# *Molecular Rotations of Glucides in Relation to their Structures. II.*
## *The Conformation and the Absolute Configuration of Aldopyranoses.*
## *Physical Meaning of Hudson's Isorotation Rule*

By Shukichi YAMANA

(Received October 1, 1956)

## Introduction

The problem of stereochemical structure of the aldopyranose-ring in its aqueous solution is not yet solved. By x-ray analysis of the crystals of aldopyranoses, Cox, Goodwin and Wagstaff concluded that the aldopyranose-ring is composed of five coplanar C atoms and one O atom (the ring-O-atom) situated outside the plane. Such a ring is called Cox's flat ring. They presumed, moreover, that aldopyranose molecules retain Cox's flat ring even in aqueous solutions[1].

From the results of the studies on cuprammonium-glycoside complexes, Reeves concluded that an aldopyranose molecule has a slightly distorted hexagonal structure oriented in one of the Sachse strainless ring[2] conformations, and that all of D-galactose, D-glucose and D-mannose have a chair-form ring of special type (according to Reeves' symbol, C 1 conformation[3],[*1].

On the other hand, Hudson reported of the quantitative relation between the structure of pyranoses and the value of their molecular rotations, and found Hudson's isorotation rule, but he could not explain the fact that the magnitude of the anomeric difference[*2] of mannose is smaller than those of other pyranoses[4]. Freudenberg explained the above-described fact, paying attention to the orientation of the OH group, which combines with C$^2$-atom, but his explanation did not imply any physical or mathematical equations[5]. Kauzmann, Walter and Eyring discussed this rule from the standpoint of the one-electron theory, but they insisted upon the fact that the OH group is not isotropic and the orientations of O—H bonds are complex, and they did not give any decisive explanation for this rule[6]. In short, the physical meaning of Hudson's isorotation rule and of the deviation of mannose from this is not yet determined. The author discussed in the preceding article[7] the absolute configuration of $\gamma$ lactones by using Kirkwood's treatment of OH group, regarding it as nearly isotropic. By using this treatment, the absolute configuration of aldopyranoses was examined as follows[*3]; The method of investigation was quite similar to that used for the study of $\gamma$-lactones. It was, first, to assume a molecular model, and next, to calculate the variation of the molecular rotation of the plane polarized light of the wave-length of D line at 20°C, $(\varDelta[\mathrm{M}]_{\mathrm{D}}^{20})$, caused by the orientation-change of one unit group in the molecule by using Kirkwood's polarizability theory[8]; lastly, to examine the sign of the proportionality-constant $\kappa$, by making the

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[1] E. G. Cox, T. H. Goodwin and (Miss) A. I. Wagstaff, *J. Chem. Soc.*, **1953**, 1495, part 2.

[2] U. Sachse, *Z. Phys. Chem.*, **10**, 203 (1892).

[3] R. E. Reeves, *J. Am. Chem. Soc.*, **72**, 1499 (1950).

[*1] By X-ray analysis, T. R. R. McDonald and C. A. Beevers came to the conclusion that the structure of $\alpha$-D-glucose molecule in crystalline state is almost the same as that of Reeves' C 1 conformation, but its bond lengths and valency angles are not simple (ref. T. R. R. Mc Donald and C. A. Beevers, *Acta. Cryst.*, **5**, 654 (1952)).

[*2] This is the difference in optical rotation of $\alpha$ and $\beta$ aldoses.

[4] C. S. Hudson and K. P. Monroe, *J. Am. Chem. Soc.*, **41**, 1141 (1919).

[5] K. Freudenberg and W. Kuhn, *Ber.*, **64**, 703 (1931).

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

[7] S. Yamana, This Bulletin, **30**. 203 (1957).

[*3] Then, unexpectedly, it became possible to presume the conformation of the aldopyranose-ring, and moreover, to understand the physical meaning of Hudson's isorotation rule.

