Pergamon

Tetrahedron 57 (2001) 8521–8530

TETRAHEDRON

Diastereoselective synthesis of enantiopure γ-amino-β-hydroxy acids by Reformatsky reaction of chiral α-dibenzylamino aldehydes

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Received 28 February 2001; revised 18 June 2001; accepted 2 August 2001

Abstract—*N*,*N*-Dibenzylamino aldehydes **1** react with Reformatsky's reagent leading to *anti*-γ-dibenzylamino-β-hydroxy esters **2** as the major stereoisomers. Treatment of **2** with TFA followed by hydrogenolysis on Pearlman's catalyst yields the corresponding γ-amino-β-hydroxy acids **10**. Contrarily, some *N*-butoxycarbonyl (Boc) amino aldehydes lead to *syn*-γ-*tert*-butoxycarbonylamino-β-hydroxy esters as the major product.

1. Introduction

The synthesis of γ-amino-β-hydroxy acids has recently received increasing interest because they are peptide components which act as protease inhibitors of aspartic acid.[1] The activity of these substrates depends on the stereochemistry and thus a great number of stereoselective synthesis has been developed.[2] In this way, the diastereoselective reduction of γ-amino-β-keto esters[3] and related compounds[4] has been frequently used in the synthesis of *anti* adducts with moderate selectivities,[3a–e] although $NaBH_4$ reduction of chiral γ-(*N*,*N*-dibenzylamino)-β-keto esters yields *syn* diastereoisomers in good diastereomeric ratios.[3f,g]

The stereoselective aldol reaction of protected α-amino aldehydes with ester enolates also allowed the preparation of these compounds. In this way, the lithium enolate of ethyl acetate adds stereoselectively to *N*,*N*-dibenzylamino aldehydes leading to *anti* adducts in good dr,[5] whereas the addition of the same enolate to Cbz- or butoxycarbonyl (Boc)-amino aldehydes yields *syn* diastereoisomers with moderate selectivity.[6] Excellent dr[7] in favor of *anti* adducts, including some stereoselective aldolic reaction of L-proline derivatives,[8] are obtained when Lewis acids are used as catalysts in these condensations.

On the contrary, there are scarcely references on synthesis of these compounds by Reformatsky reaction on α-amino aldehydes.[9] For example, *syn*-γ-amino-α,α-difluoro-β-hydroxy esters has been prepared as the major diastereomer by reaction of *N*-Boc-amino aldehydes with ethyl bromodifluoroacetate under Reformatsky conditions in THF at room temperature, and the same isomer was obtained as single product when the reaction was carried out at reflux of the same solvent.[9a]

As a part of a project directed to the use of α-amino aldehydes in the synthesis of chiral targets,[10] we present now the results on the Reformatsky reaction of a variety of chiral α-amino aldehydes.

2. Results and discussion

N,*N*-Dibenzylamino aldehydes **1a**–**f** react with *tert*-butoxycarbonylmethylzinc bromide leading to γ-dibenzylamino-β-hydroxy esters **2a**–**f** in good chemical yields and moderate diastereoselectivities. The major diastereomer formed was always *anti* (Scheme 1 and Table 1).

Different experimental conditions has been tested on α-amino aldehyde **1b** (entries 2–6 in Table 1) and the better reaction conditions were when 3 equiv. of Reformatsky reagent at 0°C and THF as solvent were used (entry 3). Other reaction conditions, such as the use of only 2 equiv. of zinc reagent (entry 2), a decrease (entry 4) or an increase (entry 5) of the reaction temperature, or the use of THF–diethyl ether as solvent (entry 6) did not increase the stereoselection and decreased the yield of the reaction.

α-Amino aldehydes **1a**,**c**–**f** reacted with Reformatsky reagent in the above experimental conditions leading to γ-dibenzylamino-β-hydroxy esters **2a**,**c**–**f** with moderate stereoselectivities, which are practically independent on

Keywords: diastereoselective synthesis; amino alcohols; amino aldehydes; amino acids.

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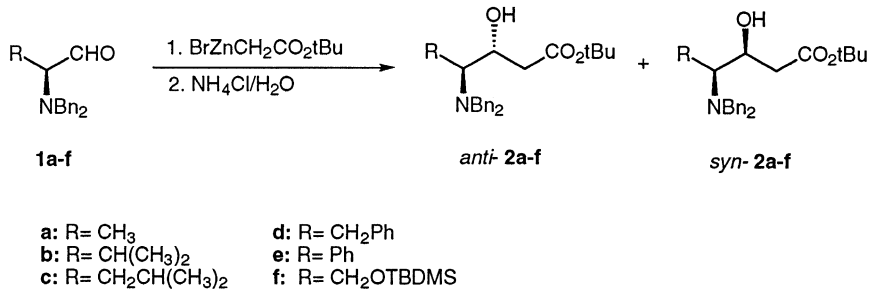
PII: S0040-4020(01)00804-3



Scheme 1.

Table 1. Stereoselective addition of $BrZnCH_2CO_2tBu$ to *N,N*-dibenzylamino aldehydes **1a–f**

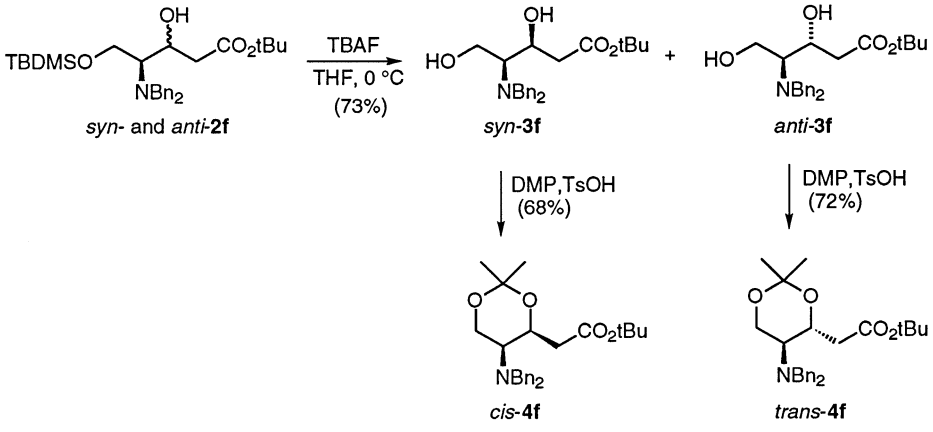
Entry	1	Solvent	Temperature (°C)	*t* (h)	2	Yield (%)[a]	*anti*/*syn*[b]
1	**1a**	THF	0	2	**2a**	69	78:22
2	**1b**[c]	THF	0	19	**2b**	35[d]	80:20
3	**1b**	THF	0	5	**2b**	82	80:20
4	**1b**	THF	−78 to 0	6/16	**2b**	30[e]	78:22
5	**1b**	THF	66	1	**2b**	68	75:25
6	**1b**	THF/Et_2O (1/4)	0	20	**2b**	40	78:22
7	**1c**	THF	0	1.5	**2c**	87	78:22
8	**1d**	THF	0	1.5	**2d**	70	74:26
9	*ent*-**1e**	THF	0	2	*ent*-**2e**	75	62:38
10	**1f**	THF	0	2	**2f**	78	76:24

Unless otherwise noted, reactions were run with 3 equiv. of Reformatsky reagent.
[a] Numbers correspond to combined yield of pure and isolated diastereoisomers.
[b] The diastereomeric ratio was determined by integration of the ^1H NMR spectra of the reaction mixture.
[c] Reaction was run with 2 equiv. of Reformatsky reagent.
[d] 21% of amino aldehyde **1b** was recovered.
[e] 25% of amino aldehyde **1b** was recovered.

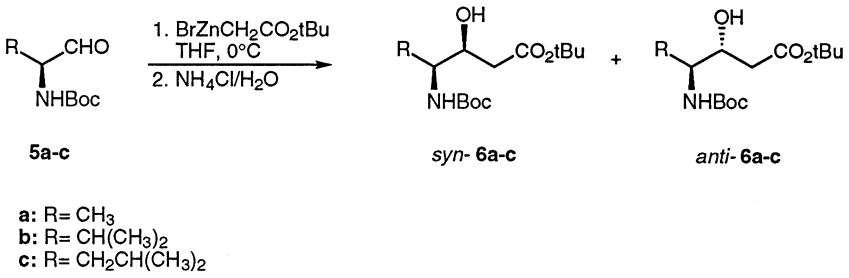
the size of the substituent or even the presence of the additional heteroatom at the chain. It is interesting to note that the worst stereoselection was obtained for (*R*)-phenylglycinal derivative *ent*-**1e** (entry 9).

Diastereomeric γ-dibenzylamino-β-hydroxy esters **2a**,**c–e** were easily separated by flash chromatography on silica gel and their structure confirmed by comparison of their spectral data with those previously described[3g] for **2b–d**, or by ^1H NMR. In this way, the proton at C-3 appeared downfield for *anti* than for *syn* diastereomers, whereas the vicinal coupling constant ($^{1,3}J$) for proton at C-3 and C-4 was higher for *syn* than for *anti*-derivatives.[10b,11] Diastereoisomers *syn*- and *anti*-**2f** was only isolated by flash chromatography after desilylation with TBAF in THF at 0°C to *syn*- and *anti*-**3f**, which, after separation were converted into dioxanes *cis*- and *trans*-**4f**, respectively by treatment with 2,2-dimethoxypropane (TsOH, 50°C) (Scheme 2). The stereochemistry of *cis*- and *trans*-**4f** was established on the basis of the coupling constant[12] for protons at C-4 and C-5 which was smaller ($^{1,3}J$=8.6 Hz) for *cis*-**4f** than for *trans*-**4f** ($^{1,3}J$=9.9 Hz).

The influence of the protecting group at the nitrogen was tested on α-aminoaldehydes **5a–c** where the two benzyl groups have been changed by an electron withdrawing *t*-Boc group on the nitrogen. Interestingly, the reaction of **5b** with *tert*-butoxycarbonylmethylzinc bromide in THF at



Scheme 2.



Scheme 3.

0°C yielded 76% of a mixture (1:2) of *anti*- and *syn*-**6b** as major diastereomer, obtained as minor component for the dibenzylamino valinal **1b**. When the reaction was carried out at reflux of THF the same mixture of isomers was obtained but only in 59% yield. This behavior is not general because, in the same reaction conditions, *N*-Boc protected **5a** and **5c** derived from alaninal or leucinal give to an equimolar mixture of the corresponding *anti*-**6a**,**c** and *syn*-**6a**,**c** in 77 and 68% yield, respectively. These results are in agreement with previously reported data[6] indicating that electron-withdrawing substituents at the nitrogen decrease the stereoselection. The better stereodiscrimination observed for **5b** could be attributed to the size of the alkyl substituent in the valine derivative (Scheme 3).

