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The reaction of amines with an electrogenerated base. Improved synthesis of arylcarbamic esters

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Abstract

The electrogenerated base of 2-pyrrolidone reacts with amines and anilines yielding the corresponding alkyl and aryl carbamates, after addition of carbon dioxide and ethyl iodide. Arylcarbamic esters are obtained in very good yields under mild reaction conditions with respect to the methods so far reported. © 2000 Elsevier Science Ltd. All rights reserved.

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Organic carbamates find several applications in the chemical, pharmaceutical and agricultural industries in the syntheses of intermediates, polymers, medical drugs, pesticides, herbicides and fungicides.¹ In classical organic syntheses, this class of compounds finds extensive utilization as protecting groups of the amine functionality in the preparation of polypeptides or other natural substances.² Consequently, alternative syntheses of carbamates to the classical methods, which employ toxic and corrosive reagents like phosgene and its derivatives, have been studied and proposed in the last few years.³

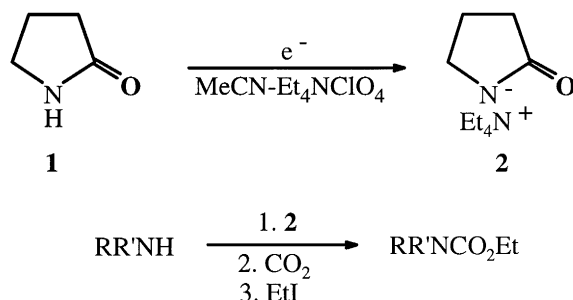
Our research group is engaged in the electrochemical synthesis of carbamic esters using carbon dioxide, a cheap and abundant reagent, as a raw material and potential source of carbon. We found that linear and cyclic carbamates may be obtained by reaction of electrochemically generated tetraethylammonium carbonate (TEAC) and tetraethylammonium peroxodicarbonate (TEAPC) with aryl and alkyl amines, followed, if necessary, by the addition of a suitable alkylating reagent. TEAC and TEAPC were obtained by electrolysis carried out in solutions (MeCN–Et₄NClO₄) saturated with CO₂^{4a} (E=–2.1 V versus SCE) or with a mixture of O₂–CO₂^{4b,c} (E=–1.0 V versus SCE). Both methods provide carbamates in good to excellent yields. Aryl amines were found to be less reactive than the corresponding aliphatic ones.

The electrochemical reduction of CO₂ to CO₂^{•–}, in aprotic solvents, involves three competing pathways yielding oxalate, carbonate (plus CO in equimolar amounts) and formate anions.⁵ The product

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distribution is strongly affected by the cathodic material, the current density and the concentration of CO_2 and H_2O . Consequently, the selective formation of TEAC requires careful choice and control of the conditions of electrolysis.⁶ Moreover, the weak oxidizing power of TEAPC solutions has been observed by several authors.⁷ Therefore, the use of TEAPC as a carboxylating agent towards aminic substrates containing easily oxidizable functional groups is not recommended.

Here we present a novel electrochemical synthesis of alkyl- and arylcarbamic esters that does not resort to the direct reduction of CO_2 or O_2 . This synthesis is based upon the reaction of amines and anilines with a 2-pyrrolidone electrogenerated base (associated with the Et_4N^+ cation)⁸ (**2**) followed by sequential addition of carbon dioxide and ethyl iodide (Scheme 1). Electrogenerated bases (EGBs) are usually obtained by cathodic reduction of appropriate precursors (not necessarily bases), the so-called probases (PBs) (e.g. azocompounds, activated alkenes, oxygen, 2-pyrrolidone). The widespread applications of electrogenerated bases in electro-organic synthesis have been extensively reviewed⁹ and new possible utilizations have been recently suggested.¹⁰



Scheme 1. Reaction of amines with the EGB of 2-pyrrolidone

The EGB was obtained by reduction of 2-pyrrolidone on a Pt cathode under galvanostatic control.⁸ The anion **2** was able to deprotonate different aliphatic and aromatic amines yielding the corresponding tetraethylammonium amides or anilides,[†] which can then react with carbon dioxide and EtI to give the required carbamate. The yield of carbamate was affected by different parameters including the molar ratio pyrrolidone:amine and the number of faradays per mole of probase supplied to the electrodes. Some results are reported in Table 1, entries 1–9. The highest yields for ethyl cyclohexyl carbamate were obtained when a molar ratio of pyrrolidone:amine of 2:1 and 1.5 F per mole of probase were used (entry 6). As reported in Table 1, the reaction with anilines allows arylcarbamic esters to be obtained in very good yields, especially if compared with the results of our previous methods employing TEAC, TEAPC, or with the other ‘phosgene-free’ methods reported in the literature.^{3,4a,b,12} In any case, the reaction yields were affected by the nature and the position of the substituent (either EWG or EDG) present on the aromatic ring.

