was taken up in acetone (50 ml.), potassium acetate (5 g.) was added and the mixture boiled for 20 hours. The acetone was distilled, water was added and the product extracted with methylene chloride. After removal of solvent, the crude product was dissolved in methanol (25 ml.) and a solution of sodium bisulfite (1 g.) in water (15 ml.) added and the mixture boiled for one hour. The solution was then concentrated *in vacuo*, water was added and the crude XIa (an oil) isolated by methylene chloride extraction. Chromatography of the oil on 200 g. of neutral alumina gave in the benzene–ether (4:1) fractions, 670 mg. of XIa, m.p. 188–190°. Acetone recrystallization gave the analytical specimen, m.p. 195–196.5°, $[\alpha]D$ +135°; λ_{max} 241 mμ, ε 15,500; λ_{max}^{KBr} 1230, 1590, 1640, 1710, 1740 cm.$^{-1}$.

Anal. Calcd. for $C_{24}H_{34}O_5$: C, 71.61; H, 8.51; O, 19.88. Found: C, 71.64; H, 8.40; O, 19.83.

6α-Methyl-Δ⁴-pregnene-17α,21-diol-3,20-dione Diacetate (XIb).—A solution of XIa (760 mg.), glacial acetic acid (50 ml.), acetic anhydride (13 ml.) and *p*-toluenesulfonic acid·$1H_2O$ (760 mg.) was allowed to stand for one hour at 25° before pouring into ice-water. When the excess anhydride had hydrolyzed the product was extracted with ethyl acetate and the extract washed to neutrality with bicarbonate and water. Evaporation of solvent and crystallization of the residue from acetone–ether gave 260 mg. of 17,21-diacetate XIb, m.p. 203–204°. Recrystallization from acetone–hexane yielded material of m.p. 216–218°, $[\alpha]D$ +51°; λ_{max} 241 mμ, ε 16,600; λ_{max}^{KBr} 1230, 1600, 1660, 1720, 1740 cm.$^{-1}$.

Anal. Calcd. for $C_{26}H_{36}O_6$: C, 70.24; H, 8.16. Found: C, 70.48; H, 8.13.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE OHIO STATE UNIVERSITY]

Synthesis of Amino Sugars by Reduction of Hydrazine Derivatives; D- and L-Ribosamine, D-Lyxosamine[1-3]

BY M. L. WOLFROM, F. SHAFIZADEH, R. K. ARMSTRONG AND T. M. SHEN HAN

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A number of amino sugar derivatives have been synthesized through the reduction of the hydrazino compounds derived from the replacement, with probable Walden inversion of *p*-tolylsulfonyloxy groups with hydrazine. Methyl 3,4-*O*-isopropylidene-2,*O*-*p*-tolylsulfonyl-β-D-arabinopyranoside, 1,2-*O*-isopropylidene-3,5-di-*O*-*p*-tolylsulfonyl-α-D-xylofuranose, 1,2-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-α-D-xylofuranose, methyl 3,5-*O*-isopropylidene-2-*O*-*p*-tolylsulfonyl-α,β-D-xylofuranoside and methyl 3,4-*O*-isopropylidene-6-*O*-*p*-tolylsulfonyl-α-D-galactopyranoside, have been converted by this method to amino sugar derivatives. A derivative of a diamino sugar is described. Crystalline D(and DL)-ribosamine (2-amino-2-deoxyribose) and D-lyxosamine (2-amino-2-deoxy-D-lyxose) are reported as hydrochlorides.

It has been shown that the reduction of sugar phenylhydrazones provides a convenient method for the synthesis of certain monosaccharide derivatives containing a primary amino group.[4] In a previous publication,[3] the reduction of hydrazino compounds, obtained by replacement of a *p*-tolylsulfonyloxy group with hydrazine, has been utilized for the synthesis of amino sugars. Peat and Wiggins[5] have shown that ammonolysis of a *p*-tolylsulfonyloxy group proceeds through an intermediate epoxide when a suitably situated hydroxyl group is available. This results in retention of configuration at the original site of the *p*-tolylsulfonyloxy group because of two successive Walden inversions at this point. The same spatial considerations apply to hydrazinolysis as shown by the identity of the end products.

