Electro-organic Reactions. Part 13.† The Anodic Acetoxylation of Methyl Oleate

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Efficient anodic mono- and di-acetoxylation of methyl oleate is described. Acetoxylation is consecutive and conditions may be adjusted to give a maximum of either 60% monoacetoxylation or 85% diacetoxylation. Both mono- and di-substituted products are a complex mixture of isomers but the products of exhaustive electrolysis are mainly 9,10-diacetoxyoctadec-7- or -11-enoate. A mechanistic rationalisation is proposed.

THE allylic functionalisation of unsaturated fatty acid esters has been much studied and oxygenated products are normally obtained by oxidation,[1] autoxidation,[2] and acetoxylation [3] using heat, light, or metal catalysts to promote reaction. Such methods often lack selectivity and are difficult to control. Acetoxylation of methyl oleate, in oxidation catalysed by palladium(II) salts,[3] drew our attention to the possibility of anodic acetoxylation of such compounds. The anodic acetoxylation of alkylaromatics both at the side chain and in the nucleus is well understood [4] to involve electron transfer from the aromatic species; similarly anodic functionalisation at allylic positions has been reported.[5] Acetoxylation of alkylaromatics may also be achieved [6] using palladium(II) salts as catalysts; substitution occurs at the side chain and at the nucleus. Although the product distributions of the anodic and palladium catalysed processes are closely similar Pd^{II} does not apparently oxidise electron rich aromatics in the absence of a base [7] and the formation of π-complexed intermediates is thought to be the key step. The similarity of the results of the two processes is, however, such that it becomes worthwhile to investigate further the anodic acetoxylation of alkenes. Methyl oleate was chosen as substrate because (a) it has been subjected to palladium catalysed acetoxylation [3] and many other methods of oxygenation, (b) the two allylic methylene groups are non-equivalent and mechanistic information may accrue from the selectivity of attack, and (c) the development of efficient and convenient syntheses of oxygenated products derived from methyl oleate is important and mimics processes involved in the deterioration of fats and oils.

RESULTS AND DISCUSSION

Ease of Oxidation.—Single sweep cyclic voltammetry [Pt bead anode, CH_3CN–Bu_4NClO_4 (0.1M), 200 mV s^{-1}] revealed that methyl oleate was not oxidised at $\leqslant 2.25$ V (*versus* Ag wire). Because preparative electrochemical oxidations of alkenes in acetonitrile are often precluded by electrode fouling, an aqueous acetonitrile solution was also examined. Oxidations which fail because of anode fouling in acetonitrile are often successful in aqueous acetonitrile.[8] However, according to cyclic voltammetry [Pt bead anode, 10% H_2O–CH_3CN (v/v), LiClO$_4$ (0.075M), CH_3CO_2Na (0.075M), CH_3CO_2H (0.075M)] no oxidation of methyl oleate was observed before oxidation of the solvent set in at $\leqslant 2.0$ V (*versus* Ag wire). Al-

† Part 12, ref. 10.

kenes are known to be difficult to oxidise, *e.g.* for oct-2-ene in acetonitrile [9] an $E_{\frac{1}{2}}$ value of $+2.23$ V (*versus* Ag–Ag$^+$) has been recorded. In cyclic voltammetric experiments lower oxidation potentials have been found [10] for cycloalkenes, particularly where the double bond bears alkyl substituents, but the peaks are often broad and ill defined.

The fact that in voltammetry the solvent system oxidises at a lower potential than methyl oleate need not preclude preparative scale electrolysis. It is often observed that in mixtures of electroactive species at preparative concentrations the observed electrode reaction is a function not only of potential but of concentration; *e.g.* conditions for the anodic oxidation in acetonitrile of mixtures of chloride ion and cyclohexene may be adjusted [11] to give either prior oxidation of chloride or oxidation of cyclohexene. Another example is the Kolbe oxidation of alkanoate ions in aqueous solution where at high current density the evolution of oxygen (a lower potential process) is completely suppressed.[12] With this encouragement preparative scale anodic oxidation of methyl olate in the presence of acetate ion was carried out under a variety of conditions.

