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Aminocyclitols. VIII. A Synthesis of Inosamines and Inosadiamines*

By Tetsuo SUAMI,† Frieder W. LICHTENTHALER†† and Seiichiro OGAWA†

† *Department of Applied Chemistry, Faculty of Engineering, Keio University, Koganei-shi, Tokyo*
†† *Institut für Organische Chemie, Technische Hochschule, 61 Darmstadt, Germany*

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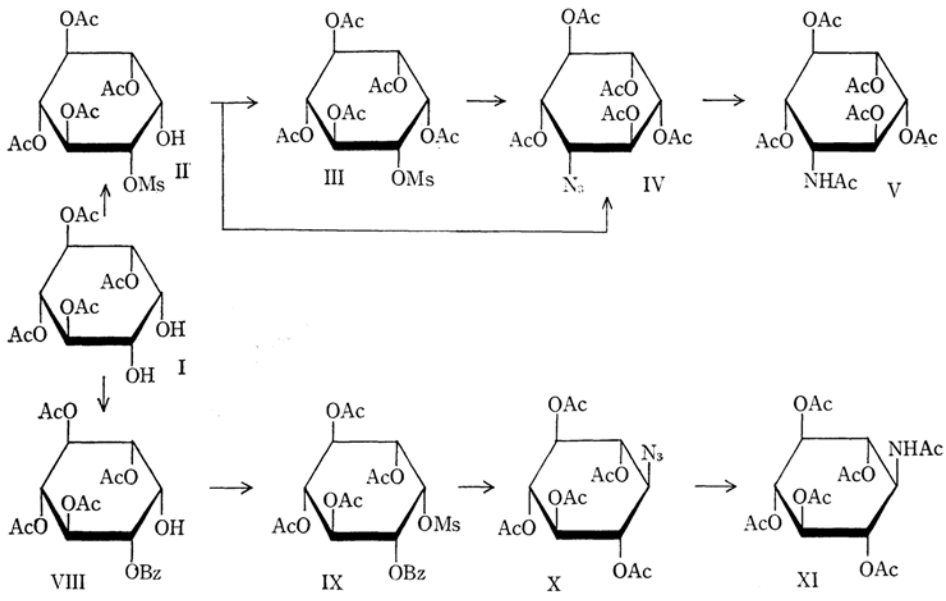
muco-Inosamine-1, *scyllo*-inosamine, *muco*-inosadiamine-1, 5 and *myo*-inosadiamine-1, 2 have been synthesized from *myo*-inositol. Their structures have also been established by a study of the NMR spectra of their acetyl derivatives. When 1, 4, 5, 6-tetra-*O*-acetyl-3-*O*-mesyl-*myo*-inositol is treated with sodium azide in boiling aqueous 2-methoxyethanol, an azido derivative is obtained. The azido compound is hydrogenated in the presence of a catalyst and subsequently acetylated to give muco-inosamine-1. The stereochemical course of the reaction has been proposed to be an anchimeric reaction. When the analogous reaction is carried out with 2, 3-di-*O*-mesyl-*myo*-inositol tetraacetate, *myo*-inosadiamine-1, 2 or *muco*-inosadiamine-1, 5 is obtained as the main product, depending on the solvent applied.

In connection with a previous communication,[1] a new synthesis of *muco*-inosamine-1,[4] *scyllo*-inosamine,[8] *muco*-inosadiamine-1, 5 and *myo*-inosadiamine-1, 2, and their structures as established by means of the NMR spectra, will be described in the present paper.

scyllo- and *muco*-1-Inosamine

1, 4, 5, 6-Tetra-*O*-acetyl-*myo*-inositol (I)[2] has been used as the starting material. By treating I with one mole of methanesulfonyl chloride in pyridine, 1, 4, 5, 6-tetra-*O*-acetyl-3-*O*-mesyl-*myo*-inositol (II) is obtained in a fairly good yield. Then the acetylation of II gives 3-*O*-mesyl-*myo*-inositol pentaacetate (III).[3] The sturctures of II and III have been established by means of the NMR spectra, along with chemical evidence.[1] The spectrum of III in chloroform (Fig. 1) reveals a sharp signal at 7.00 τ, which is assigned to the protons of an equatorial mesyloxy group.[3] The signal at 7.78 τ corresponds to an axial acetoxy group, and the

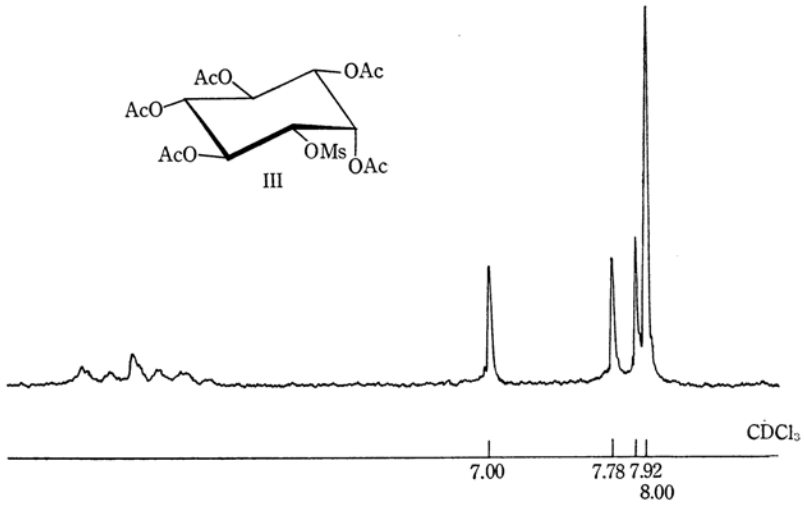


* A part of this research has been presented at the 18th Annual Meeting of the Chemical Society of Japan, Osaka, April, 1965.

1) T. Suami and S. Ogawa, This Bulletin, **37**, 1238 (1964).

