Synthesis C. Mei et al. Special Topic

Visible-Light-Driven Oxidation of *N*-Alkylamides to Imides Using Oxone/H_2O and Catalytic KBr

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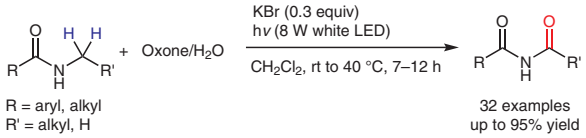

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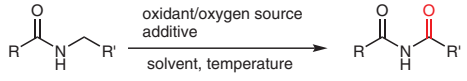
Abstract Imides are prepared conveniently by visible-light-driven oxidations of various *N*-alkylamides under mild conditions. The majority of the reactions proceed efficiently by using Oxone as the oxidant in the presence of a catalytic amount of KBr in H_2O/CH_2Cl_2 under irradiation by an 8 W white LED at room temperature. Experimental studies suggest that an imine, obtained from the substrate amide via a radical process, is the key intermediate.

Key words imides, amides, oxidation, catalysis, photochemistry

Imides are present in a broad range of pharmaceuticals, agrochemicals, and natural products.[1] They are normally prepared by a variety of reactions including condensations,[2] couplings,[3] oxidations,[4] etc., according to the different precursors employed. Among them, direct α-oxidation of *N*-benzylamides or *N*-alkylamides is one of the most straightforward methods for the synthesis of imides. Most recently, we developed a transition-metal- and halogen-free oxidation of *N*-benzylamides to their corresponding imides using $K_2S_2O_8/O_2$ as oxidants and pyridine as a phase-transfer catalyst in MeCN at 70 °C, but the method was not applicable to *N*-alkylamides.[4m] In comparison with many reports on oxidations of benzylic sp^3 C–H bonds to carbonyl groups, there are only a few effective examples related to the oxidations of α-alkyl sp^3 C–H bonds of *N*-alkylamides to afford the corresponding imides, and special oxidants such as H_5IO_6,[4b] Dess–Martin periodinane (DMP),[4c] or Selectfluor[4i] are employed in these reactions (Scheme 1). It is still desirable to explore the oxidation of *N*-alkylamides to prepare imides by using common oxidants under mild conditions. Herein, we disclose a very convenient method to produce imides from *N*-alkylamides using Oxone as the oxidant with catalytic KBr in H_2O/CH_2Cl_2 under irradiation by visible light at room temperature to 40 °C.Abstraction of hydrogen by halogen radicals is a highly powerful method for the functionalization of various C–H bonds. Meanwhile, it is feasible to combine the oxidation of halogen ions to halogens and the generation of halogen radicals from halogens under light together at room temperature in chemical synthesis. For example, visible-light-driven oxidative chlorination of alkyl sp^3 C–H bonds with NaCl[5] and carbonylation of benzylic sp^3 C–H bonds in the presence of stoichiometric KBr[6] have been successfully developed. In these reactions, Oxone ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$) is used as a very stable, cheap and effective oxidant under mild conditions. Thus, the Oxone/KBr system was selected to explore the oxidation of α-alkyl sp^3 C–H bonds of *N*-alkylamides to produce the corresponding imides under irradiation with visible light.



Method	Oxidant/ oxygen source	Additive	Solvent	Temp (°C)
Trudell (2004)[4b]	H_5IO_6 (6 equiv)	CrO_3 (0.05 equiv)	Ac_2O/ MeCN	0
Nicolaou (2005)[4c]	DMP (2 equiv)/ H_2O	–	PhF/ DMSO	85
Xu (2011)[4i]	Selectfluor (2.5 equiv)/ H_2O	CuBr (1.2 equiv)	MeCN	rt
This work	Oxone (2.0 equiv)/ H_2O	KBr (0.3 equiv)	CH_2Cl_2 irradiation using an 8 W white LED	rt–40

Scheme 1 Examples of the direct oxidation of *N*-alkylamides to imides

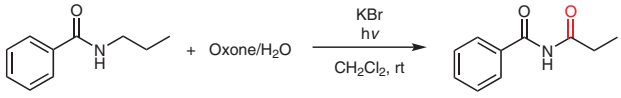
To our delight, the target imide **B1** was obtained in 41% yield from the oxidation of *N*-propylbenzamide (**A1**) with 1.5 equivalents of Oxone and 1.0 equivalent of KBr in

