IMPROVED SYNTHESIS OF 1-DEOXYNOJIRIMYCIN AND FACILE SYNTHESIS OF ITS STEREOISOMERS FROM (*S*)-PYROGLUTAMIC ACID DERIVATIVE

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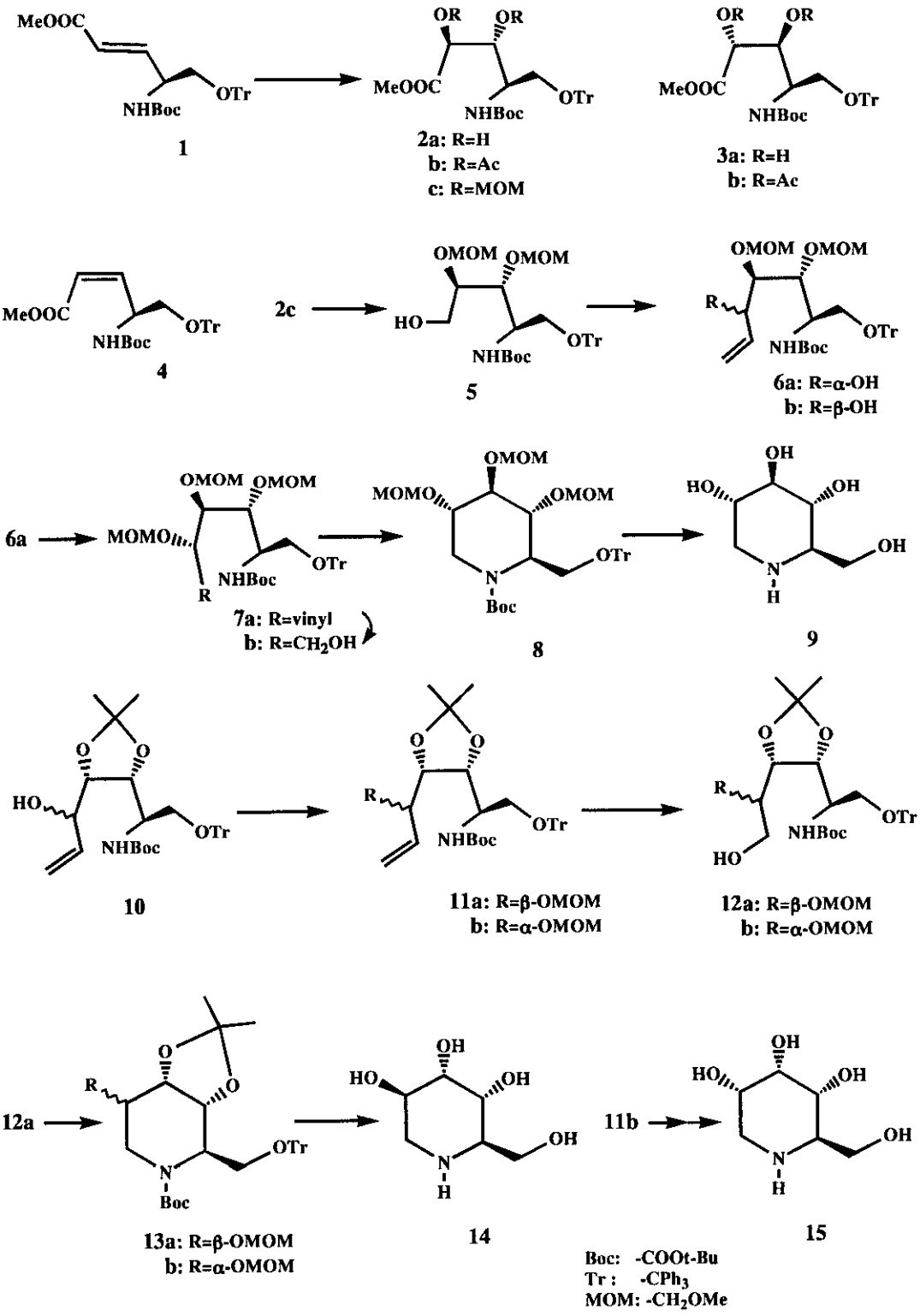
Abstract-----Improved synthesis of 1-deoxynojirimycin (**9**) from (*E*)-α,β-unsaturated ester (**1**) and facile synthesis of 1-deoxy-azasugars (**14** and **15**) from **10** where both substrates (**1** and **10**) prepared from (*S*)-pyroglutamic acid were described.

