dizes a part of the hydrol to the ketone and transforms the rest into the ether.

CAMBRIDGE, MASS.

CRYSTALLINE β-METHYL FRUCTOSIDE AND ITS TET-RACETATE.[1]

BY C. S. HUDSON AND D. H. BRAUNS.

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In a previous article[2] several methods for the preparation of tetracetyl fructose were described and it was shown that the action on fructose of acetic anhydride containing $ZnCl_2$ gives the best result and yields about 36% of the theory. This easily prepared crystalline tetracetate is a convenient material from which to start the preparation of various fructose derivatives and in the article mentioned its conversion to α-pent-acetyl fructose was described. We have now sought to use it in the preparation of a monomethoxy derivative of fructose, and have applied to it the method of methylation with methyl iodide and silver oxide which was devised by Purdie.[3] Although this method has been applied with good success to the preparation of methylated derivatives of many of the sugars, particularly by Irvine and his co-workers, fructose has never yielded but two pure derivatives. Purdie and Paul[4] prepared tetra-methyl fructose in crystalline form, and Irvine and Hynd[5] obtained a crystalline monomethyl fructose by the methylation of fructose diace-tone and showed that the methoxy group in it is attached to the terminal carbon atom farthest from the ketonic carbon. Our results show that Purdie's method of methylation succeeds excellently with fructose tetrace-tate and gives almost a quantitative yield of pure crystalline tetracetyl monomethoxy fructose, the acetyl groups of the tetracetate not being affected by the methyl iodide of neutral reaction. The substance crys-tallizes very well from petroleum ether in long prismatic needles. Its saponification with barium hydroxide has yielded a crystalline mono-methoxy fructose which does not reduce Fehling's solution until after hydrolysis by acid. This reaction differentiates the substance from Irvine and Hynd's monomethoxy fructose, which reduces strongly, and proves that our crystalline material is *methyl d-fructoside.* On the probable assumption that it is a γ-cyclo derivative, its constitution is
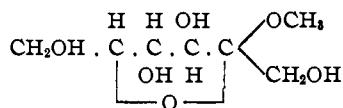
[1] Contribution from the Carbohydrate Laboratory, Bureau of Chemistry, United States Department of Agriculture.
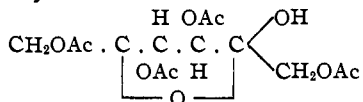
[2] THIS JOURNAL, 37, 2736 (1915).

[3] "A General Review of Purdie's Reaction," by Charles Robert Young, Memorial Volume of Scientific Papers of St. Andrews University, 500th Anniversary.

[4] J. Chem. Soc., 91, 289 (1907).
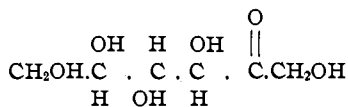
[5] Ibid.. 95, 1220 (1909).

$$\underset{\underset{\displaystyle \boxed{\rule{2.5cm}{0pt}} \text{O} \boxed{\rule{1.5cm}{0pt}}}{\text{OH H}}}{\text{CH}_2\text{OH}\,.\,\overset{\text{H}}{\text{C}}\,.\,\overset{\text{H}}{\text{C}}\,.\,\overset{\text{OH}}{\text{C}}\,.\,\text{C}} \underset{\text{CH}_2\text{OH}}{\overset{\text{OCH}_3}{\big\langle}}$$

Its formation from *tetracetyl d-fructose* establishes the configuration of that substance similarly as

$$\underset{\underset{\boxed{\rule{2.5cm}{0pt}} \text{O} \boxed{\rule{1.5cm}{0pt}}}{\text{OAc H}}}{\text{CH}_2\text{OAc}\,.\,\overset{\text{H}}{\text{C}}\,.\,\overset{\text{OAc}}{\text{C}}\,.\,\text{C}\,.\,\text{C}} \underset{\text{CH}_2\text{OAc}}{\overset{\text{OH}}{\big\langle}}$$