H_2O/CH_2Cl_2 under indoor lighting (a 30 W fluorescent light at a distance of 1.5 m) at room temperature (Table 1, entry 1). No reaction occurred when H_2O, KBr or light, respectively, was not present (Table 1, entries 5–7), implying that the reaction is a visible-light-driven process with KBr as an essential additive in aqueous solution. Other common solvents including MeCN and $MeNO_2$ were not suitable for this reaction. In addition, no significant improvement in the yield was observed by simple tuning of the amounts of KBr and Oxone (Table 1, entries 1–4). When 0.5 equivalents of KBr were used along with additional Oxone (2.2 equiv), the yield was 51%, which represents a quantitative yield based on KBr (Table 1, entry 4). However, when the fluorescent light was replaced with a household 8 W white LED bulb (at a distance of 0.15 m), the yield of the imide **B1** was enhanced dramatically in the presence of catalytic KBr (Table 1, entries 8–10). For example, **B1** was obtained in 85% yield after 7 hours by using 2.0 equivalents of Oxone in the presence of 0.3 equivalents of KBr (Table 1, entry 9). NaBr could also be employed as the catalytic additive to afford **B1** in 69% yield, but KCl and KI were not suitable under identical conditions (see the Supporting Information). Under a nitrogen atmosphere, the oxidation of *N*-alkylamides to imides still proceeded smoothly (Table 1, entry 11), indicating that the oxygen source was not O_2 from air in this carbonylation of C–H bonds.

A series of *N*-alkylbenzamides with different *N*-alkyl groups and substituents on the phenyl rings was tested under the optimized conditions (see Table 1, entry 9) in visible-light-driven oxidations (Scheme 2). When the *N*-alkyl groups were methyl, propyl, and dimethylpropyl, the yields of the corresponding imides were moderate to excellent (64–94%), regardless of the substituent on the benzene ring (F, Cl, Br, OMe or CF_3). In contrast, in the cases of ethyl and methylbutyl groups, several of the yields were less than 50%. However, multi-carbonyl-containing product **B27** was obtained in a yield of 87% from the corresponding amino acid derivative. *N*-Propionylpicolinamide (**B28**), a heterocyclic amide, was produced in 44% yield. In addition, aliphatic imides (**B29**–**B32**) could be prepared in high yields. No products were obtained when *N*,*N*-dipropylbenzamide (**A33**) and ethyl benzoate (**A34**) were employed as substrates. In addition, this method was not suitable for *N*-benzylamide substrates such as *N*-benzylacetamide (**A35**), which mainly afforded benzoic acid (**C**) under the optimized conditions.

Moreover, it was found that *N*-alkylbenzamides containing tertiary α-sp^3 C–H bonds were decomposed into their corresponding benzamides and ketones under the standard conditions, which is an effective method for the cleavage of sp^3 C–N bonds from these amides at room temperature (Scheme 3).

Table 1 Investigation of the Reaction Conditions[a]

