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Synthesis of non proteinogenic dipeptides by asymmetric hydrogenation

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Summary. N-Boc protected non-proteinogenic dipeptides with D,L-and L,L-configuration were prepared by catalytic asymmetric hydrogenation of the corresponding dehydrophenylalanyl-(L)-phenylalanine derivatives. The configuration of the new stereogenic centre depends first of all on the catalyst configuration and is less influenced by the substrate configuration. Diastereomeric excesses in the range of 80–96% de could be increased up to 99% by recrystallization. Analytical data of selected new compounds are given.

Keywords: Amino acids – Non-proteinogenic dipeptides – Dehydrodipeptides – Diastereoselectivity – N-Boc-Dehydroamino acids – Asymmetric hydrogenation – Chiral rhodium catalysts

Abbreviations: PINDOPHOS: 2,3-O,N-bis(diphenylphosphino)-1-(4-indolyloxy)-2-hydroxy-3-isopropylamino propane; PROPRAPHOS: 2,3-O,N-bis(diphenylphosphino)-1-(naphthoxy)-2-hydroxy-3-isopropylamino propane; BDPB: 1,4-bis(diphenylphosphino)butane.

Introduction

Biologically active small peptides play an increasing role in drug design. Sequences of four to ten residues are conformationally flexible, and the kind of peptide – receptor interaction is not easy to predict. The result can be an agonistic or an antagonistic effect, depending on structural, conformational, stereoelectronic, and dynamic properties in the course of interaction with the receptor. Emerging approaches in the molecular design of receptor-selective peptide ligands are given in an excellent review (Hruby et al., 1990). The incorporation of D-amino acids into biologically active peptides to stabilize conformations and to protect the peptides from enzymic degradation has been widely applied in the synthesis of LHRH antagonists (Reissmann et al., 1994; Pinski et al., 1995; Kutscher et al., 1997). Peptides with partly D-configuration

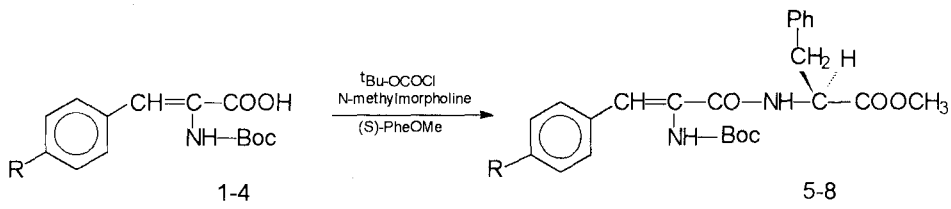
have been also used as enkephalin agonists (Morgan et al., 1977, somatostatin analogues (Wynants et al., 1988) and others. Besides this configurational change from proteinogenic to non-proteinogenic peptides bulky side chain groups can optimize the steric and stereoelectronic requirements for interaction with a particular receptor. The hopeful development of LHRH antagonists as antitumor agent in human hormon sensitive breast cancer and prostatic cancer is a good illustration of this strategic concept (Kutscher et al., 1997).

As a consequence of our investigations to synthesize non-proteinogenic amino acids by catalytic asymmetric hydrogenation (Kreuzfeld et al., 1996 a) we checked the possibility to hydrogenate dehydrodipeptides bearing different protective groups as an alternative route in comparison to the classical peptide synthesis (Döbler et al., 1999). Here we like to report on our experience in the enantioselective hydrogenation of some selected N-Boc-dehydrophenylalanyl-(L)-phenylalanine esters to N-Boc-(D)-phenylalanyl-(L)-phenylalanine esters.

Results and discussion

First unpublished experiments to hydrogenate N-Cbz-protected dehydrodipeptides showed unacceptable slow hydrogenation rates. We had expected that the retarding influence of this protective group would be significant in comparison to acetyl- or benzoyl-protected derivatives. But, in fact, these substrates are unfit to be hydrogenated under the conditions we used usually in this reaction.

