Shaking 2.2 g. of the above product with water for a minute resulted in decomposition with evolution of heat. After standing overnight the product solidified. Recrystallization of 1.9 g. of the product from petroleum ether gave crystals (XXII) melting at 60–61°.

Anal. Found: C, 62.70; H, 6.92; Cl, 17.13. Calcd. for $C_{11}H_{14}ONCl$: C, 62.41; H, 6.68; Cl, 16.77.

B. With Nitrosyl Chloride.—A solution of 2 g. (0.011 mole) of N-benzylisobutyroamide in 6 ml. of benzene was treated with 2.35 g. (0.011 mole) of phosphorus pentachloride at 30–40°. After solution was complete 10.6 g. (0.011 mole) of 7% solution of nitrosyl chloride in carbon tetrachloride was added dropwise. The mixture was maintained at 5–10° for 3.5 hr. with stirring and then poured into ice-water. The carbon tetrachloride layer was washed with sodium bicarbonate and dried. After removal of the carbon tetrachloride, 2.2 g. of oil was obtained. Distillation gave 1.2 g. of product boiling at 120–130° under 3 mm., yield 50.2%. This substance solidified immediately and melted at 56–58°. A mixed m.p. with an authentic sample of XXII was not depressed.

Anal. Found: C, 62.60; H, 6.93; N, 6.46. Calcd. for $C_{11}H_{14}ONCl$: C, 62.41; H, 6.68; N, 6.61.

Reaction of N-Benzyl-N-nitrosopropionamide with Phosphorus Pentachloride.—A mixture of 3.5 g. (0.018 mole) of the nitrosoamide and 3.8 g. (0.018 mole) of phosphorus pentachloride was heated 40–45° for 20 minutes, and then was poured into ice-water. After 30 min. 500 ml. of 0.2% solution of 2,4-dinitrophenylhydrazine in 2 *N* hydrochloric acid was added and the mixture was heated for a few minutes. The crystalline product was collected and washed with water, ether and ethyl acetate to give 0.5 g. of yellow hydrazone, melting at 221–225°, yield 7.7%. Recrystallization from ethyl acetate gave a product melting at 229°.

Anal. Found: C, 54.09; H, 4.21; N, 19.27. Calcd. for $C_{16}H_{15}N_5O_5$: C, 53.78; H, 4.23; N, 19.60.

A suspension of 0.5 g. of the hydrazone in 50 ml. of ethanol was hydrogenated using Raney nickel and 61 kg. per cm.^{2} pressure of hydrogen. The reduced mixture was filtered and evaporated to dryness after acidifying with hydrochloric acid. The residue was treated with 10 ml. of 6 *N* hydrochloric acid and heated at 100° for 3 hr. After evaporating to dryness, the residue was dissolved in a small portion of water and purified with Amberlite. The eluate with 2 *N* acetic acid was decolorized with charcoal, filtered and evaporated to dryness. To the residue was added ethanol and the colorless crystals were separated. This substance was violet in ninhydrin reaction and its R_f of a paper chromatogram eluted with phenol was 0.52, as was that of alanine.

Reaction of the Imidochloride of N-2-Phenylethylacetamide with Nitrosyl Chloride.—To a solution of 1.7 g. (0.010 mole) of the amide was added at 0°, 45 ml. of a solution of 2.2 g. (0.010 mole) of phosphorus pentachloride in carbon tetrachloride. After a few minutes, 9 g. (0.010 mole) of 7.5% solution of nitrosyl chloride in carbon tetrachloride was added and the mixture was stirred at room temperature for 1 hr., then maintained at 45° for additional 1.5 hr. The colorless precipitate was collected, treated with water and 0.8 g. of the starting material was recovered. After washing and drying, carbon tetrachloride was removed from the filtrate and the residue was kept standing for a day. Recrystallization of the residue gave 0.2 g. of II, yield, 10.0%.

A solution of 1 g. (0.0061 mole) of the amide in 3 ml. of phosphorus oxychloride was treated with 1.3 g. (0.0062 mole) of phosphorus pentachloride at 40°. The mixture, when cooled in an ice–salt-bath, absorbed 0.45 g. (0.0069 mole) of nitrosyl chloride. After standing for 40 hr. at room temperature, the mixture was poured into ice-water, and the material which separated was recrystallized from ethanol to give 0.2 g. of II, yield 16.9%.

Reaction of the Nitrosoamide I with Phosphorus Oxychloride or Phosphorus Trichloride.—In 2 ml. (0.022 mole) of phosphorus oxychloride 0.5 g. (0.0026 mole) of I was dissolved. The mixture was heated at 45–50° for 3 hr., and then poured into ice-water. After standing for 2 days, white crystals had separated. The product was collected and recrystallized from ethanol to give 0.4 g. of II, yield 80%.

A mixture of 0.5 g. (0.0026 mole) of I and 0.23 ml. (0.0026 mole) of phosphorus trichloride was maintained at 45–50° for 1 hr. and then poured into ice-water. The crystalline material was collected and washed with ether. From the ether-insoluble product 0.2 g., (yield 36.4%) of I was obtained; the ether-soluble product was *ca.* 30 mg. of X (yield 6%).

[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, UNIVERSITY OF CALIFORNIA, BERKELEY 4, CALIF.]

Cyclizations of Dialdehydes with Nitromethane. VII.[1] Preparation of *neo*-Inosadiamine-1,4[2]

BY FRIEDER W. LICHTENTHALER AND HERMANN O. L. FISCHER[3]

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Cyclization of glyoxal with nitromethane at *p*H 10 yielded 1,4-dideoxy-1,4-dinitro-*neo*-inositol which upon hydrogenation gave the corresponding *neo*-inosadiamine-1,4. Structural assignment was accomplished by means of the proton nuclear magnetic resonance spectra of acetyl derivatives.

Introduction

Interest in the chemistry of the inosamines has been stimulated by their occurrence as a component of certain antibiotics.[4] Neoinosamine-2 has been isolated from hygromycin A,[5,6] while *scylloinosadiamine-1,3* (*streptamine*) occurs as part of the streptomycin molecule. The monoinosamines have been thoroughly investigated and, as a result of this, more than half of the thirty-two theoretically possible isomers have been synthesized and characterized in the last fifteen years. On the other hand, the configuration of only one of the ninety possible stereoisomeric inosadiamines, namely, streptamine, has been elucidated by unequivocal synthesis.[4,7–9] There are, however,

(1) Paper VI in this series: A. C. Richardson and H. O. L. Fischer, *J. Am. Chem. Soc.*, **83**, 1132 (1961).

(2) Presented in part at the Meeting of the American Chemical Society, New York, N. Y., September, 1960.

(3) Deceased, March 9, 1960.

(4) S. J. Angyal and L. Anderson, *Advances in Carbohydrate Chem.*, **14**, 184 (1959).

(5) J. B. Patrick, R. P. Williams, C. W. Waller and B. L. Hutchings, *J. Am. Chem. Soc.*, **78**, 2652 (1956).

(6) R. L. Mann and D. O. Wolf, *ibid.*, **79**, 120 (1957).

(7) M. L. Wolfrom, S. M. Olin and W. F. Polglase, *ibid.*, **72**, 1724 (1950).

(8) H. Straube-Rieke, H. A. Lardy and L. Anderson, *ibid.*, **75**, 694 (1953).

(9) K. Heyns and H. Paulsen, *Ber.*, **89**, 1152 (1956).

