Aminocyclitols. XXIX. Synthesis of Inosadiamines *via* 1,3-Biimino-1,3-dideoxy-inositols[1]

Tetsuo SUAMI, Seiichiro OGAWA, Hayashi UCHINO, and Masaru UCHIDA

Department of Applied Chemistry, Faculty of Engineering, Keio University, Hiyoshi, Yokohama 223

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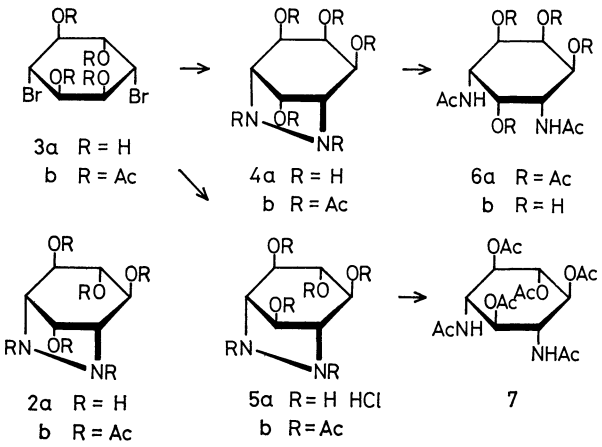
Hydrazinolysis of DL-1,4-dibromo-1,4-dideoxy-*chiro*-inositol (**3a**), followed by catalytic hydrogenation and acetylation, afforded di-*N*-acetyl-tetra-*O*-acetyl-*neo*-inosadiamine-1,3 (**6a**) and -*scyllo*-inosadiamine-1,3 (**7**) in 18% and 24% yields, respectively. From the intact hydrazinolyzate of **3a**, two new stereoisomeric 1,3-biimino-1,3-dideoxy-inositols (**4a** and **5a**) could be isolated, and their structures were established by correlating to the corresponding inosadiamines. A similar hydrazinolysis of 3,6-di-*O*-*p*-tolylsulfonyl-*muco*-inositol (**12**) gave sole crystalline 1,3-biimino compound (**13a**), whose structure was followed from its conversion into known di-*N*-acetyl-tetra-*O*-acetyl-*myo*-inosadiamine-4,6 (**14**). PMR spectra of four 1,3-biimino compounds were discussed.

We described a convenient synthesis of a biologically useful aminocyclitol, *myo*-inosadiamine-1,3, by hydrazinolysis of 1,3-di-*O*-*p*-tolylsulfonyl-*myo*-inositol (**1**) followed by hydrogenation.[2] The formation of 6,7-diazabicyclo[3.2.1]octane-2,3,4,8-tetrol (**2a**) of *myo*-configuration, which may be termed 1,3-biimino-1,3-dideoxy-*myo*-inositol,[3] was demonstrated by isolation of the free base. The synthesis seems to provide a convenient method for preparing an unaccessible inosadiamine having two amino groups in *cis*-1,3-positions from readily available di-*O*-*p*-tolylsulfonyl- or dihalodideoxy-inositol. On the other hand, the use of mono- or di-alkyl hydrazine gave *N*-alkyl- or di-*N*-alkyl-inosadiamine, *viz.*, *N*-methyl-*myo*-inosadiamine-1,3 and actinamine.[5]

In the present paper, we wish to report the synthesis of three new stereoisomers of 1,3-biimino-1,3-dideoxy-inositol and their conversion into the corresponding inosadiamines. In order to demonstrate the reaction mechanism of the hydrazinolysis, displacement reactions with azide ion were also studied.

Firstly, the hydrazinolysis of DL-1,4-dibromo-1,4-dideoxy-*chiro*-inositol (**3a**)[6] obtained by a drastic bromination reaction of *epi*-inositol was investigated. On treatment with hydrazine, two epoxide intermediates are expected to be formed by participation of vicinal *trans*-situated hydroxyl groups, since **3a** has two bromine atoms in *cis*-1,4 positions; this may satisfy the steric requirement for formation of a 1,3-biimino bridge. When **3a** was treated with excess hydrazine in boiling 2-methoxyethanol and the hydrazinolyzate was then subjected to hydrogenation and acetylation, di-*N*-acetyl-tetra-*O*-acetyl-*neo*-inosadiamine-1,3 (**6a**) and -*scyllo*-inosadiamine-1,3 (**7**) were isolated in 18 and 24% yields, respectively. The former was further characterized by conversion into its di-*N*-acetyl derivative (**6b**). The structure of **6a** was established by the following spectral evidence. The PMR spectrum of **6a** in dimethylsulfoxide-d_6 (DMSO-d_6) revealed six acetyl methyl protons as four singlets (2 : 2 : 1 : 1) at τ 8.27, 8.06, 7.90, and 7.88, which according to Lichtenthaler *et al.*,[7] can be readily assigned to two equatorial acetamido, and two equatorial, one axial and one axial acetoxy groups, respectively. On addition of deuterium oxide (D_2O) 2-proton sextet at τ 5.66 collapsed to a quartet (J=2.7 and 12 Hz), indicating that the signal was due to two magnetically equivalent protons at C–1 and C–3. Accordingly, the 2-proton quartet at τ 5.00 was assigned to the equivalent protons at C–4 and C–6, and the two narrow triplets (J=2.7 Hz) at τ 4.67 and 4.34 to H–2 and H–5, respectively. The structure of **6a** was thus fully established.

