Manipulating L-Aspartic and L-Glutamic Acids – Diastereoselective Synthesis of Enantiopure β-Amino-γ-hydroxy Acids and γ-Amino-δ-hydroxy Acids

José M. Andrés,^[a] Eva M. Muñoz,^[a] Rafael Pedrosa,*^[a] and Alfonso Pérez-Encabo^[a]

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Enantiopure (3S,4R)- and (3S,4S)-3-amino-4-hydroxyhexanoic acids and (4S,5R)- and (4S,5S)-4-amino-5-hydroxyheptanoic acid derivatives have been prepared by stereodivergent synthesis from L-aspartic and L-glutamic acids, respectively. The stereochemistry at the carbon atom attached to the amino group was determined from the starting material, but

α-Unsubstituted β-amino-γ-hydroxy acids are interesting compounds because they are components of peptides of pharmacological interest,^[1] and biological activity.^[2-5] Additionally, they can be used as enzymatic inhibitors,^[6] and can be transformed into 4-hydroxy-β-lactams,^[7] or β-amino-γ-butyrolactones^[8] which are intermediates to β-amino alcohols,^[9] antibiotic β-lactams,^[10,11] and macrolides.^[12]

β-Amino-γ-hydroxy acids have been prepared from αhydroxy-β-lactams with hydroxylated substituents at C-4,^[13] by degradation of β-lactams^[14] or, more recently, by sodium cyanoborohydride reduction of chiral γ-hydroxy *tert*-butyl alkenoates with moderate diastereoselectivity.^[15] Dihydroxylation of γ,δ-unsaturated β-amino esters^[16] or palladium(II)-catalyzed intramolecular aminocarbonylation of *endo* carbamates^[17] also give β-amino-γ-hydroxy acid derivatives in good yields. In spite of their interest, surprisingly there are not antecedents on the diastereoselective synthesis of γ-amino-δ-hydroxy acids, to the best of our knowledge.

Recently, we have prepared both *threo*- and *erythro*- β -hydroxynorvalines by diastereo-divergent synthesis from (*S*)-serine-derived *N*,*N*-dibenzyl- α -amino aldehydes,^[18] and now we report on the preparation of enantiopure *syn*- and *anti*-aminohydroxy acids from amino aldehyde derivatives **1a**, **b**. These compounds were obtained from L-aspartic and L-glutamic acids in 40% and 32%, respectively, by benzyl-ation, lithium aluminum hydride (LAH) reduction, monoprotection as *tert*-butyldimethylsilyl ether (TBDMS) and Swern oxidation.^[19,20] α -Amino aldehydes **1a**, **b** were transformed into *syn*- and *anti*-3-amino-1,4-diols **2a** and *syn*- and *anti*-4-amino-1,5-diol derivatives **2b** in good yields and

 [a] Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Valladolid Doctor Mergelina s/n, 47011 Valladolid, Spain Fax: (internat.) + 34-983/423013 E-mail: pedrosa@qo.uva.es the configuration at C-4 or C-5 is controlled by diastereoselective alkylation with diethylzinc or ethylmagnesium bromide. The protection of the carboxylic group as OBO orthoester improved the yields in the final products. (© Wiley-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, Germany, 2003)

excellent dr's by reaction with diethylzinc or ethylmagnesium bromide (Scheme 1 and Table 1).



Scheme 1. Reagents and conditions: (i) Et_2Zn , toluene/hexane, 0 °C. 76% for *syn*-**2a**, 67% for *syn*-**2b**. (ii) EtMgBr, Et_2O , 0 °C. 70% for *anti*-**2a**, 73% for *anti*-**2b**.

As expected, the reaction of **1a** with diethylzinc in toluene/hexane at 0 °C gives *syn-***2a** as a single diastereomer, and **1b** yields, under the same experimental conditions, a mixture of *syn-***2b** and *anti-***2b** in good *dr* (87:13), indicating that the addition occurs in agreement with a chelated intermediate.^[18] On the contrary, **1a** and **1b** react with ethylmagnesium bromide leading to *anti-***2a**, as a single isomer, and *anti-***2b** and *syn-***2b** in a *dr* 92:8^[21] in agreement with a nonchelated model.^[22,23]

The stereochemistry of diastereoisomers *syn*- and *anti*-2a, **b** was determined as described previously,^[24,25] and confirmed by the ¹H NMR spectroscopic data of the oxazolidinones prepared by debenzylation followed by treatment with triphosgene (Scheme 2). The vicinal coupling constants between the protons at C-4 and C-5 in oxazolidinones 3a, b derived from *syn*-2a, b ($^{1,3}J = 6.3$ Hz and $^{1,3}J =$

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Entry ^[a]	Amino aldehyde	RM	Amino alcohol	Yield (%) ^[b]	syn/anti ^[c]
1	1a	Et_2Zn	syn -2a	76	> 95:5 ^[d]
2	1a	EtMgBr	anti-2a	70	< 5:95 ^[d]
3	1b	Et_2Zn	syn-2b	67	87:13
4	1b	EtMgBr	anti-2b	73	8:92

Table 1. Addition of Et₂Zn and EtMgBr to amino aldehydes 1a and 1b

^[a] Reactions were run at 0 °C. ^[b] Numbers correspond to combined yield of pure and isolated diastereoisomers. ^[c] The diastereomeric ratio was determined by integration of the ¹H NMR spectra of the reaction mixture. ^[d] Only one diastereomer was detected by ¹H NMR spectroscopy.

5.7 Hz, respectively) are smaller than those derived from *anti-***2a**, **b** ($^{1,3}J = 7.6$ Hz and $^{1,3}J = 7.5$ Hz) indicating a *trans* relationship for the former and a *cis* stereochemistry for the later.^[26,27]



Scheme 2. Reagents and conditions: (i) 1. $H_2/Pd(OH)_2/C$, MeOH. 2. (CCl₃O)₂CO, DIPEA, CH₂Cl₂, room temp. 72% for *trans*-3a, 46% for *trans*-3b, 70% for *cis*-3a, 50% for *cis*-3b

The transformation of **2a**, **b** into the aminohydroxy acids **7a**, **b** was achieved as summarized in Scheme 3 by protection of the secondary alcohol by reaction with (2-methoxyethoxy)methyl chloride (MEMCl) in dichloromethane at room temp., deprotection of the primary hydroxy group by treatment with tetra-*n*-butylammonium fluoride (TBAF) in THF at 0 °C, and subsequent oxidation. First, we attempt the preparation of the acids by two-steps oxidation of **5a**, **b** as described previously for 2-dibenzylamino-1,3-diols,^[18] but this protocol fails for these compounds. Swern oxidation of *syn*-**5a** lead to a complex reaction mixture where it was possible to detect (¹H NMR) dibenzylamine and α , β -unsaturated aldehydes. This fact points to that the β -amino- γ -hydroxy aldehyde is not stable and decomposes by retrocondensation to the amine and the unsaturated aldehyde.

Alternatively we tested the direct oxidation of amino alcohols **5a**, **b** with pyridinium dichromate (PDC), but this oxidation previously required a change of the benzyl protection of the amino group into urethane. This process occurred in one step by hydrogenolysis of **5a**, **b** on Pd(OH)₂/ C in the presence of di-*tert*-butyl dicarbonate leading to **6a**, **b** which were oxidized into **7a**, **b** by treatment with PDC (5 equiv.) in DMF at room temp. This protocol allowed the synthesis of protected aminohydroxy acids **7a**, **b** from **2a**, **b** in four steps with total yields of 22-31%. Compounds *syn*and *anti*-**7a** were transformed into the 3-amino-4-hydroxy acids *syn*-**8a** and *anti*-**8a** in low yields (18 and 20%) by de-



Scheme 3. Reagents and conditions: (i) MEMCl, DIPEA, CH_2Cl_2 , room temp. (ii) TBAF, THF, 0 °C. (iii) H_2 , $Pd(OH)_2/C$, Boc_2O , MeOH. (iv) PDC, DMF, room temp. (v) 1. HCl 2 N, room temp. 2. Propylene oxide, EtOH, reflux. (vi) Ac₂O, pyridine, room temp.

protection with 2 N solution of HCl at $rt^{[28]}$ followed by treatment with propylene oxide in absolute ethanol. The stereochemistry for *syn*-**8a** was confirmed by lactonization to the known^[14] *cis*-**9** by reaction with Ac₂O in pyridine at room temp. (Scheme 3).

A shorter approach to *syn*- and *anti*-**8a** from L-aspartic acid was attempted. The idea was to reduce selectively the carboxylic group at C-1 maintaining the carboxylic group at C-4, avoiding the protection of the secondary hydroxylic group and the final oxidation of the primary one. The first attempt was done by selective monoesterification^[29] of aspartic acid to **10a** which was transformed into **11a** by re-

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ductive dibenzylation with benzaldehyde and sodium cyanoborohydride in water at pH = 7 followed by reduction with diborane of the carboxylic acid,^[30] but the final compound was obtained in only 13%. In an alternative transformation, 10a was protected as benzyloxycarbonyl derivative 12a and then converted into 13a by reaction with ethyl chloroformate followed by in situ reduction with sodium borohydride in THF/MeOH.^[31] The change of Z protective group by two benzyl substituents was tried by hydrogenolysis with Pd/C in a solution of hydrochloric acid in methanol followed by dibenzylation with benzyl bromide and potassium carbonate in refluxing acetonitrile. Unfortunately, the only isolated product was lactone 14a. Trying to circumvent this problem, 13a was protected as TBDMS ether 15a that was subjected to the change of protective group at nitrogen as described for 13a. In this case compound 16a was isolated in high yield, but it was transformed by deprotection with 1% hydrochloric acid in THF or acetic acid in water-THF into a mixture of lactone 14a and 3-N,N-dibenzyl-4-hydroxybutyrate 11a. This acid lactonized quantitatively into 14a after a few days in the refrigerator (Scheme 4).



Finally, we tested a different protective group of the terminal carboxylic group to avoid the easy lactonization process. To this end, the known compound $17a^{[32]}$ was converted, in excellent yield, into the 2,6,7-trioxabicyclo[2.2.2]octane (OBO) orthoester **19a** by treatment with cesium carbonate and reaction with 3-bromomethyl-3methyloxetane in DMF to **18a** followed by treatment with boron trifluoride-diethyl ether at 0 °C in dichloromethane. LAH reduction of **19a** lead to **20a** that was deprotected



Scheme 4. Reagents and conditions: (i) 1. CH₃COCl, MeOH, 0 °C. 2. Propylene oxide, EtOH, reflux. (ii) ZCl, K_2CO_3 , H_2O/Et_2O , 20 °C. (95%). (iii) 1. ClCO₂Et, 4-methylmorpholine, THF, -10 °C. 2. NaBH₄, MeOH, 0 °C. (48%). (iv) 1. H₂, Pd-C, HCl in MeOH. 2. BnBr, K_2CO_3 , CH₃CN, reflux. (66%). (v) TBDMSCl, imidazole, DMF, 20 °C. (85%). (vi) 1. H₂, Pd-C, MeOH, room temp. 2. BnBr, K_2CO_3 , CH₃CN, reflux. (75%). (vii) 1% HCl in THF, 0 °C. **11a** (34%), plus **14a** (26%)

Scheme 5. Reagents and conditions: (i) 1. Cs_2CO_3 , H_2O , 20 °C. 2. 3-(Bromomethyl)-2-methyloxetane, DMF, 20 °C. (81%). (ii) BF₃·Et₂O, CH₂Cl₂, -30 °C. (90%). (iii) LAH, THF, 0 °C. (78%). (iv) 1. H₂, Pd(OH)₂/C, MeOH, room temp. 2. BnBr, K₂CO₃, CH₃CN, room temp. (73%). (v) (COCl)₂, DMSO, Et₃N, CH₂Cl₂, -78 °C. (95%). (vi) Et₂Zn, hexane/toluene, 0 °C. (70%). (vii) EtMgBr, THF/Et₂O, 0 °C. (62%). (viii) 2 N HCl THF/H₂O, reflux. 64% for *trans*-**26a**, and 52% for *syn*-**24a**. (ix) H₂, Pd(OH)₂-C, MeOH/H₂O (1:1). (60%)

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by hydrogenolysis with palladium hydroxide on carbon and dibenzylated with benzyl bromide and potassium carbonate to give **21a**. Swern oxidation of the protected amino alcohol lead to the OBO-*N*,*N*-dibenzylamino aldehyde **22a** in very good yield (Scheme 5).

