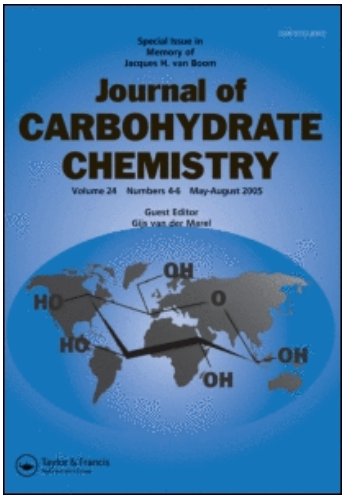

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NOVEL SYNTHESIS OF PENTA-N,O-ACETYLVALIOLAMINE

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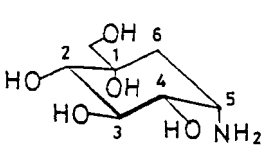
ABSTRACT

Penta-N,O-acetylvaliolamine (**11**), a derivative of microbial α-D-glucosidase inhibitor, was prepared from the chiral azido-containing cyclohexene derivative derived from D-glucose. Novel rearrangement of the C-C double bond accompanying reduction of the azido group was a key step for the preparation.

INTRODUCTION

A unique aminocyclitol, valiolamine[1] (**1**), is one of the microbial secondary metabolites isolated from the fermentation broth of Streptomyces hygroscopicus subsp. limoneus as well as valienamine[2] (**2**) and other similar analogs. These compounds and their N-substituted derivatives, both natural[3] and artificial[4] ones, exhibit a pronounced inhibitory effect on intestinal α-D-glucosidases such as maltase, sucrase, and so on. In general, such inhibitory activities of **1** and of its N-substituted derivatives are more potent than those of the other aminocyclitols and of their corresponding N-substituted derivatives, respectively. Horii et al.[5] succeeded in the first preparation of **1** by means of stereoselective conversion of other aminocyclitols such as **2**; whereas Ogawa and Shibata[6] reported the synthesis of racemic modification of penta-N,O-acetylvaliolamine (**11**). The present paper describes novel preparation of chiral **11** from 1L-(1,3,4/2)-4-azido-



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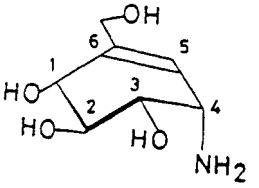

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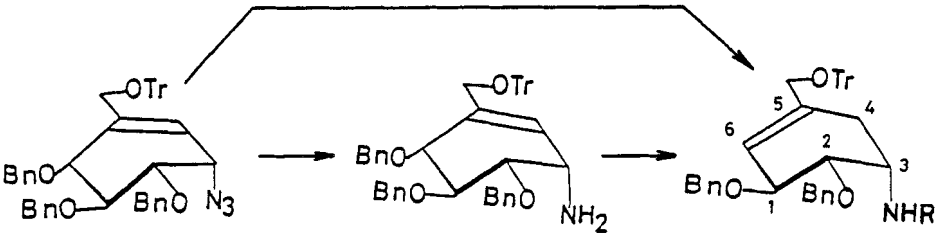
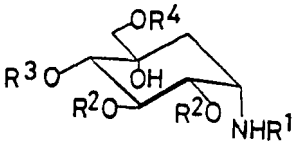


3 4 5 R = H

6 R = Ac

7 R = Cbz



8 R^1=Cbz, R^2=Bn, R^3=H, R^4=Tr

9 R^1=Cbz, R^2=Bn, R^3=Ac, R^4=Tr

10 R^1=Cbz, R^2=Bn, R^3=R^4=Ac

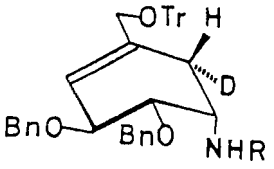
11 R^1=R^2=R^3=R^4=Ac

Scheme 1

1,2,3-tri-O-benzyl-6-(trityloxymethyl)-5-cyclohexene-1,2,3-triol[7] (3) derived from D-glucose as a synthetic precursor of 2.