On the other hand, the reaction of **3a** or its acetyl derivative (**3b**) with sodium azide in aqueous 2-



Scheme 1.

1) Presented at the 25th Annual Meeting of the Chemical Society of Japan Tokyo, 12th October 1971.

2) T. Suami and S. Ogawa, This Bulletin, **40**, 1295 (1967); T. Suami, S. Ogawa, Y. Naito, and H. Sano, *J. Org. Chem.*, **33**, 2831 (1968).

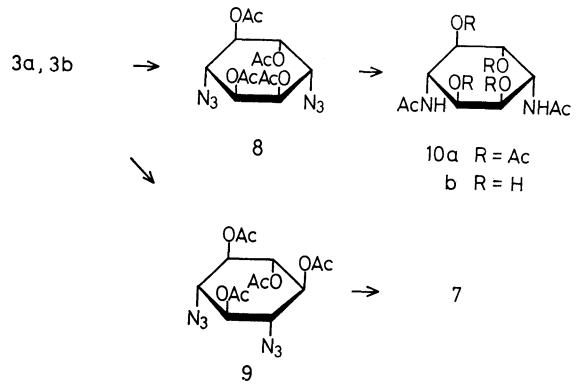
3) According to the *R,S*-notation of configuration,[4] compound **2a** should be named 6,7-diazabicyclo[3.2.1]octane-2*R*,3*R*,4*S*,8*S*-tetrol. Since this designation lacks derivational perspicuity and is somewhat cumbersome, we prefer, for the sake of simplicity, the designation 1,3-biimino-1,3-dideoxy-*myo*-inositol for **2a**, retaining the respective configuration prefix of the basal inositol. Similarly, **4a** of 2*R*,3*S*,4*S*,8*S* configuration is termed 1,3-biimino-1,3-dideoxy-*neo*-inositol; **5a** (2*R*,3*R*,4*S*,8*R*)=1,3-biimino-1,3-dideoxy-*scyllo*-inositol; **13a** (2*R*,3*S*,4*S*,8*R*)=4,6-dideoxy-4,6-biimino-*myo*-inositol.

4) R. S. Cahn, C. K. Ingold, and V. Prelog, *Experientia*, **12**, 81 (1956); *Angew. Chem. Int. Ed. Engl.*, **5**, 385 (1966).

5) T. Suami, S. Ogawa, and H. Sano, This Bulletin, **43**, 1843 (1970).

6) T. Suami, S. Suzuki, M. Uchida, and S. Yanagida, *ibid.*, **42**, 2672 (1969).

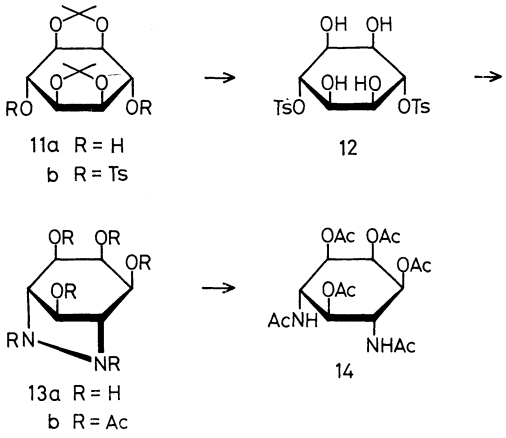
7) F. W. Lichtenthaler and P. Emig, *Carbohyd. Res.*, **7**, 121 (1968); F. W. Lichtenthaler, G. Bambach, and P. Emig, *Chem. Ber.*, **102**, 994 (1969).



