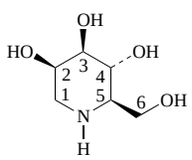
A new approach to 1-deoxy-azasugars: asymmetric synthesis of 1-deoxymannojirimycin and 1-deoxyaltronojirimycin

Yi-Ming Xu and Wei-Shan Zhou*

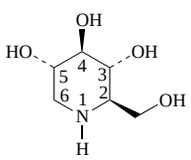
Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, China

A concise and flexible method, based upon the kinetic resolution of racemic α-furfuryl amine derivatives, for the asymmetric synthesis of 1-deoxy-azasugars is described. (−)-1-Deoxymannojirimycin 1a has been synthesized in nine steps (5.8% overall yield) from the α-furfurylamine derivative 3 and its enantiomer (+)-1-deoxymannojirimycin 1b has been similarly synthesized in nine steps (3.7% overall yield) from (*S*)-3. (−)- and (+)-1-Deoxyaltronojirimycin, 16a and 16b, have also been synthesized in five steps (overall yields 21.5% and 25.4%, respectively) from the intermediates 9a and 9b, respectively.

Naturally occurring polyhydroxylated piperidine alkaloids such as (−)-1-deoxymannojirimycin **1a** and (+)-1-deoxynojirimycin **2**, which can be regarded as 1-deoxy-azasugars, have received much attention in recent years. Deoxymannojirimycin **1a**, isolated from *Lonchocarpus* sp.,[1] is a moderate inhibitor of several α-mannosidases[2] and a good inhibitor of mammalian α-fucosidase.[3] Deoxynojirimycin **2**, first prepared by hydrogenation of a streptomyces product nojirimycin isolated from mulberries,[4] is an inhibitor of a number of glucosidases,[5] and it has potential for use in the therapy of diabetes mellitus, hyperlipoproteinemia, cancer and arthritis.[6] Because of the biological activity of these compounds as well as their structure, the latter characterized by four contiguous chiral centres and high density of functionality, much effort has been directed toward their stereoselective synthesis.[7] Although the majority of these syntheses seem to lack both flexibility and general applicability, two published recently and employing the dihydropyridone system as a building block for the preparation of 1-deoxymannojirimycin[6b] and 1-deoxyallonojirimycin,[8] are notable for their flexible, albeit multi-stage, nature. In view of these problems development of concise and flexible methods for the construction of such 1-deoxy-azasugars continues to be of importance in probing structure–activity correlations.



1a

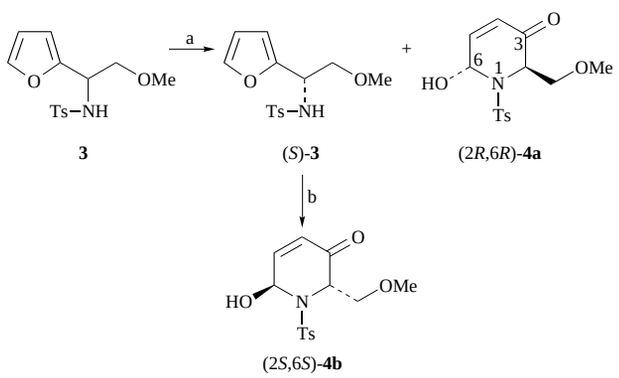


2

The numbering system shown in formula **1a** has been used only for compounds **1a**, **1b** and **16a**, **16b**; the numbering system used in the systematic names for all other compounds is shown in formula **2**

Our group has previously developed an efficient method for kinetic resolution of racemic α-furfurylamine derivatives by using a modified Sharpless asymmetric epoxidation reagent.[9] This reaction afforded two versatile chiral building blocks, both of which are very suitable for elaboration to a variety of alkaloid skeletons.[10] Here we report the application of this method to the synthesis of (−)- and (+)-1-deoxymannojirimycin, **1a**[11] and **1b**, as well as (−)- and (+)-1-deoxyaltronojirimycin, **16a** and **16b**, which are analogues of **1a** and **1b**.

We envisioned that kinetic resolution of the α-furfurylamine derivative **3** by the reported procedure[9] would yield (2*R*,6*R*)-**4a** and (*S*)-**3** which could be converted into the enantiomer of **4a** by treatment with *m*-CPBA (Scheme 1). Both **4a** and its enantiomer **4b** are potential building blocks for the synthesis of 1-deoxy-azasugars since the double bond and the carbonyl group may be further functionalized. In view of this our strategy has a potential to generate all isomers of 1-deoxy-azasugars.



3 (*S*)-**3** (2*R*,6*R*)-**4a**

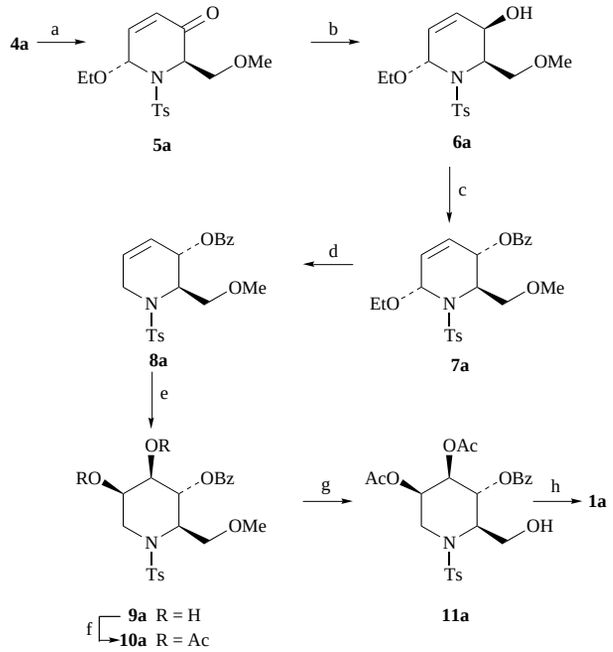
(2*S*,6*S*)-**4b**

Scheme 1 *Reagents and conditions:* a, $Ti(OPr^i)_4$, L-(+)-DIPT, TBHP, silica gel, CaH_2, CH_2Cl_2, 25 °C, 3 days; b, *m*-CPBA, CH_2Cl_2, RT

Initially, we report on the use of **4a** as a building block for the synthesis of (−)-1-deoxymannojirimycin **1a**.

As depicted in Scheme 2, treatment of **4a** with triethyl orthoformate generated **5a**, reduction of which with $NaBH_4$ and $CeCl_3 \cdot 7H_2O$ afforded solely the alcohol **6a**. In this, the configuration of the hydroxy group was assigned by 2D-NOESY spectroscopic analysis and found to be the reverse of that desired for the target molecule. Inversion of this configuration was successfully achieved by employing a Mitsunobu reaction. Removal of the ethoxy group of **7a** by $NaBH_4$ in formic acid, followed by Sharpless asymmetric dihydroxylation[12] led exclusively to the diol **9a** which was protected to give diacetate **10a**. Although attempts to remove the methyl group in **10a** selectively with Me_3SiI failed, demethylation proceeded smoothly with BBr_3. Since 2D-NOESY analysis of **11a** (see Fig. 1) showed that there is no NOE correlation between H_3 and H_4, nor between H_2 and H_3, the Mitsunobu reaction is clearly successful with stereospecific introduction of β-dihydroxy groups at C_5 and C_4.