Diastereomers *syn*- and *anti*-**6b**,**c** can be separated by flash chromatography and their stereochemistry was determined because they were obtained from **2a**–**c** by hydrogenation in ethyl acetate in the presence of palladium hydroxyde on carbon and di-*tert*-butyl dicarbonate.[13]

The change in the sense of stereoselection depending on the protecting group attached to the nitrogen was tested on (L)-prolinal derivatives **7a**–**b**. *N*-Benzyl derivative **7a** was transformed into a mixture (7:3) of *syn*- and *anti*-**8a** in 52% yield by reaction with the Reformatsky reagent (3 equiv.) in THF at 0°C for 12 h. *N*-Boc prolinal **7b** reacted more easily because in the same reaction conditions was yielded a mixture (1:2) of *syn*- and *anti*-**8b** in 72% yield after stirring for only 3 h at 0°C. Once again, the presence of benzyl group at the nitrogen lead to the *syn* diastereomer as major product whereas the *anti* product was formed predominantly in the *N*-Boc derivatives (Scheme 4).

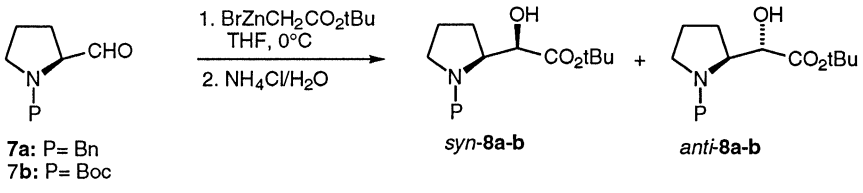
Both the de and stereochemistry for *syn*- and *anti*-**8a** were determined by ^{1}H NMR. The methine proton attached to the carbon bearing the OH group appeared upfield for the *syn* (3.85 ppm) adduct than for *anti* (4.23 ppm) adduct and the vicinal coupling constant for compound *syn* ($^{1,3}J$=5.6 Hz) is higher than for *anti* derivative ($^{1,3}J$=2.7 Hz). [10b,11]

The stereochemistry for *syn*- and *anti*-**8b** was determined by chemical correlation with the product obtained from *syn*- and *anti*-**8a** by hydrogenolysis with $Pd(OH)_2$ on carbon and Boc_2O in ethyl acetate.[13]

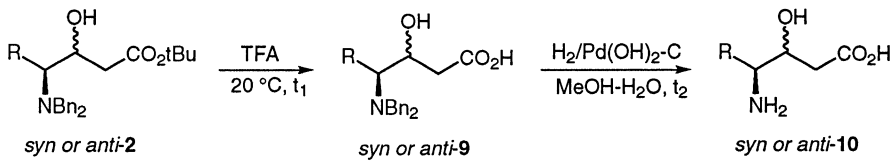
γ-Dibenzylamino-β-hydroxy esters **2a**–**e**, after separation by flash chromatography, were transformed in two steps into γ-amino-β-hydroxy acids, as depicted in Scheme 5. Compounds *anti*- and *syn*-**2a**–**e** were converted into *anti*- and *syn*-**9a**–**e** by deprotection with trifluoroacetic acid at rt[14] in good yield, and debenzylation of **9** by hydrogenolysis on $Pd(OH)_2$/C in methanol–water yielded *anti*- and *syn*-**10a**–**e** without any apreciable racemization (Scheme 5 and Table 2).

It was not possible to separate diastereomers *anti*- and *syn*-**2b** by column chromatography, and then the mixture was transformed into *N*-Boc derivatives **6b** by hydrogenolysis on $Pd(OH)_2$-C in the presence of Boc_2O, and then isolated as pure enantiomers by flash chromatography on silica gel. Both *anti*- and *syn*-**6b** were transformed in one step into γ-amino-β-hydroxy acids *anti*-**10b** and *syn*-**10b** by treatment with TFA at 0°C (Scheme 6).

In summary, the proposed methodology allows the synthesis of enantiopure γ-amino-β-hydroxy acids from α-amino



Scheme 4.

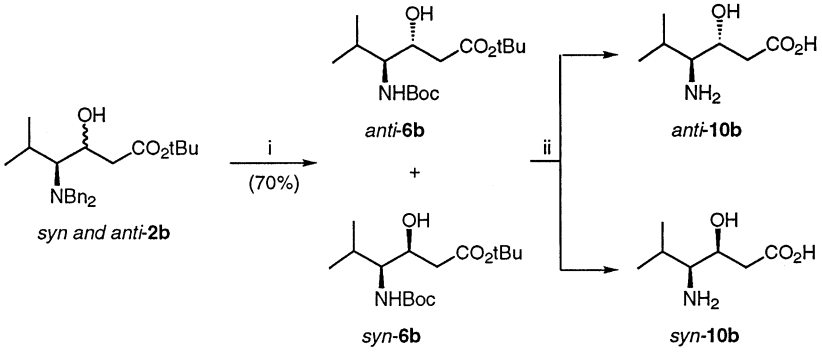


Scheme 5.

Table 2. Hydrolysis and debenzylation of γ-dibenzylamino-β-hydroxy esters *syn*- and *anti*-**2**

Compound	t_1 (h)	**9**	Yield (%)[a]	t_2 (h)	**10**	Yield (%)[a]
anti-**2a**	6	*anti*-**9a**	70	16	*anti*-**10a**	95
syn-**2c**	2	*syn*-**9c**	73	2	*syn*-**10c**	88
anti-**2c**	1.5	*anti*-**9c**	98	6	*anti*-**10c**	77
syn-**2d**	3	*syn*-**9d**	81	22	*syn*-**10d**	99
anti-**2d**	4	*anti*-**9d**	85	26	*anti*-**10d**	97
ent-syn-**2e**	5	*ent-syn*-**9e**	95	19	*ent-syn*-**10e**	91
ent-anti-**2e**	4.5	*ent-anti*-**9e**	87	19	*ent-anti*-**10e**	95

[a] Numbers correspond to isolated compounds.



Scheme 6. *Reagents and conditions*: (i) H_2, $Pd(OH)_2$–C, Boc_2O, EtoAc, 12 h. (ii) (1) Flash chromatography (silica gel, hexane/AcOEt 20/1). (2) TFA, 20°C, 1 h. (2) Propylene oxide, EtOH, reflux, 0.5 h.

aldehyde derivatives in moderated de and good chemical yields.

3. Experimental

3.1. General

The reactions were carried out in oven-dried glassware, under argon atmosphere, and using anhydrous solvents. Starting *N*,*N*-dibenzyl α-amino aldehydes **1a**–**f** were prepared as previously described.[10a,15] Amino aldehydes **7a** and **7b** were prepared by Swern oxidation of *N*-benzyl and *N*-Boc-L-prolinol. Reformatsky reagent was prepared from *tert*-butyl α-bromoacetate by a described method.[16] The ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were registered on a Bruker AC 300 or Bruker AMX 300, using TMS as internal standard. IR spectra were recorded on a Philips PU 9706 Spectrometer, as film or KBr dispersion. Optical rotations were measured on a Perkin–Elmer 241 Polarimeter in a 1 dm cell. Microanalyses were performed with a Perkin–Elmer 2400-CHN elemental analyser.

3.2. Reaction of amino aldehydes with $BrZnCH_2CO_2tBu$. General method

To a solution of amino aldehyde (3 mmol) in anhydrous THF (15 mL) at 0°C under argon was added dropwise a 0.5 M solution of $BrZnCH_2CO_2tBu$ in THF (18 mL, 6 mmol, 3 equiv). The mixture was stirred at that temperature until the reaction was finished (TLC), and then quenched with a saturated solution of aqueous ammonium chloride (30 mL). The THF was removed and the aqueous phase was extracted with dichlorometane (3×15 mL). The combined organic layers were washed with brine, and dried over anhydrous Na_2SO_4. The solvents were eliminated under vacuum and the residue was purified by flash chromatography (silica gel, hexane–ethyl acetate: 8/1–20/1).

3.2.1. *tert*-Butyl (3*S*,4*S*)-4-(*N*,*N*-dibenzylamino)-3-hydroxypentanoate (*syn*-2a). 15% yield. Colorless oil. $[\alpha]^{23}_D$=+34.7 (*c*=1.0, $CHCl_3$). IR (film): 3380, 1710, 1150, 740, 690 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.03 (d, 1H, *J*=6.7 Hz, C*H*$_3$); 1.41 (s, 9H, C(C*H*$_3$)$_3$); 2.17 (dd, 1H, J_1=15.1, J_2=8.1 Hz, C*H*HCO$_2$*t*Bu); 2.32 (dd, 1H, J_1=15.1, J_2=3.7 Hz, CH*H*CO$_2$*t*Bu); 2.65 (m, 1H, C*H*N); 3.31 (d, 2H, *J*=13.3 Hz, 2PhC*H*H); 3.85 (d, 2H, *J*=13.3 Hz, 2PhCH*H*); 3.93 (ddd, 1H, J_1=9.4, J_2=8.1, J_3=3.7 Hz, C*H*OH); 4.31 (br s, 1H, O*H*); 7.20–7.35 (m, 10H, *H*arom). ^{13}C NMR ($CDCl_3$): 8.0 (*C*H$_3$); 28.0 (C(*C*H$_3$)$_3$); 40.5 (*C*H$_2$CO$_2$*t*Bu); 53.3 (*C*H$_2$Ph); 57.9 (*C*HN); 68.3 (*C*HOH); 80.6 (*C*(CH$_3$)$_3$); 127.2, 128.5, 129.0 (*C*Harom); 138.8 (*C*arom); 171.1 (*C*O$_2$*t*Bu). Anal. Calcd for $C_{23}H_{31}NO_3$: C, 74.76; H, 8.46; N, 3.79. Found: C, 74.88; H, 8.31; N, 3.70.

3.2.2. *tert*-Butyl (3*R*,4*S*)-4-(*N*,*N*-dibenzylamino)-3-hydroxypentanoate (*anti*-2a). 54% yield. Colorless oil. $[\alpha]^{23}_D$=+17.6 (*c*=1.0, $CHCl_3$). IR (film): 3460, 1705, 1250, 750, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.15 (d, 1H, *J*=6.7 Hz, C*H*$_3$); 1.43 (s, 9H, C(C*H*$_3$)$_3$); 2.12 (dd, 1H, J_1=16.6, J_2=9.7 Hz, C*H*HCO$_2$*t*Bu); 2.63 (dq, 1H, J_1=6.7, J_2=8.2 Hz, C*H*N); 2.98 (dd, 1H, J_1=16.6, J_2=2.1 Hz, CH*H*CO$_2$*t*Bu); 3.10 (br s, 1H, O*H*); 3.41 (d, 2H, *J*=13.7 Hz, 2PhC*H*H); 3.74 (d, 2H, *J*=13.7 Hz, 2PhCH*H*); 3.95 (ddd, 1H, J_1=9.7, J_2=8.2, J_3=2.1 Hz, CHOH); 7.15–7.40 (m, 10H, *H*arom). ^{13}C NMR ($CDCl_3$): 8.2 (*C*H$_3$); 28.0 (C(*C*H$_3$)$_3$); 40.2 (*C*H$_2$CO$_2$*t*Bu); 54.3 (*C*H$_2$Ph); 56.8 (*C*HN); 70.2

(*C*HOH); 81.0 (*C*(CH_3)$_3$); 126.8, 128.2, 128.7 (*C*Harom); 139.8 (*C*arom); 173.1 (*C*O_2tBu). Anal. Calcd for $C_{23}H_{31}NO_3$: C, 74.76; H, 8.46; N, 3.79. Found: C, 74.54; H, 8.33; N, 3.68.

