Electroorganic reactions. Part 58†. Revisiting the cleavage of oxalate ester radical-anions

James H.P. Utley* and Shalini Ramesh

Department of Chemistry, Queen Mary College (University of London), Mile End Road, London, UK, E1 4NS
E-Mail: j.utley@qmul.ac.uk

Dedicated to Professsor Henry J. Shine on his 80th birthday

(received 26 Mar 03; accepted 28 May 03; published on the web 29 May 03)

Abstract

Electrochemically-generated radical-anions of oxalate esters undergo cleavage. For those of ethyl 4-substituted benzyl oxalates the rates of cleavage have been measured by cyclic voltammetry combined with digital simulation. Consideration of substituent effects and earlier product studies presents compelling evidence for an EC mechanism with the cleavage resulting in oxalate anions and benzyl radicals.

Keywords: Electrochemical reduction, reductive cleavage, oxalate esters, radical-anions, kinetics of reductive cleavage

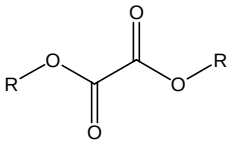
Introduction

The electrochemical reduction, with cleavage, of oxalate esters was introduced as a method for the deoxygenation of alcohols and vicinal diols.[2,3,4] This is difficult to achieve by direct reduction of alcohols because very negative potentials are required[5] and in any event the hydroxyl anion is a poor leaving group. Derivatives such as tosylates[6], methanesulfonates[7], diethylphosphates[8], and acetates[9] are more easily cleaved by cathodic reduction but only at very negative potentials.

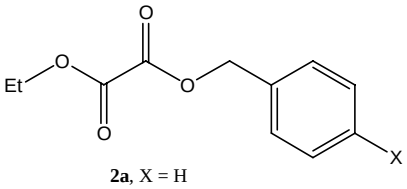
Conversion of hydroxyl into oxalate esters ($R^1OOC.COOR^2$) was found greatly to reduce the reduction potential and for benzylic or allylic alcohols and vicinal diols cathodic cleavage, in aprotic solvent, of the R-O function took place.[2,3,4] In these cases electron transfer is to the central dicarbonyl function so the oxalate group acts as both electrophore and leaving group. In practice competing hydrolysis by adventitious water in the basic conditions of electrolysis precluded preparative-scale electrolysis of preformed esters. However, *in situ* formation by transesterification during co-electrolysis of benzylic or allylic alcohols and diethyl oxalate led to

† For Part 57 see reference 1

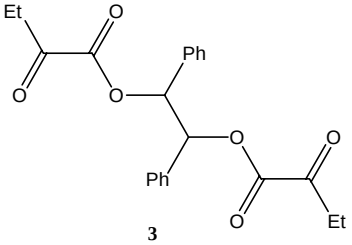
efficient 1F cleavage of hydroxyl in the added alcohol.[3,4] Coulometry, qualitative cyclic voltammetry and product studies were best explained[2] in terms of the initially formed radical-anions cleaved to radical ($R^{1\cdot}$ and $R^{2\cdot}$) and carboxylate anion ($R^2OOC.CO_2^-$ and $R^1OOC.CO_2^-$). In this context we report here on the direct observation by cyclic voltammetry of several relevant radical-anions and the measurement of their rates of cleavage and of substituent effects on the same. The oxalate esters involved in this study are as below.



1a, R = Et
1b, R = $PhCH_2$



2a, X = H
2b, X = Me
2c, X = MeO
2d, X = Cl



3

Results and Discussion

Review of product studies

From many examples the pattern of reductive cleavage is exemplified by the reactions of the compounds **1 – 3**, as set out in Table 1.

