Stereoselectivity in the Oxidation of 5-Thioglucose Derivatives with 3-Chloroperoxybenzoic Acid

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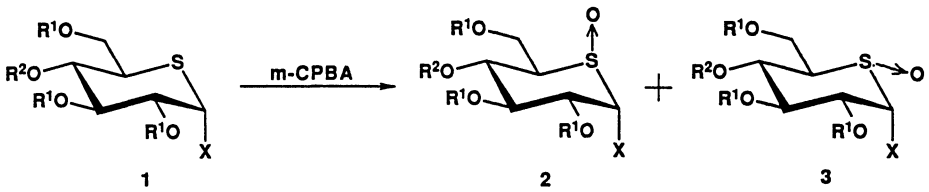
5-Thio-α-D-glucopyranose derivatives were oxidized with 3-chloroperoxybenzoic acid in various conditions to give axial and equatorial sulfoxides. Structure of an axial sulfoxide obtained was determined by X-ray crystallography. Configuration of other sulfoxides was determined by ^{1}H NMR spectroscopy according to empirical rules of chemical shift. The anomeric substituent was decisive for the stereoselectivity and the ratios of axial to equatorial sulfoxide were 3—11.5 for methoxy derivatives and 0.4—1.0 for acetoxy derivatives.

With the recent progress in the asymmetric synthesis using optically active sulfoxides as chiral auxiliary,[1] establishment of the methodology for preparing optically active sulfoxides has been an important subject.[1b] Among them the method by oxidation of sulfides has been left unexplored in the prediction of the stereoselectivity. A lot of studies have been made on the stereoselectivity in the oxidation of cyclic sulfides[2-4] including 5-thioaldopyranoses,[5] but any consistent explanation for the origin of the selectivity has not been made owing to the lack of systematic investigation. However, 5-thioglucopyranose is a convenient substrate for the study of stereoselectivity in the oxidation because it has a sterically fixed pyranoid ring and easily modifiable substituents. In this paper, we would like to report a remarkable difference in the stereoselectivity between 1-*O*-methyl and 1-*O*-acetyl derivatives of 5-thio-α-D-glucopyranose in the oxidation with 3-chloroperoxybenzoic acid (mCPBA) and discuss about the substituent effects.

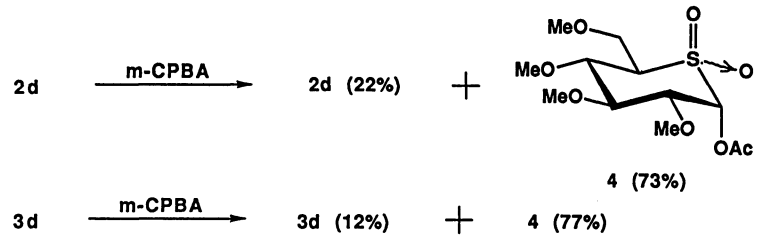
Table 1. Oxidation of 5-Thioglucose Derivatives **1** with mCPBA

	Compound			Solvent	Temp/°C[a]	Product	
	X	R^1	R^2			ax(**2**) : eq(**3**)[b]	Yield/%
1a	MeO	Me	Me	CH_2Cl_2	−20	85 : 15	86
					0	83 : 17	86
					RT	81 : 19	73
				CH_3CN	−20	86 : 14	85
					RT	87 : 13	43
1b	MeO	Ac	Me	CH_2Cl_2	−20	85 : 15	92
					0	83 : 17	96
					RT	76 : 24	93
				CH_3CN	−20	87 : 13	74
					RT	86 : 14	97
1c	MeO	Ac	Ac	CH_2Cl_2	−20	83 : 17	86
					0	80 : 20	96
					RT	75 : 25	87
				CH_3CN	−20	92 : 8	66
					RT	90 : 10	98
1d	AcO	Me	Me	CH_2Cl_2	−20	35 : 65	85
					0	38 : 62	96
					RT	41 : 59	89
				CH_3CN	−20	34 : 66	85
					RT	38 : 62	100
1e	AcO	Me	Ac	CH_2Cl_2	−20	31 : 69	93
				CH_3CN	−20	39 : 61	60
				AcOEt	−20	30 : 70	75
1f	AcO	Ac	Ac	CH_2Cl_2	−20	29 : 71	69
					0	32 : 68	86
					RT	34 : 66	88
				CH_3CN	−20	51 : 49	32
					RT	51 : 49	87
1g	H	Ac	Ac	CH_2Cl_2	−20	44 : 56[c]	85
				CH_3CN	−20	67 : 33[c]	85

a) RT; 20—30 °C. b) Determined by 100 MHz ^{1}H NMR. In the cases of **1d** and **1e**, the ratios were estimated by the isolated yields. c) Determined by 500 MHz ^{1}H NMR.



Scheme 1.



Scheme 2.

