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Supplementary Material Available: Complete experimental details and spectral data (^{1}H NMR, ^{13}C NMR, and IR) for the preparation of β-keto esters and all cyclizations not given in the Experimental Section (27 pages). Ordering information is given on any current masthead page.

Bornanesultam-Directed Asymmetric Synthesis of Crystalline, Enantiomerically Pure Syn Aldols

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Abstract: *N*-acylsultams **2** furnish, via aldolization of their enolates **16** with aldehydes, diastereomerically pure, crystalline syn aldols. The absolute configuration of the product is controlled by the choice of the enolate counterion: **16**, M = B → **3**; **16**, M = Li or Sn(IV) → **5**. Hydroperoxide-assisted hydrolysis/esterification or reductive cleavage provided enantiomerically pure methoxycarbonyl aldols (**12** and **13**) or 1,3-diols (**11**) with recovery of auxiliary **1**. The chiral serricornin precursor **14** was thus prepared.

Asymmetric aldol reactions have attracted widespread interest over the past decade, promoting considerable gain in insight and methodology.[1] Nevertheless, applications in synthesis would greatly benefit from the prospect of purifying the initially formed aldol products by crystallization. As a complement to a previous communication,[2] this article reports the first example which meets this and other relevant criteria (accessibility, versatility of chiral auxiliary as well as yields, metal-directed diastereo- and π-face selectivities of reactions).

Results

Sultam **1** (as well as its antipode readily available on a kg-scale[3]) were smoothly acylated with acylchlorides/NaH to provide starting acylsultams **2**.

Boron-Mediated Aldolizations. We first addressed the firmly established dibutylboryl enolate methodology.[4] Treatment of acylsultams **2** with freshly prepared dibutylboryl triflate/EtN(*i*Pr)$_2$ (1.1 mol equiv) at −5 °C in CH_2Cl_2, followed by addition of an aldehyde R^2CHO at −78 °C provided, on workup, syn aldols **3** (Scheme I, Table I entries 1, 2, 4, 6-9, 11, 12). Although major isomers **3** were usually isolated in good yields, conversions **2** → **3** often remained incomplete. Employing an excess of Bu_2BOTf/EtN(*i*Pr)$_2$ resulted in lower stereoselectivities.

More conveniently and more efficiently, aldols **3** were obtained by using in situ prepared diethylboryl triflate/EtN(*i*Pr)$_2$ (2 mol equiv, entries 3, 5, 10) following a protocol described for *N*-acyloxazolidinone/azetidinone aldolizations.[5] HPLC analysis of the crude products **3** showed (independent of the boryl triflate) very high diastereomeric purity which was increased to virtually

Scheme 1

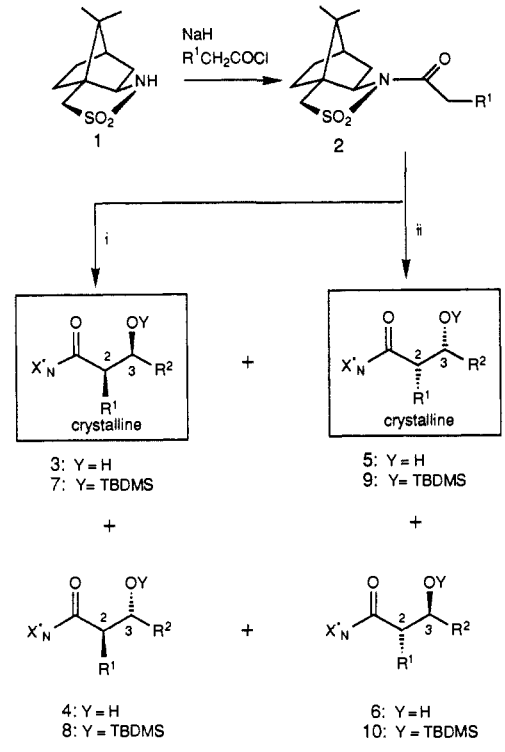

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Table I. Boron-Mediated Asymmetric Aldolizations: 2 → 3

		sultam aldehyde boron-subst.			product ratio				de (%)
		R^1	R^2	R	3/5/4 + 6	major prod.	yield (%) FC[b]	yield (%) cryst.	cryst.
1	a	Me	Ph	Bu	99:1:0	**3a**		80	>99
2	b	Me	Me	Bu	>99:<1:0	**3b**	78	69	>99
3	c	Me	Et	Et	98:2:0	**3c**	83	80	>99
4	d	Me	*i*Pr	Bu	97:3:0	**3d**	73	71	>99
5	d	Me	*i*Pr	Et	97.3:2.7:0	**3d**	82	76	>99
6	e	Me	MeCH=CH	Bu	>98:<2:0	**3e**	59	54	>99
7	f	Me	*p*-MeOPh	Bu	97.5:2.5:0	**3f**		48	>99
8	g	Et	Ph	Bu	97.5:0:2.5:0	**3g**		70	>99
9	h	Et	Me	Bu	94.2:2.3:3.5:0	**3h**	73	65	>99
10	h	Et	Me	Et	96:1.5:2.5:0	**3h**	87	82	>99
11	i	Et	*i*Pr	Bu	98.9:1.1:0	**3i**	80	66	>99
12	j	*n*Bu	Ph	Bu	>98:<1:<1	**3i**		64	>99

[a] The anti products were generally not assigned either structure **4** or **6** except product **6a** which was compared with an authentic sample.[12] [b] FC = flash chromatography.

Table II. Li(I)- or Sn(IV)-Mediated Asymmetric Aldolizations: 2 → 5

		R^1	R^2	metal	product ratio[a] 3/5/4 + 6	major prod.	yield (%) cryst.	de (%) cryst.
13	a	Me	Ph	Li(I)	10:75.7:9.1:5.2	**5a**	55	98[b]
14	a	Me	Ph	Sn(IV)	7.4:85.2:0:7.4	**5a**	67	>99
15	d	Me	*i*Pr	Li(I)	15:76.3:8.6	**5d**		
16	d	Me	*i*Pr	Sn(IV)	12.6:84.8:2.5	**5d**	44	>99
17	k	Me	*n*Pr	Sn(IV)	21:79:0	**5k**	53[c]	>95[b]
18	e	Me	MeCH=CH	Sn(IV)	5:64.5:30	**5e**	44	>99
19	g	Et	Ph	Li(I)	6.6:87.8:5.6	**5g**	59	>99
20	g	Et	Ph	Sn(IV)	10.2:80.5:9.2	**5g**	64	>99
21	i	Et	*i*Pr	Sn(IV)	0:82.2:16.7	**5i**	47	>99
22	l	Et	MeCH=CH	Sn(IV)	2:66.2:31.7	**5l**	31	>99

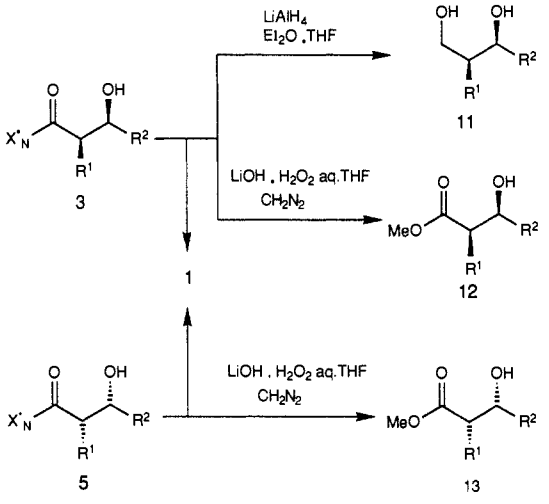
[a] The minor isomer observed in entry 17 was tentatively assigned. [b] By ^{1}H NMR analysis. [c] Oil purified by flash chromatography (FC).

