Molecular Rotations of Glucides in Relation to their Structures. I. The Absolute Configuration of γ-Lactones

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Introduction

About the problem of the absolute configuration of an optically active molecule, several studies were undertaken from the standpoint of X-ray analysis of a substance[1], or by calculation of the signs of optical rotatory powers of appropriate molecules[2].

Referring to the hypothesis that the sign of the optical rotatory power of a molecule under investigation is determined by Kirkwood's term $g^{(0)}$, Wood, Fickett and Kirkwood presumed the absolute configuration of the enantiomorph of 2, 3-epoxybutane[2]. They first divided the molecule of 2, 3-epoxybutane into the following unit groups; a three-membered ring with attached hydrogen atoms and two methyl groups which combine with the ring. Next, by using experimental data, they calculated the partial rotations caused by dynamical coupling effects between these unit groups. However, for lack of experimental data in relation to the three-membered ring, they could not calculate the partial rotations caused by the dynamical coupling effects with which the three-membered ring is concerned. Therefore, they resorted to a quasi-empirical evaluation of them, by using the experimental datum of the optical rotatory power of configurationally related 1, 2-epoxypropane. Formerly, Kirkwood proposed a convenient method of calculation of the partial rotation caused by the dynamical coupling effect of OH group, in calculating the optical rotatory power of secondary butyl alcohol[3],[*1]. To evaluate the optical rotatory powers of polypeptides of alanine, Murakami used a concept of bond-interaction in place of the idea of group-interaction and proposed a method of calculation of the partial rotation caused by the dynamical coupling effect of C=O bond. He demonstrated also that the observed values of optical rotatory power were proportional to the values calculated by Kirkwood's polarizability theory[4]. It was explained that the contribution of the one-electron effect[5] is much smaller than that of the dynamical coupling effect[6].

The author presumed the absolute configuration of γ lactones of a five-membered ring, by using a method[*2] which was devised by adopting the conception of Freudenberg's Verschiebungssatz[7] on the basis of Kirkwood's group-interaction method[3] and Murakami's bond-interaction method[4]. In order to avoid the difficulty caused by the impossibility of calculation of the terms with which the five-membered ring is concerned, a new method, different from Kirkwood's, was proposed[*3].

Theoretical Formulae

The molecular rotation of plane polarized light of wave-length λ by an optically active substance is given as follows[3],

$$[\mathrm{M}]=\frac{288\pi^2 N}{\lambda^2}\cdot\frac{n^2+2}{3}g. \qquad (1)$$

where N is Avogadro's number and n is the refractive index of the medium (solution or pure liquid). If every one of the substituent groups of the molecule—strictly speaking, unit groups made by division of the molecule — has its own optical axis of cylindrical symmetry,

$$g \doteqdot g^{(0)}=\frac{1}{6}\sum_{i>k=1}^{N}\alpha_i\alpha_k\beta_i\beta_k G_{ik}\vec{R}_{ik}(\vec{b}_i\times\vec{b}_k)$$[*4]

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1) A. F. Peerdeman, A. J. van Bommel and J. M. Bijvoet, *Koninkl. Ned. Akad. Wetensckap. Proc.*, B. **54**, 16 (1951).

2) W. W. Wood, W. Fickett and J. G. Kirkwood, *J. Chem. Phys.*, **20**, 561 (1952).

3) J. G. Kirkwood, *J. Chem. Phys.*, **5**, 479 (1937).

[*1] Ref. "Molecular Model and Data Used" in this article.

4) H. Murakami, This Bulletin, **27**, 246 (1954), **28**, 583 (1955).

In these papers, the author presumed that the proportional constant depends upon the quantitative ratio between various isomers in the equilibrium state.

5) W. J. Kauzmann, J. E. Walter and H. Eyring, *Chem. Rev.*, **26**, 339 (1940).

6) W. Kuhn, *Z. Electrochem.*, **56**, 506 (1952).

[*2] The idea of this method had already been demonstrated in the previous paper, (S. Yamana, This Bulletin, **23**, 259 (1950)).

7) K. Freudenberg und W. Kuhn, *Ber.*, **64**, 726 (1931).

[*3] Ref. "Method Proposed" in this paper.

