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The direct amidation of α-diketones with amines *via* TBHP-promoted oxidative cleavage of C(sp^2)–C(sp^2) bonds†

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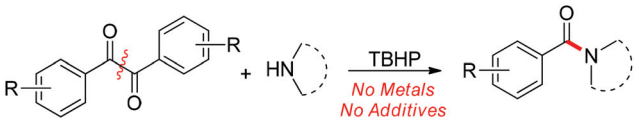
A novel and efficient direct amidation of α-diketones with amines *via* TBHP-promoted oxidative cleavage of C(sp^2)–C(sp^2) bonds has been developed. The strategy provides an alternative approach to amides under metal-free conditions.

Recently, C–C bond cleavage has emerged as a powerful tool for formation of new C–C or C–X bonds, which has been widely applied in organic synthesis owing to direct transformation into useful molecules.[1] So far, several C–C cleavage modes have been reported in the literature, such as the energy relief of ring strain,[2] the formation of a stable chelate complex,[3] and the selective cleavage of substrates with various leaving groups.[4] Generally, transition metals are often used to activate C–C bonds because of their high activity.[4,5] Despite these breakthroughs by using transition-metal catalysis,[1,6] developing metal-free approaches to these transformations is still desirable, especially in pharmaceutical synthesis. To our knowledge, C(sp^2)–C(sp^2) bond cleavage, involving α-diketones that does not require metals or metal complexes, has been rarely investigated.

The amide C–N bond is one of the most abundant and important units existing in natural products, marketed drugs and proteins.[7] For example, a hugely diverse array of biologically compounds, such as mitomycin C,[7h] tadalafil,[7i] and so on, have been broadly studied. The development of routes towards amides has always been a hot topic in organic synthesis in keeping with their importance. Some most common methodologies are as follows: (1) the coupling reaction of a carboxylic acid or its derivative with an amine;[8] (2) transition-metal-catalyzed amidation of aryl halides with nitrogen-containing reagents as well as the catalytic oxidative coupling reactions of alcohols with amines;[9] (3) the direct carbonylation of alkenes or alkynes;[10] (4) transition-metal catalyzed cleavage of C–C bonds, and some others.[11]



Scheme 1 Formation of amides from α-diketones with amines.

Although there has been much progress in this field, there are still partial limitations in these reported protocols for the synthesis of amides and their derivatives.[12] For instance, metal pollution, excessive starting materials and by-products may be a problem in these methodologies.[9–11] Therefore, it is desirable to develop environmentally friendly approaches to amides. Herein, we firstly report a novel metal-free amidation of α-diketones with amines *via* oxidative cleavage mode of α-diketones promoted by *tert*-butyl hydroperoxide (TBHP), which provides a direct approach to various amides (Scheme 1).

Based on our previous work,[6d] we initiated our investigation by testing the reaction of α-diketone (**1a**) with piperidine (**2a**) in THF, using TBHP as oxidant, as shown in Table 1. To our delight, α-diketone (**1a**) could react with piperidine (**2a**) in THF, in the presence of TBHP at 80 °C, and 45% yield of amide **3a** was obtained (Table 1, entry 1). It should be noted that *tert*-butyl benzoate was also formed in the reaction. In order to figure out beneficial factors, various bases were then screened in the reaction. When 1 equiv. of K_2CO_3 was added into the reaction, 73% yield of **3a** was obtained (Table 1, entry 2), whereas when 2 equiv. of K_2CO_3 was used, no improved yield of **3a** was observed (Table 1, entry 3). Other bases, such as Na_2CO_3, K_3PO_4 and KOH did not enhance the yields of **3a** (Table 1, entries 4–6). However, the reaction of **1a** with **2a** did not occur if a stronger base ^{t}BuOLi was used, even though **1a** was completely consumed (Table 1, entry 7). The commercially available organic bases, DABCO and DBU, showed poor performance in the model reaction and afforded the desired

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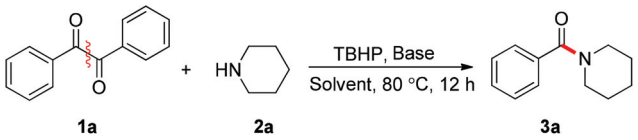
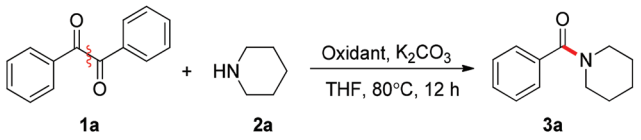
Table 1 Effect of bases and solvents on the amidation reaction of α-diketone **1a** with piperidine (**2a**)[a]