In the case of 1,2:5,6-di-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-α-D-glucofuranose, wherein the *p*-toluenesulfonate is not adjacent to any free hydroxyl group, Lemieux and Chu[6] have proved that ammonolysis, or hydrazinolysis, of the *p*-tolylsulfonyloxy group proceeds with Walden inversion to yield a derivative of 3-amino-3-deoxy-D-allose. We have likewise proved that hydrazinolysis of 3,4-*O*-isopropylidene-2-*O*-*p*-tolylsulfonyl-β-L-arabinopyranoside proceeds with Walden inversion since the crystalline, unsubstituted amino sugar hydrochloride, m.p. 142–148 dec., $[\alpha]D$ −15.6 → +6.7° (water), is not identical with that obtained[7] by the definitive C5–C6 degradation of 2-amino-2-deoxy-D-galactose to 2-amino-2-deoxy-L-arabinose hydrochloride, m.p. 153–155° dec., $[\alpha]D$ +174 → +115° (water), according to the procedure established for the synthesis of 2-amino-2-deoxy-D-xylose from 2-amino-2-deoxy-D-glucose by Wolfrom and Anno.[8] Since only two possibilities are involved, this allows the 2-amino-2-deoxy-L-ribose configuration to be assigned to the 2-amino-2-deoxy-α-L-pentose hydrochloride, $[\alpha]^{22}D$ +6.7° (water, equilibrium), previously reported.[3] It is established by comparison with the 2-amino-2-deoxy-D-xylose hydrochloride, dec. 165–167°, $[\alpha]D$ +40° (final), obtained by Wolfrom and Anno,[8] that the hydrazino group on C2 of the D-xylose derivatives herein described also entered with Walden inversion, resulting in 2-amino-2-deoxy-α-D-lyxose hydrochloride, dec. 148–155°, $[\alpha]D$ +54 → −36° (water).

The present work is concerned with the synthesis of amino sugars prepared from *p*-toluenesulfonate derivatives of D-arabinose, D-xylose and D-galactose. It should be noted that the interest in the synthesis and investigation of the amino sugars is considerably enhanced by the isolation of a variety of useful antibiotics such as streptomycin, carbomycin, erythromycin,[9] puromycin,[10] strepto-

(1) Supported by Grant No. CY-3232 from the Department of Health, Education and Welfare, Public Health Service, National Institutes of Health, Bethesda 14, Md.

(2) Reported in part in *Abstract Papers Am. Chem. Soc.*, **134**, 11D (1958).

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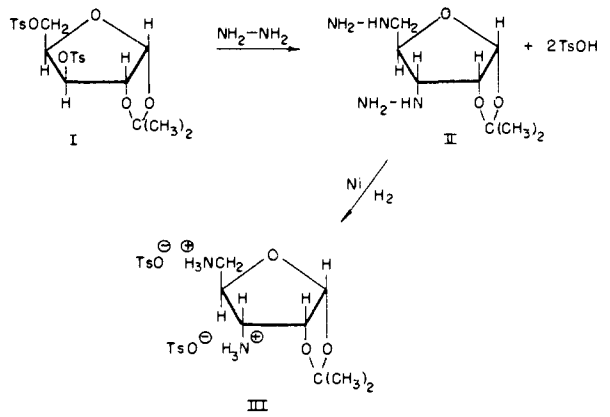

thricin,[11] amicetin,[12] neomycin[13] and kanamycin,[14] which contain unusual amino sugars.

2-Amino-2-deoxy-α-D-ribose hydrochloride was prepared by the same method as described[3] for the L-enantiomorph. This involved the treatment of methyl 3,4-*O*-isopropylidene-2-*O*-*p*-tolylsulfonyl-β-D-arabinopyranoside[15] with hydrazine and the reduction of the resulting hydrazino compound to furnish methyl 2-amino-2-deoxy-3,4-*O*-isopropylidene-β-D-ribopyranoside. This was obtained as the salicylaldehyde Schiff base and converted to methyl 2-amino-2-deoxy-β-D-ribopyranoside, isolated as the hydrochloride and the benzaldehyde Schiff base. Acetylation of the glycoside and subsequent strong acid hydrolysis provided 2-amino-2-deoxy-α-D-ribose, which crystallized as the hydrochloride. The properties and physical constants of these compounds were consistent with those described for the L-series. The hydrochloride of the racemic form is described. It is a true racemic compound.

