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

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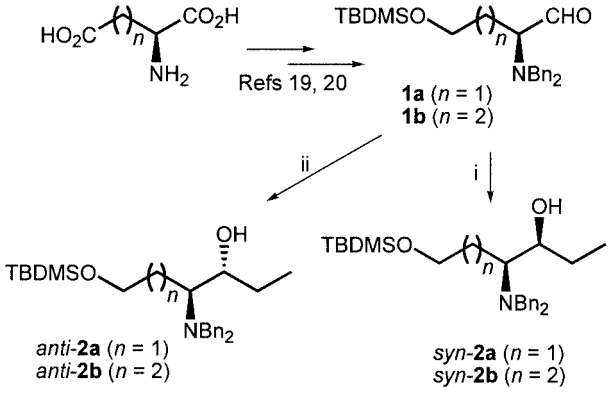
Enantiopure (3*S*,4*R*)- and (3*S*,4*S*)-3-amino-4-hydroxyhexanoic acids and (4*S*,5*R*)- and (4*S*,5*S*)-4-amino-5-hydroxyheptanoic acid derivatives have been prepared by stereodivergent synthesis from L-aspartic and L-glutamic acids, respectively. The stereochemistry at the carbon atom attached to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

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 α-hydroxy-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 benzylation, 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 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 non-chelated model.[22,23]

The stereochemistry of diastereoisomers *syn*- and *anti*-**2a, b** was determined as described previously,[24,25] and confirmed by the ^{1}H 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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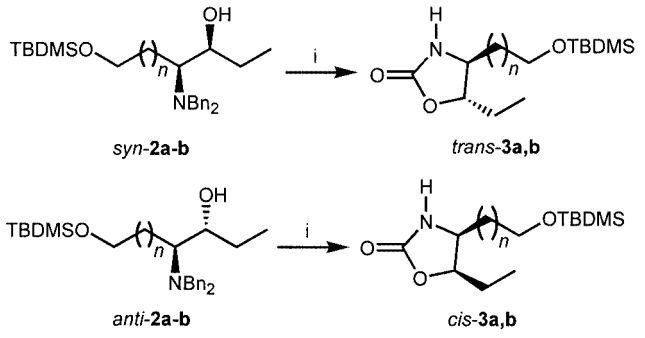
Table 1. Addition of Et_2Zn and EtMgBr to amino aldehydes **1a** and **1b**

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

[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.

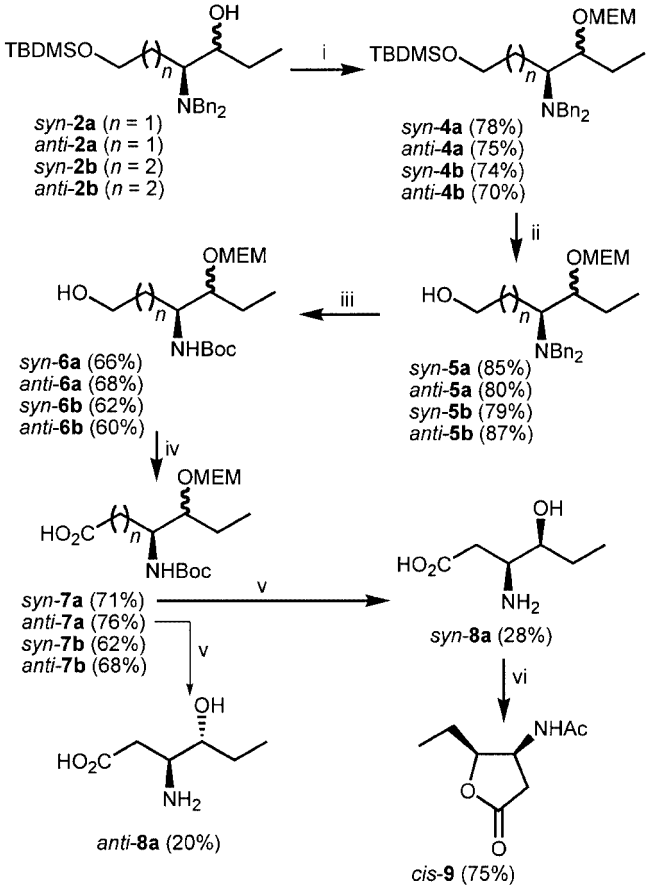
5.7 Hz, respectively) are smaller than those derived from *anti*-**2a, b** ($^{1,3}J$ = 7.6 Hz and $^{1,3}J$ = 7.5 Hz) indicating a *trans* relationship for the former and a *cis* stereochemistry for the later.[26,27]



Scheme 2. Reagents and conditions: (i) 1. H_2/$Pd(OH)_2$/C, MeOH. 2. $(CCl_3O)_2CO$, DIPEA, CH_2Cl_2, 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.

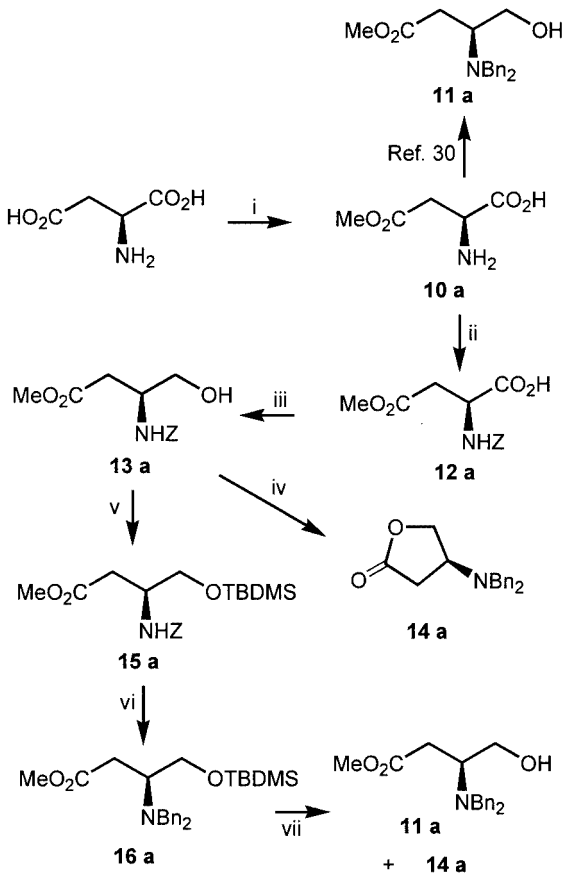
Alternatively we tested the direct oxidation of amino alcohols **5a, b** with pyridinium dichromate (PDC), but this oxidation previously required a change of the benzyl protection of the amino group into urethane. This process occurred in one step by hydrogenolysis of **5a, b** on $Pd(OH)_2$/C in the 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 deprotection 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 Ac_2O in pyridine at room temp. (Scheme 3).



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) Ac_2O, pyridine, room temp.

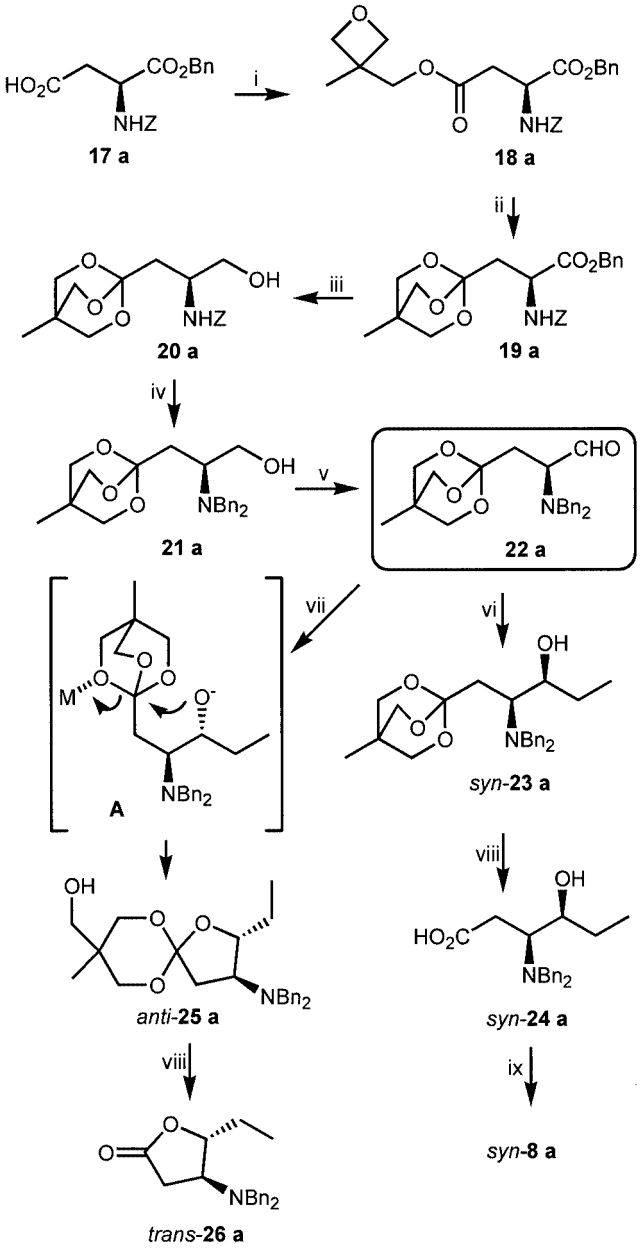
A shorter approach to *syn*- and *anti*-**8a** from L-aspartic acid was attempted. The idea was to reduce selectively the carboxylic group at C-1 maintaining the carboxylic group at C-4, avoiding the protection of the secondary hydroxylic group and the final oxidation of the primary one. The first attempt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

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).



