Electrolyses of Some α-Keto-carboxylic Acids

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The Kolbe reaction is largely suppressed when α-oxobutyric and α-oxovaleric acids are electrolysed in methanol with sodium added, by formation of a mixture of three methyl esters: (1) of unsubstituted acid with one carbon atom less than the electrolysed acid, (2) of electrolysed α-keto-acid, (3) of α-hydroxy-acid with the same carbon chain as the electrolysed α-keto-acid. Evidence is provided that α-hydroxy-esters are formed by reduction of α-keto-esters and that the hydrogen comes from the hydroxy-group of methanol. The reduction does not occur when the keto-group is further removed from the ester group or when the methyl group is attached to the carbonyl group of the α-keto-ester.

THE electrolyses of α-substituted carboxylic acids in aqueous solution resulted in the Kolbe reaction being largely or totally suppressed.[1] Thus, although normal coupling of the Kolbe type occurred with some carboxylic acids containing a keto-group further from the carboxyl group,[2] negligible coupling was observed in electrolysis of pyruvic acid in aqueous solution, which was reported to yield mainly acetic acid.[3]

Previous studies [4-10] have been confined to the electrolyses in methanol of α- or ring-substituted phenylacetic acids in which methoxylation has been observed.

The present work involves the electrolyses in methanol and sodium at constant current (1A) of some aliphatic α-keto-carboxylic acids and describes the competitive processes which largely suppress the Kolbe reaction.

RESULTS AND DISCUSSION

Pyruvic (Ia), α-oxobutyric (Ib), and α-oxovaleric (Ic) acids were electrolysed in methanol (see Table). In all cases the diketones (II) resulting from the Kolbe reaction were only the minor products. Pyruvic acid gave methyl acetate (IIIa), corresponding to the acid with one carbon atom less than the electrolysed acid, and (Ib) and (Ic), besides the methyl esters (IIIb) and (IIIc), afforded α-oxo- (IVb, c) and α-hydroxy- (Vb, c) methyl esters of the acids (Ib) and (Ic).

Electrolyses of some α-keto-carboxylic acids in methanol and sodium

Electrolysed acids	Electrolysed products (% yields)			
R·CO·CO_2H (I)	R·CO·COR (II)	R·CO_2Me (III)	R·CO·CO_2Me (IV)	R·CH(OH)·CO_2Me (V)
R = Me (a)	18·5	81·5		
R = Et (b)	Traces	73·0	16·1	7·6
R = Pr^n (c)	6·3	65·5	5·0	23·5

In order to investigate the correlation between these competitive processes, as well as the origin of the α-hydroxy-esters, the transformations occurring during

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[2] H. Hofer, *Ber.*, 1900, **33**, 650.
[3] V. Fr. Fichter and S. Lurie, *Helv. Chim. Acta*, 1933, **16**, 885.
[4] B. Wladislaw and A. M. J. Ayres, *J. Org. Chem.*, 1962, **27**, 281.
[5] B. Wladislaw, *Chem. and Ind.*, 1962, 1868.
[6] B. Wladislaw and A. Giora, *J. Chem. Soc.*, 1964, 1037.
[7] B. Wladislaw and A. Giora, *J. Chem. Soc.*, 1965, 5747.
[8] B. Wladislaw, A. Giora, and G. Vicentini, *J. Chem. Soc.* (*B*), 1966, 586.
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[10] B. Wladislaw and H. Viertler, *J. Chem. Soc.* (*B*), 1968, 576.

the electrolysis of the α-oxovaleric acid (Ic) in methanol were followed by g.l.c.[10] Figure 1 shows that electrolysis of the acid (curve A) takes 1·6 times as long as expected on the basis of the current and the amount of the acid. The formation of methyl butyrate (curve B), which is the main electrolysis product, is simultaneous with that of diketone (curve C). The maximum yields for both compounds are reached when there is no keto-acid (curve A) in the electrolysis product. Methyl α-oxovalerate (curve D), which is produced slowly since the beginning of the electrolysis, starts to decrease in the electrolysis mixture after passage of *ca.* 1·3 faraday equivalents and disappears after passage of *ca.* 2·7 faraday equivalents. At that stage the maximum yield for the α-hydroxyvalerate (curve E) is produced. This compound, which appears also at the beginning of the electrolysis and follows the formation of the keto-ester, is produced continuously even when the keto-ester is decreasing. Figure 1 suggests that the α-keto-ester undergoes reduction to α-hydroxy-ester. This is supported by the transformation of methyl α-oxovalerate into methyl α-hydroxyvalerate by electrolysis in methanol in the presence of