Scheme 2.

methoxyethanol under reflux followed by acetylation afforded tetra-*O*-acetyl-diazidodideoxy-*chiro*-inositol (**8**) in 68% yield, together with a small amount of tetra-*O*-acetyl-1,3-diazido-1,3-dideoxy-*scyllo*-inositol (**9**)[8] which was characterized by conversion into **7**. Hydrogenation of **8** and subsequent acetylation afforded hitherto unknown di-*N*-acetyl-tetra-*O*-acetyl-inosadiamine (**10a**) which was further converted into the di-*N*-acetyl derivative (**10b**). From the reaction sequence, the formation of **9** as the minor product suggested that the major diazidodideoxy-inositol should have 1,2- or 1,4-*chiro*-configuration. The physical and spectral properties of the former[9] were found to be quite different from those of **8**. In the PMR spectrum of **8** in deuteriochloroform ($CDCl_3$), the pattern of the signals due to the ring protons were shown to be substantially similar to those of **3b**.[6] The PMR spectrum of **10a** in DMSO-d_6 revealed four singlets (1 : 1 : 3 : 1) in the vicinity of τ 8; one equatorial (τ 8.22) and one axial (τ 8.11) acetamido groups, and three equatorial (τ 8.08) and one axial (τ 7.98) acetoxy groups, suggesting *chiro*-configuration.[7] Thus the structure of **8** was tentatively assigned to DL-tetra-*O*-acetyl-1,4-diazido-1,4-dideoxy-*chiro*-inositol. The preferential diaxial attack of azide ion at the intermediary epoxides can be assumed to be the prevailing mechanism for this azidolysis reaction.

The course of the nucleophilic displacement by hydrazine evidently differs from that of azide ion, and, the formation of a biimino bridge might be proposed in the hydrazinolysis of **3a**. Isolation of these anticipated intermediates was thus attempted. The crude hydrazinolyzate of **3a** was treated with Amberlite IRA-400 (OH^-) and successive treatment with aqueous ethanol gave the crystalline 1,3-biimino compound (**4a**) in 15% yield. From the mother liquor of **4a** upon acetylation, a small amount (1%) of di-*N*-acetyl-tetra-*O*-acetyl-1,3-biimino compound (**5b**) could be isolated, which afforded a monohydrochloride (**5a**) in 85% yield on hydrolysis with 3 M hydrochloric acid. Acetylation of **4a** in the usual way gave the hexaacetyl derivative (**4b**) which was found to differ entirely from **5b**. Neither **4b** nor **5b** showed any absorption in the amide II region in IR or a signal due to NH-protons in PMR spectra. Hydrogenation of **4a** followed by acetylation afforded **6a** in 73% yield. The PMR spectra of **4a** and **5a** (free base) in D_2O also supported the proposed structure. Consequently, the configuration of 1,3-biimino-1,3-dideoxy-inositol (**4a**) is unambiguously established to be *neo*- (2*R*, 3*S*, 4*S*, 8*S*), whilst **5a** is conclusively assigned to *scyllo*-configuration (2*R*, 3*R*, 4*S*, 8*R*).



Scheme 3.

Hydrazinolysis of 3,6-di-*O*-*p*-tolylsulfonyl-*muco*-inositol (**12**) was then carried out. Compound **12** was prepared from 1,2 : 4,5-di-*O*-isopropylidene-*muco*-inositol (**11a**)[10] by a reaction sequence involving *p*-toluenesulfonylation and de-*O*-acetylation (**11a**→**11b**→**12**). A similar treatment of **12** with hydrazine gave the sole crystalline 1,3-biimino compound (**13a**) in 52% yield. Acetylation of **13a** gave the hexaacetyl derivative (**13b**) in 73% yield, whose IR and PMR spectra showed a presence of a secondary amido group. Hydrogenation of **13a** and the subsequent acetylation afforded di-*N*-acetyl-tetra-*O*-acetyl-*myo*-inosadiamine-4,6 (**14**)[11] in 43 % yield. Thus the structure of **13a** was readily assigned to *myo*-configuration (2*R*, 3*S*, 4*S*, 8*R*).

The reaction of the corresponding dimesylate, 3,6-di-*O*-methylsulfonyl-*muco*-inositol, with excess sodium azide gave, by preferential diaxial cleavage of the intermediate epoxide, 3,6-diazido-3,6-dideoxy-*muco*-inositol almost exclusively.[12] In the case of hydrazinolysis, on the contrary, the hydrazino group introduced previously attacks the second epoxide intermolecularly to form a 1,3-biimino bridge.

