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Stereocontrolled Synthesis of All Four Stereoisomers of Fully Protected 2-Amino-3-hydroxypentanoic Acid from Imines Derived from D-Glyceraldehyde

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Abstract

N-Benzylimines derived from conveniently protected (*R*)-glyceraldehyde underwent diastereoselective phenylmagnesium bromide addition to afford the corresponding aminodiols, whose absolute configuration at the newly formed stereogenic carbon depends on the *O*-protecting group. These compounds can be easily transformed into optically pure *N*-*tert*-butoxycarbonyl-1-phenyl-2,3-epoxy-1-propylamines, which are key intermediates in the synthesis of 2-*tert*-butoxycarbonylamino-3-acetyloxypentanoates of *erythro* and *threo* configuration.

Keywords: Addition reactions, amino acids and derivatives, asymmetric synthesis, Grignard reagents, imines.

Introduction

α-Amino-β-hydroxy acids of varying complexity are important as components of complex biomolecules such as biologically active peptides (*e.g.* Echinocandins, Vancomycin, Ristocetin A, Teicoplanin, Bouvardin, Cyclosporine A), toxic peptides, peptidases, the polyoxins, and enzyme inhibitors [1]. They are also useful intermediates in the synthesis of other compounds such as β-lactam antibiotics [2], aminosugars [3], chiral ligands [4] and β-fluoro amino acids [5].

These compounds present a considerable challenge in terms of stereochemical control and synthetic efficiency and among the various procedures described for their stereoselective

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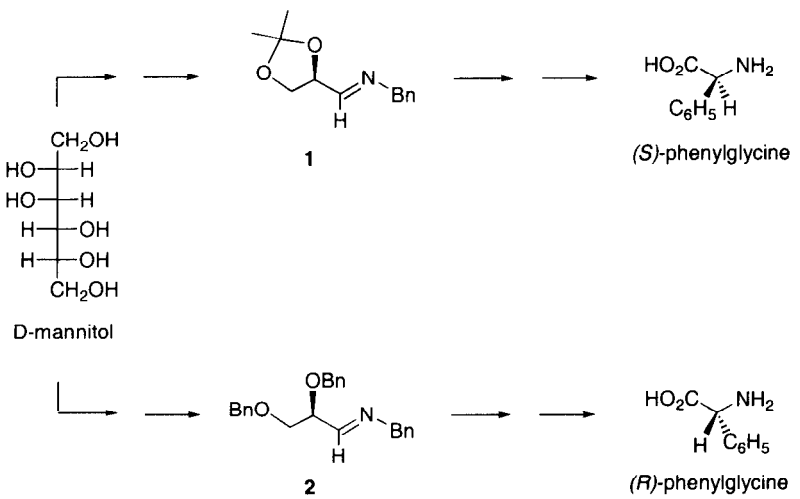
synthesis [6-14], those routes based on aldol condensations between a chiral glycine derivative and the appropriate aldehyde or ketone are usually the most efficient and versatile [12]. Although some of these procedures give good stereoselectivity, the stereochemical control of the different stereogenic carbon atoms in the molecule usually requires the use of various chiral auxiliaries. When the biological response of a series of compounds has to be evaluated, a synthetic approach leading to the maximum number stereochemical variations and substitution patterns would be desirable. Furthermore, a synthetic scheme that makes use of parallel, repetitive transformations from a single precursor should be preferred.

Carbohydrates and modified carbohydrates represent one of the most convenient classes of chiral synthons and templates in the stereoselective synthesis of enantiomerically pure compounds [15]. In this context carbon-carbon bond forming reactions from D-glyceraldehyde derivatives, easily obtained from D-mannitol, are particularly attractive.



Scheme 1

We have recently described a strategy for the synthesis of both enantiomers of phenylglycine from conveniently protected imines, derived from D-glyceraldehyde, as chiral templates [16] (Scheme 1). In our strategy, treatment of *N*-benzylimines derived from 2,3-diisopropylidene-D-glyceraldehyde or 2,3-di-*O*-benzyl-D-glyceraldehyde with phenylmagnesium bromide gave the corresponding addition compounds as single diastereoisomers. The absolute configuration of these compounds, determined through their conversion into the amino acid, depended on the choice of protecting group, which exerts control over the steric course of the nucleophilic addition.

We now wish to report the development of a general and simple methodology for the synthesis of the four stereoisomers of α-amino-β-hydroxy acids from these single, inexpensive, and easily available starting materials. The synthesis proceeds to give high optical purity and an

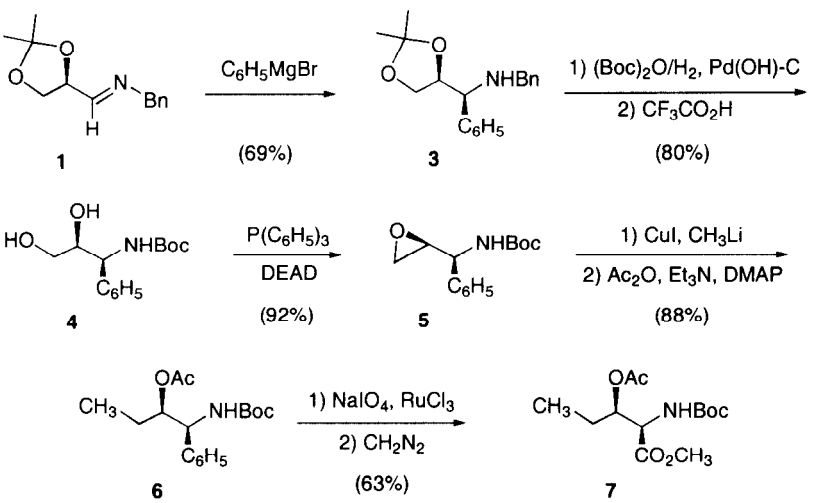
acceptable overall yield. The stereodivergent synthesis of the four isomers of 2-amino-3-hydroxypentanoic acid was selected as a model for establishing the methodology.

Results and discussion

Synthesis of fully protected (2R,3S)- and (2R,3R)-2-amino-3-hydroxypentanoic acid

(2*S*,3*S*)-3-*tert*-Butoxycarbonylamino-3-phenyl-1,2-propanediol (**4**) was prepared, as previously described [16], from the *N*-benzylimine derived from 2,3-diisopropylidene-D-glyceraldehyde. Addition of phenylmagnesium bromide to the imine gave the corresponding amine **3** of 2*S*,3*S* configuration, which was converted into the desired *N*-Boc amino diol by hydrogenolysis in the presence of di-*tert*-butyldicarbonate followed by acidic hydrolysis. From this compound a stereodivergent route to fully protected (2*R*,3*R*)- and (2*R*,3*S*)-2-amino-3-hydroxypentanoic acid has been developed.

