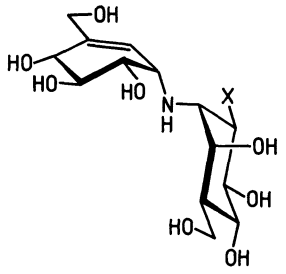
  Bull. Chem. Soc. Jpn., 56, 2326—2329 (1983) [Vol. 56, No. 8

Synthetic Studies on the Validamycins. VIII. Synthesis of DL-2-Deoxyvalidoxylamine B and Related Compound[1,2]

Seiichiro OGAWA, Hiroyuki ITO, and Tetsuo SUAMI*
Department of Applied Chemistry, Faculty of Science and Technology, Keio University, Hiyoshi, Kohoku-ku, Yokohama 223
(Received October 16, 1982)

DL-2-Deoxyvalidoxylamine B and its diastereomer have been synthesized by the reaction of the protected DL-valienamine and the anhydro derivative of (hydroxymethyl)cyclohexanetetrol followed by removal of the protecting groups.

In connection with the previous paper,[3] the synthesis of the 2-deoxy analog (**2**) of validoxylamine B (**1**) and its related compounds is described. In the present study, a nucleophilic substitution reaction of the protected DL-valienamine and the anhydro derivative of (hydroxymethyl)cyclohexanetetrol was undertaken to build up a pseudo-disaccharide structure.

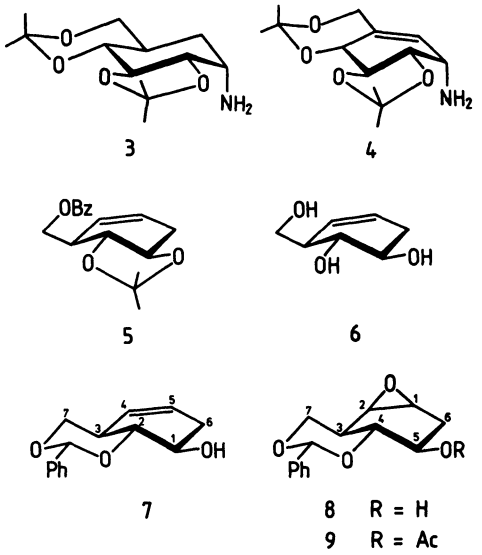


Validoxylamine B (1): X = OH
2-Deoxyvalidoxylamine B (2): X = H

Scheme 1.

DL-1,2-Anhydro-4,7-*O*-benzylidene-(1,2,3,5/4)-3-hydroxymethyl-1,2,4,5-cyclohexanetetrol (**8**) was prepared from DL-1,2-*O*-isopropylidene-(1,3/2)-3-benzoyloxymethyl-4-cyclohexene-1,2-diol (**5**)[1b] by the following sequence. *O*-Deacylation of **5** with methanolic sodium methoxide, followed by treatment with Amberlite IR-120B (H^+), gave the triol **6** in 76% yield. Treatment of **6** with α,α-dimethoxytoluene in *N,N*-dimethylformamide (DMF) in the presence of *p*-toluenesulfonic acid gave the benzylidene derivative **7** in 62% yield. Compound **7** was oxidized with *m*-chloroperoxybenzoic acid (*m*CPBA) to give almost specifically the β-epoxide **8** in 77% yield, together with a small proportion of the α-epoxide (9%). The mixture of the epoxides was directly treated with acetic anhydride in pyridine and the products were separated to give the acetate **9** of **8** in 88% yield. The structure of **8** was determined by the ^{1}H NMR spectrum, in which the C-4 proton resonated slightly lower field (δ 3.62) compared with that of the α-epoxide (δ 3.30), indicating that the C-4 proton which was situated close to the oxygen atom of the epoxide ring was deshielded by this moiety. The epoxidation seemed to be controlled by steric hindrance.

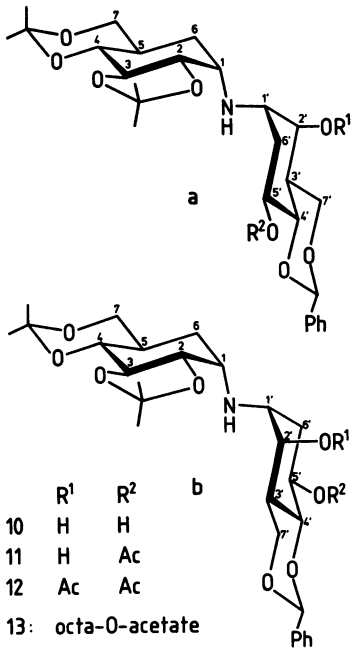
Reaction of an equimolar amount of the di-*O*-isopropylidene derivative (**3**)[4] of DL-validamine and **8** was carried out in 2-propanol in a sealed tube at



Scheme 2.

