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Synthesis of Carbonates and Related Compounds from Carbon Dioxide via Methanesulfonyl Carbonates

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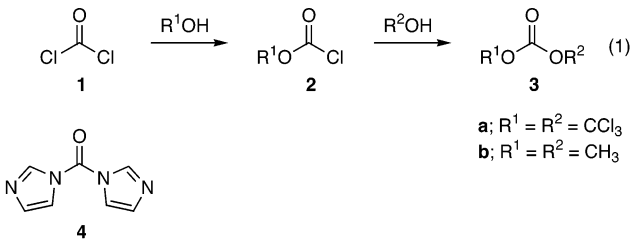
Carbonate anions resulting from reaction of primary or secondary alcohols with carbon dioxide, when added to methanesulfonic anhydride in cooled acetonitrile solution, yield methanesulfonyl carbonates, a new class of synthetic intermediate. Base-mediated reaction of the methanesulfonyl carbonates with alcohols, thiols, and amines yields carbonates, thiocarbonates, and carbamates, respectively. Overall yields for the three steps vary from 19% to 42%.

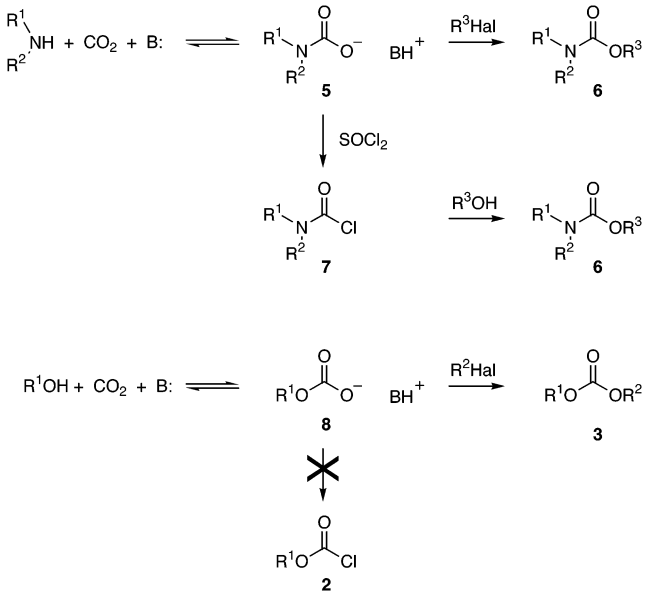
Introduction

Carbonates **3** are most commonly prepared from phosgene **1** via chloroformates **2** (eq 1).[1] While this route has the benefits of simplicity, generality, and high yields, there are significant problems with the use of highly toxic phosgene.[2] The use of solid phosgene equivalents such as bis(trichloromethyl) carbonate (triphosgene) **3a** or carbonyl diimidazole **4** can be recommended for small-scale preparations, but they are expensive, and ultimately such reagents are derived from phosgene.[3] In fact, industrially phosgene is still the most widely used carbonyl source (80% of usage), with the remainder largely accounted for by dimethyl carbonate **3b**. Synthesis of dimethyl carbonate does not have to be from phosgene, but the main alternative process is methanol carbonylation, which involves another toxic gas, carbon monoxide.[4]



Carbon dioxide is an alternative carbonyl source and, in contrast to phosgene and carbon monoxide, it is quite harmless, as well as being abundant and cheap. In fact, a good deal of progress has been made in harnessing carbon dioxide for carbamate (urethane) synthesis.[5−7] Amines react readily with carbon dioxide in the presence of base to form carbamate anions **5**. Of particular relevance to our work are processes in which the base permits substantial delocalization in its conjugate acid (typically amidine, pentaalkyl guanidine, or phosphazene bases are used), ion pairing is reduced, and the anion is rendered sufficiently nucleophilic to be alkylated to form carbamates **6** (Scheme 1).[5] Similarly, anion **5** can be

SCHEME 1



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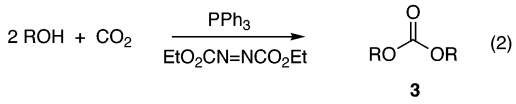
intercepted by thionyl chloride (or similar reagents) and transformed to a carbamoyl chloride **7** (or an isocyanate from a primary amine).[6] Further reaction with an alcohol leads to the carbamate targets.

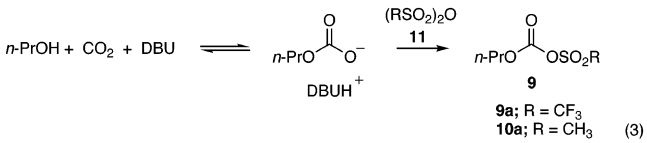
Alcohols also react with carbon dioxide to form carbonate anions **8**. However, the analogous alkylation to form carbonates directly is successful only in a limited number of cases.[8] Furthermore, reaction with thionyl chloride does not yield chloroformates **2**. In short, the carbamate chemistry cannot be directly extended to carbonate synthesis. The carbonate anions can be activated using Mitsunobu-type chemistry (eq 2), but the intermediates are not isolable.[9] Therefore, this chemistry can only be used for the synthesis of *symmetrical* carbonates.