The (*Z*)-2-N-Boc-3-phenylpropenoic acid derivatives **1–4** were prepared analogously to Shin et al. (1985) by saponification of the corresponding esters (Kreuzfeld et al., 1993; Krause et al., 1996; Kreuzfeld et al., 1996 b). Coupling with methyl (L)-phenylalaninate using the mixed anhydride technique yielded the dehydrodipeptides **5–8** (Scheme 1).



1-4 5-8

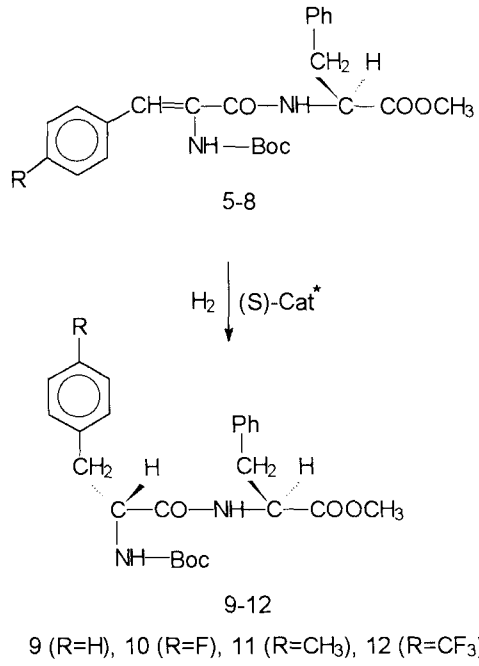
1(R=H), 2 (R=F), 3 ($R=CH_3$), 4 ($R=CF_3$)

5 (R=H), 6 (R=F), 7 ($R=CH_3$), 8 ($R=CF_3$)

Scheme 1. Dehydrodipeptide synthesis

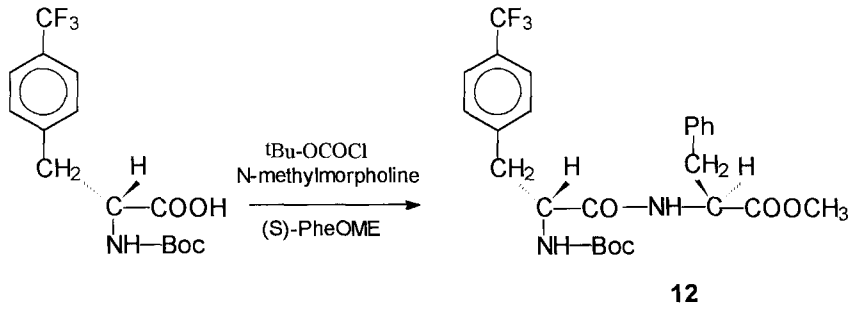
In order to induce D-configuration in the new stereogenic centre catalysts with (S)-configuration were used (Scheme 2).

The catalyst PINDOPHOS-Rh (Kreuzfeld et al., 1996 b) as well as PROPRAPHOS-Rh (Krause et al., 1992) showed nearly the same diastereoselection in the range of 60–70% de. Increased diastereoselectivities



Scheme 2. Dipeptide synthesis

were observed, when the (R)-catalysts was used, leading to 77–92% de the L,L-diastereomers. This is a configuration-assisted effect of the substrates, which has been also observed when the achiral catalyst $[BDPBRh]^+BF_4^-$ was used (13–19% excess of the L,L-diastereomers). The average hydrogenation time in the presence of this catalyst, needed for 50% of conversion (about 20min.), was significantly shorter than in case of the more bulky chiral catalysts (60–70min.). For a correct peak assignment of the hydrogenation products in the HPLC analysis alternatively compound **12** was synthesized on traditional way according to Scheme 3:



Scheme 3. Alternative synthesis of **12**

The hydrogenation experiments were performed in a standard apparatus as described in earlier work for the dehydroamino acids: 1.0mmol of substrate, 15ml of methanol at 25°C and 0.1MPa hydrogen pressure, 0.01mmol of catalyst. After the conversion was complete, a sample was taken for HPLC analysis. To isolate the peptides the solvent was evaporated under reduced