Scheme 4. Reagents and conditions: (i) 1. CH_3COCl, MeOH, 0 °C. 2. Propylene oxide, EtOH, reflux. (ii) ZCl, K_2CO_3, H_2O/Et_2O, 20 °C. (95%). (iii) 1. $ClCO_2Et$, 4-methylmorpholine, THF, −10 °C. 2. $NaBH_4$, MeOH, 0 °C. (48%). (iv) 1. H_2, Pd-C, HCl in MeOH. 2. BnBr, K_2CO_3, CH_3CN, reflux. (66%). (v) TBDMSCl, imidazole, DMF, 20 °C. (85%). (vi) 1. H_2, Pd-C, MeOH, room temp. 2. BnBr, K_2CO_3, CH_3CN, reflux. (75%). (vii) 1% HCl in THF, 0 °C. **11a** (34%), plus **14a** (26%)

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-3-methyloxetane 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 5. Reagents and conditions: (i) 1. Cs_2CO_3, H_2O, 20 °C. 2. 3-(Bromomethyl)-2-methyloxetane, DMF, 20 °C. (81%). (ii) $BF_3{\cdot}Et_2O$, CH_2Cl_2, −30 °C. (90%). (iii) LAH, THF, 0 °C. (78%). (iv) 1. H_2, $Pd(OH)_2/C$, MeOH, room temp. 2. BnBr, K_2CO_3, CH_3CN, room temp. (73%). (v) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C. (95%). (vi) Et_2Zn, hexane/toluene, 0 °C. (70%). (vii) EtMgBr, THF/Et_2O, 0 °C. (62%). (viii) 2 N HCl THF/H_2O, reflux. 64% for *trans*-**26a**, and 52% for *syn*-**24a**. (ix) H_2, $Pd(OH)_2$-C, MeOH/H_2O (1:1). (60%)

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-4-hydroxyhexanoic 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**.

