4.29 s (3), 4.17 vw, 3.80 s (2), 3.59 vw; benzoate IXc, 11.38 vs (1), 9.83 m, 8.04 w, 7.03 s, 6.56 w, 6.33 w, 5.75 w, 5.34 m, 4.50 s (2), 4.27 m, 3.95 s (3), 3.56 m, 3.29 w, 3.09 w.

Nuclear Magnetic Resonance Spectra.—Spectra were determined on a Varian A-60 n.m.r. spectrometer (Varian Associates, Palo Alto, Calif.). Tetramethylsilane (τ 10.00) was used as internal standard. Deuteration was performed by shaking the prepared sample with 1 drop of deuterium oxide for 30 min.

Acknowledgment.—The authors thank Mr. W. N. Turner for the n.m.r. data. H. El Khadem is indebted to the Educational and Cultural Exchange Program of the Department of State for a Fulbright Grant.

Synthesis of Amino Compounds in the Sugar Series by Reduction of Hydrazine Derivatives. Two Epimeric Pairs of 1,2-Diamino-1,2-dideoxyalditols[1-3]

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Hydrogenation of the hexosulose bis(phenylhydrazones) derived from D-glucose and D-xylose has afforded the two respective epimeric pairs of 1,2-diamino-1,2-dideoxyalditols. The products were isolated as their crystalline bis(salicylaldehyde Schiff base) derivatives. Structural identification of the former pair was effected by comparison with authentic samples, that of the latter by identification with the hydrogenation product of 2-amino-2-deoxy-D-lyxose phenylhydrazone, and that of 2-amino-2-deoxy-D-lyxose oxime hydrochloride. The dihydrohalide salts of three of the bases were characterized.

In earlier work reported from this laboratory,[4] 1,2-diamino-1,2-dideoxy-D-mannitol (**3**) was isolated from the reduction products of D-*arabino*-hexosulose bis(phenylhydrazone), "D-glucosazone" (**1**), as its crystalline bis(salicylaldehyde Schiff base) derivative. The yield, however, was quite low and it was postulated that the chelation of the osazone function[5-8] may have been responsible. Work by Mester[9] has indicated that 2 *N* ethanolic potassium hydroxide is required before "D-glucosazone" will undergo the formazan reaction. The diazo coupling fails in pyridine. Mester concluded that the strongly basic medium opened the chelate ring (**1**) and permitted the osazone to exhibit the anticipated chemical behavior.

Applying Mester's conditions to the hydrogenation of D-*arabino*-hexosulose bis(phenylhydrazone) and using Raney nickel as catalyst, we have found that the yield of 1,2-diamino-1,2-dideoxy-D-mannitol as its bis(salicylaldehyde Schiff base) is considerably improved, and in addition, an essentially equivalent amount of the epimeric 1,2-diamino-1,2-dideoxy-D-glucitol (**2**) is obtained as its bis(salicylidene) derivative, previously prepared only by reduction of the oxime of 2-amino-2-deoxy-D-glucose. The epimeric Schiff bases were identified by comparison with authentic samples.[4,10] Separation of the isomers could be effected by fractional recrystallization from 95% ethanol. The isomeric composition was determined by comparison of the optical rotation and optical rotatory dispersion curves of the crude product mixture with those of the pure epimers. The precision of the measurements was decreased in the former experiment by the color of the dissolved reaction mixture and in the latter by the ultraviolet absorption of the Schiff bases which necessitated the use of very dilute solutions with the accompanying decrease in the differences of observed optical rotation (Figure 1). However, both methods indicated approximately equimolar amounts of the two isomers.

The Schiff bases were hydrolyzed with dilute mineral acids to the corresponding amine salts.

D-*threo*-Pentosulose bis(phenylhydrazone), from D-xylose, was similarly hydrogenated and again two isomeric diaminoalditols were isolated as their bis(salicylidene) derivatives. Separation was effected by fractional recrystallization. Structural identification was achieved by a procedure analogous to that used previously.[4] 2-Amino-2-deoxy-D-lyxose hydrochloride was treated with phenylhydrazine and heated to initial formation of the osazone. After removal of the osazone, the reaction mixture, containing the phenylhydrazone (**4**) of the amino sugar, was hydrogenated. The product (**5**), isolated as its bis(salicylaldehyde Schiff base), was shown to be identical with the higher melting isomeric Schiff base from the osazone reduction. Hydrogenation of 2-amino-2-deoxy-D-lyxose oxime (**6**) hydrochloride gave the same results. Therefore, the higher melting product was 1,2-dideoxy-1,2-bis(salicylideneamino)-D-lyxitol and the low-melting isomer must be the epimeric 1,2-dideoxy-1,2-bis(salicylideneamino)-D-xylitol. The isomeric composition was determined by the optical rotatory dispersion procedure and again the crude reaction mixture was found to contain essentially equivalent amounts of the two epimers (Figure 2).

