Asymmetric Aldol Type Reactions of Acetate Imide Enolates

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Titanium-mediated chelation-controlled aldol type reactions of acetate thioimide enolates with representative aldehydes proceed with high π-facial differentiation. An investigation of the influence of the nature of the imide enolate ligands and the Lewis acids in the non-chelation-controlled aldol bond construction process of acetate imide enolates reveals that alternation of either the boryl geometry or imide enolate ligand leads to π-facial selectivity switch.

Introduction

Asymmetric aldol type reactions employing chiral boron enolates have received significant synthetic and mechanistic attention.[1] The well-established Zimmerman–Traxler pericyclic chairlike transition-state model has been proposed to explain the stereochemical outcome of various aldol addition processes.[2] This chairlike transition-state hypothesis also accounts very well for the general observation that the aldol reactions from α-substituted boron enolates exhibited exceptionally high stereoselection.[3] However, the transition from the propionate to the acetate enolate is unexpectedly accompanied by the disappointingly low levels of asymmetric induction.[1b,c,3b,c] Recently, although impressive progress in this area has been made using metal complexes with chiral ligands,[4] chiral silyl ketene acetals,[5] chiral silyl enol ethers,[6] chiral promoter systems,[7] auxiliary substituents,[3c,e] chiral borolane triflates,[8] or chiral chelatable metal enolates (eg., $Sn(OTf)_2$),[9] the underlying causes of the insufficient aldol stereoselectivity of boryl acetate enolates are still not completely clear at present.[1b,c,3c,8] All the established approaches have their individual strengths and weakness. To develop an efficient approach for the construction of enantiomerically pure β-hydroxy carboxylic acids and to get insight into the origin of the nonexistent stereodifferentiation of α-unsubstituted enolates, we sought to evaluate the influence of the nature of Lewis acids and the imide enolate ligands. We wish to describe an enantioselective acetate titanium enolate aldolization which offers a practical alternative to the use of other methods and to record the remarkable effect that the nature of either the boryl geometry or imide enolate ligand has on influencing the π-facial selection of acetate boryl enolates.

Results and Discussion

Previous reports from our laboratory have documented a novel method for switching between chelation- and non-chelation-controlled aldol reactions of chiral propionate imide enolates.[3i] The excellent diastereoselectivity obtained with propionate titanium and boron imide enolates and the dramatic π-facial selectivity switch for chlorotitanium-mediated aldolizations prompted us to examine the acetate imide enolates derived from *N*-acetyloxazolidinone **2O** and *N*-acetyloxazolidinethione **2S**, wherein considerable structural homology exists between them but the physical property of the exocyclic ring carbonyl is quite different from that of thiocarbonyl. At the outset of the present study, we surveyed mainly the camphor-derived acetate boryl imide enolates for reaction facial selection. The requisite imides were synthesized according to Scheme 1. Acylation of the previously reported oxazolidinone **1O** and oxazolidinethione **1S**[3i] with acetyl chloride in the presence of sodium hydride led to a nearly quantitative yield of imides **2O** and **2S**, respectively. The aldol additions of dibutylboryl enolates **3a** and **3b** to the representative aldehydes were carried out by a standard procedure.[3b] Table 1 summarizes the results of aldol reactions of **3a** and **3b** where a direct comparison can be made upon the influence of the nature of imide enolates upon the π-facial selection. The stereochemical identity of the aldol adducts was confirmed by conversion of the aldols **5**, **6**, **7**, and **8** to the corresponding acids **9** and **10**

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Scheme 1

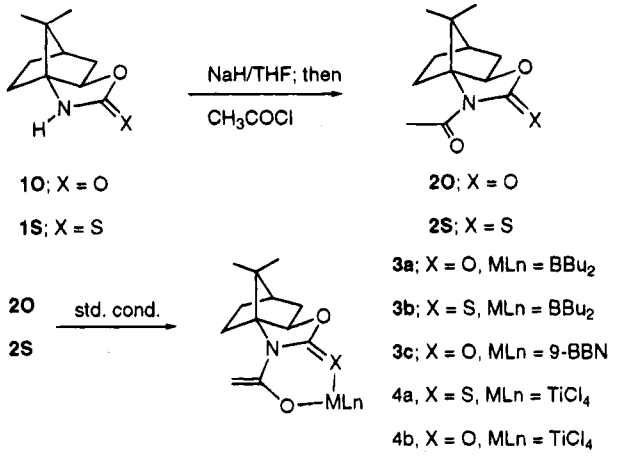


Table 1. Enolate Ligand–Dependent Aldol Reactions of Acetate Enolates 3a and 3b with Representative Aldehydes

entry	electrophile	enolate	ratio[a] 5(7):6(8)	yield[b] (%)
1	*n*-PrCHO	**3a**	73:27	71
2		**3b**	25:75	83
3	*i*-PrCHO	**3a**	70:30	61
4		**3b**	24:76	69
5	$CH_3CH{=}CHCHO$	**3a**	65:35	62
6		**3b**	8:92	69
7	PhCHO	**3a**	56:44	82
8		**3b**	25:75	74

[a] Ratios determined by 300-MHz ^{1}H NMR. [b] Combined isolated yield of all diastereomers.

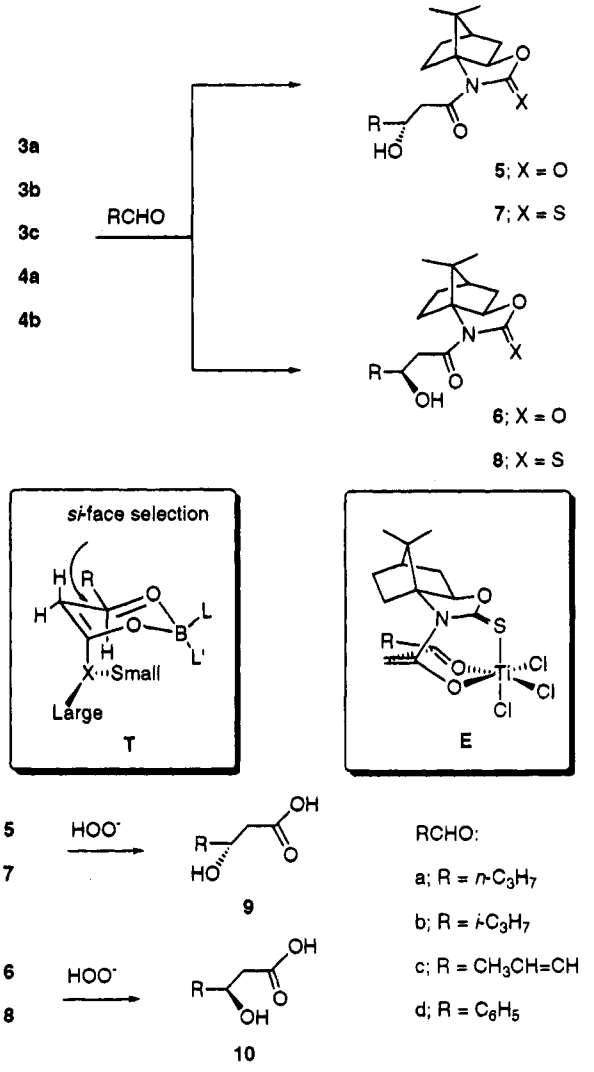
Table 2. Lithium Hydrogen Peroxide Hydrolysis of Carboximides 5 (7) and 6 (8)

entry	imide	β-hydroxy acid[a]	configuration	yield, %
1	**5a** (**7a**)	**9a**	*R*	78
2	**6a** (**8a**)	**10a**	*S*	81
3	**5b** (**7b**)	**9b**	*S*	76
4	**6b** (**8b**)	**10b**	*R*	80
5	**5c** (**7c**)	**9c**	*S*	84
6	**6c** (**8c**)	**10c**	*R*	82
7	**5d** (**7d**)	**9d**	*S*	86
8	**6d** (**8d**)	**10d**	*R*	8

