

Remote Anodic Oxidation of Carboxylic Acids in Fluorosulphuric Acid: a Synthesis of Lactones and Unsaturated Cyclic Ketones

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The oxidation of octanoic, heptanoic, 4-methylpentanoic, and 5-methylhexanoic acids at a smooth platinum anode in fluorosulphuric acid containing potassium fluorosulphate (1M) at 273 K is described. Oxidation leads to cleavage of a C-H bond and formation of a cationic centre at a place in the carbon skeleton remote from the functional group. The final products isolated are 5- and 6-membered ring compounds, lactones, and unsaturated cyclic ketones, and the ratio of products depends on the length of time the anolyte solution is left prior to work-up. A mechanism which explains the formation of all products is suggested.

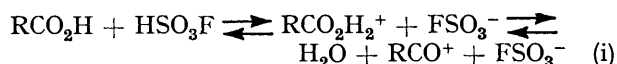
PREVIOUS papers^{1,2} have reported the oxidation of alkanes at a smooth platinum anode in the strongly

¹ J. Bertram, M. Fleischmann, and D. Pletcher, *Tetrahedron Letters*, 1971, 349.

acidic solvent, fluorosulphuric acid to which had been added a carboxylic acid; in the medium, the carboxylic

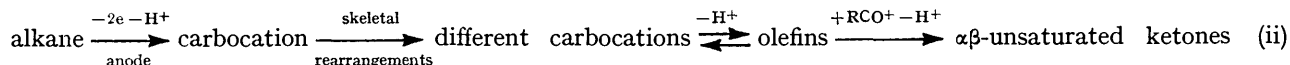
² J. Bertram, J. P. Coleman, M. Fleischmann, and D. Pletcher, *J.C.S. Perkin II*, 1973, 374.

acids act as bases because of the equilibria (i). The



products from these anodic oxidations were $\alpha\beta$ -unsaturated ketones and could all be rationalised by the reaction scheme (ii).

The present paper is the first of a series extending



the investigation to the anodic oxidation of functionalised aliphatic molecules. The basic concept of these studies is that compounds which are not solvolysed in this highly acidic solvent and which do not contain a functional group which is itself oxidised anodically might be expected to 'behave as alkanes' and undergo oxidation in the alkyl chain. Moreover almost all organic molecules are bases in fluorosulphuric acid and it is likely that the functional group will be protonated; it was hoped that the presence of this positive charge would direct the oxidation process to a position in the carbon skeleton remote from the functional group and therefore, at least with compounds of medium chain length, introduce selectivity in the site of oxidation (*cf.* n-alkanes, oxidation of which occurs at all secondary C-H sites).

This paper describes the anodic oxidation of four carboxylic acids in fluorosulphuric acid containing potassium fluorosulphate (1M) and it is shown that the primary oxidation process does occur at a site remote from the functional group, in this case $-\text{CO}_2^+\text{H}_2$ because of the equilibria (i). In this way it is possible to synthesise compounds which are either bifunctional or potentially bifunctional.

RESULTS AND DISCUSSION

Cyclic Voltammetry.—Cyclic voltammograms were recorded for a series of carboxylic acids in fluorosulphuric acid-potassium fluorosulphate (1.0M) and data taken from these *i*-*E* curves are shown in Table I. Hexanoic and 4-methylpentanoic acids give cyclic voltammograms where at potentials just prior to the anodic oxidation of the solvent/electrolyte, there is an oxidation current due to the carboxylic acids; peaks are not, however, observed. All the other acids give well formed, although irreversible, oxidation peaks (see Figure). Indeed the current functions, $i_p/\nu^{1/2}c$, are independent of the potential scan rate, ν ; hence the oxidation processes are diffusion-controlled and may be considered to be simple electron-transfer processes. No peaks for the reduction of stable intermediates are observed even at rapid potential scan rates.

As in the case of the alkanes,¹ it can be seen that the oxidation potentials become less anodic with increasing length of the carbon skeleton. Also the branched-chain acids are oxidised more readily than their straight chain analogues. Furthermore, the acids are oxidised less

readily than the corresponding alkane, owing to the influence of the positive charge on the $-\text{CO}_2^+\text{H}_2$ group.

