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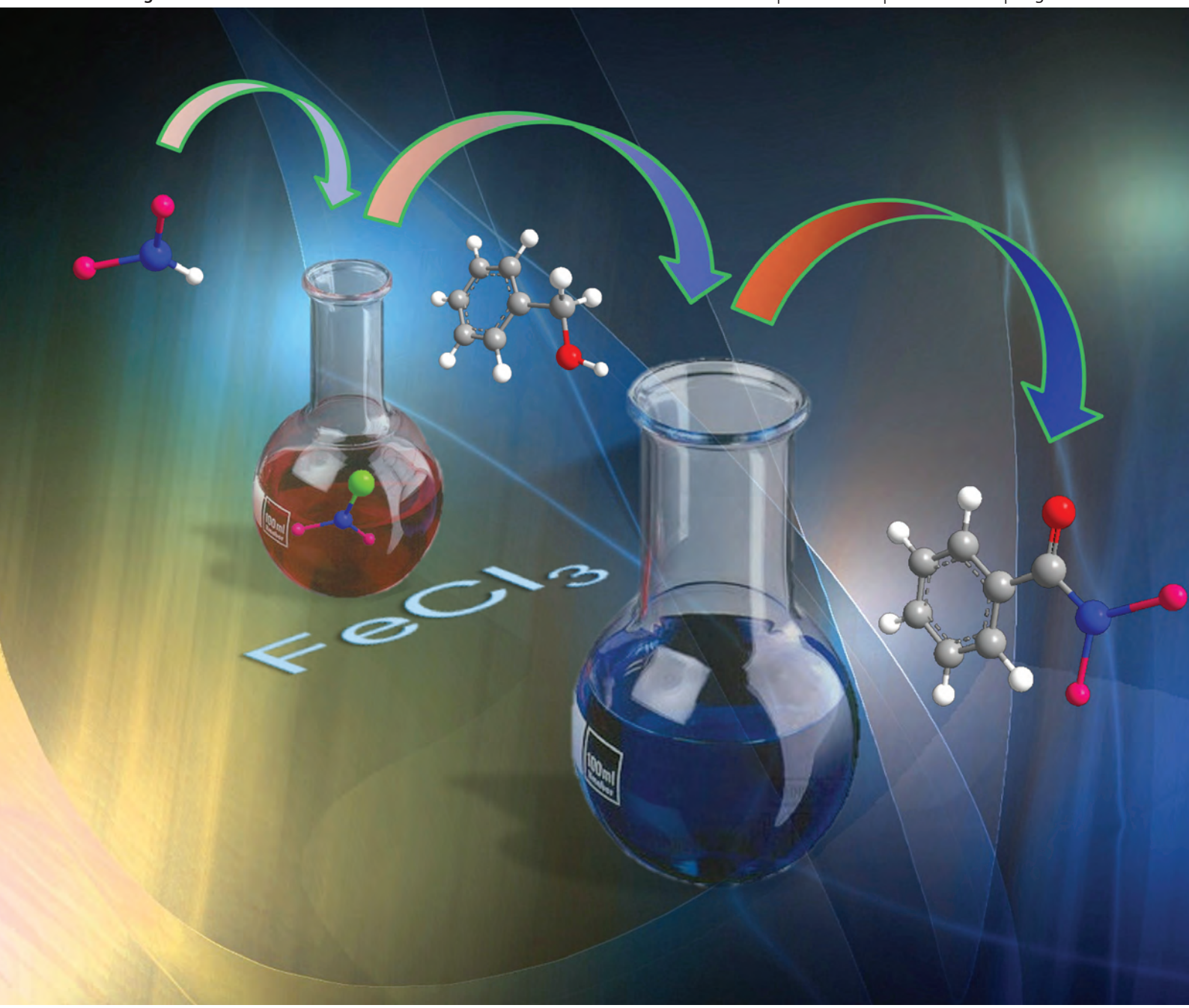

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Lidia De Luca *et al.*

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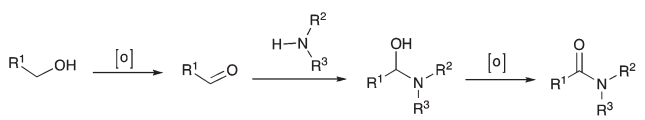
Silvia Gaspa, Andrea Porcheddu and Lidia De Luca*

A new iron-catalysed oxidative amidation of differently substituted benzylic alcohols with mono- and di-substituted amines was developed.