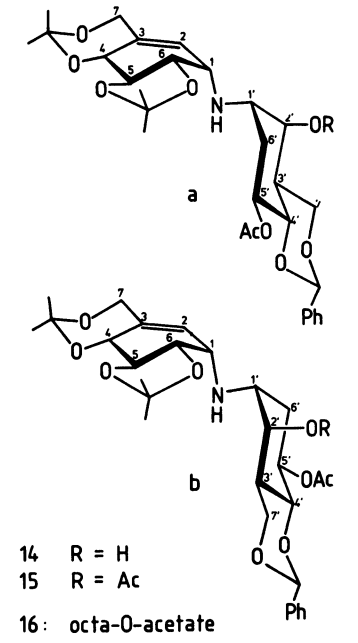
120 °C. After 44 h, the starting materials were almost consumed and the formation of two new components was observed by TLC. The products were fractionated by chromatography on silica gel with 2-butanone–toluene (1 : 30) as an eluent to give the diastereoisomeric secondary amines **10a** (42%) and **10b** (44%) as an oil. Their structures were supported by analytical data and ^{1}H NMR spectroscopy. The NMR spectral pattern was nearly identical with each other except for a small difference of the chemical shifts of the signals due to the C-1′ protons. Therefore, it was impossible to assign the exact structures to each diastereomers in this stage.

Next, the similar reaction of **3** and **9** was carried out to give an inseparable mixture of secondary amines **11a** and **11b** in 83% yield. Treatment of the mixture with acetic anhydride in pyridine gave the di-*O*-acetyl derivatives, which could clearly be separated by a silica gel column to give **12a** (31%) and **12b** (64%). The latter compound was shown to be identical with the bis(acetate) derived from **10b**. The structures of **12a** and **12b** were postulated on the basis of ^{1}H NMR spectroscopy, taking account of the data which had been observed to differentiate the diastereomers of validoxylamine A or B.[5,6] The ^{1}H NMR spectra of **12a** and **12b** revealed the signals for H-1′ as a quartet (J=3 Hz) at δ 2.94 and 3.07, and those for H-2′ as a doublet of doublets (J=2.5 and 3 Hz) at δ 4.72 and 4.93, respectively. The slight deshielding of the signals



Scheme 3.

observed for **12b** might be explained by a proximity of C-2′ proton to the oxygen atoms of the 2,3-*O*-isopropylidene group. Therefore, the structures of **12a** and **12b** were tentatively assigned as shown in Scheme 3. Deprotection of **12a** and **12b** by treatment with 1 M hydrochloric acid (1 M=1 mol dm^{-3}) at reflux temperature, followed by acetylation, gave the corresponding octa-*O*-acetyl derivatives **13a** (82%) and **13b** (82%), respectively.



Scheme 4.

Finally, the reaction of the di-*O*-isopropylidene derivative **4**[5] of DL-valienamine and **9** was carried out by the similar way. The reaction was completed within 26 h to give 82% yield of a mixture of secondary amines **14a** and **14b** as a homogeneous oil. They were converted into the di-*O*-acetyl derivatives and separated by chromatography on silica gel to give **15a** (46%) and **15b** (54%). The ^{1}H NMR spectra of **15a** and **15b** showed the signals for H-2′ at δ 4.85 and 4.93, and those for H-3′ at δ 2.66 and 2.86, respectively. Studies of their Dreiding models indicated that the 5,6-*O*-isopropylidene group was situated close to C-2′ and C-3′ protons enough to affect, if any difference, the chemical shifts of their signals in the one diastereomer. Therefore, on the basis of the down-field shifts of H-2′ and H-3′ signals of **15b**, the relative configurations of **15a** and **15b** were tentatively assigned as shown in Scheme 4.[7] The protecting groups of **15a** and **15b** were removed to give the free bases, which were characterized by converting into the corresponding octa-*O*-acetyl derivatives **16a** (73%) and **16b** (87%), respectively.