Preparative Scale Electrolyses.—The results of preparative scale anodic oxidation are summarised in Table 1. The identification and characterisation of products are discussed in a subsequent section.

Controlled potential electrolysis in aqueous acetonitrile (Table 1, entry 1) could not be taken to completion; despite the application of periodic pulsing to 0 V the current fell at 0.6 F mol^{-1} presumably because of anode fouling. Subsequent electrolysis was at constant current density in acetic acid solution. This electrolyte system conducts poorly and it was found necessary to employ an undivided, Dinh-Nguyen cell.[13] In this manner exhaustive electrolysis of methyl oleate was possible. Best results were obtained at a smooth platinum disc anode. In one experiment (entry 5) a carbon cloth anode was used which gave poor conversion of olate into acetoxylated products and, even at low conversion, favoured diacetoxylation. The low efficiency of this reaction is probably due to competition from concomitant acetate oxidation which is known to proceed well at low current densities on carbon.[14]

Much information can be gleaned from the results of an experiment which involved analysis of samples withdrawn at intervals during electrolysis (Table 1, entry 4). The results are displayed in the Figure. The consecutive

acetoxylation of oleate and monoacetoxylated oleate is revealed clearly. The acetoxy group would be expected to be, if anything, slightly activating toward further

(F mol⁻¹)(0·44) (0·88) (1·32) (1·76) (2·20) (2·64) (3·08)(3·52)(3·96)
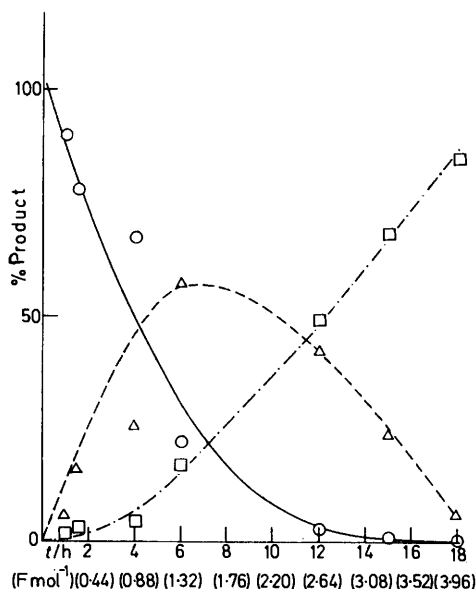
Anodic acetoxylation of methyl oleate: ○, oleate; △, monoacet-oxyoleate; □, diacetoxyoleate

oxidation as is found for anodic acetoxylation of alkyl-aromatics.[4] Such an effect should diminish with increasing separation of the acetoxy group and the double bond. The results given in the Figure may, by computerised simulation,[15] be accommodated in a scheme which,

Combined acetoxylated products were isolated by preparative scale t.l.c. The mass spectra of the mixtures showed them to consist of both monoacetoxy isomers (Found: m/e, 354.2781. Calc. for $C_{21}H_{38}O_4$: M, 354.2770) and diacetoxy isomers (Found: m/e, 412.2836 Calc. for $C_{23}H_{40}O_6$: M, 412.2825). Subsequent analysis was by g.l.c. A detailed analysis of the final product mixture for experiment 4 (Table 1) was carried out using g.l.c.–m.s. after the acetoxy compounds had been converted into trimethylsilyl ethers.[3] Three peaks corresponding to substituted oleate products were examined by mass spectrometry. That of lowest retention time (peak 1, 8 min) related to mono-oxygenated products (ca. 6%), a similarly small peak (peak 2) of retention time 18 min related to di-oxygenated products, and the major broad peak (peak 3) at 21—25 min contained a mixture of di-oxygenated products. It is convenient separately to discuss the mass spectra obtained by sampling the peaks. Mass spectrometry reveals that peak 2 is due mainly to methyl 9-(or 10)-acetoxy-10(or 9)-trimethylsiloxyoctadecanoate, derived from silylation of a partially hydrolysed diacetate mixture. It is therefore an artefact of the experimental procedure and discussion is concentrated on peaks 1 and 3.