α-Amino aldehyde derivative 22a reacts with diethylzinc (2 equiv.) in hexane/toluene at 0 °C leading to syn-23a as a single diastereomer in 70%. The stereochemistry of this compound was determined by X-ray diffraction studies^[33] (Figure 1), and the configuration at the stereocenter was, as expected, the predicted by the Cram-chelated model. This compound was transformed into syn-3-dibenzylamino-4hydroxyhexanoic acid (syn-24a) by hydrolysis of the OBO group with 2 N HCl in THF/water, and syn-24a lead to enantiopure β -amino- γ -hydroxy acid *syn*-**8a** by hydrogenolysis on Pd(OH)₂/C in methanol/water. The reaction of the amino aldehyde 22a with ethylmagnesium bromide (2 equiv.) in diethyl ether at 0 °C gave the spiranic adduct anti-25a as a single diastereomer in 62%. This orthoester was transformed into the lactone trans-26a, derived from anti-8a, as described for compound syn-23a.



Figure 1. ORTEP representation of X-ray for compound syn-23a

The formation of the spiranic orthoester *anti*-**25a** can be explained as a consequence of the intramolecular displacement of one of the alkoxy group of the OBO derivative by the intermediate alkoxide **A** formed by reaction of **22a** with the Grignard derivative (Scheme 5).

In summary, the disclosed methodology constitutes a stereodivergent synthesis of enantiopure 3-amino-4-hydroxyhexanoic acids or 4-amino-5-hydroxyheptanoic acid derivatives from easily available L-aspartic and L-glutamic acids, respectively. The key step of the transformation is the diastereoselective alkylation of the chiral α -amino aldehydes, obtained from the corresponding amino acids, by zinc or magnesium derivatives. The election of the protective group of the additional carboxylic group has been shown to be crucial for the total yield of the process. The

best results were obtained by protection of that functional group as OBO orthoester derivatives.

Experimental Section

General: The reactions were carried out in oven-dried glassware, under argon, and using anhydrous solvents. Starting *N*,*N*-dibenzyl- α -amino aldehydes **1a**-**b** were prepared by a modified described method.^[19,20] Diethylzinc (1 M solution in hexanes) is commercially available. The ¹H NMR (300 MHz) and ¹³C NMR (75 MHz) spectra were registered with a Bruker AC 300 or Bruker AMX 300, TMS was used as internal standard. IR spectra were recorded with a Philips PU 9706 Spectrometer, as film or KBr dispersion. Optical rotations were measured with a Perkin–Elmer 241 Polarimeter in a 1-dm cell. Microanalyses were performed with a Perkin–Elmer 2400-CHN elemental analyser.

Amino Alcohol syn-2a: A solution of amino aldehyde 1a (2.0 g, 5 mmol) in anhydrous toluene (60 mL) at 0 °C (ice bath) under argon was added dropwise to 10 mL of 1 M solution of diethylzinc in hexane (10 mmol, 2 equiv.). The mixture was stirred at 0 °C until the reaction was finished (TLC), and then guenched with aqueous saturated solution of ammonium chloride (70 mL). The organic layer was separated and the aqueous phase was extracted with diethyl ether (3 \times 50 mL). The combined organic layers were washed with brine, and dried with anhydrous Na₂SO₄. The solvents were eliminated under vacuum and the residue was purified by flash chromatography (silica gel, hexane/EtOAc, 25:1): 1.63 g (3.8 mmol, 76%). Colorless oil. $[\alpha]_{D}^{20} = +28.3$ (c = 1.0, CHCl₃). IR (film): $\tilde{v} =$ 3400, 740, 695 cm⁻¹. ¹H NMR (CDCl₃): $\delta = 0.11$ [s, 6 H, $Si(CH_3)_2$, 0.93 (t, J = 7.4 Hz, 3 H, CH_3CH_2), 0.94 [s, 9 H, C(CH₃)₃], 1.18 (m, 1 H, CHHCH₃), 1.58 (m, 2 H, CHHCH₃ and CHHCHN), 2.01 (m, 1 H, CHHCHN), 2.56 (m, 1 H, CHN), 3.43 (m, 1 H, CHOH), 3.45 (d, J = 13.3 Hz, 2 H, CHHPh), 3.73 (t, J = 7.0 Hz, 2 H, TBDMSOCH₂), 3.86 (d, J = 13.3 Hz, 2 H, CHHPh), 4.39 (br. s, 1 H, OH), 7.20-7.40 (m, 10 H, H_{arom.}) ppm. ¹³C NMR $(CDCl_3): \delta = -5.3 (SiCH_3), 10.1 (CH_3CH_2), 18.4 [C(CH_3)_3], 26.0$ [C(CH₃)₃], 26.6 (CH₂CH₃), 29.4 (TBDMSOCH₂CH₂), 54.0 (CH₂Ph), 59.4 (CHN), 62.0 (TBDMSOCH₂), 71.7 (CHOH), 127.1, 128.4, 129.1 (CH_{arom}), 139.1 (C_{arom}) ppm. C₂₆H₄₁NO₂Si (427.7): calcd. C 73.01, H 9.66, N 3.27; found C 73.11, H 9.82, N 3.12.

Amino Alcohol syn-2b: Compound syn-2b was obtained from amino aldehyde 1b (2.06 g, 5 mmol) by reaction with Et₂Zn as described for compound syn-2a. The product was purified by flash chromatography (silica gel, hexane/EtOAc, 30:1): 1.48 g (3.35 mmol, 67%). Colorless oil. $[\alpha]_{D}^{20} = +36.8$ (c = 1.0, CHCl₃). IR (film): $\tilde{v} = 3420, 740, 695 \text{ cm}^{-1}$. ¹H NMR (CDCl₃): $\delta = 0.10$ (s, 3 H, CH_3Si), 0.11 (s, 3 H, CH_3Si), 0.91 (t, J = 6.2 Hz, 3 H, CH₃CH₂), 0.95 [s, 9 H, C(CH₃)₃], 1.16 (m, 1 H, CHHCH₃), 1.34 (m, 1 H, CHHCHN), 1.60 (m, 1 H, CHHCH₃), 1.66 (m, 2 H, CH₂CH₂CHN), 1.80 (m, 1 H, CHHCHN), 2.43 (m, 1 H, CHN), 3.43 (m, 1 H, CHOH), 3.45 (d, J = 13.2 Hz, 2 H, CHHPh), 3.64 $(t, J = 6.2 \text{ Hz}, 2 \text{ H}, \text{TBDMSOC}H_2), 3.88 (d, J = 13.2 \text{ Hz}, 2 \text{ H},$ CHHPh), 4.47 (br. s, 1 H, OH), 7.20–7.35 (m, 10 H, H_{arom}) ppm. ¹³C NMR (CDCl₃): $\delta = -5.3$ [(CH₃)₂Si], 10.2 (CH₃CH₂), 18.3 [C(CH₃)₃], 22.0 (CH₂CHN), 25.9 [C(CH₃)₃], 26.7 (CH₂CH₃), 32.4 (CH₂CH₂CHN), 53.9 (CH₂Ph), 62.4 (CHN), 62.9 (TBDMSOCH₂), 71.7 (CHOH), 127.1, 128.4, 129.1 (CH_{arom.}), 138.9 (C_{arom.}) ppm. C₂₇H₄₃NO₂Si (441.7): calcd. C 73.41, H 9.81, N 3.17; found C 73.54, H 10.01, N 2.98.

Amino Alcohol *anti*-2a: A solution of EtMgBr (8.4 mmol, 1.25 equiv.) in diethyl ether (12 mL) at 0 °C was added dropwise to a

solution of amino aldehyde 1a (2.7 g, 6.7 mmol) in diethyl ether (12 mL). After stirring at this temperature for 1 h, saturated NH₄Cl (40 mL) was added and the mixture was extracted with diethyl ether (2 \times 20 mL). The combined organic layers were washed with brine, dried with anhydrous Na₂SO₄ and the solvent evaporated under vacuum. After flash chromatography (silica gel: hexane/ EtOAc, 15:1), the compound anti-2a was obtained as a colorless oil: 2.01 g (4.7 mmol, 70%). $[\alpha]_{D}^{20} = +10.7$ (c = 1.0, CHCl₃). IR (film): $\tilde{v} = 3420, 740, 690 \text{ cm}^{-1}$. ¹H NMR (CDCl₃): $\delta = 0.03$ (s, 3 H, SiC H_3), 0.05 (s, 3 H, SiC H_3), 0.87 (t, J = 7.4 Hz, 3 H, CH₃CH₂), 0.87 [s, 9 H, C(CH₃)₃], 1.37 (m, 1 H, CHHCH₃), 1.73 (m, 2 H, CHHCH₃ and CHHCHN), 2.01 (m, 1 H, CHHCHN), 2.69 (m, 1 H, CHN), 3.00 (d, J = 5.8 Hz, 1 H, OH), 3.53 (d, J =13.8 Hz, 2 H, CHHPh), 3.58 (m, 2 H, TBDMSOCHH and CHOH), 3.71 (d, J = 13.8 Hz, 2 H, CHHPh), 3.84 (m, 1 H, TBDMSOCHH), 7.20-7.40 (m, 10 H, H_{arom.}) ppm. ¹³C NMR $(CDCl_3): \delta = -0.5 [Si(CH_3)_2], 10.2 (CH_3CH_2), 18.2 [C(CH_3)_3],$ 25.9 [C(CH₃)₃], 27.8 (CH₂CH₃), 28.5 (TBDMSOCH₂CH₂), 54.7 (CH₂Ph), 59.4 (CHN): 62.4 (TBDMSOCH₂), 72.9 (CHOH), 126.8, 128.1, 128.8 (CH_{arom}), 139.9 (C_{arom}) ppm. C₂₆H₄₁NO₂Si (427.7): calcd. C 73.01, H 9.66, N 3.27; found C 73.23, H 9.86, N 3.09.

Amino Alcohol anti-2b: Compound anti-2b was obtained from amino aldehyde 1b (2.06 g, 5 mmol) by reaction with EtMgBr as described for compound anti-2a. The product was purified by flash chromatography (silica gel, hexane/EtOAc, 20:1): 1.61 g (3.65 mmol, 73%). Colorless oil. $[\alpha]_{D}^{20} = +24.4$ (c = 1.0, CHCl₃). IR (film): $\tilde{v} = 3420, 740, 690 \text{ cm}^{-1}$. ¹H NMR (CDCl₃): $\delta = 0.04$ (s, 3 H, CH₃Si), 0.05 (s, 3 H, CH₃Si), 0.90 [s, 9 H, C(CH₃)₃], 0.92 $(t, J = 7.3 \text{ Hz}, 3 \text{ H}, CH_3CH_2), 1.35 (m, 1 \text{ H}, CHHCH_3), 1.54 (m, 1 \text{ H}$ 3 H, CHHCH₃, CHHCH₂CHN), 1.75 (m, 2 H, CHHCHN), 2.16 (br. s, 1 H, OH), 2.64 (m, 1 H, CHN), 3.58 (m, 3 H, CHOH, TBDMSOCH₂), 3.67 (s, 4 H, CH₂Ph), 7.20-7.35 (m, 10 H, H_{arom}) ppm. ¹³C NMR (CDCl₃): $\delta = -5.3$ [(CH₃)₂Si], 11.0 (CH₃CH₂), 18.3 [C(CH₃)₃], 21.3 (CH₂CHN), 25.9 [C(CH₃)₃], 27.6 (CH₂CH₃), 30.6 (CH₂CH₂CHN), 54.9 (CH₂Ph), 60.5 (CHN), 63.0 (TBDMSOCH₂), 72.5 (CHOH), 126.9, 128.2, 128.9 (CH_{arom}), 140.0 (Carom.) ppm. C₂₇H₄₃NO₂Si (441.7): calcd. C 73.41, H 9.81, N 3.17; found C 73.68, H 9.97, N 2.95.

Oxazolidinone trans-3a: A solution of compound syn-2a (86 mg, 0.2 mmol) in MeOH (5 mL) and Pd(OH)₂/C (25 mg) was stirred for 1 h under hydrogen. The catalyst was removed by filtration through celite, washed with methanol, and the solvent was evaporated under reduced pressure. A stirred solution of the residue and diisopropylethylamine (87 µL, 0.5 mmol, 2.5 equiv.) in anhydrous CH2Cl2 (6 mL) at 0 °C was added to triphosgene (30 mg, 0.1 mmol, 0.5 equiv.). The reaction solution was warmed to room temperature with stirring for 2 h. H₂O (2.5 mL) and EtOAc (20 mL) were added to the mixture, and the organic phase was separated, dried with anhydrous MgSO₄, concentrated under reduced pressure and chromatographed (silica gel, hexane/EtOAc, 3:1) to afford trans-3a as colorless oil: 39 mg (0.14 mmol, 72%). $[\alpha]_{D}^{20} = -39.1$ (c = 0.4, CHCl₃). ¹H NMR (CDCl₃): $\delta = 0.07$ [s, 6 H, (CH₃)₂Si], 0.90 [s, 9 H, $(CH_3)_3C$], 1.03 (t, J = 7.1 Hz, 3 H, CH_2CH_3), 1.75 (m, 4 H, CH_2CH_3 and CH_2CHN), 3.58 (ddd, $J_1 = 8.6$, $J_2 = 6.3$, $J_3 =$ 4.0 Hz, 1 H, CHNH), 3.76 (m, 2 H, TBDMSOCH₂), 4.16 (ddd, J₁ = 6.7, J₂ = 6.3, J₃ = 5.7 Hz, CHO), 5.30 (br. s, 1 H, NH) ppm. C13H27NO3Si (273.4): calcd. C 57.10, H 9.95, N 5.12; found C 57.18, H 9.69, N 5.32.