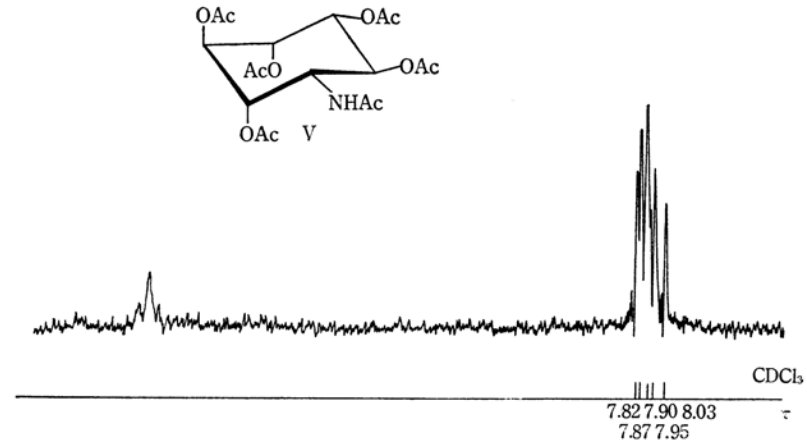
2) S. J. Angyal, P. T. Gilham and C. G. Macdonald, *J. Chem. Soc.*, **1957**, 1417.

3) T. Suami, F. W. Lichtenthaler and S. Ogawa, This Bulletin, **38**, 754 (1965).



p. p. m., $H \rightarrow$

Fig. 1



p. p. m., $H \rightarrow$

Fig. 2

signals at 7.92 and 8.00 τ with a 1 : 3-intensity are expected from four equatorial acetoxy groups.

When III is treated with sodium azide in boiling aqueous 2-methoxyethanol and subsequently acetylated, an azido acetate (IV) is obtained. Upon the catalytic reduction of IV, followed by acetylation, hexaacetyl-*muco*-inosamine-1 (V) is obtained in 32% yield; it has been identified by a mixed melting point determination.[4] V can also be prepared from II by an analogous reaction sequence.

Considering the configuration of the product obtained, the demesylation of III seems to proceed through an intermediate formation of a dioxolane-ring by participation of the vicinal, trans-orientated acetoxy group, which is then cleaved by a nucleophilic attack of the azide ion in the manner of a diaxial opening.[3]

V can also be prepared in 40% yield from II by treatment with ammonia in methanol under pressure and by subsequent acetylation. Since the first step of this reaction is a de-*O*-acetylation, the formation of V must proceed via an oxirane ring between C-3 and C-4, a ring which is diaxially opened.[5]

The stereochemical courses of these reactions are analogous to an attack of the acetate ion on

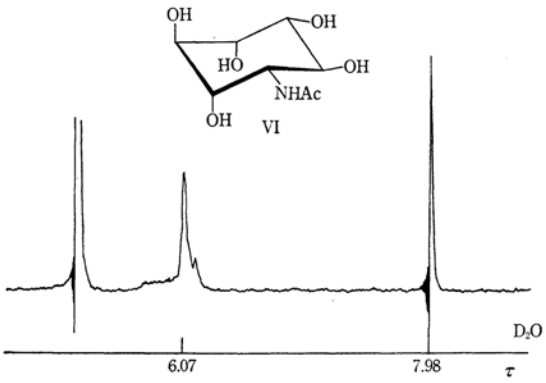
4) M. Nakajima, A. Hasegawa and N. Kurihara, *Chem. Ber.*, **95**, 2708 (1962): The melting point determination has kindly been carried out by Professor Minoru Nakajima of Kyoto University.

5) E. W. Bodycote, W. N. Haworth and E. L. Hirst, *J. Chem. Soc.* **1934**, 151; R. W. Jeanloz and A. M. C. Rapin, *J. Org. Chem.*, **28**, 2978 (1963); R. S. Tipson, "Advances in Carbohydrate Chemistry," Vol. 8, Academic Press, New York (1953), pp. 176—177.

the anchimeric intermediate acetoxonium ion[6] and to an opening of a highly-strained oxirane ring by a nucleophile.[7]

NMR-spectroscopical data support the muco-configuration: the hexaacetate V shows sharp signals at 8.03 τ, as is to be expected from an equatorial acetamido group, and at 7.82, 7.87, 7.90 and 7.95 τ (1 : 1 : 1 : 2), arising from three axial and two equatorial acetoxy groups.

The NMR spectrum of *N*-acetyl-*muco*-inosamine-1 (VI), prepared by the de-*O*-acetylation of V, in D_2O (Fig. 3) reveals one sharp signal at 7.98 τ due to the acetamido group in an equatorial orientation.

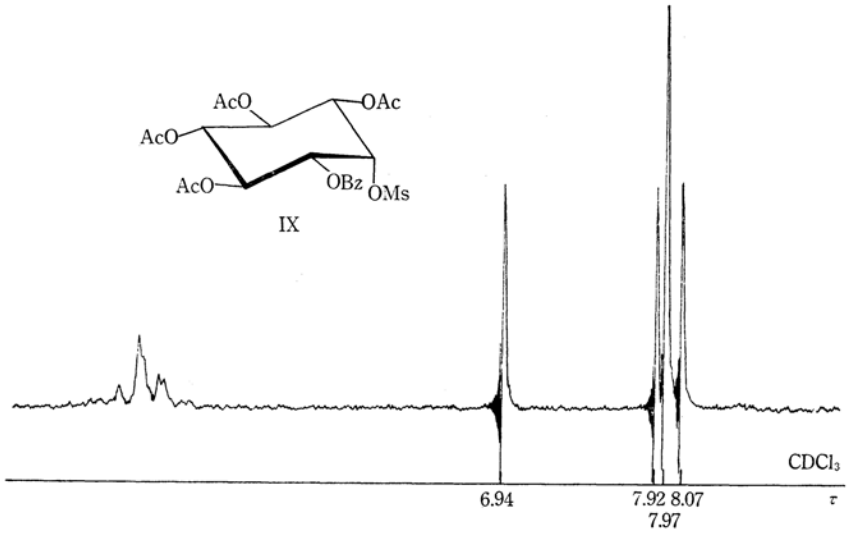


p. p. m., $H \rightarrow$

Fig. 3

When the demesylation of III with sodium azide is carried out in dimethylformamide instead of in 2-methoxyethanol, an as-yet-unidentified hexaacetyl-inosamine (VII) is obtained besides V, and this substance shows a remarkable depression in a mixed melting point determination with hexaacetyl-*rac*-inosamine-2.[8]