3.2.3. *tert*-Butyl (3*S*,4*S*)- and (3*R*,4*S*)-4-(*N*,*N*-dibenzylamino)-3-hydroxy-5-methylhexanoate (*syn*-2b and *anti*-2b). 82% yield. Colorless oil. ^{1}H NMR ($CDCl_3$): 1.05 (d, 1H, *J*=6.7 Hz, CH_3); 1.15 (d, 1H, *J*=6.8 Hz, CH_3); 1.46 (s, 9H, C(CH_3)$_3$ *syn*); 1.48 (s, 9H, C(CH_3)$_3$ *anti*); 2.21 (m, 1H, C*H*(CH_3)$_2$ *anti*); 2.32 (dd, 1H, J_1=16.0, J_2=10.6 Hz, C*H*HCO_2tBu *anti*); 2.40 (dd, 1H, J_1=6.6, J_2=5.4 Hz, C*H*N *anti*); 2.64 (dd, 1H, J_1=16.0, J_2=2.1 Hz, CH*H*CO_2tBu *anti*); 3.15 (d, 1H, *J*=5.5 Hz, O*H anti*); 3.56 (d, 1H, *J*=13.1 Hz, PhC*H*HN *syn*); 3.69 (d, 1H, *J*=13.6 Hz, PhC*H*H *anti*); 3.75 (d, 1H, *J*=13.6 Hz, PhCH*H anti*); 4.00 (d, 1H, *J*=13.1 Hz, PhCH*H*N *syn*); 4.23 (m, 1H, C*H*OH *syn*); 4.28 (ddd, 1H, J_1=10.6, J_2=5.4, J_3=2.1 Hz, C*H*OH *anti*); 7.20–7.35 (m, 10H, *H*arom). ^{13}C NMR ($CDCl_3$): [*syn* 20.1 (*C*H_3); 23.3 (*C*H_3); 25.8 (*C*H(CH_3)$_2$); 28.1 (C(*C*H_3)$_3$); 41.5 (*C*H_2); 54.5 (*C*H_2Ph); 65.2 (*C*HN); 66.1 (*C*HOH); 80.6 (*C*(CH_3)$_3$); 127.0, 128.3, 129.0 (*C*Harom); 139.3 (*C*arom); 171.8 (*C*O_2tBu)] [*anti* 20.1 (*C*H_3); 23.3 (*C*H_3); 26.4 (*C*H(CH_3)$_2$); 28.1 (C(*C*H_3)$_3$); 40.9 (*C*H_2); 55.2 (CH_2Ph); 65.5 (*C*HN); 66.9 (*C*HOH); 80.9 (*C*(CH_3)$_3$); 127.0, 128.3, 129.0 (*C*Harom); 139.7 (*C*arom); 172.6 (*C*O_2tBu)].

3.2.4. *tert*-Butyl (3*S*,4*S*)-4-(*N*,*N*-dibenzylamino)-3-hydroxy-6-methylheptanoate (*syn*-2c). 19% yield. Colorless oil. $[\alpha]^{23}_D$=−11.1 (*c*=1.0, MeOH) [Lit.[3g] $[\alpha]^{23}_D$=−2.5 (*c*=0.2, $CHCl_3$) for (3*R*,4*R*) diastereomer]. IR (film): 3460, 1710, 1150, 750, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): 0.90 (d, 6H, *J*=6.3 Hz, 2CH_3); 1.30 (m, 1H, C*H*HCHN); 1.43 (s, 9H, C(CH_3)$_3$); 1.54 (m, 1H, CH*H*CHN); 1.67 (m, 1H, C*H*(CH_3)$_2$); 2.27 (dd, 1H, J_1=15.6, J_2=3.9 Hz, C*H*HCO_2tBu); 2.34 (dd, 1H, J_1=15.6, J_2=7.9 Hz, CH*H*CO_2tBu); 2.51 (m, 1H, C*H*N); 3.44 (d, 2H, *J*=13.5 Hz, 2PhC*H*H); 3.92 (d, 2H, *J*=13.5 Hz, 2PhCH*H*); 3.96 (dt, 1H, J_1=7.9, J_2=3.9 Hz, C*H*OH); 7.15–7.35 (m, 10H, *H*arom). ^{13}C NMR ($CDCl_3$): 22.7 (*C*H_3); 23.3 (*C*H_3); 26.0 (*C*H(CH_3)$_2$); 28.0 (C(*C*H_3)$_3$); 34.7 (*C*H_2CHN); 40.6 (*C*H_2CO_2tBu); 54.1 (*C*H_2Ph); 59.5 (*C*HN); 68.7 (*C*HOH); 80.7 (*C*(CH_3)$_3$); 127.0, 128.3, 129.0 (*C*Harom); 139.4 (*C*arom); 171.8 (*C*O_2tBu).

3.2.5. *tert*-Butyl (3*R*,4*S*)-4-(*N*,*N*-dibenzylamino)-3-hydroxy-6-methylheptanoate (*anti*-2c). 68% yield. Colorless oil. $[\alpha]^{23}_D$=−13.0 (*c*=1.0, $CHCl_3$). IR (film): 3480, 1715, 1150, 740, 690 cm^{-1}. ^{1}H NMR ($CDCl_3$): 0.67 (d, 3H, *J*=6.5 Hz, CH_3); 0.90 (d, 3H, *J*=6.6 Hz, CH_3); 1.21 (m, 1H, C*H*HCHN); 1.45 (s, 9H, C(CH_3)$_3$); 1.65 (m, 1H, CH*H*CHN); 1.86 (m, 1H, C*H*(CH_3)$_2$); 2.29 (dd, 1H, J_1=16.2, J_2=10.0 Hz, C*H*HCO_2tBu); 2.45 (dd, 1H, J_1=16.2, J_2=2.9 Hz, CH*H*CO_2tBu); 2.55 (m, 1H, C*H*N); 3.09 (br s, 1H, O*H*); 3.61 (d, 2H, *J*=13.8 Hz, 2PhC*H*H); 3.73 (d, 2H, *J*=13.8 Hz, 2PhCH*H*); 4.28 (ddd, 1H, J_1=10.0, J_2=4.3, J_3=2.9 Hz, C*H*OH); 7.15–7.35 (m, 10H, *H*arom). ^{13}C NMR ($CDCl_3$): 22.4 (*C*H_3); 23.3 (*C*H_3); 24.9 (*C*H(CH_3)$_2$); 28.1 (C(*C*H_3)$_3$); 35.1 (*C*H_2CHN); 40.7 (*C*H_2CO_2tBu); 54.5 (*C*H_2Ph); 58.3 (*C*HN); 67.6 (*C*HOH); 81.1 (*C*(CH_3)$_3$); 126.8, 128.2, 128.9 (*C*Harom); 140.2 (*C*arom); 172.6 (*C*O_2tBu). Anal. Calcd for $C_{26}H_{37}NO_3$: C, 75.87; H, 9.06; N, 3.40. Found: C, 76.02; H, 8.90; N, 3.32.

3.2.6. *tert*-Butyl (3*S*,4*S*)-4-(*N*,*N*-dibenzylamino)-3-hydroxy-5-phenylpentanoate (*syn*-2d). 18% yield. Colorless oil. $[\alpha]^{23}_D$=+14.1 (*c*=1.3, $CHCl_3$) [Lit.[3g] $[\alpha]^{23}_D$=+11.5 (*c*=1.3, $CHCl_3$)]. IR (film): 3500, 1715, 1150, 745, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.39 (s, 9H, C(CH_3)$_3$); 2.04 (dd, 1H, J_1=16.0, J_2=2.4 Hz, C*H*HCO_2tBu); 2.40 (dd, 1H, J_1=16.0, J_2=9.5 Hz, CH*H*CO_2tBu); 2.76 (m, 1H, C*H*N); 2.86 (dd, 1H, J_1=13.3, J_2=8.3 Hz, C*H*HPh); 3.11 (dd, 1H, J_1=13.3, J_2=4.7 Hz, CH*H*Ph); 3.42 (d, 2H, *J*=13.5 Hz, 2PhC*H*HN); 3.94 (ddd, 1H, J_1=9.5, J_2=6.5, J_3=2.4 Hz, C*H*OH); 4.50 (d, 2H, *J*=13.5 Hz, 2PhCH*H*N); 4.07 (br s, 1H, O*H*); 7.15–7.35 (m, 15H, *H*arom). ^{13}C NMR ($CDCl_3$): 27.9 (*C*H_3); 30.6 (C*C*H_2Ph); 40.5 (*C*H_2CO_2tBu); 54.3 (N*C*H_2Ph); 62.8 (*C*HN); 67.8 (*C*HOH); 80.6 (*C*(CH_3)$_3$); 125.9, 126.9, 128.2, 128.4, 128.8, 129.1 (*C*Harom); 139.2, 140.1 (*C*arom); 172.2 (*C*O_2tBu).

3.2.7. *tert*-Butyl (3*R*,4*S*)-4-(*N*,*N*-dibenzylamino)-3-hydroxy-5-phenylpentanoate (*anti*-2d). 52% yield. Colorless oil. $[\alpha]^{23}_D$=+4.2 (*c*=0.75, $CHCl_3$). IR (film): 3420, 1700, 1140, 740, 690 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.43 (s, 9H, C(CH_3)$_3$); 2.22 (dd, 1H, J_1=16.3, J_2=10.1 Hz, C*H*HCO_2tBu); 2.63 (dd, 1H, J_1=16.3, J_2=2.5 Hz, CH*H*CO_2tBu); 2.90 (m, 1H, C*H*N); 3.07 (m, 3H, CH_2Ph, O*H*); 3.64 (d, 2H, *J*=13.9 Hz, 2PhC*H*HN); 3.73 (d, 2H, *J*=13.9 Hz, 2PhCH*H*N); 4.26 (ddd, 1H, J_1=10.1, *J*2=4.9, J_3=2.5 Hz, C*H*OH); 7.10–7.35 (m, 15H, *H*arom). ^{13}C NMR ($CDCl_3$): 28.0 (*C*H_3); 32.1 (C*C*H_2Ph); 40.7 (*C*H_2CO_2tBu); 54.5 (N*C*H_2Ph); 63.0 (*C*HN); 68.6 (*C*HOH); 81.0 (*C*(CH_3)$_3$); 125.7, 126.7, 128.1, 128.6, 129.4 (*C*Harom); 139.6, 141.1 (*C*arom); 172.6 (*C*O_2tBu). Anal. Calcd for $C_{29}H_{35}NO_3$: C, 78.17; H, 7.92; N, 3.14. Found: C, 77.89; H, 7.78; N, 3.05.

