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Note

Formation of a dioxane derivative in the acid-catalysed dehydration of erythritol : trans-2,5-di-(1,2-dihydroxyethyl)-1,4-dioxane

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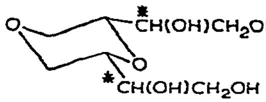
Although the acid-catalysed dehydration of alditols has been widely studied[1,2], except in the case of glycerol [3–5] no products have been reported as arising from the intermolecular elimination of water. As part of another study, we recently had cause to prepare 1,4-anhydroerythritol from erythritol. Using the reaction conditions of Klosterman and Smith[6], but a modified isolation procedure involving continuous chloroform extraction instead of distillation, we obtained, as well as the expected compound, a substance formed by a dehydration reaction between two molecules of erythritol. We report here evidence on its structure.

After purification through its acetate, the new product had m.p. 201–202°, and its elemental analysis and a molecular weight determination on its acetate suggested the molecular formula $C_8H_{16}O_6$. It consumed 2 mol. of sodium metaperiodate, and the simplicity of parts of the n.m.r. spectrum of its acetate suggested that the molecule contained an element of symmetry leading to equivalences amongst some of the protons in the derivative. For example, only two absorptions (τ 7.93 and 7.94) could be detected for the methyl protons in acetoxyl groups, and there appeared to be only one absorption (at τ 5.03) for methine protons in the structural unit -CH(OAc)-. On this evidence, two structures **1** and **3**, which have a centre and a plane of symmetry, respectively, seemed worthy of consideration. Degradation of the compound by application in sequence of periodate oxidation, borohydride reduction, and acetylation yielded *trans*-2,5-diacetoxymethyl-1,4-dioxane identical with a sample prepared by acetylation of authentic *trans*-2,5-dihydroxymethyl-1,4-dioxane. Similar treatment of compound **3** should yield *cis*-2,6-diacetoxymethyl-1,4-dioxane. The unknown compound therefore has the overall structure **1** and is *trans*-2,5-di-(1,2-dihydroxyethyl)-

1 R = H
2 R = OAc



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Carbon atoms denoted C* have opposite configurations.

1,4-dioxane. A complete definition of the structure requires determination of the relative configuration at the two secondary carbon atoms in the four carbon sub-units of **1**. However, owing to the difficulty of degrading a 1,4-dioxane in a stereospecific manner, this information has not been obtained.

In view of many the reported preparations of 1,4-anhydroerythritol[6–11], it is remarkable that the dioxane derivative **1** has not been noted previously, but this may result from the usual isolation procedure of direct distillation.

When 1,4-anhydroerythritol was subject to the acidic conditions used for its preparation, both erythritol and **1** could be detected (g.l.c.) as well as unchanged starting material. It is understandable, therefore, why the highest yields of 1,4-anhydroerythritol are obtained in syntheses where the product is removed under reduced pressure directly from the reaction mixture[10,11].

EXPERIMENTAL

G.l.c. was performed on a Perkin–Elmer F-11 instrument [2-m columns packed with *A* Carbowax (operating temperature 200°) or *B* Apiezon (operating temperature 145° or 200°)]. Periodate uptake was determined by the method of Aspinall and Ferrier[12]. The mass spectrum was recorded on a Hitachi Perkin–Elmer RMU-6E spectrometer, and n m.r. spectra were recorded at 100 MHz on a Varian HA-100 instrument with Me_4Si as an internal standard.

Reaction of erythritol with aqueous sulphuric acid. — A solution of erythritol (12 g) in a mixture of water (12 g) and conc. sulphuric acid (12 g) was heated under reflux for 15 h. The solution was diluted with water (50 ml), filtered, and passed through a column (4.5 × 50 cm) of Amberlite IRA-400(HO^-) resin. The eluent was concentrated to yield a thick syrup which contained a suspended white solid. The syrup was transferred to a Soxhlet thimble and continuously extracted with chloroform for 10 h. The extract was concentrated, and the residue was distilled to yield 1,4-anhydroerythritol (3.5 g, 37%), b.p. 86–88°/0.1 mmHg, n_D^{22} 1.4812; lit.[6] b.p. 160–165° (bath)/0.17 mmHg, n_D^{24} 1.4370; lit.[9] b.p. 144°/2–3 mmHg, n_D^{20} 1.4767; lit.[10] b.p. 105–107°/0.205 mmHg, n_D^{26} 1.478. Treatment of the foregoing compound with *p*-nitrobenzoyl chloride in pyridine yielded 1,4-anhydroerythritol 2,3-bis(*p*-nitrobenzoate), m.p. 176–177°; lit.[6] m.p. 173–174°.

