New Optically Active 2*H*-Azirin-3-amines as Synthons for Enantiomerically Pure 2,2-Disubstituted Glycines

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

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

Dedicated to Professor *Edgar Heilbronner* on the occasion of his 80th birthday

The synthesis of novel 2,2-disubstituted 2*H*-azirin-3-amines with a chiral amino group is described. Chromatographic separation of the diastereoisomer mixture yielded the pure diastereoisomers (1′*R*,2*R*)-**4a**–**e** and (1′*R*,2*S*)-**4a**–**e** (*Scheme 1*, *Table 1*), which are synthons for the (*R*)- and (*S*)-isomers of isovaline, 2-methylvaline, 2-cyclopentylalanine, 2-methylleucine, and 2-(methyl)phenylalanine, respectively. The configuration at C(2) of the synthons was determined by X-ray crystallography relative to the known configuration of the chiral auxiliary group. The reaction of **4** with thiobenzoic acid, benzoic acid, and the dipeptide Z-Leu-Aib-OH (**12**) yielded the monothiodiamides **10**, the diamides **11** (*Scheme 2*, *Table 3*), and the tripeptides **13** (*Scheme 3*, *Table 4*), respectively.

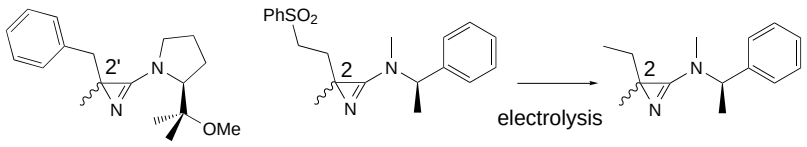
1. Introduction. – Peptides containing non-protein amino acids are of considerable interest due to their biological activity. A common modification to naturally occurring α-amino acids is the substitution of the H-atom at the C(α) atom by an alkyl group. These so-called α,α-disubstituted α-amino acids (2,2-disubstituted glycines) restrict the conformational flexibility of peptides and stabilize or promote secondary structures, such as β-turns or helices [1–4]. A convenient synthetic access to such peptides is the so-called 'azirine/oxazolone method', in which 2,2-disubstituted 2*H*-azirin-3-amines are used as amino-acid synthons [5] (*cf.* [6]). This method has been used successfully in the synthesis of peptaibols [7–12], endothiopeptides [13–17], conformationally restricted cyclic peptides [18–20], and cyclic depsipeptides [21–28].

For the incorporation of chiral, enantiomerically pure α,α-disubstituted glycines, optically pure synthons are needed. Recently, we reported the preparation of the first examples of such synthons for optically pure Phe(2Me) (see **1**) [29] and Iva (see **2**) [30]. The Iva synthons have been prepared *via* sulfone derivative **3**, and the diastereoisomers **3a** and **3b** could be separated by means of column chromatography. Electrochemical cleavage of the phenylsulfonyl group of the pure diastereoisomers then gave the synthons **2a** and **2b** for (*S*)- and (*R*)-Iva, respectively.

Based on these first successful syntheses, it was of interest to expand the number of 2*H*-azirin-3-amines available as optically pure amino-acid synthons, to work out a direct synthesis of the Iva building blocks, and to find a chiral auxiliary group, which can be used generally. In the present paper, we describe the preparation of a series of new optically pure 2*H*-azirin-3-amines which have potential use in peptide synthesis.

---

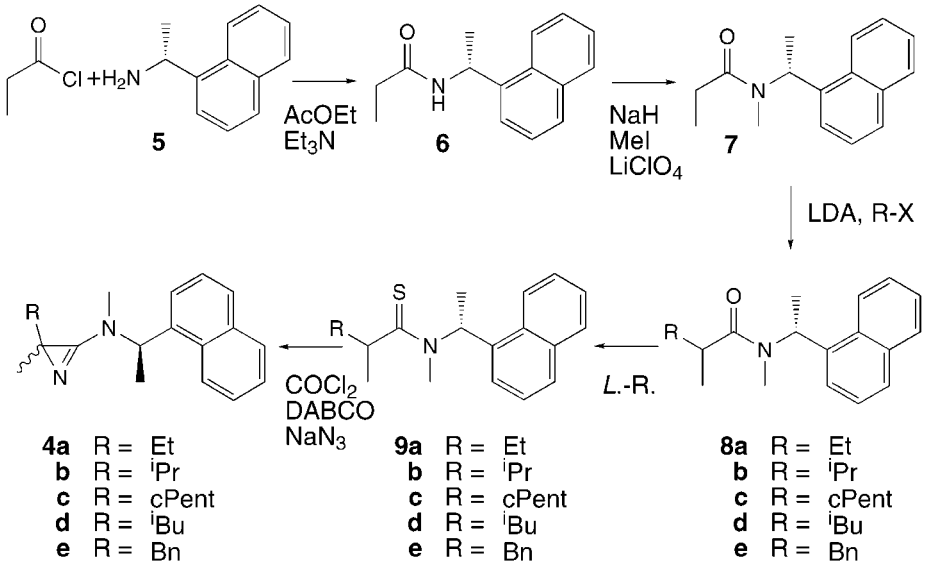
[1]) Part of the projected Ph.D. thesis of *K. B.*, Universität Zürich.



1a (2'*R*) **3a** (2*S*) **2a** (2*S*)
b (2'*S*) **b** (2*R*) **b** (2*R*)

2. Results. – 2.1. *Preparation of the Azirines.* The 2*H*-azirin-3-amines **4a**–**e** (*Scheme 1*), *i.e.*, synthons for isovaline (Iva), 2-methylvaline (Val(2Me)), 2-cyclopentylalanine (Ala(2cPent)), 2-methylleucine (Leu(2Me)), and 2-methylphenylalanine (Phe(2Me)) (*Table 1*), were prepared in gram quantities. In all experiments, the commercially available (*R*)-[1-(naphthalen-1-yl)ethyl]amine (**5**) was used as the chiral auxiliary group.

Scheme 1



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

Table 1. *Synthesis of* 2H-*Azirin-3-amines* **4**. Yields in [%].

R	Amide **8**	Thioamide **9**	Azirine **4**	Synthon for
Et	**a** (84)	**a** (88)	**a** (58)	Iva
^{i}Pr	**b** (93)	**b** (75)	**b** (53)	Val(2Me)
cPent	**c** (41[a]))	**c** (58[b]))	**c** (62)	Ala(2cPent)
^{i}Bu	**d** (82)	**d** (99)	**d** (56)	Leu(2Me)
Bn	**e** (90)	**e** (94)	**e** (59)	Phe(2Me)

[a]) Yield relative to converted starting material **7**, 74%. [b]) Yield relative to converted starting material **8c**, 94%.

The five diastereoisomer pairs of **4a**–**e** were prepared according to *Scheme 1* (*Table 1*), by following previously described protocols (*cf.* [29]). The chiral auxiliary group was introduced by coupling amine **5** with propanoyl chloride to give amide **6** in quantitative yield. The *N*-methylation of the latter was achieved in 98% yield with MeI in THF in the presence of $LiClO_4$ which was added to avoid *O*-methylation [30]. The *N*-methylated amide **7** was deprotonated with lithium diisopropylamide (LDA) and alkylated with the respective alkyl halides R–X to give the amides **8a**–**e** as diastereoisomer mixtures. The latter were converted to the corresponding thioamides **9a**–**e** (diastereoisomer mixtures) with *Lawesson* reagent. Finally, the synthesis of the azirines **4a**–**e** was achieved by consecutive treatment of **9a**–**e** 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. The yields of these transformations are summarized in *Table 1*.

Separation of the (*R*,*S*)- and (*R*,*R*)-diastereoisomers of **4a**–**e** 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*.

Table 2. *Chromatographic Separation of (*R,S*)- and (*R,R*)-Diastereoisomers of* **4a**–**e**

	R	Separation method	Amount separated	R_f Values[d])
4a	Et	MPLC[a]) (5×)	1.5 g	0.33, 0.29
4b	^{i}Pr	CC[b]), MPLC[a])	2.0 g	0.33, 0.29
4c	cPent	CC[c]), MPLC[a])	1.2 g	0.28, 0.23
4d	^{i}Bu	CC[b]) (3×)	1.7 g	0.36, 0.31
4e	Bn	CC[b]), MPLC[a])	2.9 g	0.32, 0.24

[a]) AcOEt. [b]) Hexane/AcOEt 3 : 1. [c]) Hexane/AcOEt 2 : 1. [d]) Hexane/AcOEt 1 : 1.

2.2. *Determination of the Relative Configuration of the 2*H-*Azirin-3-amines* **4**. In every case, it was possible to obtain crystals suitable for X-ray diffraction analysis from one of the two diastereoisomers (see ORTEP plots [31] in the *Fig*). The configuration at C(2) of the azirine ring was determined relative to the known (*R*)-configuration of the chiral auxiliary group. The absolute configurations of the molecules were not confirmed crystallographically, but can be assigned on the basis of the known absolute configuration in the substituted amino group.

2.3. *Conversion of Azirines* **4a**–**e** *to Amino-Acid Derivatives.* To demonstrate 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 thiobenzoic acid [29][32][33] (*cf.* [14][15]) and, in some cases, with benzoic acid according to *Scheme 2*. A typical reaction was carried out with equimolar amounts of **4** and the acid in CH_2Cl_2 at room temperature. The yields and reaction times are summarized in *Table 3*. It is obvious that the reactions with thiobenzoic acid proceed faster and in better yields than with benzoic acid.

In addition, the optically pure synthons **4a**–**e** were used to incorporate (*R*)- and (*S*)-configured 2,2-disubstituted glycines (α,α-disubstituted α-amino acids), respectively, into model tripeptides Z-Leu-Aib-Xaa-N(Me)R (**13**) by coupling **4** with the dipeptide Z-Leu-Aib-OH (**12**; *Scheme 3*). Typically, these reactions were carried out in

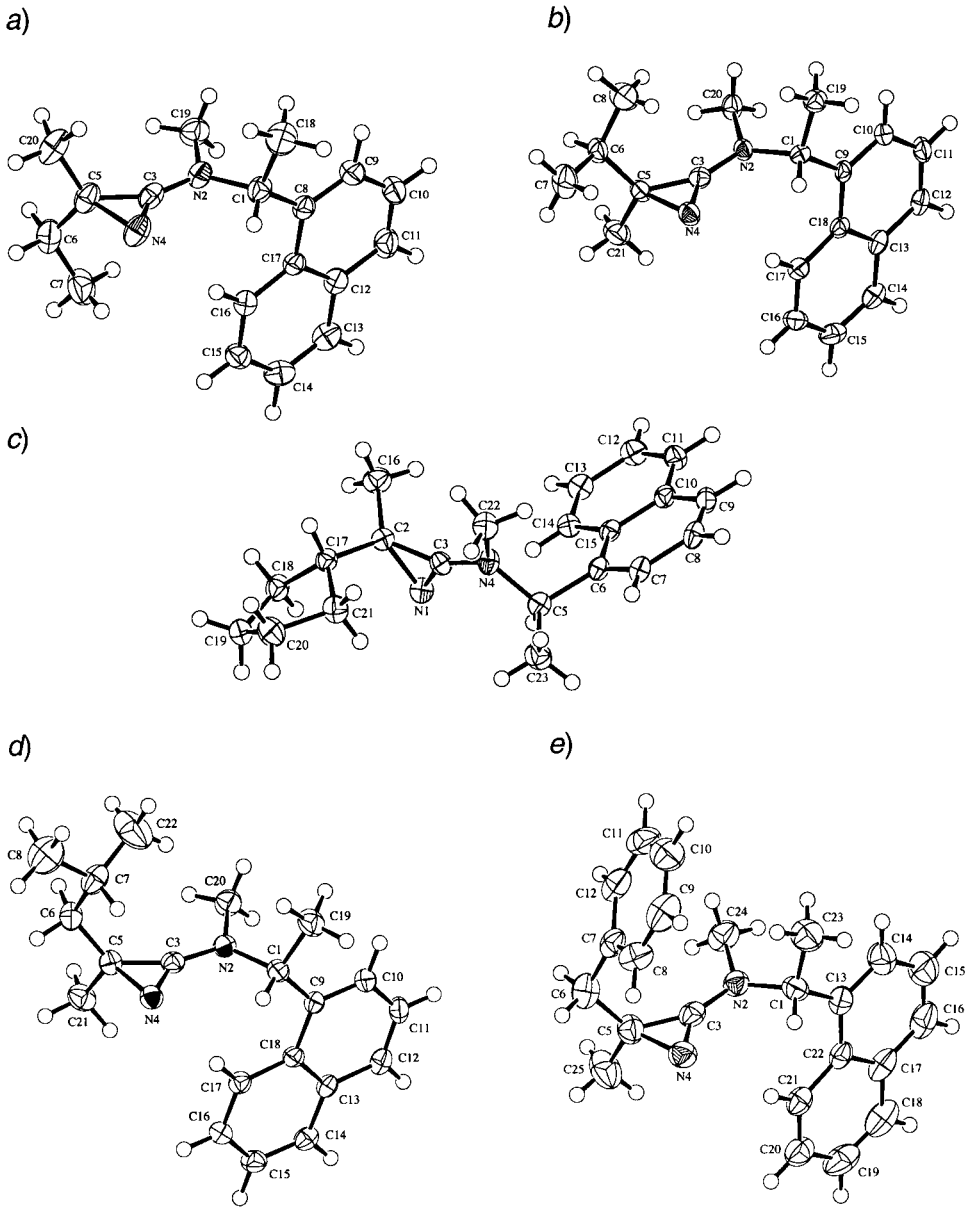
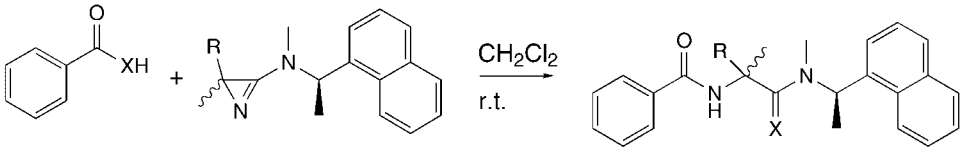


Figure. *ORTEP Plots* [31] *of the molecular structures of* a) *(1′*R,2R*)*-**4a** (synthon for (*R*)-Iva), b) *(1′*R,2S*)*-**4b** (synthon for (*S*)-Val(2Me)), c) *(1′*R,2S*)*-**4c** (synthon for (*S*)-Ala(2cPent)), d) *(1′*R,2S*)*-**4d** (synthon for (*S*)-Leu(2Me)), *and* e) *(1′*R,2S*)*-**4e** (synthon for (*S*)-Phe(2Me)) (50% Probability ellipsoids, arbitrary numbering of atoms).

Scheme 2[a])



[a]) For **a**–**e**, see *Scheme 1* or *Table 3*.

Table 3. *Reaction of the 2*H-*Azirin-3-amines* **4** *with Thiobenzoic Acid and Benzoic Acid* (in CH_2Cl_2 at room temperature)

Azirine **4**	R	Reaction with PhCOSH			Reaction with PhCOOH		
		Thioamide **10**	Yield [%]	Reaction time [h]	Amide **11**	Yield [%]	Reaction time [h]
(1′*R*,2*S*)-**4a**	Et	(1′*R*,1*S*)-**10a**	93	19	(1′*R*,1*S*)-**11a**	84	39
(1′*R*,2*R*)-**4a**		(1′*R*,1*R*)-**10a**	99	19	(1′*R*,1*R*)-**11a**	90	40
(1′*R*,2*S*)-**4b**	^{i}Pr	(1′*R*,1*S*)-**10b**	98	48			
(1′*R*,2*R*)-**4b**		(1′*R*,1*R*)-**10b**	94	23			
(1′*R*,2*S*)-**4c**	cPent	(1′*R*,1*S*)-**10c**	95	19			
(1′*R*,2*R*)-**4c**		(1′*R*,1*R*)-**10c**	68	2			
(1′*R*,2*S*)-**4d**	^{i}Bu	(1′*R*,1*S*)-**10d**	95	17			
(1′*R*,2*R*)-**4d**		(1′*R*,1*R*)-**10d**	99	15			
(1′*R*,2*S*)-**4e**	Bn	(1′*R*,1*S*)-**10e**	97	18	(1′*R*,1*S*)-**11e**	79	44
(1′*R*,2*R*)-**4e**		(1′*R*,1*R*)-**10e**	96	20	(1′*R*,1*R*)-**11e**	92	64

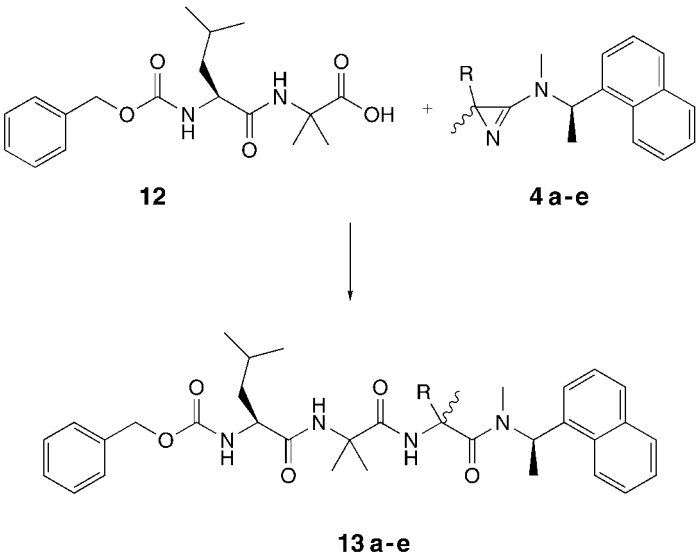
CH_2Cl_2 at room temperature with equimolar amounts of **4** and **12**. The yields and reaction times are summarized in *Table 4*.

In conclusion, novel 2,2-disubstituted 2*H*-azirin-3-amines with a chiral substituted amino group were prepared. After chromatographic separation of the diastereoisomers, these new optically active synthons for 2,2-disubstituted glycines were successfully reacted with several acids and incorporated into a model tripeptide. Therefore, these synthons can easily be used in peptide synthesis as building blocks for enantiomerically pure α,α-disubstituted α-amino acids.

Table 4. *Reaction of the 2*H-*Azirin-3-amines* **4** *with Z-Leu-Aib-OH* (**12**) (in CH_2Cl_2 at room temperature)

Azirine **4**	R	Tripeptide **13**	Yield [%]	Reaction time
(1′*R*,2*S*)-**4a**	Et	(*S*,*S*,*R*)-**13a**	77	67 h
(1′*R*,2*R*)-**4a**		(*S*,*R*,*R*)-**13a**	83	67 h
(1′*R*,2*S*)-**4b**	^{i}Pr	(*S*,*S*,*R*)-**13b**	67	5.5 d
(1′*R*,2*R*)-**4b**		(*S*,*R*,*R*)-**13b**	69	2 d
(1′*R*,2*S*)-**4c**	cPent	(*S*,*S*,*R*)-**13c**	39	5.5 d
(1′*R*,2*R*)-**4c**		(*S*,*R*,*R*)-**13c**	38	4 d
(1′*R*,2*S*)-**4d**	^{i}Bu	(*S*,*S*,*R*)-**13d**	64	2 d
(1′*R*,2*R*)-**4d**		(*S*,*R*,*R*)-**13d**	60	4 d
(1′*R*,2*S*)-**4e**	Bn	(*S*,*S*,*R*)-**13e**	59	40 h
(1′*R*,2*R*)-**4e**		(*S*,*R*,*R*)-**13e**	62	48 h

Scheme 3[a])



[a]) For **a**–**e**, see *Scheme 1* or *Table 4*.

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*. Solvents were purified by standard procedures. Thin-layer chromatography (TLC): *Merck* TLC aluminium sheets, silica gel *60* F_{254}. Prep. TLC: *Merck* PLC plates (glass), silica gel *60* F_{254}, 2 mm. Column chromatography (CC): *Uetikon-Chemie* 'Chromatographiegel' *C-560*. Medium-pressure liquid chromatography (MPLC): *Merck LiChroprep Si 60*, 15–25 μ; column: *Kronlab HPP-VPC* 540 × 40 mm or *Kronlab 4/98 – PRO* 480 × 30 mm; detection at λ 254 nm. M.p. *Mettler-FP-5* apparatus or *Büchi 510* apparatus; uncorrected. IR Spectra: *Perkin-Elmer-781* spectrophotometer or *Perkin-Elmer-1600-FT-IR* spectrophotometer; in KBr unless otherwise stated; absorptions in cm^{-1}. ^1H- (300 MHz) and ^{13}C-NMR (75.5 MHz) Spectra: *Bruker ARX-300* instrument; in $CDCl_3$ at 300 K unless otherwise stated; δ in ppm, coupling constants J in Hz; ^{13}C-signal multiplicity from DEPT spectra. MS: *Finnigan SSQ-700* or *-MAT-90* instrument for CI; *Finnigan-TSQ-700* triple quadrupole spectrometer for ESI; *m/z* (rel.%).

2. *Synthesis of the Azirines*. 2.1. N-*Methyl*-N-*[(*R*)-1-(naphthalen-1-yl)ethyl]propanamide* (**7**). N-*[(*R*)-1-(Naphthalen-1-yl)ethyl]propanamide* (**6**). To a soln. of (*R*)-[1-(naphthalen-1-yl)ethyl]amine (**5**; 10.874 g, 63.502 mmol) in AcOEt (400 ml) at 0°, Et_3N (9 ml, 6.5 g, 65 mmol) was added, and the mixture was stirred for 5 min. Within 60 min, propanoyl chloride (5.50 ml, 5.82 g, 63 mmol) was added, keeping the temp. below 4°. After further stirring for 20 min at 0°, the mixture was washed with 1N HCl and sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated: 14.8 g (quant.) of **6**. Crystalline, colorless solid. M.p. 124.4–124.7°. R_f (AcOEt) 0.47, R_f (hexane/AcOEt 1:1) 0.25. IR: 3305*s*, 3195*w*, 3170*w*, 3060*w*, 3055*w*, 2970*s*, 2930*m*, 2875*m*, 2740*w*, 1965*w*, 1915*w*, 1865*w*, 1800*w*, 1770*w*, 1730*w*, 1635*s*, 1600*m*, 1565*w*, 1530*s*, 1445*m*, 1425*m*, 1400*m*, 1370*s*, 1340*m*, 1300*w*, 1270*w*, 1260*w*, 1230*s*, 1170*m*, 1125*m*, 1095*m*, 1070*m*, 1040*w*, 1020*m*, 995*m*, 965*m*, 920*m*, 910*m*, 865*m*, 840*w*, 800*s*, 780*s*, 685*m*, 675*m*. ^1H-NMR: 8.10 (*d*, J = 8.0, 1 arom. H); 7.87 (*d*, J = 7.5, 1 arom. H); 7.80 (*d*, J = 7.9, 1 arom. H); 7.6–7.4 (*m*, 4 arom. H); 5.95–5.9 (*m*, CH); 5.78 (br., NH); 2.17 (*qd*, J = 7.6, 1.2, CH_2); 1.66 (*d*, J = 6.7, *Me*CH); 1.14

(*t*, *J* = 7.6, *Me*CH_2). ^{13}C-NMR: 172.6 (*s*, CO); 138.3, 133.9, 131.1 (3*s*, 3 arom. C); 128.7, 128.3, 126.5, 125.8, 125.1, 123.4, 122.4 (7*d*, 7 arom. CH); 44.4 (*d*, CH); 29.7 (*t*, CH_2); 20.6 (*q*, *Me*CH); 9.8 (*q*, *Me*CH_2). CI-MS (NH_3): 245 (19, $[M+NH_4]^+$), 229 (15), 228 (100, $[M+1]^+$), 155 (7, $[M-MeCH_2CONH]^+$). Anal. calc. for $C_{15}H_{17}NO$ (227.16): C 79.26, H 7.54, N 6.16; found: C 79.55, H 7.74, N 6.01.