Entry	Base	Solvent	Yield[b] (%)
1	—	THF	45
2	K_2CO_3	THF	73
3	K_2CO_3	THF	70[c]
4	Na_2CO_3	THF	40
5	K_3PO_4	THF	53
6	KOH	THF	55
7	^{t}BuOLi	THF	0
8	DABCO	THF	32
9	DBU	THF	28
10	K_2CO_3	$PhCH_3$	54
11	K_2CO_3	EtOAc	52
12	K_2CO_3	MTBE	36
13	K_2CO_3	DCE	21
14	K_2CO_3	DMF	0
15	K_2CO_3	DMSO	0

[a] *Reaction conditions*: α-Diketone (**1a**, 0.50 mmol), piperidine (**2a**, 1.0 mmol), TBHP (70% in H_2O, 2.0 mmol), base (0.50 mmol), THF (2.0 mL), 80 °C, sealed tube, 12 h. [b] Isolated yield. [c] K_2CO_3 (1.0 mmol, 2.0 equiv.). MTBE = methyl tertiary butyl ether. DCE = 1,2-dichloroethane.

Table 2 Effect of oxidants on the amidation reaction of α-diketone **1a** with piperidine (**2a**)[a]



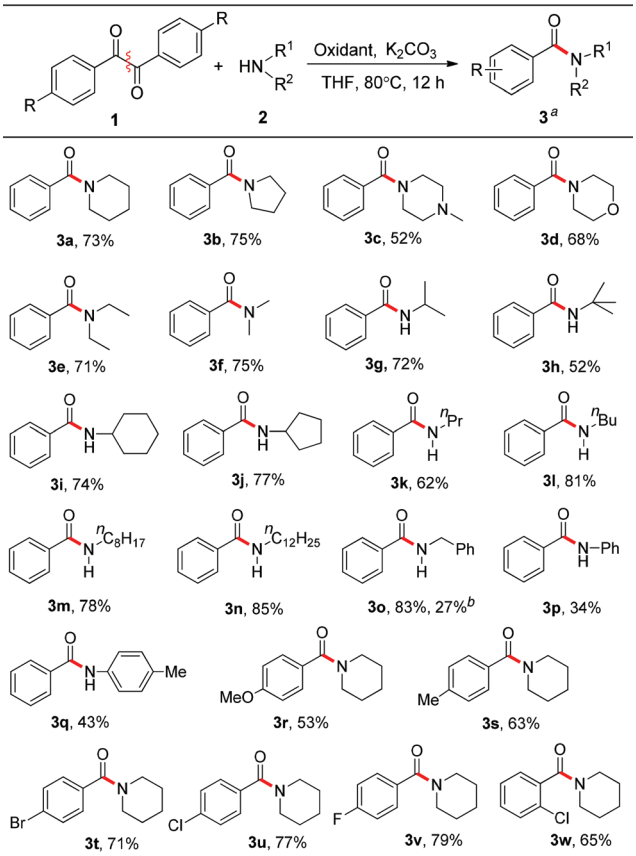
Entry	Oxidant	Additive	Yield[b] (%)
1	TBHP	—	73
2	TBHP	I_2	0
3	$(PhCOO)_2$	—	45
4	$(^t$BuO$)_2$	—	40
5	PhCOO^{t}Bu	—	36
6	H_2O_2	—	34
7	$K_2S_2O_8$	—	0
8	Ag_2O	—	0
9	$CuSO_4$	—	0
10	TBHP	—	57[c]
11	TBHP	—	73[d]
12	TBHP	—	73[e]

[a] *Reaction conditions*: α-diketone (**1a**, 0.50 mmol), piperidine (**2a**, 1.0 mmol), oxidant (2.0 mmol, 4.0 equiv.), K_2CO_3 (0.50 mmol), THF (2.0 mL), 80 °C, sealed tube, 12 h. [b] Isolated yield. [c] 3.0 equiv. of TBHP. [d] 5.0 equiv. of TBHP. [e] 20 h.

