Electrogenerated Base-Promoted Synthesis of Organic Carbonates from Alcohols and Carbon Dioxide

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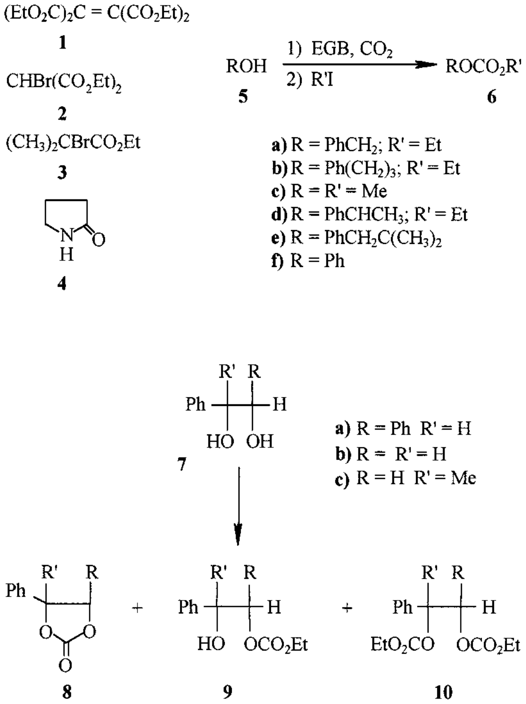
Electrogenerated bases promote the reaction between primary alcohols and carbon dioxide to give organic carbonates in excellent yields. Secondary alcohols are converted in moderate yields, whereas tertiary alcohols and phenols are unreactive. 1,2-Diols give a mixture of both cyclic and linear di- and monocarbonates. These latter are intermediates in the reaction pathway leading to the cyclic derivatives.

Introduction

Organic carbonates are an important class of compounds whose versatility allows their application in several fields of the chemical and pharmaceutical industry. Recently, the utilization of organic carbonates and the methods for their synthesis have been extensively reviewed.[1] The most important routes to these esters involve the direct or indirect use of phosgene, a very toxic and corrosive reagent. Other available methods use carbon monoxide, drastic conditions and/or metal catalysts, whose potential environmental impact should not be underestimated. We have already described a new approach to organic carbonates based on the electrocarboxylation of alcohols and 1,2-diols following activation of carbon dioxide by either cathodic reduction[2,3]or electrogenerated superoxide anion.[3,4] Both methods allow the synthesis of linear and cyclic carbonates under very mild and safe conditions, but not in very high yields. Therefore, we have reconsidered the synthesis of organic carbonates from alcohols and carbon dioxide with the aim of increasing the yield of the process. Starting from the hypothesis that the first step of the reaction involves substrate deprotonation, we decided to use electrogenerated bases (EGBs), which can be obtained by reducing suitable probases (PBs). The usefulness of EGBs in organic electrosynthesis is well documented[5] and the possibility of generating bases of different stability and reactivity by simply controlling the nature of the counterion[6] is of utmost utility.

The efficiency of some representative EGBs in the carboxylation of benzyl alcohol **5a**, which was selected as a model compound, has been tested. Under normal conditions, the 2-pyrrolidone anion arising from PB **4** gives the highest yield of carbonate **6a**. The experimental parameters of the reaction involving **4** and **5a** were subsequently optimized. Finally, under optimized conditions, representative alcohols and 1,2-diols (Scheme 1) have been subjected to the carboxylation process, to establish the generality and limits of this new procedure.



Scheme 1.

Results and Discussion

Probases **1–4** have been tested in the carboxylation reaction of benzyl alcohol **5a**. Tetraethyl ethylenetetracarboxylate (**1**) has been reduced on a mercury pool cathode under potentiostatic control in the presence of **5a** and CO_2, employing different PB concentrations and the different current amounts necessary for its complete reduction to EGB. The results of the HPLC analyses carried out on the reaction mixture obtained after addition of an excess of EtI

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Table 1. Carboxylation of benzyl alcohol **5a** (2 mmol): choice of the experimental conditions (Pt anode; catholyte = CH_3CN/0.1 M TEAP)