[a] The chiral auxiliary **1** was recovered in >90% yield.

of known absolute configuration[3c,4b,5a,b,10] using the standard LiOOH-hydrolysis conditions (Table 2).[11] While **3a** and **3b** provided only modest stereoselection, we discovered that the stereochemical sense of the addition varies with the nature of the imide enolates (cf. Table 1). The sense of facial selectivity from thioimide enolate **3b** is opposite to that obtained from imide enolate **3a**. Thioimide boryl enolate **3b** affords principally aldols expected from the addition of enolate to the *re*-face of the aldehyde carbonyl (Scheme 2). This sense of facial selectivity is opposite to that obtained from the well-documented pericyclic chair model represented by **T**, which has been set forth by Evans[1a,2b] and Masamune[6] as the preferred transition state for aldol reactions of dibutylboryl and borolanyl acetate enolates. This initial finding was intriguing, since it pointed out the alteration of the physical property of the imide enolate ligand, exocyclic

Scheme 2



carbonyl, has a strong effect on the aldol facial selection of chiral acetate boryl enolates. These observations are in marked contrast to those of our previous investigations with the propionate boryl imide enolates.[3i] The implication from the above data is that the absence of α-methyl substitution to exacerbate the steric interactions in aldol transition states promotes the importance of other steric parameters in governing the energies of aldol transition states, thereby regulating facial selection. It occurred to us that the boryl nature might also operate to influence the stereochemical outcome of the acetate boryl enolate aldol reactions. In this regard, no attention has been given to the effect of boryl geometry (cyclic vs acylic structure) in influencing the aldol asymmetric induction of acetate enolate.[12] The observation of Mukaiyama *et al.* and Masamune and co-workers with respect to the dramatic enolization stereoselectivity switch by alteration of the boryl geometry (*n*-Bu_2B-OTf vs 9-BBN-OTf)[13] prompted us to examine 9-BBN-OTf-assisted aldolizations. As expected, it was found that a unique reversal

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(11) Evans, D. A.; Britton, T. C.; Ellman, J. A. *Tetrahedron Lett.* **1987**, *28*, 6141.

(12) Cyclic boryl triflates-mediated aldol reactions are rare. See: (a) A single example of low levels of asymmetric induction exhibited for acetate 9-BBN enolate is described by Masamune and co-workers, see ref 1c. (b) In another example, Masamune disclosed that the stereoselection was generally high for chiral borolane triflate-assisted aldolization of acetate enolate, see ref 8.

(13) (a) Inoue, T.; Uchimaru, T.; Mukaiyama, T. *Chem. Lett.* **1977**, 153. (b) Hirama, M.; Garvey, D. S.; Lu, D.-L.; Masamune, S. *Tetrahedron Lett.* **1979**, 3937.

Table 3. Influence of Boryl Geometry on Aldolizations of Acetate Enolates 3a and 3c with Representative Aldehydes

entry	electrophile	enolate	ratio[a] **5**:**6**	yield[b] (%)
1	*n*-PrCHO	**3a**	73:27	71
2		**3c**	29:71	61
3	*i*-PrCHO	**3a**	70:30	61
4		**3c**	40:60	67
5	CH_3CH=CHCHO	**3a**	65:35	62
6		**3c**	33:67	58
7	PhCHO	**3a**	56:44	82
8		**3c**	36:64	60

[a] Ratios determined by 300-MHz ^{1}H NMR. [b] Combined isolated yield of all diastereomers.

Table 4. Enantioselective Aldolizations of Acetate Enolates 4a with Representative Aldehydes

entry	electrophile	$TiCl_4$ (equiv)	ratio[a] **5**(**7**):**6**(**8**)	yield[b] (%)
1	*n*-PrCHO	1.0	5:95	85
2	*i*-PrCHO	1.0	6:94	86
3	CH_3CH=CHCHO	1.5	7:93	86
4	PhCHO	1.0	9:91	91

[a] Ratios determined by 300-MHz ^{1}H NMR. [b] Combined isolated yield of all diastereomers.

in the absolute stereochemistry of the major aldols was observed in the aldolizations of 9-BBN enolate **3c** derived from **2O** as compared to the aldol adducts obtained with dibutylboryl enolate **3c** (Table 3). These comparative experiments highlight that the contributions to aldol chirality transfer due to the nature of stereochemical control elements such as boryl geometry and the enolate ligand should not be underestimated. This would be especially important in the aldol additions of α-unsubstituted boryl enolates and, as a result, the degrees of asymmetric induction are limited by the judicious choice of boryl triflate and enolate ligand.[8] The limited utility of acetate boron enolate aldol reactions led us to examine alternative metal enolates. Considering the excellent selectivity obtained with chiral propionate titanium imide[14] and thioimide enolates,[3i] it was anticipated that acetate titanium thioimide enolate **4a** should give highly selective aldolizations under chelation control. With this in mind, titanium enolate **4a** was obtained via the sequential addition of 1−1.5 equiv of $TiCl_4$ and 1.1 equiv of diisopropylethylamine to a precooled (−70 °C) solution of **2S** (0.5 M in CH_2Cl_2). Condensation of the resulting titanium enolate with representative aldehydes at −70 °C and extractive workup afford the aldol adducts in good yield. We were pleased to observe that the aldol additions from acetate enolate **4a** exhibited consistently useful levels of asymmetric induction (Table 4, typically >90:10) and provided the aldol stereomers **8** expected from chelation control (cf. Scheme 2, chelated titanium coformer **E**).[3i] As a control experiment, we also carried out the comparative aldolizations of acetate titanium imide enolate **4b** derived from **2O**. Under similar conditions, the enolate **4b** provided a roughly 1:1 ratio of two diastereomeric aldols. Considering the strong affinity of thiocarbonyl toward association with chlorotitanium,[3i,15] we contended that the high levels of chirality transfer exhibited for thioimide titanium enolate **4a** was due to sufficient conformer control by ring thiocarbonyl.[16] This direct aldolization comparison exemplifies once more that the increased chelating potential of enolate ligand is an important stereochemical control element in chelation-controlled aldol reactions.

Conclusions

The preceding studies highlight the capability of achieving high stereocontrol in titanium-mediated acetate enolate aldol reactions using thioimide and an unexpectedly strong dependence of the acetate boryl enolate aldol bond construction process on the nature of the enolate ligand and boryl geometry which has been proven to have little, if any, contribution to diastereoface differentiation in propionate boryl enolate aldol reactions.[3b,i] This aldol stereoselection switch by alternation of the nature of reaction variables is partially responsible for the unexpected difficulty of achieveing high stereocontrol in α-unsubstituted boryl enolate additions. More importantly, acetate titanium thioimide enolate **4a** represents a useful chiral acetate synthon. Its advantages include consistently useful levels of asymmetric induction, a relatively low price of $TiCl_4$ compared to other metal acids (e.g., R_2BOTf and $Sn(OTf)_2$), a one-step process,[17] as well as effective and nondestructive chiral auxiliary removal. The remarkable ease of preparation of **2S** together with the aforementioned advantages make Ti-thioimide enolate an attractive choice for the construction of enantiomerically pure β-hydroxy carboxylic acids.