We have been interested in the synthesis of dendritic carbamates using carbon dioxide.[10] One synthetic plan involved the formation of carbamoyl chlorides as in Scheme 1. However, we were repeatedly frustrated by the failure of the **5** to **7** transformation (Scheme 1) with these more complex substrates, which did not appear to be stable to thionyl chloride under the reaction conditions. We reasoned that both this problem and, more importantly, the failure of carbonate anions **8** to yield chloroformates **2** under the same conditions could be circumvented by *sulfonation* of **5** or **8** to give sulfonate analogues of **7** and **2**, respectively. Herein, we describe the development of this idea in the context of carbonate synthesis and, more briefly, its extension to thiocarbonate and carbamate synthesis.

Results and Discussion

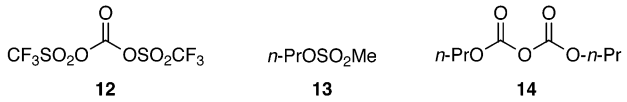
We started our studies with the synthesis of *n*-propyl sulfonyl carbonates **9a** and **10a**. Propanol was chosen as the test substrate since we anticipated that it would be easy to remove excess alcohol from reaction mixtures and we selected diazabicycloundecene (DBU) as base, since it is commercially available (pentaalkyl guanidine bases are not and phosphazene bases are very expensive). The trifluoromethanesulfonyl carbonate **9a** was our initial target, since we reasoned that reaction of the carbonate anion with the highly electrophilic anhydride **11** (R = CF_3) would be fast.



A number of experiments were attempted in which carbon dioxide was bubbled through a solution of *n*-propanol and DBU in acetonitrile then triflic anhydride **11** (R = CF_3) was added, with variations in reaction conditions and equivalents of anhydride. In all cases, analysis of the evaporated reaction mixture showed a large number of products (^{19}F NMR spectroscopy indicated the presence of 10 organofluorine compounds from one experiment), with no evidence for the presence of the sulfonyl carbonate **9a**. The only encouragement came from the observation of a small amount of di-*n*-propyl dicarbonate. However, isopropyl *n*-propyl carbonate was also identified, indicating that isomerization was occurring under the reaction conditions. We concluded that the trifluoromethanesulfonyl intermediates were simply too reactive. This is consistent with a report of carbonyl ditriflate **12** that decomposes above −20 °C.[11]

As high reactivity of the sulfonyl reagent seemed to be far from essential, we decided to investigate the analogous methanesulfonyl (mesyl) compounds. Methanesulfonic anhydride **11** (R = CH_3) is a cheap, easily handled reagent. Additionally, we expected the ^{1}H and ^{13}C NMR signals of the methyl signal to be simple to interpret yet sensitive to the environment in the proposed intermediates.

Carbon dioxide was bubbled through a solution of *n*-propanol and DBU (1 equiv) in acetonitrile at −42 °C. Methanesulfonic anhydride (1.1 equiv) was added, and after the mixture had been stirred for a short time, the solvent was evaporated. The ^{1}H NMR spectrum of the mixture showed the presence of four products. Two were unambiguously identified as di-*n*-propyl carbonate and *n*-propyl mesylate. A third compound had a methyl signal at 3.39 ppm that integrated 3:2 to one of the downfield methylene signals from the propyl group and was thus thought to be the desired sulfonyl carbonate intermediate **10a**. The fourth compound contained only propyl signals but could not be identified immediately.



The mixture was analyzed by GCMS. In agreement with the ^{1}H NMR spectrum, four components were observed in the GC trace. The first two peaks were identified by their mass spectra as di-*n*-propyl carbonate and *n*-propyl mesylate, but we were surprised to find that the third and fourth peaks were also identified by their mass spectra to be di-*n*-propyl carbonate and *n*-propyl mesylate! We realized that the sulfonyl carbonate **10a** is likely to decarboxylate on GC analysis, yielding the mesylate **13**, and this led us to the structure of the fourth unidentified product which we now know to be di-*n*-propyl dicarbonate **14**, which will decarboxylate to the carbonate on heating.[13]

Having identified all four products of reaction of *n*-propanol with carbon dioxide and methanesulfonyl anhydride, we were able to propose a rather complicated reaction scheme to explain our observations (Scheme 2). Both components in the initial equilibrium can react with

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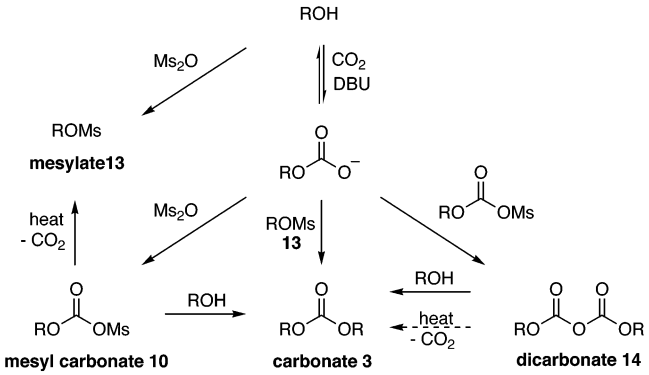
SCHEME 2



mesyl anhydride to yield the mesylate and mesyl carbonate. However, both these products can react further with carbonate anion to yield carbonate and dicarbonate, respectively, the latter being transformed to carbonate by decarboxylation or reaction with alcohol. These pathways, though interesting, are only productive if symmetrical carbonates are desired. Otherwise, it is essential to stop the reaction at the mesyl carbonate **10** to permit reaction with a different nucleophile in a second step.

