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Ethylation of Thiolaevoglucosan to a Crystalline Sulfonium Salt and Reaction of the Latter with Nucleophiles

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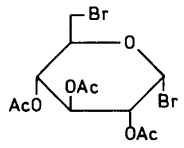
Tri-*O*-acetyl-thiolaevoglucosan (*3b*) was alkylated with triethyloxonium tetrafluoroborate to give the crystalline sulfonium salt (*5b*) in high yield. Reaction of *5b* with hard nucleophiles resulted in attack at C-1 to give products of type *7* and *8*, while soft sulfur nucleophiles attacked at C-6 to give *9*. A sulfur-linked disaccharide was prepared in this way.

Nucleophilic displacement reactions performed on carbohydrates containing an alkylthio group often result in migration of this group, explained through the intermediacy of a cyclic sulfonium ion. Thus, episulfonium ions account for the stereospecific migration of an alkylthio group between two adjacent carbon atoms.[1,2] Migration of an *S*-alkyl group between other carbon atoms, presumably



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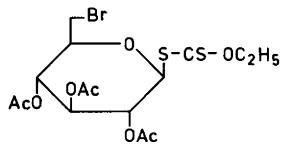

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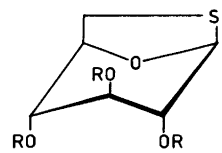

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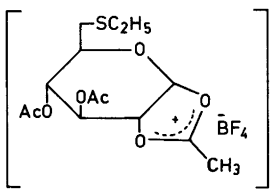

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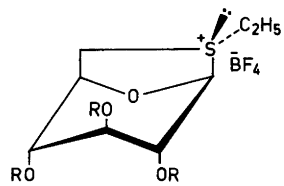

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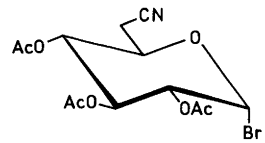

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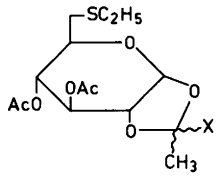

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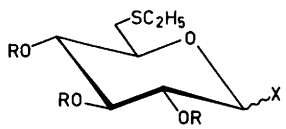

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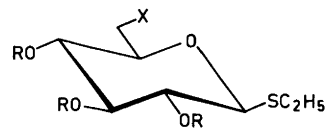

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a: R = H
b: R = Ac

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Table 1. Reaction of the sulfonium salt (*5b*) with nucleophiles.

Nucleophile (X^-)	Products[a] (%) 7	*β-8b*	*α-8b*	*9b*	*3b*
CH_3O^-		95			
CH_3COO^-		50	traces		
N_3^-	97				
CN^-	20			27	14
Br^-			33	19	10
$C_2H_5O-CS-S^-$				65	
$C_6H_5-CH_2-S^-$				63	
1-Thio-β-D-glucopyranose tetraacetate$^-$				57	

[a] X = corresponding nucleophile (Fig. 1).

involving five-[3] and six-membered[4] cyclic sulfonium ions, has also been observed. Thus, Harness and Hughes reported[4] that the benzyl thioglycosides of 5-thio-L-arabinopyranose were obtained when the dibenzyldithioacetal of 5-*O*-tosyl-L-arabinose was treated with potassium iodide, a reaction supposedly involving a six-membered cyclic sulfonium ion. Migration of an *S*-methyl group from C-1 to C-6 was observed[5] when methyl 1-thio-6-*O*-tosyl-β-D-glucopyranoside was treated with methanol, giving methyl 6-*S*-methyl-6-thio-α-D-glucopyranoside. The intermediate in this reaction is most likely a 5-membered cyclic sulfonium ion similar to that of *5*. But neither in this case,[5] nor in the examples mentioned above,[1-4] have sulfonium salts been isolated or even observed.

