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Pseudo-sugars. VII. Synthesis of Pseudo-hexopyranose Derivatives with α- and β-Gluco Configurations[1]

Seiichiro Ogawa,* Tatsushi Toyokuni, Takashi Kondoh, Yoshihisa Hattori, Shinichi Iwasaki, Masaru Suetsugu, and Tetsuo Suami

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

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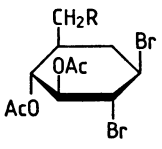
Several derivatives of pseudo-hexopyranose (5-hydroxymethyl-1,2,3,4-cyclohexanetetrol) with α-gluco, (1,2,4/3,5), and β-gluco, (1,3,5/2,4), configurations were synthesized starting from the compounds obtained by *cis*-hydroxylation and oxyamination of DL-di-*O*-acetyl-(1,3/2)-3-bromomethyl-5-cyclohexene-1,2-diol. The ^{1}H NMR chemical shifts of the acetyl methyl protons of the several acetyl derivatives of *N*-(*p*-tolylsulfonyl)-pseudo-glucosamines are discussed.

In connection with the preceding paper of this series,[2] the synthesis of pseudo-hexopyranose (5-hydroxymethyl-1,2,3,4-cyclohexanetetrol) derivatives having α- and β-gluco configurations are described. It has been hoped that pseudo-sugars, biologically interesting analogs, *e.g.* of glucose, galactose, and mannose, will be accepted by some enzymes or biological systems in place of corresponding true sugars, and may have useful biological properties.[3] On the other hand, pseudo-amino sugars related to 2-amino-2-deoxy-, 6-amino-6-deoxy-, and 2,6-diamino-2,6-dideoxy-D-glucose, components of some clinically important amino sugar antibiotics,[4] are also expected to be useful for study on a structure-activity relationship of the antibiotics.

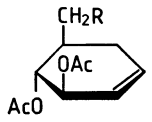
In the present study, *cis*-hydroxylation and oxyamination reactions of the unsaturated derivatives (**3** and **4**) of pseudo-hexopyranoses were carried out.

Debromination of DL-di-*O*-acetyl-(1,3/2,4,6)-3,4-dibromo-6-bromomethyl-1,2-cyclohexanediol (**1**)[5] with an excess of zinc dust in acetic acid at 70 °C for 10 min gave DL-di-*O*-acetyl-(1,3/2)-3-bromomethyl-5-cyclohexene-1,2-diol (**3**) in 92% yield. The ^{1}H NMR spectrum of **3** showed the signals for two acetoxyl groups as singlets at δ 2.01 and 2.03, and those for the H-2 and H-6 protons as a triplet of doublets (J= 3, 7.5, and 7.5 Hz) and a broad doublet (J=*ca.* 11 Hz) at δ 5.02 and 5.77, respectively. Treatment of **1** with 4 molar equivalent of sodium benzoate in 80% aqueous ethanol under reflux for 2 d gave the 7-*O*-benzoate (**2**) in 66% yield. The structure was confirmed by the ^{1}H NMR spectrum that showed the down-field shift of the signal for the C-7 methylene group resulting from the replacement of the bromine atom by a benzoyloxyl group. Compound **2** was debrominated similarly with zinc dust to give DL-di-*O*-acetyl-(1,3/2)-3-benzoyloxymethyl-5-cyclohexene-1,2-diol (**4**) in 70% yield, which was also obtained from **3** by treatment with sodium benzoate in refluxing aqueous 2-methoxyethanol for 5 h. The above results confirmed the proposed structures of **3** and **4**. These olefins may be considered as the pseudo-glycal derivatives, versatile intermediates, for the preparation of pseudo-sugar derivatives.

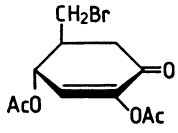
Oxidation of **3** with osmium tetraoxide and hydrogen peroxide in *t*-butyl alcohol, followed by acetylation with acetic anhydride in pyridine, gave mainly a crystalline DL-tetra-*O*-acetyl-(1,2,4/3,5)-5-bromomethyl-1,2,3,4-cyclohexanetetrol (**6**) in 37% yield, together with a small proportion of a sirupy DL-*trans*-2,4-diacetoxy-5-bromomethyl-2-cyclohexanone (**5**), which was isolated in 7.5% yield by chromatography on silica gel. The structure of **5** was tentatively assigned by the elemental analysis and ^{1}H NMR spectral data, the latter of which showed the presence of two acetoxyl groups (δ 2.15 and 2.22) and an olefinic proton (doublet, J=2.5 Hz, δ 6.47), and the remarkable down-field shift of the signal (broad doublet, δ 2.72) for the C-7 methylene protons. In the ^{1}H NMR spectrum of **6**, the signals for H-1, H-2, H-3,



	R
1	Br
2	OBz



	R
3	Br
4	OBz



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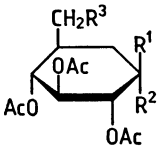
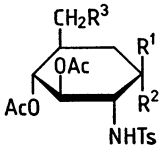


	R^1	R^2	R^3
6	H	OAc	Br
7	H	OAc	OAc
8	H	OAc	N_3
9	H	OAc	NHAc
10	H	OAc	H
11	OAc	H	OAc
12	OAc	H	Br
13	OAc	H	N_3
14	OAc	H	NHAc
15	OAc	H	H



	R^1	R^2	R^3
16	H	OH	Br
17	H	OAc	Br
18	H	OH	OBz
19	H	OAc	OBz
20	H	OH	OAc
21	H	OAc	OAc
22	H	OH	N_3
23	H	OH	NHAc
24	H	OAc	NHAc
25	H	OH	H
26	H	OMs	Br
27	H	OMs	N_3
28	N_3	H	N_3
29	H	OMs	NHAc
30	NHAc	H	NHAc
31	H	H	NHAc
32	OAc	H	OAc

and H-4 protons appeared as a quartet (J=3.5 Hz), a doublet of doublets (J=3.5 and 10.5 Hz), a triplet (J=10.5 Hz), and a triplet (J=10.5 Hz) at δ 5.39, 4.87, 5.23, and 4.94, respectively, which indicated the equatorial-axial-axial-axial conformations for H-1, H-2, H-3, and H-4, being consistent with the assigned structure. Treatment of **6** with an excess of sodium acetate in refluxing aqueous 2-methoxyethanol, followed by conventional acetylation, gave DL-penta-*O*-acetyl-(1,2,4/3,5)-5-hydroxymethyl-1,2,3,4-cyclohexanetetrol (pseudo-α-DL-glucopyranose) (**7**)[6] in 70% yield. Similar treatment of **6** with sodium azide gave the corresponding C-7 azido derivative (**8**) in 80% yield, which was subsequently converted to the acetamide (**9**) in 31% yield[7] by hydrogenation in ethanol containing acetic anhydride in the presence of Raney nickel T-4.[8] Hydrogenolysis of **6** in ethyl acetate with Raney nickel and Amberlite IR-45 (OH^-) gave the 7-deoxy compound (**10**) in 70% yield. The ^1H NMR spectra of **6**—**9** substantially resemble one another in the region for ring protons, except for signals for the exocyclic methylene groups carrying the different functions.

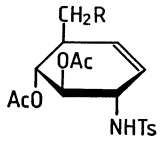
In order to synthesize the same series of compounds with the β-gluco configurations, DL-tetra-*O*-acetyl-(1,3,5/2,4)-5-bromomethyl-1,2,3,4-cyclohexanetetrol (**12**) was prepared, in 91% yield, by treatment of the corresponding C-7 acetate (**11**)[9] with 10% hydrogen bromide in acetic acid in a sealed tube at 80 °C overnight. The corresponding C-7 azido (**13**), acetamido (**14**), and deoxy derivatives (**15**) were obtained analogously starting from **12** in appropriate yields. The structures were confirmed similarly by the ^1H NMR spectral data.