Propanamide **7**. At 0°, NaH (1.1 g, 46 mmol; washed with hexane) was added to a soln. of **6** (7.010 g, 30.84 mmol) and $LiClO_4$ (3.612 g, 33.95 mmol) in abs. THF (100 ml). After stirring for 10 min at 0°, MeI (2.5 ml (5.7 g, 40 mmol) was added, and after further stirring for 10 min at 0°, the soln. was heated under reflux for 2.5 h. Addition of a new portion of NaH (1.1 g, 46 mmol; washed with hexane) and MeI (2 ml, 32 mmol) was followed by heating under reflux for 20 min. Then, the mixture was carefully poured on ice, acidified with 1N HCl, extracted with CH_2Cl_2, dried ($MgSO_4$), and evaporated. CC (hexane/AcOEt 1:1) yielded 7.297 g (98%) of **7**. Pale yellow solid. M.p. 61.8–62.4°. R_f (Et_2O) 0.40, R_f (hexane/AcOEt 1:1) 0.34. IR: 3040*m*, 2970*m*, 2930*m*, 2900*m*, 2870*m*, 1645*s*, 1630*s*, 1595*m*, 1570*m*, 1550*w*, 1530*w*, 1505*m*, 1485*m*, 1480*m*, 1465*m*, 1450*m*, 1445*m*, 1415*m*, 1395*m*, 1375*m*, 1345*m*, 1320*m*, 1285*s*, 1235*m*, 1210*m*, 1165*m*, 1120*m*, 1090*m*, 1060*m*, 1040*m*, 1025*m*, 1000*m*, 980*m*, 960*w*, 910*w*, 895*w*, 870*w*, 810*s*, 780*s*, 755*m*, 740*w*, 720*w*, 660*w*, 615*w*. ^{1}H-NMR: 8.05–8.0 (*m*, 1 arom. H); 7.85–7.8 (*m*, 2 arom. H); 7.55–7.45 (*m*, 4 arom. H); 6.64 (*q*, *J* = 7.6, CH); 2.46 (*s*, MeN); 2.32 (*q*, *J* = 7.6, CH_2); 1.60 (*d*, *J* = 6.8, *Me*CH); 1.20 (*t*, *J* = 7.5, *Me*CH_2). ^{13}C-NMR: 173.0 (*s*, CO); 136.2, 133.7, 131.9 (3*s*, 3 arom. C); 128.5, 126.6, 125.8, 124.7, 123.9 (5*d*, 7 arom. CH); 47.7 (*d*, CH); 29.0 (*q*, MeN); 27.2 (*t*, CH_2); 15.7 (*q*, *Me*CH); 9.3 (*q*, *Me*CH_2). CI-MS (NH_3): 243 (15), 242 (100, $[M+1]^+$), 241 (6, $M^{+\cdot}$). Anal. calc. for $C_{16}H_{19}NO$ (241.33): C 79.63, H 7.94, N 5.80; found: C 79.84, H 8.08, N 5.83.

2.2. *Iva Synthon. (*RS*)-*N*,2-Dimethyl*-N-*[(*R*)-1-(naphthalen-1-yl)ethyl]butanamide* (**8a**). Within 7 min, 2N LDA in THF/heptane/ethylbenzene (14.7 ml, 29.4 mmol) was added to a soln. of **7** (7.074 g, 29.31 mmol) and $LiClO_4$ (3.194 g, 30.02 mmol) in abs. THF (70 ml) at −78°, and the mixture was stirred for 1 h at −78°. Then, EtBr (2.65 ml, 3.87 g, 35.5 mmol) was added at −78°. After 40 min, the mixture was warmed to −55° within 4 h and stored for another 18 h at −30°. The resulting soln. was carefully poured on ice, neutralized with 1N HCl (keeping the mixture still slightly basic), extracted with CH_2Cl_2, dried ($MgSO_4$), and evaporated. CC (hexane/AcOEt 5:1) yielded 6.650 g (84%) of **8a**. Colorless solid. M.p. 126.1–126.9°. R_f (hexane/AcOEt 1:1) 0.54 and 0.49, resp., for the diastereoisomers. IR: 2960*s*, 2920*s*, 2870*m*, 2850*m*, 1635*s*, 1595*m*, 1505*m*, 1460*s*, 1455*s*, 1435*m*, 1405*s*, 1370*m*, 1350*m*, 1335*m*, 1320*m*, 1295*m*, 1280*m*, 1250*m*, 1235*m*, 1210*m*, 1200*w*, 1165*m*, 1110*m*, 1100*w*, 1085*m*, 1050*m*, 1025*m*, 1005*w*, 980*w*, 960*w*, 900*w*, 810*s*, 785*s*, 750*m*, 730*w*, 710*w*, 665*w*, 620*w*. ^{1}H-NMR: 8.05–7.95 (*m*, 1 arom. H); 7.85–7.8 (*m*, 2 arom. H); 7.5–7.4 (*m*, 4 arom. H); 6.67, 6.66 (2*q*, *J* = 6.8, CHN); 2.6–2.5 (*m*, CHCO, MeN); 1.9–1.7 (*m*, 1 H of CH_2); 1.60, 1.58 (2*d*, *J* = 6.8, *Me*CHN); 1.5–1.35 (*m*, 1 H of CH_2); 1.16, 1.09 (2*d*, *J* = 6.8, *Me*CHCO); 0.93, 0.87 (2*t*, *J* = 7.4, *Me*CH_2). ^{13}C-NMR: 175.7, 175.6 (2*s*, CO); 136.4, 136.3, 133.7, 131.9, 131.9 (5*s*, 3 arom. C); 128.4, 126.4, 126.4, 125.8, 124.7, 124.2, 124.1 (7*d*, 7 arom. CH); 47.7, 47.6 (2*d*, CHN); 38.0 (*d*, *C*HCO); 29.0, 29.0 (2*q*, MeN); 27.0, 26.9 (2*t*, CH_2); 17.3, 17.0, 15.8, 15.5, 12.0 (5*q*, *Me*CHN, *Me*CHCO, *Me*CH_2). CI-MS (NH_3): 271 (20), 270 (100, $[M+1]^+$). Anal. calc. for $C_{18}H_{23}NO$ (269.39): C 80.25, H 8.61, N 5.20; found: C 80.36, H 8.72, N 5.43.

*(*RS*)-*N*,2-Dimethyl*-N-*[(*R*)-1-(naphthalen-1-yl)ethyl]butanethioamide* (**9a**). To a soln. of **8a** (6.49 g, 24.1 mmol) in abs. toluene (30 ml), *Lawesson* reagent (5.86 g, 1.2 equiv.) was added, the mixture stirred for 17 h at 90° and 2 h at 110° and then cooled to r.t., the precipitate filtered and washed with Et_2O, and the filtrate evaporated. CC (hexane/AcOEt 10:1) yielded 6.06 g (88%) of **9a**. Pale yellow oil. Recrystallization from CH_2Cl_2, Et_2O, and hexane gave colorless crystals. M.p. 145.5–146.7°. R_f (hexane/AcOEt 5:1) 0.38 and 0.34, resp., for the diastereoisomers. IR: 2970*s*, 2920*s*, 2860*m*, 2840*m*, 1595*m*, 1505*m*, 1475*s*, 1455*s*, 1440*s*, 1405*s*, 1370*m*, 1350*w*, 1335*m*, 1320*s*, 1295*m*, 1270*m*, 1240*s*, 1170*m*, 1135*w*, 1110*m*, 1080*m*, 1045*m*, 1020*m*, 990*w*, 970*w*, 950*m*, 910*w*, 875*w*, 810*s*, 785*s*, 745*w*, 720*w*, 675*w*, 620*w*, 605*w*. ^{1}H-NMR: 8.0–7.9 (*m*, 1 arom. H); 7.85–7.8 (*m*, 2 arom. H); 7.6–7.45 (*m*, 4 arom. H, CHN); 2.85–2.75 (*m*, CHCS); 2.69 (*s*, MeN); 2.05–1.9 (*m*, 1 H of CH_2); 1.69, 1.68 (2*d*, *J* = 6.7, *Me*CHCS); 1.65–1.5 (*m*, 1 H of CH_2); 1.23, 1.21 (2*d*, *J* = 6.6, 6.5, *Me*CHN); 0.91, 0.87 (2*t*, *J* = 7.4, *Me*CH_2CS). ^{13}C-NMR: 209.4, 209.2 (2*s*, CS); 135.8, 135.7, 133.7, 132.1, 132.1 (5*s*, 3 arom. C); 129.0, 128.5, 126.8, 126.2, 125.3, 125.2, 125.0, 124.7, 124.6 (9*d*, 7 arom. CH); 56.9, 56.7 (2*d*, *C*HCS); 44.6, 44.4 (2*d*, CHN); 33.2, 33.1 (2*q*, MeN); 30.9, 30.3 (2*t*, CH_2); 21.1, 14.1, 13.8, 12.2, 12.1 (5*q*, *Me*CHCS, *Me*CHN, *Me*CH_2). CI-MS (NH_3): 287 (6), 286 (37, $[M+1]^+$), 133 (6), 132 (100, $[M-naphthCHCH_2+1]^+$). Anal. calc. for $C_{18}H_{23}NS$ (285.45): C 75.74, H 8.12, N 4.91; found: C 75.57, H 8.09, N 4.72.

*(*RS*)-2-Ethyl-2*,N*-*dimethyl*-N-*[(*R*)-1-(naphthalen-1-yl)ethyl]-2*H*-azirin-3-amine* (**4a**). To a soln. of **9a** (2.868 g, 10.05 mmol) and 3 drops of abs. DMF in abs. CH_2Cl_2 (20 ml) at 0°, 2N phosgene in toluene (6 ml, 12 mmol) was added, the mixture stirred for 40 min at 0°, and the solvent evaporated. The residue was dissolved in abs. THF (15 ml), DABCO (1.141 g, 10.17 mmol) was added, and the soln. was stirred for 25 min at 0°. After filtration, NaN_3 (1.314 g, 20.02 mmol) was added, the mixture stirred for 50 h at r.t. and then filtered over *Celite*,

and the filtrate evaporated. The residue was dissolved in CH_2Cl_2, washed twice with aq. $NaHCO_3$ soln. and once with sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated. CC (hexane/AcOEt 2:1) yielded 1.544 g (58%) of **4a** as pale yellow oil. The two diastereoisomers were separated by repeated MPLC (AcOEt): 0.674 g of (1′*R*,2*S*)-**4a** (R_f (hexane/AcOEt 1:1) 0.33) as colorless crystals and 0.705 g of (1′*R*,2*R*)-**4a** (R_f 0.29) as an oil, from which it was possible to grow crystals for X-ray crystal-structure determination.

*Data of (1′*R,2S*)*-**4a**: M.p. 63–64°. IR: 3440*m*, 3060*m*, 3040*m*, 2960*s*, 2910*m*, 2870*m*, 1825*w*, 1760*s*, 1715*m*, 1695*m*, 1680*w*, 1670*w*, 1660*w*, 1645*w*, 1630*w*, 1620*w*, 1610*w*, 1600*m*, 1570*w*, 1550*w*, 1530*w*, 1505*m*, 1485*w*, 1460*m*, 1450*m*, 1410*m*, 1395*w*, 1370*m*, 1340*w*, 1320*m*, 1265*m*, 1255*m*, 1235*m*, 1200*m*, 1165*m*, 1120*w*, 1105*m*, 1085*m*, 1040*m*, 1000*m*, 975*w*, 960*w*, 925*m*, 870*w*, 860*w*, 805*w*, 785*s*, 755*w*, 745*w*, 720*m*, 695*w*, 660*w*, 650*w*, 640*w*, 610*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO, 350 K): 8.1–8.05 (*m*, H–C(8)(naphth)); 7.95–7.9 (*m*, H–C(5)(naphth)); 7.9–7.85 (*m*, H–C(4)(naphth)); 7.55–7.5 (*m*, 4 H(naphth)); 5.48 (*q*, *J* = 6.9, CHN); 2.76 (*s*, MeN); 1.70 (*d*, *J* = 6.9, *Me*CHN); 1.65–1.45 (*m*, CH_2); 0.98 (*s*, Me–C(2)); 0.76 (*t*, *J* = 7.5, *Me*CH_2). ^{13}C-NMR (75.5 MHz, (D_6)DMSO, 350 K): 165.2 (*s*, C(3)); 135.6 (*s*, C(1)(naphth)); 133.2 (*s*, C(4a)(naphth)); 130.6 (*s*, C(8a)-(naphth)); 128.2 (*d*, CH(5)(naphth)); 127.7 (*d*, CH(4)(naphth)); 125.6, 125.1, 124.6, 123.4 (4*d*, 4 CH(naphth)); 122.6 (*d*, CH(8)(naphth)); 53.7 (*d*, CHN); 42.9 (*s*, C(2)); 32.2 (*q*, MeN); 29.4 (*t*, CH_2); 22.6 (*q*, *Me*–C(2)); 17.0 (*q*, *Me*CHN); 8.9 (*q*, *Me*CH_2). CI-MS (NH_3): 268 (20), 267 (100, $[M+1]^+$), 265 (6), 209 (6), 111 (6). Anal. calc. for $C_{18}H_{22}N_2$ (266.39): C 81.16, H 8.32, N 10.52; found: C 81.21, H 8.37, N 10.73.

*Data of (1′*R,2R*)*-**4a**: M.p. 90–91°. IR: 3060*w*, 3040*w*, 2960*s*, 2930*m*, 2900*m*, 2870*m*, 1825*w*, 1760*s*, 1645*w*, 1600*m*, 1555*w*, 1545*w*, 1505*m*, 1460*m*, 1450*m*, 1410*m*, 1395*w*, 1370*m*, 1340*w*, 1320*m*, 1270*m*, 1250*m*, 1235*m*, 1200*m*, 1160*m*, 1100*m*, 1085*m*, 1040*m*, 1010*w*, 990*w*, 980*w*, 960*w*, 925*w*, 870*w*, 855*w*, 810*s*, 785*s*, 745*w*, 725*w*, 695*w*, 640*w*, 610*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO, 350 K): 8.1–8.05 (*m*, H–C(8)(naphth)); 7.95–7.9 (*m*, H–C(5)(naphth)); 7.88 (*d*, *J* = 7.7, H–C(4)(naphth)); 7.6–7.5 (*m*, 1 H(naphth)); 5.48 (*q*, *J* = 6.9, CHN); 2.78 (*s*, MeN); 1.71 (*d*, *J* = 6.9, *Me*CHN); 1.55–1.25 (*m*, CH_2); 1.21 (*s*, Me–C(2)); 0.60 (*t*, *J* = 7.5, *Me*CH_2). ^{13}C-NMR (75.5 MHz, (D_6)DMSO, 350 K): 165.3 (*s*, C(3)); 135.5 (*s*, C(1)(naphth)); 133.2 (*s*, C(4a)(naphth)); 130.5 (*s*, C(8a)(naphth)); 128.1 (*d*, CH(5)(naphth)); 127.7 (*d*, CH(4)(naphth)); 125.6, 125.1, 124.6, 123.5 (4*d*, 4 CH(naphth)); 122.6 (*d*, CH(8)(naphth)); 53.7 (*d*, CHN); 42.8 (*s*, C(2)); 32.1 (*q*, MeN); 29.3 (*t*, CH_2); 23.1 (*q*, *Me*–C(2)); 16.9 (*q*, *Me*CHN); 8.8 (*q*, *Me*CH_2). CI-MS (NH_3): 269 (6), 268 (20), 267 (100, $[M+1]^+$), 227 (6), 184 (8). Anal. calc. for $C_{18}H_{22}N_2$ (266.39): C 81.16, H 8.32, N 10.52; found: C 80.95, H 8.05, N 10.52.

2.3. *Val(2Me) Synthon. (*RS*)-*N*,2,3-Trimethyl*-N*-[(*R*)-1-(naphthalen-1-yl)ethyl]butanamide* (**8b**). Within 10 min, a soln. of 2N LDA (6 ml, 12 mmol) was added to a soln. of **7** (2.802 g, 11.61 mmol) and $LiClO_4$ (1.243 g, 11.68 mmol) in abs. THF (30 ml) at −78°, and the mixture was stirred for 35 min at −78°. Then, ^{i}PrI (1.4 ml, 2.4 g, 14 mmol) was added at −78°. After 1 h, the mixture was warmed to r.t. and stirred for 2 h. As TLC showed unconsumed **7**, another portion of ^{i}PrI (0.5 ml, 5 mmol) was added. Then, the mixture was cooled to −78° and 2N LDA (2 ml, 4 mmol) was added. After 45 min, the mixture was warmed to r.t. and stirred for further 30 min. The resulting soln. was carefully poured on ice, neutralized with 1N HCl (keeping the mixture still slightly basic), extracted with Et_2O, dried ($MgSO_4$), and evaporated. CC (hexane/AcOEt 5:1) yielded 3.064 g (93%) of **8b**. Pale yellow solid. M.p. 94.5–94.7°. R_f (hexane/AcOEt 1:1) 0.55 and 0.49, resp., for the diastereoisomers. IR: 3040*m*, 2960*s*, 2930*s*, 2870*m*, 1930*w*, 1820*w*, 1620*s*, 1615*s*, 1550*w*, 1510*m*, 1480*s*, 1470*s*, 1460*s*, 1450*s*, 1405*s*, 1385*m*, 1370*m*, 1350*m*, 1325*m*, 1280*m*, 1260*m*, 1240*m*, 1210*m*, 1180*m*, 1170*m*, 1140*w*, 1125*w*, 1105*s*, 1075*m*, 1040*m*, 1025*m*, 980*m*, 970*w*, 920*w*, 910*w*, 890*w*, 870*w*, 800*m*, 785*s*, 765*m*, 750*w*, 720*w*, 665*w*, 640*w*, 625*w*. ^{1}H-NMR: 8.1–8.0 (*m*, 1 arom. H); 7.85–7.8 (*m*, 2 arom. H); 7.55–7.45 (*m*, 4 arom. H); 6.7–6.65 (*m*, CHN); 2.50, 2.49 (2*s*, MeN); 2.35–2.3 (*m*, CHCO); 2.05–1.95 (*m*, Me_2CH); 1.61, 1.58 (2*d*, *J* = 6.6, 6.8, *Me*CHN); 1.13, 1.09 (2*d*, *J* = 6.8, *Me*CHCO); 0.96, 0.93, 0.88 (3*d*, *J* = 6.7, 6.8, 6.6, Me_2CH). ^{13}C-NMR: 175.9, 175.7 (2*s*, CO); 136.3, 133.6, 131.9 (3*s*, 3 arom. C); 128.4, 126.4, 126.3, 125.9, 124.7, 124.4, 124.2 (7*d*, 7 arom. CH); 47.7, 47.6, 43.2, 43.1 (4*d*, CHN, *C*HCO); 31.3, 30.4 (2*d*, Me_2*C*H); 29.3, 29.1 (2*q*, MeN); 21.7, 21.5, 19.4, 19.0 (4*q*, *Me*CHN, *Me*CHCO); 15.8, 15.4, 15.3, 14.4 (4*q*, Me_2CH). CI-MS (NH_3): 285 (20), 284 (100, $[M+1]^+$). Anal. calc. for $C_{19}H_{25}NO$ (283.41): C 80.52, H 8.89, N 4.94; found: C 80.79, H 8.74, N 4.94.

*(*RS*)-*N*,2,3-Trimethyl*-*N*-[(*R*)-1-(naphthalen-1-yl)ethyl]butanethioamide* (**9b**). To a soln. of **8b** (3.842 g, 13.56 mmol) in abs. toluene (15 ml), *Lawesson* reagent (3.295 g, 8.147 mmol, 1.2 equiv.) was added, and the mixture was stirred for 62 h at 110°. After cooling to r.t., the precipitate was filtered and washed with Et_2O and the filtrate evaporated. Twice repeated CC (hexane/AcOEt 10:1) yielded 3.032 g (75%) of **9b** as a pale yellow oil and 0.433 g (13%) of starting **8b**. **9b**: R_f (hexane/AcOEt 10:1) 0.30 and 0.25, resp., for the diastereoisomers. IR ($CHCl_3$): 3060*w*, 2960*s*, 2870*w*, 1600*w*, 1505*m*, 1480*s*, 1460*m*, 1445*m*, 1405*s*, 1385*w*, 1370*m*, 1330*m*, 1260*m*, 1245*m*, 1170*w*, 1110*w*, 1075*m*, 1045*w*, 1000*w*, 960*w*, 920*w*, 910*w*, 865*w*, 850*w*, 840*w*. ^{1}H-NMR: 8.05–7.95 (*m*, 1 arom. H); 7.85–7.8 (*m*, 2 arom. H); 7.6–7.45 (*m*, 4 arom. H, CHN); 2.70 (*s*, MeN); 2.65–2.5 (*m*, CHCS); 2.35–2.25 (*m*, Me_2CH); 1.7–1.6 (*m*, *Me*CHN); 1.25–1.2 (*m*, *Me*CHCS); 1.0–0.95, 0.9–0.85 (2*m*, Me_2CH).