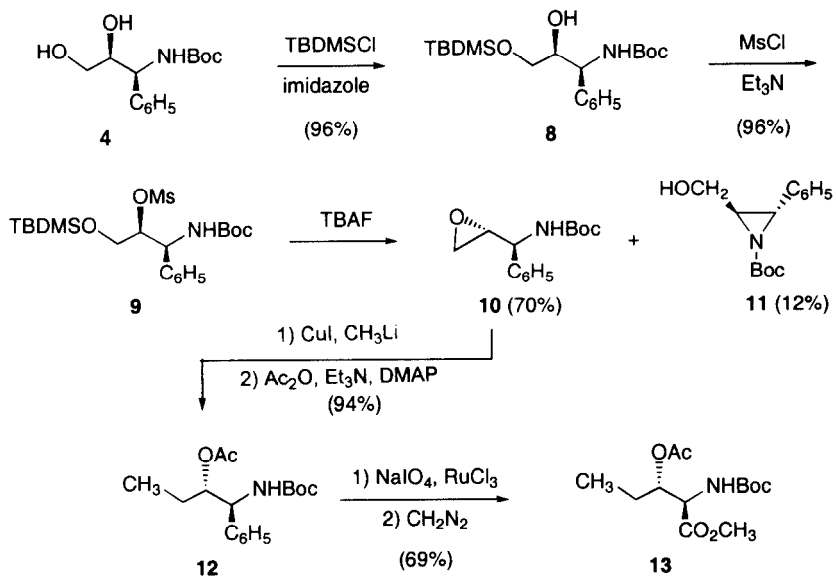
Oxirane **5**, of *S* configuration on the stereogenic carbon of the epoxy moiety, was obtained in 92% yield by treatment of *N*-Boc amino diol **4** with triphenylphosphine and diethyl azodicarboxylate. Subsequent treatment of this compound with lithium methylcuprate cleanly led to the regioselective nucleophilic ring opening to afford (1*S*,2*R*)-*N*-*tert*-butoxycarbonyl-1-phenyl-2-hydroxybutylamine, which was acetylated in 88% overall yield (two steps). Finally, as shown in Scheme 2, treatment of compound **6** with an excess of sodium periodate in the presence of ruthenium trichloride, followed by esterification of the resulting carboxylic acid by the action of diazomethane, cleanly afforded the desired methyl (2*R*,3*R*)-2-*tert*-butoxycarbonylamino-3-acetyloxypentanoate in 29% overall yield from imine **1**.



Scheme 2

The 1*S*,2*R* absolute configuration of compound **6** was unambiguously established by X-ray analysis and provided additional confirmation of the stereochemical course of the oxirane ring opening by the action of the organometallic reagent.

Our synthetic strategy for the (2*R*,3*S*)-diastereoisomer relies on the possibility of performing an inversion of configuration at the stereogenic carbon of the epoxy moiety during its synthesis. With this aim in mind, the primary alcohol in compound **4** was selectively protected in 96% yield by treatment with *tert*-butyldimethylsilyl chloride/imidazole in DMF, which allowed the mesylation of the secondary hydroxyl moiety by the action of methanesulfonyl chloride in a basic medium. Subsequent treatment of compound **9** with TBAF in THF led to the corresponding alcohol, which immediately cyclised *in situ* to afford the desired epoxide **10**, of opposite configuration at the stereogenic center, in 70% yield. A small amount of aziridine **11** (12%), probably produced by intramolecular nucleophilic attack of the nitrogen atom present in the molecule was also isolated. The addition of lithium methylcuprate to compound **10** occurred regioselectively to give (1*S*,2*S*)-*N*-*tert*-butoxycarbonyl-1-phenyl-2-hydroxybutylamine, which was acetylated to afford compound **12** in 94% overall yield (two steps). In the final steps, oxidative cleavage of the phenyl ring was performed by treatment with excess sodium periodate in the presence of ruthenium trichloride to afford the carboxylic acid. Esterification of this compound with diazomethane led to the methyl 2-*tert*-butoxycarbonylamino-3-acetyloxypentanoate of 2*R*,3*S* configuration in 23% overall yield from imine **1** according to Scheme 3.

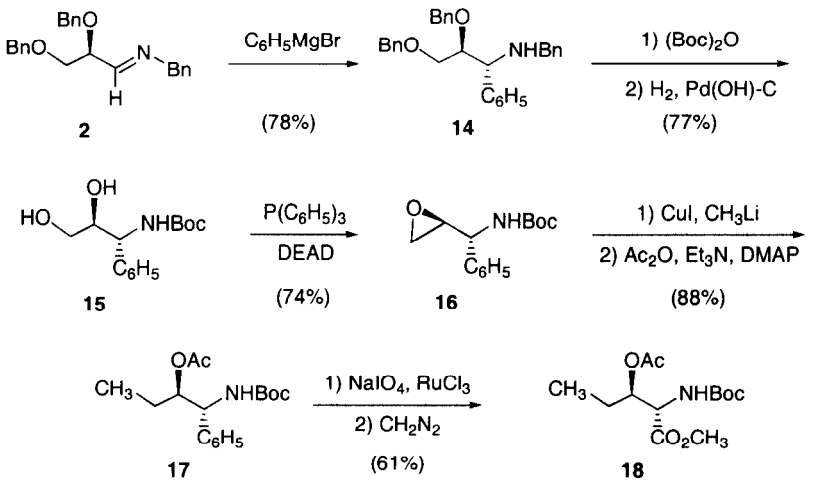


Scheme 3

Synthesis of fully protected (2S,3R)- and (2S,3S)-2-amino-3-hydroxypentanoic acid.

Addition of phenylmagnesium bromide to the *N*-benzylimine derived from 2,3-di-*O*-benzyl-D-glyceraldehyde gave the corresponding amine **14** of 1*R*,2*S* configuration from which (2*S*,3*R*)-3-*tert*-butoxycarbonylamino-3-phenyl-1,2-propanediol (**15**) was prepared by treatment with di-*tert*-butyldicarbonate followed by hydrogenolysis in the presence of palladium hydroxide, as previously described [16]. This compound was the starting material for the stereodivergent synthesis of fully protected (2*S*,3*R*)- and (2*S*,3*S*)-2-amino-3-hydroxypentanoic acid.

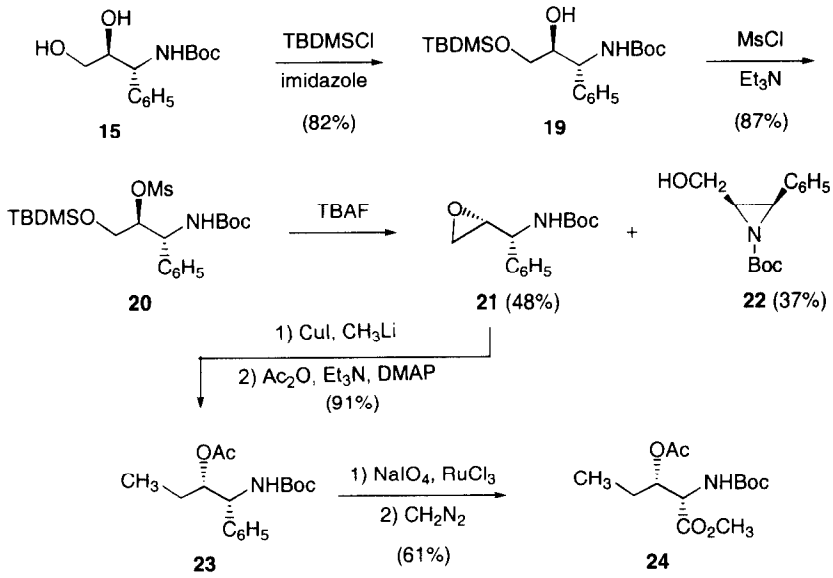
Treatment of *N*-Boc amino diol **15** with triphenylphosphine and diethyl azodicarboxylate afforded oxirane **16**, of *S* configuration at the stereogenic carbon of the epoxy moiety, in 74% yield together with a little of the corresponding aziridine. The presence of the aziridine was not problematic since it could be removed easily by chromatography. Application of the reaction sequence described above to epoxide **16** provided the desired enantiomerically pure methyl (2*S*,3*R*)-2-*tert*-butoxycarbonylamino-3-acetyloxypentanoate in 24% overall yield from imine **2** (Scheme 4).



