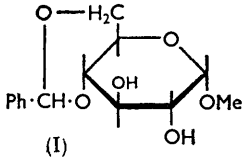
544. *The O-Toluene-p-sulphonyl Derivatives of 1,5-Anhydro-4,6-O-benzylidene-D-glucitol.**

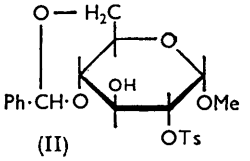
By F. H. Newth.

It has been shown that selective acylation of 1,5-anhydro-4,6-*O*-benzylidene-D-glucitol occurs at position 2, and that the epoxide produced from the 2,3-di-*O*-toluene-*p*-sulphonyl derivative has the *allo*-configuration. This is parallel to the reactions of the corresponding derivatives of methyl α-D-glucoside and it is concluded, therefore, that in this case the glycosidic methoxyl group does not exert any profound directing influence.

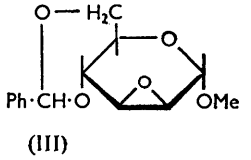
In the well-established sequence for the conversion of methyl 4,6-*O*-benzylidene-α-D-glucoside (I) into the corresponding derivative of D-altrose (VI) by alkaline hydrolysis of either the *manno*-epoxide [1] (III) or the *allo*-epoxide [2] (V) there are two features which have not received attention. The first is the selective formation of the 2-toluene-*p*-sulphonyl ester (II) and the second is the alkaline hydrolysis of the 2,3-ditoluene-*p*-sulphonyl ester (IV). Careful experimental work by Richtmyer and Hudson has shown that only methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-alloside (V) and no methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannoside (III) is formed.



(I)



(II)



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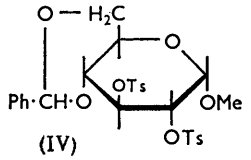
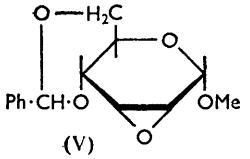


(IV)



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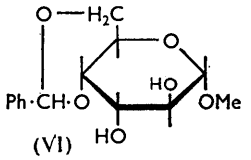
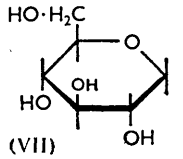


(VI)

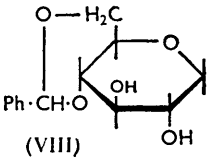
(Ts = p-$C_6H_4Me\cdot SO_2$)

The equivalent reactions of the *O*-toluene-*p*-sulphonyl derivatives of 1,5-anhydro-4,6-*O*-benzylidene-D-glucitol have now been investigated to see whether the origin of these orientations lies in the glycosidic methoxyl group. Its influence could be either steric because of its axial disposition or electronic by virtue of its being part of the acetal system and thus able to induce positive character at $C_{(1)}$.

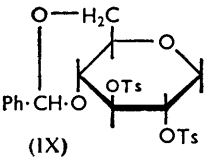
In continuing their study of the 1,5-anhydrohexitols, Zissis and Richtmyer [3] have prepared 1,5-anhydro-D-altritol from 1,5-anhydro-D-glucitol (poligalitol) (VII). The



(VII)



(VIII)



(IX)

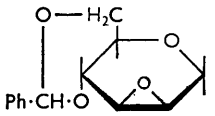
constitution of 1,5-anhydro-4,6-*O*-benzylidene-D-glucitol (VIII) was established by periodate oxidation and the epoxide obtained by alkaline hydrolysis of the 2,3-ditoluene-*p*-sulphonate (IX) could have had either the *manno*- (X) or the *allo*-configuration (XI). By

* An abstract of this paper was presented at the XVIth Internat. Congr. of Pure Appl. Chem., Paris, 1957.