100% de by flash chromatography (FC) and crystallization (entries 2–7, 9–11) or simply by direct crystallization (entries 1, 8, 12). Aldols **3** were further characterized as their crystalline *O-tert*-butyldimethylsilyl (TBDMS derivatives **7** (100% de by GC).

Li(I)- or Sn(IV)-Mediated Aldolizations. Counterion effects on the π-face discrimination and diastereoselectivity of aldolizations have been amply described.[6-10] To explore the role of the enolate counterion, propionylsultam **2a** was successively treated with LICA (−78 °C),[11] an (alkyl)metal halide ($ZnCl_2$,[6] Me_2AlCl, $EtAlCl_2$,[7] $CeCl_3$,[8] Cp_2ZrCl_2,[9] and Bu_3SnCl,[6] −78 to 0 °C) and benzaldehyde (−78 °C). HPLC and ^{1}H NMR analyses of the crude products formed from the Al(III), Zn(II), and Ce(III) enolates revealed low stereoselectivities resulting in mixtures of aldols **3a–6a**; attempted Zr(IV)- or Sn(II)[10]-mediated aldolizations failed to give discernible products (Table V, Experimental Section). As a notable exception, syn aldol **5a** was obtained in reasonably high selectivity via the Li(I) or Bu_3Sn enolate.

Recently, a reversed sense of induction was also observed on aldolizations of boron versus lithium, zinc, and tin(IV) enolates derived from α-silyloxyketones,[6a] α-haloacetyloxazolidinones,[6b] and acylthiazolidinethiones.[6c] The analogous reversal of topicity found with Li(I) and Sn(IV) enolates derived from sultams **2** is even more remarkable since the major syn aldols **5** were easily purified by FC and crystallization as summarized in Table II.

Scheme II



Thus, kinetically controlled deprotonation of propionylsultam **2a** with *n*-BuLi,[11] followed by treatment of the resulting lithium enolate with benzaldehyde at −78 °C, afforded pure syn aldol **5a** (55% yield, 98% de, entry 13) with configurations at C(2) and C(3) opposite to those of **3a**.

Transmetalation of the lithiated sultam **2a** with Bu_3SnCl (1.2 mol equiv, −78 °C, 1 h), addition of benzaldehyde (−78 °C), workup, FC, and crystallization provided aldol **5a** in 67% yield and in >99% de (Table II, entry 14). Further examination of Table II shows that pure aldols **5** were generally obtained in somewhat higher yields by using the Sn(IV) versus Li(I) methodology (cf., entries 13/14, 15/16, and 19/20). Only in aldolizations involving (*E*)-crotonaldehyde did formation of anti products become seriously competitive (entries 18 and 22). Nevertheless, purification by FC/crystallization was so efficient that in all but one case (**5k**, entry 17, oil, >95% de) aldols **5** were obtained in virtually 100% de (in 31–67% yield).

Stereochemical Assignment and Nondestructive Cleavage of the Aldol Products. Product ratios 3/4/5/6 followed directly from a comparison with independently prepared mixtures of aldols **3–6**

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(11) Treatment of acylsultams **2** with lithium cyclohexylisopropylamide (LICA, −78 °C) gave transient lithium enolates **16** with equal stereoselectivity (cf. Table V, Experimental Section) but caused some deprotonation at C(10).

Table III. Hydroperoxide-Assisted Saponification/Esterifications **3** → **1** + **12** and **5** → **1** + **13**

				methoxycarbonyl aldol				
R^1	R^2	sultam aldol	sultam **1** yield (%)	product	yield (%)	config.	$[\alpha]_D$[a]	$[\alpha]_D$ (lit.[a] ref)
Me	Ph	**3a**	91	**12a**	83	(2*R*,3*R*)	+23.5°	+23.2° (4b)
Me	Me	**3b**	95	**12b**	71	(2*R*,3*S*)	-13.5°	+14.3°[b] (21a)
Me	*i*Pr	**3d**	90	**12d**	84	(2*R*,3*S*)	+7.5°	+7.7° (4b)
Et	Ph	**3g**	89	**12g**	76	(2*R*,3*R*)	+13.5°	+12.0° (6c)
Me	Ph	**5a**	92	**13a**	76	(2*S*,3*S*)	-20.8°	
Me	*i*Pr	**5d**	91	**13d**	91	(2*S*,3*R*)	-7.1°	
Me	*n*Pr	**5k**	87	**13k**	84	(2*S*,3*R*)	+12.1°	
Me	MeCH=CH	**5e**	91	**13e**	86	(2*S*,3*R*)	+11.5°	
Et	Ph	**5g**	94	**13g**	83	(2*S*,3*S*)	-13.0°	
Et	*i*Pr	**5i**	93	**13i**	92	(2*S*,3*R*)	-7.4°	+7.6°[b] (6c)
Et	MeCH=CH	**5l**	94	**13l**	52	(2*S*,3*R*)	-7.1°	

[a] In $CHCl_3$ except **12b**, measured in MeOH. [b] $[\alpha]_D$ reported for the antipode.

Table IV. Reductive Cleavage **3** → **1** + **11**

				diol **11**			
	R^1	R^2	sultam **1** yield (%)	yield (%)	config	$[\alpha]_D$	$[\alpha]_D$ (lit. ref)
a	Me	Ph	88	75	(2*S*,3*R*)	+57.8°	
b	Me	Me	90	79	(2*S*,3*S*)	+6.0°	
d	Me	*i*Pr	93	91	(2*S*,3*S*)	+9.2°	+11.3° (21b)

(HPLC, ^{1}H NMR) and of their TBDMS ethers **7**–**10** (GC, cf., Experimental Section). The major products **3** (Table I) or **5** (Table II) were easily assigned the syn configuration based on the ^{1}H NMR vicinal coupling constants $J(2,3)$ = 2–4 Hz (**3**) and 4.0–6.5 Hz (**5**) as well as the ^{13}C NMR signals corresponding to R^1 = Me: δ = 10.8–12 ppm (**3a–3f**, **5a**, **5d**, **5f**, **5g**, **5k**).[1b] In comparison, anti aldol **6a**[12] exhibited ^{1}H and ^{13}C NMR values of $J(2,3)$ = 8.5 Hz and δ_{R^1} = Me = 14.8 ppm, respectively.

Mild hydroperoxide-assisted saponification[13] of sultam aldols **3** or **5** gave recovered sultam **1** (89–95%) and, after treatment of the resulting carboxylic acids with CH_2N_2, the corresponding, enantiomerically pure syn methoxycarbonylaldols **12** or **13** (56–93%, ^{1}H NMR: $J(2,3)$ = 3.5–5.6 Hz, Scheme II, Table III).

The absolute configurations of **12a**, **12b**, **12d**, **12g**, **13a**, and **13i** were determined by comparing their optical rotations with reference values.

Alternatively, reductive cleavage of aldol products **3a**, **3b**, and **3d** with $LiAlH_4$ gave recovered auxiliary **1** as well as enantiomerically pure 1,3-diols **11a**, **11b**, and **11d**, respectively (Table IV).

