12. Enantioselective Synthesis of α-*N*-Alkylamino Acids *via* Sultam-Directed 'Enolate' Hydroxyamination

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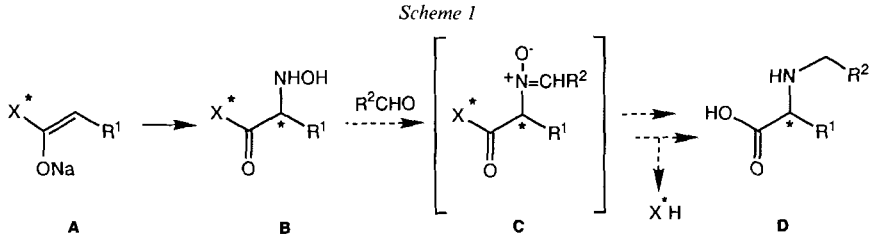
Crystalline *N*-hydroxyamino-acid derivatives **4**, readily available from non-chiral acyl chlorides **2** and sultams **1**, were treated with aldehydes in the presence of $NaBH_3CN$ to give *N*-alkylhydroxylamines **5**. *N,O*-Hydrogenolysis of **5** and saponification of **6** furnished (*S*)-*N*-alkylamino acids **7** in high optical purity. Similarly, (*R*)-*N*-alkylamino acids **12** were obtained from the antipodal acylsultams **8**.

Introduction. – α-*N*-Alkylamino acids (particularly the *N*-methyl derivatives) are constituents of various naturally occurring peptides [1] such as the immunosuppressive agent cyclosporine A [2]. Their incorporation into peptide analogs leads to profound conformational changes [3] as well as to an increase in lipophilicity and resistance to proteolysis. These effects may elicit useful pharmacological properties [4]. Moreover, several *N*-alkylamino acids have been found to be biologically active in their own right [5].

Consequently, a number of synthetic routes to optically pure *N*-alkylamino acids have been developed. The majority of these methods are limited to modifications of chiral, α-amino- [6] or α-hydroxy acids [7]. Nevertheless, short '*ab initio*' approaches, involving the generation of C(α)-chirality[1]), would be more suitable for the preparation of chiral, isotopically labelled, or other *N*-alkylamino acids derived from non-proteinogenic amino acids.

To this end, we considered taking advantage of the recently published, ~ 100% π-face selective, hydroxyamination of chiral enolates **A** → **B** (*Scheme 1*) [9].

Scheme 1

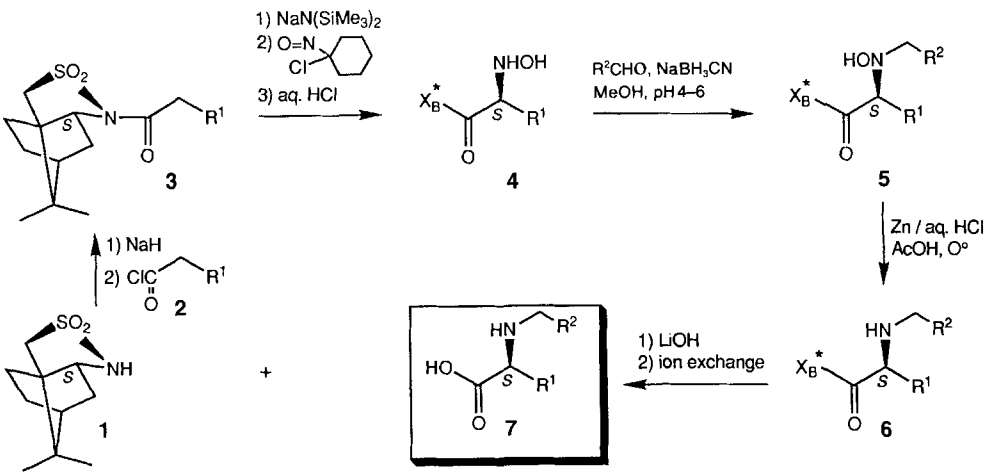


[1]) For the enantioselective preparation of *N*-alkylamino acids by Pd-catalyzed asymmetric allylic amination, see [8].

Condensation of hydroxylamines **B** with aldehydes, reduction of nitrone intermediates **C**, and recovery of the auxiliary **X*H** should conveniently provide *N*-monoalkylated amino acids **D** without significant epimerization.

Results. – Putting this plan into practice, acylation of (2*S*)-bornane-10,2-sultam (**1**) and hydroxyamination of **3** were carried out as previously described (*Scheme 2*) [9].

Scheme 2



a R^1 = Me, R^2 = H; **b** R^1 = Me_2CH, R^2 = H; **c** R^1 = Me_2CHCH_2, R^1 = H; **d** R^1 = $PhCH_2$, R^2 = H; **e** R^1 = $PhCH_2$, R^2 = Me; **f** R^1 = $PhCH_2$, R^2 = Me_2CH; **g** R^1 = $MeOCOCH_2$, R^2 = H.

The resulting, crystalline, diastereoisomerically pure hydroxylamines **4** smoothly underwent reductive *N*-alkylation [10] with methanolic formaldehyde in the presence of sodium cyanoborohydride at pH 4–6 affording crystalline *N*-methylhydroxylamine products **5** (*Table, Entries 1–4* and *7*). Similarly, *N*-ethyl- or *N*-isobutyl derivatives **5** were obtained in good yields employing acetaldehyde or isobutyraldehyde (*Entries 5* and *6*). *N,O*-hydrogenolysis of *N*-alkylhydroxylamines **5** with Zn dust (excess, 1N aq. HCl/AcOH 2:1, 0°) afforded crystalline (*N*-alkylamino)acylsultams **6**. Mild saponification of **6** with 0.3N LiOH (THF/H_2O 2:1, 0°) and extraction (CH_2Cl_2) furnished recovered sultam **1** (80–96%). Stirring of the neutralized aq. phase with ion-exchange resin (*Amberlite IR-120*) and elution of the resin with 7N aq. NH_3 provided (*S*)-*N*-alkylamino acids **7**. (*R*)-*N*-alkylamino acids **12** are equally accessible by this general protocol using the antipodal sultam *ent*-**1** (*Entries 8–11*, *Scheme 3*).

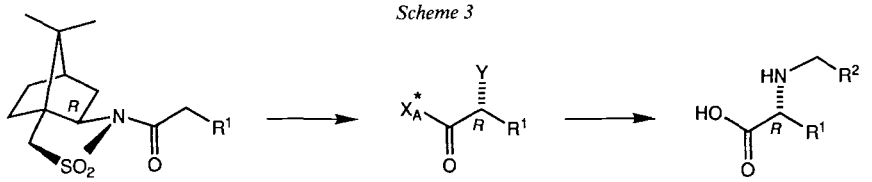
The absolute configurations of **7** and **12** follow from those of hydroxylamines **4** and **9**, respectively [9]. *C*-Functionalized, optically pure *N*-alkylamino acids can also be obtained such as the neurobiologically interesting [11] (*S*)- and (*R*)-*N*-methylaspartic acids **7g** and **12g** (*Entries 7* and *11*), respectively. In this context, it is worth mentioning that the deprotonation/hydroxyamination of **3** and **8**, R^1 = CH_2COOMe occurs regioselectively

Table. *Transformation of* N-*[2-(*N*-Hydroxyamino)acyl]bornane-10,2-sultams into Enantiomerically Pure α-* N-*Alkylamino Acids* **4** → **7** *and* **9** → **12**

Entry	[2-(*N*-Hydroxyamino)acyl]-sultam		Aldehyde	{2-[(Alkyl)(hydroxy)amino]acyl}sultam		[2-(Alkylamino)acyl]-sultam		*N*-Alkylamino Acid			
		R_1	R_2		Yield [a]		Yield [a]		Yield [b]	e.e. [b]	Configuration
1	**4**	Me	H	**5a**	67 (80)	**6a**	74 –	**7a**	91	96.8	*S*
2	**4**	Me_2CH	H	**5b**	80 (98)	**6b**	82 (94)	**7b**	90	> 99	*S*
3	**4**	Me_2CHCH_2	H	**5c**	86 (100)	**6c**	76 (87)	**7c**	100	> 99	*S*
4	**4**	$PhCH_2$	H	**5d**	82 (98)	**6d**	75 (90)	**7d**	92	> 99	*S*
5	**4**	$PhCH_2$	Me	**5e**	78 (90)	**6e**	86 –	**7e**	92	> 99	*S*
6	**4**	$PhCH_2$	Me_2CH	**5f**	77[c]) –	**6f**	71 (87)	**7f**	98	> 99	*S*
7	**4**	$MeOCOCH_2$	H	**5g**	78 (95)	**6g**	78 (92)	**7g**[d])	94	> 99	*S*
8	**9**	Me	H	**10a**	64 –	**11a**	74 (92)	**12a**	94	93	*R*
9	**9**	$PhCH_2$	Me	**10e**	78 (90)	**11e**	89 –	**12e**	91	> 99	*R*
10	**9**	$PhCH_2$	Me_2CH	**10f**	71[c]) –	**11f**	88 (95)	**12f**	90	> 99	*R*
11	**9**	$MeOCOCH_2$	H	**10g**	78 (96)	**11g**	78 (92)	**12g**[d])	94	96.4	*R*

[a]) After crystallization (yield of crude product in parentheses). [b]) Crude *N*-alkylamino acid. [c]) After flash chromatography. [d]) $R^1 = HOOCCH_2$.