RESULTS AND DISCUSSION

We found that reduction of 3 with lithium aluminum hydride in boiling diethyl ether unexpectedly gave 1D-(1/2,3)-3-amino-1,2-di-O-benzyl-5-(trityloxymethyl)-6-cyclohexene-1,2-diol (5) as a major product; whereas 3 underwent regular reduction of its azido group to give 1L-(1,3,4/2)-4-amino-1,2,3-tri-O-benzyl-6-(trityloxymethyl)-5-cyclohexene-1,2,3-triol (4) when a similar treatment was conducted below 0 °C. Compound 4 was also obtainable in preferable yield when 3 was reduced with sodium borohydride – nickel chloride.[8] For the unexpected conversion of 3 to 5, the quality of the reducing agent was the crucial factor. Thus, employment of lithium aluminum hydride from a freshly opened container was the best for the preparation of 5. The structure of 5 was elucidated on the basis of the results of physical and chemical analyses of its N-acetyl and N-benzyloxycarbonyl derivatives, 6 and 7. The ^{1}H NMR spectra and elemental analyses of 6 and 7 suggested that one of the benzyloxy groups had been removed during the reaction of 3 to 5. As shown in Fig. 1, the ^{1}H NMR spectrum of 6 reveals a couple of doublet of doublets signals at δ 2.04 and δ 2.18, which are assignable to the methylene protons newly generated. NOE (nuclear Overhawser effect) was observed between the signals at δ 2.04 and δ 5.52 due to the NH proton, but never between the signals at δ 2.18 and δ 5.52. These facts indicate that the signal at δ 2.04 is assignable to the α-oriented proton, which is in cis relationship to the neighboring NH group. The protons at C-1 and C-6 appeared as broad singlets at δ 4.04 and δ 5.92, respectively. In order to clarify the mechanism concerning the production of 5 from 3, the following experiments were conducted.



12 R = H

13 R = Ac

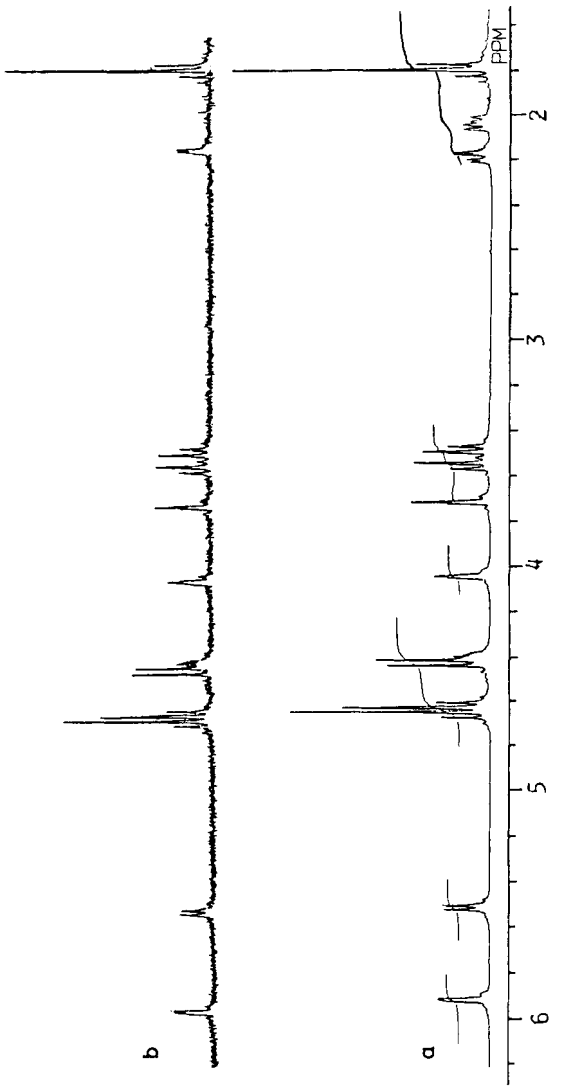


Fig. 1. Patial ^{1}H NMR spectra (500 MHz) of **6** (a) and the corresponding 4-C-deuterio derivative (**13**) (b) in $CDCl_3$.