1-Deoxynojirimycin and its stereoisomers show interesting biological activities such as glycosidase inhibitory activity[1a-c] and their synthesis has been a subject of recent research.[1c-f] We have already reported the synthesis of 1-deoxynojirimycin from (*S*)-pyroglutamic acid [2] and the improvement of stereoselectivity for the newly formed asymmetric centers.[3] In continuation of our studies on the synthesis of chiral polyhydroxylated amines, we describe here a further improvement for the synthesis of 1-deoxynojirimycin (**9**) and the facile synthesis of 1-deoxyazasugars (**14** and **15**) from (*S*)-pyroglutamic acid.

We have found the dihydroxylation of **1** with potassium osmate (0.08 equiv.) using hydroquinidine 1,4-phthalazinediyl diether (0.20 equiv.) as a chiral ligand[4] in the presence of $K_3Fe(CN)_6$ (3 equiv.), K_2CO_3 (3 equiv.), and $MeSO_2NH_2$ (1 equiv.) in *tert*-BuOH-H_2O (1:1) at 0°C for 12 h gives the diol (**2a**) as a sole diastereomer in 84% yield. A complete diastereoselectivity for this dihydroxylation was confirmed by conversion of the crude diol into the corresponding diacetate, and the diacetate (**3b**) was not detected in the ^1H NMR spectrum of the crude poduct. On the other hand, the double asymmetric induction for the dihydroxylation of (*Z*)-α,β-unsaturated ester (**4**)[5] was not effective (up to 20% d.e. was observed using hydroquinidine 1,4-phthalazinediyl diether and hydroquinine 1,4-phthalazinediyl diether as chiral ligands, while 31% d.e. was obtained without chiral ligand[5]).

The alcohol (**5**) was obtained from **2a** *via* the corresponding MOM ether (**2c**) by the same procedure as reported previously.[3] A high diastereoselectivity was also observed for the introduction of vinyl group to the aldehyde derived from **5** by the method of Swern.[6] Thus, the reaction of the aldehyde with the reagent prepared from vinylmagnesium bromide and copper bromide-dimethyl sulfide complex[7] at -78°C


MeOOC
NHBoc
OTr
1
OR
OR
2a: R=H
b: R=Ac
c: R=MOM
3a: R=H
b: R=Ac
4
2c
OMOM
HO
5
R
6a: R=α-OH
b: R=β-OH
6a
MOMO
7a: R=vinyl
b: R=CH2OH
Boc
8
OH
9
10
11a: R=β-OMOM
b: R=α-OMOM
12a: R=β-OMOM
b: R=α-OMOM
13a: R=β-OMOM
b: R=α-OMOM
14
11b
15
Boc: -COOt-Bu
Tr : -CPh3
MOM: -CH2OMe

gave **6a** and **6b** in a ratio of 15:1 in 51% yield. The major diastereomer (**6a**) was converted into a corresponding MOM ether (**7a**) and was treated with ozone in methylene chloride followed by reductive work-up with $NaBH_4$ to give the alcohol (**7b**) in 53% yield. Mesylation (methanesulfonyl chloride (MsCl), triethylamine (TEA), CH_2Cl_2) followed by cyclization with potassium *tert*-butoxide in THF gave the fully protected piperidine derivative (**8**) in 71% yield. Hydrolysis of **8** with MeOH-10% HCl (1:1) at 70°C followed by treatment with Dowex 50W-X8 (H^+ form) gave 1-deoxynojirimycin (**9**) (mp 195-197°C, $[\alpha]_D$ +46.5° (c=0.5, H_2O), lit.,[1b] mp 196°C, $[\alpha]_D$ +47° (H_2O)) in 80% yield.
1-Deoxyazasugars (**14** and **15**) were synthesized starting from the inseparable diastereomeric mixture (**10**), which was prepared from (*S*)-pyroglutamic acid for the synthesis of 1,7a-diepialexine.[8] The compound (**10**) was converted into the corresponding MOM ethers (89% yield, **11a** : **11b**= 2.3:1), which were separated by column chromatography. Major diastereomer (**11a**) was transformed to the alcohol (**12a**, O_3, then $NaBH_4$), which was then cyclized into the piperidine derivative (**13a**) *via* mesylate (MsCl, TEA, CH_2Cl_2; then *tert*-BuOK, THF) in 62% yield. Cleavage of all protecting groups in **13a** with acidic conditions (MeOH:10% HCl=1:1, 70°C) gave **14** (hydrochloride of **14**: mp 103-105°C, $[\alpha]_D$ +54.3°(H_2O)) in 85% yield. In the same reaction sequence, **11b** was converted into **15** (mp 149-150°C, $[\alpha]_D$ +28.1° (c=0.8, H_2O), lit.,[9] $[\alpha]_D$ +25.7° (c=0.65, H_2O)) in 58% yield.

