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Factors Influencing Stereoselectivity of Sulfur Oxidation: Substituent Effects on the Oxidation of 5-Thioglycopyranose Derivatives

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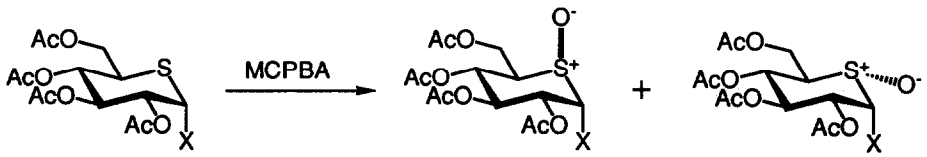
Abstract: Various 5-thioglycopyranose derivatives, including 5-thiogalactopyranose, 5-thiomannopyranose, and 1-substituted-5-thioglucopyranose derivatives, were oxidized to the sulfoxides with *m*-chloroperoxybenzoic acid (MCPBA) and 2-benzenesulfonyl-3-(*m*-nitrophenyl)-oxaziridine (BSNPO) in order to probe the origin of the reversal stereoselectivity observed in the MCPBA oxidation of the 1-*O*-methyl and 1-*O*-acetyl derivatives of 5-thio-α-D-glucopyranose. Analyses, using σ_p values, of the stereoselectivity in the oxidation of 1-*O*-(*p*-substituted benzoyl)-5-thio-α-D-glucose derivatives suggested that electronic effects of the anomeric substituents significantly affect the stereoselectivity and that the electron-donating and electron-withdrawing substituents tend to afford more and less of axial/equatorial ratios of the sulfoxides, respectively. The analyses, using multisubstituent parameters, of the oxidation of 1-substituted-5-thio-α-D-glucopyranose derivatives gave insight into the substituent effect on the stereoselectivity; that is, both the electronegativity effect and the resonance effect are involved, and steric repulsion between the anomeric substituent and the oxidant contributes especially in the case of the oxidation with the bulky BSNPO. It was shown from competition experiments, however, that the oxidation rates depend solely on the inductive effect (or electronegativity effect) of the anomeric substituent. From the extended Hückel orbital calculation on the model compounds and the regioselectivities in the oxidation of α- and β-1,5-dithioglucopyranoside derivatives, it was suggested that the oxidation rate is governed, in the same manner as anomeric effect, by the interaction between the sulfur lone pair and the antibonding orbital of the glycosidic bond. From these results, asymmetry of electron density on the sulfur lone pair orbital was proposed to be the origin of the stereoselectivity.

INTRODUCTION

Perturbation of π-facial selectivity in addition reactions by electronic effects of the neighboring or remote substituent has been demonstrated in recent years.[1] These findings give clues for understanding the stereoselectivity of some reactions that could not be explained by steric interactions. These studies have focused on the addition reactions of olefins and carbonyl compounds. No such studies have been reported on the oxidation of sulfur compound, though the relation between the type of oxidizing reagent and stereoselectivity have been reported.[2] On the other hand, we have recently found that the stereoselectivity in the oxidation of 5-thioglucose derivatives **1**, the ring sulfur analogs of glucose, with *m*-chloroperoxybenzoic acid (MCPBA) depends on the anomeric substituents (**X**); that is, the methyl α-glucoside **1-OMe** mainly gave the axial sulfoxide **ax-2** while the α-1-acetate **1-OAc** preferentially gave the equatorial sulfoxide **eq-2** (Scheme 1).[3] Steric effects



X	ax-2:eq-2
OMe	83:17
OAc	29:71
H	44:56

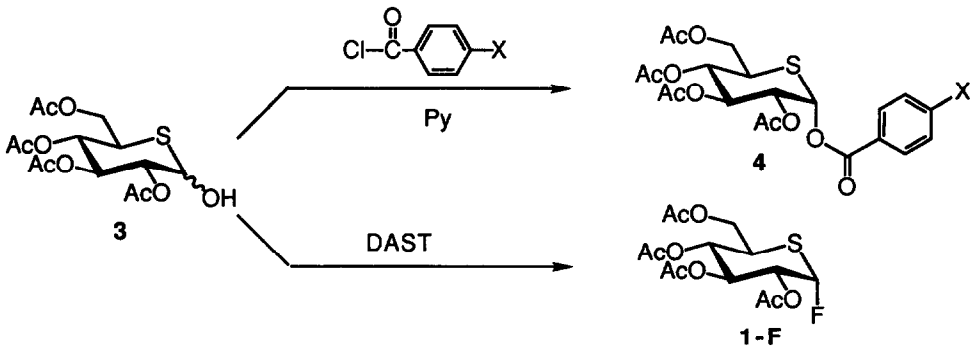
Scheme 1

seemed not to be the main factors of the reversal stereoselectivity because the acetoxyl and methoxy groups, which are almost the same in size, lead to opposite selectivity while the less hindered 1-deoxy derivative **1-H** afforded little selectivity. Neither electrostatic interactions nor hydrogen bonding was considered to be important because of the lack of solvent effects. The interaction between the sulfur lone pair orbital and the antibonding orbital of the glycosidic bond (n-σ^*), which is supposed to be the origin of the anomeric effect,[4] was proposed as the most plausible cause for the origin of the reversal stereoselectivity. A detailed study is however required to elucidate the general factors influencing the stereoselectivity in sulfur oxidation. Thus, in this paper we explore how the anomeric substituents affect the stereoselectivity. It is noteworthy that high rigidity of pyranose ring make 5-thiosugars suitable probes for the investigation because the each substituent, which may effect the stereoselectivity, is forced to remain the same position from the reaction center during oxidation reaction. The oxidation of 5-thiosugars with configurations other than glucose was also examined.

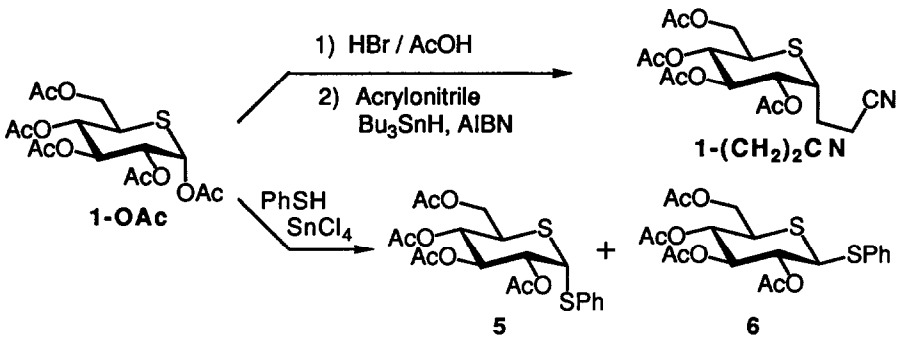
RESULTS AND DISCUSSION

Preparation of Substrates

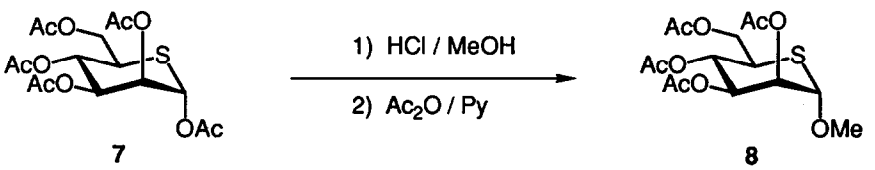
The 1-*O*-(*p*-substituted benzoyl)-5-thio-α-D-glucopyranose derivatives **4** were prepared from 2,3,4,6-tetra-*O*-acetyl-5-thioglucopyranose (**3**)[5] with the corresponding *p*-substituted benzoyl chloride in pyridine (Scheme 2). The corresponding β-anomers were barely detectable by ^{1}H NMR spectroscopy. Treatment of **3** with *N*,*N*-diethylaminosulfur trifluoride (DAST) gave 2,3,4,6-tetra-*O*-acetyl-5-thio-α-D-glucopyranosyl fluoride (**1-F**).[6]



Scheme 2

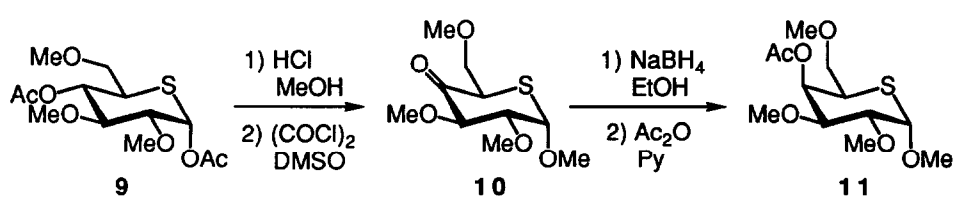


Scheme 3



Scheme 4

Treatment of 1,2,3,4,6-penta-*O*-acetyl-5-thio-α-D-glucopyranose (**1-OAc**)[5,7] with 30% hydrogen bromide in acetic acid followed by "C-glycosidation"[8] with acrylonitrile, tri-*n*-butyltin hydride, and α,α'-azobisisobutyronitrile (AIBN) gave 1-(2',3',4',6'-tetra-*O*-acetyl-5-thio-α-D-glucopyranosyl)-propionitrile (**1-$(CH_2)_2$CN**). Treatment of **1-OAc** with benzenethiol and tin(IV) chloride gave α and β anomers of phenyl thioglycosides (**5** and **6**) that were separated by column chromatography (Scheme 3). Methanolysis of 1,2,3,4,6-penta-*O*-acetyl-5-thio-α-D-mannopyranose (**7**)[9] followed by acetylation gave methyl 2,3,4,6-tetra-*O*-acetyl-5-thio-α-D-mannopyranoside (**8**, Scheme 4). Methanolysis of 1,4-di-*O*-acetyl-2,3,6-tri-*O*-methyl-5-thio-α-D-glucopyranose (**9**)[5] followed by Swern oxidation gave methyl 2,3,6-tri-*O*-methyl-5-thio-α-D-*xylo*-hexopyranosid-4-ulose (**10**). Reduction of the carbonyl group of **10** with sodium borohydride followed by acetylation gave methyl 4-*O*-acetyl-2,3,6-tri-*O*-methyl-5-thio-α-D-galactopyranoside (**11**, Scheme 5). The configuration at the C-4 of **11** was confirmed by the small coupling constants ($J_{3,4}$ = 3.0, $J_{4,5}$ = 0 Hz) in the ^{1}H NMR spectrum.