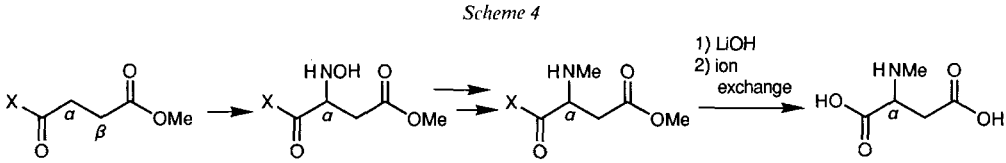
Scheme 3



a $R^1 = Me$, $R^2 = H$; **e** $R^1 = PhCH_2$, $R^2 = Me$; **f** $R^1 = PhCH_2$, $R^2 = Me_2CH$; **g** $R^1 = MeOCOCH_2$, $R^2 = H$.

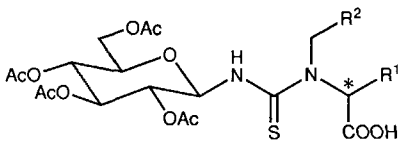
at C(α) (adjacent to the acylsultam group) and not at C(β)[2]). The methoxycarbonyl group is, furthermore, compatible with the subsequent reductive alkylation/*N,O*-hydrogenolysis steps, until it is hydrolyzed together with the acylsultam moiety (*Scheme 4*).

Scheme 4



3g X = X_B^*
8g X = X_A^*
4g X = X_B^*
9g X = X_A^* (C(α)*R*)
6g X = X_B^* (C(α)*S*)
10g X = X_A^* (C(α)*R*)
7g (C(α)*S*)
12g (C(α)*R*)

[2]) We assume that the electron-withdrawing nature of the sultam moiety and its capacity to stabilize a 'C(α)-enolate' by chelation [9] favors C(α) over C(β) deprotonation.



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The enantiomeric excess (e.e.) of **7** and **12** were readily determined by reverse-phase HPLC analysis of the corresponding thiourea derivatives **13**, obtained with 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl isothiocyanate (GITC) [12].

It is interesting to note that the thioureas from (*S*)-*N*-methyl- and *N*-ethylamino acids **7** elute *prior* to the (*R*)-diastereoisomers obtained from **12**. However, the elution order is reversed with *N*-isobutylphenylalanine, *i.e.* the thiourea **13**, prepared from (*R*)-**12f**, elutes prior to its diastereoisomer derived from (*S*)-**7f**.

The crude *N*-alkylamino acids **7** and **12** were enantiomerically pure within the limits of this HPLC analysis. Only the *N*-methylalanines **7a** and **12a** show 1.6 to 3.9% cross contamination. More extensive epimerization occurred, not surprisingly, during reductive methylation of diastereoisomerically pure hydroxylamine **4** (R^1 = Ph), which gave a 75:25 mixture of **5** (R^1 = Ph, R^2 = Me) and its C(2′)-epimer (^{1}H-NMR).

Conclusion. – In summary, this five-step conversion of non-chiral acid chlorides **2** into enantiomerically pure α-*N*-alkylamino acids **7** or **12** represents an attractive route to this class of compounds given the easy accessibility[3]) and recoverability of sultam **1** and its antipode, and last but not least, the crystallinity of most intermediates. Its most obvious potential lies in the synthesis of chiral, isotope-labelled, or other *N*-alkylamino acids which are not directly available from proteinogenic amino acids.

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Experimental Part

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 (Na-benzophenone), toluene (Na), CH_2Cl_2 (CaH_2), EtOH, MeOH (Mg). Unless otherwise stated, all combined org. extracts were dried with $MgSO_4$. Column flash chromatography (FC): SiO_2 (*Merck, Kieselgel 60*, 0.040–0.060 mm). GC: *Hewlett-Packard 5790A*, integrator *HP 3390A*, capillary column (fused silica, *OV-1*, 0.2 mm i.d., 12 m), 10 psi H_2; t_R in min (area-%). HPLC: Column *Brownlee OS-224-Spheri-5, RP-18*, 5 μm, 40°, 220 × 4.6 mm; solvents: *A*: 0.01M NaH_2PO_4 in MeCN/H_2O 9:1, pH 2.8; *B*: 0.01M NaH_2PO_4 in MeCN/MeOH/H_2O 6:1:3, pH 3.4; gradient: 25–65% *B* in 35 min, detector: 250 nm; t_R in min (area-%). M.p.: *Kofler* hot stage; uncorrected: $[\alpha]_D$: *Perkin-Elmer 241* polarimeter, in $CHCl_3$, at 25 ± 2°, unless otherwise specified. IR: *Polaris Mattson Instruments*, in $CHCl_3$, unless otherwise specified. NMR spectra (*Bruker AMX-400* or *Varian XL-200*), in $CDCl_3$, unless otherwise specified; standard $CHCl_3$ (δ = 7.27 ppm), *J* in Hz. MS: *Varian CH-4* or *Finnigan 4023* at 70 eV, *m/z* (rel.-%). HR-MS: *VG 7070-E*.

Preparation of N-*Acylsultams* **3** *and* **8**. The *N*-acylsultams **3** (R^1 = Me, Me_2CH, Me_2CHCH_2, $PhCH_2$; *Entries 1–6*) and **8** (R^1 = Me, $PhCH_2$; *Entries 8* and *9*) were prepared as described in [9b].

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[3]) Sultam **1** and its antipode *ent*-**1** are commercially available on a kg-scale from *NEWPORT Synthesis Ireland Ltd., Dublin/Ireland.*

(2S)-N-[3'-(Methoxycarbonyl)propionyl]bornane-10,2-sultam (**3**; R^1 = $MeOCOCH_2$). Following the *General Procedure* published in [9b], (2*S*)-Bornane-10,2-sultam (**1**; 2.0 g, 9.3 mmol) was acylated with 3-(methoxycarbonyl)propionyl chloride. Crystallization of the crude product from Et_2O/hexane provided pure **3** (2.72 g, 90%). M.p. 94–95°. $[\alpha]_D$ = +90, $[\alpha]_{578}$ = +94, $[\alpha]_{546}$ = +108, $[\alpha]_{436}$ = +188, $[\alpha]_{365}$ = +308 (*c* = 0.50). IR, NMR, and MS identical with those of **8** (R^1 = CH_2COOMe). HR-MS: 298.1104 ($[C_{15}H_{23}NO_5S - CH_3O]^+$, calc. 298.1113).

(2R)-N-[3'-(Methoxycarbonyl)propionyl]bornane-10,2-sultam (**8**; R^1 = $MeOCOCH_2$). Following the *General Procedure* published in [9b], (2*R*)-bornane-10,2-sultam (*ent*-**1**; 2.5 g, 11.6 mmol) was acylated with 3-(methoxycarbonyl)propionyl chloride (1.85 g, 12.3 mmol). Crystallization of the crude product from Et_2O/hexane gave pure **8** (3.6 g, 94%). M.p. 93–95°. $[\alpha]_D$ = −90.3, $[\alpha]_{578}$ = −94.5, $[\alpha]_{546}$ = −107.6, $[\alpha]_{436}$ = −186.2, $[\alpha]_{365}$ = −304.1 (*c* = 1.45). IR: 2950, 1740, 1700, 1400, 1325, 1275, 1240, 1160. ^{1}H-NMR (400 MHz): 0.97 (*s*, 3 H); 1.18 (*s*, 3 H); 1.35–1.41 (2 H); 1.85–1.98 (3 H); 2.05 (*dd*, *J* = 14, 8, 1 H); 2.16 (*m*, 1 H); 2.62 (*dt*, *J* = 16, 6, 1 H); 2.73 (*ddd*, *J* = 16, 8, 6, 1 H); 3.01 (*dt*, *J* = 16, 6, 1 H); 3.08 (*ddd*, *J* = 16, 8, 6, 1 H); 3.44 (*d*, *J* = 14, 1 H); 3.51 (*d*, *J* = 14, 1 H); 3.68 (*s*, 3 H); 3.87 (*dd*, *J* = 8, 5, 1 H). ^{13}C-NMR (100 MHz): 172.0 (*s*); 170.3 (*s*); 65.24 (*d*); 52.9 (*t*); 51.86 (*q*); 48.65 (*s*); 47.81 (*s*); 44.7 (*d*); 38.37 (*t*); 32.84 (*t*); 30.38 (*t*); 28.37 (*t*); 26.48 (*t*); 20.81 (*q*); 19.91 (*q*). MS: 300 (0.2, $[C_{15}H_{23}NO_5S - 29]^+$), 298 (3), 116 (5.5), 115 (100), 87 (4.2), 59 (6.4), 55 (14.3). HR-MS: 115.0423 ($[C_{15}H_{23}NO_5S - C_{10}H_{16}NO_2S]^+$, calc. 115.0395).

Preparation of N-[2'-(Hydroxyamino)acyl]bornane-10,2-sultams **4** *and* **9**. The (*N*-hydroxyamino)acylsultams **4** (R^1 = Me, Me_2CH, Me_2CHCH_2, $PhCH_2$; *Entries 1–6*) and **9** (R^1 = Me, $PhCH_2$; *Entries 8* and *9*) were prepared as described in [9b].