3.2.8. *tert*-Butyl (3*R*,4*R*)-4-(*N*,*N*-dibenzylamino)-3-hydroxy-4-phenylbutanoate (*ent-syn*-2e). 28% yield. Colorless solid, mp 131–132°C (from hexane–ethyl acetate). $[\alpha]^{23}_D$=−112.9 (*c*=1.0, $CHCl_3$). IR (KBr): 3410, 1720, 1150, 740, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.36 (s, 9H, C(CH_3)$_3$); 2.01 (dd, 1H, J_1=15.5, J_2=8.2 Hz, C*H*HCO_2tBu); 2.08 (dd, 1H, J_1=15.5, J_2=3.3 Hz, CH*H*CO_2tBu); 3.02 (d, 2H, *J*=13.3 Hz, 2PhC*H*H); 3.54 (d, 1H, *J*=11.0 Hz, C*H*N); 3.98 (d, 2H, *J*=13.3 Hz, 2PhCH*H*); 4.39 (br s, 1H, O*H*); 4.69 (ddd, 1H, J_1=11.0, J_2=8.2, J_3=3.3 Hz, C*H*OH); 7.15–7.45 (m, 15H, *H*arom). ^{13}C NMR ($CDCl_3$): 27.8 (*C*H_3); 40.4 (*C*H_2CO_2tBu); 53.3 (*C*H_2Ph); 65.2 (*C*HN); 66.6 (*C*HOH); 80.2 (*C*(CH_3)$_3$); 127.2, 128.0, 128.3, 128.4, 128.8, 129.7 (*C*Harom); 133.1, 138.3 (*C*arom); 170.7 (*C*O_2tBu). Anal. Calcd for $C_{28}H_{33}NO_3$: C, 77.93; H, 7.71; N, 3.25. Found: C, 77.71; H, 7.73; N, 3.14.

3.2.9. *tert*-Butyl (3*S*,4*R*)-4-(*N*,*N*-dibenzylamino)-3-hydroxy-4-phenylbutanoate (*ent-anti*-2e). 47% yield. Colorless oil. $[\alpha]^{23}_D$=−86.2 (*c*=0.9, $CHCl_3$). IR (film): 3480, 1715, 1150, 750, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.47 (s, 9H, C(CH_3)$_3$); 2.29 (dd, 1H, J_1=16.4, J_2=9.8 Hz, C*H*HCO_2tBu); 2.57 (d, 1H, *J*=2.7 Hz, O*H*); 3.06 (d, 2H, *J*=13.7 Hz, 2PhC*H*H); 3.18 (dd, 1H, J_1=16.4, J_2=2.4 Hz, CH*H*CO_2tBu); 3.61 (d, 1H, *J*=9.3 Hz, C*H*N); 3.86 (d, 2H, *J*=13.7 Hz, 2PhCH*H*); 4.71 (ddd, 1H, J_1=9.8, J_2=9.3, J_3=2.4 Hz, C*H*OH); 7.20–7.50 (m, 15H, *H*arom). ^{13}C NMR ($CDCl_3$): 28.0 (*C*H_3); 40.4 (*C*H_2CO_2tBu); 54.4 (*C*H_2Ph); 66.5 (*C*HN); 67.6 (*C*HOH); 80.9 (*C*(CH_3)$_3$); 126.9, 127.5,

128.0, 128.4, 128.7, 129.8 (*C*Harom); 134.6, 139.2 (*C*arom); 172.5 (CO_2tBu). Anal. Calcd for $C_{28}H_{33}NO_3$: C, 77.93; H, 7.71; N, 3.25. Found: C, 77.76; H, 7.68; N, 3.16.

3.2.10. *tert*-Butyl (3*S*,4*S*)- and (3*R*,4*S*) 4-(*N*,*N*-dibenzylamino)-5-(*tert*-butyldimethylsilyloxy)-3-hydroxypentanoate (*syn*-2f and *anti*-2f). 78% yield. Colorless oil. ^{1}H NMR ($CDCl_3$): 0.11 (s, 3H, SiCH_3); 0.12 (s, 3H, SiCH_3); 0.94 (s, 9H, SiC(CH_3)$_3$); 1.41 (s, 9H, OC(CH_3)$_3$ *syn*); 1.44 (s, 9H, OC(CH_3)$_3$ *anti*); 2.14 (dd, 1H, J_1=16.2, J_2=9.8 Hz, C*H*HCO_2tBu *anti*); 2.20 (dd, 1H, J_1=15.2, J_2=8.6 Hz, C*H*HCO_2tBu *syn*); 2.39 (dd, 1H, J_1=15.2, J_2=3.2 Hz, CH*H*CO_2tBu *syn*); 2.62 (m, 1H, C*H*N); 2.86 (dd, 1H, J_1=16.2, J_2=2.6 Hz, CH*H*CO_2tBu *anti*); 3.25 (d, 1H, *J*=4.1 Hz, O*H*); 3.60 (d, 2H, *J*=13.4 Hz, 2PhC*H*H *syn*); 3.65 (d, 2H, *J*=13.7 Hz, 2PhC*H*H *anti*); 3.89 (d, 2H, *J*=13.7 Hz, 2PhCH*H anti*); 3.91 (d, 2H, *J*=13.4 Hz, 2PhCH*H syn*); 4.04 (m, 2H, CH_2OTBDMS); 4.24 (m, 1H, C*H*OH); 7.15–7.35 (m, 10H, *H*arom). ^{13}C NMR ($CDCl_3$): [*syn* −5.6 and −5.5 (Si*C*H_3); 18.1 (Si*C*(CH_3)$_3$); 25.9 (SiC(*C*H_3)$_3$); 28.0 (OC(*C*H_3)$_3$); 40.5 (*C*H_2CO_2tBu); 54.5 (*C*H_2Ph); 59.3 (*C*H_2O); 62.6 (*C*HN); 65.2 (*C*HOH); 80.4 (O*C*(CH_3)$_3$); 127.1, 128.3, 129.0 (*C*Harom); 139.2 (*C*arom); 171.2 (CO_2tBu)] [*anti* −5.6 and −5.5 (Si*C*H_3); 18.1 (Si*C*(CH_3)$_3$); 25.9 (SiC(*C*H_3)$_3$); 28.1 (OC(*C*H_3)$_3$); 40.8 (*C*H_2CO_2tBu); 55.2 (*C*H_2Ph); 60.3 (*C*H_2O); 61.3 (*C*HN); 68.2 (*C*HOH); 80.7 (O*C*(CH_3)$_3$); 126.8, 128.2, 128.8 (*C*Harom); 139.9 (*C*arom); 172.6 (CO_2tBu)].

3.3. Desilylation of the mixture of diastereomers *syn*- and *anti*-2f

To a solution of **2f** (250 mg, 0.5 mmol) in THF (5 mL), at 0°C, was slowly added a solution of tetrabutylammonium fluoride (237 mg, 0.75 mmol) in THF (7 mL). The mixture was stirred for 2 h at 0°C, and quenched by addition of water (8 mL). The aqueous phase was extracted with ether (3×1 mL) and the combined organic extracts were washed with brine, dried (Na_2SO_4), concentrated and chromatographed (silica gel, hexane/ethyl acetate 5/1) to yield 33 mg (0.085 mmol) of *syn*-**3f** and 107 mg (0.27 mmol) of *anti*-**3f** (73% combined yield).

3.3.1. *tert*-Butyl (3*S*,4*S*)-4-(*N*,*N*-dibenzylamino)-3,5-dihydroxypentanoate (*syn*-3f). Colorless oil. $[\alpha]^{23}_D$=−3.8 (*c*=1.0, $CHCl_3$). IR (film): 3370, 1700, 1240, 750, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.43 (s, 9H, C(CH_3)$_3$); 2.35 (dd, 1H, J_1=16.3, J_2=4.4 Hz, C*H*HCO_2tBu); 2.43 (dd, 1H, J_1=16.3, J_2=7.1 Hz, CH*H*CO_2tBu); 2.70 (m, 1H, C*H*N); 3.63 (dd, 1H, J_1=11.3, J_2=6.7 Hz, C*H*HOH); 3.69 (dd, 1H, J_1=11.3, J_2=5.1 Hz, CH*H*OH); 3.72 (d, 2H, *J*=13.2 Hz, 2PhC*H*H); 4.01 (d, 2H, *J*=13.2 Hz, 2PhCH*H)*; 4.21 (ddd, 1H, J_1=8.9, J_2=7.2, J_3=4.5 Hz, C*H*OH); 7.20–7.35 (m, 10H, *H*arom). ^{13}C NMR ($CDCl_3$): 28.0 (*C*H_3); 39.9 (*C*H_2CO_2tBu); 54.4 (*C*H_2Ph); 58.1 (*C*H_2OH) 62.4 (*C*HN); 66.8 (*C*HOH); 81.6 (*C*(CH_3)$_3$); 127.2, 128.4, 129.2 (*C*Harom); 139.1 (*C*arom); 172.3 (CO_2tBu). Anal. Calcd for $C_{23}H_{31}NO_4$: C, 71.66; H, 8.11; N, 3.63. Found: C, 71.41; H, 8.04; N, 3.75.

3.3.2. *tert*-Butyl (3*R*,4*S*)-4-(*N*,*N*-dibenzylamino)-3,5-dihydroxypentanoate (*anti*-3f). Colorless solid, mp 75–76°C (from hexane). $[\alpha]^{23}_D$=−10.6 (*c*=0.9, MeOH). IR (KBr): 3430, 3360, 1710, 1680, 750, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.46 (s, 9H, C(CH_3)$_3$); 2.20 (dd, 1H, J_1=17.0, J_2=10.0 Hz, C*H*HCO_2tBu); 2.63 (m, 1H, C*H*N); 2.74 (dd, 1H, J_1=17.0, J_2=2.4 Hz, CH*H*CO_2tBu); 3.68 (d, 2H, *J*=13.6 Hz, 2PhC*H*H); 3.77 (d, 2H, *J*=13.6 Hz, 2PhCH*H*); 3.87 (dd, 1H, J_1=11.3, J_2=6.0 Hz, C*H*HOH); 3.97 (dd, 1H, J_1=11.3, J_2=5.3 Hz, CH*H*OH); 4.31 (ddd, 1H, J_1=10.0, J_2=7.0, J_3=2.4 Hz, C*H*OH); 7.20–7.35 (m, 10H, *H*arom). ^{13}C NMR ($CDCl_3$): 28.0 (*C*H_3); 40.3 (*C*H_2CO_2tBu); 54.6 (*C*H_2Ph); 59.1 (*C*H_2OH) 61.8 (*C*HN); 68.3 (*C*HOH); 81.5 (*C*(CH_3)$_3$); 127.1, 128.3, 128.9 (*C*Harom); 139.3 (*C*arom); 172.9 (CO_2tBu). Anal. Calcd for $C_{23}H_{31}NO_4$: C, 71.66; H, 8.11; N, 3.63. Found: C, 71.45; H, 8.08; N, 3.81.