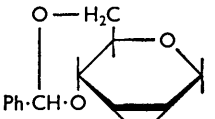
[1] Robertson and Griffith, *J.*, 1935, 1193.
[2] Richtmyer and Hudson, *J. Amer. Chem. Soc.*, 1941, **63**, 1727.
[3] Zissis and Richtmyer, *ibid.*, 1955, **77**, 5154.

analogy with the reactions in the glucoside series, it was denoted as 1,5:2,3-dianhydro-4,6-*O*-benzylidene-D-allitol (XI). Alkaline hydrolysis of the epoxide led predominantly to 1,5-anhydro-4,6-*O*-benzylidene-D-altritol (XII), the axial isomer, in conformity with the Fürst and Plattner rule [4] whichever the configuration.

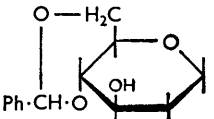
It has now been shown that Zissis and Richtmyer's assumption of epoxide configuration was correct and, further, that 1,5-anhydro-4,6-*O*-benzylidene-D-glucitol (VIII) is selectively acylated at position 2 as is the corresponding derivative of methyl α-D-glucoside.



(X)

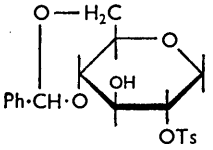


(XI)

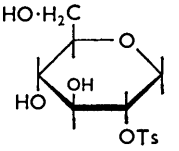


(XII)

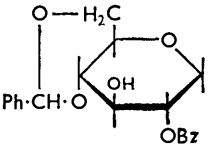
The restrained reaction of 1,5-anhydro-4,6-*O*-benzylidene-D-glucitol with toluene-*p*-sulphonyl chloride (1 mol.) in pyridine yielded a monotoluene-*p*-sulphonate which was identical with that which accompanies the formation of the 2,3-di-toluene-*p*-sulphonate.[3] This was shown to be 1,5-anhydro-4,6-*O*-benzylidene-2-*O*-tosyl-D-glucitol (XIII) by the fact that the 1,5-anhydro-*O*-tosyl-D-glucitol (XIV), obtained by acidic hydrolysis of the benzylidene residue, consumed 1 mol. of periodate. Monobenzoylation of the diol (VIII) gave 1,5-anhydro-2-*O*-benzoyl-4,6-*O*-benzylidene-D-glucitol (XV). The structure of this follows from the difference between its *O*-toluene-*p*-sulphonyl derivative (XVI) and 1,5-anhydro 3-*O*-benzoyl-4,6-*O*-benzylidene-2-*O*-tosyl-D-glucitol (XVII) obtained from (XIII). Both sulphonic and carboxylic esterification have occurred at position 2 and the conformational formulæ (Ia) and (VIIIa) show that it cannot be the glycosidic methoxyl group which is solely responsible for this orientation. It is not at present apparent why the 2-hydroxyl group should react rather than that at position 3 which is also equatorial.



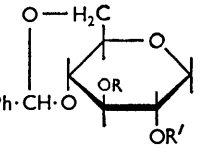
(XIII)



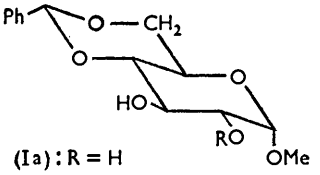
(XIV)



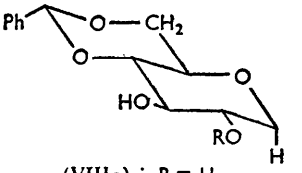
(XV)



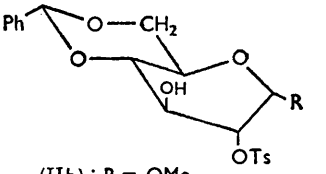
(XVI): R = Ts, R′ = Bz
(XVII): R = Bz, R′ = Ts



(Ia): R = H
(IIa): R = Ts



(VIIIa): R = H
(XIIIa): R = Ts



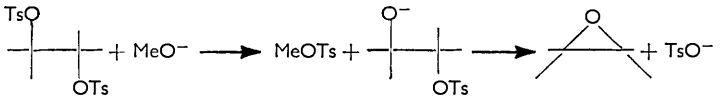
(IIb): R = OMe
(XIIIb): R = H

1,5-Anhydro-4,6-*O*-benzylidene-2-*O*-tosyl-D-glucitol (XIII) was treated with sodium methoxide at 0° and was smoothly converted into an epoxide which must be 1,5:2,3-dianhydro-4,6-*O*-benzylidene-D-mannitol (X). It is interesting to compare the ease of this reaction with the more severe conditions which are required to hydrolyse the corresponding methyl α-D-glucoside [1] (II). It has been suggested [5] that in a diequatorial system, such as that which is present here, there must be a conformational shift to the boat form (IIb) and (XIIIb) when both groups are axial and suitably placed for intramolecular nucleophilic displacement. To attain this diaxial state, the *cis*-groups at positions 1 and 2 in (IIa) and

