Supporting information

Electrochemical TEMPO-Catalyzed Multicomponent C(sp³)-H α-Carbamoylation of Free Cyclic Secondary Amines.

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1. General information

Unless otherwise stated, commercially available materials were used as received. Reactions were monitored by thin-layer chromatography (TLC) analysis using precoated silica gel aluminium foils (with fluorescent indicator 254 nm). Spots were visualized by UV irradiation or Kagi stain. Column chromatography was performed on silica gel (230-400 mesh, 40-63 µm).

$^1$H (300 MHz), $^{13}$C (75 MHz) and $^{19}$F (282 MHz) NMR spectra were recorded on a Bruker spectrometer. HRMS Spectra were recorded on a JEOL JMS-GC Mate II apparatus. Melting points were detected with a Wagner Munz Kofler hot bench.

Cyclic voltammetry (CV) was performed with a Metrohm Autolab PGSTAT101 potentiostat connected to a Nova software interface. CV was performed in a three-electrode cell connected to a Schlenk line under argon at 20 °C with a scan rate of 0.5 V·s$^{-1}$. The working electrode was a glassy carbon disk ($d = 1$ mm), the counter electrode a platinum wire of ca. 0.2 cm$^2$ apparent area. The reference was a saturated calomel electrode (SCE) separated from the solution by a bridge filled with 3 mL of CH$_3$CN (containing nBu$_4$NBF$_4$ 0.3 M).

Reversed-phase analytical HPLC was performed with Agilent Technologies 1200 series machine. Column: PROTO 200 C18 with 3 µm particles from Higgins analytical Inc., 100 mm length and 4.6 mm internal diameter. Method used was a custom method “default method” (Table 1), flow rate: 1 mL/min.

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>H$_2$O (%)</th>
<th>CH$_3$CN (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>95</td>
<td>5</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>12</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>13</td>
<td>95</td>
<td>5</td>
</tr>
</tbody>
</table>

Table 1 Default method for analytical HPLC
Reversed-phase preparative HPLC was performed with Agilent Technologies 1260 series machine. Column: Nucleodur C18 Htec. with 5 µm particles from Macherey-Nagel, 250 mm length and 16 mm internal diameter. Method used was a custom method “default method” (Table 2), flow rate: 14 mL/min.

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>H2O (%)</th>
<th>CH3CN (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>95</td>
<td>5</td>
</tr>
<tr>
<td>30</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>40</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>41</td>
<td>95</td>
<td>5</td>
</tr>
</tbody>
</table>

Table 2 Default method for preparative HPLC

Electrosynthesis was performed under constant current (12 mA or 6 mA) after the indicated reaction time with IKA ElectraSyn 2.0 in a 5 mL cell equipped with a graphite plate as anode and a nickel plate as cathode, or with a Metrohm Autolab PGSTAT101 potentiostat connected to a Nova software interface in a 5 mL cell equipped with a graphite plate as anode and a nickel plate as cathode and the distance of the 2 electrodes were kept the same as with IKA ElectraSyn 2.0.
2. Cyclic voltammetry

a) Shift of the oxidation potential of pyrrolidine under acidic conditions

b) TEMPO oxidation in the presence of acetic acid

As already reported,[1],[2] CV for TEMPO is modified under acidic conditions. Indeed, the reduction of TEMPO is easier in the presence of 25 equiv of AcOH with a $E_{\text{p,red}}$ at -1.0 V vs SCE (vs -1.75 V vs SCE in the absence of acid). On the reverse scan, there are two oxidation peaks: the first one ($E_{\text{p,ox}} = +0.65$ V) for TEMPO and the second one ($E_{\text{p,ox}} = +1.14$ V) standing for the oxidation of TEMPOH$_2^+$. 

Cyclic Voltammetry towards oxidation potentials (0.3 M of Bu$_4$NBF$_4$ in MeCN, 20°C, 0.5 V.s$^{-1}$, glassy carbon as working electrode (d = 1 mm), Pt wire as counter electrode and SCE as reference electrode) for 20 mM of pyrrolidine (black), with 1 equiv of AcOH (red) and with 2.5 equiv of AcOH (blue).
Cyclic Voltammetry towards oxidation potentials (0.3 M of $^n$Bu$_4$NBF$_4$ in MeCN, 20°C, 0.5 V.s$^{-1}$, glassy carbon as working electrode ($d = 1$ mm), Pt wire as counter electrode and SCE as reference electrode) for 2 mM of TEMPO (black) and with 25 equiv of AcOH (red).
Cyclic Voltammetry towards reduction potentials (0.3 M of \( \text{Bu}_4\text{NBF}_4 \) in MeCN, 20°C, 0.5 V.s\(^{-1}\), glassy carbon as working electrode (d = 1 mm), Pt wire as counter electrode and SCE as reference electrode) for 2 mM of TEMPO (black) and with 25 equiv of AcOH (red).

c) TEMPO oxidation in the presence of pyrrolidine

After addition of 10 equiv of pyrrolidine to a solution of TEMPO, the oxidation peak for TEMPO dramatically increases with the loss of its reverse scan. Such evolution is consistent with an electrocatalytic effect: after oxidation of TEMPO to TEMPO\(^+\), the latter reacts with pyrrolidine through a hydride transfer\(^{[3]}\) to generate the corresponding iminium and TEMPOH. Due to the high potential applied, the latter is immediately oxidized to TEMPO regenerating the catalyst. This mechanism could explain the electrocatalytic effect observed for TEMPO in the presence of pyrrolidine.
Cyclic Voltammetry towards oxidation potentials (0.3 M of $n$-Bu$_4$NBF$_4$ in MeCN, 20°C, 0.5 V.s$^{-1}$, glassy carbon as working electrode ($d = 1$ mm), Pt wire as counter electrode and SCE as reference electrode) for 2 mM of TEMPO (black) and with 10 equiv of pyrrolidine (blue).
Cyclic Voltammetry towards oxidation potentials (0.3 M of "Bu4NBF4 in MeCN, 20°C, 0.5 V.s⁻¹, glassy carbon as working electrode (d = 1 mm), Pt wire as counter electrode and SCE as reference electrode) for 2 mM of TEMPO (black), 2 mM of TEMPO with 20 mM of pyrrolidine (blue) and 20 mM of pyrrolidine (brown).

d) TEMPO oxidation in the presence of pyrrolidine and acetic acid under relevant experimental conditions

In the presence of both pyrrolidine (10 equiv) and AcOH (25 equiv), the electrocatalytic peak is still observed for TEMPO oxidation but at a lower extent due to the lower concentration of free pyrrolidine under such acidic conditions. Moreover, when the electrogenerated oxoammonium reacts with pyrrolidine, the formed TEMPOH is in equilibrium with TEMPOH₂⁺ (pKa about 7), which is oxidized at +1.2 V vs SCE according to a two-electron process. The oxoammonium is thus regenerated and could react with free pyrrolidine.
Cyclic Voltammetry towards oxidation potentials (0.3 M of Bu₄NBF₄ in MeCN, 20°C, 0.5 V.s⁻¹, glassy carbon as working electrode (d = 1 mm), Pt wire as counter electrode and SCE as reference electrode) for 2 mM of TEMPO (black), 2 mM of TEMPO with 20 mM of pyrrolidine (blue) and 2 mM of TEMPO with 20 mM of pyrrolidine and 50 mM of AcOH (green).

Therefore, we propose that the electrogenerated oxoammonium TEMPO⁺ reacts with pyrrolidine to form the iminium and the TEMPOH, which is partly protonated under acidic conditions. TEMPOH/TEMPOH₂⁺ are oxidized at the anode regenerating the oxoammonium.

In the scanned range of potentials, the isocyanide turned out to be non-electroactive as shown in the voltammogram below.
Cyclic Voltammetry towards oxidation potentials (0.3 M of *Bu₄NBF₄ in MeCN, 20°C, 0.5 V.s⁻¹, glassy carbon as working electrode (d = 1 mm), Pt wire as counter electrode and SCE as reference electrode) for 20 mM of *t*-BuNC (red), 2 mM of TEMPO (black), 2 mM of TEMPO with 20 mM of pyrrolidine (blue) and 2 mM of TEMPO with 20 mM of pyrrolidine and 50 mM of AcOH (green).

3. Calibration of product 4 with standard on analytical HPLC

Standard: *N*-cyclohexylformamide

Six samples of mixture of standard and product 4 were prepared according to Table 3 and then dissolved in 2 mL H₂O/ACN (9:1).

<table>
<thead>
<tr>
<th>No.</th>
<th>Mass of standard (mg)</th>
<th>Mass of product 4 (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>49.7</td>
<td>5.0</td>
</tr>
<tr>
<td>2</td>
<td>51.7</td>
<td>9.9</td>
</tr>
<tr>
<td>3</td>
<td>50.0</td>
<td>15.1</td>
</tr>
<tr>
<td>4</td>
<td>52.0</td>
<td>20.0</td>
</tr>
<tr>
<td>5</td>
<td>51.7</td>
<td>25.0</td>
</tr>
<tr>
<td>6</td>
<td>49.8</td>
<td>30.3</td>
</tr>
</tbody>
</table>
**Table 3 Sample preparation**

Each of the samples was injected 3 times into the analytical HPLC. The areas of both peaks were integrated and the ratios were calculated. Combined with the actual amount of standard and product 4 in the samples, the calibration curve (Figure 1) of product 4 with N-cyclohexylformamide was calculated.

![Graph](image)

**Figure 1** Calibration curve of product 4 with N-cyclohexylformamide as standard

4. **Condition screening**

All the reactions in condition screening were done with N-cyclohexylformamide as a standard inside the reaction mixtures before the reactions started. The HPLC yields were calculated with the calibration curve (Figure 1) above.
a) Solvent

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>HPLC yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CH₃CN</td>
<td>54</td>
</tr>
<tr>
<td>2</td>
<td>DCM</td>
<td>46</td>
</tr>
<tr>
<td>3</td>
<td>DMF</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>HF₆P</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>THF* (Bu₄NBF₄)</td>
<td>8</td>
</tr>
<tr>
<td>6</td>
<td>Isopropanol* (Bu₄NBF₄)</td>
<td>9</td>
</tr>
</tbody>
</table>

* Bu₄NBF₄ was used as electrolyte instead of Bu₄NBF₄ because of solubility issue.

b) Electrolyte

<table>
<thead>
<tr>
<th>Entry</th>
<th>Electrolyte</th>
<th>HPLC yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Et₄NBF₄ (1 eq)</td>
<td>54</td>
</tr>
<tr>
<td>7</td>
<td>Et₄NPF₆ (1 eq)</td>
<td>48</td>
</tr>
<tr>
<td>8</td>
<td>Et₄NOTs (1 eq)</td>
<td>26</td>
</tr>
<tr>
<td>9</td>
<td>Bu₄NOAc (1 eq)</td>
<td>10</td>
</tr>
<tr>
<td>10</td>
<td>Bu₄NBF₄ (1 eq)</td>
<td>42</td>
</tr>
<tr>
<td>11</td>
<td>Bu₄NBF₄ (5 eq)</td>
<td>37</td>
</tr>
<tr>
<td>12</td>
<td>Bu₄NBF₄ (10 eq)</td>
<td>42</td>
</tr>
<tr>
<td>13</td>
<td>/</td>
<td>20</td>
</tr>
</tbody>
</table>
c) Proton source

<table>
<thead>
<tr>
<th>Entry</th>
<th>Proton source</th>
<th>HPLC yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>AcOH (2.5 eq)</td>
<td>54</td>
</tr>
<tr>
<td>14</td>
<td>AcOH (1 eq)</td>
<td>8</td>
</tr>
<tr>
<td>15</td>
<td>AcOH (1.5 eq)</td>
<td>32</td>
</tr>
<tr>
<td>16</td>
<td>AcOH (2 eq)</td>
<td>48</td>
</tr>
<tr>
<td>17</td>
<td>AcOH (4 eq)</td>
<td>44</td>
</tr>
<tr>
<td>18</td>
<td>AcOH (2.5 eq) + 0.5 eq CH₃OH (no TEMPO)</td>
<td>33</td>
</tr>
<tr>
<td>19</td>
<td>AcOH (2.5 eq) + 1 eq HFP</td>
<td>35</td>
</tr>
<tr>
<td>20</td>
<td>AcOH (2.5 eq) + 1 eq H₂O</td>
<td>45</td>
</tr>
<tr>
<td>21</td>
<td>AcOH (2.5 eq) + 2 eq H₂O</td>
<td>36</td>
</tr>
<tr>
<td>22</td>
<td>AcOH (2.5 eq) + 4 eq H₂O</td>
<td>37</td>
</tr>
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</table>

d) Catalyst

<table>
<thead>
<tr>
<th>No.</th>
<th>Catalyst</th>
<th>HPLC yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TEMPO (0.1 eq)</td>
<td>54</td>
</tr>
<tr>
<td>23</td>
<td>TEMPO (0.3 eq)</td>
<td>40</td>
</tr>
<tr>
<td>24*</td>
<td>TEMPO (0.05 eq)</td>
<td>42</td>
</tr>
<tr>
<td>25</td>
<td>/</td>
<td>32</td>
</tr>
<tr>
<td>26</td>
<td>AcNH-TEMPO (0.1 eq)</td>
<td>50</td>
</tr>
</tbody>
</table>

