

(76%) of b. p. 155–157°;  $d^{20}$ , 1.3539, and  $n^{20D}$  of 1.53694, together with some high boiling fractions;  $M_D$  (calcd.), 58.92;  $M_D$  (found), 59.26.

*Anal.* Calcd. for  $C_{11}H_{18}O_2Br$ : Br, 31.11. Found: Br, 31.16, 31.25, 31.09.

**2,5-Dimethyltetrahydrofuran.**—Redistilled Eastman Kodak Co. 2,5-dimethylfuran of b. p. 91–94° (10 parts) was reduced in the presence of Raney nickel (1 part) in a high pressure hydrogenator as in the case of the furan itself. However, high temperatures must be avoided during the hydrogenation. The reduced product boiled from 89–91° (uncorr.), which is somewhat less than the boiling points reported for the compound prepared by other methods.

**$\alpha$ -Methyl- $\delta$ -chloroamyl Acetate.**—A mixture of 106 g. (1.06 mole) of 2,5-dimethyltetrahydrofuran and 204 g. (2.83 mole) of acetyl chloride was allowed to react in the presence of 10 mg. of zinc chloride. The mixture was then refluxed for one-half hour, carefully hydrolyzed and then worked up in the usual way, giving 145 g. of the chloro ester, a yield of 77%. The product had a b. p. of 85.5–87° at 15 mm. or 94–95° at 20 mm.;  $d^{20}$ , 1.0132;  $n^{20D}$  1.43288;  $M_D$  (calcd.), 45.74;  $M_D$  (found), 45.67.

*Anal.* Calcd. for  $C_8H_{16}O_2Cl$ : Cl, 19.87. Found: Cl, 20.16, 20.30.

**$\alpha$ -Methyl- $\delta$ -bromoamyl Acetate.**—The reaction of 50 g. (0.5 mole) of 2,5-dimethyltetrahydrofuran, 70 g. (0.57 mole) of acetyl bromide and 5 mg. of zinc chloride took place with considerable violence. From the mixture 75 g. of product of b. p. 105–107° at 20 mm. was obtained. Although several redistillations were made, no ester could

be obtained whose analysis corresponded to pure  $\alpha$ -methyl- $\delta$ -bromoamyl acetate, as in the case of the  $\delta$ -bromobutyl acetate, probably on account of the presence of dibromide.

*Anal.* Calcd. for  $C_8H_{16}O_2Br$ : Br, 35.85. Found: Br, 38.44, 38.37, 38.60.

**Tetramethylene Chlorohydrin.**—A mixture of 60 g. of  $\delta$ -chlorobutyl acetate, 120 cc. of methanol and 0.7 cc. of concd. hydrochloric acid was warmed at 40° for three and a half days. At the end of this period most of the methyl acetate and methanol was removed by distillation under diminished pressure, being careful not to overheat the residue, since the tetramethylene chlorohydrin gives hydrogen chloride and tetrahydrofuran when heated.<sup>9</sup> A further quantity of 60 cc. of methanol was then added to the residue, and this mixture was again heated at 50° for six hours and then at 30° for seventeen, when the mixture was distilled, giving 36.5 g. of the  $\delta$ -chlorobutanol of b. p. 64–65° at 3 mm., an 80% yield.

### Summary

Acetyl chloride will react with tetrahydrofuran to give  $\delta$ -chlorobutyl acetate with certain other products. The yield of  $\delta$ -chloro ester is improved by the addition of a trace of zinc chloride. Other acyl halides react similarly both with the tetrahydrofuran and 2,5-dimethyltetrahydrofuran.

The work is being continued and extended.

(9) Kirner and Richter, *THIS JOURNAL*, **51**, 2505 (1929).

TROY, N. Y.