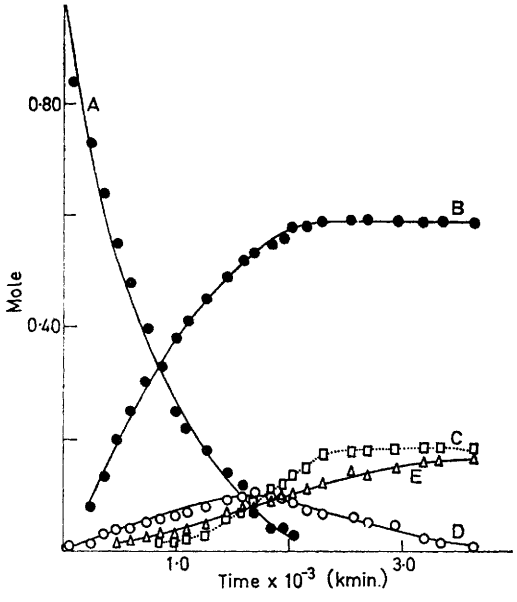


FIGURE 1 Electrolysis of α-oxovaleric acid in absolute methanol at 6° ± 1°. Anodic current density 0·059 A cm.$^{-1}$. Calculated time for passage of 1 equiv. of electricity, 1·4 × 10^3 min. A, Electrolysed acid; B, methyl butyrate; C, octane-4,5-dione; D, methyl α-oxovalerate; E, methyl α-hydroxyvalerate

acetic acid (Figure 2). The same transformation took place without addition of acetic acid. Thus, the α-keto-ester, which is formed during the electrolysis of α-keto-acid, may be considered as the precursor of the α-hydroxy-ester.

Electrolysis in methanol of α-hydroxyvaleric acid does not lead to oxidation, but produces butyraldehyde, while methyl α-hydroxyvalerate, alone or with acetic acid, remains unaltered. This rules out the occurrence of a reversible oxidation–reduction process, before or after esterification of the α-oxovaleric acid.

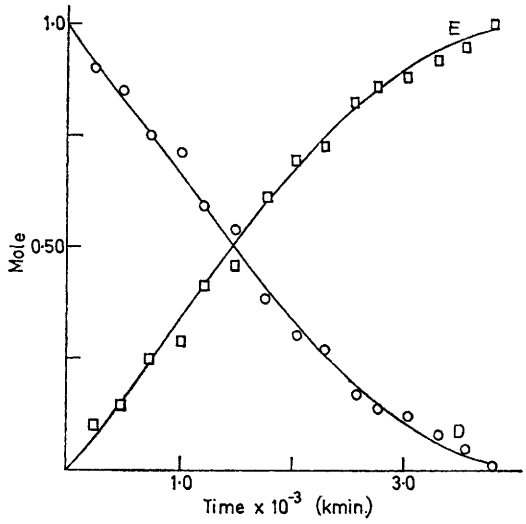
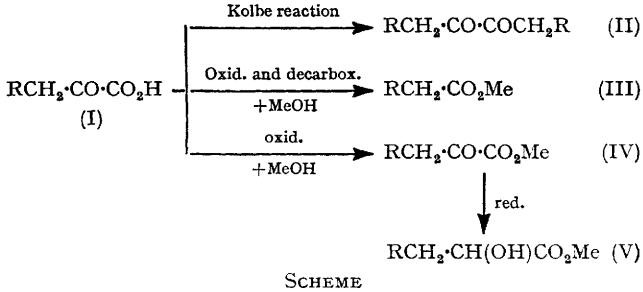


FIGURE 2 Electrolysis of methyl α-oxovalerate in absolute methanol at 6° ± 1°. Anodic current density 0·059 A cm.$^{-1}$. D, Methyl α-oxovalerate; E, methyl α-hydroxyvalerate