*2.5 mA·cm⁻², 6 h, 2.7F/mol.
e) tBuNC

\[
\text{\begin{align*}
\text{5 mA cm}^{-2} \\
\text{Ni} & \quad \text{Graphite} \\
\text{Catalyst} \\
\text{Et}_{4}NBF_{4} (1 \text{ equiv}) \\
\text{ACN} (0.17 \text{ M}), \text{rt, 3 h} \\
\end{align*}}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>tBuNC</th>
<th>HPLC yield (%)</th>
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<tbody>
<tr>
<td>1</td>
<td>1.5 eq</td>
<td>54</td>
</tr>
<tr>
<td>27</td>
<td>2.0 eq</td>
<td>51</td>
</tr>
</tbody>
</table>

f) Cathode

\[
\text{\begin{align*}
\text{5 mA cm}^{-2} \\
\text{Ni} & \quad \text{Graphite} \\
\text{Catalyst} \\
\text{TEMPO (10 mol\%)} \\
\text{Et}_{4}NBF_{4} (1 \text{ equiv}) \\
\text{Solvent} (0.17 \text{ M}), \text{rt, 3 h} \\
\end{align*}}
\]

<table>
<thead>
<tr>
<th>No.</th>
<th>Cathode</th>
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<tbody>
<tr>
<td>1</td>
<td>Ni</td>
<td>54</td>
</tr>
<tr>
<td>28</td>
<td>Pt</td>
<td>47</td>
</tr>
<tr>
<td>29</td>
<td>Ni foam</td>
<td>56</td>
</tr>
<tr>
<td>30</td>
<td>Stainless steel</td>
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g) Quantity of electricity

<table>
<thead>
<tr>
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<th>Time (h)</th>
<th>Q (F/mol)</th>
<th>HPLC yield (%)</th>
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<tbody>
<tr>
<td>1</td>
<td>3</td>
<td>2.69</td>
<td>54</td>
</tr>
<tr>
<td>35</td>
<td>4</td>
<td>3.58</td>
<td>57 (55)*</td>
</tr>
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</table>
h) Concentration

<table>
<thead>
<tr>
<th>Entry</th>
<th>Concentration (mM)</th>
<th>Time (h)</th>
<th>HPLC yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.17</td>
<td>3</td>
<td>54</td>
</tr>
<tr>
<td>38</td>
<td>0.50</td>
<td>9</td>
<td>64 (60)*</td>
</tr>
</tbody>
</table>

*Isolated yield

5. General procedure for electrosynthesis

Et$_4$NBF$_4$ (326 mg, 1.50 mmol, 1 equiv), TEMPO (23 mg, 0.15 mmol, 0.1 equiv), substrate (1.50 mmol, 1 equiv), acid (3.75 mmol, 2.5 equiv) and isocyanide (2.25 mmol, 1.5 equiv) were dissolved in 3 mL anhydrous CH$_3$CN in a 5 mL cell. The cell was then equipped with a graphite anode and a nickel cathode, and electrolysis was performed at a constant current of 12 mA (~ 5 mA/cm$^2$) for 9 hours. After the reaction time indicated, the reaction mixture was diluted with ethyl acetate (80 mL), washed with a saturated NaHCO$_3$ aqueous solution (10 mL), and then washed with a saturated NH$_4$Cl aqueous solution (7 mL *3). The organic phase was then dried over MgSO$_4$, filtered off, and concentrated _in vacuo_. The crude mixture was purified by preparative HPLC or column chromatography to give the desire product. In some cases, the product exists in the form of several rotamers, and changing the deuterated solvent induces a variation in relative proportions.
6. Experimental and characterization of electrochemical multicomponent α-carbamoylation products

![Chemical Structure](image)

Chemical Formula: C_{11}H_{20}N_{2}O_{2}
Molecular Weight: 212.2930

1-acetyl-N-(tert-butyl)pyrrolidine-2-carboxamide\(^{[4]}\) (4)

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and acetic acid (3a) (215 µL, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 4 (191 mg, 60% yield) was obtained as a white solid after purification by preparative HPLC.

In \(^1\)H NMR timescale, two rotamers (15:1 ratio in C\(_6\)D\(_6\), 6:1 ratio in CDCl\(_3\) and 15:1 ratio in toluene-\(d_8\)) were observed. **Melting point:** 122-124 °C. **Major rotamer:**

\(^1\)H NMR (300 MHz, C\(_6\)D\(_6\)): \(\delta = 7.42\) (br s, 1H), 4.29 (d, \(J = 7.0\) Hz, 1H), 2.69 (td, \(J = 9.4, 2.6\) Hz, 1H), 2.45-2.27 (m, 2H), 1.98-1.78 (m, 1H), 1.55 (s, 3H), 1.36 (s, 9H), 1.31-1.20 (m, 1H), 1.18-1.07 (m, 1H) ppm.

\(^{13}\)C NMR (75 MHz, C\(_6\)D\(_6\)): \(\delta = 170.7, 169.9, 60.5, 50.9, 47.9, 28.8, 26.9, 25.1, 22.0\) ppm. **HRMS (EI+):** calcd for C\(_{11}\)H\(_{20}\)N\(_2\)O\(_2\)[M]\(^+\): 212.1519, found: 212.1523. **Characteristic peaks for the minor rotamer:**

\(^1\)H NMR (300 MHz, C\(_6\)D\(_6\)): \(\delta = 5.32\) (br s, 1H), 3.58 (dd, \(J = 8.4, 3.0\) Hz, 1H), 3.38-3.26 (m, 2H), 1.73 (s, 3H), 1.14 (s, 9H) ppm.

\(^{13}\)C NMR (75 MHz, C\(_6\)D\(_6\)): \(\delta = 203.9, 47.0, 30.1, 28.5\) ppm.

**Major rotamer:**

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 6.98\) (br s, 1H), 4.45 (dd, \(J = 8.1, 1.8\) Hz, 1H), 3.62-3.49 (m, 1H), 3.40 (td, \(J = 9.6, 7.1\) Hz, 1H), 2.45-2.34 (m, 1H), 2.21-2.11 (m, 1H), 2.10 (s, 3H), 2.01-1.91 (m, 1H), 1.83-1.69 (m, 1H), 1.31 (s, 9H) ppm.

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta = 171.0, 170.3, 60.4, 51.1, 48.5, 28.8, 27.3, 25.2, 22.7\) ppm. **Characteristic peaks for the minor rotamer:**

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 5.17\) (br s, 1H), 4.15 (dd, \(J = 8.4, 3.3\) Hz, 1H), 2.03 (s, 3H),
1.34 (s, 9H) ppm. $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ = 63.1, 51.6, 46.9, 32.2, 23.1, 22.5 ppm.

**Major rotamer:** $^1$H NMR (300 MHz, tol-$d^8$): $\delta$ = 7.41 (br s, 1H), 4.25 (d, $J$ = 8.0 Hz, 1H), 2.74 (td, $J$ = 9.3, 2.4 Hz, 1H), 2.47 (td, $J$ = 9.8, 7.0 Hz, 1H), 2.38-2.28 (m, 1H), 1.94-1.82 (m, 1H), 1.56 (s, 3H), 1.35-1.27 (m, 1H), 1.33 (s, 9H), 1.22-1.11 (m, 1H) ppm. $^{13}$C NMR (75 MHz, tol-$d^8$): $\delta$ = 170.6, 169.8, 60.4, 50.8, 47.9, 28.8, 26.9, 25.1, 21.8 ppm. **Characteristic peaks for the minor rotamer:** $^1$H NMR (300 MHz, tol-$d^8$): $\delta$ = 5.44 (br s, 1H), 3.60 (dd, $J$ = 8.5, 2.7 Hz, 1H), 3.38-3.25 (m, 2H), 1.73 (s, 3H), 1.15 (s, 9H) ppm. $^{13}$C NMR (75 MHz, tol-$d^8$): $\delta$ = 28.4 ppm.

![Chemical Structure](image)

Chemical Formula: C$_{13}$H$_{24}$N$_2$O$_2$

Molecular Weight: 240.35

**N-(tert-butyl)-1-butyrylpyrrolidine-2-carboxamide (5)**

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and butyric acid (3b) (342 µL, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 5 (237 mg, 66% yield) was obtained as a white solid after purification by preparative HPLC. In $^1$H NMR timescale, two rotamers (15:1 ratio in C$_6$D$_6$) were observed.

**Melting point:** 103-105 °C. **Major rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta$ = 7.70 (br s, 1H), 4.46 (d, $J$ = 7.4 Hz, 1H), 2.80 (td, $J$ = 9.3, 2.4 Hz, 1H), 2.60-2.42 (m, 2H), 2.05-1.86 (m, 1H), 1.86-1.78 (m, 2H), 1.78-1.54 (m, 2H), 1.38 (s, 9H), 1.35-1.26 (m, 1H), 1.23-1.05 (m, 1H), 0.89 (t, $J$ = 7.3 Hz, 3H) ppm. $^{13}$C NMR (75 MHz, C$_6$D$_6$): $\delta$ = 172.8, 170.1, 60.3, 50.7, 47.1, 36.3, 28.9, 26.4, 25.2, 18.5, 14.0 ppm. **HRMS (EI+):** calcd for C$_{13}$H$_{24}$N$_2$O$_2$ [M]$:^+$: 240.1832, found: 240.1838. **Characteristic peaks for the minor rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta$ = 5.42
(br s, 1H), 3.81 (dd, $J = 8.5, 2.4$ Hz, 1H), 3.44 (dd, $J = 8.5, 5.4$ Hz, 2H), 1.17 (s, 9H) ppm. $^{13}$C NMR (75 MHz, C$_6$D$_6$): $\delta = 28.5$ ppm.

$N$-(tert-butyl)-1-nonanoylpyrrolidine-2-carboxamide (6)

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and nonanoic acid (3c) (654 µL, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 6 (312 mg, 67% yield) was obtained as a pale brown solid after purification by flash column chromatography. In $^1$H NMR timescale, two rotamers (10:1 ratio in C$_6$D$_6$) were observed. **Melting point:** 62-64 °C. **Major rotamer:** $^1$H NMR (400 MHz, C$_6$D$_6$): $\delta = 7.70$ (s, 1H), 4.48 (dd, $J = 8.1$, 1.5 Hz, 1H), 2.86 (td, $J = 9.1$, 2.5 Hz, 1H), 2.59 (td, $J = 9.7$, 7.1 Hz, 1H), 2.56-2.46 (m, 1H), 2.04-1.95 (m, 1H), 1.92 (t, $J = 7.2$ Hz, 2H), 1.70 (dq, $J = 22.6$, 6.6 Hz, 2H), 1.40 (s, 9H), 1.33-1.25 (m, 12H), 0.94- 0.89 (m, 3H) ppm. $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta = 173.6$, 170.4, 60.2, 50.9, 47.6, 34.7, 31.9, 29.5, 29.4, 29.2, 28.7, 26.9, 25.08, 25.05, 22.7, 14.1 ppm. **Characteristic peaks for the minor rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta = 3.46$ (m, 1H), 3.40 (t, $J = 6.5$ Hz, 1H), 2.99-2.92 (m, 1H), 2.72 (t, $J = 6.5$ Hz, 1H) ppm. **HRMS (EI+):** calcd for C$_{18}$H$_{34}$N$_2$O$_2$ [M]$^+$: 310.2615, found: 310.2611.
**N-(tert-butyl)-1-(2-ethylbutanoyl)pyrrolidine-2-carboxamide (7)**

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and 2-ethylbutyric acid (3d) (472 µL, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 7 (238 mg, 59% yield) was obtained as a yellow oil after purification by flash column chromatography. 

\[ ^1H \text{NMR (400 MHz, C}_6\text{D}_6): \delta = 7.74 \text{ (s, 1H), 4.59 (dd, J = 8.0, 1.6 Hz, 1H), 3.00 (td, J = 9.1, 2.7 Hz, 1H), 2.81 (td, J = 9.7, 7.0 Hz, 1H), 2.51 (ddt, J = 11.5, 7.0, 2.0 Hz, 1H), 1.99 (ddt, J = 21.7, 9.3, 3.8 Hz, 2H), 1.76 (ddtd, J = 16.3, 12.7, 7.4, 3.4 Hz, 2H), 1.38 (s, 9H), 1.36-1.26 (m, 3H), 1.22-1.11 (m, 1H), 0.88 (t, J = 7.4 Hz, 3H), 0.78 (t, J = 7.4 Hz, 3H) ppm.} \]

\[ ^{13}C \text{NMR (101 MHz, CDCl}_3): \delta = 176.6, 170.2, 60.0, 50.8, 47.6, 47.0, 28.7, 26.5, 26.1, 25.4, 25.0, 12.1, 11.8 ppm.} \]


**N-(tert-butyl)-1-(2-cyclopentylacetyl)pyrrolidine-2-carboxamide (8)**

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and cyclopentylacetic acid (3e) (472 µL, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product
8 (259 mg, 62% yield) was obtained as a white solid after purification by flash column chromatography. In $^1$H NMR timescale, two rotamers (21:1 ratio in C$_6$D$_6$) were observed. **Melting point:** 113-115 °C. **Major rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta$ = 7.74 (br s, 1H), 4.50 (d, $J$ = 7.2 Hz, 1H), 2.84 (td, $J$ = 9.4, 2.4 Hz, 1H), 2.57 (td, $J$ = 9.6, 6.8 Hz, 1H), 2.55-2.46 (m, 1H), 2.39 (ddd, $J$ = 23.0, 15.6, 7.4 Hz, 1H), 1.96 (d, $J$ = 6.9 Hz, 2H), 1.95-1.79 (m, 3H), 1.64-1.45 (m, 4H), 1.40 (s, 9H), 1.38-1.27 (m, 1H), 1.24-1.02 (m, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ = 172.7, 170.0, 60.3, 50.7, 47.3, 40.7, 36.8, 32.85, 28.9, 26.3, 25.40, 25.38, 25.3. **HRMS (EI+):** calcd for C$_{11}$H$_{18}$NO [M - tBuHCO]$: 180.1383$, found: $180.1386$. **Characteristic peaks for the minor rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta$ = 5.45 (br s, 1H), 3.90-3.83 (m, 1H), 3.51-3.40 (m, 2H), 1.19 (s, 9H). $^{13}$C NMR (75 MHz, C$_6$D$_6$): $\delta$ = 28.5.