We were now able to settle on a procedure that maximized the yield of the mesyl carbonate **10**, namely slow addition of a cooled suspension of the preformed carbonate anion in acetonitrile to a cooled solution of methanesulfonic anhydride, also in acetonitrile. For the *n*-propyl analogue **10a**, we were able to isolate the proposed intermediate in ca. 45% yield, though only in 90% purity, as a rather unstable oil. Characterization was only possible by ^{1}H and ^{13}C NMR spectroscopy and by mass spectrometry. The carboxyl signal at 147.83 ppm in the ^{13}C NMR spectrum is distinct from that of the carbonate (155.48 ppm), being closer in value, as expected, to that of dipropyl dicarbonate (148.64 ppm).

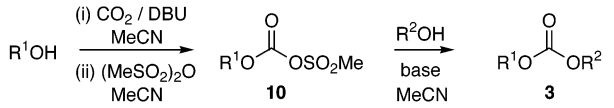
Attempts to replace the sulfonic anhydride with sulfonyl chlorides as sulfonating agents were unsuccessful. Substitution of methanesulfonic anhydride with methanesulfonyl chloride led mainly to mesylation of the alcohol, whereas use of tosyl chloride led, as with triflic anhydride, to symmetrical dicarbonates, suggesting that the intermediates in this case are too reactive for our purposes.

Synthesis of Carbonates. Having optimized the synthesis of the unstable mesyl carbonate intermediates, we proceeded to investigate their base-catalyzed reaction with a second alcohol to complete our new carbonate synthesis. The results are summarized in Table 1.

At first sight, the isolated yields for these reactions are poor. However, it should be noted that they are for three steps, the first of which (formation of the carbonate anion) is an equilibrium process. Indeed, we believe this equilibrium to be the major factor in determining the overall yield, since the only major impurity arises from mesylation of unreacted alcohol. This is consistent with our observation (vide supra) that the intermediate **10a** is only formed in ca. 45% yield.

Synthesis of the mesyl carbamate intermediate only appears to be possible in our hands with primary and secondary alcohols; use of *tert*-butyl alcohol or phenol in the first step led only to recovery of starting alcohol (entries 9 and 10). However, in the second step, phenol

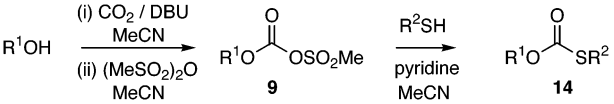
TABLE 1. Synthesis of Carbonates from Carbon Dioxide via Mesyl Carbonates



entry	R^1	R^2	base	product	isolated yield (%)
1	Me	Ph	pyridine	**3a**	26
2	*n*-Pr	*n*-Pr	pyridine	**3b**	40
3	*n*-Pr	Ph	none	**3c**	35
4	*n*-Pr	$PhCH_2$	pyridine	**3d**	28
5	$PhCH_2$	Ph	none	**3e**	25
6	$PhCH_2$	*t*-Bu	pyridine	**3f**	0
7	*i*-Pr	$PhCH_2$	pyridine	**3g**	(26)[a]
8	*t*-Bu	*n*-Pr	pyridine		no reaction
9	Ph	*n*-Pr	pyridine		no reaction

[a] NMR yield; product could not be separated by chromatography in our hands.

TABLE 2. Synthesis of Thiocarbonates from Carbon Dioxide via Mesyl Carbonates



entry	R^1	R^2	product	isolated yield (%)
1	*n*-Pr	3,5-dichlorophenyl	**14a**	37
2	$PhCH_2$	Et	**14b**	25
3	$PhCH_2$	3,5-dichlorophenyl	**14c**	19

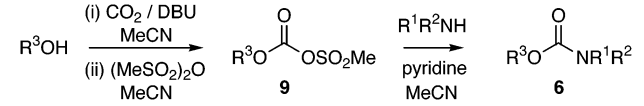
(entries 1, 3, and 5) is reactive, as well as primary alcohols. In short, this is the first synthesis of carbonates from carbon dioxide which can lead to *unsymmetrical* and to *aromatic* carbonates.

Synthesis of Thiocarbonates. An obvious extension of our new procedure was to synthesis of thiocarbonates. The results are summarized in Table 2. The particularly low yield for entry 3 is due to competing oxidation of the thiol under the reaction conditions. We believe this to be the first report of thiocarbonate synthesis from carbon dioxide.

