N-Acetylbornane-10,2-sultam: A Useful, Enantiomerically Pure Acetate Synthon for Asymmetric Aldol Reactions

Silas Bond and Patrick Perlmutter*

Department of Chemistry, Monash University, Clayton, Victoria, 3168, Australia

Received October 17, 1996
(Revised Manuscript Received May 20, 1997)

Introduction

In a projected synthesis of (+)-blastmycinone[1,2] (**1**, R = n-Bu) we needed to prepare enantiomerically-pure **2** shown in Scheme 1. We envisaged preparing **2** by a diastereoselective aldol reaction between an enantiomerically pure acetate synthon[3−5] **3** (an enolate of amide **4**, where X*$_N$ is a chiral auxiliary) and acrolein (Scheme 1).

As we have had some success with the use of dialkylboron enolates of *N*-propionylbornane-10,2-sultams (derivatives of "Oppolzer's sultams")[6] in aldol chemistry,[7,8] we decided to employ the corresponding *N-acetyl*bornane-10,2-sultam[9] as a chiral acetate synthon. On examination of the literature we were surprised to discover that no additions of the dialkylboron enolates of *N-acetyl*bornane-10,2-sultams[9] have been reported.

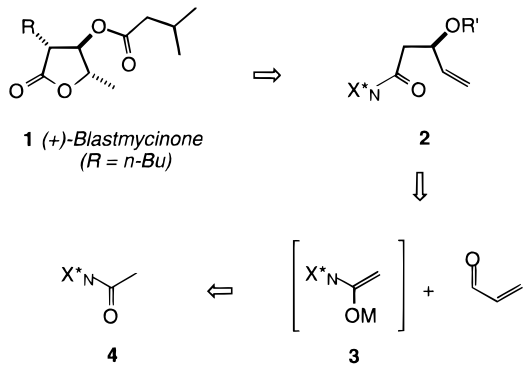
A summary of the aldol chemistry of *N*-acylbornane-10,2-sultams[6,9−11] is given in Scheme 2. Treatment of the corresponding (*Z*)-dialkylboron enolate **6**[6] or silyl ketene aminal **7**[10] with an aldehyde usually provides aldols **8** or **9**, respectively, with high diastereoselectivity.

The only report on the chemistry of the *N*-acetyl derivative **5a** describes Lewis acid promoted asymmetric aldol reactions of its corresponding silyl ketene aminals[10] (**7a**, Scheme 2). With regard to the current study it is important to note that for all these reactions, the relative stereochemistry *at the carbinol center* of the major product in each case is the same, irrespective of the starting enolate (*N*-acetyl[9] or other acyl[6]) or the reaction conditions (dialkyl boron enolate,[6] silyl ketene aminal,[10] presence[11] or absence[6] of additional Lewis acid).

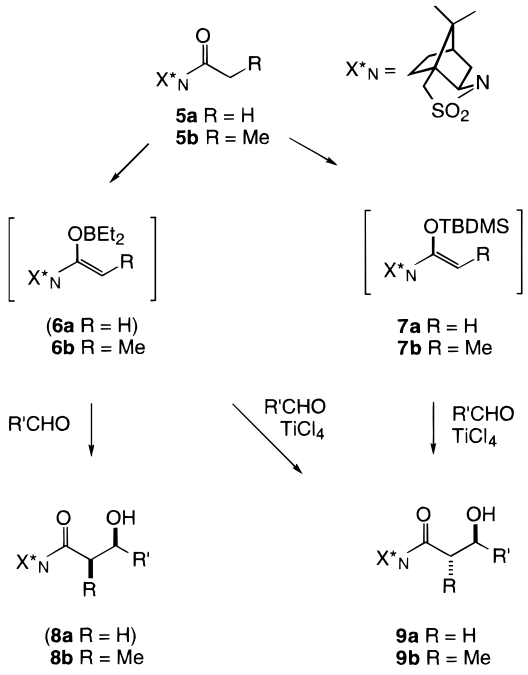
Results and Discussion

Thus we decided to examine the reaction of acrolein with the diethylboron enolate **6a** (Scheme 3). We were pleased to find that this aldol reaction proceeds in quite acceptable yields. Unlike reactions with the *N*-propionyl derivative **6b** there was no evidence of conjugate addition,[11] although dehydration of the initial adduct sometimes occurred to a small extent. We were able to obtain crystals of the major diastereomeric product which were suitable for X-ray crystallographic determination.[24] The solution is given in Figure 1 and clearly shows that the major aldol product is, in fact, **11** and not **10** (the latter