![Chemical Structure](image)

**Chemical Formula:** C$_{14}$H$_{26}$N$_2$O$_2$

**Molecular Weight:** 254.37

**N-(tert-butyl)-1-pivaloylpyrrolidine-2-carboxamide (9)**

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and pivalic acid (3f) (383 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 9 (265 mg, 69% yield) was obtained as a white solid after purification by flash column chromatography. **Melting point:** 123-125 °C. $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta$ = 7.05 (br s, 1H), 4.59 (dd, $J$ = 8.0, 2.8 Hz, 1H), 3.18-3.01 (m, 2H), 2.39-2.23 (m, 1H), 1.98-1.77 (m, 1H), 1.34 (s, 9H), 1.32-1.19 (m, 2H), 1.12 (s, 9H) ppm. $^{13}$C NMR (75 MHz, C$_6$D$_6$): $\delta$ = 177.2, 170.7, 62.1, 50.6, 48.1, 39.2, 28.9, 27.7, 26.0, 25.9 ppm. **HRMS (EI+):** calcd for C$_{14}$H$_{26}$N$_2$O$_2$ [M]+$: 254.1989$, found: $254.1992$. 

521
Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and phenyl acetic acid (3g) (510 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 10 (234 mg, 54% yield) was obtained as a white solid after purification by flash column chromatography. In $^1$H NMR timescale, two rotamers (26:1 ratio in C$_6$D$_6$) were observed. **Melting point:** 110-112 °C. **Major rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta = 7.52$ (br s, 1H), 7.24-7.11 (m, 4H), 7.09-7.01 (m, 1H), 4.47 (d, $J = 7.1$ Hz, 1H), 3.34 (d, $J = 14.5$ Hz, 1H), 3.26 (d, $J = 14.5$ Hz, 1H), 2.86 (td, $J = 9.2$, 2.4 Hz, 1H), 2.62 (td, $J = 9.7$, 7.0 Hz, 1H), 2.46-2.35 (m, 1H), 1.94-1.74 (m, 1H), 1.35 (s, 9H), 1.29-1.18 (m, 1H), 1.16-1.04 (m, 1H) ppm. $^{13}$C NMR (75 MHz, C$_6$D$_6$): $\delta =$ 170.9, 169.8, 135.4, 129.1, 128.9, 127.1, 60.5, 50.7, 47.4, 42.1, 28.9, 26.4, 25.1 ppm. **HRMS (EI+):** calcd for C$_{12}$H$_{15}$NO [M - tBuNCO]$:^+$: 189.1148, found: 189.1156. **Characteristic peaks for the minor rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta = 3.99$-3.92 (m, 1H), 1.12 (s, 9H) ppm. $^{13}$C NMR (75 MHz, C$_6$D$_6$): $\delta = 28.5$ ppm.
N-(tert-butyl)-1-(3-phenylpropanoyl)pyrrolidine-2-carboxamide (11)

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and hydrocinnamic acid (3h) (563 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 11 (308 mg, 68% yield) was obtained as a white solid after purification by flash column chromatography. In $^1$H NMR timescale, two rotamers (18:1 ratio in C$_6$D$_6$) were observed. **Melting point:** 100-102 °C. **Major rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta =$ 7.63 (br s, 1H), 7.23-7.01 (m, 5H), 4.41 (d, $J =$ 7.9 Hz, 1H), 3.02 (dt, $J =$ 14.7, 7.9 Hz, 1H), 2.92 (dt, $J =$ 14.7, 7.4 Hz, 1H), 2.74-2.61 (m, 1H), 2.51-2.31 (m, 2H), 2.24-2.03 (m, 2H), 1.98-1.78 (m, 1H), 1.38 (s, 9H), 1.31-1.19 (m, 1H), 1.19-1.03 (m, 1H) ppm. **$^{13}$C NMR** (75 MHz, C$_6$D$_6$): $\delta =$ 172.1, 169.9, 141.9, 128.8, 128.7, 126.4, 60.5, 50.7, 47.1, 36.5, 31.2, 28.9, 26.5, 25.1 ppm. **HRMS (EI+):** calcd for C$_{18}$H$_{26}$N$_2$O$_2$ [M]$^{+}$: 302.1989, found: 302.1982. **Characteristic peaks for the minor rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta =$ 5.28 (br s, 1H), 3.67 (dd, $J =$ 8.4, 3.0 Hz, 1H), 3.47-3.36 (m, 2H), 1.73 (s, 3H), 1.11 (s, 9H) ppm. **$^{13}$C NMR** (75 MHz, C$_6$D$_6$): $\delta =$ 28.4 ppm.
**Tert-butyl (2-(2-(tert-butylcarbamoyl)pyrrolidin-1-yl)-2-oxoethyl)carbamate (12)**

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and Boc-glycine (3i) (657 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 12 (210 mg, 43% yield) was obtained as a yellow solid after purification by flash column chromatography. **Melting point**: 137-139 °C. **¹H NMR** (400 MHz, C₆D₆): δ = 5.46 (s, 1H), 4.20 (d, J = 8.0 Hz, 1H), 3.49 (dd, J = 9.7, 4.6 Hz, 2H), 2.48 (td, J = 9.1, 2.5 Hz, 1H), 2.36-2.26 (m, 1H), 2.19 (td, J = 9.7, 6.8 Hz, 1H), 1.77 (h, J = 10.2 Hz, 1H), 1.46 (s, 9H), 1.34 (s, 9H), 1.21-1.11 (m, 1H), 1.01 (tt, J = 11.9, 7.5 Hz, 2H) ppm. **¹³C NMR** (101 MHz, CDCl₃): δ = 170.0, 168.6, 155.9, 79.7, 60.9, 51.1, 46.4, 43.1, 28.7, 28.4, 27.6, 24.9 ppm. **HRMS (EI⁺)**: calcd for C₁₆H₂₅N₃O₄ [M]⁺: 327.2153, found: 327.2147.

![Chemical Structure](insert)

**N-(tert-butyl)-1-(hex-5-ynoyl)pyrrolidine-2-carboxamide (13)**

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and 5-hexynoic acid (3j) (413 µL, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 13 (201 mg, 51% yield) was obtained as a yellow solid after purification by flash column chromatography. **Melting point**: 112-114 °C. **¹H NMR** (400 MHz, C₆D₆): δ = 7.54 (s, 1H), 4.45-4.35 (m, 1H), 2.81 (td, J = 9.9, 2.4 Hz, 1H), 2.53 (td, J = 9.9, 7.0 Hz, 1H), 2.50 – 2.39 (m, 1H), 2.11 (td, J = 7.0, 2.7 Hz, 2H), 1.99-1.85 (m, 3H), 1.84-1.71 (m, 3H), 1.37 (s, 9H), 1.30 (ddt, J = 11.9, 7.0, 2.4 Hz, 1H), 1.13 (ddd, J = 11.8, 7.5, 4.3 Hz, 1H) ppm. **¹³C NMR** (101 MHz, CDCl₃): δ = 172.3,
170.2, 83.5, 69.1, 60.2, 50.8, 47.4, 32.8, 28.6, 27.1, 24.9, 23.4, 17.7 ppm. **HRMS (EI+):** calcd for C\textsubscript{15}H\textsubscript{24}N\textsubscript{2}O\textsubscript{2} [M]\textsuperscript{++}: 264.1832, found: 264.1845.

\[(E)-1-(\text{but-2-enoyl})-\text{N}(\text{tert-butyl})\text{pyrrolidine-2-carboxamide (14)}\]

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and crotonic acid (3k) (323 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 14 (120 mg, 34% yield) was obtained as a yellow solid after purification by flash column chromatography. **Melting point:** 124-126 °C. **\textsuperscript{1}H NMR** (400 MHz, C\textsubscript{6}D\textsubscript{6}): \(\delta = 7.91 \text{ (s, 1H)}, 7.11 \text{ (dd, } J = 14.9, 6.9 \text{ Hz, 1H)}, 5.78 \text{ (dd, } J = 14.9, 1.7 \text{ Hz, 1H)}, 4.58 \text{ (dd, } J = 8.0, 1.5 \text{ Hz, 1H)}, 2.94 \text{ (td, } J = 9.0, 2.3 \text{ Hz, 1H)}, 2.69 \text{ (td, } J = 9.8, 6.9 \text{ Hz, 1H)}, 2.59-2.45 \text{ (m, 1H)}, 2.06-1.86 \text{ (m, 1H)}, 1.48 \text{ (dd, } J = 6.9, 1.7 \text{ Hz, 3H)}, 1.40 \text{ (s, 9H)}, 1.38-1.26 \text{ (m, 1H)}, 1.17-1.05 \text{ (m, 1H)} \text{ ppm. **HRMS (EI+):** calcd for C\textsubscript{13}H\textsubscript{22}N\textsubscript{2}O\textsubscript{2} [M]\textsuperscript{++}: 238.1676, found: 238.1683.

\[\text{N}(\text{tert-butyl})-1-(\text{3-methylbut-2-enoyl})\text{pyrrolidine-2-carboxamide (15)}\]
Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and 3,3-dimethylacrylic acid (3l) (375 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 15 (171 mg, 45% yield) was obtained as a white solid after purification by trituration in methyl-tert-butyl ether. Melting point: 94-96 °C. \(^1\)H NMR (400 MHz, C\(_6\)D\(_6\)): \(\delta = 7.88\) (s, 1H), 5.57 (s, 1H), 4.57 (dd, \(J = 8.0, 1.7\) Hz, 1H), 2.94 (td, \(J = 9.1, 2.6\) Hz, 1H), 2.73 (dd, \(J = 9.8, 7.0\) Hz, 1H), 2.55-2.49 (m, 1H), 2.16 (s, 3H), 2.04-1.85 (m, 1H), 1.54 (s, 3H), 1.40 (s, 9H), 1.32 (dtt, \(J = 12.1, 6.9, 2.5\) Hz, 1H), 1.17-1.08 (m, 1H) ppm. \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \(\delta = 170.3, 167.6, 149.8, 117.5, 59.8, 50.6, 47.7, 28.5, 26.8, 26.7, 24.9, 20.0\) ppm. HRMS (EI\(+\)): calcd for C\(_{14}\)H\(_{24}\)N\(_2\)O\(_2\) [M]\(^+\): 252.1832, found: 252.1830.

\[(E)-N-(\text{tert-butyl})-1-(2\text{-methylbut-2-enoyl})\text{pyrrolidine-2-carboxamide (16)}\]

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and tiglic acid (3m) (375 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 15 (195 mg, 51% yield) was obtained as a white solid after purification by flash column chromatography. Melting point: 125-127 °C. \(^1\)H NMR (400 MHz, C\(_6\)D\(_6\)): \(\delta = 7.41\) (s, 1H), 5.54 (q, \(J = 6.9\) Hz, 1H), 4.56 (s, 1H), 2.98 (s, 2H), 2.52 (s, 1H), 1.73 (s, 3H), 1.72-1.61 (m, 1H), 1.36 (s, 9H), 1.34 (s, 3H), 1.27-1.12 (m, 2H) ppm. \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \(\delta = 173.5, 170.3, 133.0, 127.6, 60.0, 5.1, 49.7, 28.8, 26.9, 25.3, 13.6, 13.5\) ppm. HRMS (EI\(+\)): calcd for C\(_{14}\)H\(_{24}\)N\(_2\)O\(_2\) [M]\(^+\): 252.1832, found: 252.1844.
**1-benzoyl-N-(tert-butyl)pyrrolidine-2-carboxamide (17)**

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and benzoic acid (3n) (510 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 17 (288 mg, 70% yield) was obtained as a white solid after purification by flash column chromatography. **Melting point**: 165-167 °C. **¹H NMR** (300 MHz, C₆D₆): $\delta = 7.49-7.30$ (m, 3H), 7.10-6.97 (m, 3H), 4.66 (dd, $J = 7.6, 5.1$ Hz, 1H), 3.11-2.94 (m, 1H), 2.94-2.77 (m, 1H), 2.60-2.39 (m, 1H), 1.69-1.54 (m, 1H), 1.49-1.40 (m, 1H), 1.38 (s, 9H), 1.19-1.03 (m, 1H) ppm. **¹³C NMR** (75 MHz, C₆D₆): $\delta = 170.8, 169.8, 137.3, 130.1, 128.4, 127.7, 60.6, 50.9, 50.3, 28.9, 26.5, 25.6$ ppm. **HRMS (EI⁺)**: calcd for C$_{16}$H$_{22}$N$_2$O$_2$ [M]$^{+}$: 274.1676, found: 274.1678.

