207. Asymmetric Induction at C(β) and C(α) of *N*-Enoylsultams by Organomagnesium 1,4-Addition/Enolate Trapping

by **Wolfgang Oppolzer***, **Giovanni Poli, Arend J. Kingma, Christian Starkemann,** and **Gérald Bernardinelli**

Département de Chimie Organique, Université de Genève, CH-1211 Genève 4

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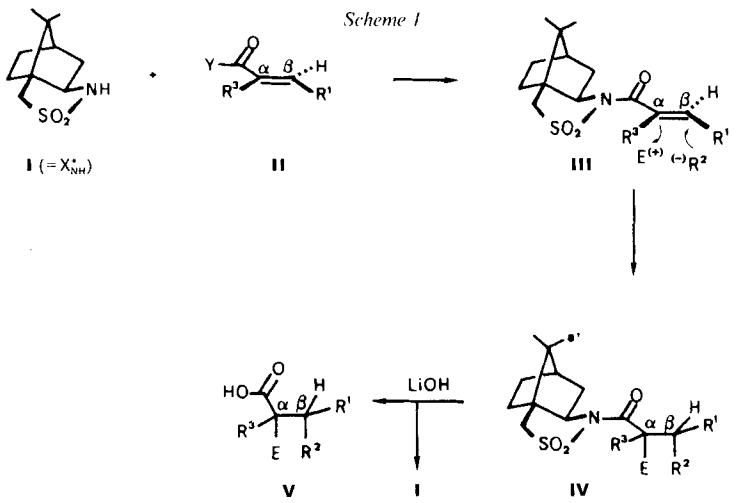
The 1,4-addition of alkylmagnesium chlorides to conjugated *N*-enoylsultams and subsequent 'enolate trapping' with aq. NH_4Cl or MeI/hexamethylphosphoric triamide generated centers of asymmetry at C(β) and/or at C(α) with good to excellent π-face differentiation as demonstrated by the conversions **1**→**2**, **1**→**4**, and **8**→**9**. This holds also for the regioselective 1,4-addition of EtMgCl to a dienoylsultam (**15**→**16**). Reactive conformations **1**$^{\neq}$, **8**$^{\neq}$, **13**, and **14** are postulated in agreement with X-ray evidence which also served for the structure determination of the product **9j**.

Introduction. – Stereoface-selective 1,4-additions of organometallic nucleophiles to conjugated carbonyl derivatives which carry a chiral auxiliary are among the most reliable approaches to enantiomerically pure C(β)-substituted carbonyl compounds[1]). As part of extensive work on asymmetric β-additions of organocopper reagents to enoates [3] [4], we showed that the same ester auxiliary may also induce chirality at C(α) in a subsequent deprotonation/electrophilic substitution step [4] [5]. However, a related 'one-pot' formation of two centers of asymmetry (at C(β) and C(α)) in an open chain[2]) *via*

Scheme 1



[1]) Review, see [1]; further references, see [2] [3].

[2]) For previously recorded cases of C(β),C(α) inductions in cyclic systems, see [2].

electrophilic trapping of the enolate intermediate is even more attractive. Recently, this goal has been achieved by alkyllithium addition/alkylation of α,β-unsaturated iron-acyl complexes [6]. Another example is the tandem hydride addition/C(α)-protonation or methylation **III**→**IV** ($R^{2(-)} = H^-$, $E^{(+)} = H^+$ or Me^+; *Scheme 1*) [7].

We continued to explore the bis-functionalization **III**→**IV** by employing C-nucleophiles $R^{2(-)}$[3]). As a complement to preliminary reports [4] [9], we describe here in detail convenient alkylmagnesium-chloride β-addition/enolate-trapping processes **III**→**IV**. As usual [4] [10], enoylsultams **III** were readily obtained by acylation of sultam **I** with NaH/acyl chlorides **II** (Y = Cl) or with Me_3Al/esters **II** (Y = OMe) and purified by crystallization.

Conjugate Addition of *Grignard* Reagents to β-Substituted (*E*)-Enoylsultams and Subsequent 'Enolate' Protonation. – We first addressed the issue of induction at C(β) (*Scheme 2*, *Table 1*). Simple alkylmagnesium chlorides added smoothly in a 1,4-fashion to β-substituted (*E*)-enoylsultams **1** to give, on subsequent treatment with aq. NH_4Cl, imides **2**/**3** in good yields. No 1,2-additions were observed, except with methyl *Grignard*

Scheme 2

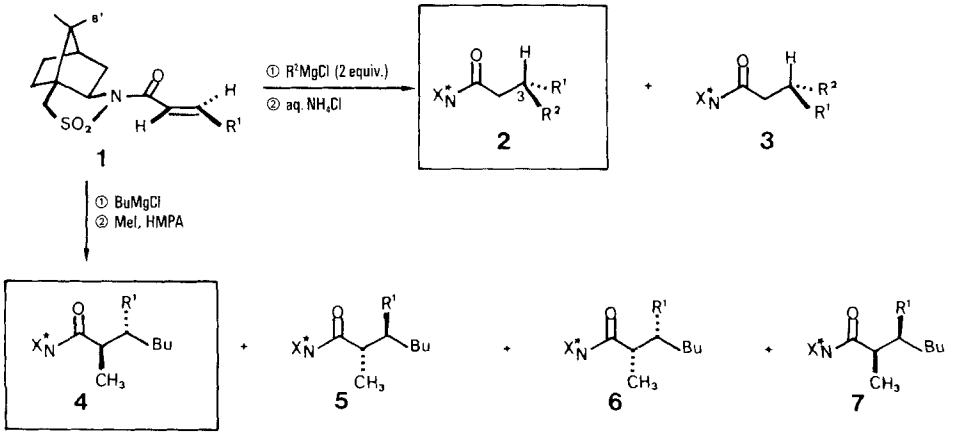


Table 1. *Conjugate Additions of R^2MgCl to β-Substituted (E)-Enoylsultams and Subsequent 'Enolate' Protonation:* **1**→**2** + **3**

	R^1	R^2	Yield [%] of **2** + **3**	Ratio **2**/**3**	Configuration of **2**
a	Me	Et	80	94.5:5.5	3*R*
b	Me	Pr	90	92.6:7.4	3*R*
c	Me	i-Pr	92	86.2:13.8	3*S*
d	Me	Bu	78	93.2:6.8	3*R*
e	Me	Hexyl	73	91.9:8.1	3*R*
f	Me	Octyl	81	90.9:9.1	3*R*
g	Et	Bu	89	94.7:5.3[a])	3*R*

[a]) By ^{1}H-NMR.

[3]) For a related organocopper addition/transmetallation/*Mannich* reaction sequence, see [8].

reagents. The extent of diastereoface differentiation was determined by capillary-GC analyses of the crude reaction mixtures. Comparisons (GC, ^{1}H-NMR) with authentic samples of **2** [11], **3a**, and **3b** [7] served to assign the absolute configurations of **2a–f**. Imide **2g** was shown to possess the (3*R*)-configuration by mild saponification (LiOH, aq. THF) to (3*R*)-3-ethylheptanoic acid, the optical rotation of which was compared with a previously reported value [12]. In all cases listed in *Table 1*, product **2** dominated significantly over its epimer **3**. Addition of the sterically more demanding i-PrMgCl to **1** (R^1 = Me) resulted in a comparatively low diastereoisomeric excess (d.e.) of **2c** (72.4%).

Conjugate Addition of *Grignard* Reagents to β-Substituted (*E*)-Enoylsultams and Subsequent 'Enolate' Methylation. – We then explored the possibility of generating, starting from **1**, a second chiral center at C(α) (*Scheme 2, Table 2*). Treatment of **1** (R^1 = Me) with BuMgCl and methylation of the resulting magnesium 'enolate' by addition of MeI/hexamethylphosphoric triamide (HMPA) afforded a 86.7:4.7:8.6 mixture **4a**/**6a**/**7a** in 80% yield. Not even a trace of the (2*S*,3*S*)-isomer **5a** could be detected by

Table 2. *Conjugate Additions of BuMgCl to β-Substituted (E)-Enoylsultams and Subsequent 'Enolate' Methylation:* **1→4 + 6 + 7**

	R^1	Yield [%] **4 + 5 + 6 + 7**	Ratio **4/5/6/7**	**4** (crystallized)				
				Yield [%]	Purity [%]	Configuration	^{1}H-NMR (δ [ppm])	
							CH_3(8′)	CH_3–C(2)
a	Me	80	86.7:0:4.7:8.6	48	97.5	2*R*,3*R*	1.19 (*s*)	1.22 (*d*)
b	Et	58	88.2:0:3.3:8.5	36	98.3	2*R*,3*R*	1.12 (*s*)	1.13 (*d*)

GC. The major product **4a** was isolated in 48% yield and 95% d.e. by crystallization and assigned the (2*R*,3*R*)-configuration based on the following evidence: sultam **1** was reacted with a mixture of the minor (2*RS*,3*SR*)- and the major (2*RS*,3*RS*)-2,3-dimethylheptanoyl chloride [13]; GC analysis of the resulting mixture showed 4 peaks (retention times: 17.73, 17.91, 18.02, 18.28) in a 1:1:1.2:1.2 ratio; accordingly, the last 2 peaks correspond to the (2*RS*,3*RS*)-isomers (see *Exper. Part*). Furthermore, taking into account the preferred formation of the (3*R*)-center in the 1,4-addition step (*Table 1*, **2d**), it follows that the major 1,4-addition/methylation product (last GC peak by coinjection) has the (2*R*,3*R*)-topicity as represented by structure **4a**. Further support for the (2*R*)-assignment of **4a** was provided by the general observation that the ^{1}H-NMR spectra of (2*R*)-2-methyl-substituted acylsultams, derived from (+)-camphor, display the *d* of CH_3–C(2) at lower field relative to the *s* of CH_3(8′) of the bornane moiety[4]). Starting from the homologue **1** with R^1 = Et, the identical 1,4-addition/methylation conditions furnished a 88.2:3.3:8.5 mixture of 3 isomeric products. The major product **4b**, obtained in *ca.* 100% d.e. by crystallization, shows ^{1}H-NMR data in agreement with the assigned (2*R*)-configuration[4]).