Preparation of sulfonium salts derived from sulfur containing carbohydrates by alkylation has been unsuccessful. Thus Bannister reported[6] that methyl α-thiolinkosaminide, a methyl thioglycoside, could not be alkylated with alkyl halides or tosylates. Similarly, alkylation of 5-thio-D-ribopyranose derivatives proved abortive.[7]

We now report on the ethylation of tri-*O*-acetyl-1,6-anhydro-6-thio-β-D-glucopyranose (*3b*)[8] (tri-*O*-acetyl-thiolaevolucosan) to give the crystalline sulfonium salt *5b*, as well as on the reaction of the latter with a series of nucleophiles. Alkylation of *3b* with methyl iodide and silver tosylate led to a syrupy sulfonium salt of type *5*, as seen from its ^1H NMR spectrum. This product was not investigated further, since alkylation performed with triethyloxonium tetrafluoroborate afforded a crystalline salt, *5b*, in 75 % yield. Only one stereoisomer of *5b* was obtained, presumably the unhindered (*S*)-epimer. This assignment is based on the assumption that this isomer represents the more stable one, due to expected steric interaction between the *S*-ethyl group and the axial 3-*O*-acetate substituent within the alternative (*R*)-epimer. Furthermore, *5b* has the same conformation as the non-alkylated product, *3b*, as seen from the coupling constants J_{23} and J_{34} (<4 Hz).

We have prepared tri-*O*-acetyl-thiolaevoglucosan in an overall yield better than that reported[8] by conversion of the 1,6-dibromo-derivative (*1*)[9] into the 6-bromo-1-xanthate (*2*) which readily gave the 1,6-thioanhydro derivative (*3a*) by treatment with sodium methoxide.

The reaction between the sulfonium salt (*5b*) and a number of nucleophiles was studied; the results (Table 1) show that the reaction takes place in a regiospecific manner, resulting from attack at one of the three α-positions: C-1, C-6 or the ethyl group. Reaction of *5b* with an alkohol or an alkoxide leads to attack at C-1, and it was hoped that pure α-glycosides could be obtained in this way. However, reaction with excess of methanol was slow (5 days), and an anomeric mixture of methyl glycosides was obtained, presumably because the reaction mixture became acidic. Reaction with one equivalent of methoxide, on the other hand, was complete within 6 h and gave pure β-glycoside. This can only be explained by anchimeric assistance from the C-2 acetoxy group giving the intermediate *4*, which by reaction with methoxide yielded the product *β-8* ($X=OCH_3$). Reaction with sodium acetate followed a similar pathway, while sodium azide yielded an orthoacid azide (*7*, $X=N_3$) in high yield, confirming the structure of the intermediate *4*. When *5b* was subjected to reaction with sulfur nucleophiles attack occurred exclusively at C-6

giving products of type *9* in good yields. Reaction with cyanide and bromide gave mixed products (see Table 1).

These results show that the sulfonium ion *5b* reacts with nucleophiles as expected, according to the accepted principle of hard and soft nucleophiles.[10] The hard oxygen nucleophiles lead to products involving the C-1 center, the soft sulfur nucleophiles attack at the soft center, C-6, while the borderline nucleophiles do not show any specificity.

Attempts to prepare a disaccharide by treatment of *5b* with the sodium salt of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose gave only the 6-*O*-acetate of di-*O*-isopropylidene-D-galactose by transesterification. A sulfur-linked disaccharide could, however, be prepared by reaction of *5b* with the sodium salt of tetra-*O*-acetyl-1-thio-β-D-glucopyranose, giving *9* (X = tetra-*O*-acetyl-1-thio-β-D-glucopyranosyl) in good yield.

The structures of the products *7* and *8* followed from their ^1H and ^{13}C NMR spectra (Experimental). In cases where X represents a sulfur substituent the structures could not be assigned to *8* or *9* by spectroscopy. Hence, chemical conversions were made. The product isolated from the reaction of *5b* with potassium xanthogenate (*8b* or *9b*, $X=S-CS-OC_2H_5$) was treated with sodium methoxide to give a thiol (*8a* or *9a*, X = SH), which was acetylated to give an *S*-acetate (*8b* or *9b*, X = S−Ac). ^1H NMR spectra of those three derivatives revealed that the signals from the H-1 proton remained nearly constant (δ ~4.5) while the signals for the two H-6 protons shifted from δ 3.6 and 3.2 in the xanthogenate to 3.0−2.6 in the thiolate and to 3.3 and 3.0 in the *S*-acetate. This proves the structure of the xanthogenate to be *9b* (X = S−CS−OEt). The thiol *9a* (X = SH) was benzylated to give a product, which, after acetylation, proved identical with the product obtained from the reaction of *5b* with phenylmethanethiolate. The sulfur-linked disaccharide obtained by reaction of *5b* with the sodium salt of 1-β-D-thio-glucopyranose tetraacetate was shown to be identical with the product isolated from reaction of *9a* (X = SNa) with acetobromoglucose.

