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MECHANISM OF THE PYRANOSIDE → FURANOSIDE ISOMERIZATION IN THE ACID-CATALYSED METHANOLYSES OF SOME METHYL HEXOPYRANOSIDES*

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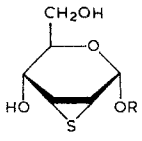
ABSTRACT

On treatment with Amberlite CG-120(H^+) resin in methanol-d_4, methyl 2,3-dideoxy-2,3-epithio-α-D-allopyranoside (**1a**) gave trideuteromethyl 2,3-dideoxy-2,3-epithio-β-D-allofuranoside (**4b**), methyl 2-*S*-benzyl-2-thio-α-D-altropyranoside (**10**) gave methyl 2-*S*-benzyl-2-thio-α-(and β)-D-altrofuranoside (**11** and **12**), 3-*S*-benzyl-3-thio-α-D-altropyranoside (**14**) was unaffected, and methyl 2-deoxy-α-D-*ribo*-hexopyranoside (**17**), methyl 2-*O*-methyl-α-D-altropyranoside (**20**), and methyl 2-deoxy-2-iodo-α-D-altropyranoside (**23**) isomerized to the corresponding methyl furanosides. The pyranoside→furanoside isomerization is explained by a mechanism involving cyclic cation intermediates (B_1 and B_2), the inductive effect of the substituent at C-2, and the steric effect of substituents at C-2 and C-3.

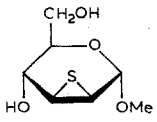
INTRODUCTION

Cation-exchange resins are well known as mild catalysts[2–7] in hydrolyses of 4,6-*O*-benzylidenehexoses, but isomerization of hexopyranoside into hexofuranoside sometimes also occurs[1]. Thus, the 4,6-*O*-benzylidene derivatives of methyl 2,3-dideoxy-2,3-epithio-α-D-allopyranoside (**1a**), methyl 2,3-dideoxy-2,3-epithio-α-D-mannopyranoside (**2**), and methyl 2,3-di-*S*-benzyl-2,3-dithio-α-D-altropyranoside (**3**) were hydrolyzed and isomerized to give methyl 2,3-dideoxy-2,3-epithio-β-D-allofuranoside (**4a**), methyl 2,3-dideoxy-2,3-epithio-α-D-mannofuranoside (**5**), and methyl 2,3-di-*S*-benzyl-2,3-dithio-α-D-altrofuranoside (**6**), respectively. It was suggested[1] that the isomerizations were caused by the S-substituent at C-2 and/or C-3. We now report on the isomerization of **1a** in CD_3OD. This reaction was studied in order to examine the incorporation of the OCD_3 group into the resulting furanoside.

*Thiosugars; Part III[1].



1a R = Me
1b R = CD_3



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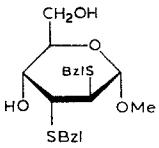

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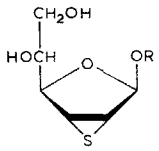
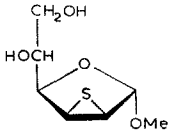


4a R = Me
4b R = CD_3
4c R = H



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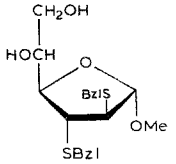

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RESULTS AND DISCUSSION

In order to examine the influence of a catalyst on the isomerization of methyl 2,3-dideoxy-2,3-epithio-α-D-allopyranoside (**1a**) into the furanoside (**4a**), various acids, namely, Amberlite CG-120(H^+) resin, and oxalic, toluene-*p*-sulphonic, hydrochloric, and sulphuric acids, were used as catalysts. The isomerization proceeded smoothly with each catalyst, and there was no specificity among these acids as shown in Table I.

TABLE I

ACID-CATALYZED ISOMERIZATION OF METHYL 2,3-DIDEOXY-2,3-EPITHIO-α-D-ALLOPYRANOSIDE (**1a**) INTO METHYL 2,3-DIDEOXY-2,3-EPITHIO-β-D-ALLOFURANOSIDE (**4a**)

Amount of **1** *(mg)*	*Acid*		*Solvent (ml)*	*Temp. (degrees)*	*Time (h)*	*Yield of* **4** *(%)*
100	Amberlite CG-120 (H^+)	(0.315 g)	Dry MeOH (7)	55	5	84.4
500	Oxalic acid	(1.5 g)	80% MeOH (50)	Reflux	10	62.0
100	Toluene-*p*-sulphonic acid	(0.195 g)	Dry MeOH (10)	55	4	79.6
101	Conc. HCl	(0.05 ml)	Dry MeOH (10)	55	2	86.2
100	Conc. H_2SO_4	(0.01 ml)	Dry MeOH (10)	55	2	88.9
100	3M HCl–MeOH	(10 ml)		55	2	75.0

The reaction of **1a** using the resin (H^+ form) in methanol-d_4 was then studied, and the effect of incorporation of the OCD_3 group into the furanoside was determined in order to clarify the mechanism of the isomerization. Table II shows the result, which is compared with the yield of the product obtained from **1a** by the reaction in methanol. The ratio of trideuteromethyl 2,3-dideoxy-2,3-epithio-α-D-allopyranoside