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[2] Preliminary communication: Abstracts, 147th National Meeting of the American Chemical Society, Philadelphia, Pa., April 1964, p. 14C.

[3] Previous publication on this subject: M. L. Wolfrom, J. Bernsmann, and D. Horton, *J. Org. Chem.*, **27**, 4505 (1962).

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[8] M. L. Wolfrom, G. Fraenkel, D. R. Lineback, and F. Komitsky, Jr., *J. Org. Chem.*, **29**, 457 (1964).

[9] L. Mester, *J. Am. Chem. Soc.*, **77**, 4301 (1955).

[10] These compounds have recently been obtained by the alternate route of reduction of D-*arabino*-hexosulose 1-(*N*-methylphenylhydrazone) 2-oxime for the 1,2-diamino-1,2-dideoxy-D-mannitol derivative and by a modification of our procedure[4] for the epimeric 1,2-diamino-1,2-dideoxy-D-glucitol derivative: G. Henseke and R. Neinass, *Ber.*, **97**, 733 (1964).

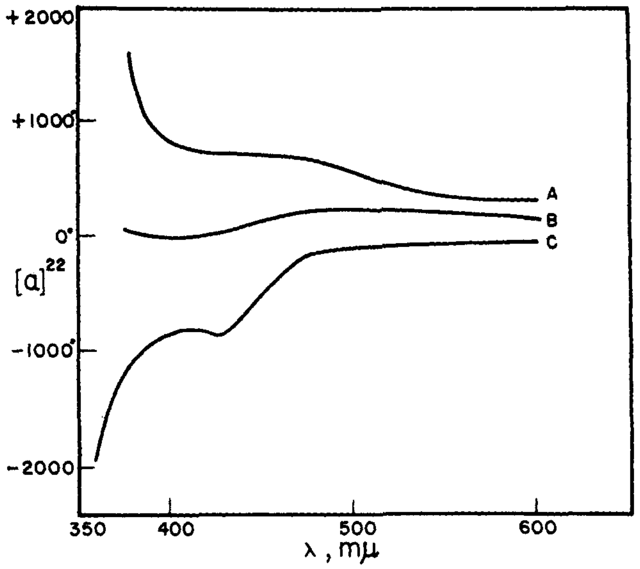


Figure 1.—Optical rotatory dispersion of 1,2-dideoxy-1,2-bis-(salicylideneamino)-D-mannitol (A), reaction mixture (B), and 1,2-dideoxy-1,2-bis(salicylideneamino)-D-glucitol (C).

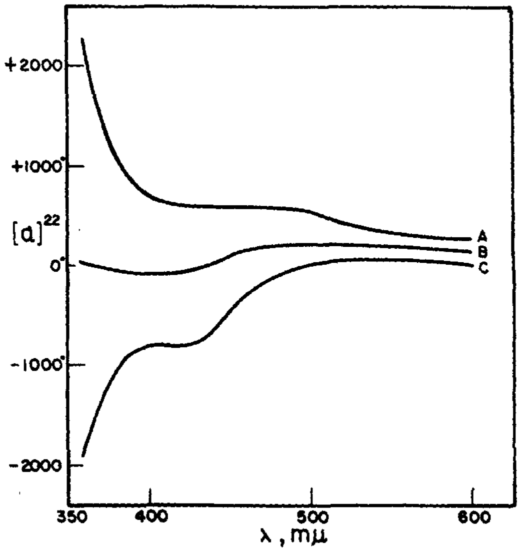


Figure 2.—Optical rotatory dispersion of 1,2-dideoxy-1,2-bis-(salicylideneamino)-D-lyxitol (A), reaction mixture (B), and 1,2-dideoxy-1,2-bis(salicylideneamino)-D-xylitol (C).