(2S,2'S)-N-[2'-(Hydroxyamino)-3'-(methoxycarbonyl)propionyl]bornane-10,2-sultam (**4**; R^1 = $MeOCOCH_2$). Following the *General Procedure* published in [9b], acylsultam **3** (R^1 = $MeOCOCH_2$; 1.09 g, 3.31 mmol) was treated successively with *1*) sodium hexamethyldisilazane, *2*) 1-chloro-1-nitrosocyclohexane, and *3*) aq. 1N HCl. The crude product (1.0 g, 84%) was crystallized from AcOEt/hexane to give **4** (0.77 g, 65%). M.p. 155–156°. $[\alpha]_D$ = +67, $[\alpha]_{578}$ = +70, $[\alpha]_{546}$ = +79.4, $[\alpha]_{436}$ = +130, $[\alpha]_{365}$ = +192.9 (*c* = 1.70). IR, NMR, and MS identical with those of **9** (R^1 = $MeOCOCH_2$). HR-MS: 118.0523 ($[C_{15}H_{24}N_2O_6S - C_{11}H_{16}NO_3S]^+$, calc. 118.0504).

(2R,2'R)-N-[2'-(Hydroxyamino)-3'-(methoxycarbonyl)propionyl]bornane-10,2-sultam (**9**; R = $MeOCOCH_2$). Following the *General Procedure* published in [9b] acylsultam **8** (R = $MeOCOCH_2$; 1.11 g, 3.4 mmol) was treated successively with *1*) sodium hexamethyldisilazane, *2*) 1-chloro-1-nitrosocyclohexane, and *3*) aq. 1N HCl. The crude product (0.98 g, 81%) was crystallized from AcOEt/hexane to give **9** (0.75 g, 62%). M.p. 155–156°. $[\alpha]_D$ = −54.6, $[\alpha]_{578}$ = −56.7, $[\alpha]_{546}$ = −63.9, $[\alpha]_{436}$ = −104.1, $[\alpha]_{365}$ = −153.6 (*c* = 0.97). IR: 3550, 3300, 2960, 1730, 1700, 1450, 1325, 1300, 1275, 1125. ^{1}H-NMR (400 MHz): 0.98 (*s*, 3 H); 1.20 (*s*, 3 H); 1.36–1.43 (2 H); 1.88–1.98 (3 H); 2.06 (*m*, 1 H); 2.17 (*m*, 1 H); 2.69 (*dd*, *J* = 16, 8, 1 H); 2.95 (*dd*, *J* = 16, 6.5, 1 H); 3.47 (*d*, *J* = 14, 1 H); 3.55 (*d*, *J* = 14, 1 H); 3.70 (*s*, 3 H); 3.95 (*dd*, *J* = 8, 5, 1 H); 4.51 (*t*, *J* = 7, 1 H); 5.25 (br. *s*, 1 H); 6.31 (br. *s*, 1 H). ^{13}C-NMR (100 MHz): 171.08 (*s*); 170.82 (*s*); 65.38 (*d*); 61.16 (*d*); 53.07 (*t*); 51.99 (*q*); 49.0 (*s*); 47.92 (*s*); 44.64 (*d*); 38.13 (*t*); 33.45 (*t*); 32.78 (*t*); 26.52 (*t*); 20.61 (*q*); 19.94 (*q*). MS: 361 (3.3, $[C_{15}H_{24}N_2O_6S + 1]^+$), 216 (4), 179 (4.8), 135 (10.1), 118 (100), 102 (27), 86 (67.6), 77 (10.3), 67 (19.1), 58 (43.9), 55 (35.5). HR-MS: 118.0504 ($[C_{15}H_{24}N_2O_6S - C_{11}H_{16}NO_3S]^+$, calc. 118.0504).

Reductive Amination of N-[2'-(Hydroxyamino)acyl]bornane-10,2-sultams. General Procedure. The hydroxylamine derivative **4** or **9** (1.14 mmol) was dissolved in a 1M methanolic soln. of aldehyde (35 ml). Then, sodium cyanoborohydride (4.14 mmol) was added, the pH was adjusted to 4–6 with methanolic HCl (prepared from AcCl/MeOH 1:5 (*v*/*v*)) at 0°, and the mixture was stirred at r.t. until completion of the reaction (TLC). Addition of 1N aq. HCl (20 ml), evaporation of MeOH, partitioning of the aq. phase between CH_2Cl_2 and sat. aq. $NaHCO_3$ soln., drying ($MgSO_4$), and evaporation of the org. extracts followed by purification of the residue by flash chromatography (FC) and/or crystallization yielded *N*-{2'-[(alkyl)(hydroxy)amino]acyl}bornane-10,2-sultams **5** or **10**, respectively.

(2S,2'S)-N-{2'-[(Hydroxy)(methyl)amino]propionyl}bornane-10,2-sultam (**5a**). Using the *General Procedure*, **4** (R^1 = Me; 0.29 g, 0.96 mmol) was converted to crude **5a** (0.24 g, 80%). FC (AcOEt/hexane 3:2) afforded pure **5a** (0.2 g, 67%). M.p. 119–122°. $[\alpha]_D$ = +561, $[\alpha]_{578}$ = +565, $[\alpha]_{546}$ = +571.5, $[\alpha]_{436}$ = +612.5, $[\alpha]_{365}$ = +679 (*c* = 0.20). IR: 3550, 2950, 1680, 1330, 1275, 1240, 1130. ^{1}H-NMR (400 MHz): 0.98 (*s*, 3 H); 1.19 (*s*, 3 H); 1.36 (*d*, *J* = 6.5, 3 H); 1.27–1.41 (2 H); 1.87–2.13 (5 H); 2.71 (*s*, 3 H); 3.44 (*d*, *J* = 14, 1 H); 3.54 (*d*, *J* = 14, 1 H); 3.92 (*dd*, *J* = 8, 5, 1 H); 4.05 (*q*, *J* = 6.8, 1 H); 5.76 (br. *s*, 1 H). ^{13}C-NMR (100 MHz): 172.89 (*s*); 65.66 (*d*); 65.55 (*d*); 53.29 (*t*); 48.53 (*s*); 47.79 (*s*); 44.90 (*q*); 44.85 (*d*); 38.72 (*t*); 33.06 (*t*); 26.41 (*t*); 20.98 (*q*); 19.94 (*q*); 14.15 (*q*). MS: 316 (1.0), 185 (1.5), 151 (10), 136 (12), 93 (20), 74 (45), 58 (100). HR-MS: 151.1380 ($[C_{14}H_{24}N_2O_4S - C_4H_7NO_4S]^+$, calc. 151.1361).

(2S,2'S)-N-{*2'-[(Hydroxy)(methyl)amino]-3'-methylbutanoyl*}*bornane-10,2-sultam* (**5b**). Using the *General Procedure*, **4** (R^1 = i-Pr; 0.46 g, 1.39 mmol) was converted to crude **5b** (0.47 g, 98%). Recrystallization from CH_2Cl_2/hexane furnished pure **5b** (0.38 g, 80%). M.p. 196–197°. $[\alpha]_D = +82.4$, $[\alpha]_{578} = +87.1$, $[\alpha]_{546} = +100$, $[\alpha]_{436} = +173.6$, $[\alpha]_{365} = +278.6$ ($c = 0.70$). IR: 3550, 3375, 2970, 1700, 1460, 1350, 1230, 1150, 1060. ^{1}H-NMR (200 MHz): 0.93 (*d*, *J* = 7, 3 H); 0.95 (*s*, 3 H); 1.05 (*d*, *J* = 7, 3 H); 1.18 (*s*, 3 H); 1.3–1.5 (2 H); 1.8–2.3 (6 H); 2.7 (*s*, 3 H); 3.45 (*d*, *J* = 13.5, 1 H); 3.55 (*d*, *J* = 13.5, 1 H); 3.8 (*d*, *J* = 10, 1 H); 3.95 (*dd*, *J* = 7.5, 5, 1 H); 5.5 (br. *s*, 1 H). ^{13}C-NMR (50 MHz): 171.3 (*s*); 74.14 (*d*); 65.58 (*d*); 53.26 (*t*); 48.07 (*s*); 47.68 (*s*); 44.62 (*d*); 44.11 (*q*); 39.00 (*t*); 32.96 (*t*); 28.36 (*d*); 26.31 (*t*); 20.73 (*q*); 19.91 (*q*); 19.69 (*q*); 19.16 (*q*). MS: 344 (0.3, $C_{16}H_{28}N_2O_4S^{+\cdot}$), 301 (4.8), 102 (100), 86 (75), 84 (25), 55 (14). HR-MS: 86.0605 ($[C_{16}H_{28}N_2O_4S - C_{12}H_{20}NO_3S]^{+\cdot}$, calc. 86.0605).

