[CONTRIBUTION FROM THE BUREAU OF CHEMISTRY AND SOILS, UNITED STATES DEPARTMENT OF AGRICULTURE]

# Concerning "β"-2,3,4,6-Tetraacetyl-*d*-glucose

BY S. B. HENDRICKS, O. R. WULF AND U. LIDDEL

During a general study of the absorption of organic compounds in the infra-red region of the spectrum in progress in this Laboratory, an attempt was made to obtain information about the structures of the sugar hydrazones and oximes. In the course of this work, which now does not hold much of promise, various acetylated hexoses and pentoses were prepared. Results of some observations, that started in a rather accidental manner, on β-2,3,4,6-tetraacetyl-*d*-glucose are described below.

Two different 2,3,4,6-tetraacetyl-*d*-glucoses are described in the literature and, in harmony with sugar nomenclature, are designated as α and β. The β-form, as prepared by Fischer and Delbrück,[1] melted at 117°, but later investigators, particularly Georg[2,3] using Fischer and Delbrück's method of preparation, obtained materials melting near 135° with somewhat more negative optical activities. Georg[2] concerned himself about these differences, accounting for the depressed melting points by presence of alkaline impurities from the melting point tubes. Actually more abstruse factors are present and further study shows that the differences in properties of the various preparations arise from admixture of two different molecular forms to which peculiar interest attaches because of the nature of their mutarotations.

Samples of "β"-2,3,4,6-tetraacetyl-*d*-glucose prepared after the method of Fischer and Delbrück gave, when crude, melting points between 118 and 128° and specific optical activities from +28 to +7° in ethyl alcohol. Melting points and optical activities were brought into agreement with the values found by Georg, m. p. 138°, $[\alpha]^{25}\text{D}$ −3.0°, by recrystallization from ether. Several samples of this recrystallized material (later referred to as Ia) after standing for two years had melting points near 120° and positive optical rotations. Recrystallization of the altered materials from ether changed them back into Ia. Change of Ia to this second form (later referred to as Ib) could also be effected by several days' heating in carbon tetrachloride or benzene solutions.

That the explanation for these observations is not simply the presence of impurities is best shown by the absorptions of the various materials in the infra-red region, 6000–7500 cm.$^{-1}$. Absorption due to the presence of OH groups is found near 7000 cm.$^{-1}$ [4] and since tetraacetylglucose contains only one OH group measurements in this region are particularly valuable for characterizing its possible molecular forms. According to the present technique measurements are made on carbon tetrachloride solutions, preferably about 0.02 molal, since it is undesirable to have RH groupings present in the solvent. Samples of the two forms of "β"-2,3,4,6-tetraacetyl-*d*-glucose gave the molal absorptions shown in Fig. 1, Ia showing two maxima and Ib a single maximum. Absorption curves for α-2,3,4-triacetyl-*d*-xylose and β-2,3,4,6-tetraacetyl-*d*-galactose are also shown in Fig. 1 in order that one unfamiliar with this type of measurement might have a more general basis for evaluating the work.

The specific optical activity of Ib in ethyl alcohol indicates that it might be a compound[5] containing three parts of Ia and one part of α-2,3,4,6-tetraacetyl-*d*-glucose. This possibility is not supported by the optical activity in chloroform and is definitely eliminated by the absorption data. It would not be possible to derive the absorption curve for Ib from any mixture, $x$Ia + $y$I (hypothetical), with $x = y$ since then I (hypothetical) would have negative absorption values.

That Ia and Ib are strictly isomorphous is shown by the microscopic examination, the identity of their x-ray powder diffraction patterns, and by the fact that the transition in the solid state takes place without destruction of single crystals. This isomorphism suggests that the geometrical shapes of Ia and Ib are similar.

Thirteen or more reasonable forms can be suggested for the configurations of Ia and Ib; α and β on the 1 carbon atom, ortho acetate formation between the OH in the 1-position and the 2- or 3-acetyl group either of which might exist in *d*

---

(1) Fischer and Delbrück, *Ber.*, **42,** 2779 (1909).

