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Application of the Cyanohydrin Synthesis to D-Altrose[1]

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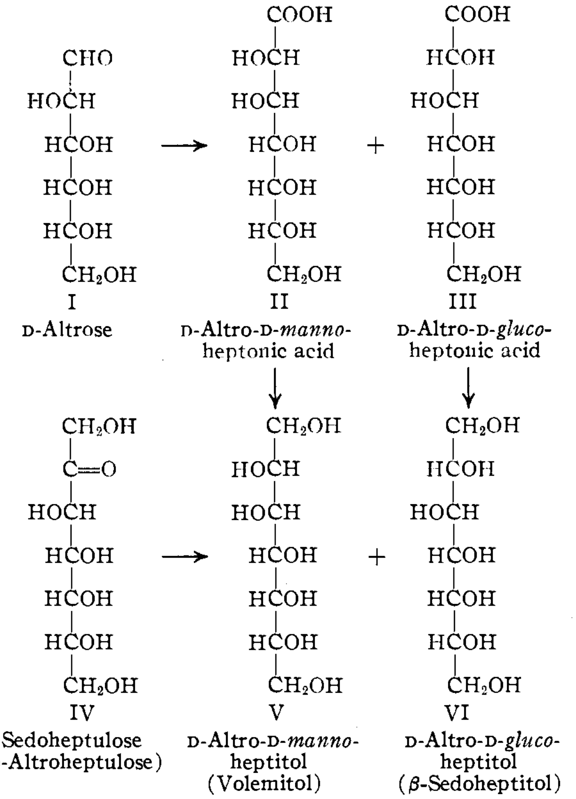
The addition of hydrogen cyanide to D-altrose has yielded a mixture of D-altro-D-*manno*-heptonic acid (55%) and D-altro-D-*gluco*-heptonic acid (13%); the acids were separated and characterized through crystalline derivatives. Their respective configurations have been established not only by the application of empirical rules of rotation but also by the reduction of their lactones to the corresponding sirupy sugars and subsequent hydrogenation to volemitol and β-sedoheptitol, whose structures had been proved earlier in a conclusive manner. The preparation of D-altrose has been improved, and tetraacetyl-β-D-altropyranose and several derivatives of the two D-altroheptoses have been described.

The addition of hydrogen cyanide to aldohexoses has been described previously with the four sugars D-galactose, D-glucose, D-gulose and D-mannose.[2] Now that crystalline D-altrose (I) has become available in this Laboratory, we have studied its reaction with cyanide, and have prepared a number of derivatives of the two D-altroheptonic acids and of the two D-altroheptoses obtained from them by reduction of their lactones with sodium amalgam.

The classical method of lengthening the carbon chain of an aldose by the addition of hydrogen cyanide, followed by saponification of the resulting mixture with barium hydroxide, has yielded the expected D-altro-D-*manno*-heptonic acid (II) as its crystalline lactone in a yield of 51%, with an additional 4% of this isomer being recovered as the phenylhydrazide. The more soluble phenylhydrazide of the D-altro-D-*gluco*-heptonic acid (III) could then be isolated from the mother liquors in a 13% yield. The relative proportion of the acids II and III was about 4 to 1; this observation is in complete agreement with previous experiences in the galactose, glucose, gulose and mannose series as expressed by Hann, Merrill and Hudson[3] in the simple generalization that *the isomer which is more readily accessible is the one that carries its hydroxyls on carbon atoms 2 and 4 in trans relationship*.

Preliminary identification of our crystalline lactone as that of D-altro-D-*manno*-heptonic acid (II) was secured through application of the empirical rules relating rotation to configuration among the phenylhydrazides,[4] amides[5] and benzimidazoles.[6] These derivatives, as may be noted from Table I, were all levorotatory. On the other hand, the more soluble phenylhydrazide and the corresponding benzimidazole and barium salt[7] were dextrorotatory as would be expected for derivatives of D-altro-D-*gluco*-heptonic acid (III). A crystalline lactone of this second acid could not be obtained.


