119. Novel Open-Chain and Cyclic Conformationally Constrained (*R*)- and (*S*)-α,α-Disubstituted Tyrosine Analogues

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Dedicated to Prof. *A. Eschenmoser* on the occasion of his 70th birthday

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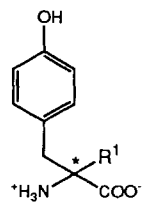
A series of novel open-chain and cyclic conformationally constrained (*R*)- and (*S*)-α,α-disubstituted tyrosine analogues **1a–e** were synthesized in good yields and high optical purities (*Schemes 1* and *2*). The absolute configurations of these tyrosine analogues were unambiguously determined based on the X-ray structures of the precursor diastereoisomeric peptides of type **4** and **5**. Four of these structures are described (*Figs. 1–4*), showing β-turn type-I geometries for dipeptides **4b**, **5b**, and **4c** and an extended conformation for peptide **5c** (*Table 3*). The conversion of the free amino acids **1a–c** into suitably protected building blocks **11a–d** and **15d,e** for peptide synthesis is discussed (*Schemes 3* and *4*).

1. Introduction. – L-Tyrosine (Tyr) belongs to the twenty coding amino acids occurring in proteins and has received special attention in recent years due to the fact that Tyr is involved in important cell signalling pathways. Phosphorylation of specific Tyr residues by tyrosine kinases and their dephosphorylation by tyrosine phosphatases are emerging as key mechanisms to activate, modulate, or translocate proteins [1]. The crystal structures of phosphotyrosine-containing peptides bound to src homology-2 (SH2) [2] [3] domains have promoted the design of inhibitors based on modified phosphorylated and non-phosphorylated Tyr analogues. Conformationally constrained Tyr analogues were also used in the field of δ opioid receptor antagonists [4].

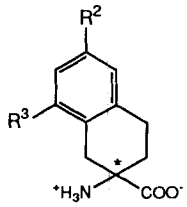
In recent years, there has been a growing interest in incorporating conformationally constrained amino acids into small-to-medium-sized bioactive peptides to modulate their low-energy conformations and elucidate structure-activity relationships. We and others have particularly focused on the study of the α,α-disubstituted (*R*)- and (*S*)-amino acids [5] [6]. Such amino acids can stabilize different types of β-turn [7–10], 3_{10}- and α-helical [4] [5] [7], as well as extended [11] conformations, when incorporated into different positions of small-to-medium-sized peptides.

In this paper we describe a novel and concise synthesis of the open-chain (*R*)- and (*S*)-Tyr analogues **1a–c** (*Scheme 1*) and their related tetralin-based cyclic analogues (*R*)- and (*S*)-**1d,e** (*Scheme 2*) following our general approach to synthesize optically pure open-chain and cyclic amino acids [7–9]. The 8-hydroxytetralin derivatives (*R*)- and (*S*)-**1e** were described earlier and used as building blocks by our group for the design and synthesis of a series of novel templates for the N-terminal, α-helical stabilization of small-to-medium-sized peptides ('N'-caps) [12].

[1]) Part of Ph. D. Thesis of *R. R.*, University of Zürich, 1995.



(*R*)- and (*S*)-**1a** R^1 = Me
(*R*)- and (*S*)-**1b** R^1 = ^{i}Pr
(*R*)- and (*S*)-**1c** R^1 = Ph



(*R*)- and (*S*)-**1d** R^2 = OH, R^3 = H
(*R*)- and (*S*)-**1e** R^2 = H, R^3 = OH

Based on the X-ray structures of **4b,c** and **5b,c** (*Figs. 1–4*), the absolute configurations of the novel Tyr analogues **1b** and **1c** were unambiguously determined. The interesting conformational aspects of peptides **4b,c** and **5b,c** will be discussed in *Chapt. 4*. In addition to this, we present a general strategy to orthogonally protect the three functional groups of the Tyr analogues **1**, featuring the (*tert*-butyl)diphenylsilyl (^{t}BuPh$_2$Si) group [13] for the protection of the phenolic group. Thus, the open-chain doubly protected (*N*-(benzyloxy)carbonyl (Z) and *O*-(*tert*-butyl)diphenylsilyl) tyrosine analogues (*S*)-**11a**, (*R*)-**11b**, and (*R*)-**11c** (*Scheme 3*), the cyclic analogue (*S*)-**11d**, and the doubly protected (*N*-(*tert*-butoxy)carbonyl (Boc) and *O*-(*tert*-butyl)diphenylsilyl) analogues (*S*)-**15d** and (*S*)-**15e** (*Scheme 4*) constitute orthogonally protected Tyr building blocks ready for incorporation into peptides.

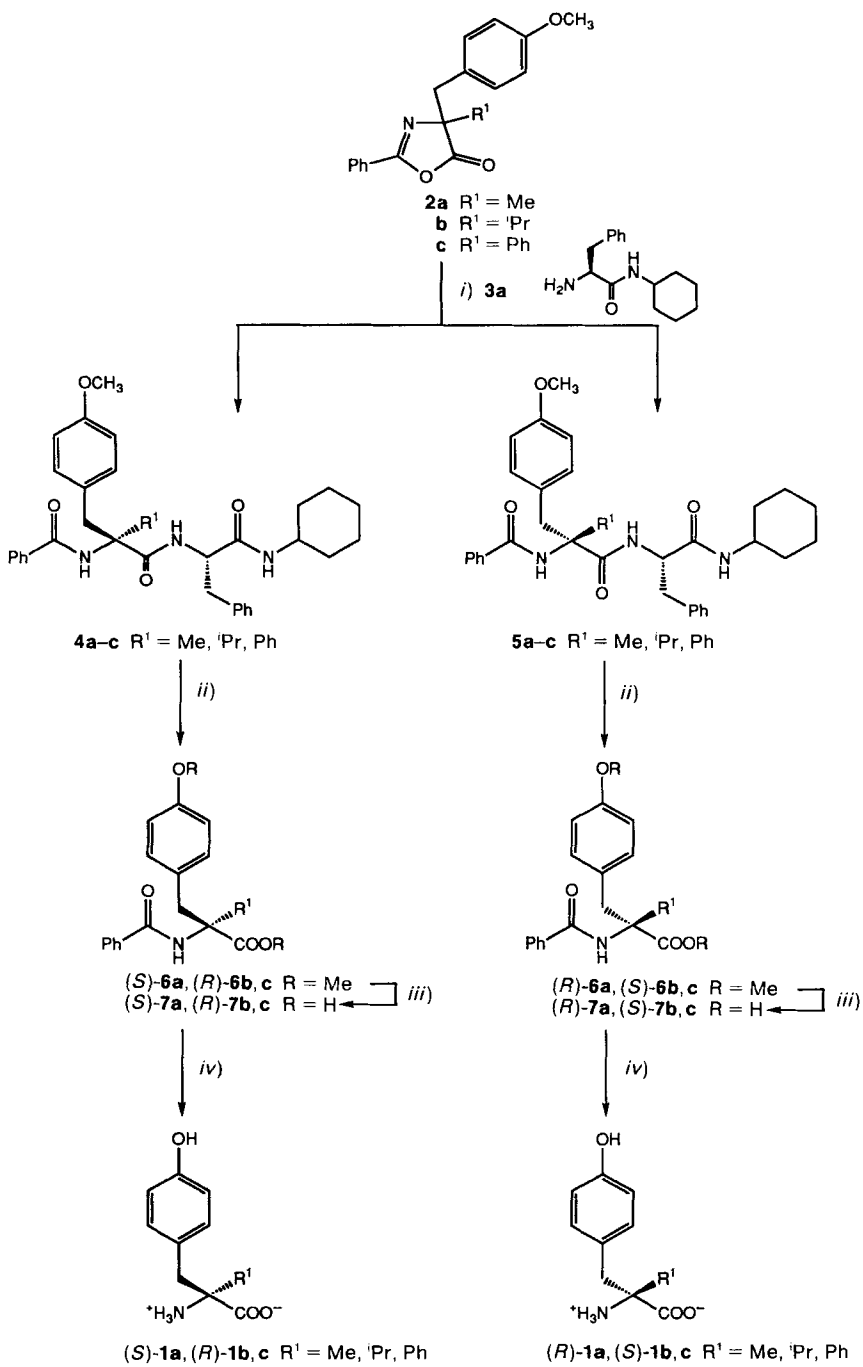
2. Synthesis of the Open-Chain and Cyclic Tyr Analogues 1a–e. – The synthesis of the open-chain analogues **1a–c** started from the racemic 4,4-disubstituted 2-phenyloxazol-5(4*H*)-ones **2a–c** [14], which reacted smoothly with L-phenylalanine cyclohexylamide (**3a**) in *N*-methylpyrrolidin-2-one (NMP) at 90° (*Method A*; *Scheme 1*). The resulting diastereoisomeric peptides **4a–c** and **5a–c** were obtained in good yields (*Table 1*) after flash chromatography (FC) [15] and/or crystallization (see *Exper. Part*). The absolute configurations at the quaternary centres in these peptides were unambiguously determined based on the crystal structures of **4b,c** and **5b,c**. The stereoplots of the correspond-

Table 1. *Synthesis of the Peptides* **4a–e** *from Oxazol-5(4H)-ones* **2a–e**

Starting material	Peptide	R^1	R^2	R^3	R^4	*n*	Yield [%][a]	$[\alpha]_D^{20}$ (*c*, solvent)
rac-**2a**	**4a**	Me	–	–	–	–	40	+10.0 (0.2, $CHCl_3$)
	5a	Me	–	–	–	–	42	+46.0 (0.2, $CHCl_3$)
rac-**2b**	**4b**	^{i}Pr	–	–	–	–	41	−6.0 (0.2, $CHCl_3$)
	5b	^{i}Pr	–	–	–	–	40	+47.5 (0.2, $CHCl_3$)
rac-**2c**	**4c**	Ph	–	–	–	–	44	+21.0 (0.2, $CHCl_3$)
	5c	Ph	–	–	–	–	43	−40.5 (0.2, $CHCl_3$)
rac-**2d**	**4d**	–	MeO	H	NC_4H_8	2	41	−2.0 (0.4, EtOH)
	5d	–	MeO	H	NC_4H_8	2	42	−18.0 (0.5, EtOH)
rac-**2e**	**4e**	–	H	MeO	NHC_6H_{11}	1	45	−21.0 (0.2, MeOH)
	5e	–	H	MeO	NHC_6H_{11}	1	46	+12.0 (0.2, MeOH)

[a]) Yield based on isolated and purified material.

Scheme 1



i) NMP, 80°. *ii*) CF_3SO_3H, MeOH, 80°. *iii*) BBr_3, CH_2Cl_2. *iv*) Conc. HCl, dioxane, 100°.

ing ORTEP drawings are shown in *Figs. 1–4*. The related cyclic amino acids **1d, e** were prepared in a similar fashion starting from the corresponding oxazol-5(4*H*)-ones **2d, e** [7] and treatment with **3a** or **3b** according to *Method A* (*Scheme 2*). The diastereoisomeric peptides **4d, e** and **5d, e** were separated by FC [15] in good yields (*Table 1*). It turned out that the separation of **2d** was easier to perform with **3b** [7], whereas for **2e**, we chose again **3a** [8]. The absolute configurations in the tetralin-based Tyr analogues were established earlier by X-ray analysis [7].

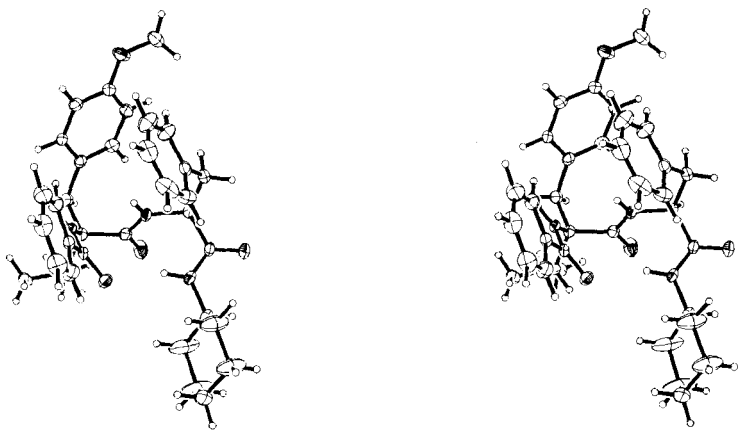


Fig. 1. *Stereoplot* (ORTEP) *of* **4b**

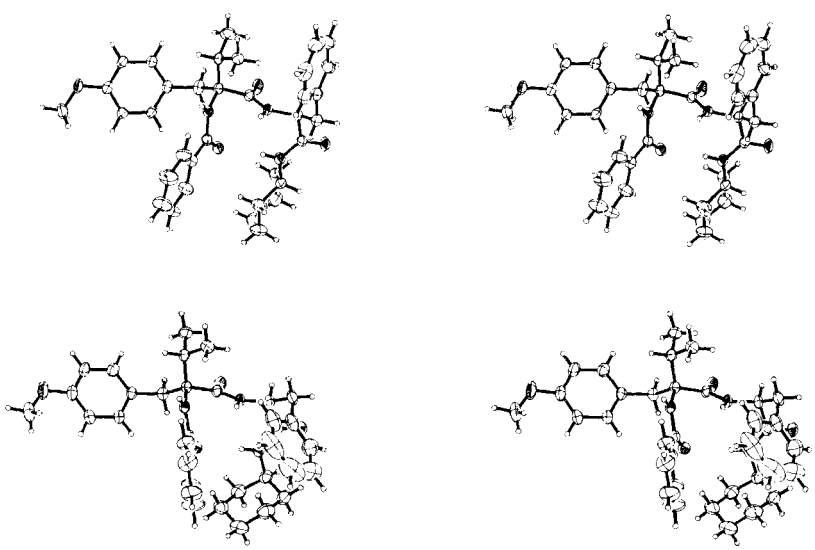


Fig. 2. *Stereoplot* (ORTEP) *of* **5b** *and* **5b′** (two independent molecules in the asymmetric unit)

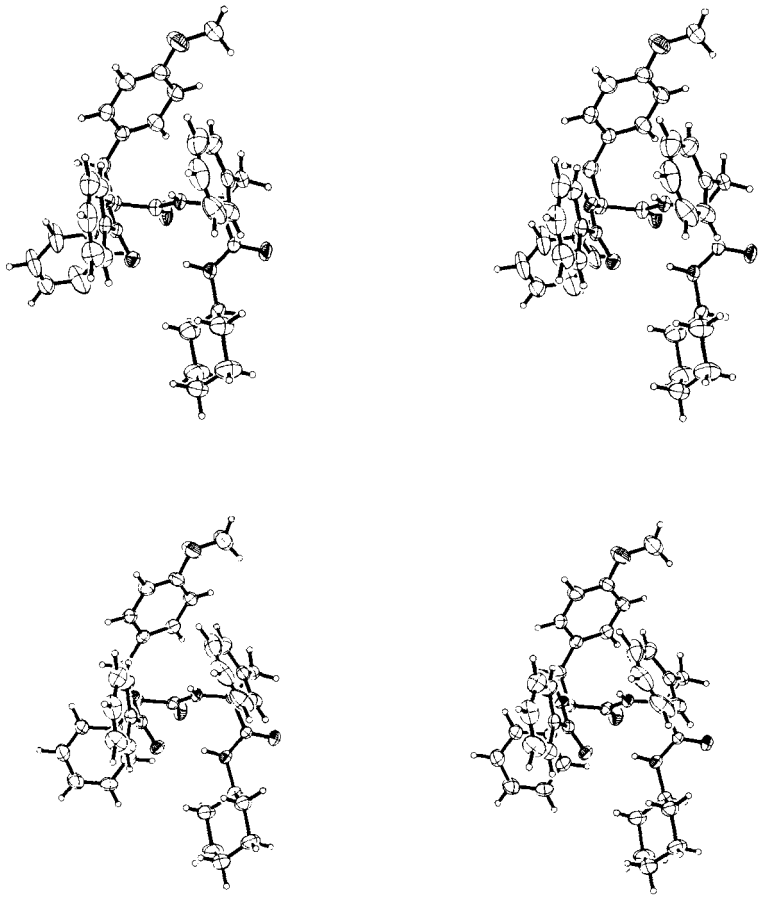


Fig. 3. *Stereoplot* (ORTEP) *of* **4c** *and* **4c'** (two independent molecules in the asymmetric unit)