(2) Georg, *Helv. Chim. Acta*, **15,** 924 (1932).

(3) Note also Haworth, Hirst and Teece, *J. Chem. Soc.*, 1405 (1930).

(4) Wulf and Liddel, THIS JOURNAL, **57,** 1464 (1935).

(5) R. C. Hockett and C. S. Hudson, *ibid.*, **53**, 4454, 4455 (1931).

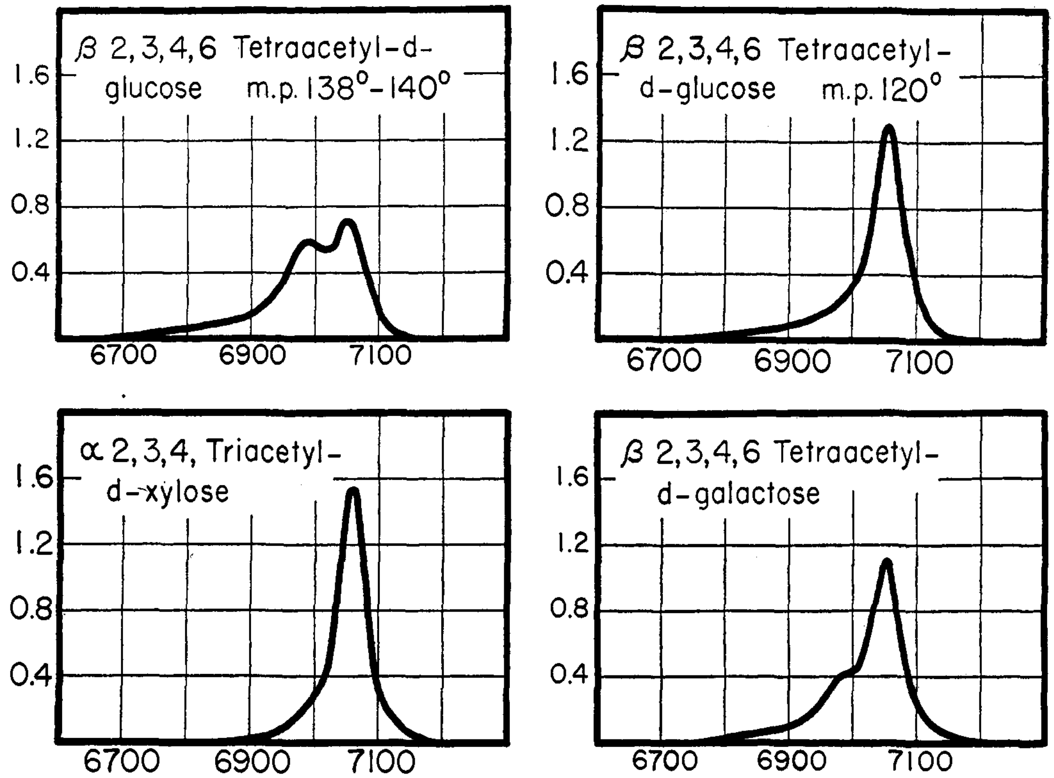

Fig. 1.—Molar absorption coefficients (ordinates) of some acetylated sugar derivatives in dilute carbon tetrachloride solution against frequency in wave numbers (abscissa).

or *l* forms, aldehydo and *cis* and *trans* isomers. Neither Ia nor Ib is probably the α form since it would have a considerably more positive optical activity.[6] Neither form gave the usual aldehyde tests nor did they react with diazomethane which was tried at the suggestion of Dr. G. E. Hilbert of this Laboratory. It was thought that an ortho acetate would be a sufficiently strong acid to be methylated by diazomethane. The presumptive conclusion then is that the materials are *cis* and *trans* ring isomers, the danger being that the chemical tests are not trustworthy.

