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Synthetic Studies on the Validamycins. VII. Synthesis of DL-2-Deoxyhydroxyvalidamine and DL-2-Deoxyvalienamine[1,2]

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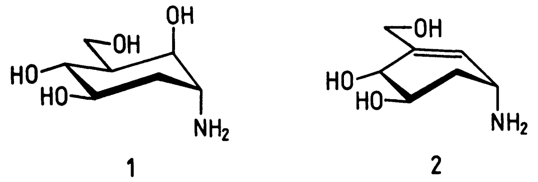
Synthesis of the 2-deoxy analogs of DL-hydroxyvalidamine and DL-valienamine starting from DL-1,2-di-*O*-acetyl-(1,3,5/2)-5-bromo-3-bromomethyl-1,2-cyclohexanediol is described.

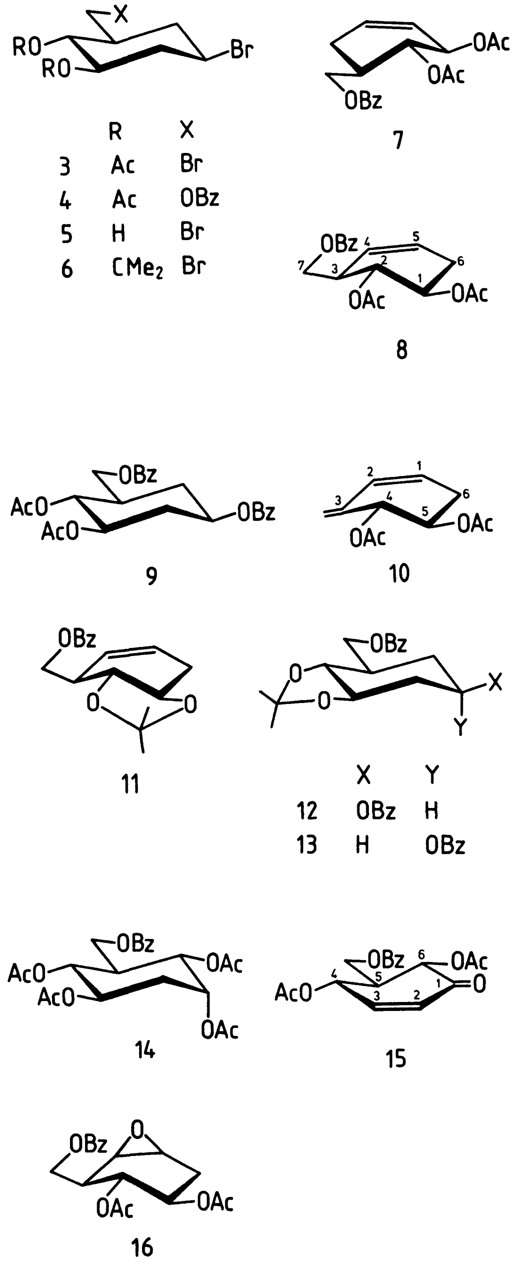
In connection with the previous paper,[3] DL-2-deoxyhydroxyvalidamine (**1**), DL-2-deoxyvalienamine (**2**), and the related cyclitol derivatives were synthesized starting from the readily available DL-1,2-di-*O*-acetyl-(1,3,5/2)-5-bromo-3-bromomethyl-1,2-cyclohexanediol (**3**),[4] following mainly the sequence previously employed for the synthesis of DL-hydroxyvalidamine.[3]



Scheme 1.

Treatment of **3** with 2 molar equiv. of sodium benzoate in 90% aqueous *N*,*N*-dimethylformamide (DMF) at 75 °C gave the monobenzoate **4** in 52% yield. When **4** reacted with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in toluene at reflux temperature, two olefins **7** and **8** were obtained, after chromatography on silica gel, in 48 and 25% yields, respectively. On the other hand, treatment of **3** with 3 molar equiv. of sodium benzoate and a molar equiv. of lithium bromide in DMF at 120 °C for 1 h gave, after chromatography, **7** (36%), **8** (26%), dibenzoate **9** (8%), and diolefin **10** (19%). Compound **7** was identified with an authentic sample.[5] The ^{1}H NMR spectrum of **8** showed the signals of H-1 and H-2 as a triplet of doublets (δ=5.10, J=6, 11, and 11 Hz) and a triplet (δ=5.28, J=11 Hz), supporting the structural assignment. Compound **4** was first converted, by attack of a bromide ion, into its C-5 epimer, which would readily undergo elimination to give **7** and **8**. This assumption may be supported by the formation of **9**. The ^{1}H NMR spectrum of **10** revealed the signals of H-2, H-4, and H-5 as a broad doublet (δ=6.13, J=10 Hz), a doublet (δ=5.60, J=9 Hz) and a triplet of doublets (δ=5.53, J=3.6, 9, and 9 Hz), respectively, indicating the assigned structure. Compound **10** was characterized by conversion into the crystalline bis(*p*-nitrobenzoate).

In order to obtain desired **8** selectively, **3** was transformed into the 1,2-*O*-isopropylidene derivative **6**. Since introduction of the 1,2-*O*-isopropylidene-fused ring into the cyclohexane ring gave appreciable strain in it, the elimination reaction was expected to proceed regioselectively to give rise to either one of the two isomeric olefins.



Scheme 2.

O-Deacetylation of **3** was carried out with hydrobromic acid in aqueous ethanol at reflux temperature to give the dihydroxy compound **5** in 95% yield. Treatment of **5** with 2,2-dimethoxypropane in DMF in the presence of *p*-toluenesulfonic acid at 70 °C gave **6** in 97% yield. Similar treatment of **6** with sodium benzoate and lithium bromide in DMF produced a single olefin **11** in 60% yield,[6] together with the substitution products **12** (12%) and **13** (5%). The structure of

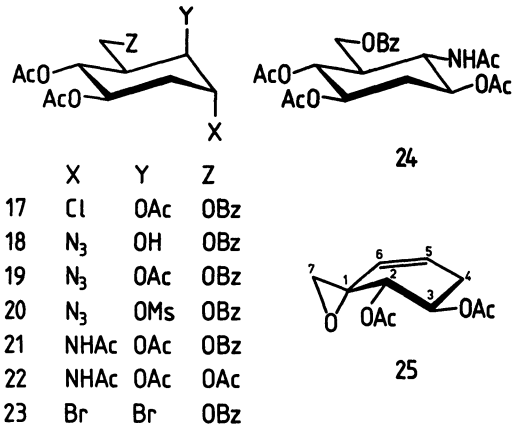
11 was confirmed by converting it into **8**. The structures of **12** and **13** were tentatively assigned by ^{1}H NMR spectroscopy. Thus, the spectra of **12** and **13** showed the signals of H-5 as a wide triplet of triplets (δ=5.20, J=5, 5, 11, and 11 Hz) and a narrow quitet (δ=5.58, J=3 Hz), respectively. Formation of **12** and **13** indicated that the ring bromine atom of **6** was first displaced by bromide ion as well as benzoate ion. The intermediate C-5 epimer of **6** would be converted into **11** *via* regioselective elimination and a small proportion of **12** *via* displacement reaction.

In order to see reactivity of **8** and to provide ^{1}H NMR spectral data of related cyclitol derivatives, synthesis of (hydroxymethyl)cyclohexanetetrol was carried out by oxidation with osmium tetraoxide in 2-propanol containing 5% hydrogen peroxide at room temperature. The products were subsequently acetylated with acetic anhydride in pyridine at room temperature and fractionated by silica-gel chromatography to give pentol peracylate **14** and α,β-unsaturated ketone **15** in 38 and 5.2% yields, respectively.[7] The ^{1}H NMR spectrum of **14** showed a quartet (J=3 Hz) at δ=5.40, which was attributed to the proton attached to the carbon atom bearing an axial acetoxyl group. The spectrum of **15** was interpreted assuming the first-order splitting. Formation of **15** involved facile β-elimination of the acetoxyl group at C-1.

