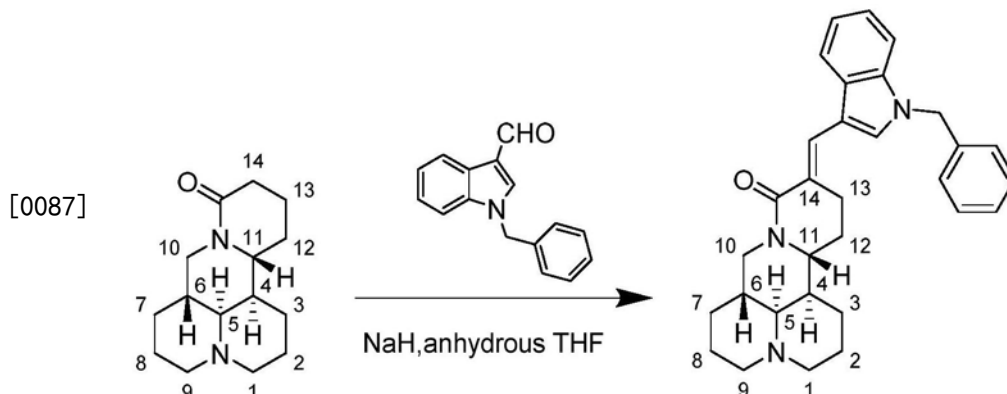
[0082] 化合物 LMY-21: 14-[N-(4-苄氧基苄基)-2-吡咯甲烯基]槐定碱: 淡黄色固体粉末, 收率 47%;

[0083] ¹H NMR (600MHz, Chloroform-d) δ 7.72 (s, 1H), 7.46-7.37 (m, 4H), 7.37-7.30 (m, 1H), 7.11-7.04 (m, 2H), 6.95-6.90 (m, 2H), 6.84-6.79 (m, 1H), 6.43 (d, J=3.8, 1.5Hz, 1H), 6.27 (t, J=3.2Hz, 1H), 5.15 (s, 2H), 5.04 (s, 2H), 3.60 (dd, J=13.6, 5.1Hz, 1H), 3.52-3.46 (m, 1H), 3.31 (t, J=13.6, 11.7Hz, 1H), 2.95-2.86 (m, 2H), 2.84-2.77 (m, 1H), 2.62-2.54 (m, 1H), 2.23-2.06 (m, 3H), 2.01 (t, J=10.8, 9.0Hz, 1H), 1.97-1.83 (m, 3H), 1.78-1.67 (m, 1H), 1.65-1.49 (m, 5H), 1.34-1.26 (m, 1H), 1.17-1.07 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ 165.30, 158.28, 136.94, 129.98, 129.14, 128.58 (2), 128.27 (2), 127.95, 127.48 (2), 125.51, 124.07, 122.08, 115.11 (2), 112.76, 108.91, 70.03, 63.58, 56.08, 55.19, 50.69, 50.25, 48.01, 39.86, 32.13, 30.08, 26.88, 24.01 (2), 21.64 (2). HRMS m/z (ESI⁺) calcd. for C₃₄H₄₀N₃O₂ [M+H⁺] 522.3121, found 522.3189. Mp: 133.6°C ~ 134.0°C

[0084] (2) LMY-22 的制备:



[0086] LMY-22的制备更加具体的为:



[0088] 具体制备LMY-22的实验方法:

[0089] 于100mL圆底烧瓶中分别加入2.4g (100mmol) 氢化钠, 50mL无水四氢呋喃, 搅拌均匀, 加入1.24g (5mmol) 槐定碱, 缓慢升温至85℃加入1.41g (6mmol) N-苄基-3-吲哚甲醛, 反应48h至终点 (TLC检测)。冷却至室温, 逐滴加入3N的盐酸中和过量的氢化钠。二氯甲烷萃取 (40mLx3), 合并有机相, 无水Na₂SO₄干燥, 减压抽滤、浓缩滤液后经硅胶柱层析 (V_{二氯甲烷}:V_{甲醇}=50:1) 纯化, 得1.185g白色固体粉末槐定碱化合物LMY-22:14-[N-苄基-3-吲哚甲烯基]槐定碱: 收率51%;

[0090] ¹H NMR (600MHz, Chloroform-d) δ8.10 (s, 1H), 7.88 (d, 1H), 7.35-7.31 (m, 2H), 7.31-7.27 (m, 3H), 7.26-7.20 (m, 2H), 7.15 (d, 2H), 5.37 (s, 2H), 3.66 (dd, J=13.5, 5.2Hz, 1H), 3.55-3.50 (m, 1H), 3.39 (t, J=13.6, 11.8Hz, 1H), 2.93 (d, J=12.1, 4.0, 1.8Hz, 1H), 2.91-2.80 (m, 2H), 2.64-2.56 (m, 1H), 2.27-2.17 (m, 2H), 2.17-2.06 (m, 2H), 2.05-1.96 (m, 1H), 1.95-1.90 (m, 2H), 1.80-1.70 (m, 1H), 1.66-1.61 (m, 1H), 1.62-1.51 (m, 4H), 1.35-1.23 (m, 1H), 1.21-1.11 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ165.60, 136.85, 136.13, 128.88 (2), 128.74, 128.55, 127.83, 126.72 (2), 125.55, 125.18, 122.77, 120.48, 119.64, 112.51, 109.79, 63.35, 55.98, 55.28, 50.49, 50.39, 47.92, 39.83, 31.93, 30.09, 27.00, 24.70, 23.75, 21.71, 21.58. HRMS m/z (ESI⁺) calcd. for C₃₁H₃₆N₃O [M+H⁺] 466.2858, found 466.3076. Mp: 140.1℃~145.9℃

[0091] 参考化合物LMY-22的实验方法制备化合物LMY-23~LMY-62, 化合物LMY-23~LMY-62结构鉴定数据如下:

[0092] 化合物LMY-23:14-[N-(2-甲基苄基)-3-吲哚甲烯基]槐定碱: 白色固体粉末, 收率32%;

[0093] ¹H NMR (600MHz, Chloroform-d) δ8.10 (s, 1H), 7.90 (d, 1H), 7.31-7.26 (m, 2H), 7.26-7.21 (m, 3H), 7.18 (s, 1H), 7.15-7.10 (m, 1H), 6.76 (d, J=7.6Hz, 1H), 5.32 (s, 2H), 3.66 (dd, J=13.6, 5.2Hz, 1H), 3.56-3.49 (m, 1H), 3.39 (t, J=12.6Hz, 1H), 2.96 (d, J=12.0Hz, 1H), 2.91-2.78 (m, 2H), 2.60-2.51 (m, 1H), 2.34 (s, 3H), 2.31-2.21 (m, 2H), 2.17-2.08 (m, 2H), 2.02 (m, J=16.1, 8.2, 4.8Hz, 1H), 1.98-1.86 (m, 2H), 1.82-1.72 (m, 1H), 1.67-1.61 (m, 1H), 1.61-1.49 (m, 4H), 1.35-1.25 (m, 1H), 1.21-1.13 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ165.58, 136.28, 135.61, 134.56, 130.53, 128.66, 128.38, 127.94, 127.16, 126.50, 125.58, 125.12, 122.75, 120.51, 119.66, 112.47, 109.69, 63.25, 55.91, 55.28,

50.39, 48.43, 47.89, 39.83, 31.83, 30.06, 27.02, 24.64, 23.63, 21.70, 21.52, 19.15. HRMS m/z (ESI⁺) calcd. for $C_{32}H_{38}N_3O[M+H^+]$ 480.3015, found 480.3288. Mp: 141.8°C ~ 143.6°C

[0094] 化合物 LMY-24: 14-[N-(3-甲基苄基)-3-吡啶甲烯基]槐定碱: 淡黄色固体粉末, 收率 24%;

[0095] ¹H NMR (600MHz, Chloroform-d) δ 8.10 (d, J=1.9Hz, 1H), 7.88 (dd, J=7.2, 1.5Hz, 1H), 7.32-7.27 (m, 2H), 7.28-7.18 (m, 3H), 7.11 (d, J=7.6Hz, 1H), 6.98 (s, 1H), 6.94 (d, J=7.6Hz, 1H), 5.32 (s, 2H), 3.66 (dd, J=13.5, 5.2Hz, 1H), 3.55-3.50 (m, 1H), 3.39 (t, 1H), 2.97-2.79 (m, 3H), 2.67-2.55 (m, 1H), 2.32 (s, 3H), 2.27-2.17 (m, 2H), 2.17-2.06 (m, 1H), 2.03-1.97 (m, 1H), 1.97-1.86 (m, 3H), 1.83-1.69 (m, 1H), 1.66-1.61 (m, 1H), 1.62-1.51 (m, 4H), 1.33-1.26 (m, 1H), 1.20-1.11 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ 165.59, 138.64, 136.80, 136.18, 128.77, 128.72, 128.61 (2), 127.44, 125.57, 125.13, 123.85, 122.73, 120.44, 119.59, 112.43, 109.82, 63.40, 56.01, 55.26, 50.53, 50.38, 47.91, 39.85, 31.98, 30.08, 27.02, 24.72, 23.79, 21.69, 21.59, 21.43. HRMS m/z (ESI⁺) calcd. for $C_{32}H_{38}N_3O[M+H^+]$ 480.3015, found 480.3019. Mp: 103.8°C ~ 109.7°C

[0096] 化合物 LMY-25: 14-[N-(4-甲基苄基)-3-吡啶甲烯基]槐定碱: 淡黄色固体粉末, 收率 49%;

[0097] ¹H NMR (600MHz, Chloroform-d) δ 8.10 (s, 1H), 7.88 (d, 1H), 7.32-7.27 (m, 2H), 7.27-7.19 (m, 2H), 7.13 (d, J=7.9Hz, 2H), 7.05 (d, J=7.9Hz, 2H), 5.33 (s, 2H), 3.66 (dd, J=13.5, 5.1Hz, 1H), 3.55-3.49 (m, 1H), 3.38 (t, J=13.5, 11.7Hz, 1H), 2.94-2.89 (m, 1H), 2.89-2.79 (m, 2H), 2.64-2.55 (m, 1H), 2.34 (s, 3H), 2.27-2.16 (m, 2H), 2.17-2.10 (m, 1H), 2.06 (t, J=11.0, 9.0Hz, 1H), 2.03-1.94 (m, 1H), 1.95-1.86 (m, 2H), 1.79-1.69 (m, 1H), 1.65-1.62 (m, 1H), 1.63-1.50 (m, 4H), 1.35-1.30 (m, 1H), 1.20-1.11 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ 165.62, 137.57, 136.12, 133.80, 129.53 (2), 128.74, 128.52, 126.75 (2), 125.59, 125.07, 122.70, 120.42, 119.61, 112.41, 109.81, 63.49, 56.07, 55.25, 50.61, 50.19, 47.94, 39.87, 32.06, 30.11, 29.71, 27.02, 23.89, 21.70, 21.64, 21.10. HRMS m/z (ESI⁺) calcd. for $C_{32}H_{38}N_3O[M+H^+]$ 480.3015, found 480.2929. Mp: 146.8°C ~ 152.8°C

[0098] 化合物 LMY-26: 14-[N-(3,5-二甲基苄基)-3-吡啶甲烯基]槐定碱: 浅棕色固体粉末, 收率 43%;

[0099] ¹H NMR (600MHz, Chloroform-d) δ 8.10 (s, 1H), 7.89 (d, J=7.6, 0.9Hz, 1H), 7.34-7.27 (m, 2H), 7.27-7.21 (m, 2H), 6.93 (s, 1H), 6.78 (s, 2H), 5.29 (s, 2H), 3.66 (dd, J=13.5, 5.1Hz, 1H), 3.55-3.49 (m, 1H), 3.38 (t, J=13.5, 11.7Hz, 1H), 2.94-2.85 (m, 2H), 2.85-2.80 (m, 1H), 2.64-2.58 (m, 1H), 2.28 (s, 6H), 2.25-2.20 (m, 1H), 2.19-2.11 (m, 1H), 2.07 (t, J=10.9, 9.0Hz, 1H), 2.02-1.96 (m, 1H), 1.96-1.86 (m, 3H), 1.79-1.70 (m, 1H), 1.63 (d, J=13.8, 4.4, 2.8Hz, 1H), 1.63-1.48 (m, 4H), 1.35-1.26 (m, 1H), 1.20-1.11 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ 165.62, 138.52 (2), 136.78, 136.22, 129.50, 128.70, 128.64, 125.59, 125.09, 124.57 (2), 122.70, 120.39, 119.57, 112.37, 109.83, 63.50, 56.06, 55.26, 50.61, 50.35, 47.95, 39.90, 32.07, 30.12, 27.05, 24.74, 23.90, 21.70, 21.65, 21.30 (2). HRMS m/z (ESI⁺) calcd. for $C_{33}H_{40}N_3O[M+H^+]$ 494.3171, found 494.3210. Mp: 140.6°C ~ 140.7°C

[0100] 化合物 LMY-27: 14-[N-(4-叔丁基苄基)-3-吡啶甲烯基]槐定碱: 白色固体粉末, 收

率34%;

[0101] ^1H NMR (600MHz, Chloroform- d) δ 8.10 (s, 1H), 7.88 (d, $J=7.6, 0.9\text{Hz}$, 1H), 7.36-7.32 (m, 2H), 7.32-7.28 (m, 2H), 7.27-7.20 (m, 2H), 7.08 (d, 2H), 5.34 (s, 2H), 3.67 (dd, $J=13.5, 5.2\text{Hz}$, 1H), 3.56-3.50 (m, 1H), 3.39 (t, $J=13.6, 11.7\text{Hz}$, 1H), 2.97-2.91 (m, 1H), 2.92-2.81 (m, 2H), 2.66-2.57 (m, 1H), 2.29-2.17 (m, 2H), 2.18-2.10 (m, 1H), 2.10 (t, 1H), 2.05-1.97 (m, 1H), 1.97-1.87 (m, 3H), 1.82-1.70 (m, 1H), 1.67-1.49 (m, 4H), 1.31 (s, 9H), 1.30-1.26 (m, 1H), 1.22-1.11 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.60, 150.82, 136.15, 133.90, 128.71, 128.63, 126.43 (2), 125.77 (2), 125.61, 125.08, 122.70, 120.42, 119.61, 112.41, 109.84, 63.37, 55.99, 55.27, 50.50, 50.05, 47.91, 39.84, 34.54, 31.95, 31.31 (3), 30.08, 27.02, 24.73, 23.75, 21.69, 21.57. HRMS m/z (ESI^+) calcd. for $\text{C}_{35}\text{H}_{44}\text{N}_3\text{O}[\text{M}+\text{H}^+]$ 522.3484, found 522.3563. Mp: $131.6^\circ\text{C} \sim 136.2^\circ\text{C}$

[0102] 化合物 LMY-28: 14-[N-(3,5-二叔丁基苄基)-3-吡啶甲烯基]槐定碱: 淡黄色固体粉末, 收率29%;

[0103] ^1H NMR (600MHz, Chloroform- d) δ 8.10 (s, 1H), 7.87 (d, 1H), 7.39-7.35 (m, 2H), 7.27-7.25 (m, 2H), 7.22 (t, $J=7.5, 7.1, 1.0\text{Hz}$, 1H), 7.01 (d, $J=1.8\text{Hz}$, 2H), 5.35 (s, 2H), 3.66 (dd, $J=13.6, 5.1\text{Hz}$, 1H), 3.55-3.49 (m, 1H), 3.39 (t, $J=13.6, 11.7\text{Hz}$, 1H), 2.93 (d, $J=12.0\text{Hz}$, 1H), 2.90-2.81 (m, 2H), 2.63-2.55 (m, 1H), 2.26-2.17 (m, 2H), 2.15-2.03 (m, 2H), 2.02-1.87 (m, 3H), 1.80-1.70 (m, 1H), 1.63 (d, $J=10.4\text{Hz}$, 1H), 1.61-1.51 (m, 4H), 1.35-1.30 (m, 1H), 1.28 (s, 18H), 1.20-1.11 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.66, 151.43 (2), 136.35, 135.75, 128.65, 128.47, 125.78, 125.06, 122.59, 121.78, 121.30 (2), 120.35, 119.58, 112.29, 109.78, 63.42, 56.00, 55.27, 50.78, 50.51, 47.95, 39.92, 31.94, 31.38 (6), 30.09, 29.71 (2), 27.06, 24.69, 23.79, 21.68, 21.60. HRMS m/z (ESI^+) calcd. for $\text{C}_{39}\text{H}_{52}\text{N}_3\text{O}[\text{M}+\text{H}^+]$ 578.4110, found 578.4356. Mp: $159.7^\circ\text{C} \sim 161.3^\circ\text{C}$

[0104] 化合物 LMY-29: 14-[N-(2-氯苄基)-3-吡啶甲烯基]槐定碱: 黄色固体粉末, 收率31%;

[0105] ^1H NMR (600MHz, Chloroform- d) δ 8.10 (s, 1H), 7.90 (d, 1H), 7.45 (d, $J=8.0, 1.2\text{Hz}$, 1H), 7.31 (s, 1H), 7.30-7.21 (m, 4H), 7.13 (t, $J=7.6, 1.2\text{Hz}$, 1H), 6.66 (d, $J=7.7, 1.6\text{Hz}$, 1H), 5.47 (s, 2H), 3.67 (dd, $J=13.5, 5.2\text{Hz}$, 1H), 3.56-3.50 (m, 1H), 3.39 (t, $J=13.6, 11.7\text{Hz}$, 1H), 2.95-2.85 (m, 2H), 2.85-2.79 (m, 1H), 2.65-2.57 (m, 1H), 2.30-2.17 (m, 2H), 2.19-2.10 (m, 1H), 2.07 (t, $J=10.0\text{Hz}$, 1H), 2.03-1.96 (m, 1H), 1.96-1.90 (m, 2H), 1.80-1.69 (m, 1H), 1.66-1.60 (m, 1H), 1.62-1.50 (m, 4H), 1.29-1.27 (m, 1H), 1.21-1.11 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.53, 136.10, 134.48, 132.43, 129.61, 129.03, 128.67, 128.62, 127.94, 127.34, 125.53, 125.37, 122.96, 120.64, 119.72, 112.81, 109.69, 63.47, 58.43, 56.05, 55.26, 50.59, 47.98, 39.89, 32.05, 30.11, 27.03, 24.73, 23.87, 21.70, 21.63. HRMS m/z (ESI^+) calcd. for $\text{C}_{31}\text{H}_{35}\text{ClN}_3\text{O}[\text{M}+\text{H}^+]$ 500.2469, found 500.2249. Mp: $131.8^\circ\text{C} \sim 133.0^\circ\text{C}$

[0106] 化合物 LMY-30: 14-[N-(4-氯苄基)-3-吡啶甲烯基]槐定碱: 白色固体粉末, 收率33%;

[0107] ^1H NMR (600MHz, Chloroform- d) δ 8.08 (s, 1H), 7.88 (d, $J=7.3\text{Hz}$, 1H), 7.29 (d, $J=$

