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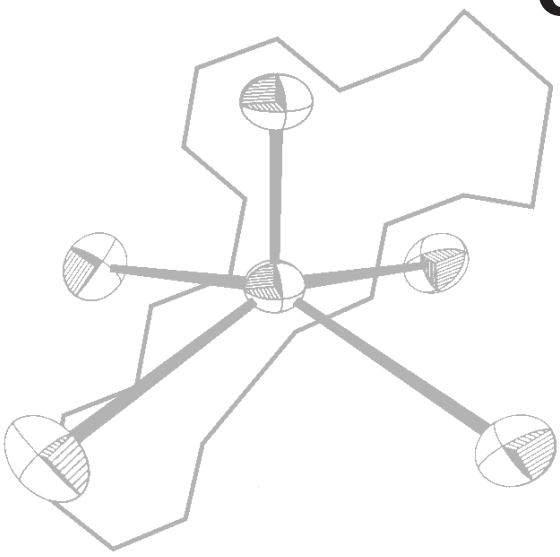

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Investigations into the Chemistry of Some 1,6-Epithio and 1,6-Episeleno β-D-Glucopyranoses

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Derivatives of 1,6-dideoxy-1,6-epithio-β-D-glucopyranose have been shown to undergo oxidation reactions to afford the corresponding sulfoxides and sulfones. The sulfoxides participate in Pummerer reactions to afford the corresponding α-acetoxy sulfides which were then oxidized further. None of the sulfoxides, sulfones or α-acetoxy sulfides prepared were particularly efficient glycosyl donors. Also presented are crystal structures of 1,6-dideoxy-1,6-epithio-β-D-glucopyranose *S,S*-dioxide and 1,6-dideoxy-1,6-episeleno-β-D-glucopyranose, interesting analogues of 1,6-anhydro-β-D-glucopyranose.

Keywords. Episeleno; epithio; glucopyranose; oxidation; sulfoxides; sulfones; Pummerer reactions; X-ray crystal structures.

1,6-Anhydro sugars are routinely employed in the construction of a variety of carbohydrate-based molecules. Of particular importance in this class of sugars is the conformational constraint enforced on the sugar by the 1,6-anhydro bridge and the protection afforded to the two most reactive hydroxyls, at C1 and C6 which, together, provide 1,6-anhydro sugars with a good deal of synthetic potential not present in other, simple sugar derivatives, such as glycosides. The analogous molecules containing sulfur or selenium have, particularly in the case of sulfur, been known for some time. Nevertheless, investigations into the reactions and properties of these molecules have been limited, owing in part to the difficulty in preparing these compounds.

The first synthesis of 'thiolevoglucosan' (1) was achieved in 1963 by Akagi and coworkers.[1] The method relied on the early introduction of sulfur at C1 of a hexopyranose, via an anomeric thioacetate, and then exposure of the derived thiolate ion (sodium methoxide) to a leaving group conveniently located at C6, thus installing the 1,6-epithio bridge. Acetylation of the crude material then provided 'tri-*O*-acetyl thioglucosan' (2) in a moderate yield. A number of related syntheses has since been reported that similarly rely on base treatment of molecules having a thioester at C1 or C6 and a good leaving group at C6 or C1, respectively.[2,3]

Recently, we reported a synthesis of thiolevoglucosan which relied on the treatment of a doubly activated hexopyranose, such as (3), having leaving groups at both C1 and C6, with sulfide ion prepared by treatment of hydrogen sulfide with triethylamine.[4] In related work, treatment of the same bromide (3) with sodium hydrogen selenide (prepared by treatment of elemental selenium with sodium borohydride in ethanol[5]) provided the novel 'tri-*O*-acetyl selenolevoglucosan' (4) in 56% yield.[4] We also attempted to prepare the 1,6-epidithio sugar (5) by treatment of the bromide (3) with the 'disulfide transfer' reagent, benzyltriethylammonium tetrathiomolybdate. This combination gave not the desired 1,6-epidithio sugar (5) but rather the 1,6-epithio sugar (2), in a very surprising yield (88%), presumably through a redox process.[4] This method now appears to constitute the most reliable and simplest preparation of thiolevoglucosans.

Recently, Lowary and Bundle reported the unanticipated preparation of a thioglucosan by treatment of the 6-*O*-tosyl derivative of an ethylthio β-D-glucoside with sodium iodide.[6] Finally, the *exo*-sulfoxide (6) has been prepared stereoselectively by the action of peracetic acid on the sulfide (1). X-ray crystallography was used to assign the stereochemistry of the resultant sulfoxide.[7]

The limited investigations into the oxidation chemistry of thioglucosan (1) warranted further studies into the preparation of derivatives containing the thioglucosan core. In addition, the novel preparation of a thioglucosan by Lowary and Bundle merited consideration of their method as an alternative preparation of thioglucosan.

To this end, the tosylate (7) was prepared by treatment of ethyl 1-thio-β-D-glucopyranoside with tosyl chloride, followed by acetylation of the crude material after workup. Treatment of the tosylate (7) with sodium iodide in refluxing butanone provided the triacetate (2) in a disappointing yield of 31%, with no improvement on the alternative syntheses outlined in the literature.[1–4]

Dimethyldioxiran (DMDO) is a potent, yet mild, oxidant, the attractiveness of which is enhanced owing to the volatil-

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ity of the only by-product of its use, acetone.[8] The use of DMDO for the oxidation of sulfur in thioglycosides has been demonstrated to a limited extent, showing its utility for the preparation of sulfoxides and sulfones. The preparation of sulfoxides is, in general, less efficient than that of the corresponding sulfone owing to competing oxidation to the sulfone. Thus, Gervay and coworkers have reported that treatment of a *C*-glycoside sulfide with an excess of DMDO afforded the corresponding sulfone in quantitative yield, whereas treatment of the same *C*-glycoside with an equivalent of *meta*-chloroperbenzoic acid afforded a mixture of the corresponding sulfoxides in only 34% yield.[9] Similarly, Berkowitz and coworkers found that treatment of a thioglycoside with DMDO afforded the corresponding sulfoxides in 77% yield; interestingly, however, a cautious treatment of the same thioglycoside with a slight excess of DMDO afforded only the major sulfoxide diastereoisomer and the corresponding sulfone.[10]

Here, the phenyl thioglycoside (8) was treated with 1.2 equiv. of DMDO in acetone to afford, after evaporation of the solvent and chromatography, the sulfoxides (9) in 64% yield. By comparison, oxidation of the same thioglycoside with *meta*-chloroperbenzoic acid afforded the same sulfoxides in 85% yield.[11] In a similar approach, the benzoylated sulfoxides (10) were prepared in 84% yield by treatment of the thioglycoside (11) with *meta*-chloroperbenzoic acid.

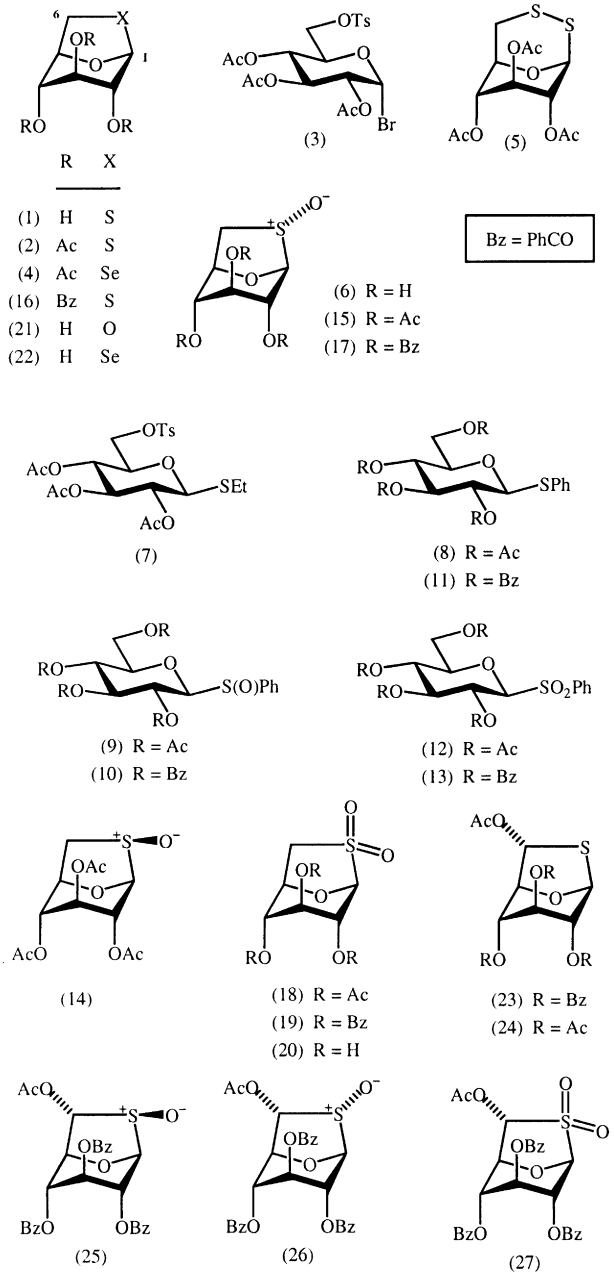
It has recently been suggested in the case of some 1-thio α-D-mannopyranosides that the observed stereoselectivity in the oxidation to the corresponding sulfoxide is a result of the oxidation of the least hindered lone-pair of the preferred conformation as predicted by the *exo*-anomeric effect.[12] In the case of a 1-thio-β-D-glucopyranoside, the *exo*-anomeric effect allows for the prediction of the preferred conformation, but it is not obvious which lone-pair on the sulfur will be less sterically hindered. Presumably, small differences in the steric environment of each lone-pair on the sulfur atoms in (8) and (11) give rise to the observed, small diastereoselectivities. That one lone-pair on the sulfur in a 1-thio-β-D-glucopyranoside is more crowded than the other could explain the results observed by Berkowitz and coworkers above.[10] An alternative explanation for the observed diastereoselectivity in the oxidation of some 1-thio-β-D-galactopyranosides has been proposed.[13]

Whilst the reagent of choice for the conversion of thioglycosides into sulfoxides appeared to be *meta*-chloroperbenzoic acid, treatment of the two thioglycosides, (8) and (11), with an excess of DMDO rapidly provided the sulfones (12) and (13), respectively, in almost quantitative yields.

