有机化学 DOI: 10.6023/cjoc202302018 研究论文
Chinese Journal of Organic Chemistry ARTICLE

基于钴催化吲哚酰胺与二炔和单炔的[4＋2]环化反应合成 γ-咔啉酮

贝文峰 潘 健 冉冬梅 刘伊琳 杨 震* 冯若昆*
(绍兴文理学院化学化工学院 浙江省精细化学品传统工艺替代技术研究重点实验室 浙江绍兴 312000)

摘要 采用廉价易得的过渡金属钴盐为催化剂, 实现了 3-吲哚甲酰胺与炔烃的 C—H/N—H 活化环化反应, 制备了一系列 γ-咔啉酮类化合物. 实验表明反应的最佳条件为: 10 mol%乙酰丙酮钴为催化剂, 1.0 equiv.乙酰丙酮锰为氧化剂, 2.0 equiv.特戊酸钠为碱, 三氟乙醇为溶剂, 120 ℃搅拌 24 h. 该方法具有良好的底物适用性, 各种芳基或烷基取代的 1,3-丁二炔均可以在标准条件下与 3-吲哚甲酰胺反应, 并以中等到良好的收率得到 3-炔基取代的 γ-咔啉酮类化合物. 此外, 当使用端炔和内炔作为环化试剂时, 反应也可以以较好的产率和较高的选择性得到目标产物. 该反应使用廉价金属钴和锰为催化体系, 不需要额外配体和吲哚氮保护基团, 为合成具有广泛应用价值的 γ-咔啉酮类化合物提供了一种有机合成方法.

关键词 钴催化; 吲哚甲酰胺; 炔烃; [4＋2]环化; γ-咔啉酮

Cobalt-Catalyzed [4＋2] Annulation of Indole Carboxamide with Diynes and Monoacetylene: Direct Access to γ-Carbolinones

Bei, Wenfeng Pan, Jian Ran, Dongmei Liu, Yilin Yang, Zhen* Feng, Ruokun*
(*Zhejiang Key Laboratory of Alternative Technologies for Fine Chemicals Process*, *College of Chemistry and Chemical Engineering*, *Shaoxing University*, *Shaoxing*, *Zhejiang 312000*)

Abstract A cobalt-catalyzed annulation of the C(sp^2)—H/N—H bond of 3-indolecarboxamides with alkynes assisted by 8-aminoquinoline is reported for the preparation of γ-carbolinones. The research results indicated that under the optimal reaction conditions, the isolated yield was up to 90% with $Co(acac)_2$ (10 mol%) as catalyst, $Mn(acac)_3$ (1.0 equiv.) as oxidant, NaOPiv (2.0 equiv.) as base, trifluoroethanol (2.0 mL) as solvent at 120 ℃ for 24 h. The protocol has a broad scope for alkynes. Both 1,4-diarylbuta-1,3-diynes and dialkyl diynes could react with *N*-(quinolin-8-yl)-1*H*-indole-3-carboxamide, giving the desired products in moderate to good yield. It was noteworthy that terminal and internal alkynes were found to be applicable to this transformation, affording the γ-carbolinones in good yield and high selectivity. This method has the advantages of applying cheap and commercially available cobalt and manganese salts as the catalytic system, requiring no additional ligands and indole nitrogen protecting groups, providing a new method for the synthesis of γ-carbolinone compounds with wide application value.

Keywords cobalt-catalysis; indole carboxamide; alkynes; [4＋2] annulation; γ-carbolinones

咔啉酮骨架广泛存在于天然产物和药物分子结构中[1]. 其中, 含 γ-咔啉酮骨架的化合物由于其具有良好的生物活性而受到广泛关注, 如化合物 **I** 是一种 5-HT_3 受体拮抗剂[2], 化合物 **II** 是一种拓扑异构酶 I 抑制剂[3], 化合物 **III** 是具有抗菌活性的天然产物异白叶藤碱[4](图 1).

传统合成 γ-咔啉酮化合物常采用分子内的环化反应, 如 Clark 课题组[2]报道了 1,2-二甲基吲哚-3 甲酰胺先与正丁基锂和 *N*,*N*-二甲基甲酰胺(DMF)作用, 后经盐酸脱羟基处理得到 γ-咔啉酮衍生物(Scheme 1a); Fresneda 课题组[5]以叶立德试剂和醛作为原料, 经过八步得到 3-(2-叠氮苯基)取代喹啉酮, 而后在邻二甲苯中加热到 150 ℃得到目标化合物(Scheme 1b); Chen 课题组[6]发展了以 4-羟基喹啉酮为原料, 先与肼反应得到 4-肼基

* Corresponding authors. E-mail: fengshenghm86@usx.edu.cn; 33168466@qq.com
Received February 16, 2023; revised May 10, 2023; published online May 23, 2023.
Project supported by the Zhejiang Provincial Natural Science Foundation (No LQ15B020002), the Shaoxing Science and Technology Plan (No. 2018C10017), the National College Students' Innovation and Entrepreneurship Training Program (Nos. 202110349018, 202210349010) and the Scientific Research Program of Zhejiang Provincial Education Department (No. Y202043097).
浙江省自然科学基金(No. LQ15B020002)、绍兴市科技计划(No. 2018C10017)、国家级大学生创新创业训练计划(Nos. 202110349018, 202210349010)和浙江省教育厅科研计划(No. Y202043097)资助项目.

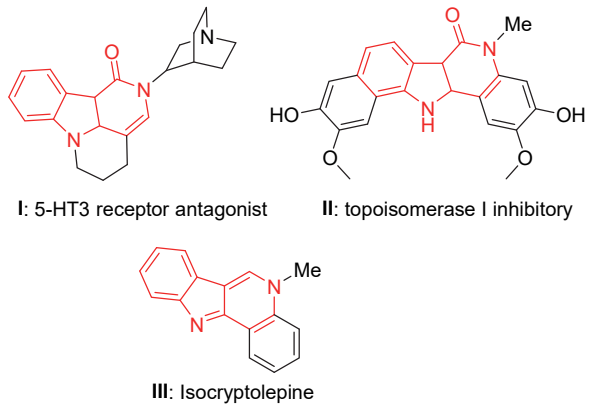


图 1 γ-咔啉酮骨架的化合物的应用举例

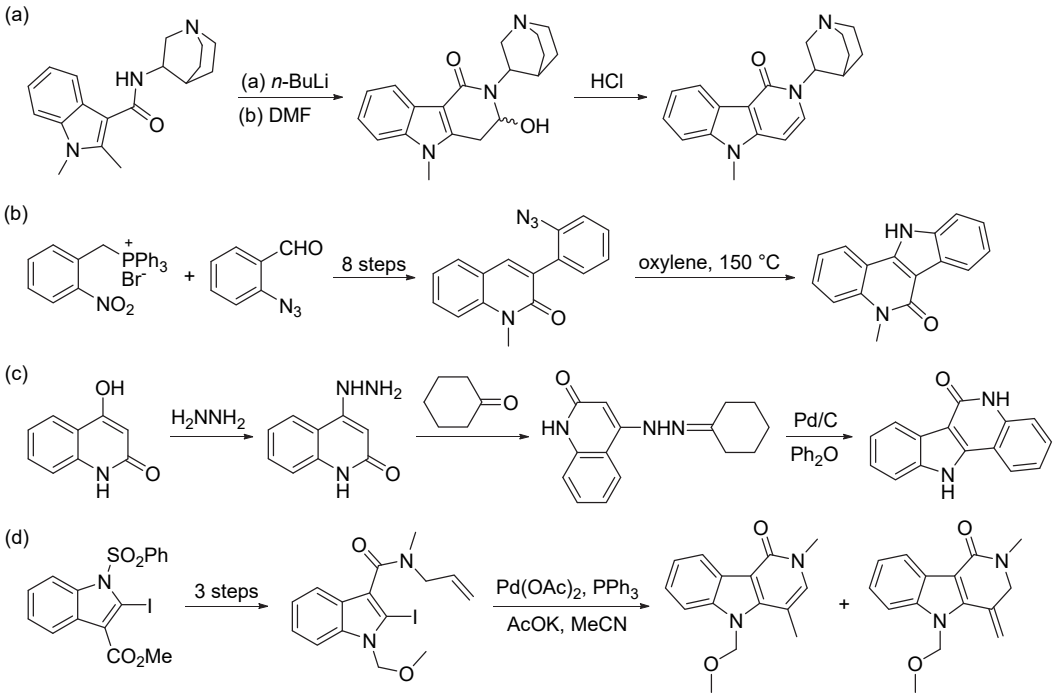
Figure 1 Examples for the application of γ-carbolinone skeleton

喹啉酮, 再与环己酮反应制备腙, 最后在 Pd/C 条件下实现 γ-咔啉酮化合物的合成(Scheme 1c); 此外, Beccalli 课题组[7]报道了一种基于分子内 Heck 反应合成 γ-咔啉酮化合物的方法(Scheme 1d). 综上所述, 这些方法均需要较长的合成步骤, 而且反应成本较高. 因此, 发展高效、快捷地合成此类化合物的方法具有十分重要的研究价值.

近年来, 过渡金属催化的碳氢键活化反应逐渐成为合成、修饰复杂分子的重要途径, 因此在生物医药、材料科学、药学以及其它行业中有着广泛的应用[8]. 基于该方法, Li 课题组[9]发展了一种基于钯催化吲哚-2-甲酰胺经分子内双 C(sp^2)—H 活化和 1,2-酰基迁移反应制备 γ-咔啉酮的方法(Scheme 2a); Yao 和 Lin 课题组[10]报道了一种钯催化吲哚-3-甲酰胺与碘苯经过两次碳氢键活化反应合成目标化合物的方法(Scheme 2b); 此外, Jiao 课题组[11]报道了钯催化吲哚-3-甲酰胺与内炔经[4+2]环加成反应制备 γ-咔啉酮(Scheme 2c). 此后, Zhang 课题组[12]开发了基于铜催化双导向基辅助的吲哚-3-甲酰胺与苯炔的[4+2]环化反应制备此类化合物的方法(Scheme 2d). 然而, 上述方法均需要贵金属钯或者使用较大量的铜作为催化剂, 发展廉价金属催化合成 γ-咔啉酮的方法受到化学工作者的青睐. 近期, Liu 和 Zeng 课题组[13]发展了基于廉价金属钴催化双齿配体辅助的吲哚-3-甲酰胺与炔烃经[4+2]环加成反应制备 γ-咔啉酮的方法, 而且研究发现水杨醛作为配体时可以促进反应的进行(Scheme 2e). 基于本课题组及其他课题组在钴催化碳氢键活化反应中的工作基础[14], 我们发展了一种基于钴催化吲哚-3-甲酰胺与二炔、内炔及单炔的[4+2]环加成反应高效合成 γ-咔啉酮化合物的方法, 该方法的优点有: (1)使用廉价金属钴作为催化剂; (2)不需添加配体; (3)使用廉价金属锰作为氧化剂; (4)吲哚氮无需保护基, 降低了反应的成本(Scheme 2f).

