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Metal-Free Synthesis of Unsymmetrical Ureas and Carbamates from 

CO₂ and Amines via Isocyanate Intermediates

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ABSTRACT

A mild and metal-free synthesis of aryl isocyanates from arylamines under an atmosphere of CO₂ has been developed. The carbamic acid intermediate, derived from the arylamine starting material and CO₂ in the presence of DBU, is dehydrated by activated sulfonium reagents to generate the corresponding isocyanate. The latter can be detected by in situ IR and trapped by various amines and alcohols to make unsymmetrical ureas and carbamates, respectively. Dicarbamates can also be prepared in good yields via the mild dehydration of the corresponding dicarbamic acids.
INTRODUCTION

Isocyanates are highly valuable intermediates in organic synthesis. They are readily converted into the ureas and carbamates found in many biologically active compounds and polymers such as polyurethanes (Scheme 1).\(^1\) The scale of their worldwide production, which surpasses millions of tons annually, clearly illustrates their importance as synthetic intermediates. Notably, (di)isocyanates derived from arylamines are of particular interest as building blocks in the pharmaceutical industry and in the manufacturing of polyurethanes (Scheme 1b). The applications of these polymers across sectors as diverse as the medical, automotive and building/construction industries, continue to grow.\(^2\text{-}^3\)

Scheme 1. Synthesis of ureas and carbamates from isocyanates and their industrial relevance.

Despite the importance of isocyanates, ureas and carbamates, and the scale of their annual production, their industrial synthesis usually relies on the reaction of toxic phosgene (or phosgene equivalents) with amines (Scheme 2a).\(^2\text{-}^4\text{,}^5\) Besides the health risks associated with the use of phosgene, there are also major concerns associated with its
production and storage.\textsuperscript{6} Due to these issues, significant research efforts have been dedicated to the development of new methods for the production of isocyanates, avoiding the use of phosgene gas.\textsuperscript{2,7,8,9,10} Carbon dioxide has emerged as an ideal C1-building block to replace phosgene since it is abundant, non-toxic and renewable.\textsuperscript{11,12} Significant progress has been made towards the synthesis of isocyanates, ureas and carbamates using CO\textsubscript{2}, however many reports require harsh reaction conditions (high pressures and temperatures) due to the thermodynamic stability of CO\textsubscript{2}.\textsuperscript{13,14} Thus, the development of mild conditions for the laboratory synthesis of isocyanates, ureas and carbamates from aromatic amines and CO\textsubscript{2} should be of significant interest and value.\textsuperscript{15} Herein we describe a metal-free method for the preparation of unsymmetrical ureas and carbamates, via the corresponding isocyanate intermediates, using CO\textsubscript{2} under atmospheric pressure.\textsuperscript{16}

The synthesis of isocyanates from arylamines and CO\textsubscript{2} is often plagued by the formation of symmetrical urea products resulting from the rapid reaction of unreacted amine with the newly generated isocyanate. Thus, efficient and complete conversion of the arylamine starting material is necessary for the clean generation of the isocyanate product. Strong dehydrating agents (such as POCl\textsubscript{3} or SOCl\textsubscript{2}) have been used to convert the carbamic acid intermediate derived from the reaction of amines with CO\textsubscript{2} to the isocyanate, while consuming the equivalent of H\textsubscript{2}O produced in the process. The use of POCl\textsubscript{3} and SOCl\textsubscript{2} potentially limits the functional group compatibility of these reactions.\textsuperscript{12a,17} Mitsunobu-type protocols have also been employed.\textsuperscript{18} Treating the carbamic acid with dialkylazodicarboxylates and trialkylphosphines produces the isocyanate, along with the stoichiometric waste inherently associated with the Mitsunobu reaction. We wondered if
a dimethylsulfonium reagent (A) could effect the dehydration of carbamic acid intermediates to generate isocyanates under mild conditions without the need for high pressure equipment and hazardous reagents (Scheme 2b, This Work).

**Scheme 2. Synthesis of aryl isocyanates, ureas and carbamates**

RESULTS AND DISCUSSION

Our synthesis of isocyanates relies on the rapid formation of carbamic acid derivatives under an atmosphere of CO$_2$ and the dehydration of this intermediate under Swern-like conditions.$^{19}$ The optimal reaction conditions for isocyanate formation, and subsequent quench with $n$-butylamine to generate the unsymmetrical urea, are demonstrated in Table 1.$^{20}$ Either TFAA or oxalyl chloride can be used to generate the activated dimethyl
sulfonium reagent, providing the urea product in excellent yields (entries 1 and 2). Under these reaction conditions, no products resulting from the Pummerer rearrangement are observed. We chose TFAA as the ideal activating reagent since the use of oxalyl chloride required lower reaction temperatures and slow addition of reagents. Control reactions revealed that DBU is necessary for the formation of the carbamic acid intermediate. In the absence of DBU or with substoichiometric quantities of DBU, little to no product was formed, and significant amounts of trifluoroacetylated aniline were isolated (entries 3 and 7). Replacing DBU with TMEDA did not yield any of the desired product (entry 8). Interestingly, TFAA appears to mediate this reaction in the absence of DMSO, although diminished yield (35%) of the unsymmetrical urea was observed under these conditions (entry 5). Overall, while the reaction requires stoichiometric quantities of DBU, DMSO and TFAA to obtain high yields, it should be noted that the resulting waste can be removed from the desired product without the need for chromatography (see below for the synthesis of 4a).
Table 1. Reaction optimization

<table>
<thead>
<tr>
<th>entry</th>
<th>change from standard conditions</th>
<th>% yield&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>93 (89)</td>
</tr>
<tr>
<td>2</td>
<td>oxalyl chloride instead of TFAA</td>
<td>95</td>
</tr>
<tr>
<td>3</td>
<td>no DBU</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>no TFAA</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>no DMSO</td>
<td>35</td>
</tr>
<tr>
<td>6&lt;sup&gt;c&lt;/sup&gt;</td>
<td>no Et&lt;sub&gt;3&lt;/sub&gt;N</td>
<td>50</td>
</tr>
<tr>
<td>7</td>
<td>DBU (0.5 equiv)</td>
<td>31</td>
</tr>
<tr>
<td>8</td>
<td>TMEDA instead of DBU</td>
<td>0</td>
</tr>
</tbody>
</table>

<sup>a</sup>Reactions were performed using aniline (1.0 mmol, 1.0 equiv), DBU (1.0 equiv), DMSO (1.0 equiv), TFAA (1.0 equiv), Et<sub>3</sub>N (1.0 equiv) and n-butylamine (1.0 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (0.17 M) and under an atmosphere of CO<sub>2</sub>. <sup>b</sup>NMR yields using diphenylacetonitrile or 1,3,5-trimethoxybenzene as an internal standard (isolated yield in parentheses). <sup>c</sup>The reaction was quenched with MeOH instead of n-BuNH<sub>2</sub>.

