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New Synthesis of Oxazolidin-2-ones

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Abstract: Electrochemically generated tetraethylammonium peroxydicarbonate (TEAPC) and tetraethylammonium carbonate (TEAC) react under very mild conditions, with 1,2-amino alcohols affording, after addition of tosyl chloride, the corresponding oxazolidin-2-ones in fair to good yields.

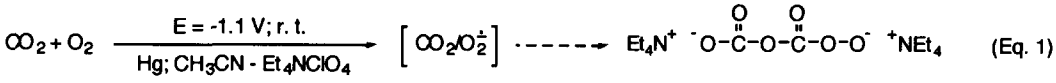
Keywords: amino alcohols; carboxylation; electrochemistry; oxazolidinones.

Chiral oxazolidin-2-ones (Evans' chiral auxiliaries[1]) are perhaps amongst the most useful chiral auxiliaries used in asymmetric synthesis.[2a] Typical chemical syntheses of oxazolidin-2-ones employ toxic and harmful reagents (*e.g.*, phosgene, isocyanates, etc.) and/or involve high temperatures.[2a] At present, diethyl carbonate is the normal reagent of choice for the preparation of Evans' auxiliaries (120 °C, 10 % cat. K_2CO_3).[2b]

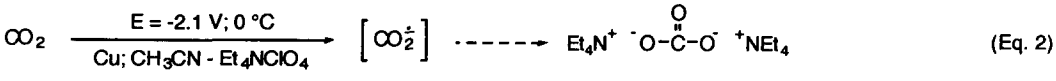
Recently, we studied the reactivity of electrochemically generated tetraethylammonium peroxydicarbonate (TEAPC)[3] or tetraethylammonium carbonate (TEAC)[4] solutions as carboxylating agents, towards amines[4,5] and alcohols.[6]

We have since studied the reactivity of these solutions towards 1,2-amino alcohols, hoping to obtain the synthesis of oxazolidin-2-ones; here we wish to report the relevant results.

Electrochemically generated TEAPC (Eq. 1) and TEAC (Eq. 2) solutions react with 1,2-amino alcohols affording, after addition of tosyl chloride, the corresponding oxazolidin-2-ones in fair to good yields.

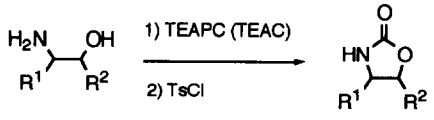


(Eq. 1)



(Eq. 2)

In a typical procedure, the amino alcohol (1.0 mmol) was added to a stirred solution of TEAPC or TEAC (1.5 mmol) in MeCN - TEAP (30 ml) at room temperature. After 2 h, a fivefold molar excess of tosyl chloride was added and the mixture was allowed to stand at 25 °C for 10 h. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel to afford the corresponding oxazolidin-2-one.



(Eq. 3)

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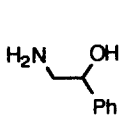
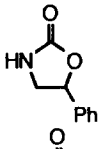
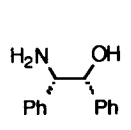
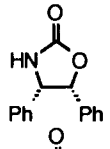
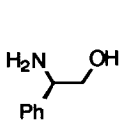
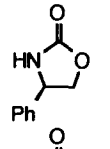
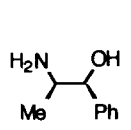
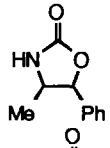
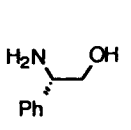
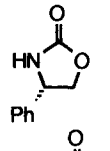
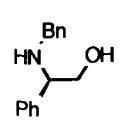
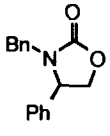
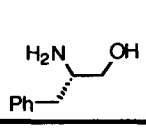
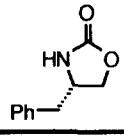
The behaviour of amino alcohols bearing primary and/or secondary alcohol and amine groups was investigated (Table 1). In every case oxazolidin-2-ones were isolated in good to high yields, irrespective of the carboxylating agent used (TEAPC or TEAC). In addition, we verified that the absolute configurations of all chiral atoms were unchanged.

Table 1. Reactions of Amino alcohols with TEAPC or TEAC and TsCl in MeCN-TEAP[a]

Entry	Substrate	Product[b]	Yield (%)[c]	Entry	Substrate	Product[b]	Yield (%)[c]
1			86[d] ; 61[e]	5			74[d] ; 72[e]
2			74[d] ; 77[e]	6			85[d] ; 84[e]
3			71[d] ; 77[e]	7			57[d] ; 58[e]
4			63[d] ; 74[e]				

[a] A molar ratio TEAPC or TEAC/amino alcohol of 1.5 was used; a fivefold molar excess of TsCl was added after 2 h. [b] All products were identified by comparison with authentic samples of commercially available products (entries 2-6) or with literature data (entry1),[7] except for (*R*)-(-)-*N*-benzyl-4-phenyloxazolidin-2-one (entry 7).[8] [c] Isolated yields, based on the starting amino alcohol. [d] Reaction with TEAPC. [e] Reaction with TEAC.

In conclusion, this method allows the synthesis of chiral oxazolidin-2-ones in a very mild way and in fair to good yields.

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8. **(*R*)-(-)-*N*-benzyl-4-phenyloxazolidin-2-one.** ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.41-7.09 (m, 10H, ar), 4.85 (d, 1H, J = 14.8 Hz, PhC*H*$_2$N), 4.59-4.45 (m, 2H, OC*H*$_2$), 4.17-4.04 (m, 1H, PhC*H*), 3.61 (d, 1H, J = 14.8 Hz, PhC*H*$_2$N). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 162.82, 137.44, 135.42, 129.32, 129.11, 128.72, 128.68, 127.96, 127.25, 69.60, 58.76, 45.85. GC-MS m/z: 253 (M^+, 10 %), 162 (M^+-Bn, 5 %), 104 ($PhCHCH_2^+$, 100 %), 91 ($PhCH_2^+$, 41 %). $[\alpha]_D^{20}$ = - 83.0 (c = 1.0, $CHCl_3$).