The electrolysis of **2a** (entry 1) is typical for preformed esters of benzylic alcohols from which only low yields of the hydrocarbon cleavage product are obtained; this has been attributed to competing rapid hydrolysis by adventitious water. However, the esters of vicinal diols such as **3** (entries 2 and 3) are smoothly converted into alkenes, *trans*-stilbene in the case cited. The formation of exclusively *trans*-stilbene from both *meso* and (±) diols suggests stepwise loss of the leaving groups, as concerted loss would lead to *cis*-stilbene from the *meso* isomer and *trans*-stilbene from the (±) isomer. The competition from hydrolysis is suppressed by co-electrolysis of the benzylic alcohols with an excess of diethyl oxalate. It has been shown by monitoring the reactions by cyclic voltammetry[2] that mixed esters are formed *in situ* by transesterification.

Table 1. Selected results of preparative-scale electrolyses[a] of oxalate esters[2]

Entry	Substrate	$-E_{red}$	Products (% yield)
1	**2a**	1.30	$PhCH_3$ (7); $PhCH_2OH$ (8)
2	*meso*-**3**	1.20[b]	t-PhCH:CHPh (80)
3	(±) **3**	1.20[b]	t-PhCH:CHPh (75)
4	$PhCH_2OH$ + **1a**	1.60	$PhCH_3$ (73): $PhCH_2OH$ (20)
5	Ph_2CHOH + **1a**	1.60	Ph_2CH_2 (70)
6	Ph_2CHOH + **1a** + H_2O (5% w/v)	1.60	Ph_2CHOH (97)
7	4-$Ph.C_6H_4.CH_2CH_2CH_2OH$ + **1a**	1.55	4-$Ph.C_6H_4.CH_2CH_2CH_2OH$ (96)

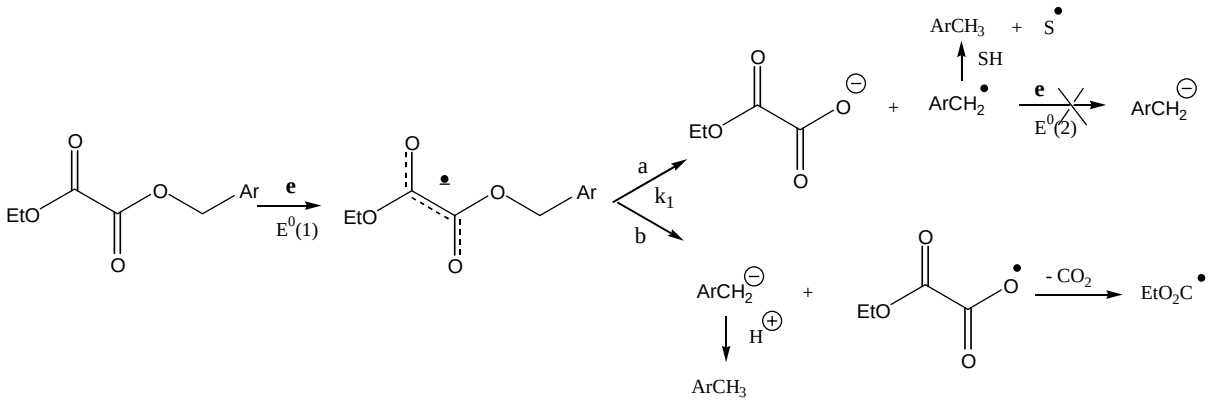
[a] Hg cathode; DMF-Bu_4NClO_4 (0.1 M); V *vs.* Ag/AgI; 1F.
[b] 2F.

Even so, relatively dry conditions must be maintained because comparison of entries 5 and 6 shows that the addition of water (5% w/v) diverts the reaction from substantially alkane formation to almost complete hydrolysis. The result in entry 7 illustrates the necessity for benzylic activation; even using the co-electrolysis method no cleavage to alkane for 4-$Ph.C_6H_4.CH_2CH_2CH_2OH$ is observed and the starting material is recovered unchanged.