Scheme 5

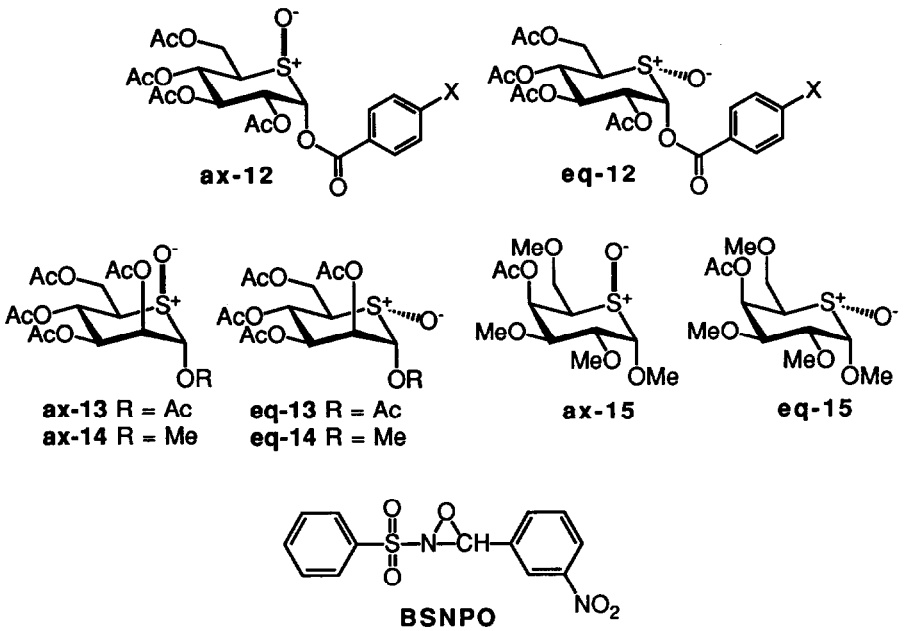
Oxidation

MCPBA oxidation of the 5-thiosugars was carried out under conditions (–20 °C, 15 min in dichloromethane) previously reported.[3] The oxidation with 2-benzenesulfonyl-3-(*m*-nitrophenyl)-oxaziridine (BSNPO),[10] which is similar to MCPBA in oxidation mechanism, was also examined with some 5-thiosugars (reflux, 1 h in 1,2-dichloroethane) for comparison. The yields and axial / equatorial ratios of the sulfoxides thus obtained (Scheme 6) are presented in Table 1. The stereochemistry of the sulfoxides was determined from the empirical rules of the chemical shifts in their ^{1}H NMR spectra wherein axial H-2 and axial H-4 signals of the axial sulfoxides resonate at much lower field (0.3—0.8 ppm) than those of the thioglycosides because of deshielding effect, and the H-1 signals of the equatorial sulfoxides are at lower field (~0.3 ppm) than those of the axial sulfoxides.[3] Isomeric ratios were determined by the relative intensities of either H-1 (in most cases), H-2, or H-4 signals for each isomer in the ^{1}H NMR spectra of the isomeric mixtures.

Table 1. Oxidation of the 5-Thiosugar Derivatives.

substrates	reagents	products	yield, %	ax:eq
1-H	BSNPO	**2-H**	100	31:69[a]
1-OMe		**2-OMe**	95	68:32[b]
1-OAc		**2-OAc**	88	36:64[b]
1-F	MCPBA	**2-F**	20[c]	62:38[a]
	BSNPO		43	54:46[a]
1-$(CH_2)_2CN$	MCPBA	**2-$(CH_2)_2CN$**	75	66:34[a]
	BSNPO		83	60:40[a]
4-H	MCPBA	**12-H**	50	38:62[b]
	BSNPO		90	57:43[b]
4-OMe	MCPBA	**12-OMe**	70	42:58[a]
	BSNPO		74	59:41[b]
4-Cl	MCPBA	**12-Cl**	49	36:64[a]
	BSNPO		87	49:51[b]
4-CF_3	MCPBA	**12-CF_3**	51	27:73[a]
	BSNPO		83	46:54[b]
4-NO_2	MCPBA	**12-NO_2**	55	24:76[b]
	BSNPO		69	36:64[b]
7	MCPBA	**13**	77	4:96[a]
8		**14**	74	25:75[a]
11		**15**	76	52:48[a]

[a]Determined by 500 MHz NMR. [b]Determined by 100 MHz NMR. [c]Prolongation of reaction time to 1 h gave 44% yield of products with the same ax:eq ratio.



Scheme 6

Analyses of Stereoselectivity

One possible explanation for the reversal of stereoselectivity observed on going from methyl glycosides to 1-O-acetates is that equatorial attack of MCPBA is favored by a hydrogen bonding interaction between MCPBA and the acetyl group of the 1-acetate **1-OAc**. *Syn* selectivity has indeed been observed in the epoxidation of β-acetoxy olefins with MCPBA and has been ascribed to the hydrogen bonding between the carbonyl oxygen of the olefins and MCPBA.[11] If an acetyl group is present near the axial side of the sulfur lone pair in the 5-thiosugar derivative, then MCPBA might prefer axial attack with the assistance of hydrogen bonding. To test the possibility, the 5-thiomannose derivatives **7** and **8** and the 5-thiogalactose derivative **11**, which have the axial acetoxyl group at C-2 or C-4 and would bear the carbonyl oxygen near the axial side of the sulfur lone pair, were oxidized with MCPBA. Compared with the oxidation of the methyl 5-thioglucopyranoside **1-OMe** (Scheme 1), the rate of the formation of axial sulfoxides clearly decreased in the oxidation of the methyl 5-thiomannopyranoside **8** and the methyl 5-thiogalactopyranoside **11**. Furthermore, the oxidation of the 5-thiomannose pentaacetate **7** gave better equatorial selectivity than that of the corresponding 5-thioglucopyranose **1-OAc**. From these results the acetoxyl group is considered to inhibit rather than to assist the attack of MCPBA and it is therefore unlikely that the equatorial selectivity observed in the oxidation of **1-OAc** is consequence of hydrogen bonding.

To look into the effect of the electronic properties of the anomeric substituents toward stereoselectivity, oxidation of the 1-*O*-(*p*-substituted benzoyl)-5-thioglucose derivatives **4** with MCPBA and BSNPO was performed. As a result, slight but significant change in the stereoselectivity was observed with modifications of the para substituent. Correlation analyses was performed for both MCPBA and BSNPO oxidation (Figure 1).

Plots of the log **ax-12/eq-12** vs σ_p[12] reveal excellent linear correlations for each oxidation; that is, the stereoselectivity is affected by electronic effects from the C-1 substituents. Obviously, the equatorial selectivity increases with the electron-accepting ability of the anomeric substituent. The slopes (*a* in the regression equations log **ax-12/eq-12** = $a\ \sigma_p + b$) are almost the same for both oxidations, indicating that sensitivity of the stereoselectivity to the electronic effects of the para substituents is similar for both. BSNPO has the secondary carbon atom and the secondary amine next to the oxygen atom that contributes to the oxidation reaction and therefore is much bulkier than MCPBA which has the hydrogen and the oxygen atoms next to the reactive oxygen. Accordingly, the steric repulsion between BSNPO and the axial substituent at C-1 can bias the attack of BSNPO toward the opposite side of the C-1 substituent, i.e., the axial attack. This is considered to be the reason the intercept value (*b*) in the regression line of the BSNPO oxidation is much larger than that of the MCPBA oxidation. These results suggest a correlation between stereoselectivity and the electronic effects of the C-1 substituent but the type of electronic effect which influences the stereoselectivity was not clear.

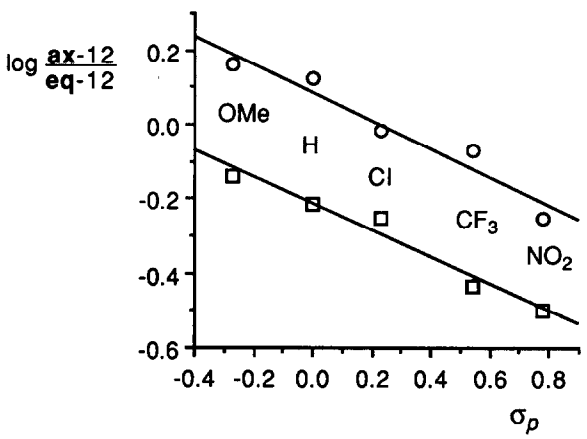


Figure 1. Plots of log **ax-12/eq-12** vs σ_p for the oxidations of **4** and least-squares linear regression analyses: (O) BSNPO, log **ax-12/eq-12** = $-0.379\sigma_p + 8.580 \times 10^{-2}$ (r^2 = 0.939); (□) MCPBA, log **ax-12/eq-12** = $-0.359\sigma_p - 0.215$ (r^2 = 0.964).

The electronic properties of a substituent can be classified into three types according to the way in which they are transmitted to the reaction center: the electric field associated with the substituent dipole (field effect), the electronegativity (χ) of the substituent group, and the ability of a substituent to act as a π-electron donor or acceptor (resonance effect).[13] To evaluate which of the effects is of importance to the stereoselectivity, regression analyses were performed for the oxidation of the five C-1 substituted derivatives **1-X** (**X = H, OMe, OAc, F,** $(CH_2)_2CN$), i.e., the plots of log **ax-2/eq-2** vs σ_I (the total polar effect including both field and inductive effects),[14] σ_χ (electronegativity),[15] or σ_R (resonance effect)[14] as a substituent constant (Table 2). However no single substituent parameter gave a significant correlation with the stereoselectivity (r^2<0.5). This implies that more than two effects could be involved and therefore analyses with the linear combination of multisubstituent parameters should be performed.

Table 2. Substituent Parameters Used for the Analyses of **ax-2:eq-2** Product Ratios.

X	σ_I	σ_χ	σ_R	υ
OMe	0.30	0.39	–0.58	0.36
OAc	0.38	0.42	–0.23	0.48[d]
H	0	0	0	0
$(CH_2)_2CN$	0.09[a]	0.06[b]	–0.12[c]	0.68[e]
F	0.54	0.53	–0.48	0.27

[a]Calculated from eq 11 of Table 45 in reference 14. [b]$\chi_{(CH_2)_2CN}$ (2.37) was calculated from eq 2—4 in reference 15. [c]Calculated from eq12 of Table 45 in reference 14. [d]The value for ethoxy group was used as an approximation. [e]The value for propyl group was used as an approximation.

As has already been shown in the oxidation of 5-thiomannose **7**, **8** and 5-thiogalactose **11** derivatives with MCPBA and the oxidation of 1-*O*-(*p*-substituted benzoyl)-5-thioglucose derivatives **4** with BSNPO, steric effects would not be negligible for the analyses. Though several steric substituent constants have been postulated, e.g., Taft's E_S value[16] and Charton's υ value,[17] we chose the υ value because the values for three out of the five C-1 substituents examined in the analyses are available and many examples of the values enabled us to make approximation for the remaining two substituents as shown in Table 2. Thus the regression analyses of the stereoselectivity with the multisubstituent parameters including σ_I, σ_χ, σ_R, and υ were performed.

Table 3. Statistical Analyses of Substituent Effects on the **ax-2:eq-2** Product Ratios Using Multisubstituent Parameters.[a]

reagents	parameters	ρ_I	ρ_χ	ρ_R	ρ_υ	b	r^2
MCPBA	σ_I, σ_R	–1.986	—	–2.383	—	-1.254×10^{-2}	0.842
	σ_χ, σ_R	—	–2.321	–2.924	—	-3.655×10^{-2}	0.957
	σ_I, σ_R, υ	–1.990	—	–2.388	0.199	-8.409×10^{-2}	0.863
	σ_χ, σ_R, υ	—	–2.308	–2.908	0.185	–0.102	0.969
BSNPO	σ_I, σ_R	–0.888	—	–1.421	—	–0.173	0.673
	σ_χ, σ_R	—	–1.141	–1.734	—	–0.175	0.763
	σ_R, υ	—	—	–0.782	0.469	–0.393	0.674
	σ_I, σ_R, υ	–0.923	—	–1.385	0.554	–0.352	0.891
	σ_χ, σ_R, υ	—	–1.162	–1.696	0.511	–0.341	0.963

[a]Values presented are from general equation: $\log$ **ax-2:eq-2** $= \rho_I\sigma_I + \rho_\chi\sigma_\chi + \rho_R\sigma_R + \rho_\upsilon\upsilon + b$.