Finally, deprotection of **11a** by sodium naphthalenide followed by chromatography on a column of Dowex-50 (H^+) gave



Scheme 2 *Reagents and conditions:* a, $HC(OEt)_3$, $BF_3{\cdot}OEt_2$, 4 Å molecular sieves THF, 0 °C (76.5%); b, $NaBH_4$, $CeCl_3{\cdot}7H_2O$, MeOH −30 °C (72.3%); c, DEAD–TPP, $PhCO_2H$, THF, RT (91.7%); d, $NaBH_4$, HCO_2H, 0 °C (86.7%); e, $(DHQ)_2$-PHAL, OsO_4, $K_3Fe(CN)_6$, K_2CO_3, Bu^{t}OH–H_2O, RT, 2 days (84.8%); f, Ac_2O, pyridine, DMAP, RT (100%); g, BBr_3, CH_2Cl_2, −78 °C (71.6%); h, Na–naphthalene, DME, −60 °C (50.7%)

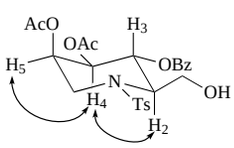


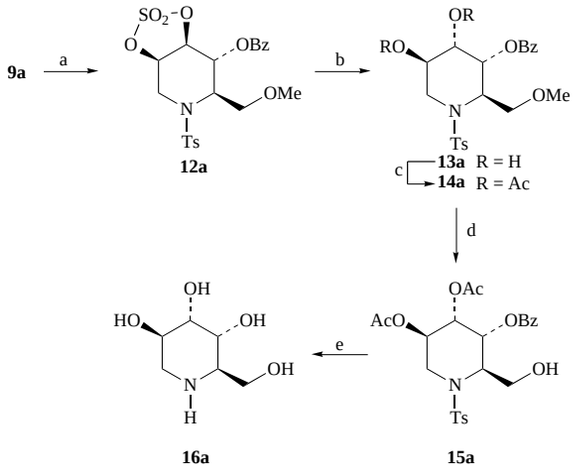
Fig. 1 NOE correlations in **11a**

(−)-1-deoxymannojirimycin **1a** in 5.8% overall yield from **3**, mp 185 °C, $[\alpha]_D^{20}$ −27† (*c* 0.1 in MeOH) [lit.,[13] mp 185–187 °C, $[\alpha]_D^{20}$ −26.7 (*c* 0.12 in MeOH)]. The ^{1}H NMR and the mass spectra of **1a** were identical with those of an authentic sample.[14]

According to our strategy, we treated (*S*)-**3**, the slow reaction product of kinetic resolution, with *m*-CPBA to obtain **4b**. In parallel with the reactions shown in Scheme 2 (+)-1-deoxymannojirimycin **1b**, the enantiomer of **1a**, was synthesized *via* **5b**, **6b**, **7b**, **8b**, **9b**, **10b** and **11b** in 3.9% overall yield; it had mp 175 °C, $[\alpha]_D^{20}$ +28.3 (*c* 0.17 MeOH); **5b**, **6b**, **7b**, **8b**, **9b**, **10b** and **11b** represent the enantiomers of **5a**, **6a**, **7a**, **8a**, **9a**, **10a** and **11a**.

For the synthesis of (−)-1-deoxyaltronojirimycin **16a** the above-mentioned synthetic intermediate **9a** was used (Scheme 3). Thus, **9a** was first converted into the cyclic sulfate **12a** by a reported procedure.[15] However **12a** failed to undergo ring-opening when treated with ammonium benzoate. We found, however, that treatment of **12a** with 20% H_2SO_4 gave two products **9a** and **13a** (1:1); with 50% H_2SO_4 the reaction produced only **13a**. Compound **13a** was protected to give diacetate **14a** which when demethylated with BBr_3 afforded **15a**. The configuration of **15a** was deduced from its 2D NOESY spectrum (see Fig. 2); this indicated that there was an NOE correlation between H_3 and H_4, but no NOE correlation between H_4 and H_5; on the other hand, H_5 had an NOE correlation with the benzoate protons, in contrast to H_3 and H_4 which did not. The configuration of **13a** was, therefore, confirmed. From this

† $[\alpha]_D$ Values given in units of 10^{-1} deg cm^2 g^{-1}.



Scheme 3 *Reagents and conditions:* a, (*i*) $SOCl_2$, NEt_3, CCl_4; (*ii*) $NaIO_4$, $RuCl_3{\cdot}3H_2O$ (72.9%); b, 50% H_2SO_4(aq.), THF (76.5%); c, Ac_2O, pyridine, DMAP, RT (100%); d, BBr_3, CH_2Cl_2, −78 °C (79.2%); e, Na–naphthalene, DME, −60 °C (48.7%)

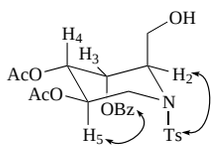


Fig. 2 NOE correlations in **15a**

evidence ring-opening of the cyclic sulfate **12a** occurs at C_4 rather than at C_5 as expected.

Deprotection of **15a** by sodium naphthalenide at −60 °C followed by chromatography on a column of Dowex-50(H^+) gave (−)-1-deoxyaltronojirimycin **16a** (overall yield of 21.5% in five steps), mp 175 °C, $[\alpha]_D^{20}$ −30.7 (*c* 0.13 in MeOH).

In a similar way, (+)-1-deoxyaltronojirimycin **16b** was synthesized in five steps from **9b** in an overall yield of 25.4%.

In summary, (−)-, (+)-1-deoxymannojirimycin, **1a** and **1b**, and (−)-, (+)-1-deoxyaltronojirimycin, **16a** and **16b**, have been synthesized; the method is based upon kinetic resolution of the α-furfurylamine derivative **3**. Work on (+)-1-deoxynojirimycin **2** and other analogues is in progress.

Experimental

All non-aqueous reactions were carried out under nitrogen. Tetrahydrofuran (THF), diethyl ether and dimethyl ether (DME) were distilled from Na–benzophenone. Dichloromethane was distilled from CaH_2. Titanium(IV) isopropoxide was purified by reduced pressure distillation and stored under an inert atmosphere. Diisopropyl tartrate (DIPT) was obtained from Tokyo Chemical Industry Co., Ltd. *tert*-Butyl hydroperoxide (TBHP) was obtained from Merck-Schuchardt Co. and purified before use according to a standard procedure.[16] Calcium hydride was obtained from Fluka Co. Mps were measured on a Büchi 535 melting-point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were measured on a Bruker AM-300 (300 MHz) with $CDCl_3$ as solvent unless otherwise noted, and values are reported in ppm using TMS as internal standard. IR spectra were measured on a Schimadzu IR 400 spectrometer. MS spectra were conducted on an HP5890 spectrometer or a Finnigan MAT-8430 spectrometer. The optical rotations, $[\alpha]_D^{20}$, were measured on a Perkin-Elmer 241 MC automatic polarimeter in a 1-dm cell and are recorded in units of 10^{-1} deg cm^2 g^{-1}. Elemental analyses were performed by the Analytical department of this Institute.