Synthesis of Carbamates. As discussed above, there are already good methods for the synthesis of carbamates from carbon dioxide, all of which rely on initial reaction of the *amine* with carbon dioxide. It was of interest to us to investigate the alternative route, namely initial reaction of an *alcohol* with carbon dioxide, followed by the reaction of an intermediate with an amine. Our results are presented in Table 3.

To complete the investigation, we briefly investigated the reactivity of an N-analogue of mesyl carbonates **9**, the mesyl carbamate **15**. Using very similar reaction conditions, carbon dioxide was bubbled through a cooled acetonitrile solution of diethylamine in the presence of DBU (eq 3). Once again, we were unable to isolate pure **15**, but were able to obtain ^{1}H and ^{13}C NMR data consistent with the proposed structure. Again, the carbamoyl signal in the ^{13}C NMR spectrum (148.00 ppm) was distinctive. It should be noted that there is literature precedent for intermediate **15** since an analogous intermediate derived from a primary amine has been pro-

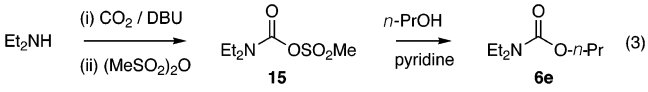
TABLE 3. Synthesis of Carbamates from Carbon Dioxide via Mesyl Carbonates



entry	R^3	R^1	R^2	product	isolated yield (%)
1	*n*-Pr	Bu	H	**6a**	42
2	*n*-Pr	Ph	H	**6b**	21
3	$PhCH_2$	*n*-Pr	H	**6c**	(48)[a]
4	$PhCH_2$	Ph	H	**6d**	28
5	*n*-Pr	Et	Et	**6e**	35

[a] NMR yield; product could not be separated by chromatography in our hands.

posed.[12] In that case, elimination of sulfonic acid to yield the corresponding isocyanate was observed.



(3)

Reaction of **15** with *n*-propanol under our standard conditions led smoothly to the known carbamate **6e** (eq 3). The increased yield as compared with the syntheses via mesyl carbonates is consistent with our proposal that the yield is mainly determined by the initial equilibrium.

Conclusion

Carbonate anions resulting from reaction of primary or secondary alcohols with carbon dioxide, when added to methanesulfonic anhydride in cooled acetonitrile solution, yield methanesulfonyl carbonates, a new class of synthetic intermediate. Base-catalyzed reaction of the methanesulfonyl carbonates with alcohols, thiols, and amines yields carbonates, thiocarbonates, and carbamates, respectively. Yields for the three steps vary from 19% to 42%, probably being limited by the initial equilibrium. To our knowledge, this is the first route from carbon dioxide to unsymmetrical carbonates, to aromatic carbonates, and to thiocarbonates. Other advantages of the procedure are that carbon dioxide can be used at atmospheric pressure and that the base used, DBU, is readily available.

Experimental Section

General Methods. Carbon dioxide was supplied by BOC gases (99%+). NMR spectra were obtained in $CDCl_3$ or acetone-d_6 with TMS as internal standard.

Propyl Methanesulfonyl Carbonate 10a. *n*-Propanol (0.4 mL, 5.35 mmol) and DBU (1 mL, 6.70 mmol) were dissolved in anhydrous MeCN (12 mL). CO_2 was bubbled subsurface, and the solution was cooled to −42 °C for 45 min. The mixture was allowed to warm to −20 °C and was transferred by cannula over 30 min to methanesulfonic anhydride (1.86 g, 10.7 mmol; 2 equiv) in MeCN (4 mL) at the same temperature. The mixture was stirred for 10 min, diluted with Et_2O (50 mL), and washed with H_2SO_4 (0.5 M, 2 × 50 mL) and brine (60 mL). The ethereal solution was dried with anhydrous potassium carbonate and filtered, and the solvent was removed in vacuo to give an oil (493 mg). The product could not separated from *n*-propyl mesylate.[14] Integration of the methanesulfonyl signals of the product and *n*-propyl mesylate in the ^1H NMR spectrum showed that the product was 90% of the oil, overall yield 45%: ^1H NMR ($CDCl_3$) δ 1.00 (3H, t, J = 7 Hz, CH_3CH$_2$CH$_2$O), 1.77 (2H tq, J = 7, 7 Hz, CH$_3$CH_2CH$_2$O), 3.39 (3H, s, CH$_3$SO$_2$), 4.27 (2H, t, J = 7 Hz, CH$_3$CH$_2$CH_2O); ^{13}C NMR ($CDCl_3$) δ 9.94 (*C*H$_3$CH$_2$CH$_2$O), 21.61 (CH$_3$*C*H$_2$CH$_2$O), 39.65 (CH$_3$SO$_2$), 72.37 (CH$_3$CH$_2$*C*H$_2$O), 147.83 (C═O); MS (EI) m/z = 182. Addition of 1 drop of Et_3N or DBU to the NMR sample gave no *n*-propyl mesyl carbonate on reanalysis.