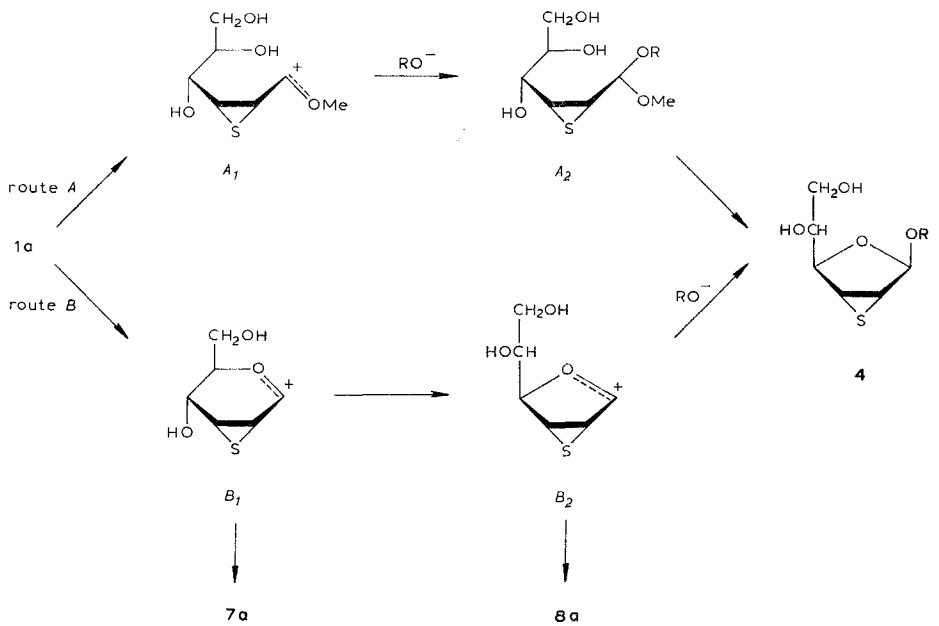
(**1b**) to **1a** was determined from the decrease of the p.m.r. signal of MeO-1 at δ 3.40 in **1a**. After a reaction time of 30 min, the recovered pyranoside was a mixture of **1a** (3.0%) and **1b** (30.7%). After 300 min, all of the methoxyl group in **1a** had exchanged with OCD_3. Also, as the p.m.r. spectra of the furanoside obtained after reaction times of 30 and 300 min contained no signal for MeO-1, the furanoside is trideuteromethyl 2,3-dideoxy-2,3-epithio-β-D-allofuranoside (**4b**). The furanoside **4a** was

TABLE II

METHANOLYSES[a] OF METHYL 2,3-DIDEOXY-2,3-EPITHIO-α-D-ALLOPYRANOSIDE (**1a**) AND METHYL 2,3-DIDEOXY-2,3-EPITHIO-β-D-ALLOFURANOSIDE (**4a**)

Material	*Solvent*	*Reaction time (min)*	*Yield of products (%)*			
			1a	**1b**	**4a**	**4b**
1a	MeOH	15	46.2		49.1	
1a	MeOH	40	23.2		66.7	
1a	MeOH	300	5.0		84.8	
1a	CD_3OD	30	3.0	30.7	—	65.4
1a	CD_3OD	300	—	8.2	—	76.3
4a	MeOH	300	—		88.3	
4a	CD_3OD	30	—	—	70.6	19.9
4a	CD_3OD	300	—	—	2.7	85.8

[a]With Amberlite CG-120(H^+) resin in dry MeOH or CD_3OD at 55°.

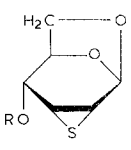


Scheme 1. Alternative pathways for 1a in acid media

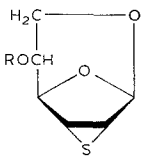
unaffected on treatment with the resin in dry methanol. The incorporation of the OCD_3 group on treatment of **4a** with resin–methanol-d_4 was not complete after 300 min (Table II). This fact suggests that **4b** produced by treatment of **1a** in methanol-d_4 does not involve **4a** as an intermediate.

In the isomerization **1a**→**4a**, two reaction pathways should be considered, as in the hydrolysis of D-glucopyranosides[8,9], involving (Scheme 1) acyclic (A_1 and A_2) and cyclic intermediates (B_1 and B_2). As the furanoside produced by the isomerization of **1a** in methanol-d_4 consists of **4b** only, route *B* is the reaction pathway.

Treatment of **1a** with the resin in dry tetrahydrofuran gave **4a** (9%), 2,3-dideoxy-2,3-epithio-β-D-allofuranose (**4c**, 12.0%), 1,6-anhydro-2,3-dideoxy-2,3-epithio-β-D-allopyranose (**7a**, 26.4%), and 1,6-anhydro-2,3-dideoxy-2,3-epithio-β-D-allofuranose (**8a**, 15.9%). The formation of **4c** is probably due to the participation of water absorbed by the resin. When the reaction was monitored by t.l.c., the reactions **4c**→**7a**→**8a** were detected. When the mixture of **4a**, **4c**, **7a**, and **8a** had been formed in tetrahydrofuran, methanol was added and the mixture was heated to afford **4a** in 82% yield. Thus, the formation of **7a** and **8a** can be explained only *via* route *B*, involving the intermediates B_1 and B_2.



7a R = H
7b R = Bz

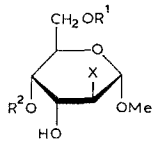


8a R = H
8b R = Bz

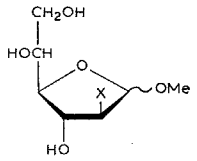
The structures of **7a** and **8a** were established on the basis of their n.m.r. spectra and those of the monobenzoates **7b** and **8b** (see Experimental).