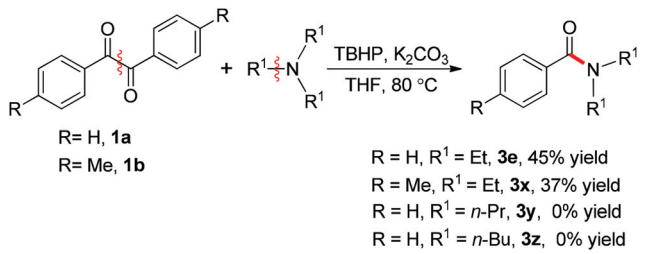
amide **3a** in only 32 and 28% yields, respectively (Table 1, entries 8 and 9). Subsequently, several common solvents were examined in the reaction. An inferior result was obtained when toluene was used as the reaction medium (Table 1, entry 10). The reactions of **1a** with **2a** also took place in ethyl acetate, MTBE (methyl tertiary butyl ether) and DCE (1,2-dichloroethane), providing the corresponding product **3a** in 52, 36 and 21% yields, respectively (Table 1, entries 11, 12 and 13). However, polar solvents, such as DMF and DMSO, seemed to hinder the amidation process completely (Table 1, entries 14 and 15).

Next, a variety of oxidants were evaluated for the amidation of **1a** with **2a** and the results are listed in Table 2. With THF as solvent, TBHP was used to promote the reaction, which generated the desired product **3a** in 73% yield (Table 2, entry 1). However, it was found that I_2 obviously shut down the transformation totally (Table 2, entry 2). We found that the model reaction could proceed in the presence of $(PhCOO)_2$ and generated **3a** in 45% yield (Table 2, entry 3). The use of PhCOO^{t}Bu or $(^t$BuO$)_2$ was also less efficient (Table 2, entries 4 and 5). Although H_2O_2 has broadly been used as a green oxidant in organic synthesis, when it was employed in the reaction, a low yield of **3a** was obtained (Table 2, entry 6). In addition, inorganic oxidants such as $K_2S_2O_8$, Ag_2O and $CuSO_4$ resulted in no formation of the desired product **3a** (Table 2, entries 7–9). The reaction seems to be dependent on the oxidant loading because the yield dramatically decreased when less than 4.0 equiv. of TBHP was employed (Table 2, entries 10 and 11). However, longer reaction time (more than 12 h) did not improve the yield of amide **3a** when the reaction was carried out in THF at 80 °C (Table 2, entry 12).

Having established the optimized reaction conditions, we subsequently explored the generality of substrates with a range of α-diketones and amines, as summarized in Scheme 2. It was found that the reaction of α-diketone (**1a**) with various amines gave good yields. For the cyclic secondary amines, piperidine and cyclopentylamine gave higher yields (leading to products **3a** and **3b**) than those derived from 1-methylpiperazine and morpholine (**3c** and **3d**, 52 and 68% yields). The acyclic aliphatic amines **2e** and **2f** also gave the corresponding amides in comparable yields to **2a** and **2b**. When propan-2-amine **2g** reacted with **1a**, 72% yield of **3g** was obtained. As expected, the sterically bulky *tert*-butylamine only gave **3h** in 52% yield, since presumably the *tert*-butyl group hindered the reaction. When cyclohexanamine (**2i**) and cyclopentanamine (**2j**) were tested, improved yields of the desired products **3i** and **3j** were achieved. Good to excellent yields were obtained when aliphatic amines, such as *n*-propylamine (**2k**), *n*-butylamine (**2l**), *n*-octylamine (**2m**), *n*-dodecylamine (**2n**) and benzylamine (**2o**) reacted with **1a**. It is worth noting that the same amide **3o** could be obtained from the reaction of dibenzylamine with α-diketone (**1a**) in 27% yield, and no other amide was isolated. Unfortunately, conducting the reaction with aryl amines (**2p** and **2q**) and **1a** afforded the desired amides **3p** and **3q** in only 34 and 43% yields, respectively. In addition, it was found that several 4,4′-disubstituted α-diketones exhibited different activity when they reacted with piperidine. The results showed that electron-withdrawing groups on the benzene ring gave better yields of the corresponding products (**3r**, **3s** *vs.* **3t**, **3u**, **3v**). The chloro group in the *ortho*-position of α-diketone led to 65% yield of amide **3w**.



