The conversion of aryl and heteroaryl methylketones to the corresponding secondary or tertiary amides

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Secondary or tertiary amides have been prepared directly from aryl, heteroaryl methyl ketones using an iodine–amine–NaOH system which afforded the expected products in good yields in an aqueous medium. The present method has the advantages of using inexpensive reagents, mild reaction condition and ease of manipulation.

Keywords: iodine, amide, water, Lieben iodoform reaction

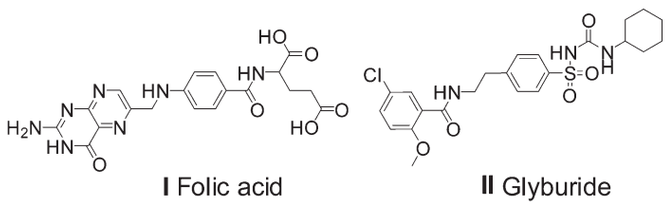
The formation of amides is an important topic in organic synthesis. The amide unit is a biological activity structural component of biomolecules and commercial drugs (Scheme 1).[1] Traditionally, amides have been successfully prepared using reactions such as the Beckmann rearrangement,[2–4] Ritter reaction,[5–7] Chapman rearrangement,[8,9] Haller–Bauer reaction,[10–11] Passerini reaction,[12,13] Wolff rearrangement,[14] and Schmidt reaction.[15–17] Apart from these conventional methods for the synthesis of amides, many alternative strategies have been reported.[18–25] Typically the direct amidation of activated carboxylic acid derivatives with amines is a convenient approach to amides.[18,19] The transition-metal-catalysed carbonylation of aryl halides or alkenes in the presence of nucleophiles is an important atom-economic reaction that can be applied to the synthesis of amides.[20,21] In addition, a recent conceptually economical amidation from alcohols has been explored with highly active transition-metal catalysts such as Ru-,[22,23] Rh-,[24] and Ag-[25] producing two molecules of hydrogen as the only stoichiometric byproduct. Although various methods for preparations of amides are available, the development of an efficient, economic and environmental friendly method is still desirable. Recently, we reported direct transformation of methyl ketones or carbinols to corresponding primary amides.[26] We now report an efficient method for the preparation of secondary and tertiary amides in the presence of iodine and various amines in aqueous media.

Initially, we expected to obtain intermediate **5** in one pot from *p*-methoxyacetophenone **1** in the presence of copper (II) oxide (1 equivalent), iodine (1 equivalent), and aqueous ammonia (1 equivalent) in methanol (Scheme 2).[27] Heating the reaction mixture at 100°C in a sealed tube for 10h gave the desired product in 46% yield. Meanwhile, α-iodoketone **2**[28] was obtained in 16% yield together with the 4-methoxybenzoate **4**[29] in 10% yield (Table 1, Entry 1). It was interesting to find that the unexpected product 4-methoxybenzamide **3**[26] was obtained in 5% yield. When *t*-butyl alcohol was used as the solvent, the ester was not detected owing to steric hindrance (Table 1, Entry 2).[30] To our disappointment, changing metal oxides did not reduce the amount of the byproducts (Table 1, entries 3–6). It was notable, however, that this transformation

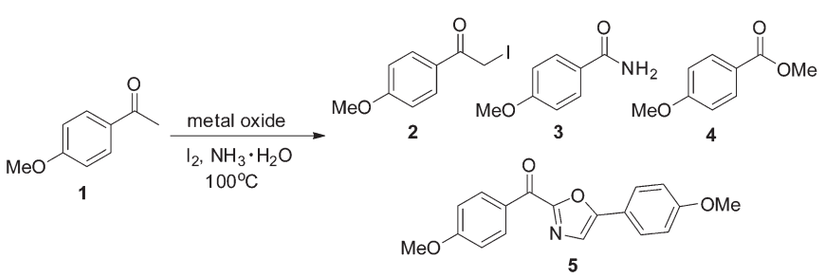
Table 1 Effect of the basicity on the amidation[a]