Within every combination of the four parameters examined, avoiding the duplication of σ_I and σ_χ, the examples that exhibited significant ($r^2 > 0.6$) correlation with the stereoselectivity are shown in Table 3. In the analyses with two parameters, so called dual substituent parameter (DSP) analysis,[18] all sets that demonstrate

significant correlation with the stereoselectivity include σ_R as a fragment parameter. This indicates that at least resonance effect is involved in the electronic effects and affects the stereoselectivity. Though involvement of resonance effects in aliphatic systems seems unlikely, it is reported[19] that in some cases, e.g., the ultraviolet absorption (ν_{CN}) of YCH_2CN, a resonance effect of substituents apparently is transmitted through the aliphatic skeleton to perturb some properties. Another fragment of DSP, σ_χ, gave a better correlation than σ_I for both the MCPBA and BSNPO oxidations. The σ_I values originate from experimental data and therefore they contain terms of electrostatic effects (field effects), electronegativity effect, and other minor effects.[13] Accordingly, the above results show that electronegativity effect, not field effect, would be one of the significant effects on the stereoselectivity. The field effect has its origin in charge-charge, charge-dipole, or dipole-dipole interaction ("through space") between a substituent and the reaction center;[13] hence the lack of contribution from these effects is consistent with the lack of solvent effects on the stereoselectivity (*vide supra*). On the other hand, the electronegativity effect originates from the partial ionic character of the sigma bond between a substituent and its bonded atom of the molecular framework; therefore, the interaction range is short and the transmission mode of this effect is "through bond."[13] These characteristics would make the electronegativity effect difficult to transmit to the reaction center, i.e., the sulfur atom, directly. The third term, υ, appears only in combination with σ_R in the DSP analysis of the BSNPO oxidation. This suggests that steric effects are very important in the BSNPO oxidation as described earlier.

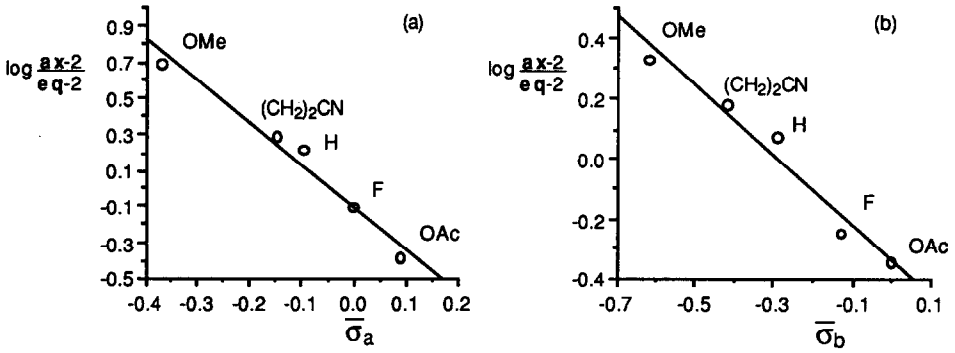


Figure 2. Plots of log **ax-2/eq-2** vs multisubstituent parameter ($\bar{\sigma}$) for the oxidation of **1** with MCPBA (a) and BSNPO (b). For the graphical displays, the equation was transformed as follows: $\log$ **ax-2/eq-2** $= \rho_\chi\sigma_\chi + \rho_R\sigma_R + \rho_\upsilon\upsilon + b = \rho_\chi\bar{\sigma}$, where $\bar{\sigma} = \sigma_\chi + \sigma_R\rho_R/\rho_\chi + \upsilon\rho_\upsilon/\rho_\chi$.

The lower correlations in the DSP analyses, using σ_R and σ_I or σ_χ, of the BSNPO oxidation than those of the MCPBA oxidation can be ascribed to the lack of steric parameters. Therefore the analyses with three parameters including υ were performed and all possible combinations gave improvement in correlations compared with the corresponding DSP analyses without υ. The best correlation was obtained with a combination of σ_χ, σ_R, and υ for both the MCPBA oxidation and the BSNPO oxidation (Figure 2), suggesting that electronegativity, resonance, and steric effects are the main factors influencing the stereoselectivity. The larger coefficient of υ (ρ_υ) for the BSNPO oxidation, as compared with that for the MCPBA oxidation, again indicates a large steric bias between BSNPO and the anomeric substituent. In some cases improvement in correlation by adding further

parameters may be fortuitous but the consistency seen in the analyses for the two oxidants, and the excellent correlation coefficients, support the validity of the multisubstituent parameter analyses.

From the results of the analyses with multisubstituent parameters, the following correlations between the properties of the anomeric substituents and the stereoselectivity in the oxidation of 5-thioglucose derivatives are made: (1) electronegative substituents tend to afford the equatorial sulfoxide, (2) substituents with electron-donating resonance effects tend to afford the axial sulfoxides, (3) bulky substituents tend to afford axial sulfoxides, (4) the effect of (3) is small for the MCPBA oxidation and significant for the BSNPO oxidation.

Competition Experiment

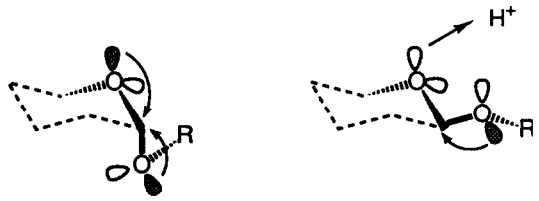
That the stereoselectivity, i.e., the product ratio of the axial sulfoxide to the equatorial sulfoxide (ax:eq), reflects the *intramolecular* relative rate $k_{ax}:k_{eq}$ raises the simple question whether the mode of the substituent effects observed for the *intramolecular* relative rate is also observed for *intermolecular* relative rates. Thus, competition experiments with the compounds **1-H**, **1-OMe**, **1-OAc**, and **1-F** were carried out. Equimolar mixtures of two of thiosugars were stirred with 0.25 equiv. of MCPBA in dichloromethane at –20°C for 15 min. The product ratio was determined from the relative intensities in the ^{1}H NMR spectra of the crude mixture. The product ratios for **2-H**:**2-OMe**, **2-OMe**:**2-OAc**, and **2-OAc**:**2-F** were >20:1, 2:1, and >20:1 respectively. The approximate order of the relative rate is therefore F << OAc < OMe << H. Qualitatively speaking, this order is the same as that of σ_I or σ_χ but not of σ_R nor υ. Therefore the major factor of the substituent effect that affects the oxidation rate would be field or electronegativity effect, and the contribution from resonance (or steric) effects is considered to be negligible unlike the substituent effects on the stereoselectivity. This suggests that the mechanism through which the substituent affects the oxidation rate is independent of that for the stereoselectivity.

Table 4. Relative Rates of MCPBA Oxidation of **1** and Calculated HOMO Energy (eV) of the Model Compound **16**.

X	relative rate	HOMO energy
H	>200	–12.46
OMe	2	–12.61
OAc	1	–12.64
F	<0.01	–12.70

A negative correlation between the inductive effect of the substituent and the reaction rate has been observed in the electrophilic addition reactions toward substituted olefins and has been ascribed to the concerted decrease of the highest occupied molecular orbital (HOMO) energy with the increase of inductive effect.[20] Similarly, the HOMO energy is thought to be important in the linear free energy relationship observed in the oxidation of the 5-thioglucose **1**, since the HOMO energy of CH_3SCH_2X **16**[21] (which is a model for the 5-thiosugar derivatives **1**) calculated by extended Hückel method[22] (Table 4) is found to correlate either with σ_I (r^2 = 0.993) or σ_χ (r^2 = 0.996). Although this correlation could be explained simply by perturbation of the HOMO energy by the bond polarity transmitted through bonds (S-C-X) or through space, orbital interaction between the HOMO, i.e., the sulfur lone pair orbital (n), and the antibonding orbital (σ^*) of the glycosidic linkage is the most probable origin

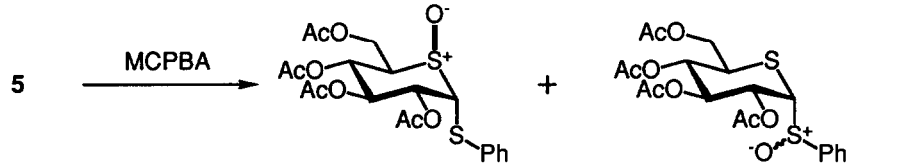
as follows. It is reported that the strength of an anomeric effect, the tendency of the substituent at the anomeric position to take axial orientation in a pyranose ring, correlates with the electronegativity or the inductive effect of the substituent.[23] This phenomenon has been explained by the interaction between the lone pair orbital (n) of the ring oxygen and the antibonding orbital (σ*) of the glycosidic bond:[4] the more electronegative the anomeric substituent is, the larger the interaction energy of n-σ* becomes with decrease in the energy of σ*. This orbital interaction could exert a large effect on HOMO energy of the 5-thiosugar derivatives.



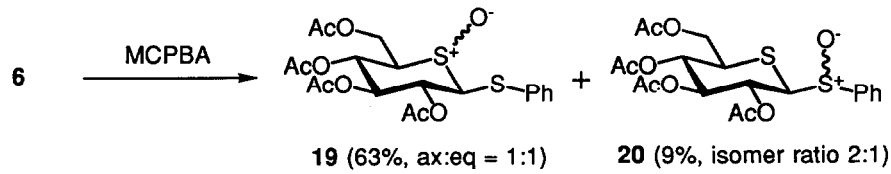
gg (α-glucoside) ***gt*** (β-glucoside)

Figure 3. Relationship between the conformation and the basisity of the oxygen atom in acetal compounds.

The most stable conformation in a generalized acetal ROCHOR is the *gauche-gauche* (*gg*) conformation, since two stabilizing interactions (i.e., n-σ*) are involved while in the *trans-gauche* (*tg*) conformation only one such interaction exists (Figure 3).[24] It has therefore been suggested that the basisity of ring oxygen is higher in β-glucosides (*tg*) than in α-glucosides (*gg*) since the ring oxygen of β-glucosides, unlike α-glucosides, is not involved in n-σ* interaction.[24,25] This argument is applicable to the relative nucleophilicity of the sulfur atoms in dithioacetals if the nucleophilicity is governed mainly by the n-σ* interaction as well. Thus the α and β anomers of phenyl-1,5-dithioglucopyranosides **5** and **6** were oxidized with MCPBA to give the corresponding *endo*- and *exo*- sulfoxides in the ratio (**17**:**18** ≈) 13:73 and (**19**:**20** ≈) 63:9, respectively (Scheme 7). These results demonstrate the higher nucleophilicity of the ring sulfur in the β-glucoside **6** than in the α-glucoside **5**, and hence point the importance of the n-σ* interaction on the oxidation rates.



