Copper-Catalyzed C–N Bond Formation through C–H/N–H Activation: A Novel Approach for the Synthesis of Multisubstituted Ureas

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General Information

All manipulations were carried out under air atmosphere. Tert-Butyl hydroperoxide (70 % solution in water) was purchased from Acros Organics and used without further purification. Column chromatography was generally performed on silica gel (200-300 mesh) and reactions were monitored by thin layer chromatography (TLC) using UV light to visualize the course of the reactions. 1H NMR and 13C NMR spectra were recorded in CDCl3 at Bruker ARX-300 MHz spectrometer with chemical shifts referenced to SiMe4 as internal standard. Chemical shifts are reported in parts per million (ppm) and referenced to the residual solvent resonance. Coupling constant (J) are reported in hertz (Hz). Standard abbreviations indicating multiplicity were used as follows: s = singlet, d = double, t = triplet, dd = double doublet, tt = triple triplet, q = quartet, m = multiplet, b = broad. HRMS were recorded on an Agilent 6210 TOF LC/MS equipped with electrospray ionization (ESI) probe operating in positive or negative ion mode.

General Procedure for the synthesis of ureas 3a–3x:

The N-alkoxyarylamides (0.5 mmol), N, N-disubstituted formamide (26 mmol), CuCl2·2H2O (0.015 mmol, 3 mol%), TBHP (1.5 mmol, 0.2 mL of a 70% aqueous solution) were added to a test tube in air. The reaction mixture was stirred at room temperature for 5 h and was quenched with a saturated solution of Na2SO3 (for removal of excess TBHP) and extracted with ethyl acetate. The organic solvent was removed under vacuum and purification by chromatography on a silica gel column afforded the desired product.

General Procedure: The synthesis of N-alkoxy benzamides
Method A:

Methoxylamine hydrochloride (840 mg, 10 mmol) and potassium carbonate (2.76 g, 20 mmol) were dissolved in a mixture of water (25 mL) and EtOAc (50 mL), and cooled to 0 °C upon which acyl chloride (10 mmol) was added dropwise. The reaction was then allowed to warm to r.t. and stirred for between 5 h and overnight. The product was isolated by diluting the mixture with EtOAc/H₂O and separating the layers, the organic phase was then washed with brine and dried over MgSO₄, filtered and concentrated to give the product which was then recrystallized (EtOAc/Hex) to give the target compound (1a-1m). Procedure described in Fisher et al. J. Org. Chem. 1993, 58, 3643.

Method B:

N-hydroxybenzamide (1.4 g, 10 mmol) and NaOH (0.44 g, 11 mol) were dissolved in a mixture of water (2 mL) and EtOH (30 mL), and the alkyl bromide (11 mol) were added dropwise. The reaction was then allowed to warm to reflux and stirred for 16 h. The solvent was removed and diluted with EtOAc/H₂O and separated the layers, the organic phase was then washed with brine and dried over MgSO₄, filtered and concentrated which was then purified by column chromatography on silica gel (EtOAc/Hex=1:1) to give the compound (1n-1t). Procedure described in Morris T. Reagan et al. J. Am. Chem. Soc. 1968, 90, 4096.

The data of new substrates

N-methoxy-2,4,6-trimethylbenzamide (1h). white solid, 33% yield, mp. 146-148°C. ¹H NMR (300 MHz, CDCl₃) δ 8.85 (s, 1H), 6.75 (s, 2H), 3.80 (s, 3H), 2.23 (s, 3H), 2.19 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 167.7, 139.3, 135.3, 130.6, 128.2, 64.3, 21.2, 18.9; HRMS (ESI): calculated for C₁₁H₁₅NNaO₂: 216.0995 [M+Na]⁺; found: 216.0982.