The leaving group

The relevant possibilities for cleavage from the oxalate radical-anions are given in the Scheme 1; the electron transfer to give a radical-anion followed by rate determining cleavage is a classical EC reaction (**E**lectron transfer-**C**hemical step), with no subsequent electron transfer. Given that the benzylic group has to be part of the leaving group, with C-O cleavage, either a or b are the key steps. Benzylic activation can be understood in both events because both the benzylic radical and anion would be stabilised by conjugation. However, the carboxylate anion would be stable whereas the carboxylate radical would rapidly decarboxylate, according to literature precedent. The acetoxyl radical ($CH_3CO_2^{\cdot}$) has a half lifetime[10] of a few nanoseconds and such radicals are transient intermediates in the Kolbe anodic oxidation of carboxylate anions to give alkanes[11]. For cleavage according to b (Scheme) the $EtO_2C.CO_2^{\cdot}$ radical would be expected to decarboxylate to give $EtO_2C^{\cdot}$ and this entity is shown,[12] by addition to butadiene, to be formed in the anodic oxidation of $EtO_2C.CO_2^{-}$. However, carbon dioxide was not a gaseous product in the cathodic reduction of diethyl oxalate[2]. Furthermore, ^1H NMR and IR spectra of the residue from one electrolysis (Table 1, entry 4) showed characteristic features also found for $Bu_4NO_2C.CO_2Et$.

Consequently the favoured reaction is probably route a. Because only 1F reaction is found there appears to be no further electron transfer such as often found when benzylic radicals are formed. This is unusual but benzylic radicals are known to survive further reduction where the first electron transfer to the substrate is at a less negative potential than the reduction potential of the benzylic radical formed by subsequent reaction[13,14]. This situation could apply here because the reduction potentials of the oxalate esters [$E^0(1)$] are relatively low (Table 2) and could plausibly be less negative that those required for benzylic radical reduction [$E^0(2)$]. We propose that the reactions are completed by hydrogen abstraction from the solvent (DMF).



Scheme 1. Pathways for the fragmentation of oxalate ester radikal-anions.

Kinetics of cleavage and substituent effects

Each of the oxalate esters listed in Table 2 showed quasi-reversible reduction on cyclic voltammetry within the scan rate range of 0.5 – 90 V s^{-1}, depending on the substitution pattern. Qualitatively, the radical-anion of 4-chlorobenzyl ethyl oxalate (**2d**) underwent the fastest reaction and diethyl oxalate (**1a**) the slowest.

Table 2. Standard redox potentials for oxalate esters[a]

Oxalate	**1a**	**1b**	**2a**	**2b**	**2c**	**2d**
$-E^0(1)$	1.79	1.68	1.78	1.76	1.73	1.77

Cyclic voltammetry in range 0.5 – 90 V s^{-1}; V *vs*. SCE, Hg/Pt cathode, DMF-Bu_4NPF_6 (0.1 M), substrate concentration. 2 mM.

Digital simulation of the voltammograms (BAS DigiSim 3.03) offered the opportunity both to test the simple EC mechanism illustrated in the Scheme and, if successful, to estimate the rates of C-O cleavage (k_1 in the Scheme, routes a or b). By assuming the EC mechanism and using several experimentally determined parameters (diffusion coefficients, E^0 values) excellent fits of experimental curves were obtained by allowing k_1 to float. An example is given in Figure 1.

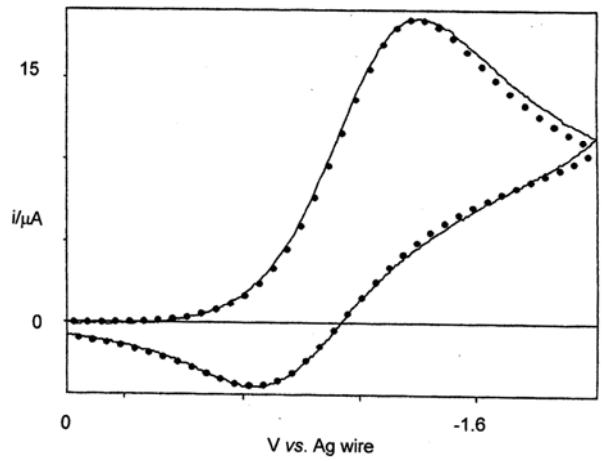


Figure 1. Experimental (solid line) and simulated (closed circles) voltammogram for 4-methoxybenzyl ethyl oxalate (**2c**) [2mM in DMF-Bu_4NPF_6 (0.1 M); Hg/Pt cathode; scan rate 10 V s^{-1}].

