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

THE ISOMERIC TETRACETATES OF XYLOSE, AND OBSERVATIONS REGARDING THE ACETATES OF MELIBIOSE, TREHALOSE AND SUCROSE.

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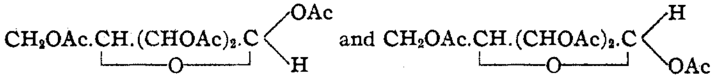
Crystalline xylose tetracetate has been prepared by Stone[1] through the action of acetic anhydride and sodium acetate upon the sugar, and he records its melting point as 123.5–4.5° and its specific rotation in absolute alcohol —25.43°. Bader[2] has found the substance to melt slightly higher, 126°. We have recently converted this tetracetate to an isomeric form by heating it in acetic anhydride solution with a trace of zinc chloride, as will presently be described. The new tetracetate and the one prepared by Stone represent a pair of isomers similar to the alpha and beta forms of the pentacetates of mannose and glucose and the octacetates of cellose, maltose and lactose, and their structures may accordingly be written, assuming a gamma lactonyl ring,



$$\mathrm{CH_2OAc.\underbrace{CH.(CHOAc)_2.C}_{O}}\left\langle\begin{matrix}\mathrm{OAc}\\ \mathrm{H}\end{matrix}\right. \quad \text{and} \quad \mathrm{CH_2OAc.\underbrace{CH.(CHOAc)_2.C}_{O}}\left\langle\begin{matrix}\mathrm{H}\\ \mathrm{OAc}\end{matrix}\right.$$

Since the specific rotations of the two tetracetates in chloroform solution (*vide infra*) are, respectively, —25° for Stone's form and +49° for the new isomer, it is highly probable that the latter is a derivative of the strongly dextrorotatory alpha form of xylose, and the former a derivative of the hypothetical beta xylose,[3] and in conformity with this view we will designate the new tetracetate as the alpha form and Stone's tetracetate as the beta modification. We have sought to complete the evidence on this point by correlating one of these tetracetates directly with crystalline alpha xylose by acetylating this sugar with acetic anhydride and pyridine at 0°, but the reaction has yielded both tetracetates, due doubtless to a partial transformation of alpha xylose to its beta form in advance of the acetylation.

Rearrangement of β-Xylose Tetracetate to the Isomeric Alpha Form.—A considerable quantity of the β-tetracetate was prepared according to Stone's directions, using the proportions one part fused sodium acetate, four parts pure xylose, and sixteen parts acetic anhydride, and pouring the reaction mixture into water as soon as the xylose had dissolved. After recrystallizing the tetracetate from water and from 95% alcohol until its rotatory power reached a constant value, the m. p. of the pure sub-

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[1] *Am. Chem. J.*, 15, 653 (1893).

[2] *Chem. Ztg.*, 19, 55 (1895).

[3] THIS JOURNAL, 31, 76 (1909).

stance was found to be 128° (corr.). Its specific rotations in several solvents are recorded in Table I. The yield of pure β-tetracetate was 22 grams from 25 grams of xylose. When this tetracetate was dissolved in acetic anhydride containing a small amount of zinc chloride and the solution was heated on the steam bath, a change in specific rotation from —23.3° to the constant final value +71.8° was observed, only four minutes, or less, being required for the completion of the mutarotation. The product was poured into cold water and a partial crystallization of the insoluble sirupy layer soon took place. The mass was thinned with alcohol and the crystals removed. They proved to be the original β-tetracetate. The sirupy alcoholic mother liquor, on cooling with ice, gave fine, flaky crystals which could be filtered while cold, though they melted somewhat below room temperature. They appear to be an unstable alcoholate of α-xylose tetracetate, but a trustworthy analysis of them could not be obtained on account of the fact that they readily change to crystals of α-tetracetate, without alcohol, on recrystallization. Estimations of the alcoholic content of the crystals by direct evaporation and also by specific-gravity measurements of their distillate on boiling with water, showed percentages varying from 12 to 33, indicating that the crystals were mixtures of alcoholate and alcohol-free tetracetate. When the crystals of the alcoholate were dissolved in a little alcohol at room temperature, there crystallized spontaneously the new α-xylose tetracetate. In another case, a batch of crystals of the alcoholate was found to change entirely to crystals of the new tetracetate, free of alcohol, on standing several days in alcohol near 0°. The α-tetracetate was recrystallized from alcohol until its specific rotation reached the constant values that are recorded in Table I. The substance melts at 59° (corr.). The yield is about 50% of the weight of the β-tetracetate. For analysis the compound was dried in a vacuum desiccator over KOH.