(2S,2'S)-N-{*2'-[(Hydroxy)(methyl)amino]-4'-methylpentanoyl*}*bornane-10,2-sultam* (**5c**). Using the *General Procedure*, **4** ($R^1 = Me_2CHCH_2$; 0.54 g, 1.57 mmol) was converted into crude **5c** (0.56 g, 100%). FC (CH_2Cl_2/AcOEt 8:2) gave pure **5c** (0.48 g, 86%). M.p. 191–193°. IR: 3550, 3350, 2950, 1680, 1460, 1330, 1270, 1160, 1130, 1070. ^{1}H-NMR (400 MHz): 0.93 (*d*, *J* = 7, 3 H); 0.96 (*d*, *J* = 7, 3 H); 0.98 (*s*, 3 H); 1.19 (*s*, 3 H); 1.38–2.15 (10 H); 2.72 (*s*, 3 H); 3.44 (*d*, *J* = 13.6, 1 H); 3.53 (*d*, *J* = 13.6, 1 H); 3.91 (*dd*, *J* = 8, 5, 1 H); 4.13 (*dd*, *J* = 8, 6, 1 H); 5.54 (br. *s*, 1 H). ^{13}C-NMR (50 MHz): 172.7 (*s*); 66.6 (*d*); 65.8 (*d*); 53.14 (*t*); 48.37 (*s*); 47.74 (*s*); 44.67 (*q*); 44.63 (*d*); 38.79 (*t*); 37.03 (*t*); 32.90 (*t*); 26.31 (*t*); 24.36 (*d*); 23.21 (*q*); 21.91 (*q*); 20.72 (*q*); 19.87 (*q*). MS: 360 (22.6, $[C_{17}H_{30}N_2O_4S + 2]^{+\cdot}$), 359 (30.1), 358 (1.4), 116 (100), 100 (46.6), 93 (26.9), 79 (26.1), 73 (37.4), 57 (83), 55 (64). HR-MS: 285.1257 ($[C_{17}H_{30}N_2O_4S - C_4H_9O]^{+\cdot}$, calc. 285.1273).

(2S,2'S)-N-{*2'-[(Hydroxy)(methyl)amino]-3'-phenylpropionyl*}*bornane-10,2-sultam* (**5d**). Using the *General Procedure*, **4** ($R^1 = PhCH_2$; 0.43 g, 1.14 mmol) was converted to crude **5d** (0.44 g, 98%). FC (CH_2Cl_2/AcOEt 5:1) gave pure **5d** (0.36 g, 82%). M.p. 172–174°. $[\alpha]_D = -77.6$, $[\alpha]_{578} = -73.3$. $[\alpha]_{546} = -58.1$, $[\alpha]_{436} = +35$, $[\alpha]_{365} = +187.8$ ($c = 0.58$). IR: 3550, 3370, 3020, 2980, 1680, 1500, 1475, 1370, 1175. ^{1}H-NMR (400 MHz): 0.98 (*s*, 3 H); 1.16 (*s*, 3 H); 1.36–1.41 (2 H); 1.88–2.15 (5 H); 2.71 (*s*, 3 H); 3.11–3.14 (2 H); 3.43 (*d*, *J* = 13.5, 1 H); 3.52 (*d*, *J* = 13.5, 1 H); 3.93 (*t*, *J* = 8, 1 H); 4.31 (*m*, 1 H); 5.58 (br. *s*, 1 H); 7.21–7.34 (5 H). ^{13}C-NMR (50 MHz); 172.03 (*s*); 137.51 (*s*); 129.64 (*d*); 129.53 (*d*); 128.33 (*d*); 126.51 (*d*); 70.07 (*d*); 65.37 (*d*); 53.03 (*t*); 48.52 (*s*); 47.79 (*s*); 45.21 (*q*); 44.79 (*d*); 38.84 (*t*); 34.20 (*t*); 32.95 (*t*); 26.33 (*t*); 20.87 (*q*); 19.91 (*q*). MS: 393 (1.5, $[C_{20}H_{28}N_2O_4S + 1]^{+\cdot}$), 392 (0.5), 301 (8.2), 151 (10.3), 150 (100), 134 (11), 132 (12.5), 91 (58.3), 77 (16.6), 55 (19.3). HR-MS: 148.0732 ($[C_{20}H_{28}N_2O_4S - C_{11}H_{18}NO_3S]^{+\cdot}$, calc. 148.0762).

(2S,2'S)-N-{*2'-[(Ethyl)(hydroxy)amino]-3'-phenylpropionyl*}*bornane-10,2-sultam* (**5e**). Using the *General Procedure*, **4** ($R^1 = PhCH_2$; 0.21 g, 0.55 mmol) was converted to crude **5e** (0.20 g, 90%). Crystallization from EtOH gave pure **5e** (0.175 g, 78%). M.p. 173–176°. $[\alpha]_D = +94.2$, $[\alpha]_{578} = +99.0$, $[\alpha]_{546} = +113.6$, $[\alpha]_{436} = +201.9$, $[\alpha]_{365} = +345.6$ ($c = 1.03$). IR: 3570, 3386, 3025, 2965, 1692, 1455, 1336, 1212, 1135. ^{1}H-NMR (400 MHz): 0.97 (*s*, 3 H); 1.11 (*t*, *J* = 8, 3 H); 1.15 (*s*, 3 H); 1.35–1.39 (2 H); 1.86–1.93 (3 H); 2.05–2.15 (2 H); 2.76 (*dq*, *J* = 14, 7, 1 H); 2.84 (*dq*, *J* = 14, 7, 1 H); 3.12 (*dd*, *J* = 14, 6, 1 H); 3.18 (*dd*, *J* = 14, 6, 1 H); 3.42 (*d*, *J* = 14, 1 H); 3.50 (*d*, *J* = 14, 1 H); 3.91 (*t*, *J* = 7, 1 H); 4.33 (br. *s*, 1 H); 5.37 (br. *s*, 1 H); 7.20–7.33 (5 H). ^{13}C-NMR (100 MHz): 172.36 (*s*); 137.97 (*s*); 129.69 (*d*); 128.17 (*d*); 126,29 (*d*); 69.2 (*d*); 65.4 (*d*); 53.1 (*t*); 51.6 (*t*); 48.48 (*s*); 47.77 (*s*); 44.8 (*d*); 38.9 (*t*); 33.8 (*t*); 33.0 (*t*); 26.4 (*t*); 20.9 (*q*); 19.9 (*q*); 12.8 (*q*). MS: 407 (1.3, $[C_{21}H_{30}N_2O_4S + 1]^{+\cdot}$), 315 (13.5), 164 (100), 146 (10.4), 131 (11.5), 100 (39.3), 91 (81.1), 79 (22.5), 77 (18.5), 56 (49.6), 55 (27.1). HR-MS: 164.1103 ($[C_{21}H_{30}N_2O_4S - C_{11}H_{16}NO_3S]^{+\cdot}$, calc. 164.1075).

(2S,2'S)-N-{*2'-[(Hydroxy)(isobutyl)amino]-3'-phenylpropionyl*}*bornane-10,2-sultam* (**5f**). Using the *General Procedure*, **4** ($R^1 = PhCH_2$; 0.27 g, 0.71 mmol), and isobutyraldehyde gave an oil, which was chromatographed (CH_2Cl_2/AcOEt 9:1) to yield pure **5f** as a colorless solid (0.24 g, 77%). M.p. 85–88°. $[\alpha]_D = +95.1$, $[\alpha]_{578} = +99.0$, $[\alpha]_{546} = +113.6$, $[\alpha]_{436} = +202.9$, $[\alpha]_{365} = +347.6$ ($c = 1.03$). IR: 3550, 3380, 2970, 1700, 1450, 1330, 1260, 1150. ^{1}H-NMR (400 MHz): 0.78 (*d*, *J* = 7, 3 H); 0.81 (*d*, *J* = 7, 3 H); 0.97 (*s*, 3 H); 1.16 (*s*, 3 H); 1.35–1.40 (2 H); 1.87–2.12 (5 H); 2.52 (*dd*, *J* = 13, 8, 1 H); 2.57 (*dd*, *J* = 13, 7, 1 H); 3.11 (*dd*, *J* = 14, 6, 1 H); 3.18 (*dd*, *J* = 14, 8, 1 H); 3.41 (*d*, *J* = 14, 1 H); 3.50 (*d*, *J* = 14, 1 H); 3.91 (*t*, *J* = 7, 1 H); 4.30 (br. *t*, *J* = 7, 1 H); 5.33 (br. *s*, 1 H); 7.19–7.32 (5 H). ^{13}C-NMR (100 MHz): 172.22 (*s*); 137.92 (*s*); 129.74 (*d*); 129.50 (*d*); 128.62 (*d*); 128.07 (*d*); 126.23 (*d*); 69.54 (*d*); 65.32 (*d*); 65.12 (*t*); 53.09 (*t*); 48.51 (*s*); 47.80 (*s*); 44.87 (*d*); 38.83 (*t*); 33.38 (*t*); 32.97 (*t*); 26.40 (*t*); 26.21 (*d*); 20.79 (*q*); 20.40 (*q*); 20.36 (*q*); 19.88 (*q*). MS: 435 (8.4, $[C_{23}H_{34}N_2O_4S + 1]^{+\cdot}$), 434 (0.8), 343 (14.2), 192 (45.7), 176 (7.6), 136 (20.05), 128 (17.4), 107 (12.15), 91 (62.85), 77 (15.1), 67 (19.7), 57 (100), 55 (30.4). HR-MS: 343.1719 ($[C_{23}H_{34}N_2O_4S - C_7H_7]^{+\cdot}$, calc. 343.1691).

