D-Galactose behaved like D-mannose with regard to color formation. D-Galactose had a more pronounced tendency to form reversion products than D-mannose: one spot in the disaccharide region and another in the trisaccharide region appeared on the paper chromatogram upon heating for 1 min. at 98° in 1.0*N* hydrochloric acid. After 30 min. heating the two spots were still faint; after 50 min. they appeared stronger, and after 87 min. higher molecular weight reversion products were also detectable on the paper chromatograms. Di- and trisaccharide spots appeared faintly on the paper chromatograms after heating D-galactose with 4.0*N* hydrochloric acid 126 min.

D-Fructose was heated with 0.1*N* hydrochloric acid and 4.0*N* hydrochloric acid for up to 120 min. Although the formation of brown colored, solid resinous products occurred very early, D-fructose was still present in solution after 30 min. treatment with 4.0*N* hydrochloric acid but was completely destroyed after 60 min. D-Fructose did not produce any reversion product. The chromatogram revealed a spot corresponding to 5-hydroxymethyl-2-furaldehyde. Three very faint spots were revealed on the chromatograms following the steam treatment. They are located between the dextrose and the maltose spot and appear only in the reaction with the lower concentration of hydrochloric acid. The spots are attributed to bimolecular fructose anhydrides in very low concentration.

L-Sorbose was treated with 0.1*N* hydrochloric acid up to 75 min. and with 4.0*N* hydrochloric acid up to 30 min. L-Sorbose was still detected after 20 min. treatment with 4.0*N* hydrochloric acid but not after 30 min. No formation of reversion products was observed but 5-hydroxymethyl-2-furaldehyde and very minor amounts of three compounds, believed to be bimolecular sorbose anhydrides, were present. L-Sorbose behaved in this respect like the other ketose, D-fructose.

Maltose was heated with 0.1*N* hydrochloric acid up to 60 min. and with 0.5*N* hydrochloric acid up to 30 min. Maltose could still be detected after 30 min. treatment with 0.5*N* hydrochloric acid. During the time the degradation of maltose into two molecules of D-glucose took place, and before all the maltose was hydrolyzed, reversion products were formed.

Sucrose was treated in 0.05*N* hydrochloric acid up to 30 min. and in 1.0*N* hydrochloric acid up to 40 min. The chromatograms showed that the sucrose was hydrolyzed completely into D-glucose and D-fructose after 5 min. in 0.05*N* hydrochloric acid and before the appearance of reversion products. Prolonged treatment with hydrochloric acid produces reversion products. The reversion products occupy the same positions on the chromatograms as the reversion products obtained with D-glucose alone. Their presence is attributed to the glucose moiety of sucrose.

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DECATUR, ILL.

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2-Deoxy-D-ribose. VI.[1] The Preparation of Derivatives of 3-Deoxy-D-*ribo*-hexonic Acid and 3-Deoxy-D-*arabino*-hexonic Acid Therefrom. Some Observations on the Kiliani Synthesis

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Derivatives of 3-deoxy-D-*ribo*-hexonic acid and 3-deoxy-D-*arabino*-hexonic acid are most easily prepared in pure form through the addition of hydrogen cyanide to 2-deoxy-D-ribose, the total yield being 80%. A variety of substances derived from these acids, including 3-deoxy-D-*ribo*-hexitol and 3-deoxy-D-*arabino*-hexitol, are described. With 2-deoxy-D-ribose and D-ribose in the usual Kiliani synthesis, hydrolysis of the epimeric nitriles is spontaneous and rapid, requiring no special step in the procedure.

The 3-deoxyhexoses, 3-deoxy-D-*ribo*-hexose (3-deoxy-D-glucose), and 3-deoxy-D-*arabino*-hexose (3-deoxy-D-mannose), as well as some of their derivatives, are of biochemical as well as of theoretical interest. Unfortunately, however, the synthetic methods which have been used for the preparation of these two substances[2,3] are of such complexity and length as to render the sugars themselves relatively inaccessible. In the course of the present work we have investigated some alternative and potentially simpler synthetic pathways to these two 3-deoxyhexoses.