Results and Discussion

Oxidation Reaction: At first, 1-*O*-methyl **1c** and 1-*O*-acetyl **1f** derivatives of 5-thio-α-D-glucopyranose were oxidized with mCPBA at −20 °C in dichloromethane (Scheme 1, Table 1). The ratios of axial to equatorial sulfoxide obtained, i.e. **2c**:**3c** and **2f**:**3f**, were estimated by their intensities of ^{1}H NMR signals of the diastereomeric mixture, and their configurations were determined by the empirical rules of chemical shift in the ^{1}H NMR spectra in conbination with X-ray analysis described later. Thus, it was found that axial sulfoxide **2c** was preferentially obtained (**2c**:**3c**≈5:1) from the 1-*O*-methyl derivative **1c**, while equatorial sulfoxide **3f** was preferentially obtained (**2f**:**3f**≈3:7) from the 1-*O*-acetyl derivative **1f**. A finding of this distinct reverse stereoselectivity prompted us to investigate the substituent effect at other than anomeric position and the effects of other factors such as solvent and temperature on the stereoselectivity in detail. Thus three kinds of both 1-*O*-methyl (**1a—c**)[6] and 1-*O*-acetyl (**1d—f**)[6,7] derivatives of 5-thio-D-glucopyranose and 1-deoxy analog **1g**[8] were subjected to oxidation in various conditions (Table 1). In the oxidation of series of the substrates, the following tendencies were observed, i.e., preferential formation of axial and equatorial (except for **1f** in acetonitrile) sulfoxides when the anomeric substituent is methoxyl and acetoxyl groups respectively, and ineffectiveness of substituents other than anomeric position on the stereoselectivity. On the other hand, less stereoselectivity was observed in the oxidation of the 1-deoxy derivative **1g**. In addition, reasonable dependence of the isomer ratio on the reaction temperature was observed. In the polar solvent (acetonitrile), the ratios of axial sulfoxides were significantly increased only in the cases of two tetra-acetates (**1f** and **1g**) compared with those in dichloromethane.

Although any overoxidation was not observed in the above oxidation of 5-thioglucose derivatives, the sulfone derivative **4** was obtained from both the axial (**2d**) and the equatorial (**3d**) sulfoxides (Scheme 2) at room temperature under the same conditions, i.e., the same reaction time and the same amount of mCPBA. This result shows a marked difference of reaction rate between the sulfoxide formation and the sulfone formation; actually the sulfoxide formation went to completion as soon as mCPBA was added, in contrast with slow formation of the sulfone. In the sulfone formation, each of the recovered sulfoxides did not contain the corresponding isomer, indicating no in situ isomerization between axial and equatorial sulfoxide in the mCPBA oxidation. Thus it was suggested that the formation of the sulfoxides are kinetically controlled.

Johnson and McCants[2] have investigated the stereoselectivity in the oxidation of 4-substituted thianes with various reagents and proposed a steric approach control for the oxidation with peroxides. In our case, however, steric effects are thought to be less important because the preferred isomer of sulfoxide obtained are different from each other in the oxidation of 5-thioglucose having methoxyl and acetoxyl groups, both of which are bulkier than a hydrogen atom of 1-deoxy analog, at the anomeric position. Furthermore either hydrogen-bonding between mCPBA and an oxygen atom of the substrate or dipole-dipole interaction between incipient S-O bond and C-O bond at the anomeric position is hard to be applied for the explanation of stereoselectivity, because polar and Lewis-basic solvent, i.e., acetonitrile has no significant effect on the stereoselectivity.

Though the obtained experimental data are insufficient for explanation of the stereoselectivity, the observed phenomenon, a kind of 1,2-asymmetric induction, may depend orbital interactions. Klein and Stollar[3] have attributed the preferential equatorial attack of an electrophile for thiane derivatives to relatively higher electron density of 3p orbital at equatorial side. This kind of stereoelectronic effect is most plausible. Detailed investigation is now in progress.

Assignment of Configuration: The configuration

Table 2. Bond Distances (l/Å) of **2b**[a]

S-O(S)	1.492(7)	O(3)-C(31)	1.34(1)	C(1)-C(2)	1.53(1)
S-C(1)	1.839(9)	O(4)-C(4)	1.41(1)	C(2)-C(3)	1.48(1)
S-C(5)	1.833(9)	O(4)-C(41)	1.41(1)	C(3)-C(4)	1.52(1)
O(1)-C(1)	1.42(1)	O(6)-C(6)	1.43(1)	C(4)-C(5)	1.53(1)
O(1)-C(11)	1.41(1)	O(6)-C(61)	1.34(1)	C(5)-C(6)	1.51(1)
O(2)-C(2)	1.46(1)	O(21)-C(21)	1.19(1)	C(21)-C(22)	1.48(1)
O(2)-C(21)	1.33(1)	O(31)-C(31)	1.19(1)	C(31)-C(32)	1.53(1)
O(3)-C(3)	1.44(1)	O(61)-C(61)	1.18(1)	C(61)-C(62)	1.51(1)

a) Numbers in parentheses are estimated standard deviations.

