Cyclizations of Dialdehydes with Nitromethane. IX.[1] Nitrogenous Heptulosans

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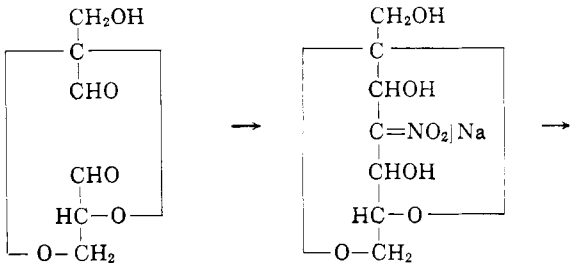
Received August 28, 1962

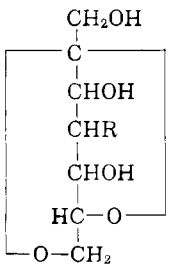
The synthesis of three 2,7-anhydro-4-nitro-4-deoxy-β-D-heptulopyranoses and of the corresponding 4-amino sugars by way of the nitromethane method is described. The products are presumed to bear their nitrogen functions in equatorial positions, *i.e.*, to possess any three of the *ido*, *gulo*, *altro*, and *allo* configurations.

In contrast to the vast amount of knowledge that has accumulated in the field of nitrogenous five- and six-carbon sugars, little is known about their seven-carbon homologs. In fact, we are not aware of any that occur in nature, and only three 2-acetamido-2-deoxy-aldoheptoses[2] and a number of 1-nitro-1-deoxyheptitols[3] have been synthesized. In this paper we wish to report on the synthesis of some members of a new group of nitrogen derivatives in the seven-carbon sugar family. They are 4-nitro- and 4-amino-4-deoxyheptulosans. Their synthesis was accomplished by applying the nitromethane cyclization, which has been described in preceding papers of this series, to the dialdehyde I that is readily obtainable from sedoheptulosan.[4]

When the dialdehyde I was condensed in *methanolic* solution with one molecular equivalent of nitromethane in the presence of one molecular equivalent of sodium methoxide, solid *aci*-nitro sodium salts were obtained, in various fractions comprising three stereoisomers, in nearly quantitative total yield. On the basis of earlier experiences with this method[5] we assigned to the products structure II (2,7-anhydro-4-*aci*-nitro-4-deoxy-β-D-heptulopyranose sodium salts). The least soluble of them, salt IIa, crystallized directly out of the reaction solution and amounted to 14% of the total salts formed.



I II



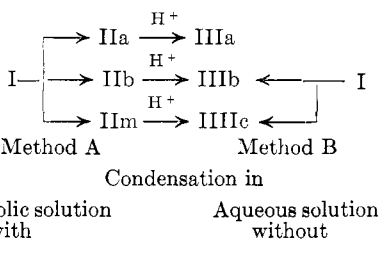
III. R = NO_2
IV. R = NH_3]Cl

The mother liquor upon prolonged standing deposited, in similar yield, a second salt, IIb, which differed from the first in the infrared spectrum as well as, most strikingly, in its rotatory behavior in water. Whereas IIa exhibits a virtually constant levorotation ($[\alpha]_D$ $-51° \rightarrow -50°$), a fresh solution of IIb is strongly dextrorotatory, with the initial value of $[\alpha]_D$ $+115°$ decreasing rapidly, turning negative and reaching a final value of $-92°$ after several hours. A third isomer, IIc, was recognized to exist in the mother liquor of the condensation solution although it could not be isolated directly from the latter. It was obtained in solid form when the free crystalline nitrodeoxyheptulosan IIIc described below was reconverted into the sodium salt. This salt IIc shows a mutarotation of $[\alpha]_D$ $-138.5° \rightarrow -73°$, which is opposite in sense to that of IIb. As was established earlier,[1] mutarotations of *aci*-nitro glycoside salts are indicative of spontaneous epimerizations taking place at carbon atoms adjacent to the nitro groupings.