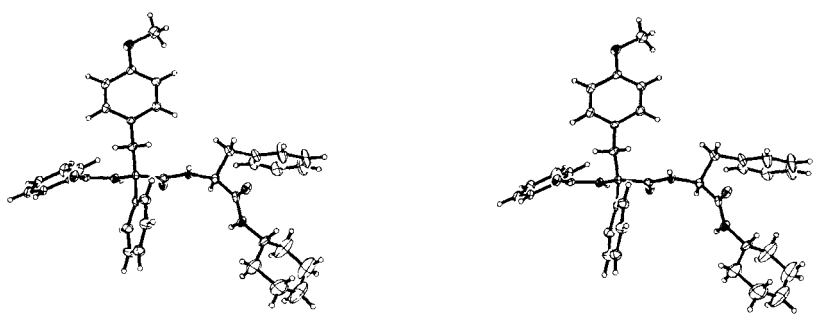
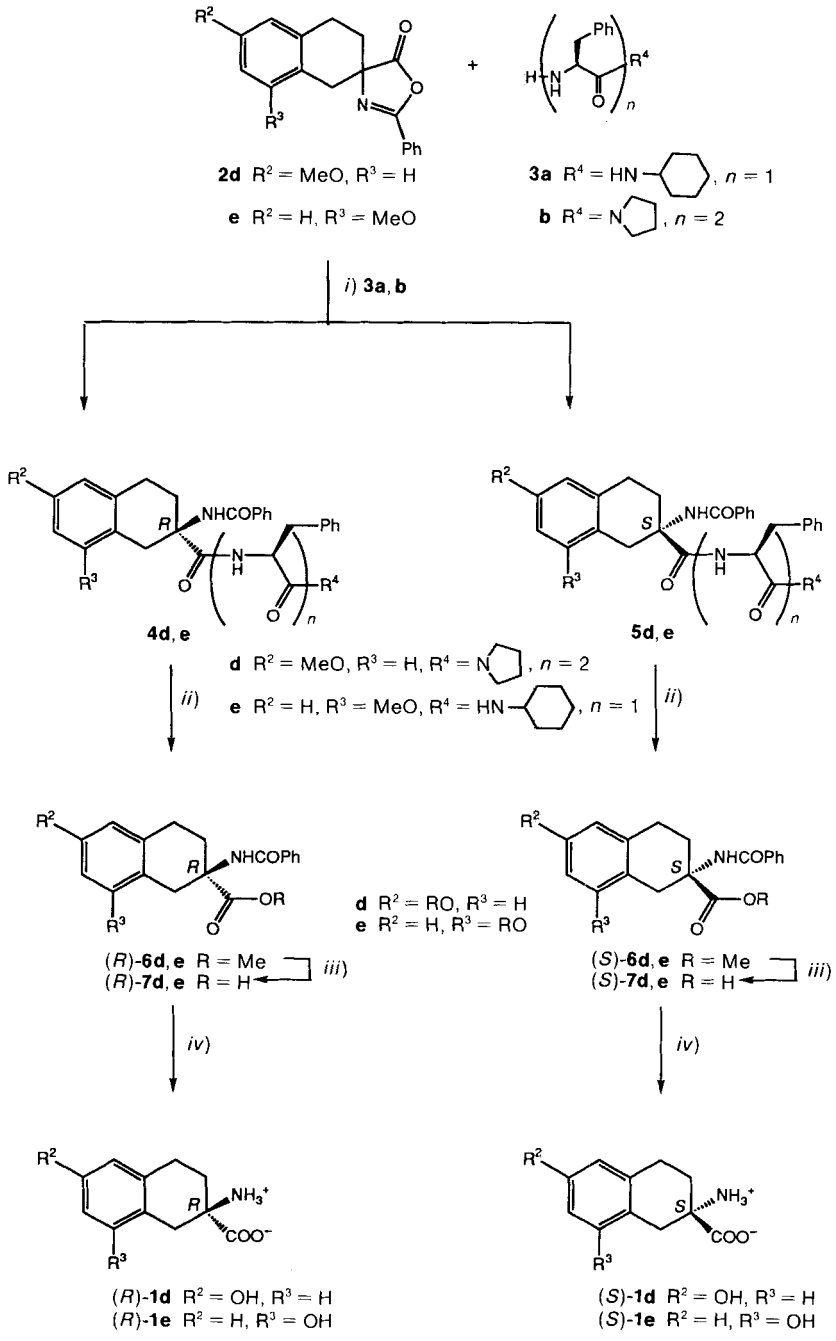


Fig. 4. *Stereoplot* (ORTEP) *of* **5c**

Scheme 2



i) NMP, 80°. *ii*) CF_3SO_3H, MeOH, 80°. *iii*) BBr_3, CH_2Cl_2. *iv*) Conc. HCl, dioxane, 100°.

Table 2. *Cleavage of Peptides* **4a–e** *and* **5a–e** *to (*R*)- and (*S*)-***6a–e*** *(Method B)*

Peptide	Product	$[\alpha]_D^{20}$ (*c*, solvent)	Yield [%][a])
4a	(*S*)-**6a**	+79.5 (0.2, $CHCl_3$)	91
5a	(*R*)-**6a**	−78.0 (0.2, $CHCl_3$)	91
4b	(*R*)-**6b**	+119.5 (0.2, $CHCl_3$)	97
5b	(*S*)-**6b**	−117.5 (0.2, $CHCl_3$)	92
4c	(*R*)-**6c**	+98.0 (0.2, CH_2Cl_2)	94
5c	(*S*)-**6c**	−97.0 (0.2, CH_2Cl_2)	99
4d	(*R*)-**6d**	−68.0 (0.4, CH_2Cl_3)	92
5d	(*S*)-**6d**	+67.7 (0.3, $CHCl_3$)	94
4e	(*R*)-**6e**	−142.5 (0.2, $CHCl_3$)	93
5e	(*S*)-**6e**	+138.5 (0.2, $CHCl_3$)	94

[a]) Based on isolated and purified material.

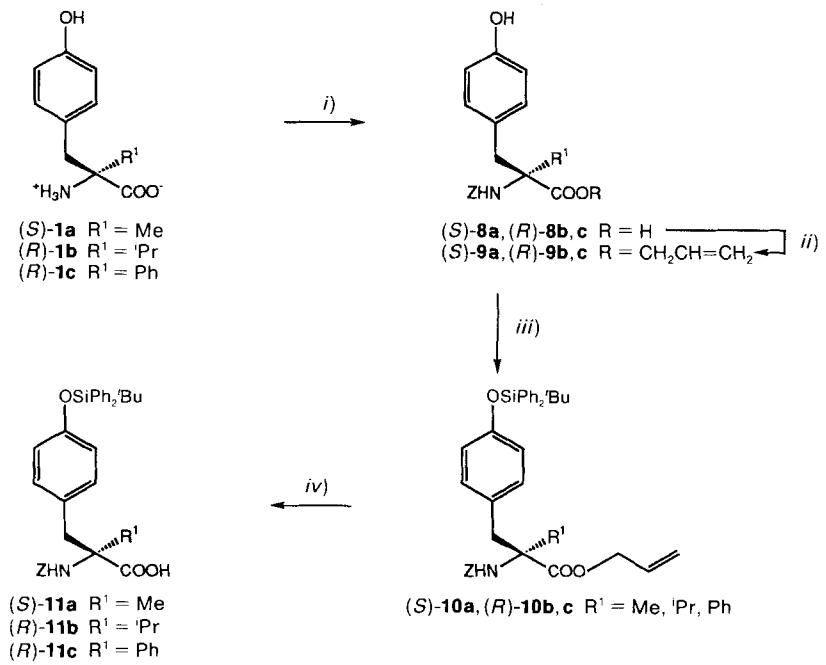
The diastereoisomeric peptides **4a–e** and **5a–e** were individually treated with CF_3SO_3H in MeOH at 80° (*Method B*) to form the optically pure methyl esters (*R*)- and (*S*)-**6a–e** (*Schemes 1* and *2*) in high yields (*Table 2*), along with the CF_3SO_3H salts of **3a, b** which could be recovered in > 90% yield. As previously shown, the enantiomeric purity of the compounds was essentially 100%, which was double-checked by anal. HPLC on a *Chiracel OD* column. The mechanism of the selective amide cleavage was discussed previously [7]. Treatment of (*R*)- and (*S*)-**6a–e** with excess BBr_3 resulted in ether and ester cleavages to form the corresponding acids (*R*)- and (*S*)-**7a–e** (*Method C*) in high yields. Finally, hydrolysis of the acids (*R*)- and (*S*)-**7a–e** with aqueous HCl (37%) in dioxane at 100° (*Method D*) gave the optically pure open-chain and cyclic Tyr analogues **1a–e** in high yields, after precipitation at neutral pH (*Method D*).

3. Synthesis of the Orthogonally Doubly Protected Open-Chain and Cyclic Tyr Analogues (*R*)- and (*S*)-11a–d and (*R*)- and (*S*)-15d, e. – As the optically pure open-chain and cyclic Tyr analogues **1a–e** are potentially interesting amino acids for incorporation into short peptides, the corresponding building blocks with suitable protecting groups were required. Previous experience has shown that the phenolic groups would need protection due to the slower coupling rates of these sterically hindered amino acids. From earlier work [16], we knew that certain trisubstituted silyl-protected phenols are quite stable to aqueous (*e.g.* 2N aq. HCl, dioxane, room temperature) as well as to nonaqueous hydrolytic conditions (CF_3COOH, CH_2Cl_2, 0°). We, therefore, chose the ^{t}BuPh$_2$Si group for transient protection of the tyrosine phenol OH in combination with the *N*-Boc or the *N*-Z group. First, the sterically more demanding open-chain Tyr analogues (*S*)-**1a**[2]), (*R*)-**1b**[2]), and (*R*)-**1c**[2]) (*Scheme 3*) and (*S*)-**1d**[2]) (*Scheme 4*) were Z-protected using the method of *Kricheldorf* [17] (*Method E, Scheme 3*) to give the corresponding Z-protected amino acids (*S*)-**8a**, (*R*)-**8b, c**, and (*S*)-**8d** in good yields. These were conveniently converted to the corresponding prop-2-enyl esters (*S*)-**9a**, (*R*)-**9b, c**, and (*S*)-**9d** using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and CH_2=$CHCH_2Br$ in DMF (*Method F*)[3]). The

[2]) Both enantiomers of the free amino acids **1a–e** were converted to the protected building blocks; all compounds are described in the *Exper. Part*, but only one enantiomer is illustrated in the schemes.

[3]) The silylation of (*R*)-**8a** using excess of silylating agent followed by mild hydrolysis to form directly (*R*)-**11a** gave only a very low yield due to purification problems.

Scheme 3



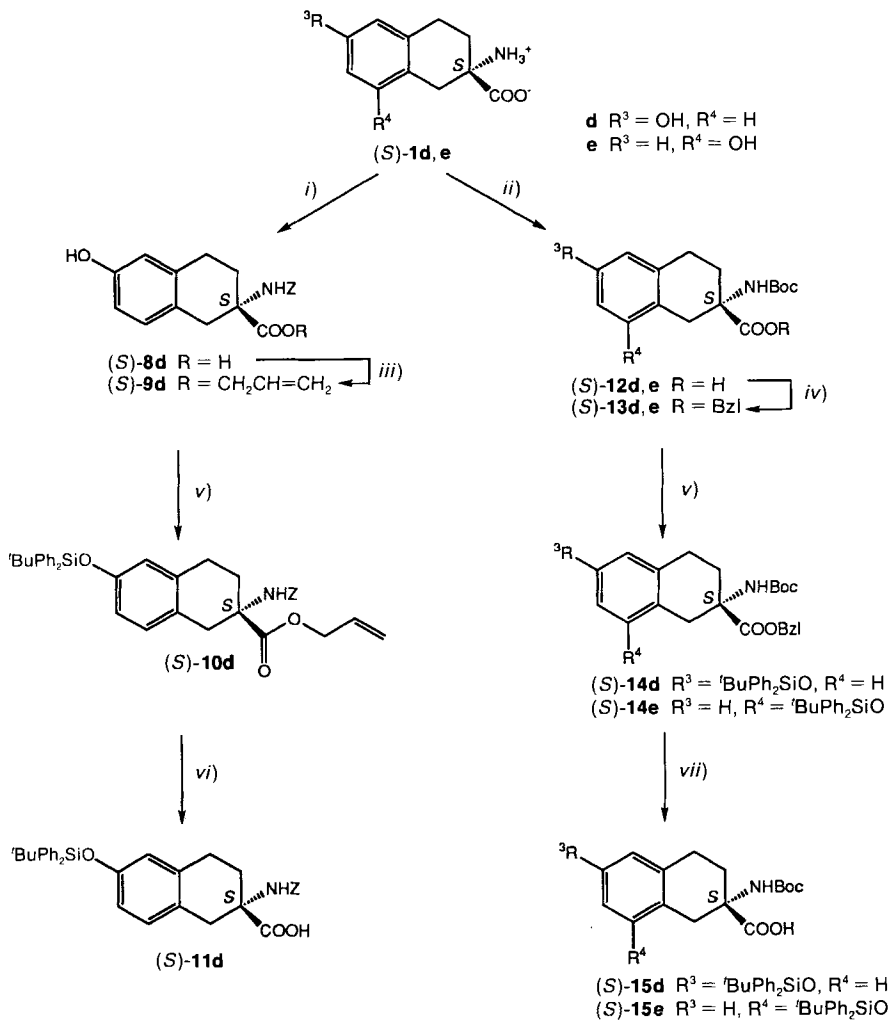
i) Me_3SiCl, $^iPr_2EtN$, Z-Cl, $CHCl_3$. *ii*) DBU, allyl bromide, DMF. *iii*) 1*H*-imidazole, $^tBuPh_2SiCl$, DMF. *iv*) *N*-Methylaniline, $[Pd(PPh_3)_4]$, DMSO/THF/0.5M HCl (aq.) 2:2:1.

$^tBuPh_2Si$-protected derivatives (*S*)-**10a**, (*R*)-**10b,c**, and (*S*)-**10d** were obtained in high yield using $^tBuPh_2SiCl$ and 1*H*-imidazole in DMF [13] (*Method G*). Finally, mild deprotection of the prop-2-enyl esters using $[Pd(PPh_3)_4]$ and *N*-methylaniline in DMSO/THF/0.5N HCl 2:2:1 [18] (*Method H*) gave the desired open-chain, orthogonally doubly protected Tyr analogues (*S*)-**11a**, (*R*)-**11b**, (*R*)-**11c**, and (*S*)-**11d** (*Schemes 3* and *4*).

Following another protocol, we protected the sterically less demanding tetralin-based analogues (*S*)-**1d,e**[2]) first with a Boc group using again the *Kricheldorf* [17] method (*Method I*), giving (*S*)-**12d,e**, and then converted them to the corresponding benzyl esters (*S*)-**13d,e** in high yields using DBU and benzyl bromide in DMF (*Method K*). Silylation (*Method G*) as mentioned before proceeded smoothly to give the corresponding $^tBuPh_2Si$-protected derivatives (*S*)-**14d,e**, which were converted to the doubly-protected Tyr analogues (*S*)-**15d,e** (*Scheme 4*) by hydrogenation (*Method L*).