With these results in hand, the oxidation of the triacetate (2) was examined. Treatment of (2) with *meta*-chloroperbenzoic acid in dichloromethane at 0° resulted in the rapid conversion to two new, high-polarity compounds (t.l.c.). These compounds were separated and identified as the *endo*-sulfoxide (14) (7%) and the *exo*-sulfoxide (15) (84%). The *endo*-stereochemistry of (14) was assigned on the basis of the large downfield shift of H2 relative to that of the sulfide (2), attributed to deshielding by the anisotropic S–O bond.[14] Deacetylation of (15) provided the triol (6), previously prepared by Novotny and coworkers but characterized only by X-ray crystallography.[7]

The tribenzoate (16) was treated with *meta*-chloroperbenzoic acid to afford only the *exo*-sulfoxide (17), the increased stereoselectivity presumably resulting from the increased bulk of the benzoate group at C3, compared with the acetate group in (2). In the two cases above, the predominant sulfoxide obtained was that of the *exo*-configuration. Presumably, the oxidant reacts with the most exposed lone-pair on sulfur to afford the corresponding sulfoxide.

The next compounds to be investigated were the sulfones. The triacetate (2) was treated with an excess of *meta*-chloroperbenzoic acid at room temperature for two days, resulting in, initially, a fast conversion to the sulfoxides (14) and (15) (t.l.c.), followed by a slower conversion into the sulfone (18), eventually isolated in a yield of 95%. Whilst



the yield of the reaction was excellent, the use of a large excess of *meta*-chloroperbenzoic acid and the prolonged reaction time were not ideal, prompting an attempt at the oxidation using DMDO. Indeed, treatment of the triacetate (2) with an excess of DMDO rapidly provided the sulfone (18) in a quantitative yield, with no requirement for purification. Similarly, the tribenzoate (16), upon treatment with DMDO, was converted in good yield into the sulfone (19), although at a lower rate. The tri-*O*-benzoyl sulfone (19) was a remarkably refractory material, possessing only a slight solubility in chloroform and only marginally better solubility in dimethyl sulfoxide. Deacetylation of the tri-*O*-acetyl sulfone (18) with sodium methoxide in methanol provided the triol (20), the structure being confirmed by a single-crystal X-ray diffraction analysis (Fig. 1).

X-Ray crystal structures have already been determined for glucosan (21),[15] thioglucosan (1)[16] and its *exo*-sulfoxide (6).[7] To complete the glycosan series, the crystal structure of selenoglucosan (22) was determined (Fig. 1).

Table 1 summarizes the C 1–X and C 6–X bond lengths from all of the known crystal structures for simple glucosan derivatives. It is of interest to note that the unit cell of the sulfoxide (6) contains two crystallographically independent molecules, possessing almost the same conformation. On the other hand, the unit cell of the selenoglucosan (22), the only crystallographically characterized selenium-containing member of the array, contains two independent molecules having quite different conformations, namely one in a 'twisted' $B_{3,O}$ conformation and the other in a slightly deformed $^1C_4$ conformation. The series containing oxygen, sulfur and selenium exhibits an increase in the C 1–X and C 6–X bond lengths, as would be expected, the greatest increase being from oxygen to sulfur [Δ(C 1–X) = 0.38_8 Å, Δ(C 6–X) = 0.38_3 Å)], with a smaller increase from sulfur to selenium [Δ(C 1–X) = 0.12_5, 0.18_3 Å; Δ(C 6–X) = 0.12_3, 0.12_2 Å]; the latter, nevertheless, may be sufficient to begin to tip the balance of conformational stability in favour of the new form.

The trend in bond lengths for the sequence containing thioglucosan (1), the sulfoxide (6) and the sulfone (20) is less obvious; however, there appears to be a slight increase in the length of the C 1–S bond. The C 6–S bond through the series shows no such trend; however, it is only in the sulfone (20) that the C 6–S bond is shorter than the C 1–S bond.

Table 1. Selected bond lengths and conformations in glucosan derivatives

Derivative	Atom X	C 1–X (Å)[A]	C 6–X (Å)[A]	Conformation
(21)[15]	O	1.427(4)	1.444(5)	$^1C_4$
(1)[16]	S	1.815[B]	1.827[B]	$^1C_4$
(22)	Se	1.94(1), 1.998(9)	1.95(1), 1.94(1)	$^1C_4$, $B_{3,O}$
(6)[7]	*exo*-SO	1.828(3), 1.821(4)	1.835(4), 1.868(4)	$^1C_4$
(20)	SO_2	1.825(3)	1.779(2)	$^1C_4$

[A] Error in value shown in parentheses.
[B] Errors in measurement are not quoted in ref. 16.

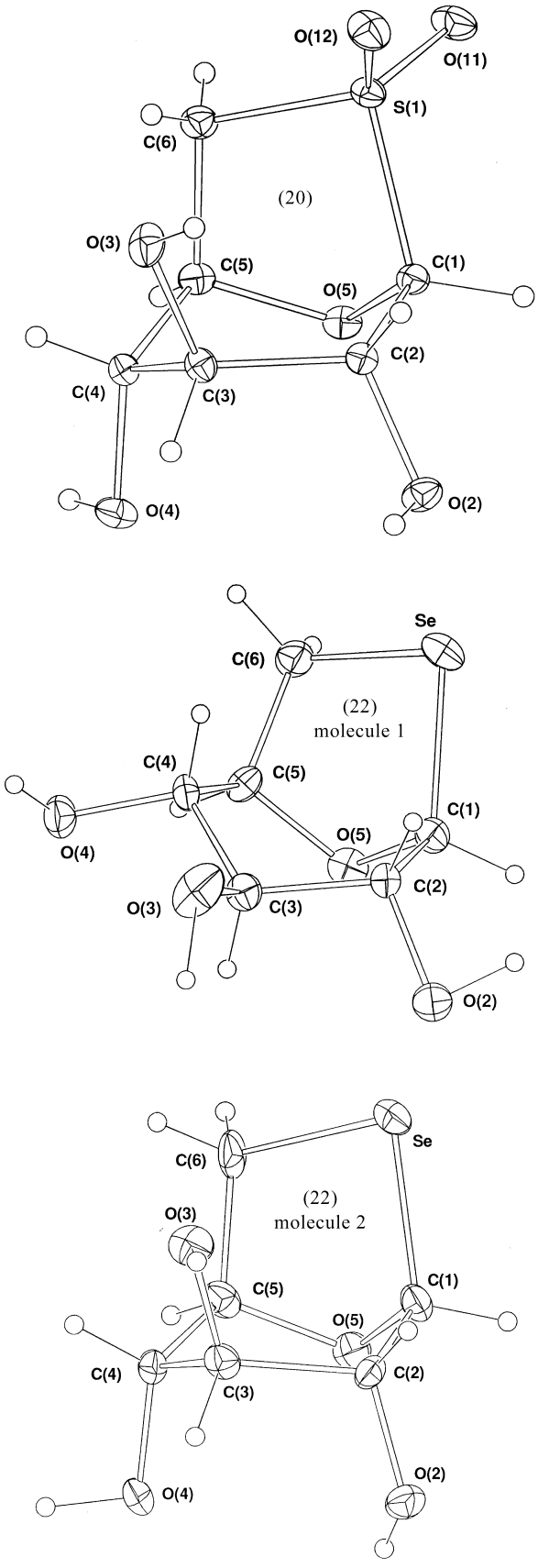


Fig. 1. Projections of (20) and (22) (two molecules) in the orientation of the schema (approximately), showing the two conformers of (22). 20% thermal ellipsoids are shown for the non-hydrogen atoms, hydrogen atoms having arbitrary radii of 0.1 Å.

