[CONTRIBUTION FROM THE ORGANIC CHEMICAL RESEARCH SECTION, LEDERLE LABORATORIES, RESEARCH DIVISION, AMERICAN CYANAMID CO.]

# A New Synthesis of Inosamines. The Synthesis of L-*neo*-Inosamine-1 and L-Inosamine-5

BY GEORGE R. ALLEN, JR.

RECEIVED SEPTEMBER 10, 1956

Two new inosamines, L-*neo*-inosamine-1 (IV) and L-inosamine-5 (V), have been prepared by the ammonolysis and hydrolysis of L-1,2-anhydro-3,4;5,6-di-*O*-isopropylidene-*allo*-inositol (I). This represents a new synthesis of inosamines. Structural assignments for these inosamines and certain of their derivatives are discussed.

The most common synthetic method for the preparation of inosamines has been the reduction of an oxime or phenylhydrazone derivative of an inosose. In this manner, *myo*-inosamine-2[1,3-5] and *scyllo*-inosamine[3-5] were obtained from *myo*-inosose-2,[6] and similarly DL-*epi*-inosamine-2[3,7] and DL-*myo*-inosamine-4[8] were obtained from DL-*epi*-inosose-2.[9] Another method, which was used by H. O. L. Fischer and co-workers,[10] involved the cyclization and reduction of 6-deoxy-6-nitro-D-glucose (or L-idose). This procedure is of limited value since a complex mixture of inosamines is obtained. We wish to report the synthesis of two new inosamines, L-*neo*-inosamine-1 and L-inosamine-5, by the reaction of ammonia with L-1,2-anhydro-3,4;5,6-di-*O*-isopropylidene-*allo*-inositol (I).[11,12] This procedure illustrates a new pathway to inosamines.

When compound I was treated with ammoniacal methanol at 100°, there was obtained an 87% yield of a gum, the elemental analysis of which corresponded to that of a di-*O*-isopropylideneinosamine. Since the epoxide ring can react at either the $C_1$- or $C_2$-positions,[13] it seemed probable that this product represented a mixture of L-2,3;4,5-di-*O*-isopropylidene-*neo*-inosamine-1 (II) and 1,2;3,4-di-*O*-isopropylidene-L-inosamine-5 (III). This was demonstrated in the following manner.

Dilute acid hydrolysis of this gum, followed by deionization with Amberlite IRA-400 (OH) resin,[14] gave an aqueous solution of the free bases. Partial concentration of this solution precipitated a crystalline product (A) with a satisfactory analysis for an inosamine ($C_6H_{13}NO_5$) in 30% yield (based on I). The mother liquor was taken to dryness to give a gum which was completely acetylated and then de-*O*-acetylated to yield a crystalline N-acetylinosamine (B). The over-all yield from I of B ($C_8H_{15}NO_6$) was 31%. That this material was not merely the N-acetyl derivative of product A was shown in two ways.

Conversion of inosamine A to the N-acetylinosamine (C) and comparison of this product with B by melting point, specific rotation and infrared spectra showed the two compounds to be different. Furthermore, acid hydrolysis of B gave an amorphous solid with satisfactory analysis for an inosamine. Although this material could not be crystallized, comparison of this inosamine (D) with inosamine A by specific rotation and infrared spectra indicated the two to be different.

The unequivocal assignment of structure to these inosamines and their derivatives was determined as follows. The two possible inosamine structures are IV and V, and the corresponding N-acetyl derivatives are VI and VII. Since only inositols with *cis*-glycols can form isopropylidene derivatives,[15] it would be expected that VI should yield two di-*O*-isopropylidene derivatives whereas VII should give only one such derivative. In fact, treatment of compound C (the N-acetyl derivative of inosamine A) with acetone in the presence of cupric sulfate and ethanesulfonic acid gave two di-*O*-isopropylidene derivatives which must be VIII and IX. The two derivatives were fortuitously separated by crystallization from ether. (Structural assignments for these di-*O*-isopropylidene derivatives will be discussed below.) Compound B (the N-acetyl derivative of inosamine D) gave only one di-*O*-isopropylidene derivative (X). Thus, inosamine A is L-*neo*-inosamine-1 (IV) and inosamine D is L-inosamine-5 (V).