^{13}C-NMR: 209.6, 209.3 (2*s*, CS); 135.8, 135.6, 133.6, 133.6, 132.1, 131.9 (6*s*, 3 arom. C); 128.9, 128.5, 128.4, 126.8, 126.7, 126.1, 126.1, 125.3, 125.2, 125.0, 124.9, 124.7, 124.6 (13*d*, 7 arom. C); 56.7, 56.5, 50.2, 50.0 (4*d*, CHN, *C*HCS); 35.0, 33.3 (2*d*, Me_2*C*H); 33.5 (*q*, MeN); 22.0, 21.5 (2*q*, *Me*CHN); 20.9, 19.7, 19.4, 19.1, 14.0, 13.6 (6*q*, *Me*CHCS, Me_2CH). CI-MS (NH_3): 302 (5), 301 (20), 300 (100, $[M+1]^+$), 146 (8). Anal. calc. for $C_{19}H_{25}NS$ (299.48): C 76.20, H 8.41, N 4.68; found: C 76.26, H 8.60, N 4.68.

*(*RS*)-2-Isopropyl-2,*N*-dimethyl-*N*-[(*R*)-1-(naphthalen-1-yl)ethyl]-2*H*-azirin-3-amine* (**4b**). To a soln. of **9b** (4.130 g, 13.79 mmol) and 4 drops of abs. DMF in abs. CH_2Cl_2 (13 ml), 2N phosgene in toluene (8.5 ml, 19 mmol) was added at 0°. The mixture was stirred for 25 min at 0° and 30 min at r.t. and the solvent evaporated. The residue was dissolved in abs. THF (15 ml), DABCO (1.575 g, 14.04 mmol) was added, and the soln. was stirred for 20 min at 0°. After filtration, NaN_3 (1.803 g, 27.74 mmol) was added, the mixture stirred for 27 h at r.t. and then filtered over *Celite*, the filter cake washed with Et_20, the filtrate evaporated. The residue was dissolved in CH_2Cl_2, washed with aq. $NaHCO_3$ soln. (2×) and sat. aq. NaCl soln. (1×), dried ($MgSO_4$), and evaporated. CC (hexane/AcOEt 3:1) and MPLC (AcOEt) gave 2.040 g (53%) of **4b**, *i.e.* 787 mg of crystalline (1′*R*,2*S*)-**4b** (R_f (hexane/AcOEt 1:1) 0.33), 1172 mg of (1′*R*,2*R*)-**4b** (R_f 0.29) as a pale yellow oil, and 81 mg of (1′*R*,2*S*)/(1′*R*,2*R*)-**4b** (pale yellow oil). The structure of (1′*R*,2*S*)-**4b** was determined by X-ray crystallography.

*Data of (1′*R*,2*S*)-***4b***: M.p. 92–92.5°. IR: 3432*w*, 3044*w*, 2957*s*, 2936*m*, 1764v*s*, 1597*w*, 1510*w*, 1458*m*, 1410*w*, 1381*w*, 1368*m*, 1318*w*, 1236*w*, 1199*m*, 1138*w*, 1098*w*, 1052*s*, 1008*w*, 949*w*, 810v*s*, 786*s*, 726*w*, 614*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO, 373 K): 8.1–8.05 (*m*, 1 arom. H); 7.95–7.85 (*m*, 2 arom. H); 7.6–7.5 (*m*, 4 arom. H); 5.56 (*q*, *J* = 6.9, CHN); 2.69 (*s*, MeN); 1.80 (*sept.*, *J* = 6.8, Me_2CH); 1.72 (*d*, *J* = 6.9, *Me*CHN); 1.09 (*s*, Me–C(2)); 0.89, 0.81 (2*d*, *J* = 6.8, Me_2CH). ^{13}C-NMR (75.5 MHz, (D_6)DMSO, 373 K): 165.1 (*s*, C(3)); 135.3, 133.1, 130.6 (3*s*, 3 arom. C); 128.1, 127.7, 125.5, 125.1, 124.5, 123.6, 122.6 (7*d*, 7 arom. CH); 53.0 (*d*, CHN); 46.0 (*s*, C(2)); 33.1 (*d*, $(Me)_2$CH); 32.0 (*q*, MeN); 20.6 (*q*, *Me*–C(2)); 18.7, 18.0 (2*q*, Me_2CH); 17.0 (*q*, *Me*CHN). ESI-MS (MeOH): 363 (10), 313 (65, $[M+MeOH+1]^+$), 281 (100, $[M+1]^+$), 155 (12, $[naphthCHMe]^+$). Anal. calc. for $C_{18}H_{23}NO$ (269.39): C 81.38, H 8.63, N 9.99; found: C 81.12, H 8.70, N 9.87.

*Data of (1′*R*,2*R*)-***4b***: IR: 3434*w*, 3050*w*, 2960*s*, 2870*m*, 1760v*s*, 1599*w*, 1510*w*, 1454*m*, 1412*w*, 1376*w*, 1321*w*, 1239*w*, 1196*m*, 1170*w*, 1102*w*, 1082*w*, 1047*m*, 982*w*, 944*w*, 864*w*, 804*m*, 780v*s*, 726*w*, 696*w*, 631*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO, 373 K): 8.15–8.1 (*m*, 1 arom. H); 7.95–7.85 (*m*, 2 arom. H); 7.65–7.5 (*m*, 4 arom. H); 5.55 (*q*, *J* = 6.9, CHN); 2.72 (*s*, MeN); 1.73 (*d*, *J* = 6.9, *Me*CHN); 1.75–1.65 (*m*, Me_2CH); 1.21 (*s*, Me–C(2)); 0.84, 0.74 (2*d*, *J* = 6.8, 6.9, Me_2CH). ^{13}C-NMR (75.5 MHz, (D_6)DMSO, 373 K): 165.1 (*s*, C(3)); 135.3, 133.1, 130.5 (3*s*, 3 arom. C); 128.0, 127.6, 125.5, 125.0, 124.5, 123.6, 122.6 (7*d*, 7 arom. CH); 53.1 (*d*, CHN); 45.9 (*s*, C(2)); 33.2 (*d*, Me_2*C*H); 31.7 (*q*, MeN); 20.9 (*q*, *Me*–C(2)); 18.7, 18.0 (2*q*, Me_2CH); 16.4 (*q*, *Me*CHN). CI-MS (NH_3): 326 (6), 282 (21), 281 (100, $[M+1]^+$), 155 (15, $[naphthCHMe]^+$).

2.4. *Ala(2cPent) Synthon. (*RS*)-2-Cyclopentyl-*N*-methyl-*N*-[(*R*)-1-(naphthalen-1-yl)ethyl]propanamide* (**8c**). Within 20 min, a soln. of 2N LDA (17.5 ml, 35 mmol) was added to a soln. of **7** (6.999 g, 29.002 mmol) and $LiClO_4$ (3.088 g, 29.025 mmol) in abs. THF (70 ml) at 0°, and the mixture was stirred for 7 min at 0°. Then, cyclopentyl bromide (3.1 ml, 4.3 g, 28.9 mmol) was added at 0° within 20 min. After 3 h, the mixture was warmed to r.t. and stirred for 2 h. TLC showed still unconsumed **7**. The mixture was stored at 4° for 18 h, then poured carefully on ice, extracted with Et_2O, dried ($MgSO_4$), and evaporated. CC (hexane/AcOEt 5:1) yielded 3.921 g (44%) of **8c** as a colorless oil and 2.859 g (41%) of starting **7**. **8c**: R_f (hexane/AcOEt 2:1) 0.47 and 0.38, resp., for the diastereoisomers. IR (neat): 3049*w*, 2955v*s*, 2868*m*, 1738*w*, 1634v*s*, 1511*m*, 1461*s*, 1403*s*, 1372*m*, 1277*m*, 1240*m*, 1170*w*, 1110*m*, 1087*w*, 1044*m*, 806*s*, 782v*s*, 724*w*, 671*w*, 629*w*. ^{1}H-NMR: 8.05–8.0 (*m*, 1 arom. H); 7.85–7.8 (*m*, 2 arom. H); 7.55–7.45 (*m*, 4 arom. H); 6.7–6.65 (*m*, CHN); 2.50 (*s*, MeN); 2.45–2.2 (*m*, 2 H); 1.95–1.8 (*m*, 2 H); 1.60, 1.58 (2*d*, *J* = 6.1, 6.7, *Me*CHN); 1.55–1.5 (*m*, 4 H); 1.16, 1.10 (2*d*, *J* = 6.7, *Me*CHCO); 1.15–0.9 (*m*, 1 H). ^{13}C-NMR: 175.9, 175.8 (2*s*, CO); 136.5, 136.3, 133.6, 132.0, 131.9 (5*s*, 3 arom. C); 128.4, 128.3, 126.4, 126.3, 125.8, 124.7, 124.4, 124.2 (8*d*, 7 arom. CH); 47.6, 47.5, 43.8, 43.2, 42.0 (5*d*, CHN, *C*HCO, CH(cPent)); 31.5, 31.4, 30.2, 30.1, 25.1, 25.0 (6*t*, 4 CH_2); 29.2, 29.1 (2*q*, MeN); 16.8, 16.4, 15.8, 15.4 (4*q*, 2 Me). CI-MS (NH_3): 311 (23), 310 (100, $[M+1]^+$). Anal. calc. for $C_{21}H_{27}NO$ (309.45): C 81.51, H 8.79, N 4.53; found: C 81.28, H 8.59, N 4.50.

*(*RS*)-2-Cyclopentyl-*N*-methyl-*N*-[(*R*)-1-(naphthalen-1-yl)ethyl]propanethioamide* (**9c**). To a soln. of **8c** (3.703 g, 11.966 mmol) in abs. toluene (10 ml), *Lawesson* reagent (2.903 g, 7.177 mmol, 1.2 equiv.) was added, the mixture stirred for 7 h at 130° and then cooled to r.t., the precipitate filtered and washed with Et_2O, and the filtrate evaporated. CC (hexane/AcOEt 10:1) yielded 2.242 g (58%) of **9c** as colorless oil and 1.436 g (39%) of starting **8c**. **9c**: R_f (hexane/AcOEt 5:1) 0.41 and 0.26, resp., for the diastereoisomers. IR (neat): 3048*m*, 2950*s*, 2866*s*, 1934*w*, 1820*w*, 1736*m*, 1598*m*, 1510*s*, 1478*s*, 1406v*s*, 1371*s*, 1320*s*, 1240*s*, 1173*m*, 1111*s*, 1073*s*, 1045*s*, 990*m*, 970*m*, 930*m*, 868*w*, 805*s*, 780v*s*, 726*w*, 695*m*, 642*w*. ^{1}H-NMR: 8.0–7.95 (*m*, 1 arom. H); 7.85–7.8 (*m*, 2 arom. H); 7.6–7.55 (*m*, CHN); 7.55–7.45 (*m*, 4 arom. H); 2.8–2.45 (*m*, 2 H); 2.71, 2.69 (2*s*, MeN); 2.35–1.85 (*m*, 2 H);

1.69, 1.68 (2*d*, *J* = 6.6, 6.7, Me); 1.65–1.45 (*m*, 4 H); 1.24, 1.23 (2*d*, *J* = 6.5, 6.2, Me); 1.2–0.75 (*m*, 2 H). ^{13}C-NMR: 209.3, 209.2 (2*s*, CS); 135.9, 135.5, 133.6, 132.0 (4*s*, 3 arom. C); 128.9, 128.4, 128.3, 126.7, 126.1, 125.2, 125.1, 124.9, 124.8, 124.6 (10*d*, 7 arom. C); 56.7, 56.4, 49.3, 49.0, 47.6, 46.2 (6*d*, 3 CH); 33.2 (*q*, MeN); 31.8, 31.5, 30.5, 25.2, 25.1 (5*t*, 4 CH_2); 20.6, 20.3, 14.0, 13.6 (4*q*, 2 Me). CI-MS (NH_3): 327 (16), 326 (100, $[M+1]^+$), 172 (9, $[M-\text{naphthCHCH}_2+1]^+$). Anal. calc. for $C_{21}H_{27}NS$ (325.52): C 77.49, H 8.39, N 4.30, S 9.85; found: C 77.37, H 8.25, N 4.25, S 9.69.

*(*RS*)-2-Cyclopentyl-2,*N*-dimethyl-*N*-[(*R*)-1-(naphthalen-1-yl)ethyl]-2*H*-azirin-3-amine* (**4c**). To a soln. of **9c** (2.097 g, 6.442 mmol) and 3 drops of abs. DMF in abs. CH_2Cl_2 (10 ml) at 0°, 2N phosgene soln. in toluene (4.2 ml, 8.4 mmol) was added, stirred for 15 min at 0° and 10 min at r.t., and evaporated. The residue was dissolved in abs. THF (10 ml), DABCO (0.729 g, 6.498 mmol) was added, and the soln. was stirred for 20 min at 0°. Then, NaN_3 (0.848 g, 13.046 mmol) was added, the mixture stirred for 8 h at r.t. and then filtered over *Celite*, the filter cake washed with Et_2O, and the filtrate evaporated. CC (hexane/AcOEt 2:1) followed by MPLC (AcOEt) yielded 0.415 g of crystalline (1′*R*,2*S*)-**4c** (R_f (hexane/AcOEt 1:1) 0.28) and 0.818 g (1′*R*,2*R*)-**4c** (R_f 0.23) as a pale yellow oil. Total yield of **4c**: 1.233 g (62%). The structure of (1′*R*,2*S*)-**4c** was determined by X-ray crystallography.

*Data of (1′*R*,2*S*)-***4c***: M.p. 95–96°. IR: 3046*w*, 2956*s*, 2867*m*, 1764v*s*, 1597*w*, 1510*w*, 1443*w*, 1410*w*, 1319*w*, 1236*w*, 1197*m*, 1100*w*, 1055*s*, 1025*w*, 903*w*, 810*s*. ^{1}H-NMR (300 MHz, (D_6)DMSO, 373 K): 8.1–8.05 (*m*, 1 arom. H); 7.95–7.85 (*m*, 2 arom. H); 7.6–7.5 (*m*, 4 arom. H); 5.52 (*q*, *J* = 6.8, CHN); 2.71 (*s*, MeN); 2.15–2.05 (*m*, CH); 1.72 (*d*, *J* = 6.9, *Me*CHN); 1.7–1.45, 1.4–1.25, 1.2–1.1 (3*m*, 4 CH_2); 1.06 (*s*, Me–C(2)). ^{13}C-NMR (75.5 MHz, (D_6)DMSO, 373 K): 165.1 (*s*, C(3)); 135.4, 133.1, 130.6 (3*s*, 3 arom. C); 128.1, 127.7, 125.5, 125.1, 124.5, 123.6, 122.6 (7*d*, 7 arom. CH); 53.2 (*d*, CHN); 45.2 (*d*, CH); 44.6 (*s*, C(2)); 32.0 (*q*, MeN); 28.4, 28.0, 24.4, 24.3 (4*t*, 4 CH_2); 22.1 (*q*, *Me*–C(2)); 16.7 (*q*, *Me*CHN). ESI-MS (MeOH): 635 (7, $[2M+\text{Na}]^+$), 419 (8), 339 (32, $[M+\text{MeOH}]^+$), 329 (100, $[M+\text{Na}]^+$), 307 (66, $[M+1]^+$), 155 (25, [naphthCHMe]$^+$), 153 (27). Anal. calc. for $C_{21}H_{26}N_2$ (306.45): C 82.31, H 8.55, N 9.14; found: C 82.49, H 8.21, N 9.12.

*Data of (1′*R*,2*R*)-***4c***: IR (neat): 3049*w*, 2949*s*, 2866*m*, 1759v*s*, 1598*w*, 1510*w*, 1450*w*, 1413*w*, 1374*w*, 1319*w*, 1239*w*, 1196*w*, 1102*w*, 1056*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO, 373 K): 8.15–8.1 (*m*, 1 arom. H); 7.95–7.85 (*m*, 2 arom. H); 7.6–7.5 (*m*, 4 arom. H); 5.52 (*q*, *J* = 6.8, CHN); 2.74 (*s*, MeN); 2.0–1.9 (*m*, CH); 1.72 (*d*, *J* = 6.9, *Me*CHN); 1.65–1.6, 1.55–1.25, 1.2–1.0 (3*m*, 4 CH_2); 1.23 (*s*, Me–C(2)). ^{13}C-NMR (75.5 MHz, (D_6)DMSO, 373 K): 165.2 (*s*, C(3)); 135.4, 133.1, 130.5 (3*s*, 3 arom. C); 128.0, 127.6, 125.5, 125.0, 124.5, 123.6, 122.6 (7*d*, 7 arom. CH); 53.3 (*d*, CHN); 45.2 (*d*, CH); 44.4 (*s*, C(2)); 31.8 (*q*, MeN); 28.4, 28.0, 24.3, 24.2 (4*t*, 4 CH_2); 22.5 (*q*, *Me*–C(2)); 16.6 (*q*, *Me*CHN). ESI-MS (MeOH + NaI): 330 (24, $[M+\text{Na}+1]^+$), 329 (100, $[M+\text{Na}]^+$), 155 (4, [naphthCHMe]$^+$). Anal. calc. for $C_{21}H_{26}N_2$ (306.45): C 82.31, H 8.55, N 9.14; found: C 82.07, H 8.25, N 9.22.

2.5. *Leu(2Me) Synthon. (*RS*)-*N*,2,4-Trimethyl-*N*-[(*R*)-1-(naphthalen-1-yl)ethyl]pentanamide* (**8d**). Within 10 min, a soln. of 2N LDA (21 ml, 42 mmol) was added to a soln. of **7** (8.291 g, 34.355 mmol) and $LiClO_4$ (3.656 g, 34.36 mmol) in abs. THF (80 ml) at −78°, and the resulting mixture was stirred for 25 min at −78°. Then, ^{i}BuI (5 ml, 7.9 g, 43 mmol) was added at −78° and the mixture slowly warmed to −20° (7 h) and stored overnight at −30°. The soln. was poured carefully on ice, extracted with Et_2O, dried ($MgSO_4$), and evaporated. CC (hexane/AcOEt 5:1, then 2:1) yielded 8.382 g (82%) of **8d** as a colorless solid and 1.322 g (16%) of starting **7**. After recrystallization (CH_2Cl_2, AcOEt, hexane) of an aliquot of **8d**, colorless crystals were obtained. M.p. 131.4–132.0°. R_f (hexane/AcOEt 1:1) 0.56 and 0.50, resp., for the diastereoisomers. IR: 3080*w*, 3060*w*, 3040*m*, 2950*m*, 2930*m*, 2900*m*, 2860*m*, 1960*w*, 1940*w*, 1830*w*, 1680*w*, 1640*m*, 1630*s*, 1595*m*, 1550*w*, 1530*w*, 1510*m*, 1470*s*, 1460*s*, 1455*m*, 1445*m*, 1430*m*, 1400*m*, 1385*m*, 1370*m*, 1350*m*, 1340*m*, 1325*m*, 1285*m*, 1235*m*, 1210*m*, 1175*m*, 1165*m*, 1130*w*, 1110*s*, 1080*m*, 1040*m*, 1025*m*, 1010*w*, 980*w*, 960*w*, 915*w*, 880*w*, 810*s*, 785*s*, 755*w*, 730*w*, 660*w*, 620*w*. ^{1}H-NMR: 8.0–7.95 (*m*, 1 arom. H); 7.85–7.8 (*m*, 2 arom. H); 7.55–7.45 (*m*, 4 arom. H); 6.7–6.65 (*m*, CHN); 2.75–2.65 (*m*, CHCO); 2.50, 2.50 (2*s*, MeN); 1.8–1.6, 1.3–1.05, 0.9–0.75 (3*m*, 15 H, Me_2CHCH_2CHMe, *Me*CHN). ^{1}H-NMR (only 1 diastereoisomer, R_f 0.56): 8.0–7.95 (*m*, 1 arom. H); 7.85–7.8 (*m*, 2 arom. H); 7.55–7.45 (*m*, 4 arom. H); 6.66 (*q*, *J* = 6.8, CHN); 2.75–2.65 (*m*, CHCO); 2.51 (*s*, MeN); 1.8–1.7 (*m*, CH_2); 1.60 (*d*, *J* = 6.9, *Me*CHCO); 1.3–1.25 (*m*, Me_2CH); 1.07 (*d*, *J* = 6.8, *Me*CHN); 0.91, 0.90 (2*d*, *J* = 6.5, Me_2CH). ^{13}C-NMR: 176.0 (*s*, CO); 136.5, 133.7, 132.0 (3*s*, 3 arom. C); 128.5, 126.5, 126.4, 125.9, 124.8, 124.2 (6*d*, 7 arom. CH); 47.8 (*d*, CHN); 43.2, 43.0 (2*t*, CH_2); 34.2, 34.1 (2*d*, *C*HCO); 29.1 (*q*, MeN); 25.9, 25.7 (2*d*, Me_2CH); 22.9, 22.7 (2*q*, Me_2CH); 17.9, 17.5, 15.8, 15.6 (4*q*, *Me*CH, *Me*CH_2). ^{13}C-NMR (only 1 diastereoisomer, R_f 0.56): 175.9 (*s*, CO); 136.4, 133.7, 131.9 (3*s*, 3 arom. C); 128.4, 126.4, 125.8, 124.7, 124.2 (5*d*, 7 arom. CH); 47.7 (*d*, CHN); 43.0 (*t*, CH_2); 34.1 (*d*, *C*HCO); 29.0 (*q*, MeN); 25.9 (*d*, Me_2CH); 22.8, 22.6 (2*q*, Me_2CH); 17.8, 15.7 (2*q*, *Me*CH, *Me*CH_2). CI-MS (NH_3): 299 (20), 298 (100, $[M+1]^+$). Anal. calc. for $C_{20}H_{27}NO$ (297.44): C 80.76, H 9.15, N 4.71; found: C 80.80, H 8.98, N 4.73.