Sulfoxides with α-protons, upon treatment with acylating reagents such as acetic anhydride, are prone to rearrangement to α-acetoxy sulfides.[17] This reaction, known as the Pummerer rearrangement, effectively achieves an oxidation adjacent to sulfur, thus providing a route to thioacetals.[18,19] The benzoylated sulfoxide (17) was treated with sodium acetate and acetic anhydride at reflux, resulting in a slow but smooth conversion into a new compound. Workup, followed by flash chromatography, provided the α-acetoxy sulfide (23) (91%). The stereochemistry of the newly formed centre at C 6 was assigned on the basis of the very small magnitude of the coupling constant between H 5 and H 6 ($J \approx 0$ Hz) which, by an inspection of models, could only result from the acetoxy group being present in the *exo*-configuration.[20] In a similar fashion, the triacetate (15) was treated with acetic anhydride and sodium acetate, resulting in a slightly faster conversion into the tetraacetate (24).

Both of the Pummerer rearrangements on the *exo*-sulfoxides (15) and (17) shown above were stereoselective, affording products with the same *exo*-configuration as the starting sulfoxide. This result is possibly a consequence of the migration of the acetate group through a close-contact ion pair. Alternatively, the stereoselectivity of this reaction may result from the addition of acetate to the least hindered side of an intermediate cation.[17]

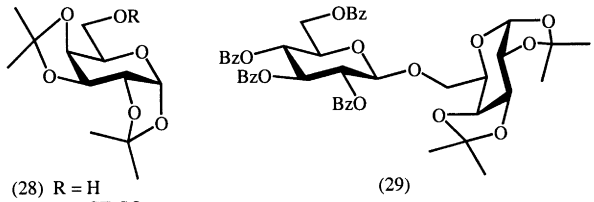
The oxidation of these α-acetoxy sulfides was the next reaction to be investigated. Thus, the α-acetoxy sulfide (23) was treated briefly with *meta*-chloroperbenzoic acid, affording two sulfoxides, (25) and (26) (a combined yield of 87%), in the ratio of 1 : 5. Again, the stereochemistry of the newly formed stereogenic centres was assigned on the basis of a downfield shift of H 2 caused by the *endo*-sulfoxide of the (*S*)-*S*-oxide (25). In these cases, the reduced stereoselectivity in the oxidation of (23) compared with that of (16) is most likely a result of the increased hindrance of the *exo*-face of (23) by the newly installed acetoxy group.

Finally, the α-acetoxy sulfide (23) was treated with an excess of DMDO, resulting in a quantitative conversion into the sulfone (27). This work provided access to a number of potential glycosyl donors, namely the sulfoxide (17), the sulfone (19), the α-acetoxy sulfide (23), and the α-acetoxy sulfone (23). Our next piece of work details investigations into the utility of these compounds as glycosyl donors.

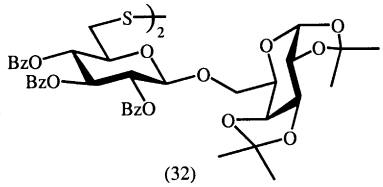
The construction of the glycosidic bond through the use of glycosyl sulfoxides has gained a great deal of popularity since the original disclosure by Kahne and coworkers that such glycosyl donors may be activated with triflic anhydride in the presence of a hindered base; even sterically hindered acceptor alcohols gave the reaction in good yield.[21] The outstanding utility of this glycosylation protocol has been demonstrated in a synthesis of the Le^a, Le^b and Le^x blood group antigenic determinants through the singular use of the sulfoxide glycosylation protocol to generate both α- and β-linkages.[22] Mechanistic studies have been performed that indicate that the actual reactive intermediate may, in fact, be a glycosyl triflate and that the reaction may be conducted with only half an equivalent of triflic anhydride.[23,24] More recently, glycosyl sulfenates have also been implicated as intermediates.[25] A number of alternative promoters for the reaction has since been developed.[24,26–30]

The established reliability of the sulfoxide glycosylation protocol prompted an investigation into the activation of the sulfoxide (17) as a glycosyl donor. Initially, however, the model sulfoxide (10) was treated with the alcohol (28) and triflic anhydride in the presence of 2,6-di-t-butylpyridine, resulting in a complex mixture of products. Repetition of this reaction, but with the omission of the base, resulted in the clean formation of the disaccharide (29) in good yield (78%). Glycosylation under Kahne's conditions with base, with benzoylated donors such as (10), has been shown to afford equimolar mixtures of orthoesters and glycosides; however, it has been shown that without base the reaction proceeds cleanly to afford glycosides in good yield.[23,26] Presumably, the sulfenic acid liberated during the reaction causes rearrangement of intermediate orthoesters to afford the desired glycosides.

Treatment of a suspension of the sulfoxide (17) and the alcohol (28) in ether with triflic anhydride afforded none of


(28) R = H
(30) R = CF_3SO_2

(29)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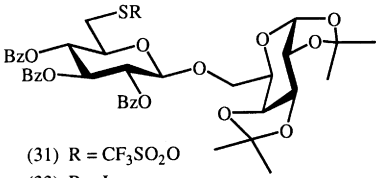
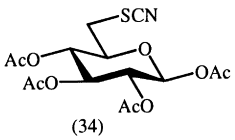

(31) R = CF_3SO_2O
(33) R = I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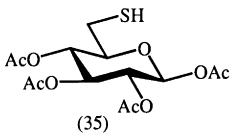
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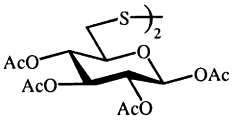
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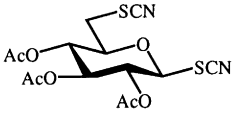
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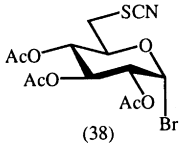
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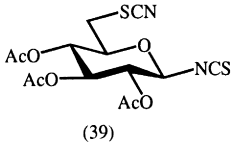
(39)

the desired disaccharide, but only the triflate (30).[31] Undoubtedly, the low solubility of the sulfoxide (17) in ether prevented glycosylation and the alternative sulfonylation reaction occurred. The reaction was repeated using 1,2-dichloroethane as the solvent; however, only polar products appeared to be formed (t.l.c). Under the assumption that this polar material arose from the decompostion of an intermediate sulfenyl triflate, e.g. (31), the reaction was attempted again but with tetrabutylammonium iodide added in order to promote the formation of the disulfide (32) by way of the sulfenyl iodide (33). Encouragingly, the disulfide (32) was formed, although in a poor yield (29%).

With these only partially successful results available, the sulfoxide method was set aside in favour of investigations into glycosylations using the sulfone (19). Again, the model sulfone (13) was the initial focus of the investigation. Ferrier and coworkers[32] and, more recently, Ley and coworkers[33,34] have reported preliminary investigations into the use of sulfones as glycosyl donors. The reaction of sulfones with alcohols is characterized by the very mild conditions required for activation, namely magnesium bromide etherate and sodium bicarbonate. Thus, a mixture of the sulfone (13), the alcohol (28), magnesium bromide etherate and sodium bicarbonate was ultrasonicated at 40° for 3 h. After this time, there appeared to be no change (t.l.c.) and the reaction was abandoned. The lack of reaction shown by the donor (13) is not overly surprising—Ley has only been able to activate 2-deoxy glycosyl sulfones, a class of sugars well known for their lability toward acid hydrolysis.[33,34] As a result, the glycosylation of the alcohol (28) with the sulfones (19) and (27) was not attempted.

The last compound to be investigated for its ability to function as a glycosyl donor was the α-acetoxy sulfide (23). By analogy with the successful use of thioglucosans as glycosyl donors, it was hoped that the thioacetal of (23) could act as a glycosyl donor. In the event, a solution of the α-acetoxy sulfide (23) and the alcohol (28) was treated with *N*-iodosuccinimide/triflic acid. After a prolonged treatment, no reaction other than degradation of the starting materials was evident and the reaction was abandoned.

We still maintained an interest in the unusual disulfide (5) and made an attempt at its synthesis. Initially, however, we treated the thiocyanate (34) with benzyltriethylammonium tetrathiomolybdate, according to the procedure of Prabhu and coworkers, to give an easily separated mixture of the thiol (35) and the disulfide (36).[35] It was hoped that an analogous treatment of the dithiocyanate (37) with the same reagent would provide the desired disulfide (5). Unexpectedly, treatment of the bromide (38) with potassium thiocyanate gave not the dithiocyanate (37), but rather the isothiocyanate (39). The change in linkage was demonstrated by the application of infrared spectroscopy and ^{13}C n.m.r. spectroscopy. At this stage, our investigations drew to a close; however, it has been reported that glycosyl thiocyanates may be readily prepared from benzoylated glycosyl bromides, with little formation of the isomeric isothiocyanates.[36]

Experimental

General experimental procedures have been given previously.[37]