PMR Spectra. The PMR spectra of the three stereoisomeric 1,3-biimino-1,3-dideoxy-inositols (**4a**, **5a**, and **13a**) together with **2a** were discussed. Since all the molecules have a plane of symmetry, the H-1 and H-5, and H-2 and H-4 protons are magnetically equivalent thus simplifying the interpretation of the signals. In **2a**, **4a**, and **5a**, a first-order analysis was successfully applied to interpret the signals from the ring protons. In **13a**, however, the signals due to

8) This compound could not be isolated in a crystalline state.
9) N. Kurihara, T. Kurokawa, and M. Nakajima, *Agr. Biol. Chem.* (Tokyo), **31**, 1166 (1967).
10) S. J. Angyal and R. M. Hoskinson, *J. Chem. Soc.*, **1962**, 2985.
11) T. Suami and S. Ogawa, This Bulletin, **38**, 2026 (1965); **40**, 1925 (1967).
12) T. Suami, F. W. Lichtenthaler, and S. Ogawa, *ibid.*, **40**, 1488 (1967).

TABLE 1. CHEMICAL SHIFTS OF 1,3-BIIMINO-1,3-DIDEOXY-INOSITOL[a)]

Compound	H-1,5	H-2,4	H-3	H-8
2a	6.72(d)	6.32(t)	6.54(t)	5.38(s)
4a	6.47(d)	5.93(t)	6.18(t)	5.12(s)
5a	6.77(d)	6.48(t)	5.81(t)	5.58(t)
13a	6.43(t)	5.94(m)	5.94(m)	5.57(t)

a) Measured at 60 MHz in D_2O with sodium 3-(trimethylsilyl)-1-propanesulfonate as an internal reference. Chemical shifts are given in terms of τ-values, the signals being denoted by s (singlet), d (doublet), t (triplet), and m (complex multiplet).

TABLE 2. COUPLING CONSTANTS OF 1,3-BIIMINO-1,3-DIDEOXY-INOSITOL[a)]

Compound	$J_{1,2}$ ($J_{4,5}$)	$J_{1,8}$ ($J_{5,8}$)	$J_{2,3}$ ($J_{3,4}$)	$J_{2,8}$
2a	2.0	0	4.2	0
4a	5.0	0	4.7	0
5a	~1.0	4.7	6.6	~1.0
13a	4.0	4.7	—	~1.0

a) Values (Hz) are of first-order.

H-2, H-3, and H-4 protons overlapped to give rise to a complex multiplet (Tables 1 and 2).

Assignment of the configuration of the hydroxyl group at C-8 was based on the following results. The H-8 proton appeared as a triplet (J=4.7 Hz) at τ 5.58 and 5.57 in **5a** and **13a**, respectively, which shows that the dihedral angle $\phi_{1,8}$ and $\phi_{5,8}$ would approach 40°. The sharp singlets at τ 5.38 and 5.12 in **2a** and **4a**, respectively, could be assigned to H-8 protons, indicating that the dihedral angles $\phi_{1,8}$ and $\phi_{5,8}$ were nearly 90°.[13] In this case the *cisoid* protons (axial) resonated at lower field than the *transoid* protons (equatorial). The former might have been strongly deshielded by two axial hydroxyls at C-2 and C-4.[14,15]

In the PMR spectrum of **4a** (Fig. 1), the 2H-triplet at τ 5.94, 1H-triplet at τ 6.18, and 2H-doublet at τ 6.47 were assigned to H-2 and H-4, H-3, and H-1 and H-5, respectively. The observed coupling constants of $J_{1,2}$ and $J_{2,3}$ corresponded to the dihedral angles $\phi_{1,2}$ (45°) and $\phi_{2,3}$ (45°), which were derived from a molecular model of **4a**, the chair conformation being slightly distorted by incorporation of the 1,3-biimino bridge.[16] The coupling constants were shown to be in good accordance with the corresponding values of 1,5-lactone of (−)-quinic acid ((−)-quinide).[15]

However a remarkable flattening of the chair conformation was deduced from the PMR spectra, when three axial hydroxyl groups were located at C-2, C-3,

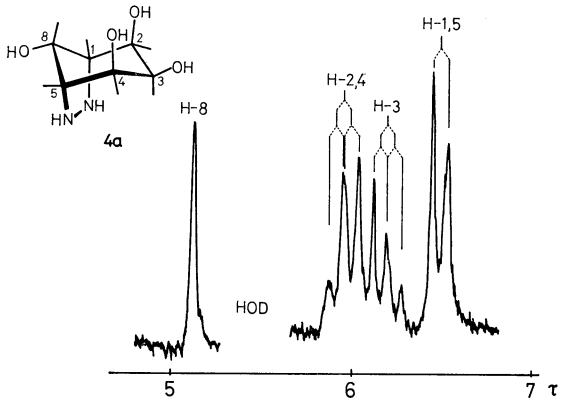


Fig. 1. Partial PMR spectrum (D_2O) of 1,3-biimino-1,3-dideoxy-*neo*-inositol (**4a**).

and C-4. In the PMR spectrum of **2a**, the small value of $J_{1,2}$ (2.0 Hz) may be rationalized by such a distortion that would increase the dihedral angles $\phi_{1,2}$ and $\phi_{2,3}$. Since $J_{1,2}$ was found to accord with the corresponding value of 3,4-*O*-isopropylidene-(−)-quinide,[15] the dihedral angle $\phi_{1,2}$ is likely to be nearly 60°.