In analogy to the monomesylation of tetraacetyl-*myo*-inositol (I→II), a selective monobenzoylation to the 3-*O*-benzoyl derivative should also be possible by treating I with benzoyl chloride under appropriate conditions. When one mole of benzoyl chloride is added to I in pyridine at 5°C, a tetra-*O*-acetyl-3-*O*-benzoyl derivative (VIII) is obtained in a good yield. It can easily be mesylated with methanesulfonyl chloride to 3-*O*-benzoyl-2-*O*-mesyl-*myo*-inositol tetraacetate (IX). This product IX is quite different in its physical properties from the 2-*O*-benzoyl-3-*O*-mesyl-*myo*-inositol tetraacetate (XIX) prepared by the benzoylation of II. Also, their NMR spectra are distinctly different (cf. Figs. 4 and 5 respectively). The spectrum of IX reveals a sharp signal at 6.94 τ corresponding to an axial mesyloxy group, while in the case of XIX the signal of the mesyl protons is shifted to a higher field (6.98 τ), as is to be expected from an equatorial mesyloxy group. Therefore, it is reasonable to conclude that IX is 3-*O*-benzoyl-2-*O*-mesyl-*myo*-inositol tetraacetate. It must be noticed that benzoyl chloride attacks an equatorial hydroxyl group rather than an axial one, as does *p*-toluenesulfonyl chloride[9] or methanesulfonyl chloride[1].



p. p. m., $H \rightarrow$

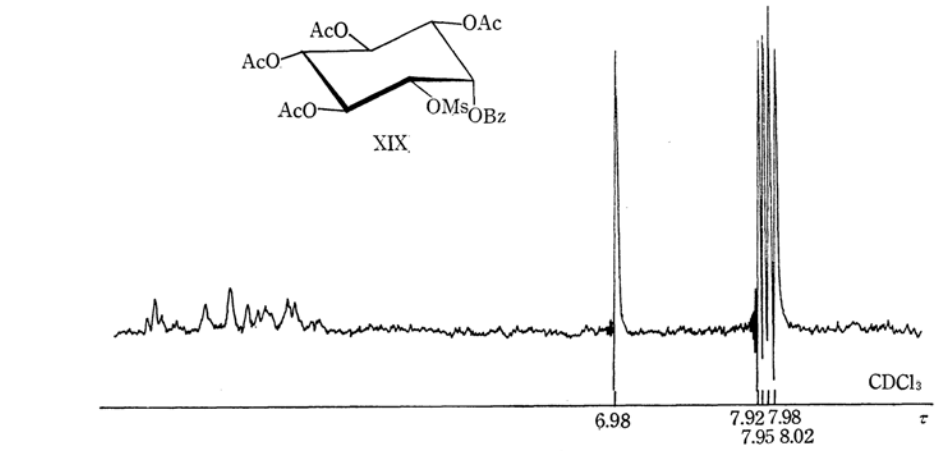
Fig. 4

6) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Rinehart & Winston, New York (1959), pp. 565—566.

7) E. Eliel, in M. S. Newman, "Steric Effects in Organic Chemistry," J. Wiley & Sons, New York (1956), pp. 130—134; M. Nakajima, A. Hasegawa and F. W. Lichtenthaler, *Ann. Chem.*, **669**, 75 (1963).

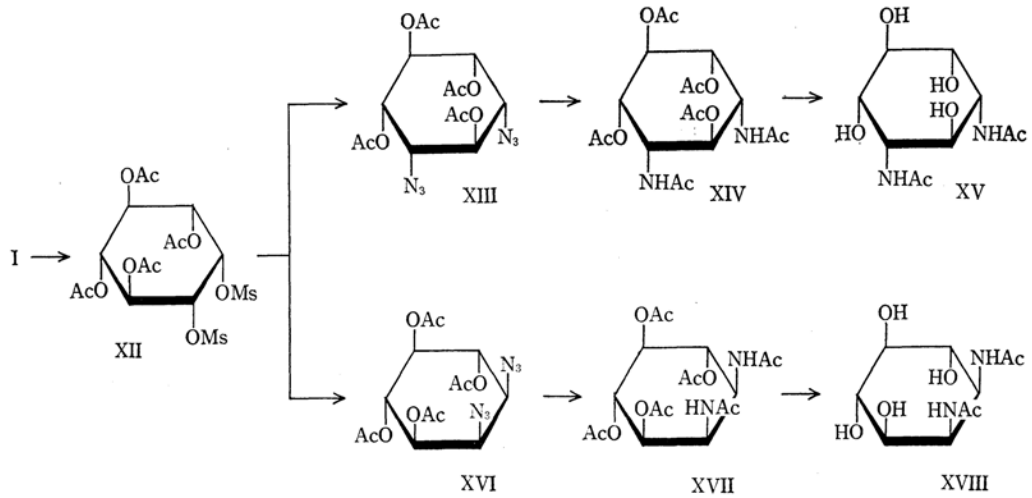
8) M. Nakajima, N. Kurihara and A. Hasegawa, *Chem. Ber.*, **95**, 141 (1962); an authentic sample of hexaacetyl-*rac*-inosamine-2 has been presented by Professor Minoru Nakajima of Kyoto University.

9) S. J. Angyal and L. Anderson, "Advances in Carbohydrate Chemistry," Vol. XIV, Academic Press, New York (1959), p. 167.



p. p. m., $H \rightarrow$

Fig. 5



When IX is treated with sodium azide in boiling aqueous 2-methoxyethanol, an azido compound (X) is obtained; upon hydrogenation and subsequent acetylation, this compound yields hexaacetyl-*scyllo*-inosamine (XI).[10]

In the case of compound IX, the two vicinal acyloxy groups are located in an anchimerically-unassisted cis configuration to the mesyloxy group. Thus a neighboring group participation is improbable, and a direct S_N2 mechanism[11] must be proposed for the demesylation of IX with sodium azide.

