Inositol Derivatives. 8. Azidolysis of Tri- and Tetra-sulfonates of *myo*-Inositol[1]

Tetsuo SUAMI, Seiichiro OGAWA, Shuichi OKI, and Hideo KUNITOMO
Department of Applied Chemistry, Faculty of Engineering, Keio University, Hiyoshi, Yokohama 223
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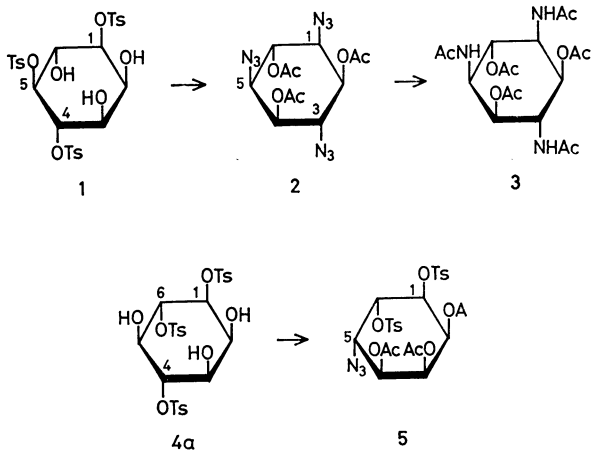
Reactions of the azide ion with four trisulfonates (1,4,5-, 1,4,6-, 1,5,6-, and 4,5,6-) and one tetrasulfonate (1,4,5,6-) of *myo*-inositol were studied. The structures of the new azido compounds were established by PMR spectroscopy and reaction sequences. The mechanism of neighboring-group participation reactions were discussed.

In continuation of the preceding work,[2] studies have been made on the azidolysis of four tritosylates (1,4,5,-1,4,6-, 1,5,6-, and 4,5,6-) of *myo*-inositol and some of their 2,3-*O*-cyclohexylidene derivatives, together with 1,4,5,6-tetra-*O*-tosyl-*myo*-inositol.

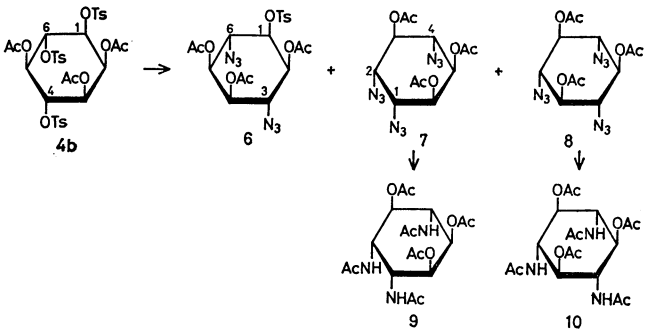
1,4,5-Tritosylate. Refluxing of 1,4,5-tri-*O*-tosyl-*myo*-inositol (**1**)[3] with sodium azide in 90% aqueous 2-methoxyethanol for 22 hr, followed by acetylation, exclusively gave crystalline triazidotrideoxyinositol triacetate (**2**) in 42% yield. Hydrogenation of **2** and subsequent acetylation gave the corresponding hexaacetyl inosatriamine (**3**) in 54% yield. Compound **2** was assigned to 1,3,5-triazido-1,3,5-trideoxy-*muco*-inositol triacetate on the basis of elemental analysis and IR and well-defined PMR spectra. In the PMR spectrum in deuteriochloroform ($CDCl_3$) (Table 1), the H-3 wide triplet (τ 5.80) shifted downfield remarkably as compared with two-proton double doublet (τ 6.02) due to two equivalent equatorial protons on C-1 and C-5, attributable to the deshielding effect of two *syn*-axial azido groups on C-1 and C-5.[4] The PMR spectrum of **3** in dimethylsulfoxide-d_6 (DMSO-d_6) also supported its *muco*-1,3,5 configuration. Thus, the acetyl methyl protons appearing as four singlets (2:1:1:2) at τ 8.18, 8.07, 8.04, and 7.87, could be ascribed to two equatorial and one axial acetamido, and one equatorial and two axial acetoxy groups, respectively.[5] The H-6 wide triplet (J=10 Hz) appeared in a lower field (τ 4.75) due to deshielding effect of two *syn*-axial acetoxy groups on C-2 and C-4.[4] It is interesting to note that, in the favored conformation of **2**, the two substituents located in *syn*-axial orientation appear to be not the acetoxy but the azido groups, in contrast with that of **3**, whose substituents on the same carbons were of *syn*-equatorial orientation.



Scheme 1

It is reasonable to deduce that the azidolysis proceeds *via* neighboring-group participation reaction initiated by the intramolecular attack of the 3-hydroxyl group to C-4 leading to the intermediate 3,4-epoxide. From the structure of **2**, it is feasible that the intermediate epoxides formed successively are opened by azide ion in *trans*-diaxial manner.

1,4,6-Tritosylates. On treatment with sodium azide under similar conditions to those for **1**, 1,4,6-tri-*O*-tosyl-*myo*-inositol (**4a**)[3] yielded, after subsequent acetylation, the monoazido compound (**5**) as the sole crystalline product in 6% yield. The structure of **5** was deduced to be 5-azido-5-deoxy-1,6-di-*O*-tosyl-*allo*-inositol triacetate on the basis of its PMR spectrum, which exhibited the H-5 signal as a double doublet (J=3 and 10 Hz) at τ 5.86.[6] Mechanistically, the 5-hydroxyl group is likely to form the 4,5-epoxide which is opened diaxially by azide ion.