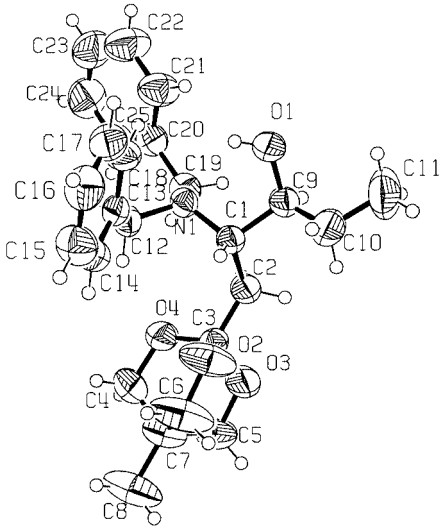


Figure 1. ORTEP representation of X-ray for compound *syn*-**23a**

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 ^{1}H NMR (300 MHz) and ^{13}C 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 quenched with aqueous saturated solution of ammonium chloride (70 mL). The organic layer was separated and the aqueous phase was extracted with diethyl ether (3 × 50 mL). The combined organic layers were washed with brine, and dried with anhydrous Na_2SO_4. 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, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3400, 740, 695 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 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, $C(CH_3)_3$], 1.18 (m, 1 H, CHHCH$_3$), 1.58 (m, 2 H, CHHCH$_3$ 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, TBDMSOCH_2), 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. ^{13}C NMR ($CDCl_3$): δ = −5.3 (SiCH_3), 10.1 (CH_3CH_2), 18.4 [$C(CH_3)_3$], 26.0 [$C(CH_3)_3$], 26.6 (CH_2CH_3), 29.4 (TBDMSOCH$_2$CH_2), 54.0 (CH_2Ph), 59.4 (*C*HN), 62.0 (TBDMSOCH_2), 71.7 (*C*HOH), 127.1, 128.4, 129.1 ($CH_{arom.}$), 139.1 ($C_{arom.}$) ppm. $C_{26}H_{41}NO_2Si$ (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 Et_2Zn 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, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3420, 740, 695 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 0.10 (s, 3 H, CH_3Si), 0.11 (s, 3 H, CH_3Si), 0.91 (t, J = 6.2 Hz, 3 H, CH_3CH_2), 0.95 [s, 9 H, $C(CH_3)_3$], 1.16 (m, 1 H, CHHCH$_3$), 1.34 (m, 1 H, CHHCHN), 1.60 (m, 1 H, CHHCH$_3$), 1.66 (m, 2 H, CH_2CH_2CHN), 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 Hz, 2 H, TBDMSOCH_2), 3.88 (d, J = 13.2 Hz, 2 H, CHHPh), 4.47 (br. s, 1 H, OH), 7.20−7.35 (m, 10 H, $H_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$): δ = −5.3 [$(CH_3)_2$Si], 10.2 (CH_3CH_2), 18.3 [$C(CH_3)_3$], 22.0 (CH_2CHN), 25.9 [$C(CH_3)_3$], 26.7 (CH_2CH_3), 32.4 (CH_2CH_2CHN), 53.9 (CH_2Ph), 62.4 (*C*HN), 62.9 (TBDMSOCH_2), 71.7 (*C*HOH), 127.1, 128.4, 129.1 ($CH_{arom.}$), 138.9 ($C_{arom.}$) ppm. $C_{27}H_{43}NO_2Si$ (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 NH_4Cl (40 mL) was added and the mixture was extracted with diethyl ether (2 × 20 mL). The combined organic layers were washed with brine, dried with anhydrous Na_2SO_4 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, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3420, 740, 690 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.03 (s, 3 H, SiCH_3), 0.05 (s, 3 H, SiCH_3), 0.87 (t, *J* = 7.4 Hz, 3 H, CH_3CH_2), 0.87 [s, 9 H, C(CH_3)$_3$], 1.37 (m, 1 H, C*H*HCH$_3$), 1.73 (m, 2 H, CH*H*CH$_3$ and C*H*HCHN), 2.01 (m, 1 H, CH*H*CHN), 2.69 (m, 1 H, C*H*N), 3.00 (d, *J* = 5.8 Hz, 1 H, O*H*), 3.53 (d, *J* = 13.8 Hz, 2 H, C*H*HPh), 3.58 (m, 2 H, TBDMSOC*H*H and C*H*OH), 3.71 (d, *J* = 13.8 Hz, 2 H, CH*H*Ph), 3.84 (m, 1 H, TBDMSOCH*H*), 7.20−7.40 (m, 10 H, $H_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$): δ = −0.5 [Si(*C*H$_3$)$_2$], 10.2 (*C*H$_3$CH$_2$), 18.2 [*C*(CH$_3$)$_3$], 25.9 [C(*C*H$_3$)$_3$], 27.8 (*C*H$_2$CH$_3$), 28.5 (TBDMSOCH$_2$*C*H$_2$), 54.7 (*C*H$_2$Ph), 59.4 (*C*HN): 62.4 (TBDMSO*C*H$_2$), 72.9 (*C*HOH), 126.8, 128.1, 128.8 (*C*H$_{arom.}$), 139.9 (*C*$_{arom.}$) ppm. $C_{26}H_{41}NO_2Si$ (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, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3420, 740, 690 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.04 (s, 3 H, SiCH_3), 0.05 (s, 3 H, SiCH_3), 0.90 [s, 9 H, C(CH_3)$_3$], 0.92 (t, *J* = 7.3 Hz, 3 H, CH_3CH_2), 1.35 (m, 1 H, C*H*HCH$_3$), 1.54 (m, 3 H, CH*H*CH$_3$, C*HH*CH$_2$CHN), 1.75 (m, 2 H, C*HH*CHN), 2.16 (br. s, 1 H, O*H*), 2.64 (m, 1 H, C*H*N), 3.58 (m, 3 H, C*H*OH, TBDMSOC*H*$_2$), 3.67 (s, 4 H, C*H*$_2$Ph), 7.20−7.35 (m, 10 H, $H_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$): δ = −5.3 [(*C*H$_3$)$_2$Si], 11.0 (*C*H$_3$CH$_2$), 18.3 [*C*(CH$_3$)$_3$], 21.3 (*C*H$_2$CHN), 25.9 [C(*C*H$_3$)$_3$], 27.6 (*C*H$_2$CH$_3$), 30.6 (*C*H$_2$CH$_2$CHN), 54.9 (*C*H$_2$Ph), 60.5 (*C*HN), 63.0 (TBDMSO*C*H$_2$), 72.5 (*C*HOH), 126.9, 128.2, 128.9 (*C*H$_{arom.}$), 140.0 (*C*$_{arom.}$) ppm. $C_{27}H_{43}NO_2Si$ (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 CH_2Cl_2 (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. H_2O (2.5 mL) and EtOAc (20 mL) were added to the mixture, and the organic phase was separated, dried with anhydrous $MgSO_4$, 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, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 0.07 [s, 6 H, (CH_3)$_2$Si], 0.90 [s, 9 H, (CH_3)$_3$C], 1.03 (t, *J* = 7.1 Hz, 3 H, CH$_2$CH_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, C*H*NH), 3.76 (m, 2 H, TBDMSOCH_2), 4.16 (ddd, J_1 = 6.7, J_2 = 6.3, J_3 = 5.7 Hz, C*H*O), 5.30 (br. s, 1 H, N*H*) ppm. $C_{13}H_{27}NO_3Si$ (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%). $[\alpha]_D^{20}$ = −12.9 (*c* = 0.4, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 0.10 [s, 6 H, (CH_3)$_2$Si], 0.90 [s, 9 H, (CH_3)$_3$C], 1.06 (t, *J* = 7.4 Hz, 3 H, CH$_2$CH_3), 1.65 (m, 4 H, C*HH*CH$_3$ and CH_2CHN), 3.78 (m, 2 H, TBDMSOCH_2), 3.92 (ddd, J_1 = 8.8, J_2 = 7.6, J_3 = 4.4 Hz, 1 H, C*H*N), 4.51 (ddd, J_1 = 9.7, J_2 = 7.6, J_3 = 4.2 Hz, 1 H, C*H*O), 5.75 (br. s, 1 H, N*H*) 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. $[\alpha]_D^{20}$ = −43.5 (*c* = 1.1, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3260, 1740, 1460, 1385 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.06 (s, 6 H, CH_3Si), 0.89 (s, 9 H, CCH_3), 1.02 (t, *J* = 7.4 Hz, 3 H, CH_3CH$_2$), 1.55−1.80 (m, 6 H, CH_2CHN, CH_2CH$_2$CHN, CH_2CH$_3$), 3.48 (m, 1 H, C*H*N), 3.65 (t, *J* = 5.5 Hz, 2 H, TBDMSOCH_2), 4.10 (dt, J_1 = 5.7, J_2 = 6.7 Hz, 1 H, C*H*O), 6.17 (br. s, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$): δ = −5.4 [(*C*H$_3$)$_2$Si], 9.0 (*C*H$_3$CH$_2$), 18.3 [*C*(CH$_3$)$_3$], 25.9 [C(*C*H$_3$)$_3$], 27.7 (*C*H$_2$CH$_3$), 28.7 (*C*H$_2$CHN), 32.6 (TBDMSOCH$_2$*C*H$_2$), 57.5 (*C*HN), 62.5 (TBDMSO*C*H$_2$), 83.8 (*C*HO), 159.2 (NH*C*O$_2$) ppm. $C_{14}H_{29}NO_3Si$ (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). $[\alpha]_D^{20}$ = −9.6 (*c* = 1.9, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3250, 1730, 1450, 1380 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.06 [s, 6 H, (CH_3)$_2$Si], 0.89 [s, 9 H, C(CH_3)$_3$], 1.06 (t, *J* = 7.3 Hz, 3 H, CH_3CH$_2$), 1.45−1.85 (m, 6 H, CH_2CH$_3$, CH_2CH$_2$CHN, CH_2CHN), 3.66 (m, 2 H, TBDMSOCH_2), 3.78 (m, 1 H, C*H*N), 4.50 (ddd, J_1 = 9.6, J_2 = 7.5, J_3 = 4.4 Hz, 1 H, C*H*O), 6.17 (br. s, 1 H, N*H*) ppm. ^{13}C NMR ($CDCl_3$): δ = −5.4 [(*C*H$_3$)$_2$Si], 10.4 (*C*H$_3$CH$_2$), 18.2 [*C*(CH$_3$)$_3$], 22.4 (*C*H$_2$CH$_3$), 25.9 [C(*C*H$_3$)$_3$], 26.9 (*C*H$_2$CHN), 29.2 (TBDMSOCH$_2$*C*H$_2$), 55.5 (*C*HN), 62.6 (TBDMSO*C*H$_2$), 81.7 (*C*HO), 159.6 (NH*C*O$_2$) ppm. $C_{14}H_{29}NO_3Si$ (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 CH_2Cl_2 (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 NH_4Cl (35 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 25 mL), and the combined organic layers were washed with brine, dried ($MgSO_4$), 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, $CHCl_3$). IR (film): $\tilde{\nu}$ = 740, 700 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.04 (s, 3 H, SiCH_3), 0.05 (s, 3 H, SiCH_3), 0.41 (t, *J* = 7.4 Hz, 3 H, CH_3CH$_2$), 0.88 [s, 9 H, C(CH_3)$_3$], 1.58 (m, 1 H, C*H*HCH$_3$), 1.81 (m, 2 H, CH*H*CH$_3$ and C*H*HCHN), 1.96 (m, 1 H, CH*H*CHN), 2.81 (m, 1 H, C*H*N), 3.37 (s, 3 H, OCH_3), 3.42 (d, *J* = 13.4 Hz, 2 H, C*H*HPh), 3.44 (m, 1 H, C*H*OMEM), 3.51 (m, 2 H, CH_2O), 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, OCH*H*O), 7.15−7.40 (m, 10 H, C$H_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$): δ = −5.3 [Si (*C*H$_3$)$_2$], 9.7 (*C*H$_3$CH$_2$), 18.3 [*C*(CH$_3$)$_3$], 23.9 (*C*H$_2$CH$_3$), 26.0 [C(*C*H$_3$)$_3$], 27.4 (TBDMSOCH$_2$*C*H$_2$), 54.0 (*C*HN), 55.4 (*C*H$_2$Ph), 59.0 (O*C*H$_3$), 61.0 (TBDMSO*C*H$_2$), 67.2 (O*C*H$_2$CH$_2$O), 71.7 (OCH$_2$*C*H$_2$O), 81.80 (*C*HOH), 95.2 (O*C*H$_2$O), 126.6, 127.9, 129.2 (*C*H$_{arom.}$), 140.9 (*C*$_{arom.}$) ppm. $C_{30}H_{49}NO_4Si$ (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, $CHCl_3$). IR (film): $\tilde{\nu}$ = 740, 695 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.04 (s, 3 H, $SiCH_3$), 0.06 (s, 3 H, $SiCH_3$), 0.62 (t, J = 7.4 Hz, 3 H, CH_3CH_2), 0.89 [s, 9 H, $C(CH_3)_3$], 1.53 (m, 1 H, $CHHCH_3$), 1.70 (m, 2 H, $CHHCH_3$ and $CHHCHN$), 1.96 (m, 1 H, $CHHCHN$), 2.72 (m, 1 H, CHN), 3.40 (s, 3 H, OCH_3), 3.55 (m, 2 H, OCH_2CH_2O), 3.57 (d, J = 13.6 Hz, 2 H, $CHHPh$), 3.73 (m, 5 H, $TBDMSOCH_2$, $CHOMEM$, OCH_2CH_2O), 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. ^{13}C NMR ($CDCl_3$): δ = −0.5 [$Si(CH_3)_2$], 9.3 (CH_3CH_2), 18.9 [$C(CH_3)_3$], 24.6 (CH_2CH_3), 26.0 [$C(CH_3)_3$], 29.7 ($TBDMSOCH_2CH_2$), 54.4 (CH_2Ph), 55.2 (CHN), 59.0 (OCH_3), 62.1 ($TBDMSOCH_2$), 67.4 (OCH_2CH_2O), 71.8 (OCH_2CH_2O), 79.3 ($CHOMEM$), 95.0 (OCH_2O), 126.7, 128.0, 128.9 ($CH_{arom.}$), 140.3 ($C_{arom.}$) ppm. $C_{30}H_{49}NO_4Si$ (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 (CH_2Cl_2/hexane, 2:1): 1.22 g (2.3 mmol, 74%). Colorless oil. $[\alpha]_D^{20} = +25.1$ (c = 1.0, $CHCl_3$). IR (film): $\tilde{\nu}$ = 1600, 1490, 1450, 1360, 1250, 750, 700 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.07 [s, 6 H, $(CH_3)_2Si$], 0.48 (t, J = 7.4 Hz, 3 H, CH_3CH_2), 0.92 [s, 9 H, $C(CH_3)_3$], 1.57 (m, 4 H, $CHHCH_3$, $CHHCHN$, CH_2CH_2CHN), 1.78 (m, 2 H, $CHHCH_3$, $CHHCHN$), 2.53 (m, 1 H, CHN), 3.37 (s, 3 H, OCH_3), 3.45 (d, J = 13.4 Hz, 2 H, $CHHPh$), 3.52 (m, 3 H, $CHOMEM$, OCH_2CH_2O), 3.59 (m, 2 H, $TBDMSOCH_2$), 3.68 (m, 2 H, OCH_2CH_2O), 3.95 (d, J = 13.4 Hz, 2 H, $CHHPh$), 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. ^{13}C NMR ($CDCl_3$): δ = −5.3 [$(CH_3)_2Si$], 9.9 (CH_3CH_2), 18.3 [$C(CH_3)_3$], 20.3 (CH_2CH_3), 24.1 (CH_2CHN)), 26.0 [$C(CH_3)_3$], 30.7 (CH_2CH_2CHN), 55.3 (CH_2Ph), 57.6 (CHN), 59.0 (OCH_3), 63.2 ($TBDMSOCH_2$), 67.3 (OCH_2CH_2O), 71.7 (OCH_2CH_2O), 81.5 ($CHOMEM$), 95.3 (OCH_2O), 126.6, 128.0, 129.2 ($CH_{arom.