Next, several carbocyclic analogs of glucosamine derivatives were synthesized from **3** and **4**. Treatment of **3** with osmium tetroxide and chloramine T in chloroform–water (1:1) in the presence of triethylbenzylammonium chloride at 60 °C for 40 h, (essentially the procedure of Sharpless and his coworkers)[10] gave a mixture of at least four products. The major product was easily separated by crystallization from ethanol–ether to give DL-3,4-di-*O*-acetyl-(1,2,4/3,5)-5-bromomethyl-2-(*p*-toluenesulfonamido)-1,3,4-cyclohexanetriol (**16**) in 31% isolated yield, which was further characterized as the triacetate (**17**).[11] In the ^1H NMR spectrum of **17**, the signals for H-2, H-3, and H-4 protons appeared as a triplet of doublets (J=3, 11, and 11 Hz), a triplet (J=11 Hz), and a triplet (J=11 Hz) at δ 3.49, 5.09, and 4.88, respectively. Upon deuteration, a doublet (J=11 Hz, δ 5.42) due to the amido proton disappeared and the H-2 signal changed to a doublet of doublets (J=3 and 11Hz). Therefore, the conformations of H-1, H-2, and H-3 were shown to be equatorial-axial-axial, supporting the structure assigned above. Similar *cis*-oxyamination of **4** gave mainly the pseudo-glucosamine derivative (**18**) in 30% yield, which was converted to triacetate (**19**). The structure of **18** could be correlated to that of **16** by comparison of the ^1H NMR spectral data.[12]

Treatment of **16** with sodium acetate in refluxing aqueous 2-methoxyethanol gave its triacetate (**20**) in 57% yield, which was further acetylated to give the tetraacetate (**21**). The ^1H NMR spectrum of **20** resembled that of **16** in the region for ring protons, apart from that the signal for the C-7 methylene protons was shifted down field.

Azidolysis of **16** with sodium azide in *N*,*N*-dimethylformamide (DMF) at 80 °C for 2 h gave the azido derivative (**22**) in 90% yield, which was converted to the corresponding acetamide (**23**) in 57% yield. Tetra-*N*,*O*-acetyl derivative (**24**) was prepared. Hydrogenolysis of **16** gave the C-7 debromo compound (**25**) in 82% yield. The ^1H NMR spectra of **22**—**25** were all consistent with the assigned structures.

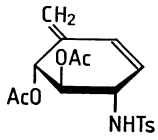
On the other hand, to obtain the derivatives having the β-gluco configuration, an inversion of the C-1 configuration was attempted by a direct substitution reaction of the 1-*O*-methanesulfonate (**26**) of **16**. Thus, **26** was prepared in 69% yield by treatment of **16** with an excess of methanesulfonyl chloride in pyridine. Azidolysis of **26** with 1.5 molar equivalent of sodium azide in DMF at 80 °C for 2 h gave preferentially the C-7 azido derivative (**27**) in 68% yield. While, on treatment with 5 molar equivalent of sodium azide at 85 °C for a prolonged period (20 h), the diazido derivative (**28**) was obtained mainly in 71% yield. Hydrogenation of **27** and **28** followed by acetylation gave the corresponding acetamide (**29**) and diacetamide (**30**) in 65 and 66% yields, respectively. As the side product of the hydrogenation of **28**, DL-1,2-di-*O*-acetyl-(1,3/2,6)-3-acetamidomethyl-6-(*p*-toluenesulfonamido)-1,2-cyclohexanediol (**31**) was isolated in 18% yield, which might arise from the elimination of the C-4 azido group under slightly basic conditions.



R

33 OAc

34 NHAc



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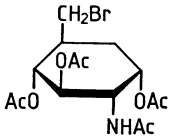

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Reaction of **26** with an excess of sodium acetate in DMF at 80 °C for 20 h gave a mixture of products from which DL-tetra-*O*-acetyl-(1,3,5/2,4)-5-hydroxymethyl-2-(*p*-toluenesulfonamido)-1,3,4-cyclohexanetriol (**32**), DL-1,2-di-*O*-acetyl-(1,3/2,6)-3-hydroxymethyl-6-(*p*-toluenesulfonamido)-4-cyclohexene-1,2-diol (**33**), and DL-1,2-di-*O*-acetyl-(1/2,6)-3-methylene-6-(*p*-toluenesulfonamido)-4-cyclohexene-1,2-diol (**35**) were isolated in 10, 28, and 7% yields, respectively, by chromatography on silica gel. The structures were determined by the elemental analysis and ^1H NMR spectral data. The ^1H NMR spectrum of **32** in chloroform-*d* showed the signal for the H-2 proton as a quartet (J=10 Hz) at δ 3.65, which changed to a triplet upon deuteration, indicating the *trans*-diaxial arrangement of H-1 and H-2. The structure of **33** was assigned by the appearance of two-proton singlet at δ 5.50 attributable to two olefinic protons. In the spectrum of **35**, the signals for the exocyclic methylene protons appeared as a broad singlet at δ 4.96

Table 1. Chemical shifts of acetyl methyl protons[a)]

Compound	1-OAc	3-OAc	4-OAc	7-OAc
16		1.62	2.00	
17	2.06	1.76	1.99	
18		1.64	1.97	
19	2.10	1.78	1.98	
20		1.60	1.97	2.02
21	2.05	1.72	1.97	2.01
22		1.61	2.01	
25		1.60	1.97	
26		1.66	2.01	
27		1.60	2.00	
32	1.71[b)]	1.79[b)]	1.97	2.03

a) Taken at 90 MHz in $CDCl_3$ with reference to TMS. Chemical shifts are given in terms of δ-values. b) Assignments may be reversed.

and 5.06.[13)]

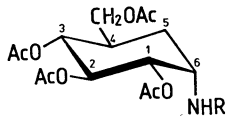
The elimination occurred predominantly in the reaction of **29** with sodium acetate in DMF giving rise to DL-1,2-di-*O*-acetyl-(1,3/2,6)-3-acetamidomethyl-6-(*p*-toluenesulfonamido)-4-cyclohexene-1,2-diol (**34**) in 59% yield. The ^1H NMR spectrum showed the signals for two olefinic protons as two triplets of doublets (J=2, 2, and 12 Hz) at δ 5.34 (H-4) and 5.57 (H-5).

The olefins **33**, **34**, and **35** thus obtained may be good precursors for preparation of branched-chain amino- and diaminocyclitols. Removal of the *N*-(*p*-tolylsulfonyl) group can usually be performed by the influence of sodium in liquid ammonia. Alternatively, on treatment with 20% hydrogen bromide in acetic acid in a sealed tube at 70 °C overnight, **16** gave the corresponding tri-*O*-acetyl amine hydrobromide, which was successively acetylated to the peracetyl derivative (**36**) in 69% yield. This procedure may be used for a small scale deprotection of *N*-(*p*-tolylsulfonyl) derivatives.

We are studying to prepare glycosides of **20** and **22**, which would provide the pseudo analogs of antibiotic trehalosamine and its related compounds.[14)]

Assignment of Acetyl Methyl Protons of N-(p-*Tolylsulfonyl) Derivatives of Pseudo-glucosamine.* Comparison of the ^1H NMR spectra of **16**, **17**, **20**, and **21** allowed to assign all the signals due to the acetyl methyl protons (Table 1). The appreciable up-field shift of the signal for the C-3 equatorial acetoxyl group is observed (at least 0.20 ppm), which may be attributed to a shielding effect by the aromatic ring of the C-2 equatorial *p*-toluenesulfonamido group being in the position perpendicular to the acetyl methyl protons.[15,16a)] Whereas, the C-1 axial acetoxyl group resonates slightly up-shifted by *ca.* 0.10 ppm in the region of δ 2.05—2.10.[16)] These results are consistent with the structure of **32**, in which the presence of two equatorial acetoxyl groups at C-1 and C-3 may be supported by appearance of two up-shifted acetyl signals.

The *N*-(*p*-tolylsulfonyl) derivative (**37**) of validamine was prepared[17)] in order to see the shielding effect of the axially oriented *p*-toluenesulfonamido function. The ^1H NMR spectrum of **37** revealed the acetyl signals as two singlets at δ 1.79 and 2.00 in a ratio of 1:3, while, those of the peracetyl derivative (**38**)[9)]



37 R = Ts
38 R = Ac

showed three singlets at δ 1.99, 2.01, and 2.03 in a ratio of 1:2:2. Therefore, the C-1 acetoxymethyl-signal seems to be shifted to higher field by at least 0.20 ppm due to the C-6 axail *p*-toluenesulfonamido group.