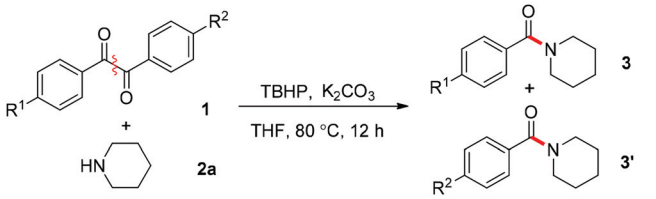
Scheme 2 TBHP-promoted amidation of α-diketones with amines. *Reaction conditions*: α-diketone (**1**, 0.50 mmol), amine (**2**, 0.50 mmol), TBHP (70% in H_2O, 2.0 mmol), K_2CO_3 (0.50 mmol), THF (2.0 mL), 80 °C, sealed tube, 12 h. [a] Isolated yields. [b] Dibenzylamine as amine source.

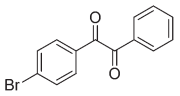
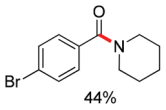
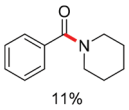
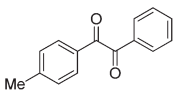
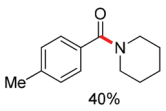
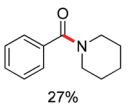
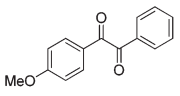
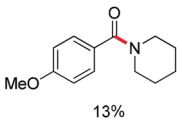
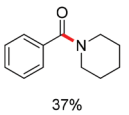
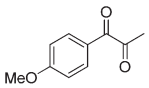
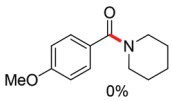


Scheme 3 TBHP-promoted amidation of α-diketones with tertiary amines. *Reaction conditions*: α-diketone (**1a** or **1b**, 0.50 mmol), amine (0.50 mmol), TBHP (70% in H_2O, 2.0 mmol), K_2CO_3 (0.50 mmol), THF (2.0 mL), 80 °C, sealed tube, 12 h.

On the other hand, it is well known that the cleavage of the inert C–N bond is extremely difficult, generally requiring the presence of transition metals and additives.[13] However, in the course of our efforts on amidation reactions, we found that the treatment of α-diketones with triethylamine also led to the formation of the corresponding amides, as shown in Scheme 3. The results indicated that both α-diketones **1a** and **1b** reacted with triethylamine and afforded the corresponding products in 45% (**3e**) and 37% (**3x**) yields. Unfortunately, the coupling reactions of α-diketones with other tertiary amines, such as tripropylamine and tributylamine, were not successful.

Table 3 TBHP-promoted reaction of α-diketones with piperidine[a]

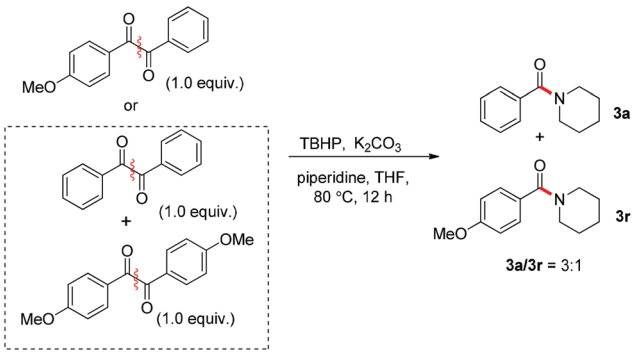


Entry	1	3, yield[b] (%)	3′, yield[b] (%)
1		 44%	 11%
2		 40%	 27%
3		 13%	 37%
4		 0%	 0%

