Among the other products obtained from this reaction are three isomeric compounds which appear to be diphenyldiisobutyrylcyclobutanes.

MADISON, WISCONSIN RECEIVED JULY 27, 1934

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

Three Crystalline Hexaacetates of *d*-α-Mannoheptose[1]

BY EDNA MONTGOMERY AND C. S. HUDSON

Hudson and Monroe[2] have described two hexaacetates of *d*-α-mannoheptose, of specific rotations $[\alpha]^{20}_D$ +24 and −31° in chloroform, respectively. In a re-investigation of this subject we find that the dextrorotatory acetate, which was produced by acetylating the sugar with acetic anhydride and sodium acetate, was evidently not obtained pure in the earlier work because the pure substance is now found to have the rotation +34°. This acetate is of the beta series because we have now transformed it in a mixture of acetic acid and acetic anhydride containing sulfuric acid as a catalyst, to a new crystalline hexaacetate of the sugar, of specific rotation +120.8°, the alpha form. The difference between the molecular rotations of this α,β pair is 40,000, in fair agreement with the values for many such pairs in the case of other sugars, for example, the α- and β-glucose pentaacetates, which show a difference of 38,000. The levorotatory acetate, the rotation of which we now find to be −34°, is not formed by rearrangement of the beta acetate, as reported by Hudson and Monroe; it accompanies the beta form as a product of the acetylation of the sugar with acetic anhydride and sodium acetate. We have now determined that it is of the open chain aldehydo type, since it is produced from *d*-α-mannoheptose ethyl mercaptal pentaacetate by the action of mercuric chloride in the presence of cadmium carbonate (Wolfrom's method[3]). This appears to be the first instance of the production of an aldehydo acetate from an aldose by direct acetylation of the sugar. The aldehydo acetate does not appear to be affected by the sulfuric acid transforming solution, as its rotation therein remains constant and it is recoverable therefrom. We now regard sulfuric acid as a preferable catalyst to zinc chloride in the transformation of alpha and beta acetates; there is less decomposition, the reaction proceeds at room temperature, and the products are more readily isolated.

Experimental

Preparation of β-*d*-[α-Mannoheptose] Hexaacetate.—Pure mannoheptose (40 g.) was acetylated with sodium acetate and acetic anhydride in the customary way, care being taken to keep the temperature of the solution below 90° so that a colorless sirup was obtained, which crystallized from aqueous alcoholic solution in 58% yield, of $[\alpha]^{20}_D$ +26.4° in chloroform. It was recrystallized four times from 10 parts of 50% ethyl alcohol. The product (25 g.), dried to constant weight at 70° and 5 mm., melted sharply at 107° and had an $[\alpha]^{20}_D$ value of +34.1° (c = 1.30, U. S. P. chloroform), and these properties remained unchanged after further recrystallizations.

Anal. Acetyl: 0.3169 g. used 41.14 cc. of 0.1 *N* NaOH. Calcd. for six acetyl groups, 41.17 cc. Calcd. for $C_{19}H_{26}O_{13}$: C, 49.33; H, 5.67. Found: C, 49 [illegible], 5.62.

Transformation of β-*d*-[α-Man[illegible]ose] Hexaacetate to its Alpha Isomer.—The pure beta hexaacetate (5 g.) was dissolved in the isomerizing reagent described below, making a 30-cc. solution. The change in $[\alpha]^{20}_D$ value of the solution, complete in twenty-four hours at 20°, was from +33.9 to +111°. The transformed acetate was isolated and purified by the usual procedure, the dry sirup obtained crystallizing from ether (10 cc.) containing a few drops of petroleum ether in radiating clusters of long prisms (3.8 g.), which were recrystallized twice from the same solvent (3.2 g.), m. p. 75–76°, $[\alpha]^{20}_D$ +120.8° (c = 1.30, U. S. P. chloroform). Further recrystallizations did not change its properties.

Anal. Acetyl: 0.4041 g. used 52.55 cc. of 0.1 *N* NaOH. Theoretical for six acetyl groups, 52.50 cc. Calcd. for $C_{19}H_{26}O_{13}$: C, 49.33; H, 5.67. Found: C, 49.39; H, 5.65.

Isomerizing Reagent.—A solution of sulfuric acid in acetic anhydride and acetic acid (2 to 1) was made by dropping 4.56 cc. of concentrated sulfuric acid (95%) into a mixture of 137.1 cc. of acetic anhydride (95%) and 58.5 cc. of acetic acid (99.5%) cooled to −17°, slowly enough to avoid coloring.

Aldehydo-*d*-α-Mannoheptose Hexaacetate by Acetylation of the Sugar.—The crude acetate (10 g.) was crystallized from the concentrate of the combined alcoholic mother liquors obtained by recrystallizing the crude β-*d*-[α-mannoheptose] hexaacetate (51 g.). The aldehydo acetate was extracted several times with warm ether and the insoluble portion was recrystallized twice from hot acetone (50 cc.). The tabular crystals (4.5 g.) melted at

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[1] Publication authorized by the Surgeon General, U. S. Public Health Service.

[2] Hudson and Monroe, THIS JOURNAL, **46**, 978 (1924).

[3] Wolfrom, *ibid.*, **51**, 2188 (1929).