myo-1, 2 and *muco*-1, 5-Inosadiamine

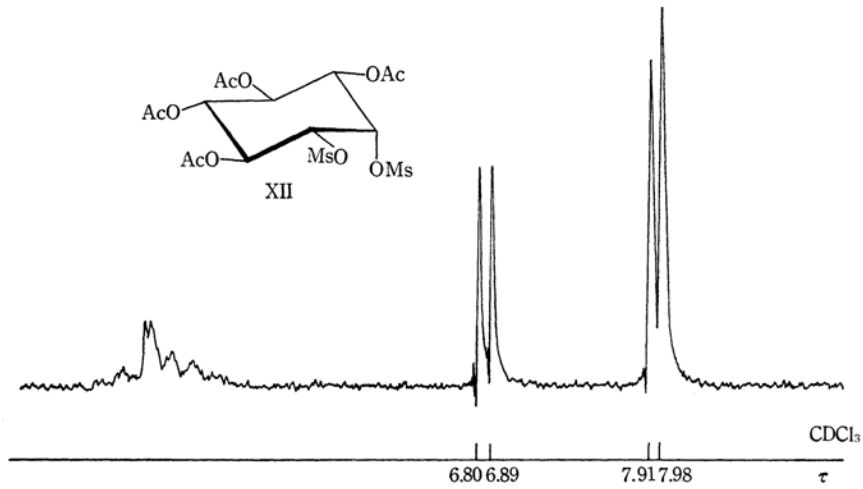
Upon the treatment of tetraacetyl-*myo*-inositol (I) with two moles of methanesulfonyl chloride in pyridine, 2,3-di-*O*-mesyl-*myo*-inositol tetraacetate (XII) is obtained in a good yield. Its NMR spectrum (Fig. 6) reveals two sharp signals at 6.80 and 6.89 τ, corresponding to an axial and an equatorial mesyloxy group respectively.

By treating XII with sodium azide in aqueous 2-methoxyethanol, a diazido derivative (XIII) is obtained; this is converted to hexaacetyl-*muco*-inosadiamine-1, 5 (XIV) by hydrogenation and by subsequent acetylation.

The structure of XIV as a *m*-inosadiamine and its *muco*-1, 5-configuration is established on the basis of the following data: 1) The hexaacetate XIV is easily de-*O*-acetylated with methanolic ammonia to its di-*N*-acetate (XV), which, upon periodation, consumes 2.2 mol. of periodate in 43 hr. Thus the two acetamido groups must be located in a 1, 3-position. 2) Since the hexaacetate XIV is insoluble in chloroform, the NMR spectrum was measured in pyridine and in d_6-dimethylsulfoxide (DMSO). In pyridine, signals

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

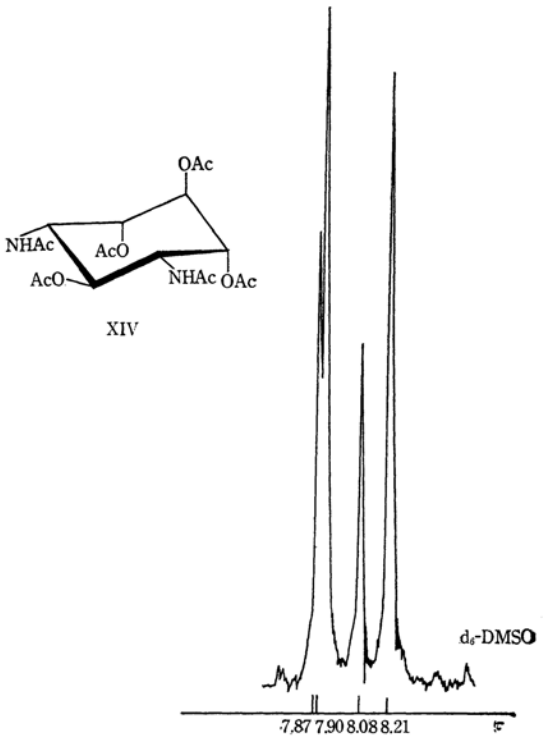
11) B. R. Baker and A. H. Haines, *J. Org. Chem.*, **28**, 442 (1963).