*(*RS*)*-N,*2,4-Trimethyl*-N-*[(*R*)-1-(naphthalen-1-yl)ethyl]pentanethioamide* (**9d**). To a soln. of **8d** (2.516 g, 8.459 mmol) in abs. toluene (15 ml), *Lawesson* reagent (2.134 g, 10.55 mmol) was added, the mixture stirred for 18 h at 110°, cooled to r.t. and filtered, the precipitate washed with Et_2O, and the filtrate evaporated. CC (hexane/AcOEt 10:1) yielded 2.614 g (99%) of **9d**. Recrystallization from hexane/Et_2O gave colorless crystals. M.p. 123.4–124.3°. R_f (hexane/AcOEt 5:1) 0.41 and 0.35, resp., for the diastereoisomers. IR ($CHCl_3$): 2960*s*, 2930*s*, 2860*m*, 2450*w*, 2420*w*, 2390*w*, 1600*w*, 1505*m*, 1480*s*, 1445*s*, 1405*s*, 1385*m*, 1370*m*, 1350*w*, 1320*m*, 1290*m*, 1260*m*, 1250*m*, 1170*m*, 1140*w*, 1110*m*, 1075*m*, 1060*m*, 1050*m*, 1040*m*, 1025*w*, 985*m*, 970*w*, 955*w*, 920*w*, 900*w*, 865*w*, 845*w*. ^{1}H-NMR: 7.95–7.8 (*m*, 3 arom. H); 7.6–7.45 (*m*, 4 arom. H, CHN); 3.05–3.0 (*m*, CHCS); 2.70 (*s*, MeN); 1.85–0.65 (*m*, 15 H, Me_2CHCH_2CH*Me*, *Me*CHN). ^{13}C-NMR: 209.1, 208.9 (2*s*, CS); 135.4, 133.2, 131.7 (3*s*, 3 arom. C); 128.5, 128.1, 126.4, 125.7, 124.8, 124.6, 124.2, 124.1 (8*d*, 7 arom. CH); 56.4, 56.3 (2*d*, CHN); 46.3 (*t*, CH_2); 40.1 (*d*, *C*HCS); 32.6 (*q*, MeN); 25.2, 25.0 (2*d*, Me_2*C*H); 22.6, 22.2, 22.0, 20.9, 20.7, 13.5, 13.3 (7*q*, *Me*$_2$CHCH$_2$*Me*, *Me*CHN). CI-MS (NH_3): 315 (19), 314 (100, $[M+1]^+$), 169 (7), 160 (25), 155 (7, [naphthCHMe]$^+$). Anal. calc. for $C_{20}H_{27}NS$ (313.51): C 76.62, H 8.68, N 4.47, S 10.23; found: C 76.88, H 8.52, N 4.57, S 10.27.

*(*RS*)-2-Isobutyl-2,*N*-dimethyl*-N-*[(*R*)-1-(naphthalen-1-yl)ethyl]-2*H*-azirin-3-amine* (**4d**). To a soln. of **9d** (1.756 g, 5.601 mmol) and 4 drops of abs. DMF in abs. CH_2Cl_2 (8 ml), 2N phosgene soln. in toluene (3.4 ml, 6.8 mmol) was added at 0°. The soln. was stirred for 10 min at 0° and 30 min at r.t. and evaporated. The residue was dissolved in abs. THF (8 ml), DABCO (0.633 g, 5.643 mmol) was added, and the soln. was stirred for 1.5 h at 0°. After filtration, NaN_3 (0.733 g, 11.277 mmol) was added, the mixture stirred for 22 h at r.t. and then filtered over *Celite*, and the filtrate evaporated. The residue was dissolved in CH_2Cl_2, washed with aq. $NaHCO_3$ soln. (2×) and sat. aq. NaCl soln. (1×), dried ($MgSO_4$), and evaporated. CC (hexane/AcOEt 3:1) yielded 0.921 g (56%) of **4d** as a pale yellow oil. A diastereoisomer mixture (1.7 g) was separated by repeated CC (hexane/AcOEt 3:1): 0.768 g of (1′*R*,2*S*)-**4d** as colorless crystals (R_f (hexane/AcOEt 1:1) 0.36) and 0.755 g (1′*R*,2*R*)-**4d** as a pale yellow oil (R_f 0.31). The structure of (1′*R*,2*S*)-**4d** was determined by X-ray crystallography.

*Data of (1′*R,2S*)-***4d***: M.p. 73.6–74.1°. IR: 3070*w*, 3040*m*, 2960*s*, 2960*s*, 2905*m*, 2870*m*, 1755*s*, 1600*w*, 1510*m*, 1465*m*, 1450*m*, 1445*m*, 1410*w*, 1385*m*, 1380*m*, 1365*m*, 1315*m*, 1270*m*, 1260*w*, 1235*m*, 1195*m*, 1160*m*, 1130*w*, 1110*w*, 1095*w*, 1050*s*, 1015*w*, 960*w*, 940*w*, 920*w*, 810*s*, 785*s*, 725*w*, 650*w*, 625*w*, 615*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO, 373 K): 8.1–8.05 (*m*, 1 arom. H); 7.95–7.85 (*m*, 2 arom. H); 7.55–7.5 (*m*, 4 arom. H); 5.48 (*q*, *J* = 6.9, CHN); 2.74 (*s*, MeN); 1.69 (*d*, *J* = 6.9, *Me*CHN); 1.65–1.6 (*m*, Me_2CH); 1.58 (*dd*, *J* = 14.0, 6.1, 1 H of CH_2); 1.29 (*dd*, *J* = 13.5, 5.5, 1 H of CH_2); 0.98 (*s*, Me–C(2)); 0.91, 0.89 (2*d*, *J* = 7.1, 6.6, Me_2CH). ^{13}C-NMR (75.5 MHz, (D_6)DMSO, 373 K): 165.1 (*s*, C(3)); 135.6, 133.2, 130.6 (3*s*, 3 arom. C); 128.2, 127.8, 125.7, 125.2, 124.7, 123.6, 122.7 (7*d*, 7 arom. CH); 53.6 (*d*, CHN); 46.1 (*t*, CH_2); 41.5 (*s*, C(2)); 32.2 (*q*, MeN); 29.3 (*d*, Me_2*C*H); 23.5 (*q*, *Me*–C(2)); 23.0, 22.3 (2*q*, Me_2CH); 16.9 (*q*, *Me*CHN). CI-MS (NH_3): 296 (22), 295 (100, $[M+1]^+$), 251 (6), 186 (17), 184 (16). Anal. calc. for $C_{20}H_{26}N_2$ (294.43): C 81.59, H 8.90, N 9.51; found: C 81.39, H 8.65, N 9.42.

*Data of (1′*R,2R*)-***4d***: IR (neat): 3050*w*, 2952*s*, 2869*m*, 1758v*s*, 1510*w*, 1452*w*, 1414*w*, 1372*w*, 1319*w*, 1262*w*, 1194*w*, 1170*w*, 1116*w*, 1056*w*, 970*w*, 938*w*, 863*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO, 373 K): 8.05–8.0 (*m*, 1 arom. H); 7.95–7.9 (*m*, 2 arom. H); 7.6–7.5 (*m*, 4 arom. H); 5.49 (*q*, *J* = 6.9, CHN); 2.74 (*s*, MeN); 1.70 (*d*, *J* = 6.9, *Me*CHN); 1.50 (*sept.*, *J* = 6.6, Me_2CH); 1.31 (*dd*, *J* = 13.9, 6.9, 1 H of CH_2); 1.22 (*s*, Me–C(2)); 1.1–1.0 (br., 1 H of CH_2); 0.80, 0.76 (2*d*, *J* = 6.6, Me_2CH). ^{13}C-NMR (75.5 MHz, (D_6)DMSO, 373 K): 165.2 (*s*, C(3)); 135.5, 133.2, 130.6 (3*s*, 3 arom. C); 128.2, 127.8, 125.6, 125.2, 124.6, 123.6, 122.7 (7*d*, 7 arom. CH); 53.5 (*d*, CHN); 46.0 (*t*, CH_2); 41.5 (*s*, C(2)); 31.9 (*q*, MeN); 24.2 (*d*, Me_2*C*H); 24.0 (*q*, *Me*–C(2)); 22.9, 22.3 (2*q*, Me_2CH); 16.8 (*q*, *Me*CHN). ESI-MS (MeOH): 327 (10, $[M+MeOH+1]^+$), 295 (100, $[M+1]^+$), 155 (43, [naphtCHMe]$^+$), 141 (38, $[M-naphthCHCH_2+1]^+$). Anal. calc. for $C_{20}H_{26}N_2$ (294.43): C 81.59, H 8.90, N 9.51; found: C 81.59, H 8.61, N 9.48.

2.6. *Phe(2Me) Synthon. (*RS*)-*N,*2-Dimethyl*-N-*[(*R*)-1-(naphthalen-1-yl)ethyl]-3-phenylpropanamide* (**8e**). Within 20 min, a soln. of 2N LDA (11.5 ml, 23.0 mmol) was added to a soln. of **7** (4.633 g, 19.20 mmol) in abs. THF (50 ml) at 0°. Then, benzyl bromide (2.3 ml, 3.3 g, 19.3 mmol) was added within 55 min keeping the temp. below 5°. After 60 min, the mixture was poured carefully on ice, extracted with Et_2O, dried ($MgSO_4$), and evaporated. CC (hexane/AcOEt 5:1) yielded 5.723 g (90%) of **8e** as a pale yellow oil. Recrystallization from Et_2O and hexane gave colorless crystals. M.p. 105–105.5°. R_f (hexane/AcOEt 2:1) 0.41 and 0.32, resp., for the diastereoisomers. IR: 3030*w*, 2974*m*, 2933*m*, 2916*w*, 2872*w*, 1628v*s*, 1508*m*, 1475*s*, 1453*s*, 1453*s*, 1410*s*, 1372*w*, 1350*w*, 1322*w*, 1279*m*, 1238*w*, 1213*w*, 1164*w*, 1128*m*, 1108*m*, 1088*m*, 1043*m*, 1026*w*, 982*w*, 812*s*, 790*s*, 760*m*, 744*m*, 735*w*, 700*s*. ^{1}H-NMR: 8.0–7.5 (*m*, 3 arom. H); 7.5–7.1 (*m*, 9 arom. H); 6.61 (*q*, *J* = 6.8, CHN); 3.15–3.05, 2.95–2.8, 2.75–2.65 (3*m*, CHCO, CH_2); 2.46, 2.22 (2*s*, MeN); 1.58, 1.43 (2*d*, *J* = 6.8, 6.9, *Me*CHN); 1.18, 1.16 (2*d*, *J* = 6.8, 6.7, *Me*CHCO). ^{13}C-NMR: 175.1, 174.9 (2*s*, CO); 140.3, 140.1, 136.3, 136.0, 133.7, 131.9 (6*s*, 4 arom. C); 129.0, 128.9, 128.4, 128.3, 128.2, 126.6, 126.4, 126.1, 125.9, 125.8, 124.8, 124.7, 124.1, 124.0 (14*d*, 12 arom. CH);

47.9, 47.8 (2*d*, CHN); 40.4, 39.9 (2*t*, CH_2); 38.7, 38.5 (2*d*, *C*HCO); 28.9, 28.8 (2*q*, MeN); 17.9, 17.1 (2*q*, *Me*CHCO); 15.6, 15.5 (2*q*, *Me*CHN). CI-MS (NH_3): 333 (23), 332 (100, $[M+1]^+$), 227 (18), 199 (7). Anal. calc. for $C_{23}H_{25}NO$ (331.43): C 83.35, H 7.60, N 4.23; found: C 83.33, H 7.59, N 4.14.

*(*RS*)-*N,*2-Dimethyl*-N-*[(*R*)-1-(naphthalen-1-yl)ethyl]-3-phenylpropanethioamide* (**9e**). To a soln. of **8e** (5.50 g (16.6 mmol)) in abs. toluene (20 ml), *Lawesson* reagent (4.0 g, 1.2 equiv.) was added, the mixture stirred for 17 h at 110° and then cooled to r.t., the precipitate filtered and washed with Et_2O, and the filtrate evaporated. After CC (hexane/AcOEt 5:1), the solvent was evaporated, and the formed precipitate was filtered yielding 1.949 g of a pure diastereoisomer of **9e** as colorless crystals. The filtrate was evaporated and the residue dried: 3.466 g of a pale yellow solid diastereoisomer mixture **9e**/**9e′**. Total yield of **9e**: 5.415 g (94%). M.p. (**9e**) 140.5–141.0°. R_f (hexane/AcOEt 5:1) 0.35 and 0.29, resp., for **9e** and **9e′**. IR: 3442*w*, 3047*w*, 3008*w*, 2974*s*, 2950*m*, 2927*s*, 2911*s*, 2845*m*, 1598*w*, 1509*s*, 1482v*s*, 1444v*s*, 1407v*s*, 1368*s*, 1323*s*, 1295*s*, 1254v*s*, 1213*w*, 1174*s*, 1141*w*, 1114v*s*, 1082*s*, 1050*s*, 1038*m*, 1026*m*, 1009*w*, 984*s*, 968*s*, 929*w*, 906*w*, 873*w*, 852*w*, 810v*s*, 793v*s*, 785v*s*, 755v*s*, 726*w*, 708v*s*, 677*w*, 625*w*, 613*w*. ^{1}H-NMR: 7.95–7.9, 7.85–7.8 (2*m*, 3 arom. H); 7.55–7.4, 7.35–7.3, 7.25–7.1 (3*m*, 9 arom. H, CHN); 3.3–3.2 (*m*, CH_2); 2.9–2.85 (*m*, CHCS); 2.70 (*s*, MeN of **9e′**); 2.32 (*s*, MeN of **9e**); 1.67 (*d*, *J* = 6.7, *Me*CHN of **9e′**); 1.50 (*d*, *J* = 6.7, *Me*CHN of **9e**); 1.31 (*d*, *J* = 6.2, *Me*CHCS of **9e**); 1.25 (*d*, *J* = 6.4, *Me*CHCS of **9e′**). ^{13}C-NMR: 208.1 (*s*, CS); 140.0, 139.9, 135.5, 133.6, 132.0 (5*s*, 4 arom. C); 129.2, 129.1, 129.0, 128.9, 128.5, 128.4, 128.2, 128.2, 127.0, 126.7, 126.3, 126.0, 125.2, 125.2, 124.9, 124.3 (16*d*, 12 arom. CH); 56.9, 56.7 (2*d*, *C*HCS); 44.9, 44.6 (2*d*, CHN); 44.2, 43.1 (*t*, CH_2); 33.0 (*q*, MeN); 21.9, 20.8 (2*q*, *Me*CHN); 13.8, 13.7 (2*q*, *Me*CHCS). CI-MS (NH_3; **9e**): 349 (15), 348 (61, $[M+1]^+$), 195 (11), 194 (100, $[M-\text{naphthCHCH}_2+1]^+$). Anal. calc. for $C_{23}H_{25}NS$ (347.50): C 79.50, H 7.25, N 4.03, S 9.23; found: C 79.41, H 7.13, N 3.98, S 9.26.

*(*RS*)-2-Benzyl-2,*N*-dimethyl*-N-*[(*R*)-1-(naphthalen-1-yl)ethyl]-2*H*-azirin-3-amine* (**4e**). To a soln. of **9e** (5.135 g (14.78 mmol)) and 5 drops of abs. DMF in abs. CH_2Cl_2 (15 ml) at 0°, 2N phosgene in toluene (9 ml, 18 mmol) was added and the mixture was stirred for 30 min at 0° and evaporated. The residue was dissolved in abs. THF (15 ml), DABCO (1.662 g, 14.82 mmol) was added, and the mixture was stirred for 20 min at 0°. After filtration, NaN_3 (1.922 g, 29.57 mmol) was added, the suspension stirred for 18 h at r.t. and then filtered over *Celite*, the filter cake washed with Et_2O and AcOEt, and the filtrate evaporated. The residue was dissolved in CH_2Cl_2, the soln. washed with aq. $NaHCO_3$ soln. (2×) and the aq. soln. with CH_2Cl_2 (1×) and the combined org. phase dried ($MgSO_4$) and evaporated. CC (hexane/AcOEt 3:1) followed by MPLC (AcOEt) yielded 1.362 g of (1′*R*,2*S*)-**4e** (R_f (hexane/AcOEt 1:1) 0.32) and 1.526 g of (1′*R*,2*R*)-**4e** (R_f 0.24). Total yield of **4e**: 2.888 g (59%). Crystallization of (1′*R*,2*S*)-**4e** from AcOEt afforded suitable crystals for X-ray crystal structure determination. (1′*R*,2*R*)-**4e** was obtained as an oil.

*Data of (1′*R,2S*)-***4e***: M.p. 109.5–110.5°. IR: 3441*m*, 3052*m*, 2972*s*, 2918*m*, 1765v*s*, 1741*m*, 1600*m*, 1510*m*, 1494*w*, 1452*m*, 1374*m*, 1318*m*, 1265*m*, 1240*m*, 1204*m*, 1168*m*, 1103*m*, 1071*m*, 1028*w*, 985*w*, 955*w*, 808*m*, 784*s*, 705*s*, 622*w*, 602*w*, 576*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO, 373 K): 8.05–8.0, 7.95–7.85, 7.55–7.45, 7.3–7.15 (4*m*, 12 arom. H); 5.41 (*q*, *J* = 6.9, CHN); 2.9–2.7 (*m*, CH_2); 2.61 (br. *s*, MeN); 1.53 (*d*, *J* = 6.9, *Me*CHN); 1.04 (br. *s*, Me–C(2)). ^{13}C-NMR (75.5 MHz, (D_6)DMSO, 373 K): 164.8 (*s*, C(3)); 138.1, 135.3, 133.2, 130.6 (4*s*, 4 arom. C); 129.1, 128.2, 127.8, 127.3, 125.8, 125.4, 125.2, 124.7, 123.6, 122.7 (10*d*, 12 arom. CH); 53.2 (*d*, CHN); 43.7 (*t*, CH_2); 42.4 (*s*, C(2)); 32.3 (*q*, MeN); 22.8 (*q*, *Me*–C(2)); 16.5 (*q*, *Me*CHN). CI-MS (NH_3): 330 (24), 329 (100, $[M+1]^+$). Anal. calc. for $C_{23}H_{24}N_2 \cdot 0.25\ C_4H_7O_2$ (347.50): C 82.31, H 7.41, N 8.00; found: C 82.53, H 7.25, N 8.29.

*Data of (1′*R,2R*)-***4e***: IR (neat): 3059*m*, 2974*m*, 2938*m*, 1760v*s*, 1614*s*, 1511*m*, 1495*s*, 1454*s*, 1373*s*, 1320*m*, 1240*m*, 1188*m*, 1080*s*, 1030*m*, 985*w*, 954*w*, 866*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO, 373 K): 8.05–7.9, 7.55–7.5, 7.25–7.1 (3*m*, 12 arom. H); 5.43 (*q*, *J* = 6.9, CHN); 2.70 (br. *s*, MeN); 2.57 (br., CH_2); 1.65 (*d*, *J* = 6.9, *Me*CHN); 1.19 (br. *s*, Me–C(2)). ^{13}C-NMR (75.5 MHz, (D_6)DMSO, 373 K): 165.1 (*s*, C(3)); 138.2, 135.7, 133.2, 130.5 (4*s*, 4 arom. C); 128.8, 128.2, 127.8, 127.4, 125.8, 125.4, 125.2, 124.7, 123.5, 122.6 (10*d*, 12 arom. CH); 53.8 (*d*, CHN); 44.0 (*t*, CH_2); 42.4 (*s*, C(2)); 32.3 (*q*, MeN); 22.9 (*q*, *Me*–C(2)); 17.0 (*q*, *Me*CHN). CI-MS (NH_3): 330 (22), 329 (100, $[M+1]^+$).

3. *Reactions of* **4a**–**e** *with Thiobenzoic and Benzoic Acid*. 3.1. *Reactions of* **4a**. N-*{(*S*)-1-Methyl-1-{[methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}thioxomethyl}propyl}benzamide* ((1′*R*,1*S*)-**10a**). To thiobenzoic acid (53 mg, 0.38 mmol), a soln. of (1′*R*,2*S*)-**4a** (101 mg, 0.38 mmol) in abs. CH_2Cl_2 (5 ml) was added, and the mixture was stirred for 19 h at r.t. Evaporation and prep. TLC (hexane/AcOEt 1:1) gave 143 mg (93%) of (1′*R*,1*S*)-**10a**. Colorless foam. M.p. 88–91°. R_f (hexane/AcOEt 1:1) 0.35. IR: 3426*w*, 3211*m*, 3051*w*, 2974*w*, 2933*w*, 1659*s*, 1600*w*, 1579*w*, 1510v*s*, 1479v*s*, 1374*s*, 1333*w*, 1238*w*, 1174*w*, 1112*w*, 1071*m*, 1044*w*, 894*w*, 867*w*. ^{1}H-NMR: 9.86 (br. *s*, NH); 8.0–7.95, 7.9–7.85, 7.8–7.75, 7.6–7.45 (4*m*, 12 arom. H, CHN); 3.05–2.95 (*m*, 1 H of CH_2 of Iva); 2.85 (*s*, MeN); 2.05–1.95 (*m*, 1 H of CH_2 of Iva); 1.82 (*s*, Me(3) of Iva); 1.78 (*d*, *J* = 6.7, *Me*CHN); 0.87 (*t*, *J* = 7.4, Me(4) of Iva). ^{13}C-NMR: 205.0 (*s*, CS); 164.1 (*s*, CO); 135.8, 134.9, 133.7, 131.9 (4*s*, 4 arom. C); 131.0, 129.3, 128.7, 128.4, 127.0, 126.9, 126.3, 125.4, 125.0, 123.7 (10*d*, 12 arom. CH); 64.9 (*s*, C(2) of Iva); 61.4

(*d*, CHN); 35.9 (*q*, MeN); 28.5 (*t*, CH_2(3) of Iva); 23.8, 13.1, 8.9 (3*q*, *Me*CHN, Me(3) of Iva, Me(4) of Iva). CI-MS (NH_3): 407 (7), 406 (28), 405 (100, $[M+1]^+$), 283 (12, $[M-PhCONH_2]^+$), 252 (10), 251 (66, $[M-naphthCHCH_2+1]^+$), 217 (9), 155 (5, $[naphtCHMe]^+$). Anal. calc. for $C_{25}H_{28}N_2OS$ (404.58): C 74.22, H 6.98, N 6.92, S 7.93; found: C 74.15, H 6.86, N 6.75, S 7.73.