Epoxidation of **8** with *m*-chloroperoxybenzoic acid (*m*CPBA) and sodium hydrogencarbonate in 1,2-dichloroethane at room temperature yielded almost exclusively the epoxide **16** in 80% yield, together with an isomeric epoxide (<7%). Treatment of **16** with sodium azide and ammonium chloride in aqueous 2-methoxyethanol at 75 °C gave the single azido compound **18** in 76% yield through *trans*-diaxial opening of the epoxide ring. The ^{1}H NMR spectrum of **18** exhibited a quartet (J=2.5 Hz) at δ=3.83, which was ascribed to the axial proton on the carbon atom bonding to the azido function. Treatment of **16** with sodium acetate and ammonium chloride followed by acetylation gave the chloride **17** in 58% yield. The structure of **17** was shown to correspond with that of **18** by comparison of their ^{1}H NMR spectra. Accordingly, the structure of **16** was established as shown in Scheme 2 on the basis of the above results and the ^{1}H NMR spectral data. It was thought that the peroxy acid may attack **8** from less hindered side, since there is no polar substituent on the α-carbon atom that would influence the direction of the attack of the peroxy acid.

Compound **18** was converted into the triacetate **19** or the mesylate **20** in good yield. Hydrogenation of **19** with Raney nickel in ethanol followed by the conventional acetylation afforded the peracyl derivative **21** of **1** in 60% yield. Alternatively, ammonolysis of **16** with methanolic ammonia in a sealed tube at 90 °C for 15 h followed by acetylation gave, after chromatography, three amides **21** (17%), **22** (31%), and **24** (19%). The structure of **22** was determined by comparison of the ^{1}H NMR spectrum with that of **21**. The ^{1}H NMR spectrum of **24** was in accord with that of the product derived by *trans*-diequatorial opening of the epoxide.

On the other hand, **20** was treated with DBU in toluene at reflux temperature for 6 h gave the olefin **28** in 76% yield. The ^{1}H NMR spectrum of **28** showed a broad doublet (δ=6.12, J=3 Hz) and a narrow multiplet (δ=4.10), which were assigned to H-4 and H-5, respectively. Reduction of the azido group was effected by hydrogen sulfide in aqueous pyridine at room temperature,[8] and, after acetylation, the amide **29** was obtained in 65% yield. In the ^{1}H NMR spectrum of **29**, the olefinic proton appeared as a broad doublet (J=3.5 Hz) at δ=6.03. This is indicative of the pseudo-axial conformation of the acetamido group.[9] Compound **29** was a 2-deoxy analog of valienamine.

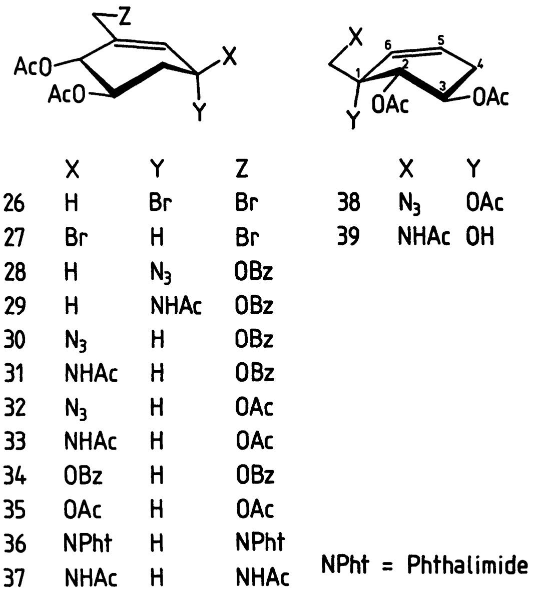


	X	Y	Z
17	Cl	OAc	OBz
18	N_3	OH	OBz
19	N_3	OAc	OBz
20	N_3	OMs	OBz
21	NHAc	OAc	OBz
22	NHAc	OAc	OAc
23	Br	Br	OBz

24

25

Scheme 3.



	X	Y	Z
26	H	Br	Br
27	Br	H	Br
28	H	N_3	OBz
29	H	NHAc	OBz
30	N_3	H	OBz
31	NHAc	H	OBz
32	N_3	H	OAc
33	NHAc	H	OAc
34	OBz	H	OBz
35	OAc	H	OAc
36	NPht	H	NPht
37	NHAc	H	NHAc

	X	Y
38	N_3	OAc
39	NHAc	OH

NPht = Phthalimide

Scheme 4.

The 5-epimer of **2** and related cyclitols were prepared according to the following sequence. Compound **8** reacted with bromine in carbon tetrachloride at room temperature to give dibromide **23** in 47% yield as the only product. The ^{1}H NMR spectrum of **23** showed the signal of C-1 proton as a triplet of doublets (J=6, 9.5, and 9.5 Hz) at δ=5.38 somewhat lower-field as compared with that (δ=4.85) of **4**. It may be attributable to the presence of the bromine atom in a 1,3-diaxial position. Treatment of **23** with sodium azide in DMF at 120 °C gave azide **30** in 91% yield as the sole product.

The structure was assigned by comparison of its ^{1}H NMR spectrum with that of **28**. In contrast, the signal of C-4 olefinic proton appeared as a broad singlet (δ=5.99) in the case of **30**. Upon similar reduction followed by acetylation, **30** was converted into amide **31** in 58% yield. Reaction of **23** with benzoate ion in DMF similarly gave dibenzoate **34** in 62% yield. The reactions of **23** seemed to involve first the ready elimination of hydrobromic acid between C-3 and C-4. The intermediate allyl bromide was then substituted by the nucleophile *via* direct S_N2 reaction.

In addition, alternative synthetic route for deoxyvalienamine derivatives was studied starting from **10**, which could readily be prepared by treatment of **3** with DBU in toluene at reflux temperature. Reaction of **10** with bromine in carbon tetrachloride at 0 °C yielded a stereoisomeric mixture of 1,4-addition products **26** and **27** in 54% yield, together with a small amount of crystalline tetrabromide. Without further separation, the mixture of **26** and **27** was treated with an excess of sodium benzoate in 90% aqueous DMF at room temperature to give the dibenzoate **34** in 30% yield. The epimer of **34** was not isolated in pure form because of their similar mobility on TLC. Compound **34** was converted into the corresponding tetraacetate **35**. When the mixture was treated with potassium phthalimide in DMF at room temperature, a single bis(phthalimide) **36** was obtained in 58% yield selectively. Treatment of **36** with butylamine in methanol, followed by acetylation gave the bis(acetamide) **37** in 98% yield. The ^{1}H NMR spectrum was consistent with the assigned structure.

On the other hand, epoxidation of **10** with *m*CPBA in dichloromethane and phosphate buffer solution (pH 8) afforded mainly crystalline spiro epoxide **25** in 50% yield.[10] Azidolysis of **25** with sodium azide and ammonium chloride in DMF at 60 °C resulted in preferential attack at C-7 by azide ion to give only azide **38** in 92% yield. The structure of **38** was supported by ^{1}H NMR signal of the branched-chain methylene protons which appear at somewhat higher-field (AB-quartet, δ=3.60 and 3.83) than those (δ=4.15 and 4.51) of the related 1-*C*-acetoxymethyl compound.[11] Reduction of **38** with hydrogen sulfide followed by acetylation gave the amide **39** in quantitative yield. However, treatment of **25** with sodium azide and sulfuric acid in aqueous acetone at room temperature yielded, after acetylation, mainly the azide **32** in 48% yield. Similar reduction followed by acetylation gave the amide **33**, whose ^{1}H NMR spectrum showed the olefinic proton as a broad singlet (δ=4.70) and was comparable with **31** in the vicinity of the signals due to ring protons.

