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钯催化 *N*,*N*-二甲基甲酰胺与胺高效合成甲酰胺

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摘要 报道了一种醋酸钯催化 *N*,*N*-二甲基甲酰胺(DMF)与各类胺高效合成甲酰胺化合物的方法. 该反应体系简单, 具有催化效率高, 不需要其它溶剂及共催化剂, 底物普适范围广的优点, 为合成甲酰胺化合物提供了一种快速, 实用的方法.

关键词 醋酸钯; *N*,*N*-二甲基甲酰胺(DMF); 胺; *N*-甲酰化

Pd-Catalyzed *N*-Formylation of Amines with *N*,*N*-Dimethylformamide

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Abstract A highly efficient protocol for the transamidation of *N*,*N*-dimethylformamide (DMF) and amines has been developed, utilizing a catalytic amount $Pd(OAc)_2$. This methodology has a broad substrate scope for aliphatic, aromatic, and heterocyclic amines. And this process is simple and easily performed without solvent and co-catalyst.

Keywords $Pd(OAc)_2$; *N*,*N*-dimethylformamide (DMF); amines; *N*-formylation

甲酰胺广泛存在于天然产物中, 常是药物的药效官能团, 其衍生物多具有显著的生物活性[1]. 在有机合成反应中,甲酰基是胺类化合物中氨基最有效的保护基团之一[2], 形成的甲酰胺也是合成异氰化合物, 甲脒的重要前体[3]. 另外, 甲酰胺还可作为 Lewis 碱催化剂催化烷基化和硅氢加成反应[4].

早在 1955 年, Fieser 等[5]就成功利用甲酸为原料实现了苯胺的甲酰化. 随后, 各种甲酰化试剂相应被报道, 如三氯乙醛[6], 甲酸铵[7], 甲酸酯[8], 甲酸盐[9]等. 但其中有许多方法存在使用毒性试剂, 反应条件不温和, 底物适应范围小等缺点. *N*,*N*-二甲基甲酰胺(DMF)具有低毒、廉价、易分离等优点, 是一种理想的酰化试剂[10]. 硼试剂在催化胺与 DMF 合成甲酰胺化合物中具有很好的活性, 如 $B(OH)_3$[11], $B(OCH_2CF_3)_3$[12], 苯基硼酸[13]等. 另外, 过渡金属催化剂在该反应中的应用研究也取得了新的进展, 例如 Jagtap 等[14]报道的镍催化剂以及 Guo 等[15]报道的钯催化剂. 虽然这些催化剂都能成功催化转化胺与 DMF 合成甲酰胺化合物, 但这些体系仍存在需要共催化剂, 配体, 反应温度高, 底物普适范围小等问题. 因此, 探究一种高效, 简单的催化体系来实现氨基的甲酰化仍具有重要的意义.

以理想的甲酰化试剂 DMF 为原料, 通过对各种钯催化剂的筛选, 以获得无溶剂, 无共催化剂的简单催化合成甲酰胺的反应体系. 研究表明, 该体系以三乙胺为碱, 在 $Pd(OAc)_2$ 催化下能获得优异的甲酰胺产物收率, 广泛的底物适应范围.

1 结果与讨论

1.1 钯催化剂对胺甲酰化反应活性的影响

首先以 DMF 与 3-(2-氨乙基)吲哚的反应为模板反应, 考察多种钯化合物在胺甲酰化反应中的催化活性, 实验结果如表 1 所示. 不难发现, 在没有其它溶剂及活化剂的条件下, 钯化合物都能成功催化 3-(2-氨乙基)吲哚与 DMF 合成甲酰胺, 其中 $Pd(OAc)_2$ 催化该反应最终能获得 54%的产物分离收率, 而 $Pd(OH)_2$, $PdCl_2$,

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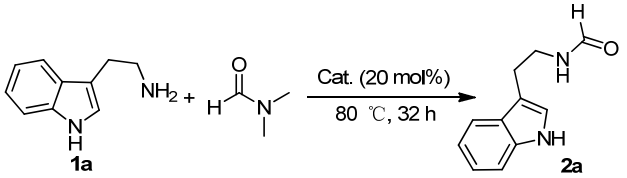
$Pd(NO_3)_2$, $Pd(dppf)Cl_2$, $Pd(COD)Cl_2$, $Pd(acac)_2$, $(Pd(Allyl)Cl)_2$催化3-(2-氨乙基)吲哚与DMF合成甲酰胺的活性都较低. 当将催化剂的用量降低至 10 mol%时, 产物的收率降低至35%(表1, Entry 5). 因此, 我们选择$Pd(OAc)_2$为最优催化剂, 催化剂用量为 20 mol%, 并对反应条件做了进一步筛选.

