[CONTRIBUTION FROM THE POLARIMETRY SECTION OF THE BUREAU OF STANDARDS, UNITED STATES DEPARTMENT OF COMMERCE][1]

RELATIONS BETWEEN ROTATORY POWER AND STRUCTURE IN THE SUGAR GROUP. XIII.[2] A CLASSIFICATION OF VARIOUS SUBSTANCES OF THE MANNOSE AND RHAMNOSE SERIES ACCORDING TO RING TYPES

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RECEIVED MARCH 18, 1926 PUBLISHED MAY 5, 1926

Exceptional Comparative Rotations in the Mannose, Rhamnose and Lyxose Series

The rotations of mannose and its derivatives have been considered exceptional in the respect that the numerical relations which hold fairly closely among the rotations of a large number of substances of the sugar group[3] do not apply at all well in the mannose series. Ten years ago it was noticed[4] that the rotations of the α- and β-mannose penta-acetates differ by a smaller value ($\Delta[M]_D = 31{,}300$) than the normal (38,000). Later it was found[5] through an indirect experimental method involving corresponding solubility and rotation measurements that the rotation of the then unknown alpha form of mannose has a value, $[\alpha]_D = +34$, which is greatly different from that which had been calculated previously,[3] (+76); from the rotations of α- and β-glucose and β-mannose. Recently it was shown[6] that the rotation of chloro-acetyl mannose ($[\alpha]_D = +90$) measured by Brauns[7] is very much smaller than the value that is to be expected (about +125), from the rotations of the mannose penta-acetates. These measurements, which have led to the recognition of the exceptional character of the comparative rotations in the mannose series, seem substantially correct, as Levene[8] has confirmed the value for α-mannose penta-acetate and has found for α-mannose, which he succeeded in crystallizing for the first time, $[\alpha]_D = +30$ by direct measurement, and Brauns was careful to recrystallize his chloro-acetyl mannose to constant rotation. There can be no doubt that the deviations found in the mannose series are real and that in two cases, namely, for α-mannose and chloro-acetyl mannose, they are very large. The deviation of the penta-acetates is not so large.

It has been found[5] that the α- and β-forms of rhamnose and likewise

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[1] Published by permission of the Director of the Bureau of Standards.

[2] Article XII was published in THIS JOURNAL, **48**, 503 (1926).

[3] Hudson, *ibid.*, **31**, 66 (1909).

[4] Hudson and Dale, *ibid.*, **37**, 1280 (1915).

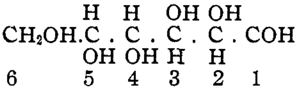
[5] Hudson and Yanovsky, *ibid.*, **39**, 1013 (1917).

[6] Hudson, *ibid.*, **46**, 462 (1924).

[7] Brauns, *ibid.*, **44**, 401 (1922).

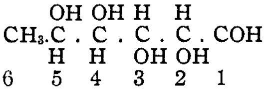
[8] Levene, *J. Biol. Chem.*, **57**, 329 (1923); **59**, 129, 141 (1924).

those of lyxose differ in rotation by much smaller amounts ($\Delta[M]_D$ = 10,100 and 6200, respectively) than the normal value (about 17,000 to 19,000), in which respect these sugars resemble mannose, the forms of which differ by 9200. Since mannose, rhamnose and lyxose have a like type of configuration for their carbon atoms 2, 3 and 4 (Irvine's nomenclature, see Formulas I, II and III) it was suggested that "the exceptional value of the difference for these sugars may be dependent upon this type of configuration."



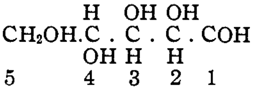
$$\underset{6}{\mathrm{CH_2OH}}.\underset{\substack{\mathrm{OH}\\5}}{\overset{\mathrm{H}}{\mathrm{C}}}\,.\,\underset{\substack{\mathrm{OH}\\4}}{\overset{\mathrm{H}}{\mathrm{C}}}\,.\,\underset{\substack{\mathrm{H}\\3}}{\overset{\mathrm{OH}}{\mathrm{C}}}\,.\,\underset{\substack{\mathrm{H}\\2}}{\overset{\mathrm{OH}}{\mathrm{C}}}\,.\,\underset{1}{\mathrm{COH}}$$

