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Enantioselective synthesis of S-substituted ω-amino-α-thiohydroxycarboxylic acids via sulfenylation of 2-(ω-aminoalkyl)-oxazolines

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Abstract: Optically active ω-benzenesulfonylamino-α-methylthio- and ω-benzenesulfonylamino-α-phenylthiocarboxylic acids **7** were synthesized by stereoselective α-sulfenylation of 2-(ω-benzenesulfonylaminoalkyl)-1,3-oxazolines **3** with disulfides in the presence of LDA, followed by hydrolysis. Twofold α-sulfenylation affording 2-[ω-benzenesulfonylamino-α,α-bis-(methylthio)-alkyl]- or 2-[ω-benzenesulfonylamino-α,α-bis-(phenylthio)-alkyl]-1,3-oxazolines **8** was observed as side reaction. Phenylselenylation of 2-(ω-benzenesulfonylaminoalkyl)-1,3-oxazolines **3** also occurs twice affording the 2-[3-benenesulfonylamino-α,α-bis-(phenylselenyl)-propyl]-1,3-oxazoline **18**. © 1997 Elsevier Science Ltd

ω-Amino-α-thiohydroxycarboxylic acids exhibit interesting biological properties.[1,2] Racemic compounds in this series can be obtained mostly by substitution of the corresponding α-halo-compounds with S-nucleophiles[1–3] or α-sulfenylation of lactams.[4] In the optically active series, however, only two γ-aminobutanoic acids have been reported, which were obtained from the corresponding optically active ω-amino-2-brom-carboxylic acid[5] or by nucleophilic ring opening of an aziridinecarboxylic acid.[6]

We envisaged the synthesis of ω-amino-α-thiohydroxycarboxylic acids by asymmetric α-sulfenylation of ω-aminoacid derivatives. Although asymmetric α-sulfenylation has been reported with non-functionalized 3-acyl-1,3-oxazolidine-2-ones (Evans auxiliary)[7,8], no results were published in the ω-aminoacyl-series so far. Recently we developed an asymmetric synthesis of α-branched ω-aminocarboxylic acids via highly stereoselective α-alkylation of chiral 2-(ω-aminoalkyl)-1,3-oxazolines[9] similar to Meyers[10] well-known protocol but not following its stereochemical model. We report now the application of this approach to the synthesis of ω-amino-α-thiohydroxycarboxylic acids **7** (Scheme 1). Up to now α-sulfenylation of 2-alkyl-1,3-oxazolines has not been reported at all.

The starting 2-(ω-aminoalkyl)-1,3-oxazolines **3** were obtained from the corresponding aminoalcohol **2** as chiral auxiliary and a derivative (lactam acetal or lactim ether) of lactam **1** as reported before.[9,16]

The α-sulfenylation of **3** could be achieved with excess of LDA (3 equivalents) and dimethyldisulfide or diphenyldisulfide **4**. Reaction temperature of −78°C (compare entries 10, 14, 15 in Table 1) and 1.5 equivalents of disulfide **5** (compare entries and 1, 2, 10 and 11) turned out to be useful. The resulting 2-(ω-amino-α-methylthioalkyl)- or 2-(ω-amino-α-phenylthioalkyl)-1,3-oxazolines **5** (see Table 1) were obtained with good diastereoselectivities. In a number of cases the yields of oxazolines **5** were lowered by partial hydrolysis of the oxazoline ring to corresponding amides **6** (see Table 1, entries 10, 12) or by twofold sulfenylation to corresponding α,α-disulfenylated ω-aminoalkyloxazolines **8** (see Table 1, entries 1, 2, 3, 5, 7). Those by-products could be removed by column chromatography. Disulfenylation predominates if excess higher than 1.5 equivalents of disulfide (see entries 2, 3) was used or in particular if the reaction temperature was increased from −78°C to −40°C (see Table 1, compare entry 2 with entry 4 and entry 10 with entry 15). In general, dimethyldisulfide exhibited a

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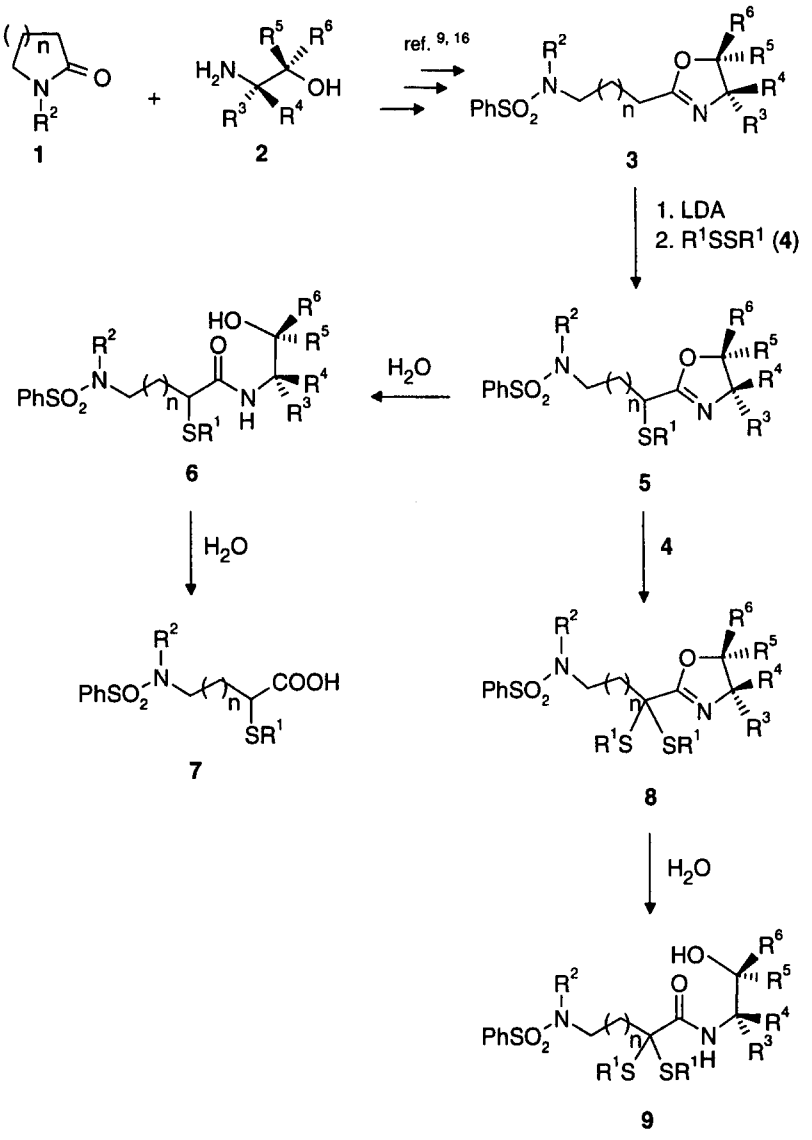


Scheme 1.

greater tendency to disulfenylation than diphenyldisulfide. The application of triethylborane which had a remarkable stereoselectivity improving effect in the alkylation of 2-(ω-aminoalkyl)-1,3-oxazolines **3**[9] turned out to be disadvantageous in the sulfenylation (see entries 3, 6, 12, 13). A reaction of the disulfide **4** with triethylborane was indicated preventing α-sulfenylation (see entry 6, 13) unless higher excess of **4** was used (see entries 3 and 12). It has to be mentioned that no stereoselective monosulfenylation of 2-(ω-benzenesulfonylaminopentyl)-1,3-oxazolines **3** (n=3) could be achieved. If dimethyldisulfide was used only disulfenylated product **8** (see entry 8) was obtained while diphenyldisulfide formed the corresponding 2-(ω-amino-α-phenylthiopentyl)-1,3-oxazoline **5** as 58: 42 diastereomeric mixture (entry 18). In the 2-(ω-aminopropyl)-series however diasteriomerically pure α-monosulfenylated products **5** (n=1) were obtained either directly from the sulfenylation mixture (see Table 1) or by chromatographic separation of the diastereomeric mixture in almost all cases.