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[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY OF PRINCETON UNIVERSITY]

## Studies in the Ketone Sugar Series. IX. The Validity of Hudson's Rules of Isorotation in the *l*-Sorbose Series. $\beta$ -Ethylsorbose and its Tetraacetate

BY EUGENE PACSU

By the discovery<sup>1</sup> of the true  $\alpha$ -pentaacetylfructose <2,6> and by the subsequent<sup>2</sup> interconversion of this substance and the  $\beta$ -pentaacetate, there has become known for the first time in the ketose group an  $\alpha,\beta$ -pair, the mutual relationship of the members of which has been definitely proved. According to Hudson's rules of isorotation, the different  $a_x$  constants that may be calculated from this true  $\alpha,\beta$ -pair and the  $\beta$ -derivatives of *d*-fructose should be of general applicability for all the ketoses and their derivatives. These  $a_x$  constants, with the exception of  $a_{OH}$  for chloroform solution, have been found to be throughout larger than the corresponding  $A_x$  constants in the aldose series. Difference between the values of

$a_x$  and  $A_x$  is, of course, to be expected, since the constants represent, in the latter series, the molecular rotations of carbon atom 1, H-C-X, whereas in the ketose series they express the rotational values of carbon atom 2, ROH<sub>2</sub>C-C-X, where R designates a hydrogen atom in the free ketoses and their glycosides, and an acetyl group in the acetylated products. According to the rules of isorotation, the difference in structure or configuration of the basal chain,  $b_x$ , of the ketoses should not alter to any large extent the values of the  $a_x$  constants. If large deviations be found, it would not necessarily follow that the principle of optical superposition as applied by Hudson is of no general validity, because it is possible that the deviating "constants" have been calculated from the molecular rotations of com-

(1) Pacsu and Cramer, *THIS JOURNAL*, **57**, 1944 (1935).

(2) Cramer and Pacsu, *ibid.*, **59**, 711 (1937).

TABLE I  
*l*-SORBOSE AND ITS DERIVATIVES WITH THEIR MELTING POINTS, MOLECULAR WEIGHTS, SPECIFIC AND MOLECULAR ROTATIONS, AND CALCULATED ROTATIONS

Substance <sup>a</sup>	M. p., °C.	Mol. wt.	[α] <sub>D</sub>	Mol. rot.	[α] <sub>D</sub> calcd. from	
					$a_x + b_{\alpha,\beta}$	$a_x + b_{\alpha}$ and $a_x + b_{\beta}$
α-Sorbose tetraacetate	100.8	348	-19.4	-6,750	-36.8	-17.2
α-Sorbose pentaacetate	97.0	390	-56.4	-22,000	-71.6	-54.1
α-Acetochlorosorbose	67.0	367	-83.4	-30,600	-108.5	-89.9
α-Methylsorbose tetraacetate	89.5	362	-52.6	-19,100	-71.7	[-52.6]
α-Ethylsorbose tetraacetate	75.0	376	-54.6	-20,500	-76.4	-58.2
β-Sorbose pentaacetate	113.8	390	74.4	29,000	96.8	79.4
β-Methylsorbose tetraacetate	75.0	362	79.8	28,900	98.7	[79.8]
β-Ethylsorbose tetraacetate	86.0	376	82.7	31,000	102.5	84.3
α-Methylsorbose	122.0	194	-88.7	-17,200	-134.0	[-88.7]
α-Ethylsorbose	116.0	208	-73.9	-15,400	-120.0	-77.4
β-Methylsorbose	106.2	194	39.0	7,600	84.5	[39.0]
β-Ethylsorbose	...	208	31.0	6,500	73.5	31.2
α-Sorbose	161.0	180	-43.1	-7,850	-92.5	-43.3

<sup>a</sup> The rotations of the acetates refer to chloroform solutions and those of the other substances to aqueous solutions.

pounds which are not true α,β-stereoisomeric pairs. The history of the application of Hudson's rules in sugar chemistry shows that such errors frequently have been made in the past. Only a few years ago it was discovered<sup>3</sup> that neither "α"-pentaacetylfructose nor "α"-chloroacetylfructose possesses any ring structure in its molecule. Yet, the rotations of these compounds had been used together with those of the true β-compounds for calculations at a time when the correctness of the assigned structural formulas of these "α"-compounds had not been questioned. Also in the aldose series it recently has been shown<sup>4</sup> that the α-ethyl- and α-benzylthioglucosides are furanosides and not the diastereoisomers of the pyranoid β-compounds as earlier workers had believed.

In view of all these recent cases, where the apparent invalidity of Hudson's rules has been traced back to erroneous assumptions regarding the chemical structures of the "α,β-pairs," it appears to be necessary to ascertain the stereochemical relationship of the constituents of a reference pair, before using their rotational data for computations. This seems to be of special importance in instances where the results of the calculations indicate a failure of the principle of optical superposition. Such a failure of Hudson's rules has been recorded by Schlubach and Graefe<sup>5</sup> in their paper dealing with the preparation of new *l*-sorbose derivatives and with the numerical relationship of rotations in the *l*-sorbose series.

