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Electrochemical Studies on Haloamides. Part XII[1]. Electrosynthesis of Oxazolidine-2,4-diones

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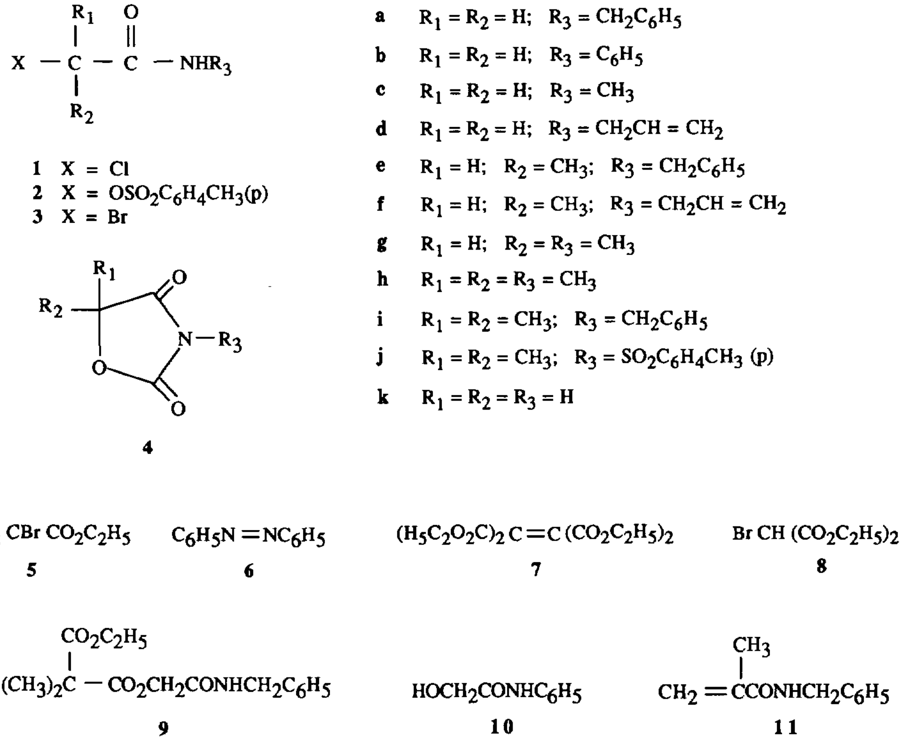
Abstract: Electrogenerated bases promote the carboxylation of NH-protic carboxamides bearing a leaving group at the position 2 to give oxazolidine-2,4-diones. The process is believed to involve acid-base reaction with the substrate, carboxylation of its conjugate base to the corresponding carbamate and ring-closure following intramolecular S_N2 reaction. A variety of oxazolidine-2,4-diones, including clinically used trimethadione® and malidone®, have been prepared in high to excellent yield, which established the scope and generality of this new ring-forming process.

INTRODUCTION

Oxazolidine-2,4-diones are a class of biologically active compounds. They are employed as anticonvulsants, in particular in the symptomatic treatment of absence seizures [2]. 3,5,5-Trimethyloxazolidine-2,4-dione (trimethadione®) is the most active, but even 5-ethyl-3,5-dimethyloxazolidine-2,4-dione (paramethadione®) and 3-allyl-5-methyloxazolidine-2,4-dione (malidone®) display interesting therapeutic properties [3]. Moreover, the recent discovery of the herbicidal activity of several compounds belonging to this class has remarkably improved the search for more efficient syntheses. Among the available methods, the most common routes to 3-substituted derivatives involve the reaction between aryl or alkyl isocyanates and α-hydroxyesters to give urethans, later cyclized by heating, or the introduction of the substituent at the position 3 in the pre-formed heterocycle[2]. In any case, the use of toxic and hazardous reagents and/or drastic conditions is required.