The simulations and comparisons with experimental voltammograms were carried out for a range of scan rates and at several substrate concentrations and these data are displayed in Table 3. The fact that simulation using the EC mechanism gives essentially the same rate constants for the rate-determining cleavage step for several scan rates and concentrations is compelling evidence for the mechanism given in the Scheme. Similarly, the evidence for the leaving groups being the oxalate anion ($EtO_2C.CO_2^-$) and benzyl radical, reviewed above, is very strong.

For the 4-substituted benzyl ethyl oxalates there is a distinct substituent effect on the rate of cleavage (Table 3). The radical-anions of the benzyl esters **1b** and **2a** cleave much more rapidly than that of diethyl oxalate (**1a**); the rate for **1b** is increased more than 50-fold and for **2a** more than 20-fold. Relative to the rate for benzyl ethyl oxalate (**2a**) 4-Me and 4-MeO cause modest increases in cleavage rate whereas 4-Cl causes a 6.6-fold increase.

The Hammett plot (Figure 2) reveals poor correlation and this is arguably more consistent with loss of benzyl radical than loss of benzyl anion, i.e. a transition state in which the breaking C-O bond is polarised with negative charge on the oxygen and a developing radical centre at the carbon. The alternative, negative charge on the carbon and a developing radical centre at the oxygen, would probably be subject to more pronounced substituent effects, e.g. it is unlikely that the electron-withdrawing groups, Me and MeO, would enhance the rate. In any event the other evidence about the direction of cleavage is very strong. We conclude, therefore, that the mechanism is well described by route a in the Scheme.

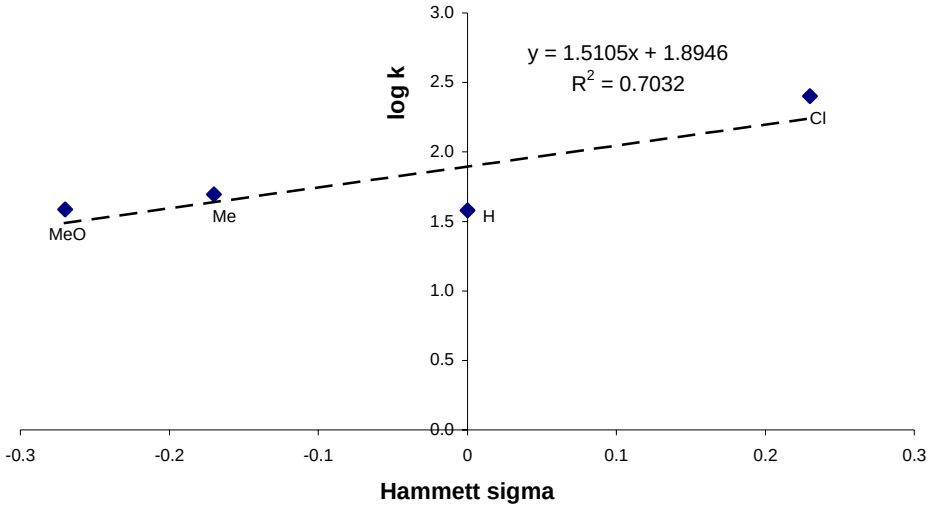


Figure 2. Attempted Hammett correlation for ethyl 4-X-benzyl oxalate radical anion cleavage.