Oxazolidinone *cis*-**3a**: This compound was prepared from *anti*-**2a** (86 mg, 0.20 mmol) by the same procedure as for *trans*-**3a**. It was obtained as colorless oil: 38 mg (0.14 mmol, 70%). $[\alpha]_{D}^{D0} = -12.9$ (c = 0.4, CHCl₃). ¹H NMR (CDCl₃): $\delta = 0.10$ [s, 6 H, (CH₃)₂Si],

0.90 [s, 9 H, $(CH_3)_3$ C], 1.06 (t, J = 7.4 Hz, 3 H, CH_2CH_3), 1.65 (m, 4 H, $CHHCH_3$ and CH_2CHN), 3.78 (m, 2 H, TBDMSOC H_2), 3.92 (ddd, $J_1 = 8.8$, $J_2 = 7.6$, $J_3 = 4.4$ Hz, 1 H, CHN), 4.51 (ddd, $J_1 = 9.7$, $J_2 = 7.6$, $J_3 = 4.2$ Hz, 1 H, CHO), 5.75 (br. s, 1 H, NH) ppm. $C_{13}H_{27}NO_3Si$ (273.4): calcd. C 57.10, H 9.95, N 5.12; found C 56.92, H 9.78, N 5.24.

Oxazolidinone *trans*-**3b**: Oxazolidinone *trans*-**3b** was prepared from *syn*-**2b** (88 mg, 0.2 mmol) using the same procedure as for *trans*-**3a**, and purified by flash chromatography (silica gel, hexane/EtOAc, 3:1): 26 mg (0.09 mmol, 46%). Colorless oil. $[a]_{D}^{20} = -43.5$ (c = 1.1, CHCl₃). IR (film): $\tilde{v} = 3260$, 1740, 1460, 1385 cm⁻¹. ¹H NMR (CDCl₃): $\delta = 0.06$ (s, 6 H, CH₃Si), 0.89 (s, 9 H, CCH₃), 1.02 (t, J = 7.4 Hz, 3 H, CH₃CH₂), 1.55–1.80 (m, 6 H, CH₂CHN, CH₂CH₂CHN, CH₂CH₃), 3.48 (m, 1 H, CHN), 3.65 (t, J = 5.5 Hz, 2 H, TBDMSOCH₂), 4.10 (dt, $J_1 = 5.7$, $J_2 = 6.7$ Hz, 1 H, CHO), 6.17 (br. s, 1 H, NH) ppm. ¹³C NMR (CDCl₃): $\delta = -5.4$ [(CH₃)₂Si], 9.0 (CH₃CH₂), 18.3 [C(CH₃)₃], 25.9 [C(CH₃)₃], 27.7 (CH₂CH₃), 28.7 (CH₂CHN), 32.6 (TBDMSOCH₂CH₂), 57.5 (CHN), 62.5 (TBDMSOCH₂), 83.8 (CHO), 159.2 (NHCO₂) ppm. C₁₄H₂₉NO₃Si (287.5): calcd. C 58.49, H 10.17, N 4.87; found C 58.32 H 10.38, N 4.75.

Oxazolidinone *cis*-**3b**: Oxazolidinone *cis*-**3b** was prepared from *anti*-**2b** (88 mg, 0.2 mmol) using the same procedure as for *trans*-**3a**, and purified by flash chromatography (silica gel, hexane/EtOAc, 3:1): 29 mg (0.1 mmol, 50%). Colorless solid. M.p. 100–102 °C (from hexane). $[\alpha]_{20}^{20} = -9.6$ (c = 1.9, CHCl₃). IR (KBr): $\tilde{v} = 3250$, 1730, 1450, 1380 cm⁻¹. ¹H NMR (CDCl₃): $\delta = 0.06$ [s, 6 H, (*CH*₃)₂Si], 0.89 [s, 9 H, C(*CH*₃)₃], 1.06 (t, J = 7.3 Hz, 3 H, *CH*₃CH₂), 1.45–1.85 (m, 6 H, *CH*₂CH₃, *CH*₂CH₂CHN, *CH*₂CHN), 3.66 (m, 2 H, TBDMSOC*H*₂), 3.78 (m, 1 H, *CHN*), 4.50 (ddd, $J_1 = 9.6$, $J_2 = 7.5$, $J_3 = 4.4$ Hz, 1 H, *CHO*), 6.17 (br. s, 1 H, *NH*) ppm. ¹³C NMR (CDCl₃): $\delta = -5.4$ [(*CH*₃)₂Si], 10.4 (*CH*₃CH₂), 18.2 [*C*(CH₃)₃], 22.4 (*CH*₂CH₃), 25.9 [C(*CH*₃)₃], 26.9 (*CH*₂CHN), 29.2 (TBDMSOCH₂CH₂), 55.5 (*C*HN), 62.6 (TBDMSOCH₂), 81.7 (*C*HO), 159.6 (NHCO₂) ppm. C₁₄H₂₉NO₃Si (287.5): calcd. C 58.49, H 10.17, N 4.87; found C 58.26, H 10.36, N 4.69.

Protected Aminodiol syn-4a: A solution of syn-2a (1.32 g, 3 mmol) and diisopropylethylamine (1.62 mL, 9.3 mmol) in CH₂Cl₂ (25 mL) at 0 °C was added dropwise to MEM chloride (1.02 mL, 9 mmol). After 16 h at room temperature, the reaction was quenched with saturated aqueous NH₄Cl (35 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 25 mL), and the combined organic layers were washed with brine, dried (MgSO₄), concentrated and chromatographed (silica gel, hexane/EtOAc, 20:1) to give syn-4a as a colorless oil: 1.21 g (2.34 mmol, 78%). Colorless oil. $[\alpha]_{D}^{20} = +25.6$ (c = 1.0, CHCl₃). IR (film): $\tilde{v} = 740, 700 \text{ cm}^{-1}$. ¹H NMR (CDCl₃): $\delta =$ 0.04 (s, 3 H, SiCH₃), 0.05 (s, 3 H, SiCH₃), 0.41 (t, J = 7.4 Hz, 3 H, CH₃CH₂), 0.88 [s, 9 H, C(CH₃)₃], 1.58 (m, 1 H, CHHCH₃), 1.81 (m, 2 H, CHHCH₃ and CHHCHN), 1.96 (m, 1 H, CHHCHN), 2.81 (m, 1 H, CHN), 3.37 (s, 3 H, OCH₃), 3.42 (d, J = 13.4 Hz, 2 H, CHHPh), 3.44 (m, 1 H, CHOMEM), 3.51 (m, 2 H, CH₂O), 3.68 (m, 4 H, CH_2O and $CH_2OTBDMS$), 3.95 (d, J = 13.4 Hz, 2 H, CH*H*Ph), 4.64 (d, J = 7.0 Hz, 1 H, OC*H*HO), 4.71 (d, J =7.0 Hz, 1 H, OCHHO), 7.15-7.40 (m, 10 H, CH_{arom}) ppm. ¹³C NMR (CDCl₃): $\delta = -5.3$ [Si (CH₃)₂], 9.7 (CH₃CH₂), 18.3 $[C(CH_3)_3],$ 23.9 $(CH_2CH_3),$ 26.0 $[C(CH_3)_3],$ 27.4 (TBDMSOCH₂CH₂), 54.0 (CHN), 55.4 (CH₂Ph), 59.0 (OCH₃), 61.0 (TBDMSOCH₂), 67.2 (OCH₂CH₂O), 71.7 (OCH₂CH₂O), 81.80 (CHOH), 95.2 (OCH₂O), 126.6, 127.9, 129.2 (CH_{arom}), 140.9 (Carom.) ppm. C₃₀H₄₉NO₄Si (515.8): calcd. C 69.86, H 9.58, N 2.72; found C 69.74, H 9.78, N 2.80.

Protected Aminodiol anti-4a: This compound was obtained from amino alcohol anti-2a (1.92 g, 4.5 mmol) by the method described for syn-4a, and purified by flash chromatography (hexane/EtOAc, 20:1): 1.74 g (3.37 mmol, 75%). Colorless oil. $[\alpha]_D^{20} = -9.0$ (c = 1.0, CHCl₃). IR (film): $\tilde{v} = 740$, 695 cm⁻¹. ¹H NMR (CDCl₃): $\delta =$ 0.04 (s, 3 H, SiCH₃), 0.06 (s, 3 H, SiCH₃), 0.62 (t, J = 7.4 Hz, 3 H, CH₃CH₂), 0.89 [s, 9 H, C(CH₃)₃], 1.53 (m, 1 H, CHHCH₃), 1.70 (m, 2 H, CHHCH₃ and CHHCHN), 1.96 (m, 1 H, CHHCHN), 2.72 (m, 1 H, CHN), 3.40 (s, 3 H, OCH₃), 3.55 (m, 2 H, OCH₂. CH_2O), 3.57 (d, J = 13.6 Hz, 2 H, CHHPh), 3.73 (m, 5 H, TBDMSOC H_2 , CHOMEM, OC H_2 CH $_2$ O), 3.74 (d, J = 13.6 Hz, 2 H, CHHPh), 4.75 (d, J = 7.0 Hz, 1 H, OCHHO), 4.81 (d, J = 7.0 Hz, 1 H, OCHHO), 7.20-7.40 (m, 10 H, CH_{arom}) ppm. ¹³C NMR (CDCl₃): $\delta = -0.5$ [Si(CH₃)₂], 9.3 (CH₃CH₂), 18.9 26.0 29.7 $[C(CH_3)_3],$ 24.6 $(CH_2CH_3),$ $[C(CH_3)_3],$ (TBDMSOCH₂CH₂), 54.4 (CH₂Ph), 55.2 (CHN), 59.0 (OCH₃), 62.1 (TBDMSOCH₂), 67.4 (OCH₂CH₂O), 71.8 (OCH₂CH₂O), 79.3 (CHOMEM), 95.0 (OCH₂O), 126.7, 128.0, 128.9 (CH_{arom}), 140.3 (C_{arom.}) ppm. C₃₀H₄₉NO₄Si (515.8): calcd. C 69.86, H 9.58, N 2.72; found C 69.68, H 9.84, N 2.92.

Protected Aminodiol syn-4b: The compound syn-4b was obtained from amino alcohol syn-2b (1.37 g, 3.1 mmol) by the method described for syn-4a, and purified by flash chromatography (CH₂Cl₂/ hexane, 2:1): 1.22 g (2.3 mmol, 74%). Colorless oil. $[\alpha]_D^{20} = +25.1$ $(c = 1.0, \text{CHCl}_3)$. IR (film): $\tilde{v} = 1600, 1490, 1450, 1360, 1250, 750,$ 700 cm⁻¹. ¹H NMR (CDCl₃): $\delta = 0.07$ [s, 6 H, (CH₃)₂Si], 0.48 (t, J = 7.4 Hz, 3 H, CH₃CH₂), 0.92 [s, 9 H, C(CH₃)₃], 1.57 (m, 4 H, CHHCH₃, CHHCHN, CH₂CH₂CHN), 1.78 (m, 2 H, CHHCH₃, CHHCHN), 2.53 (m, 1 H, CHN), 3.37 (s, 3 H, OCH₃), 3.45 (d, J = 13.4 Hz, 2 H, CHHPh), 3.52 (m, 3 H, CHOMEM, OCH₂-CH₂O), 3.59 (m, 2 H, TBDMSOCH₂), 3.68 (m, 2 H, OCH₂CH₂O), 3.95 (d, J = 13.4 Hz, 2 H, CH*H*Ph), 4.64 (d, J = 7.0 Hz, 1 H, OCHHO), 4.71 (d, J = 7.0 Hz, 1 H, OCHHO), 7.15–7.40 (m, 10 H, $H_{arom.}$) ppm. ¹³C NMR (CDCl₃): $\delta = -5.3$ [(CH₃)₂Si], 9.9 (CH₃CH₂), 18.3 [C(CH₃)₃], 20.3 (CH₂CH₃), 24.1 (CH₂CHN)), 26.0 [C(CH₃)₃], 30.7 (CH₂CH₂CHN), 55.3 (CH₂Ph), 57.6 (CHN), 59.0 (OCH₃), 63.2 (TBDMSOCH₂), 67.3 (OCH₂CH₂O), 71.7 (OCH₂-CH₂O), 81.5 (CHOMEM), 95.3 (OCH₂O), 126.6, 128.0, 129.2 (CH_{arom.}), 140.9 (C_{arom.}) ppm. C₃₁H₅₁NO₄Si (529.8): calcd. C 70.27, H 9.70, N 2.64; found C 70.47, H 9.88, N 2.38.