4.0Hz, 2H), 7.26 (d, J=10.3Hz, 4H), 7.07 (d, J=8.1Hz, 2H), 5.34 (s, 2H), 3.66 (dd, J=13.6, 5.2Hz, 1H), 3.56-3.49 (m, 1H), 3.39 (t, J=12.6Hz, 1H), 2.97-2.77 (m, 2H), 2.66-2.56 (m, 1H), 2.29-2.17 (m, 2H), 2.18-2.10 (m, 1H), 2.07 (t, 1H), 2.01-1.96 (m, 2H), 1.97-1.86 (m, 2H), 1.79-1.69 (m, 1H), 1.67-1.61 (m, 1H), 1.62-1.50 (m, 4H), 1.37-1.29 (m, 1H), 1.21-1.11 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.50, 135.99, 135.36, 133.70, 129.08 (2), 128.76, 128.26, 128.03 (2), 125.51, 125.35, 122.92, 120.62, 119.76, 112.78, 109.64, 63.45, 56.04, 55.26, 50.58, 49.76, 47.95, 39.87, 30.11, 29.71, 27.01, 24.74, 23.87, 21.71, 21.65. HRMS m/z (ESI^+) calcd. for $\text{C}_{31}\text{H}_{35}\text{ClN}_3\text{O}$ [$\text{M}+\text{H}^+$] 500.2469, found 500.2798. Mp: 150.2°C~152.8°C

[0108] 化合物 LMY-31:14-[N-(2,6-二氯苄基)-3-吡啶甲烯基]槐定碱:白色固体粉末,收率38%;

[0109] ^1H NMR (600MHz, Chloroform- d) δ 8.03 (s, 1H), 7.84 (d, J=7.9Hz, 1H), 7.54 (d, J=8.2Hz, 1H), 7.43 (d, J=8.0Hz, 2H), 7.35-7.27 (m, 2H), 7.23 (t, J=7.5Hz, 1H), 7.12 (s, 1H), 5.58 (s, 2H), 3.64 (dd, J=13.6, 5.1Hz, 1H), 3.53-3.46 (m, 1H), 3.35 (t, J=12.6Hz, 1H), 2.91 (d, J=12.0Hz, 1H), 2.87-2.73 (m, 2H), 2.55-2.46 (m, 1H), 2.26-2.14 (m, 2H), 2.14-2.08 (m, 1H), 2.05 (t, J=9.9Hz, 1H), 2.00-1.91 (m, 1H), 1.93-1.85 (m, 2H), 1.79-1.68 (m, 1H), 1.62 (d, J=13.9Hz, 1H), 1.59-1.49 (m, 4H), 1.35-1.23 (m, 1H), 1.19-1.09 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.56, 136.85 (2), 136.30, 131.66, 130.45, 128.92 (2), 128.41, 127.51, 125.57, 125.30, 122.69, 120.45, 119.58, 112.52, 109.78, 63.44, 56.02, 55.26, 50.55, 47.92, 45.34, 39.91, 31.98, 30.09, 27.15, 24.45, 23.83, 21.70, 21.62. HRMS m/z (ESI^+) calcd. for $\text{C}_{31}\text{H}_{34}\text{Cl}_2\text{N}_3\text{O}$ [$\text{M}+\text{H}^+$] 534.2079, found 534.2446. Mp: 147.5°C~150.1°C

[0110] 化合物 LMY-32:14-[N-(2-溴苄基)-3-吡啶甲烯基]槐定碱:白色固体粉末,收率47%;

[0111] ^1H NMR (600MHz, Chloroform- d) δ 8.10 (s, 1H), 7.90 (d, 1H), 7.65-7.61 (m, 1H), 7.31 (s, 1H), 7.29-7.22 (m, 3H), 7.18-7.13 (m, 2H), 6.63-6.57 (m, 1H), 5.44 (s, 2H), 3.67 (dd, 1H), 3.59-3.52 (m, 1H), 3.40 (t, J=12.6Hz, 1H), 2.98 (d, J=11.6Hz, 1H), 2.94-2.84 (m, 2H), 2.67-2.57 (m, 1H), 2.35-2.24 (m, 2H), 2.24-2.11 (m, 1H), 2.10-2.01 (m, 1H), 2.01-1.88 (m, 3H), 1.80 (t, J=13.3Hz, 1H), 1.70-1.64 (m, 1H), 1.63-1.55 (m, 4H), 1.35-1.29 (m, 1H), 1.21-1.13 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.55, 136.09, 136.00, 132.88, 129.30, 128.67 (2), 127.99, 127.97, 125.57, 125.32, 123.00, 122.24, 120.69, 119.69, 112.78, 109.76, 63.18, 55.93, 55.27, 50.49, 50.35, 47.77, 39.71, 31.67, 29.89, 26.95, 24.66, 23.40, 21.62, 21.34. HRMS m/z (ESI^+) calcd. for $\text{C}_{31}\text{H}_{35}\text{BrN}_3\text{O}$ [$\text{M}+\text{H}^+$] 544.1964, found 544.2314. Mp: 133.7°C~134.2°C

[0112] 化合物 LMY-33:14-[N-(3-溴苄基)-3-吡啶甲烯基]槐定碱:白色固体粉末,收率45%;

[0113] ^1H NMR (600MHz, Chloroform- d) δ 8.08 (s, 1H), 7.89 (d, J=7.6Hz, 1H), 7.43 (d, J=7.9, 1.9Hz, 1H), 7.35 (s, 1H), 7.30-7.23 (m, 4H), 7.18 (t, J=7.9Hz, 1H), 7.01 (d, J=7.7Hz, 1H), 5.34 (s, 2H), 3.66 (dd, J=13.6, 5.2Hz, 1H), 3.56-3.50 (m, 1H), 3.39 (t, J=

13.5, 11.7 Hz, 1H), 2.95-2.91 (m, 1H), 2.91-2.80 (m, 2H), 2.66-2.57 (m, 1H), 2.27-2.19 (m, 2H), 2.19-2.12 (m, 1H), 2.09 (t, J=10.0 Hz, 1H), 2.02-1.96 (m, 1H), 1.97-1.87 (m, 3H), 1.80-1.70 (m, 1H), 1.63 (d, J=13.5, 6.3, 3.2 Hz, 1H), 1.62-1.49 (m, 3H), 1.39-1.29 (m, 1H), 1.22-1.11 (m, 1H). ^{13}C NMR (151 MHz, CDCl_3) δ 165.50, 139.22, 136.02, 131.04, 130.51, 129.73 (2), 128.75, 128.29, 125.60, 125.34, 125.24, 122.99, 120.66, 119.77, 112.87, 109.61, 63.42, 56.02, 55.27, 50.55, 49.76, 47.94, 39.86, 32.01, 30.09, 27.00, 24.75, 23.83, 21.70, 21.61. HRMS m/z (ESI^+) calcd. for $\text{C}_{31}\text{H}_{35}\text{BrN}_3\text{O}$ [$\text{M}+\text{H}^+$] 544.1964, found 544.2219. Mp: 135.6°C ~ 135.8°C

[0114] 化合物 LMY-34: 14-[N-(4-溴苄基)-3-吡啶甲烯基]槐定碱: 白色固体粉末, 收率 39%;

[0115] ^1H NMR (600 MHz, Chloroform- d) δ 8.09 (s, 1H), 7.88 (d, 1H), 7.44 (d, J=8.2 Hz, 2H), 7.25 (s, 1H), 7.24 (s, 2H), 7.22 (d, J=8.4 Hz, 1H), 7.00 (d, J=8.0 Hz, 2H), 5.30 (s, 2H), 3.67 (dd, J=13.6, 5.4 Hz, 1H), 3.59-3.53 (m, 1H), 3.44 (t, J=12.5 Hz, 1H), 3.05 (d, J=12.1 Hz, 1H), 3.00-2.93 (m, 1H), 2.90-2.83 (m, 1H), 2.65-2.58 (m, 1H), 2.40-2.32 (m, 2H), 2.32-2.21 (m, 1H), 2.17-2.06 (m, 2H), 2.05-1.98 (m, 1H), 1.94 (d, J=5.4 Hz, 1H), 1.86-1.76 (m, 1H), 1.69-1.65 (m, 1H), 1.66-1.52 (m, 4H), 1.35-1.29 (m, 1H), 1.25-1.16 (m, 1H). ^{13}C NMR (151 MHz, CDCl_3) δ 165.51, 135.98, 135.89, 132.02 (2), 128.76, 128.62, 128.35 (2), 125.54, 125.36, 122.94, 121.75, 120.66, 119.74, 112.74, 109.66, 62.65, 55.58, 55.45, 49.92, 49.81, 47.78, 39.60, 29.98, 29.71, 26.91, 24.65, 23.06, 21.81, 21.35. HRMS m/z (ESI^+) calcd. for $\text{C}_{31}\text{H}_{35}\text{BrN}_3\text{O}$ [$\text{M}+\text{H}^+$] 544.1964, found 544.2314. Mp: 151.3°C ~ 153.9°C

[0116] 化合物 LMY-35: 14-[N-(3-甲氧基苄基)-3-吡啶甲烯基]槐定碱: 淡黄色固体粉末, 收率 27%;

[0117] ^1H NMR (600 MHz, Chloroform- d) δ 8.09 (s, 1H), 7.88 (d, 1H), 7.32-7.27 (m, 2H), 7.27-7.20 (m, 3H), 6.83 (dd, J=8.3, 2.5 Hz, 1H), 6.74-6.67 (m, 2H), 5.34 (s, 2H), 3.75 (s, 3H), 3.66 (dd, J=13.5, 5.1 Hz, 1H), 3.55-3.49 (m, 1H), 3.38 (t, J=13.5, 11.7 Hz, 1H), 2.93-2.84 (m, 2H), 2.84-2.78 (m, 1H), 2.65-2.56 (m, 1H), 2.25-2.16 (m, 2H), 2.17-2.10 (m, 1H), 2.05 (t, J=10.9, 9.0 Hz, 1H), 2.01-1.92 (m, 1H), 1.91-1.90 (m, 2H), 1.79-1.69 (m, 1H), 1.66-1.62 (m, 1H), 1.64-1.48 (m, 4H), 1.35-1.25 (m, 1H), 1.20-1.11 (m, 1H). ^{13}C NMR (151 MHz, CDCl_3) δ 165.58, 160.02, 138.49, 136.16, 129.96, 128.72, 128.52, 125.50, 125.24, 122.77, 120.47, 119.64, 118.99, 112.93, 112.65, 112.54, 109.76, 63.55, 56.09, 55.24, 55.23, 50.65, 50.32, 47.96, 39.89, 32.12, 30.13, 27.02, 24.73, 23.96, 21.69, 21.67. HRMS m/z (ESI^+) calcd. for $\text{C}_{32}\text{H}_{38}\text{N}_3\text{O}_2$ [$\text{M}+\text{H}^+$] 496.2964, found 496.3064. Mp: 134.3°C ~ 135.7°C

[0118] 化合物 LMY-36: 14-[N-(4-甲氧基苄基)-3-吡啶甲烯基]槐定碱: 白色固体粉末, 收率 29%;

[0119] ^1H NMR (600 MHz, Chloroform- d) δ 8.08 (s, 1H), 7.87 (d, J=7.4, 1.3 Hz, 1H), 7.33-7.19 (m, 4H), 7.12-7.08 (m, 2H), 6.88-6.84 (m, 2H), 5.30 (d, J=9.5 Hz, 2H), 3.79 (s, 3H), 3.66 (dd, J=13.5, 5.1 Hz, 1H), 3.54-3.48 (m, 1H), 3.37 (t, J=13.5, 11.7 Hz, 1H), 2.93-

2.83 (m, 2H), 2.83-2.78 (m, 1H), 2.59 (m, 1H), 2.24-2.10 (m, 3H), 2.04 (t, $J=10.8, 9.0\text{Hz}$, 1H), 2.00-1.86 (m, 3H), 1.73 (m, 1H), 1.66-1.47 (m, 5H), 1.36-1.26 (m, 1H), 1.20-1.10 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.58, 159.23, 136.07, 128.80, 128.77, 128.37, 128.19 (2), 125.50, 125.13, 122.68, 120.41, 119.62, 114.25 (2), 112.39, 109.80, 63.57, 56.10, 55.30, 55.23, 50.67, 49.90, 47.96, 39.90, 32.15, 30.15, 27.03, 24.72, 24.00, 21.70 (2). HRMS m/z (ESI^+) calcd. for $\text{C}_{32}\text{H}_{38}\text{N}_3\text{O}_2[\text{M}+\text{H}^+]$ 496.2964, found 496.3337. Mp: $204.0^\circ\text{C} \sim 205.1^\circ\text{C}$

[0120] 化合物 LMY-37: 14-[N-(3,5-二甲氧基苄基)-3-吡啶甲烯基]槐定碱: 白色固体粉末, 收率 33%;

[0121] ^1H NMR (600MHz, Chloroform- d) δ 8.09 (s, 1H), 7.87 (d, $J=7.7\text{Hz}$, 1H), 7.33-7.27 (m, 2H), 7.27-7.19 (m, 2H), 6.38 (s, 1H), 6.29 (s, 2H), 5.29 (s, 2H), 3.73 (s, 6H), 3.66 (dd, $J=13.6, 5.2\text{Hz}$, 1H), 3.55-3.50 (m, 1H), 3.39 (t, 1H), 2.96-2.91 (m, 1H), 2.91-2.81 (m, 2H), 2.65-2.56 (m, 1H), 2.29-2.23 (m, 2H), 2.23-2.17 (m, 1H), 2.16-2.06 (m, 1H), 1.97-1.90 (m, 2H), 1.90-1.85 (m, 2H), 1.80-1.70 (m, 1H), 1.66-1.61 (m, 1H), 1.61-1.52 (m, 3H), 1.35-1.29 (m, 1H), 1.21-1.11 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.58, 161.22 (2), 139.29, 136.21, 128.71, 128.54, 125.54, 125.22, 122.78, 120.47, 119.63, 112.54, 109.75, 104.89 (2), 99.32, 67.98, 63.42, 56.01, 55.33 (2), 55.27, 50.53, 50.43, 47.93, 39.85, 30.10, 29.71, 27.00, 24.72, 21.69, 21.60. HRMS m/z (ESI^+) calcd. for $\text{C}_{33}\text{H}_{40}\text{N}_3\text{O}_3[\text{M}+\text{H}^+]$ 526.3070, found 526.3104. Mp: $198.1^\circ\text{C} \sim 199.2^\circ\text{C}$

[0122] 化合物 LMY-38: 14-[N-(2-溴-5-甲氧基苄基)-3-吡啶甲烯基]槐定碱: 淡黄色固体粉末, 收率 44%;

[0123] ^1H NMR (600MHz, Chloroform- d) δ 8.09 (s, 1H), 7.91-7.87 (m, 1H), 7.51 (d, $J=8.8\text{Hz}$, 1H), 7.29 (d, $J=7.7\text{Hz}$, 1H), 7.28-7.21 (m, 3H), 6.71 (dd, $J=8.8, 3.0\text{Hz}$, 1H), 6.16 (d, $J=3.0\text{Hz}$, 1H), 5.38 (s, 2H), 3.66 (dd, $J=13.6, 5.2\text{Hz}$, 1H), 3.56 (s, 3H), 3.55-3.50 (m, 1H), 3.39 (t, $J=13.6, 11.7\text{Hz}$, 1H), 2.94-2.86 (m, 2H), 2.85-2.80 (m, 1H), 2.65-2.56 (m, 1H), 2.30-2.17 (m, 2H), 2.19-2.10 (m, 1H), 2.11-2.05 (m, 1H), 2.04-1.95 (m, 1H), 1.97-1.86 (m, 2H), 1.80-1.69 (m, 1H), 1.66-1.61 (m, 1H), 1.61-1.51 (m, 4H), 1.36-1.24 (m, 1H), 1.21-1.11 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.53, 159.41, 137.07, 136.10, 133.49, 128.65, 128.52, 125.54, 125.38, 122.99, 120.65, 119.73, 114.53, 114.14, 112.87, 112.43, 109.70, 63.47, 56.04, 55.33, 55.26, 50.58, 50.49, 47.96, 39.89, 32.03, 30.11, 27.03, 24.74, 23.87, 21.69, 21.63. HRMS m/z (ESI^+) calcd. for $\text{C}_{32}\text{H}_{37}\text{BrN}_3\text{O}_2[\text{M}+\text{H}^+]$ 574.2069, found 574.2172. Mp: $162.3^\circ\text{C} \sim 163.7^\circ\text{C}$

[0124] 化合物 LMY-39: 14-[N-(2-萘基亚甲基)-3-吡啶甲烯基]槐定碱: 棕色固体粉末, 收率 37%;

[0125] ^1H NMR (600MHz, Chloroform- d) δ 8.12 (s, 1H), 7.90 (d, 1H), 7.85-7.79 (m, 2H), 7.79-7.74 (m, 1H), 7.59 (s, 1H), 7.51-7.46 (m, 2H), 7.34 (d, $J=11.6\text{Hz}$, 2H), 7.30-7.21 (m, 3H), 5.51 (s, 2H), 3.66 (dd, $J=13.6, 5.3\text{Hz}$, 1H), 3.55-3.49 (m, 1H), 3.40 (t, $J=12.6\text{Hz}$, 1H), 2.98 (d, $J=12.0\text{Hz}$, 1H), 2.94-2.83 (m, 2H), 2.64-2.56 (m, 1H), 2.33-2.22 (m, 2H), 2.18 (t, $J=10.1\text{Hz}$, 1H), 2.14-2.00 (m, 2H), 1.99-1.86 (m, 2H), 1.84-1.73 (m, 1H), 1.67-

1.61 (m, 1H), 1.62-1.50 (m, 4H), 1.27-1.23 (m, 1H), 1.22-1.12 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.57, 136.24, 134.27, 133.31, 132.90, 128.84, 128.79, 128.63, 127.85, 127.74, 126.48, 126.19, 125.63 (2), 125.11, 124.64, 122.85, 120.56, 119.62, 112.56, 109.86, 63.04, 55.80, 55.29, 50.62, 50.21, 47.79, 39.66, 29.92, 29.72, 26.91, 24.66, 23.33, 21.63, 21.33. HRMS m/z (ESI^+) calcd. for $\text{C}_{35}\text{H}_{38}\text{N}_3\text{O}$ [$\text{M}+\text{H}^+$] 516.3015, found 516.3042. Mp: 111.2°C~115.6°C

[0126] 化合物 LMY-40: 14-[N-(4-三氟甲氧基苄基)-3-吡啶甲烯基]槐定碱: 白色固体粉末, 收率24%;