We now report an electrochemical synthesis of 3-substituted oxazolidine-2,4-diones which overcomes these drawbacks. The starting point of this investigation has been given by the results of a precedent study [1] concerning the carboxylation of 2-haloacetamides *via* their electrodic reduction in the presence of CO_2. 3-Benzyloxazolidine-2,4-dione has been recognized in the mixture obtained from 2-bromo-*N*-benzylacetamide; its formation has been ascribed to the addition of the conjugate base of the starting amide (deriving from an autoprotonation reaction of the first formed carbanion [4]) to CO_2, followed by cyclization of the resulting carbamate ion. Of course, no more than 50% yield of cycle could be achieved by this way. However, the conjugate base of the haloamide could be yielded quantitatively by reaction of the latter with an electrogenerated base (EGB), formed by reducing an appropriate probase (PB). The major advantages of this technique include the possibility to generate anionic species *in situ*, under mild conditions and controlling factors as base strenght and concentration. On this basis, we have planned the synthesis of oxazolidine-2,4-diones starting from amides bearing a good leaving group at the position 2, using CO_2 and EGBs. (Scheme 1).



$X-C(R_1)(R_2)-C(=O)-NHR_3$

1 X = Cl
2 X = $OSO_2C_6H_4CH_3$(p)
3 X = Br

4

a $R_1 = R_2 = H$; $R_3 = CH_2C_6H_5$
b $R_1 = R_2 = H$; $R_3 = C_6H_5$
c $R_1 = R_2 = H$; $R_3 = CH_3$
d $R_1 = R_2 = H$; $R_3 = CH_2CH = CH_2$
e $R_1 = H$; $R_2 = CH_3$; $R_3 = CH_2C_6H_5$
f $R_1 = H$; $R_2 = CH_3$; $R_3 = CH_2CH = CH_2$
g $R_1 = H$; $R_2 = R_3 = CH_3$
h $R_1 = R_2 = R_3 = CH_3$
i $R_1 = R_2 = CH_3$; $R_3 = CH_2C_6H_5$
j $R_1 = R_2 = CH_3$; $R_3 = SO_2C_6H_4CH_3$ (p)
k $R_1 = R_2 = R_3 = H$

$(CH_3)_2CBrCO_2C_2H_5$ **5**

$C_6H_5N{=}NC_6H_5$ **6**

$(H_5C_2O_2C)_2C{=}C(CO_2C_2H_5)_2$ **7**

$BrCH(CO_2C_2H_5)_2$ **8**

$(CH_3)_2C(CO_2C_2H_5)-CO_2CH_2CONHCH_2C_6H_5$ **9**

$HOCH_2CONHC_6H_5$ **10**

$CH_2{=}C(CH_3)CONHCH_2C_6H_5$ **11**

SCHEME 1

RESULTS AND DISCUSSION

The results of the HPLC analyses carried out on the solutions obtained from the reduction of PBs **5**-**7** in the presence of 2-chloro-*N*-benzylacetamide **1a** and CO_2 are reported in Table 1 (entries 1-3); **1a** has been selected as model compound because of its reduction potential value, which is compatible with those of the employed probases. By using ethyl 2-bromo-2-methylpropanoate **5** as PB, oxazolidine-2,4-dione **4a** is formed in low yield together with malonic derivative **9** and some unreacted **1a** (entry 1). The presence of **9** in the reduction mixture suggests that reaction pathways other than the acid-base reaction involve the electrochemically generated carbanion. A possible reactions sequence to **9** requires the carboxylation of the EGB and the alkylation of the intermediate carboxylate ion by starting **1a**. Better yield of **4a** have been obtained employing PBs **6**,**7** and among these tetraethyl ethylenetetracarboxylate **7** has given the higher value. Accordingly, **7** has been reduced in the presence of **1a** and CO_2 under different experimental conditions in a search for their optimization. In any case, carring out the electrolysis under galvanostatic control or changing the nature of the cathode or the solvent, very good yields of **4a** have been observed (Table 1, entries 4-6). However, the best yield of **4a** has been achieved by potentiostatic reduction of **7** at a mercury cathode and using DMF as solvent. Under these conditions, the electrolysis of **7** in the presence of CO_2 and several amides electroinactive at the working potential (**1-3**, Scheme 1), gives the corresponding oxazolidine-2,4-diones **4**. HPLC or GC analysis of the electrolyzed solutions are reported in Table 2.

