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SHORT COMMUNICATION

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Sulfur and Nitrogen Mustard Carbonate Analogues

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Sulfur and nitrogen half-mustard compounds lose their aggressive properties when the chlorine atom is replaced by a carbonate moiety. The anchimeric effect of the novel mustard carbonate analogues is investigated. The reaction follows first-order kinetics, does not need any base, and occurs with –OH, –NH and acidic –CH nucleophiles. Most of these molecules are unexplored and might provide a novel strategy for the preparation of compounds previously not easily accessible.

Introduction

Bis(2-chloroethyl) sulfide and bis(2-chloroethyl)(ethyl)-amine (Figure 1), respectively, known as sulfur and nitrogen mustards, have been used as chemical weapons for the first time in World War I for their acutely toxic vesicant properties.[1] The toxicity of these compounds is strictly related to their high reactivity. In fact, sulfur and nitrogen mustard, as well as their monofunctional analogous half-mustards, i.e., 2-chloroethyl methyl sulfide and (2-chloroethyl)dimethylamine (Figure 1), readily eliminates a chloride ion by *intramolecular* nucleophilic substitution due to the sulfur and nitrogen anchimeric effect, to form a cyclic episulfonium/aziridinium ion.[2] Furthermore, in contact with the human skin, they release HCl and can also permanently alkylate the guanine nucleotide in DNA strands, which is particularly harmful to cellular health.[1] Nevertheless, sulfur and nitrogen (half-)mustards are of great interest as electrophiles; in fact, they are extensively employed in inorganic synthesis,[3] organic synthesis[4] and in the preparation of numerous pharmaceutical intermediates.[5]

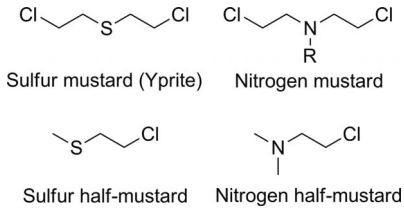


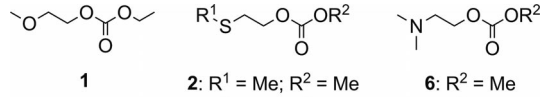
Figure 1. Sulfur and nitrogen (half-) mustards.

Herein we report the synthesis and a preliminary account on the chemical behaviour of sulfur and nitrogen half-mustard carbonate analogues: The replacement of a chlorine atom by a carbonate moiety not only results in harmless compounds, but most importantly gives open access to reactive intermediates so far only poorly exploited.

Dialkyl carbonates (DACs) in general, and dimethyl carbonate (DMC) in particular, are well-recognized green reagents and solvents for new synthetic pathways,[6] i.e., for cyclic compounds[7] and varnish formulations.[8] DMC, nowadays synthesised by CO_2 insertion into epoxides,[6b] has shown surprising high selectivity with different monodentate and bidentate nucleophiles.[9] In fact, the reactivity of the two electrophilic centers of DMC can be explained according to the Hard-Soft Acid-Base (HSAB) theory and modulated by temperature, which – very often – is a key factor. In fact, DMC acts as methoxycarbonylation agent by a $B_{Ac}2$ mechanism at reflux temperature (T = 90 °C), while it acts as methylating agent via a $B_{Al}2$ mechanism at higher temperature (T > 150 °C). Both reactions give as by-product only methanol and eventually CO_2.

We already reported some examples where substituting chlorine chemistry with DMC and taking advantage of the related $B_{Ac}2/B_{Al}2$ reaction mechanism resulted in quite unexpected outcomes, i.e., the selective *mono*-C-methylation of CH_2-acidic compounds such as arylacetonitriles, intermediates for the synthesis of anti-inflammatory drugs.[10]

In this work, we account for the first time on the synthesis and chemical behaviour of nitrogen and sulfur half-mus-



1

2: R^1 = Me; R^2 = Me
3: R^1 = Me; R^2 = Et
4: R^1 = Ph; R^2 = Me
5: R^1 = Ph; R^2 = Et

6: R^2 = Me
7: R^2 = Et

Figure 2. Sulfur and nitrogen half-mustard carbonate analogues **2**–**7** and the carbonate **1** used as reference compound for this study.