d-Mannose I



$$\underset{6}{\mathrm{CH_3}}.\underset{\substack{\mathrm{H}\\5}}{\overset{\mathrm{OH}}{\mathrm{C}}}\,.\,\underset{\substack{\mathrm{H}\\4}}{\overset{\mathrm{OH}}{\mathrm{C}}}\,.\,\underset{\substack{\mathrm{OH}\\3}}{\overset{\mathrm{H}}{\mathrm{C}}}\,.\,\underset{\substack{\mathrm{OH}\\2}}{\overset{\mathrm{H}}{\mathrm{C}}}\,.\,\underset{1}{\mathrm{COH}}$$

l-Rhamnose II



$$\underset{5}{\mathrm{CH_2OH}}.\underset{\substack{\mathrm{OH}\\4}}{\overset{\mathrm{H}}{\mathrm{C}}}\,.\,\underset{\substack{\mathrm{H}\\3}}{\overset{\mathrm{OH}}{\mathrm{C}}}\,.\,\underset{\substack{\mathrm{H}\\2}}{\overset{\mathrm{OH}}{\mathrm{C}}}\,.\,\underset{1}{\mathrm{COH}}$$

d-Lyxose III

Normal Comparative Rotations in These Series

It may seem on first thought that the foregoing summary of these exceptional comparative rotations can lead only to the conclusion that the quantitative relations between rotation and structure, which hold for so many sugars and various of their derivatives, completely fail to apply in the mannose, rhamnose and lyxose series. However, before such a view is accepted let there be considered the following additional facts which clearly show that the comparative rotations of many pairs of substances of these series have quite normal values. It has been remarked[9] that α-*d*-mannose (+30)[10] and α-methyl *d*-mannoside (+79), likewise α-*l*-rhamnose (—7.7) and α-methyl *l*-rhamnoside (—62.5) and also α-*d*-lyxose (+5.5), α-methyl *d*-lyxoside[11] (+59.5) and α-benzyl *d*-lyxoside (+80.5) differ in rotation by the normal values obtained from the analogous derivatives of glucose. Similarly, the rotations of α-methyl *d*-mannoside (+79) and α-methyl *l*-rhamnoside (—62.5) were shown[9] to differ by the normal amount obtained from β-methyl *d*-glucoside (—32.5) and β-methyl *d*-isorhamnoside (—55.2). The configuration of the group of carbon atoms 2, 3 and 4 of mannose, rhamnose and lyxose occurs also in α-glucoheptose and it was shown[9] that the rotation of β-methyl *d*-α-glucoheptoside (—74.6) differs normally from that of β-*d*-α-glucoheptose (—28.4) and that the α- and β-hexa-acetates of α-glucoheptose differ in rotation normally.[12] Lastly, it is recalled that Dale[13] has drawn attention to a remarkable agreement between the specific rotation of three isomeric triacetyl methyl *l*-rhamnosides that Fischer, Bergmann and Rabe[14] have described (designated by

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[9] Hudson, THIS JOURNAL, **47**, 268 (1925).

[10] In order to make the designation of isomers unmistakable the $[\alpha]_D$ value will be appended to the names of many substances in this article.

[11] Phelps and Hudson, THIS JOURNAL, **48**, 503 (1926).

[12] Hudson and Yanovsky, *ibid.*, **38**, 1575 (1916).

[13] Dale, *ibid.*, **46**, 1046 (1924).

[14] Fischer, Bergmann and Rabe, *Ber.*, **53**, 2362 (1920).

them as α, β and γ modifications, of $[\alpha]_D$ = —53.5, +45.7 and +28.0, respectively, in acetylene tetrachloride) and those of the three isomeric tetra-acetyl-methyl *d*-mannosides which he prepared. Reversing the signs of the rotations of the *l*-rhamnose derivatives gives the rotations in the *d*-rhamnose series and these are compared in Table I with the values of Dale's *d*-mannose derivatives. Such a comparison is logical because *d*-rhamnose and *d*-mannose have closely similar structures, the symmetric carbon 6 group of *d*-mannose (CH_2OH) becoming CH_3 in *d*-rhamnose. The parallelism of the rotations in the two series is striking and it caused Dale to designate his isomers by the same symbols that Fischer, Bergmann and Rabe used for the rhamnose derivatives, and in support of such designation Dale also observed that the correlated forms show close similarity in chemical reactions. Thus, the γ-isomers retain one combined acetyl group under drastic conditions of alkaline hydrolysis, a behavior that is unique among substances of the sugar group. Although the structures of these various isomers are not yet definitely known it seems very probable from the fact of the existence of Dale's parallelism that the correlated forms have like structures, including like ring structures and that the change of Carbon 6 from the grouping $CH_2OOC_2H_3$ to CH_3 has only a minor influence on the rotation of glycoside acetates. Such a conclusion conforms with the previous observation[9] that the rotations of methyl *d*-rhamnoside and methyl *d*-mannoside differ ($\Delta[M]_D$ = 4200, fairly closely) by the normal amount found from methyl *d*-glucoside and methyl *d*-isorhamnoside, namely, $\Delta[M]_D$ = 3500 in water. Apparently the analogous coefficient for the acetylated glycosides in chloroform is very much smaller and has approximately the same value for the three pairs of acetylated glycosides; in consequence, Dale's correlation has been readily detectable even in the absence of full knowledge of the structures.