In 1910 J. U. Nef[4] noted that among the saccharinic acids produced by the isomerization of D-glucose[5] with a large excess of hot sodium hydroxide were the two 3-deoxyhexonic acids, 3-deoxy-D-*ribo*-hexonic acid ("α-D-glucometasaccharinic acid") and 3-deoxy-D-*arabino*-hexonic acid ("β-D-glucometasaccharinic acid"). Using the mixture produced according to Nef's directions, Sowden[6] carried the process one step further with a Ruff degradation to

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(1) 2-Deoxy-D-ribose. V: C. Pedersen and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **82**, 5210 (1960).

(2) Crystalline 3-deoxy-D-glucose: J. W. Pratt and N. K Richtmyer, *J. Am. Chem. Soc.*, **79**, 2597 (1957).

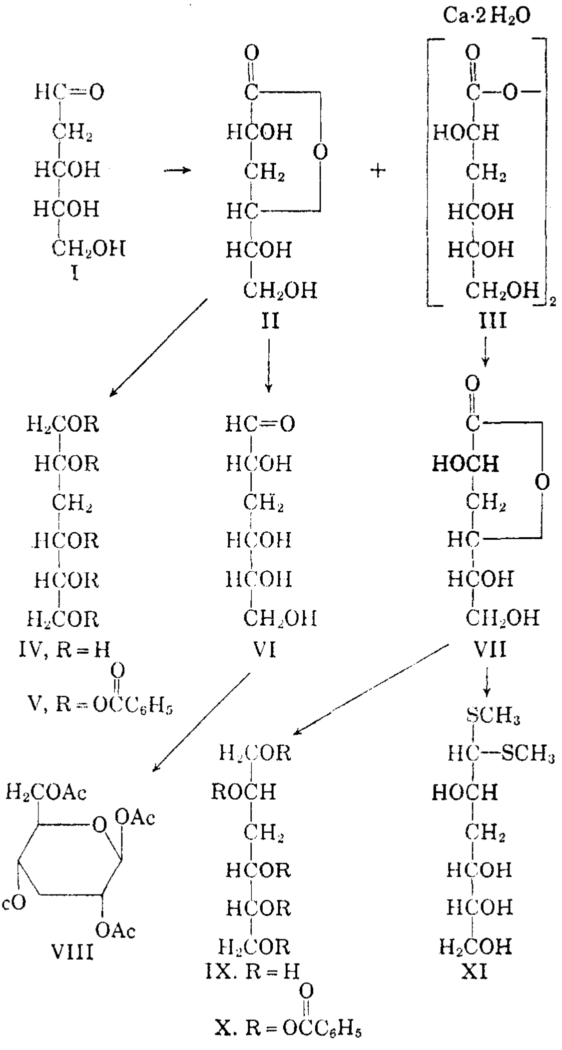
(3) H. R. Bolliger and D. A. Prins, *Helv. Chim. Acta*, **29**, 1061 (1946); crystalline 3-deoxy-D-mannose: G. Rembarz, *Chem. Ber.*, **93**, 622 (1960).

(4) J. U. Nef, *Ann.*, **376**, 1 (1910).

(5) These saccharinic acids, being deoxyhexonic acids ($C_6H_{12}O_6$), are, formally, isomers of D-glucose ($C_6H_{12}O_6$).

obtain 2-deoxy-D-ribose (I) as its anilide in about 8% yield. Diehl and Fletcher[7] simplified this preparation of 2-deoxy-D-ribose, chiefly through use of a modified initial isomerization which involved relatively brief heating of a mixture of D-glucose monohydrate with calcium hydroxide. Because of these developments, a worker can now produce about twenty-five grams of 2-deoxy-D-ribose per day using common laboratory equipment and this biochemically important sugar is thus comparatively accessible.