Cyclic voltammograms of the isolated lactone products gave no oxidation wave within the potential range used, but those of the $\alpha\beta$ -unsaturated ketones did, at $-E_{p/2}$ *ca.* 1.5 V. Fortunately, these latter compounds are formed after electrolysis is complete and therefore do not undergo further oxidation.

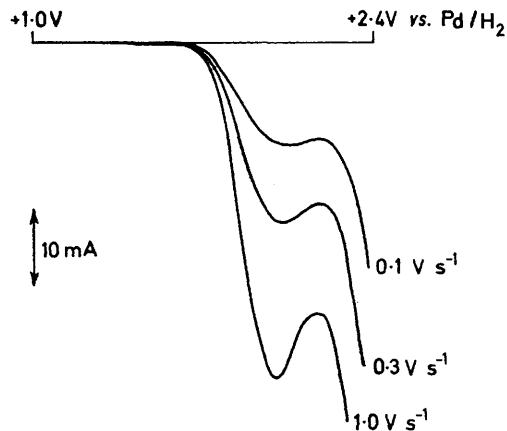
Preparative Experiments.—Controlled potential oxidations were carried out on solutions of four of the carboxylic acids in fluorosulphuric acid-potassium

TABLE I

Cyclic voltammetric data for carboxylic acid oxidations at a platinum electrode in fluorosulphuric acid-potassium fluorosulphate (1.0M). Potential scan rate 0.5 V s⁻¹. Potentials quoted *versus* the Pd/H₂ electrode in this solution

Acid	E_p/V	$(E_p - E_{p/2})/\text{mV}$
Hexanoic	Oxidation close to that for SO_3F^-	
4-Methylpentanoic	Oxidation close to that for SO_3F^-	
Heptanoic	1.95	140
5-Methylhexanoic	1.91	150
Octanoic	1.84	140
Nonanoic	1.74	130
Decanoic	1.64	120

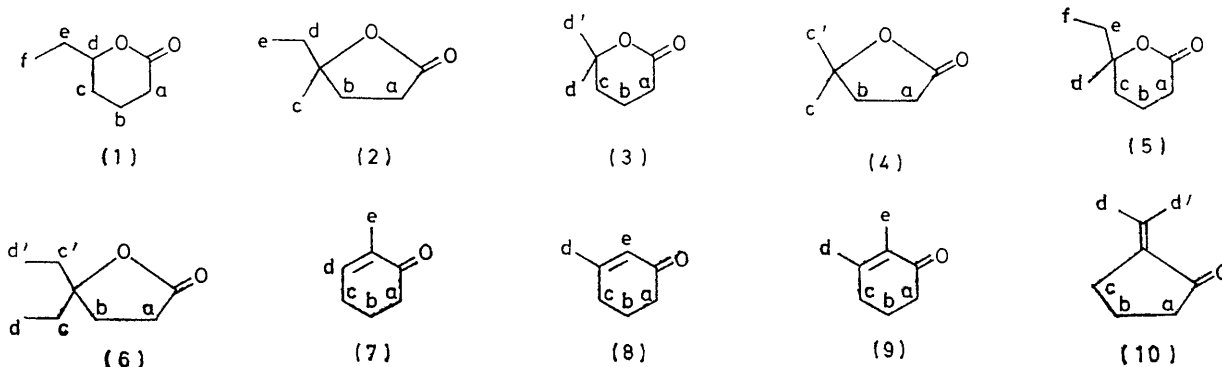
fluorosulphate (1.0M). The products were isolated and purified by g.l.c. and were identified by analysis of their spectroscopic data, as well as comparison of their



Linear potential sweep experiments for a solution of octanoic acid (0.1M) and potassium fluorosulphate (1.0M) in fluorosulphuric acid at a Pt electrode (1 cm²)

spectra with those of authentic samples, if available. The products identified are shown in Table 2. Those isolated if the anolytes were not quenched immediately at the end of the electrolysis were different from those isolated when the anolytes were quenched straight away.

In the latter case the major products were always γ - or δ -lactones, which are potentially bifunctional compounds and tend to become cyclic $\alpha\beta$ -unsaturated ketones. The overall yields were in the range 40–70%. Optical rotation measurements on compounds (1), (2), and (5) showed the products to be racemic mixtures.