Protected Amino-diol anti-4b: The compound anti-4b was obtained from amino alcohol anti-2b (1.55 g, 3.5 mmol) by the method described for *syn*-4a, and purified by flash chromatography (CH₂Cl₂): 1.30 g (2.45 mmol, 70%). Colorless oil. $[\alpha]_{D}^{20} = -3.4$ (c = 1.0, CHCl₃). IR (film): $\tilde{v} = 1595$, 1490, 1450, 1360, 745, 700 cm⁻¹. ¹H NMR (CDCl₃): $\delta = 0.02$ (s, 3 H, CH₃Si), 0.03 (s, 3 H, CH₃Si), 0.62 (t, J = 7.4 Hz, 3 H, CH_3CH_2), 0.88 [s, 9 H, $C(CH_3)_3$], 1.49 (m, 3 H, CHHCH₃, CHHCHN and CHHCH₂OTBDMS), 1.70 (m, 3 H, CHHCH₃, CHHCHN and CHHCH₂OTBDMS), 2.56 (m, 1 H, CHN), 3.37 (s, 3 H, OCH₃), 3.52 (m, 4 H, OCH₂CH₂O and CH₂OTBDMS), 3.53 (d, J = 13.8 Hz, 2 H, CHHPh), 3.71 (m, 3 H, CHOMEM and OCH₂CH₂O), 3.76 (d, J = 13.8 Hz, 2 H, CH*H*Ph), 4.72 (d, *J* = 7.0 Hz, 1 H, OC*H*HO), 4.77 (d, *J* = 7.0 Hz, 1 H, OCHHO), 7.15-7.35 (m, 10 H, H_{arom}) ppm. ¹³C NMR $(CDCl_3): \delta = -5.3 [(CH_3)_2Si], 9.4 (CH_3CH_2), 18.3 [C(CH_3)_3], 21.9$ (CH₂CH₃), 24.9 (CH₂CHN), 26.0 [C(CH₃)₃], 31.3 (CH₂CH₂CHN), 54.3 (CH₂Ph), 58.1 (CHN), 59.0 (OCH₃), 63.2 (TBDMSOCH₂), 67.4 (OCH₂CH₂O), 71.8 (OCH₂CH₂O), 79.1 (CHOMEM), 95.1 (OCH₂O), 126.7, 128.0, 128.9 (CH_{arom.}), 140.4 (C_{arom.}) ppm. C31H51NO4Si (529.8): calcd. C 70.27, H 9.70, N 2.64; found C 70.38, H 9.90, N 2.44.

Amino Alcohol syn-5a: A solution of syn-4a (1.14 g, 2.2 mmol) in THF (20 mL) at 0 °C was slowly added to a solution of tetrabutylammonium fluoride (1.05 g, 3.3 mmol) in THF (5 mL). The mixture was stirred at 0 °C during 8 h, and the reaction was quenched by addition of water (20 mL). The aqueous phase was extracted with diethyl ether (2 \times 25 mL), and the combined organic extracts were washed with brine, dried (Na2SO4), concentrated and chromatographed (silica gel, hexane/EtOAc, 3:2) to yield syn-5a as colorless oil: 0.75 g (1.87 mmol, 85%). Colorless oil. $[\alpha]_{D}^{20} = -35.8$ (c = 1.0, CHCl₃). IR (film): $\tilde{v} = 3440$, 750, 700 cm⁻¹. ¹H NMR $(CDCl_3)$: $\delta = 0.68$ (t, J = 7.4 Hz, 3 H, CH_3CH_2), 1.57 (m, 1 H, CHHCH₃), 1.74 (m, 2 H, CHHCH₂OH y CHHCH₃), 1.92 (m, 1 H, CHHCH₂OH), 2.83 (m, 1 H, CHN), 3.15 (br. s, 1 H, OH), 3.40 (s, 3 H, OCH₃), 3.50-3.70 (m, 6 H, OCH₂CH₂O, CHOMEM and CH₂C*H*HOH), 3.63 (d, *J* = 13.2 Hz, 2 H, C*H*HPh), 3.84 (m, 1 H, CH₂CH*H*OH), 3.85 (d, J = 13.2 Hz, 2 H, CH*H*Ph), 4.71 (d, J =10.1 Hz, 1 H, OCHHO), 4.72 (d, J = 10.1 Hz, 1 H, OCHHO), 7.20–7.40 (m, 10 H, $H_{\rm arom}$) ppm. ¹³C NMR (CDCl₃): $\delta = 9.5$ (CH₃CH₂), 24.3 (CH₂CH₃), 27.6 (CH₂CHN), 54.8 (CH₂Ph), 56.6 (CHN), 58.9 (OCH₃), 61.7 (CH₂OH), 67.6 (OCH₂CH₂O), 71.8 (OCH₂CH₂O), 81.4 (CHOMEM), 95.2 (OCH₂O), 126.8, 128.1, 129.2 (CH_{arom}), 140.0 (C_{arom}) ppm. C₂₄H₃₅NO₄ (401.5): calcd. C 71.79, H 8.79, N 3.49; found C 71.51, H 8.67, N 3.71.

Amino Alcohol anti-5a: The amino alcohol anti-5a was obtained from anti-4a (1.47 g, 2.85 mmol) by the method described for syn-5a and purified by flash chromatography (silica gel, hexane/EtOAc, 3:2): 0.92 g (2.28 mmol, 80%). Colorless oil. $[\alpha]_D^{20} = -55.0$ (c = 1.1, CHCl₃). IR (film): $\tilde{v} = 3420, 740, 695 \text{ cm}^{-1}$. ¹H NMR (CDCl₃): $\delta = 0.71$ (t, J = 7.5 Hz, 3 H, CH_3CH_2), 1.50 (m, 1 H, $CHHCH_3$), 1.60 (m, 1 H, CHHCHN), 1.75 (m, 1 H, CHHCH₃), 2.12 (m, 1 H, CHHCHN), 2.80 (m, 1 H, CHN), 3.39 (s, 3 H, OCH₃), 3.46 (d, J = 13.5 Hz, 2 H, CHHPh, 3.55 (m, 2 H, OCH₂CH₂O), 3.62 (m, 1 H, CHHOH), 3.74 (m, 3 H, OCH₂CH₂O and CHHOH), 3.88 (m, 1 H, CHOMEM), 3.90 (d, J = 13.5 Hz, 2 H, CHHPh), 4.79 (d, *J* = 7.1 Hz, 1 H, OCHHO), 4.86 (d, *J* = 7.1 Hz, 1 H, OCHHO), 7.20–7.35 (m, 10 H, CH_{arom}) ppm. ¹³C NMR (CDCl₃): $\delta = 9.4$ (CH₃CH₂), 24.8 (CH₂CH₃), 27.3 (CH₂CHN), 54.1 (CH₂Ph), 58.2 (CHN), 58.9 (OCH₃), 62.6 (CH₂OH), 67.7 (OCH₂CH₂O), 71.6 (OCH₂CH₂O), 77.4 (CHOMEM), 94.9 (OCH₂O), 127.0, 128.2, 129.0 (CHarom.), 139.2 (Carom.) ppm. C24H35NO4 (401.5): calcd. C 71.79, H 8.79, N 3.49; found C 71.70, H 8.62, N 3.63.

Amino Alcohol syn-5b: The amino alcohol syn-5b was obtained from syn-4b (1.06 g, 2 mmol) by the method described for syn-5a and purified by flash chromatography (silica gel, hexane/EtOAc, 2:1): 657 mg (1.58 mmol, 79%). Colorless oil. $[\alpha]_{D}^{20} = +54.4$ (c = 1.0, CHCl₃). IR (film): $\tilde{v} = 3380$, 755, 705 cm⁻¹. ¹H NMR $(CDCl_3)$: $\delta = 0.47$ (t, J = 7.4 Hz, 3 H, CH_3CH_2), 1.45–1.85 (m, 6 H, CHHCH3, CH2CHHCHN), 2.15 (br. s, 1 H, OH), 2.55 (m, 1 H, CHN), 3.39 (s, 3 H, OCH₃), 3.45 (d, J = 13.4 Hz, 2 H, CHHPh), 3.55 (m, 5 H, CHOMEM, OCH₂CH₂O and CH₂OH), 3.65 (m, 1 H, OCHHCH₂O), 3.84 (m, 1 H, OCHHCH₂O), 3.98 (d, J = 13.4 Hz, 2 H, CH*H*Ph), 4.64 (d, J = 7.2 Hz, 1 H, OC*H*HO), 4.72 (d, J = 7.2 Hz, 1 H, OCHHO), 7.20–7.40 (m, 10 H, $H_{arom.}$) ppm. ¹³C NMR (CDCl₃): $\delta = 9.9$ (CH₃CH₂), 20.3 (CH₂CHN), 24.0 (CH₂CH₃), 30.6 (CH₂CH₂CHN), 55.3 (CH₂Ph), 57.7 (CHN), 59.1 (OCH₃), 63.0 (CH₂OH), 67.6 (OCH₂CH₂O), 71.9 (OCH₂-CH₂O), 81.5 (CHOMEM), 95.3 (OCH₂O), 126.7, 128.0, 129.2 (CH_{arom}), 140.8 (C_{arom}) ppm. C₂₅H₃₇NO₄ (415.6): calcd. C 72.26, H 8.97, N 3.37; found C 72.52, H 9.15, N 3.12.

Amino Alcohol *anti*-5b: The amino alcohol *anti*-5b was obtained from *anti*-4b (1.27 g, 2.4 mmol) by the method described for *syn*-5a and purified by flash chromatography (silica gel, hexane/EtOAc, 2:1): 870 mg (2.09 mmol, 87%). Colorless oil. $[\alpha]_{D}^{20} = -23.2$ (c = 1.0, CHCl₃). IR (film): $\tilde{v} = 3440$, 750, 695 cm⁻¹. ¹H NMR (CDCl₃): $\delta = 0.66$ (t, J = 7.5 Hz, 3 H, CH₃CH₂), 1.61 (m, 6 H, CHHCH₂CHN, CHHCH₃, CHHCHN), 2.61 (m, 1 H, CHN), 3.38 (s, 3 H, OCH₃), 3.54 (d, J = 13.8 Hz, 2 H, CHHPh), 3.56 (m, 4 H, OCH₂CH₂O), 3.71 (m, 2 H, CH₂OH), 3.78 (m, 1 H, CHOMEM), 3.79 (d, J = 13.8 Hz, 2 H, CHHPh), 4.75 (d, J = 7.0 Hz, 1 H, OCHHO), 4.80 (d, J = 7.0 Hz, 1 H, OCHHO), 7.20–7.40 (m, 10 H, $H_{arom.}$) ppm. ¹³C NMR (CDCl₃): $\delta = 9.4$ (CH₃CH₂), 22.1 (CH₂CHN), 24.9 (CH₂CH₃), 31.1 (CH₂CH₂CHN), 54.2 (CH₂Ph), 58.1 (CHN), 59.0 (OCH₃), 62.9 (CH₂OH), 67.5 (OCH₂CH₂O), 71.7 (OCH₂CH₂O), 78.9 (CHOMEM), 95.1 (OCH₂O), 126.7, 128.0, 128.9 (CH_{arom.}), 140.1 ($C_{arom.}$) ppm. C₂₅H₃₇NO₄ (415.6): calcd. C 72.26, H 8.97, N 3.37; found C 72.16, H 8.90, N 3.31.

Amino Alcohol syn-6a: A solution of dibenzylamino alcohol syn-5a (574 mg, 1.43 mmol) in EtOAc (15 mL) was added to di-tert-butyl dicarbonate (468 mg, 2.15 mmol, 1.5 equiv.) and Pd(OH)₂/C (145 mg) in one portion. The mixture was stirred under 1 hydrogen and the reaction monitored by TLC. When the reaction was completed, the catalyst was removed by filtration through celite and washed with EtOAc (25 mL). The solvent was concentrated under reduced pressure and the residue purified by flash chromatography (silica gel, hexane/EtOAc, 1:1): 303 mg (0.94 mmol, 66%). Colorless oil. $[\alpha]_{D}^{20} = +13.9$ (c = 1.0, CHCl₃). IR (film): $\tilde{v} = 3450$, 1690 cm⁻¹. ¹H NMR (CDCl₃): $\delta = 0.91$ (t, J = 7.4 Hz, 3 H, CH₃CH₂), 1.45 [s, 9 H, (CH₃)₃C], 1.65 (m, 4 H, CH₂CH₃, HOCH₂CH₂), 3.39 (s, 3 H, CH₃O), 3.49 (m, 1 H, CHOMEM) 3.55 (m, 2 H, OCH₂-CH₂O), 3.66 (m, 2 H, CH₂OH), 3.75 (m, 2 H, OCH₂CH₂O), 3.89 (m, 1 H, CHN), 4.70 (d, J = 7.1 Hz, 1 H, OCHHO), 4.80 (d, J = 7.1 Hz, 1 H, OCHHO), 4.95 (d, J = 9.4 Hz, 1 H, NH) ppm. ¹³C NMR (CDCl₃): $\delta = 9.7$ (CH₂CH₃), 24.3 (CH₂CH₃), 28.2 [(CH₃)₃C], 36.4 (CH₂CHN), 48.3 (CHN), 58.6 (CH₂OH), 58.9 (OCH₃), 67.2 (OCH₂CH₂O), 71.6 (OCH₂CH₂O), 79.6 [C(CH₃)₃], 80.6 (CHOMEM), 94.7 (OCH₂O), 157.3 (CO₂tBu) ppm. C15H31NO6 (321.41): calcd. C 56.05, H 9.72, N 4.36; found C 55.80, H 9.75, N 4.30.