First, treatment of **4** with freshly opened lithium aluminum hydride in boiling diethyl ether also resulted in **5**, suggesting that **4** would be an intermediate located between **3** and **5**. Second, treatment of **3** with lithium aluminum deuteride under the same reaction conditions gave a mixture of **4** and the 4-C-deuterio compound, **12**, which underwent N-acetylation to give **13**; the ^{1}H NMR spectrum of **13** revealed only one H-4 signal at δ 2.17 assignable to the β-proton (see Fig. 1). These results suggested that the α-amino group of the intermediate **4** would help a hydride attack C-4 from the α-side by chelating lithium aluminum hydride.

Towards the preparation of **11**, further processing of **7** was carried out. Compound **7** was oxidized at 60-70 °C with a catalytic amount of osmium tetroxide in the presence of trimethylamine N-oxide,[9] giving a valiolamine derivative **8** in 58% yield. Apparently, cis-dihydroxylation of the C-C double bond took place exclusively from the α-side, as no compound, which should have been produced by the attack from the opposite side, was detected. In the ^{1}H NMR spectrum of **8** (in chloroform-d), singlets at δ 2.51 and δ 2.66 were assigned to the hydroxyl protons generated and which disappeared by addition of deuterium oxide. The H-2 signal appeared at δ 3.75 as a doublet. Compound **8** underwent acetylation of only secondary hydroxyl group at C-2 by treatment with acetic anhydride and base, giving **9**. Compound **9** revealed the H-2 signal at δ 4.94 as a doublet with $J_{2,3}$ 9.52 Hz in the ^{1}H NMR spectrum. The value of such coupling constant indicates a trans diaxial relationship between H-2 and H-3, ascertaining the configuration of the substituents at C-2 (and also at C-1) of **8** and **9**. The trityl group of **9** was removed with acetic acid and the resulting primary hydroxyl group was acetylated to give the diacetate **10**. Compound **10** was catalytically hydrogenated with palladium on carbon for simultaneous removal of the benzyl and the benzyloxycarbonyl groups and the product was then acetylated in the usual way, giving **11**.

EXPERIMENTAL

General Procedures. Optical rotations were determined with a Perkin-Elmer Model 241MC polarimeter. IR spectra were recorded with a Shimadzu IR-27 spectrophotometer, for thin films on KRS or, for

potassium bromide disk. ^{1}H NMR spectra were recorded at 400 MHz or 500 MHz with a JEOL JNM-GX 400 or a JEOL JNM-GX 500 spectrometers, using tetramethylsilane as the internal standard, for solutions in chloroform-d. Thin-layer chromatography was conducted on precoated plates (layer thickness 0.2 mm; E. Merck, Darmstadt, Germany) of silica gel $60F_{254}$. Chromatography was performed on columns of silica gel Merck (70-230 mesh; E. Merck, Darmstadt, Germany). Preparative thin-layer chromatography was performed on precoated plates (layer thickness 2 mm; E. Merck, Darmstadt, Germany) of silica gel $60F_{254}$. Solvent extracts were dried with anhydrous sodium sulfate unless otherwise specified; and solutions were concentrated under diminished pressure.