TABLE I

DALE'S CORRELATION OF THE ROTATIONS OF THE ISOMERIC ACETYLATED METHYL RHAMNOSIDES AND MANNOSIDES

Substance	$[\alpha]_D$ of the isomers α-form	 β-form	 γ-form	Remarks
Methyl *l*-rhamnoside triacetate	−53.5	+45.7	+28.0	Measured in acetylene tetrachloride
Methyl *d*-rhamnoside triacetate	+53.5	−45.7	−28.0	Obtained by reversing signs
Methyl *d*-mannoside tetra-acetate	+49.1	−46.8	−26.6	Measured in chloroform

These numerous examples of normal comparative rotations in the mannose, rhamnose and lyxose series make it evident that the conclusion stated at the beginning of this section cannot be accepted. It is clearly proved, on the contrary, that along with many exceptional comparative rotations there are many in these series that are quite according to rule.

An Hypothesis Concerning the Occurrence of Derivatives of Various Ring Types in These Series[15]

The discussion of the data has now led by induction to an interesting problem. Why do some of the comparisons give normal values and others abnormal ones? In a specific case, for example, why is the rotation of α-mannose (30) normal with reference to that of α-methyl mannoside (79) but abnormal with respect to that of β-mannose (—17)? When the problem is thus reduced to specific formulation, an hypothesis that is both simple and probable almost suggests itself. *Let it be assumed that among the known derivatives of mannose there occur substances of various ring types and that substances belonging to the same ring type show normal comparative rotations.* Since α-mannose and α-methyl mannoside differ normally in rotation, it follows from this hypothesis that they have the same ring, for example, 1,5, but since α- and β-mannose differ abnormally it follows that β-mannose possesses some other ring, for example, 1,4. Such a view does not today seem improbable. The view of earlier days that the 1,4-butylene ring is to be assumed in the sugar group to the exclusion of other rings, which arose from the fact that the earlier known lactones of the aldonic acids appear to be of this structure, has been modified by subsequent experimental researches. The discovery of a third methyl glucoside (the sirupy, distillable so-called γ-form of Fischer[16]), of the two forms of gluconic and of mannonic lactone,[17] of derivatives of the so-called γ-forms of glucose,[18] fructose,[19] mannose[20] and arabinose,[21] of the four crystalline galactose penta-acetates,[22] of the second form of α-mannoheptose hexa-acetate which must differ in ring structure from the first form,[23] and the evidence that methyl xyloside,[24] arabinoside[25] and galactoside[26] possess 1,5-amylene rings and that two tetramethyl mannonic lactones exist,[27] show that various ring types occur in the sugar group. Doubtless certain types of configuration strongly favor certain ring forms, but it must be expected that some sugar structures may readily form sev-

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[15] This hypothesis was stated in Article VII of this series [Hudson, This Journal, **47**, 272 (1925)] on the basis of the experimental evidence there advanced.

[16] Fischer, *Ber.*, **47**, 1980 (1914).

[17] Nef, *Ann.*, **403**, 331 (1914).

[18] Irvine, Fyfe and Hogg, *J. Chem. Soc.*, **107**, 524 (1915). Pacsu, *Ber.*, **58**, 1455 (1925).

[19] Irvine and Robertson, *J. Chem. Soc.*, **109**, 1305 (1916).

[20] Irvine and Burt, *ibid.*, **125**, 1343 (1924).

[21] Baker and Haworth, *ibid.*, **127**, 365 (1925).

[22] Hudson and Johnson, This Journal, **38**, 1223 (1916).

[23] Hudson and Monroe, *ibid.*, **46**, 979 (1924).

[24] Hirst and Purves, *J. Chem. Soc.*, **123**, 1352 (1923).

[25] Hirst and Robertson, *ibid.*, **127**, 358 (1925).

[26] Pryde, *ibid.*, **123**, 1808 (1923).

