201. Asymmetric Alkylations of a Sultam-Derived Glycine Equivalent: Practical Preparation of Enantiomerically Pure α-Amino Acids

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Alkylation of the chiral glycine derivative **2** with 'activated' organohalides under ultrasound-assisted phase-transfer catalysis or with activated and nonactivated organohalides in anhydrous medium provides (mostly crystalline) alkylation products **3**. Acidic hydrolysis of the pure products **3** gives (aminoacyl)sultams **4** which by mild saponification furnish pure α-amino acids **5** in good overall yields from **2**, along with recovered auxiliary **1** (*Scheme 1*). Pure ω-protected α,ω-diamino acids and α-amino-ω-(hydroxyamino)acids **12**–**16** are readily accessible from (ω-haloacyl)sultams **3** *via* reaction with N-nucleophiles followed by acidic and basic hydrolyses (*Scheme 2*). A reliable determination of the enantiomeric purity of α-amino acids using HPLC analysis of their *N*-(3,5-dinitrobenzoyl)prolyl derivatives **17** is presented.

1. Introduction. – Chiral glycine enolate equivalents are attractive pivotal templates for the syntheses of optically pure α-amino acids[1]). Particularly, alkylations of cyclic glycine enolates derived from bis-lactim ethers [2], imidazolidinones [3], and oxazinones [4] were shown to be tremendously useful. This holds despite some problems associated with the cleavage of the auxiliary ring system and the recovery of the chiral information. Acyclic enolates, obtained from glycine imines [5] or glycinyl pyrrolidines [6], were employed to a lesser extent.

Recently, we communicated the *C*-alkylation of the glycylsultam **2** *via* its enolate as part of a versatile approach to α-amino acids [7]. We now wish to present in full detail the preparation of glycine derivative **2** (which is now commercially available[2]), its alkylation, and the efficient transformation of the alkylation products into optically pure α-amino acids.

2. Alkylations of Chiral Glycine Derivative 2. – 2.1. *Preparation of Glycylsultam* **2**. Crystalline glycine derivative **2** was readily prepared in 81% yield (on a *ca.* 50-g scale) by Me_3Al-mediated acylation of sultam **1** with methyl *N*-[bis(methylthio)methylidene]glycinate[3]) (*Scheme 1*).

2.2. *Alkylation of* **2** *under Phase-Transfer Catalysis* (PTC). Intrigued by the previously observed benzylation of glycine derivative **2** under phase-transfer conditions [7], we then explored this promising protocol[4]) using the allylation of **2** as a reference reaction. Initial attempts involving vigorous stirring of **2** and allyl iodide in aq. LiOH/

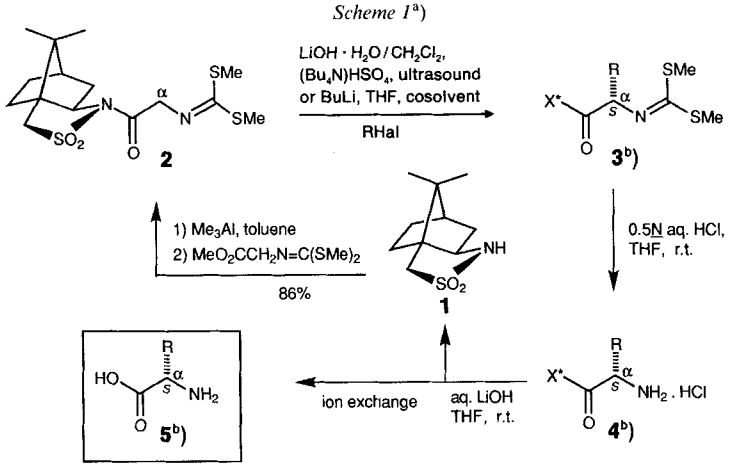
[1]) For reviews on asymmetric α-amino acid synthesis, see [1].

[2]) Glycine derivative **2** and its enantiomer are available from *Oxford Asymmetry Ltd.*, Abingdon/UK.

[3]) For the preparation of ethyl *N*-[bis(methylthio)methylidene]glycinate and its transformation into (±)-α-amino acids, see [8].

[4]) For alkylations of achiral *N*-(diphenylmethylidene)glycinates under chiral phase transfer catalysis, see [9].

Scheme 1[a])



[a]) X*H = **1**. [b]) For R, see *Tables 1* and *2*.

$(Bu_4N)HSO_4/CH_2Cl_2$ required 24 to 48 h for complete conversion of **2** and suffered from competitive hydrolysis of the *N*-acyl group. This problem was solved by the use of ultrasound which dramatically increased the rate of alkylation. Thus, ultrasonication (75 W output) with insertion of the probe into a mixture of glycine derivative **2** (11 g), $LiOH \cdot H_2O$ (50 mol-equiv.), $(Bu_4N)HSO_4$ (1.1 mol-equiv.), and allyl iodide (1.2 mol-equiv.) in CH_2Cl_2/H_2O 30:1 (290 ml) for 5 min at −10° led to complete conversion of **2**, giving, after workup and crystallization, pure alkylation product **3a** in 79% yield (*Scheme 1*; *Table 1, Entry 1*).

Table 1. *Phase Transfer Catalyzed Alkylations of Sultam-Derived Glycine* **2** *with 'Activated' Halides RHal* (**2**→**3**)

Entry	R	Hal	Product	d.e. of **3** [%][a])		Yield of **3** [%]	M.p. of **3** [°C]
				crude	cryst. (FC)	cryst. (FC)	
1	CH_2=$CHCH_2$	I	**3a**	88.1	99.6	79	81–83
2	(*Z*)-BnOCH_2CH=$CHCH_2$	I	**3b**	89.0	(98.4)	(86)	oil
3	(*Z*)-(*t*-Bu)Me_2SiOCH_2CH=$CHCH_2$	Br	**3c**	85.6	(99.3)	(69)	oil
4	$PhCH_2$	I	**3d**	90.7	99.9	77	132–133
5	*p*-Br–$C_6H_4CH_2$	Br	**3e**	86.2	99.5	79	163–164
6	(Naphthalen-1-yl)CH_2	I	**3f**	89.2	99.0	(85)	74–75
7	*t*-BuO_2CCH_2	I	**3g**	98.5	100.0	81	142–143
8	Me	I	**3h**	83.9	99.6	71	118–119

[a]) By HPLC.

Applying these optimized conditions to the reaction of glycine derivative **2** with further 'activated' alkylating agents such as allylic or benzylic iodides and bromides, as well as *t*-butyl iodoacetate and MeI, provided alkylation products **3b–h** in 83.9–98.5% d.e. (*Table 1, Entries 2–8*). The diastereoisomeric purity of the crude products, determined by comparison (HPLC) with 1:1 mixtures of the corresponding α-epimers, was in most cases enhanced to > 99% d.e. by direct crystallization, without recurring to chro-

matography. Only products **3b** and **3c** were obtained as oils and, thus, purified by FC. A major limitation of the otherwise attractive phase-transfer procedure came forth during an attempted alkylation of glycine derivative **2** with BuI which led to complete *N*-acyl cleavage without any detectable C(α)-butylation.

2.3. *Alkylation of* **2** *under Anhydrous Conditions.* Successive treatment of **2** with *1*) BuLi (THF, −78°) and *2*) hexamethylphosphoramide (HMPA; 3 mol-equiv.) and 3 equiv. of allyl-, benzyl-, or methyl iodide or *tert*-butyl bromoacetate/Bu_4NI, stirring at −50° for 16 h (or warming from −78° to room temperature, *Entry 11*), and workup provided alkylation products **3a**, **d**, **g**, **h** in initially 94.7–98.4% d.e. (*Table 2, Entries 9–12*).

Table 2. *Aprotic Alkylation of Sultam-Derived Glycine* **2** *with BuLi/RHal/THF and Cosolvent* (**2**→**3**)

Entry	R	Hal	Cosolvent	Product	d.e. of **3** [%][a])		Yield of **3** [%]	M.p. of **3** [°C]
					crude	cryst. (FC)	cryst. (FC)	
9	$CH=CHCH_2$	I	HMPA	**3a**	96.8	> 99	87	83–84
10	$PhCH_2$	I	HMPA	**3d**	94.7	> 99	93	132–133
11	t-BuO_2CCH_2	Br[b])	HMPA	**3g**	98.4	> 99	96	142–144
12	Me	I	HMPA	**3h**	96.4	> 99	87	119–120
13	Bu	I	HMPA	**3i**	95.6	> 99	86	95–97
14	Bu	I	DMPU		98.2	> 99	83	95–97
15	i-Bu	I	HMPA	**3j**	95.6	> 99	85	125–127
16	i-Bu	I	DMPU		95.4	> 99	67	125–127
17	i-Pr	I	HMPA	**3k**	97.7	(> 99)	(95)	amorphous solid
18	i-Pr	I	DMPU		96.8	(> 99)	(66)	amorphous solid
19	$ClCH_2$	I	DMPU	**3l**	92.9	98	65	142–145
20	$Cl(CH_2)_3$	I	DMPU	**3m**	93.1	99.7	72	115–117
21	$I(CH_2)_4$	I	DMPU	**3n**	93.5	98.3	78	90–91
22	$I(CH_2)_5$	I	DMPU	**3o**	95.3	> 99	78	73–75
23	$I(CH_2)_6$	I	DMPU	**3p**	95.3	99.9	77	79–80

[a]) By GC (*Entries 9, 10,* and *12–18*) or by HPLC (*Entries 11* and *19–23*). [b]) In the presence of Bu_4NI.

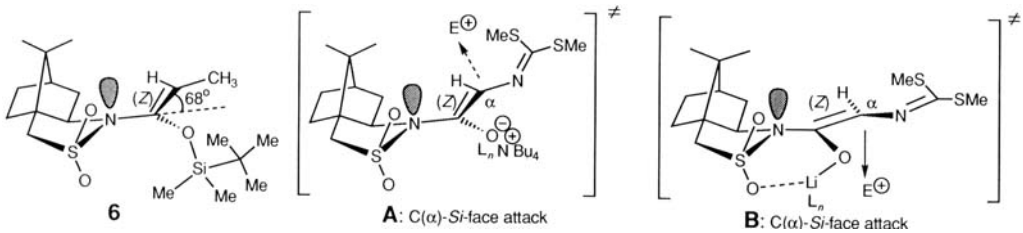
The thus observed π-face selectivities and the chemical yields of crystallized pure products (87–96%) exceeded even those achieved under phase-transfer conditions (*Table 1, Entries 1, 4, 7,* and *8*). We were also pleased to find equally efficient and π-face-selective alkylations of lithiated **2** with nonactivated and secondary iodides (BuI, i-BuI, and i-PrI (5 mol-equiv.)) in the presence of HMPA (7 mol-equiv.; −78°→room temperature; *Entries 13, 15,* and *17*).

We then varied the cosolvent using the butylation of lithiated **2** as a reference reaction. In the absence of HMPA, the alkylation product **3i** was obtained in only 10% yield, along with unchanged **2** (53%) and free sultam **1** (35%). Replacing HMPA by nontoxic cosolvents like 3,4,5,6-tetrahydro-1,3-dimethylpyrimidin-2(1*H*)-one (DMPU; 24 vol-%) [10], 1,3-dimethylimidazolidin-2-one (DMEU; 14 vol-%) [11], or dimethylformamide (DMF; 14 vol-%) furnished crude **3i** in 95.3–98.2 *d.e.* and in yields of 95, 90, and 41%, respectively. Best results were obtained when a solution of glycine derivative **2** in THF/DMPU 76:24 was treated with BuLi (or $NaN(SiMe_3)_2$) at −78° and then with BuI (−78°→room temperature). The face selectivity and chemical yield of pure **3i** match those observed in THF/HMPA (*cf. Entries 13* and *14*). Applying the optimum conditions of *Entry 14*, glycine derivative **2** was also smoothly alkylated in THF/DMPU with i-BuI,

i-PrI, and ω-halo-α-iodoalkanes (*Entries 16* and *18–23*). Products **3i–p** ($\geq$ 93% d.e. by GC or HPLC) could be separated from their (αR)-epimers by chromatography and, moreover, in all but one case (**3k**), purified to *ca.* 100% d.e. by crystallization.

The (αS)-configuration of products **3** (*Tables 1* and *2*) was assigned by their comparison (HPLC, NMR) with authentic samples of the (αR)-epimers (**3a**, **d**, **h**, **j**, **k**)[5]) and by conversion into the corresponding free amino acid **5** (*vide infra*).

2.4. *Rationalization of the Observed π-Face Discriminations.* It thus follows that alkylations of glycine derivative **2** generate almost exclusively the (αS)-configuration in products **3**, whether carried out under phase-transfer or anhydrous conditions. An understanding of this π-face discrimination in the phase-transfer alkylation mode is difficult due to the general lack of structural information about PTC-generated enolates [13]. We assume that the acylsultam **2** is deprotonated at the solvent interface and that the (Z)-enolate is transported into the organic phase as an ion pair with the Bu_4N^+ cation. In the rate-determining step, the ion pair is alkylated in the organic layer. In view of NOE studies with $(Bu_4N)^+BH_4^-$ solutions [14], it is plausible that the ion pair is tightly associated. The resulting bulk of the enolate O-atom may further increase through enolate aggregation and/or hydration. To avoid repulsions between the bulky associated enolate O-atom and the bornanesultam skeleton, we postulate a preferred transition-state conformation **A**. Conformation **A** resembles that of the *O*-[(*tert*-butyl)dimethylsilyl]-substituted-ketene *N*,*O*-acetal **6**, whose X-ray diffraction analysis exhibits an S–N–C=C torsion angle of −68°, which means that the olefinic π-orbitals and the lone electron pair on the N-atom are out of plane [15]. Since *N*,*O*-acetal **6** underwent highly selective aldolizations at the C(α)-*Si*-face, *i.e.* opposite to the sterically demanding SO_2 group [15], it appears reasonable to expect the same faciality in the alkylations of the PTC-generated enolates of **2**.



The observed reaction topicity for alkylations **2** → **3** in anhydrous media are in agreement with a kinetically controlled formation of a Li-chelated (Z)-enolate which is attacked by the alkylating agent from the face opposite to the lone electron pair on the N-atom (transition-state model **B**). This C(α)-*Si*-face attack parallels the stereochemistry found in reactions of acylsultam-derived lithium and sodium enolates with alkylating agents [16] [17], 1-chloro-1-nitrosocyclohexane [12], *N*-bromosuccinimide (NBS) [18], carboxylic acid chlorides [17], aldehydes [17] [19], and iminium salts [20].

3. Conversion of the Alkylation Products into Pure (*S*)-α-Amino Acids. – Selective *N*-deprotection of **3** by mild acidic hydrolysis (0.5N aq. HCl/THF, room temperature)

[5]) For the preparation of enantiomerically pure α-amino acids *via* electrophilic amination of sultam-derived enolates with 1-chloro-1-nitrosocyclohexane, see [12].

furnished amine hydrochlorides **4** which could be isolated and characterized (*e.g.* **4d**). In general, the crude salts **4** were directly saponified with LiOH (4 mol-equiv., aq. THF, room temperature). Extraction (CH_2Cl_2) gave recovered sultam **1** (83–100%). Acidification of the aq. phase to pH 4–5, adsorption on ion-exchange resin (*Amberlite IR 120*, H^+) and desorption with aq. NH_4OH solution provided *ca.* 100% enantiomerically pure (*S*)-amino acids **5** in 84–100% overall yield from **3** (*Table 3*).

Table 3. *(S)-α-Amino Acids* **5** *by Deprotection/Hydrolysis of Alkylation Products* **3** (**3**→**4**→**5**)

Entry	R		Yield [%] of sultam **1**	Yield [%] of amino acid **5**	e.e. [%] of amino acid **5**
1	CH_2=$CHCH_2$	**5a**	> 99	> 99	> 99.8
2	(*Z*)-(*t*-Bu)Me_2SiOCH_2CH=$CHCH_2$	**5c**	97.4	93[a])	–[a])
3	$PhCH_2$	**5d**	> 99	> 99	> 99.8
4	*t*-BuO_2CCH_2	**5g**	84	75[b])	> 99.8[b])
5	Me	**5h**	98	> 99	> 99.8
6	Bu	**5i**	> 99	> 99	> 99.8
7	i-Bu	**5j**	95	> 99	99.5
8	i-Pr	**5k**	83	84	> 99.8

[a]) **5c** was obtained as desilylated α-amino ω-hydroxy acid, m.p. 215–216°, and converted into enantiomerically pure lactone **18** (*Scheme 3*).