Entry	Metal oxide	Temp/°C	Slovent	Conv/%	Yield/%[c]			
					2	3	4	5
1	CuO	100	MeOH	81	16	5	10	46
2	CuO	100	*t*-BuOH	80	12	10	–	55
3	MgO	100	*t*-BuOH	81	10	12	–	50
4	CrO_3	100	*t*-BuOH	100	10	18	–	68
5	ZnO	100	*t*-BuOH	89	11	20	–	48
6	MnO_2	100	*t*-BuOH	70	8	38	–	15
7	CuO	100	H_2O	88	–	80	–	5
8	None[b]	90	H_2O	82		80	–	–
9	None[b]	60	H_2O	86		83	–	–

[a] Reaction conducted with 1 mmol of acetophenone, 1 mmol of metal oxide and 1 mmol of I_2 in 10h.
[b]Reaction conducted with 1 mmol of acetophenone, 3 mmol of $NH_3{\cdot}H_2O$ and 3 mmol of I_2 in 1h.
[c] Isolated yields.



Scheme 1



Scheme 2

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took place smoothly in H_2O to give the amide in 80% yields (Table 1, Entry 7). We also found that the transformation of compound **1** to **3** could be achieved in good yield without a metal oxide in aqueous ammonia at 90°C (Table 1, Entry 8). A higher conversion was observed upon heating the reaction mixture to 60°C for one hour (Table 1, Entry 9). Based on these result, we proposed a tandem Lieben-Haller-Bauer reaction mechanism for the direct transformation of methyl ketones or carbinols to corresponding primary amides.[26]

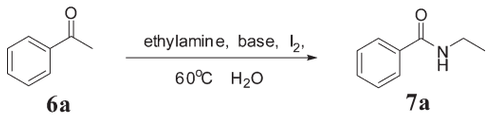
In the course of further work on preparing amides, we now report the tandem Lieben–Haller–Bauer reaction using several other amines in place of ammonia in an aqueous media. Acetophenone (**6a**) was used as a model substrate in the presence of molecular iodine and ethylamine in water for 4 hours to investigate the best condition for the synthesis of amides. Unfortunately, as shown in Table 2, a low conversion of methyl ketone to the corresponding secondary amide was observed (Table 2, Entry 1). We speculated that basicity of ethylamine might be too weak to induce the Lieben-iodoform process in aqueous media. Therefore, the screening reactions were performed with respect to a variety of bases. The results are summarised in Table 2 and show that NaOH was the best base for performing the conversion. Several parallel reactions were performed with the other bases such as K_2CO_3, Et_3N, DMAP, and pyridine (Table 2, entries 2–6). On the basis of the above-described results, two possibilities should be taken into consideration. (i) The inorganic base was more suitable than the organic base for the Lieben-iodoform process under aqueous conditions.[31,32] (ii) Sodium hypoiodite formed from NaOH could be important to promote the Lieben-iodoform process.[33–36]

Encouraged by these results, a number of primary and secondary amines were subjected to the optimised set of conditions to examine the effectiveness of this procedure. As shown in Table 3, it was obvious that moderate to good yields were obtained for most amines. However, tert-butylamine did not give the expect product because of steric hindrance (Table 3, Entry 4). Meanwhile, aniline failed to give the corresponding secondary amide (Table 3, Entry 10). We ssuggest that aniline is not a good nucleophilic reagent because the conjugation of phenyl ring leads the N atom losing its nucleophilicity in the reaction.