While the yield of 2-deoxy-D-ribose from D-glucose in this two-step process is low, it may be recalled that even pure salts of aldonic acids normally give no more than 45% of the corresponding lower-carbon sugar in the Ruff degradation.[8] One may assume, then, that the highly complex mixture resulting from the alkaline isomerization of D-glucose contains substantial quantities of the epimeric 3-deoxyhexonic acids. If these could be isolated from the mixture in an efficient manner, they should provide, through conventional reduction procedures, a practical source of the two epimeric 3-deoxyhexoses. In our hands, however, all attempts to separate substantial quantities of the two 3-deoxyaldonic acids from the isomerization mixture have proved laborious and unsatisfactory, the only product isolable in a simple and efficient fashion being the relatively insoluble lactone of the branched-chain saccharinic acid 2-*C*-methyl-D-*ribo*-pentonic acid ("α-D-glucosaccharinic acid").[9,10] However, while the desired 3-deoxyhexonic acids are difficult to isolate from the isomerization mixture, they are readily separable from each other. Attention was therefore turned to the addition of hydrogen cyanide to 2-deoxy-D-ribose (I), a synthetic pathway which had the added attraction of being suitable for the preparation of labeled materials. Using a carbonate-buffered solution of sodium cyanide,[11] the addition was found to take place in normal fashion, 3-deoxy-D-*ribo*-hexonic acid being isolated as its lactone (II, 56% yield) and 3-deoxy-D-*arabino*-hexonic acid as the dihydrate of its calcium salt (III, 24% yield). The direct addition of sodium cyanide in cold but unbuffered aqueous solution gave the same products in substantially the same proportions but in somewhat lower yields. Paper chromatography of the lactones of the two acids (II and VII) showed that preparation of epimerically pure materials requires particular care here; the rotation of one of the chromatographically pure individuals (see Experimental) was found to differ to a small but significant extent from the values previously recorded. The pure lactones were further characterized through the picrates of the two corresponding 2-substituted benzimidazoles, the signs of the rotations of these products being opposite as might be predicted from the benzimidazole rule.[12]



3-Deoxy-D-*ribo*-hexonic acid lactone (II) was reduced with sodium borohydride to the corresponding crystalline hexose (VI, "3-deoxy-D-glucose") which was further characterized as its tetraacetate[2,13] (VIII). Reduction of 3-deoxy-D-*arabino*-hexonic acid lactone in buffered solution with sodium amalgam afforded a crude, amorphous 3-deoxy-D-*arabino*-hexose which was converted

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(6) J. C. Sowden, *J. Am. Chem. Soc.*, **76**, 3541 (1954); *Biochem. Preparations*, **5**, 75 (1957).

(7) H. W. Diehl and H. G. Fletcher, Jr., *Arch. Biochem. Biophys.*, **78**, 386 (1958); *Biochem. Preparations*, **8**, in press (1961).

(8) H. G. Fletcher, Jr., H. W. Diehl, and C. S. Hudson, *J. Am. Chem. Soc.*, **72**, 4546 (1950).

(9) J. C. Sowden, *Advances in Carbohydrate Chem.*, **12**, 35 (1957).

(10) J. C. Sowden and D. R. Strobach, *J. Am. Chem. Soc.*, **82**, 3707 (1960).

(11) H. S. Isbell, J. V. Karabinos, H. L. Frush, N. B. Holt, A. Schwebel, and T. T. Galkowski, *J. Research Natl. Bur. Standards*, **48**, 163 (1952).

(12) This rule, normally applied to the free benzimidazoles, is described and discussed by N. K. Richtmyer, *Advances in Carbohydrate Chem.*, **6**, 175 (1951).

(13) M. Černý and J. Pacák, *Collection Czechoslov. Chem. Communs.*, **21**, 1003 (1956).

into its dimethyl dithioacetal (XI), a crystalline derivative recently reported by Rembarz.[8] A pure sample of the dithioacetal was demercaptalated to the free sugar; unlike Rembarz[8] we were unable to obtain the latter in crystalline form. In passing, it may be mentioned that 3-deoxy-D-*ribo*-hexose failed, in our hands, to yield a crystalline dimethyl dithioacetal.

Complete reduction of the two epimeric lactones with sodium borohydride gave the two 3-deoxyhexitols IV and IX. While both of these proved to be amorphous, each gave a crystalline pentabenzoate (V and X).

COMMENT ON THE KILIANI SYNTHESIS

A variety of techniques have been described for the addition of hydrogen cyanide to reducing sugars. The directions which Pratt and Richtmyer[14] gave for D-ribose illustrate a widely used procedure. The sugar is treated with cold aqueous sodium cyanide until the Fehling test is negative and then the strongly alkaline solution is boiled until the ammonia, formed by the hydrolysis of the epimeric nitriles, is expelled. It appears to be generally assumed that this latter treatment is necessary in order to hydrolyze the nitriles. However, the heating involves visible decomposition; Isbell and his co-workers[11] avoided this undesirable feature by aerating the solution at 60° in order to remove the ammonia. In the course of the present work it was found that the nitriles from 2-deoxy-D-ribose hydrolyze spontaneously in carbonate-buffered solution at room temperature; decationization, followed by removal of the slight excess of hydrogen cyanide, gave a product which failed to evolve ammonia when heated with strong sodium hydroxide. A similar result was observed when 2-deoxy-D-ribose was treated with cold, aqueous sodium cyanide.

