JOC*Note*

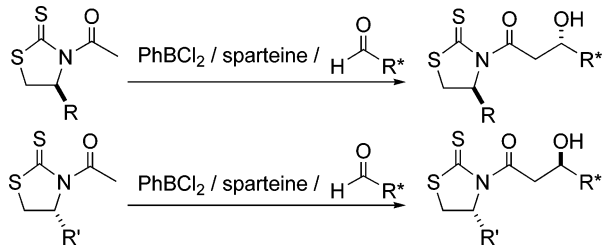
Double Diastereoselective Acetate Aldol Reactions with Chiral *N*-Acetyl Thiazolidinethione Reagents

Yingchao Zhang and Tarek Sammakia*

Department of Chemistry and Biochemistry, University of Colorado, Boulder, Colorado 80309-0215

sammakia@colorado.edu

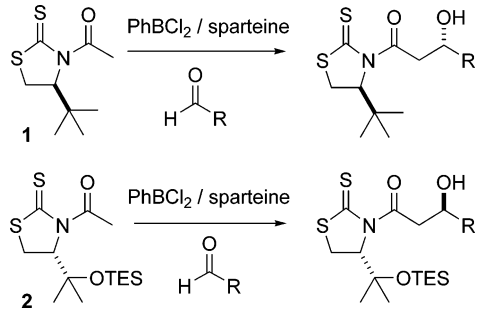
Received March 14, 2006



Double diastereoselective acetate aldol reactions using the *N*-acetyl thiazolidinethione-based chiral auxiliaries **1** and **2** and chiral aldehydes are described. Aldehydes that bear α-alkyl stereocenters exhibit moderate levels of double diastereoselection, while those that bear α- or *β*-alkoxy substitution exhibit little to no double diastereoselection. In all cases studied, the stereoselectivity of the reaction is dictated by the reagent, not the substrate.

We recently described a new chiral auxiliary-based method for performing asymmetric acetate aldol reactions[1,2] using the *N*-acyl thiazolidinethione auxiliaries **1** and **2** (Scheme 1).[3] Upon enolization with $PhBCl_2$ and sparteine, these pseudo-enantiomeric reagents provide good yields and high diastereoselectivities in aldol reactions with a variety of achiral aldehydes, including α- and *β*-oxygenated aliphatic aldehydes, and allow for the synthesis of either stereochemistry at the hydroxyl group of the aldol product. This note describes the use of these reagents in reactions with chiral, nonracemic aldehydes and examines the extent of double diastereoselection[2a] observed in these reactions. Additionally, to assess the efficacy of this process for the synthesis of polyacetate-derived natural products, aldehydes which are representative of the types of structures and protecting groups which one might encounter in a polyacetate synthesis are used.

SCHEME 1. Asymmetric Acetate Aldol Reactions with the Pseudo-Enantiomeric Thiazolidinethione Reagents 1 and 2



Since the seminal work of Heathcock, double diastereoselection has been recognized as an important issue to be addressed in the coupling of two chiral fragments via the aldol reaction.[4] In matched cases, useful increases in selectivities can be observed, whereas mismatched cases can cause significant erosions or reversals in selectivity. At times, subtle structural features can influence the magnitude and sense of asymmetric induction in aldol reactions with chiral aldehydes.[5] For example, in reactions of achiral propionate or ethyl ketone enolates with

(1) For selected reviews on the aldol reaction, see: (a) Evans, D. A.; Nelson, J. V.; Taber, T. R. *Top. Stereochem.* **1982**, *13*, 1. (b) Heathcock, C. H. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 2, pp 181−238. (c) Arya, P.; Qin, H. P. *Tetrahedron* **2000**, *56*, 917. (d) Kim, B.-M.; Williams, S. F.; Masamune, S. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 2, pp 239−275. (e) Cowden, C. J.; Paterson, I. *Org. React.* **1997**, *51*, 1. (f) Machajewski, T. D.; Wong, C. H. *Angew. Chem., Int. Ed.* **2000**, *39*, 1353. (g) Carreira, E. M. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley: New York, 2000. For recent advances in asymmetric synthesis with chiral imide auxiliaries, see: (h) Evans, D. A.; Shaw, J. T. *Actual. Chim.* **2003**, 35. For a review with examples of the use of the aldol reaction in total synthesis, see: (i) Norcross, R. D.; Paterson, I. *Chem. Rev.* **1995**, *95*, 2041.