The isomerization of **1a** and **2** should be influenced strongly by the steric effect of the 2,3-epithio ring. Because the 2,3-epithio ring requires coplanarity of C-1,2,3,4, the intermediate furanoid cation will be attacked by methoxyl anions on the least-hindered side. This concept is supported by examples of pyranoid→furanoid isomerizations in bicyclic compounds[10–13].

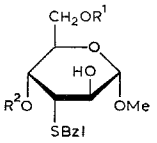
In order to compare the effect of a substituent at C-2 or C-3, methyl 2-*S*-benzyl-4,6-*O*-benzylidene-2-thio-α-D-altropyranoside (**9**) and methyl 3-*S*-benzyl-4,6-*O*-benzylidene-3-thio-α-D-altropyranoside (**13**) were treated with the resin. With the resin in 80% methanol at 55°, **9** gave methyl 2-*S*-benzyl-2-thio-α-D-altropyranoside (**10**) after 1.5 h, but with longer reaction times (25 and 50 h), methyl 2-*S*-benzyl-2-thio-α-D-altrofuranoside (**11**) and the β anomer of **11** (**12**) were formed at the expense of **10**. Treatment of **12** with resin–methanol gave **10** and **11**, as shown on t.l.c. The ratios of the yields of **10**, **11**, and **12** depended on the reaction time (Table III), and these products were interconvertible.



9 R^1, R^2 = PhCH, X = SBzl
10 $R^1 = R^2$ = H, X = SBzl
17 $R^1 = R^2$ = H, X = H
19 R^1, R^2 = PhCH, X = OMe
20 $R^1 = R^2$ = H, X = OMe
22 R^1, R^2 = PhCH, X = I
23 $R^1 = R^2$ = H, X = I



11 X = SBzl (α-anomer)
12 X = SBzl (β-anomer)
18 X = H (β-anomer)
21 X = OMe (α,β-mixture)
24 X = I (α,β-mixture)



13 R^1, R^2 = PhCH
14 $R^1 = R^2$ = H

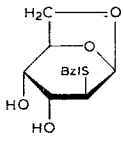


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TABLE III

HYDROLYSIS[a] OF METHYL 2-*S*-BENZYL-4,6-*O*-BENZYLIDENE-2-THIO-α-D-ALTROPYRANOSIDE (**9**)

Reaction time (h)	*Yield of products* (%)		
	10	**11**	**12**
1.5	78.0	—	—
25	15.6	65.5	16.1
50	7.2	47.6	18.1

[a]With Amberlite CG-120(H^+) resin in 80% MeOH at 55°.

On treatment of the 3-thio derivative (**13**) with resin–methanol at 55° for 100 h, methyl 3-*S*-benzyl-3-thio-α-D-altropyranoside (**14**, 75%) was the only product identified. The above results reveal that the pyranoside→furanoside isomerization is caused by the S-substituent at C-2.

When a solution of **9** in 80% acetone was boiled for 8 h in the presence of oxalic acid as the catalyst, 1,6-anhydro-2-*S*-benzyl-2-thio-α-D-altropyranose (**15**, 3%) and 2-*S*-benzyl-2-thio-D-altrose (**16**, 30.5%) were formed, together with **10** (10.2%). Under similar conditions, **13** gave **14** (70%). The conversion of **9** into **11** and **12** with resin–80% methanol, and into **15** and **16** with oxalic acid–80% acetone, is attributable to the effect of both the acid and the reaction solvent.

2-Deoxyglycosides are hydrolysed much faster in acid than the corresponding glycosides[14–17], and Armour *et al.*[17] have invoked a cyclic carbonium-ion intermediate. Owing to a weaker electron-withdrawing effect by the methylene group at position 2 in comparison with a CH(OH) group, protonation of MeO-1 in methyl 2-deoxyglycosides is promoted, and the loss of MeO-1 is facilitated. If the electronegativity of the atom attached to C-2 is used as a measure of the reactivity in hydrolyses, it is noteworthy that the value (2.50) for sulphur is closer to that (2.1) of hydrogen than that (3.5) of oxygen. Thus, the derivatives having an S-substituent at C-2 are hydrolyzed as rapidly as are 2-deoxyglycosides. Therefore, the hydrolysis and

the isomerisation of **10** should be facilitated by the inductive effect of the S-substituent. In order to prove this point, the hydrolyses of glycosides having a 2-substituent of weaker electron-withdrawing effect than hydroxyl, *e.g.*, methyl 2-deoxy-α-D-*ribo*-hexopyranoside (**17**), methyl 2-*O*-methyl-α-D-altropyranoside (**20**), and methyl 2-deoxy-2-iodo-α-D-altropyranoside (**23**), were examined.

When **17** was treated with resin–methanol at 55° for 40 h, methyl 2-deoxy-β-D-*ribo*-hexofuranoside (**18**, 47%) was obtained. Treatment of methyl 4,6-*O*-benzylidene-2-*O*-methyl-α-D-altropyranoside (**19**) with resin–80% methanol at 55° for 2 h produced **20** (96.5%), but after 280 h, methyl 2-*O*-methyl-α(and β)-D-altrofuranosides (**21**, 24.1%) were formed and the yield of **20** was reduced (59.2%). The p.m.r. spectrum of **21** revealed two signals for anomeric protons (δ 4.75 and 4.85) which indicated an ~2:1 αβ-mixture.