Entry	PB[a] (mmol)	mF[b]	T [°C]	E [V] or I [mA cm^{-2}]	Products (yield%[c])
1	**1** (1.0)	2.0	25	–1.0	**5a** (68), **6a** (31)
2	**1** (1.5)	3.0	25	–1.0	**5a** (52), **6a** (35)
3	**1** (2.0)	4.0	25	–1.0	**5a** (46), **6a** (40)
4	**1** (3.0)	6.0	25	–1.0	**5a** (33), **6a** (46)
5	**1** (4.0)	8.0	25	–1.0	**5a** (30), **6a** (49)
6	**1** (5.0)	10.0	25	–1.0	**5a** (28), **6a** (50)
7	**2** (4.0)	6.1[d]	25	–0.5	**5a** (36), **6a** (32)
8	**3** (4.0)	8.0	25	–1.0	**5a** (65), **6a** (24)
9	**4** (5.0)	4.0	25	15	**5a** (20), **6a** (63)
10	**4** (10.0)	8.0	25	15	[e] **6a** (65)
11	**4** (5.0)	4.0	0	15	**5a** (18), **6a** (78)
12	**4** (5.0)	4.0	–25	15	**5a** (27), **6a** (68)
13	**4** (5.0)	4.0	–50	15	**5a** (24), **6a** (58)
14	**4** (5.0)	6.0	0	15	**6a** (88)
15	**4** (10.0)	8.0	0	15	**6a** (78)
16	**4** (5.0)[f]	6.0	0	15	**5a** (67), **6a** (31)

[a] A Hg pool (probases **1**–**3**) or a Pt gauze (probase **4**) was used as cathode. – [b] Total current amount in mF. – [c] HPLC analysis. – [d] Compound **2** undergoes competitive dimerization. – [e] Unidentified products did not allow to quantify **5a**. – [f]DMF was used as solvent.

are reported in Table 1 (entries 1–6). As expected, higher yields of benzyl ethyl carbonate **(6a)** are observed by increasing the PB concentration; they achieve a maximum value when the PB concentration is twice that of the substrate. However, we considered an equimolar concentration of PB (and thus, theoretically, two equivalents of EGB[7]) as a good compromise between chemical yield and current consumption and chose such conditions to test the other probases. When using diethyl bromomalonate **(2)** and ethyl 2-bromo-2-methylpropionate **(3)** the yield of **6a** decreases (Table 1, entries 7,8).[7] On the other hand, the EGB arising from 2-pyrrolidone **(4)** promotes the highest yield in the conversion of **5a** into carbonate **6a** (Table 1, entry 9).[8] In these conditions further increases of the PB concentration and of the current amount do not increase the carbonate yield (Table 1, entry 10).

The reduction of **4** was carried out on a platinum gauze cathode under galvanostatic control. The reduction potential value of **4** is very negative, but its EGB is stable enough to be generated and then utilized after the current is switched off, thus allowing its use even with substrates electroactive at the working potential.[5d] Since it gives the higher yield of **6a** (cf. entries 3,7–9 in Table 1), compound **4** was selected to carry out all the other carboxylation reactions. The next step of the research was the optimization of the experimental conditions. We first investigated the influence of the temperature on the formation of **6a**, in the range from +25 °C to –50 °C. HPLC analyses of these solutions are reported in Table 1 (entries 9,11–13) and show 0 °C to be the optimum electrolysis temperature. Another set of experiments was carried out in order to establish the influence of the PB concentration and of the employed electricity (Table 1, entries 11,14,15). The best yield of **6a** was obtained using 5 mmol of PB and a current value of 6.0 mF. A further increase of the PB concentration and of the total current amount produces a decrease in the carbonate yield and a greater number of unidentified products, some of which arise from interactions between the EGB and the solvent, as ascertained on the basis of their IR spectra. To eliminate these undesired reactions, *N,N*-dimethylformamide was used instead of acetonitrile under otherwise identical experimental conditions, but the drastic decrease in the carbonate yield (Table 1, entry 16) excluded the possibility of employing this solvent. Therefore, the optimized conditions for the carboxylation of **5a** (2 mmol) to **6a** require the reduction of pyrrolidone **4** (5 mmol) in acetonitrile (50 mL) at 0° C with a consumption of 6.0 mF of current.

