986. *Aspects of Stereochemistry. Part IX.* Structure of the Di-O-benzylidenetetritols.*

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A 1,3:2,4-distribution of the cyclic acetal rings in the di-*O*-benzylidene derivatives of erythritol and L-threitol is demonstrated by the formation of 1,3-*O*-benzylidene derivatives on graded acidic hydrolysis. Since the configuration of the monobenzylidene derivatives has been established (preceding paper) the structure of the dibenzylidene compounds may be defined completely. 1,3:2,4-Di-*O*-benzylidene-L-threitol has an " O-inside " structure. Possible effects of hydrogen bonding in the reaction of glycerol and the higher polyhydric alcohols with aldehydes are considered.

WHEREAS in the acid-catalysed reaction of pentitols and the higher polyhydric alcohols with aldehydes, six-membered cyclic acetals are formed preferentially,[1] the five-membered analogues are the predominant products in glycerol–aldehyde reactions.[2] The reaction pattern in the former group has been rationalised [3] but that of the glycerol–aldehyde series has not.[4] Since the tetritols are intermediate with respect to the above two groups of polyhydric alcohols it is surprising that there has been no report on the pattern of their reaction with aldehydes although numerous cyclic acetal derivatives are known.[1] We have now shown that, with respect to their reaction with benzaldehyde, the tetritols may be included with the higher polyhydric alcohols.

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* Part VIII, preceding paper.

[1] Barker and Bourne, *Adv. Carbohydrate Chem.*, 1952, **7**, 137.

[2] Hill, Whelen, and Hibbert, *J. Amer. Chem. Soc.*, 1928, **50**, 2235; Trister and Hibbert, *Canad. J. Res.*, 1936, **14**, *B*, 415; van Roon, *Rec. Trav. chim.*, 1929, **48**, 175.

[3] (*a*) Barker, Bourne, and Whiffen, *J.*, 1952, 3865; (*b*) Mills, *Adv. Carbohydrate Chem.*, 1955, **10**, 1.

[4] Brimacombe, Foster, and Haines, *J.*, 1960, 2582.

Di-*O*-benzylidene-erythritol was first described by Fischer [5] and the derivative has since been frequently used to characterise the tetritol. Graded hydrolysis of di-*O*-benzylidene-erythritol at 50° with hydrochloric acid in aqueous dioxan gave an optically inactive mono-*O*-benzylidene compound the infrared spectrum of which in Nujol or potassium chloride, or in carbon tetrachloride solution, was indistinguishable from that of 1,3-*O*-benzylidene-L-erythritol.[6] Further, the infrared spectra, in the hydroxyl stretching region,[7,8] of dilute solutions ($\not> 0{\cdot}005$M) of the mono-*O*-benzylidene-erythritol and 1,3-*O*-benzylidene-L-erythritol showed closely similar absorption patterns of free and intramolecularly bonded hydroxyl groups. Finally, the di-*O*-acetates of the mono-*O*-benzylidene-erythritol and 1,3-*O*-benzylidene-L-erythritol gave indistinguishable proton magnetic resonance spectra. Thus, the graded hydrolysis product may be assigned the structure 1,3-*O*-benzylidene-DL-erythritol and its precursor a 1,3:2,4-distribution of the cyclic acetal residues, on the assumption that no acetal rearrangement occurred during the graded hydrolysis.

In the preceding paper [6] 1,3-*O*-benzylidene-L-erythritol was shown to have the configuration (II); therefore 1,3:2,4-di-*O*-benzylidene-erythritol must have the bicyclic structure (I) which is related to *trans*-decalin and has two equatorial phenyl groups, a thermodynamically very stable structure. 1,3.2,4-Di-*O*-benzylidene-erythritol is an interesting example of the group of compounds which are optically inactive because of a centre of symmetry; the product of partial hydrolysis is a DL-mixture. It is likely that other dialkylidene and diarylidene derivatives of erythritol [1] have a 1,3:2,4-distribution of the cyclic acetals.