Treatment of methyl 4,6-*O*-benzylidene-2-deoxy-2-iodo-α-D-altropyranoside (**22**) with resin–methanol for 2 h gave **23** (58.9%), whereas after 53 h, methyl 2-deoxy-2-iodo-α(and β)-D-altrofuranoside (**24**, 28.8%) and 2-deoxy-2-iodo-D-altrose (**25**, 5.9%) were obtained together with **23** (20.9%). The p.m.r. spectrum of **24** contained signals for anomeric protons at δ 5.30 and 5.52, indicating an αβ-ratio of ~1:1.

The results of the acid-catalysed methanolyses of **17**, **20**, and **23** prove that pyranoside–furanoside isomerization is caused by the inductive effect of a substituent at C-2. However, since **10**, **20**, and **23** gave the isomerization products as αβ-mixtures, the steric effects of substituents at C-2 and C-3 should also be considered. For the altrose derivatives, the intermediates B_1 and B_2 (Scheme 1) are supposed to be in equilibrium. An aqueous solution of D-altrose at equilibrium contains[18] 67% of pyranose and 33% of furanose forms, and the ratio of furanoside to pyranoside for D-xylose in methanolic hydrogen chloride increases in the order of 3-*O*-methyl, 2-*O*-methyl, and 2,3-di-*O*-methyl derivatives[19]. These phenomena are due to a nonbonded interaction of the substituents at C-2 and C-3.

EXPERIMENTAL

General procedures. — Amberlite CG-120(H^+) resin was prepared in the usual way, washed with acetone, and dried at room temperature. Melting points are uncorrected. Specific rotations were measured with an automatic polarimeter (JASCO). P.m.r. spectra were recorded with JNM-60H (JEOL) or HA-100 (Varian) instruments for solutions in chloroform-*d* unless otherwise noted; in order to determine OCD_3 incorporation, 10% solutions were used. I.r. spectra were recorded with a DS-701 (JASCO) instrument, and mass spectra were recorded with a JMS-O1-SG (JEOL) spectrometer. The purity of compounds was assessed by t.l.c. on Wakogel B-O (Wako Chemical Co.) and detection by charring with sulphuric acid. Tetrahydrofuran was dried over sodium hydroxide for a month, and then distilled from $LiAlH_4$ and stored over metallic Na. The isotopic purity of the methanol-d_4 (Merck) used was 99%. Column chromatography was performed on silicic acid (Mallinckrodt Chem. Co.) with the solvent systems specified.

Isomerization of methyl 2,3-dideoxy-2,3-epithio-α-D-allopyranoside (**1a**). — (*a*) *With Amberlite CG-120(H^+) resin.* A mixture of **1a**[1] (100 mg), resin (315 mg), and dry methanol (7 ml) was stirred for 15 min at 55° and then filtered. Concentration of the filtrate *in vacuo* gave a syrup which was eluted from silica gel with chloroform–ethyl acetate (1:1) to give first methyl 2,3-dideoxy-2,3-epithio-β-D-allofuranoside[1] (**4a**; 54.1 mg, 54.1%). Recrystallization from benzene gave needles (49.1 mg, 49.1%), m.p. 133.5°. Eluted second was **1a** (46.2 mg, 46.2%).

This procedure was applied generally with methanol or methanol-d_4. After the reaction of **1a** in methanol-d_4 for 30 min, the proportion of **1b** to **1a** was determined from the decrease of the p.m.r. signal for MeO-1 at δ 3.40 in relation to that for the anomeric proton at δ 5.13. An observed decrease to 9% for the recovered pyranoside (33.7 mg, 33.7%) indicated a mixture of **1a** (3.0%) and **1b** (30.7%). The results shown in Table II were obtained by a similar procedure.

(*b*) *With oxalic acid.* A mixture of **1a** (500 mg), oxalic acid (1.5 g), and 80% methanol (50 ml) was boiled under reflux for 10 h, cooled, and stirred with barium carbonate (7.5 g) for 24 h at room temperature. The filtered mixture was concentrated *in vacuo* to dryness, and the crystalline residue was eluted from silica gel with chloroform–ethyl acetate (1:1) to give first **4a** (0.31 g, 62.0%) and then **1a** (24.5 mg, 4.8%).

(*c*) *With toluene-p-sulphonic acid.* To a solution of toluene-*p*-sulphonic acid (194 mg) in dry methanol (10 ml), **1a** (100 mg) was added. The mixture was stirred at 55° and then neutralized with Amberlite IRA-400(HO^-) resin, filtered, and concentrated *in vacuo*. Crystallization of the residue from benzene gave **4a** (79.6 mg, 79.6%).

The treatment of **1a** with the other acids indicated in Table I was carried out in a similar manner.

Treatment of methyl 2,3-dideoxy-2,3-epithio-β-D-allofuranoside (**4a**) *with Amberlite CG-120(H^+) resin in methanol.* — A mixture of **4a** (100 mg), resin, and dry methanol (7 ml) was stirred for 300 min at 55°. The product, purified as described for **1a**, was **4a** (88.3 mg, 88.3%). This procedure was also applied with methanol-d_4, and the proportions of **4b** to **4a** were determined as described above. The results are shown in Table II.