The high negative rotation of methyl fructoside (-172 in water) in comparison with that of β-fructose (-133 in water) indicates that it is a beta derivative. It is not hydrolyzed by the enzymes of yeast nor by emulsin and does not show mutarotation, behaving quite like the only other known methyl ketoside, methyl *l*-sorboside.[1]

[1] Fischer, *Ber.*, **28**, 1145 (1895). The antipode has been prepared by Lobry de Bruyn and van Ekenstein (*Rec. trav. chim.*, **19**, 1 (1900)). There appears to be sufficient evidence at hand to permit the designation of this sorboside and its antipode as alpha derivatives, and, this being the case, their formation by the methylation of sorbose or its antipode with methyl alcohol and HCl falls in with what appears to be a general rule among the sugars that *this reaction produces the alpha isomer in considerable excess over the beta form*, doubtless because the equilibrium between the two isomers in methyl alcoholic solution is considerably towards the alpha form. The evidence in point consists in the fact that the specific rotation of methyl sorboside is —88 in comparison with —42 for sorbose. Since the structure of sorbose has been shown by Fischer to be

$$\underset{\text{H}\quad \text{OH}\quad \text{H}}{\text{CH}_2\text{OH}.\text{C}\ .\ \overset{\text{OH}}{\text{C}}.\overset{\text{H}}{\text{C}}\ .\ \overset{\overset{\text{O}}{\|}}{\text{C}}.\text{CH}_2\text{OH}}$$

we consider that in the designation of the alpha and beta forms of its derivatives, according to the plan which one of us has suggested for the sugars (Hudson, THIS JOURNAL, **31**, 72 (1909)), sorbose should be considered as a relative of *l*-glucose, because both may be regarded as higher sugars from *l*-glycerose, CH₂OH.C.COH. The designation of the alpha and beta derivatives of *l*-glucose has been so made that the alpha form is more levorotatory than the beta, just as the alpha and beta forms of *d*-glucose have been so chosen that the alpha is more dextrorotatory than the beta. By this method of naming, α,*l*-glucose is the optical antipode of α,*d*-glucose, and β,*l*-glucose and β,*d*-glucose are likewise so related, which seems desirable in any system of nomenclature. Since sorbose is here considered as a levo sugar the possible alpha and beta *l*-sorbosides should be named so that the alpha form is the more levorotatory. Although only one methyl *l*-sorboside has been prepared in crystalline form, the fact that it is more levorotatory (—88) than the parent sugar *l*-sorbose (—42) indicates, by analogy with the other sugars, that the unknown *l*-methyl sorboside is less levorotatory than the sugar, and hence less so than the known *l*-sorboside; the latter is accordingly to be named the alpha form.

In this connection we would mention that sorbose has been designated by Fischer

Since the employment of tetracetyl fructose for the synthesis of other compounds makes knowledge of its structure desirable we thought it

as d-sorbose because on reduction it yields the same sorbite as does d-glucose. This designation was a subject of discussion between Rosanoff (THIS JOURNAL, **28,** 114 (1906)), who suggested the name l-sorbose on account of the structural relationship of the sugar to l-glycerose and l-glucose, and Fischer (*Ber.*, **40,** 102 (1907)), who preferred d-sorbose, because as a matter of history the structure of sorbose was proved in part through the reduction of it and of d-glucose to the same form of sorbite. According to our understanding of Fischer's point of view, as given in his article, he regarded the naming as a matter of convention and preference, since the fundamental structure configurations which he proved for the sugars are in no way affected by the nomenclature that may be adopted for distinguishing the d- and l-forms of the sugars, and he was of the opinion that any advantage to be gained by changing his designation of sorbose from d- to l- was not sufficient to outweigh the temporary confusion that always occurs when historical names are changed. Against this view it is to be said that at the present time the conditions are somewhat different from what they were in 1907 when the discussion between Rosanoff and Fischer took place, because it was not known at that time that a general relation exists in the sugar group between the rotatory powers of the alpha and beta forms of the sugars and their derivatives. The naming of these forms as alpha or beta according to this general relation among their rotatory powers, which seems very desirable because it furnishes in many cases at present the only method of distinguishing the members of the two series, becomes greatly confused unless the d- and l-forms of the sugars are selected on the basis of the structural relationships that follow from the cyanhydrin synthesis in the sugar group. We consider therefore that it is advisable, in order to prevent the increase of confusion in the nomenclature of the sugar derivatives, to apply the term l-sorbose to the sugar which Fischer has shown to have the configuration mentioned. The other sugars to which the same remarks apply are xylose, gulose, idose and threose.