Experimental

Melting points were determined on a Büchi 510 capillary melting point apparatus and are uncorrected. Solutions were concentrated below 50 °C under reduced pressure. Catalytic hydrogenations were carried out in a Parr shaker type apparatus in the initial hydrogen pressure of 3.4 kg/cm² at ambient temperature. Unless otherwise noted, ^1H NMR spectra were taken on a Varian EM-390 (90 MHz) spectrometer in chloroform-*d* ($CDCl_3$) or dimethyl-d_6 sulfoxide (DMSO-d_6) with reference to tetramethylsilane as an internal standard. The peak positions are given in terms of δ-values and values given for coupling constants are of first-order. TLC was performed on precoated silica gel 60 F-254 plaques (Merck, Darmstadt; 0.25 mm thickness). The silica gel used for a column chromatography was Wakogel C-300 (Wako Pure Chemical Industries, Ltd.).

DL-*Di-O-acetyl-(1,3/2,4,6)-3,4-dibromo-6-benzoyloxymethyl-1,2-cyclohexanediol (2).* A mixture of DL-di-*O*-acetyl-(1,3/2,4,6)-3,4-dibromo-6-bromomethyl-1,2-cyclohexanediol (**1**, 2 g),[4)] sodium benzoate (2.56 g, 4 molar equivalent), and 80% aqueous ethanol (50 ml) was refluxed for 2 d. The reaction mixture was allowed to stand in a refrigerator overnight, and the resulting crystals were collected by filtration. Recrystallization from ethanol gave **2** (1.44 g, 66%) as colorless plates: mp 154—155 °C. ^1H NMR ($CDCl_3$, 60 MHz)[18)] δ 1.96 (3H, s) and 2.03 (3H, s) (OAc), 3.80—4.30 (4H, m, H-3, H-4, and CH_2OBz), 4.70—5.35 (2H, m, H-1 and H-2), 7.05—7.90 (5H, m, phenyl).

Found: C, 44.00; H, 4.15; Br, 32.52%. Calcd for $C_{18}H_{20}BrO_6$: C, 43.93; H, 4.10; Br, 32.47%.

DL-*Di-O-acetyl-(1,3/2)-3-bromomethyl-5-cyclohexene-1,2-diol (3).* To a solution of **1** (10 g) in acetic acid (70 ml) was added zinc dust (5.76 g) in three portions at 70 °C. The reaction mixture was stirred vigorously at 70 °C for 10 min and then cooled immediately, and the white precipitates and an excess of zinc dust were removed by filtration. The filtrate was concentrated to give a sirup which crystallized from ethanol–water to give **3** (5.96 g, 92%) as plates: mp 83—84 °C. ^1H NMR ($CDCl_3$) δ 2.01 (3H, s) and 2.03 (3H, s) (OAc), 3.19—3.52 (2H, m, CH_2Br), 5.02 (1H, td, J=3, 7.5, and 7.5 Hz, H-2), 5.29—5.53 (2H, m, H-1 and H-5), 5.63—5.91 (1H, broad d, J=*ca.* 11 Hz, H-6).

Found: C, 45.16; H, 5.04; Br, 27.70%. Calcd for $C_{11}H_{15}BrO_4$: C, 45.37; H, 5.20; Br, 27.44%.

DL-*Di-O-acetyl-(1,3/2)-3-benzoyloxymethyl-5-cyclohexene-1,2-diol (4).* *a)* A stirred suspension of **2** (1 g) and zinc dust (0.53 g) in acetic acid (10 ml) was heated at 70 °C for 0.5 h. After cooling, the reaction mixture was processed as described for the preparation of **3**. The crystalline product was recrystallized from ethanol to give **4** (0.47 g, 70%)

as prisms: mp 75—76.5 °C. ^{1}H NMR ($CDCl_3$) δ 2.02 (6H, s, two OAc), 4.22 (1H, dd, J=5.3 and 12 Hz, H-7), 4.40 (1H, dd, J=4.2 and 12 Hz, H-7'), 5.25 (1H, dd, J=7.7 and 10.5 Hz, H-2), 5.40—5.66 (2H, m, H-1 and H-5), 5.69—5.99 (1H, broad d, J=*ca.* 11 Hz, H-6), 7.34—7.60 (2H, m) and 7.93—8.12 (2H, m) (phenyl).

Found: C, 64.82; H, 6.09%. Calcd for $C_{18}H_{20}O_6$: C, 65.05; H, 6.07%.

b) A mixture of **3** (1.5 g) and sodium benzoate (1.5 g, 2 molar equivalent) in 80% aqueous 2-methoxyethanol (30 ml) was refluxed for 5 h. Then the mixture was concentrated to dryness and the residue was treated with acetic anhydride (10 ml) and pyridine (10 ml) at amibient temperature overnight. An insoluble material was removed by filtration and the filtrate was concentrated. The residue was dissolved in chloroform (20 ml) and passed through a short column of alumina. The filtrate and washings were combined and concentrated. Recrystallization of the residue from ethanol–hexane gave **4** (1.15 g, 67%) as prisms: mp 75—76 °C. This compound was identical with the compound obtained from **2**.

*Oxidation of **3** with Osmium Tetroxide.* *a)* To a solution of **3** (4.37 g) in *t*-butyl alcohol (75 ml) and 35% hydrogen peroxide (15 ml) was added a solution of osmium tetroxide (0.16 g) in *t*-butyl alcohol (15 ml), and the mixture was kept at 30 °C for 24 h under dark. At that time, TLC indicated the disappearance of **3** and the formation of three components (R_f 0.45, 0.38, and 0.34) in 1:1 2-butanone–toluene. The reaction mixture was concentrated and the residue was treated with acetic anhydride and pyridine in usual way. Evaporation of the excess reagent gave a sirup, which was crystallized from ethanol to give DL-tetra-*O*-acetyl-(1,2,4/3,5)-5-bromomethyl-1,2,3,4-cyclohexanetetrol (**6**, 2.24 g, 36.5%). Recrystallization from ethanol gave an analytical sample: mp 137—138 °C. ^{1}H NMR ($CDCl_3$) δ 1.98 (3H, s), 2.00 (3H, s), 2.06 (3H, s), and 2.12 (3H, s) (OAc), 3.34 (2H, d, J=4.5 Hz, C$\underline{H}_2$Br), 4.87 (1H, dd, J=3.5 and 10.5 Hz, H-2), 4.94 (1H, t, J=10.5 Hz, H-4), 5.23 (1H, t, J=10.5 Hz, H-3), 5.39 (1H, q, J=3.5 Hz, H-1).

Found: C, 43.79; H, 5.18; Br, 19.74%. Calcd for $C_{15}H_{21}BrO_8$: C, 44.02; H, 5.17; Br, 19.53%.

The mother liquor from **6** was concentrated and the sirupy residue (2.3 g) was chromatographed on a silica-gel column (40 g) with 1:6 2-butanone–toluene as an eluent. The fractions containing the faster moving component were collected and concentrated to give DL-*trans*-2,4-diacetoxy-5-bromomethyl-2-cyclohexenone (**5**, 0.34 g, 7.5%) as a chromatographically homogeneous sirup. ^{1}H NMR ($CDCl_3$, 60 MHz)[18] δ 2.15 (3H, s) and 2.22 (3H, s) (OAc), 2.72 (2H, broad d, J=2.5 Hz, ring methylene), 3.50 (2H, broad d, J=2.5 Hz, C$\underline{H}_2$Br), 5.70 (1H, symmetric m, H-4), 6.47 (1H, d, J=2.5 Hz, H-3).