N-(prop-2-yn-1-yl)oxy)benzamide (1p). white solid, 78% yield, mp. 85-87°C. ¹H NMR (300 MHz, CDCl₃) δ 9.93 (s, 1H), 7.76 (d, J=7.7, 2H), 7.43 (m, 3H), 4.60 (s, 2H), 2.51 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 166.5, 132.2, 131.5, 128.67, 127.4, 78.0, 76.4, 63.6; HRMS (ESI): calculated for C₁₀H₉NNaO₂: 198.0526 [M+Na]⁺; found: 198.0520.
**N-(isopentyloxy)benzamide (1r).** yellow oil, 65% yield. $^1$H NMR (300 MHz, CDCl$_3$) δ 10.31 (s, 1H), 7.76 (d, $J$=7.3, 2H), 7.48–7.26 (m, 3H), 3.97 (t, $J$=6.8, 2H), 1.65 (m, 1H), 1.50 (q, $J$=6.8, 2H), 0.86 (s, 3H), 0.83 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 166.2, 132.0, 131.8, 128.5, 127.3, 75.3, 36.7, 25.0, 22.6; HRMS (ESI): calculated for C$_{12}$H$_{17}$NNaO$_2$: 230.1152 [M+Na]$^+$; found: 230.1147.

**2-(3-chlorophenyl)-N-methoxyacetamide(1y).** white solid, 82% yield, mp. 72–74°C. $^1$H NMR (300 MHz, CDCl$_3$) δ 11.05 (s, 1H), 7.26 (s, 1H), 7.17–7.10 (m, 3H), 3.66 (s, 3H), 3.35 (s, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 168.3, 136.5, 134.1, 129.7, 129.1, 127.3, 127.1, 63.8, 39.1; HRMS (ESI): calculated for C$_9$H$_{11}$ClNO$_2$: 200.0473 [M+H]$^+$; found: 200.0462.

**Table S1: Optimization of reaction conditions.**

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<th>Entry</th>
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\(^{a}\) Reaction conditions: 0.5 mmol N-methoxybenzamide, 3 mol% Cu catalyst, 52 equiv N, N-dimethylformamide, r.t, 3.0 equiv oxidant, 5h. \(^{b}\) Isolated yield. \(^{c}\) 6 equiv N, N-dimethylformamide.

### Transformations of the multisubstituted N-acyl ureas

In order to further show the synthetic application, we tried our best to transform the N-acyl ureas into other diverse derivatives. Although many methods reported by other groups had been tested, \(^{1}\) the N-deprotected product could not be detected. The compound 3d was selected as the substrate in the transformation.

\[
\begin{align*}
\text{hv} &> 290 \text{ nm, MeOH} \\
\text{SmI\(_2\), THF} \\
10 \text{ mol% Pd/C, EtOH, H\(_2\)} \\
\text{NaH, THF} \\
\text{TiCl\(_3\), EtOH} \\
\end{align*}
\]

The TEMPO adduct spectrum of the MI


### Effect of the radical scavenger

CuCl\(_2\)-2H\(_2\)O (0.015 mmol), TBHP (1.5 mmol) were placed in a dry sealable tube. To this, dried DMF (2.0 mL), N-methoxybenzamide (0.5 mmol) (1a) and TEMPO (3.0 equiv) were added. The tube was sealed, and stirred for one night at room temperature. Then it was detected with MS, no product (3a) were found and the TEMPO adduct was detected. It indicated that the reaction proceeded through the activation of the sp\(^2\) C–H of formamides by a radical mechanism.

### The TEMPO adduct Spectrum of the MI
Compound characterizations

\[
\text{N-(dimethylcarbamoyl)-N-methoxybenzamide (3a). colorless oil, 77\% yield.} 
\]

\[\text{\textsuperscript{1}H NMR (300 MHz, CDCl}_3\text{) } \delta 7.80-7.62 (m, 2H), 7.47-7.22 (m, 3H), 3.97 (s, 3H), 3.11 (s, 3H), 2.99 (s, 3H); \text{\textsuperscript{13}C NMR (75 MHz, CDCl}_3\text{) } \delta 151.9, 148.2, 130.4, 130.4, 128.5, 126.1, 63.0, 37.0, 36.9; \text{HRMS (ESI): calculated for C}_{11}\text{H}_{14}\text{N}_2\text{NaO}_3: 245.0896 [M+Na\textsuperscript{+}]; found: 245.0894.} \]

\[
\text{N-(dimethylcarbamoyl)-4-fluoro-N-methoxybenzamide (3b). colorless oil, 69\% yield.} 
\]