Roughly 70% of the *aci*-nitro salts formed in the nearly quantitative condensation reaction did not crystallize spontaneously. However, by means of simple general techniques the total condensation products could be obtained in solid state. Thus, the remainder of the products after the collection of most of the crystallizable IIa was worked up giving fractions of material whose aqueous solutions were all levorotatory and exhibited considerable mutarotations. These salt fractions were not stereochemically homogeneous but could nevertheless be utilized for further preparative work. For the sake of convenient reference they are herein given a common designation, salt IIm.

By deionization with cation exchange resin the salts II were converted into free 2,7-anhydro-4-nitro-4-deoxy-β-D-heptulopyranoses (III). Thus, we have obtained three beautifully crystalline isomers, IIIa, IIIb and IIIc (method A).

Alternatively, the nitroheptulosans IIIb and IIIc could be prepared directly, without the isolation of *aci*-nitro salts, by conducting the nitromethane condensation of the dialdehyde in *aqueous* solution in the presence of one equivalent of sodium hydroxide followed by deionization (method B). The latter method is the preferred one for the preparation of IIIc.



(1) Paper VIII in this series: H. H. Baer, *J. Am. Chem. Soc.*, **84**, 83 (1962).

(2) R. Kuhn and G. Baschang, *Ann.*, **636**, 164 (1960).

(3) J. C. Sowden and R. Schaffer, *J. Am. Chem. Soc.*, **73**, 4662 (1951); J. C. Sowden and H. O. L. Fischer, *ibid.*, **68**, 1511 (1946); J. C. Sowden and D. R. Strobbach, *ibid.*, **82**, 954 (1960).

(4) J. W. Pratt, N. K. Richtmyer, and C. S. Hudson, *ibid.*, **74**, 2200 (1952).

(5) See ref. 1, and the preceding papers I–VII.

The characteristic physical data of the nitrodeoxyheptulosans are given in Table I, and their ways of formation are indicated in the preceding scheme (p. 1287).

TABLE I

PHYSICAL CONSTANTS OF THREE ISOMERIC NITRODEOXYHEPTULOSANS III

Compound	M.p., °C.	$[\alpha]^{23}D$ in H_2O	R_f[a]
IIIa	176	−60°	
IIIb	203	+69°	0.58
IIIc	159	−176.5°	0.52

[a] See Experimental.

Catalytic hydrogenation of the nitrodeoxyheptulosans III readily afforded the corresponding 2,7-anhydro-4-amino-4-deoxy-β-D-heptulopyranoses which were isolated as their crystalline hydrochlorides IV. The constants of the new amino sugars are given in Table II. They were produced immediately in chromatographically pure state when the pure, uniform nitro compounds were hydrogenated. However one need not always employ, in the preparation of the amines, homogeneous crystalline nitro compounds; rather, sirupy mixtures may be used since the amine hydrochlorides crystallize without difficulty. Thus, the product obtained upon acidification of the heterogeneous salt IIm, followed by hydrogenation, represented a mixture of amino sugars from which pure IVc could be crystallized in fair yield. Similarly, sirups remaining after the collection of all the nitro products which crystallized in the experiments of method B have been hydrogenated and have furnished crystalline mixtures of amino sugars.

TABLE II

SPECIFIC ROTATIONS AND R_{gm}-VALUES OF THREE ISOMERIC AMINODEOXYHEPTULOSAN HYDROCHLORIDES IV

Compound	$[\alpha]^{23}D$ in H_2O	$R_{glucosamine}$[a]
IVa	−55°	1.04
IVb	+39°	1.30
IVc	−126°	1.00

[a] See Experimental.