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tard carbonate analogues (Figure 2), which showed to maintain the chemical behaviour of the parent chlorine compounds, while losing their toxic properties.

Results and Discussion

Sulfur half-mustard carbonate alkyl 2-(alkylthio)ethyl carbonates **2**–**5**, nitrogen half-mustard carbonates alkyl 2-(dimethylamino)ethyl carbonates **6** and **7**, and ethyl 2-methoxyethyl carbonate **1** (Figure 2) have all been synthesised in quantitative yield by treating the related commercially available alcohol with the corresponding DAC by a $B_{Ac}2$ mechanism and using – in some cases – potassium carbonate as a catalyst.

Although very simple compounds, most of these carbonates, i.e., methyl 2-(methylthio)ethyl carbonate (**2**), ethyl 2-(methylthio)ethyl carbonate (**3**), methyl 2-(phenylthio)ethyl carbonate (**4**), ethyl 2-(phenylthio)ethyl carbonate (**5**), and ethyl 2-(dimethylamino)ethyl carbonate (**7**), resulted to be unexpectedly novel, as evidence of a chemistry not yet explored.

It is noteworthy that the carbonate analogues of the half-mustards **2**–**7**, isolated as pure compounds, are stable, do not smell, and do not show any vesicant properties or harm for the experimentator.

In order to investigate their reactivity as electrophiles, sulfur and nitrogen half-mustard carbonate analogues were treated with a simple nucleophile, i.e., phenol. The reactions were conducted in an autoclave at 180 °C by using preferably acetonitrile as solvent and without any base (Scheme 1).

Table 1 accounts on different aspects of the chemical behavior of carbonates **1**–**7**. The reaction of phenol with diethyl carbonate (DEC) and ethyl 2-methoxyethyl carbonate (**1**) was used as test reaction. Phenol and DEC, employed as reagent and solvent (Entry 1, Table 1), gave – as only product – ethoxybenzene (**13**) in low conversion (33%). On the other hand, phenol did not react at all with ethyl 2-methoxyethyl carbonate (**1**) (Entry 2, Table 1), most probably due to the absence of an anchimeric effect. However, when the same reaction was carried out in the presence of a base (i.e. K_2CO_3), ethoxybenzene (**13**) formed as the main product together with a small amount of (2-methoxyethoxy)benzene (**8**) (Entry 3, Table 1). This result demonstrates that the bimolecular substitution ($B_{Al}2$ mechanism) is predominant in base-promoted DAC reactions. In the same way, the reaction of phenol with DEC in the presence of base resulted in the quantitative formation of ethoxybenzene (**13**) after only 2 h (Entry 1, Table 1 footnote [d]).

Table 1. Reaction of phenol with sulfur and nitrogen half-mustard carbonate analogues.[a]

Entry	Carbonate	Solvent	Time [h]	Conversion[b] [%]	Product (yield [%])	k[c] [h^{-1}]
1[d]	DEC	DEC	24	33	**13** (100)	–
2	**1**	CH_3CN	24	0	**8** (0)	–
3[e]	**1**	CH_3CN	24	97	**8** (28)	–
					13 (72)	
4	**2**	CH_3CN	24	100	**9** (100)	–
5	**3**	CH_3CN	24	81	**9** (100)	0.082
6[e]	**3**	CH_3CN	24	100	**9** (58)	
					13 (41)	
7	**3**	Cyclohexane	46	70	**9** (100)	0.015
8	**3**	DMF	48	94	**9** (17)	0.098
9	**4**	CH_3CN	24	36	**10** (45)	–
10	**5**	CH_3CN	24	50	**10** (16)	–
11	**6**	CH_3CN	5	100	**11** (100)	–
12	**7**	CH_3CN	5	100	**11** (100)	1.385[f]