[0127] ^1H NMR (600MHz, Chloroform- d) δ 8.08 (s, 1H), 7.87 (d, $J=7.5\text{Hz}$, 1H), 7.29 (d, $J=5.5\text{Hz}$, 1H), 7.25 (d, $J=4.0\text{Hz}$, 2H), 7.26-7.20 (m, 1H), 7.19-7.13 (m, 4H), 5.38 (s, 2H), 3.67 (dd, $J=13.6, 5.5\text{Hz}$, 1H), 3.62-3.56 (m, 1H), 3.45 (t, $J=12.7\text{Hz}$, 1H), 3.13 (d, $J=12.2\text{Hz}$, 1H), 3.10-3.03 (m, 1H), 2.91-2.84 (m, 1H), 2.67-2.59 (m, 1H), 2.53-2.44 (m, 3H), 2.30-2.18 (m, 1H), 2.17-2.04 (m, 2H), 2.02-1.90 (m, 2H), 1.76-1.69 (m, 1H), 1.69-1.53 (m, 4H), 1.29-1.25 (m, 1H), 1.25-1.19 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.45, 148.74, 135.97, 135.56, 128.73, 128.51, 128.05 (2), 125.80, 125.04, 123.01, 121.40 (2), 120.70, 120.39 (d, $J=257.3\text{Hz}$), 119.66, 112.65, 109.71, 62.58, 55.65, 55.32, 49.88, 49.66, 47.36, 39.34, 29.70, 29.48, 26.78, 24.53, 22.47, 21.49, 20.81. HRMS m/z (ESI^+) calcd. for $\text{C}_{32}\text{H}_{35}\text{F}_3\text{N}_3\text{O}_2$ [$\text{M}+\text{H}^+$] 550.2681, found 550.2813. Mp: 182.1°C~185.7°C

[0128] 化合物 LMY-41: 14-[N-(4-苄氧基苄基)-3-吡啶甲烯基]槐定碱: 淡黄色固体粉末, 收率34%;

[0129] ^1H NMR (600MHz, Chloroform- d) δ 8.09 (s, 1H), 7.88 (d, $J=7.7\text{Hz}$, 1H), 7.45-7.37 (m, 4H), 7.37-7.20 (m, 5H), 7.10 (d, $J=8.3\text{Hz}$, 2H), 6.94 (d, $J=8.3\text{Hz}$, 2H), 5.30 (s, 2H), 5.05 (s, 2H), 3.66 (dd, $J=13.5, 5.1\text{Hz}$, 1H), 3.56-3.50 (m, 1H), 3.39 (t, $J=12.6\text{Hz}$, 1H), 2.93 (d, $J=11.9\text{Hz}$, 1H), 2.90-2.80 (m, 2H), 2.64-2.55 (m, 1H), 2.30-2.17 (m, 2H), 2.17-2.11 (m, 1H), 2.08 (t, $J=9.9\text{Hz}$, 1H), 2.05-1.96 (m, 1H), 1.97-1.85 (m, 2H), 1.80-1.70 (m, 1H), 1.68-1.62 (m, 1H), 1.62-1.51 (m, 4H), 1.36-1.25 (m, 1H), 1.21-1.10 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.59, 158.44, 136.78, 136.07, 129.10, 128.76, 128.61 (2), 128.40, 128.20 (2), 128.03, 127.45 (2), 125.56, 125.08, 122.70, 120.44, 119.62, 115.21 (2), 112.40, 109.81, 70.07, 63.48, 56.06, 55.25, 50.60, 49.90, 47.91, 39.85, 32.05, 30.09, 27.01, 24.71, 23.85, 21.69, 21.62. HRMS m/z (ESI^+) calcd. for $\text{C}_{38}\text{H}_{42}\text{N}_3\text{O}_2$ [$\text{M}+\text{H}^+$] 572.3277, found 572.3361. Mp: 109.9°C~111.2°C

[0130] 化合物 LMY-42: 14-[5-甲基-N-(3-溴苄基)-3-吡啶甲烯基]槐定碱: 黄色固体粉末, 收率41%;

[0131] ^1H NMR (600MHz, Chloroform- d) δ 8.06 (s, 1H), 7.68 (s, 1H), 7.41 (dd, $J=7.9, 2.0\text{Hz}$, 1H), 7.35-7.27 (m, 1H), 7.23 (s, 1H), 7.17 (t, $J=7.8\text{Hz}$, 1H), 7.13 (d, $J=8.3\text{Hz}$, 1H), 7.07 (d, $J=8.4, 1.5\text{Hz}$, 1H), 6.99 (d, $J=7.7\text{Hz}$, 1H), 5.29 (s, 2H), 3.66 (dd, $J=13.6, 5.2\text{Hz}$, 1H), 3.55-3.48 (m, 1H), 3.38 (t, $J=13.5, 11.8\text{Hz}$, 1H), 2.92 (d, 1H), 2.89-2.80 (m, 2H), 2.64-2.56 (m, 1H), 2.49 (s, 3H), 2.25-2.10 (m, 2H), 2.10-2.04 (m, 1H), 2.03-1.94 (m, 1H), 1.96-1.86 (m, 3H), 1.79-1.69 (m, 1H), 1.66-1.61 (m, 1H), 1.62-1.50 (m, 4H), 1.35-

1.29 (m, 1H), 1.20-1.10 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.55, 139.37, 134.38, 130.97, 130.48, 130.08, 129.68, 129.04, 128.35, 125.43, 125.21 (2), 124.55, 122.96, 119.47, 112.35, 109.31, 63.47, 56.05, 55.25, 50.59, 49.79, 47.93, 39.86, 32.05, 30.10, 27.00, 24.74, 23.87, 21.69, 21.63, 21.50. HRMS m/z (ESI^+) calcd. for $\text{C}_{32}\text{H}_{37}\text{BrN}_3\text{O}$ [$\text{M}+\text{H}^+$] 558.2120, found 558.2194. Mp: 101.9°C ~ 108.7°C

[0132] 化合物 LMY-43: 14-[5-甲基-N-(4-苄氧基苄基)-3-吡啶甲烯基]槐定碱: 白色固体粉末, 收率 53%;

[0133] ^1H NMR (600MHz, Chloroform- d) δ 8.07 (s, 1H), 7.67 (s, 1H), 7.46-7.37 (m, 4H), 7.34 (t, $J=7.2\text{Hz}$, 1H), 7.23 (s, 1H), 7.19 (d, $J=8.3\text{Hz}$, 1H), 7.07 (t, $J=7.9\text{Hz}$, 3H), 6.92 (d, $J=8.2\text{Hz}$, 2H), 5.26 (s, 2H), 5.04 (s, 2H), 3.67 (dd, $J=13.5, 5.2\text{Hz}$, 1H), 3.57-3.51 (m, 1H), 3.40 (t, $J=12.6\text{Hz}$, 1H), 2.98 (d, $J=12.0\text{Hz}$, 1H), 2.92-2.82 (m, 2H), 2.65-2.55 (m, 1H), 2.49 (s, 3H), 2.33-2.22 (m, 2H), 2.20-2.10 (m, 1H), 2.09-2.00 (m, 1H), 1.98-1.87 (m, 3H), 1.84-1.74 (m, 1H), 1.69-1.52 (m, 5H), 1.35-1.24 (m, 1H), 1.22-1.13 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.65, 158.40, 136.80, 134.44, 129.85, 129.23, 129.05, 128.60 (2), 128.50, 128.14 (2), 128.02, 127.45 (2), 125.77, 124.59, 124.29, 119.32, 115.18 (2), 111.87, 109.51, 70.06, 63.24, 55.94, 55.27, 50.40, 49.95, 47.79, 39.74, 31.82, 29.98, 26.96, 24.66, 23.54, 21.68, 21.52, 21.46. HRMS m/z (ESI^+) calcd. for $\text{C}_{39}\text{H}_{44}\text{N}_3\text{O}_2$ [$\text{M}+\text{H}^+$] 586.3434, found 586.3514. Mp: 191.9°C ~ 192.5°C

[0134] 化合物 LMY-44: 14-[5-甲氧基-N-(3-溴苄基)-3-吡啶甲烯基]槐定碱: 黄色固体粉末, 收率 37%;

[0135] ^1H NMR (600MHz, Chloroform- d) δ 8.04 (s, 1H), 7.39 (d, $J=8.1, 1.9\text{Hz}$, 1H), 7.31-7.27 (m, 2H), 7.23 (s, 1H), 7.15 (t, $J=7.8\text{Hz}$, 1H), 7.09 (d, $J=8.9\text{Hz}$, 1H), 6.97 (d, $J=7.7\text{Hz}$, 1H), 6.89-6.85 (m, 1H), 5.25 (s, 2H), 3.86 (s, 3H), 3.64 (dd, $J=13.6, 5.2\text{Hz}$, 1H), 3.54-3.48 (m, 1H), 3.36 (t, 1H), 2.91 (d, $J=12.1, 2.6\text{Hz}$, 1H), 2.89-2.79 (m, 2H), 2.62-2.53 (m, 1H), 2.26-2.16 (m, 2H), 2.15-2.05 (m, 1H), 2.03-1.93 (m, 1H), 1.94-1.85 (m, 3H), 1.79-1.69 (m, 1H), 1.64-1.59 (m, 1H), 1.59-1.51 (m, 4H), 1.31-1.25 (m, 1H), 1.19-1.09 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.57, 154.97, 139.28, 131.03, 131.00, 130.48, 129.65, 129.36, 128.75, 125.35, 125.19, 124.93, 122.96, 113.60, 112.39, 110.59, 100.84, 63.32, 55.97, 55.87, 55.24, 50.48, 49.94, 47.89, 39.79, 31.92, 30.06, 26.96, 24.70, 23.72, 21.69, 21.55. HRMS m/z (ESI^+) calcd. for $\text{C}_{32}\text{H}_{37}\text{BrN}_3\text{O}_2$ [$\text{M}+\text{H}^+$] 574.2069, found 574.2172. Mp: 128.1°C ~ 131.0°C

[0136] 化合物 LMY-45: 14-[5-甲氧基-N-(4-苄氧基苄基)-3-吡啶甲烯基]槐定碱: 黄色固体粉末, 收率 34%;

[0137] ^1H NMR (600MHz, Chloroform- d) δ 8.06 (d, $J=1.9\text{Hz}$, 1H), 7.43-7.36 (m, 4H), 7.35-7.28 (m, 2H), 7.25 (s, 1H), 7.17 (d, $J=8.9\text{Hz}$, 1H), 7.09-7.05 (m, 2H), 6.94-6.90 (m, 2H), 6.90-6.86 (m, 1H), 5.24 (s, 2H), 5.03 (s, 2H), 3.87 (s, 3H), 3.66 (dd, $J=13.5, 5.2\text{Hz}$, 1H), 3.56-3.50 (m, 1H), 3.39 (t, $J=12.6\text{Hz}$, 1H), 2.97 (d, $J=12.0\text{Hz}$, 1H), 2.92-2.80 (m, 2H), 2.62-2.54 (m, 1H), 2.34-2.21 (m, 2H), 2.19-2.09 (m, 1H), 2.08-1.99 (m, 1H), 1.99-1.85 (m, 3H), 1.84-1.74 (m, 1H), 1.68-1.52 (m, 5H), 1.33-1.26 (m, 1H), 1.22-1.11 (m, 1H). ^{13}C NMR

(151MHz, CDCl_3) δ 165.66, 158.43, 154.86, 136.78, 131.13, 129.35, 129.11, 128.85, 128.60 (2), 128.15 (2), 128.02, 127.45 (2), 125.66, 124.35, 115.19 (2), 113.37, 111.94, 110.79, 100.72, 70.05, 63.24, 55.95, 55.88, 55.24, 50.41, 50.13, 47.76, 39.71, 31.81, 29.95, 26.95, 24.64, 23.52, 21.65, 21.43. HRMS m/z (ESI^+) calcd. for $\text{C}_{39}\text{H}_{44}\text{N}_3\text{O}_3$ [$\text{M}+\text{H}^+$] 602.3383, found 602.3427. Mp: 118.8°C ~ 121.9°C

[0138] 化合物 LMY-46: 14-[5-溴-N-(3-溴苄基)-3-吡啶甲烯基]槐定碱: 浅棕色固体粉末, 收率 43%;

[0139] ^1H NMR (600MHz, Chloroform- d) δ 8.01-7.91 (m, 2H), 7.41 (dd, $J=8.1, 1.9\text{Hz}$, 1H), 7.31-7.26 (m, 2H), 7.24 (s, 1H), 7.17 (t, $J=7.9\text{Hz}$, 1H), 7.08 (d, $J=8.7\text{Hz}$, 1H), 6.96 (d, $J=7.7\text{Hz}$, 1H), 5.28 (s, 2H), 3.63 (dd, $J=13.6, 5.2\text{Hz}$, 1H), 3.53-3.48 (m, 1H), 3.34 (t, $J=12.7\text{Hz}$, 1H), 2.94-2.87 (m, 1H), 2.86-2.78 (m, 2H), 2.59-2.52 (m, 1H), 2.26-2.16 (m, 2H), 2.14-2.03 (m, 1H), 2.01-1.94 (m, 1H), 1.95-1.83 (m, 3H), 1.78-1.68 (m, 1H), 1.65-1.49 (m, 5H), 1.28-1.22 (m, 1H), 1.17-1.08 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.18, 138.74, 134.63, 131.19, 130.57, 130.35, 129.64, 129.22, 126.36, 125.82, 125.16, 124.47, 123.06, 122.42, 114.07, 112.32, 111.20, 63.36, 55.99, 55.22, 50.52, 49.92, 47.92, 39.83, 31.95, 30.01, 26.95, 24.72, 23.76, 21.64, 21.52. HRMS m/z (ESI^+) calcd. for $\text{C}_{31}\text{H}_{34}\text{Br}_2\text{N}_3\text{O}$ [$\text{M}+\text{H}^+$] 622.1069, found 622.1469. Mp: 138.0°C ~ 146.3°C

[0140] 化合物 LMY-47: 14-[5-溴-N-(4-苄氧基苄基)-3-吡啶甲烯基]槐定碱: 黄色固体粉末, 收率 35%;

[0141] ^1H NMR (600MHz, Chloroform- d) δ 8.01-7.94 (m, 2H), 7.43-7.36 (m, 4H), 7.33 (t, $J=7.1\text{Hz}$, 1H), 7.31-7.27 (m, 1H), 7.24 (s, 1H), 7.14 (d, $J=8.7\text{Hz}$, 1H), 7.05 (d, $J=8.2\text{Hz}$, 2H), 6.92 (d, $J=8.3\text{Hz}$, 2H), 5.24 (s, 2H), 5.03 (s, 2H), 3.64 (dd, $J=13.6, 5.2\text{Hz}$, 1H), 3.54-3.48 (m, 1H), 3.36 (t, $J=12.6\text{Hz}$, 1H), 2.94 (d, $J=11.9\text{Hz}$, 1H), 2.87-2.78 (m, 2H), 2.59-2.51 (m, 1H), 2.29-2.16 (m, 2H), 2.15-2.06 (m, 2H), 2.03-1.85 (m, 3H), 1.80-1.70 (m, 1H), 1.66-1.50 (m, 5H), 1.33-1.27 (m, 1H), 1.19-1.09 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.28, 158.54, 136.72, 134.70, 130.38, 129.31, 128.61 (2), 128.16 (2), 128.05, 127.45 (2), 125.87, 125.55, 124.74, 122.30, 115.27 (2), 114.63, 113.87, 111.89, 111.40, 70.07, 63.32, 55.98, 55.24, 50.49, 50.12, 47.90, 39.82, 31.92, 30.02, 26.97, 24.69, 23.73, 21.67, 21.54. HRMS m/z (ESI^+) calcd. for $\text{C}_{38}\text{H}_{41}\text{BrN}_3\text{O}_2$ [$\text{M}+\text{H}^+$] 650.2382, found 650.2816. Mp: 112.3°C ~ 120.1°C

[0142] 化合物 LMY-48: 14-[6-氯-N-(3-溴苄基)-3-吡啶甲烯基]槐定碱: 棕色固体粉末, 收率 39%;

[0143] ^1H NMR (600MHz, Chloroform- d) δ 7.99 (d, $J=1.9\text{Hz}$, 1H), 7.76 (d, $J=8.5\text{Hz}$, 1H), 7.44 (d, $J=7.9, 1.9\text{Hz}$, 1H), 7.32-7.27 (m, 1H), 7.25-7.16 (m, 4H), 6.99 (d, $J=7.7\text{Hz}$, 1H), 5.28 (s, 2H), 3.65 (dd, $J=13.6, 5.2\text{Hz}$, 1H), 3.57-3.51 (m, 1H), 3.38 (t, $J=12.6\text{Hz}$, 1H), 2.97 (d, $J=12.1\text{Hz}$, 1H), 2.92-2.80 (m, 2H), 2.63-2.54 (m, 1H), 2.34-2.22 (m, 2H), 2.20-2.11 (m, 1H), 2.08-1.87 (m, 4H), 1.84-1.73 (m, 1H), 1.71-1.52 (m, 5H), 1.26 (d, $J=10.7\text{Hz}$, 1H), 1.21-1.12 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.25, 138.67, 136.42, 131.25, 130.62, 129.63, 129.05, 128.79, 127.25, 126.22, 125.16, 124.78, 123.11, 121.39, 120.69, 112.96,

109.64, 63.20, 55.93, 55.26, 50.39, 49.78, 47.80, 39.73, 29.90, 29.70, 26.89, 24.65, 23.48, 21.62, 21.38. HRMS m/z (ESI⁺) calcd. for C₃₁H₃₄BrClN₃O [M+H⁺] 578.1574, found 578.1658. Mp: 150.1°C ~ 154.7°C

[0144] 化合物 LMY-49:14-[6-氯-N-(4-苄氧基苄基)-3-吡啶甲烯基]槐定碱:黄色固体粉末, 收率44%;

[0145] ¹H NMR (600MHz, Chloroform-d) δ 8.02 (s, 1H), 7.76 (d, J=8.5Hz, 1H), 7.41 (d, J=7.7Hz, 2H), 7.39 (d, J=7.4Hz, 2H), 7.33 (dd, J=9.4, 4.9Hz, 1H), 7.28 (t, J=3.6Hz, 1H), 7.23 (s, 1H), 7.16 (d, J=8.5Hz, 1H), 7.06 (d, J=8.2Hz, 2H), 6.93 (d, J=8.3Hz, 2H), 5.20 (s, 2H), 5.03 (s, 2H), 3.65 (dd, J=13.7, 5.2Hz, 1H), 3.55-3.46 (m, 1H), 3.39 (t, J=12.6Hz, 1H), 2.99 (d, J=12.0Hz, 1H), 2.93-2.77 (m, 2H), 2.59-2.51 (m, 1H), 2.28 (d, J=14.5Hz, 1H), 2.19 (t, J=10.0Hz, 1H), 2.12-2.01 (m, 2H), 1.97-1.85 (m, 3H), 1.77 (t, J=13.4Hz, 1H), 1.66-1.49 (m, 5H), 1.34-1.27 (m, 1H), 1.20-1.11 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ 165.34, 158.56, 136.74, 136.45, 130.81, 128.98, 128.62 (2), 128.59, 128.21 (2), 128.05, 127.47 (2), 125.70, 125.01, 121.13, 120.53, 115.31 (2), 114.71, 112.46, 109.89, 70.07, 62.91, 55.75, 55.31, 50.16, 49.97, 47.82, 44.38, 39.64, 29.92, 26.86, 24.61, 23.30, 21.69, 21.36. HRMS m/z (ESI⁺) calcd. for C₃₈H₄₁ClN₃O₂ [M+H⁺] 606.2887, found 606.3263. Mp: 144.7°C ~ 153.5°C