Table 1. Asymmetric hydrogenation of dehydrodipeptide esters

Substrate	Catalyst	Dipeptide esters	Diastereomeric ratio	de (%)	after one crystallization	
	(S)-PIN		D,L/L,L			
5		9	80.2/19.8	60.4	98.6/1.4	97.2
6		10	79.8/20.2	59.6	97.9/2.1	98.6
7		11	79.9/20.1	59.8	97.9/2.1	95.8
8		12	86.5/13.5	73.0	96.6/3.3	93.4
	(R)-PIN		L,L/D,L			
5		**	88.7/11.3	77.4	99.6/0.4	99.2
6		**	88.9/11.1	77.8	99.8/0.2	99.6
7		**	88.0/12.0	76.0	99.8/0.2	99.6
8		**	95.9/4.1	91.8	99.9/0.1	99.8

** These compounds have not been used for further analytical purpose.

pressure and the residue recrystallized from ethyl acetate/hexane to give an optical purity in the range of 90–99% de. The results are summarized in Table 1.

As can be seen from Table 1 the configuration-induced effect of the subtrates is evident. Consequenly, when the dehydrodipeptide has D-configuration and the catalyst with (S)-configuration is used, non-proteinogenic dipeptides with D,D-configuration can be prepared by this method in high optical purity. On the other hand each imaginable combination can be realized in the traditional way, when the corresponding non-coded amino acids are available. An example is given in compound **12**, Scheme 3. The advantage of the described methods to prepare this kind of dipeptides is their smoothly removable protective group as an essential for peptide building blocks.

Material and methods

The optical rotation was measured on a GYROMAT-HP polarimeter (Fa. Dr. Kernchen, Seelze). The diastereomeric excess (% de) was determined by HPLC on a Hewlett-Packard 1090 chromatograph series II, fitted with a 250 × 4.6 mm CHIRACEL OD-H column (eluent: n-hexane/isopropanol). Melting points are uncorrected and were determined on a Galen ™III (Cambridge Instruments). The mass spectra were recorded on an AMD 402/3 spectrometer (EI, source temperature 200°C). NMR spectra were recorded on a Bruker ARX 400 spectrometer at ambient temperature, chemical shifts are given in ppm relatively to internal TMS (δ scale). Under these conditions, several resonances appear broadened or even split due to the hindered rotation about the C-N amide bond. The assignment of the NH resonances has been confirmed by exchange with D_2O.

(Z)-2-N-Boc-3-phenyl-propenoic acid derivatives **(1–4)**

The following procedure for *(Z)-2-tert-Butyloxycarbonylamino-3-phenyl-propenoic acid* **1** is illustrative: To a solution of 3.11 g (10 mmol) of the methyl ester (Kreuzfeld et al., 1993) in dioxane (35 ml) was added a solution of LiOH × H_2O (923 mg, 22 mmol) in water (12 ml) with stirring. The resulting turbid mixture was stirred for 6 hours at room temperature and then diluted with water (15 ml). After filtration the filtrate was acidified with 1N

HCl to precipitate the acid. The microcrystalline product was filtered off, washed with water and dried over KOH. Yield 2.05 g (78%), mp 169–171°C. Recrystallized from ethanol/water: 1.94 g (74%), mp 171–174°C. Anal. calcd. for $C_{14}H_{17}NO_4$ (263.3), calcd. C 63.86 H 6.51 N 5.32; found: C 63.91 H 6.40 N 5.32. MS: 263.2 (M^+), 207.1 (M^+ − butene), 172.2 (M^+ − O-tert-Bu − H_2O), 163.3 (M^+ − butene − CO_2), 56.9 (tert-butyl). ^{1}H NMR (acetone-d_6): δ 1.38 (br s, CMe_3), 7.30 (br s, CH olef.), 7.49 (br, NH), 7.67, 7.38, 7.33 (CH aromat., ortho, meta, para). ^{13}C NMR (acetone-d_6): δ 28.3 ($C\underline{Me}_3$), 80.2 ($\underline{C}Me_3$), 132.0 (br, CH olef.), 127.1 (C olef. two signals), 130.7, 129.8 para, 129.2 (CH aromat.), 135.2 (C aromat.), 154.3 (CO amide, two signals), 167.2 (CO acid).

