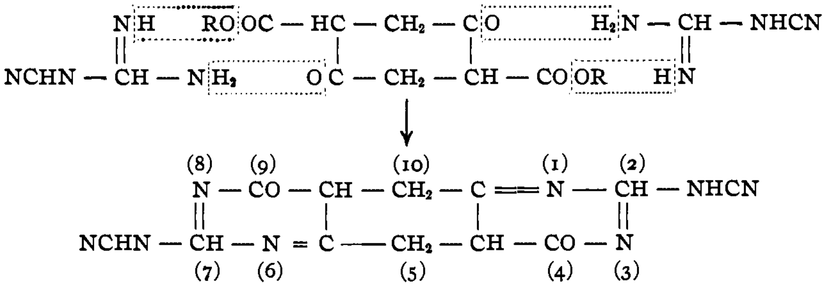
and by its infusibility. At about 320° it darkens in color without melting. Analysis of the product gave the following results:

Calc. for $C_{12}H_8N_8O_2$: N, 37.8; C, 48.6; H, 3.0. Found: N, 37.2; C, 48.5; H, 2.7.

The condensation evidently takes place as indicated below, and consists in the elimination of two molecules of water and two of alcohol, between one of succinylosuccinic ester and two of dicyanodiamide.



The product is therefore 2,7-dicyanoamino-4,9-diketotetrahydro-1,3,6,8-naphthotetrazine.

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INDIRECT MEASUREMENTS OF THE ROTATORY POWERS OF SOME ALPHA AND BETA FORMS OF THE SUGARS BY MEANS OF SOLUBILITY EXPERIMENTS.

BY C. S. HUDSON AND E. YANOVSKY.

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At the present time the crystalline alpha and beta modifications of lactose and of glucose are known in a condition closely approaching purity and their rotatory powers have in consequence been directly measured. The view that the mutarotation of lactose and glucose is due to the slow establishment of an equilibrium in solution between the respective alpha and beta forms of these sugars leads to the presumption that the many other sugars which show mutarotation exist in alpha and beta forms likewise. Such modifications have, indeed, been crystallized in the cases of galactose, rhamnose, gentiobiose and possibly melibiose, but it appears doubtful whether the isomers have been fully separated in these cases. For the remaining crystalline sugars which show mutarotation and, therefore, probably exist in two modifications, namely, xylose, arabinose, lyxose, ribose, mannose, fructose, α-glucoheptose, maltose, cellose, and a few rarer sugars, only one crystalline form has ever been prepared.

It has been suggested by one of us[1] that the difference between the

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[1] Hudson, THIS JOURNAL, 31, 66 (1909).

molecular rotations of the alpha and beta forms of the sugars is a constant quantity, or nearly so, for all the aldoses, and by use of this relationship the rotatory powers of several of the unknown forms have been calculated from those of the known modifications. Thus, since the specific rotations of alpha and beta lactose are 90° and 35°, respectively, and that of beta maltose (so named because it shows upward mutarotation) is 118°, the rotation of the unknown alpha maltose is calculated to be $118 + (90 - 35) = 173°$. In the present investigation we have sought to obtain experimental evidence regarding the rotations of these unknown forms of the mutarotating sugars. The principle which has been used is that the rotation of the unknown form may be measured either by observing the maximum rate of solution of the corresponding known isomer or by measuring the latter's initial and final solubility, a method which has previously been described and applied in the case of the alpha and beta forms of lactose.[1]

Description of the Method. Experiments with *d*-Glucose.

The theory of the maximum rate of solution of any mutarotating sugar may be taken from the considerations that were presented regarding lactose in the former article. Thus if an excess of pure crystalline alpha glucose is shaken continuously at constant temperature with a solvent in which it is only slightly soluble, so that the laws of dilute solutions apply, the initial solubility (S_o), the final solubility (S_∞), and the solubility (S) at any time (t) since the beginning of the experiment, are connected by the relation $1/t \log [(S_\infty - S_o)/(S - S_o)] = k_2$, where k_2 is the velocity-coefficient expressing the rate at which unit concentration of dissolved beta glucose changes to the alpha form. The analogous coefficient for the reverse change of alpha to beta is k_1, and the value of the sum of these coefficients ($k_1 + k_2$) may be obtained independently from measurements of the rate of mutarotation of either form of the sugar, as has previously been shown.[2] It was also there proved that the equilibrium-constant (K) for the reversible reaction is equal to k_1/k_2, and also to $(S_\infty - S_o)/S_o$. It is evident that the ratio (K) of the amounts of the beta and alpha forms that are present when equilibrium is attained may be found either by determining k_1 and k_2 from combined measurements of the rate of mutarotation ($k_1 + k_2$) and the maximum rate of solution of the known form (k_2), or by observing the initial and final solubilities of this substance. With this ratio determined and the specific rotations of alpha glucose and the equilibrium mixture known, it is possible to calculate the rotatory power of the beta form. Since the solubilities are more easily and accurately observed than the rates of mutarotation and solution, we have usually

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[1] Hudson, THIS JOURNAL, 26, 1067 (1904); see also Lowry, *J. Chem. Soc.*, 85, 1551 (1904); *Z. physik. Chem.*, 44, 487 (1903).

[2] *Loc. cit.*, p. 1067.

chosen to measure only them, though in the case of two sugars (see under mannose and fructose) the values of K have been determined by both methods with agreeing results.

In order to measure S_0 it was necessary to use crystalline alpha glucose which was free from impurities, especially the beta isomer. To accomplish this purification alpha glucose was prepared by the method which Hudson and Dale[1] have described and was then shaken one or two minutes with 80% alcohol to dissolve any traces of the very soluble beta form. In such cases an experimental check upon the purity of the final crystals was obtained by measuring the initial solubility of the sugar several times in succession, using the residual crystals from one experiment as the starting material in the subsequent one; purity and freedom from the isomeric form are shown when these successive initial solubility measurements agree. This test has been found quite necessary and has been applied to all the sugars studied.

The Solubilities of Anhydrous Alpha Glucose in 80% Ethyl Alcohol.—The highest value previously recorded for the specific rotation of anhydrous alpha glucose is 110°[2] but glucose of this rotation was found to show irregular and high values for S_0 in comparison with samples of the same crystals which had been shaken two minutes at 20° with 80% alcohol to dissolve any traces of beta glucose. The undissolved crystals were found to have an initial specific rotation of +113.4° in water, +115.2° in 80% alcohol and +121.5° in absolute methyl alcohol. These values are accordingly accepted as the rotations of pure anhydrous alpha glucose. After mixing approximately 20 g. of this purified material with 200 cc. of 80% alcohol and shaking vigorously at 20° during 5 minutes, a portion of the solution was filtered from the undissolved crystals, kept overnight or a drop of ammonia added to complete the mutarotation, and read in a 200 mm. tube in a saccharimeter. Since the rotations of all the sugars are proportional to the concentration closely enough for the accuracy of the present measurements, the relative initial and final solubilities may be conveniently expressed by the rotations of the solutions. Thus, the initially-saturated solution of alpha glucose in 80% alcohol rotated in stable condition +6.8° Ventzke in a 200 mm. tube. In all the experiments mentioned in this article the temperature was 20° unless otherwise stated. The concentration of this solution may be obtained from the observed specific rotation of anhydrous glucose in 80% alcohol, 59.0°, as 2.0 g. per 100 cc. That this value really represents initial saturation was proved by the fact that portions of the solution which were removed from the crystals 3 or 7 minutes after starting the shaking gave the same readings. The rate of mutarotation of glucose in 80% alcohol at 20°

[1] THIS JOURNAL, 39, 322 (1917).

[2] Hudson and Dale, *Loc. cit.*

is so slow, requiring over four hours for its half completion, that there is ample time for initially saturating the solution before the production of the beta form in solution causes the concentration to increase appreciably. To obtain the final solubility of anhydrous alpha glucose it was found necessary to avoid the crystallization of alpha glucose monohydrate which takes place on long standing of the solution, and to produce final saturation by adding a drop of strong ammonia to the solution and stirring gently for one hour. In the experiment cited above the final solubility was +15.2° by the same units of estimation, corresponding to 4.5 g. glucose in 100 cc. The increase of solubility was thus 15.2 — 6.8 = 8.4, which may be taken as a measure of the concentration of β-glucose in the solution that had reached equilibrium, 6.8 being the concentration of the alpha form. A dilute solution of glucose in 80% alcohol which has reached equilibrium consists, therefore, of 6.8/15.2 = 0.447 parts of alpha glucose to 8.4/15.2 = 0.553 parts of beta glucose.[1] Since the initial specific rotation of anhydrous α-glucose in 80% alcohol is +115.2°, as mentioned, and the final specific rotation, when equilibrium had been reached, was found to be +59.0°, the specific rotation of beta glucose (x) in 80% alcohol may be obtained from the equation $0.447\ (115.2) + 0.553\ (x) = 59.0$ or $x = +14°$. In a repetition of this experiment the values $S_0 = 6.3$ and $S_\infty = 14.75$ were obtained, which lead to $x = +15°$. The direct measurement of the initial specific rotation of pure anhydrous beta glucose in 80% alcohol was +20.3°, which gives an idea of the accuracy of the method under somewhat unfavorable conditions because the solution in which S_∞ was measured was necessarily unstable, being supersaturated with respect to alpha glucose hydrate ($C_6H_{12}O_6.H_2O$) which always crystallized in time from it. The value of S_∞ is the highest concentration that the solution reached during the experiments; if it were 16.7° in place of 15.2° in the first experiment the calculated value of x would agree with the observed 20.3°.