[*4] The error of signs in reference (3) is corrected in reference 2).

$$G_{ik}=\frac{1}{R^3_{ik}}\left[\vec{\boldsymbol{b}}_i\cdot\vec{\boldsymbol{b}}_k-3\frac{(\vec{\boldsymbol{b}}_i\cdot\vec{\boldsymbol{R}}_{ik})(\vec{\boldsymbol{b}}_k\cdot\vec{\boldsymbol{R}}_{ik})}{R^2_{ik}}\right]$$

$$\vec{\boldsymbol{R}}_{ik}=\vec{\boldsymbol{R}}_k-\vec{\boldsymbol{R}}_i$$

where α_i (mean polarizability of group or bond i) $=(3/4\pi N)\cdot\sum\limits_{s}^{(i)}A_s$, but A_s is atomic refraction; β_i (anisotropy ratio of the polarizability of group or bond i) $=\alpha_{11}^{(i)}-\alpha_{22}^{(i)}/\alpha_i$, but $\alpha_{11}^{(i)}$ and $\alpha_{22}^{(i)}$ are components of α_i parallel and perpendicular to $\vec{\boldsymbol{b}}_i$ and β_i can be calculated from the depolarization-degree $\varDelta$ of light, scattered by vapor; $\vec{\boldsymbol{b}}_i$ (unit vector along the optical symmetry axis of group or bond i) and $\vec{\boldsymbol{R}}_i$ (vector distance from the center of mass of the molecule to the center of mass of group or bond i) are determined from the geometry of the molecule.

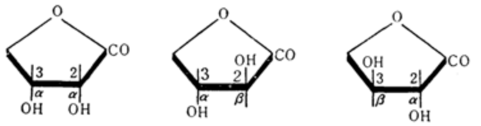
Molecular Model and Data Used

γ-Lactones to which the calculations were applied and their corresponding molecular rotations, are as follows,

Name	Unit Groups	$[M]_D^{20}$(W)	Lit.
D-erythronic γ-lactone	[CO, $(OH)^{2\alpha}$,*5, $(OH)^{3\alpha}$, Ring]*6	-86.5^0	(a)
D-threonic γ-lactone	[CO, $(OH)^{2\beta}$, $(OH)^{3\alpha}$, Ring]	-36.6^0	(b)
L-threonic γ-lactone	[CO, $(OH)^{2\alpha}$, $(OH)^{3\beta}$, Ring]	36.6^0	(b)

Square brackets [ ], written on the right side of these names imply unit groups of the corresponding γ-lactone molecules, and any two members of these unit groups in the same square bracket couple together to produce their own partial molecular rotation. (ref. Fig. 1). Haworth's perspective formulae of these γ-lactones are shown in Fig. 1.

It was concluded that all of four carbon atoms and one oxygen atom of the aldofuranose ring lie on one plane — namely, the γ-lactone ring plane — from the results of investigations measuring the dipole moment[8)] of an aldofuranose molecule and examining its crystal with X ray[9)].



D-Erythronic-γ-lactone D-Threonic-γ-lactone L-Threonic γ-lactone

Fig. 1. Haworth's perspective formulae

In order to simplify the calculations, the values of bond lengths and valency angles were assumed as follows*7,

(1) The lengths of C—C and C—O bonds in the γ-lactone ring are all 1.54Å, that is to say, the γ-lactone ring plane is a regular pentagon and the length of its side is 1.54Å.

(2) C=O bond (its length is 1.24Å)[c)] projects out from C^1-atom*8, in the direction of the extension line from the center of the ring to C^1-atom.

(3) The hydroxyl oxygen atom (represented by O^h) and H atom combine with C atom of the γ-lactone ring and the angle $\angle O^hCH$ (tetrahedral angle = 109°28′) is bisected by the γ-lactone ring plane. The length of C-O^h bond is 1.42 Å*9. The refractive indices of aqueous solutions of three γ-lactones given in Fig. 1, whose concentrations are suitable for measurement of the optical rotatory power, can be considered equal*10.

Concerning the experimental data and the manner of treatment of OH groups and of C=O bond, the following two methods of treatment were employed.