Ethyl 2,3,4-Tri-O-*acetyl-6*-O-*(*p*-tolylsulfonyl)-1-thio*-β-D-*glucoside (7)*

Ethyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucoside[38,39] (2.00 g, 5.10 mmol) was suspended in dry MeOH (20 ml) and treated with a small piece of sodium metal at room temperature. The suspension rapidly dissolved and, after 20 min, t.l.c. indicated complete conversion to a higher polarity compound. The solvent was evaporated and the residue was taken up in dry pyridine (10 ml) and TsCl (1.4 g, 7.3 mmol) was added to the solution at 0°. The mixture was stirred overnight at room temperature under N_2. Ac_2O (3 ml) was added and the solution was allowed to stand for 10 min. Water (5 ml) was added and the mixture, after 10 min, was subjected to the usual workup (EtOAc). The residue, after evaporation of the solvent, was taken up in EtOH and allowed to crystallize to give the *tosylate* (7) as colourless needles (1.42 g, 55%), m.p. 116–117° (EtOH), $[\alpha]_D$ –5.9° (Found: C, 50.2; H, 5.5. $C_{21}H_{28}O_{10}S_2$ requires C, 50.0; H, 5.6%). ^1H n.m.r. (300 MHz) δ 1.19, t, *J* 7.5 Hz, CH_2CH_3; 1.96, 1.96, 2.01, 3s, 9H, Ac; 2.42, s, Ar**Me**; 2.54–2.66, m, C**H**$_2$CH$_3$; 3.72, ddd, $J_{4,5}$ 10.1, $J_{5,6}$ 3.0, 5.6 Hz, H 5; 4.02, dd, $J_{6,6}$ 11.0 Hz, H 6; 4.09, dd, H 6; 4.41, d, $J_{1,2}$ 10.1 Hz, H 1; 4.89, dd, $J_{3,4}$ 9.5 Hz, H 4; 4.92, dd, $J_{2,3}$ 9.3 Hz, H 2; 5.15, dd, H 3; 7.30–7.32, 7.72–7.75, 2m, 4H, Ar. ^{13}C n.m.r. (75.5 MHz) δ 14.81, CH_2CH_3; 20.49, 20.53, 20.64, 3C, CO**Me**; 21.62, Ar**Me**; 24.06, **C**H$_2$CH$_3$; 67.73, C 6; 68.52, 69.60, 73.57, 75.43, C 2,3,4,5; 83.37, C 1; 128.04, 129.85, 132.36, 145.12, Ar; 169.30, 169.42, 170.09, 3C, CO.

2,3,4-Tri-O-*acetyl-1,6-dideoxy-1,6-epithio*-β-D-*glucose (2)*

A solution of the tosylate (7) (516 mg, 1.02 mmol) and NaI (270 mg, 1.80 mmol) in butanone (10 ml) was heated under reflux for 2 h. The solvent was evaporated and the residue partitioned between EtOAc and water. The organic phase was separated and washed with aqueous sodium thiosulfate solution, then brine and dried. The residue was purified by flash chromatography (30% EtOAc/petrol) to afford the triacetate (2) as a clear oil (98 mg, 31%). The ^1H n.m.r. (300 MHz) spectrum of this material agreed with that reported in the literature.[4]

(R)- *and* (S)-*Phenylsulfinyl Tetra*-O-*acetyl*-β-D-*glucopyranoside (9)*

A solution of phenyl tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (8)[38,39] (220 mg, 0.500 mmol) in acetone (3 ml) was treated with DMDO (6 ml of 0.1 M in acetone, 0.6 mmol; –78°, 3 min). The solvent was evaporated under reduced pressure to afford a white, crystalline solid that was purified by flash chromatography (50–75% EtOAc/petrol) to afford the sulfoxides (9) as a white, crystalline powder (147 mg, 64%, 1 : 3). The ^1H n.m.r. spectrum was largely in accordance with that given in the literature.[40] Partial ^1H n.m.r. (300 MHz) δ 3.57, ddd, $J_{4,5}$ 10.1, $J_{5,6}$ 2.3, 5.8 Hz, H 5 minor; 3.67, ddd, $J_{4,5}$ 10.2, $J_{5,6} \approx J_{5,6}$ 3.6 Hz, H 5 major. ^{13}C n.m.r. (75.5 MHz) δ 20.32, 20.36, 20.42, 4C, Me; 61.16, 61.53, C 6; 67.16, 67.22, 67.54, 73.40, 73.60, 76.05, 76.30, C 2,3,4,5; 89.64, 91.99, C 1; 125.51–138.77, Ph; 168.76, 169.06, 169.13, 169.92, 170.15, 4C, CO.

(R)- *and* (S)-*Phenylsulfinyl Tetra*-O-*benzoyl*-β-D-*glucopyranoside (10)*

meta-Chloroperbenzoic acid (80%, 270 mg, 1.25 mmol) was added to a solution of phenyl tetra-*O*-benzoyl-1-thio-β-D-glucopyranoside (11)[41] (688 mg, 1.00 mmol) in dry CH_2Cl_2 (20 ml) at 0° under N_2. After 5 min, t.l.c. indicated a trace of starting material remaining so further *meta*-chloroperbenzoic acid (20 mg, 0.09 mmol) was added and the mixture was stirred for another 5 min. Aqueous KI solution (10%, 2 ml) and saturated aqueous $NaHCO_3$ solution (6 ml) were added and the mixture was stirred for 20 min. The mixture was washed with aqueous sodium thiosulfate solution (0.5 M) and the organic phase was separated, dried and the solvent evaporated. The residue was purified by flash chromatography (0–50% EtOAc/toluene) to give the sulfoxides (10) as a clear foam (593 mg, 84%, 2 : 3). ^1H n.m.r. (300 MHz) for the major diastereoisomer: δ 4.21, ddd, $J_{4,5}$ 9.8, $J_{5,6}$ 2.7, 4.4 Hz, H 5; 4.40, dd, $J_{6,6}$ 12.4 Hz, H 6; 4.66, dd, H 6; 4.87, d, $J_{1,2}$ 9.8 Hz, H 1; 5.54, dd, $J_{3,4}$

≈ $J_{4,5}$ 9.8 Hz, H 4; 5.70, dd, $J_{2,3}$ 9.3 Hz, H 2; 5.95, dd, H 3; 7.07–8.05, m, Ph. ^{1}H n.m.r. (300 MHz) for the minor diastereoisomer: δ 4.12, ddd, $J_{4,5}$ 9.7, $J_{5,6}$ 2.8, 6.4 Hz, H 5; 4.43, dd, $J_{6,6}$ 12.4 Hz, H 6; 4.53, dd, H 6; 4.59, d, $J_{1,2}$ 9.6 Hz, H 1; 5.61, dd, $J_{3,4}$ ≈ $J_{4,5}$ 9.7 Hz, H 4; 5.91, dd, $J_{1,2}$ ≈ $J_{2,3}$ 9.6 Hz, H 2; 6.01, dd, H 3; 7.07–8.05, m, Ph. ^{13}C n.m.r. (75.5 MHz) δ 62.11, 62.91, C 6; 67.91, 68.11, 68.34, 73.72, 73.81, 76.73, 77.08, C 2,3,4,5; 90.72, 92.93, C 1; 125.46–138.22, Ph; 164.91, 165.78, 4C, CO.

Phenylsulfonyl Tetra-O-*acetyl*-β-D-*glucopyranoside (12)*

A solution of phenyl tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (8)[38,39] (220 mg, 0.500 mmol) in acetone (2 ml) was treated with DMDO (12 ml of 0.1 M in acetone, 1.2 mmol; 0°, 5 min). The solvent was evaporated under reduced pressure to afford a white, crystalline solid. This solid was purified by flash chromatography (50% EtOAc/petrol) to give the sulfone (12) as white needles (224 mg, 95%), m.p. 189–190° (Pr^{i}OH; lit.[42] 188–189°), $[\alpha]_D$ –27.9° (lit.[43] –26.9°).

Phenylsulfonyl Tetra-O-*benzoyl*-β-D-*glucopyranoside (13)*

The 1-thio-β-D-glucoside (11) (505 mg, 734 μmol) was treated with a solution of DMDO (30 ml of 0.1 M in acetone, 3 mmol; 0°, 10 min). At this stage, t.l.c. indicated the formation of a new compound of slightly higher polarity. The solvent was evaporated and the residue was dried under vacuum to give a white, crystalline solid (535 mg). This material was taken and recrystallized to give the *sulfone* (13) as fine needles, m.p. 180–181.5° (CH_2Cl_2/petrol), $[\alpha]_D$ +1.9° (Found: C, 66.9; H, 4.6. $C_{40}H_{32}O_{11}S$ requires C, 66.7; H, 4.5%). ^{1}H n.m.r. (500 MHz) δ 4.19, ddd, $J_{4,5}$ 9.9, $J_{5,6}$ 2.7, 4.9 Hz, H 5; 4.38, dd, $J_{6,6}$ 12.4 Hz, H 6; 4.64, dd, H 6; 4.88, dd, $J_{1,2}$ 9.8 Hz, H 1; 5.50, dd, $J_{2,3}$ 9.7 Hz, H 2; 5.78, dd, $J_{3,4}$ 9.8 Hz, H 4; 5.92, dd, H 3; 7.26–7.61, 7.77–8.00, 2m, Ph. ^{13}C n.m.r. (125.8 MHz) δ 61.99, C 6; 67.63, 68.21, 73.56, 76.75, C 2,3,4,5; 89.21, C 1; 128.32–130.44, 133.27–134.49, Ph; 164.93, 165.03, 165.72, 4C, CO.