In the case of octanoic acid, a controlled potential coulometric experiment showed that the current decreased smoothly with time and 1.8 electrons per molecule

TABLE 2

Products from the anodic oxidation of the carboxylic acids in fluorosulphuric acid–potassium fluorosulphate (1.0M). In general 2 Faraday mol⁻¹ charge was passed during the electrolyses

Acid	t/h ^a	Products and yields (%) ^b
Heptanoic	0	(1) (30), (2) (2), (3) (1½), (7) (2)
	48	(2) (17), (7) (20), (8) (2)
4-Methylpentanoic	0	(4) (25)
	20	(4) (23)
5-Methylhexanoic	0	(3) (60)
	48	(3) (26), (8) (42)
Octanoic	0	(5) (63), (6) (trace), (9) (trace), (10) (trace)
	22	(9) (34), (10) (26)

^a Time after the electrolysis the anolyte was left prior to work-up. ^b Based on charge consumed during the electrolysis.

of acid were transferred during the electrolysis. N.m.r. spectra were run at regular intervals for the resulting anolyte solution and at no time during the 2 days following the completion of the electrolysis were any olefinic protons detected.

On one occasion the anolyte from an oxidation of 5-methylhexanoic acid was worked up by addition to [¹⁸O]water. Mass spectrometry of the lactone formed showed that there was no incorporation of the labelled oxygen atom into the product.

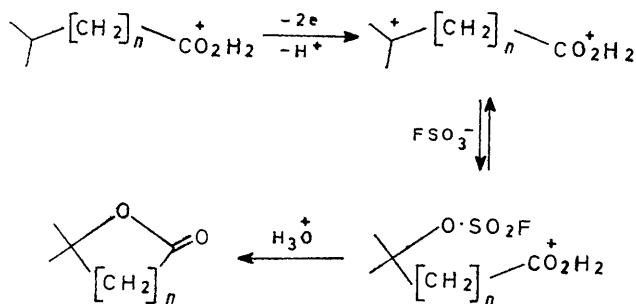
Mechanism.—The n.m.r. evidence indicates that the electroactive species is the protonated carboxylic acid RCO₂H₂⁺. This conclusion is based on the small paramagnetic shift (*ca.* 0.4–0.5 p.p.m.) relative to that reported for MeCO⁺ (*ca.* 2 p.p.m.).³ By analogy with alkane oxidation, the primary product will be a carbocation formed by cleavage of the weakest C–H bond in the substrate.

When the anolyte is worked up immediately after

termination of the electrolysis the major products are always γ - or δ -lactones. The simplest situation arises from the oxidation of the branched-chain acids, where there is a single product; the anode reaction will cleave the tertiary C–H bond and the product arises by the sequence shown in Scheme 1. With the straight-chain

acids, the situation is more complex, both because of the occurrence of carbocation rearrangements (secondary to tertiary) prior to ring closure and because, particularly with increasing carbon chain length, there is the possibility that oxidation will occur at several places on the carbon skeleton and a complex mixture of carbocations will be formed. Certainly, both straight-chain acids give lactones derived from stable tertiary carbocations.

On standing in fluorosulphuric acid, the lactones are slowly converted into cyclic unsaturated ketones in most