Scheme 2

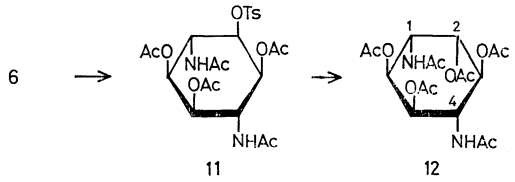
On the other hand, when the triacetate (**4b**)[3] was treated with sodium azide under identical conditions, three azido compounds were formed, which were successively separated by fractional crystallization from ethanol and methanol to give one diazido compound (**6**) (34%), and two triazido compounds (**7** (9%) and **8** (2%)). Syrupy **8**, which was later obtained in a crystalline form, was further characterized by converting it into known hexaacetyl *scyllo*-inosatriamine-1,3,5 (**10**).[7] The structure of **8** was then established to be 1,3,5-triazido-1,3,5-trideoxy-*scyllo*-inositol triacetate.[8] From the data of analysis and IR and PMR spectra **6** and **7** were assigned to 3,6-diazido-3,6-dideoxy-1-*O*-tosyl-*muco*-inositol triacetate and 1,2,4-triazido-1,2,4-trideoxy-*chiro*-inositol triacetate,[9] respec-

Table 1. PMR spectral data in $CDCl_3$ at 60 MHz[a)]

Compound	H_1 ($J_{1,2}$)	H_2 ($J_{2,3}$)	H_3 ($J_{3,4}$)	H_4 ($J_{4,5}$)	H_5 ($J_{5,6}$)	H_6 ($J_{1,6}$)	OAc	Others
2	6.02 dd (4)	4.82 dd (8)	5.80 t (8)	4.82 dd (4)	6.02 dd (6)	4.60 t (6)	7.82 (9) [b)]	
6		(4.5)	5.88 t (4.5)		(9)	5.85 t (9)	8.08 (3) 7.92 (3) 7.89 (3)	7.50 (3) OTs
7	6.0 m	6.0 m (10)	4.66 t (10)	6.20 t (10)	4.91 dd (3.5)	4.57 t (3.5)	7.93 (3) 7.82 (3) 7.73 (3)	
8	6.36 t (10)	4.92 t (10)	6.36 t (10)	4.92 t (10)	6.36 t (10)	4.92 t (10)	7.82 (9)	
21	5.08 dd (4)	(8)	5.78 t (8)		(6)	5.66 t (6)	7.86 (3) 7.84 (3) 7.80 (3)	6.87 (3) OMs
23a	4.78 t (3.5)	6.00 dd (8)	4.86 dd (10)	6.39 dd	6.0 m	6.0 m (3.5)	7.80 (3)	6.79 (3) OMs
27b	4.97 dd (3.5)	6.03 dd (11)	4.64 t (11)	6.05 t (11)	4.72 dd (3)	4.35 dd (4)	7.88 (3) 7.77 (3) 7.74 (3)	6.73 (3) OMs

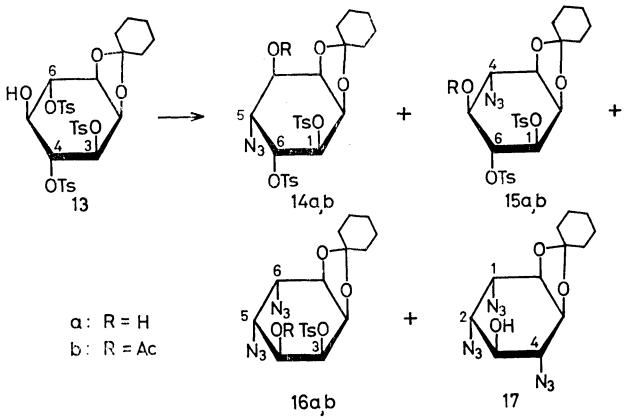
a) Chemical shifts are given in terms of τ-values. Values given for coupling constants (Hz) are of firts order. Abbreviations: s (singlet); d (doublet); t (triplet); dd (double doublet); m (complex multiplet). b) Values in parenthesis show number of protons.

tively. The PMR spectrum of **6** exhibited the H-3 signal as a narrow triplet and H-6 signal as a wide triplet at τ 5.88 and 5.85, respectively. The downfield shift of H-6 axial proton as compared with H-3 equatorial proton might be attributed to the deshielding effect of two *syn*-axial acetoxy groups on C-2 and C-4.[4] The structure of **6** was finally confirmed by transforming it into known hexaacetyl *chiro*-inosadiamine-1,4 (**12**)[10] in the following way. On reduction and



Scheme 3

subsequent acetylation, **6** gave 3,6-diacetamido-3,6-dideoxy-1-*O*-tosyl-*muco*-inositol triacetate (**11**). Without further purification, this was refluxed with sodium acetate in 90% aqueous 2-methoxyethanol followed by acetylation to afford **12** in 61% yield with an inversion of the configuration at C-1. The PMR spectral data of **7** established the axial orientation for H-3, H-4, and H-5, and the equatorial orientation for H-6. The PMR spectrum of hexaacetyl inosatriamine (**9**) derived from **7** showed the acetyl methyl protons as four singlet (2: 1: 2: 1) at τ 8.21, 8.10, 8.06, and 7.85, which were assigned to two equatorial and one axial acetamido, and two equatorial and one axial acetoxy groups, respectively.[5] These chemical shifts were found to be very similar to those of **12**. Consequently, the configuration of **7** was proved to be *chiro*-1,3,4. From these results, the azidolysis reactions of **4a** and **4b** should involve quite different mechanisms. In the case of **4b**, the initial formation of the intermediate 3,4- or/and 5,6-cyclic acetoxonium ion might be proposed.



Scheme 4

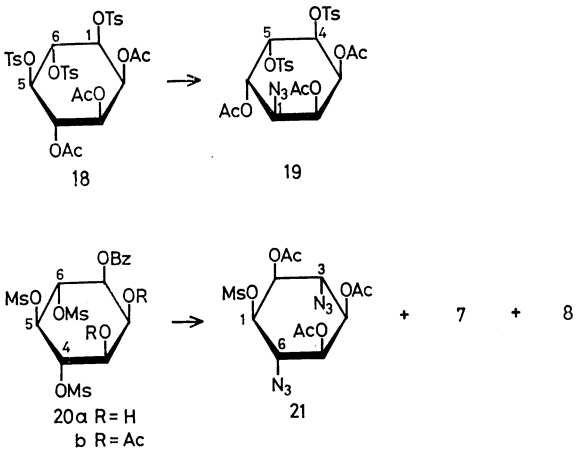
1,2-*O*-Cyclohexylidene-3,4,6-tri-*O*-tosyl-*myo*-inositol (**13**)[3] was subjected to a similar azidolysis. In compound **13**, the neighboring-group participation of the 3-hydroxyl group to C-4 as would be expected in the azidolysis of **5** was not possible, since the two hydroxyl groups at C-2 and C-3 were blocked by *O*-cyclohexylidene group. The reaction was monitored by tlc. After 3 hr, **13** disappeared completely and the formation of two major components (**14a** and **15a**) was detected. **15a**, a slightly faster-moving component, was then disappeared slowly and the third component **16a** was formed. By a prolonged treatment, **16a** was converted almost completely into the more faster-moving component (**17**), while **14a** remained unchanged during the course of the reaction. Thus, when **13** was allowed to react with sodium azide on being refluxed in 90% aqueous 2-methoxyethanol for 3 hr, monoazido compounds (**14a** and **15a**) and a diazido compound (**16a**) were obtained in 26, 28, and 7% yields, respectively, after separation by fractional crystallization from ethanol or ethyl acetate. When the reaction time