17 (13%) **18** (73%, isomer ratio 4:1)



19 (63%, ax:eq = 1:1) **20** (9%, isomer ratio 2:1)

Scheme 7

Model for Origin of the Stereoselectivity

The mechanism of oxygen transfer from peracids to sulfides has been investigated from both the kinetic[26] and theoretical[27] points of view. These reactions have the following mechanistic features: (1) Peracids are electrophilic toward sulfides.[26] (2) The oxidation are second-order reactions (first order for each component) and hence the transition state contains both peracid and sulfide.[26] (3) A reagent-like early transition state has been supported by relatively small reaction constants (ρ) and the lack of salts effect.[26] (4) The transition state model that the peracid approaches the sulfur atom along the axis of 3p orbital has been suggested by *ab initio* calculation using oxaziridine and hydrogen sulfide as model compounds.[27] (5) In the frontier molecular orbital (FMO) theory, these reactions involve the interaction between HOMO (3p-like lone pair) of the sulfide and the lowest unoccupied molecular orbital (LUMO) of the peracid.[27]

One can then draw a rough model of transition state of the oxidation as shown in Figure 4. Although the bonding state and hybridization of the product sulfoxide are complicated,[27] it is sufficient for this discussion to consider which is the energetically more favored of the two transition structures in which the each oxygen atom transferred from the peracid is located on the axis of the 3p orbital above and below the C-S-C plane, respectively.

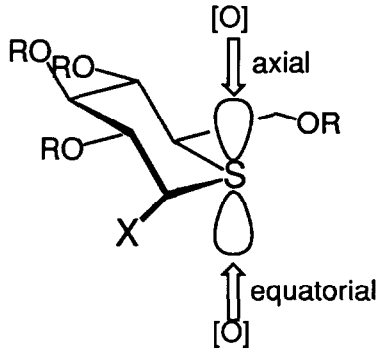


Figure 4. Transition-state geometry for the oxidation of **1**.

Some models explaining how the electronic properties of neighboring bond affect the π-facial selectivity of addition reactions to carbonyl compounds or olefins are based on a significant bond formation in the transition states (TS).[1a-k] For example, in Cieplak model,[1a] preferred anti attack with respect to the most electron-donationg neighboring bond (σ) is explained by stabilization of TS due to interaction of σ with antibonding orbital of the incipient bond ($\sigma^*_{\neq}$). In the sulfur oxidation, however, the contribution of an incipient bond in the TS to the stabilization by orbital interaction is hard to accept because the TS is such that an oxidant is *approaching* the lone pair of the sulfur atom from far away and any significant bond would not be formed. As the TS is very close to the substrate, it is more reasonable to suppose that the difference of the TS energies between the two attack routes would simply reflect the difference between each lobe of the lone pair orbitals, i.e., asymmetry of the 3p orbital in the substrate. Asymmetry of p orbitals has been proposed as origin of the π-facial selectivity in some addition reactions, e.g., *exo*-face selectivity in electrophilic additions to norbornene[29] and *endo*-face selectivity in [4+2] cycloaddition reactions of isodicyclopentadiene,[11,30] where distortion of the π orbitals by the mixing of another component of canonical orbitals is postulated. Similarly, if the 3p orbital of the

sulfur lone pair is distorted, stereoselectivity in the oxidation could be perturbed. In principle, such an orbital distortion can be monitored by a low temperature X-ray charge density study.[31] A study on trans-2,5-dichloro-1,4-dioxane was recently reported and it was manifested that the lone pair orbital of the oxygen atom is 2p-like but the lobe anti to the Cl atom is fused with the C-O bond at the anomeric position although it is not clear whether this phenomenon is related with anomeric effect.[32] If this fusion holds in the sulfur lone pair of the 5-thioglucose derivatives, the shape can be roughly depicted as Figure 5. The upper lobe of the sulfur lone pair, fused with the C-S bond, is situated so that it can interact with the anomeric substituent not only through a σ bond but also through hyperconjugation. Therefore the upper lobe, independent of the lower lobe, can be perturbed either by electronegativity or resonance effects of the X group. In other words, the electron density at the upper lobe of HOMO should be determined by electron withdrawal or electron donation from the X group. When the X group is highly electronegative and the resonance effect is negligible, the electron density of the upper lobe would be less than that of the lower one; hence the oxidants would preferably attack the lower lobe to afford the equatorial sulfoxide. On the other hand, when the electron-donationg resonance effect of the X group is important, the electron density of the upper lobe would be greater than that of the lower one. Hence the oxidants would preferentially attack the upper lobe to afford the axial sulfoxide.

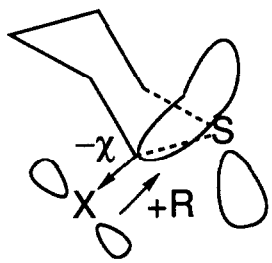


Figure 5. Model of lone pair orbital distortion of the ring sulfur atom of the 5-thiopyranoses.

From Klopman's theorem,[33] stabilization energy (ΔE) in the interaction of HOMO and LUMO is inversely proportional to the energy separation of the HOMO (E_{HOMO}) and LUMO (E_{LUMO}) and proportional to the square of their overlap (S) as shown in eq 1.

$$\Delta E \propto \frac{S^2}{E_{LUMO} - E_{HOMO}} \qquad (1)$$

The absolute rate of the oxidation is considered to be under the control of the denominator of eq 1 because it is correlated with calculated E_{HOMO} as has been discussed. The larger inductive effect of X is, the larger n-σ^*_{CX} interaction energy would be. As the lone pair orbital is the larger part of the HOMO, E_{HOMO}, and simultaneously the ΔE, is decreased by the n-σ* interaction. On the other hand, the stereoselectivity is considered to be controlled by effectiveness of overlap between the HOMO of the 5-thioglucose derivative and LUMO of the oxidant; i.e., the numerator of eq 1, because there is no asymmetry in orbital energy. Interestingly, this argument is consistent with the above discussions in that the stereoselectivity is under control of asymmetry in the electron density of the sulfur lone pair orbital and the effects of the X group on the stereoselectivity and the oxidation rate are independent of each other.

CONCLUSION

A large dependence of the stereoselectivity in sulfur oxidation on the electronic properties of the neighboring substituent was demonstrated for the first time by making use of rigid and sterically defined 5-thioglucopyranose derivatives as substrates. The multisubstituent parameter analyses resolved the effect of the neighboring substituent on the stereoselectivity into electronegativity, resonance, and steric effects. The oxidation rate was found to be dependent mainly on electronegativity or inductive effect. Though the latter is easily understandable from FMO theory, there has been no model to explain the electronic effects of the former. Our novel model is based on the assumption that the upper lobe of the sulfur lone pair is fused with the other bond. To verify this, low temperature X-ray charge density study of the 5-thio-α-D-glucose derivative would be necessary. Furthermore, to clarify whether the observed phenomena are specific for the 5-thiosugars, studies on simpler sulfides should be performed.

EXPERIMENTAL

Melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. Optical rotations were determined with a JASCO DIP-4 polarimeter. Column chromatography was performed on Wako gel C-300 with solvent system specified. ^{1}H NMR spectra were obtained with a JEOL JNM-PS100 (100 MHz) or a JNM-GX500 (500 MHz) spectrometer. ^{13}C NMR spectra were obtained with a JEOL JNM-FX90Q spectrometer. Chemical shifts were recorded as δ values in parts per million (ppm) from tetramethylsilane as an internal standard in deuteriochloroform. High-resolution mass spectra (HRMS) were obtained with a JEOL JMS-SX102 spectrometer.

General Procedure for the Preparation of 1-Benzoates 4. To a stirred solution of **3** (0.3 mmol) in pyridine (1.5 mL) was added an appropriately substituted benzoyl chloride (1 mmol) at 0 °C. After stirring for 2 h at room temperature, the mixture was poured into ice water and extracted with $CHCl_3$. The extracts were washed with aqueous $NaHCO_3$, dried over $MgSO_4$, and concentrated. The residue was chromatographed on silica gel, with hexane-EtOAc (3:1—2:1), to give a syrupy product.

2,3,4,6-Tetra-*O*-acetyl-1-*O*-benzoyl-5-thio-α-D-glucopyranose (4-H): Yield 90%; $[\alpha]_D^{29}$ +223° (c 1.6, $CHCl_3$); ^{1}H NMR δ 8.24—7.44 (m, 5H, Ar), 6.48 (d, 1H, J = 3.0 Hz, H-1), 5.70—5.34 (m, 3H, H-2, H-3, H-4), 4.51 (dd, 1H, J = 5.2, 12.0 Hz, H-6a), 4.15 (dd, 1H, J = 2.8, 12.0 Hz, H-6b), 3.76 (ddd, 1H, J = 10.8, 2.8, 5.2 Hz, H-5), 2.15 (s, 6H, 2 x $COCH_3$), 2.09 and 2.03 (each s, 3H, $COCH_3$). Anal. Calcd for $C_{21}H_{24}O_{10}S$: C, 53.84; H, 5.16; S, 6.84. Found: C, 53.71; H, 4.99; S, 6.64.

2,3,4,6-Tetra-*O*-acetyl-1-*O*-(4-methoxybenzoyl)-5-thio-α-D-glucopyranose (4-OMe): Yield 85%; $[\alpha]_D^{21}$ +214° (c 1.2, $CHCl_3$); ^{1}H NMR δ 8.08 and 7.03 (each d, 2H, J = 8.5 Hz, Ar), 6.41 (d, 1H, J = 3.0 Hz, H-1), 5.75—5.31 (m, 3H, H-2, H-3, H-4), 4.47 (dd, 1H, J = 4.8, 11.8 Hz, H-6a), 4.13 (dd, 1H, J = 3.0, 11.8 Hz, H-6b), 3.96 (s, 3H, OCH_3), 3.76 (ddd, 1H, J = 10.2, 4.8, 3.0 Hz, H-5), 2.12 (s, 6H, 2 x $COCH_3$), 2.07 and 2.01 (each s, 3H, $COCH_3$). Anal. Calcd for $C_{22}H_{26}O_{11}S$: C, 53.01; H, 5.26; S, 6.43. Found: C,

52.90; H, 5.23; S, 6.37.

2,3,4,6-Tetra-*O*-acetyl-1-*O*-(4-chlorobenzoyl)-5-thio-α-D-glucopyranose (4-Cl): Yield 100%; ^{1}H NMR δ 8.00 and 7.47 (each d, 2H, *J* = 8.0 Hz, Ar), 6.39 (d, 1H, *J* = 2.0 Hz, H-1), 5.72—5.24 (m, 3H, H-2, H-3, H-4), 4.46 (dd, 1H, *J* = 4.8, 12.0 Hz, H-6a), 4.11 (dd, 1H, *J* = 3.0, 12.0 Hz, H-6b), 3.72 (m, 1H, H-5), 2.12 (s, 6H, 2 x $COCH_3$), 2.08 and 2.00 (each s, 3H, $COCH_3$). Anal. Calcd for $C_{21}H_{23}ClO_{10}S$: C, 50.15; H, 4.61; Cl, 7.05. Found: C, 49.91; H, 4.72; Cl, 6.09.