Experimental Section

General Procedures. ^{1}H NMR spectra were recorded on the following instruments: a Bruker AM–250, JEOL–EX270 (270 MHz) and Bruker AMX–600. Chemical shifts are given in δ (ppm) relative to TMS. The coupling constants (J) are given in Hz. ^{13}C NMR spectra were recorded on the Bruker AM–250 (250 MHz) and JEOL–EX270 (270 MHz) machines.

Melting points were measured using a Reichert microscope melting point apparatus or in a capillary tube using an electrothermal melting point apparatus and were uncorrected.

Elemental analyses were run by the elemental analysis service at University College London.

Table 3. Rate constants estimated by digital simulation of cyclic voltammograms

Substrate	Scan rate ($V\ s^{-1}$)	Concentration (mM)	k_1 (s^{-1})
Diethyl oxalate (**1a**)	0.5	3	1.41
	0.6		1.55
	0.7		1.67
	0.8		1.82
	0.5	5	1.57
	0.6		1.70
	0.7		1.84
	0.8		1.97
			1.69 ± 0.14
	40	2	90.8
Dibenzyl oxalate (**1b**)	60		91.0
	80		89.8
	40	4	88.5
	60		88.7
	80		90.5
			89.9 ± 0.9
	10	2	31.3
Ethyl benzyl oxalate (**2a**)	20		32.9
	25		35.1
	30		39.4
	10	4	34.1
	20		41.7
	25		43.6
	30		45.1
			37.9 ± 4.5
	15	2	46.3
Ethyl 4-methylbenzyl oxalate	18		48.8
(**2b**)	20		49.6
	15	4	48.2
	18		51.3
	20		53.0
			49.5 ± 1.76

Table 3. Continued

Substrate	Scan rate ($V\ s^{-1}$)	Concentration (mM)	k_1 (s^{-1})
	10	2	37.9
Ethyl 4-methoxybenzyl oxalate	20		36.2
(**2c**)	30		36.3
	10	3	42.6
	20		42.7
	30		36.3
			38.6 ± 2.66
	70	2	249.8
Ethyl 4-chlorobenzyl oxalate (**2d**)	80		252.1
	90		246.4
	70	3	254.2
	80		257.1
	90		251.1
			251.9 ± 2.68

Electrochemical Instrumentation

Cyclic voltammetry and digital simulation

At low scan rates (< 1 V s^{-1}) a VersaStat EG&G Princeton Applied Research potentiostat interfaced with a PC *via* National Instruments GPIB-PCII/IIA (General Purpose Interface Board) was used. The controlling software was Model 270/250 Research Electrochemistry Software v 4.00. For faster scan rates (1-100 V s^{-1}) a software-controlled EG&G Princeton Applied Research potentiostat Model 263A was used with IR compensation. Solutions were degassed prior to measurements by nitrogen bubbling and measurements were made in an atmosphere of dry nitrogen. Before addition of the substrate (1-5 mM) a background run was made to allow subsequent subtraction. Digital simulation used BAS DigiSim 3.03 software.

Cells, electrodes and electrolytes

A conventional undivided three-electrode glass cell was used. The working electrode was gold (Au) (diameter 1 mm) or platinum (Pt) (diameter 0.5 or 1 mm) coated with mercury (Hg). The reference electrode was a silver wire immersed in the electrolyte and contained in a glass tube with a porous glass tip. This electrode was calibrated by determining the reversible reduction potential of anthracene after each set of measurements. This varied from day-to-day but allowed conversion to values *vs.* SCE. The E° value for anthracene in 0.1 M TBAI/DMF solution is -1.902V *vs.* SCE.[15]

DMF (HPLC grade) was stirred over anhydrous calcium hydride overnight, then filtered and distilled (30°C at 1mmHg), under nitrogen, onto freshly baked (150°C) 4Å molecular sieves to

ensure the dryness. The solvent-electrolyte solution was passed into the cell through a column of activated neutral alumina (grade 1) immediately before the measurements were made[16].