1L-(1,3,4/2)-4-Amino-1,2,3-tri-O-benzyl-6-(trityloxymethyl)-5-cyclohexene-1,2,3-triol (4): a) by sodium borohydride-nickel chloride reduction. A 4% ethanolic solution of nickel chloride hexahydrate (15 mL) was added dropwise to a solution of 1L-(1,3,4/2)-4-azido-1,2,3-tri-O-benzyl-6-(trityloxymethyl)-5-cyclohexene-1,2,3-triol[7] (**3**, 3.2 g, 4.5 mmol) and sodium borohydride (1.5 g, 39.7 mmol) in 1,4-dioxane – 2-propanol (1:5 v/v, 150 mL); the mixture was stirred for 3 h at room temperature, treated with celite, filtered, concentrated, and extracted with diethyl ether (50 mL). The extract was successively washed with aqueous sodium hydrogen carbonate and brine, dried with anhydrous potassium carbonate, and concentrated. The residue was chromatographed with 4:1 (v/v) benzene – ethyl acetate as the eluant, to give **4** (2.4 g, 77%) as a syrupy compound; $[\alpha]_D^{25}$ -0.78° (c 1.29, $CHCl_3$); ν_{max}^{film} 3300 cm^{-1} (NH_2); δ_H (400 MHz): 1.50 (bs, 2H, NH_2), 3.57 (m, 2H, H-4 and H-3), 3.69 (d, 1H, J 13.4 Hz, TrOC$\underline{H}_2$ x 1/2), 3.74 (d, 1H, J 13.4 Hz, TrOC$\underline{H}_2$ x 1/2), 3.89 (dd, 1H, J 9.76 and 7.08 Hz, H-2), 4.14 (d, 1H, J 7.08 Hz, H-1), 4.48-4.94 (m, 6H, PhC$\underline{H}_2$ x 3), 5.97 (bd, 1H, J 3.66 Hz, H-5).

Anal. Calcd for $C_{47}H_{45}NO_7$: C, 82.07; H, 6.59; N, 2.04. Found: C, 81.91; H, 6.65; N, 1.91.

b) By lithium aluminum hydride reduction. Lithium aluminum hydride (30 mg, 0.8 mmol) was added to a solution of **3** (40 mg, 0.056 mmol) in diethyl ether (6 mL) below 0 °C; the mixture was stirred for 2 h at 0° C, carefully diluted with water (ca. 1 mL) and then with saturated aqueous potassium sodium tartrate, and extracted with diethyl ether. The extract was washed with water, dried with anhydrous potassium carbonate,

and concentrated; the residue was chromatographed with 60:40:1 (v/v) benzene – ethyl acetate – triethylamine as the eluant to give **4** (28 mg, 72%).

Conversion of 3 to 1D-(1/2,3)-3-amino-1,2-di-O-benzyl-5-(trityloxymethyl)-6-cyclohexene-1,2-diol (5): a) from 3. Freshly opened lithium aluminum hydride (2.5 g, 66 mmol) was added in portions at 0-5 °C to a solution of **3** (3.14 g, 4.4 mmol) in diethyl ether (180 mL); the mixture was heated under reflux for 1 h, treated successively with ethyl acetate, methanol, and aqueous potassium sodium tartrate and extracted with ethyl ether (200 mL x 2). The extract was washed with brine, dried with anhydrous potassium carbonate, and concentrated. The residue was chromatographed with 99:1 (v/v) chloroform – methanol as the eluant, to give **5** (2.1 g, 80%); $[\alpha]_D^{25}$ +35.6° (c 0.62, $CHCl_3$); ν_{max}^{film} 3300 cm^{-1} (NH_2); δ_H (400 MHz): 1.53 (bs, 2H, NH_2), 2.02 (dd, 1H, J 17.4 and 6.9 Hz, H-4α), 2.22 (dd, 1H, J 17.4 and 4.4 Hz, H-4β), 3.31 (m, 1H, H-3), 3.50 (d, 1H, J 13.2 Hz, $TrOCH_2$ x 1/2), 3.52 (d, 1H, J 13.2 Hz, $TrOCH_2$ x 1/2), 3.65 (dd, 1H, J 2.7 and 4.9 Hz, H-2), 4.13 (bs, 1H, H-1), 4.58-4.69 (m, 4H, $PhCH_2$ x 2), 5.85 (bs, 1H, H-6).