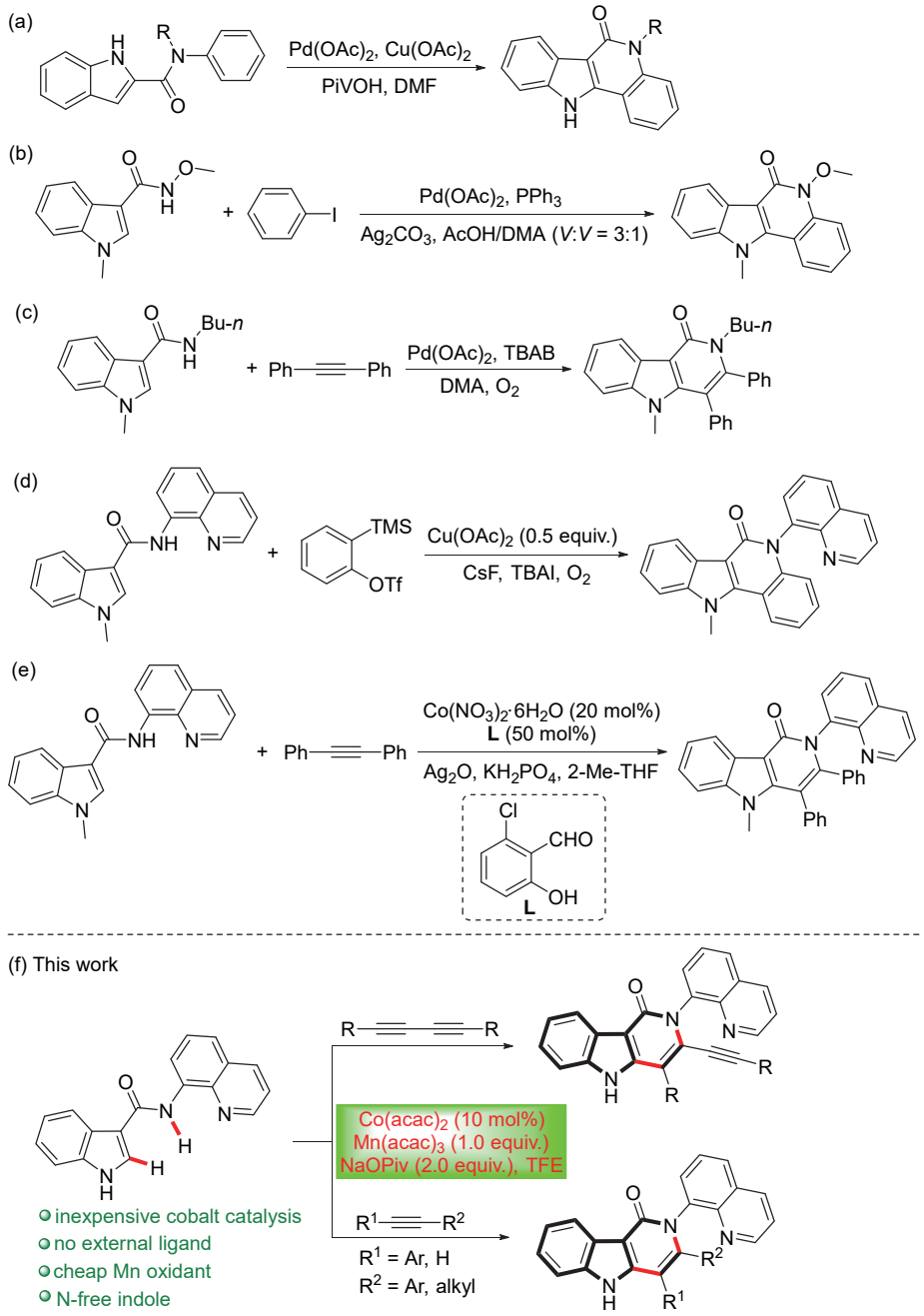
1 结果与讨论

首先, 选用 *N*-(8-喹啉基)-3-吲哚甲酰胺(**1**)与 1,4-二苯基-1,3-丁二炔(**2a**)作为模板反应, 在醋酸钴、乙酸锰、特戊酸钠、三氟乙醇(TFE)、100 ℃的条件下反应 24 h, 结果发现有痕量的产物生成(表 1, Entry 1). 此后, 通过



图式 1 传统合成 γ-咔啉酮化合物的方法

Scheme 1 Traditional synthetic methods for γ-carbolinones



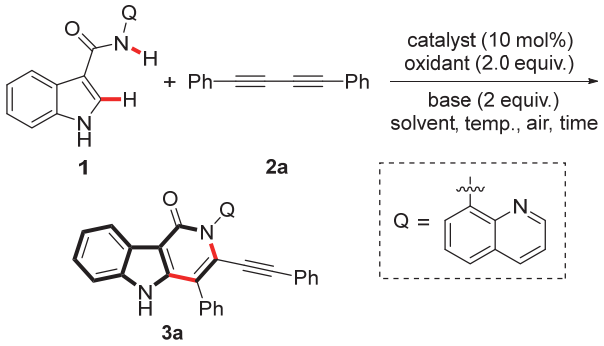
图式 2 基于碳氢键活化反应合成 γ-咔啉酮化合物的方法总结

Scheme 2 A summary of the synthetic methods for γ-carbolinones via C—H activation

对不同钴催化剂的筛选，发现当使用乙酰丙酮钴作为催化剂，其他条件不变时，该反应可以以 76%的产率得到 γ-咔啉酮化合物，而其它钴盐如氯化钴、氟化钴、七水合硫酸钴作为催化剂时，反应产率并未得到明显改善(表 1, Entries 2～5). 在得到最佳催化剂后，进一步对反应所需氧化剂进行了优化. 研究发现以银盐作为氧化剂时的产率均低于乙酸锰(表 1, Entries 6～8). 当使用其它锰盐，如 2.0 equiv.的乙酰丙酮锰作为氧化剂时，反应的产率仅为 42%(表 1, Entry 9)，而当乙酰丙酮锰的用量降低至 1.0 equiv.时，反应的产率提升至 82%(表 1, Entry 10). 继续降低乙酰丙酮锰的用量，反应产率降至 40%(表 1, Entry 11). 而降低乙酸锰的用量会导致反应产率明显下降(表 1, Entry 12). 在此基础上，进一步对反应所需的碱进行了筛选，发现无论是磷酸盐、碳酸盐还是乙酸盐，反应产率均不如特戊酸钠(表 1, Entries 13～18). 通过系列实验考察溶剂包括甲醇、乙醇、六氟异丙醇的影响，结果表明三氟乙醇作为溶剂时效果最好(表 1, Entries 19～21)，而使用非质子性溶剂，如 1,2-二氯乙烷、甲苯时反应微弱(表 1, Entries 22～23). 实验结果表明，降低反应温度不利于目标反应的发生(表 1, Entry

表 1 反应条件优化 [a]

Table 1 Optimization of reaction conditions



Entry	Catalyst	Oxidant	Base	Solvent	Yield[b]/%
1	$Co(OAc)_2$	$Mn(OAc)_2$	NaOPiv	TFE	Trace
2	$CoCl_2$	$Mn(OAc)_2$	NaOPiv	TFE	Trace
3	CoF_2	$Mn(OAc)_2$	NaOPiv	TFE	11
4	$CoSO_4•7H_2O$	$Mn(OAc)_2$	NaOPiv	TFE	20
5	$Co(acac)_2$	$Mn(OAc)_2$	NaOPiv	TFE	76
6	$Co(acac)_2$	AgOAc	NaOPiv	TFE	10
7	$Co(acac)_2$	Ag_2O	NaOPiv	TFE	17
8	$Co(acac)_2$	Ag_2CO_3	NaOPiv	TFE	27
9	$Co(acac)_2$	$Mn(acac)_3$	NaOPiv	TFE	42
10	$Co(acac)_2$	$Mn(acac)_3$	NaOPiv	TFE	82[c]
11	$Co(acac)_2$	$Mn(acac)_3$	NaOPiv	TFE	40[d]
12	$Co(acac)_2$	$Mn(OAc)_2$	NaOPiv	TFE	56[e]
13	$Co(acac)_2$	$Mn(acac)_3$	NaH_2PO_4	TFE	35
14	$Co(acac)_2$	$Mn(acac)_3$	K_2HPO_4	TFE	38
15	$Co(acac)_2$	$Mn(acac)_3$	Na_2CO_3	TFE	56
16	$Co(acac)_2$	$Mn(acac)_3$	$NaHCO_3$	TFE	71
17	$Co(acac)_2$	$Mn(acac)_3$	$KHCO_3$	TFE	57
18	$Co(acac)_2$	$Mn(acac)_3$	NaOAc	TFE	75
19	$Co(acac)_2$	$Mn(acac)_3$	NaOPiv	MeOH	18
20	$Co(acac)_2$	$Mn(acac)_3$	NaOPiv	EtOH	16
21	$Co(acac)_2$	$Mn(acac)_3$	NaOPiv	HFIP	57
22	$Co(acac)_2$	$Mn(acac)_3$	NaOPiv	DCE	Trace
23	$Co(acac)_2$	$Mn(acac)_3$	NaOPiv	Toluene	Trace
24	$Co(acac)_2$	$Mn(acac)_3$	NaOPiv	TFE	80[f]
25	**$Co(acac)_2$**	**$Mn(acac)_3$**	**NaOPiv**	**TFE**	**90[g]**
26	$Co(acac)_2$	$Mn(acac)_3$	NaOPiv	TFE	53[h]

[a] Reaction conditions: **1a** (0.1 mmol, 1.0 equiv.), **2a** (0.2 mmol, 2.0 equiv.), catalyst (10 mol%), oxidant (0.2 mmol, 2.0 equiv.), base (0.2 mmol, 2.0 equiv.), solvent (2.0 mL), air atmosphere, 24 h. [b] Isolated yield. [c] $Mn(acac)_3$ (1.0 equiv.) [d] $Mn(acac)_3$ (0.5 equiv.). [e] $Mn(OAc)_2$ (1.0 equiv.). [f] The temperature was 80 ℃. [g] The temperature was 120 ℃. [h] The temperature was 140 ℃.