\[\text{\textsuperscript{1}H NMR (300 MHz, CDCl}_3\text{) } \delta 7.80-7.62 (m, 2H), 7.15-6.89 (m, 2H), 3.95 (s, 3H), 3.10 (s, 3H), 2.99 (s, 3H); \text{\textsuperscript{13}C NMR (75 MHz, CDCl}_3\text{) } \delta 165.7, 162.4, 149.6 (d, } J=332.3, 128.1 (d, } J=9.0, 126.6(d, } J=3.0, 115.6 (d, } J=21.2, 63.0, 36.9, 36.8; \text{HRMS (ESI): calculated for C}_{11}\text{H}_{13}\text{FN}_2\text{NaO}_3: 263.0802 [M+Na\textsuperscript{+}]; found: 263.0811.} \]

\[
\text{4-chloro-N-(dimethylcarbamoyl)-N-methoxybenzamide (3c). colorless oil, 58\% yield.} 
\]

\[\text{\textsuperscript{1}H NMR (300 MHz, CDCl}_3\text{) } \delta 7.64 (d, } J=8.4, 2H), 7.33 (d, } J=8.4, 2H), 3.96 (s, 3H), 3.10 (s, 3H), 2.99 (s, 3H); \text{\textsuperscript{13}C NMR (75 MHz, CDCl}_3\text{) } \delta 151.8, 147.4, 136.4, 129.0, 128.8, 127.4, 63.1, 37.0, 36.9; \text{HRMS (ESI): calculated for C}_{11}\text{H}_{13}\text{ClN}_2\text{NaO}_3: 279.0507 [M+Na\textsuperscript{+}]; found: 279.0513.} \]

\[
\text{4-bromo-N-(dimethylcarbamoyl)-N-methoxybenzamide (3d). colorless oil, 59\% yield.} 
\]
\[ ^1H\text{ NMR (300 MHz, CDCl}_3 \delta 7.61-7.55 (m, 2H), 7.52-7.46 (m, 2H), 3.96 (s, 3H), 3.11 (s, 3H), 3.00 (s, 3H); }^{13}C\text{ NMR (75 MHz, CDCl}_3 \delta 151.8, 147.5, 131.8, 129.5, 127.6, 124.8, 63.2, 37.0, 36.9; }\text{HRMS (ESI): calculated for C}_{11}H_{13}BrN_2NaO_5: 323.0002 [M+Na]^+; found: 323.0001.}\]

\[
\text{N-\text{(dimethylcarbamoyl)-N-methoxy-4-nitrobenzamide (3e). colorless oil, 56% yield. } ^1H\text{ NMR (300 MHz, CDCl}_3 \delta 8.22-8.16 (m, 2H), 7.89-7.83 (m, 2H), 4.00 (s, 3H), 3.12 (s, 3H), 3.00 (s, 3H); }^{13}C\text{ NMR (75 MHz, CDCl}_3 \delta 151.5, 148.7, 146.5, 136.6, 126.8, 123.7, 63.5, 37.0, 36.9; }\text{HRMS (ESI): calculated for C}_{11}H_{13}N_3NaO_5: 290.0747 [M+Na]^+; found: 290.0745.}\]

\[
\text{2-chloro-N-\text{(dimethylcarbamoyl)-N-methoxybenzamide (3f). colorless oil, 63% yield. } ^1H\text{ NMR (300 MHz, CDCl}_3 \delta 7.67-7.64 (m, 1H), 7.43-7.25 (m, 3H), 3.99 (s, 3H), 3.09 (s, 3H), 2.94 (s, 3H); }^{13}C\text{ NMR (75 MHz, CDCl}_3 \delta 151.4, 147.2, 132.8, 131.9, 131.2, 130.3, 130.0, 126.9, 63.1, 36.8; }\text{HRMS (ESI): calculated for C}_{11}H_{13}ClN_2NaO_5: 279.0507 [M+Na]^+; found: 279.0503.}\]

\[
\text{N-\text{(dimethylcarbamoyl)-N-methoxy-1-naphthamide (3g). colorless oil, 56% yield. } ^1H\text{ NMR (300 MHz, CDCl}_3 \delta 8.71 (d, J=8.5, 1H), 7.94-7.77 (m, 3H), 7.65-7.44 (m, 3H), 4.09 (s, 3H), 3.10 (s, 3H), 2.95 (s, 3H); }^{13}C\text{ NMR (75 MHz, CDCl}_3 \delta 151.9, 148.4, 133.8, 130.9, 130.7, 128.5, 127.9, 127.6, 127.2, 126.2, 125.8, 124.9, 63.0, 36.7; }\text{HRMS (ESI): calculated for C}_{13}H_{16}N_2NaO_5: 295.1053 [M+Na]^+; found: 295.1056.}\]