The interpretation of mass spectra on the basis of allylic fragmentation follows that described previously[3] and is summarised in Table 2 and the associated formulae. Peak 3 is seen to be due to a mixture of dihydroxy-octadecenoate (V) and dihydroxyoctadecanoate (IV), with one hydroxy substituent scattered between C-8 and

TABLE 1

Anodic acetoxylation of methyl oleate

Entry	Anode [a]	Electrolyte	Current density (A cm⁻²)	Charge (F mol⁻¹)	Oleate	Product [c] (%) Mono-OAc	Di-OAc	Unknown
1	Pt	90% v/v MeCN–H₂O; LiClO₄ (0.1M–NaOAc (0.1M)	(anode potential) [b] [+2.1 V (vs. Ag wire)]	0.6		Current fell at 0.6 F mol⁻¹		
2	Pt	HOAc–LiClO₄(0.2M)	0.035	28.0	13.8	40.0	40.4	5.9
3	Pt	HOAc–LiClO₄ (0.1M)	0.007	4.5	2.4	31.8	59.5	6.3
4	Pt	HOAc–LiClO₄ (0.1M)	0.008	Samples analysed in range 0–4 F mol⁻¹		see Figure		
5	C (cloth)	HOAc–LiClO₄ (0.1M)	0.008	3.1	68.4	9.2	17.4	5.0

[a] Entry 1, divided H cell, carbon cathode; entries 2—5 Dhin-Ngyuen cell, Hg cathode. [b] Periodic pulsing to 0 V required to maintain current. [c] Analysis by g.l.c.

assuming kinetics pseudo-first order in oleate and mono-acetoxyoleate, gives the relative rates for oleate to mono-acetoxyoleate (k_1) and monoacetoxyoleate to diacetoxy-oleate (k_2) as $k_1/k_2 = 1.4$. Thus a small deactivating effect is observed. These latter results must however be interpreted with great caution because in such hetero-geneous oxidation the relative rates of reaction may well be governed by unknown (and unknowable) surface effects and/or transport to and from the anode of react-ants, reactive intermediates, and products.

It is clear, however, that by careful choice of the conditions monoacetoxylation may be optimised at ca. 60% and diacetoxylation at ca. 85% yield.

Identification and Characterisation of Products.—

-11, and the other hydroxy between C-9 and -12 (Table 2). The relative abundance of the fragment ions at m/e 215 and 259 indicates that the 9,10-dihydroxy derivative is the main component of this mixture. Peak 1 is due to a mixture of allylic hydroxyoctadecenoate (I), non-allylic hydroxyoctadecenoate (II), and hydroxyocta-decanoate (III) with hydroxy substituent distributed between C-8 and -11 (Table 2).

*Mechanism.—*The major features to be accommodated in the mechanism are: (a) consecutive acetoxylation takes place with the oleate consumed after ca. 2 F mol⁻¹ (Figure); (b) the major product of diacetoxylation is 9,10-substituted; and (c) saturated and unsaturated products are observed.

These observations are consistent with the pathways summarised in the Scheme. Whenever cationic intermediates are involved there is the possibility of hydride shifts with effective double bond migration and the formation of diacetates other than 9,10-disubstituted. This would account for the great variety of minor products which are formed. It is unlikely that significant

spectra of the corresponding TMS ethers suggests that the Δ^7- and Δ^{11}-isomers predominate; the ions most probably arise via allylic fragmentation.

The sequential formation of diacetates from monoacetates (Figure) rules out the formation to any great extent of saturated diacetates via quenching of monoacetoxy cations at the one-electron oxidation stage.

TABLE 2

Analyses of mono- and dihydroxy-derivatives by g.l.c.–m.s.