<sup>21</sup>In situ monitoring by IR spectroscopy clearly demonstrated the formation of an isocyanate intermediate using both the TFAA and oxalyl chloride mediated protocols. Upon transferring the solution of the carbamic acid intermediate to the activated dimethylsulfoxonium reagent (A, Scheme 2) at low temperature, a signal at 2265 cm<sup>-1</sup> corresponding to phenyl isocyanate appeared. This signal increased in strength upon addition of Et<sub>3</sub>N to the reaction mixture, indicating complete conversion to the isocyanate product. This signal disappeared upon quenching the reaction with n-butylamine since the isocyanate intermediate was consumed to generate the unsymmetrical urea.
Under our optimized conditions, a range of aryl and alkyl amines (1) could be converted to unsymmetrical ureas (2) and carbamates (3) in one pot, via the isocyanate, by quenching the reactions with amines or alcohols, respectively (Schemes 3 and 4). Simple arylamines, as well as those bearing electron-donating and electron-withdrawing groups, yielded the corresponding ureas 2a-d,g,i,k and carbamates 3a,b,e in good to excellent yields. Substituents such as a ketone (2e), thioether (2h), nitrile (2j) and nitro (3c-d) functional group were tolerated. 2-Aminothiophene could also be converted to urea 2j and carbamate 3f in good yields (78% and 67%, respectively). An arylamine bearing halide substituents was converted to urea 2f in 92% yield, providing useful synthetic handles for subsequent transformations. Aniline derivatives with ortho substituents generated the isocyanate intermediates in high yields, as illustrated by the formation of ureas 2f and 2h in 92% and 82%, respectively. Aliphatic amines, including benzylic amines and a methyl ester-protected amino acid, could also be converted to ureas 2l-o in good to excellent yields (Scheme 3). Of note, under our mild reaction conditions, epimerization of enantioenriched amino acid derivative 2o and benzylic amine 2n was not observed.
Scheme 3. Synthesis of unsymmetrical ureas from amines and CO$_2$\textsuperscript{$a,b$}

\[
\begin{align*}
\text{N} & \text{H} \\
\text{H} & \text{N} \\
\text{H} & \text{N} \\
\end{align*}
\]

1. Reactions were performed using aryl amine (or alkyl amine) (1.0 mmol, 1.0 equiv), DBU (1.0 equiv), DMSO (1.0 equiv), TFAA (1.0 equiv), Et$_3$N (1.0 equiv) and amine (1.0 equiv) in CH$_2$Cl$_2$ (0.17 M) and under an atmosphere of CO$_2$. \textsuperscript{b} Isolated yields represent the average yield for 2 reactions. \textsuperscript{c} Using 2.0 equivalents of DBU. \textsuperscript{d} Using 1.4 equivalents of DBU.
Scheme 4. Synthesis of carbamates from arylamines and CO$_2$ $^{a,b}$

Reactions were performed using arylamine (1.0 mmol, 1.0 equiv), DBU (1.0 equiv), DMSO (1.0 equiv), TFAA (1.0 equiv), Et$_3$N (1.0 equiv) and alcohol (1.0 equiv) in CH$_2$Cl$_2$ (0.17 M) and under an atmosphere of CO$_2$. $^b$Isolated yields represent the average yield for 2 reactions. $^c$Using 2.0 equivalents of DBU. $^d$Using aryl diamine (0.5 mmol, 1.0 equiv), DBU (3.0 equiv), DMSO (2.0 equiv), TFAA (2.0 equiv), Et$_3$N (2.0 equiv) and alcohol (11.0 equiv).

The isocyanate intermediates can be trapped with a variety of nucleophiles, including aliphatic and arylamines (Scheme 3). Both primary and secondary amines afforded the products in good to excellent yields. Heterocycles are also compatible, as illustrated by the formation of indoline- and 2-aminothiazole-derived ureas 2$k$ and 2$i$ in 83% and 80%, respectively. Quenching the isocyanate with an alcohol yields the carbamate (Scheme 4). Using this strategy, Cbz- and alloc-protected arylamines 3$b,c,f$ could be prepared from simple amines, CO$_2$ and the corresponding alcohol. Unfortunately, tert-butanol was not
an efficient nucleophile in this transformation even after prolonged reaction times. Boc-protected arylamine was not detected in the $^1$H NMR of the crude reaction mixture; instead only unreacted isocyanate and tert-butanol were observed.

Finally, we set out to prepare the methyl carbamates of 4,4'-methylene diphenyl diisocyanate (MDI) and 2,4-toluene diisocyanate (TDI), which are relevant building blocks for the polyurethane industry, from aryl diamines, CO$_2$ and the dimethyl sulfonium reagent (A) generated in situ from DMSO and TFAA. We anticipated that this reaction would be challenging due the difficulty in preparing a dicarbamic acid intermediate under an atmosphere of CO$_2$ and its likely poor solubility in organic solvents. The quantitative formation of the dicarbamic acid derivative and its subsequent clean dehydration would also be essential to avoid polymerization over diisocyanate formation. A brief reoptimization of the reaction conditions revealed that using a slight excess of DBU (3.0 equivalents, or 1.5 equivalents per amine) enabled the clean formation of the methyl ester derivatives 4a and 4b in 87% and 81%, respectively.$^{22}$ For the synthesis of 4a, a simple aqueous wash of the reaction mixture removed reaction side products and afforded the desired product in 90% purity.