The branched-chain aminocyclitols and cyclitols described in this paper are not only biologically interesting compounds, but also useful model substances for structural elucidation of pseudonitrogen disaccharides reported in the accompanying paper.[12]

Experimental

Unless otherwise noted, melting points were determined on a Mitamura Riken micro hot stage apparatus and are uncorrected. ^{1}H NMR spectra were taken on a Varian EM-360 (60 MHz) or a Varian EM-390 (90 MHz) in chloroform-*d* ($CDCl_3$) with reference to tetramethylsilane as an internal standard. The peak positions are given in terms of δ-values. Values given for coupling constants are of first-order. TLC was performed on precoated silica gel 60 F-254 plates (Merck, Darmstadt; 0.25 mm thickness). The silica gel for a column chromatography was Wakogel C-300 (Wako Pure Chemical Industries, Ltd.). Organic solutions were dried over anhydrous sodium sulfate. Solutions were concentrated below 50 °C under reduced pressure.

DL-*1,2-Di-O-acetyl- (1,3,5/2)- 3-benzoyloxymethyl-5 - bromo - 1,2 cyclohexanediol (**4**).* A mixture of DL-1,2-di-*O*-acetyl-(1,3,-5/2)-5-bromo-3-bromomethyl-1,2-cyclohexanediol (**3**)[4] (2.0 g), sodium benzoate (1.56 g, 2 molar equiv.), and 90% aqueous DMF was stirred at 75 °C for 10 h, and then concentrated. The residue was extracted with ethyl acetate and the extracts were filtered through a short column of alumina. The filtrate was concentrated and the residue was crystallized from ethanol to give 1.15 g (52%) of **4**: mp 121—123 °C.** ^{1}H NMR (90 MHz) δ=2.03 (6H, s, OAc), 4.00 (1H, tt, $J_{4eq,5}=J_{5,6cq}=4$ Hz, $J_{4ax,5}=J_{5,6ax}=12$ Hz, H-5), 4.18 (1H, dd, $J_{3,7}=5$ Hz, $J_{gem}=11.5$ Hz, H-7), 4.35 (1H, dd, $J_{3,7'}=3$ Hz, H-7′), 4.85 (1H, ddd, $J_{1,2}=9.5$ Hz, $J_{1,6eq}=4.5$ Hz, $J_{1,6ax}=11$ Hz, H-1), 5.10 (1H, t, $J_{2,3}=9.5$ Hz, H-2), 7.34—7.74 (3H, m) and 8.01—8.17 (3H, m) (phenyl).

Found: C, 52.13; H, 5.22; Br, 19.64%. Calcd for $C_{18}H_{21}BrO_6$: C, 52.31; H, 5.21; Br, 19.33%.

*Reaction of **4** with DBU.* A mixture of **4** (0.20 g), DBU (0.36 ml), and toluene (6 ml) was refluxed for 14 h. The reaction mixture was diluted with toluene (20 ml) and the solution was washed with 1 M hydrochloric acid (1 M=1 mol dm^{-3}), saturated sodium hydrogencarbonate, and water, and dried. Evaporation of the solvent gave an oil (0.17 g) which was chromatographed on a silica gel with ethyl acetate–hexane (1 : 5) as an eluent. The first fraction gave crystals which were recrystallized from ethanol to give 96 mg (48%) of DL-1,2-di-*O*-acetyl-(1,3/2)-3-benzoyloxymethyl-5-cyclohexene-1,2-diol (**7**) as prisms: mp 75.5—76 °C,** identical with an authentic sample (mp 75—76.5 °C).

The second fraction gave crystals which were recrystallized from ethanol to give 50 mg (25%) of DL-1,2-di-*O*-acetyl-(1,3/2)-3-benzoyloxymethyl-4-cyclohexene-1,2-diol (**8**) as prisms: mp 76—78 °C.** ^{1}H NMR (90 MHz) δ=2.03 (6H, s, OAc), 4.20 (1H, dd, $J_{3,7}=5.5$ Hz, $J_{gem}=10.5$ Hz, H-7), 4.43 (1H, dd, $J_{3,7'}=5$ Hz, H-7′), 5.10 (1H, td, $J_{1,2}=J_{1,6ax}=11$ Hz, $J_{1,6eq}=6$ Hz, H-1), 5.28 (1H, t, $J_{2,3}=11$ Hz, H-2), 5.50—5.79 (2H, m, H-4 and H-5), 7.28—7.66 (3H, m) and 7.95—8.11 (2H, m) (phenyl).

Found: C, 65.15; H, 6.07%. Calcd for $C_{18}H_{20}O_6$: C, 65.05; H, 6.07%.

*Reaction of **3** with Sodium Benzoate in DMF.* A mixture of **3** (0.30 g), sodium benzoate (0.35 g), lithium bromide (0.17 g), and dry DMF (10 ml) was stirred at 120—130 °C for 1 h, and then concentrated. The residue was extracted with ethyl acetate and the extracts was passed through a short column of alumina. The filtrate was concentrated to give an oil (0.27 g), which was chromatographed on a silica-gel column (15 g) with ethyl acetate–hexane (1 : 4) as an eluent. The first fraction gave 32 mg (19%) of DL-*trans*-4,5-diacetoxy-3-methylene-1-cyclohexene (**10**) as an oil. ^{1}H NMR (90 MHz) δ=2.00 (3H, s) and 2.08 (3H, s) (OAc), 2.63 (1H, br dt, $J_{1,6eq}=J_{5,6eq}=5$ Hz, $J_{gem}=16.5$ Hz, H-6eq), 4.90—5.12 (3H, m, H-5 and exocyclic methylene), 5.35—5.73 (2H, m, H-4 and H-5), 6.13

** Determined on a Büchi 510 capillary melting point apparatus.

(1H, br d, $J_{1,2}=10$ Hz, H-2). This compound was identical with a sample later derived by an unequivocal route.

The second fraction gave 97 mg (36%) of **7**. The third fraction gave 70 mg (26%) of **8**. The fourth fraction gave crystals which were recrystallized from ethanol to give 28 mg (8%) of DL-1,2-di-*O*-acetyl-5-*O*-benzoyl-(1,3,5/2)-3-benzoyloxymethyl-1,2,5-cyclohexanetriol (**9**) as needles: mp 126—128 °C. ^{1}H NMR (90 MHz) $\delta=2.02$ (3H, s) and 2.04 (3H, s) (OAc), 4.23 (1H, dd, $J_{3,7}=4.5$ Hz, $J_{gem}=11$ Hz, H-7), 4.40 (1H, dd, $J_{3,7'}=4$ Hz, H-7′), 4.86—5.30 (3H, m, H-1, H-2, and H-5), 7.32—8.18 (10H, m, phenyl).

Found: C, 66.28; H, 5.89%. Calcd for $C_{25}H_{26}O_8$: C, 66.07; H, 5.77%.

DL-*(1,3,5/2)-5-Bromo-3-bromomethyl-1,2-cyclohexanediol (5).* A mixture of **3** (15.0 g) and ethanol (300 ml) containing 47% hydrobromic acid (30 ml) was heated at reflux for 6 h. The reaction mixture was neutralized with 2 M sodium hydroxide (120 ml) and concentrated until precipitates appeared. The solution was extracted with chloroform (100 ml), and the extracts were washed with water thoroughly and dried. Evaporation of the solvent gave crystals which were recrystallized from chloroform to give 11.0 g (95%) of **5** as needles: mp 108—110 °C.

Found: C, 29.37; H, 4.05; Br, 55.71%. Calcd for $C_7H_{12}Br_2O_2$: C, 29.20; H, 4.20; Br, 55.49%.

DL-*1,2-O-Isopropylidene-(1,3,5/2)-5-bromo-3-bromomethyl-1,2-cyclohexanediol (6).* To a solution of **5** (7.0 g) in dry DMF (80 ml) was added 2,2-dimethoxypropane (30 ml) and a catalytic amount of *p*-toluenesulfonic acid, and the mixture was heated at 70—80 °C for 2 h. The reaction mixture was concentrated with a small amount of sodium hydrogencarbonate to give an oil which was dissolved in chloroform and passed through a short column of alumina. The filtrate was concentrated and the residue was crystallized from ethanol to give 7.7 g (97%) of **6** prisms: mp 59—60.5 °C.