[0146] 化合物 LMY-50:14-[6-甲氧基-N-(3-溴苄基)-3-吡啶甲烯基]槐定碱:黄色固体粉末, 收率45%;

[0147] ¹H NMR (600MHz, Chloroform-d) δ 8.03 (s, 1H), 7.74 (d, J=8.7Hz, 1H), 7.42 (d, 1H), 7.36-7.27 (m, 1H), 7.21-7.12 (m, 2H), 7.00 (d, J=7.7Hz, 1H), 6.89 (d, J=8.7, 2.2Hz, 1H), 6.69 (s, 1H), 5.26 (s, 2H), 3.82 (s, 3H), 3.65 (dd, J=13.6, 5.2Hz, 1H), 3.55-3.48 (m, 1H), 3.37 (t, J=12.6Hz, 1H), 2.91 (d, J=11.8Hz, 1H), 2.88-2.79 (m, 2H), 2.63-2.54 (m, 1H), 2.26-2.10 (m, 2H), 2.06 (t, J=9.9Hz, 1H), 2.02-1.94 (m, 1H), 1.95-1.85 (m, 3H), 1.79-1.69 (m, 1H), 1.65-1.60 (m, 1H), 1.60-1.51 (m, 4H), 1.34-1.29 (m, 1H), 1.20-1.09 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ 165.50, 157.12, 139.19, 136.83, 131.00, 130.50, 129.70, 127.35, 125.53, 125.38, 125.23, 123.04, 122.98, 120.40, 112.88, 110.03, 93.51, 63.47, 56.05, 55.73, 55.23, 50.59, 49.67, 47.93, 39.85, 32.05, 30.08, 26.96, 24.70, 23.86, 21.67, 21.60. HRMS m/z (ESI⁺) calcd. for C₃₂H₃₇BrN₃O₂ [M+H⁺] 574.2069, found 574.2466. Mp: 101.1°C ~ 106.5°C

[0148] 化合物 LMY-51:14-[N-(4-(4-甲基苄氧基)苄基)-3-吡啶甲烯基]槐定碱:淡黄色固体粉末, 收率48%;

[0149] ¹H NMR (600MHz, Chloroform-d) δ 8.11 (s, 1H), 7.89 (d, 1H), 7.33-7.28 (m, 4H), 7.27 (d, J=3.9Hz, 1H), 7.24-7.22 (m, 1H), 7.20 (d, J=7.9Hz, 2H), 7.09 (d, J=8.8Hz, 2H), 6.94-6.91 (m, 2H), 5.28 (s, 2H), 4.99 (s, 2H), 3.68 (dd, J=13.5, 5.3Hz, 1H), 3.57-3.52 (m, 1H), 3.42 (d, J=13.6, 11.6Hz, 1H), 3.01 (d, J=12.1, 4.0, 1.8Hz, 1H), 2.94-2.84 (m, 2H), 2.63-2.57 (m, 1H), 2.37 (s, 3H), 2.33-2.23 (m, 2H), 2.19 (dd, J=11.1, 9.0Hz, 1H), 2.16-2.02 (m, 1H), 2.01-1.88 (m, 3H), 1.84-1.75 (m, 1H), 1.68-1.53 (m, 5H), 1.32-1.29 (m, 1H), 1.23-1.14 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ 165.60, 158.51, 137.82, 136.08, 133.74,

129.29 (2), 129.00, 128.79, 128.54, 128.47, 128.19 (2), 127.60 (2), 125.64, 122.71, 120.45, 119.61, 115.19 (2), 112.37, 109.85, 70.00, 63.02, 55.79, 55.35, 50.21, 49.90, 47.87, 39.75, 31.62, 30.05, 26.98, 24.70, 23.44, 21.76, 21.47, 21.22. HRMS m/z (ESI⁺) calcd. for C₃₉H₄₄N₃O₂ [M+H⁺] 586.3434, found 586.3911. Mp: 183.5°C ~ 184.0°C

[0150] 化合物 LMY-52: 14-[N-(4-(4-叔丁基苄氧基)苄基)-3-吡啶甲烯基]槐定碱: 淡黄色固体粉末, 收率 57%;

[0151] ¹H NMR (600MHz, Chloroform-d) δ 8.11 (s, 1H), 7.89 (d, J=7.6, 0.9Hz, 1H), 7.44-7.42 (m, 2H), 7.38-7.35 (m, 2H), 7.32 (d, J=8.3, 0.9Hz, 1H), 7.28 (d, J=3.2Hz, 1H), 7.27-7.21 (m, 2H), 7.11-7.08 (m, 2H), 6.97-6.91 (m, 2H), 5.30 (s, 2H), 5.01 (s, 2H), 3.67 (dd, J=13.5, 5.2Hz, 1H), 3.56-3.51 (m, 1H), 3.40 (t, J=13.5, 11.7Hz, 1H), 3.00-2.94 (m, 1H), 2.91-2.84 (m, 2H), 2.64-2.57 (m, 1H), 2.31-2.19 (m, 2H), 2.17-2.10 (m, 2H), 2.07-1.87 (m, 3H), 1.82-1.73 (m, 1H), 1.68-1.50 (m, 5H), 1.35 (d, J=2.5Hz, 9H), 1.34-1.28 (m, 1H), 1.22-1.13 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ 165.58, 158.59, 151.12, 136.08, 133.71, 129.00, 128.78, 128.55, 128.44, 128.19 (2), 127.44 (2), 125.57 (2), 125.08, 122.70, 120.44, 119.62, 115.15 (2), 112.39, 109.84, 69.96, 63.28, 55.93, 55.29, 50.42, 49.92, 47.89, 39.82, 34.61, 31.88, 31.36 (3), 30.08, 27.01, 24.72, 23.68, 21.72, 21.56. HRMS m/z (ESI⁺) calcd. for C₄₂H₅₀N₃O₂ [M+H⁺] 628.3903, found 628.3989. Mp: 133.3°C ~ 133.8°C

[0152] 化合物 LMY-53: 14-[N-(4-(4-氟苄氧基)苄基)-3-吡啶甲烯基]槐定碱: 淡黄色固体粉末, 收率 32%;

[0153] ¹H NMR (600MHz, Chloroform-d) δ 8.11 (s, 1H), 7.88 (d, J=7.6Hz, 1H), 7.40-7.36 (m, 2H), 7.31-7.19 (m, 4H), 7.10-7.04 (m, 4H), 6.92-6.88 (m, 2H), 5.27 (s, 2H), 4.97 (s, 2H), 3.66 (dd, J=13.5, 5.2Hz, 1H), 3.55-3.49 (m, 1H), 3.40 (t, J=12.6Hz, 1H), 2.99 (d, J=11.9Hz, 1H), 2.93-2.82 (m, 2H), 2.62-2.55 (m, 1H), 2.32-2.22 (m, 2H), 2.14-2.00 (m, 2H), 1.98-1.86 (m, 3H), 1.82-1.72 (m, 1H), 1.66-1.51 (m, 5H), 1.31 (d, J=17.1Hz, 1H), 1.21-1.11 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ 165.56, 162.49 (d, J=246.3Hz), 158.24, 136.06, 132.55 (d, J=3.0Hz), 129.35, 129.30, 129.28, 128.78, 128.49, 128.23 (2), 125.61, 125.04, 122.72, 120.47, 119.60, 115.57, 115.43, 115.17 (2), 112.37, 109.85, 69.36, 63.01, 55.79, 55.32, 50.22, 49.87, 47.83, 39.71, 31.62, 29.99, 26.95, 24.69, 23.40, 21.72, 21.43. HRMS m/z (ESI⁺) calcd. for C₃₈H₄₁FN₃O₂ [M+H⁺] 590.3183, found 590.3315. Mp: 92.2°C ~ 97.4°C

[0154] 化合物 LMY-54: 14-[N-(4-(4-氯苄氧基)苄基)-3-吡啶甲烯基]槐定碱: 淡黄色固体粉末, 收率 51%;

[0155] ¹H NMR (600MHz, Chloroform-d) δ 8.09 (d, J=2.3Hz, 1H), 7.90-7.82 (m, 1H), 7.35 (s, 4H), 7.32-7.28 (m, 2H), 7.25-7.21 (m, 2H), 7.09 (dd, J=9.3, 2.8Hz, 2H), 6.92-6.88 (m, 2H), 5.30 (s, 2H), 5.00 (s, 2H), 3.67 (dd, J=13.5, 5.2Hz, 1H), 3.57-3.51 (m, 1H), 3.41 (t, J=13.6, 11.7Hz, 1H), 3.00-2.95 (m, 1H), 2.91-2.84 (m, 2H), 2.64-2.57 (m, 1H), 2.31-2.21 (m, 2H), 2.18-2.09 (m, 1H), 2.08-2.00 (m, 1H), 2.00-1.88 (m, 3H), 1.82-1.73 (m, 1H), 1.67-1.53 (m, 5H), 1.31-1.26 (m, 1H), 1.22-1.13 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ 165.57, 158.15, 136.05, 135.29, 133.82, 129.36, 128.78 (2), 128.74 (2), 128.62, 128.40, 128.20

(2), 125.57, 125.12, 122.71, 120.45, 119.65, 115.18 (2), 112.43, 109.79, 69.26, 63.16, 55.87, 55.33, 50.33, 49.87, 47.87, 39.79, 31.78, 30.08, 27.00, 24.71, 23.57, 21.76, 21.54. HRMS m/z (ESI⁺) calcd. for C₃₈H₄₁ClN₃O₂ [M+H⁺] 606.2887, found 606.3364. Mp: 190.6 °C ~ 194.1 °C

[0156] 化合物 LMY-55: 14-[N-(4-(4-溴苄氧基)苄基)-3-吡啶甲烯基]槐定碱: 淡黄色固体粉末, 收率 47%;

[0157] ¹H NMR (600MHz, Chloroform-d) δ 8.09 (d, J=1.9Hz, 1H), 7.87 (dd, J=7.3, 1.3Hz, 1H), 7.53-7.48 (m, 2H), 7.31-7.27 (m, 4H), 7.25-7.20 (m, 2H), 7.11-7.07 (m, 2H), 6.92-6.88 (m, 2H), 5.29 (s, 2H), 4.99 (s, 2H), 3.67 (dd, J=13.5, 5.2Hz, 1H), 3.56-3.51 (m, 1H), 3.41 (t, J=13.5, 11.7Hz, 1H), 3.01-2.96 (m, 1H), 2.93-2.83 (m, 2H), 2.63-2.56 (m, 1H), 2.32-2.21 (m, 2H), 2.20-2.09 (m, 2H), 2.08-1.99 (m, 1H), 2.00-1.88 (m, 2H), 1.82-1.72 (m, 1H), 1.68-1.54 (m, 5H), 1.31-1.27 (m, 1H), 1.23-1.13 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ 165.56, 158.13, 136.05, 135.82, 131.73 (2), 129.37, 129.03 (2), 128.76, 128.41, 128.20 (2), 125.59, 125.10, 122.72, 121.93, 120.46, 119.64, 115.18 (2), 112.43, 109.80, 69.28, 63.11, 55.84, 55.32, 50.29, 49.87, 47.84, 39.77, 31.74, 30.05, 27.00, 24.70, 23.52, 21.75, 21.50. HRMS m/z (ESI⁺) calcd. for C₃₈H₄₁BrN₃O₂ [M+H⁺] 650.2382, found 650.2816. Mp: 185.1 °C ~ 185.9 °C

[0158] 化合物 LMY-56: 14-[N-(4-(4-三氟甲氧基苄氧基)苄基)-3-吡啶甲烯基]槐定碱: 淡黄色固体粉末, 收率 29%;

[0159] ¹H NMR (600MHz, Chloroform-d) δ 8.10 (s, 1H), 7.87 (d, J=7.6Hz, 1H), 7.44 (d, J=8.3Hz, 2H), 7.31-7.26 (m, 2H), 7.24-7.20 (m, 4H), 7.09 (d, J=8.4Hz, 2H), 6.90 (d, J=8.4Hz, 2H), 5.28 (s, 2H), 5.01 (s, 2H), 3.65 (dd, J=13.5, 5.2Hz, 1H), 3.54-3.49 (m, 1H), 3.38 (t, J=12.6Hz, 1H), 2.96 (d, J=12.0Hz, 1H), 2.92-2.82 (m, 2H), 2.63-2.54 (m, 1H), 2.33-2.22 (m, 2H), 2.19-2.08 (m, 1H), 2.03 (dd, J=11.4, 6.1Hz, 1H), 1.97-1.85 (m, 3H), 1.83-1.73 (m, 1H), 1.66-1.51 (m, 5H), 1.30 (d, J=16.7Hz, 1H), 1.20-1.10 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ 165.52, 158.15, 148.86, 136.05, 135.53, 129.41, 128.83 (2), 128.77, 128.49, 128.26 (2), 125.58, 125.02, 122.73, 121.09 (2), 120.47, 120.46 (d, J=257.3Hz), 119.57, 115.14 (2), 112.36, 109.86, 69.12, 63.17, 55.90, 55.25, 50.35, 49.86, 47.78, 39.71, 31.74, 29.92, 26.93, 24.68, 23.46, 21.62, 21.39. HRMS m/z (ESI⁺) calcd. for C₃₉H₄₁F₃N₃O₃ [M+H⁺] 656.3100, found 656.3270. Mp: 114.8 °C ~ 115.1 °C

[0160] 化合物 LMY-57: 14-[5-甲氧基-N-(4-(4-甲基苄氧基)苄基)-3-吡啶甲烯基]槐定碱: 淡黄色固体粉末, 收率 52%;

[0161] ¹H NMR (600MHz, Chloroform-d) δ 8.06 (d, J=2.0Hz, 1H), 7.32-7.29 (m, 3H), 7.24 (s, 1H), 7.18 (dd, J=16.3, 8.4Hz, 3H), 7.09-7.05 (m, 2H), 6.93-6.90 (m, 2H), 6.88 (dd, J=8.8, 2.4Hz, 1H), 5.24 (s, 2H), 4.99 (s, 2H), 3.88 (s, 3H), 3.66 (dd, J=13.5, 5.1Hz, 1H), 3.54-3.49 (m, 1H), 3.38 (t, J=13.5, 11.7Hz, 1H), 2.92 (d, J=11.9, 4.0, 1.8Hz, 1H), 2.88-2.80 (m, 2H), 2.62-2.55 (m, 1H), 2.37 (s, 3H), 2.28-2.17 (m, 2H), 2.19-2.09 (m, 1H), 2.06 (dd, J=10.9, 9.0Hz, 1H), 2.02-1.86 (m, 3H), 1.80-1.70 (m, 1H), 1.66-1.52 (m, 5H), 1.30 (d, J=17.7Hz, 1H), 1.20-1.11 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ 165.68, 158.49, 154.85,

137.81, 133.73, 131.14, 129.35, 129.28 (2), 129.03, 128.80, 128.11 (2), 127.59 (2), 125.55, 124.47, 115.18 (2), 113.37, 111.98, 110.77, 100.72, 70.00, 63.49, 56.07, 55.87, 55.23, 50.61, 50.12, 47.92, 39.85, 32.09, 30.13, 27.01, 24.69, 23.90, 21.71, 21.66, 21.22. HRMS m/z (ESI⁺) calcd. for C₄₀H₄₆N₃O₃ [M+H⁺] 616.3539, found 616.3630. Mp: 95.8°C ~ 99.3°C

[0162] 化合物 LMY-58: 14-[5-甲氧基-N-(4-(4-叔丁基苄氧基)苄基)-3-吡啶甲烯基]槐定碱: 淡黄色固体粉末, 收率 59%;

[0163] ¹H NMR (600MHz, Chloroform-d) δ 8.07 (d, J=1.9Hz, 1H), 7.42 (d, J=6.8, 2.0Hz, 2H), 7.38-7.35 (m, 2H), 7.31 (d, J=2.4Hz, 1H), 7.26 (s, 1H), 7.18 (d, J=8.9Hz, 1H), 7.10-7.07 (m, 2H), 6.95-6.92 (m, 2H), 6.89 (dd, J=8.8, 2.4Hz, 1H), 5.25 (s, 2H), 5.00 (s, 2H), 3.89 (s, 3H), 3.67 (dd, J=13.6, 5.3Hz, 1H), 3.57-3.51 (m, 1H), 3.41 (t, J=13.6, 11.6Hz, 1H), 3.00-2.95 (m, 1H), 2.92-2.83 (m, 2H), 2.64-2.57 (m, 1H), 2.32-2.21 (m, 2H), 2.17-2.12 (m, 1H), 2.08-1.99 (m, 1H), 2.00-1.88 (m, 3H), 1.83-1.73 (m, 1H), 1.67-1.56 (m, 5H), 1.35 (s, 9H), 1.34-1.28 (m, 1H), 1.23-1.14 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ 165.70, 158.58, 154.86, 151.12, 133.70, 131.14, 129.37, 129.03, 128.82, 128.12 (2), 127.44 (2), 125.64, 125.56 (2), 124.43, 115.14 (2), 113.40, 111.99, 110.78, 100.72, 69.95, 63.16, 55.88 (2), 55.33, 50.34, 50.14, 47.88, 39.77, 34.61, 31.80, 31.36 (3), 30.11, 26.99, 24.67, 23.59, 21.78, 21.56. HRMS m/z (ESI⁺) calcd. for C₄₃H₅₂N₃O₃ [M+H⁺] 658.4009, found 658.4464. Mp: 93.0°C ~ 98.7°C

[0164] 化合物 LMY-59: 14-[5-甲氧基-N-(4-(4-氟苄氧基)苄基)-3-吡啶甲烯基]槐定碱: 淡黄色固体粉末, 收率 41%;

[0165] ¹H NMR (600MHz, Chloroform-d) δ 8.05 (s, 1H), 7.39-7.35 (m, 2H), 7.30 (d, J=2.5Hz, 1H), 7.24 (s, 1H), 7.15 (dd, J=8.9, 2.0Hz, 1H), 7.08-7.03 (m, 4H), 6.92-6.85 (m, 3H), 5.23 (s, 2H), 4.97 (s, 2H), 3.87 (s, 3H), 3.65 (dd, J=13.6, 5.2, 1.8Hz, 1H), 3.53-3.47 (m, 1H), 3.37 (t, 1H), 2.93-2.88 (m, 1H), 2.87-2.78 (m, 2H), 2.61-2.53 (m, 1H), 2.24-2.16 (m, 2H), 2.16-2.09 (m, 1H), 2.07-2.01 (m, 1H), 2.00-1.84 (m, 3H), 1.78-1.68 (m, 1H), 1.65-1.50 (m, 5H), 1.29 (d, J=17.3Hz, 1H), 1.19-1.09 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ 165.65, 162.48 (d, J=246.3Hz), 158.22, 154.85, 132.55, 131.11, 129.36, 129.34, 129.31, 129.28, 128.80, 128.15 (2), 125.50, 124.52, 115.56, 115.42, 115.15 (2), 113.37, 111.99, 110.77, 100.72, 69.36, 63.47, 56.06, 55.85, 55.22, 50.61, 50.09, 47.93, 39.85, 32.07, 30.13, 27.00, 24.70, 23.90, 21.71, 21.67. HRMS m/z (ESI⁺) calcd. for C₃₉H₄₃FN₃O₃ [M+H⁺] 620.3288, found 620.3416. Mp: 108.1°C ~ 111.6°C