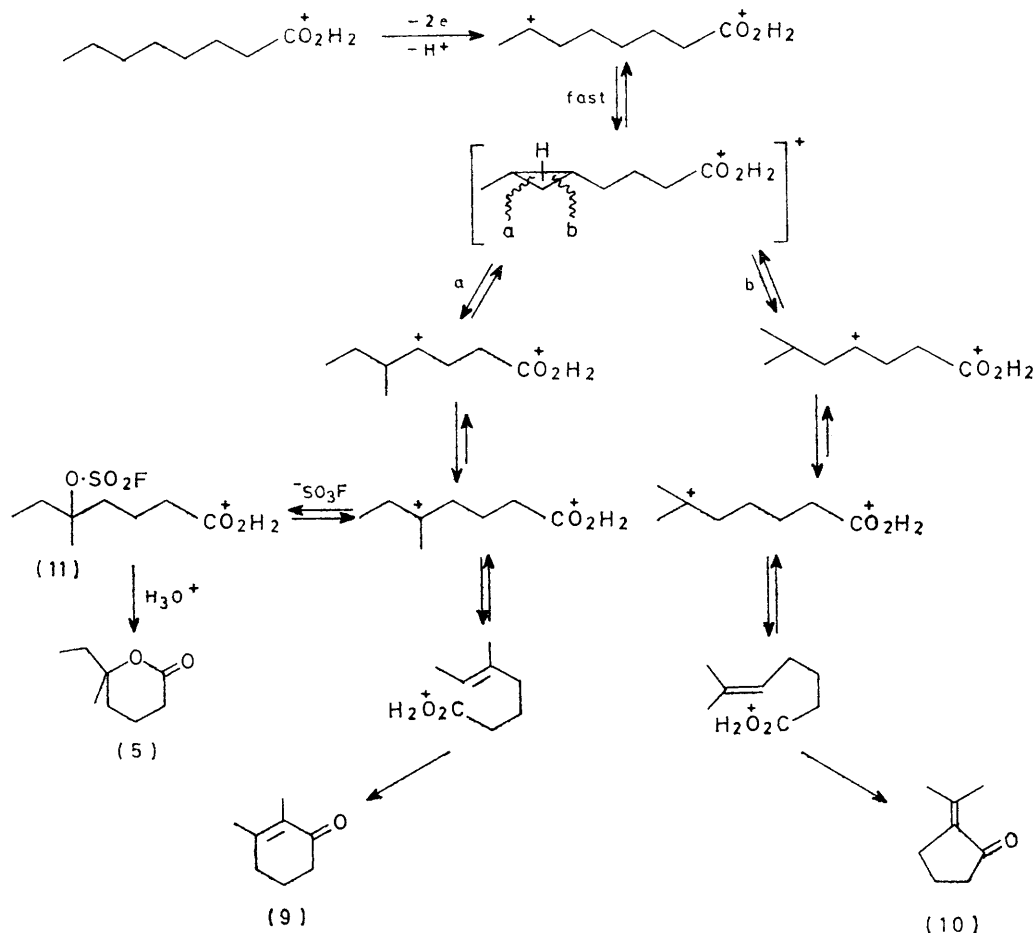
cases. The formation of these products is, however, clearly preceded by a very slow chemical reaction. It is suggested that they arise by the reaction sequence described in Scheme 2 (in which octanoic acid is used as an example), where loss of HSO₃F is the slow step as indicated by the inability to find olefinic proton signals in the n.m.r. spectrum of the anolyte. Compound (11) is believed to occur as the sulphonate ester as shown, not only because the n.m.r. spectrum of the anolyte showed only a small paramagnetic shift (*ca.* 0.4 p.p.m.) of the methyl and methylene protons (CH₃·C·CH₂·CH₃) of (11) [much lower than the expected shift (*ca.* 2 p.p.m.)

³ G. Olah, W. S. Tolgyesi, S. J. Kuhn, M. E. Moffatt, I. Bastein, and E. B. Baker, *J. Amer. Chem. Soc.*, 1963, **85**, 1328.

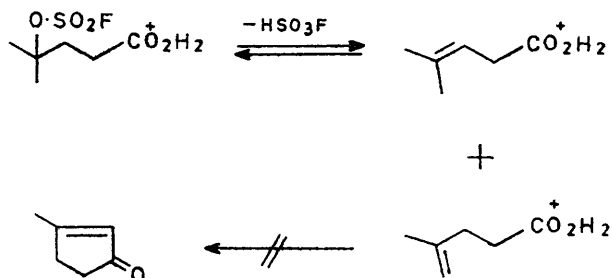
reported³], but also because the lactone formed from oxidation of 5-methylhexanoic acid showed no ¹⁸O incorporation when [¹⁸O]water was used during work-up. In the case of 4-methylpentanoic acid, the fact that no

sium fluorosulphate,² 3-methylcyclohex-2-enone,⁴ and 2-isopropylidencyclopentanone⁵ were prepared by the published methods.

The electrochemical experiments were carried out using a



ketone is isolated is most probably due to the unfavourable equilibrium shown in Scheme 3.



EXPERIMENTAL

The carboxylic acids (B.D.H. or Pfaltz and Bauer) were used as supplied. Fluorosulphuric acid (Fluorochem) was distilled, once, at atmospheric pressure, before use. Potas-

⁴ L. I. Smith and G. F. Rouault, *J. Amer. Chem. Soc.*, 1943, **65**, 631.