[4]) This trend seems to be independent of the substitution and configuration at C(β). Corresponding ^{1}H-NMR data for (2*S*)-2-methylacylsultams were observed for **3a** (1.18 (*s*), 1.16 (*d*) [7]), **3b** (1.18 (*s*), 1.16 (*d*) [7]), and **6a** (1.08 (*s*), 0.99 (*d*) [14]).

Conjugate Addition of *Grignard* Reagents to *N*-Methacryloylsultam and Subsequent 'Enolate' Protonation. – As an alternative method to create a chiral center at C(α) of a carbonyl compound, we then subjected α-substituted enoylsultams **8** to the alkylmagnesium-chloride addition/protonation sequence. The alkylmagnesium chloride (1–2 M solution in Et_2O) was added at −80° to a solution of *N*-methacryloylsultam **8** (R^1 = H) in toluene; warming up to room temperature within 15 min, quenching of the *in situ*-prepared Mg enolate at −95° with an emulsion of sat. aq. NH_4Cl solution in THF afforded *C*-methyl-substituted *N*-acylsultams **9** (R^1 = H) with high diastereofacial differentiation (*Scheme 3*, *Table 3*)[5]).

Even MeMgCl gave conjugate adducts **9a**/**10a** (9:1) although in only 45% yield due to concurrent 1,2-addition. Higher alkyl *Grignard* reagents furnished products **9** (R^1 = H)/**10** (R^1 = H) in ratios ranging from 91.5: 8.5 up to 97:3 (80–93% yield) from which the major epimer **9** (R^1 = H) was routinely isolated in virtually pure form and in good yield by flash chromatography and/or crystallization (see **9b–e**). The (2*R*)-configurations of **9**

Scheme 3

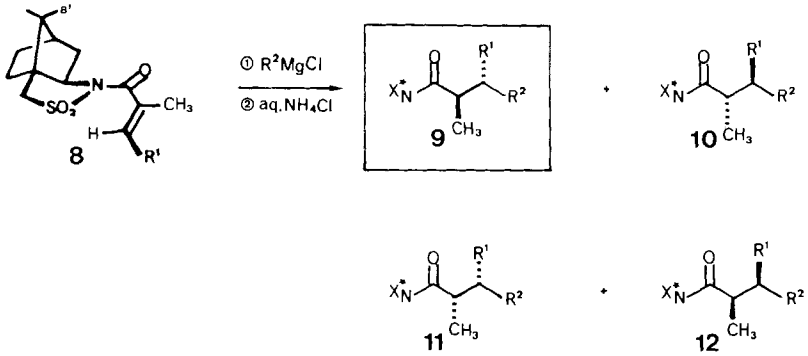


Table 3. *Conjugate Additions of R^2MgCl to* N-*Methacryloylsultam and Subsequent 'Enolate' Protonation:* **8**(R^1 = H)→**9**(R^1 = H) + **10**(R^1 = H)

	R^2	Yield [%] **9**(= **12**) + **10**(= **11**)	Ratio **9**/**10**	**9** (purified)				
				Yield [%]	d.e. [%]	Configuration	^{1}H-NMR (δ [ppm])	
							CH_3(8′)	CH_3–C(2)
a	Me	45	90:10	–[a])	–[a])	2*R*	1.17 (*s*)	1.22 (*d*)
b	Et	92	95:5	70[b])	97.2	2*R*	1.16 (*s*)	1.20 (*d*)
c	Pr	80	97:3	70[b])	99.6	2*R*	1.14 (*s*)	1.19 (*d*)
d	i-Pr	93	95.6:4.4	84[c])	98.0	2*R*	1.13 (*s*)	1.16 (*d*)
e	Bu	81	91.5:8.5	62[c])	100	2*R*	1.13 (*s*)	1.17 (*d*)

[a]) Not purified.
[b]) Flash chromatography.
[c]) Crystallization.

[5]) Compared to *Table 3, Entry* **c**, significantly lower induction (→(2*R*)) was observed on protonation of the transient enolate **14** (R^1 = H, R^2 = Pr) with MeOH (52% d.e.) or with 2,6-di(*tert*-butyl)-4-methylphenol (74% d.e.).

agree with their ^{1}H-NMR spectra and were confirmed in the case of **9a** and **9b** by comparison with authentic samples [7][6]). It is interesting to note that the 1,4-addition/protonation **8**→**9** (*Tables 3* and *4*) reveals a π-face discrimination at C(α) which is opposite to that of the 1,4-addition/methylation process **1**→**4**.

Conjugate Additions of *Grignard* Reagents to α,β-Disubstituted (*E*)-Enoylsultams and Subsequent 'Enolate' Protonations. – Encouraged by the excellent stereodifferentiations for **8**→**9** with R^1 = H, we then studied the generation of two contiguous centers of chirality by submitting α,β-disubstituted (*E*)-enoylsultams to similar conjugate addition/protonation conditions (*Scheme 3*, *Table 4*). A solution of an alkylmagnesium chloride (2.2 mol-equiv. in Et_2O) was added at −80° to a solution of an enoylsultam **8** (R^1 = alkyl) in Et_2O/THF 5:1. To complete the *Michael*-type reaction, the mixture was slowly warmed to −40° and kept at −40° overnight. Protonation at −70° using again an emulsion of sat. aq. NH_4Cl solution in THF provided mixtures of 2–3 of the 4 possible stereoisomeric products **9**–**12** with isomer **9** largely prevailing. In each case (*Table 4*), the major isomer **9** was efficiently purified by flash chromatography and crystallization[7]). Mild saponifica-

Table 4. *Conjugate Addition of R^2MgCl to α,β-Disubstituted (E)-Enoylsultams and Subsequent 'Enolate' Protonation:* **8**→**9** + **11** + **12**

	R^1	R^2	Yield [%] **9** + **10** + **11** + **12**	Ratio **9**/**10**/**11**/**12**	**9** (crystallized) Yield [%]	Purity [%]	Configuration	^{1}H-NMR (δ [ppm]) $CH_3(8')$	CH_3–C(2)
f	Me	Et	90	99.0:0:1.0:0	81	99.7	2*R*,3*R*	1.15 (*s*)	1.18 (*d*)
g	Me	Bu	73	98.2:0.2:0.9:0.7	66	100	2*R*,3*R*	1.19 (*s*)	1.22 (*d*)
h	Me	Ph	–[a])	97.0:0:2.4:0.6	48	99.3	2*R*,3*S*	1.10 (*s*)	1.21 (*d*)
i	Et	Bu	90	97.0:0:2.6:0.4	78	100	2*R*,3*R*	1.12 (*s*)	1.13 (*d*)
j	Bu	Et	82	96.5:0:1.4:2.1	60	99.8	2*R*,3*S*	1.06 (*s*)	1.07 (*d*)

[a]) Not determined.

tion of **9f** furnished sultam auxiliary **I** and (2*R*,3*R*)-2,3-dimethylpentanoic acid [15] which exemplifies the overall transformation **II**→**V** and serves as evidence for the (2*R*,3*R*)-configuration of **9f**. Products **9g** and **9i** were readily shown to possess also the (2*R*,3*R*)-topicity by identifying them with the above described addition/methylation products **4a** and **4b**, respectively. All products **9** display ^{1}H-NMR spectra in accord with a (2*R*)-configuration[4]). This applies also to the 3-phenyl derivative **9h** which has been ascribed the (3*S*)-configuration based on analogy. Unequivocal proof for the (2*R*,3*S*)-chirality of **9j** was obtained by means of an X-ray-diffration analysis (*Figure*) accounting for the known configuration of the camphor-derived sultam moiety as well as for a least-squares refinement of the absolute-structure parameter *x* [16].

Accordingly, *Table 4* reveals synthetically relevant inductions at C(β) and C(α)(→(2*R*)) of **9** which derive solely from the auxiliary **I**. The synthesis of **9i** and **9j** thus exemplify the option to alternate the developing configuration at C(β)(→(3*R*) or (3*S*))

[6]) For comparison (GC, ^{1}H-NMR), mixtures **9c**/**10c** and **9d**/**10d** were prepared by acylation of sultam **I** with the corresponding racemic acyl chlorides.

[7]) The configurations of the minor products were not assigned except for **11f**, **11g**, **12g**, and **12j** (= **9i**) (GC comparison with authentic samples, see *Exper. Part*).

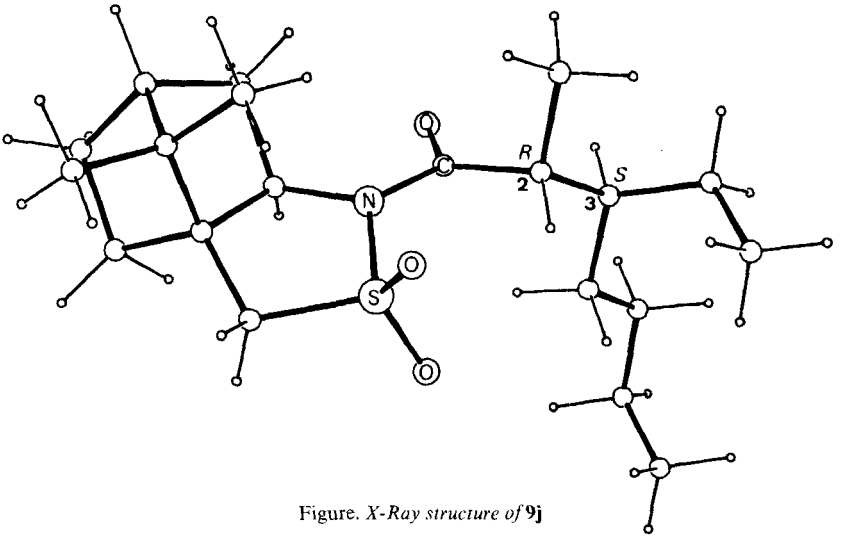


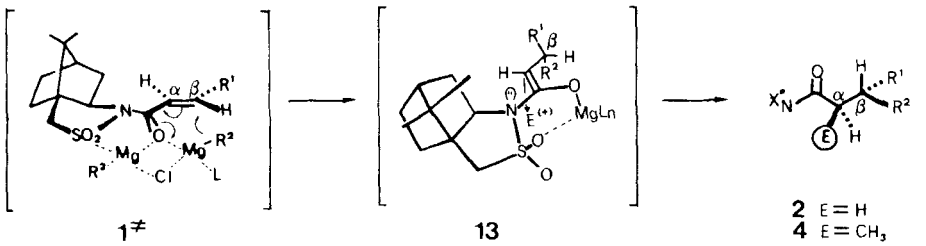
Figure. *X-Ray structure of* **9j**

by permutation of R^1 and the '*Grignard* substituent' R^2 independent of the stereochemical outcome at C(α)(→(2*R*)).