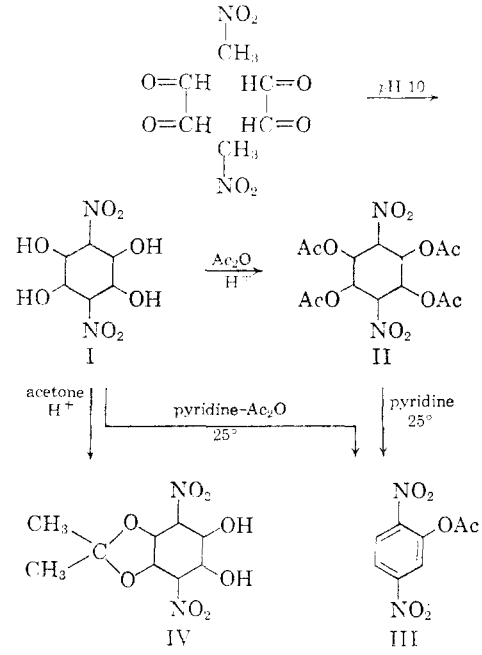
several reports on the preparation of inosadiamines other than streptamine. The cyclization and subsequent reduction of a 6-deoxy-6-nitrohexosamine yielded another *m*-inosadiamine besides streptamine.[7] The hydrogenation of rhodizonic acid 1,4-diimine has been reported to give *p*-inosadiamines, presumably a mixture of isomers.[10] A number of inosadiamines has been obtained by amination of the two available dibromo-dideoxyinositols,[11,12] but because of the probable formation of epoxide intermediates, it is not known with certainty whether the amino groups have the *o*-, *m*- or *p*-arrangement. The problem of assigning the configurations to these inosadiamines, which is complicated by their rather difficult preparation and the numerous diastereomers possible, still remains to be solved.

Our interest in this problem was prompted by the recent development in this Laboratory of a cyclization reaction of dialdehydes with nitromethane.[1,13] By extension of this method to glyoxal, whose tendency to cyclize has been shown in other reactions,[14] we have developed a convenient experimental method for the preparation of *p*-inosadiamines. Furthermore, it could be shown that the application of the proton nuclear magnetic resonance gives one a powerful tool for elucidating configurations of inosamines and inosadiamines.

Results

Glyoxal, in the form of a commercially available 30% aqueous solution, was allowed to react with excess nitromethane at about *p*H 10. A substance soon precipitated from the reaction mixture, and it had, after repeated recrystallization, the composition required for a 1,4-dideoxy-1,4-dinitroinositol (dec. above 260°). The yield, based on the assumption that the glyoxal solution contained only pure monomeric glyoxal, was 10.2% (8.1% of recrystallized material). A determination of the free aldehyde groups under conditions similar to those of the condensation revealed that the 30% glyoxal solution contained only 4.2% of monomeric glyoxal. On this basis, the yield was 72.5%.

Designation of the condensation product as a 1,4-dideoxy-1,4-dinitroinositol was based on elemental analysis, on conversion to a tetra-*O*-acetate (II) thus indicating four hydroxyl groups, and on transformation to a known aromatic compound. By treatment of the tetraacetate II with pyridine–acetic anhydride below 40°, *O*-acetyl-2,5-dinitrophenol (*III*) was immediately formed, thus establishing the cyclic nature of the isolated product. This aromatization is analogous to that of the deoxy-nitro-inositols or their penta-acetates, which yielded the diacetate of 5-nitroresorcinol.[15] In our case, due to the proton-activating effect of *two* nitro groups, the transformation was accomplished under milder conditions.



Attempts were made by means of paper chromatography to obtain information regarding the configurational purity of the isolated dinitroinositol. Whereas nitro sugars are separated easily by paper chromatography, no satisfactory solvent system was found for the 1,4-dinitroinositol. In contrast, chromatograms of the condensation solution, after isolation of I, showed in 1-butanol–acetic acid–water (4:1:5) several spots other than I which remained at the starting line, and the methanolic mother liquor of the recrystallization of I contained at least three compounds other than I.

The acetonation of the 1,4-dideoxy-1,4-dinitroinositol (I) with acetone containing 0.4% sulfuric acid led to a mono-isopropylidene derivative (IV) in 68% yield. This, however, required the repeated acetonation of the unreacted dinitroinositol recovered in yields of 58–65% from the reaction mixture each time. Thus, under these conditions the reaction apparently proceeds only to an equilibrium, consisting of about 60% of the dinitroinositol and 40% of the mono-isopropylidene compound IV. No di-isopropylidene derivative was formed.

Compound IV did not consume any periodate in aqueous methanolic solution in the course of four days. Acetylation could not be accomplished, since under basic conditions dehydration to aromatic products occurred, whereas acid conditions caused hydrolysis of the isopropylidene group. Deacetonation of IV with acetic acid–water at 100° gave a dinitroinositol in 84% yield with prop-

(10) G. Quadbeck and E. Röhm, *Ber.*, **89**, 1645 (1956).

(11) M. L. Wolfrom, F. Radell, R. M. Husband and G. E. McCasland, *J. Am. Chem. Soc.*, **79**, 160 (1957).

(12) A. E. E. Menzel, M. Moore and O. Wintersteiner, *ibid.*, **71**, 1268 (1949).

(13) H. H. Baer and H. O. L. Fischer, *Proc. Nat. Acad. Sci.*, **44**, 991 (1958); *J. Am. Chem. Soc.*, **81**, 5184 (1959); **82**, 3709 (1960); H. H. Baer, *Ber.*, **93**, 2865 (1960); A. C. Richardson and H. O. L. Fischer, *Proc. Chem. Soc.*, 431 (1960).

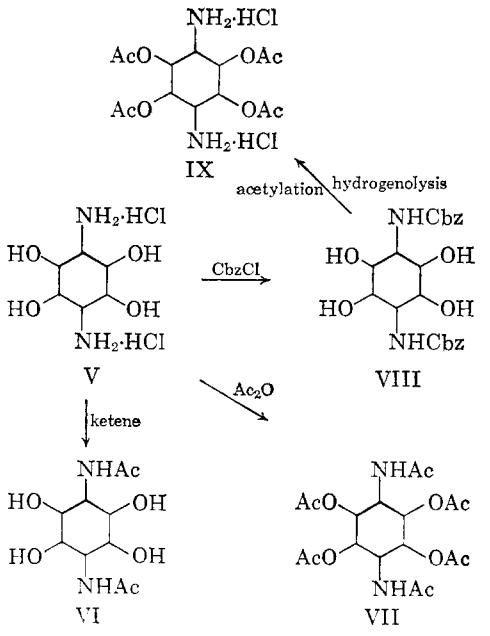
(14) B. Homolka, *Ber.*, **54**, 1393 (1921); R. Kuhn, G. Quadbeck and E. Röhm, *Ann.*, **565**, 1 (1949).

(15) J. M. Grosheintz and H. O. L. Fischer, *J. Am. Chem. Soc.*, **70**, 1479 (1948).

erties slightly different from I (dec. above 265°). A weak infrared absorption at 1660 cm.$^{-1}$ in the spectrum of I, indicative of an ethylenic double bond, was absent in the deacetonated material, suggesting that I is contaminated with traces of a partly dehydrated product.

