Electrochemical Reduction of Some α-Oxo-esters in Methanol at a Platinum Cathode

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The reactivities towards cathodic reduction for some aliphatic and aromatic α-oxo-esters, in methanol, at a platinum cathode are reported. The relative rates for the reduction follow the order: α-oxovalerate > α-oxobutyrate > phenylglyoxylate > 4-chlorophenylglyoxylate > 4-methoxycarbonylphenylglyoxylate. No reduction occurred with oxomalonate, 4-methoxyphenylglyoxylate, or 4-nitrophenylglyoxylate. An explanation for these differences in reactivities is suggested on the basis of electronic effects, steric inhibition of coplanarity, and hemiacetal formation.

IT was reported previously[1] that in the electrolyses of some long-chain α-oxo-acids the corresponding α-hydroxy-esters were identified as secondary products. Proof was provided that the formation of these compounds occurred in two consecutive steps, involving anodic esterification of the α-oxo-acids by methanol employed as solvent to give α-oxo-esters and further cathodic reduction of the latter. It was considered of interest to reinvestigate the electrochemical reduction of α-oxo-esters as a possible synthetic route to α-hydroxy-esters. However, the preliminary electrolytic experiments, undertaken with methyl α-oxovalerate and pyruvate, showed that, although the former was reduced quantitatively, the latter remained unaltered. In order to obtain some insight into the relationship between structure and reactivity toward cathodic reduction it became of interest to investigate a large number of α-oxo-esters.

TABLE 1

Electrolytic reduction of some α-oxo-esters in methanol containing sodium methoxide

Electrolysed oxo-esters $RCO{\cdot}CO_2Me$	Electrolytic equivalent (faraday)	Products of electrolysis (% peak area) Hydroxy-esters	Recovered oxo-esters	Secondary products
(1) R = Pr^n	1·5[1]	94	6	
	3[a]	42	58	
(2) R = Me	2[1]		85	
	7	91		9
(3) R = Ph	5	86	14	
	5[a]	62	38	
	5[b]	92	8	
(4) R = $4\text{-}ClC_6H_4$	5	64	26	10
(5) R = $4\text{-}MeO_2CC_6H_4$	3	42	53	5
(6) R = CO_2Et[c]	5[d]		100[e]	
(7) R = $4\text{-}MeOC_6H_4$	5		100[e]	
(8) R = $4\text{-}O_2NC_6H_4$	5		80[e]	

[a] 0·15M-$Bu^n_4N^+ClO_4^-$. [b] 0·01M-$Bu^n_4N^+ClO_4^-$. [c] Me substituted by Et. [d] In ethanol containing 0·15M-$Bu^n_4N^+ClO_4$. [e] % Yield.

This paper deals with the electrochemical studies of some aliphatic and aromatic representatives of this class of compounds.

RESULTS AND DISCUSSION

The α-oxo-esters listed in Table 1 were submitted to prolongated electrolyses (*ca.* 3—5 faradays), in methanol containing sodium methoxide. The phenylglyoxylate (3) afforded the corresponding α-hydroxy-ester in good yield. However methyl 4-chlorophenylglyoxylate (4) and 4-methoxycarbonylphenylglyoxylate (5) were transformed only partially into their corresponding hydroxy-esters. No reduction occurred with ethyl oxomalonate (6), 4-methoxyphenylglyoxylate (7), and 4-nitrophenylglyoxylate (8), which were recovered unchanged after electrolysis. It is noteworthy that methyl pyruvate (2), which had been recovered unchanged from an electrolytic experiment with up to *ca.* 2 faradays,[1] was later reduced, in good yield, after passage of 7 faradays. The substitution of tetra-n-butylammonium perchlorate for sodium methoxide in the electrolyses of the compounds (1) and (3) lead to a similar reductive trend.

The relative rates for the reduction of the compounds (3)—(5) and methyl α-oxobutyrate (9) were estimated following the courses of their electrolyses by g.l.c. The results are shown in the Figure.

Two groups of curves are observed, those that descend and those that ascend, corresponding to the oxo-esters and hydroxy-esters, respectively. The Figure indicates that, after passage of 2 and 3 faradays, there is complete reduction of α-oxovalerate (1) and α-oxobutyrate (9), respectively. However, at this stage, only 60% of either phenylglyoxylate (3) or 4-chlorophenylglyoxylate (4) is transformed into the corresponding hydroxy-ester. Although the reduction of the phenylglyoxylate (3) is nearly complete after passage of 6 faradays, only 80% of 4-chlorophenylglyoxylate (4) is reduced at this stage. The reactivity of 4-methoxycarbonylphenylglyoxylate (5) is still lower, because after passage of 2 and 6 faradays no more than *ca.* 30 and 80%, respectively, of hydroxy-ester is produced.