Chemical Electronics potentiostat and a pulse generator type R.B.1. *i-E* Curves were recorded on a Hewlett-Packard 1035 X-Y recorder and an electronic integrator was used to measure the amount of current passed.

A two-compartment cell was used for voltammetry. One compartment (5 cm³) contained the working electrode (Pt wire), area 0.6 cm², surrounded by a helical Pt wire secondary electrode. The other compartment contained the reference electrode (Pd/H₂)² and was connected to the former by a Luggin capillary.

All preparative oxidations were carried out in a three-compartment cell. The anode compartment (ca. 25 cm³) was separated from the cathode by a No. 2 glass sinter. A 3.5 cm² Pt gauze anode was used. The reference electrode (Pd/H₂) was separated from the working electrode by a Luggin capillary. The secondary electrode was a Pt sheet (area 4 cm²).

N.m.r. spectra were recorded on either a Perkin-Elmer R-12 or a Varian HA-100 instrument. I.r. spectra were measured on a Perkin-Elmer 157G spectrometer. Mass

⁵ R. Cernubert and C. Borrel, *Bull. Soc. chim. France*, 1930, 958.

spectra were measured on an AEI MS 12 mass spectrometer and u.v. spectra on a Pye-Unicam SP 800A instrument, and optical rotations were measured with an ETL-NPL 143A automatic polarimeter. G.l.c. was carried out with a Pye 104 chromatograph with a flame ionisation detector. A column (0.3 × 90 cm) of 10% PEGA and 1% H₃PO₄ on Celite was used for analytical experiments and a column (0.5 × 160 cm) of 15% PEGA and 1% H₃PO₄ was used for preparative experiments.

Preparative Electrolysis; General Method.—The cell was filled with fluorosulphuric acid containing potassium fluorosulphate (1.0M) and immersed in an ice-bath. The acid (ca. 10 mmol) was added to the anode compartment and the solution was stirred magnetically. Electrolysis was carried out, at the same temperature, with a controlled anode potential of +1.8 to +2.0 V vs. a Pd/H₂ reference electrode, until ca. 1000 C had been passed. The electrode was kept clean by a short cathodic pulse (100 ms) to +0.3 V every 3 s.

At the end of electrolysis the anolyte was quenched by adding, dropwise, to crushed ice. The resulting acidic solution was neutralised with sodium carbonate, and sodium chloride was added to saturate the solution further. The organic material was extracted with ether (4 × 200 ml). The extract was dried (Na₂SO₄) and evaporated under vacuum below 30°. The products were separated by preparative g.l.c. when necessary and analysed accordingly. The yields of the products quoted are based on the charge passed. The organic yields cannot be lower than these values.

(a) *4-Methylpentanoic acid.* The acid (1.3 ml) was oxidised at 2.1 V. The crude liquid obtained after evaporation was subjected to g.l.c. and g.l.c.–mass spectroscopic analyses. The result showed that four products were obtained. The first three, with lower retention times (ca. 30% yield), had high molecular weight (170) and the fourth (23%) had a molecular weight of 114. The major product (last peak) was purified by distillation under vacuum [b.p. 78.0–80.0° at 10 mmHg (lit.,⁶ 79.5° at 10 mmHg)] and identified as 4-methylpentan-4-olide (4), ν_{\max} (film) 1765 cm⁻¹ (C=O of γ -lactone), *m/e* 114 (*M*⁺), 99, 81, 70, 55, and 43 (cf. ref. 7), δ (CDCl₃) 1.44 (6H, s, H_{c,c'}), 2.15 (2H, t of d, J 6 and 2 Hz, H_a), and 2.64 (2H, t of d, J 6 and 2 Hz, H_b).

(b) *5-Methylhexanoic acid.* The acid (1.0 ml, 7 mmol) was oxidised at +2.0 V. (i) When the anolyte was worked up immediately after electrolysis (1080 C) a crude liquid (410 mg, 60%) was obtained. G.l.c. analysis showed only one major peak. Distillation of the crude material under vacuum gave a liquid, b.p. 100–103° at 4 mmHg (lit.,⁸ 102° at 4 mmHg), identified as 5-methylhexan-5-olide (3), ν_{\max} (film) 1740 cm⁻¹ (C=O of γ -lactone) (cf. refs. 9 and 10), *m/e* 128 (*M*⁺), 113, 85, 69, 56, 43, and 41 (identical with reported values⁷), δ (CDCl₃) 1.40 (6H, s, H_{d,d'}), 1.80 (4H, m, H_{b,c}), and 2.48 (2H, t, J 5 Hz, H_a).