4. X-Ray Structures of 4b,c, and 5b,c. – The absolute configuration of the α-isopropyltyrosines **1b** and the α-phenyltyrosines **1c** were determined by X-ray crystallography of the *N*-benzoyl-protected L-Phe cyclohexylamide derivatives **4b** and **5b**, and **4c** and **5c**, respectively. Whereas dipeptide **5c** is almost completely extended (*Fig. 4*), the three dipeptides **4b**, **5b**, and **4c** exhibit a β-turn type-I conformation [19] with the two amino acids at the ($i + 1$) and ($i + 2$) positions (*Figs. 1–3*). An intramolecular H-bond between the benzoyl C=O group and the cyclohexylamide NH group is formed in each of these

Scheme 4



i) Me_3SiCl, $^iPr_2EtN$, Z-Cl, $CHCl_3$. *ii*) Me_3SiCl, $(^iPr)_2EtN$, Boc_2O, CH_2Cl_2. *iii*) DBU, allyl bromide, DMF. *iv*) DBU, benzyl bromide, DMF. *v*) 1*H*-Imidazole, ^{t}BuPh$_2$SiCl, DMF. *vi*) *N*-Methylaniline, $[Pd(PPh_3)_4]$, DMSO/THF/0.5M HCl (aq.) 2:2:1. *vii*) H_2, 10% Pd/C, EtOH.

structures. The H-bond distances, as well as the torsional angles of the peptide backbone are listed in *Table 3*. Two of these compounds each crystallized with two independent molecules in the asymmetric unit (**5b**/**5b′** and **4c**/**4c′**), each adopting very similar β-turn type-I structures. The close similarity of all five independent β-turn structures is clearly borne out by the backbone superposition shown in *Fig. 5*. Interestingly, the conformational behavior of the isopropyl derivatives **4b** and **5b** does not depend on the inversion of chirality at the quaternary C(α) centre. In all but one of the five β-turn structures, the

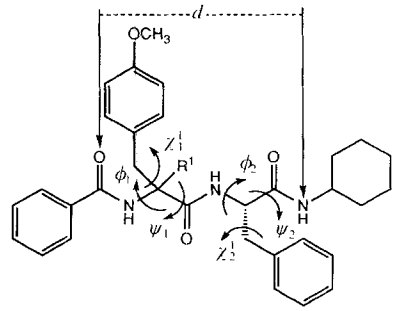


Table 3. *Torsion Angles* [°] *and H-Bond Distances* d [Å] *in* **4b**, **c** *and* **5b**, **c**

	Absolute configuration	Φ_1	Ψ_1	Φ_2	Ψ_2	X_1^1	X_2^1	d [Å]	Structural motif [19]
4b	(*R*,*S*)	−56.5	−27.1	−74.8	−10.0	+58.1	+40.0	2.92	β-turn I (α,α)
5b	(*S*,*S*)	−53.6	−26.8	−85.0	−7.5	+55.3	+64.4	2.96	β-turn I (α,α)
5b′	(*S*,*S*)	−57.2	−30.8	−81.4	−13.8	+47.7	−58.1	2.96	β-turn I (α,α)
4c	(*R*,*S*)	−62.7	−13.3	−81.5	−8.5	+57.9	+41.8	2.97	β-turn I (α,α)
4c′	(*R*,*S*)	−64.4	−14.7	−80.2	−5.7	+57.0	+45.0	2.97	β-turn I (α,α)
5c	(*S*,*S*)	+179.9	+174.6	−133.2	+117.5	−52.5	−179.9	[a])	extended (εβε)

[a]) Extended conformation.

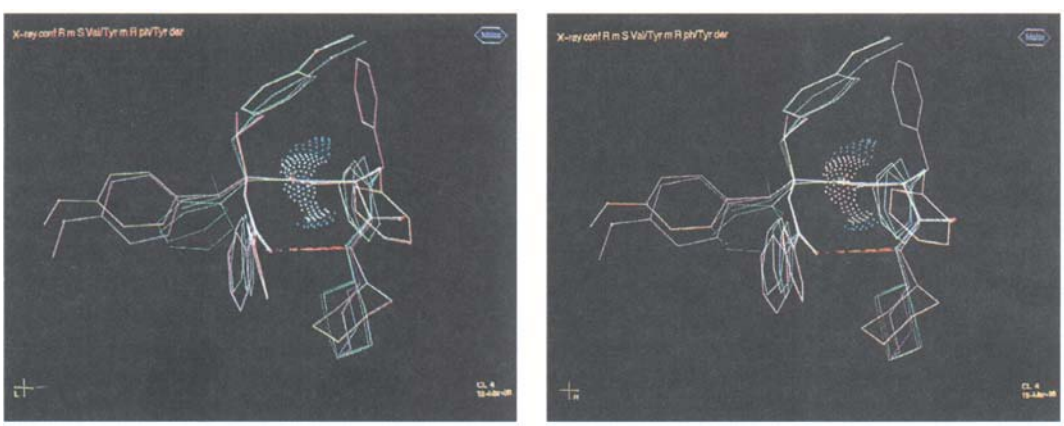


Fig. 5. *Backbone superposition of the five independent β-turn structures* **4b**, **5b**, **5b′**, **4c**, *and* **4c′** (see *Table 3*)

Phe side chains adopt the less common *endo*-conformation ($0 < \chi^1 < +120°$), thereby shielding the central amide peptide NH group and preventing it from engaging in H-bonding. A similar folding was described recently for a related tripeptide [8]. The crystal structure of the (*S*)-isopropyltyrosine derivative **5b** is also remarkable in that the two independent molecules of the asymmetric unit exhibit an N-equatorial and an N-axial cyclohexylamide unit, respectively. The latter conformation, which is stabilized by crystal packing forces, is rarely seen in crystal structures [8].

5. Conclusions. – Based on the methodology previously developed in our group, we were able to synthesize on large scales, in good yields, and with high optical purities novel α,α-disubstituted tyrosine analogues in both enantiomeric forms. These constrained amino acids were successfully converted to orthogonally doubly protected building blocks with free carboxylic acid groups suitable for peptide synthesis. Based on the crystal structures of tripeptidic derivatives, these tyrosine analogues are of interest for both the induction or stabilization of turn conformations in peptides and the study of substrate interactions with kinases and phosphatases.

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Experimental Part

General. See [8]. ISP and ISN = ion-spray (positive and negative, resp.) ionization.

General Methods. Method A. To a stirred soln. of crude **2** (20 mmol) in NMP (100 ml) was added **3** (40 mmol). The soln. was stirred for 36 h at 90°, cooled to r.t., and poured onto ice (100 g), 2N aq. HCl (250 ml), and AcOEt (250 ml). The aq. layer was extracted with AcOEt (2 × 100 ml), the combined org. phase washed with H_2O (2 × 100 ml) and sat. brine (200 ml), dried (Na_2SO_4), and evaporated. The diastereoisomeric peptides were separated and purified as indicated.

Method B. To a stirred mixture of peptide **4** or **5** (5.0 mmol) in freshly distilled MeOH (25 ml) was added CF_3SO_3H (1.32 ml, 15.0 mmol) under Ar at 0°. The mixture was then heated for 20 h at 80°, cooled to r.t., and evaporated. The residue was extracted with 2N aq. HCl (50 ml) and AcOEt (50 ml), the org. phase washed with H_2O (50 ml) and brine (50 ml), dried (Na_2SO_4), and evaporated, the residue suspended in CH_2Cl_2, and **3**·CF_3SO_3H filtered off and washed with CH_2Cl_2 (2 × 5 ml). The filtrate was evaporated and chromatographed (SiO_2 (120 g), hexane/AcOEt 4:1): amino acid methyl ester **6** as a white solid.

Method C. To a stirred soln. of **6** (5.0 mmol) in freshly distilled CH_2Cl_2 (20 ml) was added BBr_3 (2.17 ml, 22.5 mmol) in CH_2Cl_2 (20 ml) under Ar at 0°. The soln. was stirred for 4 h at r.t. and poured onto ice (20 g), sat. aq. NH_4Cl soln. (50 ml), and CH_2Cl_2 (50 ml). The aq. layer was extracted with CH_2Cl_2 (2 × 25 ml), the combined org. phase dried (Na_2SO_4) and evaporated, and the residue recrystallized from Et_2O/hexane 1:1: **7** as a white solid.

Method D. To a stirred mixture of **7** (2.5 mmol) and dioxane (5 ml) was added 37% aq. HCl soln. (8 ml) at 0° and heated in a pyrrolysis tube at 100° for 4 h. The mixture was cooled to r.t. and poured onto ice (10 g), 1N aq. HCl (50 ml), and Et_2O (100 ml), the aq. layer washed with Et_2O (2 × 25 ml), concentrated to 30 ml *in vacuo*, and brought to pH *ca.* 7 by addition of 6N aq. NaOH, and the precipitate filtered off and dried (P_2O_5) in a desiccator overnight: **1** as an amorphous solid.

Method E. To a stirred soln. of **1** (5 mmol) in $CHCl_3$ (10 ml) in a pyrrolysis tube was added, under Ar at 0°, chlorotrimethylsilane (Me_3SiCl; 3.1 ml, 25 mmol). The mixture was heated for 1 h at 70° and then cooled to 0°, $^iPr_2EtN$ (3.42 ml, 20 mmol) added, and the mixture stirred for 1 h at 70°. The soln. was recooled to 0°, benzyl chloroformate (Z-Cl; 1.41 ml, 10 mmol) added, and the mixture stirred for 17 h at 80° and poured onto ice (50 g), 0.5N aq. HCl (100 ml), and AcOEt (100 ml). The org. layer was washed with H_2O (20 ml) and sat. brine (2 × 25 ml), dried (Na_2SO_4), and evaporated and the residue purified as described: **8**.

Method F. To a stirred soln. of **8** (2.0 mmol) in DMF (12 ml) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 358 µl, 2.4 mmol) and allyl bromide (338 µl, 4.0 mmol) under Ar at 0°. The soln. was stirred for 17 h at r.t. and then evaporated. The residue was extracted with AcOEt (100 ml) and ice-cold 0.5N aq. HCl (100 ml), the org. phase washed with H_2O (50 ml) and sat. brine (50 ml), dried (Na_2SO_4), and evaporated and the residue chromatographed (SiO_2 (80 g), hexane/AcOEt 3:1): **9** as a white solid.

Method G. To a stirred soln. of **9** or **13** (1.0 mmol) in DMF (5 ml) was added 1*H*-imidazole (204 mg, 3.0 mmol) and $^tBuPh_2SiCl$ (307 µl, 1.2 mmol) under Ar at 0°. The soln. was stirred for 17 h at r.t. and then evaporated, the residue extracted with AcOEt (50 ml) and precooled 0.5N aq. HCl (50 ml), the org. phase washed with H_2O (20 ml) and sat. brine (50 ml), dried (Na_2SO_4), and evaporated, and the residue chromatographed (SiO_2 (60 g), hexane/AcOEt 10:1): **10** or **14**, resp., as colorless oil.

Method H. To a stirred soln. of **10** (1.0 mmol) in DMSO/THF/0.5N aq. HCl 2:2:1 (12.5 ml) was added dropwise *N*-methylaniline (*ca.* 2.5 ml) until the pH reached *ca.* 4. Ar was bubbled through the mixture for 15 min, $[Pd(PPh_3)_4]$ (173 mg, 0.15 mmol) added, and the mixture stirred for 17 h at r.t. under Ar. The mixture was poured onto ice (50 g), 0.5N aq. HCl (100 ml), and CH_2Cl_2 (100 ml), the org. phase washed with H_2O (20 ml) and sat. brine (50 ml), dried (Na_2SO_4), and evaporated, and the product purified by filtration on SiO_2 (30 g) with $CHCl_3$, then $CHCl_3$/MeOH 9:1: **11** as a white foam.

Method I. To a stirred soln. of **1** (4 mmol) in CH_2Cl_2 (10 ml) in a pyrrolysis tube was added, under Ar at 0°, Me_3SiCl (1.73 ml, 14.5 mmol). The mixture was heated for 1 h at 50° and then cooled to 0°, $^iPr_2EtN$ (2.74 ml, 16.0 mmol) added, and the mixture stirred for 1 h at 50°. The soln. was recooled to 0°, di(*tert*-butyl)dicarbonate (2.62 g, 12.0 mmol) added, and the mixture stirred for 17 h at 50° and poured onto ice (20 g), 1N aq. NaOH (50 ml), and CH_2Cl_2 (50 ml). The aq. layer was washed with CH_2Cl_2 (2 × 20 ml), adjusted to pH 2 with 1N aq. HCl, and extracted with AcOEt (2 × 100 ml). The org. phase was washed with H_2O (50 ml) and sat. brine (2 × 25 ml), dried (Na_2SO), and evaporated: **12**.

Method K. According to *Method F*, with **12** (2.0 mmol), DMF (12 ml), DBU (358 µl, 2.4 mmol), and benzyl bromide (284 µl, 2.4 mmol): **13** as a white solid.

Method L. To a prehydrogenated mixture of 10% Pd/C (25 mg) in EtOH (10 ml) was added a soln. of **14** (2 mmol) in EtOH (10 ml). The mixture was stirred vigorously under H_2 for 4 h and filtered over *Speedex*, the filtrate evaporated, and the resulting white foam dried under h.v.: **15** in quantitative yield.

(S)-2-Methyltyrosine ((*S*)-**1a**). From (*S*)-**7a** (1.10 g, 3.67 mmol) according to *Method D:* 540 mg (75.4%) of (*S*)-**1a**. White solid. M.p. (dec.) > 310°. $[\alpha]_D = -16.0$ (*c* = 0.10, H_2O/MeCN 1:1). IR (KBr): 3426*w* (br.), 3252*m*, 3120*m* (br.), 3020*m*, 2979*w*, 2495*w* (br.), 1638*m*, 1645*s*, 1581*s*, 1516*s*, 1450*m*, 1369*s*, 1268*m*, 1243*s*, 1125*w*, 598*w*, 553*m*. ^{1}H-NMR (250 MHz, DCl/D_2O): 7.17, 6.90 (2*d*, *AA'BB'*, J_{AB} = 8.5, 4 arom. H); 3.32, 3.07 (2*d*, J_{AB} = 14.5, CH_2); 1.65 (*s*, Me). MS: 195 (2, M^+), 150 (12), 108 (24), 107 (55), 88 (100), 77 (16), 42 (77).

*(R)-Enantiomer (R)-***1a**. From (*R*)-**7a** (850 mg, 2.84 mmol) according to *Method D:* 450 mg (96%) of (*R*)-**1a**. Light-brown solid. M.p. (dec.) > 300°. $[\alpha]_D = -17.0$ (*c* = 0.2, H_2O/MeCN 1:1). MS, IR, and ^{1}H-NMR: in close agreement with those of (*S*)-**1a**.

(R)-2-(1-Methylethyl)tyrosine ((*R*)-**1b**). From (*R*)-**7b** (520 mg, 1.59 mmol) according to *Method D*: 250 mg (70.4%) of (*R*)-**1b**. Light-brown solid. M.p. (dec.) > 295°. $[\alpha]_D = +10.0$ (*c* = 0.2, 1N HCl). IR (KBr): 3421*w* (br.), 3260*m*, 3058*m*, 2971*m*, 2597*w* (br.), 2485*w* (br.), 1634*s*, 1614*s*, 1581*s*, 1513*s*, 1447*m*, 1398*s*, 1253*m*, 1243*s*, 1176*w*, 839*w*, 621*w*. ^{1}H-NMR (250 MHz, DCl/D_2O): 7.18, 6.89 (2*d*, *AA'BB'*, J_{AB} = 8.6, 4 arom. H); 3.36, 3.10 (2*d*, J_{AB} = 14.7, CH_2); 2.38 (*sept.*, *J* = 7.0, Me_2CH); 2.38 (*t*, *J* = 7.0, Me_2CH). MS: 223 (2, M^+), 178 (12), 116 (100), 107 (46), 70 (86), 43 (35).

*(S)-Enantiomer (S)-***1b**. From (*S*)-**7b** (750 mg, 2.29 mmol) according to *Method D:* 405 mg (79%) of (*S*)-**1b**. Light-brown solid. M.p. (dec.) > 300°. $[\alpha]_D = -11.8$ (*c* = 0.2, 1N HCl). MS, IR, and ^{1}H-NMR: in close agreement with those of (*R*)-**1b**.

(R)-2-Phenyltyrosine ((*R*)-**1c**). From (*R*)-**7c** (1.35 g, 3.73 mmol) according to *Method D*: 920 mg (96%) of (*R*)-**1c**. Light-brown solid. M.p. (dec.) > 310°. $[\alpha]_D = +19.9$ (*c* = 0.1, 1N aq. HCl/MeOH 1:1). IR (KBr): 3413*m* (br.), 3261*s*, 2721*m*, 1634*s*, 1612*s*, 1586*s*, 1377*s*, 1237*s*, 1104*m*, 1041*m*, 735*w*, 693*m*. ^{1}H-NMR (250 MHz, CD_3OD): 7.65–7.55 (*m*, 5 arom. H); 7.14 (*d*, *J* = 8.4, 2 arom. H); 6.77 (*d*, *J* = 8.4, 2 arom. H); 3.76 (*d*, *J* = 15.4, 1 aliph. H); 3.64 (*d*, *J* = 15.4, 1 aliph. H). ISP-MS: 257.9 (100, $[M + H]^+$), 240.8 (63).