XII

p. p. m., $H \rightarrow$

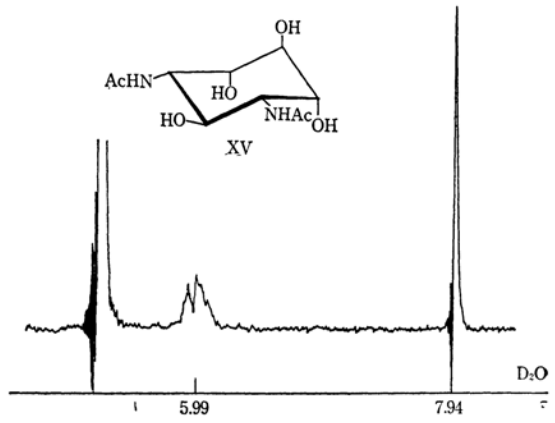
Fig. 6



XIV

p. p. m., $H \rightarrow$

Fig. 7



XV

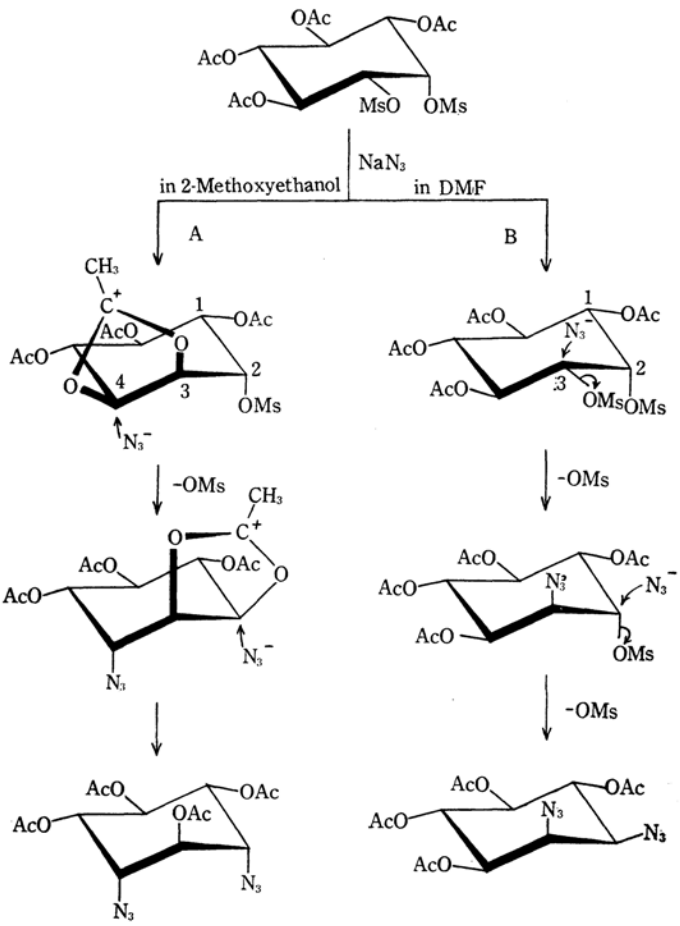
p. p. m., $H \rightarrow$

Fig. 8

were obtained in the 8 τ-region; however, when compared with the signals in similar compounds, these signals showed no apparent correlation with the configuration. In d_6-DMSO however, nicely-resolved signals for the acetyl groups were obtained in the 8 τ-region (Fig. 7): a four signal pattern with a 1 : 2 : 1 : 2-intensity. Since the absorption ranges obtained for axial and equatorial acetoxy or acetamido-groups in chloroform solution[12] cannot be applied for other solvents, a series of compounds have been measured in d_6-DMSO; on the basis of these measurements the following ranges could be established: a) acetoxy-groups, axial 7.86—7.91 τ; equatorial 8.05—8.11 τ; b) equatorial acetamido-groups 8.19—8.30 τ.[13] Subsequently, the NMR-signals of XIV in d_6-DMSO can be convincingly assigned to three axial acetoxy groups, 7.87 τ (1) and 7.90 τ (2), one equatorial acetoxy group (8.08 τ), and two equatorial acetamido groups (8.21 τ), thus establishing the *muco*-1, 5-configuration for XIV.

The di-*N*-acetate (XV) has, in its NMR-spectrum in D_2O (Fig. 8), one sharp signal at 7.94 τ, showing the presence of two sterically-equivalent

12) F. W. Lichtenthaler, *Chem. Ber.*, **96**, 2047 (1963).
13) F. W. Lichtenthaler, H. Leinert and H. P. Albrecht, *Tetrahedron Letters*, in press.



(equatorial) acetamido-groups, thus supporting the *muco*-1, 5-configuration.

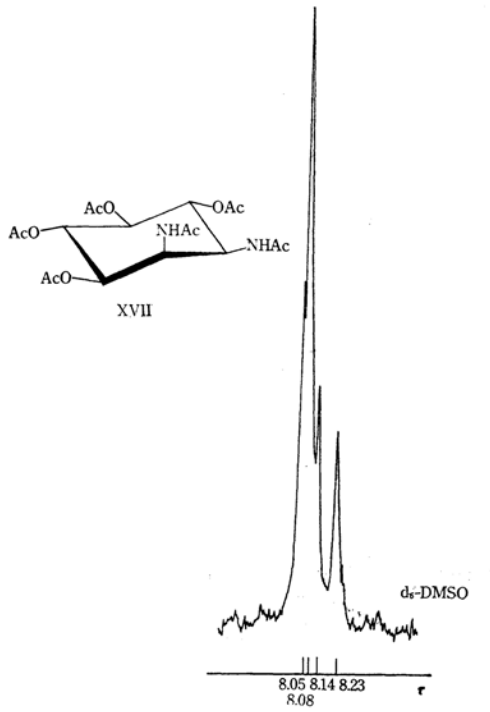
The course of the reaction can be explained by assuming the formation of an acetoxonium ion in an anchimeric mechanism with the displacement of the mesyloxy group on C-3. Then an nucleophilic attack by an azide ion can occur in the manner of a trans-diaxial opening of a dioxolane ring.[6] Now again, a mesyloxy group and an acetoxy group are in a trans orientation, resulting in the formation of another acetoxonium ion and subsequent clevage by the azide ion. This reaction sequence is shown in the following chart (course A).

When XII is treated with ammonia under pressure, the same *muco*-inosadiamine-1, 5 is obtained. In this reaction, de-*O*-acetylation takes place at first and an oxirane ring may be formed;[5] this ring is then cleaved by the nucleophilic attack of ammonia in the manner described above.

When XII is reacted with sodium azide in aqueous dimethylformamide instead of 2-methoxyethanol and subsequently treated in a manner analogous to that in which XIV is obtained, hexaacetyl-*myo*-inosadiamine-1, 2 (XVII) is obtained.

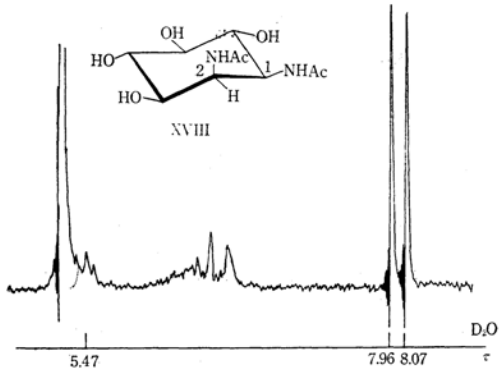
The structural and configurational proof was obtained from the following data; the NMR spectrum of XVII in d_6-DMSO (Fig. 9) gives two sharp signals, with an equal intensity, at 8.14 and 8.23 τ; these signals are to be assigned to an axial and an equatorial acetamido group respectively. The four equatorial acetoxy groups give two signals with a 1 : 3-intensity at 8.05 and 8.08 τ. The NMR spectrum of the di-*N*-acetate (XVIII), obtained by the de-*O*-acetylation of XVII with methanolic ammonia is shown in Fig. 10: two sharp signals, with an intensity of 1 : 1, at 7.96 and 8.07 τ, corresponding to an axial and an equatorial acetamido group respectively. Furthermore, it shows a triplet at 5.47 τ (J= 3.5 c. p. s.), as i expected[14] for the C-2-hydrogen in XVIII. Also, XVIII consumes 3.3 mol. of periodate in 43 hr., showing that the two acetamido groups are in a vicinal position, thus establishing unequivocally the *myo*-1, 2-configuration. Considering the structure and configuration of the product obtained, a quite different mechanism must operate in the course of this reaction; the

14) G. Slomp and F. A. MacKellar, ibid., **12** 521 (1962).



p. p. m., $H \rightarrow$

Fig. 9



p. p. m., $H \rightarrow$

Fig. 10

replacement of the mesyloxy groups on C-2 and C-3 must proceed predominantly through a direct S_N2 mechanism and, hence, Walden inversions must occur on C-2 and C-3 (course B).