General Procedure for Synthesis of Carbonates 3, Thiocarbonates 14, and Carbamates 6 from Alcohols. An alcohol (9.9 mmol) and DBU (1.25 equiv) were dissolved in anhydrous MeCN (12 mL), CO_2 was bubbled subsurface, and the solution was cooled to −42 °C for 45 min. The mixture was allowed immediately to warm to −30 °C and was transferred by cannula over 60 min to methanesulfonic anhydride (1.25 equiv) in MeCN (6 mL) at the same temperature. Once the reaction reached room temperature, the second nucleophile (1.3 equiv) and pyridine (1.4 equiv) dissolved in MeCN (1 mL) were added dropwise. The addition was exothermic and required cooling in ice−water. The reaction was subsequently stirred at room temperature overnight. Ethyl acetate (50 mL) was added, and the solution was washed with H_2SO_4 (0.2 M, 2 × 50 mL) and brine (50 mL). The organic layer was dried (K_2CO_3) and filtered, and the solvent was removed in vacuo. The purification methods are described below for each product.

Methyl Phenyl Carbonate 3a.[15] The general procedure was followed using methanol and with the following amendment. After the addition of the carbonate salt was complete, the reaction was allowed to warm to 7 °C. Phenol (1.3 equiv) was dissolved in MeCN (1 mL) with pyridine (1.4 equiv) and added to the mesyl carbonate. A temperature increase to 24 °C was noted, and the reaction was cooled back to 7 °C. A precipitate had formed within 30 s; no further change was observed within 48 h. The reaction was diluted with Et_2O (40 mL) and washed with HCl (0.2 M, 2 × 40 mL), NaOH (0.125 M, 40 mL), and brine (40 mL). The product was isolated as a colorless oil in 26% yield. Purity by ^1H NMR spectroscopy was >95%: IR (film) 1763 cm^{-1} (C═O); ^1H NMR ($CDCl_3$) δ 3.91 (3H, s, CH$_3$), 7.16−7.41 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 55.37, 121.01 (Ar), 126.06 (C-4), 129.48 (Ar), 151.07 (C-1), 154.28 (C═O); HRMS (EI) calcd 152.0473, found 152.0429.

Di-*n*-propyl Carbonate 3b.[16] The general procedure was followed with *n*-propanol as both starting alcohol and second nucleophile. The product was extracted with Et_2O and isolated by evaporation in 40% yield: ^1H NMR (400 MHz, $CDCl_3$) δ 0.97 (6H, t, J = 7 Hz, CH$_3$), 1.70 (4H, tq, J = 7 Hz, 7 Hz, CH_2CH$_2$O), 4.09 (4H, t, J = 7 Hz, CH$_2$O); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 10.21 (CH$_3$), 22.08 (CH$_2$), 69.45 (CH$_2$), 155.48 (C═O); HRMS (EI) calcd 146.0943, found 146.0949.

Phenyl *n*-Propyl Carbonate 3c.[17] The general procedure was followed with *n*-propanol as starting alcohol and phenol as second nucleophile and with the following amendment. No pyridine was added, and the reaction was heated with phenol at 40 °C for 22 h. The crude oil was purified by flash chromatography (SiO_2, cyclohexane/CH_2Cl_2) and isolated as a clear oil in 35% yield: IR (film) 1761 cm^{-1} (C═O); ^1H NMR δ 1.00 (3H, t, J = 7 Hz, CH$_3$), 1.77 (2H, tq, J = 7 Hz, 7 Hz, CH_2CH$_2$O), 4.22 (2H, t, J = 7 Hz, CH$_2$O), 7.16−7.48 (5H, overlapping m, Ph); ^{13}C NMR δ 10.20 (CH$_3$), 22.00 (CH$_2$), 70.34 (CH$_2$), 121.10 (Ar), 125.97 (C-4), 129.47 (Ar), 151.19 (C-1), 153.81 (C═O); MS (EI) m/z = 180 (M^+). Anal. Calcd for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.31; H, 6.66.

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Benzyl *n*-Propyl Carbonate 3d.[18] The general procedure was followed with benzyl alcohol as starting alcohol and *n*-propanol as second nucleophile and with the following amendment. A 5 mL (2.3 mmol) aliquot of the reaction was removed when at 0 °C, to which was added benzyl alcohol (0.3 mL, 2.90 mmol; 1.3 equiv) and pyridine (0.25 mL, 3.09 mmol; 1.39 equiv). TLC after 1 h showed a new product. There was no further change in the reaction during 3 days. The reaction was diluted with Et_2O (40 mL), washed with HCl (0.125 M, 2 × 40 mL) and brine (40 mL), dried (K_2CO_3), and filtered. Isolation by flash chromatography (SiO_2, 1:1 cyclohexane/CH_2Cl_2) yielded a colorless oil in 28% yield: IR (film) 1745 cm^{-1} (C═O); ^1H NMR (300 MHz, $CDCl_3$) δ 0.96 (3H, t, J = 7 Hz, CH_3CH$_2$CH$_2$O), 1.69 (2H, tq, J = 7 Hz, 7 Hz, CH$_3$CH_2CH$_2$O), 4.10 (2H, t, J = 7 Hz, CH$_3$CH$_2$CH_2O), 5.15 (2H, s, PhCH_2O), 7.31−7.41 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 10.18 (CH_3CH$_2$CH$_2$O), 22.01 (CH$_3$CH_2CH$_2$O), 69.81 (PhCH_2O), 70.08 (CH$_3$CH$_2$CH_2O), 128.32 (Ar), 128.49 (C-4), 128.59 (Ar), 135.36 (C-1), 155.27 (C═O); MS (EI) m/z = 194. Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 67.68; H, 7.18.