24); 升高温度至 120 ℃时反应产率提升到 90%(表 1, Entry 25), 继续升高体系温度反应产率有所下降(表 1, Entry 26). 综上, 确定该反应最佳反应条件为: $Co(acac)_2$ (10 mol%)为催化剂, $Mn(acac)_3$ (1.0 equiv.)为氧化剂, NaOPiv (2.0 equiv.)为碱, TFE (2.0 mL)为溶剂, 120 ℃环境下反应 24 h.

在得到最佳反应条件后, 对各种二炔的底物适用性进行了考察. 首先, 对吲哚-3-甲酰胺(**1**)与 1,4-二芳基-1,3-丁二炔的反应进行了考察(表 2, Entries 1～7). 实验结果表明, 当苯环上有供电子取代基, 如甲基、乙基、叔丁基及甲氧基时反应产率略高于苯环上带有吸电子取代基, 如氟(表 2, Entries 2～7). 其次, 考察了烷基二炔的底物适用性(表 2, Entries 8～12). 研究结果显示, 支链烷基取代的二炔可以以中等收率得到目标产物(**3h**). 烷基氯取代基团的存在并不干扰反应的发生(**3i**). 带有环状结构取代基的二炔, 如 1,4-二环己基取代的二炔可以以 55%的收率得到相应的产物(**3j**). 此外, 当二炔中含有氧时反应不受影响, 仍可以以 53%的收率得到炔基取代的 γ-咔啉酮化合物(**3k**). 值得注意的是, 将反应的氧化剂换为乙酸锰时, 位阻较大的 1,4-二(三甲基硅基)二炔也可以与吲哚-3-甲酰胺(**1**)反应, 并以 63%的收率得到目标化合物 **3l**.

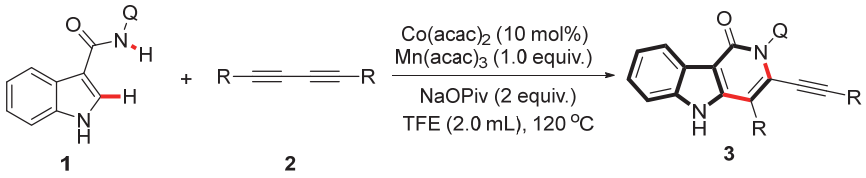
接着, 考察了吲哚-3-甲酰胺与单炔的反应, 如表 3 所示. 实验结果表明, 无论端炔还是内炔作为底物时, 反应条件仍然适用, 可以以中等到良好的收率得到 γ-咔啉酮化合物, 而且芳香炔烃作为底物时, 反应表现明显的电子效应(表 3, Entries 1～7). 供电子取代的苯乙炔, 如甲基、乙基及甲氧基取代苯乙炔反应产率比吸电子苯乙炔, 如氯、氰基和硝基取代苯乙炔产率高(表 3, Entries 2～7). 烷基端炔的产率高于芳基端炔, 但是反应产物有一定的区域选择性, 其原因可能与炔烃的电子效应有关, 如随着链的增长, 反应产率略有下降, 但是选择性提高(表 3, Entries 8～10); 环基炔烃, 如环丙基乙炔、环己基乙炔作为底物时, 反应产率降低, 反应选择性分别为大于 20∶1 和 6∶1(表 3, Entries 11～12). 值得一提的是, 苯基炔丙基醚作为反应底物时, 反应以 48%的产率得到高选择性的产物(表 3, Entries 13). 此外, 内炔, 如 1,2-二苯乙炔、1-苯基-1-丁炔也可以在标准条件下以中等收率得到目标化合物(表 3, Entries 14～15).

为了探究该方法的应用价值, 尝试了克级反应, 如 Scheme 3 所示. 当使用 4 mmol 吲哚-3-甲酰胺与 1,4-二苯基-1,3-丁二炔在标准条件下反应时, 反应仍可以平稳进行, 且以 76%的产率得到 3-炔基取代的 γ-咔啉酮化合物.

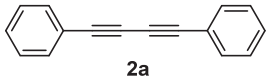
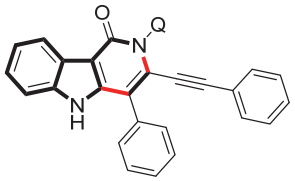
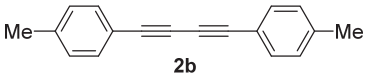
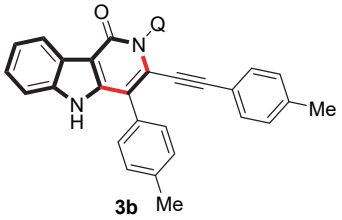
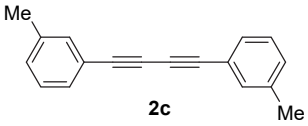
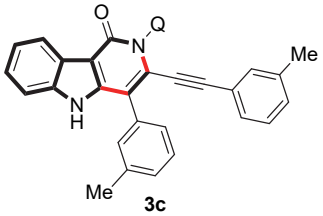
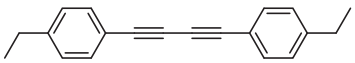
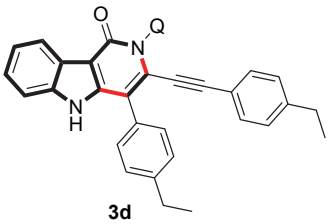
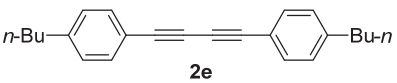
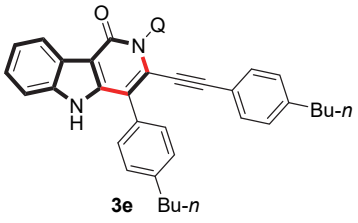
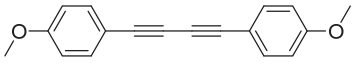
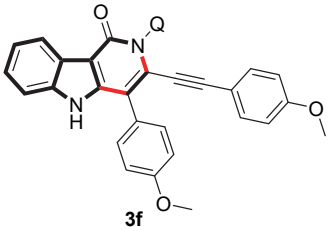
结合钴催化 C-H/N-H[4＋2]环化反应的文献报道及上述实验结果[13,15], 提出了可能的反应机理, 如 Scheme 4 所示. 首先乙酰丙酮钴被三价锰氧化成三价钴, 其与

表 2 二炔底物适用性考察 [a]

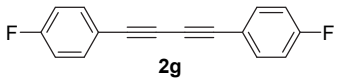
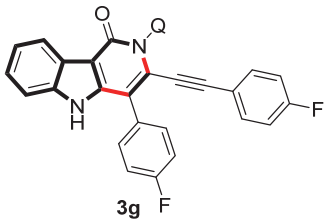
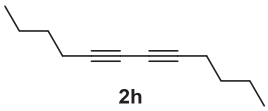
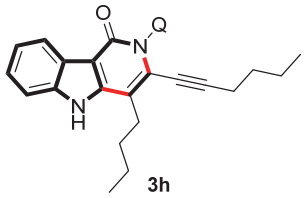
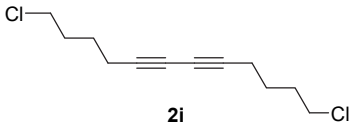
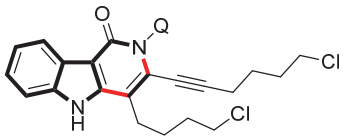
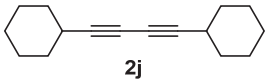
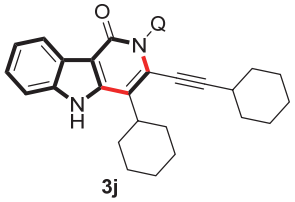
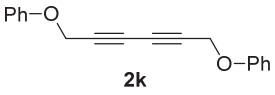
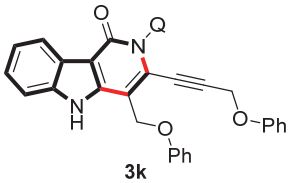
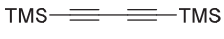
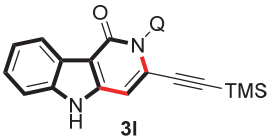
Table 2 Evaluation of the scope of diynes



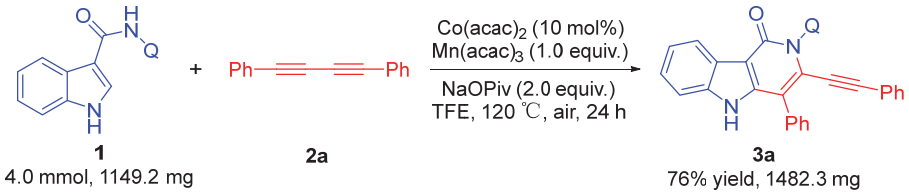
1 **2** **3**

Entry	Substrate **2**	Product **3**	Yield[b]/%
1	 **2a**	 **3a**	90
2	 **2b**	 **3b**	64
3	 **2c**	 **3c**	75
4	 **2d**	 **3d**	86
5	 **2e**	 **3e**	88
6	 **2f**	 **3f**	75

续表

Entry	Substrate **2**	Product **3**	Yield[b]/%
7	 **2g**	 **3g**	58
8	 **2h**	 **3h**	71
9	 **2i**	 **3i**	68
10	 **2j**	 **3j**	55
11	 **2k**	 **3k**	53
12	 **2l**	 **3l**	63[c]

[a] Reaction conditions: **1** (0.1 mmol), **2** (2 equiv.), $Co(acac)_2$ (10 mol%), $Mn(acac)_3$ (1 equiv.), NaOPiv (2 equiv.), TFE (2 mL), 120 ℃, 24 h. [b] Isolated yield. [c] $Mn(OAc)_2$ (2 equiv.), 80 ℃, 3 h.