Experimental

General Methods. The same method was used as described in the preceding paper.[1b]

DL-*(1,3/2)-3-Hydroxymethyl-4-cyclohexene-1,2-diol (6).* A mixture of DL-1,2-*O*-isopropylidene-(1,3/2)-3-benzoyloxymethyl-4-cyclohexene-1,2-diol (**5**)[1b] (2.8 g) and 1 M methanolic sodium methoxide (4 ml) in methanol (20 ml) was stirred at room temperature for 30 min. The reaction mixture was treated with Amberlite IR-120B (H$^+$) (4 ml) at room temperature for 2 h and then concentrated. The residue was crystallized from ethanol to give 1.1 g (76%) of **6**: mp 100—101 °C.

Found: C, 58.10; H, 8.17%. Calcd for $C_7H_{12}O_3$: C, 58.32; H, 8.39%.

DL-*2,7-O-Benzylidene-(1,3/2)-3-hydroxymethyl-4-cyclohexene-1,2-diol (7).* To a solution of **6** (1.08 g) in dry DMF (10 ml) was added α,α-dimethoxytoluene (1.36 ml) and a trace of *p*-toluenesulfonic acid, and the mixture was stirred at 60 °C under reduced pressure for 2 h. The reaction mixture was treated with sodium hydrogencarbonate and diluted with ethyl acetate (20 ml). The solution was washed thoroughly with water, dried, and concentrated. The residue was crystallized from ethanol to give 1.07 g (62%) of **7** as needles: mp 120—122 °C. ^{1}H NMR ($CDCl_3$) δ=3.45 (1H, dd, $J_{3,7ax}$=5 Hz, J_{gem}=10.5 Hz, H-7ax), 3.65 (1H, $J_{1,2}=J_{2,3}$=8 Hz, H-2), 4.00 (1H, td, $J_{1,6ax}$=8 Hz, $J_{1,6eq}$=6.5 Hz, H-1), 4.22 (1H, dd, $J_{3,7eq}$=4.5 Hz, H-7eq), 5.22 (1H, br d, $J_{4,5}$=*ca.* 9 Hz, H-4), 5.52—5.86 (1H, m, H-5), 5.60 (1H, s, benzylic), 7.32—7.75 (5H, m, phenyl).

Found: C, 72.39; H, 6.87%. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94%.

DL-*1,2-Anhydro-4,7-O-benzylidene-(1,2,3,5/4)-3-hydroxymethyl-1,2,4,5-cyclohexanetetrol (8).* To a solution of **7** (0.10 g) in 1,2-dichloroethane (2 ml) was added *m*CPBA (0.21 g, *ca.* 2 molar equiv.) and sodium hydrogencarbonate (0.21 g), and the mixture was vigorously stirred at room temperature for 1 h. Excess of the peroxy acid was destroyed by washing with a solution of sodium thiosulfate (0.16 g) in water (5 ml), and the organic layer was washed with water and dried. Evaporation of the solvent gave an oil (0.11 g) that was chromatographed on a silica-gel column (5 g) with 2-butanone–toluene (1 : 5) as an eluent. The major fraction (R_f 0.22) gave a crystalline product which was recrystallized from ethanol to give 82 mg (77%) of **8**: mp 111.5—112.5 °C. ^{1}H NMR ($CDCl_3$) δ=2.97 (1H, br d, J=4.5 Hz) and 3.05 (1H, br t, J=4.5 Hz) (H-1, H-2), 3.50—3.82 (2H, m, H-4, H-5), 3.95 (1H, t, $J_{3,7ax}$=10.5

Hz, J_{gem}=10.5 Hz, H-7ax), 4.30 (1H, dd, $J_{3,7eq}$=4 Hz, H-7eq), 5.52 (1H, s, benzylic), 7.30—7.65 (5H, m, phenyl).

Found: C, 67.48; H, 6.44%. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50%.

The minor fraction (R_f 0.18) gave an oily product (10 mg, 9%), which was considered by ^{1}H NMR spectrum to be a stereoisomer of **8**, but further characterization was not attempted. ^{1}H NMR ($CDCl_3$) δ=2.56—2.82 (1H, m, H-2), 2.96—3.23 (1H, m, H-1), 3.30 (1H, t, $J_{3,4}=J_{4,5}$=10 Hz, H-4), 4.34 (1H, dd, $J_{3,7eq}$=5 Hz, J_{gem}=10.5 Hz, H-7eq), 5.53 (1H, s,benzylic), 7.31—7.60 (5H, m, phenyl).