Experimental Section

General. Diisopropylethylamine and dichloromethane were dried by distillation under N_2 from calcium hydride. Sodium hydride (80% dispersion in mineral oil), Bu_2B-OTf (1 M in CH_2Cl_2), 9-BBN-OTf (0.5 M in Hexane), and $TiCl_4$ (1 M in CH_2Cl_2) were purchased from Aldrich Chemical Co. All aldehydes were freshly distilled prior to use. Unless otherwise noted, all nonaqueous reactions were carried out under a dry nitrogen atmosphere with oven-dried glassware. Flash chromatography was done on E. Merck silica gel 60 (230−400 mesh).[18] Melting points (Pyrex capillary) are uncorrected. Concentrations for rotation data are given as g/100 mL of solvent. Enantiomeric excesses (ee) were determined by 300 MHz ^{1}H NMR. All NMR spectra were measured in $CDCl_3$ solution. Chemical shifts are expressed in ppm downfield from internal tetramethylsilane; coupling constants are expressed in hertz.

***N*-Acetyl-(1*S*,5*R*,7*R*)-10,10-dimethyl-3-oxo-2-aza-4-oxatricyclo[5.2.1.0^{1,5}]decane (2O).** To a solution of sodium hydride (1.8 g, 75 mmol) in 200 mL of anhydrous THF at 0 °C was added a solution of (9.05 g, 50 mmol) of oxazolidinone **1O** in 100 mL of dry THF. The mixture was stirred at 0 °C for 30 min, allowed to warm to room temperature for an additional 5 h, and then recooled to 0 °C. To the above solution was added via cannula a solution of 4.3 mL (60 mmol) of acetyl chloride in 30 mL of dry THF. The resulting solution was stirred at 0 °C for 1 h and 25 °C for 2 h. The reaction mixture

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(15) Fowles, G. W. A.; Rice, D. A.; Wilkins, J. D. *J. Chem. Soc.* **1971**, 1920.

(16) In order to gain some insight into the chelate effect difference between titanium imide enolates **4a** and **4b**, a relative rate comparison between **4a** and **4b** formation was carried out at −78 °C. Sequential treatment of a mixture of equimolar quantities of **2O** and **2S** (1.0 equiv) with 1.0 equiv of $TiCl_4$ and then 1.0 equiv of diisopropylethylamine at −78 °C followed by quench with aldehyde provided exclusive aldol derived from **2S**. These observations imply that the intramolecular complexation of $TiCl_4$ with thiocarbonyl is relatively large compared to that obtained with ring carbonyl, thereby leading to the preference of thiocarbonyl coordination to $TiCl_4$ Lewis acid.

(17) Helmchen and Oppolzer have demonstrated a two-step $TiCl_4$-mediated enantioselective aldolizations of chiral acetate (*tert*-butyl)-dimethylsilyl enolates, see refs 5a and 5b.

(18) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

was recooled to 0 °C and quenched with 3 N HCl (15 mL). Following removal of the THF in vacuo on the rotary evaporator, the residue was diluted with 300 mL of dichloromethane and 50 mL of water. The organic extract was washed successively with saturated aqueous sodium bicarbonate and brine, dried ($MgSO_4$), and concentrated in vacuo to yield **2O** (10.9 g, >98%) as a viscous oil, which was used without purification. A small portion was purified by flash chromatography on silica gel for analysis: R_f 0.35 (30% hexane/dichloromethane); IR (neat) 2960, 1770, 1704, 1456, 1370, 1316, 1278, 1052 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.25 (dd, J = 8.1, 4.5 Hz, 1H), 2.98−1.22 (m, with s at 2.53, 10 H), 1.13 and 1.02 (2s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 172.0, 155.4, 84.8, 72.2, 48.2, 42.4, 34.6, 25.9, 25.7, 24.8, 21.4, 19.1; $[\alpha]^{25}_D$ +68.4° (*c* 4.8, $CHCl_3$); high-resolution MS *m/e* calcd for $C_{12}H_{17}NO_3$ 223.1208, found 223.1208. Anal. Calcd for $C_{12}H_{17}NO_3$: C, 64.57; H, 7.62; N, 6.28. Found: C, 63.98; H, 7.75; N, 6.04.

***N*-Acetyl-(1*S*,5*R*,7*R*)-10,10-dimethyl-3-thioxo-2-aza-4-oxatricyclo[5.2.1.0^{1,5}]decane (2S).** To a solution of sodium hydride (1.8 g, 75 mmol) in 150 mL of anhydrous THF, stirred at 0 °C under dry N_2, was added via cannula a precooled (0 °C) solution of 9.85 g (50 mmol) of **1S**[1f] in 100 mL of dry THF. The mixture was stirred at 0 °C for 25 min, and 4.3 mL (4.73 g, 60 mmol, 1.2 equiv) of acetyl chloride was added dropwise over 10 min. The solution is stirred at that temperature for 30 min, and the reaction was quenched with trifluoroacetic acid (80 mmol). THF was removed by rotary evaporation, the resultant slurry was diluted with CH_2Cl_2 (300 mL), and the CH_2Cl_2 solution was washed with two 50 mL portions of saturated aqueous sodium bicarbonate and 50 mL of brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give 11.0 g (92%) of the title compound as a white solid. An analytical sample was prepared by recrystallization from dichloromethane/hexane to afford colorless, crystalline solid: mp 129−130 °C; IR (KBr) 2956, 1710, 1365, 1332, 1275, 1188, 1170 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.45 (dd, J = 8.4, 3.9 Hz, 1H), 2.94−1.19 (m, with s at 2.78, 10H), 1.14 and 1.06 (2s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.4, 172.3, 89.4, 76.5, 49.2, 42.5, 34.8, 27.3, 26.0, 25.3, 21.5, 19.2; $[\alpha]^{25}_D$ −64.9° (*c* 7.2, $CHCl_3$); high-resolution MS *m/e* calcd for $C_{12}H_{17}NO_2S$ 239.0980, found 239.0979. Anal. Calcd for $C_{12}H_{17}NO_2S$: C, 60.28; H, 7.17; N, 5.86. Found: C, 60.07; H, 7.26; N, 5.92.

General Procedure for the Aldol Type Reaction of Boron Enolates. To a solution of **2O** or **2S** (1 mmol) in 4 mL of CH_2Cl_2 cooled to 0 °C was added 1 mL (1 M in CH_2Cl_2) of Bu_2B-OTf or 2 mL of 9-BBN-OTf (0.5 M in hexane). After stirring at 0 °C for 10 min, slow addition of diisopropylethylamine (1 M in CH_2Cl_2, 1.1 mL, 1.1 mmol) and further stirring for 25 min at 0 °C, the reaction mixture was cooled to −78 °C. To the above enolate solution was slowly added a solution of aldehyde (1.2 mmol) in 1 mL of CH_2Cl_2. The reaction mixture was stirred at −78 °C for 2 h, allowed to warm to 0 °C, and then quenched with aqueous phosphate buffer (pH = 7), 6 mL of methanol, and 4 mL of 30% H_2O_2. The aqueous layer was extracted with two portions of CH_2Cl_2 (2 × 15 mL). The combined organic extracts were washed with saturated aqueous NH_4Cl (4 mL), and brine (4 mL), dried ($MgSO_4$), and concentrated in vacuo. The residue was subjected to ^1H NMR analysis and purified by flash chromatography on silica gel (15% ethyl acetate/hexane).

