

# OPTICAL ROTATION AND RING STRUCTURE IN THE SUGAR GROUP

## THE OPTICAL ROTATION OF THE VARIOUS ASYMMETRIC CARBON ATOMS IN THE HEXOSE AND PENTOSE SUGARS

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### ABSTRACT

The specific rotations of  $\alpha$ -*d*-gulose (+61.6),  $\alpha$ -methyl *d*-guloside (+106) and  $\beta$ -methyl *d*-guloside (−83), which are reported for the first time, complete the data necessary for the calculation of the optical rotatory power of each of the various asymmetric carbon atoms in the hexose sugars. The values for the optical rotatory power of the various asymmetric carbon atoms in both the hexose and pentose series are calculated first, from the optical rotations of the methyl glycosides, and, secondly, from the optical rotations of the sugars. The values from the glycosides are slightly higher, but of the same order as the values obtained from the sugars indicating that the normal forms of *d*-glucose, *d*-galactose,  $\alpha$ -*d*-mannose and  $\alpha$ -*d*-gulose have the same ring structure as the corresponding glycosides (1, 5). The slightly larger values for the glycosides indicates that the replacement of the hydroxyl group in the sugars by a methoxy group alters the rotation of all the asymmetric carbon atoms. The utilization of the values given is illustrated by the explanation of certain deviations from Hudson's second rule of isorotation and the prediction of the optical rotations of the at present unknown hexose sugars and methyl glycosides.

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### I. INTRODUCTION

In 1875 van't Hoff<sup>1</sup> formulated the rule of optical superposition and illustrated it quite plainly in its application to the carbohydrate field. This rule states the optical rotation of the molecule is the algebraic sum of the constituent asymmetric carbon atoms, the

<sup>1</sup> La Chimie dans L'Espace, van't Hoff, Rotterdam; 1875.

rotations of the individual atoms changing from  $+a$  to  $-a$  when the atomic configuration is replaced by its mirror image. Van't Hoff illustrated this rule quite plainly in its application to the carbohydrate field as will be discussed below. However, at that time the experimental data were lacking to establish its validity in the sugar group. In 1909 the development of experimental carbohydrate chemistry was sufficient for Hudson<sup>2</sup> to apply the superposition rule by his method of considering only the rotations of the first asymmetric carbon and the rest of the molecule and to determine the optical rotation of the first carbon atom and the rotation of the rest of the molecule. He compared all kinds of derivatives by his method and by this way of comparison showed that the principle of optical superposition holds approximately. In order to make comparisons between substances whose structure differs considerably he made a number of rules ("isorotation") or approximations. The correlation of rotation in the sugar group by him and others showed that there exist many deviations<sup>3</sup> from his rules, which indicate that the influence of a given group on the rotatory power of the various asymmetric carbon atoms is manifested throughout the sugar molecule.

A test of the theory of optical superposition was anticipated by van't Hoff<sup>4</sup> in 1894, who states that when there are several asymmetric carbon atoms their action is to be added or subtracted. "Thus for the four pentose types COH (CHOH)<sub>3</sub>, we should have the following rotations:

No. 1	No. 2	No. 3	No. 4
$\begin{array}{c} +A \\ +B \\ +C \end{array}$	$\begin{array}{c} +A \\ +B \\ -C \end{array}$	$\begin{array}{c} +A \\ -B \\ +C \end{array}$	$\begin{array}{c} -A \\ +B \\ +C \end{array}$

and since the sum of No. 2, No. 3, and No. 4 is equal to  $A+B+C$ , the rotation of arabinose (probably the highest) should be equal to the rotations of xylose, ribose, and the expected fourth type taken together."<sup>5</sup>

Van't Hoff's idea may be put in the form of four simultaneous equations which contain only three variables, and if the experimental values of A, B, and C, determined from any three of the equations check the fourth equation, his theory as applied in the given case is definitely proved. If one had a similar series of compounds, which checked, it would be strong evidence that all the compounds in the series had similar structures. The realization of the experimental proof of this reasoning has not been possible because of the lack of knowledge and sufficient experimental data. The problem is far more complicated than van't Hoff could anticipate at that early date. However, in the light of modern knowledge upon the ring structure of the sugars it should now be possible to reach the desired goal if the necessary data were available.

<sup>2</sup> Hudson, J. Am. Chem. Soc., **31**, p. 69; 1909.

<sup>3</sup> Böeseken, The Configuration of the Saccharides, A. W. Sijthoff's, Leyden.

<sup>4</sup> Van't Hoff, The Arrangement of Atoms in Space (translated by Eilcoart), Longmans, Green & Co., p. 160; 1898.

<sup>5</sup> Discovered since, and called lyxose.

The author is attempting to prepare those compounds necessary for the calculation and *checking* of the optical rotatory power of all the different asymmetric carbon atoms in the hexose sugars and methyl glycosides. The investigation, which is still in progress, has been successful, in that the optical rotations of  $\alpha$ -*D*-gulose and  $\alpha$ - and  $\beta$ -methyl *D*-gulosides have been determined. These values complete the data necessary for the computation of the optical rotation of each of the several asymmetric carbon atoms in the hexose sugars and in the methyl glycosides. The values obtained for the rotatory power of the different asymmetric carbon atoms are of particular interest because they are the primary values from which the optical rotation of all the normal aldohexose sugars and methyl glycosides may be calculated. The numerical values for the at present unknown normal forms of *D*-idose, *D*-talose, *D*-allose, and *D*-altrose and the corresponding methyl glycosides are predicted. An attempt is being made to prepare and measure the optical rotation of one or more forms of *D*-idose. If the optical rotations which may be found in the future check the predicted values, it will be strong evidence that all the sugars involved in the calculations have similar ring structures.