Scheme 4

Application of a synthetic strategy similar to that described above to aminodiol **15**, in order to perform an inversion of configuration at the stereogenic carbon of the epoxy moiety, allowed the synthesis of the (1*R*,2*R*)-2,3-epoxypropylamine **21**. This compound was necessary for the synthesis of the 2*S*,3*S* diastereomer of methyl (2*S*,3*S*)-2-*tert*-butoxycarbonylamino-3-acetyloxypentanoate. Thus the primary alcohol in compound **15** was converted into its *tert*-butyldimethylsilylether before mesylation of the secondary hydroxyl moiety. Subsequent hydrolysis of the *tert*- butyldimethylsilylether moiety gave rise to immediate cyclisation to the epoxide together with a substantial amount of undesired aziridine. The isolated epoxide **21** was

transformed into the desired methyl (2*S*,3*S*)-2-*tert*-butoxycarbonylamino-3-acetyloxypentanoate by following the same reaction sequence as described above for the other diastereoisomers. In this case the overall yield from imine **2** was only 11% (Scheme 5).



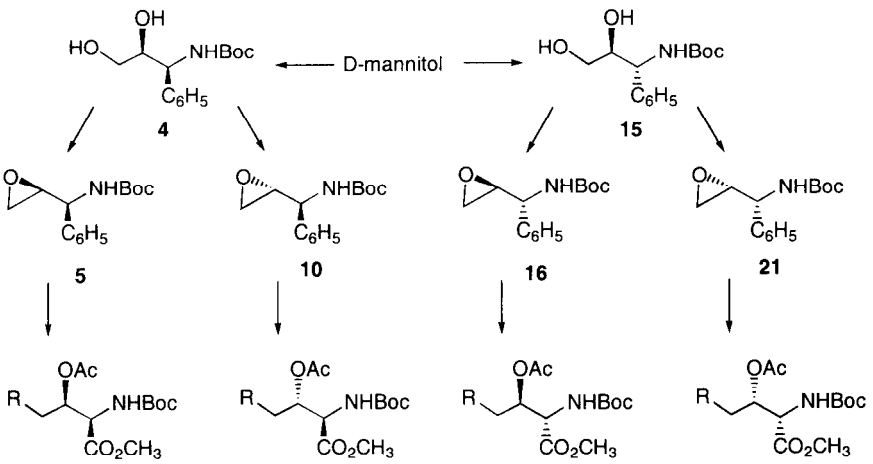
Scheme 5

At this stage the optical purity of the four stereoisomers of methyl 2-*tert*-butoxycarbonylamino-3-acetyloxypentanoate was confirmed by Eu(hfc)$_3$ ^{1}H NMR. On addition of 0.2 equiv of lanthanide shift reagent, a sufficient amount to cause splitting in a racemic mixture, only one set of signals corresponding to a single enantiomer was observed in each case. Accordingly, an optical putity of >98% for compounds **7**, **13**, **18** and **24** was found, demonstrating that essentially no racemization had occurred during the reactions of imines **1** and **2** at the beginning of the synthesis.

Conclusion

In summary, we have designed a versatile, stereodivergent methodology that allows the synthesis of enantiomerically pure *erythro* and *threo* α-amino β-hydroxy acids of any absolute configuration from *N*-benzylimines derived from conveniently protected (*R*)-glyceraldehyde, which is readily available from D-mannitol. Starting from 2,3-diisopropylidene-D-glyceraldehyde or 2,3-di-*O*-benzyl-D-glyceraldehyde, (2*S*,3*S*)-3-*tert*-butoxycarbonylamino-3-phenyl-1,2-propanediol (**4**) or (2*S*,3*R*)-3-*tert*-butoxycarbonylamino-3-phenyl-1,2-propanediol (**15**) are obtained upon addition of phenylmagnesium bromide to the corresponding *N*-benzylimines followed by removal of the *O*-protecting groups. From **4** and **15**, oxiranes of *S* or

R configuration at the ring are obtained by choosing the appropriate synthetic route. Finally, regioselective ring opening of the oxirane with an organometallic reagent provides α-amino-β-hydroxyacid precursors of any of the four possible stereochemistries, in enantiomerically pure form (Scheme 6). The synthesis of the four stereoisomers of fully protected 2-amino-3-hydroxypentanoic acid by application of this synthetic strategy gives grounds to believe that this methodology can be applied to the synthesis of a wide variety of α-amino-β-hydroxyacids from a single and easily available starting material.



Scheme 6

Experimental

Methods and Materials. Melting points were determined using a Büchi capillary melting point apparatus and are not corrected. Infrared spectra were recorded on a Perkin-Elmer 1600FT spectrophotometer as neat liquids or as nujol dispersions, and prominent peaks are expressed in cm^{-1}. NMR spectra were recorded on Varian Unity-300 or Bruker ARX-300 instruments operating at 300 MHz for ^1H NMR and at 75 MHz for ^{13}C NMR. The chemical shifts (δ) are reported in parts per million and the coupling constants (*J*) in Hertz. The following abbreviations are used: s, singlet; d, doublet; t, triplet; m, multiplet; bs, broad signal; bd, broad doublet; dd, doublet of doublets, ddd, doublet of doublet of doublets. The ^1H-NMR and ^{13}C-NMR spectra of *N*-Boc protected compounds were not conclusive at room temperature due to the presence of a dynamic equilibrium between rotamers caused by the restricted rotation of the nitrogen–carbon bond of the urethane group. In order to overcome this problem NMR spectra of these compounds were acquired at 333 K. Optical rotations were measured on a Perkin-Elmer 241-C polarimeter at 25 °C with concentrations given in g/100 mL. Elemental analyses were performed using a Perkin-Elmer 200 C,H,N,S elemental analyser. Electron impact mass spectra were obtained on a high resolution VG-autospec spectrometer.

Chemicals. All reactions were carried out in dry solvents. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. Diethyl ether was distilled from $LiAlH_4$. Chloroform and methylene chloride were distilled from P_2O_5. Dimethylformamide was dried for 2 days with 3A molecular sieves. Whenever possible the reactions were monitored by TLC. TLC was performed on precoated silica gel polyester plates and products were visualised using UV light (254 nm) and anisaldehyde/sulphuric acid/ethanol (2:1:100). Column chromatography was performed using silica gel (Kiesegel 60). Chemicals for reactions and the lanthanide shift reagent were used as purchased from The Aldrich Chemical Co. Ethereal solutions of diazomethane were generated from *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine. **CAUTION**, diazomethane is a very harmful and hazardous reagent and must be handled with caution. Compounds **1**, **2**, **3**, **4**, **14** and **15** were synthesized according to our previously described procedures [16].

(1S,2S)-N-tert-Butoxycarbonyl-1-phenyl-2,3-epoxy-1-propylamine **(5).**
A solution of triphenylphosphine (172 mg, 0.66 mmol), diethyl azodicarboxylate (115 mg, 0.66 mmol) and compound **4** (167 mg, 0.62 mmol) in dry chloroform (10 mL) was stirred overnight under reflux. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on a silica gel column. Elution with ether/hexanes (2:3) gave 143 mg (92% yield) of the title compound **5** as a white solid. M.p. 90 °C (lit. [17] m.p. 90–91 °C); $[\alpha]^{25}_D$ = +22.9 (*c* 1, $CHCl_3$) {lit. [17] $[\alpha]^{23}_D$ = +22.4 (*c*2.74, $CHCl_3$)}; IR (nujol) 3372, 1685 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.40 (s, 9H), 2.48 (dd, 1H, *J* = 5.1 Hz, *J* = 2.7 Hz), 2.75 (dd, 1H, *J* = 5.1 Hz, *J* = 3.9 Hz), 3.25 (ddd, 1H, *J* = 5.1 Hz, *J* = 3.9 Hz, *J* = 2.7 Hz), 4.71 (bs, 1H), 5.02 (bs, 1H), 7.25–7.35 (m, 5H); ^{13}C NMR (75 MHz,$CDCl_3$) δ 28.3, 45.8, 53.8, 55.4, 80.0, 127.1, 127.9, 128.6, 138.0, 155.1; Anal. Calcd. for $C_{14}H_{19}NO_3$: C, 67.45; H, 7.68; N, 5.62. Found: C, 67.52; H, 7.59; N, 5.26.