N-*{(*S*)-1-Methyl-1-{{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}oxomethyl}propyl}benzamide* ((1′*R*,1*S*)-**11a**). As described for (1′*R*,1*S*)-**10a**, with benzoic acid (46 mg, 0.38 mmol), (1′*R*,2*S*)-**4a** (100 mg, 0.38 mmol), and CH_2Cl_2 (4 ml); 39 h at r.t.: 123 mg (84%) of (1′*R*,1*S*)-**11a**. Colorless foam. M.p. 74–76°. R_f (hexane/AcOEt 1:1) 0.30. IR: 3348*m*, 3052*w*, 2976*m*, 1718*w*, 1660*s*, 1612v*s*, 1579*m*, 1511*s*, 1481*s*, 1391*m*, 1290*w*, 1240*w*, 1172*w*, 1105*m*, 1084*m*, 1044*w*, 925*w*, 881*w*. ^{1}H-NMR: 8.41 (br. *s*, NH); 7.9–7.8, 7.6–7.4 (2*m*, 12 arom. H); 6.68 (*q*, *J* = 6.8, CHN); 2.85–2.8 (*m*, 1 H of CH_2 of Iva); 2.60 (*s*, MeN); 1.9–1.85 (*m*, 1 H of CH_2 of Iva); 1.75 (*s*, Me(3) of Iva); 1.68 (*d*, *J* = 6.8, *Me*CHN); 0.91 (*t*, *J* = 7.4, Me(4) of Iva). ^{13}C-NMR: 172.4, 165.1 (2*s*, 2 CO); 135.5, 135.2, 133.7, 131.8 (4*s*, 4 arom. C); 131.1, 130.0, 128.8, 128.6, 128.4, 126.8, 126.6, 126.0, 125.2, 124.8, 123.4 (11*d*, 12 arom. CH); 62.2 (*s*, C(2) of Iva); 50.9 (*d*, CHN); 30.0 (*q*, MeN); 27.6 (*t*, CH_2(3) of Iva); 22.1, 15.0, 8.8 (3*q*, *Me*CHN, Me(3) of Iva, Me(4) of Iva). ESI-MS (MeOH): 427 (16, $[M+K]^+$), 416 (30), 411 (98, $[M+Na]^+$), 389 (13, $[M+1]^+$), 267 (28, $[M-PhCONH_2]^+$), 235 (44, $[M-naphthCHCH_2+1]^+$), 204 (100, $[M-naphthCH(Me)NMe]^+$), 176 (78, $[M-naphthCH(Me)N(Me)CO]^+$), 155 (50, $[naphtCHMe]^+$). Anal. calc. for $C_{25}H_{28}N_2O_2 \cdot 0.5\ H_2O$ (397.52): C 75.54, H 7.35, N 7.05; found: C 75.59, H 7.33, N 6.63.

N-*{(*R*)-1-Methyl-1-{{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}thioxomethyl}propyl}benzamide* ((1′*R*,1*R*)-**10a**). As described for (1′*R*,1*S*)-**10a**, with thiobenzoic acid (53 mg, 0.38 mmol), (1′*R*,2*R*)-**4a** (101 mg, 0.38 mmol), and CH_2Cl_2 (5 ml); 19 h at r.t.: 152 mg (99%) of (1′*R*,1*R*)-**10a**. Colorless foam. M.p. 84–86°. R_f (hexane/AcOEt 1:1) 0.36. IR: 3424*w*, 3208*m*, 3051*w*, 2973*m*, 2875*w*, 1733*w*, 1659*s*, 1600*w*, 1579*w*, 1510v*s*, 1479v*s*, 1375*s*, 1330*m*, 1273*w*, 1240*m*, 1174*w*, 1113*w*, 1071*m*, 1043*m*, 1028*w*, 895*w*, 867*w*. ^{1}H-NMR: 9.86 (br. *s*, NH); 8.0–7.95, 7.9–7.85, 7.65–7.6, 7.55–7.45 (4*m*, 12 arom. H, CHN); 3.0–2.9 (*m*, 1 H of CH_2 of Iva); 2.87 (*s*, MeN); 1.95–1.85 (*m*, 1 H of CH_2 of Iva); 1.91 (*s*, Me(3) of Iva); 1.74 (*d*, *J* = 6.7, *Me*CHN); 0.78 (*t*, *J* = 7.4, Me(4) of Iva). ^{13}C-NMR: 205.0 (*s*, CS); 164.1 (*s*, CO); 135.8, 134.8, 133.6, 131.9 (4*s*, 4 arom. C); 131.0, 129.2, 128.6, 128.4, 126.9, 126.3, 125.6, 125.0, 124.2 (9*d*, 12 arom. CH); 64.9 (*s*, C(2) of Iva); 61.0 (*d*, CHN); 36.3 (*q*, MeN); 28.3 (*t*, CH_2(3) of Iva); 24.8, 13.0, 9.1 (3*q*, *Me*CHN, Me(3) of Iva, Me(4) of Iva). CI-MS (NH_3): 407 (8), 406 (28), 405 (100, $[M+1]^+$), 283 (15, $[M-PhCONH_2]^+$), 251 (48, $[M-naphthCHCH_2+1]^+$). Anal. calc. for $C_{25}H_{28}N_2OS \cdot 0.33\ H_2O$ (404.58): C 73.13, H 7.04, N 6.82; found: C 73.11, H 6.90, N 6.58.

N-*{(*R*)-1-Methyl-1-{{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}oxomethyl}propyl}benzamide* ((1′*R*,1*R*)-**11a**). As described for (1′*R*,1*S*)-**10a**, with benzoic acid (46 mg, 0.38 mmol), (1′*R*,2*R*)-**4a** (100 mg, 0.38 mmol), and CH_2Cl_2 (4 ml); 40 h at r.t.: 132 mg (90%) of (1′*R*,1*R*)-**11a**. Colorless foam. M.p. 79–81°. R_f (hexane/AcOEt 1:1) 0.29. IR: 3342*w*, 3052*w*, 2977*w*, 1718*w*, 1611v*s*, 1579*w*, 1511*s*, 1481*s*, 1393*w*, 1240*w*, 1172*w*, 1098*w*, 1083*m*, 1044*w*, 913*w*, 881*w*. ^{1}H-NMR: 8.38 (br. *s*, NH); 8.1–8.05, 8.0–7.8, 7.55–7.4 (3*m*, 12 arom. H); 6.72 (*q*, *J* = 6.8, CHN); 2.85–2.7 (*m*, 1 H of CH_2 of Iva); 2.63 (*s*, MeN); 1.9–1.75 (*m*, 1 H of CH_2 of Iva); 1.84 (*s*, Me(3) of Iva); 1.66 (*d*, *J* = 6.8, *Me*CHN); 0.79 (*t*, *J* = 7.4, Me(4) of Iva). ^{13}C-NMR: 172.5, 165.1 (2*s*, 2 CO); 135.5, 135.1, 133.6, 131.8 (4*s*, 4 arom. C); 130.0, 128.5, 128.4, 126.8, 126.6, 126.0, 126.0, 125.3, 124.8, 123.9 (9*d*, 12 arom. CH); 62.0 (*s*, C(2) of Iva); 50.6 (*d*, CHN); 30.3 (*q*, MeN); 27.6 (*t*, CH_2(3) of Iva); 22.4, 15.2, 8.9 (3*q*, *Me*CHN, Me(3) of Iva, Me(4) of Iva). ESI-MS (MeOH): 799 (9, $[2M+1]^+$), 677 (15), 661 (7), 603 (9), 427 (15, $[M+K]^+$), 416 (88), 411 (100, $[M+Na]^+$), 408 (91), 389 (17, $[M+1]^+$), 339 (10), 307 (61), 267 (23, $[M-PhCONH_2]^+$), 235 (35, $[M-naphthCHCH_2+1]^+$), 204 (88, $[M-naphthCH(Me)NMe]^+$), 176 (55, $[M-naphthCH(Me)N(Me)CO]^+$), 155 (59, $[naphtCHMe]^+$). Anal. calc. for $C_{25}H_{28}N_2O_2 \cdot 0.5\ H_2O$ (397.52): C 75.54, H 7.35, N 7.05; found: C 75.62, H 7.22, N 6.56.

3.2. *Reactions of* **4b**. N-*{(*S*)-1,2-Dimethyl-1-{{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}thioxomethyl}propyl}benzamide* ((1′*R*,1*S*)-**10b**). As described for (1′*R*,1*S*)-**10a**, with thiobenzoic acid (30 mg, 0.217 mmol), (1′*R*,2*S*)-**4b** (60 mg, 0.214 mmol), and CH_2Cl_2 (2 ml), 48 h at r.t.: 88 mg (98%) of (1′*R*,1*S*)-**10b**. Colorless foam. M.p. 79–82°. R_f (hexane/AcOEt 1:1) 0.47. ^{1}H-NMR: 7.94 (br. *s*, NH); 7.9–7.8, 7.65–7.4 (2*m*, 12 arom. H, CHN); 2.80 (*s*, MeN); 2.35 (*sept.*, *J* = 6.8, C(3) of Val(2Me)); 1.92 (*s*, Me(3) of Val(2Me)); 1.74 (*d*, *J* = 6.7, *Me*CHN); 1.22, 1.05 (2*d*, *J* = 6.8, 6.7, 2 Me(4) of Val(2Me)). ^{13}C-NMR: 205.4 (*s*, CS); 165.5 (*s*, CO); 135.4, 133.6, 131.9 (3*s*, 4 arom. C); 131.2, 129.0, 128.6, 126.9, 126.8, 126.2, 125.4, 125.0, 124.2 (9*d*, 12 arom. CH); 67.7 (*s*, C(2) of Val(2Me)); 60.8 (*d*, CHN); 36.3 (*q*, MeN); 35.4 (*d*, C(3) of Val(2Me)); 21.8, 18.4, 18.1, 12.9 (4*q*, Me(3) of Val(2Me), 2 Me(4) of Val(2Me), *Me*CHN). CI-MS (NH_3): 421 (9), 420 (29), 419 (100, $[M+1]^+$), 266 (14), 265 (82, $[M-naphthCHCH_2+1]^+$), 231 (9). Anal. calc. for $C_{26}H_{30}N_2OS \cdot 0.33\ H_2O$ (424.16): C 73.55, H 7.28, N 6.60; found: C 73.39, H 7.43, N 6.28.

N-*{(*R*)-1,2-Dimethyl-1-{{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}thioxomethyl}propyl}benzamide* ((1′*R*,1*R*)-**10b**). As described for (1′*R*,1*S*)-**10a**, with thiobenzoic acid (30 mg, 0.217 mmol), (1′*R*,2*R*)-**4b** (60 mg,

0.214 mmol), and CH_2Cl_2 (2 ml); 23 h at r.t.: 85 mg (94%) of (1′*R*,1*R*)-**10b**. Colorless foam. M.p. 153–154°. R_f (hexane/AcOEt 1:1) 0.43. ^{1}H-NMR: 8.42 (br. *s*, NH); 7.9–7.8, 7.65–7.35 (2*m*, 12 arom. H, CHN); 2.83 (*s*, MeN); 2.27 (*sept.*, *J* = 6.8, C(3) of Val(2Me)); 2.01 (*s*, Me(3) of Val(2Me)); 1.74 (*d*, *J* = 6.7, *Me*CHN); 1.20, 1.05 (2*d*, *J* = 6.9, 6.6, 2 Me(4) of Val(2Me)). ^{13}C-NMR: 205.7 (*s*, CS); 165.1 (*s*, CO); 135.5, 135.2, 133.5, 132.0 (4*s*, 4 arom. C); 131.1, 129.0, 128.4, 128.3, 127.2, 126.9, 126.3, 125.4, 124.9, 124.6 (10*d*, 12 arom. CH); 67.5 (*s*, C(2) of Val(2Me)); 61.0 (*d*, CHN); 36.6 (*q*, MeN); 35.2 (*d*, C(3) of Val(2Me)); 21.7, 18.5, 13.2 (3*q*, Me(3) of Val(2Me), 2 Me(4) of Val(2Me), *Me*CHN). CI-MS (NH_3): 421 (8), 420 (27), 419 (100, $[M+1]^+$), 266 (6), 265 (37, $[M-$naphthCHCH$_2+1]^+$), 231 (7). Anal. calc. for $C_{26}H_{30}N_2OS \cdot 0.2\ H_2O$ (422.20): C 73.97, H 7.26, N 6.63; found: C 74.08, H 7.54, N 6.57.

3.3. *Reactions of* **4c**. N-*{(*S*)-1-Cyclopentyl-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-thioxoethyl}benzamide* (1′*R*,1*S*)-**10c**). As described for (1′*R*,1*S*)-**10a**, with thiobenzoic acid (44 mg, 0.318 mmol), (1′*R*,2*S*)-**4c** (93 mg, 0.304 mmol), and CH_2Cl_2 (2 ml); 19 h at r.t.; prep. TLC (hexane/AcOEt 2:1): 128 mg (95%) of (1′*R*,1*S*)-**10c**. Colorless foam. M.p. 88–91°. R_f (hexane/AcOEt 2:1) 0.31. IR: 3432*m*, 2946*m*, 2868*m*, 1667*s*, 1600*w*, 1579*w*, 1510*s*, 1478v*s*, 1376*s*, 1330*m*, 1280*w*, 1232*w*, 1174*w*, 1107*w*, 1060*m*, 1016*w*. ^{1}H-NMR: 7.9–7.8, 7.7–7.3 (2*m*, 12 arom. H, CHN, NH); 2.81 (*s*, MeN); 2.59 (*quint.*, *J* = 8.4, CH(3) of Ala(2cPent); 1.99 (*s*, Me(3) of Ala(2cPent)); 1.9–1.8 (*m*, 2 H of cPent); 1.74 (*d*, *J* = 6.7, CHN*Me*); 1.7–1.5 (*m*, 6 H of cPent). ^{13}C-NMR: 205.3 (*s*, CS); 165.5 (*s*, CO); 135.8, 135.1, 133.6, 132.0 (4*s*, 4 arom. C); 131.2, 128.8, 128.5, 126.8, 126.7, 126.1, 125.4, 125.0, 124.4 (9*d*, 12 arom. CH); 67.4 (*s*, C(2) of Ala(2cPent)); 60.6 (*d*, CHN); 47.7 (*d*, C(3) of Ala(2cPent)); 35.8 (*q*, MeN); 28.0, 27.8, 25.2 (3*t*, 4 CH_2 of cPent); 23.6, 12.9 (2*q*, 2 Me). ESI-MS (MeOH/CH_2Cl_2/NaI): 911 (15, $[2M+Na]^+$), 467 (100, $[M+Na]^+$), 291 (57, $[M-$naphthCHCH$_2+1]^+$). Anal. calc. for $C_{28}H_{32}N_2OS$ (444.64): C 75.64, H 7.25, N 6.30; found: C 75.14, H 7.14, N 6.42.

N-*{(*R*)-1-Cyclopentyl-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-thioxoethyl}benzamide* ((1′*R*,1*R*)-**10c**). As described for (1′*R*,1*S*)-**10a**, with thiobenzoic acid (42 mg, 0.311 mmol), (1′*R*,2*R*)-**4c** (94 mg (0.307 mmol)), and CH_2Cl_2 (2 ml); 2 h at r.t.; prep. TLC (hexane/AcOEt 2:1): 128 mg (68%) of (1′*R*,1*R*)-**10c**. Colorless solid. M.p. 104–105°. R_f (hexane/AcOEt 2:1) 0.31. IR: 3309*w*, 3053*w*, 2952*s*, 2870*m*, 1740*m*, 1668*s*, 1641*s*, 1600*w*, 1579*w*, 1512v*s*, 1476v*s*, 1383v*s*, 1331*m*, 1230*s*, 1156*m*, 1104*w*, 1061*s*, 1014*m*, 970*w*, 932*w*, 856*w*. ^{1}H-NMR: 7.95 (*d*, *J* = 8.5, 1 arom. H); 7.85–7.8, 7.75–7.3 (2*m*, 11 arom. H, CHN, NH); 2.86 (*s*, MeN); 2.59 (*quint.*, *J* = 8.4, CH(3) of Ala(2cPent); 2.04 (*s*, Me(3) of Ala(2cPent)); 2.0–1.95 (*m*, 1 H of cPent); 1.73 (*d*, *J* = 6.7, *Me*CHN); 1.7–1.45 (*m*, 7 H of cPent). ^{13}C-NMR: 205.1 (*s*, CS); 165.1 (*s*, CO); 135.4, 133.5, 132.1 (3*s*, 4 arom. C); 131.0, 128.9, 128.4, 128.1, 127.1, 126.8, 126.2, 125.3, 124.9, 124.8 (10*d*, 12 arom. CH); 66.9 (*s*, C(2) of Ala(2cPent)); 60.9 (*d*, CHN); 47.6 (*d*, C(3) of Ala(2cPent)); 36.3 (*q*, MeN); 28.1, 28.0, 25.3, 24.9 (4*t*, 4 CH_2 of cPent); 23.2, 13.2 (2*q*, 2 Me). ESI-MS (MeOH + NaI): 469 (11), 468 (32, $[M+Na+1]^+$), 467 (100, $[M+Na]^+$). Anal. calc. for $C_{28}H_{32}N_2OS \cdot 0.5\ H_2O$ (444.64): C 74.13, H 7.33, N 6.18; found: C 73.84, H 7.09, N 6.17.

3.4. *Reactions of* **4d**. N-*{(*S*)-1,3-Dimethyl-1-{{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}thioxomethyl}-butyl}benzamide* ((1′*R*,1*S*)-**10d**. As described for (1′*R*,1*S*)-**10a**, with thiobenzoic acid (26 mg, 0.19 mmol), (1′*R*,2*S*)-**4d** (54 mg, 0.18 mmol), and CH_2Cl_2 (2 ml); 17 h at r.t.: 75 mg (95%) of (1′*R*,1*S*)-**10d**. Colorless solid. M.p. 174–175°. R_f (hexane/AcOEt 1:1) 0.47. IR: 3446*w*, 3205*s*, 2956*m*, 2869*w*, 1660v*s*, 1600*w*, 1579*w*, 1512*s*, 1480v*s*, 1394*s*, 1373*s*, 1332*w*, 1303*w*, 1228*w*, 1175*w*, 1103*w*, 1068*w*, 1001*w*, 912*w*, 871*w*, 810*m*. ^{1}H-NMR: 10.20 (br. *s*, NH); 8.05–8.0, 7.9–7.85, 7.75–7.7, 7.6–7.45 (4*m*, 12 arom. H, CHN); 3.04 (*dd*, *J* = 15.3, 7.4, 1 H of CH_2(3) of Leu(2Me)); 2.85 (*s*, MeN); 1.89 (*dd*, *J* = 15.3, 4.9, 1 H of CH_2(3) of Leu(2Me)); 1.79 (*d*, *J* = 6.8, *Me*CHN); 1.77 (*s*, Me(3) of Leu(2Me)); 1.7–1.6 (*m*, CH(4) of Leu(2Me)); 0.95, 0.88 (2*d*, *J* = 6.6, 6.7, 2 Me(5) of Leu(2Me)). ^{13}C-NMR: 205.7 (*s*, CS); 164.1 (*s*, CO); 136.2, 135.1, 133.8, 132.0 (4*s*, 4 arom. C); 131.1, 129.4, 128.8, 128.5, 127.2, 127.0, 126.4, 125.5, 125.1, 123.9 (10*d*, 12 arom. CH); 64.8 (*s*, C(2) of Leu(2Me)); 61.7 (*d*, CHN); 44.1 (*t*, C(3) of Leu(2Me)); 36.3 (*q*, MeN); 25.4 (*d*, C(4) of Leu(2Me)); 24.6, 24.3, 23.4, 12.9 (4*q*, Me(3) of Phe(2Me), *Me*CHN, 2 Me(5) of Leu(2Me)). ESI-MS (MeOH/NaI): 457 (9), 456 (33, $[M+Na+1]^+$), 455 (100, $[M+Na]^+$). Anal. calc. for $C_{27}H_{32}N_2OS \cdot 0.33\ H_2O$ (438.64): C 73.93, H 7.51, N 6.39, S 7.31; found: C 74.07, H 7.65, N 6.33, S 7.48.

N-*{(*R*)-1,3-Dimethyl-1-{{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}thioxomethyl}butyl}benzamide* ((1′*R*,1*R*)-**10d**. As described for (1′*R*,1*S*)-**10a**, with thiobenzoic acid (26 mg, 0.19 mmol), (1′*R*,2*R*)-**4d** (54 mg, 0.18 mmol), and CH_2Cl_2 (2 ml); 15 h at r.t.: 78 mg (99%) of (1′*R*,1*R*)-**10d**. Colorless foam. M.p. 78–81°. R_f (hexane/AcOEt 1:1) 0.40. IR: 3424*w*, 3211*w*, 3053*w*, 2955*m*, 2868*w*, 1735*w*, 1657*s*, 1600*w*, 1579*w*, 1510v*s*, 1477v*s*, 1394*s*, 1372*m*, 1332*w*, 1302*w*, 1231*w*, 1173*w*, 1105*w*, 1066*w*, 1042*m*, 1028*w*, 970*w*, 911*w*, 869*w*. ^{1}H-NMR: 10.09 (br. *s*, NH); 8.0–7.85 (*m*, 5 arom. H); 7.70 (*q*, *J* = 6.7, CHN); 7.63 (*d*, *J* = 7.1, 1 arom. H); 7.55–7.45 (*m*, 6 arom. H); 1.96 (*dd*, *J* = 15.4, 9.8, 1 H of CH_2(3) of Leu(2Me)); 2.84 (*s*, MeN); 1.88 (*s*, Me(3) of Leu(2Me)); 1.83 (*dd*, *J* = 15.3, 3.7, 1 H of CH_2(3) of Leu(2Me)); 1.74 (*d*, *J* = 6.7, *Me*CHN); 1.5–1.4 (*m*, CH(4) of Leu(2Me)); 0.93, 0.51 (2*d*, *J* = 6.5, 6.7, 2 Me(5) of Leu(2Me)). ^{13}C-NMR: 205.5 (*s*, CS); 164.2 (*s*, CO); 136.2, 134.8, 133.8, 132.0 (4*s*, 4 arom. C); 131.1, 129.4, 128.7, 128.5, 127.0, 126.8, 126.4, 125.8, 125.1, 124.5 (10*d*, 12 arom. CH); 65.0

(*s*, C(2) of Leu(2Me)); 61.0 (*d*, CHN); 43.8 (*t*, C(3) of Leu(2Me)); 36.5 (*q*, MeN); 25.7 (*d*, C(4) of Leu(2Me)); 25.8, 24.4, 22.7, 13.2 (4*q*, Me(3) of Phe(2Me), *Me*CHN, 2 Me(5) of Leu(2Me)). ESI-MS (MeOH/NaI): 457 (8), 456 (33, $[M+Na+1]^+$), 455 (100, $[M+Na]^+$) Anal. calc. for $C_{27}H_{32}N_2OS \cdot 0.3\ H_2O$ (438.64): C 73.93, H 7.51, N 6.39, S 7.31; found: C 74.06, H 7.64, N 6.25, S 7.38.