The nature and the yields of the reaction products suggest some considerations. The yield of oxazolidine-2,4-dione is always very high when the substituent at the nitrogen atom is an alkyl group, whereas it decreases remarkably when an aryl group is present. In the mixture obtained from the reduction of **7** in the presence of **2b** and CO_2, only 40% of **4b** has been recovered together with the unexpected *N*-phenylglycolamide **10**. The low yield of the cyclic compound can be attributed to the poor nucleophilicity of the anion, owing to the charge delocalization on the aromatic ring. The formation of **10** can be ascribed to a homogeneous electron transfer reaction involving the radical anion of **7** and the substrate and giving the radical anion of **2b** which evolves to a sulphinate anion and an alkoxy radical, further reducible at the working potential. This behaviour of the EGB of **7** has been already described [5]. The electron transfer reaction occurs only when the carboxylation process is slow, that is when a substituent lowering the nucleophilicity is present at the nitrogen atom.

Concerning the leaving group effect, if the intramolecular S_N2 reaction takes place on a primary carbon, the nature of the leaving group does not influence the yield of the cycle. On the contrary, if the cyclization involves

Table 1. Synthesis of *N*-Benzyloxazolidine-2,4-dione **4a** from 2-Chloro-*N*-benzylacetamide **1a**: Choose of the Most Appropriate Conditions.

Entry	Cathode	SSE[a]	Probase	Molar ratio PB/substrate	-E(V)	Products (yield%)[b]
1	Hg	A	**5**	1.1	1.2	**4a** (33), **1a** (16) **9** (40)
2	Hg	A	**6**	0.5	1.5	**4a** (85)
3	Hg	A	**7**	0.5	1.2	**4a** (93)
4	Hg	B	**7**	0.5	1.2	**4a** (85)
5	C	A	**7**	0.5	1.2	**4a** (85)
6	Hg	A	**7**	0.6	c	**4a** (89), **1a** (4)

[a] Solvent Supporting Electrolyte system: A = DMF - 0.1 mol l^{-1} TEAP; B = AN - 0.1 mol l^{-1} TEAP. [b] HPLC analysis. [c] The electrolysis, performed under galvanostatic control (I = 5.0 mA cm^{-2}), was stopped after the flow of 1F per mol of amide.

a secondary carbon, the yield of oxazolidine-2,4-dione strictly depends on the leaving group nature. For the same substrate, the yield of the cyclic compound is lower when the leaving group is chloride than when is *p*-toluenesulfonate (see yields of **4e** from **1e** and **2e**). For this reason, 3-allyl-5-methyloxazolidine-2,4-dione **4f** (malidone®) has been synthesized in excellent yield from **2f**.

The successive goal has been the one-step synthesis of 3,5,5-trialkyloxazolidine-2,4-diones starting from *N*,2,2-trisubstituted acetamides. The peak potential values of **7** and **3i** on Hg cathode are very close, making impossible the selective reduction of the PB in the presence of this substrate.Unfortunately, any attempt carried out under different experimental conditions in order to obtain **2i** from **3i** and silver *p*-toluenesulfonate, has given acrylamide **11** in almost quantitative yield. Therefore, the electrolysis of **7** has been performed in the presence of **3i** and CO_2 at vitreous carbon cathode. In fact, it is well known that the reduction potential of the C-Br bond, contrary to that pertinent to an olefinic double bond, is shifted toward more negative value by changing C for Hg as cathode, thus making possible the selective discharge at the electrode of **7** also in the presence of **3i**. Moreover, the electrode nature does not significantly influence the yield of the heterocycle (entries 3,5 in Table 1). Analysis of the electrolyzed solution showed the presence of only **11** and unreacted **3i**. The formation of **11** can be ascribed to a β-elimination reaction that occurs preferentially to an S_N2. Possibly, the acidity of the hydrogen atom on the carbon at the β position with respect to the carbonyl group is of the same order of magnitude of that of the amide hydrogen and the stability of the product drives the acid-base reaction between the EGB and the substrate to wards the formation of **11**. In order to increase the acidity of the NH group, the nature of the *N*-substituent has been changed. 2-bromo-2-methyl-*N*-tosylpropanamide **3j** has been synthesized, whose deprotonation can be performed even by the EGB from diethyl bromomalonate **8** [6]. The peak potential value of **8** allows its reduction in the presence of CO_2 and **3j** on Hg cathode. The EGB from **8** is able to selectively deprotonate the amide group (**11** is no more formed), but the conjugate base of the substrate, owing to the presence of a strong electronwithdrawing group as the tosyl, is not able to attack CO_2 and **3j** is recovered by extraction with $CHCl_3$ after treatment with mineral acid. On this basis, we have tried to obtain 3,5,5-trisubstituted oxazolidine-2,4-diones, through electrochemically induced alkylation of the parent 3,5-disubstituted compounds. Accordingly, **5** has been reduced in

Table 2. Synthesis of Oxazolidine-2,4-diones. PB: Tetraethyl ethylenetetracarboxylate **7**; Molar Ratio PB/substrate = 0.5; DMF - 0.1 mol l^{-1} TEAP; E = - 1.2 V; Hg Cathode; Pt Anode.