Table 3. Bond Angles (ϕ/°) of **2b**[a]

S-C(1)-O(1)	107.4(5)	O(6)-C(6)-C(5)	111.3(7)
S-C(1)-C(2)	109.7(6)	O(6)-C(61)-O(61)	123.6(9)
S-C(5)-C(4)	110.2(5)	O(6)-C(61)-C(62)	110.7(8)
S-C(5)-C(6)	108.4(6)	O(21)-C(21)-C(22)	126.5(8)
O(S)-S-C(1)	106.7(4)	O(31)-C(31)-C(32)	125.1(9)
O(S)-S-C(5)	106.6(3)	O(61)-C(61)-C(62)	124.3(9)
O(1)-C(1)-C(2)	109.6(7)	C(1)-S-C(5)	96.0(4)
O(2)-C(2)-C(1)	106.5(6)	C(1)-O(1)-C(11)	113.4(7)
O(2)-C(2)-C(3)	106.3(6)	C(1)-C(2)-C(3)	115.6(7)
O(2)-C(21)-O(21)	122.3(8)	C(2)-O(2)-C(21)	118.8(6)
O(2)-C(21)-C(22)	111.2(7)	C(2)-C(3)-C(4)	112.7(6)
O(3)-C(3)-C(2)	107.5(6)	C(3)-O(3)-C(31)	118.5(6)
O(3)-C(3)-C(4)	106.4(6)	C(3)-C(4)-C(5)	111.6(6)
O(3)-C(31)-O(31)	124.1(8)	C(4)-O(4)-C(41)	115.5(7)
O(3)-C(31)-C(32)	110.6(8)	C(4)-C(5)-C(6)	113.1(7)
O(4)-C(4)-C(3)	109.2(6)	C(6)-O(6)-C(61)	114.6(7)
O(4)-C(4)-C(5)	109.0(6)		

a) Numbers in parentheses are estimated standard deviations.

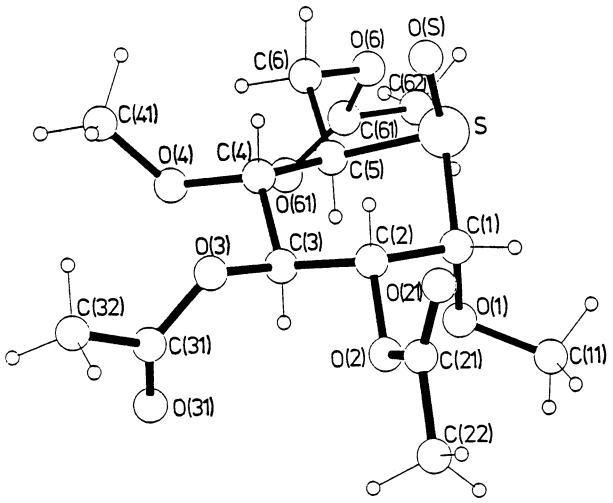


Fig. 1. Molecular structure and atomic numbering of **2b**.

Table 4. Selected Torsion Angles (ϕ/°)[a]

S-C(1)-O(1)-C(11)	103.3(7)	O(21)-C(21)-O(2)-C(2)	2 (1)
S-C(1)-C(2)-O(2)	179.4(5)	O(31)-C(31)-O(3)-C(3)	2 (1)
S-C(1)-C(2)-C(3)	61.6(8)	O(61)-C(61)-O(6)-C(6)	348 (1)
S-C(5)-C(4)-O(4)	174.0(5)	C(1)-S-C(5)-C(4)	60.2(6)
S-C(5)-C(4)-C(3)	294.6(7)	C(1)-S-C(5)-C(6)	184.5(6)
S-C(5)-C(6)-O(6)	64.9(8)	C(1)-C(2)-O(2)-C(21)	98.2(8)
O(S)-S-C(1)-O(1)	171.7(5)	C(1)-C(2)-C(3)-C(4)	301 (1)
O(S)-S-C(1)-C(2)	52.6(7)	C(2)-O(2)-C(21)-C(22)	182.5(7)
O(S)-S-C(5)-C(4)	310.8(7)	C(2)-C(1)-S-C(5)	303.3(6)
O(S)-S-C(5)-C(6)	75.0(6)	C(2)-C(1)-O(1)-C(11)	222.4(8)
O(1)-C(1)-S-C(5)	62.3(6)	C(2)-C(3)-O(3)-C(31)	233.3(8)
O(1)-C(1)-C(2)-O(2)	61.6(8)	C(2)-C(3)-C(4)-C(5)	59.8(9)
O(1)-C(1)-C(2)-C(3)	304 (1)	C(3)-O(3)-C(31)-C(32)	186.1(7)
O(2)-C(2)-C(3)-O(3)	66.1(7)	C(3)-C(2)-O(2)-C(21)	222.0(7)
O(2)-C(2)-C(3)-C(4)	183.0(6)	C(3)-C(4)-O(4)-C(41)	112.8(8)
O(3)-C(3)-C(2)-O(1)	184.0(6)	C(3)-C(4)-C(5)-C(6)	173.1(7)
O(3)-C(3)-C(4)-O(4)	297.9(8)	C(4)-C(3)-O(3)-C(31)	112.4(8)
O(3)-C(3)-C(4)-C(5)	177.3(6)	C(5)-C(4)-O(4)-C(41)	235.0(8)
O(4)-C(4)-C(3)-C(2)	180.3(7)	C(5)-C(6)-O(6)-C(61)	91.0(9)
O(4)-C(4)-C(5)-C(6)	52.4(9)	C(6)-O(6)-C(61)-C(62)	181.0(8)
O(6)-C(6)-C(5)-C(4)	187.4(7)		

a) Numbers in parentheses are estimated standard deviations.

