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THE SYNTHESIS AND CHEMICAL PROPERTIES OF METHYL 2,3,6-TRI-O-BENZOYL-4-DEOXY-4-THIOCYANO-α-D-GLUCOPYRANOSIDE

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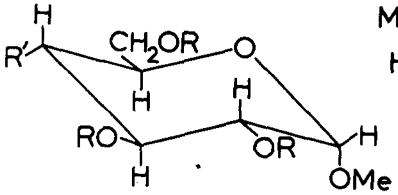
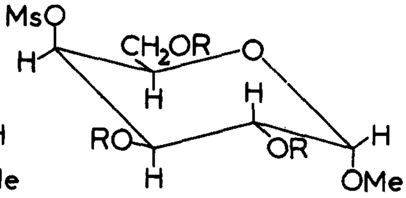
In connection with our programme dealing with thioglycosides as " enzyme inducers " (1), we report in this communication the synthesis and chemical properties of methyl 2,3,6-tri-O-benzoyl-4-deoxy-4-thiocyano-α-D-glucopyranoside (I). On sodium methoxide treatment this gives the sodio-derivative of methyl-4-deoxy-4-thio-α-D-glucopyranoside (II), which is a key intermediate for the preparation of the sulphur-containing analogues of maltose, cellobiose and lactose.



[I] R=COPh; R'=SCN
[II] R=H; R'=SNa



[III] R=COPh

Although it is sometimes difficult to carry out substitution reactions on some secondary pyranose-sugar sulphonates, the sulphonyl esters on C-4 of glucopyranose or galactopyranose derivatives can be displaced by strong nucleophiles in dimethylformamide solution with inversion (2,3).

Treatment of the readily available (4,5) methyl 2,3,6-tri-O-benzoyl-4-O-methylsulphonyl-α-D-galactopyranoside (III)* with potassium thiocyanate at 140° for 22 hours, furnished methyl 2,3,6-tri-O-benzoyl-4-deoxy-4-thiocyano-α-D-glucopyranoside (I) in a yield of 47 %, m.p. 194-194.5°, $[\alpha]_D^{29}$ + 60.3° (c 0.53, $CHCl_3$) ; found : C, 63.41 ; H, 4.62 ; N, 2.53 ; S, 5.81 ; $C_{29}H_{25}O_8NS$; requires C, 63.43 ; H, 4.57 ; N, 2.59 ; S, 5.85.

That the thiocyano group is attached to C-4 of the ring was shown by a sequence involving Raney nickel desulphurization, followed by debenzoylation and reacetylation of the crude product. The isolated substance was methyl 2,3,6-tri-O-acetyl-4-deoxy-α-D-xylo-hexopyranoside (IV) (78 %)[based on the thiocyanate (I)] m.p.75-76°, $[\alpha]_D^{30}$+138° (c 0,5, $CHCl_3$) ; found: C, 51.17 ; H, 6.46 ; $C_{13}H_{20}O_8$; requires C, 51.2 ; H, 6.6 Hedgley, Overend and Rennie (6b) give m.p. 74°, $[\alpha]_D$ + 135.2° (c 0.9, $CHCl_3$).

This route represents an excellent procedure for preparing 4-deoxy-D - xylo-hexopyranose. Alternative sequences for synthesizing this deoxy-sugar have been reported (6), using less readily available starting material.

The N.M.R. spectrum of (I) is completely consistent with the gluco configuration having the C-1 conformation. The H-3 and H-4 signals are clearly recognizable as triplets with large first-order coupling constants (J = 10 c.p.s.). These protons are diaxially related and flanked by axial protons on C-2 and C-5.