Found: C, 36.88; H, 4.90; Br, 48.89%. Calcd for $C_{10}H_{16}Br_2O_2$: C, 36.61; H, 4.92; Br, 48.72%.

*Reaction of **6** with Sodium Benzoate in DMF.* A mixture of **6** (0.50 g), sodium benzoate (0.55 g), lithium bromide (0.16 g), and dry DMF (10 ml) was stirred at 105—110 °C for 2 h. The reaction mixture was processed similarly as described in the reaction of **3** and the products were fractionated by chromatography on silica gel with 2-butanone–toluene (1 : 30) as an eluent.

The first fraction gave 0.26 g (60%) of DL-1,2-*O*-isopropylidene-(1,3/2)-3-benzoyloxymethyl-4-cyclohexene-1,2-diol (**11**) as an oil. ^{1}H NMR (90 MHz) $\delta=1.44$ (6H, s, isopropylidene), 3.47 (1H, t, $J_{1,2}=J_{2,3}=9$ Hz, H-2), 3.72 (1H, td, $J_{1,6eq}=5$ Hz, $J_{1,6ax}=9$ Hz, H-1), 4.28 (1H, dd, $J_{3,7}=7$ Hz, $J_{gem}=11$ Hz, H-7), 4.57 (1H, dd, $J_{3,7'}=5$ Hz, H-7′), 5.51—5.56 (2H, m, H-4 and H-5), 7.28—7.73 (3H, m) and 8.00—8.26 (2H, m) (phenyl). Compound **11** did not give a satisfactory analytical data, and the mass spectrum was measured:[13] Found: *m/e* 194.1295. Calcd for $C_{17}H_{20}O_4$: M$^+$ 194.1307.

Compound **11** (4.6 g) was treated with 50% aqueous acetic acid (50 ml) at room temperature for 30 min. and then mixture was concentrated. The residue was treated with acetic anhydride (20 ml) and pyridine (30 ml) at room temperature overnight. The reaction mixture was concentrated and the product was recrystallized from ethanol to give 5.1 g (96%) of **8**, identical with the compound obtained before.

The second fraction gave 72 mg (12%) of DL-5-*O*-benzoyl-1,2-*O*-isopropylidene-(1,3,5/2)-3-benzoyloxymethyl-1,2,5-cyclohexanetriol (**12**) as an oil. ^{1}H NMR (90 MHz) $\delta=1.44$ (6H, s, isopropylidene), 3.32 (1H, t, $J_{1,2}=J_{2,3}=9$ Hz, H-2), 3.52 (1H, td, $J_{1,6eq}=3$ Hz, $J_{1,6ax}=9$ Hz, H-1), 4.22 (1H, dd $J_{3,7}=6.5$ Hz, $J_{gem}=11$ Hz) and 4.49 (1H, dd, $J_{3,7'}=3.5$ Hz) ($C\underline{H}_2OBz$), 5.20 (1H, tt, $J_{4eq,5}=J_{5,6eq}=5$ Hz, $J_{4ax,5}=J_{5,6ax}=11$ Hz H-5).

The third fraction gave 31 mg (6%) of DL-5-*O*-benzoyl-1,2-*O*-isopropylidene-(1,3/2,5)-3-benzoyloxymethyl-1,2,5-cyclohexanetriol (**13**) as an oil. ^{1}H NMR (90 MHz) $\delta=1.47$, (6H, s, isopropylidene), 3.35 (1H, dd, $J_{1,2}=9$ Hz, $J_{2,3}=10.5$, Hz, H-2), 3.88 (1H, ddd, $J_{1,6eq}=4$ Hz, $J_{1,6ax}=11$ Hz, H-1) 4.33 (1H, dd, $J_{3,7}=6$ Hz, $J_{gem}=11$ Hz) and 4.56 (1H, dd, $J_{3,7'}=5$ Hz) ($C\underline{H}_2OBz$), 5.58 (1H, quintet, $J=3$ Hz, H-5).

Found for **12**: *m/e* 395.1523, and for **13**: *m/e* 410.1754, 395.1475. Calcd for $C_{24}H_{26}O_6$: M$^+$, 410.1728, M$^+-15$, 395.1493.

*Oxidation of **8** with Osmium Tetraoxide.* To a solution of **8** (0.10 g) in *t*-butyl alcohol (2.2 ml) containing 6% hydrogen peroxide was added a solution of osmium tetraoxide (0.65 ml, 0.013 mmol), and the mixture was stirred at room temperature for 20 h. The reaction mixture was diluted with water (2 ml) and sodium sulfite was added until the peroxide was consumed. The mixture was concentrated and the residue was acetylated in the usual way. The product was chromatographed on a silica-gel column with 2-butanone–toluene (1 : 12) as an eluent. The first fraction gave crystals which were recrystallized from ethanol to give 42 mg (38%) of DL-1,2,4,5-tetra-*O*-acetyl-(1,2,4/3,5)-3-benzoyloxymethyl-1,2,4,5-cyclohexanetetrol (**14**) as prisms: mp 145—146 °C. ^{1}H NMR (90 MHz) $\delta=1.98$ (3H, s), 1.99 (3H, s), 2.02 (3H, s), and 2.10 (3H, s) (OAc), 4.28 (2H, m, $C\underline{H}_2OBz$), 4.90 (1H, dd, $J_{1,2}=3$ Hz, $J_{2,3}=11$ Hz, H-2), 5.03—5.30 (2H, m, H-4 and H-5), 5.40 (1H, q, $J=3$ Hz, H-5), 7.11—7.99 (5H, m, phenyl).

Found: C, 58.69; H, 5.89%. Calcd for $C_{22}H_{26}O_{10}$: C, 58.66; H, 5.82%.

The second fraction gave crystals which were recrystallized from ethanol to give 5.4 mg (5.2%) of DL-*r*-4,*c*-6-diacetoxy-*t*-5-benzoyloxymethyl-2-cyclohexanone (**15**) as prisms: mp 109—110 °C. ^{1}H NMR (90 MHz) $\delta=2.10$ (3H, s) and 2.15 (3H, s) (OAc), 2.75 (1H, ddd, $J_{4,5}=10$ Hz, $J_{5,6}=13$ Hz, $J_{5,7}=3$ Hz, H-5), 4.39 (2H, d, $J=3$ Hz, $C\underline{H}_2OBz$), 5.45 (1H, d, H-6), 5.77 (1H, ddd, $J_{2,4}=2$ Hz, $J_{3,4}=2.5$ Hz, H-4), 6.10 (1H, dd, $J_{2,3}=10.5$ Hz, H-3), 6.77 (1H, dd, H-2).

Found: C, 62.17; H, 5.36%. Calcd for $C_{18}H_{18}O_7$: C, 62.42; H, 5.24%.

DL-*4,5-Di-O-acetyl-1,2-anhydro-(1,2,3,5/4)-3-benzoyloxymethyl-1,2,4,5-cyclohexanetetrol (16).* A suspension of **8** (1.0 g), *m*CPBA (1.06 g, *ca.* 1.5 molar equiv), and sodium hydrogencarbonate (0.72 g) in 1,2-dichloroethane (20 ml) was vigorously stirred at room temperature for 18 h. The reaction mixture was diluted with water (20 ml) and sodium sulfite was added to destroy the peracid. The organic layer was washed with water thoroughly and dried. Evaporation of the solvent gave crystals which were recrystallized from ethanol to give 0.84 g (80%) of **16** as needles: mp 96—99 °C. ^{1}H NMR (90 MHz) $\delta=2.01$ (6H, s, OAc), 3.18 (1H, t, $J_{1,2}=J_{2,3}=4.5$ Hz, H-2), 3.40 (1H, ddd, $J_{1,6eq}=3.5$ Hz, $J_{1,6ax}=6.5$ Hz, H-1), 4.37 (1H, dd, $J_{3,7}=7$ Hz, $J_{gem}=11$ Hz, H-7), 4.56 (1H, dd, $J_{3,7'}=5$ Hz, H-7′), 4.82 (1H, td, $J_{4,5}=J_{5,6ax}=9.5$ Hz, $J_{5,6eq}=7.5$ Hz, H-5), 5.11 (1H, t, $J_{3,4}=9.5$ Hz H-4), 7.30—7.58 (3H, m) and 7.96—8.12 (3H, m) (phenyl).