表 1 钯催化剂对胺甲酰化反应活性的影响

Table 1 Pd-catalyzed *N*-formylation of amine



Entry	Catalyst	Yield[b]/%
1	$Pd(NO_3)_2$	39
2	$Pd(OH)_2$	22
3	$PdCl_2$	33
4	$Pd(OAc)_2$	54
5[c]	$Pd(OAc)_2$	35
6	$Pd(dppf)Cl_2$	30
7	$Pd(COD)Cl_2$	30
8	$Pd(acac)_2$	20
9	$(Pd(Allyl)Cl)_2$	37

[a] Reagents and conditions: 2-(1*H*-indol-3-yl)-ethylamine (1 mmol), catalyst (0.2 mmol). [b] Isolated yield. [c] Catalyst (0.1 mmol).

1.2 碱对胺甲酰化反应活性的影响

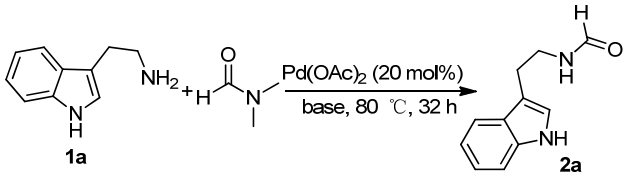
在钯催化反应体系中, 碱是影响催化活性的重要因素. 因此, 我们在该反应体系中考察了多种碱对反应活性的影响, 实验结果如表 2 所示. 从表 2 可见, 碱对$Pd(OAc)_2$催化胺甲酰化反应活性有较大影响, 其中加入K_2CO_3, $Ba(OH)_2$, CH_3COOK, 该反应活性降低; 加入Cs_2CO_3, NEt_3, ethylenediamine, pyridine, 反应活性明显提高. 尤其是当碱为NEt_3时, 产物分离收率能明显提升到 81%. 继续考察 NEt_3 与催化剂的比例对催化活性的影响. 实验结果表明, 当碱/催化剂提高到 4 时, 产物分离收率高达 94%, 但继续提高比例时, 催化活性降低. 因此, 该催化体系的最佳反应条件为: $Pd(OAc)_2$ (20 mol%), NEt_3 (碱/催化剂=4).

1.3 DMF 对胺甲酰化反应活性的影响

通过对催化剂、碱进行筛选后, 我们继续对 DMF 的量进行了考察, 实验结果如表3所示. 从表3可见, 当向体系中加入 1 equiv. DMF 时, 发现能够以 25%的分离产率得到目标产物, 随着 DMF 增加到 8 equiv.时, 产物的分离收率可达到最高为 94%, 继续增加后, 目标产物的产率没有明显变化. 综上所述, 得到最优反应条件为$Pd(OAc)_2$ (20 mol%), NEt_3 (碱/催化剂=4), DMF (8.0 equiv.).

表 2 碱对胺甲酰化反应活性的影响

Table 2 Effect of different bases on the *N*-formylation of amine



Entry	Base	Base/catal.	Yield[b]/%
1	K_2CO_3	2	33
2	Cs_2CO_3	2	60
3	$Ba(OH)_2$	2	38
4	LiOH	2	41
5	CH_3COOK	2	34
6	NEt_3	0	54
7	NEt_3	2	81
8	NEt_3	4	94
9	NEt_3	6	68
10	Ethylenediamine	2	60
11	Pyridine	2	74

[a] Reagents and conditions: 2-(1*H*-Indol-3-yl)-ethylamine (1 mmol), $Pd(OAc)_2$ (0.2 mmol). [b] Isolated yield.