Introduction

The amide bond is one of the most significant functional groups contained in many natural products, polymers, pharmaceuticals and synthetic intermediates.[1] The classical method for amide synthesis is the acylation of amines with carboxylic acid derivatives (acid chlorides, anhydrides, active esters, *etc.*).[2] Several alternative strategies such as the Staudinger reaction,[3] the Schmidt reaction,[4] the Beckmann rearrangement,[5] the direct amide formation from unactivated carboxylic acids with amines[6] and the oxidative amidation of aldehydes[7] have been developed. However, many of these methods have the innate drawbacks of producing a stoichiometric amount of waste product and of using highly hazardous reagents. The direct amidation of alcohols with amines can be a potentially elegant alternative pathway since it uses cheap, abundant and stable starting materials.[8] To date, the oxidative amidation of alcohols is essentially promoted by homogeneous Ru- and Rh-based catalysts. Heterogeneous Ag-[9] and Au-based[10] catalysts were recently reported too. Usually, these strategies consist of the oxidation of an alcohol to the corresponding aldehyde that reacts with an amine. The hemiaminal intermediate is subsequently oxidized to give the corresponding amide (Scheme 1).



Scheme 1 Oxidative amidation of alcohols *via* hemiaminal intermediate formation.

Dipartimento di Chimica e Farmacia, Università degli Studi di Sassari, Via Vienna 2, Sassari, Italy. E-mail: ldeluca@uniss.it; Fax: +39-079-212069; Tel: +39-079-213529

†Electronic supplementary information (ESI) available: Experimental procedures, characterization of products, and copies of ^{1}H NMR and ^{13}C NMR spectra are provided. See DOI: 10.1039/c3ob40170g

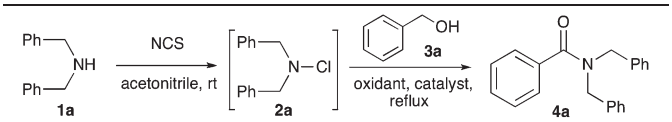
Nevertheless, most of the developed methodologies showed excellent activity only with sterically unhindered alcohols and unhindered amines. Furthermore they suffer from drawbacks derived from the formation and stability of the hemiaminal intermediate and the use of expensive and toxic transition metal catalysts. Therefore, the development of alternative routes to amide bond formation from alcohols remains an area of active research. Recently, Wang *et al.*[11] reported a pioneering I_2-mediated synthesis of *N*,*N*-dimethyl aryl amides starting from benzylic alcohols and dimethylformamide, *via* a radical pathway.

Indubitably it is a fundamentally different approach to amide synthesis, which deserves to be further developed. In this context, we wish to report a new and efficient procedure for the oxidative amidation of alcohols with *N*-chloroamines, prepared *in situ* from the corresponding amines, by the use of TBHP as an oxidant and iron(III) chloride as a catalyst and under base-free conditions. The use of iron salts as catalysts seems very attractive with respect to catalysis based on precious metals, because of their relative non-toxicity, easy availability and low price. Recently, our group has developed new protocols for the iron[12] and copper[13] catalysed amidation of aldehydes. Encouraged by our previous results, we have tested the possibility to perform an oxidative amidation of alcohols in view of their stability, availability and inexpensiveness compared to aldehydes.

Results and discussion

We began our investigation by treating dibenzylamine **1a** (1 equiv.) with *N*-chlorosuccinimide (NCS) (1.1 equiv.) in acetonitrile at room temperature. After 3 h, the corresponding *N*-benzyl-*N*-chloro-1-phenylmethanamine **2a** was quantitatively formed. This reaction mixture, containing the *N*-chloroamine generated *in situ*, was consecutively treated, without any purification, with benzyl alcohol **3a** (5 equiv.), $Cu(OAc)_2{\cdot}H_2O$ (14 mol%) and *tert*-butyl hydroperoxide (TBHP 70% aqueous solution, 5 equiv.) under reflux, for 2 h, generating the amide