[b]) **5g** was obtained from **3g** as free (*S*)-aspartic acid by successive treatment with CF_3CO_2H (r.t., 2 h), aq. HCl/THF, and aq. LiOH/THF, followed by ion exchange.

In the case of **3g**, the *t*-Bu ester was cleaved (CF_3CO_2H, room temperature) prior to the usual hydrolysis sequence giving free (*S*)-aspartic acid **5g** (75% from **3g**, *Entry 4*). The (*S*)-configurations and enantiomeric purities of amino acids **5** ($\geq$ 95% e.e.) were readily determined by GC comparison (*Chirasil-Val*) of their *N*-trifluoroacetyl isopropyl esters [21] with racemic and enantiomerically pure authentic samples.

4. Pure ω-Protected (*S*)-α,ω-Diamino Acids and (*S*)-α-Amino-ω-(hydroxyamino) Acids. – 4.1. *N-Nucleophile ω-Halide Displacement/Hydrolysis.* With amino- and carboxylprotected α-amino-ω-halo acid derivatives **3l–p** (*see Scheme 1* and *Table 2*) in hand, we explored the displacement of the halide atom by N-nucleophiles as a potential approach to optically pure α,ω-diamino acids and their derivatives (*Table 4*)[6]).

Indeed, treatment of halides **3m,p** *with* NaN_3 *in DMEU and subsequent acidic and* basic hydrolysis afforded α-amino-ω-azido acids **12** (98–100% e.e.) and the recovered auxiliary **1** in high yields (*Scheme 2*). The ω-halide atom in **3m** and **3n** was also efficiently displaced by *O*-benzyl-*N*-tosyl-hydroxylamine [23]/$KN(SiMe_3)_2$ or with *O*-benzyl acetohydroxamate [24]/K_2CO_3 in the case of **3n**, without apparent N-acyl cleavage or C(α)-epimerization. The resulting ω-protected [α-amino-ω-(hydroxyamino)acyl]*sultams* **8m,n** (83–93%) were subjected to consecutive acidic and basic hydrolysis providing, in addition to recovered sultam **1** (92–93%), optically pure N^{ω}-(benzyloxy)-N^{ω}-tosyl-substituted ornithine and lysine **13m** and **13n**, respectively (93–94%; *Entries 5* and *6*). Acidic removal of the bis(methylthio)methylidene group from **9n**, followed by saponification of the

[6]) For recent syntheses of enantiomerically pure α,ω-diaminoheptanoic(octanoic) acids, N^{δ}-(benzyloxy)-N^{δ}-tosylornithine, and α-amino-ω-[(benzyloxycarbonyl)amine]heptanoic(octanoic) acids, see [22a], [22b], and [22c], respectively.

Table 4. *N^{ω}-Protected α,ω-Diamino Acids* **12–16** *by ω-Halide Displacement/Hydrolysis* (**3**→**7–11**→**12–16**)

Entry	ω-Halide	*n*	X	N-Nucleophile	Displacement products **7–11**				Sultam **1**	Amino acids **12–16**		
						Yield [%]	R^1	R^2	Yield [%]		Yield [%][a]	e.e. [%][b]
1	**3m**	1	Cl	NaN_3	**7m**	–[c]		N_2	95	**12m**	78	> 99.5
2	**3n**	2	I	NaN_3	**7n**	–[c]		N_2	95	**12n**	91	97.8
3	**3o**	3	I	NaN_3	**7o**	–[c]		N_2	95	**12o**	100	> 99.5
4	**3p**	4	I	NaN_3	**7p**	–[c]		N_2	95	**12p**	100	> 99.5
5	**3m**	1	Cl	$TsNH(OBn)/KN(SiMe_3)_2$	**8m**	83	Ts	OBn	93	**13m**	93	97.2
6	**3n**	2	I	$TsNH(OBn)/KN(SiMe_3)_2$	**8n**	93	Ts	OBn	93	**13n**	94	> 99.5
7	**3n**	2	I	$AcNH(OBn)/K_2CO_3$	**9n**	68	Ac	OBn	92	**14n**	72	–[d]
8	**3n**	2	I	$TsNHPh/KN(SiMe_3)_2$	**10n**	98	Ts	Ph	97	**15n**	94	97.1
9	**3o**	3	I	KOCN/BnOH	**11o**	74	H	Z	97	**16o**	88	> 99.5
10	**3p**	4	I	KOCN/BnOH	**11p**	71	H	Z	97	**16p**	92	> 99.5

[a]) Yields of **12** from **3** (2 steps); yields of **13–16** from **8–11** (1 step).

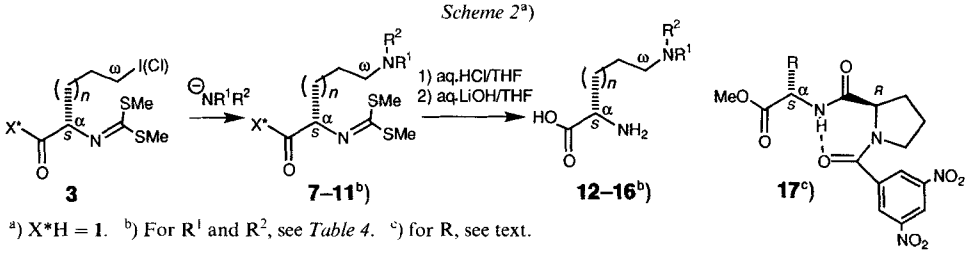
[b]) HPLC (*Lichrosorb Si 60, Entries 1, 9, and 10*) or *Bakerbond R-DNBPG*, hexane/i-PrOH of α-{[(*R*)-*N*-(3,5-dinitrobenzoyl)prolyl]amino} acid methyl esters **17**; in all cases, the minor isomer eluted earlier.

[c]) Crude azide displacement products **7** were directly hydrolyzed to **12**.

[d]) E.e. not determined.

acylsultam moiety alone (2 mol-equiv. LiOH, 1 h) or together with the *N*-acetyl group (4 mol-equiv. LiOH, 24 h) in aq. THF at room temperature provided (*S*)-N^{ε}-acetyl-N^{ε}-(benzyloxy)lysine (**14n**) or (*S*)-N^{ε}-(benzyloxy)lysine. Thus obtained ω-protected derivatives of (*S*)-N^{δ}-hydroxyornithine (**13m**) and (*S*)-N^{ε}-hydroxylysine (**13n**, **14n**) are important precursors for syntheses of hydroxamate siderophore peptides [25]. Similar treatment of (ω-iodoacyl)sultam **3n** with $TsNHPh/KN(SiMe_3)_2$, followed by acidic/basic hydrolysis of isolated intermediate **10n**, furnished (*S*)-N^{ε}-phenyl-N^{ε}-tosyl-lysine (**15n**; 92% from **3n**). Displacement of the I-atom in acylsultams **3o** and **3p** with potassium cyanate/benzyl alcohol/DMEU at 100°[7]) and hydrolysis of the resulting carbamates **11o** and **11p** yielded N^{ω}-(benzyloxycarbonyl)-protected 2,7-diaminoheptanoic and 2,8-diaminooctanoic acids **16o** and **16p**, respectively (65% from **3o** or **3p**).

Scheme 2[a])



3 **7–11**[b]) **12–16**[b]) **17**[c])

[a]) X*H = **1**. [b]) For R^1 and R^2, see *Table 4*. [c]) for R, see text.

The depicted (*S*)-configuration of α,ω-diamino acid derivatives **12–16** was assigned by chiroptic comparison with published data (*Entries 5–7*). The optical purities of compounds **12–16** varied between 97 and > 99% and were determined as described in *Chapt. 4.2.*

[7]) For the preparation of carbamates by reaction of organic halides with KOCN/ROH in *N*-methylpyrrolidin-2-one or in DMF, see [26a] and [26b], respectively.

4.2. *Determination of the Optical Purity.* Initial attempts to determine the enantiomeric purity of temperature-sensitive and/or non-volatile amino acids **12–16** by GC analysis of their *N*-(trifluoroacetyl) isopropyl esters [21] failed. Unsatisfactory separations were also observed in HPLC analyses either of *N*-(3,5-dinitrobenzoyl) methyl esters of **12–16** using a chiral column (*Bakerbond R-DNBPG*) or of derivatives of **12–16** with 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranyl isothiocyanate (GITC) [27a], α-methoxy-α-methylnaphthalene-1-acetic acid [27b], (+)-1-(9*H*-fluorenyl)-9-ethylethyl chloroformate [27c], (*S*)-flunoxaprofen [27d], dibenzoyltartarimide [27e], as well as *N*-[(naphthalene-2-yl)sulfonyl]prolyl chloride [27f] using non-chiral capillary columns.

Much more gratifying was the phosphonic anhydride mediated acylation [28] of the amino acid methyl esters with (*R*)-*N*-(3,5-dinitrobenzoyl)proline [29] and HPLC analyses of the resulting dipeptide esters **17**[8]). 'Base-line separations' were observed with (α*RS*)-**17**, R = $(CH_2)_3N_3$, R = $(CH_2)_4NHZ$ and R = $(CH_2)_5NHZ$ (*Table 4, Entries 1, 9,* and *10*), and using the achiral column *Lichrosorb Si 60*. In the remaining cases, it was preferable to employ the chiral column *Bakerbond R-DNBPG*. HPLC Comparison of the dipeptide esters **17**, R = i-Pr, R = $(CH_2)_3N(OBn)Ts$, and R = $(CH_2)_4N(OBn)Ts$ with (α*RS*)-derivatives obtained from racemic amino acid methyl esters showed that the dipeptide esters of (α*R*)-amino acids were eluted faster from the chiral column than their (α*S*)-epimers.

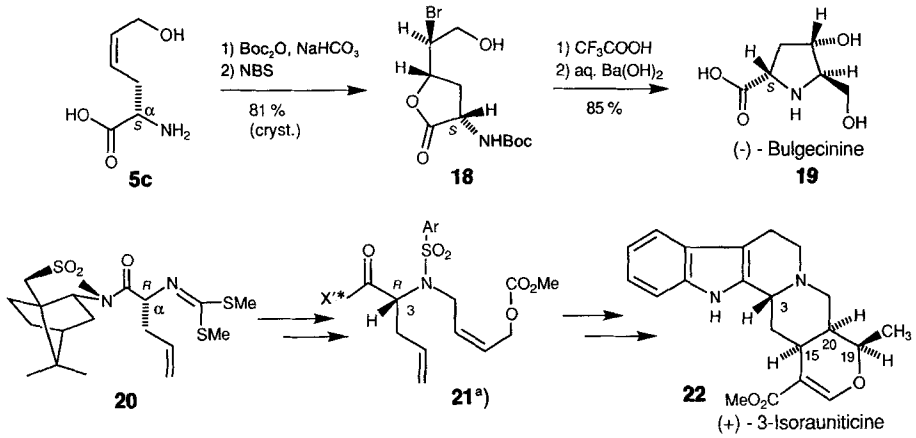
5. Enantiomerically Pure α-Amino Acid Derivatives with an Alk-2-enyl Side Chain as Building Blocks in Organic Synthesis. – The described α-amino acids are not only of interest *per se* or in peptide synthesis, but, furthermore, serve as chiral building blocks for the preparation of more complex (non-peptide) molecules, chiral reagents, and catalysts. *E.g.*, (ω-haloacyl)sultams **3m** and **3n** are potential synthetic precursors of (*S*)-proline and (*S*)-pipecolic acid *via* acidic removal of the bis(methylthio)methylidene group followed by straightforward internal alkylation, analogous to the cyclization of deprotected **18** → **19** (*Scheme 3*). This synthesis of the glycopeptide constituent (−)-bulgecinine (**19**), as communicated by *Ohfune* and *coworkers* [31], relies on the preparation of the *N*-Boc-protected derivative of **5c** from (*S*)-*N*-Boc-α-allylglycine in 7 steps. Amino acid **5c**, which was much more conveniently prepared by our route, was thus acylated with Boc_2O. Following *Ohfunes'* protocol, the resulting *N*-Boc derivative was subjected to a diastereoselective bromolactonization with *N*-bromosuccinimide (NBS) to give, after recrystallization, pure bromolactone **18**. Deprotection of **18** with CF_3COOH, cyclization of the free amine with $Ba(OH)_2$, and isolation using ion-exchange resin provided pure (−)-bulgecinine **19** in 50% overall yield from our glycine derivative **2**.

Another example illustrates the use of the antipode of glycine derivative **2** to obtain (α*R*)-amino acids. Hence, phase transfer catalyzed allylation of *ent*-**2**, carried out on a 45-g scale, provided **20** (= *ent*-**3a**) which, *via* a Pd-catalyzed cyclization of **21**, served as a key precursor for a synthesis of the alkaloid (+)-3-isorauniticine [32].

6. Conclusion. – In summary, this alkylation approach to enantiomerically pure α-amino acids complements the approach involving sultam-directed, electrophilic enolate aminations [12]. It also compares very favorably with those previously published

[8]) To our knowledge, the determination of the enantiomeric purity of α-amino acids by HPLC analysis of their *N*-(3,5-dinitrobenzoyl)prolyl derivatives is without direct precedence. For related analyses of amino acid *N*-(naphthylsulfonyl)prolyl- and *N*-tosylprolyl derivatives, see [27f] and [27g], respectively. For NMR studies of *N*-benzoylprolylvaline methyl ester, see [30].

Scheme 3



a) X'*H = *ent*-**1**.

[1–6][9]) given the easy accessibility of glycine derivative **2** and its antipode[2]), the efficient formation of crystalline alkylation products (*ca.* 100% d.e., even with nonactivated primary and secondary alkyl iodides), and, last but not least, the mild and efficient cleavage conditions. Its value in the synthesis of chiral, isotope-labelled α-amino acids was recently demonstrated [34]. Reactions of glycine derivative **2** with further C-electrophiles and applications of these results toward alkaloid syntheses will be reported in due course.

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Experimental Part

1. *General.* All reactions were carried out under Ar with magnetic stirring, unless otherwise specified. Solvents were dried by distillation from drying agents as follows: Et_2O, THF, toluene (Na metal); CH_2Cl_2, HMPA, DMPU, DMEU, Et_3N, pyridine, *N*-methylmorpholine, *N*-ethylpiperidine and diisopropylethylamine (CaH_2). (*Z*)-1-(Benzyloxy)-4-iodobut-2-ene was prepared by treatment of (*Z*)-4-(benzyloxy)but-2-en-1-ol (*Aldrich*) with methyltriphenoxyphosphonium iodide in DMF *cf.* [35]. *tert*-Butyl iodoacetate, benzyl iodide, (naphthalen-1-yl)methyl iodide, 1,5-diiodopentane, and 1,6-diiodohexane were prepared by refluxing NaI and the corresponding alkyl bromides in acetone, and the crude products were purified by distillation or directly used for phase transfer catalyzed alkylation (*tert*-butyl iodoacetate, benzyl iodide, (naphthalen-1-yl)methyl iodide). *Amberlite-IR-120* ion-exchange resin (H^+ form, *Fluka*) was washed successively with 1N NaOH, H_2O, and 1N aq. HCl prior to use. Ultrasound: high-intensity ultrasonic processor (600-W model, *Sonics & Materials, Inc.*), standard horn, 1/2″ tip (13 mm), inserted into the middle of the reaction mixture, continuous sonication, energy output 75 W. Workup denotes extraction with an org. solvent, drying of the org. phase ($MgSO_4$), and evaporation *in vacuo*. Flash chromatography (FC): *Merck 9385* silica gel. GC: *Hewlett-Packard 5790a*, integrator *HP 3390*, 10 psi H_2, capillary columns (fused silica, 0.22 mm i.d., 12 m); *A*, *OV-1*, 100°,10°/min to 270°, unless otherwise specified; *B*, *Chirasil-*

[9]) Exploratory alkylations of the *N*-diphenylmethylidene analogue of glycine derivative **2** with benzyl iodide gave the corresponding α-benzylated product in slightly lower diastereoisomeric excess or chemical yield [33a]; *cf.* [33b].

