Stereochemistry of organic compounds(41) : On the optical contributions and solvent effects of sulfur atoms at C1 of glycopyranosides

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Stereochemistry of Organic Compounds XLI[1)]
On the Optical Contributions and Solvent Effects of Sulfur Atoms at C_1 of Glycopyranosides

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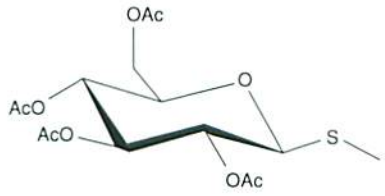
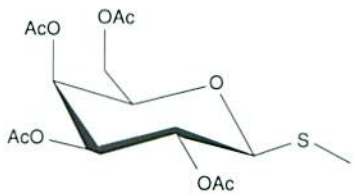
In our earlier studies[1-2)], we reported on the optical contributions in the thioglycosides having bulky chromophores such as nitrophenyl groups at S atoms. In cases like these, since nitrophenyl groups dominated the optical contribution, the effects of the S atoms were not observed clearly, whereas the C_1-thiol of the D-glucopyranoside derivative[3)] without the bulky chromophore showed the negative Cotton effect at 274 nm. It has been suggested that the Cotton effect is based on the S atom due to the $n \rightarrow \sigma^*$ transition. Therefore, the S atom dominates the optical contribution.

This paper will discuss in detail these results. In order to evaluate these effects, the thioglycosides containing methyl (Compounds **I**～**II**) and cyanomethyl (Compounds **III**～**IV**) were employed. For the purpose of comparison, measurements of pentaacetylglucopyranoside (Compound **V**)[3)] were newly carried out in various solvents. The following compounds were examined, and these structures are illustrated in Figure 1.

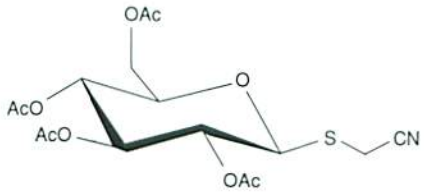
Methyl 2,3,4,6-tetra-*O*-acetyl-β-D-



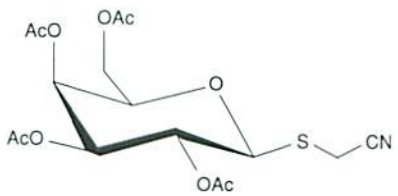
I



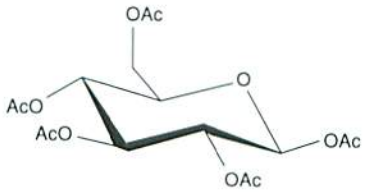
II



III



IV



V

Figure 1 Compounds **I**～**V** examined

thioglucopyranoside (Compound **I**),

Methyl 2,3,4,6-tetra-*O*-acetyl-β-D-thiogalactopyranoside (Compound **II**),

Cyanomethyl 2,3,4,6-tetra-*O*-acetyl-β-D-thioglucopyranoside (Compound **III**),

Cyanomethyl 2,3,4,6-tetra-*O*-acetyl-β-D-thiogalactopyranoside (Compound **IV**),

1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranoside (Compound **V**).

For this purpose, the optical contributions were investigated by means of rotatory dispersion (RD), circular dichroism (CD), and ultraviolet absorption (UV) spectra, using acetonitrile (CH_3CN), ethanol (EtOH) and water (H_2O) as polar solvents and dioxane and tetrahydrofuran (THF) as non-polar solvents. In addition, the proton nuclear magnetic resonance (^{1}H-NMR) spectra were measured in dimethyl sulfoxide-d_6 (DMSO-d_6).

Results and Discussion

The RD, CD and UV curves of Compounds **I**~**IV** are shown in Figures 2 ~ 5 in dioxane, tetrahydrofuran, acetonitrile, ethanol and water, respectively. The data of RD, CD and UV are summarized in Table 1. However, Compounds **I** and **II** did not dissolve in water, so there is no data for them in relation to water in Table 1. The specific rotations $[\alpha]_{589}^{n}$ using Xe-lamp of Compounds **I**~**IV** are shown in Table 2.

Moreover, pentaacetyl-β-D-glucopyranoside (Compound **V**) will be employed for comparison, and the data of Compound **V** in dioxane and ethanol appears in Table 1.