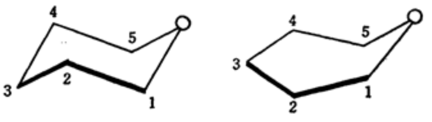
[8] J. G. Kirkwood, *J. Chem. Phys.*, **5**, 479 (1937).

| Name | Unit Groups | $[M]_D^{20}$(w) | Lit. |
|---|---|---|---|
| α-D-Galactose | [$(OH)^{1\alpha}$, $(OH)^{2\alpha}$, $(OH)^{3\beta}$, $(OH)^{4\beta}$, $(CH_2OH)^{5\beta}$, Ring] | 261.0° | (a) |
| β-D-Galactose | [$(OH)^{1\beta}$, $(OH)^{2\alpha}$, $(OH)^{3\beta}$, $(OH)^{4\beta}$, $(CH_2OH)^{5\beta}$, Ring] | 97.6° | (a) |
| α-D-Glucose | [$(OH)^{1\alpha}$, $(OH)^{2\alpha}$, $(OH)^{3\beta}$, $(OH)^{4\alpha}$, $(CH_2OH)^{5\beta}$, Ring] | 198.2° | (a) |
| β-D-Glucose | [$(OH)^{1\beta}$, $(OH)^{2\alpha}$, $(OH)^{3\beta}$, $(OH)^{4\alpha}$, $(CH_2OH)^{5\beta}$, Ring] | 34.7° | (a) |
| α-D-Mannose | [$(OH)^{1\alpha}$, $(OH)^{2\beta}$, $(OH)^{3\beta}$, $(OH)^{4\alpha}$, $(CH_2OH)^{5\beta}$, Ring] | 53.8° | (b) |
| β-D-Mannose | [$(OH)^{1\beta}$, $(OH)^{2\beta}$, $(OH)^{3\beta}$, $(OH)^{4\alpha}$, $(CH_2OH)^{5\beta}$, Ring] | −29.3° | (b) |

calculated value of $\Delta[M]_D^{20}$ proportional to its observed value. However, as it was impossible to calculate the terms concerning the aldopyranose-ring, a new method was applied[*4].

### Molecular Model and Data Used

Reeves' C 1 conformation and Cox's flat ring were used as the molecular model of the aldopyranose-ring for calculation. These are shown in Fig. 1.



Reeves' C 1 conformation Cox's flat ring

Fig. 1. Aldopyranose-ring
○, ring-O-atoms.

In order to simplify the calculations, the values of bond lengths and valency angles are assumed as follows, by referring to the data in the original papers. That is to say, as for Reeves' C 1 conformation[3)], the lengths of C—C and C—O bonds in the ring are assumed to be all 1.54 Å, and that of C—O bond which projects out of the ring to be 1.42 Å[*5]. The valency angles of C and O atoms are assumed to be a tetrahedral angle (109° 28′). According to Cox's investigations, the geometry of Cox's flat ring is as follows[1)]. The lengths of C—C and C—O bonds in the molecule are 1.54 Å and 1.46 Å respectively. As for the corner-angles of the ring, the valency angles of C atoms lie between 113° and 116°, the corresponding limits of the valency angle of O atom being 90° and 106°. Then the author used 114° as the valency angle of C atom which is the mean value of 113° and 116°, therefore the valency angle of O atom became 92°[*6]. If the hydroxyl oxygen is symbolized by $O^h$, $O^h$ atom and H atom combine with the same C atom of the ring and the angle ∠$HCO^h$ which is tetrahedral angle, 109° 28′, must be bisected by the plane which is determined by three atoms, namely, C atom and the two atoms besides H- and $O^h$- atoms attached to this C atom. The unit groups of the aldopyranose molecules were given in square brackets, as shown on the top of this page[*7].

It is assumed that the orientation of OH group in $(CH_2OH)^{5\beta}$ as regards the aldopyranose-ring is definite and similar in all of the above-described aldopyranoses. The values of the optical properties of OH group and H atom, used in the preceding article[7)] were used without any correction. The refractive indices of aqueous solutions of D-galactose, of D-glucose and of D-mannose, whose concentrations are suitable for measurement of the optical rotatory power, are nearly equal (1.34)[*8].