Starting amide	Products (yield %)
1a	**4a** (93)[a]
2a	**4a** (95)[a]
2b	**4b** (40)[a], **10** (30)[a]
1c	**4c** (89)[b]
1d	**4d** (92)[b]
1e	**4e** (51)[a], **1e** (48)[a]
2e	**4e** (99)[a]
2f	**4f** (95)[b]
2g	**4g** (86)[b]
3i[c]	**11** (34)[a], **3i** (65)[a]
3j[d]	**3j** (100)[a,e]
1k[f]	**4a** (54)[g]

[a] HPLC analysis. [b] GC analysis. [c] Vitreous carbon cathode. [d] **8** was employed as PB (E = - 0.6 V; molar ratio PB/substrate = 1.5). [e] After acidification. [f] Molar ratio PB/substrate = 1. [g] After alkylation *in situ* with $PhCH_2Br$

the presence of **4e** and methyl iodide: work-up of the electrolyzed mixture has given **4i** in good overall yield (75% from **2e**). The method has been extended to the synthesis of trimethadione® **4h**, by reducing **5** in the presence of **4g** and MeI. In this case the overall yield of **4h** is lower (~ 60% from **2g**) but still quite satisfactory.

Finally, in order to verify the usefulness of the electrochemical method also for the synthesis of 3-unsubstituted derivatives , the primary amide **1k** has been submitted to the carboxylation-cyclization process. As is known that these compounds are acidic enough to undergo acid-base reaction with the EGB [2], two equivalents of **7** have been reduced: **4k** has been recovered after extraction with organic solvents of the acidified electrolysis mixture. Alternatively, alkylation of the conjugate base of **4k** can be performed *in situ*, obtaining the corresponding 3-alkyloxazolidine-2,4-dione in good yield.

CONCLUSIONS

An electrochemical method for the synthesis of oxazolidine-2,4-diones, a class of biologically active compounds, starting from amides bearing a leaving group at the position 2 has been developed. 3,5-Disubstituted derivatives are obtained in excellent yield with a one-step procedure, while a two-step process, both electrochemical, gives 3,5,5-trisubstituted oxazolidinediones in good overall yield. The new synthetic method needs mild reaction conditions and the use of inexpensive and easy available reagents. If compared with the traditional chemical syntheses, where toxic and hazardous reagents and/or drastic conditions are required, the electrochemical method can be considered really advantageous.

EXPERIMENTAL

General. Column chromatography (c.c.) was performed on Merck silica gel (70-230 mesh; 100g per 1g of reaction mixture). Melting points were taken upon a Tottoli apparatus and are uncorrected. IR spectra were recorded on a Perkin Elmer 281B grating spectrophotometer. ^{1}H-NMR spectra were recorded for solutions in $CDCl_3$, using a Varian EM-390 spectrometer and the chemical shift values are reported relative to Me_4Si as internal standard. HPLC analyses were carried out on a Perkin Elmer system made up from a Series 4 LC, an LC 85B spectrophotometric detector, an LC Autocontrol and a Nelson 1020 data station, using a Merck Hibar LiChrocart (250-4; 7 μm) RP-18 column. A CH_3CN-H_2O 35:65 mixture was used as eluent in the analysis of the solutions containing **4a,e,g**. In all the other analyses, a CH_3CN-H_2O mixture in linear gradient from 1:9 to 9:1 in 25 min was employed. The flow was always 1 ml min^{-1}. GC analyses were carried out with a Perkin Elmer 8500 GC using a J and W fused silica megabore DB-WAX (30 m) column in the temperature range 130-150°C, depending on the nature of the oxazolidinedione. Quantitative HPLC and GC analyses were carried out with the internal standard method. All new compounds gave satisfactory elemental analyses (C ± 0.3% ; H ± 0.2%; N ± 0.2%). The electrochemical apparatus, the cells and the reference electrode were already described[7]. The values of the working potentials are reported relative to SCE.