Table 1. Results of α-sulfenylation of ω-aminoalkyl-oxazolines **3**

entry	R^1	R^2	n	R^3	R^4	R^5	R^6	Reaction conditions	d. r.	Configuration[2]	Products / Yield (%)			
											5	**6**	**8**	**9**
1	Me	Me	1	H	Et	H	H	1.5 equ. **4**	81:19	*(R)*	**a**/69	-	**a**/21	-
2								3 equ. **4**	88:12		**a**/22	-	**a**/32	-
3								5 equ. **4**, 3 equ.BEt_3	80:20		**a**/20[3]	-	**a**/21	-
4								3 equ. **4**, -40°C			-	-	-	**a**/92
5	Me	Me	1	Me	H	Ph	H	1.5 equ. **4**	>90:10	*(S)*	**b**/40	-	**b**/ 59	-
6								1.5 equ. **4**, 3 equ.BEt_3			-	-	-	-
7	Me	Me	1	MOM	H	H	Ph	1.5 equ. **4**	90:10	*(R)*	**c**/47	-	**c**/40	-
8	Me	Me	3	Me	H	Ph	H	1.5 equ. **4**			-	-	**d**/73	-
9	Me	H	1	Me	H	Ph	H	1.5 equ. **4**	65:35	*(S)*	**e**/52	-	-	-
10	Ph	Me	1	H	Et	H	H	1.5 equ. **4**	80:20	*(R)*	**f**/50	**f**/10	-	-
11								3 equ. **4**	80:20		**f**/60	-	-	-
12								4 equ. **4**, 3 equ.BEt_3	>90:10		-	**f**/31[4]	-	-
13								1.5 equ. **4**, 1.5 equ. BEt_3			-	-	-	-
14								1.5 equ. **4**, -90°C	82:18		**f**/51	-	-	-
15								1.5 equ. **4**, -40°C			-	-	**f**/28[4]	-
16	Ph	Me	1	Me	H	Ph	H	1.5 equ. **4**	64:36	*(S)*	**g**/32[4]	-	-	-
17	Ph	Me	1	MOM	H	H	Ph	1.5 equ. **4**	>90:10	*(R)*	**h**/38	-	-	-
18	Ph	Me	3	Me	H	Ph	H	1.5 equ. **4**	58:42	*(S)*	**i**/44[4]	-	-	-

[1] see General Procedure in the experimental part
[2] configuration of the major isomer in α-position of **5**
[3] 40% of starting material **3** was recovered
[4] ~20% of starting material **3** was recovered

Hydrolysis of the sulfenylated 2-(ω-benzenesulfonylaminoalkyl)-1,3-oxazolines **5** was achieved in aqueous HCl giving the corresponding ω-benzenesulfonylamino-α-methylthio- or ω-benzenesulfonylamino-α-phenylthiocarboxylic acids **7** in high yields (see Table 2).

The elucidation of the absolute configuration of α-sulfenylated ω-benzenesulfonylaminocarboxylic acids **7** and their precursors **5** was based on the independent synthesis of the carboxylic acids **7a** and **7b** starting from the commercially available (*S*)-(+)-2,4-diaminobutanoic acid dihydrochloride **10**

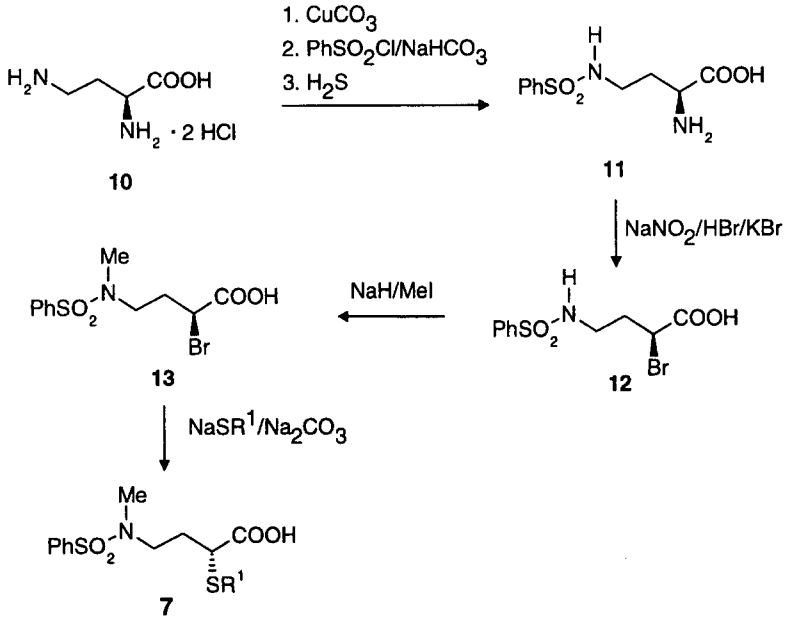
Table 2. α-Sulfenylated ω-benzenesulfonylaminocarboxylic acids **7**

entry	R^1	R^2	n	Configuration and substituent in 4-position of **3**	ee (%)	**7**[1] yield (%)	$[\alpha]_D^{20}$ (c in g/100mL $CHCl_3$)
1	Me	Me	1	(*R*)-Et	>90[2]	(*R*)-**a**/92	+ 7.2 (0.90)
2	Me	Me	1	(*S*)-MOM	80	(*R*)-**a**/96	+ 5.9 (0.47)
3	Me	Me	1	(*S*)-Me	>90	(*S*)-**a**/quant.	- 8.1 (0.07)
4	Ph	Me	1	(*R*)-Et	>90[2]	(*R*)-**b**/77	+ 6.8 (0.74)
5	Ph	Me	1	(*S*)-MOM	>90	(*R*)-**b**/66	+ 6.8 (0.95)
6	Ph	Me	3	(*S*)-Me	16	(*S*)-**c**/quant.	- 7.6 (0.25)

[1] configuration was determined by independed synthesis of **7a** and **7b** according to Scheme 2

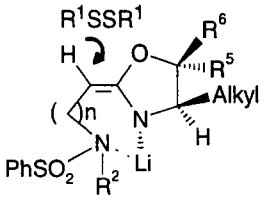
[2] after prior removal of the minor diastereoisomer **5** by chromatography

according to Scheme 2. After transformation[11] to the γ-benzenesulfonylamino acid **11** the α-amino group was substituted by bromide with retention of configuration adopting a known procedure.[12] The resulting (*S*)-4-benzenesulfonylamino-2-bromo-butanoic acid **12** was N-methylated[13] and reacted with sodium methylthiolate[14] or -phenylthiolate[15] affording **7a** and **7b**, respectively (see Experimental). Since this type of substitution of bromine by S-nucleophiles at other α-bromocarboxylic acids is known to occur by inversion[14] the resulting dextrorotatory 4-(N-benzenesulfonyl-N-methylamino)-2-mercaptobutanoic acids **7a** and **7b** possess (*R*)-configuration. Based on this configuration the ω-benzenesulfonylaminocarboxylic acids **7** obtained by α-sulfenylation according to Scheme 1 were assigned (*R*) for positive optical rotation and (*S*) for negative α-values.

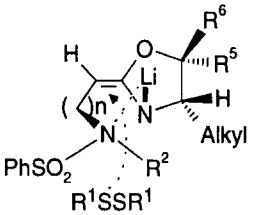


Scheme 2.

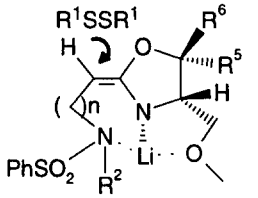
Considering the stereodirecting effects of substituents in the oxazoline ring of the starting oxazolines **3** on the α-sulfenylation (see Scheme 1 and Table 1) it turned out that as expected substituents at position 4 are governing. 4-(*R*)-Alkyl groups implied α-(*R*) products **5** and vice versa. Unlike the known α-alkylation of oxazolines **3**[9] the sulfenylation gives opposite configurations in the products **5** if the chelating MOM-substituent (R^3=MeOCH or a non-chelating alkyl substituents (R^3=alkyl) are found at position 4 of the oxazoline ring (see Table 1, compare entries 5 with 7 and 16 with 17). Unlike in Meyers cases for the α-alkylation of 2-alkyl-1,3-oxazolines where (*Z*)-azaenolates are formed 2-(ω-benzenesulfonylamino-alkyl)-1,3-oxazolines **3** afford (*E*)-azaenolates on treatment with LDA such as shown in Schemes 3–5 due to chelation of the Li-atom with the ω-benzenesulfonylamino group. Because of the shielding effect of the benzenesulfonyl–aminoalkyl bridge the attack of the disulfide **4** is not likely to occur via S–Li-interaction, but from the side opposite to the Li-atom. These models (Schemes 3–5) well explain the stereochemical outcome of all cases investigated.



Scheme 3.