*(S)-Enantiomer (S)-***1c**. From (*S*)-**7c** (1.20 g, 3.32 mmol) according to *Method D:* 820 mg (96%) of (*S*)-**1c**. Light-brown solid. M.p. (dec.) > 310°. $[\alpha]_D = -27.3$ (*c* = 0.11, 1N aq. HCl/MeOH 1:1). MS, IR, and ^{1}H-NMR: in close agreement with those of (*R*)-**1c**.

(R)-2-Amino-1,2,3,4-tetrahydro-6-hydroxynaphthalene-2-carboxylic Acid ((*R*)-**1d**). From (*R*)-**7d** (2.0 g, 6.42 mmol) according to *Method D:* 1.22 g (91.7%) of (*R*)-**1d**. Light-brown solid. M.p. (dec.) > 275°. $[\alpha]_D = -4.6$ (*c* = 0.175, 1N HCl). IR (KBr): 3438*s* (br.), 3367*m*, 3133*s* (br.), 3031*m*, 2947*w*, 2832*w*, 1648*s*, 1625*w*, 1565*s*, 1500*s*, 1450*m*, 1405*s*, 1371*w*, 1327*w*, 1281*m*, 1249*m*, 1216*w*, 1155*m*, 1047*m*, 835*w*, 578*w*. ^{1}H-NMR (250 MHz, DCl/D_2O 1:1): 7.18, 6.75 (2*d*, *J* = 8.0, 2 arom. H); 6.73 (*s*, 1 arom. H); 3.38, 3.01 (2*d*, J_{AB} = 16.8, CH_2); 3.05–2.75 (*m*, 2 aliph. H); 2.45–2.3 (*m*, 1 aliph. H); 2.25–2.1 (*m*, 1 aliph. H). ISP-MS: 208.2 (100, $[M + H]^+$), 191.2 (64).

*(S)-Enantiomer (S)-***1d**. From (*S*)-**7d** (2.50 g, 8.03 mmol) according to *Method D:* 1.23 g (74.0%) of (*S*)-**1d**. Light-brown solid. M.p. (dec.) > 280°. $[\alpha]_D = +4.0$ (*c* = 0.093, H_2O/MeCN 1:1). MS, IR, and ^{1}H-NMR: in close agreement with those of (*R*)-**1d**.

(R)-2-Amino-1,2,3,4-tetrahydro-8-hydroxynaphthalene-2-carboxylic Acid ((*R*)-**1e**). From (*R*)-**7e** (9.16 g, 29.4 mmol) according to *Method D:* 4.76 g (83%) of (*R*)-**1e**. Light-brown solid. M.p. (dec.) > 272°. $[\alpha]_D = -5.0$ (*c* = 0.1, 1N HCl). IR (KBr): 3257*s*, 2759*w*, 2641*w*, 2538*w*, 1652*s*, 1587*s*, 1501*s*, 1462*s*, 1402*s*, 1221*s*, 1137*m*, 1092*w*,

1071*w*, 1025*w*, 947*w*, 781*m*, 706*w*. ^{1}H-NMR (250 MHz, DCl/D_2O 1:1): 9.45 (br. *s*, 1 COOH); 7.65 (br. *s*, 1 OH, NH_2); 6.89 (*t*, J = 7.7, 1 arom. H); 6.62, 6.52 (2*d*, J = 7.7, 2 arom. H); 3.07, 2.68 (2*d*, J_{AB} = 18.1, 2 aliph. H); 2.65–2.4 (*m*, 2 aliph. H); 2.1–1.9 (*m*, 1 aliph. H); 1.9–1.7 (*m*, 1 aliph. H). MS: 207 (23, M^+), 190 (13), 162 (100), 145 (64), 120 (50), 91 (26). Anal. calc. for $C_{11}H_{13}NO_3$ (207.23): C 63.76, H 6.32, N 6.76; found: C 63.75, H 6.25, N 6.54.

*(S)-Enantiomer (S)-***1e**. From (*S*)-**7e** (4.3 g, 13.81 mmol) according to *Method D*: 2.28 g (80%) of (*S*)-**1e**. White solid. M.p. (dec.) > 270°. $[\alpha]_D$ = +7.0 (c = 0.2, 1N HCl). MS, IR, and ^{1}H-NMR: in close agreement with those of (*R*)-**1e**.

N^2-*[(S)-*N^2*-Benzoyl-*$O^{4'}$*,2-dimethyltyrosyl]-(S)-phenylalanine Cyclohexylamide* (**4a**) *and (R,S)-Isomer* **5a**. From rac-*4-(4-methoxybenzyl)-4-methyl-2-phenyl-1,3-oxazol-5(4*H*)-one* (**2a**; 4.0 g, 13.54 mmol) according to *Method A*. Recrystallization from AcOEt/hexane gave 2.90 g (39.5%) of **4a**. White solid. M.p. (dec.) > 230°. $[\alpha]_D$ = +10.0 (c = 0.2, $CHCl_3$). IR (KBr): 3424*w*, 3292*m*, 3062*w*, 3006*w*, 2934*w*, 2885*w*, 1680*m*, 1659*s*, 1633*s*, 1580*w*, 1513*s*, 1305*w*, 1252*m*, 1178*w*, 1035*w*, 1035*w*, 718*w*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.6–7.4 (*m*, 5 arom. H); 7.15–6.8 (*m*, 9 arom. H); 6.56 (br. *s*, 2 NH); 6.12 (br. *d*, J = 8.1, NH); 4.7–4.55 (*m*, $PhCH_2CH$); 3.85–3.65 (*m*, CHNH); 3.79 (*s*, MeO); 3.35–3.25, 2.9–2.75 (2*m*, *ABX*, $PhCH_2CH$); 3.16, 2.98 (2*d*, *AB*, J_{AB} = 14.1, $MeOC_6H_4CH_2$); 1.9–1.55 (*m*, 6 aliph. H); 1.65 (*s*, Me); 1.45–1.0 (*m*, 4 aliph. H). FAB-MS: 542 (45, $[M + H]^+$), 217 (100), 109 (35), 91 (80).

After crystallization, the filtrate was evaporated and the residue chromatographed (SiO_2 (300 g), CH_2Cl_2/MeOH 6:1→4:1). Recrystallization from AcOEt/EtOH gave 3.05 g (41.6%) of **5a**. M.p. 176–178°. $[\alpha]_D$ = +46.0 (c = 0.2, $CHCl_3$). IR (KBr): 3434*w*, 3337*s*, 3301*m*, 3062*w*, 2980*w*, 2936*w*, 2857*w*, 1665*s*, 1644*s*, 1580*s*, 1534*m*, 1510*s*, 1448*m*, 1295*w*, 1249*m*, 1176*w*, 1032*w*, 702*m*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.6–7.5 (*m*, 3 arom. H); 7.5–7.4 (*m*, 2 arom. H); 7.25–7.05 (*m*, 5 arom. H); 7.0–6.9 (*m*, 2 arom. H); 6.55–6.45 (*m*, 2 arom. H, 1 NH); 6.25–6.15 (br. *m*, 2 NH); 4.75–4.6 (*m*, $PhCH_2CH$); 3.85–3.65 (*m*, CHNH); 3.76 (*s*, MeO); 3.40, 3.23 (2*d*, *AB*, J_{AB} = 14.1, $MeOC_6H_4CH_2$); 3.35–3.2, 3.1–3.0 (2*m*, *ABX*, $PhCH_2CH$); 1.95–1.55 (*m*, 5 aliph. H); 1.45–1.05 (*m*, 5 aliph. H); 1.32 (*s*, Me). FAB-MS: 542 (65, $[M + H]^+$), 217 (100), 109 (40), 91 (95).

N^2-*[(R)-*N^2*-Benzoyl-*O^4*-methyl-2-(1-methylethyl)tyrosyl]-(S)-phenylalanine Cyclohexylamide* (**4b**) *and (S,S)-Isomer* **5b**. From rac-*4-(4-methoxybenzyl)-4-(1-methylethyl)-2-phenyl-1,3-oxazol-5(4*H*)-one* (**2b**; 3.0 g, 9.28 mmol) according to *Method A*. Chromatography (SiO_2 (600 g), Et_2O/hexane 3:1) and recrystallization from AcOEt/hexane gave 2.17 g (40.9%) of **4b**. White solid. M.p. 212.5–214.5°. $[\alpha]_D$ = −6.0 (c = 0.2, $CHCl_3$). IR (KBr): 3422*m*, 3290*m*, 3062*w*, 2933*m*, 1681*s*, 1658*s*, 1680*m*, 1637*s*, 1579*w*, 1530*m*, 1512*s*, 1483*m*, 1451*m*, 1302*w*, 1251*m*, 1179*w*, 692*w*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.65–7.55 (*m*, 2 arom. H); 7.55–7.35 (*m*, 3 arom. H); 7.2–7.05 (*m*, 5 arom. H); 7.02–6.72 (2*d*, *AA'BB'*, J_{AB} = 8.7, 4 arom. H); 6.94 (br. *s*, NH); 6.86 (br. *d*, J = 8.1, NH); 5.73 (br. *d*, J = 8.1, NH); 4.6–4.5 (*m*, $PhCH_2CH$); 3.8–3.65 (*m*, CHNH); 3.73 (*s*, MeO); 3.53, 3.29 (2*d*, *AB*, J_{AB} = 13.8, $MeOC_6H_4CH_2$); 3.25–3.15, 3.0–2.75 (2*m*, $PhCH_2CH$, Me_2CH); 1.9–1.5 (*m*, 5 aliph. H); 1.45–0.85 (*m*, 5 aliph. H); 1.06, 0.99 (2*d*, J = 6.9, Me_2CH). ISP-MS: 592.6 (100, $[M + Na]^+$), 570.7 (90, $[M + H]^+$), 552.2 (30), 471.5 (20), 324.3 (60).

Further elution yielded, after recrystallization from AcOEt/EtOH, 2.12 g (40.0%) of **5b**. M.p. 133.5–135.0°. $[\alpha]_D$ = +47.5 (c = 0.2, $CHCl_3$). IR (KBr): 3425*w* (br.), 3316*w* (br.), 3062*w*, 3030*w*, 2931*m*, 1641*s*, 1512*s*, 1483*m*, 1450*w*, 1301*m*, 1250*m*, 1179*w*, 1034*w*, 698*w*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.6–7.35 (*m*, 5 arom. H); 7.2–7.05 (*m*, 5 arom. H); 6.98, 6.69 (2*d*, *AA'BB'*, J_{AB} = 8.7, 4 arom. H); 6.56 (br. *d*, J = 8.0, NH); 6.45 (br. *d*, J = 8.1, NH); 6.31 (br. *s*, NH); 4.75–4.6 (*m*, $PhCH_2CH$); 3.85–3.65 (*m*, CHNH); 3.73 (*s*, MeO); 3.55, 3.44 (2*d*, *AB*, J_{AB} = 14.1, $MeOC_6H_4CH_2$); 3.25–3.05 (*m*, *ABX*, $PhCH_2CH$); 2.25 (*sept.*, J = 6.8, Me_2CH); 2.0–1.5 (*m*, 5 aliph. H); 1.45–1.05 (*m*, 5 aliph. H); 1.09, 0.72 (2*d*, J = 6.9, Me_2CH). ISP-MS: 592.5 (100, $[M + Na]^+$), 552.2 (10), 471.4 (15), 324.3 (60).

N^2-*[(R)-*N^2*-Benzoyl-*O^4*-methyl-2-phenyltyrosyl]-(S)-phenylalanine Cyclohexylamide* (**4c**) *and (S,S)-Isomer* **5c**. From rac-*2-(4-methoxybenzyl)-2,4-diphenyl-1,3-oxazol-5(4*H*)-one* (**2c**; 1.0 g, 2.80 mmol) according to *Method A*. Chromatography (SiO_2 (250 g) Et_2O→Et_2O/i-PrOH 99:1) and crystallization from AcOEt/hexane gave 750 mg (44.4%) of **4c**. White solid. M.p. 217–219°. $[\alpha]_D$ = +21.0 (c = 0.2, $CHCl_3$). IR (KBr): 3059*w*, 3030*w*, 2940*w*, 1810*s*, 1660*s*, 1612*w*, 1510*s*, 1448*m*, 1301*w*, 1250*s*, 1176*m*, 1061*m*, 699*m*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.75–7.65 (*m*, 2 arom. H); 7.6–7.3 (*m*, 8 arom. H); 7.2–7.1 (*m*, 3 arom. H, 1 NH); 7.0–6.85 (*m*, 4 arom. H); 6.75–6.65 (*m*, 2 arom. H); 6.53 (br. *d*, J = 8.1, 1 NH); 6.44 (br. *d*, J = 7.1, 1 NH); 4.55–4.45 (*m*, $PhCH_2CH$); 4.06, 3.59 (2*d*, *AB*, J_{AB} = 14.1, $MeOC_6H_4CH_2$); 3.8–3.65 (*m*, CHNH); 3.74 (*s*, MeO); 3.05–2.9, 2.6–2.45 (2*m*, *ABX*, $PhCH_2CH$); 1.95–1.55 (*m*, 5 aliph. H); 1.45–0.85 (*m*, 5 aliph. H). ISP-MS: 626.6 (35, $[M + Na]^+$), 604.5 (55, $[M + H]^+$), 358.3 (20), 330.0 (20), 247.4 (100).

Further elution yielded, after crystallization from AcOEt/hexane, 720 mg (42.6%) of **5c**. M.p. > 192°. $[\alpha]_D$ = −40.5 (c = 0.2, $CHCl_3$). IR (KBr): 3412*w*, 3355*m*, 3062*w*, 3030*w*, 2932*m*, 2854*w*, 1651*s*, 1610*s*, 1512*s*, 1478*s*, 1447*w*, 1432*w*, 1250*w*, 1180*w*, 1033*w*, 698*m*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.7–7.6 (*m*, 2 arom. H); 7.55–7.05 (*m*, 13 arom. H, 1 NH); 6.7–6.55 (*m*, 4 arom. H); 6.19 (br. *d*, J = 8.1, NH); 6.05 (br. *d*, J = 8.1, NH); 4.65–4.45 (*m*,

$PhCH_2CH$); 3.80, 3.56 (2*d*, *AB*, J_{AB} = 14.1, $MeOC_6H_4CH_2$); 3.8–3.6 (*m*, CHNH); 3.72 (*s*, MeO); 3.2–2.95 (2*m*, *ABX*, $PhCH_2CH$); 1.85–1.5 (*m*, 5 aliph. H); 1.4–0.9 (*m*, 5 aliph. H). ISP-MS: 604.5 (20, $[M + H]^+$), 358.3 (15), 321.8 (15), 247.4 (100).

$N^{2,2'}$-[(R)-2-Benzamido-1,2,3,4-tetrahydro-6-methoxynaphthalene-2-carbonyl]-(S)-phenylalanyl-(S)-phenylalanine $N^{1,3}$,$N^{1,3}$-(Tetramethylene)amide (**4d**) *and (S,S,S)-Isomer* **5d** [7].

N^2-[(R)-2-Benzamido-1,2,3,4-tetrahydro-8-methoxynaphthalene-2-carbonyl]-(S)-phenylalanine Cyclohexylamide (**4e**) *and (S,S)-Isomer* **5e**. From *rac*-**2e** (12.6 g, 41.0 mmol) according to *Method A*. Crystallization from AcOEt and recrystallization from AcOEt/hexane 6:1 gave 10.44 g (46%) of **5e**. White solid. M.p. 186–188°. $[\alpha]_D$ = +12.0 (*c* = 0.2, MeOH). IR (KBr): 3414*m* (br.), 3331*m* (br.), 3028*w*, 2931*s*, 2854*m*, 1647*s*, 1585*s*, 1528*s*, 1470*s*, 1340*w*, 1286*m*, 1255*s*, 1102*m*, 775*w*, 704*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.58 (*d*, *J* = 7.2, 2 arom. H); 7.55–7.45 (*m*, 1 arom. H); 7.45–7.35 (*m*, 2 arom. H); 7.3–7.1 (*m*, 6 arom. H); 6.75–6.65 (*m*, 2 arom. H); 6.6–6.5 (br. *m*, 2 NH); 6.26 (br. *s*, 1 NH); 4.66 (*q*, *J* = 8.0, CHNH); 3.80 (*s*, MeO); 3.8–3.65 (*m*, CHNH); 3.35–3.25, 3.15–3.05 (2*m*, *ABX*, $PhCH_2CH$); 3.19–2.96 (2*d*, *AB*, J_{AB} = 17.5, 2 aliph. H); 2.9–2.7 (*m*, 2 aliph. H); 2.65–2.55 (*m*, 1 aliph. H); 2.0–1.9 (*m*, 1 aliph. H); 1.9–1.75 (*m*, 2 aliph. H); 1.75–1.55 (*m*, 3 aliph. H); 1.4–1.05 (*m*, 5 aliph. H). ISP-MS: 576.4 (15, $[M + Na]^+$), 554.6 (100, $[M + H]^+$).