2,3,4,6-Tetra-*O*-acetyl-1-*O*-(4-trifluoromethylbenzoyl)-5-thio-α-D-glucopyranose (4-CF_3): Yield 85%; $[\alpha]_D^{21}$ +187° (c 1.7, $CHCl_3$); ^{1}H NMR δ 8.20 and 7.78 (each d, 2H, *J* = 8.0 Hz, Ar), 6.40 (d, 1H, *J* = 3.0 Hz, H-1), 5.72—5.28 (m, 3H, H-2, H-3, H-4), 4.42 (dd, 1H, *J* = 5.0, 12.0 Hz, H-6a), 4.10 (dd, 1H, *J* = 3.0, 12.0 Hz, H-6b), 3.72 (ddd, 1H, *J* = 11.0, 5.0, 3,0 Hz, H-5), 2.11 (s, 6H, 2 x $COCH_3$), 2.05 and 1.98 (each s, 3H, $COCH_3$). Anal. Calcd for $C_{22}H_{23}F_3O_{10}S$: C, 49.25; H, 4.32. Found: C, 49.05; H, 4.26.

2,3,4,6-Tetra-*O*-acetyl-1-*O*-(4-nitrobenzoyl)-5-thio-α-D-glucopyranose (4-NO_2): Yield 85%; $[\alpha]_D^{23}$ +218° (c 1.1, $CHCl_3$); ^{1}H NMR δ 8.56—8.31 (m, 4H, Ar), 6.55 (d, 1H, *J* = 1.2 Hz, H-1), 5.84—5.38 (m, 3H, H-2, H-3, H-4), 4.55 (dd, 1H, *J* = 5.0, 12.0 Hz, H-6a), 4.22 (dd, 1H, *J* = 2.6, 12.0 Hz, H-6b), 3.83 (ddd, 1H, *J* = 8.0, 5.0, 2.6 Hz, H-5), 2.19 (s, 6H, 2 x $COCH_3$), 2.14 and 2.07 (each s, 3H, $COCH_3$). Anal. Calcd for $C_{21}H_{23}NO_{12}S$: C, 49.12; H, 4.51; N, 2.73; S, 6.24. Found: C, 48.94; H, 4.73; N, 2.59; S, 6.36.

2,3,4,6-Tetra-*O*-acetyl-5-thio-α-D-glucopyranosyl Fluoride (1-F). To a stirred solution of **3** (1.73g, 4.75 mmol) in dry tetrahydrofuran (17 mL) was slowly added DAST (0.77 mL, 5.83 mmol) at –30 °C. The solution was stirred for 15 min at room temperature. After cooling to –30 °C, the reaction was quenched with methanol. Solvent was removed by evaporation. The residue was diluted with $CHCl_3$ and washed with aqueous $NaHCO_3$. The organic layer was dried over $MgSO_4$ and concentrated. The residue was chromatographed on silica gel, with hexane-EtOAc (5:2), to give a crude product (1.71 g), which was crystallized with diethyl ether and recrystallized from ethanol to yield 988 mg (57%) of **1-F**: mp 95—96 °C (lit.,[6] 102—103 °C); $[\alpha]_D^{23}$ +138° (c 1.0, $CHCl_3$) {lit.,[6] $[\alpha]_D$ +106° (c 1.0, $CHCl_3$)}; ^{1}H NMR δ 5.79 (dd, 1H, *J* = 48.0, 2.3 Hz, H-1), 5.48 (dd, 1H, *J* = 10.0, 10.0 Hz, H-3), 5.34 (dd, 1H, *J* = 10.0, 10.0 Hz, H-4), 5.17 (ddd, 1H, *J* = 23.5, 2.3, 10.0 Hz, H-2), 4.39 (dd, 1H, *J* = 4.9, 12.2 Hz, H-6a), 4.10 (dd, 1H, *J* = 3.1, 12.2 Hz, H-6b), 3.62 (ddd, 1H, *J* = 10.0, 4.9, 3.1 Hz, H-5), 2.09, 2.08, 2.05, and 2.02 (each s, 3H, $COCH_3$). Anal. Calcd for $C_{14}H_{19}FO_8S$: C, 45.89; H, 5.23. Found: C, 45.71; H, 4.98.

1-(2',3',4',6'-Tetra-*O*-acetyl-5-thio-α-D-glucopyranosyl)-propionitrile (1-$(CH_2)_2CN$). To a stirred solution of **1-OAc** (324 mg, 0.80 mmol) in dichloromethane (3 mL) was slowly added 30% hydrogen bromide in acetic acid (2 mL) at 0 °C. After stirring for 1 h, the mixture was poured into ice water and extracted with $CHCl_3$. The organic layer was wshed with aqueous $NaHCO_3$, dried over $MgSO_4$, and concentrated. Benzene (25 mL) and acrylonitrile (1.6 mL, 24 mmol) was added to the residue. To the mixture was slowly added a solution of tri-n-butyltin hydride (0.23 mL, 0.86 mmol) and AIBN (32 mg, 0.2 mmol) in benzene (16 mL) at reflux under argon. After 14 h the mixture was concentrated, diluted with $CHCl_3$, and washed with

aqueous sodium fluoride. The insoluble material was removed by filtration. The organic layer was dried over $MgSO_4$ and concentrated. The residue was chromatographed on silica gel, with hexane-EtOAc (2:1—3:2), to give **1-$(CH_2)_2$CN** (32 mg, 12%): mp 103—106 °C; $[\alpha]_D^{29}$ +99° (c 0.99, $CHCl_3$); ^{1}H NMR δ 5.34 (dd, 1H, *J* = 4.9, 9.4 Hz, H-2'), 5.22 (dd, 1H, *J* = 9.4, 9.4 Hz, H-3'), 5.18 (dd, 1H, *J* = 9.4, 9.4 Hz, H-4'), 4.29 (dd, 1H, *J* = 5.5, 12.0 Hz, H-6'a), 4.10 (dd, 1H, *J* = 3.5, 12.0 Hz, H-6'b), 3.28 (ddd, 1H, *J* = 9.4, 5.5, 3.5 Hz, H-5'), 3.10 (ddd, 1H, *J* = 12.0, 3.7, 4.9 Hz, H-1'), 2.70 (ddd, 1H, *J* = 8.0, 5.0, 16.8 Hz, H-2a), 2.52 (ddd, 1H, *J* = 8.0, 8.0, 16.8 Hz, H-2b), 2.29 (dddd, 1H, *J* = 3.7, 8.0, 8.0, 14.3 Hz, H-1a), 2.09, 2.07, 2.03, and 2.02 (each s, 3H, $COCH_3$), 2.0—1.9 (m, 1H, H-1b); ^{13}C NMR δ 170.4, 169.7, and 169.3 (C=O), 118.6 (C≡N), 73.2, 72.4, and 70.6 (C-2', C-3', C-4'), 61.4 (C-6'), 40.9 and 38.9 (C-1', C-5'), 23.2 (C-2), 20.7, 20.6, and 20.5 ($COCH_3$), 15.5 (C-1). Anal. Calcd for $C_{17}H_{23}NO_8S$: C, 50.86; H, 5.77; N, 3.49; S, 7.99. Found: C, 50.61; H, 5.76; N, 3.69; S, 7.76.

Phenyl 2,3,4,6-Tetra-*O*-acetyl-1,5-dithio-α- and β-D-glucopyranoside (5 and 6). To a stirred solution of **1-OAc** (248 mg, 0.610 mmol) and benzenethiol (0.09 mL, 0.876 mmol) in dichloromethane (2.5 mL) was slowly added tin(IV) chloride (0.09 mL, 0.769 mmol) at 0 °C. After stirring for 45 min at room temperature the mixture was diluted with $CHCl_3$, washed with aqueous $NaHCO_3$, and concentrated. The residue was chromatographed on silica gel, with hexane-EtOAc (4:1), to give the α-isomer **5** (99 mg, 36%) in an earlier fraction, the β-isomer **6** (89 mg, 32%) in a later fraction, and the mixture of **5** and **6** (52 mg, 18%).

5. mp 99—102 °C; $[\alpha]_D^{21}$ +294° (c 0.89, $CHCl_3$); ^{1}H NMR δ 7.56—7.30 (m, 5H, Ar), 5.60 (dd, 1H, *J* = 9.5, 9.5 Hz, H-3), 5.29 (dd, 1H, *J* = 4.0, 9.5 Hz, H-2), 5.29 (dd, 1H, *J* = 9.5, 10.5 Hz, H-4), 4.80 (d, 1H, *J* = 4.0 Hz, H-1), 4.42 (dd, 1H, *J* = 6.0, 11.5 Hz, H-6a), 4.11(dd, 1H, *J* = 3.0, 11.5 Hz, H-6b), 3.82 (ddd, 1H, *J* = 10.5, 6.0, 3.0 Hz, H-5), 2.11 (s, 9H, 3 x $COCH_3$), 1.91 (s, 3H, $COCH_3$); ^{13}C NMR δ 170.3, 169.8, and 169.5 (C=O), 133.5, 129.1, and 128.4 (Ar), 75.0, 72.4, and 71.1 (C-2, C-3, C-4), 61.2 (C-6), 52.7 (C-1), 40.0 (C-5), 20.5 ($COCH_3$). Anal. Calcd for $C_{20}H_{24}O_8S_2$: C, 52.62; H, 5.30; S, 14.05. Found: C, 52.20; H, 4.95; S, 13.66.

6. mp 95—97 °C; $[\alpha]_D^{21}$ +30° (c 1.3, $CHCl_3$); ^{1}H NMR δ 7.55—7.34 (m, 5H, Ar), 5.25 (dd, 1H, *J* = 10.0, 10.0 Hz, H-4), 5.20 (dd, 1H, *J* = 10.0, 10.0 Hz, H-2), 5.06 (dd, 1H, *J* = 10.0, 10.0 Hz, H-3), 4.23 (dd, 1H, *J* = 5.5, 12.2 Hz, H-6a), 4.11 (d, 1H, *J* = 10.0 Hz, H-1), 4.07 (dd, 1H, *J* = 3.4, 12.2 Hz, H-6b), 3.22 (ddd, 1H, *J* = 10.0, 5.5, 3.4 Hz, H-5), 2.08, 2.05, 2.01, and 2.00 (each s, 3H, $COCH_3$); ^{13}C NMR δ 170.5, 169.7, 169.4, and 169.3 (C=O), 133.7, 133.5, 131.5, 129.2, and 128.9 (Ar), 74.6, 73.9, and 71.8 (C-2, C-3, C-4), 61.2 (C-6), 51.6 (C-1), 44.5 (C-5), 20.6 and 20.5 ($CO\underline{C}H_3$). Anal. Calcd for $C_{20}H_{24}O_8S_2$: C, 52.62; H, 5.30; S, 14.05. Found: C, 52.72; H, 5.31; S, 14.04.