Stereochemical Rationalization, Regio- and Face-Selective Addition of Ethylmagnesium Chloride to [(*E*,*E*)-2,4-Hexadienoyl]sultam. – The stereoface differentiations observed throughout this work are consistent with the transition-state topologies presented in *Schemes 4* and *5*. Focussing this discussion first on the 1,4-additions to C(α)-unsubstituted enoylsultams **1**, it appears that the conformation found in crystalline **1**, with R^1 = Me (C=O/SO_2 antiperiplanar, C=O/C(α),C(β) s-*cis*, and a pyramidal N-atom) [17], differs from that of transition state **1**$^{\neq}$ (*Scheme 4*) which features rather a Mg-chelated SO_2/C=O synperiplanar disposition.

This explains the need of > 2 mol-equiv. of alkylmagnesium chloride for achieving successful 1,4-additions to enoylsultams **1** and **8**. We thus assume delivery of R^2 to **1**$^{\neq}$ from the bottom side, opposite to the lone pair on the N-atom[8]) *via* a 6-membered cyclic

Scheme 4

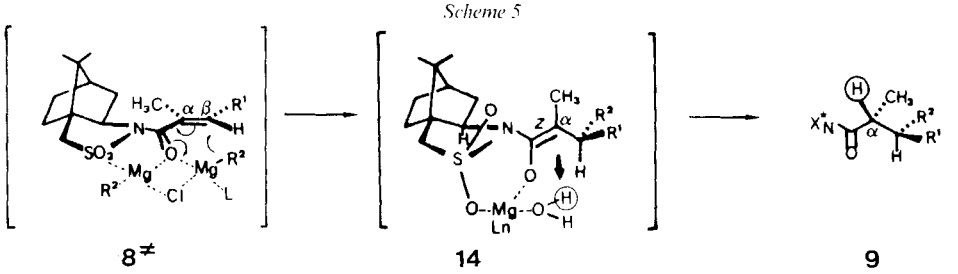


[8]) The possibility of a π-face-directing bias of the pyramidal N-atom on the electrophilic attack of enamines and *N,O*-ketene acetals was first evoked by *Eschenmoser* and coworkers [18]. Similar stereoelectronic control of nucleophilic 1,4-additions to enoylsultams **1** and **8** may be operational. The above postulate relates even more closely to the stereoface-selective reactions of electrophiles with *O*-metalated *N,O*-ketene acetals such as **13** and other reported examples [7] [8] [19].

mechanism [20] which is compatible with the depicted C=O/C(α),C(β) s-*cis* conformation. During this process, the C=O/C(α),C(β) s-*cis* conformation apparently translates into the 'enolate' (*Z*)-configuration of **13**[9]). To explain the subsequent stereoface-selective methylations **13**→**4**, we propose for **13** the depicted conformation which parallels that of the *O*-pivaloyl derivative of **13** with R^1 = Pr and R^2 = H [9] [22]. Sterically or stereoelectronically[8]) auxiliary-directed electrophilic attack from the bottom side of **13** provides the (2*R*)-products **4** with good π-face differentiation despite the counteracting bias of the C(β)-center ($R^2 > R^1$).

Examination of *Scheme 3* and *Table 4* reveals that *Grignard* reagents undergo 1,4-additions to α,β-disubstituted (*E*)-enoyl sultams **8** from the same π-face as they do with the β-monosubstituted (*E*)-enoyl derivatives **1**. We believe that the C=O/SO_2 antiperiplanar and C=O/C(α),C(β) s-*trans* conformation of **8**, as indicated by X-ray evidence [9] [17], is irrelevant in this reaction series. It is much more plausible to assume again a chelation by Mg (C=O/SO_2 synperiplanar) and the operation of a cyclic transition state C=O··Mg··R^2··C(β) which enforces the C=O/C(α),C(β) s-*cis* conformation of $\mathbf{8}^{\neq}$, regardless of the C(α)-methyl/bornane repulsion (*Scheme 5*).

Scheme 5



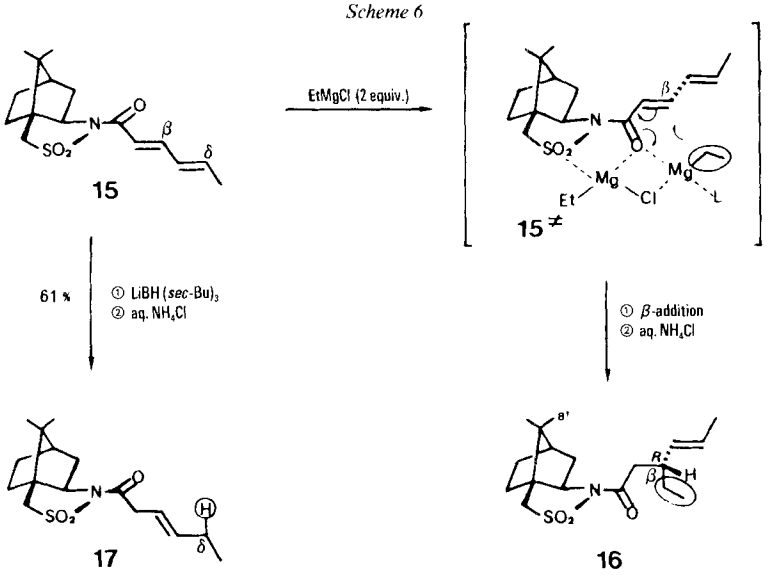
$\mathbf{8}^{\neq}$ **14** **9**

This reactive s-*cis* conformation of $\mathbf{8}^{\neq}$ would entail the stereoselective formation of (*Z*)-enolates **14**[9]) which was confirmed by ^{1}H-NMR and X-ray studies of the *O*-acetyl derivative of **14** and its (*E*)-isomer (R^1 = H, R^2 = Et) [9] [22]. To rationalize the face differentiation on protonations of (*Z*)-enolates **14** (which is opposite to that of **13**), we propose a conformation with the lone electron pair on the N-atom in the nodal plane of the π-system. This geometry, similar to that of the (*E*)-*O*-acetyl derivative of **14** [9] [22], minimizes repulsion between the C(α)-methyl group and the auxiliary unit. Furthermore, chelation of the enolate and the lower SO_2 O-atom by Mg as well as association of the latter with H_2O complies plausibly with a protonation from the C(α)-*Si*(front) face of **14**.

Referring again to the postulated six-membered cyclic transition states $\mathbf{1}^{\neq}$ and $\mathbf{8}^{\neq}$, experimental support was provided by the regioselective 1,4-addition of EtMgCl to (*E*,*E*)-hexadienoylsultam **15** which gave, after crystallization, the (*E*)-3-ethyl-4-hexenoyl product **16** (69% yield) in *ca.* 100% d.e. (*Scheme 6*). Saponification of **16** (LiOH, aq. THF, r.t.) and hydrogenation of the resulting (*E*,3*R*)-3-ethyl-4-hexenoic acid (H_2, Rh/Al_2O_3) gave the known (3*S*)-3-ethylhexanoic acid [23] which revealed readily the (3*R*)-

[9]) For the influence of C(α)- and C(β)-substituents on the s-*cis*/s-*trans*-conformation of α,β-unsaturated ketones and their stereoselective conversion to (*Z*)- or (*E*)-enolates by conjugate hydride additions, see [21].

Scheme 6



configuration of **16**. However, it is the obvious preference for C(β)-addition which reflects the steric constraints of a cyclic transition state since attack at C(δ) would imply an 8-membered ring containing a *trans*-olefinic bond. In contrast, hydride was delivered by *L-Selectride* (= LiBH(*sec*-Bu)$_3$) regioselectively at C(δ) of **15** affording *N*-[(*E*)-3-hexenoyl]sultam **17** [9] [14]. It is worth noting that the smooth and selective transformation **15**→**16** is of interest for organic synthesis in view of possible π-face-selective functionalizations at the olefinic C-atoms and at C(α).

Conclusions. – The evidence presented here leaves no doubt about the potential of the tandem alkylmagnesium addition/enolate trapping for the synthesis of enantiomerically pure compounds. It exemplifies once more the wide applicability and practical advantages of the sultam **I** (and its enantiomer) as a chiral auxiliary [4] [9]. Further work on the scope and limitations of this new methodology is in progress.

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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 (Na), THF (Na), toluene (K). MeMgCl (3M in Et_2O) and EtMgCl (2M in Et_2O) were purchased from *Aldrich*. Solns. (0.8–1.2M) of the other *Grignard* reagents in Et_2O were prepared from alkyl chlorides and Mg powder (*Merck*, 0.1–0.3 mm). Their concentrations were determined by addition of a measured excess of aq. HCl and 'back-titration' with 0.1N aq. NaOH using phenolphthalein as indicator. 'Workup' denotes extraction with an org. solvent, washing of the org. phase with sat. aq. NaCl soln., drying ($MgSO_4$), and evaporation (rotatory evaporator). Column flash chromatography (FC): SiO_2 (*Merck 9385*). GC: *Hewlett-Packard 5790A*, integrator *HP 3390*, capillary column (fused silica, 0.2 mm i.d., 12 m), *OV-1*, 10 psi

H_2; A: 150°, 10 min→10°/min→250°; B: 150°, 10 min→7.5°/min→250°; C: 160°, 10 min→7.5°/min→250°; D: 160°, 10 min→10°/min→250°, unless otherwise specified; retention time in min (area %). M.p.: *Kofler* hot stage; uncorrected. [α]: *Perkin-Elmer-241* polarimeter; in $CHCl_3$, unless otherwise specified. IR: *Perkin-Elmer 257*, $CHCl_3$ unless otherwise specified. ^{1}H-NMR at 360 MHz, unless otherwise specified; ^{13}C-NMR at 50 MHz, unless otherwise specified; standard tetramethylsilane ($\delta = 0$ ppm); J in Hz. MS: m/z (rel.-%).

***N*-Enoylsultams 1.** – *(2R)-Bornane-10,2-sultam* (**I**). Auxiliary **I** [4] [9] [17] was prepared from (+)-(1*S*)-camphor-10-sulfonyl chloride following the procedure described for the preparation of its antipode [24].