I D-Altrose
II D-Altro-D-*manno*-heptonic acid
III D-Altro-D-*gluco*-heptonic acid
IV Sedoheptulose (D-Altroheptulose)
V D-Altro-D-*manno*-heptitol (Volemitol)
VI D-Altro-D-*gluco*-heptitol (β-Sedoheptitol)

Conclusive proof of the correctness of the formulas thus assigned to the acids, as well as additional support for the validity of the "rules," was obtained through reduction of the two lactones with sodium amalgam to their respective sirupy altroheptoses and subsequent catalytic hydrogenation to the corresponding polyols. The product from the crystalline lactone was found to be identical with the naturally occurring D-altro-D-*manno*-heptitol, usually known as volemitol (V). The product from the second lactone was D-altro-D-*gluco*-heptitol, usually known as β-sedoheptitol (VI). Both polyols are obtainable by the similar reduction of naturally occurring sedoheptulose[8] (D-altroheptulose, IV), the ketoheptose that forms a common phenylosazone with our two new aldoheptoses; the configuration of each of the two polyols has been established previously in a definitive manner, particularly through the researches of Ettel[9] and of Merrill, Haskins, Hann and Hudson.[10]

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(1) Presented in part before the Division of Sugar Chemistry at the Boston Meeting of the American Chemical Society, April 2, 1951.

(2) For a recent review of these syntheses, see C. S. Hudson, *Advances in Carbohydrate Chem.*, **1**, 1 (1945).

(3) R. M. Hann, A. T. Merrill and C. S. Hudson, THIS JOURNAL, **66**, 1912 (1944); *cf.* J. G Maltby, *J. Chem. Soc.*, **123**, 1404 (1923); 1629 (1926); 2769 (1929).

(4) P. A. Levene, *J. Biol. Chem.*, **23**, 145 (1915); C. S. Hudson, THIS JOURNAL, **39**, 462 (1917).

(5) C. S. Hudson, *ibid.*, **40**, 813 (1918).

(6) N. K. Richtmyer and C. S. Hudson, *ibid.*, **64**, 1612 (1942).

(7) See P. A. Levene, *J. Biol. Chem.*, **23**, 145 (1915), and P. A. Levene and G. M. Meyer, *ibid.*, **26**, 355 (1917), for the rule of rotation for salts of aldonic acids.

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

(9) V. Ettel, *Collection Czechoslov. Chem. Communs.*, **4**, 504, 513 (1932).

(10) A. T. Merrill, W. T. Haskins, R. M. Hann and C. S. Hudson, THIS JOURNAL, **69**, 70 (1947).

TABLE I

COMPARISON OF ROTATIONS OF SUBSTANCES IN THE D-ALTRO-D-*manno*-HEPTOSE, D-MANNOSE AND D-GALA-L-*manno*-HEPTOSE SERIES

Solvent: chloroform (C), *N* hydrochloric acid (H), pyridine (P) or water (W)

	D-Altro-D-*manno*-heptose series		D-Mannose series		D-Gala-L-*manno*-heptose series	
	$[\alpha]^{20}\text{D}$	$[M]^{20}\text{D}$	$[\alpha]\text{D}$	$[M]\text{D}$	$[\alpha]\text{D}$	$[M]\text{D}$
Lactone (W)	+40.4°	+8400	+51.5°[a]	+9200	−52.3°[a]	−10,900
Phenylhydrazide (W)	− 5.8	−1800	− 8.1[a]	−2300	+ 8.5[a]	+2700
Amide (W)	− 9.0	−2000	−17.3[a]	−3400	+14.3[a]	+3200
Benzimidazole (H)	−17.7	−5300	−23.7[b]	−6400	+18.5[b]	+5500
Diethyl mercaptal (P)	± 0.0	±0	− 2.8[c]	− 800	− 9.7[d]	−3100
Sugar α-acetate (C)	+66.5	+30,700	+55.0[a]	+21,500	......	......

[a] From the tables in "Polarimetry, Saccharimetry, and the Sugars," by F. J. Bates and Associates, U. S. Government Printing Office, Washington, 1942. [b] W. T. Haskins and C. S. Hudson, THIS JOURNAL, **61**, 1266 (1939). [c] E. Pacsu and C. von Kary, *Ber.*, **62**, 2811 (1929). [d] R. M. Hann and C. S. Hudson, THIS JOURNAL, **59**, 1898 (1937).