Table 1 Oxidative amidation of alcohols: optimization of the reaction conditions[a]



Entry	Oxidant	Catalyst	Yield[b] (%)
1	TBHP	$Cu(OAc)_2{\cdot}H_2O$	20
2	TBHP	$FeCl_3{\cdot}6H_2O$	96
3	TBHP	$FeCl_2{\cdot}4H_2O$	98
4	TBPB	$FeCl_3{\cdot}6H_2O$	35
5	Benzoyl peroxide	$FeCl_3{\cdot}6H_2O$	32
6	H_2O_2	$FeCl_3{\cdot}6H_2O$	—
7	Oxone	$FeCl_3{\cdot}6H_2O$	—
8[c]	TBHP	$FeCl_3{\cdot}6H_2O$	27
9[d]	TBHP	$FeCl_3{\cdot}6H_2O$	30
10[e]	TBHP	$FeCl_3{\cdot}6H_2O$	58

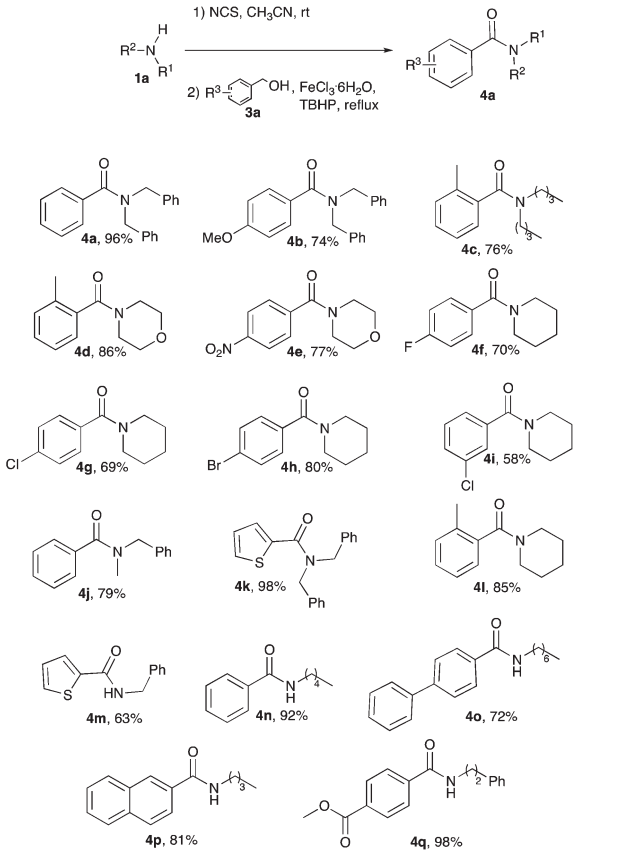
[a] Reaction conditions: dibenzylamine **1a** (1 equiv.), *N*-chlorosuccinimide (NCS) (1.1 equiv.), in acetonitrile at room temperature for 3 h. To this reaction mixture were added benzyl alcohol **3a** (5 equiv.), catalyst (14 mol%) and oxidant (5 equiv.) under reflux, until the disappearance of *N*-chloro amine monitored by TLC. [b] Yield refers to the isolated product after column chromatography. [c] Reaction performed using 2.5 equiv. of **3a**. [d] Reaction performed using 2.5 equiv. of TBHP. [e] Reaction performed at room temperature for 74 h.

4a in only 20% yield (Table 1, entry 1). In order to find the optimum reaction conditions, different parameters of the second step such as catalyst, oxidant, stoichiometric mole ratio of reactants and temperature were examined.

We performed the same reaction by the use of $FeCl_3{\cdot}6H_2O$ instead of $Cu(OAc)_2{\cdot}H_2O$, obtaining the product **4a** with a significant improvement of yield (96%) (Table 1, entry 2). Excellent results in terms of yields (98%) were obtained using $FeCl_2{\cdot}4H_2O$ (Table 1, entry 3), but, on the whole, $FeCl_3$ was chosen to catalyse the reaction due to its own stability. Next the role of the oxidant has been evaluated. Very poor results in terms of yield were observed employing different peroxides: *tert*-butyl peroxybenzoate and benzoyl peroxide were used, giving respectively 35% and 32% yields (Table 1, entries 4–5). No product formation was observed using classical oxidizing reagents such as H_2O_2 and oxone (Table 1, entries 6–7).

