New Optically Active 2*H*-Azirin-3-amines as Synthons for Enantiomerically Pure 2,2-Disubstituted Glycines: Synthesis of Synthons for Tyr(2Me) and Dopa(2Me), and Their Incorporation into Dipeptides

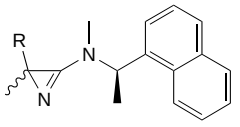
by **Kathrin A. Brun**[1]), **Anthony Linden**, and **Heinz Heimgartner***

Organisch-chemisches Institut der Universität Zürich, Winterthurerstrasse 190, CH-8057 Zürich

Dedicated to Professor *Dieter Seebach* on the occasion of his 65th birthday

The synthesis of novel unsymmetrically 2,2-disubstituted 2*H*-azirin-3-amines with chiral auxiliary amino groups is described. Chromatographic separation of the mixture of diastereoisomers yielded (1′*R*,2*S*)-**2a**,**b** and (1′*R*,2*R*)-**2a**,**b** (*c.f. Scheme 1* and *Table 1*), which are synthons for (*S*)- and (*R*)-2-methyltyrosine and 2-methyl-3′,4′-dihydroxyphenylalanine. Another new synthon **2c**, *i.e.*, a synthon for 2-(azidomethyl)alanine, was prepared but could not be separated into its pure diastereoisomers. The reaction of **2** with thiobenzoic acid, benzoic acid, and the amino acid Fmoc-Val-OH yielded the monothiodiamides **11**, the diamides **12** (*cf. Scheme 3* and *Table 3*), and the dipeptides **13** (*cf. Scheme 4* and *Table 4*), respectively. From **13**, each protecting group was removed selectively under standard conditions (*cf. Schemes 5–7* and *Tables 5–6*). The configuration at C(2) of the amino acid derivatives (1*R*,1′*R*)-**11a**, (1*R*,1′*R*)-**11b**, (1*S*,1′*R*)-**12b**, and (1*R*,1′*R*)-**12b** was determined by X-ray crystallography relative to the known configuration of the chiral auxiliary group.

1. Introduction. – Recently, we reported the preparation of new optically active 2*H*-azirin-3-amines **1** as synthons for enantiomerically pure 2,2-disubstituted glycines (α,α-disubstituted α-amino acids) [1].

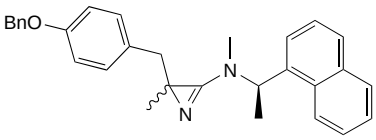


R = Et, ^{i}Pr, cyclopentyl, ^{i}Bu, Bn

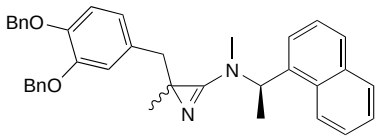
1

It has been shown that these 2*H*-azirin-3-amines can successfully be used in peptide synthesis [1][2]. All prepared 2*H*-azirin-3-amines **1** possess aliphatic or aromatic side chains. It was of interest to extend the series of available synthons to examples with functionalized side chains, *e.g.*, side chains with OH groups. In the present paper, the synthesis of 2*H*-azirin-3-amines **2a** and **2b** with protected phenolic hydroxy groups as synthons for enantiomerically pure 2-methyltyrosine (Tyr(2Me)) and 2-methyl-3′,4′-dihydroxyphenylalanine (Dopa(2Me)), and their use in peptide synthesis are described. Additionally, the new 2*H*-azirin-3-amine **2c** with a N_3 group in the side chain is presented as the unexpected product of an attempt to prepare **2d**, a benzyl (Bn)-protected synthon for Ser(2Me).

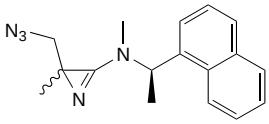
[1]) Part of the Ph.D. thesis of *K. A. B.*, Universität Zürich, 2002.



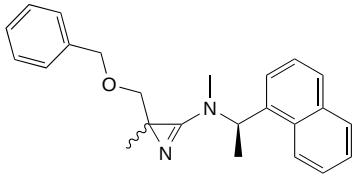
2a



2b



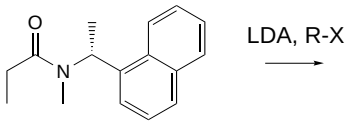
2c



2d

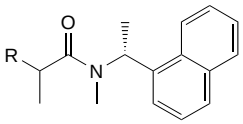
2. Results. – 2.1. *Preparation of the 2*H*-Azirines.* The 2*H*-azirin-3-amines **2a**–**c** (*Scheme 1*), *i.e.*, synthons for 2-methyltyrosine (Tyr(2Me)), 2-methyl-3′,4′-dihydroxyphenylalanine (Dopa(2Me)), and 2-(azidomethyl)alanine (Ala(2AMe)) (*Table 1*), were prepared in gram quantities. As reported in our previous paper [1], the commercially available (*R*)-[1-(naphthalen-1-yl)ethyl]amine (**3**) was used as the chiral auxiliary group in all experiments.

Scheme 1



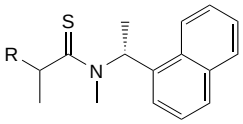
4

LDA, R-X



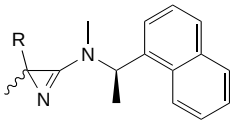
5a R = 4-$BnOC_6H_4CH_2$
b R = 3,4-$(BnO)_2C_6H_3CH_2$
c R = 4-$BnOCH_2$

L.-R.



10a R = 4-$BnOC_6H_4CH_2$
b R = 3,4-$(BnO)_2C_6H_3CH_2$
c R = 4-$BnOCH_2$

$COCl_2$
DABCO
NaN_3



2a R = 4-$BnOC_6H_4CH_2$
b R = 3,4-$(BnO)_2C_6H_3CH_2$
c R = N_3CH_2

LDA = lithium diisopropylamide; *L*.-R. = *Lawesson* reagent; DABCO = 1,4-diazabicyclo[2.2.2]octane.

The three pairs of diastereoisomers of **2a**–**c** were prepared according to *Scheme 1* (*Table 1*) by applying the previously described protocols (*cf.* [3]). The chiral auxiliary group was introduced as described for **1a**–**e** [1]. The amide **4** [1] was deprotonated with

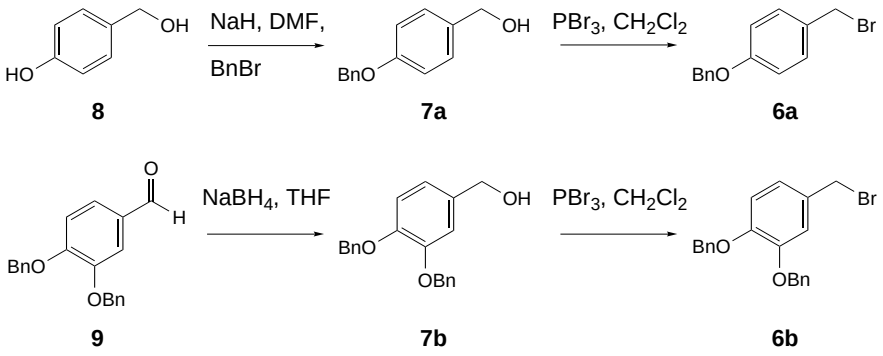
Table 1. *Synthesis of 2*H-*Azirin-3-amines* **2** (Yields in [%])

R	Alcohol **7**	Bromide **6**	Amide **5**	Thioamide **10**	Azirine **2**	Synthon
4-$BnOC_6H_4CH_2$	**a** (90)	**a** (quant.)	**a** (92)	**a** (78)	**a** (81)	Tyr(2Me)
3,4-$(BnO)_2C_6H_3CH_2$	**b** (quant.)	**b** (quant.)	**b** (88)	**b** (85)	**b** (62)	Dopa(2Me)
4-$BnOCH_2$			**c** (92)	**c** (49)		
N_3CH_2					**c** (26)	Ala(2AMe)

lithium diisopropylamide (LDA) and alkylated with the respective halides R–X to give the amides **5a**–**c** as mixtures of diastereoisomers.

The halides **6a** and **6b**, which were used for the synthesis of **5a** and **5b**, respectively, were prepared from the corresponding benzylic alcohols **7a** and **7b**, which were obtained from phenol **8** and aldehyde **9**, respectively [4] (*Scheme 2*). The amide **5c** was prepared by alkylation with benzyl chloromethyl ether (**6c**), which was commercially available.

Scheme 2



The amides **5a**–**c** were then converted to the corresponding thioamides **10a**–**c** (mixtures of diastereoisomers) by treatment with *Lawesson* reagent. Finally, the synthesis of the azirines **2a**–**c** was achieved by consecutive reaction of **10a**–**c** with $COCl_2$ solution in CH_2Cl_2, deprotonation with 1,4-diazabicyclo[2.2.2]octane (DABCO) in THF, and treatment with NaN_3 (*cf.* [1]). The yields of these transformations are given in *Table 1*. The conversion of **10c** under the conditions described leads to the unexpected product **2c** instead of **2d**. During the reaction sequence described, the BnO group of the side chain was replaced by the N_3 group. This substitution could be prevented neither by using less than 1 equiv. of NaN_3 nor by adding NaN_3 very slowly to the intermediate chloroenamine; therefore, it is suspected that the substitution is faster than the formation of the azirine.

Separation of the (*R*,*S*)- and (*R*,*R*)-diastereoisomers of **2a** and **2b** was achieved by means of column chromatography (CC; SiO_2), followed by MPLC (SiO_2). The detailed procedures and solvent systems are summarized in *Table 2*.

The diastereoisomers of azirine **2c** could not be separated by means of chromatography, neither by TLC, CC, and MPLC nor by GC. The two diastereoisomers could not be differentiated with NMR techniques either.

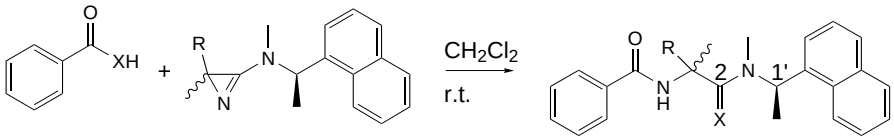
Table 2. *Chromatographic Separation of the (*R,S*)- and (*R,R*)-Diastereoisomers of* **2a** *and* **2b**

	R	Separation method	Amount separated	R_f-Values[c])
2a	4-$BnOC_6H_4CH_2$	CC[a]), MPLC[b])	1.5 g	0.25, 0.16
2b	3,4-$(BnO)_2C_6H_3CH_2$	CC[a]) (3×), MPLC[b])	4.9 g	0.29, 0.20

[a]) Hexane/AcOEt 2 : 1. [b]) AcOEt. [c]) Hexane/AcOEt 1 : 1.

2.2. *Reaction of 2*H-*Azirines* **2a – c** *with Thiocarboxylic and Carboxylic Acids.* With the aim of demonstrating that the new, optically pure amino-acid synthons show analogous chemical behavior in reactions with thiocarboxylic and carboxylic acids as the already known 2*H*-azirin-3-amines (*cf.* [5]), they were reacted with PhCOSH (*cf.* [1][3][6–9]) and PhCOOH (*cf.* [1][3][7]) (*Scheme 3*). A typical reaction was carried out with equimolar amounts of **2** and the acid in CH_2Cl_2 at room temperature. The yields and reaction times are given in *Table 3*. It is obvious that the reactions with PhCOSH proceeded faster and gave the products in better yields than with PhCOOH. The same difference has been observed with azirines **1a – e** [1]. In the case of the Tyr(2Me) synthon **2a**, the (1′*R*,2*S*)-diastereoisomer reacts significantly slower and gave the products in lower yields than its (1′*R*,2*R*)-isomer. On the other hand, such a different behavior of the Dopa(2Me) synthons **2b** was not observed.

Scheme 3[a])



X = S, O **2a-c** **11a-c** X = S **12a-b** X = O

[a]) For **a – c**, see *Scheme 1*.

Table 3. *Reaction of the 2*H-*Azirin-3-amines* **2** with *PhCOSH and PhCOOH* (in CH_2Cl_2 at room temperature)

Azirine **2**	R	Reaction with PhCOSH			Reaction with PhCOOH		
		Thioamide **11**	Yield [%]	Reaction time [h]	Amide **12**	Yield [%]	Reaction time [h]
(1′*R*,2*S*)-**2a**	4-$BnOC_6H_4CH_2$	(1*S*,1′*R*)-**11a**	64	18	(1*S*,1′*R*)-**12a**	39	19
(1′*R*,2*R*)-**2a**		(1*R*,1′*R*)-**11a**	90	2.5	(1*R*,1′*R*)-**12a**	67	23
(1′*R*,2*S*)-**2b**	3,4-$(BnO)_2C_6H_3CH_2$	(1*S*,1′*R*)-**11b**	89	3	(1*S*,1′*R*)-**12b**	91	336
(1′*R*,2*R*)-**2b**		(1*R*,1′*R*)-**11b**	88	20	(1*R*,1′*R*)-**12b**	90	314
2c	N_3CH_2	**11c**	97	4.5			

2.3. *Determination of the Relative Configuration of the New Synthons.* As most of the prepared azirines were not crystalline compounds or, in the case of (1′*R*,2*S*)-**2a**, suitable crystals for the X-ray crystallographic analysis could not be obtained, the configurations were determined in derivatives **11** and **12**. Suitable crystals were

obtained from the four products of the conversion of (1′*R*,2*R*)-**2a**, (1′*R*,2*S*)-**2b** and (1′*R*,2*R*)-**2b** with PhCOSH and PhCOOH, respectively, *i.e.* from the monothiodiamides (1*R*,1′*R*)-**11a** and (1*R*,1′*R*)-**11b**, and the diamides (1*S*,1′*R*)-**12b** and (1*R*,1′*R*)-**12b** (see *Fig.*). The configuration at C(2) of the amino acid derivatives (C(4) in the *Figure*) was determined relative to the known (*R*)-configuration of the chiral auxiliary group. Except for (1*R*,1′*R*)-**11a**, the absolute configurations of the molecules were not confirmed crystallographically, but could be assigned on the basis of the known absolute configuration of the amino substitutent.

2.4. *The Use of Azirines* **2a** *and* **2b** *in Peptide Chemistry.* The optically pure amino acid synthons **2a** and **2b** were used to incorporate the corresponding (*S*)- and (*R*)-configured 2,2-disubstituted glycines (α,α-disubstituted α-amino acids), respectively, into dipeptides of the type Fmoc-Val-Xaa-N(Me)NaphthEt **13** by coupling **2** with Fmoc-valine (Fmoc-Val-OH, *Scheme 4*). Typically, these reactions were carried out in CH_2Cl_2 at room temperature with equimolar amounts of **2** and Fmoc-Val-OH. The yields and reaction times are listed in *Table 4*. As can be seen, the coupling of the Dopa(2Me) synthons **2b** is slower than in the case of the Tyr(2Me) synthons **2a**, probably due to increased sterical hindrance resulting from the second Bn protecting group in the side chain.

Scheme 4

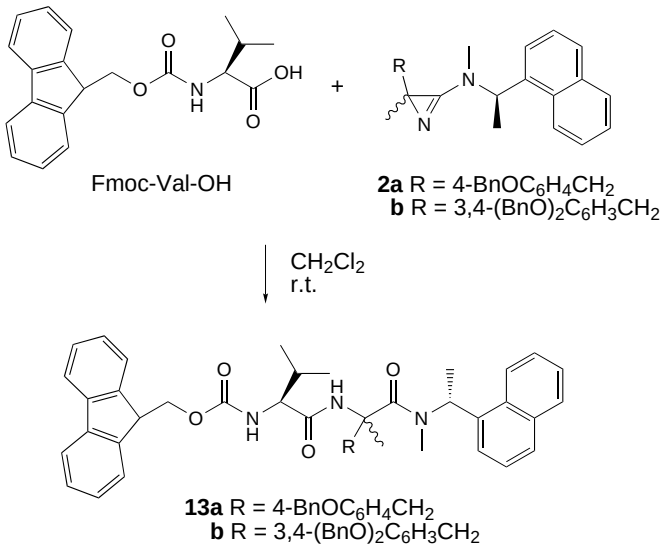


Table 4. *Reaction of the* 2H-*Azirin-3-amines* **2** *with Fmoc-Val-OH* (in CH_2Cl_2 at room temperature)

Azirine **2**	R	Dipeptide **13**	Yield [%]	Reaction time [h]
(1′*R*,2*S*)-**2a**	4-$BnOC_6H_4CH_2$	(*S*,*S*,*R*)-**13a**	52	20
(1′*R*,2*R*)-**2a**		(*S*,*R*,*R*)-**13a**	70	66
(1′*R*,2*S*)-**2b**	3,4-(BnO)$_2C_6H_3CH_2$	(*S*,*S*,*R*)-**13b**	56	137
(1′*R*,2*R*)-**2b**		(*S*,*R*,*R*)-**13b**	58	142

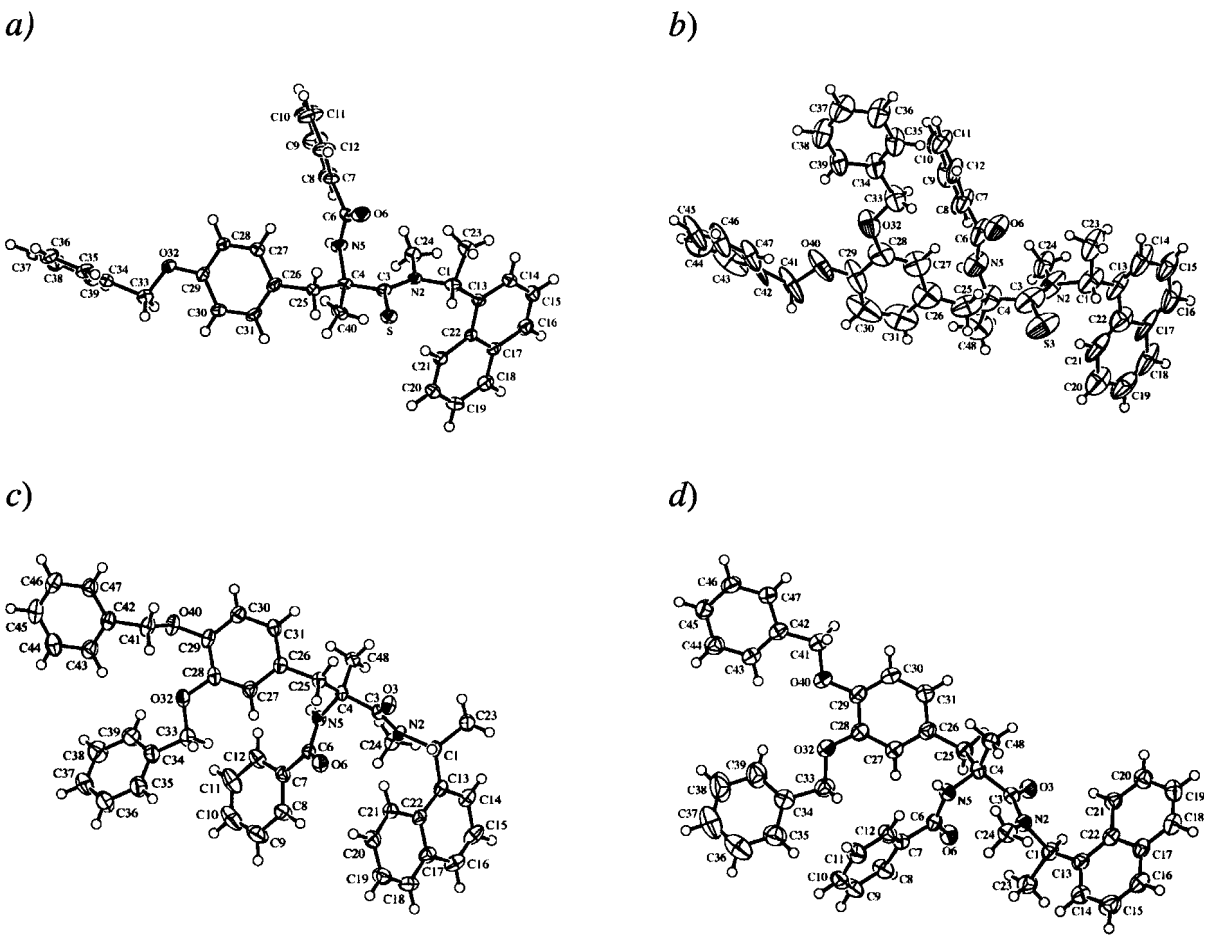
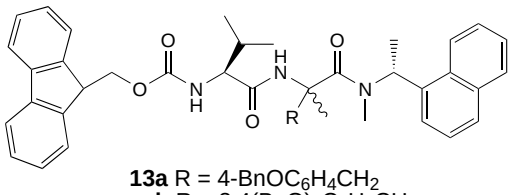


Figure. *ORTEP Plots* [10] *of the molecular structures of* a) *(1*R,*1′*R*)*-**11a** (derivative of (*R*)-Tyr(2Me)), b) *(1*R,*1′*R*)*-**11b** (derivative of (*R*)-Dopa(2Me)), c) *(1*S,*1′*R*)*-**12b** (derivative of (*S*)-Dopa(2Me)), *and* d) *(1*R,*1′*R*)*-**12b** (derivative of (*R*)-Dopa(2Me)) (50% Probability ellipsoids, arbitrary numbering of atoms)

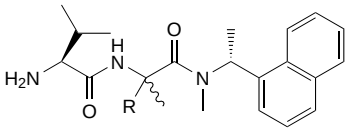
Each of the protecting groups of the dipeptides **13** was removed selectively under standard conditions. The Fmoc group at the N-terminus was cleaved under basic conditions with Et_2NH to give the dipeptides **14** (*Scheme 5*). Typically, these reactions were carried out without solvent at room temperature and in an excess of Et_2NH. The yields and reaction times are given in *Table 5*.