Tetrabutylammonium hexaflorophosphate was recrystallised from ethyl acetate. The recrystallised product was then dried in a vacuum desiccator.

Oxalates

Diethyl oxalate (1a). (Aldrich) Was washed three times with sodium bicarbonate, once with distilled water and then dried in magnesium sulphate. The solvent was evaporated off and the product was distilled off (185°C). The distilled diethyl oxalate was then dried over anhydrous sodium carbonate before use.

Ethyl benzyl oxalate (2a)[2]. Ethyl oxalyl chloride (1.36 ml, 0.012 mole) was added slowly at room temperature to a dry ether (50 ml) solution of the benzyl alcohol (1.26 ml, 0.012 mole) and pyridine (0.99 ml, 0.012 mole). This mixture was refluxed for 12 hours under nitrogen. The precipitate of pyridinium hydrochloride was filtered off and the organic layer washed with sodium bicarbonate ($NaHCO_3$) and then dried over $MgSO_4$. The solvent was evaporated to give an oily product (1.78g, 70%); ^{1}H NMR δ_H (270 MHz, $CDCl_3$): 7.3 (5H, m, Ar-H), 5.2 (2H, s, CH_2), 4.35 (2H, q, J = 5.5Hz, CH_2) and 1.4 (3H, t, J = 5.5Hz, CH_3); ^{13}C NMR δ_C (62.5 MHz, $CDCl_3$): 155.9, 140.9, 128.7, 127.4, 71.6, 58.9 and 13.3.

Dibenzyl oxalate (1b)[17]. Was prepared from oxalyl chloride and two equivalents of benzyl alcohol according to the above procedure. The product was obtained as a white solid (46%); m.p. 57-60°C (lit.[ref] 58-60°C); ^{1}H NMR δ_H (270 MHz, $CDCl_3$): 7.45-7.30 (10H, m, Ar-H) and 5.2 (4H, s, CH_2); ^{13}C NMR δ_C (62.5 MHz, $CDCl_3$): 155.9, 140.9, 128.7, 127.4, 127.0 and 71.6.

Ethyl 4-methyl benzyl oxalate (2b). Was prepared by the above procedure from ethyloxalyl chloride and 4-methylbenzyl alcohol to give white solid (76%); $C_{12}H_{14}O_4$ requires: C, 64.85; H, 6.35; O, 28.80 %. Found: C, 63.84; H, 6.47; O, 28.72 %); ^{1}H NMR δ_H (270 MHz, $CDCl_3$): 7.35 (2H, d, J = 12Hz, Ar-H), 6.9 (2H, d, J = 12Hz, Ar-H), 5.2 (2H, s, CH_2), 4.35 (2H, q, J = 7.4Hz, CH_2), 3.8 (3H, s, CH_3), and 1.35 (3H, t, J = 7.4Hz, CH_3); ^{13}C NMR δ_C (62.5 MHz, $CDCl_3$) : 155.9, 137.9, 136.6, 129.4, 127.2, 71.6, 58.9, 20.9 and 13.3.

Ethyl 4-methoxybenzyl oxalate (2c). Was prepared by the above procedure from ethyloxalyl chloride and 4-methoxybenzyl alcohol to give white solid (76%); $C_{12}H_{14}O_5$ requires: C, 60.50; H, 5.92; O, 33.58 %. Found: C, 60.44; H, 5.72; O, 34.72 %); m.p. 40-43°C; ^{1}H NMR δ_H (270 MHz, $CDCl_3$): 7.35 (2H, d, J = 12Hz, Ar-H), 6.9 (2H, d, J = 12Hz, Ar-H), 5.2 (2H, s, CH_2), 3.8 (3H, s, CH_3), 4.35 (2H, q, J = 7.5Hz, CH_2) and 1.35 (3H, t, J = 7.5Hz, CH_3); ^{13}C NMR δ_C (62.5 MHz, $CDCl_3$) : 160.9, 155.9, 133.2, 128.3, 114.3, 71.6, 58.9, 56.0 and 13.1.