TABLE II

COMPARISON OF ROTATIONS OF SUBSTANCES IN THE D-ALTRO-D-*gluco*-HEPTOSE, D-GLUCOSE AND D-GALA-L-*gluco*-HEPTOSE SERIES

Solvent: chloroform (C), *N* hydrochloric acid (H), methyl cellosolve (MC), pyridine (P) or water (W)

	D-Altro-D-*gluco*-heptose series		D-Glucose series		D-Gala-L-*gluco*-heptose series	
	$[\alpha]^{20}\text{D}$	$[M]^{20}\text{D}$	$[\alpha]\text{D}$	$[M]\text{D}$	$[\alpha]\text{D}$	$[M]\text{D}$
Phenylhydrazide (W)	+13.4°	+4200	+12°[a]	+3400	−7.8°[b]	−2500
Benzimidazole (H)	+ 9.7	+2900	+ 8.7[c]	+2300	−14.4[d]	−4300
Phenylosazone, initial (MC)	−61[e]	−23,700	−59.5[f]	−21,300	+68.6[f]	+26,600
Phenylosazone, final	−45[e]	−17,500	−44.7[f]	−16,000	+30.0[f]	+11,700
Phenylosotriazole (P)	−71.7[e]	−21,200	−81.6[g]	−21,600	+80.3[h]	+23,700
Sugar α-acetate (C)	+107	+49,400	+102[a]	+39,700	−55.8[b]	−25,800

[a] From the tables in "Polarimetry, Saccharimetry, and the Sugars," by F. J. Bates and Associates, U. S. Government Printing Office, Washington, 1942. [b] R. M. Hann and C. S. Hudson, THIS JOURNAL, **59**, 548 (1937). [c] N. K. Richtmyer and C. S. Hudson, *ibid.*, **64**, 1612 (1942). [d] D. A. Rosenfeld, J. W. Pratt, N. K. Richtmyer and C. S. Hudson, *ibid.*, in press. [e] Average values; see Experimental part. [f] W. T. Haskins, R. M. Hann and C. S. Hudson, unpublished measurements from this Laboratory. [g] R. M. Hann and C. S. Hudson, THIS JOURNAL, **66**, 735 (1944). [h] W. T. Haskins, R. M. Hann and C. S. Hudson, *ibid.*, **69**, 1050 (1947).

In several earlier papers from this Laboratory[11] attention was called to the similarity of the properties of each of the higher-carbon sugars to those of the corresponding hexose which possessed like configurations at carbon atoms 2, 3, 4 and 5. The two new series of D-altroheptoses now permit additional comparisons, and Table I brings together the rotational data on derivatives of D-altro-D-*manno*-heptose, D-mannose, and another heptose with a manno configuration at the reducing end, namely, D-gala-L-*manno*-heptose. Table II includes derivatives of the epimeric D-altro-D-*gluco*-heptose, D-glucose, and D-gala-L-*gluco*-heptose series, although the phenylosazones and phenylosotriazoles may be placed equally well in the first table. Again the similarities of molecular rotations are marked, except for the open-chain mercaptals; however, such derivatives have been noted as exceptions before.[11b,c,d,e]

Experimental

D-Altrose (I) was prepared in the following manner. Methyl α-D-glucoside was first transformed to methyl 4,6-benzylidene-α-D-altroside as described in preceding papers.[12] While the direct acetolysis of the benzylidene compound yields pentaacetyl-α-D-altrose,[13] the mother liquors contain considerable benzylidenediacetate (m.p. 44–45°) which prevents a completely satisfactory isolation of the product. Accordingly, each 25-g. batch of the benzylidene compound was hydrolyzed to methyl α-D-altroside,[12b] which for the immediate purpose was not crystallized but its aqueous solution merely concentrated *in vacuo* to a stiff sirup. Acetolysis of this material was effected by adding 150 ml. of cold acetic anhydride containing 1.5 ml. of concentrated sulfuric acid, keeping the mixture cooled until solution was complete, and then leaving it at room temperature for three days. The acetolysis mixture was poured on ice, neutralized with solid sodium bicarbonate, and the product extracted with chloroform; the extract was washed, dried, and concentrated in the usual manner. Crystallization with ether and pentane gave an average yield of 22 g. of pentaacetyl-α-D-altrose as rectangular, plate-like prisms of m.p. 118–119° and $[\alpha]^{20}\text{D}$ +63.0° in chloroform (*c*, 5).[12b]