With respect to the amount of benzyl alcohol **3a** in the procedure, it was found that 5 equiv. were optimal. The decrease in the amount to 2.5 equiv. was detrimental (Table 1, entry 8). Likewise, the decrease in the amount of *tert*-butyl hydroperoxide (TBHP) from 5 equiv. to 2.5 equiv. led to a collapse of the yield (30%) (Table 1, entry 9). It was possible to perform the reaction at room temperature (Table 1, entry 10), but this involved a considerable lengthening of the reaction time (74 h) and a substantial yield reduction (58%). After finding the best performing reaction conditions, the methodology was tested with an array of commercially available alcohols and amines. As illustrated in Scheme 2, the methodology was applied to different substrates to afford a wide range of variously substituted amides in moderate to excellent yields.

When aliphatic alcohols, such as 1-octanol and 2,2-dimethyl-1-propanol, were employed as the substrates, no



Scheme 2 Oxidative amidation of alcohols: investigation of the substrate scope of the reaction.

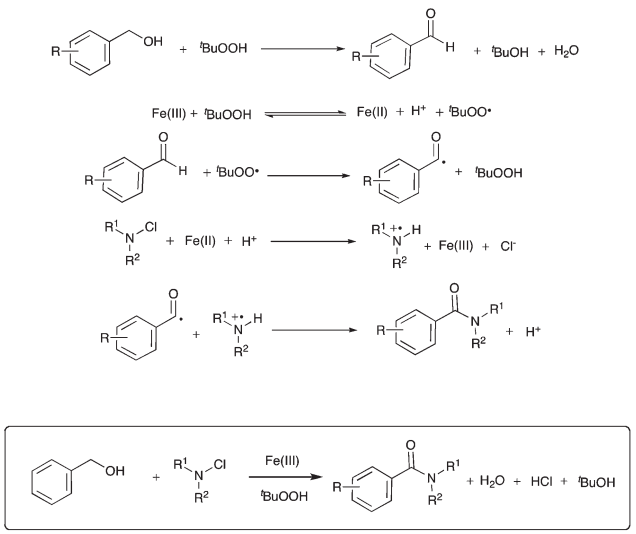
corresponding amides were obtained, since aliphatic alcohols were not oxidized to the corresponding aldehydes under the optimized reaction conditions.

Neither the electronic properties nor the steric effects of substituents on the aromatic ring of benzylic alcohols were found to have any influence on the reaction. Both electron-donating groups, such as benzylic C–H (Scheme 2, entries **4c** and **4d** and **4l**) and OMe (Scheme 2, entry **4b**), and withdrawing groups, such as NO_2 (Scheme 2, entry **4e**), were well tolerated providing the desired amides in good yields. Benzylic alcohol with carbonyl substituents like ester gave good results too (Scheme 2, **4q**). The reaction carried out on alcohols with halide substituents on the aromatic ring gave the corresponding amides, which could be further transformed by traditional cross-coupling reactions (Scheme 2, entries **4f–i**).

To prove the synthetic utility of the methodology, thiophene-2-carbaldehyde was subjected to optimized reaction conditions, giving the desired heteroaryl amides (Scheme 2, entries **4k** and **4m**) in good yield.

When the aromatic ring was replaced by hindered biphenyl or naphthyl groups, the corresponding amides were obtained in 72% and 81% yields respectively (Scheme 2, entries **4o** and **4p**).

The reaction was tested with a series of *N*,*N*-dialkyl-amines showing excellent tolerance. Acyclic (Scheme 2, entries **4a–c**, **4j**



Scheme 3 Proposed mechanism and global reaction.

and **4k**) as well as cyclic amines (Scheme 2, entries **4d–i** and **4l**) showed to be effective in this reaction. Furthermore mono-substituted amines gave the corresponding *N*-mono-substituted amides in good yields (Scheme 2, entries **4m–q**).

On the basis of previous studies[12,13] a possible reaction mechanism is shown in Scheme 3.