\[
\text{N-\text{(dimethylcarbamoyl)-N-methoxy-2,4,6-trimethylbenzamide (3h). colorless oil, 77% yield. } ^1H\text{ NMR (300 MHz, CDCl}_3 \delta 6.86 (s, 2H), 3.94 (s, 3H), 3.03 (s, 3H), 2.90 (s, 3H), 2.41 (s, 6H), 2.27 (s, 3H); }^{13}C\text{ NMR (75 MHz, CDCl}_3 \delta 151.5, 147.4, 139.5, 138.2, 128.7, 127.2, 62.7, 36.8, 21.2, 20.1; }\text{HRMS (ESI): calculated for C}_{14}H_{20}N_2NaO_5: 287.1366 [M+Na]^+; found: 287.1371.}\]

\[
\text{N-\text{(dimethylcarbamoyl)-N,4-dimethoxybenzamide (3i). colorless oil, 74% yield. } ^1H\text{ NMR (300 MHz, CDCl}_3 \delta 7.67-7.59 (m, 2H), 6.90-6.82 (m, 2H), 3.92 (s, 3H), 3.78 (s, 3H), 3.09 (s, 3H), 2.97 (s, 3H); }^{13}C\text{ NMR (75 MHz, CDCl}_3 \delta 161.3, 152.0, 148.1, 127.6, 122.7, 113.9, 62.74, 55.3, 36.8, 36.7; }\text{HRMS (ESI): calculated for C}_{13}H_{16}N_2NaO_4: 275.1002 [M+Na]^+; found: 275.1005.}\]
N-(dimethylcarbamoyl)-N-methoxycinnamamide (3j). colorless oil, 75% yield. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.49–7.39 (m, 2H), 7.38–7.24 (m, 3H), 6.97 (d, $J=16.1$, 1H), 6.68 (d, $J=16.1$, 1H), 3.93 (s, 3H), 3.11 (s, 3H), 3.01 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 151.7, 149.5, 135.5, 135.0, 129.0, 128.8, 127.2, 118.2, 62.9, 36.9, 36.8; HRMS (ESI): calculated for C$_{13}$H$_{16}$N$_2$NaO$_3$: 271.1053 [M+Na]$^+$; found: 271.1065.

N-(dimethylcarbamoyl)-N-methoxythiophene-2-carboxamide (3k). colorless oil, 75% yield. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.35–7.29 (m, 2H), 7.04–6.96 (m, 1H), 3.94 (s, 3H), 3.10 (s, 3H), 3.01 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 151.5, 145.1, 133.1, 128.2, 127.8, 127.2, 63.0, 36.9, 36.8; HRMS (ESI): calculated for C$_9$H$_{12}$N$_2$NaO$_3$: 251.0461 [M+Na]$^+$; found: 251.0450.

N-(dimethylcarbamoyl)-N-methoxyfuran-2-carboxamide (3l). colorless oil, 80% yield. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.46–7.42 (m, 1H), 6.67 (d, $J=3.4$, 1H), 6.43–6.39 (m, 1H), 3.94 (s, 3H), 3.06 (s, 3H), 2.97 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 151.5, 144.5, 141.6, 112.1, 111.9, 111.5, 63.3, 37.0, 36.8; HRMS (ESI): calculated for C$_9$H$_{12}$N$_2$NaO$_4$: 235.0689 [M+Na]$^+$; found: 235.0681.

N-(dimethylcarbamoyl)-N-ethoxybenzamide (3m). colorless oil, 75% yield. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.77–7.68 (m, 2H), 7.42–7.31 (m, 3H), 4.21 (q, $J=7.0$, 2H), 3.11 (s, 3H), 2.99 (s, 3H), 1.32 (t, $J=7.0$, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 152.1, 148.1, 130.6, 130.2, 128.4, 126.0, 70.6, 36.8, 14.6; HRMS (ESI): calculated for C$_{13}$H$_{16}$N$_2$NaO$_3$: 259.1053 [M+Na]$^+$; found: 259.1057.