From the known α-tetraacetate of *l*-sorbose the authors have prepared the α-pentaacetate and the

α-acetochloro compound. From the latter, by the replacement of the chlorine atom with an acetoxy or methoxy group, the β-pentaacetate and the β-methylsorbose tetraacetate have been obtained. Deacetylation of the glycoside has yielded the β-methylsorbose. Since the publication of Schlubach's work, Whistler and Hixon<sup>6</sup> have prepared the α-ethylsorbose and its tetraacetate, and in the Experimental Part of this paper the corresponding β-isomers are described. In the preparation of the latter compounds it has been found that the reaction between α-acetochlorosorbose and ethyl alcohol, just as in the fructose series, does not give rise exclusively to the true β-ethylsorbose tetraacetate. This sorbose is only the product of a side reaction, the main reaction being the formation of a new ethylsorbose tetraacetate possessing ortho ester structure. On account of its sirupy nature, the latter compound has not been investigated closely. Table I contains the data of all the *l*-sorbose derivatives which have been used for calculations in the present publication.

In carrying out their computations, Schlubach and Graefe have assumed that the two methylsorbosides and their acetates constitute true α,β-stereoisomeric pairs. From the molecular rotations of these pairs they have obtained  $b_{\text{sorb.}} = -4800^7$  and  $b_{\text{sorb. ac.}} = 4900$ . Using these values, Schlubach and Graefe have calculated from the molecular rotations of the α-derivatives the different  $a_x$  constants; these values were found to be 4400 to 9250 units smaller than those

(3) Pacsu and Rich, *THIS JOURNAL*, **54**, 1697 (1932); **55**, 3018 (1933).

(4) Green and Pacsu, *ibid.*, **59**, 1205 (1937).

(5) Schlubach and Graefe, *Ann.*, **532**, 211 (1937).

(6) Whistler and Hixon, *THIS JOURNAL*, **60**, 563 (1938).

(7) The authors give +4800, which is obviously a clerical error.

of the corresponding constants determined by Pacsu and Cramer<sup>1</sup> from the rotations of the whole group of the fructose derivatives (Table II).

TABLE II

COMPARISON OF THE  $a_x$  VALUES OF SCHLUBACH AND GRAEFE<sup>8</sup> AND THE CORRESPONDING  $a_x$  VALUES DETERMINED FOR THE KETOSES BY PACSU AND CRAMER<sup>1</sup>

$a_x$ values (S. and G.) (for acetylated sorboside derivatives in chloroform)	$a_x$ values (P. and C.) (for acetylated fructose derivatives in chloroform)	Difference
$a_{OH}$ 12,300	17,750	-5,450
$a_{OMe}$ 24,000	30,850	-6,850
$a_{OEt}$ 25,400 <sup>a</sup>	33,650	-8,250
$a_{OAc}$ 26,900	32,850	-5,950
$a_{Cl}$ 35,500	44,750	-9,250
For deacetylated sorboside derivatives in water	For deacetylated ketose derivatives in water	
$a_{OMe}$ 12,400	21,200	-8,800
$a_{OEt}$ 15,700 <sup>a</sup>	20,100	-4,400
$a_{OH}$ 3,050 <sup>a</sup>	11,800 <sup>a,b</sup>	-8,750

<sup>a</sup> Addition of the present author. <sup>b</sup> Calculated from the rotation of the basal chain in the two methylfructosides  $\langle 2,6 \rangle$ ,  $b_{fruct.} = -12,200$ , and the initial rotation of  $\beta$ -fructose ( $-24,000$ ).