In the case of **5a** having three axial substituents on both sides of the cyclohexane ring, a very small $J_{1,2}$ (less than 1.0 Hz) was observed, while $J_{2,3}$ (6.6 Hz) seems to indicate that the six-membered ring exists in a flattened boat conformation rather than in a chair form. The evidence for this can be deduced from the down-field shift of H-3 (τ 5.18) as compared with that of **2a** (τ 6.54), since the difference can be attributed to considerable deformation of the ring conformation with respect to carbons C_2–C_3–C_4. The non-bonded interaction between three axial hydroxyl groups at C-2, C-4, and C-8 was presumably sufficient to cause the six-membered ring to exist in this conformation.

A long range coupling ($J_{2,8}$ and $J_{4,8}$) was observed in **5a** and **13a**, which could be substantially accounted for by W-letter rule.[17]

On the other hand, the PMR spectra of the hexaacetyl derivatives of 1,3-biimino-1,3-dideoxy-inositols were expected to be complex owing to the hindered rotation of acetamido groups.[18] In **2b** and **4b**, the symmetry of the molecules was to some extent lost, and the six ring protons revealed individual signals.

The PMR spectrum of **4b** (Fig. 2) was interpreted as follows. By analogy with the assignment of the PMR spectrum of **4a**, the singlet at τ 4.12 and the triplet (J=5.0 Hz) at τ 5.02 could be assigned to H-8 and H-3 protons, respectively. Irradiation at the triplet (J=5.0 Hz) at τ 4.25 simplified the H-3 triplet to a doublet, and the doublet (J=5.0 Hz) at τ 5.30 to a singlet. Consequently, the triplet at τ 4.25 was assigned to H-2 (H-4) and the doublet at τ 5.30 to H-1 (H-5). The complex multiplet centered at τ 4.60

13) A. C. Oehlsclager and L. H. Zalkow, *J. Org. Chem.*, **30**, 4205 (1965); C. W. Jefford, B. Waegell, and K. Ramey, *J. Amer. Chem. Soc.*, **87**, 2191 (1965).

14) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day Inc. (1964), pp. 183—191.

15) E. Haslam and M. J. Turner, *J. Chem. Soc., C*, **1971**, 1496.

16) M. Karplus, *J. Amer. Chem. Soc.*, **85**, 2870 (1963). The dihedral angles were measured by using Buchi's Dreiding-stereomodels.

17) L. M. Jackman and S. Sternhell, "Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press 2nd Ed. (1969), p. 334.

18) H. Paulsen and K. Todt, *Advan. Carbohyd. Chem.*, **23**, 115 (1968).

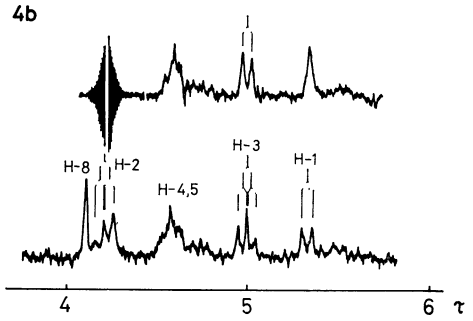


Fig. 2. Partial PMR spectrum ($CDCl_3$) of di-*N*-acetyl-tetra-*O*-acetyl-1,3-biimino-1,3-dideoxy-*neo*-inositol (**4b**), measured on a Varian Associates HA-100D (100 MHz) spectrometer.

should be attributed to H-4 (H-2) and H-5 (H-1) protons. We see from comparison with their counterparts that H-2 (H-4) and H-5 (H-1) protons are markedly deshielded (0.70 and 0.35 ppm, respectively) by the amide carbonyl groups most probably in a *cis*-relationship to them. Thus, it was deduced that the planes of two-secondary acetamido groups were somewhat twisted from that of the biimino ring due to the repulsion between the amido methyl groups.

