The Rotatory Dispersion and Stereochemistry of Organic Compounds. VII.[1] Monosulfides and Disulfides Derived from Glucose and Glucosamine

By Yojiro TSUZUKI, Koko TANABE, Masuo AKAGI and Setsuzo TEJIMA

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In previous papers[1-3] the rotatory dispersion (RD) and stereochemistry of sugar xanthates have been studied, and it has been shown that the Cotton effect is due to the weak absorption band of the $-\mathrm{S}-\overset{\mathrm{S}}{\overset{\|}{\mathrm{C}}}-$ group.

The present paper deals with the studies made of some monosulfides as well as disulfides containing an –S–S– group with the object of investigating the rotatory contribution of the sulfur atoms.

Since it has often been observed[4-7] that optically active disulfides in general are characterized by anomalously large rotations, it appears that it would be particularly interesting to investigate, by means of RD, how the –S–S– group contributes to the optical activity of the disulfides newly synthesized from D-glucose and D-glucosamine.

The following compounds will be investigated:

Bis(2-acetamido-2-deoxy-β-D-glucopyranosyl)-sulfide (compound I),

Bis(2-acetamido-2-deoxy-3, 4, 6-tri-*O*-acetyl-β-D-glucopyranosyl) sulfide (compound II),

Bis(2-acetamido-2-deoxy-β-D-glucopyranosyl)-D-disulfide (compound III),

1, 6-Anhydro-1, 6-sulfide-2, 3, 4-tri-*O*-acetyl-β-glucopyranose (compound IV),

Bis(2, 3, 4, 6-tetra-*O*-acetyl-β-D-glucopyranosyl) sulfide (compound V),

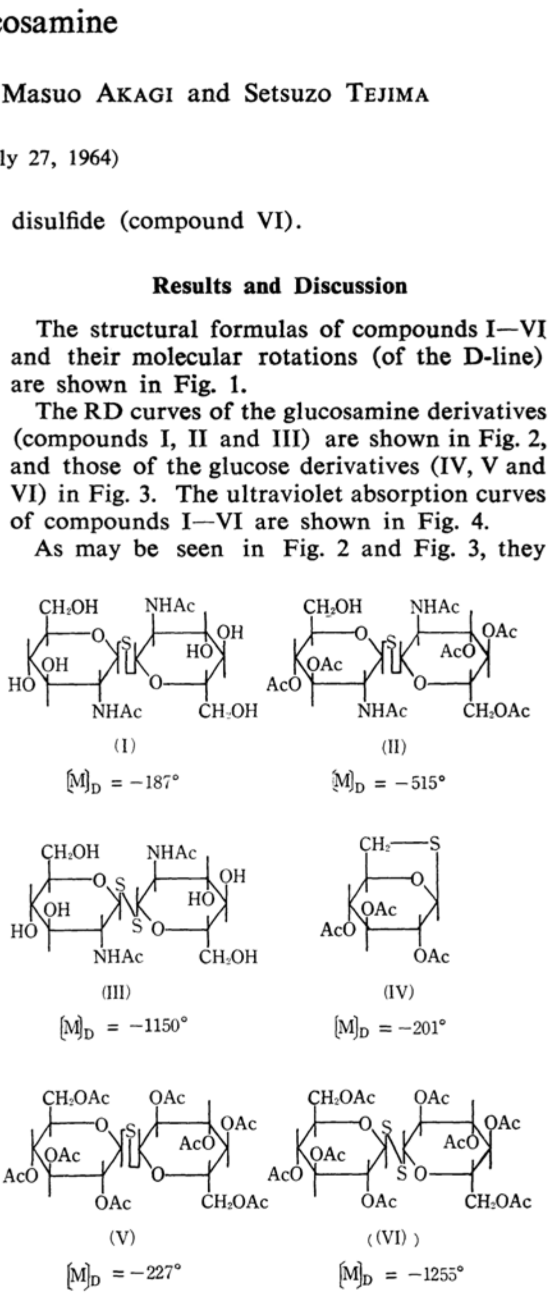
Bis(2, 3, 4, 6-tetra-*O*-acetyl-β-D-glucopyranosyl) disulfide (compound VI).