An attempt was made to prepare the di-*aci*-sodium salt of the dinitro compound I by treatment with the theoretical amount of sodium methoxide. However, a yellow, non-crystalline, hygroscopic mass was obtained in 70–80% yield, whose analysis for C, H, N and Na, was too low for the expected product. Upon acidification of the salt with dilute hydrochloric acid, compound I was reisolated in a yield of 35%. None of the isomeric 1,4-dinitroinositols which might be formed by isomerization during these steps could be isolated. However, a chromatogram of the reaction mixture did indicate three components in addition to I.

The hydrogenation of the dinitro compound I could not be accomplished with platinum as catalyst under various conditions, whereas Raney Nickel T4 catalyst, prepared according to Nishimura,[16] was found to be very effective. When used in dimethylformamide–acetic acid (1:1), the reduction was completed in about four hours, giving a 90% yield of a *p*-inosadiamine dihydrochloride (V). The dinitroinositol, obtained by



deacetonation of the mono-isopropylidene derivative, and a dinitroinositol sample, recovered from acetonation, were also hydrogenated. Both of these compounds as well as V yielded the same *p*-inosadiamine dihydrochloride, as was indicated by the identity of the infrared spectra, the response to periodation and the chromatographic behavior. Consequently, the dinitroinositol obtained by deacetonation of IV has the same configuration as I, indicating that the isolated condensation product I represents a pure single isomer.

(16) S. Nishimura, *Bull. Chem. Soc. Japan*, **32**, 61 (1959).

The purity of the dinitroinositol also was indicated by the excellent yields in which the derivatives of the *p*-inosadiamine were obtained. The free *p*-inosadiamine was prepared from the dihydrochloride V by treatment with the theoretical amount of sodium hydroxide, while addition of sulfuric acid gave the *p*-inosadiamine sulfate. The di-*N*-acetate VI, obtained in quantitative yield from the free inosadiamine by treatment with ketene, had a m.p. of 325–258° dec.; whereas those of the previously reported di-*N*-acetylinosadiamines with unknown configuration are considerably lower.[11,12] The hexaacetate VII did not melt below 370° or show any decomposition. The m.p. reported for the *p*-inosadiamine hexaacetate of Quadbeck and Röhm[10] is 340–355°. Those of the other previously described diaminoinositols, which could possibly have the amino groups in *p*-position, are 146°, 149°,[12] 170–173°, 293–303°,[11] thus indicating that our compound is not identical with any of them.

In order to elucidate the configuration of this inosadiamine, attempts were made to deaminate the *p*-inosadiamine and its tetra-*O*-acetyl-derivative IX to the corresponding inositols, although it is known that this reaction can take place with either inversion or retention of configuration.[1] The deaminations done under conditions used previously[6,17–19] failed to yield identifiable products. The tetra-*O*-acetylinosadiamine dihydrochloride (IX) was prepared in 71% yield *via* carbobenzoxylation, acetylation and subsequent hydrogenolysis. It was essential, however, to conduct the hydrogenolysis in an acidic medium. Otherwise acyl migration occurred due to the basicity of the resulting diamine, as was found in the hydrogenolysis of di-N-carbobenzoxy-tetra-*O*-acetylstreptamine.[17] The latter, hydrogenated with the addition of the theoretical amount of *N* hydrochloric acid, yielded readily tetra-*O*-acetylstreptamine dihydrochloride, m.p. 253–254° (reported[20] 260°). An attempted preparation of the tetra-*O*-acetylinosadiamine *via* the Schiff bases with benzaldehyde and salicylaldehyde, followed by acetylation and subsequent acid hydrolysis was not successful. Thus, the blocking of the amino groups by carbobenzoxylation is to be preferred.

The glyoxal–nitromethane condensation was also studied with glyoxal tetraacetate as starting material, using sodium methoxide as the basic agent, both for deacetylation of the glyoxal tetraacetate and to provide the necessary alkalinity for the condensation. From the reaction mixture, a yellow mass precipitated, being the impure di-*aci*-sodium salt of a 1,4-dinitroinositol. Its infrared spectrum was identical with the di-*aci*-sodium salt obtained from 1,4-dinitroinositol (I). Acidification with *N* hydrochloric acid gave a crystalline substance in a yield of only 4.2%, identical in all its properties with I. The mother liquor

(17) O. Wintersteiner and A. Klingsberg, *J. Am. Chem. Soc.*, **73**, 2917 (1951).

(18) T. Posternak, *Helv. Chim. Acta*, **33**, 1597 (1950).

(19) T. Posternak, W. H. Schopfer and R. Huguenin, *ibid.*, **40**, 1875 (1957).

(20) L. Anderson and H. A. Lardy, *J. Am. Chem. Soc.*, **71**, 1268 (1949).