Under these conditions, several representative alcohols and 1,2-diols (**5** and **7** in Scheme 1) were subjected to the EGB-promoted carboxylation process. The results of the analyses carried out on the corresponding reaction mixtures are reported in Table 2 and allow us to draw some conclusions. The primary alcohols **5a–c** are converted into the corresponding carbonates in excellent yields (entries 1–3). Under the same experimental conditions, the secondary alcohol **5d** gives a lower yield of **6d** (entry 4). A higher conversion can be obtained by increasing the current value to 8.0 mF (entry 5), although a further increase of the PB concentration and of the total current amount (see Experimental Section) does not produce better results (entry 6). The tertiary alcohol **5e** and phenol **5f** do not undergo the carboxylation reaction. It is likely that steric hindrance and/or the unfavorable deprotonation equilibrium between EGB and **5e**[9] do not allow the carbonate formation. On the other hand the poor nucleophilicity of the **5f** anion is probably responsible for the unsuccessful formation of **6f**. When diols **7a–c** are subjected to the above-described procedure, complex mixtures are obtained in which the cyclic carbonates **8a–c** and linear monocarbonates **9a–c** are present, together with the dicarbonates **10a,b** starting from **7a,b** (Table 2, entries 9–16). Once again, the value of the PB concentration and the current amount affect the course of the reaction. In the case of **7a,** the yield of cyclic carbonate reaches a maximum for a current value of 6.0 mF and a further increase and/or a higher PB concentration only bring about higher yields of dicarbonate **10a** (Table 2, entries 9–12). A similar behavior is observed for **7b**, although higher yields of **8b** and **10b** are obtained by increasing PB and total current amounts (Table 2, entries 13,14). Finally, the yield of **8c** is essentially unaffected by these parameters (Table 2, entries 15,16). It has already been proved that the linear carbonates **9** are intermediates in the reaction pathway yielding to the formation of **8**. Actually, samples of compounds **9**, independently synthesized by chemical methods, were converted into **8** when treated under carboxylation conditions.[3] Further evidence has been collected during the present study: both the treatment of isolated **9** under workup conditions and the simple use of longer reaction times promote the conversion of **9** into **8**. The dicarbonates **10** have never been detected in the reaction mixtures obtained employing the two previously reported methods of electrocarboxylation.[3] It is likely that the conjugate base of **4** is strong enough to deprotonate both OH groups, which are subsequently carboxylated. The formation of **10c** from **7c** is probably prevented for the reasons suggested before in the case of **5e**. It is interesting to note that the formation of the cyclic carbonates takes place with total retention of the absolute configuration. Actually, starting from *meso*-**7a,** only *cis*-**8a** is obtained. This is in agreement with a reaction mechanism which does not involve the cleavage of the C–O bond at the chiral carbon atom.

Table 2. Carboxylation of **5a–f** and **7a–c** (PB = **4**; Pt anode and cathode; catholyte = CH_3CN/0.1 M TEAP; T = 0 °C; I = 15 $mAcm^{-2}$)

Entry	Substrate	mF[a]	Products (yield%[b])
1	**5a**	6.0	**6a** (88) [74]
2	**5b**	6.0	**5b** (20), **6b** (80) [66]
3	**5c**	6.0	**6c** (90)
4	**5d**	6.0	**6d** (34) [31]
5	**5d**	8.0	**6d** (50)
6	**5d**	12.0	**6d** (52)
7	**5e**	6.0	**5e** (98)
8	**5f**	6.0	**5f** (51)[c]
9	**7a**	4.0	**7a** (71), **8a** (20), **9a** (7), **10a** (2)
10	**7a**	6.0	**7a** (63), **8a** (29), **9a** (4), **10a** (4)
11	**7a**	8.0	**7a** (62), **8a** (30), **9a** (2), **10a** (5)
12	**7a**	12.0	**7a** (50), **8a** (29) [30], **9a** (5) [2], **10a** (12) [7]
13	**7b**	6.0	**7b** (45), **8b** (18) [24], **9b** (11) [4], **10b** (9) [9]
14	**7b**	12.0	**7b** (38), **8b** (28), **9b** (10), **10b** (16)
15	**7c**	6.0	**7c** (62), **8c** (19) [27], **9c** (18) [9]
16	**7c**	12.0	**7c** (55), **8c** (21), **9c** (15)

[a] Total current amount in mF. – [b] HPLC (GC in entry 3) yields are given in parentheses; isolated yields in square brackets. – [c] PhOEt was detected by HPLC analysis.

