Synthesis and *X*-Ray Crystallographic Studies of Dithiepan Derivatives of Carbohydrates

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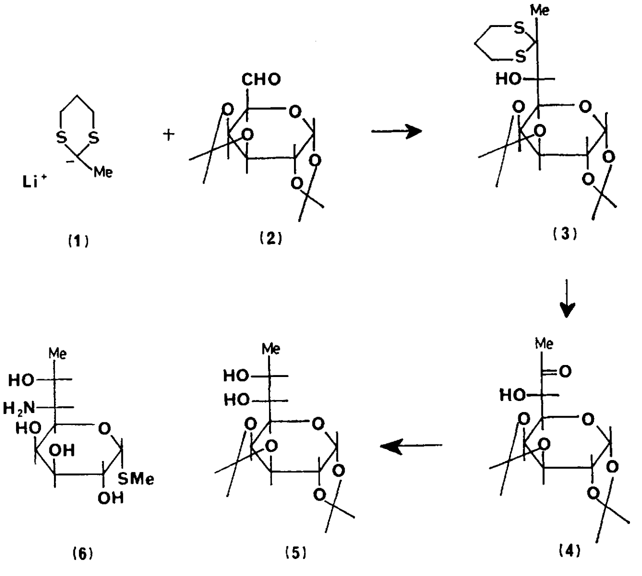
Summary Nucleophilic addition of 2-lithio-2-methyl-1,3-dithian to the dialdehyde (**2**) gives the two diastereoisomers (**3**) and (**7**); compound (**7**) was transformed into a new class of carbohydrate dithiepan derivatives (**11**)-(**13**).

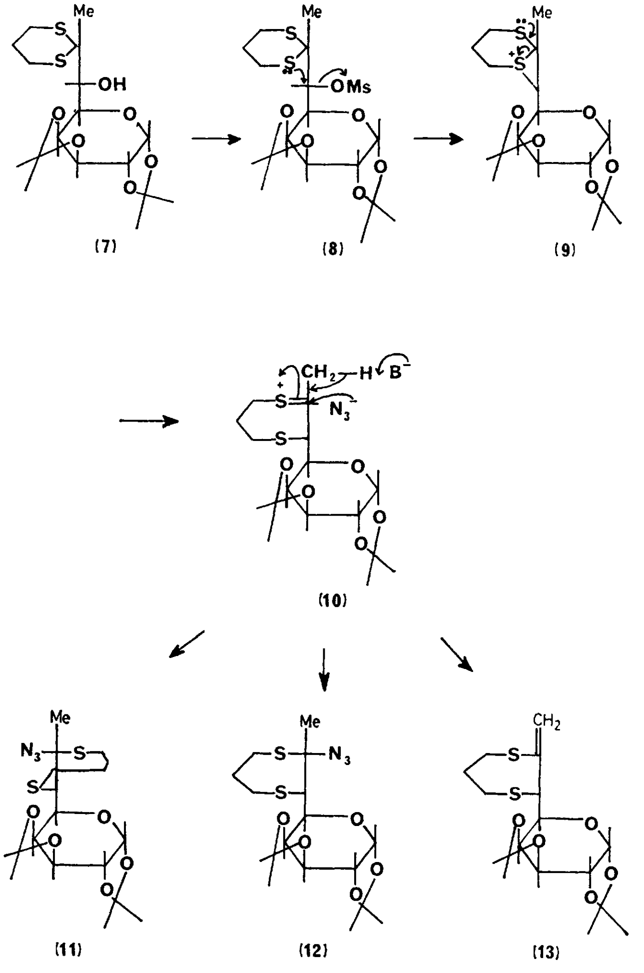
The recent discovery of several antibiotics[1,2] containing octose groups of unusual functionality, which include aldgamycin E, quinocycline complex antibiotics, lincomycin, and apramycin[3] has stimulated the search for a synthesis of octose derivatives from the more abundant hexoses. The construction of such molecules requires suitable chain-branching or chain-extension of a hexose by two functionalized carbon atoms. We have considered[4] nucleophilic addition of a 2-lithio-1,3-dithian derivative to a ketose or aldose.



Scheme 1

Here we report the stereocontrolled preparation of the two diastereoisomers (**3**) and (**7**), and their transformations into the octopyranose (**5**), and into a new class of carbohydrate dithiepan derivatives [(**11**)—(**13**)].