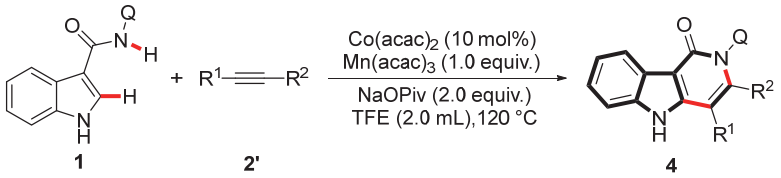
图式 3 克级反应

Scheme 3 Gram reaction

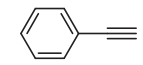
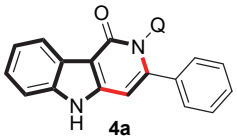
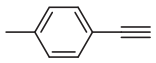
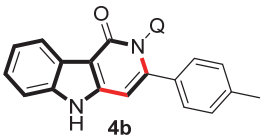
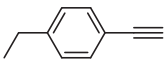
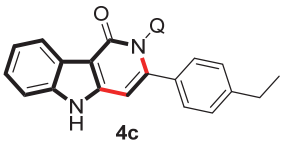
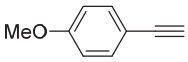
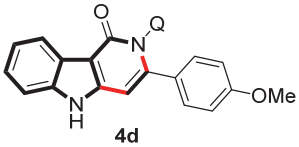
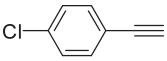
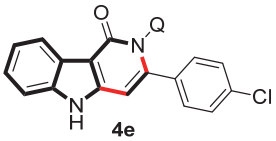
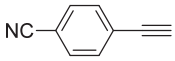
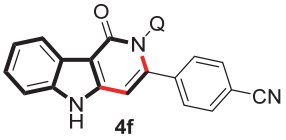
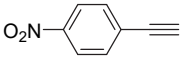
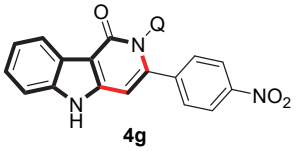
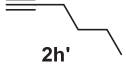
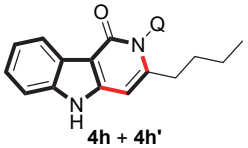
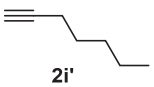
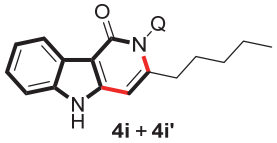
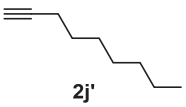
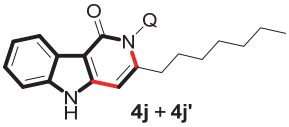
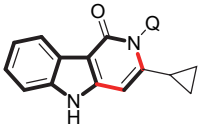
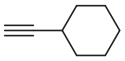
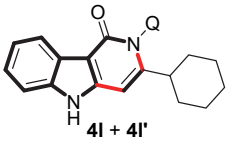
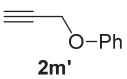
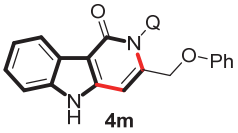
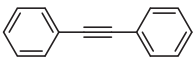
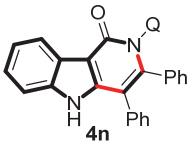
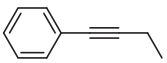
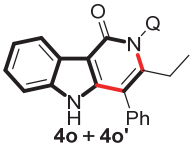
吲哚-3-甲酰胺络合形成中间体 **A**. 中间体 **A** 在碱的作用下, 经过碳氢键活化形成 C—Co 键, 得到中间体 **B**. 中间体 **B** 与炔烃先发生配位形成中间体 **C**, 而后通过插入反应得到中间体 **D**. 中间体 **D** 经过还原消除得到目标产物及一价钴, 一价钴在氧化剂作用下氧化成二价钴完成催化循环.

表 3 单炔底物适用性考察 [a]

Table 3 Evaluation of the scope of monoacetylenes



1 2' 4

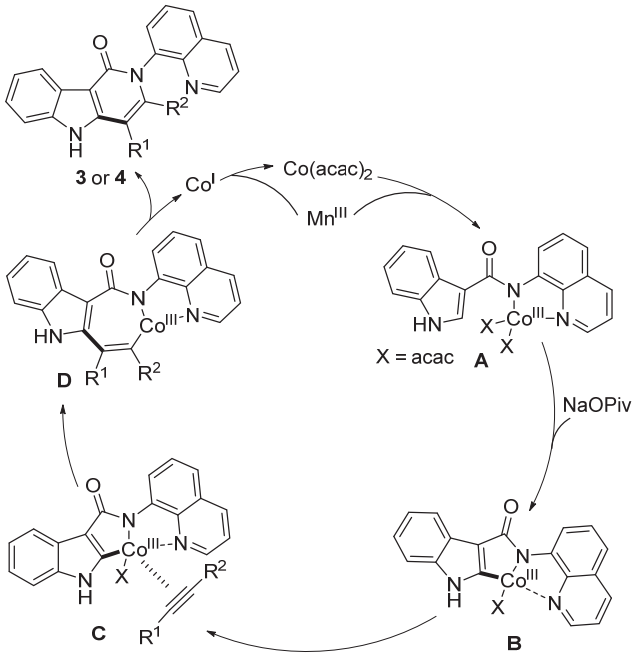
Entry	Substrate 2	Product 4	Yield[b]/%
1	 2a'	 4a	60
2	 2b'	 4b	73
3	 2c'	 4c	65
4	 2d'	 4d	62
5	 2e'	 4e	41
6	 2f'	 4f	32
7	 2g'	 4g	28
8	 2h'	 4h + 4h'	91 (2.5:1)
9	 2i'	 4i + 4i'	88 (6:1)
10	 2j'	 4j + 4j'	83 (6:1)
11	 2k'	 4k + 4k'	51 (>20:1)
12	 2l'	 4l + 4l'	46 (6:1)
13	 2m'	 4m	48 (>20:1)
14	 2n'	 4n	71
15	 2o'	 4o + 4o'	78 (4:1)

[a] Reaction conditions: **1** (0.1 mmol), **2** (2 equiv.), $Co(acac)_2$ (10 mol%), $Mn(acac)_3$ (1 equiv.), NaOPiv (2 equiv.), TFE (2 mL), 120 ℃, 24 h. [b] Isolated yield.

2 结论

综上所述，研究了廉价金属钴催化的吲哚-3-甲酰胺与炔烃的[4＋2]环加成反应. 该反应具有良好的底物适用性，二炔、端炔或内炔均可以以中等到良好的产率得到目标化合物. 而且反应中使用了廉价钴和锰作为催

化剂和氧化剂, 反应条件较温和, 为 γ-咔啉酮化合物的制备提供了一种简便高效的有机合成方法.



图式 4 可能的反应机理
Scheme 4 Plausible reaction mechanism

3 实验部分

3.1 仪器与试剂

除非另有说明, 本反应所使用的玻璃器皿均在烘箱干燥后予以使用. ^{1}H NMR 和 ^{13}C NMR 使用核磁共振仪(Brucker Advance DMX (400 MHz 和 100 MHz)型)进行表征, 内标为 TMS; 熔点用 WRS-1C 在熔点管中进行测定; 高分辨率质谱(HRMS)使用 XEVO G2-XS QTOF/H-CLASS (ESI 源)进行测定; 红外光谱使用 Nicolet-470 傅里叶转换红外光谱仪进行表征. 在薄层色谱(TLC)分析过程中, 使用的是商品化的硅胶板, 用紫外灯(ZF-1, 254 nm, 365 nm)检测化合物荧光. 柱层析所用硅胶为 200～300 目. 所有商品化试剂均购自安耐吉、毕得医药, 不经进一步处理直接使用.

3.2 实验方法

在装有搅拌子的干燥 25 mL 高温耐压管中, 加入 *N*-(喹啉-8-基)-3-吲哚甲酰胺(**1**, 0.1 mmol), 炔烃(0.2 mmol, 2.0 equiv.), 乙酰丙酮钴(II) (0.01 mmol, 10 mol%), 乙酰丙酮锰(III) (0.1 mmol, 1.0 equiv.), 特戊酸钠(0.2 mmol, 2.0 equiv.), 三氟乙醇(2 mL), 于 120 ℃环境下反应 24 h. 反应结束, 冷却至室温, 加入二氯甲烷稀释, 通过硅藻土过滤, 并用二氯甲烷洗涤(5 mL×3). 减压浓缩滤液, 以硅胶为固定相, 丙酮和二氯甲烷为洗脱剂分离得到目标产物.

3.3 产物数据

4-苯基-3-(苯乙炔基)-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**3a**): 44 mg, 90% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.68 (s, 1H), 8.85～8.87 (m, 1H), 8.54～8.56 (m, 1H), 8.22～8.24 (m, 1H), 8.12 (d, J=8.0 Hz, 1H), 7.98～8.01 (m, 1H), 7.84 (t, J=8.0 Hz, 1H), 7.73～7.74 (m, 2H), 7.52～7.64 (m, 5H), 7.35～7.37 (m, 1H), 7.20～7.28 (m, 2H), 7.13～7.15 (m, 2H), 6.34 (d, J=8.0 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 158.6, 151.0, 144.6, 142.3, 138.7, 137.7, 136.4, 133.6, 130.8, 130.5, 130.2, 129.3, 129.1, 128.7, 128.6, 128.4, 126.7, 126.2, 124.5, 124.4, 121.9, 121.2, 120.6, 120.5, 114.9, 112.1, 107.8, 97.8, 84.4; HRMS (ESI$^+$) calcd for $C_{34}H_{22}N_3O$ $[M+H]^+$ 488.1757, found 488.1760.