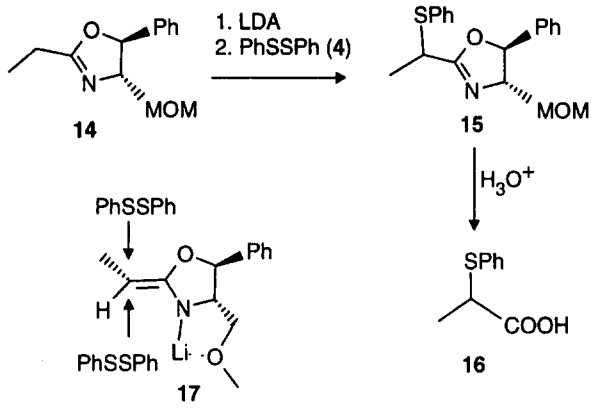
Scheme 4.



Scheme 5.

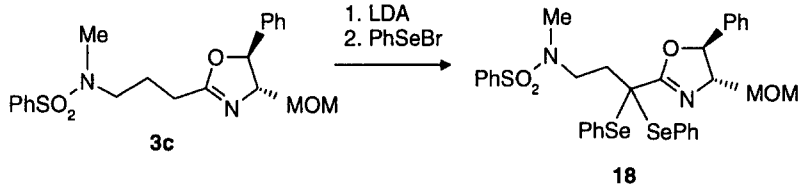
We also investigated typical 2-alkyloxazolines lacking functional groups in the alkyl chain, which were extensively used by Meyers in α-alkylations. But following a similar sulfenylation procedure as applied in Scheme 1 for **3** the 2-ethyloxazoline **14**[17] gave the 2-(α-phenylthioethyl)-oxazoline **15** with much lower stereoselectivity (d.r. 55: 45) than in cases of **3**. As compared with the known (*R*)-(+)-2-phenylthiopropionic acid[18] the positive [α]-value (α_D^{20}=+1.7) of the mixture of enantiomeric **16** revealed that the major stereoisomer was derived from a chelated *re*-attack at the (*Z*)-enolate **17**. Obviously chelated (*re*) and non-chelated (*si*) attack of the diphenyldisulfide occurs almost to the same extent (Scheme 6).

We further tried to apply phenylselenylbromide in the α-functionalization of 2-(ω-aminoalkyl)-1,3-oxazolines **3**. It was not possible to stop the reaction at the stage of monoselenylation and only the 2-[3-benzenesulfonylamino-α,α-bis-(phenylselenyl)-propyl]-1,3-oxazoline **18** could be obtained



Scheme 6.

even if excess of **3** was used. Presumably the envisaged monoselenylation product is more acidic than the starting material **3** thus giving immediate twofold selenylation to **18** (Scheme 7).



Scheme 7.

The aforementioned results demonstrate the first asymmetric synthesis of 4-benzenesulfonylamino-2-methylthio- and 4-benzenesulfonylamino-2-phenylthiobutanoic acids **7**. Either of the two enantiomers **7** can be prepared in a predictable way by choosing the suitably configured aminoalcohol **2** as chiral auxiliary.

Experimental

^1H NMR and ^{13}C NMR spectra were recorded at 300 and 75.5 MHz respectively on a Brunker AC-300. The splitting patterns were designated as follows: s (singlet), d (doublet), dd (double doublet), t (triplet), q (quartet), qd (quartet doublet), quint (quintet), m (multiplet), and br (broad). The diastereomeric ratios were determined from ^{13}C NMR spectra obtained before chromatographic purification (^{13}C NMR-shifts in brackets correspond to the minor diastereoisomer) and in some cases by HPLC. Optical rotation was determined with a Perkin Elmer polarimeter 241 using a 0.6 ml cell. EI-Mass spectra (HP 5995 A) were measured at 70eV. CI-high-resolution mass spectra were recorded on a VG Autospec, Finnigan (NH_3). For preparative column chromatography silicagel (0.04–0.063 mm, MERCK) was used.

Starting materials **3** were usually obtained by ring transformation of lactam acetals or lactim ethers with aminoalcohols **2**.[16] (*S*)-(+)-2,4-Diaminobutanoic acid dihydrochloride was purchased from Aldrich.

General procedure for α-sulfenylation of 3 to 2-(ω-benzenesulfonylamino-2-sulfenylalkyl)-1,3-oxazolines 5 and to 2-(ω-benzenesulfonylamino-2,2-disulfenylalkyl)-1,3-oxazolines 8 or corresponding amides 6 and 9 (Table 1).

A solution of oxazoline **3** (1.0 mmol) in dry THF (5 mL) was added to a solution of LDA (3 mmol, from 0.52 mL of diisopropylamine and 2.78 mL of 1.6 M n-BuLi in hexane) at −78°C under argon.

The resulting dark yellow solution was stirred at −78°C for 30 min. A solution of disulfide **4** (1.5 mmol) in 3 ml THF was added dropwise over 10 min. The resulting, almost pale yellow solution was stirred for 2 h at −78°C and was then allowed to reach room temperature overnight. The reaction mixture was poured into saturated NH_4Cl solution (30 mL) and extracted with dichloromethane (4×10 mL), dried (Na_2SO_4) and concentrated. Final purification by column chromatography on silica gel gave compounds **5**, **6**, **8** and **9** as oils with exception of **8f** (white solid) (see Table 1) (R_f for **5** and **8**=0.6–0.7; for **6** and **9**=0.4–0.6; ethyl acetate/hexane=7/3). In some cases (**5a**, **5f**) it was possible to isolate the main diastereoisomer **5** by chromatography. Variation of temperature or of ratios of reactants or the addition of BEt_3 after deprotonation according to Table 1 gave unfavorable results.

(4R)-2-[(1R)-1-Methylthio-3-(N-benzenesulfonyl-N-methyl-amino)-propyl]-4-ethyl-1,3-oxazoline ***5a***

Pale yellow oil, $[\alpha]_D^{20}$=+20.2 (c 0.44, $CHCl_3$); ^1H NMR ($CDCl_3$) δ/ppm, J/Hz: 0.85–0.91 (t, J=7.6, 3H, CH_3); 1.16–1.21 (t, J=7.1, 1H, CH_2); 1.41–1.75 (2×m, 2H, CH_2); 1.82–2.05 (m, 1H, CH_2); 2.08 (s, 3H, CH_3-S); 2.67 (s, 3H, CH_3-N); 3.07–3.11 (m, 2H, CH_2-N); 3.33–3.46 (m, 1H, CH-S); 3.84–3.90 (m, 1H, CH_2-O); 3.97–4.06 (m, 1H, CH-N); 4.25–4.32 (m, 1H, CH_2-O); 7.41–7.54 (m, 3H, Ph); 7.70–7.84 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$) δ/ppm: 10.3 (10.2) CH_3; 14.1 (14.6) CH_3-S; 28.9 (28.8) CH_2; 30.1 (30.2) CH_2; 35.6 CH_3-N; 40.0 (39.9) CH-S; 48.4 CH_2-N; 67.8 CH-N; 72.6 (72.7); CH_2-O; 127.4 2×CH_{Ph}; 129.4 2×CH_{Ph}; 132.9 CH_{Ph}; 137.8 C_{Ph}; 166.3 C=N. EI-MS, m/z (%): 356 (M^+, 2); 355 (M−1, 1.5); 184 (47); 141 (43); 77 (100); 73 (25); 42 (37). $C_{16}H_{24}O_3N_2S_2$ (356.49): Exact mass calcd. 356.1228 found 356.1227.

(4S,5S)-2-[(1S)-1-Methylthio-3-(N-benzenesulfonyl-N-methyl-amino)-propyl]-4-methyl-5-phenyl-1,3-oxazoline ***5b***

Colorless oil, $[\alpha]_D^{20}$=−35.8 (c 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ/ppm, J/Hz: 0.93–0.97 (d, J=7.1, 3H, CH_3); 1.21–1.25 (m, 1H, CH_2); 1.75–1.85 (m, 1H, CH_2); 2.17 (s, 3H, CH_3-S); 2.69 (s, 3H, CH_3-N); 2.99–3.12 (m, 2H, CH_2-N); 3.14–3.21 (m, 1H, CH-S); 4.40–4.43 (m, 1H, CH-N); 5.57–5.61 (d, J=9.8, 1H, CH-O); 7.18–7.45 (m, 5H, Ph); 7.47–7.54 (m, 3H, Ph); 7.63–7.75 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$) δ/ppm: 14.4 CH_3-S; 18.3 CH_3; 34.9 CH_2; 35.7 CH_3-N; 40.2 CH-S; 48.6 CH_2-N; 65.3 CH-N; 84.6 CH-O; 127.6 2×CH_{Ph}; 127.8 2×CH_{Ph}; 128.4 2×CH_{Ph}; 129.5 2×CH_{Ph}; 132.9 CH_{Ph}; 133.2 CH_{Ph}; 137.9 C_{Ph}; 141.6 C_{Ph}; 166.9 C=N. EI-MS, m/z (%): 419 (M^++1, 3); 418 (M^+, 10); 240 (19); 184 (23); 144 (25); 141 (57); 98 (47); 77 (100); 44 (65). $C_{21}H_{26}O_3N_2S_2$ (418.56): Anal. calcd. H 6.26, N 6.69, S 15.32. found H 6.45, N 5.96, S 15.32.