(*Z*)-2-tert-Butyloxycarbonylamino-3-(4-fluorophenyl)propenoic acid **2**: from the corresponding ester (Krause, 1996): yield 2.49 g (89%), mp 171–173°C, recrystallized from EtOH/water: 2.26 g (80%), mp 172–175°C, $C_{14}H_{16}FNO_4$ (281.3), calcd. C 59.78 H 5.73 N 5.05; found C 59.69 H 5.65 N 5.05. MS: 281 (M^+), 225.3 (M^+ − butene), 207 (M^+ − BuOH), 190.2 (M^+ − O-tert-Bu − H_2O), 181.3 (M^+ − butene − CO_2), 56.9 (tert-butyl). ^{1}H NMR (acetone-d_6): δ 1.37 (br s, CMe_3), 7.29 (br s, CH olef.), 7.48 (br, NH), 7.72, 7.15 (CH aromat.). ^{13}C NMR (acetone-d_6): δ [J(^{13}C, ^{19}F)] 28.3 ($C\underline{Me}_3$), 80.2 ($\underline{C}Me_3$), 126.7 (br, C olef.), 130.9 (br, CH olef.), 116.1 [d, 22 Hz] and 132.9 [d, 8 Hz] (CH aromat.), 131.7 [d, 3 Hz] and 163.5 [d, 248 Hz] (C aromat.), 154.3 (CO amide, two signals), 167.1 (CO acid).

(*Z*)-tert-Butyloxycarbonylamino-3-(4-methyl-phenyl)propenoic acid **3**: from the corresponding ester (Kreuzfeld, 1996 b): yield 2.3 g (83%), mp 166–170°C (EtOH/water) $C_{15}H_{19}NO_4$ (277.3), calcd. C 64.96 H 6.91 N 5.05; found C 65.20 H 6.80 N 5.15 MS: 277.1 (M^+), 221.2 (M^+ − butene), 203.3 (M^+ − BuOH), 186.2 (M^+ − O-tert-Bu − H_2O), 177.1 (M^+ − butene − CO_2), 56.9 (tert-butyl). ^{1}H NMR (acetone-d_6): δ 1.39 (br s, CMe_3), 2.32 (s, CH_3), 7.29 (br s, CH olef.), 7.42 (br, NH), 7.20, 7.57 (CH aromat.). ^{13}C NMR (acetone-d_6): δ 21.3 (CH_3 aromat.), 28.4 ($C\underline{Me}_3$), 80.0 ($\underline{C}Me_3$), 126.2 (C olef., two signals), 132.6 (br, CH olef.), 129.9, 130.8 (CH aromat.), 132.3, 140.0 (C aromat.), 154.4 (CO amide, two signals), 167.3 (CO acid).

(*Z*)-tert-Butyloxycarbonylamino-3-(4-methyl-phenyl)propenoic acid **4**: from the corresponding ester (Krause, 1996): yield 2.67 g (81%), mp 166–168°C (EtOH/water) $C_{15}H_{16}F_3NO_4$ (331.3), calcd. C 54.38 H 4.87 N 4.23; found C 54.33 H 4.94 N 4.35 MS: 331.2 (M^+), 275 (M^+ − butene), 231.1 (M^+ − butene − CO_2), 257.1 (M^+ − BuOH), 231.1 (M^+ − butene − CO_2), 57.0 (tert-butyl). ^{1}H NMR (acetone-d_6): δ 1.37 (br s, CMe_3), 7.30 (br s, CH olef.), 7.66 br, NH), 7.72, 7.82 (CH aromat.). ^{13}C NMR (acetone-d_6): δ [J(^{13}C, ^{19}F)] 28.3 ($C\underline{Me}_3$), 80.5 ($\underline{C}Me_3$), 128.9 (br, CH olef.), 125.1 [q, 272 Hz] (CF_3), 129.1, 129.2 (C olef.), 125.9 [q, 4 Hz] and 130.9 (CH aromat.), 129.5 [q, 30 Hz] and 139.6 (C aromat.), 153.8, 153.9 (CO amide), 166.7 (CO acid).