(2S,2'S)-N-{*2'-[(Hydroxy)(methyl)amino]-3'-(methoxycarbonyl)propionyl*}*bornane-10,2-sultam* (**5g**). Using the *General Procedure*, **4** ($R^1 = MeOCOCH_2$; 0.2 g, 0.55 mmol) yielded crude **5g** (0.2 g, 95%). FC (AcOEt/hexane 5:1) and crystallization (AcOEt/hexane) gave pure **5g** (0.16 g, 78%). M.p. 143–144°. $[\alpha]_D = +72.6$, $[\alpha]_{578} = +75.5$, $[\alpha]_{546} = +85.8$, $[\alpha]_{436} = +149.0$, $[\alpha]_{365} = +241.5$ ($c = 1.06$). IR, NMR, and MS identical with those of **10g**.

(2R,2'R)-N-*{2-[(Hydroxy)(methyl)amino]propionyl}bornane-10,2-sultam* (**10a**). Using the *General Procedure*, **9** (R^1 = Me; 0.33 g, 1.1 mmol) afforded, after FC (AcOEt/hexane 3:2), pure **10a** (0.22 g, 64%). M.p. 119–122°. $[\alpha]_D = -561$, $[\alpha]_{578} = -565$, $[\alpha]_{546} = -571.5$, $[\alpha]_{436} = -612.5$, $[\alpha]_{365} = -679$ ($c = 0.20$). IR, NMR, and MS identical with those of **5a**. HR-MS: 74.0571 ($[C_{14}H_{24}N_2O_4S - C_{11}H_{16}NO_3S]^{+\cdot}$, calc. 74.0606).

(2R,2'R)-N-*{2'-[(Hydroxy)(ethyl)amino]-3'-phenylpropionyl}bornane-10,2-sultam* (**10e**). Using the *General Procedure*, **9** ($R^1 = PhCH_2$; 0.36 g, 0.95 mmol) furnished crude **10e** (0.345 g, 90%). Crystallization from EtOH gave pure **10e** (0.30 g, 78%). M.p. 165–168°. $[\alpha]_D = -93$, $[\alpha]_{578} = -97.4$, $[\alpha]_{546} = -112.3$, $[\alpha]_{436} = -198.2$, $[\alpha]_{365} = -337.7$ ($c = 1.14$). IR, NMR, and MS identical with those of **5e**. HR-MS: 164.1070 ($[C_{21}H_{30}N_2O_4S - C_{11}H_{16}NO_3S]^{+\cdot}$, calc. 164.1075).

(2R,2'R)-N-*{2'-[(Hydroxy)(isobutyl)amino]-3'-phenylpropionyl}bornane-10,2-sultam* (**10f**). Using the *General Procedure*, **9** ($R^1 = PhCH_2$; 0.50 g, 1.31 mmol) and isobutyraldehyde gave an oil, which was chromatographed (CH_2Cl_2/AcOEt 9:1) to yield pure **10f** as a colorless solid (0.406 g, 71%). M.p. 97–100°. $[\alpha]_D = -112.4$ ($c = 0.59$, 20°). IR, NMR, and MS identical with those of **5f**.

(2R,2'R)-N-*{2'-[(Hydroxy)(methyl)amino]-3'-(methoxycarbonyl)propionyl}bornane-10,2-sultam* (**10g**). Using the *General Procedure*, **9** ($R^1 = MeOCOCH_2$; 0.26 g, 0.72 mmol) gave crude **10g** (0.26 g, 96%). FC (AcOEt/hexane 5:1) and crystallization from AcOEt/hexane afforded pure **10g** (0.21 g, 78%). M.p. 143–144°. $[\alpha]_D = -69.5$, $[\alpha]_{578} = -72.4$, $[\alpha]_{546} = -82.8$, $[\alpha]_{436} = -140.9$, $[\alpha]_{365} = -225.7$ ($c = 1.05$). IR: 3560, 3350, 2960, 1730, 1690, 1430, 1330, 1275, 1230, 1160, 1125. ^{1}H-NMR (400 MHz): 1.00 (*s*, 3 H); 1.20 (*s*, 3 H); 1.35–1.41 (2 H); 1.88–2.12 (5 H); 2.71 (*s*, 3 H); 2.85 (*dd*, $J = 16, 7$, 1 H); 2.92 (*dd*, $J = 16, 7$, 1 H); 3.44 (*d*, $J = 14$, 1 H); 3.53 (*d*, $J = 14$, 1 H); 3.70 (*s*, 3 H); 3.98 (*dd*, $J = 8, 5$, 1 H); 4.42 (*t*, $J = 7$, 1 H); 5.62 (br. *s*, 1 H). ^{13}C-NMR (100 MHz): 171.38 (*s*); 170.54 (*s*); 65.93 (*d*); 65.83 (*d*); 53.27 (*t*); 52.01 (*q*); 48.39 (*s*); 47.72 (*s*); 45.07 (*q*); 44.55 (*d*); 38.55 (*t*); 33.23 (*t*); 31.13 (*t*); 26.28 (*t*); 21.21 (*q*); 19.92 (*q*). MS: 375 (5.8, $[C_{16}H_{26}N_2O_6S + 1]^+$), 374 (0.6), 132 (100), 116 (8.2), 113 (18.7), 100 (69.55), 93 (12.65), 84 (10.7), 79 (14.3), 77 (9.6), 72 (36.5), 67 (16.4), 59 (20.7), 55 (45.1), 45 (10.6). HR-MS: 132.0661 ($[C_{16}H_{26}N_2O_6S - C_{11}H_{16}NO_3S]^{+\cdot}$, calc. 132.0661).

N,O-*Hydrogenolysis of* N-*{2'-[(Alkyl)(hydroxy)amino]acyl}bornane-10,2-sultams. General Procedure.* A mixture of *N*-alkylhydroxylamine **5** or **10** (0.53 mmol) and Zn dust (3.0 g) in 1N HCl/AcOH soln. (2:1, 12 ml) was stirred at 0° for 2 d. Then, the mixture was filtered through glass wool, and the Zn was washed with AcOH. The filtrate was evaporated, and the residue was partitioned between CH_2Cl_2 and sat. aq. $NaHCO_3$ soln. The combined org. extracts were dried ($MgSO_4$) and evaporated. The crude product was purified by FC and/or crystallization.

(2S,2'S)-N-*[2'-(Methylamino)propionyl]bornane-10,2-sultam* (**6a**). Using the *General Procedure*, **5a** (0.12 g, 0.38 mmol) was reduced with Zn. The crude oil was crystallized from hexane to give pure **6a** (0.081 g, 74%). M.p. 110–112°. $[\alpha]_D = +59.8$, $[\alpha]_{578} = +64.3$, $[\alpha]_{546} = +69.6$, $[\alpha]_{436} = +113.4$, $[\alpha]_{365} = +161.6$ ($c = 1.12$). IR: 3320, 2950, 1700, 1450, 1370, 1275, 1240, 1140. ^{1}H-NMR (400 MHz): 0.98 (*s*, 3 H); 1.19 (*s*, 3 H); 1.27 (*d*, $J = 6.5$, 3 H); 1.25–1.41 (2 H); 1.88–2.16 (5 H); 2.36 (*s*, 3 H); 3.45 (*d*, $J = 14$, 1 H); 3.53 (*d*, $J = 14$, 1 H); 3.88–3.95 (2 H). ^{13}C-NMR (100 MHz): 176.16 (*s*); 65.65 (*d*); 57.52 (*d*); 53.09 (*t*); 48.68 (*s*); 47.82 (*s*); 44.75 (*d*); 38.77 (*t*); 33.64 (*q*); 32.97 (*t*); 26.43 (*t*); 20.86 (*q*); 19.93 (*q*); 17.96 (*q*). MS: 119 (1.3, $[C_{14}H_{24}N_2O_3S - 181]^{+\cdot}$), 93 (1.15), 77 (1.1), 59 (4.3), 58 (100), 56 (4.1), 55 (2.95). HR-MS: 58.0660 ($[C_{14}H_{24}N_2O_3S - C_{11}H_{16}NO_3S]^{+\cdot}$, calc. 58.0657).

(2S,2'S)-N-*[2'-(Methylamino)-3'-methylbutanoyl]bornane-10,2-sultam* (**6b**). Using the *General Procedure*, **5b** (0.18 g, 0.53 mmol) was reduced with Zn to give crude **6b** (0.165 g, 94%). FC (CH_2Cl_2/AcOEt 5:1) afforded pure **6b** (0.14 g, 82%). M.p. 167–168°. $[\alpha]_D = +89.4$, $[\alpha]_{578} = +93.0$, $[\alpha]_{546} = +105.3$, $[\alpha]_{436} = +175.1$, $[\alpha]_{365} = +259.8$ ($c = 1.22$). IR: 3300, 2950, 1680, 1450, 1380, 1130, 1050. ^{1}H-NMR (200 MHz): 0.93 (*s*, 3 H); 0.95 (*s*, 3 H); 1.00 (*s*, 3 H); 1.15 (*s*, 3 H); 1.3–1.5 (2 H); 1.8–2.3 (6 H); 2.35 (*s*, 3 H); 3.42 (*d*, $J = 13.5$, 1 H); 3.51 (*d*, $J = 13.5$, 1 H); 3.53 (*d*, $J = 8$, 1 H); 3.9 (*dd*, $J = 7.5, 5.5$, 1 H). ^{13}C-NMR (50 MHz): 174.81 (*s*); 67.23 (*d*); 65.48 (*d*); 53.10 (*t*); 48.39 (*s*); 47.74 (*s*); 44.55 (*d*); 38.77 (*t*); 33.41 (*q*); 32.90 (*t*); 29.32 (*d*); 26.31 (*t*); 20.76 (*q*); 20.21 (*q*); 19.88 (*q*); 17.65 (*q*). MS: 285 (0.6, $[C_{16}H_{28}N_2O_3S - C_3H_7]^+$, 86 (100), 71 (6), 70 (5), 55 (10). HR-MS: 86.0969 ($[C_{16}H_{28}N_2O_3S - C_{11}H_{16}NO_3S]^{+\cdot}$, calc. 86.0970.