Found: C, 61.92; H, 5.81%. Calcd for $C_{18}H_{20}O_7$: C, 62.06; H, 5.79%.

A trace of a stereoisomeric epoxide (8 mg, 7%) was obtained as an oil. ^{1}H NMR (90 MHz) $\delta=2.02$ (3H, s) and 2.07 (3H, s) (OAc), 3.07 (1H, d, $J_{1,2}=3.5$ Hz, H-2), 3.30 (1H, m, H-1), 4.35 (1H, dd, $J_{3,7}=3$ Hz, $J_{gem}=10$ Hz, H-7), 4.72 (1H, dd, $J_{3,7'}=4$ Hz, H-7′), 4.78—5.16 (2H, m, H-4 and H-5), 7.32—7.60 (3H, m) and 7.98—8.14 (2H, m) (phenyl).

DL-*1,2-Di-O-acetyl-(1,3,4/2,5)-3-benzoyloxymethyl-5-chloro-1,2-*

4-cyclohexanetriol (17). A mixture of **16** (0.10 g), sodium acetate (47 mg), and ammonium chloride (46 mg) in 90% aqueous 2-methoxyethanol (5 ml) was heated at 80 °C for 5 h, and then concentrated. The residue was treated with acetic anhydride and pyridine in the usual way. The product was purified by a silica-gel column with 2-butanone–toluene (1 : 10) as an eluent. The main fraction gave crystals which were recrystallized from ethanol to give 54 mg (44%) of **17**: mp 96—97 °C. ^{1}H NMR (90 MHz) δ=2.07 (3H, s) and 2.10 (6H, s) (OAc), 2.80—3.20 (1H, m, H-3), 4.25—4.70 (3H, m, H-5 and $C\underline{H}_2OBz$), 5.30—5.65 (2H, m, H-1 and H-2).

Found: C, 56.55; H, 5.40; Cl, 8.55%. Calcd for $C_{20}H_{23}ClO_8$: C, 56.28; H, 5.43; Cl, 8.31%.

DL-*1,2-Di-O-acetyl-(1,3,4/2,5)-5-azido-3-benzoyloxymethyl-1,2,4-cyclohexanetriol (18).* A mixture of **16** (0.20 g), sodium azide (0.11 g), ammonium chloride (0.11 g), and 90% aqueous 2-methoxyethanol (10 ml) was stirred at 75 °C for 3 h, and then concentrated. The residue was taken up in chloroform (20 ml) and the solution was filtered through a short column of alumina. The filtrate was concentrated and the residue was chromatographed on a silica-gel column (10 g) with 2-butanone–toluene (1 : 10) as an eluent. The main fraction gave crystals which were recrystallized from ethanol to give 0.17 g (76%) of **18** as needles: mp 107—109 °C. ^{1}H NMR (90 MHz) δ=2.00 (3H, s) and 2.03 (3H, s) (OAc), 3.35 (1H, d, J=4.5 Hz, OH), 3.83 (1H, q, J=2.5 Hz, H-5), 3.95 (1H, t, J=2.5 Hz, H-4), 4.20 (1H, dd, $J_{3,7}$=4.5 Hz, J_{gem}=11.5 Hz, H-7), 4.65 (1H, dd, $J_{3,7'}$=9 Hz, H-7′), 5.09 (1H, td, $J_{1,2}$=$J_{1,6ax}$=9 Hz, $J_{1,6eq}$=7.5 Hz, H-1), 5.29 (1H, t, $J_{2,3}$=9 Hz, H-2), 7.33—7.74 (3H, m) and 7.98—8.17 (2H, m) (phenyl).

Found: C, 54.97; H, 5.41; N, 10.45%. Calcd for $C_{18}H_{21}N_3O_7$: C, 55.24; H, 5.41; N, 10.74%.

DL-*1,2,4-Tri-O-acetyl-(1,3,4/2,5)-5-azido-3-benzoyloxymethyl-1,2,4-cyclohexanetriol (19).* Compound **18** (49 mg) was treated with acetic anhydride and pyridine in the usual way. The product was purified by passage through a short column of alumina with chloroform, giving 55 mg (100%) of **19** as an oil. ^{1}H NMR (90 MHz) δ=2.02 (3H, s) and 2.04 (6H, s) (OAc), 3.94 (1H, q, J=3.5 Hz, H-5), 4.10—4.50 (2H, m, $C\underline{H}_2OBz$), 7.36—7.73 (3H, m) and 7.98—8.17 (phenyl).

Found: C, 55.55; H, 5.43; N, 9.46%. Calcd for $C_{20}H_{23}N_3O_8$: C, 55.42; J, 5.35; N, 9.70%.

DL-*1,2-Di-O-acetyl-4-O-methylsulfonyl-(1,3,4/2,5)-5-azido-3-benzoyloxymethyl-1,2,4-cyclohexanetriol (20).* To a solution of **18** (0.17 g) in pyridine (3 ml) was added methanesulfonyl chloride (0.067 ml) dropwise under ice cooling, and then the mixture was stirred at room temperature for 16 h. Ethyl acetate (6 ml) was added to the mixture and it was washed thoroughly with saturated sodium hydrogencarbonate and water and dried. Removal of the solvent gave a crude product which was chromatographed on a silica-gel column with 2-butanone–toluene. The main fraction gave 177 mg (87%) of **21** as an oil. ^{1}H NMR (90 MHz) δ=2.03 (3H, s) and 2.06 (3H, s) (OAc), 3.07 (3H, s, OMe), 4.94 (1H, dd, $J_{3,4}$=3 Hz, $J_{4,5}$=3.5 Hz, H-4).

Found: C, 48.77; 5.05; N, 8.69; S, 6.63%. Calcd for $C_{19}H_{23}N_3O_9S$: C, 48.61; H, 4.94; N, 8.95; S, 6.83%.

DL-*1,2,4-Tri-O-acetyl-(1,3,4/2,5)-5-acetamido-3-benzoyloxymethyl-1,2,4-cyclohexanetriol (21).* A solution of **19** (55 mg) in ethanol (6 ml) in the presence of Raney nickel T-4[14] was hydrogenated in Parr shaker type apparatus in the initial hydrogen pressure of 3.4 kg/cm^2 at room temperature for 32 h. The product was acetylated in the usual way and purified by chromatography on silica gel with ethanol–toluene (1 : 10). The main fraction gave 35 mg (60%) of **21** as an oil. ^{1}H NMR (90 MHz) δ=1.97 (3H, s), 2.03 (6H, s), and 2.04 (3H, s) (NAc and OAc), 6.05 (1H, br d, J=7.5 Hz, NH).

Found: C, 58.50; H, 6.25; N, 2.97%. Calcd for $C_{22}H_{27}NO_9$: C, 58.79; H, 6.06; N, 3.12%.

Ammonolysis of 16. A mixture of **16** (0.10 g) and ethanol (10 ml) saturated with ammonia at 5 °C was heated in a sealed tube at 90 °C for 15 h. The reaction mixture was concentrated and the residue was treated with acetic anhydride and pyridine in the usual way. Excess reagent was removed by evaporation and the products (0.17 g) were fractionated by chromatography on silica gel (8 g) with ethanol–toluene (1 : 12) as an eluent.