The different reaction mechanisms caused by a change in solvent in the displacement of a mesyloxy group have been reported in previous communications;[3,15] this is another valid example of a solvent effect on a stereochemical course of the reaction. That is, in 2-methoxyethanol an anchimeric reaction is predominant, while a direct S_N2 reaction is dominant in dimethylformamide.

15) B. R. Baker and H. S. Sachdev, *J. Org. Chem.*, **28**, 2132 (1963).

Experimental

The melting points reported were determined on a Mitamura Riken micro hot stage. The melting points marked with asterisks were measured in a liquid bath and are uncorrected. The infrared spectra were determined by pressed potassium bromide disks. The NMR spectra of the samples were determined at a frequency of 60 Mc. p. s. in deuteriochloroform, deuterium oxide or deuteriodimethylsulfoxide with tetramethylsilane, sodium trimethylsilylpropanesulfonate or tetramethylsilane respectively as an internal standard. The peak positions are given in τ-values.

1, 4, 5, 6-Tetra-*O*-acetyl-3-*O*-mesyl-*myo*-inositol (II).—To a stirred solution of 3.45 g. of 1, 4, 5, 6-tetra-*O*-acetyl-*myo*-inositol (I) in 40 ml. of pyridine, 1.5 g. of methanesulfonyl chloride was added at 5°C. The mixture was kept at room temperature overnight and then poured into ice and water, after which the solution was evaporated under reduced pressure to dryness. The residue was digested with cold water, and the product was collected by filtration. The crude product (3.9 g.) was recrystallized from methanol to give 2.7 g. (72%) of colorless crystals at *210—213°C. Further recrystallization afforded an analytical sample of II, m. p. *210.5—212°C.

Found: C, 41.86; H, 5.31; S, 7.83. Calcd. for $C_{15}H_{22}O_{12}S$: C, 42.25; H, 5.20; S, 7.52%.

3-*O*-Mesyl-*myo*-inositol Pentaacetate (III).—A 200 mg. portion of II was treated with 3 ml. of acetic anhydride in pyridine at 90°C. The mixture was then evaporated under reduced pressure to dryness, and the residue was crystallized from a mixtrue of methanol and petroleum ether to give 220 mg, of white crystals melting at 158—160°C. Recrystallization from ethanol furnished 193 mg. (87.7%) of colorless needles, m. p. 159—161°C.

Found: C, 43.42; H, 5.34; S, 6.58. Calcd. for $C_{17}H_{24}O_{13}S$: C, 43.59; H, 5.17; S, 6.85%.

2-*O*-Mesyl-*myo*-inositol Pentaacetate.—To a stirred mixture of 37 mg. of 1, 3, 4, 5, 6-penta-*O*-acetyl-*myo*-inositol[16] and 0.5 ml. of pyridine, 0.1 g. of methanesulfonyl chloride was added. After it had stood overnight at room temperature, the mixture was poured into 1 ml. of cold water. The solution was then evaporated to dryness, and the residue was crystallized from ethanol to give 15 mg. of colorless needles melting at 190—192°C.

Found: C, 43.45; H, 5.35. Calcd. for $C_{17}H_{24}O_{13}S$: C, 43.59; H, 5.17%.

Hexaacetyl-*muco*-inosamine-1 (V).—a) A mixture of III (0.907 g.), sodium azide (0.255 g.) and 90% aqueous 2-methoxyethanol was refluxed for 16 hr. A brown mixture was evaporated under reduced pressure to dryness. The residue was dissolved in 10 ml. of ethanol, and an insoluble material was removed by filtration. The filtrate was then evaporated to give a brown oil, which showed an infrared absorption characteristic of an azide group at 2100 cm^{-1}. Then the oil was acetylated with acetic anhydride in pyridine to give an oily product (IV).

IV was hydrogenated in 20 ml. of ethanol over Raney nickel T4[17] under 50 p.s.i.g. of initial hydrogen pressure for 6 hr. After the catalyst had been removed,

16) E. L. May, ibid., **17**, 286 (1952).
17) S. Nishimura, This Bulletin, **32**, 61 (1959).

the filtrate was evaporated and the residue was acetylated with acetic anhydride in pyridine to yield 0.273 g. (32.3%) of crystals melting at 204°C after sintering at 190°C. Recrystallizations from methanol gave rhombic crystals of V melting at 205—205.5°C.

Found: C, 50.08; H, 5.97; N, 3.30. Calcd. for $C_{18}H_{25}NO_{11}$: C, 50.11; H, 5.84; N, 3.23%.

b) A mixture of II (1.02 g.), sodium azide (0.32 g.) and 90% aqueous 2-methoxyethanol was heated under reflux for 15 hr. The reaction mixture was then treated in the manner described above, giving 0.409 g. (39.2%) of crystals melting at 204—205°C after sintering at 197°C. Recrystallization from ethanol afforded crystals melting at 205—205.5°C.

c) A mixture of II (1.00 g.), sodium azide (1.00 g.) and 90% aqueous dimethylformamide was heated under reflux for 40 hr. The mixture was treated in the manner described above to give 0.26 g. (25%) of crude hexaacetyl-inosamine, m. p. 170—190°C. Fractional recrystallizations from a mixture of ethanol and ether gave 0.10 g. (9.6%) of V, m. p. 197—199°C. and 0.03 g. of an unidentified product (VII), m. p. *175—178°C.

When VII was mixed with an authentic sample of hexaacetyl-*roc*-inosamine-2, a remarkable depression of the melting point was observed.

IR: 3260, 1685, 1655, 1550 (amide), 1750 cm^{-1} (OAc).

Found: C, 49.95; H, 6.59; N, 3.43%.

After hydrolysis with 6 N hydrochloric acid, VII gave a single spot of R_f 0.26 in ascending paper chromatography in an ethyl acetate - pyridine - acetic acid - water (5 : 5 : 1 : 3) system[18] at 20°C (R_f of D-glucosamine hydrochloride: 0.35).

d) A mixture of III (7.08 g.) and 350 ml. of methanol saturated with ammonia was heated at 110°C for 24 hr. in an autoclave. After it had then been cooled, the mixture was evaporated in vacuo and the residue was acetylated with acetic anhydride (10 ml.) and sodium acetate (0.5 g.) at 100°C for 2 hr. to give a crude product. The product was recrystallized from ethanol to yield colorless crystals of V (2.52 g., 40.5%), m. p. 204.5—205°C. From the mother liquor, an unidentified product (0.22 g.), m. p. 192—218°C, was obtained.