DL-*5-O-Acetyl-1, 2-anhydro-4, 7-O-benzylidene-(1,2,3,5/4)-3-hydroxymethyl-1,2,4,5-cyclohexanetetrol (9).* Compound **7** (0.33 g) was treated with acetic anhydride (5 ml) in pyridine (5 ml) at room temperature overnight. The reaction mixture was concentrated to give the acetate as an oil. Without further purification, it was treated with *m*CPBA similarly as described in the preparation of **8**. The crude product was purified by chromatography on silica gel (25 g) with 2-butanone–toluene (1 : 20) as an eluent. The major fraction [R_f 0.45, 2-butanone–toluene (1 : 5)] gave crystals which were recrystallized from ethanol to give 0.37 g (88%) of **9** as needles: mp 126—130 °C. ^{1}H NMR ($CDCl_3$) δ=2.03 (3H, s, OAc), 2.31 (1H, td, $J_{3,4}=J_{3,7ax}$=11.5 Hz, $J_{3,7eq}$=5 Hz, H-3), 2.68 (1H, ddd, $J_{1,6eq}$=4.5 Hz, $J_{5,6eq}$=8 Hz, J_{gem}16 Hz, H-6eq), 3.04 (1H, d, J=4.5 Hz) and 3.14 (1H, t, J=4.5 Hz) (H-1, H-2), 3.95 (1H, dd, $J_{4,5}$=10 Hz, H-4), 4.02 (1H, t, J_{gem}= 11.5 Hz, H-7ax), 4.38 (1H, dd, H-7eq), 4.98 (1H, br td, $J_{5,6ax}$ =8 Hz, H-5), 5.56 (1H, s, benzylic), 7.30—7.59 (5H, m, phenyl).

Found: C, 66.22; H, 6.35%. Calcd for $C_{16}H_{18}O_5$: C, 66.19; H, 6.25%.

This compound was identical with a sample obtained by acetylation of **8**.

The minor fraction (R_f 0.42) gave an oily product (25 mg, 6%), whose ^{1}H NMR spectrum was in accord with that expected for a stereoisomer of **9**, but further characterization was not attempted. ^{1}H NMR ($CDCl_3$) δ=2.01 (3H, s, OAc), 2.68 (1H, d, $J_{1,2}$=4.5 Hz, H-2), 2.95—3.23 (1H, m, H-1), 3.49 (1H, t, $J_{3,7ax}$=11 Hz, J_{gem}=11 Hz, H-7ax), 3.75 (1H, dd, $J_{3,4}$=11 Hz, $J_{4,5}$=10 Hz, H-4), 4.35 (1H, dd, $J_{3,7eq}$=5 Hz, H-7eq), 4.97 (1H, td, $J_{5,6eq}$ =10 Hz, $J_{5,6eq}$=6.5 Hz, H-5), 5.51 (1H, s, benzylic), 7.30—7.59 (5H, m, phenyl).

Reaction of DL-*2,3 : 4,7-Di-O-isopropylidene-(1,2,4/3,5)-2,3,4-trihydroxy-5-(hydroxymethyl)cyclohexylamine (3) and 8.* A mixture of **3**[4] (64 mg, 0.24 mmol) and **8** (59 mg, 0.24 mmol) in 2-propanol (0.5 ml) was heated in a sealed tube at 120 °C for 44 h. Formation of two components was detected by TLC [R_f 0.44 and 0.40, ethanol–toluene (1 : 5)]. The reaction mixture was concentrated and the residue was chromatographed on a silica-gel column (7 g) with ethanol–toluene (1 : 30) as an eluent. The first fraction was fractionated again by a silica-gel column (3.5 g) with 2-butanone–toluene (1 : 3) to give **3** (10 mg) and 52 mg (42%) of DL-*N*-[4,7-*O*-benzylidene-(1,4/2,3,5)-2,4,5-trihydroxy-3-(hydroxymethyl)-cyclohexyl]-2,3 : 4,7-di-*O*-isopropylidene-(1,2,4/3,5)-2,3,4-tri-hydroxy-5-(hydroxymethyl)cyclohexylamine (**10a**) as an oil. The second fraction gave 54 mg (44%) of the diastereomer **10b** as an oil. ^{1}H NMR ($CDCl_3$) for **10a**, δ=1.44 (9H, s) and 1.50 (3H, s) (isopropylidene), 2.85 (1H, q, J=3 Hz, H-1′), 5.58 (1H, s, benzylic), 7.32—7.62 (5H, m, phenyl), and for **10b**, δ=1.44 (9H, s) and 1.50 (3H, s) (isopropylidene), 2.91 (1H, q, J=3 Hz, H-1′), 5.57 (1H, s, benzylic), 7.30—7.62 (5H, m, phenyl).

