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SYNTHESIS OF 1,6-THIOANHYDRO-D-GLUCITOL*

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ABSTRACT

Treatment of 2,4-*O*-benzylidene-1,6-di-*O*-tosyl-D-glucitol (**1**) with potassium thiolbenzoate afforded the 6-*S*-benzoyl compound **2** and its 5-benzoate **4**, the structure of which was proved chemically. When **1** was acetylated and then treated with the thiolate, the acetylated 6-*S*-benzoyl compound **19** was obtained in good yield in addition to some 1,6-di-*S*-benzoyl derivative **21**. Treatment of **19** with acetic anhydride–acetic acid–sulfuric acid afforded 2,3,4,5-tetra-*O*-acetyl-6-*S*-acetyl-1-*O*-tosyl-D-glucitol (**26**), which was converted by sodium methoxide into a mixture of 1,5-anhydro-6-thio-D-glucitol (**28**) and 1,6-thioanhydro-D-glucitol (**29**). These two compounds were isolated as their acetates (**30** and **31**) by column chromatography, or by converting **28** into its *S*-trityl derivative (**32**).

INTRODUCTION

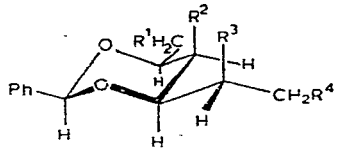
The interesting biological properties of 2,5-anhydro-3,4-di-*O*-methanesulphonyl 1,6-thioanhydro-D-glucitol[1,2] led us to initiate a study of the structure–activity relationships in this type of hexitol derivative. In order to study the role of the 2,5-anhydro bridge, the synthesis of 1,6-thioanhydro-D-glucitol was undertaken.

RESULTS AND DISCUSSION

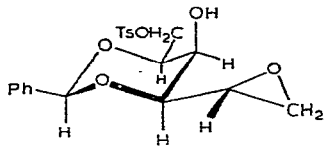
When the readily available[3] 2,4-*O*-benzylidene-1,6-di-*O*-tosyl-D-glucitol (**1**) was treated with 1 equivalent of potassium thiolbenzoate, one of the tosyloxy groups was replaced by an *S*-benzoyl group. However, in addition to compound **2**, which could be isolated in relatively low yields only, a mono-*O*-benzoyl derivative was also formed.

This by-product arises from the reaction of **1** or **2** with benzoic acid formed by oxidation of liberated benzaldehyde. The amount of the *O*-benzoyl derivative

*1,6-Thioanhydrohexitols: Part VI. Parts I–V of this series had the general title "Hexitol derivatives containing a 1,4-oxathiane ring". Part V: J. Kuszmann and P. Sohár, *Acta Chim. (Budapest)*, in press.



1 $R^1 = R^4 = OTs, R^2 = R^3 = OH$
2 $R^1 = OTs, R^2 = R^3 = OH, R^4 = SBz$
3 $R^1 = OTs, R^2 = OBz, R^3 = OH, R^4 = SBz$
4 $R^1 = OTs, R^2 = OH, R^3 = OBz, R^4 = SBz$
5 $R^1 = OTs, R^2 = OAc, R^3 = OBz, R^4 = SBz$
6 $R^1 = OTs, R^2 = R^3 = OBz, R^4 = SBz$
7 $R^1 = OTs, R^2 = OMs, R^3 = OBz, R^4 = SBz$
8 $R^1 = OTs, R^2 = OMs, R^3 = OH, R^4 = SH$
9 $R^1 = OTs, R^2 = OMs, R^3 = OH, R^4 = S—/_2$
10 $R^1 = OTs, R^2 = OMs, R^3 = OAc, R^4 = SAc$
11 $R^1 = OTs, R^2 = OMs, R^3 = OAc, R^4 = S—/_2$
12 $R^1 = OTs, R^2 = R^3 = OMs, R^4 = SBz$
17 $R^1 = OTs, R^2 = R^3 = OH, R^4 = Br$
18 $R^1 = OTs, R^2 = R^3 = OAc, R^4 = Br$
19 $R^1 = OTs, R^2 = R^3 = OAc, R^4 = SBz$
20 $R^1 = R^4 = OTs, R^2 = R^3 = OAc$
21 $R^1 = R^4 = SBz, R^2 = R^3 = OAc$
22 $R^1 = R^4 = SH, R^2 = R^3 = OH$
23 $R^1 = R^4 = SAc, R^2 = R^3 = OAc$
24 $R^1 = OTs, R^2 = R^3 = OAc, R^4 = SAc$
25 $R^1 = OTs, R^2 = R^3 = OH, R^4 = S—/_2$



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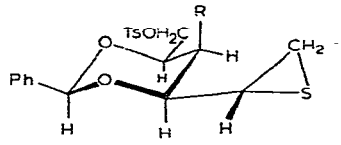
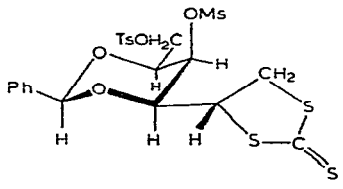