Scheme 5



13a R = 4-$BnOC_6H_4CH_2$
b R = 3,4-$(BnO)_2C_6H_3CH_2$

Et_2NH
r.t.



14a R = 4-$BnOC_6H_4CH_2$
b R = 3,4-$(BnO)_2C_6H_3CH_2$

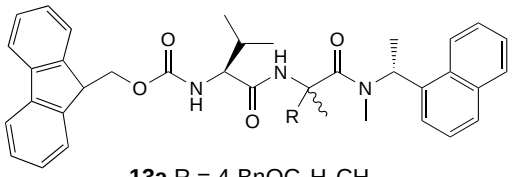
Table 5. *Removal of the Fmoc Group of the Dipeptides* **13** *with Et_2NH and Cleavage of the Bn Groups in the Side Chains with Pd/C and H_2*

13	R	**14**	Yield [%]	Reaction time [h]	**15**	Yield [%]	Reaction time [h]
(*S*,*S*,*R*)-**13a**	4-$BnOC_6H_4CH_2$	(*S*,*S*,*R*)-**14a**	quant.	1	(*S*,*S*,*R*)-**15a**	47	48
(*S*,*R*,*R*)-**13a**		(*S*,*R*,*R*)-**14a**	94	2	(*S*,*R*,*R*)-**15a**	71	40
(*S*,*S*,*R*)-**13b**	3,4-$(BnO)_2C_6H_3CH_2$	(*S*,*S*,*R*)-**14b**	87	1	(*S*,*S*,*R*)-**15b**	60	22
(*S*,*R*,*R*)-**13b**		(*S*,*R*,*R*)-**14b**	77	4	(*S*,*R*,*R*)-**15b**	85	25

The Bn protecting groups of the side chains were removed by hydrogenolysis to give dipeptides **15** (*Scheme 6*). Typically, these reactions were carried out in MeOH with a catalytic amount of Pd/C (10% on charcoal) and H_2 at room temperature. The yields and reaction times are collected in *Table 5*.

The amide group at the C-terminus was hydrolyzed under acidic conditions to give the dipeptide acids **16** (*Scheme 7*). Optimal conditions for the hydrolysis of amides with this special chiral auxiliary group have been determined earlier [2]. Typically, these reactions were carried out in 3N HCl (MeCN/H_2O 1:1) at 60°. For the hydrolysis of **13** to the dipeptide acids **16**, however, the solubility of the dipeptide amides (*S*,*S*,*R*)-**13a** and (*S*,*S*,*R*)-**13b** in the 1:1 mixture of MeCN/H_2O was insufficient; longer reaction times would have been neccessary, which leads to increased decomposition. Therefore,

Scheme 6

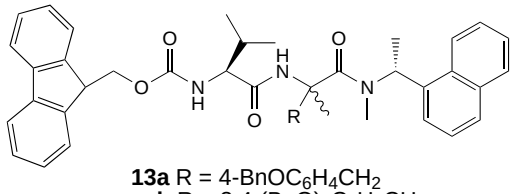


13a R = 4-$BnOC_6H_4CH_2$
b R = 3,4-$(BnO)_2C_6H_3CH_2$

H_2, Pd/C
MeOH

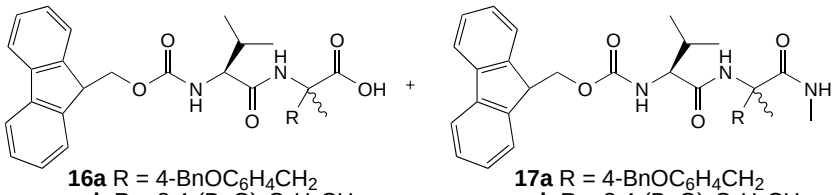
15a R = 4-$HOC_6H_4CH_2$
b R = 3,4-$(HO)_2C_6H_3CH_2$

Scheme 7



13a R = 4-$BnOC_6H_4CH_2$
b R = 3,4-$(BnO)_2C_6H_3CH_2$

3N HCl (MeCN/H_2O)
60°



16a R = 4-$BnOC_6H_4CH_2$
b R = 3,4-$(BnO)_2C_6H_3CH_2$

17a R = 4-$BnOC_6H_4CH_2$
b R = 3,4-$(BnO)_2C_6H_3CH_2$

the ratio of MeCN and H_2O was changed, while keeping the concentration of HCl constant (3N). The reaction conditions, yields and reaction times are given in *Table 6*.

Surprisingly, an undesired side reaction of the amino group took place, leading to the product **17** (*Scheme 7*), which cannot be hydrolyzed further under the possible reaction conditions. This side product was fully characterized in the case of (*S*,*S*)-**17a**. The formation of these side products can be explained by an acid-catalyzed cleavage of the benzylic C–N bond of the amide group under the more drastic hydrolysis conditions.

3. Conclusions. – It can be stated that the new synthons were successfully used for the synthesis of dipeptides. Each protecting group could be removed selectively, but

Table 6. *Hydrolysis of the Dipeptide Amides* **13** (in 3N HCl (MeCN/H_2O) at 60°)

Dipeptide **13**	R	MeCN/H_2O 1:1				MeCN/H_2O 2:1			MeCN/H_2O 3:1		
		Yield [%]		Recovered **13** [%]	Reaction time [h]	Yield [%]		Reaction time [h]	Yield [%]		Reaction time [h]
		16	**17**			**16**	**17**		**16**	**17**	
(*S*,*S*,*R*)-**13a**	4-$BnOC_6H_4CH_2$	8	33	49	5	27	68	1.75			
(*S*,*R*,*R*)-**13a**		51	30	19	3						
(*S*,*S*,*R*)-**13b**	3,4-$(BnO)_2C_6H_3CH_2$	9	–	78	3	22	67	1	30	42	1
(*S*,*R*,*R*)-**13b**		25	19	55	3						

one limitation in the use of the chiral auxiliary group has to be mentioned: after successful coupling to give the peptide amide, the auxiliary group has to be cleaved by acid hydrolysis. In some cases, the yields after the hydrolysis are poor. The resulting side product is of no use for further reactions in peptide synthesis.

We thank the analytical services of our institute for NMR and mass spectra and for elemental analyses. Financial support by the *Swiss National Science Foundation*, *F. Hoffmann-La Roche AG*, Basel, and the *Stiftung für wissenschaftliche Forschung an der Universität Zürich* is gratefully acknowledged. *K. A. B.* thanks the '*Stipendienfonds der Basler Chemischen Industrie*' for a scholarship.

Experimental Part

1. *General.* See [1].

2. *Synthesis of the 2*H*-Azirines.* 2.1. *Tyr(2Me) Synthon*. 2.1.1. *[4-(Benzyloxy)phenyl]methanol* (**7a**). To an orange soln. of (*4-hydroxyphenyl*)*methanol* (**8**; 10.011 g, 80.643 mmol) in DMF (220 ml) at 0°, NaH (3.5 g, *ca.* 80 mmol; washed with hexane) was added. At r.t., BnBr (9.5 ml, 80 mmol) was added, and the mixture was stirred for 6 h, while the color was changing to blue-green. The soln. was evaporated (10 mbar, 50°), and the residue was dissolved in CH_2Cl_2 and washed with H_2O. The color of the soln. turned to orange, and after evaporation, the residue solidified overnight. CC (hexane/AcOEt 2:1) yielded 15.463 g (90%) of **7a**. M.p. 84.5–85°. R_f (hexane/AcOEt 2:1) 0.13. IR: 3322*s*, 3060*m*, 3034*m*, 2915*m*, 2866*m*, 1956*w*, 1888*w*, 1610*s*, 1585*m*, 1513v*s*, 1469*m*, 1454*s*, 1423*m*, 1382*s*, 1299*m*, 1246v*s*, 1173*s*, 1112*m*, 1082*w*, 998v*s*, 936*w*, 914*m*, 863*m*, 812*s*, 777*s*, 740v*s*, 716*m*, 696v*s*, 640*m*, 615*m*. ^{1}H-NMR (CD_3OD): 7.45–7.25 (*m*, 7 arom. H); 7.0–6.95 (*m*, 2 arom. H); 5.06, 4.59 (2*s*, 2 CH_2); 1.63 (br. *s*, OH). ^{13}C-NMR (CD_3OD): 158.3 (*s*, 1 arom. CO); 136.9, 133.3 (2*s*, 2 arom. C); 130.0, 128.5, 127.9, 127.3 (4*d*, 7 arom. CH); 114.9 (*d*, 2 arom. CH); 70.0, 64.9 (2*t*, 2 CH_2). EI-MS (NH_3): 214 (15, $M^{+\bullet}$), 91 (100, $C_7H_7^+$). Anal. calc. for $C_{14}H_{14}O_2$ (214.26): C 78.48, H 6.59; found: C 78.22, H 6.62.

2.1.2. *4-(Benzyloxy)-1-(bromomethyl)benzene* (**6a**). To a soln. of **7a** (7.035 g, 32.834 mmol) in CH_2Cl_2 (150 ml) under Ar at 0°, PBr_3 (3.2 ml, 33.7 mmol) was added dropwise. The mixture was kept dark with Al foil around the flask. After 1.5 h, the mixture was warmed to r.t. and stirred for another 30 min. The soln. was poured on ice and extracted with Et_2O; the org. phase was dried ($MgSO_4$) and evaporated (keeping in the dark as long as possible): 9.184 g (quant. yield) of **6a**, which was very unstable (decomposition within several h) and had to be used for further reactions immediately. M.p. 85–86°. R_f (hexane/AcOEt 2:1) 0.54. R_f (hexane/AcOEt 5:1) 0.42. IR: 3030*m*, 2934*m*, 2874*w*, 1612*m*, 1579*m*, 1515v*s*, 1466*w*, 1454*m*, 1384*m*, 1316*w*, 1298*m*, 1253v*s*, 1231*s*, 1204*m*, 1173*s*, 1126*w*, 1098*w*, 1082*w*, 1007*s*, 919*w*, 866*w*, 838*m*, 810*w*, 743v*s*, 699*s*, 598*s*. ^{1}H-NMR (CD_3OD): 7.45–7.3 (*s*, 7 arom. H); 6.93 (*dt*, $J = 8.7, 2.5, 2$ arom. H); 5.05 (*s*, CH_2O); 4.48 (*s*, CH_2Br). ^{13}C-NMR (CD_3OD): 158.8 (*s*, 1 arom. CO); 136.6, 130.1 (2*s*, 2 arom. C); 130.4, 128.5, 127.9, 127.3 (4*d*, 7 arom. CH); 115.1 (*d*, 2 arom. CH); 70.0 (*t*, CH_2O); 33.7 (*t*, CH_2Br). EI-MS: 278 (1, $M^{+\bullet}$, ^{81}Br), 276 (1, $M^{+\bullet}$, ^{79}Br), 198 (4), 197 (26, $[M-Br]^+$), 119 (8), 107 (14, $C_7H_7O^+$), 93 (13), 91 (100, $C_7H_7^+$), 79 (16), 78 (9), 77 (27, $C_6H_5^+$), 69 (9), 67 (5), 65 (17, $C_5H_5^+$), 51 (8, $C_4H_3^+$).

2.1.3. *(*RS*)-2-[4-(Benzyloxy)benzyl]*-N-*methyl*-N-*[(*R*)-1-(naphthalen-1-yl)ethyl]propanamide* (**5a**). To a soln. of N-*methyl*-N-*[(*R*)-1-(naphthalen-1-yl)ethyl]propanamide* (**4** [1]; 6.868 g, 28.459 mmol) in abs. THF (30 ml) at 0°, 2N LDA in THF/heptane/PhEt (17 ml, 34.0 mmol) was added within 30 min. Then, **6a** (7.894 g, 28.482 mmol) in abs. THF (40 ml) was added within 35 min, keeping the temp. below 5°. After 60 min, the

mixture was carefully poured on ice, extracted with Et_2O, dried ($MgSO_4$), and evaporated. CC (hexane/AcOEt 4:1, then 2:1) yielded 11.419 g (92%) of **5a**. Colorless oil. R_f (hexane/AcOEt 2:1) 0.34 and 0.26, resp., for the diastereoisomers. IR ($CHCl_3$): 3007*s*, 2875*w*, 2359*w*, 1731*w*, 1625v*s*, 1510v*s*, 1464*m*, 1454*m*, 1409*m*, 1376*m*, 1297*m*, 1248*s*, 1109*m*, 1084*w*, 1043*w*, 1025*m*, 916*w*, 864*w*, 837*w*, 807*m*. ^{1}H-NMR: 8.0–7.75 (*m*, 3 arom. H); 7.5–7.25 (*m*, 9 arom. H); 7.14, 7.04 (2*d*, J = 8.6, 2 arom. H); 6.89, 6.73 (2*d*, J = 8.6, 2 arom. H); 6.62, 6.60 (2*q*, J = 6.7, CHN); 5.04, 4.95 (2*s*, PhCH_2O); 3.1–2.95, 2.9–2.8, 2.7–2.55 (3*m*, CH_2C*H*); 2.43, 2.20 (2*s*, MeN); 1.57, 1.41 (2*d*, J = 6.8, 1 Me); 1.18, 1.14 (2*d*, J = 6.7, 1 Me). ^{13}C-NMR: 175.1, 175.0 (2*s*, CO); 157.2, 157.1, 137.1, 136.3, 136.0, 133.6, 132.7, 132.5, 131.9 (9*s*, 6 arom. C); 130.0, 129.9, 128.5, 128.3, 127.8, 127.3, 126.5, 126.4, 125.8, 124.8, 124.7, 124.1, 114.7, 114.6 (14*d*, 16 arom. CH); 69.9 (*t*, PhCH_2O); 47.8 (*d*, CHN); 39.6, 39.1 (2*t*, CH_2); 38.9, 38.7 (2*d*, *C*HCO); 28.9, 28.8 (2*q*, MeN); 17.9, 17.2, 15.6, 15.5 (4*q*, 2 Me). CI-MS (NH_3): 455 (16, $[M+NH_4]^+$), 440 (11), 439 (43), 438 (100, $[M+1]^+$), 108 (14, $[PhCH_2O+1]^+$). Anal. calc. for $C_{30}H_{31}NO_2$ (437.58): C 82.35, H 7.14, N 3.20; found: C 82.40, H 7.22, N 3.04.

2.1.4. *(*RS*)-2-[4-(Benzyloxy)benzyl]-*N*-methyl-*N*-[(*R*)-1-(naphthalen-1-yl)ethyl]propanethioamide* (**10a**). To a soln. of **5a** (5.970 g, 13.64 mmol) in abs. toluene (15 ml), *Lawesson* reagent (3.3 g, 1.2 equiv.) was added; the mixture was stirred for 3.5 h at 125°, cooled to r.t., the precipitate was washed with Et_2O, and the filtrate was evaporated. CC (hexane/AcOEt 5:1) yielded 4.797 g (78%) of **10a**. Colorless solid. M.p. 128–129°. R_f (hexane/AcOEt 5:1) 0.27 and 0.21, resp., for the diastereoisomers. IR: 3444*w*, 3039*w*, 2967*m*, 2923*m*, 1613*m*, 1582*w*, 1510v*s*, 1486v*s*, 1453*s*, 1406v*s*, 1377*m*, 1322*s*, 1297*m*, 1249v*s*, 1172*s*, 1110*s*, 1085*m*, 1044*s*, 1028*m*, 987*m*, 969*m*, 904*w*, 841*m*, 805*s*, 778v*s*, 732*s*, 694*m*, 678*w*, 624*w*. ^{1}H-NMR: 7.9–7.8 (*m*, 3 arom. H); 7.5–7.3 (*m*, 9 arom. H, CHN); 7.16 (*d*, J = 8.6, 2 arom. H); 6.86 (*d*, J = 8.6, 2 arom. H); 5.05 (*s*, PhCH_2O); 3.25–3.15 (*m*, CH_2); 2.85–2.8 (*m*, CSCH); 2.30 (*s*, MeN); 1.47 (*d*, J = 6.8, Me); 1.30 (*d*, J = 6.1, Me). ^{13}C-NMR: 208.3 (*s*, CS); 157.2 (*s*, 1 arom. C–O); 137.1, 135.6, 133.6, 132.3, 132.0 (5*s*, 5 arom. C); 130.1, 128.8, 128.5, 127.8, 127.3, 126.7, 126.0, 125.2, 124.8, 124.4, 114.7 (11*d*, 16 arom. CH); 69.9 (*t*, Ph*C*H$_2$O); 56.8 (*d*, CHN); 45.0 (*d*, *C*HCS); 43.3 (*t*, CH_2); 32.9 (*q*, MeN); 21.9, 13.9 (2*q*, *Me*CHN, *Me*CHCS). ESI-MS (CH_2Cl_2, MeOH): 492 (6, $[M+K]^+$), 484 (16, $[M+MeOH]^+$), 476 (13, $[M+Na]^+$), 454 (100, $[M+1]^+$), 300 (82, $[M-naphthCHCH_2+1]^+$), 266 (36), 155 (20, $[naphthCHMe]^+$). Anal. calc. for $C_{30}H_{31}NOS$ (453.65): C 79.43, H 6.89, N 3.09, S 7.07; found: C 79.31, H 6.94, N 3.03, S 6.97.

2.1.5. *(*RS*)-2-[4-(Benzyloxy)benzyl]-2,*N*-dimethyl-*N*-[(*R*)-1-(naphthalen-1-yl)ethyl]-2*H*-azirin-3-amine* (**2a**). To a soln. of **10a** (1.959 g, 4.32 mmol) and 4 drops of abs. DMF in abs. CH_2Cl_2 (10 ml) at 0°, 2N $COCl_2$ in toluene (2.6 ml, 5.2 mmol) was added, the mixture was stirred for 25 min at 0°, and the solvent was evaporated. The residue was dissolved in abs. THF (10 ml), DABCO (0.488 g, 4.35 mmol) was added, and the soln. was stirred for 15 min at 0°. Then, NaN_3 (0.569 g, 8.75 mmol) was added, the mixture was stirred for 20 min at 0° and 7 h at r.t., and then filtered over *Celite*, the filter cake was washed with Et_2O, and the filtrate was evaporated. CC (hexane/AcOEt 2:1, then 1:1) yielded 1.525 g (81%) of **2a**. The two diastereoisomers were separated by means of MPLC (AcOEt).