1-(2-Furyl)-2-methoxy-*N*-tosylethylamine 3[17]

A 500-cm^3 round three-necked flask was charged with $SnCl_2$

(7.6 g) and THF (10 cm^3) under N_2 to which a solution of LiBr (3.5 g) in THF (15 cm^3) and chloromethoxymethane (3.1 cm^3) was added at room temperature (RT). After 10 min, the reaction mixture was cooled to −78 °C and BuLi (1.6 mol dm^{-3}; 100 cm^3) was added to it dropwise. After the mixture had been stirred at −78 °C for 1 h, a solution of *N*-furfuryltoluene-*p*-sulfonamide (10 g) in THF (40 cm^3) was added to it. After 30 min, the reaction mixture was warmed to −30 °C and then treated with saturated aqueous NH_4Cl and extracted with ethyl acetate. The combined extracts were washed with brine, dried (Na_2SO_4), concentrated under reduced pressure and the residue flash column chromatographed on silica gel (light petroleum–ethyl acetate, 7:1) to give **3** (4.8 g, 40.5%) as a solid, mp 97.8 °C; ν_{max}(KBr)/cm^{-1} 3300, 3050, 2900, 1603 and 1460; δ_H 7.59 (2 H, d, *J* 8.3, Ph), 7.19 (2 H, d, *J* 8.3, Ph), 7.13 (1 H, m, 5-H), 6.12 (1 H, dd, *J* 1.8, 3.2, 4-H), 6.03 (1 H, d, *J* 3.2, 3-H), 5.14 (1 H, d, *J* 7.4, NH), 4.53 (1 H, m, α-H), 3.60 (1 H, dd, *J* 5.3, 9.7, CH_{2a}OCH_3), 3.44 (1 H, dd, *J* 4.9, 9.7, CH_{2b}OCH_3), 3.20 (3 H, s, OCH_3) and 2.33 (3 H, s, Ts-CH_3); *m/z* 295 (M^+), 250 ($M^+ - CH_2OCH_3$) and 155 (Ts^+) (Found: C, 56.88; H, 5.71; N, 4.58. Calc. for $C_{14}H_{17}NO_4S$: C, 56.93; H, 5.80; N, 4.74%).

(*S*)-1-(2-Furyl)-2-methoxy-*N*-tosylethylamine (*S*)-3 and (2*R*,6*R*)-*N*-tosyl-6-hydroxy-2-methoxymethyl-1,2,3,6-tetrahydropyridin-3-one 4a[9]

To a solution of $Ti(OPr^i)_4$ (0.99 cm^3, 3.4 mmol) in CH_2Cl_2 (6 cm^3) was added CaH_2 (14 mg), silica gel (31 mg) and L-(+)-DIPT (0.85 cm^3, 4.1 mmol) successively under N_2 at −20 °C. After 10 min, a solution of (±)-**3** (1.0 g, 3.4 mmol) in CH_2Cl_2 (6 cm^3) was added to the reaction mixture which was then stirred for a further 10 min before anhydrous TBHP (7.01 mol dm^{-3}; 1.45 cm^3, 10.2 mmol) was injected into it. After the reaction mixture had been stirred for 3 days at RT, 10% aqueous tartaric acid (10 cm^3) was added to it at −20 °C. Vigorous stirring was continued for 4 h at RT until the aqueous layer became clear. After separation of the organic layer, the aqueous layer was washed with CH_2Cl_2 (×3). The organic layer was filtered off through a pad of silica gel and the filtrate was concentrated under reduced pressure. The residue was dissolved in ether (10 cm^3) and treated with saturated aqueous $FeSO_4$ (10 cm^3) for 10 min at 0 °C. The organic layer was washed with brine, dried (Na_2SO_4) and concentrated under reduced pressure to afford an oil which was purified by flash column chromatography on silica gel (light petroleum–ethyl acetate, 9:1) to afford a mixture of (*S*)-**3** and L-(+)-DIPT. This mixture was dissolved in a mixture of THF–H_2O (3:1; 8 cm^3) and treated with LiOH·H_2O (0.16 g) for 2 h at 0 °C. The organic layer was separated, washed with brine, dried (Na_2SO_4) and concentrated under reduced pressure to give (*S*)-**3** (0.44 g, 44%), $[\alpha]_D^{20}$ −5.4 (*c* 1.0 EtOH). The spectral data (IR, ^1H NMR) were identical with those of (±)-**3**. The above silica gel column was then washed with light petroleum–ethyl acetate (5:1) to produce **4a** (0.45 g, 42.7%), mp 101.3 °C; [*α*] +3.24 (*c* 2.9 EtOH); ν_{max}(film)/cm^{-1} 3370, 2920, 1700, 1600 and 1450 cm^{-1}; δ_H 7.77 (2 H, d, *J* 8.2, Ph), 7.30 (2 H, d, *J* 8.2, Ph), 6.94 (1 H, dd, *J* 5.0, 10.3, 5-H), 6.08 (1 H, d, *J* 10.3, 4-H), 5.95 (1 H, dd, *J* 5.0, 11.4, 6-H), 4.77 (1 H, d, *J* 11.6, OH), 4.54 (1 H, m, 2-H), 3.69 (1 H, dd, 2.1, 9.6, C$H_a$$H_b$OMe), 3.44 (1 H, dd, *J* 2.5, 9.6, C$H_a$$H_b$OMe), 3.23 (3 H, s, OMe) and 2.42 (3 H, s, Ts-Me); *m/z* 311 (M^+), 294 ($M^+ - H_2O$) and 155 (Ts^+) (Found: C, 54.12; H, 5.31; N, 4.30. Calc. for $C_{14}H_{17}NO_5S$: C, 54.01; H, 5.50; N, 4.50%).

(2*R*,6*R*)-1-Tosyl-6-ethoxy-2-methoxymethyl-1,2,3,6-tetrahydropyridin-3-one 5a

To a solution of **4a** (1.1 g, 3.54 mmol) in THF (10 cm^3) were added 4 Å molecular sieves (165 mg), triethyl orthoformate (1.47 cm^3, 8.84 mmol) and BF_3·Et_2O (45 mm^3) at 0 °C. After the reaction mixture had been stirred for 3 h at 0 °C it was diluted with water (10 cm^3) and extracted with ether. The combined extracts were washed with brine and dried (Na_2SO_4). Flash chromatography on silica gel (light petroleum–ethyl acetate, 6:1) afforded **5a** (917 mg, 76.5%) as a solid, mp 71.8 °C; $[\alpha]_D^{20}$ −1.71 (*c* 2.75 EtOH). ν_{max}(KBr)/cm^{-1} 2900, 1700, 1600 and 1450; δ_H 7.58 (2 H, d, *J* 8.2, Ph), 7.25 (2 H, d, *J* 8.2, Ph), 6.77 (1 H, dd, *J* 4.4, 10.4, 5-H), 5.82 (1 H, d, *J* 10.4, 4-H), 5.64 (1 H, d, *J* 4.4, 6-H), 4.55 (1 H, t, *J* 7.1, 2-H), 4.05 (1 H, dd, *J* 7.1, 9.4, C$H_a$$H_b$OMe), 3.84 (1 H, dd, *J* 7.7, 10.0, C$H_a$$H_b$OMe), 3.69 (2 H, m, OC$H_2$Me), 3.39 (3 H, s, OC$H_3$), 2.41 (3 H, s, Ts-Me) and 1.26 (3 H, t, *J* 7.0, OCH_2*Me*); *m/z* 294 (M^+ − EtO), 249 (M^+ − EtO − CH_2OMe) and 155 (Ts^+) (Found: C, 56.40; H, 6.03; N, 4.02. Calc. for $C_{16}H_{21}NO_5S$: C, 56.62; H, 6.24; N, 4.13%).