2-(8-喹啉基)-4-(4-甲基苯基)-3-(4-甲基苯乙炔基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**3b**): 31 mg, 64% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.61 (s, 1H), 8.84 8.86 (m, 1H), 8.53～8.55 (m, 1H), 8.20～8.23 (m, 1H), 8.11 (d, J=8.0 Hz, 1H), 7.96～7.98 (m, 1H), 7.82 (t, J=8.0 Hz, 1H), 7.57～7.62 (m, 4H), 7.42 (d, J=8.0 Hz, 2H), 7.33～7.37 (m, 1H), 7.23～7.27 (m, 1H), 6.96 (d, J=8.0 Hz, 2H), 6.25 (d, J=8.0 Hz, 2H), 2.44 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 158.6, 150.9, 144.6, 143.0, 142.4, 139.2, 138.6, 137.8, 137.6, 136.3, 130.7, 130.6, 130.2, 130.1, 129.6, 129.2, 129.0, 128.7, 126.7, 126.2, 124.4, 121.9, 121.1, 120.4, 117.6, 114.4, 112.1, 107.6, 98.1, 84.0, 20.9 (2C); HRMS (ESI$^+$) calcd for $C_{36}H_{26}N_3O$ $[M+H]^+$ 516.2070, found 516.2072.

2-(8-喹啉基)-4-(3-甲基苯基)-3-(3-甲基苯基乙炔基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**3c**): 39 mg, 75% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.68 (s, 1H), 8.86 (d, J=4.0 Hz, 1H), 8.56 (d, J=12.0 Hz, 1H), 8.23 (d, J=8.0 Hz, 1H), 8.14 (d, J=8.0 Hz, 1H), 7.99 (d, J=8.0 Hz, 1H), 7.83 (t, J=8.0 Hz, 1H), 7.58～7.62 (m, 2H), 7.48～7.55 (m, 3H), 7.34～7.39 (m, 2H), 7.26 (t, J=8.0 Hz, 1H), 7.03 (d, J=8.0 Hz, 2H), 6.17 (t, J=4.0 Hz, 1H), 6.10 (s, 1H), 2.44 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 158.7, 151.0, 144.7, 142.3, 138.7, 137.9, 137.8 (2C), 136.4, 133.5, 131.0, 130.8, 130.7, 130.0, 129.1, 129.0, 128.8, 128.5 (2C), 127.5, 127.3, 126.7, 126.3, 124.5, 124.4, 122.0, 121.2, 120.5 (2C), 114.8, 112.1, 107.8, 98.2, 84.3, 21.2, 20.6; HRMS (ESI$^+$) calcd for $C_{36}H_{26}N_3O$ $[M+H]^+$

516.2070, found 516.2065.

4-(4-乙基苯基)-3-((4-乙基苯基)乙炔基)-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**3d**): 46 mg, 86% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.68 (s, 1H), 8.84～8.85 (m, 1H), 8.54 (dd, J=8.0, 4.0 Hz, 1H), 8.20～8.22 (m, 1H), 8.13 (d, J=8.0 Hz, 1H), 7.95～7.97 (m, 1H), 7.79～7.83 (m, 1H), 7.56～7.65 (m, 4H), 7.43 (d, J=8.0 Hz, 2H), 7.33～7.38 (m, 1H), 7.23～7.27 (m, 1H), 6.97 (d, J=8.3 Hz, 2H), 6.26 (d, J=8.0 Hz, 2H), 2.72 (q, J=16.0 Hz, 8.0 Hz, 2H), 2.44 (q, J=16.0 Hz, 8.0 Hz, 2H), 1.26 (t, J=8.0 Hz, 3H), 1.01 (t, J=8.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 158.7, 151.0, 145.5, 144.7, 143.9, 142.5, 138.7, 137.9, 136.4, 130.9, 130.8, 130.4, 130.3, 129.1, 128.7, 128.1, 128.0, 126.9, 126.3, 124.5, 124.4, 122.0, 121.2, 120.5, 118.0, 114.6, 112.2, 107.7, 98.2, 84.1, 28.1, 28.0, 15.6, 15.1; HRMS (ESI$^+$) calcd for $C_{38}H_{30}N_3O$ [M＋H]$^+$ 544.2383, found 544.2390.

4-(4-丁基苯基)-3-((4-丁基苯基)乙炔基)-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**3e**): 53 mg, 88% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.66 (s, 1H), 8.84～8.86 (m, 1H), 8.52～8.54 (m, 1H), 8.21 (d, J=8.0 Hz, 1H), 8.14 (d, J=8.0 Hz, 1H), 7.95～7.96 (m, 1H), 7.80 (t, J=8.0 Hz, 1H), 7.56～7.64 (m, 4H), 7.34～7.41 (m, 3H), 7.25 (t, J=8.0 Hz, 1H), 6.94 (d, J=8.0 Hz, 2H), 6.26 (d, J=8.0 Hz, 2H), 2.69 (t, J=8.0 Hz, 2H), 2.41 (t, J=8.0 Hz, 2H), 1.60～1.67 (m, 2H), 1.31～1.41 (m, 4H), 1.12～1.18 (m, 2H), 0.92 (t, J=8.0 Hz, 3H), 0.79 (t, J=8.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 158.7, 151.0, 144.7, 144.0, 142.5, 142.4, 138.7, 137.9, 136.4, 130.9, 130.7, 130.3, 130.2, 129.1, 128.7, 128.5, 126.9, 126.2, 124.4, 121.9, 121.2, 120.5, 118.0, 114.7, 112.1, 107.7, 98.2, 84.1, 34.7, 34.6, 33.1, 32.6, 21.7, 21.5, 13.8, 13.7; HRMS (ESI$^+$) calcd for $C_{42}H_{38}N_3O$ [M＋H]$^+$ 600.3009, found 600.3027.

4-(4-甲氧基苯基)-3-((4-甲氧基苯基)乙炔基)-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**3f**): 41 mg, 75% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.63 (s, 1H), 8.86 (d, J=4.0 Hz, 1H), 8.53 (d, J=8.0 Hz, 1H), 8.21 (d, J=8.0 Hz, 1H), 8.15 (d, J=4.0 Hz, 1H), 7.97 (d, J=8.0 Hz, 1H), 7.81 (t, J=8.0 Hz, 1H), 7.67 (d, J=8.0 Hz, 2H), 7.56～7.62 (m, 2H), 7.36 (t, J=8.0 Hz, 1H), 7.26 (t, J=8.0 Hz, 1H), 7.17 (d, J=8.0 Hz, 2H), 6.73 (d, J=8.0 Hz, 2H), 6.34 (d, J=8.0 Hz, 2H), 3.85 (s, 3H), 3.65 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 159.9, 159.2, 158.7, 151.0, 144.7, 142.8, 138.7, 138.0, 136.4, 132.0, 131.7, 130.8, 129.0, 128.7, 127.0, 126.2, 125.7, 124.5, 124.4, 121.9, 121.1, 120.5, 114.4, 114.1, 113.9, 112.6, 112.1, 107.5, 98.4, 83.4, 55.3 (2C); HRMS (ESI$^+$) calcd for $C_{36}H_{26}N_3O_3$ [M＋H]$^+$ 548.1969, found 548.1971.

4-(4-氟苯基)-3-((4-氟苯基)乙炔基)-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**3g**): 30 mg, 58% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.71 (s, 1H), 8.85～8.87 (m, 1H), 8.53～8.56 (m, 1H), 8.22 (dd, J=8.0, 4.0 Hz, 1H), 8.12 (d, J=8.0 Hz, 1H), 7.98～8.00 (m, 1H), 7.83 (d, J=8.0 Hz, 1H), 7.75～7.79 (m, 2H), 7.57～7.61 (m, 2H), 7.42～7.47 (m, 2H), 7.35～7.39 (m, 1H), 7.24～7.28 (m, 1H), 7.02～7.07 (m, 2H), 6.39～6.42 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 163.4, 160.9, 158.6, 151.1, 144.6, 142.3, 138.7, 137.7, 136.4, 132.7, 132.6, 132.5, 130.8, 129.9, 129.6, 129.2, 128.7, 126.7, 126.2, 124.6, 124.4, 122.0, 121.3, 120.5, 117.0, 116.3, 116.0, 115.7, 115.5, 113.9, 112.1, 107.8, 97.0, 83.9; ^{19}F NMR (376 MHz, DMSO) δ: －108.8, －113.4; HRMS (ESI$^+$) calcd for $C_{34}H_{20}F_2N_3O$ [M＋H]$^+$ 524.1569, found 524.1577.

4-丁基-3-(己-1-炔-1-基)-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**3h**): 32 mg, 71% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.96 (s, 1H), 8.78～8.79 (m, 1H), 8.47～8.49 (m, 1H), 8.11～8.13 (m, 1H), 8.05 (d, J=8.0 Hz, 1H), 7.71～7.79 (m, 2H), 7.54～7.60 (m, 2H), 7.35 (t, J=8.0 Hz, 1H), 7.21 (t, J=8.0 Hz, 1H), 2.89 (t, J=8.0 Hz, 2H), 1.94 (t, J=8.0 Hz, 2H), 1.61～1.69 (m, 2H), 1.40～1.49 (m, 2H), 0.93 (t, J=8.0 Hz, 3H), 0.71～0.84 (m, 2H), 0.52～0.67 (m, 5H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 158.8, 150.7, 144.7, 143.7, 138.3, 138.1, 136.3, 130.6, 128.8, 127.3, 126.1, 124.6, 124.1, 121.8, 120.9, 120.5, 112.8, 111.6, 107.1, 100.9, 74.6, 31.6, 29.3, 27.7, 22.1, 20.6, 18.1, 13.9, 13.3. HRMS (ESI$^+$) calcd for $C_{30}H_{30}N_3O$ [M＋H]$^+$ 448.2383, found 448.2390.