[a] Carbonate (1.0 mol-equiv.) and phenol (3.0 mol-equiv.) in acetonitrile (100 mL) at 180 °C in an autoclave. [b] Calculated by GC–MS analysis using *p*-xylene as internal standard. [c] First-order kinetics constant, calculated according to the disappearance of the starting carbonate. [d] Reaction perfomerd in the presence of 1.0 mol-equiv. of K_2CO_3 resulted in 100% conversion into ethoxybenzene (**13**) after 2 h. [e] Reaction performed in the presence of 1.0 mol-equiv. of K_2CO_3. [f] First-order kinetics were calculated by using carbonate (1.0 mol-equiv.) and phenol (1.0 mol-equiv.) in acetonitrile (100 mL) at 180 °C in an autoclave.

Conversely, when phenol was treated with the sulfur half-mustard carbonate analogues **2** and **3** under neutral conditions, the chemical behaviour observed was different: methyl 2-phenoxyethyl sulfide (**9**) formed in quantitative yield (Entries 4 and 5, Table 1). This provides evidence that the 2-(methylthio)ethyl moiety is crucial for the reaction to occur, most probably due to the anchimeric effect of the sulfur atom (Figure 3).

The reaction of phenol and ethyl 2-(methylthio)ethyl carbonate (**3**) was also conducted in the presence of a base. In this case, the sulfide **9** still formed as the main product, but ethoxybenzene (**13**) was also present in 41% yield (Entry 6, Table 1) showing the concurrence of the $B_{Al}2$ pathway (Entry 3, footnote [e], Table 1). This result proves the importance of the sulfur neighboring effect in the mustard carbonate analogues. It is also evident that the anchimeric

1: X = O; R^1 = Me; R^2 = Me
3: X = S; R^1 = Me; R^2 = Et
4: X = S; R^1 = Ph; R^2 = Me
5: X = S; R^1 = Ph; R^2 = Et
6: X = N(Me); R^1 = Me; R^2 = Me
7: X = N(Me); R^1 = Me; R^2 = Et

8: X = O; R^1 = Me
9: X = S; R^1 = Me
10: X = S; R^1 = Ph
11: X = N(Me); R^1 = Me

12: R^2 = Me
13: R^2 = Et

Scheme 1. Reaction of phenol with half-mustard carbonate analogues **2**–**7**.

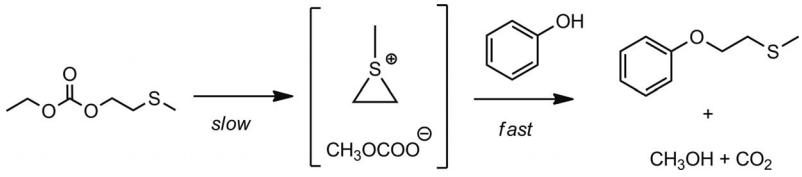


Figure 3. Reaction mechanism of sulfur half-mustard carbonate **3** with phenol.

effect does not need the presence of base, which – on the contrary – resulted counterproductive. It is noteworthy that the absence of the base represents an advantage in terms of waste minimization.

The reaction between the sulfur half-mustard carbonate **3** and phenol was then investigated by employing different solvents. Cyclohexane resulted as a fair solvent, compared to acetonitrile, in terms of conversion and selectivity (Entry 7, Table 1), although the reaction required 46 h to achieve 70% conversion of the starting material. *N*,*N*-Dimethylformamide (DMF) showed a poor selectivity (Entry 8, Table 1). Besides, when dimethyl sulfoxide, tetrahydrofuran or toluene were employed, the formation of methyl 2-phenoxyethyl sulfide (**9**) was not observed, although the starting carbonate slowly diminished over time (24 h). Acetonitrile resulted as the best solvent for the reaction studied (Entry 5, Table 1). The effect of the solvent on the half-mustard reactivity well agrees with what was recently reported in the literature for functionalized aziridinium salts with acetonitrile being the best solvent and THF the worst.[11]