Benzyl Phenyl Carbonate 3e.[19] The general procedure was followed with benzyl alcohol as starting alcohol and phenol as second nucleophile and with the following amendment. The product was extracted with Et_2O. Yield by ^1H NMR was 31%. The crude oil was purified by flash chromatography (SiO_2, 5:4 cyclohexane/ CH_2Cl_2) and isolated as clear oil: IR (thin film) 1762; ^1H NMR (300 MHz, $CDCl_3$) δ 5.27 (2H, s, CH_2), 7.16−7.47 (10H, overlapping m, Ar); ^{13}C NMR (75.5 MHz, $CDCl_3$) 70.32 (CH_2), 121.01 (Ar), 126.04 (Ar), 128.54 (Ar), 128.67 (Ar), 128.75 (Ar), 129.46 (Ar), 134.73 (Bn, C-1), 151.08 (Ph, C-1), 153.65 (C═O); MS (EI) m/z = 228. Anal. Calcd for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30. Found: C, 73.49; H, 5.23.

Benzyl Isopropyl Carbonate 3g.[20] Isopropyl alcohol (0.4 mL, 5.22 mmol) was dried over 4 Å molecular sieves and then stirred with DBU (0.78 mL, 5.22 mmol) in MeCN (7 mL). CO_2 was bubbled subsurface, and then the reaction was cooled to −42 °C. CO_2 was bubbled for a further 45 min at this temperature. The resulting carbonate suspension was transferred to a solution of methanesulfonic anhydride (1.052 g, 6.04 mmol; 1.16 equiv) in MeCN (3.5 mL) at the same temperature, over 90 min, by cannula. After being warmed to 5 °C, the reaction was split into two aliquots. Benzyl alcohol (0.35 mL, 3.38 mmol) and pyridine (0.25 mL, 3.13 mmol) were added to an aliquot. After 1 min, a precipitate formed and the temperature rose to 23 °C. The reaction was cooled to 5 °C again and stirred overnight. The reaction was filtered and added to Et_2O (30 mL). The organic layer was washed with HCl (0.2M, 2 × 30 mL) and brine (30 mL). The solvent was removed in vacuo to give 282 mg. Analysis indicated the required product, benzyl alcohol, benzyl mesylate, and a small amount of diisopropyl carbonate in the ratio 26:39:2:1. Yield by ^1H NMR was 108 mg (21%): ^1H NMR ($CDCl_3$) δ 1.30 (6H, d, J = 6 Hz, CH_3), 4.89 (1H, septet, J = 6 Hz, CH), 5.14 (2H, s, CH_2), 7.35−7.39 (5H, overlapping m, Ar); ^{13}C NMR ($CDCl_3$) δ 21.73 (CH_3), 69.25 (CH_2), 72.10 (CH), 128.27 (Ar), 128.40 (C-4), 128.51 (Ar), 135.32 (C-1), 154.59 (C═O); HRMS (CI) calcd for $C_{11}H_{14}O_3$ 195.1021, found 195.1019.

***n*-Propyl *S*-3,5-Dichlorophenyl Thiocarbonate 14a.** The general procedure was followed with *n*-propanol as starting alcohol and 3,5-dichlorothiophenol as second nucleophile and with the following amendment. Analysis by TLC after 1 h showed a negligible amount of thiol remaining. The reaction was stirred overnight at ambient temperature. The crude mixture was diluted with Et_2O (50 mL) and washed with H_2SO_4 (0.2 M, 2 × 50 mL), NaOH (0.1 M, 2 × 50 mL), and brine (50 mL). The solution was dried (K_2CO_3) and filtered, and the solvent was removed in vacuo. Purification by flash chromatography (SiO_2, 24:1 cyclohexane/CH_2Cl_2) yielded **14a** as a clear oil in 37% yield: IR (film) 1731 cm^{-1} (C═O); ^1H NMR (250 MHz, $CDCl_3$) δ 0.96 (3H, t, J = 7 Hz, CH_3), 1.72 (2H, tq, J = 7 Hz, 7 Hz, CH_2), 4.23 (2H, t, J = 7 Hz, CH_2), 7.40 (1H, t, J = 2 Hz, H-4), 7.44 (2H, apparent d, J = 2 Hz, H-2 and H-6); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 10.21 (CH_3), 22.00 (CH_2CH$_2$O), 70.15 (CH$_2$CH_2O), 129.67 (C-4), 130.92 (C-1), 132.57 (C-2), 135.14 (C-3), 168.05 (C═O); HRMS (EI) calcd 263.9779, found 263.9774. Anal. Calcd for $C_{10}H_{10}Cl_2O_2S$: C, 45.30; H, 3.80. Found: C, 45.25; H, 3.71.