Irvine and Garrett (*J. Chem. Soc.*, **97,** 1277 (1910)) have mentioned in connection with the provisional naming of the two fructose diacetones by Fischer (α-form, $[\alpha]_D^{20} = -161$ and β-form, $[\alpha]_D^{20} = -34$) that "the analogy to α- and β-glucosides in describing these compounds is not maintained in some respects. Thus the α-form * * * * is more easily hydrolyzed than the β-isomeride * * * *. This holds true not only for the removal of the acetone residue from the $3:4$ position but also for the glucosidic acetone group." According to the plan which we are following the more levorotatory of these fructose diacetones should be designated the beta form and the other the alpha because fructose is a d-series sugar, and since Fischer's use of the α- and β-designations for these substances was only provisional, for the purpose of distinguishing them, we suggest that these names be now reversed, as indicated, since it is possible to assign the substances to the alpha and beta series on the basis of their rotations. When this is done it is seen that the analogy to α- and β-glucosides in regard to the relative ease of hydrolysis, holds. This may serve very well as an example of the advantages that come from a uniform system of naming the alpha and beta, and also the d- and l-, forms of the sugars, as it is probable that many more analogies between structure and physical properties or chemical reactivities will be found among the alpha and beta derivatives of the sugars.

Since Purdie and Paul's crystalline tetramethyl fructose shows mutarotation in water from $[\alpha]_D^{20} = -125$ to -121, and Irvine and Hynd's monomethoxy fructose mutarotates from -70 to -53, they are both to be regarded as beta derivatives. Likewise, Irvine and Garrett's fructose monacetone, $[\alpha]_D^{20} = -159$, is doubtless a beta compound because it was prepared from β-fructose diacetone, $[\alpha]_D^{20} = -161$.

well to regenerate crystalline fructose from it by saponification and definitely identify the sugar, which had not been done before.

It appears very probable on theoretical grounds that β-methyl fructoside is one of the components of the uncrystallizable sirup which Fischer[1] obtained by the condensation of fructose with methyl alcohol, using HCl as a catalyst.

Experimental.

Preparation and Properties of β-Tetracetyl Methyl Fructoside.—Sixty grams of powdered fructose tetracetate, 375 g. of freshly prepared silver oxide and 340 cc. of methyl iodide were boiled on the water bath for six hours in a 2-liter Erlenmeyer flask with reflux condenser which was supplied with ice water in order to prevent loss of the solvent. The boiling of the methyl iodide (b. p. 44°) is not really essential because the reaction can be carried out quite as well at room temperature by shaking the mixture. In recovering the excess of MeI it is advisable to distil from a flask with a large bottom to prevent bumping. The residue from the distillation was mixed with some ether, filtered on a large Büchner funnel and the silver oxide washed with ether. The ether was evaporated in the air and the resulting colorless syrup soon crystallized. The first time that the reaction was carried out long standing of the sirup in a desiccator and occasional stirring with petroleum ether was necessary to induce crystallization, but in subsequent preparations crystallization took place readily even without seeding. The yield of the product, which was nearly pure as prepared, was almost the theoretical. For purification the crystals were boiled in a large flask with petroleum ether and the hot solution filtered and allowed to evaporate slowly in the air. In this way beautiful prismatic needles were obtained. The solubility of tetracetyl methyl fructoside in hot petroleum ether is only about 1 g. in 400 cc., but no other suitable solvent for recrystallization was found, as the substance is very soluble in all usual solvents excepting petroleum ether and water and in the latter it is almost insoluble. A second recrystallization from petroleum ether did not change the rotatory power or melting point. The substance melts at 75–76°, is colorless and odorless, and has a bitter taste. Analysis proves it to be a tetracetyl monomethoxy fructose.