### Method Proposed

Partial molecular rotations of the plane polarized light of wave-length of D line at 20°C, represented by $[\mu]_D^{20}$, caused by the dynamical coupling effect between any two members of unit groups (except $(CH_2OH)^{5\beta}$ and Ring) in the aldopyranose molecule, were calculated according to Kirkwood's polarizability theory[8)]. The results of the calculation with regard to Reeves' C 1 conformation are given in Table I.

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[*4] Concerning this method, refer to "Method Proposed" in this article.

[*5] This is the mean value of lengths of C-O bonds in α-D-glucose. (ref. *1).

[*6] In order to see the magnitude of deviation of $[\mu]_{D\ \mathrm{calcd}}^{20}(3/n^2+2)$, caused by a small deviation in bond length or in valency angle, the author tried the other type of Cox's flat ring. In this ring, the valency angle of C atom and of O atom is 116° and 101.5° respectively, and lengths of C-C and C-O bonds in the molecule are 1.54 Å and 1.48 Å (ref. M. Kimura, *J. Chem. Soc. Japan.* **71**, 18 (1950)).respectively. $[\mu]_{D\ \mathrm{calcd}}^{20}(3/n^2+2)$, caused by the dynamical coupling effect of the unit groups in this molecular model is given in each parenthesis in Table II.

[*7] $(OH)^{1\alpha}$ means OH group which combines with 1-position of the aldopyranose-ring, in α orientation. (ref. L. F. Fieser, *J. Am. Chem. Soc.*, **72**, 623 (1950).)

a) C. N. Riiber, J. Minsaas and R. T. Lyche, *J. Chem. Soc.*, **1929**, 2173.

b) C. N. Riiber und J. Minsaas, *Ber.*, **60**, 2402 (1927).

[*8] ref. *10 in the preceding paper (7) cf. "International Critical Tables of Numerical Data," Vol. 2, p 351,347.

| | $2\alpha$ | $3\beta$ | $4\beta$ | $(CH_2OH)^{5\beta}$ | Ring | Sum |
|---|---|---|---|---|---|---|
| $1\alpha$ | 6.5 | 1.7 | 0 | $(1\alpha)\times(CH_2OH)^{5\beta}$,[*10] | $(1\alpha)\times$Ring | $8.2+(1\alpha)\times(CH_2OH)^{5\beta}+(1\alpha)\times$Ring |
| $1\beta$ | $-6.5$ | 0 | 0 | $(1\beta)\times(CH_2OH)^{5\beta}$ | $(1\beta)\times$Ring | $-6.5+(1\beta)\times(CH_2OH)^{5\beta}+(1\beta)\times$Ring |

TABLE I

$[\mu]^{20}_{\mathrm{Dcalcd}}\ (3/n^2+2,)$ CAUSED BY THE DYNAMICAL COUPLING EFFECT BETWEEN ANY TWO MEMBERS OF UNIT GROUPS (EXCEPT $(CH_2OH)^{5\beta}$ AND RING), WITH REGARD TO REEVES' C 1 conformation[*9]

| | $4\beta$ | $4\alpha$ | $3\beta$ | $3\alpha$ | $2\beta$ | $2\alpha$ |
|---|---|---|---|---|---|---|
| $1\alpha$ | 0 | 0 | 1.7 | 0 | 0 | 6.5 |
| $1\beta$ | 0 | 0 | 0 | $-1.7$ | 6.5 | $-6.5$ |
| $2\alpha$ | 1.7 | 0 | 6.5 | $-6.5$ | | |
| $2\beta$ | 0 | $-1.7$ | $-6.5$ | 0 | | |
| $3\alpha$ | 0 | 6.5 | | | | |
| $3\beta$ | 6.5 | $-6.5$ | | | | |

Note: $1\alpha$ is an abbreviated symbol of $(OH)^{1\alpha}$, and so on.