Treatment of **1a** *with Amberlite CG-120(H^+) resin in dry tetrahydrofuran.* — (*a*) Resin (7.5 g) was added to a solution of **1a** (2.2 g) in dry tetrahydrofuran (230 ml), and the mixture was stirred for 10 h at 55°. The filtered solution was then concentrated *in vacuo* to give a syrup which was eluted from silica gel with chloroform to give first 1,6-anhydro-2,3-dideoxy-2,3-epithio-β-D-allopyranose (**7a**; 484.1 mg, 26.4%), m.p. 82–83°. Recrystallization from light petroleum gave colourless needles, m.p. 86.5–87.0°, $[\alpha]_D^{27.5}$ +103° (*c* 0.93, chloroform), ν_{max}^{KBr} 3490 cm^{-1} (OH), λ_{max}^{EtOH} 261.5 nm (ε 74). P.m.r. data (100 MHz): δ 2.45 (broad, 1 H, OH), 3.15 (q, 1 H, $J_{1,2}$ <1, $J_{2,3}$ 6 Hz, H-2), 3.57 (q, 1 H, $J_{2,3}$ 6, $J_{3,4}$ 7 Hz, H-3), 3.77 (q, 1 H, $J_{3,4}$ 7, $J_{4,5}$ 2.5 Hz, H-4), 3.86 (q, 1 H, $J_{5,6exo}$ 7.5, $J_{6,6}$ 8 Hz, H-6*exo*), 3.97 (d, 1 H, $J_{6,6}$ 8 Hz, H-6*endo*), 4.40 (q, 1 H, $J_{4,5}$ 2.5, $J_{5,6exo}$ 7.5 Hz, H-5), and 5.27 (d, 1 H, $J_{1,2}$ <1 Hz, H-1). Mass spectrum: *m/e* 160.0179 ($C_6H_8O_3S$: calc. *m/e* 160.0194).

Anal. Calc. for $C_6H_8O_3S$: C, 45.00; H, 5.04. Found: C, 45.10; H, 5.03.

Eluted second was 1,6-anhydro-2,3-dideoxy-2,3-epithio-β-D-allofuranose (**8a**; 292.9 mg, 15.9%), m.p. 107–109°. Recrystallization from ether gave colourless needles, m.p. 112.0–113.0°, $[\alpha]_D^{27.5}$ +101.5° (*c* 0.99, chloroform), ν_{max}^{KBr} 3410 cm^{-1} (OH), λ_{max}^{EtOH} 262.5 nm (ε 64). P.m.r. data (100 MHz): δ 3.16 (broad, 1 H, OH), 3.35 (d, 1 H, $J_{2,3}$ 4.5 Hz, H-2), 3.48 (d, 1 H, $J_{2,3}$ 4.5 Hz, H-3), 3.63 (m, 1 H, H-5), 3.77 (m, 1 H, $J_{6,6'}$ 13.5 Hz, H-6*exo*), 4.26 (q, 1 H, $J_{5,6endo}$ 3, $J_{6,6'}$ 13.5 Hz, H-6*endo*), 4.29 (t, 1 H, $J_{4,5}$ 2, $J_{4,6exo}$ 2 Hz, H-4), and 5.35 (s, 1 H, H-1). Mass spectrum: *m/e* 160.0205 ($C_6H_8O_3S$: calc. *m/e* 160.0194).

Anal. Calc. for $C_6H_8O_3S$: C, 45.00; H, 5.04. Found: C, 45.01; H, 5.16.

Eluted third was methyl 2,3-dideoxy-2,3-epithio-β-D-allofuranoside (**4a**; 198.5 mg, 9.0%) identical with an authentic sample[1]. Eluted fourth was 2,3-dideoxy-2,3-epithio-β-D-allofuranose (**4c**; 246.4 mg, 12.0%), m.p. 97–99°. Recrystallization from acetone–light petroleum gave needles, m.p. 98–99°, identical with an authentic sample[20].

The n.m.r. spectra of **7a** and **8a** correspond to those of 1,6-anhydropyranoses[21] and 1,6-anhydrofuranoses[22–24], respectively.

(*b*) To a solution of **1a** (51.6 mg) in dry tetrahydrofuran (3.5 ml), resin (156.9 mg) was added. After stirring for 5.5 h at 55°, **1a** had disappeared (t.l.c.; chloroform–ethyl acetate, 1.2:1). After cooling to room temperature, dry methanol (3.5 ml) was added, and the mixture was stirred for 40 min (no change observed on t.l.c.) and then at 55° for 5 h (t.l.c. then revealed only **4a**). The cooled mixture was filtered through Celite and concentrated *in vacuo* to give **4a**, m.p. 132–133°. Recrystallization from benzene gave needles, m.p. 133.5° (41.0 mg, 82%), identical with an authentic sample[1].

*1,6-Anhydro-4-*O*-benzoyl-2,3-dideoxy-2,3-epithio-β-*D*-allopyranose* (**7b**). — Conventional treatment of **7a** (64.5 mg) with pyridine (1 ml) and benzoyl chloride (1.5 mol.) and elution of the product from silica gel with chloroform gave syrupy **7b** (95.5 mg, 89.8%) which gradually crystallized. Purification by sublimation *in vacuo* gave needles, m.p. 97–97.5°, $[\alpha]_D^{21}$ +128° (*c* 0.35, chloroform), ν_{max}^{KBr} 1715 cm^{-1} (C=O). P.m.r. data: δ 3.18 (d, 1 H, $J_{2,3}$ 6.7 Hz, H-2), 3.60 (t, 1 H, $J_{2,3}$ 6.7, $J_{3,4}$ 6.7 Hz, H-3), 4.67 (t, 1 H, $J_{5,6endo} = J_{5,6exo} = 4.5$ Hz, H-5), 5.12 (d, 1 H, $J_{3,4}$ 6.7 Hz, H-4), and 5.85 (s, 1 H, H-1). Mass spectrum: *m/e* 264 (M).