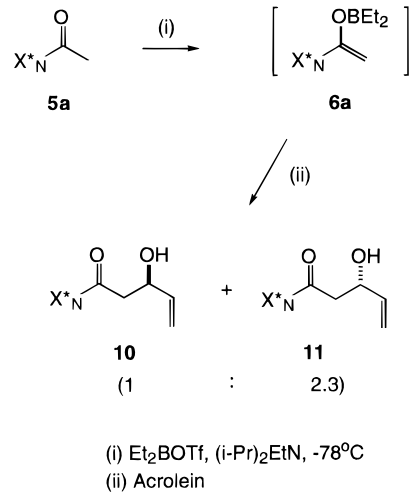
Scheme 1



Scheme 2



Scheme 3



(1) Birch, A. J.; Cameron, D. W.; Harada, Y.; Rickards, R. W. *J. Chem. Soc.* **1961**, 889−895.
(2) Li, W.; Nihira, T.; Sakuda, S.; Nishida, T.; Yamada, Y. *J. Ferm. Bioeng.* **1992**, *74*, 214−217.
(3) Otsuka, K.; Ishizuka, T.; Kimura, K.; Kunieda, T. *Chem. Pharm. Bull.* **1994**, *42*, 748−750.
(4) Cooke, J. W. B.; Davies, S. G.; Naylor, A. *Tetrahedron* **1993**, *49*, 7955−7966.
(5) Oppolzer, W.; Marco-Contelles, J. *Helv. Chim. Acta* **1986**, *69*, 1699−1703.
(6) Oppolzer, W.; Blagg, J.; Rodriguez, I.; Walther, E. *J. Am. Chem. Soc.* **1990**, *112*, 2767−2772.
(7) Mavropoulos, I.; Perlmutter, P. *Tetrahedron Lett.* **1996**, *37*, 3751−3754.
(8) Bratt, K.; Garavelas, A.; Perlmutter, P.; Westman, G. *J. Org. Chem.* **1996**, *61*, 2109−2117.
(9) Oppolzer, W.; Starkemann, C. *Tetrahedron Lett.* **1992**, *33*, 2439−2442.
(10) Oppolzer, W.; Starkemann, C.; Rodrigues, I.; Bernardinelli, G. *Tetrahedron Lett.* **1991**, *32*, 61−64.
(11) Oppolzer, W.; Lienard, P. *Tetrahedron Lett.* **1993**, *34*, 4321−4324.

S0022-3263(96)01953-6 CCC: $14.00

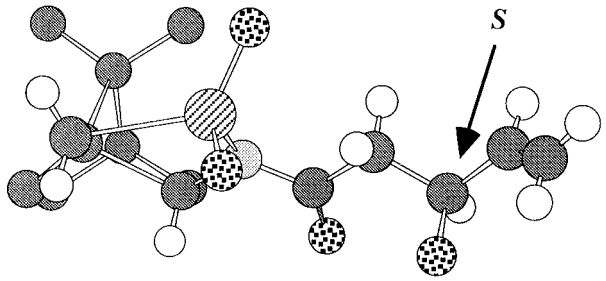
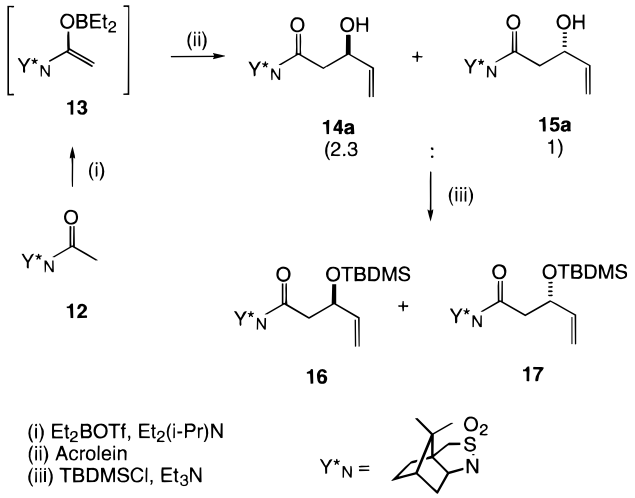
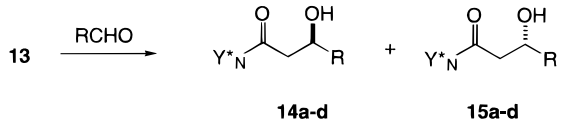


Figure 1. X-ray crystal structure of **11** (some hydrogens omitted for clarity).

Scheme 4



Scheme 5



would have been expected by analogy with aldol reactions of the diethylboron enolates of *N*-propionylbornane-10,2-sultams (see Scheme 2)). By comparison, reaction of the lithium enolate of **5a** gave an almost equal ratio of aldol products.