Benzyl *S*-Ethyl Thiocarbonate 14b. The general procedure was followed with benzyl alcohol as starting alcohol and ethanethiol as second nucleophile. Purification by flash chromatography (SiO_2, 24:1 cyclohexane/CH_2Cl_2) gave the isolated product as a clear oil in 25% yield: IR (film) 1702 cm^{-1} (C═O); ^1H NMR ($CDCl_3$) δ 1.32 (3H, t, J = 7 Hz, CH_3CH$_2$S), 2.88 (2H, q, J = 7 Hz, CH$_2$S), 5.23 (2H, s, CH$_2$O), 7.32−7.37 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 14.96 (CH_3), 25.38 (CH$_2$S), 68.71 (CH$_2$O), 128.56 (Bn), 128.52 (Bn), 128.44 (Bn), 135.23 (C-1), 164.31 (C═O); HRMS (EI) calcd 196.05580, found 196.05581. Anal. Calcd for $C_{10}H_{12}O_2S$: C, 61.20; H, 6.16. Found: C, 61.05; H, 6.11.

Benzyl *S*-3,5-Dichlorophenyl Thiocarbonate 14c. The general procedure was followed with *n*-propanol as starting alcohol and 3,5-dichlorothiophenol as second nucleophile and with the following amendment. A NaOH wash (0.1 M, 40 mL) was also carried out. ^1H NMR spectroscopy of the crude product showed a mixture of disulfide and ca. 33% product. Flash chromatography (SiO_2, 24:1 cyclohexane/CH_2Cl_2) of the crude oil gave 19% of product free from disulfide: IR (film) 1731 cm^{-1} (C═O); ^1H NMR ($CDCl_3$) δ 5.27 (2H, s, CH_2), 7.35−7.41 (6H, overlapping m, Ar), 7.44 (2H, apparent d, J = 2 Hz, H′-2 and H′-6); ^{13}C NMR ($CDCl_3$) 70.01 (CH_2), 128.59 (Bn), 128.71 (Bn), 128.83 (Bn), 129.80 (Ar, C-4), 130.62 (Ar C-1), 132.60 (Ar C-2), 135.19 (Ar C-3, C−Cl), 135.76 (Bn C-1), 168.09 (C═O); HRMS (CI) calcd (M^+ + 18) 330.0122, found 330.0127.

***n*-Propyl *N*-*n*-Butyl Carbamate 6a.** The general procedure was followed with *n*-propanol as starting alcohol and *n*-butylamine as second nucleophile. Purification by flash chromatography (SiO_2, cyclohexane/CH_2Cl_2) yielded **6a** as a clear oil in 42% yield: IR (film) 3336, 1695; ^1H NMR ($CDCl_3$) δ 0.89−0.96 (6H, 2 overlapping t, CH_3), 1.27−1.55 (4H, 2 overlapping m, CH_2CH_2CH$_2$N), 1.62 (2H, tq, J = 7 Hz, 7 Hz, CH_2CH$_2$O), 3.17 (2H, m, J = 6 Hz, CH$_2$N), 4.01 (2H, t, J = 7 Hz, CH$_2$O), 4.69 (1H, br, N−H); ^{13}C NMR (50.6 MHz, $CDCl_3$) δ 10.29 (CH_3CH$_2$CH$_2$O), 13.69 (CH_3CH$_2$CH$_2$CH$_2$NH), 19.84 (CH$_3$CH_2CH$_2$CH$_2$NH), 22.34 (CH$_3$CH_2CH$_2$O), 32.05 (CH$_3$CH$_2$CH_2CH$_2$NH), 40.62 (CH$_3$CH$_2$CH$_2$CH_2NH), 66.25 (CH$_3$CH$_2$CH_2O), 156.79 (C═O); HRMS (CI) calcd. 160.1337, found 160.1332. Anal. Calcd for $C_8H_{17}NO_2$: C, 60.35; H, 10.76; N, 8.80. Found: C, 60.05; H, 10.71; N, 8.68.

***n*-Propyl *N*-Phenyl Carbamate 6b.**[21] The general procedure was followed with *n*-propanol as starting alcohol and aniline as second nucleophile and with DBU (1 equiv). Crystallization from cyclohexane yielded **6b** as a white solid in 28% yield: IR (CH_2Cl_2) 1709 cm^{-1} (C═O); ^1H NMR ($CDCl_3$) δ 0.98 (3H, t, J = 7 Hz, CH_3), 1.70 (2H, tq, J = 7 Hz, 7 Hz, CH_2CH$_2$O), 4.13 (2H, t, J = 7 Hz, CH_2), 6.64 (1H, br, NH), 7.03−7.08 (1H, apparent t, J = 7 Hz, H-4), 7.27−7.40 (4H, m, Ar);^{13}C NMR ($CDCl_3$) δ 10.33 (CH_3), 22.24 (CH_2), 66.83 (CH_2), 118.58 (C-2), 123.29 (C-4), 129.01 (C-3), 137.93 (C-1), 153.69 (C═O); MS (EI) m/z = 179. Anal. Calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. Found: C, 67.05; H, 7.33; N, 7.81.

