Electrosynthesis of cyclic carbamates from aziridines and carbon dioxide

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A new and selective synthesis of five-membered ring cyclic carbamates involving nickel-catalyzed CO_2 incorporation into aziridines under mild electrochemical conditions was carried out in good yields.

Within our ongoing interest in carbon dioxide incorporation into small heterocyclic ring systems,[1,2] we present here our results on carbon dioxide incorporation into aziridines for the synthesis of 2-oxazolidones. 2-Oxazolidones are an important class of heterocyclic five-membered ring compounds.[3] These cyclic carbamates show good antibacterial properties[4,5] and are widely used in pharmaceutical chemistry.[6]

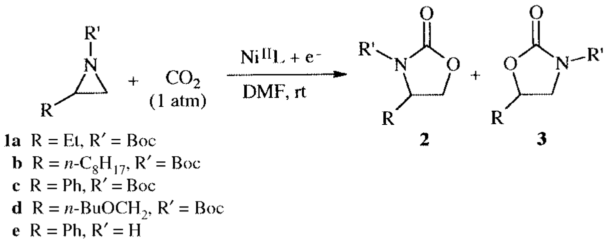
Their synthesis generally proceeds through the condensation of 1,2-aminoalcohols with toxic carbonyl derivatives such as phosgene[7] or cyanic acid (from urea decomposition).[8] The direct addition of CO_2 to β-amino alcohols at high pressure and temperature has been described in the patent literature.[9] Other methods of synthesis of 2-oxazolidones include the reaction of epoxides with cyanuric acid[10] or isocyanates[11] or the reaction of alkenes with *N*-bromosuccinimide and isocyanates.[12] 2-Oxazolidones can also be obtained from α-ketols and isocyanates or chloroformates.[13]

The direct functionalization of aziridines to cyclic carbamates has been reported *via* flash vacuum pyrolysis at 600 °C in the presence of ethyl chlorocarbonate[14] and by reaction with CO_2 at high pressure (50 atm, 60 °C) in the presence of tetraphenylantimony halides.[15]

We describe now a new and selective method of 2-oxazolidone synthesis using a simple electrochemical procedure, by which the cyclic carbamates **2** and **3** can be obtained in good yields from the direct reaction of substituted aziridines **1** with CO_2. Carbon dioxide insertion into the C–N bond of the aziridine ring takes place under very mild conditions, at room temperature and with atmospheric carbon dioxide pressure (Scheme 1). This new carboxylation reaction widens the field of utilization of CO_2 as a C-1 building block for organic chemicals.[16]

The reaction was catalyzed by a Ni(II) complex (10 mol%) and was carried out in a single-compartment cell fitted with a consumable magnesium anode and an inert cathode (*e.g.* stainless steel). Electrolyses were conducted at constant intensity in DMF as the solvent, and $[Ni(bipy)_3][BF_4]_2$ (bipy = 2,2′-bipyridine) was shown to be an efficient catalyst for this carboxylation. This same Ni(II)–bipy complex has already been used as a catalyst in other carbon dioxide incorporation reactions (*e.g.* into alkynes[17] or diynes[18]).

The electrochemical carboxylation of the *N*-Boc protected aziridine **1a**[19] led to the cyclic carbamates as a 60 : 40 mixture of two regioisomers **2a** and **3a** in 83% yield and 60% aziridine conversion (Table 1, entry 1). The major isomer corresponds to the incorporation of CO_2 at the less hindered side of the monosubstituted aziridine. No reaction occurred in the absence of current and in the absence of the nickel catalyst a very low yield of cyclic carbamates was obtained (< 10%).



Scheme 1

From a mechanistic point of view, oxidation of the magnesium rod to Mg^{2+} ions in solution takes place at the anode. At the cathode, the reduction of the Ni(II) complex to Ni(0) occurs reversibly at −1.2 V *vs.* SCE. Cyclic voltammetry showed that upon addition of **1a** to the Ni(II)–bipy solution, the reduction peak of the Ni(II)/Ni(0) transition at −1.2 V became irreversible. This was taken to indicate that the electrogenerated Ni(0) reacted with **1a** by a possible insertion into the C–N bond of the aziridine ring. The oxidative addition of Ni(0) complexes to oxirane rings has already been reported.[20]

Table 1 Ni-catalyzed electrochemical CO_2 incorporation into aziridines[a]

Entry	Aziridine	Catalyst[b]	Conditions[c]	Conversion (%)	Carbamate yield[d] (%)	Ratio **2** : **3**
1	**1a**	Ni–bipy	Mg/st. steel KBr	60	83	60 : 40
2	**1a**	Ni–bipy	Mg/Ni KBr	20	100	75 : 25
3	**1a**	Ni–bpy	Mg/C KBr	45	88	50 : 50
4	**1a**	Ni–bipy	Al/st. steel KBr	30	50	66 : 34
5	**1a**	Ni–bipy	Mg/st. steel NBu_4BF_4	30	85	76 : 24
6	**1a**	Ni–bipy	Mg/st. steel KCl	45	75	73 : 27
7	**1a**	Ni–cyclam	Mg/st. steel KBr	85	94	75 : 25
8	**1b**	Ni–cyclam	Mg/st. steel KBr	65	93	67 : 33
9	**1c**	Ni–cyclam	Mg/st. steel KBr	99	94	78 : 22
10	**1d**	Ni–cyclam	Mg/st. steel KBr	99	100	86 : 14
11	**1e**	Ni–cyclam	Mg/st. steel KBr	63	100	84 : 16