of the sulfoxide **2b** was determined to be axial by X-ray crystallography (Fig. 1). The data given in Tables 2—4 represent a typical characteristic of the sulfoxide with the angles of two C-S-O (106.6° in average) and C-S-C (96.0°) (Table 3) and the rather longer S-O bond (1.492 Å, Table 2), as compared with acyclic sulfoxides.[9] The average torsion angle (60.5°, Table 4) around the ring of **2b** is larger than those of penta-*O*-acetyl-5-thio-α-D-glucopyranose (58.2°)[10] and methyl 5-thio-α-D-ribopyranoside (57.4°).[11] The torsion angle of the glycosidic bond (103.1°, Table 4) is much larger than that expected from exo-anomeric effect (60°).[12]

The ^{1}H NMR data of **2b** reveals a deshielding effect

Table 5. ^{1}H NMR Data (Chemical Shifts (δ/ppm) and Coupling Constants/Hz) of **1**, **2**, **3**(**a**—**f**), and **4**

Compd	H-1	H-2	H-3	H-4	H-5	H-6a	H-6b	Others
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$	
1a[a]	4.55	—3.2—3.7—			2.99	3.80	—	3.38, 3.45, 3.51, 3.57, and 3.61(OMe)
	1.5	—[b]	—	9.0	4.0	1.2	9.5	
2a[c]	4.62	——————2.7—4.0——————						3.44, 3.53, 3.57, 3.60, and 3.62(OMe)
	2.5	—	—	—	—	—	—	
3a[c]	4.96	——————2.7—4.0——————						3.4—3.9(OMe)
	2.0	—	—	—	—	—	—	
1b[a]	4.56	5.09	5.42	3.54	3.23	4.36	4.36	2.05, 2.08, 2.10(Ac), 3.41, and 3.44(OMe)
	2.8	9.8	8.5	11.0	3.5	3.5	0	
2b[c]	4.75	5.67	5.46	3.88	3.10	4.41	4.80	2.10(Ac×2), 2.14(Ac), 3.46, and 3.62(OMe)
	2.2	10.0	8.5	11.0	9.2	4.0	11.0	
3b[c]	5.00	—	5.31	———	2.7—5.1	———		2.11, 2.12, 2.17(Ac), 3.49, and 3.92(OMe)
	0	9.0	9.0	—	—	—	—	
1c[c]	4.67	5.06	5.36	5.19	3.35	4.51	3.92	1.94, 1.96, 1.98, 2.03(Ac), and 3.47(OMe)
	3.0	10.0	8.8	10.0	4.2	2.8	12.0	
2c[d]	4.84	5.75	5.55	5.63	3.24	4.43	4.48	2.02, 2.06, 2.10, 2.11(Ac), and 3.64(OMe)
	2.4	10.0	10.0	11.2	8.7	4.6	11.5	
3c[d]	5.05	5.00	5.55	5.17	3.74	4.30	4.72	2.02, 2.05, 2.09, 2.10(Ac), and 3.89(OMe)
	~0	10.7	11.3	11.8	~0	~0	12.7	
1d[a]	6.06	———3.02—3.62———				3.72	—	2.08(Ac), 3.32, 3.40(OMe), and 3.77(OMe×2)
	2.5	—	—	—	4.8	—	9.8	
2d[d]	6.24	3.97	3.44	3.81	2.86	3.60	3.95	2.15(Ac), 3.44, 3.49, 3.57, and 3.63(OMe)
	2.8	9.8	9.8	9.8	9.8	4.3	9.2	
3d[d]	6.54	3.27	3.45	3.31	3.15	3.77	3.90	2.25(Ac), 3.43, 3.47, 3.60, and 3.61(OMe)
	2.0	9.6	9.6	11.6	2.0	2.0	10.0	
4[c]	5.97	3.71	3.35	—[e]	3.20	—3.9—4.0—		2.20(Ac), 3.41, 3.45(OMe), and 3.61(OMe×2)
	3.0	9.4	9.4	10.5	2.0	4.3	—	
1e[a]	6.16	3.53	3.40	5.12	———3.44—3.38———			2.12, 2.15(Ac), 3.31, 3.45, and 3.52(OMe)
	3.2	9.4	9.4	10.5	—	—	—	
2e[c]	6.29	4.10	—	5.44	3.01	—3.4—3.9—		2.15, 2.19(Ac), 3.42, 3.51, and 3.55(OMe)
	3.0	10.2	11.5	9.2	4.5	11.8	—	
3e[d]	6.58	3.41	3.54	5.15	3.32	3.58	3.79	2.15, 2.28(Ac), 3.34, 3.48, and 3.50(OMe)
	2.0	10.0	10.0	11.9	—	2.6	10.3	
1f[c]	6.10	———5.0—5.6———			3.58	4.04	4.36	2.00, 2.02, 2.05, 2.08, and 2.18(Ac)
	2.5	—	—	9.8	3.0	4.8	12.0	
2f[d]	6.32	5.86	5.53	5.68	3.24	4.42	4.50	2.03, 2.04, 2.08, 2.11, and 2.24(Ac)
	2.8	10.4	10.4	10.4	9.2	4.4	11.9	
3f[d]	6.55	5.20	5.53	5.25	3.58	4.27	4.73	2.01, 2.05, 2.06, 2.10, and 2.33(Ac)
	2.4	10.4	10.4	11.2	~2	~2	11.1	

