[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Beta to Alpha Conversion of Fully Acetylated Sugars by Alkali

BY M. L. WOLFROM AND DONALD R. HUSTED

In some work carried out in this Laboratory on a reaction involving *β-d*-glucose pentaacetate, it was found that this *β*-form had been isomerized unexpectedly to *α-d*-glucose pentaacetate. This change was obtained under conditions entirely different from those recorded in the literature for effecting the conversion of a fully acetylated *β*-form of a sugar to the corresponding *α*-isomer. Such a conversion had been produced previously by treating the *β*-pentaacetate in acetic anhydride solution with either zinc chloride[1] or sulfuric acid;[2] or by treatment with stannic chloride in chloroform.[3] The experimental conditions which we found effective for producing this conversion were studied in considerable detail in order to determine the agent producing the change. We believe that the effective agent was a very mild alkalinity. This is in contrast to the acidic conditions previously used to cause the shift. This result can be harmonized with modern theories of sugar mutarotation, since both acidic and basic catalysts are effective in the transformation of a non-substituted reducing sugar into its *alpha* and *beta* forms.[4]

The procedure used by us was to shake a solution or suspension of the completely acetylated *β*-form of the sugar in a suitable non-aqueous solvent with solid sodium hydroxide and a suitable drying agent. Anhydrous and alcohol-free ether as well as dioxane were found to be suitable solvents but were most effective when used in an equal mixture. No difference was found in the action of commercial or highly purified dioxane. Either sodium or anhydrous calcium sulfate (Drierite) was suitable as drying agent, such an agent apparently being required to protect the reaction mixture from becoming too alkaline. The sodium hydroxide was essential. These conditions are those of incipient alkaline deacetylation and some deacetylation always occurred. Consequently, this reaction is not the equal of the previously established methods for preparative purposes, but we believe that it is of theoretical interest, particularly in its relation to the study of the interconversion of isomeric sugar structures.

The reaction was extended successfully to *β-d*-mannose pentaacetate, *β-d*-galactose pentaacetate and *β*-lactose octaacetate.

Experimental

***α-d*-Glucose Pentaacetate.**—An amount of 25 cc. of dry dioxane (a high grade commercial product dried with sodium or anhydrous calcium sulfate (Drierite)) and 25 cc. of diethyl ether (anhydrous and alcohol-free) were placed in a citrate pressure bottle and approximately 3 g. of sodium and 3 g. of crushed, solid sodium hydroxide were added. This mixture was shaken mechanically for approximately fifteen minutes and then 3 g. of pure *β-d*-glucose pentaacetate was added quickly and the mixture shaken for a period of four to six hours. Some dark brown sludge formed and the solution was colored brown. After a little experience the completeness of the reaction could be judged by this color. At the end of the shaking, some Carboraffin was added and the mixture rapidly filtered with suction into a flask containing a few cc. of acetic acid. The acidified filtrate was light yellow in color and showed a specific rotation varying from +70 to +90°. The residue obtained after solvent removal under reduced pressure was crystallized from 95% ethanol (Carboraffin), the first crop of crystals being *α-d*-glucose pentaacetate of good purity; m. p. 110–111° (unchanged on admixture with known material of the same purity); $[\alpha]$ +96°[5] ($CHCl_3$); average yield approximately 1.2 g., maximum 1.5 g.; acetyl, 13.0 cc. 0.1 *N* NaOH per 100 mg. (calcd., 12.8 cc.). After several recrystallizations the following constants were obtained: m. p. 112–113°; $[\alpha]^{22}$ +98.5° (*c*, 3; $CHCl_3$). Hudson and Dale[6] record for *α-d*-glucose pentaacetate the constants: m. p. 113°; $[\alpha]^{20}$ +101.5° ($CHCl_3$).

When the conditions described above were adhered to rigidly, no *β*-form was isolated from the reaction. If the reaction was stopped short of completion, some *β*-form could be isolated. After a little experience, the results described above could be obtained in about 90% of the trials, the limitations being that if the reaction was stopped short of the optimum point some *β*-form was obtained, while if the reaction was allowed to proceed too far or if too much moisture was accidentally introduced, deacetylation resulted.

It was thought at first that the rearrangement might have been effected by impurities contained in the dioxane but no difference was noted when dioxane was used that had been purified by the method of Kraus and Vingee.[7]

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(1) (a) E. Erwig and W. Koenigs, *Ber.*, **22**, 1464 (1889); (b) C. S. Hudson and J. M. Johnson, THIS JOURNAL, **37**, 1270 (1915).

(2) L. Maquenne and W. Goodwin, *Bull. soc. chim.*, [3] **31**, 854 (1904); Edna Montgomery and C. S. Hudson, THIS JOURNAL, **56**, 2463 (1934).

(3) E. Pacsu, *Ber.*, **61B**, 137 (1928).

(4) T. M. Lowry and G. F. Smith, "Rapports sur les Hydrates de Carbone," Dixième Conférence de l'Union Internationale de Chimie, Liége, 1930, pp. 79–121.

(5) All of the recorded rotations were measured to the D-line of sodium.

(6) C. S. Hudson and J. K. Dale, THIS JOURNAL, **37**, 1264 (1915).

(7) C. A. Kraus and R. A. Vingee, *ibid.*, **56**, 511 (1934).