13 R = OMs
15 R = OH



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increased with prolongation of the reaction time, especially at elevated temperatures. When pyridine was used as the reaction solvent, formation of the *O*-benzoyl derivative was substantially diminished. Theoretically, the benzoyl group could be situated at O-3 or O-5 (**3** or **4**), and therefore the compound was separately acetylated, benzoylated, and mesylated. However, the n.m.r. data (Table I) of the mixed esters (**5**, **6**, and **7**) provided no further evidence of the presumed structures, When the mesyl derivative **7** was treated with 1 equiv. of sodium methoxide, the mesyloxy group remained intact and, depending on the duration of the treatment, either the thiol **8** or the corresponding disulfide **9** could be isolated. The n.m.r. spectra of the acetylated derivatives (**10** and **11**) of **8** and **9** proved the presence of the *O*-mesyl, *O*-acetyl, and *S*-acetyl groups, as well as the absence of an epithio group, which should be formed from a 3-*O*-benzoyl-5-*O*-mesyl derivative (derived from **3**). Consequently, the mesyl group in **7** is located at O-3 and the benzoyl group at O-5.

The ready formation of a 5,6-epithio group from a 5-*O*-mesyl compound was also demonstrated. Thus, the di-*O*-mesyl derivative **12**, obtained on mesylation of **2**, gave 2,4-*O*-benzylidene-5,6-epithio-3-*O*-mesyl-1-*O*-tosyl-L-iditol (**13**) on treatment with sodium methoxide. The structure of **13** was proved chemically by converting the known 5,6-epoxide[3] (**14**) with thiourea into the 5,6-epithio compound **15** (inversion at C-5), which on mesylation afforded **13**. The epithio derivative **13** could be converted

TABLE I

P.M.R. DATA[a] FOR 2,4-*O*-BENZYLIDENE DERIVATIVES **2**, **4–13**, **15–17**, AND **19–25**

Compound	*Acetyl Me*	*Tosyl Me*	*Mesyl Me*	*PhCH*	*Other protons*
2	—	2.40	—	5.55	OH: 4.85d (8 Hz) and 5.35d (6 Hz)[b]
4	—	2.35	—	5.65	—
5	2.00	2.30	—	5.68	—
6	—	2.28	—	5.75	—
7	—	2.30	3.00	5.70	—
8	—	2.40	3.15	5.60	SH: 1.55t (9 Hz)
9	—	2.43	3.12	5.60	—
10	2.05	2.45	3.10	5.70	SAc: 2.35
11	2.05	2.50	3.35	5.90	—
12	—	2.50	3.25 3.35	5.90	—
13	—	2.45	3.20	5.65	epithio CH_2 2.2–2.8, CH 3.4
15	—	2.45	—	5.60	epithio CH_2 2.2–2.8, CH 3.4
16	—	2.45	3.20	5.75	—
17	—	2.40	—	5.55	OH: 4.77d (8 Hz) and 5.25d (5 Hz)[b]
19	1.98 2.02	2.38	—	5.60	—
20	2.00[c]	2.37 2.42	—	5.58	—
21	1.98 2.12	—	—	5.65	—
22	—	—	—	5.60	OH: 4.58d (8 Hz) and 5.10d (5 Hz)[b]
23	2.02 2.12	—	—	5.63	SAc: 2.35[c]
24	1.98 2.02	2.40	—	5.60	SAc: 2.33
25[d]	—	2.38	—	5.55	

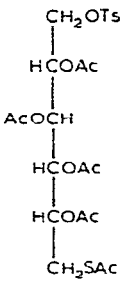
[a] δ scale. [b] $(CD_3)_2SO$. [c] Intensity, 6H. [d] Acetone-d_6.

smoothly into the cyclic trithiocarbonate **16** on treatment with carbon disulfide and potassium hydroxide in methanol.

As large-scale separation of the 6-*S*-benzoyl compound **2** from its 5-*O*-benzoyl derivative was difficult, another synthetic approach was investigated. The epoxide[3] **14**, when treated in acetone with aqueous hydrogen bromide, yielded the 6-bromo-6-deoxy derivative **17**, and the acetate (**18**) of **17** was converted into the 6-*S*-benzoyl ester **19**. As acetylation of **2** also yielded **19**, the location of the *S*-benzoyl group at C-6 was established. However, the overall yield of conversion **1**→**14**→**17**→**18**→**19** was not satisfactory, and therefore a third variation was worked-out.

When the di-*O*-tosyl derivative **1** was acetylated (to give **20**) and then treated with potassium thiolbenzoate, the desired 6-*S*-benzoyl compound **19** was formed, together with the 1,6-di-*S*-benzoyl ester **21**, which could be isolated easily by recrystallization. Treatment of **21** with sodium methoxide afforded the 1,6-dithiol **22**, which gave **23** on acetylation.