N-Acetyl-*muco*-inosamine-1 (VI).—A 297 mg. portion of V was added to 25 ml. of methanol saturated with ammonia. The mixture was kept at room temperature overnight and evaporated under reduced pressure; a colorless oil was thus obtained. The product was washed with 5 ml. of ethyl acetate and crystallized from 90% ethanol to yield 118 mg. (77.7%) of colorless plate melting at 222—224°C. The second crop, m. p. 221.5—224°C (14 mg., 86.5%), was recovered from the mother liquor. Recrystallization from ethanol gave fine plates melting at 223—225°C.

Found: C, 43.55; H, 6.96; N, 6.37. Calcd. for $C_8H_{15}O_6N$: C, 43.43; H, 6.84; N, 6.33%.

1, 4, 5, 6-Tetra-*O*-acetyl-3-*O*-benzoyl-*myo*-inositol (VIII).—To a solution of 9.4 g. of I in 60 ml. of pyridine there was added, portion by portion, 3.5 ml. of benzoyl chloride at 5°C. The mixture was kept at room temperature for 20 hr. and then poured into 100 ml. of ice and water. The solution was extracted four times with chloroform (50 ml.), and the extracts were washed with water. After it had been dried over anhydrous sodium sulfate, the chloroform was evaporated in vacuo to give a crystalline residue. The crystals were washed with ethanol. The crude product (8.9 g., 73%) melted at *201.5—203°C. A second crop (1.3 g., 84%) was obtained from the washings. Recrystallization from ethanol afforded fine needles which melted at *202—203°C.

Found: C, 55.81; H, 5.26; Calcd. for $C_{21}H_{24}O_{11}$: C, 55.76; H, 5.35%.

1, 4, 5, 6-Tetra-*O*-acetyl-2-*O*-mesyl-3-*O*-benzoyl-*myo*-inositol (IX).—To a solution of 8.0 g. of VIII in 80 ml. of pyridine, 3.5 g. of methanesulfonyl chloride was added. The mixture was kept at room temperature for 2 days, and then poured into 300 ml. of ice and water. The precipitate was collected and washed with ethanol. The crude product weighed 8.0 g. (85%). Recrystallization from 2-methoxyethanol gave colorless rhombics (6.34 g., 67%) which melted at 240.5—242°C.

Found: C, 50.08; H, 5.07; S, 5.78. Calcd. for $C_{22}H_{26}O_{13}S$: C, 49.80; H, 4.94; S, 6.04%.

1-Azido-1-deoxy-*scyllo*-inositol Pentaacetate (X).—A mixture of 5.0 g. of IX, 2.0 g. of sodium azide and 170 ml. of 90% aqueous 2-methoxyethanol was refluxed for 20 hr. The brown mixture was evaporated under reduced pressure, and the residue was acetylated by heating it with acetic anhydride and pyridine at 100°C for 1 hr. After the solution had cooled, the insoluble material was removed and the filtrate was evaporated under reduced pressure to give a partly-crystallized residue. The residue was triturated with ethanol and filtered to yield 3.02 g. (77%) of crystals melting at *200—203°C. Recrystallization from ethanol gave colorless needles (2.04 g.) melting at *205—205.5°C.

Found: C, 46.57; H, 5.05; N, 9.78. Calcd. for $C_{16}H_{21}N_3O_{10}$: C, 46.26; H, 5.10; N, 10.12%.

Hexaacetyl-*scyllo*-inosamine (XI).—X (0.547 g.) was dissolved in glacial acetic acid (30 ml.) and hydrogenated at room temperature in a Parr shaker type apparatus at an initial pressure of 50 p.s.i.g. of hydrogen over Adams platinum oxide (33 mg.) for 13 hr. The catalyst was then removed, and the filtrate was evaporated in vacuo. The residual oil was treated with 10 ml. of pyridine - acetic anhydride (1 : 1) to give crude hexaacetyl-*scyllo*-inosamine (0.518 g., 91.3%) melting at *269—272°C with decomposition after sintering at 230°C. Recrystallization from 2-methoxyethanol gave colorless needles (0.397 g.) melting at *271—272°C with decomposition after coloring at 240°C. (Lit.[8,10] m. p. 275—276 and 288°C)

Found: C, 50.56; H, 5.79; N, 3.22. Calcd. for $C_{18}H_{22}NO_{11}$: C, 50.11; H, 5.84; N, 3.23%.

The NMR spectrum was superimposable upon that of an authentic sample.

N-Acetyl-*scyllo*-inosamine, m. p. *285—286°C (decomp), was prepared by an ordinary method of selective deacetylation [Lit.[10] m. p. 289—301°C (decomp.)].

1, 4, 5, 6-Tetra-*O*-acetyl-2, 3-di-*O*-benzoyl-*myo*-inositol.—A mixture of I (1 g.), benzoyl chloride (1 ml.) and pyridine (5 ml.) was heated on a boiling-water bath for 30 min. After it had been cooled, the mixture was diluted with cold water and the precipitate was collected and washed with water. The crude

18) F. G. Fischer and H. Dorfel, *Hoppe-Seyler's Z. physiol. Chem.*, **301**, 224 (1955).

product weighed 1.46 g. (91%) and melted at 157—163°C. The analytical sample was obtained by recrystallizations from methanol; it melted at 180.5—182°C.

Found: C, 60.31; H, 4.89. Calcd. for $C_{28}H_{28}O_{12}$: C, 60.43; H, 5.07%.

1, 4, 5, 6-Tetra-*O*-acetyl-2-*O*-benzoyl-3-*O*-mesyl-*myo*-inositol.—A mixture of II (0.408 g.), benzoyl chloride (0.5 ml.) and pyridine (5 ml.) was treated similarly to give 0.285 g. (56%) of crystals melting at 150—153°C. The analytical sample was obtained by recrystallization from ethanol m. p. *152—154.5°C, 154—155.5°C.