The first fraction gave 25 mg (19%) of DL-1,2,5-tri-*O*-acetyl-(1,3,5/2,4)-4-acetamido-3-benzoyloxymethyl-1,2,5-cyclohexanetriol (**24**) as crystals: mp 136—140 °C. ^{1}H NMR (90 MHz) δ=2.03 (3H, s), 2.06 (6H, s), and 2.09 (3H, s) (NAc and OAc), 4.14 (1H, dd, $J_{3,7}$=6.5 Hz, J_{gem}=11 Hz, H-7), 4.32 (1H, dd, $J_{3,7'}$=7 Hz, H-7′), 4.46 (1H, 0.3 ppm width m, H-4), 4.90—5.45 (3H, m, H-1, H-2, and H-5), 6.44 (1H, br d, J=7.5 Hz, NH), 7.39—7.57 (3H, m) and 7.70—7.90 (2H, m) (phenyl).

Found: C, 58.50; H, 6.25; N, 2.97%. Calcd for $C_{22}H_{27}NO_9$: C, 58.79; H, 6.06; N, 3.12%.

The second fraction gave 22 mg (17%) of **21** as an oil, identical with the compound obtained before.

The third fraction gave 41 mg (31%) of DL-1,2,4,7-tetra-*O*-acetyl-(1,3,4/2,5)-5-acetamido-3-hydroxymethyl-1,2,4-cyclohexanetriol (**22**) as an oil. ^{1}H NMR (90 MHz) δ=2.00 (3H, s), 2.04 (9H, s), and 2.10 (3H, s) (NAc and OAc), 4.04 (1H, dd, $J_{3,7}$=6 Hz, J_{gem}=11 Hz, H-7), 4.23 (1H, dd, $J_{3,7'}$=7 Hz, H-7′), 4.02—4.31 (1H, m, H-5), 4.88—5.34 (3H, m, H-1, H-2, and H-4), 6.10 (1H, m, NH).

Found: C, 52.76; H, 6.56; N, 3.45%. Calcd for $C_{17}H_{25}NO_9$: C, 52.71; H, 6.51; N, 3.62%.

DL-*1,2-Di-O-acetyl-(1/2,5)-5-azido-3-benzoyloxymethyl-3-cyclohexene-1,2-diol (28).* A mixture of **20** (157 mg), DBU (0.15 ml), and toluene (9 ml) was refluxed for 6 h. The reaction mixture was washed successively with 1 M hydrochloric acid, saturated sodium hydrogencarbonate, and water, and dried. The solvent was removed and the crude product was chromatographed on a silica-gel column with 2-butanone–toluene (1 : 10) to give 95 mg (76%) as an oil. ^{1}H NMR (90 MHz) δ=2.00 (3H, s) and 2.03 (3H, s) (OAc), 4.10 (1H, m, H-5), 4.76 (2H, br s, $C\underline{H}_2OBz$), 5.12 (1H, ddd, $J_{1,2}$=5 Hz, $J_{1,6eq}$=3.5 Hz, $J_{1,6ax}$=7 Hz, H-1), 5.45 (1H, br d, H-2), 6.12 (1H, br d, $J_{4,5}$=3 Hz, H-4).

Found: C, 57.71; H, 5.18; N, 11.03%. Calcd for $C_{18}H_{19}N_3O_6$: C, 57.90; H, 5.13; N, 11.25%.

DL-*1,2-Di-O-acetyl-(1,2/5)-5-acetamido-3-benzoyloxymethyl-3-cyclohexene-1,2-diol (29).* To a solution of **28** (62 mg) in pyridine (1.5 ml) and water (1.5 ml) was bubbled with hydrogen sulfide for 2 h. Nitrogen was introduced to remove an excess of hydrogen sulfide for 30 min, and the mixture was concentrated. The residue was acetylated in the usual way and purified by chromatography on silica gel with ethanol–toluene (1 : 10). The main fraction gave crystals which were recrystallized from ethanol to give 43 mg (65%) of **24** as crystals: mp 135—136 °C. ^{1}H NMR (90 MHz) δ=1.96 (6H, s) and 2.00 (3H, s) (NAc and OAc), 4.72 (2H, br s, $C\underline{H}_2OBz$), 5.09 (1H, ddd, $J_{4,5}$=5 Hz, $J_{5,6eq}$=3.5 Hz, $J_{5,6ax}$=8 Hz, H-5), 5.41 (1H, br d, H-4), 6.00 (1H, d, NH), 6.03 (1H, br d, $J_{1,2}$=3.5 Hz, H-2).

Found: C, 61.87; H, 6.07; N, 3.52%. Calcd for $C_{20}H_{23}NO_7$: C, 61.69; H, 5.95; N, 3.60%.

DL-*1,2-Di-O-acetyl-(1,3,4/2,5)-3-benzoyloxymethyl-4,5-dibromo-1,2-cyclohexanediol (23).* To a solution of **8** (0.10 g) in carbon tetrachloride (2 ml) was added bromine (0.1 ml) in carbon tetrachloride (2 ml) and the mixture was stirred at room temperature for 2 h. The reaction mixture was treated with Amberlite IRA-400 (OH$^-$) (3 ml) and then concentrated to give a crude oil which was crystallized from ethanol to give 70 mg (47%) of **23** as crystals: mp 109—110 °C. ^{1}H NMR (90 MHz) δ=2.00 (3H, s) and 2.03 (3H, s) (OAc), 4.23 (1H, dd, $J_{3,7}$=8 Hz, J_{gem}=11 Hz, H-7), 4.47 (1H, dd, $J_{3,7'}$=5.5 Hz, H-7'), 4.56—4.76 (2H, m, H-4 and H-5), 5.18—5.60 (2H, m, H-1 and H-2), 7.12—8.03 (5H, m, phenyl).

Found: C, 43.79; H, 4.09; Br, 32.15%. Calcd for $C_{18}H_{20}Br_2O_6$: C, 43.93; H, 4.10; Br, 32.47%.

DL-*1,2-Di-O-acetyl-(1,5/2)-5-azido-3-benzoyloxymethyl-3-cyclohexene-1,2-diol (**30**).* A mixture of **23** (0.28 g), sodium azide (91 mg), and DMF (10 ml) was stirred at 120 °C for 30 min. The reaction mixture was concentrated to give a solid residue which was suspended with chloroform and passed through a short column of silica gel. The filtrate was concentrated to give 0.19 g (91%) of **30** as an oil. ^{1}H NMR (90 MHz) δ=2.00 (3H, s) and 2.04 (3H, s) (OAc), 3.94—4.23 (1H, m, H-5), 4.75 (2H, s, C$\underline{H}_2$OBz), 5.00 (1H, ddd, $J_{1,2}$=7 Hz, $J_{1,6\text{eq}}$=3 Hz, $J_{1,6\text{ax}}$=9.5 Hz, H-1), 5.62 (1H, br d, H-2), 5.99 (1H, br s, H-4), 7.13—8.04 (5H, m, phenyl).

Found: C, 58.03; H, 5.28; N, 11.31%. Calcd for $C_{18}H_{19}N_3O_6$: C, 57.91; H, 5.13; N, 11.25%.

DL-*1,2-Di-O-acetyl-(1,5/2)-5-acetamido-3-benzoyloxymethyl-3-cyclohexene-1,2-diol (**21**).* Compound **30** (0.13 g) was reduced similarly as described in the preparation of **29**. The crude amine was acetylated in the usual way and the product was purified by chromatography on silica gel with chloroform and then with ethanol–toluene (1 : 5) as an eluent . The main fraction gave crystals which were recrystallized from ethanol to give 80 mg (58%) of **31** as crystals: mp 162—163 °C. ^{1}H NMR (90 MHz) δ=1.93 (3H, s), 1.99 (3H, s), and 2.00 (3H, s) (NAc and OAc), 4.69 (2H, s, C$\underline{H}_2$OBz), 5.50—5.76 (2H, m, H-1 and H-2), 5.90 (1H, br s, H-4), 7.11—8.01 (5H, m, phenyl).

