been solvated. A final recrystallization from ethanol gave the original, higher-melting form with m.p. 145–147° and $[\alpha]^{20}\text{D}$ +29.4° in chloroform (*c* 1.2).

Anal. Calcd. for $C_{35}H_{36}O_{14}S_4$: C, 51.97; H, 4.49; S, 15.85. Found: C, 52.24; H, 4.55; S, 15.65.

2,7-Anhydro-3,4-*O*-isopropylidene-β-D-*manno*-heptulopyranose.—A mixture of 1.0 g. of the anhydride II, 10 g. of anhydrous copper sulfate and 100 ml. of acetone was stirred mechanically for 48 hours, filtered and the solution concentrated to a sirup (1.26 g.) that crystallized spontaneously. From acetone–pentane there was obtained 0.85 g. of the *O*-isopropylidene derivative; it separated as clusters of acicular prisms and, after three recrystallizations, melted at 106–107° and showed $[\alpha]^{20}\text{D}$ −21.8° in water (*c* 2). Assignment of the *O*-isopropylidene group to the 3,4-positions is by analogy with 1,6-anhydro-β-D-mannopyranose and similar compounds.

Anal. Calcd. for $C_{10}H_{16}O_6$: C, 51.72; H, 6.95. Found: C, 51.70, 51.91; H, 6.91, 6.95.

1,6-Anhydro-β-D-mannopyranose from D-Mannose in Acid Solution and Isolation as Its 2,3-*O*-Isopropylidene Derivative.—Preliminary experiments showed that D-mannose suffered only negligible loss of rotatory power when a 0.1 *M* solution in 0.2 *N* hydrochloric acid was heated at 40° and at 60°. When a 0.2 *M* solution in 0.2 *N* hydrochloric acid was equilibrated overnight at 20° it showed $[\alpha]^{20}\text{D}$ +13.99°; after the solution had been heated at 80° for 3 and 6 hours, the rotations were +13.82 and +13.70°, respectively. For the attempted isolation of the expected very small amount of anhydride, three portions of D-mannose, totaling 144.13 g. and made to 4 liters at 20° in volumetric flasks with 0.2 *N* sulfuric acid, were allowed to stand overnight at that temperature. The rotations were $[\alpha]^{20}\text{D}$ +13.98, +13.96 and +14.06°. The first liter portion was heated 24 hours at about 70° and then showed $[\alpha]^{20}\text{D}$ +13.38°. The second liter portion was heated 32 hours at about 83° and then showed $[\alpha]^{20}\text{D}$ +13.24°. The third, 2-liter portion was heated 24 hours at about 83° and then showed $[\alpha]^{20}\text{D}$ +13.17°. These final values correspond to the presence of 0.5, 0.6 and 0.7%, respectively, of 1,6-anhydro-β-D-mannopyranose, calculated on the assumption that the solutions contained only D-mannose and its known anhydride. Reducing sugar determinations by the ferricyanide method indicated a small loss but the values were not considered reliable because the apparent change was less than the limit of accuracy of the method. Ultraviolet absorption data showed that less than 0.2% of 5-(hydroxymethyl)-2-furaldehyde was generated by heating D-mannose under these conditions.

The unchanged D-mannose in the 4 liters of solution was sacrificed by heating with excess barium hydroxide, and then neutralizing, filtering, deionizing and concentrating in the usual manner. The sirupy residue had a levorotation corresponding to 0.62 g. of the expected anhydride, but it weighed 9 g. and still contained material that reduced Fehling solution. Accordingly, it was treated again with barium hydroxide and the new sirup weighed 3.1 g. and had a levorotation corresponding to 0.91 g. (0.70%) of the expected anhydride. When an attempt to isolate 1,6-anhydro-β-D-mannopyranose by direct crystallization was unsuccessful, the sirup was extracted with 300 ml. of acetone at room temperature and the extract shaken with 10 g. of anhydrous copper sulfate for 42 hours. The filtered and concentrated solution crystallized readily. The product, isolated in two batches with the aid of 2-propanol and 1-butanol, weighed 0.87 g. (0.54%) and after one recrystallization from 1-butanol was identified as 1,6-anhydro-2,3-*O*-isopropylidene-β-D-mannopyranose[10] by melting point and mixed melting point of 160–161° and specific rotation $[\alpha]^{20}\text{D}$ −57.5° in water (*c* 1.8). Knauf, Hann and Hudson[10] reported m.p. 161–162° and $[\alpha]^{20}\text{D}$ −58.8° in water (*c* 2.08).