EXPERIMENTAL

General methods.---------Melting points were determined on a hot stage apparatus and are uncorrected. IR spectra were measured with a JEOL JIR-110 FT-IR spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-FX100 (100 Mz) spectrometer. Data are recorded in parts per million (ppm) downfield from internal tetramethylsilane. MS spectra were taken on a JEOL JMS-D302 spectrometer. Optical rotations were measured in $CHCl_3$ solution at 20°C on a JASCO DIP-360 polarimeter unless otherwise mentioned. The organic solvents were dried over $MgSO_4$ before vacuum evaporation and a column chromatography was carried out with silica gel (Wakogel C-200).

1,1-Dimethylethyl *N*-[(1*R*,2*R*,3*S*)-2,3-dihydroxy-3-methoxycarbonyl-1-(trityloxymethyl)propanyl]carbamate (2a) Potassium osmate dihydrate (54.5 mg, 0.15 mmol) was added to a mixture of hydroquinidine 1,4-phthalazinedil diether (288 mg, 0.37 mmol), $K_3Fe(CN)_6$ (1.82 g, 5.5 mmol), K_2CO_3 (770 mg, 5.5 mmol), and $MeSO_2NH_2$ (174 mg, 1.85 mmol) in a *tert*-BuOH-H_2O (1:1, 18 mL) at rt. Then, **1** (900 mg, 1.85 mmol) was added at 0°C. After being stirred at 0°C for 12 h, Na_2SO_3 (4 g) was added and the mixture was stirred for 30 min, and extracted with AcOEt. The organic extracts were washed with H_2O, 1 N aqueous KOH, H_2O, and saturated aqueous NaCl. Drying followed by evaporation gave a residue, which was purified by column chromatography (AcOEt:hexane=2: 1) to give **2a** (805 mg, 84%) as an oil, $[\alpha]_D$ -7.9° (c=1.5); IR ν_{max} 3444, 1748, 1708, 1166, 1086 cm^{-1}; ^1H NMR ($CDCl_3$): 1.41 (9H, s, *t*-Bu), 2.80-3.02(1H, br s, OH), 3.15-3.29 (1H, m, CH), 3.49-3.96(2H, m, 2xCH), 3.75(3H, s, OCH_3), 3.96-4.46(3H, m, 2xCH, OH), 5.15(1H, d, *J*=8 Hz, NH), 7.07-7.78 (15H, m, aromatic protons); ^{13}C NMR ($CDCl_3$): 27.92(q), 52.09(d), 62.13(t), 70.76(d), 71.54(d), 79.72(s), 86.49(s), 126.70, 127.48, and 128.20(each d), 143.27(s),

156.23(s), 172.60(s); MS *m/z* 520(M^+-1). A part of the crude diol was converted to the corresponding diacetate (excess pyridine and acetic anhydride, room temperature, 13 h). Diacetate (**3b**) was not detected in the ^1H NMR spectrum of the crude diacetate.

1,1-Dimethylethyl *N*-[(1*R*,2*R*,3*R*,4*S*)- and (1*R*,2*R*,3*R*,4*R*)-2,3-Bis(methoxymethoxy)-4-hydroxy-1-trityloxymethyl-5-hexenyl]carbamate (6a and 6b) The preparation of alcohol (**5**) and Swern oxidation were peformed by the same procedure as previously described.[3] [Vinyl-Cu]·$MgBr_2$ prepared by addition of vinylmagnesium bromide (4.2 mL of 1.0 M solution in THF) to the copper bromide-dimethyl sulfide complex (816 mg, 4 mmol) in ether-dimethyl sulfide (5:1, 5 mL) was added at -78°C to the crude aldehyde prepared from **5c** (480 mg, 0.83 mmol). After being stirred at -78°C for 1 h, the mixture was treated with saturated aqueous NH_4Cl (10 mL) and extracted with AcOEt. The organic layers were washed with half-saturated aqueous NaCl. Drying followed by evaporation gave a residue, which was purified by column chromatography (AcOEt:hexane=1:2.5) to give **6a** (241 mg, 48%, $[\alpha]_D$ -15.0° (c=1.1), lit.,[3] $[\alpha]_D$ -15.3° (c=1)) and **6b** (16 mg, 3.2%, $[\alpha]_D$ -22.5° (c=1.6), lit.,[3] $[\alpha]_D$ -22.0° (c=1)) as oils, which were identical to the authentic samples.[3]

