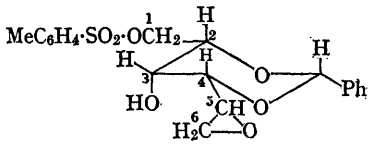
Synthesis of 1,3-Anhydro-D-glucitol

By E. HASLAM and T. RADFORD
(*Department of Chemistry, University of Sheffield*)

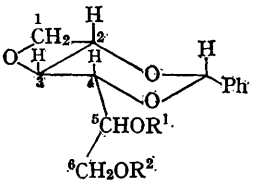
IN the course of the synthesis of a natural product the action of base on the epoxide[1] (I) was investigated. Rather surprisingly the 1,3-anhydro-D-glucitol derivative (II; $R^1 = R^2 = H$) was formed and this behaviour contrasts with that of the related methylene bridged compound (III; $R^1 = R^2 = H$) which on similar treatment[2] yields the expected 1,5-anhydro-2,4-methylene-D-glucitol. The oxetan

[1] L. Vargha, *Ber.*, 1935, **68**, 1377.
[2] S. B. Baker, *Canad. J. Chem.*, 1954, **32**, 628.

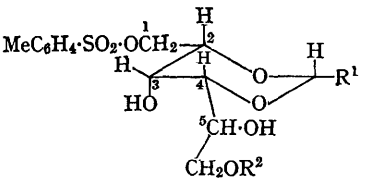
(II; $R^1=R^2=H$) readily formed a diacetate (II; $R^1=R^2=CO\cdot Me$) and a monotrityl-monoacetate (II; $R^1=CO\cdot Me$, $R^2=CPh_3$) and when hydrogenated it yielded the crystalline 1,3-anhydro-D-glucitol (IV; R=H; m.p. 98—99°, $[\alpha]_D$ −1°) which was characterised as its bisisopropylidene and tetra-acetate derivatives. The 6-*O*-methyl



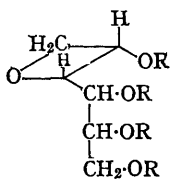
(I)



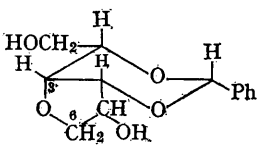
(II)



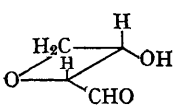
(III)



(IV)



(V)



(VI)

and 6-*O*-ethyl analogues of the benzylidene-oxetan (II; $R^1=H$, $R^2=Me$, and II; $R^1=H$, $R^2=Et$) were prepared by base hydrolysis of the corresponding glucitols[1] (III; $R^1=Ph$, $R^2=Me$ and III; $R^1=Ph$, $R^2=Et$) or by treatment of the bis-(toluene-*p*-sulphonate) (III; $R^1=Ph$; $R^2=SO_2\cdot C_6H_4\cdot Me$) with methanolic or ethanolic caustic soda. The ethyl derivative (II; $R^1=H$, $R^2=Et$) was incidentally identical with a compound previously described by Vargha[1] but for which no structure was suggested. The action of alkali in the presence of benzyl alcohol on the epoxide (I) or the bis-(toluene-*p*-sulphonate) (III; $R^1=Ph$, $R^2=SO_2\cdot C_6H_4\cdot Me$) gave the benzyl ether (II; $R^1=H$, $R^2=PhCH_2$) which when hydrogenated afforded 1,3-anhydro-D-glucitol (IV; R=H) identical with the product described above.

Comparison of the proton magnetic resonance spectra of the methyl, ethyl, and benzyl ethers and of the parent compound (II; $R^1=R^2=H$) confirmed the suggested relationship and permitted the formulation of these compounds as oxetan derivatives. The spectra of the methyl and ethyl ether monoacetates (II; $R^1=CO\cdot Me$, $R^2=Me$ and II; $R^1=CO\cdot Me$, $R^2=Et$) were identical with that of the parent diacetate (II; $R^1=R^2=CO\cdot Me$) in the region τ 4·5 to τ 6·3 (absorption attributable to the benzylic proton and protons attached directly to C-1—C-6) except that the characteristic absorption of the C-6 methylene protons in the diacetate (τ 5·4—5·6) was shifted and appeared in the ethers as a sharp doublet at τ 6·28, concomitant with the change in structural environment from a position adjacent to an ester to that of an ether grouping. A similar correlation was also possible for the benzyl ether monoacetate (II; $R^1=CO\cdot Me$, $R^2=PhCH_2$) although this compound also displayed a two-proton singlet (τ 5·46) due to the additional benzylic protons. The formation of anhydro-derivatives from (III; $R^1=Ph$, $R^2=Me$, and III; $R^1=Ph$, $R^2=Et$) under basic conditions can only be satisfactorily rationalised in terms of ring closure between C-1 and the hydroxyl at C-3 or C-5. Bearing in mind the structural relationship of these compounds to the product of solvolysis of (I), which was clearly not a derivative of 1,5-anhydro-D-glucitol, these cyclisations and hence the original transformation of (I) have therefore been formulated as occurring between C-1 and the C-3 hydroxyl with the production of oxetans. These structural assignments were also supported by the interpretations of the proton magnetic resonance spectra of the other oxetan derivatives; the uptake of periodate by 1,3-anhydro-D-glucitol was however abnormal (~3·5 moles) and this results presumably from further decomposition of the initially formed β-hydroxy-aldehyde (VI).

In view of the renewed interest[3-5] in carbohydrate oxetans it is interesting to observe the formation from the epoxide (I) of a further compound of this type and in circumstances where alternative ring closures to 5-, 6-, or 7-membered oxide rings are theoretically possible. Presumably the projected cyclisation of the epoxide (I) and the toluene-*p*-sulphonate esters (III; R^1=Ph, R^2=Me, and III; R^1=Ph, R^2=Et) to the 1,5-anhydro-D-glucitol structure is not observed because of the unfavourable conformation of the transition state to these products; although in the case of the epoxide (I) it is not clear why the formation of the oxetan (II; R^1=R^2=H) is preferred over the cyclisation to the 3,6-anhydro-compound (V).

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[4] P. W. Austin, J. G. Buchanan, and E. M. Oakes, *Chem. Comm.*, 1965, 374.
[5] G. E. Ustyuzhanin, N. S. Tikhomorova-Sidorova, and S. N. Danilov, *J. Gen. Chem.* (*U.S.S.R.*), 1963, **33**, 445.