Acknowledgment.—The authors wish to thank Mr. John T. Sipes and Miss Rosemary Richtmyer, as well as several earlier workers in this Laboratory, for their preparations of D-*manno*-heptulose; Mr. William M. Jones and Mrs. Anne H. Wright for obtaining the infrared and ultraviolet absorption spectra, respectively; and Dr. William C. Alford and his associates of the Institutes' microanalytical laboratory for carrying out the microanalyses.

BETHESDA 14, MARYLAND

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH]

Crystalline 3-Deoxy-α-D-*ribo*-hexose. Preparation and Properties of 1,6-Anhydro-3-deoxy-β-D-*arabino*-hexopyranose, 1,6-Anhydro-3-deoxy-β-D-*ribo*-hexopyranose and Related Compounds[1,2]

BY JAMES W. PRATT AND NELSON K. RICHTMYER

RECEIVED DECEMBER 14, 1956

3-Deoxy-D-*arabino*-hexose and 3-deoxy-D-*ribo*-hexose have been shown to form their 1,6-anhydrides in aqueous acid to the extent of 29 and 10%, respectively. The 1,6-anhydrides were characterized as their di-*O*-acetyl derivatives. 3-Deoxy-α-D-*ribo*-hexopyranose and the phenyl 3-deoxy-α- and β-D-*ribo*-hexopyranosides have been obtained crystalline.

When LaForge and Hudson[3] established that hot aqueous acid acts on sedoheptulose (= D-*altro*-heptulose) to form a non-reducing anhydride, they were led to assume that this sugar is unique in this respect since their observation had no precedent, and, of course, many sugars had previously been subjected to such conditions on many occasions. An extension of this idea to include all sugars possessing the *altro* configuration was strongly suggested by the fact that D-altrose exhibits the same property.[4] Subsequently, the results of a number of investigations in this Laboratory have shown that although the amount of anhydride at equilibrium varies from more than 90% to less than 1%, the reaction is quite general among the aldohexoses, aldoheptoses and heptuloses.

Reeves[5] has sought to explain the ease of formation of the altrose[4] and idose[6] anhydrides in dilute aqueous acid in terms of the ring conformation of the parent aldohexose. His suggestion that the conformation of the β-D-pyranose ring exerts a con-

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[1] Presented in part before the Division of Carbohydrate Chemistry at the Atlantic City Meeting of the American Chemical Society, September 18, 1956.