This point was settled satisfactorily when it was found that ether alone could be used as a solvent if the time of shaking was prolonged to from eighteen to twenty-four hours. Purified dioxane could also be used alone but then the reaction likewise proceeded at a very slow rate. The sodium used in the procedure served merely as a drying agent, since anhydrous calcium sulfate (Drierite) could be substituted for it without affecting the yield. When sodium was used and the solid sodium hydroxide omitted, a very low yield of α-glucose pentaacetate was obtained. This small amount of conversion was undoubtedly due to the slight quantity of sodium hydroxide produced by unavoidable contamination with moisture. All of these experiments pointed to the conclusion that the active interconverting agent was the sodium hydroxide. When α-*d*-glucose pentaacetate was used initially, it was recovered unchanged in approximately 50% yield but no β-form was isolated. This would indicate either that the equilibrium was displaced to favor the α-form or that the β-isomer was more readily deacetylated.

α-*d*-Galactose Pentaacetate.—Pure β-*d*-galactose pentaacetate (3.0 g.) was treated exactly as described for β-*d*-glucose pentaacetate except that the time of shaking was from five to seven hours. The acidified filtrate showed a specific rotation of from +60 to +80°. The sirup obtained after solvent removal under reduced pressure was dissolved in ethanol, treated with Carboraffin, filtered and the ethanol removed under reduced pressure. The residual sirup was dissolved in chloroform and the solution washed successively with 5% hydrochloric acid, 5% aqueous sodium bicarbonate and then with water, dried, the solvent removed under reduced pressure and the residual sirup crystallized from a small amount of hot ethanol; yield 0.8 to 1.0 g.; m. p. 94–95° (mixed m. p. unchanged); $[\alpha]^{27}$ +104° (*c*, 3.7; $CHCl_3$). Hudson and Parker[8] record for α-*d*-galactose pentaacetate the constants: m. p. 96°; $[\alpha]^{20}$ +107° ($CHCl_3$).

α-*d*-Mannose Pentaacetate.—Pure β-*d*-mannose pentaacetate (3.0 g.) was treated exactly as described for β-*d*-glucose pentaacetate except that the time of shaking was from four to four and one-half hours. The acidified filtrate showed a specific rotation of approximately +45°. The sirup obtained after solvent removal was crystallized from hot water; yield 1.2 g.; m. p. 73–74°; $[\alpha]^{33}$ +59° (*c*, 2.6; $CHCl_3$; 2-dm. semimicro tube). After one further recrystallization the substance showed the constants: m. p. 74–75° (mixed m. p. unchanged); $[\alpha]^{28}$ +60° (*c*, 3.3; $CHCl_3$; 2-dm. semimicro tube). Levene and Bencowitz[9] record for α-*d*-mannose pentaacetate the constants: m. p. 75°; $[\alpha]^{22}$ +55° ($CHCl_3$).

α-Lactose Octaacetate.—Pure β-lactose octaacetate (3.0 g.; m. p. 90°; $[\alpha]$ −4.2°, $CHCl_3$) was treated exactly as described for β-*d*-glucose pentaacetate and the sirup obtained after solvent removal was dissolved in ethanol (Carboraffin) and the ethanol removed under reduced pressure. The residual sirup was triturated with several portions of cold water and obtained crystalline from either ethanol or ether by slow evaporation of the solvent. α-Lactose octaacetate is difficult to crystallize and the yield was very low; m. p. 149–150°; $[\alpha]^{21}$ +51° (*c*, 2.9; $CHCl_3$; 2-dm. semimicro tube). On one further recrystallization the melting point was 152° (mixed m. p. unchanged). Hudson and Johnson[1b] record for α-lactose octaacetate the constants: m. p. 152°; $[\alpha]^{20}$ +54° ($CHCl_3$).

Summary

1. A method was found for converting β-*d*-glucose pentaacetate to the α-form, using sodium hydroxide as the reagent.
2. The method was extended to the corresponding fully acetylated derivatives of *d*-galactose, *d*-mannose and lactose. It is probably of general application.

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[8] C. S. Hudson and H. O. Parker, THIS JOURNAL, **37**, 1589 (1915).

[9] P. A. Levene and I. Bencowitz, *J. Biol. Chem.*, **72**, 627 (1927)

[CONTRIBUTION FROM THE GEORGE HERBERT JONES CHEMICAL LABORATORY OF THE UNIVERSITY OF CHICAGO]

The Configurations of α- and β-*p*-Bromobenzophenone Oximes

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An earlier contribution by Johnson and Stieglitz[1] from this Laboratory reported the details of an empirical method for the determination of the velocity of hydrolysis of oximes. Data were reported which showed that the individual members of the pair of stereoisomeric oximes of *p*-methylbenzophenone hydrolyzed at considerably different rates.

The purpose of this study was, first, to test the generality of this difference in rates by the investigation of another pair of stereoisomeric oximes and, second, to extend the study to include a comparison of the rates of hydrolysis of the stereoisomeric forms with those of the corresponding symmetrical oximes. It was hoped that this might throw some light on the configurations of the stereoisomeric compounds. The compounds selected were the α and β forms of *p*-bromobenzophenone oxime and the related oximes of benzophenone and *p*,*p*′-dibromobenzophenone.

Preparation of Materials

Benzophenone Oxime.—This compound was prepared by the method of Fischer.[2]

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[1] Johnson and Stieglitz, THIS JOURNAL, **56**, 1904 (1934).

[2] Fischer, "Anleitung zur Darstellung organ. Prepärate," Braunschweig, 1908, p. 68.