(2*R*,3*R*,6*R*)-1-Tosyl-6-ethoxy-2-methoxymethyl-1,2,3,6-tetrahydropyridin-3-ol 6a

$CeCl_3$·$7H_2O$ (307 mg, 0.82 mmol) was added at RT to a solution of compound **5a** (559 mg, 1.65 mmol) in MeOH (10 cm^3). $NaBH_4$ (219 mg, 5.8 mmol) was added in portions at −30 °C to the mixture which was then stirred at the same temperature for 1 h. Saturated aqueous NH_4Cl was added at −10 °C to the mixture which was then extracted with ethyl acetate (3 × 10 cm^3). The combined extracts were washed with brine and dried (Na_2SO_4). Flash chromatography on silica gel (light petroleum–ethyl acetate, 7:3) then gave **6a** (407 mg, 72.3%) as a solid, mp 107.4 °C; $[\alpha]_D^{20}$ −1.8 (*c* 2.5 EtOH); ν_{max}(KBr)/cm^{-1} 3450, 2900, 1600 and 1440; δ_H 7.69 (2 H, d, *J* 8.3, Ph), 7.28 (2 H, d, *J* 8.0, Ph), 5.72 (2 H, m, 4-H, 5-H), 5.39 (1 H, d, *J* 1.8, 6-H), 4.17 (1 H, m, 3-H), 4.09 (1 H, t, *J* 9.4, 2-H), 3.87–3.79 (2 H, m, OCH_2Me), 3.63 (1 H, dd, *J* 7.1, 9.3, C$H_a$$H_b$Me), 3.53 (1 H, dd, *J* 3.7, 9.3, C$H_a$$H_b$OMe), 3.32 (3 H, s, OMe), 2.41 (3 H, s, Ts-Me) and 1.22 (3 H, t, *J* 7.0, OCH_2*Me*); *m/z* 296 (M^+ − EtO), 250 (M^+ − MeC_6H_4) and 155 (Ts^+) (Found: C, 56.37; H, 6.94; N, 4.11. Calc. for $C_{16}H_{23}NO_5S$: C, 56.29; H, 6.79; N, 4.10%).

(2*R*,3*S*,6*R*)-1-Tosyl-6-ethoxy-2-methoxymethyl-1,2,3,6-tetrahydro-3-pyridyl benzoate 7a

To a solution of **6a** (284 mg, 0.83 mmol) in dried THF (8 cm^3) were added triphenylphosphine (436 mg, 1.66 mmol), benzoic acid (203 mg, 1.66 mmol) and diethyl azodicarboxylate (DEAD) (0.26 cm^3, 1.66 mmol) at RT. After the reaction mixture had been stirred for 3 h, it was evaporated and the residue diluted with CH_2Cl_2 (30 cm^3). The resulting solution was washed with saturated aqueous $NaHCO_3$ and water and dried ($MgSO_4$). Flash chromatography on silica gel (light petroleum–ethyl acetate, 15:1) then gave **7a** (340 mg, 91.7%) as an oil; $[\alpha]_D^{20}$ +3.75 (*c* 1.2 EtOH); ν_{max}(film)/cm^{-1} 2900, 1730, 1600 and 1460; δ_H 7.75–7.64 (4 H, m, Ph), 7.52 (1 H, m, Ph), 7.35 (2 H, m, Ph), 7.10 (2 H, d, *J* 8.2, Ph), 6.17 (1 H, dd, *J* 4.2, 10.1, 4-H), 6.04 (1 H, dd, *J* 5.0, 10.1, 5-H), 5.58 (1 H, d, *J* 4.1, 3-H), 5.37 (1 H, d, *J* 5.2, 6-H), 4.36 (1 H, dd, *J* 5.0, 10.0, 2-H), 3.89 (1 H, dd, *J* 7.1, 9.4, OC$H_a$$H_b$Me), 3.72–3.62 (2 H, m, OC$H_a$$H_bMe, CH_a$$H_b$-OMe), 3.53 (1 H, dd, *J* 5.0, 10.0, C$H_a$$H_b$Me), 3.37 (3 H, s, OMe), 2.21 (3 H, s, Ts-Me) and 1.22 (3 H, t, *J* 7.0, OCH_2*Me*); *m/z* 400 (M^+ − EtO), 354 ($M^+ - CH_3C_6H_4$), 155 (Ts^+) and 105 ($C_6H_5CO^+$) (Found: C, 61.49; H, 5.96; N, 2.84. Calc. for $C_{23}H_{27}NO_6S$: C, 62.00; H, 6.11; N, 3.14%).

(2*R*,3*S*)-1-Tosyl-2-methoxymethyl-1,2,3,6-tetrahydro-3-pyridyl benzoate 8a

$NaBH_4$ (87 mg, 2.3 mmol) was added in portions to a solution of **7a** (340 mg, 0.76 mmol) in 88% formic acid (8 cm^3) at 0 °C. After being stirred for 1 h the mixture was evaporated under reduced pressure and water (5 cm^3) was added to the residue. The resulting mixture was extracted with ethyl acetate (3 × 10 cm^3) and the combined extracts were washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4) and evaporated under reduced pressure. Flash chromatography on silica gel (light petroleum–ethyl acetate, 10:1) then gave **8a** (256 mg, 86.7%) as a solid, mp 92.5 °C; $[\alpha]_D^{20}$ +14.8 (*c* 1.0 EtOH); ν_{max}(KBr)/cm^{-1} 2900, 1720, 1600 and 1460 cm^{-1}; δ_H 7.89 (2 H,

m, Ph), 7.75 (2 H, d, *J* 8.3, Ph), 7.55 (1 H, m, Ph), 7.34 (2 H, m, Ph), 7.16 (2 H, d, *J* 8.1, Ph), 6.04 (2 H, m, 4-H, 5-H), 5.45 (1 H, d, *J* 4.2, 3-H), 4.56 (1 H, t, *J* 7.0, 2-H), 4.11 (1 H, dd, *J* 4.2, 18.4, C*H*$_a$H$_b$OMe), 3.73 (1 H, dd, *J* 1.7, 18.4, CH$_a$*H*$_b$OMe), 3.48 (2 H, m, C*H*$_2$OMe), 3.33 (3 H, s, OMe) and 2.34 (3 H, s, Ts-Me); *m/z* 356 ($M^+ - CH_2OMe$), 234 ($M^+ + 1 - MeC_6H_4Ph$), 155 (Ts^+) and 105 ($PhCO^+$) (Found: C, 62.96; H, 5.90; N, 5.54. Calc. for $C_{21}H_{23}NO_5S$: C, 62.82; H, 5.77; N, 3.49%).

(2*R*,3*S*,4*R*,5*R*)-1-Tosyl-4,5-dihydroxy-2-methoxymethyl-3-piperidyl benzoate 9a