(1S,2R)-N-tert-Butoxycarbonyl-1-phenyl-2-acetyloxy-1-butylamine **(6).**
A 1.6M solution of methyllithium in ether (6.52 mL, 10.44 mmol) was added dropwise to a suspension of CuI (994 mg, 5.22 mmol) in dry ether (30 mL) at –35 °C under argon. After being stirred for 30 min at –35 °C a solution of compound **5** (260 mg, 1.04 mmol) in dry ether (2 mL) was added and the mixture was stirred for additional 1 h at the same temperature. The reaction mixture was diluted with ethyl acetate (20 mL) and carefully quenched at –35 °C with saturated NH_4Cl (15 mL). After the addition of water (10 mL) the reaction mixture was allowed to warm up to room temperature with vigorous stirring, the organic layer was separated and the aqueous layer extracted with ethyl acetate (3 × 15 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*, and the residue purified by filtration through silica gel (ether/hexanes 3:2). A solution of the obtained amino alcohol (256 mg, 0.96 mmol), triethylamine (117 mg, 1.15 mmol), dimethylaminopyridine (10 mg, 0.08 mmol) and acetic anhydride (108 mg, 1.06 mmol) in dry methylene chloride (15 mL) was stirred at room temperature for 30 min under argon. The reaction mixture was treated with ether (30 mL) and washed with 1M aqueous $KHSO_4$ (20 mL). The organic layer was collected, the

aqueous layer extracted with ether (3 × 15 mL) and the combined organic layers were dried over anhydrous $MgSO_4$, filtered, concentrated *in vacuo*, and the residue purified by flash chromatography on silica gel. Elution with ether/hexanes (1:2) gave 282 mg (88% overall yield) of the title compound **6** as a white solid. M.p. 145 °C; $[\alpha]^{25}_D$ = +53.2 (*c* 1, $CHCl_3$); IR (nujol) 3374, 1725, 1683 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, 3H, *J* = 7.5 Hz), 1.39 (s, 9H), 1.45–1.60 (m, 2H), 1.95 (s, 3H), 4.84 (dd, 1H, *J* = 8.7 Hz, *J* = 5.1 Hz), 5.04 (bs, 1H), 5.07, (ddd, 1H, *J* = 7.8 Hz, *J* = 5.1 Hz, *J* = 5.1 Hz), 7.20–7.35 (m, 5H); ^{13}C NMR (75 MHz,$CDCl_3$) δ 9.7, 20.6, 23.6, 28.2, 57.2, 76.4, 79.6, 127.3, 127.4, 128.6 138.8, 155.0, 170.4; Anal. Calcd. for $C_{17}H_{25}NO_4$: C, 66.43; H, 8.20; N, 4.56. Found: C, 66.38; H, 8.28; N, 4.50.

Methyl (2R,3R)-2-tert-butoxycarbonylamino-3-acetyloxypentanoate **(7).**
A solution of compound **6** (160 mg, 0.52 mmol) in a mixture of ethyl acetate/acetonitrile/water (1:1:8) (10 mL) was treated with $NaIO_4$ (3.2 mg, 15 mmol) and $RuCl_3.H_2O$ (6.2 mg, 0.03 mmol). On completion of the addition the mixture was vigorously stirred at room temperature for 24 h and then extracted with ether (3 × 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The resulting residue was dissolved in ether and extracted with saturated aqueous $NaHCO_3$. The aqueous layer was carefully acidified at 0 °C with 1M aqueous $KHSO_4$ and then extracted with ether (3 × 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The crude acid was dissolved in ether (10 mL) and a solution of diazomethane in ether was added dropwise until the yellow colour of the diazomethane solution persisted during several minutes. The solution was then concentrated *in vacuo* and the residue purified by flash chromatography on silica gel. Elution with ether/hexanes (1:1) gave 95 mg (63% overall yield) of the title compound **7** as an oil. $[\alpha]^{25}_D$ = –3.9 (*c* 0.86, $CHCl_3$); IR (neat) 3378, 1747, 1718 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.92 (t, 3H, *J* = 7.5 Hz), 1.42 (s, 9H), 1.54–1.73 (m, 2H), 2.02 (s, 3H), 3.74 (s, 3H), 4.54 (dd, 1H, *J* = 8.4 Hz, *J* = 3.3 Hz), 4.97, (ddd, 1H, *J* = 8.7 Hz, *J* = 5.1 Hz, *J* = 3.3 Hz), 5.20 (bs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.7, 20.7, 23.7, 28.3, 52.2, 56.2, 75.5, 80.2, 155.1, 170.1, 170.5; HRMS(EI) Calcd. for $C_8H_{14}O_6$ (M^+ – $NCO_2{}^tBu$): 174.0892. Found: 174.0897.

(2S,3S)-3-tert-Butoxycarbonylamino-1-tert-butyldimethylsilyloxy-3-phenyl-2-propanol **(8).**
A solution of compound **4** (500 mg, 1.87 mmol), *tert*-butyldimethylsilylchloride (311 mg, 2.06 mmol) and imidazole (279 mg, 4.10 mmol) in dry dimethylformamide (10 mL) was stirred at room temperature for 24 h. The mixture was diluted with ether (40 mL) and washed with saturated aqueous NH_4Cl (20 mL). The organic layer was treated with water, the organic layer separated and the aqueous layer extracted with ether (3 × 15 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was purified by flash chromatography on a silica gel column. Elution first with ether/hexanes (1:5) and then with ether/hexanes (1:1) gave 681 mg (96% yield) of the title compound **8** as a white solid. M.p. 44 °C (lit. [18] m.p. 43.5–45.5 °C); $[\alpha]^{25}_D$ = +26.1 (*c* 1, $CHCl_3$) {lit. [18] $[\alpha]^{23}_D$ =

+25.9 (*c* 0.21, $CHCl_3$)}; IR (nujol) 3411, 1697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.03 (s, 3H), 0.05 (s, 3H), 0.91 (s, 9H), 1.38 (s, 9H), 2.43 (d, 1H, *J* = 6.6 Hz), 3.44 (dd, 1H, *J* = 10.5 Hz, *J* = 4.8 Hz), 3.56 (dd, 1H, *J* = 10.5 Hz, *J* = 4.2 Hz), 3.82–3.90 (m, 1H), 4.80 (dd, 1H, *J* = 8.4 Hz, *J* = 5.1 Hz), 5.77 (bs, 1H), 7.15–7.35 (m, 5H); ^{13}C NMR (75 MHz,$CDCl_3$) δ –5.6, –5.5, 18.2, 25.9, 28.4, 58.3, 64.3, 73.3, 79.5, 127.2, 127.4, 128.5, 139.7, 155.6; Anal. Calcd. for $C_{20}H_{35}NO_4Si$: C, 62.95; H, 9.25; N, 3.67. Found: C, 62.82; H, 9.11; N, 3.71.