}$), 140.9 ($C_{arom.}$) ppm. $C_{31}H_{51}NO_4Si$ (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 (CH_2Cl_2): 1.30 g (2.45 mmol, 70%). Colorless oil. $[\alpha]_D^{20} = -3.4$ (c = 1.0, $CHCl_3$). IR (film): $\tilde{\nu}$ = 1595, 1490, 1450, 1360, 745, 700 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.02 (s, 3 H, CH_3Si), 0.03 (s, 3 H, CH_3Si), 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, $CHHCH_3$, $CHHCHN$ and $CHHCH_2OTBDMS$), 1.70 (m, 3 H, $CHHCH_3$, $CHHCHN$ and $CHHCH_2OTBDMS$), 2.56 (m, 1 H, CHN), 3.37 (s, 3 H, OCH_3), 3.52 (m, 4 H, OCH_2CH_2O and $CH_2OTBDMS$), 3.53 (d, J = 13.8 Hz, 2 H, $CHHPh$), 3.71 (m, 3 H, $CHOMEM$ and OCH_2CH_2O), 3.76 (d, J = 13.8 Hz, 2 H, $CHHPh$), 4.72 (d, J = 7.0 Hz, 1 H, $OCHHO$), 4.77 (d, J = 7.0 Hz, 1 H, $OCHHO$), 7.15−7.35 (m, 10 H, $H_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$): δ = −5.3 [$(CH_3)_2Si$], 9.4 (CH_3CH_2), 18.3 [$C(CH_3)_3$], 21.9 (CH_2CH_3), 24.9 (CH_2CHN), 26.0 [$C(CH_3)_3$], 31.3 (CH_2CH_2CHN), 54.3 (CH_2Ph), 58.1 (CHN), 59.0 (OCH_3), 63.2 ($TBDMSOCH_2$), 67.4 (OCH_2CH_2O), 71.8 (OCH_2CH_2O), 79.1 ($CHOMEM$), 95.1 (OCH_2O), 126.7, 128.0, 128.9 ($CH_{arom.}$), 140.4 ($C_{arom.}$) ppm. $C_{31}H_{51}NO_4Si$ (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 × 25 mL), and the combined organic extracts were washed with brine, dried (Na_2SO_4), 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, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3440, 750, 700 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.68 (t, J = 7.4 Hz, 3 H, CH_3CH_2), 1.57 (m, 1 H, $CHHCH_3$), 1.74 (m, 2 H, $CHHCH_2OH$ y $CHHCH_3$), 1.92 (m, 1 H, $CHHCH_2OH$), 2.83 (m, 1 H, CHN), 3.15 (br. s, 1 H, OH), 3.40 (s, 3 H, OCH_3), 3.50−3.70 (m, 6 H, OCH_2CH_2O, $CHOMEM$ and CH_2CHHOH), 3.63 (d, J = 13.2 Hz, 2 H, $CHHPh$), 3.84 (m, 1 H, CH_2CHHOH), 3.85 (d, J = 13.2 Hz, 2 H, $CHHPh$), 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, $H_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$): δ = 9.5 (CH_3CH_2), 24.3 (CH_2CH_3), 27.6 (CH_2CHN), 54.8 (CH_2Ph), 56.6 (CHN), 58.9 (OCH_3), 61.7 (CH_2OH), 67.6 (OCH_2CH_2O), 71.8 (OCH_2CH_2O), 81.4 ($CHOMEM$), 95.2 (OCH_2O), 126.8, 128.1, 129.2 ($CH_{arom.}$), 140.0 ($C_{arom.}$) ppm. $C_{24}H_{35}NO_4$ (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, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3420, 740, 695 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 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, $CHHCH_3$), 2.12 (m, 1 H, $CHHCHN$), 2.80 (m, 1 H, CHN), 3.39 (s, 3 H, OCH_3), 3.46 (d, J = 13.5 Hz, 2 H, $CHHPh$), 3.55 (m, 2 H, OCH_2CH_2O), 3.62 (m, 1 H, $CHHOH$), 3.74 (m, 3 H, OCH_2CH_2O 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. ^{13}C NMR ($CDCl_3$): δ = 9.4 (CH_3CH_2), 24.8 (CH_2CH_3), 27.3 (CH_2CHN), 54.1 (CH_2Ph), 58.2 (CHN), 58.9 (OCH_3), 62.6 (CH_2OH), 67.7 (OCH_2CH_2O), 71.6 (OCH_2CH_2O), 77.4 ($CHOMEM$), 94.9 (OCH_2O), 127.0, 128.2, 129.0 ($CH_{arom.}$), 139.2 ($C_{arom.}$) ppm. $C_{24}H_{35}NO_4$ (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, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3380, 755, 705 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.47 (t, J = 7.4 Hz, 3 H, CH_3CH_2), 1.45−1.85 (m, 6 H, $CHHCH_3$, $CH_2CHHCHN$), 2.15 (br. s, 1 H, OH), 2.55 (m, 1 H, CHN), 3.39 (s, 3 H, OCH_3), 3.45 (d, J = 13.4 Hz, 2 H, $CHHPh$), 3.55 (m, 5 H, $CHOMEM$, OCH_2CH_2O and CH_2OH), 3.65 (m, 1 H, $OCHHCH_2O$), 3.84 (m, 1 H, $OCHHCH_2O$), 3.98 (d, J = 13.4 Hz, 2 H, $CHHPh$), 4.64 (d, J = 7.2 Hz, 1 H, $OCHHO$), 4.72 (d, J = 7.2 Hz, 1 H, $OCHHO$), 7.20−7.40 (m, 10 H, $H_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$): δ = 9.9 (CH_3CH_2), 20.3 (CH_2CHN), 24.0 (CH_2CH_3), 30.6 (CH_2CH_2CHN), 55.3 (CH_2Ph), 57.7 (CHN), 59.1 (OCH_3), 63.0 (CH_2OH), 67.6 (OCH_2CH_2O), 71.9 (OCH_2CH_2O), 81.5 ($CHOMEM$), 95.3 (OCH_2O), 126.7, 128.0, 129.2 ($CH_{arom.}$), 140.8 ($C_{arom.}$) ppm. $C_{25}H_{37}NO_4$ (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, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3440, 750, 695 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.66 (t, J = 7.5 Hz, 3 H, CH_3CH$_2$), 1.61 (m, 6 H, CHHCH$_2$CHN, CHHCH$_3$, CHHCHN), 2.61 (m, 1 H, CHN), 3.38 (s, 3 H, OCH_3), 3.54 (d, J = 13.8 Hz, 2 H, CHHPh), 3.56 (m, 4 H, OCH_2CH_2O), 3.71 (m, 2 H, CH_2OH), 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. ^{13}C NMR ($CDCl_3$): δ = 9.4 (CH_3CH_2), 22.1 (CH_2CHN), 24.9 (CH_2CH_3), 31.1 (CH_2CH_2CHN), 54.2 (CH_2Ph), 58.1 (CHN), 59.0 (OCH_3), 62.9 (CH_2OH), 67.5 (OCH_2CH_2O), 71.7 (OCH$_2$$CH_2$O), 78.9 (CHOMEM), 95.1 (OCH_2O), 126.7, 128.0, 128.9 ($CH_{arom.}$), 140.1 ($C_{arom.}$) ppm. $C_{25}H_{37}NO_4$ (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, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3450, 1690 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.91 (t, J = 7.4 Hz, 3 H, CH_3CH$_2$), 1.45 [s, 9 H, (CH_3)$_3$C], 1.65 (m, 4 H, CH_2CH$_3$, HOCH$_2$CH_2), 3.39 (s, 3 H, CH_3O), 3.49 (m, 1 H, CHOMEM) 3.55 (m, 2 H, OCH$_2$-CH_2O), 3.66 (m, 2 H, CH_2OH), 3.75 (m, 2 H, OCH_2CH$_2$O), 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. ^{13}C NMR ($CDCl_3$): δ = 9.7 (CH$_2$$CH_3$), 24.3 ($CH_2CH_3$), 28.2 [($CH_3$)$_3$C], 36.4 ($CH_2$CHN), 48.3 (CHN), 58.6 ($CH_2$OH), 58.9 (O$CH_3$), 67.2 (OCH$_2$$CH_2$O), 71.6 (O$CH_2CH_2$O), 79.6 [$C$(CH$_3$)$_3$], 80.6 (CHOMEM), 94.7 (OCH_2O), 157.3 (CO_2tBu) ppm. $C_{15}H_{31}NO_6$ (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. $[\alpha]_D^{20} = -62.2$ ($CHCl_3$, c = 1.0). IR (film): $\tilde{\nu}$ = 3340, 1680 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.94 (t, J = 7.4 Hz, 3 H, CH_3CH$_2$), 1.45 (m, 2 H, CHHCH$_3$ and CHHCH$_2$OH; 1.46 [s, 9 H, C(CH_3)$_3$], 1.62 (m, 1 H, CHHCH$_3$), 1.81 (m, 1 H, CHHCH$_2$OH), 3.40 (s, 3 H, OCH_3), 3.60 (m, 7 H, OCH_2CH_2O, CHOMEM, CHHOH, OH), 3.82 (m, 2 H, CHHOH, CHN), 4.73 (d, J = 7.1 Hz, 1 H, OCHHO), 4.81 (d, J = 7.1 Hz, 1 H, OCHHO), 5.86 (d, J = 9.1 Hz, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$): δ = 10.1 (CH_3CH_2), 25.4 (CH_2CH_3), 28.2 [C(CH_3)$_3$], 31.4 (CH_2CHN), 48.9 (CHN), 58.3 (CH_2OH), 58.9 (OCH_3), 67.5 (OCH_2CH_2O), 71.4 (OCH$_2$$CH_2$O), 79.4 [$C$(CH$_3$)$_3$], 85.7 (CHOMEM), 96.6 (OCH_2O), 157.2 (CO_2tBu) ppm. $C_{15}H_{31}NO_6$ (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, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3400, 1670, 1480, 1440, 1350, 750 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.91 (t, J = 7.4 Hz, 3 H, CH_3CH$_2$), 1.43 [s, 9 H, C(CH_3)$_3$], 1.56 (m, 6 H, CHHCH$_3$, CHHCHN, CH_2CH$_2$CHN), 3.40 (s, 3 H, OCH_3), 3.48 (m, 1 H, CHOMEM), 3.57 (m, 2 H, OCH_2CH$_2$O), 3.65 (m, 4 H, OCH$_2$CH_2O and CH_2OH), 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, OCHHO), 4.82 (d, J = 10.5 Hz, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$): δ = 9.8 (CH_3CH_2), 24.0 (CH_2CH_3), 28.2 [C(CH_3)$_3$], 28.9 (CH_2CHN), 29.4 (CH_2CH_2CHN), 51.4 (CHN), 58.8 (OCH_3), 62.1 (CH_2OH), 67.2 (OCH_2CH_2O), 71.6 (OCH$_2$$CH_2$O), 78.8 [$C$(CH$_3$)$_3$], 80.3 (CHOMEM), 94.7 (OCH_2O), 156.1 (NHCO_2) ppm. $C_{16}H_{33}NO_6$ (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, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3340, 1685, 1450, 1365 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 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, CH_2CH$_2$CHN, CHHCH$_3$), 3.40 (s, 3 H, OCH_3), 3.47 (m, 1 H, CHOMEM), 3.58 (m, 2 H, OCH_2CH$_2$O), 3.66 (m, 4 H, CH_2OH, OCH$_2$CH_2O), 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. ^{13}C NMR ($CDCl_3$): δ = 10.2 (CH_3CH_2), 25.2 (CH_2CH_3), 25.5 (CH_2CHN), 28.4 [C(CH_3)$_3$], 29.0 (CH_2CH_2OH), 52.2 (CHN), 59.0 (OCH_3), 62.6 (CH_2OH), 67.4 (OCH_2CH_2O), 71.7 (OCH$_2$$CH_2$O), 78.9 [$C$(CH$_3$)$_3$], 85.0 (CHOMEM), 96.3 (OCH_2O), 156.2 (NHCO_2) ppm. $C_{16}H_{33}NO_6$ (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 × 25 mL), the combined ethereal layers were washed with H_2O and saturated NaCl solution, dried ($MgSO_4$) 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, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3280, 1700 cm^{-1}.^1H NMR ($CDCl_3$): δ = 0.93 (t, J = 7.4 Hz, 3 H, CH$_2$CH_3), 1.44 [s, 9 H, (CH_3)$_3$C], 1.56 (m, 2 H, CH_2CH$_3$), 2.61 (m, 2 H, CH_2CO$_2$H), 3.40 (s, 3 H, CH_3O), 3.57 (m, 1 H, CHO-MEM), 3.57 (m, 2 H, OCH$_2$CH_2O), 3.68 (m, 1 H, OCHHCH$_2$O), 3.78 (m, 1 H, OCHHCH$_2$O), 4.16 (m, 1 H, CHN), 4.72 (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. ^{13}C NMR ($CDCl_3$): δ = 9.7 (CH$_2$$CH_3$), 24.1 ($CH_2CH_3$), 28.3 [C($CH_3$)$_3$], 37.4 ($CH_2$CHN), 48.8 (CHN), 58.9 ($CH_3$O), 67.4 (OCH$_2$$CH_2$O), 71.6 (O$CH_2CH_2$O), 79.5 [$C$(CH$_3$)$_3$], 80.0 (CHOMEM), 95.0 (OCH_2O), 155.7 (CO_2tBu), 175.5 (CO_2H) ppm. $C_{15}H_{29}NO_7$ (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, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3340, 1700 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.95 (t, J = 7.4 Hz, 3 H, CH$_2$CH_3), 1.44 [s, 9 H, (CH_3)$_3$C]], 1.54 (m, 2 H, CH_2CH$_3$), 2.56 (m, 2 H, CH_2CO$_2$H), 3.40 (s, 3 H, CH_3O), 3.58 (m, 3 H, CHOMEM), OCH-$_2$CH_2O), 3.68 (m, 1 H, OCHHCH$_2$O), 3.78 (m,1 H, OCHHCH$_2$O), 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. ^{13}C NMR ($CDCl_3$): δ = 9.7 (CH_3CH_2), 24.9 (CH_2CH_3), 28.2 [(CH_3)$_3$C], 34.4 (CH_2CO_2H), 49.8 (CHN), 58.8 (CH_3O), 67.4 (CH_2O), 71.5 (CH_2O), 79.2 [(CH$_3$)$_3$$C$], 83.1 (CHOMEM), 96.1 (OCH_2O), 155.5 (NHCO_2tBu), 176.3 (CO_2H) ppm. $C_{15}H_{29}NO_7$ (335.4): calcd. C 53.72, H 8.72, N 4.18; found C 53.81, H 8.75, N 4.11.