The reaction of *5b* with cyanide gave *7* (X = CN), *3b*, and a third compound. The latter was shown to be a β-thioglycoside by converting it into the α-bromide (*6*) on treatment with bromine in carbon tetrachloride.[11] Thus the compound had the structure *9b* (X = CN).

EXPERIMENTAL

Melting points are uncorrected. Optical rotations were measured on a Perkin Elmer 141 polarimeter. NMR spectra were obtained on Bruker WH-90 and HX-90 instruments. Acetylated products were measured in $CDCl_3$ and non-acetylated compounds in D_2O. TMS was used as internal reference in ^1H and ^{13}C NMR spectra in $CDCl_3$, and for ^{13}C NMR spectra in D_2O dioxane (67.40 p.p.m.) was used. Preparative TLC was performed on 1 mm layers of silica gel (Merck PF_{254}). All evaporations were performed *in vacuo*. Microanalyses were performed by NOVO microanalytical laboratory.

Tri-O-acetyl-6-bromo-6-deoxy-α-D-glucopyranosyl bromide (1).[9] Penta-*O*-acetyl-β-D-glucopyranose (60 g) was placed in a glass tube and cooled to −78 °C. Hydrogen bromide (~200 ml) was condensed into the tube. It was then placed in an iron tube which was closed and kept at room temperature for 6 days. After this time it was again cooled to −78 °C and opened. The reaction mixture was then poured into dichloromethane (~300 ml) and left in the hood until most of the hydrogen bromide had evaporated. The remaining mixture was diluted with more dichloromethane and washed twice with water, with aqueous $NaHCO_3$, dried ($MgSO_4$), and the solvent was evaporated. Crystallization of the product from chloroform − pentane gave 46 g (69 %) of (*1*), m.p. 168−170 °C (lit.[9] 173 °C). ^1H NMR: δ 6.67 (H-1); 5.59 and 5.19 (H-3 and H-4); 4.87 (H-2); 4.33 (H-5); 3.62 (H-6); 3.44 (H-6′); J_{12} 4.0 Hz; $J_{23}=J_{34}=J_{45}$ 9.5; J_{56} 2.6; $J_{56'}$ 4.0; $J_{66'}$ 12.0.

2,3,4-Tri-O-acetyl-6-bromo-6-deoxy-β-D-glucopyranosyl xanthogenate (2). 2,3,4-Tri-*O*-acetyl-6-bromo-6-deoxy-α-D-glucopyranosyl bromide (*1*) (20 g) and potassium ethyl xanthogenate (8.1 g, 1.1 eqv.) were dissolved in oxygen-free acetonitrile (500 ml) and heated to 60 °C for 1h. After filtration, the filtrate was concentrated to a syrup. This was dissolved in chloroform, the solution was washed with water, dried ($MgSO_4$) and evaporated. The product was crystallized from ether − pentane to give 20 g (91 %) of *2*, m.p. 93−98 °C. Recrystallization from ether − pentane gave a product with m.p. 107.5−108.5 °C. $[\alpha]_D^{20} = +15.2°$ (*c*. 1.0, $CHCl_3$). Anal. $C_{15}H_{21}BrO_8S_2$: C,H,S. ^1H NMR: δ 5.51 (H-1); 5.33 (H-3); 5.16 (H-2); 5.04 (H-4); 4.67 (−O−CH_2); 3.86 (H-5); 3.50 (H-6); 3.38 (H-6′); 1.45 (−CH_3); 2.07, 2.04, 2.01 (OAc).