(2S,2'S)-N-*[2'-(Methylamino)-4'-methylpentanoyl]bornane-10,2-sultam* (**6c**). Using the *General Procedure*, **5b** (0.29 g, 0.8 mmol) was reduced with Zn to give crude **6c** (0.24 g, 87%). FC (CH_2Cl_2/AcOEt 5:1) afforded pure **6c** (0.21 g, 76%). M.p. 123–125°. $[\alpha]_D = -122.6$, $[\alpha]_{578} = -120.5$, $[\alpha]_{546} = -113.2$, $[\alpha]_{436} = -72.7$, $[\alpha]_{365} = -26.9$ ($c = 0.78$). IR: 3320, 2950, 1690, 1460, 1325, 1270, 1230, 1160, 1130, 1060. ^{1}H-NMR (200 MHz): 0.93 (*d*, $J = 7$, 3 H); 0.96 (*d*, $J = 7$, 3 H); 1.00 (*s*, 3 H); 1.20 (*s*, 3 H); 1.3–2.2 (10 H); 2.35 (*s*, 3 H); 3.45 (*d*, $J = 14$, 1 H); 3.55 (*d*, $J = 14$, 1 H); 3.82–3.94 (2 H). ^{13}C-NMR (50 MHz): 175.72 (*s*); 65.42 (*d*); 60.26 (*d*); 53.03 (*t*); 48.58 (*s*); 47.75 (*s*); 44.56 (*d*); 40.45 (*t*); 38.74 (*t*); 33.42 (*q*); 32.85 (*t*); 26.34 (*t*); 24.58 (*d*); 23.49 (*q*); 21.63 (*q*); 20.72 (*q*); 19.85 (*q*). MS: 100 (100, $[C_{17}H_{30}N_2O_3S - C_{11}H_{18}NO_3S]^{+\cdot}$), 98 (2.5), 79 (2.0), 67 (2.6), 58 (13.75), 55 (4.1). HR-MS: 98.0952 ($[C_{17}H_{30}N_2O_3S - C_{11}H_{18}NO_3S]^{+\cdot}$, calc. 98.0969).

(2S,2'S)-N-*[2'-(Methylamino)-3'-phenylpropionyl]bornane-10,2-sultam* (**6d**). Using the *General Procedure*, **5d** (0.21 g, 0.53 mmol) was reduced with Zn to give crude **6d** (0.18 g, 90%). Recrystallization from CH_2Cl_2/hexane gave pure **6d** (0.15 g, 75%). M.p. 192–194°. $[\alpha]_D = -140.9$, $[\alpha]_{578} = -138.4$, $[\alpha]_{546} = -125.5$, $[\alpha]_{436} = -48.2$, $[\alpha]_{365} = +61.8$ ($c = 0.45$). IR: 3320, 3020, 2960, 1680, 1475, 1450, 1380, 1275, 1170. ^{1}H-NMR (400 MHz): 0.96 (*s*, 3 H); 0.99 (*s*, 3 H); 1.18–1.42 (2 H); 1.88–2.17 (5 H); 2.32 (*s*, 3 H); 2.70 (*dd*, $J = 14$, 8, 1 H); 3.15 (*dd*, $J = 14$,4, 1 H); 3.46 (*d*, $J = 13.5$, 1 H); 3.54 (*d*, $J = 13.5$, 1 H); 3.94 (*dd*, $J = 7$, 5, 1 H); 4.12 (*dd*, $J = 8$, 4, 1 H); 7.26–7.29 (5 H). ^{13}C-NMR (50 MHz): 174.60 (*s*); 137.85 (*s*); 129.48 (*d*); 128.27 (*d*); 126.43 (*d*); 65.42 (*d*); 63.39 (*d*); 52.99 (*t*); 48.66 (*s*); 47.78 (*s*); 44.62 (*d*); 38.68 (*t*); 37.78 (*t*); 33.68 (*q*); 32.87 (*t*); 26.33 (*t*); 20.82 (*q*); 19.85 (*q*). MS: 148 (23.7, $[C_{20}H_{28}N_2O_3S - 228]^{+\cdot}$), 134 (100), 91 (17.3), 77 (8.5), 55 (10.9). HR-MS: 134.0953 ($[C_{20}H_{28}N_2O_3S - C_{11}H_{16}NO_3S]^{+\cdot}$, calc. 134.0970).

(2S,2'S)-N-*[2'-(Ethylamino)-3'-phenylpropionyl]bornane-10,2-sultam* (**6e**). Using the *General Procedure*, **5e** (0.12 g, 0.3 mmol) was reduced with Zn. The resulting crude foam was crystallized from hexane to yield pure **6e** (0.1 g, 86%). M.p. 195–197° (dec.). $[\alpha]_D = +58.9$, $[\alpha]_{578} = +60.7$, $[\alpha]_{546} = +69.3$, $[\alpha]_{436} = +123.2$, $[\alpha]_{365} = +200$ ($c = 0.28$). IR: 3015, 2965, 1690, 1455, 1335, 1200, 1135. ^{1}H-NMR (400 MHz): 0.98 (*s*, 3 H); 0.99 (*t*, $J = 8$, 3 H); 1.16 (*s*, 3 H); 1.36–1.42 (2 H); 1.87–1.98 (3 H); 2.10–2.18 (2 H); 2.50 (*dq*, $J = 14$, 7, 1 H); 2.57 (*dq*, $J = 14$, 7, 1 H); 2.73 (*dd*, $J = 14$, 8, 1 H); 3.14 (*dd*, $J = 14$, 4, 1 H); 3.45 (*d*, $J = 14$, 1 H); 3.53 (*d*, $J = 14$, 1 H); 3.92 (*t*, $J = 8$, 1 H); 4.17 (*dd*, $J = 8$, 4, 1 H); 7.21–7.29 (5 H). ^{13}C-NMR (100 MHz): 174.95 (*s*); 138.09 (*s*); 129.65 (*d*); 128.17 (*d*); 126.35 (*d*); 65.53 (*d*); 61.84 (*d*); 53.12 (*t*); 48.71 (*s*); 47.83 (*s*); 44.81 (*d*); 41.4 (*t*); 38.7 (*t*); 38.2 (*t*); 33.0 (*t*); 26.4 (*t*); 20.8 (*q*); 19.9 (*q*); 15.3 (*q*). MS: 300 (1.0, $[C_{21}H_{30}N_2O_3S - C_7H_6]^+$, 299 (5.4), 216 (2), 148 (100), 119 (5.8), 104 (2.5), 91 (18.1), 77 (8.6), 56 (22.6). HR-MS: 216.0981 ($[C_{21}H_{30}N_2O_3S - C_{11}H_{12}NO]^+$, calc. 216.1058).

(2S,2'S)-N-*[2'-(Isobutylamino)-3'-phenylpropionyl]bornane-10,2-sultam* (**6f**). Using the *General Procedure*, **5f** (0.16 g, 0.37 mmol) was reduced with Zn to give crude **6f** (0.136 g, 87%). Crystallization from Et_2O provided pure compound **6f** (0.11 g, 71%). M.p. 134–136°. $[\alpha]_D = +64.3$, $[\alpha]_{578} = +67.3$, $[\alpha]_{546} = +76.5$, $[\alpha]_{436} = +132.6$, $[\alpha]_{365} = +212.2$ ($c = 0.98$). IR: 3320, 3020, 2970, 1680, 1450, 1330, 1260, 1230, 1130. ^{1}H-NMR (400 MHz): 0.73 (*d*, $J = 6$, 3 H); 0.78 (*d*, $J = 6$, 3 H); 0.98 (*s*, 3 H); 1.17 (*s*, 3 H); 1.32–1.45 (2 H); 1.6 (*m*, 1 H); 1.85–1.97 (3 H); 2.10–2.15 (2 H); 2.25 (*dd*, $J = 12$, 6, 1 H); 2.34 (*dd*, $J = 12$, 7, 1 H); 2.72 (*dd*, $J = 14$, 8, 1 H); 3.12 (*dd*, $J = 14$, 4, 1 H); 3.43 (*d*, $J = 14$, 1 H); 3.52 (*d*, $J = 14$, 1 H); 3.92 (*dd*, $J = 8$, 7, 1 H); 4.12 (*dd*, $J = 9$, 4, 1 H); 7.17–7.32 (5 H). ^{13}C-NMR (100 MHz): 175.04 (*s*); 138.30 (*s*); 129.70 (*d*); 128.06 (*d*); 126.24 (*d*); 65.47 (*d*); 62.02 (*d*); 54.83 (*t*); 53.12 (*t*); 48.69 (*s*); 47.82 (*s*); 44.83 (*d*); 38.72 (*t*); 38.02 (*t*); 32.98 (*t*); 28.45 (*d*); 26.43 (*t*); 20.77 (*q*); 20.40 (*q*); 20.23 (*q*); 19.90 (*q*). MS: 417 (0.2, $[C_{23}H_{34}N_2O_3S - H]^+$, 329 (2.7), 328 (7.4), 327 (40.6), 177 (13.8), 176 (100), 135 (9.15), 120 (27.3), 91 (13.2), 77 (4.1), 57 (21.7), 55 (6.5). HR-MS: 327.1750 ($[C_{23}H_{34}N_2O_3S - C_7H_7]^+$, calc. 327.1758).