The treatment of 1,2-*O*-isopropylidene-3,5-di-*O*-*p*-tolylsulfonyl-α-D-xylofuranose[16] (I) with hydrazine and subsequent hydrogenation of the product (II) with Raney nickel catalyst provided 3,5-diamino-3,5-dideoxy-1,2-*O*-isopropylidene-α-D-ribofuranose di-*p*-toluenesulfonate (III). The D-ribose configuration has been assigned to this compound on the assumption that, as in the case of the closely related 1,2:5,6-di-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-α-D-glucofuranose,[3] the direct replacement of the sulfonyloxy group with hydrazine is accompanied by a Walden inversion. Substance III is unusual in being a derivative of a diamino sugar.

Application of the same reaction to 1,2-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-α-D-xylofuranose[17] provided 5-amino-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose *p*-toluenesulfonate. This amino sugar has been previously prepared in this Laboratory through the reduction of 1,2-*O*-isopropylidene-5-*aldehydro*-α-D-xylopentodiofuranose phenylhydrazone[4]; it had also been prepared by Akiya and Osawa through reaction of the tosyl derivative with ammonia.[18]

Similar treatment of 3,5-*O*-isopropylidene-2-*O*-*p*-tolylsulfonyl-α-β-D-xylofuranoside[19] produced methyl 2-amino-2-deoxy-3,5-*O*-isopropylidene-D-lyxofuranoside,[20] isolated as the salicylaldehyde Schiff base. Hydrolysis of this substance with dilute hydrochloric acid produced 2-amino-2-deoxy-α-D-lyxose hydrochloride.

In the galactose series, methyl α-D-galactopyranoside was treated with acetone and phosphorus pentoxide. Preferential tosylation of the resulting methyl 3,4-*O*-isopropylidene-α-D-galactopyranoside gave the 6-*O*-*p*-tolylsulfonyl derivative. Reaction of this compound with hydrazine and subsequent reduction gave methyl 6-amino-6-deoxy-3,4-*O*-isopropylidene-α-D-galactopyranoside *p*-toluenesulfonate. A similar compound, 6-amino-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose, has been previously prepared by Freudenberg and Doser.[20]

Experimental

Methyl 2-Deoxy-3,4-*O*-isopropylidene-2-salicylideneamino-β-D-ribopyranoside.—A mixture of 20 g. of methyl 3,4-*O*-isopropylidene-2-*O*-*p*-tolylsulfonyl-β-D-arabinopyranoside[15] was heated with 100 g. of anhydrous hydrazine at 145° for 20 hr. After cooling, the partially crystalline reaction mixture was extracted with four 100-ml. portions of ether. The extract was evaporated to a sirup and treated with 100 ml. of water. The aqueous solution, still containing some hydrazine, was treated with Raney nickel catalyst for 2 hr. This resulted in the destruction of the excess hydrazine with evolution of ammonia and nitrogen. The reaction mixture was then hydrogenated in the Parr apparatus at 3-atm. pressure for 18 hr., using Raney nickel catalyst. The reduction product was concentrated to 20 ml. and treated with 3 ml. of salicylaldehyde and a sufficient amount of absolute ethanol to provide a clear solution. The solution was heated at 60° for 1 hr. and water was added to incipient turbidity, resulting in crystallization. The yellow product of methyl 2-deoxy-3,4-*O*-isopropylidene-2-salicylideneamino-β-D-ribopyranoside was recrystallized from aqueous ethanol; yield 2.2 g., m.p. 116–117°, $[\alpha]^{25}D$ −110° (*c* 2.42, chloroform); X-ray powder diffraction data were identical in all respects to that reported for methyl 2-deoxy-3,4-*O*-isopropylidene-2-salicylideneamino-β-L-ribopyranoside.[3]

Anal. Calcd. for $C_{16}H_{21}NO_5$: C, 62.52; H, 6.89; N, 4.56. Found: C, 62.67; H, 6.91; N, 4.81.