The configurations of our new sugar derivatives have not been established as yet. However, Richardson and Fischer,[6] having investigated the course of the nitromethane condensation with the homologous dialdehyde from levoglucosan, adduced experimental proof that in all their nitro sugars the NO_2 group had adopted an equatorial position, and they suggested for a reason the large steric interference which an axial NO_2 would encounter from the anhydride bridge. It is therefore very likely that our products III (and hence IV, too) also carry equatorially linked nitrogen atoms, *i.e.*, that they possess any three of the *gulo*, *altro*, *allo* and *ido* configurations.

A comparison of the molecular rotations of the pair of homologs, 1,6-anhydro-β-D-gulopyranose (M_D +8165)[7] and 2,7-anhydro-β-D-guloheptulopyranose (M_D +7620),[8] suggests that the corresponding 3-amino-3-deoxygulosan hydrochloride (M_D +9100)[6] has its homolog in IVb (M_D +8900). A comparison of 1,6-anhydro-β-D-altropyranose (M_D −34,800)[9] with 2,7-anhydro-β-D-altroheptulopyranose (sedoheptulosan, M_D −28,000)[4] might allow the conclusion that 3-amino-3-deoxyaltrosan hydrochloride (M_D −34,100)[6,10] and IVc (M_D −28,800) are homologs. A similar tentative assignment for IVa cannot be made at present for lack of pertinent data.

(6) Part VI of this series, *J. Am. Chem. Soc.*, **83**, 1132 (1961).

(7) L. C. Stewart and N. K. Richtmyer, *ibid.*, **77**, 1021 (1955).

(8) By reversal of the sign of rotation of the known enantiomorph; L. C. Stewart, N. K. Richtmyer, and C. S. Hudson, *ibid.*, **74**, 2206 (1952).

(9) N. K. Richtmyer and C. S. Hudson, *ibid.*, **61**, 214 (1939).

(10) L. F. Wiggins, *J. Chem. Soc.*, 18 (1947).

(11) Pyridine–ethyl acetate–water–acetic acid (5:5:3:1, v./v.), with pyridine–ethyl acetate–water (6:40:11, v./v.) in the bottom of the tank; F. G. Fischer and H. Dörfel, *Z. physiol. Chem.*, **301**, 224 (1955).

Experimental

The melting points were determined in an aluminum block. The optical rotations were measured in 2-dm. tubes in carbon dioxide-free water; *c*, approximately 1 unless otherwise stated. Evaporations were done *in vacuo* at 35–40° (bath temperature).

Paper Chromatography.—The descending technique on Whatman no. 1 paper was used. The nitro compounds were irrigated with 1-butanol–acetic acid–water (4:1:5 v./v., upper layer, with the lower layer in the bottom of the tank) and made visible by spraying with *N* aqueous sodium hydroxide–methanol–butanol (1:2:7, v./v.) and inspection under an ultraviolet lamp. The amino derivatives were chromatographed with the Fischer–Dörfel[11] solvent system and detected with a ninhydrin spray, glucosamine hydrochloride being used as a speed standard. The R_{gm}-values given refer to a freshly set up solvent system; in older tanks the values tend to become somewhat lower.

Dialdehyde (I) from Sedoheptulosan.—Crystalline sedoheptulosan hydrate[4] (10.5 g., 0.05 mole) was added, in the course of 10 min., to an ice-cooled solution of 21.4 g. of sodium metaperiodate (0.1 mole) in 250 ml. of water. The reaction mixture then was allowed to assume room temperature and to stand in the dark for 4 hr., during which period 45 ml. of a *M* sodium bicarbonate solution (90% of 1 molar equiv.) was gradually added. Thereafter the solution was concentrated to beginning crystallization, mixed with two volumes of ethanol, chilled, and filtered. The inorganic filter residue was washed with ethanol and the filtrate further concentrated. This procedure was repeated, usually three to four times, until no more crystalline material could be removed. Finally a colorless sirup of I resulted that was deemed sufficiently free of salts (sodium iodate and formate) when it dissolved clearly in three volumes of cold methanol.