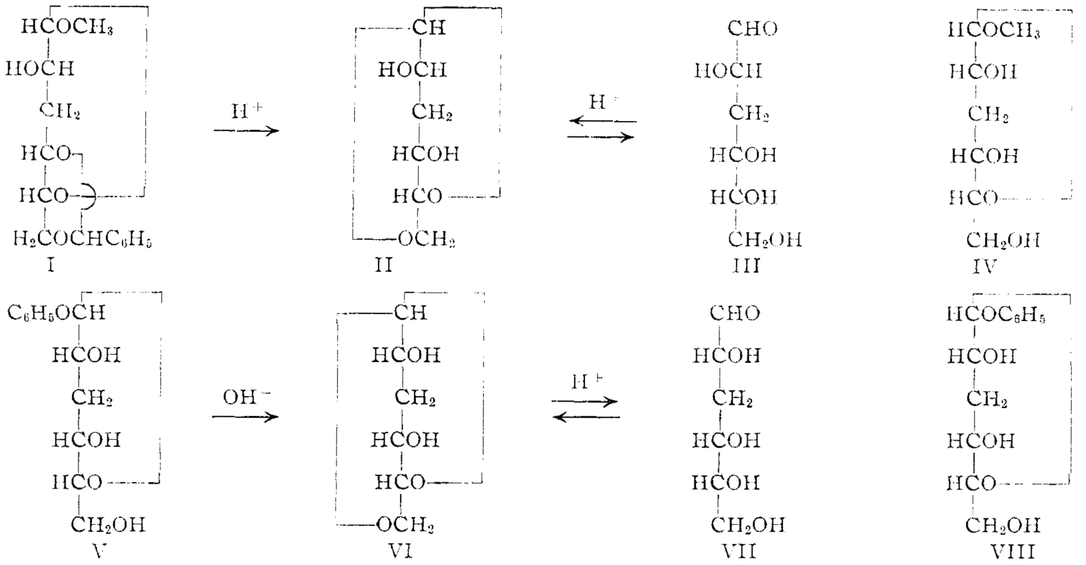
[2] For the preceding paper on anhydro sugars see E. Zissis, L. C. Stewart and N. K. Richtmyer, THIS JOURNAL, **79**, 2593 (1957).

[3] F. B. LaForge and C. S. Hudson, *J. Biol. Chem.*, **30**, 61 (1917).

[4] N. K. Richtmyer and C. S. Hudson, THIS JOURNAL, **57**, 1716 (1935).

[5] (a) R. E. Reeves, *ibid.*, **72**, 1499 (1950); (b) *Advances in Carbohydrate Chem.*, **6**, 107 (1951).

[6] E. Sorkin and T. Reichstein, *Helv. Chim. Acta*, **28**, 1 (1945).



trolling influence should, perhaps, be broadened to include the α-D-pyranose ring as well, since we are dealing with a complex equilibrium and thus are concerned mainly with the question of thermodynamic stability. The stability of the anhydride itself is perhaps the most important factor; next in importance is the question of the relative stabilities of any and all of the tautomers, anomers and conformational isomers of the free sugar.

Since the generality of the reaction has been established, we are faced with the modified problem of evaluating the several steric factors which influence the extent to which the "forward" reaction proceeds (sugar ⇄ anhydride). Reeves' "instability factors"[7] serve as a useful guide in this area, but in the light of recent data they are somewhat inadequate except for idose and altrose at one end of the scale and glucose and mannose at the other.

From some recent data, particularly the amount of 1,6-anhydroallose[8] which resulted from this reaction, we have been led to the idea that the hydroxyl group on C3 plays a very prominent role in controlling the point of equilibrium. If this is true, a 3-deoxy sugar should react much more readily than the less reactive member of a 3-epimeric pair. A diminished reactivity compared with the more reactive epimer would be expected since a favorably situated hydroxyl not only would not interfere with bridge formation but, by introducing an "instability factor" in the opposite chair conformation, would increase the probability of the favorable orientation. In order to test this hypothesis we have prepared 3-deoxy-D-*arabino*-hexose, which is related to D-mannose and D-altrose, and 3-deoxy-D-*ribo*-hexose, related to D-glucose and D-allose. Our hypothesis is supported by the observations that at equilibrium in aqueous acid the amount of anhydride (molar basis) formed from 3-deoxy-D-*arabino*-hexose is 29% (*cf.* from D-mannose <1%[2]; from D-altrose 57%[4]); and from 3-deoxy-D-*ribo*-hexose 10% (*cf.* from D-glucose 2% or less[9]; from D-allose 14%[8]). We are at present engaged in extending this study to the remaining 3-deoxy-D-hexoses, and for this reason prefer not to argue too strongly for the hypothesis until the remaining data are available.