Synthesis of the dehydrodipeptides **5–8**

The following procedure for *N-[(Z)-N-Boc-(phenyl)dehydroalanyl]-(L)-phenylalanine methyl ester* **5** is illustrative. A: 2.16 g of L-Phenylalanine methyl ester hydrochloride (10 mmol) were dissolved in warm DMF (20 ml). After cooling to room temperature 1.12 ml (10 mmol) N-methylmorpholine was added. B: 2.63 g **1** (10 mmol) were dissolved with stirring in dry THF (50 ml), cooled under argon to −15°C and neutralized with N-methylmorpholine (1.12 ml, 10 mmol). Isobutyl chloroformate (1.32 ml, 10 mmol) was added and about one minute later solution A. The ice bath was removed and the mixture warmed to room temperature with stirring. Precipitated N-methylmorpholino hydrochloride was separated by suction and the salt washed with some milliliters of dry THF. After evaporation of the solvent under reduced pressure the residue was dissolved in 150 ml of ethyl acetate and successively washed with water (50 ml), 0.5 N $KHCO_3$ (50 ml), 0.5 N HCl (50 ml) and water (50 ml). The organic phase was dried (Na_2SO_4) and the solvent evaporated under reduced pressure. Yield 3.19 g (75%), recrystallized from EtOAc/hexane: 2.96 g (70%), mp 129–131°C, $[a]_D^{25}$ 67.8 (c1, $CHCl_3$), $C_{24}H_{28}N_2O_5$ (424.5), calcd. C 67.91 H 6.65 N 6.69; found C 67.75 H 6.45 N 6.73, MS: 424 (M^+), 368 (M^+ − butene), 351 (M^+ − O-tert-Bu), 91 ($PhCH_2$), 57 (tert-Bu). ^{1}H NMR ($CDCl_3$): δ 1.41 (s, CMe_3), 3.21 (d, CH_2

Table 2. ^{1}H NMR data of the dipeptides **9–12** in acetone-d_6. Chemical shifts δ, homonuclear coupling constants J in brackets. Index *(1)* refers to the Boc-protected, R-substituted phenylalanine moiety (drawn on the left in Scheme 2), index *(2)* refers to the phenylalanine ester moiety (drawn on the right in Scheme 2)

Compound	**9**	**10**	**11**	**12**
R=	H	F	CH_3	CF_3
^{t}Bu	1.32	1.32	1.32	1.30
CH_2 *(1)*	3.04	3.02	2.98	3.14
[^3J/Hz]	[5.0]	[5.4]	[5.8]	[5.4]
	2.77	2.74	2.73	2.84
[^3J/Hz]	[8.9]	[8.7]	[8.5]	[9]
[^2J/Hz]	[14.0]	[13.9]	[14.0]	[13.8]
CH *(1)*	4.37	4.34	4.33	4.43
NH *(1)*	5.96	5.99	5.94	6.03
phenylene	7.2 (m)	7.12	7.01 (*)	7.55
		6.96		7.33
R	7.2 (m)	–	2.25	–
OCH_3	3.65	3.66	3.65	3.66
CH_2 *(2)*	3.10	3.12	3.09	3.13
[^3J/Hz]	[5.6]	[5.4]	[5.6]	[5.6]
	2.98	2.97	2.97	2.98
[^3J/Hz]	[7.9]	[8.1]	[7.9]	[8.3]
[^2J/Hz]	[13.7]	[13.8]	[13.9]	[13.8]
CH *(2)*	4.70	4.69	4.69	4.72
NH *(2)*	7.57	7.60	7.53	7.66
phenyl	7.2 (m)	7.28	7.27	7.28 *(meta)*
		7.21	7.19	7.21 *(o/p)*

(*) AA′BB′ pattern

benzyl), 3.72 (s, OCH_3), 4.99 (dt, ^3J(NH, CH) = 7.5 Hz, ^3J(CH, CH_2) = 5.6 Hz; CH aliph.), 5.89 (br, NH), 6.75 (d, NH), 7.07 (s, CH, olef.), 7.15, 7.29, 7.37, 7.43 (CH aromat.).