When the pyranose (**2**) was treated with equimolar quantities of the dithian (**1**) in dry tetrahydrofuran (—20°, 20 h), compound (**3**) was obtained as the major product (42%); M^+ 392, m.p. 106—109°, $[\alpha]_D$ — 36° (*c* 1·22, $CHCl_3$). The absolute configuration at the newly formed asymmetric centre [C-6 in (**3**)] was established from circular dichroism studies. Compound (**3**) has a negative Cotton effect, which corresponds in sign and location (230 nm) with that of 6-*C*-(1′,3′-dithian-2′-yl)-1,2:3,4-di-*O*-isopropylidene-α-D-*glycero*-D-*galacto*-heptopyranose.[7] The D-*glycero* configuration of the latter was also proved by chemical correlations. The minor product (17%) was compound (**7**); M^+ 392, m.p. 111—112°, $[\alpha]_D$ — 53° (*c* 1·7, $CHCl_3$) which has been described previously.[4] Only the diastereoisomer (**7**) was obtained (34%) when hexamethyl phosphorictriamide was used as solvent in the addition reaction.



Scheme 2

Treatment of (**3**) with mercuric chloride and cadmium carbonate in absolute ethanol (80°, 1 h) gave the ketone (**4**), which was then reduced with sodium borohydride to give the octopyranose (**5**) [60% from (**3**)] (Scheme 1); m.p. 149·5—151°, $[\alpha]_D$ — 57·4° (*c* 1·4, $CHCl_3$) identical (by m.p., mixed m.p., $[\alpha]_D$, and chromatographic mobility) with an authentic sample synthesised[5] by a different route. The diol (**3**) has previously been converted[6] into thiolincosaminide (**6**) and lincomycin.

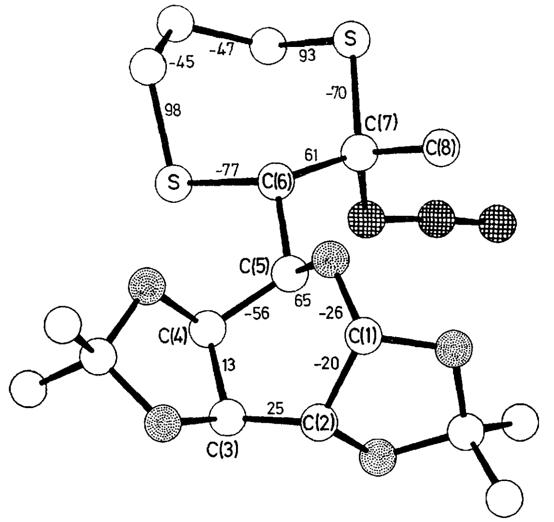


FIGURE. Molecular structure of 7-azido-8-deoxy-1,2:3,4-di-*O*-isopropylidene-6,7-*S*,*S*-trimethylene-6,7-dithio-α-L-*threo*-D-*galacto*-octopyranose (**11**) showing the principal torsional angles in degrees.

The alcohol (**7**) gave a mesylate[4] (**8**) and it was of interest to investigate the behaviour of this mesylate towards displacement reactions in view of presence of the neighbouring thio function.

Treatment of the mesylate (**8**) with sodium azide in dimethylformamide (80°, 5 h) gave compounds (**11**) (12%), m.p. 115—118°, $[\alpha]_D$ +137° (*c* 0·92, $CHCl_3$), M^+ 417; (**12**) (15%), M^+ 417; (**13**) (28%), M^+ 375.†

Colourless crystals of (**11**) were grown from ethanol. The material crystallises in the orthorombic space group $P2_12_12_1$ with cell dimensions: $a = 9{\cdot}599$, $b = 10{\cdot}83$ and $c = 19{\cdot}558$ Å. The structure was solved by direct methods, using the phase function.[8] *X*-Ray intensity for 1965 independent reflections data were collected on a Philips diffractometer and were refined by least-square procedures[9] to a conventional value of 5·7%. A view of the molecule is shown in the Figure.

The formation of compounds (**11**)—(**13**) may be rationalised by an initial intramolecular displacement to give the episulphonium ion (**9**); this opens with ring enlargement to give (**10**), which is either attacked by azide ion leading to (**11**) and (**12**) or loses a proton giving the alkene (**13**) (Scheme 2).

These products (**11**)—(**13**) represent the first examples of heterocyclic dithiepan derivatives of carbohydrates.

All new compounds gave satisfactory elemental analyses.

We thank Professor Szarek for a sample of the diol (**5**).

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† Structures (**12**) and (**13**) were assigned on the basis of ^1H and ^{13}C n.m.r. and [for (**12**)] i.r. spectra.

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