The filtrate was evaporated and purified by chromatography (SiO_2 (1 kg), Et_2O/i-PrOH 99.5:0.5). Crystallization from AcOEt/hexane 1:1 gave 10.25 g (45%) of **4e**. M.p. 191–192°. $[\alpha]_D$ = −21.0 (*c* = 0.2, MeOH). IR (KBr): 3423*m* (br.), 3334*m* (br.), 3061*w*, 3029*w*, 2931*m*, 2853*w*, 1648*s*, 1585*m*, 1525*s*, 1286*w*, 1256*m*, 1097*w*, 706*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.55–7.45 (*m*, 3 arom. H); 7.45–7.35 (*m*, 2 arom. H); 7.2–7.05 (*m*, 6 arom. H); 6.89 (br. *d*, *J* = 8.2, 1 NH); 6.75–6.7 (*m*, 2 arom. H); 6.34 (br. *d*, *J* = 8.4, 1 NH); 6.21 (br. *s*, 1 NH); 4.8–4.7 (*m*, CHNH); 3.85 (*s*, MeO); 3.8–3.7 (*m*, CHNH); 3.3–3.2, 3.15–3.05 (2*m*, *ABX*, $PhCH_2CH$); 3.05–2.83 (2*d*, *AB*, J_{AB} = 18.5, 2 aliph. H); 2.85–2.75 (*m*, 1 aliph. H); 2.7–2.55 (*m*, 2 aliph. H); 2.3–2.2 (*m*, 1 aliph. H); 2.0–1.55 (*m*, 5 aliph. H); 1.45–1.1 (*m*, 5 aliph. H). ISP-MS: 576.5 (30, $[M + Na]^+$), 554.6 (100, $[M + H]^+$).

Methyl (S)-N^2-Benzoyl-$O^{4'}$,2-dimethyltyrosinate ((*S*)-**6a**). From **4a** (2.40 g, 4.43 mmol) according to *Method B*. Recrystallization from Et_2O/hexane gave 1.32 g (91%) of (*S*)-**6a**. M.p. 96–97°. $[\alpha]_D$ = +79.5 (*c* = 0.2, $CHCl_3$). IR (KBr): 3338*w* (br.), 3061*w*, 2996*w*, 2949*w*, 1738*s*, 1644*s*, 1610*m*, 1580*m*, 1456*m*, 1330*m*, 1299*m*, 1248*s*, 1118*s*, 1033*m*, 843*w*, 715*m*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.75–7.65 (*m*, 2 arom. H); 7.55–7.35 (*m*, 3 arom. H); 7.05–6.95 (*m*, 2 arom. H); 6.83 (br. *s*, NH); 6.8–6.7 (*m*, 2 arom. H); 3.81, 3.75 (2*s*, 2 MeO); 3.69, 3.22 (2*d*, *AB*, J_{AB} = 14.1, $MeOC_6H_4CH_2$); 1.79 (*s*, Me). MS. 327 (1, $M^{+\cdot}$), 206 (48), 121 (37), 105 (100), 77 (38), 43 (76).

(R)-Enantiomer (R)-**6a**. From **5a** (2.0 g, 3.69 mmol) according to *Method B*. Recrystallization from Et_2O/hexane gave 1.10 g (91%) of (*R*)-**6a**. White solid. M.p. 96.0–97.5°. $[\alpha]_D$ = −78.0 (*c* = 0.2, $CHCl_3$). IR, MS, and ^{1}H-NMR: in close agreement with those of (*S*)-**6a**.

Methyl (R)-N^2-Benzoyl-$O^{4'}$-methyl-2-(1-methylethyl)tyrosinate ((*R*)-**6b**). From **4b** (2.0 g, 3.50 mmol) according to *Method B:* 1.20 g (96.5%) of (*R*)-**6b**. Oil. $[\alpha]_D$ = +119.5 (*c* = 0.2, $CHCl_3$). IR (film): 3411*w*, 3062*w*, 2958*m*, 2836*w*, 1729*s*, 1664*s*, 1612*m*, 1581*w*, 1513*s*, 1486*s*, 1441*s*, 1368*s*, 1286*m*, 1249*s*, 1210*m*, 1128*w*, 1035*m*, 840*w*, 715*m*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.7–7.65 (*m*, 2 arom. H); 7.55–7.35 (*m*, 3 arom. H); 7.04 (br. *s*, NH); 7.05–6.95 (*m*, 2 arom. H); 6.75–6.65 (*m*, 2 arom. H); 3.93, 3.33 (2*d*, *AB*, J_{AB} = 13.6, $MeOC_6H_4CH_2$); 3.85 (*s*, MeO); 3.73 (*s*, MeO); 3.07 (*sept.* *J* = 6.9, Me_2CH); 1.19, 0.95 (2*d*, *J* = 6.9, Me_2CH). MS: 355 (1, $M^{+\cdot}$), 243 (27), 175 (24), 121 (38), 77 (38), 105 (100), 77 (52).

(S)-Enantiomer (S)-**6b**. From **5b** (2.0 g, 3.50 mmol) according to *Method B:* 1.15 g (92.4%) of (*S*)-**6b**. Oil. $[\alpha]_D$ = −117.5 (*c* = 0.2, $CHCl_3$). IR, MS, and ^{1}H-NMR: in close agreement with those of (*R*)-**6b**.

Methyl (R)-N^2-Benzoyl-$O^{4'}$-methyl-2-phenyltyrosinate ((*R*)-**6c**). From **4c** (2.80 g, 4.64 mmol) according to *Method B*. Chromatography (SiO_2, AcOEt/hexane 1:2) gave 1.15 g (94%) of (*R*)-**6c**. M.p. 178–180°. $[\alpha]_D$ = +98.0 (*c* = 0.2, CH_2Cl_2). IR (KBr): 3413*s*, 3004*w*, 2947*w*, 2830*w*, 1734*s*, 1665*s*, 1612*m*, 1580*m*, 1512*s*, 1481*s*, 1447*m*, 1249*m*, 1209*m*, 1183*m*, 718*m*, 699*m*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.73–7.70 (*d*, *J* = 6.8, 2 arom. H); 7.5–7.2 (*m*, 8 arom. H, 1 NH); 7.1–6.9 (*m*, 2 arom. H); 6.8–6.7 (*m*, 2 arom. H); 4.24, 3.85 (2*d*, *AB*, J_{AB} = 13.3, $PhCH_2$); 3.75 (*s*, 2 MeO). MS: 389 (< 1, M^+), 268 (66), 121 (32), 105 (100), 77 (24). Anal. calc. for $C_{24}H_{23}NO_4$ (389.43): C 74.02, H 5.95, N 3.60; found: C 73.72, H 5.97, N 3.53.

(S)-Enantiomer (S)-**6c**. From **5c** (2.50 g, 4.14 mmol) according to *Method B*. Chromatography (SiO_2, AcOEt/hexane 1:4) gave 1.61 g (99.8%) of (*S*)-**6c**. M.p. 171–173°. $[\alpha]_D$ = −97.0 (*c* = 0.2, CH_2Cl_2). IR, MS, and ^{1}H-NMR: in close agreement with those of (*R*)-**6c**.

(R)-Methyl 2-Benzamido-1,2,3,4-tetrahydro-6-methoxynaphthalene-2-carboxylate ((*R*)-**6d**) *and (S)-Enantiomer (S)-***6d** [7].

(R)-Methyl 2-Benzamido-1,2,3,4-tetrahydro-8-methoxynaphthalene-2-carboxylate ((*R*)-**6e**) *and (S)-Enantiomer (S)-***6e** [7].

(S)-N²-Benzoyl-O⁴',2-dimethyltyrosine ((*S*)-**7a**). From (*S*)-**6a** (1.20 g, 3.67 mmol) according to *Method C*. Recrystallization from Et_2O/hexane gave 1.05 g (95.6%) of (*S*)-**7a**. M.p. 219.5–222°. $[\alpha]_D = +27.0$ (*c* = 0.2, EtOH). IR (KBr): 3338*m*, 3066*w*, 2981*w*, 2808*w*, 2719*w*, 1710*s*, 1637*s*, 1579*w*, 1549*s*, 1514*s*, 1462*w*, 1340*w*, 1262*w*, 1125*m*, 843*w*, 733*m*. ^{1}H-NMR (250 MHz, (D_6)DMSO): 12.40 (br. *s*, 1 COOH); 9.20 (*s*, 1 OH); 8.10 (*s*, 1 NH); 7.85–7.7 (*m*, 2 arom. H); 7.6–7.4 (*m*, 3 arom. H); 6.87–6.62 (2*d*, *AA'BB'*, $J_{AB} = 8.4$, 4 arom. H); 3.84, 2.93 (2*d*, *AB*, $J_{AB} = 13.2$, CH_2); 1.13 (*s*, Me). MS: 299 (< 1, M^+), 178 (41), 107 (36), 105 (100), 77 (44).

*(R)-Enantiomer (R)-***7a**. From (*R*)-**6a** (1.00 g, 3.05 mmol) according to *Method C*. Recrystallization from Et_2O/hexane gave 895 mg (95%) of (*R*)-**7a**. M.p. 220–222°. $[\alpha]_D = -25.0$ (*c* = 0.2, EtOH). IR, MS, and ^{1}H-NMR: in close agreement with those of (*S*)-**7a**.

(R)-N²-Benzoyl-O⁴'-methyl-2-(1-methylethyl)tyrosine ((*R*)-**7b**). From (*R*)-**6b** (810 mg, 2.28 mmol) according to *Method C*. Recrystallization from AcOEt/hexane gave 640 mg (85.7%) of (*R*)-**7b**. M.p. 199–203°. $[\alpha]_D = +130.4$ (*c* = 0.2, EtOH). IR (KBr): 3390*w* (br.), 3101*w* (br.), 3025*m*, 2986*m*, 2811*w*, 1716*s*, 1644*s*, 1596*m*, 1532*s*, 1514*s*, 1459*w*, 1375*w*, 1256*m*, 1199*s*, 890*w*, 730*m*. ^{1}H-NMR (250 MHz, (D_6)DMSO): 13.15 (br. *s*, 1 COOH); 9.14 (*s*, 1 OH); 7.75–7.67 (*m*, 2 arom. H); 7.6–7.35 (*m*, 3 arom. H, 1 NH); 6.86, 6.56 (2*d*, *AB*, $J_{AB} = 8.3$, 4 arom. H); 3.5–3.2 (*m*, CH_2); 2.55–2.4 (*m*, Me_2CH); 1.10, 0.94 (2*d*, *J* = 6.6, Me_2CH). MS: 327 (< 1, M^+), 206 (38), 161 (22), 107 (20), 105 (100), 77 (38).

*(S)-Enantiomer (S)-***7b**. From (*S*)-**6b** (0.95 g, 2.67 mmol) according to *Method C*. Recrystallization from AcOEt/hexane gave 800 mg (91.5%) of (*S*)-**7b**. M.p. 198–202°. $[\alpha]_D = -129.5$ (*c* = 0.2, EtOH). IR, MS, and ^{1}H-NMR: in close agreement with those of (*R*)-**7b**.

(R)-N²-Benzoyl-O⁴'-methyl-2-phenyltyrosine ((*R*)-**7c**). From (*R*)-**6c** (1.65 g, 4.23 mmol) according to *Method C*. Recrystallization from Et_2O/hexane gave 1.42 g (99%) of (*R*)-**7c**. Amorphous solid. $[\alpha]_D = +100.5$ (*c* = 0.2, MeOH). IR (KBr): 3413*s* (br.), 3089*s* (br.), 3026*s*, 3000*w*, 1731*s*, 1638*s*, 1601*s*, 1576*m*, 1514*s*, 1485*s*, 1248*s*, 1188*s*, 834*m*, 719*m*, 693*m*. ^{1}H-NMR (250 MHz, $CDCl_3$): 13.60 (br. *s*, 1 COOH); 9.21 (*s*, 1 OH); 7.89 (*s*, 1 NH); 7.7 (*m*, 2 arom. H); 7.6–7.3 (*m*, 8 arom. H); 6.83 (*d*, *J* = 8.4, 2 arom. H); 6.56 (*d*, *J* = 8.4, 2 arom. H); 3.80 (*dd*, *AB*, $J_{AB} = 14.0$, 25, 2 aliph. H). ISP-MS: 360 (100, $[M - H]^+$), 316 (75).

*(S)-Enantiomer (S)-***7c**. From (*S*)-**6c** (1.56 g, 4.00 mmol) according to *Method C*. Recrystallization from Et_2O/hexane gave 1.22 g (85%) of (*S*)-**7c**. Amorphous solid. $[\alpha]_D = -100$ (*c* = 0.1, MeOH). IR, MS, and ^{1}H-NMR: in close agreement with those of (*R*)-**7c**.

(R)-2-Benzamido-1,2,3,4-tetrahydro-6-hydroxynaphthalene-2-carboxylic Acid ((*R*)-**7d**). From (*R*)-**6d** (3.00 g, 8.84 mmol) according to *Method C*. Recrystallization from Et_2O/hexane gave 2.65 g (96.3%) of (*R*)-**7d**. M.p. 210–212°. $[\alpha]_D = -31.0$ (*c* = 0.2, EtOH). IR (KBr): 3400*s* (br.), 3026*w*, 2937*w*, 2848*w*, 1718*s*, 1642*s*, 1576*w*, 1509*s*, 1542*m*, 1356*w*, 1285*m*, 1234*s*, 1153*w*, 816*w*, 691*w*. ^{1}H-NMR (250 MHz, (D_6)DMSO): 12.34 (*s*, 1 COOH); 9.04 (*s*, 1 OH); 8.37 (*s*, 1 NH); 7.75, 7.42 (2*d*, *J* = 7.0, 4 arom. H); 7.55–7.45 (*m*, 1 arom. H); 7.85, 6.51 (2*d*, *J* = 8.2, 2 arom. H); 6.48 (*s*, 1 arom. H); 3.26, 3.05 (2*d*, *J* = 18.0, CH_2); 2.8–2.5 (*m*, 2 aliph. H); 2.5–2.4 (*m*, 1 aliph. H); 2.05–1.9 (*m*, 1 aliph. H). MS: 311 (< 1, M^+), 190 (100), 145 (52), 105 (45), 77 (36).

*(S)-Enantiomer (S)-***7d**. From (*S*)-**6d** (2.40 g, 7.07 mmol) according to *Method C*. Recrystallization from Et_2O/hexane gave 2.18 g (99.0%) of (*S*)-**7d**. M.p. 210–212°. $[\alpha]_D = +31.5$ (*c* = 0.1, EtOH). IR, MS, and ^{1}H-NMR: in close agreement with those of (*R*)-**7d**.

(R)-2-Benzamido-1,2,3,4-tetrahydro-8-hydroxynaphthalene-2-carboxylic Acid ((*R*)-**7e**). From (*R*)-**6e** (5.06 g, 14.9 mmol) according to *Method C*. Recrystallization from Et_2O/hexane gave 3.48 g (75%) of (*R*)-**7e**. Amorphous solid. $[\alpha]_D = -84.3$ (*c* = 0.3, MeOH). IR (KBr): 3366*s* (br.), 3032*w*, 2937*w*, 2614*w*, 1718*s*, 1643*s*, 1587*m*, 1523*s*, 1487*m*, 1466*m*, 1278*m*, 1184*w*, 1082*w*, 786*w*, 716*m*. ^{1}H-NMR (250 MHz, (D_6)DMSO): 12.32 (*s*, 1 COOH); 9.27 (*s*, 1 OH); 8.47 (*s*, 1 NH); 7.9–7.7 (*m*, 2 arom. H); 7.6–7.4 (*m*, 3 arom. H); 6.69 (*t*, *J* = 7.7, 1 arom. H); 6.6–6.5 (*m*, 2 arom. H); 3.05 (*s*, 2 aliph. H); 2.9–2.6 (*m*, 2 aliph. H); 2.6–2.4 (*m*, 1 aliph. H); 2.1–1.9 (*m*, 1 aliph. H). MS: 311 (< 1, M^+), 293 (1), 265 (3), 190 (87), 145 (78), 122 (70), 105 (100), 77 (87).