**N-(tert-butyl)-1-(2-methylbenzoyl)pyrrolidine-2-carboxamide (18)**

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and o-toluic acid (3o) (510 mg, 3.75 mmol,
2.5 equiv), and following the aforementioned general procedure, product 18 (356 mg, 82% yield) was obtained as a white paste after purification by flash column chromatography. $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta = 7.57$ (brs, 1H), 7.09-6.99 (m, 2H), 6.99-6.88 (m, 2H), 4.64 (dd, $J = 8.1$, 3.1 Hz, 1H), 2.82-2.73 (m, 1H), 2.69-2.61 (m, 1H), 2.57-2.48 (m, 1H), 2.23 (s, 3H), 1.79-1.67 (m, 1H), 1.40 (s, 9H), 1.39-1.29 (m, 1H), 1.24-1.13 (m, 1H) ppm. $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta = 171.5$, 169.8, 136.9, 133.9, 130.7, 129.3, 126.1, 125.4, 60.0, 51.2, 49.3, 28.9, 26.9, 25.1, 18.9 ppm. HRMS (EI+): calcd for C$_{17}$H$_{24}$N$_2$O$_2$ [M]$^{+}$: 288.1832, found: 288.1838.

$N$-(tert-butyl)-1-(2-fluorobenzoyl)pyrrolidine-2-carboxamide (19)

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and 2-fluorobenzoic acid (3p) (525 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 19 (224 mg, 51% yield) was obtained as a white solid after purification by flash column chromatography. In $^1$H NMR timescale, two rotamers (15:1 ratio in C$_6$D$_6$) were observed. Melting point: 125-127 °C. Major rotamer: $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta = 7.27$-7.18 (m, 2H), 6.88-6.78 (m, 1H), 6.76-6.64 (m, 2H), 4.68 (dd, $J = 8.2$, 3.5 Hz, 1H), 3.00 (ddd, $J = 10.3$, 7.8, 5.3 Hz, 1H), 2.76 (dt, $J = 10.3$, 7.3 Hz, 1H), 2.48-2.33 (m, 1H), 1.76-1.59 (m, 1H), 1.50-1.35 (m, 1H), 1.40 (s, 9H), 1.23-1.10 (m, 1H) ppm. $^{13}$C NMR (75 MHz, C$_6$D$_6$): $\delta = 169.6$, 166.1, 158.8 (d, $J_{C-F} = 247.0$ Hz), 131.3 (d, $J_{C-F} = 8.0$ Hz), 129.0 (d, $J_{C-F} = 3.9$ Hz), 126.1 (d, $J_{C-F}$
= 17.8 Hz), 124.6 (d, J_C_F = 3.4 Hz), 115.9 (d, J_C_F = 21.5 Hz), 60.6, 50.9, 48.5 (d, J_C_F = 3.1 Hz), 28.8, 27.2, 24.9 ppm. $^{19}$F NMR (282 MHz, C$_6$D$_6$): $\delta$ = -116.1 ppm. HRMS (EI+): calcd for C$_{11}$H$_{11}$FNO [M - tBuNHCO]$^+$: 192.0819, found: 192.0825. **Characteristic peaks for the minor rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta$ = 5.01 (br s, 1H), 3.88-3.81 (m, 1H), 3.77-3.67 (m, 2H), 1.07 (s, 9H) ppm. $^{13}$C NMR (75 MHz, C$_6$D$_6$): $\delta$ = 47.1, 32.1, 28.4 ppm. $^{19}$F NMR (282 MHz, C$_6$D$_6$): $\delta$ = -115.1 ppm.

![Chemical structure](image)

Chemical Formula: C$_{17}$H$_{24}$N$_2$O$_2$
Molecular Weight: 288.39

**N-(tert-butyl)-1-(3-methylbenzoyl)pyrrolidine-2-carboxamide (20)**

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and m-toluic acid (3q) (510 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 20 (284 mg, 66% yield) was obtained as a white solid after purification by flash column chromatography. **Melting point:** 166-168 °C. $^1$H NMR (400 MHz, C$_6$D$_6$): $\delta$ = 7.43 (br s, 1H), 7.32 (s, 1H), 7.26 (d, J = 7.6 Hz, 1H), 7.00 (t, J = 7.6 Hz, 1H), 6.92 (d, J = 7.6 Hz, 1H), 4.78-4.66 (m, 1H), 3.13-3.00 (m, 1H), 2.99-2.87 (m, 1H), 2.64-2.40 (m, 1H), 2.02 (s, 3H), 1.64 (hept, J = 6.9 Hz, 1H), 1.52-1.42 (m, 1H), 1.39 (s, 9H), 1.20-1.06 (m, 1H) ppm. $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ = 171.1, 170.0, 138.1, 136.3, 130.8, 128.1, 127.6, 124.0, 60.3, 51.0, 50.4, 28.6, 27.0, 25.3, 21.3 ppm. HRMS (EI+): calcd for C$_{17}$H$_{24}$N$_2$O$_2$ [M]$^+$: 288.1832, found: 288.1825.
**N-(tert-butyl)-1-(3-(trifluoromethyl)benzoyl)pyrrolidine-2-carboxamide (21)**

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and 2-(trifluoromethyl)benzoic acid (3r) (713 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 21 (166 mg, 32% yield) was obtained as a white solid after purification by trituration in methyl-tert-butyl ether. **Melting point:** 190-192 °C.

**^1H NMR** (400 MHz, C6D6): δ = 7.90 (s, 1H), 7.44 (d, J = 7.9 Hz, 1H), 7.34 (d, J = 7.9 Hz, 1H), 7.14 (br s, 1H), 6.90 (t, J = 7.9 Hz, 1H), 4.62 (dd, J = 8.1, 4.9 Hz, 1H), 3.04-2.93 (m, 1H), 2.81-2.69 (m, 1H), 2.58-2.45 (m, 1H), 1.70 (hept, J = 6.8 Hz, 1H), 1.57-1.48 (m, 1H), 1.46 (s, 9H), 1.16 (dt, J = 13.0, 6.8 Hz, 1H) ppm. **^13C NMR** (101 MHz, CDCl3): δ = 169.9, 169.4, 137.2, 131.1 (q, J_{C,F} = 32.8 Hz), 130.5, 129.1, 127.1 (q, J_{C,F} = 3.7 Hz), 124.3 (q, J_{C,F} = 3.7 Hz), 123.7 (q, J_{C,F} = 273.0 Hz), 60.9, 51.4, 50.6, 28.8, 27.5, 25.6 ppm. **^19F NMR** (376 MHz, CDCl3): δ = -62.8 ppm. **HRMS (EI+):** calcd for C12H11F3NO [M - CONH'Bu]^+: 242.0787, found: 242.0782.

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**N-(tert-butyl)-1-(3-chlorobenzoyl)pyrrolidine-2-carboxamide (22)**
Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and 2-chlorobenzoic acid (3s) (587 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 22 (173 mg, 37% yield) was obtained as a white solid after purification by trituration in methyl-tert-butyl ether. **Melting point:** 187-189 °C. \(^{1}H\) NMR (400 MHz, C\(_6\)D\(_6\)): \(\delta = 7.47\) (s, 1H), 7.13 (d, \(J = 7.9\) Hz, 1H), 7.01 (d, \(J = 7.9\) Hz, 1H), 6.70 (t, \(J = 7.9\) Hz, 1H), 4.53 (dd, \(J = 8.1, 4.8\) Hz, 1H), 2.85 (dt, \(J = 10.4, 7.0\) Hz, 1H), 2.73 – 2.61 (m, 1H), 2.52 – 2.39 (m, 1H), 1.60 (tt, \(J = 13.7, 7.0\) Hz, 1H), 1.45 – 1.35 (m, 1H), 1.36 (s, 9H), 1.07 (dq, \(J = 12.9, 6.8\) Hz, 2H) ppm. \(^{13}C\) NMR (101 MHz, CDCl\(_3\)): \(\delta = 169.9, 169.4, 138.1, 134.5, 130.4, 129.9, 127.4, 125.2, 60.7, 51.2, 50.5, 28.8, 27.3, 25.5\) ppm. **HRMS (EI+):** calcd for C\(_{16}\)H\(_{21}\)ClN\(_2\)O\(_2\) [M]\(^{+}\): 308.1286, found: 308.1290.

\[
\begin{align*}
\text{Chemical Formula: } & \quad \text{C}_{16}\text{H}_{21}\text{BrN}_{2}\text{O}_{2} \\
\text{Molecular Weight: } & \quad 353.26
\end{align*}
\]

**1-(3-bromobenzoyl)-\(N\)-(tert-butyl)pyrrolidine-2-carboxamide (23)**

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and 2-bromobenzoic acid (3t) (754 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 23 (216 mg, 41% yield) was obtained as a white solid after purification by flash column chromatography. **Melting point:** 195-197 °C. \(^{1}H\) NMR (400 MHz, C\(_6\)D\(_6\)): \(\delta = 7.65\) (s, 1H), 7.57 (d, \(J = 8.2\) Hz, 1H), 7.43 (d, \(J = 7.7\) Hz, 1H), 7.30 (d, \(J = 7.8\) Hz, 1H), 6.71 (s, 1H), 4.60 (dd, \(J = 7.6, 5.7\) Hz, 1H), 3.59 – 3.51 (m, 1H), 3.48 – 3.37 (m, 1H), 2.49 – 2.39 (m, 1H), 2.11 – 1.99 (m, 2H), 1.88 – 1.77 (m, 1H), 1.36
(s, 9H) ppm. \(^{13}\text{C NMR}\) (101 MHz, CDCl\(_3\)): \(\delta = 169.9, 169.3, 138.3, 133.4, 130.3, 130.1, 125.7, 122.6, 60.7, 51.3, 50.6, 28.8, 27.3, 25.5 \) ppm. \textbf{HRMS (EI+)}: calcd for C\(_{16}\)H\(_{21}\)BrN\(_2\)O\(_2\) [M]\(^+\): 352.0781, found: 352.0794.

\[ \text{N-}(\text{tert-butyl})-1-(4\text{-fluorobenzoyl})\text{pyrrolidine-2-carboxamide (26)} \]

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 \(\mu\)L, 2.25 mmol, 1.5 equiv) and 2-bromobenzoic acid (3w) (525 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 26 (307 mg, 70% yield) was obtained as a white solid after purification by flash column chromatography. In \(^1\text{H NMR} \) timescale, two rotamers (21:1 ratio in C\(_6\)D\(_6\)) were observed. \textbf{Melting point}: 177-179 °C. \textbf{Major rotamer}: \(^1\text{H NMR}\) (300 MHz, C\(_6\)D\(_6\)): \(\delta = 7.29-7.19 \) (m, 3H), 6.71-6.61 (m, 2H), 4.59 (t, \(J = 6.1 \) Hz, 1H), 3.05-2.87 (m, 1H), 2.85-2.68 (m, 1H), 2.58-2.35 (m, 1H), 1.71-1.55 (m, 1H), 1.50-1.40 (m, 1H), 1.37 (s, 9H), 1.17-1.01 (m, 1H) ppm. \(^{13}\text{C NMR}\) (75 MHz, C\(_6\)D\(_6\)): \(\delta = 169.8, 169.6, 163.9 \) (d, \(J_{C,F} = 249.6 \) Hz), 133.2 (d, \(J_{C,F} = 2.4 \) Hz), 130.1 (d, \(J_{C,F} = 8.5 \) Hz), 115.3 (d, \(J_{C,F} = 21.7 \) Hz), 60.8, 50.9, 50.3, 28.8, 26.7, 25.6 ppm. \(^{19}\text{F NMR}\) (282 MHz, C\(_6\)D\(_6\)): \(\delta = -110.0 \) ppm. \textbf{HRMS (EI+)}: calcd for C\(_{11}\)H\(_{11}\)FNO [M - CONH\textsuperscript{t}Bu\textsuperscript{+}]: 192.0819, found: 192.0820. \textbf{Characteristic peaks for the minor rotamer}: \(^1\text{H NMR}\) (300 MHz, C\(_6\)D\(_6\)): \(\delta = 7.36-7.31 \) (m, 2H), 6.75-6.71 (m, 2H), 3.56-3.43 (m, 1H) ppm. \(^{13}\text{C NMR}\) (75 MHz, C\(_6\)D\(_6\)): \(\delta = 115.1 \) (d, \(J_{C,F} = 21.6 \) Hz) ppm. \(^{19}\text{F NMR}\) (282 MHz, C\(_6\)D\(_6\)): \(\delta = -110.9 \) ppm.
**N-(tert-butyl)-1-(furan-2-carbonyl)pyrrolidine-2-carboxamide (27)**