was extended to 22 hr, compound **14a**, **16a**, and a triazido compound (**17**) were isolated in 26, 1.4, and 13% yields, respectively, after fractionation by a silica gel chromatography. Since **13** yielded the 4,5-epoxide selectively on treatment with sodium methoxide,[11] the intermediary-formation of the same epoxide might be postulated as in the azidolysis of **13**. The monoazido compounds are therefore formed through nucleophilic cleavage of the 4,5-epoxide by azide ion. The 5-azido compound seems to be less reactive for further substitution as compared with the 4-azido compound, because of lack of the participating group. Compounds **14a** and **15a** were thus reasonably assigned to 5-azido-2,3-*O*-cyclohexylidene-5-deoxy-1,6-di-*O*-tosyl-*allo*-inositol and 4-azido-2,3-*O*-cyclohexylidene-4-deoxy-1,6-di-*O*-tosyl-*myo*-inositol, respectively. Compound **15a** would readily undergo nucleophilic substitution *via* the intermediate 5,6-epoxide to give 5,6-diazido-1,2-*O*-cyclohexylidene-5,6-dideoxy-3-*O*-tosyl-*allo*-inositol (**16a**) as a predominant product, which was further transformed into a triazido compound (**17**), 1,2,4-triazido-5,6-*O*-cyclohexylidene-1,2,4-trideoxy-*chiro*-inositol. The structure of **17** was confirmed by its conversion into **7** by hydrolysis with 80% aqueous acetic acid followed by acetylation.

The tentatively assigned structures of **14a**, **15a**, and **16a** were supported by the PMR spectra of their corresponding acetyl derivatives (**14b**, **15b**, and **16b**). The PMR spectrum of **14b** showed a double doublet (J=3.5 and 9.5 Hz) at τ 5.78, which was ascribed to the proton attached to the carbon atom carrying the azido group. In the spectrum of **15b**, H-4 signal appeared as a multiplet, which was coupled with the adjacent signal due to H-3 proton. The PMR spectrum of **16b** exhibited three narrow multiplets at τ 6.00, 4.98, and 4.68 in the ratio 1:1:1, ascribable to three pairs of protons being vicinally located: H-5 and H-6, H-1 and H-2, and H-3 and H-4, respectively.

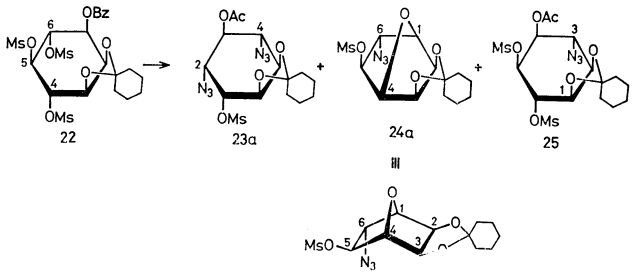
Hydrolysis of **14a** followed by acetylation gave **5** in 55% yield, supporting the proposed structure of **5**.

1,5,6-Tritosylate. Treatment of 1,5,6-tri-*O*-tosyl-*myo*-inositol triacetate (**18**)[3] with sodium azide under the usual conditions, followed by acetylation, gave predominantly the monoazido compound (**19**) in 26% yield. Tlc showed the formation of a trace of the more faster-moving component, probably the diazido compound, in addition to **19**. The structure of **19** was assigned to 1-azido-1-deoxy-4,5-di-*O*-tosyl-*allo*-inositol triacetate on the basis of its PMR spectrum. The two double doublets (τ 5.90 and 4.34) showed splittings of 3.5 and 10.5 Hz, coupled with each other. Thus they were ascribed to H-1 and H-6 protons, respectively. Compound **19** should be formed by diaxial scission of the intermediate 4,5-epoxide with azide ion.



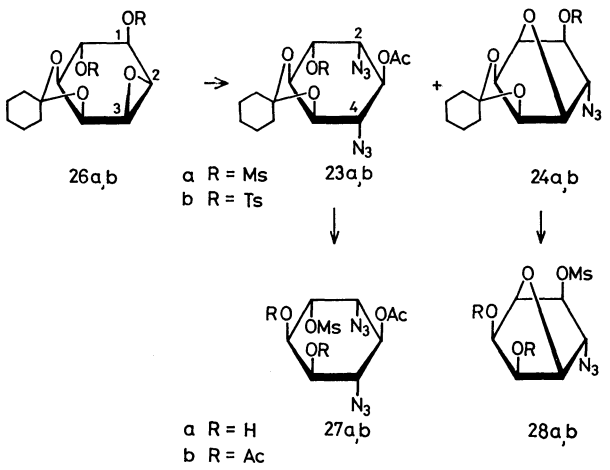
Scheme 5

4,5,6-Trisulfonates. 1-*O*-Benzoyl-4,5,6-tri-*O*-mesyl-*myo*-inositol (**20**)[12] was subjected to azidation. The products were fractionated by silica gel column chromatography to afford the monoazido compound (**21**), **7** and **8** in 31, 14, and 9.5% yields, respectively. The PMR spectrum of **21** (Table 1) was very close to that of **6**. Thus its structure was assigned to the corresponding 3,6-diazido-3,6-dideoxy-1-*O*-mesyl-*muco*-inositol. If the reaction is initiated by the participation of 1-benzoyloxy or 3-hydroxyl group to C-6 or C-4, the diaxial opening of the cyclic intermediates with azide ion should proceed preferentially to yield **21** as the predominant product along with the minor **8**. Compound **7** should have arisen from **21** by further direct S_N2 substitution of 1-mesyloxy group with azide ion. For the sake of confirmation, **21** was treated with sodium azide under the same conditions, but **7** was found to be only slightly formed by tlc. It was thus necessary to deduce an alternative reaction mechanism. We reported that the direct S_N2 displacement reaction of 5-tosyloxy function with chloride ion occurred readily in the tosylation of 1,2-*O*-cyclohexylidene-*myo*-inositol and its related compound.[12] By analogy with this, the initial substitution of the 5-mesyloxy group might be also feasible, and would account for the formation of **7** as well as **8** in relatively good yields.