N-[(E)-2-Butenoyl]bornane-10,2-sultam (**1**, R^1 = Me). Prepared according to [10] [24].

N-[(E)-2-Pentenoyl]bornane-10,2-sultam (**1**, R^1 = Et). A soln. of **I** (3.4 g, 15.8 mmol) in toluene (40 ml) was added dropwise at r.t. to a stirred suspension of NaH (23.8 mmol) in toluene (42 ml). After 1 h, (*E*)-2-pentenoyl chloride (3.79 g, 32 mmol) was added slowly, and the mixture was stirred at r.t. for 3 h. Workup, FC (hexane/EtOAc 85:15), and crystallization (EtOH) gave **1** (R^1 = Et; 3.63 g, 78%). GC (A): 14.05. M.p. 130–131°. IR: 2970, 1680, 1640, 1480, 1455, 1415, 1375, 1235. ^{1}H-NMR: 0.94 (*s*, 3H); 1.06 (*t*, *J* = 7.5, 3H); 1.16 (*s*, 3H); 1.3–1.45 (2H); 1.83–1.96 (3H); 2.05–2.2 (2H); 2.23–2.33 (2H); 3.45 (*d*, *J* = 13.5, 1H); 3.53 (*d*, *J* = 13.5, 1H); 3.94 (*dd*, *J* = 8, 5.5, 1H); 6.56 (*dt*, *J* = 15, 2, 1H); 7.15 (*dt*, *J* = 15, 6.5, 1H). ^{13}C-NMR: 164.20 (*s*); 152.19 (*d*); 119.99 (*d*); 65.09 (*d*); 53.12 (*t*); 48.42 (*s*); 47.75 (*s*); 44.66 (*d*); 38.48 (*t*); 32.80 (*t*); 26.47 (*t*); 25.66 (*t*); 20.84 (*q*); 19.90 (*q*); 12.17 (*q*). MS: 297 (1, $C_{15}H_{23}NO_3S^+$), 268 (0.6), 233 (1), 218 (1.5), 204 (7), 83 (100), 55 (24). HR-MS: 297.1411 ($C_{15}H_{23}NO_3S^+$, calc. 297.1400).

N-(2-Methyl-2-propenoyl)bornane-10,2-sultam (**8**, R^1 = H). Following the procedure for the preparation of **1** (R^1 = Et), successive treatment of **I** (500 mg, 2.32 mmol) with NaH (3.48 mmol) and 2-methyl-2-propenoyl chloride (0.46 ml, 4.71 mmol), workup, FC (hexane/EtOAc 85:15), and crystallization (EtOH) furnished **8** (R^1 = H; 502 mg, 76%). GC (A): 8.60. M.p. 149–150°. IR: 2970, 1680, 1640, 1455, 1415, 1340. ^{1}H-NMR: 1.00 (*s*, 3H); 1.22 (*s*, 3H); 1.3–1.5 (2H); 2.0 (*d*, *J* = 1.5, 3H); 1.8–2.1 (5H); 3.42 (*d*, *J* = 14, 1H); 3.55 (*d*, *J* = 14, 1H); 4.06 (*dd*, *J* = 8, 5.5, 1H); 5.68 (*d*, *J* = 1.5, 1H); 5.72 (*s*, 1H). ^{13}C-NMR: 171.20 (*s*); 138.88 (*s*); 124.27 (*t*); 65.38 (*d*); 53.47 (*t*); 47.95 (*s*); 47.62 (*s*); 45.16 (*d*); 38.27 (*t*); 33.17 (*t*); 26.40 (*t*); 21.27 (*q*); 19.81 (*q*); 18.67 (*q*). MS: 283 (0.3, $C_{14}H_{21}NO_3S^+$), 214 (1.3), 204 (2.4), 191 (3.9), 176 (4.7), 162 (0.9), 150 (1.8), 134 (6.2), 119 (3.1), 108 (8.1), 69 (100). HR-MS: 283.1240 ($C_{14}H_{21}NO_3S^+$, calc. 283.1243).

N-[(E)-2-Methyl-2-butenoyl]bornane-10,2-sultam (**8**, R^1 = Me). Prepared according to [10].

N-[(E)-2-Methyl-2-pentenoyl]bornane-10,2-sultam (**8**, R^1 = Et). Following the procedure described previously [10] for the preparation of *N*-[(*E*)-2-hexenoyl]bornane-10,2-sultam, (*E*)-2-methyl-2-pentenoic acid (1.14 g, 10 mmol) was converted (oxalyl chloride) into its acyl chloride which served to acylate **I** (1.06 g, 5 mmol), giving after crystallization (hexane), **8** (R^1 = Et; 1.32 g, 85%). GC (150°, 10°/min→270°): 5.62. M.p. 131–132°. IR: 2970, 1680, 1485, 1460, 1415, 1395, 1375, 1335, 1310, 1290, 1250, 1185, 1170, 1130, 1100, 1060, 1035, 985. ^{1}H-NMR: 1.00 (*s*, 3H); 1.07 (*t*, *J* = 7.5, 3H); 1.25 (*s*, 3H); 1.40 (*dt*, *J* = 9, 7.5, 2H); 1.87 (br. *s*, 3H); 1.83–2.08 (5H); 2.13–2.33 (2H); 3.37 (*d*, *J* = 14, 1H); 3.47 (*d*, *J* = 14, 1H); 4.03 (*dd*, *J* = 7.5, 5, 1H); 6.22 (*dt*, *J* = 9, 1.5, 1H). ^{13}C-NMR: 172.44 (*s*); 143.97 (*d*); 129.88 (*d*); 65.37 (*d*); 53.48 (*t*); 47.79 (*s*); 47.65 (*s*); 45.19 (*d*); 38.20 (*t*); 33.17 (*t*); 26.50 (*t*); 21.78 (*t*); 21.29 (*q*); 19.88 (*q*); 12.85 (*q*); 12.75 (*q*). MS: 311 (12, $C_{16}H_{25}NO_3S^+$), 247 (7), 232 (7), 218 (29), 204 (7), 190 (8), 152 (9), 97 (100), 69 (40). HR-MS: 311.1544 ($C_{16}H_{25}NO_3S^+$, calc. 311.1555).

N-[(E)-2-Methyl-2-heptenoyl]bornane-10,2-sultam (**8**, R^1 = Bu). At r.t., 2M $AlMe_3$ in hexane (3 ml, 6 mmol) was added dropwise to a soln. of **I** (961 mg, 4.47 mmol) in toluene (20 ml). After stirring for 15 min, ethyl (*E*)-2-methyl-2-heptenoate (1.08 g, 6.3 mmol) was added, and the resulting mixture was heated at 90° for 6 d. Workup and FC (hexane/EtOAc 82:18) gave **8** (R^1 = Bu; 651 mg, 42%) which was crystallized (hexane). GC (C): 18.50. M.p. 88°. IR (CCl_4): 2950, 2940, 2850, 1675, 1325. ^{1}H-NMR: 0.82 (*t*, *J* = 7, 3H); 0.90 (*s*, 3H); 1.16 (*s*, 3H), 1.2–1.43 (6H); 1.80 (*d*, *J* = 1.5, 3H); 1.81–2.0 (5H); 2.05–2.25 (2H); 3.34 (*d*, *J* = 14, 1H); 3.44 (*d*, *J* = 14, 1H); 4.00 (*dd*, *J* = 7.5, 4.5, 1H); 6.26 (*dq*, *J* = 7.5, 1.5, 1H). ^{13}C-NMR: 172.38 (*s*); 142.65 (*d*); 130.35 (*s*); 65.35 (*d*); 53.47 (*t*); 47.76 (*s*); 47.60 (*s*); 45.17 (*d*); 38.17 (*t*); 33.15 (*t*); 30.49 (*t*); 28.22 (*t*); 26.45 (*t*); 22.36 (*t*); 21.24 (*q*); 19.83 (*q*); 13.84 (*q*); 12.85 (*q*). MS: 339 (3, $C_{18}H_{29}NO_3^+$), 324 (1), 218 (10), 135 (11), 126 (22), 125 (100), 107 (7), 95 (11), 82 (13), 69 (22), 55 (53). HR-MS: 339.1912 ($C_{18}H_{29}NO_3S^+$, calc. 339.1916).

N-[(E,E)-2,4-Hexadienoyl]bornane-10,2-sultam (**15**). A mixture of sorbic acid (100 mg, 0.9 mmol) and oxalyl chloride (567 mg, 4.5 mmol) was stirred at r.t. for 12 h and then evaporated. Bulb-to-bulb distillation of the residue (70–75° (bath)/10 Torr) furnished (*E,E*)-2,4-hexadienoyl chloride (112 mg, 84%). Following the procedure described for the preparation of **1** (R^1 = Et), acylation of **I** (178 mg, 0.83 mmol) with (*E,E*)-2,4-hexadienoyl chloride (112 mg, 0.75 mmol), workup, FC (hexane/EtOAc 4:1), and crystallization (hexane) gave **15** (161 mg, 69%). GC (C): 18.67. M.p. 110–111°. IR: 2970, 2920, 2890, 1680, 1640, 1610, 1340, 1270, 1250, 1210, 1160, 1130, 1115, 1060, 1000. ^{1}H-NMR: 0.88 (*s*, 3H); 1.10 (*s*, 3H); 1.23–1.45 (2H); 1.8–1.93 (6H); 1.98–2.15 (2H); 3.41 (*d*,

J = 13.5, 1 H); 3.47 (*d*, J = 13.5, 1 H); 3.92 (*dd*, J = 7.5, 5, 1 H); 6.12–6.32 (2 H); 6.50 (*d*, J = 15, 1 H); 7.35 (*dd*, J = 15, 10, 1 H). ^{13}C-NMR: 164.50 (*s*); 145.87 (*d*); 141.10 (*d*); 130.01 (*d*); 118.21 (*d*); 65.10 (*d*); 53.09 (*t*); 48.36 (*s*); 47.72 (*s*); 44.62 (*d*); 38.46 (*t*); 32.76 (*t*); 26.45 (*t*); 20.77 (*q*); 19.86 (*q*); 18.74 (*q*). MS: 309 (8, $C_{16}H_{23}NO_3S^{+\cdot}$), 294 (2), 135 (3), 95 (100), 67 (70). HR-MS: 309.1369 ($C_{16}H_{23}NO_3S^{+\cdot}$, calc. 309.1399).

