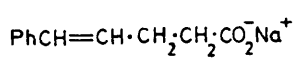
Anodic Oxidation. Part XII.[1] Synthesis of 5-Methoxy-5-phenylpentan-4-olide

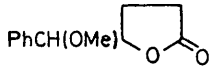
By **F. Mpandasoni Banda** and **Roger Brettle,*** Department of Chemistry, The University, Sheffield S3 7HF

Electrochemical oxidation of sodium (*E*)-5-phenylpent-4-enoate in methanol gives a mixture of *erythro*- and *threo*-5-methoxy-5-phenylpentan-4-olide.

We report that electrolysis of sodium (*E*)-5-phenylpent-4-enoate (1) in methanol using a platinum anode and an uncontrolled anode potential gives essentially only two products, in almost equal amounts, identified as *erythro*- and *threo*-5-methoxy-5-phenylpentan-4-olide (2) on the

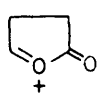


(1)



(2)

basis of the following considerations. G.l.c.–mass spectroscopy showed that the two products had identical mass spectra, and high resolution measurements on a sample of each, separated by preparative t.l.c., showed them to have the molecular formulae $C_{12}H_{14}O_3$. The presence in each of a γ-lactone ring was established by the strong absorption at 1770 cm^{-1} and by a fragment ion at *m/e* 85 corresponding to the fragment (3); the base peaks



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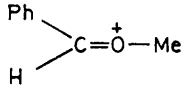

(4)

(*m/e* 121) corresponded to the same cleavage but with retention of charge on the other fragment (4). The n.m.r. spectra of the two products were similar and established the presence in each compound of one methoxy-group, derived from the solvent (τ 6·70 and 6·73); the remaining absorptions were in accord with the proposed structures.

The conversion of (1) into the two forms of (2), based on starting material consumed, was >90%. A similar mixture of *erythro*- and *threo*-5-methoxy-5-phenylpentan-4-olide was also prepared, but in lower overall yield and by a more involved and less convenient route, as follows. Epoxidation of methyl (*E*)-5-phenylpent-4-enoate, followed by acid-catalysed methanolysis, gave methyl *erythro*- and *threo*-4-hydroxy-5-methoxy-5-phenylpentanoates, which on saponification and treatment with acid gave the mixture of lactones. The regiospecific opening of the oxiran ring to give the 4-hydroxy-5-methoxy-compounds and the lack of stereospecificity in the creation of the chiral centres at C-4 and C-5 are consistent with the formation of a benzylic cation as an intermediate in the ring-opening process.

Our results in the electrolysis differ profoundly from the early results of Fichter and Kenstenholz [2] on the electrolysis of potassium 5-phenylpent-4-enoate in water–methanol–pyridine under similar conditions; surprisingly their major product was 4-phenylbut-3-en-1-ol. However, cases in which a γ-lactone is formed by the cyclisation of a carboxylate group onto a $\gamma\delta$-olefinic bond during the electrolysis of olefinic dicarboxylic acids are known,[3] and intramolecular acyloxylation leading to γ- or δ-lactones has been reported to occur on electrolysis of a number of aromatic carboxylic acids.[4] In none of these examples [3,4] is there incorporation of a methoxy-group from the solvent. The process now reported is more closely related to the electrochemical cyclisation of 3-furylpropan-1-ols in methanol,[5] where cyclisation of the oxygen atom of the side chain onto the furan ring is accompanied by incorporation of a methoxy-group from the solvent.

EXPERIMENTAL

N.m.r. spectra were recorded on Perkin-Elmer R12A or Varian HA-100 instruments for solutions in $CDCl_3$ with tetramethylsilane as internal standard. I.r. spectra were measured on a Pye Unicam SP 200 spectrophotometer. G.l.c.–mass spectrometry was performed on a Pye 104 chromatograph with a 6 ft glass column packed with FFAP on Chromosorb G operating at 210° and connected by a

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Biemann separator to an A.E.I. MS12 mass spectrometer. Accurate mass measurements were made with an A.E.I. MS9 instrument.