0.2731 and 0.3082 g. substance gave 0.4982 and 0.5613 g. CO_2 and 0.1498 and 0.1682 g. H_2O.

Found: C, 49.75 and 49.67%; H, 6.14 and 6.10%. Theoretical for $C_6H_7O.OCH_3(C_2H_3O_2)_4$: 49.70 and 6.12%.

A methoxyl determination with 0.2484 g. substance gave 0.1581 g. AgI corresponding to 8.41% OCH_3. Theoretical 8.56%.

For the quantitative estimation of acetyl the substance was saponified by shaking 0.3000 g. with 75 cc. 0.1 N sodium hydroxide during one

[1] *Ber.*, **28**, 1145 (1895).

hour at 0° and titrating with 0.1 N sulfuric acid and phenolphthalein. The amount of acetic acid produced was found to be 66.45%. In a similar experiment of 2 hours' duration the value 66.31% was found and in a third lasting 2$\frac{1}{2}$ hours the value was 66.19%. The theoretical quantity for a tetracetylmethyl fructoside is 66.30%. Evidently the saponification is complete after one hour.

The molecular weight was determined by the lowering of the freezing point of benzene. In three experiments, 1.4330, 3.1622 and 4.8405 g. β-tetracetyl methyl fructoside per 100 g. benzene gave the respective depressions 0.210°, 0.449° and 0.672°, from which the values 341, 352 and 360 are calculated for the molecular weight in comparison with the theoretical value 362.

The specific rotation was measured in chloroform solution. 2.000 g. of once recrystallized β-tetracetyl methyl fructoside were made up to 25 cc. with chloroform[1] and the solution was found to read in a 1 dcm. tube at 20° with sodium light 9.95 circular degrees to the left, hence $[\alpha]_D^{20} = -124.4$. After a second recrystallization from petroleum ether, the substance rotated 9.97 circular degrees to the left in a similar solution, hence $[\alpha]_D^{20} = -124.6$, which is taken as the specific rotation of pure β-tetracetyl methyl fructoside.

Preparation and Properties of β-Methyl Fructoside.—The method of saponification which was used for the quantitative estimation of acetic acid in β-tetracetyl methyl fructoside was found unsuitable for the preparation and isolation of β-methyl fructoside because the latter could not be obtained free from sodium acetate by repeated recrystallization from alcohol. The following procedure gave the desired result:

Seventy grams of crystalline barium hydroxide (Ba(OH)$_2$ + 8H$_2$O) were dissolved in one liter of water on the steam bath and filtered into a bottle with a glass stopper. The solution was cooled with ice to about 5°, and although it was supersaturated at this temperature several experiments were performed without crystallization occurring. To it were added 20 grams powdered tetracetyl methyl fructoside, which required about half an hour's time, with occasional shaking, for complete solution. The liquid was kept one hour longer in ice and was then saturated with CO_2 and filtered. The amount of sulfuric acid necessary to precipitate the dissolved barium acetate was calculated to be 221.0 cc. normal H$_2$SO$_4$, since this amount is equivalent to the acetic acid that is obtainable from 20 g. of tetracetyl methyl fructoside. A somewhat smaller amount, 210 cc. of acid, was added with stirring and the mixture was centrifuged for a couple of hours or kept in the ice-box for a couple of days in order to separate as much as possible of the suspended barium sulfate. The milky liquid

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[1] *Chloroformum purificatum.* U. S. P.

was distilled *in vacuo* and some attention was needed in the beginning to prevent its foaming over into the receiver. After considerable concentration the solution could be filtered clear and by carefully adding 0.1 N H_2SO_4 to the filtrate it was brought to the stage where it gave only a slight precipitate with sulfuric acid. On evaporating this solution in a vacuum desiccator it soon crystallized to a solid mass. By repeated crystallization from hot absolute alcohol beautiful crystals were obtained which were free of ash. By slow evaporation large, thin plates were formed, which often measured 1 cm. square. The yield was about 80% of the theory.