2,7-Anhydro-4-*aci*-nitro-4-deoxy-β-D-heptulopyranose Sodium Salts (II).—The sirupy dialdehyde obtained above was dissolved in 100 ml. of methanol. The solution was chilled in ice–water, 2.7 ml. of nitromethane (1 molar equiv.) was added, and then 36.5 ml. of a chilled sodium methoxide solution (containing 3 g. of sodium per 100 ml.) was dropped in with swirling in the course of 10 min. The reaction mixture was then kept overnight in the refrigerator.

The first crop of crystals which had slowly appeared was collected and washed with ice-cold methanol. The yield of the desiccator-dried, yellowish-white product was 1.65 g. **Salt IIa.** $[\alpha]^{23}D$ −50.8° → −49.8° (final after 26 hr.). Vapor phase chromatography of a solution in water indicated the presence of methanol of crystallization.

Anal. Calcd. for $C_7H_{10}O_7NNa \cdot CH_3OH$ (275.2): N, 5.09; Na, 8.37. Found: N, 5.64; Na, 8.35.

A second crop of IIa separated from the mother liquor that was kept at 4°, and was collected after 3 days; 0.53 g., $[\alpha]^{23}D$ −52.3° → −50.8°. The infrared spectra of the first and second crops were identical.

When after removal of the crystalline IIa the mother liquor was placed in the refrigerator again, another crop of crystals was deposited in the course of several days. It was **salt IIb** which after washing with cold methanol weighed 1.9 g. (desiccator-dried); $[\alpha]^{23}D$ +115.0° (3 min.) → −92.0° (final, 16 hr.). Vapor phase chromatography (Perkin–Elmer fractometer, Model 154, W-column) indicated the presence in the crystals of methanol of crystallization.

Anal. Calcd. for $C_7H_{10}O_7NNa \cdot {}^1/_2CH_3OH$ (259.2): C, 34.80; H, 4.65; Na, 8.90. Found: C, 35.22; H, 4.99; Na, 8.96.

The infrared spectrum of IIb differed markedly from that of IIa, especially in the regions of 1550–1570, 1325–1350, 1130, and 900–700 cm.$^{-1}$.

In a number of otherwise identical experiments we did not wait for the slow formation of a second crop of IIa nor for the crystallization of IIb. Rather, the reaction solution upon collection of the first crop of IIa (*i.e.*, about 17 hr. after the start of the nitromethane condensation) was immediately worked up to give mixed salt fractions of generally similar however varying size and composition. These fractions are referred to as **salt IIm**. The following description is typical.

The combined filtrate and washings obtained upon collection of the first crop of crystals (IIa) was evaporated to dryness and the solid residue triturated with approximately 50 ml. of a mixture of methanol and ethanol (2:1). Insoluble matter was filtered off and washed with the same solvents. Its dry weight was 4.64 g.; $[\alpha]^{23}D$ −51.9° → −76.2° (final). From the filtrate another crop was precipitated by the addition of excess ethanol; 2.07 g., $[\alpha]D$ −69.2° → −82.0° (final). The filtrate from this precipitate was brought to dryness and the residue of evaporation then triturated with a little ethanol. The major part remained undissolved and was isolated and washed with ethanol; 3.05 g., $[\alpha]^{23}D$ −14.8° → −65.7° (final). The ethanolic extract and washings were finally evaporated yielding 0.47 g. of a solid, $[\alpha]^{23}D$ +2° → −22.4° (final). The combined yield of these fractions IIm was 10.23 g. When added to the 1.65 g. of previously separated IIa the total yield in sodium salts II was 97% based upon the starting sedoheptulosan hydrate. The sodium contents of the fractions of IIm from this and similar experiments were found to be 8.4, 8.1, 8.4, 8.6, 8.5, 8.5, 8.7, 8.0%.