#### 1. DETERMINATION OF RING STRUCTURE BY THE AGREEMENT WITH OR DEVIATION FROM THE THEORY OF OPTICAL SUPERPOSITION

At the time when van't Hoff first presented the theory of optical superposition the reducing sugars were considered to be true aldehydes. Subsequently it has been found that the sugars and glycosides exist in two isomeric forms ( $\alpha$  and  $\beta$ ) which contain an additional asymmetric carbon atom. In 1883 Tollens<sup>6</sup> had suggested a ring structure for the reducing sugars, but discovery of the two methyl glycosides by Emil Fischer<sup>7</sup> in 1893 marks the beginning of the modern concept of the structure of the sugars. The optical rotation of the pseudo-aldehydic carbon atom was determined in 1909 by C. S. Hudson, who by a series<sup>8</sup> of brilliant researches has developed the theory of optical superposition into the most useful tool at the disposal of sugar chemists. Hudson<sup>9</sup> has considered the rotation of the pseudo-aldehydic carbon as  $+a$  in the  $\alpha$  (dextro) sugars,  $-a$  in the  $\beta$  sugars, and the rotation of the rest of the molecules as  $b$ . The rotation of the  $\alpha$ -*D*-form is equal to  $b+a$  and the rotation of the  $\beta$ -*D*-form is equal to  $b-a$ . He has shown from the available data, first, that the difference between the molecular rotations of the  $\alpha$  and  $\beta$  forms of all the aldehyde sugars and their derivatives ( $2a$ ) is a nearly constant quantity, and, secondly, that the  $\alpha$  and  $\beta$  forms of those derivatives of any aldose sugar in which only the first carbon is affected have molecular rotations whose sum is approximately equal to the sum ( $2b$ ) of the molecular rotations of the  $\alpha$  and  $\beta$  forms of the sugar. Certain exceptions were found to the above rules, particularly in the mannose, rhamnose, and lyxose series, which led to

<sup>6</sup> Tollens, Ber., 16, p. 921; 1883.

<sup>7</sup> Fischer, Ber., 26, p. 2400; 1893.

<sup>8</sup> Hudson, Relations Between Rotatory Power and Structure in the Sugar Group, B. S. Sci. Paper No. 533.

<sup>9</sup> See footnote 2, p. 1042.



the hypothesis<sup>10</sup> "that among the known derivatives of mannose and rhamnose there occur substances of various ring types (which accounts for the observed exceptional comparative rotations) and that substances belonging to the same ring type show normal comparative rotations (which accounts for the normal values)." The hypothesis and allocation of the various substances to the different series which he postulated was vigorously attacked by Haworth and Hirst.<sup>11</sup> They regard  $\alpha$ - and  $\beta$ -mannose as being not necessarily dissimilar in ring structure and believe that the divergence in optical rotation may be caused by the special arrangement of hydroxyl groups in mannose and the related sugars rhamnose and lyxose. In their studies they found a new form of lyxose whose rotation ( $-70$ ) is also exceptional. However, Hudson's hypothesis has recently received additional support in the preparation by Dale<sup>12</sup> of a calcium chloride double compound of a new form of  $\alpha$ -*d*-mannose whose rotation agrees with the rotation calculated by Hudson for a certain ring form of  $\beta$ -*d*-mannose.

A comparison of the optical rotations of the sugars and glycosides only indicates that a given series of compounds have or have not a common ring form. The ring structure of said series is assumed to be the same as the ring structure of any substance in the series whose ring structure is established by other methods. The ring structures of these key substances are derived from the results obtained by methylation studies.

## 2. DETERMINATION OF RING STRUCTURE OF THE GLYCOSIDES FROM METHYLATION STUDIES

In 1903 Purdie and Irvine<sup>13</sup> showed that the hydroxyl groups in methyl glucoside could be replaced by methoxyl groups by means of methyl iodide and silver oxide. Since all the hydroxyl groups in the resulting pentamethyl glucose are blocked the ring structure is assumed to be fixed. The normal isomeric  $\alpha$  and  $\beta$  pentamethyl glucoses, when hydrolyzed by acids, are converted into tetramethyl glucoses. Both of the tetramethyl glucoses exhibit mutarotation and give the same final rotatory power which shows that  $\alpha$  and  $\beta$  tetramethyl glucose have the same ring structure. Recently Wolfrom and Lewis<sup>14</sup> have shown that tetramethyl glucose may be transformed by dilute alkalis directly to tetramethyl mannose, which shows that tetramethyl mannose and tetramethyl glucose have similar ring structures. Direct evidence on the location of the ring may be obtained by the oxidation of the methylated sugars to the corresponding sugar acids. Charlton, Haworth and Peat<sup>15</sup> found that those lactones prepared from the normal forms of glucose, galactose, mannose, arabinose, and xylose, by first methylating the aldoses and then submitting them to oxidation with bromine water, exhibited a rapid change in rotation when dissolved in water. This rapid change<sup>16</sup> indicates that 1,5 lactones were formed. This conclusion

<sup>10</sup> Hudson, J. Am. Chem. Soc., **48**, p. 1434, 1926.

<sup>11</sup> Haworth and Hirst, J. Chem. Soc., p. 1221; 1928.

<sup>12</sup> J. K. Dale, B. S. Jour. Research, **3**, p. 459; 1929; J. Am. Chem. Soc., **51**, p. 2788; 1929.

<sup>13</sup> Purdie and Irvine, J. Chem. Soc., **83**, p. 1021; 1903; **85**, p. 1049; 1904.

<sup>14</sup> Wolfrom and Lewis, J. Am. Chem. Soc., **50**, p. 837; 1928.