To assess the generality of the method and to evaluate the electronic influence of the aromatic ring substituent, various other aromatic ketones (**6**) were examined under the optimised conditions (Table 4). Acetophenone and its derivatives were readily transformed into the corresponding secondary amides with moderate to good yields (63–89%). It was obvious that an electron withdrawing substituent (*e.g.* $–NO_2$, –Br) on the benzene ring gave a considerable increase in the yield (Table 4, entries 1–3), and the corresponding products **8a–c** were obtained in good yield. In contrast, when the benzene rings bear electron-donating groups (Table 4, entries 4–6), the corresponding products **8d–f** were obtained in slight lower yields. Encouraged by the results obtained with aryl methyl ketones, we turned our attention to the heteroaryl methyl ketones. The presence of heteroatoms, including oxygen (**8g**) and sulfur (**8h**) in the substrate, did not affect the overall efficiency, and the corresponding amides were obtained. An attempt to perform the reaction with 2-naphthyl methyl ketone (**8i**) also succeeded in moderate yield (Table 4, Entry 9).

A possible reaction mechanism is shown in Fig. 1. The acetophenone undergoes the formation of enolate ion under basic condition provided by NaOH, and three sequential α-halogenations take place to afford the α,α,α-triiodomethyl ketone. This is the mechanism of the Lieben iodoform reaction.[31,32] However, α,α,α-triiodomethyl ketone does not undergo rapid hydrolysis to afford the iodoform and a carboxylate in the presence of primary or secondary amines. Instead, α,α,α-triiodomethyl ketone, which is a nonenolizable ketone, is attacked by the amine as a nucleophilic reagent, and this is accompanied by the cleavage of a carbon–carbon bonds leading to benzamide and iodoform. This process is a Haller–Bauer reaction.[37,38] Meanwhile, NaOH can act as a base to neutralise the hydrogen iodide, formed in the process of Lieben iodoform

Table 2 Effect of the basicity on the amidation[a]

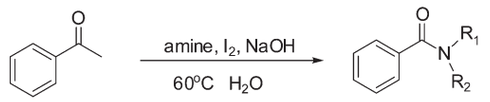


6a **7a**

Entry	Base	Yield/%[b]
1	—	35
2	NaOH	78
3	K_2CO_3	51
4	Et_3N	5
5	DMAP	30
6	Pyridine	36
7	NaOH[c)]	87

[a] Reaction conducted with 1 mmol of acetophenone, 3 mmol of ethylamine (35%), 1 nmmol base and 3 mmol of I_2 in 4h.
[b] Isolated yield.

Table 3 Preparation of amides from acetophenone with various amines[a]

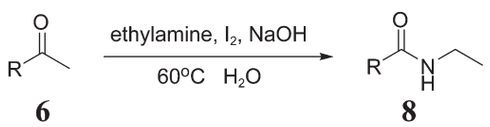


6a **7a-j**

Entry	Amine	Product	Yield[b]/%
1	Ethanamine	**7a**	87
2	Methanamine	**7b**	88
3	n-Butylamine	**7c**	60
4	t-Butylamine	**7d**	NR
5	n-Octadecylamine	**7e**	35
6	Dimethylamine	**7f**	55
7	Diethylamine	**7g**	52
8	Piperidine[c]	**7h**	56
9	Morpholine	**7i**	44
10	Aniline	**7j**	NR

[a] Reaction conducted with 1 mmol of acetophenone, 3 mmol of ethylamine, 3 mmol of I2 and 3mmol NaOH in 4h.
[b] Isolated yields.
[c] Reaction conducted in 6h.

Table 4 Preparation of secondary amides from ethylamine with various methyl ketones



6 **8**

Entry	R	Product	Yield[a]/%
1	3,4-$Cl_2C_6H_3$	**8a**	81
2	4-$NO_2C_6H_4$	**8b**	89
3	4-BrC_6H_4	**8c**	84
4	4-MeC_6H_4	**8d**	78
5	Piperonyl	**8e**	71
6	4-$EtOC_6H_4$	**8f**	76
7	2-Thienyl	**8g**	70
8	2-Furyl	**8h**	86
9	2-Naphthyl	**8i**	63

[a] Isolated yield.