Scheme 6

The azidolysis of the 2,3-*O*-cyclohexylidene derivative (**22**)[12] was carried out. Following the reaction by tlc, the formation of two major components was shown, together with two minor components which gradually disappeared with prolonged treatment. After 45 hr, the products were fractionated with a silica gel column to afford the diazido compound (**23a**) (8%), and monoazido compounds (**24a** (9%) and **25** (1.5%)). Since the reaction might proceed *via* the cyclic intermediate, 1,6-benzoxonium ion, azidolysis of an epoxide with a similar configuration was studied. Epoxides, 2,3-anhydro-4,5-*O*-cyclohexylidene-1,6-di-*O*-mesyl-*epi*-inositol (**26a**)[12] and -1,6-di-*O*-tosyl-*epi*-inositol (**26b**)[11] were subjected to azidolysis. Compounds **23a**,**b** and **24a**,**b** were obtained as expected from **26a**,**b** in comparatively good yields.

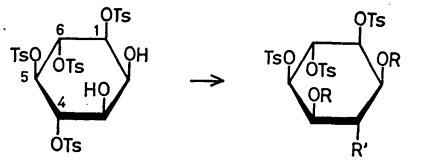


Scheme 7

Removal of the cyclohexylidene group of **23a** led to dihydroxyl compound (**27a**) which gave triacetate (**27b**). Similarly, **24a** was converted into dihydroxyl compound (**28a**) and diacetate (**28b**). On the basis of elemental analysis and IR and PMR spectra, **23a** and **24a** were assigned to 3-*O*-acetyl-2,4-diazido-5,6-*O*-cyclohexylidene-2,4-dideoxy-1-*O*-mesyl-*chiro*-inositol and 1,4-anhydro-6-azido-2,3-*O*-cyclohexylidene-6-deoxy-5-*O*-mesyl-*epi*-inositol, respectively. In the PMR spectrum of **27b**, a pattern of the signals due to the ring protons was shown to be essentially similar to that of 2,4-diazido-2,4-dideoxy-*chiro*-inositol tetraacetate,[2] supporting the proposed structure.

In the first step of the azidolysis, it is mechanistically reasonable to conclude that the 2,3-epoxide ring is opened by azide ion to give rise to 2- and 3-azido compounds, both of which are lacking in the participating groups for nucleophilic substitution of the sulfonyloxy group in a vicinal position. Thus in the case of the latter, substitution of the sulfonyloxy group at C-1 would proceed in direct S_N2 fashion to give **23a**. In the case of the former, a direct S_N2 attack on C-1 is considerably interrupted by steric and electronic effects due to the adjacent azido group, but the hydroxyl group at C-3 can attack the rear-side of C-6 intramolecularly in a boat-like conformation, resulting in the transannular epoxide (**24a**).[2,13]

The PMR spectral data of **24a** and its derivatives (Table 2) were consistent with the assigned structures. The C-2 and C-3 protons appeared at τ 5.31 and 5.67, respectively, as the AB quartet. The downfield shift of the former might be accounted for by assuming the proximity effect[14] and/or a strong magnetic field, excerted by the 6-*endo* azido group. No detectable coupling could be observed between the bridge head proton H-1 or H-4 and H-2 *endo* or H-3 *endo* protons, supporting the bicyclic structure. The coupling constants measured from **24a**, **24b**, and **28** were in good accord with those of bicyclo[2.2.1]heptane system.[15]



Scheme 8

1,4,5,6-Tetratosylate. Reaction of 1,4,5,6-tetra-*O*-tosyl-*myo*-inositol (**29**)[3] with sodium azide in the usual way gave the monoazido compound (**30a**) selectively in 62% yield, which was converted into the diacetate (**30b**). By a similar reaction with sodium acetate followed by acetylation, **29** yielded the triacetyl compound (**30c**) in 63% yield. The reactions seem to proceed *via* the intermediate 3,4-epoxide, followed by nucleophilic attack in diaxial manner. Exclusive products would possess *muco*-configuration. The PMR spectra of **30b** and **30c** supported the assigned structures. In **30b**, the acetyl methyl protons appeared as a single peak at τ 8.09, indicating a symmetrical structure. In **30c**, three acetoxy groups occurred as two singlets (2: 1) at τ 8.18 and 8.02, satisfying *muco*-configuration. The structures of **30a** and **30c** could thus be established as 3-azido-3-deoxy-1,5,6-tri-*O*-tosyl-*muco*-inositol and 2,3,4-tri-*O*-tosyl-*muco*-inositol triacetate, respectively.

TABLE 2. PMR DATA OF DERIVATIVES OF 1,4-ANHYDRO-*epi*-INOSITOL IN $CDCl_3$ AT 60 MHz[a]

	24a	**24b**	**28b**
H_1	5.55 d	5.72 d	5.17 d
H_2	5.31 d	5.31 d	4.62 d
H_3	5.67 d	5.74 d	4.87 d
H_4	5.45—5.55 m	5.53 s	5.38 s
H_5	5.45—5.55 m	5.47 dd	5.60—5.80 m
H_6	5.88 dd	5.94 dd	5.25 m
OAc			7.87[b]
OMs	6.86		6.78
OTs		7.50	
$J_{1,2}$	0	0	0
$J_{2,4}$	5.5	6.0	6.7
$J_{3,4}$	0	0	0
$J_{4,5}$	—	1.0	—
$J_{5,6}$	6.0	5.5	—
$J_{1,6}$	2.0	2.3	—

a) see Table 1. b) Singlet due to two acetoxy groups.

Experimental

Unless otherwise noted, 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 obtained on a Varian Associates A-60D (60 MHz) spectrometer at a concentration of approximately 10% $CDCl_3$ or DMSO-d_6, with tetramethylsilane as an internal standard. Chemical shifts are given in terms of τ-values, signals being denoted by s (singlet), d (doublet), dd (double doublet), t (triplet), or m (complex multiplet). Values given for coupling constants are of first-order. All the solutions were concentrated with a rotary evaporator at 40—50 °C under reduced pressure, a trace of residual pyridine being removed by coevaporation with toluene. Catalytic hydrogenations were carried out with a Parr shaker apparatus in the presence of Raney nickel T-4[16] catalyst in the initial hydrogen pressure of 3.5 kg/cm^2 at room temperature. Tlc was performed on silica gel

(Wakogel B-10, Wako Pure Chemica lIndustries, Ltd.) using a mixture of 2-butanone and toluene. The spots were indicated by heating above 150 °C after spraying with 30% sufuric acid.