[27] Levene and Meyer, *J. Biol. Chem.*, **60**, 167 (1924).

eral types of rings. There is, indeed, nothing improbable in the view that mannose can crystallize from solution in two forms of different ring structures. The hypothesis will now be applied in union with Dale's correlation to obtain a classification of various derivatives of mannose and rhamnose according to ring types. It will be shown that the substances fall into three groups the rings of which will be provisionally designated 1,A, 1,B and 1,C.

Ring Types in the Mannose and Rhamnose Series

Substances of the 1,A Ring Type.—Let the ring of α-methyl *d*-mannoside (79) be denoted 1,A to distinguish it from other rings, leaving the allocation of A for subsequent consideration. Referring to the aldehyde formula for mannose (I), the designation of the ring as (1,A) signifies that it is formed between Carbon 1 and some other carbon of the molecule which will be designated provisionally as[28] A. Since α-mannose (30) differs in rotation from α-methyl mannoside (1,A) (79) by the normal amount, as has been shown,[9] the 1,A ring must be assigned to this form of the sugar. The molecular rotation of α-methyl *d*-mannoside (1,A) is to be written $b_{\text{mannose (1,A)}} + a_{\text{Me}} = (79)\ (194) = +15{,}300$, where $b_{\text{mannose (1,A)}}$ denotes the rotation of the chain of mannose of this ring type and a_{Me} is the rotation of the end asymmetric carbon atom of the methyl glycosides, which has been shown[29] to have the value +18,500. Substituting, there is obtained $b_{\text{mannose (1,A)}} = -3200$ *in water.* From this coefficient the rotations in water of the α- and β-forms of mannose (1,A) and the β-form of methyl mannoside (1,A) may be calculated in the usual manner, as shown in the first part of Table II. The coefficient a_{OH} has been shown[30] to have the value +8500.

TABLE II

CALCULATED ROTATIONS OF SUBSTANCES OF THE 1,A-RING TYPE IN THE MANNOSE SERIES

(Coefficients: $a_{\text{OH}} = 8500$, $a_{\text{Me}} = 18{,}500$, $A_{\text{Ac}} = 19{,}100$, $A_{\text{Me}} = 26{,}900$, $\text{A}_{\text{Cl}} = 39{,}800$, $b_{\text{mannose (1,A)}} = -3200$, $B_{\text{mannose (1,A)}} = -9100$.)

Substance	Molecular rotation[a]	Mol. wt.	$[\alpha]_D$ calcd.
α-*d*-Mannose (1,A)	$b_{\text{mn. (1,A)}} + a_{\text{OH}} = -3{,}200 + 8{,}500$	180	$+29^b$
β-*d*-Mannose (1,A)	$b_{\text{mn. (1,A)}} - a_{\text{OH}} = -3{,}200 - 8{,}500$	180	-65^b
β-Methyl *d*-mannoside (1,A)	$b_{\text{mn. (1,A)}} - a_{\text{Me}} = -3{,}200 - 18{,}500$	194	-112^b
α-*d*-Mannose penta-acetate (1,A)	$B_{\text{mn. (1,A)}} + A_{\text{Ac}} = -9{,}100 + 19{,}100$	390	$+26^c$
β-*d*-Mannose penta-acetate (1,A)	$B_{\text{mn. (1,A)}} - A_{\text{Ac}} = -9{,}100 - 19{,}100$	390	-72^c
β-Methyl *d*-mannoside tetra-acetate (1,A)	$B_{\text{mn. (1,A)}} - A_{\text{Me}} = -9{,}100 - 26{,}900$	362	-99^c
α-Chloro-acetyl *d*-mannose (1,A)	$B_{\text{mn. (1,A)}} + \text{A}_{\text{Cl}} = -9{,}100 + 39{,}800$	367	$+84^c$

[a] "Mannose" is abbreviated to "mn." [b] In water. [c] In chloroform.

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[28] This follows the proposal of Bergmann and Miekeley [*Ber.*, **54**, 2150 (1921)] for designating rings in the sugar group.

[29] Ref. 9, p. 270.

[30] Ref. 6, p. 488.