In a separate experiment, crude material obtained by concentration of the solution from the deionization step was trifluoroacetylated[13,14] and subjected to g.l.c. analysis (column *B*). It contained (% by weight of injected material) 1,4-anhydroerythritol (47%), erythritol (15%), and **1** (14%).

The material remaining in the extractor thimble was continuously extracted with methanol for 4 h, and the extracts were then concentrated to give a solid (3.8 g) which, after two recrystallisations from methanol, had m.p. 195–198°. A portion of this material when treated with acetic anhydride in pyridine yielded, after two crystallisations of the product from ethyl acetate–light petroleum, the acetate **2** (1.0 g), m.p. 128–130°, mol. wt. (vapour pressure osmometry in chloroform) 373. N.m.r.

data* ($CDCl_3$): τ 5.03 (se, H-b), 5.58 (q, H-a), 5.89 (q, H-a′), 6.14 (q, H-d), 6.38 (q, H-c), 6.52 (d, H-d′), 7.93 (s) and 7.94 (s) (Ac). The mass spectrum contained a significant peak at *m/e* 256 ($M-2CH_3COOH$).

Anal. Calc. for $C_{16}H_{24}O_{10}$: C, 51.1; H, 6.4. Found: C, 50.9; H, 6.4.

The acetate **2** (0.8 g) was deacetylated by treatment with methanol containing a trace of sodium methoxide to yield, after crystallisation of the product from methanol, *trans*-2,5-di-(1,2-dihydroxyethyl)-1,4-dioxane (**1**) (0.4 g, 91%), m.p. 201–202°; **1** reduced 2 mol. of sodium metaperiodate.

Anal. Calc. for $C_8H_{16}O_6$: C, 46.15; H, 7.75. Found: C, 45.9; H, 7.55.

Degradation of trans-*2,5-di-(1,2-dihydroxyethyl)-1,4-dioxane.* — To a solution of **1** (0.104 g) in water (5 ml), a solution of sodium metaperiodate (0.217 g) in water (5 ml) was added. After 0.5 h at room temperature, a solution of barium chloride dihydrate (0.106 g) in water (5 ml) was added and stirring was continued for a further 0.5 h. Sufficient sodium hydrogen carbonate was added to basify the reaction mixture which was then filtered through Kieselguhr. Sodium borohydride (0.25 g) in water (5 ml) was added to the filtrate and, after 1 h, the mixture was neutralized with acetic acid and concentrated to dryness. Acetic anhydride (5 ml) and pyridine (1 ml) were added to the residue and, after 12 h at room temperature, the mixture was poured into saturated aqueous sodium hydrogen carbonate. Extraction of the solution with chloroform, followed by concentration of the extracts, gave a solid which was crystallised from ethyl acetate–light petroleum to yield *trans*-2,5-diacetoxymethyl-1,4-dioxane (55 mg, 48%), m.p. 128–129°, which was identical [g.l.c. (column *A*), i.r., n.m.r., and mass spectrum, mixed m.p. 128–129°] with an authentic sample, m.p. 128–129°, prepared by acetylation of the known[15,16] *trans*-2,5-dihydroxymethyl-1,4-dioxane, m.p. 93-94°.

Anal. Calc. for $C_{10}H_{16}O_6$: C, 51.7; H, 6.95. Found: C, 51.8; H, 7.0

Treatment of 1,4-anhydroerythritol with aqueous sulphuric acid. — A solution of 1,4-anhydroerythritol (0.4 g) in sulphuric acid (0.5 g) and water (0.5 ml) was heated under reflux for 15 h. The mixture was diluted with water (15 ml), filtered, and neutralised by passage through a column of Amberlite IRA-400(HO^-) resin. The eluate was concentrated, and g.l.c. analysis (column *B*) of the residue, after trifluoroacetylation[13,14], showed it to contain 1,4-anhydroerythritol, erythritol, and **1** in the ratios (by weight) 10.6:1:1.3.

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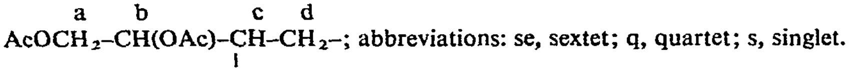
*Letters used to designate the protons in acetate **2** are according to the scheme:



$\overset{a}{AcOCH_2}-\overset{b}{CH(OAc)}-\underset{|}{\overset{c}{CH}}-\overset{d}{CH_2}-$; abbreviations: se, sextet; q, quartet; s, singlet.

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