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Synthesis of Thiodisaccharide Sulfoxides and Sulfones – Determination of the Configuration of the Sulfur Stereocentre

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The oxidation of per-*O*-acetyl *S*-(1→3)- and *S*-(1→4)-linked thiodisaccharides containing glucose, gulose and galactose residues with an excess of *m*-chloroperbenzoic acid gave the corresponding sulfoxides or sulfones. Sulfones were formed when the oxidation reaction was left for longer times. The sulfoxides were obtained as diastereomeric mixtures due to the chirality of the sulfur atom. Both diastereoisomers of the *S*-(1→3)-linked thiodisaccharide sulfoxides were isolated by column chromatography, whereas the *S*-(1→4)-linked analogues could not be separated. The absolute configuration of the sulfur stereocentre of the sulfoxides was assigned using NMR spectroscopy, taking into account the preferred conformations of the molecules, and the shielding/deshielding of proton signals caused by the anisotropy of the S=O bond and related effects. Most of the thiodisaccharide sulfoxides were successfully *O*-deacetylated with MeOH/Et_3N/H_2O, but the sulfones underwent elimination reactions under these conditions. Therefore, the oxidation was performed on unprotected thiodisaccharides, and the corresponding sulfones were obtained in very good yields.

Introduction

Thiooligosaccharides have attracted attention in the area of glycobiology as tools for studying various biological processes.[1] They are particularly useful probes for enzyme inhibition studies. The replacement of the interglycosidic oxygen atom by a sulfur atom in thiooligosaccharides generally gives stability to the thioglycosidic linkage towards hydrolysis by glycosidases, and increases the potential of such molecules to act as inhibitors of these enzymes.[2] In our laboratory, we have synthesized a number of thiodisaccharides that proved to be inhibitors of specific glycosidases.[3–7] The molecular basis of the inhibition of the β-galactosidase from *E. coli* by selected *S*-disaccharides has been studied by using a combination of NMR spectroscopy and molecular modelling techniques.[8]

The sulfur atom of thiosugars can be oxidized to the corresponding sulfoxides or sulfones. Many such molecules have been shown to have interesting biological activities. Thus, Witczak and co-workers[9] studied the oxidation of 3-deoxy-*S*-(1→4)-disaccharides, and the diasteromeric mixtures of the resulting *S*-oxides inhibited the proliferation of selected murine and human tumor cell lines. Cumpstey et al.[10] have prepared pseudodisaccharides non-glycosidically linked through sulfoxide or sulfone groups, and these compounds were tested for binding to proteins. The oxidation of carbohydrate molecules that contain more than one sulfur atom has been described. For instance, the oxidation of 1,5-dithioglycopyranosides took place at the *endo* or the *exo* sulfur atom.[11,12] Some thiosugar thioglycosides have been oxidized to give sulfoxides that differ in the oxidation site (*endo* or *exo*) and/or the chirality of the respective sulfur atoms.[13] Similarly to their precursors, these sulfoxides showed oral antithrombotic activity, which depended on both the location and the configuration of the sulfoxide.

The synthesis of chiral non-racemic sulfoxides has been a subject of constant interest, as these compounds have been used in numerous asymmetric reactions, including Michael addition, C–C bond formation, carbonyl reduction, Diels–Alder cycloaddition, etc.[14] In the field of carbohydrates, selectively protected monosaccharides have been used as chiral sulfinate derivatives, which are useful for the synthesis of both enantiomers of dialkyl, diaryl, or alkyl aryl sulfoxides.[14,15] Moreover, sulfoxides derived from common thioglycosides are widely used as glycosyl donors in glycosylation reactions. Since its introduction in 1989, Kahne's sulfoxide glycosylation method[16] has proved to be one of the more powerful techniques available for the formation of glycosidic bonds.[17] The application of this procedure to a wide range of carbohydrates, including extremely complex and sensitive ones, has prompted the development of highly efficient reactions for the oxidation of thioglycosides and for the determination of the configuration of the sulfur atom.[18] It has been established that the diastereoselectivity of the oxidation depends on the stereochemistry of the monosaccharide, the anomeric configuration, and the nature of the substituents on the hydroxy

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groups, among many other factors. For the assignment of the configuration of sulfoxides, NMR methods, molecular modelling, and X-ray crystallography have been used.[18–21]

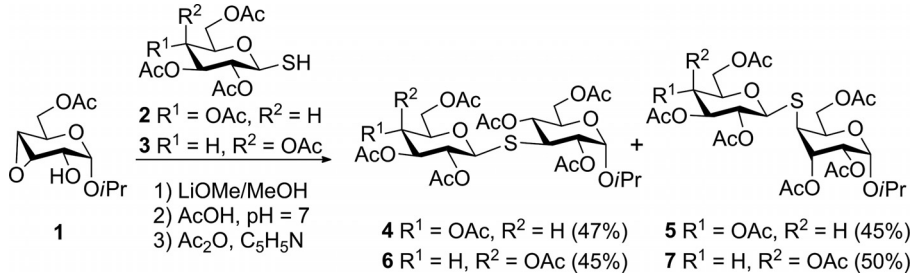
In this paper, we describe the synthesis of *S*-oxide (i.e., sulfoxide) and *S*,*S*-dioxide (i.e., sulfone) derivatives of *S*-(1→3)- and *S*-(1→4)-linked thiodisaccharides. The configuration of the sulfur chiral centre of the sulfoxides was assigned using NMR spectroscopy, taking into account the shielding and deshielding effects caused by the relative orientation of the sulfoxide group in the preferred conformation of the molecules. The unprotected sulfoxide and sulfone thiodisaccharides were also synthesized.

Results and Discussion

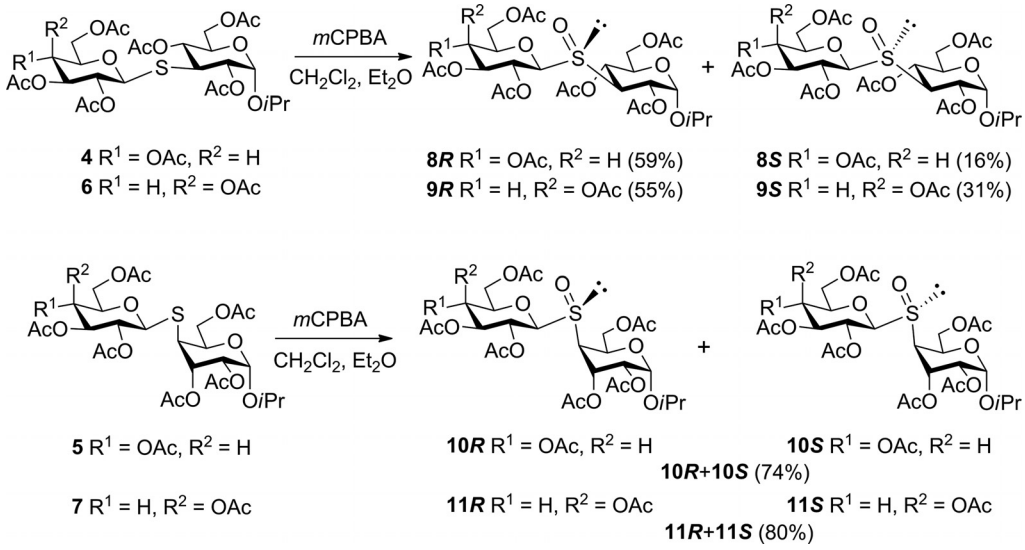
Thiodisaccharides **4**–**7** were prepared (45–50% yield) by the ring-opening reaction of the epoxide functionality of sugar oxirane **1**, with 1-thioaldose derivatives **2** and **3** as nucleophiles (Scheme 1).[7,22] The thiodisaccharides have *S*-(1→3)- or *S*-(1→4)-linkages, and have Glc*p* or Gal*p* units at the non-reducing end.

The interglycosidic sulfur atom of compounds **4**–**7** was oxidized with an excess of *m*-chloroperbenzoic acid (*m*CPBA) at room temperature for 2 h, to give the corresponding sulfoxides (Scheme 2). For example, the oxidation of *S*-(1→3)-linked disaccharide **4** gave a mixture of diastereoisomeric sulfoxides (ratio ca. 4:1), which could be separated by column chromatography. The structures of the products and the chiralities of the respective sulfoxide groups were established by the use of high-field 1D and 2D-NMR spectroscopy. The major product of the oxidation reaction of **4**, the chromatographically less polar sulfoxide, was assigned the *R* configuration, as described below. For the assignment of configuration, it was necessary to determine the conformation of the starting thiodisaccharide (i.e., **4**) and also those of the oxidation products (i.e., **8***R* and **8***S*). Analysis of the coupling constants indicated that, as expected, both of the glucopyranose residues of **4** adopt the $^4C_1$ conformation. The NOESY spectrum confirmed this conclusion, since the 4-thio-Glc*p* unit showed characteristic intraresidue NOE enhancements between 2-H and 4-H, and between 3-H and 5-H. Similarly, the Glc*p* non-reducing terminal residue showed cross-peaks for 1′-H with both 3′-H and 5′-H, and for 2′-H with 4′-H, consistent with a $^4C_1$ conformation for this residue.

The conformation of thiodisaccharides has been studied using a combination of theoretical calculations and NMR spectroscopy.[8,23] Due to the length and flexibility of the C–S bond, many conformations may be formed by rotation through the torsion angles ϕ (i.e., 1′-H–C-1′–*S*–C-4) and ψ (i.e., C-1′–*S*–C-4–4-H). The presence of characteristic inter-residue NOE enhancements has been used to experimen-



Scheme 1. Synthesis of thiodisaccharides **4**–**7**.



Scheme 2. Oxidation of thiodisaccharides **4**–**7** to give diasteromeric sulfoxides **8**–**11**.

tally detect the existence of conformers formed by rotation through the ϕ and ψ torsion angles.[7,8,23] The NOESY spectrum of **4** showed interresidue NOE enhancements between 1′-H and 3-H, and between 1′-H and 4-H, which seems to confirm the respective *syn* ϕ/*syn* ψ and *syn* ϕ/*anti* ψ conformations around the thioglycosidic linkage. It has been reported that these conformations are preferred for the analogous thiodisaccharides,[8,23] and it is worth mentioning that they are stabilized by the favourable interactions of the sulfur lone-pair disposed *anti* to the C-1′–O-1′ bond (the *exo*-anomeric effect).

Similarly to thiodisaccharide **4**, the NMR spectra of **8***R* and **8***S* the coupling constants for the 2-H, 3-H, and 4-H protons of both Glc*p* units were large, indicating that these protons were axially orientated, and that both rings of **4** had $^4C_1$ conformations. The intraresidue NOE enhancements observed (i.e., 3-H–5-H, 1′-H–3′-H, 1′-H–5′-H, and 2′-H–4′-H) confirmed the $^4C_1$ conformation for the Glc*p* units of sulfoxide **8***R*. Cross-peaks observed between 1′-H and 3-H, and between 1′-H and 4-H in the NOESY spectrum of this compound suggest the presence of the *syn* ϕ/*syn* ψ and *syn* ϕ/*anti* ψ conformers, respectively (a weak correlation between 1′-H and 2-H was also observed; Figure 1). Interestingly, both thiodisaccharide **4** and its sulfoxide **8***R* seem to adopt the same conformations for the thioglycosidic linkage, probably due to the fact that these conformers are stabilized by the *exo*-anomeric effect. In agreement with our results, it has been reported that common β-*R*-sulfinyl glycosides exist in a major conformation stabilized by the *exo*-anomeric effect.[20]

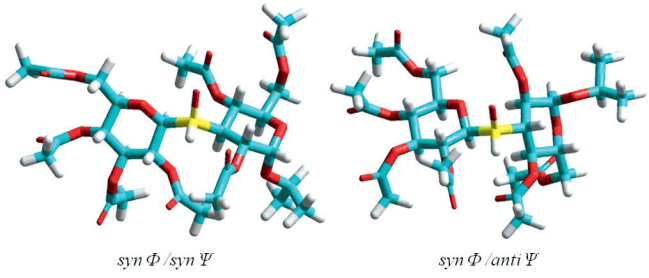


Figure 1. Conformations of **8***R*, based on NOE enhancements.