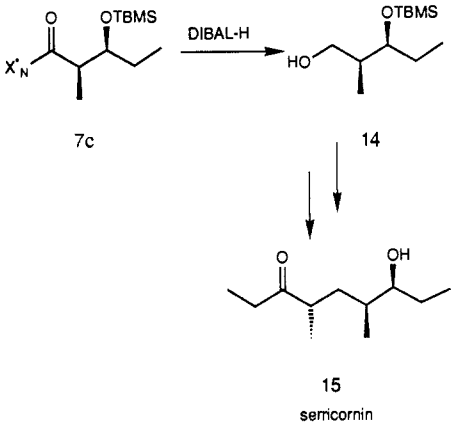
Illustrating the preparative value of this method, silyl ether **7c** was cleaved with DIBAL-H to provide alcohol **14**, a precursor for the synthesis of the cigarette beetle pheromone serricornin[14] (**15**, Scheme III).

Stereochemical Rationalization: Dichotomy between Boron- and Lithium- or Tin(IV)-Mediated Aldolizations. Enolate Configurations. Treating acylsultams **2** with a dialkylboryl triflate/N-(*i*Pr)$_2$Et apparently gave boryl enolates **16**, $ML_n = BR_2$ (Scheme IV), assigned the *Z* configuration based on generally accepted arguments.[1,5] An ^{1}H NMR study indicates the formation of a single boryl enolate from propionylsultam **2a**.

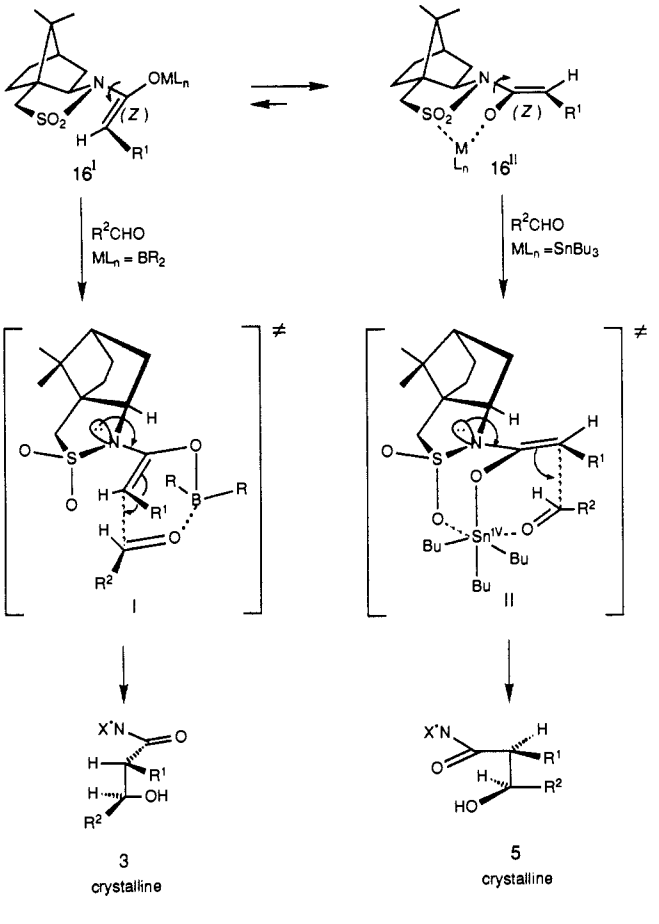
Lithium enolates **16**, M = Li, generated by deprotonation of acylsultams **2** with *n*-BuLi, were assigned the *Z* configuration via correlation of **16g**, M = Li, with the corresponding (*Z*)-*O*-pivaloyl-*N*,*O*-ketene acetal.[15] Transmetalation **16**, M = Li → **16**, M = $SnBu_3$, is assumed to retain the stereochemical integrity.

All three enolates **16**, M = B, Li and Sn(IV) seem to be in equilibrium between the electrostatically favored N-SO_2/C-OML_n s-trans conformation **16**$^{\text{I}}$ and the chelate-enforced s-cis conformation **16**$^{\text{II}}$.[16]

Scheme III



Scheme IV



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Aldolization. The rate-determining step **16** → **3** or **16** → **5** most plausibly proceeds via Zimmerman/Traxler-type transition states implying a coordination of aldehyde R^2CHO with the enolate counterion.[1] Since the maximal coordination number of dialkylboron(III) is four, it cannot simultaneously bind three oxygen atoms (enolate, aldehyde, SO_2 group) in contrast to Li(I) and $Bu_3Sn(IV)$ which possess higher coordination potentials. Thus (regardless of the equilibrium position **16**^{I} ⇄ **16**^{II}), the observed topicities conform with transition state I for the boron-mediated aldolization and chelated transition state II for the Li(I)- and Sn(IV)-mediated reaction.[6] Both transition states account for a selective aldehyde approach from the bottom face of **16**, opposite to the lone electron pair on the nitrogen atom, in analogy to other electrophiles (iminium salt,[17] primary alkyl halides,[15b] NBS,[18] etc.).

Conclusion

This work exemplifies once more the general applicability of sultam **1** (and its antipode) as a practical chiral auxiliary.[19] Its use in the preparation of enantiomerically pure syn aldols compares very favorably with other methods. The potential of this chirophore in asymmetric synthesis, e.g., of anti aldols,[12] is being further explored.

Experimental Section

General Methods. All reactions were carried out under Ar or N_2 with magnetic stirring unless otherwise specified. Solvents were dried by distillation from drying reagents as follows: CH_2Cl_2 (CaH_2), THF (Na), toluene (K), Et_2O (Na), DMF (CaH_2), and MeOH ($MgOMe_2$). Dibutylboron triflate was prepared according to the method of Mukaiyama and stored in a Schlenk tube under nitrogen.[20]

Column flash chromatography (FC): SiO_2 (Merck 9385). HPLC: Waters ALC\GPC-244 (Li Chrosorb, Si60 5 μm), hexane/EtOAc 4:1, 5:1, or 6:1, 1 cm^3/min, unless otherwise stated, retention time in minutes (area %). GC: Hewlett Packard 5790A, integrator HP3390, capillary column (fused silica, 0.2 mm i.d., 12 m). OV-1, 10 psi H_2; A, 160°, 10 min → 10°/min → 270°; B, 100°, isotherm; C, 125°, → 5°/min → 250°; D, 150°, 5 min, 10°/min → 260°; E, 200°, 10 min, → 10°/min → 270°; retention time in min (area %). Mp: Kofler hot stage apparatus, uncorrected. [α]: Perkin-Elmer-241 polarimeter; in $CHCl_3$ at 20 °C, unless otherwise stated. IR: Mattson Instruments Polaris, $CHCl_3$ unless otherwise stated. ^{1}H NMR at 360 MHz in $CDCl_3$ unless otherwise stated; ^{13}C NMR at 50 MHz in $CDCl_3$ unless otherwise stated; standard tetramethylsilane (δ = 0 ppm): *J* in Hz. MS: *m/z* (rel intensity %).

***N*-Acylsultams. General Procedure.** A solution of (2*R*)-bornane-10,2-sultam **1**[3] (2.0 g, 9.3 mmol) in toluene (40 mL) was added dropwise to a suspension of NaH (606 mg, 55% dispersion in mineral oil, 13.9 mmol) in toluene (10 mL), and the mixture was stirred for 2 h at room temperature. Addition of freshly distilled acid chloride (13.9 mmol) in toluene (40 mL), stirring for 2 h, followed by addition of saturated aqueous NH_4Cl, separation of the toluene layer, extraction of the aqueous phase (Et_2O), drying of the combined organic layers ($MgSO_4$), evaporation and crystallization gave the respective *N*-acylsultam.