*Data of (1′*R*,2*S*)-***2a***: M.p. 68–69°. R_f (hexane/AcOEt 1:1) 0.25. IR (neat): 3033*m*, 2974*m*, 2937*m*, 1761v*s*, 1610*s*, 1583*m*, 1510v*s*, 1454*s*, 1419*m*, 1374*s*, 1298*m*, 1240v*s*, 1176*s*, 1107*m*, 1067*m*, 1026*s*, 954*w*, 915*w*, 862*w*, 839*m*, 805*s*, 782*s*, 738*s*, 697*s*, 621*w*. ^{1}H-NMR ((D$_6$)DMSO, 370 K): 8.05–8.0 (*m*, 1 arom. H); 7.95–7.9 (*m*, 1 arom. H); 7.87 (*d*, J = 7.8, 1 arom. H); 7.55–7.3 (*m*, 9 arom. H); 7.11 (*d*, J = 8.6, 2 arom. H); 6.92 (*d*, J = 8.6, 2 arom. H); 5.41 (*q*, J = 6.9, CHN); 5.09 (*s*, PhCH_2O); 2.84, 2.76 (*AB*, J = 14.5, CH_2C(2)); 2.61 (br. *s*, MeN); 1.54 (*d*, J = 6.9, *Me*CHN); 1.05 (br. *s*, MeC(2)). ^{13}C-NMR ((D$_6$)DMSO, 370 K): 164.8 (*s*, C(3)); 156.5 (*s*, 1 arom. CO); 137.0, 135.4, 133.1, 130.6, 130.5 (5*s*, 5 arom. C); 130.0, 128.1, 127.7, 127.7, 127.0, 126.8, 125.7, 125.1, 124.6, 123.5, 122.6, 114.2 (12*d*, 16 arom. CH); 69.2 (*t*, Ph*C*H$_2$O); 53.4 (*d*, CHN); 42.8 (*t*, *C*H$_2$–C(2)); 42.5 (*s*, C(2)); 32.3 (*q*, MeN); 22.7, 16.5 (2*q*, *Me*–C(2), *Me*CHN). ESI-MS (MeOH): 469 (9), 468 (38), 467 (100, $[M+MeOH]^+$), 436 (8), 435 (26, $[M+1]^+$), 281 (5, $[M-naphthCHCH_2+1]^+$), 155 (6, $[naphthCHMe]^+$). Anal. calc. for $C_{30}H_{30}N_2O$ (434.58): C 82.91, H 6.96, N 6.45; found: C 82.62, H 6.77, N 6.61.

*Data of (1′*R*,2*R*)-***2a***: R_f (hexane/AcOEt 1:1) 0.16. IR (neat): 3033*m*, 2972*s*, 2910*s*, 1758v*s*, 1610*s*, 1582*m*, 1510v*s*, 1453*s*, 1415*m*, 1373*s*, 1297*s*, 1240v*s*, 1175*s*, 1107*s*, 1064*s*, 1026*s*, 954*w*, 913*w*, 862*m*, 841*m*, 803*s*, 781*s*, 738*s*, 697*s*, 617*w*. ^{1}H-NMR ((D$_6$)DMSO, 380 K): 8.05–7.85 (*m*, 3 arom. H); 7.55–7.5 (*m*, 4 arom. H); 7.5–7.1 (*m*, 5 arom. H); 7.05–7.0 (*m*, 2 arom. H); 6.85–6.8 (*m*, 2 arom. H); 5.42 (*q*, J = 6.9, CHN); 5.05 (*s*, PhCH_2O); 2.70 (*s*, MeN); 2.6–2.55 (*m*, CH_2C(2)); 1.65 (*d*, J = 6.9, *Me*CHN); 1.19 (*s*, MeC(2)). ^{13}C-NMR ((D$_6$)DMSO, 380 K): 165.1 (*s*, C(3)); 156.4 (*s*, 1 arom. CO); 133.9, 135.7, 133.1, 130.5, 130.4 (5*s*, 5 arom. C); 129.7, 128.1, 127.7, 127.6, 127.0, 126.8, 125.6, 125.0, 124.6, 123.4, 122.5, 114.2 (12*d*, 16 arom. CH); 69.2 (*t*, Ph*C*H$_2$O); 53.8 (*d*, CHN); 43.0 (*t*, *C*H$_2$–C(2)); 42.5 (*s*, C(2)); 32.1 (*q*, MeN); 22.8, 16.9 (2*q*, *Me*–C(2), *Me*CHN). ESI-MS (MeOH): 468 (36), 467 (100, $[M+MeOH]^+$), 435 (54, $[M+1]^+$), 281 (19, $[M-naphthCHCH_2+1]^+$), 155 (37, $[naphthCHMe]^+$). Anal. calc. for $C_{30}H_{30}N_2O$ (434.58): C 82.91, H 6.96, N 6.45; found: C 82.67, H 6.93, N 6.35.

2.2. *Dopa(2Me) Synthon.* 2.2.1. *3,4-Bis(benzyloxy)benzenemethanol* (**7b**). A soln. of *3,4-bis(benzyloxy)-benzaldehyde* (**9**, 12.797 g, 40.195 mmol) in abs. THF (100 ml) was added dropwise to a suspension of $NaBH_4$ (1.56 g, 41.237 mmol) in abs. THF (200 ml). The mixture was stirred for 4.5 h at r.t., and then the reaction was quenched by dropwise addition of H_2O (40 ml). The resulting mixture was passed through a *Celite* pad. The filtrate was dried ($MgSO_4$) and evaporated: 13.169 g of crude **7b** (quant.) as a colorless solid. M.p. 73–73.5°. R_f (hexane/AcOEt 1:1) 0.30. IR: 3288*s*, 3063*m*, 3034*m*, 2918*m*, 2874*m*, 1605*w*, 1589*m*, 1515v*s*, 1467*w*, 1455*s*, 1424*m*, 1386*s*, 1292*w*, 1257v*s*, 1228*s*, 1164*m*, 1130v*s*, 1069*w*, 1047*w*, 1004v*s*, 942*w*, 914*w*, 860*w*, 809*m*. ^{1}H-NMR: 7.45–7.25 (*m*, 10 arom. H); 6.99 (*d*, $J = 1.8$, 1 arom. H); 6.9–6.8 (*m*, 2 arom. H); 5.15, 5.14 (2*s*, 2 CH_2); 4.56 (*s*, PhCH_2O); 1.57 (*s*, OH). ^{13}C-NMR: 149.1, 148.5 (2*s*, 2 arom. CO); 137.2, 137.2, 134.4 (3*s*, 3 arom. C); 128.4, 127.7, 127.2, 127.2, 120.1 (5*d*, 11 arom. CH); 115.2, 114.1 (2*d*, 2 arom. CH); 71.4, 71.2 (2*t*, 2 CH_2); 65.1 (*t*, CH_2OH). CI-MS (NH_3): 338 (15, $[M + NH_4]^+$), 304 (8), 303 (100, $[M - OH]^+$). Anal. calc. for $C_{21}H_{20}O_3$ (320.39): C 78.73, H 6.29; found: C 78.38, H 6.47.

2.2.2. *1,2-Bis(benzyloxy)-4-(bromomethyl)benzene* (**6b**). To a soln. of **7b** (12.022 g, 37.523 mmol) in abs. CH_2Cl_2 (200 ml) at 0° under Ar, PBr_3 (3.6 ml, 37.9 mmol) was added dropwise. After 30 min, the mixture was warmed to r.t. and stirred for 1 h. The soln. was poured on ice and extracted with Et_2O; the org. phase was dried ($MgSO_4$) and evaporated: 14.350 g (quant. yield) of **6b**. This compound was unstable and had to be quickly reacted further. R_f (hexane/AcOEt 2:1) 0.44. IR (neat): 2966*s*, 1955*w*, 1774*m*, 1724*w*, 1604*s*, 1514v*s*, 1454v*s*, 1383*s*, 1266v*s*, 1012v*s*, 909*s*, 807*s*, 732v*s*, 695v*s*, 653*s*, 606*s*. ^{1}H-NMR: 7.45–7.25 (*s*, 10 arom. H); 6.99 (*d*, $J = 1.9$, 1 arom. H); 6.9–6.85 (*m*, 2 arom. H); 5.15, 5.14 (2*s*, 2 CH_2O); 4.43 (*s*, CH_2Br). ^{13}C-NMR: 149.2, 149.0 (2*s*, 2 arom. CO); 137.0, 136.9, 130.8 (3*s*, 3 arom. C); 128.4, 127.8, 127.3, 127.1, 122.3 (5*d*, 11 arom. CH); 115.9, 114.7 (2*d*, 2 arom. CH); 71.3, 71.2 (2*t*, CH_2O); 34.0 (*t*, CH_2Br).

2.2.3. *(*RS*)-2-[3,4-Bis(benzyloxy)benzyl]-*N*-methyl-*N*-[(*R*)-1-(naphthalen-1-yl)ethyl]propanamide* (**5b**). As described for **5a**, with LDA (2N soln., 17.5 ml, 35.0 mmol), **4** [1] (7.005 g, 29.027 mmol), and abs. THF (30 ml); 30 min at 0°; with **6b** (11.121 g, 29.015 mmol), and abs. THF (30 ml); addition within 35 min, below 5°; 2 h at 0°; CC (hexane/AcOEt 5:1, then 4:1): 13.814 g (88%) of **5b**. Colorless oil. R_f (hexane/AcOEt 1:1) 0.49 and 0.42, resp., and R_f (hexane/AcOEt 2:1) 0.28 and 0.22, resp., for the diastereoisomers. IR (neat): 3034*s*, 2967*s*, 1952*w*, 1736*s*, 1630v*s*, 1509v*s*, 1261v*s*, 1135v*s*, 1024v*s*, 909*m*, 851*s*, 805v*s*, 735*s*, 697v*s*, 622*m*, 597*m*. ^{1}H-NMR: 7.95–7.75 (*m*, 3 arom. H); 7.5–7.2 (*m*, 14 arom. H); 6.85–6.55 (*m*, 3 arom. H, CHN); 5.2–5.0 (*m*, 2 PhCH_2O); 3.05–2.95, 2.85–2.75, 2.6–2.45 (3*m*, CH_2CH); 2.37, 2.12 (2*s*, MeN); 1.55, 1.38 (2*d*, $J = 6.8$, 1 Me); 1.15–1.1 (*m*, 1 Me). ^{13}C-NMR: 175.1, 174.9 (2*s*, CO); 148.7, 148.5, 147.4, 137.5, 137.4, 137.3, 136.0, 133.6, 133.6, 131.9 (10*s*, 8 arom. C); 128.4, 128.3, 127.6, 127.5, 127.3, 127.2, 126.6, 126.4, 125.8, 124.7, 124.0, 124.0, 122.0, 121.9, 116.3, 115.4, 115.1 (17*d*, 20 arom. CH); 71.4, 71.2 (2*t*, PhCH_2O); 47.8 (*d*, CHN); 40.0, 39.4 (2*t*, CH_2); 38.8, 38.5 (2*d*, CHCO); 28.9, 28.8 (2*q*, MeN); 17.9, 17.1, 15.6 (3*q*, 2 Me). ESI-MS (MeOH, CH_2Cl_2, NaI): 566 (100, $[M + Na]^+$), 544 (8, $[M + 1]^+$), 404 (17, $[M - N(Me)naphthEt + MeOH]^+$), 322 (22). Anal. calc. for $C_{37}H_{37}NO_3$ (543.71): C 81.74, H 6.86, N 2.58; found: C 81.97, H 6.87, N 2.53.

2.2.4. *(*RS*)-2-[3,4-Bis(benzyloxy)benzyl]-*N*-methyl-*N*-[(*R*)-1-(naphthalen-1-yl)ethyl]propanethioamide* (**10b**). As described for **10a**, with **5b** (12.742 g, 23.44 mmol), abs. toluene (30 ml), and *Lawesson* reagent (5.665 g, 1.2 equiv.); 5 h at 130°; 2 × CC (hexane/AcOEt 4:1): 11.149 g (85%) of **10b**. Colorless oil. R_f (hexane/AcOEt 2:1) 0.44 and 0.40, resp., for the diastereoisomers. IR (neat): 2927*s*, 1952*w*, 1822*w*, 1732*s*, 1600*s*, 1514v*s*, 1504v*s*, 1470*s*, 1455v*s*, 1404*s*, 1254*s*, 1136*s*, 910*m*, 846*m*, 773*s*, 738*s*, 696*s*, 611*m*. ^{1}H-NMR: 7.9–7.7 (*m*, 3 arom. H); 7.55–7.15 (*m*, 14 arom. H, CHN); 6.85–6.6 (*m*, 3 arom. H); 5.2–5.0 (*m*, 2 PhCH_2O); 3.25–3.05, 2.85–2.8 (2*m*, $CHCH_2$); 2.57, 2.20 (2*s*, MeN); 1.64, 1.43 (2*d*, $J = 6.8$, 6.7, 1 Me); 1.26, 1.18 (2*d*, $J = 6.0$, 6.3, 1 Me). ^{13}C-NMR: 208.1, 208.0 (2*s*, CS); 148.6, 148.4, 147.4 (3*s*, 2 arom. CO); 137.4, 135.6, 133.6, 133.5 (4*s*, 6 arom. C); 128.9, 128.9, 128.5, 128.3, 128.2, 127.7, 127.5, 127.3, 127.2, 127.1, 126.9, 126.7, 126.0, 125.2, 124.9, 124.4, 122.1, 116.4, 115.4, 114.9 (20*d*, 20 arom. CH); 71.4, 71.2 (2*t*, 2 PhCH_2O); 56.8, 56.6 (2*d*, CHN); 44.9, 44.7 (2*d*, CHCS); 43.7, 42.6 (2*t*, CH_2); 32.9 (*q*, MeN); 21.9, 20.8, 13.7 (3*q*, *Me*CHN, *Me*CHCS). CI-MS (NH_3): 561 (9), 560 (18, $[M + 1]^+$), 407 (30), 406 (100, $[M - naphthCHCH_2 + 1]^+$), 316 (36). Anal. calc. for $C_{37}H_{37}NO_2S$ (559.77): C 79.39, H 6.66, N 2.50, S 5.73; found: C 79.22, H 6.95, N 2.44, S 5.43.

2.2.5. *(*RS*)-2-[3,4-Bis(benzyloxy)benzyl]-2,*N*-dimethyl-*N*-[(*R*)-1-(naphthalen-1-yl)ethyl]-2*H*-azirin-3-amine* (**2b**). As described for **2a**, with **10b** (8.149 g, 14.56 mmol), 4 drops of abs. DMF, abs. CH_2Cl_2 (15 ml), and 2N $COCl_2$ in toluene (9 ml, 18 mmol); 15 min at 0°; evaporation; abs. THF (20 ml), and DABCO (1.634 g, 14.57 mmol); 20 min at 0°; NaN_3 (1.893 g, 29.123 mmol); 20 min at 0°; 26 h at r.t.; CC (hexane/AcOEt 2:1): 4.913 g (62%) of **2b**. The diastereoisomers were separated by means of CC and MPLC (AcOEt), and each was obtained as an oil.

*Data of (1′*R*,2*S*)-***2b***:* R_f (hexane/AcOEt 1:1) 0.29. IR (neat): 3034*m*, 2973*s*, 2912*s*, 1952*w*, 1760v*s*, 1588*s*, 1504v*s*, 1454v*s*, 1425*s*, 1373*s*, 1264v*s*, 1136v*s*, 1102*m*, 1067*s*, 1025*s*, 910*w*, 852*m*. ^{1}H-NMR ((D_6)DMSO, 373 K):

8.05–7.95, 7.95–7.9, 7.85–7.8 (3*m*, 3 arom. H); 7.55–7.25 (*m*, 14 arom. H); 6.94 (*d*, *J* = 8.3, 1 arom. H); 6.93 (*d*, *J* = 1.7, 1 arom. H); 6.71 (*dd*, *J* = 8.1, 2.1, 1 arom. H); 5.38 (*q*, *J* = 6.9, CHN); 5.08, 5.07 (2*s*, 2 PhC*H*$_2$O); 2.79, 2.73 (*AB*, *J* = 14.7, CH$_2$C(2)); 2.56 (br. *s*, MeN); 1.52 (*d*, *J* = 6.9, *Me*CHN); 1.01 (br. *s*, MeC(2)). ^{13}C-NMR ((D$_6$)DMSO, 373 K): 164.7 (*s*, C(3)); 148.0, 146.8, 137.2, 137.1, 135.4, 133.1, 131.7, 130.6 (8*s*, 8 arom. C); 128.1, 127.7, 127.6, 127.0, 126.8, 125.6, 125.1, 124.6, 123.5, 122.5, 122.2, 117.0, 115.1 (13*d*, 20 arom. CH); 70.7, 70.6 (2*t*, 2 PhCH$_2$O); 53.4 (*d*, CHN); 43.2 (*t*, *C*H$_2$–C(2)); 42.3 (*s*, C(2)); 32.3 (*q*, MeN); 22.7, 16.6 (2*q*, *Me*–C(2), *Me*CHN). ESI-MS (CH$_2$Cl$_2$, MeOH, NaI): 574 (28), 573 (68, [*M* + MeOH + 1]$^+$), 564 (14), 563 (34, [*M* + Na]$^+$), 542 (39), 541 (100, [*M* + 1]$^+$). Anal. calc. for C$_{37}$H$_{36}$N$_2$O$_2$ (540.71): C 82.19, H 6.71, N 5.18; found: C 82.05, H 6.66, N 4.94.

*Data of (1′*R*,2*R*)-***2b***: R_f (hexane/AcOEt 1:1) 0.20. IR (neat): 3034*m*, 2939*m*, 1952*w*, 1760v*s*, 1588*m*, 1513v*s*, 1454*s*, 1425*s*, 1374*s*, 1264v*s*, 1136*s*, 1066*s*, 1025*s*, 911*w*, 854*w*. ^{1}H-NMR ((D$_6$)DMSO, 373 K): 8.0–7.85 (*m*, 3 arom. H); 7.5–7.25 (*m*, 14 arom. H); 6.87 (*d*, *J* = 8.2, 1 arom. H); 6.82 (*d*, *J* = 1.6, 1 arom. H); 6.64 (*dd*, *J* = 8.1, 1.8, 1 arom. H); 5.40 (*q*, *J* = 6.8, CHN); 5.04, 4.91 (2*s*, 2 PhC*H*$_2$O); 2.97, 2.63, 2.53 (3 br., CH$_2$–C(2), MeN); 1.62 (*d*, *J* = 6.9, *Me*CHN); 1.17 (*s*, MeC(2)). ^{13}C-NMR ((D$_6$)DMSO, 373 K): 165.1 (*s*, C(3)); 148.0, 146.8, 137.1, 137.0, 135.6, 133.2, 131.8, 130.5 (8*s*, 8 arom. C); 128.2, 127.7, 127.6, 127.6, 127.0, 126.8, 125.7, 125.1, 124.6, 123.4, 122.5, 121.9, 116.7, 115.1 (14*d*, 20 arom. CH); 70.6, 70.5 (2*t*, 2 PhCH$_2$O); 53.7 (*d*, CHN); 43.7 (*t*, *C*H$_2$–C(2)); 42.5 (*s*, C(2)); 32.1 (*q*, MeN); 22.9, 16.9 (2*q*, *Me*–C(2), *Me*CHN). ESI-MS (CH$_2$Cl$_2$, MeOH, NaI): 573 (65, [*M* + MeOH + 1]$^+$), 541 (100, [*M* + 1]$^+$). Anal. calc. for C$_{37}$H$_{36}$N$_2$O$_2$ (540.71): C 82.19, H 6.71, N 5.18; found: C 82.17, H 6.55, N 5.38.