[4] Mills, cited by Newth and Homer, *J.*, 1953, 989.
[5] Newth, *J.*, 1956, 441.

(XIIIa) must move past each other and will show interaction appropriate to their size. The different reactivities shown by (II) and (XIII) are attributed to the different passing interactions: OTs/OMe and OTs/H.

1,5:2,3-Dianhydro-4,6-*O*-benzylidene-D-mannitol (X) was compared with the dianhydride obtained by Zissis and Richtmyer from 1,5-anhydro-4,6-*O*-benzylidene-2,3-di-*O*-tosyl-D-glucitol (IX): the two compounds were clearly different. The 2,3-ditoluene-*p*-sulphonate must give the allitol (XI) and this is parallel to the behaviour of methyl 4,6-*O*-benzylidene-2,3-di-*O*-tosyl-α-D-glucoside (IV). The factors controlling epoxide formation from di-*O*-sulphonyl compounds are little known, but a preliminary appraisal has been given recently.[6] Angyal and Gilham [7] represent the reaction by the sequence:



and the more accessible sulphonyl group is that which is removed first. In the diesters (IV) and (IX) primary attack must be at the 2-group and although the reason for this is not yet apparent, it cannot be attributed to the presence or absence of the glycosidic methoxyl group.

Experimental

1,5-*Anhydro*-4,6-O-*benzylidene*-D-*glucitol*.—The compound, m. p. 165—166°, was prepared as described by Zissis and Richtmyer [3] (Found: C, 61·9; H, 6·4. Calc. for $C_{13}H_{16}O_5$: C, 61·9; H, 6·4%).

1,5-*Anhydro*-4,6-O-*benzylidene*-2-O-*tosyl*-D-*glucitol*.—1,5-Anhydro-4,6-*O*-benzylidene-D-glucitol (252 mg.) was dissolved in dry pyridine (2 ml.) and cooled to −10°. Toluene-*p*-sulphonyl chloride (190 mg., 1 mol.) was added and the mixture kept at 5° for 48 hr. The crystalline material obtained on pouring the solution into water recrystallised from ethanol, and 1,5-*anhydro*-4,6-O-*benzylidene*-2-O-*tosyl*-D-*glucitol* (260 mg.) had m. p. 174—175° (alone or mixed with 1,5-anhydro-4,6-*O*-benzylidene-*O*-tosyl-D-glucitol, m. p. 175—179°, kindly supplied by Dr. N. K. Richtmyer) (Found: C, 58·9; H, 5·6. $C_{20}H_{22}O_7S$ requires C, 59·1; H, 5·4%).

1,5-*Anhydro*-2-O-*tosyl*-D-*glucitol*.—1,5-Anhydro-4,6-*O*-benzylidene-2-*O*-tosyl-D-glucitol (200 mg.) was boiled in methanol (5 ml.) containing 3N-hydrochloric acid (0·5 ml.) for 20 min., then kept for 18 hr. Water (5 ml.) was added, the acid neutralised with silver carbonate, and benzaldehyde extracted with ether. The inorganic material was removed at a centrifuge and evaporation of the solution provided crystalline 1,5-*anhydro*-2-O-*tosyl*-D-*glucitol* (125 mg.). Recrystallised from ethyl acetate, it had m. p. 158—159° (Found: C, 49·1; H, 5·6. $C_{13}H_{18}O_7S$ requires C, 49·1; H, 5·6%): it reduced 1·02 mol. of sodium metaperiodate during 49 hr.