Val (*Altech Associates Inc.*), 2 min 100°, 5°/min to 140°; t_R in min (area %). HPLC: *Waters ALC/GPC-244*, UV (254 nm) detector, *Mega/Carlo-Erba* integrator, t_R in min (area %); *A*, *Merck Hibar*, *LiChrosorb Si 60*, 5 μm, 250 × 4 mm, hexane/AcOEt 9:1, 2 ml/min, unless otherwise specified; *B*, *Bakerbond R-DNBPG*, 250 × 4.6 mm, hexane/i-PrOH 4:1, 2 ml/min, unless otherwise specified. M.p.: *Kofler* hot stage; uncorrected. $[\alpha]_D$: *Perkin Elmer-241* polarimeter; in $CHCl_3$ at 20°, unless otherwise specified. IR: *Mattson Instruments Polaris* and *Perkin-Elmer 1600* FT-IR; in $CDCl_3$, unless otherwise specified; ν_{max} in cm^{-1}. NMR: in $CDCl_3$, unless otherwise specified; standard: tetramethylsilane ($\delta = 0$ ppm); ^1H, *Bruker AMX 400* (400 MHz) and *Varian XL-200* (200 MHz); ^{13}C, *Varian Xl-200* (50 MHz). MS (EI, 70 eV): *m/z* (rel. intensity in %).

2. *Starting Materials. (2R)-N-{N-[Bis(methylthio)methylidene]glycyl}bornane-10,2-sultam* (**2**). A 2M Me_2Al soln. in hexane (60 ml, 120 mmol) was added dropwise, without cooling and without external heating, to a soln./suspension of (2*R*)-bornanesultam **1** (21,5 g, 100 mmol) in dry toluene (200 ml). The mixture started to boil under reflux, and **1** got dissolved. Stirring of the soln. for 30 min, addition of methyl *N*-[bis(methylthio)methylidene]glycinate [8] (29 g, 150 mmol, 1.2 equiv.) in toluene (80 ml), heating of the mixture at 50° for 24 h, cooling (ice bath), dropwise addition of MeOH (100 ml), stirring for 30 min, addition of H_2O (80 ml), stirring for 1 h, filtration through *Celite*, washing of the *Celite* with AcOEt, drying of the combined org. phases ($MgSO_4$), evaporation, and crystallization (EtOH) furnished **2** (46 g, 81%). M.p. 107–109°. HPLC (*A*): 18.50. $[\alpha]_D = -115.6$, $[\alpha]_{578} = -120.7$, $[\alpha]_{546} = -138.1$, $[\alpha]_{436} = -243.6$, $[\alpha]_{365} = -409.9$ ($c = 3.27$). IR: 2970, 2920, 1720, 1570, 1460, 1390, 1370, 1340, 1270, 1240, 1130. ^1H-NMR (200 MHz): 0.96 (*s*, 3 H); 1.18 (*s*, 3 H); 1.30–1.48 (2 H); 1.82–1.95 (3 H); 2.07 (*dd*, $J = 14, 8$, 1 H); 2.15–2.26 (1 H); 2.40 (*s*, 3 H); 2.51 (*s*, 3 H); 3.42 (*d*, $J = 14$, 1 H); 3.50 (*d*, $J = 14$, 1 H); 3.91 (*dd*, $J = 8, 5$, 1 H); 4.60 (*d*, $J = 18$, 1 H); 4.70 (*d*, $J = 18$, 1 H). ^{13}C-NMR: 168.05 (*s*); 164.05 (*s*); 65.19 (*d*); 55.48 (*t*); 52.77 (*t*); 48.84 (*s*); 47.73 (*s*); 44.67 (*d*); 38.27 (*t*); 32.76 (*t*); 26.38 (*t*); 20.70 (*q*); 19.80 (*q*); 15.00 (*q*); 14.54 (*q*). MS: 376 (0.2, $C_{15}H_{24}N_2O_3S_3^{+\cdot}$), 329 (100), 135 (55), 107 (25), 93 (30), 79 (20), 72 (18), 61 (60).

*(Z)-1-Bromo-4-[(*tert*-butyl)dimethylsiloxy]but-2-ene*. NaH (1.35 g, 60% dispersion in mineral oil, 28 mmol) was washed with hexane and then suspended in THF (55 ml). Addition of a soln. of (*Z*)-but-2-ene-1,4-diol (2.47 g, 28 mmol), stirring for 45 min at r.t., addition of (*t*-Bu)Me_2SiCl (4.22 g, 28 mmol), stirring for 45 min, aq. workup (Et_2O), and FC (hexane/AcOEt 4:1) gave (*Z*)-1-[(*tert*-butyl)dimethylsilyloxy]but-2-en-4-ol (5.19 g). PPh_3 (6.3 g, 24 mmol) was added to a soln. of NBS (4.32 g, 24 mmol) in DMF (20 ml) which became hot during the addition. After cooling the resulting red suspension to r.t., a soln. of (*Z*)-4-[(*tert*-butyl)dimethylsiloxy]but-2-en-1-ol (5.96 g, 20 mmol) in DMF (20 ml) was added and the mixture stirred at r.t. for 20 min. Addition of a sat. aq. Na_2SO_3 soln., workup (hexane), and FC (hexane/Et_2O 4:1) provided (*Z*)-1-bromo-4-[(*tert*-butyl)dimethylsilyloxy]but-2-ene (oil; 5.17 g, 75% from (*Z*)-but-2-ene-1,4-diol). IR: 3020, 2980, 2880, 2840, 1470, 1400, 1380, 1350, 1245, 1200. ^1H-NMR: 0.00 (*s*, 6 H); 0.81 (*s*, 9 H); 3.92–3.95 (2 H); 4.21–4.25 (2 H); 5.55–5.71 (2 H). MS: 265 (0.5, $C_{10}H_{21}BrOSi^{+\cdot}$), 209 (27), 207 (28), 185 (27), 139 (38), 137 (39), 129 (13), 127 (62), 75 (58), 73 (66), 59 (26), 57 (100).

3. *Alkylations of Sultam-Derived* N*-Protected Glycine* **2**. *General Procedure A (Phase-Transfer Catalysis)*. $LiOH \cdot H_2O$ (50 mol-equiv.) was added to a mixture of **2** (1.0 equiv.), $(Bu_4N)HSO_4$ (1.1 mol-equiv.), and alkylating halide (1.2 mol-equiv.) in CH_2Cl_2/H_2O 30:1 (10 ml/mmol) at −10°, and the mixture was immediately sonicated for 2–8 min. Filtration of the biphasic mixture, evaporation of the filtrate, trituration of the residue with Et_2O (50 ml/mmol), filtration from Bu_4NX (X = I or Br), washing of the filtrate (H_2O, then sat. aq. NaCl soln.), drying (Na_2SO_4), evaporation, and crystallization (or FC) of the residue afforded alkylation products **3**.

General Procedure B (BuLi, THF/HMPA). A 1.6M BuLi soln. (1.1 equiv.) in hexane was added over 1 h at −78° to stirred 0.2M **2** in THF. After stirring for 1 h at −78°, a soln. of the alkylating agent (3 mol-equiv.) in HMPA (3 mol-equiv.) was added over 30 min. Warming of the mixture to r.t. over 2–3 h (unless otherwise specified), evaporation of the THF below 40° *in vacuo*, workup (Et_2O), FC, and crystallization furnished alkylation products **3**.

General Procedure C (BuLi, THF/DMPU). A. 1.6M BuLi soln. (1.1 equiv.) in hexane was added over 1 h at −78° to stirred 0.2M **2** in THF. After stirring for 1 h at −78°, DMPU (1.58 ml/mmol, 24%) was added over 30 min. Subsequent addition of the alkyl halide (5.0 equiv.), warming of the mixture to r.t. over 2–3 h (unless otherwise specified), evaporation of the THF below 40° *in vacuo*, workup (Et_2O), FC, and crystallization furnished alkylation products **3**.

(2R)-N-{(2S)-2-{[Bis(methylthio)methylidene]amino}pent-4-en-1-oyl}bornane-10,2 sultam (**3a**). Using the *General Procedure A*, alkylation of **2** (11.0 g, 29 mmol) with allyl iodide (sonication for 5 min, −10°), workup, and crystallization (EtOH) gave (after FC of the mother liquors) pure **3a** (9.54 g, 79.0%). HPLC (*A*): 11.72 (99.8), 7.65 (0.2). M.p. 81–83°. $[\alpha]_D = -55.3$, $[\alpha]_{578} = -57.3$, $[\alpha]_{546} = -64.6$, $[\alpha]_{436} = -106.3$, $[\alpha]_{365} = -165.1$ ($c = 2.41$). IR: 3020, 2980, 2880, 1700, 1640, 1570, 1340, 1270, 1240, 1130, 900. ^1H-NMR (200 MHz): 0.96 (*s*, 3 H); 1.18 (*s*, 3 H); 1.24–1.45 (2 H); 1.82–1.95 (3 H); 2.00–2.08 (2 H); 2.42 (*s*, 3 H); 2.55 (*s*, 3 H); 2.58–2.78 (2 H); 3.42 (*d*, $J = 13$, 1 H); 3.51 (*d*, $J = 13$, 1 H); 3.92 (*t*, $J = 6$, 1 H); 5.0–5.16 (3 H); 5.88 (*ddt*, $J = 17, 10, 7$, 1 H). ^{13}C-NMR: 170.89 (*s*); 161.99

(*s*); 133.73 (*d*); 117.70 (*t*); 65.35 (*d*); 64.54 (*d*); 53.11 (*t*); 48.42 (*s*); 47.72 (*s*); 44.65 (*d*); 38.83 (*t*); 38.40 (*t*); 32.83 (*t*); 26.43 (*t*); 20.73 (*q*); 19.85 (*q*); 15.30 (*q*); 14.76 (*q*). MS: 416 (0.5, $C_{18}H_{28}N_2O_3S_3^+$), 369 (100), 327 (5), 296 (12), 174 (72), 135 (95), 126 (58), 107 (34), 101 (42), 93 (43), 79 (33).

Using the *General Procedure B*, alkylation of **2** (377 mg, 1 mmol) with allyl iodide (THF/HMPA, −50°, 16 h), workup, and crystallization (EtOH) gave **3a** (364 mg, 87%; d.e. > 99%) showing the same m.p., [α], IR, NMR, and MS as described above.

(2R)-N-{*(2S,Z)-6-(Benzyloxy)-2-{[bis(methylthio)methylidene]amino}hex-4-en-1-oyl}bornane-10,2-sultam* (**3b**). Using the *General Procedure A*, alkylation of **2** (5.46 g, 14.5 mmol) with (*Z*)-1-(benzyloxy)-4-iodo-but-2-ene (sonication for 4 min, −10°) workup, and FC (hexane/Et_2O 2:1) afforded **3b** (oil; 6.61 g, 85%). HPLC (*A*): 19.91 (0.8), 24.73 (99.2). $[\alpha]_D = -50.2$, $[\alpha]_{578} = -52.3$, $[\alpha]_{546} = -59.2$, $[\alpha]_{436} = -97.7$ (*c* = 1.68). IR: 3020, 2980, 2880, 2840, 1710, 1570, 1450, 1340, 1270, 1240, 1130. ^{1}H-NMR (200 MHz): 0.95 (*s*, 3 H); 1.14 (*s*, 3 H); 1.23–1.47 (2 H); 1.76–1.95 (3 H); 1.99–2.80 (*m*, 2 H); 2.41 (*s*, 3 H); 2.53 (*s*, 3 H); 2.56–2.80 (2 H); 3.36–3.54 (2 H); 3.86–3.99 (3 H); 4.49 (*s*, 2 H); 5.02 (*t*, *J* = 5.39, 1 H); 5.58–5.86 (2 H); 7.26–7.40 (5 H). ^{13}C-NMR: 170.89 (*s*); 162.46 (*s*); 138.59 (*s*); 129.94 (*d*); 129.85 (*d*); 129.20 (*d*); 128.80 (*d*, 2 C); 127.73 (*d*); 127.43 (*d*); 71.68 (*t*); 70.57 (*t*); 65.39 (*d*); 64.72 (*d*); 53.16 (*t*); 48.48 (*s*); 47.76 (*s*); 44.65 (*d*); 38.47 (*t*); 37.58 (*t*); 32.87 (*t*); 26.47 (*t*); 20.76 (*q*); 19.88 (*q*); 15.34 (*q*); 14.84 (*q*). MS: 537 (0.05, $[C_{26}H_{36}N_2O_4S_3 + 1]^+$), 489 (1), 459 (0.05), 445 (0.05), 429 (0.05), 415 (0.2), 381 (0.4), 375 (1), 294 (0.8), 216 (0.4), 186 (0.6), 156 (0.8), 135 (6), 107 (6), 91 (100), 79 (13), 67 (13), 55 (12).

(2R)-N-{*(2S,Z)-2-{[Bis(methylthio)methylidene]amino}-6-[(*tert*-butyl)dimethylsilyloxy]hex-4-en-1-oyl}-bornane-10,2-sultam* (**3c**). Using the *General Procedure A*, alkylation of **2** (3.765 g, 10 mmol) with (*Z*)-1-bromo-4-[(*tert*-butyl)dimethylsilyloxy]but-2-ene (sonication for 5 min, −10°), workup, and FC (hexane/Et_2O 2:1) gave **3c** (3.838 g, 68.5%). HPLC (*A*): 9.59 (0.39), 15.86 (99.7). $[\alpha]_D = -54.4$, $[\alpha]_{578} = -56.6$, $[\alpha]_{546} = -64.2$, $[\alpha]_{436} = -106.2$, $[\alpha]_{365} = -161.3$ (*c* = 2.905). IR: 3020, 2980, 2880, 1700, 1570, 1470, 1460, 1410, 1370, 1270, 1140, 1070, 840. ^{1}H-NMR: 0.00 (*s*, 6 H); 0.83 (*s*, 9 H); 0.92 (*s*, 3 H); 1.10 (*s*, 3 H); 1.23–1.38 (2 H); 1.78–1.90 (3 H); 1.98–2.03 (2 H); 2.36 (*s*, 3 H); 2.50 (*s*, 3 H); 2.52 (*m*, 1 H); 2.66 (*m*, 1 H); 3.37 (*d*, *J* = 14, 1 H); 3.45 (*d*, *J* = 14, 1 H); 3.88 (*t*, *J* = 6, 1 H); 4.20 (*d*, *J* = 6, 2 H); 4.94 (*t*, *J* = 6, 1 H); 5.42 (*m*, 1 H); 5.55 (*m*, 1 H). ^{13}C-NMR: 170.10 (*s*); 162.38 (*s*); 133.17 (*d*); 124.62 (*d*); 65.40 (*d*); 64.69 (*d*); 59.65 (*t*); 53.20 (*t*); 48.53 (*s*); 47.82 (*s*); 44.71 (*d*); 38.44 (*t*); 32.91 (*t*); 32.83 (*t*); 26.50 (*t*); 26.0 (*q*, 3 C); 20.80 (*q*); 19.92 (*q*); 18.34 (*s*); 15.43 (*q*); 14.83 (*q*); −5.121 (*q*, 2 C). MS: 561 (0.5, $[C_{25}H_{44}N_2O_3S_3Si + 1]^+$), 513 (5), 503 (2), 455 (2), 429 (0.5), 415 (4), 384 (10), 375 (13), 351 (0.5), 329 (0.5), 255 (0.5), 186 (30), 166 (10), 135 (30), 107 (40), 93 (55), 73 (100).

The minor (α*R*)-epimer of **3c** was isolated in 4.2% yield. HPLC (*A*): 9.12. IR: 3020, 2980, 2880, 1700, 1570, 1470, 1460, 1410, 1370, 1270, 1140, 1070, 840. ^{1}H-NMR: 0.00 (*s*, 6 H); 0.83 (*s*, 9 H); 0.89 (*s*, 3 H); 1.07 (*s*, 3 H); 1.18–1.38 (2 H); 1.76–1.85 (3 H); 1.95–2.10 (2 H); 2.28 (*s*, 3 H); 2.40 (*m*, 1 H); 2.48 (*s*, 3 H); 2.64 (*m*, 1 H); 3.35 (*d*, *J* = 14, 1 H); 3.39 (*d*, *J* = 14, 1 H); 3.85 (*dd*, *J* = 8, 5, 1 H); 4.15–4.28 (2 H); 4.80 (*t*, *J* = 6, 2 H); 5.38 (*m*, 1 H); 5.53 (*m*, 1 H). MS: 562 (1.5, $[C_{25}H_{44}N_2O_4S_3Si + 2]^+$), 513 (3), 503 (3.5), 455 (1.5), 429 (1.2), 415 (3), 384 (6), 375 (12), 351 (0.4), 329 (0.9), 318 (2), 288 (2), 260 (2), 186 (31), 166 (9), 154 (4), 135 (33), 124 (7), 107 (44), 93 (51), 73 (100), 57 (38).