"β"-2,3,4,6-Tetraacetyl-*d*-glucose as prepared after the method of Weizmann and Haskelberg[7] showed a rather peculiar behavior. The crude material was similar in optical activity and melting point to that prepared according to the method of Fischer and Delbrück but many recrystallizations from ether did not change it into Ia. Large crystals with intermediate melting points (125–131°) could be grown from ether solutions and various fractions from these solutions had the same characteristics. It would seem either that some minor impurity difficult to separate is present or that an obscure catalyst is needed.

## Experimental

**"β"-2,3,4,6-Tetraacetyl-*d*-glucose** was prepared from acetobromoglucose and moist silver carbonate after the method of Fischer and Delbrück save that the acetone was evaporated after reaction for a few minutes at 0°. The crude residue was immediately washed with ether and recrystallized from dry ether; yield 40–60%. Crude crystalline materials (m. p.'s 105–120°) upon standing gave odors of acetic acid and could not then be recrystallized from ether.

A number of methods of purification were tried and some of these are indicated schematically below, starting materials, solvent, number of recrystallizations, and final melting points, optical activities, etc., being given: (a) crude, twice ethyl acetate, m. p. 122–125°, $[\alpha]^{20}\text{D}$ +15° (1.3% in $C_2H_5OH$) calcd. for $C_{14}H_{20}O_{10}$: C, 48.25; H, 5.79. Found: C, 48.33; H, 5.94. (b) crude, twice amyl acetate, m. p. 125–128°, twice dry ether, m. p. 136–138°, $[\alpha]^{20}\text{D}$ −3° (1.0% in $C_2H_5OH$); (c) crude, four times from dry ether, m. p. 136–138°, twice benzene, m. p. 138–140°, $[\alpha]^{20}\text{D}$ $-4.2 \longrightarrow +75°$ after ten days (1.9% in $C_2H_5OH$) $+18.8° \longrightarrow +78°$ after ten days (1.7% in $CHCl_3$). Five grams of (c) was dissolved in 10 cc. of freshly distilled nitromethane and set aside in the ice box.

---

[6] Schlubach and Wolf, *Ber.*, **62**, 1507 (1929), have prepared a form of 2,3,4,6-tetraacetyl-*d*-glucose having $[\alpha]\text{D}$ +139.4° (in ethyl alcohol) and have designated it as α.

[7] Weizmann and Haskelberg, *J. Chem. Soc.*, 1023 (1935).

A single crystal weighing *ca.* 3 mg. separated during two days, m. p. 138°, the mother liquor was concentrated and the material was thrown out with ether. The final fraction had a melting point of 138°. Acetylation of (b) yielded pentaacetyl-*d*-glucose melting at 130°, unchanged upon mixing with an authentic sample.

**Transformation of Material Melting at 138 to 120° Form.**—Four separate samples of (b) above were set aside for two years at the end of which time they had the following melting points: (d) 114–118°, (e) 119–120°, (f) 118–124°, (f′) strong odor of acetic acid, material quite spongy. Sample (d) was recrystallized twice from ether and gave (g) with a melting point of 136–139°. Five grams of (d) kept at 60° in carbon tetrachloride solution for two days gave 1.0 g. of material melting at 120–120.5°, $[\alpha]^{20}\mathrm{D}$ $+30° + \longrightarrow$ (1% in $C_2H_5OH$). Five grams of (c) heated, near the boiling point, for three days with 800 cc. of carbon tetrachloride upon concentration to 200 cc. gave 1.5 g. of crystals, m. p. 120–122° (h) $[\alpha]^{20}\mathrm{D}$ $+32.6 \longrightarrow +79°$ after ten days (1.9% in $C_2H_5OH$) $+40° \longrightarrow$ (1.6% in $CHCl_3$). Five grams of (c) refluxed with 50 cc. of benzene gave (j) about 1.0 g. of crystals, m. p. 114–117° $[\alpha]^{20}\mathrm{D}$ +36° (1.6% in $C_2H_5OH$) +46° (1.4% in $CHCl_3$). Sirups from (h) and (j) were not brought to crystallization upon long standing and repeated addition of (c) in 0.5-g. amounts.