The Solubilities of Anhydrous Alpha Glucose in Absolute Methyl Alcohol.—Since this solvent dissolves the sugar sparingly and the rate of mutarotation is slow the initial and final solubilities could be measured and the specific rotation of the beta form calculated from the data. The initial specific rotation of freshly dissolved pure anhydrous alpha glucose was found to be +121.5°, as mentioned, and the constant rotation +70.45°.

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[1] It is not intended that this statement should indicate that dissolved glucose consists only of two molecular configurations. Such an assumption would not only be rather improbable but for the present calculations is unnecessary. The statement is only a short form of expression of the experimental measurements of the initial and final solubilities, and, insofar as we can now see, the method which is here used *to measure indirectly the rotatory power of beta glucose through observations made upon the alpha form* would not be affected by the development of new ideas on the constitution of dissolved glucose.

The initial solubility was +3.45° V. (corresponding to 0.85 g. per 100 cc. solution) and the final +6.7° V. (1.6 g.). In this case $0.515\ (121.5) + 0.485\ x = 70.45$ and $x = +16°$. Direct observation gave +16.5° for the initial specific rotation of pure β-glucose in this solvent.

The Solubilities of Alpha Glucose Hydrate in 80% Ethyl Alcohol.—The pure hydrate ($C_6H_{12}O_6.H_2O$) was prepared by allowing crystals of any form of pure glucose to stand several days at room temperature covered with 80% alcohol, as it is the stable phase under these conditions. The pure hydrate (15.320 g.) lost 9.14% (1.401 g.) during six hours' drying to constant weight at 75° in a vacuum, the theoretical quantity being 9.09%. Its constant specific rotation was 47.9° in water (= 52.2° as anhydrous sugar), 54.4° in 80% alcohol (= 59.3°) and its initial rotation in 80% alcohol was 105.0° (= 114.5°). In one experiment $S_0 = 4.4°$ V. (1.3 g. anhydrous sugar) and $S_\infty = 10.5°$ (3.0 g.), hence, if the calculations be referred to the anhydrous substance, $0.419\ (114.5) + 0.581\ x = 59.3°$ and $x = 19.0°$. In a second experiment $S_0 = 4.5°$, $S_\infty = 10.6°$, hence $x = 19.0+°$. These values agree closely with that directly observed for pure beta glucose in 80% alcohol (+20.3°). It seems likely that the good agreement in these experiments is due to the fact that alpha glucose hydrate is the stable solid phase of the system and accordingly the substance may be prepared free from its isomers and its final solubility measured accurately without dealing with supersaturated solutions, as in the case of anhydrous alpha glucose in 80% alcohol or, as will now be described, in the experiments with beta glucose.

The Solubilities of Beta Glucose in 80% Ethyl Alcohol.—The beta crystals which were used showed an initial specific rotation of +19.7° in water at 20°, and +20.3° in 80% alcohol. Beta glucose is much more soluble than the anhydrous alpha form or its hydrate and in one experiment $S_0 = 16.5°$ (4.9 g. per 100 cc. solution) and $S_\infty = 30.9°$ (9.1 g.), hence, if y denote the specific rotation of the anhydrous alpha form, $0.534\ (20.3) + 0.466y = 59.0°$ or $y = +103°$. In a second experiment $S_0 = 16.2°$ and $S_\infty = 29.7°$, hence, $y = +105°$. These values agree well enough with the directly measured +115.2°, when it is remembered that the finally saturated solution is an unstable one and can only be obtained by using ammonia to catalyze the mutarotation, and also that it is quite a difficult matter to make certain that beta glucose is fully free from the alpha isomer.

Does S_0 Remain Constant during the Measurement of S_∞?—In developing the theory of the method it was accepted that the true solubility of the solid phase (*e. g.*, alpha glucose) is S_0, and that at the end of the experiment, when S_∞ total sugar is in solution, S_0 of it still represents the true solubility of the solid. This assumes that the solubility of the alpha form is not influenced by the presence of the beta modification in solution, and while this assumption appears warranted as the limiting case for dilute solutions, it seems altogether probable that with increasing total sugar concentration the solubility of the alpha form may change somewhat, probably increasing. The elimination of this source of error in the measurements dealing with the unknown forms of the sugars has been sought through the employment of sufficiently strong alcohol to reduce the total dissolved sugar to the lowest amounts that could be measured with the accuracy desired. In order to obtain direct evidence upon this question, the initial and final solubilities of alpha lactose hydrate were measured, first in 40% alcohol and next in a solution containing 6.5 g. glucose in 100 cc. 40% alcohol. The solubilities were not affected by the presence of the glucose, and it seems reasonable to suppose, therefore, that the initial solubility of α-lactose is also not affected by the presence of β-lactose in the moderate amounts that are present in the saturated 40% alcoholic solution. A similar conclusion can be drawn from the fact that the previously recorded solubility experiments on α-glucose hydrate in 80% alcohol indicate that when equilibrium is reached the solution contains 42% α-glucose and 58% β-glucose, while the directly observed initial rotations of the two forms in this solvent (+115° and +20°) and the constant rotation (59°) indicate that the equilibrium mixture consists of $(59 - 20)/(115 - 20) = 41\%$ α-glucose and 59% β-glucose. The results of these two independent methods of measurement agree within the limits of error.

A Method for the Reduction of the Measurements of the Specific Rotations of the Alpha or Beta Forms in Aqueous Alcohol to the Corresponding Values for Aqueous Solution. Experiments with Glucose. —It is necessary to carry out the measurements of the initial and final solubilities of the sugars in aqueous alcohol in order to have a liquid of low solvent power, and in consequence the calculated specific rotations from such measurements refer to aqueous alcohol rather than to water. For purposes of comparison it is desirable to know the value in water, and to accomplish this reduction a method has been used which will now be illustrated by the data from the measurements on glucose.

Four and one-half g. of pure anhydrous glucose were dissolved in 20 cc. water, the solution allowed to complete its mutarotation overnight, and then 80 g. of absolute alcohol were added to it, the volume measured (120 cc.) and the solution immediately read in a saccharimeter. The specific rotation was +52.0, which is almost exactly the accepted value for aqueous solution. The equilibrium ratio between the alpha and beta forms in this freshly prepared alcoholic solution must be the same as that which obtained in the aqueous solution from which it was prepared because the change of equilibrium, as indicated by the mutarotation, is a slow process. It has been mentioned that the initial specific rotations of alpha glucose in water and in 80% alcohol are 113.4 and 115.2, which are nearly alike, hence, since the specific rotation of the same equilibrium mixture of the alpha and beta forms in water and in 80% alcohol is +52 in both cases, the specific rotation of beta glucose in water must be almost the same, or within one to two degrees of its value in 80% alcohol. It results in this case that the experimental value for the rotation of β-glucose in 80% alcohol, as obtained from the solubility measurements upon α-glucose, can be applied without change to aqueous solution; this has been found to hold also in the case of several other sugars, but for arabinose and galactose and some others there is a considerable difference, as will be shown later.

On longer standing the solution of glucose in 80% alcohol slowly changed in specific rotation from the recorded initial value +52 to become constant at about 58°; this change is evidently due to the shifting of the equilibrium between the forms of glucose.

The Rate of Mutarotation of Glucose in Aqueous Ethyl Alcohol.—In describing the experiments on the solubilities of glucose it was mentioned that a solvent must be chosen in which the mutarotation takes place very slowly so that the initial solubility can be measured before any considerable amount of the dissolved sugar changes to its isomeric form. Aqueous alcohol proved to meet this requirement, as is shown by the following measurements of the mutarotation of alpha glucose in alcohol-water mixtures. The solutions were prepared by the use of absolute alcohol which had been distilled first with the addition of a drop of conc. H_2SO_4 and then from a little NaOH. The measurements were made at 20°, in tubes 200 mm. long, and the concentrations of sugar were in the range between 5 and 10%. The mutarotation followed the unimolecular formula $1/t \log [(r_0 - r_\infty)/(r - r_\infty)] = k_1 + k_2$, and the values of the velocity coefficient, using minutes and decimal logarithms, are as follows:

% alcohol by weight	0	20	40	60	70	80
$(k_1 + k_2)$	0.0065	0.0048	0.0030	0.00182	0.00156	0.00114

Experiments with Lactose.