表 3 DMF 对胺甲酰化反应活性的影响

Table 3 Effect of DMF on the *N*-formylation of amine

Entry	DMF/equiv.	Yield[b]/%
1	1	25
2	2	40
3	4	62
4	6	85
5	8	94
6	10	92
7	12	91

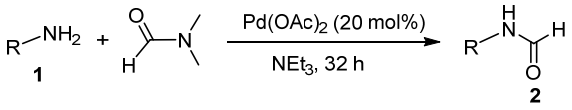
[a] Reagents and conditions: 2-(1*H*-Indol-3-yl)-ethylamine (1 mmol), $Pd(OAc)_2$ (0.2 mmol), NEt_3 (0.8 mmol). [b] Isolated yield.

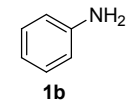
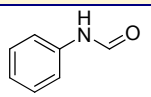
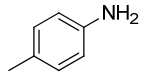
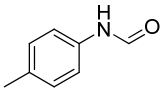
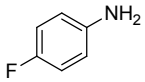
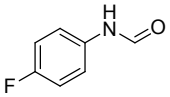
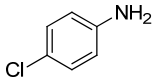
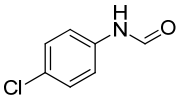
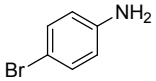
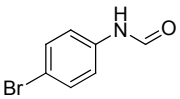
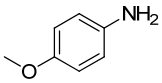
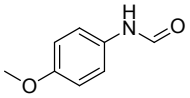
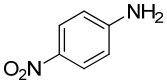
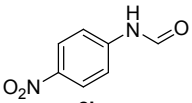
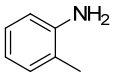
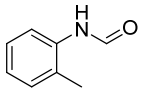
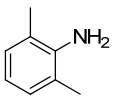
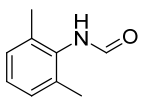
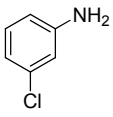
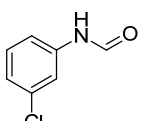
1.4 反应底物的普适性研究

在最优化的反应条件下、为了探究该方法的普遍性和适用范围, 考察了各种胺, 例如芳胺、杂环芳胺、烷基胺等, 在无溶剂条件下, 分别与 DMF 进行反应, 反应结果如表 4 所示. 从表 4 可见, 该体系催化芳香伯胺都具有较好的催化活性(Entries 1～10), 在 80 ℃条件下, 能获得 60%～93%的分离收率, 对位带有吸电子基团或是供电子基团对反应收率都没有较大影响. 但当底物含有邻位取代基时, 由于较大的空间位阻, 使反应收率降低(Entries 8, 9). 该体系催化芳香仲胺时需要较高的温度, 在 140 ℃条件下, 最高能达 75%分离收率, 可见仲胺的活性要明显低于伯胺. 随后考察了烷基胺在该体系中的普适性, 从 Entries 13～17 可见, 在 140 ℃条件下, 能获得 78%～93%的分离收率. 杂环芳胺在该体系催化

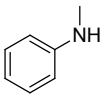
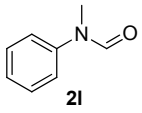
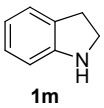
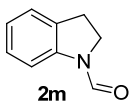
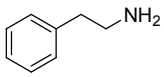
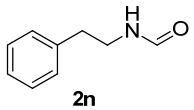
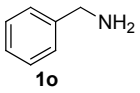
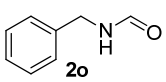
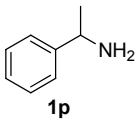
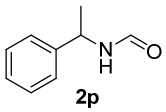
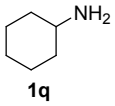
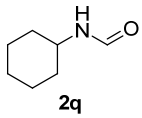
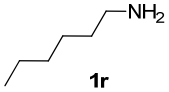
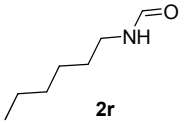
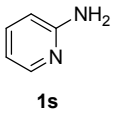
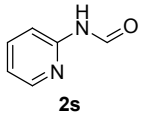
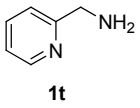
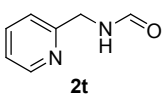
表 4 醋酸钯催化胺甲酰化反应

