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Aminocyclitols. XIV. The Synthesis of Streptamine and Actinamine

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Streptamine, actinamine and *scyllo*-inosatriamine-1, 3, 5 have been synthesized from 1, 2, 3, 5-tetra-*O*-acetyl-4, 6-diazido-4, 6-dideoxy-*myo*-inositol. Hydrolysis of this compound gave 5-*O*-acetyl-4, 6-diazido-4, 6-dideoxy-*myo*-inositol, which was a key compound for the synthesis of streptamine and *scyllo*-inosatriamine-1, 3, 5, and 4, 6-diazido-4, 6-dideoxy-*myo*-inositol which was derived to actinamine. PMR spectra were mainly used to establish the configurations of the new compound obtained.

In connection with the previous papers of this series,[1] new synthetic routes to streptamine,[2,3] actinamine[4] and *scyllo*-inosatriamine-1, 3, 5 from the previously described 1, 2, 3, 5-tetra-*O*-acetyl-4, 6-diazido-4, 6-dideoxy-*myo*-inositol (I)[3] have been accomplished in our laboratory.

Streptamine. An attempted de-*O*-acetylation of I in methanolic ammonia at 5°C to hydrolyzed the acetoxy groups on C-1, 2 and 3 led to the formation of 5-*O*-acetyl-4, 6-diazido-4, 6-dideoxy-*myo*-inositol (II) in a yield of 95.4%.

To prove the configuration of II, this compound was methylated with methyl iodide and silver oxide in dimethylformamide to give 5-*O*-acetyl-4, 6-diazido-4, 6-dideoxy-1, 2, 3-tri-*O*-methyl-*myo*-inositol. The configuration of this compound was unequivocally established by its proton magnetic resonance (PMR) spectrum in deuteriochloroform (Fig. 1). The protons of an acetoxy group revealed the sharp signal at τ 7.85 (3H). This fact suggested that there was an axial acetoxy group on C-2 or an equatorial one on C-5. The chemical shift of an axial acetoxy group generally appears at τ 7.78—7.89, and that of an equatorial one at τ 7.94—8.02.[5] But in the present case, there are two azido groups on the neighboring carbon atoms of C-5 and they might shift the signal of an equatorial group on C-5 to a considerably lower field. The protons of equatorial methoxy groups revealed the signal at τ 6.51 (6H) and those