Anal. Calc. for $C_{13}H_{12}O_4S$: C, 59.09; H, 4.58. Found: C, 59.00; H, 4.56.

*1,6-Anhydro-5-*O*-benzoyl-2,3-dideoxy-2,3-epithio-β-*D*-allofuranose* (**8b**). — Benzoylation of **8a**, followed by elution of the product from silica gel, gave **8b** (49.9 mg), m.p. 87–91°. Purification by sublimation *in vacuo* gave needles (41.9 mg, 95.3%), m.p. 138–139°, $[\alpha]_D^{13.5}$ +7° (*c* 0.3, chloroform), ν_{max}^{KBr} 1715 cm^{-1} (C=O). P.m.r. data: δ 3.53 (d, 1 H, $J_{2,3}$ 4.5 Hz, H-2), 3.49 (d, 1 H, $J_{2,3}$ 4.5 Hz, H-3), 3.95 (d, 1 H, $J_{6,6'}$ 13.5 Hz, H-6*exo*), 4.42 (q, 1 H, $J_{5,6endo}$ 3, $J_{6,6'}$ 13.5 Hz, H-6*endo*), 4.47 (t, 1 H, $J_{4,5}$ 2, $J_{4,6exo}$ 2 Hz, H-4), 4.99 (m, 1 H, H-5), and 5.42 (s, 1 H, H-1). Mass spectrum: *m/e* 264 (M).

Anal. Calc. for $C_{13}H_{12}O_4S$: C, 59.09; H, 4.58. Found: C, 59.21; H, 4.29.

Hydrolysis of methyl 2-S-benzyl-4,6-O-benzylidene-2-thio-α-D-altropyranoside (**9**). — (*a*) *With Amberlite CG-120(H^+) resin.* A mixture of **9**[6] (500 mg), resin (2.3 g), and 80% methanol (50 ml) was stirred for 50 h at 55° and then filtered, and the filtrate was concentrated *in vacuo* to dryness. Elution of the residue (yellow syrup) from silica gel with chloroform–methanol (9.5:0.5) gave, first, syrupy methyl 2-*S*-benzyl-2-thio-α-D-altropyranoside (**10**; 28 mg, 7.2%), $[\alpha]_D^{19}$ +59° (*c* 0.57, chloroform); ν_{max}^{film} 3460 (OH), 1600, 1495, and 700 cm^{-1} (phenyl). P.m.r. data: δ 3.32 (s, 3 H, OMe), 3.82 (s, 2 H, CH_2-S), 4.68 (s, 1 H, H-1), and 7.35 (s, 5 H, Ph).

Anal. Calc. for $C_{14}H_{20}O_5S$: C, 55.99; H, 6.71. Found: C, 55.75; H, 6.59.

Eluted second was a mixture of two products (t.l.c.) which was rechromatographed on silica gel by elution with ether to give, first, syrupy methyl 2-*S*-benzyl-2-thio-α-D-altrofuranoside (**11**; 184 mg, 47.6%), $[\alpha]_D^{19}$ +29° (*c* 0.53, chloroform); ν_{max}^{film} 3400 (OH), 1600, 1450, and 700 cm^{-1} (phenyl). P.m.r. data: δ 3.30 (s, 3 H, OMe), 3.87 (s, 2 H, CH_2-S), 4.78 (d, 1 H, $J_{1,2}$ 2.3 Hz, H-1), and 7.37 (s, 5 H, Ph). Mass spectrum: *m/e* 300 (M) and 91 (base peak).

Anal. Calc. for $C_{14}H_{20}O_5S$: C, 55.99; H, 6.71; S, 10.67. Found: C, 56.16; H, 6.88; S, 10.56.

Eluted second was methyl 2-*S*-benzyl-2-thio-β-D-altrofuranoside (**12**; 70 mg, 18.1%), m.p. 107–108°, $[\alpha]_D^{19}$ +14° (*c* 0.2, chloroform); ν_{max}^{KBr} 3380, 3290 (OH), 1600, 1495, and 700 cm^{-1} (phenyl). P.m.r. data: δ 3.33 (s, 3 H, OMe), 392 (s, 2 H, CH_2-S), 4.62 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), and 7.39 (s, 5 H, Ph). Mass spectrum: *m/e* 300 (M) and 91 (base peak).

Anal. Calc. for $C_{14}H_{20}O_5S$: C, 55.99; H, 6.71; S, 10.67. Found: C, 55.84; H, 6.70; S, 10.40.

The products and yields of other related experiments are listed in Table III.

To a solution of **11** (50 mg) in methanol (0.2 ml) was added a solution of sodium metaperiodate (71 mg) in water (1.8 ml), and the mixture was stored for 2 h. Addition of a solution of dimedone (0.12 g) in water (20 ml) to the steam distillate of the reaction mixture gave a product (50 mg, 73.5%) which, after recrystallisation from ethanol, had m.p. 190–191° alone or in admixture with the dimethone obtained from formaldehyde. In a similar manner, **12** gave formaldehyde, but **10** did not. The $[\alpha]_D$ values and the $J_{1,2}$ values (*cf.* Ref. 25) confirm the α and β configuration of **11** and **12**.