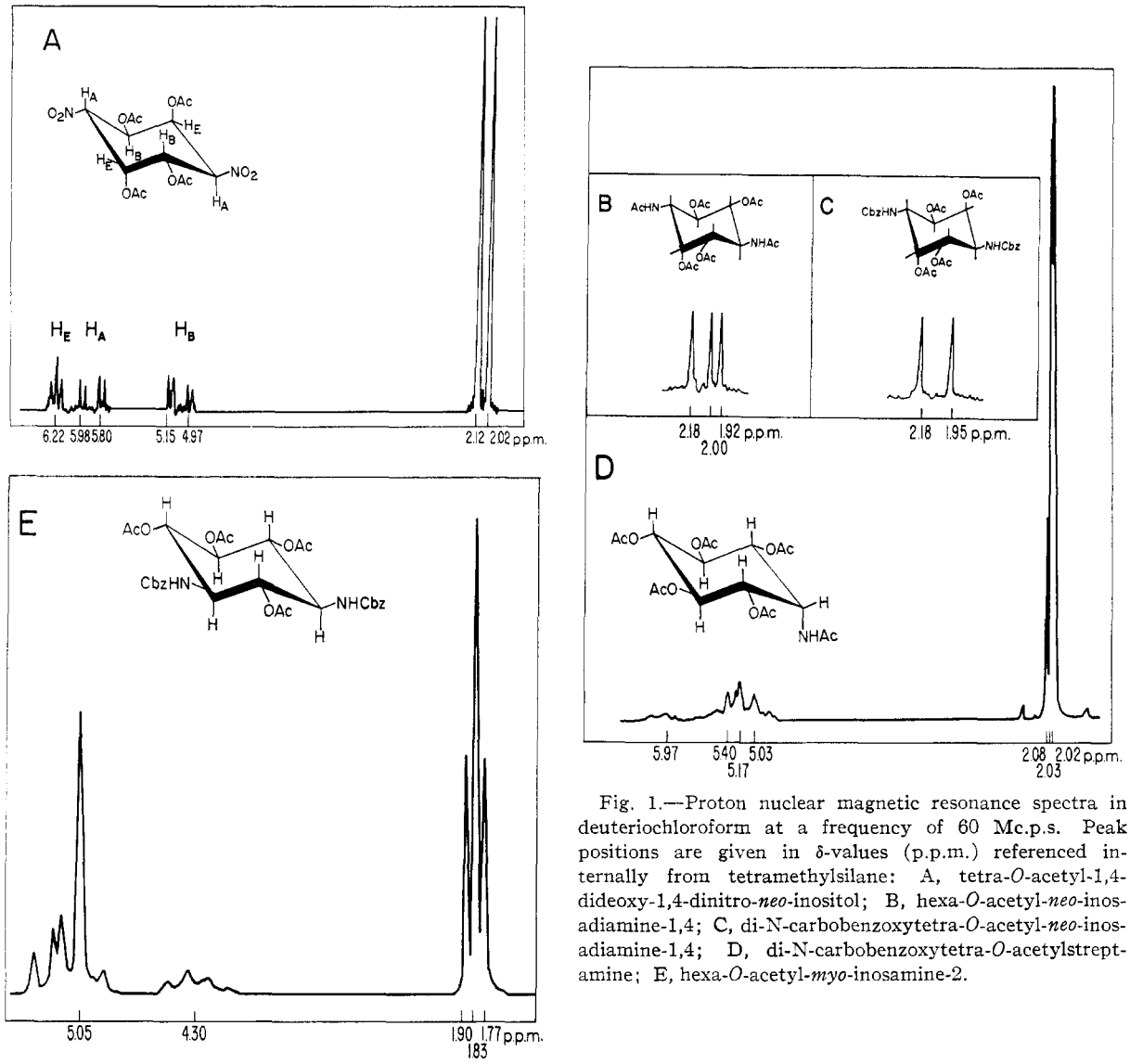


Fig. 1.—Proton nuclear magnetic resonance spectra in deuteriochloroform at a frequency of 60 Mc.p.s. Peak positions are given in δ-values (p.p.m.) referenced internally from tetramethylsilane: A, tetra-*O*-acetyl-1,4-dideoxy-1,4-dinitro-*neo*-inositol; B, hexa-*O*-acetyl-*neo*-inosadiamine-1,4; C, di-N-carbobenzoxytetra-*O*-acetyl-*neo*-inosadiamine-1,4; D, di-N-carbobenzoxytetra-*O*-acetylstreptamine; E, hexa-*O*-acetyl-*myo*-inosamine-2.

apparently contained four isomeric 1,4-dinitroinositols other than I, according to spots on the chromatogram (R_f 0.21, 0.47, 0.74 and 0.8 in butanol–acetic acid–water 4:1:5).

Stereochemical Considerations and N.m.r. Spectra.—In the glyoxal–nitromethane condensation any of the 20 possible isomeric 1,4-dideoxy-1,4-dinitroinositols would be expected. Since the enantiomorphs of the D,L-forms would accumulate as racemates in the course of the reaction, only 14 compounds, 8 *meso* forms and 6 racemates, have to be considered. The fact that the compound obtained forms a mono-*O*-isopropylidene derivative eliminates with certainty the isomers having *trans*-(e,e)- or -(a,a)-hydroxyl pairs on both sides of the ring: namely, the *scyllo*, *myo*-2,5-(D,L), *neo*-2,5, *muco*-1,4 (D,L) and (±)-2,5 (D,L) configurations. From the remaining 9 isomeric compounds, four would be expected to give a mono-*O*-isopropylidene derivative due to a *cis*-(e,a)-hydroxyl pair on one side of the ring (*myo*-1,4, (±)-1,4, *epi*-1,4 and *allo*-2,5; all being D,L-pairs) whereas five should be able to form di-*O*-isopropylidene derivatives (*neo*-1,4, *epi*-3,6, *cis*, *allo*-1,4 and *muco*-3,6; all being *meso* forms).

The formation of the mono-isopropylidene derivative IV from I suggested that the latter had only one pair of *cis*-hydroxyl groups. However, one could expect a considerable amount of steric hindrance from the nitro groups and the failure to form a di-isopropylidene derivative is insufficient evidence to rule out two pairs of *cis*-hydroxyls in I.

The application of the proton nuclear magnetic resonance technique to these compounds, however, has been found to be a powerful tool for establishing configurations. Lemieux, Kullnig, Bernstein and Schneider already have shown on some hexaacetylinositols that the signals of the protons of an axial acetoxy group appear at lower field than those of an equatorial acetoxy group.[21] We have confirmed these observations with a hexaacetylinosamine of known structure, with a streptamine

(21) R. U. Lemieux, R. K. Kullnig, H. J. Bernstein and W. G. Schneider, *J. Am. Chem. Soc.*, **80**, 6098 (1958).

derivative and also with the new compounds described herein.

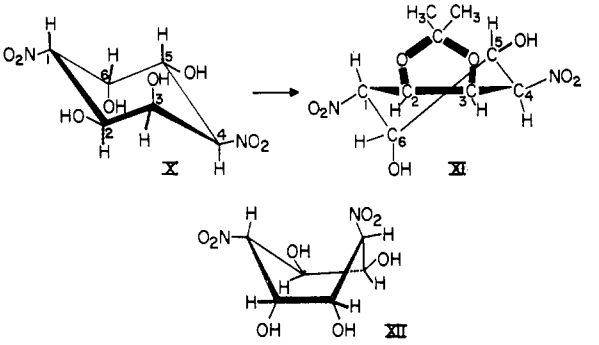
The n.m.r. spectrum of hexaacetyl-*myo*-inosamine-2[22] (Fig. 1, D) reveals three sharp signals of a relative intensity 1:2:3, as expected from the protons of the axial acetamido group (2.08 p.p.m.) and the five equatorial acetoxy groups (2.03 and 2.02 p.p.m.) which are split, since the acetoxy groups at carbon 1 and 3, although equatorial, are not equivalent with those at carbon 4, 5 and 6. The pattern of the ring protons indicates one equatorial proton (around 5.97 p.p.m.) and six protons in the region of 5.0–5.4 p.p.m., originating from the five axial ring hydrogens and the amino hydrogen.

Di-N-carbobenzoxy-tetra-*O*-acetylstreptamine (Fig. 1, E) gave a spectrum with a sharp signal of a 1:2:1 relative intensity, centered around 1.8 p.p.m., which would be expected for the three different kinds of acetoxy groups. The quartet signal centered around 4.30 p.p.m. is from the two protons on the carbons with amino groups. Their large spacing indicates an axial–axial spin coupling to each of the hydrogens on the adjacent carbon and a spin coupling of about the same size to the amino hydrogen, thus explaining the quartet of lines. All other hydrogens, except the aromatic protons, fall into the group of lines around 5.05 p.p.m. No signals appeared around 5.50 p.p.m., revealing that, in full agreement with the configuration assigned to streptamine on the basis of chemical observations, all ring hydrogens are axial.

From the dinitroinositol described above, the tetra-*O*-acetyl derivative was found to be suitable for n.m.r. investigation. Its spectrum (Fig. 1, A) shows a strong, sharp equal intensity doublet in the region of 2.1 p.p.m. originating from the protons of the four acetoxy groups. They are equivalent in pairs, thus indicating that two are in an equatorial and two in an axial position. The six ring-protons fall into three spin–spin multiplet patterns, labeled H_A, H_B and H_E, and are thus also equivalent in pairs. The four equal intensity doublets (H_A and H_B) display a large splitting characteristic of axial–axial spin-coupling and a smaller coupling which must be due to the adjacent equatorial protons. Therefore, H_A and H_B together represent 4 axial protons and H_E two equatorial protons. As a result of this, 13 of the 14 theoretically possible compounds can be eliminated, since only an isomer of *neo*-1,4-configuration can give rise to the observed spin–spin multiplets of the ring hydrogens. The signal of the two equivalent equatorial protons H_E is split by spin–spin interactions with the two adjacent axial protons (H_A and H_E), giving rise to the observed 1:2:1 triplet for H_E. The bands of the two kinds of axial protons in the molecule, H_A, attached to the carbon with the nitro group, and H_B, attached to the carbon with an acetoxy-group, are split into four doublets by the neighboring axial and equatorial protons.