As seen in Figure 2, the RD curves of Compound **I** contribute to the negative over 220 nm in all solvents. Even in the short wavelength region, the RD contributes

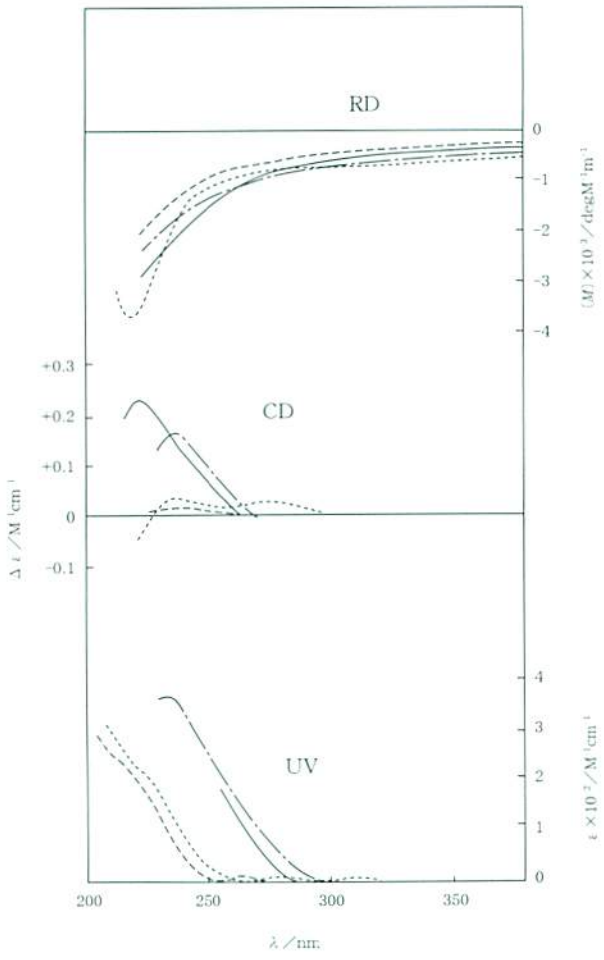


Figure 2. RD, CD and UV of **I** (—— in dioxane, – – – in THF, – – – – in CH_3CN, ····· in EtOH).

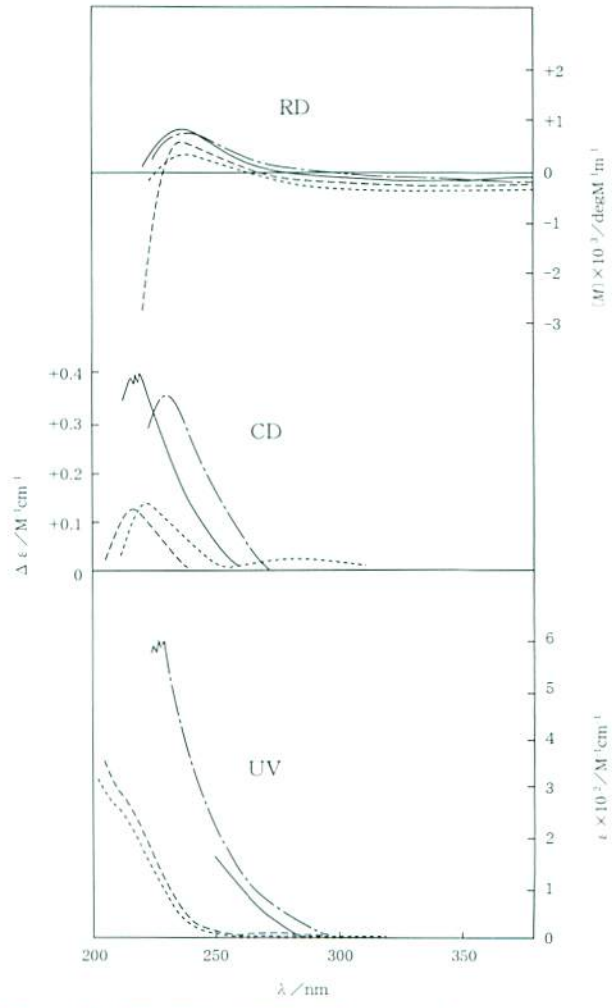


Figure 3. RD, CD and UV of **II** (—— in dioxane, – – – in THF, – – – – in CH_3CN, ····· in EtOH).