***N*-Propionylbornane-10,2-sultam (2a).** Colorless crystals from MeOH (2.19 g, 87%); GC(A) 9.19; mp 153–154 °C; $[\alpha]_D$ = −108.38° (*c* 2.65).

***N*-Butanoylbornane-10,2-sultam (2g).** Colorless crystals from CH_2Cl_2/hexane, 2.18 g (82%); GC(A) 11.89; mp 86–87 °C; $[\alpha]_D$ = −96.0° (*c* 0.84).

***N*-Hexanoylbornane-10,2-sultam (2j).** Oil, FC (hexane/Et_2O 1:1), 2.86 g (98%); GC(A) 15.36; $[\alpha]_D$ = −84.87° (*c* 1.33).

Aldol Reactions of *N*-Acylsultams 2 via Their Dialkylboron Enolates. Using Freshly Distilled Dibutylboryl Triflate. *n*-Bu_2BOTf (1.0 N in CH_2Cl_2, 1.1 mol equiv) was added dropwise to a stirred solution of the appropriate *N*-acylsultam **2** in CH_2Cl_2 (1.4 mL, 0.37 mmol) at −5 °C. After stirring at −5 °C for 5 min, slow addition of (iPr)$_2$EtN (1.1 mol equiv) and further stirring for 30 min at −5 °C to −3 °C, the mixture was cooled to −78 °C. Addition of freshly distilled aldehyde (5.0 mol equiv), stirring for 15 min at −78 °C, quenching with aqueous phosphate buffer (pH = 7, 0.6 mL, 0.37 mmol), extraction (Et_2O) followed by washing of the combined organic extracts (saturated aqueous NH_4Cl), drying ($MgSO_4$), and evaporation gave the crude product which was subjected to HPLC analysis. Purification by FC (hexane/EtOAc 4:1) and/or crystallization furnished the pure (2*R*)-aldol diastereoisomer **3**.

Using in Situ Prepared Diethylboryl Triflate. CF_3SO_3H (3.7 mmol) was added to a 1 M solution of BEt_3 (hexane, 3.7 mmol) at room temperature, and the mixture was stirred at 40 °C (until gas evolution has ceased). After successive addition of acylsultam **2** (1.85 mmol) in CH_2Cl_2 (7 mL) and 1 M NEt(iPr)$_2$ (CH_2Cl_2, 3.9 mmol), stirring at −5 °C for 30 min, addition of the corresponding aldehyde at −78 °C, stirring at −78 °C for 75 min and workup, the reaction mixture was analyzed and purified as described above.

***O*-TBDMS Derivatives 7.** 2,6-Lutidine (2.0 mol equiv) followed by *tert*-butyldimethylsilyltriflate (1.5 mol equiv) was added at 0 °C to a solution of **3** (CH_2Cl_2, 0.1 mmol/mL). After stirring (0 °C to room temperature, 10 min), saturated aqueous NH_4Cl was added, and the aqueous phase was extracted (Et_2O). Drying ($MgSO_4$), evaporation, and crystallization gave **7**.

***N*-[(2*R*,3*R*)-2-Methyl-3-hydroxy-3-phenylpropanoyl]bornane-10,2-sultam (3a). Using Freshly Distilled Bu_2BOTf.** Propionylsultam **2a** (97 mg, 0.36 mmol) and benzaldehyde (80 μL, 0.72 mmol) gave a crude reaction mixture, HPLC (4:1) 7.25 (8), 12.4 (88), 15.2 (0.9), which was crystallized from CH_2Cl_2/hexane to provide pure aldol **3a** (107 mg, 80%): HPLC (4:1) 12.39; mp 191–192 °C; $[\alpha]_D$ = −98.5° (*c* 0.65).

***N*-[(2*R*-3*S*)-3-Hydroxy-2-methylbutanoyl]bornane-10,2-sultam (3b). Using Freshly Distilled Bu_2BOTf.** Propionylsultam **2a** (100 mg, 0.37 mmol) and acetaldehyde gave a crude reaction mixture: HPLC (4:1, 1.5 cm^3/min) 16.7 (96). FC (hexane/EtOAc 3:1) and crystallization (MeOH) provided pure aldol **3b** (79.8 mg, 69%): HPLC (4:1, 1.5 cm^3/min) 14.73; mp 96–97 °C; $[\alpha]_D$ = −84.9° (*c* 0.67). *O*-TBDMS derivative **7b**: crystallized from MeOH, 73%; GC(A) 19.39; mp 127–130 °C.

***N*-[(2*R*,3*S*)-3-Hydroxy-2-methylpentanoyl]bornane-10,2-sultam (3c). Using in Situ Prepared Et_2BOTf.** Propionylsultam **2a** (500 mg, 1.85 mmol) and propanal gave a crude reaction mixture: HPLC (6:1) 9.6 (4.3), 22.5 (82.8), 29.4 (1.8). FC (hexane/EtOAc 4:1) and crystallization from methanol provided pure aldol **3c** (485 mg, 80%): mp 120–121 °C; HPLC (6:1) 23.2; $[\alpha]_D$ = −99.3° (*c* 1.06). *O*-TBDMS derivative **7c**: crystallized from MeOH, 95%; GC(D) 15.48; mp 131–133 °C.

***N*-[(2*R*,3*S*)-3-Hydroxy-2,4-dimethylpentanoyl]bornane-10,2-sultam (3d). Using Freshly Distilled Bu_2BOTf.** Propionylsultam **2a** (231 mg, 0.85 mmol) and isobutyraldehyde gave a crude reaction mixture: HPLC (4:1) 7.2 (8.9), 9.4 (86.5), 13.6 (2.6). FC (hexane/EtOAc 4:1) and crystallization from hexane provided pure aldol **3d** (207 mg, 71%): HPLC (4:1) 9.44; mp 113–114 °C; $[\alpha]_D$ = −83.7° (*c* 0.77). *O*-TBDMS derivative **7d**: crystallized from MeOH, 73%; GC(A) 20.50; mp 173–174 °C.

Via in Situ Prepared Et_2BOTf. Propionylsultam **2a** (100 mg, 0.37 mmol) and isobutyraldehyde (−78 °C, 30 min, then −65 °C, 40 min) gave a crude reaction mixture: HPLC (6:1) 15.4 (97.3), 26.3 (2.7). FC (hexane/EtOAc 6:1 → 3:1) and crystallization (Et_2O/hexane) afforded pure aldol **3d** (97 mg, 76%), identical with the above-described sample of **3d**.

***N*-[(*E*)-(2*R*,3*S*)-2-Methyl-3-hydroxy-4-hexenoyl]bornane-10,2-sultam (3e). Using Freshly Distilled Bu_2BOTf.** Propionylsultam **2a** (98 mg, 0.36 mmol) and (*E*)-crotonaldehyde gave a crude reaction mixture: HPLC (4:1) 5.2 (20.6), 8.3 (76.5). FC (hexane/EtOAc 4:1) and crystallization (CH_2Cl_2/hexane) provided the pure aldol **3e** (66.0 mg, 54%): HPLC (4:1) 8.31; mp 118–119 °C; $[\alpha]_D$ = −93.6° (*c* 0.77). *O*-TBDMS derivative **7e**: crystallized from MeOH, 86%; GC(A) 19.79; mp 110–111 °C.