Firstly, benzyl alcohol is oxidized, by TBHP, to benzaldehyde.[14] The Fe(III) reacts with TBHP forming the *tert*-butylperoxy radical, Fe(II) and H^+ following the mechanism demonstrated by Barton and co-workers.[15] The *tert*-butylperoxy radical abstracts hydrogen from aldehyde to generate an acyl radical, as reported by Wan,[16] and the *N*-chloroamine, after protonation, is converted to an amino radical by a redox reaction as well documented by Minisci.[17] Finally, the acyl radical and the amino radical couple to form the desired amide.[12,13]

Conclusions

In conclusion we have reported a novel example of C–N bond formation *via* a new iron catalysed direct oxidative amidation of alcohols with *N*-chloroamines, prepared *in situ* from amines. The methodology was employed to prepare amides directly from substituted benzylic alcohols and primary and secondary amines. The procedure appears to be simple and convenient and uses cheap, stable and easily available reagents.

Experimental section

All reagents and solvents were as obtained from commercial sources. All the reactions were carried out under an N_2 atmosphere using standard techniques. Column chromatography was generally performed on silica gel (pore size 60 Å, 40–63 μm particle size) and reactions were monitored by thin-layer chromatography (TLC). Analysis was performed with Merck Kieselgel 60 F254 plates and visualized using UV light at 254 nm and $KMnO_4$ staining. ^{1}H NMR and ^{13}C NMR spectra were measured on a Bruker Avance III 400 spectrometer (400 MHz or 100 MHz, respectively) with $CDCl_3$ as a solvent and recorded in ppm relative to the internal tetramethylsilane standard. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; q, quartet; br, broad. The coupling constants, *J*, are reported in hertz (Hz). The IR spectra were recorded on a Jasco FTIR-480 Plus Fourier Transform spectrometer. Melting points were determined in open capillary tubes and are uncorrected. High resolution mass spectroscopy data of the product were collected on a Waters Micromass GCT instrument.

General procedure for the synthesis of amides 4a–q

An amine (0.32 mmol) was added to a solution of *N*-chlorosuccinimide (0.352 mmol) in 10 mL of acetonitrile under an N_2 atmosphere and at room temperature. The reaction was monitored by TLC until the disappearance of the amine (1–2 hours), and then an alcohol (1.6 mmol), TBHP (1.6 mmol, 0.22 mL of a 70 wt% in water) and $FeCl_3{\cdot}6H_2O$ (0.045 mmol) were added under an N_2 atmosphere.

The resulting reaction mixture was heated in an oil bath at 85 °C (the reaction was monitored by TLC until the disappearance of *N*-chloroamine). Then the reaction mixture was quenched with 20 mL of a saturated solution of Na_2SO_3 (for the removal of excess TBHP) and extracted three times with 40 mL of diethyl ether. The combined organic phases were dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The crude product was purified by silica gel column chromatography to provide the desired amides **4a–q**.

***N*,*N*-Dibenzylbenzamide (4a).**[13] Prepared according to the general procedure. The product was purified by flash chromatography on silica gel (v/v petroleum ether–AcOEt = 4.2/0.8), R_f = 0.44, to afford a white solid in 96% yield (m.p. 113–115 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.39 (s, 2H), 4.70 (s, 2H), 7.13–7.15 (m, 2H), 7.24–7.39 (m, 11H), 7.48–7.51 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 46.8, 51.4, 126.7, 127.0, 127.5, 128.4, 128.5, 128.7, 129.6, 136.2, 172.2; IR (neat) ν = 3058, 3028, 2924, 1633, 1494, 1452, 1423, 1362, 1265, 1143, 1076, 1027, 991, 736, 700.

***N*,*N*-Dibenzyl-4-methoxybenzamide (4b).**[13] Prepared according to the general procedure. The product was purified by flash chromatography on silica gel (v/v petroleum ether–AcOEt = 3.8/1.2), R_f = 0.38, to afford a white solid in 74% yield (m.p. 119–121 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.80 (s, 3H), 4.48 (br s, 2H), 4.67 br (s, 2H), 6.88 (d, J = 8.8 Hz, 2H), 7.2–7.38 (m, 10H), 7.48 (d, J = 8.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 44.1, 55.2, 60.3, 113.8, 126.9, 127.5, 128.2, 128.5, 128.7, 136.9, 160.2, 172.2; IR (neat) ν = 3062, 2924, 2853, 1629, 1513, 1494, 1421, 1363, 1265, 1176, 1030, 993, 738, 701.