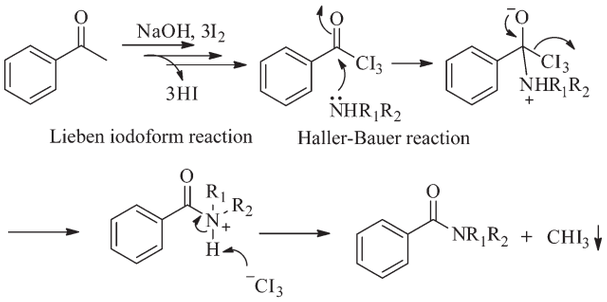


Fig. 1 The possible reaction mechanism.

reaction. In addition, water as a solvent is indispensable to this reaction because the iodoform that is formed during the reaction is insoluble in hot water and can further promote the transformation.

In conclusion, an efficient approach to secondary and tertiary amides in the presence of iodine and amines has been developed in aqueous media. The reaction provides an efficient method for the preparation of secondary and tertiary amides. It further confirms the rationality of the tandem Lieben–Haller–Bauer reaction mechanism. The advantages of the present method in term of good yields, mild reaction conditions, ease of manipulation, and inexpensive reagents, should make it a valuable alternative to existing methods.

Experimental

Methyl ketones **8a–i**, amines **7a–j** and other reagents were obtained from commercial suppliers and used without further purification. TLC analysis was performed using pre-coated glass plates. Column chromatography was performed using silica gel (200–300 mesh). IR spectra were recorded on a PE-983 spectrophotometer as KBr pellets and were reported in cm^{-1}. ^1H and ^{13}C NMR spectra were recorded on a Varian Mercury 600 or 400 spectrometer operating at 600 or 400 and 150 or 100 MHz. Chemical shifts are reported in ppm, relative to the internal standard of tetramethylsilane (TMS). Electron impact (EI) mass spectra were acquired using a Finnegan Trace MS spectrometer. Melting points were determined using XT-4 apparatus and not corrected. HRMS were obtained on a Bruker 7-tesla FT-ICR MS equipped with an electrospray source (Billelica, MA,USA).

*Synthesis of amides (***7***); general procedure*

Finely powdered NaOH (120 mg, 3.0 mmol) and iodine (762 m g, 3.0 mmol) were added to a well-stirred solution of methyl ketone (1.0 mmol) and amine in water (20 mL). The mixture was stirred for 5 min and then heated to 60°C for about 4h. After disappearance of the reactant (monitored by TLC), the mixture was extracted by EtOAc (3×50 mL) and washed with saturated $Na_2S_2O_3$ (3×50 mL). The organic layer was dried over anhydrous sodium sulfate. The solvent was evaporated and the residue was purified by column chromatography (petroleum ether/ethyl acetate) to give the target products in good yield.

*Synthesis of oxazole (***5***); general procedure*

Finely powdered CuO (80 mg, 1.0 mmol) and iodine (254 m g, 1.0 mmol) were added to a well-stirred solution of methyl ketone (1.0 mmol) and aqueous ammonia (35%, 100mg, 1mmol) in *t*-butyl alcohol (20 mL). The mixture was stirred for 5 min and then heated to 100°C for about 10h. After disappearance of the reactant (monitored by TLC), the mixture was extracted by EtOAc (3×50 mL) and washed with saturated $Na_2S_2O_3$ (3×50 mL). The organic layer was dried over anhydrous sodium sulfate. The solvent was evaporated and the residue was purified by column chromatography (petroleum ether/ethyl acetate) to give the target products.

2-(4-Methoxyphenylcarbonyl)-5-(4-methoxyphenyl)-oxazole (**5a**): M.p. 145–146 °C (lit.[39] 153–155 °C). IR (KBr): 3443, 3126, 2977, 2836, 1645, 1598, 1567, 1482, 1424, 1306, 1248, 1157, 1069, 952, 828, 772 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.53 (d, 2H, *J* = 8.8 Hz), 7.76 (d, 2H, *J* = 8.4 Hz), 7.48 (s, 1H), 7.00 (t, 4H, *J* = 8.4 Hz), 3.88 (d, 2H, *J* = 15.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.0, 164.1, 160.9, 156.8, 154.0, 133.2, 128.3, 127.0, 122.3, 119.5, 114.5, 113.7, 55.5, 55.4. MS (EI, 70 ev) *m/z*: 309 (21%), 135 (100), 107 (5), 92 (7), 77 (13).