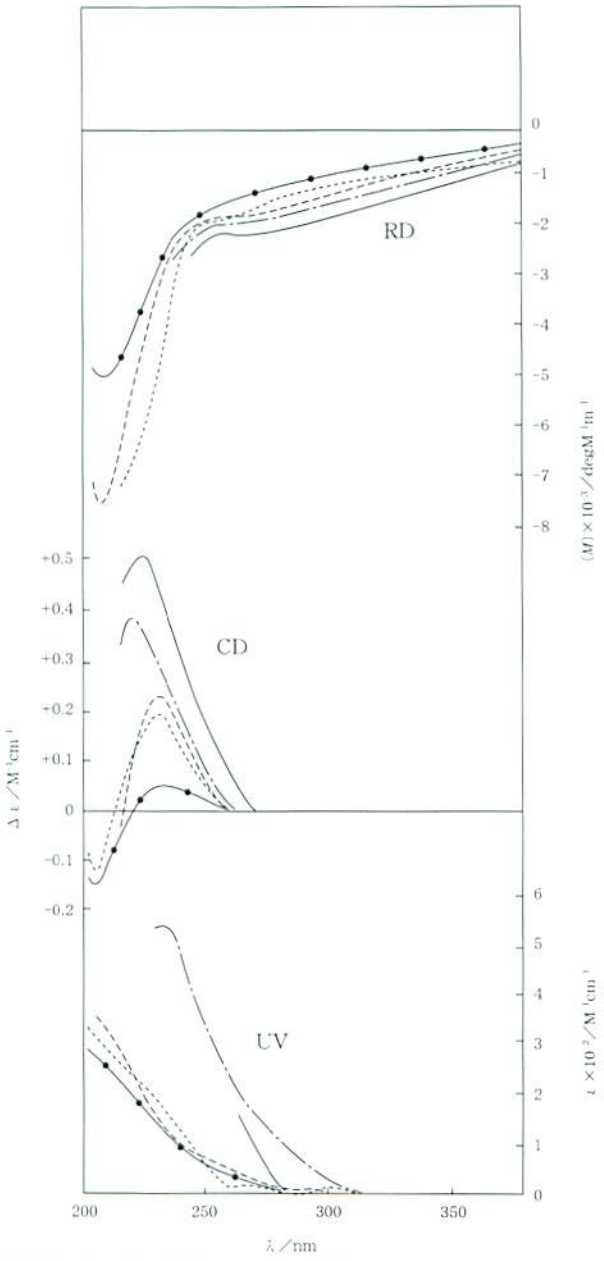


Figure 4. RD, CD and UV of **III** (—— in dioxane, – – – in THF, – · – · – in CH_3CN, ····· in EtOH, —•—•— in H_2O).

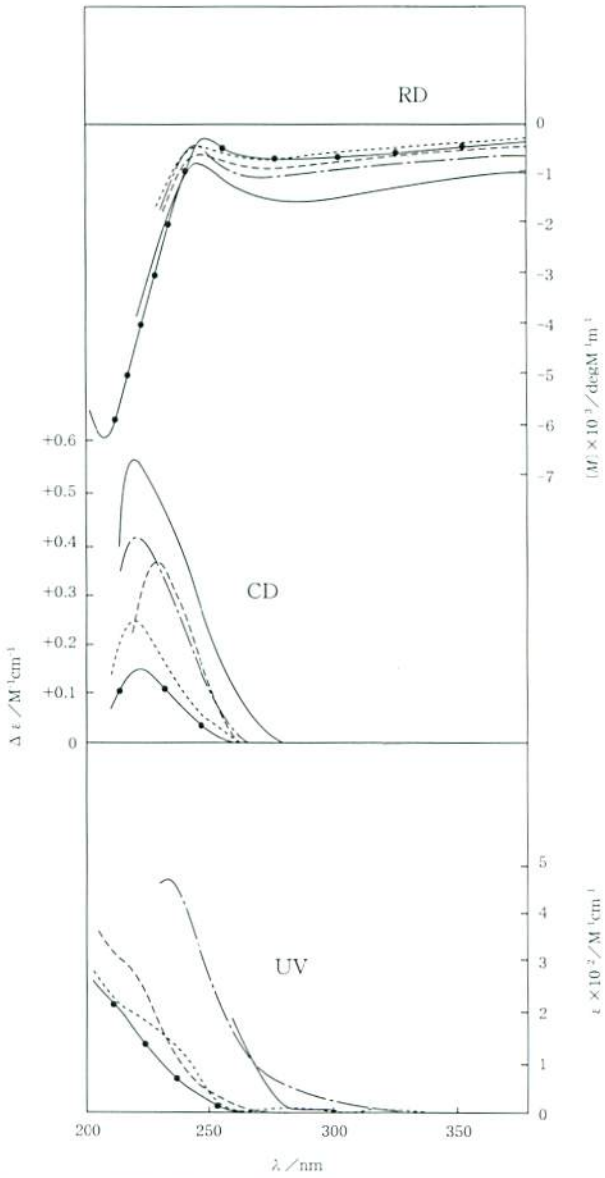


Figure 5. RD, CD and UV of **IV** (—— in dioxane, – – – in THF, – · – · – in CH_3CN, ····· in EtOH, —•—•— in H_2O).