(2S,2'S)-N-*[3'-(Methoxycarbonyl)-2'-(methylamino)propionyl]bornane-10,2-sultam* (**6g**). Using the *General Procedure*, **5g** (0.11 g, 0.3 mmol) was reduced with Zn to give crude **6g** (oil, 0.092 g, 92%) which was crystallized from hexane yielding pure **6g** (0.078, 78%). M.p. 104–106°. $[\alpha]_D = +50.3$, $[\alpha]_{578} = +52.4$, $[\alpha]_{546} = +59.2$, $[\alpha]_{436} = +97.3$, $[\alpha]_{365} = +139.5$ ($c = 1.47$). IR, NMR, and MS identical with those of **11g**.

(2R,2'R)-N-*[2'-(Methylamino)propionyl]bornane-10,2-sultam* (**11a**). Using the *General Procedure*, **10a** (0.22 g, 0.69 mmol) was reduced with Zn to give crude **11a** (oil, 0.19 g, 92%) which was subjected to FC (AcOEt/hexane 5:1) and crystallization from hexane affording pure **11a** (0.15 g, 74%). M.p. 110–112°. $[\alpha]_D = -59.8$, $[\alpha]_{578} = -64.3$, $[\alpha]_{546} = -69.6$, $[\alpha]_{436} = -113.4$, $[\alpha]_{365} = -161.6$ ($c = 1.12$). IR, NMR, and MS identical with those of **6a**. HR-MS: 58.0640 ($[C_{14}H_{24}N_2O_3S - C_{11}H_{16}NO_3S]^+$, calc. 58.0657).

(2R,2'R)-N-*[2'-(Ethylamino)-3'-phenylpropionyl]bornane-10,2-sultam* (**11e**). Using the *General Procedure*, **10e** (0.20 g, 0.49 mmol) was reduced with Zn, and the crude product was crystallized from hexane to give pure **11e** (0.17 g, 88.5%). M.p. 199–201° (dec.). $[\alpha]_D = -73.9$, $[\alpha]_{578} = -76.5$, $[\alpha]_{546} = -87.8$, $[\alpha]_{436} = -150.4$, $[\alpha]_{365} = -240$ ($c = 1.15$). IR, NMR, and MS identical with those of **6e**. HR-MS: 299.1432 ($[C_{21}H_{30}N_2O_3S - C_7H_7]^+$, calc. 299.1429).

(2R,2'R)-N-*[2'-(Isobutylamino)-3'-phenylpropionyl]bornane-10,2-sultam* (**11f**). Using the *General Procedure*, **10f** (293 mg, 0.67 mmol) was reduced with Zn to give crude **11f** (268 mg, 95%). FC and crystallization from Et_2O provided pure **11f** (249 mg, 88%). M.p. 136–138°. $[\alpha]_D = -77.8$, $[\alpha]_{578} = -81.2$, $[\alpha]_{546} = -92.6$, $[\alpha]_{436} = -159.0$, $[\alpha]_{365} = -251.6$ ($c = 0.298$). IR, NMR, and MS identical with those of **6f**.

(2R,2'R)-N-*[3'-(Methoxycarbonyl)-2'-(methylamino)propionyl]bornane-10,2-sultam* (**11g**). Using the *General Procedure*, **10g** (0.16 g, 0.43 mmol) was reduced with Zn to give crude **11g** (0.14 g, 92%) as an oil, which was crystallized from hexane affording pure **11g** (0.12 g, 78%). M.p. 104–106°. $[\alpha]_D = -56.7$, $[\alpha]_{578} = -58.2$, $[\alpha]_{546} = -65.7$, $[\alpha]_{436} = -107.5$, $[\alpha]_{365} = -159.7$ ($c = 0.67$). IR: 3350, 2960, 1740, 1690, 1450, 1330, 1270, 1230, 1140. ^{1}H-NMR (400 MHz): 0.99 (*s*, 3 H); 1.18 (*s*, 3 H); 1.32–1.45 (2 H); 1.83–1.99 (3 H); 2.17–2.20 (2 H); 2.34 (*s*, 3 H); 2.53 (*dd*, $J = 16$, 8, 1 H); 2.84 (*dd*, $J = 16$, 6, 1 H); 3.46 (*d*, $J = 14$, 1 H); 3.54 (*d*, $J = 14$, 1 H); 3.69 (*s*, 3 H); 3.94 (*dd*, $J = 8$, 5, 1 H); 4.31 (*dd*, $J = 8$, 6, 1 H). ^{13}C-NMR (100 MHz): 173.19 (*s*); 171.06 (*s*); 65.39 (*d*); 58.27 (*d*);

52.99 (*t*); 51.85 (*q*); 48.75 (*s*); 47.81 (*s*); 44.72 (*d*); 38.71 (*t*); 35.79 (*t*); 32.91 (*t*); 32.69 (*q*); 26.40 (*t*); 20.82 (*q*); 19.90 (*q*). MS: 130 (8, $([C_{16}H_{26}N_2O_5S - C_6H_{26}NO_2]^+$, 116 (100), 84 (24.5), 74 (9), 57 (13.8), 56 (11.8), 55 (11). HR-MS: 116.0653 ($[C_{16}H_{26}N_2O_5S - C_{11}H_{16}NO_3S]^+$, calc. 116.0711).

Saponification of N-*[2-(Alkylamino)acyl]bornane-10,2-sultams and Determination of the Enantiomeric Purity of Resulting* N-*Methyl(alkyl)amino Acid. General Procedure.* A 1N LiOH soln. (1 ml) was added to a soln. of *N*-[2-(*N*-alkylamino)acyl]bornane-10,2-sultam **6** or **11** (0.25 mmol) in THF (2 ml), and the mixture was stirred at 0° until completion of the reaction (TLC). Then, the THF was evaporated, and the resulting aq. phase was partitioned between CH_2Cl_2 and H_2O. The combined org. extracts were washed with H_2O, dried ($MgSO_4$), and evaporated to give the bornane-10,2-sultam auxiliary (85–100%). Acidification of the combined aq. layers to pH 7, addition of ion-exchange resin (*Amberlite IR-120*, 2.0 g) stirring for 16 H, filtration, washing of the resin with dist. H_2O (until the filtrate remained clear upon addition of $AgNO_3$/EtOH), stirring of the resin with 7N aq. NH_3 soln. (40 ml) for 4 h, filtration and evaporation of the filtrate, addition of THF/toluene or EtOH/Et_2O, evaporation, and drying of the solid residue *in vacuo* provided the corresponding *N*-methyl(alkyl)amino acid. To determine its enantiomeric excess, a soln. of 2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyl isothiocyanate (GITC, 2 mg) in MeCN (0.1 ml) was added to a soln. of the corresponding *N*-alkylamino acid (0.1 mg) and NEt_3 (2 µl) in MeCN/H_2O 1:1 (0.1 ml). The mixture was kept at r.t. for 20 min. Addition of a 4M aq. soln. of NH_3 (20 µl), stirring for 5 min, and addition of a 4M aq. soln. of AcOH (0.3 ml) gave a soln. from which samples (20 µl) were directly injected into the chromatograph for HPLC analysis.

(2S)-N-*Methylalanine* (**7a**). Using the *General Procedure*, **6a** (0.033 g, 0.11 mmol) was saponified to give recovered **1** (0.019 g, 83%) and **7a** (0.010 g, 91%). $[\alpha]_D = +5.6$ (*c* = 1.0, H_2O). IR (KBr): 3650–3450, 3200–2300, 1580, 1475, 1400, 1350, 1100, 1050, 825, 670. ^{1}H-NMR (200 MHz, D_2O): 1.29 (*d*, *J* = 7.2, 3 H); 2.51 (*s*, 3 H); 3.42 (*q*, *J* = 7.2, 1 H). ^{13}C-NMR (50 MHz, D_2O): 174.85 (*s*); 58.82 (*d*); 30.89 (*q*); 14.49 (*q*). MS: 149 (28), 103 (8), 91 (12), 73 (10), 58 (100). HPLC (thiourethane **13**): 8.87 (58.96), 10.82 (0.96).