[0166] 化合物 LMY-60: 14-[5-甲氧基-N-(4-(4-氯苄氧基)苄基)-3-吡啶甲烯基]槐定碱: 淡黄色固体粉末, 收率 53%;

[0167] ¹H NMR (600MHz, Chloroform-d) δ 8.05 (d, J=1.8Hz, 1H), 7.33 (d, J=1.0Hz, 4H), 7.29 (d, J=2.4Hz, 1H), 7.23 (s, 1H), 7.14 (d, J=8.9Hz, 1H), 7.05 (d, J=8.5Hz, 2H), 6.90-6.84 (m, 3H), 5.22 (s, 2H), 4.97 (s, 2H), 3.86 (s, 3H), 3.64 (dd, J=13.5, 5.1Hz, 1H), 3.52-3.47 (m, 1H), 3.36 (t, J=13.5, 11.7Hz, 1H), 2.90 (d, J=12.1, 4.0, 1.8Hz, 1H), 2.87-2.77 (m, 2H), 2.60-2.53 (m, 1H), 2.25-2.07 (m, 3H), 2.04 (dd, J=10.9, 9.0Hz, 1H), 2.00-1.84

(m, 3H), 1.78-1.68 (m, 1H), 1.64-1.51 (m, 5H), 1.29 (d, J=17.5Hz, 1H), 1.18-1.09 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.63, 158.13, 154.85, 135.31, 133.76, 131.11, 129.39, 129.36, 128.80, 128.74 (4), 128.15 (2), 125.48, 124.53, 115.15 (2), 113.37, 112.00, 110.76, 100.72, 69.22, 63.47, 56.06, 55.86, 55.22, 50.61, 50.07, 47.92, 39.85, 32.07, 30.13, 27.00, 24.70, 23.90, 21.71, 21.66. HRMS m/z (ESI^+) calcd. for $\text{C}_{39}\text{H}_{43}\text{ClN}_3\text{O}_3$ [$\text{M}+\text{H}^+$] 636.2993, found 636.3120. Mp: 113.6°C ~ 116.7°C

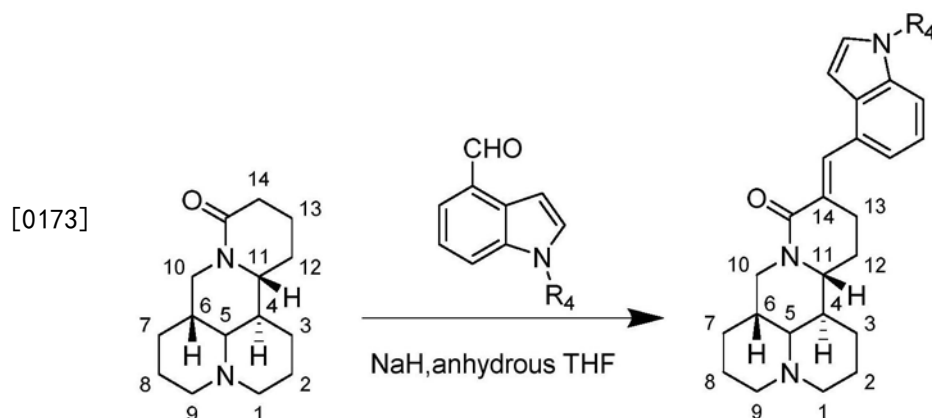
[0168] 化合物 LMY-61: 14-[5-甲氧基-N-(4-(4-溴苄氧基)苄基)-3-吡啶甲烯基]槐定碱: 淡黄色固体粉末, 收率 55%;

[0169] ^1H NMR (600MHz, Chloroform- d) δ 8.05 (d, J=1.8Hz, 1H), 7.50 (d, J=8.4Hz, 2H), 7.30-7.27 (m, 4H), 7.24 (s, 1H), 7.16 (d, J=8.9Hz, 1H), 7.07 (d, 2H), 6.89 (d, J=8.5Hz, 2H), 5.25 (s, 2H), 4.98 (s, 2H), 3.88 (s, 3H), 3.66 (dd, J=13.6, 5.2Hz, 1H), 3.55-3.48 (m, 1H), 3.42-3.34 (m, 1H), 2.95-2.89 (m, 1H), 2.89-2.80 (m, 2H), 2.63-2.54 (m, 1H), 2.26-2.17 (m, 2H), 2.16-2.10 (m, 1H), 2.08 (t, J=9.9Hz, 1H), 2.02-1.85 (m, 3H), 1.79-1.70 (m, 1H), 1.66-1.50 (m, 5H), 1.31-1.26 (m, 1H), 1.20-1.12 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.65, 158.11, 154.85, 135.82, 131.72 (2), 131.10, 129.41, 129.35, 129.03 (2), 128.77, 128.13 (2), 125.53, 124.53, 121.92, 115.17 (2), 113.40, 112.03, 110.74, 100.72, 69.28, 63.43, 56.03, 55.87, 55.25, 50.57, 50.10, 47.90, 39.84, 32.04, 30.13, 27.01, 24.69, 23.84, 21.74, 21.65. HRMS m/z (ESI^+) calcd. for $\text{C}_{39}\text{H}_{43}\text{BrN}_3\text{O}_3$ [$\text{M}+\text{H}^+$] 680.2488, found 680.2886. Mp: 110.0°C ~ 114.9°C

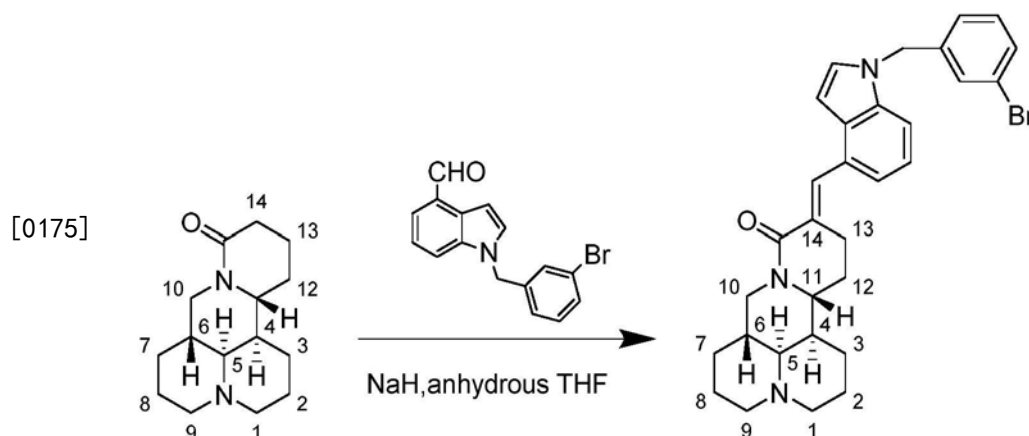
[0170] 化合物 LMY-62: 14-[5-甲氧基-N-(4-(4-三氟甲氧基苄氧基)苄基)-3-吡啶甲烯基]槐定碱: 淡黄色固体粉末, 收率 38%;

[0171] ^1H NMR (600MHz, Chloroform- d) δ 8.05 (d, J=1.9Hz, 1H), 7.47-7.43 (m, 2H), 7.31-7.22 (m, 5H), 7.16 (d, J=8.9Hz, 1H), 7.10-7.07 (m, 2H), 6.93-6.90 (m, 2H), 5.26 (s, 2H), 5.03 (s, 2H), 3.88 (s, 3H), 3.66 (dd, J=13.6, 5.2Hz, 1H), 3.55-3.50 (m, 1H), 3.42-3.36 (m, 1H), 2.93 (d, J=12.0Hz, 1H), 2.90-2.81 (m, 2H), 2.64-2.56 (m, 1H), 2.28-2.18 (m, 2H), 2.18-2.06 (m, 1H), 2.03-1.97 (m, 1H), 1.97-1.88 (m, 3H), 1.80-1.71 (m, 1H), 1.67-1.55 (m, 5H), 1.30 (d, J=17.7Hz, 1H), 1.22-1.11 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.65, 158.14, 154.86, 148.90, 148.89, 135.50, 131.10, 129.47, 129.35, 128.82 (2), 128.77, 128.15 (2), 125.55, 124.54, 121.12 (2), 115.14 (2), 113.42, 112.04, 110.73, 100.72, 69.15, 63.42, 56.04, 55.87, 55.25, 50.56, 50.10, 47.88, 39.83, 32.03, 30.11, 27.00, 24.69, 23.81, 21.73, 21.63. HRMS m/z (ESI^+) calcd. for $\text{C}_{40}\text{H}_{43}\text{F}_3\text{N}_3\text{O}_4$ [$\text{M}+\text{H}^+$] 686.3206, found 686.3303. Mp: 88.3°C ~ 97.6°C

[0172] (3) LMY-63 的制备:



[0174] LMY-63的制备更加具体的如下：



[0176] 具体制备LMY-63的实验方法：

[0177] 于100mL圆底烧瓶中分别加入2.4g (100mmol) 氢化钠, 50mL无水四氢呋喃, 搅拌均匀, 加入1.24g (5mmol) 槐定碱, 缓慢升温至85℃加入1.878g (6mmol) N-(3-溴苄基)-4-吲哚甲醛, 反应48h至终点(TLC 检测)。冷却至室温, 逐滴加入3N的盐酸中和过量的氢化钠。二氯甲烷萃取(40mL×3), 合并有机相, 无水Na₂SO₄干燥, 减压抽滤、浓缩滤液后经硅胶柱层析(V_{二氯甲烷}:V_{甲醇}=50:1)纯化, 得1.032g棕色固体粉末槐定碱化合物LMY-63:14-[N-(3-溴苄基)-4-吲哚甲烯基]槐定碱: 收率38%;

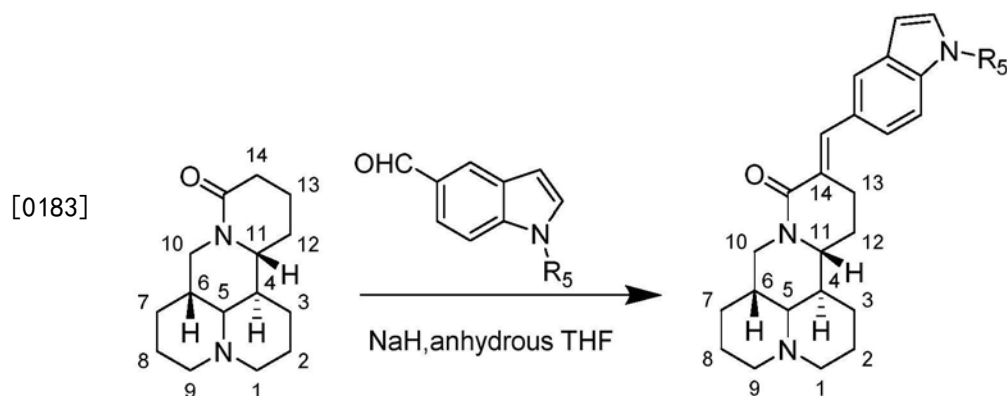
[0178] ¹H NMR (600MHz, Chloroform-d) δ8.14 (s, 1H), 7.40 (d, J=9.7Hz, 1H), 7.31 (d, J=28.8Hz, 1H), 7.24-7.13 (m, 4H), 7.09 (t, J=9.0Hz, 1H), 7.05-6.95 (m, 1H), 6.67 (d, J=3.2Hz, 1H), 5.30 (s, 2H), 3.72-3.60 (m, 1H), 3.60-3.50 (m, 1H), 3.43 (t, J=12.9, 11.6Hz, 1H), 2.97 (d, J=12.3Hz, 1H), 2.95-2.85 (m, 2H), 2.67-2.57 (m, 1H), 2.32-2.21 (m, 2H), 2.17 (t, J=9.9Hz, 1H), 2.12-2.02 (m, 2H), 2.00-1.89 (m, 3H), 1.85-1.72 (m, 1H), 1.69-1.63 (m, 1H), 1.63-1.47 (m, 3H), 1.34-1.30 (m, 1H), 1.23-1.12 (m, 1H). ¹³C NMR (151MHz, CDCl₃) δ165.39, 139.69, 136.15, 132.34, 130.88, 130.41 (2), 129.83, 128.77, 128.58, 128.43, 125.39, 122.92, 121.51, 120.49, 109.46, 101.28, 63.24, 55.89, 55.57, 50.34, 49.64, 48.09, 40.12, 30.00, 29.71, 27.56, 24.12, 23.55, 21.49, 21.42. HRMS m/z (ESI⁺) calcd. for C₃₁H₃₅BrN₃O [M+H⁺] 544.1964, found 544.2314. Mp: 159.8℃~161.0℃

[0179] 参考化合物LMY-63的实验方法制备化合物LMY-64, 化合物LMY-64结构鉴定数据如下：

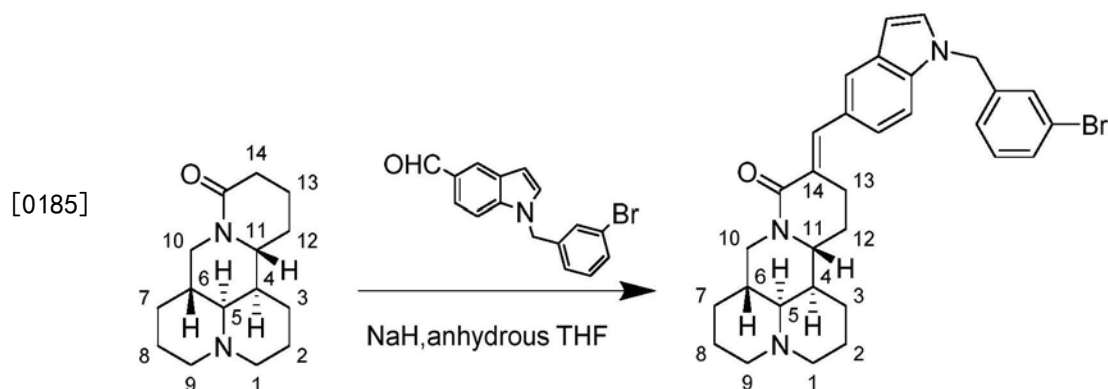
[0180] 化合物LMY-64:14-[N-(4-苄氧基苄基)-4-吲哚甲烯基]槐定碱:棕色固体粉末,收率54%;

[0181] ^1H NMR (600MHz, Chloroform- d) δ 8.16 (s, 1H), 7.44-7.37 (m, 4H), 7.36-7.32 (m, 1H), 7.30-7.27 (m, 1H), 7.19 (t, $J=7.8\text{Hz}$, 1H), 7.16 (d, $J=3.2\text{Hz}$, 1H), 7.09 (t, $J=7.8\text{Hz}$, 3H), 6.95-6.91 (m, 2H), 6.65 (d, $J=3.2\text{Hz}$, 1H), 5.26 (s, 2H), 5.04 (s, 2H), 3.66 (dd, $J=13.7, 5.4\text{Hz}$, 1H), 3.60-3.56 (m, 1H), 3.45 (t, $J=12.7\text{Hz}$, 1H), 3.05 (d, $J=12.2\text{Hz}$, 1H), 2.99-2.89 (m, 2H), 2.62 (t, $J=12.4\text{Hz}$, 1H), 2.39-2.23 (m, 3H), 2.19-2.10 (m, 1H), 2.09-2.02 (m, 1H), 2.00-1.91 (m, 3H), 1.88-1.79 (m, 1H), 1.70-1.44 (m, 4H), 1.34-1.28 (m, 1H), 1.24-1.15 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.44, 158.36, 136.85, 136.19, 132.59, 130.21, 129.59, 128.60 (2), 128.56, 128.40, 128.30 (2), 128.10, 128.00, 127.44 (2), 121.20, 120.28, 115.12 (2), 109.67, 100.73, 70.06, 62.94, 55.71, 55.63, 50.07, 49.75, 48.00, 40.03, 29.95, 29.71, 27.54, 24.10, 23.24, 21.52, 21.30. HRMS m/z (ESI^+) calcd. for $\text{C}_{38}\text{H}_{42}\text{N}_3\text{O}_2$ $[M+H]^+$ 572.3277, found 572.3654. Mp: 141.0°C ~ 146.4°C

[0182] (4) LMY-65的制备:



[0184] LMY-65的制备更加具体的如下:



[0186] 具体制备LMY-65的实验方法:

[0187] 于100mL圆底烧瓶中分别加入2.4g (100mmol) 氢化钠, 50mL无水四氢呋喃, 搅拌均匀, 加入1.24g (5mmol) 槐定碱, 缓慢升温至85°C加入1.878g (6mmol) N-(3-溴苄基)-5-吲哚甲烯基, 反应48h至终点(TLC 检测)。冷却至室温, 逐滴加入3N的盐酸中和过量的氢化钠。二氯甲烷萃取(40mLx3), 合并有机相, 无水 Na_2SO_4 干燥, 减压抽滤、浓缩滤液后经硅胶柱层析($V_{\text{二氯甲烷}}:V_{\text{甲醇}}=50:1$)纯化, 得0.977g白色固体粉末槐定碱化合物LMY-65:14-[N-(3-溴苄基)-5-吲哚甲烯基]槐定碱:收率36%;

[0188] ^1H NMR (600MHz, Chloroform- d) δ 7.91 (s, 1H), 7.67 (s, 1H), 7.41 (d, $J=8.0\text{Hz}$, 1H), 7.30 (d, $J=20.8\text{Hz}$, 1H), 7.27-7.20 (m, 2H), 7.20-7.14 (m, 2H), 7.02 (d, $J=7.8\text{Hz}$, 1H), 6.59 (d, $J=3.1\text{Hz}$, 1H), 5.29 (s, 2H), 3.63 (dd, $J=13.6, 5.3\text{Hz}$, 1H), 3.54 (m, $J=12.2, 7.7, 4.5\text{Hz}$, 1H), 3.41 (t, $J=12.7\text{Hz}$, 1H), 3.06-2.95 (m, 2H), 2.96-2.84 (m, 1H), 2.73-2.64 (m, 1H), 2.35-2.24 (m, 2H), 2.20 (t, $J=10.1\text{Hz}$, 1H), 2.14-2.02 (m, 2H), 2.00 -1.88 (m, 3H), 1.84-1.74 (m, 1H), 1.68-1.63 (m, 1H), 1.63-1.47 (m, 3H), 1.36-1.30 (m, 1H), 1.22-1.11 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.64, 139.62, 135.74, 135.72, 130.92, 130.43, 129.79, 128.89, 128.68, 127.96, 127.79, 125.35, 124.36, 122.94, 122.66, 109.34, 102.66, 63.04, 55.76, 55.48, 50.18, 49.59, 48.06, 39.95, 31.38, 29.96, 27.43, 23.71, 23.35, 21.55, 21.35. HRMS m/z (ESI^+) calcd. for $\text{C}_{31}\text{H}_{35}\text{BrN}_3\text{O}$ [$\text{M}+\text{H}^+$] 544.1964, found 544.2123. Mp: $112.9^\circ\text{C}\sim 127.7^\circ\text{C}$