Kirkwood's Treatment[3)].— It is supposed that OH group has its optical axis of cylindrical symmetry directed along its bond to C atom, and the optical center of OH group is located at O atom*11. Values of mean polarizability α and of anisotropy

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*5 $(OH)^{2\alpha}$ means OH group, which combines with 2-position of the ring in α-orientation. (ref. L. F. Fieser, *J. Am. Chem. Soc.*, **72**, 623 (1950)).

*6 Because of the small polarizabilities of H atom and C-H bond, they can be neglected.

a) Ruff, *Ber.*, **32**, 3679 (1899).

b) K. Gätzi and T. Reichstein, *Helv. Chim. Acta.*, **20**, 1298 (1937).

8) H. Hilbert and J. S. Allen, *J. Am. Chem. Soc.*, **54**, 4115 (1932).

9) E. G. Cox and T. H. Goodwin, *J. Chem. Soc.*, **1932**, 1844.

*7 In the calculation of the optical rotatory power by Kirkwood's polarizability theory, a small deviation in atomic distance or in valency angle causes only a small deviation in the calculated value of optical rotatory power. Concerning a concrete example of the magnitude of this deviation, refer to the next paper "Molecular Rotations of Glucides in Relation to their Structures. II."

c) M. Kimura and Y. Kurita, *J. Chem. Soc. Japan*, **72**, 396 (1951).

*8 C^1-atom means the C atom at 1-position of the ring.

*9 The mean value of lengths of C-O bonds in α-D-glucose. (ref. T. R. R. Mc Donald and C. A. Beevers, *Acta Cryst.*, **5**, 654 (1952)).

*10 For determination of optical rotatory power of a sugar-group substance, about 2% aqueous solution is used in general, and the value of n of it is about 1.34.

*11 This manner of treatment was rejected by Gorin, J. Walter and H. Eyring (*J. Chem. Phys.*, **6**, 824 (1938)), because it regards a single OH group as isotropic. The author of this paper, however, thought that this was very convenient and useful for approximate estimation of partial rotation of the OH group, especially when optical rotatory power of such a substance which has many OH groups in its molecule as a sugar was the subject. Besides, for lack of data for C-O and O-H bonds, OH group cannot be divided into its component bonds.

ratio β of OH group are 1.04×10^{-24} (cc)[d] and 0.35[e] respectively.

Murakami's Treatment.[4]—It is supposed that C=O bond has its optical axis of cylindrical symmetry directed along itself. The optical center of C=O bond is located at its center of mass. Value of $\alpha\beta$ of C=O bond is $(19.4-8.0)\times10^{-25}=1.14\times10^{-24}$ (cc)[f].

Method Proposed

Partial molecular rotations of the plane polarized light of wave-length of D line at 20°C, represented by the notation $[\mu]^{20}_{D}$, caused by the dynamical coupling effect between any two members of unit groups in the molecular model of γ-lactone, were calculated by using Eq. (1). Of course, the molecular rotation is the sum of the partial molecular rotations, namely

$$[M]^{20}_{D}=\Sigma[\mu]^{20}_{D}$$

where Σ means the summation over all $[\mu]^{20}_{D}$s possible. Therefore, for the calculated values, the following equation can be obtained.

$$[M]^{20}_{D\mathrm{calcd}}=\Sigma[\mu]^{20}_{D\mathrm{calcd}} \tag{2}$$

where the suffix calcd means the calculated value. For the observed values,

$$[M]^{20}_{D\mathrm{obs}}=\Sigma[\mu]^{20}_{D\mathrm{obs}}{}^{*12} \tag{3}$$

The results of calculation are given in Table I.

TABLE I

$[\mu]^{20}_{D\mathrm{calcd}}\,(3/n^2+2)$, CAUSED BY THE DYNAMICAL COUPLING EFFECT BETWEEN ANY TWO MEMBERS OF UNIT GROUPS (EXCEPT RING), WITH REGARD TO HAWORTH'S PERSPECTIVE FORMULAE

	3β	3α	2β	2α
CO	4.9	−4.9	21.0	−21.0
2α	4.4	0		
2β	0	−4.4		

Note: 2α is an abbreviated symbol of $(OH)^{2\alpha}$, and so on.