Anal. Calcd for $C_{40}H_{39}NO_3 \cdot 1.3H_2O$: C, 79.39; H, 6.93; N, 2.31. Found: C, 79.46; H, 6.69; N, 2.36.

b) From 4. Freshly opened lithium aluminum hydride (30 mg, 0.8 mmol) was added to a solution of **4** (40 mg, 0.058 mmol) in diethyl ether (8 mL) at room temperature; the mixture was heated under reflux for 1 h, cooled, and worked up in the same way as described in the preparation of **4** from **3** by lithium aluminum hydride reduction (method b) to give **5** (24 mg, 71%).

1D-(1/2,3)-3-Acetamido-1,2-di-O-benzyl-5-(trityloxymethyl)-6-cyclohexene-1,2-diol (6). Acetic anhydride (1 mL) was added at 0 °C to a solution of **5** (175 mg, 0.3 mmol) in dichloromethane (2 mL) and pyridine (2 mL); the mixture was stirred overnight at room temperature, diluted with water (10 mL), stirred for further 2 h, and extracted with dichloromethane (10 mL x 3). The extract was successively washed with 1 M hydrochloric acid and brine and concentrated. The residue was chromatographed with 9:1 (v/v) benzene – ethyl acetate as the eluant to give amorphous powdery **6** (155 mg, 83%); $[\alpha]_D^{25}$ +23.5° (c 1.24, $CHCl_3$); ν_{max}^{KBr} 3400 cm^{-1} (NH), 1655 and 1540 cm^{-1} (CONH); δ_H (500 MHz): 1.80 (s,

3H, $C\underline{H}_3CO$), 2.04 (dd, 1H, J 16.8 and 9.7 Hz, H-4α), 2.18 (dd, 1H, J 16.8 and 5.8 Hz, H-4β), 3.48 (d, 1H, J 12.8 Hz, $TrOC\underline{H}_2$ x 1/2), 3.56 (d, 1H, J 12.8 Hz, $TrOC\underline{H}_2$ x 1/2), 3.72 (bs, 1H, H-2), 4.04 (bs, 1H, H-1), 4.40-4.44 (m, 2H, H-3 and $PhC\underline{H}_2$ x 1/2), 4.60-4.67 (m, 3H, $PhC\underline{H}_2$ x 3/2), 5.52 (d, 1H, J 8.8 Hz, NH), 5.92 (bs, 1H, H-6).

Anal. Calcd for $C_{42}H_{41}NO_4$: C, 80.87; H, 6.62; N, 2.25. Found: C, 80.49; H, 6.59; N, 2.13.

1D-(1/2,3)-1,2-Di-O-benzyl-3-(benzyloxycarbonylamino)-5-(trityloxymethyl)-6-cyclohexene-1,2-diol (7). A solution of benzyloxycarbonyl chloride (210 mg, 1.23 mmol) in dichloromethane (2 mL) was added dropwise at 0 °C to a solution of **5** (582 mg, 1 mmol) in pyridine (4 mL) and dichloromethane (5 mL); the mixture was stirred overnight at room temperature, diluted with water (20 mL), stirred for further 2 h, and extracted with dichloromethane (20 mL x 3). The extract was successively washed with 1M hydrochloric acid, aqueous sodium hydrogencarbonate, and brine, dried, and concentrated. The residue was chromatographed with 98:2 (v/v) benzene – ethyl acetate as the eluant to give syrupy **7** (597 mg, 83%); $[\alpha]_D^{31}$ +27.0° (c 1.00, $CHCl_3$); ν_{max}^{film} 3400 cm^{-1} (NH), 1720 and 1510 cm^{-1} (OCONH); δ_H (400 MHz): 2.09 (dd, 1H, J 16.85 and 9.28 Hz, H-4α), 2.21 (dd, 1H, J 16.85 and 5.85 Hz, H-4β), 3.49 (d, 1H, J 13.2 Hz, $TrOC\underline{H}_2$ x 1/2), 3.55 (d, 1H, J 13.2 Hz, $TrOC\underline{H}_2$ x 1/2), 3.77 (bs, 1H, H-2), 4.03 (bs, 1H, H-1), 4.20 (m, 1H, H-3), 4.48-4.69 (m, 4H, $PhC\underline{H}_2$ x 2), 4.98 (d, 1H, J 8.79 Hz, NH), 5.06 (s, 2H, $PhC\underline{H}_2OCO$), 5.88 (bs, 1H, H-6).