Thus, the pathways shown in the Scheme can be suggested for the electrolyses of the long-chain α-keto-acids in methanol. The esters (III) are the expected products of anodic methoxylation, which usually occurs when the formation of normal coupling products (II) is partially suppressed.[11] The keto-esters (IV) are formed from the electrolysed acids (I) and methanol, this reaction already having been reported.[12–14] The formation of α-hydroxy-esters (V) in the electrolyses of α-keto-acids through the corresponding α-keto-esters (IV), or in the electrolyses of the α-keto-esters in methanol, at the low-overpotential platinum electrode is of interest, since it has



SCHEME

not been described before. β-Keto-esters were reduced at the lead electrode and in acidic catholyte and reported to give hydrocarbons with hydrogenolysis of the ester group.[15,16] Glyoxylic acid was described to give

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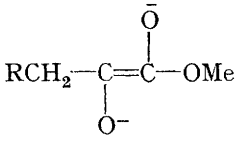
[14] R. G. Woolford, J. Soong, and W. S. Lin, *Canad. J. Chem.*, 1967, **45**, 1837.
[15] M. J. Allen, 'Organic Electrode Processes,' Chapman and Hall Ltd., London, 1958, pp. 47—72.
[16] F. D. Popp and P. Schultz, *Chem. Rev.*, 1962, **62**, 29.

tartaric acid when reduced at an iron, nickel, or silver electrode in a neutral or alkaline medium, whereas at a lead, cadmium, or mercury cathode the more highly reduced succinic acid was obtained.[15]

Electrolysis of methyl α-oxovalerate in MeOD produces methyl α-hydroxyvalerate with an α-C–D bond, showing that the hydrogen atom at the α-carbon comes from the hydroxyl group of methanol. It was also verified that the reduction does not occur when the keto-group is further from the ester group nor when the methyl group is directly bonded to the carbonyl group of the α-keto-ester, as methyl laevulinate and methyl pyruvate remained unaltered when electrolysed in methanol. It can also be seen (Table) that the reduction is much slower in the electrolysis of the α-oxobutyric acid, in which only *ca.* 33% of the α-keto-ester was transformed into α-hydroxy-ester, than in that of α-oxovaleric acid, in which this transformation occurred in *ca.* 85%. In an electrolytical experiment with up to *ca.* 3 faraday equivalents only *ca.* 50% of the α-oxobutyric acid was reduced, the methyl α-oxovalerate being converted totally into the corresponding hydroxy-ester in these conditions.

These results seem to indicate that the reduction of the keto-group at the platinum cathode requires the presence of the neighbouring electron-withdrawing methoxycarbonyl group and the absence of the electron-donating methyl group. It seems reasonable to suggest that the methoxycarbonyl group favours the two-electron change of the carbon in the charged mesomeric form, which was suggested for the electroreduction of ketones.[15] It is possible that the reduction of the α-keto-esters at the platinum cathode proceeds *via* the dienolate anion (VI), similar to that suggested for the reduction of benzil to benzoin.[17]



(VI)

The reduction of the methyl α-oxovalerate and α-oxobutyrate at the platinum cathode in methanol is a new route to the corresponding α-hydroxy-esters.

EXPERIMENTAL

M.p.s were determined on a Kofler microhot-stage apparatus. I.r. spectra were measured with a Perkin-Elmer model 221 spectrophotometer with a sodium chloride prism, on solutions in carbon tetrachloride. For g.l.c. a Perkin-Elmer 226 instrument with a hydrogen flame ionization detector (FS-1265 column) and CG 10-P instrument with thermal conductivity detector (Apiezon-M column) were used. The analyses were carried out with programmed temperatures. N.m.r. spectra were recorded at 60 Mc./sec. on a Perkin-Elmer R10 spectrometer on solutions in carbon tetrachloride. Chemical shifts are given on the τ scale; tetramethylsilane was used for internal references.