*(S)-Enantiomer (S)-***7e**. From (*S*)-**6e** (1.95 g, 5.75 mmol) according to *Method C*. Recrystallization from Et_2O/hexane gave 1.75 g (97.8%) of (*S*)-**7e**. Amorphous solid. $[\alpha]_D = +84.3$ (*c* = 0.3, MeOH). IR, MS, and ^{1}H-NMR: in close agreement with those of (*R*)-**7e**.

(S)-2-[(Benzyloxy)carbonylamino]-3-(4-hydroxyphenyl)-2-methylpropanoic Acid (= *(S)-N²-[(Benzyloxy)carbonyl]-2-methyltyrosine*; (*S*)-**8a**). From (*S*)-**1a** (2.0 g, 10.2 mmol) according to *Method E*. The residue was suspended in Et_2O, and the impurities were filtered off to give, after evaporation and drying, 3.29 g (98%) of (*S*)-**8a**. Oil. $[\alpha]_D = +22.0$ (*c* = 0.1, CH_2Cl_2). IR (KBr): 3399*w* (br.), 3334*m* (br.), 3120*m* (br.), 3031*w*, 2944*w* (br.), 1703*s*, 1614*w*, 1515*s*, 1454*m*, 1266*m*, 1230*m*, 1100*w*, 1060*m*, 699*w*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.4–7.25 (*m*, 5 arom. H); 6.83, 6.61 (2*d*, *AA'BB'*, $J_{AB} = 8.4$, 4 arom. H); 5.50 (br. *s*, 1 NH); 5.25–5.0 (*m*, $PhCH_2O$); 3.37, 3.06 (2*d*, $J_{AB} = 13.7$, $ArCH_2$); 1.67 (*s*, Me). MS: 329 (> 1, M^+), 107 (100), 91 (70), 77 (21), 42 (18).

(R)-Enantiomer (R)-**8a**. From (*R*)-**1a** (200 mg, 1.02 mmol) according to *Method E*. The residue was suspended in Et_2O, and the impurities were filtered off to give, after evaporation and drying, (*R*)-**8a** as an oil which was not further purified and converted direction to (*R*)-**11a**.

(R)-2-[(Benzyloxy)carbonylamino]-3-(4-hydroxyphenyl)-2-(1-methylethyl)propanoic Acid (= *(R)*-N^2-*[(Benzyloxy)carbonyl]-2-(1-methylethyl)tyrosine*; (*R*)-**8b**). From (*R*)-**1b** (230 mg, 1.03 mmol) according to *Method E*. The residue was suspended in Et_2O, and the impurities were filtered off to give, after evaporation and drying, 230 mg (62%) of (*R*)-**8b**. Oil. $[\alpha]_D = +37.0$ ($c = 0.1$, MeOH). IR (KBr): 3407*s* (br.), 3033*w*, 2969*m*, 1707*s* (br.), 1614*m*, 1515*s*, 1450*m*, 1372*w*, 1347*w*, 1261*s*, 1225*s*, 1103*m*, 1064*m*, 1021*m*, 838*w*, 772*w*, 698*w*. ^{1}H-NMR (250 MHz, (D_6)DMSO): 13.05 (br. *s*, 1 OH); 9.17 (*s*, 1 OH); 7.45–7.3 (*m*, 5 arom. H); 6.77, 6.54 (2*d*, *AB*, $J_{AB} = 8.4$, 4 arom. H); 6.45 (*s*, 1 NH); 5.06 (*s*, $PhCH_2O$); 3.22, 3.10 (2*d*, *AB*, $J_{AB} = 13.9$, $ArCH_2$); 2.25–2.1 (*m*, Me_2CH); 1.01, 0.86 (2*d*, *AB*, $J_{AB} = 6.8$ Me_2CH). ISN-MS: 364.4 (100, $[M - H]^-$).

(S)-Enantiomer (S)-**8b**. From (*S*)-**1b** (190 mg, 0.851 mmol) according to *Method E*. The residue was suspended in Et_2O, and the impurities were filtered off to give, after evaporation and drying, 213 mg (70%) of (*S*)-**8b**. Oil. $[\alpha]_D = -34.5$ ($c = 0.1$, MeOH). MS, IR, and ^{1}H-NMR: in close agreement with those of (*R*)-**8b**.

(R)-2-[(Benzyloxy)carbonylamino]-3-(4-hydroxyphenyl)-2-phenylpropanoic Acid (= *(R)*-N^2-*[(Benzyloxy)carbonyl]-2-phenyltyrosine*; (*R*)-**8c**). From (*R*)-**1c** (900 mg, 3.50 mmol) according to *Method E*. During workup, the mixture was stirred in ice/0.5N HCl/$CHCl_3$. The product precipitated which was filtered and dried under vacuum over P_2O_5: 980 mg (72%) of (*R*)-**8c**. Grey solid. M.p. 190–192°. $[\alpha]_D = +26.0$ ($c = 0.1$, MeOH). IR (KBr): 3417*s*, 3031*w*, 1733*s*, 1692*s*, 1615*m*, 1512*s*, 1451*m*, 1273*m*, 1240*m*, 1175*m*, 1090*m*, 1064*m*, 1026*m*, 842*w*, 731*w*, 696*m*. ^{1}H-NMR (250 MHz, (D_6)DMSO): 13.43 (br. *s*, 1 OH); 9.21 (*s*, 1 OH); 7.5–7.25 (*m*, 10 arom. H); 6.83 (*s*, 1 NH); 6.70, 6.53 (2*d*, *AB*, $J_{AB} = 8.5$, 4 arom. H); 5.12, 4.95 (2*d*, *AB*, $J_{AB} = 11.5$, $PhCH_2O$); 3.66, 3.54 (2*d*, *AB*, $J_{AB} = 14.0$, $ArCH_2$). EI-MS: 413.3 (54, $[M + Na]^+$), 392.3 (83, $[M + H]^+$), 217.0 (75), 91.2 (100).

(S)-Enantiomer (S)-**8c**. From (*S*)-**1c** (800 mg, 3.11 mmol) according to *Method E*. During workup, the mixture was stirred in ice/0.5N HCl/$CHCl_3$. The product precipitated which was filtered and dried under vacuum over P_2O_5: 810 mg (67%) of (*S*)-**8c**. Grey solid. M.p. 190–192°. $[\alpha]_D = -23.0$ ($c = 0.1$, MeOH). MS, IR, and ^{1}H-NMR: in close agreement with those of (*R*)-**8c**.

(S)-2-[(Benzyloxy)carbonylamino]-6-hydroxy-1,2,3,4-tetrahydronaphthalene-2-carboxylic Acid ((*S*)-**8d**). From (*S*)-**1d** (400 mg, 1.93 mmol) according to *Method E*. The residue was filtered on SiO_2 (10 g) with $CHCl_3 \rightarrow CHCl_3$/MeOH 9:1. Then the product was dissolved in $CHCl_3$ and washed with 0.5N HCl and sat. brine, dried (Na_2SO_4), evaporated, and dried overnight under h.v.: 514 mg (78%) of (*S*)-**8d**. White solid. M.p. 159–160°. $[\alpha]_D = +43.0$ ($c = 0.1$, MeOH). IR (KBr): 3402*s* (br.), 2951*w*, 1714*s* (br.), 1617*m*, 1505*s*, 1454*m*, 1374*w*, 1274*s*, 1232*s*, 1150*m*, 1067*m*, 742*w*, 698*w*. ^{1}H-NMR (250 MHz, (D_6)DMSO): 12.50 (br. *s*, 1 OH); 9.04 (*s*, 1 OH); 7.53 (*s*, 1 NH); 7.4–7.25 (*m*, 5 arom. H); 6.85–6.75 (*m*, 1 arom. H); 6.55–6.4 (*m*, 2 arom. H); 5.1–4.9 (*m*, $PhCH_2O$); 3.1–2.8 (*m*, 2 aliph. H); 2.8–2.55 (*m*, 2 aliph. H); 2.3–2.15 (*m*, 1 aliph. H); 2.0–1.8 (*m*, 1 aliph. H). ISN-MS: 340.3 (18, $[M - H]^-$), 232.2 (100).

(R)-Enantiomer (R)-**8d**. From (*R*)-**1d** (400 mg, 1.93 mmol) according to *Method E*. The residue was purified by stirring in ice-cold $CHCl_3$, filtering off the product, evaporating the filtrate, and repeating until all of the product was isolated: 586 mg (89%) of (*R*)-**8d**. White solid. M.p. 173–174°. $[\alpha]_D = -45.0$ ($c = 0.1$, MeOH). MS, IR, and ^{1}H-NMR: in close agreement with those of (*S*)-**8d**.

Prop-2-enyl (S)-2-[(Benzyloxy)carbonylamino]-3-(4-hydroxyphenyl)-2-methylpropanoate ((*S*)-**9a**). From (*S*)-**8a** (500 mg, 1.52 mmol) according to *Method F*: 484 mg (86%) of (*S*)-**9a**. Amorphous solid. $[\alpha]_D = +13.0$ ($c = 0.1$, $CHCl_3$). IR (KBr): 3359*s* (br.), 3065*w*, 2942*w*, 1701*s* (br.), 1614*m*, 1515*s*, 1452*m*, 1377*w*, 1325*w*, 1266*s*, 1226*s*, 1115*m*, 1059*m*, 698*w*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.45–7.3 (*m*, 5 arom. H); 6.83, 6.64 (2*d*, *AB*, $J_{AB} = 8.5$, 4 arom. H); 6.0–5.8 (*m*, CH_2=$CHCH_2$); 5.38 (br. *s*, 1 NH); 5.4–5.0 (*m*, CH_2=CH_2, $PhCH_2O$); 4.77 (br. *s*, OH); 4.62 (br. *s*, CH_2CHCH_2); 3.35, 3.10 (2*d*, *AB*, $J_{AB} = 13.8$, $ArCH_2$); 1.63 (*s*, Me). ISN-MS: 368.2 (100, $[M - H]^-$).

Prop-2-enyl (R)-2-[(Benzyloxy)carbonylamino]-3-(4-hydroxyphenyl)-2-(1-methylethyl)propanoate ((*R*)-**9b**). From (*R*)-**8b** (207 mg, 0.579 mmol) according to *Method F*: 192 mg (83%) of (*R*)-**9b**. Oil. $[\alpha]_D = +45.0$ ($c = 0.1$, $CHCl_3$). IR (film): 3406*s* (br.), 3032*w*, 2969*m*, 1716*s* (br.), 1615*m*, 1514*s*, 1451*m*, 1371*w*, 1264*s*, 1021*m*, 937*w*, 841*w*, 769*w*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.45–7.3 (*m*, 5 arom. H); 6.82, 6.56 (2*d*, *AB*, $J_{AB} = 8.5$, 4 arom. H); 6.05–5.9 (*m*, CH_2=$CHCH_2$); 5.72 (*s*, 1 NH); 5.45–5.25 (*m*, CH_2=$CHCH_2$); 5.20, 5.01 (2*d*, *AB*, $J_{AB} = 12.3$, $PhCH_2O$); 4.7–4.6 (*m*, CH_2=$CHCH_2$); 4.57 (*s*, 1 OH); 3.61, 3.22 (2*d*, *AB*, $J_{AB} = 13.7$, $ArCH_2$); 2.75–2.4 (*m*, Me_2CH); 1.11, 0.92 (2*d*, *AB*, $J_{AB} = 6.8$ Me_2CH). ISP-MS: 398.5 (100, $[M - H]^+$), 354.4 (81), 320.3 (46).

(S)-Enantiomer (S)-**9b**. From (*S*)-**8b** (224 mg, 0.626 mmol) according to *Method F*: 142 mg (57%) of (*S*)-**9b**. Oil. $[\alpha]_D = -39.0$ ($c = 0.1$, $CHCl_3$). MS, IR, and ^{1}H-NMR: in close agreement with those of (*R*)-**9b**.

Prop-2-enyl (R)-2-[(Benzyloxy)carbonylamino]-3-(4-hydroxyphenyl)-2-phenylpropanoate ((*R*)-**9c**). From (*R*)-**8c** (600 mg, 1.53 mmol) according to *Method F:* 603 mg (91.3%) of (*R*)-**9c**. White solid. M.p. 89–90°. $[\alpha]_D = +19.0$ ($c = 0.1$, $CHCl_3$). IR (KBr): 3421*w* (br.), 3273*w* (br.), 2858*m*, 1732*w*, 1703*s*, 1614*m*, 1496*s*, 1448*m*, 1276*s*, 1030*s*, 753*w*, 698*m*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.5–7.25 (*m*, 10 arom. H); 6.78, 6.59 (2*d*, *AB*, $J_{AB} = 8.4$, 4 arom. H); 6.18 (*s*, 1 NH); 6.85–6.7 (*m*, CH_2=C*H*CH_2); 5.25–5.15 (*m*, CH_2CHCH_2); 5.11, 4.95 (2*d*, *AB*, $J_{AB} = 12.3$. PhCH_2O); 4.65 (*s*, 1 OH); 4.56 (*d*, $J = 4.5$, CH_2CHCH_2); 3.77, 3.90 (2*d*, *AB*, $J_{AB} = 13.3$, ArCH_2). ISP-MS: 454.3 (100, $[M + Na]^+$), 432.2 (50, $[M + H]^+$).

*(S)-Enantiomer (S)-***9c**. From (*S*)-**8c** (500 mg, 1.28 mmol) according to *Method F*: 737 mg (95.7%) of (*S*)-**9c**. White solid. M.p. 91–92°. $[\alpha]_D = -20.0$ ($c = 0.1$, $CHCl_3$). MS, IR, and ^{1}H-NMR: in close agreement with those of (*R*)-**9c**.

Prop-2-enyl (S)-2-[(Benzyloxy)carbonylamino]-6-hydroxy-1,2,3,4-tetrahydronaphthalene-2-carboxylate ((*S*)-**9d**). From (*S*)-**8d** (260 mg, 0.762 mmol) according to *Method F:* 188 mg (65%) of (*S*)-**9d**. White solid. M.p. 118–119°. $[\alpha]_D = +52.0$ ($c = 0.1$, $CHCl_3$). IR (KBr): 3346*s*, 1712*s*, 1613*m*, 1548*s*, 1510*w*, 1454*m*, 1301*s*, 1276*s*, 1146*w*, 1065*m*, 742*w*, 698*w*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.4–7.25 (*m*, 5 arom. H); 6.88 (*d*, $J = 8.1$, 1 arom. H); 6.65–6.55 (*m*, 2 arom. H); 6.0–5.8 (*m*, CH_2=C*H*CH_2); 5.35–5.15 (*m*, CH_2=$CHCH_2$); 5.06 (*s*, PhCH_2O); 5.02 (*s*, 1 NH); 4.66 (*s*, CH_2=$CHCH_2$, OH); 3.21, 2.92 (2*d AB*, $J_{AB} = 16.0$, 2 aliph. H); 2.85–2.75 (*m*, 2 aliph. H); 2.6–2.45 (*m*, 1 aliph. H); 2.25–2.05 (*m*, 1 aliph. H). ISN-MS: 380.4 (100, $[M - H]^-$).

*(R)-Enantiomer (R)-***9d**. From (*R*)-**8d** (380 mg, 1.11 mmol) according to *Method F*: 320 mg (76%) of (*R*)-**9d**. White solid. M.p. 240–243°. $[\alpha]_D = -49.0$ ($c = 0.1$, $CHCl_3$). MS, IR, and ^{1}H-NMR: in close agreement with those of (*S*)-**9d**.