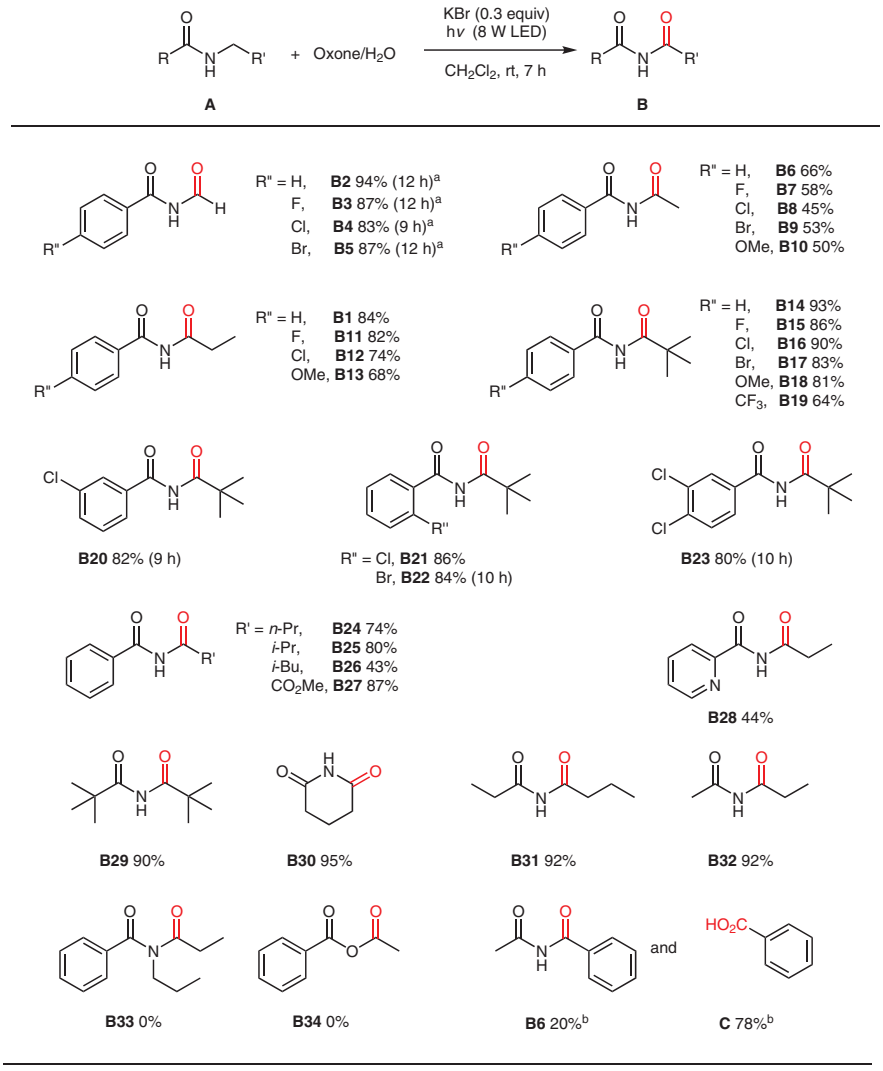


A1 **B1**

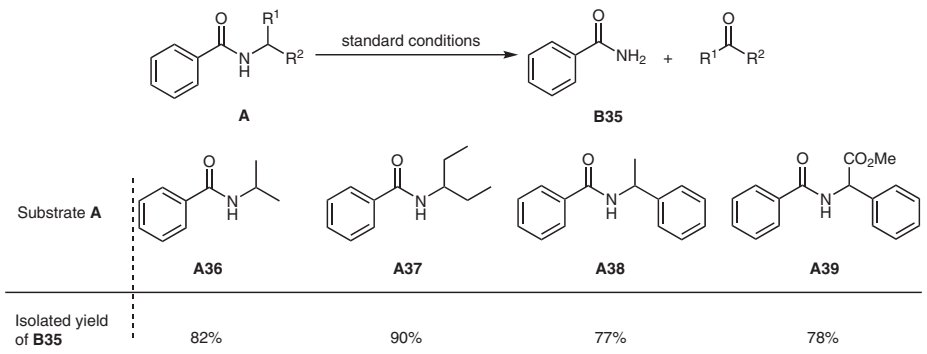
Entry	Oxone (equiv)	KBr (equiv)	Time (h)	Yield (%)[b]
1	1.5	1.0	12	41
2	2.0	1.0	12	67
3	2.5	1.0	12	61
4	2.2	0.5	8	51
5[c]	2.0	1.0	12	–
6	2.0	–	12	–
7[d]	2.0	1.0	12	–
8	2.2	0.5	7	70
9	2.0	0.3	7	85
10	2.0	0.2	7	51
11[e]	2.2	0.3	7	83
12	2.5	0.3	7	80
13	1.5	0.3	7	63

[a] *Conditions*: *N*-propylbenzamide (**A1**) (0.25 mmol, 1 equiv), H_2O (11 mmol, 44 equiv, 0.2 mL), CH_2Cl_2 (1.5 mL), air, rt, 30 W fluorescent light (at a distance of 1.5 m) (entries 1–6), or an 8 W white LED (at a distance of 0.15 m) (entries 8–12).
[b] Yield of isolated product.
[c] Reaction without H_2O.
[d] Reaction run in the dark.
[e] Reaction under N_2.