***N*-[(2*R*,3*R*)-2-Methyl-3-hydroxy-3-(4-methoxyphenyl)propanoyl]-bornane-10,2-sultam (3f). Using Freshly Distilled Bu_2BOTf.** Propionylsultam **2a** (100 mg, 0.37 mmol) and anisaldehyde gave a crude reaction mixture: HPLC (4:1) 6.8 (>2), 16.5 (95), 21.1 (2.4). FC (hexane/EtOAc 3:1) and crystallization (MeOH) afforded pure aldol **3f** (72 mg, 48%): HPLC (4:1) 16.99; mp 153–155 °C; $[\alpha]_D$ = −93.2° (*c* 0.86). *O*-TBDMS derivative **7f**: crystallized from MeOH, 85%; GC(A) 25.51; mp 96–98 °C.

***N*-[(2*R*,3*R*)-2-(Hydroxybenzyl)butanoyl]bornane-10,2-sultam (3g). Using Freshly Distilled Bu_2BOTf.** Butanoylsultam **2g** (268 mg, 0.94 mmol) and benzaldehyde gave a crude reaction mixture: HPLC (4:1) 6.6 (2), 9.7 (2.4), 11.2 (93.7), which was crystallized (CH_2Cl_2/hexane) to furnish pure aldol **3g** (257 mg, 70%): HPLC (4:1) 11.85; mp 219–220 °C; $[\alpha]_D$ = −86.6° (*c* 0.716). *O*-TBDMS derivative **7g**: crystallized from MeOH, 82%; GC(A) 23.13; mp 170–172 °C.

***N*-[(2*R*,3*S*)-2-Ethyl-3-hydroxybutanoyl]bornane-10,2-sultam (3h). Using Freshly Distilled Bu_2BOTf.** Butanoylsultam **2g** (104 mg, 0.365 mmol) and acetaldehyde gave a crude reaction mixture: HPLC (4:1) 8.7

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(6), 9.9 (3.3), 10.3 (2.1), 15.4 (88.5). FC (hexane/EtOAc 3:1) and crystallization (MeOH) provided pure aldol **3h** (77.6 mg, 65%): HPLC (4:1 hexane/EtOAc, 1.5 mL/min) 14.98; mp 166 °C; $[\alpha]_D = -118.49°$ (*c* 0.384). *O*-TBDMS derivative **7h**: crystallized from MeOH, 53%; GC(A) 19.84; mp 170–172 °C.

Via in Situ Prepared Et_2BOTf. Butanoylsultam **2g** (100 mg, 0.35 mmol) and acetaldehyde gave a crude reaction mixture: HPLC (4:1) 4.2 (5.7), 9.7 (3.7), 14.8 (90.6). FC (hexane/EtOAc 4:1) and crystallization (MeOH) afforded pure aldol **3h** (94 mg, 82%); HPLC (4:1) 14.8; mp 166–167 °C, identical with the above-described sample of **3h**.

***N*-[(2*R*,3*S*)-2-Ethyl-3-hydroxy-4-methylpentanoyl]bornane-10,2-sultam (3i). Using Freshly Distilled Bu_2BOTf.** Butanoylsultam **2g** (52 mg, 0.185 mmol) and isobutyraldehyde gave a crude reaction mixture; HPLC (4:1) 9.6 (97.6), 12.9 (1.08); FC (hexane/EtOAc 4:1) and crystallization (MeOH) afforded pure aldol **3i** (43.2 mg, 66%): HPLC (4:1) 8.77; mp 159–160 °C. $[\alpha]_D = -143.8°$ (*c* = 0.32): *O*-TBDMS derivative **7i**: crystallized from MeOH, 77% GC(A) 20.85; mp 140–142 °C.

***N*-[(2*R*,3*R*)-2-(Hydroxybenzyl)hexanoyl]bornane-10,2-sultam (3j). Using Freshly Distilled Bu_2BOTf.** Hexanoylsultam **2j** (101 mg, 0.323 mmol) and benzaldehyde (100 μL, 1.1 mmol) furnished a crude reaction mixture, HPLC (5:1) 6.9 (17.1), 12.8 (80.8), which was crystallized from CH_2Cl_2/hexane to give pure aldol **3j** (86.0 mg, 64%): HPLC (5:1) 12.74; mp 148–149 °C; $[\alpha]_D = -89.2°$ (*c* 0.62). *O*-TBDMS derivative **7j**: viscous oil, (81%); GC(A) 24.33.

^1H NMR Study of Boron Enolate 16, $ML_n = BBu_2$. Bu_2BOTf (1.0 M in CD_2Cl_2, 100 μL, 0.1 mmol) was added dropwise to a stirred solution of *N*-propionylsultam **2a** (25.0 mg, 0.09 mmol) in CD_2Cl_2 (0.7 mL) at −5 °C. After stirring (−5 °C, 5 min), $Et(iPr)_2N$ (17 μL, 0.1 mmol) was added, and the solution was transferred via a canula into a NMR tube which was subsequently sealed under nitrogen: ^1H NMR (CD_2Cl_2, 200 MHz, −8.7 °C, signals of interest) 3.20 (s, 2 H, C(10) protons), 3.80 (t, *J* = 6.5, C(2) proton), 4.39 (q, *J* = 6.8, 1 H, vinyl proton).

Lithium-Mediated Aldolizations. A solution of *n*-BuLi (1.6 M, hexane, 1.1 mol equiv) was added over 30 min at −78 °C to a solution of the appropriate *N*-acylsultam **2** in THF (5 mL). After stirring the resulting lithium enolate solution at −78 °C for 30 min, freshly distilled aldehyde (2.0–5.0 mol equiv) was added. Stirring at −78 °C for 1 h, addition of 10% aqueous citric acid, extraction (Et_2O), drying ($MgSO_4$), and evaporation of the extracts gave the crude product mixture which was analyzed by HPLC. Subsequent FC and crystallization provided the pure syn aldol **5**.

Tin(IV)-Mediated Aldolizations. Freshly distilled Bu_3SnCl (1.2 mol equiv) was added to the solution of the above-described lithium enolate at −78 °C. Stirring the mixture for 1 h, addition of the aldehyde, further stirring for 1 h at −78 °C, followed by workup gave crude aldol **5**, analyzed and purified as described above.

***N*-[(2*S*,3*R*)-2-Methyl-3-hydroxy-3-phenylpropanoyl]bornane-10,2-sultam (5a). A: Lithium-Mediated Aldolization. *N*-Propanoylsultam 2a** (250 mg, 0.92 mmol) was treated, as described above, with *n*-BuLi (1.6 M hexane, 630 μL). Addition of benzaldehyde (140 μL, 1.38 mmol) to the resulting lithium enolate solution gave a crude reaction mixture: HPLC (4:1) 10.47 (15.2), 12.37 (75.7), 29.8 (9). FC (hexane/EtOAc 4:1) followed by crystallization (MeOH) afforded pure aldol **5a** (190 mg, 55%): HPLC (6:1) 23.05 (98); mp 77.5–79 °C.