1,5-*Anhydro*-2-O-*benzoyl*-4,6-O-*benzylidene*-D-*glucitol*.—1,5-Anhydro-4,6-*O*-benzylidene-D-glucitol (252 mg.) in pyridine (2 ml.) was treated at −10° with benzoyl chloride (0·116 ml.) and kept at 0° for 3 hr., then poured into water, giving a crystalline precipitate which separated into two fractions when recrystallised from ethanol. The first was 1,5-*anhydro*-2,3-*di*-O-*benzoyl*-4,6-O-*benzylidene*-D-*glucitol* (85 mg.), m. p. 162—163° (Found: C, 70·7; H, 5·5. $C_{27}H_{24}O_7$ requires C, 70·5; H, 5·2%). The second was 1,5-*anhydro*-2-O-*benzoyl*-4,6-O-*benzylidene*-D-*glucitol* (60 mg.), m. p. 133—134° (Found: C, 67·8; H, 5·7. $C_{20}H_{20}O_6$ requires C, 67·4; H, 5·6%).

1,5-*Anhydro*-2-O-*benzoyl*-4,6-O-*benzylidene*-3-O-*tosyl*-D-*glucitol*.—1,5-Anhydro-2-*O*-benzoyl-4,6-*O*-benzylidene-D-glucitol (25 mg.) in pyridine (0·1 ml.) was treated with toluene-*p*-sulphonyl chloride (20 mg.) for 4 hr. The mixture was poured into water; 1,5-*anhydro*-2-O-*benzoyl*-4,6-O-*benzylidene*-3-O-*tosyl*-D-*glucitol*, recrystallised from ethanol, had m. p. 192° (Found: C, 63·3; H, 5·2. $C_{27}H_{26}O_8S$ requires C, 63·5; H, 5·1%).

1,5-*Anhydro*-3-O-*benzoyl*-4,6-O-*benzylidene*-2-O-*tosyl*-D-*glucitol*.—1,5-Anhydro-4,6-*O*-benzylidene-2-*O*-tosyl-D-glucitol (50 mg.) in pyridine (0·5 ml.) was treated with benzoyl chloride (0·05 ml.) for 3 hr. The mixture was poured into water; 1,5-*anhydro*-3-O-*benzoyl*-4,6-O-*benzylidene*-2-O-*tosyl*-D-*glucitol*, recrystallised from ethanol, had m. p. 200° (m. p. in admixture

[6] Newth, *Quart. Rev.*, 1959, **13**, 30.
[7] Angyal and Gilham, *J.*, 1957, 3691.

with the above isomer: 170—185°) (Found: C, 63·3; H, 5·1%). The infrared spectra of the two compounds showed differences in the region of molecular absorption (9—15 μ), the 2-*O*-benzoyl-3-*O*-tosyl derivative having bands displaced to longer wavelength and with different relative intensity.

1,5:2,3-*Dianhydro*-4,6-O-*benzylidene*-D-*mannitol*.—1,5-Anhydro-4,6-*O*-benzylidene-2-*O*-tosyl-D-glucitol (60 mg.) in chloroform (0·3 ml.) was treated with methanol (0·3 ml.) containing sodium (10 mg.) and kept at 0° for 14 hr. The alkali was neutralised with carbon dioxide, the solution evaporated, and the residue extracted with chloroform. Evaporation of the extract gave crystalline 1,5:2,3-*dianhydro*-4,6-O-*benzylidene*-D-*mannitol* (25 mg.). Recrystallised from ethanol this had m. p. 138—139°, $[\alpha]_D^{22}$ −13·2° (*c* 0·85 in chloroform) (Found: C, 66·5; H, 5·9. $C_{13}H_{14}O_4$ requires C, 66·6; H, 6·0%). In admixture with the 1,5:2,3-dianhydro-4,6-*O*-benzylidene-D-hexitol, m. p. 129—130°, $[\alpha]_D^{20}$ +35°, of Zissis and Richtmyer[3] (kindly supplied by Dr. N. K. Richtmyer), there was a depression to 95—103°. That compound must, therefore, be 1,5:2,3-dianhydro-4,6-*O*-benzylidene-D-allitol.

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