***N*,*N*-Dibutyl-2-methylbenzamide (4c).** Prepared according to the general procedure. The product was purified by flash chromatography on silica gel (v/v petroleum ether–AcOEt =

4/1), R_f = 0.51, to afford a pale yellow oil in 76% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.74 (t, J = 7.2 Hz, 2H), 0.98 (t, J = 7.4 Hz, 2H), 1.1 (q, J = 7.4 Hz, 2H), 1.37–1.47 (m, 4H), 1.6–1.7 (m, 2H), 2.28 (s, 3H), 3.04 (t, J = 7.4 Hz, 2H), 3.3 (br s, 2H), 3.65 (br s, 2H), 7.12–7.25 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 14.1, 19.1, 19.9, 20.6, 29.8, 30.8, 44.2, 48.2, 125.8, 125.9, 128.6, 130.4, 134.1, 137.4, 171.4; IR (neat) ν = 2958, 2931, 2869, 1633, 1463, 1423, 1376, 1301, 1261, 746. HRMS (EI) ([M^+]) Calcd for $C_{16}H_{25}NO$: 247.1936, Found: 247.1933.

Morpholino(*o*-tolyl)methanone (4d).[18] Prepared according to the general procedure. The product was purified by flash chromatography on silica gel (v/v petroleum ether–AcOEt = 2.5/2.5), R_f = 0.31, to afford a yellow oil in 86% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.32 (s, 3H), 3.24 (br d, J = 4.5 Hz, 2H), 3.57 (br t, J = 4.5 Hz, 2H), 3.76–3.84 (br m, 4H), 7.14–7.3 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.1, 41.9, 47.3, 66.9, 67.0, 125.8, 126.0, 129.1, 130.5, 134.2, 135.6, 170.1; IR (neat) ν = 3054, 2983, 2923, 2859, 1633, 1431, 1265, 1157, 704.

Morpholino(4-nitrophenyl)methanone (4e).[18] Prepared according to the general procedure. The product was purified by flash chromatography on silica gel (v/v petroleum ether–AcOEt = 2.5/2.5), R_f = 0.23, to afford a white solid in 77% yield (m.p. 98–101 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.41–3.82 (br m, 8H), 7.61 (d, J = 8.8 Hz, 2H), 8.31 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 42.6, 48.0, 66.8, 124.0, 128.2, 141.4, 148.5, 168.1; IR (neat) ν = 2922, 2856, 1637, 1523, 1435, 1352, 1279, 1113, 1012, 895, 839, 735.

(4-Fluorophenyl)(piperidin-1-yl)methanone (4f).[19] Prepared according to the general procedure. The product was purified by flash chromatography on silica gel (v/v petroleum ether–AcOEt = 3/2), R_f = 0.2, to afford a pale yellow oil in 70% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.57 (br s, 2H), 1.71 (br s, 4H), 3.37 (br s, 2H), 3.71 (br s, 2H), 7.08–7.12 (m, 2H), 7.39–7.43 (m, 2H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.6, 25.7, 26.6, 43.2, 48.9, 115.3, 115.6, 129.0, 129.1, 132.4, 132.5, 161.9, 164.4, 169.4; IR (neat) ν = 2942, 1628, 1442, 1265, 1157, 1004, 847, 739.

(4-Chlorophenyl)(piperidin-1-yl)methanone (4g).[19] Prepared according to the general procedure. The product was purified by flash chromatography on silica gel (v/v petroleum ether–Et_2O = 3/2), R_f = 0.2, to afford a white solid in 69% yield (m.p. 59–61 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.54 (br, s, 2H), 1.70 (br s, 4H), 3.35 (br s, 2H), 3.71 (br s, 2H), 7.34–7.41 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.5, 25.6, 26.6, 43.2, 48.9, 128.4, 128.7, 134.8, 135.4, 169.2; IR (neat) ν = 2937, 1629, 1440, 1277, 1090, 1003, 737.