Anal. Calcd for $C_{48}H_{45}NO_5$: C, 80.53; H, 6.34; N, 1.96. Found: C, 80.42; H, 6.31; N, 1.97.

Reduction of 3 with lithium aluminum deuteride to 1D-(1/2,3,4)-3-acetamido-1,2-di-O-benzyl-4-deuterio-5-(trityloxymethyl)-5-cyclohexene-1,2-diol (12) and its conversion to N-acetate (13). Freshly opened lithium alminium deuteride (12 mg, 0.29 mmol) was added to a solution of **3** (20 mg, 0.028 mmol) in diethyl ether (4 mL) at room temperature; the mixture was heated under reflux for 2 h, cooled, treated with ethyl acetate (0.5 mL) and methanol (0.5 mL), diluted with saturated aqueous potassium sodium tartrate, and extracted with diethyl ether. The extract was washed with water, dried with anhydrous potassium carbonate, and concentrated; the residue was purified by preparative TLC with

19:1 (v/v) chloroform – methanol as the developing agent to give **4** (8 mg, 43%) and **12** (6 mg, 37%). To a solution of **12** in methanol (1 mL) was added acetic anhydride (0.2 mL) and the mixture was stirred at room temperature for 3 h, concentrated, and chromatographed with 5:1 (v/v) benzene – ethyl acetate as the eluant, to give **13** (4 mg, 63%); δ_H (500 MHz): 1.81 (s, 3H, CH_3CO), 2.17 (d, 1H, J 5.8 Hz, H-4β), 3.48 (d, 1H, J 12.8 Hz, $TrOCH_2$ x 1/2), 3.55 (d, 1H, J 12.8 Hz, $TrOCH_2$ x 1/2), 3.72 (bs, 1H, H-2), 4.05 (bs, 1H, H-1), 4.39-4.45 (m, 2H, H-3 and $PhCH_2$ x 1/2), 4.61-4.68 (m, 3H, $PhCH_2$ x 3/2), 5.49 (d, 1H, J 8.9 Hz, NH), 5.92 (bs, 1H, H-6).

1L-(1,2,4,5/3)-3,4-Di-O-benzyl-5-(benzyloxycarbonylamino)-1-C-(trityloxymethyl)-cyclohexane-1,2,3,4-tetrol (8). Osmium tetroxide (2.5 mg, 0.01 mmol) was added to a solution of **7** (300 mg, 0.42 mmol) and trimethylamine-N-oxide dihydrate (93 mg, 0.84 mmol) in t-butanol (10 mL) containing pyridine (0.5 mL); the mixture was stirred in argon atmosphere for 6 h at 60-70 °C, treated with a 20% aqueous solution of sodium hydrogen sulfite (2 mL) at room temperature, diluted with saturated brine (20 mL), and extracted with dichloromethane (20 mL x 3). The extract was washed with water, dried, and concentrated. The residue was chromatographed with 96:4 (v/v) benzene – ethyl acetate as the eluant to give syrupy **8** (182 mg, 58%); $[\alpha]_D^{25}$ +3.5° (c 1.65, $CHCl_3$); ν_{max}^{film} 3400 cm^{-1} (OH and NH), 1720 and 1510 cm^{-1} (OCONH); δ_H (400 MHz): 1.85 (dd, 1H, J 12.7 and 1.0 Hz, H-6a), 1.88 (bd, 1H, J 12.7 Hz, H-6b), 2.51 (s, 1H, OH), 2.66 (s, 1H, OH), 2.87 (d, 1H, J 8.79 Hz, $TrOCH_2$ x 1/2), 3.21 (d, 1H, J 8.79 Hz, $TrOCH_2$ x 1/2), 3.55 (dd, 1H, J 9.28 and 4.1 Hz, H-4), 3.67 (dd, 1H, J 9.28 and 9.03 Hz, H-3), 3.75 (d, 1H, J 9.03 Hz, H-2), 4.48-5.05 (m, 5H, $PhCH_2$ x 2 and H-5), 5.10 (s, 2H, $PhCH_2$), 6.21 (d, 1H, J 9.53 Hz, NH).