Table 1 Peak Data of CD, RD and UV spectra

Compound	spectrum	solvent	λ_{max}/nm($\Delta\varepsilon$/M^{-1}cm^{-1};[M]/deg M^{-1}m^{-1};ε/M^{-1}cm^{-1})
I	CD	dioxane	221(+0.218)
		THF	234(+0.172)
		CH_3CN	232(+0.0252)
		EtOH	280(+0.0260), 232(+0.339)
	RD	dioxane	—
		THF	—
		CH_3CN	—
		EtOH	221(−3550)
	UV	dioxane	292(2.98)

		THF	228(386)
		CH_3CN	264(10.6), 224-209(207-304, shoulder)
		EtOH	303(4.01), 271(10.6), 229-209(173-308, shoulder)
II	CD	dioxane	220(+0.404)
		THF	230(+0.368)
		CH_3CN	217(+0.123)
		EtOH	283(+0.0222), 222(+0.139)
	RD	dioxane	234(+1020)
		THF	234(+984)
		CH_3CN	234(+699)
		EtOH	236(+465)
	UV	dioxane	298(1.92)
		THF	228(610)
		CH_3CN	292-262(3.38-6.75, shoulder), 228-210(115-314, shoulder)
		EtOH	303(5.00), 271(6.11), 221-208(171-283, shoulder)
III	CD	dioxane	223(+0.504)
		THF	220(+0.387)
		CH_3CN	230(+0.227)
		EtOH	231(+0.197), 205(-0.128)
		H_2O	314(4.17), 229(+0.0464), 204(-0.151)
	RD	dioxane	258(−2190), 254(−2150)
		THF	262(−1950, I)
		CH_3CN	261(−1730, I), 207(−7710)
		EtOH	256(−1720, I)
		H_2O	209(−5120)
	UV	dioxane	294(8.13)
		THF	233(561)
		CH_3CN	224-210(203-232, shoulder)
		EtOH	297(8.92), 268(21.8), 235-209(165-285, shoulder)
		H_2O	229-210(127-259, shoulder)
IV	CD	dioxane	221(+0.580)
		THF	220(+0.422)
		CH_3CN	228(+0.358)
		EtOH	220(+0.241)
		H_2O	221(+0.145)
	RD	dioxane	276(−1500), 245(−697)
		THF	274(−967), 245(−427)
		CH_3CN	272(−737), 245(−389)
		EtOH	265(−617), 245(−431)
		H_2O	275(−669), 248(−258), 208(−6290)
	UV	dioxane	292(7.30)
		THF	232(478)
		CH_3CN	229-209(151-329, shoulder)
		EtOH	324(6.52), 294-259(5.04-8.59, shoulder), 235-210(159-236, shoulder)
		H_2O	319(3.95), 226-210(122-231, shoulder)
V	CD	dioxane	222(+0.566)
		EtOH	220(+0.213)
	RD	dioxane	236(+933)
		EtOH	238(+554)
	UV	dioxane	297-261(6.96-11.8, shoulder)
		EtOH	295-264(3.42-6.84, shoulder), 210(250)

Table 2 $[\alpha]_{589}^{25}$ (deg, $l=$ 1cm, $c\fallingdotseq 0.1$ g·ml^{-1}) in four Solvents by Xe-lamp

Compound	dioxane	THF	CH_3CN	EtOH
I	−43.9	−50.0	−42.1	−51.6
II	−28.8	−17.5	−38.1	−32.3
III	−84.4	−76.7	−75.4	−101
IV	−77.9	−55.6	−55.8	−67.5

to the negative, and not at all to the positive, due to the effect of the C_1-S-CH_3 group. And, because of the strong negative background rotation, the positive peaks of the Cotton effects are not visible around 230-250 nm. In the CD curves of Compound **I**, the CD maxima contribute to the blue-shift in non-polar solvents, and in the case of non-polar solvents, the CD values and the blue-shift are larger in dioxane than in THF. The CD maxima in polar solvents are only 1/5 to 1/8 in value compared to the CD maxima in non-polar solvents.