Further confirmation of the structural assignments was obtained as follows. Hydrolysis of VI with aqueous barium hydroxide (2.5 hours on the steam-bath) gave the parent inosamine IV in 88% yield. The same hydrolytic treatment of VII was ineffective, and starting material was recovered to the extent of 82%. Since there is this striking dif-

(1) The system of nomenclature proposed by Fletcher and his associates[2] is used in this paper.

(2) H. G. Fletcher, Jr., L. Anderson and H. A. Lardy, *J. Org. Chem.*, **16**, 1238 (1951).

(3) H. E. Carter, R. K. Clark, Jr., B. Lytle and G. E. McCasland, *J. Biol. Chem.*, **175**, 683 (1948).

(4) L. Anderson and H. A. Lardy, THIS JOURNAL, **72**, 3141 (1950).

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

(6) T. Posternak, *ibid.*, **24**, 1045 (1941).

(7) E. L. May and E. Mosettig, *J. Org. Chem.*, **14**, 1137 (1949).

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

(9) T. Posternak, *Helv. Chim. Acta*, **19**, 1333 (1936).

(10) (a) J. M. Grosheintz and H. O. L. Fischer, THIS JOURNAL, **70**, 1476 (1948); (b) B. Iselin and H. O. L. Fischer, *ibid.*, **70**, 3946 (1948).

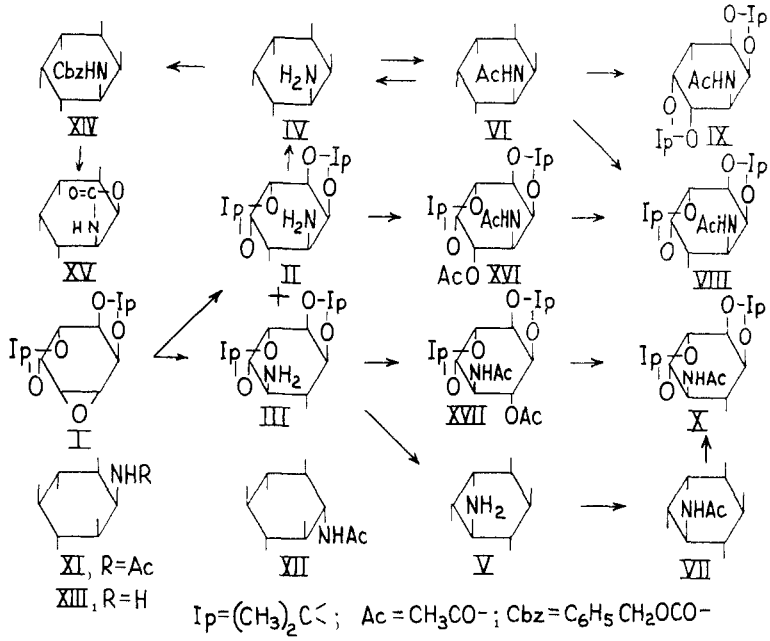
(11) S. J. Angyal and N. K. Matheson, *ibid.*, **77**, 4343 (1955).

(12) The preparation of these inosamines has been reported independently by L. Anderson [Abstracts of the 130th Meeting of the American Chemical Society, Atlantic City, N. J., September, 1956, p. 27D].

(13) S. J. Angyal, *Chemistry & Industry*, 1230 (1954). It is pertinent to point out that *neo*-inositol and L-inositol are formed in almost equal yield when I is treated with dilute sulfuric acid solution.[12]

(14) A synthetic anion exchange resin of the modified amine type produced by Rohm and Haas Co.