Alkyl 2-(phenylthio)ethyl carbonates **4** and **5** were also treated with phenol (Entries 9 and 10, Table 1). In this cases, a low conversions of the starting carbonates and modest selectivity were observed (45% and 16%, respectively). These results might be ascribed to the lower nucleophilicity of the sulfur atom compared to the carbonates **2** and **3**.

Table 1 reports also the reactivity of the nitrogen half-mustard analogues alkyl 2-(dimethylamino)ethyl carbonates **6** and **7**. Both carbonates reacted readily with phenol to give as sole product dimethyl(2-phenoxyethyl)amine (**11**) in quantitative yield (Entries 11 and 12, Table 1). It is noteworthy that the reactions involving nitrogen half-mustard carbonates **6** and **7** were much faster than the ones of sulfur mustard analogues **2**–**5**. This is almost certainly ascribed to the easier formation of the aziridinium cation as the reaction intermediate.

In order to prove the reaction mechanism, some kinetics studies were carried out both on sulfur and nitrogen half-mustard compounds. The reaction kinetics of ethyl 2-(methylthio)ethyl carbonate (**3**) with phenol was investigated in different solvents resulting always in first-order kinetics (rate constants reported in Entries 5, 7 and 8, Table 1).

Figure 4 depicts the reaction kinetics of ethyl 2-(dimethylamino)ethyl carbonate (**7**) with phenol (1:1 molar ratio) in acetonitrile according to the reaction conditions reported in Entry 12, Table 1. By plotting the experimental values of $\ln(C_0/C)$ and $1/C$ against the first- and second-order rate equations, respectively, it is evident that the reaction fits first-order kinetics (Figure 4) and corroborates the reaction mechanism reported in Figure 3.

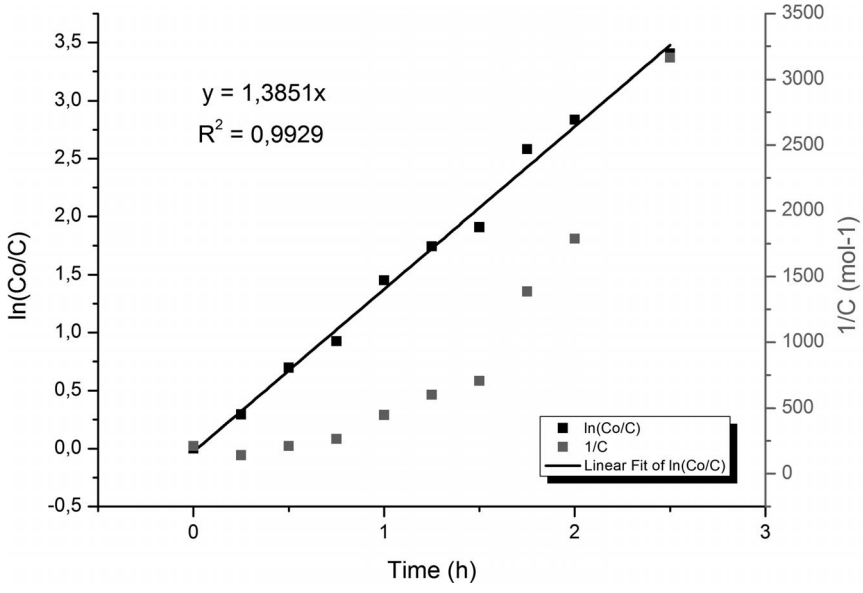
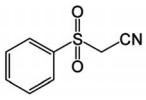
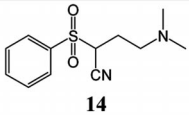
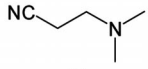
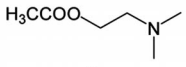
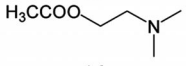
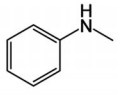
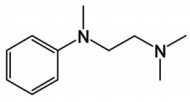


Figure 4. Comparison between first- (black) and second-order (grey) kinetics of the reaction of carbonate **7** with phenol (1:1 molar ratio in an autoclave 180 °C) where *C* is the concentration of the carbonate **7** (mol/L); *p*-xylene was used as internal reference.