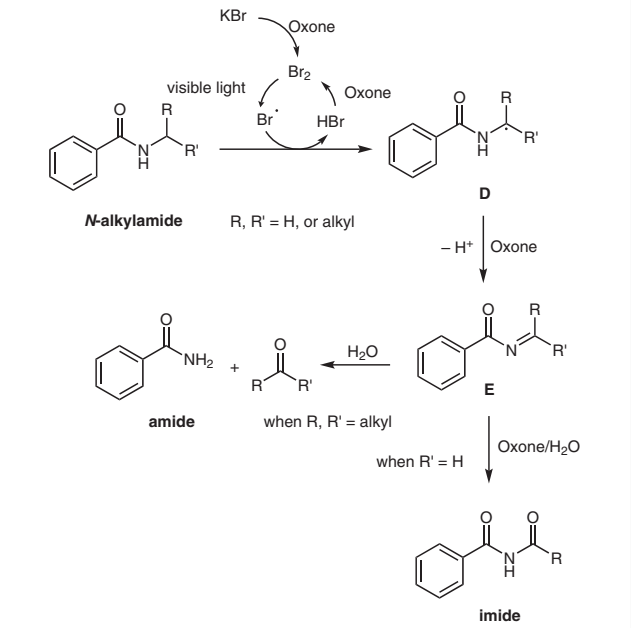
Based on the above results and related reports,[4,6,7] a possible reaction mechanism for the oxidation of *N*-alkylamides to imides can be proposed (Scheme 4). Firstly, the α-sp^3 C–H bond of the *N*-alkylamide is cleaved by a bromine radical to afford the radical intermediate **D** and HBr, which occurs via abstraction of hydrogen from the C–H bond adjacent to NHCO through a radical process. In this system, bromine anions can be oxidized by Oxone to bromine, and bromine radicals are produced from bromine under visible light. Next, radical **D** is oxidized further to give imine **E** as a key intermediate,[4c,4i,7] which does not undergo monobromination or dibromination as in the carbonylation of benzylic sp^3 C–H bonds under visible light.[6a] This is supported by the fact that *N*,*N*-dialkylamides or alkyl benzoates are not available in these oxidations since they cannot be transformed into imines or similar structures. When the imine **E** is derived from an *N*-alkylbenzamide containing a tertiary α-sp^3 C–H bond or an *N*-benzylamide substrate, it is easily hydrolyzed to give the corresponding amide. Alternatively, after further reactions with water and Oxone, **E** is converted into the target imide, as confirmed by previous work.[4i,8]



Scheme 2 Oxidation of *N*-alkylamides to imides. *Conditions*: **A** (0.25 mmol, 1 equiv), Oxone (0.50 or 0.55 mmol, 2.0 or 2.2 equiv), KBr (0.075 mmol, 0.3 equiv), H_2O (11 mmol, 44 equiv, 0.2 mL), CH_2Cl_2 (1.5 mL), 8 W white LED (at a distance of 0.15 m), air, rt, 7 h; yields are those of isolated products (unless otherwise noted). [a] Reaction at 40 °C. [b] ^1H NMR yield.



Scheme 3 Cleavage of C–N bonds of *N*-alkylamides containing tertiary α-sp^3 C–H bonds



Scheme 4 A proposed mechanism

In summary, we have reported a straightforward and transition-metal-free method to prepare imides from *N*-alkylamides under mild conditions, which proceeds via a visible-light-driven oxidation using Oxone as the oxidant in the presence of catalytic KBr in H_2O/CH_2Cl_2 at room temperature to 40 °C. A number of imides have been prepared from *N*-alkylamide substrates, but not from *N*,*N*-dialkylamides. In addition, the C–N bonds of *N*-alkylbenzamides containing tertiary α-sp^3 C–H bonds could be cleaved to give the corresponding amides and ketones under the same conditions, implying that imine intermediates are potentially involved. Further studies on the scope, mechanism and applications of this methodology are in progress.

Unless otherwise noted, all reagents were obtained from commercial sources and were used without purification. Solvents were distilled before use. The procedures used for the synthesis of the substrates are described in the Supporting Information. Flash chromatography was performed on General-Reagent silica gel (200–300 mesh). Visible light was provided by a Philips 8W white LED (E27, 220-240V, 50/60Hz, 600lm, 64mA). Melting points were recorded using a INESA SGW X-4 melting point apparatus. NMR spectra were obtained using a Varian Mercury 400 plus instrument, a Bruker AVANCE III HD 400 instrument (400 MHz for ^{1}H, 100 MHz for ^{13}C and 376 MHz for ^{19}F), or a Bruker AVANCE III HD 500 instrument (500 MHz for ^{1}H, and 125 MHz for ^{13}C). Data are reported as follows: chemical shift (δ) using the residual proton signal of the solvent as an internal standard [δ 7.26 ($CDCl_3$)] or TMS (δ 0.00), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (*J*) in Hz, integration. HRMS were measured with an ACQUITYTM UPLC & Q-TOF MS Premier instrument.