General Procedure for the Aldol Reaction of Chlorotitanium Enolates. To a solution of **2O** or **2S** (1 mmol) in 2 mL of CH_2Cl_2 cooled to −70 °C was added 1−1.5 mL (1 M in CH_2Cl_2) of $TiCl_4$. After stirring at −70 °C for 10 min and slow addition of diisopropylethylamine (1 M in CH_2Cl_2, 1.1 mL, 1.1 mmol), the reaction mixture was stirred for an additional 10−20 min at −70 °C. To the above enolate solution was slowly added a solution of aldehyde (1.2 mmol) in 1 mL of CH_2Cl_2. The reaction mixture was stirred at −70 °C for 0.5 h and then quenched with 6 mL of saturated aqueous ammonium chloride. The aqueous layer was extracted with two portions of CH_2Cl_2 (2 × 15 mL). The combined organic extracts were washed with saturated aqueous NH_4Cl (4 mL) and brine (4 mL), dried ($MgSO_4$), and concentrated in vacuo. The residue was subjected to ^1H NMR analysis and purified by flash chromatography on silica gel (15% ethyl acetate/hexane).

***N*-[(*R*)-3-Hydroxyhexanoyl]-(1*S*,5*R*,7*R*)-10,10-dimethyl-3-oxo-2-aza-4-oxatricyclo[5.2.1.0^{1,5}]decane (5a) and *N*-[(*S*)-3-Hydroxyhexanoyl]-(1*S*,5*R*,7*R*)-10,10-dimethyl-3-oxo-2-aza-4-oxatricyclo[5.2.1.0^{1,5}]decane (6a).** As described above, acetyloxazolidinone **2O** (446 mg, 2 mmol), n-Bu_2B-OTf (1 M in CH_2Cl_2, 2 mmol), and n-butyraldehyde (1 M in CH_2Cl_2, 2.4 mmol) provided a crude reaction mixture. Diastereomer analysis [300 MHz ^1H NMR integration of the C-2 methylene protons (CH_2C=O) and/or C-3 methine proton (C*H*(OH))] of the unpurified adduct revealed the presence of two aldols in the ratio of 73:27. The pale yellow oil was purified by flash chromatography on silica gel (15% ethylacetate/hexane) afforded 305 mg (52%) of **5a** and 113 mg (19%) of **6a**. In an experiment otherwise identical with that described above, **2O** was treated with a solution of 9-BBN-OTf (0.5 M in hexane, 2 mmol) and then quenched with aldehyde. Workup and ^1H NMR analysis gave a 29:71 ratio of aldol adducts **5a** and **6a**. **5a**: IR (neat) 3536, 2964, 1786, 1702, 1076, 1052 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.23 (dd, J = 8.4, 4.2 Hz, 1H), 4.02 (m, 1H), 3.10 (dd, J = 17.1, 9.3 Hz, 1H), 2.99−2.89 (m with dd at 2.95, J = 17.1, 2.7 Hz, 2H), 2.28−1.20 (m, 11H), 1.11 and 1.01 (2S, 6H), 0.91 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 174.5, 155.3, 84.8, 72.3, 68.1, 48.3, 43.4, 42.3, 38.8, 34.7, 25.9, 25.7, 21.5, 19.1, 18.6, 13.9; $[\alpha]^{25}_D$ +23.3° (*c* 2.1, $CHCl_3$); high-resolution MS *m/e* calcd for $C_{16}H_{25}NO_4$ 295.1776, found 295.1786. Anal. Calcd for $C_{16}H_{25}NO_4$: C, 65.08; H, 8.47; N, 4.74. Found: C, 64.61; H, 8.71; N, 4.95. **6a**: IR (neat) 3488, 2964, 1782, 1704, 1076, 1052 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.23 (dd, J = 8.4, 4.5 Hz, 1H), 4.10 (m, 1H), 3.25 (dd, J = 17.7, 2.7 Hz, 1H), 2.97−2.77 (m with dd at 2.82, J = 17.7, 9.6 Hz, 2H), 2.28−1.20 (m, 11H), 1.12 and 1.01 (2S, 6H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 174.2, 155.1, 84.8, 72.3, 67.4, 48.2, 43.6, 42.3, 38.4, 34.7, 25.9, 25.6, 21.4, 19.1, 18.6, 13.9; $[\alpha]^{25}_D$ +55.0° (*c* 0.75, $CHCl_3$); high-resolution MS *m/e* calcd for $C_{16}H_{25}NO_4$ 295.1776, found 295.1786. Anal. Calcd for $C_{16}H_{25}NO_4$: C, 65.08; H, 8.47; N, 4.74. Found: C, 64.71; H, 8.77; N, 4.91.

***N*-[(*S*)-3-Hydroxy-4-methylpentanoyl]-(1*S*,5*R*,7*R*)-10,10-dimethyl-3-oxo-2-aza-4-oxatricyclo[5.2.1.0^{1,5}]decane (5b) and *N*-[(*R*)-3-Hydroxy-4-methylpentanoyl]-(1*S*,5*R*,7*R*)-10,10-dimethyl-3-oxo-2-aza-4-oxatricyclo[5.2.1.0^{1,5}]decane (6b).** As described above, acetyloxazolidinone **2O** (223 mg, 1 mmol), n-Bu_2B-OTf (1 M in CH_2Cl_2, 1 mmol), and isobutyraldehyde (1 M in CH_2Cl_2, 1.2 mmol) provided a crude reaction mixture. Diastereomer analysis [300 MHz ^1H NMR integration of the C-2 methylene protons (CH_2C=O) and/or C-3 methine proton (C*H*(OH))] of the unpurified adduct revealed the presence of two aldols in the ratio of 70:30. The pale yellow oil was purified by flash chromatography on silica gel (15% ethyl acetate/hexane) afforded 126 mg (43%) of **5b** and 54 mg (18%) of **6b**. In an experiment otherwise identical with that described above, **2O** was treated with a solution of 9-BBN-OTf (0.5 M in hexane, 2 mmol) and then quenched with aldehyde. Workup and ^1H NMR analysis gave a 29:71 ratio of aldol adducts **5b** and **6b**. **5b**: mp 78−79 °C; IR (KBr) 3488, 2968, 1784, 1708, 1076, 1054 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$) δ 4.26 (dd, J = 8.1, 4.2 Hz, 1H), 3.80 (m, 1H), 3.16 (dd, J = 16.5, 10.2 Hz, 1H), 3.07 (d, J = 5.1 Hz, 1H), 2.95 (dd, J = 16.5, 2.4 Hz, 2H), 2.31−1.18 (m, 7H), 1.12 and 1.01 (2s, 6H), 0.95 and 0.93 (2d, J = 6.9 Hz, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 174.7, 155.4, 84.8, 73.3, 72.4, 48.3, 42.3, 40.5, 34.6, 33.4, 25.9, 25.7, 21.5, 19.0, 18.3, 17.6; $[\alpha]^{25}_D$ −23.2° (*c* 10.5, $CHCl_3$); high-resolution MS *m/e* calcd for $C_{16}H_{25}NO_4$ 295.1784, found 295.1780. Anal. Calcd for $C_{16}H_{25}NO_4$: C, 65.08; H, 8.47; N, 4.74. Found: C, 64.80; H, 8.66; N, 4.80. **6b**: IR (neat) 3456, 2964, 1784, 1702, 1076, 1052 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$) δ 4.25 (dd, J = 8.1, 4.2 Hz, 1H), 3.90 (m, 1H), 3.26 (dd, J = 17.1, 2.4 Hz, 1H), 3.02−2.82 (m with dd at 2.86, J = 17.1, 9.9 Hz, d at 2.76, J = 3.9 Hz, 3H), 2.30−1.17 (m, 7H), 1.14 and 1.03 (2s, 6H), 0.98 and 0.97 (2d, J = 6.9 Hz, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 174.5, 155.1, 84.8, 74.5, 72.3, 48.2, 42.4, 40.8, 34.6, 33.1, 25.9, 25.6, 21.4, 19.1, 18.4, 17.6; $[\alpha]^{25}_D$ −64.8° (*c* 3.1, $CHCl_3$); high-resolution MS *m/e* calcd for $C_{16}H_{25}NO_4$