Let the acetyl derivatives in the mannose series now be considered. The acetylation of α-methyl mannoside (+79), to which the 1,A ring has been assigned, was found by Dale[13] to yield almost quantitatively the beautifully crystalline and pure α-methyl *d*-mannoside tetra-acetate (+49.1). The 1,A ring is assigned to this substance because it is held that the acetylation of a methyl glycoside does not shift the ring. The evidence for this view is the well recognized general observation that the acetylation of a methyl glycoside followed by the de-acetylation of the resulting acetate gives back the original glycoside. The molecular rotation of α-methyl *d*-mannoside tetra-acetate (1,A) is written $B_{\text{mannose (1,A)}} + A_{\text{Me}} = (49.1)(362) = +17{,}800$, where $B_{\text{mannose (1,A)}}$ denotes the rotation of the acetylated chain of mannose of this (1,A) ring type. Substituting the known value[6] of A_{Me} (26,900) gives $B_{\text{mannose (1,A)}} =$ *—9100 in chloroform.* From this value of the acetylated chain the rotations of the corresponding α- and β-mannose penta-acetates, of β-methyl mannoside tetra-acetate and α-chloro-acetyl mannose, all of the 1,A-ring type, may be calculated in the usual way, as shown in detail in the second part of Table II. The value of A_{Ac} has been shown[6] to be 19,100. The value of A_{Cl} used heretofore[31] was 37,900, but the recent revision of the rotation of α-chloro-acetyl *d*-xylose by Brauns[32] and that of α-chloro-acetyl lactose[33] lead to the revised value $A_{\text{Cl}} =$ *39,800 in chloroform*, as the average of A_{Cl} from the rotations of the α-chloro-acetyl derivatives of xylose, glucose, lactose, maltose and cellobiose.

Passing now to the *l*-rhamnose series, it is recalled that Dale's parallelism is strong evidence that α-methyl *l*-rhamnoside triacetate (—53.5) possesses the same ring as α-methyl *d*-mannoside tetra-acetate (+49.1), namely, the assigned 1,A ring. Since this triacetate results from the acetylation of α-methyl *l*-rhamnoside (—62.5), the same 1,A ring must be assigned to the latter. If the rotation of the *l*-rhamnose chain, of the 1,A-ring type is $b_{l\text{-rhamnose (1,A)}}$, the molecular rotation of α-methyl *l*-rhamnoside is written $b_{l\text{-rhamnose (1,A)}} - a_{\text{Me}}{}^{34} = (-62.5)(178) = -11{,}100$, and hence $b_{l\text{-rhamnose (1,A)}} =$ *+7400 in water.* In like manner from the rotation of the triacetate (—53.5) in acetylene tetrachloride there is obtained the rotation of the acetylated rhamnose chain of 1,A-ring type, $B_{l\text{-rhamnose (1,A)}} =$ *+10,600*, as a provisional value for either acetylene tetrachloride or chloroform solution. It would be preferable to know the rotation of the triacetate in chloroform, but it has been shown[6] that acetyl sugar derivatives rotate nearly the same in the two solvents. From these coefficients there have been calculated the rotations of various members of the

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[31] Hudson and Phelps, THIS JOURNAL, **46**, 2592 (1924).

[32] Brauns, *ibid.*, **47**, 1280 (1925).

[33] Hudson and Kunz, *ibid.*, **47**, 2052 (1925).

[34] The minus sign is here used for an α-glycoside because of the fact that the sugar belongs in the *l*-series.

l-rhamnose (1,A) series in the usual way. The calculations are analogous to those of Table II and the details may accordingly be omitted; the resulting rotations are recorded in Table III in the column pertaining to the 1,A ring.

Substances of 1,B-Ring Type.—It has already been shown that the hypothesis leads clearly to the conclusion that β-mannose (—17) differs from α-mannose (1,A)(+30) in ring structure. Let its ring be designated (1,B), leaving the allocation of B for later consideration. Since its ring is different from that of α-mannose, the mutarotation of α- and β-mannose is not as simple a reaction as it has been supposed to be (the establishment of equilibrium between an α- and a β-form of the same ring type) but involves a change in ring structure. These forms of mannose have in the past been named α and β because of the directions of their mutarotation, but it is now seen that their difference of ring structure makes this evidence inapplicable. The correlation shown earlier in this article between α-mannose (+30) and α-methyl mannoside (+79) proves, however, that the naming of this α-form is correct. If it were a β-form of the sugar its correlated methyl mannoside would be less dextrorotatory than it, whereas the reverse is the case, which indicates that the compared substances are of the α-series.[35]

The question whether the so-called β-mannose (—17), of the new 1,B-ring structure, is an α- or β-form remains to be decided. It can be shown by the following evidence that it is the true beta isomer of its ring type. If it is assumed that it is a beta form its molecular rotation is to be written $b_{\text{mannose (1,B)}} - a_{\text{OH}} = (-17)\ (180) = -3100$ and it follows that $b_{\text{mannose (1,B)}} = 5400$ *in water.* The rotation of the corresponding β-methyl mannoside (1,B) is to be written $b_{\text{mannose (1,B)}} - a_{\text{Me}} = 5400 - 18{,}500 = -13{,}100$ and hence its $[\alpha]_D = -(13{,}100)/194 = -68$. Only one methyl mannoside is known, the alpha form of the 1,A ring, hence the calculated rotation refers at present to a hypothetical compound. It can be shown, however, that the corresponding rhamnoside is a known substance. The rotation of β-methyl *d*-rhamnoside (1,B) must be less in the dextro direction than that of β-methyl *d*-mannoside (1,B) by 4200, since this is