Found: C, 43.14; H, 4.50; Br, 26.34%. Calcd for $C_{11}H_{13}BrO_5$: C, 43.30; H, 4.29; Br, 26.19%.

b) To a mixture of **3** (4 g), 35% hydrogen peroxide (15 ml), and *t*-butyl alcohol (75 ml) was added a solution of osmium tetroxide (0.2 g) in *t*-butyl alcohol (40 ml) and the reaction mixture was stirred at 25 °C overnight. The mixture was processed similarly as described in *a)* and the product directly crystallized from ethanol to give **6** (2.6 g, 46%) as prisms: mp 137—138 °C.

DL-*Penta*-O-*acetyl*-*(1,2,4/3,5)*-*5*-*hydroxymethyl*-*1,2,3,4*-*cyclohexanetetrol* (**7**). A mixture of **6** (0.82 g), anhydrous sodium acetate (0.49 g), and 90% aqueous 2-methoxyethanol (20 ml) was refluxed for 20 h. The reaction mixture was concentrated and the residue was treated with acetic anhydride and pyridine in the usual way. The reaction mixture was filtered and the filtrate was concentrated. The residue was triturated with chloroform and the suspension was passed through a short column of alumina. The filtrate was concentrated and the residue was crystallized from ethanol–ether to give **7** (0.32 h, 42%) as needles mp 110—111 °C. ^{1}H NMR ($CDCl_3$) δ 1.99 (3H, s) 2.00 (3H, s), 2.03 (3H, s), 2.05 (3H, s), and 2.13 (3H, s) (OAc), 3.86 (1H, dd, J=3.5 and 11 Hz, H-7), 4.11 (1H, dd, J=4.5 and 11 Hz, H-7'), 4.89 (1H, dd, J=3 and 10.5 Hz, H-2), 4.99 (1H, dd, J=9 and 10.5 Hz, H-4), 5.39 (1H, t, J=10.5 Hz, H-3), 5.41 (1H, q, J=3 Hz, H-1).

Found C, 52.65; H, 6.18%. Calcd for $C_{17}H_{24}O_{10}$: C, 52.57; H, 6.23%.

DL-*Tetra*-O-*acetyl*-*(1,2,4/3,5)*-*5*-*azidomethyl*-*1,2,3,4*-*cyclohexanetetrol* (**8**). A mixture of **6** (0.82 g), sodium azide (0.78 g), and 90% aqueous 2-methoxyethanol (20 ml) was refluxed for 20 h. The reaction mixture was concentrated and the residue was treated with acetic anhydride and pyridine in usual way. The reaction mixture was processed as described for the preparation of **7** to give crystals which were recrystallized from ethanol–ether to give **8** (0.55 g, 74%) as prisms: mp 85—86 °C. ^{1}H NMR ($CDCl_3$, 60 MHz)[18] δ 2.00 (6H, s), 2.07 (3H, s), and 2.13 (3H, s) (OAc), 3.27—3.35 (2H, m, CH_2N_3), 4.85 (1H, dd, J=3 and 9.5 Hz, H-2), 4.92 (1H, broad t, J=9.5 Hz, H-4), 5.38 (1H, broad t, J=9.5 Hz, H-3), 5.45 (1H, q, J=3 Hz, H-1).

Found: C, 48.77; H, 5.81; N, 11.53%. Calcd for $C_{15}H_{21}N_3O_8$: C, 48.52; H, 5.70; N, 11.32%.

DL-*Tetra*-O-*acetyl*-*(1,2,4/3,5)*-*5*-*acetamidomethyl*-*1,2,3,4*-*cyclohexanetetrol* (**9**). A solution of **8** (0.3 g) in ethanol (10 ml) containing acetic anhydride (0.4 ml) was hydrogenated in the presence of Raney nickel T-4[8] overnight. The catalyst was removed by filtration and the filtrate was concentrated. The product was purified by passage through a short column of alumina with chloroform. The filtrate was concentrated and the residue was crystallized from ethanol–ether to give **9** (0.10 g, 31%) as needles: mp 150—151 °C. ^{1}H NMR ($CDCl_3$, 60 MHz)[18] δ 1.99 (9H, s) and 2.08 (6H, s) (NAc and OAc), 3.33—3.95 (2H, m, C$\underline{H}_2$NHAc), 4.78 (1H, broad t, J=9.5 Hz, H-4), 4.84 (1H, dd, J=3 and 9.5 Hz, H-2), 5.33 (1H, q, J=3 Hz, H-1), 5.40 (1H, broad t, J=9.5 Hz, H-3), 6.07 (1H, t, J=5.5 Hz, N$\underline{H}$).

Found: C, 52.87; H, 6.49; N, 3.65%. Calcd for $C_{17}H_{25}NO_9$: C, 52.71; H, 6.51; N, 3.62%.

DL-*Tetra*-O-*acetyl*-*(1,2,4/3,5)*-*5*-*methyl*-*1,2,3,4*-*cyclohexanetetrol* (**10**). A solution of **6** (0.8 g) in ethyl acetate (10 ml) was hydrogenated in the presence of Raney nickel T-4 (one spoonful) and Amberlite IR-45 (OH^-) (5 ml) overnight. The catalyst and the resin were removed by filtration and the filtrate was concentrated. The residue was crystallized from ethanol to give **10** (0.45 g, 70%) as plates: mp 137—138 °C. ^{1}H NMR ($CDCl_3$) δ 0.93 (3H, d, J=6 Hz, methyl), 1.98 (6H, s), 2.03 (3H, s), and 2.10 (3H, s) (OAc), 4.71 (1H, t, J=10.5 Hz, H-4), 4.87 (1H, dd, J=3 and 10.5 Hz, H-2), 5.30 (1H, t, J=10.5 Hz, H-3), 5.31 (1H, q, J=3 Hz H-1).

Found: C 54.82; H, 6.69%. Calcd for $C_{15}H_{22}O_8$: C, 54.54: H, 6.71%.

DL-*Tetra*-O-*acetyl*-*(1,3,5/2,4)*-*5*-*bromomethyl*-*1,2,3,4*-*cyclohexanetetrol* (**12**). A mixture of DL-penta-*O*-acetyl-(1,3,5/2,4)-5-hydroxymethyl-1,2,3,4-cyclohexanetetrol (**11**, 1.0 g)[9] and 10% hydrogen bromide in acetic acid (4.5 ml) was heated in a sealed tube at 80 °C for 16 h. The reaction mixture was poured into ice–water (40 ml) and the precipitates were collected by filtration. Recrystallization from ethanol gave **12** (0.88 g, 83%) as plates: mp 128—129.5 °C. ^{1}H NMR ($CDCl_3$, 60 MHz)[18] δ 1.98 (3H, s), 2.00 (3H,

s), 2.03 (3H, s), and 2.06 (3H, s) (OAc), 3.38 (1H, broad d, J=4 Hz, C$\underline{H}_2$Br), 4.8—5.2 (4H, m, H-1, H-2, H-3, and H-4).

Found: C, 44.20; H, 5.19; Br, 19.67%. Calcd for $C_{15}H_{21}BrO_8$: C, 44.03; H, 5.17; Br, 19.52%.

DL-*Tetra*-O-*acetyl*-*(1,3,5/2,4)*-*5*-*azidomethyl*-*1,2,3,4*-*cyclohexanatetrol* (**13**). A mixture of **12** (0.2 g), sodium azide (0.06 g), and 90% aqueous *N,N*-dimethylformamide (DMF) (5 ml) was stirred at 80 °C for 7 h. The reaction mixture was concentrated and the residue was processed as described for the preparation of **8**. The crude product was recrystallized from ethanol to give **13** (0.16 g, 85%) as prisms: mp 101—102 °C. ^{1}H NMR ($CDCl_3$) δ 1.97 (3H, s), 1.99 (3H, s), 2.02 (3H, s), and 2.03 (3H, s) (OAc), 3.22 (1H, dd, J=6 and 13 Hz, H-7), 3.39 (1H, dd, J=5 and 13 Hz, H-7′), 4.67—5.20 (4H m, H-1, H-2, H-3, and H-4).

Found: C, 48.61; H, 5.71; N, 11.28%. Calcd for $C_{15}H_{21}N_3O_8$: C, 48.52; H, 5.70; N, 11.32%.