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and 2-furoic acid (3x) (420 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 27 (190 mg, 48% yield) was obtained as a white solid after purification by flash column chromatography. **Melting point:** 142-144 °C. **$^1$H NMR** (300 MHz, C$_6$D$_6$): $\delta$ = 7.52 (br s, 1H), 7.10-7.00 (m, 1H), 6.87-6.80 (m, 1H), 5.91 (dd, $J$ = 3.3, 1.6 Hz, 1H), 4.64 (d, $J$ = 7.1 Hz, 1H), 3.50 (t, $J$ = 7.9 Hz, 1H), 3.20 (dd, $J$ = 17.4, 9.2 Hz, 1H), 2.54-2.32 (m, 1H), 2.11-1.84 (m, 1H), 1.34 (s, 9H), 1.24-1.04 (m, 2H) ppm. **$^{13}$C NMR** (75 MHz, C$_6$D$_6$): $\delta$ = 169.9, 159.2, 149.3, 144.2, 117.2, 111.6, 61.8, 50.8, 48.3, 28.8, 26.2, 25.7 ppm. **HRMS (EI+):** calcld for C$_9$H$_{10}$NO$_2$ [M - CONH'Bu]$^+$: 164.0706, found: 164.0706.

**N-(tert-butyl)-1-(thiophene-2-carbonyl)pyrrolidine-2-carboxamide (28)**

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and 2-thiophenecarboxylic acid (3y) (480 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure,
product 28 (144 mg, 34% yield) was obtained as a white solid after purification by flash column chromatography. **Melting point:** 138-140 °C. **$^1$H NMR** (300 MHz, $^1$H$_2$O): $\delta = 7.45$ (br s, 1H), 7.16 (1H), 6.86 (dd, $J = 5.1$, 1.1 Hz, 1H), 6.61 (dd, $J = 5.1$, 3.8 Hz, 1H), 4.80-4.46 (m, 1H), 3.35-3.16 (m, 1H), 3.14-2.95 (m, 1H), 2.54-2.27 (m, 1H), 2.04-1.75 (m, 1H), 1.34 (s, 9H), 1.30-1.21 (m, 2H) ppm. **$^{13}$C NMR** (75 MHz, $^1$H$_2$O): $\delta = 169.8$, 163.0, 139.9, 130.4, 130.3, 127.3, 62.1, 50.9, 49.3, 28.8, 26.4, 25.7 ppm. **HRMS (EI+):** calcd for C$_9$H$_{11}$NOS [M]$^{+}$: 181.0556, found: 181.0555.

![Chemical Formula: C$_{23}$H$_{28}$N$_2$O$_2$ Molecular Weight: 328.46](image)

**N-cyclohexyl-1-(3-phenylpropanoyl)pyrrolidine-2-carboxamide (29)**

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), cyclohexyl isocyanide (2b) (280 $\mu$L, 2.25 mmol, 1.5 equiv) and hydrocinnamic acid (3g) (563 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 29 (308 mg, 62% yield) was obtained as a white solid after purification by flash column chromatography. In $^1$H NMR timescale, two rotamers (9:1 ratio in C$_6$D$_6$) were observed. **Melting point:** 157-159 °C. **Major rotamer: $^1$H NMR** (300 MHz, C$_6$D$_6$): $\delta = 7.64$ (d, $J = 6.9$ Hz, 1H), 7.23-7.11 (m, 4H), 7.11-7.03 (m, 1H), 4.48 (d, $J = 7.7$ Hz, 1H), 4.09-3.88 (m, 1H), 3.02 (td, $J = 14.4$, 7.4 Hz, 1H), 2.97 (td, $J = 14.4$, 7.4 Hz, 1H), 2.72-2.62 (m, 1H), 2.50 (dd, $J = 11.9$, 6.7 Hz, 1H), 2.40 (dt, $J = 9.9$, 6.9 Hz, 1H), 2.24-2.05 (m, 2H), 2.01-1.78 (m, 3H), 1.62-1.46 (m, 2H), 1.38-0.99 (m, 8H) ppm. **$^{13}$C NMR** (75 MHz, C$_6$D$_6$): $\delta = 172.1$, 169.8, 141.9, 128.9, 128.7, 126.4, 60.0, 48.3, 47.1, 36.5, 33.2, 33.1, 31.2, 26.6, 25.9,
25.2, 24.9, 24.8 ppm. HRMS (EI+): calcd for C_{20}H_{28}N_{2}O_{2} [M]^{+}: 328.2145, found: 328.2155. **Characteristic peaks for the minor rotamer:** \(^1\)H NMR (300 MHz, C\(_6\)D\(_6\)): \(\delta = 5.34 (d, J = 8.1 \text{ Hz}, 1\text{H}), \) 3.83-3.75 (m, 2\text{H}), 3.51-3.40 (m, 2\text{H}) ppm.

![Chemical Structure](image)

Chemical Formula: C\(_{21}\)H\(_{24}\)N\(_2\)O\(_2\)

Molecular Weight: 336.44

**N-benzyl-1-(3-phenylpropanoyl)pyrrolidine-2-carboxamide (30)**

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), benzyl isocyanide (2c) (274 \(\mu\)L, 2.25 mmol, 1.5 equiv) and hydrocinnamic acid (3g) (563 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 30 (224 mg, 42% yield) was obtained as a white solid after purification by flash column chromatography. In \(^1\)H NMR timescale, two rotamers (15:1 ratio in C\(_6\)D\(_6\)) were observed. **Melting point:** 88-90 °C. **Major rotamer:** \(^1\)H NMR (300 MHz, C\(_6\)D\(_6\)): \(\delta = 7.83 (br \text{ t}, J = 6.0 \text{ Hz}, 1\text{H}), 7.27-7.20 (m, 2\text{H}), 7.15-6.99 (m, 8\text{H}), 4.49-4.32 (m, 3\text{H}), 3.02-2.84 (m, 2\text{H}), 2.73-2.59 (m, 1\text{H}), 2.45-2.30 (m, 2\text{H}), 2.15-2.06 (m, 2\text{H}), 1.94-1.74 (m, 1\text{H}), 1.30-1.10 (m, 2\text{H}) ppm. \(^{13}\)C NMR (75 MHz, C\(_6\)D\(_6\)): \(\delta = 172.1, 170.9, 141.8, 139.7, 128.82, 128.76, 128.7, 127.9, 127.3, 126.4, 59.9, 47.0, 43.5, 36.5, 31.2, 27.1, 25.0 \text{ ppm}.** HRMS (EI+): calcd for C\(_{21}\)H\(_{24}\)N\(_2\)O\(_2\) [M]^{+}: 336.1832, found: 336.1826. **Characteristic peaks for the minor rotamer:** \(^1\)H NMR (300 MHz, C\(_6\)D\(_6\)): \(\delta = 6.10 (br \text{ t}, J = 6.3 \text{ Hz}, 1\text{H}), 4.21 (dd, J = 14.7, 6.4 \text{ Hz}, 1\text{H}), 4.10 (dd, J = 14.7, 6.1 \text{ Hz}, 1\text{H}), 3.82 (dd, J = 8.6, 2.4 \text{ Hz}, 1\text{H}), 3.46-3.29 (m, 2\text{H}) ppm.
1-(3-phenylpropanoyl)-N-(2,4,4-trimethylpentan-2-yl)pyrrolidine-2-carboxamide (31)

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), tert-Octyl isocyanide (2d) (394 µL, 2.25 mmol, 1.5 equiv) and hydrocinnamic acid (3g) (563 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 31 (538 mg, 66% yield) was obtained as a white solid after purification by flash column chromatography. In $^1$H NMR timescale, two rotamers (21:1 ratio in C$_6$D$_6$) were observed. **Melting point:** 95-97 °C. **Major rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta$ = 7.64 (br s, 1H), 7.22-7.11 (m, 4H), 7.10-7.02 (m, 1H), 4.48 (d, $J = 7.8$ Hz, 1H), 3.08-2.88 (m, 2H), 2.77-2.64 (m, 1H), 2.57-2.35 (m, 2H), 2.27-2.07 (m, 2H), 2.01 (d, $J = 14.8$ Hz, 1H), 1.97-1.78 (m, 1H), 1.70 (d, $J = 14.8$ Hz, 1H), 1.46 (s, 3H), 1.42 (s, 3H), 1.33-1.20 (m, 1H), 1.18-1.05 (m, 1H), 1.01 (s, 9H) ppm. $^{13}$C NMR (75 MHz, C$_6$D$_6$): $\delta$ = 172.1, 169.2, 141.9, 128.9, 128.8, 126.5, 60.7, 54.6, 51.0, 47.1, 36.6, 31.7, 31.5, 31.2, 30.0, 29.4, 26.3, 25.1 ppm. **HRMS (EI+):** calcd for C$_{22}$H$_{34}$N$_2$O$_2$ [M]+: 358.2615, found: 358.2625. **Characteristic peaks for the minor rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta$ = 5.58 (br s, 1H), 3.71 (dd, $J = 8.4$, 2.1 Hz, 1H), 3.49-3.38 (m, 2H), 0.85 (s, 9H) ppm.
Methyl (3-phenylpropanoyl)prolylglycinate (32)

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), methyl isocyanooacetate (2e) (137 µL, 2.25 mmol, 1.5 equiv) and hydrocinnamic acid (3g) (563 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 32 (117 mg, 28% yield) was obtained as a white solid after purification by flash column chromatography. In \(^1\text{H NMR}\) timescale, two rotamers (9:1 ratio in C\(_6\)D\(_6\)) were observed. **Melting point:** 85-87 °C. **Major rotamer:** \(^1\text{H NMR}\) (300 MHz, C\(_6\)D\(_6\)): \(\delta = 7.93\) (br t, \(J = 5.7\) Hz, 1H), \(7.27-7.09\) (m, 4H), \(7.09-6.99\) (m, 1H), \(4.54\) (d, \(J = 7.5\) Hz, 1H), \(3.86\) (dd, \(J = 17.8, 6.0\) Hz, 1H), \(3.74\) (dd, \(J = 17.8, 5.7\) Hz, 1H), \(3.19\) (s, 3H), \(3.03\) (t, \(J = 7.6\) Hz, 2H), \(2.74\) (td, \(J = 9.3, 1.9\) Hz, 1H), \(2.47-2.32\) (m, 2H), \(2.30-2.09\) (m, 2H), \(1.93-1.72\) (m, 1H), \(1.31-1.11\) (m, 2H) ppm. \(^{13}\text{C NMR}\) (75 MHz, C\(_6\)D\(_6\)): \(\delta = 172.2, 171.5, 170.2, 141.9, 128.9, 128.7, 126.4, 59.5, 51.4, 47.0, 41.2, 36.6, 31.3, 26.8, 24.9\) ppm.