295.1784, found 295.1780. Anal. Calcd for $C_{16}H_{25}NO_4$: C, 65.08; N, 8.47; N, 4.74. Found: C, 64.73; H, 8.67; N, 4.81.

***N*-[(*S*)-3-Hydroxy-4-hexenoyl]-(1*S*,5*R*,7*R*)-10,10-dimethyl-3-oxo-2-aza-4-oxatricyclo[5.2.1.0^{1,5}]decane (5c) and *N*-[(*R*)-3-Hydroxy-4-hexenoyl]-(1*S*,5*R*,7*R*)-10,10-dimethyl-3-oxo-2-aza-4-oxatricyclo[5.2.1.0^{1,5}]decane (6c).** As described above, acetyloxazolidinone **2O** (223 mg, 1 mmol), *n*-Bu_2B-OTf (1 M in CH_2Cl_2, 1 mmol), and crotonaldehyde (0.10 mL, 86 mg, 1.2 mmol) provided a crude reaction mixture. Diastereomer analysis [300 MHz ^{1}H NMR integration of the C-2 methylene protons (CH_2C=O) and/or C-3 methine proton (C*H*(OH))] of the unpurified adduct revealed the presence of two aldols in the ratio of 65:35. The pale yellow oil was purified by flash chromatography on silica gel (15% ethyl acetate/hexane) afforded 118 mg (40%) of **5c** and 63.5 mg (22%) of **6c**. In an experiment otherwise identical with that described above, **2O** was treated with a solution of 9-BBN-OTf (0.5 M in hexane, 2 mmol) and then quenched with aldehyde. Workup and ^{1}H NMR analysis gave a 33:67 ratio of aldol adducts **5c** and **6c**. **5c**: IR (neat) 3520, 2960, 1780, 1704, 1078, 1052 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.74 (ddq, J = 15.3, 6.0, 0.9 Hz, 1H), 5.53 (ddq, J = 15.3, 6.6, 1.2 Hz, 1H), 4.48 (m, 1H), 4.23 (dd, J = 8.1, 4.2 Hz, 1H), 3.26 (dd, J = 17.1, 9.0 Hz, 1H), 3.15 (bs, 1H), 2.99 (dd, J = 17.1, 3.3 Hz, 1H), 2.91−1.19 (m with dd at 1.66, J = 6.3, 0.9 Hz, 10H), 1.10 and 0.99 (2s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 173.9, 155.1, 131.9, 127.2, 84.8, 72.3, 69.0, 48.3, 43.4, 42.3, 34.6, 25.9, 25.7, 21.4, 19.0, 17.6; $[\alpha]^{25}_D$ +38.5° (*c* 1.1, $CHCl_3$); high-resolution MS *m*/*e* calcd for $C_{16}H_{23}NO_4$ 293.1618, found 293.1631. Anal. Calcd for $C_{16}H_{23}NO_4$: C, 65.53; H, 7.85; N, 4.78. Found: C, 65.42; H, 7.95; N, 4.74. **6c**: IR (neat) 3468, 2964, 1780, 1704, 1076, 1052 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.75 (ddq, J = 15.3, 6.3, 0.9 Hz, 1H), 5.41 (ddq, J = 15.3, 6.6, 1.5 Hz, 1H), 4.58 (m, 1H), 4.23 (dd, J = 8.1, 4.2 Hz, 1H), 3.29 (dd, J = 17.4, 3.3 Hz, 1H), 3.15 (bs, 1H), 2.97 (dd, J = 17.4, 9.0 Hz, 1H), 2.91−1.18 (m with dd at 1.68, J = 6.3, 1.5 Hz, 10H), 1.15 and 1.02 (2s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 173.5, 155.1, 131.8, 127.4, 84.9, 72.4, 68.6, 48.2, 43.6, 42.4, 34.7, 25.9, 25.6, 21.4, 19.1, 17.6; $[\alpha]^{25}_D$ +73.8° (*c* 0.7, $CHCl_3$); high-resolution MS *m*/*e* calcd for $C_{16}H_{23}NO_4$ 293.1618, found 293.1621. Anal. Calcd for $C_{16}H_{23}NO_4$: C, 65.53; H, 7.85; N, 4.78. Found: C, 65.24; H, 7.99; N, 4.82.

***N*-[(*S*)-3-Hydroxy-3-phenylpropionyl]-(1*S*,5*R*,7*R*)-10,10-dimethyl-3-oxo-2-aza-4-oxatricyclo[5.2.1.0^{1,5}]decane (5d) and *N*-[(*R*)-3-Hydroxy-3-phenylpropionyl]-(1*S*,5*R*,7*R*)-10,10-dimethyl-3-oxo-2-aza-4-oxatricyclo[5.2.1.0^{1,5}]decane (6d).** As described above, acetyloxazolidinone **2O** (446 mg, 2 mmol), *n*-Bu_2B-OTf (1 M in CH_2Cl_2, 2 mmol), and benzaldehyde (0.25 mL, 260 mg, 2.4 mmol) provided a crude reaction mixture. Diastereomer analysis [300 MHz ^{1}H NMR integration of the C-2 methylene protons (CH_2C=O) and/or C-3 methine proton (C*H*(OH))] of the unpurified adduct revealed the presence of two aldols in the ratio of 56:44. The pale yellow oil was purified by flash chromatography on silica gel (15% ethyl acetate/hexane) afforded 302 mg (46%) of **5d** and 237 mg (36%) of **6d**. In an experiment otherwise identical with that described above, **2O** was treated with a solution of 9-BBN-OTf (0.5 M in hexane, 2 mmol) and then quenched with aldehyde. Workup and ^{1}H NMR analysis gave a 36:64 ratio of aldol adducts **5d** and **6d**. **5d**: IR (neat) 3450, 2964, 1780, 1708, 1490, 1456, 1076, 1052 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62−7.24 (m, 5H), 5.16 (dd, J = 9.6, 3.0 Hz, 1H), 4.24 (dd, J = 8.1, 4.5 Hz, 1H), 3.66 (s, 1H), 3.53 (dd, J = 16.8, 9.6 Hz, 1H), 3.21 (dd, J = 16.8, 3.0 Hz, 1H), 3.03−1.21 (m, 7H), 1.13 and 1.01 (2s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 173.7, 155.1, 142.5, 128.5, 127.7, 125.8, 84.9, 72.4, 70.6, 48.3, 45.0, 42.3, 34.6, 25.9, 25.7, 21.4, 19.1; $[\alpha]^{25}_D$ −30.4° (*c* 0.4, $CHCl_3$); high-resolution MS *m*/*e* calcd for $C_{19}H_{23}NO_4$ 329.1628, found 329.1627. **6d**: mp 64−65 °C; IR (KBr) 3456, 2964, 1782, 1704, 1492, 1454, 1074, 1054 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43−7.25 (m, 5H), 5.26 (dd, J = 9.6, 2.7 Hz, 1H), 4.22 (dd, J = 8.1, 4.5 Hz, 1H), 3.47 (dd, J = 17.4, 2.7 Hz, 1H), 3.25 (dd, J = 17.4, 9.6 Hz, 1H), 2.99−1.20 (m, 8H), 1.15 and 1.02 (2s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 173.4, 155.0, 142.4, 128.5, 127.7, 125.8, 84.9, 72.3, 69.9, 48.2, 45.3, 42.3, 34.6, 25.9, 25.5, 21.4, 19.1; $[\alpha]^{25}_D$ −85.8° (*c* 8.4, $CHCl_3$); high-resolution MS *m*/*e* calcd for $C_{19}H_{23}NO_4$ 329.1628, found 329.1627.