In order to test the method as fully as possible upon sugars for which the two isomeric forms are known before using it to learn the rotatory powers of the unknown forms of other sugars experiments were made with alpha lactose hydrate to supplement those on glucose which have just been described. The pure substance, $C_{12}H_{22}O_{11}.H_2O$, was prepared by recrystallizing lactose from water and allowing the crystals to stand under 40% alcohol one week to insure that no unstable isomers were present. The initial specific rotation of this hydrate in water is recorded[1] as 86.0° (for $C_{12}H_{22}O_{11}$), but we find a higher value, +90.0°, in water, and 81.0 in 40% alcohol. The final specific rotation of anhydrous lactose in water

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[1] Hudson, THIS JOURNAL, 30, 1780 (1908).

is generally accepted to be 55.3, and we find the same value in 40% alcohol. The initial solubility of alpha lactose hydrate in 40% alcohol was +3.5° V. (1.10 g. anhydrous sugar per 100 cc. solution), the final solubility was +7.6° V. (2.4 g.), hence, if x is the specific rotation of beta lactose, $0.460\ (81.0) + 0.540x = 55.3$, and $x = 33°$. In a second experiment $S_0 = 3.4°$ and $S_\infty = 7.4°$, hence, $x = 33°$. The value which one of us[1] has observed for pure beta lactose in water is 35°, and we conclude, therefore, that beta lactose has appreciably the same rotation in water and in 40% alcohol. On the other hand, the alpha hydrate has different values in these solvents, namely, 90 in water and 81 in 40% alcohol, as mentioned. This difference shows itself in an independent experiment which will now be described.

Reduction of the Rotation of Alpha Lactose Hydrate in 40% Alcohol to Its Value in Water.—In 180 g. water 7.174 g. of lactose ($C_{12}H_{22}O_{11}.H_2O$) were dissolved, the solution was allowed to stand overnight to complete the mutarotation, 120 g. of absolute alcohol were then added, the volume measured (331 cc.), and the specific rotation immediately after mixing was found to be 52.5°, on the basis of anhydrous sugar. In repetitions of this experiment the same value was found on two other occasions. The final specific rotation of anhydrous lactose in water is 55.3, as mentioned. The difference, 2.8°, must be due to the influence of the solvents on the rotation of alpha lactose since it has just been shown that beta lactose has the same rotations in them. The proportion of the two forms in the 40% alcoholic solution immediately after the addition of the alcohol is given by the equation $81z + 33(1 - z) = 52.5$, if z denotes the quantity of the alpha form, hence $z = 41\%$. If the difference in rotation in the two solvents that is due to this proportion of alpha is 2.8°, the difference that would be caused by 100% pure alpha form is $(2.8)/(0.4) = 7°$. Hence it is concluded from this experiment that alpha lactose has an initial rotation in water 7° higher than the similar value in 40% alcohol. This agrees very well with the directly observed difference, which is 9°, as mentioned.

Experiments with Galactose.

Both the alpha and beta forms of *d*-galactose have been known in the crystalline state but there has been some uncertainty regarding the purity of the beta modification. For our solubility experiments we used very pure alpha galactose ($C_6H_{12}O_6$) which had been kept several days under 60% alcohol to remove any traces of the beta form; its constant or final specific rotation was 80.5 in water, 72.8 in 60% alcohol, 73.1 in 80% alcohol, and its initial rotation was 144.0 in water, 140.6 in 60% alcohol, and 127.2 in 80% alcohol.

The Solubility of α-Galactose in 80% Alcohol.—The initial solubility

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[1] Hudson, This Journal, 30, 1780 (1908).

S_0 was 1.15° V. (corresponding to 0.27 g. in 100 cc. solution) and the final S_∞ was 2.75 (0.65 g.), which indicate that the equilibrium mixture consists of 41.8% alpha and 58.2% beta galactose. The specific rotation of the beta sugar x is calculated from the equation $0.418\ (127.2) + 0.582x = 73.1$ to be $x = 34°$ in 80% alcohol. A second experiment gave $S_0 = 1.15°$ V., $S_\infty = 2.8$ and, hence $x = 35°$. Since the sugar is very sparingly soluble in this strength of alcohol, and the uncertainty of the measurements is thereby increased, the experiments were repeated in 60% alcohol.

The Solubility of α-Galactose in 60% Alcohol.—S_0 was found to be 4.65° V. (1.1 g.), S_∞ was 12.9 (3.1 g.), hence $x = 34$. In three repetitions x was found to have the values 34, 33 and 33.

Reduction of the Rotation of β-Galactose in 60% Alcohol to Its Value in Water.—A solution of 3.433 g. galactose in 40 cc. water was kept overnight to complete its mutarotation and then 60 g. of absolute alcohol were added, the volume measured (114 cc.) and the solution immediately read in a 200 mm. tube. The reading 12.5° V. corresponds to $[\alpha]_D = 72°$, and this value was found in two repetitions. Since the rotation of α-galactose is nearly the same in water (144) and in 60% alcohol (141), the considerable change from 80.5 to 72° must be due principally to a change in the specific rotation of β-galactose. The proportions of the alpha and beta forms present immediately after the addition of the alcohol may be calculated from the equation $34z + 140.6\ (1 - z) = 72$, hence z, the amount of the beta form, is 64%. If the drop from 80.5 to 72 is due to the 64% of the beta form, the drop for 100% pure β-galactose would be $8.5/0.64 = 13°$. Applying this correction the specific rotation of β-galactose in water becomes $34 + 13 = 47°$. Tanret[1] has found the value 53 for this constant. Since the difference in the rotations of α- and β-glucose is 94°, the calculated value for β-galactose, from that observed for α-galactose (144°), is $144 - 94 = 50°$. The agreement of the three values, 47, 53 and 50, is sufficiently close. We have sought to repeat Tanret's measurement in an attempt to lower his value, but it was not possible to reach a lower rotation than 52°. These experiments will now be described.

Preparation and Purification of β-Galactose.—Twenty grams of galactose were dissolved in 50 cc. hot water to establish equilibrium between the α and β forms and the solution was cooled to 0° and poured into 500 cc. of absolute alcohol which was kept cold with an ice and salt bath. With vigorous stirring an abundant crystallization was obtained in 2 minutes and about seven g. of galactose, of initial rotation about 65°, were immediately filtered off. To obtain the best results in this very rapid crystallization, it is advisable to seed with crystals from a previous similar experiment. This mixture of α- and β-galactose was separated by dissolving 10 g. of it quickly in 10 cc. ice-cold water, filtering and adding

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[1] *Bull. soc. chim.*, [3] 15, 195 (1896).

250 cc. cold absolute alcohol and stirring for one minute. After two such recrystallizations, crystals showing an initial rotation of about 53° were obtained, and when these were shaken with cold 80% alcohol one or two minutes, to dissolve out the remaining traces of α-galactose, and filtered, the undissolved crystals rotated 52°, which is the lowest value yet found for β-galactose. The yield was 3 or 4 g. from 20 g. of pure galactose. If the recrystallization of the mixture rotating 65° is not to be carried out immediately, the crystals should be washed with alcohol, followed by ether, and kept dry in a desiccator, because in moist condition the mixture changes to α-galactose on standing many hours.

A Peculiarity in the Mutarotation of Galactose.—It has been mentioned that an aqueous solution of galactose which had reached equilibrium showed the reading of 12.5° V. immediately after the addition of enough absolute alcohol to bring the solvent up to 60% alcohol. This reading corresponds to $[\alpha]_D = 72°$, which is very near the final constant value for this solvent, 73°. It would be expected that the specific rotation would increase gradually from 72 to 73, or stay constant if it is assumed that this difference of one degree is experimental error. Instead, however, the reading of 12.5 decreased to 12.0 and after a day became constant at 12.5. In other trials an initial reading of 19.0 changed to 18.2 and then back to 19.1, and a reading of 13.7 decreased to 13.2 and then returned to 13.7. This exceptional behavior of galactose is being investigated further as it appears to indicate that there may be side reactions occurring during the mutarotation of this sugar. Arabinose shows the same peculiar behavior, as will be more fully described further on.

Experiments with Mannose.

Only one crystalline form of this sugar, its anhydrous β-modification ($C_6H_{12}O_6$), is known. The very pure sugar which was prepared from vegetable ivory by the method that Hudson and Sawyer[1] have described, was kept under 80% alcohol several days to insure the presence of only the β form. Its final specific rotation in water for a 3% solution was +14.6 at 20°, and its initial rotation was —17.0.

The Solubility of β-Mannose in 80% Alcohol.—S_0 was found to be 3.55° V. (= 2.4 g.), S_∞ was 19.3 (= 13.0 g.), hence the equilibrium mixture consists of 82% α-mannose and 18% β-mannose. Since the initial and final specific rotations of β-mannose in this solvent were found to be —14.9 and +25.7 the specific rotation of α-mannose in 80% alcohol, x, is calculated from $0.18\ (-14.9) + 0.82\ (x) = 25.7$ to be $x = +35°$. In three repetitions of this measurement the values 35, 34 and 34 were found.

The Solubility of β-Mannose in Absolute Methyl Alcohol.—The initial specific rotation in this solvent was —16.5, the final +30.1, S_0 was 1.35° V.

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[1] THIS JOURNAL, 39, 470 (1917).

(= 0.78 g.), and S_∞ 7.67 (= 4.4 g.), hence $x = +40°$. A repetition gave the value 38°.