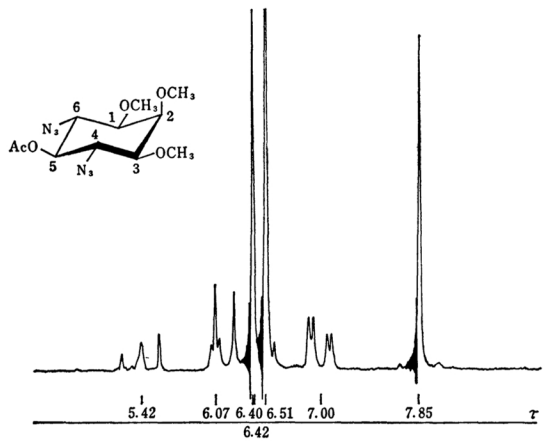


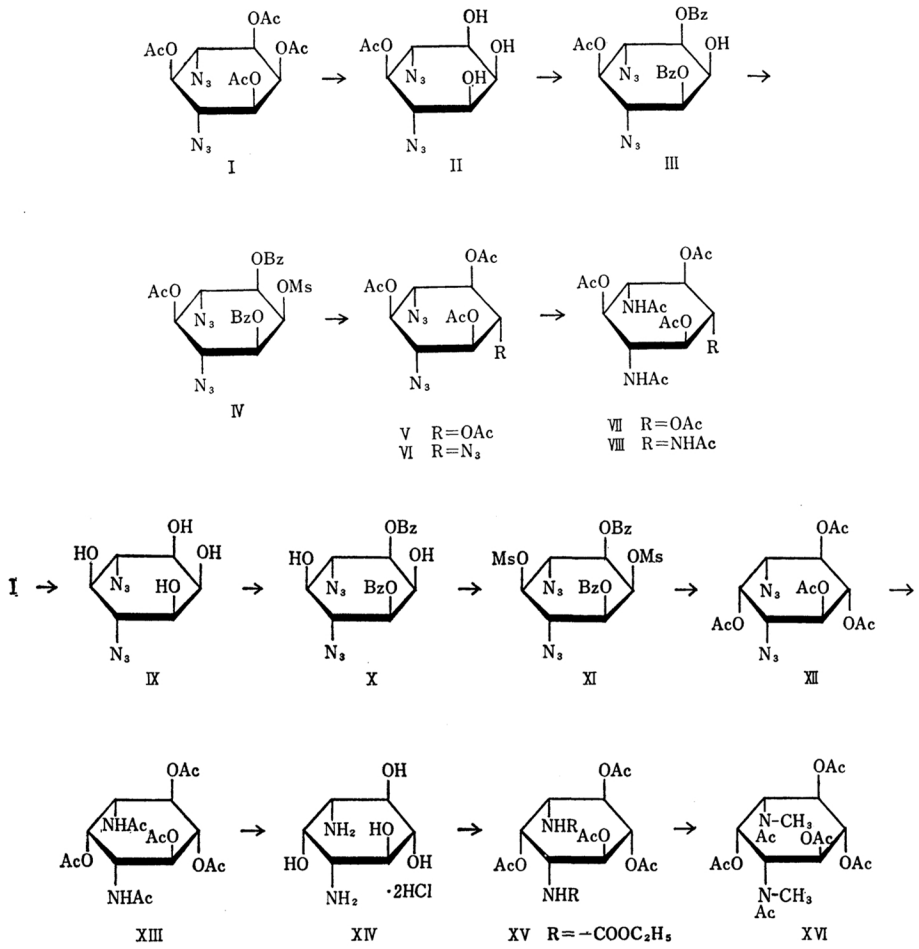
Fig. 1. PMR spectrum at 60 Mcps of 5-*O*-acetyl-4, 6-diazido-4, 6-dideoxy-1, 2, 3-tri-*O*-methyl-*myo*-inositol in $CDCl_3$.

of an axial methoxyl group showed the signal at τ 6.40 (3H).[6]

The signals of the ring protons presented the more information. That is, the quartet at τ 7.00 was attributed to the protons on C-1 and C-3 coupling with the neighboring protons with J_{aa} (9.9 cps) and J_{ae} (2.2 cps).[7] The triplet at τ 6.07 was assigned to the equatorial proton on C-2, since it showed a small coupling with H-1 and H-3 ($J_{aa}=J_{ea}=2.2$ cps). The axial proton (triplet, $J_{aa}=9.9$ cps) attached to C-5 appeared at relatively lower field, τ 5.42. Therefore, the remaining methoxyl group was considered to be attached to C-2. These PMR data consisted with the above described configuration of II.

Since there were two equatorial hydroxyl groups and one axial one in II, a selective benzoylation

1) T. Suami and S. Ogawa, This Bulletin, **37**, 1238 (1964).
2) M. L. Wolfrom, S. M. Olin and W. J. Polglasse, *J. Am. Chem. Soc.*, **72**, 1724 (1950); K. Heyns and H. Paulsen, *Chem. Ber.*, **89**, 1152 (1956).
3) T. Suami and S. Ogawa, This Bulletin, **38**, 2026 (1965).
4) P. F. Wiley, *J. Am. Chem. Soc.*, **84**, 1514 (1962); G. Slomp and F. A. MacKellar, *Tetrahedron Letters*, **12**, 521 (1962); M. Nakajima, N. Kurihara, A. Hasegawa and T. Kurokawa, *Ann. Chem.*, **689**, 243 (1965); T. Suami and S. Ogawa, This Bulletin, **40**, 1295 (1967).
5) F. W. Lichtenthaler, *Chem. Ber.*, **96**, 2047 (1963).
6) R. U. Lemieux, R. K. Kulling, H. J. Bernstein and W. G. Schneider, *J. Am. Chem. Soc.*, **80**, 6098 (1958).
7) W. F. Trager, F. F. Vincenzi and A. G. Huitric, *J. Org. Chem.*, **27**, 3006 (1962).



of equatorial hydroxyl groups must be possible.[8] When II was treated with benzoyl chloride in pyridine under ice-cooling, 5-*O*-acetyl-4, 6-diazido-1, 3-di-*O*-benzoyl-4, 6-dideoxy-*myo*-inositol (III) was obtained in a 84.2% yield.