(2R)-N-{*(2S)-2-{[Bis(methylthio)methylidene]amino}-3-phenylpropan-1-oyl}bornane-10,2-sultam* (**3d**). Using the *General Procedure A*, alkylation of **2** (1.1 g, 2.9 mmol) with benzyl iodide (sonication for 3 min, −10°), workup, and crystallization (EtOH) gave **3d** (1.0842 g, 77.4%). HPLC (*A*): 14.9 (0.1), 22.6 (99.9). M.p. 132–133°. $[\alpha]_D = -109.2$, $[\alpha]_{578} = -114.0$, $[\alpha]_{546} = -130.2$, $[\alpha]_{436} = -227.4$, $[\alpha]_{365} = -374.9$ (*c* = 1.6). IR: 3020, 2980, 2880, 1700, 1570, 1450, 1340, 1270, 1240, 1140. ^{1}H-NMR (200 MHz): 0.86 (*s*, 3 H); 0.90 (*s*, 3 H); 1.20–1.40 (2 H); 1.76–1.94 (4 H); 2.02 (*dd*, *J* = 13, 7.5, 1 H); 2.41 (*s*, 3 H); 2.48 (*s*, 3 H); 3.03 (*dd*, *J* = 13, 7.5, 1 H); 3.32 (*dd*, *J* = 13, 6, 1 H); 3.40 (*d*, *J* = 14, 1 H); 3.43 (*d*, *J* = 14, 1 H); 3.87 (*dd*, *J* = 8, 5, 1 H); 5.23 (*dd*, *J* = 7.5, 6, 1 H); 7.13–7.32 (5 H). ^{13}C-NMR: 170.95 (*s*); 162.79 (*s*); 137.21 (*s*); 129.97 (*d*); 128.07 (*d*); 126.50 (*d*); 66.82 (*d*); 65.31 (*d*); 53.14 (*t*); 48.39 (*s*); 47.68 (*s*); 44.70 (*d*); 40.31 (*t*); 38.29 (*t*); 32.87 (*t*); 26.44 (*t*); 20.59 (*q*); 19.83 (*q*); 15.49 (*q*); 14.86 (*q*). MS: 467 (0.1, $[C_{22}H_{30}N_2O_3S_3 + 1]^+$), 436 (0.1), 419 (97), 375 (32), 346 (53), 304 (10), 274 (5), 224 (44), 176 (18), 151 (47), 135 (100), 103 (35), 93 (35), 91 (32).

Using the *General Procedure B*, alkylation of **2** (377 mg, 1 mmol) with benzyl iodide (THF/HMPA, −55°, 16 h), workup, and crystallization (EtOH) gave **3d** (435 mg, 93%; d.e. > 99%) showing the same m.p., [α], IR, NMR, and MS as described above.

(2R)-N-{*(2S)-2-{[Bis(methylthio)methylidene]amino}-3-(4-bromophenyl)propan-1-oyl}bornane-10,2-sultam* (**3e**). Using the *General Procedure A*, alkylation of **2** (1.1 g, 2.9 mmol) with 4-bromobenzyl bromide (sonication for 4 min, −10°), workup, and crystallization (EtOH) gave **3e** (1.274 g, 85.2%). HPLC (*A*): 13.83 (0.3), 23.75 (99.7). M.p. 163–164°. $[\alpha]_D = -102.0$ $[\alpha]_{578} = -106.8$, $[\alpha]_{546} = -121.6$, $[\alpha]_{436} = -213.0$, $[\alpha]_{365} = -350.8$ (*c* = 0.5). IR: 3020, 2980, 2880, 1700, 1570, 1490, 1350, 1270, 1230, 1120. ^{1}H-NMR (200 MHz): 0.88 (*s*, 3 H); 0.92 (*s*, 3 H);

1.15–1.45 (2 H); 1.76–1.92 (4 H); 2.02 (*dd*, J = 14, 8, 1 H); 2.39 (*s*, 3 H); 2.47 (*s*, 3 H); 3.00 (*dd*, J = 7.5, 13, 1 H); 3.25 (*dd*, J = 6, 13, 1 H); 3.38 (*d*, J = 15, 1 H); 3.48 (*d*, J = 15, 1 H); 3.88 (*dd*, J = 8, 5, 1 H); 5.17 (*dd*, J = 7.5, 6.2, 1 H); 7.15 (*d*, J = 7, 2 H); 7.35 (*d*, J = 7, 2 H). ^{13}C-NMR: 170.1 (*s*); 163.12 (*s*); 136.3 (*s*); 131.7 (*d*); 131.2 (*d*); 120.6 (*s*); 66.4 (*d*); 65.3 (*d*); 53.1 (*t*); 48.4 (*s*); 47.7 (*d*); 44.7 (*d*); 38.3 (*t*); 39.7 (*t*); 32.9 (*t*); 26.4 (*t*); 20.4 (*q*); 19.8 (*q*); 15.4 (*q*); 14.9 (*q*). MS: 499 (38, $[C_{22}H_{29}BrN_2O_3S_3 - 46]^+$), 426 (30), 375 (39), 304 (22), 209 (18), 135 (100), 93 (29).

*(2*R*)-*N*-{(2*S*)-2-{[Bis(methylthio)methylidene]amino}-3-(naphthalen-1-yl)propan-1-oyl}bornane-10,2-sultam* (**3f**). Using the *General Procedue A*, alkylation of **2** (1.1 g, 2.9 mmol) with (naphthalen-1-yl)methyl iodide (sonication for 3 min, −10°), workup, and FC (hexane/Et_2O 2:1) provided **3f** (amorphous solid; 1.274 g, 85.2%). HPLC (*A*): 14.05 (0.5), 20.42 (99.5). M.p. 74–75°. $[\alpha]_D$ = −86.0, $[\alpha]_{578}$ = −89.6, $[\alpha]_{546}$ = −102.5, $[\alpha]_{436}$ = −182.3, $[\alpha]_{365}$ = −316.9 (c = 0.645). IR: 3030, 3020, 2980, 2880, 1700, 1570, 1450, 1360, 1270, 1250, 1150. ^{1}H-NMR (200 MHz): 0.58 (*s*, 3 H); 0.84 (*s*, 3 H); 1.15–1.40 (2 H); 1.65–2.05 (5 H); 2.34 (*s*, 3 H); 2.41 (*s*, 3 H); 3.41–3.82 (5 H); 5.50 (*t*, J = 7.5, 1 H); 7.32–7.55 (4 H); 7.68–7.82 (2 H); 8.34 (*d*, J = 6, 1 H). ^{13}C-NMR: 171.2 (*s*); 162.5 (*s*); 138.8 (*s*); 133.2 (*s*); 132.6 (*s*); 128.7 (*d*); 128.3 (*d*); 127.5 (*d*); 125.7 (*d*); 125.4 (*d*); 125.2 (*d*); 124.8 (*d*); 66.4 (*d*); 65.3 (*d*); 53.1 (*t*); 48.3 (*s*); 47.6 (*s*); 44.7 (*d*); 38.2 (*t*); 36.9 (*t*); 32.9 (*t*); 26.4 (*t*); 20.4 (*q*); 19.8 (*q*); 15.5 (*q*); 14.8 (*q*). MS: 469 (2.4, $[C_{26}H_{32}N_2O_3S_3 - 47]^+$), 375 (6), 274 (3), 253 (1), 226 (8), 198 (3), 181 (37), 167 (3), 153 (100), 141 (76), 135 (48), 127 (10), 115 (26), 107 (42), 93 (61).

*(2*R*)-*N*-{(2*S*)-2-{[Bis(methylthio)methylidene]amino}-3-[(*tert*-butyl)oxycarbonyl]propan-1-oyl}bornane-10,2-sultam* (**3g**). Using the *General Procedure A*, alkylation of **2** (1.1 g, 2.9 mmol) with *tert*-butyl iodoacetate (sonication for 3 min, −10°), workup, and crystallization (EtOH) gave **3g** (1.156 g, 80.7%). HPLC (*A*): 15.98 (> 99.9), 19.65 (< 0.1). M.p. 142–143°. $[\alpha]_D$ = −37.8, $[\alpha]_{578}$ = −39.2, $[\alpha]_{546}$ = −44.0, $[\alpha]_{436}$ = −70.4, $[\alpha]_{365}$ = −99.2 (c = 2.355). IR: 2980, 1710, 1680, 1570, 1370, 1340, 1270, 1160, 1130. ^{1}H-NMR (200 MHz): 0.95 (*s*, 3 H); 1.19 (*s*, 3 H); 1.32–1.50 (2 H); 1.42 (*s*, 9 H); 1.84–2.20 (5 H); 2.38 (*s*, 3 H); 2.56 (*s*, 3 H); 2.80 (*dd*, J = 15, 6.5, 1 H); 2.96 (*dd*, J = 15, 6.5, 1 H); 3.40 (*d*, J = 14, 1 H); 3.48 (*d*, J = 14, 1 H); 3.93 (*dd*, J = 5, 8, 1 H); 5.18 (*t*, J = 6.5, 1 H). ^{13}C-NMR: 170.08 (*s*); 169.50 (*s*); 163.66 (*s*); 80.77 (*s*); 65.319 (*d*); 61.93 (*d*); 53.008 (*t*); 48.676 (*s*); 47.86 (*s*); 44.61 (*d*); 39.48 (*t*); 37.94 (*t*); 32.75 (*t*); 28.06 (*q*); 26.55 (*t*); 20.55 (*q*); 19.92 (*q*); 15.24 (*q*); 14.77 (*q*). MS: 443 (0.3, $[C_{21}H_{34}N_2O_3S_3 - 37]^+$), 387 (4), 341 (1), 339 (1), 323 (0.3), 296 (0.4), 248 (3), 192 (7), 172 (7), 135 (24), 109 (10), 107 (13), 100 (15), 93 (21), 57 (100).

Using the *General Procedure B*, alkylation of **2** (377 mg, 1 mmol) with *tert*-butyl bromoacetate/0.1 mol-equiv. Bu_4NI (THF/HMPA), workup, and crystallization (EtOH) gave **3g** (453 mg, 96%; d.e. > 99%) showing the same m.p., [α], IR, NMR, and MS as described above.

*(2*R*)-*N*-{(2*S*)-2-{[Bis(methylthio)methylidene]amino}propan-1-oyl}bornane-10,2-sultam* (**3h**). Using the *General Procedure A*, alkylation of **2** (1.1 g, 2.9 mmol) with MeI (sonication for 3 min, −10°), workup, crystallization (EtOH), and FC of the mother liquors gave **3h** (0.799 g, 70.6%). HPLC (*A*): 10.29 (0.2), 15.36 (99.8). M.p. 118–119°. $[\alpha]_D$ = −70.0, $[\alpha]_{578}$ = −72.8, $[\alpha]_{546}$ = −82.5, $[\alpha]_{436}$ = −137.8, $[\alpha]_{365}$ = −213.3 (c = 1.765). IR: 3020, 2950, 2920, 1880, 1700, 1570, 1320, 1280, 1240, 1130, 1100, 1060. ^{1}H-NMR (200 MHz): 0.97 (*s*, 3 H); 1.16 (*s*, 3 H); 1.26–1.43 (2 H); 1.50 (*d*, J = 7, 3 H); 1.80–1.88 (3 H); 2.15–2.60 (2 H); 2.43 (*s*, 3 H); 2.55 (*s*, 3 H); 3.42 (*d*, J = 13.65, 1 H); 3.51 (*d*, J = 13.65, 1 H); 3.92 (*t*, J = 6.35, 1 H); 5.10 (*q*, J = 7.3, 1 H). ^{13}C-NMR: 172.29 (*s*); 161.41 (*s*); 65.20 (*d*); 60.66 (*d*); 53.06 (*t*); 48.52 (*s*); 47.76 (*s*); 44.62 (*d*); 38.32 (*t*); 32.79 (*t*); 26.43 (*t*); 20.68 (*q*); 19.87 (*q*); 19.84 (*q*); 15.15 (*q*); 14.69 (*q*). MS: 390 (0.2, $C_{16}H_{26}N_2O_3S_3^+$), 375 (5), 343 (96), 315 (2), 270 (18), 148 (100), 135 (90), 109 (45), 93 (35), 75 (90).

Using the *General Procedure B*, alkylation of **2** (377 mg, 1 mmol) with MeI (THF/HMPA, −50°, 16 h), workup, and crystallization (hexane) gave **3h** (350 mg, 87%; d.e. > 99%) showing the same m.p., [α], IR, NMR, and MS as described above.

*(2*R*)-*N*-{(2*S*)-2-{[Bis(methylthio)methylidene]amino}hexan-1-oyl}bornane-10,2-sultam* (**3i**). Using the *General Procedure B*, alkylation of **2** (377 mg, 1 mmol) with BuI (THF/7 mol-equiv. of HMPA, −50°, 16 h), workup, and crystallization (hexane) gave **3i** (364 mg, 87%). GC (*A*): 12.73 (< 0.1), 13.09 (> 99.9). M.p. 95–97° $[\alpha]_D$ = −72.2, $[\alpha]_{578}$ = −77.1, $[\alpha]_{546}$ = −87.3, $[\alpha]_{436}$ = −146.6, $[\alpha]_{365}$ = −232.1 (c = 1.12). IR: 2970, 2920, 1710, 1570, 1330, 1270, 1130, 1110. ^{1}H-NMR: 0.88 (*t*, J = 7.0, 3 H); 0.97 (*s*, 3 H); 1.17 (*s*, 3 H); 1.26–1.45 (6 H); 1.83–2.10 (7 H); 2.43 (*s*, 3 H); 2.55 (*s*, 3 H); 3.43 (*d*, J = 14, 1 H); 3.50 (*d*, J = 14, 1 H); 3.93 (*t*, J = 6.5, 1 H); 4.94 (*dd*, J = 7.5, 5.0, 1 H). ^{13}C-NMR: 171.87 (*s*); 161.51 (*s*); 65.34 (*d*); 65.19 (*d*); 53.15 (*t*); 48.46 (*s*); 47.80 (*s*); 44.62 (*d*); 38.47 (*t*); 34.47 (*t*); 32.85 (*t*); 27.95 (*t*); 26.49 (*t*); 22.40 (*t*); 20.70 (*q*); 19.92 (*q*); 15.31 (*q*); 14.85 (*q*); 13.95 (*q*). MS: 432 (5, $C_{19}H_{32}N_2O_3S_3^+$), 417 (15), 385 (90), 312 (32), 190 (72), 135 (100), 93 (42), 69 (58).

Using the *General Procedure C*, alkylation of **2** (50 mg, 0.133 mmol) with BuI (THF/DMPU), workup, FC (hexane/Et_2O 2:1), and crystallization (hexane/Et_2O) gave **3i** (47.5 mg, 83%; d.e. > 99%) showing the same m.p., [α], IR, NMR, and MS as described above.