Reduction of the Rotation of α-Mannose in 80% Alcohol to Its Value in Water.—A solution of 17.69 g. pure mannose in 20 cc. water was kept overnight to complete its mutarotation and then 80 g. of absolute alcohol were added, the volume measured (128 cc.) and the solution immediately read in a 200 mm. tube. The reading 12.0° V. corresponds to $[\alpha]_D = +15°$ which is nearly identical with the constant value for water. Two repetitions gave the same result. Since the initial specific rotation of β-mannose in water (—17) is nearly the same as in 80% alcohol (—15), and a mixture of the α and β forms rotates nearly the same in the two solvents, as shown, it is evident that the rotation of the α form is about the same in water as in 80% alcohol, namely +34°. However, this value is much different from what would be expected from the fact that the two forms of glucose differ in rotation by 94°, because the addition of 94° to the value for β-mannose (—17) gives +77°.[1] In order to check the experimental determination in this case the equilibrium ratio between the α and β forms of mannose was determined by the following second method.

The Maximum Rate of Solution of β-Mannose in 80% Alcohol.—An excess of pure crystalline β-mannose was shaken continuously with 80% alcohol at 20°, portions of the solution were filtered off at successive intervals and their concentrations measured by reading their constant rotations in a 200 mm. tube in a saccharimeter. The reaction follows the unimolecular order, and the value of k_1, the coefficient which measures the rate at which unit concentration of α-mannose changes in solution to the β form, is 0.00077. The unimolecular coefficient for the mutarotation of mannose ($k_1 + k_2$) in 80% alcohol was measured in the usual way

t (min.).	S (degrees Ventzke).	$k_1 = \frac{1}{t} \log \frac{S_0 - S_\infty}{S - S_\infty}$.
0	3.55 (= S_0)	.....
15	3.9	0.00065
45	4.85	0.00083
75	5.7	0.00085
105	6.25	0.00078
135	6.95	0.00078
175	7.8	0.00078
215	8.65	0.00079
260	9.5	0.00079
300	10.15	0.00080
1800	18.15	0.00062
∞	19.3 (= S_∞)	.....
		Average, 0.00077

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[1] See also THIS JOURNAL, 31, 75 (1909).

and found to be 0.00363 in the same units, hence k_2 is 0.00286 and the equilibrium ratio between the alpha and beta forms is 0.00286/0.00077, hence the equilibrium mixture consists of 79% α-mannose and 21% β-mannose, which agrees within the limits of error with the value from the solubility determinations. It is evident, therefore, that the difference between the rotations of the α- and β-mannoses is not as large as in the case of the glucoses (94°) but is approximately $35 + 17 = 52$. This conclusion recalls the fact that the α- and β-pentacetates of mannose have been found[1] to differ in rotation by a value, 80°, which is considerably less than the difference for the corresponding glucose pentacetates, 98°. It appears, therefore, that the change from the glucose to the mannose chain does have considerable influence upon the rotatory power of the terminal asymmetric carbon atom.

The Final Specific Rotation of Mannose in Water.—The rotation of mannose is influenced considerably by the concentration of the solution, as is shown from the following table in which the concentrations are expressed as grams per 100 cc. solution, the readings as degrees Ventzke with a 200 mm. tube, and the specific rotations as circular degrees dextrorotation for sodium light:

Concentration.	Reading.	Specific rotation.
3.250	2.75	14.6
4.579	3.85	14.5
10.202	8.3	14.1
16.890	13.25	13.6
20.539	15.9	13.4
30.049	22.8	13.1
39.708	29.3	12.8
50.000	35.6	12.3
60.000	41.15	11.9
70.000	46.05	11.4
80.000	50.4	10.9

Experiments with Fructose.

Only one modification of this ketose is known in the crystalline state, namely, β-fructose, but its upward (—133 to —92) mutarotation indicates the existence of the hypothetical α form. One of us has also shown that the α form is liberated from sucrose during the hydrolysis of that sugar by invertase.[2] The following experiments show that β-fructose exhibits a maximum rate of solution like the other mutarotating sugars. The fructose which was used was very pure, having been recrystallized many times, and to insure the presence of only the β form, the crystals (anhydrous $C_6H_{12}O_6$) were kept several days under 80% alcohol. Their initial specific rotation in water at 20°, in a concentration of about 10%, was —133.5 and their final $[\alpha]_D^{20} = -92.0$.

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[1] Hudson and Dale, THIS JOURNAL, 37, 1280 (1915).

[2] Hudson, *Ibid.*, 31, 655 (1909).

Solubility of β-Fructose in 80% Alcohol.—S_0 was found to be —53.2° V. (= 13.4 g.), S_∞ = —108.7 (= 27.4 g.), hence the equilibrium proportions are 49% β-fructose and 51% α form. The constant specific rotation of fructose in this solvent was —68.6 (in 10% concentration) and the initial $[\alpha]_D^{20}$ for β-fructose was the same as in water, —133.5, hence, $[\alpha]_D^{20}$ for α-fructose is calculated by the equation 0.49 (—133.5) + 0.51 (x) = —68.6 to be x = —7. A second experiment showed S_0 = —54.7, S_∞ = —107.2, and x = —1, while two further trials indicated x = —7 and —8. The value —7 is accordingly assigned as the specific rotation of α-fructose in 80% alcohol.

Solubility of β-Fructose in 95% Alcohol.—The initial specific rotation of the sugar in this solvent was —122, and the constant final value —52.5. S_0 was —5.5 (= 1.8 g.), S_∞ = —12.8 (= 4.2 g.), hence the equilibrium mixture consists of 43% β- and 57% α-fructose, and the specific rotation of the α-form in this solvent is calculated from these data to be x = 0.

Solubility of β-Fructose in Absolute Methyl Alcohol.—The initial and final specific rotations of the β form in this solvent were —122 and —61.4, respectively, S_0 was —18.5 (= 5.2 g.), and S_∞ was —39.3 (= 11.1 g.); hence, there was present in equilibrium 47% β- and 53% α-fructose. The calculated $[\alpha]_D^{20}$ for the α form is accordingly —8.

Reduction of the Rotation of α-Fructose in 80% Alcohol to Its Value in Water.—A solution of 20.11 g. fructose in 20 cc. water was allowed to come to equilibrium and then 80 g. of absolute alcohol were added, the volume measured (128 cc.) and the rotation immediately read in a 200 mm. tube. Its value —80.1° V. corresponded to $[\alpha]_D^{20}$ = —88, and in four repetitions the values —88, —88.5, —87, —89, were found. In all cases $[\alpha]_D^{20}$ finally became constant at —71. This value is slightly higher than that mentioned previously (—68.6) because the concentrations in the two cases differed; thus, a solution containing 17.1 g. fructose in 100 cc. 80% alcohol showed a specific rotation of —71, and the same solution diluted to a double volume showed a specific rotation of —69. Since the rotation immediately after dilution (—88) is less than that in water for this concentration (—93),[1] and since β-fructose rotates the same in the two solvents (initial $[\alpha]_D^{20}$ = —133.5) we conclude that α-fructose is more levorotatory in water than in 80% alcohol. The proportion of the α-isomer

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[1] Strictly speaking the comparable value for aqueous solution should be obtained by diluting the fructose solution with water in place of alcohol and reading the rotation immediately, but experiments have shown that the values obtained in this way do not differ enough from those of the stable aqueous solution to have any considerable effect upon the present studies. Thus, an 80% solution of fructose which was diluted to 5% with water and measured immediately changed in rotation on standing only to the extent of 3%. In our present experiments the concentrations before dilution with alcohol are not so great as 80%, and any correction would be entirely within experimental errors. This remark applies throughout the article.

in solution immediately after adding the alcohol, y, is obtained from the equation $133.5\ (1 - y) + 7y = 88$ to be $y = 36\%$. If the difference $93 - 88 = 5$ is due to 36% α-fructose the difference for the pure substance would be $5/0.36 = 14$. The specific rotation of α-fructose in water is accordingly taken to be $-7 - 14 = -21$.

Maximum Rate of Solution of β-Fructose in 80% Alcohol.—In the experiments on the solubility of the sugar in this solvent samples were removed at intervals from the continuously shaken mixture of solvent and crystals and the following maximum rate of solution was observed at 20°:

t (min.).	r (V°. 200 mm. tube).	$k_1 = \frac{1}{t} \log \frac{r_0 - r_\infty}{r - r_\infty}$.
0	—53.2	....
30	—68.6	0.0047
50	—76.7	0.0049
70	—83.7	0.0049
90	—88.4	0.0048
120	—96.0	0.0053
180	—99.6	0.0044
250	—103.4	0.0041
330	—106.8	0.0044
∞	—108.7	....
		Average, 0.0047

In a repetition of this measurement $r_0 = -54.7$, $r_\infty = -107.2$ and the average for k_1 was again 0.0047. As has been mentioned before, k_1 expresses the rate at which unit concentration of the α form changes in solution to the β-modification. Likewise, k_2 expresses the rate at which unit concentration of the β changes to the α form. If the concentrations of the two forms are (A) and (B) when equilibrium is attained, $(A)\ k_1 = (B)\ k_2$, hence, $(A)/(B) = k_2/k_1$. It has been shown by the measurements of S_0 and S_∞ that $A = 51\%$, $B = 49\%$. Since k_1 has been found to be 0.0047, k_2 is calculated from the above equation to be 0.0049 and, therefore, the unimolecular coefficient for the mutarotation of fructose ($k_1 + k_2$) is calculated to be 0.0096. A direct measurement of this coefficient from observations of the mutarotation of a freshly prepared solution of fructose in 80% alcohol at 20° showed the value 0.0091 in good agreement with the calculations.