As we required, for future work, the opposite stereochemistry at the carbinol center to that obtained in **11**, we switched to the enantiomeric series (i.e. using enolate **13** derived from *N*-acetyl-2(*S*)-bornane-10,2-sultam **12** (Scheme 4). As expected, adduct **14a** was the major product. Purification of this aldol mixture was difficult so it was converted into a mixture of the corresponding TBDMS ethers from which the desired diastereomer **16** was easily obtained pure ($[\alpha]_D$ 54.0, *c* 1.05, $CHCl_3$) by crystallization from ethanol.

Although the diastereoselectivity for each of these aldols was not great (≈2.3:1 in favor of **11** or **14a**), we were interested to establish whether this unexpected diastereoselectivity was a more general phenomenon or merely peculiar to reactions with acrolein. The results for the aldol reactions of **13** with some typical aldehydes (Scheme 5) are collected in Table 1. Consistent with our results with acrolein, in each of the cases we examined, the major adduct was **14** and not **15**. In fact the diastereoselectvity was found to be much better than that for acrolein, ranging from 81:19 to 91:9.[12,13]

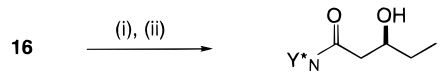
The stereochemistry of the adducts from reactions of **13** with acrolein and propanal (entry 2) was chemically

Table 1. Results for Aldol Reactions of 13

entry	aldehyde (RCHO) R	products[a] (**14**:**15**)
1	**a**, R = vinyl	70:30
2	**b**, R = ethyl	91:9
3	**c**, R = isopropyl	90:10
4	**d**, R = phenyl	81:19

[a] Ratios were determined by analytical HPLC on a Porasil column (eluant: ethyl acetate/hexane).

Scheme 6



(i) Conc. HCl/THF (1:10), r.t.
(Ii) Pd/C, H_2, r.t.

correlated. Thus, desilylation of **16** followed by catalytic reduction gave material identical with the major propanal aldol adduct (Scheme 6). For aldol reactions with isobutyraldehyde (entry 3) and benzaldehyde (entry 4), the stereochemistry of the major adduct in each case was established by hydrolysis to the corresponding known β-hydroxy acid[14] and comparison of their optical rotations.

Asymmetric aldol reactions involving dialkylboron enolate intermediates generally proceed through chair-like transition states (i.e. **19**, Figure 2). Were this the case in the present study, then the major diastereomeric products should have been **15a**−**d** in reactions with enolate **13**. The finding that the major products were, in fact, **14a**−**d** suggests that a different transition state is involved. We propose that a boatlike transition state (i.e. **18**, Figure 2) is responsible for the observed diastereoselection. Similar transition states have been described before[15] and are thought to be important in aldol reactions involving chiral enolates of methyl ketones.[16−20] In this regard it may be more appropriate to consider the enolates derived from *N*-acetylsultams as part of this family of acetyl enolates (i.e. including *N*-acetyl and "*C*-acetyl" derivatives).[21] The torsional strain experienced by **18** is, most likely, smaller than the unfavorable pseudo-1,3-diaxial interaction (between one of the boron ligands and the auxiliary) evident in **19**. Preference for the boat conformation **18**, with "R" occupying the sterically-less demanding pseudoequatorial position, leads to

(12) The use of 1 equiv each of diethylboron triflate and diisopropylethylamine gave identical stereoselection but with significant quantities of unchanged starting material.

(13) In response to a referee's suggestion we prepared purified diethylboron triflate (see ref 15) and repeated several of the reactions listed in Table 1. In all cases, the results were, within experimental error, the same as those obtained using diethylboron triflate generated "in situ". This precludes the possibility of ethylboron ditriflate being responsible for our results (see Boeckman, R. K., Jr.; Johnson, A. T.; Musselman, R. A. *Tetrahedron Lett.* **1994**, *35*, 8521−8524).

(14) Helmchen, G.; Leikauf, U.; Taufer-Knopfel, I. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 874−875.

(15) Evans, D. A.; Nelson, J. V.; Taber, T. R. *J. Am. Chem. Soc.* **1981**, *103*, 3099−3111.

(16) Gustin, D. J.; VanNieuwenhze, M. S.; Roush, W. R. *Tetrahedron Lett.* **1995**, *36*, 3443−3446.-

(17) Bernardi, F.; Robb, M. A.; Suzzi-Valli, G.; Tagliavini, E.; Trombini, C.; Umani-Ronchi, A. *J. Org. Chem.* **1991**, *56*, 6472−6475.

(18) Goodman, J. M.; Kahn, S. D.; Paterson, I. *J. Org. Chem.* **1990**, *55*, 3295−3303.

(19) Li, Y.; Paddon-Row, M. N.; Houk, K. N. *J. Org. Chem.* **1990**, *55*, 481−493.

(20) Bernardi, A.; Capelli, A. M.; Gennari, C.; Goodman, J. M.; Paterson, I. *J. Org. Chem.* **1990**, *55*, 3576−3581.