The remaining free hydroxyl group on C-2 in III was in an axial position, and consequently its mesylation with methanesulfonyl chloride for a short time resulted in a poor yield. When this reaction was carried out for a prolonged period (4 days), 5-*O*-acetyl-4, 6-diazido-1, 3-di-*O*-benzoyl-4, 6-dideoxy-2-*O*-methanesulfonyl-*myo*-inositol (IV) was obtained in a 83.2% yield.

Then the displacement of methanesulfonyloxy group of IV by an acetate ion might occur only in the direct S_N2 reaction, because the two neighboring benzoyloxy groups were located in an anchimerically unassisted *cis* configuration to the methanesulfonyloxy group. When IV was treated with sodium acetate in boiling 2-methoxyethanol and subsequently acetylated, 2, 4, 5, 6-tetra-*O*-acetyl-1, 3-diazido-1, 3-dideoxy-*scyllo*-inositol was obtained (V) in a 37.4% yield.

A catalytic hydrogenation of V, followed by acetylation, gave hexaacetyl-streptamine (VII) in a 80.0% yield, which was identified with an authentic sample obtained from streptomycin,[9] by an infrared spectrum.

***scyllo*-Inosatriamine-1, 3, 5.** When IV was heated in 2-methoxyethanol with sodium azide, instead of sodium acetate, a triazido derivative (VI) was obtained as a syrup. The product was hydrolyzed in 6 N hydrochloric acid and then acetylated with acetic anhydride in pyridine. The product was hydrogenated in the presence of platinum catalyst under a hydrogen stream and the reduction product was acetylated to give colorless long needles, mp 310—315°C, in a 35.0% yield.

The replacement reaction of methanesulfonyloxy group by an azide ion is expected to occur in a direct S_N2 mechanism in view of the same type of

8) E. J. Reist, R. R. Spencer, D. F. Calkins, B. R. Baker and L. Goodman, *J. Org. Chem.*, **30**, 2312 (1965); T. Suami, F. W. Lichtenthaler and S. Ogawa, This Bulletin, **39**, 170 (1966).

9) R. L. Peck, R. P. Graber, A. Walti, E. W. Peel, C. E. Hoffhine, Jr., and K. Folkers, *J. Am. Chem. Soc.*, **68**, 29 (1946).

reaction described above, and hence the product, VIII, must be hexaacetyl-*scyllo*-inosatriamine-1, 3, 5.

The configuration was confirmed by its PMR spectrum. The spectrum of VIII in deuterium oxide revealed two signals at τ 7.95 (9H) and τ 8.07 (9H), which were attributed to three equatorial acetoxy groups and three equatorial acetamido groups respectively.[10] The ring protons on the carbons which bore acetamido groups appeared at τ 5.73 (3H) as a triplet (J=10.1 cps) indicating that the three protons were conformationally equivalent and located in the *trans*-diaxial arrangements with the neighboring protons. The protons on the carbon which had acetoxy groups appeared at τ 4.85 (3H) as a triplet (J=10.1 cps) showing the same arrangements as described above. These PMR data were compatible with the above mentioned structure of VIII.