(15) S. J. Angyal and C. G. MacDonald, *J. Chem. Soc.*, 686 (1952). There are two known examples of a *trans*-glycol reacting with acetone to form a ketal. However, each involves the formation of a tri-*O*-isopropylideneinositol from a di-*O*-isopropylideneinositol. Angyal and MacDonald have explained the formation of a tri-*O*-isopropylidene derivative as a special situation in which the normal steric hindrance to ketal formation between *trans*-hydroxyl groups is diminished by withdrawal of axial groups from their usual position by prior ketal formation between *cis*-hydroxyl groups.




ference in the behavior toward this alkaline hydrolytic treatment, it is reasonable to presume that this difference results from a facilitation of hydrolysis by neighboring group participation of an adjacent *cis*-hydroxyl group, which is present only in VI.[16,17] Identical behavior toward this barium hydroxide hydrolytic treatment was observed with the known N-acetylinosamines, 2-acetamido-2-deoxy-*myo*-inositol (XI)[3] and 1-acetamido-1-deoxy-*scyllo*-inositol (XII).[3] Compound XI, which has two *cis*-hydroxyl groups adjacent to the acetamido group, gave *myo*-inosamine-2 (XIII)[3-5] in 84% yield. The same treatment of XII, in which neither of the hydroxyl groups adjacent to the acetamido group is *cis*, resulted in a 95% recovery of this material.

Additionally, when IV was treated with carbobenzyloxy chloride, L-1-carbobenzyloxyamino-1-deoxy-*neo*-inositol (XIV) was formed in 66% yield. Treatment of XIV with methanolic sodium methoxide in dimethylformamide gave an amorphous product with a fairly satisfactory analysis for the desired cyclic carbamate XV. That this material contained XV was implied by a comparison of the infrared spectra of XIV and XV. The amide I and amide II bands[20] of the carbobenzyloxy derivative XIV appear at 5.91 and 6.49 $\mu$, respectively, whereas the amide bands of the cyclic carbamate XV appear at 5.74 and 6.28 $\mu$, respectively. This shift to a lower wave length may be considered indicative of the formation of a strained ring system, as in XV. Similar *trans* esterifications of a carbobenzyloxyamino group have been observed previously in the inosamine series[21] and the sugar series.[22]

The specific structures (VIII and IX) of the di-*O*-isopropylidene derivatives of L-1-acetamido-1-deoxy-*neo*-inositol (VI) were determined in the following manner. A mixture of II and III, obtained by the ammonolysis of I, was acetylated to give a mixture of the diacetates XVI and XVII. Alumina chromatography of the diacetates resulted in their partial separation. Catalytic de-*O*-acetylation of the more rapidly eluted substance gave a crystalline compound which could be VIII or X. This compound was identical by melting point, mixed melting point and infrared spectral comparisons with the *ether-soluble* di-*O*-isopropylidene derivative (either VIII or IX) prepared from VI. The only possible common structure is L-1-acetamido-1-deoxy-2,3;4,5-di-*O*-isopropylidene-*neo*-inositol (VIII). Therefore, the *ether-insoluble* derivative obtained by acetonation of VI must be L-1-acetamido-1-deoxy-2,3;4,5-di-*O*-isopropylidene-*neo*-inositol (IX).

The second fraction from the alumina column was catalytically de-*O*-acetylated to give crystalline 5-acetamido-5-deoxy-1,2;3,4-di-*O*-isopropylidene-L-inositol (X). This sample was identical according to melting point, mixture melting point and infrared spectra with that obtained by the acetonation of 5-acetamido-5-deoxy-L-inositol (VII).

**Acknowledgment.**—The author wishes to thank Drs. H. M. Kissman and M. J. Weiss for helpful discussions, and is indebted to Mr. J. Poletto for the large scale preparation of certain intermediates and to Mr. G. W. Drake of The Rubber Research Institute of Malaya, Kuala Lumpur, for a generous grant of quebrachitol. Microanalyses were carried out by Mr. L. Brancone and staff and spectroscopic and polarimetric work by Mr. W. Fulmor and staff.