(21) For examples of Lewis-acid promoted *anti*-aldol reactions which would be expected to provide the opposite stereochemical result at the newly-formed carbinol center to those described here see: Raimundo, B. C.; Heathcock, C. H. *Synlett* **1995**, 1213−1214 and references cited therein.

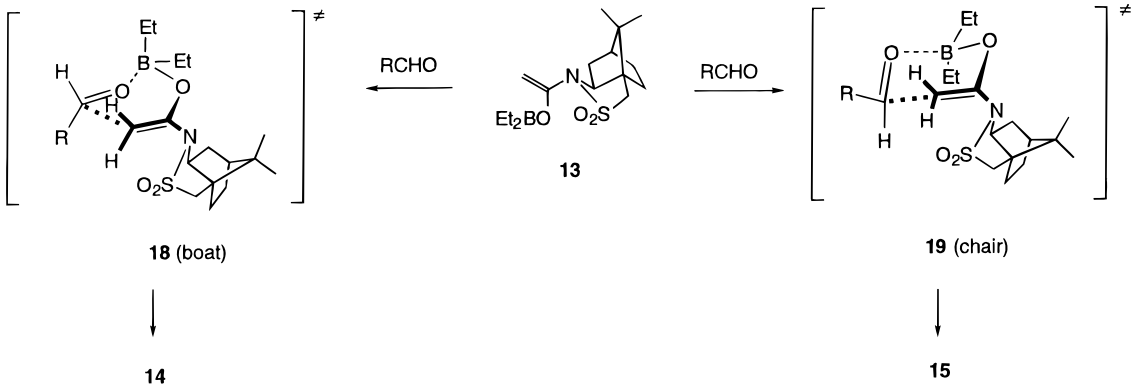


Figure 2.

the correct diastereomeric product. Reactions of the α,β-unsaturated aldehydes, acrolein and benzaldehyde, showed poorer diastereoselectivity than the two saturated aldehydes. It is plausible that there may be a small electronic preference for reaction via a chairlike transition state for the former aldehydes the result of which would be a reduction in diastereoselectivity.

In summary, we have demonstrated that diethylboron enolates of *N*-acetylbornane sultams react with aldehydes with good diastereoselectivity. Although this stereoselectivity is different to that observed in the reactions of other, closely related chiral enolates it appears to be reliable and predictable. It is proposed that the reaction proceeds through a boatlike transition state. Consequently this study has uncovered a useful, enantiomerically pure acetate synthon.

Experimental Section

General Methods. Toluene, CH_2Cl_2, and DMF were all dried by distillation from CaH_2. Benzaldehyde, propanal, acrolein, and isobutyraldehyde were all freshly distilled prior to use. All reactions were conducted under a nitrogen atmosphere.

Flash chromatography was carried out using SiO_2 (230−400 mesh). HPLC analyses were performed using a SiO_2 column (3.9 mm × 300 mm) with both UV and refractive index detectors. The eluant was hexanes/ethyl acetate mixtures and a flow rate of 1 mL/min was used. Retention times are in minutes (area %).

Melting points were measured on a hot stage melting point apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded at 200 MHz or 300 MHz and 50 MHz, respectively, in either $CDCl_3$ or d_6-acetone.

(2*S*)-*N*-Acetylbornane-10,2-sultam (12).[9] Toluene (150 mL) was added to (2*S*)-bornane-10,2-sultam[22,23] (10 g, 46.5 mmol) and NaH (2.1 g, 80% dispersion in mineral oil, 70 mmol) under N_2. This mixture was stirred at rt for 2 h after which time freshly distilled acetyl chloride (5 mL, 70.3 mmol) in toluene (50 mL) was added slowly. Stirring was continued for a further 2 h, and the reaction was quenched with saturated aqueous NH_4Cl (100 mL). After separation of the toluene layer, the aqueous layer was extracted with ether (2 × 25 mL), the combined organic extracts were dried ($MgSO_4$) and filtered, and the solvent removed to yield a white solid which was recrystallized from ethyl acetate/petroleum ether to yield colorless crystals (9.8 g, 82%): mp 138−139°; HPLC (4:1), 7.58; $[\alpha]^{19}_D$ +104.8 (*c* 1.06, $CHCl_3$); IR (Nujol) 1687, 1425, 1324, 1140, 986 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.97 (s, 3H), 1.15 (s, 3H), 1.30−1.43 (m, 2H), 1.83−2.07 (m, 4H), 2.10−2.19 (m, 3H), 2.40 (s, 3H), 3.42 (d, *J* = 13.8 Hz, 1H), 3.50 (d, *J* = 13.8 Hz, 1H), 3.84 (dd, *J* = 7.7, 5.1 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 19.8, 20.7, 23.1, 26.3, 32.7, 38.3, 44.5, 47.6, 48.3, 52.7, 65.1, 168.5; HRMS calcd for M^+: *m*/*z* 257.109, found 257.108; MS *m*/*z* 257 (M^+, 4%), 135 (59), 134 (100), 132 (43), 119 (38), 108 (48), 93 (45), 67 (35).