No influence of the hindered rotation of acetamido groups was observed in the PMR spectrum of **5b**. This might be due to the existence of a rotamer having a plane of symmetry resulting from the deformation of the cyclohexane ring.

Experimental

Melting points were determined on a Mitamura Riken micro hot stage and are uncorrected. IR spectra were measured on a Jasco IR-E spectrophotometer in KBr disks. PMR spectra were measured on Varian Associates A-60D (60 MHz) and HA-100D (100 MHz) spectrometer at a concentration of approximately 10% deuteriochloroform ($CDCl_3$), deuterium oxide (D_2O), or dimethylsulfoxide-d_6 (DMSO-d_6), with tetramethylsilane or sodium 3-(trimethylsilyl)-1-propanesulfonate, respectively, as internal standard. Chemical shifts are given in terms of τ-values, and signals being denoted by s (singlet), d (doublet), t (triplet), dd (double doublet), or m (complex multiplet). Values given for coupling constants are of first-order. All solutions were concentrated by a rotary evaporator at 40—50 °C under reduced pressure.

Hydrazinolysis of DL-*1,4-dibromo-1,4-dideoxy*-chiro-*inositol* (**3a**). *Preparation of di*-N-*acetyl-tetra*-O-*acetyl*-neo-*inosadiamine-1,3* (**6a**) *and* -scyllo-*inosadiamine-1,3* (**7**). A mixture of **3a** (1.00 g), anhydrous hydrazine (0.50 ml), and 2-methoxyethanol (50 ml) was refluxed for 90 min and the solution was evaporated to dryness. The residue was dissolved in water (50 ml) and, after treatment with Amberlite IRA-400 (OH^-) (10 ml), the solution was hydrogenated in the presence of Adam's platinum catalyst (50 mg) in a Parr shaker type apparatus (under 3.4 kg/cm² of initial hydrogen pressure) for 20 hr at room temperature. The catalyst was filtered off and the filtrate was evaporated to dryness. The residue was treated with acetic anhydride (5 ml) and pyridine (5 ml) overnight at room temperature. The reaction mixture was evaporated and the crude mixture was fractionated by crystallization from ethanol. The first crystals (0.40 g, 23.5%) were identified as **7** by the mode of melting (mp 245—249 °C with transition) and a comparison of its IR spectra with that of an authentic sample.[19] Crystals (0.31 g, 18%) of **6a** were then isolated, mp 280—285 °C. An analytical sample was obtained by further recrystallization from ethanol, mp 282—285 °C. IR: 3300, 1660, 1555 (NHAc), and 1755 cm^{-1} (OAc), PMR data are in the text.

Found: C, 50.44; H, 6.32; N, 6.39%. Calcd for $C_{18}H_{26}N_2O_{10}$: C, 50.23; H, 6.09; N, 6.51%.

Di-N-*acetyl*-neo-*inosadiamine-1,3* (**6b**). Compound **6a** (150 mg) was treated with methanolic ammonia (15 ml) overnight at room temperature. The mixture was evaporated to give a crystalline residue which was crystallized from 90% aqueous ethanol to give an analytical sample (60 mg, 68%) of **6b**, mp 313 °C (dec.). IR: 1635 and 1555 cm^{-1} (NHAc).

Found: C, 43.10; H, 7.22; N, 9.90%. Calcd for $C_{10}H_{18}N_2O_6 \cdot H_2O$: C, 42.88; H, 7.14; N, 10.00%.

Azidation Reaction of **3a** *or* **3b**. *Preparation of* DL-*Di*-N-*acetyl-tetra*-O-*acetyl-1,4-diazido-1,4-dideoxy*-chiro-*inositol* (**8**) *and* (**7**). A mixture of DL-tetra-*O*-acetyl-1,4-dibromo-1,4-dideoxy-*chiro*-inositol (**3b**)[4] (1.00 g), sodium azide (1.40 g), and 90% aqueous 2-methoxyethanol (50 ml) was refluxed for 25 hr. The mixture was then evaporated and dried by codistillation with dry toluene several times. The residue was treated with acetic anhydride (20 ml) and pyridine (20 ml) overnight at room temperature. An insoluble material was removed by filtration and the filtrate was evaporated to give an oily product, which was extracted with chloroform and purified by a short column of active aluminum oxide. The solvent was evaporated and the crude product was crystallized from ethanol to afford colorless needles (0.89 g, 68%) of **8**, mp 109—113 °C. Recrystallization from ethanol gave an analytical sample, mp 112—114 °C. IR: 2150 (N_3), and 1750 cm^{-1} (OAc). PMR ($CDCl_3$): τ 7.95 (3, s, OAc), 7.91 (6, s, 2OAc), 7.84 (3, s, OAc), 6.18 (1, t, H-4, J=10.5 Hz), and 4.96 (1, dd, H-5, J=3 and 10.5 Hz).