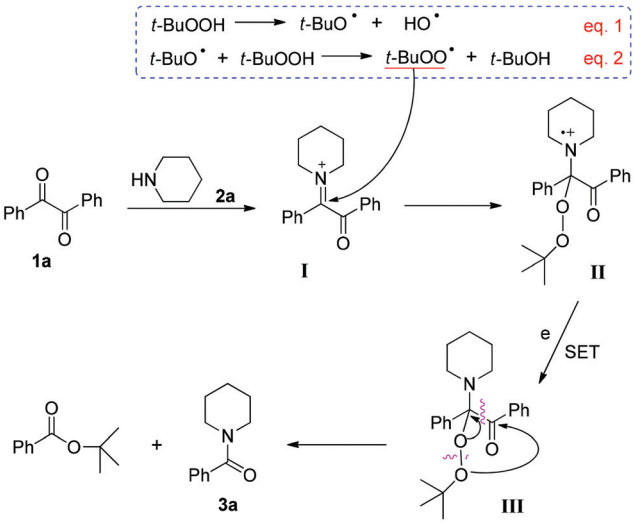
[a] *Reaction conditions*: α-diketone (**1**, 0.50 mmol), piperidine (**2a**, 0.50 mmol), TBHP (70% in H_2O, 2.0 mmol), K_2CO_3 (0.50 mmol), THF (2.0 mL), 80 °C, sealed tube, 12 h. [b] Isolated yield.

Then, our continued efforts focused on the selective formation of amides by the reactions of representative asymmetric α-diketones with piperidine, and the results are given in Table 3. It was found that asymmetric α-diketones, with Br, Me or MeO groups on one of the benzene rings, exhibited different activity when they reacted with piperidine, and moderate to good yields of mixed products were obtained, with ratios of 44 : 11 to 13 : 37. However, when the aromatic/aliphatic α-diketone, 1-(4-methoxyphenyl)propane-1,2-dione reacted with piperidine, no product was detected (Table 3, entry 4). Additionally, we noticed that the amides were isolated as the main products with moderate yields and the other possible by-products formed by radical reactions, such as self-coupling of aminyl radicals, radical coupling with THF, the solvent, and so on, may be present in the system, which accounts for the moderate yields of the corresponding amides **3**.

In order to obtain some information on competition experiments, the reaction of asymmetric 1,2-bis(4-methoxyphenyl)-ethane-1,2-dione with piperidine was carried out under the given conditions shown in Scheme 4. It was found that a 3/1 molar ratio of amides **3a**/**3r** could be obtained. On the other hand, a mixture of 1.0 eq. of 1,2-diphenylethane-1,2-dione and 1,2-bis(4-methoxyphenyl)ethane-1,2-dione was reacted with an



Scheme 4 Competition experiments. *Reaction conditions*: α-diketone (0.50 mmol), piperidine (0.50 mmol), TBHP (70% in H_2O, 2.0 mmol), K_2CO_3 (0.50 mmol), THF (2.0 mL), 80 °C, sealed tube, 12 h.



Scheme 5 Proposed reaction mechanism.

equal equivalent of piperidine under similar reaction conditions, and a comparable ratio of **3a**/**3r** (3/1) was also observed. These results showed that the introduction of a substituent on the phenyl ring of the 1,2-diketone molecules dramatically affects the yields of the corresponding amide products.

Although the exact mechanism of this reaction is not clear up till now, a plausible pathway for the amidation of α-diketone with piperidine is described in Scheme 5. Initially, an intermediate **I** was generated *via* the condensation of benzil (**1a**) with piperidine (**2a**). The obtained **I** then reacted with a *tert*-butylperoxy free radical generated from the reactions of eqn (1) and (2)[14] in Scheme 5 *via* homolytic cleavage of *tert*-butyl hydroperoxide to generate intermediate **II**, which underwent a SET process to afford intermediate **III**.[15] Finally, an intramolecular C–C bond cleavage of **III** occurs to afford the desired amide product **3a** and *tert*-butyl benzoate as side product. It should be noted that the involvement of radical species could be verified by addition of TEMPO (radical scavenger), which significantly suppressed the coupling reaction of **1a** with **2a**, with no formation of product **3a**.

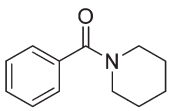
In conclusion, we have established a novel approach to amides through TBHP-mediated direct amidation of α-diketones with amines *via* oxidative cleavage of $C(sp^2)$–$C(sp^2)$ bonds under metal-free conditions.[16] A wide range of amides can be obtained in moderate to good yields through this protocol, which offers a new and alternative way for the construction of amides and further application into other reactions is ongoing in our laboratory.