Table 4 $Pd(OAc)_2$-catalyzed *N*-formylation of amines



Entry	Substrate	Product	Temp./℃	Yield[b]/%
1	 **1b**	 **2b**	80	89
2	 **1c**	 **2c**	80	92
3	 **1d**	 **2d**	80	93
4	 **1e**	 **2e**	80	91
5	 **1f**	 **2f**	80	90
6	 **1g**	 **2g**	80	85
7	 **1h**	 **2h**	80	88
8	 **1i**	 **2i**	80	72
9	 **1j**	 **2j**	80	60
10	 **1k**	 **2k**	80	75

续表

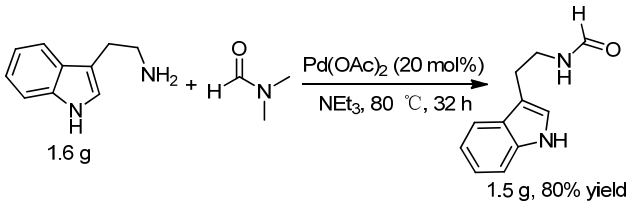
Entry	Substrate	Product	Temp./℃	Yield[b]/%
11	 **1l**	 **2l**	140	64
12	 **1m**	 **2m**	140	75
13	 **1n**	 **2n**	140	93
14	 **1o**	 **2o**	140	89
15	 **1p**	 **2p**	140	85
16	 **1q**	 **2q**	140	78
17	 **1r**	 **2r**	140	83
18	 **1s**	 **2s**	120	82
19	 **1t**	 **2t**	120	87

[a] Reagents and conditions: amines (1 mmol), $Pd(OAc)_2$ (0.2 mmol), NEt_3 (0.8 mmol), 32 h. [b] Isolated yield.

下也能获得最高 87%的分离收率. 最后为了考察该催化体系的实际应用价值, 我们做了放大实验, 如 Scheme 1 所示. 当 3-(2-氨乙基)吲哚的量增加至 10 mol 时, 最终能达到 80%的产物收率.

2 结论

综上所述, 通过对金属钯、碱的筛选, 发现了一种在无溶剂条件下使用 $Pd(OAc)_2$ 作催化剂, 三乙胺作碱, 催化 DMF 和各类胺进行氨基甲酰化反应的方法. 该方法具有催化体系简单、产率高、适用范围广等优点, 为



图式 1 克级甲酰化反应
Scheme 1 Gram scale *N*-formylation reaction

催化胺甲酰化反应合成甲酰胺化合物提供了一条新的途径.

3 实验部分

3.1 仪器与试剂

除特别说明外, 所用试剂均为化学纯或分析纯. 实验所用试剂均购于 Adamas 试剂公司. 熔点测定使用河南省予华仪器有限公司 X-5 型显微熔点仪; 核磁共振氢谱采用 JEOL NMR 400 型核磁共振仪测定, DMSO-d_6 为溶剂; 质谱采用 LCO Advantage 型质谱仪测定.

3.2 实验方法

在 10 mL 的反应试管中, 加入胺(1.0 mmo1)、醋酸钯(0.2 mmol)、三乙胺(0.8 mmol)、DMF (8.0 mmol), 搅拌使其混合均匀, 继续在设定温度下搅拌一定时间, 用薄层层析色谱法(TLC)监测. 反应完全后, 加入 10 mL 水, 搅拌, 乙酸乙酯(10 mL×3), 萃取, 分液, 收集有机相并用无水硫酸钠干燥, 旋蒸, 除去溶剂得粗产品. 然后, 运用柱层层析色谱法进行分离提纯. 目标化合物的结构经 ^{1}H NMR, ^{13}C NMR 和 HRMS 确证.

3.3 产物表征

N-[2-(1*H*-吲哚基-3)-乙基]-甲酰胺(**2a**): 获得产物有两种构象异构体, 比例为 9∶1. 棕色油状物; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.89 (s, 1H), 8.15 (s, 0.9H), 8.07 (s, 0.9H), 7.83 (s, 0.1H), 7.58 (d, J=8.0 Hz, 1H), 7.39 (d, J=4.0 Hz, 1H), 7.21 (s, 1H), 7.09～7.13 (m, 1H), 7.01～7.05 (m, 1H), 5.80 (s, 0.1H), 3.42～3.45 (m, 2H), 2.87～2.91 (m, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 164.96 (minor), 161.59 (major), 136.77 (major), 136.62 (minor), 127.68 (major), 127.63 (minor), 123.59 (minor), 123.25 (major), 121.47 (major), 121.35 (minor), 118.79 (major), 118.75 (major), 118.59 (minor), 118.47 (minor), 112.09 (major), 111.91 (major), 111.71 (minor), 111.54 (minor), 42.29 (minor), 38.56 (major), 27.75 (minor), 25.65 (major); HRMS calcd for $C_{11}H_{12}N_2ONa$ [M+Na$^+$] 211.0847, found 211.0839.