β-Methyl fructoside melts at 119–120°. The crystals are colorless, odorless and have a pure, sweet taste. The taste of the α- and β-methyl glucoside is sweet followed by bitter. The fructoside is easily soluble in water and hot alcohol, slightly soluble in hot acetone and ethyl acetate. Its aqueous solution is not reduced by boiling with Fehling's solution. After hydrolyzing it by boiling its aqueous solution with a mineral acid and neutralizing the cooled solution, it readily reduces Fehling's solution on boiling. This reaction proves, in connection with the analysis recorded below, that the prepared substance is a methyl fructoside and also shows that in the described tetracetyl fructose the glucosidic hydroxyl is not acetylated.

0.2943 and 0.2246 g. subs. gave 0.4675 and 0.3576 g. CO_2 and 0.1905 and 0.1457 g. H_2O.

Found: C, 43.32 and 43.42%; H, 7.24 and 7.26%. Theoretical for $C_6H_{11}O_5$-(OCH_3): 43.27 and 7.27%.

A methoxyl determination with 0.2486 g. substance gave 0.2993 AgI corresponding to 15.92% OCH_3. Theoretical 15.98%.

The molecular weight of the substance was determined by the lowering of the freezing point of water. In three experiments 1.2063, 2.5524 and 3.7749 g. in 100 g. water gave the respective depressions 0.13°, 0.259° and 0.384°, from which the values 172, 182 and 182 are calculated for the molecular weight in comparison with the theoretical value 194 for a methyl fructoside.

The specific rotation of the substance was measured in water. 2.5012 g. β-methyl fructoside were made up to 25 cc. with water and a reading of 17.2 circular degrees to the left was obtained in a 1 dcm. tube at 20° with sodium light; hence $[\alpha]_D^{20} = -171.9°$. After a further crystallization from hot alcohol 2.5048 g. substance made up in the same manner rotated 17.23 circular degrees to the left; hence $[\alpha]_D^{20} = -172.1°$, which is taken as the specific rotation of pure β-methyl fructoside.

In a high vacuum β-methyl fructoside can be sublimed. The sublimate was found to have the same melting point and specific rotation as men-

tioned above for the pure material prepared by crystallization from solvents.

The substance is not hydrolyzed by the enzymes of yeast or by emulsin. 0.100 g. β-methyl fructoside was dissolved in 10 cc. of water and after the addition of some fresh top fermentation yeast the solution was kept at room temperature in a fermentation tube. No gas was produced after 48 hours, but under the same conditions several cc. of CO_2 were produced from 0.100 g. fructose. For testing the action of emulsin a solution of 0.100 g. β-methyl fructoside in 8 cc. of water was mixed with 0.100 g. emulsin and the whole kept in a closed bottle at 35° for 48 hours, and as checks there were kept under the same conditions a solution of 0.100 g. amygdalin and 0.100 g. emulsin in 8 cc. of water and a mixture of 0.100 g. emulsin with 8 cc. water. After 48 hours the solutions were filtered and the filters washed with water. The three filtrates were boiled with Fehling's solution under the conditions of the quantitative determination of glucose by Allihn's method. Only the filtrate from the amygdalin mixture reduced Fehling's solution; the Cu obtained by glowing and reducing the precipitate weighed 0.1383 g. corresponding to 0.0703 g. glucose; calculated for 0.100 g. amygdalin, 0.0704 g. glucose.