Furthermore, it has been pointed out by Schlubach and Graefe that if the calculations be based on the molecular rotations of the two sorbose pentaacetates instead of the acetylated methylsorbosides, the value of  $b_{sorb. ac.}$  becomes only 3500 instead of 4900, and all the  $a_x$  values will be 1400 units smaller. This fact could be regarded as an indication that there might be a difference in the structure of the  $\alpha$ - and  $\beta$ -derivatives, since the substitution of an acetoxyl group for a methoxyl group should not influence the rotation of the basal chain to such a large extent. The other fact that the  $a_x$  values in the sorbose series deviate so greatly (4400-9250 or more) from the  $a_x$  values for the fructose derivatives could be construed as confirmatory evidence that once again incorrect " $\alpha, \beta$ -pairs" have been used for calculations. However, application of the periodic acid oxidation method of Jackson and Hudson<sup>8</sup> gave results which indicate that both the  $\alpha$ - and  $\beta$ -sorbosides possess pyranoid ring structures. Such a structure already has been established by Whistler and Hixon<sup>9</sup> for the  $\alpha$ -alkylsorbosides. Therefore, the results of the above calculations would appear to indicate a complete failure of Hudson's rules in the ketose series (column 6, Table I). However, it will be shown in the following calcu-

lations that *the isorotation rules hold closely in the sorbose series provided that the  $a_x$  constants for the fructose derivatives are applied separately to the  $\alpha$ - and  $\beta$ -sorboside derivatives.*

From the molecular rotation of  $\alpha$ -methylsorboside tetraacetate ( $-19,100$ ) and the  $a_{OMe}$  constant for the fructose series, the value of the basal chain is calculated to be  $b_{\alpha-sorb. ac.}^{10} = 11,750$ , from the equation:  $-19,100 = -30,850 + b_{\alpha-sorb. ac.}$ . Combination of  $b_{\alpha-sorb. ac.}$  with the different  $a_x$  constants for the fructose derivatives gives the calculated specific rotations of *all the  $\alpha$ -sorboside derivatives*. The values obtained agree satisfactorily with those found by experiment (column 7, Table I). From the molecular rotation of  $\beta$ -methylsorboside tetraacetate a new value for the basal chain,  $b_{\beta-sorb. ac.} = -1950$ , is obtained from the equation:  $28,900 = 30,850 + b_{\beta-sorb. ac.}$ . Combination of this new value with the  $a_x$  constants for the fructose series gives the specific rotations of *all the  $\beta$ -sorboside derivatives*. Again, the agreement between calculated and observed values is quite satisfactory (column 7, Table I). Similar results are obtained if calculations be carried out by the use of the molecular rotations of the two methylsorbosides. From the  $[M]$  value of  $\alpha$ -methylsorboside ( $-17,200$ ) and  $a_{OMe} = 21,200$ , which is the constant for the fructose derivatives, the value of the basal chain is calculated to be  $b_{\alpha-sorb.} = 4000$  from the equation:  $-17,200 = -21,200 + b_{\alpha-sorb.}$ . From the molecular rotation of the  $\beta$ -methylsorboside (7600) a new value for the basal chain is calculated to be  $b_{\beta-sorb.} = -13,600$ , from the equation:  $7600 = 21,200 + b_{\beta-sorb.}$ . Combination of the respective basal chain values with the  $a_x$  constants for the fructose series gives the rotations of the  $\alpha$ - and  $\beta$ -sorboside derivatives, the agreement between calculated and found values being satisfactory (column 7, Table I).

The principle that underlies these calculations is Hudson's glycoside-sugar corollary<sup>11</sup> from his rules of optical isorotation. He showed that the difference between the molecular rotation of a given glycoside and that of its parent sugar,  $A_{OMe} - A_{OH}$ , has the same numerical value (10,000) and the proper sign throughout the sugar group. He found it "a very noteworthy fact that the normal value of the difference holds for

(8) Jackson and Hudson, *THIS JOURNAL*, **58**, 378 (1936); *Science*, **85**, 51 (1937); *THIS JOURNAL*, **59**, 994 (1937).

(9) Whistler and Hixon, *ibid.*, **59**, 2047 (1937).

(10) The symbols  $b_\alpha$ ,  $b_\beta$  and  $b_{\alpha,\beta}$  indicate that their values were obtained from the  $\alpha$ -form, or  $\beta$ -form, or the  $\alpha, \beta$ -pair of the sugar derivatives.