3.5. *Reactions of* **4e**. N-*{(*S*)-1-Benzyl-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-thioxoethyl}benzamide* ((1′*R*,1*S*)-**10e**. As described for (1′*R*,1*S*)-**10a**, with thiobenzoic acid (43 mg, 0.31 mmol), (1′*R*,2*S*)-**4e** (100 mg, 0.31 mmol), and CH_2Cl_2 (2 ml); 18 h at r.t.; CC (hexane/AcOEt 5:1): 139 mg (97%) of (1′*R*,1*S*)-**10e**. M.p. 93–96°. R_f (hexane/AcOEt 1:1) 0.45. IR: 3410*m*, 2929*w*, 1655*m*, 1618*m*, 1578*w*, 1509*s*, 1478v*s*, 1388*s*, 1375*s*, 1331*w*, 1241*w*, 1104*w*, 1063*m*, 1044*w*, 876*w*. ^{1}H-NMR: 9.31 (br. *s*, NH); 7.95–7.85, 7.8–7.75, 7.7–7.35, 7.2–7.05 (4*m*, 17 arom. H, CHN); 4.20, 3.35 (*AB*, $J=14.4$, CH_2(3) of Phe(2Me)); 2.90 (*s*, MeN); 1.91 (*s*, Me(3) of Phe(2Me)); 1.64 (*d*, $J=6.7$, *Me*CHN). ^{13}C-NMR: 204.1 (*s*, CS); 164.8 (*s*, CO); 136.2, 135.6, 135.0, 133.6, 132.0 (5*s*, 5 arom. C); 131.2, 130.0, 129.2, 128.6, 128.5, 127.9, 127.1, 126.9, 126.2, 125.4, 125.0, 123.9 (12*d*, 17 arom. CH); 64.6 (*s*, C(2) of Phe(2Me)); 61.2 (*d*, CHN); 41.8 (*t*, Ph*C*H$_2$); 36.7 (*q*, MeN); 24.3, 12.7 (2*q*, Me(3) of Phe(2Me), *Me*CHN). ESI-MS (MeOH + NaI): 489 (100, $[M+Na]^+$), 473 (46, $[M+Li]^+$), 317 (13), 313 (36, $[M-naphthCHCH_2+1]^+$), 279 (10), 238 (10), 176 (6), 155 (59, $[naphtCHMe]^+$). Anal calc. for $C_{30}H_{30}N_2OS \cdot 0.2\ H_2O$ (470.25): C 76.62, H 6.52, N 5.96, S 6.82; found: C 76.64, H 6.64, N 5.78, S 6.96.

N-*{(*S*)-1-Benzyl-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-oxoethyl}benzamide* ((1′*R*,1*S*)-**11e**). As described for (1′*R*,1*S*)-**10a**, with benzoic acid (38 mg, 0.31 mmol), (1′*R*,2*S*)-**4e** (100 mg, 0.31 mmol), and CH_2Cl_2 (2 ml); 44 h at r.t. CC (CH_2Cl_2/MeOH 100:1) gave 109 mg (79%) of (1′*R*,1*S*)-**11e**. M.p. 178–179°. R_f (CH_2Cl_2/MeOH 20:1) 0.61. R_f (CH_2Cl_2/MeOH 100:1) 0.19. IR: 3434v*s*, 3049*m*, 2942*m*, 1662*s*, 1613*s*, 1529*m*, 1455*w*, 1396*w*, 1333*w*, 1236*w*, 1172*w*, 1138*w*, 1074*w*, 802*w*, 778*w*, 720*w*, 697*w*, 659*w*. ^{1}H-NMR: 7.97 (br. *s*, NH); 7.85–7.8, 7.75–7.7, 7.55–7.35, 7.3–7.25, 7.15–7.1 (5*m*, 17 arom. H); 6.55 (*q*, $J=6.8$, CHN); 4.01, 3.26 (*AB*, $J=14.4$, CH_2(3) of Phe(2Me)); 2.67 (*s*, MeN); 1.83 (*s*, Me(3) of Phe(2Me)); 1.56 (*d*, $J=6.8$, *Me*CHN). ^{13}C-NMR: 171.7 (*s*, CO); 165.6 (*s*, Ph*C*O); 136.5, 135.4, 135.2, 133.6, 131.8 (5*s*, 5 arom. C); 131.2, 129.8, 128.7, 128.6, 128.4, 128.2, 126.9, 126.7, 126.0, 125.2, 124.8, 123.4 (12*d*, 17 arom. CH); 61.8 (*s*, C(2) of Phe(2Me)); 50.9 (*d*, CHN); 40.2 (*t*, C(3) of Phe(2Me)); 30.7 (*q*, MeN); 22.4, 14.6 (2*q*, *Me*CHN, Me(3) of Phe(2Me)). ESI-MS (MeOH): 924 (11, $[2M+Na]^+$), 489 (86, $[M+K]^+$), 473 (100, $[M+Na]^+$), 451 (15, $[M+1]^+$), 297 (14, $[M-naphthCHCH_2+1]^+$), 266 (6, $[M-naphthCH(Me)NMe]^+$). Anal. calc. for $C_{30}H_{30}N_2O_2 \cdot 0.2\ H_2O$ (454.18): C 79.34, H 6.74, N 6.17; found: C 79.29, H 6.70, N 6.07.

N-*{(*R*)-1-Benzyl-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-thioxoethyl}benzamide* ((1′*R*,1*R*)-**10e**. As described for (1′*R*,1*S*)-**10a**, with thiobenzoic acid (43 mg, 0.31 mmol), (1′*R*,2*R*)-**4e** (100 mg, 0.31 mmol), and CH_2Cl_2 (2 ml); 20 h at r.t.; CC (hexane/AcOEt 5:1): 136 mg (96%) of (1′*R*,1*R*)-**10e**. M.p. 188.5–189°. R_f (hexane/AcOEt 1:1) 0.43. IR: 2980*m*, 2938*m*, 1656v*s*, 1599*w*, 1580*w*, 1510v*s*, 1482v*s*, 1446*s*, 1385*s*, 1366*s*, 1320*m*, 1304*m*, 1244*w*, 1216*w*, 1173*w*, 1109*w*, 1064*s*, 1025*m*, 805*w*, 781*s*, 757*w*, 729*m*, 710*m*, 693*w*. ^{1}H-NMR: 8.0–7.75, 7.7–7.35, 7.2–7.0 (3*m*, NH, 17 arom. H, CHN); 4.00, 3.64 (*AB*, $J=14.1$, CH_2(3) of Phe(2Me)); 2.91 (*s*, MeN); 1.81 (*s*, Me(3) of Phe(2Me)); 1.74 (*d*, $J=6.7$, *Me*CHN). ^{13}C-NMR: 204.2 (*s*, CS); 165.1 (*s*, CO); 136.9, 135.4, 134.7, 133.6, 132.1 (5*s*, 5 arom. C); 131.6, 130.5, 129.0, 128.5, 128.0, 127.1, 126.8, 126.7, 126.1, 125.7, 124.9, 124.6 (12*d*, 17 arom. CH); 64.2 (*s*, C(2) of Phe(2Me)); 60.4 (*d*, CHN); 44.2 (*t*, C(3) of Phe(2Me)); 36.0 (*q*, MeN); 25.2, 13.4 (2*q*, Me(3) of Phe(2Me), *Me*CHN). ESI-MS (MeOH/MeCN 1:1 + 0.1% HCOOH): 467 (46, $[M+Na]^+$), 433 (14), 314 (22), 313 (100, $[M-naphthCHCH_2+1]^+$), 155 (10, $[naphtCHMe]^+$). Anal. calc. for $C_{30}H_{30}N_2OS \cdot 0.2\ H_2O$ (470.25): C 76.62, H 6.52, N 5.96, S 6.82; found: C 76.56, H 6.61, N 5.86, S 6.72.

N-*{(*R*)-1-Benzyl-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-oxoethyl}benzamide* ((1′*R*,1*R*)-**11e**. As described for (1′*R*,1*S*)-**10a**, with benzoic acid (38 mg, 0.31 mmol), (1′*R*,2*R*)-**4e** (100 mg, 0.31 mmol), and CH_2Cl_2 (2 ml); 64 h at r.t.; CC (CH_2Cl_2/MeOH 100:1): 127 mg (92%) of (1′*R*,1*R*)-**11e**. M.p. 172–173°. R_f (CH_2Cl_2/MeOH 20:1) 0.56. R_f (CH_2Cl_2/MeOH 100:1) 0.11. IR: 3407*s*, 3372*s*, 3060*m*, 2978*m*, 1656*s*, 1636*s*, 1611v*s*, 1580*w*, 1531*m*, 1510*m*, 1483*m*, 1454*m*, 1392*m*, 1333*w*, 1256*w*, 1173*w*, 1106*w*, 1073*m*, 1044*w*, 1029*w*, 808*w*, 782*w*, 717*w*, 702*w*, 673*w*, 649*w*. ^{1}H-NMR: 8.05–8.0, 7.85–7.8, 7.7–7.65, 7.55–7.35, 7.15–7.0 (5*m*, 17 arom. H); 6.77 (*q*, $J=6.8$, CHN); 6.68 (*s*, NH); 3.64, 3.62 (*AB*, $J=14.2$, CH_2(3) of Phe(2Me)); 2.66 (*s*, MeN); 1.66 (*d*, $J=6.9$, *Me*CHN); 1.58 (*s*, Me(3) of Phe(2Me)). ^{13}C-NMR: 171.5 (*s*, CO); 166.0 (*s*, Ph*C*O); 137.0, 135.8, 134.5, 133.7, 132.0 (5*s*, 5 arom. C); 131.4, 130.7, 128.5, 128.4, 128.0, 126.8, 126.6, 126.5, 125.8, 125.3, 124.7, 124.1 (12*d*, 17 arom. CH); 60.4 (*s*, C(2) of Phe(2Me)); 50.4 (*d*, CHN); 41.0 (*t*, C(3) of Phe(2Me)); 29.9 (*q*, MeN); 22.2, 15.1 (2*q*, *Me*CHN, Me(3) of Phe(2Me)). ESI-MS (MeOH): 489 (4, $[M+K]^+$), 473 (6, $[M+Na]^+$), 451 (2, $[M+1]^+$), 297 (100, $[M-naphthCHCH_2+1]^+$), 266 (92, $[M-naphthCH(Me)NMe]^+$), 238 (23, $[M-naphthCH(Me)N(Me)CO]^+$), 186 (10), 155 (9, $[naphthCHMe]^+$). Anal. calc. for $C_{30}H_{30}N_2O_2 \cdot 0.2\ H_2O$ (454.18): C 79.34, H 6.74, N 6.17; found: C 79.51, H 6.75, N 6.13.

4. *Synthesis of Model Peptides.* 4.1. N-*[(Benzyloxy)carbonyl]leucyl-α-aminoisobutyric Acid* (Z-Leu-Aib; **12**). *Benzyl {1-{{{1,1-Dimethyl-2-[methyl(phenyl)amino]-2-oxoethyl}amino}oxomethyl}-3-methylbutyl}carbamate* (Z-Leu-Aib-N(Me)Ph). To a soln. of Z-leucine (4.147 g, 15.631 mmol) in abs. Et_2O (50 ml), 2,2,*N*-trimethyl-*N*-phenyl-2*H*-azirin-3-amine (3.014 g, 17.297 mmol) in abs. Et_2O (20 ml) was added at 0°, and the mixture was stirred for 2 h. Petroleum ether 50–60° (80 ml) was added, and after 1 h, the precipitate was filtered, the filtrate evaporated, and the residue recrystallized from CH_2Cl_2/Et_2O/petroleum ether: 6.122 g (89%) of Z-Leu-Aib-N(Me)Ph. Colorless crystals. M.p. 135.2–135.7°. R_f (CH_2Cl_2/MeOH 20:1) 0.41. IR: 3290*s*, 3060*m*, 2960*s*, 2930*m*, 2870*m*, 1710*s*, 1670*s*, 1630*s*, 1590*s*, 1545*s*, 1540*s*, 1495*s*, 1470*m*, 1450*m*, 1435*m*, 1415*m*, 1395*s*, 1365*s*, 1285*m*, 1275*s*, 1240*s*, 1210*m*, 1170*m*, 1120*m*, 1090*s*, 1070*m*, 1045*m*, 1030*m*, 780*m*, 765*m*, 740*m*, 705*s*, 670*m*, 665*m*, 610*m*. ^{1}H-NMR: 7.4–7.25, 7.2–7.15 (2*m*, 10 arom. H); 6.63 (br. *s*, NH); 5.2–5.05 (*m*, PhCH_2O, NH); 3.95–3.85 (*m*, CH(2) of Leu); 3.25 (*s*, MeN); 1.65–1.4 (*m*, CH_2(3) and CH(4) of Leu, 2 Me(3) of Aib); 0.9–0.85 (*m*, 2 Me(5) of Leu). ^{13}C-NMR: 173.0, 170.5 (2*s*, 2 CO); 156.0 (*s*, CO (urethane)); 144.3, 136.3 (2*s*, 2 arom. C); 129.3, 128.4, 128.1, 128.0, 128.0, 127.9 (6*d*, 10 arom. CH); 66.8 (*t*, Ph*C*H_2O); 58.2 (*s*, C(2) of Aib); 53.5 (*d*, C(2) of Leu); 41.5 (*t*, C(3) of Leu); 41.3 (*q*, MeN); 24.5 (*d*, C(4) of Leu); 25.8, 23.0, 21.8 (3*q*, 2 Me(3) of Aib, 2 Me(5) of Leu). CI-MS (NH_3): 441 (15), 440 (56, $[M+1]^+$), 334 (20), 333 (100, $[M-Ph(Me)N]^+$), 332 (7), 108 (7). Anal. calc. for $C_{25}H_{33}N_3O_4 \cdot 0.33\ H_2O$ (445.56): C 67.39, H 7.62, N 9.43; found: C 67.36, H 7.81, N 9.53.

Z-Leu-Aib-OH (**12**). A soln. of Z-Leu-Aib-N(Me)Ph (5.969 g, 13.58 mmol) in 3N HCl in THF/H_2O 1:1 (50 ml) was stirred for 14 h at r.t. Then, 1N HCl (20 ml) was added, the mixture extracted with Et_2O (3×), and the org. soln. dried ($MgSO_4$) and evaporated: 4.742 g (99%) of **12**. Colorless foam. Recrystallization from Et_2O and petroleum ether gave colorless crystals. M.p. 118.4–119.0°. R_f (CH_2Cl_2/MeOH 10:1) 0.40–0.11. IR: 3350*s*, 3270*s*, 3200*m*, 3180*m*, 3170*m*, 3160*m*, 3130*m*, 3120*m*, 3100*m*, 3080*s*, 3060*m*, 3050*m*, 2950*s*, 2860*m*, 1725*s*, 1715*s*, 1690*s*, 1660*s*, 1650*s*, 1550*s*, 1530*s*, 1470*s*, 1450*m*, 1435*m*, 1395*m*, 1385*m*, 1365*m*, 1305*m*, 1280*s*, 1310*m*, 1230*s*, 1170*s*, 1130*m*, 1120*m*, 1050*s*, 790*m*, 750*m*, 740*m*, 695*s*, 655*m*. ^{1}H-NMR: *ca.* 10 (br., COOH); 7.35–7.3 (*m*, 5 arom. H); 7.08 (*s*, NH of Aib); 5.70 (*d*, $J=8.2$, NH of Leu); 5.10 (*s*, PhCH_2O); 4.35–4.3 (*m*, CH(2) of Leu); 1.7–1.45 (*m*, CH_2(3) and CH(4) of Leu, 2 Me(3) of Aib); 0.95–0.9 (*m*, 2 Me(5) of Leu). ^{13}C-NMR: 177.1, 172.4 (2*s*, COOH, CO (amide)); 156.6 (*s*, CO (urethane)); 136.0 (*s*, 1 arom. C); 128.4, 128.1, 127.9 (3*d*, 5 arom. CH); 67.1 (*t*, Ph*C*H_2O); 56.7 (*s*, C(2) of Aib); 53.4 (*d*, C(2) of Leu); 41.2 (*t*, C(3) of Leu); 24.6 (*d*, C(4) of Leu); 24.3, 22.7, 21.9 (3*q*, 2 Me(3) of Aib, 2 Me(5) of Leu). CI-MS (NH_3): 368 (16, $[M+H_2O]^+$), 352 (18), 351 (100, $[M+1]^+$), 217 (10). Anal. calc. for $C_{18}H_{26}N_2O_5$ (350.41): C 61.70, H 7.48, N 7.99; found: C 62.02, H 7.39, N 7.97.

4.2. *Tripeptides Z-Leu-Aib-Xaa(2Me)-NR*$_2$. *Benzyl {(*S*)-1-{{{1,1-Dimethyl-2-{{(*S*)-1-methyl-1-{{methyl-[(*R*)-1-(naphthalen-1-yl)ethyl]amino}oxomethyl}propyl}amino}-2-oxoethyl}amino}oxomethyl}-3-methylbutyl}-carbamate* (Z-Leu-Aib-(*S*)-Iva-N(Me)(naphthEt); (*S*,*S*,*R*)-**13a**). To a soln. of **12** (377 mg, 1.08 mmol) in abs. CH_2Cl_2 (5 ml), (1′*R*,2*S*)-**4a** (300 mg (1.13 mmol)) in abs. CH_2Cl_2 (5 ml) was added at 0°, and the mixture was stirred for 67 h at r.t. Evaporation and CC (hexane/AcOEt 2:1, then 1:1) gave 509 mg (77%) of (*S*,*S*,*R*)-**13a**. Colorless solid. M.p. 158–159°. R_f (CH_2Cl_2/MeOH 20:1) 0.28. IR: 3320*m*, 3050*m*, 2980*m*, 2880*m*, 1710*m*, 1695*s*, 1665*s*, 1660*s*, 1650*m*, 1630*m*, 1625*m*, 1615*m*, 1610*s*, 1540*s*, 1530*s*, 1515*s*, 1505*s*, 1495*s*, 1470*m*, 1465*m*, 1455*m*, 1390*m*, 1385*m*, 1370*m*, 1330*m*, 1315*m*, 1305*m*, 1290*m*, 1260*m*, 1220*m*, 1195*m*, 1170*m*, 1110*m*, 1080*m*, 1045*m*, 1030*m*, 805*m*, 780*m*, 740*m*, 700*m*. ^{1}H-NMR: 7.9–7.8 (*m*, NH, 3 arom. H); 7.55–7.45 (*m*, 4 arom. H); 7.3–7.25 (*m*, 5 arom. H); 6.73 (*s*, NH); 6.61 (*q*, $J=6.6$, CHN); 5.30 (*d*, $J=6.6$, NH of Leu); 5.10 (br. *s*, PhCH_2O); 4.15–4.1 (*m*, CH(2) of Leu); 2.53 (*s*, MeN); 2.45–2.4 (*m*, CH(4) of Leu); 1.9–1.5 (*m*, CH_2(3) of Leu, CH_2(3) and Me(3) of Iva, 2 Me(3) of Aib, *Me*CHN); 0.94 (*d*, $J=6.0$, 2 Me(5) of Leu); 0.85 (*t*, $J=7.4$, *Me*CH_2 of Iva). ^{13}C-NMR: 172.0, 171.8, 171.4 (3*s*, 3 CO (amide)); 156.2 (*s*, CO (urethane)); 136.1, 135.4, 133.6, 131.8 (4*s*, 4 arom. C); 128.7, 128.5, 128.4, 128.1, 127.8, 126.6, 125.9, 125.2, 124.8, 123.7 (10*d*, 12 arom. CH); 67.0 (*t*, Ph*C*H_2O); 61.5, 57.5 (2*s*, C(2) of Aib, C(2) of Iva); 54.1, 50.7 (2*d*, Me*C*HN, C(2) of Leu); 41.3, 27.9 (2*t*, C(3) of Leu, C(3) of Iva); 29.9 (*q*, MeN); 24.7 (*d*, C(4) of Leu); 25.1, 22.9, 22.1, 21.8, 14.9, 8.6 (6*q*, *Me*CHN, 2 Me(3) of Aib, Me(3) of Iva, Me(4) of Iva, 2 Me(5) of Leu). ESI-MS (MeOH + NaI): 640 (40, $[M+Na+1]^+$), 639 (100, $[M+Na]^+$). Anal. calc. for $C_{36}H_{48}N_4O_5$ (616.80): C 70.10, H 7.84, N 9.08; found: C 70.03, H 7.85, N 8.97.

*Benzyl {(*S*)-1-{{{1,1-Dimethyl-2-{{(*R*)-1-methyl-1-{{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}oxomethyl}propyl}amino}-2-oxoethyl}amino}oxomethyl}-3-methylbutyl}carbamate* (Z-Leu-Aib-(*R*)-Iva-N(Me)(naphthEt); (*S*,*R*,*R*)-**13a**). As described for (*S*,*S*,*R*)-**13a**, with **12** (378 mg, 1.08 mmol), CH_2Cl_2 (5 ml), (1′*R*,2*R*)-**4a** (302 mg, 1.13 mmol), and CH_2Cl_2 (5 ml); 67 h at r.t.: 553 mg (83%) of (*S*,*R*,*R*)-**13a**. Colorless foam. M.p. 94–96°. R_f (CH_2Cl_2/MeOH 20:1) 0.29. IR: 3320*m*, 3050*w*, 2960*m*, 2880*m*, 1705*s*, 1690*s*, 1680*s*, 1670*s*, 1620*s*, 1615*s*, 1550*m*, 1530*s*, 1525*s*, 1510*s*, 1505*s*, 1500*s*, 1470*m*, 1465*m*, 1390*m*, 1330*m*, 1310*m*, 1285*m*, 1240*s*, 1220*m*, 1195*m*, 1170*m*, 1120*w*, 1100*m*, 1080*m*, 1045*m*, 1030*m*, 805*m*, 780*m*, 760*m*, 755*m*, 700*m*, 695*m*. ^{1}H-NMR: 7.95–7.9

(*m*, NH, 1 arom. H); 7.85–7.8 (*m*, 2 arom. H); 7.55–7.45 (*m*, 4 arom. H); 7.3–7.25 (*m*, 5 arom. H); 6.73 (br., NH); 6.62 (*q*, *J* = 6.7, MeC*H*N); 5.28 (*d*, *J* = 6.7, NH of Leu); 5.10 (br., PhCH_2O); 4.15–4.1 (*m*, CH(2) of Leu); 2.55 (*s*, MeN); 2.45–2.4 (*m*, CH(4) of Leu); 1.8–1.45 (*m*, CH_2(3) of Leu, CH_2(3) and Me(3) of Iva, 2 Me(3) of Aib, *Me*CHN); 0.94 (*d*, *J* = 6.0, 2 Me(5) of Leu); 0.76 (*t*, *J* = 7.5, *Me*CH_2 of Iva). ^{13}C-NMR: 172.0, 171.4 (2*s*, 3 CO (amide)); *ca*. 156 (*s*, CO (urethane)); 136.1, 135.3, 133.6, 131.8 (4*s*, 4 arom. C); 128.7, 128.4, 128.1, 127.9, 126.6, 126.0, 125.3, 124.8, 124.1 (9*d*, 12 arom. CH); 67.0 (*t*, PhCH_2O); 61.3, 57.5 (2*s*, C(2) of Aib, C(2) of Iva); 54.2, 50.5 (2*d*, Me*C*HN, C(2) of Leu); 41.3, 28.0 (2*t*, C(3) of Leu, C(3) of Iva); 30.2 (*q*, MeN); 24.7 (*d*, C(4) of Leu); 25.0, 22.9, 22.0, 21.9, 15.1, 8.6 (6*q*, *Me*CHN, 2 Me(3) of Aib, Me(3) of Iva, Me(4) of Iva, 2 Me(5) of Leu). ESI-MS (MeOH + NaI): 640 (40, $[M+Na+1]^+$), 639 (100, $[M+Na]^+$). Anal. calc. for $C_{36}H_{48}N_4O_5 \cdot H_2O$ (634.82): C 68.11, H 7.70, N 8.83; found: C 67.97, H 7.68, N 8.68.

