Oxidative Ring Opening of Pyranosides and Furanosides

By S. J. ANGYAL* and K. JAMES

(*School of Chemistry, The University of New South Wales, Kensington, N.S.W.* 2033, *Australia*)

Summary Chromium trioxide in acetic acid oxidizes fully-acetylated methyl hexofuranosides and β-pyranosides (but not α-pyranosides) to methyl 4-oxo- and 5-oxo-glycconates, respectively.

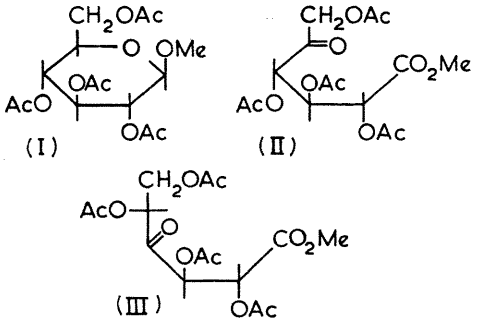
IT has been shown that methoxy-groups can be converted into formate groups by oxidation with chromium trioxide in glacial acetic acid.[1] This reaction could extend the use of methyl ethers as protecting groups for synthetic purposes in the carbohydrate field, as our results have indicated that yields obtained in this reaction are of the order of 60% or higher.[2]

In an attempt to extend this method to the removal of glycosidic methyl groups rather surprising results were obtained. In a typical experiment a suspension of chromium trioxide (3·0 g.) in glacial acetic acid (30 ml.) was stirred vigorously at room temperature with methyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside (1·0 g.). Oxidation was slower than usual with methyl ethers, and after 4·5 hr. 40% of the starting material was still present [estimated by g.l.c. analysis using a 4 ft. glass column of LAC IR-296 (1·5%) on chromosorb W (100—120 mesh) at 225°]. Column chromatography on silicic acid gave the 1-*O*-formyl derivative (m.p. 121—123°) containing 5% of the starting material (by g.l.c.), the n.m.r. spectrum of which showed the isolated formyl proton at δ 8·18 and the absence of a glycosidic methyl group.

On the other hand, the β-derivative (I) reacted rapidly with chromium trioxide undergoing oxidative opening of the pyranose ring to give methyl 2,3,4,6-tetra-*O*-acetyl-D-*xylo*-5-hexulosonate ("5-oxogluconate") (II), m.p. 59—60°, $[\alpha]_D^{24}$ — 5·8° (*c* 1·65, $CHCl_3$), in 76% yield; the reaction was

complete in 1 hr. The structure of this compound was assigned on the basis of its n.m.r. spectrum (60 MHz.; $CDCl_3$). Four acetyl groups and one methyl group are still present but the signal of the latter has shifted to the position (δ 3·78) characteristic for methyl carboxylates; a two-proton singlet (δ 4·87) for 6-H indicates that there is no hydrogen atom on C-5; and the remaining three protons appear in two doublets (δ 5·35 and 5·51) and a triplet (δ 5·74, $J_{2,3}$ and $J_{3,4}$ 4·3 Hz.), indicating an isolated system of three hydrogen atoms on consecutive carbon atoms.

That this type of reaction is general, providing the glycosidic methyl group has the β-configuration in a pyranose ring, has been demonstrated by oxidation of the fucoside, galactoside, and alloside. Crystalline 5-keto-esters were obtained in each case. The n.m.r. spectrum of the compound obtained from methyl 2,3,4-tri-*O*-acetyl-β-D-fucopyranoside furnishes additional evidence for the assignment of the keto-group to C-5. The signal of the C-6 methyl group, which appears as a doublet at δ 1·23 in the precursor, is replaced by a singlet at δ 2·07 in the product.



In contrast to the methyl pyranosides, both anomers of the methyl furanosides undergo this oxidative ring opening. The product obtained from the oxidation of methyl 2,3,5,6-tetra-*O*-acetyl-α- and -β-D-glucofuranosides has been shown to be methyl 2,3,5,6-tetra-*O*-acetyl-D-*glycero*-L-*threo*-4-hexulosonate (III) on the basis of its n.m.r. spectrum. A methyl ester group appears at δ 3·78; there are two isolated protons (2-H and 3-H) showing as an AB pattern (δ_A 5·88, δ_B 5·70, $J_{A,B}$ 2·4 Hz.); and the remaining three protons (6-H, 6′-H, and 5-H) appear as a typical ABX pattern (δ_6 4·63, δ_6 4·28, δ_5 5·52; $J_{6,6'}$ 12·3, $J_{5,6}$ 3·2, and $J_{5,6'}$ 6·0 Hz.). There is no proton, therefore, on C-4.

The two acetylated methyl D-mannofuranosides are also oxidised to a keto-ester, methyl 2,3,5-tetra-*O*-acetyl-D-*glycero*-L-*erythro*-4-hexulosonate. All these reactions proceed rapidly and the keto-esters appear to be their only products.

This reaction provides a ready method for obtaining the rare 5-hexulosonic acids and the practically unexplored 4-hexulosonic acids in high yield. Further reactions of these compounds are potentially valuable. Reduction of the keto group would provide glyconic acids epimerized on C-4 or C-5. Reduction of the ester group (by the method of Jones and Reid[3]) would provide a synthesis of the rare 3-hexuloses.

(*Received, April 15th*, 1969; *Com.* 517.)

[1] I. T. Harrison and S. Harrison, *Chem. Comm.*, 1966, 752.
[2] S. J. Angyal and K. James, submitted for publication in *Carbohydrate Res.*
[3] J. K. N. Jones and W. W. Reid, *Canad. J. Chem.*, 1955, **33**, 1682.