2.3. *Ser(2Me) Synthon.* 2.3.1. *(*RS*)-3-(Benzyloxy)-2,*N*-dimethyl*-N*-[(*R*)-1-(naphthalen-1-yl)ethyl]propanamide* (**5c**). As described for **5a**, with LDA (2N soln., 16 ml, 32.0 mmol), **4** [1] (6.302 g, 26.11 mmol), abs. THF (65 ml), and a 60% soln. of benzyl chlormethyl ether (6.1 ml, *ca.* 26 mmol); addition within 20 min, below 5°; 45 min at 0°; CC (hexane/AcOEt 4:1, then 2:1) yielded 8.696 g (92%) of **5c**. Colorless oil. R_f (hexane/AcOEt 2:1) 0.31 and 0.24, resp., for the diastereoisomers. IR (neat): 3421*w*, 3030*w*, 2974*s*, 2935*m*, 2862*m*, 1951*w*, 1818*w*, 1633v*s*, 1511*s*, 1454*s*, 1411*s*, 1372*m*, 1324*m*, 1296*m*, 1240*m*, 1209*m*, 1172*m*, 1103*s*, 1044*s*, 1027*s*, 910*w*, 805*s*, 782v*s*, 737*s*, 698*s*. ^{1}H-NMR: 8.05–7.95 (*m*, 1 arom. H); 7.85–7.75 (*m*, 2 arom. H); 7.5–7.1 (*m*, 9 arom. H); 6.65–6.6 (*m*, CHN); 4.6–4.4 (*m*, PhC*H*$_2$O); 3.9–3.75, 3.55–3.45, 3.05–2.95 (3*m*, CH$_2$CH); 2.51, 2.49 (2*s*, MeN); 1.59, 1.58 (2*d*, *J* = 6.8, 1 Me); 1.17, 1.08 (2*s*, *J* = 6.9, 1 Me). ^{13}C-NMR: 174.3, 174.0 (2*s*, CO); 141.0, 138.5, 136.2, 136.0, 133.7, 131.9 (6*s*, 4 arom. C); 128.5, 128.4, 128.3, 128.2, 128.1, 127.4, 127.3, 126.8, 126.5, 126.4, 125.8, 124.8, 124.7, 124.2, 124.0 (15*d*, 12 arom. CH); 73.4, 73.3 (2*t*, PhCH$_2$O); 65.1 (*t*, *C*H$_2$CH); 47.9 (*d*, CHN); 37.2 (*d*, *C*HCH$_2$); 29.1 (*q*, MeN); 15.6, 14.4, 14.2 (3*q*, 2 Me). CI-MS (NH$_3$): 363 (27), 362 (100, [*M* + 1]$^+$), 332 (10), 242 (8), 208 (17, [*M* – naphthCHCH$_2$ + 1]$^+$), 200 (7), 155 (6, [naphthCHMe]$^+$). Anal. calc. for C$_{24}$H$_{27}$NO$_2$ (361.48): C 79.74, H 7.53, N 3.87; found: C 79.77, H 7.82, N 3.80.

2.3.2. *(*RS*)-3-(Benzyloxy)-2,*N*-dimethyl*-N*-[(*R*)-1-(naphthalen-1-yl)ethyl]propanethioamide* (**10c**). As described for **10a**, with **5c** (8.407 g, 23.26 mmol), abs. toluene (25 ml), and *Lawesson* reagent (5.634 g, 1.2 equiv.); 6 h at 130°; CC (hexane/AcOEt 5:1) yielded 4.323 g (49%) of **10c**. Slightly yellow oil. R_f (hexane/AcOEt 2:1) 0.44. IR (neat): 2930*s*, 1594*s*, 1485v*s*, 1452v*s*, 1407*s*, 1370*m*, 1296*m*, 1258v*s*, 1178*m*, 1112v*s*, 984*s*, 805*s*, 782*s*, 739*m*, 698*s*, 620*w*. ^{1}H-NMR: 7.95–7.8, 7.6–7.15, 6.95–6.85 (3*m*, 12 arom. H, CHN); 4.6–4.4 (*m*, PhC*H*$_2$O); 4.0–3.8, 3.7–3.6, 3.35–3.2 (3*m*, CHCH$_2$); 2.72, 2.72 (2*s*, MeN); 1.69, 1.68 (2*d*, *J* = 6.8, 6.7, 1 Me); 1.26, 1.22 (2*d*, *J* = 6.6, 1 Me). ^{13}C-NMR: 206.6, 206.3 (2*s*, CS); 138.4, 135.6, 133.6, 132.0 (4*s*, 4 arom. C); 132.8, 128.9, 128.5, 128.3, 128.2, 127.5, 127.4, 126.8, 126.7, 126.1, 125.2, 124.9, 124.8, 124.6, 124.4, 114.0, 113.8 (17*d*, 12 arom. CH); 76.4, 75.8, 73.4 (3*t*, 2 CH$_2$O); 56.7, 56.6 (2*d*, CHN); 43.2, 43.2 (2*d*, *C*HCS); 33.3 (*q*, MeN); 18.1, 13.8 (3*q*, 2 Me). CI-MS (NH$_3$): 379 (14), 378 (49, [*M* + 1]$^+$), 348 (14), 225 (14), 224 (100, [*M* – naphthCHCH$_2$ + 1]$^+$), 194 (28, [*M* – naphthEtNMe + 1]$^+$). Anal. calc. for C$_{24}$H$_{27}$NOS (377.55): C 76.43, H 7.21, N 3.71, S 8.49; found: C 76.22, H 7.48, N 3.47, S 8.26.

2.3.3. *(*RS*)-2-(Azidomethyl)-2,*N*-dimethyl*-N*-[(*R*)-1-(naphthalen-1-yl)ethyl]-2*H*-azirin-3-amine* (**2c**). As described for **2a**, with **10c** (2.510 g, 6.65 mmol), 4 drops of abs. DMF, abs. CH$_2$Cl$_2$ (10 ml), and 2N COCl$_2$ in toluene (4.3 ml, 8.6 mmol); 15 min at 0°; 30 min at r.t.; evaporation; with abs. THF (10 ml), DABCO (0.768 g, 6.85 mmol); 40 min at 0°; NaN$_3$ (0.431 g, 6.63 mmol); 1 h at 0°, dilution with abs. THF (25 ml); 24 h at r.t.; CC (hexane/AcOEt 5:1): 0.498 g (26%) of the unexpected azirine **2c**. R_f (hexane/AcOEt 1:1) 0.28. IR (neat): 3410*w*, 3051*w*, 2976*m*, 2917*w*, 2098v*s*, 1767v*s*, 1619*w*, 1599*w*, 1510*w*, 1450*m*, 1420*w*, 1375*m*, 1318*w*, 1278*s*, 1193*m*, 1170*m*, 1103*m*, 1073*m*, 989*w*, 956*w*, 890*w*, 865*w*. ^{1}H-NMR (300 MHz, (D$_6$)DMSO, 370 K): 8.1–8.05 (*m*, 1 arom. H); 7.95–7.9 (*m*, 2 arom. H); 7.6–7.5 (*m*, 4 arom. H); 5.48 (*q*, *J* = 6.9, CHN); 3.38, 3.27 (*AB*, *J* = 13.2, CH$_2$N$_3$); 2.84 (*s*, MeN); 1.73 (*d*, *J* = 6.9, *Me*CHN); 0.93 (br. *s*, MeC(2)). ^{13}C-NMR (75.5 MHz, (D$_6$)DMSO, 350 K): 162.7 (*s*, C(3)); 135.2, 133.2, 130.6 (3*s*, 3 arom. C); 128.2, 127.9, 125.8, 125.2, 124.7, 123.6, 122.5 (7*d*, 7 arom. CH); 56.8 (*t*, CH$_2$N$_3$); *ca.* 54 (*d*, CHN); *ca.* 42 (*s*, C(2)); 32.7 (*q*, MeN); 20.2, 17.1 (2*q*, 2 Me). CI-MS (NH$_3$): 295 (20), 294

(100, $[M+1]^+$), 267 (9), 266 (46, $[M-N_2+1]^+$), 254 (14), 253 (9), 242 (7), 203 (13), 184 (27, [naphthEtNMe]$^+$), 170 (7), 142 (10), 140 (6, $[M-\text{naphthCHCH}_2+1]^+$), 125 (17), 112 (5), 97 (18). Anal. calc. for $C_{17}H_{19}N_5$ (293.37): C 69.69, H 6.53, N 23.87; found: C 69.49, H 6.64, N 23.76.

3. *Reactions of the Azirines* **2a**–**2c** *with PhCOSH and PhCOOH.* 3.1. *Reactions of (1′*R*,2*S*)-***2a***.* 3.1.1. N-*((*S*)-1-[4-(Benzyloxy)benzyl]-1-methyl-2-[methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino]-2-thioxoethyl)benzamide* ((1*S*,1′*R*)-**11a**). To PhCOSH (32 mg, 0.23 mmol), a soln. of (1′*R*,2*S*)-**2a** (100 mg, 0.23 mmol) in abs. CH_2Cl_2 (2 ml) was added, and the soln. was stirred for 18 h at r.t. Evaporation, CC (hexane/AcOEt 3:1), and prep. TLC (hexane/AcOEt 1:1) gave 84 mg (64%) of (1*S*,1′*R*)-**11a**. M.p. 94–95°. R_f (hexane/AcOEt 1:1) 0.47. IR: 3418*m*, 2925*s*, 1732*w*, 1656*m*, 1611*w*, 1580*w*, 1510v*s*, 1478v*s*, 1374*m*, 1241*m*, 1176*w*, 1104*w*, 1063*m*, 1044*w*, 1025*w*, 878*w*, 804*w*, 781*m*, 714*w*, 696*w*. ^{1}H-NMR: 9.25 (br. *s*, NH); 7.9–7.85, 7.8–7.75, 7.6–7.3 (3*m*, 17 arom. H, CHN); 7.00 (*d*, *J* = 8.6, 2 arom. H); 6.83 (*d*, *J* = 8.6, 2 arom. H); 5.01 (*s*, PhC*H*$_2$O); 4.10, 3.29 (*AB*, *J* = 14.6, CH_2(3) of Tyr(2Me)); 2.88 (*s*, MeN); 1.90 (*s*, Me(3) of Tyr(2Me)); 1.65 (*d*, *J* = 6.7, NCH*Me*). ^{13}C-NMR: 204.4 (*s*, CS); 164.8 (*s*, CO); 157.8 (*s*, 1 arom. CO); 137.0, 135.8, 135.2, 133.7, 132.1 (5*s*, 6 arom. C); 131.2, 131.1, 129.3, 128.7, 128.6, 127.9, 127.5, 127.2, 127.0, 126.3, 125.5, 125.1, 124.0, 114.5 (14*d*, 21 arom. CH); 70.0 (*t*, PhCH_2O); 64.9 (*s*, C(2) of Tyr(2Me)); 61.2 (*d*, CHN); 41.1 (*t*, C(3) of Tyr(2Me)); 36.8 (*q*, MeN); 24.4, 12.9 (2*q*, Me(3) of Tyr(2Me), NCH*Me*). ESI-MS (CH_2Cl_2, MeOH, NaI): 597 (10), 596 (34), 595 (100, $[M+\text{Na}]^+$), 579 (76). Anal. calc. for $C_{37}H_{36}N_2O_2S$ (572.77): C 77.59, H 6.34, N 4.89, S 5.60; found: C 77.65, H 6.59, N 4.52, S 5.44.

3.1.2. N-*((*S*)-1-[4-(Benzyloxy)benzyl]-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-oxoethyl)benzamide* ((1*S*,1′*R*)-**12a**). As described for (1*S*,1′*R*)-**11a**, with PhCOOH (28 mg, 0.23 mmol), (1′*R*,2*S*)-**2a** (100 mg, 0.23 mmol), and abs. CH_2Cl_2 (2 ml); 19 h at r.t.; prep. TLC (hexane/AcOEt 1:1): 49 mg (38%) of (1*S*,1′*R*)-**12a**. M.p. 192–193°. R_f (hexane/AcOEt 1:1) 0.37. IR: 3311*m*, 3049*w*, 2976*w*, 1654*s*, 1615v*s*, 1579*m*, 1511v*s*, 1479*m*, 1545*m*, 1393*m*, 1336*w*, 1302*m*, 1246*s*, 1179*m*, 1106*w*, 1068*m*, 1039*w*, 1026*w*, 882*w*, 838*w*, 802*m*, 779*m*, 726*m*, 696*m*, 658*w*, 648*w*, 613*w*. ^{1}H-NMR: 7.95 (br. *s*, NH); 7.85–7.7, 7.55–7.25 (2*m*, 17 arom. H); 7.05 (*d*, *J* = 8.6, 2 arom. H); 6.86 (*d*, *J* = 8.7, 2 arom. H); 6.56 (*q*, *J* = 6.8, CHN); 5.01 (*s*, PhC*H*$_2$O); 3.92, 3.19 (*AB*, *J* = 14.5, CH_2(3) of Tyr(2Me)); 2.65 (*s*, MeN); 1.80 (*s*, Me(3) of Tyr(2Me)); 1.57 (*d*, *J* = 6.8, NCH*Me*). ^{13}C-NMR: 171.8, 165.7 (2*s*, 2 CO); 157.9 (*s*, 1 arom. CO); 137.0, 135.5, 135.4, 133.7, 131.9 (5*s*, 6 arom. C); 131.3, 130.9, 128.9, 128.7, 128.6, 127.9, 127.5, 126.9, 126.1, 125.3, 124.9, 123.6, 114.7 (13*d*, 21 arom. CH); 70.0 (*t*, PhCH_2O); 62.0 (*s*, C(2) of Tyr(2Me)); 51.0 (*d*, CHN); 39.5 (*t*, C(3) of Tyr(2Me)); 30.8 (*q*, MeN); 22.4, 14.8 (2*q*, NCH*Me*, Me(3) of Tyr(2Me)). ESI-MS (CH_2Cl_2, MeOH): 595 (11, $[M+\text{K}]^+$), 579 (19, $[M+\text{Na}]^+$), 403 (36, $[M-\text{naphthCHCH}_2+1]^+$), 372 (100, $[M-\text{naphthEt(Me)N}]^+$), 344 (66, $[M-\text{naphthEt(Me)NCO}]^+$), 155 (7, [naphthCHMe]$^+$). Anal. calc. for $C_{37}H_{36}N_2O_3\cdot 0.33\ H_2O$ (562.71): C 78.97, H 6.57, N 4.98; found: C 78.94, H 6.49, N 4.92.

3.2. *Reactions of (1′*R*,2*R*)-***2a***.* 3.2.1. N-*((*R*)-1-[4-(Benzyloxy)benzyl]-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-thioxoethyl)benzamide* ((1*R*,1′*R*)-**11a**). As described for (1*S*,1′*R*)-**11a**, with PhCOSH (33 mg, 0.24 mmol), (1′*R*,2*R*)-**2a** (100 mg, 0.23 mmol), and abs. CH_2Cl_2 (2 ml); 2.5 h at r.t.; prep. TLC (hexane/AcOEt 1:1): 119 mg (90%) of (1*R*,1′*R*)-**11a**. Crystals suitable for an X-ray crystal-structure determination were obtained from Et_2O/CH_2Cl_2/hexane. The configuration at C(2) of Tyr(2Me) is (*R*). M.p. 147–148°. R_f (hexane/AcOEt 1:1) 0.44. IR: 3412*m*, 3051*w*, 2933*m*, 1659*s*, 1607*w*, 1579*w*, 1509v*s*, 1480*s*, 1453*m*, 1384*m*, 1366*m*, 1322*w*, 1296*m*, 1234v*s*, 1179*m*, 1109*w*, 1065*m*, 1026*w*, 1008*w*, 921*w*, 865*w*, 840*w*, 807*w*, 782*s*, 718*w*, 696*w*, 652*w*, 610*w*. ^{1}H-NMR: 8.0–7.65, 7.6–7.3 (2*m*, NH, 17 arom. H, CHN); 6.94 (*d*, *J* = 8.6, 2 arom. H); 6.73 (*d*, *J* = 8.7, 2 arom. H); 4.98 (*s*, PhC*H*$_2$O); 3.95, 3.53 (*AB*, *J* = 14.3, CH_2(3) of Tyr(2Me); 2.90 (*s*, MeN); 1.82 (*s*, Me(3) of Tyr(2Me)); 1.82 (*d*, *J* = 6.7, NCH*Me*). ^{13}C-NMR: 204.4 (*s*, CS); 165.1 (*s*, CO); 157.7 (*s*, 1 arom. CO); 137.0, 135.4, 134.9, 133.7, 132.2 (5*s*, 6 arom. C); 131.5, 131.4, 129.3, 129.1, 128.6, 128.0, 127.5, 127.2, 126.9, 126.2, 125.9, 125.0, 124.8, 114.6 (14*d*, 21 arom. CH); 70.0 (*t*, PhCH_2O); 64.5 (*s*, C(2) of Tyr(2Me)); 60.4 (*d*, CHN); 43.3 (*t*, C(3) of Tyr(2Me)); 36.1 (*q*, MeN); 25.3, 13.5 (2*q*, Me(3) of Tyr(2Me), NCH*Me*). ESI-MS (MeOH, $CHCl_3$): 861 (12, [2 ($M-\text{naphthCHCH}_2+1$) + Na]$^+$), 575 (18), 574 (41), 573 (100, $[M+1]^+$), 420 (15), 419 (47, $[M-\text{naphthCHCH}_2+1]^+$). Anal. calc. for $C_{37}H_{36}N_2O_2S$ (572.77): C 77.59, H 6.34, N 4.89, S 5.60; found: C 77.45, H 6.21, N 4.77, S 5.38.

3.2.2. N-*((*R*)-1-[4-(Benzyloxy)benzyl]-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-oxoethyl)benzamide* ((1*R*,1′*R*)-**12a**). As described for (1*S*,1′*R*)-**11a**, with PhCOOH (28 mg, 0.23 mmol), (1′*R*,2*R*)-**2a** (100 mg, 0.31 mmol), and abs. CH_2Cl_2 (2 ml); 23 h at r.t.; prep. TLC (hexane/AcOEt 1:1): 86 mg (67%) of (1*R*,1′*R*)-**12a**. R_f (hexane/AcOEt 1:1) 0.34. M.p. 163–164°. IR: 3416*w*, 3361*m*, 3054*w*, 2977*w*, 1655*s*, 1619v*s*, 1580*m*, 1533*s*, 1510v*s*, 1480*s*, 1454*s*, 1392*s*, 1301*m*, 1240*s*, 1177*m*, 1107*w*, 1073*m*, 1043*w*, 1026*m*, 922*w*, 867*w*, 838*w*, 806*m*, 781*s*, 719*m*, 696*m*, 672*w*, 648*w*, 612*w*. ^{1}H-NMR: 8.05–8.0, 7.85–7.8, 7.7–7.65, 7.55–7.3 (4*m*, 17 arom. H); 6.93 (*d*, *J* = 8.6, 2 arom. H); 6.80 (*s*, NH); 6.8–6.75 (*m*, CHN); 6.73 (*d*, *J* = 8.7, 2 arom. H); 4.97 (*s*,

PhCH_2O); 3.60, 3.54 (*AB*, $J = 14.3$, CH_2(3) of Tyr(2Me)); 2.67 (*s*, MeN); 1.66 (*d*, $J = 6.8$, NCH*Me*); 1.60 (*s*, Me(3) of Tyr(2Me)). ^{13}C-NMR: 171.7, 166.1 (2*s*, 2 CO); 137.1, 135.9, 134.8, 133.8, 132.1 (5*s*, 6 arom. C); 131.7, 131.5, 129.3, 128.6, 128.6, 128.0, 127.4, 126.9, 126.7, 125.9, 125.5, 124.8, 124.3, 114.6 (14*d*, 21 arom. CH); 70.0 (*t*, PhCH$_2$O); 60.8 (*s*, C(2) of Tyr(2Me)); 50.4 (*d*, CHN); 40.2 (*t*, C(3) of Tyr(2Me)); 30.1 (*q*, MeN); 22.4, 15.3 (2*q*, NCH*Me*, Me(3) of Tyr(2Me)). ESI-MS (CH_2Cl_2, MeOH): 595 (6, $[M+K]^+$), 579 (8, $[M+Na]^+$), 403 (30, $[M-$naphthCHCH$_2+1]^+$), 372 (100, $[M-$naphthEt(Me)N$]^+$), 344 (69, $[M-$naphthEt(Me)NCO$]^+$), 155 (6, [naphthCHMe]$^+$). Anal. calc. for $C_{37}H_{36}N_2O_3 \cdot 0.5\ H_2O$ (565.71): C 78.56, H 6.59, N 4.95; found: C 78.37, H 6.59, N 4.72.