A 25-cm^3 round bottom flask was charged with *tert*-butyl alcohol (6 cm^3), water (6 cm^3), $K_3Fe(CN)_6$ (862 mg, 2.6 mmol), K_2CO_3 (361 mg, 2.6 mmol), $(DHQ)_2$-PHAL (2 mg) and a solution of OsO_4 in toluene (25 mg cm^{-3}; 0.9 cm^3). Compound **8a** (350 mg, 0.87 mmol) was then added to the resulting heterogeneous slurry which was then vigorously stirred at RT for 2 days. The reaction was quenched by addition of Na_2SO_3 (989 mg) to the mixture and this was followed by ethyl acetate (5 cm^3), added after 20 min. The resulting mixture was extracted with ethyl acetate (3 × 5 cm^3) and the combined extracts were dried (Na_2SO_4) and evaporated. Subsequent purification by flash chromatography on silica gel (light petroleum–ethyl acetate, 1:1) gave **9a** (322 mg, 84.8%) as a solid, mp 131.5 °C; $[\alpha]_D^{20}$ −6.13 (*c* 1.5 EtOH); ν_{max}(film)/cm^{-1} 3400, 2900, 1720, 1600 and 1450; δ_H 7.85 (2 H, m, Ph), 7.66–7.56 (3 H, m, Ph), 7.42 (2 H, t, *J* 7.6, Ph), 7.07 (2 H, d, *J* 8.3, Ph), 5.28 (1 H, dd, *J* 1.1, 3.2, 3-H), 4.33 (1 H, m, 2-H), 3.93–3.80 (5 H, m, C*H*$_2$OMe, 4-H, 5-H, 6-H$_a$), 3.41 (3 H, s, OMe), 3.22 (1 H, m, 6-H$_b$) and 2.27 (3 H, s, Ts-Me); *m/z* 390 ($M^+ - CH_2OMe$), 372 ($M^+ - H_2O - CH_2OMe$), 105 ($PhCO^+$) and 91 ($MeC_6H_4^+$) (Found: C, 57.73; H, 5.97; N, 2.97. Calc. for $C_{21}H_{25}NO_7S$: C, 57.92; H, 5.79; N, 3.22%).

(2*R*,3*S*,4*R*,5*R*)-1-Tosyl-4,5-diacetoxy-2-methoxymethyl-3-piperidyl benzoate 10a

To a solution of **9a** (312 mg, 0.9 mmol) in pyridine (1 cm^3) was added acetic anhydride (0.5 cm^3) and *N*,*N*-dimethylaminopyridine (DMAP; 1 mg). The reaction mixture was stirred for 24 h at RT after which it was evaporated under reduced pressure and the residue treated with water (3 cm^3). The resulting mixture was extracted with ethyl acetate (3 × 5 cm^3) and the combined extracts were washed successively with saturated aqueous $CuSO_4$ and brine, dried (Na_2SO_4) and evaporated. Purification of the residue by flash chromatography on silica gel (light petroleum–ethyl acetate, 4:1) gave **10a** (372 mg, 100%) as a solid, mp 133.8 °C; $[\alpha]_D^{20}$ −3.46 (*c* 1.5 $CHCl_3$); ν_{max}(film)/cm^{-1} 2900, 1750, 1730, 1600 and 1450; δ_H 7.83 (2 H, d, *J* 7.2, Ph), 7.68 (2 H, d, *J* 8.3, Ph), 7.57 (1 H, t, *J* 6.3, Ph), 7.41 (2 H, t, *J* 7.7, Ph), 7.05 (2 H, d, *J* 8.2, Ph), 5.36 (2 H, s, 4-H, 5-H), 5.12 (1 H, m, 3-H), 4.51 (1 H, t, *J* 8.1, 2-H), 3.94 (1 H, dd, *J* 5.3, 13.6, 6-H$_a$), 3.82 (1 H, t, *J* 8.9, C*H*$_a$H$_b$OMe), 3.70 (1 H, dd, *J* 7.5, 10.1, CH$_a$*H*$_b$OMe), 3.42 (3 H, s, OMe), 3.33 (1 H, dd, *J* 11.4, 13.6, 6-H$_b$), 2.24 (3 H, s, Ts-Me), 2.14 (3 H, s, MeCO) and 2.03 (3 H, s, MeCO); *m/z* 474 ($M^+ - CH_2OMe$), 414 ($M^+ + 1 -$ AcO − CH_2OH), 155 (Ts^+) and 105 ($PhCO^+$) (Found: C, 58.01; H, 5.83; N, 2.66. Calc. for $C_{25}H_{29}NO_9S$: C, 57.79; H, 5.63; N, 2.70%).

(2*R*,3*S*,4*R*,5*R*)-1-Tosyl-4,5-diacetoxy-2-hydroxymethyl-3-piperidyl benzoate 11a

A dried 25-cm^3 round bottom flask was charged with **10a** (324 mg, 0.62 mmol) and CH_2Cl_2 (5 cm^3) under N_2 at RT; a solution of BBr_3 in CH_2Cl_2 (1 mol dm^{-3}; 6.2 cm^3) was then added at −78 °C to the flask. After 1 h the reaction mixture was warmed to −20 °C at which temperature stirring was continued for 5 h. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (3 cm^3) to the mixture which was then extracted with ethyl acetate (3 × 5 cm^3). The combined extracts were washed with brine, dried (Na_2SO_4) and concentrated under reduced pressure. Subsequent flash chromatography on silica gel (light petroleum–ethyl acetate, 3:2) gave **11a** (226 mg, 71.6%) as a solid, mp 45.5 °C, $[\alpha]_D^{20}$ −2.0 (*c* 2.75 EtOH); ν_{max}(film)/cm^{-1} 3350, 1740, 1720, 1600 and 1450; δ_H 7.76 (2 H, d, *J* 7.3, Ph), 7.66 (2 H, d, *J* 8.2, Ph), 7.59 (1 H, t, *J* 7.4, Ph), 7.40 (2 H, t, *J* 7.7, Ph), 7.00 (2 H, d, *J* 8.1, Ph), 5.33 (1 H, t, *J* 3.1, 5-H), 5.21 (1 H, d, *J* 2.7, 4-H), 5.11 (1 H, m, 3-H), 4.25 (1 H, t, *J* 7.0, 2-H), 4.13–3.98 (2 H, m, C*H*$_2$OMe), 3.88 (1 H, dd, *J* 6.1, 11.4, 6-H$_a$), 3.41 (1 H, dd, *J* 11.3, 13.6, 6-H$_b$), 2.18 (3 H, s, Ts-Me), 2.14 (3 H, s, CH_3CO) and 2.04 (3 H, s, MeCO); *m/z* 474 ($M^+ - CH_2OH$), 414 ($M^+ - C_6H_4$), 250 ($M^+ - C_6H_4 -$ PhCO − AcO), 155 (Ts^+) and 105 ($PhCO^+$) (Found: C, 56.92; H, 5.36; N, 2.43. Calc. for $C_{24}H_{27}NO_9S$: C, 57.02; H, 5.38; N, 2.77%).

(−)-1-Deoxymannojirimycin 1a

A solution of sodium naphthalenide in DME was prepared by addition of DME (1.5 cm^3) to a mixture of sodium (39 mg, 9.7 mmol) and naphthalene (222 mg, 9.7 mmol). The resulting mixture was stirred at RT for 1 h. To a solution of **11a** (55 mg, 0.11 mmol) in DME (2 cm^3) was added sodium naphthalenide (0.6 cm^3) under N_2 at −60 °C. The reaction mixture was stirred for 1 h at −60 °C and then quenched by the addition of saturated aqueous NH_4Cl (2 cm^3) at −30 °C. The resulting mixture was separated and the organic layer was extracted with water (3 × 5 cm^3). The combined aqueous solutions were washed with ether and concentrated under reduced pressure. The residue was chromatographed on Dowex-50(H^+) (first elution with MeOH, then concentrated aqueous NH_3) to afford **1a** (9 mg, 50.7%) as a solid, mp 185 °C; $[\alpha]_D^{20}$ −27 (*c* 0.1 MeOH) [lit.,[13] mp 185–187 °C, $[\alpha]_D^{20}$ −26.7 (0.12 in MeOH)]; $\delta_H(D_2O)$ 4.07 (1 H, m, 5-H), 3.85 (2 H, d, *J* 3.7 C*H*$_2$OH), 3.72–3.62 (2 H, m, 3-H, 4-H), 3.08 (1 H, dd, *J* 1.9, 14.3, 6-H$_a$), 2.83 (1 H, d, br, *J* 14.3, 6-H$_b$) and 2.55 (1 H, m, 2-H) [Found (HRMS): *m/z*, 163.0866. Calc. for $C_6H_{13}NO_4$: 163.0844].