Amino Alcohol anti-6a: The compound anti-6a was obtained from anti-5a (602 mg, 1.5 mmol) by the method described for syn-6a. Yield: 328 mg (1.02 mmol, 68%). Colorless oil. $[\alpha]_{D}^{20} = -62.2$ (CHCl₃, c = 1.0). IR (film): $\tilde{v} = 3340$, 1680 cm⁻¹. ¹H NMR $(CDCl_3)$: $\delta = 0.94$ (t, J = 7.4 Hz, 3 H, CH_3CH_2), 1.45 (m, 2 H, CHHCH₃ and CHHCH₂OH; 1.46 [s, 9 H, C(CH₃)₃], 1.62 (m, 1 H, CHHCH₃), 1.81 (m, 1 H, CHHCH₂OH), 3.40 (s, 3 H, OCH₃), 3.60 (m, 7 H, OCH₂CH₂O, CHOMEM, CHHOH, OH), 3.82 (m, 2 H, CH*H*OH, C*H*N), 4.73 (d, J = 7.1 Hz, 1 H, OC*H*HO), 4.81 (d, J = 7.1 Hz, 1 H, OCHHO), 5.86 (d, J = 9.1 Hz, 1 H, NH) ppm. ¹³C NMR (CDCl₃): $\delta = 10.1$ (CH₃CH₂), 25.4 (CH₂CH₃), 28.2 [C(CH₃)₃], 31.4 (CH₂CHN), 48.9 (CHN), 58.3 (CH₂OH), 58.9 (OCH₃), 67.5 (OCH₂CH₂O), 71.4 (OCH₂CH₂O), 79.4 [C(CH₃)₃], 85.7 (CHOMEM), 96.6 (OCH₂O), 157.2 (CO₂tBu) ppm. C₁₅H₃₁NO₆ (321.4): calcd. C 56.05, H 9.72, N 4.36; found C 55.75, H 9.69, N 4.21.

Amino Alcohol *syn***-6b**: The amino alcohol *syn***-6b** was obtained from *syn***-5b** (582 mg, 1.4 mmol) by the method described for *syn***-6a** and purified by flash chromatography (silica gel, hexane/EtOAc, 2:1): 292 mg (0.87 mmol, 62%). Colorless oil. $[\alpha]_{D}^{20} = +12.1$ (c = 0.8, CHCl₃). IR (film): $\tilde{v} = 3400$, 1670, 1480, 1440, 1350, 750 cm⁻¹. ¹H NMR (CDCl₃): $\delta = 0.91$ (t, J = 7.4 Hz, 3 H, CH₃CH₂), 1.43 [s, 9 H, C(CH₃)₃], 1.56 (m, 6 H, CHHCH₃, CHHCHN, CH₂CH₂CHN), 3.40 (s, 3 H, OCH₃), 3.48 (m, 1 H, CHOMEM), 3.57 (m, 2 H, OCH₂CH₂O), 3.65 (m, 4 H, OCH₂CH₂O and CH₂OH), 3.82 (m, 1 H, CHN), 4.70 (d, J = 7.1 Hz, 1 H, OCHHO), 4.79 (d, J = 7.1 Hz, 1 H, OCH*H*O), 4.82 (d, J = 10.5 Hz, 1 H, N*H*) ppm. ¹³C NMR (CDCl₃): $\delta = 9.8$ (*C*H₃CH₂), 24.0 (*C*H₂CH₃), 28.2 [C(*C*H₃)₃], 28.9 (*C*H₂CHN), 29.4 (*C*H₂CH₂CH₂O), 51.4 (*C*HN), 58.8 (OCH₃), 62.1 (*C*H₂OH), 67.2 (OCH₂CH₂O), 71.6 (OCH₂CH₂O), 78.8 [*C*(CH₃)₃], 80.3 (*C*HOMEM), 94.7 (OCH₂O), 156.1 (NHCO₂) ppm. C₁₆H₃₃NO₆ (335.4): calcd. C 57.29, H 9.92, N 4.18; found C 57.08, H 10.06, N 4.02.

Amino Alcohol anti-6b: The amino alcohol anti-6b was obtained from anti-5b (831 mg, 2 mmol) by the method described for syn-6a and purified by flash chromatography (silica gel, hexane/EtOAc, 1:1): 403 mg (1.2 mmol, 60%). Colorless oil. $[\alpha]_{D}^{20} = -48.0$ (c = 1.0, CHCl₃). IR (film): $\tilde{v} = 3340$, 1685, 1450, 1365 cm⁻¹. ¹H NMR $(CDCl_3)$: $\delta = 0.94$ (t, J = 7.4 Hz, 3 H, CH_3CH_2), 1.44 [s, 9 H, $C(CH_3)_3$], 1.60 (m, 6 H, CHHCHN, CH₂CH₂CHN, CHHCH₃), 3.40 (s, 3 H, OCH₃), 3.47 (m, 1 H, CHOMEM), 3.58 (m, 2 H, OCH2CH2O), 3.66 (m, 4 H, CH2OH, OCH2CH2O), 3.81 (m, 1 H, CHN), 4.71 (d, J = 7.2 Hz, 1 H, OCHHO), 4.80 (d, J = 7.2 Hz, 1 H, OCHHO), 5.45 (d, J = 9.6 Hz, 1 H, NH) ppm. ¹³C NMR $(CDCl_3): \delta = 10.2 (CH_3CH_2), 25.2 (CH_2CH_3), 25.5 (CH_2CHN),$ 28.4 [C(CH₃)₃], 29.0 (CH₂CH₂OH), 52.2 (CHN), 59.0 (OCH₃), 62.6 (CH₂OH), 67.4 (OCH₂CH₂O), 71.7 (OCH₂CH₂O), 78.9 [C(CH₃)₃], 85.0 (CHOMEM), 96.3 (OCH₂O), 156.2 (NHCO₂) ppm. C₁₆H₃₃NO₆ (335.4): calcd. C 57.29, H 9.92, N 4.18; found C 57.11, H 10.12, N 4.00.

Amino Acid syn-7a: A solution of syn-6a (289 mg, 0.9 mmol) in freshly distilled DMF (4 mL) was slowly added to PDC (1.69 g, 4.5 mmol, 5 equiv.). The orange suspension was stirred at room temperature overnight, and quenched by addition of H_2O (30 mL). The solution was extracted with diethyl ether $(10 \times 25 \text{ mL})$, the combined ethereal layers were washed with H₂O and saturated NaCl solution, dried (MgSO₄) and the volatiles were evaporated. The residue was purified by flash chromatography (silica gel, hexane/EtOAc, 1:4) to yield syn-7a as colorless oil: 214 mg (0.64 mmol, 71%). Colorless oil. $[\alpha]_{D}^{20} = +14.8$ (c = 0.7, CHCl₃). IR (film): $\tilde{v} =$ 3280, 1700 cm⁻¹.¹H NMR (CDCl₃): $\delta = 0.93$ (t, J = 7.4 Hz, 3 H, CH₂CH₃), 1.44 [s, 9 H, (CH₃)₃C], 1.56 (m, 2 H, CH₂CH₃), 2.61 (m, 2 H, CH₂CO₂H), 3.40 (s, 3 H, CH₃O), 3.57 (m, 1 H, CHO-MEM), 3.57 (m, 2 H, OCH₂CH₂O), 3.68 (m, 1 H, OCHHCH₂O), $3.78 \text{ (m, 1 H, OCHHCH}_2\text{O}), 4.16 \text{ (m, 1 H, CHN}), 4.72 \text{ (d, } J =$ 7.1 Hz, 1 H; OCHHO), 4.77 (d, J = 7.1 Hz, 1 H, OCHHO), 5.05 (d, J = 9.4 Hz, 1 H, NH) ppm. ¹³C NMR (CDCl₃): $\delta = 9.7$ (CH₂CH₃), 24.1 (CH₂CH₃), 28.3 [C(CH₃)₃], 37.4 (CH₂CHN), 48.8 (CHN), 58.9 (CH₃O), 67.4 (OCH₂CH₂O), 71.6 (OCH₂CH₂O), 79.5 [C(CH₃)₃], 80.0 (CHOMEM), 95.0 (OCH₂O), 155.7 (CO₂tBu), 175.5 (CO₂H) ppm. C₁₅H₂₉NO₇ (335.4): calcd. C 53.72, H 8.72, N 4.18; found C 53.76, H 8.77, N 4.14.

Amino Acid anti-7a: The protected amino acid anti-7a was obtained by oxidation of anti-6a (257 mg, 0.8 mmol) by the procedure described for syn-7a. Yield: 204 mg (0.61 mmol, 76%). Colorless oil. $[\alpha]_{D}^{20} = -43.7$ (c = 1.0, CHCl₃). IR (film): $\tilde{v} = 3340$, 1700 cm⁻¹. ¹H NMR (CDCl₃): $\delta = 0.95$ (t, J = 7.4 Hz, 3 H, CH₂CH₃), 1.44 [s, 9 H, (CH₃)₃C]], 1.54 (m, 2 H, CH₂CH₃), 2.56 (m, 2 H, CH₂CO₂H), 3.40 (s, 3 H, CH₃O), 3.58 (m, 3 H, CHOMEM), OCH-₂CH₂O), 3.68 (m, 1 H, OCHHCH₂O), 3.78 (m, 1 H, OCHHCH₂O), 4.03 (m, 1 H, CHN), 4.71 (d, J = 7.1 Hz, 1 H, OCHHO), 4.77 (d, J = 7.1 Hz, 1 H, OCHHO), 5.82 (d, J = 9.2 Hz, 1 H, NH) ppm. ¹³C NMR (CDCl₃): δ = 9.7 (CH₃CH₂), 24.9 (CH₂CH₃), 28.2 [(CH₃)₃C], 34.4 (CH₂CO₂H), 49.8 (CHN), 58.8 (CH₃O), 67.4 (CH₂O), 71.5 (CH₂O), 79.2 [(CH₃)₃C], 83.1 (CHOMEM), 96.1 (OCH₂O), 155.5 (NHCO₂tBu), 176.3 (CO₂H) ppm. C₁₅H₂₉NO₇ (335.4): calcd. C 53.72, H 8.72, N 4.18; found C 53.81, H 8.75, N 4.11.

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Amino Acid syn-7b: The compound syn-7b was obtained by oxidation of syn-6b (201 mg, 0.6 mmol) by the procedure described for syn-7a and purified by flash chromatography (silica gel, hexane/ EtOAc, 2:1): 130 mg (0.37 mmol, 62%). Colorless oil. $[\alpha]_{D}^{20} = -25.3$ $(c = 1.2, \text{ CHCl}_3)$. ¹H NMR (CDCl₃): $\delta = 0.98$ (t, J = 7.4 Hz, 3 H, CH₃CH₂), 1.44 (m, 2 H, CHHCH₃), 1.53 [s, 9 H, C(CH₃)₃], 2.05 (m, 2 H, CHHCHN), 2.49 (m, 2 H, CHHCO₂H), 3.39 (s, 3 H, OCH₃), 3.55 (t, J = 4.6 Hz, 2 H, OCH₂CH₂O), 3.72 (m, 2 H, OCH₂-CH2O), 3.80 (m, 1 H, CHOMEM), 4.43 (m, 1 H, CHN), 4.75 (d, J = 7.1 Hz, 1 H, OCHHO), 4.78 (d, J = 7.1 Hz, 1 H, OCHHO) ppm. ¹³C NMR (CDCl₃): $\delta = 10.2$ (CH₃CH₂), 18.6 (CH₂CH₃), 22.0 (CH₂CHN), 27.9 [C(CH₃)₃], 32.0 (CH₂CO₂H), 58.8 (CHN), 59.0 (OCH₃), 67.3 (OCH₂CH₂O), 71.6 (OCH₂CH₂O), 79.6 (CHO-MEM), 82.8 [C(CH₃)₃], 95.4 (OCH₂O), 149.7 (NHCO₂), 174.9 (CO₂H) ppm. C₁₆H₃₁NO₇ (349.4): calcd. C 55.00, H 8.94, N 4.01; found C 54.83, H 9.15, N 3.90.