2-(Thiophen-3-yl-carbonyl)-5-(thiophen-3-yl)-oxazole (**5b**): M.p. 170–171 °C, IR (KBr): 3121, 1597, 1510, 1467, 1267, 1139, 1068, 952, 850, 817, 659cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.05 (d, 1H, *J* = 2.4 Hz), 7.95 (d, 1H, *J* = 5.6 Hz), 7.83 (t, 1H, *J* = 2.0 Hz), 7.45 (d, 3H, *J* = 1.6 Hz), 7.38 (m, 1H, *J* = 2.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ =137.0, 128.5, 127.3, 125.9, 124.8, 123.8, 123.5. MS (EI, 70 ev) *m/z*: 260 (86%), 232 (26), 176 (14), 111 (100), 83 (23), 77 (4). HRMS (EI) *m/z* Calcd for $C_{12}H_7NO_2S_2$ $(M+Na)^+$ 283.9810. Found 283.9811.

N-Ethylbenzamide (**7a**): M.p. 64–65 °C (lit.[40] 64–65 °C). IR (KBr): 3318, 3080, 2979, 2934, 2870, 1636, 1604, 1549, 1488, 1432, 1358, 1311, 1145, 868, 720, 695 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.77 (d, 2H, *J* = 7.2 Hz), 7.46 (t, 1H, *J* = 7.2 Hz), 7.38 (t, 2H, *J* = 7.2 Hz), 6.56 (br s, 1H), 3.48 (m, 2H, *J* = 7.2 Hz), 1.22 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ =167.5, 134.7, 131.2, 128.4, 126.8, 34.9, 14.8. MS (EI, 70 ev) *m/z*: 149 (26%), 148 (29), 105 (89), 82 (100), 77 (61).

N-Methylbenzamide (**7b**): M.p. 78–79 °C. lit.[41] 79–80 °C). IR (KBr): 3330, 3065, 2932, 2803, 1688, 1667, 1594, 1541, 1447, 1412, 1293, 1219, 1178, 1159, 1070, 925, 807, 749, 689, cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): ^1H NMR (600 MHz, $CDCl_3$): δ = 8.33 (d, 2H, *J* = 7.8 Hz), 7.62 (t, 1H, *J* = 7.2 Hz), 7.48 (t, 2H, *J* = 7.2 Hz), 7.17 (br s, 1H), 2.97 (d, 3H, *J* = 4.8 Hz). ^{13}C NMR (150 MHz, $CDCl_3$): δ =187.7, 162.4, 134.3, 133.2, 131.1, 128.4, 26.0. MS (EI, 70 ev) *m/z*: 135 (10%), 134 (16), 105 (70), 82 (100), 77 (60).

N-Butylbenzamide (**7c**): M.p. 72–73 °C (lit.[42] 72–73 °C). IR (KBr): 3313, 3065, 2959, 2931, 2872, 1639, 1541, 1491, 1513, 1407, 1465, 1377, 1309, 1225, 1185s, 1154, 1075, 1028, 947, 852, 803 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ =7.77 (d, 2H, *J* = 7.2Hz), 7.46 (t, 1H, *J* = 7.2 Hz), 7.39 (t, 2H, *J* = 7.2 Hz), 6.53 (br s, 1H), 3.42 (q, 2H, *J* = 6.6 Hz), 1.58 (t, 2H, *J* = 7.2Hz), 1.39 (q, 2H, *J* = 7.2 Hz), 0.93 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 167.6, 134.7, 131.1, 128.3, 126.8, 39.7, 31.6, 20.1, 13.7. MS (EI, 70 ev) *m/z*: 177 (10%), 135 (34), 104 (100), 77 (55).