It may be concluded (Table 1 and Figure) that the

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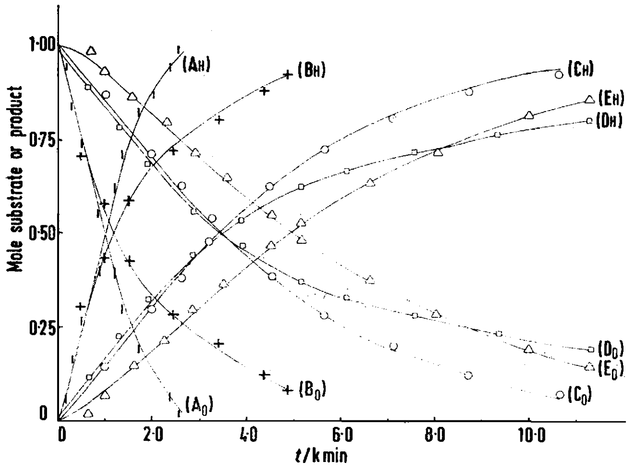
[1] B. Wladislaw and J. P. Zimmermann, *J. Chem. Soc.* (*B*), 1970, 290.

relative rates for the reduction of the α-oxo-esters follow the order: α-oxovalerate > α-oxobutyrate > phenylglyoxylate > 4-chlorophenylglyoxylate > 4-methoxycarbonylphenylglyoxylate.

These results at first sight seem surprising. The fact that phenylglyoxylate is less reactive than α-oxovalerate, that both methoxy- and nitro-substituents decrease the occurrence of reduction and that, in the aliphatic series, the reactivity increases with lengthening of the carbon chain, indicates clearly that some other factors, besides electronic ones, are also operating.

The inertness of the 4-nitro-derivative (8) toward electrochemical reduction can hardly be explained by electronic effects, since the electron-withdrawing nitro-group should interact with the carbonyl group in such a way as to destabilize the reactant, making it more reactive. Insight into the behaviour of this compound was obtained from its i.r. spectrum in methanolic solution, which showed that the carbonyl stretching band at 1700 cm^{-1}, present in chloroform, had practically vanished. A plausible explanation for both the i.r. spectra and the lack of reactivity is that 4-nitrophenylglyoxylate, in methanolic solution, forms a hemiacetal to an appreciable extent.



Cathodic reductions of: (A) methyl α-oxovalerate; (B) methyl α-oxobutyrate; (C) methyl phenylglyoxylate; (D) methyl 4-chlorophenylglyoxylate and (E) methyl 4-methoxycarbonylphenylglyoxylate. Calculated time for passage of 1 faraday, 1·60 kmin. H, Hydroxy-ester; O, oxo-ester

The decrease of the reactivity of the chloro (4) and methoxycarbonyl (5) derivatives by comparison with unsubstituted phenylglyoxylate (3) seems also to be due to the existence of the oxo–hemiacetal equilibrium in these compounds. Evidence for such equilibria were obtained from examination of the u.v. spectra of these compounds (Table 2). The oxo-esters (4) and (5) in methanolic solution, show a large decrease of the intensity of the $n \longrightarrow \pi^*$ absorption bands, by comparison with those in carbon tetrachloride, n-hexane, or chloroform.

TABLE 2

$n \longrightarrow \pi^*$ Band for some α-oxo-esters and some apparent equilibrium constants K for hemiacetal formation

$RCO{\cdot}CO_2Me$	CCl_4 λ/nm (log ε)	n-C_6H_{14} λ/nm (log ε)	$CHCl_3$ λ/nm (log ε)	MeOH λ/nm (log ε)	K
(1)		342 (1·21)		326 (0·80)	1·4
(2)		332 (1·20)		323 (0·46)	4·0
(3)	348 (1·63)	350 (1·56)	341 (1·73)	340 (1·60)	
(4)	352 (1·85)	353 (1·82)	347 (1·94)	345 (1·58)	
(5)	358 (1·87)		352 (1·92)	342 (1·32)	
(6) [a]	373 (1·49)		369 (1·38)	no absorp.	
(7)			295 (4·18)	291 (4·24)	
(9) R = Et		329 (1·22)		320 (0·66)	2·2

[a] Et for Me.

Table 2 indicates that hemiacetal formation also occurs in the aliphatic series. Ethyl oxomalonate (6), which was not reduced, shows complete suppression of the $n \longrightarrow \pi^*$ band in methanol by comparison with n-hexane. It is noteworthy that the isolation of a number of stable hemiacetals of some oxomalonates has been reported.[2]

Extensive suppression of the $n \longrightarrow \pi^*$ band was observed in the spectrum of methyl pyruvate (2) in methanolic solution but the effect was smaller in the case of α-oxobutyrate (9). However, the spectrum of α-oxovalerate (1) in methanol shows only a slight decrease of the $n \longrightarrow \pi^*$ band when compared with that in carbon tetrachloride. The differences in the reactivity toward hemiacetal formation in the aliphatic α-oxo-esters (1), (2), and (9) may be estimated by the apparent equilibrium constants K. These are shown to decrease upon increasing the chain length $[K(2) > K(9) > K(1)]$. It is significant that this is also the order of reactivity toward cathodic reduction. Therefore, it seems reasonable to suggest that the lack or large decrease of reactivities of oxomalonate (6) and pyruvate (2) may be due, at least partly, to hemiacetal formation.

The decrease in hemiacetal formation with the lengthening of the carbon chain also suggests some steric requirements.