Actinamine. I was hydrolyzed in boiling 6 N hydrochloric acid to give 4, 6-diazido-4, 6-dideoxy-*myo*-inositol (IX). There are four hydroxyl groups, of which three functional groups on C-1, C-3 and C-5 are equatorial and that on C-2 is axial in the favored conformation of IX. The selective *O*-benzoylation of equatorial hydroxyl groups in the presence of axial one must be possible. Also considering from the above described difficulty in the hydrolysis of acetoxy group on C-5, it might be assumed that the hydroxyl group on C-5 has a comparatively low reactivity. When IX was benzoylated with benzoyl chloride in pyridine at low temperature, 4, 6-diazido-1, 3-di-*O*-benzoyl-4, 6-dideoxy-*myo*-inositol (X) was obtained.

Then X was treated with an excess amount of methanesulfonyl chloride for three days to yield 4, 6-diazido-1, 3-di-*O*-benzoyl-4, 6-dideoxy-2, 5-di-*O*-methanesulfonyl-*myo*-inositol (XI) in a 40% yield. The displacement of methanesulfonyloxy groups of XI by acetate ions in 2-methoxyethanol occurred in the direct S_N2 mechanism to give 2, 4, 5, 6-tetra-*O*-acetyl-1, 3-diazido-1, 3-dideoxy-*myo*-inositol (XII) in a 17.0% yield, after acetylation.

A catalytic hydrogenation of XII, followed by acetylation, gave hexaacetyl-*myo*-inosadiamine-1, 3 (XIII)[11] in a 72.0% yield. Hydrolysis of XIII in 6 N hydrochloric acid afforded *myo*-inosadiamine-1, 3 dihydrochloride (XIV).

Then XIV was treated with ethyl chloroformate in an alkaline solution and the product was acetylated to give 2, 4, 5, 6-tetra-*O*-acetyl-*N*, *N'*-di-ethoxycarbonyl-*myo*-inosadiamine-1, 3 (XV) in a yield of 85.0%. Reduction of XV with an excess amount of lithium aluminum hydride, followed by acetylation, afforded hexaacetyl-actinamine (XVI) in a 44.5% yield, which was the component of the antibiotic actinospectacin produced by Streptomyces spectabilis[12] and flavopersicus.[13] XVI was identified with an authentic sample[14] by a mixed melting point determination and an infrared spectrum.

N-Methylation was also successfully carried out with formaldehyde, but the yield of actinamine was relatively low compared with the above described process.

Experimental

The melting points reported were determined on a Mitamura Riken micro hot stage and uncorrected. The infrared spectra were determined by pressed potassium bromide disks. The PMR spectra of the samples were recorded on a Japan Electron Optics JNM-C-60 spectrometer at a frequency of 60 Mcps in deuteriochloroform, deuterium oxide or deuteriodimethylsulfoxide (d_6-DMSO) with tetramethylsilane, sodium trimethylsilylpropanesulfonate or tetramethylsilane, respectively, as an internal standard. The peak positions are expressed by τ-values.

5-*O*-Acetyl-4, 6-diazido-4, 6-dideoxy-*myo*-inositol (II). 1, 2, 3, 5-Tetra-*O*-acetyl-4, 6-diazido-4, 6-dideoxy-*myo*-inositol (I) (8.1 g) was added to methanol (290 m*l*) previously saturated with ammonia at 0—5°C and the solution was stored in a refrigerator for 17 hr. Then the solution was evaporated under reduced pressure below 40°C to give an oily residue, which was crystallized by triturating with water (10 m*l*). The crystals were collected by filtration and washed with a small amount of cold water. The yield was 4.1 g (76%), mp 193—197°C. Recrystallization from ethanol gave colorless crystals (3.6 g, 65%) melting at 195—197°C.

Found: C, 35.33; H, 4.51; N, 30.37%. Calcd for $C_8H_{12}N_6O_5$: C, 35.29; H, 4.44; N, 30.88%. PMR: (d_6-DMSO) equatorial acetoxy group, τ 7.90 (3H).

The filtrate was evaporated under reduced pressure to dryness and acetylated with a mixture of acetic anhydride and pyridine to recover I (2.5 g), mp 148—149°C. The yield of II based on these results was 92%.