Found: C, 61.59; H, 6.01; N, 3.80%. Calcd for $C_{20}H_{23}NO_7$: C, 61.69; H, 5.96; N, 3.60%.

DL-*1,2-Di-O-acetyl-5-O-benzoyl-(1,5/2)-3-benzoyloxymethyl-3-cyclohexene-1,2,5-triol (**34**).* A mixture of **23** (0.10 g), sodium benzoate (44 mg), and DMF (5 ml) was stirred at 120 °C for 30 min, and then concentrated. The residue was suspended in ethyl acetate and the mixture was passed through a short column of silica gel. The filtrate was concentrated and the residue was recrystallized from ethanol to give 57 mg (62%) of **34** as crystals: mp 107—108.5 °C. ^{1}H NMR (90 MHz) δ=2.04 (6H, s, OAc), 4.82 (2H, s, C$\underline{H}_2$OBz), 5.15 (1H, ddd, $J_{1,2}$=6.5 Hz, $J_{1,6\text{eq}}$=3.5 Hz, $J_{1,6\text{ax}}$=9 Hz, H-1), 5.55—5.90 (2H, m, H-2 and H-5), 6.18 (1H, br s, H-4), 7.22—8.10 (10H, m, phenyl).

Found: C, 66.41; H, 5.38%. Calcd for $C_{25}H_{24}O_8$: C, 66.36; H, 5.35%.

Compound **34** was *O*-deacylated by treatment with methanolic sodium methoxide in methanol and then acetylated in the usual way to give the tetraacetate **35** as an oil. ^{1}H NMR (60 MHz) δ=1.96 (3H, s) and 1.99 (9H, s) (OAc), 4.29 (1H, d) and 4.61 (1H, d) (J_{gem}=12 Hz, C$\underline{H}_2$OAc), 4.97 (1H, ddd, $J_{1,2}$=6 Hz, $J_{1,6\text{eq}}$=4 Hz, $J_{1,6\text{ax}}$=10 Hz, H-1), 5.53 (1H, br d, H-2), 5.20—5.50 (1H, m, H-5), 5.85 (1H, br s, H-4).

Found: C, 54.45; H, 5.95%. Calcd for $C_{15}H_{20}O_8$: C, 54.87; H, 6.14%.

*Alternative Preparation of **10** from **3**.* A mixture of **3** (3.0 g), DBU (6 ml), and toluene (6 ml) was refluxed for 90 min, and then allowed to stand in a refrigerator overnight. Precipitates were removed by filtration and the filtrate was washed successively with 1 M hydrochloric acid, saturated sodium hydrogencarbonate, and water, and dried. Evaporation of the solvent gave 1.28 g (76%) of **10** as an oil, identical with the sample obtained before by the different reaction conditions.

Compound **10** (0.80 g) was *O*-deacylated by treatment with methanolic sodium methoxide to give the dihydroxy compound: ^{1}H NMR (90 MHz, CD_3OD) δ=2.13 (1H, br dd, $J_{5,6\text{ax}}$=18 Hz, H-6ax), 2.51 (1H, dt, $J_{1,6\text{eq}}$=$J_{5,6\text{eq}}$=5.5 Hz, H-6eq), 3.60 (1H, ddd, $J_{4,5}$=9 Hz, H-5), 4.00 (1H, dt, $J_{4,7}$=$J_{4,7'}$=2.5 Hz, H-4), 4.98 (1H, br s) and 5.25 (1H, br s) (exocyclic methylene), 5.63 (1H, m, H-1), 6.12 (1H, br d, $J_{1,2}$=*ca.* 10 Hz, H-2). It was then treated with *p*-nitrobenzoyl chloride in pyridine in the usual way to give, after recrystallization from ethanol, 0.75 g of the bis(*p*-nitrobenzoate): mp 187—188 °C.

Found: C, 59.16; H, 3.95; N, 6.36%. Calcd for $C_{21}H_{16}N_2O_8$: C, 59.44; H, 3.80; N, 6.60%.

*Reaction of **10** with Bromine in Carbon Tetrachloride.* To a cooled solution of **10** (1.99 g) in carbon tetrachloride (25 ml) was added a solution (2 ml) of bromine–carbon tetrachloride (1 : 3, v/v), and the mixture was stirred at −8 °C for 30 min. The mixture was concentrated and the products were roughly fractionated by a silica-gel column with 2-butanone–toluene (1 : 6) as an eluent. The main fraction gave 1.8 g (54%) of a mixture of DL-1,2-di-*O*-acetyl-(1/2,5)- (**26**) and (1,5/2)-5-bromo-3-bromomethyl-3-cyclohexene-1,2-diol (**27**): ^{1}H NMR (90 MHz) δ=2.03 (3H, s) and 2.10 (3H, s) (OAc), 2.36 (2H, br t, $J_{1,6}$=9 Hz, $J_{5,6}$=8 Hz, H-6 and H-6'), 3.91 (2H, br s, C$\underline{H}_2$Br), 4.75 (1H, br q, J=8 Hz, H-5), 5.23 (1H, q, J=9 Hz, H-1), 5.71 (1H, d, $J_{1,2}$=9 Hz, H-2), 6.19 (1H, d, $J_{4,5}$=8 Hz, H-4). The spectrum showed that **26** was the major product. Attempts to prepare a pure sample by chromatography failed, because of the high lability. Therefore, a crude mixture was directly used in the following experiments.

A trace of a tetrabromide was obtained: mp 158—160 °C; ^{1}H NMR (60 MHz) δ=2.05 (3H, s) and 2.15 (3H, s) (OAc), 3.65 (1H, d) and 4.15 (1H, d) (J=12 Hz, C$\underline{H}_2$Br).

Found: C, 25.08; H, 2.70; Br, 60.49%. Calcd for $C_{11}H_{14}Br_4O_4$: C, 24.94; H, 2.66; Br, 60.32%.

*Reaction of **26** and **27** with Sodium Benzoate.* A mixture of **26** and **27** (1.29 g), sodium benzoate (2.0 g), and 90% aqueous DMF (9 ml) was stirred at room temperature overnight. Water was added and the mixture was extracted with ethyl acetate (30 ml). The extracts were dried and concentrated to give crystals which were recrystallized from ethanol to give 0.30 g (30%) of **34**: mp 100—101 °C, identical with a sample derived from **23**.

*Reaction of **26** and **27** with Potassium Phthalimide.* A mixture of **26** and **27** (0.53 g), potassium phthalimide (1.06 g), and DMF (15 ml) was stirred at room temperature overnight. The reaction mixture was diluted with ethyl acetate and washed with water thoroughly. The organic layer was dried and concentrated to give crystals. Recrystallization from ethyl acetate gave 0.42 g (58%) of DL-1,2-di-*O*-acetyl-(1,5/2)-5-phthalimido-3-phthalimidomethyl-3-cyclohexene-1,2-diol (**36**) as crystals: mp 206—207 °C. ^{1}H NMR (60 MHz) δ=1.97 (3H, s) and 2.10 (3H, s) (OAc), 4.06 (1H, d) and 4.50 (1H, d) (J=15 Hz, C$\underline{H}_2$N), 7.76 (8H, m, phenyl).

Found: C, 64.31; H, 4.59; N, 5.65%. Calcd for $C_{27}H_{22}N_2O_8$: C, 64.55; H, 4.41; N, 5.57%.