(2) For reviews of asymmetric acetate aldol reactions, see: (a) Masamune, S.; Choy, W.; Petersen, J. S.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1. (b) Braun, M. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 24. For selected examples of asymmetric acetate aldol reactions, see: (c) Iwasawa, N.; Mukaiyama, T. *Chem. Lett.* **1983**, 297. (d) Braun, M.; Devant, R. *Tetrahedron Lett.* **1984**, *25*, 5031. (e) Nagao, Y.; Yamada, S.; Kumagai, T.; Ochiai, M.; Fujita, E. *J. Chem. Soc., Chem. Commun.* **1985**, 1418. (f) Helmchen, G.; Leikauf, U.; Taufer-Knöpfel, I. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 874. (g) Nagao, Y.; Hagiwara, Y.; Kumagai, T.; Ochiai, M.; Inoue, T.; Hashimoto, K.; Fujita, E. *J. Org. Chem.* **1986**, *51*, 2391. (h) Masamune, S.; Sato, T.; Kim, B. M.; Wollmann, T. A. *J. Am. Chem. Soc.* **1986**, *108*, 8279. (i) Devant, R.; Mahler, U.; Braun, M. *Chem. Ber.* **1988**, *121*, 397. (j) Duthaler, R. O.; Herold, P.; Lottenbach, W.; Oertle, K.; Riediker, M. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 495. (k) Corey, E. J.; Imwinkelried, R.; Pikul, S.; Xiang, Y. B. *J. Am. Chem. Soc.* **1989**, *111*, 5493. (l) Oppolzer, W.; Starkemann, C. *Tetrahedron Lett.* **1992**, *33*, 2439. (m) Yan, T. H.; Hung, H. C.; Hung, A. W.; Lee, H. C.; Chang, C. S. *J. Org. Chem.* **1994**, *59*, 8187. (n) Yan, T. H.; Hung, A. W.; Lee, H. C.; Chang, C. S.; Liu, W. H. *J. Org. Chem.* **1995**, *60*, 3301. (o) González, Á.; Aiguadé, J.; Urpí, F.; Vilarrasa, J. *Tetrahedron Lett.* **1996**, *37*, 8949. (p) Gabriel, T.; Wessjohan, L. *Tetrahedron Lett.* **1997**, *38*, 4387. (q) Bond, S.; Perlmutter, P. *J. Org. Chem.* **1997**, *62*, 6397. (r) Palomo, C.; Gonzalez, A.; Garcia, J. M.; Landa, C.; Oliarbide, M.; Rodríguez, S.; Linden, A. *Angew. Chem., Int. Ed.* **1998**, *37*, 180. (s) Saito, S.; Hatanaka, K.; Kano, T.; Yamamoto, H. *Angew. Chem., Int. Ed.* **1998**, *37*, 3378. (t) Fukuzawa, S.-i.; Matsuzawa, H.; Yoshimitsu, S.-i. *J. Org. Chem.* **2000**, *65*, 1702. (u) Guz, N. R.; Phillips, A. J. *Org. Lett.* **2002**, *4*, 2253. (v) Hodge, M. B.; Olivo, H. F. *Tetrahedron* **2004**, *60*, 9397.

(3) (a) Zhang, Y.; Sammakia, T. *Org Lett.* **2004**, *6*, 3139. (b) Zhang, Y.; Phillips, A. J.; Sammakia, T. *Org Lett.* **2004**, *6*, 23.

(4) (a) Heathcock, C. H.; White, C. T. *J. Am. Chem. Soc.* **1979**, *101*, 7076. (b) Heathcock, C. H.; Pirrung, M. C.; Buse, C. T.; Hagen, J. P.; Young, S. D.; Sohn, J. E. *J. Am. Chem. Soc.* **1979**, *101*, 7077. (c) Heathcock, C. H.; White, C. T.; Morrison, J. J.; VanDerver, D. *J. Org. Chem.* **1981**, *46*, 1296. (d) Heathcock, C. H.; Pirrung, M. C.; Lampe, J.; Buse, C. T.; Young, S. D. *J. Org. Chem.* **1981**, *46*, 2290.