3.3.3. *tert*-Butyl (3*S*,4*S*)-4-(*N*,*N*-dibenzylamino)-3,5-isopropylidendioxypentanoate (*cis*-4f). To a solution of aminodiol *syn*-**3f** (20 mg, 0.05 mmol) in 2,2-dimethoxypropane (1 mL), at room temperature, was added TsOH·H_2O (4 mg). The mixture was stirred at 45°C for 4 h, and then quenched with aqueous saturated solution of $NaHCO_3$. The aqueous phase was extracted with ethyl acetate and dried over anhydrous $MgSO_4$. The solvents were eliminated under vacuum and the residue was purified by flash chromatography (silica gel, hexane/ethyl acetate 8/1) to yield 15 mg of compound *cis*-**4f** (0.035 mmol, 68%) as a colorless oil. $[\alpha]^{23}_D$=+26.8 (*c*=0.7, $CHCl_3$). IR (film): 1720, 750, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.39 (s, 3H, CH_3); 1.40 (s, 3H, CH_3); 1.42 (s, 9H, C(CH_3)$_3$); 2.27 (dd, 1H, J_1=15.6, J_2=8.6 Hz, C*H*HCO_2tBu); 2.39 (dd, 1H, J_1=15.6, J_2=3.2 Hz, CH*H*CO_2tBu); 2.69 (m, 1H, C*H*N); 3.58 (dd, 1H, J_1=10.2, J_2=5.6 Hz, C*H*HCHN); 2.59 (d, 2H, *J*=13.2 Hz, 2PhC*H*H); 3.76 (dd, 1H, J_1=10.2, J_2=6.1 Hz, CH*H*CHN); 4.00 (d, 2H, *J*=13.2 Hz, 2PhCH*H*); 4.07 (dt, 1H, J_1=8.6, J_2=3.2 Hz, C*H*OH); 7.20–7.35 (m, 10H, *H*arom).^{13}C NMR ($CDCl_3$): 24.4 (*C*H_3); 28.1 (C(CH_3)$_3$); 40.8 (*C*H_2CO_2tBu); 54.4 (*C*H_2Ph); 57.1 (*C*H_2OH); 61.2 (*C*HN); 66.0 (*C*HOH); 80.6 (*C*(CH_3)$_3$); 100.2 ($O_2C(CH_3)_2$); 127.2, 128.4, 129.1 (*C*Harom); 139.1 (*C*arom); 171.5 (CO_2tBu). Anal. Calcd for $C_{26}H_{35}NO_4$: C, 73.38; H, 8.29; N, 3.29. Found: C, 73.19; H, 8.20; N, 3.35.

3.3.4. *tert*-Butyl (3*R*,4*S*)-4-(*N*,*N*-dibenzylamino)-3,5-isopropylidendioxypentanoate (*trans*-4f). This compound was obtained from *anti*-**3f** (45 mg, 0.12 mmol), by the method described for *cis*-**4f**. Yield: 36 mg (0.082 mmol, 72%). Colorless oil. $[\alpha]^{23}_D$=+48.2 (*c*=0.7, $CHCl_3$). IR (film): 1720, 750, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.28 (s, 3H, CH_3); 1.40 (s, 3H, CH_3); 1.44 (s, 9H, C(CH_3)$_3$); 2.02 (dd, 1H, J_1=15.3, J_2=9.9 Hz, C*H*HCO_2tBu); 2.70 (m, 1H, C*H*N); 2.86 (dd, 1H, J_1=15.3, J_2=2.4 Hz, CH*H*CO_2tBu); 3.49 (d, 2H, *J*=13.6 Hz, 2PhC*H*H); 3.87 (dd, 1H, J_1=11.9, J_2=5.6 Hz, C*H*HCHN); 3.93 (d, 2H, *J*=13.6 Hz, 2PhCH*H*); 3.95 (dd, 1H, J_1=11.9, J_2=6.4 Hz, CH*H*CHN); 4.29 (dt, 1H, J_1=9.9, J_2=2.4 Hz, C*H*OH); 7.20–7.35 (m, 10H, *H*arom). ^{13}C NMR ($CDCl_3$): 21.4 (*C*H_3); 26.5 (*C*H_3); 28.1 (C(*C*H_3)$_3$); 39.8 (*C*H_2CO_2tBu); 54.6 (*C*H_2Ph); 57.6 (*C*HN); 57.9 (*C*H_2OH); 67.5 (*C*HOH); 80.3 (*C*(CH_3)$_3$); 99.2 ($O_2C(CH_3)_2$); 127.1, 128.3, 128.8 (*C*Harom); 139.3 (*C*arom); 171.0 (CO_2tBu). Anal. Calcd for $C_{26}H_{35}NO_4$: C, 73.38; H, 8.29; N, 3.29. Found: C, 73.25; H, 8.18; N, 3.23.

3.3.5. *tert*-Butyl (3*S*,4*S*)- and (3*R*,4*S*)-4-(*N*-*tert*-butoxy-

carbonylamino)-3-hydroxypentanoate (*syn*-6a and *anti*-6a)77% yield. Colorless oil. ^{1}H NMR ($CDCl_3$): 1.12 (d, 3H, J=6.8 Hz, CH_3 *anti*); 1.21 (d, 3H, J=6.8 Hz, CH_3 *syn*); 1.44 (s, 9H, C(CH_3)$_3$); 1.46 (s, 9H, C(CH_3)$_3$); 2.30–2.50 (m, 2H, CH_2); 3.46 (br s, 1H, O*H anti*); 3.50 (br s, 1H, O*H syn*); 3.63 (m, 1H, C*H*N); 3.93 (m, 1H, C*H*OH *syn*); 3.99 (m, 1H, C*H*OH *anti*); 4.86 (br s, 1H, N*H*). ^{13}C NMR ($CDCl_3$): 14.8 (*C*H$_3$ *anti*); 18.3 (*C*H$_3$ *syn*); 27.9, 28.3 (C(*C*H$_3$)$_3$); 39.2 (*C*H$_2$ *anti*); 39.7 (*C*H$_2$ *syn*); 49.7 (*C*HN); 70.6 (*C*HOH); 79.1, 81.1 (*C*(CH$_3$)$_3$); 155.4 (N*C*O$_2$*t*Bu *anti*); 155.7 (N*C*O$_2$*t*Bu *syn*); 172.0 (*C*O$_2$*t*Bu *anti*); 172.4 (*C*O$_2$*t*Bu *syn*).

3.3.6. *tert*-Butyl (3*S*,4*S*)-4-(*N*-*tert*-butoxycarbonylamino)-3-hydroxy-5-methylhexanoate (*syn*-6b). 51% yield. Colorless oil. $[\alpha]^{23}_D$=−38.2 (c=1.0, $CHCl_3$). IR (film): 3400, 1710, 1150 cm^{-1}. ^{1}H NMR ($CDCl_3$): 0.95 (d, 3H, J=6.8 Hz, CH_3); 0.98 (d, 3H, J=6.7 Hz, CH_3); 1.44 (s, 9H, C(CH_3)$_3$); 1.46 (s, 9H, C(CH_3)$_3$); 1.86 (m, 1H, C*H*(CH$_3$)$_2$); 2.35 (dd, 1H, J_1=16.8, J_2=2.7 Hz, C*H*HCO$_2$*t*Bu); 2.48 (dd, 1H, J_1=16.8, J_2=10.1 Hz, CH*H*CO$_2$*t*Bu); 3.12 (m, 1H, C*H*N); 3.44 (br s, 1H, O*H*); 4.21 (d, 1H, J=10.1 Hz, C*H*OH); 4.87 (d, 1H, J=10.1 Hz, N*H*). ^{13}C NMR ($CDCl_3$): 19.5 (*C*H$_3$); 19.7 (*C*H$_3$); 28.0, 28.3 (C(*C*H$_3$)$_3$); 30.2 (*C*H(CH$_3$)$_2$); 40.0 (*C*H$_2$CO$_2$*t*Bu); 59.5 (*C*HN); 66.9 (*C*HOH); 78.9, 81.2 (C(CH$_3$)$_3$); 156.3 (N*C*O$_2$*t*Bu); 172.9 (*C*O$_2$*t*Bu). Anal. Calcd for $C_{16}H_{31}NO_5$: C, 60.54; H, 9.84; N, 4.41. Found: C, 60.66; H, 9.74; N, 4.51.

3.3.7. *tert*-Butyl (3*R*,4*S*)-4-(*N*-*tert*-butoxycarbonylamino)-3-hydroxy-5-methylhexanoate (*anti*-6b). 25% yield. Colorless solid mp 95–96°C (from hexane). $[\alpha]^{23}_D$=+11.8 (c=1.0, $CHCl_3$). IR (film): 3440, 3380, 1690, 1150 cm^{-1}. ^{1}H NMR ($CDCl_3$): 0.87 (d, 3H, J=6.8 Hz, CH_3); 0.93 (d, 3H, J=6.8 Hz, CH_3); 1.45 (s, 9H, C(CH_3)$_3$); 1.47 (s, 9H, C(CH_3)$_3$); 2.14 (m, 1H, C*H*(CH$_3$)$_2$); 2.38 (dd, 1H, J_1=16.5, J_2=8.9 Hz, C*H*HCO$_2$*t*Bu); 2.52 (dd, 1H, J_1=16.5, J_2=2.9 Hz, CH*H*CO$_2$*t*Bu); 3.50 (m, 2H, C*H*N and O*H*); 3.87 (m, 1H, C*H*OH); 4.46 (d, 1H, J=10.1 Hz, N*H*). ^{13}C NMR ($CDCl_3$): 16.0 (*C*H$_3$); 20.1 (*C*H$_3$); 27.4 (*C*H(CH$_3$)$_2$); 28.0, 28.3 (C(*C*H$_3$)$_3$); 39.3 (*C*H$_2$CO$_2$*t*Bu); 58.5 (*C*HN); 69.0 (*C*HOH); 79.3, 81.2 (*C*(CH$_3$)$_3$); 156.2 (N*C*O$_2$*t*Bu); 172.6 (*C*O$_2$*t*Bu). Anal. Calcd for $C_{16}H_{31}NO_5$: C, 60.54; H, 9.84; N, 4.41. Found: C, 60.56; H, 9.72; N, 4.53.

3.3.8. *tert*-Butyl (3*S*,4*S*)-4-(*N*-*tert*-butoxycarbonylamino)-3-hydroxy-6-methylheptanoate (*syn*-6c). 35% yield. Colorless oil. $[\alpha]^{23}_D$=−17.2 (c=1.0, $CHCl_3$). IR (film): 3400, 1705, 1160 cm^{-1}. ^{1}H NMR ($CDCl_3$): 0.92 (d, 6H, J=6.4 Hz, CH_3); 1.20–1.60 (m, 2H, CH_2CHN); 1.44 (s, 9H, C(CH_3)$_3$); 1.46 (s, 9H, C(CH_3)$_3$); 1.66 (m, 1H, C*H*(CH$_3$)$_2$); 2.39 (dd, 1H, J_1=16.7, J_2=3.6 Hz, C*H*HCO$_2$*t*Bu); 2.47 (dd, 1H, J_2=16.7, J_2=9.2 Hz, CH*H*CO$_2$*t*Bu); 3.43 (br s, 1H, O*H*); 3.60 (m, 1H, C*H*N); 3.97 (m, 1H, C*H*OH); 4.74 (d, 1H, J=9.4 Hz, N*H*). ^{13}C NMR ($CDCl_3$): 22.1 (*C*H$_3$); 22.9 (*C*H$_3$); 24.6 (*C*H(CH$_3$)$_2$); 27.9, 28.3 (C(*C*H$_3$)$_3$); 39.7 (*C*H$_2$CHN); 41.7 (*C*H$_2$CO$_2$*t*Bu); 51.8 (*C*HN); 69.6 (*C*HOH); 78.9, 81.1 (*C*(CH$_3$)$_3$); 155.9 (N*C*O$_2$*t*Bu); 172.6 (*C*O$_2$*t*Bu). Anal. Calcd for $C_{17}H_{33}NO_5$: C, 61.60; H, 10.04; N, 4.23. Found: C, 61.78; H, 10.12; N, 4.28.