2,7-Anhydro-4-nitro-4-deoxy-β-D-heptulopyranoses (III). A. From the Sodium Salts (II).—One part of a salt II was generally dissolved in 50 parts of ice-cold water and at once stirred for 10 min. with a cation-exchange resin (22 ml. of Amberlite IR-120 [H^+] per gram of II). The resin was filtered off, washed exhaustively with water, and the filtrate evaporated to dryness, finally with the addition of two consecutive portions of ethanol. Colorless crystalline residues of III were thus obtained.

Nitrodeoxyheptulosan IIIa.—The product obtained from 1.60 g. of salt IIa was triturated with a little ethyl acetate and after short standing at 0° collected on a Büchner funnel and washed with cold ethyl acetate. The yield of crude IIIa was 640 mg., with m.p. 167° dec. and $[\alpha]^{23}D$ −55.8°. Another 32 mg. crystallized from the mother liquor upon storage at 4°. Two recrystallizations from boiling ethanol with the addition of a few drops of water gave beautiful needles that melted at 173.5° and showed $[\alpha]^{23}D$ −60°. The highest melting point observed was 176°.[12]

Anal. Calcd. for $C_7H_{11}O_7N$ (221.2): C, 38.01; H, 5.01; N, 6.33. Found: C, 38.67; H, 5.28; N, 6.52.

Nitrodeoxyheptulosan IIIb.—The product obtained from 1.50 g. of salt IIIb was triturated with a small amount of ice-cold ethanol. After 1.5 hr., 990 mg. of platelets showing $[\alpha]^{23}D$ +67.9° and m.p. 202° dec. were isolated; from the filtrate additional crops amounting to 164 mg. and melting at 197–199° were obtained. Total yield, 85%. The product was proved by its infrared spectrum and R_f value to be identical with IIIb described under B.

All the inhomogeneous fractions of salt IIm were deionized in the same manner and invariably yielded crystalline dextrorotatory IIIb amounting to 10–20% of the products of deionization, while the bulk of these products consisted of strongly levorotatory sirups. Although it was possible to obtain from the sirups impure crystals of **nitrodeoxyheptulosan IIIc** amounting to 14–22% (m.p. 143–145°, $[\alpha]^{23}D$ −125°; −137.5°), it was more satisfactory for the preparation of this isomer to use method B. The sirups, however, could be utilized in hydrogenation experiments whereby they afforded crystalline aminodeoxyheptulosan IVc as described later.

(12) Material with virtually the same rotation but with m.p. 176° was obtained in separate experiments. In general it was difficult to raise the melting point of samples of IIIa by recrystallization because of the instability of the compound in hydroxylic solvents. Thus, the material invariably gave streaking spots on paper chromatograms, and crystals recovered from aqueous optical rotation solutions melted 8–10° lower than before. When a sample was refluxed in propanol for 2 hr., a complete transformation resulted as demonstrated by hydrogenation followed by paper chromatography, which showed predominantly a new amine (R_{gm} 1.20) and no IVa (R_{gm} 1.04). In the preparation of IIIa from IIa the mother liquor was similarly shown to contain a product giving rise to the unknown amine (R_{gm} 1.20).

B. By Nitromethane Condensation in Aqueous Solution.—Sirupy dialdehyde I (0.05 mole) was dissolved in 50 ml. of water containing 3 drops of phenolphthalein indicator. The solution was carefully adjusted with *N* sodium hydroxide to the point of a slight pink coloration remaining for at least 1 min.; about 4 ml. of the base was required. Under swirling in an ice bath 2.7 ml. of nitromethane was now added at once and 50 ml. of *N* sodium hydroxide was dropped in over a period of 10 min. The stoppered reaction vessel was allowed to stand at room temperature for 17 hr. The slightly yellow solution was then chilled again with ice, stirred vigorously with 70 ml. of Amberlite IR-120 (H^+) for 15 min., filtered, and, after exhaustive washing with water of the resin, decolorized with activated charcoal. The colorless solution afforded a sirupy mixture of nitrodeoxyheptulosans III by evaporation and dehydration with ethanol.