1,3,5-Triazido-1,3,5-trideoxy-muco-*inositol Triacetate (2).* A mixture of 1,4,5-tri-*O*-tosyl-*myo*-inositol (**1**)[3] (1.50 g), sodium azide (1.50 g), and 90% aqueous 2-methoxyethanol (75 ml) was refluxed for 22 hr. The reaction mixture was then evaporated to dryness and the residue was treated with acetic anhydride (10 ml) and pyridine (10 ml) overnight at room temperature. An insoluble material was removed by filtration and the filtrate was evaporated to yield an oil which was purified by passing through a short alumina column with chloroform as an eluent. The solution was concentrated and the product was crystallized from ether to afford crystals (0.37 g, 42%) of **2**. Recrystallization from ethanol–ether afforded an analytical sample (0.33 g, 37%), mp 92—93 °C.

Found: C, 37.81; H, 3.95; N, 33.19%. Calcd for $C_{12}H_{15}N_9O_6$: C, 37.79; H, 3.97; N, 33.07%.

Hexaacetyl muco-*Inosatriamine-1,3,5 (3).* A solution of **2** (100 mg) in ethanol (10 ml) was hydrogenated for 6 hr. The catalyst was filtered off and the filtrate was evaporated to dryness. The residue was treated with acetic anhydride (1.5 ml) and pyridine (2 ml) overnight at room temperature. The reaction mixture was evaporated to give a crystalline residue which was recrystallized from ethanol–ether to give tiny needles (60 mg, 54%) of **3**, mp 259—260 °C (decomp.).

Found: C, 50.49; H, 6.42; N, 9.99%. Calcd for $C_{18}H_{27}N_3O_9$: C, 50.34; H, 6.34; N, 9.79%.

*5-Azido-5-deoxy-1,6-di-*O*-tosyl*-allo-*inositol Triacetate (5).* A mixture of 1,4,6-tri-*O*-tosyl-*myo*-inositol (**4a**)[3] (2.0 g), sodium azide (2.0 g), and 90% aqueous 2-methoxyethanol (50 ml) was refluxed for 22 hr. The mixture was evaporated to dryness and the residue was acetylated in the usual manner. Tlc showed the formation of one major component and two minor components. The products were extracted with chloroform and the extracts were evaporated to give an oil which was crystallized from ethanol to give needles (0.14 g, 6.3%) of **5**, mp 157—158 °C. Recrystallization from ethanol afforded a pure sample, mp 158—160 °C. PMR ($CDCl_3$): τ 8.13, 7.92, 7.90 (3-proton s, OAc), 7.50 (3-proton s, $OSO_2C_6H_4C\underline{H}_3$).

Found: C, 48.97; H, 4.70; N, 6.31; S, 9.98%. Calcd for $C_{26}H_{29}N_3O_{12}S_2$: C, 48.82; H, 4.57; N, 6.57; S, 10.02%.

*Azidolysis of 1,4,6-tri-*O*-tosyl*-myo-*inositol Triacetate (4b).*[3] A mixture of **4b** (3.25 g), sodium azide (3.85 g), and 90% aqueous 2-methoxyethanol (100 ml) was refluxed for 16 hr. The reaction mixture was then treated in a similar way to that for **1** to give a crystalline mixture (1.04 g), mp 121—134 °C. Tlc (1:4 2-butanone–toluene) indicated the formation of two major components. Fractional crystallization from ethanol gave two crystals: 3,6-diazido-3,6-dideoxy-1-*O*-tosyl-*muco*-inositol triacetate (**6**), yield 0.73 g (33.8%), mp 134—135 °C, and 1,2,4-triazido-1,2,4-trideoxy-*chiro*-inositol triacetate (**7**), yield 0.122 g (8.7%), mp 112—113 °C. Analytical samples of **6** and **7** were obtained by recrystallization from ethanol and dried *in vacuo* over phosphorus pentoxide overnight at room temperature.

6: Found: C, 45.09; H, 4.51; N, 16.35; S, 6.00%. Calcd for $C_{19}H_{22}N_6O_9S$: C, 44.70; H, 4.34; N, 16.46; S, 6.28%.

7: Found: C, 38.05; H, 3.96; N, 33.30%. Calcd for $C_{12}H_{15}N_9O_6$: C, 37.80; H, 3.97; N, 33.06%.

Evaporation of the mother liquor gave a syrup which was shown by tlc to consist of a faster-moving major component together with traces of **6** and **7**. The syrupy crude 1,3,5-triazido-1,3,5-trideoxy-*scyllo*-inositol triacetate (**8**) was, without further purification, hydrogenated in an ethanol solution (10 ml) for 5.5 hr. The product was treated with acetic anhydride (5 ml) and pyridine (5 ml) overnight at room temperature, and the mixture was then evaporated to give an oil, which crystallized upon addition of methanol to give plates (40 mg, 2.2%) of hexaacetyl *scyllo*-inosatriamine-1,3,5 (**10**), which did not melt below 330 °C, but sublimed at 305 °C turning brown at 310 °C (lit,[7] mp 310—315 °C). The compound was identified with an authentic sample[7] by comparison of IR spectra.

Hexaacetyl chiro-*Inosatriamine-1,2,4 (9).* A solution of **7** (0.20 g) in ethanol (30 ml) was hydrogenated for 20 hr. After the catalys had been removed by filtration, the solution was evaporated and the residue was acetylated in the usual way to give crystalline product. Recrystallization from ethanol afforded crystals (136 mg, 60.4%) of **9**, mp 167—168 °C. Recrystallization from ethanol gave an analytical sample as needles, mp 166—169 °C.

Found: C, 48.51; H, 6.25; N, 9.33%. Calcd for $C_{18}H_{27}N_3O_9\cdot H_2O$: C, 48.31; H, 6.51; N, 9.39%.

Preparation of Hexaacetyl chiro-*Inosadiamine-1,4 (12) from 6.* Compound **6** (0.91 g) was hydrogenated in an ethanol solution (150 ml) for 16 hr. The product was acetylated in the usual manner to give syrupy 1-*O*-tosyl-*muco*-inosadiamine-3,6 triacetate (**11**). Without further purification, **11** was treated with anhydrous sodium acetate (0.80 g) in refluxing 90% aqueous 2-methoxyethanol (45 ml) for 45 hr, and the reaction mixture was then evaporated to dryness and subsequently acetylated to give a crystalline compound, which was crystallized from chloroform to afford crystals (0.47 g, 61%) of **12**, mp 126—131 °C (lit,[10] 127—129 °C). This compound was identified with an authentic sample by comparison of their IR and PMR (DMSO-d_6) spectra.