N,N-Dimethylformamide (DMF, Aldrich) was distilled from activated alumina under reduced pressure. Acetonitrile (AN, Carlo Erba RS for HPLC) was distilled twice from CaH_2 and P_2O_5, respectively. Tetraethylammonium perchlorate (TEAP, Fluka) was purified as previously described[7]. The solution of the supporting electrolyte (0.1 mol l^{-1}) in the chosen solvent was percolated on activated alumina just before using.

Chemistry. Haloacetamides **1a,d,e,3i** were obtained by allowing the chloro(bromo)acyl chloride(bromide) and the corresponding amine (1:2 molar ratio) to react in CH_2Cl_2 solution at 0°C for 2h. After extraction with H_2O, 1 mol l^{-1} HCl and H_2O, the solution was dried (Na_2SO_4) and the solvent was removed under reduced pressure. **1a,e,3i** were purified by crystallization, **1d** by c.c. (light petroleum/acetone 1:1). **1c** was synthesized by reacting methyl chloroacetate and methylamine (35% in water) in 1:1 molar ratio in CH_3OH; after evaporation of the solvent, the solid residue was purified by crystallization.

N-Benzylchloroacetamide **1a**: m.p. 93-94°C (cyclohexane) (lit.[8] m.p. 93.5-94.5°C); *N*-methylchloroacetamide **1c**: m.p. 43 - 44°C (Et_2O) (lit.[9] m.p. 45 - 46°C); *N*-allylchloroacetamide **1d**: oil[10]; *N*-benzyl-2-chloropropanamide **1e**: m.p. 80 - 81°C (cyclohexane) (lit.[11] m.p. 80-82°C); *N*-benzyl-2-bromo-2-methylpropanamide **3i**: m.p. 71-72°C (light petroleum) (lit.[12] m.p. 72°C).

O-Tosylglycolamides **2a,b,e,g** were prepared by reacting the corresponding bromoamide with silver toluene-4-sulfonate. A solution of amide (5.7 mmol) and silver salt (7.1 mmol) in CH_3CN (40 ml) was refluxed under stirring for 12 h. After cooling, the solid was filtered off and the solvent was removed under reduced pressure. The residue was purified by c.c. (light petroleum-AcOEt 3:2 as eluent) and further crystallization. *N*-Benzyl-*O*-tosylglycolamide **2a**: m.p. 119-120°C (benzene-cyclohexane) (lit. [5] m.p. 119-120°C); *N*-phenyl-*O*-tosylglycolamide **2b**: m.p. 119-120°C (benzene-cyclohexane) (lit. [5] m.p. 119-120°C); *N*-benzyl-*O*-tosyllactamide **2e**: m.p. 72-73°C (cyclohexane); IR (nujol) ν: 3230, 1650, 1590 and 1550 cm^{-1}; ^1H-NMR δ (ppm) 1.47 (d, 3H, CH_3CH), 2.43 (s, 3H, CH_3), 4.45 (d, 2H, CH_2N), 4.95 (q, 1H, CHO), 6.6-7.0 (br s, 1H, NH), 7.1-7.5 (m, 7H, arom) and 7.87 (d, 2H, arom); *N*-allyl-*O*-tosyllactamide **2f**: m.p. 77-78°C (cyclohexane); IR (nujol) ν: 3220, 3080, 1650, 1590 and 1570 cm^{-1}; ^1H-NMR δ (ppm) 1.40 (d, 3H, CH_3CH), 2.43 (s, 3H, CH_3), 3.85 (t, 2H, CH_2N), 4.93 (q, 1H, CHO), 5.0-5.4 (m, 2H, CH_2=C), 5.5-6.1 (m, 1H, CH=C), 6.3-6.9 (br s, 1H, NH), 7.30 (d, 2H, arom) and 7.85 (d, 2H, arom); *N*-methyl-*O*-tosyllactamide **2g**: m.p. 78-80°C (cyclohexane); IR (nujol) ν: 3280, 1660 and 1580 cm^{-1}; ^1H-NMR δ (ppm) 1.23 (d, 3H, CH_3CH), 2.50 (s, 3H, CH_3), 2.80 (d, 3H, CH_3N), 4.90 (q, 1H, CHO), 6.1-6.9 (br s, 1H, NH), 7.30 (d, 2H, arom) and 7.83 (d, 2H, arom).