3.3. *Reactions of (1′*R*,2*S*)*-**2b**. 3.3.1. N-*((*S*)-1-[3,4-Bis(benzyloxy)benzyl]-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-thioxoethyl)benzamide* ((1*S*,1′*R*)-**11b**). As described for (1*S*,1′*R*)-**11a**, with PhCOSH (36 mg, 0.26 mmol), (1′*R*,2*S*)-**2b** (142 mg, 0.26 mmol), and abs. CH_2Cl_2 (2 ml); 3 h at r.t.; prep. TLC (hexane/AcOEt 3:2): 158 mg (89%) of (1*S*,1′*R*)-**11b**. Colorless foam. M.p. 85–87°. R_f (hexane/AcOEt 1:1) 0.46. IR: 3418*m*, 3195*w*, 3060*w*, 2934*w*, 1656*m*, 1601*w*, 1579*w*, 1510v*s*, 1478v*s*, 1374*s*, 1332*w*, 1267*s*, 1220*m*, 1161*w*, 1138*m*, 1063*m*, 1044*w*, 1021*m*, 877*w* ^{1}H-NMR: 9.32 (br. *s*, NH); 7.9–7.85, 7.75–7.7, 7.55–7.25 (3*m*, 22 arom. H, CHN); 6.8–6.75 (*m*, 2 arom. H); 6.6–6.55 (*m*, 1 arom. H); 5.10 (*s*, PhCH_2O); 4.88, 4.85 (*AB*, $J = 12.0$, PhCH_2O); 4.08, 3.27 (*AB*, $J = 14.3$, CH_2(3) of Dopa(2Me)); 2.80 (*s*, MeN); 1.86 (*s*, Me(3) of Dopa(2Me)); 1.58 (*d*, $J = 6.7$, NCH*Me*). ^{13}C-NMR: 204.2 (*s*, CS); 164.5 (*s*, CO); 148.6, 147.8 (2*s*, 2 arom. CO); 137.3, 137.2, 135.5, 135.0, 133.6, 129.8 (6*s*, 7 arom. C); 131.2, 129.2, 128.6, 128.5, 128.3, 127.6, 127.2, 127.2, 126.9, 126.2, 125.4, 124.9, 123.9, 122.8, 117.1, 114.9 (16*d*, 25 arom. CH); 71.3, 71.0 (2*t*, 2 PhCH$_2$O); 64.7 (*s*, C(2) of Dopa(2Me)); 61.1 (*d*, CHN); 41.5 (*t*, C(3) of Dopa(2Me)); 36.6 (*q*, MeN); 24.2, 12.8 (2*q*, Me(3) of Dopa(2Me), NCH*Me*). ESI-MS (MeOH, NaI): 702 (55), 701 (100, $[M+Na]^+$), 423 (7). Anal. calc. for $C_{44}H_{42}N_2O_3S \cdot 0.2\ H_2O$ (682.49): C 77.43, H 6.26, N 4.10, S 4.70; found: C 77.45, H 6.37, N 4.06, S 4.75.

3.3.2. N-*((*S*)-1-[3,4-Bis(benzyloxy)benzyl]-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-oxoethyl)benzamide* ((1*S*,1′*R*)-**12b**). As described for (1*S*,1′*R*)-**11a**, with PhCOOH (68 mg, 0.56 mmol), (1′*R*,2*S*)-**2b** (300 mg, 0.56 mmol), and abs. CH_2Cl_2 (4 ml); 14 d at r.t.; CC (hexane/AcOEt 2:1) and prep. TLC (hexane/AcOEt 1:1): 335 mg (91%) of (1*S*,1′*R*)-**12b**. Colorless solid. Crystals suitable for an X-ray crystal-structure determination were obtained from AcOEt/MeOH/hexane. The configuration at C(2) in Dopa(2Me) is (*S*). R_f (hexane/AcOEt 1:1) 0.38. M.p. 180–181°. IR: 3310*m*, 3049*w*, 2940*w*, 1656*s*, 1610v*s*, 1535*m*, 1509*s*, 1480*m*, 1454*m*, 1423*w*, 1397*m*, 1265*s*, 1230*w*, 1157*w*, 1138*w*, 1071*m*, 1026*w*, 883*w*. ^{1}H-NMR: 7.93 (br. *s*, NH); 7.85–7.8 (*m*, 3 arom. H); 7.75 (*d*, $J = 7.0$, 1 arom. H); 7.5–7.25 (*m*, 18 arom. H); 6.83 (*d*, $J = 8.2$, 1 arom. H); 6.77 (*d*, $J = 1.9$, 1 arom. H); 6.65 (*dd*, $J = 8.2$, 2.0, 1 arom. H); 6.53 (*q*, $J = 6.7$, CHN); 5.10 (*s*, PhCH_2O); 4.89, 4.80 (*AB*, $J = 11.9$, PhCH_2O); 3.87, 3.18 (*AB*, $J = 14.6$, CH_2(3) of Dopa(2Me)); 2.60 (*s*, MeN); 1.77 (*s*, Me(3) of Dopa(2Me)); 1.53 (*d*, $J = 6.8$, NCH*Me*). ^{13}C-NMR: 171.7, 165.4 (*s*, 2 CO (amide)); 148.8, 148.0 (2*s*, 2 arom. CO); 137.3, 137.1, 135.3, 133.6, 131.8, 130.0 (6*s*, 7 arom. C); 131.3, 128.7, 128.5, 128.3, 128.3, 127.6, 127.2, 126.8, 126.0, 125.2, 124.8, 123.5, 122.5, 117.1, 115.0 (15*d*, 25 arom. CH); 71.4, 71.0 (2*t*, 2 PhCH$_2$O); 61.8 (*s*, C(2) of Dopa(2Me)); 50.9 (*d*, CHN); 39.7 (*t*, C(3) of Dopa(2Me)); 30.6 (*q*, MeN); 22.4, 14.7 (2*q*, Me(3) of Dopa(2Me), NCH*Me*). ESI-MS (MeOH, NaI): 685 (100, $[M+Na]^+$). Anal. calc. for $C_{44}H_{42}N_2O_4$ (662.83): C 79.73, H 6.39, N 4.23; found: C 79.61, H 6.38, N 4.22.

3.4. *Reactions of (1′*R*,2*R*)*-**2b**. 3.4.1. N-*((*R*)-1-[3,4-Bis(benzyloxy)benzyl]-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-thioxoethyl)benzamide* ((1*R*,1′*R*)-**11b**). As described for (1*S*,1′*R*)-**11a**, with PhCOSH (36 mg, 0.26 mmol), (1′*R*,2*R*)-**2b** (143 mg, 0.26 mmol), and abs. CH_2Cl_2 (2 ml); 20 h at r.t.; prep. TLC (hexane/AcOEt 1:1): 156 mg (88%) of (1*R*,1′*R*)-**11b**. Crystals suitable for an X-ray crystal-structure determination were obtained from Et_2O/hexane. The configuration at C(2) in Dopa(2Me) ist (*R*). R_f (hexane/AcOEt 1:1) 0.42. M.p. 83–86°. IR: 3424*m*, 2933*w*, 1656*w*, 1510v*s*, 1479*m*, 1384*w*, 1267*m*, 1138*w*, 1065*w*, 1024*w*. ^{1}H-NMR: 7.95–7.9, 7.85–7.8, 7.7–7.65, 7.6–7.55, 7.5–7.2 (5*m*, 22 arom. H, CHN, NH); 6.71 (*d*, $J = 1.7$, 1 arom. H); 6.66 (*d*, $J = 8.2$, 1 arom. H); 6.48 (*dd*, $J = 8.2$, 1.9, 1 arom. H); 5.06 (*s*, PhCH_2O); 4.73, 4.70 (*AB*, $J = 12.0$, PhCH_2O); 3.92, 3.53 (*AB*, $J = 14.4$, CH_2(3) of Dopa(2Me)); 2.86 (*s*, MeN); 1.73 (*s*, Me(3) of Dopa(2Me)); 1.72 (*d*, $J = 6.8$, NCH*Me*). ^{13}C-NMR: 204.2 (*s*, CS); 164.8 (*s*, CO); 148.5, 147.7 (2*s*, 2 arom. CO); 137.3, 137.0, 135.4, 133.6, 130.4 (5*s*, 7 arom. C); 131.5, 129.0, 128.6, 128.3, 128.2, 127.6, 127.6, 127.2, 127.0, 126.8, 126.1, 125.7, 124.9, 124.6, 123.2, 117.3, 114.9 (17*d*, 22 arom. CH); 71.3, 70.7 (2*t*, 2 PhCH$_2$O); 64.2 (*s*, C(2) of Dopa(2Me)); 60.3 (*d*, CHN); 43.9 (*t*, C(3) of Dopa(2Me)); 35.8 (*q*, MeN); 25.0, 13.4 (2*q*, Me(3) of Dopa(2Me), NCH*Me*). HPLC-ESI-MS: 1379 (9, $[2M+Na]^+$), 1003 (26), 903 (8), 827 (11), 701 (100, $[M+Na]^+$), 509 (40, $[M-$naphthCHCH$_2+1]^+$). Anal. calc. for $C_{44}H_{42}N_2O_3S \cdot 0.25\ H_2O$ (683.39): C 77.33, H 6.27, N 4.12, S 4.69; found: C 77.29, H 6.80, N 4.25, S 4.84.

3.4.2. N-*((*R*)-1-[3,4-Bis(benzyloxy)benzyl]-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-oxoethyl)benzamide* ((1*R*,1′*R*)-**12b**). As described for (1*S*,1′*R*)-**11a**, with PhCOOH (68 mg, 0.56 mmol),

(1′*R*,2*R*)-**2b** (300 mg, 0.56 mmol), and abs. CH_2Cl_2 (4 ml); 13 d at r.t.; CC (hexane/AcOEt 2:1): 330 mg (90%) of (1*R*,1′*R*)-**12b**. Colorless solid. Crystals suitable for an X-ray crystal-structure determination were obtained from AcOEt. The configuration at C(2) in Dopa(2Me) is (*R*). M.p. 103–104°. R_f (hexane/AcOEt 1:1) 0.36. M.p. 87–89°. IR: 3340*m*, 3052*w*, 2980*m*, 2938*m*, 1657*s*, 1611v*s*, 1536*s*, 1512v*s*, 1482*s*, 1454*s*, 1424*m*, 1376*s*, 1333*m*, 1266v*s*, 1232*s*, 1166*m*, 1138*s*, 1069*s*, 1039*m*, 1027*m*, 908*w*, 847*w*. ^{1}H-NMR: 8.1–8.0, 7.85–7.7, 7.55–7.2 (3*m*, 22 arom. H); 6.76 (*q*, *J* = 6.7, CHN); 6.7–6.65 (*m*, 2 arom. H); 6.48 (*dd*, *J* = 8.2, 2.0, 1 arom. H); 5.06 (*s*, PhC*H*$_2$O); 4.72, 4.68 (*AB*, *J* = 12.0, PhC*H*$_2$O); 3.53 (*s*, CH_2(3) of Dopa(2Me)); 2.64 (*s*, MeN); 1.66 (*d*, *J* = 6.8, NCH*Me*); 1.51 (*s*, Me(3) of Dopa(2Me)). ^{13}C-NMR: 171.5, 165.8 (*s*, 2 CO (amide)); 148.5, 147.6 (2*s*, 2 arom. CO); 137.3, 137.0, 135.9, 134.3, 133.7, 130.4 (6*s*, 7 arom. C); 131.6, 128.6, 128.5, 128.3, 128.2, 127.6, 127.2, 126.8, 126.5, 125.8, 125.3, 124.7, 124.1, 123.3, 117.4, 115.0 (16*d*, 25 arom. CH); 71.3, 70.7 (2*t*, 2 PhC*H*$_2$O); 60.4 (*s*, C(2) of Dopa(2Me)); 50.3 (*d*, CHN); 40.5 (*t*, C(3) of Dopa(2Me)); 29.9 (*q*, MeN); 22.2, 14.1 (2*q*, Me(3) of Dopa(2Me), NCH*Me*). ESI-MS (MeOH, NaI): 685 (87, $[M+Na]^+$), 509 (48, $[M-$naphthCHCH$_2+1]^+$), 478 (100, $[M-$naphthEt(Me)N$]^+$), 450 (59, $[M-$naphthEt(Me)NCO$]^+$), 203 (32), 181 (35), 155 (23, [naphthCHMe]$^+$). Anal. calc. for $C_{44}H_{42}N_2O_4 \cdot 1.5\ H_2O$ (689.86): C 76.60, H 6.57, N 4.06; found: C 76.88, H 6.62, N 4.60.

3.5. *Reactions of* **2c**. 3.5.1. N-*((*(R)*-1-(Azidomethyl)-1-methyl-2-{methyl[(*R)*-1-(naphthalen-1-yl)ethyl]-amino}-2-thioxoethyl)benzamide* (**11c**). As described for (1*S*,1′*R*)-**11a**, with PhCOSH (38 mg, 0.28 mmol), **2c** (80 mg, 0.27 mmol), and abs. CH_2Cl_2 (2 ml); 4.5 h at r.t.; prep. TLC (hexane/AcOEt 2:1): 110 mg (97%) of **11c**. Colorless foam. R_f (hexane/AcOEt 2:1) 0.24. M.p. 64–66°. IR: 3416*w*, 3051*w*, 2934*w*, 2100v*s*, 1665*w*, 1600*w*, 1580*w*, 1511*m*, 1480*s*, 1390*s*, 1282*w*, 1242*w*, 1172*w*, 1105*w*, 1066*w*, 1045*w*, 1025*w*. ^{1}H-NMR: 7.85–7.8, 7.65–7.3 (2*m*, 12 arom. H, CHN, NH); 4.48, 4.36 (*AB*, *J* = 18.4, CH_2); 2.77 (*s*, MeN); 1.77 (*d*, *J* = 6.7, NCH*Me*); 1.75 (*s*, Me(3)). ^{13}C-NMR: 202.2 (*s*, CS); 165.4 (*s*, CO); 134.9, 134.1, 133.6 (3*s*, 4 arom. C); 131.5, 129.2, 128.5, 127.3, 126.7, 126.2, 125.4, 124.9, 124.3 (9*d*, 12 arom. CH); 64.6 (*s*, C(2)); 60.4 (*d*, CHN); 57.3 (*t*, CH_2); 35.8 (*q*, MeN); 22.4, 13.0 (2*q*, NCH*Me*, Me(3)). ESI-MS (MeOH, NaI): 489 (7), 454 (40, $[M+Na]^+$), 404 (45, $[M-N_2+1]^+$), 309 (9, $[M-N_3+1]^+$), 384 (10), 372 (11), 250 (15, $[M-N_2-$naphthCHCH$_2+1]^+$), 187 (8), 155 (100, [naphthCHMe]$^+$).

4. *Synthesis of Model Peptides*. 4.1. *Dipeptides with (*S*)-Tyr(2Me)*. 4.1.1. *[(*9H*-Fluoren-9-yl)methyl]* N-*((*S*)-1-{[((*S*)-1-[4-(Benzyloxy)benzyl]-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-oxoethyl)amino]-carbonyl}-2-methylpropyl)carbamate* (*Fmoc-Val-(*S*)-Tyr(2Me)(OBn)-NMe(naphthEt)*, (*S*,*S*,*R*)-**13a**). To Fmoc-Val-OH (236 mg, 0.695 mmol), a soln. of (1′*R*,2*S*)-**2a** (302 mg, 0.695 mmol) in abs. CH_2Cl_2 (6 ml) was added, and the mixture was stirred for 20 h at r.t. Evaporation, CC (hexane/AcOEt 3:2), and prep. TLC (hexane/AcOEt 1:1) yielded 282 mg (52%) of (*S*,*S*,*R*)-**13a**. Colorless foam. M.p. 98–99°. R_f (hexane/AcOEt 1:1) 0.33. IR: 3334*w*, 3040*w*, 2962*m*, 1724*s*, 1676*s*, 1615*s*, 1511v*s*, 1451*s*, 1391*m*, 1330*w*, 1240*s*, 1178*w*, 1107*w*, 1071*w*, 1027*w*, 805*w*, 782*m*, 759*w*, 741*m*, 697*w*. ^{1}H-NMR: 7.85–7.8, 7.75–7.7, 7.6–7.2 (3*m*, 20 arom. H, NH of Tyr(2Me)); 6.95 (*d*, *J* = 8.6, 2 arom. H); 6.78 (*d*, *J* = 8.6, 2 arom. H); 6.54 (*q*, *J* = 6.7, CHN); 5.28 (*d*, *J* = 8.0, NH of Val); 4.90 (br., PhC*H*$_2$O); 4.45–4.3 (*m*, CH_2O of Fmoc); 4.22 (*t*, *J* = 6.9, CH of Fmoc); 4.02 (br., CH(2) of Val); 3.68, 3.01 (*AB*, *J* = 15.0, CH_2(3) of Tyr(2Me)); 2.56 (*s*, MeN); 2.2–2.15 (*m*, CH(3) of Val); 1.66 (*s*, Me(3) of Tyr(2Me)); 1.52 (*d*, *J* = 6.6, *Me*CHN); 0.97, 0.90 (2*d*, *J* = 6.5, 6.7, 2 Me(4) of Val). ^{13}C-NMR: 171.2, 169.3 (2*s*, 2 CO (amide)); 157.8 (*s*, CO (urethane)); 143.7, 141.2, 136.9, 135.4, 133.7, 131.8, 128.2 (7*s*, 10 arom. C); 130.6, 128.7, 128.6, 128.4, 127.8, 127.6, 127.3, 127.0, 126.5, 125.9, 125.2, 124.9, 124.8, 123.5, 119.9, 114.7 (16*d*, 24 arom. CH); 69.8, 66.8 (2*t*, 2 CH_2O); 61.7 (*s*, C(2) of Tyr(2Me)); 60.6 (*d*, C(2) of Val); 50.8, 47.2 (2*d*, CH of Fmoc, CHN); 39.8 (*t*, C(3) of Tyr(2Me)); 31.0 (*d*, C(3) of Val); 30.5 (*q*, MeN); 22.3, 19.1, 17.5, 14.6 (4*q*, CHN*Me*, Me(3) of Tyr(2Me), 2 Me(4) of Val). ESI-MS (CH_2Cl_2, MeOH, NaI): 796 (100, $[M+Na]^+$). Anal. calc. for $C_{50}H_{51}N_3O_5 \cdot H_2O$ (791.99): C 75.83, H 6.75, N 5.31; found: C 76.10, H 6.90, N 5.37.

4.1.2. *(*S*)-2-{[(*S*)-2-Amino-3-methyl-1-oxobutyl]amino}-2-[4-(benzyloxy)benzyl]-*N*-methyl-*N*-[(*R*)-1-(naphthalen-1-yl)ethyl]propanamide* (*H-Val-(*S*)-Tyr(2Me)(OBn)-NMe(naphthEt)*, (*S*,*S*,*R*)-**14a**). To (*S*,*S*,*R*)-**13a** (52 mg, 0.067 mmol), Et_2NH (1 ml) was added, and the soln. was stirred for 1 h and evaporated. Prep. TLC (hexane/AcOEt 1:1) gave 37 mg (quant. yield) of (*S*,*S*,*R*)-**14a**. M. p. 69–70°. R_f (AcOEt) 0.17. IR: 3324*w*, 2960*m*, 1674*m*, 1614*s*, 1511v*s*, 1386*m*, 1331*w*, 1301*w*, 1240*m*, 1177*w*, 1107*w*, 1068*w*, 806*w*, 782*m*, 738*w*, 696*w*. ^{1}H-NMR ($CDCl_3$): 8.1–7.85 (*m*, 3 arom. H); 7.6–7.3 (*m*, 9 arom. H); 7.1–6.7 (*m*, 4 arom. H); 6.55 (*q*, *J* = 6.6, CHN); 5.03 (*m*, PhC*H*$_2$O); 3.81 (*d*, *J* = 3.8, CH(2) of Val); 3.40, 3.10 (*AB*, *J* = 14.2, CH_2(3) of Tyr(2Me); 2.60 (*s*, MeN); 2.3–2.2 (*m*, CH(3) of Val); 1.59 (*s*, Me(3) of Tyr(2Me); 1.52 (*d*, *J* = 6.7, CHN*Me*); 1.12, 1.10 (2*d*, *J* = 7.5, 6.1, 2 Me(4) of Val). ^{13}C-NMR: 172.4, 171.7 (2*s*, 2 CO (amide)); 157.7 (*s*, 1 arom. C); 136.9, 135.7, 133.6, 131.9 (4*s*, 5 arom. C); 131.1, 128.5, 128.2, 127.8, 127.3, 126.6, 125.9, 125.1, 124.7, 124.1, 114.6 (11*d*, 16 arom. CH); 69.9 (*t*, PhC*H*$_2$O); 60.6 (*d*, C(2) of Val); 60.3 (*s*, C(2) of Tyr(2Me)); 50.4 (*d*, CHN); 40.6 (*t*, C(3) of Tyr(2Me)); 30.4 (*d*, C(3) of Val); 23.0, 19.5, 15.9, 14.6 (4*q*, MeN, CHN*Me*, Me(3) of Tyr(2Me), 2 Me(4) of Val). ESI-MS (MeOH,

NaI): 600 (19), 574 (25, $[M+Na]^+$), 552 (100, $[M+1]^+$), 398 (39, $[M-naphthCHCH_2+1]^+$), 155 (7, $[naphthCHMe]^+$). Anal. calc. for $C_{35}H_{41}N_3O_3 \cdot 0.5\ H_2O$ (560.74): C 74.97, H 7.55, N 7.49; found: C 75.04, H 7.38, N 7.19.