Found: C, 49.66; H, 5.00; S, 6.17. Calcd. for $C_{22}H_{26}O_{13}S$: C, 49.80; H, 4.94; S, 6.04%.

2, 3-Di-*O*-mesyl-*myo*-inositol Tetraacetate (XII).—To a solution of 1.0 g. of I in 10 ml. of pyridine, 1.3 g. of methanesulfonyl chloride was added under ice cooling. The mixture was treated in the manner described for II to give 1.25 g. (87.5%) of the product, m. p. *205.5—209°C. Recrystallizations from ethanol afforded 1.12 g. (78.5%) of needles, m. p. *211—213°C.

Found: C, 38.34; H, 4.98; S, 12.48. Calcd. for $C_{16}H_{24}O_{14}S_2$: C, 38.10; H, 4.80; S, 12.72%.

A mixed melting point determination with II showed a remarkable depression.

Hexaacetyl-*muco*-inosadiamine-1, 5 (XIV). — a) A mixture of XII (2.06 g.), sodium azide (1.05 g.) and 95% aqeous 2-methoxyethanol (75 ml.) was refluxed for 19 hr. The mixture was then treated in the manner described for V a) to give 193 mg. of the crude product, m. p. *282—283°C (decomp.). Recrystallizations from ethanol afforded 134 mg. (7.6%) of the crystals, m. p. *305—306°C.

Found: C, 50.14; H, 6.22; N, 6.50. Calcd. for $C_{18}H_{26}N_2O_{10}$: C, 50.23; H, 6.09; N, 6.51%.

No other crystalline isomer could be obtained from the mother liquor.

b) A mixture of XII (3.0 g.) and methanol (180 ml.) which had previously been saturated with ammonia was heated in an autoclave at 110°C for 20 hr. Then the reaction mixture was treated in the manner described for V c) to give 646 mg. (25.0%) of the crude XIV, m. p. *292.5—294.5°C (decomp.). Recrystallizations from ethanol gave 438 mg. (16.9%) of colorless needles, which melted at *306.5—307°C.

Di-*N*-acetyl-*muco*-inosadiamine-1, 5 (XV).—XIV (100 mg.) was selectively deacetylated by the ordinary method described for VI to give 66 mg. of the crude product of XV, m. p. 235—237°C. Recrystallization from aqueous alcohol gave 43 mg. (71%) of colorless plates, m. p. 238.5—239°C.

Found: C, 45.25; H, 7.09; N, 10.38. Calcd. for $C_{10}H_{18}N_2O_6$: C, 45.79; H, 6.92; N, 10.68%.

Periodate Oxidation.—A 21.9 mg. portion of XV was treated with 25 ml. of a 0.0301 M sodium metaperiodate solution at 15°C. Iodometric titrations with sodium arsenite[19] showed that 2.18 mol. of periodate was consumed per mole of XV in 43 hr.

***muco*-Inosadiamine-1, 5 Dihydrochloride.**—XIV (300 mg.) was heated in 6 N hydrochloric acid on a boiling water bath for 1.5 hr. The solution was then evaporated under reduced pressure to give a crystalline residue. The residue was recrystallized from a mixture of methanol and ethanol to give 175 mg. (60.6%) of crystals melting at *300°C (decomp.) after coloring at 260°C.

Found: C, 29.24; H, 6.28; N, 10.74; Cl, 27.83. Calcd. for $C_6H_{14}N_2O_4 \cdot 2HCl$: C, 28.70; H, 6.42; N, 11.15; Cl, 28.24%.

Hexaacetyl-*myo*-inosadiamine-1, 2 (XVII). — A mixture of XII (5.0 g.), sodium azide (3.0 g.) and 80% aqueous dimethylformamide (120 ml.) was refluxed for 18 hr. The reaction mixture was then evaporated under reduced pressure and extracted with ethanol (30 ml. × 3). The extracts were evaporated in vacuo to dryness, pyridine - acetic anhydride (1 : 1) (50 ml.) was added, and the mitture was kept at room temperature overnight. The insoluble material was removed, and the solution was evaporated under reduced pressure to give an oil. This oil was dissolved in ethanol (20 ml.) and kept in a refrigerator overnight. The precipitate (the starting material) was filtered off and treated again with toluene (20 ml.) in a similar manner. The filtrate was evaporated, and the residual oil was dissolved in ethanol (20 ml.) containing Adams platinum oxide (100 mg.). The mixture was hydrogenated at room temperature in a Parr shaker-type apparatus at an initial pressure of 50 p.s.i.g. of hydrogen for 20 hr. The catalyst was filtered off, and the filtrate was evaporated. The residual oil was treated again with pyridine-acetic anhydride (1 : 1) (10 ml.) and crystallized from ethanol/ether to give the crude product (152 mg.), which melted at *270—274°C with decomposition after sintering at 260°C. The second crop was obtained from the mother liquor, 123 mg., melting at *250—262°C with decomposition after sintering at 245°C. The total yield was 6.4%. The crude product was recrystallized from ethanol with carbon to give colorless needles (151 mg.) which melted at *275—277°C with decomposition after sintering at 267°C.

Found: C, 50.14; H, 6.18; N 6.67. Calcd. for $C_{18}H_{26}N_2O_{10}$: C. 50.23; H, 60.9; N, 6.51%.

Di-*N*-acetyl-*myo*-inosadiamine-1, 2 (XVIII). — XVII (150 mg.) was treated in the manner described for XV to give 85.9 mg. (94.1%) of crystals, m. p. 262—264°C The analytical sample was obtained, by recrystallization from a mixture of ethanol, ether and water, as plates melting at 270—271°C.

Found: C, 45 62; H, 6.85; N, 10.47. Calcd. for $C_{10}H_{18}N_2O_6$: C, 45.79; H, 6.92; N, 10.68%.

Periodate Oxidation. — A 25.1 mg. portion of XVIII was dissolved in 50 ml. of a 0.0301 M sodium metaperiodate solution at 15°C. Iodometric titrations with sodium arsenite[17] showed that 3.30 mol. of periodate was consumed per mole of XVIII in 43 hr.

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19) J. M. Bobbitt, "Advances in Carbohydrate Chemistry," Vol. XI, Academic Press, New York (1956), pp. 1—41.