*Azidolysis of 1,2-*O*-Cyclohexylidene-3,4,6-tri-*O*-tosyl*-myo-*inositol (13).*[3] *a)*: A mixture of **13** (6.0 g), sodium azide (6.0 g), and 90% aqueous 2-methoxyethanol (90 ml) was refluxed, and the progress of the reaction was followed by tlc (1:4 2-butanone–toluene). After 3 hr, **13** disappeared completely in the reaction mixture. It was then evaporated to dryness and the residue was extracted with hot ethyl acetate (3×50 ml). The extract was concentrated to give a crystalline mixture, whose tlc showed the formation of major three components along with a trace of a faster-moving component. Crystallization from ethyl acetate gave crystals (1.29 g, 26%) of 5-azido-5-deoxy-2,3-*O*-cyclohexylidene-1,6-di-*O*-tosyl-*allo*-inositol (**14a**), mp 165—169 °C. The crystals were shown by IR spectrum to contain ethyl acetate. Recrystallization twice from ethanol gave an analytical sample, mp 163.5—164 °C.

Found: C, 52.77; H, 5.52; N, 7.08; S, 10.37%. Calcd for $C_{26}H_{31}N_3O_9S_2$: C, 52.60; H, 5.26; N, 7.08; S, 10.80%.

Compound **14a** (0.33 g) was treated with acetic anhydride (2 ml) and pyridine (3 ml) overnight at room temperature. The reaction mixture was evaporated with toluene to give a syrup which was crystallized from ethanol–ether to afford crystals (0.33 g, 94%) of the acetate (**14b**), mp 163.5—165.5 °C. Recrystallization from ethanol–chloroform gave an analytical sample, mp 150—151 °C. PMR ($CDCl_3$): τ 7.86 (3-proton s, OAc), 7.52 (6-proton s, $OSO_2C_6H_4C\underline{H}_3$).

Found: C, 52.70; H, 5.22; N, 6.47; S, 10.08%. Calcd for $C_{28}H_{33}N_3O_{10}S_2$: C, 52.90; H, 5.23; N, 6.61; S, 10.09%.

The mother liquor of **14a** was concentrated to a small volume and allowed to stand at room temperature yielding thin needles, which were recrystallized from ethanol to afford tiny needles (1.37 g, 27.8%) of 4-azido-4-deoxy-2,3-*O*-cyclohexylidene-1,6-di-*O*-tosyl-*myo*-inositol (**15a**), mp 173—175 °C, after melting and resolidifying at 165—167 °C.

Found: C, 52.90; H, 5.17; N, 7.05; S, 11.10%. Calcd

for $C_{26}H_{31}N_3O_9S_2$: C, 52.60; H, 5.26; N, 7.08; S, 10.80%.

Compound **15a** (0.36 g) was acetylated as described above to give crystals, which were recrystallized from chloroform–ethanol to afford crystals (0.37 g, 95%) of the acetate (**15b**), mp 156.5—158.5 °C. PMR ($CDCl_3$): τ 7.94 (3-proton s, OAc), 7.55 (6-proton s, $OSO_2C_6H_4C\underline{H}_3$), 5.71 (dd, $J_{1,2}$= 3.5 Hz, $J_{2,3}$=5 Hz, H-2).

Found: C, 53.14; H, 5.44; N, 6.43; S, 10.14%. Calcd for $C_{2,}H_{33}N_3O_{10}S_2$: C, 52.90; H, 5.23; N, 6.61; S, 10.09%.

The mother liquor of **15a**, kept at room temperature for a long time, yielded crystals which were recrystallized from ethanol to afford pure crystals (0.26 g, 6.9%) of 5,6-diazido-1,2-*O*-cyclohexylidene-5,6-dideoxy-3-*O*-tosyl-*allo*-inositol(**16a**), mp 142—143.5 °C.

Found: C, 49.18; H, 5.20; N, 17.97; S, 7.15%. Calcd for $C_{19}H_{24}N_6O_6S$: C, 49.12; H, 5.21; N, 18.10; S, 6.90%.

Acetylation of **16a** gave a homogeneous syrupy acetate (**16b**), which did not crystallize in spite of several attempts.

b): A mixture of **13** (10.0 g), sodium azide (10.0 g), and 90% aqueous 2-methoxyethanol (200 ml) was refluxed for 22 hr, when, tlc showed the formation of a faster-moving component, together with **14a** and **16a**. The reaction mixture was evaporated to dryness and the residue was extracted with ethyl acetate (3×100 ml). The extracts were purified by passing through a short alumina column and then concentrated to a syrup, which was crystallized from ethyl acetate to give crystals (1.76 g, 21.4%) of **14a**, mp 145—148 °C. The mother liquor was evaporated to give a syrup which was chromatographed on a silica gel column (90 g) with 1:6 2-butanone–toluene as an eluent. The three fractions were separated in accord with the results of tlc.

Fraction 1 gave a syrup which slowly crystallized upon trituration with ligroin, affording needles (0.61 g, 13.2%) of 1,2,4-triazido-5,6-*O*-cyclohexylidene-1,2,4-trideoxy-*chiro*-inositol (**17a**), mp 95—97 °C.

Found: C, 42.55; H, 5.01; N, 37.53%. Calcd for $C_{12}H_{17}N_9O_3$: C, 42.98; H, 5.11; N, 37.60%.

Fraction 2 gave crystals (0.089 g, 1.4%) of **16a**, mp 140—142 °C, after crystallization from ethanol.

Fraction 3 gave crystals (0.372 g) of **14a**, mp 142—145 °C, after crystallization from ethanol. The total yield of **14a** was then 26%.

Acetylation of **17a** gave a homogeneous syrupy acetate (**17b**) which did not crystallize in spite of several attempts.

Treatment of **17a** (0.30 g) with refluxing 80% aqueous acetic acid (10 ml) for 1.5 hr, followed by acetylation, gave crystals (0.26 g, 65%) of **7**, mp 111.5—112.5 °C. The compound was identified with a sample obtained from **4b**.