Found for **10a**: C, 64.20; H, 7.73; N, 2.56%, and for **10b**, C, 64.41; H, 7.57; N, 2.75%. Calcd for $C_{27}H_{39}NO_8$: C, 64.14; H, 7.78; N, 2.77%.

Reaction of 3 and 9. A mixture of **3** (93 mg, 0.37 mmol) and **9** (100 mg, 0.34 mmol) in 2-propanol (0.7 ml) was heated in a sealed tube at 120 °C for 26 h. The reaction mixture was concentrated and the residue was chromatographed on a silica-gel column [7 g, 2-butanone–toluene (1 : 3)]. The major fraction [R_f 0.29, ethanol–toluene (1 : 8)] gave crystals which were recrystallized from ethanol to give 157 mg (83%) of a mixture of the diastereomers of DL-*N*-[5-*O*-acetyl-4,7-*O*-benzylidene-(1,4/2,3,5)-2,4,5-trihydroxy-3-(hydroxymethyl)-cyclohexyl]-2,3 : 4,7-di-*O*-isopropylidene-(1,2,4/3,5)-2,3,4-tri-hydroxy-5-(hydroxymethyl)cyclohexylamine (**11a** and **11b**) as homogeneous crystals: mp 117—119 °C. ^{1}H NMR ($CDCl_3$) δ=1.44 (9H, s) and 1.50 (3H, s) (isopropylidene), 2.03 (3H, s, OAc), 2.94 (0.5H, q) and 2.97 (0.5H, q) (J=3 Hz, H-1′), 4.96—5.30 (1H, m, H-5), 5.56 (1H, s, benzylic), 7.29—7.60 (5H, m, phenyl).

Found: C, 63.40; H, 7.43; N, 2.44%. Calcd for $C_{29}H_{41}NO_9$: C, 63.60; H, 7.55; N, 2.56%.

Diastereomers 12a and 12b of DL-N-[*2,5-Di-O-acetyl-4,7-O-benzylidene-(1,4/2,3,5)-2,4,5-trihydroxy-3-(hydroxymethyl)cyclohexyl]-2,3 : 4,7-di-O-isopropylidene-(1,2,4/3,5)-2,3,4-trihydroxy-5-(hydroxymethyl)cyclohexylamine.* A mixture of **11a** and **11b** (90 mg) was treated with acetic anhydride (1 ml) and pyridine (1 ml) at room temperature overnight. Formation of two components was detected by TLC [R_f 0.47 and 0.44, ethanol–toluene (1 : 8)]. The products were fractionated by chromatography on a silica-gel column (5 g) with 2-butanone–toluene (1 : 10) as an eluent to give in turn 30 mg (31%) of **12a** and 62 mg (64%) of **12b** as a homogeneous oil. ^{1}H NMR ($CDCl_3$) for **12a**, δ=1.45 (9H, s) and 1.50 (3H, s) (isopropylidene), 2.05 (3H, s) and 2.11 (3H, s) (OAc), 2.57 (1H, tdd, $J_{2',3'}$=2.5 Hz, $J_{3',7'eq}$=4.5 Hz, $J_{3',4'}=J_{3',7'ax}$=11 Hz, H-3′), 4.72 (1H, dd, H-2′), 5.17 (1H, ddd, $J_{4',5'}$=10 Hz, $J_{5',6'eq}$ =5 Hz, $J_{5',6'ax}$=11.5 Hz, H-5′), 5.56 (1H, s, benzylic), 7.29—7.59 (5H, m, phenyl), and for **12b**, δ=1.45 (6H, s), 1.48 (3H, s), and 1.50 (3H, s) (isopropylidene), 2.04 (3H, s) and 2.10 (3H, s) (OAc), 2.57 (1H, tdd, $J_{2',3'}$=2.5 Hz, $J_{3',7'eq}$=5 Hz, $J_{3',4'}=J_{3',7'ax}$=11.5 Hz, H-3′), 3.07 (1H, q, $J_{1',2'}=J_{1',6'eq}=J_{1',6'ax}$=3 Hz, H-1′), 4.93 (1H, dd, H-2′), 5.17 (1H, ddd, $J_{4',5'}$=10 Hz, $J_{5',6'eq}$=5 Hz, $J_{5',6'ax}$=11.5 Hz, H-5′), 5.54 (1H, s, benzylic), 7.28—7.62 (5H, m, phenyl).