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, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.98 (t, J = 7.4 Hz, 3 H, CH_3CH$_2$), 1.44 (m, 2 H, CHHCH$_3$), 1.53 [s, 9 H, C(CH$_3$)$_3$], 2.05 (m, 2 H, CHHCHN), 2.49 (m, 2 H, CHHCO$_2$H), 3.39 (s, 3 H, OCH$_3$), 3.55 (t, J = 4.6 Hz, 2 H, OCH$_2$CH$_2$O), 3.72 (m, 2 H, OCH$_2$-CH$_2$O), 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. ^{13}C NMR ($CDCl_3$): δ = 10.2 (CH$_3$CH$_2$), 18.6 (CH$_2$CH$_3$), 22.0 (CH$_2$CHN), 27.9 [C(CH$_3$)$_3$], 32.0 (CH$_2$CO$_2$H), 58.8 (CHN), 59.0 (OCH$_3$), 67.3 (OCH$_2$CH$_2$O), 71.6 (OCH$_2$CH$_2$O), 79.6 (CHO-MEM), 82.8 [C(CH$_3$)$_3$], 95.4 (OCH$_2$O), 149.7 (NHCO$_2$), 174.9 (CO$_2$H) ppm. $C_{16}H_{31}NO_7$ (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, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.96 (t, J = 7.5 Hz, 3 H, CH_3CH$_2$), 1.47 (m, 1 H, CHHCH$_3$), 1.54 [s, 9 H, C(CH$_3$)$_3$], 1.70 (m, 1 H, CHHCH$_3$), 2.00 (m, 2 H, CHHCHN), 2.36 (ddd, J_1 = 17.6, J_2 = 10.0, J_3 = 2.2 Hz, 1 H, CHHCO$_2$H), 2.72 (dt, J_1 = 17.6, J_2 = 10.0 Hz, 1 H, CHHCO$_2$H), 3.37 (s, 3 H, OCH$_3$), 3.52 (m, 2 H, OCH$_2$CH$_2$O), 3.61 (m, 2 H, OCH$_2$CH$_2$O), 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. ^{13}C NMR ($CDCl_3$): δ = 10.1 (CH$_3$CH$_2$), 17.3 (CH$_2$CH$_3$), 24.2 (CH$_2$CHN), 27.9 [C(CH$_3$)$_3$], 32.5 (CH$_2$CO$_2$H), 58.8 (OCH$_3$), 59.3 (CHN), 67.3 (OCH$_2$CH$_2$O), 71.6 (OCH$_2$CH$_2$O), 79.1 (CHO-MEM), 82.6 [C(CH$_3$)$_3$], 94.6 (OCH$_2$O), 149.5 (NHCO$_2$), 175.4 (CO$_2$H) ppm. $C_{16}H_{31}NO_7$ (349.4): calcd. C 55.00, H 8.94, N 4.01; found C 54.88, H 8.97, N 3.96.