This experience with 2-deoxy-D-ribose raised two questions: 1) are the nitriles from other sugars as readily hydrolyzed and, if so, 2) are the proportions of the two epimeric products formed affected by the heating which is normally part of the procedure? Heating of the strongly alkaline solution resulting from the reaction of aqueous sodium cyanide with an aldose would appear to favor epimerization of the products. The procedure of Pratt and Richtmyer[14] was therefore repeated with D-ribose, omitting the expulsion of the ammonia. The yield of calcium D-altronate hemiheptahydrate (35%) and of D-allonolactone (25%) indicated a ratio almost identical with that obtained by the earlier authors.[15] Obviously, trials in a variety of series would be necessary in order to ascertain whether the customary heating of the Kiliani reaction mixture may lead to significant epimerization of the products.

EXPERIMENTAL[16]

*3-Deoxy-*D-ribo*-hexono-γ-lactone* (II) *and calcium 3-deoxy-*D-arabino*-hexonate dihydrate* (III) *from 2-deoxy-*D*-ribose* (I). The conditions for this reaction are essentially those described by Isbell *et al.*[11] Sodium cyanide (2.01 g., 97% sodium cyanide) and sodium hydroxide (1.49 g.) were dissolved in 186 ml. of water and the solution frozen on the walls of a spherical, 1-l. flask. A solution of 5.0 g. of 2-deoxy-D-ribose in 186 ml. of 0.2*M* sodium bicarbonate was then added and the mixture stirred gently at room temperature until homogeneous. After 16 hr. the odor of ammonia was apparent and the colorless solution showed no reducing power with Fehling solution. Four identical batches were pooled and deionized by passage through a column (6.8 × 45 cm.) of Amberlite IR-120-H$^+$. The effluent and washings were concentrated *in vacuo* (60° bath) to a thin, pale-yellow sirup which was diluted with 50 ml. of absolute ethanol. The ethanol was removed *in vacuo* and the process repeated with 50 ml. of ethanol and then with 25 ml. of ethanol. Dilution of the viscous sirup with 25 ml. of acetone and seeding gave well formed octahedra of 3-deoxy-D-*ribo*-hexono-γ-lactone (6.87 g., $[\alpha]^{20}_{D}$ + 23.1° in water). The mother liquor was concentrated *in vacuo* and a small amount of water evaporated from the residue to remove all of the acetone. The sirup was then dissolved in *ca.* 60 ml. of water and sufficient calcium hydroxide added to cause a permanent, light-pink color with phenolphthalein. The excess of base was neutralized with carbon dioxide, the solution heated to boiling and filtered through Celite. It was then concentrated to a volume of *ca.* 20 ml. On standing at room temperature the solution deposited the dihydrate of calcium 3-deoxy-D-*arabino*-hexonate: 7.64 g., 24%, $[\alpha]^{20}_{D}$ −23° in water. Recrystallized from water, it showed $[\alpha]^{20}_{D}$ −24° in water (*c* 0.6). Nef[4] reported $[\alpha]_D$ −23.3°. The main mother liquor was freed of calcium ions by passage through a column (3.4 × 37 cm.) of Amberlite IR-120-H$^+$ and the solution then concentrated *in vacuo* to a sirup. Residual water was removed by evaporating absolute alcohol from the material and the sirup was then dissolved in a little acetone to give a second crop (6.7 g.) of 3-deoxy-D-*ribo*-hexono-γ-lactone, $[\alpha]^{20}_{D}$ + 23° in water. The lactone (total yield 56%) was recrystallized from acetone (17 parts) and then from water (0.5 part). Paper chromatography in ethyl acetate–acetic acid–formic acid–water (18:3:1:4, v./v.),[17] followed with a periodate-benzidine spray,[18] then showed the material to be homogeneous. Thus purified, the lactone melted at 108–109°[19] and had a rotation $[\alpha]^{20}_{D}$ +27°[20] in water (*c* 0.7). Nef[4] reported m.p. 104° and $[\alpha]_D$ +25.3° (water) for this compound. In saturated aqueous

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[14] J. W. Pratt and N. K. Richtmyer, *J. Am. Chem. Soc.*, **77**, 1906 (1955).