(4S,5R)-2-[(1R)-1-Methylthio-3-(N-benzenesulfonyl-N-methyl-amino)-propyl]-4-methoxymethyl-5-phenyl-1,3-oxazoline ***5c***

d.r.: 90:10; colorless oil, $[\alpha]_D^{20}$=−9.9 (c 0.91, $CHCl_3$); ^1H NMR ($CDCl_3$) δ/ppm, J/Hz: 1.73–1.77 (m, 1H, CH_2); 1.90–1.97 (m, 1H, CH_2); 2.16 (s, 3H, CH_3-S); 2.69 (s, 3H, CH_3-N); 3.11–3.18 (m, 2H, CH_2-N); 3.21–3.28 (m, 1H, CH-S); 3.32 (s, 3H, CH_3-O); 3.41–3.49 (m, 1H, CH_2-O); 3.51–3.55 (m, 1H, CH_2-O); 4.07–4.12 (q, 1H, CH-N); 5.28–5.30 (d, J=6.6, 1H, CH-O); 7.19–7.30 (m, 5H, Ph); 7.42–7.53 (m, 3H, Ph); 7.69–7.73 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$) δ/ppm: 14.3 (14.5) CH_3-S; 30.3 (30.5) CH_2; 35.7 CH_3-N; 40.3 (40.7) CH-S; 48.5 (48.1) CH_2-N; 59.6 CH_3-O; 74.4 CH_2-O; 74.8 CH-N; 83.9 (83.3) CH-O; 127.6 2×CH_{Ph}; 127.8 2×CH_{Ph}; 128.4 2×CH_{Ph}; 129.5 2×CH_{Ph}; 132.9 CH_{Ph}; 133.2 CH_{Ph}; 137.9 C_{Ph}; 141.6 C_{Ph}; 167.1 C=N. EI-MS, m/z (%): 448 (M^+, 0.5); 184 (27); 141 (42); 77 (100); 45 (55); 42 (21). $C_{22}H_{28}O_4N_2S_2$ (448.59): Anal. calcd. C 58.90, H 6.29, N 6.24, S 14.29. found C 58.44, H 6.23, N 6.31, S 14.36.

(4S,5S)-2-[(1R)-1-Methylthio-3-(N-benzenesulfonyl-amino)-propyl]-4-methyl-5-phenyl-1,3-oxazoline ***5e***

d.r.: 65:35; pale yellow oil, $[\alpha]_D^{20}=-25.1$ (c 1.8, $CHCl_3$); ^1H NMR ($CDCl_3$) δ/ppm, J/Hz: 0.74–0.77 (d, J=7.4, 3H, CH_3); 1.63–1.79 (2×m, 2H, CH_2); 2.02 (s, 3H, CH_3-S); 3.01–3.08 (m, 2H, CH_2-N); 3.29–3.32 (m, 1H, CH-S); 4.24–4.27 (m, 1H, CH-N); 5.46–5.50 (d, J=9.8, 1H, CH-O); 7.05–7.20 (m, 5H, Ph); 7.36–7.44 (m, 3H, Ph); 7.68–7.74 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$) δ/ppm: 14.3 (14.4) CH_3-S; 18.2 CH_3; 31.3 (31.6) CH_2; 40.6 (40.8) CH-S; 41.4 (41.2) CH_2-N; 68.5 CH-N; 84.8 CH-O; 126.4 2×CH_{Ph}; 127.7 2×CH_{Ph}; 128.4 2×CH_{Ph}; 128.7 2×CH_{Ph}; 129.5 CH_{Ph}; 131.2 CH_{Ph}; 137.1 C_{Ph}; 140.4 C_{Ph}; 168.1 C=N. EI-MS, m/z (%): 404 (M^+, 0.6); 188 (40); 141 (38); 134 (50); 111 (30); 77 (100); 55 (25); 44 (74). $C_{20}H_{24}O_3N_2S_2$ (404.53): Exact mass calcd. 404.1228. found 404.1225.

(4R)-2-[3-(N-Benzenesulfonyl-N-methyl-amino)-(1R)-1-phenylthio-propyl]-4-ethyl-1,3-oxazoline ***5f***

Colorless oil, $[\alpha]_D^{20}=+27.6$ (c 0.21, $CHCl_3$); ^1H NMR ($CDCl_3$) δ/ppm, J/Hz: 0.75–0.81 (t, J=7.5, 3H, CH_3); 1.18–1.55 (2×m, 2H, CH_2); 1.90–2.00 (m, 1H, CH_2); 2.05–2.17 (m, 1H, CH_2); 2.62 (s, 3H, CH_3-N); 3.03–3.17 (m, 2H, CH_2-N); 3.36–3.45 (m, 1H, CH-S); 3.73–3.79 (m, 1H, CH_2-O); 3.81–3.95 (m, 1H, CH-N); 4.18–4.27 (m, 1H, CH_2-O); 7.11–7.26 (m, 3H, Ph); 7.32–7.53 (m, 5H, Ph); 7.67–7.70 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$) δ/ppm: 10.3 (10.5) CH_3; 28.7 (28.8) CH_2; 30.8 (30.9) CH_2; 35.5 CH_3-N; 43.0 (43.1) CH-S; 48.4 (48.2) CH_2-N; 67.8 CH-N; 72.8 CH_2-O; 127.5 2×CH_{Ph}; 127.9 2×CH_{Ph}; 128.4 2×CH_{Ph}; 129.3 2×CH_{Ph}; 130.2 CH_{Ph}; 133.2 CH_{Ph}; 135.2 C_{Ph}; 137.7 C_{Ph}; 166.1 C=N. EI-MS, m/z (%): 418 (M^+, 1.4); 277 (100); 249 (31); 234 (58); 221 (46); 184 (68); 168 (94); 141 (30); 77 (52); 55 (23); 42 (26). $C_{21}H_{26}O_3N_2S_2$ (418.56): Anal. calcd. C 60.26, H 6.26, N 6.69, S 15.32. found C 59.90, H 6.20, N 6.35, S 15.14.

(4S,5S)-2-[3-(N-Benzenesulfonyl-amino)-(1S)-1-phenylthio-propyl]-4-methyl-5-phenyl-1,3-oxazoline ***5g***

d.r.: 64:36, pale yellow oil, $[\alpha]_D^{20}=-34.0$ (c 1.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ/ppm, J/Hz: 0.65–0.67 (d, J=7.0, 3H, CH_3); 2.03–2.31 (m, 2H, CH_2); 2.70 (s, 3H, N-CH_3); 3.17–3.34 (t, J=6.5, 2H, CH_2-N); 3.93–3.98 (t, J=7.4, 1H, CH-S); 4.36–4.43 (m, 1H, CH-N); 5.58–5.62 (d, J=9.9, 1H, CH-O); 7.12–7.33 (m, 8H, Ph); 7.46–7.56 (m, 5H, Ph); 7.73–7.77 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$) δ/ppm: 17.8 (18.1) CH_3; 30.5 (30.2) CH_2; 35.2 CH_3-N; 42.6 (42.9) CH-S; 48.3 (48.8) CH_2-N; 65.0 CH-N; 84.3 (84.6) CH-O; 126.2 4×CH_{Ph}; 127.4 2×CH_{Ph}; 128.0 4×CH_{Ph}; 128.2 2×CH_{Ph}; 129.1 CH_{Ph}; 132.6 CH_{Ph}; 132.9 CH_{Ph}; 146.3 C_{Ph}; 147.2 C_{Ph}; 166.3 C=N. EI-MS, m/z (%): 480 (M^+, 0.1); 339 (10); 230 (15); 184 (39); 141 (58); 109 (22); 77 (100); 44 (42); 42 (32). $C_{26}H_{28}O_3N_2S_2$ (480.63): Anal. calcd. C 64.97, H 5.87, N 5.83, S 13.34. found C 64.47, H 5.55, N 5.98, S, 12.67.