<sup>15</sup> Charlton, Haworth and Peat, J. Chem. Soc., p. 89; January, 1926.

<sup>16</sup> Levene and Simms, J. Biol. Chem., **65**, p. 31; 1925.

has been confirmed by the degradation of the various methylated sugar acids by nitric acid oxidation to the expected products. Thus tetramethyl gluconic acid prepared from the normal tetramethyl glucose on nitric acid oxidation gave a 70 per cent yield of xylotrimethoxyglutaric acid,<sup>17</sup> which indicates that the methylated sugar has a 1,5 ring structure.

The formation of the third methyl glucoside (the distillable so-called  $\gamma$ -form of Fischer<sup>18</sup>) and other similar compounds indicates that in a sugar solution an equilibrium<sup>19</sup> may exist between a number of different ring forms. As pointed out by Phelps and Purves the ring structure of a methylated sugar which might be prepared from such a solution would not determine the ring structure of the original sugar. When substitution is on the pseudo-aldehydic carbon atom as in the glycosides, the oxygen ring is more stable and probably it does not migrate upon further methylation. Hence, it may be assumed that the correct ring structure of glycosides is obtained from methylation studies, but that the ring structures of the sugars are not established by methylation.

It has been shown by methylation studies that  $\alpha$ - and  $\beta$ -methyl glucosides,<sup>20</sup>  $\alpha$ - and  $\beta$ -methyl galactosides,<sup>21</sup>  $\alpha$ -methyl mannoside,<sup>22</sup>  $\alpha$ - and  $\beta$ -methyl arabinosides,<sup>23</sup>  $\alpha$ - and  $\beta$ -methyl xylosides,<sup>24</sup> and  $\alpha$ -methyl lyxoside<sup>25</sup> have a 1,5-ring structure. The only glycosides whose rotations were used and which have not been shown by methylation studies to have a 1,5-ring structure are the author's newly prepared  $\alpha$ - and  $\beta$ -methyl gulosides.<sup>26</sup> In this article it has been assumed that their ring structure is the same as the ring structure of the other crystalline glycosides.

The ring structures of the sugars were allocated by means of the concept that there occur different ring forms in the sugar group which may be detected by the wide deviation from Hudson's rules of isorotation. The rotation of each sugar was compared with the rotation of the corresponding glycoside by means of the following equations:

$$[M]_D (\text{glycoside}) = B' \pm 18,500.$$

$$[M]_D (\text{sugar}) = B \pm 8,500.$$

If the values of  $B$  and  $B'$  agree approximately it is assumed that the two substances have similar ring structures. The only exceptions as previously found by Hudson were in the mannose and lyxose series. A comparison of the numerical values shows that  $B$  ( $-3,100$ ) from  $\alpha$ - $d$ -mannose ( $+30$ ) agrees with the value of  $B'$  ( $-3,170$ ) from  $\alpha$ -methyl  $d$ -mannoside ( $+79$ ) and hence it is assumed

<sup>17</sup> Haworth, Hirst and Miller, *J. Chem. Soc.*, p. 2436; 1927.

<sup>18</sup> Fischer, *Ber.*, **47**, p. 1980; 1914.

<sup>19</sup> Phelps and Purves, *B. S. Jour. Research*, **3**, p. 247; 1929; *J. Am. Chem. Soc.*, **51**, p. 2443; 1929.

<sup>20</sup> Haworth, Hirst, and Miller, *J. Chem. Soc.*, p. 2436; 1927.

<sup>21</sup> Haworth, Ruell, and Westgarth, *J. Chem. Soc.*, **125**, p. 2468; 1924; Pryde, *J. Chem. Soc.*, **123**, p. 1808; 1923.

<sup>22</sup> Goodyear and Haworth, *J. Chem. Soc.*, p. 3136; 1927.

<sup>23</sup> Haworth, Hirst, and Learner, *J. Chem. Soc.*, p. 2432; 1927.

<sup>24</sup> Hirst and Purves, *J. Chem. Soc.*, **123**, p. 1352; 1923; Phelps and Purves, *J. Am. Chem. Soc.*, **51**, p. 2443; 1929; also *B. S. Jour. Research*, **3**, p. 247; 1929.

<sup>25</sup> Hirst and Smith, *J. Chem. Soc.*, p. 3147; 1923.

<sup>26</sup> It is planned to methylate the two methyl gulosides and determine their probable ring structure. The calculations are published at this time because it will be some time before the methylation studies are completed.

that they belong to the same series. The value of  $B$  (+5,440) from  $\beta$ - $d$ -mannose (-17) does not check the value from the methyl glycoside (-3,170) which indicates that it has a different ring structure and it is therefore excluded from the calculations. The value of  $B$  (-2,000) from  $\beta$ - $d$ -lyxose (-70) does not check the value of  $B'$  (-8,760) from  $\alpha$ -methyl  $d$ -lyxoside and so it is also excluded from the calculations. The values of  $B$  and  $B'$  as well as the data used in the calculations are given in Table 1.

