Ring Expansion of a Glycoside

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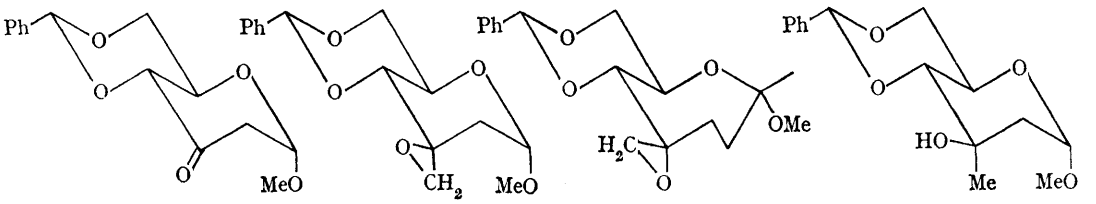
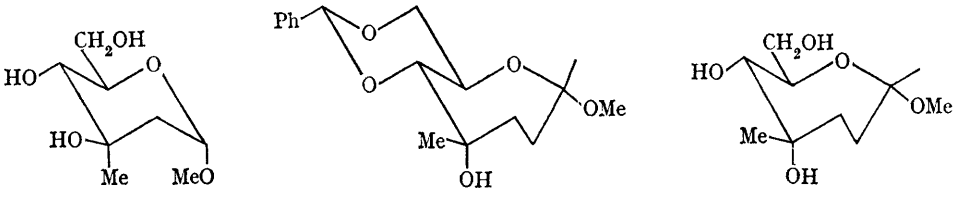
Two crystalline epoxides have been isolated from the multi-component system which results from treatment of methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*erythro*-hexopyranosid-3-ulose (I) in methanol with excess of diazomethane in ether at room temperature.[1] One of the epoxides (II) {m.p. 116·5—117°, $[\alpha]_D$ + 119° (ethyl acetate), M.W. 278 ± 2} on reduction ($LiAlH_4$) gave a product (IV), m.p. 79—79·5°, $[\alpha]_D$ + 122° (ethanol) isomeric with the substance obtained from the reaction between the glycopyranosidulose (I) and methylmagnesium iodide.[2] As the latter product has been shown[2] previously to have the *ribo*-configuration, the new branched-chain glycoside (IV) must belong to the *arabino*-series, a configurational assignment supported by the n.m.r. spectrum of the



(I) (II) (III) (IV)



(V) (VI) (VII)

epoxide (II) (proton count 18) (spectra were measured with a Varian A-60 n.m.r. spectrometer equipped with an integrator; all compounds were examined in solution in deuterochloroform, and with tetramethylsilane as the internal reference), by high-resolution infrared-spectral analysis[3] of the hydroxyl stretching region of the reduction product (IV), and by periodate oxidation[4] (1 mol. consumed in 10 hr.) and the M_G-value[5] (0·13 in borate buffer, pH 9·2) of the product (V) from the debenzylidenation of compound (IV).

The other epoxide (III) {obtained in 30% yield, m.p. 154—154·5°, $[\alpha]_D$ + 122° (ethyl acetate)} gave a positive test for a 2-deoxy-sugar and liberated benzaldehyde on acidification. Elemental analysis and M.W. determination by a chemical method[6] (found M.W. 296 ± 2) indicated that compounds (II) and (III) were not isomeric but differed by a methylene group: from the n.m.r. spectrum of epoxide (III) an unambiguous proton count of 20 was obtained. The assignment of signals in the spectrum of (III) was as follows: the five protons at τ 2·60 were clearly the phenyl protons, and the singlet at τ 4·50 was due to the acetal proton. The singlet at τ 6·63 (3 protons) was assigned to the methoxyl group at C-1 and the two protons in the two sharp doublets at τ 7·45 and 6·80 formed a typical AB system and were assigned to the protons of the epoxide ring. The anomeric proton in epoxide (III) gave rise to a quartet at τ 5·30 with $J_{1,2}$ = 8·0 c./sec. but in epoxide (II) the quartet due to the anomeric proton at τ 5·12 has $J_{1,2}$ = 4·0 c./sec. A model of epoxide (III) shows that the anomeric proton is quasi-axial and thus accounts for the large splitting observed. The multiplet in the region τ 5·60—6·40 (4 protons) was no more complex than that observed in the region τ 5·60—6·30 (4 protons) of the spectrum of epoxide (II) and was assigned to the protons H-4, H-5, H-6 *ax.* and H-6 *eq.* In the high-field region the multiplet at τ 8·00—8·80 (4 protons) was assigned to the protons of the methylene groups at C-2 and C-3. The n.m.r. spectrum of epoxide (III) precludes all structures containing a methyl substituent or a ring of the trimethylene oxide-type and is fully consistent with the structure shown.

Reduction of epoxide (III) with lithium aluminium hydride gave a crystalline branched-chain methyl heptoside derivative (VI) {66%, m.p. 102—102·5°, $[\alpha]_D$ + 130° (ethanol)}. The n.m.r. spectra of compounds (III) and (VI) were very similar. In the spectrum of (VI) the disappearance of the two sharp doublets at τ 6·80 and 7·45 (2 protons) and the appearance of a singlet at τ 8·65 (3 protons) was consistent with the reductive cleavage of the epoxide in (III) to form a methyl substituent in (VI). The multiplet at τ 7·40—8·50 (5 protons) was assigned to the four protons of the two methylene groups and the hydroxylic proton.

Debenzylidenation of compound (VI) yielded a crystalline glycoside (VII), m.p. 90—90·5°, $[\alpha]_D$ + 147° (ethanol): the extent and rate of its periodate

oxidation (1 mol. consumed in 65 min.) supports the structure and configuration shown. The *ribo*-configuration is further supported by the M_G-value (0·30) of compound (VII) measured in borate buffer, pH 9·2.

Apparently compound (III) arises from (I) by ring expansion on treatment with diazomethane. Although ring expansions of cyclic ketones are well known,[7] as far as we are aware this is the first reported example of a ring expansion of this type in carbohydrates.

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[1] See W. G. Overend and N. R. Williams, *J. Chem. Soc.*, 1965, 3446, for treatment of glycopyranosiduloses with diazomethane.
[2] B. Flaherty, W. G. Overend, and N. R. Williams, *J. Chem. Soc.* (*C*), 1966, 398.
[3] R. J. Ferrier, W. G. Overend, G. A. Rafferty, H. M. Wall, and N. R. Williams, *Proc. Chem. Soc.*, 1963, 133.
[4] Method of R. J. Ferrier and G. O. Aspinall, *Chem. and Ind.*, 1957, 1216.
[5] A. B. Foster, *Adv. Carbohydrate Chem.*, 1957, **12**, 81.
[6] W. C. J. Ross, *J. Chem. Soc.*, 1950, 2257.
[7] See E. P. Kohler, M. Tishler, H. Potter, and H. T. Thompson, *J. Amer. Chem. Soc.*, 1939, **61**, 1057.