Compound **14a** (0.28 g) was successively hydrolyzed and acetylated as described above to give crystals (0.17 g, 55%) of **5**, mp 157—159 °C, after recrystallization from chloroform–ethanol. The compound was identified with a sample obtained from **4a**.

*1-Azido-1-deoxy-4,5-di-*O*-tosyl-*allo*-inositol Triacetate (**19**).* A mixture of 1,5,6-tri-*O*-tosyl-*myo*-inositol triacetate (**18**)[3] (0.50 g), sodium azide (0.50 g), and 90% aqueous 2-methoxyethanol (15 ml) was refluxed for 6 hr. The reaction mixture was then treated in a similar way to that for **4b** to give crystals (0.11 g, 26.4%) of **19**, mp 179.5—180.5 °C. Recrystallization from chloroform–ethanol, mp 182—183 °C.

Found: C, 49.22; H, 4.76; N, 6.34; S, 10.11%. Calcd for $C_{26}H_{29}N_3O_{12}S_2$: C, 48.82; H, 4.57; N, 6.57; S, 10.03%.

*1-*O*-Benzoyl-4,5,6-tri-*O*-mesyl-*myo*-inositol (**20a**).* 1-*O*-Benzoyl-2,3-*O*-cyclohexylidene-4,5,6-tri-*O*-mesyl-*myo*-inositol (**22**)[12] (3.0 g) was treated with refluxing 80% aqueous acetic acid (60 ml) for 3 hr. On being cooled to room temperature, the resulting crystals were collected by filtration: yield 1.98 g (77%), mp 215—221 °C. An additional crop (0.31 g, total yield 89%) was obtained by evaporation of the water layer. An analytical sample melted at 228—230 °C.

Found: C, 36.99; H, 4.46; S, 18.51%. Calcd for $C_{16}H_{23}O_{13}S_3$: C, 37.10; H, 4.27; S, 18.21%.

Acetylation of **20a** (1.5 g) in the usual manner gave the diacetate (**20b**): yield 1.74 g (99%), mp 209—212 °C. Recrystallization from chloroform–ethanol afforded an analytical sample, mp 214—216 °C.

Found: C, 39.80; H, 4.51; S, 15.94%. Calcd for $C_{20}H_{27}O_{15}S_3$: C, 39.74; H, 4.31; S, 16.21%.

*Azidolysis of **20a**.* A mixture of **20a** (2.0 g), sodium azide (1.25 g), and 90% aqueous 2-methoxyethanol (75 ml) was refluxed for 28 hr. The reaction mixture was then treated in a similar way to that for **4b** to give a syrupy mixture of azido acetates. Tlc showed the formation of three major components. The mixture was chromatographed on a silica gel column (80 g) with 1:6 2-butanone–toluene as an eluent. The three fractions were separated in accord with the results of tlc.

Fraction 1 gave needles (0.14 g, 9.5%) of **8**, mp 127—132 °C, after crystallization from methanol.

Found: C, 37.80; H, 3.97; N, 33.06%. Calcd for $C_{12}H_{15}N_9O_6$: C, 37.69; H, 3.93; N, 32.85%.

Fraction 2 gave needles (0.20 g, 13.6%) of **7**, mp 109—111 °C, after crystallization from ethanol.

Fraction 3 gave crystals (0.51 g, 30.5%) of 3,6-diazido-3,6-dideoxy-1-*O*-mesyl-*muco*-inositol triacetate (**21**), mp 111—113 °C, after crystallization from chloroform–methanol.

Found: C, 35.95; H, 4.18; N, 19.35; S, 7.38%. Calcd for $C_{13}H_{18}N_6O_9S$: C, 36.14; H, 4.15; N, 19.32; S, 7.11%.

*Azidolysis of 1-*O*-Benzoyl-2,3-*O*-cyclohexylidene-4,5,6-tri-*O*-mesyl-*myo*-inositol (**22**).* A mixture of **22** (2.0 g), sodium azide (0.90 g), and 90% aqueous 2-methoxyethanol (70 ml) was refluxed for 45 hr. The reaction mixture was then treated in a similar way to that for **13**, and the resulting product was acetylated in the usual way to give a syrup which was purified by being passed through a short alumina column with chloroform. The solution was concentrated to afford a small amount of crystals (92 mg) of 3-*O*-acetyl-2,4-diazido-5,6-*O*-cyclohexylidene-2,4-dideoxy-1-*O*-mesyl-*chiro*-inositol (**23a**), mp 127—129 °C. The mother liquor was evaporated to give a syrup which was chromatographed on a silica gel column (100 g) with 1:9 2-butanone–toluene as an eluent. The three fractions were separated in accord with the results of tlc.

Fraction 1 gave crystals (35 mg, total yield 7.7%) of **23a**, mp 128—129 °C, after crystallization from ethanol–ether.

Found: C, 42.00; H, 5.18; N, 19.72; S, 7.36%. Calcd for $C_{15}H_{22}N_6O_7S$: C, 41.86; H, 5.15; N, 19.52; S, 7.45%.

Fraction 2 gave crystals (116 mg, 8.7%) of 1,4-anhydro-6-azido-2,3-*O*-cyclohexylidene-6-deoxy-5-*O*-mesyl-*epi*-inositol (**24a**), mp 127—128.5 °C, after crystallization from ethanol–ether. An analytical sample melted at 130—132 °C.

Found: C, 45.56; H, 5.50; N, 12.24; S, 9.06%. Calcd for $C_{13}H_{19}N_3O_6S$: C, 45.21; H, 5.55; N, 12.17; S, 9.28%.

Fraction 3 gave crystals (27 mg, 1.5%), mp 190—191 °C. The structure was deduced to be 2-*O*-acetyl-3-azido-4,5-*O*-cyclohexylidene-3-deoxy-1,6-di-*O*-mesyl-*muco*-inositol (**25**).

PMR (DMSO-d_6): τ 7.80 (3-proton s, OAc), 6.83, 6.74 (3-proton s, OMs).

Found: C, 39.92; H, 5.01; N, 8.40; S, 13.13%. Calcd or $C_{12}H_{25}N_3O_{10}S_2$: C, 39.75; H, 5.21; N, 8.69; S, 13.26%.