2,3,4-Tri-O-acetyl-1,6-anhydro-6-thio-β-D-glucopyranose (3b). To a solution of sodium (4.5 g) in methanol (270 ml) 18.5 g of *2* was added with stirring. After 2 h a few drops of water were added and after 5 min the mixture was neutralized with acetic acid and evaporated. Pyridine was added and evaporated and the remaining product was dissolved in pyridine (25 ml) and acetic anhydride

(20 ml, 2 eqv.) was added. After standing at room temperature for 2 h or more, chloroform was added and the solution was washed with water, 4 N hydrochloric acid, aqueous $NaHCO_3$, dried ($MgSO_4$), and evaporated. The crude product (9 g) was recrystallized from ethanol to give 4.5 g (38 %) of *3b*, m.p. 86–88 °C (lit: 93–94°,[8] 79–81°[12]). ^{1}H NMR: δ 5.41 (H-1); 4.91 (H-3); 4.73 (H-2); 4.67 (H-4); 4.59 (H-5); 3.16 (H-6_{exo}); 3.06 (H-6_{endo}); 2.14, 2.09 (OAc). ^{13}C NMR: 81.8 ppm (C-1); 79.7 (C-5); 74.4 (C-2); 72.2 (C-4); 69.2 (C-3); 34.6 (C-6).

*2,3,4-Tri-*O*-acetyl-1,6-anhydro-6-thio-β-*D*-glucopyranose-(*S*)-S-ethylsulfonium tetrafluoroborate (*5b*).* Thiolaevoglucosane triacetate (*3b*), (2.19 g) was added to a solution of 1.51 g (1.1 eqv.) of triethyloxonium tetrafluoroborate in dichloromethane (8 ml). The solution was kept at room temperature for 20 h during which time the sulfonium salt (*5b*) crystallized. Ether was added and the product collected by filtration. Recrystallization from acetone–ether gave 2.23 g (74 %) of *5b*, followed by another crystallization from the same solvent to give an analytical specimen, m.p. 156–158 °C. $[\alpha]_D^{20} = -65.5°$ (*c.* 0.9, acetone). Anal. $C_{14}H_{21}BF_4O_7S$: C,H,S. A lower melting (114–116 °C) modification having the same composition and optical rotation was occasionally obtained. ^{1}H NMR (acetone-d_6): δ 6.42 (H-1); 5.49 (H-5); 5.09 (H-3); 4.7–4.9 (H-2, H-4); 4.35 (H-6_{endo}); 3.82 (H-6_{exo}); 3.51 and 1.51 ($-CH_2-CH_3$); 2.0 (OAc); J_{12} <3 Hz; J_{23} <4; J_{34} <4; J_{45} <4; $J_{56'}$ 8; $J_{66'}$ 14; J_{Et} = 7.4. Kept in a desiccator over potassium hydroxide the product is stable.

*Reaction of the sulfonium salt (*5b*) with nuclophiles.* The following reactions were monitored by TLC (ether–pentane 4:1). Work up was performed when the starting material had disappeared.

Reaction with sodium methoxide. To 433 mg of *5b* in dry acetonitrile (10 ml), 10 ml of a 0.103 M (=1.0 eqv.) solution of sodium methoxide in methanol was added. After 6 h at room temperature the reaction mixture was neutral, and the solvent was evaporated. The resulting syrup was acetylated in pyridine (10 ml) with acetic anhydride (1 ml). Work up as described above gave 341 mg (91 %) of almost pure *β-8b* (X = OCH_3). Purification by preparative TLC (ether–pentane 2:1) gave a product (215 mg, 57 %), which was recrystallized from ether–pentane, m.p. 73.5–74.5 °C. $[\alpha]_D^{20} = -6.7°$ (*c.* 0.6, $CHCl_3$). Anal. $C_{15}H_{24}O_8S$. C,H,S. ^{1}H NMR: δ 5.26 (H-3); 5.02 (H-4); 5.00 (H-2); 4.47 (H-1); 3.68 (H-5); 3.52 (OCH_3); 2.70 (H-6, H-6'); 2.66 and 1.26 ($-CH_2-CH_3$); 2.06, 2.0 (OAc); J_{12} 7.2 Hz; $J_{23} = J_{34} = J_{45}$ 9.0; $J_{56} = J_{56'} \sim 6$; J_{Et} 7.5.