3.3.9. *tert*-Butyl (3*R*,4*S*)-4-(*N*-*tert*-butoxycarbonylamino)-3-hydroxy-6-methylheptanoate (*anti*-6c). 33% yield. Colorless oil. $[\alpha]^{23}_D$=−9.6 (c=1.1, $CHCl_3$). IR (film): 3400, 1700, 1160 cm^{-1}. ^{1}H NMR ($CDCl_3$): 0.91 (d, 3H, J=6.4 Hz, CH_3); 0.93 (d, 3H, J=6.4 Hz, CH_3); 1.30 (m, 2H, CH_2CHN); 1.44 (s, 9H, C(CH$_3$)$_3$); 1.46 (s, 9H, C(CH_3)$_3$); 1.66 (m, 1H, C*H*(CH$_3$)$_2$); 2.39 (m, 2H, CH_2CO$_2$*t*Bu); 3.55 (br s, 1H, O*H*); 3.64 (m, 1H, C*H*N); 3.97 (m, 1H, C*H*OH); 4.69 (d, 1H, J=9.2 Hz, N*H*). ^{13}C NMR ($CDCl_3$): 21.5 (CH$_3$); 23.7 (*C*H$_3$); 24.6 (*C*H(CH$_3$)$_2$); 28.0, 28.3 (C(*C*H$_3$)$_3$); 38.6 (*C*H$_2$); 39.1 (*C*H$_2$); 52.5 (*C*HN); 71.3 (*C*HOH); 79.3, 81.3 (*C*(CH$_3$)$_3$); 156.0 (N*C*O$_2$*t*Bu); 172.2 (*C*O$_2$*t*Bu). Anal. Calcd for $C_{17}H_{33}NO_5$: C, 61.60; H, 10.04; N, 4.23. Found: C, 61.68; H, 9.86; N, 4.25.

3.3.10. *tert*-Butyl (3*S*,2′*S*)-3-[*N*-benzyl-2′-pyrrolidinyl]-3-hydroxypropionate (*syn*-8a). 36% yield. Colorless oil. $[\alpha]^{23}_D$=−31.8 (c=0.9, $CHCl_3$). IR (film): 3400, 1710, 740, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.47 (s, 9H, C(CH_3)$_3$); 1.70 (m, 3H, NCHC*H*HCH_2); 1.94 (m, 1H, NCHCH*H*); 2.35 (dd, 1H, J_1=15.4, J_2=9.2 Hz, C*H*HCO$_2$*t*Bu); 2.36 (m, 1H, NC*H*H); 2.50 (dd, 1H, J_1=15.4, J_2=3.9 Hz, CH*H*CO$_2$*t*Bu); 2.84 (ddd, 1H, J_1=8.0, J_2=5.6, J_3=3.3 Hz, C*H*N); 2.92 (m, 1H, NCH*H*); 3.53 (d, 1H, J=13.2 Hz, C*H*HPh); 3.85 (ddd, 1H, J_1=9.3, J_2=5.6, J_3=3.9 Hz, C*H*OH); 4.04 (d, 1H, J=13.2 Hz, CH*H*Ph); 7.20–7.35 (m, 5H, *H*arom). ^{13}C NMR ($CDCl_3$): 24.0 (*C*H$_2$); 27.6 (*C*H$_2$); 27.9 (*C*H$_3$); 40.0 (*C*H$_2$CO$_2$*t*Bu); 54.1 (*C*H$_2$Ph); 60.9 (N*C*H$_2$); 67.2 (*C*HN); 70.2 (*C*HOH); 80.6 (*C*(CH$_3$)$_3$); 127.0, 128.2, 128.6 (*C*Harom); 138.8 (*C*arom); 171.7 (*C*O$_2$*t*Bu). Anal. Calcd for $C_{18}H_{27}NO_3$: C, 70.79; H, 8.91; N, 4.59. Found: C, 70.98; H, 8.86; N, 4.56.

3.3.11. *tert*-Butyl (3*R*,2′*S*)-3-[*N*-benzyl-2′-pyrrolidinyl]-3-hydroxypropionate (*anti*-8a). 16% yield. Colorless oil. $[\alpha]^{23}_D$=−46.0 (c=1.2, $CHCl_3$). IR (film): 3440, 1715, 750, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.48 (s, 9H, C(CH_3)$_3$); 1.73 (m, 4H, NCHCH_2CH_2); 2.24 (m, 1H, NC*H*H); 2.30 (dd, 1H, J_1=15.4, J_2=5.1 Hz, C*H*HCO$_2$*t*Bu); 2.50 (dd, 1H, J_1=15.4, J_2=8.3 Hz, CH*H*CO$_2$*t*Bu); 2.61 (m, 1H, C*H*N); 2.95 (m, 1H, NCH*H*); 3.30 (d, 1H, J=13.0 Hz, C*H*HPh); 4.11 (d, 1H, J=13.0 Hz, CH*H*Ph); 4.23 (ddd, 1H, J_1=8.3, J_2=5.1, J_3=2.7 Hz, C*H*OH); 7.20–7.35 (m, 5H, *H*arom). ^{13}C NMR ($CDCl_3$): 23.0 (*C*H$_2$); 23.7 (*C*H$_2$); 28.0 (*C*H$_3$); 39.4 (*C*H$_2$CO$_2$*t*Bu); 54.1 (*C*H$_2$Ph); 58.0 (N*C*H$_2$); 65.7 (*C*HN); 66.6 (*C*HOH); 80.6 (*C*(CH$_3$)$_3$); 126.9, 128.1, 128.6 (*C*Harom); 138.8 (*C*arom); 171.0 (*C*O$_2$*t*Bu). Anal. Calcd for $C_{18}H_{27}NO_3$: C, 70.79; H, 8.91; N, 4.59. Found: C, 70.94; H, 8.95; N, 4.52.

3.3.12. *tert*-Butyl (3*S*,2′*S*)-3-[*N*-*tert*-butoxycarbonyl-2′-pyrrolidinyl]-3-hydroxypropanoate (*syn*-8b). 24% yield. Colorless oil. $[\alpha]^{23}_D$=−46.5 (c=0.9, $CHCl_3$). IR (film): 3400, 1720, 1680 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.46 (s, 18H, 2C(CH_3)$_3$); 1.86 (m, 4H, NCHCH_2CH_2); 2.32 (dd, 1H, J_1=15.2, J_2=8.4 Hz, C*H*HCO$_2$*t*Bu); 2.43 (dd, 1H, J_1=15.2, J_2=3.3 Hz, CH*H*CO$_2$*t*Bu); 3.30 (m, 1H, NC*H*H); 3.50 (m, 1H, NCH*H*); 3.93 (dd, 1H, J_1=7.3, J_2=3.6 Hz, C*H*N); 4.10 (m, 1H, C*H*OH); 4.80 (br s, 1H, O*H*). ^{13}C NMR ($CDCl_3$): 24.0 (*C*H$_2$); 27.9, 28.2 (*C*H$_3$); 41.0 (*C*H$_2$CO$_2$*t*Bu); 47.2 (N*C*H$_2$); 61.7 (*C*HN); 72.3 (*C*HOH); 80.0, 80.6 (*C*(CH$_3$)$_3$); 157.2 (N*C*O$_2$*t*Bu); 171.2 (*C*O$_2$*t*Bu).

Anal. Calcd for $C_{16}H_{29}NO_5$: C, 60.93; H, 9.27; N, 4.44. Found: C, 61.11; H, 9.42; N, 4.36.

3.3.13. *tert*-Butyl (3*R*,2′*S*)-3-[*N*-*tert*-butoxycarbonyl-2′-pyrrolidinyl]-3-hydroxypropanoate (*anti*-8b). 48% yield. Colorless oil. $[\alpha]^{23}_D=-29.6$ (c=0.8, $CHCl_3$). IR (film): 3440, 1725, 1690 cm^{-1}. ^1H NMR ($CDCl_3$): 1.46 (s, 18H, CH_3); 1.79 (m, 4H, NCHCH_2CH_2); 2.34 (m, 2H, CH_2CO$_2t$Bu); 3.27 (m, 1H, NCHH); 3.48 (m, 1H, NCHH); 3.91 (m, 1H, CHN); 4.16 (m, 1H, CHOH). ^{13}C NMR ($CDCl_3$): 23.9 (*C*H_2); 26.9 (*C*H_2); 27.9, 28.3 (*C*H_3); 38.9 (*C*H_2CO$_2t$Bu); 47.5 (N*C*H_2); 61.8 (*C*HN); 69.8 (*C*HOH); 80.0, 80.7 (*C*(CH$_3$)$_3$); 155.9 (N*C*O$_2t$Bu); 171.7 (CH$_2$*C*O$_2t$Bu). Anal. Calcd for $C_{16}H_{29}NO_5$: C, 60.93; H, 9.27; N, 4.44. Found: C, 61.13; H, 9.37; N, 4.50.

3.4. Conversion of γ-(*N*,*N*-dibenzylamino)-β-hydroxy-esters 2 into γ-(*N*,*N*-dibenzylamino)-β-hydroxyacids 9. General method

A solution of **2** (1 mmol) in TFA (7 mL) was stirred at rt until the reaction was finished (TLC). The solvent was evaporated and methanol (2×5 mL) was added and evaporated twice to give the intermediate salt as a yellow solid. This salt was treated with saturated $NaHCO_3$ to pH 7 and extracted with dichlorometane (3×5 mL). The combined organic layers were washed with brine (5 mL), dried over anhydrous Na_2SO_4, filtered and evaporated. The residue was purified by chromatography (EtOAc/hexane 3/2).

3.4.1. (3*R*,4*S*)-4-(*N*,*N*-Dibenzylamino)-3-hydroxypentanoic acid (*anti*-9a). 70% yield. Colorless oil. $[\alpha]^{23}_D=+10.9$ (c=0.9, MeOH). IR (film): 3350, 1690, 740, 690 cm^{-1}. ^1H NMR ($CDCl_3$): 1.17 (d, 3H, J=5.5 Hz, CH_3); 2.30 (m, 1H, CHN); 2.82 (m, 2H, CH_2CO$_2$H); 3.44 (d, 2H, J=13.4 Hz, 2PhCHH); 3.86 (d, 2H, J=13.4 Hz, 2PhCHH); 4.07 (m, 1H, CHOH); 6.17 (br s, 2H, OH and CO$_2H$); 7.20–7.40 (m, 10H, *H*arom). ^{13}C NMR ($CDCl_3$): 8.2 (*C*H_3); 40.6 (*C*H_2CO$_2$H); 54.3 (*C*H_2Ph); 58.2 (*C*HN); 69.0 (*C*HOH); 127.6, 128.4, 129.3 (*C*Harom); 136.8 (*C*arom); 177.3 (*C*O$_2$H). Anal. Calcd for $C_{19}H_{23}NO_3$: C, 72.82; H, 7.40; N, 4.47. Found: C, 72.99; H, 7.29; N, 4.59.