*Azidolysis of 2,3-Anhydro-4,5-*O*-cyclohexylidene-1,6-di-*O*-mesyl-epi-inositol (**26a**).*[12] *a)*: A mixture of **26a** (1.0 g), sodium azide (0.66 g), ammonium chloride (0.27 g), and 90% aqueous 2-methoxyethanol (50 ml) was refluxed for

24 hr. The reaction mixture was then treated in a similar way to that for **13**. The syrupy azido compounds thus obtained were crystallized from ethanol–ether to give crystals (246 mg, 28.3%) of **24a**, mp 127—128.5 °C. The mother liquor was evaporated to dryness and the residue was acetylated in the usual way to give a syrup which was crystallized from ethanol–ether to afford crystals (360 mg, 33.3%) of **23a**, mp 128—129 °C.

b): Under the same conditions except for the absence of ammonium chloride, **26a** (1.0 g) afforded **23a** (230 mg, 21.3%), mp 128—129 °C, and **24a** (303 mg, 34.9%), mp 127—128.5 °C.

Azidolysis of 2,3-Anhydro-4,5-O-cyclohexylidenle-1,6-di-O-tosyl-epi-inositol (26b).[11] Compound **26b** (1.0 g) was refluxed with sodium azide (0.59 g) and ammonium chloride (0.24 g) in 2-methoxyethanol (30 ml) for 22 hr. The reaction mixture was treated in a similar way to that for **13** to give crystals (373 mg, 39.7%) of 1,4-anhydro-6-azido-2,3-*O*-cyclohexylidene-6-deoxy-5-*O*-tosyl-*epi*-inositol (**24b**), mp 115—123 °C. Recrystallization from ethanol gave an analytical sample, mp 126—127 °C.

Found: C, 54.24; H, 5.44; N, 9.62; S, 7.87%. Calcd for $C_{19}H_{23}N_3O_6S$: C, 54.15; H, 5.50; N, 9.97; S, 7.61%.

The mother liquor was concentrated and acetylated in the usual way to give a syrup. Tlc indicated the formation of one major component in addition to **24b**, which was probably diazido compound (**23b**) corresponding to **23a**. The syrup did not crystallize.

*3-O-Acetyl-2,4-diazido-2,4-dideoxy-1-O-mesyl-*chiro*-inositol (27a).* Compound **23a** (854 mg) was treated with refluxing 80% aqueous acetic acid (20 ml) for 1.5 hr, and then the reaction mixture was evaporated to dryness. The residual syrup crystallized spontaneously to give crystals (538 mg, 77.4%) of **27a**, mp 101—104 °C. Recrystallization from ethanol gave an analytical sample, mp 102—104 °C.

Found: C, 31.10; H, 4.12; N, 24.01; S, 8.86%. Calcd for $C_9H_{14}N_6O_7S$: C, 30.86; H, 4.03; N, 23.99; S, 9.15%.

Compound **27a** (100 mg) was acetylated in the usual way to give crystals (92 mg, 74%) of 2,4-diazido-2,4-dideoxy-1-*O*-mesyl-*chiro*-inositol triacetate (**27b**), mp 114—116 °C. Recrystallization from chloroform–ethanol gave an analytical sample, mp 115.5—117 °C.

Found: C, 35.90; H, 4.17; N, 19.48; S, 7.27%. Calcd for $C_{13}H_{18}N_6O_9S$: C, 35.95; H, 4.18; N, 19.35; S, 7.38%.

*1,4-Anhydro-6-azido-6-deoxy-5-O-mesyl-*epi*-inositol (28a).* Compound **24a** (0.50 g) was refluxed with 80% aqueous acetic acid (15 ml) for 1.5 hr. After cooling, the resulting crystals were collected by filtration: yield 162 mg (42%), mp 177.5—178 °C. Another crop of crystals was obtained by evaporation of the filtrate: yield 103 mg. The total yield of **28a** was 69%. An analytical sample was obtained by recrystallization from ethanol, mp 177—178 °C.

Found: C, 31.71; H, 4.13; N, 15.92; S, 12.11%. Calcd for $C_7H_{11}N_3O_6S$: C, 31.70; H, 4.18; N, 15.84; S, 12.09%.

Compound **28a** (67 mg) was acetylated in the usual way to give crystals (83 mg, 95%) of the diacetate (**28b**), mp 141—142 °C, after crystallization from ethanol. An analytical sample was obtained by recrystallization from chloroform–ethanol, mp 158.5—159 °C.

Found: C, 37.67; H, 4.27; N, 12.02; S, 8.93%. Calcd for $C_{11}H_{15}N_3O_8S$: C, 37.82; H, 4.33; N, 12.03; S, 9.18%.

*3-Azido-3-deoxy-1,5,6-tri-O-tosyl-*muco*-inositol (30a).* A mixture of 1,4,5,6-tetra-*O*-tosyl-*myo*-inositol (**29**)[3] (2.0 g), sodium azide (2.0 g), and 90% aqueous 2-methoxyethanol (50 ml) was refluxed for 15 hr. The reaction mixture was evaporated and the residue was extracted with 2-butanone (2×20 ml). The extract was passed through an alumina column and then evaporated to give crystals (0.98 g, 62%) of **30a**, mp 162—163.5 °C. Recrystallization from ethanol afforded an analytical sample, mp 168.5—169.5 °C.

Found: C, 49.02; H, 4.61; N, 6.16; S, 14.50%. Calcd for $C_{27}H_{29}N_3O_{11}S_3$: C, 48.57; H, 4.38; N, 6.29; S, 14.41%.

Compound **30a** (0.33 g) was acetylated in the usual way to give crystals which were recrystallized from chloroform–ethanol to afford plates (0.32 g, 84%) of the diacetate (**30b**), mp 172.5—173 °C.

Found: C, 49.89; H, 4.67; N, 5.48; S, 12.50%. Calcd for $C_{31}H_{33}N_3O_{13}S_3$: C, 49.52; H, 4.42; N, 5.59; S, 12.80%.

*2,3,4-Tri-O-tosyl-*muco*-inositol Triacetate (30c).* A mixture of **29** (2.0 g), anhydrous sodium acetate (2.0 g), and 90% aqueous 2-methoxyethanol (50 ml) was refluxed for 19 hr. The reaction mixture was treated in a similar way to that for **4b**, and the product was crystallized from ethyl acetate–ether to give crystals (1.2 g, 63%) of **30c**, mp 162.5—163.5 °C.

Found: C, 51.81; H, 4.87; S, 12.29%. Calcd for $C_{33}H_{36}O_{15}S_3$: C, 51.55; H, 4.72; S, 12.51%.

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