(11) Hudson, *THIS JOURNAL*, **47**, 268 (1925).

mannose and rhamnose," although "these sugars . . . exhibit a considerable and similar deviation from the principle of optical superposition when the rotations of their respective  $\alpha$  and  $\beta$  forms are compared." He also suggested that "the known  $\alpha$  forms of mannose ( $[\alpha]_D + 30$ ) and methyl mannoside (+79), rhamnose (-7.7) and methyl rhamnoside (-62.5) . . . possess ring structures common to the respective members of each pair" and "that the  $\beta$  forms of these sugars, the rotations of which have been shown to differ from those of the respective  $\alpha$  forms by a much smaller amount than is required by the principle, possess rings that are different from those of the  $\alpha$  forms." At present, it is recognized that "rings that are different" cannot in these cases be rings that differ in the number of their members (pyranoid and furanoid rings), since the  $\alpha$ - and  $\beta$ -derivatives of these sugars and also those of *l*-sorbose and *d*-fructose possess six-membered rings throughout. It seems probable that the difference may be ascribed to a new type of isomerism that is not apparent in the customary  $\alpha,\beta$ -stereoisomeric formulas, an isomerism which very well can be accounted for by the existence of any or all of the two possible *trans* and six *cis* ring conformations<sup>12</sup> constituted on the Sachse principle. The numerical value of this new factor ( $F$ ) can be obtained easily from either equation

$$[M]_{\alpha} = +A_x + (B_{\alpha,\beta} + F) \text{ and}$$

$$[M]_{\beta} = -A_x + (B_{\alpha,\beta} - F)$$

where  $A_x$  represents the "normal" values valid for *all* the aldoses. Until the exact physical significance of  $F$  is fully understood and it becomes definitely known for which particular sugars this additional optical factor must be considered, it is only a matter of convenience to assume that  $F = 0$  in the arabinose-glucose series, where the majority of the most common aldoses belong. Consequently, the  $A_x$  values obtained from the  $\alpha,\beta$ -stereoisomeric pairs of these sugars and derivatives will represent the "normal" values valid for *all* the aldoses. From  $\alpha$ -methylmannopyranoside ( $[M]_{\alpha} = 15,250$ ) and  $\beta$ -methylmannopyranoside ( $[M]_{\beta} = -13,200$ ), the value of the basal chain is calculated to be  $B_{\alpha,\beta\text{-man.}} = 1025$ . These two substances do not obey Hudson's rules, since the half of the difference of their rotations gives  $A'_{\text{OMe}} = 14,225$ , instead of the "normal" value of  $A_{\text{OMe}} = 18,700$ , obtained from the members of the

arabinose-glucose series. From either modified equation:  $[M]_{\alpha} = A_{\text{OMe}} + (B_{\alpha,\beta\text{-man.}} + F)$  and  $[M]_{\beta} = -A_{\text{OMe}} + (B_{\alpha,\beta\text{-man.}} - F)$  the value of  $F$  is calculated to be  $-4475$ . This represents the numerical value of the contribution of the new optical factor (ring conformation) to the total rotation of the molecule. According to the above arbitrary assumption, this factor does not occur, or it cancels out, in the glucose type of sugars. By the aid of  $F$  the rotation of  $\alpha$ -mannose is calculated to be  $[M]_{\alpha} = A_{\text{OH}} + (B_{\alpha,\beta\text{-man.}} + F)$ , that is:  $8450 + 1025 - 4475 = 5000$ , where  $A_{\text{OH}} = 8450$  represents the "normal" value obtained from the members of the glucose type of aldoses for *all* the aldehyde sugars. Similarly, the molecular rotation of  $\beta$ -mannose is calculated from the equation:  $[M]_{\beta} = -A_{\text{OH}} + (B_{\alpha,\beta\text{-man.}} - F)$  to be  $-2950$ . Then the specific rotation of  $\alpha$ -mannose becomes  $5000/180 = 28^{\circ}$  and that of  $\beta$ -mannose,  $-2950/180 = -16.4^{\circ}$ , which values agree excellently with the observed respective values of  $+29.9$  and  $-16.3^{\circ}$ .