N-Propionylbenzamide (B1); Typical Procedure

N-Propylbenzamide (**A1**) (40.8 mg, 0.25 mmol, 1.0 equiv), Oxone (307.8 mg, 0.50 mmol, 2.0 equiv), KBr (8.9 mg, 0.075 mmol, 0.3 equiv), H_2O (198.2 mg, 44 equiv, 0.2 mL) and CH_2Cl_2 (1.5 mL) were added to a 15 mL sealed tube containing a magnetic stir bar. The reaction mixture was stirred at room temperature for 7 hours under irradiation with an 8 W white LED. After completion of the reaction, saturated Na_2SO_3 (5.0 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organics were washed with brine (10 mL), dried over Mg_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography on silica gel (EtOAc/PE, 1:6) to afford *N*-propionylbenzamide (**B1**).[3b]

White solid; yield: 37.7 mg (85%); mp 93–94 °C (Lit.[3b] 93–94 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.54 (br s, 1 H), 7.84 (d, *J* = 7.2 Hz, 2 H), 7.61 (t, *J* = 7.6 Hz, 1 H), 7.51 (t, *J* = 8.0 Hz, 2 H), 3.04 (q, *J* = 7.2 Hz, 2 H), 1.23 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.8, 166.0, 133.3, 133.0, 129.1, 128.0, 31.5, 8.4.

N-Formylbenzamide (B2)[9]

White solid; yield: 35 mg (94%); mp 106–108 °C (Lit.[9] 108–112 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.37 (d, *J* = 9.6 Hz, 1 H), 8.96 (br s, 1 H), 7.90 (d, *J* = 8.0 Hz, 2 H), 7.67 (t, *J* = 7.6 Hz, 1 H), 7.55 (t, *J* = 7.6 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.8, 164.7, 134.2, 131.3, 129.3, 128.2.

4-Fluoro-*N*-formylbenzamide (B3)[9]

White solid; yield: 36.4 mg (87%); mp 161–162 °C (Lit.[9] 161–165 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.02 (br s, 1 H), 9.42 (d, *J* = 9.2 Hz, 1 H), 8.15–7.98 (m, 2 H), 7.34–7.17 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.4 (d, J_{C-F} = 256 Hz), 165.6, 164.8, 130.9 (d, J_{C-F} = 9 Hz), 127.4 (d, J_{C-F} = 3 Hz), 116.6 (d, J_{C-F} = 22 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –103.3.

4-Chloro-*N*-formylbenzamide (B4)[10]

White solid; yield: 38.1 mg (83%); mp 183–174 °C (Lit.[10] 183–187 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.59 (br s, 1 H), 9.37 (d, *J* = 9.6 Hz, 1 H), 7.91 (d, *J* = 8.4 Hz, 2 H), 7.53 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.6, 164.1, 140.8, 129.7, 129.6, 129.5.

4-Bromo-*N*-formylbenzamide (B5)[9]

White solid; yield: 49.6 mg (87%); mp 178–180 °C (Lit.[9] 211–215 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.36 (d, *J* = 9.5 Hz, 1 H), 9.30 (br s, 1 H), 7.83–7.76 (m, 2 H), 7.74–7.65 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.7, 163.6, 132.7, 130.1, 129.5, 129.4.

N-Acetylbenzamide (B6)[4g]

White solid; yield: 26.9 mg (66%); mp 115–117 °C (Lit.[4g] 115–117 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.36 (br s, 1 H), 7.92 (d, *J* = 7.2 Hz, 2 H), 7.60 (t, *J* = 7.2 Hz, 1 H), 7.50 (t, *J* = 8.0 Hz, 2 H), 2.61 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.1, 166.1, 133.5, 132.9, 129.2, 128.0, 25.9.

***N*-Acetyl-4-fluorobenzamide (B7)**[11]

White solid; yield: 26.3 mg (58%); mp 112–113 °C (Lit.[11] 111–112 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.23 (br s, 1 H), 8.06–7.88 (m, 2 H), 7.24–7.12 (m, 2 H), 2.61 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.2, 165.9 (d, J_{C-F} = 255 Hz), 164.9, 130.6 (d, J_{C-F} = 9 Hz), 128.9 (d, J_{C-F} = 3 Hz), 116.3 (d, J_{C-F} = 22 Hz), 25.8.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –104.7.

***N*-Acetyl-4-chlorobenzamide (B8)**[11]

White solid; yield: 22.2 mg (45%); mp 135–136 °C (Lit.[11] 136–137 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.51 (br s, 1 H), 7.79 (d, *J* = 8.8 Hz, 2 H), 7.50 (d, *J* = 8.8 Hz, 2 H), 2.62 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.2, 165.1, 139.9, 131.1, 129.43, 129.39, 25.8.