**CONCLUSION**

In summary, we have developed a metal-free synthesis of unsymmetrical ureas and carbamates from amines and CO$_2$ under mild reaction conditions. An activated dimethylsulfonium reagent, reminiscent of those used in Swern oxidation protocols, mediates this transformation. A wide range of aryl and aliphatic amines can be converted to unsymmetrical ureas and carbamates, via the isocyanate intermediate, in high yield and with little to no symmetrical urea byproduct.
EXPERIMENTAL SECTION

General information

All reactions were performed using anhydrous solvents in oven-dried flasks unless otherwise specified. Anhydrous CH$_2$Cl$_2$ was purchased from Sigma-Aldrich and was used as received. TFAA was purchased from Sigma-Aldrich and used as received (stored under air). Reagent grade DMSO was purchased from Sigma-Aldrich and was stored over 4 Å molecular sieves before use. All other chemicals were purchased from Sigma-Aldrich, Fisher Scientific and Combi-Blocks, and were used without further purification. NMR solvents (CDCl$_3$, DMSO-d$_6$, acetone-d$_6$) were purchased from Cambridge Isotope Laboratories, Inc. or Sigma-Aldrich. Proton chemical shifts are reported in ppm with respect to TMS (δ 0.00) for CDCl$_3$ or to the residual proton resonance in DMSO-d$_6$ (δ 2.50) and acetone-d$_6$ (δ 2.05). Carbon chemical shifts were internally referenced to the solvent resonances in CDCl$_3$ (δ 77.2 ppm), DMSO-d$_6$ (δ 39.5) and acetone-d$_6$ (δ 29.8 and 206.3). Peak multiplicities are designated by the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; J, coupling constant in Hz. Complex multiplicities were reported as a combination of the above abbreviations to provide an appropriate descriptor for the observed pattern (i.e., dt – doublet of triplets). All synthesized compounds were characterized by $^1$H, $^{19}$F and $^{13}$C NMR, HRMS, IR and melting point (when applicable). $^1$H, $^{19}$F and $^{13}$C NMR were recorded on Varian MercuryPlus 400 MHz, Bruker AvanceIII-400 MHz, Agilent DD2-500 MHz equipped with XSens cold probe, Agilent DD2-500 with oneNMR probe and Agilent DD2-600 MHz spectrometers. Mass spectra were obtained by the University of Toronto Advanced Instrumentation for Molecular Structure (AIMS) mass spectrometry facility; high
resolution mass spectra (HRMS) were recorded on a JEOL AccuTOF model JMS-T1000LC mass spectrometer equipped with an IONICS Direct Analysis in Real Time (DART) ion source. HPLC was performed with a Shimadzu HPLC equipped with a chiral column and UV detector (254 nm). Chiral HPLC column (Chiralpak® IG 87325A) was purchased from Chiral Technologies, Inc. HPLC solvents (Hexanes and iPrOH) were purchased from Sigma-Aldrich. Flash chromatography on silica gel (60 Å, 230-400 mesh, from Silicycle) was performed. Solvent ratios for chromatography are reported as v/v ratios. Analytical thin-layer chromatography (TLC) was performed on Merck silica gel 60 F254 pre-coated plates and visualized with a UV lamp and KMnO₄ stain. Infrared FTIR spectra from in situ reaction monitoring were obtained on a Mettler Toledo instrument equipped with 6.3 mm AgX DiComp probe. FTIR spectrum were obtained on a Perkin Elmer spectrometer equipped with an ATR sampling head.

**General procedures for the synthesis of ureas**

**General procedure A for the synthesis of ureas using TFAA:** A solution of DMSO (0.07 mL, 1.00 mmol, 1.00 eq) in 3.0 mL CH₂Cl₂ under an atmosphere of CO₂ (balloon) was cooled to the appropriate temperature (-60 °C using a dry ice/chloroform bath or -78 °C using an acetone/dry ice bath). TFAA (0.15 mL, 1.00 mmol, 1.00 eq) was added dropwise to the cold solution. The resulting mixture was stirred at low temperature for 5 minutes. In a second flask, CO₂ was bubbled through a solution of amine (1.00 mmol, 1.00 eq) and DBU (0.15 mL, 1.00 mmol, 1.00 eq) in 3.0 mL CH₂Cl₂ at room temperature. This mixture was cannula transferred to the first (cold) solution. The resulting cold mixture was stirred at low temperature for 10 minutes. Triethylamine (0.14 mL, 1.00
mmol, 1.00 eq) was added and the mixture was stirred for 10 minutes. The solution was allowed to slowly warm to room temperature and was left to stir for an additional 10 minutes. The amine (1.00 mmol, 1.00 eq) was added rapidly to the flask followed by 5 minutes of rapid stirring. The mixture was concentrated under reduced pressure to afford the crude material, which was purified by flash chromatography on silica gel to afford the desired product.

**General procedure B for the synthesis of ureas using oxalyl chloride:** A solution of oxalyl chloride (0.09 mL, 1.00 mmol, 1.00 eq) in 3.0 mL CH₂Cl₂ under an atmosphere of CO₂ (balloon) was cooled to the appropriate temperature (-60 °C using a dry ice/chloroform bath or -78 °C using an acetone/dry ice bath). DMSO (0.07 mL, 1.00 mmol, 1.00 eq) was added dropwise to the cold solution as a solution in 1.0 mL CH₂Cl₂. The resulting mixture was stirred at low temperature for 5 minutes. In a second flask, CO₂ was bubbled through a solution of amine (1.00 mmol, 1.00 eq) and DBU (0.15 mL, 1.00 mmol, 1.00 eq) in 3.0 mL CH₂Cl₂ at room temperature. This mixture was cannula transferred to the first (cold) solution. The resulting cold mixture was stirred at low temperature for 10 minutes. Triethylamine (0.14 mL, 1.00 mmol, 1.00 eq) was added and the mixture was stirred for 10 minutes. The solution was allowed to slowly warm to room temperature and was left to stir for an additional 10 minutes. The amine (1.00 mmol, 1.00 eq) was added rapidly to the flask followed by 5 minutes of rapid stirring. The mixture was concentrated under reduced pressure to afford the crude material, which was purified by flash chromatography on silica gel to afford the desired product.
1-Butyl-3-phenylurea (2a): This compound was synthesized from aniline (1.55 mmol scale) using general procedure A (TFAA method) at -60 °C. Purification by flash column chromatography on silica gel (35% EtOAc/Hexanes) afforded 265 mg (1.38 mmol, 89%) of the desired product as a white solid. Second trial of reaction yielded 255 mg (1.33 mmol, 86%) of the desired product. Average yield: 88%. Exhibited spectral data identical to a previous report.\textsuperscript{23}

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}, 298K): δ 7.26-7.18 (m, 4H), 7.01-6.96 (m, 1H), 6.81 (br s, 1H), 5.09 (br s, 1H), 3.14 (td, J = 7.2, 5.7 Hz, 2H), 1.61-1.44 (m, 2H), 1.30-1.17 (m, 2H), 0.83 (t, J = 7.2 Hz, 3H). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}, 298K): δ 156.2, 138.8, 129.2, 123.6, 121.0, 40.1, 32.2, 20.1, 13.8.