N-苯基甲酰胺(**2b**): 获得产物有两种构象异构体, 比例为 3∶1. 黄色固体, m.p. 47～48 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.18 (s, 1H), 8.80 (d, J=6.0 Hz, 0.25H), 8.30 (s, 0.75H), 7.61 (d, J=4.0 Hz, 1.5H), 7.31～7.34 (m, 2H), 7.21 (d, J=4.0 Hz, 0.5H), 7.06～7.09 (m, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 163.05 (minor), 160.10 (major), 138.86 (minor), 138.78 (major), 129.91 (minor), 129.38 (major), 124.15 (minor), 124.11 (major), 119.65 (major), 118.02 (minor); HRMS calcd for C_7H_7NO-Na [M+Na$^+$] 144.0425, found 144.0424.

N-(4-甲基苯基)甲酰胺(**2c**): 获得产物有两种构象异构体, 比例为 3∶1. 白色固体, m.p. 47～49 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.09 (s, 1H), 8.73 (d, J=6.0 Hz, 0.25H), 8.26 (s, 0.75H), 7.50 (d, J=6.0 Hz, 1.5H), 7.12 (d, J=4.0 Hz, 2H), 7.09 (d, J=4.0 Hz, 0.5H), 2.26 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 162.97 (minor), 159.84 (major), 136.45 (minor), 136.30 (major), 133.22 (minor), 133.04 (major), 130.29 (minor), 129.73 (major), 119.62 (major), 118.20 (minor), 20.96 (major), 20.82 (minor); HRMS calcd for C_8H_9NONa [M+Na$^+$] 158.0582, found 158.0580.

N-(4-氟苯基)甲酰胺(**2d**): 获得产物有两种构象异构体, 比例为3∶1. 白色固体, m.p. 62～64 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.18 (s, 0.75H), 10.09 (d, J=4.0 Hz, 0.25H), 8.65 (d, J=6.0 Hz, 0.25H), 8.22 (s, 0.75H), 7.57 (d, J=8.0 Hz, 1.5H), 7.16～7.19 (m, 0.5H), 7.08～7.13 (m, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 163.21 (minor), 159.99 (major), 158.08 (minor), 157.45 (major), 135.29 (minor), 135.20 (major), 121.36 (major), 120.04 (minor), 116.63 (minor), 116.04 (major); HRMS calcd for C_7H_6FNONa [M+Na$^+$] 162.0331, found 162.0324.

N-(4-氯苯基)甲酰胺(**2e**): 获得产物有两种构象异构体, 比例为 4∶1. 白色固体, m.p. 100～102 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.27 (s, 0.8H), 10.18 (d, J=4.0 Hz, 0.2H), 8.75 (d, J=6.0 Hz, 0.2H), 8.25 (s, 0.8H), 7.58 (d, J=4.0 Hz, 1.6H), 7.32 (d, J=4.0 Hz, 2H), 7.17 (d, J=4.0 Hz, 0.4H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 163.04 (minor), 160.22 (major), 137.91 (minor), 137.67 (major), 129.73 (minor), 129.26 (major), 127.98 (minor), 127.67 (major), 121.20 (major), 119.47 (minor); HRMS calcd for $C_7H_6ClNONa$ [M+Na$^+$] 178.0036, found 178.0036.

N-(4-溴苯基)甲酰胺(**2f**): 获得产物有两种构象异构体, 比例为 4∶1. 白色固体, m.p. 113～115 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.29 (s, 0.8H), 10.19 (d, J=6.0 Hz, 0.2H), 8.79 (d, J=6.0 Hz, 0.2H), 8.30 (s,

0.8H), 7.57 (d, J=4.0 Hz, 1.6H), 7.49 (d, J=6.0 Hz, 2H), 7.16 (d, J=4.0 Hz, 0.4H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 162.98 (minor), 160.25 (major), 138.33 (minor), 138.06 (major), 132.61 (minor), 132.17 (major), 121.58 (major), 119.83 (minor), 115.90 (minor), 115.69 (major); HRMS calcd for $C_7H_6BrNONa$ [M+Na$^+$] 221.9530, found 221.9514.