Table 1 and Figure 2 confirm that the mustard carbonate analogues have a behaviour similar to that of the parent chlorine compounds,[12] i.e., the anchimeric effect follows the order N > S >> O; no base is necessary; the reaction follows first-order kinetics; the solvent effect is similar to the one recently observed for aziridinium salts; besides, the novel carbonate compounds do not smell and do not show any toxic or vesicant effects.

The exploitation of this reaction was next investigated by treating several nucleophiles with ethyl 2-(dimethylamino)-ethyl carbonate (**7**) at 180 °C in an autoclave in acetonitrile and under neutral conditions. The results are reported in Table 2.

Table 2. Reaction of different nucleophiles with nitrogen half-mustard carbonate **7** in the absence of a base.[a]

Entry	Nucleophile	Time [h]	Product [%]	GC-MS area [%] (isolated yield [%])
1		7	 **14**	94 (81)
2	KCN	4	 **15**	50 (40)
3	CH_3COOH	4	 **16**	60 (28)
4	CH_3COOK	3	 **16**	70 (40)
5		5	 **17**	45 (30)

[a] Nucleophile/carbonate (3:1) molar ratio in acetonitrile at 180 °C in an autoclave. The conversion of the carbonate **7**, calculated by GC–MS analysis using *p*-xylene as internal standard, was always quantitative. The isolated yields for compounds **15**–**17** were modest, because purification of these compounds by column chromatography was sometimes difficult, possibly due to their polarity.

The nucleophiles selected included an organic CH_2-acidic compound, i.e., (phenylsulfonyl)acetonitrile (Entry 1, Table 2); salts, i.e., potassium cyanide and potassium acetate (Entries 2 and 4, Table 2); a carboxylic acid, i.e., acetic acid (Entry 3, Table 2); and an amine, i.e., *N*-methylaniline (Entry 5, Table 2). In all these cases, the reactions – monitored until complete disappearance of the starting carbonate **7** – showed the formation of the expected substituted compounds **14**–**17** as the main products together with small amounts of several by-products that were not isolated. In particular, dimethyl[2-(*N*-methylanilino)ethyl]amine (**17**) was formed in low yield (Entry 5, Table 2). Potassium cyanide also gave a poor selectivity, probably as a result of the low solubility in the reaction mixture. All the alkylated products **14**–**17** were isolated and fully characterized (see Supporting Information).

The results reported in Table 2 prove that the novel mustard carbonates react with a wide range of nucleophiles, i.e., CH- and OH-acidic compounds, carboxylic acids, amines and inorganic anions, and give the corresponding products in the absence of any base. The reaction between phenol and the nitrogen half-mustard carbonate **6** was also performed on a preparative scale by starting from 5.0 g of phenol, and the resulting product **11** was isolated in 70% yield (see Experimental Section).

Conclusions

Replacement of the chlorine atom by a carbonate moiety in half-nitrogen and -sulfur mustard compounds gave new, unexplored and safe compounds that showed good reactivity and might give open access to a variety of compounds previously not easily accessible. The reactions involving the half-mustard carbonate analogues and a nucleophile proceed through an *intramolecular* S_N2 mechanism promoted by the sulfur and nitrogen anchimeric effect, which is the rate-determining step; the subsequent nucleophilic attack, being faster, does not influence the reaction rate.