Then, $[\mu]^{20}_{\mathrm{Dcalcd}}(3/n^2+2)$, caused by the dynamical coupling effects between OH group situated in the 1-position of D-galactose molecule and the other unit groups in this molecule are as shown on the top of this page.

If the orientation of $(OH)^1$ group of D-galactose molecule changes from $\beta$ to $\alpha$, then the calculated value of the optical rotatory power of this molecule changes and the value of this change is as follows,

$$\begin{aligned}\Delta[M]^{20}_{\mathrm{Dcalcd}} &= \sum\Delta[\mu]^{20}_{\mathrm{Dcalcd}} = [\{8.2+(1\alpha)\\ &\quad \times(CH_2OH)^{5\beta}+(1\alpha)\times\mathrm{Ring}\}\ \text{minus}\\ &\quad \{-6.5+(1\beta)\times(CH_2OH)^{5\beta}\\ &\quad +(1\beta)\times\mathrm{Ring}\}]\ (n^2+2)/3,\\ &= (14.7+L)\ \ (n^2+2)/3\end{aligned}$$

where

$$\begin{aligned}L \equiv &(1\alpha)\times(CH_2OH)^{5\beta}-(1\beta)\\ &\times(CH_2OH)^{5\beta}+(1\alpha)\times\mathrm{Ring}\\ &-(1\beta)\times\mathrm{Ring}.\end{aligned}$$

The corresponding $\Delta[M]^{20}_{\mathrm{Dobs}}$ is given by, $\{[M]^{20}_{\mathrm{Dobs}}$ of $\alpha$-D-galactose$\}$ minus $\{[M]^{20}_{\mathrm{Dobs}}$ of $\beta$-D-galactose$\}$. This is $(261.0-97.6)=163.4$. These two values must be made equal to each other by using a proportionality-constant $\kappa$. Then

$$163.4=\kappa(14.7+L)\ \ (n^2+2)/3. \tag{1}$$

Of course, the left side and the right side of Eq. (1) show the observed value and the calculated value of the anomeric difference of D-galactose, respectively. By using the method like that mentioned above, two other equations are obtained.

From D-glucose,

$$163.5=\kappa(14.7+L)\ \ (n^2+2)/3 \tag{2}$$

and from D-mannose,

$$83.1=\kappa(-4.8+L)\ \ (n^2+2)/3 \tag{3}$$

The left side of (1) is nearly equal to that of (2), and this fact is well known as Hudson's isorotation rule[9]. The right side of (1) is equal to that of (2). In other words, the calculated value of the anomeric difference of D-galactose and that of D-glucose is equal. Now, the above-described calculation can be said to bear satisfactory results to explain Hudson's isorotation rule. On the other hand, the anomeric difference of D-mannose is given by Eq. (3), but it is apparent that these values are different from those in Eqs. (1) and (2). Namely, the anomeric difference of D-mannose is different from those of D-galactose and D-glucose. From Eq. (2) minus Eq. (3), $\kappa=12.37/n^2+2$, where $n^2$ is always positive, then $\kappa>0$. This result means that the Fischer convention from which Reeves' C 1 conformation is derived, is a structurally correct representation of the absolute configuration.

Next, the author applied the method which is analogous to that used in the case of Reeves' C 1 conformation above, to the

TABLE II

$[\mu]^{20}_{\mathrm{Dcalcd}}(3/n^2+2)$, CAUSED BY THE DYNAMICAL COUPLING EFFECT BETWEEN ANY TWO MEMBERS OF UNIT GROUPS (EXCEPT $(CH_2OH)^{5\beta}$ AND RING), WITH REGARD TO COX'S FLAT RING[*11]