In the ketose group the values of  $a_{\text{OMe}} - a_{\text{OH}}$  for  $\alpha$ -*l*-sorbose and  $\beta$ -*d*-fructose and their corresponding methyl glycosides are constant (9500) and practically identical with those for the aldoses (10,000).<sup>13</sup> However, the  $a_x$  values from the sorbose derivatives are entirely at variance with the  $a_x$  constants calculated from the fructose derivatives (Table II). Here again, just as in the aldose group, at present, it is only a matter of convenience to decide which values should be chosen as the "normal" values valid for *all* the ketoses, that is, which one of the two ketoses possesses *strictly* comparable  $b$  parts in its  $\alpha$ - and  $\beta$ -forms. It is suggested that until no contradictory evidence is discovered, the  $a_x$  values derived from the fructose derivatives should be used as the "normal" values for all the ketoses. Then in the calculation of the rotations of those ketoses and their derivatives which do not obey Hudson's rules, *e. g.*, *l*-sorbose, a factor  $F$  must be added to the value of  $b_{\alpha,\beta}$  for all the  $\alpha$ -forms and subtracted from  $b_{\alpha,\beta}$  for all the  $\beta$ -isomers. From  $\alpha$ -methylsorbopyranoside ( $[M]_{\alpha} = -17,200$ ) and  $\beta$ -methylsorbopyranoside ( $[M]_{\beta} = 7600$ ) the constant  $b_{\alpha,\beta} = -4800$  is obtained. From either equation:  $[M]_{\alpha} = -a_{\text{OMe}} + (b_{\alpha,\beta\text{-sorb.}} + F)$  and  $[M]_{\beta} = a_{\text{OMe}} + (b_{\alpha,\beta\text{-sorb.}} - F)$ , where  $a_{\text{OMe}} = 21,200$  represents the "normal" value obtained

(12) Haworth, "The Constitution of Sugars," Edward Arnold and Co., London, 1929, p. 91.

(13) Since all the  $A_x$  constants for the aldoses are different from the  $a_x$  constants for the ketoses, the agreement is probably fortuitous.

from the two methylfructopyranosides, the value of  $F$  is calculated to be 8800. Addition of  $F = 8800$  to  $b_{\alpha,\beta\text{-sorb.}} = -4800$  gives  $b_{\alpha\text{-sorb.}} = 4000$  for all the  $\alpha$ -sorbitose derivatives and subtraction of  $F = 8800$  from  $b_{\alpha,\beta\text{-sorb.}} = -4800$  gives  $b_{\beta\text{-sorb.}} = -13,600$  for all the corresponding  $\beta$ -isomers. Similarly, from the acetylated  $\alpha$ - and  $\beta$ -methylsorbopyranosides  $F = 6850$  is obtained, which when added to, or subtracted from,  $b_{\alpha,\beta\text{-sorb. ac.}} = 4900$ , gives  $b_{\alpha\text{-sorb. ac.}} = 11,750$  for all the acetylated  $\alpha$ -sorbitose derivatives and  $b_{\beta\text{-sorb. ac.}} = -1950$  for all the corresponding  $\beta$ -forms. The very satisfactory agreement between the values calculated on this basis and the actually observed values of all the *l*-sorbitose derivatives (column 7, Table I) leads to the conclusion that Hudson's rules of isorotation hold closely in the *l*-sorbitose series and that measurements of the factor  $F$  for various sugars may furnish evidence concerning ring conformations.

**Addendum.**—The possibilities of the construction of two *trans*- and six *cis*-models of sugars on the Sachse principle have been discussed and explored by Haworth.<sup>12</sup> However, our attempts to build up these different forms by using the latest atom models<sup>14</sup> based on the true atomic dimensions resulted in the surprising discovery that only one *trans*- and one *cis*-conformation of a hexopyranose could be constructed. The skeleton models of these two conformations are shown in the sketches Figs. 1 and 2.

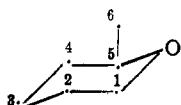


Fig. 1.

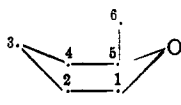


Fig. 2.

In any other conformation more or less obstruction occurs between certain atoms or atomic groups such as the terminal  $-\text{CH}_2\text{OH}$  group, the hydrogen atom and the hydroxyl group of one or more ring carbon atoms, thus making the construction of the molecule impossible. Since theoretical considerations<sup>15</sup> indicate that the *cis*-forms would seem to be unstable due to large repulsion both in the ring and among the subsidiary groups, there remains only one *trans*-form (Fig. 1) from which all the hexopyranoses and their derivatives must be derived. Under such circumstances the physical significance of  $F$  appears to be the disturbing effect of the differ-