DL-*Tetra*-O-*acetyl*-*(1,3,5/2,4)*-*5*-*acetamidomethyl*-*1,2,3,4*-*cyclohexanetetrol* (**14**). A solution of **13** (0.10 g) in ethanol (20 ml) was hydrogenated in the presence of Raney nickel T-4 (one spoonful) overnight. The catalyst was removed by filtration and the filtrate was concentrated. The residue was acetylated in the usual way. The product was crystallized from ethanol to give **14** (60 mg, 58%) as needles: mp 210—211 °C. ^{1}H NMR ($CDCl_3$) δ 1.97 (12H, s) and 2.06 (3H, s) (NAc and OAc), 2.75 (1H, td, J=5, 5, and 14 Hz, H-7, changes to a doublet of doublets with 5 and 14 Hz splittings on deuteration), 3.69 (1H, ddd, J= 3, 8, and 14 Hz, H-7′, changes to a doublet of doublets with 3 and 14 Hz splittings on deuteration), 4.63—5.16 (4H, m, H-1, H-2, H-3, and H-4), 5.99 (1H, broad dd, J=5 and 8 Hz, N$\underline{H}$, disappears on deuteration).

Found: C, 52.80; H, 6.46; N, 3.50%. Calcd for $C_{17}H_{25}NO_9$: C, 52.71; H, 6.51; N, 3.62%.

DL-*Tetra*-O-*acetyl*-*(1,3,5/2,4)*-*5*-*methyl*-*1,2,3,4*-*cyclohexanetetrol* (**15**). A solution of **12** (0.2 g) in ethyl acetate (15 ml) was hydrogenated as described for the preparation of **10**. The product was recrystallized from ethanol to give **15** (0.13 g, 82%) as prisms: mp 110—111 °C. ^{1}H NMR ($CDCl_3$) δ 0.94 (3H, d, J=6 Hz, methyl), 1.12—2.02 (3H, m, H-5, H-6, and H-6′), 1.97 (3H, s), 1.98 (3H, s), 2.00 (3H, s), and 2.02 (3H, s) (OAc), 4.59—5.17 (4H, m, H-1, H-2, H-3, and H-4).

Found: C, 54.41; H, 6.69%. Calcd for $C_{15}H_{22}O_8$: C, 54.54; H, 6.71%.

DL-*3,4-Di*-O-*acetyl*-*(1,2,4/3,5)*-*2*-*(*p-*toluenesulfonamido)*-*5*-*bromomethyl*-*1,3,4*-*cyclohexanetriol* (**16**). To a solution of **3** (1.5 g, 5.2 mmol) in chloroform (25 ml) was added a solution of osmium tetroxide in *t*-butyl alcohol (2.6 ml, 0.052 mmol), chloramine T (trihydrate) (1.82 g), triethylbenzylammonium chloride (0.06 g), and water (25 ml). The mixture was stirred at 60 °C for 40 h. At that time, TLC indicated the formation of the major (R_f 0.64) and three minor components (R_f 0.60, 0.49, and 0.45), together with a trace of **3** (R_f 0.85) in 1:8 ethanol–toluene. Sodium hydrogensulfite (1.5 g) was added to the mixture and it was refluxed for 5 h. Chloroform (50 ml) was added to the cooled mixture, and the organic layer was separated, washed successively with 1% aqueous sodium hydroxide and brine, and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a sirup from which the major product was crystallized out on addition of ethanol. Recrystallization from ethanol gave **16** (0.76 g, 31%) as prisms: mp 196—197 °C. ^{1}H NMR ($CDCl_3$) δ 1.62 (3H, s) and 2.00 (3H, s) (OAc), 2.42 (3H, s, tosyl methyl), 3.01 (1H, d, J=4 Hz, O$\underline{H}$, disappears on deuteration), 3.18—3.51 (1H, m, H-2), 3.32 (2H, d, J=4 Hz, C$\underline{H}_2$Br), 4.07—4.26 (1H, m, H-1), 4.86 (1H, J=10 Hz, H-4), 5.09 (1H, t, J= 10 Hz, H-3), 5.62 (1H, d, J=8 Hz, N$\underline{H}$, disappears on deuteration), 7.28 (2H, d) and 7.75 (2H, d) (J=9 Hz, phenyl).

Found: C, 44.94; H, 5.04; N, 2.78%. Calcd for $C_{18}H_{24}BrNO_7S$: C, 45.20; H, 5.06; N, 2.93%.

Acetylation of **16** (0.1 g) in the usual way gave the triacetate (**17**), which was recrystallized from ethanol to give an analytical sample (0.07 g, 66%) as prisms: mp 192—193 °C. ^{1}H NMR ($CDCl_3$) δ 1.76 (3H, s), 1.99 (3H, s), and 2.06 (3H, s) (OAc), 2.40 (3H, s, tosyl methyl), 3.29 (2H, d, J= 3 Hz, C$\underline{H}_2$Br), 3.49 (1H, ddd, J=3, 9, and 11 Hz, H-2, changes to a doublet of doublets with 3 and 11 Hz splittings on deuteration), 4.88 (1H, t, J=11 Hz, H-4), 5.09 (1H, t, J=11 Hz, H-3), 7.42 (2H, d) and 7.69 (2H, d) (J=9 Hz, phenyl).

Found: C, 45.96; H, 5.07; N, 2.46%. Calcd for $C_{20}H_{26}BrNO_8S$: C, 46.16; H, 5.04; N, 2.69%.

DL-*3,4-Di*-O-*acetyl*-*(1,2,4/3,5)*-*5*-*benzoyloxymethyl*-*2*-*(*p-*toluenesulfonamido)*-*1,3,4*-*cyclohexanetriol* (**18**). To a solution of **4** (2 g, 6 mmol) in chloroform (30 ml) was added a solution of osmium tetroxide in *t*-butyl alcohol (4.5 ml, 0.09 mmol), chloramine T (trihydrate) (2.1 g), benzyltriethylammonium chloride (0.07 g), and water (30 ml), and the mixture was heated at 60 °C under stirring for 2 d. At that time, TLC indicated the formation of one major (R_f 0.45) and one minor products (R_f 0.28), together with **4** (R_f 0.75) in 1:10 ethanol–toluene. The reaction mixture was processed as described for the preparation of **16**. The crude product was purified by passage through a short column of caoline and silica gel with chloroform. Recrystallization from toluene gave **18** (0.93 g, 30%) as prisms: mp 150—152 °C. ^{1}H NMR ($CDCl_3$) δ 1.64 (3H, s), 1.97 (3H, s) (OAc), 2.38 (3H, s, tosyl methyl), 3.41 (1H, dd, J=2.5 and 10 Hz, H-2), 4.99 (1H, t, J=9 Hz, H-4), 5.17 (1H, t, J=9 Hz, H-3), 5.85 (1H d J=9 Hz N$\underline{H}$), 7.18—8.13 (9H, m, phenyl).

Found: C, 57.74; H, 5.70; N, 2.55; S, 6.15%. Calcd for $C_{25}H_{29}NO_9S$: C, 57.79; H, 5.63; N, 2.70; S, 6.17%.

Compound **18** was converted into the triacetate (**19**) by the conventional manner. An analytical sample was obtained by recrystallization from ethanol: mp 200—201 °C. ^{1}H NMR ($CDCl_3$) δ 1.78 (3H, s), 1.98 (3H, s), and 2.10 (3H, s) (OAc), 2.40 (3H, s, tosyl methyl), 3.55 (1H, td, J=5, 9, and 9 Hz, H-2), 4.23 (2H, d, J=4 Hz, C$\underline{H}_2$OBz), 4.91—5.20 (3H, m, H-1, H-3, and H-4), 5.28 (1H, d, J= 9 Hz, N$\underline{H}$), 7.13—8.13 (9H, m, phenyl).

Found: C, 57.46; H, 5.57; N, 2.36; S, 5.50%. Calcd for $C_{27}H_{31}NO_{10}S$: C, 57.74; H, 5.56; N, 2.49; S, 5.71%.