(4S,5R)-2-[3-(N-Benzenesulfonyl-N-methyl-amino)-(1R)-1-phenylthio-propyl]-4-methoxymethyl-5-phenyl-1,3-oxazoline ***5h***

Pale yellow oil, $[\alpha]_D^{20}=-17.5$ (c 0.20, $CHCl_3$); ^1H NMR ($CDCl_3$) δ/ppm, J/Hz: 2.03–2.25 (m, 2H, CH_2); 2.77 (s, 3H, CH_3-N); 3.26–3.31 (t, J=6.5, 2H, CH_2-N); 3.32 (s, 3H, CH_3-O); 3.61–3.67 (t, J=6.6, 2H, CH_2-O); 3.92–3.97 (m, 1H, CH-S); 4.31–4.37 (m, 1H, CH-N); 5.44–5.47 (d, J=7.9, 1H, CH-O); 7.22–7.37 (m, 8H, Ph); 7.46–7.57 (m, 5H, Ph); 7.72–7.79 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$) δ/ppm: 30.0 CH_2; 35.8 CH_3-N; 42.6 CH-S; 47.9 CH_2-N; 59.2 CH_3-O; 73.2 CH_2-O; 74.2 CH-N; 84.4 CH-O; 125.7 4×CH_{Ph}; 127.9 2×CH_{Ph}; 128.6 4×CH_{Ph}; 129.1 2×CH_{Ph}; 132.6 2×CH_{Ph}; 132.8 CH_{Ph}; 146.5 C_{Ph}; 148.6 C_{Ph}; 167.5 C=N. EI-MS, m/z (%): 510 (M^+, 0.3); 369 (17); 260 (17); 141 (63); 91 (28); 77 (100); 55 (35); 51(26); 45 (70). $C_{27}H_{30}O_4N_2S_2$ (510.65): Anal. calcd. C 63.50, H 5.92, N 5.48. found C 63.11, H 5.64, N 5.28.

(4S,5S)-2-[3-(N-Benzenesulfonyl-N-methyl-amino)-(1S)-1-phenylthio-pentyl]-4-methyl-5-phenyl-1,3-oxazoline ***5i***

d.r.: 58:42, colorless oil, $[\alpha]_D^{20}=-67.7$ (c 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$) δ/ppm, J/Hz: 0.53–0.56 (d, J=7.0, 3H, CH_3); 1.14–1.12 (m, 1H, CH_2); 1.35–1.55 (m, 4H, 2×CH_2); 1.77–1.81 (m, 1H, CH_2); 2.64 (s, 3H, N-CH_3); 2.92–2.96 (t, J=6.5, 2H, CH_2-N); 3.76–3.81 (m, 1H, CH-S); 4.28–4.35 (m, 1H, CH-N); 5.50–5.53 (d, J=9.8, 1H, CH-O); 7.05–7.09 (m, 2H, Ph); 7.12–7.32 (m, 6H, Ph); 7.40–7.52 (m, 5H, Ph); 7.68–7.72 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$) δ/ppm: 18.6 (18.8) CH_3; 25.3 CH_2; 28.1 (28.2) CH_2; 32.8 (32.9) CH_2; 35.6 CH_3-N; 46.4 (46.7) CH-S; 50.8 CH_2-N; 65.9 CH-N; 85.2 (85.1) CH-O; 126.8 2×CH_{Ph}; 128.3 2×CH_{Ph}; 128.8 2×CH_{Ph}; 129.1 2×CH_{Ph}; 129.8 2×CH_{Ph};129.9 2×CH_{Ph}; 132.8 CH_{Ph}; 133.4 CH_{Ph}; 133.6 CH_{Ph}; 137.6 C_{Ph}; 138.5 C_{Ph}; 166.4 (166.9) C=N. EI-MS, m/z (%): 446 (M^+, 0.1); 367 (13); 336 (14); 141 (35); 77 (100); 70 (26); 44 (50); 42 (37). $C_{23}H_{30}O_3N_2S_2$ (446.61): Anal. calcd. C 61.85, H 6.77, N 6.27, S 14.36. found C 61.45, H 6.61, N 6.21, S 14.09.

(2R)-4-(N-Benzenesulfonyl-N-methyl-amino)-N-[(1R)-1-hydroxymethyl-propyl]-2-phenylthiobutan-amide ***6f***

Colorless oil, $[\alpha]_D^{20}=-3.1$ (c 0.45, $CHCl_3$); ^1H NMR ($CDCl_3$) δ/ppm, J/Hz: 0.81–0.86 (t, J=7.4, 3H, CH_3); 1.21–1.29 (m, 1H, CH_2); 1.31–1.40 (m, 2H, CH_2); 1.44–1.59 (m, 1H, CH_2); 2.70 (s, 3H, CH_3-N); 2.98–3.12 (m, 2H, CH_2-N); 3.25–3.29 (t, J=6.9, 1H, CH-S); 3.73–3.4 (m, 2H, CH_2-O); 3.89–3.96 (m, 1H, CH-N); 6.77–6.80 (d, J=8.7, 1H, NH); 7.11–7.33 (m, 5H, Ph); 7.41–7.55 (m, 3H, Ph); 7.65–7.78 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$) δ/ppm: 10.6 CH_3; 26.7 CH_2; 35.9 CH_3-N; 38.5 CH_2; 38.7 CH-S; 45.5 CH_2-N; 51.4 CH-N; 62.6 CH_2-O; 126.3 2×CH_{Ph}; 126.9 2×CH_{Ph}; 127.7 2×CH_{Ph}; 127.9 2×CH_{Ph}; 129.4 CH_{Ph}; 130.4 CH_{Ph}; 133.1 C_{Ph}; 137.5 C_{Ph}; 176.8 C=O. EI-MS, m/z (%): 436 (M^+, 0.2); 435 (M^+-1, 0.5); 184 (39); 164 (37); 141 (48); 110 (21); 77 (100); 55 (40); 44 (44). $C_{21}H_{28}O_4N_2S_2$ (436.58): Exact mass calcd. 436.1490 found 436.1490.

(4R)-2-[1,1-Bis-(methylthio)-3-(N-benzenesulfonyl-N-methyl-amino)-propyl]-4-ethyl-1,3-oxazoline ***8a***

Pale yellow oil, $[\alpha]_D^{20}=+38.2$ (c 1.10, $CHCl_3$); ^1H NMR ($CDCl_3$) δ/ppm, J/Hz: 0.78–0.83 (t, J=7.4, 3H, CH_3); 1.13–1.19 (quint, 2H, CH_2); 1.36–1.45 (m, 1H, CH_2); 1.52–1.59 (m, 1H, CH_2); 1.99 (s, 6H, 2xCH_3-S); 2.69 (s, 3H, CH_3-N); 3.08–3.16 (m, 2H, CH_2-N); 3.85–3.90 (t, J=7.8, 1H, CH_2-O); 3.99–4.05 (m, 1H, CH-N); 4.23–4.29 (dd, J=9.1, 8.1, 1H, CH_2-O); 7.39–7.49 (m, 3H, Ph); 7.67–7.70 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$) δ/ppm: 10.3 CH_3; 12.6 CH_3-S; 28.9 CH_2; 34.1 CH_2; 36.0 CH_3-N; 47.6 CH_2-N; 53.8 C-S; 68.2 CH-N; 73.0 CH_2-O; 127.8 2×CH_{Ph}; 129.6 2×CH_{Ph}; 133.0 CH_{Ph}; 138.3 C_{Ph}; 164.9 C=N. EI-MS, m/z (%): 402 (M^+, 0.2); 401 (M^+-1, 0.7); 184 (93); 172 (25); 141 (74); 77 (100); 55 (21); 42 (30). $C_{17}H_{26}O_3N_2S_3$ (402.58): Anal. calcd. C 50.71, H 6.51, N 6.95, S 23.89. found C 50.57, H 6.26, N 6.24, S 23.85.

(4S,5S)-2-[1,1-Bis-(methylthio)-3-(N-benzenesulfonyl-N-methyl-amino)-propyl]-4-methyl-5-phenyl-1,3-oxazoline ***8b***

Pale yellow oil, $[\alpha]_D^{20}=-87.1$ (c 0.14, $CHCl_3$); ^1H NMR ($CDCl_3$) δ/ppm, J/Hz: 0.87–0.91 (d, J=6.9, 3H, CH_3); 1.11–1.19 (m, 2H, CH_2); 2.13 (s, 3H, CH_3-S); 2.15 (s, 3H, CH_3-S); 2.67 (s, 3H, N-CH_3); 2.93–3.01 (m, 2H, CH_2-N); 4.35–4.41 (m, 1H, CH-N); 5.42–5.46 (d, J=9.2, 1H, CH-O); 7.11–7.39 (m, 5H, Ph); 7.44–7.53 (m, 3H, Ph); 7.61–7.70 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$) δ/ppm: 12.3 CH_3-S; 12.8 CH_3-S; 18.4 CH_3; 33.9 CH_2; 35.9 CH_3-N; 47.5 CH_2-N; 58.1 C-S; 65.8 CH-N; 84.9 CH-O; 127.0 2×CH_{Ph}; 127.9 2×CH_{Ph}; 128.3 2×CH_{Ph}; 129.4 2×CH_{Ph}; 130.4 CH_{Ph}; 132.9 CH_{Ph}; 136.9 C_{Ph}; 138.3 C_{Ph}; 164.2 C=N. EI-MS, m/z (%): 464 (M^+, 4.5); 463 (M^+-1; 5); 323 (13); 187 (47); 184 (87); 141 (51); 77 (100); 73 (23); 45 (45); 42 (28). $C_{22}H_{28}O_3N_2S_3$ (464.65): Anal. calcd. C 56.86, H 6.07, N 6.03, S 20.70. found C 54.25, H 5.98, N 5.69, S, 20.96.