Maquenne and Bertrand [9] first prepared di-*O*-benzylidene-D-, -L-, and -DL-threitol and these compounds have been described subsequently by other workers.[1] The di-*O*-benzylidene-L-threitol used in this work was obtained by treating benzaldehyde with L-threitol prepared from (+)-tartaric acid [10] and had m. p. 218—220° or 224—229° depending on the conditions of isolation. These modifications are probably dimorphs since they gave indistinguishable infrared spectra (KCl discs); other workers [1] have observed similar m. p. variations.

Graded hydrolysis of di-*O*-benzylidene-L-threitol with dilute hydrochloric acid in aqueous dioxan gave 1,3-*O*-benzylidene-L-threitol (IV) identical with the product obtained by periodate oxidation and subsequent borohydride reduction of 1,3-*O*-benzylidene-L-arabinitol.[6] Thus, again on the assumption that acetal migration does not occur, the di-*O*-benzylidene-L-threitol must have a 1,3:2,4-distribution of the acetal rings. Since this arrangement would form a bicyclic system related to *cis*-decalin, two structures (III) and (V), each containing chair conformations of the dioxan rings and equatorial phenyl groups, are possible for 1,3:2,4-di-*O*-benzylidene-L-threitol. Because of less adverse non-bonded interactions, the " O-inside " structure (III) should be preferred [3b] to the " H-inside " structure (V). Moreover, the products of graded hydrolysis, (IV) and (VI), respectively, of the O- and H-inside structure are different. In the preceding paper [6] 1,3-*O*-benzylidene-L-threitol was shown to have structure (IV); therefore 1,3:2,4-di-*O*-benzylidene-L-threitol must have the O-inside structure (III).

When 1,3:2,4-di-*O*-benzylidene-erythritol and 1,3:2,4-di-*O*-benzylidene-L-threitol were subjected to graded acidic hydrolysis under the same conditions, 4% of the former and 29% of the latter compound was recovered unchanged; *i.e.*, the *trans*-fused 2,4,6,8-tetraoxabicyclo[4,4,0]decane system is more easily disrupted by acid than is the *cis*-fused system. Related results have been observed with certain 4,6-*O*-benzylidenehexopyranosides.[11]

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[5] Fischer, *Ber.*, 1894, **27**, 1524.

[6] Foster, Haines, Homer, Lehmann, and Thomas, preceding paper.

[7] Kuhn, *J. Amer. Chem. Soc.*, 1952, **74**, 2492; 1954, **76**, 4323.

[8] Cole and Jefferies, *J.*, 1956, 4391.

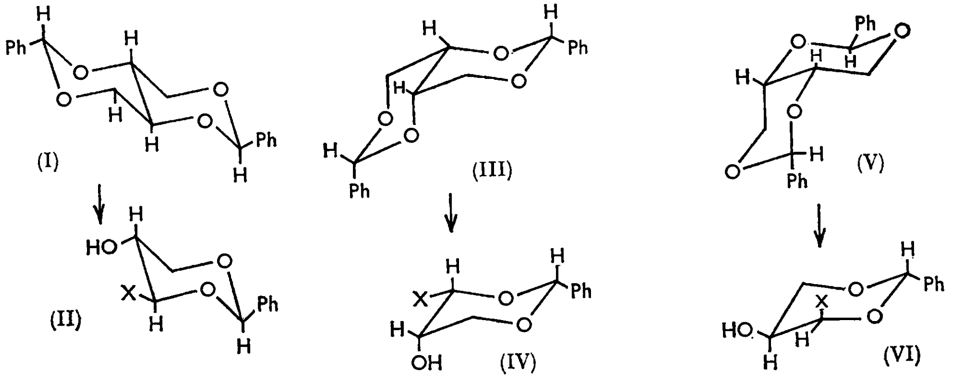
[9] Maquenne and Bertrand, *Compt. rend.*, 1901, **132**, 1565.