Ethyl 4-chlorobenzyl oxalate (2d). Was prepared from ethyloxalyl chloride and 4-chlorobenzyl alcohol according to the above procedure and the product was obtained as a white solid (90%); $C_{11}H_{11}ClO_4$ requires: C, 54.45; H, 4.57; O, 26.37 %. Found: C, 54.48; H, 4.72; O, 26.72 %); m.p. 77-79°C; ^{1}H NMR δ_H (270 MHz, $CDCl_3$): 7.35 (4H, s, Ar-H), 5.25 (2H, s, CH_2), 4.35 (2H, q, J = 7.2Hz, CH_2) and 1.4 (3H, t, J = 7.2Hz, CH_3); ^{13}C NMR δ_C (62.5 MHz, $CDCl_3$): 155.9, 139.0, 132.7, 129.1, 128.7, 71.6, 58.9 and 13.3.

Acknowledgements

We thank the EPSRC for a Studentship (to SR).

References

1. Utley, J. H. P.; Rozenberg, G. G. *J. Applied Electrochem.* **2003**, in press.
2. Islam, N.; Sopher, D. W.; Utley, J. H. P. *Tetrahedron* **1987**, *43*, 959.
3. Islam, N.; Sopher, D. W.; Utley, J. H. P. *Tetrahedron* **1987**, *43*, 2741.
4. Ellis, K. G.; Islam, N.; Sopher, D. W.; Utley, J. H. P.; Chum, H. L.; Ratcliff, M. *J. Electrochem. Soc.* **1987**, *134*, 3058.
5. Lund, H.; Doupeux, H.; Michel, M. A.; Mousset, G.; Simonet, J. *Electrochim. Acta* **1974**, *19*, 629.
6. Gerdil, R. *Helv. Chim. Acta* **1970**, *53*, 2097.
7. Shono, T.; Matsumura, Y.; Tsubata, K.; Sugihara, Y. *Tetrahedron Letters* **1979**, 2157.
8. Shono, T.; Matsumura, Y.; Tsubata, K.; Sugihara, Y. *J. Org. Chem.* **1979**, *44*, 4508.
9. Coleman, J. P.; Naser-ud-din; Gilde, H. G.; Utley, J. H. P.; Weedon, B. C. L.; Eberson, L. *J. Chem. Soc., Perkin Trans 2* **1973**, 1903.
10. Gilbert, B. G.; Holmes, R. G. G.; Marshall, P. D. R.; Norman, R. O. C. *J. Chem. Res.(S)* **1977**, 172.
11. Eberson, L.; Utley, J. H. P. Chapter on Kolbe Reaction. In *Organic Electrochemistry*; Baizer, M. M.; Lund, H., Eds.; Marcel Dekker Inc.: New York, 1983; pp 435-462.
12. Lindsay, R. V.; Peterson, M. L. *J. Amer. Chem. Soc.* **1959**, *81*, 2073.
13. Nielsen, M. F.; Spriggs, S.; Utley, J. H. P.; Gao, Y. *J. Chem. Soc., Chem. Commun.* **1994**, 1395.
14. Fry, A. J.; Porter, J. M.; Fry, P. *J. Org. Chem.* **1996**, *61*, 3191.
15. Bard, A. J.; Faulkner, L. R. *Electrochemical Methods*; Wiley: New York, 1980; p 701.
16. Fussing, I.; Güllü, M.; Hammerich, O.; Hussain, A.; Nielsen, M. F.; Utley, J. H. P. *J. Chem. Soc., Perkin Trans 2* **1996**, 649.
17. Trahanovsky, W. S. *J. Amer. Chem. Soc.* **1968**, *90*, 2839.