N-[(*Z*)-N-Boc-(4-fluorophenyl)dehydroalanyl-(L)-phenylalanine methyl ester **6**: analogously to **5**, starting from **2**. Yield 3.26 g (74%), mp 128–130°C (EtOAc/hexane), $[a]_D^{25}$ 65.0 (c1, $CHCl_3$), $C_{24}H_{27}FN_2O_5$ (442.5), calcd. C 65.14 H 6.15 N 6.33; found C 65.23 H 6.19 N 6.31, MS: 442 (M^+), 369 (M^+ – O-tert-Bu), 342 (M^+ – CO_2 – butene), 91 ($PhCH_2$), 57 (tert-Bu). ^{1}H NMR ($CDCl_3$): δ 1.41 (s, CMe_3), 3.20 (d, CH_2 benzyl), 3.73 (s, OCH_3), 4.97 (dt, ^3J(NH, CH) = 7.7 Hz, ^3J(CH, CH_2) = 5.8 Hz; CH aliph.), 5.91 (br, NH), 6.75 (d, NH), 7.06 (s, CH olef.), 7.06, 7.14, 7.27, 7.43 (CH aromat.).

N-[(*Z*)-N-Boc-(4-methylphenyl)dehydroalanyl]-(L)-phenylalanine methyl ester **7**: starting from **3**, yield 3.05 g (70%), mp 138–140°C (EtOAc/hexane), $[a]_D^{25}$ 68.31 (c1, $CHCl_3$), $C_{25}H_{30}N_2O_5$ (438.5), calcd. C 68.47 H 6.90 N 6.39; found C 68.37 H 6.71 N 6.48, MS: 438 (M^+), 364 (M^+ – tert-BuOH), 388 (M^+ – CO_2 – butene), 91 (tert-Bu). ^{1}H NMR ($CDCl_3$): 1.42 (s, CMe_3), 2.34 (s, CH_3 aromat.), 3.20 (d, CH_2 benzyl), 3.72 (s, OCH_3), 4.98 (dt, ^3J(NH, CH) = 7.5 Hz, ^3J(CH, CH_2) = 5.6 Hz; CH aliph.), 5.83 (br, NH), 6.75 (d, NH), 7.08 (s, CH olef.), 7.16, 7.18, 7.28, 7.34 (CH aromat.).

N-[(*Z*)-N-Boc-(4-trifluoromethyl)dehydroalanyl]-(L)-phenylalanine methyl ester **8**: starting from **4**, yield 3.33 g (68%), mp 135–137°C (EtOAc/hexane), $[a]_D^{25}$ 59.6 (c1, $CHCl_3$), $C_{25}H_{27}F_3N_2O_5$ (492.5), calcd. C 60.97 H 5.53 N 5.69; found C 60.78 H 5.55 N 5.68, MS: 492 (M^+), 436 (M^+ – butene), 4.19 (M^+ – O-tert-Bu), 392 (M^+ – CO_2 – butene), 91 ($PhCH_2$), 57 (tert-Bu). ^{1}H NMR ($CDCl_3$): 1.40 (s, CMe_3), 3.22 (d, CH_2 benzyl), 3.75 (s,

Table 3. ^{13}C NMR data of the dipeptides **9–12** in acetone-d_6. Chemical shifts δ, coupling constants $J(^{13}C, ^{19}F)$ in brackets

Compound	**9**	**10**	**11**	**12**
R =	H	F	CH_3	CF_3
$C\underline{Me}_3$	28.4	28.4	28.5	28.4
$\underline{C}Me_3$	79.3	79.3	79.3	79.4
OCH_3	52.3	52.3	52.3	52.4
CH_2	38.7	38.2	38.3	38.7
	38.3	38.0	38.3	38.3
CH aliph.	56.2	56.1	56.3	55.9
	54.4	54.3	54.3	54.4
phenyl	130.1	130.1	130.1	130.2
	129.2	129.2	129.2	129.2
(*para*)	127.6	127.6	127.6	127.6
(*ipso*)	137.7	137.8	137.7	137.7
phenylene	138.5	162.5	136.4	143.4
[*J*/Hz]		[242]		
	130.2	134.5	135.4	131.0
	128.9	131.9	130.0	128.9
[*J*/Hz]		[8]		[31]
	127.1	115.5	129.6	125.7
[*J*/Hz]		[21]		[4]
CO	172.4	172.4	172.4	172.4
	172.1	171.8	172.0	171.7
	156.0	156.0	156.0	156.0
R	–	–	21.0	125.5
[*J*/Hz]				[271]