Results and Discussion

The structural formulas of compounds I—VI and their molecular rotations (of the D-line) are shown in Fig. 1.

The RD curves of the glucosamine derivatives (compounds I, II and III) are shown in Fig. 2, and those of the glucose derivatives (IV, V and VI) in Fig. 3. The ultraviolet absorption curves of compounds I—VI are shown in Fig. 4.

As may be seen in Fig. 2 and Fig. 3, they



(I) $[M]_D = -187°$

(II) $[M]_D = -515°$

(III) $[M]_D = -1150°$

(IV) $[M]_D = -201°$

(V) $[M]_D = -227°$

((VI)) $[M]_D = -1255°$

Fig. 1. Structural formulas and $[M]_D$. Ac=COCH$_3$

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[1] Part VI: Y. Tsuzuki, K. Tanaka, K. Tanabe, M. Akagi and S. Tejima, This Bulletin, 37, 730 (1964).

[2] Y. Tsuzuki, K. Tanaka and K. Tanabe, ibid., 35, 1614 (1962).

[3] Y. Tsuzuki, K. Tanabe, M. Akagi and S. Tejima, ibid., 37, 162 (1964).

[4] W. J. Kauzmann and H. Eyring, *J. Chem. Phys.*, **9**, 41 (1941).

[5] L. F. Fieser, *Rec. trav. chim.*, **69**, 410 (1950).

[6] A. Fredga, *Acta Chem. Scand.*, **4**, 1307 (1950).

[7] C. Djerassi, A. Fredga and B. Sjöberg, ibid., **15**, 417 (1961).

all exhibit negative, plain, rotatory dispersion curves, since in the measured wavelength region (from 265 mμ to 700 mμ) these compounds have no optically active absorption bands.

As is evident from Fig. 4, the monosulfides **I**, II and V show no absorption maxima in the measured wavelength region (from 225 mμ to 340 mμ), in accordance with the observations that dialkyl sulfides exhibit strong absorption bands (log ε ~3) only below 210 mμ.[8] Even these "monothiodisaccharides" may be expected to have optically active absorption bands at a shorter wavelength region when we reflect upon the situation described above as well as the detailed considerations[9,10] of the ultraviolet absorption spectra of various sulfides. However, it is natural that the RD curves of I, II and V are plain in the measured wavelength region.

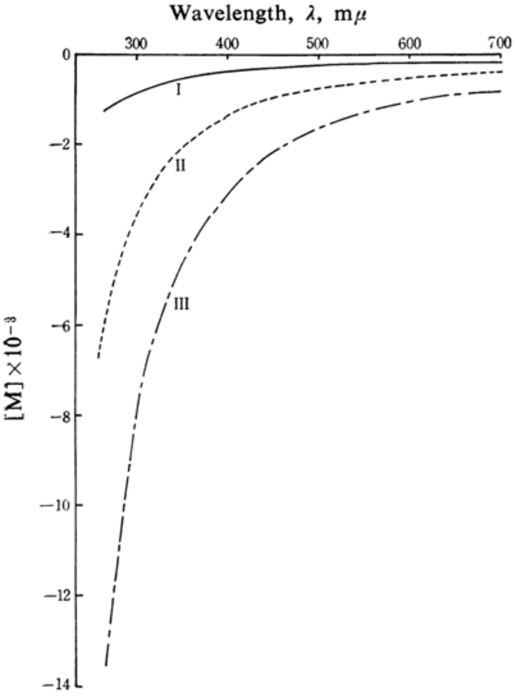

Fig. 2. RD of I—III.