In order to generate the 1,6-thioanhydro structure, **19** was treated with sodium methoxide. When the reaction was interrupted after several minutes, the 6-thiol was obtained, which was characterised as its triacetate **24**. Prolongation of the reaction time afforded the disulphide **25**, whereas decomposition occurred at elevated temperatures. The presence of the 2,4-*O*-benzylidene group prevents the attack of the thiolate anion on the equatorially oriented C-1. The *O*-benzylidene group was therefore removed by treating compound **19** with acetic anhydride–acetic acid–sulfuric acid. Under these conditions, however, not only was the *O*-benzylidene group replaced by *O*-acetyl groups, but simultaneously the *S*-benzoyl ester was changed into an *S*-acetyl derivative (**26**). 2,3,4,5-Tetra-*O*-acetyl-6-*S*-acetyl-1-*O*-tosyl-D-glucitol (**26**) was also obtained when the *S*-acetyl derivative **24** was submitted to acetolysis.



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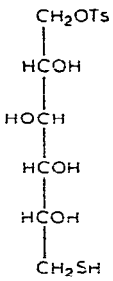

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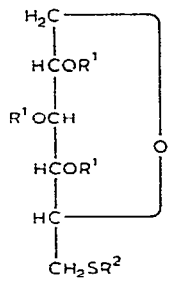
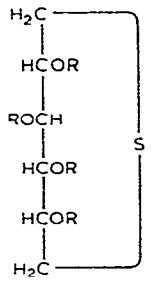


28 $R^1 = R^2 = H$
30 $R^1 = R^2 = OAc$
32 $R^1 = H$, $R^2 = Tr$
33 $R^1 = Ac$, $R^2 = Tr$



29 R = H
31 R = Ac

Treatment of **26** in chloroform with an excess of sodium methoxide gave **28** and **29**, which could not be fractionated by column chromatography. After acetylation of **28** and **29**, 2,3,4-tri-*O*-acetyl-6-*S*-acetyl-1,5-anhydro-6-thio-D-glucitol (**30**) and 2,3,4,5-tetra-*O*-acetyl-1,6-thioanhydro-D-glucitol (**31**) could be isolated by chromatography, and deacetylation then gave the thiol **28** and the 1,6-thioanhydro derivative (**29**), respectively. The tedious chromatographic fractionations could be avoided by deacetylation and tritylation of the crude mixture of **30** and **31**. The resulting 6-*S*-trityl derivative **32**, as well as methyl trityl ether, could then be extracted with ether from the evaporated mixture after addition of water, whereas the 1,6-thioanhydride **29** remained in the aqueous phase and could be recrystallized after evaporation. The 6-*S*-trityl compound **32** was freed from methyl trityl ether by treatment with methanol/HCl and subsequent column chromatography. Acetylation of **32** afforded the triacetate **33**, but attempted mesylation of **32** was unsuccessful.

To optimise the yield of 1,6-thioanhydro-D-glucitol (**29**), the reaction of **26** with sodium methoxide was investigated thoroughly. The ratio of **30** and **31**, formed after acetylation of the crude reaction mixture, was determined by g.l.c. It was found that at least 1.5 equiv. of sodium methoxide were needed for complete reaction, as the

thiol **28** also consumes methoxide. As a further increase in the proportion of base did not influence the yield, 2 equiv. were used in subsequent experiments. When the reaction was conducted at low temperatures (−40°), only deacetylation occurred, and **27** was probably formed as intermediate. This assumption is backed by t.l.c. data: the spot (R_F 0.95, solvent *G*) for **26** disappeared and a new spot (R_F 0.80) appeared, which could still be detected with 4-(*p*-nitrobenzyl)pyridine[4]. A 1,2-epoxide, which would also react with this reagent, could similarly lead to the formation of **28** and **29**. However, as no precipitation of sodium tosylate occurred at this low temperature, **27** is considered to be the intermediate. When the temperature was raised to −5°, precipitation of sodium tosylate started and **28** and **29** were formed (t.l.c.) in a ratio of ~3:7. With reaction temperatures above −5°, this ratio was shifted towards the 1,5-anhydride **28**, and a ratio of 1:1 was obtained at the boiling point (~70°) of the reaction mixture. Prolongation of the reaction time decreased the yield of **28**, probably because of oxidation to the corresponding disulphide.

EXPERIMENTAL

General methods. — Melting points are uncorrected. T.l.c. was performed on Kieselgel G with ethyl acetate (*A*), ethyl acetate–carbon tetrachloride 1:1 (*B*), 1:2 (*C*), 1:3 (*D*), 1:5 (*E*), ethanol–ethyl acetate 1:5 (*F*), and ethanol–ethyl acetate 1:9 (*G*). Detection was effected with 0.1M potassium permanganate–M sulphuric acid (1:1) at 105°, or 4-(*p*-nitrobenzyl)pyridine followed by 2M sodium hydroxide and heating at 105°. Column chromatography was performed on silicic acid, using the same solvent systems as for t.l.c. unless stated otherwise.