ent orientation of the hydroxyl groups in the  $\alpha$  and  $\beta$ -isomers of certain sugars. The occurrence of such disturbances at present cannot be predicted beyond some empirical rules, neither can the effect be measured by any chemical or physical methods. In many instances the optical effect of the orientation appears to be negligible (glucose-arabinose series) but for various sugars (mannose, sorbose, etc.) it must be eliminated from the calculations by the introduction of factor  $F$ , a characteristic constant for each of these sugars. If this conclusion regarding the nature of  $F$  be correct, then the numerical value of this factor must remain the same not only for one particular sugar and its glycosidic derivatives but for any other similarly constructed sugar and its corresponding derivatives. The structure of rhamnose is very similar to that of mannose, consequently the orientation of the hydroxyl groups should not differ to any great extent in the two sugars. Indeed, the numerical value of the factor for *d*-mannose ( $F = -4475$ ) is practically equal and opposite to that for rhamnose ( $F = 4650$ , obtained from  $\alpha$ - and  $\beta$ -methyl-*l*-rhamnopyranoside) which belongs to the *l*-series. By the use of this factor the initial rotations of  $\alpha$ - and  $\beta$ -*l*-rhamnose are calculated to be  $-5.3^\circ$  and  $41.0^\circ$ , respectively. Jacobi<sup>16</sup> observed  $-5^\circ$  and Hudson<sup>17</sup> measured  $-7.7^\circ$  for the  $\alpha$ -form, and Fischer<sup>18</sup> gave  $31.5^\circ$  for the  $\beta$ -form of a sample which probably was not quite pure.

### Experimental Part

**Preparation of  $\beta$ -Ethylsorboside Tetraacetate.**—Twelve grams of  $\alpha$ -sorbitose tetraacetate was dissolved in 150 cc. of absolute ether and the solution saturated with dry hydrogen chloride at  $-70^\circ$  in a pressure bottle. After having been warmed up to  $0^\circ$  for twelve hours, the solution was cooled and the bottle opened. The solution was evaporated four times with ether to a sirup, rotating  $-67^\circ$  in chloroform. Attempts at crystallization of the acetochloro compound from the sirupy product failed. In order to convert it into the glycoside, the crude acetochlorosorbitose was shaken with absolute ethyl alcohol and silver carbonate for several hours, then the reaction mixture was filtered and the filtrate treated with hydrogen sulfide to remove traces of silver salts. After filtration with activated carbon, the solution was evaporated to a sirup, which was stirred vigorously for ten minutes in 100 cc. of boiling water containing one drop of 0.1 *N* hydrochloric acid. The latter operation was necessary in order to decompose the large quantity of ortho ester formed from the

(14) Fisher-Hirschberger Atom Models, Fisher Scientific Co., Pittsburgh, Pa.

(15) Gorin, Kauzmann and Walter, *J. Chem. Phys.*, **7**, 327 (1939).

(16) Jacobi, *Ann.*, **272**, 170 (1892).

(17) Hudson, *This Journal*, **48**, 1424 (1926).

(18) Fischer, *Ber.*, **29**, 324 (1896).

acetochloro compound, which ortho ester prevented the crystallization of the true glycoside. The resulting solution containing sorbose tetraacetate, which is the decomposition product of the ortho ester, and oily drops of the partially soluble  $\beta$ -ethylsorbose tetraacetate, was cooled and extracted with 200 cc. of benzene in several portions. The latter solution was then extracted repeatedly with water until the aqueous extract no longer reduced Fehling's solution. The benzene solution was dried over anhydrous sodium sulfate, then evaporated to a sirup, whose 15-cc. ether solution, on addition of 30 cc. of petroleum ether, deposited 2.5 g. of crystalline  $\beta$ -ethylsorbose tetraacetate. After repeated recrystallization from the same solvents, the substance melted at  $86^\circ$  and showed  $[\alpha]^{20}_D$  82.7,  $[\alpha]^{20}_C$  66.0 and  $[\alpha]^{20}_{Hg}$  98.0 in chloroform solution (0.200 g. of substance, 10 cc. of solution, 2-dm. semimicro tube; rotations 3.31, 2.64 and 3.92° to the right, respectively). In an acetyl estimation, 0.3762 g. of the substance required 40.3 cc. of decinormal alkali; calcd. for four acetyls, 40.0 cc.