Materials.—Redistilled pyruvic acid (b.p. 70—72°/20 mm.) and methyl acetate (b.p. 56—57°) were used. Biacetyl (Fischer), b.p. 88—91°, was used as received. The following compounds were prepared as described in the appropriate references: α-oxobutyric acid, b.p. 92—95°/50 mm.;[18] α-oxovaleric acid, b.p. 80—82°/21 mm.;[18] methyl propionate, b.p. 78—79°;[19] methyl butyrate, b.p. 100—102°;[19] methyl pyruvate, b.p. 136—140°;[20] methyl α-oxobutyrate, b.p. 64—65°/16 mm.;[21] methyl α-oxovalerate, b.p. 69—70°/32 mm.;[21] methyl lactate, b.p. 143—145°;[22] methyl α-hydroxybutyrate, b.p. 160—162°;[23] methyl α-hydroxyvalerate, b.p. 92—94°/28 mm.;[23] methyl laevulinate, b.p. 193—195°;[24] α-hydroxyvaleric acid, b.p. 108—110°/2 mm.;[25] octane-4,5-dione, b.p. 75—77°/24 mm.;[26] and [*hydroxy*-$^2H_1$]methanol[27] which was shown by n.m.r. to contain *ca.* 2% of methanol.

Electrolyses.—They were performed at the platinum electrodes, in two cells: simple (A) and modified (B), which have been described.[4,10] In all experiments a current of 1 amp. was passed.

(a) *Pyruvic acid.* The solution of the acid (3·0 g.) in methanol (50 ml.) containing sodium (0·02 g.) was electrolysed in cell A until the electrode became slightly alkaline (after passage of *ca.* 3 faraday equiv.). G.l.c. (FS-1265, 40—120°) of the methanolic solution gave three peaks, which corresponded to methanol, methyl acetate, and acetyl. The peak areas for the ester and diketone were 81·5 and 18·5% respectively. The distillation of methanol gave polymeric residue (0·2 g.).

(b) *α-Oxobutyric acid.* The acid (3·0 g.) in methanol (50·0 ml.) containing sodium (0·02 g.) was electrolysed in cell A until the electrolyte became slightly alkaline (after passage of *ca.* 2 faraday equiv.). G.l.c. (FS-1265, 55—190°) of the methanolic solution gave five peaks due to methanol, methyl propionate (73·0%), hexane-3,4-dione (traces), methyl α-oxobutyrate (16·7%), and methyl α-hydroxybutyrate (7·6%). After passage of up to 3 faraday equiv. through the same electrolyte, g.l.c. chromatography showed the same percentage for the methyl propionate. The yields for the keto- and hydroxy-esters were respectively 12·0 and 14·0%.

(c) *α-Oxovaleric acid.* (i) The solution of the acid (4·0 g.) in methanol (66·5 ml.) containing sodium (0·02 g.) was electrolysed in cell A until the electrolyte became slightly alkaline (after passage of *ca.* 2 faraday equiv.). The solution was neutralised with acetic acid and the methanol evaporated. The residue was dissolved in ether and the

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[26] W. Rigby, *J. Chem. Soc.*, 1951, 795.
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solution washed with saturated potassium hydrogen carbonate solution, dried, and evaporated. The residue (1·2 g.) on distillation gave a liquid, b.p. 164—174° (0·7 g.); (ii) The acid (7·4 g.), in methanol (123 ml.) containing sodium (0·04 g.) was electrolysed in cell A until the electrolyte became slightly alkaline (after passage of *ca.* 2 faraday equiv.). Work-up as in the preceding electrolysis yielded a liquid residue (2·3 g.). This was hydrolysed with 3·5 ml. of 25% ethanolic sodium hydroxide solution to afford an acid residue (1·8 g.). Distillation gave α-hydroxyvaleric acid, b.p. 99—101°/1 mm (0·9 g.), identical (i.r. comparison) with an authentic specimen. The derivative with *p*-toluidine, m.p. 98—99° (Found: C, 69·3; H, 8·4. Calc. for $C_{12}H_{17}NO_2$: C, 69·5; H, 8·3) was prepared.[28] The mixed m.p. with the corresponding derivative of the authentic α-hydroxyvaleric acid was 97—99°. (iii) The acid (3·0 g.) in methanol (50 ml.) containing sodium (0·02 g.) was electrolysed in cell A until the electrolyte became slightly alkaline (after passage of *ca.* 2 faraday equiv.). G.l.c. (FS-1265, 100—210°) of the methanolic solution showed five peaks due to methanol, methyl butyrate (65·5%), methyl α-oxovalerate (5·0%), octane-4,5-dione (6·3%), and methyl α-hydroxyvalerate (23·1%). (iv) The acid (10 g.) in methanol (156 ml.) containing sodium (0·08 g.) was electrolysed in cell B, the temperature being maintained at 6° ± 1°. At 10 min. intervals up to 410 minutes' electrolysis (after passage of *ca.* 3 faraday equiv.) two samples (1·0 ml. each) of the electrolyte were removed and one was titrated with 0·01N-sodium hydroxide and the other analysed by g.l.c. (Apiezon M, 80—220°). The results are shown in Figure 1.