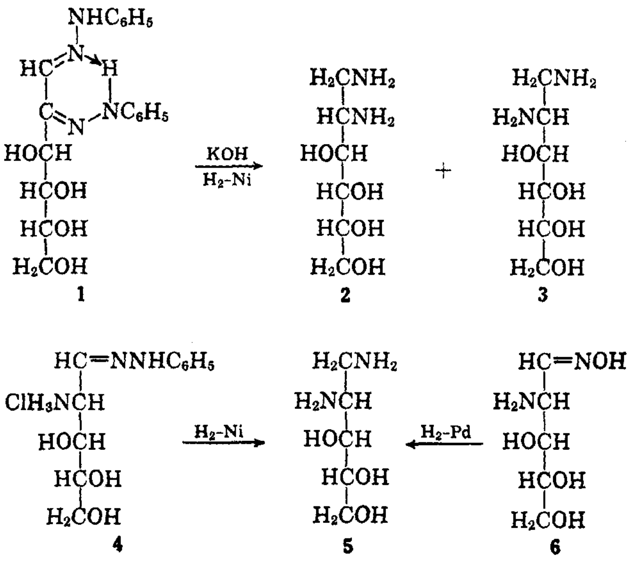
Comparison of the optical rotatory properties of the four diaminoalditol bis(Schiff bases) supports the structural assignments. The similarity of the optical rotatory dispersion curves of the 1,2-diamino-1,2-dideoxy-D-glucitol bis(salicylidene Schiff base) and the 1,2-diamino-1,2-dideoxy-D-xylitol bis(salicylidene Schiff base) (Figures 1 and 2, curves C) and of the bis(salicylidene Schiff bases) assigned the D-mannitol (Figure 1, curve A) and D-lyxitol (Figure 2, curve A) configurations complies with their stereochemical relationships.

TABLE I

OPTICAL ROTATIONS OF 1,2-DIDEOXY-1,2-BIS(SALICYLIDENEAMINO)ALDITOLS

Alditol derivative	$[\alpha]_D$[a]	Ref.
D-Glucitol	−83°	b
D-Xylitol	−106	This work
D-Mannitol	+54	b
D-Lyxitol	+31	This work

[a] In N,N-dimethylformamide (c 1–4), 20 to 23°. [b] See ref. 4.



The optical rotations at the sodium D-line in N,N-dimethylformamide show a similar correspondence (Table I).

Hydrolysis of the bis(Schiff base) of 1,2-diamino-1,2-dideoxy-D-lyxitol gave the crystalline diamine salt. The 1,2-diamino-1,2-dideoxy-D-xylitol diamine salt has not been crystallized.

Experimental[11]

Hydrogenation of D-*arabino*-Hexosulose Bis(phenylhydrazone).—A solution of 3.50 g. of D-*arabino*-hexosulose bis(phenylhydrazone) (1) in 90 ml. of 2 N ethanolic potassium hydroxide was hydrogenated for 10–16 hr. at room temperature and 3-atm. pressure in the Parr[12] apparatus using Raney nickel[13] as catalyst. The reaction mixture was filtered, neutralized with cold hydrochloric acid, concentrated to 15–20 ml., diluted with water, cooled, and filtered with Celite.[14] The filtrate was extracted with benzene, decolorized, and treated with 2 g. of sodium hydrogen carbonate. A 2.5-ml. quantity of salicylaldehyde was added portionwise at room temperature to the mechanically stirred solution. After 3 hr. the mixture was cooled, the product was collected, washed well with ice water, and dried, and the excess aldehyde was removed by washing with a 50% mixture of ether in petroleum ether; the yield was variable (54–82%).

Fractional crystallization from 95% ethanol gave two products, yellow in color. The less soluble Schiff base, 35% of the crude mixture, m.p. 221–221.5°, was identical with authentic[4] 1,2-dideoxy-1,2-bis(salicylideneamino)-D-mannitol by comparison of melting points, mixture melting points, infrared spectra, optical rotation, and X-ray powder diffraction patterns. The more soluble product, m.p. 206–206.5°, 35% of the mixture, was similarly identified as 1,2-dideoxy-1,2-bis(salicylideneamino)-D-glucitol: ultraviolet absorption spectra data[11]: $\lambda_{max}^{95\%\ EtOH}$ 206, 231 (sh), 267, 404 mμ (ϵ_{max} 26,000, 5160, 8290, 1520, respectively).

The isomeric composition of the mixture was determined by measurement of its optical activity, $[\alpha]^{24}_D$ −11 ± 8° (3, 52 ± 6%), and its optical rotatory dispersion curve (Figure 1).[15]

1,2-Diamino-1,2-dideoxy-D-mannitol Dihydrochloride (3·2-HCl).—An aqueous suspension of 1,2-dideoxy-1,2-bis(salicyl-

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[11] Melting points are corrected except where noted. X-Ray powder diffraction data refer to interplanar spacing in Å. with Cu Kα radiation. Relative intensities were estimated visually: s, strong; m, medium; w, weak; v, very. The first three strongest lines are numbered (1, strongest); multiple numbers indicate approximately equal intensities. The ultraviolet absorption analysis was made on a Cary recording spectrophotometer, Model 10, Applied Physics Corp., Pasadena, Calif. Elemental microanalyses were made by W. N. Rond.