2,3,4-Tri-O-*acetyl-1,6-dideoxy-1,6-epithio*-β-D-*glucose* (R)-S-*Oxide (14) and 2,3,4-Tri*-O-*acetyl-1,6-dideoxy-1,6-epithio*-β-D-*glucose* (S)-S-*Oxide (15)*

meta-Chloroperbenzoic acid (85%, 530 mg, 2.6 mmol) was added in two portions to a solution of the triacetate (2) (608 mg, 2.00 mmol) in dry CH_2Cl_2 (10 ml) at 0° under N_2. The mixture was stirred for 10 min, then more *meta*-chloroperbenzoic acid (85%, 50 mg, 0.25 mmol) was added. The mixture was stirred (10 min) and then treated to a workup (CH_2Cl_2) as for the preparation of (10) above. Flash chromatography (60–100% EtOAc, then 10% EtOH/EtOAc) of the residue, after the removal of solvent, gave, firstly, the endo-*sulfoxide* (14) as needles (44 mg, 7%), m.p. 119–120° (EtOAc/petrol), $[\alpha]_D$ –149° (Found: C, 44.8; H, 5.3. $C_{12}H_{16}O_8S$ requires C, 45.0; H, 5.0%). ^{1}H n.m.r. (300 MHz) δ 2.06, 2.09, 2.10, 3s, 9H, Me; 3.09, dd, $J_{5,6}$ 6.8, $J_{6,6}$ 13.5 Hz, H 6; 3.21, br d, H 6; 4.63, br d, H 5; 4.78, dd, $J_{3,4}$ 8.5, $J_{4,5}$ 2.2 Hz, H 4; 5.44, dd, $J_{2,3}$ 7.3 Hz, H 3; 5.52, br s, H 1; 5.60, dd, $J_{1,2}$ 0.85 Hz, H 2. ^{13}C n.m.r. (75.5 MHz) δ 20.63, 20.78, 20.83, 3C, Me; 55.51, C 6; 65.47, 68.26, 73.38, 81.54, C 2,3,4,5; 92.95, C 1; 169.89, 169.93, 170.58, 3C, CO.

Next to elute was the exo-*sulfoxide* (15) as chunky crystals (538 mg, 84%), m.p. 122–123.5° (Pr^{i}OH), $[\alpha]_D$ –75.0° (Found: C, 45.0; H, 4.9. $C_{12}H_{16}O_8S$ requires C, 45.0; H, 5.0%). ^{1}H n.m.r. (300 MHz) δ 2.02, 2.06, 2.07, 3s, 9H, Me; 2.78, ddd, $J_{4,6}$ 0.9, $J_{5,6}$ 8.5, $J_{6,6}$ 13.6 Hz, H 6; 3.85, d, H 6; 4.39, br s, 1H, 4.67, m, 1H, 4.76, br s, H 2,3,4; 5.14, br d, H 5; 5.26, br s, H 1. ^{13}C n.m.r. (75.5 MHz) δ 20.31, 20.38, 20.45, 3C, Me; 58.46, C 6; 64.54, 66.47, 67.41, 78.33, C 2,3,4,5; 99.56, C 1; 167.44, 168.94, 169.26, 3C, CO.

1,6-Dideoxy-1,6-epithio-β-D-*glucopyranose* (S)-S-*Oxide (6)*

A suspension of the triacetate (15) (34 mg) in dry MeOH (2 ml) was treated with a small piece of sodium at room temperature for 1 h, affording a white precipitate. Water (2 ml) was added and the precipitate dissolved. Resin (Amberlite IR-120, H^+) was added until the solution became neutral and the solvent was evaporated to afford a white, crystalline solid (20 mg). Crystallization afforded the *triol* (6) as needles, m.p. 231° (MeOH), $[\alpha]_D$ –117° (H_2O) (Found: C, 36.9; H, 5.0. $C_6H_{10}O_5S$ requires C, 37.1; H, 5.2%). ^{1}H n.m.r. (300 MHz, D_2O) δ 2.63, br dd, $J_{5,6}$ 8.6, $J_{6,6}$ 13.2 Hz, H 6; 3.40, 3.60, 3.78, 3 br s, H 2,3,4; 3.99, br d, H 6; 5.13, br d, H 5; 5.19, br s, H 1. ^{13}C n.m.r. (75.5 MHz, D_2O) δ 58.73, C 6; 67.44, 68.48, 69.15, 81.51, C 2,3,4,5; 102.35, C 1.

2,3,4-Tri-O-*benzoyl-1,6-dideoxy-1,6-epithio*-β-D-*glucose* (S)-S-*Oxide (17)*

meta-Chloroperbenzoic acid (85%, 265 mg, 1.30 mmol) was added to an ice-cold solution of the tribenzoate (16) (491 mg, 1.00 mmol) in dry CH_2Cl_2 (20 ml). The mixture was stirred under argon for 5 min. The mixture was treated to a workup (CH_2Cl_2) as for the preparation of (10) above to afford a pale yellow oil. The oil was taken up in CH_2Cl_2 and crystallized upon addition of petrol to give the *sulfoxide* (17) as pale yellow needles (498 mg, 98%), m.p. 126–128° (CH_2Cl_2/petrol), $[\alpha]_D$ –50.5°. ^{1}H n.m.r. (300 MHz) δ 3.06, ddd, $J_{4,6}$ 0.93, $J_{5,6}$ 8.5, $J_{6,6}$ 13.8 Hz, H 6; 4.14, d, H 6; 4.93, br s, 1H, 5.36–5.39, m, H 2,3,4; 5.50, br d, H 5; 5.66, br s, H 1; 7.36–7.69, 8.04–8.12, 2m, 15H, Ph. ^{13}C n.m.r. (75.5 MHz) δ 59.12, C 6; 65.68, 67.46, 68.02, 78.64, C 2,3,4,5; 100.29, C 1; 127.94–130.08, 133.77, 134.33, Ph; 163.66, 164.84, 165.05, 3C, CO. High-resolution mass spectrum (f.a.b.) *m/z* 507.1163 ($C_{27}H_{23}O_8S$ [$(M+H)^{+\bullet}$] requires 507.1114).

2,3,4-Tri-O-*acetyl-1,6-dideoxy-1,6-epithio*-β-D-*glucose* S,S-*Dioxide (18)*

(A) A solution of the triacetate (2) (304 mg, 1.00 mmol) and *meta*-chloroperbenzoic acid (85%, 510 mg, 2.5 mmol) in dry CH_2Cl_2 (5 ml) was allowed to stand at room temperature for 2 days. T.l.c. analysis indicated a fast reaction, initially, to give the sulfoxide, followed by a slow reaction to give a much less polar product. The mixture was treated to a workup (CH_2Cl_2) as for the preparation of (10) above to afford a solid residue that was purified by flash chromatography (75% EtOAc/petrol) to give the *sulfone* (18) as a white, crystalline residue (320 mg, 95%). A sample was recrystallized to give fine needles, m.p. 181–182° (EtOAc/petrol), $[\alpha]_D$ –21.7° (Found: C, 43.1; H, 4.8; S, 9.9. $C_{12}H_{16}O_9S$ requires C, 42.9; H, 4.8; S, 9.5%). ^{1}H n.m.r. (300 MHz) δ 2.12, 2.14, 2.15, 3s, 9H, Me; 3.42–3.44, m, 2H, H 6; 4.72, dd, $J_{3,4}$ 4.7, $J_{4,5}$ 2.2 Hz, H 4; 4.80, br s, H 1; 4.88–4.93, m, H 5; 5.08, br dd, $J_{2,3}$ 3.7 Hz, H 3; 5.27, br d, H 2. ^{13}C n.m.r. (75.5 MHz) δ 20.67, 20.81, 3C, Me; 50.43, C 6; 67.25, 67.96, 70.41, 76.63, C 2,3,4,5; 86.63, C 1; 169.08, 169.26, 170.11, 3C, CO. Mass spectrum (f.a.b.) *m/z* 337.40 ($C_{12}H_{17}O_9S$ [$(M+H)^{+\bullet}$] requires 337.05).

(B) The triacetate (2) (76 mg, 0.25 mmol) was treated with DMDO (20 ml of 0.1 M in acetone, 2 mmol; 0°, 20 min). The solvent was evaporated under reduced pressure to afford the sulfone (18) as a white, crystalline solid (83 mg), identical by ^{1}H n.m.r. (200 MHz) spectroscopy to the material prepared above.

1,6-Dideoxy-1,6-epithio-β-D-*glucopyranose* S,S-*Dioxide (20)*

The sulfone (18) (180 mg) was suspended in dry MeOH (5 ml) at room temperature and a small piece of sodium metal was added. After 30 min, t.l.c. analysis indicated conversion into a high polarity compound. Resin (Dowex 50, H^+) was added until the solution became neutral. The mixture was filtered and the residue evaporated to afford the *sulfone* (20) as a white, crystalline solid (109 mg). A portion of this solid was crystallized as hexagonal prisms, m.p. 208–209° (MeOH), $[\alpha]_D$ –40.6° (H_2O) (Found: C, 34.7; H, 5.2. $C_6H_{10}O_6S$ requires C, 34.3; H, 4.8%). ^{1}H n.m.r. (300 MHz, D_2O) δ 3.34–3.35, m, 2H, H 6; 3.52–3.93, m, H 2,3,4; 4.77–4.80, m, H 1,5. ^{13}C n.m.r. (75.5 MHz, D_2O) δ 49.80, C 6; 67.90, 70.28, 71.53, 78.70, C 2,3,4,5; 89.14, C 1. High-resolution mass spectrum (f.a.b.) *m/z* 210.9755 ($C_6H_{11}O_6S$ [$(M+H)^{+\bullet}$] requires 211.0276).

