SECTION C
Organic Chemistry

Anodic Oxidation. Part VIII.[1] Electrolysis of Dimethyl Sodiomalonate in Hexamethylphosphoric Triamide

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Electrolysis of dimethyl sodiomalonate in hexamethylphosphoric triamide gives tetramethyl ethane-1,1,2,2-tetracarboxylate, tetramethyl propane-1,1,3,3-tetracarboxylate, and hexamethyl propane-1,1,2,2,3,3-hexacarboxylate. Degradation of the solvent to pentamethylphosphoric triamide occurs; mechanisms for the loss of the *N*-methyl group and for its subsequent incorporation into the second of the above products are discussed.

We reported earlier [2] that the electrolysis of diethyl sodiomalonate in *NN*-dimethylformamide and *NN*-dimethylacetamide gives as one of the products tetraethyl propane-1,1,3,3-tetracarboxylate (I; R = Et) containing a one-carbon fragment which we suggested was derived from one of the *N*-methyl groups of the solvent. Since this electrochemical demethylation parallels the biological oxidative demethylation of *N*-methyl substituted carboxylic amides,[3] recent reports [4] that hexamethylphosphoric triamide, a well known electrochemical solvent,[5] undergoes biological demethylation prompted us to see if we could obtain evidence for the electrochemical *N*-demethylation of this phosphoric amide. We report now on the electrolysis of dimethyl sodiomalonate in this solvent.

Tetramethyl ethane-1,1,2,2-tetracarboxylate (II), tetramethyl propane-1,1,3,3-tetracarboxylate (I; R = Me), and hexamethyl propane-1,1,2,2,3,3-hexacarboxylate (III) could each be isolated from the electrolysis products by a combination of fractional crystallisation and t.l.c. The structure of (III), which

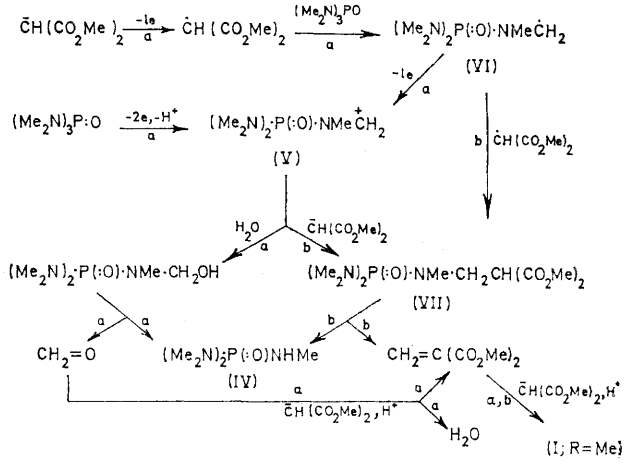
$$(RO_2C)_2CH{\cdot}CH_2{\cdot}CH(CO_2R)_2$$
(I)

$$(MeO_2C)_2CH{\cdot}CH(CO_2Me)_2$$
(II)

$$(MeO_2C)_2CH{\cdot}C(CO_2Me)_2{\cdot}CH(CO_2Me)_2$$
(III)

was not fully characterised in the earlier studies,[2] was confirmed by the microanalytical data, a molecular ion *m/e* 392 in the mass spectrum, and the n.m.r. spectrum which showed just two singlet absorptions, due to the ester methyl groups (τ 6·19) and the hydrogen atoms at C-1 and C-3 (τ 5·72), with integrated areas in the ratio 9 : 1. Analysis by g.l.c. of the water-soluble material showed the presence of hexamethylphosphoric triamide and also pentamethylphosphoric triamide (IV) (identified by its retention time and by its i.r. spectrum).

The formation of (II) and (III) in this electrolysis is unexceptional and was expected on the basis of work in other solvents.[2] The formation of both tetramethyl propane-1,1,3,3-tetracarboxylate (I; R = Me) and pentamethylphosphoric triamide (IV) strongly suggests that the 'extra' methylene group in (I; R = Me) originates as one of the *N*-methyl-groups in the solvent. A mechanism analogous to the one suggested earlier [2] to account for the formation of (I; R = Et) during the electrolysis of diethyl sodiomalonate in *NN*-dimethylacetamide, which requires the presence of a trace of water, could be operative here (Scheme: pathway a).