## Experimental[23]

**Ammonolysis of L-1,2-Anhydro-3,4;5,6-di-*O*-isopropylidene-*allo*-inositol(I).**—A mixture of 5.673 g. (0.0234 mole) of L-1,2-anhydro-3,4;5,6-di-O-isopropylidene-*allo*-inositol (I)[12] and 150 ml. of methanol saturated with ammonia at 5° was heated at 100° in a stainless steel bomb during 88 hours. The contents of the bomb was transferred to a 1000-ml. round-bottom flask. The bomb was rinsed with two 100-ml. portions of methanol, and the washings were combined with the reaction solution. The solution was concentrated to a gummy residue which was triturated with 150 ml. of water. Most of the gum dissolved, but some solid separated from the mixture. This solid was collected by filtration and dried over phosphorus pentoxide to give 0.569 g. (10% recovery) of crude **L-1,2-anhydro-3,4;5,6-di-*O*-isopropylidene-*allo*-inositol (I), m.p. 98–105°.**

The aqueous filtrate was concentrated to an amber gum. This mixture of **L-2,3;4,5-di-*O*-isopropylidene-*neo*-inosamine-1 (II) and 1,2;3,4-di-*O*-isopropylidene-L-inosamine-5**

(16) Similar observations in the sugar series have been reported by Baker and co-workers.[18]

(17) Presumably a neighboring group participation would involve reaction intermediates similar to those postulated for the O → N and N → O acyl migrations which are observed in this series. It may be noted that corresponding to our results these migrations proceed more rapidly in *cis*-1,2-aminocyclohexanol systems.[4,8,19]

(18) B. R. Baker, J. P. Joseph and R. E. Schaub, THIS JOURNAL, **77**, 5905 (1955).

(19) G. E. McCasland, *ibid.*, **73**, 2295 (1951).

(20) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954, pp. 180–192.

(21) J. B. Patrick, R. P. Williams, C. W. Waller and B. L. Hutchings, THIS JOURNAL, **78**, 2652 (1956).

(22) B. R. Baker and J. P. Joseph, *ibid.*, **77**, 15 (1955).

(23) All melting points are uncorrected. Unless otherwise stated all evaporations were carried out under reduced pressure (water-pump) on the steam-bath.

(III) was dried over phosphorus pentoxide to give 5.343 g. (87% yield) of material.

*Anal.* Calcd. for $C_{12}H_{21}NO_5$: C, 55.58; H, 8.16; N, 5.40. Found: C, 55.11; H, 8.39; N, 5.19.

A solution of 5.300 g. (0.020 mole) of the gum in 30 ml. of 0.1 *N* sulfuric acid solution was heated on the steam-bath during three hours. The cooled solution was magnetically stirred during one hour with 24 g. of Amberlite IRA-400 (OH) resin[14] and 100 ml. of water, and the mixture was filtered. The filtrate was treated with Norite and filtered to give a clear solution. The aqueous filtrate was concentrated to a volume of 15 ml. and chilled in an ice-bath. The solid which separated from the solution was collected by filtration and dried *in vacuo* over phosphorus pentoxide to give 1.025 g. of white crystals, m.p. 262–264° dec. A second crop weighing 0.280 g. was obtained by dilution of the filtrate with 15 ml. of acetone. The total yield of **inosamine A** was 30% (based on I). The material was recrystallized from water to give white crystals, m.p. 265–267° dec., $[\alpha]^{25}D$ +8.3° (*c* 1.1, water).

*Anal.* Calcd. for $C_6H_{13}NO_5$: C, 40.22; H, 7.31; N, 7.82. Found: C, 39.95; H, 7.58; N, 7.92.

The mother liquor from the separation of product A was concentrated to dryness. The residue was treated with 0.500 g. of anhydrous sodium acetate in 10 ml. of refluxing acetic anhydride during two hours. The hot mixture was filtered, and the residue was washed with 2 ml. of acetic anhydride. The combined filtrate and washing was taken to dryness; water (10 ml.) was added and then removed in the usual manner. The residue was dissolved in 25 ml. of methanol saturated with ammonia at 5° and allowed to stand at room temperature during 24 hours. The solvent was removed, and the gum was dissolved in the minimum quantity of water. The solution was treated with Norite, filtered and diluted to turbidity with ethanol. The turbid solution was chilled at −5° during 16 hours and filtered to give 1.410 g. (31% yield based on I) of **product B** as white crystals, m.p. 232–234° dec. Recrystallization of the solid from water–ethanol did not alter the melting point behavior; $[\alpha]^{25}D$ −70.4° (*c* 2.0, water).