Amino Acid anti-7b: The compound anti-7b was obtained by oxidation of anti-6b (385 mg, 1.15 mmol) by the procedure described for syn-7a and purified by flash chromatography (silica gel, hexane/ EtOAc. 2:1): 273 mg (0.78 mmol. 68%). Colorless oil. $[\alpha]_{D}^{20} =$ -104.8 (c = 1.0, CHCl₃). ¹H NMR (CDCl₃): $\delta = 0.96$ (t, J = 7.5 Hz, 3 H, CH₃CH₂), 1.47 (m, 1 H, CHHCH₃), 1.54 [s, 9 H, C(CH₃)₃], 1.70 (m, 1 H, CHHCH₃), 2.00 (m, 2 H, CHHCHN), 2.36 (ddd, $J_1 = 17.6$, $J_2 = 10.0$, $J_3 = 2.2$ Hz, 1 H, CHHCO₂H), 2.72 (dt, $J_1 = 17.6$, $J_2 = 10.0$ Hz, 1 H, CHHCO₂H), 3.37 (s, 3 H, OCH₃), 3.52 (m, 2 H, OCH₂CH₂O), 3.61 (m, 2 H, OCH₂CH₂O), 3.95 (m, 1 H, CHOMEM), 4.19 (d, J = 9.2 Hz, 1 H, CHN), 4.62 (d, J = 7.1 Hz, 1 H, OCHHO), 4.74 (d, J = 7.1 Hz, 1 H, OCHHO) ppm. ¹³C NMR (CDCl₃): $\delta = 10.1$ (CH₃CH₂), 17.3 (CH₂CH₃), 24.2 (CH₂CHN), 27.9 [C(CH₃)₃], 32.5 (CH₂CO₂H), 58.8 (OCH₃), 59.3 (CHN), 67.3 (OCH₂CH₂O), 71.6 (OCH₂CH₂O), 79.1 (CHO-MEM), 82.6 [C(CH₃)₃], 94.6 (OCH₂O), 149.5 (NHCO₂), 175.4 (CO₂H) ppm. C₁₆H₃₁NO₇ (349.4): calcd. C 55.00, H 8.94, N 4.01; found C 54.88, H 8.97, N 3.96.

(3S,4S)-3-Amino-4-hydroxyhexanoic Acid (syn-8a): 2 N HCl solution in THF/H₂O (1:1) (10 mL) was added to syn-7a (202 mg, 0.64 mmol) and the solution was stirred at room temp. overnight. The THF was eliminated in a Rotary evaporator, the mixture was extracted with diethyl ether $(2 \times 10 \text{ mL})$ and the aqueous layer was evaporated in vacuo. Anhydrous ethanol (8 mL) and a large excess of propylene oxide (4 mL) was added to the solid residue and the mixture was refluxed for 1 h. After removal of the volatiles on Rotavapor, the white residue was purified by flash chromatography (silica gel, CH₂Cl₂/MeOH/NH₄OH, 6:4:1) to give syn-8a as a colorless solid: 18 mg (0.12 mmol, 18%). [α]_D²⁰= -23.1 (c = 0.6, H₂O). ¹H NMR (D₂O): δ = 0.92 (t, J = 7.4 Hz, 3 H, CH₃), 1.40 (m, 1 H, CHHCH₃), 1.60 (m, 1 H, CHHCH₃), 2.42 (dd, J₁ = 17.0, J₂ = 8.2 Hz, 1 H, CHHCO₂H), 2.55 (dd, $J_1 = 17.0$, $J_2 = 4.7$ Hz, 1 H, CH*H*CO₂H), 3.36 (ddd, $J_1 = 8.2$, $J_2 = 7.0$, $J_3 = 4.7$ Hz, 1 H, CHN), 3.56 (m, 1 H, CHOH) ppm. ¹³C NMR (D₂O): $\delta = 11.4$ (CH₃), 28.1 (CH₂CH₃), 38.2 (CH₂CO₂H), 55.9 (CHN), 74.2 (CHOH), 180.0 (CO₂H) ppm. C₆H₁₃NO₃ (147.2): calcd. C 48.97, H 8.90, N 9.52; found C 49.07, H 8.87, N 9.73.

(35,4*R*)-3-Amino-4-hydroxyhexanoic Acid (*anti*-8a): The compound *anti*-7a (141 mg, 0.42 mmol) was deprotected by the same procedure to afford *anti*-8a as a colorless solid. M.p. 152–154 (dec) (from MeOH/Et₂O). 12 mg (0.084 mmol, 20%). $[\alpha]_{D}^{20} = -40.5$ (*c* = 0.7, H₂O). ¹H NMR (D₂O): $\delta = 0.92$ (t, J = 7.4 Hz, 3 H, CH₃), 1.45 (m, 2 H, CHHCH₃), 2.35 (dd, $J_1 = 17.0$, $J_2 = 10.1$ Hz, 1 H, CHHCO₂H), 2.52 (dd, $J_1 = 17.0$, $J_2 = 4.1$ Hz, 1 H, CHHCO₂H), 3.51 (m, 1 H, CHN), 3.69 (m, 1 H, CHOH) ppm. ¹³C NMR (D₂O): $\delta = 12.0$ (CH₃), 27.4 (CH₂CH₃), 35.4 (CH₂CO₂H), 55.4 (CHN),

74.5 (CHOH), 180.6 (CO₂H) ppm. $C_6H_{13}NO_3$ (147.2): calcd. C 48.97, H 8.90, N 9.52; found C 48.04, H 8.80, N 9.58.

Methyl (*S*)-3-Dibenzylamino-4-hydroxybutanoate (11a): This compound was obtained by desilylation of 16a with 1% HCl solution in THF. The reaction yielded a mixture of lactone 14a (26%) and 11a^[30] (34%) as unstable colorless oil. ¹H NMR (CDCl₃): $\delta = 2.24$ (dd, $J_1 = 14.5$, $J_2 = 8.3$ Hz, 1 H, CHHCO₂), 2.70 (dd, $J_1 = 14.5$, $J_2 = 5.1$ Hz, 1 H, CHHCO₂), 3.43 (d, J = 13.3 Hz, 2 H, CHHPh), 3.53 (m, 3 H, CHN, CHHOH), 3.67 (s, 3 H, OCH₃), 3.78 (d, J = 13.3 Hz, 2 H, CHHPh), 7.20–7.35 (m, 10 H, $H_{arom.}$) ppm. ¹³C NMR (CDCl₃): $\delta = 31.2$ (CH₂OC), 51.8 (OCH₃), 53.3 (CH₂Ph), 56.5 (CHN), 61.3 (CH₂OH), 127.3, 128.4, 128.9 (CH_{arom.}), 138.7 ($C_{arom.}$), 172.5 (CO₂CH₃) ppm. This compound lactonized completely after 12 h in the refrigerator.

(S)-2-[(Benzyloxycarbonyl)amino]-3-(methoxycarbonyl)propionic Acid (12a): To the L-aspartic acid β -methyl ester (10a)^[29] (2.94 g, 20 mmol) dissolved in water (70 mL), was added diethyl ether (25 mL), potassium carbonate (3.87 g, 28 mmol, 1.4 equiv.) and benzyl chloroformate (4 mL, 28 mmol, 1.4 equiv.). The solution was stirred at room temp. for 4 h, the layers were separated, the aqueous layer was washed with diethyl ether (2×30 mL) and acidified to pH 1 with 1 N HCl. The resulting solution was extracted with diethyl ether (3 \times 20 mL). The combined organic phases were dried (MgSO₄) and the solvents evaporated in vacuo to give Z derivative **12a:** 5.34 g (19 mmol, 95%). Colorless oil. $[\alpha]_{D}^{20} = +31.5$ $(c = 1.2, \text{CHCl}_3)$. ¹H NMR (CDCl₃): $\delta = 2.88$ (dd, $J_1 = 17.4, J_2 =$ 4.6 Hz, 1 H, CHHCHN), 3.07 (dd, $J_1 = 17.4$, $J_2 = 4.5$ Hz, 1 H, CHHCHN), 3.68 (s, 3 H, CO₂CH₃), 4.68 (m, 1 H, CHN), 5.12 (s, 2 H, CH_2Ph), 5.87 (d, J = 8.6 Hz, 1 H, NH), 7.20–7.30 (m, 5 H, $H_{\text{arom.}}$), 8.10 (br. s, 1 H, CO₂H) ppm. ¹³C NMR (CDCl₃): $\delta = 36.2$ (CH₂CO₂CH₃), 50.1 (CHN), 52.2 (OCH₃), 67.3 (CH₂Ph), 128.1, 128.2, 128.5 (CH_{arom}), 135.9 (C_{arom}), 156.1 (NCO₂Bn), 171.5 (CO₂CH₃), 175.1 (CO₂H) ppm. C₁₃H₁₅NO₆ (281.3): calcd. C 55.51, H 5.38, N 4.98; found C 55.83, H 5.42, N 4.96.

(S)-3-[(Benzyloxycarbonyl)amino]-4-hydroxybutanoate Methyl (13a): To a stirred solution of N-protected amino acid 12a (5.17 g, 18.4 mmol, lequiv.) in anhydrous THF (90 mL) at -10 °C, 4-methylmorpholine (2.0 mL, 18.4 mmol, 1 equiv.) was added, followed by ethyl choroformate (2.22 mL, 18.4 mmol, 1 equiv.). After 5-10 min, NaBH₄ (2.1 g, 55.2 mmol, 3 equiv.) was added in one portion. MeOH (190 mL) was then added dropwise to the mixture. The solution was stirred for additional 10 min, and then neutralized with 1 N HCl to pH 1. The organic solvents were evaporated under reduced pressure and the product was extracted with EtOAc (3 \times 20 mL). The organic phase was washed consecutively with 1 N HCl (10 mL), H₂O (10 mL), 5% aq NaHCO₃ (10 mL), H₂O (10 mL), dried (Na₂SO₄), and the solvent was evaporated under reduced pressure. The residue was purified by flash chromatography (silica gel, hexane/EtOAc, 1:1): 2.33 g (8.8 mmol, 48%). Colorless solid, m.p. 53-55 °C (from hexane/EtOAc). $[\alpha]_D^{20} = +2.1$ (c = 1.0, MeOH). IR (film): $\tilde{v} = 3350$, 1710, 1690, 740, 690 cm⁻¹. ¹H NMR (CDCl₃): $\delta = 2.63$ (d, J = 6.0 Hz, 2 H, CH₂CO₂CH₃), 2.90 (br. s, 1 H, OH), 3.66 (s, 3 H, OCH₃), 3.67 (m, 2 H, CH₂OH), 4.05 (m, 1 H, CHN), 5.08 (s, 2 H, CH₂Ph), 5.61 (d, J = 8.0 Hz, 1 H, NH), 7.34 (m, 5 H, $H_{\text{arom.}}$) ppm. ¹³C NMR (CDCl₃): δ = 35.4 (CH2CO2CH3), 49.6 (CHN), 51.6 (OCH3), 63.6 (CH2Ph), 66.6 (CH₂OH), 127.9, 128.1, 128.3 (CH_{arom.}), 136.1 (C_{arom.}), 156.1 (CO2Bn), 172.0 (CO2CH3) ppm. C13H17NO5 (267.3): calcd. C 58.42, H 6.41, N 5.24; found C 58.45, H 6.42, N 5.20.

(S)-3-Dibenzylaminobutyrolactone (14a): This compound was obtained by hydrogenolysis of 13a with palladium on carbon in a solution of HCl in methanol, followed by treatment with excess of benzyl bromide and potassium carbonate in refluxing acetonitrile. The residue was chromatographed (silica gel, hexane/EtOAc, 6:1) yielding **14a** (66%) as colorless oil. $[α]_{20}^{20} = +18.9 (c = 0.7, CHCl_3)$. IR (film): $\tilde{v} = 1770$, 1160, 745, 695 cm⁻¹. ¹H NMR (CDCl₃): $\delta = 2.54$ (dd, $J_1 = 17.8$, $J_2 = 8.1$ Hz, 1 H, CHHCO), 2.61 (dd, $J_1 = 17.8$, $J_2 = 8.1$ Hz, 1 H, CHHCO), 3.51 (d, J = 13.8 Hz, 2 H, CHHPh), 3.66 (d, J = 13.8 Hz, 2 H, CHHPh), 3.76 (m, 1 H, CHN), 4.28 (dd, $J_1 = 9.9$, $J_2 = 5.2$ Hz, 1 H, CHHO), 4.33 (dd, $J_1 = 9.9$, $J_2 = 7.1$ Hz, 1 H, CHHO), 7.20–7.40 (m, 10 H, $H_{arom.}$) ppm. ¹³C NMR (CDCl₃): $\delta = 30.7$ (CH₂COO), 54.5 (CH₂Ph), 56.0 (CHN), 71.0 (CH₂O₂C), 127.4, 128.4, 128.5 (CH_{arom.}), 138.2 (C_{arom.}), 176.2 (CO₂) ppm. C₁₈H₁₉NO₂ (281.3): calcd. C 76.84, H 6.81, N 4.98; found C 76.93, H 6.83, N 4.93.