TABLE 1.—Optical rotation of the aldose sugars and glycosides

	$[\alpha]_D^{20}$ in H <sub>2</sub> O	$[M]_D^{20}$	$[M]_D^{20}$ $\pm 8,500$ $= B$	$[M]_D^{20}$ $\pm 18,500$ $= B$	Ring from methyl- ation	Ring assigned
$\alpha$ - $d$ -glucose <sup>1</sup> -----	+113	+20,340	+11,840	-----	-----	1, 5
$\beta$ - $d$ -glucose <sup>1</sup> -----	+19	+3,420	+11,920	-----	-----	1, 5
$\alpha$ -methyl $d$ -glucoside <sup>2</sup> -----	+157.9	+30,630	-----	+12,130	1, 5	1, 5
$\beta$ -methyl $d$ -glucoside <sup>2</sup> -----	-32.5	-6,300	-----	+12,200	1, 5	1, 5
$\alpha$ - $d$ -mannose <sup>3</sup> -----	+30	+5,400	-3,100	-----	-----	1, 5
$\beta$ - $d$ -mannose <sup>3</sup> -----	-17	-3,060	+5,440	-----	-----	-----
$\beta$ - $d$ -mannose (Dale's) <sup>4</sup> -----	-65	-11,700	-3,200	-----	-----	1, 5
$\alpha$ -methyl $d$ -mannoside <sup>5</sup> -----	+79	+15,330	-----	-3,170	1, 5	1, 5
$\alpha$ - $d$ -galactose <sup>1</sup> -----	+144	+25,920	+17,420	-----	-----	1, 5
$\beta$ - $d$ -galactose <sup>1</sup> -----	+52	+9,360	+17,860	-----	-----	1, 5
$\alpha$ -methyl $d$ -galactoside <sup>2</sup> -----	+192.7	+37,380	-----	+18,880	1, 5	1, 5
$\beta$ -methyl $d$ -galactoside <sup>2</sup> -----	-0.4	-80	-----	+18,580	1, 5	1, 5
$\alpha$ - $d$ -gulose <sup>6</sup> -----	+62.6	+11,100	+2,600	-----	-----	1, 5
$\alpha$ -methyl $d$ -guloside <sup>6</sup> -----	+106	+20,600	-----	+2,100	-----	1, 5
$\beta$ -methyl $d$ -guloside <sup>6</sup> -----	-83	-16,100	-----	+2,400	-----	1, 5
$\beta$ - $d$ -arabinose <sup>1</sup> -----	-175	-26,250	-17,750	-----	-----	1, 5
$\beta$ - $l$ -arabinose <sup>1</sup> -----	+175	+26,250	+17,750	-----	-----	1, 5
$\alpha$ -methyl $l$ -arabinoside <sup>1</sup> -----	+17.3	+2,840	-----	+21,340	1, 5	1, 5
$\beta$ -methyl $l$ -arabinoside <sup>1</sup> -----	+245.5	+40,200	-----	+21,760	1, 5	1, 5
$\alpha$ - $d$ -xylose <sup>1</sup> -----	+92	+13,800	+5,300	-----	-----	1, 5
$\alpha$ -methyl $d$ -xyloside <sup>1</sup> -----	+153.9	+25,240	-----	+6,740	1, 5	1, 5
$\beta$ -methyl $d$ -xyloside <sup>1</sup> -----	-65.5	-10,740	-----	+7,760	1, 5	1, 5
$\alpha$ - $d$ -lyxose <sup>1</sup> -----	+5.5	+825	-7,625	-----	-----	1, 5
$\beta$ - $d$ -lyxose <sup>8</sup> -----	-70	-10,500	-2,000	-----	-----	-----
$\alpha$ -methyl $d$ -lyxoside <sup>9</sup> -----	+59.4	+9,740	-----	-8,760	1, 5	1, 5

<sup>1</sup> B. S. Sci. Paper No. 533.

<sup>2</sup> Bourquelot, Ann. Chim., **7**, p. 218; 1917.

<sup>3</sup> Levene and Meyer, J. Biol. Chem., **57**, p. 329; 1923; **59**, p. 129; 1924.

<sup>4</sup> Dale, J. Amer. Chem. Soc., **51**, p. 2788; 1929.

<sup>5</sup> Van Ekenstein, Rec. trav. chim., **15**, p. 223; 1896.

<sup>6</sup> These values were taken from the author's work which will be subsequently published. The rotation of  $\alpha$ - $d$ -gulose was determined from a new calcium chloride double compound of  $\alpha$ - $d$ -gulose; the methyl gulosides were fractionally crystallized to constant melting point from ethyl alcohol. The rotations may be subject to slight revision but are probably correct to  $\pm 2^\circ$ .

<sup>7</sup> Hudson and Yanovsky, J. Amer. Chem. Soc., **39**, p. 1035; 1917.

<sup>8</sup> Haworth and Hirst, J. Chem. Soc., p. 1221; 1928.

<sup>9</sup> Phelps and Hudson, J. Amer. Chem. Soc., **48**, p. 503; 1926.

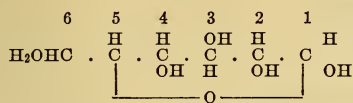
## II. CALCULATION OF THE NUMERICAL VALUE FOR THE OPTICAL ROTARY POWER OF THE VARIOUS ASYMMETRIC CARBON ATOMS

### 1. METHOD OF CALCULATION

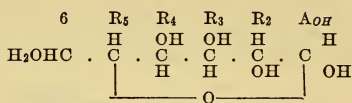
If we assume the 1, 5 ring structure for the sugars, they are represented by the formulas I, II, III, IV, V, VI, and VII. Since the  $\alpha$  and  $\beta$  forms differ only in the stereoisomeric arrangement of the pseudo-aldehydic carbon atom only one form is given. The methyl



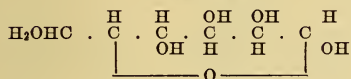
glycosides differ from the sugars only in that the hydroxyl on the first carbon is replaced by a methoxy group.



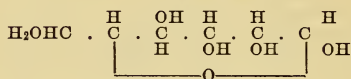
*α*-d-glucose I.



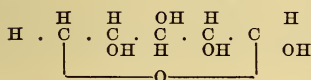
*α*-d-galactose II.