The anisotropy of the sulfoxide bond has been used to predict the configuration of the corresponding sulfur atom.[24] It has been assumed that the anisotropy of the S=O bond is acetylenic in character, with axial symmetry, and with the shielding cones oriented along the S=O bond.[25] However, additional shielding–deshielding effects must also be considered.[24–26] For instance, hydrogen atoms that are *a anti*-axial to the lone-pair electrons of the sulfoxide group are subject to a shielding influence. In contrast, significant deshielding is observed for protons that have a *syn*-axial relationship to the S=O bond.

The absolute configuration of sulfoxides **8** was assessed, taking into account the conformations deduced by NMR and by NOE experiments, as well as the anisotropy of the sulfoxide group and the resulting shielding/deshielding effects mentioned above. For each experimentally determined conformer, a minimum energy structure was calculated using molecular mechanics (MM+), and from these structures, the orientation of each proton relative to the S=O bond was established. It was evident that the major product of the oxidation of **4** had the *R* configuration, as this particular diastereoisomer explains the upfield and downfield shifts shown in Table 1. Thus, the *syn* ϕ/*syn* ψ conformation of **8***R* shows *syn*-axial interactions of the S=O group with 2′-H, 2-H, and 4-H, and the respective signals in the ^{1}H NMR spectrum should undergo the observed downfield shifts. Similarly, in the *syn* ϕ/*anti* ψ conformation of **8***R*, the C-3–3-H bond bisects the angle between the O–S bond and the lone-pair; thus, it lies in the deshielding zone of the S=O group and so the 3-H signal is also deshielded. Furthermore, in both of these two conformations, 2′-H experiences a *syn*-axial effect with the sulfoxide group, and so the 2′-H signal is the most deshielded. In contrast, 1′-H is located within the anisotropic shielding zone, and hence the 1′-H signal is slightly shielded relative to the corresponding resonance in **4**.

Table 1. Chemical shift differences between thiodisaccharide and sulfoxide protons.

	Chemical shift δ [ppm]					
	1-H	1′-H	2-H	2′-H	3-H	4-H
8*R*	5.27	4.75	5.17	5.52	3.56	5.23
8*S*	5.20	4.62	5.01	5.32	3.94	5.35
4	5.10	4.78	4.82	4.93	3.26	4.91
$\Delta\delta_{\mathbf{4}-\mathbf{8}R}$[a]	–0.17	0.03	–0.35	–0.59	–0.30	–0.32
$\Delta\delta_{\mathbf{4}-\mathbf{8}S}$	–0.10	0.16	–0.19	–0.39	–0.68	–0.44
9*R*	5.27	4.73	5.18	5.73	3.54	5.23
9*S*	5.20	4.59	5.03	5.55	3.90	5.34
6	5.10	4.77	4.82	5.14	3.27	4.92
$\Delta\delta_{\mathbf{6}-\mathbf{9}R}$	–0.17	0.04	–0.36	–0.59	–0.27	–0.31
$\Delta\delta_{\mathbf{6}-\mathbf{9}S}$	–0.10	0.18	–0.21	–0.41	–0.63	–0.42
10*R*	5.16	4.62	5.26	5.49	5.64	3.39
10*S*	5.08	4.54	4.65	5.46	5.26	3.63
5	5.03	4.71	5.35	5.06	5.32	3.30
$\Delta\delta_{\mathbf{5}-\mathbf{10}R}$	–0.13	0.09	0.09	–0.43	–0.32	–0.09
$\Delta\delta_{\mathbf{5}-\mathbf{10}S}$	–0.05	0.17	0.70	–0.40	0.06	–0.33
11*R*	5.15	4.58	5.25	5.68	5.64	3.40
11*S*	5.08	4.47	4.67	5.67	5.23	3.65
7	5.03	4.68	5.34	5.24	5.35	3.28
$\Delta\delta_{\mathbf{7}-\mathbf{11}R}$	–0.12	0.10	0.09	–0.44	–0.29	–0.12
$\Delta\delta_{\mathbf{7}-\mathbf{11}S}$	–0.05	0.21	0.67	–0.43	0.12	–0.37

[a] Positive values indicate shielding of the sulfoxide protons, and negative values, deshielding.

The ^{1}H NMR spectrum of the other sulfoxide isolated (i.e., **8***S*) showed complete overlap of the 2′-H and 3′-H signals, which appeared as multiplet due to second-order effects. In the NOESY spectrum of **8***S*, interresidue NOE enhancements were detected between 1′-H and 3-H, between 1′-H and 4-H, and between 2-H and 2′-H (or 3′-H). These contacts are indicative of the coexistence of the *syn* ϕ/*syn* ψ, *syn* ϕ/*anti* ψ, and *anti* ϕ/*anti* ψ forms in the conformational equilibrium (Figure 2). Although the 2′-H and 3′-H signals were overlapping, inspection of molecular models, or structures calculated by molecular mechanics, showed that the distance between 2-H and 3′-H would always be

too long for an NOE to be detected. Therefore, the cross-peak observed should be due to enhancement between 2-H and 2′-H, and the *anti* ϕ/*anti* ψ conformation implied by this NOE is the only one stabilized by the *exo*-anomeric effect. The presence of the *anti* ϕ/*anti* ψ and *syn* ϕ/*anti* ψ conformations would explain the downfield shift observed for the signals of 3-H and 4-H, and the slight upfield shift for 2-H, relative to those of **4**, due to the anisotropy of the sulfoxide. The 1′-H proton should be shielded, while 2′-H should be deshielded, in the *syn* ϕ/*anti* ψ and *syn* ϕ/*syn* ψ conformations, and the opposite effects should be expected for the *anti* ϕ/*anti* ψ conformer. The position of the S=O bond in the *syn* ϕ/*syn* ψ conformation suggested that 2-H, 3-H, and 4-H should be deshielded. As a result of an averaging of the opposing effects operating in **8***S*, the signals of 3-H, 4-H, and 2-H should be more strongly deshielded than the corresponding resonances in **4**, and this is consistent with experimental observation.

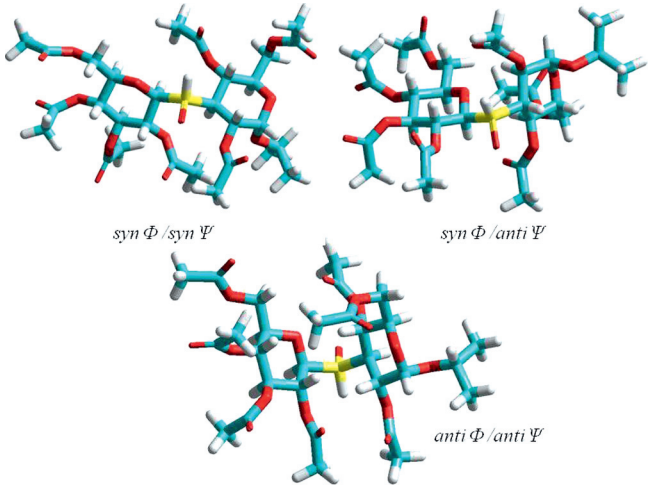


Figure 2. Conformations of **8***S*, based on NOE enhancements.

In agreement with our assignments, an *R*-glucosyl sulfoxide adopts, in the crystalline state,[19] an atomic arrangement similar to the *syn* ϕ/*syn* ψ conformation detected in solution for **8***R*. Furthermore, consistent with the behaviour of common xylopyranosyl[18] and glucopyranosyl[19,20] sulfoxides, the 2-H signal vicinal to the S=O group is shifted further downfield in the *R* isomer of the thioglycoside sulfoxide than it is in the *S* isomer. Also, in glucopyranosyl and xylopyranosyl sulfoxides, the anomeric carbon signal of the *R* diastereomer appears further upfield than that of the *S* diastereoisomer, and this too was observed for **8***R* and **8***S*.

An analysis similar to that used with **8***R* and **8***S* was carried out on sulfoxides **9***R* and **9***S*, which were obtained by oxidation of *S*-(1→3)-linked disaccharide **6**. Diastereoisomers **9***R* and **9***S* were formed in a 2:1 ratio, and they were separated by column chromatography. The change of the configuration of the distal C-4′ in **9**, compared to **8**, is expected to have practically no effect on the conformation of the interglycosidic linkage. Therefore, the shielding/deshielding effects on the protons in the neighbourhood of the S=O bond should be approximately the same. In fact, the observed chemical shift differences for **8***R* and **9***R*, as well as for **8***S* and **9***S*, with respect to the corresponding thiodisaccharides (i.e., **4** and **6**, respectively), are almost identical. The absolute configuration of *R*- and *S*-β-galactopyranosyl sulfoxides has been determined by X-ray crystallography, and the data reported is in agreement with our conclusions.[27]

The *m*CPBA oxidation of the sulfur atom of *S*-(1→4)-linked disaccharides **5** and **7** was also conducted. Diastereoisomeric mixtures of sulfoxides **10***R*,*S* and **11***R*,*S* were obtained in 74 and 80% overall yields, respectively. Unfortunately, in these cases, all the attempts to separate the diastereoisomers by column chromatography were unsuccessful. However, the NMR spectra of the mixtures of **10***R*,*S* and **11***R*,*S* were rather well resolved, and many of the signals of each individual isomer could be identified. In contrast, the NOESY spectra of **10***R*,*S* and **11***R*,*S* were quite complex, due to signal overlap, and the assignment of cross-peaks was not reliable. Based on the chemical shifts of the 2′-H and C-1 signals for the two diastereoisomers of **10**, the major component of the mixture ($\Delta\delta_{2'\text{-H}}$ = 0.03 ppm, $\Delta\delta_{\text{C-1}'}$ = –0.3 ppm) should have the *R* configuration. This isomer showed a strong downfield shift of the 2′-H and 3-H signals compared with the respective resonances in **6** (Table 1). To assign the configuration of sulfoxide **10**, we first recorded the NOESY spectrum of precursor thiodisaccharide **5**. Interresidue NOE enhancements were observed between 1′-H and 4-H, and between 2′-H and 4-H, characteristic of the *syn* ϕ/*syn* ψ and *anti* ϕ/*syn* ψ conformations, respectively. These two conformations are stabilized by the *exo*-anomeric effect. An additional NOE detected between 1′-H and 2-H suggested the presence of the *syn* ϕ/*anti* ψ conformation.