1,1-Dimethylethyl *N*-[(1*R*,2*R*,3*R*,4*S*)-2,3,4-Tris(methoxymethoxy)-1-trityloxymethyl-5-hexenyl]carbamate (7a) A mixture of **6a** (230 mg, 0.38 mmol), *N*,*N*-diethylaniline (570 mg, 3.82 mmol), and chloromethyl methy ether (310 mg, 3.82 mmol) in CH_2Cl_2 (5 mL) was stirred at rt for 48 h. After addition of AcOEt (100 mL), the mixture was washed with 5% aqueous HCl, H_2O, saturated aqueous $NaHCO_3$, and H_2O. Drying followed by evaporation gave a residue, which was purified by column chromatography(AcOEt:hexane= 1: 4) to give **7a** (176 mg, 71%) as an oil, $[\alpha]_D$ +4.3° (c=1.6, MeOH) ; IR $\nu_{max.}$ (neat) 1708, 1500, 1218, 1028 cm^{-1}; ^1H NMR($CDCl_3$): 1.40(9H, s, *t*-Bu), 3.10-4.03(5H, m, CH_2, 3xCH), 3.25, 3.28, 3.29, and 3.41 (9H, each s, 3xOCH_3), 4.10-4.35(1H, m, CH), 4.42-4.80(6H, m, 3xCH_2), 5.14-5.90(4H, m, -CH_2=CH, NH), 7.10-7.53(15H, m, aromatic protons); ^{13}C NMR($CDCl_3$): 27.97(q), 50.68(d), 55.26(q), 55.69(q), 55.99(q), 62.38(t), 77.14(d), 77.87(d), 78.41(s), 79.43(d), 86.25(s), 93.51(t), 97.51(t), 98.63(t), 119.24(t), 126.55, 127.33, and 128.26(each d), 134.05(d), 143.27(s), 155.16(s); Anal. Calcd for $C_{37}H_{49}NO_9$: C, 68.18; H, 7.58; N, 2.15. Found: C, 67.77; H, 7.85; N, 1.88.

1,1-Dimethylethyl *N*-[(1*R*,2*R*,3*R*,4*S*)-2,3,4-Tris(methoxymethoxy)-1-trityloxymethyl-5-hydroxypentyl]carbamate (7b) A solution of **7a** (170 mg, 0.26 mmol) in CH_2Cl_2 (1 mL) was added at -78°C to 2 mL of CH_2Cl_2 saturated with ozone, then ozone was bubbled for further 5 min at -78°C. Then, this solution was added to a suspension of $NaBH_4$ (61 mg, 1.6 mmol) in EtOH (2 mL) at 0°C. After being stirred at 0°C for 15 min, the mixture was diluted with AcOEt-benzene (1:2, 100 mL) and washed with half-saturated aqueous NaCl. Drying followed by evaporation gave a residue, which was purified by column chromatography (AcOEt:hexane=3:2) to give **7b** (128 mg, 75 %) as an oil, $[\alpha]_D$ -12.8° (c=1.2) ; IR $\nu_{max.}$ (neat) 3448, 1708, 1450, 1158, 1026 cm^{-1}; ^1H NMR($CDCl_3$): 1.40(9H, s, *t*-Bu), 3.10-3.31(2H, m, CH_2), 3.21, 3.30, and 3.39 (each 3H, each s, 3xOCH_3), 3.57-4.20(6H, m, CH_2, 4xCH), 4.55(4H, br s, 2xOCH_2O), 4.50-4.70(1H, m, OH), 4.66(2H, br s, OCH_2O), 5.50(1H, d, J=9 Hz, NH), 7.10-7.48(15H, m, aromatic protons); ^{13}C NMR($CDCl_3$): 28.21(q), 50.44(d), 55.70(q), 55.89(q), 56.14(q), 62.33(t), 77.14(d), 78.75(s),

80.45(d), 80.99(d), 86.49(s), 97.56(t), 98.09(t), 98.68(t), 126.75, 127.53, and 128.45(each d), 143.41(s), 155.16(s); MS *m/z* 655(M^+).