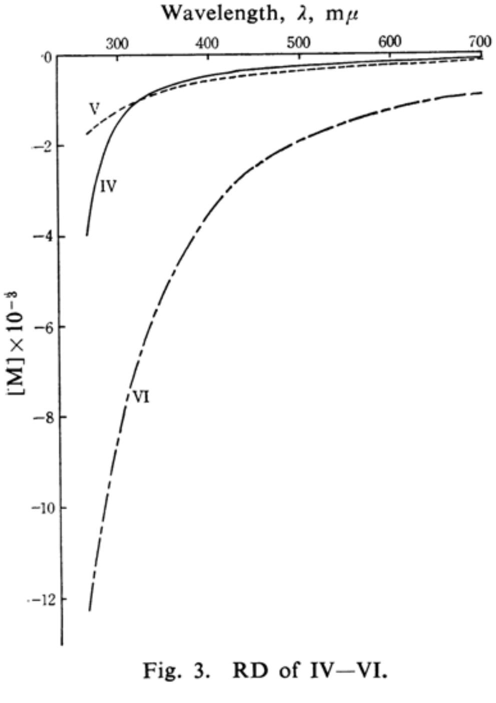

Fig. 3. RD of IV—VI.

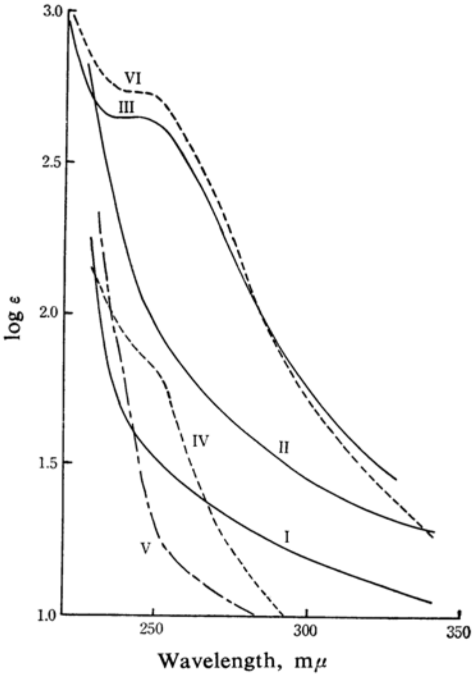

Fig. 4. UV absorption spectra.

Although the absorption due to the $n \rightarrow \pi^*$ transition of the S–S bond varies from 230 mμ to 370 mμ according to the molecular evironment, it has been reported[8,10] that dialkyl disulfides exhibit broad maxima (log ε ~2.6) in the neighborhood of 250 mμ. Compounds III and VI exhibit slight absorption maxima at 235 to 250 mμ, as may be seen in Fig. 4. It is, however, uncertain whether these absorptions are optically active or inactive. Really the dispersion curves of compounds III and VI are plain up to the possible limit of the experiment as compared with the RD curves

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[8] S. Ishida, *J. Chem. Soc. Japan* (*Nippon Kwagaku Kwaishi*), **64**, 177, 179, 382 (1943); See also N. Kharasch, "Organic Sulfur Compounds," Vol. I, Pergamon Press, Oxford (1961), p. 51.

[9] H. H. Jaffé and Milton Orchin, "Theory and Applications of Ultraviolet Spectroscopy," John Wiley & Sons, Inc., New York (1962), p. 474.

[10] G. Bergson. G. Claeson and L. Schotte, *Acta Chem. Scand.*, **16**, 1159 (1962).

of the other compounds, but they are very steep and their terminals closely approach the first extremes of the possible Cotton effects associated with the absorption bands of the disulfides.

The fact that all the RD curves (I—VI) are negative in sign may be due to the β-configuration of the C_1 of the β-D-glucopyranosides. The negative rotation of compound II is distinctly greater in value than that of compound I, probably because the optically active absorption is deeper in the former than in the latter, for its acetoxyl group has a larger polarizability than the hydroxyl group.