a) Data from Ref. 6. b) Unidentified. c) Measured at 100 MHz. d) Measured at 500 MHz. e) 3.4—3.8.

Table 6. ^{1}H NMR Data (Chemical Shifts (δ/ppm) and Coupling Constansts/Hz) of **1g**, **2g**, and **3g**

Compd	H-1a	H-1e	H-2		H-3	H-4	H-5	H-6a	H-6b	Ac
	$J_{1a,1e}$	$J_{1a,2}$	$J_{1e,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$	
1g[a]	2.67	2.88	—[b]		—	5.21	3.17	4.14	4.25	2.01, 2.02, 2.03, and 2.07
	12.8	10.1	3.9	—	10.1	9.5	3.3	5.9	11.9	
2g[c]	2.60	3.65	5.73		5.34	5.68	3.05	4.35	4.46	2.04, 2.05, 2.07, and 2.10
	13.9	12.0	3.9	9.8	9.8	11.5	9.8	4.3	12.0	
3g[c]	2.99	3.81	5.09		5.31	5.23	3.12	4.40	4.68	2.02, 2.05, 2.07, and 2.08
	11.8	12.0	3.6	9.8	9.8	11.5	1.9	2.6	12.8	

a) Data from Ref. 8. b) Unidentified. c) Measured at 500 MHz.

Table 7. Chemical Shift Difference of Ring Protons between **2** and **3** ($\Delta\delta$/ppm)

$\Delta\delta_{2-3}$	H-1e	H-1a	H-2	H-3	H-4	H-5
2a—3a	−0.34	—	—	—	—	—
2b—3b	−0.25	—	—	0.15	—	—
2c—3c	−0.21	—	0.75	0	0.46	−0.50
2d—3d	−0.30	—	0.70	−0.01	0.50	−0.29
2e—3e	−0.29	—	0.69	—	0.29	−0.31
2f—3f	−0.23	—	0.66	0	0.43	−0.34
2g—3g	−0.16	−0.39	0.64	0.03	0.45	−0.07

of axial sulfoxide for the syn-axial protons[13,14] (H-2 and H-4, Table 5). This deshielding effect is also characteristic for the other axial sulfoxides (Tables 5—7). It was found that the anomeric equatorial protons of the equatorial sulfoxides resonate at lower field (ca. 0.3 ppm) than those of the axial sulfoxides as shown in Table 7. The chemical shifts of the equatorial protons vicinal to the sulfoxide bonds of some thianes 1-oxide were measured but their difference has not been particularly pointed out.[13] On the assumption that an anisotropy of the sulfoxide bond is important for the deshielding effect, the dihedral angle between the S-O bond and the anomeric C-H bond of equatorial sulfoxides would be smaller than that of axial sulfoxides. In addition, chemical shifts (δ) of H-5 of axial sulfoxides **2** are smaller than those of equatorial sulfoxides **3**. This supports an acetylene-type anisotropy of sulfoxide bond.[14] In any case, these chemical shift difference could be used subsidiarily for the assignment.

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. Infrared spectra were recorded on a HITACHI 260-10 spectrometer. ^{1}H NMR spectra were obtained from JEOL PS-100 (100 MHz) and JNM-GX-500 (500 MHz) spectrometer. ^{13}C NMR spectra were recorded on 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. Column chromatography was carried out on Wako gel C-300 with solvent system specified.

Oxidation of 5-Thioglucose Derivatives (1) with m-CPBA. General Procedure: To a stirred solution of **1** (0.5 mmol) in the solvent given in Table 1 (1.5×10^{-2} ml mg^{-1} of **1**) was slowly added a solution of mCPBA (0.55 mmol) in the same solvent (1.5×10^{-2} ml mg^{-1} of **1**) at the temperature given in Table 1. After 15 min, the reaction mixture was diluted with chloroform and washed with aqueous $Na_2S_2O_3$ and aqueous $NaHCO_3$ successively. The chloroform layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was chromatographed on a silica-gel column (hexane/acetone 4:1—5:3) to give recovery of **1** in an early fraction and the diastereomer mixture of sulfoxide derivatives **2** and **3** in a later fraction. The yields and the diastereomer ratios are given in Table 1.