Reaction with sodium acetate. To 500 mg of *5b* in dry acetonitrile (5 ml), anhydrous sodium acetate (0.167 g, 1.7 eqv.) was added. The mixture was stirred for 23 h, and the solvent was removed. The resulting syrup was dissolved in chloroform and washed with aqueous $NaHCO_3$, water, dried ($MgSO_4$), and concentrated to give 370 mg (79 %) of crude material. A ^{1}H NMR spectrum showed that *β-8b* (X = OAc) was the main product. Besides, traces of the corresponding α-anomer together with hydrolysis products were present. Crystallization from ether–pentane gave 231 mg (41 %) of *β-8b* with m.p. 97–99 °C. Recrystallization from ethanol gave the pure product with m.p. 100.5–101.5 °C. $[\alpha]_D^{20} = +7.7°$ (*c.* 1.1, chloroform). Anal. $C_{16}H_{24}O_9S$: C,H,S. ^{1}H NMR: δ 5.77 (H-1); 5.4–5.0 (H-2, H-3, H-4); 3.87 (H-5); 2.8–2.6 (H-6, H-6'); 2.6–2.7 and 1.22 ($-CH_2-CH_3$); 2.12, 2.06, 2.04, 2.02 (–OAc); J_{12} 7.2 Hz; $J_{56} \sim 4$; $J_{56'}$ 6; J_{Et} 7.5.

Reaction with sodium azide. To 400 mg of *5b* dissolved in dry acetonitrile (10 ml), sodium azide (6.19 mg, 10 eqv.) was added. After stirring for 23 h at room temperature work-up as described above gave a syrup (345 mg, 97 %). The product was nearly pure 7 (X = N_3) as seen from its ^{1}H NMR spectrum and TLC, but failed to crystallize. Purification by preparative TLC was unsuccessful because the orthoacid derivative hydrolyzed on the silica gel. ^{1}H NMR: δ 5.81 (H-1); 5.21 (H-3); 4.94 (H-4); 4.41 (H-2); 3.89 (H-5); 2.8–2.5 (H-6, H-6'); 2.63 and 1.26 ($-CH_2-CH_3$); 2.13, 2.11 (OAc); 1.93 ($>C-CH_3$); J_{12} 5.3 Hz; J_{23} 3.0; J_{34} 2.2; J_{45} 9.2; J_{56} 4.0; $J_{56'}$ 6.3; J_{Et} 7.5. ^{13}C NMR: 97.3 ppm (C-1); 73.3 (C-2); 71.1 (C-4); 69.6 (C-3, C-5); 33.9 (C-6); 29.6 and 14.7 ($-CH_2-CH_3$); 22.3 ($>C-CH_3$); 169.1, 169.7, 170.1 and 20.7, 20.8 (OAc).

Reaction with tetrabutylammonium bromide. To 500 mg of *5b* in dry acetonitrile (5 ml), dry tetrabutylammonium bromide (3.91 mg, 1.02 eqv.) was added. After stirring for 22 h at room temperature ether (150 ml) was added and work-up as above gave a syrup (410 mg). Preparative TLC (ether–pentane 1:1) gave 4 fractions. The fastest moving fraction gave 189 mg, 38 %) of the α-bromide (*α-8b*, X = Br). ^{1}H NMR: δ 6.66 (H-1); 5.58 (H-3); 5.18 (H-4); 4.84 (H-2); 4.31 (H-5); 2.84 (H-6); 2.64 (H-6'); 2.60 and 1.26 ($-CH_2-CH_3$); 2.10, 2.07, 2.04 (OAc); J_{12} 4.0 Hz; $J_{23} = J_{34} = J_{45}$ 9.5; J_{56} 3.6; $J_{56'}$ 6.0; $J_{66'}$ 14; J_{Et} 7.5. The next fraction yielded 113 mg (23 %) of the *β*-ethylthioglucoside (*9b*, X = Br). ^{1}H NMR: δ 5.29 (H-3); 5.04 (H-2); 5.01 (H-4); 4.58 (H-1); 3.76 (H-5); 3.53 (H-6); 3.36 (H-6'); 2.76 and 1.30 ($-CH_2-CH_3$); 2.07, 2.01 (OAc); J_{12} 9.5 Hz; $J_{23} = J_{34} = J_{45}$ 9.0; J_{56} 3.0; $J_{56'}$ 6; $J_{66'}$ 12; J_{Et} 7.5. The third fraction gave 38 mg (10 %) of thiolaevoglucosan triacetate (*3b*) while the slowest moving fraction (25 mg, 6 %) was a mixture of 2,3,4- and 1,3,4-tri-*O*-acetyl-6-*S*-ethyl-6-thio-α-*D*-glucopyranose.

