

CHIROPTICAL STUDIES OF SUGARS. PART IV.
PROPOSAL OF THE GLYCOCIDIC HETEROATOM
HELICITY RULE IN 1-THIO-D-GLYCOPYRANOSIDES.

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1-Thio-D-glycopyranosides gave CD bands at 220 nm ($n \rightarrow \sigma^*$ of glycosidic sulfur). Their $[\theta]$ were shown as the sum of the two effects from ring oxygen and -OH at C-2, leading to the glycosidic heteroatom helicity rule to predict the configurations and conformations at C-1 and C-2.

Previously it has been suggested that the $\sigma \rightarrow \sigma^*$ band of the ring heteroatom might be the main band in governing the optical rotations of the sugars. Especially in 1-thio-sugars the signs and strengths of the band have been shown to be determined by the configurations and conformations of the glycosidic sulfur (Ring Heteroatom Helicity Rule)¹⁻³⁾ The stereochemical factors to determine the $[\theta]$ of the minor band due to glycosidic heteroatoms, however, has not yet been fully studied. Here we report the CD of the eight 1-thio-D-glycopyranosides. They are four glucosides (ethyl α -glucosides(I)²⁾, cyclohexyl α -glucoside(II)²⁾, ethyl β -glucoside(IV)²⁾, and cyclohexyl β -glucoside(V)²⁾), two mannosides (ethyl α -mannoside(III)⁴⁾ and ethyl β -mannoside(VI)⁵⁾), and two galactosides (n-butyl β -galactoside(VII)²⁾ and cyclohexyl β -galactoside(VIII)²⁾).

UV peaks or shoulders were observed at 209-229 nm (Band 1) and 196-216 nm (Band 2) (Table 1). They almost coincided with the UV $n \rightarrow \sigma^*$ bands of thioether group at ca. 230 nm and at ca.210 nm⁶⁻¹¹⁾ respectively. In circular dichroism (CD), on the other hand, they gave maxima (Band A) at 218-225 nm (Table 1, Fig.1), which correspond to Band 1 in their UV spectra. They showed red shifts with decreasing polarities of solvent. It shows that Band A is due to the $n \rightarrow \sigma^*$ transition of glycosidic sulfur. The results are summarized as follows.

(1) The signs and magnitudes of Band A were almost the same in the glucosides and galactosides which differ from each other in

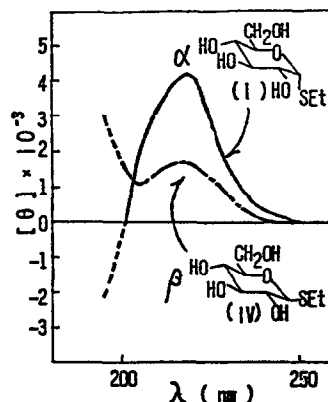


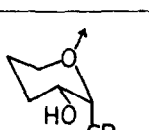
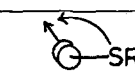
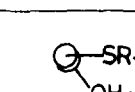
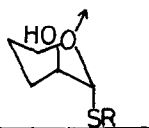

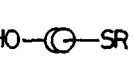
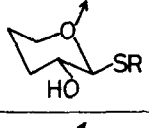
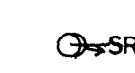
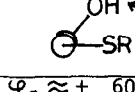
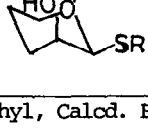
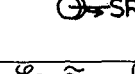
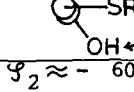
Fig.1 CD spectra of ethyl 1-thio- α -D-glucopyranoside (I) and ethyl 1-thio- β -D-glucopyranoside (IV) in aqueous solution.

Table 1 CD and UV data and calcd. values of Band A in 1-thio-D-glycopyranosides.