*Anal.* Calcd. for $C_8H_{15}NO_6$: C, 43.44; H, 6.84; N, 6.33. Found: C, 43.11; H, 7.06; N, 6.11.

In other experiments the yield of the $C_6H_{13}NO_5$ product (A) varied between 23–35% and that of the $C_8H_{15}NO_6$ product (B) varied between 27–36%.

**Preparation of N-Acetylinosamine (C).**—A mixture of 0.380 g. (2.12 mmoles) of inosamine A, 0.300 g. of anhydrous sodium acetate, and 15 ml. of acetic anhydride was allowed to reflux during 2.5 hours. The hot solution was taken to dryness; water (15 ml.) was added and removed in the usual manner. The residue was treated with 25 ml. of water and the mixture was filtered. The solid residue was recrystallized from dilute alcohol to give 0.779 g. (85% yield) of the hexaacetate as white crystals, m.p. 267.5–269.5°, $[\alpha]^{25}D$ −5.1° (*c* 0.98, water).

*Anal.* Calcd. for $C_{18}H_{25}NO_{11}$: C, 50.11; H, 5.84; N, 3.25. Found: C, 50.43; H, 6.21; N, 3.12.

A solution of 0.625 g. (1.45 mmoles) of the hexaacetate in 32 ml. of methanol saturated with ammonia at 5° was allowed to stand at room temperature during four days. The solvent was removed from the mixture. The residue was triturated with 25 ml. of ethanol and filtered to give 0.338 g. (100% yield) of the **N-acetylinosamine (C)** as white crystals, m.p. 266–268° dec. The solid was recrystallized from water–ethanol to give white crystals, m.p. 266–268° (dec.), $[\alpha]^{25}D$ −64.9° (*c* 1.1, water).

*Anal.* Calcd. for $C_8H_{15}NO_6 \cdot {}^1/_2H_2O$: C, 41.73; H, 6.95; N, 6.09. Found: C, 41.75; H, 7.41; N, 6.06.

**Hydrolysis of the N-Acetylinosamine (B).**—A solution of 0.221 g. (1.00 mmole) of the $C_8H_{15}NO_6$ product (B) and 5 ml. of 0.1 *N* sulfuric acid was allowed to reflux during two hours. The cooled solution was stirred with 90 ml. of water and 4.0 g. of Amberlite IRA-400 (OH) resin.[14] The mixture was filtered, and the filtrate was taken to dryness. The residual gum was treated with 10 ml. of ethanol, and the solvent was removed at atmospheric pressure to give 0.137 g. (77% yield) of **inosamine C** as an amorphous solid, $[\alpha]^{25}D$ −60.1° (*c* 0.57, water). All attempts to crystallize this material were unsuccessful.

*Anal.* Calcd. for $C_6H_{13}NO_5$: C, 40.22; H, 7.31; N, 7.82. Found: C, 40.05; H, 7.56; N (Dumas), 5.83, 5.62, (Kjeldahl), 7.32.

**L-1-Acetamido-1-deoxy-2,3;4,5-di-*O*-isopropylidene-*neo*-inositol (VIII) and L-1-Acetamido-1-deoxy-2,3;5,6-di-*O*-isopropylidene-*neo*-inositol (IX).**—A magnetically stirred suspension of 0.338 g. (1.47 mmoles) of the N-acetylinosamine (C) and 1.67 g. of anhydrous cupric sulfate in 22 ml. of acetone was chilled in an ice-bath. This suspension was treated with a previously cooled solution of 1.04 ml. of ethanesulfonic acid in 3 ml. of acetone. The ice-bath was removed, and the mixture was stirred for three hours at room temperature. The mixture was filtered, and the residue was washed with 25 ml. of acetone. The combined filtrate and washing was treated with a solution of 1.80 g. of sodium carbonate in 33 ml. of water. The green solution was concentrated to near dryness, and the residual solid was washed with three 25-ml. portions of chloroform. The combined chloroform washings were dried over magnesium sulfate, and the chloroform was removed to give 0.333 g. of a gum. This material was triturated with 20 ml. of anhydrous ether; a portion of the material crystallized. Filtration of the mixture gave 0.146 g. of white solid, m.p. 198.5–201.0°. The filtrate was diluted with 5 ml. of petroleum ether (b.p. 90–100°) and evaporated at atmospheric pressure until crystals began separating. The mixture was chilled to give 28 mg. of white solid, m.p. 191–200°. A mixture with the material of melting point 198.5–201.0° melted at 191–200°. The combined material was recrystallized from ethyl acetate–petroleum ether (b.p. 90–100°) to give 97.0 mg. (22% yield) of white needles, m.p. 201.5–203.5°, $[\alpha]^{25}D$ −76.1° (*c* 2.0, water).