***N*-Acetyl-4-bromobenzamide (B9)**[12]

White solid; yield: 32.1 mg (53%); mp 150–152 °C (Lit.[12] 152–154 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.16 (br s, 1 H), 7.82–7.74 (m, 2 H), 7.69–7.60 (m, 2 H), 2.60 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.0, 165.2, 132.4, 131.6, 129.5, 128.5, 25.8.

***N*-Acetyl-4-methoxybenzamide (B10)**[13]

White solid; yield: 24.1 mg (50%); mp 115–116 °C (Lit.[13] 119–119.5 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.75 (br s, 1 H), 7.84 (d, *J* = 9.2 Hz, 2 H), 6.98 (d, *J* = 8.8 Hz, 2 H), 3.88 (s, 3 H), 2.61 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.9, 165.2, 163.8, 130.1, 124.9, 114.4, 55.8, 25.8.

4-Fluoro-*N*-propionylbenzamide (B11)[3b]

White solid; yield: 40 mg (82%); mp 121–122 °C (Lit.[3b] 123–124 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.24 (br s, 1 H), 7.99–7.93 (m, 2 H), 7.18 (t, *J* = 8.4 Hz, 2 H), 3.03 (d, *J* = 7.2 Hz, 2 H), 1.21 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.0, 165.8 (d, J_{C-F} = 255 Hz), 164.9, 130.7 (d, J_{C-F} = 9 Hz), 129.1 (d, J_{C-F} = 3 Hz), 116.2 (d, J_{C-F} = 22 Hz), 31.4, 8.3.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –105.0.

4-Chloro-*N*-propionylbenzamide (B12)[14]

White solid; yield: 39.2 mg (74%); mp 140–141 °C (Lit.[14] 141–145 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.05 (br s, 1 H), 7.92–7.81 (m, 2 H), 7.66–7.43 (m, 2 H), 3.02 (q, *J* = 7.5 Hz, 2 H), 1.21 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.5, 164.8, 139.8, 131.3, 129.37, 129.34, 31.4, 8.3.

4-Methoxy-*N*-propionylbenzamide (B13)[3b]

White solid; yield: 35.2 mg (68%); mp 128–130 °C (Lit.[3b] 133–134 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.13 (br s, 1 H), 7.88 (d, *J* = 9.0 Hz, 2 H), 6.95 (d, *J* = 9.0 Hz, 2 H), 3.86 (s, 3 H), 3.01 (q, *J* = 7.0 Hz, 2 H), 1.19 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.8, 165.2, 163.6, 130.1, 125.0, 114.2, 55.6, 31.2, 8.4.

***N*-Pivaloylbenzamide (B14)**[15]

White solid; yield: 47.7 mg (93%); mp 126–127 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.55 (br s, 1 H), 7.75 (d, *J* = 8.0 Hz, 2 H), 7.59 (t, *J* = 7.6 Hz, 1 H), 7.49 (t, *J* = 7.2 Hz, 2 H), 1.33 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.3, 166.7, 134.0, 133.1, 129.0, 127.9, 40.8, 27.4.

4-Fluoro-*N*-pivaloylbenzamide (B15)

White solid; yield: 48 mg (86%); mp 126–128 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.51 (br s, 1 H), 7.78–7.70 (m, 2 H), 7.17–7.08 (m, 2 H), 1.31 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.3, 166.0, 165.5 (d, J_{C-F} = 254 Hz), 130.6 (d, J_{C-F} = 9 Hz), 130.1, 116.0 (d, J_{C-F} = 22 Hz), 40.7, 27.2.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –105.4.

HRMS (ESI-Q/TOF MS, MeCN): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{15}FNO_2$: 224.1087; found: 224.1086.

4-Chloro-*N*-pivaloylbenzamide (B16)

White solid; yield: 53.9 mg (90%); mp 138–140 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.48 (br s, 1 H), 7.71–7.62 (m, 2 H), 7.48–7.39 (m, 2 H), 1.32 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.3, 166.3, 139.3, 132.3, 129.4, 129.1, 40.7, 27.2.

HRMS (ESI-Q/TOF MS, MeCN): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{15}ClNO_2$: 240.0791; found: 240.0797.