4.1.3. *[(9*H*-Fluoren-9-yl)methyl]* N-*((*S*)-1-[[((*S*)-1-(4-Hydroxybenzyl)-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-oxoethyl)amino]carbonyl}-2-methylpropyl)carbamate* (*Fmoc-Val-(*S*)-Tyr(2Me)-NMe(naphthEt),* (*S,S,R*)-**15a**). A soln. of (*S,S,R*)-**13a** (38 mg, 0.049 mmol) and 5 mg Pd/C (10% on activated charcoal) in MeOH (1 ml) was treated with H_2 for 2 d at r.t. The mixture was filtered over *Celite*, and the filtrate was evaporated. Prep. TLC (hexane/AcOEt 1:1) gave 16 mg (47%) of (*S,S,R*)-**15a**. M.p. 111–112°. R_f (hexane/AcOEt 1:1) 0.25. IR: 3391*s*, 2963*m*, 1725*m*, 1666*s*, 1614*s*, 1514v*s*, 1450*s*, 1392*m*, 1240*m*, 1106*m*, 1071*w*, 1043*w*, 805*w*, 782*m*, 760*w*, 742*m*. ^{1}H-NMR: 7.85–7.7, 7.55–7.2 (2*m*, 15 arom. H, NH); 6.89 (*d*, *J* = 8.4, 2 arom. H); 6.65 (*d*, *J* = 9.0, 2 arom. H); 6.52 (*q*, *J* = 6.7, CHN); 5.38 (*d*, *J* = 7.5, NH of Val); 4.4–4.15 (*m*, $CHCH_2$ of Fmoc); 4.05–3.95 (*m*, CH(2) of Val); 3.64, 3.00 (*AB*, *J* = 14.6, CH_2(3) of Tyr(2Me)); 2.56 (*s*, MeN); 2.2–2.15 (*m*, CH(3) of Val); 1.64 (*s*, Me(3) of Tyr(2Me)); 1.51 (*d*, *J* = 6.6, *Me*CHN); 0.96, 0.89 (2*d*, *J* = 6.1, 6.7, 2 Me(4) of Val). ^{13}C-NMR: 171.3 (*s*, 2 CO (amide)); 155.1 (*s*, CO (urethane)); 143.7, 141.2, 135.2, 133.6, 127.5 (5*s*, 9 arom. C); 130.7, 128.7, 128.6, 127.6, 127.0, 126.6, 125.9, 125.2, 125.0, 124.8, 123.4, 119.9, 115.3 (13*d*, 19 arom. CH); 67.0 (*t*, CH_2O of Fmoc); 61.7 (*s*, C(2) of Tyr(2Me)); 60.6 (*d*, C(2) of Val); 50.8, 47.1 (2*d*, CH of Fmoc, CHN); *ca.* 40 (*t*, C(3) of Tyr(2Me)); 30.8 (*q*, MeN); 30.5 (*d*, C(3) of Val); 22.2, 19.2, 17.5, 14.6 (4*q*, CHN*Me*, Me(3) of Tyr(2Me), 2 Me(4) of Val). ESI-MS (MeOH, NaI): 706 (100, $[M+Na]^+$), 530 (18, $[M-naphthCHCH_2+1]^+$), 485 (30, $[M-BnOC_6H_4CH_2-1]^+$), 413 (36, $[M-Fmoc\text{-}Val-Bn]^+$), 397 (6, $[M-BnOC_6H_4CH_2-Fmoc]^+$). Anal. calc. for $C_{43}H_{45}N_3O_5$ (683.85): C 75.52, H 6.63, N 6.14; found: C 75.14, H 7.14, N 6.03.

4.1.4. *(*S*)-2-[4-(Benzyloxy)benzyl]-2-{[(*S*)-2-({[(9*H*-fluoren-9-yl)methoxy]carbonyl}amino)-3-methyl-1-oxobutyl]amino}-2-methylpropanoic Acid* (*Fmoc-Val-(*S*)-Tyr(2Me)(OBn)-OH,* (*S,S*)-**16a**). A soln. of (*S,S,R*)-**13a** (118 mg, 0.152 mmol) in 3N HCl ($MeCN/H_2O$ 2:1, 4.5 ml) was stirred for 105 min at 60°. The mixture was extracted with CH_2Cl_2, dried ($MgSO_4$), and evaporated. Prep. TLC (CH_2Cl_2/MeOH 20:1) gave 25 mg (27%) of (*S,S*)-**16a** and 64 mg (68%) of *[(9*H*-fluoren-9-yl)methyl]* N-*{(*S*)-1-[({(*S*)-1-[4-(benzyloxy)-benzyl]-1-methyl-2-(methylamino)-2-oxoethyl}amino)carbonyl]-2-methylpropyl}carbamate* (*Fmoc-Val-(*S*)-Tyr(2Me)-NHMe,* (*S,S*)-**17a**).

*Data of (*S,S*)*-**16a**: M.p. 72–73°. R_f (CH_2Cl_2/MeOH 20:1) 0.15. IR: 3417v*s*, 2928*s*, 1714*s*, 1682*s*, 1652*s*, 1634*m*, 1614*m*, 1538*m*, 1513v*s*, 1454*m*, 1372*w*, 1243*m*, 1119*w*, 1027*w*, 759*w*, 740*w*, 696*w*. ^{1}H-NMR: 7.71 (*d*, *J* = 7.4, 2 arom. H); 7.6–7.55, 7.4–7.2 (2*m*, 11 arom. H); 7.00 (*d*, *J* = 8.6, 2 arom. H); 6.75–6.7 (*m*, 2 arom. H, NH of Tyr(2Me)); 5.86 (*d*, *J* = 9.2, NH of Val); 4.75 (*s*, PhCH_2O); 4.4–4.2 (*m*, $CHCH_2$ of Fmoc); 4.0–3.95 (*m*, CH(2) of Val); 3.43, 3.16 (*AB*, *J* = 13.7, CH_2(3) of Tyr(2Me)); 2.15–2.0 (*m*, CH(3) of Val); 1.67 (*s*, Me(3) of Tyr(2Me)); 0.93 (br., 2 Me(4) of Val). ^{13}C-NMR: 176.6, 171.2 (2*s*, COOH, CO (amide)); 157.8, 156.5 (2*s*, CO (urethane), 1 arom. CO); 143.7, 141.2, 136.8, 127.9 (4*s*, 6 arom. C); 130.8, 128.3, 127.7, 127.3, 127.0, 125.0, 119.9, 114.6 (8*d*, 17 arom. CH); 69.7, 67.2 (2*t*, PhCH_2O, CH_2O of Fmoc); 61.3 (*s*, C(2) of Tyr(2Me)); 60.7 (*d*, C(2) of Val); 47.1 (*d*, CH of Fmoc); 40.6 (*t*, C(3) of Tyr(2Me)); 31.0 (*d*, C(3) of Val); 22.7, 19.0, 17.9 (3*q*, Me(3) of Tyr(2Me), 2 Me(4) of Val). ESI-MS (MeOH, NaI): 629 (100, $[M+Na]^+$), 552 (36), 404 (11). Anal. calc. for $C_{37}H_{38}N_2O_6 \cdot H_2O$ (624.74): C 71.14, H 6.45, N 4.48; found: C 71.51 H 6.46, N 4.20.

*Data of (*S,S*)*-**17a**: M.p. 81–82°. R_f (CH_2Cl_2/MeOH 10:1) 0.49. IR: 3366*m*, 2963*w*, 1706*s*, 1655*s*, 1545v*s*, 1511v*s*, 1451*w*, 1348*s*, 1242*m*, 1176*w*, 1079*w*, 1027*w*, 924*w*, 842*w*, 760*w*, 732*w*, 698*w*. ^{1}H-NMR: 8.0–7.7, 7.6–7.25 (2*m*, 13 arom. H); 6.95 (*d*, *J* = 8.5, 2 arom. H); 6.76 (*d*, *J* = 8.4, 2 arom. H); 6.69 (*s*, NH); 6.50 (br. *s*, NH); 5.30 (*d*, *J* = 6.4, NH of Val); 4.87 (*s*, PhCH_2O); 4.45–4.15 (*m*, $CHCH_2$ of Fmoc); 3.9-3.8 (*m*, CH(2) of Val); 3.17, 3.08 (*AB*, *J* = 13.6, CH_2(3) of Tyr(2Me)); 2.74 (*s*, MeN); 2.15–2.05 (*m*, CH(3) of Val); 1.63 (*s*, Me(3) of Tyr(2Me)); 0.93, 0.89 (2*d*, *J* = 6.8, 2 Me(4) of Val). ^{13}C-NMR: 173.7, 170.7 (2*s*, 2 CO (amide)); 157.9 (*s*, CO (urethane)); 143.6, 143.5, 141.2, 136.7 (4*s*, 7 arom. C); 130.9, 128.4, 127.8, 127.7, 127.3, 127.0, 125.0, 124.8, 119.9, 114.7 (10*d*, 17 arom. CH); 69.8, 67.0 (2*t*, PhCH_2O, CH_2O of Fmoc); 61.3 (*d*, C(2) of Val); 60.8 (*s*, C(2) of Tyr(2Me)); 47.1 (*d*, CH of Fmoc); 42.8 (*t*, C(3) of Tyr(2Me)); 30.3 (*d*, C(3) of Val); 26.6, 22.8, 19.1, 17.6 (4*q*, MeN, Me(3) of Tyr(2Me), 2 Me(4) of Val). ESI-MS (MeOH, NaI): 642 (100, $[M+Na]^+$), 236 (18, $[M-H-C(^iPr)-CO-Tyr(2Me)(OBn)-NH_2Me]^+$). Anal. calc. for $C_{38}H_{41}N_3O_5$ (619.76): C 73.64, H 6.67, N 6.78; found: C 73.41 H 6.86, N 6.56.

4.2. *Dipeptides with (*R*)-Tyr(2Me).* 4.2.1. *[(9*H*-Fluoren-9-yl)methyl]* N-*((*S*)-1-{[((*R*)-1-[4-(Benzyloxy)-benzyl]-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-oxoethyl)amino]carbonyl}-2-methylpropyl)carbamate* (*Fmoc-Val-(*R*)-Tyr(2Me)(OBn)-NMe(naphthEt),* (*S,R,R*)-**13a**). As described for (*S,S,R*)-**13a**, with Fmoc-Val-OH (195 mg, 0.575 mmol), (1′*R*,2*R*)-**2a** (250 mg, 0.575 mmol), and abs. CH_2Cl_2 (7 ml); 66 h at r.t.; prep. TLC (hexane/AcOEt 1:1): 310 mg (70%) of (*S,R,R*)-**13a**. Colorless foam. M.p. 111–113°. R_f (hexane/AcOEt 1:1) 0.39. IR: 3336*w*, 3038*w*, 2962*m*, 1724*m*, 1686*s*, 1613*s*, 1511v*s*, 1451*s*, 1390*m*, 1328*m*, 1299*m*, 1240*s*,

1177*m*, 1106*w*, 1068*m*, 1027*m*, 839*w*, 805*w*, 781*m*, 740*s*, 696*w*. ^{1}H-NMR: 8.0–7.95, 7.8–7.7, 7.55–7.25 (3*m*, 22 arom. H); 6.94 (*d*, *J* = 8.3, 2 arom. H); 6.75–6.6 (*m*, 2 arom. H, CHN, NH of Tyr(2Me)); 5.26 (*d*, *J* = 8.6, NH of Val); 4.95–4.85 (*m*, PhC*H*$_2$O); 4.35–4.15 (*m*, CH$_2$CH of Fmoc); 3.95 (br., CH(2) of Val); 3.45–3.3 (*m*, CH$_2$(3) of Tyr(2Me)); 2.57 (br. *s*, MeN); 2.1–2.05 (*m*, CH(3) of Val); 1.61 (*d*, *J* = 6.7, *Me*CHN); 1.53 (*s*, Me(3) of Tyr(2Me)); 0.91, 0.85 (2*d*, *J* = 6.3, 6.4, 2 Me(4) of Val). ^{13}C-NMR: 171.1, 169.7 (2*s*, 2 CO (amide)); 157.6, 156.2 (2*s*, CO (urethane), 1 arom. CO); 143.8, 143.6, 141.2, 136.9, 135.5, 133.6, 131.9 (7*s*, 9 arom. C); 131.3, 128.6, 128.4, 127.8, 127.6, 127.3, 127.0, 126.6, 125.9, 125.2, 125.0, 124.7, 124.2, 119.9, 114.6 (15*d*, 24 arom. CH); 69.8, 67.0 (2*t*, 2 CH$_2$O); 60.6 (*s*, C(2) of Tyr(2Me)); 60.1 (*d*, C(2) of Val); 50.4, 47.1 (2*d*, CH of Fmoc, CHN); 40.6 (*t*, C(3) of Tyr(2Me)); 30.6 (*d*, C(3) of Val); 30.3 (*q*, MeN); 22.4, 19.5, 17.2, 15.2 (4*q*, CHN*Me*, Me(3) of Tyr(2Me), 2 Me(4) of Val). ESI-MS (CH$_2$Cl$_2$, MeOH, NaI): 797 (94, [*M* + Na]$^+$), 413 (100, [*M* – Fmoc-Val – Bn]$^+$). Anal. calc. for $C_{50}H_{51}N_3O_5$ (773.97): C 77.59, H 6.64, N 5.43; found: C 77.40, H 6.72, N 5.29.

4.2.2. *(*R*)-2-[[(*S*)-2-Amino-3-methyl-1-oxobutyl]amino]-2-[4-(benzyloxy)benzyl]*-N-*methyl*-N-*[(*R*)-1-(naphthalen-1-yl)ethyl]propanamide* (*H-Val-(*R*)-Tyr(2Me)(OBn)-NMe(naphthEt)*, (*S*,*R*,*R*)-**14a**). As described for (*S*,*S*,*R*)-**14a**, with (*S*,*R*,*R*)-**13a** (100 mg, 0.129 mmol), and Et$_2$NH (2 ml); 2 h at r.t.; prep. TLC (AcOEt/MeOH 20:1): 67 mg (94%) of (*S*,*R*,*R*)-**14a**. M.p. 88–89°. R_f (AcOEt) 0.13. IR: 3291*m*, 3041*w*, 2960*w*, 1737*w*, 1670*s*, 1612v*s*, 1511v*s*, 1454*m*, 1391*m*, 1301*w*, 1240*s*, 1178*w*, 1105*w*, 1070*m*, 1042*w*, 1026*w*, 843*w*, 805*w*, 782*m*, 741*w*, 697*w*, 648*w*, 612*w*. ^{1}H-NMR: 8.05–8.0, 7.9–7.8, 7.5–7.3 (3*m*, 12 arom. H, NH); 6.98 (*d*, *J* = 8.6, 2 arom. H); 6.81 (*d*, *J* = 8.6, 2 arom. H); 6.70 (*q*, *J* = 6.6, CHN); 5.01 (*s*, PhC*H*$_2$O); 3.51, 3.33 (*AB*, *J* = 14.2, CH$_2$(3) of Tyr(2Me)); 3.45–3.25 (*m*, CH(2) of Val); 2.59 (br. *s*, MeN); 2.35–2.3 (*m*, CH(3) of Val); 1.62 (*d*, *J* = 6.8, *Me*CHN); 1.55 (*s*, Me(3) of Tyr(2Me)); 0.92, 0.75 (2*d*, *J* = 7.0, 6.8, 2 Me(4) of Val). ^{13}C-NMR: 172.4, 171.7 (2*s*, 2 CO (amide)); 157.5 (*s*, CO (urethane)); 137.0, 135.8, 133.6, 132.0, 129.3 (5*s*, 6 arom. C); 131.4, 128.5, 128.3, 127.8, 127.3, 126.6, 125.8, 125.2, 124.7, 124.3, 114.4 (11*d*, 16 arom. CH); 69.9 (*t*, PhC*H*$_2$O); 60.3 (*s*, C(2) of Tyr(2Me)); 60.2 (*d*, C(2) of Val); 50.2 (*d*, CHN); 40.8 (*t*, C(3) of Tyr(2Me)); 30.0, 30.0 (*d*, *q*, C(3) of Val, MeN); 22.6, 19.6, 15.9, 15.1 (4*q*, CHN*Me*, Me(3) of Tyr(2Me), 2 Me(4) of Val). ESI-MS (CHCl$_3$, MeOH): 552 (100, [*M* + 1]$^+$), 398 (1, [*M* – naphthCHCH$_2$ + 1]$^+$). Anal. calc. for $C_{35}H_{41}N_3O_3 \cdot 0.3\ H_2O$ (557.74): C 75.37, H 7.53, N 7.53; found: C 75.25, H 7.66, N 7.24.

4.2.3. *[(9*H*-Fluoren-9-yl)methyl]* N-*((*S*)-1-{[((*R*)-1-(4-Hydroxybenzyl)-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-oxoethyl)amino]carbonyl}-2-methylpropyl)carbamate* (*Fmoc-Val-(*R*)-Tyr(2Me)-NMe(naphthEt)*, (*S*,*R*,*R*)-**15a**). As described for (*S*,*S*,*R*)-**15a**, with (*S*,*R*,*R*)-**13a** (81 mg, 0.105 mmol), Pd/C (10% on activated charcoal, 25 mg), MeOH (2 ml), and H$_2$; 40 h at r.t.: 51 mg (71%) of (*S*,*R*,*R*)-**15a**. M.p. 131–132°. R_f (hexane/AcOEt 1:1) 0.24. IR (neat): 3301*s*, 2964*s*, 1678v*s*, 1514v*s*, 1392*s*, 1331*s*, 1225v*s*, 1173*m*, 1105*s*, 1071*s*, 1041*m*, 834*w*, 804*m*, 782*s*, 760*s*, 741*s*, 650*w*. ^{1}H-NMR: 7.96, 7.8–7.7, 7.5–7.2 (*d*, *J* = 7.8, 2*m*, 15 arom. H); 6.85 (*d*, *J* = 7.9, 2 arom. H); 6.65-6.55 (*m*, 2 arom. H, CHN, NH of Tyr(2Me)); 5.34 (*d*, *J* = 9.1, NH of Val); 4.25–4.1 (*m*, CH$_2$CH of Fmoc); 3.9–3.85 (*m*, CH(2) of Val); 3.35, 3.27 (*AB*, *J* = 14.1, CH$_2$(3) of Tyr(2Me)); 2.54 (br. *s*, MeN); 2.05–2.0 (*m*, CH(3) of Val); 1.60 (*d*, *J* = 6.4, *Me*CHN); 1.45 (*s*, Me(3) of Tyr(2Me)); 0.9–0.85 (*m*, 2 Me(4) of Val). ^{13}C-NMR: 171.1, 169.8 (2*s*, 2 CO (amide)); *ca.* 156, 154.9 (2*s*, CO (urethane), 1 arom. CO); *ca.* 144, 143.4, 141.1, *ca.* 136, 133.6, *ca.* 122 (6*s*, 8 arom. C); 131.5, 128.5, 128.3, 127.6, 127.0, 126.6, 125.9, 125.2, 125.0, 124.7, *ca.* 124, 119.9, 115.2 (13*d*, 19 arom. CH); 67.0 (*t*, CH$_2$O of Fmoc); 60.3 (*s*, C(2) of Tyr(2Me)); 60.1 (*d*, C(2) of Val); 50.5, 46.9 (2*d*, CH of Fmoc, CHN); 40.9 (*t*, C(3) of Tyr(2Me)); 30.6 (*d*, C(3) of Val); 30.3 (*q*, MeN); 22.3, 19.4, 17.3, 15.1 (4*q*, CHN*Me*, Me(3) of Tyr(2Me), 2 Me(4) of Val). ESI-MS (MeOH, CH$_2$Cl$_2$): 722 (12, [*M* + K]$^+$), 708 (12), 707 (55), 706 (100, [*M* + Na]$^+$). Anal. calc. for $C_{43}H_{45}N_3O_5 \cdot 0.5\ H_2O$ (692.86): C 74.54, H 6.69, N 6.06; found: C 74.55, H 6.61, N 5.89.