0.2584 and 0.2675 g. substance yielded 0.4640 and 0.4806 g. CO_2, and 0.1341 and 0.1378 g. H_2O.

Calc. for CHO: 49.03% C and 5.70% H. Found: 48.97 and 49.00% C, 5.81 and 5.76% H.

An acetyl estimation was made by boiling in a quartz flask with reflux quartz condenser 0.5 g. substance with 100 cc. 0.25 *N* sulfuric acid during three hours.

Calc. for xylose tetracetate: 54.09%. Found: 54.00 and 53.89% (CH_3CO).

Mol. wt. from the lowering of the freezing point in benzene. Six experiments (with 0.746 and 1.754 g. per 100 g. solvent) showed depressions varying between 0.123° and 0.267°, which indicated values for the molecular weight ranging between 303 and 329. Theoretical value, 318.

By saponifying the new xylose tetracetate with 5% alcoholic potash at 0°, xylose was regenerated, crystallized and identified. The specific rotation in water of the xylose two minutes after solution at 20°, was +86.1° and the constant rotation was +19.4°.

The Rotatory Powers of the Isomeric Xylose Tetracetates.—Table I records the specific rotatory power of the new α-tetracetate in several solvents[1] in comparison with the rotation of the β-tetracetate. The tube length in all cases was 4 dcm., the specific rotations are expressed in circular degrees for sodium light, and the concentration in grams per 100 cc. of solution, the weighings being made in air with brass weights.

TABLE I.

The Specific Rotations of the Isomeric Xylose Tetracetates.

	Chloroform.		Benzene.		99.5% Acetic acid.	
Tetracetate.	Conc.	$[\alpha]^{20}_{D}$.	Conc.	$[\alpha]^{20}_{D}$.	Conc.	$[\alpha]^{20}_{D}$.
Alpha	5.02	+89.3	5.03	+79.3	3.33	+95.3
Alpha	9.99	+88.9	10.01	+80.4	10.04	+95.8
Beta	4.99	—24.7	10.03	—22.3	10.04	— 7.3
Beta	11.07	—25.1	...	..	...	..

Difference of the Molecular Rotations of the Alpha and Beta Forms.

	Chloroform.	Benzene.	99.5% Acetic acid.
Glucose pentacetate	38,100	36,700	40,800
Xylose tetracetate	36,300	32,500	32,700

A comparison of the differences of the molecular rotations of the α- and β-xylose tetracetates with those of the α- and β-glucose pentacetates[2] is shown in the second part of Table I, where the averaged values of Table I are multiplied by 318, the molecular weight of xylose tetracetate.

It was expected from theoretical considerations[3] that these differences would be the same for the two pairs of acetylated sugars. In benzene and in acetic acid solutions, the conclusion does not hold at all well, as has been noticed previously in similar comparisons.[4] The values are fairly close in chloroform solution, the discrepancy amounting to about six degrees in specific rotation.

Preparation of Both α- and β-Xylose Tetracetates by Acetylating α-Xylose at 0° in Pyridine Solution.—Pure crystalline α-xylose (20 g.) was acetylated at 0° with a mixture of acetic anhydride (100 cc.) and commercial pyridine bases (100 cc.) according to the directions of Behrend.[5] After the sugar had dissolved, which required about 26 hours with occasional stirring, the mixture was kept at 0° 24 hours longer, but no change in its rotation after dissolving ($[\alpha]_D = +33$ approximately) was apparent. It was then poured into a large excess of water and the resulting insoluble sirupy layer partially crystallized. This was thinned with alcohol, and the crystals removed, which proved to be the β-tetracetate. By cooling the sirupy mother liquor with ice, crystallization of the alcoholate of α-xylose tetracetate, which has been described above, could be ob-

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[1] The chloroform used was *Chloroformum purificatum*, U. S. P.

[2] Hudson and Dale, THIS JOURNAL, **37**, 1264 (1915).

[3] THIS JOURNAL, **31**, 66 (1909); **37**, 1266, 1275, 1279 (1915).