(4S,5R)-2-[1,1-Bis-(methylthio)-3-(N-benzenesulfonyl-N-methyl-amino)-propyl]-4-methoxy-methyl-5-phenyl-1,3-oxazoline ***8c***

Colorless oil, $[\alpha]_D^{20}=-11.0$ (c 0.70, $CHCl_3$); ^1H NMR ($CDCl_3$) δ/ppm, J/Hz: 2.04 (s, 3H, CH_3-S); 2.06 (s, 3H, CH_3-S); 2.11–2.22 (m, 2H, CH_2); 2.60 (s, 3H, CH_3-N); 3.11–3.22 (m, 2H, CH_2-N); 3.24 (s, 3H, CH_3-O); 3.42–3.54 (m, 2H, CH_2-O); 4.09–4.13 (q, 1H, CH-N); 5.34–5.37 (d, J=6.4, 1H, CH-O); 7.19–7.27 (m, 5H, Ph); 7.42–7.54 (m, 3H, Ph); 7.69–7.71 (d, J=7.2, 2H, Ph). ^{13}C NMR ($CDCl_3$) δ/ppm: 12.4 CH_3-S; 12.5 CH_3-S; 33.7 CH_2; 35.7 CH_3-N; 47.4 CH_2-N; 58.3 C-S; 59.5 CH_3-O; 73.9 CH_2-O; 74.7 CH-N; 84.1 CH-O; 126.3 2×CH_{Ph}; 127.7 2×CH_{Ph}; 128.8 2×CH_{Ph}; 129.2 2×CH_{Ph}; 129.5 CH_{Ph}; 132.9 CH_{Ph}; 138.3 C_{Ph}; 140.7 C_{Ph}; 165.5 C=N. EI-MS, m/z (%): 448 (7); 184 (100); 141 (60); 91 (22); 77 (98); 45 (52); 42 (20). $C_{23}H_{30}O_4N_2S_2$ (494.68): Anal. calcd. C 55.84, H 6.11, N 5.66, S 19.44. found C 54.84, H 6.20, N 5.60, S 19.47.

(4S,5S)-2-[1,1-Bis-(methylthio)-3-(N-benzenesulfonyl-N-methyl-amino)-pentyl]-4-methyl-5-phenyl-1,3-oxazoline ***8d***

Pale yellow oil, $[\alpha]_D^{20}=-107.7$ (c 0.56, $CHCl_3$); ^1H NMR ($CDCl_3$) δ/ppm, J/Hz: 0.68–0.71 (d, J=6.6, 3H, CH_3); 1.14–1.35 (m, 2H, CH_2); 1.51–1.56 (m, 2H, CH_2); 1.82–1.97 (m, 2H, CH_2); 2.00 (s, 3H, CH_3-S); 2.06 (s, 3H, CH_3-S); 2.65 (s, 3H, N-CH_3); 2.88–2.95 (m, 2H, CH_2-N); 4.37–4.47 (m, 1H, CH-N); 5.57–5.61 (d, J=9.8, 1H, CH-O); 7.16–7.20 (m, 3H, Ph); 7.23–7.30 (m, 2H, Ph); 7.39–7.50 (m, 3H, Ph); 7.67–7.71 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$) δ/ppm: 12.3 CH_3-S; 12.9 CH_3-S; 18.6 CH_3; 22.8 CH_2; 27.9 CH_2; 35.0 CH_2; 35.1 CH_3-N; 50.2 CH_2-N; 60.6 C-S; 65.8 CH-N; 84.7 CH-O; 126.3 2×CH_{Ph}; 127.7 2×CH_{Ph}; 128.2 2×CH_{Ph}; 128.7 CH_{Ph}; 129.4 2×CH_{Ph}; 132.9 CH_{Ph}; 137.1 C_{Ph}; 137.7 C_{Ph}; 164.7 C=N. EI-MS, m/z (%): 446 (14); 184 (46); 141 (45); 134 (33); 77 (100); 51 (23); 44 (41); 42 (28). $C_{24}H_{32}O_3N_2S_3$ (492.70): Anal. calcd. C 58.50, H 6.55, N 6.69, S 19.52. found C 58.46, H 6.80, N 6.19, S, 19.86.

(4R)-2-[1,1-Bis-(phenylthio)-3-(N-benzenesulfonyl-N-methyl-amino)-propyl]-4-ethyl-1,3-oxazoline ***8f***

White solid, F_p=52–56°C; $[\alpha]_D^{20}=+17.3$ (c 2.56, $CHCl_3$); ^1H NMR ($CDCl_3$) δ/ppm, J/Hz: 0.68–0.73 (t, J=7.4, 3H, CH_3); 1.13–1.24 (m, 1H, CH_2); 1.28–1.37 (m, 1H, CH_2); 2.01–2.11 (m, 2H, CH_2); 2.49 (s, 3H, CH_3-N); 3.31–3.40 (m, 2H, CH_2-N); 3.69–3.79 (m, 2H, CH_2-O, CH-N); 4.16–4.21 (m, 1H, CH_2-O); 7.23–7.35 (m, 5H, Ph); 7.39–7.68 (m, 10H, Ph). ^{13}C NMR ($CDCl_3$) δ/ppm: 10.4 CH_3; 28.6 CH_2; 34.4 CH_2; 35.4 CH_3-N; 47.1 CH_2-N; 62.7 C-S; 68.2 CH-N; 72.9 CH_2-O; 127.7 2×CH_{Ph}; 129.2 2×CH_{Ph}; 129.4 2×CH_{Ph}; 129.5 2×CH_{Ph}; 130.1 CH_{Ph}; 132.9 CH_{Ph}; 135.7 2×CH_{Ph}; 135.8 2×CH_{Ph}; 136.6 CH_{Ph}; 136.8 2×C_{Ph}; 138.1 C_{Ph}; 164.5 C=N. EI-MS, m/z (%): 526 (M^+, 0.2); 525 (M^+-1, 0.5); 417 (5); 184 (100); 141 (57); 110 (31); 77 (76); 44 (21); 42 (27). $C_{27}H_{30}O_3N_2S_3$ (526.72): Anal. calcd. C 61.56, H 5.74, N 5.32, S 18.26. found C 59.94, H 5.70, N 5.04, S 18.76.

4-(N-Benzenesulfonyl-N-methyl-amino)-2,2-bis-(methylthio)-N-[(1R)-1-hydroxymethyl-propyl]-butanamide ***9a***

Colorless oil, $[\alpha]_D^{20}=+21.9$ (c 2.46, $CHCl_3$); ^1H NMR ($CDCl_3$) δ/ppm, J/Hz: 0.86–0.91 (t, J=7.4, 3H, CH_3); 1.53–1.62 (m, 2H, CH_2; 2.03 (s, 6H, 2×CH_3-S); 2.15–2.21 (m, 2H, CH_2); 2.72 (s, 3H, CH_3-N); 3.14–3.24 (m, 2H, CH_2-N); 3.51–3.67 (qd, J=3.8, 11.1, 2H, CH_2-O); 3.97–4.05 (m, 1H, CH-N); 6.95–6.98 (d, J=7.7, 1H, NH); 7.42–7.51 (m, 3H, Ph); 7.69–7.72 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$) δ/ppm: 10.7 CH_3; 13.0 CH_3-S; 13.1 CH_3-S; 25.1 CH_2; 34.2 CH_2; 36.2 CH_3-N; 47.6 CH_2-N; 52.3 C-S; 53.1 CH-N; 64.4 CH_2-O; 127.6 2×CH_{Ph}; 129.5 2×CH_{Ph}; 133.0 CH_{Ph}; 138.1 C_{Ph}; 169.6 C=O. EI-MS, m/z (%): 184 (100); 141 (54); 77 (71); 73 (21); 42 (23). $C_{17}H_{28}O_4N_2S_3$ (420.60): Anal. calcd. C 48.54, H 6.71, N 6.66. found C 48.12, H 6.39, N 5.95.