(3*S*,4*S*)-3-Amino-4-hydroxyhexanoic Acid (*syn*-8a): 2 N HCl solution in THF/H_2O (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 × 10 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, CH_2Cl_2/MeOH/NH_4OH, 6:4:1) to give *syn*-**8a** as a colorless solid: 18 mg (0.12 mmol, 18%). $[\alpha]_D^{20} = -23.1$ (c = 0.6, H_2O). ^{1}H NMR (D_2O): δ = 0.92 (t, J = 7.4 Hz, 3 H, CH$_3$), 1.40 (m, 1 H, CHHCH$_3$), 1.60 (m, 1 H, CHHCH$_3$), 2.42 (dd, J_1 = 17.0, J_2 = 8.2 Hz, 1 H, CHHCO$_2$H), 2.55 (dd, J_1 = 17.0, J_2 = 4.7 Hz, 1 H, CHHCO$_2$H), 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. ^{13}C NMR (D_2O): δ = 11.4 (CH$_3$), 28.1 (CH$_2$CH$_3$), 38.2 (CH$_2$CO$_2$H), 55.9 (CHN), 74.2 (CHOH), 180.0 (CO$_2$H) ppm. $C_6H_{13}NO_3$ (147.2): calcd. C 48.97, H 8.90, N 9.52; found C 49.07, H 8.87, N 9.73.

(3*S*,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/Et_2O). 12 mg (0.084 mmol, 20%). $[\alpha]_D^{20} = -40.5$ (c = 0.7, H_2O). ^{1}H NMR (D_2O): δ = 0.92 (t, J = 7.4 Hz, 3 H, CH$_3$), 1.45 (m, 2 H, CHHCH$_3$), 2.35 (dd, J_1 = 17.0, J_2 = 10.1 Hz, 1 H, CHHCO$_2$H), 2.52 (dd, J_1 = 17.0, J_2 = 4.1 Hz, 1 H, CHHCO$_2$H), 3.51 (m, 1 H, CHN), 3.69 (m, 1 H, CHOH) ppm. ^{13}C NMR (D_2O): δ = 12.0 (CH$_3$), 27.4 (CH$_2$CH$_3$), 35.4 (CH$_2$CO$_2$H), 55.4 (CHN), 74.5 (CHOH), 180.6 (CO$_2$H) 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. ^{1}H NMR ($CDCl_3$): δ = 2.24 (dd, J_1 = 14.5, J_2 = 8.3 Hz, 1 H, CHHCO$_2$), 2.70 (dd, J_1 = 14.5, J_2 = 5.1 Hz, 1 H, CHHCO$_2$), 3.43 (d, J = 13.3 Hz, 2 H, CHHPh), 3.53 (m, 3 H, CHN, CHHOH), 3.67 (s, 3 H, OCH$_3$), 3.78 (d, J = 13.3 Hz, 2 H, CHHPh), 7.20−7.35 (m, 10 H, $H_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$): δ = 31.2 (CH$_2$CO$_2$), 51.8 (OCH$_3$), 53.3 (CH$_2$Ph), 56.5 (CHN), 61.3 (CH$_2$OH), 127.3, 128.4, 128.9 (CH$_{arom.}$), 138.7 ($C_{arom.}$), 172.5 (CO$_2$CH$_3$) 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 × 20 mL). The combined organic phases were dried ($MgSO_4$) 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, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 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, CO$_2$CH$_3$), 4.68 (m, 1 H, CHN), 5.12 (s, 2 H, CH$_2$Ph), 5.87 (d, J = 8.6 Hz, 1 H, NH), 7.20−7.30 (m, 5 H, $H_{arom.}$), 8.10 (br. s, 1 H, CO$_2$H) ppm. ^{13}C NMR ($CDCl_3$): δ = 36.2 (CH$_2$CO$_2$CH$_3$), 50.1 (CHN), 52.2 (OCH$_3$), 67.3 (CH$_2$Ph), 128.1, 128.2, 128.5 (CH$_{arom.}$), 135.9 ($C_{arom.}$), 156.1 (NCO$_2$Bn), 171.5 (CO$_2$CH$_3$), 175.1 (CO$_2$H) ppm. $C_{13}H_{15}NO_6$ (281.3): calcd. C 55.51, H 5.38, N 4.98; found C 55.83, H 5.42, N 4.96.