This shows that the RD is slightly affected by the solvents, but the CD values are more strongly affected by solvents. Normally the CD is not affected by solvents, while the RD is affected by solvents. In this case, the results are opposite because of the transition property.

As evident in Figure 3, the RD curves of Compound **II** contribute to the change from negative to positive from the short wavelength to the long wavelength, and show the peak in the 234-236 nm range. This result is due to the weakening effect of the C_1-S-CH_3 group, because Compound **II** has a positive background due to the galactose. Therefore, it is clear that those peaks are the positive Cotton effects. From the fact that the contribution to the CD of Compound **II** shows a tendency equal to the case of **I**, we can conclude that these Cotton effects are caused by the transition of the C_1-S-methyl. Characteristic of Compounds **I** and **II** in ethanol, the CD curves show the small positive Cotton effects around 280 nm due to the transition by the Sulfur atom. Typically, in the case of β-D-glucose and β-D-galactose, the former $[\alpha]_D^{25}$ is +102° and the latter $[\alpha]_D^{25}$ is+151° in water. Also in the case of pentaacetyl β-D-glucose and β-D-galactose, the former $[\alpha]_D^{25}$ is +3.8° and the latter $[\alpha]_D^{25}$ is +25° in chloroform. Both facts show that galactose having the C_4-axial configuration totally contributes to the positive optical rotation. C_1-S-derivatives, such as Compounds **I** and **II**, show the above galactose effects.

Compounds **III** and **IV**, respectively, changed the methyl group of Compounds **I** and **II** to the cyanomethyl group. That is to say, the effect of the CN group of the electron-withdrawal in the methyl group was examined. Let's compare Compound **III** to Compound **I**. As shown in Table 2 and Figure 4, in the case of RD curves of Compound **III**, the introduction of a CN group contributes negative rotation and shows weak peaks of positive Cotton effects in all solvents. This result is different from the hidden positives peaks of Compound **I**. The CD curves of Compound **III** are more than twice the size of Compound **I**, which supports the result of the RD. The same differences in the results for Compounds **III** and **I**

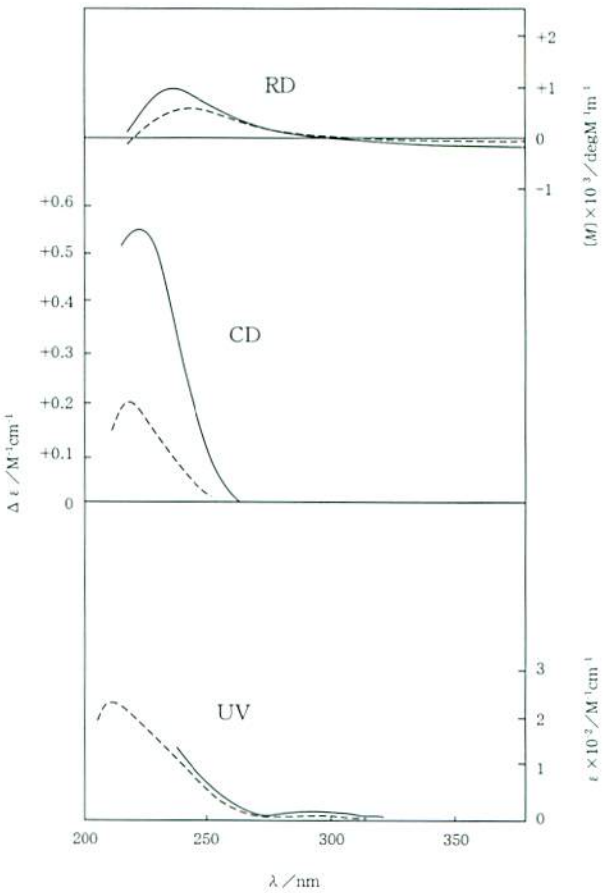


Figure 6. RD, CD and UV of **V** (—— in dioxane, ····· in EtOH).