(2S)-N-*Methylvaline* (**7b**). Using the *General Procedure*, **6b** (0.023 g, 0.07 mmol) was saponified to give recovered **1** (0.012 g, 80%) and **7b** (8.4 mg, 90%). M.p. > 230°. $[\alpha]_D = +30.9$ (*c* = 1.0, 5N aq. HCl). IR (KBr): 3200–2650, 1575, 1450, 850. ^{1}H-NMR (200 MHz, D_2O): 0.70 (*d*, *J* = 7.5, 3 H); 0.75 (*d*, *J* = 7.5, 3 H); 1.70 (*m*, 1 H); 2.15 (*s*, 3 H); 2.67 (*d*, *J* = 7.5, 1 H). ^{13}C-NMR (50 MHz, D_2O): 172.81 (*s*); 69.71 (*d*); 32.68 (*q*); 29.15 (*d*); 17.85 (*q*); 17.42 (*q*). MS: 132 (2.4, $[C_6H_{13}NO_2 - 1]^+$), 131 (0.6), 88 (69.1), 86 (100), 71 (18.8), 70 (21.2), 55 (28.7), 45 (6.3). HPLC (thiourethane **13**): 15.48 (20.61), 17.94 (0.046).

(2S)-N-*Methylleucine* (**7c**). Using the *General Procedure*, **6c** (50 mg, 0.15 mmol) was saponified to give recovered **1** (29 mg, 93%) and **7c** (20 mg, 100%). M.p. > 200° (sublimes). IR (KBr): 3200–2400, 1600, 1500, 850, 675. ^{1}H-NMR (200 MHz, D_2O): 0.74 (br. *s*, 3 H); 0.77 (br. *s*, 3 H); 1.40–1.60 (3 H); 2.50 (*s*, 3 H); 3.37 (br. *t*, *J* = 6, 1 H). ^{13}C-NMR (50 MHz, D_2O): 174.29 (*s*); 62.71 (*d*); 38.97 (*t*); 31.76 (*q*); 24.35 (*d*); 21.93 (*q*); 21.38 (*q*). MS: 146 (1.4, $[C_7H_{15}NO_2 + 1]^+$), 145 (0.7), 100 (100), 88 (40.7), 70 (10.4), 58 (94.1), 45 (12.5). HPLC (thiourethane **13**): 20.31 (25.89), 23.26 (0.031).

(2S)-N-*Methylphenylalanine* (**7d**). Using the *General Procedure*, **6d** (94 mg, 0.25 mmol) was saponified to give recovered **1** (48 mg, 90%) and **7d** (41 mg, 92%). M.p. 243–246° (dec.). $[\alpha]_D = +7.6$ (*c* = 0.5, 5N aq. HCl). IR (KBr): 3200–2300, 1625, 1485, 1475, 1450, 1430, 875, 860, 750, 700. ^{1}H-NMR (200 MHz, D_2O): 2.25 (*s*, 3 H); 2.85 (*d*, *J* = 7.5, 2 H); 3.30 (*t*, *J* = 7.5, 1 H); 7.0–7.3 (5 H). MS: 179 (3.3, $C_{10}H_{13}NO_2^+$), 148 (10), 134 (25), 119 (7.5), 102 (9.5), 88 (100), 65 (6.6). HPLC (thiourethane **13**): 21.86 (21.96), 24.47 (0.0).

(2S)-N-*Ethylphenylalanine* (**7e**). Using the *General Procedure*, **6e** (77 mg, 0.2 mmol) was saponified to give recovered **1** (37 mg, 88%) and **7e** (35 mg, 92%). M.p. 238–240° (dec.). IR (KBr): 3100–2350, 1580, 1440, 1400, 800, 750, 665. ^{1}H-NMR (400 MHz, D_2O): 1.02 (*t*, *J* = 7, 3 H); 2.77 (*dq*, *J* = 14, 7, 2 H); 2.95 (*dd*, *J* = 14, 7, 2 H); 3.58 (*t*, *J* = 7, 1 H); 7.09–7.24 (5 H). MS: 194 (0.62, $[C_{11}H_{15}NO_2 + 1]^+$), 148 (16.25), 120 (11.1), 103 (11.3), 102 (100), 91 (18.7), 77 (9.4), 65 (11.3), 56 (59.3), 46 (4.6). HPLC (thiourethane **13**): 26.44 (41.22), 27.39 (0.0).

(2S)-N-*Isobutylphenylalanine* (**7f**). Using the *General Procedure*, **6f** (50 mg, 0.12 mmol) was saponified to give recovered **1** (25 mg, 96%) and **7f** (26 mg, 98%). M.p. > 235–240° (sublimes). IR (KBr): 3200–2700, 1560, 1450, 1380, 830, 700. ^{1}H-NMR (400 MHz, D_2O): 0.71 (*d*, *J* = 4, 3 H); 0.73 (*d*, *J* = 4, 3 H); 1.66 (*m*, 1 H); 2.37 (*dd*, *J* = 12, 8, 1 H); 2.45 (*dd*, *J* = 12, 7, 1 H); 2.85 (*dd*, *J* = 14, 8, 1 H); 2.92 (*dd*, *J* = 14, 6, 1 H); 3.40 (*t*, *J* = 7, 1 H); 7.07–7.22 (5 H). MS: 222 (1.7, $[C_{13}H_{19}NO_2 + 1]^+$), 176 (11.4), 130 (91.8), 120 (29.3), 103 (12.6), 91 (38.1), 84 (10.7), 77 (18.6), 74 (51.2), 65 (19.9), 57 (100), 55 (11.8), 51 (15.5), 45 (10.3). HPLC (thiourethane **13**): 19.99 (29.55), 20.68 (0.0).

(2S)-N-*Methylaspartic Acid* (**7g**). Using the *General Procedure*, **6g** (20 mg, 0.056 mmol) was saponified to give recovered **1** (11 mg, 92.5%) and **7g** (7.5 mg, 94%). M.p. 187–190°. IR (KBr): 3600–3000, 1630, 1490, 1420, 1130, 870. ^{1}H-NMR (400 MHz, D_2O): 2.60 (*s*, 3 H); 2.82 (*dd*, *J* = 16, 6, 1 H); 2.88 (*dd*, *J* = 16, 6, 1 H); 3.72 (*t*, *J* = 6, 1 H). MS: 147 (0.7, $C_5H_9NO_4^{+\cdot}$), 102 (100), 88 (14), 84 (34.6), 60 (16.4), 57 (23.45), 56 (18.8). HPLC (thiourethane **13**): 12.44 (88.44), 13.30 (1.63).

(2R)-N-Methylalanine (**12a**). Using the *General Procedure*, **11a** (79 mg, 0.26 mmol) was saponified to give recovered *ent*-**1** (53 mg, 95%) and **12a** (26 mg, 94%). $[\alpha]_D = -5.6$ ($c = 1.0$, H_2O). IR (KBr): 3650–3450, 3200–2300, 1580, 1475, 1400, 1350, 1100, 1050, 825, 670. ^{1}H-NMR (400 MHz, D_2O): 1.27 (*d*, $J = 7.2$, 3 H); 2.46 (*s*, 3 H); 3.31 (*m*, 1 H). HPLC (thiourethane **13**): 8.60 (2.26), 10.35 (62.45).

(2R)-N-Ethylphenylalanine (**12e**). Using the *General Procedure*, **11e** (131 mg, 0.33 mmol) was saponified to give recovered **1** (63 mg, 89%) and **12e** (59 mg, 91%). M.p. 238–240° (dec.). IR (KBr): 3100–2350, 1580, 1440, 1400, 800, 750, 665. ^{1}H-NMR (400 MHz, D_2O): 1.06 (*t*, $J = 7$, 3 H); 2.86 (*dq*, $J = 14$, 7, 2 H); 3.00 (*dd*, $J = 14$, 7, 2 H); 3.66 (*t*, $J = 7$, 1 H); 7.12–7.23 (5 H). MS: 193 (0.2, $C_{11}H_{15}NO_2^{+\cdot}$), 148 (24.2), 120 (10.6), 102 (100), 91 (23.1), 77 (9.8), 56 (27.3), 46 (53). HPLC (thiourethane **13**): 26.04 (0.0), 27.27 (34.66).

(2R)-N-Isobutylphenylalanine (**12f**). Using the *General Procedure*, **11f** (223 g, 0.53 mmol) was saponified to give recovered **1** (115 mg, 91%) and **12f** (106 mg, 90%). M.p. 236–238° (dec.). HPLC (thiourethane **13**): 20.68 (15.19), 21.45 (0.0).

(2R)-N-Methylaspartic Acid (**12g**). Using the *General Procedure*, **11g** (42 mg, 0.12 mmol) was saponified to give recovered *ent*-**1** (23 mg, 92%) and **12g** (16 mg, 94%). M.p. 187–190°. IR (KBr): 3600–3000, 1630, 1490, 1420, 1130, 870. ^{1}H-NMR (400 MHz, D_2O): 2.60 (*s*, 3 H); 2.82 (*dd*, $J = 16$, 6, 1 H); 2.88 (*dd*, $J = 16$, 6, 1 H); 3.72 (*t*, $J = 6$, 1 H). MS: 148 (1.1, $[C_5H_9NO_4 + 1]^{+\cdot}$), 147 (0.7), 129 (3.9), 102 (100), 88 (18.6), 84 (49.1), 70 (12.3), 60 (46.75), 56 (42.7), 45 (47.1). HPLC (thiourethane **13**): 12.44 (0.0), 13.26 (90.10).

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