[0189] 参考化合物 LMY-65 的实验方法制备化合物 LMY-66, 化合物 LMY-66 结构鉴定数据如下:

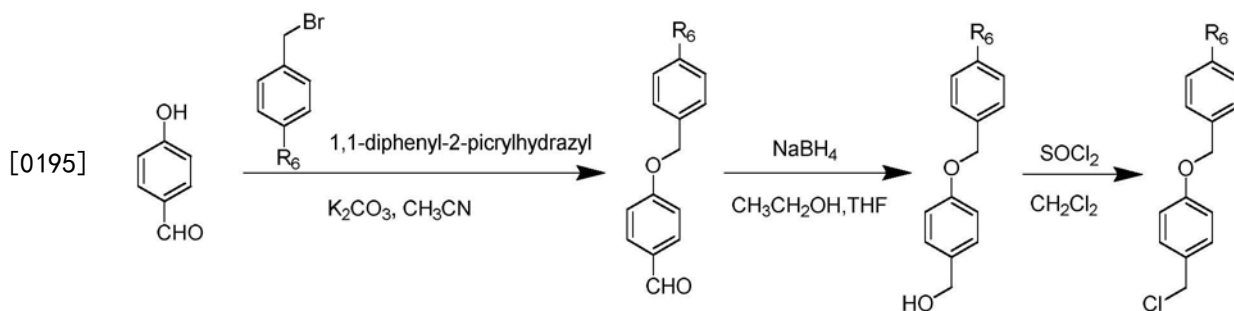
[0190] 化合物 LMY-66: 14-[N-(4-苄氧基苄基)-5-吡啶甲烯基]槐定碱: 淡黄色固体粉末, 收率 39%;

[0191] ^1H NMR (600MHz, Chloroform- d) δ 7.92 (d, $J=1.8\text{Hz}$, 1H), 7.67 (d, $J=1.5\text{Hz}$, 1H), 7.44-7.37 (m, 4H), 7.36-7.31 (m, 1H), 7.31-7.28 (m, 1H), 7.22 (dd, $J=8.6, 1.6\text{Hz}$, 1H), 7.13 (d, $J=3.2\text{Hz}$, 1H), 7.10-7.06 (m, 2H), 6.95-6.89 (m, 2H), 6.56 (d, $J=3.1\text{Hz}$, 1H), 5.24 (s, 2H), 5.03 (s, 2H), 3.63 (dd, $J=13.6, 5.1\text{Hz}$, 1H), 3.55 -3.49 (m, 1H), 3.38 (t, $J=13.8, 11.9\text{Hz}$, 1H), 3.04-2.90 (m, 2H), 2.88-2.79 (m, 1H), 2.72-2.63 (m, 1H), 2.28-2.16 (m, 2H), 2.11-2.04 (m, 2H), 2.05-1.85 (m, 4H), 1.81-1.71 (m, 1H), 1.67-1.61 (m, 1H), 1.62-1.44 (m, 3H), 1.34-1.26 (m, 1H), 1.20-1.09 (m, 1H). ^{13}C NMR (151MHz, CDCl_3) δ 165.67, 158.37, 136.84, 135.80, 135.75, 129.54, 128.89, 128.67, 128.60 (2), 128.25 (2), 128.01, 127.72, 127.68, 127.44 (2), 124.12, 122.57, 115.14 (2), 109.53, 102.10, 70.05, 63.51, 56.04, 55.37, 50.58, 49.72, 48.16, 40.11, 31.83, 30.06, 27.49, 23.87, 23.78, 21.57, 21.52. HRMS m/z (ESI^+) calcd. for $\text{C}_{38}\text{H}_{42}\text{N}_3\text{O}_2$ [$\text{M}+\text{H}^+$] 572.3277, found 572.3654. Mp: $137.6^\circ\text{C}\sim 138.4^\circ\text{C}$

[0192] 本发明还提供了化合物 LMY-51~LMY-62 的反应物 luo-51~luo-62 的合成方法, 反应物 luo-51~luo-62 依次为 N-(4-(4-甲基苄氧基)苄基)-3-吡啶甲醛、N-(4-(4-叔丁基苄氧基)苄基)-3-吡啶甲醛、N-(4-(4-氟苄氧基)苄基)-3-吡啶甲醛、N-(4-(4-氯苄氧基)苄基)-3-吡啶甲醛、N-(4-(4-溴苄氧基)苄基)-3-吡啶甲醛、N-(4-(4-三氟甲氧基苄氧基)苄基)-3-吡啶甲醛、5-甲氧基-N-(4-(4-甲基苄氧基)苄基)-3-吡啶甲醛、5-甲氧基-N-(4-(4-叔丁基苄氧基)苄基)-3-吡啶甲醛、5-甲氧基-N-(4-(4-氟苄氧基)苄基)-3-吡啶甲醛、5-甲氧基-N-(4-(4-氯苄氧基)苄基)-3-吡啶甲醛、5-甲氧基-N-(4-(4-溴苄氧基)苄基)-3-吡啶甲醛和 5-甲氧基-N-(4-(4-三氟甲氧基苄氧基)苄基)-3-吡啶甲醛, 具体如下:

[0193] 步骤 1, 制备化合物 MY-01~MY-06,

[0194] MY-01 的制备:



[0196] 具体制备MY-01的实验方法：

[0197] 于250mL圆底烧瓶中分别加入20mmol (2.44g) 对羟基苯甲醛, 20mmol (2.76g) 碳酸钾, 22 mmol (4.048g) 4-甲基溴化苄, 加入50mL乙腈搅拌均匀, 加入几毫克1,1-联苯基-2-苦基肼基, 升温至50℃, 反应24小时至终点 (TLC检测)。冷却至室温, 减压抽滤, 二氯甲烷洗涤, 收集滤液, 二氯甲烷萃取 (40 mLx3), 合并有机相, 无水Na₂SO₄干燥, 减压抽滤、浓缩滤液后得橙色固体粉末。

[0198] 于100mL三口烧瓶中分别加入1.44g (30mmol) 硼氢化钠和所得4.321g (约19mmol) 橙色固体粉末, 进行氮气保护, 加入40mL乙醇和20mL四氢呋喃, 0℃反应12小时至终点 (TLC检测)。逐滴加入3N的盐酸中和过量的硼氢化钠, 二氯甲烷萃取 (40mLx3), 合并有机相, 无水Na₂SO₄干燥, 减压抽滤、浓缩滤液后得浅黄色固体粉末。

[0199] 于250mL圆底烧瓶中加入所得的4.112g (约18mmol) 浅黄色固体粉末, 加入100mL二氯甲烷搅拌使其溶解, 于冰浴下逐滴加入1.56mL (21.6mmol) 氯化亚砷, 滴加完恢复室温, 反应1小时至终点 (TLC检测)。加水萃取, 收集有机相, 无水Na₂SO₄干燥, 减压抽滤、浓缩滤液后得4.477g白色固体粉末化合物MY-01: (4-甲基苄氧基) 苄氯: 白色固体粉末, 收率91%;

[0200] ¹H NMR (600MHz, Chloroform-d) δ7.37-7.32 (m, 4H), 7.23 (d, J=7.8Hz, 2H), 7.00-6.96 (m, 2H), 5.06 (s, 2H), 4.60 (s, 2H), 2.40 (s, 3H)。

[0201] 参考化合物MY-01的实验方法制备化合物MY-02~MY-06, 化合物MY-02~MY-06结构鉴定数据如下:

[0202] 化合物MY-02: (4-叔丁基苄氧基) 苄氧基苄氯: 白色固体粉末, 收率92%;

[0203] ¹H NMR (600MHz, Chloroform-d) δ7.47-7.44 (m, 2H), 7.40 (d, J=8.3Hz, 2H), 7.36-7.33 (m, 2H), 7.02-6.98 (m, 2H), 5.07 (s, 2H), 4.60 (s, 2H), 1.37 (d, J=0.8Hz, 9H)。

[0204] 化合物MY-03: (4-氟苄氧基) 苄氯: 白色固体粉末, 收率90%;

[0205] ¹H NMR (600MHz, Chloroform-d) δ7.45-7.41 (m, 2H), 7.36-7.33 (m, 2H), 7.10 (t, J=8.7Hz, 2H), 6.98-6.95 (m, 2H), 5.05 (s, 2H), 4.59 (s, 2H)。

[0206] 化合物MY-04: (4-氯苄氧基) 苄氯: 白色固体粉末, 收率94%;

[0207] ¹H NMR (600MHz, Chloroform-d) δ7.39 (s, 4H), 7.37-7.32 (m, 2H), 6.97-6.94 (m, 2H), 5.06 (s, 2H), 4.59 (s, 2H)。

[0208] 化合物MY-05: (4-溴苄氧基) 苄氯: 白色固体粉末, 收率91%;

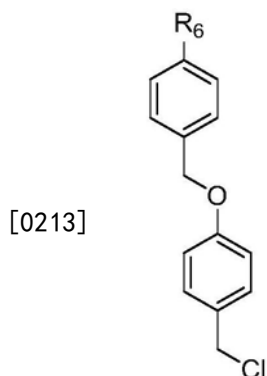
[0209] ¹H NMR (600MHz, Chloroform-d) δ7.56-7.52 (m, 2H), 7.36-7.31 (m, 4H), 6.97-6.94 (m, 2H), 5.04 (s, 2H), 4.59 (s, 2H)。

[0210] 化合物MY-06: (4-三氟甲氧基苄氧基) 苄氯: 白色固体粉末, 收率93%;

[0211] ¹H NMR (600MHz, Chloroform-d) δ7.50-7.47 (m, 2H), 7.37-7.34 (m, 2H), 7.29-7.24

(m, 2H), 6.99- 6.95 (m, 2H), 5.09 (s, 2H), 4.60 (s, 2H) .

[0212] 化合物MY-02~MY-06的结构通式:



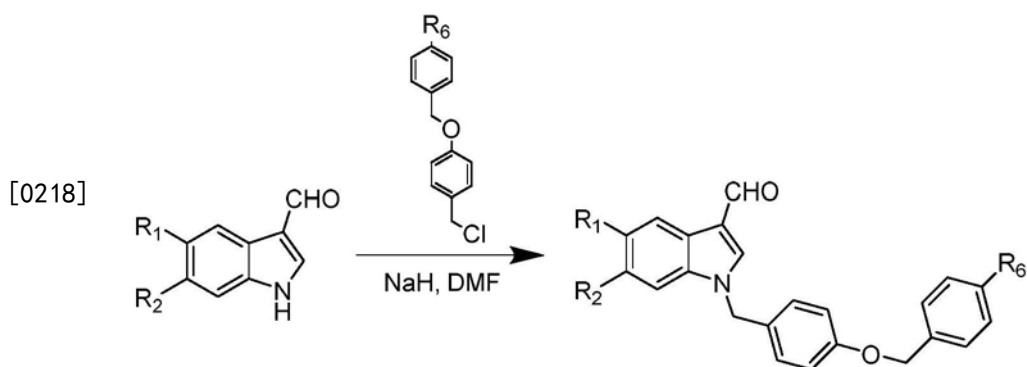
MY-01~06

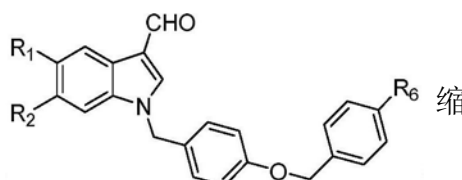
[0214] MY-01: $R_6 = \text{Me}$ MY-04: $R_6 = \text{Cl}$

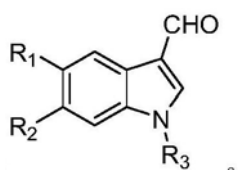
[0215] MY-02: $R_6 = \text{tBu}$ MY-05: $R_6 = \text{Br}$

[0216] MY-03: $R_6 = \text{F}$ MY-06: $R_6 = \text{OCF}_3$

[0217] 步骤2, 制备化合物1uo-51~1uo-62反应路线如下:



[0219] 为了方便表达将结构式  缩写成结构式

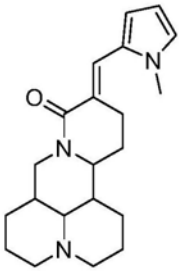
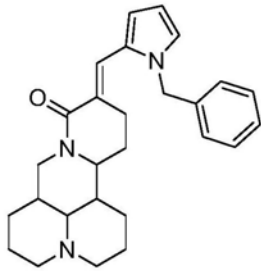
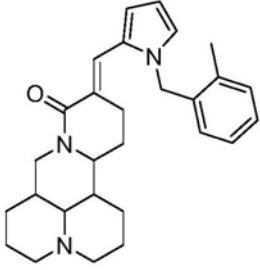
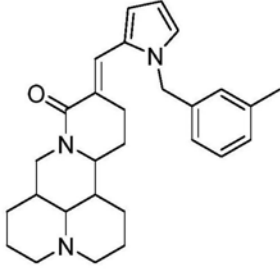


通过本发明制备的上述槐定碱吡咯、吲哚类衍生物, 其构成纯度在百分

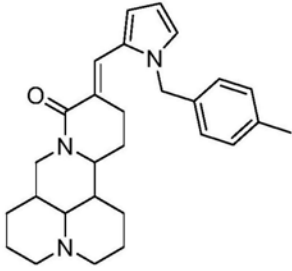
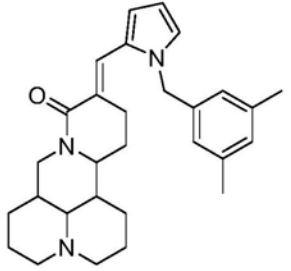
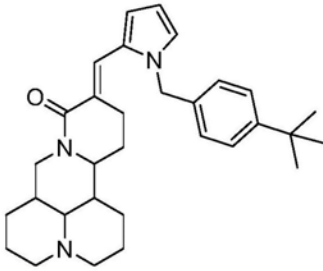
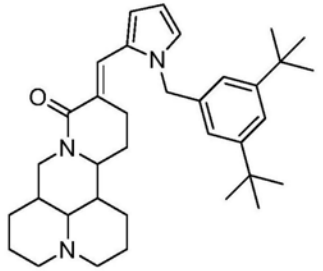
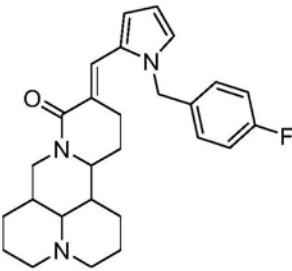
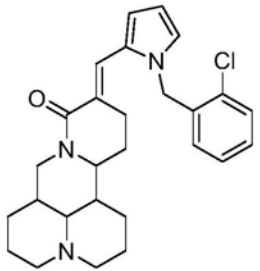
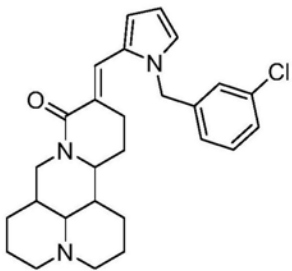
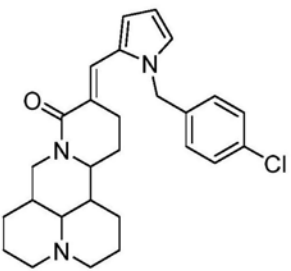
99%以上。

[0220] 以下表1给出了制备目标化合物的结构式:

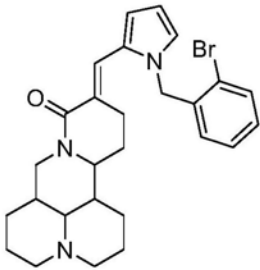
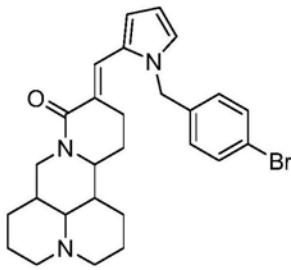
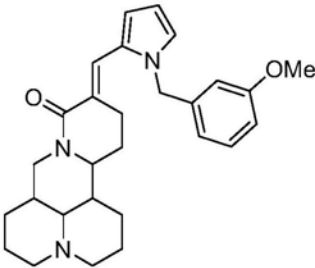
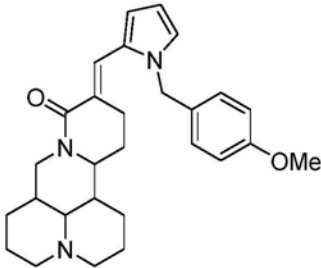
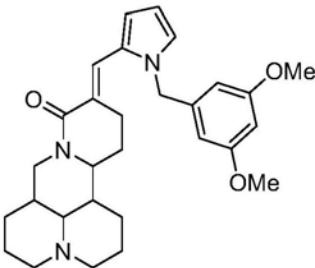
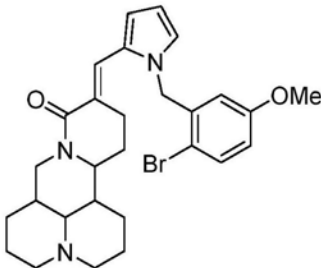
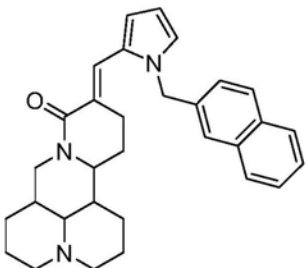
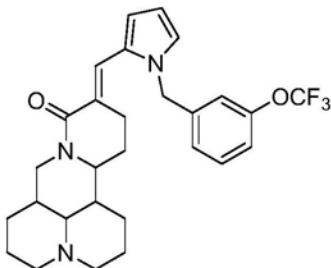
[0221]

LMY-01	 14-(N-甲基-2-吡咯甲基)槐定碱	LMY-02	 14-(N-苄基-2-吡咯甲基)槐定碱
LMY-03	 14-[N-(2-甲基苄基)-2-吡咯甲基]槐 定碱	LMY-04	 14-[N-(3-甲基苄基)-2-吡咯甲基]槐 定碱