N.m.r. spectra (60 MHz) were recorded at room temperature for $CDCl_3$ solutions (internal Me_4Si) with a JEOL 60-HL spectrometer. I.r. spectra were recorded for KBr pellets with a Perkin–Elmer 577 spectrometer. The i.r. spectra of compounds (**2**, **4–13**, **15–17**, **19**, **20**, **24**, and **25**) containing mesyl or tosyl groups showed bands at 1370–1335 (ν_{as} SO_2), 1210–1170 (ν_s SO_2), 1000–970 (ν SO), and 600–500 cm^{-1} (δ SO_2).

G.l.c. was performed on a Perkin–Elmer F-21 instrument with a U-shaped glass column (4 mm × 2 m), packed with 5% of QF-1 on 80/100-mesh Gas Chrom Q. Temperatures: inlet 220°, column 200°; carrier gas: nitrogen, 45 ml/sec.

Acetylation was carried out with acetic anhydride (2.5 equiv. for each OH and/or SH group) in pyridine (4 ml/ml of acetic anhydride).

Reaction mixtures containing sodium methoxide were neutralized with solid carbon dioxide. All evaporations were carried out with a rotary evaporator under diminished pressure, after drying of organic solutions over sodium sulphate. Light petroleum refers to the fraction having b.p. 60–80°. Optical rotations were determined in chloroform (*c* 1) unless otherwise stated.

6-S-Benzoyl-2,4-O-benzylidene-6-thio-1-O-p-tolylsulphonyl-D-glucitol (**2**). — A solution of compound **1**[3] (5.8 g) in dry acetone (100 ml) was treated with pyridine (1 ml) and potassium thiolbenzoate (2 g). After being kept at room temperature for

24 h, the slurry was heated on a steam bath for 1 h and then evaporated. The residue was partitioned between chloroform and water, the organic solution was washed with 0.5M sulfuric acid, water, and 5% aqueous sodium hydrogen carbonate, dried, and evaporated. The residue was recrystallized first from ethanol and then from acetone–light petroleum to give **2** (2.35 g, 43%), m.p. 159–160°, $[\alpha]_D^{20}$ +39°, R_F 0.65 (*B*); ν_{max}^{KBr} 3555 (OH) and 1645 cm^{-1} (*S*-benzoyl) (Found: C, 59.55; H, 5.30; S, 11.97. $C_{27}H_{28}O_8S_2$ calc.: C, 59.53; H, 5.18; S, 11.78%).

5-O-Benzoyl-6-S-benzoyl-2,4-O-benzylidene-6-thio-1-O-p-tolylsulphonyl-D-glucitol (**4**). — A solution of **1** (58 g) and potassium thiolbenzoate (18 g) in dry acetone (1 litre) was boiled for 8 h. The residue obtained after evaporation was partitioned between chloroform and water. The organic solution was washed with water, dried, and evaporated. The residue was recrystallized first from ethanol, then from ethyl acetate–carbon tetrachloride, and then twice from ethyl acetate to give **4** (4.5 g, 6.95%), m.p. 152–153°, $[\alpha]_D^{20}$ +28°, R_F 0.90 (*B*), 0.35 (*E*); ν_{max}^{KBr} 3560 (OH), 1720 (benzoyl), and 1655 cm^{-1} (*S*-benzoyl) (Found: C, 63.13; H, 5.05; S, 10.08. $C_{34}H_{32}O_9S_2$ calc.: C, 62.94; H, 4.97; S, 9.88%).

Acetylation of **4** (0.65 g) afforded **5** (0.6 g, 86.8%), m.p. 72–75°, $[\alpha]_D^{20}$ 0°, R_F 0.5 (*E*); ν_{max}^{KBr} 1740 (acetyl), 1720 (benzoyl), 1665 cm^{-1} (*S*-benzoyl) (Found: C, 62.66; H, 4.89; S, 9.22. $C_{36}H_{34}O_{10}S_2$ calc.: C, 62.60; H, 4.96; S, 9.29%).

3,5-Di-O-benzoyl-6-S-benzoyl-2,4-O-benzylidene-6-thio-1-O-p-tolylsulphonyl-D-glucitol (**6**). — A solution of **4** (0.65 g) in pyridine (3 ml) was treated with benzoyl chloride (0.3 ml) to give, after the usual work-up, **6** as a solid foam (0.7 g, 93.5%), $[\alpha]_D^{20}$ −60°, R_F 0.45 (*E*); ν_{max}^{KBr} 1725 (benzoyl) and 1665 cm^{-1} (*S*-benzoyl) (Found: C, 65.16; H, 4.79; S, 8.40. $C_{41}H_{36}O_{10}S_2$ calc.: C, 65.41; H, 4.82; S, 8.52%).

5-O-Benzoyl-6-S-benzoyl-2,4-O-benzylidene-3-O-methanesulphonyl-6-thio-1-O-p-tolylsulphonyl-D-glucitol (**7**). — A solution of **4** (0.65 g) in pyridine (3 ml) was treated with mesyl chloride (0.2 ml) to give, after the usual work-up, crude **7** (0.7 g, 96%), m.p. 78–85° (the m.p. did not alter on recrystallization from ethanol–water), $[\alpha]_D^{20}$ −7°, R_F 0.70 (*C*); ν_{max}^{KBr} 1725 (benzoyl) and 1665 cm^{-1} (*S*-benzoyl) (Found: C, 57.76; H, 4.78; S, 13.13. $C_{35}H_{34}O_{11}S_3$ calc.: C, 57.87; H, 4.72; S, 13.23%).