5-*O*-Acetyl-4, 6-diazido-1, 3-di-*O*-benzoyl-4, 6-dideoxy-*myo*-inositol (III). II (1.50 g) was dissolved in anhydrous pyridine (40 m*l*) and cooled to −3—0°C. Benzoyl chloride (1.94 g) was added dropwise under vigorous agitation. The reaction mixture was stored in a refrigerator for 24 hr and then poured into a mixture of ice and water (150 m*l*). White precipitates were collected and washed with water. Recrystallization from ethanol gave colorless plates (2.21 g, 84.2%) melting at 211—213°C.

Found: C, 55.07; H, 4.47; N, 17.26%. Calcd for $C_{22}H_{20}N_6O_7$: C, 55.00; H, 4.20; N, 17.49%. PMR:

10) F. W. Lichtenthaler and H. Leinert, *Chem. Ber.*, **99**, 903 (1966).

11) An authentic sample of hexaacetyl-*myo*-inosadiamine-1, 3 was kindly presented by Doz. Dr. F. W. Lichtenthaler of Technische Hochschule, Darmstadt, Germany.

12) D. J. Mason, A. Dietz and R. M. Smith, *Antibiotics and Chemotherapy*, **11**, 118 (1961).

13) T. J. Oliver, A. Goldstein, R. R. Bower, J. C. Holper and R. H. Otto, *ibid.*, **11**, 495 (1961).

14) We thank Dr. P. F. Wiley (Upjohn Co., Kalamazoo, Michigan, U. S. A.) for supplying a sample of the authentic material.

(d_6-DMSO) equatorial acetoxy group, τ 7.83 (3H); H-4, 6, τ 5.82 (triplet, J=10.5 cps); H-5, τ 4.75 (triplet, J=10.5 cps); H-1, 3, τ 4.67 (quartet, J=10.5 and 2.2 cps).

II was treated with an excess amount of benzoyl chloride in pyridine to afford tribenzoate quantitatively, needles, mp 156—159°C, after recrystallization from ethanol.

Found: C, 59.49; H, 4.31; N, 14.55%. Calcd for $C_{29}H_{24}N_6O_8$: C, 59.58; H, 4.14; N, 14.38%.

5-*O*-Acetyl-4, 6-diazido-4, 6-dideoxy-1, 2, 3-tri-*O*-methyl-*myo*-inositol. I (2.04 g) was dissolved in anhydrous dimethylformamide (70 m*l*), to which methyl iodide (9.3 m*l*) and silver oxide (10.3 g) was added, and the mixture was vigorously stirred at room temperature for 43 hr. An insoluble material was filtered off and washed with a small amount of dimethylformamide. The filtrate was then evaporated *in vacuo* to dryness. The residue was extracted with hot ethanol (20 m*l*×3) and the extracts were evaporated to give a crystalline residue. Recrystallization from ethanol gave colorless crystals (1.53 g, 54.6%) melting at 118—120°C. The second crop (0.13 g, 70.0%) was obtained by evaporation of the mother liquor. Analytical sample was again recrystallized from the same solvent, mp 119—120°C.

Found: C, 42.39; H, 5.91; N, 26.96%. Calcd for $C_{11}H_{18}N_6O_5$: C, 42.03; H, 5.77; N, 26.74%.

5-*O*-Acetyl-4, 6-diazido-1, 3-di-*O*-benzoyl-4, 6-dideoxy-2-*O*-methanesulfonyl-*myo*-inositol (IV). III (2.8 g) was dissolved in anhydrous pyridine (30 m*l*) and cooled in an ice bath. Methanesulfonyl chloride (1.4 g) was added dropwise under vigorous agitation. Then the reaction mixture was allowed to stand at room temperature for 4 days. The mixture was poured onto an ice and water, and the precipitates were collected and washed with cold water. The crude product was recrystallized from 2-methoxyethanol to give 2.7 g (83.2%) of needles melting at 235—237°C.

Found: C, 49.07; H, 4.67; N, 14.60; S, 5.49%. Calcd for $C_{23}H_{22}N_6O_8S$: C, 49.46; H, 3.97; N, 15.03; S, 5.74%.