(5) For discussions of 1,2- and 1,3-asymmetric induction in aldol reactions with chiral aldehydes, see: (a) Lodge, E. P.; Heathcock, C. H. *J. Am. Chem. Soc.* **1987**, *109*, 3353. (b) Evans, D. A.; Duffy, J. L.; Dart, M. J. *Tetrahedron Lett.* **1994** *35*, 8537. (c) Evans, D. A.; Dart, M. J.; Duffy, J. L.; Yang, M.; Livingston, A. B. *J. Am. Chem. Soc.* **1995**, *117*, 6619. (d) Evans, D. A.; Dart, M. J.; Duffy, J. L.; Yang, M. *J. Am. Chem. Soc.* **1996**, *118*, 4322. For a review, see: (e) Mahrwald, R. *Chem. Rev.* **1999**, *99*, 1095. See also refs 6 and 7.

10.1021/jo0605694 CCC: $33.50
Published on Web 07/13/2006

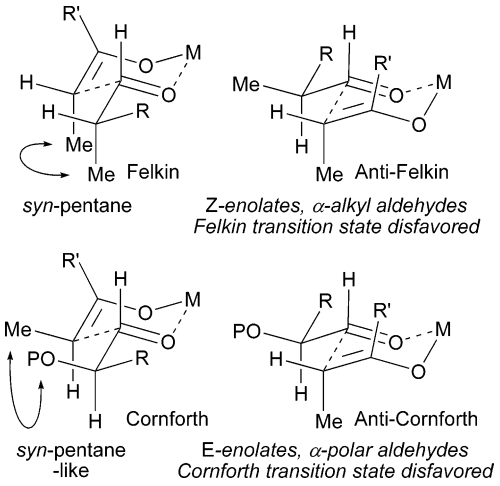


FIGURE 1. Anti-Felkin and anti-Cornforth aldol additions.

chiral aldehydes, a reversal of the ordinary Felkin−Anh selectivity can be observed when the aldehyde bears alkyl branching at the α-position, and the enolate is of the *Z*-configuration. This is thought to be due to a developing *syn*-pentane interaction between the terminal methyl group of the enolate and the methyl group at the α-position of the aldehyde which is present in the Felkin, but not the anti-Felkin, transition states (Figure 1).[1a,6] Similarly, α-heteroatom-substituted aldehydes can provide unexpected selectivities when reacting with achiral propionate or ethyl ketone enolates, though in these cases, *E*-enolates are the offending reactants. This is also thought to be due to developing *syn*-pentane-like interactions between the terminal methyl group of the enolate and the α-heteroatom group of the aldehyde which is present in the Cornforth, but not the anti-Cornforth, transition states (Figure 1).[7] Chiral auxiliary-based propionate aldol reactions are highly selective, and the stereochemical influence of the reagents usually overrides that of a chiral aldehyde.[1,2a] While aldol additions of acetate (rather than propionate) or methyl ketone (rather than ethyl ketone) substrates to chiral aldehydes should be simpler since the corresponding enolates bear a terminal methylene, the levels of asymmetric induction displayed by chiral variants of these reagents have traditionally been lower than those of propionate or ethyl ketone substrates. We, therefore, wished to explore this issue with the reagents we have developed in order to determine if they can add in a stereochemically predictable fashion to chiral aldehydes bearing α- or *β*-substituents.[8]

To study the levels of double diastereoselection in this process, we prepared substituted aldehydes in nonracemic form and subjected them to aldol reactions with our pseudo-enantiomeric reagents. These aldehydes bear either *β*-alkoxy substitution, α-alkyl substitution, or α-alkoxy substitution. These are the most commonly encountered substitution patterns in the synthesis of polyacetate fragments. Our results are shown in Table 1. All reactions were conducted under the optimized reaction conditions previously described (enolization with 1.3 equiv of **1** or **2** and $PhBCl_2$, and 2.6 equiv sparteine at 0 °C followed by addition of 1 equiv of the aldehyde at −78 or 0 °C) and proceed in good to excellent yields. We find that the extent of double diastereoselection varies according to the position and nature of the stereocenter in the aldehyde. Thus, reaction with the *β*-oxygenated aldehyde **3**, which lacks a stereocenter at the α-position, proceeds with little double diastereoselection and provides good diastereoselectivity with either reagent **1** or **2** (26:1 and 22:1, respectively, entries 1 and 2). Aldehyde **4**, on the other hand, bears an α-stereocenter and *β*-oxygenation and displays significant double diastereoselection; the matched case provides excellent selectivity (>100:1) with reagent **1**, while the mismatched case provides lower selectivity (12:1) with reagent **2** (entries 3 and 4, respectively). Similarly, aldehydes **5** and **6**, which also bear α-alkyl stereocenters, display significant double diastereoselection with the matched cases providing about 5 times higher levels of asymmetric induction than that of the mismatched cases (compare entry 5 with entry 6, and entry 7 with entry 8). D-Glyceraldehyde acetonide[9] (**7**), which bears an α-oxygenated stereocenter, provides similar selectivities with reagents **1** and **2** (13:1 and 12:1, entries 9 and 10, respectively). We also note that a variety of protecting groups, including PMB, TBS, and TES ethers, and an acetonide participate in this reaction.