Benzyl *N*-*n*-Propyl Carbamate 6c.[22] The general procedure was followed with benzyl alcohol as starting alcohol and propylamine as second nucleophile. Crystallization from hexane gave **6c**. As estimated by ^1H NMR spectroscopy, this product was 70% pure, representing a 48% yield of **6c**. No

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further purification was possible: ^{1}H NMR ($CDCl_3$) δ 0.91 (3H, t, J = 7 Hz, CH_3), 1.51 (2H, tq, J = 7 Hz, 7 Hz, CH_2CH_2N), 3.15 (2H, br m, CH_2N), 5.09 (2H, s, CH_2O), 7.28−7.37 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 11.15 (CH_3), 23.13 (CH_2), 66.52 (CH_2), 126.92 (Ar), 127.93 (Ar), 128.36 (Ar), 136.53 (C-1), 156.37 (C═O); HRMS (CI) calcd 194.1180, found 194.1181.

Benzyl *N*-Phenyl Carbamate 6d.[23] The general procedure was followed with benzyl alcohol as starting alcohol and aniline as second nucleophile. Purification by flash chromatography (SiO_2, cyclohexane/CH_2Cl_2) and recrystallization from diethyl ether/hexane gave **6d** as a white solid in 28% yield: IR 1726 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.21 (2H, s, CH_2), 6.65 (1H, br, N−H), 7.04−7.09 (1H, m, J = 7 Hz, para H of PhNH), 7.28−7.40 (9H, overlapping m, Ar); ^{13}C NMR ($CDCl_3$) δ 66.89 (CH_2), 118.70 (Ph C-4), 123.40 (Bn C-2), 128.16 (Ar), 128.21 (Ar), 128.49 (Ar), 128.91 (Ar), 135.92 (Bn C-1), 137.68 (Ph C-1), 153.44 (C═O); HRMS (EI) calcd 227.0946, found 227.0945 Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 74.02; H, 5.81; N, 6.17.

***n*-Propyl *N*,*N*-Diethyl Carbamate 6e.**[24] The general procedure was followed with *n*-propanol as starting alcohol and diethylamine as second nucleophile. Product **6e** was isolated in 35% yield, as below.

***n*-Propyl *N*,*N*-Diethyl Carbamate 6e.** Diethylamine (0.5 mL, 4.83 mmol) and DBU (0.9 mL, 6.03 mmol; 1.25 equiv) were stirred in anhydrous MeCN (8 mL). The flask was purged with CO_2 before cooling to −20 °C, and then CO_2 was bubbled subsurface for 1 h. Methanesulfonic anhydride (0.96 g, 5.51 mmol) in anhydrous MeCN (3 mL) was then transferred dropwise to the carbamate solution. After addition was complete, the solution was kept cool for 30 min and then allowed to warm to rt with stirring. *n*-Propanol (0.4 mL, 5.35 mmol) and Et_3N (0.7 mL, 5.02 mmol) were added, and after being stirred for 1 h, the reaction was heated at reflux overnight. After cooling, the solvent was removed in vacuo and the residue was dissolved in CH_2Cl_2 (100 mL), solids were filtered off, and the organic solution was washed with H_2SO_4 (0.125 M, 2 × 100 mL) and brine (100 mL). The crude product was dried ($MgSO_4$), filtered, and concentrated to dryness (510 mg). Flash chromatography (SiO_2, 4:1 hexane/EtOAc) gave the product as a clear oil (200 mg, 26%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.95 (3H, t, J = 7 Hz, CH_3CH_2CH_2O), 1.12 (6H, t, J = 7 Hz, CH_3CH_2N), 1.65 (2H, tq, J = 7 Hz, 7 Hz, CH_3CH_2-CH_2O), 3.29 (4H, br m, CH_3CH_2N), 4.03 (2H, t, J = 7 Hz, CH_3-CH_2CH_2O); ^{13}C NMR ($CDCl_3$) δ 10.54 (*C*H_3CH_2CH_2O), 14.25 (*C*H_3CH_2N), 14.39 (*C*H_3CH_2N), 22.49 (CH_3*C*H_2CH_2O), 41.43 (CH_3CH_2N), 41.74 (CH_3CH_2N), 66.59 (CH_3CH_2*C*H_2O), 156.20 (C═O); MS (CI) m/z = 160 (MH^+). Anal. Calcd for $C_8H_{17}NO_2$: C, 60.35; H, 10.76; N, 8.80. Found: C, 59.90; H, 10.76; N, 8.55.

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