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[35] Irvine and Moodie [*J. Chem. Soc.*, **87**, 1462 (1905)] have proved that α-methyl mannoside (79) is indeed an α-glycoside. They prepared its tetramethyl ether ($[\alpha]_D = 43$ in water) and by hydrolyzing this substance produced tetramethyl mannose ($[\alpha]_D = 1$ in water, final) and concluded that the greater dextrorotation of the former shows that it and its parent substance, methyl mannoside (79), belong to the α-series. Purdie and Young [*ibid.*, **89**, 1194 (1906)] have proved that α-methyl *l*-rhamnoside (—62.5) belongs in the α-series through their observation that its trimethyl ether ($[\alpha]_D = -16$ in water) is more levorotatory than the corresponding trimethyl *l*-rhamnose ($[\alpha]_D = 25$ in water, final). The present results lead independently to the same allocations and in addition they correlate the structures of α-methyl mannoside (79), α-methyl rhamnoside (—62.5), α-mannose (30) and α-rhamnose (—7.7) as being of the same ring type (1,A) (see Table III).

the difference previously found for the change from a *d*-mannoside to a *d*-rhamnoside.[9] The rotation of β-methyl *l*-rhamnoside (1,B) must have the same magnitude but opposite sign and is accordingly to be written $[M]_D$ = —(—13,100—4200) = 17,300, from which it follows that its $[\alpha]_D$ = 17,300/178 = 97 in water. This calculated value agrees closely with the rotation (95.2) that Fischer, Bergmann and Rabe[14] have recorded for a substance which they have designated β-methyl *l*-rhamnoside. The fact that there exists this rhamnoside having the rotation that is calculated from that of β-mannose (1,B)(—17) on the assumption that the latter is a true beta sugar proves the assumption to be correct and indicates also that the 1,B ring is present in what may now be designated systematically the β-methyl *l*-rhamnoside (1,B) (95) of Fischer, Bergmann and Rabe.

These assignments lead to an interesting conclusion concerning certain acetyl derivatives of the substances. Fischer, Bergmann and Rabe obtained their β-methyl *l*-rhamnoside (1,B) by the de-acetylation of its triacetate and the latter may, therefore, now be classified as β-methyl *l*-rhamnoside (1,B) tri-acetate (+45.7 in acetylene tetrachloride, see Table I), and its rotation written $B_{l\text{-rhamnose (1,B)}} + A_{\text{Me}}$ = (45.7) (304) = +13,900, from which it follows that $B_{l\text{-rhamnose (1,B)}}$ = *—13,000.* By Dale's correlation it is indicated that his β-methyl-*d*-mannoside tetra-acetate (—46.8) is the ring structural analog of the now allocated β-methyl *l*-rhamnoside (1,B) triacetate (+45.7) and is, therefore, to be designated β-methyl *d*-mannoside (1,B) tetra-acetate (—46.8). If this last assignment is correct the de-acetylation of this acetate should yield β-methyl *d*-mannoside (1,B), the $[\alpha]_D$ value of which has been calculated in the preceding paragraph to be —68 in water. This compound is now unknown but these relations indicate a known acetate from which its production by de-acetylation can be expected.

From the observed rotation of β-methyl *l*-rhamnoside (1,B), $b_{l\text{-rhamnose (1,B)}} + a_{\text{Me}}$ = +16,900, which has just been shown to agree closely with the calculated value, there is obtained $b_{l\text{-rhamnose (1,B)}}$ = *—1600 in water.* By Dale's measurement of the rotation of β-methyl *d*-mannoside (1,B) tetra-acetate in chloroform, $B_{\text{mannose (1,B)}} - A_{\text{Me}}$ = (—46.8)(362) = —16,900, from which it follows that $B_{\text{mannose (1,B)}}$ = *+10,000 in chloroform.* The four coefficients obtained in this section have now been used for the calculation in the customary way of the specific rotations of the usual substances of the *d*-mannose and *l*-rhamnose series of 1,B-ring type, and the results are recorded in Table III under the column for this ring type.