Methyl 2,3,4,6-Tetra-*O*-acetyl-5-thio-α-D-mannopyranoside (8). To a stirred solution of **7** (201 mg, 0.494 mmol) in methanol (4 mL) was slowly added a solution of hydrochloric acid (0.5 mL) in methanol (4 mL). After 1 h, the mixture was neutralized with basic lead carbonate. After removal of the insoluble material by filtration, the filtrate was concentrated. The residue was chromatographed, with $CHCl_3$-methanol (6:1), to give methyl 5-thio-α-D-mannopyranoside; *Rf* 0.33 ($CHCl_3$-methanol, 3:1), which was acetylated with acetic

anhydride and pyridine in an usual manner and chromatographed, with hexane-acetone (3:1), to give **8** (87 mg, 46%) as a syrup; $[\alpha]_D^{25}$ +103° (c 1.8, $CHCl_3$); ^1H NMR δ 5.42 (dd, 1H, *J* = 9.4, 9.4 Hz, H-4), 5.37—5.16 (m, 2H, H-2, H-3), 4.47 (d, 1H, *J* = 3.6 Hz, H-1), 4.34 (dd, 1H, *J* = 5.5, 11.8 Hz, H-6a), 4.05 (dd, 1H, *J* = 4.0, 11.8 Hz, H-6b), 3.48—3.28 (m, 1H, H-5), 3.47 (s, 3H, OCH_3), 2.19, 2.10, 2.05, and 2.01 (each s, 3H, $COCH_3$). HRMS calcd for $C_{15}H_{22}O_9SNa$: 401.0882. Found: 401.0875 ($M + Na^+$).

Methyl 2,3,6-Tri-*O*-methyl-5-thio-α-D-*xylo*-hexopyranosid-4-ulose (10). A solution of **9** (1.07 g, 3.31 mmol) and hydrochloric acid (0.9 mL) in methanol (50 mL) was refluxed for 10 h. The mixture was neutralized with aqueous $NaHCO_3$ and concentrated. Dichloromethane was added to the residue and the insoluble material was removed by filtration. After concentration of the filtrate, the residue was chromatographed, with hexane-EtOAc (5:2—1:1), to give methyl 2,3,6-Tri-O-methyl-5-thio-α-D-glucopyranoside (0.461 g); *Rf* 0.24 (hexane-EtOAc, 1:1), which was dissolved in 1.8 mL of dichloromethne (slution A). To a stirred solution of oxalyl chloride (0.11 mL, 1.26 mmol) in dichloromethane (3.2 mL) was slowly added a solution of dimethyl sulfoxide (0.31 mL, 5.50 mmol) in dichloromethane (0.9 mL) at –78 °C under argon. After 15 min, the solution A was slowly added to the mixture and stirred for 1 h. Triethylamine (0.76 mL, 5.45 mmol) was slowly added to the solution and the mixture was warmed to room temperature. The mixture was diluted with dichlorometane, washed with water, and concentrated. The residue was chromatographed, with hexane-EtOAc (1:1), to give **10** (229 mg, 28%) as a syrup: $[\alpha]_D^{23}$ +536° (c 1.0, $CHCl_3$); ^1H NMR δ 4.74 (d, 1H, *J* = 3.0 Hz, H-1), 4.12 (d, 1H, *J* = 9.8 Hz, H-3), 4.0—3.3 (m, 3H, H-5, H-6a, H-6b), 3.72 (dd, 1H, *J* = 3.0, 9.8 Hz, H-2), 3.59 (s, 6H, 2 x OCH_3), 3.52 and 3.40 (each s, 3H, OCH_3); ^{13}C NMR δ 197.4 (C-4), 89.3 (C-2), 86.4 (C-3), 82.0 (C-1), 68.3 (C-6), 59.6, 59.3, and 57.1 (OCH_3), 42.5 (C-5). Anal. Calcd for $C_{10}H_{18}O_5S$: C, 47.98; H, 7.25; S, 12.81. Found: C, 47.51; H, 7.18; S, 12.94.

Methyl 4-*O*-Acetyl-2,3,6-tri-*O*-methyl-5-thio-α-D-galactopyranoside (11). A solution of **10** (225 mg, 0.898 mmol) and sodium borohydride (52 mg, 1.37 mmol) in ethanol (11 mL) was stirred for 10 min at 0 °C. After addition of acetone, the mixture was concentrated. The residue was passed through a short coumn of silica gel, with EtOAc as eluant. The effluent was concentrated and treated with acetic anhydride and pyridine in the usual manner of acetylation. The crude product was purified by column of silica gel, with hexane-EtOAc (1:1), to give **11** (208 mg, 79%); mp 73—74 °C; $[\alpha]_D^{17}$ +264° (c 0.86, $CHCl_3$); ^1H NMR δ 5.71 (d, 1H, *J* = 4.0 Hz, H-4), 4.64 (d, 1H, *J* = 2.8 Hz, H-1), 3.74 (dd, 1H, *J* = 2.8, 9.6 Hz, H-2), 3.5—3.3 (m, 4H, H-3, H-5, H-6a, H-6b), 3.52, 3.49, 3.44, and 3.34 (each s, 3H, OCH_3), 2.17 (s, 3H, $COCH_3$); ^{13}C NMR δ 170.4 (C=O), 81.8 (C-1), 81.0 (C-2), 78.9 (C-3), 71.2 (C-6), 68.6 (C-4), 59.0, 58.4, and 56.7 (OCH_3), 39.7 (C-5), 20.9 ($COCH_3$). Anal. Calcd for $C_{12}H_{22}O_6S$: C, 48.96; H, 7.53; S, 10.89. Found: C, 49.30; H, 7.57; S, 10.84.

General Procedure for the MCPBA Oxidation. To a stirred solution of substrate (0.25 mmol) in dichloromethane (2 mL) was slowly added a solution of MCPBA (0.28 mmol) in dichloromethane (2 mL) at –20 °C. After 15 min, the mixture was diluted with $CHCl_3$ and washed with aqueous $Na_2S_2O_3$ and then aqueous $NaHCO_3$. The organic layer was dried over $MgSO_4$ and concentrated. The residue was chromatographed, with hexane-acetone (3:1—2:1), to give the mixture of axial and equatorial sulfoxides. The yield and the diastereomer

ratio are given in Table I.

General Procedure for the BSNPO Oxidation. To a stirred solution of substrate (0.25 mmol) in 1,2-dichloroethane (2 mL) was slowly added a solution of BSNPO (0.25 mmol) in 1,2-dichloroethane at reflux. After 1 h, the mixture was cooled and processed as described above for the MCPBA oxidation.

2,3,4,6-Tetra-*O*-acetyl-5-thio-α-D-glucopyranosyl Fluoride *S*-Oxide (2-F): $[\alpha]_D^{21}$ +71° (c 1.2, $CHCl_3$) for ax:eq = 62:38; $[\alpha]_D^{21}$ +54° (c 1.2, $CHCl_3$) for ax:eq = 54:46. ^1H NMR: axial isomer δ 5.83 (ddd, 1H, *J* = 30.5, 1.8, 10.5 Hz, H-2), 5.80 (dd, 1H, *J* = 37.8, 1.8 Hz, H-1), 5.70 (dd, 1H, *J* = 10.5, 10.5 Hz, H-4), 5.56 (dd, 1H, *J* = 10.5, 10.5 Hz, H-3), 4.53 (dd, 1H, *J* = 4.3, 12.2 Hz, H-6a), 4.44 (dd, 1H, *J* = 9.2, 12.2 Hz, H-6b), 3.21 (ddd, 1H, *J* = 10.5, 4.3, 9.2 Hz, H-5), 2.11 2.10, 2.07, and 2.03 (each s, 3H, $COCH_3$); equatorial isomer δ 5.90 (dd, 1H, *J* = 43.3, 1.3 Hz, H-1), 5.58 (dd, 1H, *J* = 10.5, 10.5 Hz, H-3), 5.27 (dd, 1H, *J* = 10.5, 11.7 Hz, H-4), 5.17 (ddd, 1H, *J* = 28.0, 1.3, 10.5 Hz, H-2), 4.75 (dd, 1H, *J* = 1.9, 12.7 Hz, H-6a), 4.32 (dd, 1H, *J* = 1.9, 12.7 Hz, H-6a), 3.70 (ddd, 1H, *J* = 11.7, 1.9, 1.9 Hz, H-5), 2.13, 2.09, 2.06, and 2.01 (each s, 3H, $COCH_3$). Anal. Calcd for $C_{14}H_{19}FO_9S$: C, 43.98; H, 5.01. Found: C, 43.97; H, 5.00.

1-(2',3',4',6'-Tetra-*O*-acetyl-5-thio-α-D-glucopyranosyl)-propionitrile *S*-Oxide (2-$(CH_2)_2CN$): $[\alpha]_D^{29}$ +68° (c 1.1, $CHCl_3$) for ax:eq = 66:34; $[\alpha]_D^{21}$ + 59° (c 1.3, $CHCl_3$) for ax:eq = 60:40. ^1H NMR: axial isomer δ 5.82 (dd, 1H, *J* = 4.3, 9.5 Hz, H-2'), 5.56 (dd, 1H, *J* = 9.5, 11.0 Hz, H-4'), 5.37 (dd, 1H, *J* = 9.5, 9.5 Hz, H-3'), 4.49 (dd, 1H, *J* = 4.6, 11.9 Hz, H-6'a), 4.41 (dd, 1H, *J* = 9.2, 11.9 Hz, H-6'b), 3.62 (m, 1H, H-1'), 3.23 (ddd, 1H, *J* = 11.0, 4.6, 9.2 Hz), 2.78—2.49 (m, 4H, H-1a, H-1b, H-2a, H-2b), 2.11, 2.10, 2.07, and 2.05 (each s, 3H, $COCH_3$); equatorial isomer δ 5.32 (dd, 1H, *J* = 9.8, 9.8 Hz, H-3'), 5.24 (dd, 1H, *J* = 4.1, 9.8 Hz, H-2'), 5.18 (dd, 1H, *J* = 9.8, 11.9 Hz, H-4'), 4.67 (dd, 1H, *J* = 2.3, 12.7 Hz, H-6'a), 4.33 (dd, 1H, *J* = 2.0, 12.7 Hz, H-6'b), 3.79 (m, 1H, H-1'), 3.20 (ddd, 1H, *J* = 11.9, 2.3, 2.0 Hz, H-5'), 2.32—1.80 (m, 4H, H-1a, H-1b, H-2a, H-2b), 2.14, 2.10, 2.04, and 2.02 (each s, 3H, $COCH_3$). Anal. Calcd for $C_{17}H_{23}NO_9S$: C, 48.91; H, 5.55; N, 3.36; S, 7.68. Found: C, 48.73; H, 5.65; N, 3.30; S, 7.29.