Methyl 2-Amino-2-deoxy-β-D-ribopyranoside Hydrochloride.—A suspension of 1.35 g. of methyl 2-deoxy-3,4-*O*-isopropylidene-2-salicylideneamino-β-D-ribopyranoside in 50 ml. of 2 *N* hydrochloric acid was heated at 100° for 1 hr. The resulting solution was decolorized with activated carbon and concentrated to a sirup which crystallized. Recrystallization from a mixture of methanol and ether gave methyl 2-amino-2-deoxy-β-D-ribopyranoside hydrochloride as colorless small plates; yield 0.6 g., m.p. 175–183° dec., $[\alpha]^{25}D$ −91.8° (*c* 3.04, water); X-ray powder diffraction data identical in all respects to that of the L-enantiomorph.[3]

Anal. Calcd. for $C_6H_{14}ClNO_4$: C, 36.10; H, 7.07; Cl, 17.76; N, 7.02. Found: C, 36.20; H, 7.19; Cl, 17.63; N, 7.20.

Methyl 2-Benzylideneamino-2-deoxy-β-D-ribopyranoside.—A solution of 0.5 g. of methyl 2-amino-2-deoxy-β-D-ribopyranoside in 2 ml. of water was heated with 0.3 g. of benzaldehyde and 0.4 g. of sodium bicarbonate. The reaction mixture crystallized on cooling. The product, methyl 2-benzylideneamino-2-deoxy-β-D-ribopyranoside, was ob-

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tained as colorless needles by recrystallization from ether; yield 0.45 g., m.p. 143°, $[\alpha]^{23}D$ −114° (*c* 1.85, chloroform).

Anal. Calcd. for $C_{13}H_{17}NO_4$: C, 62.15; H, 6.77; N, 5.57. Found: C, 62.17; H, 6.12; N, 5.81

2-Amino-2-deoxy-α-D-ribose (D-Ribosamine) Hydrochloride.—A mixture of 2.2 g. of methyl 2-amino-2-deoxy-β-D-ribopyranoside hydrochloride, 3.5 g. of anhydrous sodium acetate and 45 ml. of acetic anhydride was heated with continued stirring until it boiled briefly and then it was kept at 80° for 1 hr. The reaction mixture was poured into 400 ml. of ice and water and extracted with chloroform. The extract was washed with an aqueous solution of sodium bicarbonate and then with water, and concentrated to a sirup which failed to crystallize. This was hydrolyzed with 50 ml. of 4 *N* hydrochloric acid at 100° for 1 hr. Crystallization from a mixture of methanol and acetone gave 2-amino-2-deoxy-α-D-ribose hydrochloride; yield 1.45 g., m.p. 144–149° dec., $[\alpha]^{23}D$ +14.1° (initial, extrapolated) → −2.75° (*c* 2.18, water final); X-ray powder diffraction data were the same as that of the L-form.[3]

Anal. Calcd. for $C_5H_{12}ClNO_4$: C, 32.36; H, 6.52; Cl, 19.10; N, 7.55. Found: C, 32.55; H, 6.57; Cl, 19.09; N, 7.33.

2-Amino-2-deoxy-DL-ribose (DL-Ribosamine) Hydrochloride.—Equal amounts of the D- and L-forms were mixed and crystallized from methanol, acetone and ether; m.p. 169–170°; X-ray powder diffraction data[21]: 7.83m, 6.03s(2), 4.83w, 4.42m, 4.35vs(1), 3.89s(3), 3.32w, 2.78s, 2.60vw, 2.55vw, 2.47m, 2.37m, 2.02w, 1.94w. The above X-ray diffraction pattern is different from that of the D- and L-forms, and indicates the formation of a racemic compound of unknown anomeric form.

5-Amino-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose *p*-Toluenesulfonate.—A mixture of 5.0 g. of 1,2-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-α-D-xylofuranose[17] was heated with 40 g. of anhydrous hydrazine at 145° for 20 hr. The solution was concentrated to a sirup and then dissolved in water. The aqueous solution was allowed to stand with Raney nickel catalyst for 2 hr. and was then reduced on the Parr apparatus at 3-atm. for 18 hr. The mixture was filtered and the filtrate was concentrated to a sirup which crystallized. The product, 5-amino-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose *p*-toluenesulfonate, was recrystallized from a mixture of methanol, acetone and ether; yield 2.75 g., m.p. 193°, $[\alpha]^{25}D$ −5.3° (*c* 3.49, water); X-ray powder diffraction data[21]: 8.65s(3), 6.49m, 5.21s, 4.78-vs(1,1), 4.16vs(1,1), 3.96m, 3.58m, 3.44w, 3.20w, 3.09m. Akiya and Osawa[18] report m.p. 199°, $[\alpha]^{13}D$ −6°.