N-Octadecylbenzamide (**7e**): M.p. 76–77 °C (lit.[43] 82 °C). IR (KBr): 3344, 2919, 2847, 1632, 1577, 1533, 1488, 1463, 1296, 1075, 866 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ =7.76 (d, 2H, *J* = 7.6 Hz), 7.49–7.41 (m, 3H), 6.12 (br s, 1H), 3.45 (q, 2H, *J* = 6.8 Hz), 1.38–1.26 (m, 32H), 0.88 (t, 3H, *J* = 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.5, 134.9, 131.3, 128.5, 126.8, 40.1, 31.9, 29.7, 29.3, 27.0, 22.7, 14.1. MS (EI, 70 ev) *m/z*: 373 (21%), 372 (7), 344 (5), 330 (9), 316 (5), 207 (8), 190 (11), 176 (37), 148 (24), 135 (44), 105 (100), 77 (12).

N,N-Dimethylbenzamide (**7f**): Colourless oil, IR (KBr): 3496, 3344, 2936, 1646, 1596, 1580, 1450, 1405, 1316, 1246, 1145, 1063, 994, 882, 807, 757, 725 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.95 (d, 2H, *J* = 7.2 Hz), 7.65 (t, 1H), 7.51 (q, 2H, *J* = 7.8 Hz), 3.13 (s, 3H), 2.97 (s, 3H), ^{13}C NMR (150 MHz, $CDCl_3$): δ = 156.8, 134.7, 133.0, 129.7, 129.0, 37.1, 34.0. MS (EI, 70 ev) *m/z*: 149 (27%), 148 (32), 105 (100), 82 (22), 77 (63).

N,N-Diethylbenzamide (**7g**): Colourless oil, IR (KBr): 3478, 3064, 2972, 2936, 2927, 1725, 1681, 1643, 1597, 1448, 1383, 1289, 1233, 1180, 1145, 1075, 1021, 971, 941, 855, 721, 688 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, 2H, *J* = 7.2 Hz), 7.64 (t, 1H, *J* = 7.2 Hz), 7.51 (t, 2H, *J* = 7.2 Hz), 3.57 (q, 2H, *J* = 7.2 Hz), 3.25 (q, 2H, *J* = 7.2 Hz), 1.28 (q, 3H, *J* = 7.2 Hz), 1.16 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.7, 134.5, 133.2, 129.6, 128.9, 42.1, 38.8, 29.7, 14.1, 12.8. MS (EI, 70 ev) *m/z*: 177 (6 %), 135 (19), 105 (100), 84 (30), 82 (40).

Phenyl(piperidin-1-yl)methanone (**7h**): Colourless oil, IR (KBr): 3421, 2974, 2859, 1671, 1643, 1603, 1594, 1496, 1448, 1317, 1294, 1242, 1214, 1176, 1173, 1074, 1042, 973, 912 cm^{-1}, ^1H NMR (600 MHz, $CDCl_3$): δ = 7.54 (d, 1H, *J* = 7.8 Hz), 7.64 (t, 1H, *J* = 7.8 Hz), 7.52 (t, 3H, *J* = 7.8 Hz), 3.71 (s, 2H), 3.30 (t, 3H, *J* = 6.3 Hz), 1.70 (t, 4H, *J* = 3.0 Hz), 1.55 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.4, 134.6, 133.2, 129.5, 128.9, 47.0, 42.1, 26.1, 25.4, 24.3. MS (EI, 70 ev) *m/z*: 189 (22%), 147 (48), 112 (100), 105 (48), 99 (21), 85 (57), 77 (17).