[15] In carbonate-buffered solution, using the technique of Isbell *et al.* (ref. 11), but omitting the heating and aeration, D-ribose gave 36% of the calcium salt and 38% of the lactone.

[16] Melting points are corrected.

[17] R. L. Whistler and G. N. Richards, *J. Am. Chem. Soc.*, **80**, 4888 (1958).

[18] M. Viscontini, D. Hoch, and P. Karrer, *Helv. Chim. Acta*, **38**, 642 (1955).

[19] J. Kenner and G. N. Richards [*J. Chem. Soc.*, 278 (1954)] reported that 3-deoxy-D-*ribo*-hexono-γ-lactone became amorphous after heating at 60° for prolonged periods. They suggested that "some isomerization to the β-form may have occurred." In the course of the present work, a sample of the pure lactone was heated in a Pyrex vessel for 6 hr. at 110–115° (bath). The colorless melt crystallized on cooling and then showed $[\alpha]^{20}_{D}$ +25.9° in water (*c* 1.1). Paper chromatography indicated that the substance was unchanged.

[20] Samples showing a rotation of less than $[\alpha]^{20}_{D}$ +25.5° were found, on paper chromatography, to be contaminated with the epimeric lactone.

phenylmercuric nitrate solution[21] (*c* 2.7) one specimen of 3-deoxy-D-*ribo*-hexono-γ-lactone was found to mutarotate $[\alpha]^{20}_{D}$ + 25° (4 min.) → +11° (193 hr.).

3-Deoxy-D-*ribo*-hexono-γ-lactone dissolves readily in cold dioxane but rapidly crystallizes without cooling the solution. Apparently a solvate is involved but attempts to characterize it were without success owing to the fact that dioxane is rapidly lost from the solid at room temperature.

A sample of the lactone was converted to 3-deoxy-D-*ribo*-hexonic acid phenylhydrazide using the method which Bolliger and Prins[3] described for the preparation of its epimer: m.p. 108–109°, $[\alpha]^{20}_{D}$ 0° (methanol, *c* 0.94 and water, *c* 0.65). Nef[4] reported m.p. 100–103° and $[\alpha]_{D}$ 0° (water) for this compound.

3-Deoxy-D-arabino-*hexono-γ-lactone* (VII) *from calcium 3-deoxy*-D-arabino-*hexonate dihydrate* (III). An aqueous solution containing 23 g. of calcium 3-deoxy-D-*arabino*-hexonate dihydrate was freed of calcium ions by passage through a column of Amberlite IR-120-H$^+$ and then concentrated *in vacuo* to a clear, colorless sirup. Benzene (2 × 25 ml.) and then dioxane (25 ml.) were distilled *in vacuo* from this sirup to remove water. From its solution in 20 ml. of dioxane, the residue deposited 16.6 g. (54%) of 3-deoxy-D-*arabino*-hexono-γ-lactone. Recrystallized from a mixture of absolute alcohol and pentane, the lactone was obtained in chromatographically pure form: m.p. 92–93°, $[\alpha]^{20}_{D}$ + 6.4° (water, *c* 0.8). Nef[4] reported m.p. 92° and $[\alpha]_{D}$ +8.2° (water) while Richards[22] gave m.p. 89–90° and $[\alpha]^{20}_{D}$ +8.0° (water). In saturated aqueous phenylmercuric nitrate solution[21] (*c* 2.7) a sample mutarotated $[\alpha]^{20}_{D}$ + 6.1° (4 min.) → −0.5° (756 hr.).

A sample of 3-deoxy-D-*arabino*-hexono-γ-lactone was converted to 3-deoxy-D-*arabino*-hexonic acid phenylhydrazide following the directions of Bolliger and Prins[3]: m.p. 127–128°, $[\alpha]^{20}_{D}$ −47.0° (methanol, *c* 0.5); the earlier authors[3] reported m.p. 128–129° and $[\alpha]^{13}_{D}$ −46.7° (methanol, *c* 1.2).

