

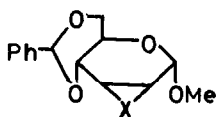
SYNTHESIS AND REACTIONS OF 2,3-DIDEOXY-2,3-EPIITHIO-MANNOSE(1)

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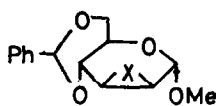
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Guthrie and Murphy(3) recently reported that methyl 4,6-O-benzylidene-2,3-anhydro- α -D-allo-pyranoside(I) reacted with thiourea in 2-propanol to give methyl 4,6-O-benzylidene-2,3-dideoxy-2,3-epithio- α -D-mannopyranoside(IV) together with methyl 4,6-O-benzylidene-2,3-dideoxy-2,3-didehydro- α -D-erythro-hexopyranoside(V), and failed to react with potassium thiocyanate to yield any quantity of the manno-episulphide. They established the structure of IV on the basis of the elemental analysis, the p.m.r. spectrum and the optical rotatory dispersion.



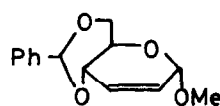
I X: O

II X: S



III X: O

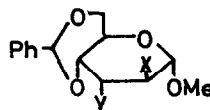
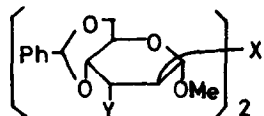
IV X: S



V

The paper prompts us to report our synthesis of the manno-episulphide(IV). When the allo-epoxide(I) and ammonium thiocyanate were reacted in 2-methoxyethanol at 100-105° for 17 hr., bis(methyl 4,6-O-benzylidene-2-deoxy- α -D-altropyranoside)-2(2')-disulphide(VI)(63.5%), m.p. 180°, $[\alpha]_D^{20} +123^\circ$ (c,1 in CHCl₃), and the expected manno-episulphide(IV)(6.7%), m.p. 158-159°, $[\alpha]_D^{16} +30^\circ$, were obtained together with a small amount of V.

The structure of VI was established by derivation to methyl 4,6-O-benzylidene-2-deoxy-S-benzyl-2-thio- α -D-altropyranoside(IX), m.p. 134-135.5° (authentic sample(4), m.p. 135-136°), after reduction by lithium aluminium hydride followed by S-benylation. The optical rotatory dispersion curve of VI showed a weak positive Cotton effect as already known in the other disulphides (5,6). $[\phi]_{430} +1010$, $[\phi]_{271} +4696$ pk., $[\phi]_{257} +4598$, $[\phi]_{240} +5260$, $[\phi]_{225} +10020$ (dioxan).



VI	X: S-S	Y: OH
VII	X: S-S	Y: OSO ₂ Me
VIII	X: S	Y: OH

IX	X: SCH ₂ Ph	Y: OH
X	X: SH	Y: OH
XI	X: H	Y: OH
XII	X: H	Y: H

CD, $[\theta]_{335}^0$, $[\theta]_{249}^0 +1978$, $[\theta]_{233}^0 +1859$, $[\theta]_{225}^0 +2670$ (dioxan). The elemental analysis of the product of m.p. 158-159^o, indicated reasonable values for the manno-episulphide(IV) constitution, and Raney nickel desulphurization in dioxan at room temperature gave methyl 4,6-O-benzylidene-2,3-dideoxy- α -D-erythro-hexopyranoside(XII), m.p. 88^o, $[\alpha]_D^{14} +117.4^o$ (c, 2 in CHCl₃), which was also obtained from allo-episulphide(II)(3,4) by the analogous desulphurization. Moreover, in the p.m.r. spectrum(7), the signals due to H-2 and H-3 showed AB quartet at τ 6.93 and 7.25 ($J = 6.9$ c/sec.), respectively; the anomeric proton(H-1) gave a singlet(τ 5.00) showing zero coupling between H-1 and H-2; and phenyl, benzylidene-methine and methoxyl protons occurred at τ 2.63, 4.52 and 6.59, respectively. The optical rotatory dispersion curve (8,9) showed a positive Cotton effect around 264 m μ . $[\phi]_{380} +332$, $[\phi]_{277} +2857$ pk., $[\phi]_{250} -5825$ tr., $[\phi]_{238} -5585$, $[\phi]_{220} -10300$ (dioxan). CD, $[\theta]_{287}^0$, $[\theta]_{264}^0 +5323$, $[\theta]_{235}^0$ (dioxan). These data supported the manno-episulphide(IV) structure for the new product, but didn't agree with the data shown for the same compound in the Guthrie's report. m.p. 173-174^o, $[\alpha]_D^{22} +130^o$, p.m.r. spectrum; τ 2.63(phenyl), 4.41(benzylidene-methine), 5.14(H-1), 6.61(methoxyl protons). O.R.D.; $[\phi]_{400} +830$, $[\phi]_{300} +1870$, $[\phi]_{265} +2330$ pk., $[\phi]_{248} +1830$ tr., $[\phi]_{227} +3120$ (dioxan). Therefore, we traced the Guthrie's procedure for the preparation of the manno-episulphide(IV) and obtained a product which was identified to be the altro-2(2')-disulphide(VI) in comparison with our sample by a mixed m.p. determination and I.R. spectra.