We established that asymmetric induction is dictated by the reagent rather than the aldehyde by reduction of the products of entries 7−10 in Table 1 with $NaBH_4$. The diols obtained from the major products of entries 7 and 8 are diastereomeric, as are those from the products of entries 9 and 10 (Scheme 2). The sense of asymmetric induction was assigned in analogy with our previous work with reagents **1** and **2**.

In conclusion, we have shown that acetate aldol reactions using thiazolidinethione reagents **1** and **2** are subject to modest double diastereoselection in reactions with chiral aldehydes. Aldehydes in which the chirality is due to the presence of an alkyl group at the α-carbon show the greatest double diastereoselection and difference in selectivity of the matched and mismatched reaction pairs. When the chirality is due to α- or *β*-oxygenation, little double diastereoselection is observed. In all cases, the stereochemistry of the product is dictated by the reagent, not the aldehyde. This study should enhance the predictability of reactions using these reagents and thereby facilitate the design of polyacetate synthesis.

Experimental Section

General Aldol Reaction Procedure: To a 10 mL round-bottom flask were added *N*-acetyl thiazolidinethione (0.250 mmol, 1.30 equiv) and CH_2Cl_2 (1.25 mL). The flask was cooled in an ice bath, and $PhBCl_2$ (33.3 *μ*L, 0.250 mmol, 1.30 equiv) was added dropwise

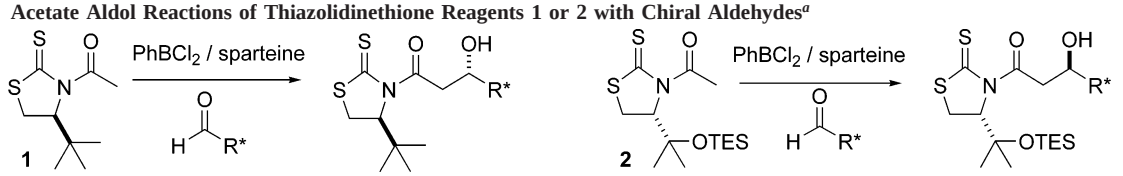
(6) (a) Roush, W. R. *J. Org. Chem.* **1991**, *56*, 4151. For an exception to this trend, see: (b) Evans, D. A.; Gage, J. R. *Tetrahedron Lett.* **1990**, *31*, 6129.

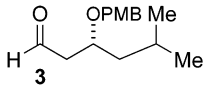
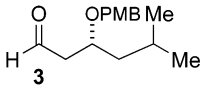
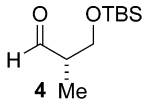
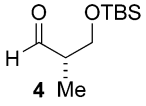
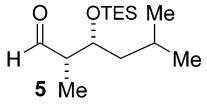
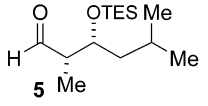
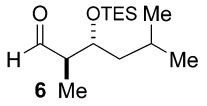
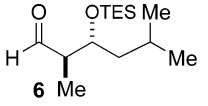
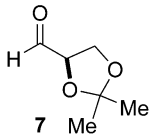
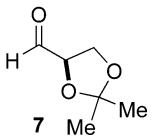
(7) In the case of the addition of propionate enolates to α-oxygenated aldehydes, the groups of Evans and Marco have recently provided evidence for the importance of the Cornforth model for asymmetric induction, which is based on a dipole-minimized conformation of the aldehyde. See: (a) Evans, D. A.; Siska, S. J.; Cee, V. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 1761. (b) Marco, J. A.; Carda, M.; Díaz-Oltra, S.; Muraga, J.; Falomir, E.; Roeper, H. *J. Org. Chem.* **2003**, *68*, 8577. (c) Cee, V. J.; Cramer, C. J.; Evans, D. A. *J. Am. Chem. Soc*, **2006**, *128*, 2920.