Alternatively (Scheme: pathway b) the intermediates (V) and (VI) in such a pathway might combine with the anion from dimethyl malonate, or the related radical formed from it by electrochemical oxidation, to give the the intermediate (VII), fragmentation of which would give pentamethylphosphoric triamide (initially as its anion) and dimethyl methylenemalonate, the precursor of (I; R = Me); *N*-(2,2-diethoxycarbonylethyl)phthalimide undergoes a similar fragmentation.[6]

[1] Part VII, T. D. Binns, R. Brettle, and G. B. Cox, *J. Chem. Soc.* (*C*), 1969, 2499.
[2] R. Brettle and J. G. Parkin, *J. Chem. Soc.* (*C*), 1967, 1352.
[3] R. E. McMahon, *J. Pharm. Sci.*, 1966, **55**, 457.
[4] A. R. Jones and J. S. Bertram, *Experimentia*, 1968, **24**, 326; A. R. Jones and H. Jackson, *Biochem. Pharmacol.*, 1968, **17**, 2247.
[5] H. Normant, *Angew. Chem. Internat. Edn.*, 1967, **6**, 1046; *Bull. Soc. chim. France*, 1968, 791.
[6] H. Bohme and L. Hafner, *Chem. Ber.*, 1966, 287.

Our results show that the analogy between electrochemical and biological oxidative *N*-demethylation in carboxylic amides can be extended to a phosphoric amide.

EXPERIMENTAL

Chloroform was evaporated on a Buchi Rotavapor R evaporator. Details of the electrolysis cell have been given previously.[7] For other general directions see earlier Parts of this series.[1]

Electrolysis of Dimethyl Sodiomalonate in Hexamethylphosphoric Triamide.—Dimethyl malonate (66·0 g., 0·5 mole) was added dropwise to a stirred suspension of sodium hydride (12·0 g., 0·5 mole) in anhydrous hexamethylphosphoric triamide (200 ml.) until reaction was complete; the solution was then electrolysed using a platinum anode and a mercury cathode at 40°. The initial current of 2 A at 100 V fell to 0·5 A after 16 hr. Tetramethyl ethane-1,1,2,2-tetracarboxylate (g.l.c., mixed m.p.[2] determination) (1·31 g.) deposited during the electrolysis was filtered off. Unchanged dimethyl malonate and hexamethylphosphoric triamide were distilled from the filtrate at 60—120°/15 mm. The residue, after 4 days, deposited more tetramethyl ethane-1,1,2,2-tetracarboxylate (0·56 g.). Further material (3·13 g.), deposited during the next 14 days, on recrystallisation from benzene afforded *hexamethyl propane*-1,1,2,2,3,3-*hexacarboxylate* (1·72 g.), m.p. 136—137: (Found: C, 46·2; H, 4·9. $C_{15}H_{20}O_{12}$ requires C, 45·9; H, 5·1%). The residue was diluted with water and extracted with chloroform; the aqueous layer was examined separately (see below). The chloroform extracts were dried and the chloroform evaporated, leaving a viscous oil which partly solidified after 2 days. Analytical g.l.c. on this solid (3·26 g.) (F and M 720; 2 column, 10% silicone-rubber, 210°) showed that it was mainly tetramethyl ethane-1,1,2,2-tetracarboxylate (R_T 1·5 min.) and hexamethyl propane-1,1,2,2,3,3-hexacarboxylate (R_T 8·6 min.). The remaining material was taken up in chloroform washed with water (3×) and the solution dried; the washings were combined with the aqueous layer from the initial extraction. Evaporation of the chloroform gave a solid (12·14 g.). Preparative t.l.c. on a part of this material (1·52 g.) gave tetramethyl propane-1,1,3,3-tetracarboxylate (0·66 g.), m.p. 42—46° (from methanol), mixed m.p.[2] 43—46°, τ 6·24 (12H, s, Me) 6·47 (2H, t, J 7·5 c./sec., C*H*) and 7·54 (2H, t, J 7·5 c./sec., CH_2).

Continuous extraction of the combined aqueous layers, with chloroform gave an oil (11·6 g.) which was shown by g.l.c. (as above, 150°) to contain only hexamethylphosphoric triamide (R_T 2·9 min.) and pentamethylphosphoric triamide (R_T 4·0 min.), which had an i.r. spectrum identical with that of an authentic sample.

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[7] Nguyen Dinh-Nguyen, *Acta Chem. Scand.*, 1958, 585; R. Brettle, N. Polgar, and W. Smith, *J. Chem. Soc.*, 1960, 2802; T. D. Binns and R. Brettle, *J. Chem. Soc.* (*C*), 1966, 336.