Comp.	Anom. Config.	Relative Geometry	CD			S o l v.	UV	
			Band A				Band 1	Band 2
			Calcd. $[\theta] \times 10^{-3}$	Obsd. $[\theta] \times 10^{-3}$	λ_{max}			
(I) Ethyl α -gluco	α	A	+ 4.4	+ 4.2 (218) + 4.1 (224) + 4.3 (225)	W M D	4.3 (209) 2.4 ^S (222) 3.5 (229)	3.0 ^S (198) 2.9 (210) 2.7 ^S (216)	
(II) Cyclohexyl α -gluco	α	A		+ 6.3 (219)	W	3.9 (211)	2.7 ^S (198)	
(III) Ethyl α -manno	α	B	+ 6.6	+ 6.6 (221) + 7.7 (225) + 7.3 (224)	W M D	4.0 (209) 0.78 ^S (220) 0.53 ^S (226)	2.2 ^S (196) 2.0 (206) 1.1 (210)	
(IV) Ethyl β -gluco	β	C	+ 2.2	+ 1.7 (217) + 2.0 (224) + 1.8 (224)	W M D	4.0 (209) 0.95 ^S (220) 2.6 (220)	2.4 ^S (196) 1.8 (206)	
(V) Cyclohexyl β -gluco	β	C		+ 3.4 (219)	W	4.1 (209)	2.8 ^S (198)	
(VI) Ethyl β -manno	β	D	- 2.2	- 2.6 ^S (216) - 3.2 (218) - 2.2 (217)	W M D	4.0 (209) 0.86 ^S (220) 1.2 ^S (220)	2.5 ^S (198) 1.9 (207) 1.9 (211)	
(VII) n-Butyl β -galacto	β	C		+ 2.7 (220)	W	4.5 (207)	3.2 ^S (198)	
(VIII) Cyclohexyl β -galacto	β	C		+ 3.3 (219)	W	5.0 (208)	3.6 ^S (198)	

Solv. (W:Water, M:Methanol, D:Dioxane). s:shoulder.

Table 2 All the possible relative geometries between glycosidic sulfur and adjacent two chromophores (ring oxygen and -OH at C-2) in ethyl 1-thio-D-glycopyranosides.

Relative Geometry	Projections from C-1		$[\theta]_{ring\ O}$ $\times 10^{-3}$	$[\theta]_{(C-2)-OH}$ $\times 10^{-3}$	Calcd. Band A $[\theta] \times 10^{-3}$
	To Ring O	To C-2			
A 			+ 6.6	- 2.2	+ 4.4
B 			+ 6.6	0	+ 6.6
C 			0	+ 2.2	+ 2.2
D 			0	- 2.2	- 2.2

R=ethyl, Calcd. Band A ; $[\theta] = [\theta]_{ring\ O} + [\theta]_{(C-2)-OH}$

configuration at C-4. These results suggest that Band A is not affected by the -OH group at C-4 which is distant from the glycosidic sulfur at C-1.

- (2) The signs and magnitudes of Band A differed in glucosides and mannosides which differ from each other in configuration at C-2. These results suggest that Band A is affected by the configuration of the -OH at C-2 which is adjacent to the glycosidic sulfur at C-1.
- (3) In anomers, Band A of the α -anomers have larger positive values than those of the β -anomers of the same glycosides. These results suggest that Band A is also affected by the ring oxygen adjacent to the glycosidic sulfur at C-1.
- (4) The magnitudes of Band A are increased on changing the size of the R in -SR (if 1.0 in R=ethyl, 1.4 in R=n-butyl, 1.7 in R=cyclohexyl) in the three sugar series at the same ratio.

The ring conformations of all the model compounds are postulated as 4C_1 chair form from the PMR studies.¹²⁾ Table 2 shows all possible relative geometries between the glycosidic sulfur and the two adjacent functional groups using their sketches and their helical projections from C-1 to the ring oxygen and from C-1 to C-2. Here \mathcal{G}_1 is the dihedral angle between (C-1)-S bond and the vector of the direction of the dipole moment of the ring oxygen and \mathcal{G}_2 is that between (C-1)-S bond and (C-2)-O bond. The signs of \mathcal{G}_1 and \mathcal{G}_2 are defined as positive and negative in anticlockwise and clockwise senses, respectively. Table 2 also shows the partial $[\theta]$ ($[\theta]_{\text{ring O}}$ and $[\theta]_{\text{(C-2)-OH}}$), together with their sums (Calcd. Band A). $[\theta]_{\text{ring O}}$ reflect the relative geometries between the glycosidic sulfur and the ring oxygen, while $[\theta]_{\text{(C-2)-OH}}$ reflect those between the glycosidic sulfur and the -OH group at C-2. Here these signs and magnitudes are based on the following assumptions.