**HRMS (EI+):** calcd for C\(_{17}\)H\(_{22}\)N\(_2\)O\(_4\) [M]\(^{++}\): 318.1574, found: 318.1587. **Characteristic peaks for the minor rotamer:** \(^1\text{H NMR}\) (300 MHz, C\(_6\)D\(_6\)): \(\delta = 6.45\) (br s, 1H), \(3.40-3.31\) (m, 1H), \(2.03-1.96\) (m, 2H), \(1.63-1.50\) (m, 2H) ppm. \(^{13}\text{C NMR}\) (75 MHz, C\(_6\)D\(_6\)): \(\delta = 61.4, 41.0, 32.0, 22.6\) ppm.
Ethyl (3-phenylpropanoyl)prolylglycinate (33)

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), ethyl isocyanatoacetate (2f) (245 µL, 2.25 mmol, 1.5 equiv) and hydrocinnamic acid (3g) (563 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 33 (156 mg, 31% yield) was obtained as a white solid after purification by flash column chromatography. In $^1$H NMR timescale, two rotamers (10:1 ratio in C$_6$D$_6$) were observed. **Melting point:** 75-77 °C. **Major rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta$ = 7.93 (br t, $J$ = 6.1 Hz, 1H), 7.28-7.10 (m, 4H), 7.09-7.02 (m, 1H), 4.54 (d, $J$ = 7.6 Hz, 1H), 3.90 (dd, $J$ = 17.9, 6.1 Hz, 1H), 3.82 (q, $J$ = 7.2 Hz, 2H), 3.74 (dd, $J$ = 17.9, 5.5 Hz, 1H), 3.04 (t, $J$ = 7.5 Hz, 2H), 2.71 (td, $J$ = 9.2, 2.0 Hz, 1H), 2.45-2.33 (m, 2H), 2.29-2.09 (m, 2H), 1.92-1.73 (m, 1H), 1.30-1.04 (m, 2H), 0.83 (t, $J$ = 7.2 Hz, 3H) ppm. **13C NMR** (75 MHz, C$_6$D$_6$): $\delta$ = 172.2, 171.4, 169.8, 141.9, 128.9, 128.7, 126.4, 60.8, 59.5, 47.0, 41.4, 36.6, 31.3, 26.7, 24.9, 14.0 ppm. **HRMS (EI+):** calcd for C$_{18}$H$_{24}$N$_2$O$_4$ [M]$^+$: 332.1731, found: 332.1733. **Characteristic peaks for the minor rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta$ = 6.00 (br t, $J$ = 5.8 Hz, 1H), 3.61 (dd, $J$ = 6.1, 3.8 Hz, 2H), 3.57-3.48 (m, 1H), 3.45-3.33 (m, 1H), 3.10 (t, $J$ = 7.5 Hz, 2H) ppm.

![Chemical Structure](image)

Chemical Formula: C$_{24}$H$_{30}$N$_2$O$_4$
Molecular Weight: 410.51

N-(3,4-dimethoxyphenethyl)-1-(3-phenylpropanoyl)pyrrolidine-2-carboxamide (34)

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), 4-(2-isocyanatoethyl)-1,2-dimethoxybenzene (2g) (245 µL, 2.25 mmol, 1.5 equiv) and hydrocinnamic
acid (3g) (430 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 34 (324 mg, 52% yield) was obtained as a white solid after purification by flash column chromatography. In $^1$H NMR timescale, two rotamers (12:1 ratio in C$_6$D$_6$) were observed. **Melting point:** 98-100 °C. **Major rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta$ = 7.45 (br t, $J$ = 5.5 Hz, 1H), 7.21-7.00 (m, 5H), 6.74-6.65 (m, 2H), 6.65-6.59 (m, 1H), 4.41 (d, $J$ = 7.6 Hz, 1H), 3.63-3.44 (m, 2H), 3.53 (s, 3H), 3.42 (s, 3H), 3.05-2.86 (m, 2H), 2.80-2.58 (m, 3H), 2.45-2.31 (m, 2H), 2.11 (t, $J$ = 7.6 Hz, 2H), 1.94-1.73 (m, 1H), 1.33-1.04 (m, 2H) ppm. $^{13}$C NMR (75 MHz, C$_6$D$_6$): $\delta$ = 172.0, 170.9, 150.3, 148.8, 132.3, 128.9, 128.8, 126.5, 121.1, 113.5, 112.7, 59.8, 55.8, 55.7, 47.0, 41.3, 36.5, 35.7, 31.2, 26.9, 25.0 ppm. **HRMS (EI+):** calcld for C$_{24}$H$_{30}$N$_2$O$_4$ [M]$^+$: 410.2200, found:410.2190. **Characteristic peaks for the minor rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta$ = 6.59-6.51(m, 3H), 5.55 (br s, 1H), 3.81-3.74 (m, 1H) ppm.

![Chemical Structure](image)

Chemical Formula: C$_{22}$H$_{28}$N$_2$O$_2$
Molecular Weight: 350.46

**N-(2,6-dimethylphenyl)-1-(3-phenylpropanoyl)pyrrolidine-2-carboxamide** (35)

Starting from pyrrolidine (1a) (107 mg, 1.5 mmol, 1 equiv), 2,6-dimethylpheynyl isocyanide (2h) (245 µL, 2.25 mmol, 1.5 equiv) and hydrocinnamic acid (3g) (430 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 35 (178 mg, 34% yield) was obtained as a white solid after purification by flash column chromatography. In $^1$H NMR timescale, two rotamers (15:1 ratio
in C\textsubscript{6}D\textsubscript{6}) were observed. **Melting point:** 141-143 °C. **Major rotamer:** \(^1\text{H NMR}\) (300 MHz, C\textsubscript{6}D\textsubscript{6}): \(\delta = 8.64 \text{ (br s, 1H)}, 7.13-6.92 \text{ (m, 8H)}, 4.62 \text{ (d, } J = 7.1 \text{ Hz, 1H)}, 3.04-2.87 \text{ (m, 2H)}, 2.79-2.69 \text{ (m, 1H)}, 2.52-2.35 \text{ (m, 2H)}, 2.23 \text{ (s, 6H)}, 2.22-2.14 \text{ (m, 2H)}, 1.90-1.72 \text{ (m, 1H)}, 1.34-1.14 \text{ (m, 2H)} \text{ ppm.} \(^{13}\text{C NMR}\) (75 MHz, C\textsubscript{6}D\textsubscript{6}): \(\delta = 172.3, 169.1, 141.7, 135.4, 135.3, 128.82, 128.76, 128.3, 126.8, 126.5, 60.1, 47.1, 36.5, 31.2, 27.0, 25.1, 18.7 \text{ ppm.} \text{HRMS (EI+:} calcd for C\textsubscript{22}H\textsubscript{26}N\textsubscript{2}O\textsubscript{2}[M]^{+*}: 3502.1989, found: 350.1994. **Characteristic peaks for the minor rotamer:** \(^1\text{H NMR}\) (300 MHz, C\textsubscript{6}D\textsubscript{6}): \(\delta = 8.64 \text{ (br s, 1H)}, 7.13-6.92 \text{ (m, 8H)}, 4.62 \text{ (d, } J = 7.1 \text{ Hz, 1H)}, 3.04-2.87 \text{ (m, 2H)}, 2.79-2.69 \text{ (m, 1H)}, 2.52-2.35 \text{ (m, 2H)}, 2.23 \text{ (s, 6H)}, 2.22-2.14 \text{ (m, 2H)}, 1.90-1.72 \text{ (m, 1H)}, 1.34-1.14 \text{ (m, 2H)} \text{ ppm.} \(^{13}\text{C NMR}\) (75 MHz, C\textsubscript{6}D\textsubscript{6}): \(\delta = 172.3, 169.1, 141.7, 135.4, 135.3, 128.82, 128.76, 128.3, 126.8, 126.5, 60.1, 47.1, 36.5, 31.2, 27.0, 25.1, 18.7 \text{ ppm.} \text{HRMS (EI+:} calcd for C\textsubscript{22}H\textsubscript{26}N\textsubscript{2}O\textsubscript{2}[M]^{+*}: 3502.1989, found: 350.1994. **Characteristic peaks for the minor rotamer:** \(^1\text{H NMR}\) (300 MHz, C\textsubscript{6}D\textsubscript{6}): \(\delta = 6.53 \text{ (br s, 1H)}, 3.92-3.83 \text{ (m, 1H)}, 3.53-3.42 \text{ (m, 2H)}, 3.12-3.04 \text{ (m, 2H)}, 1.94 \text{ (s, 6H)} \text{ ppm.}\\\\

1-acetyl-\text{N-(tert-butyl)piperidine-2-carboxamide (36)}\\

Starting from piperidine (1b) (128 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 \text{ µL}, 2.25 mmol, 1.5 equiv) and acetic acid (3a) (215 \text{ µL}, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 36 (127 mg, 37% yield) was obtained as a white solid after purification by flash column chromatography. In \(^1\text{H NMR timescale}, two rotamers (8:1 ratio in C}_6\text{D}_6) were observed. **Melting point:** 88-90 °C. **Major rotamer:** \(^1\text{H NMR}\) (300 MHz, C\textsubscript{6}D\textsubscript{6}): \(\delta = 6.28 \text{ (br s, 1H)}, 5.17 \text{ (d, } J = 5.4 \text{ Hz, 1H)}, 3.11-2.88 \text{ (m, 2H)}, 2.20-2.06 \text{ (m, 1H)}, 1.95 \text{ (qt, } J = 13.0, 3.9 \text{ Hz, 1H)}, 1.69 \text{ (s, 3H)}, 1.39-1.31 \text{ (m, 1H)}, 1.28 \text{ (s, 9H)}, 1.21-1.10 \text{ (m, 2H)}, 1.06-0.89 \text{ (m, 1H)} \text{ ppm.} \(^{13}\text{C NMR}\) (75 MHz, C\textsubscript{6}D\textsubscript{6}): \(\delta = 170.5, 170.3, 52.3, 50.6, 44.1, 28.8, 25.7, 25.6, 21.4, 20.5 \text{ ppm.} \text{HRMS (EI+:} calcd for C\textsubscript{12}H\textsubscript{22}N\textsubscript{2}O\textsubscript{2}[M]^{+*}: 226.1676, found: 226.1676. **Characteristic peaks for the minor rotamer:** \(^1\text{H NMR}\) (300 MHz, C\textsubscript{6}D\textsubscript{6}): \(\delta = 5.70 \text{ (br s, 1H)}, 4.72 \text{ (d, } J = 11.8 \text{ Hz, 1H)}, 3.99-3.85 \text{ (m, 2H)}, 3.84-3.67 \text{ (m, 2H)}, 3.54-3.44 \text{ (m, 1H)}, 3.14-3.03 \text{ (m, 2H)}, 1.91 \text{ (s, 6H)}, 1.89 \text{ (s, 6H)} \text{ ppm.}
Hz, 1H), 3.94-3.77 (m, 1H), 2.54-2.31 (m, 2H) ppm. $^{13}$C NMR (75 MHz, C$_6$D$_6$): $\delta = 28.6$ ppm.

$N$-(tert-butyl)-1-(3-phenylpropanoyl)piperidine-2-carboxamide (37)

Starting from piperidine (1b) (128 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 $\mu$L, 2.25 mmol, 1.5 equiv) and hydrocinnamic acid (3g) (430 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 37 (169 mg, 36% yield) was obtained as a white solid after purification by flash column chromatography. In $^1$H NMR timescale, two rotamers (8:1 ratio in C$_6$D$_6$) were observed. **Melting point:** 138-140 °C. **Major rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta = 7.15$-7.09 (m, 2H), 7.09-7.02 (m, 3H), 6.20 (br s, 1H), 5.19 (d, $J = 5.4$ Hz, 1H), 3.15-3.02 (m, 1H), 2.97 (dd, $J = 16.1$, 7.8 Hz, 2H), 2.87 (td, $J = 13.1$, 3.0 Hz, 1H), 2.28 (t, $J = 7.7$ Hz, 2H), 2.17-2.07 (m, 1H), 1.96 (qt, $J = 13.0$, 3.9 Hz, 1H), 1.39-1.31 (m, 1H), 1.27 (s, 9H), 1.22-1.17 (m, 1H), 1.15-1.05 (m, 1H), 0.93 (tt, $J = 12.9$, 4.2 Hz, 1H) ppm. $^{13}$C NMR (75 MHz, C$_6$D$_6$): $\delta = 172.2$, 170.4, 141.8, 128.8, 128.7, 126.4, 52.5, 50.6, 43.3, 35.4, 31.7, 28.8, 25.7, 25.6, 20.6 ppm.

**HRMS (EI+):** calcd for C$_{19}$H$_{28}$N$_2$O$_2$ [M]$^{+*}$: 316.2145, found: 316.2153. **Characterisitic peaks for the minor rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta = 5.41$ (br s, 1H), 4.79 (d, $J = 12.3$ Hz, 1H), 3.97-3.86 (m, 1H), 2.47-2.34 (m, 2H), 1.16 (s, 9H) ppm. $^{13}$C NMR (75 MHz, C$_6$D$_6$): $\delta = 28.6$ ppm.
**N-(tert-butyl)-1-pivaloylpiperidine-2-carboxamide (38)**

Starting from piperidine (1b) (128 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and pivalic acid (3e) (383 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 38 (177 mg, 44% yield) was obtained as a white solid after purification by flash column chromatography. **Melting point**: 74-76 °C. **$^1$H NMR** (400 MHz, C$_6$D$_6$): $\delta = 6.33$ (s, 1H), 5.14 (d, $J = 5.7$ Hz, 1H), 3.72 (d, $J = 13.0$ Hz, 1H), 2.82 (dd, $J = 13.0$, 2.8 Hz, 1H), 2.25 (d, $J = 13.0$ Hz, 1H), 2.11-1.94 (m, 1H), 1.44-1.36 (m, 1H), 1.28 (s, 9H), 1.25-1.19 (m, 1H), 1.21-1.13 (m, 1H), 1.14 (s, 9H), 1.13-1.03 (m, 1H) ppm. **$^{13}$C NMR** (101 MHz, CDCl$_3$): $\delta = 178.3, 170.3, 54.4, 50.9, 44.5, 38.9, 28.9, 28.3, 25.5, 25.2, 20.7$ ppm. **HRMS (EI+)**: calcd for C$_{15}$H$_{28}$N$_2$O$_2$ [M]$^{+}$: 268.2145, found: 268.2154.