Experiments with Maltose.

Only the β-modification of maltose is known in the crystalline state. A quantity of very pure recrystallized maltose was kept several days under 60% alcohol to insure its complete transformation to the stable crystalline phase which is β-maltose monohydrate ($C_{12}H_{22}O_{11}.H_2O$). The initial specific rotation of this substance in water was +112.5 (or +118 for anhydrous $C_{12}H_{22}O_{11}$), and the final rotation +129.5 (or +136 for the anhydrous sugar).

Solubility of β-Maltose Monohydrate in 60% Alcohol.—In this solvent the initial specific rotation of the hydrate was +105.7 (= 111.0 for the anhydrous sugar) and the final, 122.0 (= 128.1). S_0 was 22.7° V. (3.0 g. $C_{12}H_{22}O_{11}$), and S_∞, 35.3° (4.75 g.), hence the equilibrium mixture consisted of 64% β- and 36% α-maltose. The specific rotation of anhydrous α-maltose is calculated from the equation $0.64\ (111) + 0.36x = 128$ to be $x = 158$. Two repetitions of the experiment yielded the values 161 and 155, and the average of the three is 158.

Reduction of the Rotation of α-Maltose in 60% Alcohol to Its Value in Water.—A solution of 4.885 g. maltose hydrate in 40 cc. water was allowed to complete its mutarotation, 60 g. absolute alcohol were then added, the volume measured (115 cc.) and the rotation immediately read in a 200 mm. tube. Its value 29.9° V. corresponds to $[\alpha]_D^{20} = 128$ for anhydrous sugar. After some time the reading became constant at 131. In two repetitions of this measurement the initial values were 128 and 129, becoming constant at 131 in each case, hence 128 is chosen as the specific rotation for anhydrous maltose immediately after dilution with alcohol. The constant specific rotation of the same substance in water is 136, hence the difference $136 - 128 = 8$ must be attributed to the influence of the added alcohol upon the true specific rotations of the two forms of maltose which make up the equilibrium mixture. The proportions of the two forms in this mixture may be obtained from the equation $158\ (z) + 111\ (1 - z) = 128$ to be 36% α- and 64% β-maltose. It has been shown that the initial or true specific rotation of β-maltose is lower in 60% alcohol (111) than in water (118) by 7°, hence $(7)\ (0.64) = 4.5$ is taken as the change that is due to the β-maltose in the equilibrium mixture. The remainder of the decrease, $8 - 4.5 = 3.5°$, must be ascribed to the 36% of α-maltose present, and hence, pure α-maltose must rotate $3.5/0.36 = 10°$ less in 60% alcohol than in water. Adding this to the value found for 60% alcohol, 158, gives 168 as the specific rotation of anhydrous α-maltose in water. This value agrees very well with the one that has been calculated at the beginning of this article, 173°.

Experiments with Melibiose.

Very pure melibiose was prepared from raffinose according to the directions that have been published elsewhere,[1] and the crystalline material was kept several days under 80% alcohol to fully convert it to the stable β-melibiose dihydrate ($C_{12}H_{22}O_{11}.2H_2O$). The initial specific rotation of the hydrate in water was +113 (= 124 for $C_{12}H_{22}O_{11}$) and the final 129.5 (= 142.5). Bau[2] has found 129.6 for the final specific rotation of melibiose dihydrate in water.

Solubility of β-Melibiose Dihydrate in 80% Alcohol.—The initial

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[1] Hudson and Harding, THIS JOURNAL, **37**, 2734 (1915).

[2] *Z. Ver. Zuckerind.*, **41**, 481 (1904).

$[\alpha]_D^{20}$ in this solvent was 113 (= 124 for $C_{12}H_{22}O_{11}$), and the final 133.0 (= 146.3). S_0 was found 6.45° V. (0.76 g. anhydrous sugar), S_∞ was 10.7 (1.3 g.), hence the equilibrium mixture consists of 60% β-melibiose and 40% α-melibiose. The specific rotation of anhydrous α-melibiose is calculated from the relation $0.60 (124) + 0.40x = 146.3$ to be $x = +180$. In repetition $S_0 = 6.5$ and $S_\infty = 10.7$, hence $x = +180$. In a third measurement x was found 178, hence, the average $x = 179$ is chosen for the initial specific rotation of anhydrous α-melibiose in 80% alcohol.

Reduction of the Rotation of α-Melibiose in 80% Alcohol to Its Value in Water.—A solution of 2.637 g. β-melibiose dihydrate in 20 cc. water was kept overnight to establish equilibrium, and then 80 g. absolute alcohol were added, the volume measured (122 cc.) and the rotation immediately read in a 200 mm. tube. Its value 16.0° V. corresponds to $[\alpha]_D^{20} = 141$ for anhydrous sugar. This value is so near that previously recorded for water, 142.5, that it is not possible to say that the equilibrium mixture has appreciably different rotations in the two solvents. Since the initial specific rotations of β-melibiose in water and in 80% alcohol have the same value, 124, it must be concluded that the initial specific rotation of anhydrous α-melibiose is the same in water as has been calculated for 80% alcohol, namely, 179°. This value agrees completely with the rotation which may be calculated as has been done for maltose, since $124 + 55 = 179$. In a previous article[1] the value 175 was obtained through an independent method of calculation based upon the specific rotation of raffinose (+123), a derivative of melibiose.

While the specific rotation of the melibiose solution to which alcohol was added was 141 immediately after mixing, it slowly changed on standing to become constant at 146, which agrees with the value previously mentioned for the stable 80% alcoholic solution. This slow change is doubtless due to the slow shifting of the equilibrium ratio from its value in water to that in 80% alcohol. In repetitions of these experiments the values 140, 142, 140 and 141 were found immediately after the addition of alcohol, and they increased on standing to 146, 147, 145 and 146, respectively.

The Velocity of the Mutarotation of Melibiose.—The mutarotation of melibiose has been observed by Loiseau[2] and by Bau,[3] and from Bau's data we have calculated the unimolecular velocity coefficient $(k_1 + k_2)$ to be about 0.0082 at 20°, in terms of minutes and decimal logarithms. In repeating these observations we find that the reaction follows closely the unimolecular order and that $(k_1 + k_2)$ at 20° has the value 0.0088, which agrees well with Bau's result.

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[1] THIS JOURNAL, 38, 1569 (1916).

[2] *Z. Ver. Zuckerind.*, 40, 1050 (1903).

[3] *Ibid.*, 41, 481 (1904).

Experiments with Cellose.

Several hundred grams of cellose were prepared by the saponification of cellose octacetate, and the recrystallized very pure sugar was kept for several days under 20% alcohol to insure its complete conversion to the stable β-cellose. The isomeric α-cellose has never been prepared. The crystals of β-cellose ($C_{12}H_{22}O_{11}$) showed an initial $[\alpha]_D^{20}$ in water $= +16.0°$ and a final $[\alpha]_D^{20} = +35.0$.

The Solubility of β-Cellose in 20% Alcohol.—The initial $[\alpha]_D^{20}$ of the sugar in this solvent was $+18.5$, the final $+36.0$, S_0 was 6.7° V. (= 3.2 g.), S_∞ 9.8 (= 4.7 g.), and hence, the equilibrium mixture consists of about 67% α-cellose with 33% α-cellose. From the equation $0.67 (18.5) + 0.33x = 36.0$, the specific rotation of α-cellose in 20% alcohol is calculated to be $x = +72$. In two repetitions of this experiment x was found to be 72 and 73.

Reduction of the Rotation of α-Cellose in 20% Alcohol to Its Value in Water.—A solution of 4.439 g. cellose in 80 cc. water was allowed to reach equilibrium and then 20 g. alcohol were added, the volume measured (105 cc.), and the rotation immediately read in a 200 mm. tube. Its value 8.55° V. corresponds to $[\alpha]_D^{20} = 35$ which is the same as in aqueous solution and almost the same as the final constant rotation in 20% alcohol. A repetition of the experiment gave identical results. The initial $[\alpha]_D^{20}$ for β-cellose in 20% alcohol is so slightly different (2.5°) from its value in water, that it must be concluded from the fact that the equilibrium mixture rotates nearly the same in the two solvents, that α-cellose has nearly the same rotation in water as in 20% alcohol, namely, 72°. This agrees closely with the calculated value, since $18 + 55 = 73$.

The Velocity of the Mutarotation of Cellose.—The change of rotation of a freshly prepared solution of β-cellose in water from 16 to 35° is a slow one and it was found to follow the law of unimolecular reactions. At 20° the velocity-coefficient ($k_1 + k_2$) was 0.0047, in terms of minutes and decimal logarithms. This rate is about the same as that for lactose.

Experiments with Xylose.

Very pure recrystallized xylose ($C_5H_{10}O_5$) was kept several days under 80% alcohol to insure the presence of the stable α-xylose, and the initial $[\alpha]_D^{20}$ of the crystals was found to be $+92.0$ in water and the final rotation $+19.0$. The initial value of 100° for α-xylose which one of us has mentioned in a former article[1] was obtained from an uncertain extrapolation of older measurements by Parcus and Tollens[2] and is unquestionably too high.