Methyl 2,3,4,6-Tetra-*O*-methyl-5-thio-α-D-glucopyranoside (*R*)- and (*S*)-*S*-Oxide (2a and 3a): Oxidation of methyl 2,3,4,6-tetra-*O*-methyl-5-thio-α-D-glucopyranoside (**1a**)[6] followed by purification on a silica-gel column (hexane/acetone 4:1—3:1) gave the mixture of **2a** and **3a** as a colorless oil; $[\alpha]_D^{22}$ +177° (*c* 0.92, $CHCl_3$) for the mixture with the diastereomer ratio of 85:15; IR (neat) 1035 cm^{-1}. In the ^{13}C NMR of the mixture, only signals for **2a** were assigned: δ=56.0 (5-C), 59.2, 59.7, 61.2, 61.4 (OMe), 67.0 (6-C), 77.4, 78.8 (2-C and 4-C), 84.2 (3-C), and 89.0 (1-C).

Found: C, 46.70; H, 7.98; S, 11.40%. Calcd for $C_{11}H_{22}O_6S$: C, 46.79; H, 7.85; S, 11.36%.

Methyl 2,3,6-Tri-*O*-acetyl-4-*O*-methyl-5-thio-α-D-glucopyranoside (*R*)- and (*S*)-*S*-Oxide (2b and 3b): Oxidation of methyl 2,3,6-tri-*O*-acetyl-4-*O*-methyl-5-thio-α-D-glucopyranoside (**1b**)[6] followed by purification on a silica-gel column (hexane/acetone 2:1) gave the mixture of **2b** and **3b** as a white solid; $[\alpha]_D^{20}$ +144° (*c* 0.67, $CHCl_3$) for the mixture with the diastereomer ratio of 85:15. Recrystallization of the mixture from ethanol gave the (*R*)-sulfoxide **2b** as white crystals; mp 172—173 °C; $[\alpha]_D^{20}$ +176° (*c* 1.38, $CHCl_3$); the crystal of **2b** used for X-ray analysis was obtained by natural vaporization from the solution in hexane/acetone (2:1); mp 168—170 °C; ^{13}C NMR for **2b**: δ=20.6, 20.7 (CH_3CO), 54.5 (5-C), 59.0 (6-C), 60.5, 61.7 (OMe), 69.1 (2-C), 71.6 (3-C), 74.8 (4-C), 88.7 (1-C), 169.3, 169.6, and 170.4 (CH_3CO).

Found: C, 45.83; H, 6.09; S, 8.65%. Calcd for $C_{14}H_{22}O_9S$: C, 45.89; H, 6.05; S, 8.75%.

Methyl 2,3,4,6-Tetra-*O*-acetyl-5-thio-α-D-glucopyranoside (*R*)- and (*S*)-*S*-Oxide (2c and 3c): Oxidation of methyl 2,3,4,6-Tetra-*O*-acetyl-5-thio-α-D-glucopyranoside (**1c**)[6] followed by purification on a silica-gel column (hexane/acetone 2:1) gave the mixture of **2c** and **3c** as a colorless oil; $[\alpha]_D^{28}$ +166° (*c* 2.25, $CHCl_3$) for the mixture with the diastereomer ratio of 83:17.

Found: C, 45.88; H, 5.93; S, 7.74%. Calcd for $C_{15}H_{22}O_{10}S$: C, 45.68; H, 5.62; S, 8.13%.

1-*O*-Acetyl-2,3,4,6-tetra-*O*-methyl-5-thio-α-D-glucopyranose (*R*)- and (*S*)-*S*-Oxide (2d and 3d): Oxidation of 1-*O*-acetyl-2,3,4,6-tetra-*O*-methyl-5-thio-α-D-glucopyranose (**1d**)[6] followed by purification on a silica-gel column (hexane/acetone 5:2) gave **2d** as a colorless oil in an early fraction and **3d** as white crystals in a later fraction.

2d: $[\alpha]_D^{20}$ +247° (*c* 1.33, $CHCl_3$); IR (neat) 1050 cm^{-1}.

Found: C, 46.10; H, 7.24; S, 10.18%. Calcd for $C_{12}H_{22}O_7S$: C, 46.44; H, 7.14; S, 10.33%.

3d: Mp 88—90 °C (from petroleum ether); $[\alpha]_D^{22}$ +164° (*c* 1.13, $CHCl_3$); IR (neat) 1050 cm^{-1}.

Found: C, 46.35; H, 7.23; S, 10.28%. Calcd for $C_{12}H_{22}O_7S$: C, 46.44; H, 7.14; S, 10.33%.