1-Butyl-3-(p-tolyl)urea (2b): This compound was synthesized from p-toluidine (1.08 mmol scale) using general procedure A (TFAA method) at -60 °C. Purification by flash column chromatography on silica gel (30% EtOAc/hexanes) afforded 198 mg (0.94 mmol, 87%) of the desired product as a white solid. Second trial of reaction yielded 192 mg (0.92 mmol, 85%) of the desired product. Average yield: 86%. Exhibited spectral data identical to a previous report.\textsuperscript{24}

\textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}, 298 K): δ 7.91 (br s, 1H), 7.15 (d, J = 8.4 Hz, 2H), 7.00 (d, J = 8.6 Hz, 2H), 6.03 (br t, J = 5.8 Hz, 1H), 3.12 (td, J = 7.2, 5.7 Hz, 2H), 2.26 (s, 3H), 1.41-1.33 (m, 2H), 1.30-1.22 (m, 2H), 0.86 (t, J = 7.1 Hz, 3H). \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}, 298 K): δ 157.3, 136.7, 132.2, 129.4, 120.4, 40.0, 32.4, 20.8, 20.2, 13.9.
**N-(4-methoxyphenyl)morpholine-4-carboxamide (2c):** This compound was synthesized from p-anisidine (1.00 mmol scale) using general procedure A (TFAA method) with 2 equivalents of DBU at -78 °C. Purification by flash column chromatography on silica gel (25% EtOAc/Hexanes) afforded 205 mg (0.87 mmol, 87%) of the desired product as a white solid. Second trial of reaction yielded 207 mg (0.88 mmol, 88%) of the desired product. Average yield: 88%. Exhibited spectral data identical to a previous report.25

**1H NMR (600 MHz, CDCl₃, 298 K):** δ 7.20 (s, 1H), 7.13-7.11 (m, 2H), 6.73-6.70 (m, 2H), 3.69 (s, 3H), 3.50 (t, $J = 5.9$ Hz, 4H), 3.27 (t, $J = 4.6$ Hz, 4H).

**13C NMR (150 MHz, CDCl₃, 298 K):** δ 156.2, 155.9, 132.0, 123.3, 113.8, 66.4, 55.4, 44.1.

**1-Butyl-3-(4-fluorophenyl)urea (2d):** This compound was synthesized from p-fluoroaniline (1.53 mmol scale) using general procedure A (TFAA method) at -60 °C. Purification by flash column chromatography on silica gel (30% EtOAc/hexanes) afforded 279 mg (1.33 mmol, 87%) of the desired product as a white solid. Second trial of reaction yielded 275 mg (1.32 mmol, 86%) of the desired product. Average yield: 87%.

**1H NMR (400 MHz, DMSO-d₆, 298 K):** δ 8.39 (s, 1H), 7.39-7.35 (m, 2H), 7.06-7.00 (m, 2H), 6.07 (t, $J = 5.9$ Hz, 1H), 3.07 (q, $J = 5.9$ Hz, 2H), 1.44-1.25 (m, 4H), 0.89 (t, $J = 7.1$ Hz, 3H).

$^1$H $^1$H {19F} NMR (400 MHz, DMSO-d₆, 298 K): δ 8.38 (s, 1H), 7.37 (d, $J = 9.1$ Hz, 2H), 7.04 (d, $J = 9.1$ Hz, 2H), 6.06 (t, $J = 5.8$ Hz, 1H), 3.06 (td, $J = 6.8$, 5.6 Hz, 2H), 1.44-1.25 (m, 4H), 0.89 (t, $J = 7.1$ Hz, 3H).

$^{19}$F $^{1}$H NMR (377 MHz, DMSO-d₆, 298 K): δ -118.1.

**13C NMR (100 MHz, DMSO-d₆, 298 K):** δ 156.8 (d, $J = 236.9$ Hz), 155.2,
136.9 (d, $J = 2.4$ Hz), 119.1 (d, $J = 7.6$ Hz), 115.0 (d, $J = 22.0$ Hz), 38.7, 31.85, 19.5, 13.7. HRMS (DART-TOF+) $m/z$: [M+H]$^+$ calcd for C$_{11}$H$_{16}$FN$_2$O 211.1247; found 211.1249. IR (neat): 3360, 1562, 1504, 1211, 833 cm$^{-1}$. Melting point: 128.1-131.1 °C.

1-(3-Acetylphenyl)-3-(sec-butyl)urea (2e): This compound was synthesized from 3-aminoacetophenone (1.00 mmol scale) using general procedure A (TFAA method) at -78 °C. Purification by flash column chromatography on silica gel (35% EtOAc/Hexanes) afforded 190 mg (0.81 mmol, 81%) of the desired product as a white solid. Second trial of reaction yielded 194 mg (0.83 mmol, 83%) of the desired product. Average yield: 82%.

$^1$H NMR (400 MHz, CDCl$_3$, 298 K, mixture of rotamers in a 1.5:1 ratio): $\delta$ 8.29 (s, 1H), 7.89 (dd, $J = 1.9$, 1.0 Hz, 1H), 7.61 (ddd, $J = 8.1$, 2.3, 1.0 Hz, 1H), 7.48 (ddd, $J = 7.7$, 1.7, 1.0 Hz, 1H), 7.24 (dd, $J = 7.7$, 7.7 Hz, 1H), 5.93 (d, $J = 8.3$ Hz, 1H, major rotamer), 4.99 (d, $J = 8.2$ Hz, 1H, minor rotamer), 3.82-3.72 (m, 1H, major rotamer), 3.69-3.61 (m, 1H, minor rotamer), 2.49 (s, 3H), 1.47-1.35 (m, 2H), 1.10 (d, $J = 6.6$ Hz, 3H, major rotamer), 1.06 (dd, $J = 6.6$, 1.1 Hz, 3H, minor rotamer), 0.87 (t, $J = 7.4$ Hz, 3H, major rotamer), 0.84 (td, $J = 7.5$, 1.4 Hz, 3H, minor rotamer). $^{13}$C NMR (100 MHz, CDCl$_3$, 298 K, mixture of rotamers): $\delta$ 198.8, 158.3, 156.0, 140.3, 137.5, 129.1, 123.8, 122.0, 118.5, 47.4, 47.2, 30.2, 30.0, 26.67, 21.0, 20.9, 10.4. HRMS (DART-TOF+) $m/z$: [M+H]$^+$ calcd for C$_{13}$H$_{19}$N$_2$O$_2$ 235.1447; found 235.1447. IR (neat): 2880, 1660, 1539, 1240, 686 cm$^{-1}$. Melting point: 111.8-116.8 °C.
N-(2-Bromo-5-chlorophenyl)morpholine-4-carboxamide (2f): This compound was synthesized from 2-bromo-5-chloroaniline (1.00 mmol scale) using general procedure A (TFAA method) with 2 equivalent of DBU at -78 °C. Purification by flash column chromatography on silica gel (25% EtOAc/Hexanes) afforded 293 mg (0.92 mmol, 92%) of the desired product as a yellow oil. Second trial of reaction yielded 289 mg (0.91 mmol, 91%) of the desired product. Average yield: 92%.