Reaction of I with potassium thiocyanate in 2-methoxyethanol yielded only bis(methyl 4,6-O-benzylidene-2-deoxy- α -D-altropyranoside)-2(2')-sulphide(VIII)(75.2%). m.p. 229-231^o, $[\alpha]_D^{20} +63.5^o$ (c, 0.85 in CHCl₃), the structure of which was established by the elemental analysis and the molecular weight determination, and by Raney nickel desulphurization, which gave methyl 4,6-O-benzylidene-2-deoxy- α -D-ribo-hexopyranoside(XI), m.p. 129-131^o, identical with a sample(10) prepared

by the ring-opening reaction of I with lithium aluminium hydride.

Although the direct formation of IV from I was in the low yield as described above, it was also obtained from VI through two steps in an excellent yield. VI was treated with methanesulphonyl chloride in pyridine to give 3-methanesulphonate(VII)(96%), m.p. 171° (decomp.), $[\alpha]_D^{34.5} +185^{\circ}$ (c, 1 in CHCl_3), which was subsequently reacted with 1 mole of sodium borohydride in pyridine at room temperature to give IV(95.7%).

Attempts to learn what product could be obtained from IV by the attack of a nucleophilic reagent such as sodium benzylmercaptide, potassium ethyl xanthate or thiourea resulted only in the formation of the olefin(V), exclusive of 2,3-dithio-sugars. Recently, conversion of some epoxy compounds by potassium alkyl xanthate into the corresponding alkenes has been discussed(11, 12) in the presumption that the reactions pass through the episulphides with double inversions as intermediates. Horton and his colleagues(13,14) found the conversion of I into V by the action of a large excess of potassium ethyl xanthate in boiling 1-butanol, but the pathway of the reaction has not yet been elucidated. For isolation of an intermediate, the episulphide, the reaction was carried out in smaller amount of xanthate than the Horton's procedure in methanol or ethanol as solvent. When a solution of 1 mole of I and 2 moles of potassium ethyl xanthate using methanol was refluxed, two crystalline products were isolated. One was the altro-2(2')-sulphide(VIII)(57%), and the other(36%), m.p. $165-167^{\circ}$, $[\alpha]_D^{16} +68^{\circ}$ (c, 1 in CHCl_3), which was converted to IX by benzylation and to VI by oxidation, was characterized as methyl 4,6-O-benzylidene-2-deoxy-2-thio- α -D-altropyranoside(X) [m.p. $168-169^{\circ}$, $[\alpha]_D +80.5^{\circ}$ (CHCl_3)(15); m.p. $170-172^{\circ}$, $[\alpha]_D^{20} +77.4^{\circ}$ (CHCl_3)(16) in the literatures]. Using 1 mole of potassium ethyl xanthate in boiling ethanol, IV(6%), V(9%), VIII(36%) and unchanged starting material(5%) were obtained after chromatographic purification. Also in the case of the manno-epoxide(III), it was converted into V, in 50% yield, on treatment with potassium ethyl xanthate in boiling 1-butanol, and into the contaminated allo-episulphide(II) in boiling ethanol. After several recrystallizations, a pure material of II was obtained from the crude product in a poor yield. These results support that the formation of the olefin(V) from both epoxides (I and III) should proceed via episulphides(IV and II), respectively as anticipated in other cases(12).

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R E F E R E N C E S

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