3,5-Diamino-3,5-dideoxy-1,2-*O*-isopropylidene-α-D-ribofuranose[20] Di-*p*-toluenesulfonate.—A mixture of 10 g. of 1,2-*O*-isopropylidene-3,5-di-*O*-*p*-tolylsulfonyl-α-D-xylofuranose[16] in 100 g. of anhydrous hydrazine was heated at 135° for 40 hr. The solution was cooled and concentrated to a sirup which was dissolved in water. Raney nickel catalyst was added to the solution which was allowed to stand at room temperature for 2 hr. The reaction mixture was then hydrogenated as before. The mixture was filtered and the filtrate was concentrated to a sirup which crystallized. The product was dissolved in methanol. Addition of a mixture of acetone and ether resulted in crystallization of a compound which proved to be ammonium *p*-toluenesulfonate. The mother liquor was allowed to stand until more crystals precipitated. This product, 3,5-diamino-3,5-dideoxy-1,2-*O*-isopropylidene-α-D-ribofuranose di-*p*-toluenesulfonate, was recrystallized from a mixture of methanol, acetone and ether; yield 0.35 g., m.p. 210°, $[\alpha]^{26}D$ +23.1° (*c* 1.53, water); X-ray powder diffraction data[21]: 8.23s(3), 6.17m, 5.77vw, 5.47 vw, 5.05vs(1), 4.75vs(2), 4.40s, 4.17s, 3.46m.

Anal. Calcd. for $C_{22}H_{32}N_2O_9S_2$: C, 49.60; H, 6.05; N, 5.35; S, 12.04. Found: C, 49.75; H, 6.20; N, 4.99; S, 11.83.

Preparation of Methyl 3,4-*O*-Isopropylidene-α-D-galactopyranoside.—Methyl α-D-galactopyranoside monohydrate[22] (18 g.) was finely powdered and suspended in 1 liter of acetone containing 35 g. of phosphorus pentoxide. The mixture was vigorously stirred for 20 min. and then decanted from the insoluble material and neutralized with sodium carbonate. The neutral solution was filtered and concentrated to a sirup which was extracted with 500 ml. of benzene. This was evaporated to a sirup which was distilled at 160° and 0.1 mm. The solidified distillate (11.9 g.) was recrystallized from benzene and methyl 3,4-*O*-isopropylidene-α-D-galactopyranoside was obtained as colorless flakes, m.p. 97–98°, $[\alpha]^{27}D$ +135° (*c* 1.61, chloroform). Ault, Haworth and Hirst[23] record 101–102° and +162° (water) for this substance prepared by a somewhat different procedure.

Anal. Calcd. for $C_{10}H_{18}O_6$: C, 51.28; H, 7.69. Found: C, 50.87; H, 7.3.

In subsequent preparations the concentrated benzene extract crystallized on seeding.

Preparation of Methyl 3,4-*O*-Isopropylidene-6-*O*-*p*-tolylsulfonyl-α-D-galactopyranoside.—Methyl 3,4-*O*-isopropylidene-α-D-galactopyranoside (5 g.) and 4 g. of *p*-toluenesulfonyl chloride (1 mole equiv.) were dissolved in 25 ml. of pyridine and the solution left at room temperature for 1 day, whereupon it was poured into water and the resulting solid was crystallized from chloroform and petroleum ether. Methyl 3,4-*O*-isopropylidene-6-*O*-*p*-tolylsulfonyl-α-D-galactopyranoside was obtained as colorless crystals; yield 5.2 g., m.p. 127–128° (Iselin and Reichstein[24] quote m.p. 129–130°).