3-Deoxy-D-*arabino*-hexose (III), as its methyl 4,6-*O*-benzylidene-α-pyranoside derivative (I), was prepared uneventfully from methyl α-D-glucoside by the multistep method of Prins,[10] which employs as intermediates methyl 4,6-*O*-benzylidene-α-D-glucopyranoside, the corresponding 2-*p*-tolylsulfonyl ester, and the 2,3-anhydro-D-mannose derivative.[11] Hot, aqueous acid effected the hydrolytic removal of benzaldehyde and the aglycon, and continued heating resulted in the formation of an appreciable amount of the 1,6-anhydro sugar. The remaining free sugar was removed by heating the solution with excess barium hydroxide and subsequent deionization. Although the anhydride failed to crystallize, it was characterized through its crystalline dibenzoate and diacetate. The rotation ($[\alpha]^{20}\text{D}$ −156°) of the 1,6-anhydro-3-deoxy-β-D-*arabino*-hexopyranose (II) and the point of equilibrium between sugar and anhydride in the presence of acid were determined in solutions obtained by careful saponification of the pure diacetate. The free anhydride was not oxidized by periodate.

3-Deoxy-D-*ribo*-hexose (VII) was prepared, as its methyl 4,6-*O*-benzylidene-α-pyranoside derivative, from methyl 4,6-*O*-benzylidene-α-D-glucopyranoside also, but *via* the 2,3-di-*p*-tolylsulfonyl ester and the 2,3-anhydro-D-allose derivative.[11] Catalytic hydrogenolysis of the 2,3-anhydro compound[10,12] yielded methyl 3-deoxy-α-D-*ribo*-hexopyranoside as a sirup which was identified by the preparation of the crystalline 4,6-*O*-benzylidene derivative.

Acetylation of methyl 3-deoxy-α-D-*ribo*-hexo-

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(7) Reference 5b, p. 124.

(8) J. W. Pratt and N. K. Richtmyer, THIS JOURNAL, **77**, 1906 (1955).

(9) L. D. Ough and R. G. Rohwer, *J. Agr. Food Chem.*, **4**, 267 (1956); A. Thompson, K. Anno, M. L. Wolfrom and M. Inatome, THIS JOURNAL, **76**, 1309 (1954).

(10) D. A. Prins, THIS JOURNAL, **70**, 3955 (1948).

(11) G. J. Robertson and C. F. Griffith, *J. Chem. Soc.*, 1193 (1935).

(12) D. A. Prins, *Helv. Chim. Acta*, **29**, 1 (1946).

pyranoside followed by acetolysis produced a sirupy mixture of acetates (presumably tetraacetates). This mixture was heated with phenol in the presence of *p*-toluenesulfonic acid,[13] the product deacetylated, and phenyl 3-deoxy-β-D-*ribo*-hexopyranoside (V) obtained crystalline. Treatment of the phenyl glycoside with hot, strong caustic followed by appropriate purification afforded the desired 1,6-anhydride as a sirup which could not be induced to crystallize. A crystalline diacetate was readily obtained, however, and this derivative was used for subsequent studies in the manner outlined for the epimer. The rotation of the 1,6-anhydro-3-deoxy-β-D-*ribo*-hexopyranose (VI) is $[\alpha]^{20}\text{D}$ −79.9°. The anhydride was not oxidized by periodate.

We desired to obtain the sugar VII in as pure a form as possible, and so prepared the crystalline tetra-*O*-acetyl derivative first reported by Černý and Pacák.[14] Catalytic deacetylation of this material yielded the sugar as small needles melting at 105.5–107° and mutarotating in water from +102° (initial, extrapolated) to +32.2° (final, 3 hours); the rotatory data indicate that the 3-deoxy-*ribo*-hexose is the α-D-pyranose form. It is of interest to note that the equilibrium rotation of the sugar is in excellent agreement with the value +31.8° calculated from the data obtained by the equilibration of the anhydride in aqueous acid.