Reaction with potassium cyanide. 200 mg of *5b* and potassium cyanide (263 mg, 8.5 eqv.) was stirred

in dry acetonitrile (3 ml) for 22 h. Work-up as described above gave 166 mg of crude product. Preparative TLC (ether – pentane 4:1) gave 3 compounds. The fastest moving fraction (35 mg, 20 %) was the orthoacid derivative (*7*, X = CN). ^{1}H NMR: δ 5.84 (H-1); 5.23 (H-3); 4.96 (H-4); 4.29 (H-2); 3.88 (H-5); 2.64 – 2.78 (H-6, H-6'); 2.63 and 1.26 ($-CH_2-CH_3$); 1.94 ($>C-CH_3$); 2.14, 2.11 (OAc); J_{12} 5.2 Hz; J_{23} 2.8; J_{24} 1.0; J_{34} 2.2; J_{45} 9.2; J_{56} 4.5; $J_{56'}$ 6.2. ^{13}C NMR: 116 ppm (–CN); 97.2 (C-1); 74.0, 70.7, 69.7 (C-2, C-3, C-4); 69.3 (C-5); 33.6 (C-6) 26.8 and 14.5 ($-CH_2-CH_3$); 24.2 ($>C-CH_3$); 169.4 and 20.5, 20.6 (OAc). The next fraction gave 20 mg (14 %) of thiolaevoglucosan triacetate (*3b*). The slowest moving fraction yielded the 6-cyano-compound (*9b*) (46 mg, 27 %). ^{1}H NMR: δ 5.31 (H-3); 5.07 (H-2); 4.97 (H-4); 4.61 (H-1); 3.82 (H-5); 2.67 (H-6, H-6'); 2.76 and 1.30 ($-CH_2-CH_3$); 2.09, 2.07, 2.03 (OAc); J_{12} 10.0 Hz; $J_{23} = J_{34}$ 9.0; J_{45} 9.5; $J_{56} \sim J_{56'} \sim 6$; J_{Et} 7.5. ^{13}C NMR: 115 ppm (–CN); 83.5 (C-1); 73.4, 73.3, 71.6, 69.8 (C-2, C-3, C-4 and C-5); 21.3 (C-6); 24.2 and 14.8 (CH_2-CH_3); 169.7 and 20.5 (OAc).

Reaction with potassium ethylxanthogenate. To a solution of *5b* (1.2 g) in dry acetonitrile (15 ml) a solution of potassium ethylxanthogenate (583 mg, 1.3 eqv.) in dry acetonitrile (15 ml) was added with stirring. After 30 min the solvent was removed *in vacuo* and the residue was dissolved in chloroform, washed with aqueous $NaHCO_3$, dried ($MgSO_4$), and concentrated to a syrup. Recrystallization from ethanol gave 838 mg (65 %) of *9b* (X = –S–CS–OC_2H_5) m.p. 106.5 – 107 °C. $[\alpha]_D^{20} = +30.2°$ (*c.* 1.4, $CHCl_3$). Anal. $C_{17}H_{26}O_8S_3$: C,H,S. ^{1}H NMR: δ 5.30 (H-3); 5.03 (H-2); 5.00 (H-4); 4.53 (H-1); 3.73 (H-5); 3.64 (H-6); 3.19 (H-6'); 2.72 and 1.14 ($-CH_2-CH_3$); 2.11, 2.06, 2.02 (OAc); $J_{12} = J_{23} = J_{34} = J_{45}$ 9.0 Hz; J_{56} 3.0; $J_{56'}$ 8.5; $J_{66'}$ 14.7; J_{Et} 7.5; J_{OEt} 7.1.