The following two examples will illustrate the noticeable effect of the sulfur atom in comparison with the oxygen atom on optical rotation. As may be seen in Fig. 3, the RD curve (IV) is plain; however, its absorption curve shows a shoulder near 250 $m\mu$ (Fig. 4, IV), quite in harmony with the fact that heterocyclic sulfur compounds usually show bathochromic shifts in comparison with simple sulfides.[8] The negative RD curve (Fig. 3, IV) also descends steeply toward the absoption region, and its terminal nearly approaches the extreme of the shoulder. In this respect the thiolevoglucosan (compound IV) is distinguished from other simple sulfides. It may be stated positively that this "heterocyclic" sulfur atom contributes a strong negative rotation to thiolevoglucosan, as is evident from a comparison with levoglucosan, its corresponding oxygen compound (1, 6-anhydro-2, 3, 4-triacetyl-β-D-glucopyranose) :

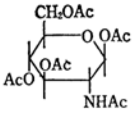
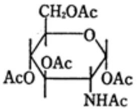
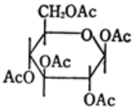
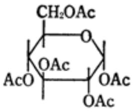
	$[\alpha]_D$	$[M]_D$
Thiolevoglucosan triacetate	−65.9°	−201°
Levoglucosan triacetate	−45.5°[11]	−131°

Next compound V (β, β-thiotrehalose octaacetate) was compared with its corresponding oxygen compound, β, β-trehalose octaacetate :

	$[\alpha]_D$	$[M]_D$
β, β-Thiotrehalose octaacetate	−32.6°	−227°
β, β-Trehalose octaacetate	−18.4°[12]	−125°

The negative value of the molecular rotation of the former (V) $[M]_D = -227°$ is far greater than that of the latter, $[M]_D = -125°$. This fact indicates that the sulfur atom of the C_1-β-configuration contributes to a greater negative rotation, as can be expected from the bathochromic shift of the C_1–S–C_1 group.

TABLE I. THE OPTICAL SUPERPOSITION OF PENTAACETATES OF GLUCOSE AND GLUCOSAMINE

		$[\alpha]_D^{20}$	$[M]_D$	
	(β)	+ 1.2°	+ 4.7= $-A+B$	$A=180$ $B=184$
	(α)	+ 93.5°	+364= $A+B$	
	(β)	+ 3.8°	+ 15= $A+B'$	$A=191$ $B'=206$
	(α)	+101.6°	+396= $A+B'$	

One may get a glimpse into the effect of the acetamido group-$NHCOCH_3$ from a comparison of the glucosamine derivative (II) with the glucose derivative (V). Their configurations differ from each other only in C_2.

From Figs. 2 and 3 it is evident that the former compound shows a far stronger RD curve of a negative sign. This fact can be interpreted as follows:

In the first place, the values of A and B of the pentaacetates of glucose and glucosamine must be taken into consideration; they are given by Hudson's rule of optical superposition.[13]

As may be seen in Table I, the values of B and B' are both positive in sign, and the B' value of glucose pentaacetate is distinctly larger than the B value of glucosamine pentaacetate. This fact indicates that the partial rotation of the group C_2-NHAc is lower than that of C_2-OAc. In a similar way, the B value of compound II is found, by applying Hudson's rule, to be smaller than that of compound V, implying that here also C_2-NHAc is lower than C_2-OAc in partial rotatory power. Thus, it is reasonable that compound II exhibits a stronger negative RD curve.

Dispersions Constants

It is to be expected that the dispersion data can be expressed by a single-term Drude equation, since the dispersions exhibit only plain curves.

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[11] C. Tanret, *Compt. rend.*, **119**, 158 (1894); P. Karrer and A. P. Smirnoff, *Helv. Chim. Acta*, **4**, 819 (1921).

[12] C. M. McClosky, R. E. Pyle and G. H. Coleman, *J. Am. Chem. Soc.*, **66**, 349 (1944); "Advances in Carbohydrate Chemistry," Vol. VI, Acad. Press, New York (1951), p. 75.