$^1$H NMR (400 MHz, CDCl$_3$, 298 K): $\delta$ 8.24 (d, $J = 2.5$ Hz, 1H), 7.36 (d, $J = 8.6$ Hz, 1H), 6.99 (br s, 1H), 6.84 (dd, $J = 8.5$, 2.5 Hz, 1H), 3.78-3.67 (m, 4H), 3.52-3.44 (m, 4H).

$^{13}$C NMR (100 MHz, CDCl$_3$, 298 K): $\delta$ 153.8, 137.6, 134.2, 132.5, 123.7, 120.9, 110.8, 66.4, 44.2. HRMS (DART-TOF+) m/z: [M+H]$^+$ calcd for C$_{11}$H$_{13}$BrClN$_2$O$_2$ 318.9849; found 318.9850. IR (neat): 2860, 1643, 1504, 1115, 860 cm$^{-1}$.

N-(p-Tolyl)pyrrolidine-1-carboxamide (2g): This compound was synthesized from p-toluidine (1.00 mmol scale) using general procedure B (oxalyl chloride method) at -78 °C. Purification by flash column chromatography on silica gel (30% EtOAc/Hexanes) afforded 170 mg (0.83 mmol, 83%) of the desired product as a white solid. Exhibited spectral data identical to a previous report.$^{26}$ Second trial of reaction yielded 172 mg (0.84 mmol, 84%) of the desired product. Average yield: 84%.

$^1$H NMR (500 MHz, CDCl$_3$, 298 K): $\delta$ 7.30-7.27 (m, 2H), 7.07-7.05 (m, 2H), 6.17 (s, 1H), 3.44-3.41 (m, 4H), 2.28 (s, 3H), 1.94-1.92 (m, 4H).

$^{13}$C NMR (125 MHz, CDCl$_3$, 298 K): $\delta$ 154.2, 136.6, 132.2, 129.3, 119.8, 45.7, 25.6, 20.7
**N-(2-(methylthio)phenyl)morpholine-4-carboxamide (2h):** This compound was synthesized from 2-(methylthio)aniline (1.00 mmol scale) using general procedure A (TFAA method) with 2 equivalents of DBU at -78 °C. Purification by flash column chromatography on silica gel (40% EtOAc/Hexanes) afforded 207 mg (0.82 mmol, 82%) of the desired product as a white solid. Second trial of reaction yielded 205 mg (0.81 mmol, 81%) of the desired product. Average yield: 82%.

**1H NMR (600 MHz, CDCl₃, 298 K):** δ 8.13 (dd, J = 8.3, 1.4 Hz, 1H), 7.81 (br, 1H), 7.43 (dd, J = 7.7, 1.6 Hz, 1H), 7.28-7.21 (m, 1H), 6.96 (dd, J = 7.5, 7.5, 1.4 Hz, 1H), 3.73-3.71 (m, 4H), 3.51-3.49 (m, 4H), 2.33 (s, 3H).

**13C NMR (150 MHz, CDCl₃, 298 K):** δ 154.6, 139.5, 133.1, 129.1, 124.4, 123.0, 119.7, 66.5, 44.1, 19.0. **HRMS** (DART-TOF+) m/z: [M+H]^+ calcd for C₁₂H₁₇N₂O₂S 253.1011; found 253.1010. **IR** (neat): 3226, 1623, 1507, 1394, 1246, 737 cm⁻¹. **Melting point:** 96.9-100.1 °C.

**1-(4-Methoxyphenyl)-3-(thiazol-2-yl)urea (2i):** This compound was synthesized from p-anisidine (1.00 mmol scale) using general procedure A (TFAA method) with 2 equivalents of DBU at -78 °C. Purification by flash column chromatography on silica gel (65% EtOAc/Hexanes) afforded 202 mg (0.80 mmol, 80%) of the desired product as a white solid. Second trial of reaction yielded 201 mg (0.80 mmol, 80%) of the desired product. Average yield: 80%. Exhibited spectral data identical to a previous report.²⁷

**1H NMR (500 MHz, DMSO-d₆, 298 K):** δ 10.54 (br s, 1H), 8.77 (s, 1H), 7.39-7.35 (m, 3H), 7.08 (d, J = 3.6 Hz, 1H), 6.91-6.87 (m, 2H), 3.72 (s, 3H). **13C NMR (125 MHz, DMSO-d₆, 298 K):** δ 160.1, 155.5, 152.2, 137.6, 132.0, 120.9, 114.5, 112.7, 55.6.
1-(3-Cyanothiophen-2-yl)-3-cyclopropylurea (2j): This compound was synthesized from 2-aminothiophene-3-carbonitrile (1.00 mmol scale) using general procedure A (TFAA method) at -78 °C. Purification by flash column chromatography on silica gel (20% EtOAc/Hexanes) afforded 162 mg (0.78 mmol, 78%) of the desired product as a white solid. Second trial of reaction yielded 161 mg (0.78 mmol, 78%) of the desired product. Average yield: 78%.

$^1$H NMR (500 MHz, CDCl$_3$, 298 K): $\delta$ 9.01 (br, 1H), 6.85 (d, $J = 6.0$ Hz, 1H), 6.68 (d, $J = 5.7$ Hz, 1H), 6.32 (s, 1H), 2.70-2.66 (m, 1H), 0.79 (br d, $J = 4.5$ Hz, 2H), 0.60 (br s, 2H).