4.2.4. *(*R*)-2-[4-(Benzyloxy)benzyl]-2-{[(*S*)-2-(([(9*H*-fluoren-9-yl)methoxy]carbonyl}amino)-3-methyl-1-oxobutyl]amino}-2-methylpropanoic Acid* (*Fmoc-Val-(*R*)-Tyr(2Me)(OBn)-OH*, (*S*,*R*)-**16a**). As described for (*S*,*S*)-**16a**, with (*S*,*R*,*R*)-**13a** (121 mg, 0.156 mmol), and 3N HCl (MeCN/H$_2$O 1:1, 5 ml); 3 h at 60°: 48 mg (51%) of (*S*,*R*)-**16a**, 24 mg (19%) of (*S*,*R*,*R*)-**13a**, and 29 mg (30%) of (*S*,*R*)-**17a**.

*Data of (*S,R*)-***16a***: M.p. 98–99°. R_f (CH$_2$Cl$_2$/MeOH 20:1) 0.16. IR: 3409*m*, 2930*w*, 1718*s*, 1511v*s*, 1451*m*, 1390*w*, 1242*s*, 1178*w*, 1119*w*, 1027*w*, 759*w*, 741*m*, 696*w*. ^{1}H-NMR: 7.73 (*d*, *J* = 7.5, 2 arom. H); 7.6–7.55, 7.4–7.25 (2*m*, 11 arom. H); 7.02 (*d*, *J* = 8.5, 2 arom. H); 6.79 (*d*, *J* = 8.6, 2 arom. H); 6.70 (*s*, NH of Tyr(2Me)); 5.89 (*d*, *J* = 9.4, NH of Val); 4.88 (*s*, PhC*H*$_2$O); 4.45–4.1 (*m*, CHCH$_2$ of Fmoc, CH(2) of Val); 3.35–3.2 (*m*, CH$_2$(3) of Tyr(2Me)); 2.05–1.95 (*m*, CH(3) of Val); 1.58 (*s*, Me(3) of Tyr(2Me)); 0.9–0.85 (*m*, 2 Me(4) of Val). ^{13}C-NMR: 176.6, 175.9 (2*s*, COOH, CO (amide)); 157.8, 156.7 (2*s*, CO (urethane), 1 arom. CO); 143.7, 141.2, 136.8, 127.9 (4*s*, 6 arom. C); 131.0, 128.4, 127.8, 127.7, 127.3, 127.0, 125.0, 119.9, 114.6 (9*d*, 17 arom. CH); 69.8, 67.3 (2*t*, PhC*H*$_2$O, CH$_2$O of Fmoc); 60.8 (*s*, C(2) of Tyr(2Me)); 60.2 (*d*, C(2) of Val); 47.0 (*d*, CH of Fmoc); 40.3 (*t*, C(3) of Tyr(2Me)); 30.9 (*d*, C(3) of Val); 23.1, 19.2, 17.5 (3*q*, Me(3) of Tyr(2Me), 2 Me(4) of Val). ESI-MS (MeOH,

NaI): 629 (100, $[M+Na]^+$). Anal. calc. for $C_{37}H_{38}N_2O_6 \cdot H_2O$ (624.74): C 71.14, H 6.45, N 4.48; found: C 71.45 H 6.48, N 4.39.

4.3. *Dipeptides with (*S*)-Dopa(2Me).* 4.3.1. *[(9*H*-Fluoren-9-yl)methyl]* N-*((*S*)-1-[[((*S*)-1-[3,4-Bis(benzyloxy)benzyl]-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-oxoethyl)amino]carbonyl}-2-methylpropyl)carbamate* (*Fmoc-Val-(*S*)-Dopa(2Me)(OBn)$_2$-NMe(naphthEt),* (*S,S,R*)-**13b**). As described for (*S,S,R*)-**13a**, with Fmoc-Val-OH (253 mg, 0.745 mmol) in abs. CH_2Cl_2 (5 ml), (1′*R*,2*S*)-**2b** (400 mg, 0.740 mmol), and abs. CH_2Cl_2 (10 ml); 137 h at r.t.: 363 mg (56%) of (*S,S,R*)-**13b**. Colorless foam. M.p. 89–90°. R_f (hexane/AcOEt 1:1) 0.42. IR: 3334*m*, 3036*w*, 2962*m*, 1724*m*, 1676*m*, 1618*s*, 1509v*s*, 1452*s*, 1375*w*, 1332*w*, 1269*m*, 1222*m*, 1138*w*, 1026*w*, 848*w*, 805*w*, 782*w*, 759*w*, 740*m*, 697*w*. ^{1}H-NMR: 7.85–7.8, 7.75–7.7, 7.5–7.15, 6.75–6.7, 6.5–6.45 (5*m*, 28 arom. H, NH, CHN); 5.21 (*d*, *J* = 6.7, NH of Val); 5.07, 5.02 (2*s*, 2 PhC*H*$_2$O); 4.45–4.35, 4.35–4.2, 4.2–4.1, 4.05–3.95 (4*m*, CH_2CH of Fmoc, CH(2) of Val); 3.65, 2.59 (*AB*, *J* = 14.7, CH_2(3) of Dopa(2Me)); 2.45 (*s*, MeN); 2.2–2.15 (*m*, CH(3) of Val); 1.56 (*s*, Me(3) of Dopa(2Me)); 1.43 (*d*, *J* = 6.7, *Me*CHN); 0.95, 0.87 (2*d*, *J* = 6.5, 6.7, 2 Me(4) of Val). ^{13}C-NMR: 171.2, 169.2 (2*s*, 2 CO (amide)); 156.1 (*s*, CO (urethane)); 148.7, 148.1, 143.7, 141.2, 137.3, 137.2, 135.4, 133.7, 131.8, 129.4 (10*s*, 12 arom. C); 128.7, 128.6, 128.3, 127.6, 127.4, 127.2, 127.0, 126.5, 125.9, 125.2, 124.9, 124.8, 123.5, 122.4, 119.9, 117.1, 115.0 (17*d*, 28 arom. CH); 71.3, 71.1 (2*t*, 2 PhC*H*$_2$O); 66.7 (*t*, CH_2O of Fmoc); 61.4 (*s*, C(2) of Dopa(2Me)); 60.6 (*d*, C(2) of Val); 50.7, 47.2 (2*d*, CH of Fmoc, CHN); 40.4 (*t*, C(3) of Dopa(2Me)); 31.0 (*d*, C(3) of Val); 30.4 (*q*, MeN); 22.3, 19.1, 17.5, 14.6 (4*q*, CHN*Me*, Me(3) of Dopa(2Me), 2 Me(4) of Val). ESI-MS (MeOH, NaI): 902 (100, $[M+Na]^+$), 613 (14). Anal. calc. for $C_{57}H_{57}N_3O_6$ (880.10): C 77.80, H 6.53, N 4.77; found: C 77.91, H 6.56, N 4.68.

4.3.2. *(*S*)-2-[[(*S*)-2-Amino-3-methyl-1-oxobutyl]amino}-2-[3,4-bis(benzyloxy)benzyl]-*N*-methyl-*N*-[(*R*)-1-(naphthalen-1-yl)ethyl]propanamide* (*H-Val-(*S*)-Dopa(2Me)(OBn)$_2$-NMe(naphthEt),* (*S,S,R*)-**14b**). As described for (*S,S,R*)-**14a**, with (*S,S,R*)-**13b** (74 mg, 0.084 mmol), and Et_2NH (2 ml); 1 h at r.t.: 48 mg (87%) of (*S,S,R*)-**14b**. M. p. 65–66°. R_f (AcOEt) 0.23. IR: 3396*w*, 2960*m*, 1674*s*, 1620v*s*, 1511v*s*, 1454*s*, 1385*m*, 1332*w*, 1269*s*, 1139*w*, 1069*m*, 1025*w*, 805*w*, 782*m*, 737*w*, 697*w*. ^{1}H-NMR: 8.17 (br. *s*, NH); 8.0–7.9, 7.8–7.75, 7.55–7.25, 6.8–6.75, 6.65–6.5 (5*m*, 20 arom. H, 2 NH, CHN); 5.15–5.05 (*m*, 2 PhC*H*$_2$O); 4.05–4.0 (*m*, CH(2) of Val); 3.65–2.85 (*m*, CH_2(3) of Dopa(2Me)); 2.45–2.4 (*m*, MeN); 2.3–2.25 (*m*, CH(3) of Val); 1.55 (*s*, Me(3) of Dopa(2Me)); 1.55–1.4 (*m*, *Me*CHN); 0.95–0.75 (*m*, 2 Me(4) of Val). ^{13}C-NMR: 171.5, 170.6 (2*s*, 2 CO (amide)); 148.5, 148.0, 137.3, 137.2, 135.6, 133.6, 131.9, 129.3 (8*s*, 8 arom. C); 128.5, 128.3, 127.7, 127.4, 127.2, 126.6, 125.9, 125.1, 124.7, 124.0, 123.2, 117.6, 114.9 (13*d*, 20 arom. CH); 71.4, 71.1 (2*t*, 2 PhCH_2O); 61.0 (*s*, C(2) of Dopa(2Me)); 59.8 (*d*, C(2) of Val); 50.4 (*d*, CHN); 41.2 (*t*, C(3) of Dopa(2Me)); 30.4 (*d*, C(3) of Val); 30.1 (*q*, MeN); 23.0, 19.4, 19.1, 16.5, 14.7 (5*q*, CHN*Me*, Me(3) of Dopa(2Me), 2 Me(4) of Val). ESI-MS (MeCN, NaI): 680 (25, $[M+Na]^+$), 658 (100, $[M+1]^+$), 504 (24, $[M-$naphthCHCH$_2+1]^+$), 473 (7, $[M-$naphthEtNMe$+1]^+$). Anal. calc. for $C_{42}H_{47}N_3O_4 \cdot 0.5\ H_2O$ (666.86): C 75.64, H 7.26, N 6.30; found: C 75.32, H 7.11, N 5.96.

4.3.3. *[(9*H*-Fluoren-9-yl)methyl]* N-*((*S*)-1-[[((*S*)-1-[3,4-Bis(hydroxy)benzyl]-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-oxoethyl)amino]carbonyl}-2-methylpropyl)carbamate* (*Fmoc-Val-(*S*)-Dopa-(2Me)-NMe(naphthEt),* (*S,S,R*)-**15b**). As described for (*S,S,R*)-**15a**, with (*S,S,R*)-**13b** (100 mg, 0.114 mmol), Pd/C (10% on activated charcoal, 5 mg), MeOH (2 ml), and H_2; 22 h at r.t.: 48 mg (60%) of (*S,S,R*)-**15b**. M.p. 127–128°. R_f (hexane/AcOEt 1:1) 0.14. IR: 3332*s*, 3050*w*, 2964*m*, 1678*s*, 1614*s*, 1511v*s*, 1450*s*, 1398*m*, 1375*m*, 1334*m*, 1285*s*, 1240*s*, 1110*m*, 1072*m*, 1043*w*, 867*w*, 805*w*, 782*m*, 760*w*, 741*m*. ^{1}H-NMR: 8.0–7.7, 7.6–7.2 (2*m*, 15 arom. H, NH); 6.67 (*d*, *J* = 8.0, 1 arom. H); 6.55–6.5 (*m*, 2 arom. H, CHN); 6.31 (*d*, *J* = 7.9, 1 arom. H); 5.71 (*d*, *J* = 9.8, NH of Val); 4.45–4.4, 4.35–4.3, 4.2–4.15, 4.05–4.0 (4*m*, $CHCH_2$ of Fmoc, CH(2) of Val); 3.7–3.65, 3.0–2.9 (2*m*, CH_2(3) of Dopa(2Me)); 2.65 (*s*, MeN); 2.15–2.1 (*m*, CH(3) of Val); 1.68 (*s*, Me(3) of Dopa(2Me)); 1.62 (*d*, *J* = 6.7, *Me*CHN); 1.04, 0.98 (2*d*, *J* = 6.6, 6.7, 2 Me(4) of Val). ^{13}C-NMR: 171.3, 169.9 (2*s*, 2 CO (amide)); 157.4 (*s*, CO (urethane)); 143.8, 143.7, 143.3, 141.2, 135.1, 133.7, 131.7, 127.5 (8*s*, 10 arom. C); 128.8, 128.7, 127.7, 127.0, 126.6, 126.0, 125.3, 125.0, 123.2, 121.3, 119.9, 117.1, 114.5 (13*d*, 18 arom. CH); 67.5 (*t*, CH_2 of Fmoc); 62.7 (*s*, C(2) of Dopa(2Me)); 61.4 (*d*, C(2) of Val); 51.1, 47.0 (2*d*, CH of Fmoc, CHN); 38.6 (*t*, C(3) of Dopa(2Me)); 30.9 (*d*, C(3) of Val); 30.8 (*q*, MeN); 21.5, 19.3, 17.9, 14.6 (4*q*, CHN*Me*, Me(3) of Tyr(2Me), 2 Me(4) of Val). ESI-MS (CH_2Cl_2, MeOH, NaI): 722 (100, $[M+Na]^+$). Anal. calc. for $C_{43}H_{45}N_3O_6 \cdot H_2O$ (717.87): C 71.95, H 6.60, N 5.85; found: C 72.23, H 6.73, N 5.69.

4.3.4. *(*S*)-2-[3,4-Bis(benzyloxy)benzyl]-2-{[(*S*)-2-([[(9*H*-fluoren-9-yl)methoxy]carbonyl}amino)-3-methyl-1-oxobutyl]amino}-2-methylpropanoic Acid* (*Fmoc-(*S*)-Dopa(2Me)(OBn)$_2$-OH,* (S,S)-**16b**). As described for (*S,S*)-**16a**, with (*S,S,R*)-**13b** (109 mg, 0.124 mmol), and 3N HCl (MeCN/H_2O 3:1, 4 ml); 1 h at 60°: 26 mg (30%) of (*S,S,*)-**16b** and 38 mg (42%) of (*S,S*)-**17b**.

*Data of (*S,S*)-*__16b__: M.p. 91–92°. R_f (CH_2Cl_2/MeOH 20:1) 0.16. IR: 3403*m*, 2962*w*, 1720*s*, 1509v*s*, 1452*s*, 1376*w*, 1265*s*, 1139*w*, 1027*w*, 759*w*, 740*m*, 696*w*, 621*w*. ^{1}H-NMR: 7.71 (*d*, *J* = 7.4, 2 arom. H); 7.53 (*d*, *J* = 6.6, 2 arom. H); 7.45–7.2 (*m*, 14 arom. H); 6.7–6.6 (*m*, 3 arom. H, NH of Dopa(2Me)); 5.79 (*d*, *J* = 9.0, NH of Val);

5.02, 4.92 (2*s*, 2 PhCH_2O); 4.35–4.1 (*m*, CHCH_2 of Fmoc); 4.0–3.9 (*m*, CH(2) of Val); 3.35, 3.11 (*AB*, J = 13.7, CH_2(3) of Dopa(2Me)); 2.05–1.9 (*m*, CH(3) of Val); 1.57 (*s*, Me(3) of Dopa(2Me)); 0.95–0.85 (*m*, 2 Me(4) of Val). ^{13}C-NMR: 176.4, 171.2 (2*s*, COOH, CO (amide)); 156.4 (*s*, CO (urethane)); 148.5, 148.2, 143.6, 141.2, 137.2, 137.1, 128.8 (7*s*, 9 arom. C); 128.3, 127.6, 127.4, 127.2, 127.0, 125.0, 122.9, 119.9, 117.1, 114.7 (10*d*, 21 arom. CH); 71.2, 70.5 (2*t*, 2 PhCH_2O, CH_2O of Fmoc); 61.0 (*d*, C(2) of Val); 60.5 (*s*, C(2) of Dopa(2Me)); 47.0 (*d*, CH of Fmoc); 41.1 (*t*, C(3) of Dopa(2Me)); 30.9 (*d*, C(3) of Val); 22.7, 19.0, 17.8 (3*q*, Me(3) of Dopa(2Me), 2 Me(4) of Val). ESI-MS (CH_2Cl_2, MeOH, NaI): 737 (14), 735 (100, $[M+Na]^+$), 661 (14), 617(10). Anal. calc. for $C_{44}H_{44}N_2O_7$ (712.84): C 74.14, H 6.22, N 3.93; found: C 74.00, H 6.30, N 3.65.

4.4. *Dipeptides with Val-(*R*)-Dopa(2Me).* 4.4.1. *[(9*H*-Fluoren-9-yl)methyl]* N-*((*S*)-1-{[((*R*)-1-[3,4-Bis-(benzyloxy)benzyl]-1-methyl-2-[methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-oxoethyl)amino]carbonyl}-2-methylpropyl)carbamate* (*Fmoc-Val-(*R*)-Dopa(2Me)(OBn)$_2$-NMe(naphthEt),* (*S*,*R*,*R*)-**13b**). As described for (*S*,*S*,*R*)-**13a**, with Fmoc-Val-OH (253 mg, 0.745 mmol) in abs. CH_2Cl_2 (5 ml), (1′*R*,2*R*)-**2b** (400 mg, 0.740 mmol), and abs. CH_2Cl_2 (10 ml); 142 h at r.t.; CC (hexane/AcOEt 3:2): 377 mg (58%) of (*S*,*R*,*R*)-**13b**. Colorless foam. M.p. 92–94°. R_f (hexane/AcOEt 1:1) 0.55. IR: 3402*m*, 3037*w*, 2963*m*, 1725*m*, 1681*s*, 1620*m*, 1510v*s*, 1452*s*, 1391*m*, 1330*w*, 1269*s*, 1222*m*, 1138*w*, 1070*m*, 1026*m*, 804*w*, 782*m*, 759*w*, 740*s*, 697*w*. ^{1}H-NMR: 7.95–7.9, 7.8–7.7, 7.5–7.2 (3*m*, 25 arom. H, CHN); 6.7-6.6 (*m*, 1 arom. H, NH); 6.55–6.5 (*m*, 2 arom. H); 5.19 (*d*, J = 8.2, NH of Val); 5.03, 5.00 (2*s*, 2 PhCH_2O); 4.35–4.25, 4.25–4.15, 3.95–3.9 (3*m*, CH_2CH of Fmoc, CH(2) of Val); 3.37, 3.29 (*AB*, J = 14.6, CH_2(3) of Dopa(2Me)); 2.51 (br. *s*, MeN); 1.65–1.5 (*m*, CH(3) of Val); 1.60 (*d*, J = 6.7, *Me*CHN); 1.43 (*s*, Me(3) of Dopa(2Me)); 0.88, 0.82 (2*d*, J = 6.3, 6.4, 2 Me(4) of Val). ^{13}C-NMR: 171.2, 169.7 (2*s*, 2 CO (amide)); 156.2 (*s*, CO (urethane)); 148.6, 148.2, 143.7, 141.3, 137.4, 135.7, 133.7, 132.0, 129.7 (9*s*, 12 arom. C); 128.6, 128.4, 127.7, 127.4, 127.3, 127.1, 126.7, 126.0, 125.1, 124.8, 124.2, 123.2, 120.0, 118.1, 115.0 (15*d*, 28 arom. CH); 71.4, 71.3 (2*t*, 2 PhCH_2O); 67.0 (*t*, CH_2O of Fmoc); 60.5 (*d*, C(2) of Val); 60.2 (*s*, C(2) of Dopa(2Me)); 50.6, 47.2 (2*d*, CH of Fmoc, CHN); 41.3 (*t*, C(3) of Dopa(2Me)); 30.7 (*d*, C(3) of Val); 30.3 (*q*, MeN); 22.6, 19.5, 17.4, 15.3 (4*q*, CHN*Me*, Me(3) of Dopa(2Me), 2 Me(4) of Val). ESI-MS (MeOH, NaI): 903 (100, $[M+Na]^+$), 824 (7), 223 (8). Anal. calc. for $C_{57}H_{57}N_3O_6 \cdot 0.3\ H_2O$ (886.11): C 77.26, H 6.56, N 4.74; found: C 77.04, H 6.55, N 5.24.