Found: C, 42.46; H, 4.59; N, 20.85%. Calcd for $C_{14}H_{18}N_6O_8$: C, 42.21; H, 4.59; N, 21.10%.

The mother liquor of **8** was evaporated and the residue was hydrogenated in an ethanol solution (20 ml) in a similar way to that for **6a**. The hydrogenate was acetylated in the usual way to give colorless needles (28 mg, 1.9%) of **7**, mp 240—245 °C, after crystallization from ethanol. This compound was identified with an authentic sample[18] by comparison of IR spectra and mixed melting point.

Almost the same result was obtained from **3a**.

DL-*Di*-N-*acetyl-tetra*-O-*acetyl*-chiro-*inosadiamine-1,4* (**10a**). A solution of **8** (0.54 g) in ethanol (50 ml) was hydrogenated in a similar way to that for **6a** for 15 hr. The catalyst was filtered off and filtrate was evaporated to dryness.

The residual product was acetylated in the usual way to give colorless needles (0.58 g, 77%) of **10a**, mp 120—126 °C. Recrystallization from acetone gave a hygroscopic crystals, mp 127—129 °C. IR: 3280, 1655, 1545 (NHAc), and 1750 cm^{-1} (OAc). PMR (DMSO-d_6): τ 2.55 (1, d, equatorial NHAc, J=9 Hz) and 1.68 (1, d, axial NHAc, J=8 Hz).

Found: C, 49.64; H, 6.14; N, 6.08%. Calcd for $C_{18}H_{26}N_2O_{10} \cdot 1/2H_2O$: C, 49.20; H, 6.19; N, 6.38%.

DL-*Di*-N-*acetyl*-chiro-*inosadiamine-1,4* (**10b**). Compound **10a** (0.20 g) was treated with methanolic ammonia (30 ml) overnight at room temperature. The solution was then evaporated to give a crystalline residue which was recrystallized from 95% ethanol to afford colorless needles (90 mg, 74%) of **10b**, mp 254—256 °C. IR: 3480, 1630,

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

1580, and 1560 cm^{-1} (NHAc). PMR (D_2O): τ 7.97 (6, s, 2 NHAc).

Found: C, 46.00; H, 7.23; N, 10.36%. Calcd for $C_{10}H_{18}N_2O_6$: C, 45.79; H, 6.92; N, 10.63%.

1,3-Biimino-1,3-dideoxy-neo-*inositol* (**4a**) *and Di*-N-*acetyl-tetra*-O-*acetyl-1,3-biimino-1,3-dideoxy*-scyllo-*inositol* (**5b**). A mixture of **3a** (2.00 g), anhydrous hydrazine (1.6 ml), and 2-methoxyethanol (100 ml) was refluxed for 2 hr, and the mixture was evaporated to dryness. The residue was dissolved in water (30 ml) and treated with Amberlite IRA-400 (OH^-) for 5 hr. The solution was evaporated and the oily residue was crystallized from water–ethanol to afford crystals (0.17 g, 14.8%) of **4a**, mp 208 °C (dec.).

Found: C, 41.11; H, 6.79; N, 15.70%. Calcd for $C_6H_{12}N_2O_4$: C, 40.91; H, 6.87; N, 15.90%.

The mother liquor of **4a** was evaporated to dryness and the residue was treated with acetic anhydride (5 ml) and pyridine (5 ml) overnight at room temperature. The mixture was evaporated and the product was crystallized from ethanol–ether to give crystals (26 mg, 1%) of **5b**, mp 213 °C. IR: 1755, 1720 (OAc), and 1680 cm^{-1} (NAc).

Found: C, 50.68; H, 5.56; N, 6.45%. Calcd for $C_{18}H_{24}N_2O_{10}$: C, 50.47; H, 5.65; N, 6.54%.

Di-N-*acetyl-tetra*-O-*acetyl-1,3-biimino-1,3-dideoxy*-neo-*inositol* (**4b**). A 20 mg-portion of **4a** was acetylated with acetic anhydride (1.5 ml) and pyridine (1.5 ml) overnight at room temperature. The product was crystallized from ethanol–ether to give crystals (15 mg, 31%) of **4b**, mp 161—162 °C. IR: 1745 (OAc), and 1635 cm^{-1} (NAc). PMR data are in the text.

Found: C, 50.49; H, 5.94; N, 6.18%. Calcd for $C_{18}H_{24}N_2O_{10}$: C, 50.47; H, 5.65; N, 6.54%.