(1S,2S)-N-tert-Butoxycarbonylamino-3-tert-butyldimethylsilyloxy-2-mesyloxy-1-phenyl-1-propylamine **(9).**

A solution of methanesulfonyl chloride (233 mg, 2.03 mmol) in dry methylene chloride (1.5 mL) was added dropwise to a solution of compound **8** (646 mg, 1.70 mmol) and triethylamine (205 mg, 2.03 mmol) in dry methylene chloride (15 mL) at 0 °C under argon. The solution was allowed to warm up to room temperature and, after stirring for 45 min, the reaction mixture was partitioned between water (10 mL) and methylene chloride (10 mL). The organic layer was separated and the aqueous layer extracted with ether (3 × 30 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash chromatography on a silica gel column. Elution with ether/hexanes (1:1) gave 750 mg (96% yield) of the title compound **9** as an oil. $[\alpha]^{25}_D$ = +10.1 (*c* 0.95, $CHCl_3$) {lit. for the enantiomer [19] $[\alpha]_D$ = –9.6 (*c* 2.0, $CHCl_3$)}; IR (neat) 3407, 1712 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.05 (s, 3H), 0.07 (s, 3H), 0.92 (s, 9H), 1.41 (s, 9H), 2.96 (s, 3H), 3.64 (dd, 1H, *J* = 11.7 Hz, *J* = 4.5 Hz), 3.72 (dd, 1H, *J* = 11.7 Hz, *J* = 4.2 Hz), 4.84–4.90 (m, 1H), 5.07 (dd, 1H , *J* = 8.1 Hz, *J* = 4.5 Hz), 5.91 (bs, 1H), 7.31 (s, 5H); ^{13}C NMR (75 MHz,$CDCl_3$) δ –5.8, –5.7, 18.0, 25.7, 28.2, 38.6, 56.4, 62.9, 79.6, 82.0, 127.2, 127.9, 128.5, 137.7, 155.2.

(1S,2R)-N-tert-Butoxycarbonyl-1-phenyl-2,3-epoxy-1-propylamine **(10).**

A 1M solution of tetrabutylammonium fluoride in THF (3.18 mL, 3.18 mmol) was added dropwise to a solution of compound **9** (730 mg, 1.59 mmol) in dry THF (15 mL) at 0 °C. The solution was then warmed up to room temperature and stirred overnight. The reaction mixture was partitioned between water (7.5 mL) and ether (7.5 mL). The organic layer was separated and the aqueous layer extracted with ether (3 × 25 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash chromatography on a silica gel column. Elution first with ether/hexanes (1:6) and then with ether/hexanes (1:3) gave 276 mg (70% yield) of the title compound **10** as a white solid [further elution with ether/hexanes (2:1) allowed the isolation of aziridine **11**]. M.p. 80 °C; $[\alpha]^{25}_D$ = +101.5 (*c* 1, $CHCl_3$); IR (nujol) 3362, 1675 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.40 (s, 9H), 2.68 (dd, 1H, *J* = 4.8 Hz, *J* = 2.7 Hz), 2.76 (dd, 1H, *J* = 4.8 Hz, *J* = 3.9 Hz), 3.25 (ddd, 1H, *J* = 5.1 Hz, *J* = 3.9 Hz, *J* = 2.7 Hz), 4.80–4.92 (m, 2H), 7.28–7.40 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.2, 44.1, 53.7, 53.8, 79.7, 126.9, 127.7, 128.7, 140.2, 155.2; Anal. Calcd. for $C_{14}H_{19}NO_3$: C, 67.45; H, 7.68; N, 5.62. Found: C, 67.38; H, 7.55; N, 5.66.

(1S,2S)-N-tert-Butoxycarbonyl-1-phenyl-2-acetyloxy-1-butylamine **(12).**
From 234 mg (0.94 mmol) of *(1S,2R)-N-tert*-butoxycarbonyl-1-phenyl-2,3-epoxy-1-propylamine (**10**), 270 mg (94% overall yield) of the title compound **12** were obtained as a white solid according to the experimental procedure described above for compound **6**. M.p. 48 °C; $[\alpha]^{25}_{D}$ = +18.1 (*c* 1.11, $CHCl_3$); IR (nujol) 3353, 1712 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, 3H, *J* = 7.5 Hz), 1.40 (s, 9H), 1.50–1.60 (m, 2H), 1.97 (s, 3H), 4.78 (dd, 1H, *J* = 9.3 Hz, *J* = 5.7 Hz), 5.03–5.10 (m, 1H), 5.09 (bs, 1H), 7.18–7.33 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.7, 20.7, 24.8, 28.4, 57.2, 77.5, 79.7, 126.7, 127.6, 128.6 140.2, 155.4, 170.6; Anal. Calcd. for $C_{17}H_{25}NO_4$: C, 66.43; H, 8.20; N, 4.56. Found: C, 66.54; H, 8.11; N, 4.49.

Methyl (2R,3S)-2-tert-butoxycarbonylamino-3-acetyloxypentanoate **(13).**
From 240 mg (0.78 mmol) of *(1S,2S)-N-tert*-butoxycarbonyl-1-phenyl-2-acetyloxy-1-butylamine (**12**), 155 mg (69% overall yield) of the title compound **13** were obtained as a white solid according to the experimental procedure described above for compound **7**. M.p. 97 °C; $[\alpha]^{25}_{D}$ = –60.0 (*c* 0.80, $CHCl_3$); IR (nujol) 3390, 1741, 1710 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.93 (t, 3H, *J* = 7.2 Hz), 1.44 (s, 9H), 1.58–1.70 (m, 2H), 1.99 (s, 3H), 3.69 (s, 3H), 4.43 (bd, 1H, *J* = 9.3 Hz), 5.05 (bs, 1H), 5.18, (ddd, 1H, *J* = 7.2 Hz, *J* = 7.2 Hz, *J* = 2.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.6, 20.6, 24.4, 28.3, 52.3, 55.8, 75.1, 80.3, 155.7, 169.8, 171.0; Anal. Calcd. for $C_{13}H_{23}NO_6$: C, 53.97; H, 8.01; N, 4.84. Found: C, 53.85; H, 8.12; N, 4.93.

(1R,2S)-N-tert-Butoxycarbonyl-1-phenyl-2,3-epoxy-1-propylamine **(16).**
From 255 mg (0.95 mmol) of *(2S,3R)-3-tert*-butoxycarbonylamino-3-phenyl-1,2-propanediol (**15**), 175 mg (74% yield) of the title compound **16** were obtained as a white solid according to the experimental procedure described above for compound **5**. M.p. 80 °C; $[\alpha]^{25}_{D}$ = –101.5 (*c* 1, $CHCl_3$); IR (nujol) 3362, 1675 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.40 (s, 9H), 2.68 (dd, 1H, *J* = 4.8 Hz, *J* = 2.7 Hz), 2.76 (dd, 1H, *J* = 4.8 Hz, *J* = 3.9 Hz), 3.23 (ddd, 1H, *J* = 5.1 Hz, *J* = 3.9 Hz, *J* = 2.7 Hz), 4.80–4.92 (m, 2H), 7.28–7.40 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.4, 44.2, 53.9, 54.0, 79.9, 127.0, 127.9, 128.8, 140.4, 155.4; Anal. Calcd. for $C_{14}H_{19}NO_3$: C, 67.45; H, 7.68; N, 5.62. Found: C, 67.53; H, 7.78; N, 5.54.