The Solubility of α-Xylose in 80% Alcohol.—The initial $[\alpha]_D^{20}$ in this solvent was 94.5, the final 32.1, S_0 was 5.1° V. (= 2.7 g.), and S_∞ 11.5

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[1] Hudson, THIS JOURNAL, 31, 76 (1909).

[2] *Ann.*, **257**, 175 (1890); also *Z. Ver. Zuckerind.*, **27**, 853 (1890).

(= 6.2 g.), hence the equilibrium mixture consists of 44% α-xylose and 56 β-xylose. The specific rotation of β-xylose is calculated from the relation $0.44\ (94.5) + 0.56x = 32.1$ to be $x = -18°$. A second measurement gave $S_0 = 5.5$, $S_\infty = 12.0$ and $x = -21$, so —20 is taken as the value for β-xylose in 80% alcohol.

Reduction of the Rotation of β-Xylose in 80% Alcohol to Its Value in Water.—A solution of 5.402 g. xylose in 20 cc. water was allowed to reach equilibrium, and then 80 g. alcohol were added, the volume measured (121 cc.), and the solution immediately read in a 4 dcm. tube. The reading 10.0° V. corresponds to $[\alpha]_D^{20} = 19$, which is identical with the constant rotation in aqueous solution. On standing the specific rotation slowly increased to 31, which is sufficiently near the value that was found for the constant rotation in 80% alcohol in the more accurate determination that has been mentioned. A second experiment gave the same values. Since the initial $[\alpha]_D^{20}$ for α-xylose is nearly the same in water (92) and in 80% alcohol (94.5) it is concluded that β-xylose must rotate approximately the same in the two solvents, or —20. This experimental value is near that which would be expected from the fact that the α- and β-glucoses differ by 94°, because this difference for a hexose (m. w. 180) corresponds in the case of a pentose (m. w. 150) to $(94)\ (180)/150 = 113°$ and the calculated value for β-xylose, by this method, if α-xylose rotates +92, is $92 - 113 = -21°$.[1] The great difference between the constant rotations in water (19) and in 80% alcohol (32.1) is due to an influence of the alcohol upon the equilibrium ratio between the two forms of xylose rather than to an influence upon the true specific rotations of the forms.

The Velocity of the Mutarotation of Xylose in Water at Various Temperatures.—The velocity-coefficient $(k_1 + k_2)$ of this unimolecular reaction was found to have the following values in terms of minutes and decimal logarithms:

Temperature.	1.	10.	20.	30.	40.
$(k_1 + k_2)$...........	0.0028	0.0075	0.0207	0.0532	0.133

The rate increases about 2.7 fold for a rise of 10° in temperature.

Experiments with Lyxose.

A supply of this pentose was prepared by oxidizing calcium *d*-galactonate with hydrogen peroxide and basic ferric acetate according to Ruff and Ollendorff's[2] directions. The very pure recrystallized lyxose was kept several days under 90% alcohol to insure the conversion of the crystals to the stable form, anhydrous α-lyxose. The initial $[\alpha]_D^{20}$ of the pure material was +5.5 in water, and the constant value was —14.0.

The Solubility of α-Lyxose in 90% Alcohol.—Its initial $[\alpha]_D^{20}$ in this solvent was +5.5, the constant value was —7.9, S_0 was —2.45° V. (= 5.4

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[1] See This Journal, 31, 76 (1909).

[2] *Ber.*, 33, 1798 (1900).

g.) and S_∞ was —3.6 (7.9 g.), hence the equilibrium mixture consists of 68% α-lyxose and 32% β-lyxose. The $[\alpha]_D^{20}$ of the unknown form, β-lyxose, may be calculated from the equation 0.68 (5.5) + 0.32 (x) = —7.9 to be x = —37. A second measurement showed S_0 = —2.6 and S_∞ = —3.9, hence x = —36.

Reduction of the Rotation of β-Lyxose in 90% Alcohol to Its Value in Water.—A solution of 9.19 g. lyxose in 15 cc. water was allowed to reach equilibrium and then 135 g. absolute alcohol were added, the volume measured (190 cc.) and the rotation immediately read in a 200 mm. tube. The reading —4.2° V. corresponds to $[\alpha]_D^{20}$ = —15, which is almost the same as for aqueous solution. After several hours' standing the solution showed the constant specific rotation of —7.5, which is nearly the same value as is recorded above from another experiment. Since the initial values for α-lyxose in water and in 90% alcohol are identical (+5.5) and since the specific rotation of the equilibrium mixture immediately after the addition of alcohol is almost the same as in aqueous solution, we conclude that the value —36 holds for the initial specific rotation of β-lyxose in both 90% alcohol and water.

The Velocity of the Mutarotation of Lyxose.—This reaction was measured in aqueous solution at 20°, was found to follow the unimolecular order and the value of its velocity coefficient ($k_1 + k_2$) was 0.065, in terms of minutes and decimal logarithms.

Experiments with Arabinose.

A supply of *d*-arabinose was prepared by oxidizing calcium *d*-gluconate with hydrogen peroxide and basic ferric acetate according to the directions of Ruff.[1] The very pure recrystallized sugar was kept several days under 80% alcohol to insure its complete conversion to the stable phase which is anhydrous β-arabinose ($C_5H_{10}O_5$). The initial $[\alpha]_D^{20}$ of the crystals was —175 in water, and the final constant levorotation —105.0.

The Solubility of β-*d*-Arabinose in 80% Alcohol.—The initial $[\alpha]_D^{20}$ of the sugar in this solvent was —173 and the final rotation was —81.7. S_0 was —3.5° V. (0.74 g.) and S_∞ was —9.2 (= 1.94 g.), hence the equilibrium mixture consists of 38% β- and 62% α-arabinose. The specific rotation of α-arabinose is calculated from the relation 0.38 (—173) + 0.62x = —81.7 to be x = —26. Four repetitions of this measurement gave the values —32, —26, —28, and —28 for x, or —28 as the average.

Reduction of the Rotation of α-*d*-Arabinose in 80% Alcohol to Its Value in Water.—A solution of 3.41 g. arabinose in 20 cc. water was kept a few hours to allow its mutarotation to become complete and then 80 g. absolute alcohol were added, the volume measured (122 cc.) and the solution immediately read in a 200 mm. tube. The reading —14.5° V. corresponds to $[\alpha]_D^{20}$ = —90°, and three repetitions of the experiment gave the

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[1] *Ber.*, 32, 550 (1899).

same value. This rotation is considerably less than that for the stable aqueous solution, —105, and since β-arabinose has nearly identical initial rotations in the two solvents, namely, —173 and —175, as mentioned, it is evident that α-arabinose is much more levorotatory in water than in 80% alcohol. The proportion of α-arabinose (y) in the 80% alcoholic solution immediately after the addition of the alcohol is found from the equation $173 (1 - y) + 28y = 90$ to be 57%. If the depression from —105 to —90 is due to 57% β form the difference in the case of the pure β-sugar would be $15/0.57 = 26°$, and the specific rotation of β-arabinose in water is, therefore, calculated to be $-28 - 26 = -54°$. This experimental value is near that which would be expected from the fact that the α- and β-glucoses differ by 94°, because the calculated value for α-arabinose by the method that was mentioned in the case of xylose is $-175 + 113 = -62°$.

A Peculiarity in the Mutarotation of Arabinose.—This pentose, which is very closely related to galactose in its configuration, shows the same anomaly that has previously been described for that sugar. The rotation of the solution mentioned in the preceding paragraph, which was —14.5 immediately after the addition of the alcohol, did not change gradually to a constant value, but instead decreased to —12.9 and then increased to —13.7, the constant final value. In three repetitions of this measurement, the corresponding values $-14.5 \longrightarrow -13.0 \longrightarrow -13.8$, $-9.4 \longrightarrow -8.4 \longrightarrow -8.9$, and $-10.0 \longrightarrow -8.9 \longrightarrow -9.5$ were found.

Experiments with Rhamnose.

The pure recrystallized rhamnose hydrate ($C_6H_{12}O_5.H_2O$) which was used in the measurements showed an initial $[\alpha]_D^{20}$ in water of —7.7° (calculated as anhydrous $C_6H_{12}O_5$), and a final rotation of +8.9. Since rhamnose beongs to the *l*-series its more levorotatory form is to be named alpha.

Solubilities of Alpha Rhamnose Hydrate in Absolute Alcohol.—The initial $[\alpha]_D^{20}$ in this solvent was —19.4 (as anhydrous sugar), the final was —9.9°, the initial solubility was —5.0° V. (corresponding to 8.6 g. $C_6H_{12}O_5$ per 100 cc. solution) and the final solubility was —5.5° (9.5 g.). The solution accordingly contains an equilibrium mixture of 91% α- and 9% β-rhamnose. The specific rotation of anhydrous β-rhamnose is calculated from the equation $0.91 (-19.4) + 0.09x = -9.9$ to be $x = 86°$. A repetition of the experiment gave the same result.