Deacetylation was accomplished by dissolving each 100 g. of pentaacetate in one liter of warm, anhydrous methanol, cooling until fine crystals began to separate, then adding 20 ml. of 2 *N* barium methoxide in methanol and leaving the mixture at 5° overnight. Enough *N* sulfuric acid was added to neutralize the barium methoxide (as determined in a separate experiment, using phenolphthalein as the indicator), 4 g. of bentonite was added to aid in coagulating the colloidal barium sulfate, and the mixture was filtered through a Buchner funnel precoated with activated carbon. The clear solution was concentrated *in vacuo* to a fairly thick sirup which was transferred to a beaker with methanol and concentrated further in a desiccator over granular calcium chloride. Inoculation with seed crystals and further standing in the desiccator yielded about 35 g. of D-altrose, with an additional amount recoverable from the combination of mother liquors.

Pentaacetyl-β-D-altropyranose.—In the course of an earlier research[12b] a sample of 2,3,4,6-tetraacetyl-β-D-altrose had been acetylated by adding the finely powdered substance to a mixture of acetic anhydride and pyridine at −10°. The product, isolated at that time as a sirup,

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[11] (a) R. M. Hann, A. T. Merrill and C. S. Hudson, THIS JOURNAL, **57**, 2100 (1935); (b) R. M. Hann and C. S. Hudson, *ibid.*, **59**, 548 (1937); (c) R. M. Hann and C. S. Hudson, *ibid.*, **59**, 1898 (1937); (d) W. D. Maclay, R. M. Hann and C. S. Hudson, *ibid.*, **60**, 1035 (1938); (e) R. M. Hann, W. D. Maclay and C. S. Hudson, *ibid.*, **61**, 1270 (1939); (f) E. M. Montgomery and C. S. Hudson, *ibid.*, **64**, 247 (1942); (g) R. M. Hann, A. T. Merrill and C. S. Hudson, *ibid.*, **66**, 1912 (1944).

[12] (a) D. A. Rosenfeld, N. K. Richtmyer and C. S. Hudson, *ibid.*, **70**, 2201 (1948); (b) N. K. Richtmyer and C. S. Hudson, *ibid.*, **63**, 1727 (1941).

[13] N. K. Richtmyer and C. S. Hudson, *ibid.*, **65**, 740 (1943).

crystallized after standing for a few years in a desiccator over soda lime. Addition of a few crystals thus obtained to the sirupy mother liquors remaining after the separation of the pentaacetyl-α-D-altrose as described above resulted in the isolation of a considerable amount of the desired pentaacetyl-β-D-altrose. It could be recrystallized by dissolving in a small amount of chloroform, adding pentane, and cooling slowly in the presence of a seed crystal. The elongated prisms were readily distinguishable from the characteristic clusters of plate-like prisms of the α-pentaacetate. After several recrystallizations in this manner the β-pentaacetate melted at 89–91°, and its rotation had become constant at $[\alpha]^{20}$D $-38.3°$ in chloroform (c, 5).

Anal. Calcd. for $C_{16}H_{22}O_{11}$: C, 49.23; H, 5.68; CH_3CO, 55.1. Found: C, 49.10; H, 5.67; CH_3CO, 55.5.

In order to relate the new pentaacetyl-β-D-altrose to the previously known α-pentaacetate, a sample of each of these acetates was treated with titanium tetrachloride as described in an earlier publication[12b] and the products were found to be identical by melting points, mixed melting points, and rotations. Since the acetochloro-α-D-altrose obtained in this manner from the α-pentaacetate had already been correlated with methyl α-D-altroside, whose pyranoid ring structure had been proved by periodate oxidation methods, these experiments established the presence of the pyranoid ring also in the new β-pentaacetate.