Morpholino(phenyl)methanone (**7i**): Colourless oil, IR (KBr): 3416, 2968, 2922, 2862, 1675, 1640, 1595, 1494, 1466, 1448, 1389, 1364, 1291, 1272, 1219, 1179, 1113, 1066, 982, 932, 870, 840, 802, 732 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.96 (d, 2H, *J* = 7.2 Hz), 7.66 (t, 2H, *J* = 7.2 Hz), 7.53 (t, 2H, *J* = 7.8 Hz), 3.80 (t, 4H, *J* = 7.8 Hz), 3.66 (t, 2H, *J* = 5.4Hz), 3.39 (t, 2H, *J* = 4.8 Hz). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 191.1, 165.4, 134.9, 132.9, 129.6, 129.0, 66.7, 66.6, 46.2, 41.5. MS (EI, 70 ev) *m/z*: 191 (25%), 105 (100), 77 (35).

3,4-Dichloro-N-ethylbenzamide (**8a**): M.p. 92–93 °C (lit.[44] 97–98 °C). IR (KBr): 3319, 3076, 2972, 2934, 1635, 1596, 1550, 1467, 1437, 1320, 1241, 1169, 1145, 1128, 1030, 897 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, 1H, *J* = 1.6 Hz), 7.6–7.58 (m, 1H), 7.47 (d, 1H, *J* = 8.4 Hz), 6.44 (br s, 1H), 3.47 (m, 2H), 1.25 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.3, 135.6, 134.5, 132.9, 130.5, 129.1, 126.0, 35.1, 14.7. MS (EI, 70 ev) *m/z*: 219 (M+1, 19%), 218 (M, 27), 217 (M-1, 31), 216 (M-2, 39), 174 (61), 172 (100), 144 (32), 108 (18).

N-ethyl-4-nitrobenzamide (**8b**): M.p. 135–136 °C (lit.[45]138–140 °C). IR (KBr): 3336, 3083, 2981, 2939, 1642, 1600, 1552, 1490, 1458, 1439, 1344, 1303, 1146, 1109, 1086s, 1014, 1024, 871, 845 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 8.28 (d, 2H, *J* = 8.8 Hz), 7.93 (d, 2H, *J* = 8.8 Hz), 6.27 (br s, 1H), 3.53 (m, 2H,), 1.29 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.4, 149.4, 140.3, 128.0, 123.7, 35.3, 14.7. MS (EI, 70 ev) *m/z*: 195 (M+1, 5%), 194 (M, 41), 193 (M-1, 49), 150 (100), 104 (29).

4-Bromo-N-ethylbenzamide (**8c**): M.p. 117–118 °C (lit.[46] 122–124 °C). IR (KBr): 3343, 3249, 3079, 2978, 2881, 1624, 1591, 1553, 1478, 1382, 1358, 1307, 1270, 1184, 1144, 1115, 1072, 1101, 960, 908, 851 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63 (d, 2H, *J* = 8.4 Hz), 7.55 (d, 2H, *J* = 8.4 Hz), 6.18 (br s, 1H), 3.48 (m, 2H, *J* = 6.8 Hz), 1.25 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.4, 133.6, 131.7, 128.4, 125.9, 35.0, 14.8. MS (EI, 70 ev) *m/z*: 229 (M+1,31%), 228 (M, 47), 227 (M-1, 33), 182 (100), 156 (34).

N-ethyl-4-methylbenzamide (**8d**): M.p. 90–91 °C (lit.[47] 96–98 °C). IR (KBr): 3259, 3066, 2972, 2934, 2877, 1628, 1549, 1508, 1473, 1357, 1302, 1145, 1104, 962 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (d, 2H, *J* = 8.4 Hz), 7.18 (d, 2H, *J* = 8.0 Hz), 6.49 (br s, 1H), 3.48–3.44 (m, 2H), 2.37 (s, 3H), 1.24–1.20 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.4, 141.5, 131.8, 129.0, 126.8, 34.7, 21.3, 14.8. MS (EI, 70 ev) *m/z*: 163 (39%), 162 (39), 119 (100), 91 (46), 65 (15).