If the theory used for the calculation of optical rotatory power is perfect and data which are used in calculation are satisfactory, the calculated value, $[M]^{20}_{D\mathrm{calcd}}$, must be equal to the observed value, $[M]^{20}_{D\mathrm{obs}}$, in sign and magnitude. However, in fact, they are not equal, owing to the imperfectness of the theory, and of assumptions and to the errors of data used. Generally, $[M]^{20}_{D\mathrm{calcd}}$ by Kirkwood's polarizability theory is equal to $[M]^{20}_{D\mathrm{obs}}$ in sign, and the magnitude of the former can be made equal to that of the latter by multiplying by a proportionality-constant[4],[*13]. Therefore,

$$[M]^{20}_{D\mathrm{obs}}=\kappa[M]^{20}_{D\mathrm{calcd}} \tag{4}$$

where κ is always positive. If the orientation of one unit group in a molecular model changes, $[M]^{20}_{D\mathrm{obs}}$ and $[M]^{20}_{D\mathrm{calcd}}$ change to $[M']^{20}_{D\mathrm{obs}}$ and $[M']^{20}_{D\mathrm{calcd}}$ respectively. By the change of the orientation of a unit group, a new molecule appears. For this new molecule,

$$[M']^{20}_{D\mathrm{obs}}=\kappa[M']^{20}_{D\mathrm{calcd}} \tag{5}$$

where $[M']^{20}_{D}$ means the molecular rotation of a new substance. From Eq. (5) minus Eq. (4),

$$[M']^{20}_{D\mathrm{obs}}-[M]^{20}_{D\mathrm{obs}}$$

$$=\kappa([M']^{20}_{D\mathrm{calcd}}-[M]^{20}_{D\mathrm{calcd}})$$

or

$$\Delta[M]^{20}_{D\mathrm{obs}}=\kappa\Delta[M]^{20}_{D\mathrm{calcd}} \tag{6}$$

In (6), as κ is always positive, if, concretely speaking, the orientation of a unit group changes in a molecule, the observed value of its optical rotatory power changes toward the same direction as the calculated value. Accordingly, in calculation, with regards to a definite molecular model, of $\Delta[M]^{20}_{D}$ due to the orientation-change of a unit group, if $\Delta[M]^{20}_{D\mathrm{calcd}}$ has the same sign as $\Delta[M]^{20}_{D\mathrm{obs}}$ this molecular model must be a structurally correct representation of the absolute configuration. On the other hand, if they are different in sign, the model used must be incorrect. In short, the problem of the absolute configuration becomes the problem of the sign of κ of Eq. (6) or (4). The author will illustrate the above-described principle, by using concrete examples. As is seen in Fig. 1, if the ori-

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[d] Landolt-Börnstein, Physikalisch-Chemische Tabellen, Hw. 2. p. 985.

[e] Values obtained by Ramakrishna-Rao; see Landolt-Börnstein, Physikalisch-Chemische Tabellen, 5th Ed., Eg. 2. p 90, 91.

[f] Sheng-Nien Wang, *J. Chem. Phys.*, **7**, 1012 (1939).

[*12] In the actual experiments, $[\mu]$ can not be observed. Then strictly speaking, $[\mu]^{20}_{D\mathrm{obs}}$ is of hypothetical character.

[*13] In this case, the value of the proportionality-constant depends upon various factors, chiefly owing to the effect of solvation.

entation of OH group which combines with 2-position of the ring in the molecular model of D-erythronic γ-lactone changes from α to β, the molecular model of D-threonic γ-lactone can be obtained, and if the orientation of OH group, which combines with 3-position of the ring in the molecular model of D-erythronic γ-lactone changes from α to β, the molecular model of L-threonic γ-lactone can be obtained. Therefore, by calculation, with regards to Haworth's perspective formulae, of $\varDelta[M]_D^{20}$ caused by the above-described two orientation-changes we can presume the absolute configuration of γ-lactones. That is to say, if $\varDelta[M]_{D\text{calcd}}^{20}$ is in the same direction as that of $\varDelta[M]_{D\text{obs}}^{20}$, Haworth's perspective formula (accordingly, Fischer convention)[10] is presumed to be a structurally correct representation of absolute configuration, and if the change is in the opposite direction, the formula is presumed to be incorrect. This method of presumption of the absolute configuration can be easily subjected to calculation with regards to D-erythronic- and D-threonic-γ-lactones, as follows; $[\mu]_{D\text{calcd}}^{20}(3/n^2+2)$, caused by the dynamical coupling effects between OH group which combines with 2-position of the ring and the other unit groups in these molecules are given below. (ref. Table I)