C-18 OTMS methyl esters [a]		Related masses	Fragment ions [a]	m/e (relative abundance, %)			
				8-OH	9-OH	10-OH	11-OH
Monohydroxy							
Peak 1							
Allylic	I	384(M)	A,B	241(12)	227(18)	271(15)	285(14)
Nonallylic	II	384(M)	C,D	245(21)	259(37)	215(43)	201(15)
Saturated	III	371(M − 15)	C,D	243(16)	229(31)	273(28)	287(14)
Dihydroxy							
Peak 3				8, x − x, 9 [b]	9, x − x, 10	10, x − x, 11	11, x − x, 12
Saturated	IV	459(M − 15)	C	229(10)	215(75)	201(27)	187(4)
			D	245(21)	259(97)	273(6)	287(5)
Unsaturated	V	457(M − 15)	A	227(14)	213(10)	199(8)	185(6)
			B	243(12)	257(22)	271(15)	285(7)
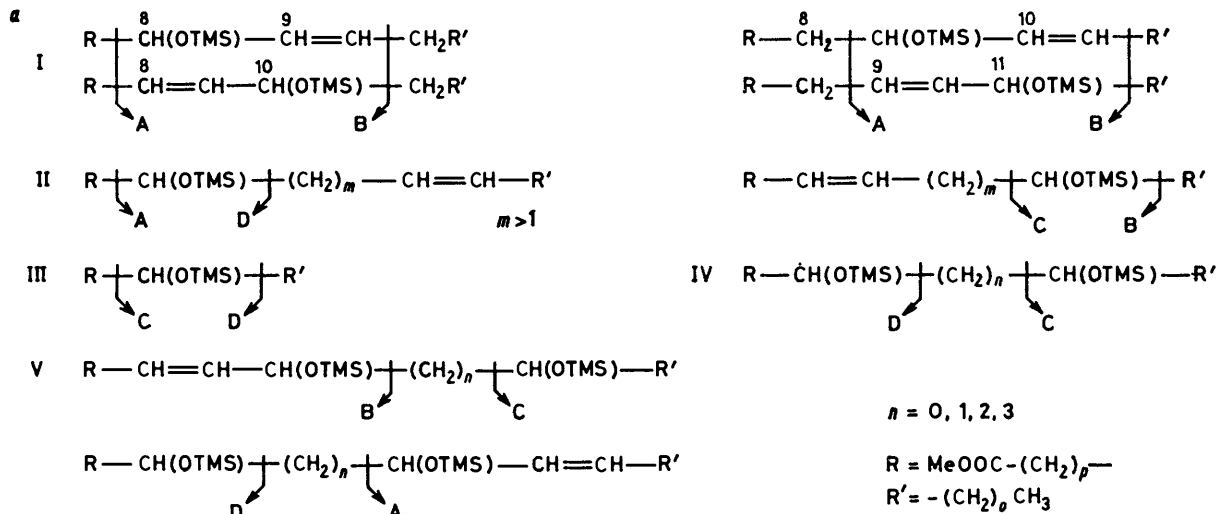
[b] 8,x means hydroxy on C-8 on ester side of molecule (R), x,9 means hydroxy on C-9 on hydrocarbon side of molecule (R').

amounts of vinylic mono- or di-acetates are formed. Such structures (i.e. enol acetates) would be expected to oxidise at the anode with cleavage [16] and, if such a fate were avoided, would hydrolyse to carbonyl compounds which were not detected.

Saturated monoacetates are present but their formation is not favoured; they cannot exceed 6% (peak 1) because it is unlikely that they would have been depleted by anodic oxidation to diacetates. If conditions were severe enough to oxidise saturated acetates then oxidation would not stop at the diacetate stage. We may conclude from this that abstraction (and/or disproportionation), the routes to saturated acetates, is not significant. This result also implies that at a later stage significant abstraction to give saturated diacetates is also unlikely which, in turn, suggests that the major products are unsaturated 9,10-diacetates. The prominence of ions at m/e 215 (RA, 75%) and 259 (RA, 97%) in the mass

EXPERIMENTAL

Electrochemical Experiments.—For both preparative and voltammetric experiments suitable combinations of the following modules were used: potentiostat (TR 70/2A), waveform generator (RB1), and electronic integrator (all Chemical Electronics Ltd.), together with an X–Y recorder (Hewlett–Packard 7035B). Constant current electrolyses were performed using either a Coutant Electronics Ltd. power supply (model LA 200.2) or a direct current power supply constructed by the Q.M.C. electronics workshop.

