The Action of Methanethiol on D-Ribose Tetra-acetates; Formation of Methyl 1,5-Dithio-β-D-ribopyranoside and 4-*S*-Methyl-4-thio-L-lyxose Dimethyl Dithioacetal

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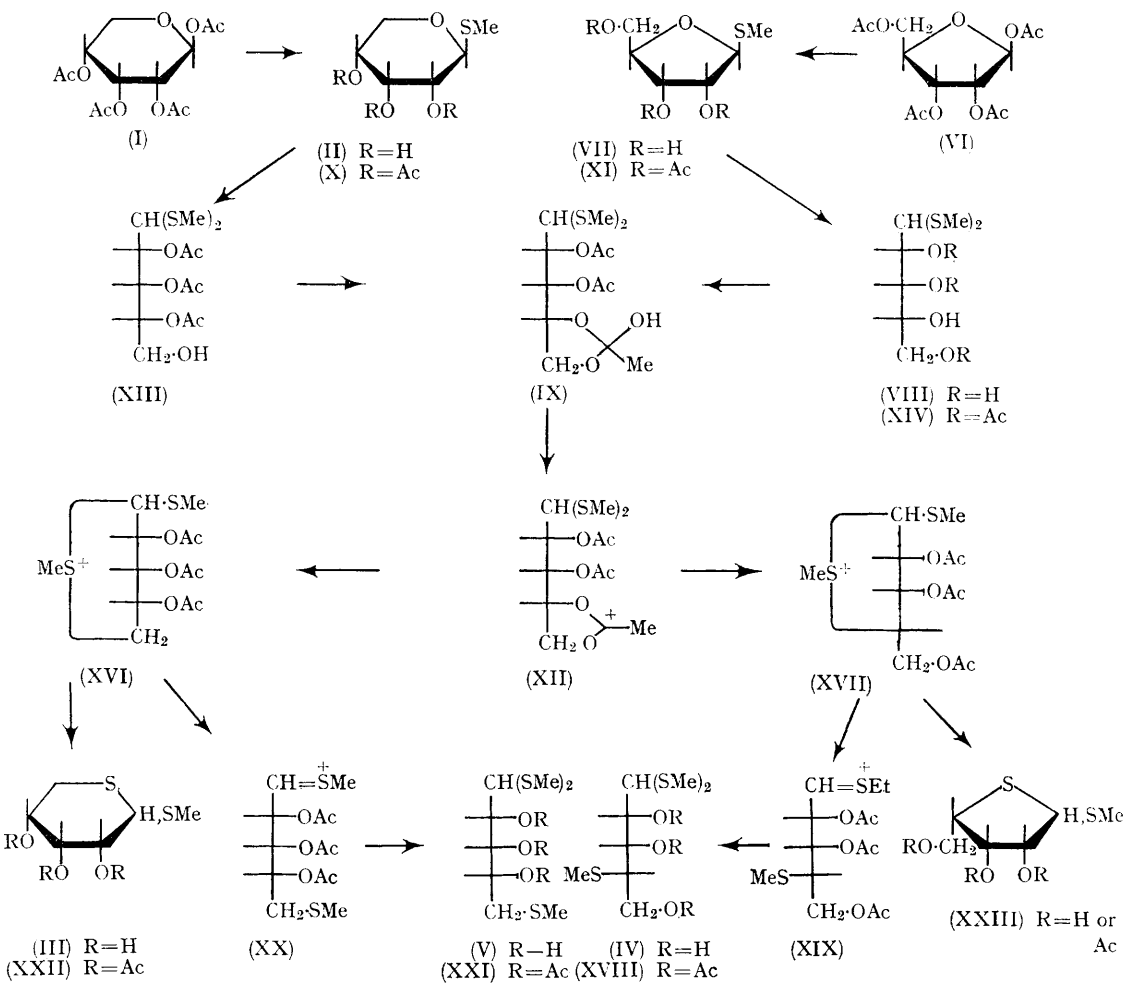
RECENT interest has centred on carbohydrate derivatives in which a sulphur atom replaces the ring oxygen atom.[1] We now report the formation of such a derivative by a novel reaction.

Reaction of 1,2,3,4-tetra-*O*-acetyl-β-D-ribopyranose (I) with methanethiol in the presence of zinc chloride and deacetylation of the products gave, in addition to the expected[2] methyl 1-thio-β-D-ribopyranoside (II), methyl 1,5-dithio-β-D-ribopyranoside (IIIb), and 4-*S*-methyl-4-thio-L-lyxose dimethyl dithioacetal (IV) together with a small amount of 5-*S*-methyl-5-thio-D-ribose dimethyl dithioacetal (V). Similar treatment of 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose (VI) for a short time gave only small amounts of methyl 1-thio-β-D-ribofuranoside (VII) and the major product was D-ribose dimethyl dithioacetal (VIII). Longer reaction times resulted in the complete disappearance of the furanoside (VII) from the products, a decrease in the amount of the dithioacetal (VIII), and the appearance, as main products, of the dithioglycoside (IIIb) and the *lyxo*-compound (IV) together with a small amount of the dithioacetal (V).