Anal. Calcd for $C_{48}H_{47}NO_7$: C, 76.88; H, 6.32; N, 1.87. Found: C, 76.53; H, 6.19; N, 1.83.

1L-(1,2,4,5/3)-2-O-Acetyl-3,4-di-O-benzyl-5-(benzyloxycarbonylamino)-1-C-(trityloxymethyl)-cyclohexane-1,2,3,4-tetrol (9). Compound **8** (165 mg, 0.22 mmol) was treated in pyridine (2 mL) and dichloromethane (2 mL) with acetic anhydride (1 mL) and worked up in the same manner as described in the preparation of **6**. The crude product was chromatographed with 97:3 (v/v) benzene – ethyl

acetate as the eluant to give syrupy **9** (142 mg, 82%); $[\alpha]_D^{24}$ +16.5° (c 1.8, $CHCl_3$); ν_{max}^{film} 3450 cm^{-1} (OH and NH), 1710-1740 cm^{-1} (CO), 1510 cm^{-1} (NH); δ_H (400 MHz): 1.71 (s, 3H, CH_3CO), 1.92 (bs, 1H, J 15.38 Hz, H-6a), 2.02 (dd, 1H, J 15.38 and 3.03 Hz, H-6b), 2.44 (s, 1H, OH), 2.89 (d, 1H, J 8.79 Hz, $TrOCH_2$ x 1/2), 2.93 (d, 1H, J 8.79 Hz, $TrOCH_2$ x 1/2), 3.63 (dd, 1H, J 10.01 and 3.2 Hz, H-4), 3.82 (dd, 1H, J 10.01 and 9.52 Hz, H-3), 4.51-5.16 (m, 7H, $PhCH_2$ x 3 and H-5), 4.94 (d, 1H, J 9.52 Hz, H-2), 6.20 (d, 1H, J 9.77 Hz, NH).

Anal. Calcd for $C_{50}H_{49}NO_8$: C, 75.83; H, 6.24; N, 1.77. Found: C, 75.91; H, 6.18; N, 1.69.