[10] Klosterman and Smith, *J. Amer. Chem. Soc.*, 1952, **74**, 5336.

[11] Professor W. G. Overend, personal communication.

Thus, the benzylidene acetal ring in the methyl 4,6-*O*-benzylidene-D-glucopyranosides (*trans*-fused system) is more acid-labile than is the corresponding portion of the methyl 4,6-*O*-benzylidene-D-galactopyranosides (*cis*-fused system).

Hibbert and his co-workers [2] established that, at equilibrium of the acid-catalysed reaction of glycerol with aldehydes, 1,3-dioxolan derivatives are the predominant products. This result was observed for a variety of aldehydes and it indicates that some effect is operative which reverses the usual order of thermodynamic stability of five- and six-membered rings. In contrast, at equilibrium of the acid-catalysed competition of equimolar amounts of ethane-1,2-diol and propane-1,3-diol for an aldehyde,[2] 1,3-dioxan derivatives predominate. A parallel result has been observed in the reaction of butane-1,2,4-triol with benzaldehyde, which yields [12] 4-hydroxymethyl-2-phenyl-1,3-dioxan as the major product and only 5—10% of 4-2'-hydroxyethyl-2-phenyl-1,3-dioxolan. These results suggest that intermolecular hydrogen bonding could be important in glycerol–aldehyde reactions since the concentration of the alcohol in the reaction mixture is high. Two types of product can be formed, *viz.*, 1,3-dioxolan derivatives with free primary hydroxyl groups and 1,3-dioxan derivatives with free secondary hydroxyl groups. The greater acidity and steric accessibility of the primary hydroxyl groups might be expected to promote more efficient intermolecular hydrogen bonding than that from the secondary hydroxyl groups,[8] and this effect could counterbalance the tendency to form six-membered rings. Intermolecular hydrogen bonding would not be significant in the competition experiments and in the butane-1,2,4-triol–aldehyde reactions since, after formation of the cyclic acetals, only primary hydroxyl groups remain unsubstituted. That intermolecular hydrogen bonding is indeed involved in controlling the glycerol–aldehyde reaction is suggested by the results of preliminary experiments [13] in which the acid-catalysed reaction of benzaldehyde with glycerol was performed in an inert solvent with progressively decreasing concentrations of the reactants. As dilution increased, intermolecular hydrogen bonding diminished and it was found that, at equilibrium, the proportion of 1,3-dioxan derivatives increased and ultimately predominated. This effect is being investigated further.



($X = CH_2{\cdot}OH$)

EXPERIMENTAL

Graded Acid Hydrolysis of 1,3:2,4-*Di*-O-*benzylidene-erythritol*.—A solution of 1,3:2,4-di-*O*-benzylidene-erythritol [5] (1 g.; m. p. 201—202°) in dioxan (90 ml.) and 0·5N-hydrochloric acid (10 ml.) was kept at 50° for 45 min. The cooled solution was neutralised with aqueous ammonia

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[12] Foster, Haines, and Stacey, *Tetrahedron*, in the press.

[13] Baggett and Foster, unpublished results.

and evaporated. The residue was extracted with boiling water (50 ml.); unchanged 1,3:2,4-di-*O*-benzylidene-erythritol remained. The cooled aqueous solution was extracted four times with chloroform (total 80 ml.). The combined and dried (Na_2SO_4) extracts were evaporated and the residue recrystallised from benzene–light petroleum (b. p. 60—80°), to yield 1,3-O-*benzylidene*-DL-*erythritol* (0·5 g.), m. p. 108—110°, $[\alpha]_D^{20} \pm 0°$ (*c* 1·5 in $CHCl_3$) (Found: C, 63·0; H, 6·8. $C_{11}H_{14}O_4$ requires C, 62·8; H, 6·7%). The infrared spectra of the L- and the DL-form in Nujol mulls or in CCl_4 solution were indistinguishable. The spectra obtained in KCl discs were variable, but prolonged grinding gave constant spectra which were indistinguishable.