General Procedure for the Aldol Reaction.[6] To 1 M triethylborane (3.2 mL, 3.2 mmol) in hexanes was added freshly distilled triflic acid (290 μL, 3.2 mmol). After 30 min, the homogeneous solution was cooled to −5 °C and the acetyl sultam **5a** or **12** (412 mg, 1.6 mmol) in CH_2Cl_2 (6.5 mL) was added, followed by diisopropylethyl amine (560 μL, 3.2 mmol) in CH_2Cl_2 (3.4 mL). The solution was stirred for a further 30 min after which time it was cooled to −78 °C and a solution of the aldehyde (2 equiv) in CH_2Cl_2 was added. The solution was stirred for an additional 3 h and then quenched at −78 °C with pH 7 phosphate buffer and allowed to warm to rt. The organic layer was separated and the aqueous layer extracted with Et_2O. The combined extracts were washed with saturated aqueous NH_4Cl, dried ($MgSO_4$), and filtered, and the solvent was evaporated.

(2*R*)-*N*-[(3*S*)-3-Hydroxy-4-penten-1-oyl]bornane-10,2-sultam (11). The general aldol procedure was followed using *N*-acetyl sultam **5a** (412 mg, 1.6 mmol) and acrolein (1.3 mL, 20 mmol) in CH_2Cl_2 (5 mL) which was added via a syringe pump (0.2 mL/min), yielding a crude aldol mixture (326 mg, 65%): HPLC (7:3), 8.93 (22), 10.46 (78). Flash chromatography (3:1, petroleum ether/ethyl acetate) and crystallization from ethyl acetate/petroleum ether yielded colorless prisms: mp 94−95 °C; HPLC (7:3), 10.17; $[\alpha]^{20}_D$ −114.9 (*c* 0.92, $CHCl_3$); IR (Nujol) 3539, 1690, 1319, 1136, 927 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.97 (s, 3H), 1.16 (s, 3H), 1.35−1.50 (m, 2H), 1.80−2.00 (m, 3H), 2.05−2.20 (m, 2H), 2.89 (dd, *J* = 16.8, 7.9 Hz, 1H), 3.01 (dd, *J* = 16.9, 4.2 Hz, 1H), 3.11 (d, *J* = 5 Hz, 1H), 3.45 (d, *J* = 17.7 Hz, 1H), 3.52 (d, *J* = 17.7 Hz, 1H), 3.89 (dd, *J* = 7.6, 5.2 Hz, 1H), 4.55−4.70 (m, 1H), 5.16 (dt, *J* = 10.4, 1.4 Hz, 1H), 5.33 (dt, *J* = 17.2, 1.5 Hz, 1H), 5.90 (td, *J* = 15.9, 10.5, 5.4 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 19.8, 20.8, 26.3, 32.7, 38.3, 42.0, 44.6, 47.7, 48.4, 52.8, 65.0, 68.8, 115.3, 138.5, 170.5; HRMS calcd for M^+: *m*/*z* 313.135, found 313.135; MS *m*/*z* 313 (M^+, 0.5%), 136 (64), 134 (91), 119 (64), 108 (90), 93 (77), 81 (100), 67 (45), 56 (71). Anal. Calcd for $C_{15}H_{23}NO_4S$: C, 57.5; H, 7.4; N, 4.5. Found: C, 57.8; H, 7.7; N, 4.3.

(2*S*)-*N*-[(3*R*)-3-Hydroxy-4-penten-1-oyl]bornane-10,2-sultam (14a). The general aldol procedure was followed using *N*-acetyl sultam **12** (412 mg, 1.6 mmol) and acrolein (1.3 mL, 20 mmol) in CH_2Cl_2 (5 mL) which was added via a syringe pump (0.2 mL/min) to yield a crude aldol mixture (350 mg, 70%): HPLC (4:1), 16.11 (30), 20.27 (70). Flash chromatography (3:1, petroleum ether/ethyl acetate) and crystallization from ethyl acetate/petroleum ether yielded colorless prisms: mp 95−96 °C; HPLC (4:1), 20.16; $[\alpha]^{20}_D$ +112.6 (*c* 1.02, $CHCl_3$); IR (Nujol) 3538, 1689, 1135, 927 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.98 (s, 3H), 1.16 (s, 3H), 1.31−1.59 (m, 2H), 1.84−1.98 (m, 3H), 2.03−2.20 (m, 2H), 2.91 (dd, *J* = 8.1, 16.7 Hz, 1H), 3.01 (dd, *J* = 3.8, 16.7 Hz, 1H), 3.11 (d, *J* = 4.6 Hz, 1H), 3.44 (d, *J* = 21.6 Hz, 1H), 3.52 (d, *J* = 21.6 Hz, 1H), 3.89 (dd, *J* = 5.1, 7.7 Hz, 1H), 4.56−4.62 (m, 1H), 5.15 (dt, *J* = 1.3, 10.5 Hz, 1H), 5.33 (dt, *J* = 1.3, 17.1 Hz, 1H), 5.89 (td, *J* = 5.3, 10.5, 17.1 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 19.7, 20.7, 26.2, 32.6, 38.2, 41.5, 44.5, 47.6, 48.4, 52.7,