Solubilities of Alpha Rhamnose Hydrate in 70% Alcohol.—The initial $[\alpha]_D^{20}$ in this solvent was —13.0° (as anhydrous sugar), the final was —3.5, the initial solubility was —3.3° V. in a 400 mm. tube (corresponding to 8.2 g. per 100 cc. solution), and the final solubility was —3.9° V. (9.6 g.). Therefore, the equilibrium mixture in this solvent consists of 85%

α-and 15% β-rhamnose. The specific rotation of β-rhamnose is calculated from the equation $0.85\ (-13) + 0.15x = -3.5$ to be $x = 50$. A second measurement gave the same result.

Reduction of the Rotation of β-Rhamnose in 70% Alcohol to Its Value in Water.—A solution of 12.87 g. rhamnose hydrate in 30 cc. water was kept several hours to allow its mutarotation to become complete and then 70 g. absolute alcohol were added, the volume measured (124 cc.) and the solution immediately read at 20° in a 400 mm. tube. The reading +4.4° V. corresponds to $[\alpha]_D^{20} = +4.0°$ for the anhydrous substance. In the course of a few hours this specific rotation changed to become constant at —3.5. The difference between the rotations in water (+8.9) and in the freshly prepared 70% alcoholic solution (+4.0) must be ascribed to the influence of change of the solvent upon the rotations of the α and β forms of rhamnose. The proportions of these forms which are present in solution immediately after the addition of the alcohol are obtained from the equation $-13y + 50\ (1 - y) = +4.0$ to be $y = 73\%$ α-rhamnose and $1 - y = 27\%$ β-rhamnose. Since the initial rotations of α-rhamnose in water and in 70% alcohol are —7.7 and —13, respectively, giving a difference of 5.3°, the depression that would be due to the influence of the change of solvent upon the 73% of α-rhamnose is $(5.3)\ (0.73) = 3.8°$. The total depression was found to be $8.9 - 4.0 = 4.9°$, hence $4.9 - 3.8 = 1.1°$ is due to the 27% of β-rhamnose. Accordingly, the change for pure β-rhamnose would be $1.1/0.27 = 4°$ and the initial specific rotation of anhydrous β-rhamnose in water is obtained from these data to be $50 + 4 = 54$. Several repetitions of these measurements gave the same result.

Experiments with α-Glucoheptose.

A supply of this sugar was prepared from *d*-glucose according to Fischer's[1] directions, and after careful recrystallization the pure material was kept under 20% alcohol several days. The initial $[\alpha]_D^{20}$ of the sugar (anhydrous $C_7H_{14}O_7$) in water was —28.4 and the final rotation —20.4. Since α-glucoheptose is a derivative of *d*-glucose, its more levorotatory form is to be named β,α-glucoheptose.

Solubilities of β,α-Glucoheptose in 20% Alcohol.—The initial rotation in this solvent was —28.3, the final —19.6, the initial solubility was —4.5 (4.0 g. per 100 cc. solution) and the final solubility —5.1 (4.5 g.). The equilibrium mixture accordingly consists of 88% β- and 12% α,α-glucoheptose. The specific rotation of the α-form in 20% alcohol is calculated from the equation $0.88\ (-28.3) + 0.12x = -19.6$ to be $x = +45$. A repetition gave the same value.

Reduction of the Rotation of α,α-Glucoheptose in 20% Alcohol to Its Value in Water.—The specific rotation of a stable solution of 4.08 g. α-glucoheptose in 80 cc. water, to which 20 g. absolute alcohol had just been

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[1] *Ann.*, **270**, 64 (1892).

added, was —20, a value nearly identical with the constant rotation in either water or 20% alcohol. Since the initial $[\alpha]_D^{20}$ of β,α-glucoheptose is nearly the same in the two solvents it is to be concluded that the unknown α,α-glucoheptose rotates the same in water as in 20% alcohol, namely, $+45°$. The difference between the rotations of the α and β forms of this sugar (m. w. 210) is accordingly $45 + 38 = 73°$, whereas the difference of 94° in the case of the α and β forms of glucose (m. w. 180) would lead one to expect $(94)(180)/210 = 81°$. The agreement is fair in view of the indirectness of the experimental measurements.

Experiments with Sucrose, Raffinose and Trehalose.

In concluding this investigation, some measurements were made for the purpose of determining whether sugars which do not occur in alpha and beta forms and do not exhibit mutarotation show a maximum rate of solution. It was to be expected that they would not do so. Supplies of very pure crystals of sucrose ($C_{12}H_{22}O_{11}$), raffinose ($C_{18}H_{32}O_{16}.5H_2O$), and trehalose ($C_{12}H_{22}O_{11}.2H_2O$) were prepared and it was found that the shaking of each of these substances with aqueous alcohol (80% in the case of sucrose, 70% with trehalose, and 50% with raffinose) at 20° yielded a finally saturated solution within five minutes after mixing, showing that the non-mutarotating sugars do not exhibit a maximum rate of solution.

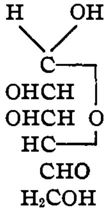
Summary and Discussion of Results.

It is generally recognized that the sugars which show mutarotation (*e. g.*, the aldoses and ketoses) differ from those which do not by the following characteristics: (1) existence in alpha and beta forms, though one of these forms may not have been isolated in the crystalline state; (2) power of combining with phenylhydrazine; and (3) of reducing Fehling's solution. It is now shown that the mutarotating sugars have another common property, namely, a measurable maximum rate of solution which is caused by the slow establishment in solution of the equilibrium between the α and β forms of the sugar. The non-reducing, non-mutarotating sugars (*e. g.*, sucrose, trehalose, raffinose) do not show this maximum rate of solution. By measuring the maximum rate of solution, or the initial and final solubilities, of many of the mutarotating sugars, it has been possible to obtain experimental evidence on the rotatory powers of those forms of these sugars which have as yet not been crystallized and measured directly. In the following table a summary is recorded of the specific rotations, in water at 20°, of the alpha and beta forms of nearly all the sugars which show mutarotation, together with the final specific rotations that refer to the equilibrium mixture of the alpha and beta forms. The values that are printed in italics have been obtained by the indirect measurements of the initial and final solubilities, as described in this article, and the other values are the result of direct observation.

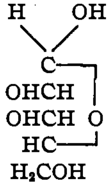
ROTATORY POWERS OF THE MUTAROTATING SUGARS.

Sugar.	M. w.	Formula.	Specific rotation in water. α Form.	Const. rot.	β Form.	Molecular rotation difference.
d-Glucose	180	$C_6H_{12}O_6$	+113.4	+52.2	+19	+16900
d-Galactose	180	$C_6H_{12}O_6$	+144.0	+80.5	+52	+16600
d-Mannose	180	$C_6H_{12}O_6$	+*34*	+14.6	—17	+9180
d-Fructose	180	$C_6H_{12}O_6$	—*21*	—92.0	—133.5	.....
d-Xylose	150	$C_5H_{10}O_5$	+92	+19	—*20*	+16800
d-Lyxose	150	$C_5H_{10}O_5$	+5.5	—14	—*36*	+6220
d-Arabinose	150	$C_5H_{10}O_5$	—*54*	—105	—175	+18100
l-Rhamnose	164	$C_6H_{12}O_5$	—7.7	+8.9	+*54*	—10000
α-Glucoheptose	210	$C_7H_{14}O_7$	+*45*	—20.4	—28.4	+15300
Lactose	342	$C_{12}H_{22}O_{11}$	+90.0	+55.3	+35	+18800
Maltose	342	$C_{12}H_{22}O_{11}$	+*168*	+136	+118	+17100
Melibiose	342	$C_{12}H_{22}O_{11}$	+*179*	+142.5	+124	+18800
Cellose	342	$C_{12}H_{22}O_{11}$	+*72*	+35	+16	+19200

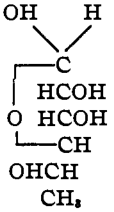
In the last column are recorded the differences between the molecular rotations of the respective alpha and beta forms of each aldose. If the rotatory power of the end asymmetric carbon atom in these aldoses has the value +A for the α-sugar and —A for the β form, and the rotation of the remainder of the structure is B, the molecular rotation of an α-sugar is A + B, and of its β form —A + B, and the difference of these values is 2A. It is to be expected, on the view that the value of A is not influenced by changes in the configuration of the remainder of the molecule, that this difference 2A is a constant for all the aldoses. The last column shows that the theory is fairly well borne out except in the case of mannose, lyxose and rhamnose. Fructose is not considered since it is a ketose and does not apply in the theory. The negative sign for the difference in the case of rhamnose is the result of the system of nomenclature for the α and β forms and is due to the fact that rhamnose is an *l*-series sugar. Now the configurations of *d*-mannose, *d*-lyxose and *l*-rhamnose are



d-Mannose.



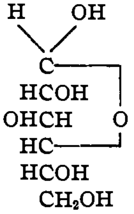
d-Lyxose.

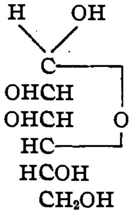


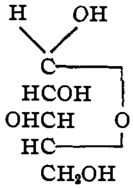
l-Rhamnose.