	CO	3α	Ring	Sum
2α	-21.0	0	$(2\alpha)\times$Ring[*14]	$-21.0+(2\alpha)\times$Ring
2β	21.0	-4.4	$(2\beta)\times$Ring	$16.6+(2\beta)\times$Ring

From Eq. (2), $\varDelta[M]_{D\text{calcd}}^{20}=\sum\varDelta[\mu]_{D\text{calcd}}^{20}$

Therefore, $\varDelta[M]_{D\text{calcd}}^{20}$ (namely, $\sum\varDelta[\mu]_{D\text{calcd}}^{20}$) due to the orientation-change of OH group which combines with 2-position from α to β in this case is $\{(16.6+(2\beta)\times\text{Ring})-(-21.0+(2\alpha)\times\text{Ring})\}(n^2+2)/3=\{37.6+(2\beta)\times\text{Ring}-(2\alpha)\times\text{Ring}\}(n^2+2)/3$

The corresponding $\varDelta[M]_{D\text{obs}}^{20}$ is given by ($[M]_{D\text{obs}}^{20}$ of D-Threonic γ-lactone) minus ($[M]_{D\text{obs}}^{20}$ of D-Erythronic γ-lactone). This is, $-36.6-(-86.5)=49.9$

By using these values, Eq. (6) becomes as below,

$$49.9=\kappa\{37.6+(2\beta)\times\text{Ring}-(2\alpha)\times\text{Ring}\}(n^2+2)/3. \qquad (7)$$

The author's purpose was to know the sign of κ, but to his regret, he was unable to calculate $(2\alpha)\times$Ring and $(2\beta)\times$Ring, owing to lack of data for α, β and $\vec{b}$ etc. of Ring. Kirkwood used a quasi-empirical method in order to avoid the difficulty of calculating $[\mu]_D$ due to a three-membered ring[*15], but the author devised a new quasi-empirical method, different from that of Kirkwood, as follows.

The same treatment was tried at 3-position of the ring, in the molecular model of D-erythronic γ-lactone as that which was carried out at 2-position, above, and the following equation was obtained.

$$123.1=\kappa\{14.2+(3\beta)\times\text{Ring}-(3\alpha)\times\text{Ring}\}(n^2+2)/3 \qquad (8)$$

On the other hand, owing to the symmetry of the γ-lactone ring plane

$$(2\alpha)\times\text{Ring}=(3\beta)\times\text{Ring}$$

and $$(2\beta)\times\text{Ring}=(3\alpha)\times\text{Ring}$$

Combining these two conditional equations with Eqs. (7) and Eq. (8)

$$\kappa=10.02/n^2+2$$

where n^2 is always positive, then $\kappa>0$[*16]. This result indicates that the Fischer convention is a structurally correct representation of absolute configuration, and this is consistent with those of Bijvoet[1] and Kirkwood[2].

Summary

The changes in optical rotatory power of γ-lactone due to orientation-changes of a unit group in the molecule were calculated by using the Kirkwood's polarizability theory with regard to molecular model, derived from Haworth's perspective formula. The Fischer convention was presumed to be the structurally correct representation of absolute configuration.

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[10] Wohl and Freudenberg, *Ber.*, **56**, 309 (1923).

[*14] $(2\alpha)\times$Ring means $[\mu]_{D\text{calcd}}^{20}(3/n^2+2)$, caused by the dynamical coupling effect between $(OH)^{2\alpha}$ group and ring.

[*15] Ref. "Introduction" of this paper.

[*16] By using n=1.34 (ref. *10). $\kappa\fallingdotseq2.64$. That is to say, $[M]_{D\text{obs}}^{20}$ is about 2.64 times as large as $[M]_{D\text{calcd}}^{20}$. The value of $\kappa(2.64)$ happens to be very consistent with the value of $\kappa=3.97/1.43=2.78$, obtained by T. C. Kwoh and H. Eyring (*J. Chem. Phys.*, **18**, 1186 (1950)) for the optical rotatory power of the acetone solution of benzoin.

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