Conjugate Additions of *Grignard* Reagents to β-Substituted (*E*)-Enoylsultams and Subsequent 'Enolate' Protonation. – *General Procedure.* At –80° *ca.* 1–2 N alkylmagnesium chloride (2.5 mol-equiv.) in Et_2O was added dropwise to 0.07 M **1** (1 mol-equiv.) in THF. The mixture was stirred at –80° for 3 h, then quenched at –60° with sat. aq. NH_4Cl soln., subjected to workup and FC thereby avoiding a separation of isomeric 1,4-adducts (as controlled by GC).

Addition of EtMgCl to **1** (R^1 = Me). Using the general procedure, **1** (R^1 = Me; 50 mg, 0.176 mmol) furnished **2a**/**3a** (44 mg, 80%). GC (A): 14.10 (94.55), 14.19 (5.45). The main product **2a** was identified as *N-[(3R)-3-methylpentanoyl]bornane-10,2-sultam* by comparison (GC, ^{1}H-NMR) with an authentic sample obtained by catalytic hydrogenation of *N*-[(*E*)-3-methyl-2-pentenoyl]bornane-10,2-sultam [11].

Addition of PrMgCl to **1** (R^1 = Me). Using the general procedure, **1** (R^1 = Me; 26 mg, 0.092 mmol) gave **2b**/**3b** (27 mg, 90%). GC (A): 15.65 (92.6), 15.78 (7.4). The main product **2b** was identified as *N-[(3R)-3-methylhexanoyl]bornane-10,2-sultam* by comparison (GC, ^{1}H-NMR) with an authentic sample obtained by catalytic hydrogenation of *N*-[(*E*)-3-methyl-2-hexenoyl]bornane-10,2-sultam [11].

Addition of i-PrMgCl to **1** (R^1 = Me). Using the general procedure, **1** (R^1 = Me; 21 mg, 0.074 mmol) gave **2c**/**3c** (22 mg, 92%). GC (A): 15.54 (86.2), 15.65 (13.8). The main product **2c** was identified as *N-[(R)-3,4-dimethylpentanoyl]bornane-10,2-sultam* by comparison (GC, ^{1}H-NMR) with an authentic sample obtained by catalytic hydrogenation of *N*-[(*E*)-3,4-dimethyl-2-pentenoyl]bornane-10,2-sultam [11].

Addition of BuMgCl to **1** (R^1 = Me). Using the general procedure, **1** (R^1 = Me; 100 mg, 0.35 mmol) gave **2d**/**3d** (94 mg, 78%). GC (A): 17.21 (93.15), 17.36 (6.85). The main product **2d** was identified as *N-[(3R)-3-methylheptanoyl]bornane-10,2-sultam* by comparison (GC, ^{1}H-NMR) with an authentic sample obtained by catalytic hydrogenation of *N*-[(*E*)-3-methyl-2-heptenoyl]bornane-10,2-sultam [11].

Addition of Hexylmagnesium Chloride to **1** (R^1 = Me). Using the general procedure, **1** (R^1 = Me; 20 mg, 0.07 mmol) gave **2e**/**3e** (19 mg, 73%). GC (A): 19.93 (91.9), 20.04 (8.1). The main product **2e** was identified as *N-[(3R)-3-methylnonanoyl]bornane-10,2-sultam* by comparison (GC, ^{1}H-NMR) with an authentic sample obtained by catalytic hydrogenation of *N*-[(*E*)-3-methyl-2-nonenoyl]bornane-10,2-sultam [11].

Addition of Octylmagnesium Chloride to **1** (R^1 = Me). Using the general procedure, **1** (R^1 = Me; 20 mg, 0.07 mmol) gave **2f**/**3f** (22 mg, 81%). GC (A): 22.23 (83.1), 22.34 (8.3). The main product **2f** was identified as *N-[(3R)-3-methylundecanoyl]bornane-10,2-sultam* by comparison (GC, ^{1}H-NMR) with an authentic sample obtained by catalytic hydrogenation of *N*-[(*E*)-3-methyl-2-undecenoyl]bornane-10,2-sultam [11].

Addition of BuMgCl to **1** (R^1 = Et). Using the general procedure, **1** (R^1 = Et; 500 mg, 1.68 mmol) gave *N-[(3R)-3-ethylheptanoyl]bornane-10,2-sultam* (**2g**; 531 mg, 89%), oil. GC (A): 16.96 (99). IR: 2960, 2930, 2880, 2860, 1690, 1480, 1460, 1415. ^{1}H-NMR: 0.82 (*t*, J = 7.5, 6 H); 0.92 (*s*, 3 H); 1.12 (*s*, 3 H); 1.14–1.42 (10 H); 1.8–2.0 (4 H); 2.03–2.1 (2 H); 2.54 (*dd*, J = 16, 6.5, 1 H); 2.68 (*dd*, J = 16, 7, 1 H); 3.43 (*d*, J = 14, 1 H); 3.50 (*d*, J = 14, 1 H); 3.88 (*t*, J = 7, 1 H); signals at 2.53 (*dd*, J = 16, 7, 0.05 H); 2.69 (*dd*, J = 16, 7, 0.05 H) assigned to isomer **3g**. ^{13}C-NMR: 171.90 (*s*); 65.16 (*d*); 52.95 (*t*); 48.17 (*s*); 47.62 (*s*); 44.59 (*d*); 39.82 (*t*); 38.50 (*t*); 35.98 (*d*); 32.94 (*t*); 32.76 (*t*); 28.56 (*t*); 26.38 (*t*); 26.18 (*t*); 22.92 (*t*); 20.71 (*q*); 19.81 (*q*); 13.99 (*q*); 10.82 (*q*). MS: 356 (0.3, $[C_{19}H_{33}NO_3S + 1]^{+\cdot}$), 355 (0.14, $C_{19}H_{33}NO_3S^{+\cdot}$), 340 (0.17), 326 (0.7), 312 (0.46), 298 (0.77), 257 (25), 151 (7), 135 (60), 107 (11), 93 (11), 71 (61), 57 (100). HR-MS: 355.2186 ($C_{19}H_{33}NO_3S^{+\cdot}$, calc. 355.2181).

Conjugate Additions of *Grignard* Reagents to β-Substituted (*E*)-Enoylsultams and Subsequent 'Enolate' Methylation. – *N-[(2R,3R)-2,3-Dimethylheptanoyl]bornane-10,2-sultam* (**4a**). At –80°, 1.0 M BuMgCl in Et_2O (5.0 ml, 5.0 mmol) was added dropwise to **1** (R^1 = Me; 500 mg, 1.76 mmol) in THF (25 ml). After stirring at –78° for 3 h, a sample was withdrawn and quenched with sat. aq. NH_4Cl soln. GC (**B**): 17.33 (84.3), 17.44 (7.9). Addition of MeI (1.1 ml, 17.7 mmol) and HMPA (1.75 ml, 10.0 mmol) at –80° to the non-quenched reaction mixture, warming up to r.t. within 16 h, and workup afforded a crude oil. GC (**B**): 17.61 (4.3), 17.79 (7.8), 18.24 (78.9). FC (hexane/EtOAc 9:1) furnished a mixture of stereoisomeric *N*-(2,3-dimethylheptanoyl)sultams (500 mg, 80%; GC (**B**): 17.62 (1.4), 17.82 (8.6), 18.37 (86.1)) from which **4a** was isolated by crystallization (hexane; 298 mg, 48%). GC (**B**): 17.79 (2.5), 18.20 (97.5). M.p. 91–92°. IR: 2970, 2940, 1695, 1460, 1390, 1330, 1265, 1132. ^{1}H-NMR: 0.91 (*t*, J = 7.5, 3 H); 0.95 (*d*, J = 6.8, 3 H); 0.99 (*s*, 3 H); 1.19 (*s*, 3 H); 1.22 (*d*, J = 7, 3 H); 1.08–1.62 (8 H); 1.8–2.0 (4 H); 2.07–2.15 (2 H); 2.92 (*dq*, J = 7, 8.8, 1 H); 3.48 (*d*, J = 14, 1 H); 3.55 (*d*, J = 14, 1 H); 3.95 (*t*, J = 6.5, 1 H). ^{13}C-NMR: 176.23 (*s*); 65.02 (*d*); 53.19 (*t*); 48.08 (*s*); 47.66 (*s*); 45.85 (*d*); 44.55 (*d*); 38.41 (*t*); 34.65 (*d*); 32.79 (*t*); 32.37 (*t*); 28.56 (*t*); 26.36 (*t*); 22.91 (*t*); 20.78 (*q*); 19.81 (*q*); 17.76 (*q*); 16.55 (*q*); 14.02 (*q*). MS: 355 (< 1,

$C_{19}H_{33}NO_3S^{+\cdot}$), 340 (1.5), 271 (50), 135 (40), 113 (50), 71 (90), 57 (100). HR-MS: 271.1232 ([$M - C_6H_{12}$]$^{+\cdot}$, $C_{13}H_{21}NO_3S^{+\cdot}$, calc. 271.1231).