Substances of 1,C-Ring Type.—Fischer, Bergmann and Rabe's so-called "γ-methyl *l*-rhamnoside triacetate" (+28.0) and Dale's "γ-methyl *d*-mannoside tetra-acetate" (—26.6) must be assigned like ring and stereochemical structures on account of Dale's correlation and their like chemical behavior on alkaline hydrolysis, as has been mentioned. Their rotations are very different from those to be expected for compounds of the 1,A- or 1,B-ring type and they are accordingly assigned a new ring, 1,C. It is not known whether they are *α*- or *β*-derivatives, but since they were both produced from bromo-acetyl sugars by the Koenigs and Knorr reaction they will here be assumed to belong in the beta series. From the rotation, then, of what may now be designated *β*-methyl *l*-rhamnoside (1,C) triacetate (+28.0), $B_{l\text{-rhamnose (1,C)}} + A_{\text{Me}} = (28.0)(304) = +8500$, there is obtained $B_{l\text{-rhamnose (1,C)}} = -18{,}400$. From the

TABLE III

CLASSIFICATION OF SUBSTANCES OF THE MANNOSE AND RHAMNOSE SERIES

		Specific rotation, $[\alpha]_D$					
		Ring[b] 1,A (= 1,5)		Ring 1,B (= 1,4)		Ring 1,C (= 1,3)	
Substance[a]	Mol. wt.	Calcd.	Obs.	Calcd.	Obs.	Calcd.	Obs.
α-*d*-Mannose	180	+29	+30	+77	...	.....	....
β-*d*-Mannose	180	−65	....	[−17]	−17	.....	....
α-Methyl *d*-mannoside	194	[+79]	+79	+123	....	.....	....
β-Methyl *d*-mannoside	194	−112	....	−68	....	.....	....
α-Methyl *d*-mannoside tetra-acetate	362	[+49.1]	+49.1	+102	....	+122	....
β-Methyl *d*-mannoside tetra-acetate	362	−99	....	[−46.8]	−46.8	[−26.6]	−26.6
α-*d*-Mannose penta-acetate	390	+26	....	+75	....	+93	....
β-*d*-Mannose penta-acetate	390	−72	....	−23	−25	−5	....
α-Chloro-acetyl *d*-mannose	367	+84	+90	+136	....	+156	....
α-*l*-Rhamnose	164	−7	−7.7	−62	....	.....	....
β-*l*-Rhamnose	164	+97	....	+42	....	.....	....
α-Methyl *l*-rhamnoside	178	[−62.5]	−62.5	−113	....	.....	....
β-Methyl *l*-rhamnoside	178	+146	....	[+95.2]	+95.2	.....	....
α-Methyl *l*-rhamnoside triacetate	304	[−53.5]	−53.5	−131	....	−149	....
β-Methyl *l*-rhamnoside triacetate	304	+123	....	[+45.7]	+45.7	[+28]	+28
α-*l*-Rhamnose tetra-acetate	332	−26	....	−97	....	−113	....
β-*l*-Rhamnose tetra-acetate	332	+89	....	+18	+13.7	+2	....

[a] Water is the solvent for mannose, rhamnose and their methyl glycosides, while the rotations of the acetylated mannose compounds refer to chloroform solution, and those of the acetylated rhamnose derivatives to acetylene tetra-chloride solution.

[b] It will be observed that structural positions for the rings are indicated in the heading. These are proved in the next article but are recorded here so that the table may serve for permanent reference.

TABLE IV

VALUES OF SOME NEW COEFFICIENTS FROM THE MANNOSE AND RHAMNOSE SERIES

	Coefficient (molecular rotation)			
Chain	Ring 1,A (= 1,5)	Ring 1,B (= 1,4)	Ring 1,C (= 1,3)	Solvent
$b_{d\text{-mannose}}$	− 3,200	+ 5,400	....	Water
$b_{l\text{-rhamnose}}$	+ 7,400	− 1,600	....	Water
$B_{d\text{-mannose}}$	− 9,100	+10,000	+17,300	Chloroform
$B_{l\text{-rhamnose}}$	+10,600	−13,000	−18,400	Note[a]

[a] These three values are obtained from measurements partly in chloroform and partly in acetylene tetra-chloride and should be regarded as provisional on this account.

rotation of the corresponding β-methyl *d*-mannoside (1,C) tetra-acetate (—26.6), $B_{\text{mannose (1,C)}} - A_{\text{Me}} = (-26.6)(362) = -9600$, there is obtained $B_{\text{mannose (1,C)}} = +17{,}300$ in chloroform. These coefficients have now been used in the calculation of the rotations of several acetyl derivatives of mannose and rhamnose, of the 1,C-ring type, by the customary formulas and the results appear in Table III.