The same compound was obtained from the acetochlorosorbose, which was prepared according to Schlubach and Graefe from the reaction of sorbose tetraacetate and liquid hydrogen chloride in an autoclave at  $0^\circ$ . Also in this case a large quantity of ortho ester accompanied the formation of the glycoside. The crystalline  $\beta$ -methylsorbose tetraacetate of Schlubach and Graefe was obtained readily by either method after the ortho ester, the main product of the reaction, had been decomposed by very dilute acid.

**$\beta$ -Ethylsorbose.**—A solution of 0.05 g. of metallic sodium in 5 cc. of absolute methyl alcohol was added to 4 g. of  $\beta$ -ethylsorbose tetraacetate dissolved in 5 cc. of the same solvent.<sup>19</sup> After two days the solution was evaporated to leave a colorless sirup, which was extracted with cold absolute ethyl alcohol. The substance, a colorless product, has not yet been obtained in crystalline form. Its specific rotation was  $31.0^\circ$  in water solution (0.4324 g. in 25 cc. rotated  $1.07^\circ$  to the right; 2-dm. tube). Reacetylation gave back the crystalline  $\beta$ -ethylsorbose tetraacetate.

**Oxidation of  $\alpha$ -Methylsorbose and  $\beta$ -Ethylsorbose by Periodic Acid.**—Jackson and Hudson<sup>8</sup> showed that the cleavage type of oxidation by periodic acid of the glycosides provides a new method for the determination of ring structure. Differentiation between the pyranosides and furanosides of the pentoses and hexoses is based on the fact that, on treatment by periodic acid, the pyranosides give rise to one mole of formic acid whereas the furanosides yield no formic acid under similar experimental conditions. Application of this method to the  $\alpha$ - and  $\beta$ -sorbosides resulted in the formation of nearly one equivalent of formic acid which was obtained by distillation under diminished pressure of the reaction mixture. This result is regarded as a definite proof of the pyranoid ring structure present in both alkyl sorbosides.

Twenty cc. of a 0.1 molar solution of crystalline periodic acid was added to 10 cc. of a 0.1 molar aqueous solution of the glycoside. After sixteen hours of standing at room temperature, the solution was mixed with 20 cc. of decinormal sodium hydroxide solution, then transferred into a 250-cc. distilling flask and evaporated to dryness under diminished pressure at a bath temperature of  $45$  to  $50^\circ$ . The receiver flask containing 10 cc. of the same standard alkali solution was cooled by running water during the distillation. The residue was then dissolved in 10 cc. of distilled water and the solution was evaporated *in vacuo*, the distillate being collected in the same receiver. Titration of the content of the receiver by decinormal acid solution showed that 9 cc. and 8.6 cc. of 0.1 molar formic acid was obtained from  $\alpha$ -methylsorbose and  $\beta$ -ethylsorbose, respectively, instead of the theoretical yield of 10 cc.

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### Summary

It has been shown that Hudson's rules of isorotation hold closely in the *l*-sorbose series provided that the  $a_x$  constants for the ketoses are applied separately to the  $\alpha$ - and  $\beta$ -derivatives.

The rotations of the  $\alpha$ - and  $\beta$ -isomers can be calculated by introduction of factor  $F$  in the equations:  $[M]_\alpha = -a_x + (b_{\alpha,\beta} + F)$  and  $[M]_\beta = a_x + (b_{\alpha,\beta} - F)$ . The numerical value of  $F$  has been determined to be 6850 for the acetylated and 8800 for the deacetylated products. Similarly, by introduction of a factor ( $F$ ) in the equations, the rotation of  $\alpha$ - and  $\beta$ -mannose can be calculated from the "normal"  $A_{OH}$  value for the aldoses. It is suggested that  $F$  represents the numerical value of the contribution of a new optical factor (ring conformations) to the total rotation of the molecule.

It has been found that the reaction between  $\alpha$ -acetochlorosorbose and methyl or ethyl alcohol gives rise to the ortho esters, as the main products and only to a small quantity of the true  $\beta$ -alkylsorbose tetraacetates. Crystalline  $\beta$ -ethylsorbose tetraacetate has been obtained and the pyranoid ring structure of  $\alpha$ -methyl- and  $\beta$ -ethylsorbose has been proved by the periodic acid oxidation method of Jackson and Hudson.

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(19) Zemlén and Pacsu, *Ber.*, **62**, 1613 (1929).