- (i) The sign of $[\theta]_{\text{ring O}}$ is positive (or negative), when \mathcal{G}_1 is positive (or negative).
- (ii) The sign of $[\theta]_{\text{(C-2)-OH}}$ is positive (or negative), when \mathcal{G}_2 is positive (or negative).
- (iii) $[\theta]_{\text{ring O}}$ is ca. 0, when \mathcal{G}_1 is ca. 0° or 180° .
- (iv) $[\theta]_{\text{(C-2)-OH}}$ is ca. 0, when \mathcal{G}_2 is ca. 0° or 180° .
- (v) When \mathcal{G}_1 is ca. 120° , $[\theta]_{\text{ring O}}$ is ca. 6.6×10^3 , from the obsd. $[\theta]$ of type B compound (III) in Table 1.
- (vi) When \mathcal{G}_2 is ca. 60° (or -60°), $[\theta]_{\text{(C-2)-OH}}$ is ca. 2.2×10^3 (or -2.2×10^3), from the average of the obsd. $|[\theta]|$ of type C compound (IV) and type D compound (VI) in Table 1.
- (vii) The signs and magnitudes of Band A are the sums of the two partial $[\theta]$ above; For example, the Calcd. Band A of type A compound is the sum of $[\theta]_{\text{ring O}}$ (ca. 6.6×10^3) and $[\theta]_{\text{(C-2)-OH}}$ (ca.

-2.2×10^3), which is ca. $+4.4 \times 10^3$.

The above assumptions well explain the obsd. Band A in Table 1. It leads us to present the above assumptions as a "glycosidic heteroatom helicity rule" in which the signs and magnitudes of Band A are mainly determined by the relative geometries between the glycosidic sulfur and its two adjacent groups. It might be used for configuration and conformation analysis at C-1 and C-2 of 1-thio-D-glycopyranosides.

The effect of the rotation around (C-1)-S bond and (C-2)-O bond might not be negligible, however, seems to be less important probably because the glycosides take almost the same conformations about these bonds so long as the R in -SR is the same. The increase of Band A on the increase of the size of the R in -SR might reflect their steric effects to the rotation around (C-1)-S bond and/or the electronic effect to the n electron on the sulfur.

REFERENCES

- 1) H.Meguro, E.Ohtaki, and K.Tuzimura, *Tetrahedron Lett.*, 4335(1977)
 - 2) E.Ohtaki, H.Meguro, and K.Tuzimura, *Tetrahedron Lett.*, 4339(1977)
 - 3) H.Meguro, E.Ohtaki, K.Tuzimura, N.A.Hughes, and L.Hough, *Tetrahedron Lett.*, 3371(1978)
 - 4) T.Ogawa and M.Matsui, *Carbohydr. Res.* 54, C17(1977), $[\alpha]_D^{24} +217.1$ (cl,water) (Found).
 - 5) J.Fried and D.G.Walz, *J.Am.Chem.Soc.* 71, 140(1949), $[\alpha]_D^{24} - 87.2$ (cl,water) (Found).
 - 6) R.M.Silverstein and G.C.Bassler, *Spectrometric Identification of Organic Compounds*, Chap.5 (John Wiley & Sons, Inc., New York, 1967)
 - 7) S.D.Thompson, D.G.Carroll, F.Watson, M.O'Donnell, and S.P.McGlynn, *J.Chem.Phys.* 45, 1367(1966)
 - 8) P.Laur, H.Häuser, J.E.Gurst, and K.Mislow, *J.Org.Chem.* 32, 498(1967)
 - 9) P.C.Cookson, G.H.Cooper, and J.Hudec, *J.Chem.Soc.(B)*, 1004(1967)
 - 10) P.Salvadori, *Chem.Commun.* 1203(1968)
 - 11) N.M.Green, W.P.Mose, and P.M.Scopes, *J.Chem.Soc.(C)*, 1330(1970)
 - 12) Glucosides and galactosides ; See ref.2).
- Mannosides ; The PMR of (III) and (VI) were studied to determine their conformations in D₂O. The chemical shifts of the anomeric protons were 5.3 ppm for α -anomer (III), 4.9 ppm for β -anomer (VI). The coupling constants between H-1 and H-2 were 1.0 cps for (III), 1.6 cps for (VI). The coupling constants between "H-2 and H-3" and "H-3 and H-4" of (VI) were 3.0 and 15.5 cps respectively. These PMR results, together with the possible similarities of the conformations with the D-glycopyranosides,¹³⁾ suggest the ⁴C₁ chair forms for (III) and (VI).
- 13) R.J.Yu and C.T.Bishop, *Can.J.Chem.* 45, 2195(1967)
 - 14) CD on a Jasco J-20, 1 mm cell, ca. 1 mg/ml, at room temperature. UV on a Beckman Acta CIII, 1 cm cell, ca. 1 mg/ml, at room temperature.
 - 15) The study was supported by the grant from the ministry of education of Japan. We thank Prof. K.Tuzimura of the former head of our laboratory for his support and encouragements. Thanks are also extended to Prof. L.Hough and Dr. A.C.Richardson of the Queen Elizabeth College for their usefull discussions and the interest.

(Received in Japan 17 April 1979)