Methyl 6-Amino-6-deoxy-3,4-*O*-isopropylidene-α-D-galactopyranoside *p*-Toluenesulfonate.—A mixture of 3.75 g. of methyl 3,4-*O*-isopropylidene-6-*O*-*p*-tolylsulfonyl-α-D-galactopyranoside in 50 g. of anhydrous hydrazine was heated at 140° for 18 hr. After cooling, the solution was concentrated to a sirup which was dissolved in water and allowed to stand for 2 hr. with Raney nickel catalyst. The reaction mixture was then reduced as before and filtered. The filtrate was concentrated to a sirup which crystallized. The product was recrystallized from a mixture of methanol, acetone and ether; yield 1.75 g., m.p. 175–176°, $[\alpha]^{20}D$ +94.6° (*c* 1.70, water); X-ray powder diffraction data[21]: 14.14s, 10.16m, 5.84s(3), 5.27w, 4.92vs(1), 4.57vs(2), 4.31vw, 4.15vw, 3.92vw, 3.74m, 3.51m, 3.40vw, 3.27w.

Anal. Calcd. for $C_{17}H_{27}NO_8S$: C, 50.36; H, 6.71; N, 3.45; S, 7.91. Found: C, 50.41; H, 6.60; N, 3.45; S, 7.99.

Methyl 2-Deoxy-3,5-*O*-isopropylidene-2-salicylideneamino-D-lyxofuranoside.[20]—A mixture of 15 g. of methyl 3,5-*O*-isopropylidene-2-*O*-*p*-tolylsulfonyl-α,β-D-xylofuranoside[19] in 50 g. of anhydrous hydrazine was heated for 20 hr. at 155°. The solution was cooled and extracted with four 100-ml. portions of ether. The ether extract was concentrated to a sirup which was dissolved in water and then allowed to stand for 2 hr. with Raney nickel catalyst. The reaction mixture was hydrogenated as described above. The mixture was filtered and the filtrate was concentrated to a sirup which was dissolved in 25 ml. of water. The aqueous solution was treated with 1 ml. of salicylaldehyde and sufficient ethanol was added to effect solution. After heating for 20 min. on the water-bath, the reaction mixture was concentrated to a sirup which crystallized. The yellow product, methyl 2-deoxy-3,5-*O*-isopropylidene-2-salicylideneamino-D-lyxofuranoside, was recrystallized from aqueous ethanol; yield 1.3 g., m.p. 109.5–110°, $[\alpha]^{23}D$ +99.5° (*c* 1.67, chloroform); X-ray powder diffraction data[21]: 10.22vs(2,2), 8.66w, 7.38vs(2,2), 5.59s, 5.04vs(1), 4.75w, 4.43s, 4.25s, 3.90m, 3.49s.

Anal. Calcd. for $C_{16}H_{21}NO_5$: C, 62.52; H, 6.89; N, 4.56. Found: C, 62.82; H, 6.99; N, 4.78.

2-Amino-2-deoxy-a-D-lyxose Hydrochloride.—A suspension of 0.8 g. of methyl 2-deoxy-3,5-*O*-isopropylidene-2-salicylideneamino-D-lyxofuranoside in 20 ml. of 2 *N* hydrochloric acid was heated in a boiling water-bath for 1 hr. The solution was decolorized with carbon and concentrated under reduced pressure to a sirup. The dried sirup was crystallized from absolute methanol–ether; yield 0.36 g. Pure material was obtained by recrystallization from abso-

(21) Interplanar spacing, Å., CuKα radiation. Relative intensity, estimated visually; s, strong; m, medium; w, weak; v, very. First three strongest lines are numbered (1, strongest); double numbers indicate approximate equal intensities.

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lute methanol; dec. 148–155°, $[\alpha]^{25}D$ +54° (initial, extrapolated) → −36° (*c* 2.3, water), X-ray powder diffraction data[21]: 6.55vw, 5.91m, 5.21w, 4.65m, 4.28vw, 4.05vs(1), 3.80vw, 3.60m, 3.42s(3), 3.29vw, 3.16m, 3.06w, 2.85m, 2.67w, 2.61s(2), 2.31w, 2.27vw, 1.95m, 1.77w, 1.74vw, 1.61w.

The substance reduced Benedict solution and exhibited a positive ninhydrin reaction.