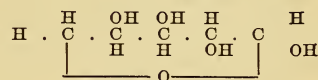
*α*-d-mannose III.



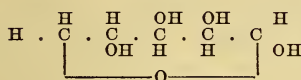
*α*-d-gulose IV.



*α*-d-xylose V.



*β*-methyl *l*-arabinose VI.



*α*-d-lyxose VII.

Considering the rotation of the first carbon atom  $a_{\text{OH}}^{27}$  in the sugars or  $a_{\text{Me}}$  in the glycosides and the rotations of the other carbon atoms in order  $R_2, R_3, R_4, R_5$ , the molecular rotations of the sugars and glycosides are given by equations which follow. The rotations of the various carbon atoms in the hexose series are designated with the capital letter  $R$ , and in the pentose series they are designated with the small letter  $r$ ; the rotations for the various carbon atoms in the glycosides are marked with an accent to distinguish them from the values derived from the sugars. The terms in the equations are considered to be positive when the hydroxyl group in the sugar lies below and negative when it lies above, as shown in Formulas (I) to (VI), inclusive.

#### HEXOSE SUGARS

- (1)  $\alpha$ -d-glucose =  $+a_{\text{OH}} + R_2 - R_3 + R_4 + R_5 = +20,300$ .
- (2)  $\beta$ -d-glucose =  $-a_{\text{OH}} + R_2 - R_3 + R_4 + R_5 = +3,420$ .
- (3)  $\alpha$ -d-mannose =  $+a_{\text{OH}} - R_2 - R_3 + R_4 + R_5 = +5,400$ .
- (4)  $\beta$ -d-mannose =  $-a_{\text{OH}} - R_2 - R_3 + R_4 + R_5 = (-11,700)$ .
- (5)  $\alpha$ -d-galactose =  $+a_{\text{OH}} + R_2 - R_3 - R_4 + R_5 = +25,900$ .
- (6)  $\beta$ -d-galactose =  $-a_{\text{OH}} + R_2 - R_3 - R_4 + R_5 = +9,360$ .
- (7)  $\alpha$ -d-gulose =  $+a_{\text{OH}} + R_2 + R_3 - R_4 + R_5 = +11,100$ .

#### HEXOSE GLYCOSIDES

- (8)  $\alpha$ -methyl *d*-glucoside =  $+a_{\text{Me}} + R'_2 - R'_3 + R'_4 + R'_5 = +30,630$ .
- (9)  $\beta$ -methyl *d*-glucoside =  $-a_{\text{Me}} + R'_2 - R'_3 + R'_4 + R'_5 = -6,300$ .
- (10)  $\alpha$ -methyl *d*-mannoside =  $+a_{\text{Me}} - R'_2 - R'_3 + R'_4 + R'_5 = +15,330$ .
- (11)  $\alpha$ -methyl *d*-galactoside =  $+a_{\text{Me}} + R'_2 - R'_3 - R'_4 + R'_5 = +37,380$ .
- (12)  $\beta$ -methyl *d*-galactoside =  $-a_{\text{Me}} + R'_2 - R'_3 - R'_4 + R'_5 = -80$ .
- (13)  $\alpha$ -methyl *d*-guloside =  $+a_{\text{Me}} + R'_2 + R'_3 - R'_4 + R'_5 = +20,600$ .
- (14)  $\beta$ -methyl *d*-guloside =  $-a_{\text{Me}} + R'_2 + R'_3 - R'_4 + R'_5 = -16,100$ .

<sup>27</sup> The rotations of the first carbon atom in the sugars  $a_{\text{OH}} = \pm 8,500$  and in the glycosides ( $a_{\text{Me}} = \pm 18,500$ ) were calculated by Hudson in 1909, see footnote 2. A value for the rotation of the second carbon atom, "the epimeric difference in rotation" was also calculated by Hudson, see footnote 10, but his value ( $2r_2 = +6,700$ ) differs considerably from the value  $2R_2 = +15,300$  as given in this paper; the difference is due to a different allocation of ring structures. The rotation of the fourth carbon atom in the pentose glycosides as given by equation (47) was also resorted to in the same article.

## PENTOSE SUGARS

- (15)  $\alpha$ -*d*-xylose =  $+a_{OH} + r_2 - r_3 + r_4 = +13,800$ .  
 (16)  $\beta$ -*d*-arabinose =  $-a_{OH} - r_2 + r_3 + r_4 = -26,250$ .  
 (17)  $\beta$ -*l*-arabinose =  $+a_{OH} + r_2 - r_3 - r_4 = +26,250$ .  
 (18)  $\alpha$ -*d*-lyxose =  $+a_{OH} - r_2 - r_3 + r_4 = +825$ .

## PENTOSE GLYCOSIDES

- (19)  $\alpha$ -methyl *d*-xyloside =  $+a_{Me} + r'_2 - r'_3 + r'_4 = +25,240$ .  
 (20)  $\beta$ -methyl *d*-xyloside =  $-a_{Me} + r'_2 - r'_3 + r'_4 = -10,740$ .  
 (21)  $\alpha$ -methyl *l*-arabinoside =  $-a_{Me} + r'_2 - r'_3 - r'_4 = +2,840$ .  
 (22)  $\beta$ -methyl *l*-arabinoside =  $+a_{Me} + r'_2 - r'_3 - r'_4 = +40,260$ .  
 (23)  $\alpha$ -methyl *d*-lyxoside =  $+a_{Me} - r'_2 - r'_3 + r'_4 = +9,740$ .