(22) Bartlett, P. D.; Knox, L. H. *Organic Synthesis*; John Wiley and Sons: New York, 1973; Collect. Vol. V; pp 196−198.

(23) Davis, F. A.; Towson, J. C.; Weismiller, M. C.; Lal, S.; Carroll, P. J. *J. Am. Chem. Soc.* **1988**, *110*, 8477−8482.

(24) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

64.9, 68.7, 115.2, 138.5, 170.4; MS *m/z* 313 (M^+, 3%), 216 (20), 151 (81), 135 (82), 139 (68), 108 (70), 93 (65), 57 (100). Anal. Calcd for $C_{15}H_{23}NO_4S$: C, 57.5; H, 7.4; N, 4.5. Found: C, 57.3; H, 7.2; N, 4.4.

(2*S*)-*N*-[(3*S*)-3-Hydroxypentan-1-oyl]bornane-10,2-sultam (14b). The general aldol procedure was followed using *N*-acetyl sultam **12** (412 mg, 1.6 mmol) and propionaldehyde (0.23 mL, 3.2 mmol) in CH_2Cl_2 (1 mL) to yield a crude aldol mixture: HPLC (4:1), 15.66 (9), 19.93 (91). Flash chromatography (3:1, petroleum ether/ethyl acetate) and crystallization from ethyl acetate/petroleum ether yielded colorless crystals (436 mg, 86%): mp 73 °C; HPLC (4:1), 20.29; $[\alpha]^{20}_D$ +125.8 (*c* 1.00, $CHCl_3$); IR (Nujol) 3412, 1660, 1337, 1140, 978 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.94 (t, J = 7.4 Hz, 3H), 0.95 (s, 3H), 1.13 (s, 3H), 1.29−1.46 (m, 2H), 1.47−1.59 (m, 2H), 1.86−2.02 (m, 3H), 2.03−2.18 (m, 2H), 2.74 (dd, J = 16.7, 8.9 Hz, 1H), 2.90 (dd, J = 16.7, 2.7 Hz, 1H), 3.40 (bs, 1H), 3.42 (d, J = 13.8 Hz, 1H), 3.49 (d, J = 13.8 Hz, 1H), 3.85 (dd, J = 7.6, 5 Hz, 1H), 3.92−4.01 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 9.7, 19.7, 20.7, 26.2, 29.2, 32.6, 38.3, 41.6, 44.5, 47.6, 48.3, 52.7, 64.9, 69.2, 171.0; MS *m/z* 315 (M^+, 0.1%), 286 (10), 216 (25), 151 (58), 135 (61), 134 (78), 119 (41), 108 (63), 93 (71), 83 (100), 79 (47), 67 (59), 59 (75), 55 (88). Anal. Calcd for $C_{15}H_{25}NO_4S$: C, 57.12; H, 7.99; N, 4.44. Found: C, 57.08; H, 8.03; N, 4.32.

(2*S*)-*N*-[(3*R*)-3-Hydroxy-4-methylpentan-1-oyl]bornane-10,2-sultam (14c). The general aldol procedure was followed using *N*-acetyl sultam **12** (412 mg, 1.6 mmol) and isobutyraldehyde (0.29 mL, 3.2 mmol) in CH_2Cl_2 (1 mL) to yield a crude aldol mixture: HPLC (4:1), 11.72 (10), 15.33 (90). Flash chromatography (3:1, petroleum ether/ethyl acetate) and crystallization from ethyl acetate/petroleum ether yielded fine needles (419 mg, 76%): mp 109−110 °C; HPLC (4:1), 15.45; $[\alpha]^{20}_D$ +118.6 (*c* 1.04, $CHCl_3$); IR (Nujol) 3558, 1674, 1327, 1134 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.92−0.98 (m, 9H), 1.16 (s, 3H), 1.45−1.35 (m, 2H), 1.74 (oct, J = 6.6 Hz, 1H), 1.88−1.98 (m, 3H), 2.03−2.19 (m, 2H), 2.76 (dd, J = 16.5, 9.5 Hz, 1H), 2.93 (dd, J = 16.6, 2.6 Hz, 1H), 2.98 (d, J = 4.1 Hz, 1H), 3.45 (d, J = 13.9 Hz, 1H), 3.52 (d, J = 13.8 Hz, 1H), 3.79−3.91 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 17.6, 18.4, 19.8, 20.8, 26.4, 32.8, 33.2, 38.4, 39.5, 44.6, 47.7, 48.4, 52.9, 65.1, 72.8, 172.0; HRMS calcd for $M^+ - 18$ (H_2O): *m/z* 311.156, found 311.155; MS *m/z* 311 ($M^+ - H_2O$, 4.5%), 286 (39), 216 (69), 151 (69), 135 (100), 134 (73), 108 (71), 93 (86), 91 (50), 79 (57), 73 (89), 69 (68), 55 (79).