146° and showed $[\alpha]^{20}_{D}$ −34° (c = 1.30, U. S. P. chloroform).

Anal. Acetyl: 0.5051 g. used 65.68 cc. of 0.1 *N* NaOH. Theoretical for six acetyl groups, 65.60 cc. Calcd. for $C_{19}H_{26}O_{13}$: C, 49.33; H, 5.67. Found: C, 49.39; H, 5.65.

Aldehydo-*d*-α-Mannoheptose Hexaacetate[4]

(A) ***d*-α-Mannoheptose Ethyl Mercaptal.**—Pure mannoheptose (20 g.) was dissolved in 36% hydrochloric acid (40 cc.) and shaken with ethyl mercaptan (20 cc.). The mixture crystallized solidly in thin plates which when recrystallized twice from liter portions of hot water and dried to constant weight weighed 23.2 g., 80% yield. The mercaptal melted at 188–190° and showed a specific rotation of $[\alpha]^{20}_{D}$ −9.2° (c = 0.93, pyridine) and −11.90° (c = 0.40, water).

Anal. Calcd. for $C_{11}H_{24}O_6S_2$: S, 20.2. Found: S, 19.98.

(B) ***d*-α-Mannoheptose Ethyl Mercaptal Hexaacetate.**—A cold solution of *d*-α-mannoheptose ethyl mercaptal (20 g.) in pyridine (144 cc.) was mixed with acetic anhydride (288 cc.) and kept overnight at 0°. The acetate was isolated and crystallized the following day by the customary procedures. It was recrystallized twice from 50% methyl alcohol (200 cc.) and dried to constant weight, 31.2 g. or 90% yield. The crystals were thin plates, which melted at 77° and showed levorotation, $[\alpha]^{20}_{D}$ −2.2° (c = 2.60, U. S. P. chloroform).

Anal. Acetyl: 0.5000 g. used 52.86 cc. of 0.1 *N* NaOH. Theoretical for six acetyl groups, 52.80 cc. Calcd. for $C_{23}H_{36}O_{12}S_2$: S, 11.27. Found: S, 11.34.

C. **Aldehydo-*d*-α-Mannoheptose Hexaacetate.**—A solution of *d*-α-mannoheptose ethyl mercaptal hexaacetate (20 g.) in acetone (100 cc.) was stirred with washed cadmium carbonate (50 g.) suspended in water (40 cc.) while a solution of mercuric chloride (43.5 g.) in acetone (110 cc.) was added slowly. The stirring was continued for twelve hours at room temperature. The reaction mixture, after standing overnight, was heated to 50° for fifteen minutes, refluxed for fifteen minutes, filtered and concentrated *in vacuo* to a dry sirup in the presence of a few grams of cadmium carbonate. The sirup was extracted with washed chloroform from which the aldehydo acetate crystallized on evaporation at room temperature. The tabular crystals were twice recrystallized from acetone. Fifteen grams, a yield of 90%, of crystalline material was obtained; m. p. 146°, not depressed by admixture with the previously mentioned levorotatory hexaacetate prepared by acetylation of the sugar with sodium acetate and acetic anhydride. The specific rotation was $[\alpha]^{20}_{D}$ −34° (c = 1.30, U. S. P. chloroform) changing to −29° overnight. A solution of the acetate (5 g.) in the isomerizing reagent failed to change in specific rotation over a period of twenty-four hours. The crystalline product (4.2 g.) which was isolated was identical with the starting material.[5]

Summary

The two hexaacetates of *d*-α-mannoheptose, the rotations of which were recorded by Hudson and Monroe as $[\alpha]^{20}_{D}$ +24 and −31°, respectively, have been reinvestigated. When fully pure the dextro form shows $[\alpha]^{20}_{D}$ +34° in chloroform. It is found to be the beta modification because it isomerizes in a solution of acetic acid and acetic anhydride containing sulfuric acid as a catalyst to a more strongly dextrorotatory hexaacetate ($[\alpha]^{20}_{D}$ +120.8° in chloroform), the alpha form, now crystallized for the first time. Sulfuric acid is preferable to zinc chloride as the catalyst in such transformations. The molecular rotational difference for the pair of hexaacetates is 40,000, in fair agreement with those found for such α,β pairs in the case of many other aldose sugars. The levorotatory acetate, the rotation of which in pure condition is now found to be −34°, proves to be an aldehydo form because it is identical with the substance which results from Wolfrom's method of synthesis of aldehydo acetates by way of the sugar mercaptal. This aldehydo hexaacetate is not affected by the previously mentioned transforming solution, which so readily isomerizes the acetates of ring structure.

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[4] The compounds described in parts A, B and C were made according to procedures described by Wolfrom.[3]

[5] Recently it has been found that the aldehydo acetate of α-mannoheptose is very rapidly formed in nearly quantitative yield when the pentaacetate (m. p. 76–77°, $[\alpha]^{20}_{D}$ −42.9° in chloroform) of a methyl α-mannoheptoside (m. p. 115°, $[\alpha]^{20}_{D}$ −111° in water) of the gamma type is dissolved in the isomerizing solution. The question whether aldehydo acetates are producible from other acetylated gamma methyl glycosides by this reaction is being studied in this Laboratory. Compare the accompanying paper by Hann and Hudson.