4-(4-氯丁基)-3-(6-氯己-1-炔-1 基)-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**3i**): 35 mg, 68% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 12.01 (s, 1H), 8.78～8.79 (m, 1H), 8.48～8.51 (m, 1H), 8.14 (dd, J=8.0, 4.0 Hz, 1H), 8.05 (d, J=8.0 Hz, 1H), 7.72～7.81 (m, 2H), 7.56～7.61 (m, 2H), 7.34～7.40 (m, 1H), 7.22 (t, J=8.0 Hz, 1H), 3.69 (t, J=4.0 Hz, 2H), 3.27～3.29 (m, 2H), 2.93 (t, J=8.0 Hz, 2H),

2.00～2.01 (m, 2H), 1.77～1.90 (m, 4H), 1.22～1.25 (m, 2H), 0.98～1.04 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 158.8, 150.8, 144.6, 143.5, 138.3, 138.0, 136.4, 130.6, 128.9, 128.8, 127.3, 126.2, 124.5, 124.3, 121.9, 121.0, 120.5, 112.4, 111.6, 107.2, 100.5, 74.8, 45.3, 44.6, 31.8, 30.3, 27.2, 26.6, 24.6, 17.7; HRMS (ESI$^+$) calcd for $C_{30}H_{28}Cl_2N_3O$ [M+H]$^+$ 516.1604, found 516.1600.

4-环己基-3-(环己基乙炔基)-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**3j**): 28 mg, 55% yield. Yellow solid, m.p. 285～286 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.67 (s, 1H), 8.79～8.80 (m, 1H), 8.48 (d, J=8.0 Hz, 1H), 8.09 (dd, J=24.0, 8.0 Hz, 2H), 7.70～7.77 (m, 2H), 7.65 (d, J=8.0 Hz, 1H), 7.56 (dd, J=8.0, 4.0 Hz, 1H), 7.35 (t, J=8.0 Hz, 1H), 7.21 (t, J=8.0 Hz, 1H), 2.18～2.24 (m, 3H), 1.86～1.91 (m, 2H), 1.72～1.75 (m, 3H), 0.78～1.25 (m, 14H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 158.7, 150.7, 144.8, 142.6, 138.3, 136.2, 130.6, 128.8, 128.7, 126.4, 126.1, 124.3, 124.2, 121.7, 120.9, 120.4, 117.0, 111.7, 107.7, 105.2, 79.2, 75.5, 30.7, 29.9, 29.0, 28.1, 26.9, 25.1, 23.2, 23.1; HRMS (ESI$^+$) calcd for $C_{34}H_{34}N_3O$ [M+H]$^+$ 500.2696, found 500.2698.

4-(苯氧基甲基)-3-(苯氧基丙-1-炔-1-基)-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**3k**): 29 mg, 53% yield. Yellow solid, m.p. 274～275 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 12.21 (s, 1H), 8.75～8.77 (m, 1H), 8.47～8.49 (m, 1H), 8.10～8.13 (m, 1H), 8.07 (d, J=8.0 Hz, 1H), 7.82～7.84 (m, 1H), 7.70 (t, J=8.0 Hz, 1H), 7.55～7.62 (m, 2H), 7.31～7.40 (m, 3H), 7.25 (t, J=8.0 Hz, 1H), 7.05～7.10 (m, 4H), 7.00 (t, J=8.0 Hz, 1H), 6.88 (t, J=8.0 Hz, 1H), 6.45 (d, J=8.0 Hz, 2H), 5.33 (s, 2H), 4.50 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 158.7, 158.5, 156.7, 150.9, 144.3, 142.6, 138.5, 137.1, 136.4, 130.5, 129.5, 129.3, 128.6, 128.4, 126.1, 124.7, 124.1, 121.9, 121.2, 121.1, 120.9, 120.5, 114.9, 114.3, 111.9, 109.0, 107.8, 95.9, 78.8, 64.0, 55.0 (2C); HRMS (ESI$^+$) calcd for $C_{36}H_{26}N_3O_3$ [M + H]$^+$ 548.1969, found 548.1971.

2-(8-喹啉基)-3-((三甲基硅基)乙炔基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**3l**): 26 mg, 63% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 12.02 (s, 1H), 8.80～8.82 (m, 1H), 8.51 (d, J=8.0 Hz, 1H), 8.16 (d, J=8.0 Hz, 1H), 8.04 (d, J=8.0 Hz, 1H), 7.82～7.85 (m, 1H), 7.76 (t, J=8.0 Hz, 1H), 7.58～61 (m, 2H), 7.36 (t, J=8.0 Hz, 1H), 7.23 (t, J=8.0 Hz, 1H), 7.03 (s, 1H), －0.35 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 159.0, 150.7, 144.7, 142.7, 138.2, 137.2, 136.2, 130.6, 129.0, 128.7, 128.5, 126.0, 124.4, 124.1, 121.8, 121.0, 120.4, 111.7, 108.1, 101.4, 100.7, 99.3, －1.1; HRMS (ESI$^+$) calcd for $C_{25}H_{22}N_3OSI$ [M+H]$^+$ 408.1527, found 408.1530.

3-苯基-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**4a**): 23 mg, 60% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.97 (s, 1H), 8.84 (d, J=4.0 Hz, 1H), 8.30 (d, J=8.0 Hz, 1H), 8.14 (d, J=8.0 Hz, 1H), 7.87 (d, J=8.0 Hz, 1H), 7.74 (d, J=8.0 Hz, 1H), 7.60 (d, J=8.0 Hz, 1H), 7.46～7.52 (m, 2H), 7.36 (t, J=8.0 Hz, 1H), 7.25 (t, J=8.0 Hz, 1H), 7.16 (d, J=8.0 Hz, 2H), 6.97～7.06 (m, 3H), 6.66 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 159.6, 150.6, 147.8, 144.6, 144.1, 137.9, 137.1, 136.5, 136.2, 131.6, 128.6 (2C) , 128.3, 128.1, 127.2, 125.7, 124.4, 123.8, 121.7, 120.8, 120.3, 111.5, 105.8, 96.3; HRMS (ESI$^+$) calcd for $C_{26}H_{18}N_3O$ [M+H]$^+$ 388.1444, found 388.1448.

3-(4-甲基苯基)-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**4b**): 29 mg, 73% yield. White solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.90 (s, 1H), 8.82～8.84 (m, 1H), 8.33～8.35 (m, 1H), 8.04 (d, J=8.0 Hz, 1H), 7.89～7.91 (m, 1H), 7.68～7.70 (m, 1H), 7.50～7.58 (m, 3H), 7.33 (t, J=8.0 Hz, 1H), 7.20～7.23 (m, 1H), 7.02 (d, J=8.0 Hz, 2H), 6.80 (d, J=8.0 Hz, 2H), 6.58 (s, 1H), 2.07 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 159.6, 150.6, 147.8, 144.6, 144.1, 137.9, 137.4, 137.2, 136.2, 133.8, 131.6, 128.6, 128.4, 128.3, 127.9, 125.8, 124.4, 123.7, 121.7, 120.7, 120.2, 111.4, 105.6, 96.2, 20.6; HRMS (ESI$^+$) calcd for $C_{27}H_{20}N_3O$ [M+H]$^+$ 402.1601, found 402.1605.

3-(4-乙基苯基)-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**4c**): 27 mg, 65% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.91 (s, 1H), 8.82～8.84 (m, 1H), 8.33～8.36 (m, 1H), 8.03 (d, J=8.0 Hz, 1H), 7.89～7.92 (m, 1H), 7.67～7.69 (m, 1H), 7.50～7.58 (m, 3H), 7.30～7.35 (m, 1H), 7.21 (t, J=8.0 Hz, 1H), 7.04 (d, J=8.0 Hz, 2H), 6.84 (d, J=8.0 Hz, 2H), 6.60 (s, 1H), 2.38 (q, J=16.0 Hz, 8.0 Hz, 2H), 0.99 (t, J=8.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 159.6, 150.7, 147.8, 144.6, 144.1, 143.6, 137.9, 137.2, 136.3, 134.0, 131.5, 128.6, 128.5, 128.3, 126.7, 125.8, 124.4, 123.7, 121.7, 120.8, 120.2, 111.5, 105.6, 96.2, 27.6, 15.1; HRMS (ESI$^+$) calcd for $C_{28}H_{22}N_3O$ [M+H]$^+$ 416.1757, found 416.1750.

3-(4-甲氧基苯基)-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**4d**): 25.8 mg, 62% yield. White solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.87 (s, 1H), 8.81～8.83 (m, 1H), 8.34～8.37 (m, 1H), 8.01～8.03 (m, 1H), 7.91～7.93 (m, 1H), 7.68～7.70 (m, 1H), 7.51～7.58 (m, 3H), 7.30～7.35 (m, 1H), 7.18～7.23 (m, 1H), 7.03～7.07 (m, 2H), 6.53～6.58 (m, 3H), 3.57 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 159.6, 158.7, 150.6, 147.6, 144.1, 137.8, 136.2, 131.6, 129.9, 128.9, 128.5, 128.3, 125.8, 124.4, 123.7, 121.7, 120.7, 120.2, 112.7, 111.4, 105.5, 96.2, 54.9; HRMS (ESI$^+$) calcd for $C_{27}H_{20}N_3O_2$ [M＋H]$^+$ 418.1550, found 418.1557.

3-(4-氯苯基)-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**4e**): 17 mg, 41% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.95 (s, 1H), 8.81～8.83 (m, 1H), 8.34～8.37 (m, 1H), 8.04 (d, *J*＝8.0 Hz, 1H), 7.93 (dd, *J*＝8.0, 4.0 Hz, 1H), 7.75～7.77 (m, 1H), 7.56～7.59 (m, 2H), 7.51～7.54 (m, 1H), 7.32～7.36 (m, 1H), 7.20～7.24 (m, 1H), 7.14～7.18 (m, 2H), 7.05～7.09 (m, 2H), 6.64 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 159.4, 150.7, 146.4, 144.3, 143.8, 137.9, 136.7, 136.2, 135.3, 132.8, 131.7, 130.4, 128.7, 128.3, 127.3, 125.8, 124.3, 123.8, 121.8, 120.8, 120.3, 111.5, 105.8, 96.4; HRMS (ESI$^+$) calcd for $C_{26}H_{17}ClN_3O$ [M＋H]$^+$ 422.1055, found 422.1048.