N-[(2R,3R)-3-Ethyl-2-methylheptanoyl]bornane-10,2-sultam (**4b**). At −85°, 1.0 M BuMgCl in Et_2O (1.5 ml, 1.5 mmol) was added dropwise to a soln. of **1** ($R^1 = C_2H_5$; 160 mg, 0.534 mmol) in THF (8 ml). After 2 h at −85°, the mixture was allowed to warm up to −65° within 3 h. A withdrawn sample was quenched with sat. aq. NH_4Cl soln. and examined by GC (B): 16.96 (92.4). Then, MeI (0.24 ml, 3.86 mmol) and HMPA (0.53 ml, 3 mmol) were added to the non-quenched reaction mixture at −85°. The mixture was slowly (within 16 h) warmed up to r.t. and submitted to workup to give a crude oil. GC (B): 18.31 (12, **2g**), 18.51 (2.5), 18.64 (6.5), 18.96 (67.8). FC gave a mixture of stereoisomeric *N*-(3-ethyl-2-methylheptanoyl)sultams (114 mg, 58%; GC (B): 18.63 (8.1), 18.96 (88.6)) from which **4b** (major) was isolated by crystallization (hexane; 72 mg, 36%). GC (C): 19.61 (1.7), 19.94 (98.3). M.p. 91–92°. IR (CCl_4): 2960, 2940, 2880, 1700, 1290, 1210. ^{1}H-NMR: 0.82 (*t*, *J* = 7.5, 3H); 0.84 (*t*, *J* = 7.0, 3H); 0.92 (*s*, 3H); 1.12 (*s*, 3H); 1.13 (*d*, *J* = 7, 3H); 1.14–1.56 (10H); 1.72 (*m*, 1H); 1.78–2.0 (3H); 2.02–2.08 (2H); 3.00 (*dq*, *J* = 8.5, 6, 1H); 3.42 (*d*, *J* = 13.5, 1H); 3.50 (*d*, *J* = 13.5, 1H); 3.90 (*t*, *J* = 6, 1H). ^{13}C-NMR: 176.31 (*s*); 65.02 (*d*); 53.12 (*t*); 48.08 (*s*); 47.61 (*s*); 44.49 (*d*); 43.24 (*d*); 40.17 (*d*); 38.39 (*t*); 32.72 (*t*); 27.94 (*t*); 27.54 (*t*); 26.36 (*t*); 24.21 (*t*); 23.15 (*t*); 20.73 (*q*); 19.80 (*q*); 16.28 (*q*); 14.04 (*q*); 11.37 (*q*). MS: 369 (0.14, $C_{20}H_{35}NO_3S^{+\cdot}$), 354 (0.5), 340 (0.2), 326 (0.25), 312 (0.14), 290 (0.28), 271 (34), 155 (14), 135 (51), 127 (30), 107 (14), 93 (15), 85 (49), 71 (100), 57 (81). HR-MS: 354.2097 ([$C_{20}H_{35}NO_3S - CH_3$]$^+$, calc. 354.2105).

Conjugate Additions of *Grignard* Reagents to *N*-(Methacryloyl)sultam 8 (R^1 = H) and Subsequent 'Enolate' Protonation. – *General Procedure.* At −80° 1–2 M alkylmagnesium chloride (2 mol-equiv.) in Et_2O was added dropwise to 0.07 M **8** (R^1 = H; 1 mol-equiv.) in toluene. Then, the mixture was allowed to reach r.t. within 15 min. After recooling to −95° (MeOH/liq. N_2), the reaction was quenched with an emulsion of THF/sat. aq. NH_4Cl and worked up to give a crude oil (analyzed by GC) which was purified by FC without altering the stereoisomer ratios (GC).

N-[(2R)-2-Methylbutanoyl]bornane-10,2-sultam (**9a**). Using the general procedure, addition of MeMgCl to **8** (R^1 = H; 65 mg, 0.23 mmol), subsequent protonation, and FC gave **I** (25%) and a 9:1 mixture (^{1}H-NMR) **9a**/**10a** (31 mg, 45%). GC (A): 10.61 (99). The major **9a** was identified by comparison (^{1}H-NMR, ^{13}C-NMR) with an authentic sample obtained *via* conjugate addition of *L-Selectride* to *N*-[(*E*)-2-butenoyl]bornane-10,2-sultam followed by methylation (MeI, HMPA) of the intermediate enolate [7] [14]. The minor **10a** was identified by comparison with authentic samples obtained either *via* conjugate addition of *L-Selectride* to *N*-[(*E*)-2-methyl-2-butenoyl] bornane-10,2-sultam followed by protonation (aq. NH_4Cl), or by acylation of **I** with (+)-(*S*)-2-methylbutyric acid [7] [14].

N-[(2R)-2-Methylpentanoyl]bornane-10,2-sultam (**9b**). Using the general procedure, addition of EtMgCl to **8** (R^1 = H; 33 mg, 0.12 mmol) and subsequent protonation gave a mixture **9b**/**10b** (31 mg, 92%). GC (A): 12.83 (4.8), 13.11 (93.1). FC furnished the major **9b** (26 mg, 70%; GC (A): 12.88 (1.4), 13.10 (98.6)), identified by comparison with an authentic sample obtained *via* addition of *L-Selectride* to *N*-(2-propylacryloyl)bornane-10,2-sultam [7] [14].

N-[(2R)-2-Methylhexanoyl]bornane-10,2-sultam (**9c**). Using the general procedure, addition of PrMgCl to **8** (R^1 = H; 629 mg, 2.22 mmol) and subsequent protonation gave **9c**/**10c** (579 mg, 80%). GC (A): 14.32 (2.8), 14.69 (91.8). FC (hexane/EtOAc 14:1) furnished the major **9c** (506 mg, 70%). GC (A): 14.32 (0.2), 14.62 (99.8). M.p. 87–88°. IR: 2960, 2940, 2880, 2860, 1695, 1480, 1470, 1460, 1415. ^{1}H-NMR: 0.86 (*t*, *J* = 7.5, 3H); 0.95 (*s*, 3H); 1.14 (*s*, 3H); 1.19 (*d*, *J* = 7, 3H); 1.2–1.46 (7H); 1.7–1.96 (4H); 2.03–2.1 (2H); 3.06 (*m*, 1H); 3.44 (*d*, *J* = 14, 1H); 3.52 (*d*, *J* = 14, 1H); 3.90 (*t*, *J* = 7, 1H). ^{13}C-NMR: 176.34 (*s*); 65.03 (*d*); 53.15 (*t*); 48.19 (*s*); 47.68 (*s*); 44.56 (*d*); 40.25 (*d*); 38.40 (*t*); 32.77 (*t*); 32.32 (*t*); 29.40 (*t*); 26.40 (*t*); 22.69 (*t*); 20.76 (*q*); 19.81 (*q*); 18.97 (*q*); 13.89 (*q*). MS: 328 (1, [$C_{17}H_{29}NO_3S + 1$]$^{+\cdot}$), 327 (< 1, $C_{17}H_{29}NO_3S^{+\cdot}$), 312 (1), 298 (1), 284 (3), 271 (12), 220 (2), 207 (0.4), 152 (7), 135 (12), 113 (29), 91 (20), 85 (100), 55 (20). HR-MS: 312.1609 ($C_{17}H_{29}NO_3S - CH_3^+$, calc. 312.1635).

N-[(2R)-2,4-Dimethylpentanoyl]bornane-10,2-sultam (**9d**). Using the general procedure, addition of i-PrMgCl to **8** (R^1 = H; 53 mg, 0.187 mmol) and subsequent protonation gave **9d**/**10d** (57 mg, 93%). GC (A): 13.44 (4.4), 13.87 (95.6). FC and crystallization (hexane) furnished the major **9d** (51 mg, 84%). GC (A): 13.43 (1), 13.88 (99). M.p. 104–105°. IR: 2960, 2940, 2890, 1695, 1480, 1470, 1460, 1415, 1395, 1375, 1370, 1330, 1270. ^{1}H-NMR: 0.84 (*d*, *J* = 6.5, 3H); 0.88 (*d*, *J* = 6.5, 3H); 0.94 (*s*, 3H); 1.13 (*s*, 3H); 1.14 (*m*, 1H); 1.16 (*d*, *J* = 7, 3H); 1.26–1.45 (2H); 1.56 (*m*, 1H); 1.75 (*ddd*, *J* = 13.5, 8.2, 6.2, 1H); 1.8–1.96 (3H); 2.0–2.08 (2H); 3.14 (*m*, 1H); 3.44 (*d*, *J* = 13.5, 1H); 3.52 (*d*, *J* = 13.5, 1H); 3.89 (*t*, *J* = 6.5, 1H). ^{13}C-NMR: 176.20 (*s*); 65.07 (*d*); 53.09 (*t*); 48.20 (*s*); 47.66 (*s*); 44.50 (*d*); 41.59 (*t*); 38.37 (*t*); 38.24 (*d*); 32.73 (*t*); 26.39 (*t*); 25.90 (*d*); 22.81 (*q*); 22.50 (*q*); 20.74 (*q*); 19.80 (*q*); 19.39 (*q*). MS: 328 (0.1, [$C_{17}H_{29}NO_3S + 1$]$^{+\cdot}$), 312 (0.4), 284 (2), 271 (12), 220 (2.5), 207 (3), 152 (5), 135 (14), 113 (31), 85 (100), 69 (10), 55 (12). HR-MS: 327.1868 ($C_{17}H_{29}NO_3S^{+\cdot}$, calc. 327.1870).

N-[(2R)-2-Methylheptanoyl]bornane-10,2-sultam (**9e**). Using the general procedure, addition of BuMgCl to **8** (R^1 = H; 60 mg, 0.21 mmol) and subsequent protonation gave **9e**/**10e** (58 mg, 81%). GC (A): 15.54 (7.5), 15.88 (80.8). FC and crystallization (hexane) furnished the major **9e** (45 mg, 62%). GC (A): 15.88 (100). M.p. 97–98°. IR: 2960, 2940, 2890, 2880, 2860, 1695, 1480, 1460, 1415. ^{1}H-NMR: 0.84 (*t*, *J* = 7, 3 H); 0.94 (*s*, 3 H); 1.13 (*s*, 3 H); 1.17 (*d*, *J* = 7, 3 H); 1.20–1.44 (9 H); 1.70–1.96 (4 H); 2.0–2.08 (2 H); 3.04 (*m*, 1 H); 3.44 (*d*, *J* = 14, 1 H); 3.50 (*d*, *J* = 14, 1 H); 3.90 (*t*, *J* = 6, 1 H). ^{13}C-NMR: 176.32 (*s*); 65.02 (*d*); 53.13 (*t*); 48.19 (*s*); 47.64 (*s*); 44.54 (*d*); 40.29 (*t*); 38.40 (*t*); 32.75 (*t*); 32.54 (*t*); 31.77 (*t*); 26.88 (*t*); 26.40 (*t*); 22.41 (*t*); 20.77 (*q*); 19.81 (*q*); 18.96 (*q*); 14.00 (*q*). MS: 342 (0.16, $[C_{18}H_{31}NO_3S + 1]^+$), 326 (0.3), 284 (1), 271 (26), 152 (8), 127 (21), 99 (23), 57 (100). HR-MS: 284.1329 ($C_{18}H_{31}NO_3S - C_4H_9^+$, calc. 284.1338).

Conjugate Additions of *Grignard* Reagents to α,β-Disubstituted (*E*)-Enoylsultams and Subsequent 'Enolate' Protonation. *General Procedure.* At −80°, 1–2M alkylmagnesium chloride (2.2 mol-equiv.) in Et_2O was added dropwise at −80° to 0.07M **8** (R^1 = alkyl, 1 mol-equiv.) in Et_2O/THF 5:1. Then, the mixture was allowed to warm up to −40° within 1 h and stirred at −40° for 16 h. After recooling to −70°, the reaction was quenched by addition of an emulsion of THF/sat. aq. NH_4Cl soln. and worked up to give a crude mixture which was analyzed by GC and purified as indicated below.