(2*S*,6*S*)-1-Tosyl-6-hydroxy-2-methoxymethyl-1,2,3,6-tetrahydropyridin-3-one 4b

A solution of *m*-CPBA (692 mg, 3.2 mmol) in CH_2Cl_2 (4 cm^3) was added to a solution of (*S*)-**3** (860 mg, 2.9 mmol) in CH_2Cl_2 (5 cm^3) at RT and the reaction mixture was stirred for 14 h. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (10 cm^3) to the mixture at 0 °C. After separation of the layers, the aqueous layer was extracted with ether (3 × 15 cm^3) and the combined extracts were washed with brine, dried (Na_2SO_4) and concentrated under reduced pressure. Subsequent flash chromatography on silica gel (light petroleum–ethyl acetate, 5:1) gave **4b** (809 mg, 89.2%) as a solid, mp 101.3 °C; $[\alpha]_D^{20}$ −2.0 (*c* 1.1 EtOH); the spectral data (IR, ^{1}H NMR) were identical with those of **4a**.

(2*S*,6*S*)-1-Tosyl-6-ethoxy-2-methoxymethyl-1,2,3,6-tetrahydropyridin-3-one 5b

As described for the preparation of its enantiomer **5a** from **4a**, compound **5b** was prepared from **4b** (780 mg, 2.5 mmol); the product (583 mg, 68.6%) had mp 72.0 °C; $[\alpha]_D^{20}$ +2.84 (*c* 2.5 EtOH). The spectral data were identical with those of **5a**.

(2*S*,3*S*,6*S*)-1-Tosyl-6-ethoxy-2-methoxymethyl-1,2,3,6-tetrahydropyridin-3-ol 6b

As described for the preparation of its enantiomer **6a** from **5a**, compound **6b** was prepared from **5b** (365 mg, 1.2 mmol); the product (289 mg, 72.2%) had mp 107.1 °C; $[\alpha]_D^{20}$ +2.04 (*c* 2.4 EtOH). The spectral data were identical with those of **6a**.

(2*S*,3*R*,6*S*)-1-Tosyl-6-ethoxy-2-methoxymethyl-1,2,3,6-tetrahydro-3-pyridyl benzoate 7b

As described for the preparation of its enantiomer **7a** from **6a**, compound **7b** was prepared from **6b** (115 mg, 0.34 mmol); the product (130 mg, 86.6%) was an oil; $[\alpha]_D^{20}$ −3.96 (*c* 2.4 EtOH). The spectral data were identical with those of **7a**.

(2*S*,3*R*)-1-Tosyl-2-methoxymethyl-1,2,3,6-tetrahydro-3-pyridyl benzoate 8b

As described for the preparation of its enantiomer **8a** from **7a**, compound **8b** was prepared from **7b** (120 mg, 0.27 mmol). The product (90 mg, 83.3%) had mp 92.5 °C; $[\alpha]_D^{20}$ −11.0 (*c* 1.0, EtOH). The spectral data were identical with those of **8a**.

(2*S*,3*R*,4*S*,5*S*)-1-Tosyl-4,5-dihydroxy-2-methoxymethyl-3-piperidyl benzoate 9b

As described for the preparation of its enantiomer **9a** from **8a**, compound **9b** was prepared from **8b** (90 mg, 0.22 mmol). The product (79 mg, 80.9%) had mp 132.0 °C; $[\alpha]_D^{20}$ −1.32 (*c* 2.5 EtOH). The spectral data were identical with those of **9a**.

(2*S*,3*R*,4*S*,5*S*)-1-Tosyl-4,5-diacetoxy-2-methoxymethyl-3-piperidyl benzoate 10b

As described for the preparation of its enantiomer **10a** from **9a**, compound **10b** was prepared from **9b** (55 mg, 0.13 mmol). The product (66 mg, 100%) had mp 134.0 °C; $[\alpha]_D^{20}$ +3.56 (*c* 2.5 $CHCl_3$). The spectral data were identical with those of **10a**.

(2*S*,3*R*,4*S*,5*S*)-1-Tosyl-4,5-diacetoxy-2-hydroxymethyl-3-piperidyl benzoate 11b

As described for the preparation of its enantiomer **11a** from **10a**, compound **11b** was prepared from **10b** (73 mg, 0.14 mmol). The product (50 mg, 70.4%) had mp 45.0 °C; $[\alpha]_D^{20}$ +2.7 (*c* 1.8 EtOH). The spectral data were identical with those of **11a**.

(+)-1-Deoxymannojirimycin 1b

As described for the preparation of its enantiomer **1a** from **11a**, compound **1b** was prepared from **11b** (44 mg, 0.09 mmol). The product (5 mg, 35.2%) had mp 185 °C; $[\alpha]_D^{20}$ +25.7 (*c* 0.17 MeOH). The spectral data were identical with those of **1a**.

(2*R*,3*S*,4*S*,5*R*)-1-Tosyl-3-benzoyloxy-2-methoxymethyl-piperidine 4,5-cyclic sulfate 12a

To a solution of **9a** (165 mg, 0.38 mmol) in dried CH_2Cl_2 (1.5 cm^3) was added Et_3N (210 mm^3, 1.52 mmol) and a solution of $SOCl_2$ (42 mm^3, 0.57 mmol) in CH_2Cl_2 (0.5 cm^3) under N_2 at 0 °C. After being stirred for 30 min the reaction mixture was diluted with cold ether (5 cm^3), washed with cold water, dried (Na_2SO_4) and concentrated under reduced pressure to give an intermediate sulfide as an oil. This crude product, dissolved in a mixture of aceonitrile (1 cm^3), CCl_4 (1 cm^3) and water (1 cm^3), was treated with $RuCl_3 \cdot 3H_2O$ (1 mg) and $NaIO_4$ (242 mg, 1.14 mmol) at 0 °C. After 2 h the reaction mixture was diluted with ether (5 cm^3) and extracted with ether (3 × 5 cm^3). The combined extracts were washed with brine, dried (Na_2SO_4) and concentrated under reduced pressure. Subsequent flash chromatography on silica gel (light petroleum–ethyl acetate, 9:1) gave **12a** (137 mg, 72.9%) as a solid, mp 111.8 °C; $[\alpha]_D^{20}$ +3.2 (*c* 1.7, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 2940, 1750, 1600 and 1450; δ_H 8.00 (2 H, m, Ph), 7.77 (2 H, d, *J* 8.2, Ph), 7.63 (1 H, m, Ph), 7.48 (2 H, m, Ph), 7.29 (2 H, m, Ph), 5.77 (1 H, t, *J* 3.6, 3-H), 5.26 (1 H, m, 5-H), 5.11 (1 H, t, *J* 4.9, 4-H), 4.51 (1 H, m, 2-H), 4.03 (1 H, m, 6-H_a), 3.62 (3 H, m, CH_2OMe-H_2, 6-H_b), 3.34 (3 H, s, OMe) and 2.42 (3 H, s, Ts-Me); *m/z* 452 ($M^+ - CH_2OMe$), 354 ($M^+ - 2 - SO_4Ph$), 155 (Ts^+), 105 ($PhCO^+$) and 91 ($MeC_6H_4^+$) (Found: C, 51.02; H, 4.59; N, 2.53. Calc. for $C_{21}H_{23}NO_9S_2$: C, 50.70; H, 4.66; N, 2.82%).