DL-*3,4,7-Tri*-O-*acetyl*-*(1,2,4/3,5)*-*5*-*hydroxymethyl*-*2*-*(*p-*toluenesulfonamido)*-*1,3,4*-*cyclohexanetriol* (**20**). A mixture of **16** (0.2 g), anhydrous sodium acetate (0.086 g), and DMF (5 ml) was heated at 80 °C for 3 d. The reaction mixture was concentrated and the residue was extracted with hot ethyl acetate (20 ml) and the extracts were washed with water. The solution was dried and concentrated to give crystals which were recrystallized from ethanol to give **20** (0.11 g, 57%) as prisms: mp 174—175 °C. ^{1}H NMR ($CDCl_3$) δ 1.60 (3H, s), 1.97 (3H, s), and 2.02 (3H, s) (OAc), 2.39 (3H, s, tosyl methyl), 3.32 (1H, td, J=3, 9, and 9 Hz, H-2), 3.81 (1H, dd, J=3 and 11 Hz, H-7), 4.05 (1H, dd, J=5 and 11 Hz, H-7′), 4.81 (1H, t, J=10 Hz, H-4), 5.03 (1H, t, J=10 Hz, H-3), 5.64 (1H, d, J=8 Hz, N$\underline{H}$), 7.23 (2H, d) and 7.68 (2H, d) (J=9 Hz, phenyl).

Found: C, 52.23; H, 5.92; N, 3.01; S, 6.76%. Calcd for $C_{20}H_{27}NO_9S$: C, 52.51; H, 5.95; N, 3.06; S, 7.01%.

Compound **20** (75 mg) was converted into the tetraacetate (**21**) by the conventional manner. The product was crystallized from ethanol to give an analytical sample (73 mg, 90%) as prisms: mp 173.5—174.5 °C. ^{1}H NMR ($CDCl_3$) δ 1.72 (3H, s), 1.97 (3H, s), 2.01 (3H, s), and 2.05 (3H, s) (OAc), 2.37 (3H, s, tosyl methyl), 3.47 (1H, dd, J= 3.2 and 10.5 Hz, H-2, on deuteration), 3.73 (1H, dd, J= 3.3 and 11.7 Hz, H-7), 4.02 (1H, dd, J=4.5 and 11.7 Hz, H-7′), 4.65—5.25 (3H, m, H-1, H-3, and H-4), 5.29 (1H, d, J=9 Hz, NH, disappears on deuteration), 7.22 (2H, d) and 7.67 (2H, d) (J=9 Hz, phenyl).

Found: C, 52.61; H, 5.76; N, 2.78; S, 6.53%. Calcd for $C_{22}H_{29}NO_{10}S$: C, 52.90; H, 5.85; N, 2.80; S, 6.42%.

DL-*3,4-Di*-O-*acetyl*-*(1,2,4/3,5)*-*5*-*azidomethyl*-*2*-*(*p-*toluenesulfonamido)*-*1,3,4-cyclohexanetriol* (**22**). A mixture of **16** (0.5 g), sodium azide (0.56 g, 4 molar equiv.), and DMF (10 ml) was heated at 80 °C for 3 h under stirring. The reaction mixture was diluted with water (4 ml) and extracted with ethyl acetate (3×5 ml), and the extracts were washed with water and dried. Evaporation of the solvent gave a crystalline residue which was recrystallized from ethanol to give **22** (0.42 g, 90%) as prisms: mp 185—186 °C. ^{1}H NMR ($CDCl_3$) δ 1.61 (3H, s) and 2.01 (3H, s) (OAc), 2.41 (3H, s, tosyl methyl), 3.16—3.47 (3H, m, H-2 and CH_2N_3), 4.02—4.23 (1H, m, H-1), 4.80 (1H, dd, J=11 and 12 Hz, H-4), 5.04 (1H, t, J=11 Hz, H-3), 5.62 (1H, d, J=8 Hz, NH), 7.24 (2H, d) and 7.69 (2H, d) (J=9 Hz, phenyl).

Found: C, 49.10; H, 5.47; N, 12.46; S, 7.04%. Calcd for $C_{18}H_{24}N_4O_7S$: C, 49.08; H, 5.49; N, 12.72; S, 7.28%.

DL-*3,4-Di*-O-*acetyl*-*(1,2,4/3,5)*-*5*-*acetamidomethyl*-*2*-*(*p-*toluenesulfonamido)*-*1,3,4-cyclohexanetriol* (**23**). A solution of **22** (0.25 g) in methanol (15 ml) containing acetic anhydride (0.1 ml) was hydrogenated in the presence of Raney nickel T-4 for 3 d. The catalyst was removed by filtration and the filtrate was concentrated to give crystals which were recrystallized from methanol to give **23** (0.14 g, 57%) as prisms: mp 233.5—234 °C. ^{1}H NMR (DMSO-d_6) δ 1.65 (3H, s), 1.76 (3H, s), and 1.90 (3H, s) (NAc and OAc), 2.32 (3H, s, tosyl methyl), 2.8—3.1 (2H, broad s, CH_2NHAc, changes to a broad doublet with 5 Hz splitting on deuteration), 4.67 (1H, t, J=11 Hz, H-4), 4.91 (1H, t, J= 11 Hz, H-3), 7.32 (2H, d) and 7.67 (2H, d) (J=9 Hz, phenyl).

Found: C, 52.61; H, 6.14; N, 5.87; S, 7.15%. Calcd for $C_{20}H_{28}N_2O_8S$: C, 52.62; H, 6.18; N, 6.14; S, 7.02%.

Compound **23** was converted to triacetate (**24**) in the conventional method. An analytical sample was prepared by recrystallization from ethanol: mp 194—195 °C. ^{1}H NMR ($CDCl_3$) δ 1.83 (3H, s), 1.96 (3H, s), and 2.07 (6H, s) (NAc and OAc), 2.41 (3H, s, tosyl methyl), 2.77 (1H, td, J=5, 5, and 14 Hz, CH_2NHAc, changes to a doublet of doublets with 5 and 14 Hz splittings on deuteration), 3.45 (1H, dd, J=4 and 11 Hz, H-2, on deuteration), 3.62 (1H, dd, J=4 and 14 Hz, H-7′, on deuteration), 4.72 (1H, t, J=11 Hz, H-4), 5.10 (1H, t, J=11 Hz, H-3), 5.51 (1H, d, J=9 Hz, NHTs), 6.02 (1H, dd, J=5 and 8 Hz, NHAc), 7.23 (2H, d) and 7.65 (2H, d) (J=9 Hz, phenyl).

Found: C, 53.16; H, 6.05; N, 5.43; S, 6.13%. Calcd for $C_{22}H_{30}N_2O_9S$: C, 53.00; H, 6.07; N, 5.62; S, 6.43%.

DL-*3,4-Di*-O-*acetyl*-*(1,2,4/3,5)*-*2*-*(*p-*toluenesulfonamido)*-*5*-*methyl*-1,3,4-*cyclohexanetriol* (**25**). A solution of **16** (0.2 g) in ethyl acetate (15 ml) was hydrogenated in the presence of Raney nickel T-4 (one spoonful) and Amberlite IR-45 (OH^-) (3 ml) overnight. The reaction mixture was processed in the usual way. The product was crystallized from ethanol to give **25** (0.14 g, 82%) as plates: mp 179.5—180 °C. ^{1}H NMR ($CDCl_3$) δ 0.88 (3H, d, J=6 Hz, methyl), 1.60 (3H, s) and 1.97 (3H, s) (OAc), 2.39 (3H, s, tosyl methyl), 3.27 (1H, broad d, H-2, changes to a doublet of doublets with 3 and 10 Hz splittings on deuteration), 3.49—4.10 (1H, m, H-1), 4.56 (1H, dd, J=9 and 10 Hz, H-4), 4.99 (1H, t, J=10 Hz, H-3), 5.34—5.80 (1H, m, NH), 7.24 (2H, d) and 7.69 (2H, d) (J=9 Hz, phenyl).

Found: C, 53.89; H, 6.24; N, 3.38; S, 7.78%. Calcd for $C_{18}H_{25}NO_7S$: C, 54.12; H, 6.31; N, 3.51; S, 8.03%.