N-(dimethylcarbamoyl)-N-propoxybenzamide (3n). colorless oil, 76% yield. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.72–7.75 (m, 2H), 7.41–7.31 (m, 3H), 4.12 (t, $J=6.6$, 2H), 3.10 (s, 3H), 2.99 (s, 3H), 1.81 – 1.63 (m, 2H), 0.96 (t, $J=7.4$, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 152.1, 148.2, 130.6, 130.1, 128.4, 126.0, 76.5, 36.8, 22.3, 10.3; HRMS (ESI): calculated for C$_{13}$H$_{18}$N$_2$NaO$_3$: 273.1210 [M+Na]$^+$; found: 273.1211.

N-(dimethylcarbamoyl)-N-isoproxybenzamide (3o). colorless oil, 67% yield. $^1$H
NMR (300 MHz, CDCl\textsubscript{3}) δ 7.79–7.69 (m, 2H), 7.44–7.30 (m, 3H), 4.50–4.33 (m, 1H), 3.10 (s, 3H), 2.99 (s, 3H), 1.31–1.29 (d, 6H); \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}) δ 152.3, 148.0, 130.8, 130.0, 128.4, 126.0, 76.4, 36.8, 21.5; HRMS (ESI): calculated for C\textsubscript{13}H\textsubscript{18}N\textsubscript{2}NaO\textsubscript{3}: 273.1210 [M+Na]\textsuperscript{+}; found: 273.1222.

\[
\begin{array}{c}
\text{N-(dimethylcarbamoyl)-N-}
\end{array}
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\textit{N-(dimethylcarbamoyl)-N-(prop-2-yn-1-yloxy)benzamide (3p).} colorless oil, 77% yield. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) δ 7.72–7.75 (m, 2H), 7.44–7.31 (m, 3H), 4.74 (d, J=2.3, 2H), 3.12 (s, 3H), 2.99 (s, 3H), 2.50 (t, J=2.3, 1H); \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}) δ 151.8, 149.5, 130.6, 130.1, 128.5, 126.3, 79.3, 75.0, 62.5, 36.9; HRMS (ESI): calculated for C\textsubscript{13}H\textsubscript{14}N\textsubscript{2}NaO\textsubscript{3}: 269.0897 [M+Na]\textsuperscript{+}; found: 269.0930.

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\textit{N-(dimethylcarbamoyl)-N-(pentyloxy)benzamide (3q).} colorless oil, 74% yield. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) δ 7.72–7.75 (m, 2H), 7.44–7.31 (m, 3H), 4.16 (t, J=6.7, 2H), 3.10 (s, 3H), 1.72 (m, 2H), 1.40–1.32 (m, 4H), 0.92 (t, J=7.0, 3H); \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}) δ 152.1, 149.5, 130.6, 130.1, 128.5, 126.0, 75.1, 36.8, 28.7, 28.0, 22.5, 14.1; HRMS (ESI): calculated for C\textsubscript{15}H\textsubscript{22}N\textsubscript{2}NaO\textsubscript{3}: 301.1528 [M+Na]\textsuperscript{+}; found: 301.1527.

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\end{array}
\]

\textit{N-(dimethylcarbamoyl)-N-(isopentyloxy)benzamide (3r).} colorless oil, 70% yield. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) δ 7.78–7.70 (m, 2H), 7.46–7.32 (m, 8H), 5.22 (s, 2H), 3.07 (s, 3H), 2.97 (s, 3H); \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}) δ 152.1, 149.0, 137.4, 130.4, 128.8, 128.5, 128.4, 128.2, 128.0, 126.2, 76.9, 36.9; HRMS (ESI): calculated for C\textsubscript{18}H\textsubscript{22}N\textsubscript{2}NaO\textsubscript{3}: 301.1528 [M+Na]\textsuperscript{+}; found: 301.1527.

\[
\begin{array}{c}
\text{N-(benzyloxy)-N-(}
\end{array}
\]