1,4-Di-*O*-acetyl-2,3,6-tri-*O*-methyl-5-thio-α-D-glucopyranose (*R*)- and (*S*)-*S*-Oxide (2e and 3e): Oxidation of 1,4-di-*O*-acetyl-2,3,6-tri-*O*-methyl-5-thio-α-D-glucopyranoside (**1e**)[6] followed by purification on a silica-gel column (hexane/acetone 4:1—2:1) gave **2e** as a colorless oil in an early fraction and **3e** as white crystals in a later fraction.

2e: $[\alpha]_D^{20}$ +207° (*c* 1.10, $CHCl_3$); IR (neat) 1065 cm^{-1}; ^{13}C NMR δ=20.6, 20.8 (CH_3CO), 56.1 (5-C), 59.0, 59.4, 61.0 (OMe), 66.9 (6-C), 68.8 (4-C), 75.8 (1-C), 77.3 (2-C), 81.1 (3-C), 168.2, and 169.6 (CH_3CO).

Found: C, 46.22; H, 6.75; S, 10.28%. Calcd for $C_{13}H_{22}O_8S$: C, 46.14; H, 6.55; S, 9.48%.

3e: Mp 169—171 °C; $[\alpha]_D^{20}$ +105° (*c* 0.96, $CHCl_3$); IR

(neat) 1065 cm^{-1}; ^{13}C NMR δ=20.4, 20.6 (CH_3CO), 58.6, 59.4 (OMe), 59.6 (5-C), 61.1 (OMe), 64.3 (6-C), 66.2 (4-C), 77.5 (2-C), 78.4 (1-C), 81.8 (3-C), and 168.9 (CH_3CO).

Found: C, 46.21; H, 6.53; S, 9.06%. Calcd for $C_{13}H_{22}O_8S$: C, 46.14; H, 6.55; S, 9.48%.

1,2,3,4,6-Penta-*O*-acetyl-5-thio-α-D-glucopyranose (*R*)- and (*S*)-*S*-Oxide (2f and 3f): Oxidation of 1,2,3,4,6-penta-*O*-acetyl-5-thio-α-D-glucopyranose (**1f**)[7] followed by puirification on a silica-gel column (hexane/acetone 5:3) gave the mixture of **2f** and **3f** as a white solid; $[\alpha]_D^{27}$ +128° (*c* 0.93, $CHCl_3$) for the mixture with the diastereomer ratio of 29:71; $[\alpha]_D^{23}$ +136° (*c* 1.17, $CHCl_3$) for the mixture with the diastereomer ratio of 51:49. Recrystallization of the mixture from ethanol gave the (*S*)-sulfoxide **3f** as white crystals; mp 175—177 °C; $[\alpha]_D^{20}$ +123° (*c* 0.85, $CHCl_3$).

Found: C, 45.74; H, 5.35; S, 7.59%. Calcd for $C_{16}H_{22}O_{11}S$: C, 45.50; H, 5.25; S, 7.59%.

2,3,4,6-Tetra-*O*-acetyl-1,5-dideoxy-1,5-epithio-D-glucitol (*S*)- and (*R*)-*S*-Oxide (2g and 3g): Oxidation of 2,3,4,6-tetra-*O*-acetyl-1,5-dideoxy-1,5-epithio-D-glucitol (**1g**)[8] followed by purification on a silica-gel column (hexane/acetone 2:1—5:3) gave the mixture of **2g** and **3g** as a white solid; mp 124—126 °C; $[\alpha]_D^{28}$ +15° (*c* 0.83, $CHCl_3$) for the mixture with the diastereomer ratio of 44:56; $[\alpha]_D^{28}$ +49° (*c* 1.31, $CHCl_3$) for the mixture with the diastereomer ratio of 67:33; ^{13}C NMR δ=20.3, 20.5, 20.5, 20.6 (CH_3CO), 47.2, 52.5, 55.4, 58.3, 59.2, 64.3, 64.5, 65.4, 66.4, 67.4, 73.4, 73.7 (1-C—6-C of both **2g** and **3g**), 168.9, 169.0, 169.5, and 170.2 (CH_3CO).

Found: C, 45.93; H, 5.58; S, 8.66%. Calcd for $C_{14}H_{20}O_9S$: C, 46.15; H, 5.53; S, 8.80%.

1-*O*-Acetyl-2,3,4,6-tetra-*O*-methyl-5-thio-α-D-glucopyranose *S*,*S*-Dioxide (4): Both **2d** and **3d** was oxidized in dichloromethane at room temperature as described above for the oxidation of **1**, respectively. The crude oil was chromatographed on a silica-gel column (hexane/acetone 5:3) to give **4** as a colorless oil in an early fraction and recovery of the sulfoxide **2d** or **3d** in later fraction; $[\alpha]_D^{30}$ +116°(*c* 0.94, $CHCl_3$); IR (neat) 1330 cm^{-1}.

Found: C, 43.91; H, 6.72; S, 9.72%. Calcd for $C_{12}H_{22}O_8S$: C, 44.16, H, 6.79; S, 9.83%.