4-(1-氧-2(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-3-基)苯甲腈(**4f**): 13 mg, 32% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 12.35 (s, 1H), 8.81～8.83 (m, 1H), 8.34～8.36 (m, 1H), 8.05 (d, *J*＝8.0 Hz, 1H), 7.92～7.95 (m, 1H), 7.81～7.83 (m, 1H), 7.48～7.61 (m, 5H), 7.32～7.36 (m, 3H), 7.20～7.24 (m, 1H), 6.72 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 159.4, 150.9, 145.8, 144.2, 143.7, 141.0, 138.0, 136.4, 136.3, 131.9, 131.2, 129.6, 128.9, 128.3, 125.8, 124.2, 124.0, 121.9, 120.9, 120.4, 118.2, 111.7, 110.7, 106.0, 96.9; HRMS (ESI$^+$) calcd for $C_{27}H_{17}N_4O$ [M＋H]$^+$ 413.1397, found 413.1402.

3-(4-硝基苯基)-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**4g**): 12 mg, 28% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 12.04 (s, 1H), 8.82～8.84 (m, 1H), 8.33～8.35 (m, 1H), 8.07 (d, *J*＝8.0 Hz, 1H), 7.93～7.95 (m, 1H), 7.85～7.87 (m, 3H), 7.56～7.61 (m, 2H), 7.52 (dd, *J*＝8.0, 4.0 Hz, 1H), 7.45～7.47 (m, 2H), 7.34～7.38 (m, 1H), 7.24 (t, *J*＝8.0 Hz, 1H), 6.74 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ: 159.3, 150.9, 146.7, 145.5, 144.1, 143.5, 142.8, 137.9, 136.3, 131.9, 130.0, 129.0, 128.3, 125.8, 124.2, 124.1, 122.3, 121.8, 121.0, 120.4, 111.6, 106.2, 97.0; HRMS (ESI$^+$) calcd for $C_{26}H_{17}N_4O_3$ [M＋H]$^+$ 433.1295, found 433.1305.

3-丁基-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**4h**)和 4-丁基-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**4h'**): 33 mg, 91% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.74 (s, 1H), 8.79～8.81 (m, 1H), 8.50～8.53 (m, 1H), 8.13～8.17 (m, 1H), 7.95 (d, *J*＝8.0 Hz, 1H), 7.74～7.87 (m, 3H, **4h**＋**4h'**), 7.57～7.62 (m, 2H, **4h**＋**4h'**), 7.52 (d, *J*＝12.0 Hz, 1H), 7.14～7.23 (m, 4H, **4h**＋**4h'**), 6.57 (s, 1H), 2.25～2.21 (m, 2H, **4h**＋**4h'**), 1.22～1.45 (m, 3H, **4h**＋**4h'**), 0.96～1.05 (m, 2H), 0.54 (t, *J*＝8.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 160.1, 158.9, 151.0, 150.9, 148.2, 144.7, 144.5, 144.4, 143.9, 138.8, 137.8, 137.6, 136.6, 136.4, 136.4, 134.4, 131.0, 129.5, 129.1, 128.8 (2C), 126.3, 124.6, 124.5, 123.6, 123.4, 122.0, 120.7, 120.5, 120.4, 120.0, 111.5, 111.2, 107.5, 106.3, 104.9, 93.5, 33.0, 31.3, 30.0, 27.2, 21.8, 21.4, 13.8, 13.3. HRMS (ESI$^+$) calcd for $C_{24}H_{22}N_3O$ [M＋H]$^+$ 368.1757, found 368.1764.

3-戊基-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**4i**)和 4-戊基-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**4i'**): 33 mg, 88% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.74 (s, 1H), 8.79～81 (m, 1H), 8.50～8.52 (m, 1H), 8.14～8.17 (m, 1H), 7.96 (d, *J*＝8.0 Hz, 1H), 7.74～7.87 (m, 2H), 7.57～7.62 (m, 1H), 7.51 (d, *J*＝8.0 Hz, 1H), 7.14～7.35 (m, 3H, **4i**＋**4i'**), 6.58 (s, 1H), 2.05～2.21 (m, 2H), 1.22～1.40 (m, 3H), 0.84～0.99 (m, 4H), 0.61～0.64 (m, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 160.1, 151.0, 148.2, 144.7, 144.5, 144.4, 143.9, 137.7, 136.6, 136.4, 134.5, 131.0, 129.1, 128.8, 126.3, 124.5, 123.4, 122.0, 120.5, 120.0, 111.2, 105.0, 93.6, 33.4, 30.5, 27.5, 21.5, 13.6; HRMS (ESI$^+$) calcd for $C_{25}H_{24}N_3O$ [M＋H]$^+$ 382.1914, found 382.1916.

3-庚基-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**4j**)和 4-庚基-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**4j'**): 34 mg, 83% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.74 (s, 1H), 8.79～8.81 (m, 1H), 8.50～8.52 (m, 1H), 8.13～8.16 (m, 1H), 7.95 (d, *J*＝8.0 Hz, 1H), 7.74～7.87 (m, 3H, **4j**＋**4j'**), 7.57～7.62 (m, 1H), 7.51 (d, *J*＝8.0 Hz, 1H), 7.14～7.35 (m, 2H, **4j**＋**4j'**), 6.57 (s, 1H), 2.06～2.21 (m,

2H), 1.21～1.35 (m, 3H), 1.03～1.10 (m, 2H), 0.80～1.00 (m, 7H, **4j**+**4j'**), 0.74 (t, *J*=8.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 160.0, 151.0, 148.2, 144.7, 144.5, 137.6, 136.5, 136.4, 131.0, 129.1, 128.8, 126.3, 124.5, 123.4, 122.0, 120.5, 120.0, 111.2, 104.9, 93.6, 33.4, 30.8, 28.2, 27.9, 27.8, 21.9, 13.8; HRMS (ESI$^+$) calcd for $C_{27}H_{28}N_3O$ [M+H]$^+$ 410.2227, found 410.2222.

3-环丙基-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**4k**): 18 mg, 51% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.94 (s, 1H), 8.79～8.80 (m, 1H), 8.48～8.50 (m, 1H), 8.12～8.14 (m, 1H), 7.98 (d, *J*=8.0 Hz, 1H), 7.83～7.85 (m, 1H), 7.75～7.78 (m, 1H), 7.57 (dd, *J*=8.0, 4.0 Hz, 1H), 7.52 (d, *J*=8.0 Hz, 1H), 7.25～7.29 (m, 1H), 7.14～7.18 (m, 1H), 6.46 (s, 1H), 1.12～1.18 (m, 1H), 0.53～0.66 (m, 2H), 0.42～0.49 (m, 1H), 0.23～0.30 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 160.1, 150.9, 149.0, 144.8, 144.6, 137.8, 137.0, 136.5, 130.9, 128.9, 128.8, 126.4, 124.4, 123.4, 121.9, 120.5, 120.0, 111.3, 105.2, 92.0, 15.2, 8.1, 6.7; HRMS (ESI$^+$) calcd for $C_{23}H_{18}N_3O$ [M+H]$^+$ 352.1444, found 352.1447.

3-环己基-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**4l**)和 3-环己基-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**4l'**): 18 mg, 46% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.72 (s, 1H), 8.79～8.80 (m, 1H), 8.50～8.53 (m, 1H), 8.12～8.17 (m, 1H), 7.95 (d, *J*=8.0 Hz, 1H), 7.73～7.86 (m, 2H), 7.58～7.62 (m, 1H), 7.52 (d, *J*=8.0 Hz, 1H), 7.14～7.35 (m, 2H), 6.58 (s, 1H), 1.70～1.97 (m, 3H, **4l**+**4l'**), 1.22～1.61 (m, 8H, **4l**+**4l'**), 1.04～1.15 (m, 1H), 0.61～0.72 (m, 1H), 0.43～0.54 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 159.8, 153.6, 151.0, 144.9, 144.6, 137.8, 136.6, 136.4, 130.8, 129.0, 128.7, 126.3, 124.5, 123.4, 122.0, 120.5, 120.0, 111.2, 105.0, 91.5, 41.6, 33.8, 32.2, 26.1, 26.0, 25.1; HRMS (ESI$^+$) calcd for $C_{26}H_{24}N_3O$ [M+H]$^+$ 394.1914, found 394.1918.

3-(苯氧基甲基)-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶[4,3-*b*]吲哚-1-酮(**4m**): 20 mg, 48% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.94 (s, 1H), 8.85～8.87 (m, 1H), 8.47～8.49 (m, 1H), 8.07～8.09 (m, 1H), 8.03 (d, *J*=8.0 Hz, 1H), 7.91～7.93 (m, 1H), 7.70 (t, *J*=8.0 Hz, 1H), 7.54～7.62 (m, 2H), 7.31～7.35 (m, 1H), 7.12～7.23 (m, 3H), 6.83～6.90 (m, 2H), 6.64 (d, *J*=12.0 Hz, 2H), 4.56 (q, *J*=20.0 Hz, 12 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 159.9, 157.4, 151.1, 144.3, 143.9, 142.2, 137.8, 136.6, 135.2, 131.1, 129.4, 129.3, 128.8, 126.3, 124.3, 123.9, 122.1, 121.1, 120.8, 120.3, 114.5, 111.5, 106.1, 95.1, 66.5; HRMS (ESI$^+$) calcd for $C_{27}H_{20}N_3O_2$ [M+H]$^+$ 418.1550, found 418.1553.

3,4-二苯基-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶并[4,3-*b*]吲哚-1-酮(**4n**): 33 mg, 71% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.37 (s, 1H), 8.88～8.90 (m, 1H), 8.28～30 (m, 1H), 8.17 (d, *J*=8.0 Hz, 1H), 7.82～7.84 (m, 1H), 7.67～7.70 (m, 1H), 7.60 (d, *J*=8.0 Hz, 1H), 7.44～7.52 (m, 2H), 7.32～7.36 (m, 1H), 7.19～7.26 (m, 7H), 6.90 (t, *J*=8.0 Hz, 1H), 6.77～6.80 (m, 1H), 6.68 (d, *J*=8.0 Hz, 1H), 6.54 (t, *J*=8.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 159.1, 150.5, 144.8, 144.6, 144.0, 138.3, 137.4, 136.1, 134.5, 134.4, 131.6, 131.1, 130.9, 129.2, 128.4, 128.2, 127.4, 127.1, 126.7, 126.2, 125.7, 124.6, 123.8, 121.6, 120.9, 120.4, 112.0, 109.4, 106.0; HRMS (ESI$^+$) calcd for $C_{32}H_{22}N_3O$ [M+H]$^+$ 464.1757, found 464.1766.