N-(4-甲氧基苯基)甲酰胺(**2g**): 获得产物有两种构象异构体, 比例为 3∶1. 白色固体, m.p. 79～80 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.05 (s, 0.75H), 9.99 (d, J=6.0 Hz, 0.25H), 8.61 (d, J=4.0 Hz, 0.25H), 8.22 (s, 0.75H), 7.53 (d, J=4.0 Hz, 1.5H), 7.13 (d, J=4.0 Hz, 0.5H), 6.90 (d, J=4.0 Hz, 2H), 3.72 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 163.11 (minor), 159.58 (major), 156.51 (minor), 155.90 (major), 131.98 (major), 131.79 (minor), 121.10 (major), 120.19 (minor), 115.10 (minor), 114.46 (major), 55.74 (minor), 55.65 (major); HRMS calcd for $C_8H_9O_2NNa$ [M+Na$^+$] 174.0531, found 174.0528.

N-(4-硝基苯基)甲酰胺(**2h**): 获得产物有两种构象异构体, 比例为 3∶1. 淡黄色固体, m.p. 196～198 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.84 (s, 0.75H), 10.74 (s, 0.25H), 9.09 (s, 0.25H), 8.44 (s, 0.75H), 8.25 (d, J=4.0 Hz, 2H), 7.85 (d, J=4.0 Hz, 1.5H), 7.45 (d, J=4.0 Hz, 0.5H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 163.31 (minor), 161.01 (major), 145.48 (minor), 144.72 (major), 143.09 (major), 143.00 (minor), 125.98 (minor), 125.59 (major), 119.51 (major), 117.07 (minor); HRMS [M+Na$^+$] calcd for $C_7H_6O_3N_2Na$ 189.0276, found 189.0278.

N-(2-甲基苯基)甲酰胺(**2i**): 获得产物有两种构象异构体, 比例为 7∶3. 淡黄色固体, m.p. 56～57 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 9.76 (d, J=6.0 Hz, 0.3H), 9.58 (s, 0.7H), 8.42 (d, J=4.0 Hz, 0.3H), 8.30 (s, 0.7H), 7.75 (d, J=4.0 Hz, 0.7H), 7.20～7.23 (m, 1.3H), 7.15 (m, 1H), 7.07～7.09 (m, 0.3H), 7.03～7.05(m, 0.7H), 2.24 (s, 0.9H), 7.22 (s, 2.1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 164.17 (minor), 160.33 (major), 136.74 (minor), 136.17 (major), 131.31 (minor), 130.91 (major), 130.81 (minor), 129.74 (major), 127.28 (minor), 126.63 (major), 125.81 (minor), 125.14 (major), 123.30 (major), 122.33 (minor), 18.36 (major), 18.22 (minor); HRMS calcd for $C_8H_{10}NO$ [M+H$^+$] 136.0762, found 136.0765.

N-(2,6-二甲基苯基)甲酰胺(**2j**): 获得产物有两种构象异构体, 比例为 5∶1. 白色固体, m.p. 158～159 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 9.47 (s, 0.83H), 9.30 (d, J=6.0 Hz, 0.17H), 8.25 (s, 0.83H), 7.98 (d, J=6.0 Hz, 0.17H), 7.11～7.12 (m, 0.5H), 7.05～7.08 (m, 2.5H), 2.21 (s, 1H), 2.15 (s, 5H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 165.22 (minor), 159.87 (major), 135.44 (minor), 135.22 (major), 134.99 (major), 134.53 (minor), 128.81 (minor), 128.23 (major), 127.31 (minor), 127.08 (major), 18.93 (minor), 18.82 (major); HRMS calcd for $C_9H_{12}NO$ [M+H$^+$] 150.0919, found 150.0918.