Conclusion

We have developed a new method of carboxylation of alcohols with CO_2 based on the employment of electrogenerated bases. It allows the formation of linear carbonates from primary and secondary alcohols in excellent to good yields, respectively. Tertiary alcohols and phenols do not react at all, so that selective carboxylation of suitable polyhydroxy compounds can be anticipated. 1,2-Diols are converted into a mixture of cyclic and linear carbonates, the latter being precursors of the former. Dicarbonates are also formed, but not when a tertiary hydroxy group is present in the molecule. If compared to the previously described electrochemical methods, the use of EGBs sharply increases the yields of organic carbonates from alcohols and CO_2. Of relevant interest, owing to its wide and multi-purpose applications in chemical industry, is the achievement of a 90% yield of dimethyl carbonate. The mild and safe conditions, which avoid the use of dangerous and polluting reagents, together with the high yields attained, make this procedure advantageous with respect to the already available methods especially for the carboxylation of primary alcohols.

Experimental Section

General Remarks: The electrochemical apparatus, the cells, and the reference electrode have already been described.[3] The value of the working potentials are reported relative to SCE. Acetonitrile (Riedel-de Haën), *N,N*-dimethylformamide (Riedel-de Haën) and tetraethylammonium perchlorate (TEAP, Fluka) were purified as previously described.[10] All the starting materials and dimethyl carbonate **6c** are commercially available. – Column chromatography (c.c.) was performed on Merck silica gel (70–230 mesh; 100 g per 1 g of crude reaction mixture). – IR, NMR, HPLC, GC and melting point apparatus were as previously described. [3] – ^1H NMR spectra were recorded as solutions in $CDCl_3$, with Me_4Si as internal standard. – HPLC analyses were carried out using a Merck Hibar LiChrocart (250–4, 5 μm) RP-18 column with a CH_3CN/H_2O mixture in a linear gradient from 35:65 to absolute CH_3CN over 20 min as eluent in the case of the solutions from **5a,b,d−f.** The same mixture, in a linear gradient from 30:70 to 60:40 over 12 min, followed by an isocratic step at this composition during 10 min, was used when starting from **7a,b**. Finally, an $MeOH/H_2O$ mixture in a linear gradient from 30:70 to 60:40 over 10 min and a further isocratic step at this composition during 10 min was employed when starting from **7c** and to quantify alcohol **7b**. The flow rate was always 1 mL min^{-1}. – GC analyses of the solution from **5c** were carried out using a Supelco Porapack PS 100 packed column (6 feet × 1/8 inch) in the range 90–190 °C. – Quantitative HPLC analyses were performed with the internal standard method, whereas a calibration curve was used in the case of GC analyses.

Chemistry: Ethyl carbonates **6**, cyclic carbonates **8,** and monocarbonates **9b,c** were prepared and characterized following a known procedure.[3,4] The monocarbonate **9a** and dicarbonates **10a,b** were obtained by reacting equimolar amounts of the corresponding diol and ethyl chloroformate according to standard procedures,[11] and purified by c.c. with a mixture of light petroleum/AcOEt (3:2) in the case of **9a** and **10a** and $CHCl_3/Me_2CO$ (95:5) in the case of **10b** as eluents.

Ethyl 2-Hydroxy-1,2-diphenylethyl Carbonate (9a): IR (film): ν = 3500, 1745 cm^{-1}. – ^1H NMR: δ = 1.18 (t, J = 7.2 Hz, 3 H, CH_3), 2.28 (s, 1 H, OH), 4.04 (q, J = 7.2 Hz, 2 H, OCH_2), 4.98 (d, J = 5.8 Hz, 1 H, C*H*OH), 5.70 (d, J = 5.8 Hz, 1 H, CHO), 7.25 (s, 10 H, arom). – ^{13}C NMR: δ= 14.10, 64.16, 76.01, 82.40, 126.96, 127.64, 127.69, 128.04, 128.11, 128.18, 128.52, 135.82, 139.25, 154.22. – $C_{17}H_{18}O_4$ (286.31): calcd. C 71.31, H 6.34; found C 71.15, H 6.24.