X-ray Analysis: The space group of **2b** was determined as $P2_12_12_1$ from the systematic absences of reflections with odd *h* for *h*00, odd *k* for 0*k*0, and odd *l* for 00*l*. A crystal with dimensions of 0.7×0.3×0.2 mm was used for data collection on a Rigaku automated four-circle diffractometer with graphite monochromated Mo $K\alpha$ radiation (λ=0.71073 Å). Accurate unit-cell dimensions were determined by least-squares calculation with 2θ values of 75 high-angle reflections measured on the diffractometer. Crystal data are summarized in Table 8.

Intensity data within the range of $3° \leq 2\theta \leq 50°$ were collected in the $2\theta/\omega$ scan mode at a scanning rate of 8° (ω) min^{-1}. The periodic check of the intensity values of five standard reflections revealed no significant variation during the course of data collection. The standard deviations were estimated by the equation of $\sigma^2(F_o)=\sigma_p^2(F_o)+qF_o^2$, , where σ_p was evaluated by counting statistics and q (=0.0182) from measurement of the monitored reflections.[15] A total of 1676 independent reflections was obtained, of which 1016 with $|F_o|>3\sigma(|F_o|)$ were used for structure determination. The intensities were corrected for Lorentz and polarization effects.

Structure Determination: The structure was solved by direct methods with the MULTAN 78 program.[16] The atomic parameters were refined by the block-diagonal least-squares method with anisotropic temperature factors. The function minimized was $\sum w(|F_o|-|F_c|)^2$, where $w=1/\sigma^2(F_o)$. All the hydrogen atoms were located geometrically and included in the structure refinement. The final R factor was 0.055 (R_w=0.085). Atomic scattering factors were taken from "International Tables for X-Ray Crystallography".[17] The final positional and thermal parameters are given in Table 9. Bond length, bond angles, and selected torsion angles are given in Tables 2—4.

Table 8. Crystal Data

$C_{14}H_{22}O_9S$
M.W.=366.39
Orthorhombic
$P2_12_12_1$
a/Å=14.886(2)
b/Å=14.479(2)
c/Å=8.2770(1)
V/Å^3=1784.0(4)
Z=4
D_x/g cm^{-3}=1.364
μ(Mo $K\alpha$)/cm^{-1}=2.26

Table 9. Fractional Coordinates and Equivalent Isotropic Temperature Factors of **2b**[a]

Atom	x	y	z	B_{eq}/Å^2
S	0.0166(2)	0.5139(2)	0.2966(3)	4.1〈10〉
O(S)	−0.0682(4)	0.4633(4)	0.2587(8)	5.4〈28〉
O(1)	0.0619(4)	0.6770(4)	0.4124(8)	4.6〈13〉
O(2)	−0.1088(4)	0.7243(4)	0.5265(8)	4.2〈20〉
O(3)	−0.1356(4)	0.5814(4)	0.7444(7)	3.9〈10〉
O(4)	−0.0037(4)	0.4473(4)	0.7670(8)	4.5〈11〉
O(6)	0.1701(4)	0.3799(5)	0.3951(8)	4.6〈13〉
O(21)	−0.2308(4)	0.7206(5)	0.374(1)	6.3〈32〉
O(31)	−0.0619(4)	0.6532(5)	0.9441(9)	5.6〈16〉
O(61)	0.2462(5)	0.4167(7)	0.616(1)	7.6〈28〉
C(1)	−0.0160(6)	0.6320(6)	0.354(1)	4.1〈16〉
C(2)	−0.0872(6)	0.6285(6)	0.486(1)	3.3〈10〉
C(3)	−0.0587(5)	0.5841(6)	0.640(1)	3.0〈6〉
C(4)	−0.0291(5)	0.4846(6)	0.616(1)	3.4〈12〉
C(5)	0.0506(5)	0.4775(6)	0.500(1)	3.5〈11〉
C(6)	0.0890(6)	0.3813(6)	0.489(1)	3.8〈9〉
C(11)	0.0998(8)	0.7390(7)	0.301(2)	5.5〈11〉
C(21)	−0.1814(6)	0.6625(6)	0.461(1)	4.0〈8〉
C(22)	−0.1903(7)	0.8606(7)	0.510(1)	5.5〈19〉
C(31)	−0.1281(6)	0.6169(7)	0.8931(1)	4.2〈13〉
C(32)	−0.2131(7)	0.598(1)	0.992(1)	6.7〈24〉
C(41)	−0.0596(8)	0.3767(8)	0.827(1)	6.4〈29〉
C(61)	0.2454(7)	0.3919(7)	0.481(1)	4.5〈9〉
C(62)	0.3269(7)	0.3910(8)	0.371(1)	5.5〈18〉

a) $B_{eq}=8\pi^2(U_1+U_2+U_3)/3$, where U_1, U_2, and U_3 are the principal components of the mean square displacement matrix U. Values in 〈 〉 are the anisotropicity defined by $(\sum(B_{eq}-8\pi^2U_i)^2/3)^{1/2}$ and those in ( ) are e.s.d.'s; they refer to the last decimal places.

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