3.4.2. (3*S*,4*S*)-4-(*N*,*N*-Dibenzylamino)-3-hydroxy-6-methylheptanoic acid (*syn*-9c). 73% yield. Colorless oil. $[\alpha]^{23}_D=-22.9$ (c=1.0, MeOH). IR (film): 3400, 1670, 750, 700 cm^{-1}. ^1H NMR ($CDCl_3$): 0.88 (d, 3H, J=6.3 Hz, CH_3); 0.99 (d, 3H, J=6.3 Hz, CH_3); 1.50 (m, 1H, CHHCHN); 1.71 (m, 2H, CHHCHN and CH(CH$_3$)$_2$); 2.19 (dd, 2H, J_1=15.6, J_2=5.0 Hz, CHHCO$_2$H); 2.81 (dd, 2H, J_1=15.6, J_2=5.2 Hz, CHHCO$_2$H); 2.85 (m, 1H, CHN); 3.57 (d, 2H, J=13.2 Hz, 2PhCHH); 4.05 (m, 1H, CHOH); 4.35 (d, 2H, J=13.2 Hz, 2PhCHH); 7.25–7.40 (m, 10H, *H*arom); 8.04 (br s, 2H, OH and CO$_2H$). ^{13}C NMR ($CDCl_3$): 21.6 (*C*H_3); 23.3 (*C*H_3); 25.3 (*C*H(CH$_3$)$_2$); 33.5 (*C*H_2CHN); 41.2 (*C*H_2CO$_2$H); 54.9 (*C*H_2Ph); 61.4 (*C*HN); 66.5 (*C*HOH); 128.6, 128.7, 130.0 (*C*Harom); 133.4 (*C*arom); 176.2 (*C*O$_2$H). Anal. Calcd for $C_{22}H_{29}NO_3$: C, 74.34; H, 8.22; N, 3.94. Found: C, 74.55; H, 8.03; N, 4.00.

3.4.3. (3*R*,4*S*)-4-(*N*,*N*-Dibenzylamino)-3-hydroxy-6-methylheptanoic acid (*anti*-9c). 98% yield. Colorless oil. $[\alpha]^{23}_D=-25.4$ (c=0.8, MeOH). IR (film): 3400, 1690, 740, 690 cm^{-1}. ^1H NMR ($CDCl_3$): 0.77 (d, 3H, J=6.6 Hz, CH_3); 0.91 (d, 3H, J=6.6 Hz, CH_3); 1.29 (m, 1H, CHHCHN); 1.64 (m, 1H, CHHCHN); 1.84 (m, 1H, CH(CH$_3$)$_2$); 2.41 (dd, 1H, J_1=16.3, J_2=9.7 Hz, CHHCO$_2$H); 2.64 (dd, 1H, J_1=16.3, J_2=2.7 Hz, CHHCO$_2$H); 2.69 (m, 1H, CHN); 3.67 (m, 4H, 2 CH_2Ph) 4.24 (m, 1H, CHOH); 6.02 (br s, 2H, OH and CO$_2H$); 7.20–7.35 (m, 10H, *H*arom). ^{13}C NMR ($CDCl_3$): 22.7 (*C*H_3); 23.0 (*C*H_3); 25.1 (*C*HCH$_3$); 34.9 (*C*H_2CHN); 40.1 (*C*H_2CO$_2t$Bu); 54.7 (*C*H_2Ph); 58.9 (*C*HN); 67.8 (*C*HOH); 127.2, 128.3, 129.1 (*C*Harom); 138.7 (*C*arom); 177.6 (*C*O$_2$H). Anal. Calcd for $C_{22}H_{29}NO_3$: C, 74.34; H, 8.22; N, 3.94. Found: C, 74.08; H, 8.10; N, 3.80.

3.4.4. (3*S*,4*S*)-4-(*N*,*N*-Dibenzylamino)-3-hydroxy-5-phenylpentanoic acid (*syn*-9d). 81% yield. Colorless oil. $[\alpha]^{23}_D=-5.8$ (c=1.0, MeOH). IR (film): 3400, 1700, 740, 700 cm^{-1}. ^1H NMR ($CDCl_3$): 2.22 (dd, 1H, J_1=15.9, J_2=3.8 Hz, CHHCO$_2$H); 2.31 (dd, 1H, J_1=15.9, J_2=7.4 Hz, CHHCO$_2$H); 2.86 (m, 1H, CHN); 2.89 (dd, 1H, J_1=12.5, J_2=9.0 Hz, CCHHPh); 3.11 (dd, 1H, J_1=12.5, J_2=3.3 Hz, CCHHPh); 3.46 (d, 2H, J=13.3 Hz, 2PhCHHN); 3.90 (m, 1H, CHOH); 4.20 (d, 2H, J=13.3 Hz, 2PhCHHN); 7.15–7.40 (m, 15H, *H*arom); 8.10 (br s, 2H, OH and CO$_2H$). ^{13}C NMR ($CDCl_3$): 30.8 (C*C*H_2Ph); 40.4 (*C*H_2CO$_2$H); 54.7 (N*C*H_2Ph); 63.2 (*C*HN); 67.1 (*C*HOH); 126.4, 127.6, 128.5, 128.7, 129.1, 129.3 (*C*Harom); 137.4, 139.0 (*C*arom); 177.6 (*C*O$_2$H). Anal. Calcd for $C_{25}H_{27}NO_3$: C, 77.09; H, 6.99; N, 3.60. Found: C, 77.12; H, 7.03; N, 3.54.

3.4.5. (3*R*,4*S*)-4-(*N*,*N*-Dibenzylamino)-3-hydroxy-5-phenylpentanoic acid (*anti*-9d). 85% yield. Colorless oil. $[\alpha]^{23}_D=-12.1$ (c=1.0, MeOH). IR (film): 3360, 1670, 740, 700 cm^{-1}. ^1H NMR ($CDCl_3$): 2.27 (dd, 1H, J_1=16.5, J_2=8.5 Hz, CHHCO$_2$H); 2.41 (dd, 1H, J_1=16.5, J_2=4.5 Hz, CHHCO$_2$H); 3.23 (m, 2H, CCH_2Ph); 3.57 (m, 1H, CHN); 3.96 (d, 2H, J=13.5 Hz, 2PhCHHN); 4.42 (d, 2H, J=13.5 Hz, 2PhCHHN); 4.78 (m, 1H, CHOH); 7.05–7.40 (m, 15H, *H*arom). ^{13}C NMR ($CDCl_3$): 29.9 (C*C*H_2Ph); 40.2 (*C*H_2CO$_2$H); 55.2 (N*C*H_2Ph); 65.1 (*C*HN), 65.5 (*C*HOH); 127.0, 128.9, 129.1, 129.9 (*C*Harom) 131.9, 136.7 (*C*arom); 174.7 (*C*O$_2$H). Anal. Calcd for $C_{25}H_{27}NO_3$: C, 77.09; H, 6.99; N, 3.60. Found: C, 77.18; H, 6.96; N, 3.65.

3.4.6. (3*R*,4*R*)-4-(*N*,*N*-Dibenzylamino)-3-hydroxy-4-phenylbutanoic acid (*ent-syn*-9e). 95% yield. Colorless oil. $[\alpha]^{23}_D=-96.5$ (c=1.6, MeOH). ^1H NMR ($CDCl_3$): 2.10 (dd, 1H, J_1=15.5, J_2=8.4 Hz, CHHCO$_2$H); 2.21(dd, 1H, J_1=15.5, J_2=1.7 Hz, CHHCO$_2$H); 3.09 (d, 2H, J=13.2 Hz, 2PhCHHN); 3.63 (d, 1H, J=10.3 Hz, CHN); 4.02 (d, 2H, J=13.2 Hz, 2PhCHHN); 4.71 (m, 1H, CHOH); 7.20–7.50 (m, 15H, *H*arom).^{13}C NMR ($CDCl_3$): 39.2 (*C*H_2); 53.6 (*C*H_2Ph); 65.2 (*C*HN); 67.0 (*C*HOH); 127.6, 128.7, 129.1, 129.9 (*C*Harom); 132.2, 137.3 (*C*arom); 176.1 (*C*O$_2$H). Anal. Calcd for $C_{24}H_{25}NO_3$: C, 76.78; H, 6.71; N, 3.73. Found: C, 76.63; H, 6.59; N, 3.69.

3.4.7. (3*S*,4*R*)-4-(*N*,*N*-Dibenzylamino)-3-hydroxy-4-phenylbutanoic acid (*ent-anti*-9e). 87% yield. Colorless oil. $[\alpha]^{23}_D=-108.4$ (c=1.0, MeOH). ^1H NMR ($CDCl_3$): 2.48 (dd, 1H, J_1=16.7, J_2=9.0 Hz, CHHCO$_2$H); 3.08 (d, 2H, J=13.6 Hz, 2PhCHH); 3.32 (dd, 1H, J_1=16.7, J_2=2.6 Hz, CHHCO$_2$H); 3.68 (d, 1H, J=9.6 Hz, CHN); 3.90

(d, 2H, J=13.6 Hz, 2PhCHH); 4.80 (ddd, 1H, J_1=9.6, J_2=9.0, J_3=2.6 Hz, CHOH); 7.20–7.55 (m, 15H, Harom). ^{13}C NMR ($CDCl_3$): 39.4 (CH_2CO_2H); 54.5 (CH_2Ph); 66.5 (CHN); 67.3 (CHOH); 127.2, 127.8, 128.2, 128.4, 128.8, 130.0 (CHarom); 133.8, 138.6 (Carom); 178.0 (CO_2H). Anal. Calcd for $C_{24}H_{25}NO_3$: C, 76.78; H, 6.71; N, 3.73. Found: C, 76.48; H, 6.75; N, 3.76.

3.5. General method for the hydrogenolysis of *N*,*N*-dibenzylamino acids 9

To a solution of the appropriate *N*,*N*-dibenzylamino acid **9** (1 mmol) in a 1:1 mixture MeOH–H_2O (10 mL) was added 20% $Pd(OH)_2$–C (50 mg) in one portion. The mixture was stirred under a hydrogen atmosphere and the reaction was monitored by TLC. After completion of the reaction, the catalyst was removed by filtration and washed with water. The solvent was concentrated under reduced pressure to afford the pure product wich was cristallized from acetone–water where necessary.

3.5.1. (3*R*,4*S*)-4-Amino-3-hydroxypentanoic acid (*anti*-10a). 95% yield. Colorless solid, mp 193–194°C. $[\alpha]^{23}_D$=−3.8 (c=0.34, H_2O) [Lit.[2g] mp 187–188°C; $[\alpha]^{23}_D$=+6.9 (c=0.18, H_2O) for the (3*S*,4*R*) isomer]. ^{1}H NMR (D_2O): 1.06 (d, 1H, J=6.8 Hz, CH_3); 2.24 (d, 2H, J=6.4 Hz, CH_2CO$_2$H); 3.28 (dq, 1H, J_1=6.8, J_2=3.0 Hz, CHN); 4.04 (dt, 1H, J_1=6.4, J_2=3.0 Hz, CHOH). ^{13}C NMR (D_2O): 13.8 (CH_3); 42.7 (CH_2); 53.2 (CHN); 70.7 (CHOH); 180.7 (CO_2H).