N-[(2R,3R)-2,3-Dimethylpentanoyl]bornane-10,2-sultam (**9f**). Using the general procedure, addition of EtMgCl to **8** (R^1 = Me; 200 mg, 0.673 mmol) and subsequent protonation gave a mixture of stereoisomers. GC (**B**): 14.67 (1), 15.13 (99). FC furnished almost pure **9f** (198 mg, 90%; GC (B): 14.65 (0.9), 15.09 (99.1)) which was crystallized from hexane (160 mg, 81%). GC (B): 14.78 (0.3), 15.28 (99.7). M.p. 118°. IR: 2970, 2880, 1690, 1520, 1330. ^{1}H-NMR: 0.86 (*t*, *J* = 7.5, 3 H); 0.91 (*d*, *J* = 6.8, 3 H); 0.95 (*s*, 3 H); 1.12 (*m*, 1 H); 1.15 (*s*, 3 H); 1.18 (*d*, *J* = 7, 3 H); 1.28–1.45 (2 H); 1.60 (*m*, 1 H); 1.78 (*m*, 1 H); 1.8–2.0 (3 H); 2.04–2.12 (2 H); 2.90 (*dq*, *J* = 9, 7, 1 H); 3.45 (*d*, *J* = 14, 1 H); 3.52 (*d*, *J* = 14, 1 H); 3.93 (*t*, *J* = 6.5, 1 H). ^{13}C-NMR: 176.18 (*s*); 65.00 (*d*); 53.18 (*t*); 48.08 (*s*); 47.66 (*s*); 45.48 (*d*); 44.55 (*d*); 38.42 (*t*); 36.01 (*d*); 32.76 (*t*); 26.38 (*t*); 25.13 (*t*); 20.79 (*q*); 19.81 (*q*); 17.15 (*q*); 16.56 (*q*); 10.67 (*q*). MS: 328 (0.26, $[C_{17}H_{29}NO_3S + 1]^+$), 327 (0.1, $C_{17}H_{29}NO_3S^+$), 312 (0.8), 298 (0.46), 271 (39), 152 (15), 135 (51), 113 (47), 93 (24), 85 (100), 55 (50). HR-MS: 327.1872 ($C_{17}H_{29}NO_3S^+$, calc. 327.1870).

N-[(2R,3R)-2,3-Dimethylheptanoyl]bornane-10,2-sultam (**9g**). Using the general procedure, addition of BuMgCl to **8** (R^1 = Me; 100 mg, 0.337 mmol) and subsequent protonation gave a mixture of stereoisomers. GC (**B**): 17.57 (0.9), 17.76 (0.7), 17.87 (0.2), 18.30 (98.2). FC furnished a mixture (87 mg, 73%; GC (**B**): 17.49 (0.9), 17.68 (0.5), 18.08 (98.6)) from which pure **9g** was crystallized (hexane; 79 mg, 66%). GC (B): 18.15 (100). M.p. 91–92°. It was identical with **4a** by comparison (GC, ^{1}H-NMR) and mixed m.p.

N-[(2R,3S)-2-Methyl-3-phenylbutanoyl]bornane-10,2-sultam (**9h**). Using the general procedure, addition of PhMgCl to **8** (R^1 = Me; 100 mg, 0.33 mmol) and subsequent protonation, workup and FC (hexane/EtOAc 8:1) gave unchanged **8** (R^1 = Me) together with a mixture of stereoisomers. GC (D): 13.50 (**8**, R^1 = Me, 13), 19.37 (2), 19.83 (0.5), 20.41 (80). Crystallization from pentane furnished almost pure **9h** (61 mg, 48%). GC (D): 19.45 (0.6), 19.91 (0.1), 20.60 (97.1). M.p. 175–176°. IR: 3070, 1690, 1340, 1190. ^{1}H-NMR: 0.89 (*d*, *J* = 7, 3 H); 0.92 (*s*, 3 H); 1.10 (*s*, 3 H); 1.21 (*d*, *J* = 7, 3 H); 1.26–1.45 (2 H); 1.82–1.96 (3 H); 2.03–2.13 (2 H); 3.03 (*m*, 1 H); 3.26 (*m*, 1 H); 3.48 (*d*, *J* = 14, 1 H); 3.52 (*d*, *J* = 14, 1 H); 3.96 (*t*, *J* = 6, 1 H); 7.20–7.34 (5 H). ^{13}C-NMR: 175.89 (*s*); 144.50 (*s*); 128.41 (*d*); 127.74 (*d*); 126.35 (*d*); 65.06 (*d*); 53.21 (*t*); 48.22 (*s*); 47.70 (*s*); 46.98 (*d*); 44.59 (*d*); 42.60 (*d*); 38.38 (*t*); 32.80 (*t*); 26.39 (*t*); 21.13 (*q*); 20.85 (*q*); 19.84 (*q*); 18.11 (*q*). MS: 375 (3, $C_{21}H_{29}NO_3S^+$), 271 (14), 161 (12), 133 (67), 105 (100), 91 (70), 77 (22). HR-MS: 375.1870 ($C_{21}H_{29}NO_3S^+$, calc. 375.1872).

N-[(2R,3R)-3-Ethyl-2-methylheptanoyl]bornane-10,2-sultam (**9i**). Using the general procedure, addition of BuMgCl to **8** (R^1 = Et; 135 mg, 0.43 mmol) and subsequent protonation gave a mixture of stereoisomers. GC (**B**): 18.52 (2.5), 18.66 (0.4), 18.99 (95.0). FC furnished 143 mg (90%; GC (B): 17.19 (2), 17.29 (0.9), 17.71 (96.9)) which were crystallized from hexane to give pure **9i** (125 mg, 78%). GC (B): 19.05 (100). M.p. 90–91°. It was identical with **4b** by comparison (GC, ^{1}H-NMR) and mixed m.p.

N-[(2R,3S)-3-Ethyl-2-methylheptanoyl]bornane-10,2-sultam (**9j**). Using the general procedure, addition of EtMgCl to **8** (R^1 = Bu; 99 mg, 0.29 mmol) and subsequent protonation gave a mixture of stereoisomers. GC (**B**): 18.78 (1.4), 18.82 (96.5), 19.15 (2.1). FC (hexane/EtOAc 6:1) furnished 88 mg (82%; GC (B): 18.91 (99.75), 19.18 (0.25)) which where crystallized from hexane to give **9j** (64 mg, 60%). M.p. 88–89°. IR (CCl_4): 2980, 2930, 2880, 1695, 1450, 1330. ^{1}H-NMR: 0.73 (*t*, *J* = 7.5, 3 H); 0.77 (*t*, *J* = 7, 3 H); 0.86 (*s*, 3 H); 1.06 (*s*, 3 H); 1.07 (*d*, *J* = 7, 3 H); 1.0–1.4 (9 H); 1.48 (*m*, 1 H); 1.68 (*m*, 1 H); 1.74–1.90 (3 H); 1.94–2.04 (2 H); 2.94 (*dq*, *J* = 9, 1 H); 3.39 (*d*, *J* = 14, 1 H); 3.44 (*d*, *J* = 14, 1 H); 3.85 (*t*, *J* = 6.5, 1 H). ^{13}C-NMR: 176.40 (*s*); 65.03 (*d*); 53.15 (*t*); 48.11 (*s*); 47.64 (*s*); 44.51 (*d*); 43.13 (*d*); 39.58 (*d*); 38.41 (*t*); 32.73 (*t*); 30.60 (*t*); 29.30 (*t*); 26.39 (*t*); 22.84 (*t*); 20.98 (*t*); 20.76 (*q*); 19.82 (*q*); 16.32 (*q*); 14.06 (*q*); 9.38 (*q*). MS: 370 (2, $[C_{20}H_{35}NO_3S + 1]^+$), 354 (4), 271 (70), 155 (70), 135 (98), 127 (75), 107 (55), 85 (100). HR-MS: 369.2371 ($C_{20}H_{35}NO_3S^+$, calc. 369.2338).

X-Ray Diffraction Analysis of **9j**. The crystals (hexane) are orthorhombic, $a = 7.8740$ (8), $b = 12.3387$ (14), $c = 21.977$ (3) Å; space group $P2_12_12_1$, $z = 4$, $d_c = 1.150$ g · cm^{-3}. Data were collected at r.t. on a *Philips PW1100 diffractometer*, (Mo$K\alpha$). The structure was solved by a direct method (MULTAN 80) and refined by a full matrix least squares analysis. The absolute configuration was confirmed by a least-squares refinement of the enantiomorph-polarity parameter [16] $x = 0.18$ (25). The final R factor based on 1902 observed reflections ($|F_0| > 3\sigma(F_0)$ and $|F_0| > 8.0$) was 0.066.

*N-[(*E,3R*)-3-Ethyl-4-hexenoyl]bornane-10,2-sultam* (**16**). Using the general procedure, addition of EtMgCl to **15** (646 mg, 2.09 mmol) and subsequent protonation gave an oil (GC (D): 17.80 (87.7), 17.93 (7.2), 18.08 (5.1)) which was crystallized from pentane at −20° to give pure **16** (488 mg, 69%). GC (C): 17.64 (100). M.p. 55–56°. IR ($CDCl_3$): 2990, 2920, 2890, 1690, 1340. ^{1}H-NMR: 0.73 (*t*, *J* = 7, 3 H); 0.85 (*s*, 3 H); 1.05 (*s*, 3 H); 1.15–1.35 (4 H); 1.54 (*dd*, *J* = 7, 1.5, 3 H); 1.7 1.9 (3 H); 1.9–2.03 (2 H); 2.40–2.56 (2 H); 2.74 (*m*, 1 H); 3.36 (*d*, *J* = 14, 1 H); 3.43 (*d*, *J* = 14, 1 H); 3.80 (*t*, *J* = 6.5, 1 H); 5.20 (*qdd*, *J* = 15, 8, 1.5, 1 H); 5.41 (*dq*, *J* = 15, 6.5, 1 H). ^{13}C-NMR: 171.02 (*s*); 133.39 (*d*); 125.72 (*d*); 65.14 (*d*); 52.96 (*t*); 48.19 (*s*); 47.64 (*s*); 44.59 (*d*); 41.29 (*t*); 40.70 (*d*); 38.48 (*t*); 32.76 (*t*); 27.71 (*t*); 26.40 (*t*); 20.74 (*q*); 19.85 (*q*); 17.85 (*q*); 11.45 (*q*). MS: 339 (17, $C_{18}H_{29}NO_3S^{+\cdot}$), 310 (10), 246 (20), 232 (17), 206 (12), 152 (60), 135 (90), 125 (99), 124 (97), 107 (65), 97 (100), 83 (98), 67 (92), 55 (97). HR-MS: 339.1892 ($C_{18}H_{29}NO_3^{+\cdot}$, calc. 339.1916).