\textit{N-(benzyloxy)-N-(dimethylcarbamoyl)benzamide (3s).} colorless oil, 64% yield. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) δ 7.78–7.72 (m, 2H), 7.46–7.30 (m, 8H), 5.22 (s, 2H), 3.07 (s, 3H), 2.97 (s, 3H); \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}) δ 152.1, 149.0, 137.4, 130.4, 128.8, 128.5, 128.4, 128.2, 128.0, 126.2, 76.9, 36.9; HRMS (ESI): calculated for C\textsubscript{18}H\textsubscript{18}N\textsubscript{2}NaO\textsubscript{3}: 321.1210 [M+Na]\textsuperscript{+}; found: 321.1204.
**N-(dimethylcarbamoyl)-N-phenethoxybenzamide (3t).** Colorless oil, 64% yield. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.84–7.77 (m, 2H), 7.46–7.23 (m, 8H), 4.45 (t, $J$=7.0, 2H), 3.15 – 3.05 (m, 5H), 3.00 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 151.9, 148.5, 138.5, 130.4, 130.3, 129.1, 128.4, 128.3, 126.2, 126.0, 75.4, 36.8, 36.7, 35.6; HRMS (ESI): calculated for C$_{18}$H$_{20}$N$_2$NaO$_3$: 335.1366 [M+Na]$^+$; found: 335.1364.

![Structure of N-(dimethylcarbamoyl)-N-phenethoxybenzamide](image)

**N-(diethylcarbamoyl)-N-methoxybenzamide (3u).** Colorless oil, 66% yield. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.79–7.67 (m, 2H), 7.43–7.32 (m, 3H), 3.96 (s, 3H), 3.41 (m, 4H), 1.24 (m, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 151.4, 148.5, 130.6, 130.3, 128.5, 126.1, 62.9, 42.4, 14.2, 13.3; HRMS (ESI): calculated for C$_{13}$H$_{18}$N$_2$NaO$_3$: 273.1210 [M+Na]$^+$; found: 273.1222.

![Structure of N-(diethylcarbamoyl)-N-methoxybenzamide](image)

**N-benzoyl-N-methoxypiperidine-1-carboxamide (3v).** Colorless oil, 43% yield. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.75–9.67 (m, 2H), 7.42–7.32 (m, 3H), 3.97 (s, 3H), 3.41 (m, 4H), 1.24 (m, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 150.8, 148.4, 130.5, 130.4, 128.5, 126.1, 62.98, 46.3, 45.5, 26.0, 25.5, 24.4; HRMS (ESI): calculated for C$_{14}$H$_{18}$N$_2$NaO$_3$: 285.1210 [M+Na]$^+$; found: 285.1207.

![Structure of N-benzoyl-N-methoxypiperidine-1-carboxamide](image)

**N-benzoyl-N-methoxymorpholine-4-carboxamide (3w).** Colorless oil, 61% yield. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.75–7.66 (m, 4H), 7.44–7.32 (m, 3H), 3.98 (s, 3H), 3.78–3.71 (m, 4H), 3.68 (s, 2H), 3.56 (s, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 150.8, 148.0, 130.5, 130.1, 128.6, 126.1, 66.6, 63.1, 45.6, 44.5; HRMS (ESI): calculated for C$_{13}$H$_{16}$N$_2$NaO$_3$: 287.1002 [M+Na]$^+$; found: 287.1000.

![Structure of N-benzoyl-N-methoxymorpholine-4-carboxamide](image)

**N-(dimethylcarbamoyl)-N-methoxy-2-phenylacetamide (3x).** Colorless oil, 52% yield. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.27–7.16 (m, 4H), 3.83 (s, 3H), 3.67 (s, 2H), 2.91 (s, 3H), 2.80 (s, 3H); HRMS (ESI): $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 151.5, 149.0, 136.8, 134.3, 129.8, 129.4, 127.5, 127.4, 62.5, 37.2, 36.8, 36.6; calculated for C$_{12}$H$_{16}$ClN$_2$O$_3$: 271.0844 [M+H]$^+$; found: 271.0851.

![Structure of N-(dimethylcarbamoyl)-N-methoxy-2-phenylacetamide](image)
$^1$H and $^{13}$C spectra of novel substrates
$^1$H and $^{13}$C spectra of novel compounds
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[Chemical structure images and spectra]