

FLUORINATION OF ACETYLATED GLYCALs

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The recent synthesis¹ of epimeric *cis* bromohexosyl fluorides from acetylated glycals has led us to investigate the reactions of these unsaturated sugars with lead tetrafluoride. Hitherto, this reagent has been employed in the synthesis of $\alpha\beta$ difluorides from halogenated olefins^{2,3} and from unsaturated steroids.⁴

Di, β -acetyl-D-arabinal was treated at 70° for 40 min. with an excess of lead tetraacetate and hydrogen fluoride in methylene dichloride. After neutralization with aqueous potassium carbonate, the methylene dichloride layer was removed and the aqueous solution was extracted with ether. From the organic extracts, a crystalline product (mp. 60-61°, $[\alpha]_D^{21}$ -24° in chloroform) was obtained, having the analytical composition of a monoacetyl dideoxydifluoropentose. Deacetylation of this material by a catalytic amount of sodium methoxide yielded a crystalline difluoride, (I) having m.p. 75°, $[\alpha]_D^{20}$ -26.0°, n_D^{20} 1.44 in methanol; Found: C. 39.0; H. 5.2; F. 25.0 Calc. for C₅H₈F₂O₃; C. 39.0; H. 5.2; F. 24.6%.

In contrast to the previously described¹ bromohexosyl fluorides, (I) was markedly stable to acidic reagents (e.g. 0.1 N sulphuric acid at 100° for 18 hr.) and towards alkalis (e.g. 0.1 N sodium methoxide at 60° for 5 hr.) The difluoride (I) consumed 0.96 moles/mole of potassium periodate, consistent with the presence of an α -glycol.

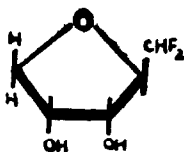
¹ P.W. Kent, F.O. Robson and V.A. Welch, J. Chem. Soc. 3273, (1963)

² A.L. Henne and T.P. Waalkes, J. Amer. Chem. Soc. 67, 1639, (1945),
68, 496 (1946)

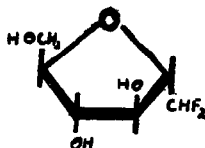
³ A.L. Henne and T.H. Newby, J. Amer. Chem. Soc. 70 130, (1948)

⁴ A. Bowers, P.G. Molton, E. Denot, M.C. Loza and R. Urquiza,
J. Amer. Chem. Soc. 84, 1050 (1962)

Proton and fluorine-19 magnetic resonance spectra of the diacetate synthesized from I, indicated the presence in the molecule of a difluoromethyl group⁵, C-CHF₂. This was confirmed by chromic acid oxidation of (I), giving one equivalent of distillable acid, identified as difluoroacetic acid by formation of the s-benzylthiuronium salt (m.p. 161-3°, Found: C. 45.85; H. 4.9; F. 13.8; C₁₀H₁₂F₂N₂OS requires C. 45.9; H. 4.6; F. 14.5%). The evidence thus indicates that the compound I has the structure of 2,5-anhydro-1-deoxy-1,1-difluoro-D-ribitol (or-D-arabitol).



I



II

The distinction between these two possibilities was made on the basis of comparison⁶ of optical rotatory changes (a) during periodate oxidation of I and methyl arabinopyranosides and (b) during borohydride reduction of the resulting "dialdehydes", and of the $[\alpha]_D$ of the p-nitrobenzoates of the final diols. In these reactions, compound I was converted into 1,1-difluoro-2-O-(2'-hydroxyethyl)-D-propane-2,3-diol bis (p-nitrobenzoate) (m.p. 86-7°, $[\alpha]_D^{20} + 7.5 \pm 2^\circ$ (c. 0.67 in chloroform) Found: F. 8.4 Calc. for C₁₉H₁₆F₂N₂O₉; F. 8.4%). Only a single asymmetric carbon atom in each of these compounds remains after oxidation.

⁵ B.H. Arison, T.V. Shen and N.R. Trenner, J.Chem.Soc.3828, (1962)

⁶ F. Smith and J.W. van Cleve, J. Amer. Chem. Soc. 77, 3091 (1955)

Optical rotatory $[\alpha]_D$ during IO_4^- oxidation and of resulting derivatives.

(I)	Methyl- α -L-arabinopyranoside ⁶	Methyl β -L-arabinopyranoside ⁶	
$[\alpha]_D$, initial compound (in H_2O)	- 35.0°	+19.7°	+235.0°
after IO_4^- oxidation (in H_2O)	+12.4°	-122.4°	+122.7°
after BH_4^- reduction of oxidation product (in EtOH)	+2.5° \pm 1°*	+6.8°	-6.9°
bis-p-nitrobenzoate (in CHCl_3)	+7.5° \pm 2° *in H_2O	+10.8	-10.2°

The difluoride (I) and methyl- α -L-arabinoside both exhibit rotational changes, similar in value and sense (see Table) and it is considered that the remaining asymmetric centre in the periodate oxidation products, is similarly orientated. On these grounds the derivative (I) is assigned to the ribo series.

With di-O-acetyl-L-arabinal, the corresponding 2,5-anhydro-1-deoxy-1,1'-difluororibitol (m.p. 75°, $[\alpha]_D^{21} + 25^\circ$ in methanol) was obtained.

In analogous reactions, triacetyl-D-glucal, treated with lead tetrafluoride and then deacetylated, gave a difluoro adduct (II, $\text{C}_6\text{H}_{10}\text{O}_4\text{F}_2$, $[\alpha]_D^{20} + 31.6$ in water), which could not be crystallised even after extensive chromatographical purification. The compound (II) consumed 1 mole/mole in periodate oxidation, and resembled the anhydrodifluororibitol (I) in its stability to acids and alkalis. The tri-O-toluene-p-sulphonate (m.p. 95°) reacted readily with sodium iodide in acetone at 110° giving a moniodide derivative (m.p. 85°, Found: C, 39.7; H, 3.63; F, 6.2; I, 19.3. Calc. for $\text{C}_{20}\text{H}_{21}\text{O}_7\text{S}_2\text{F}_2\text{I}$; C, 39.9; H, 3.51; F, 6.3; I, 21.1%) consistent with presence in II of a primary alcoholic group⁷. Chromic acid oxidation gave one equivalent of difluoroacetic acid, identified as the S^- -benzylthiuronium salt, m.p. and mixed m.p. 161-2°.

Comparison of the optical rotatory properties of II with those of

2,5-anhydro-D-mannose and -D-glucose was consistent with a manno configuration.

The reaction between lead tetrafluoride and these acetylated glycals thus leads to gem difluorides with accompanying ring contraction and differs decisively from the corresponding reaction in the steroid series where cis $\alpha\beta$ difluorides have been obtained. The formation of a gem difluoride, observed⁸ in the reaction between lead tetrafluoride and 1.1-diphenylethylene, which gives 1.1-difluoro-1,2-diphenylethane, has recently been further investigated⁹.

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⁷ J.W.H. Oldham and J.K. Rutherford, J. Amer. Chem. Soc., 54, 366, (1932)

⁸ J. Bornstein and M.R. Borden, Chem. and Ind., 441, (1958)

⁹ J. Bornstein, M.R. Borden, F. Nunes and H.I. Tavlin, J. Amer. Chem. Soc. 85, 1609, (1963).