2,4-O-Benzylidene-3-O-methanesulphonyl-6-thio-1-O-p-tolylsulphonyl-D-glucitol (**8**) *and its 6,6'-disulphide* (**9**). — A solution of crude **7** (3.5 g) in dry chloroform (15 ml) was treated with a solution of 2M methanolic sodium methoxide (2.5 ml) at room temperature. The reaction mixture was neutralized after 10 min, washed with water, dried, and evaporated. A solution of the residue in carbon tetrachloride was treated with light petroleum, and the turbid solution was filtered through charcoal and evaporated to give **9** as a solid foam (1.7 g, 68%), m.p. 45–55°, $[\alpha]_D^{20}$ +7°, R_F 0.60 (*B*); ν_{max}^{KBr} 3520 (OH) and 2580 cm^{-1} (SH) (Found: C, 48.82; H, 5.21; S, 18.35. $C_{21}H_{26}O_9S_3$ calc.: C, 48.63; H, 5.05; S, 18.55%).

When a second reaction mixture was neutralized after 48 h, the disulphide **9** was obtained after column chromatography (solvent *B*) as a solid foam (1.3 g, 52%), m.p. 55–65°, $[\alpha]_D^{20}$ +9°, R_F 0.35 (*B*); ν_{max}^{KBr} 3520 cm^{-1} (OH), no SH band (Found: C, 48.89; H, 5.00; S, 19.31. $C_{42}H_{50}O_{18}S_6$ calc.: C, 48.73; H, 4.87; S, 18.58%).

Acetylation of thiol **8** (1.2 g) gave, after recrystallization from ethyl acetate–ether, **10** (0.9 g, 64.5%), m.p. 182–184°, $[\alpha]_D^{20}$ +8°, R_F 0.75 (*B*); ν_{max}^{KBr} 1735 (acetyl) and 1685 cm^{-1} (*S*-acetyl) (Found: C, 50.02; H, 5.31; S, 15.74. $C_{25}H_{30}O_{11}S_3$ calc.: C, 49.82; H, 5.02; S, 15.96%).

Acetylation of the disulphide **9** (1.2 g) afforded **11** (1.1 g, 84.5%), m.p. 190° (dec.), $[\alpha]_D^{20}$ +10°, R_F 0.45 (*B*); ν_{max}^{KBr} 1740 cm^{-1} (acetyl), no *S*-acetyl band (Found: C, 49.30; H, 4.68; S, 17.07. $C_{46}H_{54}O_{20}S_6$ calc.: C, 49.36; H, 4.86; S, 17.19%).

6-S-Benzyol-2,4-O-benzylidene-3,5-di-O-methanesulphonyl-1-O-p-tolylsulphonyl-D-glucitol (**12**). — A solution of **2** (2.75 g) in pyridine (10 ml) was treated with mesyl chloride (1.2 g) to give, after the usual work-up, a product (3.5 g) which could be recrystallized from ethyl acetate–light petroleum to give **12** (3 g, 85.5%), m.p. 155–157°, $[\alpha]_D^{20}$ +9°, R_F 0.30 (*C*); ν_{max}^{KBr} 1660 cm^{-1} (*S*-benzoyl) (Found: C, 49.72; H, 4.68; S, 18.10. $C_{29}H_{32}O_{12}S_9$ calc.: C, 49.70; H, 4.60; S, 18.30%).

2,4-O-Benzylidene-5,6-epithio-3-O-methanesulphonyl-1-O-p-tolylsulphonyl-L-iditol (**13**). — (*a*) A solution of **12** (0.7 g) in chloroform (10 ml) was treated with a solution of M methanolic sodium methoxide (1.1 ml), kept at room temperature for 24 h, and then evaporated. A solution of the residue in chloroform was washed with water, dried, and evaporated. The residue was recrystallized first from methanol–ether and then from ethyl acetate–ether to give **13** (0.27 g, 54%), m.p. 155–156°, $[\alpha]_D^{20}$ +36°, R_F 0.65 (*C*) (Found: C, 50.53; H, 4.85; S, 19.30. $C_{21}H_{24}O_8S_3$ calc.: C, 50.38; H, 4.83; S, 19.21%).

(*b*) A solution of **15** (8.4 g) in pyridine (30 ml) was treated with mesyl chloride (2 ml) to give, after the usual work-up and recrystallization from ethyl acetate–ether, **13** (6.4 g, 64%) identical with that described in (*a*).