Experimental

Methyl 4,6-*O*-Benzylidene-3-deoxy-α-D-*arabino*-hexopyranoside (I).—Lithium aluminum hydride reduction of methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannopyranoside in the manner reported by Prins[10] led smoothly and in good yield to a product which after recrystallization, first from ether–pentane and then from aqueous methanol, melted at 111.5–113° and showed $[\alpha]^{20}\text{D}$ +95.5° in chloroform (*c* 2.2). Prins reports m.p. 111–112° and $[\alpha]^{20}\text{D}$ +107.3 ±2° in chloroform (*c* 0.941); Bolliger and Prins previously reported +95.0° (*c* 2.904) in chloroform.[15]

Anal. Calcd. for $C_{14}H_{18}O_5$: C, 63.14; H, 6.81. Found: C, 63.22; H, 6.70.

Action of Dilute Aqueous Acid on Methyl 4,6-*O*-Benzylidene-3-deoxy-α-D-*arabino*-hexopyranoside (I).—A sample of I weighing 1.0163 g. was suspended in 0.2 *N* hydrochloric acid and allowed to stand at room temperature to effect solution. After 18 hours the volume was made to 50.0 ml. with water and the optical activity observed as $\alpha^{20}\text{D}$ +6.53° in a 4-dm. tube. The solution was heated to 100° and the rotation was observed to change in 3 hours to −0.72°, unchanged by heating an additional seven hours. This treatment was repeated with 5 g. of I. After a 3.5-hour heating period the solution was transferred to a silver flask, made strongly alkaline with barium hydroxide, and heated 2 hours to destroy the remaining sugar. The solution was neutralized with solid carbon dioxide, filtered, deionized by passage through Amberlite IR-120 and Duolite A-4, and concentrated *in vacuo* to a thick sirup of 1,6-anhydro-3-deoxy-β-D-*arabino*-hexopyranose (II) which weighed 1.2 g. The material has not as yet crystallized.

1,6-Anhydro-2,4-di-*O*-benzoyl-3-deoxy-β-D-*arabino*-hexopyranose.—The sirupy anhydride (II, 1.2 g.) was dissolved in 10 ml. of dry pyridine and 2.5 ml. of benzoyl chloride added. The mixture was allowed to stand four hours at room temperature and was then poured over a mixture of ice and solid sodium bicarbonate, and worked up in the usual manner. A few crystals were obtained from a chloroform solution of the benzoate by the addition of pentane, and these were used successfully to seed the ethanol solution of the sirup which yielded 1.5 g. of water-white, prismatic needles which on further recrystallization melted at 120–121.5° and showed a rotation $[\alpha]^{20}\text{D}$ −203.7° in chloroform (*c* 1.6).

Anal. Calcd. for $C_{20}H_{18}O_6$: C, 67.79; H, 5.13. Found: C, 67.88; H, 5.21.

1,6-Anhydro-2,4-di-*O*-acetyl-3-deoxy-β-D-*arabino*-hexopyranose.—The anhydride dibenzoate (18 g.) was debenzoylated catalytically and freed from methanol by evaporation in a stream of air and from methyl benzoate by extraction with ether. The sirupy anhydride was acetylated by the acetic anhydride–fused sodium acetate procedure and the resulting product (virtually quantitative) worked up in the usual way. Recrystallized first from ether–pentane and then from 10 parts of absolute ethanol, and dried overnight at 65° the white, prismatic needles melted at 99.5–101° and showed $[\alpha]^{20}\text{D}$ −139.2° in chloroform (*c* 0.37).

Anal. Calcd. for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13; CH_3CO, 37.4. Found: C, 51.88; H, 6.30; CH_3CO, 37.1.

Optical Activity of 1,6-Anhydro-3-deoxy-β-D-*arabino*-hexopyranose (II).—The anhydride diacetate (0.4260 g.) was saponified at room temperature with 5 ml. of *N* sodium hydroxide solution. After five hours, 5 ml. of *N* hydrochloric acid was added, the volume made to 25.0 ml. with water, and the rotation observed in a 4-dm. tube: $\alpha^{20}\text{D}$ −6.76°. From this value the specific rotation of the anhydride is calculated to be $[\alpha]^{20}\text{D}$ −156°.