3-乙基-4-苯基-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶[4,3-*b*]吲哚-1-酮(**4o**)和 4-乙基-5-苯基-2-(8-喹啉基)-2,5-二氢-1*H*-吡啶[4,3-*b*]吲哚-1-酮(**4o'**): 32 mg, 78% yield. Yellow solid, m.p.＞300 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.95 (s, 1H), 8.83～8.87 (m, 1H), 8.28 (d, *J*=8.0 Hz, 1H), 8.08 (d, *J*=8.0 Hz, 1H), 7.77～7.81 (m, 1H), 7.57～7.63 (m, 3H, **4o**+**4o'**), 7.41～7.54 (m, 3H, **4o**+**4o'**), 7.33～7.37 (m, 2H), 7.15～7.28 (m, 3H, **4o**+**4o'**), 6.98～7.03 (m, 1H), 6.76～6.78 (m, 2H), 2.40～2.46 (m, 2H), 1.08 (t, *J*=8.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO) δ: 159.6, 158.9, 151.1, 150.4, 146.2, 144.5, 144.5, 144.3, 143.8, 138.1, 138.0, 137.6, 137.6, 136.6, 136.5, 136.1, 134.7, 134.5, 131.6, 131.1, 130.7, 130.6, 130.2, 129.6, 129.2, 129.1, 128.8, 128.3, 128.2, 128.0, 127.9, 127.4, 126.8, 126.2, 125.6, 124.6, 124.6, 124.5, 123.7, 123.4, 122.0, 121.6, 120.7, 120.3, 120.0, 111.7, 111.5, 108.4, 108.1, 106.1, 106.1, 104.9, 24.0, 20.5, 14.7, 13.8; HRMS (ESI$^+$) calcd for $C_{28}H_{22}N_3O$ [M+H]$^+$ 416.1757, found:416.1750.

辅助材料(Supporting Information) 化合物 **3a**～**3l**, **4a**～**4o** 的核磁共振氢谱和碳谱图. 这些材料可以免费从本刊网站(http://sioc-journal.cn/)上下载.

References

[1] (a) Larsen, L. K.; Moore, R. E.; Patterson, G. M. L. *J. Nat. Prod.* **1994**, *57*, 419.
(b) Mouaddib, A.; Joseph, B.; Hasnaoui, A.; Merour, J.-Y. *Synthesis* **2000**, 549.

(c) Jimenez, C.; Quinoa, E.; Adamczeski, M.; Hunter, L. M.; Crews, P. *J. Org. Chem.* **1991**, *56*, 3403.
(d) Griebel, G.; Perrault, G.; Simiand, J.; Cohen, C.; Granger, P.; Depoortere, H.; Françon, D.; Avenet, P.; Schoemaker, H.; Evanno, Y.; Sevrin, M.; George, P.; Scatton, B. *CNS Drug Rev.* **2003**, *9*,3.
[2] Clark, R. D.; Miller, A. B.; Berger, J.; Repke, D. B.; Weinhardt, K. K.; Kowalczyk, B. A.; Eglen, R. M.; Bonhaus, D. W.; Lee, C.-H.; Michel, A. D.; Smith, W. L.; Wong, E. H. F. *J. Med. Chem.* **1993**, *36*, 2645.
[3] Fukuda, T.; Matsuo, Y.; Matsuoka, F.; Yoshioka, N.; Onodera, G.; Kimura, M.; Ishibashi, F.; Iwao, M. *Heterocycles* **2019**, *99*, 1032.
[4] Parvatkar, P. T.; Parameswaran, P. S.; Tilve, S. G. *Curr. Org. Chem.* **2011**, *15*, 1036.
[5] Fresneda, P.; Molina, P.; Delgado, S. *Tetrahedron* **2001**, *57*, 6197.
[6] Chen, Y.-L.; Chung C.-H.; Chen, I.-L.; Chen P.-H.; Jeng, H.-Y. *Bioorg. Med. Chem.* **2002**, *10*, 2705.
[7] Beccalli, E. M.; Broggini, G.; Marchesini, A.; Rossi, E. *Tetrahedron* **2002**, *58*, 6673.
[8] (a) Pan, S.; Sarkar, S.; Ghosh, B. Sammanta, R. *Org. Biomol. Chem.* **2021**, *19*, 10516.
(b) Jacob, C.; Maes, B. U. W.; Evano, G. *Chem.-Eur. J.* **2021**, *27*, 13899.
(c) Santhoshkumar, R.; Cheng, C.-H. *Chem.-Eur. J.* **2019**, *25*, 9366.
(d) Chen, Z.; Wang, B.; Zhang, J.; Yu, W.; Liu, Z.; Zhang, Y. *Org. Chem. Front.* **2015**, *2*, 1107.
[9] Kong, L.; Zheng, Z.; Tang, R.; Wang, M.; Sun, Y.; Li, Y. *Org. Lett.* **2018**, *20*, 5696.
[10] Chen, X.; Sun, P.; Xu, J.; Wu, X.; Kong, L.; Yao, H.; Lin, A. *Tetrahedron Lett.* **2014**, *55*, 7114.
[11] Shi, Z.; Cui, Y.; Jiao, N. *Org. Lett.* **2010**, *12*, 2908.
[12] Zhang, T.-Y.; Liu, C.; Chen, C.; Liu, J.-X.; Xiang, H.-Y.; Jiang, W.; Ding, T.-M.; Zhang, S.-Y. *Org. Lett.* **2018**, *20*, 220.
[13] Huang, M.-G.; Shi S.; Li, M.; Liu, Y.-J.; Zeng, M.-H. *Org. Lett.* **2021**, *23*, 7094.
[14] (a) Gao, Y.; Zhang, M.; Wang, C.; Yang, Z.; Huang, X.; Feng, R.; Qi, C. *Chem. Commun.* **2020**, *56*, 14231.
(b) Zhang, M.; Yang, Z.; Li, R.; Huang, X.; Feng, R.; Qi, C. *Tetrahedron Lett.* **2020**, *61*, 151592.
(c) Zhang, M.; Li, R.; Yang, Z.; Feng, R. *Chin. J. Org. Chem.* **2020**, *40*, 714 (in Chinese).
(张梦帆, 李瑞鹏, 杨震, 冯若昆, 有机化学, **2020**, *40*, 714.)
(d) Wang, C.; Bei, W.; Li, W.; Wang, D.; Liu, Y.; Gong, Z.; Zeng, K.; Feng, R.; Huang, X.; Qi, C. *Tetrahedron Lett.* **2022**, *106*, 154062.
(e) Wang, C.; Dong, S.; Zhu, T.; Liu, Y.; Wu, Z.; Feng, R. *Chin. J. Org. Chem.* **2022**, *42*, 1799 (in Chinese).
(王朝彧, 董书达, 朱天阳, 刘玉琴, 武梓涵, 冯若昆, 有机化学, **2022**, *42*, 1799.)
(e) Yu, Y.; Xia, Z.; Wu, Q.; Liu, D.; Yu, L.; Xiao, Y.; Tan, Z.; Deng, W.; Zhu, G. *Chin. Chem. Lett.* **2021**, *32*, 1263.
(f) Zhang, H.; Xiao, Q.; Qi, X.-K.; Gao, X.-W.; Tong, Q.-X.; Zhong, J.-J.; *Chem. Commun.* **2020**, *56*, 12530.
(g) Xiao, Q.; Zhang, H.; Li, J.-H.; Jian J.-X.; Tong, Q.-X.; Zhong, J.-J. *Org. Lett.* **2021**, *23*, 3604.
(h) Xiao, Y.; Zhu, C.-M.; Liang, R.-B.; Huang, Y.-L.; Hai, C.-H.; Chen, J.-R.; Li, M.; Zhong, J.-J.; Huang, X.-C. *Chem. Commun.* **2023**, *59*, 2239.
(i) Yan, R.; Yu, H.; Wang, Z.-X. *Chin. J. Chem.* **2021**, *39*, 1205.
(j) Zhu, D.; Zhao, Y.; Chong, Q.; Meng, F. *Chin. J. Chem.* **2022**, *40*, 190.
[15] (a) Liu, J.; Xiao, X.; Lai, Y.; Zhang, Z. *Org. Chem. Front.* **2022**, *9*, 2256.
(b) Wang, S.; Yao, L.; Wang, J.-S.; Ying, J.; Wu, X.-F. *Mol. Catal.* **2022**, *524*, 112303.
(c) Zhai, H.; Liu, M.; Wang, C.; Qiu, S.; Wei, J.; Yang, H.; Wu, Y. *J. Org. Chem.* **2021**, *86*, 14915.
(d) Kathiravan, S.; Nicholls, I. A. *Org. Lett.* **2017**, *19*, 4758.
(e) Prakash, S.; Kuppusamy, R.; Cheng, C.-H. *ChemCatChem* **2018**, *10*, 683.
(f) Si, X.-J.; Yang, D.; Sun, M.-C.; Wei, D.; Song, M.-P.; Niu, J.-L. *Nat. Synth.* **2022**, 709.
(g) Kikuchi, J.; Yoshikai, N. *Nat. Synth.* **2022**, 674.
(h) Wang, F.; Li, X. *Chin. J. Org. Chem.* **2022**, *42*, 4350 (in Chinese).
(王芬, 李兴伟, 有机化学, **2022**, *42*, 4350.)
(i) Yao, Q.-J.; Chen, J.-H.; Song, H.; Huang, F.-R.; Shi, B.-F. *Angew. Chem., Int. Ed.* **2022**, *61*, e202202892.

(Cheng, F.)