Reaction with sodium phenylmethanethiolate. To a solution of *5b* (423 mg) in dry acetonitrile was slowly added 1.24 ml of a 0.81 M solution of sodium phenylmethanethiolate (1 eqv.) in methanol. After 3 h at room temperature the mixture was diluted with chloroform and worked up as described above to give a product which crystallized from ether – pentane to give 292 mg (63 %) of *9b* (X = –S–$CH_2-C_6H_5$) m.p. 117 – 123 °C. Recrystallization from ethanol gave a product with m.p. 125 – 126 °C; $[\alpha]_D^{20} = +5.1°$ (*c.* 1.9, $CHCl_3$). Anal. $C_{21}H_{28}O_7S$: C,H,S. ^{1}H NMR: δ 7.38 ($-C_6H_5$); 5.24 (H-3); 5.04 (H-2); 5.00 (H-4); 4.50 (H-1); 3.83 ($-CH_2-C_6H_5$); 3.62 (H-5); 2.56 (H-6, H-6'); 2.77 and 1.31 ($-CH_2-CH_3$); 2.07, 2.01, 1.98 (OAc); $J_{12} = J_{23} = J_{34} = J_{45}$ 9.5 Hz; $J_{56} = J_{56'}$ 5; J_{Et} 7.5.

*Reaction with the sodium salt of tetra-*O*-acetyl-1-thio-β-*D*-glucopyranose.* To 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranose[13] (400 mg) in dry acetonitrile 1.12 ml of a 0.9 M (0.9 eqv.) solution of sodium methoxide in methanol was added, together with 10 ml of methanol. To this mixture a solution of *5b* (462 mg, 1.0 eqv.) in dry acetonitrile (10 ml) was added. After standing for 1.5 h at room temperature three drops of the methoxide solution used above were added, and the solvents were removed *in vacuo*. The residue was extracted with chloroform and washed as described above. The crude product crystallized from ethanol to give 479 mg (57 %) of *9b* (X = 2',3',4',6'-tetra-O-acetyl-1'-thio-β-D-glucopyranosyl), m.p. 149 – 155 °C. Recrystallization from ethanol gave a product with m.p. 156.5 – 157 °C. $[\alpha]_D^{20} = -19.7°$ (*c.* 2.1, $CHCl_3$). ^{1}H NMR: δ 5.29 – 4.92 (H-2, H-3, H-4, H-5, H-2', H-3', H-4', H-5'); 4.74 and 4.57 (H-1, H-1'); 4.23 (H-6', two protons); 2.83 (H-6, two protons).

*Ethyl 1,6-dithio-β-D-glucopyranoside (*9a, *X = SH).* The 6-xanthogenate (*9b*, X = –S–CS–OEt) (265 mg) was dissolved in 1 ml of a 0.9 M (1.5 eqv.) sodium methoxide solution in methanol. After 1 h at room temperature, water (1 ml) was added and after 5 min the solution was neutralized with ion exchange resin (IR 120 – H^+). Filtration and concentration gave 128 mg (91 %) of *9a* (X = SH). ^{1}H NMR: δ 4.59 (H-1); 3.67 – 3.17 (H-2, H-3, H-4, H-5); 3.04 – 2.59 (H-6, H-6'); 2.78 and 1.30 ($-CH_2-CH_3$); $J_{12} \sim 10$ Hz; J_{Et} 7.5.