Methyl (*S*)-3-[(Benzyloxycarbonyl)amino]-4-hydroxybutanoate (13a): To a stirred solution of *N*-protected amino acid **12a** (5.17 g, 18.4 mmol, 1equiv.) 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, $NaBH_4$ (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 × 20 mL). The organic phase was washed consecutively with 1 N HCl (10 mL), H_2O (10 mL), 5% aq $NaHCO_3$ (10 mL), H_2O (10 mL), dried (Na_2SO_4), 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): $\tilde{\nu}$ = 3350, 1710, 1690, 740, 690 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 2.63 (d, J = 6.0 Hz, 2 H, CH$_2$CO$_2$CH$_3$), 2.90 (br. s, 1 H, OH), 3.66 (s, 3 H, OCH$_3$), 3.67 (m, 2 H, CH$_2$OH), 4.05 (m, 1 H, CHN), 5.08 (s, 2 H, CH$_2$Ph), 5.61 (d, J = 8.0 Hz, 1 H, NH), 7.34 (m, 5 H, $H_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$): δ = 35.4 (CH$_2$CO$_2$CH$_3$), 49.6 (CHN), 51.6 (OCH$_3$), 63.6 (CH$_2$Ph), 66.6 (CH$_2$OH), 127.9, 128.1, 128.3 (CH$_{arom.}$), 136.1 ($C_{arom.}$), 156.1 (CO$_2$Bn), 172.0 (CO$_2$CH$_3$) ppm. $C_{13}H_{17}NO_5$ (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. $[\alpha]_D^{20} = +18.9$ ($c = 0.7$, $CHCl_3$). IR (film): $\tilde{\nu} = 1770, 1160, 745, 695\ cm^{-1}$. ^1H NMR ($CDCl_3$): δ = 2.54 (dd, $J_1 = 17.8$, $J_2 = 8.1$ Hz, 1 H, C*H*HCO), 2.61 (dd, $J_1 = 17.8$, $J_2 = 8.1$ Hz, 1 H, CH*H*CO), 3.51 (d, $J = 13.8$ Hz, 2 H, C*H*HPh), 3.66 (d, $J = 13.8$ Hz, 2 H, CH*H*Ph), 3.76 (m, 1 H, C*H*N), 4.28 (dd, $J_1 = 9.9$, $J_2 = 5.2$ Hz, 1 H, C*H*HO), 4.33 (dd, $J_1 = 9.9$, $J_2 = 7.1$ Hz, 1 H, CH*H*O), 7.20−7.40 (m, 10 H, $H_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$): δ = 30.7 (CH_2COO), 54.5 (CH_2Ph), 56.0 (*C*HN), 71.0 (CH_2O_2C), 127.4, 128.4, 128.5 ($CH_{arom.}$), 138.2 ($C_{arom.}$), 176.2 (CO_2) ppm. $C_{18}H_{19}NO_2$ (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 TBDMSCl (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. $[\alpha]_D^{20} = -15.0$ ($c = 0.5$, $CHCl_3$). IR (film): $\tilde{\nu} = 3330, 1720, 730, 695\ cm^{-1}$. ^1H NMR ($CDCl_3$): δ = 0.03 [s, 6 H, $Si(CH_3)_2$], 0.87 [s, 9 H, $C(CH_3)_3$], 2.60 (m, 2 H, $CH_2CO_2CH_3$), 3.66 (s, 3 H, OCH_3), 3.68 (m, 2 H, CH_2OTBDMS), 4.11 (m, 1 H, C*H*N), 5.09 (s, 2 H, CH_2Ph), 5.35 (d, $J = 8.9$ Hz, 1 H, N*H*), 7.35 (m, 5 H, $H_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$): δ = −5.7 [$Si(CH_3)_2$], 18.1 [$C(CH_3)_3$], 25.7 [$C(CH_3)_3$], 35.2 ($CH_2CO_2CH_3$), 49.2 (*C*HN), 51.5 (OCH_3), 63.8 (TBDMSOCH_2), 66.5 (CH_2Ph), 128.0, 128.4 ($CH_{arom.}$), 136.3 ($C_{arom.}$), 155.6 (NCO_2Bn), 171.8 (CO_2CH_3) ppm. $C_{19}H_{31}NO_5Si$ (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.), K_2CO_3 (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. $[\alpha]_D^{20} = -25.3$ ($c = 1.2$, $CHCl_3$). IR (film): $\tilde{\nu} = 1725, 740, 695\ cm^{-1}$. ^1H NMR ($CDCl_3$): δ = 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, C*H*HCO_2CH_3), 2.59 (dd, $J_1 = 14.5$, $J_2 = 8.0$ Hz, 1 H, CH*H*CO_2CH_3), 3.28 (m, 1 H, C*H*N), 3.57 (s, 3 H, OCH_3), 3.62 (d, $J = 13.8$ Hz, 2 H, C*H*HPh), 3.72 (d, $J = 13.8$ Hz, 2 H, CH*H*Ph), 3.73 (d, $J = 5.5$ Hz, 2 H, TBDMSOCH_2), 7.15−7.35 (m, 10 H, $H_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$): δ = −5.7 ($SiCH_3$), −5.6 ($SiCH_3$), 18.1 [$C(CH_3)_3$], 25.8 [$C(CH_3)_3$], 33.9 (CH_2CO_2Me), 51.4 (OCH_3), 54.3 (CH_2Ph), 56.5 (*C*HN), 62.7 (TBDMSOCH_2), 126.7, 128.0, 128.7 ($CH_{arom.}$), 140.0 ($C_{arom.}$), 172.9 (CO_2CH_3) ppm. $C_{25}H_{37}NO_3Si$ (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 α-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 Et_2O (150 mL) and extracted with $NaHCO_3$ saturated solution (twice). The aqueous layer was washed with Et_2O and acidified with 10% HCl solution. The resulting oil was extracted with $CHCl_3$, washed with H_2O, dried with anhydrous Na_2SO_4 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). $[\alpha]_D^{20} = -10.5$ ($c = 1.0$, MeOH). IR (KBr): $\tilde{\nu} = 3600-2500, 1735, 1700, 1680, 750, 690\ cm^{-1}$. ^1H NMR ($CDCl_3$): δ = 2.90 (dd, $J_1 = 17.6$, $J_2 = 4.4$ Hz, 1 H, C*H*HCO_2H), 3.10 (dd, $J_1 = 17.6$, $J_2 = 4.4$ Hz, 1 H, CH*H*CO_2H), 4.68 (m, 1 H, C*H*N), 5.11 (s, 2 H, CH_2Ph), 5.17 (s, 2 H, CH_2Ph), 5.81 (d, $J = 8.6$ Hz, 1 H, N*H*), 7.30−7.35 (m, 10 H, $H_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$): δ = 36.4 (CH_2CO_2H), 50.2 (*C*HN), 67.3, 67.7 (CH_2Ph), 128.1, 128.2, 128.5, 128.6 ($CH_{arom.}$), 135.0, 135.9 ($C_{arom.}$), 156.0 (NHCO_2), 170.3 (CO_2Bn), 171.6 (CO_2H) ppm. $C_{19}H_{19}NO_6$ (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 H_2O (60 mL). $CsCO_3$ (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% $NaHCO_3$, 3% NH_4Cl (twice), saturated NaCl, dried ($MgSO_4$), 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. $[\alpha]_D^{20} = +3.0$ ($c = 1.6$, $CHCl_3$). IR (film): $\tilde{\nu} = 3310, 1710, 740, 690\ cm^{-1}$. ^1H NMR ($CDCl_3$): δ = 1.24 (s, 3 H, CH_3), 2.92 (dd, $J_1 = 17.2$, $J_2 = 4.5$ Hz, 1 H, C*H*HCHN), 3.10 (dd, $J_1 = 17.2$, $J_2 = 4.5$ Hz, 1 H, CH*H*CHN), 3.98 (d, $J = 11.1$ Hz, 1 H, CHHO_2C), 4.14 (d, $J = 11.1$ Hz, 1 H, CH*H*O_2C), 4.37 (m, 4 H, OCH_2), 4.71 (m, 1 H, C*H*N), 5.11 (s, 2 H, CH_2Ph), 5.16 (d, $J = 17.8$ Hz, 1 H, C*H*HPh), 5.20 (d, $J = 17.8$ Hz, 1 H, CH*H*Ph), 6.05 (br. s, 1 H, N*H*), 7.25−7.40 (m, 10 H, $H_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.8 (CH_3), 36.7 (CH_2CHN), 38.9 (CCH_3), 50.4 (*C*HN), 67.0, 67.5 (CH_2Ph), 68.9 (CH_2O_2C), 79.2, 79.3 (OCH_2), 128.0, 128.1, 128.3, 128.5, 128.6 ($CH_{arom.}$), 135.1, 136.1 ($C_{arom.}$), 156.0 (NHCO_2), 170.4 (CO_2), 170.6 (CO_2) ppm. $C_{24}H_{27}NO_7$ (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 CH_2Cl_2 (15 mL) and cooled to −30 °C under N_2. A solution of $BF_3{\cdot}OEt_2$ (300 μL) in CH_2Cl_2 was added, and the solution was stirred and warmed to room temperature. After 8 h, Et_3N (250 μL) in Et_2O (100 mL) was added, the solid was removed by filtration and the solution evaporated to dryness. The residue was purified by recrystallization from CH_2Cl_2/hexane to yield 3.14 g (7.1 mmol, 90%) of colorless crystals, mp. 102−103 °C (from hexane/EtOAc). $[\alpha]_D^{20} = -4.8$ ($c = 0.5$, $CHCl_3$). IR (KBr): $\tilde{\nu} = 3400, 1730, 1700, 740, 695\ cm^{-1}$. ^1H NMR ($CDCl_3$): δ = 0.73 (s, 3 H, CH_3), 2.14 (dd, $J_1 = 14.7$, $J_2 = 4.4$ Hz, 1 H, C*H*HCHN), 2.39 (dd, $J_1 = 14.7$, $J_2 = 5.8$ Hz, 1 H, CH*H*CHN), 3.77 (s, 6 H, OCH_2), 4.52 (m, 1 H, C*H*N), 5.11 (s, 2 H, CH_2Ph), 5.14 (s, 2 H, CH_2Ph), 6.07 (d, $J = 8.3$ Hz, 1 H, N*H*), 7.30−7.35 (m, 10 H, $H_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.2 (CH_3), 30.1 (CCH_3), 37.1 (CH_2CHN), 50.3 (*C*HN), 66.7 (CH_2Ph), 72.2 (OCH_2), 108.0 (CO_3), 128.0, 128.1, 128.2, 128.3, 128.4 ($CH_{arom.}$), 135.7, 136.4 ($C_{arom.}$), 156.0 (NHCO_2), 171.2 (CO_2Bn) ppm. $C_{24}H_{27}NO_7$ (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 Et_3N, hexane/EtOAc, 1:1): 1.43 g (4.2 mmol, 78%). Colorless oil. $[\alpha]_D^{20} = -5.5$ (c = 1.2, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3420, 1715, 1045, 990, 740, 700 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.79 (s, 3 H, CH_3), 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, CH_2O), 3.96 (dd, J_1 = 12.0, J_2 = 6.3 Hz, 1 H, CHHOH), 5.08 (s, 2 H, CH_2Ph), 5.60 (d, J = 7.4 Hz, 1 H, NH), 7.25−7.40 (m, 5 H, $H_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.3 (CH_3), 30.2 (CCH_3), 36.9 (CH_2CHN), 49.3 (CHN), 64.5 (CH_2OH), 66.6 (CH_2Ph), 72.4 (CH_2O), 108.3 (CO_3), 128.1, 128.4 ($CH_{arom.}$), 136.5 ($C_{arom.}$), 156.4 ($NHCO_2$) ppm. $C_{17}H_{23}NO_6$ (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 K_2CO_3 (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 Et_3N, 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, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3460, 1040, 990, 750, 700 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.80 (s, 3 H, CH_3), 1.57 (dd, J_1 = 14.3, J_2 = 9.1 Hz, 1 H, CHHCHN), 2.18 (dd, J_1 = 14.3, J_2 = 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, CH_2O), 7.20−7.40 (m, 10 H, $H_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.4 (CH_3), 30.2 (CCH_3), 32.2 (CH_2CHN), 53.0 (CH_2Ph), 54.6 (CHN), 61.7 (CH_2OH), 72.5 (CH_2O), 108.4 (CO_3), 127.0, 128.2, 129.2 ($CH_{arom.}$), 139.3 ($C_{arom.}$) ppm. $C_{23}H_{29}NO_4$ (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, $CHCl_3$). IR (film): $\tilde{\nu}$ = 1725, 1495, 1555, 1055, 750, 700 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.77 (s, 3 H, CH_3), 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, CH_2O), 7.20−7.45 (m, 10 H, $H_{arom.}$). 9.59 (s, 1 H, CHO) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.3 (CH_3), 29.9 (CH_2CHN), 30.1 (CCH_3), 54.6 (CH_2Ph), 62.1 (CHN), 72.4 (CH_2O), 108.3 (CO_3), 127.0, 128.0, 128.9 ($CH_{arom.}$), 139.2 ($C_{arom.}$), 200.9 (CHO) ppm. $C_{23}H_{27}NO_4$ (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 Et_2Zn (2 equiv.) by the method described for compounds **2a, b**. The product *syn*-**23a** was purified by flash chromatography (silica gel treated with Et_3N, 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, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3290, 1045, 990, 740, 700 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.83 (s, 3 H, CH_3), 0.86 (t, J = 7.4 Hz, 3 H, CH_3CH$_2$), 1.22 (m, 1 H, CHHCH$_3$), 1.61 (m, 1 H, CHHCH$_3$), 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, CH_2O), 7.20−7.40 (m, 10 H, $H_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$): δ = 10.3 (CH_3C), 14.5 (CH_3CH_2), 26.1 (CH_2CH_3), 30.3 (CCH_3), 32.7 (CH_2CHN), 53.5 (CH_2Ph), 57.3 (CHN), 71.8 ($CHOH$), 72.5 (CH_2O), 108.5 (CO_3), 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.