DL-*3,4-Di*-O-*acetyl*-*1*-O-*methylsulfonyl*-*(1,2,4/3,5)*-*5*-*bromomethyl*-*2*-*(*p-*toluenesulfonamido)*-*1,3,4-cyclohexanetriol* (**26**). To a solution of **16** (1.0 g) in pyridine (10 ml) was added methanesulfonyl chloride (0.36 g) under ice cooling, and then the reaction mixture was stirred at ambient temperature overnight. The mixture was poured into ice-water (50 ml) and the crystals were collected and dried. Recrystallization from ethanol gave **26** (0.81 g, 69%) as needles: mp 187—188 °C. ^{1}H NMR ($CDCl_3$) δ 1.66 (3H, s) and 2.01 (3H, s) (OAc), 2.40 (3H, s, tosyl methyl), 3.17 (3H s mesyl methyl), 3.25—3.59 (3H, m, H-3 and CH_2Br), 4.71—5.03 (3H, m, H-1, H-2, and H-3), 5.68 (1H, d, J= 8 Hz, NH), 7.26 (2H, d) and 7.68 (2H, d) (J=9 Hz, phenyl).

Found: C, 41.27; H, 4.79; N, 2.61%. Calcd for $C_{19}H_{26}BrNO_9S_2$: C, 41.01; H, 4.71; N, 2.52%.

DL-*3,4-Di*-O-*acetyl*-*1*-O-*methylsulfonyl*-*(1,2,4/3,5)*-*5*-*azidomethyl*-*2*-*(*p-*toluenesulfonamido)*-*1,3,4-cyclohexanetriol* (**27**). A mixture of **26** (0.39 g), sodium azide (0.05 g, 1.5 molar equiv.), and DMF (10 ml) was stirred at 80 °C for 2 h. The reaction mixture was processed as described for the preparation of **8**. The product was crystallized from ethanol to give **27** (0.22 g, 68%) as plates: mp 173.5—174.5 °C. ^{1}H NMR ($CDCl_3$) δ 1.60 (3H, s) and 2.00 (3H, s) (OAc), 2.40 (3H, s, tosyl methyl), 3.15 (3H, s, mesyl methyl), 3.21—3.60 (3H, m, H-3 and CH_2N_3), 4.66—5.12 (3H, m, H-1, H-2, and H-4), 5.59 (1H, d, J=8 Hz, NH), 7.29 (2H, d) and 7.66 (2H, d) (J=8 Hz, phenyl).

Found: C, 43.85; H, 4.99; N, 10.52; S, 12.48%. Calcd for $C_{19}H_{26}N_4O_9S_2$: C, 44.01; H, 5.05; N, 10.80; S, 12.36%.

DL-*1,2-Di*-O-*acetyl*-*(1,3/2,4,6)*-*4*-*azido*-*6*-*azidomethyl*-*3*-*(*p-*toluenesulfonamido)*-*1,2-cyclohexanediol* (**28**). A mixture of **26** (0.4 g), sodium azide (0.24 g, 5 molar equivalent), and DMF (10 ml) was stirred at 85 °C for 20 h. The reaction mixture was processed as described for the preparation of **8**. The product was crystallized from ethanol to give **28** (0.24 g, 71%) as prisms: mp 130—131 °C. ^{1}H NMR ($CDCl_3$) δ 1.90 (3H, s) and 2.03 (3H, s) (OAc), 2.39 (3H, s, tosyl methyl), 3.00—3.65 (4H, m, H-3, H-4, and CH_2N_3), 4.85—4.95 (2H, m, H-1 and H-2), 5.41 (1H, d, J=9 Hz, NH), 7.24 (2H, d) and 7.73 (2H, d) (J=8 Hz, phenyl).

Found: C, 46.39; H, 4.95; N, 20.76; S, 6.69%. Calcd for $C_{18}H_{23}N_7O_6S$: C, 46.45; H, 4.98; N, 21.06; S, 6.89%.

DL-*3,4-Di*-O-*acetyl*-*1*-O-*methylsulfonyl*-*(1,2,4/3,5)*-*5*-*acetamidomethyl*-*2*-*(*p-*toluenesulfonamido)*-*1,3,4-cyclohexanetriol* (**29**). A solution of **27** (0.18 g) in methanol (15 ml) containing acetic anhydride (0.11 ml) was hydrogenated in the presence of Raney nickel T-4 overnight. The product was recrystallized from ethanol to give **29** (0.12 g, 65%) as powder: mp 215—215.5 °C. ^{1}H NMR (DMSO-d_6) δ 1.55 (3H, s), 1.76 (3H, s), and 1.89 (3H, s) (NAc and OAc), 2.38 (3H, s, tosyl methyl), 2.85—3.10 (2H, m, CH_2NHAc), 3.16 (3H, s, mesyl ethyl), 3.59—3.88 (1H, m, H-3), 4.55—5.00 (3H, m, H-1, H-2, and H-4), 7.33 (2H, d) and 7.68 (2H, d) (J= 8 Hz, phenyl), 8.20 (1H, broad s, NH).

Found: C, 46.98; H, 5.63; N, 4.97; S, 11.68%. Calcd for $C_{21}H_{30}N_2O_{10}S_2$: C, 47.18; H, 5.66; N, 5.42; S, 11.99%.

DL-*1,2-Di*-O-*acetyl*-*(1,3/2,4,6)*-*4*-*acetamido*-*6*-*acetamidomethyl*-*3*-*(*p-*toluenesulfonamido)*-*1,2-cyclohexanediol* (**30**). A solution (42 mg) in methanol (5 ml) containing acetic

anhydride (0.05 ml) was hydrogenated in the presence of Raney nickel T-4 overnight. At that time, TLC indicated the disappearance of **28** and the formation of a major product along with a minor product. The mixture was fractionated on a silica-gel column with 1:3 ethanol–toluene. The fractions containing the minor product were concentrated to give DL-1,2-di-*O*-acetyl-(1,3/2,6)-3-acetamidomethyl-6-(*p*-toluensulfonamido)-1,2-cyclohexanediol (**31**, 7 mg, 18%) as powder: mp 227.5—228.5 °C. ^{1}H NMR ($CDCl_3$ and D_2O) δ 1.76 (3H, s), 1.97 (3H, s), and 2.03 (3H, s) (NAc and OAc), 2.40 (3H, s, tosyl methyl), 2.72 (1H, dd, J=4 and 14 Hz, H-7), 3.23 (1H, broad dt, J=3, 3, and ca. 9 Hz, H-6), 3.62 (1H, dd, J=3 and 14 Hz, H-7′), 4.52—4.78 (2H, m, H-1 and H-2), 7.25 (2H, d) and 7.67 (2H, d) (J=8 Hz, phenyl).

Found: C, 54.23; H, 6.16; N, 6.05%. Calcd for $C_{20}H_{28}N_2O_7S$: C, 54.53; H, 6.41; N, 6.36%.

The fractions containing the major product gave **30** (29 mg, 66%) as a homogeneous sirup, which solidified on standing. Attempts to crystallize it from several solvents failed. ^{1}H NMR ($CDCl_3$ and D_2O) δ 1.49 (3H, s), 1.87 (3H, s), 1.96 (3H, s) (NAc and OAc), 2.38 (3H, s, tosyl methyl), 2.83 (1H, dd, J=6 and 14 Hz, H-7), 3.32 (1H, dd, J=9 and 11 Hz, H-3), 3.50 (1H, dd, J=3 and 14 Hz, H-7′), 3.90 (1H, ddd, J=4, 11, and 12 Hz, H-4), 4.67 (1H, t, J=9 Hz, H-1), 4.92 (1H, t, J=9 Hz, H-2), 7.22 (2H, d) and 7.67 (2H, d) (J=8 Hz, phenyl).

Found: C, 52.77; H, 6.13; N, 8.13%. Calcd for $C_{22}H_{31}N_3O_8S$: C, 53.12; H, 6.28; N, 8.45%.