$^{13}$C NMR (125 MHz, CDCl$_3$, 298 K): $\delta$ 155.2, 153.2 (br), 123.5, 116.7, 115.6, 89.5 (br), 22.7, 7.0. HRMS (DART-TOF+) $m/z$: [M+H]$^+$ calcd for C$_{9}$H$_{10}$N$_{3}$OS 208.0545; found 208.0542. IR (neat): 3336, 2216, 1644, 1552, 1255 cm$^{-1}$. Melting point: 149.2-159.1 °C.

N-(4-Fluorophenyl)indoline-1-carboxamide (2k): This compound was synthesized from $p$-fluoroaniline (1.00 mmol scale) using general procedure A (TFAA method) at -78 °C. Purification by flash column chromatography on silica gel (20% EtOAc/Hexanes) afforded 215 mg (0.84 mmol, 84%) of the desired product as a white solid. Second trial of reaction yielded 210 mg (0.82 mmol, 82%) of the desired product. Average yield: 83%.

$^1$H NMR (600 MHz, acetone-d$_6$, 298 K): $\delta$ 8.01 (ddd, $J = 8.1$, 1.1, 0.6 Hz, 1H), 7.91 (br s, 1H), 7.64-7.61 (m, 2H), 7.17-7.16 (m, 1H), 7.14-7.11 (m, 1H), 7.07-7.03 (m, 2H), 6.89 (ddd, $J = 6.9$, 6.9, 1.2 Hz, 1H), 4.17 (dd, $J = 9.2$, 8.3 Hz, 2H), 3.21 (dd, $J = 9.1$, 8.2 Hz, 2H).

$^{13}$C NMR (125 MHz, acetone-d$_6$, 298 K): $\delta$ 158.4 (d, $J = 236.2$ Hz), 152.6, 144.0, 136.1 (d, $J = 2.6$ Hz), 130.8, 126.9, 124.4, 121.9 (d, $J = 7.7$ Hz), 121.7, 115.2, 114.7 (d, $J$
= 22.3 Hz), 47.1, 27.5. \(^{19}\text{F} \text{NMR (564 MHz, acetone-d}_6, 298 \text{ K):} \) \(\delta -122.43\). \(\text{HRMS (DART-TOF+)} \) \(m/z\) \([\text{M+H}]^+\) calcd for \(\text{C}_{15}\text{H}_{14}\text{FN}_2\text{O}\) 257.1090; found 257.1090. \(\text{IR (neat):} \) 3367, 1649, 1510, 1476, 785 cm\(^{-1}\). \text{Melting point:} 155.6-161.4 °C.

\text{1-Benzyl-3-butylurea (2l):} \) This compound was synthesized from benzylamine (1.61 mmol scale) using general procedure A (TFAA method) at -60 °C. Purification by flash column chromatography on silica gel (50% EtOAc/Hexanes) afforded 285 mg (1.38 mmol, 86%) of the desired product as a white solid. Second trial of reaction yielded 290 mg (1.40 mmol, 88%) of the desired product. Average yield: 87%. Exhibited spectral data identical to a previous report.\(^{28}\)

\(^{1}\text{H NMR (400 MHz, CDCl}_3, 298\text{K):} \) \(\delta 7.24-7.13 \) (m, 5H), 6.12 (br t, \(J = 6.0\) Hz, 1H), 5.76 (br t, \(J = 5.6\) Hz, 1H), 4.16 (d, \(J = 5.6\) Hz, 2H), 2.98 (td, \(J = 7.0, 5.5\) Hz, 2H), 1.35-1.17 (m, 4H), 0.84 (t, \(J = 7.4\) Hz, 3H). \(^{13}\text{C NMR (100 MHz, CDCl}_3, 298\text{K):} \) \(\delta 159.4, 139.8, 128.4, 127.0, 126.8, 43.8, 39.9, 32.4, 20.0, 13.8.\)

\text{N-benzylmorpholine-4-carboxamide (2m):} \) This compound was synthesized from benzylamine (1.00 mmol scale) using general procedure A (TFAA method) at -78 °C. Purification by flash column chromatography on silica gel (100% EtOAc) afforded 174 mg (0.79 mmol, 79%) of the desired product as a white solid. Second trial of reaction yielded 180 mg (0.82 mmol, 82%) of the desired product. Average yield: 81%. Exhibited spectral data identical to a previous report.\(^{29}\)
(S)-1-Butyl-3-(1-phenylethyl)urea (2n): This compound was synthesized from (S)-α-methylbenzylamine (1.62 mmol scale) using general procedure A (TFAA method) at -60 °C. Purification by flash column chromatography on silica gel (50% EtOAc/Hexanes) afforded 308 mg (1.40 mmol, 91%) of (S)-1-butyl-3-(1-phenylethyl)urea as a colorless oil. Second trial of reaction yielded 310 mg (1.41 mmol, 92%) of the desired product. Average yield: 92%. Enantiomeric excess (>99%) was determined by HPLC [Chiralpak IG, hexanes/i-PrOH 80:20, 0.98 mL/min., (minor) t_r = 5.55 min, (major) t_r = 6.42 min]. [α]D^23: -22.2° (c 1.00, CHCl_3).

Methyl (allylcarbamoyl)-L-phenylalaninate (2o): This compound was synthesized from L-alanine methyl ester (1.00 mmol scale) using general procedure A (TFAA method) with 1.40 eq of DBU at -60 °C. Purification by flash column chromatography on silica gel (40% EtOAc/Hexanes) afforded 218 mg (0.83 mmol, 83%) of the desired
product as a white solid. Enantiomeric excess (>99%) was determined by HPLC [Chiralpak IG, hexanes/i-PrOH 74:26, 0.98 mL/min., (minor) t_r = 6.95 min, (major) t_r = 10.16 min]. [α]_D^23: +51.2° (c 1.00, CHCl_3).