(2*R*,3*R*,4*R*,5*S*)-*N*-*tert*-Butoxycarbonyloxy-3,4,5-tri(methoxymethoxy)-2-(trityloxymethyl)piperidine (8) A mixture of **7b** (120 mg, 0.18 mmol), methanesulfonyl chloride (41 mg, 0.36 mmol), and TEA (37 mg, 0.36 mmol) in CH_2Cl_2 (3 mL) was stirred at 0° C for 30 min. After dilution with AcOEt, the mixture was washed with H_2O, saturated aqueous $NaHCO_3$, and H_2O. Drying followed by evaporation gave a residue, which was treated with potassium *tert*-butoxide(40 mg, 0.35 mmol) in THF (2 mL) at rt for 30 min. After dilution with AcOEt, the mixture was washed with half-saturated aqueous NaCl. Drying followed by evaporation gave a residue, which was purified by column chromatography (AcOEt:hexane =1:2) to give **8** (82 mg, yield 71%) as an oil, $[\alpha]_D$ +7.5° (c=1.4) ; IR ν max. (neat) 1688, 1418, 1038 cm^{-1}; ^1H NMR($CDCl_3$): 1.49(9H, s, *t*-Bu), 3.10-3.60(1H, m, CH_2), 3.32(6H, s, 2xCH_3), 3.45 (3H, s, OCH_3), 3.61-4.26(5H, m, 2xCH_2, 3xCH), 4.26-4.98(2H, m, 2xCH), 4.62(2H, br s, OCH_2O), 4.80(4H, br s, 2xOCH_2O), 7.11-7.64(15H, m, aromatic protons); ^{13}C NMR($CDCl_3$): 28.26(q), 39.62 and 40.74(t), 54.77(d), 55.46(q), 61.25(t), 71.73(d), 73.09(d), 75.63(d), 79.63(s), 86.35(s), 94.70 and 95.66(t), 126.75, 127.53, and 128.50(each d), 127.53, and 128.45(each d), 143.66(s), 154.96(s); MS *m/z* 636(M^+-1).

1-Deoxynojirimycin (9)

A mixture of **8** (65 mg, 0.10 mmol), 10% aqueous HCl (2 mL), and MeOH (2 mL) was stirred at 70°C for l h. After removal of the methanol *in vacuo*, the mixture was washed with AcOEt(x2) and the aqueous layer was placed on a Dowex 50W-X8 (H^+ form) column (10 ml), washed with 20 ml of H_2O, and eluted with 1 N NH_4OH. Freeze-drying of the appopriate fractions gave a residue, which was crystallized from MeOH-ether to give **9** (13 mg, 80%), which was identical to the authentic sample,[2] mp 195-197°C, $[\alpha]_D$ +46.5° (c=0.8, H_2O) ; ^{13}C NMR(D_2O, internal standard:dioxane δ=67.4): 49.56 (t), 61.35(d), 62.23(t), 71.73(d), 72.36 (d), 79.24(d).