*Benzyl {(*S*)-1-{{[2-{{(*S*)-1,2-Dimethyl-1-{{methyl[(*R*)-1-naphthalen-1-yl)ethyl]amino}oxomethyl}propyl}-amino}-1,1-dimethyl-2-oxoethyl}amino}oxomethyl}-3-methylbutyl}carbamate* (Z-Leu-Aib-(*S*)-Val(2Me)-N(Me)(naphthEt); (*S*,*S*,*R*)-**13b**). As described for (*S*,*S*,*R*)-**13a**, with **12** (453 mg, 1.29 mmol), CH_2Cl_2 (5 ml), (1′*R*,2*S*)-**4b** (361 mg, 1.29 mmol), and CH_2Cl_2 (5 ml); 5.5 d at r.t.: 542 mg (67%) of (*S*,*S*,*R*)-**13b**. Colorless foam. M.p. 96–97°. R_f (CH_2Cl_2/MeOH 20:1) 0.22. R_f (hexane/AcOEt 1:1) 0.09. IR: 3310*m*, 3060*m*, 3040*m*, 2960*m*, 2930*m*, 2870*m*, 1725*m*, 1710*m*, 1690*s*, 1680*s*, 1610*s*, 1560*m*, 1530*s*, 1505*s*, 1470*m*, 1450*m*, 1390*m*, 1370*m*, 1330*m*, 1310*m*, 1250*m*, 1240*m*, 1215*m*, 1190*m*, 1170*m*, 1125*w*, 1120*w*, 1100*m*, 1080*m*, 1045*m*, 780*m*, 695*m*. ^{1}H-NMR: 8.1–8.05, 7.85–7.75, 7.5–7.35, 7.3–7.25 (4*m*, 12 arom. H, NH); 6.72 (*q*, *J* = 6.8, MeC*H*N); 6.48 (*s*, NH); 5.16 (*d*, *J* = 7.6, NH of Leu); 5.05–4.95 (*m*, PhCH_2O); 4.1–4.0 (*m*, CH(2) of Leu); 2.50 (*s*, MeN); 2.05–1.4 (*m*, CH(3) and Me(3) of Val(2Me), 2 Me(3) of Aib, CH_2(3) and CH(4) of Leu, *Me*CHN); 1.0–0.9 (*m*, 2 Me(5) of Leu, 2 Me(4) of Val(2Me)). ^{13}C-NMR: 172.3, 172.0, 171.3 (3*s*, 3 CO (amide)); *ca*. 156 (*s*, CO (urethane)); 136.3, 135.9, 133.6, 132.0 (4*s*, 4 arom. C); 128.4, 128.3, 128.2, 127.9, 126.3, 125.8, 125.2, 124.7, 124.5 (9*d*, 12 arom. CH); 67.1 (*t*, PhCH_2O); 63.8, 57.9 (2*s*, C(2) of Aib, C(2) of Val(2Me)); 54.1, 50.0 (2*d*, Me*C*HN, C(2) of Leu); 40.9 (*t*, C(3) of Leu); 32.7 (*d*, C(3) of Val(2Me)); 24.7 (*d*, C(4) of Leu); 29.9, 25.3, 22.7, 21.8, 17.9, 17.6, 17.0, 14.6 (8*q*, MeN, *Me*CHN, 2 Me(3) of Aib, Me(3) and 2 Me(4) of Val(2Me), 2 Me(5) of Leu). ESI-MS (NaI): 659 (28), 655 (40, $[M+Na+1]^+$), 654 (100, $[M+Na]^+$). Anal. calc. for $C_{37}H_{50}N_4O_5 \cdot 0.33\ H_2O$ (636.84): C 69.78, H 7.91, N 8.80; found: C 69.94, H 8.05, N 8.59.

*Benzyl {(*S*)-1-{{[2-{{(*R*)-1,2-Dimethyl-1-{{methyl[(*R*)-1-naphthalen-1-yl)ethyl]amino}oxomethyl}propyl}-amino}-1,1-dimethyl-2-oxoethyl}amino}oxomethyl}-3-methylbutyl}carbamate* (Z-Leu-Aib-(*R*)-Val(2Me)-N(Me)(naphthEt); (*S*,*R*,*R*)-**13b**). As described for (*S*,*S*,*R*)-**13a**, with **12** (866 mg, 2.47 mmol), CH_2Cl_2 (5 ml), (1′*R*,2*R*)-**4b** (695 mg, 2.48 mmol), and CH_2Cl_2 (9 ml); 2 d at r.t.; CC (CH_2Cl_2/MeOH 100:4): 1070 mg (69%) of (*S*,*R*,*R*)-**13b**. Colorless foam. M.p. 88–89°. R_f (CH_2Cl_2/MeOH 20:1) 0.27. IR: 3300*m*, 3070*w*, 3040*w*, 2960*m*, 2870*w*, 1725*m*, 1710*s*, 1705*s*, 1695*s*, 1680*s*, 1615*s*, 1565*m*, 1550*m*, 1530*s*, 1515*s*, 1505*s*, 1465*m*, 1455*m*, 1390*m*, 1385*m*, 1370*m*, 1330*m*, 1310*w*, 1250*m*, 1220*m*, 1190*m*, 1170*m*, 1120*w*, 1100*w*, 1080*m*, 1040*m*, 780*m*, 695*m*. ^{1}H-NMR: 8.01 (*d*, *J* = 8.4, NH); 7.8–7.75 (*m*, 2 arom. H); 7.55–7.4 (*m*, 5 arom. H); 7.3–7.25 (*m*, 5 arom. H); 6.50 (*q*, *J* = 6.6, MeC*H*N); 6.42 (*s*, NH); 5.05–5.0 (*m*, PhCH_2O); 4.05–3.95 (*m*, CH(2) of Leu); 2.48 (*s*, MeN); 2.24 (*sept.*, *J* = 6.6, CH(3) of Val(2Me)); 1.59 (*d*, *J* = 6.7, *Me*CHN); 1.55–1.4, 1.2 (*m*, *s*, 2 Me(3) of Aib, Me(3) of Val(2Me), CH_2(3) and CH(4) of Leu); 1.0–0.9 (*m*, 2 Me(5) of Leu, 2 Me(4) of Val(2Me)). ^{13}C-NMR: 172.2, 171.9, 171.6 (3*s*, 3 CO (amide)); 156.2 (*s*, CO (urethane)); 135.9, 133.4, 132.0 (3*s*, 4 arom. C); 128.5, 128.4, 128.2, 127.8, 126.8, 125.8, 125.1, 124.6 (8*d*, 12 arom. CH); 67.0 (*t*, PhCH_2O); 63.6, 57.9 (2*s*, C(2) of Aib, C(2) of Val(2Me)); 54.3, 50.7 (2*d*, Me*C*HN, C(2) of Leu); 40.8 (*t*, C(3) of Leu); 33.1 (*d*, C(3) of Val(2Me)); 30.4 (*q*, MeN); 24.6 (*d*, C(4) of Leu); 25.4, 24.9, 22.8, 21.7, 17.6, 17.5, 17.4, 14.8 (8*q*, *Me*CHN, 2 Me(3) of Aib, Me(3) and 2 Me(4) of Val(2Me), 2 Me(5) of Leu). ESI-MS (NaI): 655 (45, $[M+Na+1]^+$), 654 (100, $[M+Na]^+$), 477 (6, $[M-naphthCHCH_2]^+$), 446 (5, $[M-naphthCH(Me)NMe]^+$). Anal. calc. for $C_{37}H_{50}N_4O_5 \cdot 0.33H_2O$ (636.84): C 69.78, H 7.91, N 8.80; found: C 69.94, H 7.57, N 8.62.

*Benzyl {(*S*)-1-{{[2-{{(*S*)-1-Cyclopentyl-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-oxo-ethyl}amino}-1,1-dimethyl-2-oxoethyl}amino}oxomethyl}-3-methylbutyl}carbamate* (Z-Leu-Aib-(*S*)-Ala(2c-Pent)-N(Me)(naphthEt); (*S*,*S*,*R*-**13c**). As described for (*S*,*S*,*R*)-**13a**, with **12** (234 mg, 0.67 mmol), CH_2Cl_2 (2 ml), (1′*R*,2*S*)-**4c** (205 mg, 0.67 mmol), and CH_2Cl_2 (5 ml), 5.5 d at r.t.; CC (CH_2Cl_2/MeOH 50:1): 170 mg (39%) of (*S*,*S*,*R*)-**13c**. Colorless foam. M.p. 84–85°. R_f (CH_2Cl_2/MeOH 20:1) 0.33. IR: 3308*m*, 3050*w*, 2958*s*, 2871*m*, 1681*vs*, 1610*s*, 1512*vs*, 1455*s*, 1388*s*, 1331*m*, 1311*m*, 1243*s*, 1172*m*, 1111*m*, 1055*s*, 982*w*. ^{1}H-NMR: 8.1–8.05 (*m*, 1 arom. H); 7.85–7.75 (*m*, 2 arom. H); 7.5–7.4 (*m*, 4 arom. H); 7.3–7.2 (*m*, 5 arom. H); 7.18 (*s*, NH); 6.69 (*q*, *J* = 6.8, MeC*H*N); 6.43 (*s*, NH); 5.13 (*d*, *J* = 7.5, NH of Leu); 5.03, 4.97 (*AB*, *J* = 12.2, PhCH_2O); 4.05–4.0 (*m*, CH(2) of Leu); 2.52 (*s*, MeN); 2.25–2.2 (*m*, CH(3) of Ala(2cPent)); 1.7–1.4 (*m*, *Me*CHN, 2 Me(3) of Aib, Me(3) of Ala(2cPent), CH_2(3) and CH(4) of Leu, 4 CH_2 of cPent); 0.91, 0.90 (2*d*, *J* = 6.3, 6.1, 2 Me(5) of Leu). ^{13}C-NMR: 172.3, 172.0, 171.3 (3*s*, 3 CO (amide)); 156.3 (*s*, CO (urethane)); 136.4, 135.9, 133.6, 132.0 (4*s*,

4 arom. C); 128.4, 128.2, 127.9, 126.2, 125.8, 125.2, 124.7, 124.6 (8*d*, 12 arom. CH); 67.1 (*t*, Ph*C*H$_2$O); 62.7, 57.8 (2*s*, C(2) of Aib, C(2) of Ala(2cPent)); 54.2 (*d*, CH(2) of Leu); 50.0 (*d*, Me*C*HN); 44.7 (*d*, CH(3) of Ala(2cPent)); 40.9 (*t*, C(3) of Leu); 29.8 (*q*, MeN); 27.3, 27.0, 25.5 (3*t*, 4 CH$_2$ of cPent); 24.7 (*d*, C(4) of Leu); 25.4, 25.2, 22.7, 21.8, 18.8, 14.5 (6*q*, *Me*CHN, 2 Me(3) of Aib, Me(3) Ala(2cPent), 2 Me(5) of Leu). ESI-MS (MeOH/NaI): 684 (20), 679 (87, $[M+Na]^+$), 503 (38, $[M-naphthCHCH_2+1]^+$), 472 (100, $[M-naphthCH(Me)NMe]^+$). Anal. calc. for $C_{39}H_{52}N_4O_5\cdot H_2O$ (674.91): C 69.41, H 8.06, N 8.30; found: C 69.60, H 8.06, N 7.95.

*Benzyl {(*S*)-{{{2-{{(*R*)-1-Cyclopentyl-1-methyl-2-{methyl[(*R*)-1-(naphthalen1-yl)ethyl]amino}-2-oxoethyl}-amino}-1,1-dimethyl-2-oxoethyl}amino}oxomethyl}-3-methylbutyl}carbamate* (Z-Leu-Aib-(*R*)-Ala(2cPent)-N(Me)(naphthEt); (*S*,*R*,*R*)-**13c**). As described for (*S*,*S*,*R*)-**13a**, with **12** (457 mg, 1.30 mmol), CH_2Cl_2 (5 ml), (1′*R*,2*R*)-**4c** (398 mg, 1.30 mmol), and CH_2Cl_2 (10 ml); 4 d at r.t.; CC (CH_2Cl_2/MeOH 100:1): 328 mg (38%) of (*S*,*R*,*R*)-**13c**. Colorless foam. M.p. 99–102. R_f (CH_2Cl_2/MeOH 20:1) 0.35. IR: 3322*w*, 3050*w*, 2957*s*, 2870*w*, 1680v*s*, 1612*s*, 1511v*s*, 1455*m*, 1387*m*, 1332*w*, 1242*m*, 1172*w*, 1108*w*, 1059*w*. ^{1}H-NMR: 8.01 (*d*, *J* = 8.4, 1 arom. H); 7.80, 7.77 (2*d*, *J* = 8.4, 8.3, 2 arom. H); 7.55–7.4 (*m*, 4 arom. H); 7.35–7.25 (*m*, 5 arom. H, NH); 6.53 (*q*, *J* = 6.7, MeC*H*N); 6.36 (*s*, NH); 5.17 (*d*, *J* = 6.6, NH of Leu); 5.08, 4.98 (*AB*, *J* = 12.4, PhC*H*$_2$O); 4.0–3.95 (*m*, CH(2) of Leu); 2.55–2.5 (*m*, CH(3) of Ala(2cPent), MeN); 1.85–1.45 (*m*, *Me*CHN, CH$_2$(3) and CH(4) of Leu, 4 CH$_2$ of cPent); 1.53, 1.43 (2*s*, 2 Me(3) of Aib); 1.29 (*s*, Me(3) of Ala(2cPent)); 0.90, 0.89 (2*d*, *J* = 6.3, 6.1, 2 Me(5) of Leu). ^{13}C-NMR: 172.0, 171.8, 171.5 (3*s*, 3 CO (amide)); 156.2 (*s*, CO (urethane)); 136.1, 135.8, 133.4, 132.1 (4*s*, 4 arom. C); 128.4, 128.2, 127.9, 127.8, 126.6, 125.8, 125.0, 124.9, 124.6 (9*d*, 12 arom. CH); 67.1 (*t*, Ph*C*H$_2$O); 62.3, 57.8 (2*s*, C(2) of Aib, C(2) of Ala(2cPent)); 54.4 (*d*, CH(2) of Leu); 50.6 (*d*, Me*C*HN); 45.7 (*d*, CH(3) of Ala(2cPent)); 40.8 (*t*, C(3) of Leu); 30.2 (*q*, MeN); 27.4, 25.6, 25.4 (3*t*, 4 CH$_2$ of cPent); 24.6 (*d*, C(4) of Leu); 25.3, 22.7, 21.7, 18.9, 14.7 (5*q*, *Me*CHN, 2 Me(3) of Aib, Me(3) of Ala(2cPent), 2 Me(5) of Leu). ESI-MS (MeOH/NaI): 680 (100, $[M+Na]^+$). Anal. calc. for $C_{39}H_{52}N_4O_5$ (656.89): C 71.31, H 7.98, N 8.53; found: C 71.34, H 8.07, N 8.49.

*Benzyl {(*S*)-1-{{{2-{{(*S*)-1,3-Dimethyl-1-{{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}oxomethyl}butyl}-amino}-1,1-dimethyl-2-oxoethyl}amino}oxomethyl}-3-methylbutyl}carbamate* (Z-Leu-Aib-(*S*)-Leu(2Me)-N(Me)(naphthEt); (*S*,*S*,*R*)-**13d**). As described for (*S*,*S*,*R*)-**13a**, with **12** (716 mg, 2.04 mmol), CH_2Cl_2 (5 ml), (1′*R*,2*S*)-**4d** (598 mg, 2.03 mmol), and CH_2Cl_2 (10 ml); 2 d at r.t.; CC (hexane/AcOEt 2:1): 839 mg (64%) of (*S*,*S*,*R*)-**13d**. Colorless foam. R_f (CH_2Cl_2/MeOH 20:1) 0.37. IR: 3340*m*, 3320*m*, 3040*m*, 2960*s*, 2870*m*, 1725*m*, 1710*s*, 1695*s*, 1675*s*, 1665*s*, 1650*s*, 1615*s*, 1565*m*, 1545*m*, 1530*s*, 1515*s*, 1505*s*, 1495*s*, 1490*s*, 1470*s*, 1450*s*, 1395*m*, 1385*m*, 1370*m*, 1330*m*, 1320*m*, 1245*m*, 1220*m*, 1200*m*, 1170*m*, 1105*m*, 1085*m*, 1045*m*, 1030*m*, 980*m*, 950*m*, 805*m*, 780*m*, 735*m*, 675*m*, 650*m*, 630*m*. ^{1}H-NMR: 8.28 (br. *s*, NH); 7.85–7.75 (*m*, 3 arom. H); 7.55–7.45 (*m*, 4 arom. H); 7.35–7.25 (*m*, 5 arom. H); 6.87 (br. *s*, NH); 6.58 (*q*, *J* = 6.7, MeC*H*N); 5.28 (*d*, *J* = 7.5, NH of Leu); 5.12 (br. *s*, PhC*H*$_2$O); 4.18 (br., CH(2) of Leu); 2.65–2.55 (*m*, CH(4) of Leu or of Leu(2Me)); 2.52 (*s*, MeN); 1.75–1.55 (*m*, *Me*CHN, CH$_2$(3) of Leu, CH$_2$(3) and Me(3) of Leu(2Me), CH(4) of Leu(2Me) or Leu); 0.95–0.9 (*m*, 2 Me(5) of Leu, 2 Me(5) of Leu(2Me)). ^{13}C-NMR: 172.6, 171.7, 171.2 (3*s*, 3 CO (amide)); *ca*. 156 (*s*, CO (urethane)); 136.2, 135.2, 133.7, 131.8 (4*s*, 4 arom. C); 128.8, 128.6, 128.4, 128.0, 127.9, 126.7, 126.0, 125.2, 124.8, 123.3 (10*d*, 12 arom. CH); 66.9 (*t*, Ph*C*H$_2$O); 61.1, 57.5 (2*s*, C(2) of Aib, C(2) of Leu(2Me)); 53.9, 50.9 (2*d*, Me*C*HN, C(2) of Leu); 43.2, 41.7 (2*t*, C(3) of Leu, C(3) of Leu(2Me)); 30.3 (*q*, MeN); 25.1, 24.7 (2*d*, C(4) of Leu, C(4) of Leu(2Me)); 24.5, 23.6, 23.3, 23.0, 22.8, 21.9, 14.6 (7*q*, *Me*CHN, 2 Me(3) of Aib, Me(3) of Leu(2Me), 2 Me(5) of Leu(2Me), 2 Me(5) of Leu). CI-MS (NH_3): 646 (7), 645 (17, $[M+1]^+$), 492 (29), 491 (100, $[M-naphthCHCH_2+1]^+$), 461 (7), 460 (27, $[M-naphthCH(Me)NMe]^+$), 384 (17), 383 (80, $[M-Z\text{-}Leu+1]^+$), 357 (18), 100 (9). Anal. calc. for $C_{38}H_{52}N_4O_5$ (644.86): C 70.78, H 8.13, N 8.38; found: C 71.00, H 7.91, N 8.44.