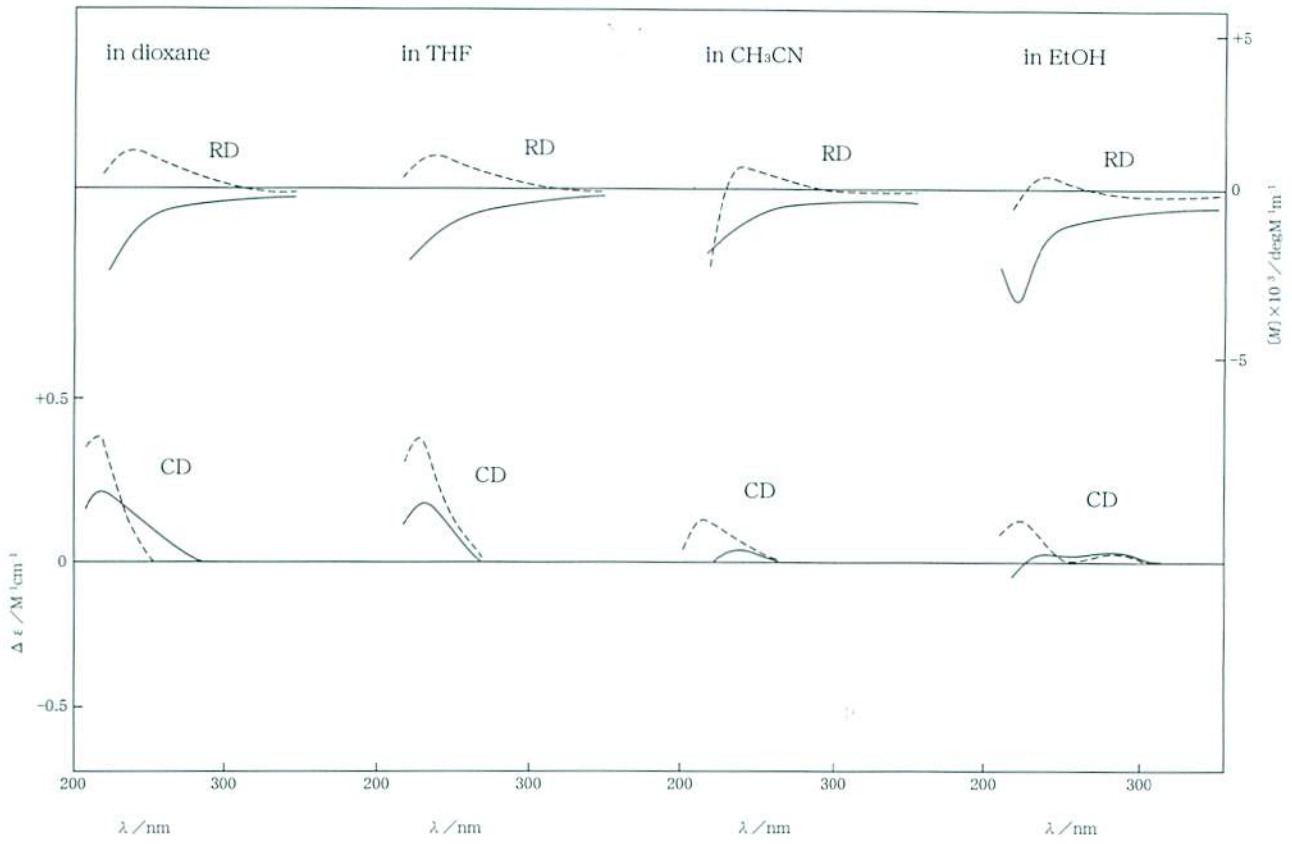


Figure 7. RD and CD of **I** and **II** in all solvents (—— **I**, ····· **II**).