1,1-Dimethylethyl *N*-[(1*R*,2*R*,3*S*,4*R*)- and (1*R*,2*R*,3*S*,4*S*)-2,3-Isopropylidenedioxy-4-methoxymethoxy-1-trityloxymethyl-5-hexenyl]carbamate (11a and 11b) These samples (**11a**, 368 mg, 62%; **11b**, 160 mg, 27%) were obtained from **10** (550 mg, 0.98 mmol) as an oil after column chromatography (AcOEt:hexane= 1: 4) in the same manner as described above for the preparation of **2c**. **11a**: $[\alpha]_D$ -42.2° (c=0.4) ; IR ν max. (neat) 1714, 1496, 1376, 1164 cm^{-1} ; ^1H NMR ($CDCl_3$):1.39(6H, s, 2xCH_3), 1.44(9H, s, *t*-Bu), 3.08-3.51(2H, m, CH_2), 3.32(3H, s, OCH_3), 4.10-4.41(4H, m, 4xCH), 4.41-4.80(2H, m, OCH_2O), 4 .90(1H, d, J=9 Hz, NH), 5.17-5.46(2H, m, C<u>H</u>$_2$=CH), 5.71-6.16(1H, m, CH_2=C<u>H</u>), 7.07-7.59(15H, m, aromatic protons);^{13}C NMR($CDCl_3$): 25.34(q), 26.31(q), 28.12(q), 49.85(d), 55.46(q), 63.35(t), 76.07(d), 79.09(s), 79.77(d), 86.16(s), 94.44(t), 108.47(s), 118.42(t), 126.70, 127.48, and 128.35(each d), 135.37(d), 143.70(s), 154.77(s). **11b**: mp 128-130°C(AcOEt-hexane) ; $[\alpha]_D$ -29.8° (c=0.5) ; IR ν max. (nujol) 1710, 1498, 1374, 1166 cm^{-1}; ^1H NMR($CDCl_3$):1.36(6H, s, 2xCH_3), 1.43(9H, s, *t*-Bu), 3.01-3.35(2H, m, CH_2), 3.38(3H, s, OCH_3), 4.03-4.80(6H, m, CH_2, 4xCH), 4.90(1H, d, J=9 Hz, NH), 5.18-5.51(2H, m, C<u>H</u>$_2$=CH), 5.60-6.01(1H, m, CH_2=C<u>H</u>), 7.07-7.59(15H, m, aromatic protons);^{13}C NMR($CDCl_3$): 24.71(q), 26.17(q), 28.17(q), 49.51(d), 55.60(q), 63.50(t), 75.44(d), 75.87(d), 78.75(d), 79.19(s), 86.16(s), 93.27(t),

108.13(s), 120.56(t), 126.75, 127.53, and 128.40(each d), 134.01(d), 143.75(s), 154.91(s); Anal. Calcd for $C_{36}H_{45}NO_7$: C, 71.62; H, 7.51; N, 2.32. Found: C, 71.33; H, 7.79; N, 2.11.

1,1-Dimethylethyl *N*-[(1*R*,2*R*,3*S*,4*R*)-2,3-Isopropylidenedioxy-4-methoxymethoxy-1-trityloxymethyl-5-hydroxypentyl]carbamate (12a) This sample (230 mg, 76%) was obtained from **11a** (300 mg, 0.50 mmol) as an oil after column chromatography (AcOEt:hexane= 2:3) in the same manner as described above for the preparation of **7b**, $[\alpha]_D$ -30.7° (c=0.6); IR $\nu_{max.}$ (neat) 3444, 1708, 1062 cm^{-1}; ^1H NMR($CDCl_3$):1.39(15H, s, 2xCH_3, *t*-Bu), 2.98-3.50(2H, m, CH_2), 3.38(3H, s, OCH_3), 3.65-3.85(3H, m, OH, CH_2), 3,98-4.55(4H, m, 4xCH), 4.60-4.97(3H, m, 2xCH, NH), 7.14-7.55(15H, m, aromatic protons); ^{13}C NMR($CDCl_3$): 25.49(q), 26.36(q), 28.12(q), 49.51(d), 55.50(q), 63.20(t), 64.47(t), 75.34(d), 77.72(s), 79.57(d), 80.45(d), 86.25(s), 97.22(t), 108.72(s), 126.75, 127.58, and 128.35(each d), 143.66(s), 155.10(s); MS *m/z* 607(M^+).

(2*R*,3*R*,4*S*,5*R*)-*N*-*tert*-Butoxycarbonyloxy-3,4-isopropylidenedioxy-5-methoxymethoxy-2-(trityloxymethyl)piperidine (13a) This sample (126 mg, 82%) was obtained from **12a** (160 mg, 0.26 mmol) as an oil after column chromatography (AcOEt:hexane= 1: 3) in the same manner as described above for the preparation of **8**, $[\alpha]_D$ -44.5° (c=0.4) ; IR $\nu_{max.}$ (neat) 1694, 1408, 1228, 1090 cm^{-1}; ^1H NMR($CDCl_3$):1.30(6H, s, 2xCH3), 1.46(9H, s, t-Bu), 2.84-3.18(3H, m, CH_2, CH), 3.32(3H, s, OCH_3), 3.50-3.83(1H, m, CH), 3.83-4.23(3H, m, 3xCH), 4.49-4.87(3H, m, CH, OCH_2O), 7.13-7.53(15H, m, aromatic protons); ^{13}C NMR($CDCl_3$): 25.44(q), 27.24(q), 27.87(q), 40.64 and 42.05(t), 51.75 and 52.63(d), 54.72(q), 62.81 and 63.50(t), 72.36 and 72.09(d), 74.07 and 74.67(d), 75.77 and 76.51(d), 79.53(s), 86.64(s), 94.73 and 94.97(t), 107.55(s), 126.65, 127.38, and 128.11(each d), 143.12(s), 154.67(s); MS *m/z* 588(M^+-1).