We assumed that similarly to **8***R* and other *R*-sulfinyl glycosides,[19,20] sulfoxide **10***R* adopts the conformations stabilized by the *exo*-anomeric effect, similar to those found for **5** (i.e., *syn* ϕ/*syn* ψ, *anti* ϕ/*syn* ψ and *syn* ϕ/*anti* ψ). The shielding/deshielding effects of the sulfoxide group operating in the *syn* ϕ/*syn* ψ form would suggest deshielding of the 2′-H, 2-H, and 3-H protons, and shielding of 1′-H and 4-H. In contrast, in the *anti* ϕ/*syn* ψ conformer, a downfield shift would be expected for the resonances of 1′-H, 2′-H, and 4-H, and an upfield shift for 2-H and 3-H. Analysis for the *syn* ϕ/*anti* ψ conformation predicted shift differences similar to those of the *syn* ϕ/*syn* ψ conformation, except for 4-H, which in this case should be shielded. Furthermore, in this conformation, 3-H undergoes further deshielding because of a *syn*-axial interaction with the sulfoxide group. Therefore, as result of an average of all the effects in the conformational equilibrium, the 2′-H and 3-H signals should be the most deshielded, as is observed experimentally.

The chemical shifts for 1′-H and 2′-H in **10***S* were similar to those of the corresponding protons in **10***R*, which suggested a similar chemical environment for these protons in both diasteroisomers. However, analysis of the effect of the anisotropy of the sulfoxide group on the vicinal protons could not be performed, as no experimental data was avail-

able to determine the conformation of the thioglycosidic linkage.

To determine the configuration of the sulfoxides of penicillin, Cooper and co-workers[24] used the McConnell point dipole approximation[28] to relate the sign and the magnitude of the chemical shift of a given proton to its spatial position relative to an anisotropic group with axial symmetry. We used this approach to check whether the calculated shifts matched with those qualitatively predicted. The expression used for the nuclear screening was:

$$\sigma = \Delta\chi \frac{(1 - 3cos^2\theta)}{3R^3} \quad (1)$$

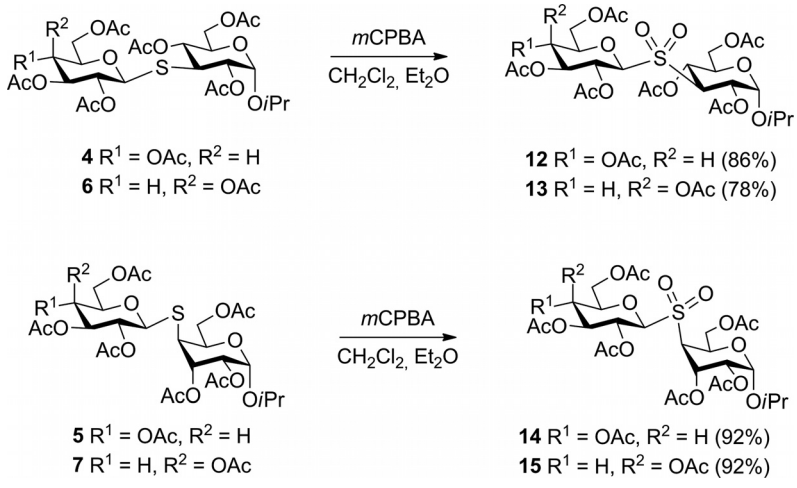
where R is the distance between the proton under study and the electrical centre of gravity of the anisotropic bond, θ is the angle between the direction R and the symmetry axis of the anisotropic bond, and $\Delta\chi$ (-32.2×10^{-30} cm^3 molecule^{-1}) is the anisotropy constant. Equation (1) was applied to selected sulfoxides, bearing in mind the assumptions and restrictions described by Cooper et al.[24] The distance R and the angle θ were measured from the conformation that corresponded to a local minimum energy calculated by molecular mechanics. For example, for the *syn* ϕ/*syn* ψ conformer of **10***R*, the σ values, defined as $\sigma = (\delta_{thiodisaccharide} - \delta_{sulfoxide})$, were calculated as follows: $\sigma_{2\text{-H}} = +0.50$, $\sigma_{3\text{-H}} = -0.14$, $\sigma_{4\text{-H}} = +0.34$, $\sigma_{1'\text{-H}} = +0.42$, and $\sigma_{2'\text{-H}} = -0.54$ (2′-H is shifted further downfield by an additional *syn* axial interaction with the S=O bond). Negative σ values indicate upfield shifts, and positive values, downfield shifts. The σ values for the *anti* ϕ/*syn* ψ were $\sigma_{2\text{-H}} = +0.34$, $\sigma_{3\text{-H}} = +0.31$, $\sigma_{4\text{-H}} = -0.31$, $\sigma_{1'\text{-H}} = -0.61$, and $\sigma_{2'\text{-H}} = -0.08$, and those for the *syn* ϕ/*anti* ψ were $\sigma_{2\text{-H}} = -0.06$, $\sigma_{3\text{-H}} = -0.46$, $\sigma_{4\text{-H}} = -0.48$, $\sigma_{1'\text{-H}} = +0.42$, and $\sigma_{2'\text{-H}} = -0.45$. Therefore, the averaged σ values for the three conformers are in agreement with the shifts predicted, and the 2′-H and 3-H signals should be more deshielded than the others, as was observed experimentally.

The configuration of the sulfur stereocentre of **11***R* and **11***S* was assigned by comparison of the chemical shift displacements ($\Delta\delta_{11-7}$) with those found for analogues **10***R* and **10***S* ($\Delta\delta_{10-5}$).

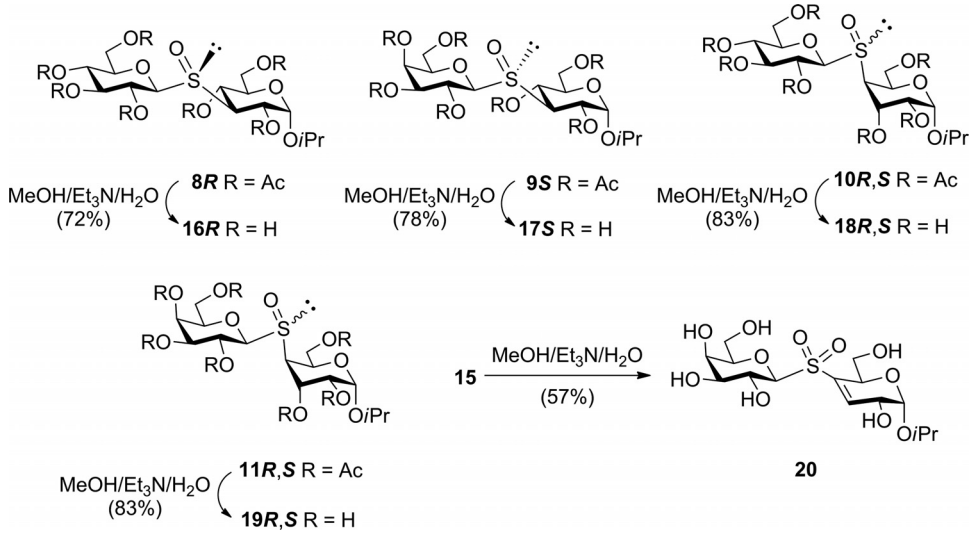
The oxidation of the sulfur atom of thiodisaccharides **4**–**7** with an excess of *m*CPBA for longer periods than those used for the oxidation to sulfoxides, led to the corresponding sulfones (i.e., **12**–**15**) in 78–92% yields (Scheme 3). As for the sulfoxides, the oxidation of the sulfur atom of **4**–**7** to give the sulfones resulted in a strong downfield shift in the ^{13}C NMR spectra of the signals of the carbons bonded to the sulfur (C-1′ $\delta \approx 89$ ppm, and C-3 or C-4 $\delta \approx 59$ ppm).

The peracetylated sulfoxide and sulfone disaccharides were deprotected by treatment with a mixture of MeOH/Et_3N/H_2O at room temperature (Scheme 4). Thus, the deprotection of sulfoxide **8***R* gave the corresponding thiodisaccharide (i.e., **16***R*; 73% yield). The ^{1}H NMR spectrum of **16***R* showed signals for the anomeric protons 1-Hα and 1′-Hβ, but at higher fields, the spectrum was rather complex, due to signal overlap. In the ^{13}C NMR spectrum of **16***R*, the signals of the carbons bonded to the sulfone group, i.e., C-1′ and C-3, were shifted downfield by 4.2 and 8.8 ppm, respectively, relative to those of the corresponding thiodisaccharide, Glc*p*-*S*-(1→3)-3-thio-Glc*p*-*Oi*Pr (**4**).

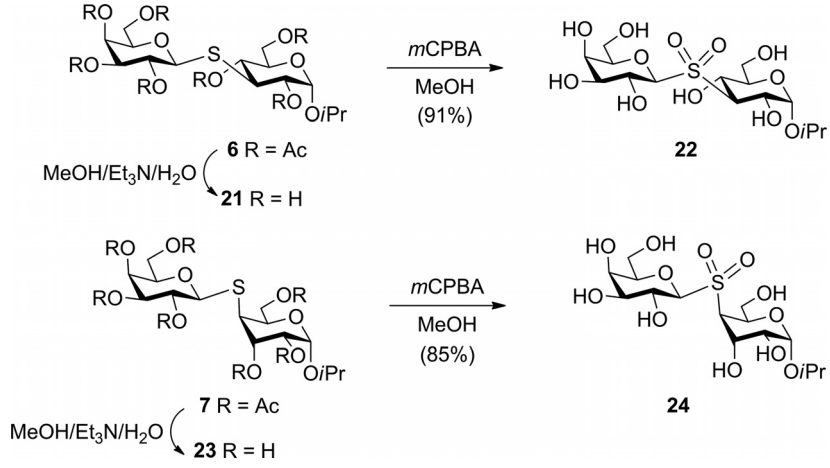
The other sulfoxides (**9***S*, **10***R*,*S*, and **11***R*,*S*) were also deacetylated with MeOH/Et_3N/H_2O to give the unprotected products in good yields (72–83%). However, in the case of **9***R*, decomposition took place during the reaction. The formation of by-products was much more significant in the deacetylation of sulfones **9**–**15**. For example, the deprotection of **15** gave α,β-unsaturated sulfone **20** as the major isolated product. The ^{1}H NMR spectrum of **20** showed a vinylic proton at $\delta = 7.00$ ppm and the anomeric protons 1-H at $\delta = 5.25$ ppm ($J = 4.0$ Hz) and 1′-H at $\delta = 4.84$ ppm ($J = 9.5$ Hz). The carbon signals of the double bond were observed at $\delta = 147.0$ and 136.0 ppm in the ^{13}C NMR spectrum of **20**. Compound **20** could arise from an initial deprotonation of C-4 (i.e., the carbon bonded to the SO_2 group) to give an anion that is stabilized by resonance with the



Scheme 3. Oxidation of thiodisaccharides to sulfones.



Scheme 4. Deprotection of thiodisaccharide sulfoxides and sulfones.



Scheme 5. Synthesis of unprotected thiodisaccharide *S*,*S*-dioxides **22** and **24** from unprotected precursors **21** and **23**.

sulfone. Subsequent elimination of the neighbouring acetoxy group would then give the corresponding alkene.

To obtain the unprotected thiodisaccharide sulfones, the deprotection of the fully acetylated thiodisaccharides, like **6** or **7**, was conducted prior to the oxidation reaction (Scheme 5). Thus, deacetylation of **6** and **7** gave the respective deprotected thiodisaccharides (i.e., **21** and **23**). These compounds were treated with an excess of *m*CPBA in CH_2Cl_2/MeOH, 1:4 to give the corresponding sulfones (i.e., **22** and **24**) in high isolated yields (90 and 84% yield, respectively).

As thioethers may undergo in vivo oxidation to give sulfoxides and sulfones, we are planning to compare the biological activity of the sulfoxides or sulfones to that of their thiodisaccharide precursors. Therefore, the evaluation of the unprotected glycosyl sulfoxides and sulfones as enzyme inhibitors, as well as antitumor agents, is underway.