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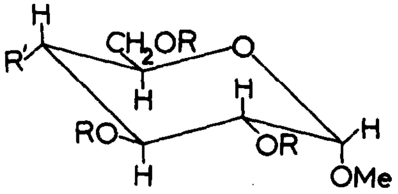
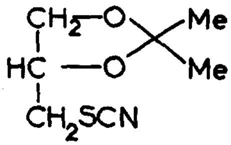


[IV] R=Ac ; R'=H

[V] R=COPh ; R'=NCS

[VI] R=Ac ; R'=SAc



[VII]

It was of interest to ascertain whether the isothiocyanate (V) under our experimental conditions, is present in either the isolated derivative (I), or in the mother liquor. Due to resonance in the thiocyanate ion, involved in the nucleophilic displacement ($\bar{S}$-C ≡ N ⟷ S = C = $\bar{N}$), the formation of both isomers (I, V) might be expected. It has been shown (7) that the α-protons adjacent to the -SCN and -NCS groups can be differentiated on the basis of their chemical shifts. Infrared spectroscopy has also been used for the detection of the isomeric products. Investigation by these methods did not reveal the presence of the isothiocyano isomer (V) (Table I).

For comparative study 1,2-O-isopropylidene-3-deoxy-3-thiocyano-glycerol (VII) was also prepared. It was obtained in good yield by the treatment of 1,2-O-isopropylidene-3-O-tosyl-glycerol with potassium thiocyanate in dimethylformamide (n_D^{19} 1.4761, b.p. 51-53°/0.02 mm ; found : C, 48.74 ; H, 6.29 ; N, 8.26 ; S,18.56 $C_7H_{11}O_2NS$; require C, 48.55 ; H, 6.40 ; N, 8.09 ; S , 18.49.

These results are in accordance with the recently reported observations (8) on the attempted isomerization of the different types of thiocyanates and isothiocyanates.

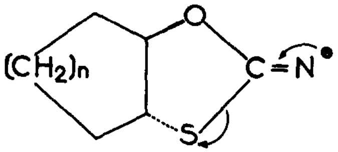
Debenzoylation of 2,3,6-tri-O-benzoyl-4-deoxy-4-thiocyano-α-D-glucopyranoside (I) with sodium methoxide, under nitrogen atmosphere, gave a sirup, which shown to be homogeneous on thin-layer chromatography. This compound was not isolated, but was acetylated using pyridine and acetic anhydride. The resulting oil could be distilled, and analysed as methyl 2,3,6-tri-O-acetyl-4-S-acetyl-4-deoxy-4-thio-α-D-glucopyranoside (VI), b.p. 145-148°/ 0.005 mm, $[\alpha]_D^{29}$ + 128° (c 0.72 ; $CHCl_3$) (found : C, 47.74 ; H, 5.99; S, 8.30 ; $C_{15}H_{22}O_9S$, requires C, 47.62 ; H, 5.86 ; S, 8.46.

In the N.M.R. spectrum of (VI) there are clearly recognizable : three equatorial O-acetyl, one S-acetyl signals as singlets at 1.97, 2.03, 2.07 and 2.30 p.p.m. respectively, and triplets of H-3 and H-4 protons with large coupling constants (J = 10 c.p.s.). The I.R. spectrum of (VI) shows the characteristic (9) equatorial C-S absorption band at 763 cm^{-1}. It is therefore apparent that the original gluco configuration of (I) was maintained during the alkaline treatment and the reacetylation procedure.

Trans - thiocyanohydrins and O-acyl thiocyanohydrins in the steroid and carbohydrate series can be converted into episulphides by basic treatment (10).

Such a reaction involves a trans-fused cyclic intermediate (VIII) whose formation requires an antiperiplanar arrangement of the functional groups. Although monocyclic systems can adopt boat or skew conformations, it was a priori improbable that basic treatment of (I), which has trans-diequatorial groups on C-3 and C-4 result in the formation of the corresponding episulphide.

In fact, sodium methoxide treatment of (I) simply cleaved the thiocyanate and benzoyl esters, furnishing after acetylation methyl-2,3,6-tri-O-acetyl-4-S-acetyl-4-deoxy-4-thio-α-D-glucopyranoside (VI).



[VIII]

Table I

Chemical shift data for α-protons in thiocyanates and isothiocyanates and infrared absorption band for thiocyanates

Compound	Chemical shift (δ)		Thiocyanate absorption band (cm^{-1})
	X= -SCN	X= -NCS	
I	3.46		2.167
VII	3.01		2.168
CH_3-CH_2-X	2.98*	3.64*	
$(H_3C)_2CH-X$	3.48*	3.95*	

* See reference (7).

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