Found for **12a**: C, 63.12; H, 7.19; N, 2.48%, and for **12b**: C, 63.24; H, 7.36; N, 2.29%. Calcd for $C_{31}H_{43}NO_{10}$: C, 63.14; H, 7.35; H, 2.38%.

Compounds **10a** and **10b** could be correlated to **12a** and **12b**, respectively, by acetylation in the usual way.

N-[*(1SR)-(1,4/2,3,5)-2,4,5-Trihydroxy-3-(hydroxymethyl)cyclohexyl*]-*(1SR)-(1,2,4/3,5)-2,3,4-trihydroxy-5-(hydroxymethyl)cyclohexylamine Octaacetate (13a).* A mixture of **12a** (30 mg) and 1 M hydrochloric acid (2 ml) was heated at reflux for 1 h. The reaction mixture was concentrated and the residue was acetylated in the usual way to give 28 mg (82%) of **13a** as an oil: R_f 0.21, 2-butanone–toluene (1 : 3). ^{1}H NMR ($CDCl_3$) δ=1.61 (1H, m, NH, disappears on deuteration), 1.98 (3H, s), 1.99 (3H, s), 2.02 (3H, s), 2.03 (9H, s), 2.07 (3H, s), and 2.11 (3H, s) (OAc), 2.82 (1H, q, J=3 Hz, H-1′), 3.27 (1H, q, J= 3 Hz, H-1). The free base showed a single spot on TLC [R_f 0.24, chloroform–methanol (3 : 1)].

Found: C, 53.62; H, 6.50; N, 2.17%. Calcd for $C_{30}H_{43}NO_{16}$: C, 53.49; H, 6.43; N, 2.08%.

N-[*(1SR)-(1,4/2,3,5)-2,4,5-Trihydroxy-3-hydroxymethyl)cyclohexyl*]-*(1RS)-(1,2,4/3,5)-2,3,4-trihydroxy-5-(hydroxymethyl)cyclohexylamine Octaacetate (13b).* Compound **12b** (62 mg) was deprotected and then acetylated similarly as described in the preparation of **13a** to give 58 mg (82%) of **13b** as an oil: R_f 0.23, 2-butanone–toluene (1 : 3). ^{1}H NMR ($CDCl_3$) δ= 1.61 (1H, m, NH, disappears on deuteration), 1.97 (3H, s),

1.975 (3H, s), 1.99 (3H, s), 2.01 (3H, s), 2.03 (3H, s), 2.035 (3H, s), 2.06 (3H, s), 2.065 (3H, s) (OAc), 2.91 (1H, q, J=3 Hz, H-1′), 3.28 (1H, q, H-1). The free base showed a single spot on TLC [R_f 0.18, chloroform–methanol (3 : 1)].

Found: C, 53.55; H, 6.52; N, 2.19%. Calcd for $C_{30}H_{43}NO_{16}$: C, 53.49; H, 6.43; N, 2.08%.

Reaction of DL-*4,7 : 5,6-Di-O-isopropylidene-(1,4,6/5)-4,5,6-trihydroxy-3-hydroxymethyl-2-cyclohexylamine (**4**) with **9**.* A mixture of **4**[6] (109 mg, 0.43 mmol) and **9** (124 mg, 0.43 mmol) in 2-propanol (1 ml) was heated in a sealed tube at 120 °C for 26 h. The reaction mixture was concentrated and the residue was chromatographed on a silica-gel column (13 g) with 2-butanone–toluene (1 : 6) as an eluent to give 191 mg (82%) of a mixture of the diastereomers of DL-*N*-[5-*O*-acetyl-4,7-*O*-benzylidene-(1,4/2,3,5)-2,4,5-trihydroxy-3-(hydroxymethyl)-cyclohexyl]-4, 7 : 5, 6-di-*O*-isopropylidene-(1,4,6/5)-4, 5, 6-trihydroxy-3-hydroxymethyl-2-cyclohexenylamine (**14a** and **14b**) as a homogeneous oil: R_f 0.48, ethanol–toluene (1 : 8). ^{1}H NMR ($CDCl_3$) δ=1.44 (6H, s), 1.47 (3H, s), and 1.54 (3H, s) (isopropylidene), 2.04 (3H, s, OAc), 2.45 (1H, m, H-3′), 3.17 (0.5H, q) and 3.30 (0.5H, q) (J=3 Hz, H-1′), 4.98—5.34 (1H, m, H-5′), 5.44 (0.5H, br d) and 5.61 (0.5H, br d) (J=*ca.* 4.5 Hz, H-2), 5.55 (1H, s, benzylic), 7.28—7.60 (5H, m, phenyl).