^1H NMR (500 MHz, CDCl_3, 298 K): δ 7.29-7.19 (m, 3H), 7.12-7.07 (m, 2H), 5.79 (ddt, J = 17.2, 10.3, 5.4 Hz, 1H), 5.20 (br d, J = 8.1 Hz, 1H), 5.13 (dq, J = 17.1, 1.7 Hz, 1H), 5.08-5.05 (m, 2H), 4.77 (dt, J = 8.1, 5.9 Hz, 1H), 3.74-3.71 (m, 2H), 3.69 (s, 3H), 3.07 (dd, J = 13.8, 5.9 Hz, 1H), 3.01 (dd, J = 13.8, 6.1 Hz, 1H). ^13C NMR (125 MHz, CDCl_3, 298 K): δ 173.4, 157.3, 136.3, 135.1, 129.3, 128.4, 126.9, 115.7, 51.0, 52.2, 42.9, 38.5.

HRMS (DART-TOF+) m/z: [M+H]^+ calcd for C_{14}H_{19}N_{2}O_{3} 263.1396; found 263.1392.

IR (neat): 3369, 1732, 1619, 1566, 1223, 697 cm^{-1}. Melting point: 96.2-101.7 °C.

**General procedures for the synthesis of carbamates**

**General procedure C for the synthesis of carbamates using TFAA:** A solution of DMSO (0.07 mL, 1.00 mmol, 1.00 eq) in 3.0 mL CH_2Cl_2 under an atmosphere of CO_2 (balloon) was cooled to the appropriate temperature (-60 °C using a dry ice/chloroform bath or -78 °C using an acetone/dry ice bath). TFAA (0.15 mL, 1.00 mmol, 1.00 eq) was added dropwise to the cold solution. The resulting mixture was stirred at low temperature for 5 minutes. In a second flask, CO_2 was bubbled through a solution of amine (1.00 mmol, 1.00 eq) and DBU (0.15 mL, 1.00 mmol, 1.00 eq) in 3.0 mL CH_2Cl_2 at room temperature. This mixture was cannula transferred to the first (cold) solution. The resulting cold mixture was stirred at low temperature for 10 minutes. Triethylamine (0.14 mL, 1.00 mmol, 1.00 eq) was added and the mixture was stirred for 10 minutes. The solution was allowed to slowly warm to room temperature and was left to stir for an
additional 10 minutes. The alcohol was added rapidly to the flask followed by 15 minutes of rapid stirring. The mixture was concentrated under reduced pressure to afford the crude material which was purified by flash chromatography on silica gel to afford the desired product.

**Methyl phenylcarbamate (3a):** This compound was synthesized from aniline (1.00 mmol scale) using general procedure C (TFAA method) at -78 °C. The reaction mixture was quenched with MeOH (0.08 ml, 2 mmol, 2 eq). Purification by flash column chromatography on silica gel (10-15% EtOAc/Hexanes) afforded 133 mg (0.88 mmol, 88%) of the desired product as a white solid. Second trial of reaction yielded 138 mg (0.91 mmol, 91%) of the desired product. Average yield: 90%. Exhibited spectral data identical to a previous report.30

**1H NMR (400 MHz, CDCl₃, 298 K):** δ 7.43 (br d, J = 7.4 Hz, 2H), 7.32-7.27 (m, 2H), 7.15 (br s, 1H), 7.09-7.05 (m, 1H), 3.77 (s, 3H).

**13C NMR (100 MHz, CDCl₃, 298 K):** δ 154.4, 138.0, 129.0, 123.5, 118.9, 52.3.

**Benzyl p-tolylcarbamate (3b):** This compound was synthesized from p-toludine (1.00 mmol scale) using general procedure C (TFAA method) at -78 °C. The reaction mixture was quenched with BnOH (0.10 ml, 1 mmol, 1 eq). Purification by flash column chromatography on silica gel (15% EtOAc/Hexanes) afforded 211 mg (0.87 mmol, 87%) of the desired product as a white solid. Second trial of reaction yielded 208 mg (0.86 mmol, 86%) of the desired product. Average yield: 87%. Exhibited spectral data identical to a previous report.30
**Allyl (4-nitrophenyl)carbamate (3c):** This compound was synthesized from p-nitroaniline (1.00 mmol scale) using general procedure C (TFAA method) with 2 equivalents of DBU at -78 °C. The reaction mixture was quenched with allyl alcohol (0.4 ml, excess). Purification by flash column chromatography on silica gel (15% EtOAc/Hexanes) afforded 187 mg (0.84 mmol, 84%) of the desired product as a white solid. Second trial of reaction yielded 199 mg (0.90 mmol, 90%) of the desired product. Average yield: 87%. Exhibited spectral data identical to a previous report.31

**Methyl (4-nitrophenyl)carbamate (3d):** This compound was synthesized from p-nitroaniline (1.00 mmol scale) using general procedure C (TFAA method) with 2 equivalents of DBU at -78 °C. The reaction mixture was quenched with MeOH (0.4 ml, excess). Purification by flash column chromatography on silica gel (30% EtOAc/Hexanes) afforded 187 mg (0.95 mmol, 95%) of the desired product as a pale yellow solid. Second trial of reaction yielded 198 mg (1.00 mmol, 100%) of the desired product. Average yield: 98%. Exhibited spectral data identical to a previous report.32
\(^1\)H NMR (400 MHz, DMSO-d\(_6\), 298 K): \(\delta\) 10.38 (br s, 1H), 8.20 (d, \(J = 9.3\) Hz, 2H) 7.69 (d, \(J = 9.3\) Hz, 2H), 3.73 (s, 3H). \(^{13}\)C NMR (100 MHz, DMSO-d\(_6\), 298 K): \(\delta\) 153.7, 145.6, 141.6, 125.0, 117.5, 52.1.

**Isopropyl (4-fluorophenyl)carbamate (3e):** This compound was synthesized from \(p\)-fluoroaniline (1.00 mmol scale) using general procedure C (TFAA method) at -78 °C. The reaction mixture was quenched with iPrOH (0.8 ml, excess). Purification by flash column chromatography on silica gel (10% EtOAc/Hexanes) afforded 181 mg (0.91 mmol, 91%) of the desired product as a white solid. Second trial of reaction yielded 193 mg (0.97 mmol, 97%) of the desired product. Average yield: 94%. Exhibited spectral data identical to a previous report.\(^{33}\)

\(^1\)H NMR (400 MHz, CDCl\(_3\), 298 K): \(\delta\) 7.38-7.29 (m, 2H), 6.99-6.92 (m, 2H), 6.88 (br s, 1H), 5.04-4.95 (m, 1H), 1.27 (d, \(J = 6.2\) Hz, 6H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\), 298 K): \(\delta\) 158.8 (d, \(J = 242\) Hz), 153.6, 134.1 (d, \(J = 2.6\) Hz), 120.7, 115.5 (d, \(J = 23.1\) Hz), 68.8, 22.0.