(2*R*,3*R*,4*S*,5*R*)-2-Hydroxymethyl-3,4,5-piperidinetriol (14) This sample (19 mg, 85%) was obtained from **13a** (80 mg, 0.14 mmol) as an oil in the same manner as described above for the preparation of **9**, $[\alpha]_D$ +17.9° (c=1.3, H_2O) ; ^1H NMR(D_2O, DHO: δ=4.70): 2.53-3.01(3H, m), 3.58-3.97(5H, m); ^{13}C NMR(D_2O, internal standard:dioxane δ=67.4): 45.42(t), 56.43(d), 61.69(t), 67.05(d), 70.22(d), 71.48(d). Hydrochloride of **14**: mp 103-105°C (MeOH-ether): $[\alpha]_D$ +54.3° (c=0.7, H_2O) ; ^1H NMR(D_2O, DHO:δ=4.70): 3.05-3.47(3H,m), 3.65-4.20(5H,m); ^{13}C NMR(D_2O, internal standard: dioxane δ=67.4): 44.78(t), 56.72(d), 59.06(t), 64.47(d), 67.05(d), 69.34(d); Anal. Calcd for $C_6H_{14}NO_4Cl$: C, 36.10; H, 7.07; N, 7.02. Found: C, 35.87; H, 7.32; N, 6.81.

Physical and nmr data of 12b, 13b, and 15 **12b**:$[\alpha]_D$ -43.9° (c=0.4) ; ^1H NMR($CDCl_3$):1.25 and 1.32(6H, each s, 2xCH3), 1.45(9H, s, *t*-Bu), 3.11-3.58(2H, m, CH_2), 3.41(3H, s, OCH_3), 3.58-3.83(3H, m, OH, CH_2), 3.85-4.50(4H, m, 4xCH), 4.69 and 4,76(2H, AB q, J=7 Hz, OCH_2O), 5.04(1H, d, J=8 Hz, NH), 7.11-7.58(15H, m, aromatic protons); ^{13}C NMR($CDCl_3$): 24.80(q), 26.60(q), 28.07(q), 50.05(d), 55.46(q), 63.35(t), 76.12(d), 79.09(s), 79.53(d), 86.06(s), 96.92(t), 107.79(s), 126.55, 127.38, and 128.31(each d), 143.60(s), 154.82(s). **13b**: $[\alpha]_D$ -42.1° (c=0.4) ; ^1H NMR($CDCl_3$) : 1.31 and 1.47(6H, each s, 2xCH_3), 1.42(9H, s, *t*-Bu), 2.92-3.60(4H, m, CH_2, 2xCH), 3.31(3H, s, OCH_3), 3.60-3.97(1H, m, CH), 4.10-4.51(3H, m, 3xCH), 4.60(2H, s, OCH_2O), 7.01-7.50(15H, m, aromatic protons); ^{13}C NMR($CDCl_3$): 23.88(q), 25.97(q), 28.17(q), 39.08 and 40,74(each t), 53.16(d),

55.26(q), 63.59(t), 70.17(d), 71.63(s), 74.21(d), 79.67(s), 86.98(s), 95.36(t), 108.33(s), 126.94, 127.62, and 128.35(each d), 143.21(s), 154.86(s). **15**: mp 149-150°C (MeOH-ether): $[\alpha]_D$ +28.1° (c=0.8, H_2O); ^1H NMR(D_2O, DHO: δ=4.70):2.39-2.87(3H, m), 3.30-3.80(4H, m), 3.90-4.05(1H, m); ^{13}C NMR(D_2O, internal standard:dioxane δ=67.4): 44.44(t), 55.36(d), 62.03(t), 68.91(d), 69.39(d), 72.27(d); Anal. Calcd for $C_6H_{13}NO_4$: C, 44.16; H, 8.03; N, 8.58. Found: C, 43.90; H, 8.37; N, 8.34.

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