1L-(1,2,4,5/3)-1-C-(Acetoxymethyl)-2-O-acetyl-3,4-di-O-benzyl-5-(benzyloxycarbonylamino)-cyclohexane-1,2,3,4-tetrol (10). p-Toluenesulfonic acid (40 mg) was added to a solution of **9** (120 mg, 0.15 mmol) in methanol (10 mL) and chloroform (5 mL); the mixture was stirred overnight at room temperature, concentrated, and extracted with chloroform (20 mL). The extract was successively washed with saturated aqueous sodium hydrogen carbonate (20 mL x 2) and brine, dried, and concentrated. The residue was chromatographed with 97:3 (v/v) chloroform – methanol as the eluant. The resulting syrupy product was acetylated in the same manner as described in the preparation of **6**. The crude product was chromatographed with 49:49:2 (v/v) benzene – chloroform – methanol as the eluant to give syrupy **10** (79 mg, 88%); $[\alpha]_D^{26}$ +13.6° (c 0.74, $CHCl_3$); ν_{max}^{film} 3400 cm^{-1} (OH and NH), 1755-1715 cm^{-1} (CH_3CO and NHCOO), 1510 cm^{-1} (NHCOO); δ_H (400 MHz): 1.76 (bs, 1H, J 14.5 Hz, H-6a), 1.95 (s, 3H, CH_3CO), 2.06 (s, 3H, CH_3CO), 2.07 (m, 1H, H-6b), 2.53 (s, 1H, OH), 3.58 (dd, 1H, J 9.52 and 4.4 Hz, H-4), 3.83 (d, 1H, J 11.23 Hz, $AcOCH_2$ x 1/2), 3.86 (dd, 1H, J 9.47 and 9.52 Hz, H-3), 3.89 (d, 1H, J 11.23 Hz, $AcOCH_2$ x 1/2), 4.52-4.58 (m, 3H, $PhCH_2$ and H-5), 4.92 (ABq, 2H, J 11.53 Hz, $PhCH_2$), 5.02 (d, 1H, J 9.47 Hz, H-2), 5.12 (s, 2H, $PhCH_2OCO$), and 6.12 (d, 1H, J 9.76 Hz, NH).

Anal. Calcd for $C_{33}H_{37}NO_9$: C, 66.92; H, 6.41; N, 2.36. Found: C, 66.78; H, 6.35; N, 2.28.

1L-(1,2,4,5/3)-5-Acetamido-1-C-(acetoxymethyl)-2,3,4-tri-O-acetyl-cyclohexane-1,2,3,4-tetrol (11). 10% Palladium on carbon (5 mg) and 0.1 M hydrochloric acid (0.5 mL) were added to a solution of **10** (36 mg, 0.06mmol) in methanol (5 mL); the mixture was vigorously stirred under

hydrogen atmosphere for 2 days at room temperature. The catalyst was filtered off and washed with water. The filtrate and washings were combined and concentrated to dryness; the residue was dissolved in pyridine (2 mL) containing 4-dimethylaminopyridine (1 mg) and treated with acetic anhydride (1 mL) for 2 h at room temperature. The mixture was diluted with water (5 mL), stirred for 2 h, and extracted with dichloromethane (10 mL x 2). The extract was washed with water, dried, and concentrated; the residue was chromatographed with 48:48:4 (v/v) benzene – chloroform – ethanol as the eluant and crystallized from dichloromethane – isopropyl ether to give **11** (17.2 mg, 71%) as prisms; mp 134-136 °C (uncorrected); $[\alpha]_D^{25}$ -15.5° (c 0.4, $CHCl_3$) [lit.[1] mp 137-138 °C, $[\alpha]_D^{25}$ -14.8° (c 1, $CHCl_3$)]; ν_{max}^{KBr} 3350 cm^{-1} (OH and NH), 1750 cm^{-1} (COO), 1660 and 1530 cm^{-1} (CONH); δ_H (400 MHz): 1.94-2.12 (m, 2H, $H_{6a,b}$), 1.99-2.10 (s x 5, 3H x 5, CH_3CO x 5), 2.87 (s, 1H, OH), 3.86 (d, 1H, J 11.48 Hz, $AcOCH_2$ x 1/2), 3.95 (d, 1H, J 11.47 Hz, $AcOCH_2$ x 1/2), 4.76 (m, 1H, H-5), 4.93 (dd, 1H, J 10.5 and 4.4 Hz, H-4), 5.04 (d, 1H, J 10.5 Hz, H-2), 5.52 (t, 1H, J 10.5 Hz, H-3), and 6.98 (d, 1H, J 8.79 Hz, NH).

Anal. Calcd for $C_{17}H_{25}NO_{10}$: C, 50.62; H, 6.25; N, 3.47. Found: C, 50.23; H, 6.11; N, 3.38.

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