Solutions (*ca.* 0·005M) of the L- and the DL-diol in CCl_4 had maxima at 3643, 3615, and 3565 $cm.^{-1}$ in the hydroxyl stretching region. The relative extinction coefficients for each set of absorptions were closely similar. These and related results will be discussed elsewhere.

2,4-*Di*-O-*acetyl*-1,3-O-*benzylidene*-L- *and* -DL-*erythritol*.—A mixture of 1,3-*O*-benzylidene-L-erythritol (0·24 g.), pyridine (8 ml.) and acetic anhydride (4 ml.) was stored overnight at room temperature. The mixture was poured into water, and the solution was saturated with sodium hydrogen carbonate and extracted with chloroform (3 × 50 ml.). Removal of the solvent from the extract and recrystallisation of the residue from benzene–light petroleum (b. p. 60—80°) gave 2,4-*di*-O-*acetyl*-1,3-O-*benzylidene*-L-*erythritol* (0·25 g., 74%), m. p. 81·5—83·5°, $[\alpha]_D$ −40° (*c* 0·27 in $CHCl_3$), $[M]_D$ −118° (Found: C, 61·5; H, 6·3. $C_{15}H_{18}O_6$ requires C, 61·2; H, 6·2%).

In essentially the same way 2,4-*di*-O-*acetyl*-1,3-O-*benzylidene*-DL-*erythritol* (61%) was prepared with m. p. 71—72°, $[\alpha]_D^{20} \pm 0°$ (*c* 1·5 in $CHCl_3$) (Found: C, 60·9; H, 6·3%).

The infrared spectra of the L- and the DL-di-*O*-acetate in Nujol mulls, in KCl discs, and in CCl_4 solution were indistinguishable, as were the proton magnetic resonance spectra of their solutions in $CHCl_3$ (preceding paper).[6]

Graded Acid Hydrolysis of 1,3:2,4-*Di*-O-*benzylidene*-L-*threitol*.—A solution of 1,3:2,4-di-*O*-benzylidene-L-threitol[9] (0·17 g.; m. p. 217—218°) in dioxan (20 ml.) and 0·5N-hydrochloric acid (2 ml.) was stored at 50° for 30 min. Concentrated aqueous ammonia (0·5 ml.) was then added and the mixture was evaporated to dryness. The residue, after removal of benzaldehyde in light petroleum (b. p. 60—80°), was extracted with water leaving unchanged dibenzylidene compound (*ca.* 50 mg.). The aqueous solution was added to a charcoal–Celite column (*ca.* 2 × 20 cm.). Elution with water removed inorganic material and L-threitol, and subsequent elution with aqueous alcohol (1 : 4 v/v), concentration of the eluate, and recrystallisation of the residue from benzene–light petroleum gave 1,3-*O*-benzylidene-L-threitol (6·4 mg.), m. p. 131—133° undepressed on admixture with authentic material.[6] The infrared spectrum (KCl disc) was indistinguishable from that of authentic material.

Comparative Hydrolysis of the 1,3:2,4-*Di*-O-*benzylidene Derivatives of Erythritol and* L-*Threitol*.—The di-*O*-benzylidene compounds (0·2 g.) were separately dissolved in dioxan (49 ml.), and 2·5N-hydrochloric acid (1 ml.) was added to each. The solutions were stored at 50° for 20 min., then neutralised with concentrated aqueous ammonia (0·5 ml.) and concentrated. The residue was extracted with water and the undissolved di-*O*-benzylidene compound was dried *in vacuo* over P_2O_5. In this way 4% of 1,3:2,4-di-*O*-benzylidene-erythritol (m. p. 201—202°) was recovered, and 29% of 1,3:2,4-di-*O*-benzylidene-L-threitol (m. p. 224—229°). In controls from which the acid was omitted the recovery of each di-*O*-benzylidene compound was 96—98%.

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