**Benzyl (3-cyanothiophen-2-yl)carbamate (3f):** This compound was synthesized from 2-aminothiophene-3-carbonitrile (1.00 mmol scale) using general procedure C (TFAA method) at -78 °C. The reaction mixture was quenched with BnOH (0.2 ml, 2 eq). Purification by flash column chromatography on silica gel (20% EtOAc/Hexanes) afforded 181 mg (0.70 mmol, 70%) of the desired product as a white solid. Second trial of reaction yielded 166 mg (0.64 mmol, 64%) of the desired product. Average yield: 67%.
\textbf{1H NMR (500 MHz, DMSO-d$_6$, 298 K):} $\delta$ 11.46 (s br, 1H), 7.45-7.29 (m, 5H), 7.15 (d, $J = 6.0$ Hz, 1H), 7.09 (d, $J = 5.8$ Hz, 1H), 5.22 (s, 2H). \textbf{13C NMR (125 MHz, DMSO-d$_6$, 298 K):} $\delta$ 154.0, 151.4, 136.3, 128.9, 128.7, 128.5, 125.9, 119.3, 114.9, 93.9 (br) 67.6.

\textbf{HRMS (DART-TOF+)} $m/z$: [M+H]$^+$ calcd for C$_{13}$H$_{11}$N$_2$O$_2$S 259.0541; found 259.0549.

\textbf{IR} (neat): 2225, 1723, 1567, 1248, 704 cm$^{-1}$.

\textbf{Melting point:} 158.8-161.9 °C.

\textbf{Dimethyl (methylenebis(4,1-phenylene))dicarbamate (4a):} This compound was synthesized from 4,4$′$-diaminodiphenylmethane (0.50 mmol scale) using general procedure C (TFAA method) with 3 equivalents of DBU at -78 °C. The reaction mixture was quenched with MeOH (0.5 ml, excess). Purification by flash column chromatography on silica gel (30% EtOAc/Hexanes) afforded 133 mg (0.42 mmol, 85%) of the desired product as a white solid. Second trial of reaction yielded 138 mg (0.44 mmol, 88%) of the desired product. Average yield: 87%. Exhibited spectral data identical to a previous report.$^{34}$

Compound 4a could also be isolated in 90% purity after simple aqueous wash (instead of flash column chromatography on silica gel). Upon completion of the reaction, the reaction mixture was diluted with dichloromethane and washed with a saturated solution of NH$_4$Cl followed by brine ($\times$3). The organic layer was dried over MgSO$_4$ and concentrated under vacuum to afford 4a in 73% yield and 90% purity.

\textbf{1H NMR (400 MHz, DMSO-d$_6$, 298 K):} $\delta$ 9.54 (s, 2H), 7.36 (d, $J = 8.4$ Hz, 4H), 7.11 (d, $J = 8.5$ Hz, 4H), 3.80 (s, 2H), 3.65 (s, 6H). \textbf{13C NMR (100 MHz, DMSO-d$_6$, 298 K):} $\delta$ 154.5, 137.5, 136.0, 129.3, 118.8, 52.0, 40.3.
**Dimethyl (4-methyl-1,3-phenylene)dicarbamate (4b):** This compound was synthesized from 2,4-diaminotoluene (0.50 mmol scale) using general procedure C (TFAA method) with 3 equivalents of DBU at -78 °C. The reaction mixture was quenched with MeOH (0.5 ml, excess). Purification by flash column chromatography on silica gel (25% EtOAc/Hexanes) afforded 96 mg (0.40 mmol, 81%) of the desired product as a white solid. Second trial of reaction yielded 95 mg (0.39 mmol, 80%) of the desired product. Average yield: 81%. Exhibited spectral data identical to a previous report.34

**1H NMR (400 MHz, DMSO-d$_6$, 298 K):** δ 9.54 (s, 1H), 8.80 (s, 1H), 7.50 (br, 1H), 7.19-7.16 (m, 1H), 7.07 (d, $J = 8.3$ Hz, 1H), 3.66-3.63 (m, 6H), 2.12 (s, 3H).

**13C NMR (100 MHz, DMSO-d$_6$, 298 K):** δ 154.7, 153.9, 137.2, 136.4, 130.2, 125.6, 115.0, 114.8, 51.6, 51.5, 17.0.

**React IR data for the formation of isocyanate**

**Experimental set-up using DMSO/oxalyl chloride reaction conditions:** Aniline (1.0 mmol) and DBU (1.0 mmol) were dissolved in CH$_2$Cl$_2$ (2.0 mL) under CO$_2$ (1 atm). This mixture was then transferred via cannula to a three-necked flask equipped with the React IR probe and containing a solution of DMSO (1.0 mmol) and oxalyl chloride (1.0 mmol) in CH$_2$Cl$_2$ at -60 °C under an atmosphere of CO$_2$ (1 atm). After 10 minutes, Et$_3$N (1.0 mmol) was added to the flask and the reaction was allowed to gradually warm to room temperature.

**SUPPORTING INFORMATION**

The Supporting Information is available free of charge on the ACS Publications website.

*In situ* IR data, HPLC traces for compounds 2n and 2o and NMR spectra (PDF)
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Notes

The authors declare no competing financial interest.

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REFERENCES


(6) Phosgene was used as a chemical weapon during WWI and is currently listed on Schedule 3 of the Chemical Weapons Convention. Schedule 3, Organisation for the Prohibition of Chemical Weapons, https://www.opcw.org/chemical-weapons-convention/annexes/annex-on-chemicals/schedule-3/ (accessed on 19/01/2017)


(15) For a review, see ref 12a. Carbamic acids can also be alkylated using electrophilic reagents (RX) to yield carbamates directly from amines and CO₂.


(20) During the course of this work, the isocyanate intermediates were not isolated due to toxicity concerns. However, isocyanate formation was confirmed by *in situ* IR spectroscopy (see Supporting Information for additional details). We anticipate that isolation should be possible based on numerous other reports involving the isolation of isocyanates.

(21) See Supporting Information for additional details.

(22) The methyl carbamate can be converted to the isocyanate based on literature procedures. See ref. 13a.


(34) Yang, Q.; Robertson, A.; Alper, H. *Org. Lett.** **2008**, *10*, 5079-5082.