4-Bromo-*N*-pivaloylbenzamide (B17)

White solid; yield: 59 mg (83%); mp 133–134 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.49 (br s, 1 H), 7.65–7.52 (m, 4 H), 1.32 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.9, 168.2, 134.5, 132.0, 131.1, 126.6, 31.8, 27.0.

HRMS (ESI-Q/TOF MS, MeCN): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{15}BrNO_2$: 284.0286; found: 284.0281.

4-Methoxy-*N*-pivaloylbenzamide (B18)

White solid; yield: 47.6 mg (81%); mp 129–130 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.55 (br s, 1 H), 7.70 (d, *J* = 8.8 Hz, 2 H), 6.91 (d, *J* = 8.8 Hz, 2 H), 3.83 (s, 3 H), 1.29 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.2, 165.7, 163.4, 130.0, 125.9, 114.0, 55.6, 40.6, 27.2.

HRMS (ESI-Q/TOF MS, MeCN): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{18}NO_3$: 236.1287; found: 236.1297.

4-Trifluoromethyl-*N*-pivaloylbenzamide (B19)

White solid; yield: 43.7 mg (64%); mp 110–112 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.66 (br s, 1 H), 7.78 (d, *J* = 8.0 Hz, 2 H), 7.69 (d, *J* = 8.0 Hz, 2 H), 1.31 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.6, 167.0, 137.4, 134.1 (q, *J* = 32.8 Hz), 128.4, 125.7 (q, *J* = 3.7 Hz), 123.6 (q, *J* = 272.7 Hz), 40.6, 27.1.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –63.1.

HRMS (ESI-Q/TOF MS, MeCN): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{15}F_3NO_2$: 274.1055; found: 274.1066.

3-Chloro-*N*-pivaloylbenzamide (B20)

White solid; yield: 49.1 mg (82%); mp 136–138 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.65 (br s, 1 H), 7.67 (t, *J* = 1.8 Hz, 1 H), 7.58–7.53 (m, 1 H), 7.50 (ddd, *J* = 8.0, 2.0, 1.0 Hz, 1 H), 7.37 (t, *J* = 8.0 Hz, 1 H), 1.30 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.4, 165.8, 135.7, 134.9, 132.7, 130.0, 128.1, 125.8, 40.7, 27.1.

HRMS (ESI-Q/TOF MS, MeCN): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{15}ClNO_2$: 240.0791; found: 240.0794.

2-Chloro-*N*-pivaloylbenzamide (B21)

White solid; yield: 51.5 mg (86%); mp 162–164 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.86 (br s, 1 H), 7.53–7.46 (m, 1 H), 7.42–7.38 (m, 2 H), 7.38–7.33 (m, 1 H), 1.27 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.2, 167.8, 135.3, 131.6, 130.1, 129.9, 129.3, 127.2, 40.3, 27.0.

HRMS (ESI-Q/TOF MS, MeCN): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{15}ClNO_2$: 240.0791; found: 240.0797.

2-Bromo-*N*-pivaloylbenzamide (B22)[16]

White solid; yield: 59.7 mg (84%); mp 162–164 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.65 (br s, 1 H), 7.58 (d, *J* = 8.0 Hz, 1 H), 7.40 (d, *J* = 4.0 Hz, 2 H), 7.35–7.27 (m, 1 H), 1.27 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.0, 168.7, 137.7, 133.0, 131.5, 128.8, 127.7, 118.4, 40.3, 27.0.

HRMS (ESI-Q/TOF MS, MeCN): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{15}BrNO_2$: 284.0286; found: 284.0288.

3,4-Dichloro-*N*-pivaloylbenzamide (B23)

White solid; yield: 54.8 mg (80%); mp 148–149 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.68 (br s, 1 H), 7.75 (s, 1 H), 7.49 (d, *J* = 1.0 Hz, 2 H), 1.29 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.6, 165.7, 137.2, 133.8, 133.2, 130.6, 130.1, 127.1, 40.6, 27.1.

HRMS (ESI-Q/TOF MS, MeCN): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{14}Cl_2NO_2$: 274.0402; found: 274.0409.

***N*-Butyrylbenzamide (B24)**[3b]

White solid; yield: 35.4 mg (74%); mp 97–99 °C (Lit.[3b] 98–99 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.19 (br s, 1 H), 7.90 (d, *J* = 7.5 Hz, 2 H), 7.58 (t, *J* = 7.5 Hz, 1 H), 7.48 (t, *J* = 7.8 Hz, 2 H), 2.98 (t, *J* = 7.5 Hz, 2 H), 1.82–1.60 (m, 2 H), 1.01 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.8, 165.9, 133.2, 132.9, 129.0, 127.9, 39.6, 17.6, 13.8.