*2-(*D-arabino-*1,3,4,5-Tetrahydroxypentyl)benzimidazole picrate.* A mixture of 3-deoxy-D-*arabino*-hexono-γ-lactone (500 mg.) with 432 mg. of *o*-phenylenediamine, 1 ml. of water, and 0.67 ml. of concd. hydrochloric acid was heated in an oil bath at 135 ± 5° for 2 hr. The sirupy residue remaining was dissolved in 5 ml. of warm water and the solution filtered through decolorizing carbon. The filtrate (10 ml.) was made alkaline with aqueous ammonia; attempts to obtain the free benzimidazole in crystalline form proved unsuccessful. The alkaline solution was therefore extracted with ether (3 × 15 ml.) to remove unchanged *o*-phenylenediamine and then concentrated to a sirup which was treated with 10 ml. of a solution which had been made by dissolving 10 g. of cupric acetate monohydrate in a minimum of ammonium hydroxide and diluting the solution to 50 ml. The grey-green precipitate was separated by centrifugation and washed with water. This copper salt was then suspended in 25% aqueous ethanol and decomposed with hydrogen sulfide. The solution was filtered through a thin bed of decolorizing carbon and concentrated *in vacuo* to a sirup (750 mg.). Picric acid (710 mg.), ethanol (7 ml.), and water (7 ml.) were then added and the mixture warmed until homogeneous. On concentration at room temperature, the solution deposited the picrate as needles. Recrystallized from 20 ml. of isopropyl alcohol, it (700 mg., 47%) melted at 170–171°. Repeated recrystallization from the same solvent gave the pure picrate: m.p. 171–172°, $[\alpha]^{20}_{D}$ −67° (dioxane, *c* 0.86).

Anal. Calcd. for $C_{18}H_{19}N_5O_{11}$ (481.37): C, 44.91: H, 3.98; N, 14.55. Found: C, 45.14; H, 4.00; N, 14.26.

*2-(*D-ribo-*1,3,4,5-Tetrahydroxypentyl)benzimidazole picrate.* 3-Deoxy-D-*ribo*-hexono-γ-lactone (500 mg.) was treated as described above for its epimer to give a product which was crystallized from a mixture of ethanol (8 ml.) and water (8 ml.). After recrystallization from water, the picrate (1.0 g., 67%) melted at 181–182°; further recrystallization from acetone-pentane afforded the pure picrate melting at 179–180° and rotating $[\alpha]^{20}_{D}$ + 84.9° (dioxane, *c* 0.86).

Anal. Calcd. for $C_{18}H_{19}N_5O_{11}$ (481.37): C, 44.91; H, 3.98; N, 14.55. Found: C, 45.00; H, 3.90; N, 14.36.

3-Deoxy-D-ribo-*hexose* (VI). 3-Deoxy-D-*ribo*-hexono-γ-lactone (1.1 g.) was dissolved in 50 ml. of water and 2 g. of sodium hydrogen oxalate added. The mixture was cooled to 0 to 5° and stirred while a solution of 0.5 g. of sodium borohydride in 10 ml. of water was added dropwise over the course of about 30 min., oxalic acid being added as necessary to maintain the *p*H at 4.5 to 5.0. Sufficient oxalic acid was then added to lower the *p*H to 3 and decompose the excess of sodium borohydride. The solution was concentrated to a volume of about 15 ml. and then diluted with 50 ml. of methanol to precipitate the major portion of the inorganic material. After filtration, the solution was again concentrated and the residue, dissolved in 50 ml. of water, freed of cations by passage through a column (3 × 30 cm.) of Amberlite IR-120-H$^+$. The solution was concentrated *in vacuo* and 50 ml. of benzene evaporated *in vacuo* from the residue. A mixture of 25 ml. of methanol and 15 ml. of benzene was then distilled *in vacuo* from the sirup and this process repeated until a flame test showed boron to be absent. The material, dissolved in 50 ml. of water, was deionized by passage through a column (3 × 30 cm.) of Duolite A-4 and then concentrated to a sirup which was diluted with 1 ml. of absolute ethanol, seeded and left at +5° for several days. The product (0.42 g., 38%) melted at 102–104°; recrystallization from absolute ethanol afforded chromatographically pure 3-deoxy-D-*ribo*-hexose melting at 105–106° and showing an equilibrium rotation of $[\alpha]^{20}_{D}$ + 32° in water (*c* 1.0). Pratt and Richtmyer[2] reported m.p. 105.5–107° and $[\alpha]^{20}_{D}$ + 32.2° for this substance. Other forms of the sugar have recently been described by Anet.[23] Admixture with a sample of the sugar kindly provided by Dr. Pratt failed to depress the melting point of the product prepared as described above.