2, 4, 5, 6-Tetra-*O*-acetyl-1, 3-diazido-1, 3-dideoxy-*scyllo*-inositol (V). A mixture of IV (0.623 g), anhydrous sodium acetate (0.624 g) and 2-methoxyethanol (20 m*l*) was refluxed for 25 hr. An insoluble material was removed by filtration and the filtrate was evaporated under reduced pressure to dryness. The residue was extracted with boiling acetone (20 m*l*×3). The extracts were evaporated to dryness and the residual oil was acetylated with acetic anhydride and pyridine. The reaction mixture was evaporated and triturated with ethanol to yield 169 mg (37.4%) of colorless plates melting at 170—171°C. Further recrystallization from ethanol did not raise its melting point.

Found: C, 42.21; H, 4.79; N, 20.88%. Calcd for $C_{14}H_{18}N_6O_8$: C, 42.21; H, 4.55; N, 21.10%. PMR: ($CDCl_3$) four equatorial acetoxy groups, τ 7.99 (3H), 7.90 (6H) and 7.80 (3H).

Hexaacetyl-streptamine (VI). V (140 mg) was dissolved in hot ethanol (30 m*l*) and hydrogenated in the presence of Adams platinum oxide (30 mg) under 50 psi of a hydrogen pressure at room temperature for 12 hr. The catalyst was filtered off and the filtrate was evaporated *in vacuo* to dryness. The residue was acetylated by acetic anhydride (7 m*l*) in pyridine (7 m*l*) at room temperature overnight. The precipitated long needles were collected by filtration and washed with ethanol. The yield was 124 mg (80.0%), transition point 238—242°C. The infrared spectrum was superimposable with that of an authentic sample derived from streptomycin.

Hexaacetyl-*scyllo*-inosatriamine-1, 3, 5 (VIII). A mixture of V (0.768 g), sodium azide (0.769 g) and 2-methoxyethanol (30 m*l*) was refluxed for 12 hr. The reaction mixture was evaporated *in vacuo* to dryness and extracted with hot acetone (20 m*l*×3). The extracts were evaporated and the residual oil was refluxed with 6 N hydrochloric acid (20 m*l*) for 1 hr. After cooling, precipitated benzoic acid was removed by filtration and the filtrate was evaporated *in vacuo* to dryness. The residual oil was treated with acetic anhydride and pyridine to give an oily 2, 4, 6-tri-*O*-acetyl-1, 3, 5-triazido-1, 3, 5-trideoxy-*scyllo*-inositol (VI). VI was hydrogenated in ethanol (10 m*l*) in the presence of Adams platinum oxide (50 mg) under 50 psi of a hydrogen pressure at room temperature for 6 hr. The catalyst was filtered off and the filtrate was evaporated to yield an oil. The oil was treated with acetic anhydride and pyridine to give 149 mg of long needles melting at 310—315°C. The another crop (57 mg) was obtained by evaporation of the mother liquor. The total yield was 35.0%. Recrystallization from ethanol gave an analytical sample.

Found: C, 50.66; H, 7.01; N, 9.56%. Calcd for $C_{18}H_{27}N_3O_9$: C, 50.34; H, 6.34; N, 9.79%. PMR: (D_2O) three equatorial acetamido groups, τ 8.08 (9H); three equatorial acetoxy groups, τ 7.95 (9H); H-1, 3, 5, τ 5.73 (triplet, J=10.1 cps); H-2, 4, 6, τ 4.85 (triplet, J=10.1 cps).

***N*, *N'*, *N''*-Triacetyl-*scyllo*-inosatriamine-1, 3, 5.** VIII (192 mg) was treated with methanolic ammonia (40 m*l*) overnight. White precipitates were collected and washed with ethanol. The product weighed 120 mg (88.5%). Recrystallization from water-ethanol afforded colorless plates (66 mg) having one mole of water of crystallization.

Found: C, 45.13; H, 7.47; N, 12.76%. Calcd for $C_{12}H_{21}N_3O_6 \cdot H_2O$: C, 44.86; H, 7.22; N, 13.08%.