The presence of a base is not required for the reaction to proceed, since – when used – it promotes unwanted by-products. It is also noteworthy that the novel half-mustard carbonate electrophiles react with several nucleophiles as well as with acetic acid.

The toxicological properties of the mustard carbonate analogues still need to be accurately investigated. Furthermore, a study of similar systems with the heteroatom in different positions, i.e., alkyl 3-(alkylthio)propyl carbonates or alkyl 4-(alkylthio)butyl carbonates (and their corresponding amino derivatives) will be carried out in order to identify the extent of the neighbouring effect.[13]

Carbonates **2**–**7** may be a good example of Green Chemistry defined as innovation at molecular level.

Experimental Section

Methods: Details on the synthetic protocols and characterization for carbonates **1**–**7** are reported in the Supporting Information.

Synthetic Protocols for Carbonates 1–7: In a typical experiment the starting alcohol (1 mol-equiv.), DEC (10 mol-equiv.) and potassium carbonate (1.1 mol-equiv.) were placed into a two-necked round-bottomed flask equipped with a reflux condenser. While being stirred magnetically, the mixture was heated at reflux temperature for 22 h. The reaction mixture was then filtered, and the solvent was evaporated.

Ethyl 2-(Methoxyethyl) Carbonate (1):[14] Colourless liquid; yield 96%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (t, J = 7.2 Hz, 3 H), 3.37 (s, 3 H), 3.60 (t, J = 4.8 Hz, 2 H), 4.19 (q, J = 7.2 Hz, 2 H), 4.26 (t, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.8, 64.8, 61.3, 58.6, 53.6, 8.8 ppm.

Methyl 2-(Methylthio)ethyl Carbonate (2): Colourless liquid; yield 80%. HRMS: calcd. for ($C_5H_{10}O_4S$ + Na) $[M]^+$ 189.0192; found 189.0192. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.14 (s, 3 H), 2.74 (t, J = 7.2 Hz, 2 H), 3.77 (s, 3 H), 4.28 (t, J = 7.2 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.2, 61.1, 49.4, 27.0, 10.4 ppm.

Ethyl 2-(Methylthio)ethyl Carbonate (3): The pure compound was obtained by distillation under vacuum; b.p. 102 °C (0.05 bar). Colourless liquid; yield 57%. HRMS: calcd. for ($C_6H_{12}O_4S$ + Na) $[M]^+$ 203.0354; found 203.0349. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.3 (t, J = 7.2 Hz, 3 H), 2.15 (s, 3 H), 2.75 (t, J = 7.2 Hz, 2 H), 4.19 (q, J = 7.2 Hz, 2 H), 4.28 (t, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.9, 66.1, 64.0, 32.3, 15.7, 14.2 ppm.

Methyl 2-(Phenylthio)ethyl Carbonate (4): The pure compound was obtained by column chromatography on silica gel using hexane/ethyl acetate (8:2). Light yellow liquid; yield 82%. HRMS: calcd. for ($C_{10}H_{12}O_4S$ + H) $[M]^+$ 229.0535; found 229.0529. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.17 (t, J = 6.8 Hz, 2 H), 3.77 (s, 3 H), 4.27 (t, J = 6.8 Hz, 2 H), 7.21 (t, J = 5.6 Hz, 1 H), 7.30 (m, 2 H), 7.40 (d, J = 6.8 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.2, 129.5, 124.7, 123.8, 121.4, 60.7, 49.5, 26.8 ppm.

Ethyl 2-(Phenylthio)ethyl Carbonate (5): The pure compound was obtained by a column chromatography on silica gel using heptane/ethyl acetate (9:1). Colourless liquid; yield 79%. HRMS: calcd. for ($C_{11}H_{14}O_4S$ + Na) $[M]^+$ 265.0505; found 265.0505. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.30 (t, J = 7.2 Hz, 3 H), 3.18 (t, J = 6.8 Hz, 2 H), 4.18 (q, J = 6.8 Hz, 2 H), 4.26 (t, J = 7.2 Hz, 2 H), 7.23 (t, J = 5.6 Hz, 1 H), 7.30 (dd, J = 7.2, 5.6 Hz, 2 H), 7.39 (d, J = 6.8 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.8, 134.8, 130.0, 129.0, 126.7, 65.8, 64.1, 32.2, 14.2 ppm.