N-(3-氯苯基)甲酰胺(**2k**): 获得产物有两种构象异构体, 比例为 3∶1. 淡黄色固体, m.p. 56～58 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.33 (s, 0.75H), 10.21 (d, J=6.0 Hz, 0.25H), 8.80 (d, J=4.0 Hz, 0.25H), 8.27 (s, 0.75H), 7.75 (s, 0.75H), 7.40 (d, J=4.0 Hz, 0.75H), 7.27～7.31 (m, 1H), 7.25～7.26 (m, 0.25H), 7.12 (d, J=4.0 Hz, 0.25H), 7.07 (d, J=4.0 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 163.11 (minor), 160.48 (major), 140.57 (minor), 140.12 (major), 134.30 (minor), 133.67 (major), 131.49 (minor), 131.06 (major), 123.84 (major), 123.69 (minor), 119.22 (major), 118.03 (major), 117.38 (major), 116.26 (major); HRMS calcd for $C_7H_6ClNONa$ [M+Na$^+$] 178.0036, found 178.0027.

N-甲基-*N*-苯基甲酰胺(**2l**): 获得产物有两种构象异构体, 比例为 9∶1. 棕色油状物; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 8.53 (s, 0.9H), 8.35 (s, 0.1H), 7.49 (d, J=4.0 Hz, 0.2H), 7.40～7.44 (m, 2H), 7.33 (d, J=4.0 Hz, 1.8H), 7.23～7.27 (m, 1H), 3.21 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 163.06 (minor), 162.55 (major), 142.56 (major), 140.95 (minor), 129.91 (major), 129.17 (minor), 126.09 (major), 125.89 (minor), 123.53 (minor), 121.99 (major), 36.61 (minor), 31.50 (major); HRMS calcd for C_8H_9NONa [M+Na$^+$] 158.0582, found 158.0577.

2,3-二氢-(1-吲哚基)甲酰胺(**2m**): 获得产物有两种构象异构体, 比例为 3∶1. 淡黄色固体, m.p. 62～64 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 9.07 (s, 0.75H), 8.51 (s, 0.25H), 7.94 (d, J=4.0 Hz, 0.25H), 7.46 (d, J=4.0 Hz, 0.75H), 7.30 (d, J=4.0 Hz, 1H), 7.18～7.22 (m, 1H), 7.03～7.07 (m, 1H), 4.13～4.17 (m, 0.5H), 3.91～3.96 (m, 1.5H), 3.10～3.15 (m, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 160.62 (minor), 158.88 (major), 141.75 (minor), 141.68 (major), 133.15 (minor), 132.23 (major), 127.80 (major), 127.52 (minor), 126.31 (major), 125.63 (minor), 124.56 (major), 124.13 (minor), 115.98 (minor), 110.35 (major), 46.95 (minor), 44.63 (major), 27.67 (minor), 27.08 (major); HRMS calcd for C_9H_9NONa [M+Na$^+$] 170.0582, found 170.0582.

N-苯乙基甲酰胺(**2n**): 获得产物有两种构象异构体, 比例为 9∶1. 淡黄色油状物; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 8.06 (s, 1H), δ: 8.01 (s, 0.9H), 7.77 (s, 0.1H), 7.28～7.31 (m, 2H), 7.19～7.23 (m, 3H), 3.31～3.36 (m, 2H), 2.72～2.76 (m, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 164.93 (minor), 161.56 (major), 139.77 (major), 139.27 (minor), 129.40 (minor), 129.14 (major), 128.85 (major), 128.59 (minor), 126.72 (minor), 126.65 (minor), 43.00 (minor), 39.24 (major), 37.66 (minor), 35.55 (major); HRMS calcd for $C_9H_{11}NONa$ [M+Na$^+$] 172.0738, found 172.0736.

N-苄基甲酰胺(**2o**): 获得产物有两种构象异构体, 比例为 9∶1. 淡黄色固体, m.p. 62～63 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 8.53 (s, 1H), 8.16 (s, 0.9H), 8.14 (d, J=6.0 Hz, 0.1H), 7.26～7.37 (m, 5H), 4.32 (d, J=2.0 Hz, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 165.44 (minor), 161.56 (major), 140.19 (minor), 139.52 (major), 128.97 (minor), 128.86 (major), 127.82 (major), 127.60 (minor), 127.57 (minor), 127.40 (minor), 45.08 (minor), 41.25 (major); HRMS calcd for C_8H_9NONa [M+Na$^+$] 158.0582, found 158.0577.