(2R)-N-{(2S)-2-{[Bis(methylthio)methylidene]amino}-4-methylpentan-1-oyl}bornane-10,2-sultam (**3j**). Using the *General Procedure B*, alkylation of **2** (377 mg, 1 mmol) with i-BuI (5 mol. equiv.: THF/7 mol-equiv. of HMPA), workup, FC (hexane/Et_2O 1:1), and crystallization (EtOH) gave **3j** (367 mg, 85%). GC (*A*): 12.30 (< 0.1), 12.56 (> 99.9). M.p. 125–127°. $[\alpha]_D = -82.7$, $[\alpha]_{578} = -87.6$, $[\alpha]_{547} = -92.6$, $[\alpha]_{436} = -162.6°$, $[\alpha]_{365} = -265.4$ (*c* = 1.37). IR: 2950, 1700, 1570, 1330, 1270, 1130, 1100. ^{1}H-NMR: 0.92 (*d*, *J* = 7, 3 H); 0.94 (*d*, *J* = 7, 3 H); 0.97 (*s*, 3 H); 1.17 (*s*, 3 H); 1.30–1.45 (2 H); 1.60–1.95 (6 H); 2.06–2.09 (2 H); 2.42 (*s*, 3 H); 2.56 (*s*, 3 H); 3.43 (*d*, *J* = 14, 1 H); 3.49 (*d*, *J* = 14, 1 H); 3.92 (*t*, *J* = 6.0, 1 H); 4.99 (*dd*, *J* = 8, 5, 1 H). ^{13}C-NMR: 172.10 (*s*); 161.46 (*s*); 65.35 (*d*); 63.83 (*d*); 53.12 (*t*); 48.43 (*s*); 47.78 (*s*); 44.58 (*d*); 43.28 (*t*); 38.43 (*t*); 32.84 (*t*); 26.46 (*t*); 25.38 (*d*); 23.09 (*q*); 21.88 (*q*); 20.73 (*q*); 19.91 (*q*); 15.28 (*q*); 14.86 (*q*). MS: 432 (0.5, $[C_{19}H_{32}N_2O_3S_3 + 2]^+$), 417 (0.5), 385 (100), 312 (30), 196 (60), 135 (50), 114 (18), 93 (15).

Using the *General Procedure C*, alkylation of **2** (50 mg, 0.133 mmol) with BuI (THF/DMPU), workup, FC (hexane/Et_2O 2:1), and crystallization (hexane/Et_2O) gave **3j** (38.1 mg, 67%; d.e. > 99%) showing the same m.p., [α], IR, NMR, and MS as described above.

(2R)-N-{(2S)-2-{[Bis(methylthio)methylidene]amino}-3-methylbutan-1-oyl}bornane-10,2-sultam (**3k**). Using the *General Procedure B*, alkylation of **2** (377 mg, 1 mmol) with i-PrI (5 mol-equiv.; THF/7 mol-equiv. of HMPA, 30 h), workup, and FC (hexane/Et_2O 1:1) gave **3k** (amorphous solid; 397 mg, 95%). GC (*A*): 11.70 (< 0.1), 12.11 (> 99.9). $[\alpha]_D = -62.5$, $[\alpha]_{578} = -65.4$, $[\alpha]_{546} = -74.2$, $[\alpha]_{436} = -126.7$, $[\alpha]_{365} = -206.4$ (*c* = 2.31). IR: 2980, 2920, 1700, 1580, 1340, 1270, 1130, 1070. ^{1}H-NMR: 0.96–0.99 (9 H); 1.17 (*s*, 3 H); 1.30–1.46 (2 H); 1.83–1.93 (3 H); 2.00–2.12 (2 H); 2.44 (*s*, 3 H); 2.54 (*s*, 3 H); 3.50 (*d*, *J* = 14, 1 H); 3.44 (*d*, *J* = 14, 1 H); 3.93 (*dd*, *J* = 7.5, 5, 1 H); 4.78 (*d*, *J* = 4.0, 1 H). ^{13}C-NMR: 171.28 (*s*); 162.10 (*s*); 69.73 (*d*); 65.27 (*d*); 53.15 (*t*); 48.37 (*s*); 47.79 (*s*); 44.53 (*d*); 38.57 (*t*); 33.26 (*d*); 32.77 (*t*); 26.52 (*t*); 20.59 (*q*); 20.02 (*q*); 19.92 (*q*); 16.87 (*q*); 15.36 (*q*); 14.88 (*q*). MS: 419 (2.5, $[C_{18}H_{28}N_2O_3S_3 + 3]^+$), 371 (10), 343 (0.3), 298 (4.2), 274 (0.3), 176 (29), 135 (50.5), 103 (29), 93 (30), 83 (40), 55 (100).

Using the *General Procedure C*, alkylation of **2** (50 mg, 0.133 mmol) with i-PrI (THF/DMPU), workup, and FC (hexane/Et_2O 1:1) gave **3k** (amorphous solid; 36.6 mg, 66%; d.e. > 99%) showing the same [α], IR, NMR, and MS as described above.

(2R)-N-{(2S)-2-{[Bis(methylthio)methylidene]amino}-3-chloropropan-1-oyl}bornane-10,2-sultam (**3l**). Using the *General Procedure C*, alkylation of **2** (500 mg, 1.33 mmol) with $ClCH_2I$ (THF/DMPU), workup, FC (hexane/Et_2O 1:1), and crystallization (hexane/Et_2O) gave **3l** (367.4 mg, 65%). HPLC (*A*): 11.69 (1), 14.99 (99). M.p. 142–145°. $[\alpha]_D = -51.0$, $[\alpha]_{578} = -51.2$, $[\alpha]_{546} = -58.1$, $[\alpha]_{436} = -93.6$, $[\alpha]_{365} = -128.0$ (*c* = 1.13). IR: 2970, 2920, 1710, 1570, 1340, 1120, 500. ^{1}H-NMR: 0.98 (*s*, 3 H); 1.20 (*s*, 3 H); 1.12–1.47 (2 H); 1.85–1.96 (3 H); 2.04–2.20 (2 H); 2.44 (*s*, 3 H); 2.58 (*s*, 3 H); 3.43 (*d*, *J* = 14, 1 H); 3.52 (*d*, *J* = 14, 1 H); 3.88–3.95 (2 H); 3.96 (*dd*, *J* = 7.5, 5, 1 H); 5.23 (*t*, *J* = 5.0, 1 H). ^{13}C-NMR: 169.0 (*s*); 166.0 (*s*); 65.66 (*d*); 65.44 (*d*); 53.12 (*t*); 48.73 (*s*); 47.92 (*s*); 45.29 (*t*); 44.54 (*d*); 38.17 (*t*); 32.77 (*t*); 26.52 (*t*); 20.59 (*q*); 19.94 (*q*); 15.36 (*q*); 14.96 (*q*). MS: 425 (1.7, $[C_{16}H_{25}ClN_2O_3S_3 + 1]^+$), 388 (0.5), 377 (20), 351 (0.4), 341 (2.4), 304 (0.9), 277 (2.5), 182 (28), 135 (76), 109 (100).

The minor (α*R*)-epimer of **3l** was also isolated (3 mg). HPLC (*A*): 10.47. IR: 2970, 2920, 1710, 1570, 1320, 1200. ^{1}H-NMR: 0.96 (*s*, 3 H); 1.13 (*s*, 3 H); 1.19–1.45 (3 H); 1.83–1.93 (3 H); 2.05–2.18 (2 H); 2.34 (*s*, 3 H); 2.59 (*s*, 3 H); 3.42–3.62 (2 H); 3.88–4.30 (2 H); 5.13 (*dd*, *J* = 8, 5, 1 H).

(2R)-N-{(2S)-2-{[Bis(methylthio)methylidene]amino}-5-chloropentan-1-oyl}bornane-10,2-sultam (**3m**). Using the *General Procedure C*, alkylation of **2** (500 mg, 1.33 mmol) with 1-chloro-3-iodopropane (THF/DMPU), workup, FC (hexane/Et_2O 1:1), and crystallization (hexane/Et_2O) gave **3m** (435.4 mg, 72.4%). HPLC (*A*): 12.04 (0.2), 17.70 (99.8). M.p. 115–117°. $[\alpha]_D = -72.4$, $[\alpha]_{578} = -75.6$, $[\alpha]_{546} = -85.8$, $[\alpha]_{436} = -145.1$, $[\alpha]_{365} = -228.3$ (*c* = 2.14). IR: 2970, 2920, 1710, 1570, 1310, 1200, 500. ^{1}H-NMR: 0.98 (*s*, 3 H); 1.17 (*s*, 3 H); 1.32–1.46 (2 H); 1.78–2.00 (5 H); 2.03–2.13 (4 H); 2.44 (*s*, 3 H); 2.56 (*s*, 3 H); 3.45 (*d*, *J* = 14, 1 H); 3.51 (*d*, *J* = 14, 1 H); 3.50–3.61 (2 H); 3.93 (*t*, *J* = 6.0, 1 H); 4.93 (*dd*, *J* = 7.5, 5, 1 H). ^{13}C-NMR: 171.02 (*s*); 167.67 (*s*); 65.30 (*d*); 64.19 (*d*); 53.07 (*t*); 48.56 (*s*); 47.83 (*s*); 44.51 (*d*); 38.43 (*t*); 32.79 (*t*); 32.08 (*t*); 29.10 (*t*); 26.47 (*t*); 20.74 (*q*); 19.89 (*q*); 15.33 (*q*); 15.09 (*q*); 13.06 (*t*). MS: 452 (0.06 $C_{18}H_{29}ClN_2O_3S_3^+$), 402 (0.5), 369 (0.3), 263 (0.5), 210 (0.5), 187 (40), 160 (30), 91 (100). Anal. calc. for $C_{18}H_{29}ClN_2O_3S_3$: C 47.72, H 6.45, N 6.18; found: C 47.81, H 6.54, N 6.25.

The minor (α*R*)-epimer of **3m** was also isolated (4 mg). HPLC (*A*): 12.04. IR: 2970, 2920, 1700, 1570, 1310, 1200, 500. ^{1}H-NMR: 0.96 (*s*, 3 H); 1.14 (*s*, 3 H); 1.30–1.44 (2 H); 1.83–2.16 (9 H); 2.35 (*s*, 3 H); 2.57 (*s*, 3 H); 3.42 (*d*, *J* = 14, 1 H); 3.45 (*d*, *J* = 14, 1 H); 3.52–3.60 (2 H); 3.92 (*dd*, *J* = 8, 5, 1 H); 4.84 (*m*, 1 H).

(2R)-N-{(2S)-2-{[Bis(methylthio)methylidene]amino}-6-iodohexan-1-oyl}bornane-10,2-sultam (**3n**). Using the *General Procedure C*, alkylation of **2** (2.0 g, 5.31 mmol) with 1,4-iodobutane (THF/DMPU), workup, FC (hexane/Et_2O 1:1), and crystallization (hexane/Et_2O) gave **3n** (2.313 g, 78%). HPLC (*A*): 10.47 (0.8), 17.06 (99.2). M.p. 90–91°. $[\alpha]_D = -59.8$, $[\alpha]_{578} = -62.8$, $[\alpha]_{546} = -71.3$, $[\alpha]_{436} = -120.7$, $[\alpha]_{365} = -191.0$ (*c* = 1.34). IR: 2970, 2920, 1710, 1570, 1330, 1110, 500. ^{1}H-NMR: 0.98 (*s*, 3 H); 1.18 (*s*, 3 H); 1.31–1.59 (4 H); 1.78–2.05 (7 H); 2.06–2.11 (2 H); 2.44 (*s*, 3 H); 2.56 (*s*, 3 H); 3.18 (*t*, *J* = 7, 2 H); 3.45 (*d*, *J* = 14, 1 H); 3.51 (*d*, *J* = 14, 1 H); 3.93 (*t*, *J* = 6, 1 H);

4.91 (*dd*, *J* = 7.5, 5, 1 H). ^{13}C-NMR: 171.45 (*s*); 162.31 (*s*); 65.32 (*d*); 64.61 (*d*); 53.11 (*t*); 48.49 (*s*); 47.81 (*s*); 44.54 (*d*); 38.45 (*t*); 33.52 (*t*); 32.96 (*t*); 32.80 (*t*); 26.71 (*t*); 26.45 (*t*); 20.83 (*q*); 19.89 (*q*); 15.27 (*q*); 14.91 (*q*); 6.74 (*t*). MS: 511 (36, $[C_{19}H_{31}IN_2O_3S_3 - MeS]^+$), 383 (30), 316 (20), 201 (60), 174 (40), 142 (95), 127 (32), 108 (32), 82 (100), 67 (35), 55 (44). Anal. calc. for $C_{19}H_{31}IN_2O_3S_3$: C 40.86, H 5.59, N 5.18; found: C 41.08, H 5.59, N 5.18.

The minor (α*R*)-epimer of **3n** was also isolated (7 mg). HPLC (*A*): 10.47. IR: 2970, 2920, 1710, 1570, 1310, 1100. ^{1}H-NMR: 0.96 (*s*, 3 H); 1.14 (*s*, 3 H); 1.21–1.50 (4 H); 1.65–2.15 (9 H); 2.35 (*s*, 3 H); 2.56 (*s*, 3 H); 3.18 (*t*, *J* = 8, 2 H); 3.42 (*d*, *J* = 14, 1 H); 3.42 (*d*, *J* = 14, 1 H); 3.47 (*d*, *J* = 14, 1 H); 3.92 (*dd*, *J* = 7.5, 5, 1 H); 4.81 (*t*, *J* = 7.0, 1 H).

*(2*R*)-*N*-{(2*S*)-2-{[Bis(methylthio)methylidene]amino}-7-iodoheptan-1-oyl}bornane-10,2-sultam* (**3o**). Using the *General Procedure C*, alkylation of **2** (500 mg, 1.33 mmol) with 1,5-diiodopentane (THF/DMPU), workup, FC (hexane/Et_2O 1:1), and crystallization (hexane/Et_2O) gave **3o** (549.7 mg, 78.3%). HPLC (*A*): 10.65 (< 0.1), 18.64 (> 99.9). M.p. 73–75°. $[\alpha]_D = -54.1$, $[\alpha]_{578} = -56.5$, $[\alpha]_{546} = -64.2$, $[\alpha]_{436} = -107.7$, $[\alpha]_{365} = -170.04$ (*c* = 1.62). IR: 2970, 2920, 1710, 1570, 1330, 1110, 500. ^{1}H-NMR: 0.98 (*s*, 3 H); 117 (*s*, 3 H); 1.31–1.48 (6 H); 1.78–2.12 (9 H); 2.43 (*s*, 3 H); 2.56 (*s*, 3 H); 3.17 (*t*, *J* = 7, 2 H); 3.45 (*d*, *J* = 14, 1 H); 3.51 (*d*, *J* = 14, 1 H); 3.93 (*t*, *J* = 6, 1 H); 4.91 (*dd*, *J* = 7.5, 5, 1 H). ^{13}C-NMR: 171.60 (*s*); 161.99 (*s*); 65.28 (*d*); 64.86 (*d*); 53.10 (*t*); 48.47 (*s*); 47.78 (*s*); 44.53 (*d*); 38.44 (*t*); 34.39 (*t*); 33.28 (*t*); 32.78 (*t*); 29.99 (*t*); 26.44 (*t*); 24.61 (*t*); 20.74 (*q*); 19.89 (*q*); 15.26 (*q*); 14.86 (*q*); 6.91 (*d*). MS: 571 (0.5, $[C_{20}H_{33}IN_2O_3S_3 - I]^+$), 557 (1), 525 (100), 452 (12), 330 (30), 135 (25), 93 (12). Anal. calc. for $C_{20}H_{33}IN_2O_3S_3$: C 41.95, H 5.81, N 4.89; found: C 42.14, H 5.85, N 5.06.

The minor (α*R*)-epimer of **3o** was also isolated (3.5 mg). HPLC (*A*): 10.65. IR: 2970, 2920, 1710, 1570, 1310, 1100. ^{1}H-NMR: 0.95 (*s*, 3 H); 1.13 (*s*, 3 H); 1.30–1.48 (6 H); 1.80–2.12 (9 H); 2.34 (*s*, 3 H); 2.57 (*s*, 3 H); 3.10–3.22 (2 H); 3.42 (*d*, *J* = 14, 1, H); 3.47 (*d*, *J* = 14, 1 H); 3.91 (*dd*, *J* = 7.5, 5, 1 H); 4.80 (*dd*, *J* = 7, 6, 1 H).