**Microscopic and X-Ray Examination.**—Samples (b) and (c) gave well-formed crystals about 2.0 × 0.5 × 0.5 mm. from ether, with parallel extinction; $\alpha\mathrm{D} = 1.483$, $\gamma\mathrm{D} = 1.495$, biaxial positive with large optic axial angle. Crystals from (g) and (h) had the same constants but differed in habit. Samples (d), (e) and (f) contained only crystals similar to (b) and (c) and showed uniform extinction. X-ray powder diffraction patterns of (j) and (c) were identical in all details (Cu K radiation).

**Attempted Methylation of 138 and 120° Materials.**—One gram ($^1/_{340}$ mole) of (c) was treated in 75 cc. of ether solution with $^1/_{25}$ mole of fresh diazomethane. No reaction was apparent and the yellow color remained after five days of standing. The ether was removed and after recrystallization 0.7 g. of material melting at 133–136° was obtained. One-half gram of (h) ($^1/_{680}$ mole) was treated in a similar manner in carbon tetrachloride solution without evident evolution of nitrogen. After five days the solution was evaporated but the residues could not be brought to crystallize.

**"β"-2,3,4,6-Tetraacetylglucose after Weizmann and Haskelberg.**[7]—Acetobromoglucose (115 g.) was treated as directed with sodium nitrite solution. After five days the acetone-rich phase was evaporated and a sirup was obtained which did not crystallize overnight but from which 10 g. of a material melting between 118–123° separated after two days' standing with ether. During a month in the presence of ether and ligroin 15 g. more of this material was obtained. These combined samples designated as (m) had $[\alpha]^{20}\mathrm{D}$ +14° (1.6% in $C_2H_5OH$) and +27° (2.4% in $CHCl_3$). The following results were obtained when purification was attempted, the number of crystallizations and melting points being indicated: one carbon tetrachloride (121–124°), two ether (125–128°), two hours of boiling ether (125–128°), residues from mother liquors (125–128°), twenty-four hours of boiling in absolute ether (fraction 1 (125–128°) fraction 2 (125–128°)), three hours of boiling in absolute ether with 0.1% acetic acid (125–128°), four hours of boiling with charcoal in ether (125–131°), absolute ether (128–131°). The final material was divided into two parts one of which was refluxed for two hours in ether solution with the silver carbonate–silver bromide residues from preparation (c) (124–131°) and the other was recrystallized from the mother liquors of (c) which contained about 10% as much of Ia (133–137°).

**Infra-red Absorption.**—Molal absorptions were measured for carbon tetrachloride solutions, usually about 0.018 molal, that were maintained near 60°. Preparation (c) gave the results shown in Fig. 1, the absorption being measured about one and one-half hours after preparation of the solution, and this slowly changed (at 60°) over a three-day period to that having a single maximum. Qualitative absorption data obtained from various samples are described below. Crude materials from the preparation after the method of Weizmann and Haskelberg gave absorptions corresponding to about equimolal mixtures of Ia and Ib, after many recrystallizations from ether the results were nearer those obtained for Ia but still indicated the presence of Ib. Samples prepared after the method of Fischer and Delbrück were examined after a single recrystallization from ether and were found to be quite pure Ia. A sample of Ia after standing for two years gave the absorption of Ib and after recrystallization from ether that of Ia.

We are indebted to Dr. R. T. Milner and Mrs. M. S. Sherman for the various microanalyses.

## Summary

"β"-2,3,4,6-Tetraacetyl-*d*-glucose can be separated into two different molecular forms having different optical activities, spectral absorptions and melting points. The form having the higher melting point usually can be obtained by recrystallization from ether. Upon standing for a long time in the solid state it changes to the second form through a complete series of solid solutions.

WASHINGTON, D. C. RECEIVED AUGUST 13, 1936