*Prop-2-enyl (S)-2-[(Benzyloxy)carbonylamino]-3-{4-[(*tert*-butyl)diphenylsilanyloxy]phenyl}-2-methylpropanoate* ((*S*)-**10a**). From (*S*)-**9a** (484 mg, 1.31 mmol) according to *Method G:* 669 mg (86%) of (*S*)-**10a**. Oil. $[\alpha]_D = +11.5$ ($c = 0.2$, $CHCl_3$). IR (KBr): 3419*w*, 3356*w* (br.), 2934*w*, 2857*w*, 1723*s* (br.), 1608*m*, 1509*s*, 1453*w*, 1427*w*, 1258*s*, 1112*m*, 1056*m*, 919*m*, 701*m*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.65–7.55 (*m*, 5 arom. H); 7.4–7.15 (*m*, 10 arom. H); 6.60, 6.49 (2*d*, *AB*, $J_{AB} = 8.5$, 4 arom. H); 5.85–5.7 (*m*, CH_2=C*H*CH_2); 5.38 (br. *s*, 1 NH); 5.25–4.9 (*m*, CH_2=$CHCH_2$, PhCH_2O); 4.50 (br. *s*, CH_2=$CHCH_2$); 3.17, 2.95 (2*d*, $J_{AB} = 13.2$, CH_2); 1.51 (*s*, Me); 1.01 (*s*, *t*-Bu). ISP-MS: 630.5 (37, $[M + Na]^+$), 625.5 (100, $[M + NH_4]^+$), 608.5 (83, $[M + H]^+$).

*Prop-2-enyl (R)-2-[(Benzyloxy)carbonylamino]-3-{4-[(*tert*-butyl)diphenylsilanyloxy]phenyl}-2-(1-methylethyl)propanoate* ((*R*)-**10b**). From (*R*)-**9b** (180 mg, 0.453 mmol) according to *Method G:* 173 mg (63%) of (*R*)-**10b**. Oil. $[\alpha]_D = +34.0$ ($c = 0.1$, $CHCl_3$). IR (film): 3419*w* (br.), 2933*w*, 2858*m*, 1722*s* (br.), 1607*m*, 1509*s*, 1427*m*, 1259*s*, 1200*w*, 1110*m*, 1020*m*, 921*s*, 742*w*, 703*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.75–7.65 (*m*, 4 arom. H); 7.45–7.2 (*m*, 11 arom. H); 6.64, 6.49 (2*d*, *AB*, $J_{AB} = 8.5$, 4 arom. H); 5.95–5.8 (*m*, CH_2=C*H*CH_2); 5.66 (*s*, 1 NH); 5.45–5.25 (*m*, CH_2=$CHCH_2$); 5.13, 4.95 (2*d*, *AB*, $J_{AB} = 12.3$, PhCH_2O); 4.65–4.45 (*m*, CH_2=$CHCH_2$); 3.56, 3.12 (2*d*, *AB*, $J_{AB} = 12.8$, ArCH_2); 2.7–2.55 (*m*, Me_2CH); 1.08 (*s*, *t*-Bu); 1.07, 0.89 (2*d*, *AB*, $J_{AB} = 6.9$ Me_2CH). ISP-MS: 653.5 (100, $[M + NH_4]^+$), 636.5 (84, $[M + H]^+$).

*(S)-Enantiomer (S)-***10b**. From (*S*)-**9b** (132 mg, 0.332 mmol) according to *Method G*: 209 mg (99.3%) of (*S*)-**10b**. Oil. $[\alpha]_D = -40.0$ ($c = 0.1$, $CHCl_3$). MS, IR, and ^{1}H-NMR: in close agreement with those of (*R*)-**10b**.

*Prop-2-enyl (R)-2-[(Benzyloxy)carbonylamino]-3-{4-[(*tert*-butyl)diphenylsilanyloxy]phenyl}-2-phenylpropanoate* ((*R*)-**10c**). From (*R*)-**9c** (585 mg, 1.36 mmol) according to *Method G:* 870 mg (95.8%) of (*R*)-**10c**. Oil. $[\alpha]_D = +19.0$ ($c = 0.1$, $CHCl_3$). IR (film): 3408*w* (br.), 2932*w* (br.), 2857*w*, 1725*s*, 1608*w*, 1508*s*, 1428*w*, 1266*s*, 1110*m*, 1027*m*, 919*m*, 700*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.75–7.65 (*m*, 4 arom. H); 7.45–7.16 (*m*, 16 arom. H); 6.61, 6.52 (2*d*, *AB*, $J_{AB} = 8.4$, 4 arom. H); 6.10 (*s*, 1 NH); 5.8–5.6 (*m*, CH_2=C*H*CH_2); 5.15–5.0 (*m*, CH_2=$CHCH_2$); 5.04, 4.89 (2*d*, *AB*, $J_{AB} = 12.3$, PhCH_2O); 4.48 (br. *s*, CH_2=$CHCH_2$); 3.83, 3.67 (2*d*, *AB*, $J_{AB} = 13.2$, ArCH_2); 1.09 (*s*, *t*-Bu). ISP-MS: 687.6 (100, $[M + NH_4]^+$), 670.5 (62, $[M + H]^+$).

*(S)-Enantiomer (S)-***10c**. From (*S*)-**9c** (496 mg, 1.15 mmol) according to *Method G*: 737 mg (95.7%) of (*S*)-**10c**. Oil. $[\alpha]_D = -20.0$ ($c = 0.1$, $CHCl_3$). MS, IR, and ^{1}H-NMR: in close agreement with those of (*R*)-**10c**.

*Prop-2-enyl (S)-2-[(Benzyloxy)carbonylamino]-6-[(*tert*-butyl)diphenylsilanyloxy]-1,2,3,4-tetrahydronaphthalene-2-carboxylate* ((*S*)-**10d**). From (*S*)-**9d** (181 mg, 0.475 mmol) according to *Method G:* 277 mg (98%) of (*S*)-**10d**. Oil. $[\alpha]_D = +39.0$ ($c = 0.1$, $CHCl_3$). IR (film): 3455*w* (br.), 2932*w*, 2857*m*, 1728*s* (br.), 1609*m*, 1499*s*, 1427*m*, 1266*s*, 1233*s*, 1120*m*, 1064*m*, 984*w*, 741*w*, 701*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.75–7.65 (*m*, 4 arom. H); 7.45–7.2 (*m*, 11 arom. H); 6.73 (*d*, $J = 8.0$, 1 arom. H); 6.56 (*d*, $J = 2.8$, 1 arom. H); 6.48 (*dd*, $J = 8.0$, 2.8, 1 arom. H); 5.95–5.75 (*m*, CH_2=C*H*CH_2); 5.35–5.15 (*m*, CH_2=$CHCH_2$); 5.06 (*s*, PhCH_2O); 4.96 (*s*, 1 NH); 4.64 (*s*, CH_2=$CHCH_2$); 3.14, 2.78 (2*d*, *AB*, $J_{AB} = 16.0$, 2 aliph. H); 2.7–2.65 (*m*, 2 aliph. H); 2.6–2.4 (*m*, 1 aliph. H); 2.15–2.0 (*m*, 1 aliph. H); 1.08 (*s*, *t*-Bu). ISP-MS: 642.4 (28, $[M + Na]^+$), 637.4 (57, $[M + NH_4]^+$), 620.4 (100, $[M + H]^+$).

(R)-Enantiomer (R)-**10d**. From (*R*)-**9d** (314 mg, 0.823 mmol) according to *Method G:* 506 mg (99%) of (*R*)-**10d**. Oil. $[\alpha]_D = -32.0$ ($c = 0.2$, $CHCl_3$). MS, IR, and ^{1}H-NMR: in close agreement with those of (*S*)-**10d**.

*(S)-2-[(Benzyloxy)carbonylamino]-3-{4-[(*tert*-butyl)diphenylsilanyloxy]phenyl}-2-methylpropanoic Acid* ((*S*)-**11a**). From (*S*)-**10a** (585 mg, 0.962 mmol) according to *Method H:* 441 mg (81%) of (*S*)-**11a**. Oil. $[\alpha]_D = +33$ ($c = 0.1$, $CHCl_3$). IR (film): 3414*s*, 2934*s*, 2858*s*, 1709*s* (br.), 1608*m*, 1509*s*, 1455*m*, 1428*w*, 1373*w*, 1111*m*, 1058*m*, 919*m*, 821*m*, 742*m*, 703*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.75–7.65 (*m*, 4 arom. H); 7.45–7.2 (*m*, 11 arom. H); 6.70, 6.57 (2*d*, *AB*, $J_{AB} = 8.6$, 4 arom. H); 5.25 (br. *s*, 1 NH); 5.04, 5.14 (2*d*, $J_{AB} = 12.0$. $PhCH_2O$); 3.20, 2.07 (2*d*, $J_{AB} = 13.6$, $ArCH_2$); 1.54 (*s*, Me); 1.08 (*s*, *t*-Bu). ISP-MS: 585.4 (65, $[M + NH_4]^+$), 568.4 (70, $[M + H]^+$), 524.4 (100). Anal. calc. for $C_{34}H_{37}NO_5Si$ (567.76): C 71.93, H 6.57, N 2.47; found: C 71.48, H 6.83, N 2.15.

(R)-Enantiomer (R)-**11a**. To a stirred soln. of crude (*R*)-**8a** in DMF (2 ml) was added 1*H*-imidazole (279.1 mg, 4.10 mmol) and ^{t}BuPh$_2$SiCl (843 mg, 5.07 mmol) under Ar at 0°. The soln. was stirred for 16 h at r.t., poured onto ice (10 g), 6N HCl (10 ml), and AcOEt (20 ml), and stirred for 24 h until only the monosilylated product remained. The org. phase was separated, washed with H_2O (20 ml) and sat. brine (50 ml), dried (Na_2SO_4), and evaporated and the residue chromatographed (SiO_2 (60 g), hexane/AcOEt 10:1 → AcOEt/EtOH 9:1): 175 mg (30%) of (*R*)-**11a**. Oil. $[\alpha]_D = -26.5$ ($c = 0.1$, $CHCl_3$).

*(R)-2-[(Benzyloxy)carbonylamino]-3-{4-[(*tert*-butyl)diphenylsilanyloxy]phenyl}-2-(1-methylethyl)propanoic Acid* ((*R*)-**11b**). From (*R*)-**10b** (162 mg, 0.255 mmol) according to *Method H:* 137 mg (90%) of (*R*)-**11b**. Oil. $[\alpha]_D = +21.0$ ($c = 0.1$, MeOH). IR (film): 3410*w* (br.), 2993*w*, 2857*m*, 1719*s* (br.), 1608*m*, 1509*s*, 1429*m*, 1257*s*, 1119*m*, 1022*w*, 821*w*, 744*m*, 703*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.7–7.6 (*m*, 4 arom. H); 7.45–7.2 (*m*, 11 arom. H); 6.72, 6.53 (2*d*, *AB*, $J_{AB} = 12.4$, 4 arom. H); 5.46 (*s*, 1 NH); 5.12, 4.97 (2*d*, *AB*, $J_{AB} = 11.8$, $PhCH_2O$); 3.41, 3.17 (2*d*, *AB*, $J_{AB} = 13.6$, $ArCH_2$); 2.75–2.4 (*m*, Me_2CH); 1.08 (*s*, *t*-Bu); 1.09, 0.93 (2*d*, *AB*, $J_{AB} = 6.9$, Me_2CH). EI-MS: 618.3 (22, $[M + Na]^+$), 596.3 (62, $[M + H]^+$), 552.3 (58), 345.1 (94), 216.9 (95), 91.1 (100).

(S)-Enantiomer (S)-**11b**. From (*S*)-**10b** (209 mg, 0.330 mmol) according to *Method H:* 159 mg (80%) of (*S*)-**11b**. Oil. $[\alpha]_D = -23.0$ ($c = 0.1$, MeOH). MS, IR, and ^{1}H-NMR: in close agreement with those of (*R*)-**11b**.

*(R)-2-[(Benzyloxy)carbonylamino]-3-{4-[(*tert*-butyl)diphenylsilanyloxy]phenyl}-2-phenylpropanoic Acid* ((*R*)-**11c**). From (*R*)-**10c** (870 mg, 1.30 mmol) according to *Method H:* 772 mg (94.3%) of (*R*)-**11c**. White solid. M.p. 89–90°. $[\alpha]_D = +26.0$ ($c = 0.1$, $CHCl_3$). IR (KBr): 3413*w* (br.), 2932*w*, 2858*m*, 1792*s* (br.), 1608*m*, 1509*s*, 1427*m*, 1262*s*, 1110*m*, 1021*w*, 919*m*, 742*m*, 700*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.75–7.65 (*m*, 4 arom. H); 7.45–7.2 (*m*, 16 arom. H); 6.60, 6.51 (2*d*, *AB*, $J_{AB} = 8.8$, 4 arom. H); 5.84 (*s*, 1 NH); 5.10, 4.92 (2*d*, *AB*, $J_{AB} = 12.2$, $PhCH_2O$); 3.61 (*s*, $ArCH_2$); 1.09 (*s*, *t*-Bu). EI-MS: 652.5 (12, $[M + Na]^+$), 630.5 (31, $[M + H]^+$), 586.5 (23), 301.3 (37), 279.3 (100).

(S)-Enantiomer (S)-**11c**. From (*S*)-**10c** (737 mg, 1.10 mmol) according to *Method H:* 660 mg (95.7%) of (*S*)-**11c**. White solid. M.p. 89–90°. $[\alpha]_D = -27.0$ ($c = 0.1$, $CHCl_3$). MS, IR, and ^{1}H-NMR: in close agreement with those of (*R*)-**11c**.

*(S)-2-[(Benzyloxy)carbonylamino]-6-[(*tert*-butyl)diphenylsilanyloxy]-1,2,3,4-tetrahydronaphthalene-2-carboxylic Acid* ((*S*)-**11d**). From (*S*)-**10d** (280 mg, 0.451 mmol) according to *Method H:* 254 mg (97%) of (*S*)-**11d**. Oil. $[\alpha]_D = +17.0$ ($c = 0.15$, MeOH). IR (KBr): 3417*w* (br.), 2932*w*, 2858*w*, 1719*s* (br.), 1609*m*, 1428*w*, 1267*s*, 1112*m*, 742*m*, 701*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.75–7.65 (*m*, 4 arom. H); 7.45–7.2 (*m*, 11 arom. H); 6.73 (*d*, $J = 8.0$, 1 arom. H); 6.57 (*d*, $J = 2.8$, 1 arom. H); 6.48 (*dd*, $J = 8.0$, 2.8, 1 arom. H); 5.08 (*s*, $PhCH_2O$); 5.00 (*s*, 1 NH); 3.23, 2.85 (2*d*, *AB*, $J_{AB} = 16.0$, 2 aliph. H); 2.7–2.45 (*m*, 3 aliph. H); 2.15–2.0 (*m*, 1 aliph. H); 1.08 (*s*, *t*-Bu). ISN-MS: 578.3 (100, $[M - H]^-$), 470.3 (75).

(R)-Enantiomer (R)-**11d**. From (*R*)-**10d** (505 mg, 0.814 mmol) according to *Method H:* 440 mg (93%) of (*R*)-**11d**. Oil. $[\alpha]_D = -18.7$ ($c = 0.1$, MeOH). MS, IR, and ^{1}H-NMR: in close agreement with those of (*S*)-**11d**.

*(S)-2-[(*tert*-Butoxy)carbonylamino]-6-hydroxy-1,2,3,4-tetrahydronaphthalene-2-carboxylic Acid* ((*S*)-**12d**). From (*S*)-**1d** (800 mg, 3.86 mmol) according to *Method I:* 985 mg (83%) of (*S*)-**12d**. Oil. $[\alpha]_D = +40.0$ ($c = 0.1$, MeOH). IR (KBr): 3339*s* (br.), 2933*w*, 1715*s* (br.), 1617*w*, 1503*s*, 1454*m*, 1394*m*, 1368*m*, 1276*m*, 1235*m*, 1164*s*, 1064*w*, 848*w*. ^{1}H-NMR (250 MHz, (D_6)DMSO): 6.95 (*d*, $J = 8.0$, 1 arom. H); 6.7–6.55 (*m*, 2 arom. H); 4.82 (*s*, 1 NH); 4.58 (*s*, 1 OH); 3.35–3.2 (*m*, 1 aliph. H); 2.95–2.7 (*m*, 3 aliph. H); 2.7–2.5 (*m*, 1 aliph. H); 2.15–2.0 (*m*, 1 aliph. H); 1.43 (*s*, *t*-BuO). MS: 307 (> 1, M^+), 233 (4), 206 (6), 190 (100), 145 (36), 57 (45).