Bromotosylamide **3j** was prepared from 2-bromopropionyl bromide and toluene-4-sulfonamide as already described [6] and purified by c.c. (light petroleum-acetone 1:1) and further crystallization. 2-Bromo-2-methyl-*N*--tosylpropanamide **3j**: m.p. 100 - 102°C (cyclohexane); IR (nujol) ν: 3270, 1710 and 1590 cm^{-1}; ^1H-NMR δ (ppm) 1.87 (s, 6H, 2 x CH_3C), 2.43 (s, 3H, CH_3), 7.30 (d, 2H, arom), 7.97 (d, 2H, arom) and 8.7-9.1 (br s, 1H, NH).

Electrochemistry. The controlled-potential electrolyses were carried out by stepwise addition of the probase to the solution of the substrate in DMF (AN) - 0.1 mol l^{-1} TEAP (50 ml) where CO_2 was bubbling. At the end of the reduction, a 2 ml sample of the electrolyzed solution was taken off for HPLC or GC analysis. The solvent was removed under reduced pressure from the remaining solution and the solid was extracted with Et_2O (5 x 30 ml). H_2O (100 ml) was added to the insoluble in ether and the mixture was extracted with $CHCl_3$ (3 x 50 ml). When it was necessary, the water was acidified (1 mol l^{-1} HCl) and extracted again with $CHCl_3$ (3 x 50 ml). The extracts were dried (Na_2SO_4) and the solvent evaporated under reduced pressure. The residues were analyzed (IR, NMR and TLC) and combined if they have the same composition. C.c. of the mixtures allowed the separation of the electrolysis products for their characterization.

Reduction of 5-7 in the presence of 1a. **5** (1.00 g, 5.1 mmol) was reduced in the presence of **1a** (0.86 g, 4.7 mmol) and CO_2. C.c. of the residue from the Et_2O extract ($CHCl_3$/AcOEt 9:1) allowed the separation of **1a** (0.09 g, 12%), 3-benzyloxazolidine-2,4-dione **4a** (0.19 g, 22%), and ethyl benzylcarbamoylmethyl 2,2-dimethylmalonate **9** (0.32 g, 25%). The results of HPLC analysis carried out on the electrolysis mixture are reported in Table 1 (entry 1).

4a: m.p. 52-54°C (2-propanol) (lit. [13] m.p. 54-55°C); IR (nujol) ν: 1810 and 1730 cm^{-1}; ^1H-NMR δ (ppm) 4.63 (s, 2H, CH_2), 4.66 (s, 2H, CH_2) and 7.6-7.3 (m, 5H, arom).

9: IR (film) ν: 3330, 1730, 1660 and 1530 cm^{-1}; ^1H-NMR δ (ppm) 1.10 (t, 3H, CH_3CH_2), 1.40 (s, 6H, 2 x CH_3), 3.95 (q, 2H, CH_2), 4.35 (d, 2H, NCH_2), 4.75 (s, 2H, OCH_2CO) and 6.8-7.3 (m, 6H, arom + NH).

The solutions obtained from the reduction of PBs **6**,**7** in the presence of **1a** and CO_2, as well as those from the reduction of **7** under different experimental conditions were analyzed by HPLC. The electrolysis conditions, the molar ratio PB/substrate, the nature and the yields of the identified products are reported in Table 1. In all the experiences, the mixtures from the Et_2O and $CHCl_3$ extracts were analyzed by ^1H-NMR and IR, in order to confirm the nature of the products.

Reduction of 7 in the presence of 2a. **7** (0.55 g, 1.7 mmol) was reduced in the presence of **2a** (1.05 g, 3.3 mmol) and CO_2. C.c. of the residue from the combined extracts gave the reduced probase and **4a** (0.48 g, 80%).