From the n.m.r. spectra of the hexa-*O*-acetyl and the di-N-carbobenzoxytetra-*O*-acetylinosadiamine (Fig. 1, B and C, respectively), only the strong signals of the acetoxy protons could be observed, due to their small solubility in solvents suitable for n.m.r. analysis. Curve B displays three equal intensity signals, to be correlated to the protons of two axial and two equatorial acetoxy groups and two acetamido groups, whereas C shows only the signals of the two kinds of acetoxy protons.[23]

At first thought there seems to be a discrepancy between the configuration assigned on the basis of the n.m.r. analysis (X) and the chemical observations. A 1,4-dinitro-*neo*-inositol having two pairs of *cis*-(e,a)-hydroxyls, might be expected to yield a di-isopropylidene derivative upon acetonation,[24] whereas experimentally only a mono-acetone compound was isolated. However, in order to form one dioxolane ring, the two hydroxyls must become eclipsed, distorting the cyclohexane ring to the half chair conformation (XI). This is possible, as revealed by Courtauld molecular models, with no or only little steric hindrance, thus accounting for the observed formation of a mono-isopropylidene derivative. When one pair of hydroxyls has been acetonated, the second pair can become eclipsed in one of two ways. The cyclohexane ring may assume the all planar conformation, highly improbable because of the required deformation of the bond angles; or it may take the boat form XII with one of the large nitro groups in the (axial)



flagstaff position and the hydrogens and hydroxyl-pairs on each side of the ring in an eclipsed position. This seems energetically improbable, thus accounting for the experimental difficulty of preparing a di-isopropylidene derivative. The n.m.r. spectra and the chemical evidence concerning the conformation are thus compatible.

Experimental

1,4-Dideoxy-1,4-dinitro-*neo*-inositol (I).—Nitromethane (300 ml.) was added to a mixture of 500 ml. of 30% aqueous glyoxal, 1000 ml. of water and 1000 ml. of methanol. The mixture was chilled in ice-water whereafter a solution of 250 g. of sodium carbonate monohydrate was added slowly in the course of 10 minutes with swirling. Scratching the flask with a glass rod soon initiated the separation of a precipitate. The mixture was kept at 5° for 5 hours and the product was filtered off and washed with water until the washings remained colorless. After being dried in a

(22) A sample was kindly provided by Dr. L. Anderson.

(23) The proton nuclear magnetic resonance spectra and their interpretations were done by Mr. L. Johnson and Dr. J. N. Shoolery of Varian Associates, Palo Alto, Calif.

(24) S. J. Angyal and P. T. Gilham, *J. Chem. Soc.*, 3691 (1957).

desiccator over phosphorus pentoxide, the product weighed 23.3 g. Keeping the reaction mixture, which contained the washings of about 400 ml. of water, in the refrigerator overnight resulted in the separation of a second crop (10.1 g.), which was isolated in the same manner. Addition of a solution of 200 g. of sodium carbonate monohydrate in 700 ml. of water to the brown red mother liquor and cooling overnight yielded another 6.0 g.

The total yield at this stage was 39.4 g. (37.8 g. and 36.2 g. in other experiments). Keeping the dark-red mother liquor at 0° for 2 days resulted only in the precipitation of a few crystals, which consisted mostly of sodium carbonate. Acidification with concentrated hydrochloric acid or addition of sodium hydroxide with subsequent acidification after 24 hours did not yield more of the product. Extraction of the mother liquor with ether, drying the ethereal solution with sodium sulfate and subsequent evaporation left a dark-red oil, which could not be crystallized.

Although the combined products (39.4 g.) analyzed correctly, they were recrystallized from 2000 ml. of hot 95% methanol, yielding in total 31.4 g. of long fine needles. In the course of the recrystallization, the yellow mother liquor of the directly precipitated and filtered crystals (25.3 g.) was concentrated to about half of its volume, yielding after heating and subsequent cooling, a second crop (6.1 g.). The substance was dried *in vacuo* at 56° for 5 hours over phosphorus pentoxide and sulfuric acid. The crystals started darkening at 250° and turned black around 275°, but without melting.

Anal. Calcd. for $C_6H_{10}O_8N_2$ (238.16): C, 30.25; H, 4.23; N, 11.76. Found: C, 30.10; H, 4.25; N, 11.81.

The yield of 39.4 g. corresponded to 10.2% (8.1% of recrystallized material) based on the glyoxal used (30 g. in 100 g. solution), with the assumption that it consisted exclusively of pure monomeric material. A determination of the free glyoxal content of the solution as described below, showed that only 4.2% of free glyoxal was present in the solution, a value which is not corrected for the terminal aldehyde groups of polymerized material. The yield based on these results was 72.5%.

Titration of the Aqueous Glyoxal According to Auerbach and Bodländer.[25]—To 1 ml. (1.26 g.) of the 30% aqueous glyoxal[26] was added 50 ml. of 0.1 *N* iodine–potassium iodide and 25 ml. each of 0.2 *N* sodium bicarbonate and 0.2 *N* sodium carbonate solution. The mixture was allowed to stand for 2 hours at room temperature, when the excess iodine was titrated with 0.1 *N* sodium thiosulfate solution, showing that 36.5 ml. of the iodine (corrected by consumption of the blank) were consumed. This corresponds to 0.9125 mmole of glyoxal in 1 ml., or 4.2 g. per 100 g.

Chromatography.—No satisfactory chromatographic separation could be accomplished. Acetone–water combinations yielded long streaks with a spot at the front, as did 1-butanol–pyridine–water and isopropyl alcohol–water mixtures and the Fischer–Dorfel solvent.[27] Use of phenol–water (4:1) and combinations of pyridine–water and 1-butanol–acetic acid–pyridine–water yielded streaked spots on the starting line. On the other hand, the condensation solution after isolation of the crude product (I), showed besides I (spot on the starting line), 6 other components on the chromatogram (1-butanol–acetic acid–water 4:1:5). The methanolic mother liquor from the recrystallization of crude I indicated, besides I, 4 other spots of R_f 0.49, 0.56, 0.68 and 0.73.

Infrared Spectrum.—The product showed the expected absorptions for hydroxyl groups (broad band at 3300 cm.$^{-1}$) and nitro groups (strong peaks at 1510 and 1385 cm.$^{-1}$), but also a weak absorption at 1660 cm.$^{-1}$.

Periodate Behavior.—The compound did not consume any periodate in the course of 4 days in aqueous solution, containing 40% dimethylformamide.

Tetra-*O*-acetyl-1,4-dideoxy-1,4-dinitro-*neo*-inositol (II).—Four grams of dinitroinositol, as obtained above, was added to a mixture of 90 ml. of acetic anhydride and 0.4 ml. of concentrated sulfuric acid. The product dissolved rapidly after heating the mixture at 60°, and immediately the tetraacetate crystallized. After standing for 2 hours at 5°, the precipitate was filtered off, washed with water, dried over phosphorus pentoxide and calcium oxide, yielding 6.15 g. (90%) of white crystals. The mother liquor was added gradually with stirring to 100 ml. of ice-water and a precipitate was filtered off, giving a second crop of 0.3 g.