[12] Parr Instrument Co., Moline, Ill.

[13] No. 28 Raney active nickel catalyst in water, Raney Catalyst Co., Chattanooga, Tenn.

[14] No. 535, Johns-Manville Co., New York, N. Y.

[15] The optical rotatory dispersion measurements were made with a Rudolph automatic recording spectropolarimeter, Model No. 260/655/850/810-614, Rudolph Instruments Engineering Co., Little Falls, N. J.

ideneamino)-D-mannitol was hydrolyzed at room temperature with a slight excess of hydrochloric acid. The solution was extracted with ether and concentrated to dryness with absolute ethanol, and the hygroscopic residue was crystallized from ethanol–water: yield 92%; m.p. 184°; $[\alpha]^{21}\mathrm{D}$ −5.0° (*c* 4.18 water); X-ray powder diffraction data[11]: 8.46 w, 5.72 s (1,1), 4.87 vw, 4.44 m (2,2), 4.15 m, 3.90 w, 3.78 m (2,2), 3.64 s (1,1), 3.50 w, 3.12 m, 3.02 vw, 2.92 m.

Anal. Calcd. for $C_6H_{18}Cl_2N_2O_4$: C, 28.47; H, 7.17; Cl, 28.01; N, 11.07. Found: C, 28.64; H, 6.89; Cl, 28.21; N, 11.30.

1,2-Diamino-1,2-dideoxy-D-glucitol Dihydrobromide (2·2-HBr).—1,2-Dideoxy-1,2-bis(salicylideneamino)-D-glucitol was similarly hydrolyzed with hydrobromic acid to give 1,2-diamino-1,2-dideoxy-D-glucitol dihydrobromide as a hygroscopic, amorphous material which crystallized on nucleation with the solid formed when the product of a previous run was allowed to stand in a desiccator over phosphorus pentaoxide: yield 97%; m.p. 146.5–147.5°; $[\alpha]^{22}\mathrm{D}$ +4.0° (*c* 5.06, water); X-ray powder diffraction data[11]: 9.12 w, 6.59 w, 5.94 vw, 5.68 m, 5.34 vw, 4.77 m, 4.59 vw, 3.93 m, 3.70 m, 3.58 vs (1), 3.43 vw, 3.28 s (2), 3.12 m, 3.05 s (3), 2.82 m.

Anal. Calcd. for $C_6H_{18}Br_2N_2O_4$: C, 21.04; H, 5.27; Br, 46.73; N, 8.19. Found: C, 21.25; H, 5.48; Br, 46.38; N, 8.76.

Hydrogenation of D-*threo*-Pentosulose Bis(phenylhydrazone).—A solution of 4.28 g. of D-*threo*-pentosulose bis(phenylhydrazone) in 90 ml. of 2 *N* ethanolic potassium hydroxide was hydrogenated under the previously employed conditions and processed in the above manner to give a binary mixture of salicylaldehyde Schiff bases, yield 2.88 g. (62%). Three recrystallizations from 95% ethanol and once from methanol–water gave a pure compound as hygroscopic yellow crystals: 37% of the mixture; m.p. 140°; $[\alpha]^{22}\mathrm{D}$ −106° (*c* 1.525, N,N-dimethylformamide); X-ray powder diffraction data[11]: 13.60 w, 11.48 s (3), 7.56 vw, 5.79 s (2), 4.75 vs (1), 4.23 m, 4.08 w, 3.87 m, 3.53 m, 3.30 w, 3.01 w.

Anal. Calcd. for $C_{19}H_{22}N_2O_5$: C, 63.67; H, 6.19; N, 7.82. Found: C, 63.45; H, 6.19; N, 7.80.

The mother liquors from the ethanol recrystallizations gave a second product which could be recrystallized as yellow needles from ethyl acetate–petroleum ether (b.p. 30–60°): yield 37% of the mixture; m.p. 187–187.5°; $[\alpha]^{22}\mathrm{D}$ +31° (*c* 1.23, *N*,*N*-dimethylformamide); this substance exhibited dimorphism, indistinguishable by melting point; X-ray powder diffraction data[11]: first form, 15.64 w, 9.31 m, 6.11 vw, 5.73 m, 5.32 w, 5.10 w, 4.95 w, 4.80 vs (1), 4.55 s (2,2), 4.18 s (2,2), 3.93 w, 3.71 s (2,2), 3.52 w, 3.31 s (2,2), 3.30 vw; second form, 8.54 m, 6.48 w, 5.85 vw, 4.98 s (1), 4.81 vw, 4.62 vw, 4.47 m, 4.30 m, 4.09 m (2,2), 3.93 m (3), 3.33 m (2,2).