*Anal.* Calcd. for $C_{14}H_{23}NO_6$: C, 55.80; H, 7.69; N, 4.65. Found: C, 55.59; H, 7.79; N, 4.50.

The filtrate from the separation of the above material was concentrated at atmospheric pressure to about 4-ml. volume and chilled in an ice-bath to give 89.0 mg. of white solid, m.p. 132–135°. This material was recrystallized from petroleum ether (b.p. 90–100°) to give 61.0 mg. (14% yield) of white crystals, m.p. 145–147°, $[\alpha]^{25}D$ −173° (*c* 2.1, water).

*Anal.* Calcd. for $C_{14}H_{23}NO_6$: C, 55.80; H, 7.69; N, 4.65. Found: C, 55.67; H, 7.95; N, 4.68.

**5-Acetamido-5-deoxy-1,2;3,4-di-*O*-isopropylidene-L-inositol (X).**—A suspension of 0.500 g. (2.26 mmoles) of the N-acetylinosamine (B) and 2.48 g. of anhydrous cupric sulfate in 32 ml. of acetone was chilled in an ice-bath during magnetic stirring. A previously chilled solution of 1.54 ml. of ethanesulfonic acid in 5 ml. of acetone was added. The ice-bath was removed, and the mixture was stirred during 17 hours and then filtered. The filtrate was diluted with a solution of 2.2 g. of sodium carbonate in 50 ml. of water, and then concentrated to near dryness. The moist, solid residue was extracted three times with 25-ml. portions of chloroform. The combined pale yellow chloroform extracts were dried over magnesium sulfate, filtered and concentrated to dryness to leave a residual glass. This glass was dissolved in 15 ml. of ether, treated with Norite, and filtered. The filtrate was diluted with 10 ml. of petroleum ether (b.p. 90–100°) and concentrated on the steam-bath at atmospheric pressure until the solution became turbid. Vigorous scratching of the container walls with a glass rod and chilling of the solution gave 0.163 g. (24% yield) of white crystals, m.p. 139–141°. This material was recrystallized from petroleum ether (b.p. 90–100°) to give white crystals, m.p. 141–142°, $[\alpha]^{25}D$ −39.3° (*c* 2.0, water).

*Anal.* Calcd. for $C_{14}H_{23}NO_6$: C, 55.80; H, 7.69; N, 4.65. Found: C, 55.61; H, 7.73; N, 4.91.

**Treatment of Certain N-Acetylinosamines with Barium Hydroxide. A. L-1-Acetamido-1-deoxy-*neo*-inositol (VI).**—A solution of 25.0 mg. (0.11 mmole) of L-1-acetamido-1-deoxy-*neo*-inositol (VI) in 1 ml. of saturated barium hydroxide was heated on the steam-bath 2.5 hours. Water (1 ml.) was added, and the solution was saturated with carbon dioxide. The solid was removed by filtration, and the filtrate was diluted with an approximately equal volume of acetone. After chilling the solution in an ice-bath during 0.5 hour, the solid was collected by filtration to give 18.0 mg. (88% yield) of white solid, m.p. 255–258° dec. A mixture of this material with the starting material melted at 225–236° dec., whereas a mixture with L-*neo*-inosamine-1 (IV) melted at 257–260° dec. The infrared spectra of the product and L-*neo*-inosamine-1 (IV) were identical.