OCH_3), 4.98 (dt, ^3J(NH, CH) = 7.5 Hz, ^3J(CH, CH_2) = 5.8 Hz; CH aliph.), 6.02 (br, NH), 6.73 (d, NH), 6.98 (s, CH olef.), 7.13, 7.29, 7.52, 7.63 (CH aromat.).

Analytical data of the dipeptides **9–12**

N-Boc-(D)-phenylalanyl-(L)-phenylalanine methyl ester **9**: mp 130–133°C (EtOAc/hexane, $[a]_D$ 46.8 (c 0.5, $CHCl_3$), 98% de by HPLC, $C_{24}H_{30}N_2O_5$ (426.5) calcd. C 67.58 H 7.09 N 6.57, found C 67.73 H 6.45 N 6.48; MS 425.9 (M^+), 369.8 (M^+ – butene), 352.9 (M^+ – O-tert-Bu), 308.8 (M^+ – H_2N-COO-tert-Bu). For ^1H NMR and ^{13}C NMR data see Tables 2 and 3.

N-Boc-D-4-fluoro-phenylalanyl-L-phenylalanine methyl ester **10**: mp 136–139°C (EtOAc/hexane), $[a]_D$ 45.2 (c 0.5, $CHCl_3$), 98.7% de (HPLC), $C_{24}H_{29}FN_2O_5$ (444.5), calcd. C 64.85 H 6.58 N 6.30, found C 65.09 H 6.54 N 6.36; MS: 443.8 (M^+), 387.8 (M^+ – butene), 370.7 (M^+ – O-tert-Bu), 326.9 (M^+ – H_2N-COO-tert-Bu). For NMR data see Tables 2 and 3.

N-Boc-D-4-methyl-phenylalanyl-L-phenylalanine methyl ester **11**: mp 139–147°C (EtOAc)/hexane), $[a]_D$ 50.1 (c 0.5, $CHCl_3$), 98.2% de (HPLC), $C_{25}H_{32}N_2O_5$ (440.5) calcd. C 68.16 H 7.32 N 6.36, found C 67.71 H 7.21 N 6.18; MS: 440.9 (M^+), 383.8 (M^+ – butene), 366.8 (M^+ – O-tert-Bu), 322.9 (M^+ – H_2N-COO-tert Bu). For NMR data see Tables 2 and 3.

N-Boc-D-4-trifluoromethyl-phenylalanyl-L-phenylalanine methyl ester **12**: mp 159–166°C (EtOAc/hexane), $[a]_D$ 45.1 (c 0.5, $CHCl_3$), 96.9% de (HPLC), $C_{25}H_{29}F_3N_2O_5$ (494.5), calcd. C 60.72 H 5.91 N 5.66, found C 60.67 H 5.80 N 5.60; MS: 493.9 (M^+), 437.8 (M^+ – butene), 421 (M^+ – O-tert-Bu), 377 (M^+ – H_2N-COO-tert-Bu). For NMR data see Tables 2 and 3.

N-Boc-D-4-trifluoromethyl-phenylalanyl-L-phenylalanine methyl ester **12**: prepared by peptide synthesis according to scheme 3, mp 164–166°C (EtOAc/hexane, $[a]_D$ 45.8 (c 0.5 $CHCl_3$), 99.4% de (HPLC), $C_{25}H_{29}F_3N_2O_5$ (494.5), found C 60.63 H 5.81 N 5.75; MS: 494 (M^+), 437.8 (M^+ − butene), 421 (M^+ − O-tert Bu). For NMR data see Tables 2 and 3.

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