Conclusions

*m*CPBA oxidation of the sulfur atom of thiodisaccharides gave the corresponding sulfoxides or sulfones. The sulfoxides were obtained as diastereomeric mixtures. Under the reaction conditions used, the oxidation of *S*-(1→3)-linked disaccharides was diastereoselective in favour of the *R*-isomer, and the mixtures of diastereomeric sulfoxides could be separated by column chromatography. In contrast, the oxidation was poorly selective in the case of *S*-(1→4)-linked disaccharides, and the diastereomeric mixtures could not be separated. The selectivity observed for the *S*-(1→3)-linked disaccharides in favour of the *R*-isomer could be due to the fact that in the populated conformations resulting from rotation around the thioglycosidic linkage, the pro-*R* lone pair of the sulfur atom is less hindered than the pro-*S*. In contrast, the two lone-pairs of the sulfur atom are almost equally hindered for the populated conformations of the *S*-(1→4)-linked disaccharides, and the approach of the oxidant to either of them is rather difficult.

The absolute configuration of the sulfur atom of sulfoxides was assigned by using NMR spectroscopy and by considering the preferred conformations of the thiodisaccharide sulfoxides, particularly around the thioglycosidic linkage, and the shielding/deshielding of the protons in sulfox-

ides, compared with the corresponding signals in their thiodisaccharide precursors. The displacement of chemical shifts is the result of the anisotropy of the S=O bond and related effects. As far as we know, this work constitutes the first report of the synthesis of diastereomerically pure thiodisaccharide sulfoxides, and also of the assignment of the absolute configurations of their sulfur stereocentres.

The *O*-deacetylation of most of the sulfoxides took place satisfactorily under mildly basic conditions, but the sulfones underwent elimination reactions that led to unsaturated products. However, oxidation of unprotected thiodisaccharides gave the expected sulfones.

Experimental Section

General Methods: Melting points were determined with a Fisher–Johns apparatus. Column chromatography was carried out with silica gel 60 (230–400 mesh). Analytical thin-layer chromatography (TLC) was carried out on silica gel 60 F254 aluminium-backed plates (layer thickness 0.2 mm). The spots were visualized by exposure to UV light and b charring with sulfuric acid (5% v/v in EtOH, containing 0.5% *p*-anisaldehyde). Optical rotations were measured at 25 °C in a 1 dm cell in the solvent indicated. Nuclear magnetic resonance (NMR) spectra were recorded at 500 MHz (^{1}H) or 125.7 MHz (^{13}C). Chemical shifts were calibrated to tetramethylsilane or to a residual solvent peak ($CHCl_3$: ^{1}H: δ = 7.26 ppm, ^{13}C: δ = 77.2 ppm). Assignments of ^{1}H and ^{13}C NMR spectra were assisted by 2D ^{1}H–COSY and 2D ^{1}H–^{13}C HSQC experiments. High-resolution mass spectra (HRMS) were obtained using the electrospray ionization (ESI) technique and Q-TOF detection. Molecular mechanics calculations (MM+) were carried out with Hyperchem Professional 8.0.3.

General Procedure for the Oxidation of the Sulfur Atom of *S*-(1→3)- and *S*-(1→4)-Linked Disaccharides (4 and 6, and 5 and 7, respectively) to Sulfoxides: *m*CPBA (80%; 31 mg, 0.144 mmol) in CH_2Cl_2 (2 mL) was added to a solution of the thiodisaccharide (50 mg, 0.072 mmol) in ethyl ether (2 mL) at 0 °C. The reaction mixture was stirred for 2 h at room temp., then it was diluted with EtOAc (30 mL). The mixture was stirred for 30 min with $NaHSO_3$ (satd. aq.; 10 mL). The organic phase was separated, and then it was stirred for a further 30 min with $NaHCO_3$ (satd. aq.; 10 mL). Finally, the organic extract was washed with $NaHCO_3$ (satd. aq.; 10 mL) and brine (10 mL), dried ($MgSO_4$), and filtered. Evaporation of the solvent followed by co-evaporation with toluene/EtOH, (1:1; 5× 10 mL) produced an oily residue. Column chromatography of the residue with hexane/EtOAc, (3:2→1:1), gave the sulfoxides as a diasteromeric mixture, which in some cases could be separated.

(2-Propyl 2,4,6-Tri-*O*-acetyl-α-D-glucopyranosid-3-yl) (2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl) (*R*)-Sulfoxide (8*R*): The major product of the oxidation of thiodisaccharide **4** was sulfoxide **8***R* (30 mg, 59%). R_f = 0.46 (hexane/EtOAc, 1:2). $[\alpha]_D^{25}$ = +45.9 (*c* = 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.13, 1.23 [2 d, *J* = 6.2 Hz, 6 H, $(CH_3)_2$CHO], 1.97–2.12 (7 s, 21 H, CH_3CO), 3.56 (t, $J_{2,3} = J_{3,4}$ = 11.3 Hz, 1 H, 3-H), 3.86 (ddd, $J_{4',5'}$ = 10.0, $J_{5',6'a}$ = 5.5, $J_{5',6'b}$ = 2.4 Hz, 1 H, 5′-H), 3.90 (m, *J* = 6.2 Hz, 1 H, Me_2CHO), 4.04–4.08 (m, 2 H, 5-H, 6b-H), 4.15 (dd, $J_{5',6'b}$ = 2.4, $J_{6'a,6'b}$ = 12.5 Hz, 1 H, 6′b-H), 4.17 (dd, $J_{5,6a}$ = 5.0, $J_{6a,6b}$ = 12.5 Hz, 1 H, 6a-H), 4.26 (dd, $J_{5',6'a}$ = 5.5, $J_{6'a,6'b}$ = 12.5 Hz, 1 H, 6′a-H), 4.75 (d, $J_{1',2'}$ = 9.7 Hz, 1 H, 1′-H), 5.08 (dd, $J_{3',4'}$ = 9.1, $J_{4',5'}$ = 10.0 Hz, 1 H, 4′-H), 5.17 (dd, $J_{1,2}$ = 3.9, $J_{2,3}$ = 11.3 Hz, 1 H, 2-H), 5.23 (t, $J_{3,4} = J_{4,5}$ = 11.3 Hz, 1 H, 4-H), 5.25 (t, $J_{2',3'} = J_{3',4'}$ = 9.2 Hz, 1 H, 3′-H), 5.27 (d, $J_{1,2}$ = 3.9 Hz, 1 H, 1-H), 5.52 (dd, $J_{1',2'}$ = 9.7, $J_{2',3'}$ = 9.2 Hz, 1 H, 2′-H) ppm. ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ = 20.6–21.0 (7 CH_3CO), 21.8, 23.2 [$(CH_3)_2$CHO], 57.5 (C-3), 61.8 (C-6′), 62.1 (C-6), 64.7 (C-4), 65.7 (C-2), 67.9, 68.0 (C-4′, C-5), 69.6 (C-2′), 71.3 (Me_2CHO), 73.5 (C-3′), 76.5 (C-5′), 85.8 (C-1′), 93.5 (C-1), 168.9, 169.1, 169.3, 169.4, 170.3, 170.4, 170.8 (CH_3CO) ppm. HRMS (ESI): calcd. for $C_{29}H_{42}NaO_{18}S$ [M + Na]$^+$ 733.1984; found 733.2002.

(2-Propyl 2,4,6-Tri-*O*-acetyl-α-D-glucopyranosid-3-yl) (2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl) (*S*)-Sulfoxide (8*S*): The minor product of the oxidation of thiodisaccharide **4** was syrupy sulfoxide **8***S* (8 mg, 16%). R_f = 0.34 (hexane/EtOAc, 1:2). $[\alpha]_D^{25}$ = +39.6 (*c* = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.10, 1.24 [2 d, *J* = 6.2 Hz, 6 H, $(CH_3)_2$CHO], 2.01–2.09 (7 s, 21 H, CH_3CO), 3.87 (ddd, $J_{4',5'}$ = 10.2, $J_{5',6'a}$ = 5.5, $J_{5',6'b}$ = 2.3 Hz, 1 H, 5′-H), 3.90 (m, *J* = 6.2 Hz, 1 H, Me_2CHO), 3.94 (dd, $J_{2,3}$ = 12.2, $J_{3,4}$ = 10.6 Hz, 3-H), 4.05 (ddd, $J_{4,5}$ = 9.8, $J_{5,6a}$ = 3.3, $J_{5,6b}$ = 4.8 Hz, 1 H, 5-H), 4.13 (dd, $J_{5,6b}$ = 4.8, $J_{6a,6b}$ = 12.3 Hz, 1 H, 6b-H), 4.17 (dd, $J_{5,6a}$ = 3.3, $J_{6a,6b}$ = 12.3 Hz, 1 H, 6a-H), 4.18 (dd, $J_{5',6'b}$ = 2.3, $J_{6'a,6'b}$ = 12.5 Hz, 1 H, 6′b-H), 4.36 (dd, $J_{5',6'a}$ = 5.6, $J_{6'a,6'b}$ = 12.5 Hz, 1 H, 6′a-H), 4.62 (m, 1 H, 1′-H), 5.01 (dd, $J_{1,2}$ = 3.7, $J_{2,3}$ = 12.2 Hz, 1 H, 2-H), 5.15 (m, 1 H, 4′-H), 5.20 (d, $J_{1,2}$ = 3.7 Hz, 1 H, 1-H), 5.32 (m, 2 H, 2′-H, 3′-H), 5.35 (dd, $J_{3,4}$ = 10.6, $J_{4,5}$ = 9.8 Hz, 1 H, 4-H) ppm. ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ = 20.5–20.9, (7 CH_3CO), 21.8, 23.3 [$(CH_3)_2$CHO], 55.3 (C-3), 62.1 (C-6′), 62.5 (C-6), 64.0 (C-4), 67.9 (C-4′), 68.1 (C-2′), 68.4 (C-5), 69.4 (C-2), 71.4 (Me_2CHO), 74.0 (C-3′), 77.2 (C-5′), 88.1 (C-1′), 93.1 (C-1), 168.8, 168.9, 169.3, 169.4 (×2), 170.6, 170.9 (CH_3CO) ppm. HRMS (ESI): calcd. for $C_{29}H_{42}NaO_{18}S$ [M + Na]$^+$ 733.1984; found 733.1996.