Equilibrium in Acid Solution between 3-Deoxy-D-*arabino*-hexose (III) and its 1,6-Anhydride (II).—The anhydride diacetate (2.3092 g.) was saponified as before. After saponification, sufficient 5 *N* hydrochloric acid was added to make the final solution (50.0 ml.) 0.6 *N* in hydrochloric acid. The solution was allowed to stand 40 days at 41° during which time the observed rotation in a 4-dm. tube changed from −18.35° (extrapolated to zero time) to −0.94°; this value did not change during an additional 20 days. An estimation of aldose sugar by the iodine–alkali method[16] gave a value of 7.12 mmoles of aldose or 71.0% on a molar basis. It is assumed that the remaining 29.0% is the anhydride II. From these data the rotation of the 3-deoxy-D-*arabino*-hexose can be calculated as $[\alpha]^{20}\text{D}$ +46.8°. This is considerably higher than the value +17.7 ±2° reported by Bolliger and Prins[15] for their sirup. However, their material had been heated 3 hours at 100° in 0.75 *N* sulfuric acid and undoubtedly contained considerable levorotatory anhydride II.

Attempted Oxidation of 1,6-Anhydro-3-deoxy-β-D-*arabino*-hexopyranose (II) with Sodium Metaperiodate.—Di-*O*-acetyl-1,6-anhydro-3-deoxy-β-D-*arabino*-hexopyranose (0.2470 g.) was saponified by treatment with 5 ml. of *N* sodium hydroxide solution at room temperature for five hours. The alkali was neutralized by the addition of *N* sulfuric acid, 5 ml. of a 0.45 *M* solution of sodium metaperiodate added, and the volume made to about 20 ml. with water. After being allowed to stand in the dark at room temperature overnight, the solution was further diluted to a volume of 25.0 ml. and 5-ml. aliquots were tested for periodate consumption. The titration difference (0.08 ml.) was of the order of the limit of experimental error.

Phenyl 3-Deoxy-β-D-*ribo*-hexopyranoside (V).—Methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside was hydrogenolyzed at 110° under a hydrogen pressure of 2000 p.s.i. in the presence of Raney nickel. Rebenzylidenation of the sirupy methyl 3-deoxy-D-*ribo*-hexoside (IV) yielded methyl 4,6-*O*-benzylidene-3-deoxy-α-D-*ribo*-hexopyranoside which showed a specific rotation in chloroform $[\alpha]^{20}\text{D}$ +121.5° (*c* 2), which is considered to be not significantly different from the reported value +115.8°.[12] In subsequent runs, the purified sirupy methyl glycoside was acetylated with acetic anhydride and sodium acetate and then acetolyzed with acetic anhydride containing 2% sulfuric acid by volume. The sirupy mixture of acetates was worked up in the usual way. To 100 g. of mixed acetates were added 100 g. of phenol and 2 g. of *p*-toluenesulfonic acid monohydrate and the fused mass was heated under reduced pressure at 65–75° for 1.5 hr.[13] The resulting product, isolated in the usual manner, failed to crystallize and so was deacetylated catalytically. On removal of solvents the mixture crystallized in part to yield 10.8 g. of material

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[13] B. Helferich and E. Schmitz-Hillebrecht, *Ber.*, **66**, 378 (1933).

[14] M. Černý and J. Pacák, *Chem. Listy*, **49**, 1848 (1955); *Collection Czechoslov. Chem. Communs.*, **21**, 1003 (1956).

[15] H. R. Bolliger and D. A. Prins, *Helv. Chim. Acta*, **29**, 1061 (1946).

[16] G. M. Kline and S. F. Acree, *Bur. Standards J. Research*, **5**, 1063 (1930).

which on recrystallization from 15 parts of hot water melted at 183–185° and showed $[\alpha]^{20}\mathrm{D}$ $-94.0°$ in water (*c* 0.27).