3.5.2. (3*S*,4*S*)-4-Amino-3-hydroxy-6-methylheptanoic acid (*syn*-10c). 88% yield. Colorless solid, mp 200–201°C (dec.) (from H_2O/acetone). $[\alpha]^{23}_D$=−21.3 (c=0.5, H_2O). [Lit.[6a] mp 201–202°C; $[\alpha]^{23}_D$=−20.0 (c=1.0, H_2O)]. ^{1}H NMR (D_2O): 0.75 (d, 3H, J=6.1 Hz, CH_3); 0.77 (d, 3H, J=6.1 Hz, CH_3); 1.34 (t, 2H, J=7.0 Hz, CH_2CHN); 1.54 (m, 1H, CHCH$_3$); 2.32 (dd, 1H, J_1=15.7, J_2=8.1 Hz, CHHCO$_2$H); 2.47 (dd, 1H, J_1=15.7, J_2=4.4 Hz, CHHCO$_2$H); 3.13 (dt, 1H, J_1=6.6, J_2=5.8 Hz, CHN); 3.89 (ddd, 1H, J_1=8.1, J_2=5.8, J_3=4.4 Hz, CHOH). ^{13}C NMR (D_2O): 23.3 (CH_3); 24.5 (CH_3); 26.2 ($CH(CH_3)_2$); 40.7 (CH_2CHN); 42.6 (CH_2CO_2H); 56.1 (CHN); 70.2 (CHOH); 179.6 (CO_2H). *Boc-derivative*: Colorless solid, mp 118–120°C (from hexane–ethyl acetate); $[\alpha]^{23}_D$=−40.0 (c=1.1, MeOH).[Lit.[2e] mp 120–121°C; $[\alpha]^{23}_D$=−40.2 (c=1.0, MeOH)].

3.5.3. (3*R*,4*S*)-4-Amino-3-hydroxy-6-methylheptanoic acid (*anti*-10c). 77% yield. Colorless solid, mp 198–199°C (from H_2O–acetone). $[\alpha]^{23}_D$=−17.8 (c=0.4, H_2O).[Lit.[6a]: mp 202–203°C (from H_2O–acetone); $[\alpha]^{23}_D$=−18.0 (c=1.0, H_2O)]. ^{1}H NMR (D_2O): 0.72 (d, 3H, J=6.5 Hz, CH_3); 0.77 (d, 3H, J=6.5 Hz, CH_3); 1.29 (m, 2H, CH_2CH); 1.47 (m, 1H, C$H(CH_3)_2$; 2.20 (dd, 1H, J_1=15.2, J_2=8.2 Hz, CHHCO$_2$H); 2.27 (dd, 1H, J_1=15.2, J_2=5.5 Hz, CHHCO$_2$H); 3.24 (m, 1H, CHN); 4.06 (m, 1H, CHOH). ^{13}C NMR (D_2O): 23.0 (CH_3); 24.8 (CH_3); 26.1 ($CH(CH_3)_2$); 38.0 (CH_2CHN); 41.7 (CH_2CO_2H); 55.7 (CHN); 70.6 (CHOH); 180.5 (CO_2H).

3.5.4. (3*S*,4*S*)-4-Amino-3-hydroxy-5-phenylpentanoic acid (3*S*,4*S*)-AHPPA (*syn*-10d).[2j] 99% yield. Colorless solid, mp 205–206°C (dec); $[\alpha]^{23}_D$=−55.0 (c=0.8, H_2O). ^{1}H NMR (D_2O): 2.28 (dd, 1H, J_1=15.6, J_2=7.8 Hz, CHHCO$_2$H); 2.42 (dd, 1H, J_1=15.6, J_2=4.5 Hz, CHHCO$_2$H); 2.67 (dd, 1H, J_1=14.3, J_2=9.3 Hz, CHHPh); 2.94 (dd, 1H, J_1=14.3, J_2=5.6 Hz, CHHPh); 3.35 (m, 1H, CHN); 3.88 (ddd, 1H, J_1=7.8, J_2=5.7, J_3=4.5 Hz, CHOH); 7.10–7.40 (m, 5H, Harom). ^{13}C NMR (D_2O): 38.0 (CH_2Ph); 43.7 (CH_2CO_2H); 59.3 (CHN); 70.1 (CHOH); 130.0, 131.6, 131.8 (CHarom); 137.8 (Carom); 180.7 (CO_2H).

3.5.5. (3*R*,4*S*)-4-Amino-3-hydroxy-5-phenylpentanoic acid (3*R*,4*S*)-AHPPA (*anti*-10d). 97% yield. Colorless solid, mp 163–164°C (from H_2O–acetone). $[\alpha]^{23}_D$=−43.8 (c=0.4, H_2O). ^{1}H NMR (D_2O): 2.29 (dd, 1H, J_1=15.2, J_2=8.2 Hz, CHHCO$_2$H); 2.36 (dd, 1H, J_1=15.2, J_2=5.5 Hz, CHHCO$_2$H); 2.62 (dd, 1H, J=14.5, 10.8 Hz, CHHPh); 2.95 (dd, 1H, J=14.5, 4.3 Hz, CHHPh); 3.46 (ddd, 1H, J=10.8, 4.3, 3.2 Hz, CHN); 4.13 (ddd, 1H, J=8.2, 5.5, 3.2 Hz, CHOH); 7.10–7.30 (m, 5H, Harom). ^{13}C NMR (D_2O): 34.9 (CH_2Ph); 42.7 (CH_2CO_2H); 59.2 (CHN); 70.5 (CHOH); 129.9, 131.6, 131.7 (CHarom); 138.0 (Carom); 180.8 (CO_2H). Anal. Calcd for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23; N, 6.69. Found: C, 62.82; H, 7.09; N, 6.74.

3.5.6. (3*R*,4*R*)-4-Amino-3-hydroxy-4-phenylbutanoic acid (*ent-syn*-10e).[17] 91% yield. Colorless solid, mp 176–177°C (from H_2O/acetone). $[\alpha]^{23}_D$=−12.8 (c=0.9, H_2O). ^{1}H NMR (D_2O): 2.09 (m, 2H, CH_2CO$_2$H); 4.10 (d, 1H, J=9.3 Hz, CHN); 4.23 (m, 1H, CHOH); 7.15–7.35 (m, 5H, Harom). ^{13}C NMR (D_2O): 42.9 (CH_2CO_2H); 62.3 (CHN); 72.2 (CHOH); 130.1, 131.9, 132.2 (CHarom); 135.8 (Carom); 180.1 (CO_2H).

3.5.7. (3*S*,4*R*)-4-Amino-3-hydroxy-4-phenylbutanoic acid (*ent-anti*-10e).[17] 95% yield. Colorless solid, mp 177–178°C. $[\alpha]^{23}_D$=−10.9 (c=0.8, H_2O). ^{1}H NMR (D_2O): 1.98 (dd, J_1=15.6, J_2=7.2 Hz, CHHCO$_2$H); 2.06 (dd, 1H, J_1=15.6, J_2=5.9 Hz, CHHCO$_2$H); 4.28 (m, 2H, CHOH and CHN); 7.20–7.35 (m, 5H, Harom). ^{13}C NMR (D_2O): 43.4 (CH_2); 60.3 (CHN); 70.9 (CHOH); 130.5, 131.3, 131.7 (CHarom); 134.7 (Carom); 180.5 (CO_2H).

3.5.8. (3*S*,4*S*)-4-Amino-3-hydroxy-5-methylhexanoic acid (*syn*-10b). A solution of *syn*-**6b** (147 mg, 0.46 mmol) in TFA (4 mL) was stirred at rt for 1 h. The solvent was evaporated and methanol (2×5 mL) was added and evaporated twice to give the intermediate salt as a colorless solid. From this compound, the free β-hydroxy-γ-aminoacid was obtained by refluxing the salt in ethanol (7 mL) with excess propylene oxide (3 mL) followed by purification by flash chromatography (silica gel, CH_2Cl_2/MeOH/NH_4OH 6/4/1), to give *syn*-**10b** as a colorless solid: 68 mg (0.42 mmol, 78%). Mp 186–188°C. $[\alpha]^{23}_D$=−5.2 (c=1.2, H_2O). ^{1}H NMR (D_2O): 0.80 (d, 3H, J=6.9 Hz, CH_3); 0.87 (d, 3H, J=6.9 Hz, CH_3); 1.87 (m, 1H, CHCH$_3$); 2.24 (dd, 1H, J_1=15.5, J_2=7.6 Hz, CHHCO$_2$H); 2.40 (dd, 1H, J_1=15.5, J_2=4.7 Hz, CHHCO$_2$H); 2.86 (m, 1H, CHN); 4.01 (m, 1H, CHOH). ^{13}C NMR (D_2O): 18.1 (CH_3); 21.1 (CH_3); 29.6 ($CHCH_3$); 41.9 (CH_2); 63.0 (CHN); 68.0 (CHOH); 178.0 (CO_2H). Anal. Calcd for $C_7H_{15}NO_3$: C, 52.16; H, 9.38; N, 8.69. Found: C, 52.02; H, 9.51; N, 8.52.

3.5.9. (3*R*,4*S*)-4-Amino-3-hydroxy-5-methylhexanoic acid (*anti*-10b). Compound *anti*-**6b** (264 mg, 0.86 mmol) was deprotected as described for *syn*-**6b** to afford *anti*-**10b** as a colorless solid: 83 mg (0.52 mmol, 60%). Mp 171–172°C. $[\alpha]^{23}_{D}$=+22.2 (*c*=0.9, H_2O). ^{1}H NMR (D_2O): 0.81 (d, 3H, *J*=7.0 Hz, CH_3); 0.83 (d, 3H, *J*=7.0 Hz, CH_3); 1.71 (m, 1H, C*H*CH_3); 2.24 (dd, 1H, J_1=15.1, J_2=9.9 Hz, C*H*HCO_2H); 2.40 (dd, 1H, J_1=15.1, J_2=3.4 Hz, CH*H*CO_2H); 2.86 (dd, 1H, J_1=8.8, J_2=4.3 Hz, C*H*N); 4.01 (ddd, 1H, J_1=9.9, J_2=4.3, J_3=3.4 Hz, C*H*OH). ^{13}C NMR (D_2O): 20.5 (*C*H_3); 20.9 (*C*H_3); 29.5 (*C*HCH_3); 38.0 (*C*H_2); 63.7 (*C*HN); 68.0 (*C*HOH); 178.0 (*C*O_2H). Anal. Calcd for $C_7H_{15}NO_3$: C, 52.16; H, 9.38; N, 8.69. Found: C, 51.95; H, 9.07; N, 8.50.

Acknowledgements

Authors thank the financial support provided by the Spanish DGESYC (Project PB98-0361) and Junta de Castilla y León (Project VA67/99).

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