*(2*R*)-*N*-{(2*S*)-2-{[Bis(methylthio)methylidene]amino}-8-iodooctan-1-oyl}bornane-10,2-sultam* (**3p**). Using the *General Procedure C*, alkylation of **2** (500 mg, 1.33 mmol) with 1,6-diiodohexane (THF/DMPU), workup, FC (hexane/Et_2O 1:1), and crystallization (hexane/Et_2O) gave **3p** (599.4 mg, 77%). HPLC (*A*): 7.99 (0.2), 13.97 (99.8). M.p. 79–80°. $[\alpha]_D = -56.8$, $[\alpha]_{578} = -60.3$, $[\alpha]_{546} = -68.1$, $[\alpha]_{436} = -114.6$, $[\alpha]_{365} = -181.5$ (*c* = 2.03). IR: 2970, 2920, 1710, 1570, 1330, 1110, 500. ^{1}H-NMR (200 MHz): 0.96 (*s*, 3 H); 1.16 (*s*, 3 H); 1.20–1.50 (8 H); 1.70–2.20 (9 H); 2.41 (*s*, 3 H); 2.54 (*s*, 3 H); 3.15 (*t*, *J* = 7.0, 2 H); 3.42 (*d*, *J* = 14, 1 H); 3.50 (*d*, *J* = 13.5, 1 H); 3.90 (*t*, *J* = 6.3, 1 H); 4.85 (*dd*, *J* = 7.5, 5, 1 H). ^{13}C-NMR: 171.68 (*s*); 161.75 (*s*); 65.24 (*d*); 64.91 (*d*); 53.01 (*t*); 48.40 (*s*); 47.74 (*s*); 44.49 (*d*); 38.39 (*t*); 34.48 (*t*); 33.35 (*t*); 32.76 (*t*); 30.25 (*t*); 27.99 (*t*); 26.41 (*t*); 25.44 (*t*); 20.70 (*q*); 19.85 (*q*); 15.21 (*q*); 14.84 (*q*); 7.18 (*d*). MS: 571 (3, $[C_{21}H_{35}IN_2O_3S_3 - Me]^+$), 539 (98), 466 (15), 411 (13), 344 (48), 268 (12), 216 (15), 135 (100), 93 (58). Anal. calc. for $C_{21}H_{35}IN_2O_3S_3$: C 43.00, H 6.01, N 4.78; found: C 43.24, H 6.00, N 4.86.

The minor (α*R*)-epimer of **3p** was also isolated (3.5 mg). IR: 2970, 2920, 1710, 1570, 1310, 1100, 500. ^{1}H-NMR: 0.95 (*s*, 3 H); 1.13 (*s*, 3 H); 1.22–1.48 (8 H); 1.78–2.12 (9 H); 2.34 (*s*, 3 H); 2.56 (*s*, 3 H); 3.13–3.20 (2 H); 3.42 (*d*, *J* = 13, 1 H); 3.46 (*d*, *J* = 13, 1 H); 3.92 (*dd*, *J* = 7.5, 5, 1 H); 4.81 (*dd*, *J* = 7, 6, 1 H).

4. *α-Amino Acids* **5**. *General Procedure D*. A 1N aq. HCl soln. (10 mol-equiv.) was added to 0.05–0.1M **3** in THF, and the mixture was stirred at r.t. for 24 h. Evaporation of the THF, washing of the residual soln. with Et_2O, and evaporation of the aq. phase gave (aminoacyl)sultam hydrochloride **4** as a solid residue. $LiOH \cdot H_2O$ (4 mol-equiv.) was added to 0.03M crude **4** in THF/H_2O 2:1, and the mixture was stirred at r.t. for 24 h. Evaporation of the THF, partition of the residue between CH_2Cl_2/H_2O, drying ($MgSO_4$), and evaporation of the org. phase furnished sultam **1**. Acidification of the aq. phase to pH 4–5, addition of *Amberlite-IR-120* ion-exchange resin (5 g/mmol), stirring of the mixture at r.t. for 15 h, filtration, washing of the resin with dist. H_2O (until the eluate remained clear upon addition of $AgNO_3$), stirring of the resin with 6N aq. NH_3 (50 ml/mmol) at r.t. for 4 h, filtration, evaporation of the filtrate, trituration of the residue with THF/toluene, evaporation, and drying of the residue *in vacuo* afforded amino acid **5**. To determine its enantiomeric excess, **5** (5 mg) was heated with a soln. of HCl in PrOH (prepared from acetyl chloride (0.3 ml) and PrOH (1 ml)) at 100° for 1 h. After evaporation, the residue was dried *in vacuo* and dissolved in CH_2Cl_2 (1 ml). $(CF_3CO)_2O$ (0.2 ml) was added at 0°, and the mixture was heated at reflux for 15 min and evaporated. The residual *N*-(trifluoroacetyl) propyl ester was compared by chiral GC with a racemic sample.

N-[(S)-2'-Amino-3-phenylpropanoyl]bornane-2,10-sultam Hydrochloride (**4d**). A 1N aq. HCl soln. (10 ml) was added to a soln. of **3d** (425 mg, 0.91 mmol) in THF (14 ml), and the mixture was stirred at r.t. for 24 h. Evaporation of the THF, washing of the residual soln. with Et_2O and evaporation of the aq. phase gave **4d**. Solid residue (366 mg, *ca.* 100%). $[\alpha]_D = -61.8$, $[\alpha]_{578} = -64.2$, $[\alpha]_{546} = -72.2$, $[\alpha]_{436} = -115.2$, $[\alpha]_{365} = -162.7$ (*c* = 1.08, MeOH, 25°). ^{1}H-NMR ((D_6)DMSO, 360 MHz): 0.87 (*s*, 3 H); 0.90 (*s*, 3 H); 1.20–1.50 (2 H); 1.60–2.10 (5 H); 3.00–4.00 (5 H); 4.40 (*m*, 1 H); 7.20–7.40 (5 H).

(S)-Allylglycine (= *(2S)-2-Aminopent-4-enoic Acid*; **5a**). According to the *General Procedure D*, **3a** (120 mg, 0.25 mmol) furnished **1** (78 mg, *ca.* 100%) and **5a** (43 mg, *ca.* 100%). ^{1}H-NMR (D_2O, 360 MHz): 2.18–2.34 (2 H);

3.26 (*t*, *J* = 6.5, 1 H); 4.93–5.03 (2 H); 5.60 (*m*, 1 H). Chiral GC of the *N*-(trifluoroacetyl) propyl ester of **5a**: 5.03 (100); racemic sample: 4.59, 50.2 (1:1).

(Z,2S)-2-Amino-6-hydroxyhex-4-enoic Acid (**5c**). According to the *General Procedure D*, **3c** (1.8 g, 3.2 mmol) furnished **1** (670 mg, 97.4%) and **5c** (430 mg, 93%). M.p. 215–216°. $[\alpha]_D = -10.5$, $[\alpha]_{578} = -11.0$, $[\alpha]_{546} = -12.4$, $[\alpha]_{436} = -23.3$, $[\alpha]_{365} = -31.6$ (*c* = 1.0, H_2O). ^{1}H-NMR (D_2O): 2.46–2.58 (2 H); 3.63 (*t*, *J* = 6, 1 H); 4.00 (*d*, *J* = 6.5, 2 H); 5.38 (*m*, 1 H); 5.68 (*m*, 1 H). MS: 146 (0.4, $C_6H_{11}NO_3^+$), 133 (0.1), 127 (3.2), 114 (0.8), 110 (1), 100 (7), 91 (0.9), 82 (66), 79 (6), 74 (93), 67 (9), 60 (3), 57 (21), 54 (100).

(S)-β-Phenylalanine (**5d**). According to the *General Procedure D*, **3d** (120 mg, 0.25 mmol) furnished **1** (55 mg, *ca.* 100%) and **5d** (41 mg, *ca.* 100%). ^{1}H-NMR (D_2O, 360 MHz): 2.81 (*dd*, *J* = 14, 8, 1 H); 2.97 (*dd*, *J* = 14, 6, 1 H); 3.58 (*m*, 1 H); 7.10–7.34 (5 H). Chiral GC (100°) of the *N*-(trifluoroacetyl) propyl ester of **5d**: 17.37 (100); racemic sample: 16.52, 17.47 (1:1).

(S)-Aspartic Acid (**5g**). According to the *General Procedure D*, **3g** (290 mg, 0.61 mmol) furnished **1** (110 mg, 84%) and **5g** (61 mg, 75%). ^{1}H-NMR (D_2O, 360 MHz): 2.31 (*dd*, *J* = 17, 9.5, 1 H); 2.54 (*dd*, *J* = 17, 4, 1 H); 3.55 (*dd*, *J* = 9.5, 4, 1 H). Chiral GC of the *N*-(trifluoroacetyl) propyl diester of **5g**: 12.66 (100); racemic sample: 12.47, 12.70 (1:1).

(S)-Alanine (**5h**). According to the *General Procedure D*, **3h** (207 mg, 0.53 mmol) furnished **1** (112 mg, 98%) and **5h** (49 mg, *ca.* 100%). ^{1}H-NMR (D_2O, 360 MHz): 1.22 (*d*, *J* = 7, 3 H); 3.50 (*q*, *J* = 7, 1 H). Chiral GC of the *N*-(trifluoroacetyl) propyl ester of **5h**: 3.20 (100); racemic sample: 2.87, 3.22 (1:1).

(S)-Norleucine (= *(2S)-2-Aminohexanoic Acid*; **5i**). According to the *General Procedure D*, **3i** (228 mg, 0.52 mmol) furnished **1** (113 mg, *ca.* 100%) and **5i** (70 mg, *ca.* 100%). ^{1}H-NMR (D_2O, 360 MHz): 0.71 (*t*, *J* = 7, 3 H); 1.08–1.18 (4 H); 1.45–1.55 (2 H); 3.24 (*m*, 1 H). Chiral GC of the *N*-(trifluoroacetyl) propyl ester **5i**: 7.19 (100); racemic sample: 6.58, 7.17 (1:1).

(S)-Leucine (**5j**). According to the *General Procedure D*, **3j** (299 mg, 0.69 mmol) furnished **1** (141 mg, 95%) and **5j** (92 mg, *ca.* 100%). ^{1}H-NMR (D_2O, 360 MHz): 0.74 (*d*, *J* = 6.5, 3 H); 0.76 (*d*, *J* = 6.5, 3 H); 1.30–1.56 (3 H); 3.30 (br. *t*, *J* = 7, 1 H). Chiral GC of the *N*-(trifluoroacetyl) propyl ester **5j**: 6.06 (0.24), 6.81 (97.38); racemic sample: 6.11, 6.78 (1:1).

(S)-Valine (**5k**). According to the *General Procedure D*, **3k** (330 mg, 0.79 mmol) furnished **1** (140 mg, 83%) and **5k** (77.3 mg, 84%). ^{1}H-NMR (D_2O, 360 MHz): 0.68–0.80 (6 H); 1.85 (*m*, 1 H); 3.05 (*m*, 1 H). Chiral GC of the *N*-(trifluoroacetyl) propyl ester of **5k**: 4.14 (100); racemic sample: 3.79, 4.06 (1:1).

5. *α-Amino-ω-azido Acids. General Procedure E.* A mixture of *ω*-halogenated alkylation product **3**, NaN_3 (3 mol-equiv.), and DMEU (5 ml/mmol of **3**) was stirred at r.t. for 48 to 72 h. Aq. workup (Et_2O), evaporation of the org. phase, and deprotection/saponification of the resulting crude *ω*-azido derivative **7**, using the *General Procedure D*, gave **1** (95–96%) and α-amino-*ω*-azido acid **12**. The latter was converted into its [-{[(*R*)-*N*-(3,5-dinitrobenzoyl)prolyl]amino} acid methyl ester **17** which was compared (HPLC (*B*)) with the derivative prepared from racemic **12** (*Table 4*).

2-Amino-5-azidopentanoic Acid (**12m**). According to the *General Procedure E*, **3m** (100 mg, 0.221 mmol) gave **12m** (solid; 27.2 mg, 77.9%). M.p. 230–232°. $[\alpha]_D = +15.0$, $[\alpha]_{578} = +16.0$, $[\alpha]_{546} = +18.8$, $[\alpha]_{436} = +32.6$, $[\alpha]_{365} = +52.1$ (*c* = 0.72, 1N aq. HCl). IR (KBr): 3200–2500, 2100, 1580, 1510, 1380. ^{1}H-NMR (D_2O): 1.42–1.60 (2 H); 1.69–1.80 (2 H); 3.23 (*t*, *J* = 7.0, 2 H); 3.59 (br. *t*, *J* = 6.0, 1 H). MS: 159 (1.4, $[C_5H_{10}N_4O_2 + 1]^+$), 113 (18), 103 (0.9), 96 (1), 85 (27), 74 (45), 68 (52), 56 (100).

2-Amino-6-azidohexanoic Acid (**12n**). According to the *General Procedure E*, **3n** (200 mg, 0.358 mmol) gave **12n** (solid; 56.0 mg, 91%). M.p. 252–255°. $[\alpha]_D = +17.3$, $[\alpha]_{578} = +19.2$, $[\alpha]_{546} = +21.9$, $[\alpha]_{436} = +37.9$, $[\alpha]_{365} = +48.6$ (*c* = 1.07, 1N aq. HCl). IR (KBr): 3200–2500, 2100, 1580, 1510, 1340. ^{1}H-NMR (D_2O): 1.19–1.37 (2 H); 1.47 (*dt*, *J* = 7, 14, 2 H); 1.63–1.79 (2 H); 3.18 (*t*, *J* = 7.0, 2 H); 3.56 (*dd*, *J* = 6.5, 5.5, 1 H). MS: 173 (16, $[C_6H_{12}N_4O_2 + 1]^+$), 127 (5.3), 110 (1.4), 99 (50), 82 (30), 70 (76), 56 (100).

2-Amino-7-azidoheptanoic Acid (**12o**). According to the *General Procedure E*, **3o** (200 mg, 0.35 mmol) gave **12o** (solid; 65 mg, 99.8%). M.p. 250° (dec.). $[\alpha]_D = +11.5$, $[\alpha]_{578} = +14.0$, $[\alpha]_{546} = +17.2$, $[\alpha]_{436} = +31.0$ (*c* = 1.0, 1N aq. HCl). IR (KBr): 3200–2600, 2100, 1650, 1500, 1380. ^{1}H-NMR (D_2O): 1.16–1.29 (4 H); 1.40–1.48 (2 H); 1.61–1.75 (2 H); 3.15 (*t*, *J* = 7.0, 2 H); 3.54 (*dd*, *J* = 6.5, 5.5, 1 H). MS: 187 (1.5, $[C_7H_{14}N_4O_2 + 1]^+$), 159 (0.4), 141 (19), 113 (6.6), 96 (17), 84 (21), 74 (43), 56 (100).

2-Amino-8-azidooctanoic Acid (**12p**). According to the *General Procedure E*, **3p** (200 mg, 0.341 mmol) gave **12p** (solid; 68.0 mg, 99.6%). M.p. 240–242°. $[\alpha]_D = +11.1$, $[\alpha]_{578} = +12.7$, $[\alpha]_{546} = +16.0$, $[\alpha]_{436} = +29.8$, $[\alpha]_{365} = +42.4$ (*c* = 0.99, 1N aq. HCl). IR (KBr): 3200–2500, 2100, 1580, 1500, 1380. ^{1}H-NMR (D_2O): 1.15–1.27 (6 H); 1.38–1.47 (2 H); 1.62–1.73 (2 H); 3.14 (*t*, *J* = 7.0, 2 H); 3.56 (*dd*, *J* = 6.5, 5.5, 1 H). MS: 201 (1.5, $[C_8H_{16}N_4O_2 + 1]^+$), 155 (26), 127 (0.9), 110 (3.5), 98 (5.9), 82 (14), 74 (39), 56 (100).