2-(Dimethylamino)ethyl Methyl Carbonate (6):[15] The pure compound was obtained by fractionated distillation under vacuum; b.p. 60–62 °C (0.05 bar). Orange liquid; yield 24%. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.96 (s, 6 H), 2.61 (t, J = 5.6 Hz, 2 H), 3.77 (s, 3 H), 4.24 (t, J = 5.6 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.7, 65.4, 57.5, 54.7, 45.5 ppm.

Ethyl 2-(Dimethylamino)ethyl Carbonate (7): The pure compound was obtained by fractionated distillation under vacuum; b.p. 73 °C (0.05 bar). Colourless liquid; yield 42%. HRMS: calcd. for ($C_7H_{15}O_3N$ + H) $[M]^+$ 162.1130; found 162.1125. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.30 (t, J = 7.2 Hz, 3 H), 2.36 (s, 6 H), 2.69 (t, J = 5.6 Hz, 2 H), 4.19 (q, J = 7.2 Hz, 2 H), 4.28 (t, J = 5.6 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.1, 65.2, 63.8, 57.6, 45.5, 14.1 ppm.

Reaction of Carbonates with Nucleophiles

Methyl (2-Phenoxyethyl) Sulfide (9):[4b] A mixture of ethyl 2-(methylthio)ethyl carbonate (300 mg, 1.83 mmol) and phenol (516 mg, 5.49 mmol) in acetonitrile (100 mL) was placed into an autoclave and heated at 180 °C while stirring for 23 h. The progress of the reaction was monitored by GC–MS. When the kinetics of the reaction was monitored, *p*-xylene (197 mg, 1.83 mmol) was added to the reaction mixture as internal standard and samples were taken at regular intervals (every hour) and analyzed by GC–MS. After disappearance of the starting carbonate, the reaction was stopped and the mixture cooled to room temperature. Then the solvent was evaporated from the clear solution. The pure compound was obtained by column chromatography on silica gel using as elution mixture hexane/ethyl acetate (9:1). A sample of the pure compound was isolated as a colorless oil. Analysis of the sample was consistent with the data reported in the literature.[4b]

(2-Phenoxyethyl) Phenyl Sulfide (10):[16] A mixture of ethyl 2-(phenylthio)ethyl carbonate (500 mg, 2.35 mmol) and phenol (665 mg, 7.07 mmol) in acetonitrile (100 mL) was placed into an autoclave and heated at 180 °C while stirring for 24 h. The progress of the reaction was monitored by GC–MS. After disappearance of the starting carbonate, the reaction was stopped and the mixture cooled to room temperature. Then the solvent was evaporated from the clear solution. The pure compound was obtained by extraction with dichloromethane/H_2O. The organic phase was separated, dried with $MgSO_4$ and the solvent evaporated. A sample of the pure compound was isolated as a colorless oil. Analysis of the sample was consistent with the data reported in the literature.

Dimethyl(2-phenoxyethyl)amine (11):[17] In a stainless steel autoclave was placed a solution of phenol (529 mg, 5.58 mmol), 2-(dimethylamino)ethyl ethyl carbonate (300 mg, 1.86 mmol) [or 2-(dimethylamino)ethyl methyl carbonate] in acetonitrile (100 mL) at 180 °C while stirring. The progress of the reaction was monitored by GC–MS. When the kinetics of the reaction was monitored, an internal standard (*p*-xylene) was added to the reaction mixture, and samples were taken at regular intervals (every hour) and analyzed by GC–MS. After disappearance of the starting carbonate, the reaction was stopped, the mixture cooled to room temperature, and the solvent evaporated. The pure compound was obtained by column chromatography on silica gel using as elution mixture dichloromethane/methanol (9:1) to recover the desired product as a brown oil in 70% yield (215 mg, 1.29 mmol). Analysis of the sample was consistent with the data reported in the literature.