(4-Bromophenyl)(piperidin-1-yl)methanone (4h).[7g] Prepared according to the general procedure. The product was purified by flash chromatography on silica gel (v/v petroleum ether–Et_2O = 3/2), R_f = 0.23, to afford a white solid in 80% yield (m.p. 75–78 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.54 (br s, 2H), 1.70 (br s, 4H), 3.26 (br s, 2H), 3.71 (br s, 2H), 7.29 (d, J = 8.5 Hz, 2H), 7.55 (d, J = 8.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.5, 25.6, 26.5, 43.3, 48.8, 123.6, 128.6, 131.6, 135.3, 169.3; IR (neat) ν = 2933, 2854, 1631, 1441, 1277, 1111, 1068, 1001, 833, 733.

(3-Chlorophenyl)(piperidin-1-yl)methanone (4i).[20] Prepared according to the general procedure. The product was purified by flash chromatography on silica gel (v/v petroleum ether–AcOEt = 3.8/1.2), R_f = 0.45, to afford a yellow oil in 58% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.55 (br s, 4H), 1.71 (br s, 4H), 3.35 (br s, 2H), 3.72 (br s, 2H), 7.27–7.40 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.5, 25.6, 26.6, 43.2, 48.8, 124.9, 127.0, 129.5, 129.8, 134.5, 138.2, 168.7; IR (neat) ν = 2931, 2856, 1631, 1566, 1439, 1280, 800, 739.

***N*-Benzyl-*N*-methylbenzamide (4j).**[7h] Prepared according to the general procedure. The product was purified by flash chromatography on silica gel (v/v petroleum ether–Et_2O = 3.5/1.5), R_f = 0.26, to afford a pale yellow oil in 79% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.89 (br s, 1.5H), 3.06 (br s, 1.5H), 4.54 (br s, 1H), 4.79 (br s, 1H), 7.20–7.47 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 33.2, 37.1, 50.8, 55.2, 126.8, 127.0, 127.6, 127.9, 128.2, 128.4, 128.8, 129.6, 136.3, 136.6, 137.1, 170.8, 171.6; IR (neat) ν = 2921, 1631, 1450, 1400, 1265, 1070, 1026, 698.

***N*,*N*-Dibenzylthiophene-2-carboxamide (4k).**[13] Prepared according to the general procedure. The product was purified by flash chromatography on silica gel (v/v petroleum ether–Et_2O = 3/2), R_f = 0.58, to afford a white solid in 98% yield (m.p. 47–50 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.75 (s, 4H), 6.98 (dd, J = 3.7 Hz, J = 5.1 Hz, 1H), 7.30–7.42 (m, 11H), 7.47 (dd, J = 1.2 Hz, J = 5.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 50.1, 126.9, 127.6, 128.6, 128.8, 129.3, 136.6, 137.7, 165.1. IR (neat) ν = 3062, 3004, 2978, 2954, 2914, 1611, 1583, 1519, 1494, 1453, 1422, 1364, 1347, 1306, 1250, 1078, 889.

Piperidin-1-yl(*o*-tolyl)methanone (4l).[12] Prepared according to the general procedure. The product was purified by flash chromatography on silica gel (v/v petroleum ether–AcOEt = 3.5/1.5), R_f = 0.38, to afford a pale yellow oil in 85% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (s, 2H), 1.66 (s, 4H), 2.31 (s, 3H), 3.17 (d, J = 4.1 Hz, 2H), 3.71 (br s, 1H), 3.79 (br s, 1H), 7.21 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.9, 24.5, 25.7, 26.5, 42.3, 47.8, 125.6, 125.8, 128.5, 130.2, 134.0, 136.7, 169.8; IR (neat) ν = 3049, 2938, 2857, 1627, 1444, 1350, 1288, 1271, 1240, 1129, 1097, 1027, 1000, 733, 700, 665.

***N*-Benzylthiophene-2-carboxamide (4m).**[21] Prepared according to the general procedure. The product was purified by flash chromatography on silica gel (v/v petroleum ether–Et_2O = 2.5/2.5), R_f = 0.35, to afford a pale yellow oil in 63% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.64 (d, J = 5.7 Hz, 2H), 6.35 (br s, 1H), 7.09 (dd, J = 3.7 Hz, J = 5.1 Hz, 1H), 7.31–7.35 (m, 1H), 7.37–7.38 (m, 4H), 7.50 (dd, J = 1.2 Hz, J = 5.1 Hz, 1H), 7.53 (dd, J = 1.1 Hz, J = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 44.0, 127.6, 127.7, 127.9, 128.1, 128.8, 130.0, 138.0, 138.7, 161.8; IR (neat) ν = 2922, 1629, 1545, 1421, 1265, 737.