(*b*) *With oxalic acid.* A mixture of **9** (2.5 g), oxalic acid (7.5 g), and acetone (250 ml) was boiled under reflux for 8 h, and then cooled, neutralised with barium carbonate (37.5 g), and filtered. The filtrate was concentrated *in vacuo* to ~50 ml, the concentrate extracted with ether, and the extract concentrated *in vacuo* to dryness. The residue (yellow syrup) was eluted from silica gel with chloroform–ethyl acetate (1:1.2) to give first 1,6-anhydro-2-*S*-benzyl-2-thio-β-D-altropyranose (**15**; 66.5 mg, 3.8%), which was crystallised from ether to afford needles (46.5 mg, 2.7%), $[\alpha]_D^{21.5}$ −75.5° (*c* 0.3, chloroform); ν_{max}^{KBr} 3450 (OH), 1495, and 700 cm^{-1} (phenyl). P.m.r. data: δ 2.74 (q, 1 H, $J_{1,2}$ 1, $J_{2,3}$ 9 Hz, H-2), 2.78 (s, 2 H, deuterium exchangeable, OH), 3.86 (s, 2 H, CH_2-S), 4.62 (m, 1 H, H-5), 5.28 (d, 1 H, $J_{1,2}$ 1 Hz, H-1), and 7.30 (s, 5 H, Ph). Mass spectrum: *m/e* 268 (M), 250 (M − 18), and 179 (base peak). The

ıemical shift for H-1 of **15** is similar to that of H-1 of 1,6-anhydro-β-D-hexopyranoses ; 5.24–5.46)[21] or 1,6-anhydro derivatives of 2-azido-2-deoxy-β-D-altropyranose and azido-3-deoxy-β-D-altropyranose (δ 5.36–5.41)[26]. The $J_{2,3}$ value (9 Hz) indicates ıat H-2 and H-3 are *trans*.

Anal. Calc. for $C_{13}H_{16}O_4S$: C, 58.20; H, 6.01. Found: C, 58.19; H, 6.15.

Eluted second was **10** (275 mg, 10.2%). Eluted third was 2-*S*-benzyl-2-thio-D-trose (**16**; 575 mg, 31.3%), which was recrystallised from acetone to afford needles, .p. 120–121°, $[\alpha]_D^{24.5}$ +63°→ −12° (equil., *c* 0.25, methanol); ν_{max}^{KBr} 3380, 3290 (OH), 495, and 700 cm^{-1} (phenyl). P.m.r. data (methyl sulphoxide-d_6): δ 2.94 (m, 1 H, -2), 2.83 (s, 2 H, CH_2-S), 4.90 (d, 1 H, collapsed to singlet on addition of D_2O, 7.5 Hz, H-1), 6.32 (d, 1 H, deuterium exchangeable, *J* 7.5 Hz, HO-1), and 7.32 , 5 H, Ph). Mass spectrum: *m/e* 286 (M) and 91 (base peak).

Anal. Calc. for $C_{13}H_{18}O_5S$: C, 54.54; H, 6.34. Found: C, 54.39; H, 6.21.

Hydrolysis of methyl 3-S-benzyl-4,6-O-benzylidene-3-thio-α-D-altropyranoside **3**). — (*a*) *With Amberlite CG-120(H^+) resin.* A mixture of **13**[7] (97 mg), resin (0.46 g), ıd 80% methanol (10 ml) was stirred for 100 h at 55° and then filtered, and the ltrate was concentrated *in vacuo* to dryness. The residue was eluted from silica el with chloroform–ethyl acetate (1:1) to give syrupy methyl 3-*S*-benzyl-3-thio-α-D-tropyranoside (**14**; 50 mg, 75%), $[\alpha]_D^{25}$ +4° (*c* 1, chloroform); ν_{max}^{film} 3300 (OH), 500, 1415, and 720 cm^{-1} (phenyl).

Anal. Calc. for $C_{14}H_{20}O_5S$: C, 55.99; H, 6.71. Found: C, 55.73; H, 6.80.

Treatment of **14** with benzaldehyde and zinc chloride, in the usual way, gave **13**.

(*b*) *With oxalic acid.* A mixture of **13** (3 g), oxalic acid (9 g), and acetone 150 ml) was boiled under reflux for 30 h, and then cooled, neutralised with barium ırbonate (45 g), and filtered. The filtrate was concentrated *in vacuo* to ~50 ml, the ɔncentrate extracted with ether, the extract concentrated *in vacuo* to dryness, and ıe residue eluted from silica gel with chloroform–ethyl acetate (1:1) to afford **14** .6 g, 70%) as a colourless syrup.

Isomerization of **11** *with Amberlite CG-120(H^+) resin.* — A mixture of **11** 48.5 mg), resin (465 mg), and methanol (15 ml) was stirred for 40 h at 55° and then ltered. The filtrate was concentrated *in vacuo* to dryness, and the residue was eluted om silica gel with chloroform–methanol (9.5:0.5) to give **10** (58 mg, 18%) and **12** 37 mg, 7.4%).

Similar treatment of **12** gave **10** and **11**, identified by t.l.c.

Methyl 2-deoxy-α-D-ribo-hexopyranoside (**17**). — (*a*) A mixture of **9** (5 g) and .aney nickel (W-4, 50 ml) in ethanol (100 ml) was stirred for 5 h at 60°, cooled, and ltered through Celite. The filtrate was concentrated, and the residue was eluted from lica gel with chloroform–methanol (9:1) to give **17** (1.268 g, 55.4%). Recrystallization om hexane gave needles, m.p. 98.5–99°, $[\alpha]_D^{18.5}$ +178° (*c* 0.25, methanol); lit.[27] ı.p. 97–99.5°, $[\alpha]_D$ +183° (*c* 0.52, methanol).