[13] C. S. Hudson and J. K. Dale, *J. Am. Chem. Soc.*, **38**, 1433 (1916).

$$[M]=\frac{R}{\lambda^2-\lambda_0{}^2}$$

Table II shows the dispersion constants obtained by the usual method of calculation from the dispersion data.

TABLE II. DISPERSION CONSTANTS

Compound	R	$\lambda_0{}^2$
I	− 56.95	0.151^2
II	−157.26	0.212^2
III	−341.00	0.220^2
IV	− 59.38	0.201^2
V	− 75.43	0.196^2
VI	−380.40	0.218^2

As may be seen in Table II, all the values of λ_0 except that of I are reasonable, representing the most probable, optically active absorption maxima. The dispersion data of III and VI in particular are precisely expressed with the single-term Drude equation, and the relations between λ^2 and $1/[M]$ become quite rectilinear (Fig. 5). Moreover, it is noticeable that the factors of the rotational strength, R, are especially high in these compounds. This fact suggests that the their ultraviolet absorptions at 235—250 mμ make so predominant contributions to the optical activity that the minor residual rotations due to other asymmetric centers may practically be ignored.

On the other hand, the dispersion data of compounds I, II, IV and V can not be so precisely expressed by the single-term equation, for the differences between the observed and the calculated values sometimes rise to five per cent, and the relations between λ^2 and $1/[M]$ deviate more or less from straight lines, rather drawing slightly convex curves. These facts suggest that the more hypsochromic C_1–S–C_1 group contributes relatively little to the optical rotation as compared with the disulfide group. Moreover, the residual partial rotation may make a considerable contribution. To elucidate this problem, however, further detailed inquiries should be made in this shorter wavelength region.

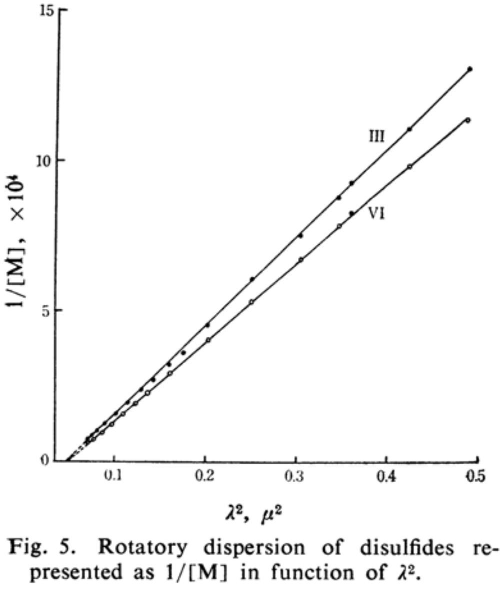

Fig. 5. Rotatory dispersion of disulfides represented as $1/[M]$ in function of λ^2.

Experimental

The rotatory dispersion was measured with a Rudolph spectropolarimeter over the wavelength region from 265 to 700 mμ. The ultraviolet absorption was measured in the same solvent as with RD measurements made with a self-recording spectrophotometer of the Hitachi EPU-II type.

Bis(2-acetamido-2-deoxy-β-D-glucopyranosyl)sulfide (Compound I).[14] — Colorless powder, m. p. 219—220°C. $[\alpha]_{\mathrm{D}}^{16}=-36.7°$ (c 1.0, H_2O).[14] The RD was measured at 22°C in water (c 0.3064). $[\alpha]_{700}^{22}$ −32.6°, $[\alpha]_{589}$ −42.4°, $[\alpha]_{265}$ −277°.

Bis(2-acetamido-2-deoxy-3,4,6-tri-O-acetyl-β-D-glucopyranosyl)sulfide (Compound II).[14]—Needles, m. p. 314—316°C (decomp.). $[\alpha]_{\mathrm{D}}^{16}=-146.4°$ (c 0.8, $CHCl_3$).[14] The RD was measured at 20.6°C in chloroform. $[\alpha]_{700}^{20.6}$ −52.8°, $[\alpha]_{589}$ −74.5°, $[\alpha]_{260}$ −973°.