B: Tin(IV)-Mediated Aldolization. Successive treatment of the above-mentioned lithium enolate with Bu_3SnCl (300 μL, 1.1 mmol) and benzaldehyde gave a crude product mixture: HPLC (6:1) 12.77 (14.8), 17.51 (85.2). FC (hexane/EtOAc 4:1) followed by crystallization (MeOH) provided pure aldol **5a** (233 mg, 67%): HPLC (6:1) 23.25 (>99); mp = 78–79 °C; $[\alpha]_D = -23.07°$ (*c* 1.04).

***N*-[(2*S*,3*R*)-3-Hydroxy-2,4-dimethylpentanoyl]bornane-10,2-sultam (5d).** *N*-Propanoylsultam (250 mg, 0.92 mmol) was converted to its tin(IV) enolate as described above. Addition of isobutyraldehyde (168 μL, 1.85 mmol) and stirring at −78 °C for 1 h and then at −60°C for another 1 h, followed by workup, gave a crude reaction mixture containing auxiliary **1** (11% by ^1H NMR): HPLC (6:1) 17.13 (2.5), 18.12 (12.6), 28.37 (84.8). FC (hexane/EtOAc 4:1) followed by crystallization furnished pure aldol **5d** (138 mg, 44%): HPLC (4:1) 20.96 (>99%); mp 128–129 °C; $[\alpha]_D = -61°$ (*c* 0.09, *T* = 22.5 °C).

[(2*S*,3*R*)-3-Hydroxy-2-methylhexanoyl]bornane-10,2-sultam (5k). *N*-Propanoylsultam (250 mg, 0.92 mmol) was converted to its tin(IV) enolate as described above. Treatment with *n*-butyraldehyde (500 μL, 5.5 mmol) and workup gave a crude product mixture: HPLC (6:1) 24.87 (78.5). FC (hexane/EtOAc 6:1) afforded pure aldol **5k**: oil (168 mg, 53%); HPLC (6:1) 23.89 (100); $[\alpha]_D = -48°$ (*c* 1.52).

***N*-[(2*S*,3*R*)-2-Methyl-3-hydroxy-(*E*)-4-hexenoyl]bornane-10,2-sultam (5e).** *N*-Propanoylsultam **2a** (250 mg, 0.92 mmol) was converted to its tin(IV) enolate as described above. Treatment with (*E*)-crotonaldehyde (155 μL, 1.84 mmol) and workup gave a crude reaction mixture: HPLC (6:1) 21.3 (30), 26.1 (5), 31.3 (64.5). FC (hexane/EtOAc 6:1) yielded a less polar anti aldol: ^1H NMR 4.13 (q, *J* = 7.5, 1 H). Crystallization of the major fraction (hexane/CH_2Cl_2) yielded pure aldol **5e** (139 mg, 44%): mp 140–141 °C; HPLC (6:1) 29.1 (>99); $[\alpha]_D = -59°$ (*c* 1.47, $CDCl_3$).

Table V. Aldolization **2a** → **3a/4a/5a/6a**: Effect of Enolate Counterion

transmetalation conditions					
metal halide	mol equiv	temp (°C)	metal	product ratio **3a/5a/4a + 6a**	yield
none	0		Li	5:91:4	53
Bu_3SnCl	1.0	0	Sn(IV)	9:89:2	64
$ZnCl_2$	1.0	0	Zn	17:52:31(28:3)	56
$EtAlCl_2$	1.0	−40	Al	36:41:23(22:1)	88
$EtAlCl_2$	2.0	−78	Al	33:34:33	
Me_2AlCl	3.0	−40	Al	15:35:50(49:1)	82
$CeCl_3$	1.25	−78	Ce	17:83:0	70
Cp_2ZrCl_2	1.1	0	Zr	complex mixture	

***N*-[(2*S*,3*S*)-2-(Hydroxybenzyl)butanoyl]bornane-10,2-sultam (5g). A: Lithium-Mediated Aldolization.** *N*-Butanoylsultam **2g** (250 mg, 0.87 mmol) was treated, as described above, with *n*-BuLi (600 μL, 0.96 mmol). Addition of benzaldehyde (185 μL, 1.74 mmol) to the resulting lithium enolate solution gave a crude reaction mixture: HPLC (6:1) 13.48 (5.6), 16.81 (94.4). FC (hexane/EtOAc 6:1) gave a less polar anti isomer: ^1H NMR 4.81 (q, *J* = 7.5, 1 H). A sample of the combined, more polar fractions was converted to the *O*-TBDMS ethers: GC(A) 22.8 (7), 23.2 (93). Crystallization (MeOH), afforded pure aldol **5g** (199 mg, 58.5%): mp 129–130 °C. HPLC (6:1) 18.19 (>99%); $[\alpha]_D = -32.7°$ (*c* 0.96).

B: Tin(IV)-Mediated Aldolization. Successive treatment of the above-mentioned lithium enolate with Bu_3SnCl (280 μL, 1.04 mmol) and benzaldehyde gave a crude product mixture: HPLC (6:1) 13.3 (9.2), 16.5 (90.8). After removal of the less polar anti isomer by FC (hexane/EtOAc 6:1) a sample was converted to the *O*-TBDMS ethers: GC(A) 22.8 (11.3), 23.1 (88.7). Crystallization (MeOH) furnished pure aldol **5g** (217 mg, 64%) identical with a sample prepared via the lithium-mediated aldolization.

***N*-[(2*S*,3*R*)-2-Ethyl-3-hydroxy-4-methylpentanoyl]bornane-10,2-sultam (5i).** *N*-Butanoylsultam **2g** (250 mg, 0.87 mmol) was converted to its tin(IV) enolate as described above. Treatment with isobutyraldehyde (500 μL, 5.5 mmol) and workup gave a crude product mixture: HPLC (6:1) 14.79 (16.7), 28.32 (82:2). FC (hexane/EtOAc 6:1) gave a less polar anti aldol: ^1H NMR 3.13 (q, *J* = 7.5, 1 H). Crystallization (hexane/CH_2Cl_2) of the combined, more polar fractions yielded pure aldol **5i** (145 mg, 46.5%): mp 165–166 °C; HPLC (6:1) 16.95 (>99%); $[\alpha]_D = -61.8°$ (*c* 1.31).

***N*-[(2*S*,3*R*)-2-Ethyl-3-hydroxy-(*E*)-4-hexenoyl]bornane-10,2-sultam (5l).** *N*-Butanoylsultam **2g** (400 mg, 1.4 mmol) was treated successively with *n*-BuLi (965 μL, 1.54 mmol), Bu_3SnCl (455 μL, 1.68 mmol), and (*E*)-crotonaldehyde (234 μL, 2.8 mmol): HPLC of crude product (6:1) 15.75 (28.5), 18.18 (2), 21.81 (66), 27.22 (3.16). FC (hexane/EtOAc 6:1) followed by crystallization (hexane/CH_2Cl_2) gave pure aldol **5l** (154 mg, 31%); mp 130.5–131.5 °C; HPLC (6:1) 20.19 (100).

Aldolization 2a → 3a/4a/5a/6a: Effect of Enolate Counterion. A 2 M solution of propionylsultam **2a** (1 mol equiv) was added dropwise at −78 °C to a freshly prepared solution of lithium cyclohexylisopropylamide (LICA, THF, 1.05 mol equiv). The resulting solution of lithium enolate was treated first with 0–3 mol equiv of a metal halide at −78 to 0 °C and then with benzaldehyde (5 mol equiv) at −78 °C. After 20 min at −78 °C, 10% aqueous citric acid was added to give, after workup, mixtures **3a/4a/5a/6a** which were analyzed by HPLC (Table V).