Experimental section

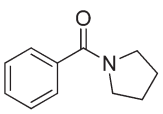
All the reactions of acetophenones and formamides were carried out under an air atmosphere. ^1H and ^{13}C NMR spectra were measured on a Bruker Avance NMR spectrometer (400 or 100 MHz, respectively) with $CDCl_3$ as solvent and recorded in ppm relative to internal tetramethylsilane standard. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; q, quartet. The coupling constants, *J*, are reported in hertz (Hz).

Typical procedure for the tandem reaction

Under air atmosphere, a sealable reaction tube with a Teflon-coated screw cap equipped with a magnetic stir bar was charged with α-diketone (benzil, **1a**, 0.50 mmol), piperidine (**2a**, 0.50 mmol), *t*-BuOOH (TBHP, 2.0 mmol), and K_2CO_3 (0.50 mmol). The rubber septum was then replaced by a Teflon-coated screw cap, and the reaction vessel placed in an oil-bath at 80 °C for 12 h. After the reaction was completed, it was cooled to room temperature and quenched with water and extracted with ethyl acetate. The resulting solution was directly filtered through a pad of silica gel using a sintered glass funnel, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (eluent: petroleum ether–ethyl acetate) to give the desired product phenyl(piperidin-1-yl)methanone (**3a**).

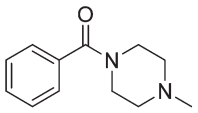


Phenyl(piperidin-1-yl)methanone, 3a. Colorless oil.[17]
^1H NMR (400 MHz, $CDCl_3$): δ 7.32 (br, 5H), 3.64 (br, 2H), 3.27 (br, 2H), 1.61–1.45 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 136.4, 129.3, 128.3, 126.7, 48.6, 43.1, 26.4, 25.6, 24.5.



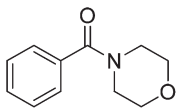
Phenyl(pyrrolidin-1-yl)methanone, 3b. White oil.[17]
^1H NMR (400 MHz, $CDCl_3$): δ 7.49–7.47 (m, 2H), 7.37–7.35 (m, 3H), 3.62 (t, J = 6.8 Hz, 2H), 3.39 (t, J = 6.4 Hz, 2H), 1.92–1.83 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.6, 137.2,

129.6, 128.1, 127.0, 49.5, 46.0, 26.3, 24.4.



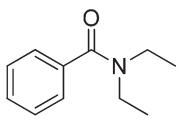
(4-Methylpiperazin-1-yl)(phenyl)methanone, 3c. Yellow solid.[18]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (br, 5H), 3.77 (br, 2H), 3.42 (br, 2H), 2.45–2.35 (m, 4H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 136.4, 129.2, 128.3, 126.7, 55.0 (2C), 47.5, 46.0, 42.0.



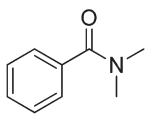
Morpholino(phenyl)methanone, 3d. White solid.[17]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (br, 5H), 3.69–3.45 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4, 135.3, 129.8, 128.5, 127.0, 66.8, 48.7, 43.1.



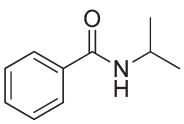
***N*,*N*-Diethylbenzamide, 3e.** Colorless oil.[19]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (br, 5H), 3.53 (br, 2H), 3.24 (br, 2H), 1.24–1.09 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3, 137.2, 129.0, 128.3, 126.2, 43.2, 39.2, 12.8.



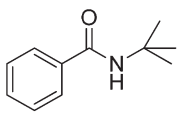
***N*,*N*-Dimethylbenzamide, 3f.** Colourless oil.[20]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (br, 5H), 3.09 (br, 3H), 2.95 (br, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 136.2, 129.5, 128.3, 127.0, 39.5, 35.3.



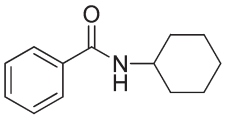
***N*-Isopropylbenzamide, 3g.** Colorless oil.[21]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76–7.75 (m, 2H), 7.49–7.41 (m, 3H), 5.94 (br, 1H), 4.34–4.26 (m, 1H), 1.28–1.26 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.9, 135.9, 131.0, 128.4, 126.6, 41.8, 22.8.



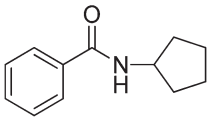
***N*-(*tert*-Butyl)benzamide, 3h.** Colorless oil.[22]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73–7.71 (m, 2H), 7.48–7.39 (m, 3H), 5.97 (br, 1H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.9, 135.9, 131.0, 128.4, 126.6, 51.5, 28.8.