For voltammetry and controlled potential electrolysis conventional glass H cells were used with sintered glass separators. The reference electrode (Ag wire) was contained in a third compartment linked to the working electrode by a sintered separator, or, for voltammetry, by a Luggin capillary. Controlled current electrolyses were carried out in a water-jacketted Dinh-Nguyen cell [13] at a platinum disc anode of 12.6 cm² area with an Hg pool cathode of 28 cm² area. In one experiment a carbon cloth anode was con-

Scheme

structed by fitting a sheath of carbon cloth over the above platinum disc.

In a typical constant current run methyl oleate (5 g, 0.017 mol) in acetic acid (30 cm³) containing dried lithium perchlorate (0.1M) was electrolysed at 0.1 A. The cell voltage was in the region 80—100 V throughout. In one experiment (Table 1, entry 4) samples (1.5 cm³) were withdrawn at intervals for analysis.

Analysis of Product Mixtures.—The essential methods as applied to acetoxyoleates (g.l.c., g.l.c.-m.s., t.l.c.) have been described as have the processes for saponification and subsubsequent silylation using bis(trimethylsilyl)trifluoroacetamide.[3]

In the present work g.l.c. was performed with glass columns (72 × 0.25 in) packed with 3% Silar 5CP on Gas-Chrom Q 80—100 mesh (Applied Science, State College, Pa), programming from 190 to 250 at 1 °C min⁻¹. The data in Table 2 were based on comparisons with reference compounds, methyl 9(10)-hydroxyoctadecanoate, 12-hydroxyoctadec-9-enoate, 12-hydroxyoctadecanoate, 9,10-dihydroxyoctadecanoate, and 10,12-dihydroxyoctadecanoate.[3]

REFERENCES

[1] M. Naudet and E. Ucciani, in ' Topics in Lipid Chemistry ', ed. F. D. Gunstone, Logos, London, 1970, vol. 2, p. 99.

[2] E. N. Frankel, in ' Symposium on Foods: Lipids and their Oxidation ', ed. W. H. Schultz, Avi, Westport, 1962, p. 51.

[3] E. N. Frankel, W. K. Rohwedder, W. E. Neff, and D. Weisleder, *J. Org. Chem.*, 1975, **40**, 3247.

[4] L. Eberson in ' Organic Electrochemistry ', ed. M. M. Baizer, Marcel Dekker, New York, 1973, pp. 781 *et seq.*

[5] N. L. Weinberg in ' Technique of Electro-organic Synthesis ', Part 1, ed. N. L. Weinberg, Wiley–Interscience, New York, 1974, pp. 355 *et seq.*

[6] L. Eberson and L. G. Gonzalez, *Acta Chem. Scand.*, 1973, **27**, 1162, 1249; G. G. Arzoumandis and F. C. Ranch, *J. Org. Chem.*, 1973, **28**, 4443.

[7] L. Eberson and L. G. Gonzalez, *Acta Chem. Scand.*, 1973, **27**, 1255.

[8] S. M. Weinreb and G. A. Epling, *J. Org. Chem.*, 1975, **40**, 1356.

[9] M. Fleischmann and D. Pletcher, *Tetrahedron Letters*, 1968, 6255.

[10] C. Adams, N. Jacobsen, and J. H. P. Utley, *J.C.S. Perkin II*, 1978, 1071.

[11] G. Faita, M. Fleischmann, and D. Pletcher, *J. Electroanalyt. Chem. Interfacial Electrochem.*, 1970, **25**, 455.

[12] T. Dickinson and W. F. K. Wynne-Jones, *Trans. Faraday Soc.*, 1962, **58**, 382, 388, 400.

[13] N. Dinh-Nguyen, *Acta Chem. Scand.*, 1958, **12**, 585.

[14] W. J. Koehl, *J. Amer. Chem. Soc.*, 1964, **86**, 4686.

[15] R. O. Butterfield, *J. Amer. Oil Chemists' Soc.*, 1969, **46**, 429.

[16] T. Shono, Y. Matsumura, and Y. Nakagawa, *J. Amer. Chem., Soc.*, 1974, **96**, 3532.