Preparation of Crystalline Fructose from Fructose Tetracetate.—One hundred and forty grams of crystalline barium hydroxide ($Ba(OH)_2$ + $8H_2O$) were dissolved in two liters of water on the steam bath and filtered into a bottle with a glass stopper. The solution was cooled with ice to about 5° and 40 g. powdered tetracetyl fructose were added and the mixture occasionally shaken. After half an hour the crystals had dissolved. The solution was kept one hour longer in ice, then saturated with CO_2 and filtered. The amount of sulfuric acid necessary to precipitate the remaining barium acetate was calculated to be 459.7 cc. of N H_2SO_4 and a somewhat larger amount, 463 cc. was added, with stirring, to the solution which was heated on the steam bath to about 50°. The barium sulfate was allowed to settle, the supernatant clear solution poured off and the remainder filtered. Barium hydroxide solution was carefully added to neutralize the excess of sulfuric acid and the filtered solution was evaporated *in vacuo* to a small volume. The clear solution, which contained only traces of barium acetate, was evaporated in a vacuum desiccator over potassium hydroxide to a thick sirup. The syrup was dissolved in warm absolute alcohol and the solution crystallized on standing in a desiccator. The crystalline fructose was separated by suction, taken up in a small amount of water and the solution filtered. After evaporation to a thick sirup the process for separating crystalline fructose was repeated and in this way 10.2 g. of pure crystalline fructose or 50% of the theory were obtained. The fructose melted at 102–104°, and its constant specific levorotation at 20° in an aqueous solution con-

taining 6.93 g. per 100 cc. was —90.9, which agrees with the recorded value for fructose at this concentration and temperature.

WASHINGTON, D. C.

A FOURTH CRYSTALLINE PENTACETATE OF GALACTOSE AND SOME RELATED COMPOUNDS.

BY C. S. HUDSON AND J. M. JOHNSON.

The method of preparation of the second pentacetate of galactose by heating the first pentacetate with acetic anhydride and a trace of $ZnCl_2$[1] furnishes an indication that the two isomers are an alpha and beta pair, because this method of rearrangement changes the beta acetates of glucose, mannose, lactose, cellose, maltose and xylose to the corresponding alpha acetates. We have now sought to transform in similar manner the third pentacetate of galactose, which one of us recently found in the mother liquors of the preparation of the first pentacetate,[2] into an isomeric form, and we find that there is produced a fourth crystalline pentacetate of galactose having properties quite distinct from those of the three known isomers.

Rearrangement of the Third Galactose Pentacetate to a Fourth Form. —A supply of 135 g. of the third pentacetate was obtained along with 940 g. of the first pentacetate by the acetylation of one kilo of pure galactose, according to the previously published directions. The specific levorotation of the recrystallized pure third form in benzene was —43.6 in 10% solution, in 99.5% glacial acetic acid —42.4 in 10% solution, both these values being near that reported previously for chloroform solution, —41.6.

On combustion 0.2003 and 0.1987 g. subs. gave 0.3622 and 0.3595 g. CO_2, and 0.1046 and 0.1020 g. H_2O.

Found: C, 49.32 and 49.34%; H, 5.84 and 5.74%. Theoretical: 49.21 and 5.68% for a galactose pentacetate.

Twenty-five grams of this third pentacetate dissolved to 100 cc. with acetic anhydride were heated with 2.5 g. $ZnCl_2$ on the steam bath until the specific rotation changed from its initial value of —41 to the constant rotation —16, which required less than fifteen minutes. On pouring the solution into water a crystallization of some unchanged third pentacetate took place. The water was extracted with chloroform, the extract was washed with $NaHCO_3$ solution and with water, dried with $CaCl_2$ and the chloroform evaporated. From the sirup, crystals of the third

[1] Hudson and Parker, THIS JOURNAL, 37, 1589 (1915).

[2] Hudson, Ibid., 37, 1591 (1915).