Anal. Calcd. for $C_{14}H_{18}O_{12}N_2$ (406.3): C, 41.40; H, 4.46; N, 6.90. Found: C, 41.62; H, 4.62; N, 6.98.

The compound had no definite melting point, but decomposed gradually above 250°. It was insoluble in cold methanol, water and acetic acid. It could be recrystallized from hot acetic acid, or better, from a small volume of hot dioxane, from which it crystallized in prisms.

Aromatization of 1,4-Dideoxy-1,4-dinitro-*neo*-inositol.—Dinitroinositol (I) (2.4 g.) was added to a mixture of 8 ml. of pyridine and 8 ml. of acetic anhydride. An exothermic reaction started, changing the color of the reaction mixture to yellow and finally dark-red. The temperature was maintained at 40° by cooling.[28] After 1 hour at room temperature, the solvents were evaporated *in vacuo*, and the brown residue was dissolved in 150 ml. of hot methanol and filtered with a little charcoal. The residue, left after evaporation of the methanol, was extracted repeatedly with ether, and the yellow ethereal solution was evaporated. The yellowish crystals were recrystallized from water–methanol (3:1), yielding 0.59 g. (27.8%) of yellowish needles, m.p. 101–102.5°.

Anal. Calcd. for $C_8H_6O_8N_2$ (226.4): C, 42.47; H, 2.68; N, 12.38. Found: C, 42.70; H, 2.70; N, 12.25.

The infrared spectra given by this product, and by a sample prepared from authentic 2,5-dinitrophenol by acetylation with pyridine and acetic anhydride, were identical. The m.p. of this authentic 2,5-dinitrophenyl acetate was not depressed by admixture with the above product. A slightly better yield of 2,5-dinitrophenyl acetate (32.3%) was obtained when the crude reaction mixture was poured into ice-water, as described above instead of evaporating the solvents.

Aromatization of Tetra-*O*-acetyl-1,4-dideoxy-1,4-dinitro-*neo*-inositol (II).—Two grams of II was dissolved in pyridine (10 ml.). After a short time, an exothermic reaction started and the solution turned yellow and finally dark-red. The temperature of the mixture was not allowed to rise above 40°. After 30 minutes, the solution was poured into ice-water with stirring and the yellow precipitate was filtered off and dried over phosphorus pentoxide and calcium oxide. The yield was 0.47 g. (41.3%) of yellowish 2,5-dinitrophenyl acetate (III), m.p. 100–102°. Two recrystallizations of this product from water–methanol (3:1) raised the m.p. to 102.5–104°.

Anal. Calcd. for $C_8H_6O_6N_2$: C, 42.47; H, 2.68; N, 12.38. Found: C, 42.53; H, 2.73; N, 12.41.

Saponification of III with 2 *N* hydrochloric acid at 100° for 30 minutes and subsequent extraction with ether gave an almost quantitative yield of 2,5-dinitrophenol, m.p. 105.5–106°. Admixture of this product with a recrystallized sample of authentic 2,5-dinitrophenol (m.p. 106.5°) showed no depression of the melting point.

Anal. Calcd. for $C_6H_4O_5N_2$ (184.11): C, 39.15; H, 2.19; N, 15.22. Found: C, 39.30; H, 2.28; N, 15.31.

2,3-*O*-Isopropylidene-1,4-dinitro-*neo*-inositol (IV).—Dinitroinositol (I) (25 g.) was added to 3000 ml. of commercial acetone containing 0.4% of concentrated sulfuric acid. After 36 hours of shaking at 37°, the brownish solution was neutralized by vigorous stirring with Amberlite CG-45, and then was evaporated *in vacuo*. The residue was transferred to an extraction thimble and extracted for 4 hours with ether in a Soxhlet apparatus. The ether-insoluble part (16.2 g., 64.8%) was starting material according to its analysis and infrared spectrum. The ether solution was evaporated *in vacuo* to about 20 ml., and the precipitate was filtered with suction and washed with ice-

(25) F. Auerbach and E. Bodländer, *Angew. Chem.*, **36**, 602 (1923).

(26) From Union Carbide Co. The analytical methods for the determination of the glyoxal content of this solution are based on the rearrangement of glyoxal with excess alkali to the sodium salt of glycolic acid. Thus the glyoxal content (30% w./w.) does not reveal the amount of free monomeric glyoxal present in the solution or at *p*H 10 (*p*H of the nitromethane condensation).

(27) F. G. Fischer and H. Dörfel, *Z. physiol. Chem.*, **301**, 224 (1955).

(28) In an early experiment, the temperature increased to 65–70° yielding a black-red solution, from which the 2,5-dinitrophenyl acetate was difficult to isolate.

cold ether. This treatment yielded 4.1 g. (14.0%) of a mono-isopropylidene derivative IV. Recrystallization from hot water with addition of a little ethanol gave needles, which started turning yellow at 205° and melted at 235° with decomposition.

Anal. Calcd. for $C_9H_{14}N_2O_8$ (278.22): C, 38.85; H, 5.07; N, 10.08. Found: C, 38.61; H, 4.96; N, 10.02.

The recovered dinitroinositol (16.2 g.) was treated again with acetone–0.4% sulfuric acid for 36 hours and worked up as above, yielding a second crop of 6.2 g. (21.2%) of IV, whereas 10.5 g. (64.8%) of the dinitroinositol was recovered. After two further repetitions of the procedure the yields presented in the following table were obtained. The overall yield after four acetonations was 67.8% of IV, whereas 15.4% of the starting material was reisolated.

	2,3-*O*-Isopropylidene derivative IV			1,4-Dinitroinositol(I) recovered		
Acetonation	G.	Yield, %	Total yield, %	G.	Yield, %	Total yield, %
First	4.1	14.0	14.0	16.2	64.8	64.8
Second	6.2	21.2	35.2	10.5	64.8	42.0
Third	4.1	14.0	49.2	6.6	62.8	26.4
Fourth	1.5	19.4	68.6	3.9	59.1	15.6

Chromatography of IV in 1-butanol-acetic acid–water (4:1:5) showed one faint spot of R_f 0.88. The compound did not consume any periodate in water–methanol (3:2) in the course of 4 days.

Deacetonation of 2,3-*O*-Isopropylidene-1,4-dideoxy-1,4-dinitro-*neo*-inositol.—One gram of the mono-isopropylidene compound IV was dissolved in 50 ml. of hot 50% acetic acid–water and refluxed for 20 minutes. When the yellow solution was kept at 4–10° for 5 hours fine, long needles separated. After isolation by filtering and washing with water the yield was 0.75 g. (87.3%). The crystals began to darken at 275°, but showed no apparent melting up to 300°. The infrared spectrum was identical with that of the dinitroinositol obtained directly from the condensation. However, it lacked the weak absorption at 1660 cm.$^{-1}$.

Anal. Calcd. for $C_6H_{10}O_8N_2$ (238.16): C, 30.25; H, 4.23; N, 11.76. Found: C, 30.35; H, 4.34; N, 11.76.

Di-*aci*-sodium Salt of 1,4-Dideoxy-1,4-dinitro-*neo*-inositol.—To a cooled solution of 2.65 g. (11 mmoles) of 1,4-dinitro-neo-inositol (I) in 1000 ml. of absolute methanol, a solution of sodium methoxide, prepared by dissolving 0.51 g. (22 mmoles) of sodium in 50 ml. of methanol, was added. The yellow mixture was stirred for 1 hour with continuous cooling, then evaporated *in vacuo* to a volume of 200 ml., and the slightly yellow precipitate filtered off after addition of 200 ml. of ether. A hygroscopic, amorphous product (2.9 g.) was obtained. However, it was impure, as shown by analysis.