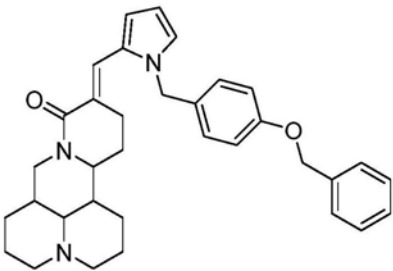
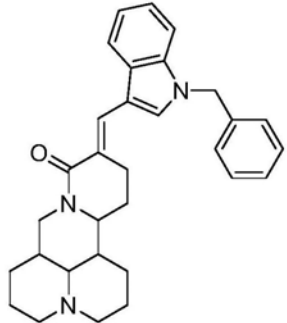
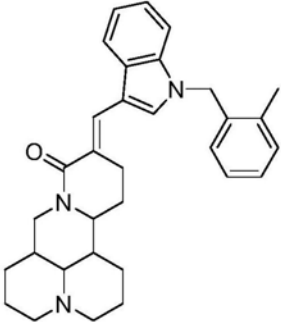
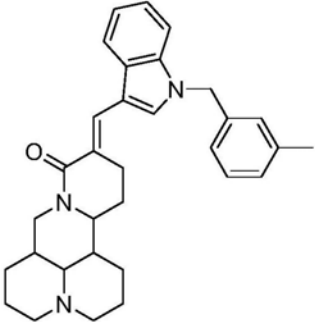
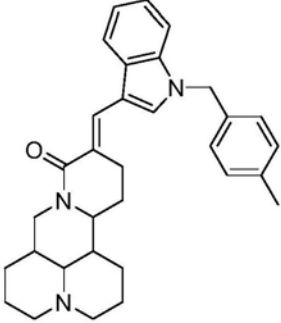
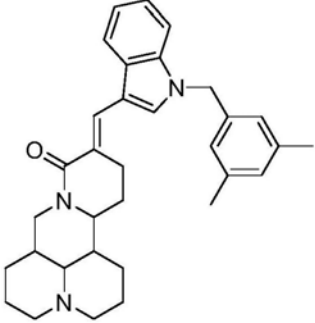
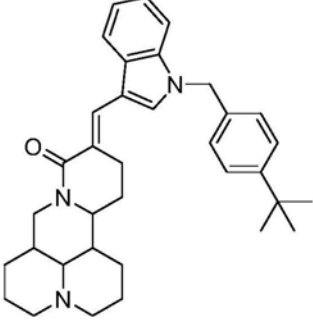
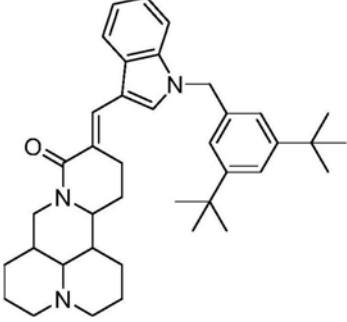
[0222]

LMY-05	 14-[N-(4-甲基苄基)-2-吡咯甲烯基]槐定碱	LMY-06	 14-[N-(3, 5-二甲基苄基)-2-吡咯甲烯基]槐定碱
LMY-07	 14-[N-(4-叔丁基苄基)-2-吡咯甲烯基]槐定碱	LMY-08	 14-[N-(3, 5-二叔丁基苄基)-2-吡咯甲烯基]槐定碱
LMY-09	 14-[N-(4-氟苄基)-2-吡咯甲烯基]槐定碱	LMY-10	 14-[N-(2-氯苄基)-2-吡咯甲烯基]槐定碱
LMY-11	 14-[N-(3-氯苄基)-2-吡咯甲烯基]槐定碱	LMY-12	 14-[N-(4-氯苄基)-2-吡咯甲烯基]槐定碱

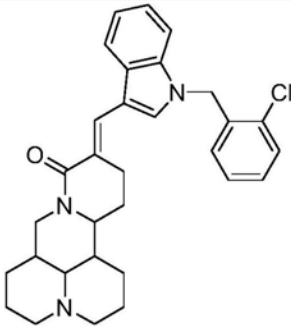
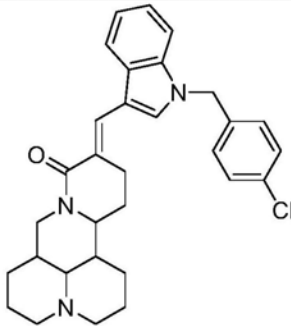
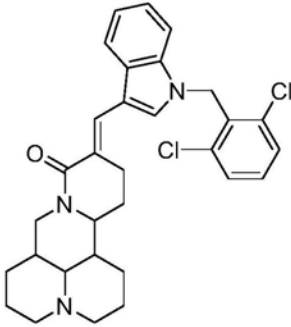
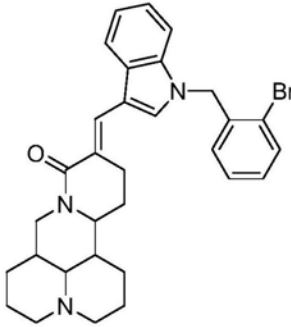
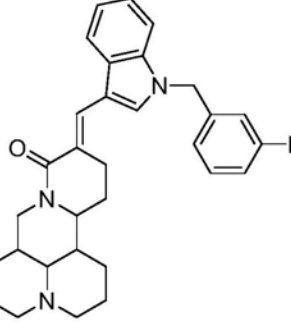
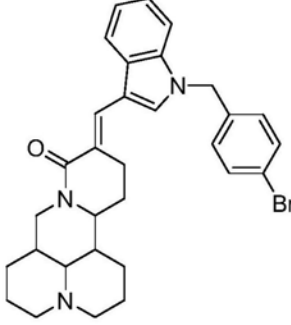
[0223]

LMY-13	 14-[N-(2-溴苄基)-2-吡咯甲烯基]槐定碱 碱	LMY-14	 14-[N-(4-溴苄基)-2-吡咯甲烯基]槐定碱 碱
LMY-15	 14-[N-(3-甲氧基苄基)-2-吡咯甲烯基] 槐定碱	LMY-16	 14-[N-(4-甲氧基苄基)-2-吡咯甲烯基] 槐定碱
LMY-17	 14-[N-(3, 5-二甲氧基苄基)-2-吡咯甲烯基]槐定碱	LMY-18	 14-[N-(2-溴-5-甲氧基苄基)-2-吡咯甲烯基]槐定碱
LMY-19	 14-[N-(2-萘基亚甲基)-2-吡咯甲烯基] 槐定碱	LMY-20	 14-[N-(4-三氟甲氧基苄基)-2-吡咯甲烯基]槐定碱

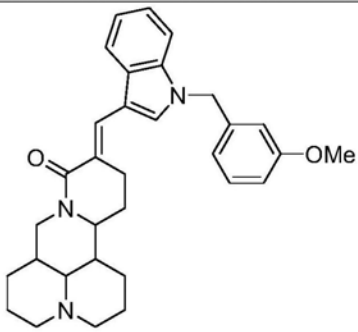
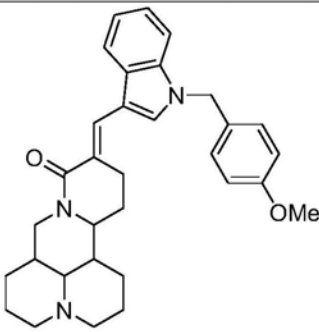
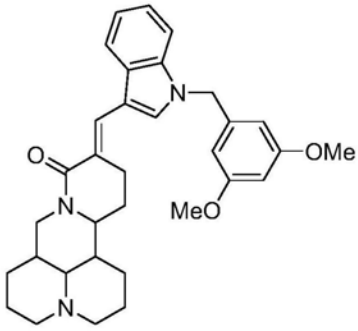
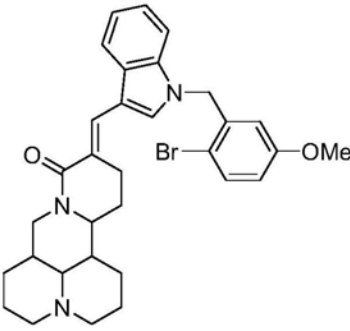
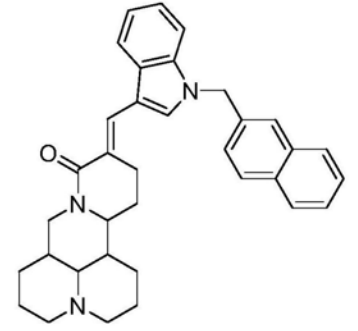
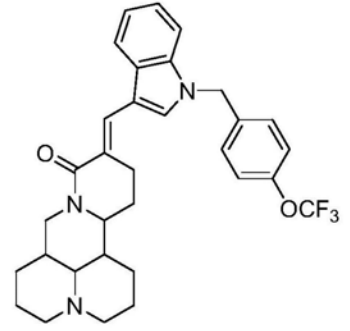
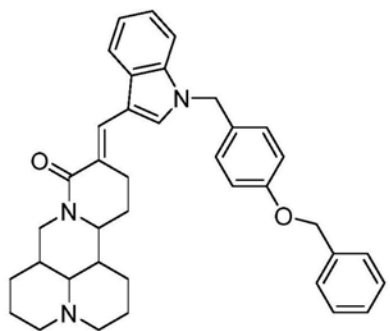
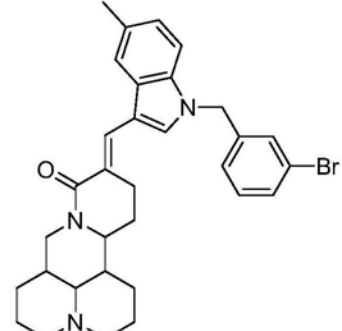
[0224]

LMY-21	 14-[N-(4-苄氧基苄基)-2-吡咯甲烯基] 槐定碱	LMY-22	 14-[N-苄基-3-吲哚甲烯基]槐定碱
LMY-23	 14-[N-(2-甲基苄基)-3-吲哚甲烯基]槐 定碱	LMY-24	 14-[N-(3-甲基苄基)-3-吲哚甲烯基]槐 定碱
LMY-25	 14-[N-(4-甲基苄基)-3-吲哚甲烯基]槐 定碱	LMY-26	 14-[N-(3, 5-二甲基苄基)-3-吲哚甲烯 基]槐定碱
LMY-27	 14-[N-(4-叔丁基苄基)-3-吲哚甲烯基]	LMY-28	 14-[N-(3,5-二叔丁基苄基)-3-吲哚甲烯

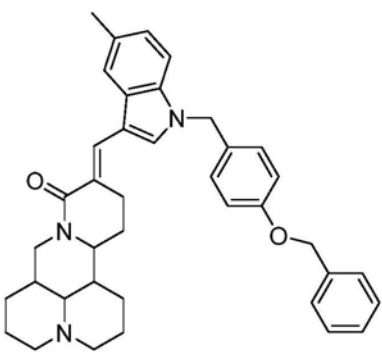
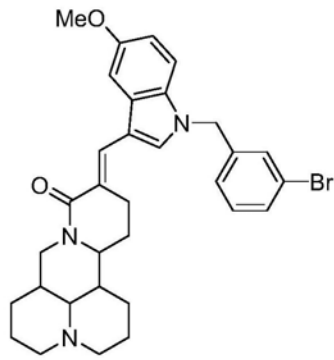
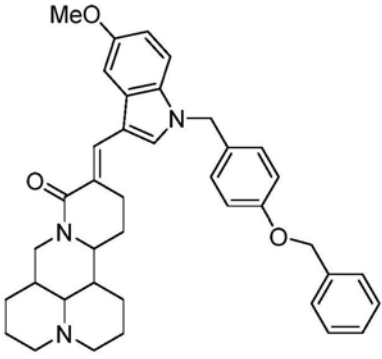
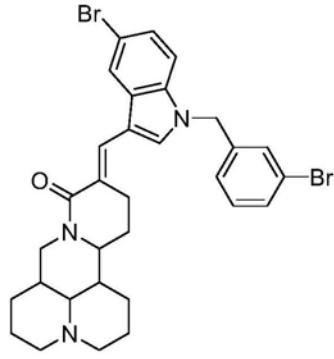
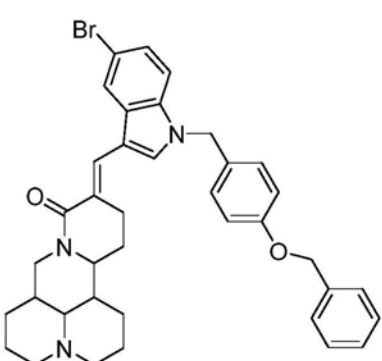
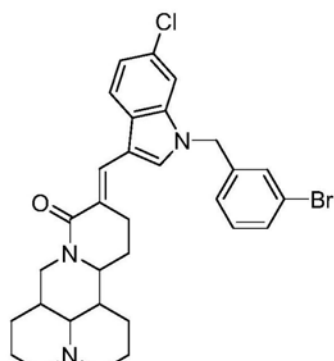
[0225]

	槐定碱		基]槐定碱
LMY-29	 14-[N-(2-氯苄基)-3-吲哚甲烯基]槐定 碱	LMY-30	 14-[N-(4-氯苄基)-3-吲哚甲烯基]槐定 碱
LMY-31	 14-[N-(2,6-二氯苄基)-3-吲哚甲烯基] 槐定碱	LMY-32	 14-[N-(2-溴苄基)-3-吲哚甲烯基]槐定 碱
LMY-33	 14-[N-(3-溴苄基)-3-吲哚甲烯基]槐定 碱	LMY-34	 14-[N-(4-溴苄基)-3-吲哚甲烯基]槐定 碱

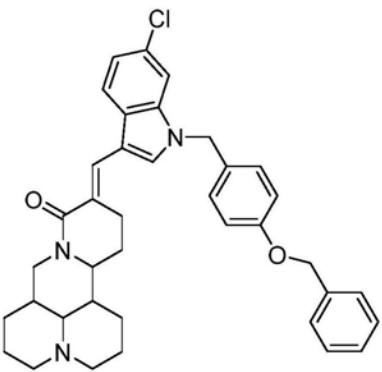
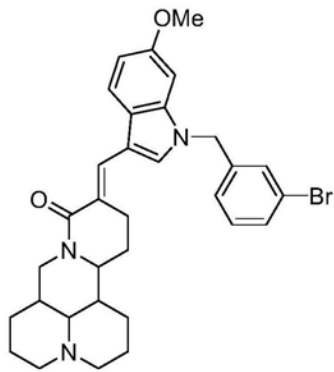
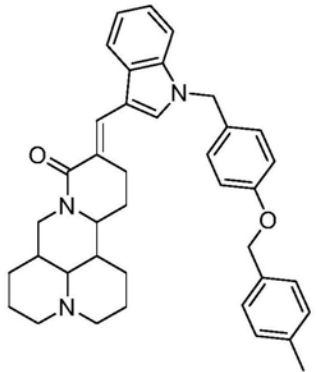
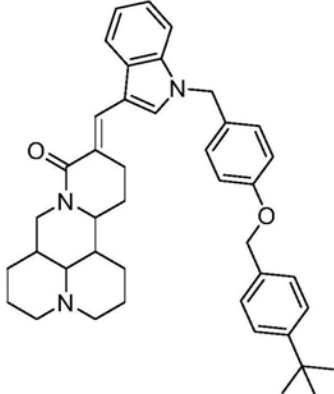
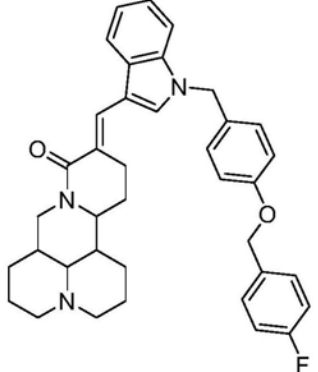
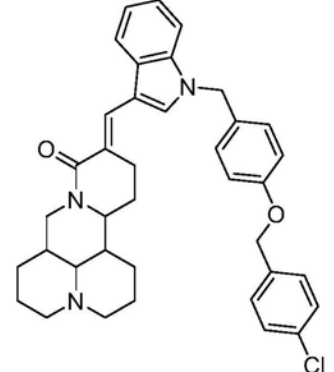
[0226]

LMY-35	 14-[N-(3-甲氧基苄基)-3-吲哚甲烯基] 槐定碱	LMY-36	 14-[N-(4-甲氧基苄基)-3-吲哚甲烯基] 槐定碱
LMY-37	 14-[N-(3,5-二甲氧基苄基)-3-吲哚甲 烯基]槐定碱	LMY-38	 14-[N-(2-溴-5-甲氧基苄基)-3-吲哚甲 烯基]槐定碱
LMY-39	 14-[N-(2-萘基亚甲基)-3-吲哚甲烯基] 槐定碱	LMY-40	 14-[N-(4-三氟甲氧基苄基)-3-吲哚甲 烯基]槐定碱
LMY-41	 LMY-41	LMY-42	 LMY-42

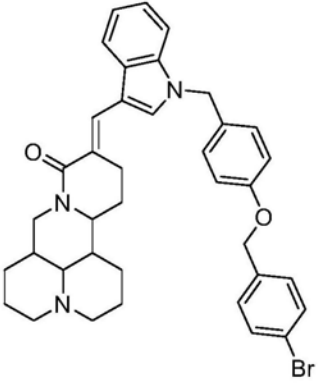
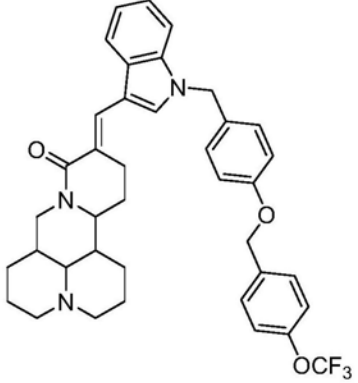
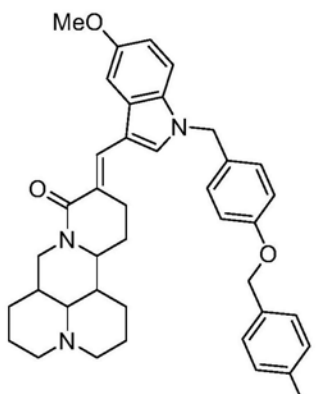
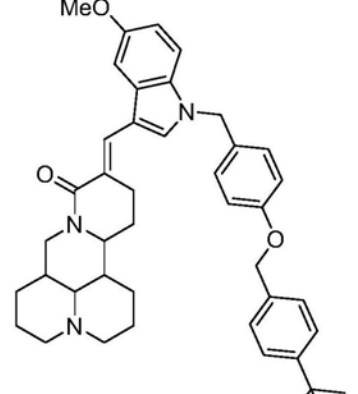
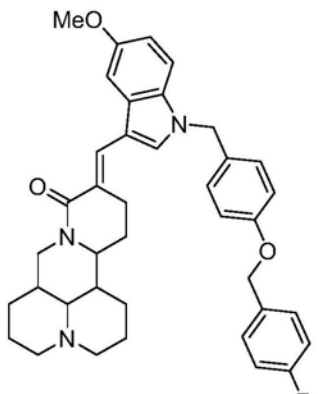
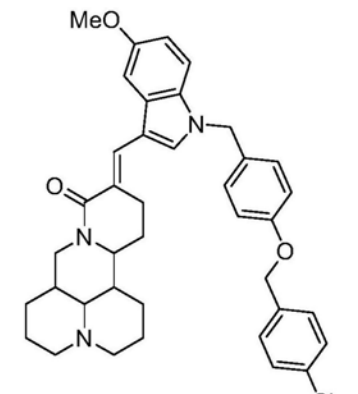
[0227]

	14-[N-(4-苄氧基苄基)-3-吡啶甲烯基] 槐定碱		14-[5-甲基-N-(3-溴苄基)-3-吡啶甲烯基] 槐定碱
LMY-43		LMY-44	
	14-[5-甲基-N-(4-苄氧基苄基)-3-吡啶 甲烯基]槐定碱		14-[5-甲氧基-N-(3-溴苄基)-3-吡啶甲 烯基]槐定碱
LMY-45		LMY-46	
	14-[5-甲氧基-N-(4-苄氧基苄基)-3-吡 啶甲烯基]槐定碱		14-[5-溴-N-(3-溴苄基)-3-吡啶甲烯基] 槐定碱
LMY-47		LMY-48	
	14-[5-溴-N-(4-苄氧基苄基)-3-吡啶甲 烯基]槐定碱		14-[6-氯-N-(3-溴苄基)-3-吡啶甲烯基] 槐定碱