6. *N^{δ}-Hydroxyornithine and N^{ε}-Hydroxylysine Derivatives. (2R)-N-{(2S)-5-[N-(Benzyloxy)-N-tosylamino]-2-{[bis(methylthio)methylidene]amino}pentanoyl}bornane-10,2-sultam* (**8m**). A 1M $KN(SiMe_3)_2$ soln. in THF (1.0 ml) was added to a soln. of *O*-benzyl-*N*-tosyl-hydroxylamine (277 mg, 1.0 mmol) in DMEU (2 ml). Then a soln. of **3m** (300 mg, 0.663 mmol) in DMEU (1 ml) was added, and the mixture was stirred at 65° for 5 h. Aq. workup (Et_2O) and FC (hexane/Et_2O 1:1) afforded **8m** (solid; 383 mg, 83%). M.p. 68–70°. $[\alpha]_D = -38.5$, $[\alpha]_{578} = -39.8$, $[\alpha]_{546} = -45.1$, $[\alpha]_{436} = -74.8$, $[\alpha]_{365} = -115.4$ ($c = 0.628$). IR: 3020, 2970, 2920, 1710, 1600, 1570, 1340, 1170. ^{1}H-NMR: 0.96 (*s*, 3 H); 1.13 (*s*, 3 H); 1.25–1.45 (3 H); 1.60–2.20 (10 H); 2.38 (*s*, 3 H); 2.40 (*s*, 3 H); 2.53 (*s*, 3 H); 3.43 (*d*, $J = 14$, 1 H); 3.49 (*d*, $J = 14$, 1 H); 3.91 (*t*, $J = 7.0$, 1 H); 4.91 (*dd*, $J = 8.0$, 5.0, 1 H); 5.10 (br. *s*, 2 H); 7.26–7.43 (7 H); 7.70–7.74 (2 H). ^{13}C-NMR: 171.17 (*s*); 162.66 (*s*); 144.56 (*s*); 135.21 (*s*); 130.08 (*s*); 129.60 (*d*, 3 C); 129.41 (*d*, 2 C); 128.58 (*d*, 2 C); 128.47 (*d*, 3 C); 79.99 (*t*); 65.27 (*d*); 64.66 (*d*); 53.23 (*t*); 53.09 (*t*); 48.51 (*s*); 47.78 (*s*); 44.48 (*d*); 38.42 (*t*); 32.77 (*t*); 32.28 (*t*); 26.44 (*t*); 23.47 (*t*); 21.58 (*q*); 20.77 (*q*); 19.85 (*q*); 15.24 (*q*); 14.83 (*q*). MS: 646 (5, $[C_{32}H_{43}N_3O_6S_4 - MeS]^+$), 538 (5), 325 (40), 224 (15), 155 (45), 91 (100).

(2R)-N-{(2S)-6-[N-Benzyloxy)-N-tosylamino]-2-{[bis(methylthio)methylidene]amino}hexanoyl}bornane-10,2-sultam (**8n**). As described for **8m**, **3n** (300 mg, 0.538 mmol) was converted (in 1 h) to **8n** (amorphous solid; 355 mg, 93%). $[\alpha]_D = -50.9$, $[\alpha]_{578} = -53.4$, $[\alpha]_{546} = -60.1$, $[\alpha]_{436} = -100.2$, $[\alpha]_{365} = -156.3$ ($c = 0.93$). IR: 3020, 2970, 2920, 1700, 1600, 1570, 1340, 1160, 900. ^{1}H-NMR: 0.97 (*s*, 3 H); 1.16 (*s*, 3 H); 1.30–1.65 (6 H); 1.82–2.09 (9 H); 2.40 (*s*, 6 H); 2.52 (*s*, 3 H); 3.45 (*d*, $J = 14$, 1 H); 3.48 (*d*, $J = 14$, 1 H); 3.92 (*t*, $J = 6.0$, 1 H); 4.89 (*dd*, $J = 8.0$, 5.0, 1 H); 5.07 (br. *s*, 2 H); 7.27–7.43 (7 H); 7.73 (*d*, $J = 8.0$, 2 H). ^{13}C-NMR: 171.48 (*s*); 162.28 (*s*); 144.53 (*s*); 135.21 (*s*); 130.09 (*s*); 129.66 (*d*, 2 C); 129.55 (*d*, 2 C); 129.39 (*d*, 2 C); 128.59 (*d*, 2 C); 128.44 (*d*); 79.97 (*t*); 67.92 (*t*); 65.24 (*d*); 64.60 (*d*); 53.21 (*t*); 48.45 (*s*); 47.74 (*s*); 44.48 (*d*); 38.41 (*t*); 34.40 (*t*); 32.75 (*t*); 26.46 (*t*); 25.56 (*t*); 23.10 (*t*); 21.57 (*q*); 20.71 (*q*); 19.85 (*q*); 15.18 (*q*); 14.80 (*q*). MS: 708 (0.1, $[C_{33}H_{45}N_3O_6S_4 + 1]^+$), 692 (0.1), 660 (25), 552 (10), 465 (10), 414 (10), 341 (8), 135 (20), 91 (100).

(S)-N^{δ}-(Benzyloxy)-N^{δ}-tosylornithine (**13m**). A soln. of **8m** (300 mg, 0.433 mmol) in 1N aq. HCl/THF 1:1 (14 ml) was stirred at r.t. for 16 h. Evaporation, dissolving the residue in THF/H_2O 2.1 (10 ml), addition of LiOH · H_2O (110 mg, 2.6 mmol), stirring at r.t. for 12 h, evaporation of the THF, addition of H_2O (8 ml), and extraction of the soln. (pH 11.0) with AcOEt yielded **1** (93%). Neutralization of the aq. phase (pH 7) with 1N aq. HCl, concentration *in vacuo*, completing the precipitation of the amino acid by keeping the mixture at 5° for 16 h, filtration, washing of the precipitate with cold H_2O and EtOH and drying *in vacuo* furnished **13m** (149 mg, 93%). M.p. 221–224° ([23]: 222.5–224.8°). $[\alpha]_D = +19.8$, $[\alpha]_{578} = +20.6$, $[\alpha]_{546} = +23.4$, $[\alpha]_{436} = +41.3$, $[\alpha]_{365} = +68.3$ ($c = 3.0$, AcOH; [23]: $[\alpha]_D = +20.7$ ($c = 3.0$, AcOH)). IR (KBr): 3300–2500, 1680, 1560, 1550–1470, 1450, 1350, 1170. ^{1}H-NMR ($CF_3COOH/CDCl_3$): 1.63–1.72 (2 H); 2.00 (br. *s*, 2 H); 2.40 (*s*, 3 H); 2.90 (br. *s*, 2 H); 4.30 (*m*, 1 H); 4.98 (*s*, 2 H); 7.25–7.70 (9 H); 7.78 (br. *s*); 8.20 (br. *s*). MS: 349 (0.1, $[C_{19}H_{23}N_2O_5S - 22]^+$), 237 (5.4), 224 (0.3), 204 (3.3), 193 (2.6), 176 (0.6), 162 (13), 114 (13), 106 (7), 91 (100), 77 (8).

(S)-N^{ε}-(Benzyloxy)-N^{ε}-tosyllysine (**13n**). As described for **13m**, **8n** (300 mg, 0.424 mmol) was converted to **13n** (162 mg, 94%). M.p. 200–205° ([36]: 204–207°). $[\alpha]_D = +18.6$, $[\alpha]_{578} = +19.5$, $[\alpha]_{546} = +22.1$, $[\alpha]_{436} = +38.1$, $[\alpha]_{365} = +63.9$ ($c = 1.02$, AcOH; [36]: $[\alpha]_D = +18.4$ ($c = 1.0$, AcOH)). IR (KBr): 3300–2500, 1700–1540, 1540–1480, 1350, 1160. ^{1}H-NMR ($CF_3COOH/CDCl_3$): 1.40–1.56 (6 H); 1.90 (br. *s*, 2 H); 2.35 (*s*, 3 H); 2.84 (br. *s*, 2 H); 4.09 (br. *s*, 1 H); 4.99 (*s*, 2 H); 7.22–7.69 (9 H); 7.82 (br.); 8.90 (br.). MS: 407 (0.1, $[C_{20}H_{26}N_2O_5S + 1]^+$), 361 (0.1), 251 (4.3), 218 (2.0), 207 (1.2), 176 (10), 155 (3.3), 128 (9.1), 106 (7), 91 (100).

(2R)-N-{(2S)-6-[N-Acetylamino-N-(benzyloxy)]-2-{[bis(methylthio)methylidene]amino}hexanoyl}bornane-10,2-sultam (**9n**). A mixture of **3n** (300 mg, 0.538 mmol), *N*-acetyl-*O*-benzyl-hydroxylamine (133 mg, 0.81 mmol) anh. K_2CO_3 (297 mg, 2.15 mmol), and acetone (20 ml) was heated at reflux for 24 h. Filtration, evaporation of the acetone, and separation of the *O*-alkylation by-products (17%) by FC (hexane/Et_2O 1:9) afforded **9n** (oil; 216.7 mg, 68%). $[\alpha_D] = -47.0$, $[\alpha]_{578} = -48.9$, $[\alpha]_{546} = -55.6$, $[\alpha]_{436} = -93.1$, $[\alpha]_{365} = -144.5$ ($c = 2.77$). IR: 3020, 2970, 1710, 1650, 1570, 1330, 1110. ^{1}H-NMR: 0.96 (*s*, 3 H); 1.15 (*s*, 3 H); 1.30–1.47 (4 H); 1.50–2.06 (9 H); 2.07 (*s*, 3 H); 2.53 (*s*, 3 H); 2.54 (*s*, 3 H); 3.43 (*d*, $J = 14$, 1 H); 3.49 (*d*, $J = 14$, 1 H); 3.62 (br. *s*, 2 H); 3.92 (*t*, 7.8, 1 H); 4.81 (*s*, 2 H); 4.92 (*dd*, $J = 8.0$, 5.0, 1 H); 7.34 (*s*, 5 H). ^{13}C-NMR: 171.51 (*s*, 2 C); 162.06 (*s*); 134.55 (*s*); 129.11 (*d*, 2 C); 128.81 (*d*); 128.62 (*d*, 2 C); 76.23 (*t*); 65.23 (*d*); 64.70 (*d*); 53.04 (*t*); 48.43 (*s*); 47.72 (*s*); 45.33 (*t*); 44.62 (*d*); 38.37 (*t*); 34.23 (*t*); 32.73 (*t*); 32.31 (*t*); 26.40 (*t*); 23.16 (*t*); 23.03 (*t*); 20.67 (*q*); 20.50 (*q*); 19.82 (*q*); 15.19 (*q*); 14.80 (*q*). MS: 595 (0.1, $C_{28}H_{41}N_3O_5S_3^+$), 548 (0.6), 488 (0.4), 442 (0.4), 393 (0.3), 353 (0.4), 305 (0.9), 271 (0.3), 259 (0.4), 91 (100).

(S)-N^{ε}-Acetyl-N^{ε}-(benzyloxy)lysine (**14n**). A soln. of **9n** (200 mg, 0.336 mmol) in 0.1N aq. HCl/THF (6.7 ml) was stirred at r.t. for 1 week. Evaporation, stirring the residue with LiOH · H_2O (28.2 mg, 0.672 mmol) at r.t. for 1 h, evaporation of the THF, addition of H_2O (8 ml), extraction of **1** with AcOEt, neutralization of the aq. phase, concentration to 5 ml, keeping the mixture at 5° for 24 h, filtration, washing (H_2O then EtOH), and drying of the precipitate gave **14n** (71.4 mg, 72%). M.p. 207–209°. $[\alpha]_D = +16.1$, $[\alpha]_{578} = +16.7$, $[\alpha]_{546} = +19.0$, $[\alpha]_{436} = +32.8$,

$[\alpha]_{365}$ = +54.9 (*c* = 1.02, AcOH). IR (KBr): 3200–2500, 1640, 1610, 1570, 1510, 1460, 1430, 1350. ^{1}H-NMR (D_2O): 1.12–1.28 (2 H); 1.48–158 (2 H); 1.61–1.77 (2 H); 1.92 (*s*, 3 H); 3.53 (*t*, *J* = 6.0, 1 H); 3.58 (*m*, 2 H); 4.80 (*s*, 2 H); 7.30 (*s*, 5 H). MS: 293 (0.2, $[C_{15}H_{22}N_2O_4 - 1]^+$), 269 (0.3), 245 (0.2), 219 (1.2), 210 (0.6), 185 (0.5), 108 (100).

(S)-N$^\varepsilon$-(Benzyloxy)lysine. Following the deprotection/saponification protocol described for **13m**, **9n** (59.5 mg, 0.1 mmol) was converted to (*S*)-*N*$^\varepsilon$-(benzyloxy)lysine (22.4 mg, 89%). M.p. 235–240° ([36]: 238–241°). $[\alpha]_D$ = +18.0, $[\alpha]_{578}$ = +19.2, $[\alpha]_{546}$ = +22.5, $[\alpha]_{436}$ = +39.2, $[\alpha]_{365}$ = +62.5 (*c* = 1.00, 1N aq. HCl; [36]: $[\alpha]_D$ = +18.1 (*c* = 1.0, 1N aq. HCl)). IR (KBr): 3200–2500, 1580, 1510. ^{1}H-NMR (D_2O): 1.13–1.30 (2 H); 1.33–1.42 (2 H); 1.60–1.75 (2 H); 2.75 (*t*, *J* = 7.5, 2 H); 3.7 (*t*, *J* = 6.0, 1 H); 4.70 (2 H, H_2O); 7.27 (*s*, 5 H). MS: 218 (0.4, $[C_{13}H_{20}N_2O_3 - 56]^+$), 190 (1.1), 162 (0.6), 144 (0.8), 128 (12.6), 108 (3.5), 99 (3), 91 (100), 84 (8), 77 (13).

7. *(S)-N$^\varepsilon$-Phenyl-N$^\varepsilon$-tosyllysine* (**15n**). *(2R)-N-{(2S)-2-{[Bis(methylthio)methylidene]amino}-6-(N-phenyl-N-tosylamino)-hexanoyl}bornane-10,2-sultam* (**10n**). As described for **8m**, *N*-tosylanilide (1.5 mol-equiv.) was alkylated with **3n** (300 mg, 0.538 mmol) affording **10n** (356 mg, 98%). M.p. 55–58°. $[\alpha]_D$ = –44.9, $[\alpha]_{578}$ = –46.6, $[\alpha]_{546}$ = –53.1, $[\alpha]_{436}$ = –89.5, $[\alpha]_{365}$ = –141.3 (*c* = 1.12). TLC (toluene/Et_2O 9:1): R_f 0.60. IR: 3020, 2920, 1710, 1600, 1570, 1480, 1340, 1160. ^{1}H-NMR: 0.96 (*s*, 3 H); 1.13 (*s*, 3 H); 1.30–1.47 (6 H); 1.76–1.96 (5 H); 2.03–2.08 (2 H); 2.40 (*s*, 3 H); 2.42 (*s*, 3 H); 2.53 (*s*, 3 H); 3.42 (*d*, *J* = 14, 1 H); 3.47 (*d*, *J* = 14, 1 H); 3.50 (*t*, *J* = 7.0, 2 H); 3.90 (*t*, *J* = 6.0, 1 H); 4.85 (*dd*, *J* = 7.5, 5.0, 1 H); 6.99–7.03 (2 H); 7.21–7.31 (5 H); 7.45 (*d*, *J* = 8, 2 H). ^{13}C-NMR: 171.47 (*s*); 162.07 (*s*); 143.14 (*s*); 139.09 (*s*); 135.31 (*s*); 129.28 (*d*, 2 C); 128.89 (*d*, 2 C); 128.79 (*d*, 2 C); 127.70 (*d*, 3 C); 65.23 (*d*); 64.73 (*d*); 53.05 (*t*); 50.29 (*t*); 48.45 (*s*); 47.75 (*s*); 44.50 (*t*); 38.40 (*t*); 34.11 (*t*); 32.75 (*t*); 27.79 (*t*); 26.41 (*t*); 22.75 (*t*); 21.50 (*q*); 20.72 (*q*); 19.85 (*q*); 15.22 (*q*); 14.83 (*q*). MS: 630 (90, $[C_{32}H_{43}N_3O_5S_4 - MeS]^+$), 522 (10), 476 (15), 435 (20), 371 (80), 260 (30), 200 (25), 155 (45), 106 (100).

(S)-N$^\varepsilon$-Phenyl-N$^\varepsilon$-tosyllysine (**15n**). As described for **13m**, **10n** (300 mg, 0.443 mmol) was converted into **15n** (157.4 mg, 95%). M.p. 225–228°. $[\alpha]_D$ = +18.4, $[\alpha]_{578}$ = +19.1, $[\alpha]_{546}$ = +22.0, $[\alpha]_{436}$ = +38.5, $[\alpha]_{365}$ = +64.1 (*c* = 1.02, AcOH). IR (KBr): 3200–2500, 1680–1560, 1480, 1350, 1150. ^{1}H-NMR ($CF_3COOH/CDCl_3$): 1.30–1.42 (2 H); 1.50–1.70 (2 H); 1.90–2.10 (2 H); 2.40 (*s*, 3 H); 3.51 (br. *s*, 2 H); 4.18 (*m*, 1 H); 6.85–6.87 (2 H); 7.20–7.30 (5 H); 7.36–7.41 (2 H); 7.66 (br. *s*); 8.28 (br. *s*). MS: 377 (0.3, $[C_{19}H_{24}N_2O_4S + 1]^+$), 260 (1.8), 221 (13), 204 (1.6), 177 (2.3), 155 (29), 128 (100), 91 (62), 84 (83), 77 (24).