***N*-Isobutyrylbenzamide (B25)**[17]

White solid; yield: 38.2 mg (80%); mp 151–152 °C (Lit.[17] 154–155.5 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.92 (br s, 1 H), 7.89 (d, *J* = 7.2 Hz, 2 H), 7.59 (t, *J* = 7.6 Hz, 1 H), 7.49 (t, *J* = 7.6 Hz, 2 H), 3.75–3.56 (m, 1 H), 1.25 (d, *J* = 6.8 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.5, 165.5, 133.2, 133.1, 129.0, 127.9, 35.1, 18.9.

***N*-(3-Methylbutanoyl)benzamide (B26)**[15]

White solid; yield: 22.1 mg (43%); mp 82–84 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.16 (br s, 1 H), 7.92 (d, *J* = 8.0 Hz, 2 H), 7.60 (t, *J* = 7.2 Hz, 1 H), 7.50 (t, *J* = 7.2 Hz, 2 H), 2.89 (d, *J* = 6.4 Hz, 2 H), 2.32–2.12 (m, 1 H), 1.03 (d, *J* = 6.8 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.8, 165.7, 133.7, 133.3, 129.1, 127.9, 46.4, 25.0, 22.8.

Methyl 2-Benzamido-2-oxoacetate (B27)[18]

White solid; yield: 45.1 mg (87%); mp 92–94 °C (Lit.[18] 92–94 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.89 (br s, 1 H), 7.93–7.87 (m, 2 H), 7.68–7.60 (m, 1 H), 7.52 (t, *J* = 7.5 Hz, 2 H), 3.98 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.7, 160.7, 134.0, 131.7, 129.3, 128.1, 54.2.

***N*-Propionylpicolinamide (B28)**

White solid; yield: 19.6 mg (44%); mp 74–76 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.45 (br s, 1 H), 8.63–8.56 (m, 1 H), 8.23 (d, *J* = 7.6 Hz, 1 H), 7.91 (td, *J* = 7.6, 1.6 Hz, 1 H), 7.52 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1 H), 2.99 (q, *J* = 7.2 Hz, 2 H), 1.22 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.7, 162.8, 148.5, 148.3, 137.9, 127.7, 123.2, 31.2, 8.3.

HRMS (ESI-Q/TOF MS, MeCN): *m*/*z* [M + Na]$^+$ calcd for $C_9H_{10}N_2O_2Na$: 201.0640; found: 201.0654.

***N*-Pivaloylpivalamide (B29)**[19]

White solid; yield: 41.7 mg (90%); mp 136–138 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.30 (br s, 1 H), 1.26 (s, 18 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 184.2, 38.7, 27.7.

Piperidine-2,6-dione (B30)[20]

White solid; yield: 26.9 mg (95%); mp 144–146 °C (Lit.[20] 144–146 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.46 (br s, 1 H), 2.60 (t, *J* = 6.4 Hz, 4 H), 2.05–1.95 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.4, 31.8, 18.1.

***N*-Propionylbutyramide (B31)**[11]

White solid; yield: 32.9 mg (92%); mp 109–110 °C (Lit.[11] 107–108 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.89 (br s, 1 H), 2.63 (q, *J* = 7.5 Hz, 2 H), 2.56 (t, *J* = 7.5 Hz, 2 H), 1.72–1.61 (m, 2 H), 1.14 (t, *J* = 7.5 Hz, 3 H), 0.96 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 175.5, 174.5, 39.4, 30.9, 18.0, 13.7, 8.5.

***N*-Acetylpropionamide (B32)**[21]

White solid; yield: 26.5 mg (92%); mp 84–86 °C (Lit.[21] 85–86 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.07 (br s, 1 H), 2.56 (q, *J* = 7.4 Hz, 2 H), 2.35 (s, 3 H), 1.15 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.0, 172.5, 30.7, 25.2, 8.5.

Benzamide (B35)[22]

White solid; yield: 23.3–27.3 mg (77–90%); mp 128–130 °C (Lit.[22] 128–130 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 6.8 Hz, 2 H), 7.54 (t, *J* = 6.8 Hz, 1 H), 7.45 (t, *J* = 7.6 Hz, 2 H), 6.21 (br s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.0, 133.6, 132.2, 128.8, 127.6.

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Supporting Information

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