**B. 5-Acetamido-5-deoxy-L-inositol (VII).**—A solution of 50.0 mg. (0.23 mmole) of the 5-acetamido-5-deoxy-L-inositol (VII) in 1.0 ml. of saturated barium hydroxide solution was heated on the steam-bath during 2.5 hours. The solution was diluted with 1 ml. of water and saturated with carbon dioxide. The mixture was filtered, and the residue was washed with 2 ml. of water. The combined aqueous solutions were diluted with 10 ml. of ethanol and chilled at −5°. The mixture was filtered to remove 6 mg. of non-organic solid and the filtrate was taken to dryness. The residue was triturated with 10 ml. of ethanol to give 41.2 mg. (82% recovery) of white solid, m.p. 228–231° dec. alone or when mixed with 5-acetamido-5-deoxy-L-inositol (VII). The infrared spectra of the recovered and starting materials were identical.

**C. 2-Acetamido-2-deoxy-*myo*-inositol (XI).**[3]—A solution of 0.243 g. (1.1 mmoles) of this material in 3 ml. of saturated barium hydroxide solution was heated on the steam-bath two hours. The cooled solution was diluted with 10 ml. of water, saturated with carbon dioxide and filtered. The filtrate was taken to dryness, and the residue was triturated with 3 ml. of water and filtered to give 0.164 g. (84% yield) of ***myo*-inosamine-2 (XIII)**[3-5] as white crystals, m.p. 275–276° dec. after darkening from 230° (reported[5] 278° dec.). A sample mixed with known *myo*-inosamine-2 melted at 275–276° dec. after darkening from 230°. The infrared spectra of the product and known *myo*-inosamine-2 were identical.

**D. 1-Acetamido-1-deoxy-*scyllo*-inositol (XII).**[3]—A solution of 1.000 g. (0.045 mole) of 1-acetamido-1-deoxy-*scyllo*-inositol[3] in 5 ml. of saturated barium hydroxide solution was heated on the steam-bath for two hours. The cooled solution was saturated with carbon dioxide and filtered. The filtrate was diluted with 90 ml. of ethanol to give 0.949 g. (95% recovery) of 1-acetamido-1-deoxy-*scyllo*-inositol (XII), m.p. 284–285° dec. (reported[3] 286–288° dec.) alone or when mixed with an authentic sample. The infrared spectra of the recovery material and the starting material were identical.

**L-1-Carbobenzyloxyamino-1-deoxy-*neo*-inositol (XIV).**—A suspension of 179 mg. (1.00 mmole) of L-*neo*-inosamine-1 (IV) in 4 ml. of water and 3 ml. of 1 *N* sodium hydroxide solution was chilled to 0° during magnetic stirring. A solution of carbobenzyloxy chloride in toluene (1 ml., equivalent to 5.2 mmoles of reagent) was added and all the solid dissolved. After stirring the solution for ten minutes, solid began precipitating. Stirring was discontinued after 30 minutes, and the mixture was shaken with 10 ml. of ether and filtered to given 0.211 g. (68% yield) of white solid. This material was recrystallized twice from water to give white needles, m.p. 235.0–236.5° dec.

*Anal.* Calcd. for $C_{14}H_{19}NO_7 \cdot {}^1/_3H_2O$: C, 52.82; H, 6.23; N, 4.40; $H_2O$, 1.89. Found: C, 53.09; H, 6.07; N, 4.59; $H_2O$ (Karl Fischer), 1.70.

**1,2-Carbonate of L-*neo*-Inosamine-1 (XV).**—A solution of 91.0 mg. (0.29 mmole) of L-1-carbobenzyloxyamino-1-deoxy-*neo*-inosamine-1 (XIV) in 8 ml. of dimethylformamide was treated with 2 ml. of 1 *N* methanolic sodium methoxide on the steam-bath during two hours while protected from the atmosphere by a calcium chloride drying tube. The initial and final *p*H of the solution was approximately 14 to *p*H test paper. The solvents were removed, and the residue was triturated with ethanol to give a solid. Filtration of the mixture gave a solid which transformed to 53 mg. (89% yield) of a gum on exposure to the atmosphere.