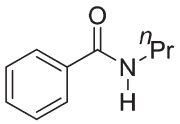
***N*-Cyclohexylbenzamide, 3i.** Colorless oil.[22]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76–7.74 (m, 2H), 7.47–7.36 (m, 3H), 6.22 (br, 1H), 3.97–3.93 (m, 1H), 2.01–1.99 (m, 2H), 1.75–1.71 (m, 2H), 1.64–1.61 (m, 1H), 1.43–1.34 (m, 2H), 1.28–1.16 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 135.1, 131.1, 128.4, 126.8, 48.7, 33.1, 25.5, 24.9.



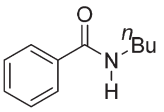
***N*-Cyclopentylbenzamide, 3j.** White solid.[22]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75–7.73 (m, 2H), 7.45–7.34 (m, 3H), 6.39 (br, 1H), 4.41–4.32 (m, 1H), 2.06–2.02 (m, 2H), 1.69–1.60 (m, 4H), 1.52–1.44 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.2, 134.9, 131.1, 128.3, 126.8, 51.6, 33.0, 23.8.



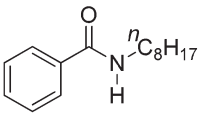
***N*-Propylbenzamide, 3k.** Colorless oil.[23]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77–7.75 (m, 2H), 7.48–7.37 (m, 3H), 6.47 (br, 1H), 3.41–3.36 (m, 2H), 1.66–1.57 (m, 2H), 0.97–0.94 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 134.8, 131.2, 128.4, 126.8, 41.7, 22.8, 11.4.



***N*-Butylbenzamide, 3l.** Colorless oil.[20]

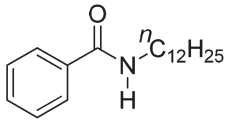
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77–7.75 (m, 2H), 7.46–7.36 (m, 3H), 6.48 (br, 1H), 3.43–3.42 (m, 2H), 1.61–1.54 (m, 2H), 1.43–1.33 (m, 2H), 0.95–0.91 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 134.8, 131.2, 128.4, 126.8, 39.8, 31.7, 20.1, 23.7.



***N*-Octylbenzamide, 3m.** White solid.[24]

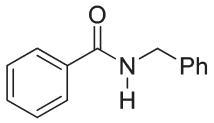
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77–7.75 (m, 2H), 7.48–7.37 (m, 3H), 6.47 (br, 1H), 3.44–3.39 (m, 2H), 1.60–1.55 (m, 2H), 1.31–1.26 (m, 10H), 0.88–0.85 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.5, 134.8, 131.2, 128.4, 126.8, 40.1, 31.7, 29.6,

29.2, 29.1, 27.0, 22.6, 14.0.



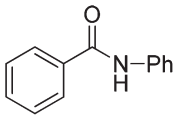
***N*-Dodecylbenzamide, 3n.** White solid.[25]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77–7.76 (m, 2H), 7.48–7.37 (m, 3H), 6.43 (br, 1H), 3.44–3.39 (m, 2H), 1.61–1.58 (m, 2H), 1.26 (br, 18H), 0.89–0.85 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.5, 134.9, 131.1, 128.4, 126.8, 40.1, 31.8, 29.6, 29.6, 29.6, 29.5, 29.5, 29.4, 29.3, 27.0, 22.6, 14.0.



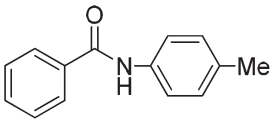
***N*-Benzylbenzamide, 3o.** White solid.[17]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81–7.79 (m, 2H), 7.51–7.47 (m, 1H), 7.42–7.40 (m, 2H), 7.35–7.29 (m, 5H), 6.73 (br, 1H), 4.63–4.61 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 138.2, 134.4, 131.4, 128.7, 128.5, 127.8, 127.5, 127.0, 44.0.



