Displacement Reactions of Acyclic Carbohydrate Derivatives. Part III.[1] Aldehyde Group Participation in 2,3,5-Tri-*O*-benzyl-4-*O*-toluene-*p*-sulphonyl-aldehydo-D-ribose

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Acidic hydrolysis of 2,3,5-tri-*O*-benzyl-4-*O*-toluene-*p*-sulphonyl-D-ribose dimethyl acetal gave 2,3,5-tri-*O*-benzyl-4-*O*-toluene-*p*-sulphonyl-aldehydo-D-ribose which was readily hydrolysed further to 2,3,5-tri-*O*-benzyl-L-lyxofuranose. Treatment of the aldehydo-compound with sodium methoxide in methanol gave methyl 2,3,5-tri-*O*-benzyl-L-lyxofuranoside. These easy displacements of the sulphonate group are rationalised in terms of neighbouring-group participation by the aldehyde group.

CASES of neighbouring-group participation by aldehyde groups are known.[2] Participation by the aldehyde group, rather than by the corresponding enol group, generally occurs by way of an addition product with a nucleophile as in the hydroxide-ion catalysed hydrolysis of methyl 2-formylbenzoate.[3] Two cases of aldehyde group participation in carbohydrate chemistry are known to occur in the presence of sodium methoxide in methanol. The D-ribofuranoside (I) containing a sulphonium group is racemised at C-4 by way of the unsaturated aldehydo-sugar (II).[4] Attack by methoxide ions at the aldehyde group, rather than at the olefinic group, then results in a mixture of D-*ribo*- (III) and L-*lyxo*-products (IV). Likewise, the L-rhamnose derivative (V) is smoothly converted by sodium methoxide into the D-allofuranoside (VII) through the epoxide (VI).[5] However, no case has been reported where a sulphonyloxy group has been displaced in this manner. The acetal (VIII) had been synthesised in connection with other work.[1] In the present context it was envisaged that acidic hydrolysis would yield the aldehyde (IX), and that treatment of this with sodium methoxide would lead to the mixture of L-lyxofuranosides (X) by the route shown.

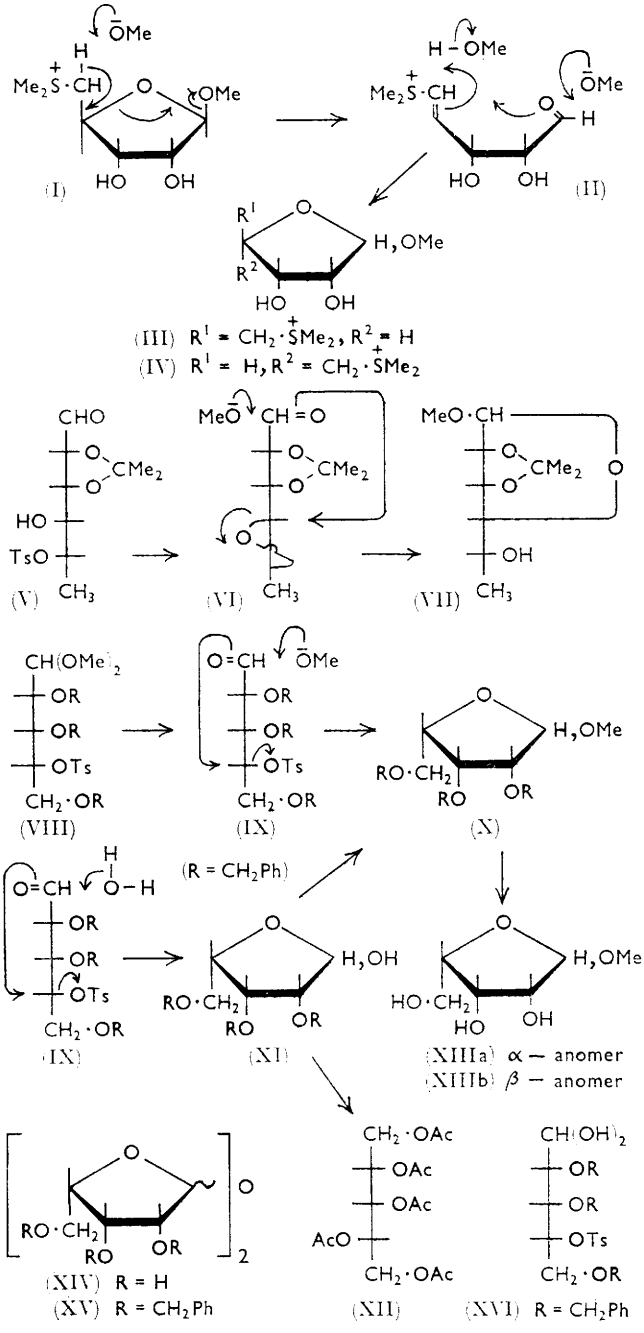
Surprisingly the acetal (VIII) was resistant to hydrolysis under mild conditions, in contrast to earlier experience with related acetals.[1] Under more vigorous conditions the acetal (VIII) slowly underwent hydrolysis and the aldehyde (IX) was formed but a second product was also obtained. This second compound arose from the aldehyde (IX); on prolonged hydrolysis it was the sole product. It contained a hydroxyl group and was shown to be 2,3,5-tri-*O*-benzyl-L-lyxofuranose (XI). Hydrogenolysis gave a sugar, chromatographically indistinguishable from D-lyxose, which on borohydride reduction gave L-lyxitol (L-arabinitol) identified as the known penta-acetate (XII).[6] Methanolysis of the sugar (XI) gave the glycosides (X) which on hydrogenolysis gave the L-lyxofuranosides (XIII); the α-anomer (XIIIa) was isolated in crystalline form and had the expected physical constants for the enantiomer of the known D-form.[7] In addition, non-reducing material was obtained with the chromatographic mobility expected for a disaccharide. This was probably composed of L-lyxofuranosyl-L-lyxofuranosides (XIV). The corresponding benzylated disaccharides (XV) could have been formed as "reversion products" in the methanolysis reaction. A similar compound, 2,2′,3,3′,5,5′-hexa-*O*-methyl-α-D-lyxofuranosyl-α-D-lyxofuranoside, was obtained when 2,3,5-tri-*O*-methyl-D-lyxofuranose was heated.[8]