Electrolysis of Sodium (E)-5-*Phenylpent*-4-*enoate*.—(*E*)-5-Phenylpent-4-enoic acid [6] (8·8 g, 0·05 mol) in methanol (200 ml) was neutralised with sodium methoxide [from sodium (1·2 g, 0·05 g atom)] in methanol (200 ml) and the resultant solution was electrolysed for 7·5 h at 23°. The undivided cell [7] had a platinum anode (10 cm^2 in area) and a mercury pool cathode. The applied potential was 100 V and the current, initially 2·5 A, had fallen to a low steady value by the end of the electrolysis. The solution was then separated from the amalgam and neutralised with acetic acid. The methanol was evaporated off and the residue was diluted with water (100 ml) and extracted with ether (2 × 100 ml). (*E*)-5-Phenylpent-4-enoic acid (5·3 g) was recovered by extraction with cold aqueous 2N-sodium hydroxide, and the neutral product (3·8 g), b.p. 130—140° at 0·5 mmHg, was shown by g.l.c. to be a mixture of two components in almost equal amounts (peak areas). Preparative t.l.c. on silica plates (benzene as developing solvent) gave each component as a viscous oil in pure (by g.l.c.) form. One isomer of 5-*methoxy*-5-*phenylpentan*-4-*olide* had τ 2·68 (s, Ph), 5·2—5·8 (m, PhC*H*·C*H*), 6·73 (s, OMe), and 7·35—8·20 (complex, CH_2·CH_2), $\nu_{max.}$ 1770 cm^{-1} (Found: C, 70·0; H, 7·1%; *m/e* 206·0938. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%; *M*, 206·0943); the other isomer had τ 2·68 (s, Ph), 5·2—5·65 (m, PhC*H*·C*H*), 6·70 (s, OMe), and 7·35—8·20 (complex, CH_2·CH_2), $\nu_{max.}$ 1770 cm^{-1} (Found: C, 69·9; H, 6·8%; *m/e* 206·0938).

Methyl (E)-5-*Phenylpent*-4-*enoate*.—(*E*)-5-Phenylpent-4-enoic acid [6] (5 g, 0·028 mol) was neutralised with methanolic sodium methoxide [from sodium (0·67 g, 0·028 g atom) and methanol (100 ml)] and the solution was then refluxed for 2 h with dimethyl sulphate (20 ml). Isolation of the product with ether gave *methyl* (E)-5-*phenylpent*-4-*enoate* (5·1 g, 96%), b.p. 95—98° at 0·3 mmHg, τ 2·71 (s, Ph), 3·27—4·06 (complex, CH=CH), 6·32 (s, CO_2Me), and 7·38—7·41 (complex, CH_2·CH_2) (Found: C, 75·7; H, 7·4. $C_{12}H_{14}O_2$ requires C, 75·8; H, 7·5%).

erythro- *and* threo-5-*Methoxy*-5-*phenylpentan*-4-*olide*.—Methyl (*E*)-5-phenylpent-4-enoate (2·85 g, 0·015 mol) in dry dichloromethane (30 ml) at 25° was treated with *m*-chloroperbenzoic acid (2·64 g, 0·016 mol) in dichloromethane (20 ml) with stirring during 10 min, and the mixture was stirred for a further 30 min. Aqueous 10% sodium sulphite (100 ml) was then added and the mixture was stirred for 5 min. The solution was extracted with ether (100 ml) and the extract washed with aqueous 5% sodium hydrogen carbonate (3 × 50 ml), water (100 ml), and saturated aqueous sodium chloride (100 ml), and dried. Evaporation gave crude methyl *threo*-4,5-epoxy-5-phenylpentanoate (2·5 g, 83%) as a viscous oil, τ 2·71 (s, Ph), 6·34 (s, CO_2Me), 6·8—7·1 (complex, PhC*H*·C*H*) and 7·5—8·2 (complex CH_2·CH_2), which was used immediately for the next step. The epoxy-ester (2·2 g, 0·011 mol) was dissolved in methanol (50 ml) containing 36N-sulphuric acid (0·2 ml) and the solution was refluxed for 18 h. Most of the methanol was distilled off, and the resultant solution was diluted with cold water (100 ml) and extracted with ether (2 × 100 ml). The combined extracts were washed with water (4 × 50 ml) and saturated aqueous sodium chloride (2 × 50 ml), and dried (Na_2SO_4). Evaporation gave a crude mixture of *erythro*- and *threo*-methyl 4-hydroxy-5-methoxy-5-phenylpentanoate (1·8 g, 69%) [τ 6·4 and 6·6 (s, CO_2Me) and 7·66 and 7·68 (s, OMe)], part of which (1·4 g, 5·9 mmol) was heated on a steam-bath with aqueous N-sodium hydroxide (20 ml) for 8 h. The solution was cooled, extracted with chloroform (100 ml), and neutralised with N-hydrochloric acid. Extraction with chloroform then gave a crude mixture (1·2 g, 91%) of *erythro*- and *threo*-4-hydroxy-5-methoxy-5-phenylpentanoic acid. Part of this mixture (1·0 g) was cyclised by refluxing for 7 h in benzene (20 ml) containing toluene-*p*-sulphonic acid (5 mg). The solution was cooled, and diluted with benzene (80 ml). The benzene solution was then washed with aqueous 5% sodium hydrocarbon carbonate (2 × 50 ml) and water (2 × 50 ml), dried, and evaporated. The residue was purified by preparative t.l.c. giving a mixture of *erythro*- and *threo*-5-methoxy-5-phenylpentan-4-olide (0·76 g, 82%), identified by its behaviour on t.l.c. and g.l.c. and by its i.r. and n.m.r. spectra.

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