8. *N$^\omega$-(Benzyloxycarbonyl)-Protected 2,7-Diaminoheptanoic and 2,8-Diaminooctanoic Acids. (2R)-N-{(2S)-7-[(Benzyloxycarbonyl)amino]-2-{[bis(methylthio)methylidene]amino}heptanoyl}bornane-10,2-sultam* (**11o**). A mixture of **3o** (100 mg, 0.175 mmol), potassium cyanate (3.0 mol-equiv.), benzyl alcohol (3.0 mol-equiv.), and DMEU (1 ml) was stirred at 100° for 24 h. Aq. workup (Et_2O) and FC (hexane/Et_2O 1:2) afforded **11o** (oil; 76.4 mg, 74%). $[\alpha]_D$ = –51.7, $[\alpha]_{578}$ = –53.8, $[\alpha]_{546}$ = –61,5, $[\alpha]_{436}$ = –104.0, $[\alpha]_{365}$ = –164.7 (*c* = 1.15). TLC (hexane/Et_2O 3:7): R_f 0.30. IR: 3420, 3020, 2970, 2920, 1710, 1570, 1510, 1340, 1250, 1140, 500. ^{1}H-NMR: 0.96 (*s*, 3 H); 1.15 (*s*, 3 H); 1.28–1.52 (8 H); 1.80–2.11 (7 H); 2.42 (*s*, 3 H); 2.54 (*s*, 3 H); 3.16 (*m*, 2 H); 3.44 (*d*, *J* = 14, 1 H); 3.47 (*d*, *J* = 14, 1 H); 3.91 (*t*, *J* = 6.0, 1 H); 4.82 (*m*, 1 H); 4.92 (*dd*, *J* = 8.0, 5.0, 1 H); 5.08 (*s*, 2 H); 7.27–7.35 (5 H). ^{13}C-NMR: 171.66 (*s*); 161.85 (*s*); 156.34 (*s*); 136.70 (*s*); 128.48 (*d*); 128.02 (*d*, 2 C); 66.49 (*t*); 65.28 (*d*); 64.86 (*d*); 53.07 (*t*); 48.44 (*s*); 47.75 (*s*); 44.52 (*d*); 40.95 (*t*); 38.42 (*t*); 34.46 (*t*); 32.77 (*t*); 29.70 (*t*); 26.43 (*t*); 25.39 (*t*); 20.70 (*q*); 19.86 (*q*); 15.22 (*q*); 14.83 (*q*). MS: 597 (3.7, $[C_{28}H_{41}N_3O_5S_3 + 2]^+$), 549 (1.7), 504 (0.3), 488 (4.5), 440 (11), 367 (0.9), 357 (1), 305 (0.7), 135 (24), 107 (29), 91 (100).

(2R)-N-{(2S)-8-[(Benzyloxycarbonyl)amino]-2-{[bis(methylthio)methylidene]amino}octanoyl}bornane-10,2-sultam (**11p**). A mixture of **3p** (200 mg, 0.341 mmol), potassium cyanate (3.0 mol-equiv.), benzyl alcohol (3.0 mol-equiv.), and DMEU (1 ml) was stirred at 100° for 24 h. Aq. workup (Et_2O) and FC (hexane/Et_2O 1:1) afforded **11p** (amorphous solid; 147 mg, 71%). $[\alpha]_D$ = –46.0, $[\alpha]_{578}$ = –47.4, $[\alpha]_{546}$ = –54.2, $[\alpha]_{436}$ = –91.9, $[\alpha]_{365}$ = –145.1 (*c* = 1.24). TLC (hexane/Et_2O 3:7): R_f 0.35. IR: 3450, 3020, 2970, 2920, 1710, 1570, 1520, 1330, 1250, 1130, 500. ^{1}H-NMR: 0.95 (*s*, 3 H); 1.16 (*s*, 3 H); 1.25–1.52 (9 H); 1.63 (br. *s*, 1 H); 1.80–2.12 (7 H); 2.42 (*s*, 3 H); 2.55 (*s*, 3 H); 3.11–3.20 (2 H); 3.4 (*d*, *J* = 14, 1 H); 3.47 (*d*, *J* = 14, 1 H); 3.92 (*t*, *J* = 6.0, 1 H); 4.79 (br. *m*, 1 H); 4.92 (*dd*, *J* = 7.5, 5.0, 1 H); 5.09 (*s*, 2 H); 7.30–7.37 (5 H). ^{13}C-NMR: 171.79 (*s*); 161.80 (*s*); 156.36 (*s*); 136.73 (*s*); 128.53 (*d*); 128.15 (*d*, 3 C); 128.08 (*d*, 2 C); 66.57 (*t*); 65.32 (*d*); 64.98 (*d*); 53.09 (*t*); 48.46 (*s*); 47.79 (*s*); 44.56 (*d*); 41.03 (*t*); 38.45 (*t*); 34.44 (*t*); 32.80 (*t*); 29.72 (*t*); 28.61 (*t*); 26.46 (*t*); 25.57 (*t*); 20.70 (*q*); 19.88 (*q*); 15.27 (*q*); 14.86 (*q*). MS: 562 (0.2, $[C_{29}H_{43}N_3O_5S_3 - MeS]^+$), 454 (0.7), 426 (0.3), 381 (1.5), 367 (0.2), 317 (0.2), 259 (11), 211 (4), 186 (5), 166 (15), 152 (3), 135 (41), 107 (62), 91 (59), 79 (100).

(2S)-2-Amino-7-[(benzyloxycarbonyl)amino]heptanoic Acid (**16o**). As described for **13m**, **11o** (59.5 mg, 0.1 mol) was converted into **16o** (26 mg, 88%). M.p. 255–257°. $[\alpha]_D$ = +14.8, $[\alpha]_{578}$ = +15.2, $[\alpha]_{546}$ = +17.7, $[\alpha]_{436}$ = +31.6, $[\alpha]_{365}$ = +56.1 (*c* = 0.61, 1N $CF_3COOH/CHCl_3$). IR (KBr): 3300, 3200–2600, 1680, 1670–1480. ^{1}H-NMR ($CF_3COOH/CHCl_3$): 1.25–1.45 (6 H); 1.90 (br. *m*, 2 H); 3.13 (br. *s*, 2 H); 3.95 (*m*, 1 H); 5.0–5.20 (2 H); 5.10 (*s*, 1 H); 6.30 (*s*, 1 H); 7.32 (*s*, 5 H). MS: 295 (0.8, $[C_{15}H_{22}N_2O_4 + 1]^+$), 249 (1.9), 220 (0.3), 203 (0.8), 187 (10), 141 (15), 108 (20), 98 (20), 91 (100), 79 (45).

(2S)-2Amino-8-[(benzyloxycarbonyl)amino]octanoic Acid (**16p**). As described for **13m**, **11p** (60.9 mg, 0.1 mmol) was converted into **16p** (283 mg, 92%). M.p. 262–265°. $[\alpha]_D = +19.7$, $[\alpha]_{578} = +20.6$, $[\alpha]_{546} = +23.4$, $[\alpha]_{436} = +42.1$, $[\alpha]_{365} = +72.9$ (*c* = 0.7, 1N $CF_3COOH/CHCl_3$). IR (KBr): 3350, 3320–2500, 1690, 1580, 1530. ^{1}H-NMR ($CF_3COOH/CDCl_3$): 1.24–1.44 (8 H); 1.90 (br. *m*, 2 H); 3.12 (br. *s*, 2 H); 4.05 (*m*, 1 H); 5.10 (br. *s*, 2 H); 6.25 (br.); 7.26–7.33 (5 H); 7.74 (br. *s*). MS: 309 (0.2, $[C_{16}H_{24}N_2O_4 + 1]^+$), 263 (1.4), 219 (0.5), 202 (1), 184 (0.8), 173 (0.6), 155 (5.0), 112 (13), 100 (5), 91 (100).

9. *Optical Purities of the Synthetic α-Amino Acid. (2R)-N-{(2RS)-2-{[bis(methylthio)methylidene]amino}-acyl}bornane-10,2-sultams.* A soln. of potassium bis(trimethylsilyl)amide (1.1 mol-equiv.) in THF was added over 1 h to 0.2M of methyl *N*-[bis(methylthio)methylidene]glycinate in THF at −78°, and the mixture was stirred at −78° for 1 h. Addition of DMPU (1.58 ml/mmol, 24 vol-%) over 5 min, followed by addition of the alkylating agent (5.0 mol-equiv.), warming of the mixture to r.t. over 2–3 h, evaporation of the THF, aq. workup (Et_2O), and FC provided racemic α-{[bis(methylthio)methylidene]amino} acid methyl esters. Analogous alkylations of methyl *N*-[bis(methylthio)methylidene]glycinate with (*Z*)-1-(benzyloxy)-4-iodobut-2-ene, 4-bromobenzyl bromide, and (naphthalen-1-yl)methyl bromide were carried out under phase-transfer catalysis (*General Procedure A*). Resulting (±)-α-{[bis(methylthio)methylidene]amino} acid methyl esters were condensed with (2*R*)-sultam **1**/$AlMe_3$ (reflux 24–48 h), as described for **2**, to give a 1:1 α-epimer mixture of the corresponding *N*-{2-{[bis(methylthio)methylidene]amino}acyl}bornane-10,2-sultam which was analyzed by GC (*A*) or HPLC (*A*).

(S)-N-[(R)-N-(3,5-Dinitrobenzoyl)prolyl]valine Methyl Ester (**17k**). $SOCl_2$ (1 ml) was added at 0° to dry MeOH (20 ml). After stirring the soln. at 0° for 10 min, solid **5k** (100 mg, 0.854 mmol) was added, and the mixture was stirred at 55° for 2 h. Evaporation and drying of the residue *in vacuo* gave the corresponding amino acid methyl ester hydrochloride. Addition of (*R*)-*N*-(3,5-dinitrobenzoyl)proline (528 mg, 2 mol-equiv.) and DMF (1 ml), cooling of the soln. to −10°, successive addition of *N*-methylmorpholine (1.1 ml, 12 mol-equiv.) and propylphosphonic anhydride (1.66 ml, 4 mol-equiv.), stirring of the mixture at −10° for 2 h, then at r.t. for 2 h, aq. workup (AcOEt), filtration through a short SiO_2 column (hexane/i-PrOH 4:1), and evaporation of the filtrate afforded **17k** (low-melting solid; 346.3 mg, 96%). $[\alpha]_D = +65.8$, $[\alpha]_{578} = +68.9$, $[\alpha]_{546} = +78.8$, $[\alpha]_{436} = +125.2$ (*c* = 1.07). HPLC (*B*, 4:1): 7.53 (0.45), 10.83 (99.55); sample prepared from (±)-valine; 7.53 (50.2), 10.76 (49.8). IR: 3400, 3050, 3000, 2950, 1740, 1690, 1630, 1570, 1350. ^{1}H-NMR: 0.93 (*d*, *J* = 7.0, 3 H); 0.99 (*d*, *J* = 7.0, 3 H); 1.90–2.52 (5 H); 3.43–3.67 (2 H); 3.76 (*s*, 3 H); 4.53 (*d*, *J* = 5.0, 1 H); 4.56 (*d*, *J* = 5.0, 1 H); 4.89 (*m*, 1 H); 8.78 (*s*, 2 H); 9.11 (*m*, 1 H). ^{13}C-NMR: 172.27 (*s*); 170.54 (*s*); 165.92 (*s*); 148.48 (*s*, 2 C); 139.57 (*s*); 127.48 (*d*, 2 C); 119.93 (*d*); 60.11 (*d*); 57.46 (*d*); 50.01 (*t*); 30.90 (*q*); 30.70 (*q*); 27.23 (*t*); 25.30 (*t*); 19.10 (*d*); 17.54 (*q*). MS: 423 (6.6, $[C_{18}H_{22}N_4O_8 + 1]^+$), 405 (0.8), 391 (0.5), 363 (0.9), 292 (5.7), 280 (0.3), 264 (38), 248 (5), 195 (100), 179 (12), 149 (55), 75 (76).

10. *Synthesis of Bulgecinine. (2S,4S,5S)-5-Bromo-2-{[(tert-butyl)oxycarbonyl]amino}-6-hydroxyhexano-4-lactone* (**18**). A mixture of **5c** (72.5 mg, 0.5 mmol), $NaHCO_3$ (0.5 mmol), di(*tert*-butyl) carbonate (0.55 mmol), and dioxane/H_2O 1:1 (1 ml) was stirred at r.t. for 24 h. Evaporation of the dioxane, addition of H_2O (5 ml), extraction (Et_2O), evaporation of the aq. phase, addition of 0.1M AcOH in THF (5 ml), and stirring of the mixture at 0° gave a soln. of the corresponding Boc-protected amino acid. Addition of NBS (0.5 mmol), stirring of the mixture at 0° for 5 min, evaporation, and aq. workup (AcOEt) gave a 89:11 stereoisomer mixture (^{1}H-NMR) which, after FC (hexane/AcOEt 1:1) and crystallization ($CHCl_3$/hexane), afforded pure **18** (131 mg, 81%). M.p. 140–142° ([31]: 139–142°). $[\alpha]_D = +45.6$, $[\alpha]_{578} = +47.6$, $[\alpha]_{546} = +53.9$, $[\alpha]_{436} = +90.7$, $[\alpha]_{365} = +139.0$ (*c* = 0.815, MeOH, 28°; [31]: $[\alpha]_D = +44.7$ (*c* = 0.78, MeOH)). IR: 3400, 3520, 2980, 2880, 1790, 1710, 1500, 1460, 1350, 1150. ^{1}H-NMR: 1.46 (*s*, 9 H); 2.25 (*ddd*, *J* = 12, 11, 10, 1 H); 2.29 (br. *m*, 1 H); 2.88 (*m*, 1 H); 3.95–4.06 (2 H); 4.17 (*q*, *J* = 10, 1 H); 4.49 (*m*, 1 H); 4.74 (*m*, 1 H); 5.12 (*m*, 1 H). ^{13}C-NMR ((D_6)DMSO): 173.89 (*s*); 155.07 (*s*); 78.42 (*s*); 75.06 (*d*); 62.46 (*t*); 57.22 (*d*); 50.23 (*d*); 32.37 (*t*); 28.00 (*q*, 3 C). MS: 323 (0.05, $[C_{11}H_{18}BrNO_3 - 1]^+$), 342 (0.05, $[M + H_2O]^+$), 313 (0.1), 300 (0.05), 294 (0.05), 282 (0.1), 279 (0.1), 269 (0.7), 224 (0.4), 196 (0.7), 145 (0.4), 126 (1.6), 100 (7.4), 82 (11), 72 (5), 59 (22), 57 (100).

(−)-Bulgecinine (**19**). A soln. of **18** (97.2 mg, 0.3 mmol) and CF_3CO_2H (10 mol-equiv.) in CH_2Cl_2 (5 ml) was heated under reflux for 3 h under N_2. Evaporation, dissolving the residue in 0.1N aq. $Ba(OH)_2$, keeping the mixture at pH 9 for 3 h, acidification to pH 1, stirring of the aq. soln. with *Amberlite-IR-120* ion-exchange resin (H^+ form, 1.0 g), for 24 h, filtration, washing of the resin with distilled H_2O (until the eluate remained clear upon addition of $AgNO_3$), stirring of the resin with 6N aq. NH_4OH soln. (30 ml), for 3 h, filtration, evaporation of the filtrate, and drying of the residue at 0.01 Torr provided **19** (amorphous solid; 46.6 mg, 97%). $[\alpha]_D = -12.8$, $[\alpha]_{578} = -13.7$ (*c* = 1.6, H_2O, 27°; [31]: $[\alpha]_D = -13.3$ (*c* = 1.5, H_2O)). ^{1}H-NMR (D_2O): 1.97 (*ddd*, *J* = 14, 7, 5, 1 H); 2.48 (*ddd*, *J* = 14, 9, 6, 1 H); 3.54–3.59 (2 H); 3.70 (*m*, 1 H); 4.03 (*dd*, *J* = 9, 6.5, 1 H); 4.20 (*m*, 1 H). ^{13}C-NMR (D_2O/dioxane): 174.76 (*s*); 71.24 (*d*); 67.54 (*d*); 60.03 (*d*); 58.75 (*t*); 37.19 (*t*).

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