3-Deoxy-β-D-ribo-*hexose tetraacetate* (VIII). One gram of 3-deoxy-D-*ribo*-hexose was acetylated with a mixture of acetic anhydride and zinc chloride in the usual manner to yield, from a mixture of ethanol and pentane, 0.6 g. (30%) of product melting at 129–130°. Recrystallized from ethanol-pentane, the pure tetraacetate (0.5 g.) melted at 130–131° and showed $[\alpha]^{20}_{D}$ −15° in chloroform (*c* 1.6). Pratt and Richtmyer[2] reported m.p. 129–130° and $[\alpha]^{20}_{D}$ −14° (chloroform); Cěrný and Pacák[13] gave m.p. 129–130° and $[\alpha]^{18}_{D}$ −20.0° (chloroform) and assigned a structure and configuration denoted by VIII to the compound.

3-Deoxy-D-arabino-*hexose dimethyl dithioacetal* (XI). 3-Deoxy-D-*arabino*-hexono-γ-lactone was reduced to the corresponding 3-deoxyhexose with sodium amalgam using the general procedure of Isbell and his associates.[24,25] The lactone (0.32 g.) was dissolved in 10 ml. of water and the solution, chilled in an ice salt bath, treated with 24 g. of sodium hydrogen oxalate to bring the *p*H to 3. While the cold suspension was vigorously stirred, sodium amalgam (36.7 g., 5% sodium) was added. After 1 hr., the major part of the spent amalgam was removed and another 36.7-g. batch added. The process was repeated once again, a total of 110 g. of amalgam being used. During the reduction the temperature was kept at −5 to 0°; the *p*H was constant at 4.5. After the third and final addition of amalgam, the mixture was stirred for 1 hr. and the major part of the inorganic salts precipitated through the addition of 75 ml. of methanol. After filtration, the solu-

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[21] On prolonged standing, aqueous solutions of the two epimeric 3-deoxyhexono-γ-lactones described here were found to contain mycelia unless phenylmercuric nitrate had been added.

[22] G. N. Richards, *J. Chem. Soc.*, 3638 (1954).

[23] E. F. L. J. Anet, *Chem. & Ind.* (*London*), 345 (1960).

[24] H. S. Isbell, H. L. Frush, and R. Schaffer, *J. Research Natl. Bur. Standards,* **54**, 201 (1955).

[25] Use of sodium borohydride and the technique described earlier in this paper for the reduction of the epimeric lactone consistently gave products heavily contaminated with the 3-deoxyhexitol.

tion was concentrated to a volume of *ca.* 20 ml. and deionized by passage through columns of Amberlite IR-120-H$^+$ and Duolite A-4. The solution was filtered through a thin bed of decolorizing carbon and concentrated *in vacuo* (0.15 mm.) to a stiff sirup (0.19 g., 59%). Paper chromatography in the ethyl acetate–acetic acid-formic acid-water system, using periodate-benzidine spray, revealed three components. The intensity of the spots indicated that the 3-deoxyhexose was slightly contaminated with the corresponding glyconolactone and glycitol. A sample (1.253 g.) of crude 3-deoxy-D-*arabino*-hexose prepared in this fashion was added to a cold mixture of 4.0 ml. of methanethiol and 1.1 ml. of concd. hydrochloric acid. In a sealed vessel the reaction mixture was held at 25° for 30 min. and then cooled in an ice bath. Water (5 ml.) and methanol (3 ml.) were then added and the solution deionized by passage through a column (1.5 × 15 cm.) of Amberlite IR-45. Solvent was removed from the effluent and benzene (5 ml.) evaporated *in vacuo* from the residual sirup. The product was then extracted with warm methylene chloride (6 × 5 ml.) and, upon concentration to a volume of *ca.* 10 ml., the combined extracts deposited 1.09 g. (59%, based on the crude sugar) of fine needles, melting at 80–82°. After recrystallization from warm methylene chloride the chromatographically pure thioacetal melted at 81–82° and showed $[\alpha]_D^{20}$ −38.4 in methanol (*c* 2.5). Rembarz[8] reported m.p. 82° and $[\alpha]_D^{18}$ −38.6° (methanol, *c* 1.6) for 3-deoxy-D-*arabino*-hexose dimethyl dithioacetal.