Evidently there is a common intermediate in these reactions of the two D-ribose tetra-acetates (I) and (VI) and we suggest that it is the ortho-acid (IX) (see Scheme 1).

The acetylated thioglycosides (X) and (XI), obtained by acetylation of the known[3] glycosides (II) and (VII), both gave rise to the dithioglycoside (IIIb) and the *lyxo*-dithioacetal (IV),



SCHEME 1

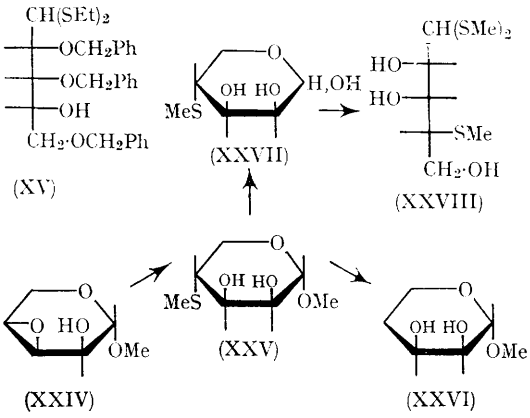
[a, α-anomer b, β-anomer]

when subjected to the above reaction conditions. The D-ribose dithioacetal (VIII) was also obtained from the reaction of the furanoside (XI) but not from the pyranoside (X). The ortho-acid (IX) and the acetoxonium ion (XII) are implicated both by the need for a common intermediate and the need to activate the acetylated dithioacetals (XIII) and (XIV) to enable the loss of a hydroxy-group by the action of the Lewis acid catalyst. By contrast the only reaction undergone by the partially benzylated dithioacetal (XV)[4] with ethanethiol and zinc chloride was a slow debenzylation. Precedent for the cyclisations to the cyclic sulphonium ions (XVI) and (XVII) is found in the formation[5] of ethyl 5-*S*-ethyl-1,5-dithio-α- and -β-L-arabinofuranosides from 5-*O*-tosyl-L-arabinose diethyl dithioacetal. The contrast in the fates of these two cyclic ions is remarkable. The acetylated *lyxo*-dithioacetal (XVIII) must arise by an opening of the cyclic ion (XVII), assisted by a mesomeric effect from the second thio-ether group, to the acyclic ion (XIX) which then reacts with solvent methanethiol. The corresponding pathway for the cyclic ion (XVI), [(XVI) → (XX) → (XXI)] is the less favoured one and instead the main reaction is a simple demethylation [(XVI) → (XXIIb)]. Simple demethylation of the ion (XVII) does not occur as no 1,4-dithioglycosides

(XXIII) were found in the reaction products. The reasons for these differences are not at present clear.

Only the β-dithioglycoside (IIIb) was obtained, the α-anomer (IIIa) was not formed. A reason for this is suggested if the two possibilities for the cyclisation of the acetoxonium ion (XII) to six-membered cyclic sulphonium ions (XVI) are considered (Scheme 2). The conformation (XIIa) leading to the α-glycoside (XVIa) has an unfavourable 1,3-diaxial interaction between the thiomethyl group at C-1 and the acetoxy-group at C-3. That leading to the β-glycoside (XVIb) is free of such interactions.

The structures of the new compounds (III), (IV), and (V) were all confirmed by synthesis. The dithio-glycoside (IIIb) together with the α-anomer (IIIa) had previously been synthesised[6] in these laboratories by the reaction of 5-thio-D-ribopyranose[7] with methanethiol. The known[8]



epoxide (XXIV) was opened with sodium methanethiolate to give the lyxoside (XXV). Proof that the epoxide opening had taken place at C-4 was obtained by reductive desulphurisation to the deoxyglycoside (XXVI) which reduced one equivalent of periodate. Hydrolysis of the lyxoside (XXV) gave the free sugar (XXVII) which on treatment with methanethiol gave the enantiomorph (XXVIII) of the *lyxo*-dithioacetal (IV). 5-*S*-Methyl-5-thio-D-ribose dithioacetal (V) was obtained directly by treatment of methyl 2,3-*O*-isopropylidene-5-*S*-methyl-5-thio-β-D-ribofuranoside[9] with methanethiol and mineral acid.

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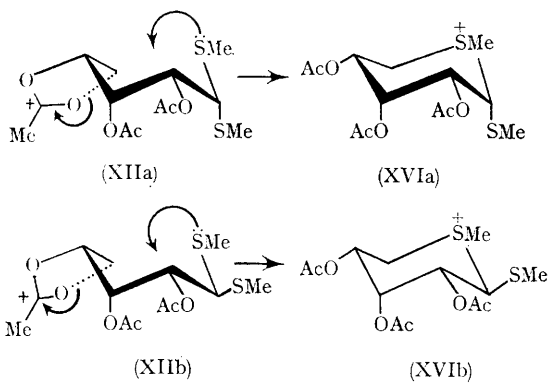

SCHEME 2

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