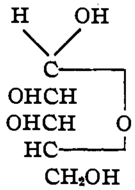
and it will be observed that these configurations are indentical (or antipodal) from the γ-carbon atom upward. It appears probable, therefore, that the exceptional value of the difference for these sugars may be dependent upon this type of configuration. Since, however, α-glucoheptose has the same configuration from the γ-carbon upward, and nevertheless shows a molecular difference nearer, though not equal, to the average value for most of the aldoses, this possible connection between structure and exceptional rotation remains in some doubt. In the case of closely related sugars, such as the four disaccharides, the agreement between theory and experiment is very good when it is recalled that it has been possible to make the measurements only by an indirect procedure.

A comparison of the configurations of the corresponding forms (either α or β thoroughout) of *d*-glucose, *d*-mannose, *d*-xylose and *d*-lyxose


d-Glucose.


d-Mannose.


d-Xylose.


d-Lyxose.

shows that the two hexoses differ by the configuration of the second carbon atom from the top, and likewise the two pentoses. This carbon atom, which is asymmetric, may accordingly be assigned the rotation $+C$ in the case of glucose and xylose and $-C$ for mannose and lyxose. From the considerations mentioned in the previous paragraph it appears that the terminal asymmetric carbon atom, of rotation A in the case of glucose and xylose ($+A$ for the α form and $-A$ for the β-modification) has a somewhat different rotation in the case of mannose and lyxose which may be denoted as A'. The rotation of the α and β forms of *d*-glucose may accordingly be written $(+A + C + D)$ and $(-A + C + D)$, respectively, where D is the rotation due to the asymmetric carbon atoms other than the two uppermost. The corresponding values for mannose are $(+A' - C + D)$ and $(-A' - C + D)$, for xylose $(+A + C + D')$ and $(-A + C + D')$ where D' is of different value from D, and for lyxose $(+A' - C + D')$ and $(-A' - C + D')$. The sums of the values for the two forms of each of these sugars are $2(C + D)$ for glucose, $2(-C + D)$ for mannose, $2(C + D')$ for xylose and $2(-C + D')$ for lyxose. Subtracting the sum for mannose from that for glucose gives 4C, and this is also the difference between the sums for xylose and lyxose. This conclusion can be tested by experiment. Using the specific rotations that are recorded in the preceding table the value of C for the two hexoses (m. w. 180) is $180\ [(113 + 19) - (34 - 17)]/4 = 5200$, and for the two pentoses (m. w. 150) is $150\ [(92 - 20) - (5 - 36)]/4 = 3900$. These values differ by 1300 in terms of molecular rotation, which corresponds to $1300/180 = 7°$ in the specific rotation of a hexose. This is not beyond the limits of the experimental errors that are involved in the indirect measurements of the rotations of the unknown forms of mannose, xylose and lyxose, and it may be concluded, therefore, that the average of these differences, 4500, represents the value of the molecular rotation of the α-carbon in these four sugars (+4500 for glucose and xylose and —4500 for mannose and lyxose).

The speeds of mutarotation of most of the sugars are indicated in the following table, the values for lyxose, α-glucoheptose, melibiose and cellose being recorded for the first time:

THE VELOCITY-COEFFICIENTS OF THE MUTAROTATION OF THE SUGARS IN WATER AT 20°.

Sugar.	$k_1 + k_2 = \frac{1}{t} \log \frac{r_0 - r_\infty}{r - r_\infty}$ (minutes and decimal logarithms).
Fructose	0.082[1]
Lyxose	0.065
Rhamnose	0.039[2]
Arabinose	0.031[3]
Fucose	0.022[4]
Xylose	0.021[3]
Mannose	0.0190[5]
α-Glucoheptose	0.0122
Galactose	0.0102[3]
Melibiose	0.0088
Maltose	0.0072[3]
Glucose	0.0065[6]
Cellose	0.0047
Lactose	0.0046[7]

The initial and final solubilities of most of the crystalline sugars are summarized in the following table:

SOLUBILITIES OF SUGARS AT 20°.

			Grams of anhydrous sugar in 100 cc. solution.	
Sugar.	Formula.	Solvent.	Init. sol.	Final sol.
α-Arabinose	$C_5H_{10}O_5$	80% alcohol	0.74	1.94
β-Cellose	$C_{12}H_{22}O_{11}$	20% alcohol	3.2	4.7
β-Fructose	$C_6H_{12}O_6$	80% alcohol	13.4	27.4
β-Fructose	$C_6H_{12}O_6$	95% alcohol	1.8	4.2
β-Fructose	$C_6H_{12}O_6$	Methyl alcohol	5.2	11.1
α-Galactose	$C_6H_{12}O_6$	60% alcohol	1.1	3.1
α-Galactose	$C_6H_{12}O_6$	80% alcohol	0.27	0.65
β,α-Glucoheptose	$C_7H_{14}O_7$	20% alcohol	4.0	4.5
α-Glucose	$C_6H_{12}O_6$	80% alcohol	2.0	4.5
α-Glucose	$C_6H_{12}O_6$	Methyl alcohol	0.85	1.6
α-Glucose Hydrate	$C_6H_{12}O_6.H_2O$	80% alcohol	1.3	3.0
β-Glucose	$C_6H_{12}O_6$	80% alcohol	4.9	9.1

[1] Hudson and Yanovsky, forthcoming publication.

[2] Osaka's calculation (*Z. physik. Chem.*, **35**, 661 (1900)) of Schnelle's results (*Dissertation*, Göttingen (1891)).

[3] Osaka's calculation from Parcus and Tollens' (*Ann.*, **257**, 160 (1890)) results.

[4] Osaka's calculation from Günther and Tollens' (*Ibid.*, **271**, 90 (1892)) results.

[5] Hudson and Sawyer, THIS JOURNAL, **39**, 470 (1917).

[6] Hudson and Dale, *Ibid.*, **39**, 320 (1917).

[7] Hudson, *Z. physik. Chem.*, 44, 487 (1903).

SOLUBILITIES OF SUGARS AT 20° (*continued*).

			Grams of anhydrous sugar in 100 cc. solution.	
Sugar.	Formula.	Solvent.	Init. sol.	Final sol.
α-Lactose hydrate	$C_{12}H_{22}O_{11}.H_2O$	40% alcohol	1.1	2.4
α-Lyxose	$C_5H_{10}O_5$	90% alcohol	5.4	7.9
β-Maltose hydrate	$C_{12}H_{22}O_{11}.H_2O$	60% alcohol	3.0	4.75
β-Mannose	$C_6H_{12}O_6$	80% alcohol	2.4	13.0
β-Mannose	$C_6H_{12}O_6$	Methyl alcohol	0.78	4.4
β-Melibiose dihydrate	$C_{12}H_{22}O_{11}.2H_2O$	80% alcohol	0.76	1.3
α-Rhamnose hydrate	$C_6H_{12}O_5.H_2O$	Absolute alcohol	8.6	9.5
α-Rhamnose hydrate	$C_6H_{12}O_5.H_2O$	70% alcohol	8.2	9.6
α-Xylose	$C_5H_{10}O_5$	80% alcohol	2.7	6.2
Sucrose	$C_{12}H_{22}O_{11}$	80% alcohol	3.7	3.7
Trehalose dihydrate	$C_{12}H_{22}O_{11}.2H_2O$	70% alcohol	1.8	1.8
Raffinose pentahydrate	$C_{18}H_{32}O_{16}.5H_2O$	50% alcohol	1.4	1.4

WASHINGTON, D. C.

[CONTRIBUTION FROM THE CARBOHYDRATE LABORATORY, BUREAU OF CHEMISTRY, UNITED STATES DEPARTMENT OF AGRICULTURE.]

THE PREPARATION OF XYLOSE.

BY C. S. HUDSON AND T. S. HARDING.

Received March 5, 1917.

The pentose sugar xylose has not been readily accessible to most investigators because it has been sold only at a very high price and its preparation has been a matter of considerable uncertainty. Since it was needed in large quantities in this laboratory, its isolation from various natural sources was studied in order to obtain, if possible, an inexpensive and accessible source and a dependable method for its preparation.

The Best Source for Xylose.—The sugar does not appear to have been noticed in the free state in nature, but it is very widely distributed among plants in the form of a condensation product, the gum xylan. By the acid hydrolysis of xylan the pentose is liberated and may be readily crystallized from the solution by the usual methods for isolating sugars. Beginning with the isolation of xylose from wood by its discoverer Koch[1] in 1886, it has been obtained also from brewer's grain,[2] straw,[3] corn cobs,[4] jute,[5] hay,[6] flax,[6] the alkaline cook liquor obtained by the action of hot

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[1] *Pharm. Z. Russland*, **25**, 619 (1886).

[2] Stone and Tollens, *Ann.*, **249**, 238 (1888).

[3] Hebert, *Ann. Agron.*, 16, 364 (1890); Bertrand, *Compt. rend.*, **114**, 1492 (1892); and *Bull. soc. chim.*, [3] **5**, 555 (1891); Schulze and Tollens, *Ann.*, **271**, 40 (1892).

[4] Stone and Lotz, *Am. Chem. J.*, 13, 348–50 (1891); *Chem. News*, **64**, 29 (1891); *Ber.*, **24**, 1657 (1891).

[5] Wheeler and Tollens, *Ann.*, **254**, 304 (1889); *Ber.*, **22**, 1046 (1889); *Z. Ver. Zuckerind.*, **26**, 848 (1889).

[6] Hebert, *Ann. Agron.*, 18, 261 (1892).