**$^{[5]}$ (39)**

Starting from 4-phenyl piperidine (1c) (242 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and acetic acid (3a) (215 µL, 3.75
mmol, 2.5 equiv), and following the aforementioned general procedure, product 36 (165 mg, 36% yield) was obtained as a white solid after purification by flash column chromatography. In $^1$H NMR timescale, two rotamers (9:1 ratio in C$_6$D$_6$) were observed. **Melting point:** 152-154 °C. **Major rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): δ = 7.21-7.14 (m, 2H), 7.14-7.01 (m, 3H), 6.38 (br s, 1H), 5.28 (dd, $J = 5.8, 1.2$ Hz, 1H), 3.44 (tt, $J = 12.4, 3.5$ Hz, 1H), 3.20-3.07 (m, 2H), 2.31 (ddt, $J = 13.4, 3.6, 1.9$ Hz, 1H), 1.72 (s, 3H), 1.52-1.42 (m, 1H), 1.40-1.32 (m, 1H), 1.31 (s, 9H), 1.26-1.17 (m, 1H) ppm. $^{13}$C NMR (75 MHz, C$_6$D$_6$): δ = 170.5, 170.3, 146.1, 128.8, 127.2, 126.7, 52.5, 50.7, 44.2, 37.9, 33.6, 32.9, 28.8, 21.5 ppm. **HRMS (EI+):** calcd for C$_{18}$H$_{26}$N$_2$O$_2$ [M]$^{+}$: 302.1989, found: 302.1985. **Characteristic peaks for the minor rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): δ = 5.79 (br s, 1H), 4.86 (d, $J = 13.4$ Hz, 1H), 3.95 (d, $J = 5.3$ Hz, 1H), 2.82-2.68 (m, 2H), 2.56 (td, $J = 13.0, 3.3$ Hz, 1H), 1.71 (s, 3H), 1.26 (s, 9H) ppm. $^{13}$C NMR (75 MHz, C$_6$D$_6$): δ = 169.4, 168.4, 145.5, 58.7, 51.2, 39.8, 38.9, 34.4, 31.8, 28.7, 21.3 ppm.

![Chemical structure](image)

**Chemical Formula:** C$_{14}$H$_{26}$N$_2$O$_3$

**Molecular Weight:** 270.37

**N-(tert-butyl)-4-pivaloylmorpholine-3-carboxamide (40)**

Starting from morpholine (1d) (131 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and pivalic acid (3e) (383 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 40 (178 mg, 44% yield) was obtained as a white solid after purification by flash column chromatography. **Melting point:** 121-123 °C. **$^1$H NMR** (300 MHz, C$_6$D$_6$): δ = 5.75 (br s, 1H), 4.71 (d, $J = 2.7$ Hz, 1H), 4.48 (d, $J = 11.6$ Hz, 1H), 3.55-3.36 (m, 2H), 3.28-3.17 (m, 1H), 3.15 (dd, $J = 11.6, 3.8$ Hz, 1H), 3.08-2.96 (m, 1H), 1.26
(s, 9H), 1.08 (s, 9H) ppm. $^{13}$C NMR (75 MHz, C$_6$D$_6$): $\delta = 177.5, 168.2, 66.7, 66.1, 55.3, 50.9, 44.7, 38.7, 28.8, 28.1$ ppm. HRMS (EI+): calcd for C$_{14}$H$_{26}$N$_2$O$_3$ [M]$^{+\ast}$: 270.1938, found: 270.1954.

$N$-(tert-buty)-4-(3-phenylpropanoyl)morpholine-3-carboxamide (41)

Starting from morpholine (1d) (131 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 $\mu$L, 2.25 mmol, 1.5 equiv) and hydrocinnamic acid (3g) (430 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 41 (229 mg, 48% yield) was obtained as a white solid after purification by flash column chromatography. In $^1$H NMR timescale, two rotamers (10:1 ratio in C$_6$D$_6$) were observed. Melting point: 127-129 °C. $^1$H NMR (400 MHz, C$_6$D$_6$): $\delta = 7.16$-7.10 (m, 3H), 7.04 (d, $J = 7.6$ Hz, 2H), 5.58 (s, 1H), 4.73 (d, $J = 3.7$ Hz, 1H), 4.25 (d, $J = 11.9$ Hz, 1H), 3.36 (dd, $J = 11.4, 3.5$ Hz, 1H), 3.32-3.21 (m, 1H), 2.96 (t, $J = 7.6$ Hz, 2H), 2.79 (td, $J = 11.4, 2.9$ Hz, 2H), 2.60 (d, $J = 14.1$ Hz, 1H), 2.19 (t, $J = 7.6$ Hz, 2H), 1.26 (s, 9H) ppm. $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta = 172.5, 168.2, 140.7, 128.6, 128.4, 126.4, 66.5, 66.0, 52.8, 51.3, 43.5, 34.8, 31.2, 28.7$ ppm. HRMS (EI+): calcd for C$_{18}$H$_{26}$N$_2$O$_3$ [M]$^{+\ast}$: 318.1938, found: 318.1946.
1-acetyl-N-(tert-butyl)azepane-2-carboxamide (42)

Starting from azepane (1e) (170 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and acetic acid (3a) (215 µL, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 42 (118 mg, 33% yield) was obtained as a white solid after purification by flash column chromatography. In $^1$H NMR timescale, two rotamers (15:1 ratio in C$_6$D$_6$) were observed. **Melting point:** 153-155 °C. **Major rotamer: $^1$H NMR (300 MHz, C$_6$D$_6$):** δ = 6.75 (br s, 1H), 4.76 (dd, $J = 12.2$, 6.5 Hz, 1H), 3.15-2.90 (m, 2H), 2.15-1.98 (m, 1H), 1.86-1.76 (m, 1H), 1.73 (s, 3H), 1.57-1.38 (m, 2H), 1.34 (s, 9H), 1.19-1.10 (m, 1H), 0.98-0.76 (m, 3H) ppm. **$^{13}$C NMR (75 MHz, C$_6$D$_6$):** δ = 171.1, 170.9, 57.5, 50.6, 44.5, 30.2, 29.4, 28.85, 28.78, 24.7, 21.4 ppm. **HRMS (EI+):** calcd for C$_{13}$H$_{23}$N$_2$O$_2$ [M - H]$^+$: 239.1754, found: 239.1757. **Characteristic peaks for the minor rotamer: $^1$H NMR (300 MHz, C$_6$D$_6$):** δ = 5.33 (br s, 1H), 4.46-4.31 (m, 1H), 3.70 (dd, $J = 11.5$, 6.1 Hz, 1H), 2.50-2.38 (m, 1H), 2.33-2.20 (m, 1H), 1.79 (s, 3H), 1.19 (s, 9H) ppm. **$^{13}$C NMR (75 MHz, C$_6$D$_6$):** δ = 63.3, 42.3, 32.0, 29.2, 28.8, 28.6, 25.9 ppm.

![Chemical Structure](image.png)

Chemical Formula: C$_{20}$H$_{30}$N$_2$O$_2$
Molecular Weight: 330.47

N-(tert-butyl)-1-(3-phenylpropanoyl)azepane-2-carboxamide (43)

Starting from azepane (1e) (170 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and hydrocinnamic acid (3g) (430 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 43 (215 mg, 43% yield) was obtained as a white solid after purification by flash column...
chromatography. In $^1$H NMR timescale, two rotamers (18:1 ratio in C$_6$D$_6$) were observed. **Melting point:** 155-157 °C. **Major rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta$ = 7.15-7.00 (m, 5H), 6.70 (br s, 1H), 4.76 (dd, $J$ = 12.2, 6.5 Hz, 1H), 3.11-2.94 (m, 4H), 2.43-2.24 (m, 2H), 2.16-1.98 (m, 1H), 1.85-1.70 (m, 1H), 1.53-1.35 (m, 2H), 1.34 (s, 9H), 1.18-1.09 (m, 1H), 0.98-0.64 (m, 3H) ppm. $^{13}$C NMR (75 MHz, C$_6$D$_6$): $\delta$ = 173.0, 170.8, 142.0, 128.9, 128.7, 126.4, 57.7, 50.6, 43.7, 35.1, 31.8, 30.2, 29.3, 28.9, 28.7, 24.6 ppm. **HRMS (EI+):** calcd for C$_{15}$H$_{20}$NO [M - CONH$^t$Bu]$^+$: 230.1539, found: 230.1534. **Characterisitic peaks for the minor rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta$ = 5.21 (br s, 1H), 4.44-4.32 (m, 1H), 3.74 (dd, $J$ = 11.5, 6.1 Hz, 1H), 1.16 (s, 9H) ppm. $^{13}$C NMR (75 MHz, C$_6$D$_6$): $\delta$ = 172.0, 171.9, 62.3, 50.8, 42.4, 35.6, 31.4, 29.2, 28.6, 25.8 ppm.

![Chemical Structure](image)

**N-(tert-butyl)-1-pivaloylazepane-2-carboxamide (44)**

Starting from azepane (1e) (170 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and pivalic acid (3e) (383 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 44 (92 mg, 22% yield) was obtained as a white solid after purification by flash column chromatography. **Melting point:** 127-129 °C. $^1$H NMR (500 MHz, C$_6$D$_6$, T = 70 °C): $\delta$ = 6.02 (s, 1H), 4.84-4.54 (m, 1H), 3.79 (d, $J$ = 15.2 Hz, 1H), 3.04 (t, $J$ = 13.0 Hz, 1H), 2.05-1.88 (m, 2H), 1.65-1.54 (m, 1H), 1.51-1.42 (m, 2H), 1.39-1.33 (m, 1H), 1.29 (s, 9H), 1.21 (s, 9H), 1.14-1.03 (m, 2H) ppm. $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ = 178.4, 171.5, 60.6, 51.0, 44.6, 39.8, 29.7, 29.1 (2C), 28.8, 28.7, 25.0 ppm. **HRMS (EI+):** calcd for C$_{16}$H$_{30}$N$_2$O$_2$ [M]$^{++}$: 282.2302, found: 282.2298.
1-benzoyl-N-(tert-butyl)azepane-2-carboxamide (45)

Starting from azepane (1e) (170 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and benzoic acid (3n) (510 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 45 (106 mg, 23% yield) was obtained as a white solid after purification by flash column chromatography. In $^1$H NMR timescale, two rotamers (4:1 ratio in C$_6$D$_6$) were observed. Melting point: 127-129 °C. **Major rotamer:** $^1$H NMR (500 MHz, C$_6$D$_6$): $\delta = 7.31$-$7.24$ (m, 2H), 7.04 (dd, $J = 5.6$, 1.8 Hz, 3H), 6.55 (s, 1H), 4.93 (dd, $J = 12.1$, 6.2 Hz, 1H), 3.35 (d, $J = 15.6$ Hz, 1H), 3.22-3.11 (m, 2H), 2.12 (q, $J = 15.0$, 11.6 Hz, 1H), 1.86 (dt, $J = 15.0$, 7.3 Hz, 1H), 1.61-1.53 (m, 1H), 1.44 (d, $J = 13.2$ Hz, 1H), 1.37 (s, 9H), 1.11-1.04 (m, 2H), 0.98-0.87 (m, 1H) ppm. $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta = 173.3$, 170.8, 137.0, 129.2, 128.6, 125.9, 58.3, 51.1, 45.8, 30.8, 29.0, 28.8, 28.7, 24.9 ppm. **HRMS (EI+):** calcd for C$_{18}$H$_{26}$N$_2$O$_2$ [M]$^{+}$: 302.1989, found: 302.1998. **Characterisitic peaks for the minor rotamer:** $^1$H NMR (400 MHz, C$_6$D$_6$): $\delta = 7.42$-$7.35$ (m, 2H), 4.74 (s, 1H), 4.61 (d, $J = 13.8$ Hz, 1H), 3.74 (t, $J = 9.3$ Hz, 1H), 2.91 (t, $J = 12.6$ Hz, 1H), 1.78-1.69 (m, 1H), 1.18 (s, 9H) ppm.
2-acetyl-N-(tert-butyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide\(^{[6]}\) (46)