N-ethylpiperonylamide (**8e**): M.p. 80–81 °C (lit.[48] 87–88 °C). IR (KBr): 3311, 3077, 2971, 2934, 2905, 1639, 1605, 1550, 1508, 1488, 1436, 1359, 1309, 1251, 1172, 1146, 1122s, 1098s, 1083, 1040, 920, 916, 880 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ =7.31–7.28 (m, 2H), 6.79 (d, 1H, *J* = 8.0 Hz), 6.24 (br s, 1H), 3.49–3.42 (m, 2H), 1.22 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.8, 150.0, 147.8, 129.0, 121.3, 107.8, 107.5, 101.5, 34.9, 14.8. MS (EI, 70 ev) *m/z*: 193 (54%), 192 (37), 149 (100), 121 (29), 65 (11).

4-Ethoxy-N-ethylbenzamide (**8f**): M.p. 93–94 °C (lit.[49] 94–96 °C). IR (KBr): 3309, 2976, 2934, 2892, 1631, 1612, 1575, 1540, 1506, 1477, 1452, 1393, 1256, 1183, 1147, 1116, 1046, 923, 853 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (d, 2H, *J* = 8.8 Hz), 6.90 (d, 2H, *J* = 4.8 Hz), 6.09 (br s, 1H), 4.07 (q, 2H, *J* = 6.8 Hz), 3.51–3.44 (m, 2H), 1.43 (t, 3H, *J* = 7.2 Hz), 1.24 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.0, 161.4, 128.5, 126.8, 114.1, 63.6, 34.8, 15.0, 14.7. MS (EI, 70 ev) *m/z*: 193 (59%), 192 (45), 149 (100), 121 (89), 93 (19).

N-Ethylthiophene-2-carboxamide (**8g**): M.p. 65–66 °C (lit.[50] 75–77 °C. IR (KBr): 3291, 3072, 2980, 2883, 1611s 1522, 1471, 1418, 1295, 1247, 1150, 1085, 913, 860 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 (br s, 1H), 7.45 (d, 1H, *J* = 4.8 Hz), 7.06 (t, 1H, *J* = 4.8 Hz), 6.30 (br s, 1H), 3.50–3.43 (m, 2H); 1.24 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.8, 139.2, 129.6, 127.8, 127.5, 34.8, 14.8. MS (EI, 70 ev) *m/z*: 155 (48%), 122 (18), 110 (100).

N-Ethylfuran-2-carboxamide (**8h**): M.p. 40–41 °C (lit.[51] 34–35 °C). IR (KBr): 3289, 3072, 2980, 2936, 2882, 1611, 1411, 1551, 1471, 1418, 1362, 1295, 1247, 1150, 1058, 913, 860 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 (t, 1H, *J* = 3.2 Hz), 7.44 (d, 1H, *J* = 5.2 Hz), 7.06–7.04 (m, 1H), 6.34 (br s, 1H), 3.50–3.43 (m, 2H), 1.23 (t, 1H, *J* = 3.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.8, 139.2, 129.6, 127.8, 127.5, 34.8, 14.8. MS (EI, 70 ev) *m/z*: 139 (18%), 110 (100), 83 (10).

N-ethyl-2-naphthamide (**8i**): M.p. 120–121 °C (lit.[52]129–130 °C). IR (KBr): 3260, 3057, 2976, 2933, 2875, 1622, 1553, 1502, 1453, 1431, 1358, 1341, 1203, 1149, 954, 915 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.28 (s, 1H), 7.91–7.81 (m, 4H), 7.58–7.50 (m, 2H), 6.33 (br s,1H), 3.59–3.52 (m, 2H), 1.30 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.5, 134.6, 132.6, 132.0, 128.8, 128.4, 127.7, 127.5, 127.2, 126.7, 123.5, 35.0, 14.9. MS (EI, 70 ev) *m/z*: 200 (M+1, 8%), 199 (M, 62), 198 (M-1, 51), 155 (100), 127 (86).

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