(1R,2R)-N-tert-Butoxycarbonyl-1-phenyl-2-acetyloxy-1-butylamine **(17).**
From 143 mg (0.57 mmol) of *(1R,2S)-N-tert*-butoxycarbonyl-1-phenyl-2,3-epoxy-1-propylamine (**16**), 155 mg (88% overall yield) of the title compound **17** were obtained as a white solid according to the experimental procedure described above for compound **6**. M.p. 48 °C; $[\alpha]^{25}_{D}$ = –18.3 (*c* 1, $CHCl_3$); IR (nujol) 3353, 1712 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, 3H, *J* = 7.5 Hz), 1.40 (s, 9H), 1.50–1.60 (m, 2H), 1.97 (s, 3H), 4.78 (dd, 1H, *J* = 9.3 Hz, *J* = 5.7 Hz), 5.03–5.10 (m, 1H), 5.09, (bs, 1H), 7.18–7.33 (m, 5H); ^{13}C NMR (75 MHz,$CDCl_3$) δ 9.7, 20.7, 24.8, 28.4, 57.3, 77.5, 79.7, 126.8, 127.6, 128.6 140.2, 155.4, 170.6; Anal. Calcd. for $C_{17}H_{25}NO_4$: C, 66.43; H, 8.20; N, 4.56. Found: C, 66.37; H, 8.23; N, 4.63.

Methyl (2S,3R)-2-tert-butoxycarbonylamino-3-acetyloxypentanoate **(18).**
From 144 mg (0.47 mmol) of *(1R,2R)-N-tert*-butoxycarbonyl-1-phenyl-2-acetyloxy-1-butylamine (**17**), 82 mg (61% overall yield) of the title compound **18** were obtained as a white solid according to the experimental procedure described above for compound **7**. M.p. 97 °C; $[\alpha]^{25}_{D}$ = +59.7 (*c* 0.81, $CHCl_3$); IR (nujol) 3390, 1741, 1710 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.93 (t, 3H, *J* = 7.2 Hz), 1.44 (s, 9H), 1.58–1.70 (m, 2H), 1.99 (s, 3H), 3.70 (s, 3H), 4.43 (bd, 1H, *J* = 9.3 Hz), 5.05 (bs, 1H), 5.18 (ddd, 1H, *J* = 7.2 Hz, *J* = 7.2 Hz, *J* = 2.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.6, 20.6, 24.4, 28.3, 52.3, 55.7, 75.1, 80.3, 155.7, 169.8. 171.0; Anal. Calcd. for $C_{13}H_{23}NO_6$: C, 53.97; H, 8.01; N, 4.84. Found: C, 54.07; H, 8.09; N, 4.76.

(2S,3R)-3-tert-Butoxycarbonylamino-1-tert-butyldimethylsilyloxy-3-phenyl-2-propanol **(19).**
From 500 mg (1.87 mmol) of *(2S,3R)-3-tert*-butoxycarbonylamino-3-phenyl-1,2-propanediol (**15**), 585 mg (82% yield) of the title compound **19** were obtained as an oil according to the experimental procedure described above for compound **8**. $[\alpha]^{25}_{D}$ = –13.2 (*c* 1, $CHCl_3$); IR (neat) 3434, 1693 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.07 (s, 6H), 0.91 (s, 9H), 1.39 (s, 9H), 2.36 (d, 1H, *J* = 3.9 Hz), 3.54 (dd, 1H, *J* = 10.2 Hz, *J* = 6.9 Hz), 3.66 (dd, 1H, *J* = 10.2 Hz, *J* = 4.8 Hz), 3.83–3.90 (m, 1H), 4.67 (dd, 1H, *J* = 8.1 Hz, *J* = 3.9 Hz), 5.77 (bs, 1H), 7.15–7.35 (m, 5H); ^{13}C NMR (75 MHz,$CDCl_3$) δ – 5.5, – 5.4, 18.3, 25.9, 28.4, 58.2, 64.6, 74.7, 79.5, 126.8, 127.4, 128.5, 141.2, 155.8; HRMS(EI) Calcd. for $C_{20}H_{35}NO_4Si$ (M^+): 381.2335. Found: 381.2336.

(1R,2S)-N-tert-Butoxycarbonylamino-3-tert-butyldimethylsilyloxy-2-mesyloxy-1-phenyl-1-propylamine **(20).**
From 495 mg (1.30 mmol) of *(2S,3R)-3-tert*-butoxycarbonylamino-1-*tert*-butyldimethylsilyloxy-3-phenyl-2-propanol (**19**), 520 mg (87% yield) of the title compound **20** were obtained as an oil according to the experimental procedure described above for compound **9**. $[\alpha]^{25}_{D}$ = –10.5 (*c* 1, $CHCl_3$); IR (neat) 3384, 1712 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.06 (s, 3H), 0.07 (s, 3H), 0.92 (s, 9H), 1.41 (s, 9H), 2.63 (s, 3H), 3.74–3.84 (m, 2H), 4.73–4.78 (m, 1H), 5.08 (dd, 1H , *J* = 9.0 Hz, *J* = 4.5 Hz), 5.29 (bs, 1H), 7.30–7.50 (s, 5H); ^{13}C NMR (75 MHz,$CDCl_3$) δ –5.6, –5.5, 18.3, 25.9, 28.4, 38.1, 55.8, 62.6, 80.0, 84.9, 126.8, 128.0, 128.8, 139.4, 155.1.

(1R,2R)-N-tert-Butoxycarbonyl-1-phenyl-2,3-epoxy-1-propylamine **(21).**
From 501 mg (1.09 mmol) of *(1R,2S)-N-tert*-butoxycarbonylamino-3-*tert*-butyldimethylsilyloxy-2-mesyloxy-1-phenyl-1-propylamine (**20**), 130 mg (48% yield) of the title compound **21** were obtained as an oil according to the experimental procedure described above for compound **10**. M.p. 89 °C; $[\alpha]^{25}_{D}$ = –23.0 (*c* 1, $CHCl_3$); IR (nujol) 3372, 1685 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.42 (s, 9H), 2.49 (dd, 1H, *J* = 5.1 Hz, *J* = 2.7 Hz), 2.72 (dd, 1H, *J* = 5.1 Hz, *J* = 3.9 Hz), 3.22 (ddd, 1H, *J* = 5.1 Hz, *J* = 3.9 Hz, *J* = 2.7 Hz), 4.69 (dd, 1H, *J* = 8.1 Hz, *J* = 5.1 Hz), 4.89 (bs, 1H), 7.25–7.35 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.4, 45.7,

53.9, 55.9, 80.0, 127.1, 128.0, 128.6, 138.5, 155.2; Anal. Calcd. for $C_{14}H_{19}NO_3$: C, 67.45; H, 7.68; N, 5.62. Found: C, 67.39; H, 7.71; N, 5.71.

(1R,2S)-N-tert-Butoxycarbonyl-1-phenyl-2-acetyloxy-1-butylamine **(23).**
From 152 mg (0.61 mmol) of *(1R,2R)-N-tert*-butoxycarbonyl-1-phenyl-2,3-epoxy-1-propylamine (**21**), 170 mg (91% overall yield) of the title compound **23** were obtained as a white solid according to the experimental procedure described above for compound **6**. M.p. 143 °C; $[\alpha]^{25}_D = -52.7$ (*c* 1, $CHCl_3$); IR (nujol) 3374, 1725, 1683 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, 3H, *J* = 7.5 Hz), 1.39 (s, 9H), 1.42–1.60 (m, 2H), 1.95 (s, 3H), 4.84 (dd, 1H, *J* = 8.4 Hz, *J* = 5.1 Hz), 5.03 (bs, 1H), 5.06, (ddd, 1H, *J* = 7.8 Hz, *J* = 5.1 Hz, *J* = 5.1 Hz), 7.20–7.35 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.8, 20.8, 23.8, 28.4, 57.4, 79.8, 127.5, 128.4 140.0, 155.2, 170.6; Anal. Calcd. for $C_{17}H_{25}NO_4$: C, 66.43; H, 8.20; N, 4.56. Found: C, 66.56; H, 8.13; N, 4.62.