***N*-[(*R*)-3-Hydroxyhexanoyl]-(1*S*,5*R*,7*R*)-10,10-dimethyl-3-thioxo-2-aza-4-oxatricyclo[5.2.1.0^{1,5}]decane (7a) and *N*-[(*S*)-3-Hydroxyhexanoyl]-(1*S*,5*R*,7*R*)-10,10-dimethyl-3-thioxo-2-aza-4-oxatricyclo[5.2.1.0^{1,5}]decane (8a).** As described above, acetyloxazolidinethione **2S** (478 mg, 2 mmol), *n*-Bu_2B-OTf (1 M in CH_2Cl_2, 2 mmol), and *n*-butyraldehyde (1 M in CH_2Cl_2, 2.4 mmol) provided a crude reaction mixture. Diastereomer analysis [300 MHz ^{1}H NMR integration of the C-2 methylene protons (CH_2C=O) and/or C-3 methine proton (C*H*(OH))] of the unpurified adduct revealed the presence of two aldols in the ratio of 25:75. The pale yellow oil was purified by flash chromatography on silica gel (15% ethylacetate/hexane) afforded 129 mg (21%) of **7a** and 387 mg (62%) of **8a**. **7a**: IR (neat) 3432, 2964, 1712, 1186 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.47 (dd, J = 8.1, 4.2 Hz, 1H), 4.05 (m, 1H), 3.54 (dd, J = 17.1, 9.3 Hz, 1H), 3.32 (dd, J = 17.1, 3.3 Hz, 1H), 3.18 (bs, 1H), 2.95−1.22 (m, 11H), 1.14 and 1.06 (2S, 6H), 0.94 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.1, 175.5, 89.8, 76.5, 68.4, 49.2, 45.4, 42.4, 38.8, 34.7, 25.9, 25.2, 21.5, 19.1, 18.5, 13.8; $[\alpha]^{25}_D$ +10.5° (*c* 1.5, $CHCl_3$); high-resolution MS *m*/*e* calcd for $C_{16}H_{25}NO_3S$ 311.1555, found 311.1553. Anal. Calcd for $C_{16}H_{25}NO_3S$: C, 61.74; H, 8.04; N, 4.50. Found: C, 61.50; H, 8.17; N, 4.76. **8a**: IR (neat) 3440, 2956, 1706, 1460, 1184 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.47 (dd, J = 8.1, 4.2 Hz, 1H), 4.18 (m, 1H), 3.74 (dd, J = 17.7, 2.4 Hz, 1H), 3.10 (dd, J = 17.7, 9.3 Hz, 1H), 2.93−1.20 (m, 12H), 1.15 and 1.06 (2S, 6H), 0.95 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.1, 175.1, 89.9, 76.5, 67.4, 49.2, 45.8, 42.7, 38.4, 34.7, 25.9, 25.0, 21.4, 19.2, 18.6, 13.9; $[\alpha]^{25}_D$ +79.6° (*c* 4.2, $CHCl_3$); high-resolution MS *m*/*e* calcd for $C_{16}H_{25}NO_3S$ 311.1555, found 311.1553. Anal. Calcd for $C_{16}H_{25}NO_3S$: C, 61.74; H, 8.04; N, 4.50. Found: C, 61.50; H, 8.16; N, 4.76.

***N*-[(*S*)-3-Hydroxy-4-methylpentanoyl]-(1*S*,5*R*,7*R*)-10,10-dimethyl-3-thioxo-2-aza-4-oxatricyclo[5.2.1.0^{1,5}]decane (7b) and *N*-[(*R*)-3-Hydroxy-4-methylpentanoyl]-(1*S*,5*R*,7*R*)-10,10-dimethyl-3-thioxo-2-aza-4-oxatricyclo[5.2.1.0^{1,5}]decane (8b).** As described above, acetyloxazolidinone **2S** (239 mg, 1 mmol), *n*-Bu_2B-OTf (1 M in CH_2Cl_2, 1 mmol), and isobutyraldehyde (1 M in CH_2Cl_2, 1.2 mmol) provided a crude reaction mixture. Diastereomer analysis [300 MHz ^{1}H NMR integration of the C-2 methylene protons (CH_2C=O) and/or C-3 methine proton (C*H*(OH))] of the unpurified adduct revealed the presence of two aldols in the ratio of 24:76. The pale yellow oil was purified by flash chromatography on silica gel (15% ethyl acetate/hexane) afforded 51 mg (16.5%) of **7b** and 164 mg (52.5%) of **8b**. **7b**: IR (neat) 3472, 2964, 1704, 1332, 1212, 1170, 1084 cm^{-1}; ^{1}H NMR (300 MHz $CDCl_3$) δ 4.45 (dd, J = 8.1, 4.2 Hz, 1H), 3.79 (m, 1H), 3.55 (dd, J = 16.8, 9.6 Hz, 1H), 3.28 (dd, J = 16.8, 2.4 Hz, 1H), 3.13 (d, J = 4.8 Hz, 1H), 2.93−1.19 (m, 8H), 1.12 and 1.03 (2s, 6H), 0.96 and 0.95 (2d, J = 6.9 Hz, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.3, 175.8, 89.9, 76.5, 73.5, 49.3, 42.6, 42.4, 34.7, 33.5, 26.0, 25.3, 21.5, 19.2, 18.4, 17.7; $[\alpha]^{25}_D$ +35.4° (*c* 0.86, $CHCl_3$); high-resolution MS *m*/*e* calcd for $C_{16}H_{25}NO_3S$ 311.1555, found 311.1554. **8b**: mp 58−59 °C; IR (neat) 3472, 2964, 1704, 1311, 1230, 1170, 1080 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.47 (dd, J = 8.1, 4.2 Hz, 1H), 3.94 (m, 1H), 3.72 (dd, J = 17.4, 2.4 Hz, 1H), 3.13 (dd, J = 17.4, 9.9 Hz, 1H), 2.93−1.20 (m, 9H), 1.15 and 1.06 (2s, 6H), 0.98 and 1.01 (2d, J = 6.9 Hz, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.2, 175.5, 89.9, 76.5, 72.7, 49.3, 43.1, 42.5, 34.7, 33.2, 26.0, 25.1, 21.5, 19.3, 18.4, 17.8; $[\alpha]^{25}_D$ +75.2° (*c* 12.3, $CHCl_3$); high-resolution MS *m*/*e* calcd for $C_{16}H_{25}NO_3S$ 311.1555, found 311.1553.