(2*R*,3*S*,4*S*,5*R*)-1-Tosyl-4,5-dihydroxy-2-methoxymethyl-3-piperidyl benzoate 13a

To a solution of **12a** (127 mg, 0.26 mmol) in THF (2 cm^3) was added 50% H_2SO_4 (0.4 cm^3) at RT. The reaction mixture was held at 40 °C for 24 h after which it was diluted with water (5 cm^3) at room temperature and extracted with ethyl acetate (3 × 5 cm^3). The combined extracts were dried (Na_2SO_4) and evaporated to give a residue which was purified by flash chromatography on silica gel (light petroleum–ethyl acetate, 1:1) to afford **13a** (85 mg, 76.5%) as an oil; $[\alpha]_D^{20}$ −3.8 (*c* 0.5, EtOH); ν_{max}(film)/cm^{-1} 3450, 2900, 1720, 1600 and 1450 cm^{-1}; δ_H 7.93 (2 H, d, *J* 7.6, Ph), 7.67 (2 H, d, *J* 8.2, Ph), 7.60 (1 H, m, Ph), 7.44 (2 H, t, *J* 7.7, Ph), 7.11 (2 H, d, *J* 8.2, Ph), 5.48 (1 H, s, 3-H), 4.52 (1 H, m, 2-H), 3.99 (3 H, m, 4-H, 5-H, 6-H_a), 3.66 (2 H, d, *J* 5.5, CH_2OMe), 3.35 (3 H, s, OMe), 3.14 (1 H, m, 6-H_b) and 2.30 (3 H, s, Ts-Me); *m/z* 436 ($M^+ - 1$), 390 ($M^+ - CH_2OMe$), 372 ($M^+ - H_2O - CH_2OMe$), 250 ($M^+ - 1 - Ts - OMe$), 155 (Ts^+), 105 ($PhCO^+$) and 91 ($MeC_6H_4^+$) (Found: C, 57.97; H, 5.99; N, 3.95. Calc. for $C_{21}H_{25}NO_7S$: C, 57.92; H, 5.79; N, 3.22%).

(2*R*,3*S*,4*S*,5*R*)-1-Tosyl-4,5-diacetoxy-2-methoxymethyl-3-piperidyl benzoate 14a

To a solution of **13a** (80 mg, 0.18 mmol) in pyridine (1 cm^3) was added acetic anhydride (0.5 cm^3) and *N*,*N*-dimethylaminopyridine (DMAP; 1 mg). The reaction mixture was stirred for 24 h at RT, after which it was evaporated under reduced pressure, diluted with water, and extracted with ethyl acetate (3 × 5 cm^3). The combined extracts were washed with saturated aqueous $CuSO_4$ and brine, dried (Na_2SO_4) and evaporated to give a residue. This was purified by flash chromatography on silica gel (light petroleum–ethyl acetate, 4:1) to yield **14a** (95 mg, 100%) as an oil; $[\alpha]_D^{20}$ −2.3 (*c* 2.0 $CHCl_3$); ν_{max}(film)/cm^{-1} 2900, 1740, 1600 and 1450; δ_H 7.84 (2 H, d, *J* 7.3, Ph), 7.70 (2 H, d, *J* 8.2, Ph), 7.61 (1 H, t, *J* 7.4, Ph), 7.43 (2 H, m, Ph), 7.08 (2 H, d, *J* 8.2, Ph), 5.56 (1 H, m, 3-H), 5.50 (1 H, dd, *J* 3.3, 10.3, 4-H), 5.18 (1 H, m, 5-H), 4.42 (1 H, s, 2-H), 4.25 (1 H, dd, *J* 5.5, 13.2, 6-H_a), 3.78 (2 H, d, *J* 3.4, CH_2OMe), 3.42 (3 H, s, OMe), 3.34 (1 H, dd, *J* 10.8, 13.3, 6-H_b), 2.27 (3 H, s, Ts-Me), 2.07 (3 H, s, MeCO) and 1.95 (3 H, s, MeCO); *m/z* 520 ($M^+ + 1$), 488 ($M^+ + 1 - OMe$), 474 ($M^+ - CH_2OMe$), 414 ($M^+ - PhCO$), 155 (Ts^+) and 105 ($PhCO^+$) (Found: C, 57.84; H, 5.34; N, 2.49. Calc. for $C_{25}H_{29}NO_9S$: C, 57.79; H, 5.63; N, 2.70%).

(2*R*,3*S*,4*S*,5*R*)-1-Tosyl-2,3-diacetoxy-5-hydroxymethyl-3-piperidyl benzoate 15a

A dried 25-cm^3 round bottom flask was charged with **14a** (87 mg, 0.17 mmol) in CH_2Cl_2 (1.5 cm^3) under N_2 at RT; a solution of BBr_3 in CH_2Cl_2 (1 mol dm^{-3}; 1.7 cm^3) was then added to it at −78 °C. After 1 h the reaction mixture was warmed to −20 °C, at which temperature it was stirred for 5 h. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (3 cm^3) to the mixture which was then extracted with ethyl acetate (3 × 5 cm^3). The combined extracts were washed with brine, dried (Na_2SO_4) and concentrated under reduced pressure. Subsequent flash chromatography on silica gel (light petroleum–ethyl acetate, 3:2) gave **15a** (67 mg, 79.2%) as an oil. $[\alpha]_D^{20}$ −3.1 (*c* 1.2 EtOH); ν_{max}(film)/cm^{-1} 3510, 1760, 1740, 1600 and 1460; δ_H 7.79 (2 H, t, *J* 7.1, Ph), 7.69 (2 H, d, *J* 8.1, Ph), 7.59 (1 H, m, Ph), 7.41 (2 H, t, *J* 7.7, Ph), 7.06 (2 H, d, *J* 8.1, Ph), 5.56 (1 H, dd, *J* 2.4, 3.1, 3-H), 5.37 (1 H, dd, *J* 3.3, 10.3, 4-H), 5.19 (1 H, m, 5-H), 4.39 (1 H, m, 2-H), 4.27 (1 H, dd, *J* 5.5, 13.6, 6-H_a), 4.00 (2 H, d, *J* 5.8, CH_2OH), 3.28 (1 H, dd, *J* 10.7, 13.6, 6-H_b), 2.23 (3 H, s, Ts-Me), 2.05 (3 H, s, CH_3CO) and 1.93 (3 H, s, CH_3CO); *m/z* 474 ($M^+ - CH_2OH$), 414 ($M^+ - MeC_6H_4$), 292 ($M^+ - 1 - PhCO - MeC_6H_4$), 250 ($M^+ - PhCO - MeC_6H_4 - AcO$), 155 ($Ts^+$), 105 ($PhCO^+$) and 91 ($MeC_6H_4^+$) (Found: C, 56.59; H, 5.30; N, 2.57. Calc. for $C_{24}H_{27}NO_9S$: C, 57.02; H, 5.38; N, 2.77%).