Anal. Calcd. for $C_{19}H_{22}N_2O_5$: C, 63.67; H, 6.19; N, 7.82. Found: C, 63.83; H, 6.63; N, 7.96.

A comparison of the optical rotatory dispersion curves of the pure compounds and that of the crude reaction mixture indicated that again an approximately equal isomeric composition had been obtained (Figure 2).

Hydrogenation of 2-Amino-2-deoxy-D-lyxose Phenylhydrazone (4).—A 0.500-g. quantity of 2-amino-2-deoxy-D-lyxose hydrochloride[16] was added to a solution of 0.392 g. of phenylhydrazine hydrochloride and 0.588 g. of sodium acetate trihydrate in 10 ml. of water. The mixture was heated for 15 min. over boiling water, cooled, and filtered from the resultant precipitate and the filtrate was hydrogenated for 11 hr. at room temperature and 3 atm. using Raney nickel[13] catalyst. The reaction mixture was filtered from the catalyst, extracted with benzene, treated with 0.5 g. of sodium hydrogen carbonate and 0.6 ml. of salicylaldehyde, and shaken mechanically for 4 hr. The precipitated product (0.336 g.) contained a red material, insoluble in organic solvents, presumably a nickel–Schiff base complex, and an ethyl acetate soluble substance, m.p. 189.5° (uncor.), mixture melting point with the high-melting isomer from the reduction of D-*threo*-pentosulose bis(phenylhydrazone) 189–190° (uncor.). Identity of the two Schiff bases was also shown by comparison of their infrared spectra, X-ray powder diffraction patterns, and optical rotations.

A 0.500-g. sample of 2-amino-2-deoxy-D-lyxose hydrochloride[16] was dissolved in 20 ml. of water, decolorized with carbon, concentrated to a thin sirup, treated with 5 ml. of 0.9 *M* ethanolic hydroxylamine (prepared from an absolute ethanolic solution of the hydrochloride which had been treated with 1 equiv. of sodium and sodium chloride removed by filtration), and left standing at room temperature for 24 hr. The reaction mixture was concentrated to a sirup and dissolved in 20 ml. of methanol, 10% of the solution was set aside, and the remainder was hydrogenated at room temperature using 5% palladium on charcoal as catalyst. The catalyst was removed and washed with methanol–water. The filtrate and washings were concentrated; the sirup was taken up in 20 ml. of water and treated with 0.5 g. of sodium hydrogen carbonate and 0.5 ml. of salicylaldehyde. The product formed on stirring at room temperature: yield, 0.194 g. A portion of this material was recrystallized once from ethyl acetate and once from ethyl acetate–petroleum ether to give a pure product, m.p. 188–188.5°, having physical properties identical with those of the product obtained from hydrogenation of the phenylhydrazone, and the higher melting isomeric Schiff base from the osazone.

The higher melting, epimeric Schiff base is therefore 1,2-dideoxy-1,2-bis(salicylideneamino)-D-lyxitol and the lower melting isomer is 1,2-dideoxy-1,2-bis(salicylideneamino)-D-xylitol.

1,2-Diamino-1,2-dideoxy-D-lyxitol Dihydrochloride (5·2HCl).—Hydrolysis of 1,2-dideoxy-1,2-bis(salicylideneamino)-D-lyxitol with dilute hydrochloric acid followed by ether extraction gave a product which crystallized from ethanol–water: yield 89%; m.p. 152°; $[\alpha]^{24}\mathrm{D}$ −10° (*c* 1.5, water); X-ray powder diffraction data[11]: 7.37 vw, 5.52 w (3), 4.22 s (1), 4.11 vw, 3.93 vw, 3.75 vw, 3.63 vw, 3.52 m (2,2), 3.37 m (2,2), 2.98 vw, 2.92 vw, 2.75 w, 2.66 w.

Anal. Calcd. for $C_5H_{16}Cl_2N_2O_3$: C, 26.91; H, 7.23; Cl, 31.80; N, 12.55. Found: C, 27.20; H, 7.30; Cl, 31.91; N, 12.72.

Acknowledgment.—The assistance of Mr. L. E. Anderson with the optical rotatory dispersion measurements is gratefully acknowledged. The 2-amino-2-deoxy-D-lyxose hydrochloride was prepared by J. Bernsmann and D. Horton.

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