Methyl (S)-3-[(Benzyloxycarbonyl)amino]-4-(tert-butyldimethylsilyloxy)butanoate (15a): This compound was prepared from 13a (1.34 g, 5.04 mmol) by reaction with TBDMSCI (1.5 equiv.) at room temp. as described previously^[19] and purified by flash chromatography (silica gel, hexane/EtOAc, 6:1): 1.64 g (4.3 mmol, 85%). Colorless oil. $[\alpha]_{D}^{20} = -15.0$ (c = 0.5, CHCl₃). IR (film): $\tilde{v} =$ 3330, 1720, 730, 695 cm⁻¹. ¹H NMR (CDCl₃): $\delta = 0.03$ [s, 6 H, Si(CH₃)₂], 0.87 [s, 9 H, C(CH₃)₃], 2.60 (m, 2 H, CH₂CO₂CH₃), 3.66 (s, 3 H, OCH₃), 3.68 (m, 2 H, CH₂OTBDMS), 4.11 (m, 1 H, CHN), 5.09 (s, 2 H, CH_2Ph), 5.35 (d, J = 8.9 Hz, 1 H, NH), 7.35 (m, 5 H, $H_{\text{arom.}}$) ppm. ¹³C NMR (CDCl₃): $\delta = -5.7$ [Si(CH₃)₂], 18.1 [C(CH₃)₃], 25.7 [C(CH₃)₃], 35.2 (CH₂CO₂CH₃), 49.2 (CHN), 51.5 (OCH₃), 63.8 (TBDMSOCH₂), 66.5 (CH₂Ph), 128.0, 128.4 (CH_{arom.}), 136.3 (C_{arom.}), 155.6 (NCO₂Bn), 171.8 (CO₂CH₃) ppm. C₁₉H₃₁NO₅Si (381.5): calcd. C 59.81, H 8.19, N 3.67; found C 59.92, H 8.28, N 3.47.

Methyl (S)-3-Dibenzylamino-4-(tert-butyldimethylsilyloxy)butanoate (16a): Compound 15a (1.58 g, 4.14 mmol) was quantitatively debenzylated over Pd/C in MeOH. A mixture of the residue, benzyl bromide (2.5 mL, 20.7 mmol, 5 equiv.), K₂CO₃ (3.43 g, 24.8 mmol, 6 equiv.) in acetonitrile (25 mL) was stirred at reflux. When the reaction was finished (TLC), the solid was separated by filtration, the filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography (silica gel, hexane/ EtOAc, 15:1): 1.24 g (3.1 mmol, 75%). Colorless oil. $[\alpha]_D^{20} = -25.3$ $(c = 1.2, \text{ CHCl}_3)$. IR (film): $\tilde{v} = 1725, 740, 695 \text{ cm}^{-1}$. ¹H NMR $(CDCl_3): \delta = 0.02 (2s, 6 H, Si(CH_3)_2], 0.87 [s, 9 H, C(CH_3)_3], 2.47$ (dd, $J_1 = 14.5$, $J_2 = 6.3$ Hz, 1 H, CHHCO₂CH₃), 2.59 (dd, $J_1 =$ 14.5, J₂ = 8.0 Hz, 1 H, CHHCO₂CH₃), 3.28 (m, 1 H, CHN), 3.57 (s, 3 H, OCH₃), 3.62 (d, J = 13.8 Hz, 2 H, CHHPh), 3.72 (d, J =13.8 Hz, 2 H, CH*H*Ph), 3.73 (d, *J* = 5.5 Hz, 2 H, TBDMSOC*H*₂), 7.15–7.35 (m, 10 H, $H_{\text{arom.}}$) ppm. ¹³C NMR (CDCl₃): $\delta = -5.7$ (SiCH₃), -5.6 (SiCH₃), 18.1 [C(CH₃)₃], 25.8 [C(CH₃)₃], 33.9 (CH₂CO₂Me), 51.4 (OCH₃), 54.3 (CH₂Ph), 56.5 (CHN), 62.7 (TBDMSOCH₂), 126.7, 128.0, 128.7 (CH_{arom.}), 140.0 (C_{arom.}), 172.9 (CO₂CH₃) ppm. C₂₅H₃₇NO₃Si (427.6): calcd. C 70.21, H 8.72, N 3.28; found C 70.07, H 8.75, N 3.32.

N-Benzyloxycarbonyl-L-aspartic Acid *a*-Benzyl Ester (17a): A solution of *N*-Benzyloxycarbonyl-L-aspartic anhydride^[32] (7.24 g, 29.0 mmol) in benzyl alcohol was heated at 90 °C for 3.5 h. The excess of BnOH was eliminated under reduced pressure and the residue was dissolved in Et₂O (150 mL) and extracted with NaHCO₃ saturated solution (twice). The aqueous layer was washed with Et₂O and acidified with 10% HCl solution. The resulting oil was extracted with CHCl₃, washed with H₂O, dried with anhydrous Na₂SO₄ and the solvent evaporated under vacuum. The residue was crystallized from hexane yielding 7.46 g of **17a** (20.9 mmol, 72%). Colorless solid, m.p. 100–102 °C (from hexane). [a]²⁰₂ = -10.5

(*c* = 1.0, MeOH). IR (KBr): $\tilde{v} = 3600-2500$, 1735, 1700, 1680, 750, 690 cm⁻¹. ¹H NMR (CDCl₃): $\delta = 2.90$ (dd, $J_1 = 17.6$, $J_2 = 4.4$ Hz, 1 H, *CH*HCO₂H), 3.10 (dd, $J_1 = 17.6$, $J_2 = 4.4$ Hz, 1 H, *CH*HCO₂H), 4.68 (m, 1 H, *CH*N), 5.11 (s, 2 H, *CH*₂Ph), 5.17 (s, 2 H, CH₂Ph), 5.81 (d, J = 8.6 Hz, 1 H, NH), 7.30–7.35 (m, 10 H, $H_{\text{arom.}}$) ppm. ¹³C NMR (CDCl₃): $\delta = 36.4$ (*C*H₂CO₂H), 50.2 (*C*HN), 67.3, 67.7 (*C*H₂Ph), 128.1, 128.2, 128.5, 128.6 (*C*H_{arom.}), 135.0, 135.9 (C_{arom.}), 156.0 (NHCO₂), 170.3 (*C*O₂Bn), 171.6 (*C*O₂H) ppm. C₁₉H₁₉NO₆ (357.4): calcd. C 63.86, H 5.36, N 3.92; found C 63.77, H 5.24, N 4.09.

Oxetane 18a: Compound 17a (8.94 g, 25 mmol) was suspended in distilled H₂O (60 mL). CsCO₃ (4.07 g, 12.5 mmol, 0.5 equiv.) was added in three portions, and the reaction was stirred vigorously. After 2 h the solution was concentrated under vacuum. The resulting white solid was dissolved in dry DMF (80 mL), and oxetane bromide (5.16 g, 31.25 mmol, 1.25 equiv.) was then added. The reaction mixture was stirred under nitrogen at room temperature for 24 h. DMF was removed using a rotary evaporator at 45 °C connected to a pump. The white crude product was dissolved in EtOAc (200 mL), washed with 5% NaHCO₃, 3% NH₄Cl (twice), saturated NaCl, dried (MgSO₄), and the solvents evaporated to dryness. The crude product was purified by flash chromatography (hexane/ EtOAc, 1:1) yielding 8.94 g of 18a (20.2 mmol, 81%) as colorless oil. $[\alpha]_{D}^{20} = +3.0 \ (c = 1.6, \text{ CHCl}_3)$. IR (film): $\tilde{v} = 3310, 1710, 740,$ 690 cm⁻¹. ¹H NMR (CDCl₃): $\delta = 1.24$ (s, 3 H, CH₃), 2.92 (dd, $J_1 = 17.2, J_2 = 4.5$ Hz, 1 H, CHHCHN), 3.10 (dd, $J_1 = 17.2, J_2 =$ 4.5 Hz, 1 H, CHHCHN), 3.98 (d, J = 11.1 Hz, 1 H, CHHO₂C), $4.14 (d, J = 11.1 Hz, 1 H, CHHO_2C), 4.37 (m, 4 H, OCH_2), 4.71$ (m, 1 H, CHN), 5.11 (s, 2 H, CH₂Ph), 5.16 (d, J = 17.8 Hz, 1 H, CHHPh), 5.20 (d, J = 17.8 Hz, 1 H, CHHPh), 6.05 (br. s, 1 H, NH), 7.25–7.40 (m, 10 H, $H_{\text{arom.}}$) ppm. ¹³C NMR (CDCl₃): δ = 20.8 (CH₃), 36.7 (CH₂CHN), 38.9 (CCH₃), 50.4 (CHN), 67.0, 67.5 (CH₂Ph), 68.9 (CH₂O₂C), 79.2, 79.3 (OCH₂), 128.0, 128.1, 128.3, 128.5, 128.6 (CH_{arom.}), 135.1, 136.1 (C_{arom.}), 156.0 (NHCO₂), 170.4 (CO2), 170.6 (CO2) ppm. C24H27NO7 (441.5): calcd. C 65.29, H 6.16, N 3.17; found C 65.55, H 6.34, N 2.97.

Amino Ester 19a: Compound 18a (3.5 g, 7.9 mmol) was dissolved in freshly distilled CH₂Cl₂ (15 mL) and cooled to -30 °C under N₂. A solution of BF₃·OEt₂ (300 µL) in CH₂Cl₂ was added, and the solution was stirred and warmed to room temperature. After 8 h, Et₃N (250 µL) in Et₂O (100 mL) was added, the solid was removed by filtration and the solution evaporated to dryness. The residue was purified by recrystallization from CH2Cl2/hexane to yield 3.14 g (7.1 mmol, 90%) of colorless crystals, mp. 102-103 °C (from hexane/EtOAc). $[\alpha]_{D}^{20} = -4.8$ (*c* = 0.5, CHCl₃). IR (KBr): $\tilde{\nu}$ = 3400, 1730, 1700, 740, 695 cm⁻¹. ¹H NMR (CDCl₃): δ = 0.73 (s, 3 H, CH₃), 2.14 (dd, J₁ = 14.7, J₂ = 4.4 Hz, 1 H, CHHCHN), 2.39 (dd, $J_1 = 14.7$, $J_2 = 5.8$ Hz, 1 H, CHHCHN), 3.77 (s, 6 H, OCH₂), 4.52 (m, 1 H, CHN), 5.11 (s, 2 H, CH₂Ph), 5.14 (s, 2 H, CH_2Ph), 6.07 (d, J = 8.3 Hz, 1 H, NH), 7.30-7.35 (m, 10 H, $H_{\text{arom.}}$) ppm. ¹³C NMR (CDCl₃): $\delta = 14.2$ (CH₃), 30.1 (CCH₃), 37.1 (CH₂CHN), 50.3 (CHN), 66.7 (CH₂Ph), 72.2 (OCH₂), 108.0 (CO_3) , 128.0, 128.1, 128.2, 128.3, 128.4 $(CH_{arom.})$, 135.7, 136.4 (Carom.), 156.0 (NHCO₂), 171.2 (CO₂Bn) ppm. C₂₄H₂₇NO₇ (441.5): calcd. C 65.29, H 6.16, N 3.17; found C 65.48, H 6.26, N 3.02.

Amino Alcohol 20a: A solution of 19a (2.4 g, 5.4 mmol) in anhydrous THF (25 mL) was added dropwise at 0 °C to a suspension of LAH (307 mg. 8.1 mmol, 1.5 equiv.) in the same solvent (25 mL). The suspension was stirred at that temperature for 0.5 h, and then treated with H_2O (0.3 mL), 15% NaOH solution (0.3 mL) and H_2O (0.9 mL), and stirred for 2 h. The white solids were removed by filtration, the solvent of the filtrate was evaporated and

the residue was purified by flash chromatography (silica gel treated with Et₃N, hexane/EtOAc, 1:1): 1.43 g (4.2 mmol, 78%). Colorless oil. $[\alpha]_{D}^{20} = -5.5$ (c = 1.2, CHCl₃). IR (film): $\tilde{v} = 3420$, 1715, 1045, 990, 740, 700 cm⁻¹. ¹H NMR (CDCl₃): $\delta = 0.79$ (s, 3 H, CH₃), 1.94 (dd, $J_1 = 15.0$, $J_2 = 5.5$ Hz, 1 H, CHHCHN), 2.06 (dd, $J_1 = 15.0$, $J_2 = 6.4$ Hz, 1 H, CHHCHN), 3.66 (m, 2 H, CHN and CHHOH), 3.86 (s, 6 H, CH₂O), 3.96 (dd, $J_1 = 12.0$, $J_2 = 6.3$ Hz, 1 H, CHHOH), 5.08 (s, 2 H, CH₂Ph), 5.60 (d, J = 7.4 Hz, 1 H, NH), 7.25–7.40 (m, 5 H, H_{arom}) ppm. ¹³C NMR (CDCl₃): $\delta = 14.3$ (CH₃), 30.2 (CCH₃), 36.9 (CH₂CHN), 49.3 (CHN), 64.5 (CH₂OH), 66.6 (CH₂Ph), 72.4 (CH₂O), 108.3 (CO₃), 128.1, 128.4 (CH_{arom}), 136.5 (C_{arom}), 156.4 (NHCO₂) ppm. C₁₇H₂₃NO₆ (337.4): calcd. C 60.52, H 6.87, N 4.15; found C 60.32, H 6.89, N 4.12.