2,3,4-Tri-O-*benzoyl-1,6-dideoxy-1,6-epithio*-β-D-*glucose* S,S-*Dioxide (19)*

The tribenzoate (16) (49 mg, 100 μmol) was treated with DMDO (10 ml of 0.1 M in acetone, 1 mmol; 0°, 2 h). T.l.c. indicated a slow but smooth conversion into a new product. The solvent was evaporated to give a white, crystalline residue (52 mg). This material was recrystal-

lized to give the *sulfone* (19) as chunky prisms, m.p. 246–248° ($CHCl_3$/petrol), $[\alpha]_D$ –26.4° (dimethyl sulfoxide, 5 ml cell) (Found: C, 62.0; H, 4.2. $C_{27}H_{22}O_9S$ requires C, 62.1; H, 4.2%). ^{1}H n.m.r. (300 MHz) δ 3.55–3.66, m, 2H, H 6; 5.08, br s, H 1; 5.12, dd, $J_{3,4}$ 4.5, $J_{4,5}$ 2.2 Hz, H 4; 5.16, m, H 5; 5.73, br d, $J_{2,3}$ 4.0 Hz, H 2; 5.79, m, H 3; 7.39–8.13, m, Ph. ^{13}C n.m.r. (75.5 MHz) δ 50.53, C 6; 68.28, 68.39, 70.95, 76.63, C 2,3,4,5; 86.93, C 1; 128.60–130.15, 133.91, 133.99, Ph; 164.87, 164.95, 165.56, 3C, CO.

*(6*R*)-6-*O*-Acetyl-2,3,4-tri*-O*-benzoyl-1,6-dideoxy-1,6-epithio*-β-D-gluco-*hexodialdo-1,5-pyranose (23)*

A mixture of the sulfoxide (17) (1.01 g, 2.00 mmol) and sodium acetate (492 mg, 6.00 mmol) in Ac_2O (25 ml) was heated under reflux under N_2 for 12 h. The solvent was evaporated under reduced pressure to give a dark oil that was subjected to the usual workup (EtOAc). The residual oil was purified by flash chromatography (0–5% EtOAc/toluene) to give the α-*acetoxy sulfide* (23) as a clear oil (1.00 g, 91%) which crystallized. A sample was recrystallized to give white needles, m.p. 123–125° (CH_2Cl_2/petrol), $[\alpha]_D$ –143.3° (Found: C, 63.3; H, 4.4. $C_{29}H_{25}O_9S$ requires C, 63.5; H, 4.4%). ^{1}H n.m.r. (300 MHz) δ 2.12, s, Me; 5.02, br d, $J_{4,5}$ 2.0 Hz, H 5; 5.09, dd, $J_{3,4}$ 5.1 Hz, H 4; 5.15, br d, $J_{2,3}$ 3.8 Hz, H 2; 5.77, br t, H 3; 5.86, br s, H 1; 6.50, br s, H 6; 7.41–7.62, 8.07–8.11, 2m, Ph. ^{13}C n.m.r. (75.5 MHz) δ 20.92, Me; 69.16, 69.96, 74.07, 82.56, 83.13, 84.36, C 1,2,3,4,5,6; 128.55–130.01, 133.66–133.76, Ph; 164.95, 165.47, 165.61, 3C, **C**OPh; 170.17, **C**OMe.

*(6*R*)-2,3,4,6-Tetra*-O*-acetyl-1,6-dideoxy-1,6-epithio*-β-D-gluco-*hexodialdo-1,5-pyranose (24)*

The sulfoxide (15) (89 mg, 280 μmol) was treated in the same manner (reflux, 8 h) as for the sulfoxide (17) to give, after flash chromatography (30–40% EtOAc/petrol), the *tetraacetate* (24) as a pale yellow oil (89 mg, 88%), $[\alpha]_D$ –218° (Found: C, 46.6; H, 4.8. $C_{14}H_{18}O_9S$ requires C, 46.4; H, 5.0%). ^{1}H n.m.r. (500 MHz) δ 2.06, 2.07, 2.11, 2.11, 4s, 12H, Me; 4.62, dd, $J_{3,4}$ 6.1, $J_{4,5}$ 2.1 Hz, H 4; 4.69–4.71, m, H 2,5; 5.12, br dd, $J_{2,3}$ 4.3 Hz, H 3; 5.53, br s, H 1; 6.24, br s, H 6. ^{13}C n.m.r. (125.8 MHz) δ 20.70, 20.81, 20.84, 4C, Me; 69.38, 69.89, 74.75, 82.43, 83.02, 84.65, C 1,2,3,4,5,6; 169.38, 169.95, 170.00, 170.21, 4C, CO.

*(6*R*)-6-*O*-Acetyl-2,3,4-tri*-O*-benzoyl-1,6-dideoxy-1,6-epithio*-β-D-gluco-*hexodialdo-1,5-pyranose* (S)-S-*Oxide (25) and (6*R*)-6-*O*-Acetyl-2,3,4-tri*-O*-benzoyl-1,6-dideoxy-1,6-epithio*-β-D-gluco-*hexodialdo-1,5-pyranose* (R)-S-*Oxide (26)*

meta-Chloroperbenzoic acid (80%, 58 mg, 280 μmol) was added to a solution of the α-acetoxy sulfide (23) (110 mg, 200 μmol) in dry CH_2Cl_2 (5 ml) at 0°. After 10 min, the mixture was treated to a workup (CH_2Cl_2) as for the preparation of (10) above. The residue, after the removal of solvent, was purified by flash chromatography (0–60% EtOAc/toluene) to give, firstly, unreacted α-acetoxy sulfide (23) (15 mg).

Next to elute was the endo-*sulfoxide* (25) as a glass (18 mg, 16%), $[\alpha]_D$ –204° (Found: C, 61.8; H, 4.5. $C_{29}H_{24}O_{10}S$ requires C, 61.7; H, 4.3%). ^{1}H n.m.r. (500 MHz) δ 2.22, s, Me; 4.76, br d, $J_{4,5}$ 2.8 Hz, H 5; 5.25, dd, $J_{3,4}$ 8.9 Hz, H 4; 5.85, br s, H 1; 6.00, d, $J_{2,3}$ 7.5 Hz, H 2; 6.24, dd, H 3; 6.27, br s, H 6; 7.13–7.61, 7.98-8.09, 2m, 15H, Ph. ^{13}C n.m.r. (125.8 MHz) δ 20.53, Me; 66.17, 68.13, 71.04, 84.16, 93.11, 95.00, C 1,2,3,4,5,6; 128.20–133.91, Ph; 165.55, 165.64, 166.08, 3C, **C**OPh; 169.47, **C**OMe.

Last to elute was the exo-*sulfoxide* (26) as needles (80 mg, 71%), m.p. 200–202° (decomposition) (CH_2Cl_2/petrol), $[\alpha]_D$ –129° (Found: C, 62.1; H, 4.4. $C_{29}H_{24}O_{10}S$ requires C, 61.7; H, 4.3%). ^{1}H n.m.r. (500 MHz) δ 2.31, s, Me; 5.16, 5.25, 5.41, 5.54, 4 br s, 4H; 5.46–5.52, m, H 1,2,3,4,5; 6.34, br s, H 6; 7.14–7.70, 8.07–8.16, 2m, 15H, Ph. ^{13}C n.m.r. (125.8 MHz) δ 20.00, Me; 65.62, 66.89, 66.95, 80.81, 86.35, 99.06, C 1,2,3,4,5,6; 128.20–133.91, Ph; 163.54, 164.80, 165.02, 3C, **C**OPh; 169.75, **C**OMe.

*(6*R*)-6-*O*-Acetyl-2,3,4-tri*-O*-benzoyl-1,6-dideoxy-1,6-epithio*-β-D-gluco-*hexodialdo-1,5-pyranose* S,S-*Dioxide (27)*

The α-acetoxy sulfide (23) (55 mg, 100 μmol) was treated with DMDO (14 ml of 0.1 M in acetone, 1.4 mmol; room temperature, 90 min), during which t.l.c. indicated a smooth conversion into one compound. The solvent was evaporated to give a white, crystalline solid (56 mg). Recrystallization gave the *sulfone* (27) as needles, m.p. 147–149° (CH_2Cl_2/petrol), $[\alpha]_D$ –80.8° (Found: C, 59.9; H, 4.4. $C_{29}H_{24}O_{11}S$ requires C, 60.0; H, 4.2%). ^{1}H n.m.r. (500 MHz) δ 2.30, s, Me; 4.99–5.01, m, H 5; 5.16, br s, H 1; 5.25, dd, $J_{3,4}$ 5.9, $J_{4,5}$ 2.7 Hz, H 4; 5.77, dd, $J_{1,2}$ 1.1, $J_{2,3}$ 4.8 Hz, H 2; 5.93, br dd, H 3; 5.95, br s, H 6; 7.24–7.63, 8.03–8.16, 2m, 15H, Ph. ^{13}C n.m.r. (125.8 MHz) δ 20.02, Me; 67.84, 68.86, 69.54, 80.54, 80.91, 88.32, C 1,2,3,4,5,6; 128.19–130.17, 133.96, 134.11, Ph; 164.93, 165.03, 165.60, 3C, **C**OPh; 169.50, **C**OMe.