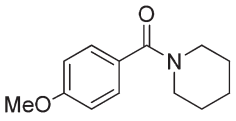
***N*-Phenylbenzamide, 3p.** White solid.[17]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (br, 1H), 7.88–7.86 (m, 2H), 7.66–7.64 (m, 2H), 7.56–7.54 (m, 1H), 7.48–7.45 (m, 2H), 7.38–7.35 (m, 2H), 7.17–7.14 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.8, 137.9, 135.0, 131.8, 129.0, 128.7, 127.0, 124.5, 120.3.



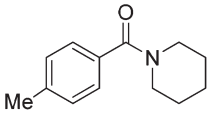
***N*-(*p*-Tolyl)benzamide, 3q.** Yellow solid.[26]

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (br, 1H), 7.87–7.85 (m, 2H), 7.54–7.51 (m, 3H), 7.46–7.43 (m, 2H), 7.17–7.15 (m, 2H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.7, 135.4, 135.1, 134.1, 131.6, 129.5, 128.6, 127.0, 120.4, 20.8.



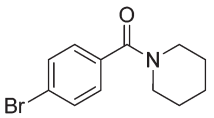
(4-Methoxyphenyl)(piperidin-1-yl)methanone, 3r. Yellow oil.[17]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.34 (m, 2H), 6.90–6.88 (m, 2H), 3.81 (s, 3H), 3.63–3.45 (m, 4H), 1.67–1.66 (m, 2H), 1.58–1.57 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 160.5, 128.8, 128.6, 113.6, 55.2, 48.7, 43.7, 29.6, 24.6.



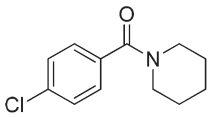
Piperidin-1-yl(*p*-tolyl)methanone, 3s. Yellow oil.[25]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.26 (m, 2H), 7.18–7.16 (m, 2H), 3.67–3.65 (m, 2H), 3.64–3.34 (m, 2H), 2.34 (s, 3H), 1.64–1.52 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4, 139.3, 133.5, 128.9, 126.8, 48.8, 43.1, 26.3, 25.7, 24.6, 21.3.



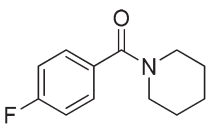
(4-Bromophenyl)(piperidin-1-yl)methanone, 3t. Yellow oil.[27]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51–7.49 (m, 2H), 7.25–7.23 (m, 2H), 3.65 (br, 2H), 3.29 (br, 2H), 1.64–1.48 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.1, 135.3, 131.5, 128.5, 123.5, 48.7, 43.1, 26.4, 25.5, 24.4.



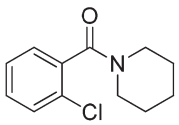
(4-Chlorophenyl)(piperidin-1-yl)methanone, 3u. Colorless oil.[17]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.30 (m, 4H), 3.66 (br, 2H), 3.30 (br, 2H), 1.64–1.50 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.1, 135.3, 134.8, 128.6, 128.3, 48.9, 43.5, 27.2, 25.9, 24.6.



(4-Fluorophenyl)(piperidin-1-yl)methanone, 3v. Colorless oil.[17]

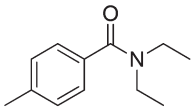
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.36 (m, 2H), 7.08–7.04 (m, 2H), 3.66 (br, 2H), 3.34 (br, 2H), 1.66–1.50 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.4, 163.2 (d, J = 247.6 Hz), 132.4 (d, J = 3.3 Hz), 129.6 (d, J = 8.3 Hz), 115.4 (d, J = 2.2 Hz), 48.9, 43.1, 26.4, 25.6, 24.5.



(2-Chlorophenyl)(piperidin-1-yl)methanone, 3w. Colorless oil.[27]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.35 (m, 1H), 7.29–7.24 (m, 3H), 3.78–3.68 (m, 2H), 3.22–3.09 (m, 2H), 1.64–1.41 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 136.4, 130.3, 129.8,

129.5, 127.5, 127.0, 47.7, 42.5, 26.2, 25.5, 24.4.



***N,N*-Diethyl-4-methylbenzamide, 3x.** Colorless oil.[28]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27–7.25 (m, 2H), 7.19–7.17 (m, 2H), 3.53 (br, 2H), 3.26 (br, 2H), 2.36 (s, 3H), 1.25–1.11 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 139.0, 134.3, 128.9, 126.3, 43.2, 38.9, 21.4, 14.2, 12.8.

Acknowledgements

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Notes and references

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