*3-Deoxy-*D-ribo-*hexitol* (IV). 3-Deoxy-D-*ribo*-hexonolactone (1.0 g.) was dissolved in 40 ml. of water and the solution added dropwise over the course of about 30 min. to a well-stirred solution of 0.7 g. of sodium borohydride in 20 ml. of water. The reaction mixture was left for another 30 min. and then passed through a column (3 × 25 cm.) of Amberlite IR-120-H$^+$. It was concentrated *in vacuo* to a stiff sirup which was freed of boric acid by repeated distillation *in vacuo* of 50-ml. portions of methanol. The sirup was then dissolved in 50 ml. of water and treated with Amberlite MB-3 in order to remove any unchanged lactone. The solution was filtered through a thin bed of decolorizing carbon and concentrated to a sirup (0.72 g., 70%) which rotated $[\alpha]_D^{20}$ −10° in water (*c* 0.9). Efforts to obtain the glycitol in crystalline form were unsuccessful. It gave a negative Fehling test and but one spot when chromatographed on paper in the ethyl acetate–acetic acid–formic acid–water system and sprayed with periodate-benzidine.

Anal. Calcd. for $C_6H_{14}O_5$ (166.17): C, 43.37; H, 8.49. Found: C, 43.46; H, 8.69.

*1,2,4,5,6-Penta-O-benzoyl-3-deoxy-*D-ribo-*hexitol* (V). 3-Deoxy-D-*ribo*-hexitol (2.3 g.) was benzoylated with benzoyl chloride in pyridine solution in the customary manner to give from 15 ml. of benzene, 4.5 g. of crystalline product. After two recrystallizations from benzene, the pentabenzoate (4.1 g., 43%) melted at 170–171° and showed $[\alpha]_D^{20}$ +19.1° in chloroform (*c* 1.1).

Anal. Calcd. for $C_{41}H_{34}O_{10}$ (686.68): C, 71.71; H, 4.99. Found: C, 71.88; H, 5.19.

*3-Deoxy-*D-arabino-*hexitol* (IX). 3-Deoxy-D-*arabino*-hexono-γ-lactone (1.4 g.) was reduced with sodium borohydride as described earlier for its epimer. The sirup was dissolved in 50 ml. of water and sufficient 0.1*N* sodium hydroxide added to make the solution just alkaline to phenolphthalein. When the pink color of the indicator had persisted for 15 min. after the last addition of the alkali, 10 g. of Amberlite MB-3, and a little decolorizing carbon were added.[26] After filtration, the solution was concentrated *in vacuo* to a sirup (1.20 g., 84%, $[\alpha]_D^{20}$ −27.0° in water, *c* 0.9) which failed to crystallize. The material gave a negative Fehling test and, on paper, a negative alkaline hydroxylamine–ferric chloride test[27] for lactone. When chromatographed on paper, using ethyl acetate–acetic acid–formic acid–water and spraying with periodate-benzidine, the preparation gave but one spot.

Anal. Calcd. for $C_6H_{14}O_5$ (166.17): C, 43.37; H, 8.49. Found: C, 43.08; H, 8.64.

*1,2,4,5,6-Penta-O-benzoyl-3-deoxy-*D-arabino-*hexitol* (X). One gram of 3-deoxy-D-*arabino*-hexitol was benzoylated in the normal manner with benzoyl chloride in pyridine solution to yield 3.7 g. of sirupy material; from a mixture of ethyl acetate (6 ml.) and pentane (9 ml.) this afforded 2.6 g. (63%) of the pentabenzoate as clusters of fine needles melting at 102–103°. Recrystallized three times from a mixture of ethyl acetate and hexane, it melted at 104–105° and rotated $[\alpha]_D^{20}$ −33.6° in chloroform (*c* 0.6). Sublimation of a sample at 1 micron pressure and 210–220° (bath), followed by recrystallization from ethyl acetate–hexane, raised the melting point to 105–106° and the rotation to $[\alpha]_D^{20}$ −34.4° (chloroform, *c* 0.6).

Anal. Calcd. for $C_{41}H_{34}O_{10}$ (585.68): C, 71.71; H, 4.99. Found: C, 71.81; H, 5.05.

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(26) This process is the method of choice for the removal of unchanged lactone from the alditol.

(27) M. Abdel-Akher and F. Smith, *J. Am. Chem. Soc.*, **73**, 5859 (1951).