(*b*) Treatment of **10** (30 mg) as in (*a*), but for 1 h, gave **17** (8 mg, 47.0%), ı.p. 98–99°.

Isomerization of **17** *with Amberlite CG-120(H^+) resin.* — A mixture of **17**

(148.5 mg), resin (465 mg), and methanol (15 ml) was stirred for 40 h at 55° and filtered, and the filtrate was concentrated *in vacuo* to dryness. The residue was eluted from silica gel with chloroform–methanol (9:1) to give first **17** (20.7 mg, 13.9%), and then methyl 2-deoxy-β-D-*ribo*-hexofuranoside (**18**; 70 mg, 47.1%). Recrystallization from chloroform gave needles, m.p. 105–109°, $[\alpha]_D^{18.5}$ −74° (*c* 0.25, methanol); lit.[27] m.p. 117–122°, $[\alpha]_D$ −46°. P.m.r. data (methyl sulphoxide-d_6): δ 5.06 (t, 1 H, *J* 4.5 Hz, H-1), 3.25 (s, 3 H, OMe), and 2.00 (t, 2 H, *J* 4.5 Hz, C–CH_2–C); lit.[27] δ 5.03 (t, 1 H, *J* 4 Hz, H-1).

Anal. Calc. for $C_7H_{14}O_5$: C, 47.18; H, 7.92. Found: C, 47.19; H, 7.73.

The furanoid structure of **18** was confirmed by the formation of formaldehyde on oxidation with sodium metaperiodate.

*Hydrolysis of methyl 4,6-*O*-benzylidene-2-*O*-methyl-α-*D*-altropyranoside* (**19**) *with Amberlite CG-120(H^+) resin.* — A mixture of **19**[28] (502.6 mg), resin (2.3 g), and 80% methanol (100 ml) was stirred for 140 h at 55°. The filtered solution was then concentrated *in vacuo* to dryness. Elution of the residue from silica gel with chloroform–methanol (9.5:0.5) gave first methyl 2-*O*-methyl-α-D-altropyranoside (**20**; 317.1 mg, 89.8%). Recrystallisation from ether gave needles, m.p. 84–85°, $[\alpha]_D^{22}$ +98.5° (*c* 0.52, methanol); lit.[28] m.p. 81–83°, $[\alpha]_D$ +111.6° (*c* 0.9, chloroform). P.m.r. data: δ 2.98 (s, 3 H, OH), 3.45 (s, 6 H, OMe), and 4.64 (s, 1 H, H-1).

Anal. Calc. for $C_8H_{16}O_6$: C, 46.15; H, 7.75. Found: C, 46.02; H, 7.87.

Eluted second was syrupy methyl 2-*O*-methyl-αβ-D-altrofuranoside (**21**; 36.9 mg, 10.4%), $[\alpha]_D^{22}$ −82° (*c* 0.49, methanol). P.m.r. data: δ 4.75 (d, *J* 1.5 Hz, H-1) and 4.85 (d, *J* 4.5 Hz, H-1); α/β ratio, 1:1. Oxidation of **21** with sodium metaperiodate gave formaldehyde.

Anal. Calc. for $C_8H_{16}O_6$: C, 46.15; H, 7.75. Found: C, 46.38; H, 7.77.

*Hydrolysis of methyl 4,6-*O*-benzylidene-2-deoxy-2-iodo-α-*D*-altropyranoside* (**22**) *with Amberlite CG-120(H^+) resin.* — A mixture of **22**[29] (1.3 g), resin (3.9 g), and 80% methanol (250 ml) was stirred for 53 h at 55°. The filtered solution was then concentrated *in vacuo* to dryness. The residue was eluted from silica gel with chloroform methanol (4:1) to give first a syrup which contained (t.l.c.) two products. Rechromatography on silica gel with chloroform–methanol (9.5:0.5) gave first methyl 2-deoxy-2-iodo-α-D-altropyranoside (**23**; 210.9 mg, 20.9%). Recrystallisation from chloroform gave needles, m.p. 107–108°, $[\alpha]_D^{22}$ +41° (*c* 0.51, methanol).

Anal. Calc. for $C_7H_{13}IO_5$: C, 27.65; H, 4.31. Found: C, 27.67; H, 4.25.

Eluted second was syrupy methyl 2-deoxy-2-iodo-αβ-D-altrofuranoside (**24**; 290.9 mg, 28.9%), $[\alpha]_D^{22}$ −7° (*c* 0.63, methanol). P.m.r. data (pyridine-d_5): δ 5.30 (d, *J* 7.5 Hz, H-1) and 5.52 (d, *J* 3.0 Hz, H-1); α/β ratio, ~1:1. Oxidation of **24** with sodium metaperiodate gave formaldehyde.

Anal. Calc. for $C_7H_{13}IO_5$: C, 27.65; H, 4.31. Found: C, 27.36; H, 4.44.

Eluted second in the first chromatography was 2-deoxy-2-iodo-D-altrose (**25**; 79.5 mg, 8.3%). Recrystallisation from acetone–light petroleum gave needles, m.p. 85°, $[\alpha]_D^{22}$ −15° → +13° (24 h, *c* 0.53, methanol). P.m.r. data: δ 5.96 (d, 1 H, *J* 8.5 Hz, H-1).

Anal. Calc. for $C_6H_{11}IO_5 \cdot H_2O$: C, 23.39; H, 4.23. Found: C, 23.74; H, 4.03. After reaction for 2 h, only **23** was obtained (58.9%).

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