Ethyl 2-Ethoxycarbonyloxy-1,2-diphenylethyl Carbonate (10a): m.p. 110–112 °C. – IR (nujol) ν = 1748 cm^{-1}. – ^1H NMR: δ = 1.12 (t, J = 7.2 Hz, 3 H, CH_3), 1.23 (t, J = 7.2 Hz, 3 H, CH_3), 4.10 (q, J = 7.2 Hz, 2 H, OCH_2), 4.11 (q, J = 7.2 Hz, 2 H, OCH_2), 5.90 (s, 2 H, 2 × CH), 7.24–7.30 (m, 10 H, arom). – ^{13}C NMR: δ= 14.08, 64.23, 79.92, 127.61, 128.06, 128.51, 135.19, 154.11. – $C_{20}H_{22}O_6$ (358.38): calcd. C 67.02, H 6.19; found C 66.85, H 6.08.

Ethyl 2-Ethoxycarbonyloxy-1-phenylethyl Carbonate (10b): IR (film) ν = 1750 cm^{-1}. – ^1H NMR: δ = 1.28 (t, J = 7.2 Hz, 3 H, CH_3), 1.30 (t, J = 7.2 Hz, 3 H, CH_3), 4.18 (q, J = 7.2 Hz, 2 H, OCH_2), 4.20 (q, J = 7.2 Hz, 2 H, OCH_2), 4.36 (d, J = 5.5 Hz, 2 H, CHC*H*$_2$), 5.87 (t, J = 5.5 Hz, 1 H, C*H*CH_2), 7.38 (s, 5 H, arom). – ^{13}C NMR: δ= 14.09, 14.14, 64.23, 68.98, 76.88, 126.62, 128.69, 128.86, 135.68, 154.28, 154.78. – $C_{14}H_{18}O_6$ (282.28): calcd. C 59.56, H 6.43; found C 59.49, H 6.31.

Electrochemistry

Reduction of Probases 1–3: The controlled-potential electrolyses were carried out at a mercury pool cathode by stepwise addition of the probase to a solution of **5a** (2 mmol) in CH_3CN/0.1 M TEAP (50 mL) where CO_2 was bubbling. The working potential value allows the selective reduction of the PB. At the end of the reduction, EtI (10 mmol) was added, and the mixture was maintained at room temperature under stirring overnight. It was then analyzed.

Reduction of Probase 4: The electrolyses were carried out under galvanostatic control ($I = 15$ mA cm^{-2}) at a platinum gauze cathode on solutions of **4** (5 mmol for current amounts up to 8.0 mF, 10 mmol for 12.0 mF) in CH_3CN/0.1 M TEAP (50 mL). After the consumption of the predetermined number of mF, the current was switched off, the substrate (2 mmol) was added to the mixture and, 10 min later, the bubbling of CO_2 was started and maintained for 1 h. EtI (MeI in the reaction of **5c**) (10 mmol) was added, the solutions were stirred overnight at room temperature, and then analyzed. When the components of the mixtures were separated, a 1 mL sample was withdrawn for HPLC analysis. The solvent was removed from the remaining solution under reduced pressure and the residue was extracted with Et_2O (5 × 30 mL). The solvent was further removed from the combined organic extracts under reduced pressure. Column chromatography of the residues [with eluent mixtures of light petroleum/AcOEt (4:1) for substrates **5a,d** and (3:2) for **5b** and **7a,b**] allowed the separation of the products, whose identity was established by comparison with known standards.

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[7] It is well established that the reduction of **1** needs 2F/mol to give the divalent EGB, whereas halo compounds such as **2** and **3** undergo a two-electron reductive cleavage to halide and carbanion. It follows that, in theory, in order to use the same number of equivalents of EGB, a twofold molar amount of **2** and **3** with respect to **1** must be employed.

[8] The reduction of **4** needs 1F/mol to give an equivalent of EGB. In general, under galvanostatic control conditions, an excess of electroactive substrate is necessary to avoid the discharge of the supporting electrolyte. Nevertheless in the literature (refs.[5d,6]) an excess of current (1.5–2.0 F/mol) is employed to ensure the complete reduction of the PB. We have chosen to use an excess of PB and 4.0 mF to compare the efficiency of this EGB with the others and, later on, to investigate the influence of PB concentration and current amount.

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