Preparations and GC Analyses of Mixtures of *N*-[(2*RS*,3*SR*)- and (2*RS*,3*RS*)-2,3-Dialkylalkanoyl]bornane-10,2-sultams. – *N-(2,3-Dimethylpentanoyl)bornane-10,2-sultams.* A 1:1 mixture of (2*RS*,3*SR*)- and (2*RS*,3*RS*)-2,3-dimethylpentanal (*'syn'* and *'anti'*, resp.; *Aldrich*) was oxidized with *Jones'* Reagent. Treatment of the resulting carboxylic-acid mixture with oxalyl chloride and acylation of **I** with the thus obtained acyl chlorides (as described for the preparation of enoylsultams) gave a mixture of stereoisomeric *N*-(2,3-dimethylpentanoyl)bornane-10,2-sultams (82%). GC (B): 14.73 (28.2), 15.04 (50.0), 15.13 (21.7).

N-(2,3-Dimethylheptanoyl)bornane-10,2-sultams. A mixture of the minor (2*RS*,3*SR*)- and the major (2*RS*,3*RS*)-2,3-dimethylheptanoic acids (*'syn'* and *'anti'*, resp.) was prepared by addition of BuCu · BF_3 to (*E*)-2-methyl-2-butenoic acid [13]. Conversion of this mixture to the acyl chlorides (oxalyl chloride) and acylation of **I** afforded a mixture of stereoisomeric *N*-(2,3-dimethylheptanoyl)bornane-10,2-sultams (96%). GC (B): 17.73 (22.7), 17.91 (22.5), 18.02 (27.8), 18.28 (26.9).

N-(3-Ethyl-2-methylheptanoyl)bornane-10,2-sultams. A 1:1 mixture of (2*RS*,3*SR*)- and (2*RS*,3*RS*)-3-ethyl-2-methylheptanoic acids (*'syn'* and *'anti'*, resp.) was prepared by addition of BuCu · BF_3 [13] to (*E*)-2-methyl-2-pentenoic acid. Conversion of this mixture to the acyl chlorides (oxalyl chloride) and acylation of **I** gave a mixture of stereoisomeric *N*-(3-ethyl-2-methylheptanoyl)bornane-10,2-sultams (70%). GC (B): 18.53 (26.5), 18.60 (23.7), 18.67 (25.9), 18.96 (23.7).

Saponifications of *N*-Acylsultams IV (→V). – *(+)-(*R*)-3-Ethylheptanoic Acid.* A 1.3 N aq. soln. of LiOH (11 ml, 14.3 mmol) was added to **2g** (d.e. 82%; 506 mg, 1.42 mmol) in THF (18 ml), and the mixture was vigorously stirred at 50° for 16 h. Evaporation, trituration of the residue with CH_2Cl_2, and evaporation of the dried extracts gave **I**. Acidification of the CH_2Cl_2-insoluble residue with 2 N aq. HCl, saturation with NaCl, extraction with CH_2Cl_2, and evaporation of the dried ($MgSO_4$) extracts gave the crude acid which was purified by FC (pentane/Et_2O 7:3) to give an oil (126 mg, 56%). $[\alpha]_D = +2.4°$; $[\alpha]_{578} = +2.5°$; $[\alpha]_{546} = +2.8°$; $[\alpha]_{436} = +4.8°$ (neat, $T = 20°$; [12]: $[\alpha]_D = +2.94°$ (neat)). IR: 3520, 3460–3000, 2960, 2860, 1710. ^{1}H-NMR ($CDCl_3$, D_2O): 0.84 (*t*, *J* = 7.5, 3 H); 0.85 (*t*, *J* = 7.5, 3 H); 1.15–1.45 (8 H); 1.78 (*m*, 1 H); 2.28 (*d*, *J* = 7, 2 H). ^{13}C-NMR: 180.55 (*s*); 38.58 (*t*); 36.14 (*d*); 32.89 (*t*); 28.66 (*t*); 26.14 (*t*); 22.82 (*t*); 13.95 (*q*); 10.64 (*q*). MS: 159 (0.7, $[C_9H_{18}O_2 + 1]^+$), 141 (0.4), 129 (14), 98 (35), 69 (26), 57 (100).

*(−)-(*2R,3R*)-2,3-Dimethylpentanoic Acid.* A mixture of **9f** (d.e. 99.4%; 150 mg, 0.459 mmol), LiOH · H_2O (192 mg, 4.59 mmol) in THF/H_2O 5:3 (8 ml) was stirred vigorously at 60° for 4 d. Following the above described extraction procedure, **I** was recovered and the crude acid chromatographed (pentane/Et_2O 3:1→1:1) giving an oil (28 mg, 48%). $[\alpha]_D = -20.2°$; $[\alpha]_{578} = -21.0°$; $[\alpha]_{546} = -24.2°$; $[\alpha]_{436} = -43.1°$; $[\alpha]_{365} = -72.1°$ (*c* = 1.04, CH_2Cl_2, $T = 20°$; [15]: $[\alpha]_D = +32.9°$ (neat, extrapolated value)). ^{1}H-NMR: 0.85 (*t*, *J* = 7.5, 3 H); 0.90 (*d*, *J* = 6.5, 3 H); 1.10 (*d*, *J* = 7.5, 3 H); 1.16 (*m*, 1 H); 1.45 (*m*, 1 H); 1.68 (*m*, 1 H); 2.38 (*quint.*, *J* = 7). ^{13}C-NMR: 182.83 (*s*); 44.30 (*d*); 37.28 (*d*); 25.77 (*t*); 16.60 (*q*); 13.62 (*q*); 11.27 (*q*).

*(−)-(*E,3R*)-3-Ethyl-4-hexenoic Acid.* A mixture of **16** (862 mg, 2.5 mmol) and LiOH · H_2O (1.06 g, 25 mmol) in THF/H_2O 2:1 (15 ml) was stirred at r.t. for 3 d. Following the above described extraction procedure furnished **I** (474 mg, 88%) and the crude acid which, on bulb-to-bulb distillation (bath 100°/3 Torr), gave an oil (274 mg, 77%). $[\alpha]_D = -13.44°$; $[\alpha]_{578} = -15.0°$; $[\alpha]_{546} = -17.19°$; $[\alpha]_{436} = -30.55°$; $[\alpha]_{365} = -50.96°$ (neat, $T = 20°$). $[\alpha]_D = -13.0°$; $[\alpha]_{578} = -13.63°$; $[\alpha]_{546} = -15.6°$; $[\alpha]_{436} = -28.21°$; $[\alpha]_{365} = -47.75°$ (*c* = 1.41, $CHCl_3$, $T = 20°$). IR (CCl_4): 3400–2700 (br.), 2980, 2940, 1710, 1450, 1420, 1290, 1030, 910. ^{1}H-NMR: 0.86 (*t*, *J* = 7.5, 3

H); 1.24–1.53 (2 H); 1.67 (*dd*, J = 6.5, 1.5, 3 H); 2.25–2.46 (3 H); 5.26 (*ddq*, J = 1.5, 15, 8, 1 H); 5.51 (*dq*, J = 6.5, 15, 1 H); 10.13 (br. *s*, 1 H). ^{13}C-NMR: 179.25 (*s*); 133.07 (*d*); 125.96 (*d*); 40.72 (*d*); 39.99 (*t*); 27.65 (*t*); 17.85 (*q*); 11.44 (*q*). MS: 142 (24, $C_8H_{14}O_2^+$), 113 (25), 97 (18), 84 (43), 71 (100), 67 (46), 55 (82). HR-MS: 142.0978 ($C_8H_{14}O_2$, calc. 142.0990).

(−)-(3S)-3-Ethylhexanoic Acid. A mixture of (−)-(*E*,3*S*)-3-ethyl-4-hexenoic acid (137 mg, 0.96 mmol) in MeOH (10 ml) and Rh/Al_2O_3 (5%; 20 mg, 0.008 mmol) was stirred under H_2 (1 atm) at r.t. for 2.5 h. Filtration, evaporation of the filtrate, and distillation of the residue (bath 100°/3 Torr) gave an oil (135 mg, 97%). $[\alpha]_D = -2.47°$; $[\alpha]_{578} = -2.57°$; $[\alpha]_{546} = -2.92°$; $[\alpha]_{436} = -4.98°$; $[\alpha]_{365} = -7.90°$ (neat, T = 25°). $[\alpha]_D = -1.86°$; $[\alpha]_{578} = -1.95°$; $[\alpha]_{546} = -2.27°$; $[\alpha]_{436} = -3.94°$; $[\alpha]_{365} = -6.21°$ (c = 2.45, $CHCl_3$, T = 25°; [23]: $[\alpha]_D = -2.50°$ (neat)). IR (CCl_4): 2970, 2920, 2880, 1710, 1470, 1410, 1290, 940. ^{1}H-NMR: 0.87 (*t*, J = 7, 3 H); 0.89 (*dt*, J = 2, 7, 3 H); 1.23–1.47 (6 H); 1.84 (*m*, 1 H); 2.29 (*d*, J = 6.5, 2 H); 11.7 (br. *s*, 1 H). ^{13}C-NMR: 180.55 (*s*); 38.56 (*t*); 35.96 (*d*); 35.55 (*t*); 26.17 (*t*); 19.63 (*t*); 14.17 (*q*); 10.63 (*q*). MS: 115 (12, $[C_8H_{16}O_2 - C_2H_5]^+$), 101 (18), 85 (40), 84 (45), 69 (28), 61 (29), 60 (100), 55 (48). HR-MS: 115.0748 ($C_{16}H_{11}O_2$, calc. 115.0758).

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