[a] *General electrochemical conditions*: into a single-compartment cell[21] of *ca.* 50 mL capacity fitted with the corresponding couple of electrodes, 40 mL of freshly distilled DMF, the supporting electrolyte (2×10^{-2} M), the Ni(II) catalyst (0.3 mmol) and aziridine **1** (3 mmol) were introduced. The solution was stirred at room temperature and CO_2 was bubbled into it at atmospheric pressure. The electrodes were connected to a stabilized constant current supply (Sodilec, EDL 36.07) and electrolyzed at 60 mA (corresponding to a current density of *ca.* 0.3 A dm^{-2}) for 7 h, until the consumption of **1** was negligible. The reaction mixture was then stirred at 50 °C overnight, hydrolyzed with aqueous HCl and extracted with ethyl acetate. The crude product was analyzed by GC, NMR and mass spectrometry, purified by column chromatography on silica gel and the identity of the carbamate products compared to the known compounds. [b] Ni–bipy = $[Ni(bipy)_3][BF_4]_2$, Ni–cyclam = $[Ni(cyclam)]Br_2$; both are 10 mol% with respect to the aziridine **1**. [c] The experimental conditions relate to the anode/cathode couple of electrodes and the supporting electrolyte (2×10^{-2} M). [d] The carbamate yields of **2** + **3** are calculated on the basis of converted aziridine.

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On the other hand, electrogenerated Ni–bipy complexes are also known to catalytically react with CO_2 to form its radical anion,[17,22] which, under the reaction conditions, undergoes reductive dimerization to oxalate.

In the electrocarboxylation of aziridines (Scheme 1), there is a competition for the electrogenerated Ni(0) complexes between two processes: (i) Ni(0) insertion into the aziridine ring followed by further CO_2 uptake and ring closure to the carbamate and (ii) CO_2 reduction to oxalate. This competition, which was very dependent on the reaction conditions, accounts for the limited aziridine conversion rates in some cases.

The influence of several factors such as the nature of the electrodes, the supporting electrolyte and of the ligand(s) attached to nickel were examined in the electrocarboxylation of **1a**. As regards the electrode, a magnesium/stainless steel couple afforded the best results, as compared to the use of carbon fiber or nickel foam as cathodes (compare Table 1, entries 1–3). When an aluminium anode was used (with several cathode materials) low aziridine conversions and low carbamate yields (*e.g.* Table 1, entry 4) were observed, with CO_2 electroreduction being favored. Among supporting electrolytes, KBr, KCl and NBu_4BF_4 were tested with Mg/stainless steel electrodes. The use of NBu_4BF_4 (Table 1, entry 5) afforded a good yield of carbamate but a low conversion of **1a** while KCl led to a conversion of 45% (Table 1, entry 6); KBr afforded the best results (Table 1, entry 1).

In the related CO_2 incorporation into oxirane rings for the synthesis of cyclic carbonates,[2] we showed that both 2,2′-bipy and cyclam ligands on nickel (cyclam = 1,4,8,11-tetraazacyclotetradecane) were effective for the CO_2 insertion reaction. In the electrocarboxylation of **1a**, the use of [Ni(cyclam)]Br_2 as the catalyst afforded **2a** and **3a** in 94% yield with 85% aziridine conversion (Table 1, entry 7). With the Ni–cyclam catalytic system the electroreduction of carbon dioxide was almost completely inhibited, in favor of aziridine carboxylation. The observed regioselectivity **2a**:**3a** was 75:25.

The reaction was then extended to the carboxylation of several monosubstituted aziridines **1b–e** with [Ni(cyclam)]Br_2 as the catalyst. Thus, aliphatic, aromatic or ether substituted *N*-Boc aziridines (Table 1, entries 8–10) led regioselectively to the corresponding carbamates in good yields and excellent conversions (Table 1, entries 9, 10). The electrocarboxylation of the non-protected N–H aziridine **1e** was also efficient and led to a 84:16 regioisomeric ratio of **2e**:**3e** in quantitative yield and with a 63% conversion (Table 1, entry 11).

In conclusion, a novel catalytic system for incorporation of CO_2 into aziridines for the synthesis of cyclic carbamates was developed. Use of stable and readily available Ni(II) complexes of cyclam or bipyridine ligands and application of simple preparative electrochemical conditions, led to efficient catalytic insertion of the carbon dioxide into the C–N bond of aziridines with regioselectivities of 60–86%.

The electrochemical method described here employs very mild experimental conditions (CO_2 pressure of 1 atm, 20 °C), as compared to existing methods, which require harsh conditions or the use of toxic starting materials such as phosgene. It is also worth noting that this reported method utilizes carbon dioxide as the starting C-1 carbon source, and constitutes a new example in the field of green and catalytic chemistry.

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