Found: C, 64.00; H, 7.25; N, 2.53%. Calcd for $C_{29}H_{39}NO_9$: C, 63.84; H, 7.20; N, 2.57%.

*Diastereomers **15a** and **15b** of* DL-N-[*2,5-Di-O-acetyl-4,7-O-benzylidene-(1,4/2,3,5)-2,4,5-trihydroxy-3-(hydroxymethyl)cyclohexyl*]-*4,7 : 5,6-di-O-isopropylidene-(1,4,6/5)-4,5,6-trihydroxy-3-hydroxymethyl-2-cyclohexenylamine.* A mixture of **14a** and **14b** (77 mg) was treated with acetic anhydride (1 ml) and pyridine (1 ml) at room temperature overnight. Formation of two components was detected by TLC [R_f 0.50 and 0.47, ethanol–toluene (1 : 8)]. The reaction mixture was concentrated and the residual products were fractionated by a silica-gel column (4.5 g) with 2-butanone–toluene (1 : 5). The first fraction (R_f 0.50) gave 38 mg (46%) of **15a** as a glass. The second fraction (R_f 0.47) gave 45 mg (54%) of **15b** as a glass. ^{1}H NMR ($CDCl_3$) for **15a**, δ=1.43 (3H, s), 1.47 (6H, s), and 1.54 (3H, s) (isopropylidene), 2.04 (3H, s) and 2.11 (3H, s) (OAc), 2.66 (1H, tdd, $J_{2',3'}$=3 Hz, $J_{3',7'_{eq}}$=5 Hz, $J_{3',4'}=J_{3',7'_{ax}}$=10.5 Hz, H-3′), 3.19 (1H, q, J=3 Hz, H-1′), 4.85 (1H, t, J=3 Hz, H-2′), 5.20 (1H, ddd, $J_{5',6'_{eq}}$=6 Hz, $J_{4',5'}$=9.5 Hz, $J_{5',6'_{ax}}$=11.5 Hz, H-5′), 5.54 (1H, s, benzylic), 5.54 (1H, br d, H-2), 7.28—7.58 (5H, m, phenyl), and for **15b**, δ=1.44 (6H, s) and 1.53 (6H, s) (isopropylidene), 2.03 (3H, s) and 2.10 (3H, s) (OAc), 2.86 (1H, tdd, $J_{2',3'}$=3 Hz, $J_{3',7'_{eq}}$=5 Hz, $J_{3',4'}=J_{3',7'_{ax}}$=11 Hz, H-3′), 3.21 (1H, q, J=3 Hz, H-1′), 4.93 (1H, t, J=3 Hz, H-2′), 5.19 (1H, ddd, $J_{5',6'_{eq}}$=5.5 Hz, $J_{4',5'}$=9.5 Hz, $J_{5',6'_{ax}}$=11 Hz, H-5′), 5.53 (1H, s, benzylic), 5.60 (1H, br d, $J_{1,2}$=5 Hz, H-2), 7.28—7.57 (5H, m, phenyl).

Found for **15a**: C, 62.52; H, 7.06; N, 2.54%, and for **15b**: C, 63.24; H, 6.94; N, 2.28%. Calcd for $C_{31}H_{41}NO_{10}$: C, 63.36; H, 7.03; N, 2.38%.

N-[*(1SR)-(1,4/2,3,5)-2,4,5-Trihydroxy-3-(hydroxymethyl)-cyclohexyl*]-*(1SR)-(1,4,6/5)-4,5,6-trihydroxy-3-hydroxymethyl-2-cyclohexenylamine Octaacetate (**16a**).* A mixture of **15a** (24 mg) and 1 M hydrochloric acid (5 ml) was heated at reflux for 2 h. The reaction mixture was concentrated and the residue was treated with acetic anhydride and pyridine in the usual way. The product was purified by passage through a short column of active alumina with chloroform. The eluate was concentrated to give 20 mg (73%) of **16a** as a glass: R_f 0.21, 2-butanone–toluene (1 : 3). ^{1}H NMR ($CDCl_3$) δ= 1.99 (3H, s), 2.03 (3H, s), 2.04 (6H, s), 2.06 (3H, s), 2.07 (6H, s), and 2.08 (3H, s) (OAc), 2.52—2.86 (1H, m, H-3′), 3.09 (1H, q, J=3 Hz, H-1′), 3.70 (1H, t, J=4 Hz, H-1), 3.96 (1H, dd, $J_{3',7'}$=5 Hz, J_{gem}=11.5 Hz) and 4.19 (1H, dd, $J_{3',7''}$= 8 Hz) ($C\underline{H}_2OAc$), 4.41 (1H, d) and 4.69 (1H, d) (J_{gem}=13 Hz, C=CH_2OAc), 5.97 (1H, br d, $J_{1,2}$=4 Hz, H-2).