2,4-O-Benzylidene-5,6-epithio-1-O-p-tolylsulphonyl-L-iditol (**15**). — To a stirred solution of epoxide **14** (2 g) in acetone (10 ml), thiourea (0.6 g) was added. After 5 min, a solid started to separate, which redissolved after 2 h of stirring. The solution was kept for 3 days at room temperature, while urea crystallized out in fine needles and the starting material (R_F 0.70) was completely consumed. The filtered solution was evaporated, and the residue was partitioned between chloroform and water. The organic solution was washed with water, dried, and evaporated to give, after recrystallization from methanol, **15** (1.7 g, 81%), m.p. 158–160°, $[\alpha]_D^{20}$ +47°, R_F 0.85 (*C*); ν_{max}^{KBr} 3560 (OH) and 3480 cm^{-1} (OH assoc.) (Found: C, 56.92; H, 5.33; S, 15.12. $C_{20}H_{22}O_6S_2$ calc.: C, 56.85; H, 5.25; S, 15.18%).

2,4-O-Benzylidene-3-O-methanesulphonyl-5,6-dithio-1-O-p-tolylsulphonyl-L-iditol 5,6-trithiocarbonate (**16**). — To a solution of potassium hydroxide (0.66 g) and carbon disulphide (0.95 ml) in methanol (20 ml), compound **13** (2.5 g) was added and the reaction mixture was boiled until complete dissolution occurred. On cooling, yellow crystals deposited, and these were filtered off after 24 h and washed with methanol to give **16** (1.9 g, 65.5%), m.p. 145–148°, $[\alpha]_D^{20}$ +128° (Found: C, 45.96; H, 4.31; S, 27.82. $C_{22}H_{24}O_8S_5$ calc.: C, 45.81; H, 4.19; S, 27.80%).

2,4-O-Benzylidene-6-bromo-6-deoxy-1-O-p-tolylsulphonyl-D-glucitol (**17**). — A solution of epoxide[3] **14** (20.3 g) in acetone (250 ml) was treated with 48% aqueous

hydrobromic acid (7 ml). The resulting slurry was neutralized after 1 h at room temperature with 5% aqueous sodium hydrogen carbonate. The solid material was filtered off, washed with water, and recrystallized from acetone to give **17** (15.5 g, 63.5%), m.p. 154–155°, $[\alpha]_D^{20}$ −6°, R_F 0.60 (*B*) (Found: C, 49.25; H, 4.79; Br, 16.53; S, 6.53. $C_{20}H_{23}BrO_7S$ calc.: C, 49.29; H, 4.76; Br, 16.40; S, 6.58%).

Acetylation of **17** (4.9 g) afforded, after recrystallization from methanol, **18** (4.2 g, 73.5%), m.p. 113–114°, $[\alpha]_D^{20}$ −6°, R_F 0.50 (*E*) (Found: C, 50.39; H, 4.80; Br, 14.14; S, 5.69. $C_{24}H_{27}BrO_9S$ calc.: C, 50.44; H, 4.76; Br, 13.98; S, 5.51%).

*3,5-Di-*O*-acetyl-6-*S*-benzoyl-2,4-*O*-benzylidene-1-*O*-*p*-tolylsulphonyl-*D*-glucitol* (**19**). — A solution of potassium thiolbenzoate (10.5 g) and the ditosyl ester **20** (33.1 g) or the bromo compound **18** (28.5 g) in acetone (350 ml) was kept for 5 days at room temperature. The resulting slurry was boiled and then evaporated. The residue was partitioned between chloroform and water, and the organic solution was washed with water, dried, and evaporated. The residue was recrystallized from ethanol to give **19** (20.7 g, 66%), m.p. 133–135°, $[\alpha]_D^{20}$ +18°, R_F 0.65 (*D*); ν_{max}^{KBr} 1740 (acetyl) and 1680 cm^{-1} (*S*-benzoyl) (Found: C, 59.23; H, 5.29; S, 10.15. $C_{31}H_{32}O_{10}S_2$ calc.: C, 59.22; H, 5.13; S, 10.20%).

Compound **19** (4.3 g, 68.5%) was also obtained on acetylation of **2** (5.4 g).

*3,5-Di-*O*-acetyl-2,4-*O*-benzylidene-1,6-di-*O*-*p*-tolylsulphonyl-*D*-glucitol* (**20**). — Acetylation of **1** (57.8 g) gave, after recrystallization from ethanol, 20 (58.5 g, 88%), m.p. 138–140°, $[\alpha]_D^{20}$ 0°, R_F 0.55 (*D*); ν_{max}^{KBr} 1740 cm^{-1} (acetyl) (Found: C, 56.26; H, 4.87; S, 9.73. $C_{31}H_{34}O_{12}S_2$ calc.: C, 56.18; H, 5.17; S, 9.68%).

*3,5-Di-*O*-acetyl-1,6-di-*S*-benzoyl-2,4-*O*-benzylidene-*D*-glucitol* (**21**). — The ethanolic mother liquor of compound **19** was evaporated, the residue was dissolved in acetone (150 ml), and potassium thiolbenzoate (5 g) was added. The mixture was boiled for 16 h and was then worked-up as described for **19**. The product was recrystallized from ethanol and then from carbon tetrachloride–light petroleum to give **21** (5.9 g, 20%), m.p. 123–124°, $[\alpha]_D^{20}$ −12°, R_F 0.85 (*D*); ν_{max}^{KBr} 1740 (acetyl), 1675 and 1655 cm^{-1} (*S*-benzoyl) (Found: C, 62.74; H, 5.14; S, 10.75. $C_{31}H_{30}O_8S_2$ calc.: C, 62.61; H, 5.09; S, 10.78%).