The ready solvolysis of the sulphonate (IX) probably occurs with neighbouring-group participation by the aldehyde group by the route shown. Alternatively it is possible that the hydrated form (XVI) of the aldehyde (IX) is involved and that the sulphonate group is displaced by a 1-hydroxyl group of the *gem*-diol (XVI). This seems less likely, because carbohydrate sulphonates are generally stable in acidic or neutral conditions even though they may undergo intramolecular displacements in the presence of bases.[9]

Although the sugar (XI) could be separated from the acetal (VIII) and the aldehyde (IX), a complete chromatographic separation of the two latter compounds could not be achieved. Treatment of the aldehyde (IX), contaminated with the acetal (VIII), with sodium methoxide in methanol resulted in the slow disappearance of the aldehyde (IX) while the acetal (VIII) remained unchanged. A separate experiment confirmed that the acetal (VIII) was stable under the conditions used. The product contained the same mixture of glycosides (X) as was obtained in the methanolysis of the sugar (XI), and hydrogenolysis gave a mixture of the methyl L-lyxofuranosides (XIII) from which the α-anomer (XIIIa) was obtained in crystalline form.

This reaction, involving displacement of a sulphonate group, is entirely analogous to the two other cases of aldehyde group participation quoted earlier. Participation by the aldehyde group is demonstrated by the fact that the attack by methoxide ions occurs at the aldehyde group and not at the sulphonate group.

[1] Part II, N. A. Hughes and P. R. H. Speakman, preceding Paper.
[2] B. Capon, *Quart. Rev.*, 1964, **18**, 83.
[3] M. L. Bender and M. S. Silver, *J. Amer. Chem. Soc.*, 1962, **84**, 4589.
[4] J. Baddiley, W. Frank, N. A. Hughes, and J. Wieczorkowski, *J. Chem. Soc.*, 1962, 1999.
[5] E. J. Reist, L. Goodman, R. R. Spencer, and B. R. Baker, *J. Amer. Chem. Soc.*, 1958, **80**, 3962.
[6] M. Abdel-Akher, J. K. Hamilton, and F. Smith, *J. Amer. Chem. Soc.*, 1951, **73**, 4691.
[7] O. Kjolberg and O. J. Tjeltveit, *Acta Chem. Scand.*, 1963, **17**, 1641.
[8] H. G. Bott, E. L. Hirst, and J. A. B. Smith, *J. Chem. Soc.*, 1930, 658.
[9] R. S. Tipson, *Adv. Carbohydrate Chem.*, 1953, **8**, 143.