Found: C, 53.82; H, 6.25; N, 2.24%. Calcd for $C_{30}H_{41}NO_{16}$: C, 53.64; H, 6.15; N, 2.09%.

The free base showed a single spot on TLC [R_f 0.44, chloroform–methanol (3 : 1)].

N-[*(1SR)-(1,4/2,3,5)-2,4,5-Trihydroxy-3-(hydroxymethyl)-cyclohexyl*]-*(1RS)-(1,4,6/5)-4,5,6-trihydroxy-3-hydroxymethyl-2-cyclohexenylamine Octaacetate (**16b**).* Compound **15b** (15 mg) was converted into **16a** similarly as described for the preparation of **16a**: yield 15 mg (87%), R_f 0.19, 2-butanone–toluene (1 : 3). ^{1}H NMR ($CDCl_3$) δ=2.00 (3H, s), 2.03 (3H, s), 2.05 (15H, s), and 2.10 (3H, s) (OAc), 2.59 (1H, m, H-3′), 3.05 (1H, q, J=3 Hz, H-1′), 3.68 (1H, m, H-1), 3.95 (1H, dd, $J_{3',7'}$=4.5 Hz, J_{gem}=11.5 Hz) and 4.20 (1H, dd, $J_{3',7''}$=9 Hz) ($C\underline{H}_2OAc$), 4.39 (1H, d) and 4.69 (J_{gem}=13 Hz, C=CCH_2OAc), 6.06 (1H, br d, $J_{1,2}$=5 Hz, H-2).

Found: C, 53.87; H, 6.28; N, 2.30%. Calcd for $C_{30}H_{41}NO_{16}$: C, 53.64; H, 6.15; N, 2.09%.

The free base showed a single spot on TLC [R_f 0.44, chloroform–methanol (3 : 1)].

The authors express their sincere thanks to Mr. Saburo Nakada for the elementary analyses. The present work was partially supported by a Grant-in-Aid for Scientific Research No. 56550617 from the Ministry of Education, Science and Culture.

References

1) a) Presented in part at the 45th National Meeting of the Chemical Society of Japan, Tokyo, April 1982, Abstr., No. 4E30; b) Previous paper of this series: S. Ogawa, H. Ito, T. Ogawa, S. Iwasaki, and T. Suami, *Bull. Chem. Soc. Jpn.*, **56**, 2319 (1983).

2) The nomenclature and numbering of cyclitols used in this paper follow IUPAC and IUB tentative rules for cyclitol nomenclature [*J. Biol. Chem.*, **243**, 5809 (1968)]. For convenience, the carbon atom of the branched-chain substituent on C-3 of the cyclohexane ring are numbered 7. All compounds described in this paper are racemic and the formulas depict only one of the respective enantiomers.

3) S. Ogawa, M. Suetsugu, T. Toyokuni, and T. Suami, *Nippon Kagaku Kaishi*, **1982**, 1721 and the references are cited therein.

4) S. Ogawa, T. Toyokuni, and T. Suami, *Chem. Lett.*, **1981**, 947; T. Toyokuni, S. Ogawa, and T. Suami, *Bull. Chem. Soc. Jpn.*, **56**, in press.

5) S. Ogawa, T. Toyokuni, Y. Iwasawa, Y. Abe, and T. Suami, *Chem. Lett.*, **1982**, 279.

6) S. Ogawa, T. Ogawa, N. Chida, T. Toyokuni, and T. Suami, *Chem. Lett.*, **1982**, 749. The similar deshielding effect was observed in the ^{1}H NMR spectrum of the corresponding 6′-acetoxy derivative.

7) Observation of chromatographic behavior of several pseudo-disaccharide derivatives obtained so far indicated that one diastereomer whose configuration corresponded to that of natural validoxylamine A moved somewhat slower than the other on TLC in several solvent systems. A similar behavior was observed in this case, correlating to the ^{1}H NMR spectral data.