***N*-Pentylbenzamide (4n).**[22] Prepared according to the general procedure. The product was purified by flash chromatography on silica gel (v/v petroleum ether–Et_2O = 2.5/2.5), R_f = 0.51, to afford a pale yellow oil in 92% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.94 (t, J = 7.1 Hz, 3H), 1.38 (m, 4H), 1.64 (t, J = 7.3 Hz, 2H), 3.47 (q, J = 7.2 Hz, 2H), 6.19 (br s, 1H), 7.42–7.53 (m, 3H), 7.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 22.4, 29.1, 29.4, 40.1, 126.8, 128.5, 131.3, 134.9, 167.5;

IR (neat) ν = 3064, 2956, 2929, 2860, 1639, 1576, 1545, 1491, 1464, 1375, 1309, 1209, 1153, 1074, 1028, 928, 877, 804, 698.

***N*-Heptylbiphenyl-4-carboxamide (4o).** Prepared according to the general procedure. The product was purified by flash chromatography on silica gel (v/v petroleum ether–AcOEt = 4/1), R_f = 0.39, to afford a pale yellow oil in 72% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, J = 6.9 Hz, 3H), 1.28–1.42 (m, 8H), 1.63–1.70 (m, 2H), 3.50 (q, J = 6.9 Hz, 2H), 6.18 (br s, 1H), 7.41 (t, J = 7.3 Hz, 1H), 7.49 (t, J = 7.7 Hz, 2H), 7.62–7.69 (m, 4H), 7.85 (d, J = 8.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.6, 27.0, 29.0, 29.7, 31.8, 40.1, 127.1, 127.2, 127.3, 127.9, 128.9, 133.5, 140.1, 144.1, 167.2; IR (neat) ν = 3041, 2922, 2852, 1630, 1537, 1469, 1265, 850, 740; HRMS (EI) ([M^+]) Calcd for $C_{20}H_{25}NO$: 295.1936, Found: 295.1938.

***N*-Butylnaphthalene-2-carboxamide (4p).**[23] Prepared according to the general procedure. The product was purified by flash chromatography on silica gel (v/v petroleum ether–Et_2O = 3/2), R_f = 0.25, to afford a white solid in 81% yield (m.p. 98–101 °C);^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (t, J = 7.3 Hz, 3H), 1.44–1.53 (m, 2H), 1.64–1.71 (m, 2H), 3.57 (q, J = 8.4 Hz, 2H), 6.00 (br s, 1H), 7.45–7.49 (m, 1H), 7.52–7.61 (m, 3H), 7.88–7.94 (m, 2H), 8.31 (d, J = 8.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 20.2, 31.8, 39.8, 124.7, 125.4, 126.4, 127.1, 128.3, 130.1, 133.7, 134.9, 169.5. IR (neat) ν = 3051, 2927, 1637, 1539, 1460, 1304, 1257, 1151, 1020, 779, 734.

Methyl 4-(phenethylcarbamoyl)benzoate (4q). Prepared according to the general procedure. The product was purified by flash chromatography on silica gel (v/v petroleum ether–Et_2O = 2/3), R_f = 0.34, to afford a white solid in 98% yield (m.p. 141–145 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.97 (t, J = 6.8 Hz, 2H), 3.76 (q, J = 6.2 Hz, 2H), 3.95 (s, 3H), 6.23 (br s, 1H), 7.25–7.38 (m, 5H), 7.76 (d, J = 8.3 Hz, 2H), 8.09 (d, J = 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.6, 41.2, 52.4, 126.7, 126.9, 128.7, 128.8, 129.8, 132.7, 138.5, 138.7, 166.3, 166.6. IR (neat) ν = 3327, 2923, 1720, 1635, 1543, 1439, 1280, 1196, 1157, 1113, 870, 821, 739, 698; HRMS (EI) ([M^+]) Calcd for $C_{17}H_{17}NO_3$: 283.1208, Found: 283.1211.

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