(ii) When the anolyte was kept at room temperature for 22 or 48 h before work-up, an orange liquid (450 mg, 70%) was obtained. G.l.c. analysis showed two major peaks, ratio 1:1 after 22 h or 1:1.5 after 48 h. The products were separated by preparative g.l.c. The first peak consisted of 3-methylcyclohex-2-enone (8), δ (CDCl₃) 1.83–

2.20 (5H, s centred at 1.97 overlapping m, H_{b,a}), 2.20–2.51 (4H, m, H_{a,c}), and 5.78br (1H, H_e); u.v. and i.r. spectra identical with those of an authentic sample. The second was identified as 5-methylhexan-5-olide (3) by comparison with the compound isolated in (i).

(iii) The acid (200 μ l, 1.4 mmol) was oxidised following the general method. The resulting anolyte (3.0 ml) was added slowly to cold (acetone–solid CO₂ bath) [¹⁸O]water (0.5 ml). The solid material was allowed to warm to ca. 0° to aid mixing, then solid sodium carbonate was added, in small portions, until evolution of gas ceased. The solid mass was then extracted with ether (4 × 50 ml). Evaporation left a yellow liquid which was analysed by g.l.c.–mass spectrometry.

(c) *Heptanoic acid.* This electrolysis was carried out at an anodic potential of +1.9 V. (i) When the solution in the anode compartment was quenched immediately after electrolysis (940 C), a yellow liquid (260 mg, 40%) was isolated. G.l.c. analysis showed three minor peaks and one major (major product 11 × minor products). The minor products were identified as 2-methylcyclohex-2-enone (7) (ca. 1%), 4-methylhexan-4-olide (2) (ca. 2%), and 5-methylhexan-5-olide (3) (ca. 1.5%) by comparison with compounds described below. The preponderant product was identified as heptan-5-olide (1) (ca. 35%) and was isolated by preparative g.l.c.; ν_{\max} (film) 1740 cm⁻¹ (C=O of γ -lactone) (cf. refs. 9 and 10), $[\alpha]_D^{21} 0^\circ$ (c 1% in EtOH), *m/e* 128 (*M*⁺), 113, 99, 86, 84, 71, 55, and 41 (cf. ref. 7), δ (CDCl₃) 1.00 (3H, t, J 5 Hz, H_f), 1.36–2.05 (6H, m, H_{b,c,e}), 2.47 (2H, t, J 4 Hz, H_a), and 4.00–4.38 (1H, m, H_d).

(ii) When the anolyte was quenched 48 h after completion of electrolysis, an orange liquid (250 mg) was obtained. G.l.c. showed two major peaks and traces of another. The products were separated by preparative g.l.c. to give as a first peak (lower *t*_R) 2-methylcyclohex-2-enone (7) (20%), ν_{\max} (film) 1680 (C=O) and 1640 cm⁻¹ (C=C), λ_{\max} (EtOH) 233 nm (ϵ 9650) [lit.,¹¹ 234 (ϵ 9660)], *m/e* 110 (*M*⁺), 99, 82, 69, 53, 39, and 32, δ (CDCl₃; 100 MHz) 1.78 (3H, q, J 1 Hz, H_e), 1.97 (2H, q, J 3 Hz, H_b), 2.20–2.52 (4H, m superimposed on t centred at 2.41, H_{a,c}), and 6.65–6.80 (1H, m, H_d). Traces of 3-methylcyclohex-2-enone (8) (ca. 2%) were observed (second peak; identified by retention time comparison with an authentic sample). The last peak was 4-methylhexan-4-olide (2) (ca. 17%), ν_{\max} (film) 1775 cm⁻¹ (C=O of γ -lactone), $[\alpha]_D^{21} 0^\circ$ (c 1% in EtOH), *m/e* 128 (*M*⁺), 113, 99, 84, 72, 69, 55, 43, 41, and 39 (as reported⁷), δ (CDCl₃) 0.97 (3H, t, J 5 Hz, H_e), 1.38 (3H, s, H_a), 1.68 (2H, t, J 5 Hz, H_d), 2.10 (2H, t, J 6 Hz, H_b), and 2.63 (2H, t of d, J 6 and 1.2 Hz, H_c).