4, 6-Diazido-1, 3-di-*O*-benzoyl-4, 6-dideoxy-2, 5-di-*O*-methanesulfonyl-*myo*-inositol (XI). I (3.0 g) was hydrolyzed with boiling 6 N hydrochloric acid (45 m*l*) for 40 min to give an oily 4, 6-diazido-4, 6-dideoxy-*myo*-inositol (IX). IX was dissolved in anhydrous pyridine (20 m*l*) and cooled to −5—0°C in an ice bath. Benzoyl chloride (2.2 m*l*) was added dropwise to the cooled solution with a vigorous agitation. After standing at room temperature for two days, the reaction mixture was poured onto an ice and water. An oily product was extracted with chloroform and the extracts were washed with 10% aqueous potassium carbonate, 5% hydrochloric acid and water successively and dried over sodium sulfate. Evaporation *in vacuo* gave an oily 4, 6-diazido-1, 3-*O*-benzoyl-4, 6-dideoxy-*myo*-inositol (X). To a solution of X in anhydrous pyridine (20 m*l*), methanesulfonyl chloride (3.4 g) was added dropwise under ice cooling. The mixture was allowed to stand at room temperature for three days and then poured onto an ice and water to yield tiny needles. The crude crystals were recrystallized from 2-methoxyethanol to afford needles (1.8 g, 40%) melting at 251—253°C with decomposition. Analytical sample was obtained by recrystallization from the same solvent.

Found: C, 44.77; H, 3.95; N, 13.83; S, 10.39%. Calcd for $C_{22}H_{22}N_6O_{10}S_2$: C, 44.44; H, 3.73; N, 14.14; S, 10.78%.

2, 4, 5, 6-Tetra-*O*-acetyl-1, 3-diazido-1, 3-dideoxy-*myo*-inositol (XII). A mixture of XI (1.6 g), anhydrous sodium acetate (1.6 g) and 2-methoxyethanol (80 m*l*) was heated under reflux for 24 hr. The reaction mixture was evaporated *in vacuo* to dryness and extracted with hot acetone (20 m*l*×3). The extracts were evaporated and treated with acetic anhydride (10 m*l*) and pyridine (10 m*l*) at room temperature overnight. The mixture was evaporated to yield an oil, which was dissolved in chloroform and placed on an alumina column. Chloroform eluates were evaporated and the residue crystallized in ethanol. Colorless crystals weighed 0.182 g (17%), mp 167—170°C. Recrystallization from ethanol afforded an analytical sample melting at 168—170°C.

Found: C, 41.75; H, 4.71; N, 21.33%. Calcd for $C_{14}H_{18}N_6O_8$: C, 42.21; H, 4.55; N, 21.10%. PMR: ($CDCl_3$) three equatorial acetoxy groups, τ 7.98 (3H) and 7.92 (6H); axial acetoxy group, τ 7.81 (3H); H-2, τ 4.31 (triplet, J=3.0 cps).

Hexaacetyl-*myo*-inosadiamine-1, 3 (XIII). XII (46 mg) was hydrogenated as described in VI. The crude product was acetylated to afford crystals (36 mg, 72%) melting at 277.5—280°C (capillary). The infrared spectrum of the crystals was superimposable with that of an authentic sample.[11]

PMR: ($CDCl_3$) two equatorial acetamido groups, τ 8.11 (6H); three equatorial acetoxy groups, τ 7.98 (3H) and 7.95 (6H); axial acetoxy groups, τ 7.76 (3H).

***myo*-Inosadiamine-1, 3 Dihydrochloride (XIV).** XIII (479 mg) was heated with 6 N hydrochloric acid (25 m*l*) on a boiling water bath for 2 hr. The solution was evaporated *in vacuo* to dryness and the residue was crystallized from water and ethanol to afford colorless needles (289 mg, 98.7%) melting at 214—234°C with decomposition.

Found: C, 27.88; H, 7.00; N, 10.46; Cl, 27.37%. Calcd for $C_6H_{16}N_2O_4Cl_2 \cdot \frac{1}{2}H_2O$; C, 27.70; H, 6.67; N, 10.77; Cl, 27.26%. The water of crystallization could be removed by drying over phosphorus pentoxide *in vacuo* at 100°C.