N-Ethylpiperidine (1.2 mol equiv) was added dropwise to a stirred mixture of $Sn(OTf)_2$ (1.2 mol equiv) and propanoylsultam **2a** (1.0 mol equiv) in CH_2Cl_2 at 0 °C. After addition of benzaldehyde (2.4 mol equiv) at −78 °C the mixture was stirred at −78 °C for 30 min and then stirred at 0 °C for 16 h. Workup and HPLC analysis showed unchanged **2a** and no **3a/4a/5a/6a** products.

Nondestructive Cleavage of Aldol Sultams. Hydroperoxide-Assisted Saponification/Esterification. General Procedure. Aqueous (30%) H_2O_2 (2.4 mol equiv) and $LiOH·H_2O$ (1.2 mol equiv) were added at 0 °C to a solution of sultam aldol **3** or **5** (1.0 mol equiv) in THF/H_2O (4:1, 0.15 mmol/mL). Stirring of the mixture at 0 °C for 3–10 h, addition of saturated aqueous Na_2SO_3 (2.0 mL), acidification with 1 N HCl, saturation with NaCl, extraction with ether, drying, and evaporation of the extracts gave an oily residue which was treated with CH_2N_2 (excess). Evaporation of the solution and crystallization of the residue (hexane/Et_2O 4:1) gave recovered auxiliary **1**. FC (hexane/Et_2O 2:1) of the mother liquor provided pure β-hydroxy ester.

(2*R*,3*R*)-Methyl 2-Methyl-3-hydroxy-3-phenylpropanoate (12a). Applying the general saponification/esterification procedure, **3a** (130 mg, 0.345 mmol) gave auxiliary **1** (67.4 mg, 91%) and hydroxy ester **12a** (55.4 mg, 83%): GC(B) 11.01; $[\alpha]_D$ = +23.5° (*c* 3.23); lit.[4b] $[a]_D$ = +23.2°, (*c* 3.2, $CHCl_3$).

(2*R*,3*S*)-Methyl 2-Methyl-3-hydroxybutyrate (12b). On applying the general saponification procedure, but modifying the workup (addition of saturated aqueous Na_2SO_4, then NaCl, extraction with CH_2Cl_2), **3b** (175 mg, 0.56 mmol) gave auxiliary **1** (112.9 mg, 95%). Acidification of the aqueous phase, extraction, evaporation, and esterification with CH_2N_2 provided hydroxy ester **12b** (52.0 mg, 71%): GC (75°, isotherm) 1.38; $[\alpha]_D$ = −13.5° (*c* 0.867, MeOH); lit. (antipode)[21a] $[\alpha]_D$ = +14.3°, *c* 5.0, MeOH, *T* = 20 °C).

(2*R*,3*S*)-Methyl 2,4-Dimethyl-3-hydroxypentanoate (12d). Applying the general saponification/esterification procedure, **3d** (125 mg, 0.35 mmol) gave auxiliary **1** (67.7 mg, 90%) and hydroxy ester **12d** (54.3 mg, 84%): GC(B) 1.59; $[\alpha]_D$ = +7.50° (*c* 2.51); lit.[4b] $[\alpha]_D$ = +7.7°, (*c* 5.4, $CHCl_3$, *T* = 25 °C).

(2*R*,3*R*)-Methyl 2-Ethyl-3-hydroxy-3-phenylpropanoate (12g). Applying the general saponification/esterification procedure, **3a** (125 mg, 0.32 mmol) gave auxiliary **1** (61.6 mg, 89%) and hydroxy ester **12g** (50.2 mg, 76%): GC(B) 15.20. $[\alpha]_D$ = +13.5°, $[\alpha]_{578}$ = +14.45° (*c* 1.55); lit.[6c] $[\alpha]_D$ = +12.0°, *c* 1.58, $CHCl_3$, 96% ee).

(2*S*,3*S*)-Methyl 2-Methyl-3-hydroxy-3-phenylpropanaote (13a). Applying the general saponification/esterification procedure, **5a** (65 mg, 0.17 mmol) gave auxiliary **1** (34.1 mg, 92%) and hydroxy ester **13a** (25.4 mg, 76%): $[\alpha]_D$ = −20.8°, $[\alpha]_{578}$ = −21.7°, $[\alpha]_{546}$ = −24.1°, $[\alpha]_{436}$ = −38.4°, $[\alpha]_{365}$ = −52.5° (*c* 1.3). IR, ^1H NMR, ^{13}C NMR, and MS are identical with those of **12a**.

(2*S*,3*R*)-Methyl 2,4-Dimethyl-3-hydroxypentanoate (13d). Applying the general saponification/esterification procedure, **5d** (100 mg, 0.29 mmol) gave auxiliary **1** (56.5 mg, 90.6%) and hydroxy ester **13d** (42 mg, 90.5%): $[\alpha]_D$ = −7.14°, $[\alpha]_{578}$ = −7.47°, $[\alpha]_{546}$ = −8.40°, $[\alpha]_{436}$ = −8.99°, $[\alpha]_{365}$ = −19.32° (*c* = 1.19). IR, ^1H NMR, ^{13}C NMR, and MS identical with those of **12d**.

(2*S*,3*R*)-Methyl 2-Methyl-3-hydroxyhexanoate (13k). Applying the general saponification/esterification procedure, **5k** (100 mg, 0.29 mmol) gave auxiliary **1** (54 mg, 87%) and hydroxy ester **13k** (39 mg, 84%): $[\alpha]_D$ = +12.05° (*c* 1.92, *T* = 25.5 °C).

(2*S*,3*R*)-Methyl 2-Methyl-3-hydroxy-(*E*)-4-hexenoate (13e). Applying the general saponification/esterification procedure, **5e** (100 mg, 0.29 mmol) gave auxiliary **1** (56.5 mg, 90.5%) and hydroxy ester **13e** (36 mg, 85.5%): GC(B) 1.66; $[\alpha]_D$ = +11.52° (*c* 0.82, *T* = 25.5 °C).

(2*S*,3*S*)-Methyl 2-Ethyl-3-hydroxy-3-phenylpropanoate (13g). Applying the general saponification/esterification procedure, **5g** (100 mg, 0.25 mmol) gave auxiliary **1** (50.05 mg, 94%) and hydroxy ester **13g** (43 mg, 82.5%): GC(B) 5.08; $[\alpha]_D$ = −12.99° $[\alpha]_{578}$ = −13.46°, $[\alpha]_{546}$ = −15.19°, $[\alpha]_{436}$ = −19.71°, $[\alpha]_{365}$ = −22.30° (*c* 1.04). IR, ^1H NMR, ^{13}C NMR, and MS identical with those of antipode **12f**.

(2*S*,3*R*)-Methyl 2-Ethyl-4-methyl-3-hydroxypentanoate (13i). Applying the general saponification/esterification procedure, 5i (120 mg, 0.33 mmol) gave auxiliary **1** (66 mg, 93%) and hydroxy ester **13i** (52.5 mg, 91.5%): GC(B) 1.85; $[\alpha]_D$ = −7.4° (*c* 0.97); lit. (antipode)[6c] $[\alpha]_D$ = +7.6°.

(2*S*,3*R*)-Methyl 2-Ethyl-3-hydroxy-4-hexenoate (13l). Applying the general saponification/esterification procedure, **5l** (100 mg, 0.28 mmol) gave auxiliary **1** (56.5 mg, 94%) and hydroxy ester **13l** (25 mg, 52%): $[\alpha]_D$ = −7.1° (*c* 0.92).