The equations just given may be solved for the optical rotations of the different asymmetric carbon atoms by adding or subtracting the equations in such a manner as to eliminate all the variables except one. The computations are given below:

## 2. CALCULATION OF OPTICAL ROTATIONS OF THE VARIOUS ASYMMETRIC CARBON ATOMS

## HEXOSE SERIES

24. $\alpha$ - <i>d</i> -galactose - $\beta$ - <i>d</i> -galactose	=	16,540 = $2a_{OH}$
25. $\alpha$ - <i>d</i> -glucose - $\beta$ - <i>d</i> -glucose	=	16,880 = $2a_{OH}$
26. $\alpha$ -methyl <i>d</i> -galactoside - $\beta$ -methyl <i>d</i> -galactoside	=	37,460 = $2a_{Me}$
27. $\alpha$ -methyl <i>d</i> -glucoside - $\beta$ -methyl <i>d</i> -glucoside	=	36,930 = $2a_{Me}$
28. $\alpha$ -methyl <i>d</i> -gulose - $\beta$ -methyl <i>d</i> -gulose	=	36,700 = $2a_{Me}$
29. $\alpha$ - <i>d</i> -glucose - $\alpha$ - <i>d</i> -mannose	=	14,900 = $2R_2$
30. $\alpha$ -methyl <i>d</i> -glucoside - $\alpha$ -methyl <i>d</i> -mannoside	=	15,300 = $2R'_2$
31. $\alpha$ - <i>d</i> -gulose - $\alpha$ - <i>d</i> -galactose	=	-14,800 = $2R_3$
32. $\alpha$ -methyl <i>d</i> -gulose - $\alpha$ -methyl <i>d</i> -galactoside	=	-16,780 = $2R'_3$
33. $\beta$ -methyl <i>d</i> -gulose - $\beta$ -methyl <i>d</i> -galactoside	=	-16,020 = $2R'_3$
34. $\alpha$ - <i>d</i> -glucose - $\alpha$ - <i>d</i> -galactose	=	-5,600 = $2R_4$
35. $\beta$ - <i>d</i> -glucose - $\beta$ - <i>d</i> -galactose	=	-5,920 = $2R_4$
36. $\alpha$ -methyl <i>d</i> -glucoside - $\alpha$ -methyl <i>d</i> -galactoside	=	-6,750 = $2R'_4$
37. $\beta$ -methyl <i>d</i> -glucoside - $\beta$ -methyl <i>d</i> -galactoside	=	-6,220 = $2R'_4$
38. $\alpha$ - <i>d</i> -gulose + $\alpha$ - <i>d</i> -mannose - $2a_{OH}$	=	<sup>28</sup> -200 = $2R_5$
39. $\beta$ -methyl <i>d</i> -gulose + $\alpha$ -methyl <i>d</i> -mannoside	=	-800 = $2R'_5$

## PENTOSE SERIES

40. $\alpha$ -methyl <i>d</i> -xyloside - $\beta$ -methyl <i>d</i> -xyloside	=	+35,980 = $2a_{Me}$
41. $\beta$ -methyl <i>l</i> -arabinoside - $\alpha$ -methyl <i>l</i> -arabinoside	=	+37,420 = $2a_{Me}$
42. $\alpha$ - <i>d</i> -xylose - $\alpha$ - <i>d</i> -lyxose	=	+12,975 = $2r_2$
43. $\alpha$ -methyl <i>d</i> -xyloside - $\alpha$ -methyl <i>d</i> -lyxoside	=	+15,500 = $2r'_2$
44. - ( $\beta$ - <i>l</i> -arabinose + $\alpha$ - <i>d</i> -lyxose) + $2a_{OH}$	=	<sup>29</sup> -10,370 = $2r_3$
45. - ( $\alpha$ -methyl <i>l</i> -arabinoside + $\alpha$ -methyl <i>d</i> -lyxoside)	=	-12,580 = $2r'_3$
46. $\alpha$ - <i>d</i> -xylose - $\beta$ - <i>l</i> -arabinose	=	-12,450 = $2r_4$
47. $\alpha$ -methyl <i>d</i> -xyloside - $\beta$ -methyl <i>l</i> -arabinoside	=	-15,020 = $2r'_4$
48. $\beta$ -methyl <i>d</i> -xyloside - $\alpha$ -methyl <i>l</i> -arabinoside	=	-13,580 = $2r'_4$

<sup>28</sup> The sum of  $\alpha$ -*d*-gulose plus  $\alpha$ -*d*-mannose =  $2R_5 + 2a_{OH}$ . The numerical value (16,710) of  $2a_{OH}$  for the hexose sugars was determined by equations (24) and (25). The value of  $2R_5$  is obtained by subtracting 16,710 from the sum of the rotations of  $\alpha$ -*d*-gulose and  $\alpha$ -*d*-mannose.

<sup>29</sup> The sum of  $\beta$ -*l*-arabinose and  $\alpha$ -*d*-lyxose =  $-2r_3 + 2a_{OH} = -27,075$ . The experimental data are not available for the determination of  $2a_{OH}$  in the pentose series by means of the original van't Hoff method. Since Hudson has shown that the rotation of the first carbon atom  $a_{OH}$  for many sugars of different types is a nearly constant quantity, the numerical value for  $2a_{OH}$  (16,710) which was found for the hexose sugars is used in solving the equation for  $2r_3$ .



## 3. SUMMARY OF RESULTS

Hexose series		Pentose series	
Sugars	Methyl glycosides	Sugars	Methyl glycosides
$a_{OH} = +8,350$	$a_{Me} = +18,520$	$^1 a_{OH} = (+8,350)$	$a_{Me} = +18,375$
$R_2 = +7,450$	$R'_2 = +7,650$	$r_2 = +6,490$	$r'_2 = +7,750$
$R_3 = -7,400$	$R'_3 = -8,200$	$r_3 = -5,185$	$r'_3 = -6,290$
$R_4 = -2,875$	$R'_4 = -3,240$	$r_4 = -6,225$	$r'_4 = -7,150$
$R_5 = -100$	$R'_5 = -400$		

<sup>1</sup> See footnote 29, p. 1048..