No indication of hemiacetal formation is obtained from the u.v. data of methyl phenylglyoxylate (3) and 4-methoxyphenylglyoxylate (7). The lack of reactivity of the latter is logically expected. The electron-donating methoxy-group has been reported to favour anodic oxidation owing to the stabilization of cationic intermediates.[3-5] Thus, this group should inhibit cationic reduction, in which the formation of anionic intermediates takes place.

The decrease in reactivity towards reduction in phenylglyoxylate, by comparison with α-oxovalerate, is probably related to the lack of coplanarity of the two carbonyl groups, as already reported.[6] Our earlier observation [1] that methyl levulinate remained unchanged when electrolysed in methanol at a platinum cathode led us to suggest that the reduction of the carbonyl

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[2] R. S. Curtiss and F. G. C. Spencer, *J. Amer. Chem. Soc.*, 1909, **31**, 1053.

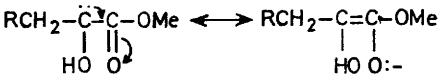
[3] B. Wladislaw and H. Viertler, *Chem. and Ind.*, 1965, 39.

[4] B. Wladislaw and H. Viertler, *J. Chem. Soc.* (*B*), 1968, 576.

[5] R. F. Garwood, Naser-Ud-Din, and B. C. L. Weedon, *Chem. Comm.*, 1968, 923.

[6] G. Oehme and A. Schellenberger, *Chem. Ber.*, 1968, **101**, 1499.

group requires the presence of a neighbouring, electron-withdrawing methoxycarbonyl group. This was confirmed as ethyl 4-oxopimelate was shown to be similarly unreactive. We previously [1] suggested that the methoxycarbonyl group may participate in the reduction process and stabilize the anionic intermediate (10a and b).



(10a) (10b)

It is noteworthy that a similar dienol structure was proposed recently [7] for the polarographic reduction of phenylglyoxylic acid. It seems reasonable to suggest that distortion of the coplanar arrangement of the two carbonyl groups would lead to a smaller contribution of the mesomeric form (10b), raising the energy of the anionic intermediate. Therefore, reactivity toward reduction should be decreased.

EXPERIMENTAL

M.p.s were on a Kofler micro-hot stage. I.r. spectra were measured with Perkin-Elmer model 337 and 457A spectrophotometers for solutions in carbon tetrachloride or as films. U.v. spectra were determined with a Beckman model DK-2A spectrophotometer at room temperature using quartz cells. ^1H N.m.r. spectra were recorded on a Varian T60 instrument for solutions in carbon tetrachloride with tetramethylsilane as internal standard. For g.l.c. a Varian 1800 instrument with a hydrogen flame ionization detector was used.

The α-oxo-esters were obtained from the corresponding hydroxy-esters by literature methods.[8-11] Previously unknown compounds were *methyl 4-methoxycarbonylmandelate*, b.p. 161° at 0·95 mmHg, m.p. 55—56° (Found: C, 59·5; H, 5·1. $C_{11}H_{12}O_5$ requires C, 58·9; H, 5·3%), $\nu_{max.}$ (CCl_4) 3530 (OH) and 1727 cm^{-1} (CO_2Me); τ 6·64 (s, OH), 6·27 [s, $CH(OH)CO_2C\mathit{H}_3$], 6·17 (s, $C_6H_4CO_2C\mathit{H}_3$), and 2·30 (q, ArH) and *methyl 4-methoxycarbonylphenylglyoxylate*, m.p. 105—106° (Found: C, 59·9; H, 4·5. $C_{11}H_{10}O_5$ requires C, 59·5; H, 4·5%), $\nu_{max.}$ (CCl_4) 1735 (CO_2Me) and 1697 cm^{-1} (CO), τ 6·07 and 6·04 (2s, $2CO_2CH_3$) and 1·90 (s, ArH).

The electrolyses were performed at the platinum electrodes in two cells, simple and modified, which have been described elsewhere.[4,12] In all experiments a current of 1A was passed and the cathodic current density was 0·059 A. The solvent was absolute methanol to which *ca.* 0·03% sodium was added.

Details of materials and individual electrolyses are specified in Supplementary Publication No. SUP 20927 (6 pp.).*

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* For details of Supplementary Publications see Notice to Authors No. 7 in *J.C.S. Perkin II*, 1972, Index Issue. Items less than 10 pp. are supplied as full-size copies.

[7] M. B. Fleury and J. C. Dufresne, *Bull. Soc. chim. France*, 1972, 844.

[8] E. Vogel and H. Schinz, *Helv. Chim. Acta*, 1950, **33**, 125.

[9] E. Baer and M. Kates, *J. Amer. Chem. Soc.*, 1945, **67**, 1482.

[10] Burroughs, Wellcome and Co., B.P. 759,014/1956 (*Chem. Abs.*, 1957, **51**, 9719*e*).

[11] F. Kogland and H. Becker, *Annalen*, 1928, **465**, 236.

[12] B. Wladislaw and A. M. J. Ayres, *J. Org. Chem.*, 1962, **27**, 281.