***N*-[(*S*)-3-Hydroxy-4-hexenoyl]-(1*S*,5*R*,7*R*)-10,10-dimethyl-3-thioxo-2-aza-4-oxatricyclo[5.2.1.0^{1,5}]decane (7c) and *N*-[(*R*)-3-Hydroxy-4-hexenoyl]-(1*S*,5*R*,7*R*)-10,10-dimethyl-3-thioxo-2-aza-4-oxatricyclo[5.2.1.0^{1,5}]decane (8c).** As described above, acetyloxazolidinone **2s** (478 mg, 2 mmol), *n*-Bu_2B-OTf (1 M in CH_2Cl_2, 2 mmol), and crotonaldehyde (0.20 mL, 172 mg, 2.4 mmol) provided a crude reaction mixture. Diastereomer analysis [300 MHz ^{1}H NMR integration of the C-2 methylene protons (CH_2C=O) and/or C-3 methine proton (C*H*(OH))] of the unpurified adduct revealed the presence of two aldols in the ratio of 8:92. The pale yellow oil was purified

by flash chromatography on silica gel (15% ethyl acetate/hexane) afforded 34 mg (5.5%) of **7c** and 392 mg (63.5%) of **8c**. **7c**: IR (neat) 3428, 2968, 1710, 1230, 1184 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.76 (ddq, J = 15.3, 6.0, 0.3 Hz, 1H), 5.57 (ddq, J = 15.3, 6.6, 0.6 Hz, 1H), 4.53 (m, 1H), 4.47 (dd, J = 8.1, 4.2 Hz, 1H), 3.65 (dd, J = 17.1, 9.0 Hz, 1H), 3.38 (dd, J = 17.1, 3.6 Hz, 1H), 3.12 (d, J = 4.2 Hz, 1H), 2.94−1.20 (m with dd at 1.71, J = 6.0, 0.6 Hz, 10H), 1.14 and 1.05 (2s, 6H, $C(CH_3)_2$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.1, 174.8, 131.9, 127.4, 89.9, 76.5, 69.4, 49.3, 45.5, 42.5, 34.7, 26.0, 25.3, 21.5, 19.2, 17.6; $[\alpha]^{25}_D$ +60.9° (*c* 1.8, $CHCl_3$); high-resolution MS *m/e* calcd for $C_{16}H_{23}NO_3S$ 309.1405, found 309.1402. **8c**: IR (neat) 3440, 2968, 1708, 1275, 1184 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.77 (ddq, J = 15.3, 6.3, 1.2, Hz, 1H), 5.59 (ddq, J = 15.3, 6.3, 0.9 Hz, 1H), 4.63 (m, 1H), 4.46 (dd, J = 8.4, 4.2 Hz, 1H), 3.67 (dd, J = 17.4, 3.3 Hz, 1H), 3.32 (dd, J = 17.4, 9.0 Hz, 1H), 2.93−1.19 (m with dd at 1.72, J = 6.3, 0.9 Hz, 11H), 1.15 and 1.06 (2s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.1, 174.5, 131.8, 127.4, 90.0, 76.5, 68.8, 49.3, 45.8, 42.5, 34.7, 26.0, 25.1, 21.5, 19.2, 17.6; $[\alpha]^{25}_D$ +74.3° (*c* 5.1, $CHCl_3$); high-resolution MS *m/e* calcd for $C_{16}H_{23}NO_3S$ 309.1405, found 309.1402.

***N*-[(*S*)-3-Hydroxy-3-phenylpropionyl]-(1*S*,5*R*,7*R*)-10,10-dimethyl-3-thioxo-2-aza-4-oxatricyclo[5.2.1.0^{1,5}]decane (7d) and *N*-[(*R*)-3-Hydroxy-3-phenylpropionyl]-(1*S*,5*R*,7*R*)-10,10-dimethyl-3-thioxo-2-aza-4-oxatricyclo[5.2.1.0^{1,5}]decane (8d).** **7d**: As described above, acetyloxazolidinone **2S** (478 mg, 2 mmol), *n*-Bu_2B-OTf (1 M in CH_2Cl_2, 2 mmol), and benzaldehyde (0.25 mL, 260 mg, 2.4 mmol) provided a crude reaction mixture. Diastereomer analysis [300 MHz ^1H NMR integration of the C-2 methylene protons (CH_2C=O) and/or C-3 methine proton (C*H*(OH))] of the unpurified adduct revealed the presence of two aldols in the ratio of 25:75. The pale yellow oil was purified by flash chromatography on silica gel (15% ethyl acetate/hexane) afforded 127 mg (18.5%) of **7d** and 383 mg (55.5%) of **8d**. **7d**: mp 94−95 °C; IR (KBr) 3424, 2964, 1708, 1488, 1456, 1311, 1214, 1170, 1080 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.41−7.26 (m, 5H), 5.17 (dd, J = 9.3, 3.3 Hz, 1H), 4.44 (d, J = 8.1, 4.2 Hz, 1H), 3.91 (dd, J = 16.8, 9.6, Hz, 1H), 3.60 (dd, J = 16.8, 3.6 Hz, 1H), 2.90−1.17 (m, 8H), 1.15 and 1.06 (2s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 187.1, 174.6, 142.5, 128.6, 127.8, 126.0, 89.9, 76.5, 71.1, 49.3, 47.0, 42.5, 34.7, 26.0, 25.2, 21.5, 19.2; $[\alpha]^{25}_D$ +60.3° (*c* 8.3, $CHCl_3$); high-resolution MS *m/e* calcd for $C_{19}H_{23}NO_3S$ 345.1406, found 345.1395. **8d**: IR (neat) 3460, 2956, 1714, 1488, 1454, 1365, 1230, 1170 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.43−7.26 (m, 5H), 5.29 (dd, J = 9.3, 2.7 Hz, 1H), 4.42 (dd, J = 8.1, 4.2 Hz, 1H), 3.84 (dd, J = 17.1, 3.0 Hz, 1H), 3.62 (dd, J = 17.1, 9.3 Hz, 1H), 3.18 (bs, 1H), 2.87−1.26 (m, 6H), 1.15 and 1.05 (m with 2s at 1.15 and 1.05, 7H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 188.0, 174.5, 142.4, 128.5, 127.7, 125.8, 90.0, 76.5, 70.2, 49.2, 47.0, 42.4, 34.6, 25.9, 24.8, 21.4, 19.2; $[\alpha]^{25}_D$ +79.1° (*c* 12.51, $CHCl_3$); high-resolution MS *m/e* calcd for $C_{19}H_{23}NO_3S$ 345.1406, found 345.1395.