(2-Propyl 2,4,6-Tri-*O*-acetyl-α-D-glucopyranosid-3-yl) (2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl) (*R*)-Sulfoxide (9*R*): The fraction eluted with hexane/EtOAc, 1:1 gave pure sulfoxide **9***R* (28 mg, 55%) as a syrup. R_f = 0.47 (hexane/EtOAc, 1:2). $[\alpha]_D^{25}$ = +58.0 (*c* = 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.13, 1.24 [2 d, *J* = 6.2 Hz, 6 H, $(CH_3)_2$CHO], 1.98, 1.99, 2.06 (×2), 2.08, 2.12, 2.17 (7 s, 21 H, CH_3CO), 3.54 (t, 1 H, $J_{2,3} = J_{3,4}$ = 11.2 Hz, 3-H), 3.90 (m, *J* = 6.2 Hz, 1 H, Me_2CHO), 4.00–4.11 (m, 4 H, 5-H, 5′-H, 6b-H, 6′b-H), 4.17 (dd, *J* = 4.8, *J* = 12.5 Hz, 1 H, 6a-H or 6′a-H), 4.23 (dd, *J* = 5.9, *J* = 11.1 Hz, 1 H, 6a-H or 6′a-H), 4.73 (d, $J_{1',2'}$ = 9.8 Hz, 1 H, 1′-H), 5.06 (dd, $J_{2',3'}$ = 10.0, $J_{3',4'}$ = 3.3 Hz, 1 H, 3′-H), 5.18 (dd, $J_{1,2}$ = 4.0, $J_{2,3}$ = 11.2 Hz, 1 H, 2-H), 5.23 (dd, $J_{3,4}$ = 11.2, $J_{4,5}$ = 9.9 Hz, 1 H, 4-H), 5.27 (d, $J_{1,2}$ = 4.0 Hz, 1 H, 1-H), 5.46 (dd, $J_{3',4'}$ = 3.3, $J_{4',5'}$ = 0.9 Hz, 1 H, 4′-H), 5.73 (t, $J_{1',2'}$ = 9.8, $J_{2',3'}$ = 10.0 Hz, 1 H, 2′-H) ppm. ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ = 20.7 (×3), 20.8 (×3), 21.0 (7 CH_3CO), 21.8, 23.2 [$(CH_3)_2$CHO], 57.5 (C-3), 61.2, 62.1 (C-6, C-6′), 65.7 (C-4), 65.7 (C-2), 66.6 (C-2′), 66.9 (C-4′), 67.9 (C-5), 71.4, 71.6 (C-3′, Me_2CHO), 75.3 (C-5′), 86.2 (C-1′), 93.4 (C-1), 168.9, 169.2, 169.6, 170.2, 170.3, 170.4, 170.8 (7 CH_3CO) ppm. HRMS (ESI): calcd. for $C_{29}H_{42}NaO_{18}S$ [M + Na]$^+$ 733.1984; found 733.1998.

(2-Propyl 2,4,6-Tri-*O*-acetyl-α-D-glucopyranosid-3-yl) (2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl) (*S*)-Sulfoxide (9*S*): The fraction eluted with hexane/EtOAc, 1:1 gave pure sulfoxide (16 mg, 31%) as a syrup. R_f = 0.35 (hexane/EtOAc, 1:2). $[\alpha]_D^{25}$ = +54.3 (*c* = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.11, 1.24 [2 d, *J* = 6.2 Hz, 6 H, $(CH_3)_2$CHO], 1.99, 2.05, 2.06 (×2), 2.08, 2.10, 2.16, (7 s, 21 H, CH_3CO), 3.90 (dd, $J_{2,3}$ = 12.2, $J_{3,4}$ = 10.2 Hz, 1 H, 3-H), 3.91 (m, 1 H, Me_2CHO), 4.06 (ddd, $J_{4,5}$ = 10.2, $J_{5,6a}$ = 3.0, $J_{5,6b}$ = 5.0 Hz, 1 H, 5-H), 4.08–4.12 (m, 3 H, 5′-H, 6b-H, 6′b-H), 4.17 (dd, $J_{5,6a}$ = 3.0, $J_{6a,6b}$ = 12.0 Hz, 1 H, 6a-H), 4.29 (dd,

$J_{5',6'a}$ = 6.4, $J_{6'a,6'b}$ = 10.9 Hz, 1 H, 6′a-H), 4.59 (d, $J_{1',2'}$ = 10.0 Hz, 1 H, 1′-H), 5.03 (dd, $J_{1,2}$ = 3.6, $J_{2,3}$ = 12.2 Hz, 1 H, 2-H), 5.17 (dd, $J_{2',3'}$ = 10.0, $J_{3',4'}$ = 3.4 Hz, 1 H, 3′-H), 5.20 (d, $J_{1,2}$ = 3.6 Hz, 1 H, 1-H), 5.34 (t, $J_{3,4}$ = $J_{4,5}$ = 10.2 Hz, 1 H, 4-H), 5.46 (dd, $J_{3',4'}$ = 3.4, $J_{4',5'}$ = 0.6 Hz, 1 H, 4′-H), 5.55 (t, $J_{1',2'}$ = $J_{2',3'}$ = 10.0 Hz, 1 H, 2′-H) ppm. ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ = 20.4, 20.7 (×2), 20.8, 20.9 (×3), (7 CH_3CO), 21.8, 23.3 [$(CH_3)_2CHO$], 55.6 (C-3), 61.6 (C-6′), 62.5 (C-6), 64.0 (C-4), 65.8 (C-2′), 67.1 (C-4′), 68.2 (C-5), 69.3 (C-2), 71.4 (Me_2CHO), 72.0 (C-3′), 76.0 (C-5′), 88.3 (C-1′), 93.1 (C-1), 168.7, 168.8, 169.4, 170.2, 170.3, 170.5, 170.9 (7 CH_3CO) ppm. HRMS (ESI): calcd. for $C_{29}H_{42}NaO_{18}S$ [M + Na]$^+$ 733.1984; found 733.1995.

(2-Propyl 2,3,6-Tri-*O*-acetyl-α-D-gulopyranosid-4-yl) (2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl) (*R*,*S*)-Sulfoxide (10*R*,*S*): Oxidation of thiodisaccharide **5** gave a diasteromeric mixture of sulfoxides **10***R*,*S* (38 mg, 74%; ratio *R*/*S*, 1:0.7). R_f = 0.36 (hexane/EtOAc, 1:2). ^{1}H NMR ($CDCl_3$, 500 MHz) data for *S* isomer: δ = 1.14, 1.25 [2 d, J = 6.2 Hz, 4.2 H, $CH(CH_3)_2$], 2.00–2.15 (CH_3CO), 3.63 (dd, $J_{3,4}$ = 2.7, $J_{4,5}$ = 2.0 Hz, 0.7 H, 4-H), 3.82–3.89 (m, 2.7 H, 5′-H overlapping with Me_2CH and 5′-H of **10***R*), 3.93 (m, J = 6.2 Hz, 0.7 H, Me_2CH), 4.12 (dd, $J_{5',6'b}$ = 3.5, $J_{6'a,6'b}$ = 12.8 Hz, 0.7 H, 6′b-H), 4.28 (dd, $J_{5',6'a}$ = 4.4, $J_{6'a,6'b}$ = 12.8 Hz, 0.7 H, 6′a-H), 4.39 (dd, $J_{5,6b}$ = 2.7, $J_{6a,6b}$ = 12.6 Hz, 0.7 H, 6b-H), 4.49 (dd, $J_{5,6a}$ = 9.1, $J_{6a,6b}$ = 12.6 Hz, 0.7 H, 6a-H), 4.54 (d, $J_{1',2'}$ = 9.8 Hz, 0.7 H, 1′-H), 4.65 (t, $J_{1,2}$ = $J_{2,3}$ = 3.9 Hz, 0.7 H, 2-H), 4.96 (m, $J_{4,5}$ = 2.0, $J_{5,6a}$ = 9.1, $J_{5,6b}$ = 2.7 Hz, 0.7 H, 5-H), 5.08 (d, $J_{1,2}$ = 3.9 Hz, 0.7 H, 1-H), 5.20 (dd, $J_{3',4'}$ = 9.3, $J_{4',5'}$ = 10.1 Hz, 0.7 H, 4′-H), 5.26 (m, 1.7 H, 3-H overlapping with 2-H of **10***R*), 5.38 (t, $J_{2',3'}$ = $J_{3',4'}$ = 9.3 Hz, 0.7 H, 3′-H), 5.46 (dd, $J_{2',3'}$ = 9.3, $J_{1',2'}$ = 9.8 Hz, 0.7 H, 2′-H) ppm. ^{13}C NMR ($CDCl_3$, 125.7 MHz) data for *S* isomer: δ = 20.6–21.3 (CH_3CO), 21.4, 23.2 [$(CH_3)_2CHO$], 60.7 (C-6′), 60.8 (C-4), 64.1 (C-3), 64.4 (C-6), 65.0 (C-5), 66.3 (C-2′), 67.3 (C-2), 67.4 (C-4′), 70.8 (Me_2CHO), 74.2 (C-3′), 77.3 (C-5′), 87.2 (C-1′), 94.7 (C-1), 168.8–170.8 (CH_3CO) ppm. ^{1}H NMR ($CDCl_3$, 500 MHz) data for *R* isomer: δ = 1.13, 1.22 [2 d, J = 6.2 Hz, 6 H, $CH(CH_3)_2$], 2.00–2.15 (CH_3CO), 3.39 (t, $J_{3,4}$ = $J_{4,5}$ = 2.7 Hz, 1 H, 4-H), 3.82–3.89 (m, 2.7 H, Me_2CH, 5′-H overlapping with 5′-H of **10***S*), 4.15 (d, $J_{5',6'b}$ = 3.2 Hz, 2 H, 6′-H), 4.20 (dd, $J_{5,6b}$ = 4.4, $J_{6a,6b}$ = 11.8 Hz, 1 H, 6b-H), 4.30 (dd, $J_{5,6a}$ = 8.0, $J_{6a,6b}$ = 11.8 Hz, 1 H, 6a-H), 4.62 (d, $J_{1',2'}$ = 9.8 Hz, 1 H, 1′-H), 4.79 (m, $J_{4,5}$ = 2.7, $J_{5,6b}$ = 4.4, $J_{5,6a}$ = 8.0 Hz, 1 H, 5-H), 5.11 (dd, $J_{3',4'}$ = 9.2, $J_{4',5'}$ = 10.1 Hz, 1 H, 4′-H), 5.16 (d, $J_{1,2}$ = 4.4 Hz, 1 H, 1-H), 5.26 (m, 1.7 H, 2-H overlapping with 3-H of **10***S*), 5.31 (t, $J_{2',3'}$ = $J_{3',4'}$ = 9.2 Hz, 1 H, 3′-H), 5.49 (dd, $J_{2',3'}$ = 9.2, $J_{1',2'}$ = 9.2 Hz, 1 H, 2′-H), 5.64 (dd, $J_{3,4}$ = 2.7, $J_{2,3}$ = 4.3 Hz, 1 H, 3-H) ppm. ^{13}C NMR ($CDCl_3$, 125.7 MHz) data for *R* isomer: δ = 20.6–21.3 (CH_3CO), 21.6, 23.2 [$(CH_3)_2CHO$], 56.6 (C-4), 61.1 (C-6′), 63.0 (C-5), 63.8 (C-6), 65.8 (C-3), 67.7 (C-2, C-4′), 69.3 (C-2′), 70.8 (Me_2CHO), 73.4 (C-3′), 76.9 (C-5′), 86.9 (C-1′), 94.3 (C-1), 168.8–170.8 (CH_3CO) ppm. HRMS (ESI): calcd. for $C_{29}H_{42}NaO_{18}S$ [M + Na]$^+$ 733.1984; found 733.2009.