*Benzyl {(*S*)-1-{{{-2-{{(*R*)-1,3-Dimethyl-1-{{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}oxomethyl}butyl}-amino}-1,1-dimethyl-2-oxoethyl}amino}oxomethyl}-3-methylbutyl}carbamate* (Z-Leu-Aib-(*R*)-Leu(2Me)-N(Me)(naphthEt); (*S*,*R*,*R*)-**13d**. As described for (*S*,*S*,*R*)-**13a**, with **12** (711 mg, 2.03 mmol), CH_2Cl_2 (5 ml), (1′*R*,2*R*)-**4d** (598 mg, 2.03 mmol), and CH_2Cl_2 (9 ml); 4 d at r.t.; CC (1. CH_2Cl_2/MeOH 50:1, 2. hexane/AcOEt 1:1): 785 mg (60%) of (*S*,*R*,*R*)-**13d**. Colorless foam. R_f (CH_2Cl_2/MeOH 20:1) 0.36. IR: 3330*m*, 3050*m*, 2960*s*, 2865*m*, 1710*s*, 1695*s*, 1680*s*, 1660*s*, 1635*m*, 1610*s*, 1550*m*, 1530*s*, 1510*s*, 1500*s*, 1495*s*, 1470*m*, 1450*m*, 1390*m*, 1385*m*, 1370*m*, 1330*m*, 1310*m*, 1260*m*, 1255*m*, 1245*m*, 1240*m*, 1220*m*, 1175*m*, 1170*m*, 1165*m*, 1160*w*, 1145*w*, 1140*w*, 1120*m*, 1105*m*, 1090*m*, 1045*m*, 1030*m*, 1010*w*, 800*m*, 780*m*, 740*m*, 695*m*. ^{1}H-NMR: 8.21 (br. *s*, NH); 7.95–7.9 (*m*, 1 arom. H); 7.85–7.8 (*m*, 2 arom. H); 7.55–7.4 (*m*, 4 arom. H); 7.3–7.25 (*m*, 5 arom. H); 6.88 (br. *s*, NH); 6.66 (*q*, *J* = 6.5, MeC*H*N); 5.35–5.3 (*m*, NH); 5.12 (br., PhC*H*$_2$O); 4.17 (br., CH(2) of Leu); 2.55–2.45 (*m*, MeN); 2.0–1.25 (*m*, 2 Me(3) of Aib, Me(3) of Leu(2Me), *Me*CHN, CH$_2$(3) and CH(4) of Leu, CH$_2$(3) and CH(4) of Leu(2Me)); 0.95–0.9, 0.6–0.55 (2*m*, 2 Me(5) of Leu, 2 Me(5) of Leu(2Me)). ^{13}C-NMR: 172.4, 171.7,

171.3 (3*s*, 3 CO (amide)); 156.2 (*s*, CO (urethane)); 136.2, 135.0, 133.8, 131.8 (4*s*, 4 arom. C); 128.8, 128.4, 128.0, 127.9, 126.4, 126.0, 125.3, 124.8, 124.1 (9*d*, 12 arom. CH); 66.9 (*t*, Ph*C*H$_2$O); 61.1, 57.5 (2*s*, C(2) of Aib, C(2) of Leu(2Me)); 54.1, 50.5 (2*d*, Me*C*HN, C(2) of Leu); 43.3, 41.6 (2*t*, C(3) of Leu, C(3) of Leu(2Me)); 30.2, 25.1 (2*q*, MeN, *Me*CHN); 25.1, 24.7 (2*d*, C(4) of Leu, C(4) of Leu(2Me)); 24.5, 24.1, 23.0, 22.9, 21.9, 15.1 (6*q*, 2 Me(3) of Aib, Me(3) of Leu(2Me), 2 Me(5) of Leu(2Me), 2 Me(5) of Leu). ESI-MS (NaI): 1314 (7, $[2M+\mathrm{Na}+1]^+$), 1313 (9, $[2M+\mathrm{Na}]^+$), 669 (12), 668 (48, $[M+\mathrm{Na}+1]^+$), 667 (100, $[M+\mathrm{Na}]^+$), 377 (6). Anal. calc. for $C_{38}H_{52}N_4O_5$ (644.86): C 70.78, H 8.13, N 8.38; found: C 70.68, H 8.22, N 8.30.

*Benzyl {(*S*)-1-{{{2-{{(*S*)-1-Benzyl-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-oxoethyl}-amino}-1,1-dimethyl-2-oxoethyl}amino}oxomethyl}-3-methylbutyl}carbamate* (Z-Leu-Aib-(*S*)-Phe(2Me)-N(Me)(naphthEt); (*S*,*S*,*R*)-**13e**). As described for (*S*,*S*,*R*)-**13a**, with **12** (355 mg, 1.01 mmol), CH_2Cl_2 (5 ml), (1′*R*,2*S*)-**4e** (331 mg, 1.01 mmol), and CH_2Cl_2 (10 ml); 40 h at r.t.; CC (hexane/AcOEt 2:1) and prep. TLC (hexane/AcOEt 1:1): 406 mg (59%) of (*S*,*S*,*R*)-**13e**. Colorless foam. M.p. 97–100°. R_f (CH_2Cl_2/MeOH 20:1) 0.42. IR: 3336*m*, 3032*w*, 2957*m*, 2871*w*, 2362*w*, 2339*w*, 1677v*s*, 1617*s*, 1497v*s*, 1455*s*, 1395*m*, 1333*w*, 1241*s*, 1172*w*, 1118*w*, 1079*m*, 1044*m*, 1029*w*, 782*m*, 736*m*, 700*m*. ^{1}H-NMR: 7.85–7.8, 7.5–7.45, 7.35–7.2, 7.1–7.05 (4*m*, 17 arom. H, 1 NH); 6.76 (br. *s*, NH); 6.52 (*q*, $J=6.7$, MeC*H*N); 5.22 (*d*, $J=7.1$, NH of Leu); 5.10 (br., PhCH_2O); 4.15–4.1 (*m*, CH(2) of Leu); 3.76, 3.19 (*AB*, $J=14.6$, CH_2(3) of Phe(2Me)); 2.60 (*s*, MeN); 1.7–1.45 (*m*, 2 Me(3) of Aib, Me(3) of Phe(2Me), CH_2(3) of Leu, CH(4) of Leu, *Me*CHN); 0.95–0.9 (*m*, 2 Me(5) of Leu). ^{13}C-NMR: 172.3, 171.4 (2*s*, 3 CO (amide)); *ca.* 156 (*s*, CO (urethane)); 136.4, 135.2, 133.6, 131.8 (4*s*, 5 arom. C); 129.8, 128.7, 128.5, 128.4, 128.1, 127.9, 126.9, 126.7, 125.9, 125.2, 124.8, 123.5 (12*d*, 17 arom. CH); 66.9 (*t*, Ph*C*H$_2$O); 61.3, 57.4 (2*s*, C(2) of Aib, C(2) of Phe(2Me)); 53.9, 50.8 (2*d*, Me*C*HN, C(2) of Leu); 41.4, 40.5 (2*t*, C(3) of Leu, C(3) of Phe(2Me)); 30.6 (*q*, MeN); 24.6 (*d*, C(4) of Leu); 25.1, 24.4, 22.9, 22.2, 21.8, 14.5 (6*q*, *Me*CHN, 2 Me(3) of Aib, Me(3) of Phe(2Me), 2 Me(5) of Leu). ESI-MS (NaI): 769 (6), 703 (11), 702 (49, $[M+\mathrm{Na}+1]^+$), 701 (100, $[M+\mathrm{Na}]^+$). Anal. calc. for $C_{41}H_{50}N_4O_5\cdot 0.33\ H_2O$ (684.88): C 71.90, H 7.46, N 8.18; found: C 71.75, H 7.45, N 8.13.

*Benzyl {(*S*)-1-{{{2-{{(*R*)-1-Benzyl-1-methyl-2-{methyl[(*R*)-1-(naphthalen-1-yl)ethyl]amino}-2-oxoethyl}-amino}-1,1-dimethyl-2-oxoethyl}amino}oxomethyl}-3-methylbutyl}carbamate* (Z−Leu−Aib−(*R*)−Phe-(2Me)−NMe(naphthEt); (*S*,*R*,*R*)-**13e**). As described for (*S*,*S*,*R*)-**13a**, with **12** (367 mg, 1.05 mmol), CH_2Cl_2 (5 ml), (1′*R*,2*S*)-**4e** (339 mg, 1.03 mmol), and CH_2Cl_2 (10 ml); 48 h at r.t.; CC (hexane/AcOEt 2:1): 434 mg (62%) of (*S*,*R*,*R*)-**13e**. Colorless foam. M.p. 99–102°. R_f (CH_2Cl_2/MeOH 20:1) 0.38. IR: 3326*m*, 3032*w*, 2957*m*, 2871*w*, 2361*w*, 1676v*s*, 1615*s*, 1511v*s*, 1455*s*, 1394*m*, 1332*w*, 1241*s*, 1172*w*, 1108*w*, 1072*m*, 1044*m*, 1029*w*, 782*m*, 738*m*, 701*m*. ^{1}H-NMR: 8.0–7.95, 7.85–7.8, 7.55–7.4, 7.3–7.25, 7.2–7.15, 7.05 (5*m*, br. *s*, 17 arom. H, 1 NH); 6.69 (*q*, $J=6.7$, MeC*H*N); 6.53 (br. *s*, NH); 5.15–5.1 (*m*, NH); 4.97, 4.84 (*AB*, $J=12.0$, PhCH_2O); 4.0–3.95 (*m*, CH(2) of Leu); 3.51, 3.47 (*AB*, $J=14.2$, CH_2(3) of Phe(2Me)); 2.63 (*s*, MeN); 1.6–1.35 (*m*, 2 Me(3) of Aib, Me(3) of Phe(2Me), CH_2(3) of Leu, CH(4) of Leu, *Me*CHN); 0.9–0.85 (*m*, 2 Me(5) of Leu). ^{13}C-NMR: 172.1, 171.6, 171.4 (3*s*, 3 CO (amide)); 156.2 (*s*, CO (urethane)); 137.0, 135.9, 133.6, 132.0 (4*s*, 5 arom. C); 130.7, 128.5, 128.4, 128.1, 127.9, 126.6, 126.5, 125.8, 125.3, 124.7, 124.1 (11*d*, 17 arom. CH); 67.1 (*t*, Ph*C*H$_2$O); 60.2, 57.6 (2*s*, C(2) of Aib, C(2) of Phe(2Me)); 54.3, 50.3 (2*d*, Me*C*HN, C(2) of Leu); 41.3, 41.0 (2*t*, C(3) of Leu, C(3) of Phe(2Me)); 30.3 (*q*, MeN); 24.6 (*d*, C(4) of Leu); 25.5, 25.1, 22.8, 22.1, 21.7, 15.0 (6*q*, *Me*CHN, 2 Me(3) of Aib, Me(3) of Phe(2Me), 2 Me(5) of Leu). ESI-MS (NaI): 846 (7), 703 (13), 702 (46, $[M+\mathrm{Na}+1]^+$), 701 (100, $[M+\mathrm{Na}]^+$). Anal. calc. for $C_{41}H_{50}N_4O_5\cdot 0.5H_2O$ (687.88): C 71.59, H 7.47, N 8.14; found: C 71.54, H 7.46, N 8.12.

5. *X-Ray Crystal-Structure Determination of (1′*R*,2*R*)-***4a***, (1′*R*,2*S*)-***4b***, (1′*R*,2*S*)-***4c***, (1′*R*,2*S*)-***4d***, and (1′*R*,2*S*)-***4e*** (see *Table 5* and *Fig.*)*[2]). All measurements were conducted at low temp. using graphite-monochromated MoK_α radiation (λ 0.71069 Å). The data collection and refinement parameters are given in *Table 5*, and views of the molecules are shown in the *Fig*. The intensities were corrected for *Lorentz* and polarization effects, and for (1′*R*,2*R*)-**4a**, an empirical absorption correction, based on azimuthal scans of several reflections [39], was also applied. Equivalent reflections, other than *Friedel* pairs, were merged. Each structure was solved by direct methods, which revealed the positions of all non-H-atoms. The structure of (1′*R*,2*S*)-**4e** contains highly disordered solvent molecules which fill a column-like cavity that runs parallel to the 6_5 axis. As the solvent for the recrystallization was AcOEt, it was assumed that the disordered solvent molecules were

---

[2]) Crystallographic data (excluding structure factors) for the structures of (1′*R*,2*R*)-**4a**, (1′*R*,2*S*)-**4b**, (1′*R*,2*S*)-**4c**, (1′*R*,2*S*)-**4d**, and (1′*R*,2*S*)-**4e** have been deposited with the *Cambridge Crystallographic Data Centre* as supplementary publications no. CCDC-160821 to CCDC-160825. 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 5. *Crystallographic Data of Compounds (1′*R,*2*R*)*-**4a**, *(1′*R,*2*S*)*-**4b**, *(1′*R,*2*S*)*-**4c**, *(1′*R,*2*S*)*-**4d**, *and (1′*R,*2*S*)*-**4e**

	(1′*R*,2*R*)-**4a**	(1′*R*,2*S*)-**4b**	(1′*R*,2*S*)-**4c**	(1′*R*,2*S*)-**4d**	(1′*R*,2*S*)-**4e**
Crystallized from	oil	hexane/Et_2O	hexane/Et_2O	AcOEt/hexane	AcOEt
Empirical formula	$C_{18}H_{22}N_2$	$C_{19}H_{24}N_2$	$C_{21}H_{26}N_2$	$C_{20}H_{26}N_2$	$C_{23}H_{24}N_2 \cdot 1/4$ $C_4H_8O_2$
M_r	266.39	280.41	306.45	294.44	350.48
Crystal color, habit	colorless, prism	colorless, prism	colorless, prism	colorless, prism	colorless, prism
Crystal dimensions [mm]	0.40×0.42 $\times 0.45$	0.20×0.40 $\times 0.45$	0.10×0.25 $\times 0.32$	0.35×0.38 $\times 0.48$	0.30×0.33 $\times 0.40$
Temperature [K]	173 (1)	173 (1)	160 (1)	173 (1)	173 (1)
Crystal system	orthorhombic	monoclinic	monoclinic	orthorhombic	hexagonal
Space group	$P2_12_12_1$	$P2_1$	$P2_1$	$P2_12_12$	$P6_5$
Z	4	2	2	4	6
Reflections for cell determination	25	25	2732	23	20
2θ Range for cell determination [°]	35 – 39	35 – 39	2 – 60	37 – 40	10 – 16
Unit cell parameters a [Å]	13.441 (2)	8.664 (2)	8.4449 (2)	7.472 (2)	16.277 (3)
b [Å]	14.400 (2)	7.655 (3)	7.6820 (2)	28.232 (1)	16.277 (3)
c [Å]	8.124 (2)	12.279 (2)	13.4962 (4)	8.383 (2)	13.119 (5)
β [°]	90	91.69 (2)	90.489 (1)	90	90
V [Å^3]	1572.3 (5)	814.0 (4)	875.52 (4)	1768.3 (5)	3010 (2)
D_x [g cm^{-3}]	1.125	1.144	1.162	1.106	1.160
$\mu(MoK_\alpha)$ [mm^{-1}]	0.0661	0.0670	0.0678	0.0645	0.0693
Transmission factors (min; max)	0.965; 1.000	–	–	–	–
Diffractometer	*Rigaku AFC5R*	*Rigaku AFC5R*	*Nonius KappaCCD*	*Rigaku AFC5R*	*Rigaku AFC5R*
Scan type	$\omega/2\theta$	$\omega/2\theta$	ϕ and ω	ω	$\omega/2\theta$
$2\theta_{max}$ [°]	60	55	60	55	55
Total reflections measured	3147	2125	24574	2815	3165
Symmetry independent reflections	3021	1997	5084	2708	2607
Reflections used ($I > 2\sigma(I)$)	2388	1536	4190	2318	1539
Parameters refined	270	190	208	304	253
Final R	0.0450	0.0432	0.0450	0.0372	0.0464
wR	0.0396	0.0384	0.0466	0.0347	0.0346
Weights: p in $w = [\sigma^2(F_o) + (pF_o)^2]^{-1}$	0.005	0.005	0.015	0.005	0.005
Goodness of fit	1.824	1.683	1.524	1.885	1.596
Secondary extinction coefficient	$1.1\ (2) \cdot 10^{-6}$	$4.3\ (4) \cdot 10^{-6}$	$1.0\ (1) \cdot 10^{-5}$	$8\ (1) \cdot 10^{-7}$	$5.8\ (8) \cdot 10^{-7}$
Final Δ_{max}/σ	0.0003	0.0002	0.0005	0.0004	0.005
$\delta\rho$ (max; min) [e Å^{-3}]	0.20; −0.16	0.19; −0.16	0.31; −0.21	0.18; −0.13	0.17; −0.15
Structure solution program	SHELXS86 [34]	SHELXS86 [34]	SHELXS97 [35]	SIR92 [36]	SHELXS86 [34]
Structure refinement program	TEXSAN [37]	TEXSAN [37]	teXsan [38]	TEXSAN [37]	teXsan [38]

AcOEt. Three solvent atoms were located in the asymmetric unit and refined with site-occupation factors of 0.5. Upon symmetry expansion, it was found that these solvent atoms are linked into an infinite chain along the 6_5 axis. The form of the chain suggests that it is built from overlapping AcOEt molecules, and the site-occupation factors for the defined atoms would be consistent with this. Thus, the ratio of solvent molecules to substrate molecules in (1′*R*,2*S*)-**4e** is *ca.* 1:4.

The non-H-atoms of each structure were refined anisotropically. All of the H-atoms in (1′*R*,2*R*)-**4a** and (1′*R*,2*S*)-**4d** were located in difference electron density maps, and their positions were allowed to refine together with individual isotropic displacement parameters. In each of the other structures, the H-atoms 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 C-atom. The H-atoms of the solvent molecule of (1′*R*,2*S*)-**4e** were not included in the model. Refinement of each structure was carried out on *F* using full-matrix least-squares procedures, which minimized the function $\Sigma w(|F_o| - |F_c|)^2$. Corrections for secondary extinction were applied. For (1′*R*,2*S*)-**4c**, five reflections 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 [40], and the scattering factors for H-atoms were taken from [41]. Anomalous dispersion effects were included in F_{calc} [42]; the values for f' and f'' were those of [43]. The values of the mass attenuation coefficients were taken from [44].

The crystals of each compound were enantiomerically pure, but the absolute configuration was not determined for any of the structures. In each case, the enantiomer used in the refinement was chosen to agree with the known (*R*)-configuration at the methyl-substituted C-atom adjacent to the naphthalene moiety. The configuration at the chiral centre in the azirine ring of each structure could then be established relative to the configuration of the known chiral centre.

REFERENCES

[1] B. V. V. Prasad, P. Balaram, *CRC Crit. Rev. Biochem.* **1984**, *16*, 307.
[2] I. L. Karle, P. Balaram, *Biochemistry* **1990**, *29*, 6747.
[3] C. Toniolo, M. Crisma, F. Formaggio, G. Valle, G. Cavicchioni, G. Precigoux, A. Aubry, J. Kamphuis, *Biopolymers* **1993**, *33*, 1061.
[4] E. Benedetti, *Biopolymers* **1996**, *40*, 3.
[5] H. Heimgartner, *Angew. Chem.* **1991**, *103*, 271.
[6] J. M. Humphrey, A. R. Chamberlin, *Chem. Rev.* **1997**, *97*, 2243.
[7] P. Wipf, H. Heimgartner, *Helv. Chim. Acta* **1990**, *73*, 13.
[8] W. Altherr, H. Heimgartner, in 'Peptides 1990', Eds. E. Giralt and D. Andreu, ESCOM Science Publishers, Leiden, 1991, p. 107.
[9] W. Altherr, H. Heimgartner, in 'Peptides 1992', Eds. C. H. Schneider and A. N. Eberle, ESCOM Science Publishers, Leiden, 1993, p. 387.
[10] W. Altherr, Dissertation, Universität Zürich, 1994.
[11] R. Luykx, C. B. Bucher, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **1996**, *79*, 527.
[12] R. T. N. Luykx, Dissertation, Universität Zürich, 2000.
[13] J. Lehmann, A. Linden, H. Heimgartner, *Tetrahedron* **1998**, *54*, 8721.
[14] J. Lehmann, A. Linden, H. Heimgartner, *Tetrahedron* **1999**, *55*, 5359.
[15] J. Lehmann, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **1999**, *82*, 888.
[16] J. Lehmann, H. Heimgartner, *Helv. Chim. Acta* **1999**, *82*, 1899.
[17] R. A. Breitenmoser, H. Heimgartner, *Helv. Chim. Acta* **2001**, *84*, 786.
[18] I. Dannecker-Dörig, H. Heimgartner, in 'Peptides 1990', Eds. E. Giralt and D. Andreu, ESCOM, Leiden, 1990, p. 460.
[19] I. Dannecker-Dörig, Dissertation, Universität Zürich, 1995.
[20] F. S. Arnhold, Universität Zürich, 1997.
[21] D. Obrecht, H. Heimgartner, *Helv. Chim. Acta* **1984**, *67*, 526.
[22] D. Obrecht, H. Heimgartner, *Helv. Chim. Acta* **1987**, *70*, 329.
[23] D. Obrecht, H. Heimgartner, *Helv. Chim. Acta* **1990**, *73*, 221.
[24] J. E. F. Magirius, Universität Zürich, 1995.
[25] J. M. Villalgordo, H. Heimgartner, *Helv. Chim. Acta* **1997**, *80*, 748.
[26] K. N. Koch, H. Heimgartner, *Helv. Chim. Acta* **2000**, *83*, 1881.
[27] K. N. Koch, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **2000**, *83*, 233.

[28] K. N. Koch, A. Linden, H. Heimgartner, *Tetrahedron* **2001**, *57*, 2311.
[29] C. B. Bucher, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **1995**, *78*, 935.
[30] C. B. Bucher, H. Heimgartner, *Helv. Chim. Acta* **1996**, *79*, 1903.
[31] C. K. Johnson, 'ORTEP II, Report ORNL-5138', Oak Ridge National Laboratory, Oak Ridge, Tennessee, 1976.
[32] C. Jenny, H. Heimgartner, *Helv. Chim. Acta* **1986**, *69*, 374.
[33] C. Strässler, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **1997**, *80*, 1528.
[34] G. M. Sheldrick, 'SHELXS86', *Acta Crystallogr., Sect. A* **1990**, *46*, 467.
[35] G. M. Sheldrick, 'SHELXS97, Program for the Solution of Crystal Structures', University of Göttingen, 1997.
[36] A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, M. C. Burla, G. Polidori, M. Camalli, 'SIR92', *J. Appl Crystallogr.* **1994**, *27*, 435.
[37] 'TEXSAN: Single Crystal Structure Analysis Software', Molecular Structure Corporation, The Woodlands, Texas, Version 5.0, 1989.
[38] 'teXsan: Single Crystal Structure Analysis Software', Molecular Structure Corporation, The Woodlands, Texas, Version 1.10, 1999.
[39] A. C. T. North, D. C. Phillips, F. S. Mathews, *Acta Crystallogr., Sect. A* **1968**, *24*, 351.
[40] E. N. Maslen, A. G. Fox, M. A. O'Keefe, in 'International Tables for Crystallography', Ed. A. J. C. Wilson, Kluwer Academic Publishers, Dordrecht, 1992, Vol. C, Table 6.1.1.1, p. 477.
[41] R. F. Stewart, E. R. Davidson, W. T. Simpson, *J. Chem. Phys.* **1965**, *42*, 3175.
[42] J. A. Ibers, W. C. Hamilton, *Acta Crystallogr.* **1964**, *17*, 781.
[43] D. C. Creagh, W. J. McAuley, in 'International Tables for Crystallography', Ed. A. J. C. Wilson, Kluwer Academic Publishers, Dordrecht, 1992, Vol. C, Table 4.2.6.8, p. 219.
[44] D. C. Creagh, J. H. Hubbell, in 'International Tables for Crystallography', Ed. A. J. C. Wilson, Kluwer Academic Publishers, Dordrecht, 1992, Vol. C, Table 4.2.4.3, p. 200.

Received April 4, 2001