DL-*1,2-Di-O-acetyl-(1,5/2)-5-acetamido-3-acetamidomethyl-3-cyclohexene-1,2-diol (**37**).* A mixture of **36** (0.50 g), butylamine (10 ml), and methanol (20 ml) was refluxed for 60 h, and then concentrated. The residue was acetylated in the usual way to give, after crystallization from ethanol, 0.32 g (98%) of **37** as crystals: mp 193—194 °C. ^{1}H NMR (60 MHz) δ=1.98 (6H, s), 2.03 (3H, s), and 2.08 (3H, s) (NAc and OAc), 3.76 (2H, d, $J_{7,\text{NH}}$=9 Hz, C$\underline{H}_2$NHAc), 5.05 (1H, ddd, $J_{1,2}$=7 Hz, $J_{1,6\text{eq}}$=4 Hz, $J_{1,6\text{ax}}$=9.5 Hz, H-1), 5.49 (1H, d, H-2), 5.71 (1H, br s, H-4), 6.10—6.50 (2H, m, N$\underline{H}$Ac).

Found: C, 54.95; H, 6.64; N, 8.37%. Calcd for $C_{15}H_{22}N_2O_6$: C, 55.20; H, 6.80; N, 8.58%.

DL-2,3-Di-O-acetyl-1,7-anhydro-(1,2/3)-1-C-hydroxymethyl-5-cyclohexene-1,2,3-triol (25). A mixture of **10** (2.0 g), *m*CPBA (3.2 g), dichloromethane (60 ml), and phosphate buffer solution[15] (pH 8) (150 ml) was stirred vigorously at room temperature for 2 h. The organic layer was washed successively with aqueous sodium sulfite, sodium hydrogencarbonate, and water, and dried. The solution was concentrated to give crystals which were recrystallized from ethanol–ether to give 1.0 g (47%) of **25** as crystals: mp 91—92 °C. ^{1}H NMR (90 MHz) δ=2.01 (3H, s) and 2.09 (3H, s) (OAc), 2.37 (1H, m, H-4), 2.60 (1H, m, H-4′), 2.82 and 2.91 (AB-quartet, J=4.5 Hz, C$\underline{H}_2$O), 5.10—5.40 (3H, m, H-2, H-3, and H-6), 5.92 (1H, dt, $J_{4,5}$=$J_{4',5}$=3.5 Hz, $J_{5,6}$=10.5 Hz, H-5).

Found: C, 58.13; H, 6.27%. Calcd for $C_{11}H_{14}O_5$: C, 58.40; H, 6.24%.

DL-1,2,3-Tri-O-acetyl-(1,2/3)-1-C-azidomethyl-5-cyclohexene-1,2,3-triol (38). A mixture of **25** (0.25 g), sodium azide (0.23 g), ammonium chloride (0.23 g), and DMF (10 ml) was stirred at 60 °C for 2 h, and then concentrated, The residual product was acetylated in the usual way in the presence of 4-diethylaminopyridine (0.20 g). An oily product was purified by chromatography on silica gel to give 0.40 g (92%) of **38** as an oil. ^{1}H NMR δ=2.00 (3H, s), 2.03 (3H, s), and 2.10 (3H, s) (OAc), 3.60 (1H, d) and 3.83 (1H, d) (J=12 Hz, C$\underline{H}_2N_3$), 5.25 (2H, br s, H-2 and H-3), 5.81 (1H, ddd, $J_{4,5}$=3.5 Hz, $J_{4',5}$=4.5 Hz, $J_{5,6}$=10.5 Hz, H-5), 6.05 (1H, dt, $J_{4,6}$=2 Hz, H-6).

Found: C, 50.00; H, 5.47; N, 13.24%. Calcd for $C_{13}H_{17}N_3O_6$: C, 50.15; H, 5.51; N, 13.50%.

DL-2,3-Di-O-acetyl-(1,2/3)-1-C-acetamidomethyl-5-cyclohexene-1,2,3-triol (39). Compound **38** (0.55 g) was reduced similarly as described in the preparation of **31**, and the product was acetylated in the usual way. The oily product was purified by a silica-gel column with 2-butanone–toluene (2 : 1) as an eluent to give 0.51 g (100%) of **39** as an oil. ^{1}H NMR (90 MHz) δ=1.93 (3H, s), 1.97 (3H, s), and 2.08 (3H, s) (NAc and OAc), 2.69 (1H, ddd, $J_{3,4}$=6 Hz, $J_{4,5}$=3 Hz, J_{gem}=18 Hz, H-4), 3.01 (1H, d) and 3.47 (1H, d) (J=13 Hz, C$\underline{H}_2$NHAc), 4.91 (1H, d, $J_{2,3}$=10.5 Hz, H-2), 5.25 (1H, td, $J_{3,4'}$=9 Hz, H-3), 5.63 (2H, br s, H-5 and H-6).

Found: C, 54.72; H, 6.32; N, 4.25%. Calcd for $C_{13}H_{19}NO_6$: C, 54.73; H, 6.71; N, 4.91%.

DL-1,2-Di-O-acetyl-(1,5/2)-5-azido-3-acetoxymethyl-3-cyclohexene-1,2-diol (32). A mixture of **25** (0.46 g), sodium azide (0.9 g), acetone (20 ml), and water (12 ml) was added concd sulfuric acid (1 g), and the mixture was stirred at room temperature for 5 d. The reaction mixture was concentrated and the residue was treated with acetic anhydride and pyridine. The product was extracted with chloroform, and the extracts were washed with water, dried, and concentrated. The product was purified by chromatography on silica gel to give 0.28 g (48%) of **32** as an oil as a main product: ^{1}H NMR (90 MHz) δ=2.03 (9H, s, OAc), 4.07 (1H, m, H-5), 4.35 (1H, d) and 4.61 (1H, d) (J=13.5 Hz, C$\underline{H}_2$OAc), 4.98 (1H, ddd, $J_{1,2}$=7 Hz, $J_{1,6eq}$=4 Hz, $J_{1,6ax}$=10.5 Hz, H-1), and 5.53 (1H, d, H-2).

Found: C, 50.31; H, 5.51; N, 13.25%. Calcd for $C_{13}H_{17}N_3O_6$: C, 50.15; H, 5.51; N, 13.50%.

DL-1,2-Di-O-acetyl-(1,5/2)-5-acetamido-3-acetoxymethyl-3-cyclohexene-1,2-diol (33). Compound **32** (0.42 g) was reduced with hydrogen sulfide similarly as described in the preparation of **29** and the product was acetylated in the usual way. The crude product was recrystallized from ethanol–ether to give 0.40 g (92%) of **33**: mp 148—149 °C; ^{1}H NMR (90 MHz) δ=1.93 (3H, s) and 2.02 (9H, s) (NAc and OAc), 4.28 (1H, d) and 4.59 (1H, d) (J=13 Hz, C$\underline{H}_2$OAc), 4.70 (1H, br s, H-5), 5.00 (1H, ddd, $J_{1,2}$=7 Hz, $J_{1,6eq}$=4 Hz, $J_{1,6ax}$=10 Hz, H-1), 5.45 (1H, d, H-2), and 5.80 (2H, m, H-4 and NH).

Found: C, 54.80; H, 6.30; N, 4.42%. Calcd for $C_{15}H_{21}NO_7$: C, 55.04; H, 6.47; N, 4.28%.

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2) The nomenclature and numbering of cyclitols used in his paper follows IUPAC and IUB tentative rules for cyclitol nomenclature [*J. Biol. Chem.*, **243**, 5809 (1968)]. For convenience, the carbon atoms of the branched-chain substituents are numbered 7. All compounds described in this paper are racemic and the formulas depict only one of the respective enantiomers.

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6) Alternatively, **6** was first treated with sodium benzoate in dimethyl sulfoxide (70 °C, 2 h) to give the corresponding benzoyloxymethyl derivative (mp 82—84 °C, 43%; Found: C, 55.42; H, 5.74; Br, 21.38%. Calcd for $C_{17}H_{21}BrO_4$: C, 55.30; H, 5.73; Br, 21.64%), which was then converted into **12** (98%) by treatment with DBU in toluene (reflux, 24 h).

7) β-Elimination of an acetoxyl group was also observed in the osmium tetraoxide-oxidation of DL-1,2-di-*O*-acetyl-(1,3/2)-3-bromomethyl-5-cyclohexene-1,2-diol.[5]

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