Anal. Calcd. for $C_6H_8N_2O_8Na_2$ (282.13): C, 25.54; H, 2.86; N, 9.93; Na, 16.30. Found: C, 24.31; H, 3.20; N, 8.92; Na, 15.39.

Acidification of the Di-*aci*-sodium Salt.—The impure di-*aci*-sodium salt (500 mg.) obtained as above was treated with 6 ml. of 2 *N* hydrochloric acid. After 2 hours, the precipitate was filtered, washed with water and dried *in vacuo* at 56°, yielding 150 mg. (35.6%) of a dinitroinositol whose m.p., infrared spectrum and other properties were identical with those of I.

Anal. Calcd. for $C_6H_{10}O_8N_2$: C, 30.25; H, 4.23; N, 11.76. Found: C, 30.19; H, 4.31; N, 11.71.

At least 3 isomers other than I could be detected in the mother liquor by paper chromatography; however, no further crystalline products could be isolated.

***neo*-Inosadiamine-1,4 Dihydrochloride (V).**—Twenty grams of dinitroinositol (I) was added to a mixture of 250 ml. of dimethylformamide and 250 ml. of acetic acid, containing 15 g. of nickel T4 catalyst.[16] The mixture was hydrogenated under normal pressure. Within 5 hours the calculated amount of 6 moles was consumed (11.2 l.), after which the catalyst was filtered off. The inosadiamine formed, being insoluble in the solvent mixture, was extracted from the catalyst with 5 *N* hydrochloric acid. Upon addition of ethanol to the extract the inosadiamine dihydrochloride precipitated. After keeping the mixture at 5° overnight, the precipitate was filtered off and washed with ice-cold ethanol, yielding 14.1 g. (58.6%) of white crystals. Evaporation of the solvents of the mother liquor left a greenish residue which was dissolved in the minimum amount of water. After addition of ethanol, the solution gave a second crop of crystals (7.5 g.) raising the yield to 89.6%. The crystals started decomposing at about 280°.

Anal. Calcd. for $C_6H_{14}O_4N_2 \cdot 2HCl \cdot 2H_2O$ (287.15): C, 25.09; H, 7.01; N, 9.76; Cl, 24.68. Found: C, 25.14; H, 7.02; N, 9.59; Cl, 24.53.

Periodate Oxidation.—The compound consumed 3.8 moles of periodate after 40 minutes, 5.6 moles after 5 hours, and reached a constant value of 6.67 moles after 4 days.

Chromatographic Behavior.—Solvents which contained water usually gave spots with considerable streaking. Others mainly consisting of organic liquids gave either no or only very slow movement. Best results were obtained with 1-butanol–ethanol–water (2:1:3), giving one large spot of R_f 0.2 without streaking.

***neo*-Inosadiamine-1,4.**—To 2.0 g. of *neo*-inosadiamine-1,4 dihydrochloride (V) was added 36 ml. of 0.4 *N* sodium hydroxide (2 molar equivalents). After a short time, crystals separated which were isolated after standing for 2 hours at 5° and washed with ethanol. The yield was 1.10 g. (88.7%) after drying over phosphorus pentoxide. A sample recrystallized from hot water began turning brown at 220°, but showed no melting up to 300°.

Anal. Calcd. for $C_6H_{14}N_2O_4$ (178.19): C, 40.45; H, 7.92; N, 15.72. Found: C, 40.38; H, 8.02; N, 15.66.

***neo*-Inosadiamine-1,4 Sulfate.**—A suspension of 100 mg. of *neo*-inosadiamine-1,4 in 10 ml. of water was treated with 5 ml. of 1 *N* sulfuric acid, giving a clear solution. A precipitate, which separated after a short time, and which was increased by addition of ethanol, was filtered off, washed with water–ethanol (1:1) and dried over phosphorus pentoxide. The yield was 120 mg. (73%) of a white substance. Recrystallized from hot water, the compound began decomposing at 290° but showed no melting up to 350°.

Anal. Calcd. for $C_6H_{14}N_2O_4 \cdot H_2SO_4 \cdot H_2O$ (294.29): C, 24.49; H, 6.17; N, 9.52; S, 10.89. Found: C, 24.51; H, 6.23; N, 9.40; S, 10.78.

Di-N-acetyl-*neo*-inosadiamine-1,4 (VI).—Inosadiamine dihydrochloride (1.44 g., 5 mmoles) was dissolved in 50 ml. of water and 50 ml. of ethanol and 1.4 ml. of triethylamine (10 mmoles) were added. Ketene was bubbled into the solution, causing a precipitate to form after a few minutes, which increased slowly. After 1 hour, the reaction mixture had become neutral and the precipitate was filtered off and washed with water and ethanol, yielding the di-N-acetate in quantitative yield. The white crystals started decomposing from 315° on, melting at 325–328° with decomposition. The compound could be recrystallized from hot water and or hot dimethyl sulfoxide. It was insoluble in all other usual organic solvents.

Anal. Calcd. for $C_{10}H_{18}O_6N_2$ (262.26): C, 45.80; H, 6.92; N, 10.68. Found: C, 45.70; H, 6.79; N, 10.56.

Hexaacetyl-*neo*-inosadiamine-1,4 (VII).—Inosadiamine dihydrochloride (1.44 g., 5 mmoles) was refluxed for 3 hours with 100 ml. of acetic anhydride and 1 g. of sodium acetate, after which the hot solution was evaporated to dryness. The residue was treated with water, filtered and washed with water and ethanol, yielding 2.05 g. (95.5%) of a white substance. Recrystallization from water (200 ml.), to which 10% ethanol had been added, yielded 1.85 g. (86%) of the hexaacetate as prisms, which did not melt up to 370°.

Anal. Calcd. for $C_{18}H_{26}N_2O_{10}$ (430.30): C, 50.20; H, 6.09; N, 6.50; acetyl, 60.0. Found: C, 50.16; H, 6.19; N, 6.35; acetyl, 58.0.

Di-N-benzylidene-*neo*-inosadiamine-1,4.—Neo-inosadiamine-1,4 (400 mg.) was refluxed with 15 ml. of benzaldehyde for 6 hours. The yellow precipitate was filtered off after cooling of the solution, yielding 700 mg. (87.7%) of a substance, which melted at 292–294° dec. after sintering.

Anal. Calcd. for $C_{20}H_{22}N_2O_4$ (354.40): C, 67.75; H, 6.26; N, 7.90. Found: C, 67.76; H, 6.34; N, 7.82.

Di-N-benzylidene-tetra-*O*-acetyl-*neo*-inosadiamine-1,4.—Di-N-benzylidene-neo-inosadiamine-1,4 (650 mg.) was suspended in 15 ml. of pyridine and 6 ml. of acetic anhydride. Heating to 70–80° gave a clear solution which was poured into 10 volumes of ice-water after standing for 3 hours. The precipitate was filtered off, washed with water and recrystallized from hot dioxane with the addition of methanol, giving 650 mg. (68%) of colorless irregular plates, m.p. 294–295°.

Anal. Calcd. for $C_{28}H_{30}O_8N_2$ (522.54): C, 64.35; H, 5.79; N, 5.36. Found: C, 63.42; H, 5.90; N, 5.35.