Bis(2-acetamido-2-deoxy-β-D-glucopyranosyl)disulfide (Compound III).[14]—Fine crystals, m. p. 212—213°C. $[\alpha]_{\mathrm{D}}=-223°$ (c 0.90, H_2O).[14] The RD was measured at 22°C in water (c 0.2293). $[\alpha]_{700}^{22}$ −161°, $[\alpha]_{589}$ −243°, $[\alpha]_{270}$ −2843°.

1,6-Anhydro-1,6-sulfide-2,3,4-tri-O-accetyl-β-D-glucopyranose (Compound IV).[15]—Colorless crystals, m. p. 93—94°C. $[\alpha]_{\mathrm{D}}^{23}=-25.2°$ (c 1.1, $CHCl_3$).[15] The RD was measured at 17.3°C in tetrahydrofuran (c 0.2883). $[\alpha]_{700}^{17.3}$ −46.5°, $[\alpha]_{589}$ −65.9°, $[\alpha]_{265}$ −1297°.

Bis(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)sulfide (Compound V).[16]—Colorless crystals, m. p. 175—176°C. $[\alpha]_{\mathrm{D}}^{18}=-38.0°$ (c 1.0, $CHCl_3$).[16] The RD was measured at 17.3°C in tetrahydrofuran (c 0.3586). $[\alpha]_{700}^{17.3}$ −27.3°, $[\alpha]_{589}$ −32.6°, $[\alpha]_{265}$ −248°.

Bis(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)disulfide (Compound VI).[17] — Colorless crystals, m. p. 143—144°C. $[\alpha]_{\mathrm{D}}=-160°$ (c 6.0, $CHCl_3$).[17] The RD was measured at 17.3°C in tetrahydrofuran (c 0.3875). $[\alpha]_{700}^{17.3}$ −122°, $[\alpha]_{589}$ −173°, $[\alpha]_{265}$ −1679°.

Summary

Measurements have been made ot the rotatory dispersions (265 to 700 mμ) and ultraviolet absorptions (225 to 340 mμ) of various thiosugars, namely, there monothiodisaccharides (I, II, V), two dithio disaccharides (III, VI),

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[14] M. Akagi, S. Tejima and M. Haga, *Chem. & Pharm. Bull.*, **9**, 360 (1961).

[15] M. Akagi, S. Tejima and M. Haga, ibid., **11**, 58 (1963).

[16] M. Akagi, S. Tejima and M. Haga, ibid., **11**, 1081 (1963).

[17] W. Schneider and A. Bonsa, *Ber.*, **64**, 1321 (1931).

and thiolevoglucosan (IV), in order to investigate the effect of sulfur atoms on optical activity.

The monosulfides, I, II and V, exhibit no absorption maxima and plain, negative RD curves. The disulfides, III and VI, exhibit absorption maxima at 235 to 250 mμ. Their negative RD curves are, accordingly, very steep, approaching the first extremes of the possible Cotton effect.

Thiolevoglucosan (IV), containing a " heterocyclic " sulfur atom, shows more bathochromic shifts than simple sulfides, and a stronger optical activity than levoglucosan. The strong rotatory contribution of the sulfur atom is also observed in acetylated thiotrehalose (V).

In thiosugars the acetamido group also shows a smaller rotatory contribution than the acetoxyl group.

The dispersion data have been analyzed by means of the Drude equation, and the physical significance of the dispersion constants has been discussed.

Department of Chemistry
Tokyo College of Science
Kagurazaka, Tokyo
(Y. T. & K. T.)

Faculty of Pharmaceutical Sciences
School of Medicine
Hokkaido University
Sapporo (M. A. & S. T.)