Anal. Calcd. for $C_{12}H_{16}O_5$: C, 60.00; H, 6.71. Found: C, 60.07; H, 6.84.

1,6-Anhydro-3-deoxy-di-*O*-acetyl-β-D-*ribo*-hexopyranose.—A suspension of 6.9 g. of phenyl 3-deoxy-β-D-*ribo*-hexopyranoside (V) in 200 ml. of 2.6 *N* aqueous sodium hydroxide was heated for 19 hours at 100° in a silver flask. The clear, pale-yellow solution was neutralized with 3 *N* sulfuric acid, concentrated *in vacuo* to a paste of sirup and crystals, and the slurry extracted thrice with 150-ml. portions of absolute ethanol. The extract was filtered, and the solvent removed *in vacuo* leaving 4.3 g. of sirup which failed to crystallize. Acetylation with acetic anhydride and sodium acetate resulted in the production of 4 g. (45% based on the phenyl glycoside) of crystalline material which on recrystallization from absolute ethanol melted at 114–116° and showed $[\alpha]^{20}\mathrm{D}$ $-74.0°$ in chloroform (*c* 0.7).

Anal. Calcd. for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13; CH_3CO, 37.4. Found: C, 52.00; H, 6.13; CH_3CO, 37.0.

Optical Activity of 1,6-Anhydro-3-deoxy-β-D-*ribo*-hexopyranose (VI).—The anhydride diacetate (0.2475 g.) was saponified in *N* sodium hydroxide at room temperature. After 3 hours an equivalent amount of *N* sulfuric acid was added, the volume made to 25.0 ml., and the rotation observed. By this procedure the anhydride VI was found to show $[\alpha]^{20}\mathrm{D}$ $-79.9°$.

Attempted Periodate Oxidation of 1,6-Anhydro-3-deoxy-β-D-*ribo*-hexopyranose (VI).—To 20.0 ml. of the solution referred to in the paragraph above was added 5 ml. of a 0.45 *M* solution of sodium metaperiodate and the volume was made to 50.0 ml. After 20 hours in the dark at 20°, the solution was found to show $[\alpha]^{20}\mathrm{D}$ $-83.4°$; after 9 days the specific rotation was $-78.5°$. These values do not differ significantly from that established for the anhydride. Periodate consumption in 20 hours was found to be 0.1 mole/mole.

Equilibrium in Acid Solution between 3-Deoxy-D-*ribo*-hexose (VII) and its 1,6-Anhydride (VI).—To 1.3953 g. of anhydride diacetate in a 50.0-ml. volumetric flask was added 6 ml. of 5 *N* sodium hydroxide solution. After 2 hours at room temperature, 10 ml. of 5 *N* hydrochloric acid was added, the volume made to the mark with water, and the solution placed in an oven at 60–62°. In five days the rotation became constant. The aldose content of the equilibrated solution, estimated by the alkali-iodine method,[15] was found to be 89.8% (molar basis). By the method given above for the epimeric system it can be shown that the specific rotation of 3-deoxy-D-*ribo*-hexose (VII) is $[\alpha]^{20}\mathrm{D}$ $+31.8°$.

3-Deoxy-D-*ribo*-hexose.—Tetra-*O*-acetyl-3-deoxy-D-*ribo*-hexose was prepared from the sirupy product of the hydrolysis of methyl 3-deoxy-α-D-*ribo*-hexopyranoside (IV) using the sodium acetate in hot acetic anhydride procedure employed by Černý and Pacák.[14] After recrystallization from absolute ethanol our product melted at 129–130° in agreement with the literature value but showed $[\alpha]^{20}\mathrm{D}$ $-14°$ in chloroform (*c* 1) in contrast with the value $-20°$ reported by the earlier authors.

Anal. Calcd. for $C_{14}H_{20}O_9$: C, 50.60; H, 6.07. Found: C, 50.45; H, 6.06.