(d) *Octanoic acid.* The acid (1.0 ml, 6 mmol) was oxidized at +1.84 V. (i) When the anolyte was quenched immediately after electrolysis (1145 C) a crude liquid was isolated (891 mg). G.l.c. analysis showed two major peaks (ratio 1.0:1.5). The first peak behaved as the starting material (g.l.c.–mass spectrum and i.r. spectrum). The second consisted of 5-methylheptan-5-olide (5) (63%), ν_{\max} (film) 1740 cm⁻¹ (C=O of δ -lactone), $[\alpha]_D^{21} 0^\circ$ (c 1% in EtOH), *m/e* 142 (*M*⁺), 127, 113, 99, 85, 70, 55, and 43 (as expected⁷), δ (CDCl₃) 0.97 (3H, t, J 3.5 Hz, H_f), 1.34 (3H, s, H_a), 1.50–2.30 (6H, m, H_{b,c,e}), and 2.25–2.50 (2H,

⁶ B. J. Clarke and R. D. Hildebrand, *J. Inst. Brewing*, 1967, **73**, 60.

⁷ E. W. Honkane, T. Moiso, and P. Karvonen, *Acta Chem. Scand.*, 1969, **23**, 537.

⁸ M. G. Zalinga, D. A. Sarkisyan, E. A. Arutyunyan, and M. T. Danguan, *Armyan khim. Zhur.*, 1967, **20**, 898.

⁹ R. R. Allen, *Chem. and Ind.*, 1965, 1950.

¹⁰ T. H. Parliament, M. W. Parliament, and I. S. Fargerson, *Chem. and Ind.*, 1966, 1845.

¹¹ E. W. Warnhoff, D. G. Martin, and W. S. Johnson, *Org. Synth.*, Coll. Vol. IV, p. 162.

m, H_a). The n.m.r. spectrum of the anolyte showed no olefinic proton signals.

(ii) The products from a similar oxidation, kept at room temperature for 22 h before quenching, gave an orange liquid (360 mg). G.l.c. analysis showed two major products (ratio 1 : 1.3) and only traces of impurities (high t_R value). The first peak was 2-isopropylidencyclopentanone (10) (26%), ν_{\max} (film) 1710 (C=O) and 1630 cm^{-1} (C=C), λ_{\max} (EtOH) 253 (ϵ 9900) and 333 nm (ϵ 61), b.p. 66–67° at 3 mmHg (lit.,⁵ 80–82° at 12 mmHg), m/e 124 (M^+), 109, 96, 82, 81, 68, 53, 41, and 39, δ (CDCl₃) 1.80 (5H, s overlapping q centred at *ca.* 1.86, H_{b,d}'), 2.20 (5H, s overlapping t centred at *ca.* 2.22, H_{e,d}), and 2.57br (2H, s, H_a). The second peak was 2,3-dimethylcyclohex-2-enone (9) (34%), ν_{\max} (film) 1660 (C=O) and 1630 cm^{-1} (C=C), λ_{\max} (EtOH) 241 (ϵ 11,630) and 308 nm (48), b.p. 68–70° at 5 mmHg (lit.,⁴ 90–96° at 14 mmHg), m/e 124 (M^+), 96, 82, 67, 53, and 39, δ (CDCl₃) 1.75 (3H, s, H_b), 1.91 (5H, s at 1.91 over-

lapping q, J 3 Hz centred at 1.97, H_{b,d}), and 2.34 (4H, m, H_{a,c}). The n.m.r. spectrum of the anolyte showed no olefinic proton signals.

Procedure for Electroanalytical Experiments.—In all experiments all compartments of the electrochemical cell were filled with the same solution: distilled fluorosulphuric acid to which a weighed amount of anhydrous potassium fluorosulphate had been added. All experiments were carried out at ice-bath temperature unless stated differently. The electrolytic solution was protected from moisture (CaCl₂ tube).

Stability of the Various Acids in Fluorosulphuric Acid-Potassium Fluorosulphate (1.0M).—The acid (40 mg) was dissolved in fluorosulphuric acid (0.5 ml) containing potassium fluorosulphonate (1.0M). The n.m.r. spectra were recorded immediately after mixing and after 10, 20, 30, 40, and 48 h.

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