General Procedure for the Hydroperoxide-Assisted Saponification. To a solution of aldol adduct **5** (**7**) or **6** (**8**) (1 equiv) in THF/H_2O (3:1, 0.2 M) at 0 °C was added a solution of LiOH (3−4 equiv) in 6 equiv of 28% H_2O_2. The resulting mixture was stirred at 0 °C for 3 h and treated with a solution of 8 equiv of Na_2SO_3 in H_2O. Following removal of the THF in vacuo on the rotary evaporator, the aqueous residue was diluted with H_2O and extracted with three portions of CH_2Cl_2. The combined CH_2Cl_2 extracts were dried ($MgSO_4$) and evaporated in vacuo to give recovered auxiliary **1O** or **1S**. The aqueous phase was acidified with 3 N HCl and extracted with three portions of ether. The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo to give an colorless oil **9** or **10**.

(*R*)-3-Hydroxyhexanoic acid (9a): IR (neat) 3430, 2962, 1707, 1401, 1260, 1017, 792 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.03 (m, 1H), 2.55 (dd, J = 16.5, 3.3 Hz, 1H), 2.45 (dd, J = 16.5, 9.0 Hz, 1H), 1.59−1.32 (m, 4H), 0.91 (t, J = 7.2 Hz, 3H); ^{13}C (75.5 MHz, $CDCl_3$) δ 177.6, 67.7, 41.0, 38.5, 18.5, 13.8; $[\alpha]^{25}_D$ −26.1° (*c* 0.4, $CHCl_3$); lit.[3c] $[\alpha]^{25}_D$ −27.3° (*c* 2.1, $CHCl_3$); high-resolution MS (CI+) *m/e* calcd for $C_6H_{13}O_3$ 133.0864, found 133.0861.

(*S*)-3-Hydroxyhexanoic acid (10a): IR and ^1H and ^{13}C NMR are identical with those of **9a**. $[\alpha]^{25}_D$ +25.7° (*c* 0.21 $CHCl_3$); lit.[6g] $[\alpha]^{25}_D$ +25.8° (*c* 0.53, $CHCl_3$); lit.[6a] $[\alpha]^{25}_D$ +28.3° (*c* 1.0, $CHCl_3$); high-resolution MS (CI+) *m/e* calcd for $C_6H_{13}O_3$ 133.0864, found 133.0861.

(*S*)-3-Hydroxy-4-methylpentanoic acid (9b): IR (neat) 3448, 2960, 1712, 1455 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.83 (dt, J = 12.3, 6.6 Hz, 1H), 2.55 (dd, J = 16.2, 3.3 Hz, 1H), 2.45 (dd, J = 16.2, 9.9 Hz, 1H), 1.74 (octet, J = 6.6 Hz, 1H), 0.95 and 0.93 (2d, J = 6.6 Hz, 6H); ^{13}C (75.5 MHz, $CDCl_3$) δ 177.7, 68.7, 38.3, 33.1, 18.2, 17.6; $[\alpha]^{25}_D$ −40.7° (*c* 3.0, $CHCl_3$); lit.[3c] $[\alpha]^{25}_D$ −42.1° (*c* 1.8, $CHCl_3$); lit.[13b] $[\alpha]^{25}_D$ −40.3° (*c* 4.6, $CHCl_3$); high-resolution MS (CI+) *m/e* calcd for $C_6H_{13}O_3$ 133.0864, found 133.0858.

(*R*)-3-Hydroxy-4-methylpentanoic acid (10b): IR and ^1H and ^{13}C NMR are identical with those of **9b**; $[\alpha]^{25}_D$ +39.9° (*c* 2.84 $CHCl_3$); lit.[6h] $[\alpha]^{25}_D$ +40.5° (*c* 0.6, $CHCl_3$); lit.[8b] $[\alpha]^{25}_D$ +40.2° (*c* 1.2, $CHCl_3$); lit.[6a] $[\alpha]^{25}_D$ +41.7° (*c* 1.0, $CHCl_3$); lit.[6g] $[\alpha]^{25}_D$ + 36.9° (*c* 1.6, $CHCl_3$); high-resolution MS (CI+) *m/e* calcd for $C_6H_{13}O_3$ 133.0864, found 133.0858.

(*S*)-(*E*)-3-Hydroxy-4-hexenoic acid (9c): IR (neat) 3476, 3010, 2955, 1707, 1638, 1308, 1227 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.74 (ddq, J = 15.8, 6.4, 0.8 Hz, 1H), 5.49 (ddq, J = 15.8, 6.6, 1.6 Hz, 1H), 4.49 (dt, J = 6.6, 6.6 Hz, 1H), 2.58 (d, J = 6.6 Hz, 2H), 1.69 (d, J = 6.4 Hz, 3H); ^{13}C (75.5 MHz, $CDCl_3$) δ 177.0, 131.5, 128.3, 68.8, 41.2, 17.5; $[\alpha]^{25}_D$ −22.2° (*c* 0.4 EtOH); high-resolution MS *m/e* calcd for $C_6H_{10}O_3$ 130.0631, found 130.0633.

(*R*)-(*E*)-3-Hydroxy-4-hexenoic acid (10c): IR and ^1H and ^{13}C NMR are identical with those of **9c**; $[\alpha]^{25}_D$ +22.5° (*c* 0.43 EtOH); high-resolution MS *m/e* calcd for $C_6H_{10}O_3$ 130.0631, found 130.0633.

(*S*)-3-Hydroxy-3-phenylpropanoic acid (9d): IR (neat) 3510, 3060, 2960, 1711, 1608, 1551, 1497, 1455 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.31−7.12 (m, 5H), 5.16 (dt, J = 8.7, 3.9 Hz, 1H), 2.85 (dd, J = 16.5, 8.7 Hz, 1H), 2.77 (dd, J = 16.8, 3.9 Hz, 1H); ^{13}C (75.5 MHz, $CDCl_3$) δ 177.2, 142.2, 128.7, 128.1, 125.7, 70.2, 42.7; $[\alpha]^{25}_D$ −21.5° (*c* 0.4, EtOH); lit.[3c] $[\alpha]^{25}_D$ −17.1° (*c* 4.1, EtOH); lit.[13a] $[\alpha]^{25}_D$ −18.9° (*c* 2.3, EtOH); lit.[13d] $[\alpha]^{25}_D$ −17.9° (*c* 2.2, 95%, EtOH); high-resolution MS *m/e* calcd for $C_9H_{10}O_3$ 166.0645, found 166.0627.

(*R*)-3-Hydroxy-3-phenylpropanoic acid (10d): IR and ^1H and ^{13}C NMR are identical with those of **9d**; $[\alpha]^{25}_D$ +20.6° (*c* 0.39 EtOH); lit.[6g] $[\alpha]^{25}_D$ +14.9° (*c* 1.94, EtOH); lit.[8c] $[\alpha]^{25}_D$ +18.9° (*c* 1.0, EtOH); lit.[6h] $[\alpha]^{25}_D$ +17.9° (*c* 2.3, 95%, EtOH); lit.[6a] $[\alpha]^{25}_D$ +60.5° (*c* 1.0, $CHCl_3$); high-resolution MS *m/e* calcd for $C_9H_{10}O_3$ 166.0645, found 166.0627.

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Supplementary Material Available: ^1H NMR spectra of compounds **5a−d**, **6a−d**, **7a−d**, and **8a−d** (20 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.

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