Rearrangement of the β-pentaacetate to the α-pentaacetate under the usual conditions of acetolysis was demonstrated by dissolving 10 g. of the pure compound in a total volume of 250 ml. of acetic anhydride containing 2.5 ml. of concentrated sulfuric acid. Equilibrium was reached within 48 hours at 20° with $[\alpha]^{20}$D being $+32.9°$. In acetic anhydride alone the α-pentaacetate had $[\alpha]^{20}$D $+70.9°$ and the β-pentaacetate $-37.6°$; on the assumption that only these two forms were present, the equilibrium mixture was estimated to contain 65% of the α-pentaacetate and 35% of the β-pentaacetate, in good agreement with the values 64 and 36%, respectively, that were reported previously[12b] from the acetolysis of 2,3,4-triacetyl-D-altrosan$<1,5>\beta<1,6>$. From the rearrangement mixture thus prepared from β-pentaacetate, 5.7 g. was isolated and identified as the anomeric α-pentaacetate.

The value of A_{Ac}, calculated from the molecular rotations of +24,590 and −14,950 for these α- and β-pentaacetates, respectively, is +19,800, which is in good agreement with the corresponding values of +20,500 and +20,700 reported from the neolactose (= 4-β-D-galactopyranosyl-D-altrose)[14] and celtrobiose (= 4-β-D-glucopyranosyl-D-altrose)[15] series, respectively. This may be considered as additional evidence that the two pentaacetates of D-altrose represent a normal α,β-pair.

D-Altro-D-*manno*-heptonic γ-Lactone.—To one hundred grams of crystalline D-altrose dissolved in 150 ml. of water and cooled in an ice-bath was added 30 ml. of liquid hydrogen cyanide and four drops of 28% aqueous ammonia. The mixture was left for three days in a refrigerator at 5°, and then showed no reducing action toward Fehling solution. In order to saponify any nitrile or amide present, the mixture was diluted to about one liter with water and boiled with 250 g. of barium hydroxide octahydrate for five hours, more water being added when necessary to maintain the original volume. Most of the barium ions were removed by the addition of 450 ml. of 3 N sulfuric acid and removal of the precipitated barium sulfate by filtration through a layer of activated carbon on a Buchner funnel; the remaining barium ions were eliminated by passing the filtrate through a column of the cation exchanger Amberlite IR-120. Concentration of the solution *in vacuo* yielded a sirup which crystallized readily when heated on the steam-bath to effect lactonization. In subsequent preparations the product usually crystallized during the concentration process. After four recrystallizations from 90% ethanol, the fine needles of D-altro-D-*manno*-heptonic lactone melted at 162–163° and showed $[\alpha]^{20}$D $+40.4°$ in water (c, 4); no mutarotation was observed in three days and accordingly the substance is presumed to be a γ-lactone. The yield of crystalline lactone from 500 g. of D-altrose was 293 g. (51%); the residual sirup weighing 206 g. was treated with phenylhydrazine as will be described later.

Anal. Calcd. for $C_7H_{12}O_7$: C, 40.39; H, 5.81. Found: C, 40.44; H, 5.81.

D-Altro-D-*manno*-heptonic Phenylhydrazide.—Six grams of the lactone was heated with 6 ml. of phenylhydrazine and 42 ml. of water for two hours on the steam-bath. The phenylhydrazide crystallized on cooling in nearly quantitative yield. After four recrystallizations from water the small flakes melted at 185–187° and showed $[\alpha]^{20}$D $-5.8°$ in water (c, 1.8).

Anal. Calcd. for $C_{13}H_{20}N_2O_7$: C, 49.36; H, 6.37; N, 8.86. Found: C, 49.25; H, 6.32; N, 8.87.

D-Altro-D-*manno*-heptonic Amide.—A suspension of 2.5 g. of the lactone in 50 ml. of absolute ethanol was saturated at room temperature with dry ammonia gas. The needles of lactone were replaced by the heavier prisms of the amide in nearly quantitative yield. After two recrystallizations from aqueous ethanol the product melted at 169–170° and showed $[\alpha]^{20}$D $-9.0°$ in water (c, 2.3).

Anal. Calcd. for $C_7H_{15}NO_7$: C, 37.33; H, 6.71; N, 6.22. Found: C, 37.20; H, 6.63; N, 6.05.