## III. DISCUSSION OF RESULTS

A comparison of the rotations of the various asymmetric carbon atoms of the sugars with the corresponding rotations from the glycosides shows that in all cases the signs of the rotations agree, and that the numerical values are of the same order. This shows that the assumption that the sugars and methyl glycosides have similar structures was justified.

The rotations of the first three carbon atoms in the pentose series are of the same order as the rotations of the corresponding atoms in the hexose series, but the rotation of the fourth carbon atom in the pentose series differs widely from the rotation of the fourth carbon atom in the hexose series. The difference in rotation of the fourth carbon atom in the hexose and pentose series was previously made the basis for the allocation of a 1,4-ring structure to glucose by Hudson. Drew and Haworth<sup>31</sup> took exception to that allocation on the grounds that the rotations for the pentoside and hexoside structures might be different because in the former case the fourth carbon atom is joined to one symmetrical and one asymmetric carbon atom, while in the latter it is joined to two asymmetric carbon atoms. The further conception which was advanced by Drew and Haworth that the carbon atoms dominating the rotatory power of a sugar are those on either side of the ring oxygen atom is not substantiated since the rotations of the intermediate carbon atoms 2, 3, and 4 are greater than the adjacent carbon atom 5. The value for the rotatory power of the fifth carbon atom is very small. It can not be explained at the present time.

## 1. COMPARISON OF THE ROTATIONS OF THE METHYL GLYCOSIDES WITH THE ROTATIONS OF THE SUGARS

A comparison may now be made between the optical rotations of the various asymmetric carbon atoms in the sugars and the corresponding rotations in the methyl glycosides. The first point is that the rotatory power of the individual asymmetric carbon atoms in the methyl glycosides is greater than the rotatory power of the corresponding atoms in the sugars. This indicates that the substitution of a

<sup>31</sup> Drew and Haworth, J. Chem. Soc., p. 2303; 1926.

hydroxyl by a methyl group affects the rotations of all the asymmetric carbon atoms in the sugar. This concept is not in agreement with the rigid application of Hudson's second rule of isorotation. According to that rule the rotation of an  $\alpha$ -methyl glycoside of a  $d$ -sugar is written  $b + a_{Me}$  and that of the alpha form of the parent sugar  $b + a_{OH}$ . The difference is  $a_{Me} - a_{OH}$ . This difference was found to have a fairly constant value, but there are several marked exceptions which were noted by Hudson.<sup>32</sup> An explanation of these deviations can be derived from the values for the optical rotatory power of the various asymmetric carbon atoms in the sugars and glycosides.

According to the theory of optical superposition the difference in molecular rotations between the methyl glycosides and the corresponding sugars is given by the following equation:

$$(49). \quad [M']_D - [M]_D = (a_{Me} \pm R'_2 \pm R'_3 \pm R'_4 \pm R'_5) - (a_{OH} \pm R_2 \pm R_3 \pm R_4 \pm R_5).$$

Since the values of  $R'$  are larger than the values of  $R$  the value of  $[M']_D - [M]_D$  will vary slightly with the structure of the sugar. In the case of arabinose, the sugar which differed most, the equation<sup>33</sup> results in all the values of  $r'$  being of like sign and the values of  $r$  being different, this gives the maximum deviation from the true value of  $a_{Me} - a_{OH}$ .

In Table 2 the values for the difference in molecular rotation of the glycosides and sugars (Hudson's  $a_{Me} - a_{OH}$ ) are compared with the values of  $a_{Me} - a_{OH}$  as obtained from the van't Hoff equation (49). The value of  $a_{Me} - a_{OH}$  as obtained from  $1/2 (2a_{Me} - 2a_{OH}) =$  approximately 10,000.

TABLE 2

	$[M]_D$	Hudson's $a_{Me} - a_{OH}$ $[M']_D - [M]_D$ <sup>1</sup>	$a_{Me} - a_{OH}$ calculations from the van't Hoff theory
$\alpha$ -methyl $d$ -glucoside.....	+30,630	+10,290	+9,955
$\alpha$ - $d$ -glucose.....	+20,340		
$\beta$ -methyl $d$ -glucoside.....	-6,300	+9,720	+10,055
$\beta$ - $d$ -glucose.....	+3,420		
$\alpha$ -methyl $d$ -galactoside.....	+37,380	+11,460	+10,395
$\alpha$ - $d$ -galactose.....	+25,920		
$\beta$ -methyl $d$ -galactoside.....	-80	+9,440	+10,505
$\beta$ - $d$ -galactose.....	+9,360		
$\alpha$ -methyl $d$ -mannoside.....	+15,330	+9,930	+9,995
$\alpha$ - $d$ -mannose.....	+5,400		
$\alpha$ -methyl $d$ -guloside.....	+20,600	+9,500	+10,035
$\alpha$ - $d$ -gulose.....	+11,100		
$\alpha$ -methyl $d$ -xyloside.....	+25,240	+11,440	+10,000
$\alpha$ - $d$ -xylose.....	+13,800		
$\beta$ -methyl $l$ -arabinoside.....	+40,260	+14,010	+10,720
$\beta$ - $l$ -arabinose.....	+26,250		

<sup>1</sup> For the beta  $d$ -sugars the value given is  $-([M']_D - [M]_D)$ , but for the  $\beta$ - $l$ -arabinose the expression is positive, which arises from the nomenclature of the  $\alpha$  and  $\beta$  forms of the  $d$ - and  $l$ -sugars.