Nitrodeoxyheptulosan IIIb.—The above sirupy residue was dissolved in 20 ml. of warm ethyl acetate with the addition of a small amount of ethanol. Upon keeping the solution overnight at 4° crystallization occurred and 1.62 g. of crude IIIb was isolated and washed with ethyl acetate. After three recrystallizations from ethanol the melting point and rotation of the colorless platelets were constant; m.p. 203.5°, $[\alpha]^{23}D$ +69.5°; R_f 0.58.

Anal. Calcd. for $C_7H_{11}O_7N$ (221.2): C, 38.01; H, 5.01; N, 6.33. Found: C, 38.72; H, 5.20; N, 6.52.

Further crops of IIIb were obtained pursuant to the isolation of IIIc described in the next paragraph.

Nitrodeoxyheptulosan IIIc.—After the isolation of the above crude IIIb the ethyl acetate mother liquor upon addition of excess ether furnished an amorphous precipitate which was filtered off, washed with ether, and dried. It weighed 3.3 g. and showed $[\alpha]D$ −125.5°. This product was dissolved in warm ethyl acetate containing a little methanol and placed in an open beaker. Evaporation in the air gave, after 2 days, a crystal-containing sirup from which by trituration with ethanol 1.22 g. of crystalline IIIc, m.p. 153°, $[\alpha]^{23}D$ −175.0°, could be isolated. Recrystallization from ethanol afforded 0.88 g. of the pure IIIc in oblong prisms of m.p. 159° and $[\alpha]^{23}D$ −176.5°; R_f 0.52.

Anal. Calcd. for $C_7H_{11}O_7N$ (221.2): C, 38.01; H, 5.01; N, 6.33. Found: C, 38.51; H, 5.24; N, 6.26.

The mother liquor of the ether precipitate was allowed to evaporate in the air to give a crystal-containing sirup. Trituration with ethyl acetate and methyl acetate furnished 710 mg. of crystals with a m.p. of 146° and $[\alpha]^{23}D$ −94°. Additional crops (160 mg. of m.p. 147° and $[\alpha]^{23}D$ −158°, and 560 mg. of m.p. 149° and $[\alpha]^{23}D$ −78.5°, respectively) were obtained from the filtrate which had been kept in the refrigerator for several days. These crystalline fractions obviously were mixtures of isomers, with relatively small proportions of the dextrorotatory IIIb being present. A total of 200 mg. of the latter (which is the least soluble) was obtained from these fractions, in fairly but not entirely pure state, by recrystallization from ethanol.

When no additional crystalline material could be obtained from the main mother liquor, the latter was evaporated to a sirup whose dry weight was 1.99 g.; $[\alpha]^{23}D$ −60.3°. The sirup was hydrogenated taking up 3 moles of hydrogen and yielding a sirupy mixture of amine hydrochlorides. Chromatography suggested the presence of the three amino sugars IV described in a following paragraph. Part of the sirup crystallized giving a preparation (640 mg., $[\alpha]D$ −78.6°) which still showed three spots on paper.

Reconversion of IIIc into Its Sodium Salt IIc.—To an ice-cold solution of 93 mg. of nitroheptulosan IIIc in 4 ml. of methanol–ethanol (1:1) 1 molar equiv. of sodium methoxide in methanol was added. The white precipitate of IIc that occurred immediately was isolated and washed with ethanol by centrifugation and was dried in a desiccator. The infrared spectrum was similar to spectra given by IIm fractions but was clearly distinct from those of IIa and IIb. $[\alpha]^{23}D$ −138.5° (1 min.) → −73° (16 hr., final; *c*, 0.5).