(2-Propyl 2,3,6-Tri-*O*-acetyl-α-D-gulopyranosid-4-yl) (2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl) (*R*,*S*)-Sulfoxide (11*R*,*S*): Oxidation of thiodisaccharide **7** gave a diasteromeric mixture of sulfoxides **11***R*,*S* (41 mg, 80%; ratio *R*/*S*, 1:0.8). R_f = 0.36 (hexane/EtOAc, 1:2). ^{1}H NMR ($CDCl_3$, 500 MHz) data for *S* isomer: δ = 1.13, 1.25 [2 d, J = 6.2 Hz, 4.8 H, $CH(CH_3)_2$], 1.97–2.15 (CH_3CO), 3.65 (dd. $J_{3,4}$ = 3.0, $J_{4,5}$ = 1.9 Hz, 0.8 H, 4-H), 3.92 (m, J = 6.2 Hz, 0.8 H, $CHMe_2$), 3.99–4.14 and 4.21–4.24 (m, 6.4 H, 5′-H, 6′a-H, 6′b-H overlapping with 6b-H, 5′-H, 6′a-H, 6′b-H of **11***R*), 4.42 (dd, $J_{5,6b}$ = 2.6, $J_{6a,6b}$ = 12.6 Hz, 0.8 H, 6b-H), 4.47 (d, $J_{1',2'}$ = 9.9 Hz, 0.8 H, 1′-H), 4.51 (dd, $J_{5,6a}$ = 9.0, $J_{6a,6b}$ = 12.6 Hz, 0.8 H, 6a-H), 4.67 (t, $J_{1,2}$ = $J_{2,3}$ = 4.0 Hz, 0.8 H, 2-H), 4.95 (dt, $J_{4,5}$ = 1.9, $J_{5,6a}$ = 9.0, $J_{5,6b}$ = 2.6 Hz, 0.8 H, 5-H), 5.08 (d, $J_{1,2}$ = 4.0 Hz, 0.8 H, 1-H), 5.22–5.26 (m, 2.6 H, 3-H, 3′-H overlapping with 2-H of **11***R*), 5.48 (dd, $J_{3',4'}$ = 3.4, $J_{4',5'}$ = 1.0 Hz, 0.8 H, 4′-H), 5.64–5.70 (m, 2.6 H, 2′-H overlapping with 2′-H, 3-H of **11***R*) ppm. ^{13}C NMR ($CDCl_3$, 125.7 MHz) data for *S* isomer: δ = 20.6–21.2 (CH_3CO), 21.4, 23.23 [$(CH_3)_2CHO$], 60.4 (C-4), 60.8, 61.1 (C-6′ of *R, S*), 64.4 (4,C-6), 65.1 (C-5), 66.4 (C-2′), 67.0 (C-4′), 67.2 (C-2), 70.8 (Me_2CHO), 72.0 (C-3′), 75.8, 76.1 (C-5′ of *R, S*), 87.6 (C-1′), 94.7 (C-1), 168.8–170.6 (7 CH_3CO) ppm. ^{1}H NMR ($CDCl_3$, 500 MHz) data for *R* isomer: δ = 1.12, 1.22 [2 d, J = 6.2 Hz, 6 H, $CH(CH_3)_2$], 1.97–2.15 (CH_3CO), 3.40 (t, $J_{3,4}$ = $J_{4,5}$ = 2.8 Hz, 1 H, 4-H), 3.85 (m, J = 6.2 Hz, $CHMe_2$), 3.99–4.14 and 4.21–4.24 (m, 6.4 H, 6b-H, 5′-H, 6′a-H, 6′b-H overlapping with 5′-H, 6′a-H, 6′b-H of isomer **11***S*), 4.30 (dd, $J_{5,6a}$ = 8.0, $J_{6a,6b}$ = 11.8 Hz, 1 H, 6a-H), 4.58 (d, $J_{1',2'}$ = 9.9 Hz, 1 H, 1′-H), 4.76 (ddd, $J_{4,5}$ = 2.8, $J_{5,6b}$ = 4.2, $J_{5,6a}$ = 8.0 Hz, 1 H, 5-H), 5.14 (dd, $J_{3',4'}$ = 3.4, $J_{2',3'}$ = 10.0 Hz, 1 H, 3′-H), 5.15 (d, $J_{1,2}$ = 4.4 Hz, 1 H, 1-H), 5.22–5.26 (m, 2.6 H, 2-H overlapping with 3-H, 3′-H of **11***S*), 5.45 (d, $J_{3',4'}$ = 3.4 Hz, 1 H, 4′-H), 5.64–5.70 (m, 2.6 H, 2′-H, 3-H overlapping with 2′-H of **11***S*). ^{13}C NMR ($CDCl_3$, 125.7 MHz) data for *R* isomer: δ = 20.6–21.2 (CH_3CO), 21.5, 23.2 [$(CH_3)_2CHO$], 56.6 (C-4), 60.8, 61.1 (C-6′ of *R, S*), 63.1 (C-5), 63.6 (C-3), 64.0 (C-6), 65.6 (C-2′), 67.1 (C-4′), 67.6 (C-2), 70.8 (Me_2CHO), 71.3 (C-3′), 75.8, 76.1 (C-5′ of *R, S*), 87.3 (C-1′), 94.3 (C-1), 168.8–170.6 (CH_3CO) ppm. HRMS (ESI): calcd. for $C_{29}H_{42}NaO_{18}S$ [M + Na]$^+$ 733.1984; found 733.2000.

General Procedure for the Oxidation of the Sulfur Atom of Thiodisaccharides 4–7 to give Sulfones 12–15: The oxidation of thiodisaccharide **4**–**7** (50 mg, 0.072 mmol) was carried out under the conditions used for the oxidation to sulfoxides, but the reaction mixtures were stirred at room temp. for longer times. When TLC monitoring of the oxidation mixture revealed the conversion of the respective sulfoxide intermediate into a single product of slightly higher R_f was complete, the mixture was diluted with EtOAc and then processed as described above for the sulfoxides. The resulting sulfones **12**–**15** were purified by column chromatography using hexane/EtOAc mixtures of increasing polarity (3:2→1:1).

(2-Propyl 2,4,6-Tri-*O*-acetyl-α-D-glucopyranoside-3-yl) (2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl) Sulfone (12): Sulfone **12** (45 mg, 86%) was isolated as a syrup. R_f = 0.53 (hexane/EtOAc, 1:2). $[\alpha]_D^{25}$ = +44.3 (c = 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.10, 1.20 [2 d, J = 6.2 Hz, 6 H, $(CH_3)_2CHO$], 1.97–2.11 (7 s, 21 H, CH_3CO), 3.85 (m, 2 H, Me_2CHO, 5′-H), 3.97 (t, $J_{2,3}$ = $J_{3,4}$ = 10.8 Hz, 3-H), 3.99 (m, 1 H, 5-H), 4.07 (dd, $J_{5,6b}$ = 2.2, $J_{6a,6b}$ = 12.3 Hz, 1 H, 6b-H), 4.12 (dd, $J_{5,6a}$ = 4.7, $J_{6a,6b}$ = 12.3 Hz, 1 H, 6a-H), 4.21 (dd, $J_{5',6'b}$ = 2.2, $J_{6'a,6'b}$ = 12.5 Hz, 1 H, 6′b-H), 4.27 (dd, $J_{5',6'a}$ = 5.8, $J_{6'a,6'b}$ = 12.5 Hz, 1 H, 6′a-H), 4.71 (d, $J_{1',2'}$ = 9.6 Hz, 1 H, 1′-H), 5.07 (t, $J_{4',5'}$ = 9.6 Hz, 1 H, 4′-H), 5.14 (dd, $J_{1,2}$ = 3.8, $J_{2,3}$ = 10.8 Hz, 1 H, 2-H), 5.16 (d, $J_{1,2}$ = 3.8 Hz, 1 H, 1-H), 5.33 (dd, $J_{2',3'}$ = 9.1, $J_{3',4'}$ = 9.6 Hz, 1 H, 3′-H), 5.37 (t, $J_{3,4}$ = $J_{4,5}$ = 10.8 Hz, 1 H, 4-H), 5.39 (dd, $J_{1',2'}$ = 9.6, $J_{2',3'}$ = 9.1 Hz, 1 H, 2′-H) ppm. ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ = 20.6–20.8 (7 CH_3CO), 21.7, 23.1 [$(CH_3)_2CHO$], 59.5 (C-3), 61.9 (C-6′), 62.1 (C-6), 62.6 (C-4), 66.6 (C-2′), 67.7 (C-5, C-4′), 68.6 (C-2), 71.5 (Me_2CHO), 73.1 (C-3′), 76.6 (C-5′), 88.6 (C-1′), 93.0 (C-1), 168.9, 169.0, 169.2, 169.4, 170.2, 170.4, 170.7, (CH_3CO) ppm. HRMS (ESI): calcd. for $C_{29}H_{42}NaO_{19}S$ [M + Na]$^+$ 749.1933; found 749.1956.

(2-Propyl 2,4,6-Tri-*O*-acetyl-α-D-glucopyranoside-3-yl) (2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl) Sulfone (13): Sulfone **13** (41 mg, 78%) was isolated as a syrup. R_f = 0.56 (hexane/EtOAc, 1:2). $[\alpha]_D^{25}$ = +54.5 (c = 0.7, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.11, 1.22 [2 d, J = 6.2 Hz, 6 H, $(CH_3)_2CHO$], 1.98–2.16, (7 s,

21 H, CH_3CO), 3.85 (m, J = 6.2 Hz, 1 H, Me_2CHO), 3.99 (m, 1 H, 5′-H), 4.00 (dd, $J_{2,3}$ = 11.2, $J_{3,4}$ = 10.5 Hz, 1 H, 3-H), 4.04–4.16 (m, 4 H, 5-H, 6b-H, 6′a-H, 6′b-H), 4.26 (dd, $J_{5,6a}$ = 5.9, $J_{6a,6b}$ = 10.1 Hz, 1 H, 6a-H), 4.63 (d, $J_{1′,2′}$ = 9.7 Hz, 1 H, 1′-H), 5.14 (dd, $J_{1,2}$ = 3.9, $J_{2,3}$ = 11.2 Hz, 1 H, 2-H), 5.15 (dd, $J_{2′,3′}$ = 10.1, $J_{3′,4′}$ = 3.3 Hz, 1 H, 3′-H), 5.18 (d, $J_{1,2}$ = 3.9 Hz, 1 H, 1-H), 5.38 (dd, $J_{3,4}$ = 10.5, $J_{4,5}$ = 9.8 Hz, 1 H, 4-H), 5.44 (d, $J_{3′,4′}$ = 3.3 Hz, 1 H, 4′-H), 5.65 (dd, $J_{1′,2′}$ = 9.7, $J_{2′,3′}$ = 10.1 Hz, 1 H, 2′-H) ppm. ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ = 20.6, 20.7 (×2), 20.8 (×3), 20.9, (CH_3CO), 21.7, 23.1 [$(CH_3)_2CHO$], 59.4 (C-3), 61.4 (C-6), 62.2 (C-6′), 62.8 (C-4), 63.4 (C-2′), 66.7 (C-4′), 67.8 (C-5), 68.5 (C-2), 71.3 (Me_2CHO), 71.5 (C-3′), 75.5 (C-5′), 89.4 (C-1′), 93.0 (C-1), 168.9, 169.0, 169.3, 169.4, 170.2, 170.4, 170.7 (CH_3CO) ppm. HRMS (ESI): calcd. for $C_{29}H_{42}NaO_{19}S$ [M + Na]$^+$ 749.1933; found 749.1951.