*General procedure for the hydrolysis of α-sulfenylated oxazolines **5** and **15** to α-sulfenylated aminoacids **7** and acid **16** (Table 2)*

A mixture of 0.5 mmol oxazoline **5** or **15** and 10 mL of 3 N aq HCl was refluxed for 3.5 h. After cooling to room temperature 10 mL of water were added and the mixture was extracted with CH_2Cl_2 (5×10 mL), dried (Na_2SO_4) and concentrated to give raw aminoacids **7** or **16** as a viscous oil. Chromatography on silica gel (ethyl acetate/hexane=9:1) was carried out to improve the purity.

*4-(N-Benzenesulfonyl-N-methyl-amino)-2-methylthio-butanoic acid **7a** [(R) or (S) see Table 2]*

Yellow viscous oil, ^{1}H NMR ($CDCl_3$) δ/ppm, J/Hz: 1.81–1.91 (m, 1H, CH_2); 1.96–2.11 (m, 1H, CH_2); 2.15 (s, 3H, CH_3-S); 2.68 (s, 3H, CH_3-N); 3.06–3.29 (2×m, 2H, CH_2-N); 3.58–3.63 (m, 1H, CH-S); 6.63 (br, 1H, OH); 7.30–7.48 (m, 3H, Ph); 7.70–7.81 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$) δ/ppm: 14.8 CH_3-S; 29.1 CH_2; 35.7 CH_3-N; 44.5 CH-S; 48.4 CH_2-N; 127.8 2×CH_{Ph}; 129.6 2×CH_{Ph}; 133.2 CH_{Ph}; 137.5 C_{Ph}; 176.9 C=O. EI-MS, m/z (%): 184 (41); 141 (59); 77 (100); 51 (23); 45 (33); 44 (54). $C_{12}H_{17}O_4NS_2$ (303.39): Anal. calcd. C 47.50, H 5.65, N 4.62. found C 47.77, H 5.63, N, 4.50.

*(R)-4-(N-Benzenesulfonyl-N-methyl-amino)-2-phenylthio-butanoic acid **7b***

Yellow viscous oil, ^{1}H NMR ($CDCl_3$) δ/ppm, J/Hz: 1.83–1.90 (m, 1H, CH_2); 2.04–2.11 (m, 1H, CH_2); 2.63 (s, 3H, CH_3-N); 3.10–3.13 (t, J=6.5, 2H, CH_2-N); 3.68–3.72 (t, J=6.9, 1H, CH-S); 5.81 (br, 1H, OH); 7.18–7.25 (m, 3H, Ph); 7.32–7.53 (m, 5H, Ph); 7.68–7.77 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$) δ/ppm: 29.9 CH_2; 35.6 CH_3-N; 47.8 CH-S; 48.3 CH_2-N; 127.8 2×CH_{Ph}; 128.9 2×CH_{Ph}; 129.5 4×CH_{Ph}; 132.5 CH_{Ph}; 133.9 CH_{Ph}; 137.5 C_{Ph}; 138.2 C_{Ph}; 177.1 C=O. EI-MS, m/z (%): 365 (M^+, 0.5); 184 (14); 141 (38); 109 (31); 96 (30); 77 (100); 51 (27); 44 (70). $C_{17}H_{19}O_4NS_2$ (365.46): Anal. calcd. C 55.87, H 5.24, N 3.83, S 17.55. found C 55.26, H 5.63, N, 3.96, S 17.04.

*(S)-6-(N-Benzenesulfonyl-N-methyl-amino)-2-phenylthio-hexanoic acid **7c** (58:42 mixture of enantiomers)*

Yellow viscous oil, ^{1}H NMR ($CDCl_3$) δ/ppm, J/Hz: 1.18–1.22 (m, 2H, CH_2); 1.28–1.33 (m, 2H, CH_2); 1.71–1.96 (2×m, 2H, CH_2); 2.63 (s, 3H, CH_3-N); 2.72–2.92 (m, 2H, CH_2-N); 3.54–3.63 (m, 1H, CH-S); 6.67 (br, 1H, OH); 7.19–7.32 (m, 5H, Ph); 7.38–7.50 (m, 3H, Ph); 7.63–7.71 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$) δ/ppm: 24.1 CH_2; 26.8 CH_2; 27.1 CH_2; 35.5 CH_3-N; 47.5 CH-S; 48.1 CH_2-N; 126.3 2×CH_{Ph}; 128.1 2×CH_{Ph}; 129.1 4×CH_{Ph}; 131.7 CH_{Ph}; 132.5 CH_{Ph}; 137.1 C_{Ph}; 138.2 C_{Ph}; 174.5 C=O. EI-MS, m/z (%): 393 (M^+, 0.5); 184 (20); 141 (51); 109 (27); 98 (28); 77 (100); 70 (24); 51 (32); 44 (60); 42 (44). $C_{19}H_{23}O_4NS_2$ (393.51): Anal. calcd. C 57.99, H 5.89, N 3.56. found C 57.25, H 6.30, N 3.69.

*Independent synthesis of α-sulfenylated 4-(N-benzenesulfonyl-N-methyl-amino)-butanoic acids **7a** and **7b** (see Scheme 2)*

To a solution of 2.0 g (17 mmol) of (*S*)-(+)-2,4-diaminobutanoic acid dihydrochloride **10** in 120 mL of hot water 3.33 g (27 mmol) of $CuCO_3$ were added in small portions. The mixture was refluxed for 2 h and filtered while still hot. After washing with another 20 mL of hot water and cooling 3.5 g (43 mmol) $NaHCO_3$ and a solution of 3.46 g (20 mmol) of benzenesulfonylchloride in 130 mL acetone were added to the combined filtrates. The mixture was vigorously stirred for 10 h at room temperature. The resulting blue precipitate (2.43 g; 49%) was collected and washed twice with 20 mL of water, then with acetone and diethyl ether. A suspension of 1.5 g of this benzenesulfonyl-protected copper complex of **10** in 50 ml of boiling water was treated with a stream of H_2S for 30 min. After treatment with 0.5 g of charcoal and 1.5 mL of 6 N HCl, the mixture was filtered. The pH of the filtrate was adjusted to 6 with 4 N NaOH. The solvent was evaporated, the resulting white solid treated with a little amount of EtOH and the remaining NaCl filtered off. The filtrate was evaporated and the remaining raw product **11** was used without further purification.

A 1 L 3 necked round bottom flask was charged with 30 mL of 1 N aq HBr solution and 1.35 g (11.4 mmol) KBr. The reaction mixture was cooled to −7°C and 4.93 mmol of raw **11** were added with stirring. 0.65 g (9.4 mmol) of $NaNO_2$ were added in small portions over 1 h keeping the internal temperature between −4 and −7°C. The mixture was vigorously stirred at this temperature for 2 h and then extracted with ethyl acetate (3×50 mL). The combined organic layers were washed with saturated aq NaCl, dried ($NaSO_4$) and evaporated. The resulting yellow oil **12** (1.08 g; 76%) was purified by column chromatography (R_f=0.35; ethyl acetate/hexane=9/1).

*(S)-4-Benzenesulfonylamino-2-bromo-butanoic acid **12***

Dark yellow oil, $[\alpha]_D^{20}$=−19.9 (c 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ/ppm, J/Hz: 1.82–1.86 (m, 1H, CH_2); 2.13–2.27 (m, 1H, CH_2); 3.73–3.81 (m, 1H, CH_2-N); 4.05–4.07 (m, 1H, CH-Br); 4.31–4.40 (m, 1H, CH_2-N); 5.41 (br, 1H, NH); 7.41–7.55 (m, 3H, Ph); 7.62–7.79 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$) δ/ppm: 34.9 CH_2; 41.0 CH_2-N; 42.7 CH-Br; 127.4 2×CH_{Ph}; 130.2 2×CH_{Ph}; 133.4 CH_{Ph}; 139.5 C_{Ph}; 174.5 C=O. EI-MS, m/z (%): 184 (48); 141 (64); 77 (100); 78 (16); 51 (22); 42 (20). $C_{10}H_{12}O_4NBrS$ (322.17): Exact mass calcd. 320.9670 found 320.9671.