(2*S*)-*N*-[(3*R*)-3-Hydroxy-3-phenylpropan-1-oyl]bornane-10,2-sultam (14d). The general aldol procedure was followed using *N*-acetyl sultam **12** (412 mg, 1.6 mmol) and benzaldehyde (0.32 mL, 3.2 mmol) in CH_2Cl_2 (1 mL) to yield a crude aldol mixture: HPLC (4:1), 15.78 (19), 20.66 (81). Flash chromatography (3:1, petroleum ether/ethyl acetate) and crystallization from ethyl acetate/petroleum ether yielded colorless crystals (433 mg, 75%): mp 167−168 °C; HPLC (4:1), 20.18; $[\alpha]^{20}_D$ +116.5 (*c* 1.05, EtOH); IR (Nujol) 3509, 1679, 1331, 1139 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.96 (s, 3H), 1.11 (s, 3H), 1.34−1.44 (m, 2H), 1.87−1.97 (m, 3H), 2.03−2.17 (m, 3H), 3.05−3.20 (m, 2H), 3.40−3.52 (m, 3H), 3.86−3.90 (m, 1H), 5.16−5.22 (m, 1H), 7.24−7.40 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 19.7, 20.7, 26.3, 32.7, 38.3, 44.1, 44.5, 47.6, 48.4, 52.7, 65.0, 70.2, 125.7, 127.6, 128.4, 142.1, 170.7; HRMS calcd for $MH^+ - 18$ (H_2O): *m/z* 346.148, found 346.147; MS *m/z* 364 (MH^+, 1%), 346 ($MH^+ - H_2O$, 77%), 258 (51), 216 (50), 151 (37), 136 (47), 135 (100), 109 (68), 105 (73), 93 (37).

(2*S*)-*N*-[(3*R*)-3-[(*tert*-Butyldimethylsilyl)oxy]-4-peten-1-oyl]bornane-10,2-sultam (16). To the crude acrolein aldol mixture (1.3 g), obtained from the reaction of *N*-acetyl sultam **12** and acrolein, were added imidazole (720 mg, 10.6 mmol), DMAP (6 mg, 0.05 mmol), and *tert*-butyldimethylsilyl chloride (700 mg, 4.7 mmol) in DMF (4 mL) and stirred at 45 °C under N_2 for 16 h. The reaction was quenched with H_2O (10 mL), extracted with CH_2Cl_2 (3 × 5 mL), and dried ($MgSO_4$). The majority of the solvent was removed *in vacuo* with the residual DMF being removed with the aid of a freeze dry apparatus to yield a solid from which **16** could be crystallized from absolute EtOH to yield fine needles (405 mg, 23% over two steps de pure, nonoptimized): mp 126−127 °C; $[\alpha]^{20}_D$ +54.0 (*c* 1.05, $CHCl_3$); IR (Nujol) 1674, 1335, 1139, 992 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.04 (s, 3H), 0.06 (s, 3H), 0.87 (s, 9H), 0.96 (s, 3H), 1.14 (s, 3H), 1.30−1.43 (m, 2H), 1.85−1.95 (m, 4H), 2.04−2.07 (m, 2H), 2.89 (dd, J = 21.6, 6.4 Hz, 1H), 2.96 (dd, J = 21.6, 6.6 Hz, 1H), 3.42 (d, J = 13.8 Hz, 1H), 3.49 (d, J = 13.8 Hz, 1H), 3.85 (t, J = 6.3 Hz, 1H), 4.66 (q, J = 6.6 Hz, 1H), 5.04 (dt, J = 10.5, 1.3 Hz, 1H), 5.20 (dt, J = 17.1, 1.6 Hz, 1H), 5.80−5.92 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ −5.0, −4.4, 18.1, 19.9, 20.8, 25.8, 26.4, 32.8, 38.4, 44.2, 44.6, 47.7, 48.3, 53.0, 65.1, 70.8, 114.9, 140.2, 169.1; MS *m/z* 426 (M^+, 3%), 370 (62), 314 (38), 172 (36), 155 (38), 138 (82), 107 (52), 93 (54), 75 (92), 73 (100), 59 (20). Anal. Calcd for $C_{21}H_{37}NO_4SSi$: C, 59.0; H, 8.7; N, 3.3. Found: C, 59.2; H, 8.7; N, 3.4.