2, 4, 5, 6-Tetra-*O*-acetyl-*N*, *N'*-di-ethoxycarbonyl-*myo*-inosadiamine-1, 3 (XV). A solution of XIV obtained from XIII (516 mg) and sodium bicarbonate (1.3 g) in water (10 m*l*) was agitated and ethyl chloroformate (0.6 m*l*) was added drop by drop under cooling. The pH of the mixture was maintained at 9 by adding sodium hydroxide solution. Then the reaction mixture was allowed to stand at room temperature overnight. The precipitates were filtered off and the filtrate was evaporated *in vacuo* to dryness. The residue was acetylated with a mixture of acetic anhydride (9 m*l*) and pyridine (9 m*l*) to yield crude crystals. Recrystallization from ethanol gave colorless plates (411 mg, 83.9%) melting at 189.5—190°C. Further recrystallization did not raise its melting point.

Found: C, 48.92; H, 5.96; N, 6.38%. Calcd for $C_{20}H_{30}N_2O_{12}$: C, 48.97; H, 6.17; N, 5.71%.

Hexaacetyl-actinamine (XVI). XV (185 mg) was dissolved in anhydrous tetrahydrofuran (20 m*l*) and the slurry of lithium aluminum hydride (1.24 g) in anhydrous tetrahydrofuran (30 m*l*) was added under cooling. The mixture was refluxed for 21 hr and then poured onto an ice and water (80 m*l*). After two days, the precipitates were filtered off and the filtrate was evaporated *in vacuo* to dryness. The residue was acetylated with a mixture of acetic anhydride (7 m*l*) and pyridine (7 m*l*) at 100°C for 3 hr. Insoluble material was filtered off and the filtrate was evaporated *in vacuo* to yield an oily product, which was dissolved in chloroform and placed on a alumina column. The column was eluted with chloroform (150 m*l*) and an excess solvent was evaporated to give the residue which was crystallized from methanol. The crystals were collected by filtration to give 77.0 mg (44.5%) of colorless plates melting at 197.5—200°C. Further recrystallization from methanol raised the melting point to 202.5—203°C. This compound was identified with an authentic sample[9] by mixed melting point determination and infrared spectra.

***N*-Methylation with Formaldehyde.** *myo*-Inosadiamine-1, 3 was obtained by treating XIV (325 mg) with Amberlite IRA-400 (10 m*l*). The free base was added to a solution of paraformaldehyde (150 mg) in water (5 m*l*) and the pH of the mixture was adjusted to 9 by adding a small amount of potassium carbonate. The mixture was heated at 60°C for 1 hr and then allowed to stand in a refrigerator overnight. Three volumes of acetone was added to the mixture and white precipitates were collected by filtration. The crude Schiff base weighed 255 mg. A solution of the crude product (234 mg) in water (5 m*l*) was hydrogenated with sodium borohydride (470 mg) for 3 hr at 0—5°C. After standing in a refrigerator overnight, the mixture was neutralyzed with acetic acid and then evaporated *in vacuo* repeatedly with methanol to dryness. After the residue was acetylated, an insoluble material was filtered off and the filtrate was evaporated *in vacuo* to yield an oily residue. The residue was dissolved in chloroform and passed through a short column of alumina. Evaporation of the excess solvent gave colorless crystals (117 mg) melting at 180—203°C. Recrystallization from methanol afforded colorless plates (67 mg) of hexaacetyl-*N*-methyl-*myo*-inosadiamine-1, 3 melting at 204—208°C.

Found: C, 51.16; H, 6.62; N, 6.18%. Calcd for $C_{19}H_{28}N_2O_{10}$: C, 51.34; H, 6.35; N, 6.30%.

From the mother liquor, small amount of colorless plates of hexaacetyl-actinamine (15 mg, mp 197—198.5°C) was obtained, which was identified with an authentic sample[14] by comparing the infrared spectra.

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