Starting from 1,2,3,4-tetrahydroisoquinoline (1f) (200 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and acetic acid (3a) (215 µL, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure changing the current to 6 mA and reaction time to 36 hours, product 46 (225 mg, 55% yield) was obtained as a white solid after purification by flash column chromatography. In \(^1\)H NMR timescale, two rotamers (18:1 ratio in C\(_6\)D\(_6\)) were observed. **Melting point:** 158-160 °C. **Major rotamer:** \(^1\)H NMR (300 MHz, C\(_6\)D\(_6\)): \(\delta = 7.15-7.12\) (m, 1H), 7.08-7.00 (m, 2H), 6.93-6.86 (m, 1H), 6.81 (br s, 1H), 5.98 (s, 1H), 3.49 (ddd, \(J = 12.7, 8.2, 4.1\) Hz, 1H), 2.93-2.85 (m, 1H), 2.73-2.64 (m, 1H), 2.25 (ddd, \(J = 13.9, 8.9, 5.3\) Hz, 1H), 1.66 (s, 3H), 1.31 (s, 9H) ppm. \(^{13}\)C NMR (75 MHz, C\(_6\)D\(_6\)): \(\delta = 170.0, 169.9, 135.6, 133.4, 128.2, 127.3, 126.6, 58.3, 51.1, 42.7, 29.0, 28.8, 21.6\) ppm. **HRMS (EI+):** calcd for C\(_{12}\)H\(_{12}\)NO\(_2\) [M - NH\(_t\)Bu]\(^+\): 202.0863, found: 202.0861. **Characteristic peaks for the minor rotamer:** \(^1\)H NMR (300 MHz, C\(_6\)D\(_6\)): \(\delta = 5.35\) (br s, 1H), 4.89 (s, 1H), 4.42-4.21 (m, 1H), 1.97 (s, 3H), 1.08 (s, 9H) ppm. \(^{13}\)C NMR (75 MHz, C\(_6\)D\(_6\)): \(\delta = 28.4\) ppm.
**N-(tert-butyl)-2-(3-phenylpropanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (47)**

Starting from 1,2,3,4-tetrahydroisoquinoline (1f) (200 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and hydrocinnamic acid (3g) (430 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure changing the current to 6 mA and reaction time to 36 hours, product 47 (282 mg, 52% yield) was obtained as a white solid after purification by flash column chromatography. In $^1$H NMR timescale, two rotamers (18:1 ratio in C$_6$D$_6$) were observed. **Melting point:** 136-138°C. **Major rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta = 7.36$ (d, $J = 7.2$ Hz, 1H), 7.20-7.01 (m, 8H), 6.89 (d, $J = 7.1$ Hz, 1H), 6.09 (s, 1H), 3.59 (ddd, $J = 12.7$, 8.5, 4.5 Hz, 1H), 3.13-2.97 (m, 2H), 2.97-2.89 (m, 1H), 2.73 (dt, $J = 15.5$, 5.3 Hz, 1H), 2.33 (ddd, $J = 15.8$, 9.3, 6.4 Hz, 1H), 2.28-2.15 (m, 2H), 1.36 (s, 9H) ppm. **$^{13}$C NMR (75 MHz, C$_6$D$_6$): $\delta = 171.9$, 170.0, 141.9, 135.6, 133.5, 128.82, 128.79, 128.4, 128.1, 127.4, 126.6, 126.4, 58.5, 51.1, 42.0, 35.7, 31.6, 29.0, 28.8 ppm. **HRMS (EI+):** calcd for C$_{18}$H$_{18}$NO [M - NH$^+$Bu]$^+$: 264.1383, found: 264.1388. **Characteristic peaks for the minor rotamer:** $^1$H NMR (300 MHz, C$_6$D$_6$): $\delta = 5.34$ (br s, 1H), 4.96 (s, 1H), 4.45-4.32 (m, 1H), 1.07 (s, 9H) ppm. **$^{13}$C NMR (75 MHz, C$_6$D$_6$): $\delta = 28.4$ ppm.

![Chemical structure of 47](image)

**N-(tert-butyl)-2-pivaloyl-1,2,3,4-tetrahydroisoquinoline-1-carboxamide (48)**

Starting from 1,2,3,4-tetrahydroisoquinoline (1f) (200 mg, 1.5 mmol, 1 equiv), tert-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and pivalic acid (3e)
(383 mg, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure changing the current to 6 mA and reaction time to 36 hours, product 48 (316 mg, 67% yield) was obtained as a white solid after purification by flash column chromatography. **Melting point**: 138-140 °C.  \(^1\)H NMR (300 MHz, C\(_6\)D\(_6\)): \(\delta = 7.12-6.99\) (m, 3H), \(6.94-6.88\) (m, 1H), \(6.77\) (br s, 1H), \(6.03\) (s, 1H), \(3.78-3.66\) (m, 1H), \(3.66-3.53\) (m, 1H), \(2.54\) (ddd, \(J = 16.5, 10.9, 5.1\) Hz, 1H), \(2.33\) (dt, \(J = 16.1, 3.2\) Hz, 1H), \(1.31\) (s, 9H), \(1.14\) (s, 9H) ppm. \(^{13}\)C NMR (75 MHz, C\(_6\)D\(_6\)): \(\delta = 171.1, 169.9, 134.6, 132.9, 128.9, 128.7, 127.1, 126.4, 59.1, 50.9, 42.3, 38.7, 29.1, 28.8, 28.1\) ppm. **HRMS (EI+)**: calcd for C\(_{14}\)H\(_{18}\)NO [M - NH\(_2\)B\(_u\)]\(^+\): 216.1383, found: 216.1383.
7. Preliminary experiments based on the use of acyclic secondary amines

To test the viability of our synthetic approach with regard to the use of acyclic secondary amines, diethylamine, the acyclic analog of pyrrolidine, was used as model substrate. In the previously optimized reaction conditions, we did witness the formation of the desired product (49), although accompanied with the generation of several unidentified byproducts. As a result, the multicomponent product 49, could only be isolated in low yield (22%), which allowed to us to conclude that acyclic secondary amines are poor reaction partners. The major characterization of product 49 is as below, and the copies of ${}^1\text{H}$ and ${}^{13}\text{C}$ NMR spectra are available in section 9.

![Chemical structure of N-\((\text{tert-buty})\)-2-\((\text{N-ethylacetamido})\)propanamide (49)](image)

**N-\((\text{tert-buty})\)-2-\((\text{N-ethylacetamido})\)propanamide (49)**

Starting from diethylamine (1g) (156 µL, 1.5 mmol, 1 equiv), \textit{tert}-butyl isocyanide (2a) (254 µL, 2.25 mmol, 1.5 equiv) and acetic acid (3a) (215 µL, 3.75 mmol, 2.5 equiv), and following the aforementioned general procedure, product 49 (70 mg, 22% yield) was obtained as a yellowish solid after purification by flash column chromatography.\textit{H NMR} (300 MHz, CDCl$_3$): $\delta$ = 6.30 (br s, 1H), 4.90 (q, $J$ = 7.2 Hz, 1H), 3.29 (q, $J$ = 7.2 Hz, 2H), 2.09 (s, 3H), 1.26-1.20 (m, 12H), 1.12 (t, $J$ = 7.2 Hz, 3H) ppm.\textit{C NMR} (75 MHz, CDCl$_3$): $\delta$ = 171.8, 171.2, 52.5, 51.0, 39.7, 28.7, 21.9, 15.5, 14.0 ppm.
8. References


9. NMR spectra of electrochemical multicomponent α-carbamoylation products

$^1$H NMR of 4 in C$_6$D$_6$

$^{13}$C NMR of 4 in C$_6$D$_6$
$^1$H NMR of 4 in CDCl$_3$

$^{13}$C NMR of 4 in CDCl$_3$
$^1$H NMR of 4 in tol-$d^8$

$^{13}$C NMR of 4 in tol-$d^8$
$^1$H NMR of 5 in C$_6$D$_6$

$^{13}$C NMR of 5 in C$_6$D$_6$
$^1$H NMR of 6 in C$_6$D$_6$

$^{13}$C NMR of 6 in CDCl$_3$
\(^1\)H NMR of 7 in C\(_6\)D\(_6\)

\(^{13}\)C NMR of 7 in CDCl\(_3\)
$^1$H NMR of 8 in C$_6$D$_6$

![H NMR spectrum](image)

$^{13}$C NMR of 8 in C$_6$D$_6$

![C NMR spectrum](image)
$^1$H NMR of 9 in C$_6$D$_6$

$^{13}$C NMR of 9 in C$_6$D$_6$
$^1$H NMR of 10 in $C_6D_6$

$^{13}$C NMR of 10 in $C_6D_6$
$^1$H NMR of 11 in C$_6$D$_6$

$^{13}$C NMR of 11 in C$_6$D$_6$
$^1$H NMR of 12 in C$_6$D$_6$

\[
\text{Boc}^+\text{H} - \text{N} - \text{C} = \text{O} - \text{N}^{\text{tBu}}
\]

13C NMR of 12 in CDCl$_3$

\[
\text{Boc}^+\text{H} - \text{N} - \text{C} = \text{O} - \text{N}^{\text{tBu}}
\]
$^{1}H$ NMR of 13 in C$_6$D$_6$

$^{13}$C NMR of 13 in CDCl$_3$
$^1$H NMR of 14 in C$_6$D$_6$

$^{13}$C NMR of 14 in CDCl$_3$
$^1$H NMR of 15 in C$_6$D$_6$

$^{13}$C NMR of 15 in CDCl$_3$
$^1$H NMR of 16

$^{13}$C NMR of 16 in CDCl$_3$
$^1$H NMR of 17 in C$_6$D$_6$

$^{13}$C NMR of 17 in C$_6$D$_6$
$^1$H NMR of 18 in C$_6$D$_6$

$^{13}$C NMR of 18 in CDCl$_3$
$^1$H NMR of 19 in C$_6$D$_6$

$^{13}$C NMR of 19 in C$_6$D$_6$
$^{19}$F NMR of 19 in C$_6$D$_6$

$^1$H NMR of 20 in C$_6$D$_6$
$^1$H NMR of 21 in C$_6$D$_6$
$^{13}$C NMR of 21 in CDCl$_3$

$^{19}$F NMR of 21 in CDCl$_3$
$^1$H NMR of 22 in C$_6$D$_6$

$^{13}$C NMR of 22 in CDCl$_3$
$^1$H NMR of 23 in C$_6$D$_6$

$^{13}$C NMR of 23 in CDCl$_3$
$^1$H NMR of 26 in C$_6$D$_6$

$^{13}$C NMR of 26 in C$_6$D$_6$
$^{19}\text{F NMR of 26 in C}_6\text{D}_6$
$^{13}$C NMR of 27 in C$_6$D$_6$

$^1$H NMR of 28 in C$_6$D$_6$
$^{13}$C NMR of 28 in C$_6$D$_6$

COSY of 28 in C$_6$D$_6$
HSQC of 28 in C$_6$D$_6$

$^1$H NMR of 29 in C$_6$D$_6$
$^{13}$C NMR of 29 in C$_6$D$_6$

$^1$H NMR of 30 in C$_6$D$_6$
$^{13}$C NMR of 30 in C$_6$D$_6$

$^1$H NMR of 31 in C$_6$D$_6$
$^{13}$C NMR of 31 in C$_6$D$_6$

$^1$H NMR of 32 in C$_6$D$_6$
$^{13}$C NMR of 32 in C$_6$D$_6$

$^1$H NMR of 33 in C$_6$D$_6$
$^{13}$C NMR of 33 in C$_6$D$_6$

$^1$H NMR of 34 in C$_6$D$_6$
$^{13}$C NMR of 34 in C$_6$D$_6$

$^1$H NMR of 35 in C$_6$D$_6$
$^{13}$C NMR of 35 in C$_6$D$_6$

DEPT of 35 in C$_6$D$_6$
$^1$H NMR of 36 in C$_6$D$_6$

$^{13}$C NMR of 36 in C$_6$D$_6$
$^1$H NMR of 37 in $C_6D_6$

$^{13}$C NMR of 37 in $C_6D_6$
$^1$H NMR of 38 in C$_6$D$_6$

$^{13}$C NMR of 38 in CDCl$_3$
$^1$H NMR of 39 in C$_6$D$_6$

![H NMR spectrum](image)

$^{13}$C NMR of 39 in C$_6$D$_6$

![C NMR spectrum](image)
$^1$H NMR of 40 in C$_6$D$_6$

$^{13}$C NMR of 40 in C$_6$D$_6$
$^1$H NMR of 41 in C$_6$D$_6$

![H NMR spectrum](image)

$^{13}$C NMR of 41 in CDCl$_3$

![C NMR spectrum](image)
$^1$H NMR of 42 in C$_6$D$_6$

$^{13}$C NMR of 42 in C$_6$D$_6$
$^1$H NMR of 43 in C$_6$D$_6$

$^{13}$C NMR of 43 in C$_6$D$_6$
$^1$H NMR of 44 in C$_6$D$_6$

$^{13}$C NMR of 44 in CDCl$_3$
$^1$H NMR of 45 in C$_6$D$_6$

$^{13}$C NMR of 45 in CDCl$_3$
$^1$H NMR of 46 in C$_6$D$_6$

$^{13}$C NMR of 46 in C$_6$D$_6$
DEPT of 46 in C₆D₆

¹H NMR of 47 in C₆D₆
$^{13}$C NMR of 47 in C$_6$D$_6$

DEPT of 47 in C$_6$D$_6$
$^1$H NMR of 48 in C$_6$D$_6$

$^{13}$C NMR of 48 in C$_6$D$_6$
$^1$H NMR of 49 in CDCl$_3$

$^{13}$C NMR of 49 in CDCl$_3$