(2-Propyl 2,3,6-Tri-*O*-acetyl-α-D-gulopyranosid-4-yl) (2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl) Sulfone (14): Sulfone **14** (48 mg, 92%) was isolated as a syrup. R_f = 0.61 (hexane/EtOAc, 1:4). $[\alpha]_D^{25}$ = +41.5 (c = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.12, 1.22 [2 d, J = 6.2 Hz, 6 H, $(CH_3)_2CHO$], 2.01, 2.02, 2.03, 2.05, 2.06, 2.08, 2.16 (7 s, 21 H, CH_3CO), 3.83 (ddd, $J_{4′,5′}$ = 10.1, $J_{5′,6′a}$ = 2.4, $J_{5′,6′b}$ = 3.6 Hz, 1 H, 5′-H), 3.86 (dd, $J_{3,4}$ = 3.7, $J_{4,5}$ = 3.0 Hz, 1 H, 4-H), 3.88 (m, J = 6.2 Hz, 1 H, Me_2CHO), 4.15 (dd, $J_{5′,6′b}$ = 3.6, $J_{6′a,6′b}$ = 12.8 Hz, 1 H, 6′b-H), 4.26 (dd, $J_{5′,6′a}$ = 2.4, $J_{6′a,6′b}$ = 12.8 Hz, 1 H, 6′a-H), 4.45 (dd, $J_{5,6b}$ = 3.0, $J_{6a,6b}$ = 12.4 Hz, 1 H, 6b-H), 4.56 (dd, $J_{5,6a}$ = 8.8, $J_{6a,6b}$ = 12.4 Hz, 1 H, 6a-H), 4.70 (d, $J_{1′,2′}$ = 9.8 Hz, 1 H, 1′-H), 4.81 (dt, $J_{4,5}$ = $J_{5,6b}$ = 3.0, $J_{5,6a}$ = 8.8, Hz, 1 H, 5-H), 5.16 (d, $J_{1,2}$ = 4.1 Hz, 1 H, 1-H), 5.18 (dd, $J_{3′,4′}$ = 9.5, $J_{4′,5′}$ = 10.1 Hz, 1 H, 4′-H), 5.34 (t, $J_{2′,3′}$ = $J_{3′,4′}$ = 9.5 Hz, 1 H, 3′-H), 5.41 (t, $J_{1,2}$ = $J_{2,3}$ = 4.1 Hz, 1 H, 2-H), 5.55 (dd, $J_{1′,2′}$ = 9.8, $J_{2′,3′}$ = 9.5 Hz, 1 H, 2′-H), 5.64 (t, $J_{2,3}$ = 4.1, $J_{3,4}$ = 3.7 Hz, 1 H, 3-H) ppm. ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ = 20.6, 20.7 (×3), 20.8, 20.9, 21.1, (CH_3CO), 21.4, 23.2 [$(CH_3)_2CHO$], 59.1 (C-4), 60.6 (C-6′), 64.0 (C-6), 64.5 (C-5), 65.1 (C-3), 66.0 (C-2′), 66.2 (C-2), 70.7 (Me_2CHO), 73.3 (C-3′), 76.8 (C-5′), 88.0 (C-1′), 67.2 (C-4′), 94.2 (C-1), 169.2, 169.4, 170.1, 170.2, 170.4, 170.5, 170.7 (CH_3CO) ppm. HRMS (ESI): calcd. for $C_{29}H_{42}NaO_{19}S$ [M + Na]$^+$ 749.1933; found 749.1948.

(2-Propyl 2,3,6-Tri-*O*-acetyl-α-D-gulopyranosid-4-yl) (2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl) Sulfone (15): Sulfone **15** (48 mg, 92%) was obtained as a syrup. R_f = 0.49 (hexane/EtOAc, 1:2). $[\alpha]_D^{25}$ = +49.3 (c = 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.11, 1.21 [2 d, J = 6.2 Hz, 6 H, $(CH_3)_2CHO$], 1.98, 2.02, 2.03, 2.05, 2.07, 2.13, 2.15 (7 s, 21 H, CH_3CO), 3.88 (m, 2 H, 4-H, Me_2CHO),4.06–4.12 (m, 2 H, 5′-H, 6′b-H), 4.16 (dd, $J_{5′,6′a}$ = 6.6, $J_{6′a,6′b}$ = 11.0 Hz, 1 H, 6′a-H), 4.47 (dd, $J_{5,6b}$ = 3.0, $J_{6a,6b}$ = 12.4 Hz, 1 H, 6b-H), 4.56 (dd, $J_{5,6a}$ = 8.7, $J_{6a,6b}$ = 12.4 Hz, 1 H, 6a-H), 4.65 (d, $J_{1′,2′}$ = 9.9 Hz, 1 H, 1′-H), 4.79 (dt, $J_{4,5}$ = $J_{5,6b}$ = 3.0, $J_{5,6a}$ = 8.7 Hz, 1 H, 5-H), 5.15 (d, $J_{1,2}$ = 3.9 Hz, 1 H, 1-H), 5.16 (dd, $J_{2′,3′}$ = 9.9, $J_{3′,4′}$ = 3.3 Hz, 1 H, 3′-H), 5.40 (dd, $J_{1,2}$ = $J_{2,3}$ = 3.9 Hz, 1 H, 2-H), 5.44 (dd, $J_{3′,4′}$ = 3.3, $J_{4′,5′}$ = 0.7 Hz, 1 H, 4′-H), 5.64 (t, $J_{2,3}$ = $J_{3,4}$ = 3.9 Hz, 1 H, 3-H), 5.72 (t, $J_{1′,2′}$ = $J_{2′,3′}$ = 9.9 Hz, 1 H, 2′-H) ppm. ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ = 20.6–20.9 (7 CH_3CO), 21.4, 23.2 [$(CH_3)_2CHO$], 59.0 (C-4), 60.8 (C-6′), 63.1 (C-2′), 64.0 (C-6), 64.8 (C-5), 65.4 (C-3), 66.4 (C-2), 66.7 (C-4′), 70.8 (Me_2CHO), 71.4 (C-3′), 75.7 (C-5′), 88.8 (C-1′), 94.2 (C-1), 169.4, 169.9, 170.0, 170.1, 170.3, 170.4, 170.6, (7 CH_3CO) ppm. HRMS (ESI): calcd. for $C_{29}H_{42}NaO_{19}S$ [M + Na]$^+$ 749.1933; found 749.1940.

General Procedure for the *O*-Deacetylation of Thiodisaccharides, Sulfoxides, and Sulfones: A solution of the per-*O*-acetylated thiodisaccharide (0.05 mmol), or the corresponding sulfoxide or sulfone (0.05 mmol), in MeOH/Et_3N/H_2O (4:1:5; 0.5 mL) was stirred at room temp. for 3 h. The mixture was concentrated, and the resulting residue was dissolved in water (1 mL). The solution was eluted through a column filled with a Dowex MR-3C mixed-bed ion-exchange resin. The deionized solution was concentrated, and the unprotected compounds were purified by dissolution in water (1 mL) and filtration through an octadecyl C18 minicolumn (Amprep, Amersham Biosciences). Evaporation of the solvent gave the unprotected thiodisaccharides or thiodisaccharide *S*-oxides.

(2-Propyl α-D-Glucopyranosid-3-yl) (β-D-Glucopyranosyl) (*R*)-Sulfoxide (16*R*): Thiodisaccharide sulfoxide **8***R* (21 mg, 0.03 mmol) was *O*-deacetylated as described above to give **16***R* (9 mg, 72%). $[\alpha]_D^{25}$ = +34.8 (c = 0.6, MeOH). ^{1}H NMR (D_2O, 500 MHz): δ = 1.20, 1.26 [2 d, J = 6.2 Hz, 6 H, $(CH_3)_2CHO$], 3.46 (t, $J_{3′,4′}$ = $J_{4′,5′}$ = 9.5 Hz, 1 H, 4′-H), 3.57 (ddd, $J_{5′,6′b}$ = 2.2, $J_{5′,6′a}$ = 6.0, $J_{4′,5′}$ = 9.5 Hz, 1 H, 5′-H), 3.59 (m, 2 H, 3-H, 3′-H), 3.72 (dd, $J_{5′,6′b}$ = 6.0, $J_{6′a,6′b}$ = 12.5 Hz, 1 H, 6′b-H), 3.76 (dd, $J_{3,4}$ = $J_{4,5}$ = 9.6 Hz, 1 H, 4-H), 3.78 (dd, $J_{5,6a}$ = 5.0, $J_{6a,6b}$ = 11.9 Hz, 1 H, 6b-H), 3.83 (ddd, $J_{5,6a}$ = 2.1, $J_{5,6b}$ = 5.0, $J_{4,5}$ = 9.6 Hz, 1 H, 5-H), 3.87 (dd, $J_{5,6a}$ = 2.1, $J_{6a,6b}$ = 11.9 Hz, 1 H, 6a-H), 3.90 (t, $J_{1′,2′}$ = $J_{2′,3′}$ = 9.5 Hz, 1 H, 2′-H), 3.93 (dd, $J_{5′,6′a}$ = 2.7, $J_{6′a,6′b}$ = 12.5 Hz, 1 H, 6′a-H), 4.03 (m, J = 6.2 Hz, 1 H, Me_2CHO), 4.11 (dd, $J_{1,2}$ = 3.9, $J_{2,3}$ = 10.7 Hz, 1 H, 2-H), 4.88 (d, $J_{1′,2′}$ = 9.7 Hz, 1 H, 1′-H), 5.09 (d, $J_{1,2}$ = 3.9 Hz, 1 H, 1-H) ppm. ^{13}C NMR (D_2O, 125.7 MHz): δ = 20.3, 22.3 [$(CH_3)_2CHO$], 60.3 (C-6), 60.4 (C-3), 60.5 (C-6′), 63.1 (C-4), 63.2 (C-2), 68.9 (C-4′), 70.3 (Me_2CHO), 71.9 (C-5), 72.7 (C-2′), 76.8 (C-3′), 80.3 (C-5′), 88.7 (C-1′), 95.2 (C-1) ppm. HRMS (ESI): calcd. for $C_{15}H_{28}NaO_{11}S$ [M + Na]$^+$ 439.1245; found 439.1238.

(2-Propyl α-D-Glucopyranosid-3-yl) (β-D-Galactopyranosyl) (*S*)-Sulfoxide (17*S*): Thiodisaccharide sulfoxide **9***S* (33 mg, 0.046 mmol) was deacetylated as described above to give **17***S* (15 mg, 78%). $[\alpha]_D^{22}$ = +105.1 (c = 0.9, MeOH). ^{1}H NMR (D_2O, 500 MHz): δ = 1.18, 1.25 [2 d, J = 6.2 Hz, 6 H, $(CH_3)_2CHO$], 3.76–3.93 (m, 7 H, 5-H, 6a-H, 6b-H, 3′-H, 5′-H, 6′a-H, 6′b-H), 3.94 (dd, $J_{3,4}$ = 9.8, $J_{2,3}$ = 11.5 Hz, 1 H, 3-H), 4.00 (t, $J_{1′,2′}$ = $J_{2′,3′}$ = 10.0 Hz, 1 H, 2′-H), 4.01 (m, J = 6.2 Hz, 1 H, Me_2CHO), 4.03 (br. s, 1 H, 4′-H), 4.04 (dd, $J_{1,2}$ = 3.6, $J_{2,3}$ = 11.5 Hz, 1 H, 2-H), 4.14 (dd, $J_{4,5}$ = 9.2, $J_{3,4}$ = 9.8 Hz, 1 H, 4-H), 4.52 (d, $J_{1′,2′}$ = 10.1 Hz, 1 H, 1′-H), 5.03 (d, $J_{1,2}$ = 3.6 Hz, 1 H, 1-H) ppm. ^{13}C NMR (D_2O, 125.7 MHz): δ = 20.2, 22.2 [$(CH_3)_2CHO$], 58.6 (C-3), 60.2, 61.1 (C-6, C-6′), 63.2 (C-4), 65.5 (C-2′), 66.5 (C-2), 68.8 (C-4′), 70.1 (Me_2CHO), 71.2 (C-5), 73.9 (C-3′), 80.3 (C-5′), 90.6 (C-1′), 94.8 (C-1) ppm. HRMS (ESI): calcd. for $C_{15}H_{28}NaO_{11}S$ [M + Na]$^+$ 439.1245; found 439.1240.