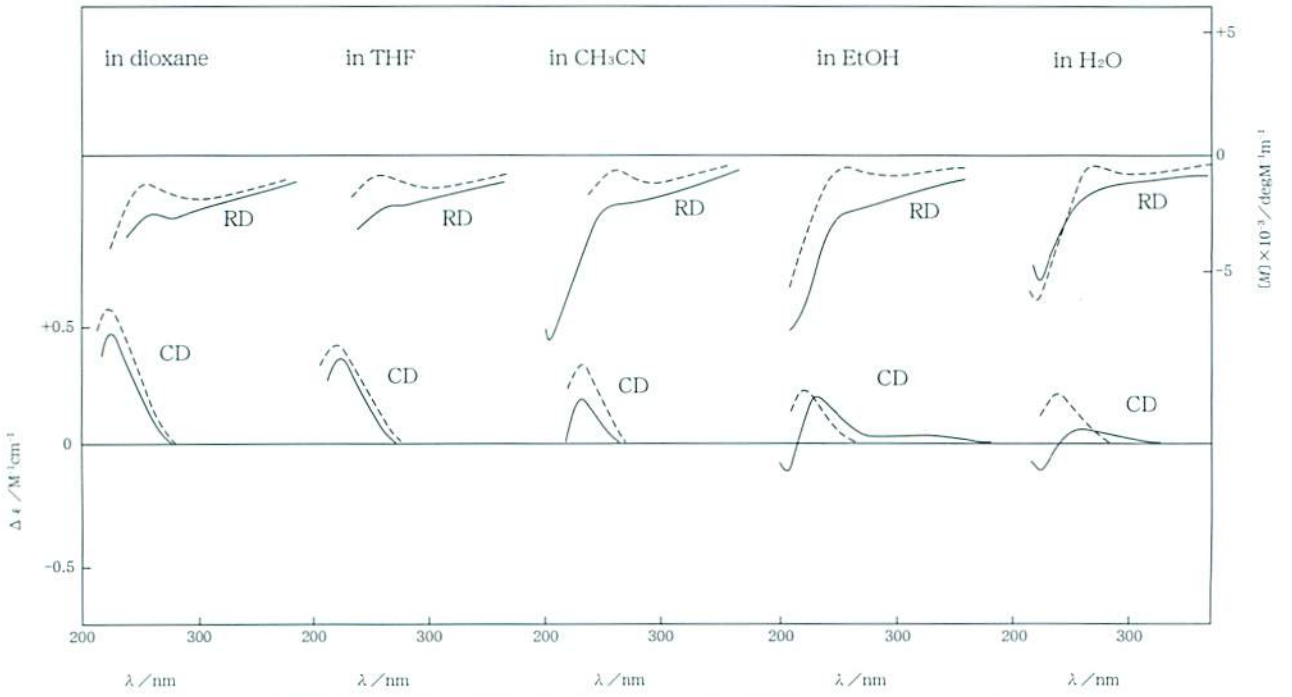
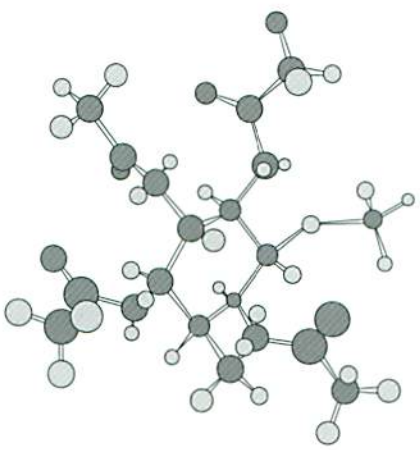
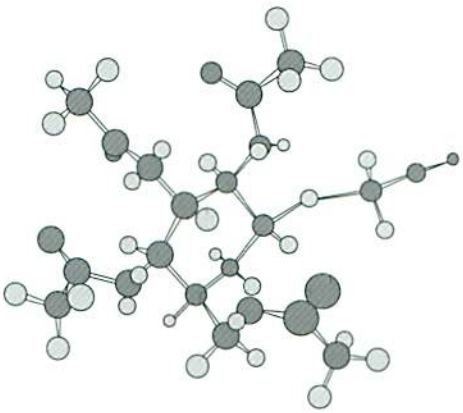


Figure 8. RD and CD of **III** and **IV** in all solvents (—— **III**, ····· **IV**).

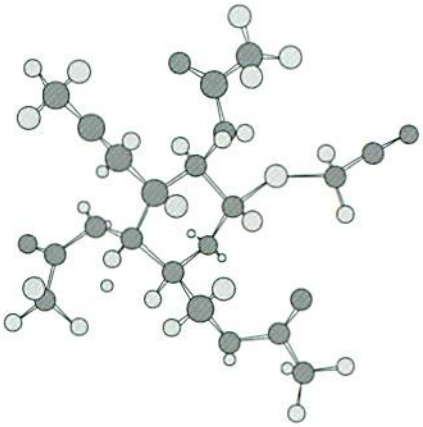


I

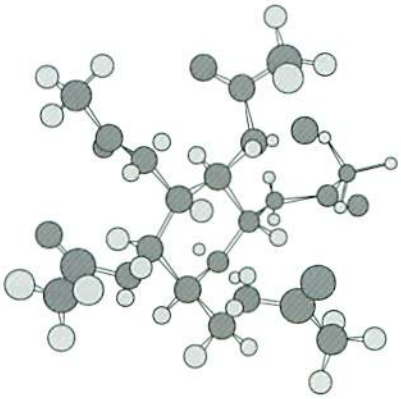
II



III



IV



V

Figure 9. Energy minimized molecular models of I~V.

exist when we compare the results of Compounds **IV** and **II**. This leads us to conclude that the cyanomethyl group in Compounds **III** and **IV** are very effective in detecting the Cotton effects of RD curves.