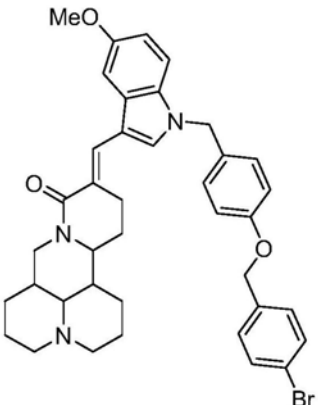
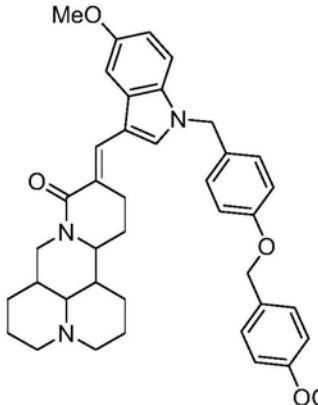
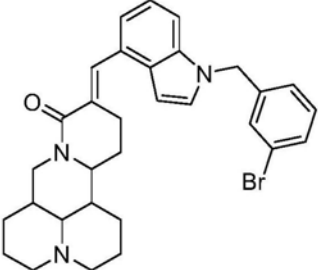
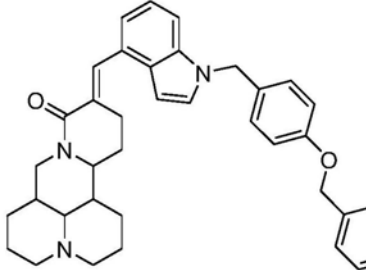
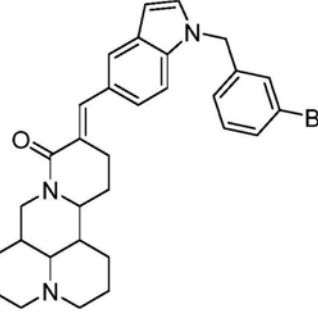
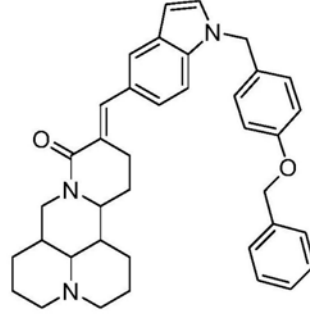
[0228]

LMY-49	 14-[6-氯-N-(4-苄氧基苄基)-3-吲哚甲 烯基]槐定碱	LMY-50	 14-[6-甲氧基-N-(3-溴苄基)-3-吲哚甲 烯基]槐定碱
LMY-51	 14-[N-(4-(4-甲基苄氧基)苄基)-3-吲哚 甲烯基]槐定碱	LMY-52	 14-[N-(4-(4-叔丁基苄氧基)苄基)-3-吲 哚甲烯基]槐定碱
LMY-53	 14-[N-(4-(4-氟苄氧基)苄基)-3-吲哚甲 烯基]槐定碱	LMY-54	 14-[N-(4-(4-氯苄氧基)苄基)-3-吲哚甲 烯基]槐定碱

[0229]

LMY-55	 14-[N-(4-(4-溴苯氧基)苄基)-3-吲哚甲 烯基]槐定碱	LMY-56	 14-[N-(4-(4-三氟甲氧基苄基)苄 基)-3-吲哚甲烯基]槐定碱
LMY-57	 14-[5-甲氧基-N-(4-(4-甲基苯氧基)苄 基)-3-吲哚甲烯基]槐定碱	LMY-58	 14-[5-甲氧基-N-(4-(4-叔丁基苯氧基) 苄基)-3-吲哚甲烯基]槐定碱
LMY-59	 14-[5-甲氧基-N-(4-(4-氟苯氧基)苄 基)-3-吲哚甲烯基]槐定碱	LMY-60	 14-[5-甲氧基-N-(4-(4-氯苯氧基)苄 基)-3-吲哚甲烯基]槐定碱

[0230]

LMY-61	 14-[5-甲氧基-N-(4-(4-溴苄氧基)苄基)-3-吡啶甲烯基]槐定碱	LMY-62	 14-[5-甲氧基-N-(4-(4-三氟甲氧基苄氧基)苄基)-3-吡啶甲烯基]槐定碱
LMY-63	 14-[N-(3-溴苄基)-4-吡啶甲烯基]槐定碱	LMY-64	 14-[N-(4-苄氧基苄基)-4-吡啶甲烯基]槐定碱
LMY-65	 14-[N-(3-溴苄基)-5-吡啶甲烯基]槐定碱	LMY-66	 14-[N-(4-苄氧基苄基)-5-吡啶甲烯基]槐定碱

[0231] 实施例2 以下通过实验进一步说明本发明的优异效果。

[0232] 所述槐定碱衍生物在体外抗肿瘤活性研究,所述肿瘤为肝癌。

[0233] 药理实验:

[0234] 肿瘤细胞:人类肝癌细胞 (HepG2) 购自美国细胞保存中心 (ATCC)。所有细胞培养在含10%FBS 和1%青霉素-链霉素的McCoy5A培养基中,并置于37℃,5%CO₂的细胞培养箱中。用MTT法进行测试,将槐定碱衍生物用DMSO溶解后用完全培养基稀释成所需浓度。取5×10⁵个对数生长期的以上细胞株,接种于96孔板中并设空白组、对照组以及给药组(100μL),每组设3个平行孔。置于37℃,5%CO₂的细胞培养箱中,24h后加入不同浓度的药物,继续培养48h后,每个孔加入20μL 5mg/ml MTT,培养箱孵育3h 离心弃上清,加入150μl DMSO,振荡混匀,酶标仪测定其A₄₉₀值。计算细胞生长抑制率,抑制率/% = (A_{对照} - A_{实验}) / (A_{对照} - A_{空白})

×100%。

[0235] 上述实验重复3次,并用Blies法计算出IC₅₀值,组间进行比较采用的是t检验法,P<0.05为有显著性差异。

[0236] 实验结果:

[0237] 表2目标化合物对HepG2细胞增殖的抑制

	Compd	IC ₅₀ (μM)	Compd	IC ₅₀ (μM)	Compd	IC ₅₀ (μM)
[0238]	LMY-01	>100	LMY-24	8.27±0.90	LMY-47	3.97±0.35
	LMY-02	10.87±0.92	LMY-25	9.39±1.01	LMY-48	7.12±0.67
	LMY-03	25.34±1.63	LMY-26	4.56±0.44	LMY-49	14.29±1.27
	LMY-04	18.09±1.21	LMY-27	4.57±0.51	LMY-50	6.15±0.58
	LMY-05	17.28±1.59	LMY-28	5.32±0.49	LMY-51	5.32±0.45
	LMY-06	14.78±1.37	LMY-29	9.05±0.88	LMY-52	6.07±0.48
	LMY-07	13.55±1.28	LMY-30	6.59±0.62	LMY-53	4.83±0.32
	LMY-08	18.12±1.64	LMY-31	9.78±0.81	LMY-54	6.17±0.58
	LMY-09	29.39±1.97	LMY-32	15.43±0.99	LMY-55	10.08±0.92
	LMY-10	17.45±1.31	LMY-33	8.62±0.98	LMY-56	6.01±0.56
	LMY-11	16.59±1.24	LMY-34	5.94±0.49	LMY-57	4.18±0.38
	LMY-12	13.53±1.11	LMY-35	8.14±0.73	LMY-58	5.86±0.41
	LMY-13	13.48±1.09	LMY-36	8.23±0.76	LMY-59	3.12±0.21
	LMY-14	12.57±1.14	LMY-37	6.88±0.61	LMY-60	3.97±0.24
	LMY-15	17.23±1.43	LMY-38	4.16±0.39	LMY-61	6.31±0.55
	LMY-16	30.12±1.91	LMY-39	12.78±0.94	LMY-62	5.72±0.42
	LMY-17	21.24±1.65	LMY-40	8.73±0.72	LMY-63	13.31±1.16
	LMY-18	9.66±0.76	LMY-41	3.08±0.40	LMY-64	15.24±1.20
	LMY-19	16.10±1.38	LMY-42	7.61±0.68	LMY-65	14.58±1.31
	LMY-20	26.51±1.94	LMY-43	7.71±0.71	LMY-66	7.25±0.80
[0239]	LMY-21	7.22±0.83	LMY-44	5.04±0.61	Sophoridine	2508±221
	LMY-22	6.95±0.47	LMY-45	1.96±0.39	Camptothecin	7.23±0.69
	LMY-23	16.32±1.35	LMY-46	12.77±1.18		

[0240] 药理实验结果表明:合成的系列槐定碱衍生物均有良好的抗肿瘤活性,在以槐定碱为对照药,与合成的LMY系列化合物通式给药的情况下,对比它们的抑制率发现,所有的化合物的抗肿瘤活性均优于对照药槐定碱,66个槐定碱衍生物中几乎所有的化合物的IC₅₀均小于30μM,其中LMY-18、LMY-21、LMY-22、LMY-24、LMY-25、LMY-26、LMY-27、LMY-28、LMY-

29、LMY-30、LMY-31、LMY-33、LMY-34、LMY-35、LMY-36、LMY-37、LMY-38、LMY-40、LMY-41、LMY-42、LMY-43、LMY-44、LMY-45、LMY-47、LMY-48、LMY-50、LMY-51、LMY-52、LMY-53、LMY-54、LMY-56、LMY-57、LMY-58、LMY-59、LMY-60、LMY-61、LMY-62、LMY-66共38个化合物对肝癌肿瘤细胞的 IC_{50} 小于 $10\mu M$,活性相比槐定碱有了极大的提高。结果显示,含有(苄氧基苄基)-3-吡啶甲烯基的化合物(LMY-21、LMY-41、LMY-43、LMY-45、LMY-47、LMY-49、LMY-51~62、LMY-64、LMY-66)均表现出很优异的抗癌活性,其中LMY-45:14-[5-甲氧基-N-(4-苄氧基苄基)-3-吡啶甲烯基]槐定碱对肝癌细胞显示出了最显著的抗癌活性, IC_{50} 的值为 $1.96\mu M$,抗肿瘤活性远远超过了母体槐定碱。

[0241] 细胞凋亡分析实验方法:

[0242] 对于细胞凋亡,将SMMC-7721和CNE2细胞按 3×10^5 密度接种于6孔板中,待细胞完全贴壁后用含不同LMY-45药物浓度的培养基继续培养24h。通过流式细胞仪及细胞凋亡检测试剂盒检测细胞凋亡比例。细胞凋亡实验分别独立重复3次。由于LMY-45具有良好的抗肿瘤活性,对其进行了进一步的细胞凋亡分析实验。

[0243] 实验结果:

[0244] 凋亡实验结果表明:在不同浓度的LMY-45药物处理24h后,在CNE2中,凋亡细胞(右下象限,AV+/PI-和右上象限,AV+/PI+)的百分比从3.19%(对照组)显著增加到8.31%($2.5\mu M$),55.30%($5\mu M$)和94.30%($10\mu M$)。在SMMC-7721中,凋亡细胞的百分比从2.24%(对照组)增加到28.99%($2.5\mu M$),95.60%($5\mu M$)和98.8%($10\mu M$)。实验结果表明LMY-45能够剂量依赖性地诱导CNE2和SMMC-7721细胞凋亡。

[0245] 本发明在于提供了一种有发展前景的抗肿瘤药物,给广大的癌症患者提供多一种治疗的可能。

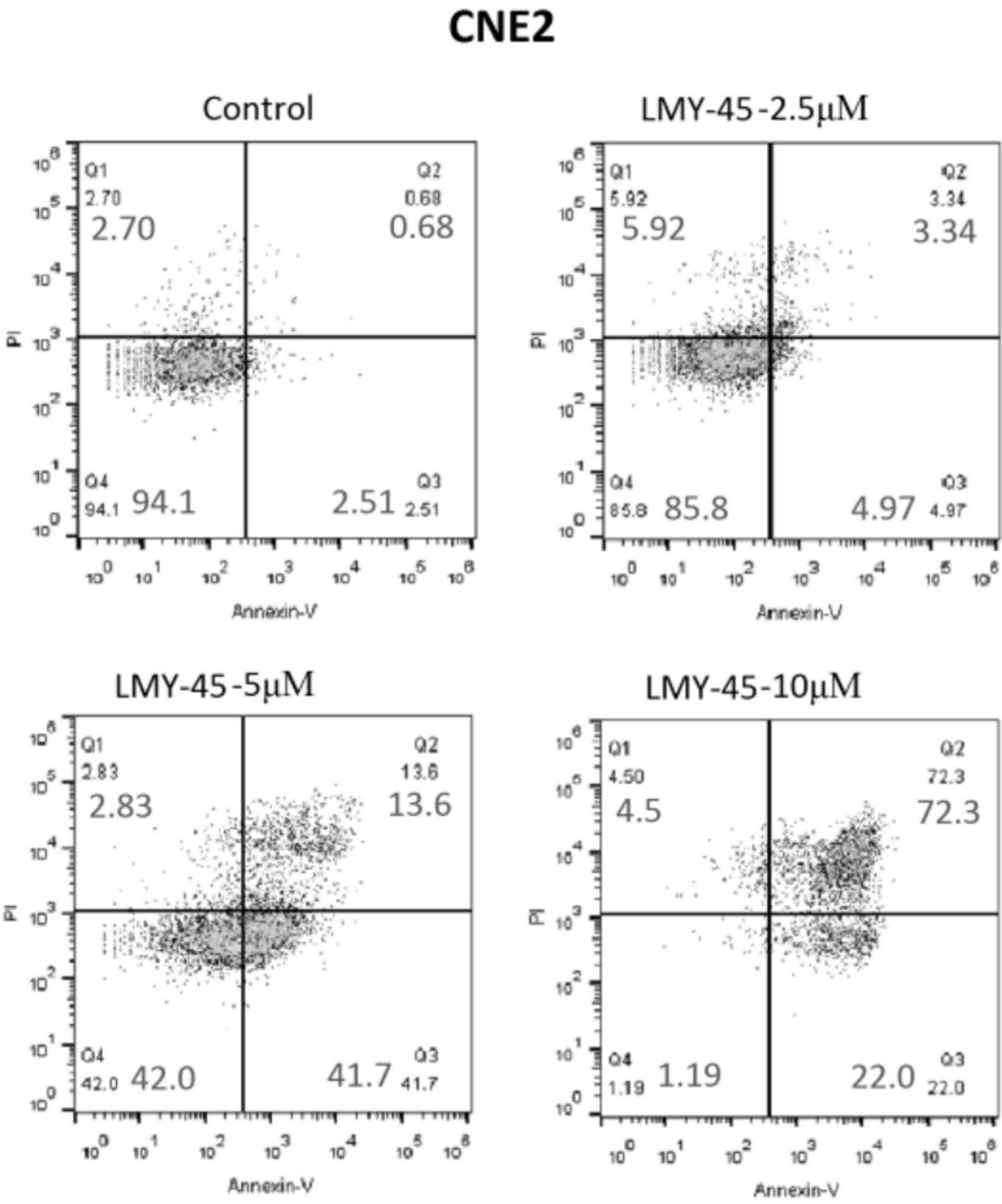


图1

SMMC-7721

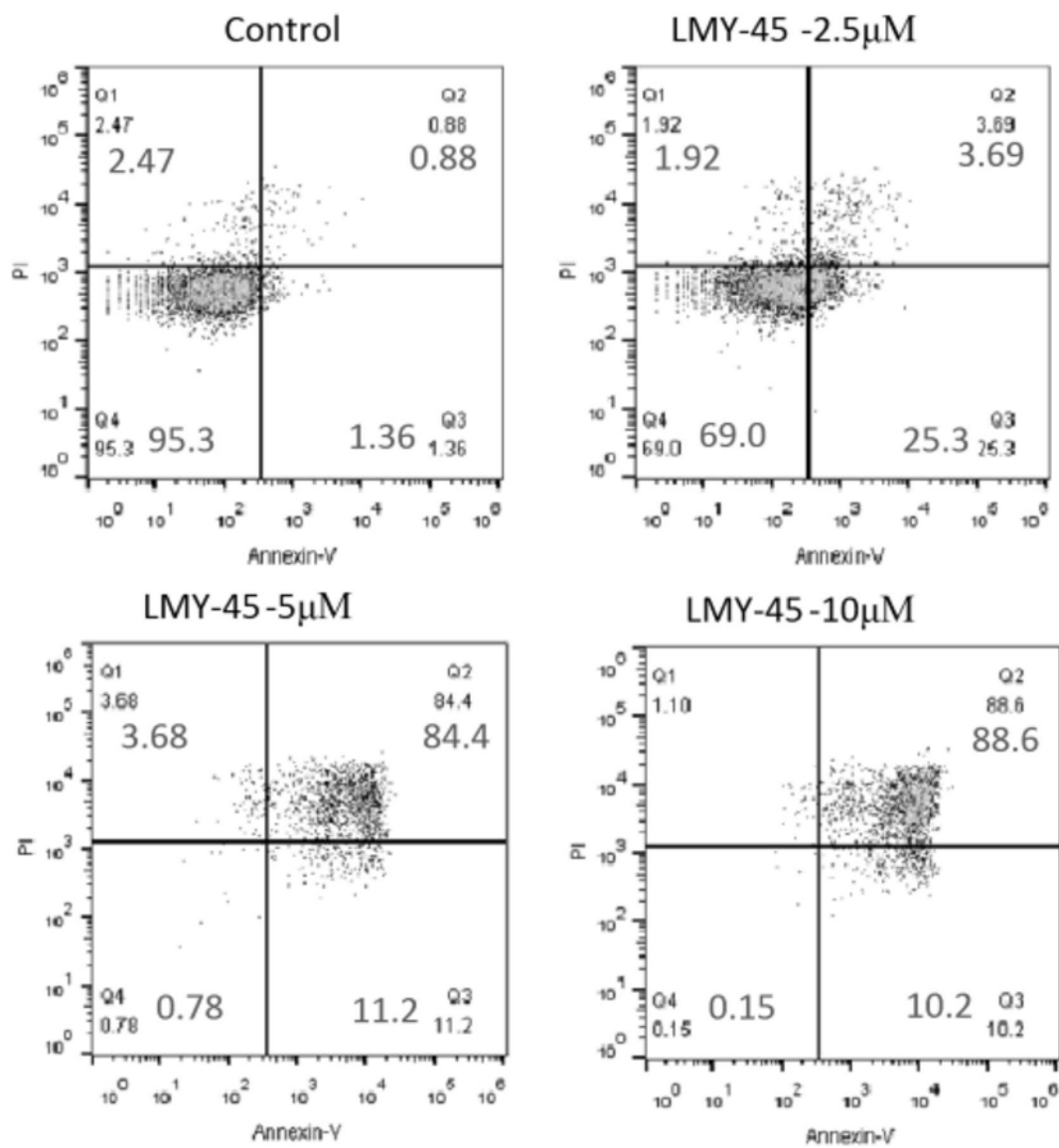


图2