To a solution of 1.0 g (3.5 mmol) of **12** in 20 mL of dry THF 0.34 g (14 mmol) of NaH were added at 0°C under Ar. After stirring for 15 min a solution of 0.99 g (7 mmol) of MeI in 10 mL of THF was dropped to the mixture at the same temperature during 10 min. The mixture was allowed to reach room temperature and was stirred overnight (12 h). After adding 30 mL of saturated aq NH_4Cl the reaction mixture was extracted with CH_2Cl_2 (3×20 mL), dried and evaporated. Purification by column chromatography on silica gel (R_f=0.5; ethyl acetate/hexane=9: 1) gave 0.45 g (45%) of **13** as an oil.

*(S)-4-(N-Benzenesulfonyl-N-methyl-amino)-2-bromo-butanoic acid **13***

Yellow oil, $[\alpha]_D^{20}$=−41.5 (c 0.45, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ/ppm, J/Hz: 2.07–2.11 (m, 1H, CH_2); 2.29–2.35 (m, 1H, CH_2); 2.69 (s, 3H, CH_3-N); 3.02–3.09 (m, 1H, CH_2-N); 3.19–3.26 (m, 1H, CH_2-N); 4.42–4.46 (dd, 1H, CH-Br); 7.43–7.56 (m, 3H, Ph); 7.71–7.78 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$) δ/ppm: 33.5 CH_2; 36.0 CH_3-N; 47.4 CH_2-N; 54.4 CH-Br; 127.6 2×CH_{Ph}; 129.6 2×CH_{Ph}; 133.1 CH_{Ph}; 137.3 C_{Ph}; 174.2 C=O. EI-MS, m/z (%): 184 (44); 141 (56); 77 (100); 51 (31); 42 (45). $C_{11}H_{14}O_4NBrS$ (336.19): Exact mass calcd. 334.9827 found 334.9825.

7a: 0.09 g (0.27 mmol) of **13** dissolved in 20 mL of dry EtOH were added dropwise to a stirred solution of 0.019 g (0.27 mmol) of NaSMe in 10 mL of EtOH/H_2O=1/1 at 0°C. 0.014 g (1.35 mmol) of $NaCO_3$ in a small amount of H_2O were added and the mixture was stirred for 24 h at room temperature. The solution was adjusted to pH 2 with 1.2 mL of conc. HCl and EtOH was evaporated. After addition of 20 mL of H_2O the reaction mixture was extracted with CH_2Cl_2 (3×10mL), dried and the solvent was evaporated. The oily residue was purified by column chromatography on silica gel (R_f=0.4; ethyl acetate/hexane=9: 1) yielding 0.087 g (95%) of **7a**: $[\alpha]_D^{20}$=+7.0 (c 1.0, $CHCl_3$).

7b: 0.06 g (0.18 mmol) of **13** were added to a solution of 0.0144 g (0.36 mmol) of NaOH in 5 mL of H_2O and 0.019 g (0.18 mmol) of thiophenol in 10 mL EtOH. The mixture was refluxed with stirring for 12 h.The mixture was adjusted to pH 2 with 1 mL of conc. HCl after cooling and the EtOH was evaporated. After addition of 15 mL of H_2O the reaction mixture was extracted with CH_2Cl_2 (3×10mL), dried and the solvent was evaporated. The oily residue was purified by column chromatography on silica gel (R_f=0.3; ethyl acetate/hexane=9:1) yielding 0.039 g (59%) of **7b**: $[\alpha]_D^{20}$=+5.2 (c 0.25, $CHCl_3$).

*Synthesis of (4S,5R)-4-methoxymethyl-5-phenyl-2-(1-phenylthio)-ethyl-1,3-oxazoline **15** and 2-phenylthio-propionic acid **16** (see Scheme 6)*

A solution of 0.5 g (2.3 mmol) of 2-ethyl-oxazoline **14**[17] in dry THF (10 mL) was added to a solution of LDA (2.8 mmol, from 0.55 mL of diisopropylamine and 2.4 mL of 1.6 M n-BuLi in hexane) at −78°C under argon. The resulting dark yellow solution was stirred at −78°C for 30 min. Then a solution of 0.75 g (3.45 mmol) diphenyldisulfide in 5 ml THF was added dropwise over 10

min. The resulting, almost pale yellow solution was stirred at −78°C for 2 h and was then allowed to reach room temperature overnight. The reaction mixture was poured into saturated NH_4Cl solution (30 mL) and extracted with dichloromethane (4×10 mL), dried (Na_2SO_4) and concentrated. Final purification by column chromatography on silica gel gave 0.45 g (59.5%) of compound **15** as an oil (R_f=0.6; ethyl acetate:hexane 7:3) with a diastereoisomeric ratio of 55:45.

15: colorless oil, $[\alpha]_D^{20}$=−23.0 (c 0.20, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ/ppm, J/Hz: 1.39–1.42 (d, J=7.1, 3H, CH_3); 3.05–3.10 (m, 1H, CH-S); 3.14 (s, 3H, CH_3-O); 3.21–3.32 (m, 1H, CH_2-O); 3.35–3.40 (m, 1H, CH_2-O); 3.85–3.94 (m, 1H, CH-N); 5.10–5.13 (d, J=6.3, 1H, CH-O); 7.00–7.32 (m, 8H, Ph); 7.44–7.45 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$) δ/ppm: 18.7 CH_3; 40.5 (40.8) CH-S; 59.6 (59.7) CH_3-O; 74.4 CH_2-O; 74.5 CH-N; 84.3 CH-O; 125.8 2×CH_{Ph}; 126.0 2×CH_{Ph}; 127.9 2×CH_{Ph}; 128.5 2×CH_{Ph}; 129.1 CH_{Ph}; 132.6 CH_{Ph}; 137.2 C_{Ph}; 141.0 C_{Ph}; 168.6 C=N. EI-MS, m/z (%): 327 (M^+, 8); 149 (13); 137 (100); 109 (40); 91 (35); 77 (31; 74 (42); 59 (36); 45 (78). $C_{19}H_{21}O_2NS$ (327.4): Anal. calcd. H 6.46, N 4.28. found H 6.28, N 4.00.

0.41 g (1.25 mmol) of **15** were hydrolyzed (see general procedure for **7** above) yielding 0.23 g (95%) of a 55:45 enantiomeric mixture of acid **16**: pale yellow oil, $[\alpha]_D^{20}$=+1.7 (c 1.0, EtOH) (for the known (*R*)-(+)-2-phenylthio-propionic acid **16** see reference[18]).

*(4S,5R)-2-[1-Bis-(phenylselenyl)-3-(N-benzenesulfonyl-N-methyl-amino)-propyl]-4-methoxymethyl-5-phenyl-1,3-oxazoline **18** (see Scheme 7)*

0.1 g (0.25 mmol) of oxazoline **3c** were deprotonated with LDA like described in the general procedure for **5** (see above). 0.09 g (0.37 mmol) of PhSeBr in 5 mL THF were added instead of R^1SSR^1. Yield: 0.075 g (54%) of a pale yellow oil; R_f=0.6; $[\alpha]_D^{20}$=+8.8 (c 0.14, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ/ppm, J/Hz: 1.99–2.12 (m, 1H, CH_2); 2.15–2.22 (m, 1H, CH_2); 2.59 (s, 3H, CH_3-N); 2.98–3.24 (2×m, 2H, CH_2-N); 3.27 (s, 3H, CH_3-O); 3.32–3.37 (m, 1H, CH_2-O); 3.43–3.52 (m, 1H, CH_2-O); 3.99–4.07 (m, 1H, CH-N); 5.23–5.25 (d, J=7.2, 1H, CH-O); 7.16–7.26 (m, 10H, Ph); 7.34–7.40 (m, 3H, Ph); 7.42–7.63 (m, 4H, Ph); 7.67–7.69 (m, 3H, Ph). ^{13}C NMR ($CDCl_3$) δ/ppm: 31.4 CH_2; 35.5 CH_3-N; 49.1 CH_2-N; 59.5 CH_3-O; 74.5 CH_2-O; 74.8 CH-N; 84.2 CH-O; 125.8–129.5 16×CH_{Ph}; 132.9 CH_{Ph}; 135.8 CH_{Ph}; 135.9 CH_{Ph}; 137.7 2×C_{Ph}; 140.9 C_{Ph}; 141.1 C_{Ph}; 167.8 C=N. EI-MS, m/z (%): 558 (1); 417 (11); 260 (25); 184 (31); 141 (49); 77 (100); 45 (75); 42(31). $C_{33}H_{34}O_4N_2SSe_2$ (712.60): Anal. calcd. C 55.62, H 4.81, N 3.93, S 4.49. found C 54.85, H 4.67, N 3.69, S 4.26.

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