*Reaction of **26** with Sodium Acetate.* A mixture of **26** (0.2 g) and anhydrous sodium acetate (0.12 g, 4 molar equiv.) in DMF (5 ml) was stirred at 80 °C for 20 h. At that time, **26** still remained in the mixture. Then the mixture was further heated at 80 °C overnight with addition of sodium acetate (0.06 g, 2 molar equivalent). The reaction mixture was processed as described for the preparation of **27**. The products were fractionated by a silica-gel column with 1:4 2-butanone–toluene. The fractions containing the faster-moving component (R_f 0.48) were concentrated to give DL-1,2-di-*O*-acetyl-(1/2,6)-3-methylene-6-(*p*-toluenesulfonamido)-4-cyclohexene-1,2-diol (**35**, 10 mg, 7%) as crystals: mp 129—130 °C. ^{1}H NMR ($CDCl_3$ and D_2O) δ 1.77 (3H, s) and 2.05 (3H, s) (OAc), 2.40 (3H, s, tosyl methyl), 4.06 (1H broad d, J=8 Hz, H-1), 4.86 (1H, broad d, J=8 Hz, H-1), 4.96 (1H, broad s, H-7), 5.06 (1H, broad s, H-7′), 5.46 (1H, broad d, J=*ca.* 10 Hz, H-5), 5.56 (1H, broad d, J=8 Hz, H-2), 7.23 (2H, d) and 7.68 (2H, d) (J=9 Hz, phenyl).

Found: C, 56.65; H, 5.48; N, 3.48%. Calcd for $C_{18}H_{21}NO_6S$: C, 56.98; H, 5.58; N, 3.69%.

The second fractions (R_f 0.24) gave crystals of DL-1,2,7-tri-*O*-acetyl-(1,3/2,6)-3-hydroxymethyl-6-(*p*-toluenesulfonamido)-4-cyclohexene-1,2-diol (**33**, 44 mg, 28%): mp 156—157 °C. ^{1}H NMR ($CDCl_3$ and D_2O) δ 1.74 (3H, s), 1.99 (3H, s), and 2.02 (3H, s) (OAc), 2.41 (3H, s, tosyl methyl), 3.88 (1H, dd, J=7 and 12 Hz, H-7), 4.06 (1H, dd, J=5 and 12 Hz, H-7′), 4.78—5.28 (3H, m, H-1 and H-2), 5.50 (2H, s, H-4 and H-5), 7.23 (2H, d) and 7.68 (2H, d) (J=8 Hz, phenyl).

Found: C, 54.60; H, 5.72; N, 3.21%. Calcd for $C_{20}H_{25}NO_8S$: C, 54.66; H, 5.73; N, 3.19%.

The third fractions gave DL-tetra-*O*-acetyl-(1,3,5/2,4)-5-hydroxymethyl-2-(*p*-toluenesulfonamido)-1,3,4-cyclohexanetriol (**32**, 15 mg, 10%) as crystals: mp 137—138 °C. Recrystallization from ethanol gave an analytical sample. ^{1}H NMR ($CDCl_3$ and D_2O) δ 1.71 (3H, s), 1.79 (3H, s), 1.97 (3H, s), and 2.03 (3H, s) (OAc), 2.37 (3H, s, tosyl methyl), 3.65 (1H, t, J=10 Hz, H-2), 3.85 (1H, dd, J=2 and 11 Hz, H-7), 4.02 (1H, dd, J=4 and 11 Hz, H-7′), 4.6—5.0 (3H, m, H-1, H-2, and H-4), 7.22 (2H, d) and 7.67 (2H, d) (J=9 Hz, phenyl).

Found: C, 52.70; H, 5.76; N, 2.75%. Calcd for $C_{22}H_{29}NO_{10}S$: C, 52.90; H, 5.85; N, 2.80%.

*Reaction of **29** with Sodium Acetate.* A mixture of **29** (0.12 g), anhydrous sodium acetate (0.055 g, 3 molar equivalent), and DMF (5 ml) was stirred at 80 °C for 2 d. The reaction mixture was concentrated and the residue was taken up in chloroform and filtered. The filtrate was concentrated and the residual product was fractionated on a silica-gel column with 1:4 ethanol–toluene as an eluent. The fractions containing the major product gave crystals of DL-1,2-di-*O*-acetyl-(1,3/2,6)-3-acetamidomethyl-6-(*p*-toluenesulfonamido)-4-cyclohexene-1,2-diol (**34**). Recrystallization from ethanol–ether gave an analytical sample (58 mg, 59%): mp 193.5—194.5 °C. ^{1}H NMR ($CDCl_3$ and D_2O) δ 1.78 (3H, s), 1.92 (3H, s), and 2.02 (3H, s) (NAc and OAc), 2.38 (3H, s, tosyl methyl), 2.90 (1H, dd, J=5 and 14 Hz, H-7), 3.64 (1H, dd, J=4 and 14 Hz, H-7′), 3.99 (1H, broad d, J=8 Hz, H-6), 4.65—5.10 (2H, m, H-1 and H-2), 5.34 (1H, td, J=2, 2, and 12 Hz, H-4), 5.57 (1H, td, J=2, 2, and 12 Hz, H-5), 7.26 (2H, d) and 7.67 (2H, d) (J=8 Hz, phenyl).

Found: C, 54.51; H, 5.96; N, 6.19; S, 7.06%. Calcd for $C_{20}H_{26}N_2O_7S$: C, 54.78; H, 5.98; N, 6.39; S, 7.31%.

*DL-1,3,4-Tri-O-acetyl-(1,2,4/3,5)-2-acetamido-5-bromomethyl-1,3,4-cyclohexanetriol (**36**).* Compound **16** (0.2 g) was heated with 20% hydrogen bromide in acetic acid (3.5 ml) in a sealed tube at 80 °C for 20 h. The mixture was poured into ice–water (50 ml) and, after overnight, the solution was extracted with chloroform (3×10 ml). The extracts were dried and concentrated to give *p*-toluenesulfonic acid (77 mg). The aqueous layer was concentrated to dryness and the residue was treated with acetic anhydride and pyridine in usual way. The product was purified by passage through a short column of alumina with chloroform. Recrystallization from ethanol–ether gave **36** (124 mg, 69%) as needles: mp 177—178 °C. ^{1}H NMR ($CDCl_3$) δ 1.96 (3H, s), 1.98 (3H, s), 2.05 (3H, s), and 2.18 (3H, s) (NAc and OAc), 3.37 (2H, d, J=4.5 Hz, CH_2Br), 4.21 (1H, td, J=3, 9, and 9 Hz, H-2), 4.82—5.30 (3H, m, H-1, H-3, and H-4), 6.23 (1H, d, J=9 Hz, NH).

Found: C, 43.94; H, 5.30; N, 3.37; Br, 19.69%. Calcd for $C_{15}H_{22}BrNO_7$: C, 44.13; H, 5.43; N, 3.43; Br, 19.57%.

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References

1) The nomenclature is based on the IUPAC-IUB Tentative Cyclitol Nomenclature Rule [*J. Biol. Chem.*, **22**, 5809 (1968)]. Alternatively, according to the proposal of McCasland,[3] 5-hydroxymethyl-1,2,3,4-cyclohexanetetrols are named as pseudo-hexopyranoses. For convenience, all the formulas depict one of the respective enantiomers.

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17) Compound **37** was prepared from DL-validamine with assistance of Messrs. N. Chida and M. Ohya: mp 152—153 °C. ^{1}H NMR ($CDCl_3$, 90 MHz) δ 1.79 (3H, s) and 2.00 (9H, s) (OAc), 3.62—3.91 (2H, m, H-6 and H-7), 4.03 (1H, dd, J=4.5 and 11.5 Hz, H-7′), 4.75 (1H, dd, J=4.5 and 10.5 Hz, H-1), 4.87 (1H, dd, J=9 and 10.5 Hz, H-3), 5.23 (1H, dd, J=9 and 10.5 Hz, H-2), 5.43 (1H, d, J=4.5 Hz, NH). Found: C, 52.85; H, 5.58; N, 2.49; S, 6.02%. Calcd for $C_{22}H_{29}NO_{10}S$: C, 52.90; H, 5.85; N, 2.80; S, 6.42%.

18) Taken on a Varian EM-360A (60 MHz) spectrometer