Reduction of 7 in the presence of 2b. **7** (0.55 g, 1.7 mmol) was reduced in the presence of **2b** (1.00 g, 3.3 mmol) and CO_2. C.c. of the residue from the Et_2O extract (light petroleum-AcOEt 7:3 as eluent) gave the reduced probase and 3-phenyloxazolidine-2,4-dione **4b** (0.17 g, 30%). Eluition with AcOEt gave *N*-phenylglycolamide **10** [14] (0.05 g, 10%).

4b: m.p. 120-122°C (2-propanol) (lit. [13] m.p. 120-121°C); IR (nujol) ν: 1810 and 1730 cm^{-1}; ^1H-NMR δ (ppm) 4.80 (s, 2H, CH_2) and 7.30 (s, 5H, arom).

Reduction of 7 in the presence of 1c. **7** (0.85, 2.7 mmol) was reduced in the presence of **1c** (0.58 g, 5.4 mmol) and CO_2. The electrolyzed solution was quenched with H_2O (150 ml) and extracted with Et_2O (3 x 50 ml) and with $CHCl_3$ (3 x 50 ml). Each of the two different combined extracts was washed with H_2O (2 x 50 ml), dried (Na_2SO_4) and the solvent was removed under reduced pressure. ^1H-NMR of the residues

from the two extracts allowed the identification of the products. The residue from the Et_2O extract was the reduced probase, that from the $CHCl_3$ extract was 3-methyloxazolidine-2,4-dione **4c** (0.26 g, 47%).
4c: m.p. 124-126°C (cyclohexane) (lit. [15] m.p. 128°C); IR (nujol) ν: 1820 and 1730 cm^{-1}; ^{1}H-NMR δ (ppm) 3.07 (s, 3H, CH_3) and 4.70 (s, 2H, CH_2).

Reduction of 7 in the presence of 1d. **7** (0.55 g, 1.7 mmol) was reduced in the presence of **1d** (0.45 g, 3.4 mmol) and CO_2. C.c. of the residue from the combined extracts (light petroleum-AcOEt 7:3 as eluent) gave the reduced probase and 3-allyloxazolidine-2,4-dione **4d** (0.37 g, 80%).
4d: oil (lit. [13] b.p.$_8$ 120-124°C); IR (film) ν: 1810 and 1720 cm^{-1}; ^{1}H-NMR δ (ppm) 4.20 (d, 2H, CH_2N), 4.76 (s, 2H, CH_2), 5.2-5.6 (m, 2H, CH_2=C) and 5.6-6.1 (m, 1H, CH=C).

Reduction of 7 in the presence of 2e. **7** (0.40 g, 1.3 mmol) was reduced in the presence of **2e** (0.85 g, 2.5 mmol) and CO_2. C.c. of the residue from the combined extracts (light petroleum-AcOEt 4:1 as eluent) gave the reduced probase and 3-benzyl-5-methyloxazolidine-2,4-dione **4e** (0.41 g, 81%).
4e: m.p. 73-75°C (2-propanol) (lit. [13] m.p. 73-75°C); IR (nujol) ν: 1820 and 1730 cm^{-1}; ^{1}H-NMR δ (ppm) 1.50 (d, 3H, CH_3), 4.77 (q, 1H, CH), 4.83 (s, 2H, CH_2) and 7.33 (s, 5H, arom).

Reduction of 7 in the presence of 1e. **7** (0.79 g, 2.5 mmol) was reduced in the presence of **1e** (0.97 g, 4.9 mmol) and CO_2. ^{1}H-NMR of the residues from the two extracts confirmed the nature of the electrolysis products, whose yields were obtained by HPLC and are reported in Table 2.

Reduction of 7 in the presence of 2f. **7** (0.47 g, 1.5 mmol) was reduced in the presence of **2f** (0.82 g, 2.9 mmol) and CO_2. C.c. of the residue from the combined extracts ($CHCl_3$-AcOEt 9:1 as eluent) gave the reduced probase and 3-allyl-5-methyloxazolidine-2,4-dione **4f** (0.33g, 77%).
4f: oil (lit. [13] b.p.$_{15}$ 125°C); IR (film) ν: 1820 and 1740 cm^{-1}; ^{1}H-NMR δ (ppm) 1.56 (d, 3H, CH_3), 4.10 (d, 2H, CH_2N), 4.85 (q, 1H, CH), 5.2-5.5 (m, 2H, CH_2=C) and 5.5-5.9 (m, 1H, CH=C).