1,3-Biimino-1,3-dideoxy-scyllo-*inositol* (**5a**). A mixture of **5b** (120 mg) and 3M-hydrochloric acid (20 ml) was refluxed for 2 hr, and the mixture was evaporated to give a glassy residue, which crystallized upon addition of aqueous ethanol to afford monohydrochloride of **5a** (51 mg, 85%), mp 147—149 °C.

Found: C, 33.55; H, 6.29; N, 12.83%. Calcd for $C_6H_{12}N_2O_4 \cdot HCl$: C, 33.89; H, 6.16%; N, 13.17%.

PMR spectrum was measured for a free base which was obtained from monohydrochloride by treatment of the aqueous solution with Amberlite IRA-400 (OH^-).

Preparation of **6a** *from* **4a**. A solution of **4a** (20 mg) in water (3 ml) was hydrogenated similarly in the presence of Adams' platinum catalyst (10 mg) overnight. The product was acetylated in the usual way to give crystals (35 mg, 73%) of **6a**, which was identified with the product obtained before by comparison of their IR spectra.

1,2 : 4,5-Di-O-*isopropylidene-3,6-di*-O-p-*tolylsulfonyl*-muco-*inositol* (**11b**). To a solution of 1,2 : 4,5-di-*O*-isopropylidene-*muco*-inositol (**11a**)[8] (1.00 g) in dry pyridine (15 ml) was added *p*-toluenesulfonyl chloride (3.8 g, 5 equiv.) and the mixture was allowed to stand at room temperature for 20 hr. After being heated over a boiling water bath for 90 min, the mixture was poured into ice and water (70 ml). The resulting crystals were collected by filtration, washed with water and dried. The crude crystals weighed 1.85 g (82%), mp 213—220 °C. Recrystallization from 2-methoxyethanol afforded an analytical sample, mp 233—234 °C. PMR ($CDCl_3$): τ 8.83 and 8.61 (6 and 6, s, 2 isopropylidene C–CH_3), 7.56 (6, s, 2 OTs C–CH_3).

Found: C, 55.32; H, 5.89; S, 11.61%. Calcd for $C_{26}H_{32}O_{10}S_2$: C, 54.91; H, 5.67; S, 11.28%.

3,6-Di-O-p-*tolylsulfonyl*-muco-*inositol* (**12**). Compound **11b** (1.20 g) was treated with boiling 90% aqueous acetic acid (30 ml) for 2 hr. The mixture was then evaporated to give a crystalline residue. The crystals were collected by triturating with ethanol: yield 0.83 g (81%), mp 221—224 °C. Recrystallization from 2-methoxyethanol afforded an analytical sample, mp 223.5—224.5 °C.

Found: C, 49.19; H, 4.89; S, 12.91%. Calcd for $C_{20}H_{24}O_{10}S_2$: C, 49.17; H, 4.95; S, 13.13%.

4,6-Biimino-4,6-dideoxy-myo-*inositol* (**13a**). A mixture of **12** (0.50 g), anhydrous hydrazine (0.5 ml), and 2-methoxyethanol (30 ml) was refluxed for 7 hr. The reaction mixture was treated as for the preparation of **4a**. The crude product was recrystallized from water–ethanol to afford crystals (95 mg, 52%) of **13a**, mp 190 °C.

Found: C, 41.14; H, 6.74; N, 15.98%. Calcd for $C_6H_{12}N_2O_4$: C, 40.91; H, 6.87; N, 15.90%.

Di-N-*acetyl-tetra*-O-*acetyl-4,6-biimino-4,6-dideoxy*-myo-*inositol* (**13b**). Compound **13a** (35 mg) was acetylated with acetic anhydride (2 ml) and pyridine (2 ml) overnight at room temperature. The product was crystallized from ethanol–ether to afford crystals (63 mg, 73%) of **13b**, mp 145—147 °C. IR: 1745 (OAc), and 1650 cm^{-1} (NAc).

Found: C, 50.70; H, 6.05; N, 6.97%. Calcd for $C_{18}H_{24}N_2O_{10}$: C, 50.47; H, 5.65; N, 6.54%.

Di-N-*acetyl-tetra*-O-*acetyl*-myo-*inosadiamine-4,6* (**14**). Compound **13a** (27 mg) was hydrogenated in a similar way to that for **4a**. Subsequent acetylation gave crystals (28 mg, 43%) of **14**, mp 280 °C. Recrystallization from ethanol afforded pure sample, mp 288 °C, which was identified with an authentic sample[11] by comparison of IR and PMR spectra.

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