Anal. Calcd. for $C_5H_{12}ClNO_4$: C, 32.36; H, 6.52; N, 7.55. Found: C, 32.34; H, 6.44; N, 7.97.

COLUMBUS 10, OHIO

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

2-Deoxy-D-ribose. II.[1] The Synthesis of 2-Deoxy-D-ribose 5-Phosphate

BY DONALD L. MACDONALD AND HEWITT G. FLETCHER, JR.

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The conversion of 2-deoxy-D-ribose to the crystalline di-(cyclohexylammonium) salt of 2-deoxy-D-ribose dimethyl acetal 5-phosphate is described. Mild acid hydrolysis of this acetal affords 2-deoxy-D-ribose 5-phosphate.

While 2-deoxy-D-ribose (2-deoxy-D-*erythro*-pentose) was recognized as a component of deoxyribonucleic acid some twenty-nine years ago,[2,3] only in the last few years has the role of this sugar in various biological systems attracted widespread attention. In particular, the phosphoric acid esters of 2-deoxy-D-ribose have been shown to be important intermediates in a variety of biochemical transformations. Friedkin and Kalckar,[4] for instance, demonstrated that the enzymatic phosphorolysis of guanine deoxyriboside afforded a 2-deoxy-D-ribose 1-phosphate which Friedkin[5] isolated as the barium and cyclohexylamine salts. Numerous other workers[6–11] have extended our knowledge of this highly labile substance. Manson and Lampen[6] demonstrated the existence of a mutase capable of converting 2-deoxy-D-ribose 1-phosphate to the 5-phosphate; the reverse reaction was found by Racker[12] who isolated the 5-phosphate as its barium salt. Racker,[12] as well as others,[8,13] has also obtained the substance through the acid hydrolysis of 2′-deoxyadenosine 5′-phosphate while Agranoff and Brady[14] described the phosphorylation of 2-deoxy-D-ribose with a ribokinase from calf liver, suggesting that 2-deoxy-D-ribose 5-phosphate was formed although this product was not actually isolated.

A deoxyribosephosphate aldolase was purified and described by Racker.[12] More recently, Domagk and Horecker[15] have shown that *Lactobacillus plantarum*, grown on D-glucose and adapted to 2-deoxy-D-ribose, has an active deoxyribosephosphate aldolase and crude extracts from this bacteria have been used by these authors to prepare 2-deoxy-D-ribose 5-phosphate as its barium or calcium salt in about 50% purity. Subsequently, an essentially pure barium salt has been obtained by this process.[16]

Klenow and Emberland[17] showed that 2-deoxy-D-ribose 1-phosphate was consumed in a system which was capable of converting D-ribose 1-phosphate to D-ribose 1,5-diphosphate, while Tarr[18] found that a crude fish muscle purine riboside phosphorylase possessing phosphoribomutase activity, acting on a mixture of 2-deoxy-D-ribose 1-phosphate and D-ribose 1,5-diphosphate, afforded 2-deoxy-D-ribose 1,5-diphosphate as well as 2-deoxy-D-ribose 5-phosphate, D-ribose 1-phosphate and D-ribose 5-phosphate.

None of the phosphates of 2-deoxy-D-ribose appears to have been made by strictly chemical means.[18a] Allerton, Overend and Stacey announced[19] the synthesis of the 3- and 5-phosphates of this sugar some years ago, but experimental details of their work have not, apparently, been published. With 2-deoxy-D-ribose readily accessible through a simplified preparation[1] we have turned our attention to the chemical synthesis of its 5-phosphate which will now be described.

The mercaptals of the pentoses offer the most direct route to 5-substituted derivatives of these sugars and, as a number of mercaptals of 2-deoxy-D-ribose have been described by Zinner,[20] the present synthesis was patterned after those previously described for D-glyceraldehyde 3-phosphate[21] and D-erythrose 4-phosphate.[22] The free sugar or, more conveniently, its anilide[1] was converted to the sir-

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(18a) Added in proof May 4, 1959. S. Lewak, R. Derache and L. Szabó [*Compt. rend.*, **248**, 1837 (1959)] have very recently announced a chemical synthesis of 2-deoxy-D-ribose 5-phosphate from 3-*O*-methyl-D-glucose 6-phosphate.

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