4.4.2. *(*R*)-2-{[(*S*)-2-Amino-3-methyl-1-oxobutyl]amino}-2-[3,4-bis(benzyloxy)benzyl]-*N*-methyl-*N*-[(*R*)-1-(naphthalen-1-yl)ethyl]propanamide* (*H-Val-(*R*)-Dopa(2Me)(OBn)$_2$-NMe(naphthEt),* (*S*,*R*,*R*)-**14b**). As described for (*S*,*S*,*R*)-**14a**, with (*S*,*R*,*R*)-**13b** (100 mg, 0.114 mmol), and Et_2NH (2 ml); 4 h at r.t.; prep. TLC (AcOEt/MeOH 20:1) and prep. TLC (CH_2Cl_2/MeOH 10:1): 58 mg (77%) of (*S*,*R*,*R*)-**14b**. M.p. 71–73°. R_f (CH_2Cl_2/MeOH 10:1) 0.45. IR: 3404*s*, 2960*m*, 1668*m*, 1623v*s*, 1512v*s*, 1454*s*, 1385*m*, 1269*s*, 1139*w*, 1070*m*, 1025*w*, 805*m*, 782*w*, 736*w*, 697*w*. ^{1}H-NMR: 8.17 (br. *s*, NH); 8.0–7.9, 7.85–7.75, 7.45–7.2, 6.95–6.55 (4*m*, 20 arom. H, 3 NH, CHN); 5.1–5.05 (*m*, 2 PhCH_2O); 4.0–3.9 (*m*, CH(2) of Val); 3.5–3.15 (*m*, CH_2(3) of Dopa(2Me)); 2.55–2.4 (*m*, MeN); 2.25–2.2 (*m*, CH(3) of Val); 1.57 (*d*, J = 6.7, *Me*CHN); 1.46 (*s*, Me(3) of Dopa(2Me)); 0.95–0.65 (*m*, 2 Me(4) of Val). ^{13}C-NMR: 171.5 (*s*, 2 CO (amide)); 148.3, 147.9, 137.3, 135.6, 133.6, 131.9, 129.9 (7*s*, 8 arom. C); 128.3, 128.3, 127.6, 127.4, 127.3, 127.2, 126.6, 125.8, 125.2, 124.8, 124.0, 123.6, 118.2, 114.8 (14*d*, 20 arom. CH); 71.5, 71.1 (2*t*, 2 PhCH_2O); 61.0 (*s*, C(2) of Dopa(2Me)); 59.4 (*d*, C(2) of Val); 50.5 (*d*, CHN); 41.7 (*t*, C(3) of Dopa(2Me)); 30.1 (*d*, C(3) of Val); 22.5, 19.0, 16.7, 15.3, 14.1 (5*q*, MeN, CHN*Me*, Me(3) of Dopa(2Me), 2 Me(4) of Val). ESI-MS (MeOH, NaI): 658 (100, $[M+1]^+$), 504 (83, $[M-naphthCHCH_2+1]^+$), 473 (27, $[M-naphthEtNMe+1]^+$), 179 (21, [dibenzofulvene]$^+$). Anal. calc. for $C_{42}H_{47}N_3O_4$ (657.85): C 76.68, H 7.20, N 6.39; found: C 76.67, H 7.23, N 6.23.

4.4.3. *[(9*H*-Fluoren-9-yl)methyl]* N-*((*S*)-1-{[((*R*)-1-[3,4-Bis(hydroxy)benzyl]-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-oxoethyl)amino]carbonyl}-2-methylpropyl)carbamate* (*Fmoc-Val-(*R*)-Dopa-(2Me)-NMe(naphthEt),* (*S*,*R*,*R*)-**15b**). As described for (*S*,*S*,*R*)-**15a**, with (*S*,*R*,*R*)-**13b** (100 mg, 0.114 mmol), 5 mg Pd/C (10% on activated charcoal), MeOH (2 ml), and H_2; 25 h at r.t.: 68 mg (85%) of (*S*,*R*,*R*)-**15b**. M.p. 131–132°. R_f (hexane/AcOEt 1:1) 0.19. IR: 3390v*s*, 2928*s*, 1681*s*, 1614*s*, 1514v*s*, 1504*s*, 1450*s*, 1392*m*, 1285*m*, 1110*m*, 1071*m*, 782*w*, 760*w*, 741*w*. ^{1}H-NMR: 7.9–7.75, 7.6–7.25 (2*m*, 15 arom. H); 6.7–6.55, 6.45–6.4 (2*m*, 3 arom. H, CHN); 6.08 (br. *s*, NH of Dopa(2Me)); 5.71 (*d*, J = 9.8, NH of Val); 4.45–4.35, 4.2–4.05 (2*m*, CHCH_2 of Fmoc, CH(2) of Val); 3.41, 3.21 (*AB*, J = 14.2, CH_2(3) of Dopa(2Me)); 2.55 (*s*, MeN); 2.1–2.05 (*m*, CH(3) of Val); 1.62 (*d*, J = 7.7, *Me*CHN); 1.34 (*s*, Me(3) of Dopa(2Me)); 0.95, 0.93 (2*d*, J = 6.5, 6.6, 2 Me(4) of Val). ^{13}C-NMR: 170.7, 170.6 (2*s*, 2 CO (amide)); 157.5 (*s*, CO (urethane)); 143.7, 143.5, 143.1, 141.2, 135.6, 133.6, 131.9, 128.1 (8*s*, 10 arom. C); 128.5, 128.4, 127.7, 127.1, 126.6, 125.9, 125.1, 124.9, 124.7, 123.9, 123.2, 119.9, 117.7, 114.5 (14*d*, 18 arom. CH); 67.7 (*t*, CH_2 of Fmoc); 60.3 (*d*, C(2) of Val); 60.0 (*s*, C(2) of Dopa(2Me)); 50.1, 47.0 (2*d*, CH of Fmoc, CHN); 40.3 (*t*, C(3) of Dopa(2Me)); 30.9 (*d*, C(3) of Val); 29.7 (*q*, MeN); 21.6, 19.6, 16.7, 14.8 (4*q*, CHN*Me*, Me(3) of Tyr(2Me), 2 Me(4) of Val). ESI-MS (CH_2Cl_2, MeOH, NaI): 810 (8), 723 (100, $[M+Na]^+$),

596 (9), 382 (8). Anal. calc. for $C_{43}H_{45}N_3O_6 \cdot H_2O$ (717.87): C 71.95, H 6.60, N 5.85; found: C 72.01, H 6.76, N 5.76.

4.4.4. *(*R*)-2-[3,4-Bis(benzyloxy)benzyl]-2-{[(*S*)-2-({[(9*H*-fluoren-9-yl)methoxy]carbonyl}amino)-3-methyl-1-oxobutyl]amino}-2-methylpropanoic Acid* (*Fmoc-(*R*)-Dopa(2Me)(OBn)$_2$-OH,* (*S,R*)-**16b**). As described for (*S,R*)-**16a**, with (*S,R,R*)-**13b** (100 mg, 0.114 mmol), and 3N HCl (MeCN/H_2O 1:1, 4 ml); 3 h at 60°: 20 mg (25%) of (*S,R*)-**16b**, 55 mg (55%) of (*S,R,R*)-**13b**, and 16 mg (19%) of (*S,R*)-**17b**.

*Data of (*S,R*)-***16b***:* M.p. 83–84°. R_f (CH_2Cl_2/MeOH 20:1) 0.29. IR: 3408*s*, 2928*m*, 1715*s*, 1513v*s*, 1453*m*, 1266*s*, 1138*w*, 1026*w*, 740*m*, 697*w*. ^{1}H-NMR: 7.73 (*d*, *J* = 7.5, 2 arom. H); 7.55–7.5 (*m*, 2 arom. H); 7.45–7.25 (*m*, 14 arom. H); 6.75–6.6 (*m*, 3 arom. H, NH of Dopa(2Me)); 5.82 (*d*, *J* = 9.0, NH of Val); 5.06, 4.99 (2*s*, 2 PhCH_2O); 4.4–4.1 (*m*, $CHCH_2$ of Fmoc, CH(2) of Val); 2.25–2.2 (*m*, CH_2(3) of Dopa(2Me)); 2.0–1.95 (*m*, CH(3) of Val); 1.51 (*s*, Me(3) of Dopa(2Me)); 0.85–0.8 (*m*, 2 Me(4) of Val). ^{13}C-NMR: 176.2, *ca.* 172 (2*s*, COOH, CO (amide)); *ca.* 157 (*s*, CO (urethane)); 148.5, 148.1, 143.6, 141.2, 137.2 (5*s*, 9 arom. C); 128.3, 127.6, 127.3, 127.2, 127.0, 125.0, 123.0, 119.9, 117.1, 114.8 (10*d*, 21 arom. CH); 71.2, 67.3 (2*t*, 2 PhCH_2O, CH_2O of Fmoc); 60.7 (*s*, C(2) of Dopa(2Me)); 60.1 (*d*, C(2) of Val); 47.0 (*d*, CH of Fmoc); 40.9 (*t*, C(3) of Dopa(2Me)); 30.9 (*d*, C(3) of Val); 23.0, 19.2, 17.5 (3*q*, Me(3) of Dopa(2Me), 2 Me(4) of Val). ESI-MS (MeOH, NaI): 736 (100, $[M+Na]^+$). Anal. calc. for $C_{44}H_{44}N_2O_7 \cdot 0.5\ H_2O$ (730.86): C 73.21, H 6.28, N 3.88; found: C 73.08, H 6.49, N 3.88.

5. *X-Ray Crystal-Structure Determination of* (1*R*,1′*R*)-**11a**, (1*R*,1′*R*)-**11b**, (1*S*,1′*R*)-**12b**, *and* (1*R*,1′*R*)-**12b** (see *Table 7* and *Figure*)[2]). All measurements were conducted at low temp. with graphite-monochromated MoK_α radiation ($\lambda = 0.71073$ Å). The data collection and refinement parameters are given in *Table 7*, and views of the molecules are shown in the *Figure*. The intensities were corrected for *Lorentz* and polarization effects, but not for absorption. Equivalent reflections, other than *Friedel* pairs, were merged. Each structure was solved by direct methods by means of SIR92 [11], which revealed the positions of all non-H-atoms.

When the peptide molecule (1*R*,1′*R*)-**12b** had been fully modelled, it was found that the unit-cell contains two quite large voids (385 Å^3 each), which are assumed to be occupied by solvent molecules. Only a few weak peaks of electron density could be located, and these did not represent any logical molecule, so the solvent molecules must be highly disordered within each cavity. Therefore, the SQUEEZE routine [12] of the program PLATON [13] was employed. This routine removes the contribution of the solvent region of the structure from the reflection intensity data and, when successful, allows the solvent molecules to be omitted entirely from the refinement model. For this structure, the procedure gave satisfactory *R* factors for the refinement and suitable geometric parameters for the peptide molecule, and there were no significant peaks of residual electron density to be found in the voids of the structure. The electron count in the solvent region was calculated to be 121 e per unit cell. It is assumed that the solvent molecules are AcOEt, as the compound was recrystallized from this solvent. If so, one molecule in each void would contribute a total of 96 e to the electron count, which falls a little short of the calculated electron count, but is not completely unreasonable. However, there is insufficient information to guarantee that the solvent molecules are indeed AcOEt, and other molecules could be conceivable. For the purposes of the calculation of M_r, the density, *F*(000) and the linear absorption coefficient, it was assumed that the solvent is indeed AcOEt, and that the ratio of peptide/AcOEt in the structure is 2:1 (4 peptide molecules plus 2 voids per unit cell).

The non-H-atoms of each structure were refined anisotropically, except for C(44) of (1*R*,1′*R*)-**11b**, which was refined only isotropically. All of the H-atoms in (1*R*,1′*R*)-**12b** were placed in geometrically calculated positions and refined with a riding model where each H-atom was assigned a fixed isotropic displacement parameter with a value equal to 1.2U_{eq} of its parent atom (1.5U_{eq} for the Me groups). For (1*R*,1′*R*)-**11b** and (1*S*,1′*R*)-**12b**, the amide H-atom was placed in the position indicated by a difference-electron-density map, and its position was allowed to refine together with an isotropic displacement parameter. All remaining H-atoms in (1*R*,1′*R*)-**11b** and (1*S*,1′*R*)-**12b**, as well as all H-atoms in (1*R*,1′*R*)-**12b** were fixed in geometrically calculated positions (d(C–H) = 0.95 Å), and each was assigned a fixed isotropic displacement parameter with a value equal to 1.2U_{eq} of its parent atom. Refinement of (1*R*,1′*R*)-**11a**, (1*R*,1′*R*)-**11b**, and (1*S*,1′*R*)-**12b** was carried out on *F* by full-matrix least-squares procedures, which minimized the function $\Sigma w(|F_o| - |F_c|)^2$. In the case of

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[2]) Crystallographic data (excluding structure factors) for (1*R*,1′*R*)-**11a**, (1*R*,1′*R*)-**11b**, (1*S*,1′*R*)-**12b**, and (1*R*,1′*R*)-**12b** have been deposited with the *Cambridge Crystallographic Data Centre* as supplementary publications no. CCDC-186661 – CCDC-186664. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0)1223-336033; email: deposit@ccdc.cam.ac.uk).

Table 7. *Crystallographic Data of Compounds (1*R*,1′*R*)*-**11a**, *(1*R*,1′*R*)*-**11b**, *(1*S*,1′*R*)*-**12b**, *and (1*R*,1′*R*)*-**12b**

	(1*R*,1′*R*)-**11a**	(1*R*,1′*R*)-**11b**	(1*S*,1′*R*)-**12b**	(1*R*,1′*R*)-**12b**
Crystallized from	Et_2O / CH_2Cl_2 / hexane	Et_2O / hexane	AcOEt / MeOH / hexane	AcOEt
Empirical formula	$C_{37}H_{36}N_2O_2S$	$C_{44}H_{42}N_2O_3S$	$C_{44}H_{42}N_2O_4$	$C_{44}H_{42}N_2O_4 \cdot 0.5\ C_4H_8O_2$
M_r [g mol^{-1}]	572.76	678.89	662.83	706.88
Crystal color, habit	colorless, plate	colorless, needle	colorless, needle	colorless, needle
Crystal dimensions [mm]	$0.08 \times 0.23 \times 0.50$	$0.05 \times 0.05 \times 0.25$	$0.02 \times 0.10 \times 0.30$	$0.08 \times 0.10 \times 0.30$
Temp. [K]	173(1)	160(1)	160(1)	160(1)
Crystal system	monoclinic	monoclinic	monoclinic	orthorhombic
Space group	$P2_1$	$P2_1$	$P2_1$	$P2_12_12_1$
Z	2	2	2	4
Reflections for cell determination	16	3364	4359	4054
2θ Range for cell determination [°]	20 – 33	4 – 50	4 – 55	4-50
Unit cell parameters a [Å]	18.869(3)	16.9854(2)	11.8540(2)	11.2289(1)
b [Å]	6.089(5)	6.0837(1)	11.0932(2)	14.2751(2)
c [Å]	14.562(3)	17.5054(2)	13.9586(3)	25.4518(3)
β [°]	112.64(1)	104.5299(5)	99.7186(9)	90
V [Å^3]	1544(1)	1751.05(4)	1809.20(6)	4079.76(8)
D_x [g cm^{-3}]	1.232	1.287	1.217	1.151
μ(MoK_α) [mm^{-1}]	0.140	0.137	0.0774	0.0744
Diffractometer	*Rigaku AFC5R*	*Nonius KappaCCD*	*Nonius KappaCCD*	*Nonius KappaCCD*
Scan type	$\omega/2\theta$	ϕ and ω	ϕ and ω	ω
$2\theta_{(max)}$ [°]	55	50	55	50
Total reflections measured	7964	53094	41965	55261
Symmetry independent reflections	7066	6111	8241	7203
Reflections with $I > 2\sigma(I)$	4756	3609	6505	5546
Parameters refined	378	450	455	455
Final R [on F; $I > 2\sigma(I)$]	0.0857	0.0953	0.0424	0.0545
wR	0.0849 [F; $I > 2\sigma(I)$]	0.0976 [F; $I > 2\sigma(I)$]	0.0419 [F; $I > 2\sigma(I)$]	0.1407 [F^2; all reflections]
Weights: w^{-1}	$\sigma^2(F_o) + (0.005F_o)^2$	$\sigma^2(F_o) + (0.018F_o)^2$	$\sigma^2(F_o) + (0.018F_o)^2$	[a])
Goodness of fit	2.706	3.232	1.309	1.028
Secondary extinction coefficient	–	3.1 (5) $\times 10^{-6}$	2.8 (3) $\times 10^{-6}$	0.033 (2)
Final Δ_{max}/σ	0.0002	0.002	0.0004	0.001
$\Delta\rho$ (max; min) [e Å^{-3}]	1.01; −0.69	0.43; −0.50	0.22; −0.21	0.40; −0.40
Structure refinement program	teXsan [22]	teXsan	teXsan	SHELXL97 [23]

[a]) $w^{-1} = \sigma^2(F_o) + (0.0969P)^2$ where $P = (F_o^2 + 2F_c^2)/3$

(1*R*,1′*R*)-**12b**, the refinement was carried out on F^2 by minimizing the corresponding function based on F^2. Corrections for secondary extinction were applied, except in the case of (1*R*,1′*R*)-**11a**. For (1*R*,1′*R*)-**11b** and (1*S*,1′*R*)-**12b**, three and six reflections, respectively, whose intensities were considered to be extreme outliers, were omitted from the final refinement. Neutral-atom scattering factors for non-H-atoms were taken from [14], and the scattering factors for H-atoms were taken from [15]. Anomalous dispersion effects were included in F_c [16]; the values for f' and f'' were those of [17]. The values of the mass attenuation coefficients were taken from [18].

The crystals of each compound were enantiomerically pure, and, in each case, the enantiomer used in the refinement was chosen to agree with the known (*R*)-configuration at the Me-substituted C-atom adjacent to the naphthalene moiety. The configuration at the stereogenic centre in the amino acid of each structure could then be established relative to the configuration of the known chiral center. In the case of (1*R*,1′*R*)-**11a**, the absolute configuration was further confirmed independently by refinement of the absolute structure parameter [19][20] during the crystal-structure determination. This parameter attained a value of $-0.04(12)$, which confirmed that the refined model represented the true enantiomorph.

The crystal of (1*R*,1′*R*)-**11b** was very small and weakly diffracting, and the overall quality of the refinement results is quite poor. The atomic parameters and derived geometry of the molecule should be considered to be only approximate, and attempts at refining the absolute structure parameter gave inconclusive results. Nonetheless, the configuration of the molecule is clearly defined. The crystal of (1*R*,1′*R*)-**11a** was also quite small and weakly diffracting, which again detracted from the quality of the results. There are significant peaks of residual electron density near the S-atom (up to 1.0 e $Å^{-3}$). However, a disordered model does not improve the results, and the structure does not appear to suffer from any other disorder or the presence of solvent.

For (1*R*,1′*R*)-**11a** and (1*R*,1′*R*)-**11b**, the amide group is not involved in any H-bonding interactions. In both (1*S*,1′*R*)-**12b** and (1*R*,1′*R*)-**12b**, the amide group forms an intermolecular H-bond with the central carbonyl O-atom of a neighboring molecule. These interactions link the molecules into infinite one-dimensional chains which run parallel to the *y*- and *x*-axes, respectively, and have graph set motifs [21] of C(5).

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