(3*S*,4*S*)-3-Dibenzylamino-4-hydroxyhexanoic Acid (*syn*-24a): A mixture of *syn*-**23a** (140 mg, 0.34 mmol) and 2 N HCl in THF/H_2O (5 mL) was stirred at reflux for 5 h. The pH of the reaction was adjusted to 6 with saturated $NaHCO_3$ solution and the mixture extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, 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, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3280, 1720, 735, 700 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 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, CHHCO$_2$H), 2.48 (dd, J_1 = 16.4, J_2 = 8.9 Hz, 1 H, CHHCO$_2$H), 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, $H_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$): δ = 9.1 (CH_3), 26.7 (CH_2CH_3), 31.3 (CH_2CO_2H), 53.8 (CH_2Ph), 59.6 (CHN), 71.5 ($CHOH$), 128.3, 128.7, 130.1 ($CH_{arom.}$), 134.8 ($C_{arom.}$), 175.3 (CO_2) ppm. $C_{20}H_{25}NO_3$ (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/Et_2O as described for *anti*-**2a, b**, and purified by flash chromatography (silica gel treated with Et_3N, hexane/EtOAc, 5:1): 127 mg (0.31 mmol, 62%). Colorless oil. $[\alpha]_D^{20} = +73.0$ (c = 1.1, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3450, 1050, 750, 700 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.88 (t, J = 7.4 Hz, 3 H, CH_3CH$_2$), 1.16 (s, 3 H, CH_3C), 1.45 (m, 1 H, CHHCH$_3$), 1.65 (m, 1 H, CHHCH$_3$), 1.72 (br. s, 1 H, OH), 2.10 (dd, J_1 = 13.5, J_2 = 9.3 Hz, 1 H, CHHCHN), 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 CH_2O), 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, J_1 = 11.0, J_2 = 4.4 Hz, 2 H, CHHO), 7.15−7.40 (m, 10 H, $H_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$): δ = 10.3 (CH_3C), 18.1 (CH_3CH_2), 27.1 (CH_2CH_3), 29.6 (CCH_3), 34.4 (CH_2CHN), 55.0 (CH_2Ph), 61.8 (CHN), 66.8, 67.1, 67.4 (CH_2O and CH_2OH), 81.2 ($CHOH$), 117.9 (CO_3), 126.9, 128.2, 128.5 ($CH_{arom.}$), 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 72.76, H 8.24, N 3.26.

(3*S*,4*R*)-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. $[\alpha]_D^{20} = +84.0$ (c = 0.4, $CHCl_3$). IR (film): $\tilde{\nu}$ = 1775, 1170, 975, 750, 700 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.90 (t, J = 7.4 Hz, 3 H, CH_3), 1.59 (m, 2 H, CH_2CH$_3$), 2.55 (dd, J_1 = 18.2, J_2 = 8.6 Hz, 1 H, CHHCO$_2$), 2.65 (dd, J_1 = 18.2, J_2 = 5.7 Hz, 1 H, CHHCO$_2$), 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, CHHPh), 4.43 (m, 1 H, CHOH), 7.20−7.40 (m, 10 H, $H_{arom.}$) ppm. ^{13}C NMR ($CDCl_3$): δ = 9.4 (CH_3), 27.4 (CH_2CH_3), 28.8 (CH_2CO_2), 54.1 (CH_2Ph), 59.2 (CHN), 83.9 ($CHOH$), 127.3, 128.4, 128.5 ($CH_{arom.}$), 138.3 ($C_{arom.}$), 175.9 (CO_2) ppm. $C_{20}H_{23}NO_2$ (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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