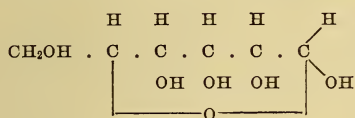
<sup>32</sup> Hudson, J. Am. Chem. Soc., 47 p. 271; 1925.

<sup>33</sup> The small letter  $r$  is used to designate the rotations in the pentose series.

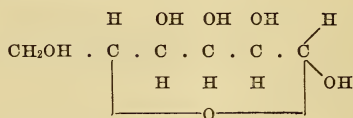
It is evident that the values calculated by the van't Hoff theory agree more closely with the value ( $a_{Me}-a_{OH}=10,000$ ) than the values calculated by Hudson. It should be emphasized that the rotations of the sugars and their corresponding methyl glycosides are given only approximately by Hudson's equations  $b \pm a_{OH}$  and  $b \pm a_{Me}$ . The value of  $b$  from the sugars may or may not equal the value of  $b$  from the methyl glycosides, depending upon the extent to which the differences in the optical rotations of the corresponding asymmetric carbon atoms in the sugars and methyl glycosides counteract each other. The optical rotations of substances of different structure, such as the sugars and glycosides, may be obtained approximately by Hudson's rules of isorotation, but it is apparent that more accurate data are obtained by comparing substances of like structure.

## 2. THE PREDICTION OF VALUES FOR THE ROTATION OF UNKNOWN SUGARS AND GLYCOSIDES

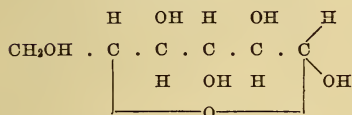
The values for the optical rotations of unknown aldohexose sugars may be obtained from the algebraic sum of the optical rotations of the different asymmetric carbon atoms in the *sugars*; while the optical rotations of the methyl glycosides may be obtained from the algebraic sum of the optical rotations of the different asymmetric carbon atoms in the *methyl glycosides*. The structures of the at present unknown hexose sugars are given by formulas VIII, IX, X, and XI.



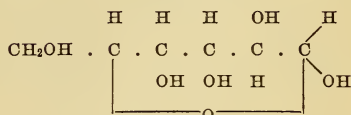
$\alpha$ -*d*-Allose (VIII)



$\alpha$ -*d*-Talose (IX)



$\alpha$ -*d*-Idose (IX)



$\alpha$ -*d*-Altrose (X)

The rotations of these unknown hexose sugars and glycosides are predicted from the following equations:

Substance		Predicted rotation			
		Alpha form		Beta form	
		$[M]_D$	$[\alpha]_D^{20}$	$[M]_D$	$[\alpha]_D^{20}$
<i>d</i> -allose.....	$= \pm a_{OH} + R_2 + R_3 + R_4 + R_5 =$	+5,425	+30	-11,275	-60
<i>d</i> -talose.....	$= \pm a_{OH} - R_2 - R_3 - R_4 + R_5 =$	+11,075	+60	-5,625	-30
<i>d</i> -idose.....	$= \pm a_{OH} - R_2 + R_3 - R_4 + R_5 =$	-3,725	-20	-20,425	-110
<i>d</i> -altrose.....	$= \pm a_{OH} - R_2 + R_3 + R_4 + R_5 =$	-9,475	-55	-26,175	-145
Methyl <i>d</i> -alloside.....	$= \pm a_{Me} + R'_2 + R'_3 + R'_4 + R'_5 =$	+14,330	+75	-22,710	-120
Methyl <i>d</i> -taloside.....	$= \pm a_{Me} - R'_2 - R'_3 - R'_4 + R'_5 =$	+21,910	+110	-15,130	-80
Methyl <i>d</i> -idoside.....	$= \pm a_{Me} - R'_2 + R'_3 - R'_4 + R'_5 =$	+5,510	+30	-31,530	-160
Methyl <i>d</i> -altroside.....	$= \pm a_{Me} - R'_2 + R'_3 + R'_4 + R'_5 =$	-970	-5	-38,010	-200



## IV. SUMMARY

1. The optical rotatory powers of all the asymmetric carbon atoms in the methyl glycosides and sugars from both the hexose and pentose series have been calculated from two entirely distinct sets of data. The rotations derived from the glycosides check approximately the rotations derived from the sugars, which indicates that the normal forms of  $\alpha$  and  $\beta$  glucose,  $\alpha$  and  $\beta$ -*d*-galactose,  $\alpha$ -*d*-mannose, and  $\alpha$ -*d*-gulose,  $\alpha$ -*d*-xylose,  $\alpha$ -*d*-lyxose, and  $\beta$ -*l*-arabinose have the same ring structures (1, 5) as the corresponding methyl glycosides.

2. The values for the optical rotatory power of the various asymmetric carbon atoms from the glycosides are slightly larger than the corresponding values from the sugars, which indicates that the replacement of the glycosidic hydroxyl in a sugar by a methoxy group affects the optical rotation of all the asymmetric carbon atoms.

3. The values for the optical rotatory powers of the different asymmetric carbon atoms should find wide application in the study of the sugars and glycosides. As examples of their utilization certain deviations in the values of  $a_{Me} - a_{OH}$  as obtained by the application of Hudson's rules of isorotation were explained; also values for the specific rotations of the at present unknown forms of *d*-allose, *d*-altrose, *d*-idose, and *d*-talose are predicted.

## ACKNOWLEDGMENTS

The writer wishes to extend his thanks to F. J. Bates, D. H. Brauns, and other members of the polarimetry section for many helpful suggestions and criticisms given by them in the preparation of this manuscript.

WASHINGTON, October 31, 1929.