N-(1-苯基乙基)甲酰胺(**2p**): 获得产物有两种构象异构体, 比例为 9∶1. 淡黄色油状物; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 8.53 (s, 0.9H), 8.32 (s, 0.1H), 8.11 (d, J=6.0 Hz, 0.1H), 8.05 (s, 0.9H), 7.33～7.37 (m, 4H), 7.23～7.27 (m, 1H), 4.98～5.05 (m, 0.9H), 4.67～4.74 (m, 0.1H), 1.43 (d, J=6.0 Hz, 0.3H), 1.37 (d, J=4.0 Hz, 2.7H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 164.48 (minor), 160.58 (major), 145.26 (minor), 144.66 (major), 128.96 (minor), 128.83 (major), 127.43 (minor), 127.27 (major), 126.48 (major), 126.40 (minor), 51.30 (minor), 47.08 (major), 23.95 (minor), 22.97 (major); HRMS calcd for $C_9H_{11}NONa$ [M + Na$^+$] 172.0738, found 172.0736.

N-环己基甲酰胺(**2q**): 淡黄色油状物; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 7.95 (d, J=6.0 Hz, 1H), 7.87 (s, 1H), 3.52～3.57 (m, 1H), 1.59～1.68 (m, 4H), 1.49 (d, J=4.0 Hz, 1H), 1.08～1.23 (m, 5H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 163.93 (minor), 160.44 (major), 50.68 (minor), 46.54 (major), 34.72 (minor), 32.84 (major), 25.66 (major), 25.35 (minor), 25.09 (minor), 24.88 (major); HRMS calcd for $C_7H_{14}NO$ [M+H$^+$] 128.1075, found 128.1078.

N-正己基甲酰胺(**2r**): 淡黄色油状物; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 7.91～7.99 (m, 2H), 3.04～3.09 (m, 2H), 1.36～1.41 (m, 2H), 1.25～1.30 (m, 6H), 0.86 (m, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 164.97 (minor), 161.38 (major), 41.38 (minor), 37.58 (major), 31.50 (major), 31.43 (minor), 29.53, 26.60 (major), 26.11 (minor), 22.63, 14.43; HRMS calcd for $C_7H_{16}NO$ [M+H$^+$] 130.1232, found 130.1234.

N-(2-吡啶基)甲酰胺(**2s**): 获得产物有两种构象异构体, 比例为 1∶1. 白色固体, m.p. 70～71 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.60 (s, 1H), 9.30 (d, J=4.0 Hz, 0.5H), 8.34 (s, 1H), 8.26 (s, 0.5H), 8.07 (d, J=4.0 Hz, 0.5H), 7.73～7.82 (m, 1H), 7.08～7.13 (m, 1H), 6.94(s, J=4.0 Hz, 0.5H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 162.66, 160.64, 152.16, 151.55, 148.69, 148.58, 139.25, 138.86, 120.30, 119.76, 114.30, 111.85; HRMS calcd for $C_6H_6N_2ONa$ [M+Na$^+$] 145.0378, found 145.0379.

N-(2-吡啶甲基)甲酰胺(**2t**): 棕色油状物; 获得产物有两种构象异构体, 比例为 9∶1. ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 8.59 (s, 1H), 8.51 (d, J=4.0 Hz, 1H), 8.18 (s, 0.9H), 8.14 (s, 0.1H), 7.75～7.79 (m, 1H), 7.31 (d, J=4.0 Hz, 1H), 7.26～7.29 (m, 1H), 4.40 (d, J=2.0 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 165.86 (minor), 161.82 (major), 159.23 (minor), 158.46 (major), 149.61 (minor), 149.41 (major), 137.44 (minor), 137.30 (major), 122.94 (minor), 122.73 (major), 121.74 (minor), 121.65 (major), 46.99 (minor), 43.30 (major); HRMS calcd for $C_7H_8N_2$-ONa [M+Na$^+$] 159.0534, found 159.0539.

辅助材料(Supporting Information) 甲酰胺化合物的 ^{1}H NMR 和 ^{13}C NMR 谱图. 这些材料可以免费从本刊网站(http://sioc-journal.cn/)上下载.

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