2,3,4,6-Tetra-*O*-acetyl-1-*O*-benzoyl-5-thio-α-D-glucopyranose *S*-Oxide (12-H): $[\alpha]_D^{26}$ +123° (c 0.87, $CHCl_3$) for ax:eq = 38:62; $[\alpha]_D^{21}$ +143° (c 1.5, $CHCl_3$), for ax:eq = 57:43. ^1H NMR: axial isomer δ 8.15—7.55 (m, 5H, Ar), 6.56 (d, 1H, *J* = 2.7 Hz, H-1), 5.99 (dd, 1H, *J* = 2.7, 9.9 Hz, H-2), 5.72—5.67 (m, 2H, H-3, H-4), 4.54 (dd, 1H, *J* = 4.4, 12.1 Hz, H-6a), 4.45 (dd, 1H, *J* = 9.3, 12.1 Hz, H-6b), 3.36 (ddd, 1H, *J* = 10.1, 4.4, 9.3 Hz, H-5), 2.11, 2.07, 2.05, and 2.02 (each s, 3H, $COCH_3$); equatorial isomer δ 8.15—7.55 (m, 5H, Ar), 6.83 (d, 1H, *J* = 1.8 Hz, H-1), 5.67 (dd, 1H, *J* = 10.1, 10.1 Hz, H-3), 5.33 (dd, 1H, *J* = 1.8, 10.1 Hz, H-2), 5.31 (dd, 1H, *J* = 10.1, 10.1 Hz, H-4), 4.77 (dd, 1H, *J* = 2.1, 12.8 Hz, H-6a), 4.29 (dd, 1H, *J* = 1.8, 12.8 Hz, H-6b), 3.70 (ddd, 1H, *J* = 10.1, 2.1, 1.8 Hz, H-5), 2.11, 2.09, 2.04, and 2.02 (each s, 3H, $COCH_3$). Anal. Calcd for $C_{21}H_{24}O_{11}S$: C, 52.06; H, 4.99; S, 6.62. Found: C, 51.84; H, 5.07; S, 6.55.

2,3,4,6-Tetra-*O*-acetyl-1-*O*-(4-methoxybenzoyl)-5-thio-α-D-glucopyranose *S*-Oxide (12-OMe): $[\alpha]_D^{18}$ +130° (c 1.7, $CHCl_3$) for ax:eq = 42:58; $[\alpha]_D^{17}$ +144° (c 0.95, $CHCl_3$). ^1H NMR: axial isomer

δ 8.10—8.00 and 7.05—6.95 (m, 5H, Ar), 6.53 (d, 1H, J = 2.8 Hz, H-1), 5.98 (dd, 1H, J = 2.8, 10.4 Hz, H-2), 5.75—5.65 (m, 2H, H-3, H-4), 4.53 (dd, 1H, J = 4.3, 12.2 Hz, H-6a), 4.44 (dd, 1H, J = 9.3, 12.2 Hz, H-6b), 3.90 (s, 3H, OCH_3), 3.36 (ddd, 1H, J = 12.0, 4.3, 9.3 Hz, H-5), 2.10, 2.07, 2.05, and 2.01 (each s, 3H, $COCH_3$); equatorial isomer δ 8.10—8.00 and 7.05—6.95 (m, 5H, Ar), 6.80 (d, 1H, J = 2.0 Hz, H-1), 5.75—5.65 (m, 1H, H-3), 5.31 (dd, 1H, J = 2.0, 10.4 Hz, H-2), 5.30 (dd, 1H, J = 10.4, 11.9 Hz, H-4), 4.77 (dd, 1H, J = 1.5, 12.2 Hz, H-6a), 4.29 (dd, 1H, J = 2.0, 12.2 Hz, H-6b), 3.90 (s, 3H, OCH_3), 3.70 (ddd, 1H, J = 11.9, 1.5, 2.0 Hz, H-5), 2.10, 2.09, 2.04, and 2.02 (each s, 3H, $COCH_3$). Anal. Calcd for $C_{22}H_{26}O_{12}S$: C, 51.36; H, 5.09; S, 6.23. Found: C, 51.29; H, 5.45; S, 5.96.

2,3,4,6-Tetra-*O*-acetyl-1-*O*-(4-chlorobenzoyl)-5-thio-α-D-glucopyranose *S*-Oxide (12-Cl): $[\alpha]_D^{18}$ +128° (c 1.0, $CHCl_3$) for ax:eq = 36:64; $[\alpha]_D^{21}$ +134° (c 1.4, $CHCl_3$) for ax:eq = 49:51. ^{1}H NMR: axial isomer δ 7.99 (d, 2H, J = 8.5 Hz, Ar), 7.53—7.50 (m, 2H, Ar), 6.54 (d, 1H, J = 2.8 Hz, H-1), 5.99 (dd, 1H, J = 2.8, 10.4 Hz, H-2), 5.70—5.65 (m, 1H, H-4), 5.65 (dd, 1H, J = 10.4, 10.4 Hz, H-3), 4.54 (dd, 1H, J = 4.3, 12.0 Hz, H-6a), 4.44 (dd, 1H, J = 9.2, 12.0 Hz, H-6b), 3.36 (m, 1H, H-5), 2.10, 2.05, 2.04, and 2.01 (each s, 3H, $COCH_3$); equatorial isomer δ 8.05 (d, 2H, J = 8.9 Hz, Ar), 7.53—7.50 (m, 2H, Ar), 6.80 (d, 1H, J = 2.3 Hz, H-1), 5.65 (dd, 1H, J = 10.7, 9.8 Hz, H-3), 5.32 (dd, 1H, J = 2.3, 10.7 Hz, H-2), 5.29 (dd, 1H, J = 9.8, 11.9 Hz, H-4), 4.77 (dd, 1H, J = 1.2, 12.8 Hz, H-6a), 4.29 (dd, 1H, J = 2.1, 12.8 Hz, H-6b), 3.66 (ddd, 1H, J = 11.9, 1.2, 2.1 Hz, H-5), 2.11, 2.09, 2.04, and 2.02 (each s, 3H, $COCH_3$). Anal. Calcd for $C_{21}H_{23}ClO_{11}S$: C, 48.61; H, 4.47; S, 6.18. Found: C, 48.97; H, 4.83; S, 5.95.

2,3,4,6-Tetra-*O*-acetyl-1-*O*-(4-trifluoromethylbenzoyl)-5-thio-α-D-glucopyranose *S*-Oxide (12-CF_3): $[\alpha]_D^{18}$ +121° (c 1.1, $CHCl_3$) for ax:eq = 27:73; $[\alpha]_D^{21}$ +119° (c 1.9, $CHCl_3$) for ax:eq = 46:54. ^{1}H NMR: axial isomer δ 8.19 (d, 2H, J = 8.2 Hz, Ar), 7.83—7.80 (m, 2H, Ar), 6.57 (d, 1H, J = 2.7 Hz, H-1), 6.00 (dd, 1H, J = 2.7, 10.1 Hz, H-2), 5.75—5.70 (m, 1H, H-4), 5.67 (dd, 1H, J = 10.1, 10.1 Hz, H-3), 4.55 (dd, 1H, J = 4.3, 12.2 Hz, H-6a), 4.45 (dd, 1H, J = 9.2, 12.2 Hz, H-6b), 3.40 (m, 1H, H-5), 2.11, 2.07, 2.06, and 2.04 (each s, 3H, $COCH_3$); equatorial isomer δ 8.25 (d, 2H, J = 7.9 Hz, Ar), 7.83—7.80 (m, 2H, Ar), 6.82 (d, 1H, J = 2.0 Hz, H-1), 5.67 (dd, 1H, J = 10.7, 9.8 Hz, H-3), 5.34 (dd, 1H, J = 2.0, 10.7 Hz, H-2), 5.30 (dd, 1H, J = 9.8, 11.9 Hz, H-4), 4.77 (dd, 1H, J = 1.4, 12.8 Hz, H-6a), 4.30 (dd, 1H, J = 2.1, 12.8 Hz, H-6b), 3.67 (ddd, 1H, J = 11.9, 1.4, 2.1 Hz, H-5), 2.11, 2.09, 2.05, and 2.03 (each s, 3H, $COCH_3$). Anal. Calcd for $C_{22}H_{23}F_3O_{11}S$: C, 47.83; H, 4.20. Found: C, 47.61; H, 4.15.

2,3,4,6-Tetra-*O*-acetyl-1-*O*-(4-nitrobenzoyl)-5-thio-α-D-glucopyranose *S*-Oxide (12-NO_2): $[\alpha]_D^{27}$ +126° (c 0.92, $CHCl_3$) for ax:eq = 24:76; $[\alpha]_D^{17}$ + 127° (c 1.7, $CHCl_3$) for ax:eq = 36:64. ^{1}H NMR: axial isomer δ 8.39—8.24 (m, 4H, Ar), 6.58 (d, 1H, J = 2.6 Hz, H-1), 6.00 (dd, 1H, J = 2.6, 10.3 Hz, H-2), 5.75—5.65 (m, 1H, H-4), 5.67 (dd, 1H, J = 10.3, 10.3 Hz, H-3), 4.56 (dd, 1H, J = 4.5, 12.2 Hz, H-6a), 4.46 (dd, 1H, J = 9.2, 12.2 Hz, H-6b), 3.21 (m, 1H, H-5), 2.11, 2.08, 2.07, and 2.02 (each s, 3H, $COCH_3$); equatorial isomer δ 8.39—8.24 (m, 4H, Ar), 6.82 (d, 1H, J = 2.1 Hz, H-1), 5.67 (dd, 1H, J = 10.7, 9.8 Hz, H-3), 5.35 (dd, 1H, J = 2.1, 10.7 Hz, H-2), 5.30 (dd, 1H, J = 9.8, 12.0 Hz, H-4), 4.78 (dd, 1H, J = 1.5, 12.8 Hz, H-6a), 4.30 (dd, 1H, J = 2.1, 12.8 Hz, H-6b), 3.67 (ddd, 1H, J = 12.0, 1.5, 2.1 Hz, H-5), 2.12, 2.10, 2.06, and 2.04 (each s, 3H, $COCH_3$). Anal. Calcd for $C_{21}H_{23}NO_{13}S$: C, 47.64; H, 4.38; N, 2.65; S, 6.06.

Found: C, 47.26; H, 4.55; N, 2.45; S, 6.05.

1,2,3,4,6-Penta-*O*-acetyl-5-thio-α-D-mannopyranose *S*-Oxide (13): $[\alpha]_D^{17}$ +64° (c 1.2, $CHCl_3$) for ax:eq = 4:96. ^1H NMR: axial isomer δ 5.96 (d, 1H, *J* = 2.6 Hz, H-1), 5.76 (dd, 1H, *J* = 2.6, 2.6 Hz, H-2), 5.52 (dd, 1H, *J* = 10.4, 11.9 Hz, H-4), 5.25 (dd, 1H, *J* = 2.6, 10.4 Hz, H-3), 4.74 (dd, 1H, *J* = 2.5, 12.8 Hz, H-6a), 4.44 (dd, 1H, *J* = 2.5, 12.8 Hz, H-6b), 3.18 (ddd, 1H, *J* = 11.9, 2.5, 2.5 Hz, H-5), 2.22, 2.20, 2.11, 2.07, and 1.98 (each s, 3H, $COCH_3$); equatorial isomer δ 6.34 (d, 1H, *J* = 4.9 Hz, H-1), 5.65 (dd, 1H, *J* = 4.9, 3.1 Hz, H-2), 5.47 (dd, 1H, *J* = 10.1, 11.6 Hz, H-4), 5.34 (dd, 1H, *J* = 3.1, 10.1 Hz, H-3), 4.74 (dd, 1H, *J* = 2.5, 12.8 Hz, H-6a), 4.29 (dd, 1H, *J* = 2.5, 12.8 Hz, H-6b), 3.39 (ddd, 1H, *J* = 11.6, 2.5, 2.5 Hz, H-5), 2.31, 2.21, 2.06, and 2.00 (each s, 3H, $COCH_3$). Anal. Calcd for $C_{16}H_{22}O_{11}S$: C, 45.50; H, 5.25; S, 7.59. Found: C, 45.51; H, 5.53; S, 7.35.