(3*R*)-3-Hydroxy-4-methylpentanoic Acid.[6,9] To **14c** (95 mg, 0.28 mmol) in THF/H_2O (4:1, 4 mL) at 0 °C was added $LiOH \cdot H_2O$ (17 mg, 0.40 mmol) and 30 wt % H_2O_2 (0.155 mL, 1.52 mmol). This was stirred at 0 °C for 3 h and then quenched with saturated Na_2SO_3 (1 mL). Concentrated NH_3 (1 mL) was added and the solution extracted with CH_2Cl_2 to yield after separation, drying ($MgSO_4$), and evaporation the sultam (60 mg, 100%). The aqueous layer was acidified with concd HCl and extracted with ether (3 × 10 mL). The combined organic extracts were dried ($MgSO_4$), and the solvent was removed to yield a colorless oil (26 mg, 65%): $[\alpha]^{20}_D$ +40.0 (*c* 1.32, $CHCl_3$) [lit.[13] $[\alpha]^{25}_D$ +40.2 (*c* 1.2, $CHCl_3$)]; ^1H NMR (200 MHz, $CDCl_3$) δ 0.91 (d, J = 5.1 Hz, 3H), 0.94 (d, J = 5.4 Hz, 3H), 1.72 (s, J = 6.6 Hz, 1H), 2.43 (dd, J = 16.2, 9.8 Hz, 1H), 2.55 (dd, J = 16.3, 3.5 Hz, 1H), 3.72−3.94 (m, 1H).

(3*R*)-3-Hydroxy-3-phenylpropanoic Acid.[6,9] To **14d** (162 mg, 0.45 mmol) in THF/H_2O (4:1, 8 mL) at 0 °C was added $LiOH \cdot H_2O$ (25 mg, 0.60 mmol) and 30 wt % H_2O_2 (0.250 mL, 2.44 mmol). This was stirred at 0 °C for 3 h and then quenched with saturated Na_2SO_3 (1 mL). Concentrated NH_3 (1 mL) was added and the solution extracted with CH_2Cl_2 to yield after separation, drying ($MgSO_4$), and evaporation the sultam (92 mg, 96%). The aqueous layer was acidified with concd HCl and extracted with ether (3 × 10 mL). The combined organic extracts were dried ($MgSO_4$), and the solvent was removed to yield a white solid (70 mg, 94%): mp 119−121 °C; $[\alpha]^{20}_D$ +17.2 (*c* 2.32, 95% EtOH) [lit.[13] $[\alpha]^{25}_D$ +17.9 (*c* 2.5, 95% EtOH)]; ^1H NMR (200 MHz, d_6-acetone) δ 2.69 (d, J = 6.6 Hz, 2H), 5.15 (t, J = 6.7 Hz, 1H), 7.21−7.43 (m, 5H).

Conversion of 16 to 14b. The silyl ether **16** (89 mg, 0.21 mmol) was stirred in a THF:concd HCl (5.5 mL, 10:1) solution at rt for 3 h after which it was diluted with water (10 mL) and extracted with ether (1 × 10 mL, 2 × 5 mL). The combined extracts were dried ($MgSO_4$) and filtered, and the solvent was evaporated to yield **14b** (60 mg, 92%) whose ^1H NMR spectrum was identical to that of the purified acrolein aldol adduct previously obtained in this work and was used without purification. The deprotected product was dissolved in absolute ethanol (1 mL), and a catalytic amount of 10% Pd/C was added. The mixture was stirred under an atmosphere of H_2 for 15 min after which time the mixture was filtered through a Celite pad and the solvent removed *in vacuo* to yield **14b** (49 mg, 81%) whose ^1H NMR spectrum was identical to a sample previously obtained in this work. HPLC (4:1), 19.57. Similar processing of a 1:1 diastereomeric of **16** and **17** yielded a 1:1 mixture of **14b** and **15b**. HPLC (4:1), 15.14, 19.77.

Acknowledgment. S.B. is grateful to the Australian Government for an Australian Postgraduate Research Award, and P.P. is grateful to the Australian Research Council for financial support. We thank Dr. G. D. Fallon for determining the X-ray crystal structure of **11**.

Supporting Information Available: ^{13}C NMR spectra for compounds **12**, **14c**, and **14d** have been provided in lieu of combustion analysis (3 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO961953B