In a typical experiment, a solution of **1** (2.0 mmol) in acetonitrile 0.1 mol L^{-1} in tetraethylammonium perchlorate (20 mL) was electrolyzed, under Ar, at 0°C , in a divided cell (Pt anode and cathode) under galvanostatic control ($I=25 \text{ mA cm}^{-2}$). After the flow of 1.5 F mol^{-1} of PB, the solution was warmed to room temperature and the amine (1.0 mmol) was added. The reaction mixture was stirred under Ar for an additional 15 min, and then carbon dioxide was bubbled into the stirred solution for 1 h, followed by the addition of a fivefold molar excess of ethyl iodide. The usual work-up⁴ gave the corresponding carbamates according to the reaction yields reported in Table 1.

[†] Several tetraethylammonium anilides (e.g. tetraethylammonium diphenylamide) have been isolated and characterized.¹¹

Table 1
Reaction of alkyl and aryl amines (1.0 mmol) with 2-pyrrolidone (PB), CO₂ and EtI (5.0 mmol) under different reaction conditions

Entry	R	R ¹	PB (mmol)	F mol ⁻¹ of PB	Yield of Carbamate (%) ^a
1	C ₆ H ₁₁	H	1.0	1.0	33
2	C ₆ H ₁₁	H	1.0	1.5	43
3	C ₆ H ₁₁	H	1.0	2.0	49
4	C ₆ H ₁₁	H	1.0	3.0	57
5	C ₆ H ₁₁	H	2.0	1.0	74
6	C ₆ H ₁₁	H	2.0	1.5	80
7	C ₆ H ₁₁	H	2.0	2.0	70
8	C ₆ H ₁₁	H	2.0	2.5	68
9	C ₆ H ₁₁	H	3.0	1.0	65
10	PhCH ₂	H	2.0	1.5	75
11	Ph(CH ₂) ₃	H	2.0	1.5	81
12	CH ₂ =CHCH ₂	H	2.0	1.5	63
13	PhCH ₂	Me	2.0	1.5	73
14	Ph	H	2.0	1.5	70
15	4-MeOPh	H	2.0	1.5	89
16	2-ClPh	H	2.0	1.5	33
17	3-ClPh	H	2.0	1.5	60
18	4-ClPh	H	2.0	1.5	80
19	3-Br-4-MePh	H	2.0	1.5	72
20	4-NO ₂ Ph	H	2.0	1.5	28

a: Yields refer to isolated carbamates and are based on the starting amine. All products were identified by comparison with authentic samples or with literature data except for Ethyl 3-bromo-4-methylphenyl-carbamate.¹³

In conclusion, a new electrochemical methodology that allows the synthesis of carbamates from primary and secondary amines and CO₂ in high yields, under mild conditions and avoiding the use of toxic and hazardous chemicals, has been designed and set up. The carboxylation of amine substrates, in solutions containing large counter-ions such as Et₄N⁺, is made possible by the deprotonating action of a 2-pyrrolidone electrogenerated base (**2**) under the reported conditions. The aryl carbamates have been obtained in remarkably high yields in comparison to the previously reported methods.

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13. Ethyl 3-bromo-4-methylphenyl carbamate. ¹H NMR (CDCl₃, 200 MHz) δ: 7.40 (d, 1H, J=8.6 Hz, Ar); 7.28 (d, 1H, J=2.5 Hz, Ar); 7.06 (dd, J=2.5; 8.6 Hz, Ar); 6.51 (brs, 1H, NH); 4.20 (q, 2H, J=7.1 Hz, CH₂CH₃), 2.34 (s, 3H, PhCH₃); 1.29 (t, 3H, J=7.1 Hz, CH₂CH₃). ¹³C NMR (CDCl₃, 50.3 MHz) δ: 153.4, 138.5, 137.1, 132.6, 120.8, 118.4, 117.6, 61.3, 22.9, 14.5. GC-MS *m/z*: 259 (100); 257 (94); 200 (32); 198 (27); 187 (34); 185 (38); 105 (42); 104 (24); 77 (36); 51 (26). Anal. calcd for C₁₀H₁₂BrNO₂: C, 46.53; H, 4.69. Found C, 46.41; H, 4.76.