Methyl 2,3,4,6-Tetra-*O*-acetyl-5-thio-α-D-mannopyranoside *S*-Oxide (14): $[\alpha]_D^{25}$ +40° (c 2.0, $CHCl_3$) for ax:eq = 25:75. ^1H NMR: axial isomer δ 5.89 (dd, 1H, *J* = 10.4, 10.4 Hz, H-4), 5.62 (dd, 1H, *J* = 3.7, 3.7 Hz, H-2), 5.38 (dd, 1H, *J* = 3.7, 10.4 Hz, H-3), 4.68 (d, 1H, *J* = 3.7 Hz, H-1), 4.55 (dd, 1H, *J* = 4.9, 11.9 Hz, H-6a), 4.47 (dd, 1H, *J* = 9.5, 11.9 Hz, H-6b), 3.66 (s, 3H, OCH_3), 3.30 (ddd, 1H, *J* = 10.4, 4.9, 9.5 Hz, H-5), 2.16, 2.12, 2.09, and 2.04 (each s, 3H, $COCH_3$); equatorial isomer δ 5.58 (dd, 1H, *J* = 4.9, 2.9 Hz, H-2), 5.40 (dd, 1H, *J* = 10.6, 10.6 Hz, H-4), 5.36 (dd, 1H, *J* = 2.9, 10.6 Hz, H-3), 4.88 (d, 1H, *J* = 4.9 Hz, H-1), 4.76 (dd, 1H, *J* = 1.8, 12.5 Hz, H-6a), 4.32 (dd, 1H, *J* = 1.8, 12.5 Hz, H-6b), 3.90 (s, 3H, OCH_3), 3.60 (ddd, 1H, *J* = 10.6, 1.8, 1.8 Hz, H-5), 2.19, 2.10, 2.05, and 1.98 (each s, 3H, $COCH_3$). HRMS calcd for $C_{15}H_{23}O_{10}S$: 395.1012. Found: 395.1023 ($M + H^+$).

Methyl 4-*O*-Acetyl-2,3,6-tri-*O*-methyl-5-thio-α-D-galactopyranoside *S*-Oxide (15): ^1H NMR: axial isomer δ 5.85—5.70 (m, 1H, H-4), 4.71 (d, 1H, *J* = 2.2 Hz, H-1), 4.17 (dd, 1H, *J* = 2.2, 10.0 Hz, H-2), 4.0—3.2 (m, 13H, H-3, H-4, H-6a, H-6b, 3 x OCH_3), 2.89 (ddd, 1H, *J* = 2.8, 6.4, 9.0 Hz, H-5), 2.13 (s, 3H, $COCH_3$); equatorial isomer δ 5.85—5.70 (m, 1H, H-4), 5.00 (d, 1H, *J* = 2.0 Hz, H-1), 4.0—3.2 (m, 15H, H-2, H-3, H-4, H-5, H-6a, H-6b, 3 x OCH_3), 2.07 (s, 3H, $COCH_3$). Anal. Calcd for $C_{12}H_{22}O_7S$: C, 46.44; H, 7.14; S, 10.33. Found: C, 46.67; H, 7.31; S, 10.18.

Phenyl 2,3,4,6-Tetra-*O*-acetyl-1,5-dithio-α-D-glucopyranoside 5-*S*-(*R*)-Oxide (17) and Phenyl 2,3,4,6-Tetra-*O*-acetyl-1,5-dithio-α-D-glucopyranoside 1-*S*-Oxide (18). The mixture of **17** and **18** was obtained following the procedure described above for the MCPBA oxidation with **5**. ^1H NMR: **17** δ 7.73—7.34 (m, 5H, Ar), 5.90 (dd, 1H, *J* = 10.7, 10.7 Hz, H-4), 5.87 (dd, 1H, *J* = 4.2, 10.0 Hz, H-2), 5.31 (dd, 1H, *J* = 10.7, 10.7 Hz, H-3), 4.87 (d, 1H, *J* = 4.2 Hz, H-1), 4.52 (dd, 1H, *J* = 4.3, 11.9 Hz, H-6a), 4.41 (dd, 1H, *J* = 9.2, 11.9 Hz, H-6b), 3.67 (ddd, 1H, *J* = 10.7, 4.3, 9.2 Hz, H-5), 2.18—2.04 (m, 12H, 4 x $COCH_3$); major isomer of **18** δ 7.73—7.34 (m, 5H, Ar), 6.04 (dd, 1H, *J* = 9.6, 9.6 Hz, H-3), 5.40 (dd, 1H, *J* = 5.0, 9.6 Hz, H-2), 5.27 (dd, 1H, *J* = 9.6, 10.7 Hz, H-4), 4.26 (dd, 1H, *J* = 5.5, 12.3 Hz, H-6a), 4.18 (d, 1H, *J* = 5.0 Hz, H-1), 4.09 (dd, 1H, *J* = 3.1, 12.3 Hz, H-6b), 4.03 (ddd, 1H, *J* = 10.7, 5.5, 3.1 Hz, H-5), 2.17, 2.07, 2.05, and 1.99 (each s, 3H, $COCH_3$); minor isomer of **18** δ 7.73—7.34 (m, 5H, Ar), 5.67 (dd, 1H, *J* = 10.2, 11.2 Hz, H-4), 5.50 (dd, 1H, *J* = 10.2, 10.2 Hz, H-3), 5.49 (dd, 1H, *J* = 5.8, 10.2 Hz, H-2),

4.60 (ddd, 1H, J = 11.2, 4.9, 3.1 Hz, H-5), 4.23 (dd, 1H, J = 4.9, 11.9 Hz, H-6a), 4.05 (dd, 1H, J = 3.1, 11.9 Hz, H-6b), 3.83 (d, 1H, J = 5.8 Hz, H-1), 2.18—2.04 (m, 12H, 4 x $COCH_3$). ^{13}C NMR: major isomer of **18** δ 169.2 (C=O), 142.6, 131.5, 129.7, 129.2, 125.1, and 125.0 (Ar), 74.6, 71.9, and 70.3 (C-2, C-3, C-4), 62.0 (C-1), 61.2 (C-6), 41.0 (C_T5), 20.5 and 20.0 ($COCH_3$).

Phenyl 2,3,4,6-Tetra-*O*-acetyl-1,5-dithio-β-D-glucopyranoside 5-*S*-Oxide (19) and Phenyl 2,3,4,6-Tetra-*O*-acetyl-1,5-dithio-β-D-glucopyranoside 1-*S*-Oxide (20). Following the procedure described above for the MCPBA oxidation with **6** gave, after column chromatography, the mixture of the equatorial isomer of **19** and the minor isomer of **20** in an earlier fraction and the mixture of the axial isomer of **19** and the major isomer of **20** in a later fraction. ^1H NMR: axial isomer of **19** δ 7.75—7.35 (m, 5H, Ar), 5.69 (dd, 1H, J = 9.7, 11.6 Hz, H-4), 5.62 (dd, 1H, J = 11.0, 9.7 Hz, H-2), 5.39 (dd, 1H, J = 9.7, 9.7 Hz, H-3), 4.46 (dd, 1H, J = 4.3, 12.0 Hz, H-6a), 4.37 (dd, 1H, J = 9.0, 12.0 Hz, H-6b), 4.01 (d, 1H, J = 11.0 Hz, H-1), 3.01 (ddd, 1H, J = 11.6, 4.3, 9.0 Hz, H-5), 2.11, 2.06, 2.05, and 2.03 (each s, 3H, $COCH_3$); equatorial isomer of **19** δ 7.75—7.35 (m, 5H, Ar), 5.32 (dd, 1H, J = 9.7, 9.7 Hz, H-3), 5.24 (dd, 1H, J = 9.7, 11.6 Hz, H-4), 5.08 (dd, 1H, J = 11.6, 9.7 Hz, H-2), 4.71 (dd, 1H, J = 2.3, 12.5 Hz, H-6a), 4.40 (dd, 1H, J = 2.3, 12.5 Hz, H-6b), 4.08 (d, 1H, J = 11.6 Hz, H-1), 3.18 (ddd, 1H, J = 11.6, 2.3, 2.3 Hz, H-5), 2.16, 2.05, 2.03, and 1.99 (each s, 3H, $COCH_3$); major isomer of **20** δ 7.75—7.35 (m, 5H, Ar), 5.60 (dd, 1H, J = 11.0, 9.6 Hz, H-2), 5.28 (dd, 1H, J = 9.6, 9.6 Hz, H-4), 5.15 (dd, 1H, J = 9.6, 9.6 Hz, H-3), 4.30 (dd, 1H, J = 4.8, 12.2 Hz, H-6a), 4.00 (dd, 1H, J = 3.2, 12.2 Hz, H-6b), 3.91 (d, 1H, J = 11.0 Hz, H-1), 3.13 (ddd, 1H, J = 9.6, 4.8, 3.2 Hz, H-5), 2.14, 2.03, 2.02, and 2.00 (each s, 3H, $COCH_3$); minor isomer of **20** δ 7.75—7.35 (m, 5H, Ar), 5.30 (dd, 1H, J = 10.4, 9.2 Hz, H-2), 5.15 (dd, 1H, J = 9.2, 9.2 Hz, H-4), 5.11 (dd, 1H, J = 9.2, 9.2 Hz, H-3), 4.22 (d, 1H, J = 10.4 Hz, H-1), 4.21 (dd, 1H, J = 5.8, 11.9 Hz, H-6a), 4.10 (dd, 1H, J = 3.7, 11.9 Hz, H-6b), 3.22 (ddd, 1H, J = 9.2, 5.8, 3.7 Hz, H-5), 2.17, 2.08, 2.02, and 2.01 (each s, 3H, $COCH_3$). ^{13}C NMR: axial isomer of **19** δ 170.2, 169.8, 169.3, and 169.1 (C=O), 133.9, 131.5, 129.6, 129.3, and 125.6 (Ar), 73.5 (C-3), 68.5 (C-1), 68.5 and 67.1 (C-2, C-4), 59.6 (C-6), 58.0 (C-5), 20.6 and 20.5 ($COCH_3$); equatorial isomer of **19** δ 170.1, 169.4, 169.1, and 168.8 (C=O), 135.2, 130.0, 129.6, 129.5, and 129.2 (Ar), 74.3 (C-3), 73.6 (C-1), 67.0 and 63.7 (C-2, C-4), 64.0 (C-5), 56.0 (C-6), 20.5, 20.3, and 20.0 ($COCH_3$).

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