Reduction of 7 in the presence of 2g. **7** (0.44 g, 1.4 mmol) was reduced in the presence of **2g** (0.72 g, 2.8 mmol) and CO_2. C.c. of the residue from the combined extracts (light petroleum-AcOEt 7:3) gave the reduced probase and 3,5-dimethyloxazolidine-2,4-dione **4g** (0.14 g, 40%).
4g: oil (lit. [15] b.p.$_{50}$ 140-144°C); IR (film) ν: 1820 and 1740 cm^{-1}; ^{1}H-NMR δ (ppm) 1.60 (d, 3H, CH_3), 3.10 (s, 3H, CH_3-N) and 4.90 (q, 1H, CH).

Reduction of 7 in the presence of 1k. **7** (1.00 g, 4.1 mmol) was reduced in the presence of **1k** (0.39 g, 4.1 mmol) and CO_2. At the end of the electrolysis, CO_2 was bubbled into the catholyte for 2h, benzyl bromide (2.1 g, 12 mmol) was added and the mixture was further stirred for 12 h. HPLC analysis showed the presence of **4a** in 54% yield.

Reduction of **7** *in the presence of* **3i***.* **7** (0.6 g, 1.9 mmol) was reduced in the presence of **3i** (0.99 g, 3.8 mmol) and CO_2 using a vitreous carbon disk (12 cm^2) as cathode. C.c. of the residue from the combined extracts (light petroleum-acetone 7:3 as eluent) gave the reduced probase, **3i** (0.48 g, 50%) and *N*-benzylmethacrylamide **11** [16] (0.17 g, 26%).

Reduction of **8** *in the presence of* **3j***.* **8** (0.68 g, 2.8 mmol) was reduced at -0.6 V on Hg cathode in the presence of **3j** (0.62 g, 1.9 mmol) and CO_2. No residue was obtained from both Et_2O and $CHCl_3$ extracts. After acidification of the H_2O solution (1 mol l^{-1} HCl), the residue from the extraction with $CHCl_3$ was **3j** (0.55 g, 92%).

The results of the HPLC or GC analysis carried out on the solutions deriving from the reduction of **7** in the presence of CO_2 and of all the substrates are reported in Table 2.

Synthesis of 3-benzyl-5,5-dimethyloxazolidine-2,4-dione **4j***.* **5** (0.3 g, 1.5 mmol) was reduced at -0.9 V in the presence of **4e** (0.16 g, 0.8 mmol) and CH_3I (0.34 g, 2.4 mmol) dissolved in 25 ml of DMF-0.1 mol l^{-1} TEAP. After evaporation of the solvent under reduced pressure, H_2O (50 ml) was added to the residue and the mixture was extracted with $CHCl_3$ (3 x 30 ml). The combined organic layers were washed with H_2O (50 ml), dried (Na_2SO_4) and the solvent removed under reduced pressure. Preparative layer chromatography (SiO_2, light petroleum-AcOEt 3:2 as eluent) gave **4j** (0.07 g, 40%). HPLC analysis allowed to extimate a 76% yield of **4j**.
4j: m.p. 57-58°C (cyclohexane) (lit. [13] m.p. 58-59°C); IR (nujol) ν: 1810 and 1730 cm^{-1}; ^1H-NMR δ (ppm) 1.53 (s, 6H, 2 x CH_3), 4.63 (d, 2H, CH_2N) and 7.30 (s, 5H, arom).

Synthesis of 3,5,5-trimethyloxazolidine-2,4-dione **4b***.* **5** (0.43 g, 2.2 mmol) was reduced at -0.9 V in the presence of **4g** (0.14 g, 1.1 mmol) and CH_3I (0.70 g, 5.2 mmol) dissolved in 25 ml of DMF - 0.1 mol l^{-1} TEAP. After work-up of the electrolyzed solution as described above, **4h** was isolated (0.06 g, 38%). GC analysis allowed to extimate a 71% yield of **4h**.
4h: m.p. 43-45°C (light petroleum) (lit. [15] m.p. 46°C); IR (nujol) ν: 1810 and 1730 cm^{-1}; ^1H-NMR δ (ppm) 1.53 (s, 6H, 2 x CH_3) and 3.05 (s, 3H, CH_3N).

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