The acetate (1.0 g.) under 10 ml. of methanol was cooled to 3° and 0.2 ml. of *N* sodium methoxide in methanol was added. Solution was effected in four hours at that temperature. After two additional hours the base was destroyed by the addition of 2 drops of glacial acetic acid and the solvents were removed *in vacuo*. The sirupy product, taken up in absolute ethanol, was induced to crystallize and yielded 0.36 g. of material in the form of clusters of very small needles. Deposition of material was remarkably slow. On recrystallization from absolute ethanol the 3-deoxy-D-*ribo*-hexose melted at 105.5–107° and showed in water (*c* 1) $[\alpha]^{20}\mathrm{D}$ $+102°$ (initial, extrapolated) $\rightarrow +97.0°$ (2.5 min.) $\rightarrow +32.2°$ (3 hours; constant).

Anal. Calcd. for $C_6H_{12}O_5$: C, 43.90; H, 7.37. Found: C, 43.79; H, 7.24.

Phenyl 3-Deoxy-α-D-*ribo*-hexopyranoside (VIII).—An attempt was made to prepare the 1,6-anhydro-3-deoxy-β-D-*ribo*-hexopyranose by the alkaline hydrolysis of a mixture of the anomeric phenyl glycopyranosides. A crystalline product was obtained which on recrystallization from ethanol-ether melted at 136–138° and showed $[\alpha]^{20}\mathrm{D}$ $+172°$ in water. Rotational and analytical data as well as the method of preparation indicate that the compound is phenyl 3-deoxy-α-D-*ribo*-hexopyranoside which, as might be expected, was not affected by hot, aqueous alkali. The substance, unlike its anomer, is very soluble in water and alcohol.

Anal. Calcd. for $C_{12}H_{16}O_5$: C, 60.00; H, 6.71. Found: C, 60.33; H, 6.88.

Acknowledgment.—The authors wish to thank Mr. John T. Sipes for the preparation of both of the 2,3-anhydro intermediates, Mr. Edward W. Tracy for assistance with several steps of the procedures, and Dr. William C. Alford and his associates of the Institutes' Microanalytical Laboratory for the elemental analyses.

BETHESDA 14, MARYLAND

[CONTRIBUTION FROM THE CHEMISTRY DIVISION, ARGONNE NATIONAL LABORATORY]

The Absence of an Amadori Rearrangement in Glucosazone Formation[1]

BY FELIX FRIEDBERG[2] AND LOUIS KAPLAN

RECEIVED JANUARY 21, 1957

Glucose-1-*t* is converted to its phenylosazone without loss of tritium. This observation invalidates any mechanism of osazone formation requiring an intermediate with two hydrogen atoms on carbon-1, including the Amadori rearrangement proposed by Weygand.

The classical scheme of Emil Fischer for osazone formation suffers from the difficulty of accounting for the oxidizing action of phenylhydrazine. In order to overcome this difficulty, Weygand[3] has proposed that the phenylhydrazone first formed rearranges, producing a carbonyl group at an adjacent carbon which then condenses with more phenylhydrazine. He has suggested two paths for the reaction, as shown by (A) and (B) in the chart. Path B, which involves an Amadori rearrangement,[4]

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[1] Work performed under the auspices of the U. S. Atomic Energy Commission.

[2] College of Medicine, Howard University. Resident Research Associate, Argonne National Laboratory, 1956.

[3] F. Weygand, *Ber.*, **73**, 1284 (1940).

[4] Although the enolization involved in path A is sometimes referred to as an Amadori rearrangement (W. W. Pigman and R. M. Goepp, Jr., "Chemistry of the Carbohydrates," Academic Press, Inc., New York, N. Y., 1948, p. 405), J. E. Hodge (*Advances in Carbohydrate Chem.*, **10**, 169 (1955)) recommends that this designation be reserved for the complete conversion of a N-substituted aldosylamine to a N-substituted 1-amino-1-deoxy-2-ketose.