*2,4-*O*-Benzylidene-1,6-dithio-*D*-glucitol* (**22**). — A solution of **21** (6 g) in chloroform (30 ml) was treated with 2M methanolic sodium methoxide (11 ml). The reaction mixture was neutralized after 15 min, washed with water, dried, and evaporated. The residue was treated with boiling acetone (15 ml), the filtered extract was concentrated to 5 ml, and light petroleum (5 ml) was added to give **22** (2.5 g, 83%), m.p. 136–138°, $[\alpha]_D^{20}$ +23° (acetone), R_F 0.60 (*B*); ν_{max}^{KBr} 3600–3000 (OH) and 2460 cm^{-1} (SH) (Found: C, 51.81; H, 6.18; S, 21.14. $C_{13}H_{18}O_4S_2$ calc.: C, 51.63; H, 6.00; S, 21.21%).

Acetylation of **22** gave a syrup, which was purified by column chromatography (solvent *E*). Recrystallization from ether–light petroleum afforded **23** (1.25 g, 33.4%), m.p. 114–116°, $[\alpha]_D^{20}$ −26°, R_F 0.50 (*E*); ν_{max}^{KBr} 1738 (acetyl) and 1688 cm^{-1} (*S*-acetyl) (Found: C, 53.47; H, 5.32; S, 13.48. $C_{21}H_{26}O_8S_2$ calc.: C, 53.60; H, 5.57; S, 13.63%).

*3,5-Di-*O*-acetyl-6-*S*-acetyl-2,4-*O*-benzylidene-1-*O*-*p*-tolylsulphonyl-*D*-glucitol*

(24). — A solution of **19** (1.26 g) in chloroform (20 ml) was treated with 4M methanolic sodium methoxide (0.5 ml). After 15 min, acetic anhydride (5 ml) and pyridine (5 ml) were added. The mixture was worked-up after 2 days to give, after recrystallization from methanol, **24** (0.4 g, 35.4%), m.p. 133–135°, $[\alpha]_D^{20}$ +21°, R_F 0.70 (*D*); ν_{max}^{KBr} 1740 (acetyl) and 1685 cm^{-1} (*S*-acetyl) (Found: C, 55.32; H, 5.13; S, 11.22. $C_{26}H_{30}O_{10}S_2$ calc.: C, 55.11; H, 5.34; S, 11.32%).

2,4-O-Benzylidene-6-thio-1-O-p-tolylsulphonyl-D-glucitol 6,6'-disulphide (**25**). — A solution of **19** (0.63 g) in chloroform (10 ml) was treated with a solution of M methanolic sodium methoxide (1.1 ml) for 24 h, then neutralized, washed with water, dried, and evaporated. The residue was recrystallized from acetone–light petroleum to give **25** (0.3 g, 68.4%), m.p. 130–132°, $[\alpha]_D^{20}$ +16° (acetone); ν_{max}^{KBr} 3600–3000 cm^{-1} (OH), no SH band (Found: C, 54.88; H, 5.52; S, 14.31. $C_{40}H_{46}O_{14}S_4$ calc.: C, 54.65; H, 5.28; S, 14.58%).

2,3,4,5-Tetra-O-acetyl-6-S-acetyl-1-O-p-tolylsulphonyl-D-glucitol (**26**). — Compound **19** (75 g) was dissolved in a mixture of acetic anhydride (375 ml), acetic acid (115 ml), and conc. sulphuric acid (10 ml). After being kept at room temperature for 15 h, the reaction mixture was slowly added to a vigorously stirred slurry of sodium hydrogen carbonate (1200 g) in water (4.5 l). The slurry was filtered, the solid material was thoroughly washed with chloroform, and the filtrate was also extracted with chloroform. The combined organic solutions were washed with water, dried, and evaporated. The residue gave, on recrystallization from methanol, **26** (41 g, 62.5%), m.p. 123–125°, $[\alpha]_D^{20}$ +38°, R_F 0.50 (*C*); ν_{max}^{KBr} 1765, 1740 (acetyl), and 1680 cm^{-1} (*S*-acetyl). N.m.r. data: δ 2.00, 2.03, 2.11 (12H, acetyl), 2.32 (*S*-acetyl), 2.45 (tosyl Me) (Found: C, 49.16; H, 5.22; S, 11.28. $C_{23}H_{30}O_{12}S_2$ calc.: C, 49.10; H, 5.36; S, 11.40%).