| | $4\beta$ | $4\alpha$ | $3\beta$ | $3\alpha$ | $2\beta$ | $2\alpha$ |
|---|---|---|---|---|---|---|
| $1\alpha$ | $-1.1$<br>$(-0.9)$ | 1.3<br>(1.0) | $-0.2$<br>(0.2) | 2.9<br>(2.4) | 1.4<br>(2.0) | 6.0<br>(5.5) |
| $1\beta$ | 0.3<br>(0.4) | $-0.1$<br>$(-0.2)$ | 1.8<br>(1.6) | $-2.1$<br>$(-2.1)$ | 6.0<br>(5.5) | $-6.4$<br>$(-6.2)$ |
| $2\alpha$ | 1.4<br>(1.4) | 0<br>(0) | 4.5<br>(4.5) | 0<br>(0) | | |
| $2\beta$ | 0<br>(0) | $-1.4$<br>$(-1.4)$ | 0<br>(0) | $-4.5$<br>$(-4.5)$ | | |
| $3\alpha$ | 4.5<br>(4.5) | 0<br>(0) | | | | |
| $3\beta$ | 0<br>(0) | $-4.5$<br>$(-4.5)$ | | | | |

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[*9] When 1.48 Å (ref. *6) is used as the value of length of C-O bond, the values 6.1 and 1.6 appears in Table 1, instead of 6.5 and 1.7 respectively.

[*10] $(1\alpha)\times(CH_2OH)^{5\beta}$ means $[\mu]^{20}_{\mathrm{Dcalcd}}\ (3/n^2+2)$, caused by the dynamical coupling effect between $(OH)^{1\alpha}$ and $(CH_2OH)^{5\beta}$.

9) C. S. Hudson, *J. Am. Chem. Soc.*, **31**, 66 (1909).

[*11] Concerning the values in parentheses, refer to *6.

case of Cox's flat ring. The results of calculation of $[\mu]_{\mathrm{D}}^{20}(3/n^2+2)$ are given in Table II.

By using these values three equations are obtained.

From D-galactose,

$$163.4=\kappa'(9.0+L')(n^2+2)/3 \qquad (4)$$

from D-glucouse,

$$163.5=\kappa'(11.8+L')(n^2+2)/3 \qquad (5)$$

and from D-mannose,

$$83.1=\kappa'(-5.2+L')(n^2+2)/3 \qquad (6)$$

where $\kappa'$ is a proportionality-constant and

$$\begin{aligned} L' \equiv\ & (1\alpha)\times(\mathrm{CH_2OH})^{5\beta}-(1\beta) \\ & \times(\mathrm{CH_2OH})^{5\beta}+(1\alpha)\times\mathrm{Ring} \\ & -(1\beta)\times\mathrm{Ring} \end{aligned}$$

in this case. From Eq. (5) minus Eq. (6),

$$\kappa'=14.19/n^2+2$$[*12]

where $n^2$ is always positive; then $\kappa'>0$. That is to say, it is concluded from the result of calculation with regard to Cox's flat ring that the Fischer convention is a structurally correct representation of the absolute configuration. But the right side of Eq. (4) is different from that of Eq. (5). In other words, the calculated value of the anomeric difference of D-galactose is different from that of D-glucose, and this is not consistent with the fact that the observed value of the anomeric difference of D-galactose is equal to that of D-glucose. In short, Hudson's isorotation rule can not be explained by using Cox's flat ring.

## Conclusion

The results of calculation and presumption in this paper are as follows,

(1) The Fischer convention is a structurally correct representation of the absolute configuration.

(2) If D-galactose, D-glucose and D-mannose are of the same type of ring structure in aqueous solution, and this type should be either Reeves' C 1 conformation or Cox's flat ring, then this common type must be the former and not the latter.

(3) Hudson's isorotation rule can be explained easily, by calculation of the anomeric difference adoption Kirkwood's polarizability theory of optical rotatory power with regard to Reeves' C 1 conformation of an aldopyranose molecule.

The author wishes to express his deepest gratitude to Professor S. Tanaka (Kyoto University) for his valuable advice and kind encouragement throughout this work.

*Department of Chemistry*
*Kyoto Gakugei University*
*Fushimi-ku, Kyoto*

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[*12] By using the values given in the parentheses in Table II, $\kappa''=15.87/n^2+2$, where $\kappa''$ is a proportionality-constant for this case.