Methyl (2S,3S)-2-tert-butoxycarbonylamino-3-acetyloxypentanoate **(24).**
From 150 mg (0.49 mmol) of *(1R,2S)-N-tert*-butoxycarbonyl-1-phenyl-2-acetyloxy-1-butylamine (**23**), 86 mg (61% overall yield) of the title compound **24** were obtained as an oil according to the experimental procedure described above for compound **7**. $[\alpha]^{25}_D = +3.6$ (*c* 0.60, $CHCl_3$); IR (neat) 3373, 1743 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.92 (t, 3H, *J* = 7.5 Hz), 1.42 (s, 9H), 1.54–1.73 (m, 2H), 2.01 (s, 3H), 3.73 (s, 3H), 4.54 (dd, 1H, *J* = 8.4 Hz, *J* = 3.3 Hz), 4.98 (ddd, 1H, *J* = 8.7 Hz, *J* = 5.1 Hz, *J* = 3.3 Hz), 5.18 (bs, 1H); ^{13}C NMR (75 MHz,$CDCl_3$) δ 9.8, 20.7, 23.7, 28.3, 52.2, 56.2, 75.5, 80.2, 155.1, 170.1, 170.5.

Single crystal X-ray diffraction analysis of **6.**
Crystallographic measurement was carried out at ambient temperature on a 4-circle Siemens P4 diffractometer using graphite monochromated molybdenum *K*α X-radiation (λ = 0.71069 Å). One equivalent set of data was collected in the range $4°<2\theta<45°$ using ω/2θ scans. No significant variation was observed in the intensity of the three standard reflections. Lorentz and polarisation corrections were applied to the data-set. The structure was solved by direct methods using SIR92 [20] and was refined by full-matrix least squares (based on F^2) using SHELXL-97 [21] which used all data for refinement. The weighting scheme was $\omega = [\sigma^2 (F_O{}^2) + (0.0927P)^2 + 0.59P]^{-1}$ where $P = (F_O{}^2 + 2F_C{}^2)/3$. All non-hydrogen atoms were refined with anisotropic thermal parameters. All hydrogen atoms were constrained to predicted positions.
$C_{17}H_{25}NO_4$, 0.52 x 0.28 x 0.20 mm, M_t = 1229.52, orthorhombic, space group $P2_12_12_1$ *a* = 5.362(5), *b* = 10.855(5), c = 31.021(5) Å, *V* = 1805.6(19) $Å^3$, *Z* = 4, ρ_{calc} = 1.131 g cm^{-3}, *F*(000) = 664.0, μ = 0.8 cm^{-1}. 2390 independent reflections measured at 293 K. Final *R* = 0.1504, ω*R* = 0.2107 for all data, *R* = 0.0699, ω*R* = 0.1617 for 1214 observed reflections with $F0 > 4\sigma F0$.

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References

[1] (a) '*Amino Acids, Peptides and Proteins*' Specialist Periodical Reports, Chem. Soc., London 1968-1995; Vol 1-28. (b) See ref 2 in Blaskovich, M. A.; Evindar, G.; Rose, N. G. W.; Wilkinson, S.; Luo, Y.; Lajoie, G. A. *J. Org. Chem.* **1998**, *63*, 3631-3646.

[2] (a) Floyd, D. M.; Fritz, A. W.; Pluscec, J.; Weaver, E. R.; Cimarusti, C. M. *J. Org. Chem.* **1982,** *47*, 5160-5167. (b) Labia, R.; Morin, C. *J. Antibiot.* **1984**, *37*, 1103-1129. (c) Miller, M. J. *Acc. Chem. Res.* **1986**, *19*, 49-56. (d) Lotz, B. T.; Miller, M. J. *J. Org. Chem.* **1993,** *58*, 618-625.

[3] Golebiowski, A.; Jurczak, J. *Synlett* **1993**, 241-245.

[4] Cossu, S.; Conti, S.; Giacomelli, G.; Farloni, M. *Synthesis* **1994**, 1429-1432.

[5] Pansare, S. V.; Vederas, J. C. *J. Org. Chem.* **1987,** *52*, 4804-4810

[6] For leading references on the asymmetric synthesis of α-amino β-hydroxy acids by reaction of organometallic reagents with aldehydes see: (a) Roemmele, R. C.; Rapoport, H. *J. Org. Chem.* **1989**, *54*, 1866-1875. (b) Williams, L.; Zhang, Z.; Ding, X.; Joullié, M. M. *Tetrahedron Lett.* **1995**, *36*, 7031-7034. (c) Kumar, J. S. R.; Datta, A. *Tetrahedron Lett.* **1997**, *38*, 473-476. (d) Laïb, T.; Chastanet, J.; Zhu, J. *Tetrahedron Lett.* **1997**, *38*, 1771-1772. (e) Blaskovich, M. A.; Evindar, G.; Rose, N. G. W.; Wilkinson, S.; Luo, Y.; Lajoie, G. A. *J. Org. Chem.* **1998**, *63*, 3631-3646. (f) Veeressa, G.; Datta, A. *Tetrahedron Lett.* **1998**, *39*, 3069-3070.

[7] For leading references on the asymmetric synthesis of α-amino β-hydroxy acids by electrophilic amination see: (a) Guanti, J.; Banfi, L.; Narisano, E. *Tetrahedron* **1988**, *44*, 5553-5562. (b) Girard, A.; Greck, C.; Ferroud, D.; Genêt, J. P. *Tetrahedron Lett.* **1996**, *37*, 7967-7970. (c) Sting, A. R.; Seebach, D. *Tetrahedron* **1996**, *52*, 279-290.

[8] For leading references on the asymmetric synthesis of α-amino β-hydroxy acids by nucleophilic opening of epoxides and azidirines see: (a) Cardani, S.; Bernardi, A.; Colombo, L.; Gennari, C.; Scolastico, C.; Venturini, I. *Tetrahedron* **1988**, *44*, 5563-5572. (b) Jung, M. E.; Jung, Y. H. *Tetrahedron Lett.* **1989**, *30*, 6637-6640. (c) Schmidt, U.; Respondek, M.; Lieberknecht, A.; Werner, J.; Fischer, P. *Synthesis* **1989**, 256-261. (d) Genet, J. P. *Pure Appl. Chem.* **1996**, *68*, 593-596. (e) Pégorier, L.; Haddad, M.; Larchevêque, M. *Synlett* **1996**, 585-586. (f) Righi, G.; Chionne, A.; D'Achille, R.; Bonini, C. *Tetrahedron: Asymmetry* **1997**, *8*, 903-907. (g) Cardillo, G.; Gentilucci, L.; Tolomelli, A.; Tomasini, C.; *J. Org. Chem.* **1998**, *63*, 3458-3462

[9] For leading references on the asymmetric synthesis of α-amino β-hydroxy acids by asymmetric dihydroxylation of α,β-unsaturated carboxylic acids see: (a) Rao, A. V. R.; Chakraborty, T. K.; Reddy,

K. L.; Rao, A. S. *Tetrahedron Lett.* **1994**, *35*, 5043-5046. (b) Hughes, P. F.; Smith, S. H.; Olson, J. T. *J. Org. Chem.* **1994**, *59*, 5799-5802. (c) Shao, H.; Goodman, M. *J. Org. Chem.* **1996**, *61*, 2582-2583.