2,7-Anhydro-4-amino-4-deoxy-β-D-heptulopyranose Hydrochlorides (IV).—The catalytic hydrogenations of the nitrodeoxyheptulosans III were performed as described in earlier work.[13] A 10% excess over the calculated amount of 1 equiv. of hydrochloric acid was provided, the starting acid concentration being approximately 0.05 *N*. The hydrogen uptake (3 molar equiv.) was usually complete and ceased after 1 to 1.5 hr. if the vessel was agitated vigorously. Evaporation of the hydrogenated

(13) H. H. Baer and H. O. L. Fischer, *J. Am. Chem. Soc.*, **82**, 3709 (1960); H. H. Baer, *Ber.*, **93**, 2865 (1960); *cf.* also ref. 1.

solutions followed by codistillation with ethanol led to the aminodeoxyheptulosans IV.

Aminodeoxyheptulosan IVa.—A 200-mg. sample of nitroheptulosan IIIa (m.p. 173.5) was hydrogenated furnishing a crystalline product, $[\alpha]^{23}D$ −46.7° (*c*, 0.5), which was revealed by paper chromatography to be not uniform. Besides the main spot of R_{gm} 1.03–1.04 there was a weaker spot of R_{gm} 1.20.[14] Recrystallization from the minimum amount of water and a tenfold excess of glacial acetic acid afforded 107 mg. of short prismatic columns which were chromatographically pure IVa; R_{gm} 1.03, $[\alpha]^{23}D$ −54.7°.

Anal. Calcd. for $C_7H_{14}O_5NCl$ (227.7): C, 36.93, H, 6.20; N, 6.15. Found: C, 37.03; H, 6.28; N, 5.94.

Aminodeoxyheptulosan IVb.—Nitrodeoxyheptulosan IIIb (130 mg.) upon hydrogenation yielded 110 mg. of elongated needle-like prisms with square, sometimes sloping, end faces. The product, IVb, was immediately chromatographically uniform (R_{gm} 1.30) and analytically pure; $[\alpha]^{23}D$ +39.0°, unchanged upon recrystallization from water–acetic acid.

Anal. Calcd. for $C_7H_{14}O_5NCl$ (227.7): C, 36.93; H, 6.20; N, 6.15; Cl, 15.57. Found: C, 37.12; H, 6.35; N, 6.00; Cl, 15.48.

In another run 280 mg. of IVa showing $[\alpha]^{23}D$ +37.5 was obtained from 315 mg. of IIIa.

Aminodeoxyheptulosan IVc.—Crystalline nitrodeoxyheptulosan IIIc (442 mg.) was hydrogenated to give 410 mg. of chromatographically uniform IVc (R_{gm} 1.00); $[\alpha]^{23}D$ −124.0°. Recrystallization from water–acetic acid gave fine needles (rapid crystallization) or rectangular prisms and platelets (slow crystallization in the air); $[\alpha]^{23}D$ −126°.

Anal. Calcd. for $C_7H_{14}O_5NCl$ (227.7): C, 36.93; H, 6.20; N, 6.15; Cl, 15.57. Found: C, 36.86; H, 6.23; N, 5.91; Cl, 15.71.

In another run 220 mg. of IVc showing $[\alpha]^{23}D$ −123.5° was obtained from 221 mg. of IIIc.

Aminodeoxyheptulosan IVc was also obtained by the hydrogenation of levorotatory, sirupy nitrodeoxyheptulosan mixtures which originated in deionization of salt IIm (previously described). Thus, 3.76 g. of a sirup ($[\alpha]^{23}D$ −90.5°) was hydrogenated and furnished a slightly yellowish, partly crystalline product which on the chromatogram showed spots of equal strength corresponding to IVb and IVc, and an unidentified faint spot of R_{gm} 1.60. Recrystallization from water–glacial acetic acid afforded 705 mg. of colorless crystals of IVc containing but a trace of IVb; $[\alpha]^{23}D$ −122.0°. The mother liquor of the recrystallization gave another 160 mg. of crystals being mainly IVc ($[\alpha]^{23}D$ −114°), as well as various mixed fractions. Similarly, a nitrodeoxyheptulosan sirup (1.3 g.) stemming from the deionization of another fraction of the salts IIm was hydrogenated to a partly crystalline amine mixture ($[\alpha]D$ −93°) whose chromatographic pattern was the same as that just described. By recrystallization from water–glacial acetic acid, 390 mg. of rather pure IVc ($[\alpha]^{23}D$ −121.5°) was obtained. The mother liquor contained both IVc and IVb; 50 mg. of the former was deposited after 3 days. The infrared spectra of the preparations of IVc obtained *via* the sirupy nitrodeoxyheptulosan mixtures were identical with that of IVc from crystalline IIIc.