Figure 6 shows the RD, CD and UV of Compound **V** in dioxane and ethanol. Because Compound **V** does not have any S atoms, the absorption bands around 280 nm were not observed. But the RD and CD were influenced by polar solvents, so small inflection points were visible. This tendency also occurs in Compounds **I**～**IV**.

In Figures 7 and 8, the isomers **I** and **II**, **III** and **IV**, respectively, are compared through RD and CD in all solvents. This data shows that galactose derivatives **II** and **IV** contribute positive rotation in RD and large positive extremes in CD. Therefore the transition moments of **II** and **IV** are large.

The CD positive extreme of all compounds registered 220～232 nm in spite of having different values and shifting wavelengths. This indicates the same conformation near the optically active absorption bands.

In order to investigate the conformation of Compounds **I**～**V**, geometry optimizations were carried out using MM2 calculations. Figure 9 shows the molecular structures created by the calculations using minimized energy. It is possible that all structures in Figure 9 propose the preferable conformation. From Figure 9, no clear differences in the structure arrangements of Compounds **I**～**V** can be seen. From these, in the C_1 thio derivatives, galactose, which has C_4-axial OAc groups, contributes to the positive compared to the glucose.

From these results, we can conclude that the presence of C_4-axial OAc groups, which is a galactose, contributes to a greater positive than just the presence of glucose. In the case of the RD curves of the glucoses, the peaks of positive Cotton effects are not visible, but in the case of the galactoses, these peaks are visible in all solvents. In other words, the information from the RD characteristics is useful for the speculation of the conformation.

Experimental

Measurements. The RD and CD were measured in dioxane, tetrahydrofuran, acetonitrile, ethanol and water at 25-27°C, in the wavelength region from 200 to 600 nm with a JASCO/UV-5 type optical rotatory dispersion recorder. The UV spectra were measured under the same conditions as the RD and CD measurements by a SHIMADZU UV-2550 PC Spectrophotometer. The ^{1}H-NMR spectra were measured on a Hitachi Model R-24B at room temperature in DMSO-d_6 as a solvent. Chemical shifts are in ppm (δ) from $SiMe_4$ as the internal standard and J-values are given in Hz.

Materials. Compounds **I**～**IV** were obtained from commercial suppliers and were used without further purification. Compound **V** was prepared according to the method as literature[4].

Methyl 2,3,4,6-tetra-*O*-acetyl-β-D-thioglucopyranoside (Compound **I**). mp 92°C ; ^{1}H-NMR δ=1.95 (s, 3H), 1.98 (s, 3H), 2.05 (s, 6H), 2.10 (s, 3H), 3.84-4.25 (m, 3H), 4.62-5.52 (m, 4H).

Methyl 2,3,4,6-tetra-*O*-acetyl-β-D-thiogalactopyranoside (Compound **II**). mp 105°C ; ^{1}H-NMR δ= 1.93 (s, 3H), 2.00 (s, 3H), 2.02 (s, 3H), 2.10 (s, 6H), 3.64-4.42 (m, 3H), 4.62-5.38 (m, 4H).

Cyanomethyl 2,3,4,6-tetra-*O*-acetyl-β-D-thioglucopyranoside (Compound **III**). mp 99°C ; ^{1}H-NMR δ=1.94 (s, 3H), 1.98 (s, 3H), 2.00 (s, 6H), 3.78 (s, 2H), 3.94-4.24 (m, 3H), 4.68-5.52 (m, 4H).

Cyanomethyl 2,3,4,6-tetra-*O*-acetyl-β-D-thiogalactopyranoside (Compound **IV**). mp 101°C ; ^{1}H-NMR δ=1.92 (s, 3H), 2.00 (s, 3H), 2.04 (s, 3H), 2.13 (s, 3H), 3.81 (s, 2H), 3.93-4.38 (m, 3H), 4.92-5.42 (m, 4H).

1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranoside (Compound **V**). mp 132°C ; ^{1}H-NMR δ=1.93 (s, 3H), 1.98 (s, 9H), 2.06 (s, 3H), 3.94-4.34 (m, 3H), 4.74-5.14 (m, 2H), 5.38 (d, J=9.2 Hz, 1H), 5.96 (d, J=8.4 Hz, 1H).

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