*6-*O*-(Tetra*-O*-benzoyl*-β-D-*glucopyranosyl)-1,2:3,4-di*-O*-isopropylidene*-α-D-*galactose (29)*

Triflic anhydride (39 μl, 240 μmol) was added dropwise over 3 min to a suspension of the sulfoxide (10) (169 mg, 240 μmol) and the alcohol (28) (52 mg, 200 μmol) in dry Et_2O (4 ml) at 0° under N_2. After 5 min, t.l.c. indicated the absence of the starting materials, so the solution was quenched by the addition of saturated aqueous $NaHCO_3$ solution (1 ml) and the mixture stirred for 5 min. The organic layer was separated, washed with brine and dried. The solvent was evaporated and the residue purified by flash chromatography (10–20% EtOAc/toluene). The residue from chromatography was treated with Ac_2O (1 ml) and pyridine (2 ml) at room temperature for 1 h. The solvent was then evaporated and the residue purified by flash chromatography (5–10% EtOAc/toluene) to give the disaccharide (29) as a clear oil (130 mg, 78%), identical by ^{1}H n.m.r. (300 MHz) spectroscopy to that reported in the literature.[44]

1,2:3,4-Di-O*-isopropylidene-6-*O*-trifluoromethylsulfonyl*-α-D-*galactose (30)*

Triflic anhydride (29 μl, 280 μmol) was added dropwise to an ice-cold suspension of the sulfoxide (17) (122 mg, 240 μmol) and the alcohol (28) (52 mg, 200 μmol) in dry Et_2O (5 ml) at 0° under N_2. After 5 min, the mixture was quenched by the addition of saturated aqueous sodium bicarbonate solution (1 ml) and the mixture stirred for 5 min. The mixture was diluted with CH_2Cl_2 and the organic layer separated and washed with brine, then dried. The solvent was evaporated and the residue crystallized from CH_2Cl_2/petrol to give the unreacted sulfoxide (17) as needles (73 mg, m.p. 128–131°). The mother liquor was evaporated and the residue was purified by flash chromatography (50% toluene/petrol, then 0–10% EtOAc/toluene) to give the D-*galacto* triflate (30) as a clear oil (54 mg, 69%), $[\alpha]_D$ –46.1° (lit.[31] –49.9°). ^{1}H n.m.r. δ 1.33, 1.44, 1.52, 3s, 12H, Me; 4.11, ddd, $J_{4,5}$ 2.0, $J_{5,6}$ 4.6, 7.5 Hz, H 5; 4.24, dd, $J_{3,4}$ 7.8 Hz, H 4; 4.35, dd, $J_{1,2}$ 5.0, $J_{2,3}$ 2.6 Hz, H 2; 4.58, dd, $J_{6,6}$ 10.7 Hz, H 6; 4.63, dd, H 6; 4.65, dd, H 3; 5.53, d, H 1. ^{13}C n.m.r. δ 24.34, 24.81, 25.81, 25.89, 4C, Me; 66.04, 70.20, 70.35, 70.62, C 2,3,4,5; 74.64, C 6; 96.09, C 1; 109.10, 110.10, 2C, **C**Me_2; 118.56, q, $J_{C,F}$ 320 Hz, CF_3.

2,3,4-Tri-O*-benzoyl-1,6-dideoxy-1,6-epithio*-β-D-*glucose (16)*

Triflic anhydride (39 μl, 280 μmol) was added dropwise over 4 min to an ice-cold solution of the sulfoxide (17) (122 mg, 240 μmol), the alcohol (28) (52 mg, 200 μmol) and Bu_4NI (148 mg, 400 μmol) in dry 1,2-dichloroethane (5 ml) at 0° under N_2. The solution immediately became very dark and was allowed to warm to room temperature. After 5 min, t.l.c. indicated a large amount of unreacted starting material. More triflic anhydride (39 μl, 280 μmol) was added, causing the disappearance of all starting material (t.l.c.). The mixture was quenched by the addition of saturated aqueous $NaHCO_3$ solution (2 ml) and aqueous sodium thiosulfate solution (0.5 M, 5 ml). The mixture was stirred for 5 min, then the organic layer was separated and dried. The solvent was evaporated and the residue purified by flash chromatography (0–15% EtOAc/toluene) to give the tribenzoate (16) as a clear oil (30 mg, 26% based on the sulfoxide), identical by ^{1}H n.m.r. (200 MHz) spectroscopy to that reported in the literature.[45]

6,6′-O-[6,6′-Dithiobis(2,3,4-tri-O-benzoyl-6-deoxy-β-D-glucosyl)]bis(1,2:3,4-di-O-isopropylidene-α-D-galactose) (32)

Triflic anhydride (78 μl, 560 μmol) was added dropwise over 4 min to an ice-cold suspension of the sulfoxide (17) (122 mg, 240 μmol) and Bu_4NI (148 mg, 400 μmol) in dry 1,2-dichloroethane (3 ml) at 0° under N_2. The solution immediately became very dark. After 5 min, an ice-cold solution of the alcohol (28) (52 mg, 200 μmol) in dry 1,2-dichloroethane (4 ml) was added. After 5 min, t.l.c. indicated the absence of the alcohol. The mixture was quenched by the addition of saturated aqueous sodium bicarbonate solution (2 ml) and aqueous sodium thiosulfate solution (0.5 M, 10 ml). The mixture was stirred for 5 min, then the organic layer was separated and dried. The solvent was evaporated and the residue purified by flash chromatography (0–20% EtOAc/toluene). The residue was treated with pyridine (2 ml) and Ac_2O (1 ml) at room temperature for 2 h, then the solvent was evaporated under reduced pressure to give an oil which was purified by flash chromatography (10–20% EtOAc/toluene) to give the disulfide (32) as a clear oil (44 mg, 29%), identical by ^{1}H n.m.r. (200 MHz) spectroscopy to that reported in the literature.[36]

Tetra-O-acetyl-6-deoxy-6-thio-β-D-glucopyranose (35) and 6,6′-Dithiobis(1,2,3,4-tetra-O-acetyl-β-D-glucose) (36)

A mixture of tetra-*O*-acetyl-6-deoxy-6-thiocyanato-β-D-glucopyranose (34)[46] (285 mg, 733 μmol) and benzyltriethylammonium tetrathiomolybdate[47] (1.34 g, 2.20 mmol) in dry MeCN (10 ml) was stirred at room temperature under N_2 overnight. The solvent was evaporated and the dark residue was slurried with CH_2Cl_2 and filtered through a plug of silica (50% EtOAc/petrol). The solvent was evaporated and the residue purified by flash chromatography (15–40% EtOAc/petrol) to give, firstly, the thiol (35) as a powder (71 mg, 27%), m.p. 100–103° (MeOH; lit.[46] 108°), $[\alpha]_D$ +9.3° (lit.[46] +9°). ^{1}H n.m.r. (500 MHz) δ 1.74, dd, $J_{6,SH}$ 7.4, 9.6 Hz, SH; 2.00, 2.02, 2.04, 2.11, 4s, 12H, Me; 2.61, ddd, $J_{5,6}$ 6.6, $J_{6,6}$ 14.3 Hz, H 6; 2.70, ddd, $J_{5,6}$ 3.0 Hz, H 6; 3.73, ddd, $J_{4,5}$ 9.7 Hz, H 5; 5.11, m, H 2,4; 5.24, t, $J_{2,3} \approx J_{3,4}$ 9.5 Hz, H 3; 5.70, d, H 1. ^{13}C n.m.r. (125.8 MHz) δ 20.54, 20.55, 20.63, 20.79, 4C, Me; 25.73, C 6; 70.15, 70.30, 72.76, 74.88, C 2,3,4,5; 91.64, C 1; 168.98, 169.23, 169.50, 170.10, 4C, CO.

Next to elute was the disulfide (36) as a microcrystalline powder (105 mg, 39%), m.p. 162–164° (MeOH; lit.[48] 164–165°), $[\alpha]_D$ +16.7° (lit.[48] +15.2°). ^{1}H n.m.r. (500 MHz) δ 2.00, 2.02, 2.05, 2.12, 4s, 12H, Me; 2.86, dd, $J_{5,6}$ 7.2, $J_{6,6}$ 14.2 Hz, H 6; 2.98, dd, $J_{5,6}$ 3.4 Hz, H 6; 3.88, ddd, $J_{4,5}$ 9.3 Hz, H 5; 5.02, t, $J_{3,4} \approx J_{4,5}$ 9.3 Hz, H 4; 5.11, dd, $J_{1,2}$ 8.3, $J_{2,3}$ 9.3 Hz, H 2; 5.23, t, $J_{2,3} \approx J_{3,4}$ 9.3 Hz, H 3; 5.71, d, H 1. ^{13}C n.m.r. (125.8 MHz) δ 20.55, 20.56, 20.69, 20.76, 4C, Me; 41.43, C 6; 70.29, 70.72, 72.67, 73.01, C 2,3,4,5; 91.60, C 1; 168.86, 169.24, 169.59, 170.06, 4C, CO.