2,3,4-Tri-O-acetyl-6-S-acetyl-1,5-anhydro-6-thio-D-glucitol (**30**) *and 2,3,4,5-tetra-O-acetyl-1,6-thioanhydro-D-glucitol* (**31**). — A solution of **26** (5.6 g) in chloroform (100 ml) and methanol (50 ml) was treated at 0° with a solution of 4M methanolic sodium methoxide (5 ml). The reaction mixture was kept at 0° for 1 h and then at room temperature for 2 h. After neutralization, the mixture was evaporated, chloroform was distilled from the residue, and then pyridine (15 ml) and acetic anhydride (10 ml) were added. The usual work-up gave a syrup that contained (g.l.c.) **30** and **31** in a ratio of 3:7; retention times, 15 and 19 min, respectively. Fractionation of this mixture by column chromatography (solvent *C*) gave first **30** (1 g, 28.7%) as a syrup, $[\alpha]_D^{20}$ +60°, R_F 0.60 (*D*); ν_{max}^{KBr} 1750 (acetyl) and 1690 cm^{-1} (*S*-acetyl). N.m.r. data: δ 1.95, 2.05, 2.08 (9H, acetyl), 2.33 (*S*-acetyl). Eluted second was **31** (1.7 g, 48.8%), m.p. 76–78° (from methanol-water), $[\alpha]_D^{20}$ −4°, R_F 0.50 (*D*); ν_{max}^{KBr} 1740 (acetyl), 1230, 1030 cm^{-1} (ester). N.m.r. data: δ 2.10 (12H, acetyl), ~2.9 (4H, m, H-1,6), ~5.3 (4H, m, H-2,3,4,5) (Found for **30**: C, 48.45; H, 5.97; S, 9.27; for **31**: C, 48.40; H, 5.88; S, 9.32. $C_{14}H_{20}O_8S$ calc.: C, 48.27; H, 5.79; S, 9.21%).

1,6-Thioanhydro-D-glucitol (**29**) *and 1,5-anhydro-6-thio-6-S-trityl-D-glucitol* (**32**). — The crude, syrupy mixture of **30** and **31**, obtained from **26** (28 g), was dissolved in methanol (300 ml), and the solution evaporated to 250 ml. 4M Methanolic sodium

methoxide (13.5 ml) was added at room temperature, followed after 15 min by trityl chloride (15 g). The reaction mixture was evaporated after 2 days, and the residue was partitioned between water and ether. Evaporation of the aqueous solution afforded a crude product (3.9 g) which was recrystallized from ethanol to give **29** (3.1 g, 34.4%), m.p. 130–131°, $[\alpha]_D^{20}$ −38° (methanol), R_F 0.30 (*F*) (Found: C, 40.17; H, 6.75; S, 17.82. $C_6H_{12}O_4S$ calc.: C, 39.98; H, 6.71; S, 17.79%).

Compound **29** was also obtained on deacetylation of **31** with sodium methoxide.

The ether solution obtained above was evaporated, the residue was triturated with 3% methanolic hydrogen chloride, and the precipitated methyl trityl ether was filtered off. The filtrate was neutralized with solid sodium hydrogen carbonate and then evaporated. The residue was purified by column chromatography (solvent *A*). Evaporation of the fractions containing the component of R_F 0.5, with recrystallization of the residue from ethyl acetate–ether, gave **32** (2.4 g, 11.5%), m.p. 157–158°, $[\alpha]_D^{20}$ −7°, R_F 0.50 (*A*) (Found: C, 71.23; H, 6.45; S, 7.61. $C_{25}H_{26}O_4S$ calc.: C, 71.06; H, 6.20; S, 7.59%).

Acetylation of **32** (0.8 g) afforded **33** (1.0 g, 91%) as a colorless syrup, $[\alpha]_D^{20}$ −4°, R_F 0.30 (*E*); ν_{max}^{KBr} 1750 (acetyl), 1590, 1485, 1445, 760, 750, 710, and 700 cm^{-1} (trityl). N.m.r. data: δ 1.98 (9H, acetyl), 2.65 (2H, m, H-6,6'), ~7.25 (15H, m, trityl).

1,5-Anhydro-6-thio-D-*glucitol* (**28**). — A solution of **30** (0.9 g) in methanol (10 ml) was treated with 4M methanolic sodium methoxide (1 ml). After 15 min, the mixture was neutralized and evaporated. The residue was purified by column chromatography (solvent *F*), yielding thiol **30** as a colorless syrup (0.30 g, 58%), $[\alpha]_D^{20}$ −15° (methanol), R_F 0.60 (*E*) (Found: S, 17.52. $C_6H_{12}O_4S$ calc.: S, 17.79%).

Tritylation of **28** afforded the 6-*S*-trityl derivative, identical with **32**.

REFERENCES

1 J. KUSZMANN AND P. SOHÁR, *Carbohyd. Res.*, 27 (1973) 157–168.
2 J. KUSZMANN AND P. SOHÁR, *Carbohyd. Res.*, 35 (1974) 97–102.
3 L. VARGHA, *Ber.*, 68 (1935) 1377–1384.
4 D. M. FRIEDMANN AND E. BOGER, *Anal. Chem.*, 33 (1961) 906–910.