*Ethyl 2,3,4-tri-*O*-acetyl-6-*S*-acetyl-1,6-dithio-β-D-glucopyranoside (*9b, *X = SAc).* A solution of *9a* (X = SH) (71 mg) was acetylated in pyridine (5 ml) with acetic anhydride (0.5 ml). Work-up in the usual way gave 82 mg (68 %) of the acetylated product (*9b*, X = SAc). ^{1}H NMR: δ 5.27 (H-3); 5.04 (H-2); 5.01 (H-4); 4.50 (H-1); 3.67 (H-5); 3.30 (H-6); 3.01 (H-6'); 2.71 and 1.29 ($-CH_2-CH_3$); 2.36 (S–Ac); 2.06, 2.01 (O–Ac); J_{12} 9.5 Hz; $J_{23} = J_{34} = J_{45}$ 9.0; J_{56} 3.2; $J_{56'}$ 6.5; $J_{66'}$ 14.5; J_{Et} 7.5.

*Ethyl 2,3,4-tri-*O*-acetyl-6-*S*-benzyl-1,6-dithio-β-D-glucopyranoside (*9b, *X = –S–$CH_2-C_6H_5$).* *9a* (X = SH) (84 mg) was dissolved in acetone (1.5 ml) and 0.4 ml of a solution of 1.97 ml benzyl chloride in 10 ml of acetone (2 eqv.) was added together with potassium carbonate (47 mg) in water (0.4 ml). After 2.5 h the mixture was diluted with water (20 ml) and extracted with pentane. The water was removed *in vacuo*, pyridine was added, evaporated, and pyridine (10 ml) and acetic anhydride (1 ml) were added. After 2 h, work-up in the usual way gave 191 mg (~100 %) of a crude product which mainly consisted of *9b* (X = –S–$CH_2-C_6H_5$). Recrystallization from ether – pentane gave 60 mg (39 %) of a product with m.p. 124.5 – 126 °C; $[\alpha]_D^{20} = +6.8°$ (*c.* 1.4, $CHCl_3$). A ^{1}H NMR spectrum was identical with that of the product described above.

*Ethyl 2,3,4-tri-*O*-acetyl-6-*S*-(2',3',4',6'-tetra-*O*-acetyl-β-D-glucopyranosyl)-1,6-dithio-β-D-gluco-*

pyranoside (9b, *X = tetra-O-acetyl-1-β-D-thio-gluco-pyranosyl)*. To 100 mg of *9a* (X = SH) in acetone (3 ml) tetra-*O*-acetyl-α-D-glucopyranosyl bromide (171 mg ~1 eqv.) was added, together with potassium carbonate (57.5 mg) dissolved in water (1 ml). After stirring for 20 h the solvents were removed *in vacuo*, pyridine was added and evaporated and the remaining substance was acetylated in pyridine (5 ml) with acetic anhydride (1 ml). Work-up in the usual way gave 300 mg of a crude product, which contained 3 compounds, as seen from TLC (ether–pentane 4:1). Separation by preparative TLC in the same solvent gave, as the fastest moving compound, 51 mg of the fully acetylated compound *9b* (X = SAc). The next fraction gave 110 mg of glucosepentaacetate; the slowest moving compound was the title compound (62.5 mg, 26%), which was crystallized from ethanol; m.p. 153–160 °C; $[\alpha]_D^{20} = -18.8°$ (*c*. 0.6, $CHCl_3$). A ^1H NMR spectrum was identical with the one described above.

2,3,4-Tri-O-acetyl-6-cyano-6-deoxy-α-D-glucopyranosyl bromide (6). The 6-cyano-compound *9b* (X = CN) (45.9 mg) was dissolved in carbon tetrachloride (6 ml) and 0.5 ml (1.1 eqv.) of a solution of bromine in carbon tetrachloride (0.281 M) was added. After 20 h the mixture was diluted with more carbon tetrachloride, which was washed successively with sodium dithionite and aqueous $NaHCO_3$, dried ($MgSO_4$) and concentrated, to give 37.6 mg (78 %) of syrupy *6*. ^1H NMR: δ 6.64 (H-1); 5.62 (H-3); 5.10 (H-4); 4.89 (H-2); 4.40 (H-5); 2.71 (H-6, H-6'); J_{12} 4.0 Hz; $J_{23} = J_{34}$ 10.0; J_{45} 9.0; $J_{56} = J_{56'}$ 5.5.

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