2-(D-*altro*-D-*manno-hepto*-Hexahydroxyhexyl)-benzimidazole.—The heating of 1.9 g. of D-altro-D-*manno*-heptonic lactone with 1.1 g. of *o*-phenylenediamine, 4 ml. of water, 1 ml. of ethanol, and 1.7 ml. of concentrated hydrochloric acid at 135° for 2.5 hours according to the directions of Moore and Link[16] gave 1.9 g. (70%) of the desired benzimidazole. Two recrystallizations from 50% ethanol yielded long needles melting at 217–219° (dec.) and showing $[\alpha]^{20}$D $-17.7°$ in N hydrochloric acid (c, 2).

Anal. Calcd. for $C_{13}H_{18}N_2O_6$: C, 52.34; H, 6.08; N, 9.39. Found: C, 52.26; H, 6.12; N, 9.57.

Reduction of D-Altro-D-*manno*-heptonic Lactone to Sirupy D-Altro-D-*manno*-heptose and the Preparation of D-Altroheptose Phenylosazone.—Forty grams of the lactone was reduced with 2000 g. of 2.5% sodium amalgam in the usual manner. The neutralized solution was concentrated *in vacuo* and freed from most of the sodium sulfate by precipitation with ethanol. The remaining ionizable material was removed by passing the aqueous solution through columns of the cation exchanger Amberlite IR-120 and the anion exchanger Duolite A-4. Final concentration of the solution *in vacuo* left a thick sirup weighing about 30 g. (average of five reductions).

Although the D-altro-D-*manno*-heptose did not form a sparingly soluble phenylhydrazone as might be expected from a heptose with the manno configuration on carbon atoms 2 to 5, it was converted readily to a phenylosazone which proved to be identical with the one first prepared by LaForge and Hudson[8] from sedoheptulose. Our product melted at 194–195° (dec.) as did also the sedoheptulose phenylosazone prepared recently by Haskins and Hudson,[17] and a mixture of the two samples showed no depression of melting point. Haskins and Hudson reported that their phenylosazone showed $[\alpha]^{20}$D $-54.4°$ in methyl cellosolve, with no mutarotation during 120 hours; our product, D-altroheptose phenylosazone, however, showed a small but consistent mutarotation under the same conditions (c, 0.4), with the $[\alpha]^{20}$D values in three determinations changing from −60.6°, −60.4° and −61.8°, to −50.7°, −49.8° and −42.5°, respectively, within six days. We also prepared the phenylosazone from sedoheptulose which had been regenerated by the action of acid on crystalline sedoheptulosan, and observed that sample to mutarotate similarly from −60.5 to −48.5° in 20 hours, and to −43.3° in ten days. In 2:3 pyridine–ethanol (v/v) solution (c, 0.4) our D-altroheptose phenylosazone mutarotated from $[\alpha]^{20}$D −69.1 to −22.5° (constant, six weeks) and our sedoheptulose phenylosazone from −69.5 to −21.2° (constant, three weeks). In pyridine solution (c, 0.4) our sedoheptulose phenylosazone changed from $[\alpha]^{20}$D −78.3 to −31.2° (constant, one month).

Additional proof of the identity of the phenylosazones from the two sources was established by converting our D-altroheptose phenylosazone to D-altroheptose phenylosotriazole as described by Haskins, Hann and Hudson.[18] The

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[14] A. Kunz and C. S. Hudson, THIS JOURNAL, 48, 1978 (1926).

[15] N. K. Richtmyer and C. S. Hudson, *ibid.*, 58, 2584 (1936).

[16] S. Moore and K. P. Link, *J. Biol. Chem.*, 133, 293 (1940).

[17] W. T. Haskins and C. S. Hudson, THIS JOURNAL, 69, 1370 (1947).

[18] W. T. Haskins, R. M. Hann and C. S. Hudson, *ibid.*, 69, 1050 (1947).

product, obtained in 52% yield, melted at 181–182° and showed $[\alpha]^{20}\text{D}$ −71.9° in pyridine (*c*, 0.8); the reported values are 181–182° and −71.5°, respectively. The melting point of a mixture of the two specimens of phenylosotriazole was not depressed.