Di-N-salicylidene-*neo*-inosadiamine-1,4.—A suspension of 1 g. of inosadiamine in 400 ml. of ethanol was refluxed for 24 hours after addition of 20 ml. of salicylaldehyde. The solid was filtered off while hot and washed with ethanol, giving 2.0 g. (92.2%) of lemon-yellow plates, m.p. 319–321° dec. after sintering at 310°.

Anal. Calcd. for $C_{20}H_{22}O_6N_2$ (386.40): C, 62.15; H, 5.74; N, 7.25. Found: C, 62.10; H, 5.65; N, 7.19.

Di-N-salicylidene-tetra-*O*-acetyl-*neo*-inosadiamine-1,4.—Two grams of di-N-salicylidene-inosadiamine was acetylated as described for the di-N-benzylidene derivative. A yield of 2.1 g. (59.2%) of colorless crystals was obtained with m.p. 257–259° after sintering.

Anal. Calcd. for $C_{32}H_{34}O_{12}N_2$: C, 60.18; H, 5.37; N, 4.39. Found: C, 59.99; H, 5.43; N, 4.43.

Di-N-carbobenzoxy-*neo*-inosadiamine-1,4 (VIII).—To an ice-cold, mechanically-stirred solution of carbobenzoxy chloride (15 ml., 0.08 mole) in toluene, a solution of inosadiamine dihydrochloride (5.74 g., 0.02 mole) in 60 ml. of water was added dropwise. The reaction was kept alkaline by the simultaneous dropwise addition of *N* sodium hydroxide (120 ml.) at the appropriate rate. After 3 hours, the reaction mixture was allowed to come to room temperature and was then shaken for 12 hours. The crystalline product was filtered off, washed first with dilute hydrochloric acid to remove starting material, then with water and finally with ethanol. After drying, 8.1 g. (87%) was obtained. For analysis, a sample was recrystallized from hot dioxane, yielding tiny needles, m.p. 285–288° dec.

Anal. Calcd. for $C_{22}H_{25}O_8N_2$ (466.5): C, 59.18; H, 5.87; N, 6.27. Found: C, 59.27; H, 6.00; N, 6.31.

Di-N-carbobenzoxy-tetra-*O*-acetyl-*neo*-inosadiamine-1,4.—Dicarbobenzoxy-inosadiamine (7.5 g.), as obtained above, was dissolved in 100 ml. of pyridine and 50 ml. of acetic anhydride by slight heating. On cooling, a precipitate appeared, which was isolated after 12 hours by filtering and washing with water and ethanol yielding 9.25 g. (94%). The analytical sample was recrystallized from chloroform–methanol (1:1), yielding hexagonal plates, m.p. 264–267°.

Anal. Calcd. for $C_{30}H_{24}O_{12}N_2$ (614.6): C, 58.61; H, 5.57; N, 4.56. Found: C, 58.54; H, 5.53; N, 4.61.

Tetra-*O*-acetyl-*neo*-inosadiamine-1,4 Dihydrochloride (IX).—Di-N-carbobenzoxy-tetra-*O*-acetylinosadiamine (7 g., 11.4 mmoles) was suspended in 300 ml. of hot dioxane and added to a prehydrogenated suspension of 1 g. of palladium black in 50 ml. of dioxane, containing 23 ml. of *N* hydrochloric acid (2 molar equivalents), and the same was hydrogenated. After 24 hours, a total of 500 ml. of hydrogen had been absorbed. The reaction mixture was filtered and the residue containing the palladium and the dihydrochloride was washed with water. Addition of ethanol to the aqueous solution resulted in precipitation of colorless crystals. After standing for 3 hours at 5°, the product was isolated by filtration, yielding 4.75 g. (86.6%) with m.p. 293–295° (capillary tube) and 284–285° (microblock).

Anal. Calcd. for $C_{14}H_{22}O_8N_2 \cdot 2HCl$ (419.25): C, 40.25; H, 5.77; N, 6.69; Cl, 16.91. Found: C, 40.15; H, 5.70; N, 6.71; Cl, 16.87.

Tetra-*O*-acetylstreptamine Dihydrochloride.—A solution of 1 g. of di-N-carbobenzoxytetra-*O*-acetylstreptamine (1.63 mmoles) in 100 ml. of dioxane was added to a prehydrogenated suspension of 300 mg. of palladium black in 50 ml. of dioxane, containing 3.25 ml. of *N* hydrochloric acid and the hydrogenation was continued. After 24 hours, the reaction mixture was filtered and the remaining catalyst washed with water. The filtrate was taken to dryness and was dissolved in the minimum amount of water. Upon addition of an ethanol–ether mixture (1:1) crystals separated, yielding 0.6 g. (84%).

Anal. Calcd. for $C_{14}H_{22}O_8N_2 \cdot 2HCl \cdot H_2O$ (437.28): C, 38.45; H, 5.99; N, 6.41; Cl, 16.22. Found: C, 38.50; H, 6.10; N, 6.34; Cl, 16.30.

The compound after being dried 5 hours over phosphorus pentoxide at 56° *in vacuo*, melted with decomposition at 249–250° (in capillary tube, not corr.) and 245–246° without apparent decomposition (Kofler block, not corr.), differing from those reported previously: 260° dec.[20] and darkening at 250° without melting up to 300°.[17]

Condensation of Glyoxal Tetraacetate with Nitromethane. To 26.2 g. (0.1 mole) of glyoxal tetraacetate, dissolved in a mixture of 500 ml. of absolute methanol and 100 ml. of chloroform, 8.1 ml. (0.15 mole) of nitromethane was added and the solution was chilled with ice. Then a sodium methoxide solution, prepared by dissolving 6.9 g. of sodium (0.3 mole) in 200 ml. of absolute methanol, was added dropwise in the course of 30 minutes, while stirring. The solution turned yellow and turbid, and a yellow, flaky substance precipitated. This was filtered off after 1 hour of continuous cooling and stirring. Being hygroscopic, it was washed quickly with consecutive portions of ice-cold ethanol, ethanol–ether and ether. After drying in a desiccator, the first crop weighed 4.45 g. Addition of ether (300 ml.) to the mother liquor and standing overnight at 0–5°, afforded a second crop of 3.4 g., thus raising the yield to 9.85 g. (70%). The material was not obtained in an analytically pure state.

Anal. Calcd. for $C_6H_8N_2O_8Na$ (282.13): C, 25.54; H, 2.86; N, 9.93; Na, 16.30. Found: C, 24.40; H, 3.30; N, 9.17; Na, 15.26.

Acidification of the Di-*aci*-sodium Salt.—Upon treatment of 5 g. (0.02 mole) of the impure di-sodium salt obtained above with *N* hydrochloric acid, crystals separated on scratching and cooling the container. After isolation and recrystallization from methanol, 0.2 g. (4.2%) of a compound identical in all its properties with 1,4-dinitro-1,4-dideoxy-*neo*-inositol (I) was obtained.

Anal. Calcd. for $C_6H_{10}O_8N_2$ (238.16): C, 30.25; H, 4.23; N, 11.76. Found: C, 30.29; H, 4.30; N, 11.70.

The aqueous mother liquor gave an oil upon evaporation, which on the paper chromatogram gave spots of R_f 0.21, 0.47, 0.65 and 0.75 (1-butanol–acetic adid–water 4:1:5)).

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