(2-Propyl α-D-Gulopyranosid-4-yl) (β-D-Glucopyranosyl) (*R*,*S*)-Sulfoxide (18*R*,*S*): Deacetylation of **10***R*,*S* (37 mg, 0.052 mmol) gave **18***R*,*S* (18 mg, 83%). As the two diastereoisomers have different stabilities in the *O*-deacetylation reaction, the configuration of the product isomers was not assigned, although the ratio of the isomers was similar to that of the starting mixture; ratio *A*:*B*, 1:0.7. ^{1}H NMR (D_2O, 500 MHz): δ = 1.20 [d, J = 6.2 Hz, 5.1 H, 2 $(CH_3)_2CHO$], 1.26, 1.27 [d, J = 6.2 Hz, 5.1 H, 2 $(CH_3)_2CHO$], 3.46 (t, J = 9.7 Hz, 1 H, 4′-H *A*), 3.49 (t, J = 9.7 Hz, 0.7 H, 4′-H *B*), 3.58 (ddd, J = 2.2, 5.6, 9.7 Hz, 1 H, 5′-H *A*), 3.66 (m, 2.7 H), 3.74–4.00 (m, 11.8 H), 4.02, 4.05 (2 m, J = 6.2 Hz, 1.7 H, Me_2CHO *A* + *B*), 4.11 (dd, J = 3.6, 5.0 Hz, 0.7 H, 3-H *B*), 4.45 (t, J = 3.5 Hz, 1 H, 3-H *A*), 4.51 (d, $J_{1′,2′}$ = 9.7 Hz, 0.7 H, 1′-H *B*), 4.65 (m, 1 H, 5-H *A*), 4.66 (d, $J_{1′,2′}$ = 9.7 Hz, 1 H, 1′-H *A*), 4.73 (m, 0.7 H, 5-H *B*), 5.12 (d, $J_{1,2}$ = 4.2 Hz, 1 H, 1-H *A*), 5.14 (d, $J_{1,2}$ = 3.6 Hz, 0.7 H, 1-H *B*) ppm. ^{13}C NMR (D_2O, 125.7 MHz): δ = 20.6, 20.7, 22.4 (×2) [$(CH_3)_2CHO$ *A* + *B*], 57.1, 60.5, 60.6, 60.9, 61.0, 64.4, 65.7, 65.9, 66.2, 66.8, 67.1, 67.2, 68.0, 68.5, 68.6, 68.9, 69.1, 72.2 (×2),

76.7, 77.1, 80.5, 80.9, 88.14 (C-1′ *B*), 93.1 (C-1′ *A*), 96.4 (C-1 *B*), 97.1 (C-1 *A*) ppm. HRMS (ESI): calcd. for $C_{15}H_{28}NaO_{11}S$ [M + Na]$^+$ 439.1245; found 439.1250.

(2-Propyl α-D-Gulopyranosid-4-yl) (β-D-Galactopyranosyl) (*R*,*S*)-Sulfoxide (19*R*,*S*): Deacetylation of **11***R*,*S* (39 mg, 0.055 mmol) gave **19***R*,*S* (19 mg, 83%; ratio *A*:*B*, 1:0.8). ^{1}H NMR (D_2O, 500 MHz): δ = 1.20 [d, J = 6.2 Hz, 5.4 H, 2 (CH_3)$_2$CHO], 1.26, 1.27 [d, J = 6.2 Hz, 5.4 H, 2 (CH_3)$_2$CHO], 3.74–4.07 (m, 21 H), 4.12 (dd, J = 3.6, 5.3 Hz, 0.8 H, 3-H *B*), 4.43 (d, $J_{1′,2′}$ = 9.8 Hz, 0.8 H, 1′-H *B*), 4.50 (t, J = 3.5 Hz, 1 H, 3-H *A*), 4.63 (d, $J_{1′,2′}$ = 9.8 Hz, 1 H, 1′-H *A*), 4.68 (m, 1 H, 5-H *A*), 4.73 (m, 0.8 H, 5-H *B*), 5.11 (d, $J_{1,2}$ = 4.2 Hz, 1 H, 1-H *A*), 5.14 (d, $J_{1,2}$ = 3.5 Hz, 0.8 H, 1-H *B*) ppm. ^{13}C NMR (D_2O, 125.7 MHz): δ = 20.7 (×2), 22.4 (×2), 57.2, 59.6, 61.0 (×2), 61.1, 61.2, 64.4, 64.5, 65.7, 65.9, 66.3, 66.5, 67.2, 68.2, 68.6, 68.8, 72.2 (×2), 73.8 (×2), 80.2, 80.3, 88.8 (C-1′ *B*), 93.5 (C-1′ *A*), 96.3 (C-1 *B*), 97.1 (C-1 *A*) ppm. HRMS (ESI): calcd. for $C_{15}H_{28}NaO_{11}S$ [M + Na]$^+$ 439.1245; found 439.1236.

(2-Propyl α-D-Erythro-hex-3-enopyranosid-4-yl) (β-D-Galactopyranosyl) Sulfone (20): Deacetylation of **15** (40 mg, 0.055 mmol) gave **20** (13 mg, 57%) as the major product. ^{1}H NMR (D_2O, 500 MHz): δ = 1.20, 1.23 [2 d, J = 6.2 Hz, 6 H, (CH_3)$_2$CHO], 3.56–4.15 (m, 10 H), 4.56 (m, 1 H, 5-H), 4.61 (d, $J_{1′,2′}$ = 9.5 Hz, 1 H, 1′-H), 5.26 (d, $J_{1,2}$ = 4.0 Hz, 1 H, 1-H), 7.00 (s, 1 H, 3-H) ppm. ^{13}C NMR (D_2O, 125.7 MHz): δ = 21.5, 23.2 [(CH_3)$_2$CHO], 61.5, 62.4, 65.2, 66.5, 69.0, 70.5, 72.5, 74.3, 80.7, 92.5 (C-1′), 95.0 (C-1), 136.0 (C-4), 147.0 (C-3) ppm. HRMS (ESI): calcd. for $C_{15}H_{28}NaO_{11}S$ [M + Na]$^+$ 437.1088; found 437.1110.

Oxidation of Unprotected Thiodisaccharides 21 and 23: Unprotected thiodisaccharide **21**[29] or **23**[7] (32 mg, 0.079 mmol) was dissolved in a mixture of CH_2Cl_2 (0.1 mL) and MeOH (4 mL), and the solution was cooled to 0 °C. *m*CPBA (80%; 54 mg, 0.25 mmol) was added, and the mixture was stirred at room temp. for 6 h. After this time, TLC ($CHCl_3$/MeOH/AcOH/H_2O, 60:30:3:5) showed complete conversion of the starting material into a single product. The solvent was evaporated in vacuo to give a solid residue, which was stirred with water (1 mL). The solid residue of *m*CPBA and *m*-chlorobenzoic acid was removed by filtration. The filtrate was passed through an octadecyl C18 minicolumn (Amprep, Amersham Biosciences), and the eluate was evaporated in vacuo to give the pure unprotected sulfone.

(2-Propyl α-D-Glucopyranoside-3-yl) (β-D-Galactopyranosyl) Sulfone (22): Sulfone **22** (31 mg, 91%) was obtained as a colourless syrup. R_f = 0.29 ($CHCl_3$/MeOH/AcOH/H_2O, 60:30:3:5). $[a]_D^{22}$ = +67.2 (c = 1.4, MeOH). ^{1}H NMR (D_2O, 500 MHz): δ = 1.19, 1.25 [2 d, J = 6.2 Hz, 6 H, (CH_3)$_2$CHO], 3.74–3.91 (m, 7 H), 3.99–4.02 (m, 2 H, 4′-H, Me$_2$C*H*O), 4.04 (dd, $J_{1,2}$ = 3.6, $J_{2,3}$ = 10.3 Hz, 1 H, 2-H), 4.08 (dd, $J_{4,5}$ = 9.0, $J_{3,4}$ = 10.3 Hz, 1 H, 4-H), 4.13 (t, $J_{2,3}$ = $J_{3,4}$ = 10.3 Hz, 1 H, 3-H), 4.18 (t, $J_{1′,2′}$ = $J_{2′,3′}$ = 9.6 Hz, 1 H, 2′-H), 4.66 (d, $J_{1′,2′}$ = 9.6 Hz, 1 H, 1′-H), 5.04 (d, $J_{1,2}$ = 3.6 Hz, 1 H, 1-H) ppm. ^{13}C NMR (D_2O, 125.7 MHz): δ = 20.3, 22.2 [(CH_3)$_2$CHO], 60.3, 60.9 (C-6, C-6′), 61.7 (C-4), 62.7 (C-3), 65.2 (C-2′), 66.5 (C-2), 68.4 (C-4′), 70.4 (Me$_2$*C*HO), 71.3 (C-5), 73.6 (C-3′), 80.0 (C-5′), 92.3 (C-1′), 94.9 (C-1) ppm. HRMS (ESI): calcd. for $C_{15}H_{28}NaO_{12}S$ [M + Na]$^+$ 455.1194; found 455.1197.

(2-Propyl α-D-Gulopyranoside-4-yl) (β-D-Galactopyranosyl) Sulfone (24): Sulfone **24** (29 mg, 85%) was obtained as a syrup. R_f = 0.47 ($CHCl_3$/MeOH/AcOH/H_2O, 60:30:3:5). $[a]_D^{22}$ = +76.7 (c = 0.8, MeOH). ^{1}H NMR (D_2O, 500 MHz): δ = 1.19, 1.24 [2 d, J = 6.2 Hz, 6 H, (CH_3)$_2$CHO], 3.73–4.10 (m, 9 H), 4.16 (t, $J_{1′,2′}$ = $J_{2′,3′}$ = 9.5 Hz, 1 H, 2′-H), 4.28 (dd, $J_{4,5}$ = 4.5, $J_{3,4}$ = 8.0 Hz, 1 H, 4-H), 4.40 (dd, $J_{2,3}$ = 3.3, $J_{3,4}$ = 8.0 Hz, 1 H, 3-H), 4.55 (ddd, $J_{4,5}$ = 4.5, J = 3.3, 8.0 Hz, 1 H, 5-H), 4.72 (d, $J_{1′,2′}$ = 9.5 Hz, 1 H, 1′-H), 5.07 (d, $J_{1,2}$ = 2.3 Hz, 1 H, 1-H) ppm. ^{13}C NMR (D_2O, 125.7 MHz): δ = 20.8, 22.3 [(CH_3)$_2$CHO], 57.9 (C-4), 59.1, 61.0 (C-6, C-6′), 65.2 (C-2′), 65.9 (C-3), 68.3, 68.9, 69.2 (×2), 72.4, 73.5 (C-3′), 80.1 (C-5′), 91.5 (C-1′), 94.8 (C-1) ppm. HRMS (ESI): calcd. for $C_{29}H_{42}NaO_{18}S$ [M + Na]$^+$ 455.1194; found 455.1194.

Supporting Information (see footnote on the first page of this article): NOESY spectra of compounds **4**, **5**, and **7**; ^{1}H and ^{13}C NMR spectra and NOESY spectra of compounds **8***R* and **8***S*; ^{1}H and ^{13}C NMR spectra of compounds **9***R*, **9***S*, **10***R*,*S*, **11***R*,*S*, **12**–**15**, **16***R*, **17***S*, **18***R*,*S*, **19***R*,*S*, **20**, **22**, and **24**; figure showing the conformations of **10***R* based on NOE enhancements.

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