(R)-Enantiomer (R)-**12d**. From (*R*)-**1d** (800 mg, 3.86 mmol) according to *Method I:* 1.01 g (85%) of (*R*)-**12d**. Oil. $[\alpha]_D = -44.0$ ($c = 0.1$, MeOH). MS, IR, and ^{1}H-NMR: in close agreement with those of (*S*)-**12d**.

*(S)-2-[(*tert*-Butoxy)carbonylamino]-8-hydroxy-1,2,3,4-tetrahydronaphthalene-2-carboxylic Acid* ((*S*)-**12e**). From (*S*)-**1e** (515 mg, 1.67 mmol) according to *Method I:* 820 mg (99.6%) of (*S*)-**12e**. Pale-yellow oil. $[\alpha]_D = +66.0$ ($c = 1.0$, MeOH). IR (KBr): 3403*s* (br.), 2933*w*, 1715*s* (br.), 1617*w*, 1503*s*, 1454*m*, 1394*m*, 1368*m*, 1276*m*, 1235*m*, 1164*s*, 1064*w*, 848*w*. ^{1}H-NMR (250 MHz, (D_6)DMSO): 12.31 (*s*, 1 OH); 9.20 (br. *s*, 1 OH); 7.07 (*s*, NH); 6.87 (*t*,

J = 8.0, arom. H); 6.6–6.5 (*m*, 2 arom. H); 2.90 (*s*, 2 aliph. H); 2.8–2.5 (*m*, 2 aliph. H); 2.6–2.3 (*m*, 1 aliph. H); 1.8–1.6 (*m*, 1 aliph. H); 1.36 (*s*, *t*-BuO). MS: 307 (> 1, M^+), 233 (11), 190 (100), 145 (73), 120 (34).

*(R)-Enantiomer (R)-***12e**. From (*R*)-**1e** (465 mg, 1.45 mmol) according to *Method I:* 401 mg (90%) of (*R*)-**12e**. White solid. M.p. 77–80°. $[\alpha]_D = -75.3$ (c = 0.1, MeOH). MS, IR, and ^{1}H-NMR: in close agreement with those of (*S*)-**12e**.

*Benzyl (S)-2-[(*tert*-Butoxy)carbonylamino]-6-hydroxy-1,2,3,4-tetrahydronaphthalene-2-carboxylate* ((*S*)-**13d**). From (*S*)-**12d** (490 mg, 1.59 mmol) according to *Method K:* 385 mg (61%) of (*S*)-**13d**. White solid. M.p. 141–142°. $[\alpha]_D = +55.0$ (c = 0.1, $CHCl_3$). IR (KBr): 3377*s*, 2949*w*, 1729*s*, 1693*s*, 1621*w*, 1585*w*, 1501*s*, 1455*m*, 1370*m*, 1278*m*, 1242*s*, 1163*s*, 1066*s*, 811*w*, 750*w*, 697*w*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.4–7.3 (*m*, 5 arom. H); 6.90 (*d*, J = 8.0, 1 arom. H); 6.7–6.55 (*m*, 2 arom. H); 5.75, 5.67 (2*d*, *AB*, J_{AB} = 16.0, PhCH_2O); 4.78 (*s*, 1 NH); 4.69 (*s*, 1 OH); 3.13, 2.86 (2*d*, J = 16.0, 2 aliph. H); 2.85–2.7 (*m*, 2 aliph. H); 2.6–2.45 (*m*, 1 aliph. H); 2.2–2.05 (*m*, 1 aliph. H); 1.37 (*s*, *t*-BuO). MS: 397 (> 1, M^+), 280 (100), 235 (22), 145 (41), 91 (77).

*(R)-Enantiomer (R)-***13d**. From (*R*)-**12d** (750 mg, 2.44 mmol) according to *Method K:* 755 mg (78%) of (*R*)-**13d**. White solid. M.p. 141–142°. $[\alpha]_D = -45.0$ (c = 0.1, $CHCl_3$). MS, IR, and ^{1}H-NMR: in close agreement with those of (*S*)-**13d**.

*Benzyl (S)-2-[(*tert*-Butoxy)carbonylamino]-8-hydroxy-1,2,3,4-tetrahydronaphthalene-2-carboxylate* ((*S*)-**13e**). From (*S*)-**12e** (800 mg, 3.60 mmol) according to *Method K:* 829 mg (80.5%) of (*S*)-**13e**. White solid. M.p. 51–65°. $[\alpha]_D = +64.5$ (c = 0.2, $CHCl_3$). IR (KBr): 3402*s*, 2935*w*, 1717*s*, 1690*s*, 1590*m*, 1498*m*, 1497*m*, 1368*m*, 1331*w*, 1279*m*, 1254*m*, 1164*s*, 1061*m*, 779*w*, 697*w*. ^{1}H-NMR (250 MHz, $CDCl_3$): 9.25 (*s*, 1 OH); 7.45–7.25 (*m*, 5 arom. H); 6.89 (*t*, J = 7.7, 1 arom. H); 6.57 (*d*, J = 7.6, 1 arom. H); 6.51 (*d*, J = 7.5, 1 arom. H); 5.2–5.1 (*m*, PhCH_2O); 3.01, 2.88 (2*d*, J = 17.5, 2 aliph. H); 2.85–2.65 (*m*, 1 aliph. H); 2.65–2.5 (*m*, 1 aliph. H); 2.3–2.15 (*m*, 1 aliph. H); 1.95–1.8 (*m*, 1 aliph. H); 1.33 (*s*, *t*-BuO). ISP-MS: 420.6 (20, $[M + Na]^+$), 415.6 (55, $[M + NH_4]^+$), 415.6 (100, $[M + H]^+$), 324.4 (78), 298.4 (31).

*(R)-Enantiomer (R)-***13e**. From (*R*)-**12e** (440 mg, 1.43 mmol) according to *Method K:* 384 mg (70%) of (*R*)-**13e**. Pale yellow solid. M.p. 56–60°. $[\alpha]_D = -62.7$ (c = 1.0, $CHCl_3$). MS, IR, and ^{1}H-NMR: in close agreement with those of (*S*)-**13e**.

*Benzyl (S)-2-[(*tert*-Butoxy)carbonylamino]-6-[(*tert*-butyl)diphenylsilanyloxy]-1,2,3,4-tetrahydronaphthalene-2-carboxylate* ((*S*)-**14d**). From (*S*)-**13d** (376 mg, 0.946 mmol) according to *Method G:* 600 mg (99.7%) of (*S*)-**14d**. White solid. M.p. 52–55°. $[\alpha]_D = +36.0$ (c = 0.1, $CHCl_3$). IR (KBr): 3433*m* (br.), 2932*m*, 1716*s* (br.), 1610*w*, 1499*s*, 1271*m*, 1273*m*, 1160*m*, 982*w*, 742*w*, 702*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.75–7.65 (*m*, 4 arom. H); 7.5–7.3 (*m*, 11 arom. H); 6.70 (*d*, J = 8.0, 1 arom. H); 6.55 (*d*, J = 2.8, 1 arom. H); 6.46 (*dd*, J = 8.0, 2.8, 1 arom. H); 5.22, 5.12 (2*d*, *AB*, J_{AB} = 16.0, PhCH_2O); 4.73 (*s*, 1 NH); 3.11, 2.74 (2*d*, J = 16.0, 2 aliph. H); 2.7–2.6 (*m*, 2 aliph. H); 2.55–2.4 (*m*, 1 aliph. H); 2.15–2.0 (*m*, 1 aliph. H); 1.37 (*s*, *t*-BuO); 1.09 (*s*, *t*-Bu). ISP-MS: 658.5 (56, $[M + Na]^+$), 636.5 (82, $[M + H]^+$), 592.4 (96), 536.6 (100).

*(R)-Enantiomer (R)-***14d**. From (*R*)-**13d** (737 mg, 1.85 mmol) according to *Method G:* 1.17 g (99.5%) of (*R*)-**14d**. White solid. M.p. 52–55°. $[\alpha]_D = -36.5$ (c = 0.1, $CHCl_3$). MS, IR, and ^{1}H-NMR: in close agreement with those of (*S*)-**14d**.

*Benzyl (S)-2-[(*tert*-Butoxy)carbonylamino]-8-[(*tert*-butyl)diphenylsilanyloxy]-1,2,3,4-tetrahydronaphthalene-2-carboxylate* ((*S*)-**14e**). From (*S*)-**13e** (207 mg, 0.521 mmol) according to *Method G:* 287 mg (87%) of (*S*)-**14e**. Oil. M.p. 52–55°. $[\alpha]_D = +44.0$ (c = 0.1, $CHCl_3$). IR (KBr): 3425*m* (br.), 2932*m*, 1717*s* (br.), 1585*w*, 1492*w*, 1465*s*, 1269*m*, 1166*m*, 785*w*, 741*w*, 702*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.75–7.6 (*m*, 4 arom. H); 7.5–7.2 (*m*, 11 arom. H); 6.8–6.6 (*m*, 2 arom. H); 6.29 (*d*, J = 7.6, 1 arom. H); 5.23 (*s*, PhCH_2O); 4.66 (*s*, 1 NH); 3.25–3.05 (*m*, 2 aliph. H); 2.85–2.7 (*m*, 2 aliph. H); 2.7–2.5 (*m*, 1 aliph. H); 2.2–2.05 (*m*, 1 aliph. H); 1.42 (*s*, *t*-BuO); 1.06 (*s*, *t*-Bu). MS: 635 (> 1, M^+), 518 (5), 461 (6), 383 (10), 91 (100).

*(R)-Enantiomer (R)-***14e**. From (*R*)-**13e** (200 mg, 0.503 mmol) according to *Method G:* 302 mg (94%) of (*R*)-**14e**. White solid. M.p. 69–70°. $[\alpha]_D = -35$ (c = 0.1, $CHCl_3$). MS, IR, and ^{1}H-NMR: in close agreement with those of (*S*)-**14e**.

*(S)-2-[(*tert*-Butoxy)carbonylamino]-6-[(*tert*-butyl)diphenylsilanyloxy]-1,2,3,4-tetrahydronaphthalene-2-carboxylic Acid* ((*S*)-**15d**). From (*S*)-**14d** (645 mg, 1.01 mmol) according to *Method L:* 434 mg (79%) of (*S*)-**15d**. White solid. M.p. 92–94°. $[\alpha]_D = +33.0$ (c = 0.1, $CHCl_3$). IR (KBr): 3433*m* (br.), 2932*m*, 1717*s* (br.), 1655*w*, 1610*w*, 1500*s*, 1428*m*, 1392*w*, 1367*w*, 1269*m*, 1239*m*, 1159*s*, 1112*m*, 822*w*, 742*w*, 704*s*. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.75–7.65 (*m*, 4 arom. H); 7.5–7.3 (*m*, 6 arom. H); 6.76 (*d*, J = 8.0, 1 arom. H); 6.56 (*d*, J = 2.8, 1 arom. H); 6.50 (*dd*, J = 8.0, 2.8, 1 arom. H); 4.75 (*s*, 1 NH); 3.24, 2.74 (2*d*, J = 16.0, 2 aliph. H); 2.7–2.6 (*m*, 3 aliph. H); 2.1–1.95 (*m*, 1 aliph. H); 1.42 (*s*, *t*-BuO); 1.09 (*s*, *t*-Bu). ISP-MS: 568.5 (43, $[M + Na]^+$), 563.6 (100, $[M + NH_4]^+$), 546.4 (37, $[M + H]^+$), 490.6 (82), 446.6 (33).

(R)-Enantiomer (R)-**15d**. From (*R*)-**14d** (1.26 g, 1.98 mmol) according to *Method G:* 831 mg (77%) of (*R*)-**15d**. White solid. M.p. 92–94°. $[\alpha]_D = -30.0$ ($c = 0.1$, $CHCl_3$). MS, IR, and ^{1}H-NMR: in close agreement with those of (*S*)-**15d**.

(S)-2-[(tert-Butoxy)carbonylamino]-8-[(tert-butyl)diphenylsilanyloxy]-1,2,3,4-tetrahydronaphthalene-2-carboxylic Acid ((*S*)-**15e**). From (*S*)-**14e** (276 mg, 0.434 mmol) according to *Method L:* 236 mg (99.6%) of (*S*)-**15e**. White solid. M.p. 115.5–116°. $[\alpha]_D = +21.5$ ($c = 0.2$, MeOH). IR (KBr): 3436*m* (br.), 2932*m*, 1715*s* (br.), 1649*w*, 1585*w*, 1465*s*, 1428*m*, 1393*w*, 1367*w*, 1267*s*, 1165*s*, 1112*m*, 772*w*, 704*m*. ^{1}H-NMR (250 MHz, (D_6)DMSO): 7.8–7.65 (*m*, 4 arom. H); 7.55–7.35 (*m*, 6 arom. H); 7.25 (*s*, 1 NH); 6.75–6.55 (*m*, 2 arom. H); 6.04 (*d*, $J = 8.0$, 1 arom. H); 3.45–3.1 (*m*, 2 aliph. H); 2.85–2.55 (*m*, 2 aliph. H); 2.35–2.2 (*m*, 1 aliph. H); 2.0–1.85 (*m*, 1 aliph. H); 1.38 (*s*, *t*-BuO); 1.02 (*s*, *t*-Bu). ISN-MS: 544.4 (100, $[M - H]^-$).

(R)-Enantiomer (R)-**15e**. From (*R*)-**14e** (295 mg, 0.464 mmol) according to *Method G:* 253 mg (99.9%) of (*R*)-**15e**. White solid. M.p. 108–110°. $[\alpha]_D = -24.0$ ($c = 0.1$, MeOH). MS, IR, and ^{1}H-NMR: in close agreement with those of (*S*)-**15e**.

X-Ray Crystal-Structure Analysis. See *Table 4.* The coordinates of **4b,c** and **5b,c** were deposited at the *Cambridge Crystallographic Data Center,* University Chemical Laboratory, 12 Union Road, Cambridge, CB2 1EZ, UK.

Table 4. *X-Ray Crystal-Structure Analysis of* **4b,c** *and* **5b,c**

	4b	**5b**	**4c**	**5c**
Crystal data				
Empirical formula	$C_{35}H_{43}N_3O_4$	$C_{35}H_{43}N_3O_4$	$C_{38}H_{41}N_3O_4$	$C_{38}H_{41}N_3O_4$
Color, habit	colorless, prismatic	colorless, prismatic	colorless, prismatic	colorless, prismatic
Crystal size [mm]	0.24 × 0.4 × 0.4	unknown	0.25 × 0.4 × 0.6	0.25 × 0.25 × 1.0
Crystal system	monoclinic	monoclinic	orthorhombic	tetragonal
Space group	$P2_1$	$P2_1$	$P2_12_12_1$	$P4_2$
Unit cell dimensions				
a [Å]	8.864(3)	11.614(2)	9.054(2)	17.794(4)
b [Å]	11.511(3)	17.222(3)	19.803(4)	
c [Å]	15.366(5)	16.412(3)	37.197(7)	10.676(5)
β [°]	98.33 (3)	96.68(3)		
Volume [Å^3]	1551.3(8)	3260.4(10)	6669.0(2)	3380.0(2)
Z	2	4	8	4
Formula weight	569.7	569.7	603.7	603.7
Density (calc.)	1.22	1.161	1.203	1.186
Absorption coefficient [mm^{-1}]	0.080	0.602	0.621	0.077
F(000)	612	1224	2576	1288
Crystallization solvent	MeCN	Propane-1,3-diol	MeOH	methylglycol
Data collection				
Radiation	MoK_α	CuK_α	CuK_α	MoK_α
Temperature [K]	233	298	298	183
2*θ* Range [deg]	0–56	0–113	0–113.5	0–56
Scan type	*ω*	2*θ*-*θ*	2*θ*-*θ*	*ω*
Scan speed [deg/min]	1.2–10.19	1.0–60.0	1.0–60	1.1–10.19
Scan range (*ω*)	0.4	0.6	0.6	0.5
Independent reflexions	3957	4501	4947	3899
Observed reflexions	2848	4386	4317	2088
Absorption correction	none	none	none	none
Solution and refinement				
Solution	direct methods	direct methods	direct methods	direct methods
Data-to-parameter ratio	7.4:1	5.8:1	5.3:1	5.1:1
Final *R* index (obs. data)	5.08	3.89	5.08	6.59

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