D-Altro-D-*manno*-heptose Diethyl Mercaptal.—Five grams of the sirupy heptose was dissolved in 5 ml. of concentrated hydrochloric acid, 5 ml. of ethyl mercaptan was added, and the mixture was kept in an ice-bath and shaken frequently for three hours. The product crystallized readily upon the addition of small pieces of ice, but the product was so soluble in ice water that only 0.6 g. was obtained on filtration. The filtrate, therefore, was neutralized with ammonium hydroxide, the solution concentrated *in vacuo* to dryness, and the residue acetylated overnight with 75 ml. of a 2:1 mixture of acetic anhydride and pyridine. The acetylated product, isolated in the usual way, was a sirup; on catalytic deacetylation with methanolic barium methoxide, it yielded an additional 1.8 g. of the mercaptal. For analysis, the D-altro-D-*manno*-heptose diethyl mercaptal was recrystallized four times from absolute ethanol. The plate-like prisms melted at 151–153° and showed $[\alpha]^{20}\text{D}$ +31.1° in water (*c*, 1.8).

Anal. Calcd. for $C_{11}H_{24}O_6S_2$: C, 41.75; H, 7.64; S, 20.26. Found: C, 41.76; H, 7.53; S, 19.88.

Hexaacetyl-D-altro-α-D-*manno*-heptose.—The acetylation of 10 g. of sirupy D-altro-D-*manno*-heptose with 100 ml. of acetic anhydride containing 1 ml. of concentrated sulfuric acid as catalyst was complete within an hour as judged by the lack of further change in rotation overnight. The reaction mixture was decomposed with ice, and the product, isolated in the usual manner, crystallized on the addition of ether and pentane in a yield of 11.6 g. The hexaacetate was recrystallized three times from chloroform by the addition of pentane, forming large, chunky prisms melting at 138–139° and showing $[\alpha]^{20}\text{D}$ +66.5° in chloroform (*c*, 2.5); these values were unchanged by two additional recrystallizations.

Anal. Calcd. for $C_{19}H_{26}O_{13}$: C, 49.35; H, 5.67; CH_3CO, 55.9. Found: C, 49.42; H, 5.68; CH_3CO, 55.5.

Hydrogenation of D-Altro-D-*manno*-heptose to D-Altro-D-*manno*-heptitol (Volemitol) (V).—Five grams of the sirupy heptose, regenerated from its crystalline α-hexaacetate by catalytic deacetylation with sodium methoxide, was shaken in 100 ml. of water with hydrogen and 9 g. of Raney nickel catalyst at 3000 p.s.i. for 24 hours at 100°. The resulting solution, which no longer reduced Fehling solution, was filtered, deionized, concentrated *in vacuo* to a sirup, and the product crystallized from 80% ethanol in a yield of 3.0 g. The once-recrystallized material was identified as volemitol by its melting point of 152–153°, a value which was unchanged when the substance was mixed with an authentic sample of volemitol prepared from sedoheptulose; by its rotation $[\alpha]^{20}\text{D}$ +57.1° in 5% ammonium molybdate (*c*, 0.41) as compared to the rotation +57.0° reported by Merrill, Haskins, Hann and Hudson[10] under the same conditions; and by its $[\alpha]^{20}\text{D}$ value of +112° in acidified molybdate solution (*c*, 0.33), in good agreement with the $[\alpha]^{20}\text{D}$ value of +109° reported recently from this Laboratory.[19]

D-Altro-D-*gluco*-heptonic Phenylhydrazide.—The 206 g. of sirup remaining after the isolation of 293 g. of crystalline D-altro-D-*manno*-heptonic lactone as described earlier was diluted to 700 ml. with water and heated with 200 ml. of phenylhydrazine for 3.5 hours on the steam-bath. Upon cooling, the relatively insoluble D-altro-D-*manno*-heptonic phenylhydrazide separated in a yield, including a second portion obtained by concentration of the mother liquor, of 35 g. (4% based on the original D-altrose). The filtrate was extracted ten times with a total of 1500 ml. of benzene to remove excess phenylhydrazine, and the aqueous solution was concentrated *in vacuo* to a sirup. The addition of ethanol resulted in the crystallization of the second D-altroheptonic phenylhydrazide. After one recrystallization from ethanol, the D-altro-D-*gluco*-heptonic phenylhydrazide weighed 118 g. (13% based on the original D-altrose). For analysis it was recrystallized thrice and formed fine needles melting at 153–155° and showing $[\alpha]^{20}\text{D}$ +13.4° in water (*c*, 3).