4-(Dimethylamino)-2-(phenylsulfonyl)butyronitrile (14): In a stainless steel autoclave was placed 2-(dimethylamino)ethyl ethyl carbonate (300 mg, 1.86 mmol) with 2-(phenylsulfonyl)acetonitrile (1.10 g, 5.58 mmol) in acetonitrile (100 mL) at 180 °C while stirring. The progress of the reaction was monitored by GC–MS. After disappearance of the starting carbonate, the reaction was stopped, the mixture cooled to room temperature, and the solvent evaporated. The pure compound was obtained by column chromatography on silica gel using as elution mixture dichloromethane/methanol (95:5) to recover the desired product **14** in 81% yield (380 mg, 1.50 mmol) as a brown oil. HRMS: calcd. for ($C_{12}H_{16}N_2O_2S$ + H) $[M]^+$ 253.1011; found 253.1005. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.25 (s, 6 H), 2.42–2.64 (m, 4 H), 4.41–4.45 (m, 1 H), 7.64 (m, 2 H), 7.76 (t, J = 6.4 Hz, 1 H), 8.02 (d, J = 7.2 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.9, 135.1, 129.5, 113.9, 55.0, 54.8, 44.8, 24.9 ppm.

3-(Dimethylamino)propanenitrile (15):[18] In a stainless steel autoclave was placed 2-(dimethylamino)ethyl ethyl carbonate (150 mg, 0.98 mmol) with potassium cyanide (192 mg, 2.95 mmol) in 100 mL of acetonitrile at 180 °C while stirring. The progress of the reaction was monitored by GC–MS. After disappearance of the starting carbonate, the reaction was stopped, the mixture cooled to room temperature, and the solvent evaporated. The pure compound was obtained by column chromatography on silica gel using as elution mixture dichloromethane/methanol (95:5) to recover the desired product in 40% yield (40 mg, 0.39) as a brown oil. Analysis of the sample was consistent with data reported in the literature.

2-(Dimethylamino)ethyl Acetate (16):[19] In a stainless steel autoclave was placed 2-(dimethylamino)ethyl ethyl carbonate (300 mg, 1.86 mmol) with acetic acid (335 mg, 5.58 mmol) (or potassium acetate 547 mg, 5.58 mmol) in 100 mL of acetonitrile at 180 °C while stirring. The progress of the reaction was monitored by GC–MS. After disappearance of the starting carbonate, the reaction was stopped, the mixture cooled to room temperature, and the solvent evaporated. In both reactions, the pure compound was obtained by column chromatography on silica gel using as elution mixture dichloromethane/methanol (95:5) to recover the desired product in 28% yield (68 mg, 0.52 mmol) (40% also in the case of potassium acetate) as a brown oil. Analysis of the sample was consistent with data reported in the literature.

Dimethyl[2-(*N*-methylanilino)ethyl]amine (17):[20] In a stainless steel autoclave was placed 2-(dimethylamino)ethyl ethyl carbonate

(300 mg, 1.86 mmol) with *N*-methylaniline (598 mg, 5.58 mmol) in 100 mL of acetonitrile at 180 °C while stirring. The progress of the reaction was monitored by GC–MS. After disappearance of the starting carbonate, the reaction was stopped, the mixture cooled to room temperature, and the solvent evaporated. The pure compound was obtained by column chromatography on silica gel using as elution mixture dichloromethane/methanol (95:5) in 30% yield (97 mg, 0.54 mmol) as a brown oil. Analysis of the sample was consistent with data reported in the literature.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR, HR-MS and GC–MS data of the pure compounds and an example of kinetics constant calculation.

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