(d) *α-Hydroxyvaleric acid.* The acid (9 g.) in methanol (120 ml.) containing sodium (0·07 g.) was electrolysed in cell B, the temperature being maintained at 6° ± 1°. By the procedure of the preceding experiment the course of the electrolysis (up to 300 min., *ca.* 2·6 faraday equiv.) was followed. The samples, which were analysed by g.l.c. (Apiezon M, 60—220°), showed, as the main peak, butyraldehyde (87·0%), and two small peaks (13·0%) which were not identified.

(e) *Methyl α-hydroxyvalerate.* (i) The ester (8 g.) in methanol (120 ml.) containing sodium (0·05 g.) was electrolysed in cell B, the temperature being maintained at 5° ± 1°. Samples (1·0 ml.) of the electrolyte were removed at 15 min. intervals up to 240 minutes' electrolysis and analysed by gas chromatography (Apiezon M, 140—220°). All samples showed two peaks, due to methanol and methyl α-hydroxyvalerate. (ii) The preceding experiment was repeated with acetic acid (3·1 g.) added to the electrolyte. The same result was obtained by g.l.c.

(f) *Methyl α-oxovalerate.* (i) The ester (11·5 g.) in methanol (150 ml.) containing sodium (0·06 g.) to which acetic acid (4·5 g.) was added, was electrolysed in cell B, the temperature being maintained at 6° ± 1°. At 15-min. intervals up to 300 minutes' electrolysis, a sample (1·0 ml.) of the electrolyte was removed and analysed by gas chromatography (Apiezon M, 140—220°). The result is shown in the Figure 2. (ii) The ester (2 g.) in methanol (50 ml.) containing sodium (0·02 g.) was electrolysed in cell A for 60 min. G.l.c. (FS-1265, 100—190°) of the methanolic solution gave three peaks due to methanol, methyl α-oxovalerate, and methyl α-hydroxyvalerate. The peak areas for the keto-ester and hydroxy-ester were 14·0 and 86·0% respectively. Distillation of methanol with a fractionating column gave a residue which, by distillation, afforded methyl α-hydroxyvalerate, b.p. 88—94°/30 mm. (0·8 g.), identified by g.l.c. (Apiezon M, 150—220°). N.m.r. spectrum showed a triplet centered at τ 5·8, assigned to the α-carbon proton. (iii) The ester (2 g.) in MeOD (50 ml.) containing sodium (0·02 g.) was electrolysed in cell A for 90 min. G.l.c. (Apiezon M, 150—220°) of the methanolic solution gave three peaks due to methanol, methyl α-oxovalerate, and methyl α-hydroxyvalerate. The peak areas for the keto-ester and hydroxy-ester were 5·5 and 94·5% respectively. Distillation of the solvent with a fractionating column and then distillation of the residue gave methyl α-hydroxyvalerate, b.p. 90—94°/30 mm. (0·9 g.), identified by g.l.c. (Apiezon M, 150—220°). In the n.m.r. spectrum the triplet at τ 5·8, assigned to the α-carbon proton, was missing.

(g) *Methyl laevulinate.* The ester (2·7 g.) in methanol (45 ml.) containing sodium (0·02 g.) was electrolysed in cell A for 90 min. G.l.c. (Apiezon M, 80—220°) of the methanolic solution gave two peaks due to methanol and methyl laevulinate.

(h) *Methyl pyruvate.* The ester (2·0 g.) in methanol (50 ml.) containing sodium (0·08 g.) was electrolysed in cell A for 60 min. The methanol was evaporated to afford a residue which by distillation gave methyl pyruvate, b.p. 66—68°/13 mm. (1·7 g.), identical (i.r. comparison) with an authentic sample.

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