Anal. Calcd. for $C_{13}H_{20}N_2O_7$: C, 49.36; H, 6.37; N, 8.86. Found: C, 49.20; H, 6.41; N, 8.76.

Regeneration of D-Altro-D-*gluco*-heptonic Lactone from Its Phenylhydrazide and the Preparation of Barium D-Altro-D-*gluco*-heptonate.—The phenylhydrazide was hydrolyzed by boiling with aqueous copper sulfate according to the method of Hann and Hudson[20]; the copper and sulfate ions were removed by treatment with hydrogen sulfide and barium hydroxide, respectively; and the clear, colorless filtrate was evaporated *in vacuo*, then heated on a steam-bath to effect lactonization. However, the product has failed so far to crystallize.

One portion of the sirupy lactone was neutralized to phenolphthalein with aqueous barium hydroxide, the solution concentrated *in vacuo*, and a crystalline barium salt obtained with the aid of 80% ethanol. The product was recrystallized three times by the slow addition of 50% ethanol to an aqueous solution of the salt. The acicular prisms of barium D-altro-D-*gluco*-heptonate showed $[\alpha]^{20}\text{D}$ +5.9° in water (*c*, 6). In *N* hydrochloric acid (*c*, 6) the barium salt mutarotated from $[\alpha]^{20}\text{D}$ +1.2° (five minutes) to +8.6° (5.5 hours, constant); the latter rotation is equivalent to +12.1° if calculated as the lactone.

Anal. Calcd. for $C_{14}H_{26}BaO_{16}$: C, 28.61; H, 4.46; Ba, 23.37. Found: C, 28.53; H, 4.57; Ba, 23.36.

2-(D-*altro*-D-*gluco*-*hepto*-Hexahydroxyhexyl)-benzimidazole.—Condensation of 1.8 g. of the sirupy lactone, which had been regenerated from the crystalline phenylhydrazide, with *o*-phenylenediamine by the procedure of Moore and Link[16] yielded 1.1 g. of crude benzimidazole. It was purified by three recrystallizations from twenty parts of 50% ethanol, forming small needles melting at 193–195° (dec.) and showing $[\alpha]^{20}\text{D}$ +9.7° in *N* hydrochloric acid (*c*, 2).

Anal. Calcd. for $C_{13}H_{18}N_2O_6$: C, 52.34; H, 6.08; N, 9.39. Found: C, 52.02; H, 6.00; N, 9.64.

Reduction of D-Altro-D-*gluco*-heptonic Lactone to Sirupy D-Altro-D-*gluco*-heptose and the Preparation of Hexaacetyl-D-altro-α-D-*gluco*-heptose.—Forty-four grams of the sirupy lactone, which had been regenerated from the phenylhydrazide, was reduced with sodium amalgam in the usual manner, furnishing 25 g. of a sirupy sugar which has not yet crystallized. Two-thirds of this sirup was subjected to acetylation with 400 ml. of acetic anhydride containing 4 ml. of concentrated sulfuric acid as catalyst, and the product was isolated in crystalline form without difficulty. The 18.5 g. of product was recrystallized to constant rotation from chloroform by the addition of ether, forming clusters of elongated, stout prisms that melted at 181–182° and showed $[\alpha]^{20}\text{D}$ +107° in chloroform (*c*, 2).

Anal. Calcd. for $C_{19}H_{26}O_{13}$: C, 49.35; H, 5.67; CH_3CO, 55.9. Found: C, 49.46; H, 5.74; CH_3CO, 55.8.

Hydrogenation of D-Altro-D-*gluco*-heptose to D-Altro-D-*gluco*-heptitol (β-Sedoheptitol) (VI).—The remaining third of the sirupy heptose (about 8 g.) was dissolved in 100 ml. of water and reduced with hydrogen and Raney nickel catalyst at 100° and 2000 p.s.i. for 24 hours. The solid product weighed 5.0 g. and, after two recrystallizations from aqueous ethanol, was identified as β-sedoheptitol by a direct comparison of melting points and rotations with an authentic sample prepared from sedoheptulose.[8]

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