(−)-1-Deoxyaltrojirimycin 16a

Sodium naphthalenide (0.69 cm^3) was added to a solution of **15a** (70 mg, 0.14 mmol) in DME (2 cm^3) under N_2 at −60 °C. The reaction mixture was stirred for 1 h at −60 °C and then quenched by the addition of saturated aqueous NH_4Cl (3 cm^3) at −30 °C. The resulting mixture was separated and the organic layer was extracted with water (3 × 5 cm^3). The combined aqueous layers were washed with ether and concentrated under reduced pressure. Subsequent chromatography of the residue

on Dowex-50(H^+) (first elution with MeOH, then concentrated aqueous NH_3) afforded **16a** (11 mg, 48.7%) as a solid, mp 175 °C; $[\alpha]_D^{20}$ −30.7 (*c* 0.13 MeOH); $\delta_H(D_2O)$ 4.06 (2 H, s, C*H*$_2$OMe), 3.97 (1 H, dd, *J* 5.0, 14.6, 3-H), 3.89 (2 H, m, 4-H, 5-H), 3.16 (1 H, dd, *J* 5.4, 13.7, 6-H$_a$), 3.06 (1 H, dd, *J* 4.5, 9.4, 2-H) and 2.98 (1 H, d, br, *J* 14.8, 6-H$_b$); $\delta_C(D_2O)$ 73.04, 71.52, 68.53, 63.13, 58.53 and 47.23; *m/z* (FABMS) 164 ($M^+ + 1$) and 133 ($M^+ + 1 - CH_2OH$).

(2*S*,3*R*,4*R*,5*S*)-1-Tosyl-3-benzoyloxy-2-methoxymethyl-piperidine 4,5-cyclic sulfate 12b

As described for the preparation of its enantiomer **12a** from **9a**, compound **12b** was prepared from **9b** (108 mg, 0.25 mmol). The product (92 mg, 74.6%) had mp 111.8 °C; $[\alpha]_D^{20}$ −3.1 (*c* 1.2 $CHCl_3$). The spectral data were identical with those of **12a**.

(2*S*,3*R*,4*R*,5*S*)-1-Tosyl-4,5-dihydroxy-2-methoxymethyl-3-piperidyl benzoate 13b

As described for the preparation of its enantiomer **13a** from **12a**, compound **13b** was prepared from **12b** (92 mg, 0.20 mmol). The product (66 mg, 82.0%) was an oil; $[\alpha]_D^{20}$ +3.0 (*c* 1.0 EtOH). The spectral data were identical with those of **13a**.

(2*S*,3*R*,4*R*,5*S*)-1-Tosyl-4,5-diacetoxy-2-methoxymethyl-3-piperidyl benzoate 14b

As described for the preparation of its enantiomer **14a** from **13a**, compound **14b** was prepared from **13b** (86 mg, 0.20 mmol). The product (97 mg, 94.5%) was an oil, $[\alpha]_D^{20}$ +2.6 (*c* 2.4 $CHCl_3$). The spectral data were identical with those of **14a**.

(2*S*,3*R*,4*R*,5*S*)-1-Tosyl-4,5-diacetoxy-2-hydroxymethyl-3-piperidyl benzoate 15b

As described for the preparation of its enantiomer **15a** from **14a**, compound **15b** was prepared from **14b** (87 mg, 0.17 mmol). The product (75 mg, 88.6%) was an oil, $[\alpha]_D^{20}$ +3.5 (*c* 3.7 EtOH). The spectral data were identical with those of **15a**.

(+)-1-Deoxyaltrojirimycin 16b

As described for the preparation of its enantiomer **16a** from **15a**, compound **16b** was prepared from **15b** (75 mg, 0.15 mmol). The product (12 mg, 49.5%) had mp 175 °C; $[\alpha]_D^{20}$ +28.3 (*c* 0.17 MeOH). The spectral data were identical with those of **16a**.

Acknowledgements

We thank the National Natural Science Foundation of China and the State Key Laboratory of Bio-Organic & Natural Products Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences for support of this work. We also thank Dr. Zhi-Min Wang for valuable discussions.

References

1 L. E. Fellows, E. A. Bell, D. G. Lynn, F. J. Pilkiewicz, I. Miura and K. Nakanishi, *J. Chem. Soc., Chem. Commun.*, 1979, 977.
2 (*a*) G. Legler, E. Julich, *Carbohydr. Res.*, 1984, **128**, 61; (*b*) U. Fuhrmann, E. Bause, G. Legler and H. Ploegh, *Nature*, 1984, **307**, 755.
3 S. V. Evans, L. E. Fellows, T. K. M. Shing and G. W. J. Fleet, *Phytochemistry*, 1985, **24**, 1953.
4 M. Yagi, T. Kouno, Y. Aoyagi and H. Murai, *Nippon Nogeikagaku Kaishi*, 1976, **50**, 571 (*Chem. Abstr.*, **86**, 167851r).
5 (*a*) S. Murso and S. Miyata, *Agric. Biol. Chem.*, 1980, **44**, 219; (*b*) U. Fuhrmann, E. Bause and H. Ploegh, *Biochim. Biophys. Acta*, 1985, **825**, 95; (*c*) A. M. Scofield, L. E. Fellows, R. J. Nash and G. W. J. Fleet, *Life Sci.*, 1986, **39**, 645.
6 (*a*) G. C. Look, C. H. Fotsch and C. H. Wong, *Acc. Chem. Res.*, 1993, **26**, 182; (*b*) G. R. Cook, L. G. Beholz and J. R. Stille, *J. Org. Chem.*, 1994, **59**, 3575 and references cited therein.
7 (*a*) A. B. Hughes and A. J. Rudge, *Natural Product Reports*, 1994, 135; (*b*) R. H. Furneaux, P. C. Tyler and L. A. Whitehouse, *Tetrahedron Lett.*, 1993, **34**, 3613 and several references cited therein.
8 H. J. Altenbach and K. Himmeldirk, *Tetrahedron Asymmetry*, 1995, **6**, 1077.
9 (*a*) W. S. Zhou, Z. H. Lu and Z. M. Wang, *Tetrahedron Lett.*, 1991, **32**, 1467; (*b*) W. S. Zhou, Z. H. Lu and Z. M. Wang, *Tetrahedron*, 1993, **49**, 2641.
10 (*a*) Z. H. Lu and W. S. Zhou, *J. Chem. Soc., Perkin Trans. 1*, 1993, 593; (*b*) Z. H. Lu and W. S. Zhou, *Tetrahedron*, 1993, **49**, 4659; (*c*) W. S. Zhou, W. G. Xie, Z. H. Lu and X. F. Pan, *Tetrahedron Lett.*, 1995, **36**, 1291.
11 Preliminary communication see Y. M. Xu and W. S. Zhou, *Tetrahedron Lett.*, 1996, **37**, 1461.
12 K. B. Sharpless, W. Amberg, Y. L. Bennani, G. A. Crispino, J. Hartung, K.-S. Jeong, H.-L. Kwong, K. Morikawa, Z.-M. Wang, D. Xu and X.-L. Zhang, *J. Org. Chem.*, 1992, **57**, 2768.
13 G. W. J. Fleet and P. W. Smith, *Tetrahedron Lett.*, 1985, **26**, 1469.
14 K. H. Park, Y. J. Yoon and S. G. Lee, *J. Chem. Soc., Perkin Trans. 1*, 1994, 2621.
15 Y. Gao and K. B. Sharpless, *J. Am. Chem. Soc.*, 1988, **110**, 7538.
16 T. Shono, Y. Matsumura, K. Tsubata and K. Uchida, *J. Org. Chem.*, 1986, **51**, 2590.
17 E. J. Corey and T. M. Eckrich, *Tetrahedron Lett.*, 1983, **24**, 3163.

Paper 6/05128*F*
Received 23*rd July* 1996
Accepted 14*th October* 1996