Further Structural Assignments in the Mannose and Rhamnose Series

By inspection of Table III it is evident that Brauns' chloro-acetyl *d*-mannose (+90) is to be assigned the structure α-chloro-acetyl *d*-mannose (1,A), and that Fischer and Oetker's[36] *d*-mannose penta-acetate (—25) is β-*d*-mannose (1,B) penta-acetate. This is an interesting conclusion because it is a fact that this penta-acetate results from the acetylation of β-mannose (1,B)(—17) at low temperature with acetic anhydride and pyridine or zinc chloride.[4] Evidently under these conditions acetylation of β-mannose (1,B) takes place substantially without isomeric change on Carbon 1 or ring shifting. It is recalled that Behrend[37] found by this method of acetylation that the α- and β-forms of glucose yield the respective α- and β-penta-acetates of glucose and he correlated the substances in this way. The present results show that Behrend's method of correlation holds for β-mannose (1,B)(—17) and its penta-acetate (—25). Whether it likewise holds for α-mannose (1,A) (+30) the present results do not indicate. From this substance Levene[8] has obtained the so-called α-mannose penta-acetate (+55) of Hudson and Dale,[4] but it is evident from an inspection of Table III that a penta-acetate of this rotation does not fit in the system. It would be expected that α-mannose (1,A) penta-acetate would rotate +26. For the present the acetate of +55 rotation will be left unclassified; the determination of its ring form and even the question whether it may not be a mixture of substances remain outstanding problems.

The *l*-rhamnose tetra-acetate (+13.75 in acetylene tetra chloride) that has been described by Fischer, Bergmann and Rabe[14] fits in the table as β-*l*-rhamnose (1,B) tetra-acetate and the known crystalline form of *l*-rhamnose (—7.7) as α-*l*-rhamnose (1,A). Both these substances thus correspond in structure with known analogous members of the mannose series.

Dale[13] has shown that β-methyl *d*-mannoside (1,C) tetra-acetate changes very rapidly at room temperature in methyl alcoholic solution, provided that a trace of hydrogen chloride is present, to β-methyl *d*-mannoside (1,B) tetra-acetate. The present knowledge of the structures of these substances leads to the conclusion that this change consists in a shifting of the ring to

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[36] Fischer and Oetker, *Ber.*, **46**, 4029 (1913).

[37] Behrend, *Ann.*, **353**, 109 (1907). Behrend and Roth, *Ann.*, **331**, 369 (1904).

another carbon atom (change from C to B) and a simultaneous shifting of an acetyl group from B to C. In other words, this reaction involves a migration of an acetyl group and a shifting of a ring. It may serve to illustrate what remarkable changes some of the sugar structures can undergo with great ease. Irvine and Burt[20] have observed that tetramethyl-γ-methyl mannoside readily rearranges to tetramethyl-α-methyl mannoside, which seems likewise to involve a shifting of the ring and a migration of a methoxy group.

Summary

A review of the experimental data shows that while many pairs of substances in the mannose, rhamnose and lyxose series exhibit comparative rotation differences that are abnormal with respect to the similar differences in the glucose series, which are regarded as the normal values, many other pairs in these series show quite normal comparative rotations. These facts lead to the hypothesis 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). Through this hypothesis it becomes possible to allocate most of the known forms and derivatives of mannose and rhamnose to three types of ring structure which are here provisionally designated 1,A, 1,B and 1,C, respectively. The proof of the precise position of these rings, which involves considerations that are not necessary to the present proof of the classifications according to ring types, follows in the next article.

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[CONTRIBUTION FROM THE POLARIMETRY SECTION OF THE BUREAU OF STANDARDS, UNITED STATES DEPARTMENT OF COMMERCE][1]

RELATIONS BETWEEN ROTATORY POWER AND STRUCTURE IN THE SUGAR GROUP. XIV.[2] THE DETERMINATION OF RING STRUCTURES IN THE GLUCOSE, MANNOSE AND RHAMNOSE SERIES

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RECEIVED MARCH 18, 1926 PUBLISHED MAY 5, 1926

The classifications according to ring types in the mannose and rhamnose series that have been shown in the preceding article can be extended to other sugar series. It has resulted that the correlations which can be established when the members of the glucose series are brought into the classification furnish a clear proof that the structural positions of the rings which have been provisionally designated 1,A, 1,B and 1,C are 1,5, 1,4

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[1] Published by permission of the Director of the Bureau of Standards.

[2] Article XIII immediately precedes this.