*Anal.* Calcd. for $C_7H_{11}NO_6$: C, 40.98; H, 5.41; N, 6.83. Found: C, 40.36; H, 5.70; N, 6.42.

The pertinent details of the infrared spectrum of the crude product are given in the discussion.

**L-1-Acetamido-1-deoxy-2,3;4,5-di-*O*-isopropylideneinositol (VIII) and 5-Acetamido-5-deoxy-1,2;3,4-di-*O*-isopropylidene-L-inositol (X).**—A mixture of 2.120 g. (8.77 mmoles) of L-1,2-anhydro-3,4;5,6-di-*O*-isopropylidene-*allo*-inositol (I) and 50 ml. of methanol saturated with ammonia at 5° was heated on the steam-bath in a stainless steel bomb for 42 hours. The contents of the bomb was transferred to a 250-ml. round-bottom flask, and the methanol was removed to give an amber gum. This gum was triturated with 50 ml. of water and filtered to remove some solid material. The aqueous filtrate was taken to dryness to give 1.967 g. (88% yield) of a mixture of **L-2,3,4,5-di-*O*-isopropylidene-*neo*-inosamine-1 (II) and 1,2;3,4-di-*O*-isopropylidene-L-inosamine-5 (III).**

This mixture was treated with 0.500 g. of anhydrous sodium acetate in 25 ml. of refluxing acetic anhydride for one hour. The excess acetic anhydride was removed by concentration, and the residue was dissolved in a mixture of 75 ml. of chloroform and 75 ml. of water. The chloroform solution was separated, dried over magnesium sulfate and taken to dryness to yield an amber gum. The latter was dissolved in 25 ml. of toluene and then taken to dryness in the usual manner to give 2.814 g. of a mixture of the diacetates. The amber gum was dissolved in 7 ml. of benzene and was chromatographed on a column (33.5 × 2.2 cm.) of "neutral" alumina.[24] The column was washed with 350 ml. of benzene, and these washings were discarded. The column was eluted with 1100 ml. of 5% ethyl acetate in benzene; fractions of 50-ml. volume were collected. Fractions 3–9 were combined and afforded, after evaporation, 0.817 g. of amber gum (product A; for further treatment see below). Fractions 10–22 gave, after evaporation, 0.638 g. of white solid (product **B**), m.p. 84–148°. The column was washed further with 450 ml. of 10% ethyl acetate in benzene; 50-ml. fractions were again collected. Fractions 3–9 afforded, after evaporation, 0.432 g. of white solid (product C), m.p. 131–148°.

Product A was treated with 25 mg. of sodium methoxide in 25 ml. of refluxing methanol for 30 minutes. The solution was taken to dryness to give a residue which was triturated with 10 ml. of ether and filtered to give 0.435 g. of white solid, m.p. 133–145°. This material was recrystallized four times from ethyl acetate–petroleum ether (b.p. 90–100°) to give 0.130 g. (5% yield) of white crystals, m.p. 145–147°. A mixture of this material with the ether soluble and lower melting di-*O*-isopropylidene derivative of L-1-acetamido-1-deoxy-*neo*-inositol (see above) melted at 145–147°. The infrared spectra of the two samples of **L-1-acetamido-1-deoxy-2,3;4,5-di-*O*-isopropylidene-*neo*-inositol (VIII)** were identical.

Product C was treated with 25 mg. of sodium methoxide in 25 ml. of refluxing methanol for 30 minutes. The methanol was evaporated, and the residue was dissolved in 15 ml. of ether, treated with Norite, filtered and taken to dryness. The residue was recrystallized twice from petroleum ether to give 0.297 g. (11% yield) of white crystals, m.p. 141–142°. A mixture of this material with a sample of **5-acetamido-5-deoxy-1,2;3,4-di-*O*-isopropylidene-L-inositol (X)** obtained from the acetonation of **5-acetamido-5-deoxy-L-inositol (VII)** melted at 141–142°. The infrared spectra of the samples from the two sources were identical.

Similar treatment of product B from the column gave a mixture of materials which could not be separated by crystallization into the pure components.

PEARL RIVER, NEW YORK

(24) A product of M. Woelm Eschwege with activity grade I.