Reductive Cleavage. General Procedure. A solution of the aldol product **3** (1.0 mol equiv) in THF/Et_2O (1:3, 4 mL/0.4 mmol) was added to a stirred suspension of $LiAlH_4$ (2.5 mol equiv) in Et_2O (1.0 mL/mmol) at 0 °C. Stirring (0 °C, 3 h), addition of saturated aqueous NH_4Cl, extraction with Et_2O, drying ($MgSO_4$), concentration, and FC (SiO_2, hexane/Et_2O, then Et_2O) gave the recovered sultam **1** and the respective, optically pure 1,3-diol **11**.

(1*R*,2*S*)-1-Phenyl-2-methylpropane-1,3-diol (11a). Applying the general reduction procedure, **3a** (130 mg, 0.35 mmol) gave auxiliary **1** (64.8 mg, 88%) and diol **11a** (43.0 mg, 75%), crystallized from Et_2O/hexane: mp 75–76 °C; GC(B) 12.68; $[\alpha]_D$ = +57.8° (*c* 0.45).

(2*S*,3*S*)-2-Methylbutane-1,3-diol (11b). Applying the general reduction procedure, **3b** (128 mg, 0.41 mmol) gave auxiliary **1** (78.2 mg, 90%) and diol **11b**, viscous oil (33.1 mg, 79%): GC(B) 1.42; $[\alpha]_D$ = +5.97° (*c* 0.32).

(2*S*,3*S*)-2,4-Dimethylpentane-1,3-diol (11d). Applying the general reduction procedure, **3d** (135 mg, 0.40 mmol) gave auxiliary **1** (75.3 mg, 93%) and diol **11d** (45.2 mg, 91%), crystallized from MeOH: mp 83 °C; GC(B) 1.57; $[\alpha]_D$ = +9.2° (*c* 0.71); lit.[21b] $[\alpha]_D$ = +11.3° (*c* 0.6, $CHCl_3$, *T* = 20 °C).

(2*S*,3*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-2-methylpentan-1-ol (14). Diisobutylaluminum hydride (1 M) (hexane 0.643 mL) was added over 10 min to a solution of **7c** (Et_2O, 95 mg, 0.214 mmol) at 0 °C. Stirring of the reaction mixture at 0 °C for 2 h, quenching with saturated aqueous NH_4Cl at −10 °C, stirring for 5 min, extraction with Et_2O, drying ($MgSO_4$), and evaporation gave a residue. Trituration with pentane provided insoluble solid sultam **1** (44 mg, 96%) and a solution which on FC (hexane/EtOAc 8:1) and bulb-to-bulb distillation (110–120 °C, bath, 1.5 Torr) provided serricornin precursor **14** (25 mg, 50%), oil: GC 70°, 3 min, 30°/min → 260°, 5.71; $[\alpha]_D$ = −4.8° (*c* 0.883, *T* = 25 °C); lit.[14b] $[\alpha]_D$ = −3.5° (*c* 1.98).

Preparation of Mixtures of Sultam Aldols 3/4/5/6 and Their *O*-TBDMS Ethers 7/8/9/10. A solution of diisopropylamine (2.0 mol equiv) in THF (1.2 mL/mmol) was cooled to −78 °C and treated with *n*-butyllithium (1.6 M in hexane, 2.0 mol equiv), allowed to warm to 0 °C (10 min), and subsequently cooled to −50 °C. A solution of propionic acid, butanoic acid, or hexanoic acid (1.0 mol equiv) in THF (0.5 mL/mmol) was added dropwise, and stirring was continued (20 °C, 1 h) whereupon a white precipitate formed. Upon cooling to −40 °C the appropriate aldehyde (1 mol equiv) was added, and stirring was continued until the white precipitate had disappeared (20 min). Addition of H_2O (5 mL), removal of THF, further addition of H_2O (50 mL) and extraction (Et_2O), followed by acidification of the aqueous phase (2 N H_2SO_4), extraction (Et_2O), and drying ($MgSO_4$) gave mixtures of racemic syn and anti β-hydroxy acids.

A solution of this mixture in DMF (3 mL/mmol) was treated with imidazole (4.0 mol equiv) and *t*$BuMe_2SiCl$ (2.0 mol equiv). After stirring (room temperature, 16 h) the reaction mixture was poured onto water and extracted (hexane). The combined organic phases were washed (saturated aqueous $NaHCO_3$), dried, evaporated, and distilled to give mixtures of racemic *syn*- and *anti*-3-((*tert*-butyldimethylsilyl)-oxy)-*tert*-butyldimethylsilyl esters.

A solution of this mixture (1.0 mol equiv) in CH_2Cl_2 (3 mL/mmol) was treated with DMF (2 drops) followed by oxaloyl chloride (1.1 mol equiv). After stirring (3 h, 20 °C), evaporation and bulb-to-bulb distillation gave the corresponding mixture of racemic *syn*- and *anti*-3-*O*-TBDMS acid chlorides.

A suspension of NaH (55% dispersion in mineral oil, 1.5 mol equiv) in toluene (25 mg/mL) was treated with a solution of sultam **1** (1.0 mol equiv) in toluene (38 mg/mL) and stirred (2 h, 20 °C). Adding a solution of the above-described acid chloride stereoisomer mixture (1.0 mol equiv in toluene) and stirring for 16 h followed by workup gave a mixture of *O*-TBDMS derivatives **7/8/9/10** which showed the following GC data: **7a–10a**(A) 22.3 (23), 22.8 (20), 22.9 (22), 23 (26); **7b–10b**(A) 18.6 (17), 18.8 (21), 19.23 (44); **7d–10d**(A) 20.0 (39), 20.2 (40), 20.5 (11), 20.6 (11); **7g–10g**(E) 18.3 (29), 19.6 (11), 18.95 (55). **7h–10h**(A) 19.4 (52), 19.7 (25), 19.8 (19). For comparison the corresponding sample was coinjected with one of these stereoisomer mixtures.

Aqueous (40%) HF (2.0 mol equiv) was added dropwise to a cooled solution of the corresponding mixture **7/8/9/10** (1.0 mol equiv) in MeCN (33 mg/mL). Stirring at 20 °C for 1.5 h and aqueous workup provided a mixture of sultam aldols **3/4/5/6** which showed the following HPLC data: **3a–6a** (4:1) 11.5 (58), 14.1 (31), 36.3 (11); **3b–6b** (4:1, 1.5 cm^3/min) 14.4 (25), 15.8 (26), 16.6 (30), 27 (19); **3d–6d** (6:1) 16.0 (11), 17.1 (56), 27.3 (12), 29 (20); **3g–6g** (5:1) 10.5 (28), 12.4 (11), 12.8 (11) >27 (~28); **3h–6h** (4:1) 13.3 (21), 13.7 (35), 20.1 (20), 26.1 (24). For comparison the corresponding sample was coinjected with one of these stereoisomer mixtures.

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Supplementary Material Available: Characterization data ([α] values, IR, ^1H NMR, ^{13}C NMR, MS, and HR MS) for **2a, 2g, 2j, 3a–j, 5a, 5d, 5e, 5g, 5i, 5k, 5l, 12a, 12b, 12d, 12g, 13e, 13i, 13k, 13l, 11a, 11b, 11d,** and **14** (12 pages). Ordering information is given on any current masthead page.