2,3,4-Tri-O-acetyl-6-deoxy-6-thiocyanato-β-D-glucosyl Isothiocyanate (39)

A solution of 2,3,4-tri-*O*-acetyl-6-deoxy-6-thiocyanato-α-D-glucosyl bromide (38)[46] (1.01 g, 2.46 mmol) and KSCN (748 mg, 7.71 mmol) in *N,N*-dimethylformamide (20 ml) was heated at 65° under N_2 for 2 h. The solvent was evaporated and the residue was partitioned between EtOAc and water. The organic phase was separated and washed sequentially with water and brine then dried ($MgSO_4$). The solvent was evaporated and the residue purified by flash chromatography (15% EtOAc/toluene) to afford a pale yellow solid. The solid was recrystallized to afford the isothiocyanate (39) as colourless plates (298 mg, 30%), m.p. 108–110° (EtOH), $[\alpha]_D$ +91.8° (Found: C, 43.2; H, 4.4. $C_{14}H_{16}N_2O_7S_2$ requires C, 43.3; H, 4.2%). I.r. (NaCl) ν_{max} 2157 (sharp, moderate SCN), 2023 (br, strong NCS), 1754 (strong CO) cm^{-1}. ^{1}H n.m.r. (300 MHz) δ 2.01, 2.07, 2.10, 3s, 9H, Me; 2.99, dd, $J_{5,6}$ 8.1, $J_{6,6}$ 14.1 Hz, H 6; 3.23, dd, $J_{5,6}$ 2.3 Hz, H 6; 3.83, ddd, $J_{4,5}$ 9.8 Hz, H 5; 4.98, t, $J_{3,4} \approx J_{4,5}$ 9.8 Hz, H 4; 5.03–5.12, m, 2H, H 1,2; 5.18–5.26, m, H 3. ^{13}C n.m.r. (75.5 MHz) δ 20.44, 20.53, 4C, Me; 35.16, C 6; 70.30, 71.77, 71.91, 74.26, C 2,3,4,5; 83.36, C 1; 111.35, SCN; 145.12, NCS; 168.96, 169.54, 169.85, 3C, CO.

Structure Determinations of (20) and (22)

Unique room-temperature single counter/'four-circle' diffractometer data sets were measured (2θ/θ scan mode; monochromatic Mo Kα radiation, λ 0.7107$_3$ Å; *T c.* 295 K) yielding *N* independent reflections, N_o with $I > 3(I)$ 'observed' absorption corrected reflections being used in the full-matrix least-squares refinements, anisotropic thermal parameter forms being refined for the non-hydrogen atoms; $(x, y, z, U_{iso})_H$ were refined for (20) and constrained at estimated values (hydroxy H located in difference maps) for (22), in which two molecules comprise the asymmetric unit. Conventional residuals *R*, R_w [statistical weights, derivative of $\sigma^2(I) = \sigma^2(I_{diff}) + 0.0004\sigma^4(I_{diff})$] on $|F|$ are quoted; neutral atom complex scattering factors were employed, computation using the Xtal 3.4 program system.[49] Pertinent results are given in Fig. 1 and Tables 1 and 2. Full details of atom coordinates, thermal parameters, non-hydrogen geometries, and structure factor amplitudes have been deposited.† Chiralities as determined crystallographically are concordant with those expected from the chemistry.

Table 2. Ring torsion angles (degrees) of glucosan derivatives (1), (6), (20), (21), (21*) and (22)
Atoms are denoted by number only, heteroatoms are italicized. Compound (21*) is the triacetate of (21)

Atoms	(21)[A,B]	(21*)[C]	(1)[D]	(6)[E]	(20)[F]	(22)[F]
5–1–2–3	–57.5(3), –57.3(3)	–53.7(4)	–53.5(2)	–55.3(4), –57.6(3)	–47.9(3)	–25(1), –56(1)
1–2–3–4	35.2(3), 35.3(3)	30.3(4)	37.2(2)	42.9(4), 43.1(4)	32.0(3)	–37(1), 37(1)
2–3–4–5	–35.1(3), –35.2(3)	–32.1(4)	–39.5(2)	–44.6(4), –42.8(4)	–36.9(3)	52(1), –37(1)
3–4–5–*5*	55.8(3), 55.8(2)	55.7(4)	57.5(2)	59.2(4), 54.8(4)	55.9(3)	–5(1), 54(1)
4–5–*5*–1	–75.3(3), –75.4(2)	–75.4(3)	–73.5(2)	–71.8(4), –68.8(4)	–71.1(3)	–58.4(9), –7(1)
5–*5*–1–2	75.8(3), 76.0(2)	75.3(3)	71.3(2)	70.1(4), 70.8(4)	67.3(3)	75.4(8), 73(1)
1–1–*5*–5	–43.6(7), –43.3(2)	–43.2(3)	–50.7(2)	–51.2(3), –51.2(3)	–54.2(2)	–44.8(8) –52.5(7)
1–*5*–5–6	43.9(3), 43.9(2)	44.6(3)	50.8(2)	51.6(4), 53.8(4)	51.2(3)	63.5(9), 54.3(9)
5–5–6–*1*	–28.6(3), –28.7(2)	–30.4(3)	–26.7(2)	–27.6(3), –30.8(4)	–21.0(3)	–47.1(9), –29.4(9)
5–6–*1*–1	3.1(3), 3.3(3)	4.7(3)	–1.4(7)	–0.7(3), 2.6(3)	–8.0(2)	18.5(8), 0.9(6)
6–*1*–1–*5*	24.8(3) 24.5(3)	23.4(3)	29.4(2)	28.2(3), 26.8(3)	35.4(2)	14.1(7), 28.7(6)
1–1–2–3	58.9(3), 58.5(3)	62.7(3)	63.3(2)	60.8(3), 59.8(4)	65.2(3)	91.2(9), 64(1)
2–1–*1*–6	–94.1(3), –93.9(3)	–96.4(3)	–90.0(2)	–91.0(3), –94.0(3)	–85.1(2)	–105.3(8), –92.9(9)
3–4–5–6	–56.4(3), –56.3(3)	–56.8(3)	–62.2(2)	–59.3(4), –62.9(4)	–62.6(3)	–12.3(1), –67(1)
4–5–6–*1*	88.5(3), 88.1(3)	86.6(3)	93.5(2)	92.1(3), 89.6(3)	98.8(3)	74(1), 92(1)

[A] Two determinations. [B] Ref. 15 and Lindberg, K. B., *Acta Chem. Scand., Ser. A*, 1974, **28**, 1181. [C] Leung, F., and Marchessault, R. H., *Can. J. Chem.*, 1974, **52**, 2516. [D] Ref. 16. [E] Ref. 7; molecules 1 and 2. [F] This work; molecules 1 and 2 for compound (22).

† Copies are available, until 31 December 2005, on application to the Australian Journal of Chemistry, P.O. Box 1139, Collingwood, Vic. 3066.

Crystal/Refinement Data

Compound (20). $C_6H_{10}O_6S$, *M* 210.2. Orthorhombic, space group $P2_12_12_1$ (D_2^4, No. 19), *a* 10.867(2), *b* 10.463(2), *c* 6.965(2) Å, *V* 792.$_0$ Å^3. D_c(*Z* = 4) 1.76$_3$ g cm^{-3}; *F*(000) 440. μ_{Mo} 4.1 cm^{-1}; specimen: 0.25 by 0.30 by 0.50 mm; $A^*_{min,\ max}$ 1.10, 1.14 (Gaussian correction). $2\theta_{max}$ 55°; *N* 1030, N_o 976; *R* 0.028, R_w 0.036 (preferred hand).

Compound (22). $C_6H_{10}O_4Se$, *M* 225.1. Monoclinic, space group $P2_1$ (C_2^2, No. 4), *a* 9.357(4), *b* 6.660(4), *c* 12.593(3) Å, β 106.28(3)°, *V* 792.$_3$ Å^3. D_c(*Z* = 4) 1.98$_5$ g cm^{-3}; *F*(000) 448. μ_{Mo} 49 cm^{-1}; specimen: 0.20 by 0.16 by 0.22 mm; $A^*_{min,\ max}$ 2.4, 2.9 (analytical correction). $2\theta_{max}$ 60°; *N* 2359, N_o 1518; *R* 0.050, R_w 0.046 (preferred hand).

Hydrogen Bonding

Hydroxyl assignments are complemented by observed/implied hydrogen-bonding interactions: in (20), O(2),H$_0$(2)···O(11) (*x* – ½, ½ – *y*, 1 – *z*) are 2.814(3), 2.24(3); O(3)···O(4) (1 – *x*, 1½ + *y*, 1½ – *z*) 2.901(3), 2.26(4); O(4),H$_0$(4)···O(2) (1½ – *x*, 1 – *y*, ½ + *z*) 2.800(3), 1.92(4); in (22), O(12),H$_0$(12)···O(24) (*x̄*–1, 1½ + *y*, *z̄*) 2.86(1), 2.$_5$ (est.); O(14)···O(23) 2.80(1) (1.$_9$); in (24), H$_0$(24)···O(22) (1 – *x*, ½ + *y*, 1 – *z*) 2.798(8) (2.$_1$) Å, for O···O < 3 Å.

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