[10] For leading references on the asymmetric synthesis of α-amino β-hydroxy acids by diastereoselective β-functionalization see: (a) Hanessian, S.; Vanasse, B. *Can. J. Chem.* **1993**, *71*, 1401-1406. (b) Easton, C. J.; Hutton, C. A.; Roselt, P. D.; Tiekink, E. R. T. *Tetrahedron* **1994**, *50*, 7327-7340. (c) Fernández-Megía, E.; Paz, M. M.; Sardina, F. J. *J. Org. Chem.* **1994**, *59*, 7643-7652.

[11] For leading references on the asymmetric synthesis of α-amino β-hydroxy acids by asymmetric aminohydroxylation of α,β-unsaturated carboxylic acids see (a) Li, G.; Chang, H. T.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 451-454. (b) Li, G.; Angert, H. H.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2813-2817. (c) Tao, B.; Schlingloff, G.; Sharpless, K. B. *Tetrahedron Lett.* **1998**, *39*, 2507-2510.

[12] For leading references on the asymmetric synthesis of α-amino β-hydroxy acids by the aldol methodology see: (a) Evans, D. A.; Weber, A. E. *J. Am. Chem. Soc.* **1987**, *109*, 7151-7157. (b) Ito, Y.; Sawamura, M.; Kobayashi, M.; Hayashi, T. *Tetrahedron Lett.* **1988**, *29*, 6321-6324. (c) Casella, L.; Gullotti, M.; Jommi, G.; Pagliarin, R.; Sisti, M. *J. Chem. Soc., Perkin Trans. 2* **1990**, 771-775. (d) Reno, D. S.; Lotz, B. T.; Miller, M. J. *Tetrahedron Lett,* **1990**, *31*, 827-830. (e) Blaser, D.; Seebach, D. *Liebigs Ann. Chem.* **1991**, 1067-1078. (f) Beulshausen, T.; Groth, U.; Schöllkopf, U. *Liebigs Ann. Chem.* **1991**, 1207-1209. (g) van der Werf, A. W.; Kellogg, R. M.; van Bolhuis, F. *J. Chem. Soc., Chem. Commun.* **1991**, 682-683. (h) Belokon, Y. N. *Pure. Appl. Chem.* **1992**, *64*, 1917-1924. (i) Soloshonok, V. A.; Avilov, D. V.; Kukhar, V. P.; Tararov, V. I.; Savel'eva, T. F.; Churkina, T. D.; Ikonnikov, N. S.; Kochetkov, K. A.; Orlova, S. A.; Pysarevsky, A. P.; Struchkov, Y. T.; Raevsky, N. I.; Belokon, Y. N. *Tetrahedron: Asymmetry* **1995**, *6*, 1741-1756. (j) Soloshonok, V. A.; Avilov, D. V.; Kukhar, V. P. *Tetrahedron: Asymmetry* **1996**, *7*, 1547-1550. (k) Ferey, V.; Le Gall, T.; Mioskowski, C. *J. Chem. Soc., Chem. Commun.* **1995**, 487-489. (l) Solladié-Cavallo, A.; Nsenda, T. *Tetrahedron Lett.* **1998**, *39*, 2191-2194. (m) Harwood, L. M.; Robertson, S. M. *Chem. Commun.* **1998**, 2641-2642.

[13] For leading references on the asymmetric synthesis of α-amino β-hydroxy acids by chemo-enzymatic aldol condensation see: (a) Saeed, A.; Young, D. W. *Tetrahedron* **1992**, *48*, 2507-2514. (b) Vassilev, V. P., Uchiyama. T.; Kajimoto, T.; Wong, C. H. *Tetrahedron Lett.* **1995**, *36*, 4081-4084. (c) Kimura, T., Vassilev, V. P.; Shen, G. J.; Wong, C. H. *J. Am. Chem. Soc.* **1997**, *119*, 11734-11742.

[14] For other approaches to the asymmetric synthesis of α-amino β-hydroxy acids see for example (a) Hirama, M.; Hioki, H.; Itô, S. *Tetrahedron Lett,* **1988**, *29*, 3125-3128. (b) Krol, W. J.; Mao, S. S.; Steele, D. L.; Townsend, C. A. *J. Org. Chem,* **1991**, *56*, 728-731. (c) Genet, J. P.; Pinel, C.; Mallart, S.; Juge, S.; Thorimbert, S.; Laffitte, J. A. *Tetrahedron: Asymmetry* **1991**, *2*, 555-567. (d) Zandbergen, P.; Brussee, J.; van der Gen, A.; Kruse, C. G. *Tetrahedron: Asymmetry* **1992**, *3*, 769-774. (e) Blank, S.; Seebach, D. *Liebigs Ann. Chem.* **1991**, 889-896. (f) Jackson, R. F. W.; Palmer, N. J.; Wythes, M. J.; Clegg, W.;

Elsegood, M. R. J. *J. Org. Chem.* **1995**, *60*, 6431-6440. (g) Yadav, J. S.; Chandrasekhar, S.; Reddy, Y. R.; Rao, A. V. R. *Tetrahedron* **1995**, *51*, 2749-2754. (h) Bycroft, M.; Herbert, R. B.; Ellames, G. J. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2439-2440. (i) delle Monache, G.; Di Giovanni, M. C.; Misiti, D.; Zappia, G. *Tetrahedron: Asymmetry* **1997**, *8*, 231-243. (j) Ciufolini, M. A.; Shimizu, T.; Swaminathan, S.; Xi, N. *Tetrahedron Lett.* **1997**, *38*, 4947-4950. (k) Cardillo, G.; Gentilucci, L.; Tolomelli, A.; Tomasini, C. *Tetrahedron Lett.* **1997**, *38*, 6953-6956. (l) Merino, P.; Franco, S.; Merchan, F. L., Tejero, T. *Tetrahedron: Asymmetry* **1997**, *8*, 3489-3496. (m) Fadnavis, N. W.; Sharfuddin, M.; Vadivel, S. K.; Bhalerao, U. T. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3577-3578. (n) Kuwano, R.; Okuda, S.; Ito, Y.; *J. Org. Chem.* **1998**, *63*, 3499-3503. (o) Alker, D.; Hamblett, G., Harwood, L. M.; Robertson, S. M.; Watkin, D. J.; Williams, C. E. *Tetrahedron* **1998**, *54*, 6089-6098.

[15] (a) Hanessian, S. *Total Synthesis of Natural Products: the Chiron Approach;* Pergamon: Oxford 1983. (b) Cintas, P. *Tetrahedron* **1991**, *47*, 6079-6111. (c) Ferrier, R. J.; Middlenton, S. *Chem. Rev.* **1993**, *93*, 2779-2831. (d) Monneret, C.; Florent, J. C. *Synlett* **1994**, 305-318. (e) Collins, P.; Ferrier, R. J. *Monosaccharides. Their Chemistry and their Roles in Natural Products;* Wiley: New York, 1995. (f) Bols, M. *Carbohydrate Building Blocks,* Wiley: New York, 1996.

[16] Badorrey, R.; Cativiela, C.; Díaz de Villegas, M. D.; Gálvez, J. A. *Tetrahedron* **1997**, *53*, 1411-1416.

[17] Castejón, P.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron* **1996**, *52*, 7063-7986.

[18] Pastó, M.; Moyano, A.; Pericàs, M. A.; Riera, A.; *Tetrahedron: Asymmetry* **1996**, *7*, 243-262.

[19] Medina, E.; Moyano, A.; Pericàs, M. A.; Riera, A. *J. Org. Chem.* **1998**, *63*, 8574-8578.

[20] Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Burla, M. C.; Polidori, G.; Camalli, M. *J. Appl. Cryst.* **1994**, *27*, 435-436.

[21] Sheldrick, G. M.; SHELXL-97. Program for the Refinement of Crystal Structures. **1997**. University of Göttingen, Germany.