EXPERIMENTAL

General techniques were as described in Part II,[1] with the following additions. The solvent system, ethyl methyl ketone saturated with water, was used for paper chromatography. α-Glycols were detected with the periodate–Schiff reagent.[10]

Acidic Hydrolysis of 2,3,5-*Tri*-O-*benzyl*-4-O-*toluene*-p-*sulphonyl*-D-*ribose Dimethyl Acetal* (VIII).—A solution of the acetal (VIII) (1·5 g.) in acetone (60 ml.) and 5N-sulphuric acid (10 ml.) was heated under reflux for 6 hr. The products were isolated with chloroform and chromatographed on silica (50 g.). Elution with benzene–ether (19 : 1) gave a mixture of the acetal (VIII) and the aldehyde (IX); elution with benzene–ether (85 : 15) gave syrupy 2,3,5-*tri*-O-*benzyl*-L-*lyxofuranose* (XI) (201 mg.) (Found: C, 74·8; H, 6·8. $C_{26}H_{28}O_5$ requires C, 74·3; H, 6·7%). Repeated chromatography of the acetal (VIII)–aldehyde (IX) mixture gave a fraction (895 mg.) with $\nu_{max.}$ 1738s cm.$^{-1}$ indicating a high proportion of the aldehyde (IX).

1,2,3,4,5-*Penta*-O-*acetyl*-L-*lyxitol* (1,2,3,4,5-*Penta*-O-*acetyl*-L-*arabinitol*) (XII).—The ether (XI) (47 mg.) was catalytically hydrogenolysed in ethanol (5 ml.) over palladium [from PdO_2 (30 mg.)] to give a sugar (16 mg.) chromatographically indistinguishable from D-lyxose. Without further purification the sugar was reduced using sodium borohydride (9 mg.) in aqueous solution. After passage of the solution through Dowex-50 (acid form) ion-exchange resin and repeated evaporation with methanol, a compound (20 mg.), chromatographically indistinguishable from L-lyxitol (L-arabinitol), was obtained. Acetylation with acetic anhydride (0·3 ml.) in pyridine (2 ml.) gave the penta-acetate (XII) (15 mg.), m. p. and mixed m. p. 75° (from ether–light petroleum).

Methyl α-L-*Lyxofuranoside* (XIIIa) *from* 2,3,5-*Tri*-O-*benzyl*-L-*lyxofuranose* (XI).—A solution of the sugar (XI) (385 mg.) in methanol (40 ml.) containing toluene-*p*-sulphonic acid (190 mg.) was heated under reflux for 15 min. and then neutralised with Dowex-2 (carbonate form) ion-exchange resin. Chromatography on silica (15 g.) and elution with benzene–ether (19 : 1) gave a product (367 mg.) which was hydrogenolysed in ethanol over palladium [from PdO_2 (350 mg.)]. Paper chromatography indicated the major product to be a methyl α-lyxofuranoside together with the β-anomer and disaccharide material. Chromatography on cellulose (35 × 1·8 cm.) and elution with ethyl methyl ketone saturated with water gave, in the early fractions, the α-*furanoside* (XIIIa) (47 mg.), m. p. 95—96° (from ethyl acetate), $[\alpha]_D$ −125° (*c* 0·3 in H_2O) (Found: C, 43·2; H, 7·4. $C_6H_{12}O_5$ requires C, 43·9; H, 7·3%) (methyl α-D-lyxofuranoside has m. p. 96·5—97°, $[\alpha]_D$ +128° [7]). Later fractions gave a mixture (20 mg.) of the α- and β-furanosides (XIIIa) and (XIIIb).

The Reaction of 2,3,5-*Tri*-O-*benzyl*-4-O-*toluene*-p-*sulphonyl-aldehydo*-D-*ribose* (IX) *with Sodium Methoxide in Methanol.*—The acetal (VIII)–aldehyde (IX) fraction (890 mg.) obtained earlier was kept in methanol (25 ml.) containing sodium methoxide [from sodium (0·3 g.)] for 6 days at room temperature after which time no aldehyde remained. The solution was neutralised with carbon dioxide and the product was isolated with chloroform. Further chromatography on silica (100 g.) [elution with benzene–ether (19 : 1)] gave a product (492 mg.) whose i.r. spectrum lacked carbonyl absorption but still showed weak sulphonate ester absorptions [due to unchanged acetal (VIII)]. Catalytic hydrogenolysis of this, in methanol containing palladium [from PdO_2 (440 mg.)], gave debenzylated material (170 mg.). Paper chromatography indicated the presence of methyl α- and β-lyxofuranosides (XIII). Chromatography on Dowex-1 (hydroxide form) ion-exchange resin (100 ml.) and elution with water (20-ml. fractions) gave, from fractions 8—10, the β-furanoside (XIIIb) (12 mg.). Fractions 33—38 contained the pure α-furanoside (XIIIa) (48 mg.), m. p. and mixed m. p. 94·5—95·5° (from ethyl acetate).

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[10] J. Baddiley, J. G. Buchanan, R. E. Handschumacher, and J. F. Prescott, *J. Chem. Soc.*, 1956, 2818.