[4] Hudson and Dale, THIS JOURNAL, **37**, 1266 (1915).

[5] *Ann.*, **331**, 369 (1904); **353**, 109 (1907).

tained. From these crystals the alcohol-free α-form was prepared according to the directions already recorded. The yield of α-tetracetate by this method is about 9 g.

Conversion of Acetochloroxylose to the β-Tetracetate.—Ryan and Ebrill[1] have prepared a tetracetate of xylose by the interaction of acetochloroxylose and silver acetate in glacial acetic acid. They call attention to the fact that the resulting tetracetate melted at 119°, which is considerably lower than the melting point found by Stone. It might be considered, therefore, that their tetracetate is an isomeric form of Stone's compound. However, they had in hand such a small quantity of their tetracetate, less than one gram, that we doubt whether it was possible to purify it sufficiently to decide this point. It is evident that the substance could not have been the new α-tetracetate of m. p. 59°. In repeating Ryan and Ebrill's preparation, we were not successful in obtaining crystalline acetochloroxylose by their method of treating xylose with acetyl chloride at 0°, but by boiling the sugar with this reagent and a trace of $ZnCl_2$ until solution was complete, acetochloroxylose was prepared in beautiful crystals, with a yield of 7.8 g. from 10 g. of xylose. It melted at 95–97° uncorr. (Ryan and Ebrill found 101°), and its specific rotation in chloroform was to the right, $[\alpha]_D^{20} = +165°$, at a concentration of 12 g. per 100 cc. A qualitative test for chlorine showed its presence. For the preparation of Ryan and Ebrill's tetracetate, 5 g. of acetochloroxylose were dissolved in 125 cc. glacial acetic acid and shaken with 4 g. silver acetate until the supernatant liquid gave no reaction for chlorine. On treating the product according to these authors' directions, we obtained 3 g. of xylose tetracetate which showed after repeated recrystallization a melting polnt of 125° (uncorr.) and a specific rotation in chloroform of —25°. The substance is indeed Stone's β-xylose tetracetate.

Conversion of the α- and β-Tetracetates to Acetobromoxylose and Its Conversion to the β-Triacetyl Methyl Xyloside.—Five grams of β-xylose tetracetate of specific rotation —25° were dissolved in 6 cc. glacial acetic acid, 17 cc. acetic acid saturated with hydrobromic acid gas were added, and the solution was kept at room temperature to observe any change in its polariscopic reading, but the reaction was so rapid that the reading had become constant within the first two minutes. The solution was poured into chloroform and the mixture was washed successively with ice-water, iced sodium bicarbonate solution, and ice-water again, and was then dried with $CaCl_2$, and evaporated *in vacuo*. The sirup was crystallized from ether and petroleum ether and 4.3 g. acetobromoxylose were obtained, of m. p. 100–101° (uncorr.), and specific rotation in chloroform +210.8°. These data agree with those found by Dale (see preceding article) for acetobromoxylose, which he recently prepared. This aceto-

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[1] *Proc. Roy. Dublin Soc.*, 11, 249 (1905–8).

bromoxylose was dissolved in methyl alcohol and by treatment with silver nitrate, β-triacetyl methyl xyloside[1] was obtained, of m. p. 115° (uncorr.) and $[\alpha]_D^{20} = -59.5°$ in chloroform solution.

Five grams of α-xylose tetracetate of specific rotation +89° were brominated as described for the other tetracetate, and there were obtained 4.1 g. of acetobromoxylose, of m. p. 94–96° (uncorr.), and specific rotation in chloroform +207.2°. This acetobromoxylose was converted as above into β-triacetyl methyl xyloside of m. p. 114–115° (uncorr.), and $[\alpha]_D^{20} = -59.3°$ in chloroform solution. Therefore, the same acetobromoxylose and the same β-triacetyl methyl xyloside were obtained from the α- and β-modifications of xylose tetracetate.