The Behavior of the *aci*-Nitro Salt IIb in Aqueous Solution.—Two 120-mg. samples of one preparation of the salt IIb were treated as follows.

Sample (a) was introduced into an ice-cold solution of 5.5 ml. 0.1*N* hydrochloric acid and 50 ml. of water. After 5 min., 5 ml. of Amberlite IR-120 (H^+) was added and the mixture was shaken for 10 min. in order to remove sodium ion. Upon filtration, the acid solution was immediately hydrogenated. Chromatographic inspection of the total residue of evaporation obtained after the hydrogenation indicated the presence of only *one* amine, namely IVb. It crystallized readily.

Sample (b) was dissolved in 30 ml. of carbon dioxide-free water at 23° and allowed to reach a constant specific rotation of −92°. After 18 hr. the solution was deionized with 5 ml. of Amberlite IR-120 (H^+), acidified with 5.5 ml. of 0.1 *N* hydrochloric acid and hydrogenated. Chromatography of the product revealed that it contained at least *two* amines, giving spots of about equal strength at R_{gm} 1.27 and R_{gm} 1.01.

Another sample of IIb was allowed to mutarotate in aqueous solution to the final $[\alpha]D$-value. By careful evaporation the solute was recovered. Its infrared spectrum was now clearly distinct from that of the starting salt IIb. It was also different from the spectrum of IIa, but it resembled closely those given by the non-uniform salts IIm.

Acknowledgment.—Preliminary experiments to this project were done in 1959 at the Max Planck Institute for Medical Research, Heidelberg, and subsequently at the National Institute of Arthritis and Metabolic Diseases, Bethesda, Md., where the author enjoyed great encouragement from and valuable discussions with Dr. N. K. Richtmyer, who also provided the sedoheptulosan, and Dr. H. G. Fletcher, Jr. A major part of the work was carried out in Ottawa with the skillful technical assistance of Mr. Frank Kienzle. Financial support by the Ontario Research Foundation is gratefully acknowledged.

(14) The occurrence of that spot obviously is connected with the instability of IIIa and the difficulty of preparing it in entirely pure state (*cf.* ref. 12). It might be possible to obtain IVa in better yield and purity by directly hydrogenating an acidified solution of IIa, *i.e.*, without isolating the intermediate nitro compound, IIIa.

Direct Epoxidation of *o*-Chlorobenzylidenemalononitrile with Hypochlorite Ion

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Received October 29, 1962

Hypochlorite ion is a nucleophile toward the electronegatively substituted olefin, *o*-chlorobenzylidenemalononitrile. The product formed with stoichiometric amounts of the reactants is the epoxide (II).

The hydrogen peroxide epoxidation of olefins activated by electron-withdrawing groups such as carbonyl and nitrile is well known.[1–4] The active reagent species is the perhydroxyl anion, which is an extraordinarily powerful nucleophile, as noted by Edwards and Pearson.[5] It would appear that hypochlorite ion, another potent nucleophile,[5] has not found use in direct epoxidation,[6] with the possible exception of a single patent[9] on the epoxidation of acrolein and alkyl-sub-

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(6) In fact, mesityl oxide, which is epoxidized[1] by perhydroxyl ion at pH 11–13, reacts with hypochlorous acid at pH 4.5 to 10 to give the chlorohydrin,[7] and under very alkaline conditions to give 3,3-dimethylacrylic acid through a haloform reaction.[8]

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