Amino Alcohol 21a: Compound 20a (1.15 g, 3.4 mmol) was transformed in the derivative 21a by debenzylation with Pd(OH)₂/C in MeOH followed by treatment with BnBr (0.85 mL, 7.1 mmol, 2.1 equiv.) and K₂CO₃ (0.94 g, 6.8 mmol, 2 equiv.) in acetonitrile (20 mL) at room temp. as described for compound 16a. After flash chromatography (silica gel treated with Et₃N, hexane/EtOAc, 3:1), the compound 21a was obtained as colorless oil: 952 mg (2.5 mmol, 73%). $[\alpha]_{D}^{20} = +34.2$ (c = 0.5, CHCl₃). IR (film): $\tilde{v} = 3460, 1040,$ 990, 750, 700 cm⁻¹. ¹H NMR (CDCl₃): $\delta = 0.80$ (s, 3 H, CH₃), 1.57 (dd, $J_1 = 14.3$, $J_2 = 9.1$ Hz, 1 H, CHHCHN), 2.18 (dd, $J_1 =$ 14.3, J₂ = 2.3 Hz, 1 H, CHHCHN), 3.20 (m, 1 H, CHN), 3.37 (d, J = 13.2 Hz, 2 H, CHHPh), 3.44 (m, 1 H, CHHOH), 3.69 (m, 1 H, CHHOH), 3.75 (d, J = 13.2 Hz, 2 H, CHHPh), 3.89 (s, 6 H, CH₂O), 7.20–7.40 (m, 10 H, $H_{\text{arom.}}$) ppm. ¹³C NMR (CDCl₃): $\delta = 14.4 (CH_3), 30.2 (CCH_3), 32.2 (CH_2CHN), 53.0 (CH_2Ph), 54.6$ (CHN), 61.7 (CH₂OH), 72.5 (CH₂O), 108.4 (CO₃), 127.0, 128.2, 129.2 (CH_{arom.}), 139.3 (C_{arom.}) ppm. C₂₃H₂₉NO₄ (383.5): calcd. C 72.04, H 7.62, N 3.65; found C 72.09, H 7.48, N 3.90.

Amino Aldehyde 22a: This compound was obtained from amino alcohol 21a (575 mg, 1.5 mmol) by Swern oxidation as described^[19,20] for compounds 1a, b: 544 mg (1.42 mmol, 95%). Colorless oil. $[\alpha]_D^{20} = -28.2$ (c = 1.1, CHCl₃). IR (film): $\tilde{v} = 1725$, 1495, 1555, 1055, 750, 700 cm⁻¹. ¹H NMR (CDCl₃): $\delta = 0.77$ (s, 3 H, CH₃), 2.02 (dd, $J_1 = 14.4$, $J_2 = 3.3$ Hz, 1 H, CHHCHN), 2.37 (dd, $J_1 = 14.4$, $J_2 = 7.4$ Hz, 1 H, CHHCHN), 3.59 (d, J = 13.4 Hz, 2 H, CHHPh), 3.65 (d, J = 13.4 Hz, 2 H, CHHPh), 3.83 (m, 6 H, CH₂O), 7.20–7.45 (m, 10 H, H_{arom}). 9.59 (s, 1 H, CHO) ppm. ¹³C NMR (CDCl₃): $\delta = 14.3$ (CH₃), 29.9 (CH₂CHN), 30.1 (CCH₃), 54.6 (CH₂Ph), 62.1 (CHN), 72.4 (CH₂O), 108.3 (CO₃), 127.0, 128.0, 128.9 (CH_{arom}), 139.2 (C_{arom}), 200.9 (CHO) ppm. C₂₃H₂₇NO₄ (381.5): calcd. C 72.42, H 7.13, N 3.67; found C 72.18, H 7.28, N 3.51.

Amino Alcohol syn-23a: This amino alcohol was obtained from 22a (191 mg, 0.5 mmol) by reaction with Et₂Zn (2 equiv.) by the method described for compounds 2a, b. The product syn-23a was purified by flash chromatography (silica gel treated with Et₃N, hexane/EtOAc, 8:1): 144 mg (0.35 mmol, 70%). Colorless solid, mp. 108-109 °C (from hexane). $[\alpha]_{D}^{20} = +31.9$ (c = 0.8, CHCl₃). IR (film): $\tilde{v} = 3290$, 1045, 990, 740, 700 cm⁻¹. ¹H NMR (CDCl₃): $\delta =$ 0.83 (s, 3 H, CH_3), 0.86 (t, J = 7.4 Hz, 3 H, CH_3CH_2), 1.22 (m, 1 H, CHHCH₃), 1.61 (m, 1 H, CHHCH₃), 1.66 (dd, $J_1 = 15.4$, $J_2 =$ 4.3 Hz, 1 H, CHHCHN), 2.18 (dd, $J_1 = 15.4$, $J_2 = 5.8$ Hz, 1 H, CHHCHN), 2.87 (m, 1 H, CHN), 3.32 (m, 1 H, CHOH), 3.56 (d, J = 13.1 Hz, 2 H, CHHPh), 3.73 (d, J = 13.1 Hz, 2 H, CHHPh), 3.92 (s, 6 H, CH₂O), 7.20-7.40 (m, 10 H, H_{arom}) ppm. ¹³C NMR $(CDCl_3): \delta = 10.3 (CH_3C), 14.5 (CH_3CH_2), 26.1 (CH_2CH_3), 30.3$ (CCH₃), 32.7 (CH₂CHN), 53.5 (CH₂Ph), 57.3 (CHN), 71.8 (CHOH), 72.5 (CH₂O), 108.5 (CO₃), 126.9, 128.2, 129.2 (CH_{arom}),

139.6 ($C_{arom.}$) ppm. $C_{25}H_{33}NO_4$ (411.5): calcd. C 72.96, H 8.08, N 3.40; found C 72.79, H 8.30, N 3.22.

(3S,4S)-3-Dibenzylamino-4-hydroxyhexanoic Acid (syn-24a): A mixture of syn-23a (140 mg, 0.34 mmol) and 2 N HCl in THF/H₂O (5 mL) was stirred at reflux for 5 h. The pH of the reaction was adjusted to 6 with saturated NaHCO₃ solution and the mixture extracted with diethyl ether (3 \times 10 mL). The combined organic layers were washed with brine, dried with MgSO₄, concentrated and chromatographed (hexane/EtOAc, 1:2) to yield syn-24a as a colorless oil: 58 mg (0.18 mmol, 52%). $[\alpha]_D^{20} = -6.1$ (c = 0.2, CHCl₃). IR (film): $\tilde{v} = 3280, 1720, 735, 700 \text{ cm}^{-1}$. ¹H NMR $(CDCl_3)$: $\delta = 0.92$ (t, J = 7.3 Hz, 3 H, CH_3), 1.28 (m, 1 H, $CHHCH_3$), 1.56 (m, 1 H, $CHHCH_3$), 2.37 (dd, $J_1 = 16.4$, $J_2 =$ 5.7 Hz, 1 H, CHHCO₂H), 2.48 (dd, $J_1 = 16.4$, $J_2 = 8.9$ Hz, 1 H, CHHCO₂H), 3.32 (m, 1 H, CHN), 3.78 (m, 1 H, CHOH), 3.90 (d, J = 12.9 Hz, 2 H, CHHPh), 4.19 (d, J = 12.9 Hz, 2 H, CHHPh), 7.20–7.40 (m, 10 H, $H_{\rm arom.}$) ppm. ¹³C NMR (CDCl₃): $\delta = 9.1$ (CH₃), 26.7 (CH₂CH₃), 31.3 (CH₂CO₂H), 53.8 (CH₂Ph), 59.6 (CHN), 71.5 (CHOH), 128.3, 128.7, 130.1 (CH_{arom.}), 134.8 (C_{arom.}), 175.3 (CO₂) ppm. C₂₀H₂₅NO₃ (327.4): calcd. C 73.37, H 7.70, N 4.28; found C 73.25, H 7.84, N 4.16.

Spirane anti-25a: This compound was obtained as a single product in the reaction of 22a (191 mg, 0.5 mmol) with EtMgBr (2 equiv.) in THF/Et₂O as described for anti-2a, b, and purified by flash chromatography (silica gel treated with Et₃N, hexane/EtOAc, 5:1): 127 mg (0.31 mmol, 62%). Colorless oil. $[\alpha]_{D}^{20} = +73.0$ (c = 1.1, CHCl₃). IR (film): $\tilde{v} = 3450$, 1050, 750, 700 cm⁻¹. ¹H NMR $(CDCl_3)$: $\delta = 0.88$ (t, J = 7.4 Hz, 3 H, CH_3CH_2), 1.16 (s, 3 H, CH₃C), 1.45 (m, 1 H, CHHCH₃), 1.65 (m, 1 H, CHHCH₃), 1.72 (br. s, 1 H, O*H*), 2.10 (dd, *J*₁ = 13.5, *J*₂ = 9.3 Hz, 1 H, C*H*HCHN), 2.18 (dd, $J_1 = 13.5$, $J_2 = 7.4$ Hz, 1 H, CHHCHN), 3.24 (m, 1 H, CHN), 3.33 (m, 4 H, CHHO and CH₂O), 3.38 (d, J = 14.0 Hz, 2 H, CHHPh), 3.80 (d, J = 14.0 Hz, 2 H, CHHPh), 3.89 (m, 1 H, CHOH), 4.03 (dd, J₁ = 11.0, J₂ = 4.4 Hz, 2 H, CHHO), 7.15–7.40 (m, 10 H, $H_{\text{arom.}}$) ppm. ¹³C NMR (CDCl₃): $\delta = 10.3$ (CH₃C), 18.1 (CH₃CH₂), 27.1 (CH₂CH₃), 29.6 (CCH₃), 34.4 (CH₂CHN), 55.0 (CH₂Ph), 61.8 (CHN), 66.8, 67.1, 67.4 (CH₂O and CH₂OH), 81.2 (CHOH), 117.9 (CO₃), 126.9, 128.2, 128.5 (CH_{arom}), 139.6 (C_{arom}) ppm. C₂₅H₃₃NO₄ (411.5): calcd. C 72.96, H 8.08, N 3.40; found C 72.76, H 8.24, N 3.26.

(3S,4R)-3-Dibenzylamino-4-ethylbutyrolactone (trans-26a): Prepared from anti-25a (123 mg, 0.3 mmol) by treatment with HCl 2 N at reflux for 1 h as described for syn-24a and purified by flash chromatography (silica gel, hexane/EtOAc, 8:1): 59 mg (0.19 mmol, 64%). Colorless oil. [α]_D²⁰ = +84.0 (c = 0.4, CHCl₃). IR (film): \tilde{v} = 1775, 1170, 975, 750, 700 cm⁻¹. ¹H NMR (CDCl₃): $\delta = 0.90$ (t, J = 7.4 Hz, 3 H, CH₃), 1.59 (m, 2 H, CH₂CH₃), 2.55 (dd, $J_1 = 18.2$, $J_2 = 8.6$ Hz, 1 H, CHHCO₂), 2.65 (dd, $J_1 = 18.2$, $J_2 = 5.7$ Hz, 1 H, CH HCO_2), 3.39 (ddd, J = 8.6, J = 5.7, J = 4.6 Hz, 1 H, CHN), 3.46 (d, J = 13.7 Hz, 2 H, CHHPh), 3.72 (d, J = 13.7 Hz, 2 H,CH*H*Ph), 4.43 (m, 1 H, C*H*OH), 7.20–7.40 (m, 10 H, H_{arom}) ppm. ¹³C NMR (CDCl₃): $\delta = 9.4$ (CH₃), 27.4 (CH₂CH₃), 28.8 (CH₂CO₂), 54.1 (CH₂Ph), 59.2 (CHN), 83.9 (CHOH), 127.3, 128.4, 128.5 (CH_{arom.}), 138.3 (C_{arom.}), 175.9 (CO₂) ppm. C₂₀H₂₃NO₂ (309.4): calcd. C 77.64, H 7.49, N 4.53; found C 77.50, H 7.45, N 4.58.

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