Observations Regarding Melibiose Octacetate.—A supply of β-melibiose octacetate was prepared by acetylating melibiose with acetic anhydride and anhydrous sodium acetate, and the substance was recrystallized until no further change in its rotation was observed. It was found to have a m. p. of 177.5° (corr.) and specific rotations in chloroform of +102.5° and in 99.5% acetic acid of +101.9°. Scheibler and Mittelmeier[2] found a m. p. of 170–171° and $[\alpha]_D$ in chloroform of +9.42°, and Bau[3] found in chloroform $[\alpha]_D = +98.1°$. 2.8 g. of this octacetate were dissolved in acetic anhydride containing a little zinc chloride and the mixture was heated on the steam bath during 35 minutes. The specific rotation was thereby changed from +107.0° to +147.3°, and longer heating caused no further increase. The solution was poured into water and after standing some days the insoluble sirupy mass was taken up in alcohol to a thick sirup. After some weeks' standing, small crystals appeared, but now after several months, we have not been able to crystallize the entire mass, and have not obtained enough crystals to make any measurements. However, on account of the large change in rotation we are of the opinion that the known octacetate of melibiose is the beta form and that the amorphous material consists largely of α-melibiose octacetate.

Observations on Trehalose Octacetate.—Trehalose octacetate was prepared according to the usual method of acetylation with acetic anhydride and anhydrous sodium acetate, a 60% yield being obtained. After recrystallization from alcohol several times, the compound melted at 96–98° (uncorr.). The same substance was obtained with a yield of 72% by acetylating the sugar with acetic anhydride and zinc chloride. Maquenne[4] found a melting point of 97–98° for this octacetate. We have measured the rotatory power of trehalose acetate, which does not seem

[1] This compound, and its method of preparation, are described in the preceding article by Dale.

[2] *Ber.*, 23, 1438 (1890).

[3] *Zeitschr. d. Ver.*, 1904, II, 507.

[4] *Compt. rend.*, 112, 947 (1891).

to have been previously recorded. 5.15 g. substance made up to 50 cc. with chloroform, in a 2 dcm. tube at 20°, rotated 96.5° V. to the right, therefore, $[\alpha]_D^{20} = +162.3°$. When this octacetate was dissolved in acetic anhydride with a small amount of zinc chloride, no change in its specific rotation of +147.4° could be detected after heating the solution to 100° repeatedly. Evidently there is only one trehalose octacetate.

Observations on Sucrose Octacetate.—Sucrose octacetate was prepared by the acetylation of sugar with acetic anhydride and pyridine bases, and also with acetic anhydride and sodium acetate. After recrystallization, it melted at 69° (uncorr.) and in chloroform $[\alpha]_D^{20} = +59.6°$. Herzfeld[1] has found the m. p. 67°. In this case again it was not possible to obtain any evidence of the existence of an isomeric sucrose octacetate, since the specific rotation of its solution in acetic anhydride containing a trace of $ZnCl_2$ did not change on heating. These results with the octacetates of trehalose and sucrose are not unexpected since the parent disaccharides are not reducing sugars, do not combine with phenylhydrazine, do not exhibit mutarotation, nor occur in alpha and beta forms, and consequently do not have the type of structure which accounts for the existence of alpha and beta modifications of the aldoses and ketoses and their derivatives.

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THE CONDENSATION OF ALDEHYDE DIACETATES AND OF PHENYLHYDRAZONES WITH 2-THIOHYDANTOIN.

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Five years ago, Wheeler and Hoffman[2] made the discovery that aromatic aldehydes can be condensed with hydantoin by boiling with glacial acetic acid and fused sodium acetate, giving compounds of Type I. Wheeler and Brautlecht[3] applied the reaction to substituted 2-thiohydantoins, and Wheeler, Nicolet and Johnson[4] showed that it worked equally well with 2-thiohydantoin itself.

These condensation products are readily reduced to benzyl (II), or substituted benzyl hydantoins,[5] and these in turn are readily hydrolyzed to phenylalanine (III), or substituted phenylalanines. In most cases this method for preparing substituted phenylalanines compares favora-

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[1] *Ber.*, 13, 267 (1880); *Z. Ver. D. Zuckerind.*, 1887, 422.

[2] H. L. Wheeler and C. Hoffman, *Am. Chem. J.*, 45, 368.

[3] H. L. Wheeler and C. A. Brautlecht, *Loc. cit.*, 446.

[4] H. L. Wheeler, B. H. Nicolet and T. B. Johnson, *Loc. cit.*, 46, 456.

[5] Wheeler and Hoffman, *Loc. cit.;* T. B. Johnson and C. A. Brautlecht, THIS THIS JOURNAL, 33, 1531 (1911).