(8) While there are examples of asymmetric acetate additions to chiral aldehydes, we know of no systematic study of double diastereoselectivity with this class of reagents and a wide range of aldehydes. For selected examples, see: (a) ref 4c. (b) Weiss, J. M.; Hofmann, H. M. R. *Tetrahedron: Asymmetry* **1997**, *8*, 3913. (c) Crimmins, M. T.; Emmitte, K. A. *Org. Lett.* **1999**, *1*, 2029. (d) Crimmins, M. T.; DeBaillie, A. C. *Org. Lett.* **2003**, *5*, 3009. (e) Vicario, J. L.; Rodriguez, D.; Badía, D.; Carrillo, L.; Reyes, E. *Org. Lett.* **2004**, *6*, 3171. (f) La Sann, C.; Muñoz, D. M.; Saunders, N.; Simpson, T. J.; Smith, D. I.; Soulas, F.; Watts, P.; Willis, C. L. *Org. Biomol. Chem.* **2005**, *3*, 1719.

(9) D-Glyceraldehyde acetonide was purchased and treated with 4 Å molecular sieves in refluxing $CHCl_3$ before use. As received, this material was largely hydrated and was not suitable for use in the aldol reaction.

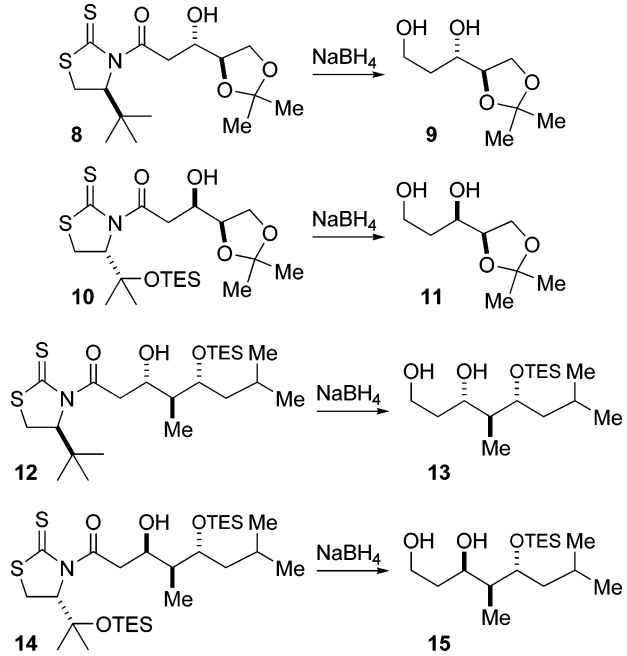
TABLE 1. Acetate Aldol Reactions of Thiazolidinethione Reagents 1 or 2 with Chiral Aldehydes[a]



entry	aldehyde	temp (°C)	dr[b]	yield (%)[c]	entry	aldehyde	temp (°C)	dr[b]	yield (%)[c]
1	 **3**	-78	26:1	79	2	 **3**	-78	22:1	81
3	 **4**	-78	>100:1	83	4	 **4**	-78	12:1	77
5	 **5**	0	23:1	75	6	 **5**	0	4.5:1	60
7	 **6**	0	4.5:1	67	8	 **6**	0	24:1	72
9	 **7**	0	13:1	79	10	 **7**	0	12:1	80

[a] For a typical experimental procedure, see Supporting Information. [b] Ratios were determined by 500 MHz ^{1}H NMR spectroscopic analysis of the crude reaction mixtures. [c] Yield of the major diastereomer after purification.

SCHEME 2. Correlation of Stereochemistry of Products



to provide an orange colored solution. After stirring for 5 min, (−)-sparteine (0.115 mL, 0.500 mmol, 2.6 equiv) was added dropwise, at which point the solution turned yellow and cloudy. After stirring for about a minute, the solution became homogeneous, but remained yellow. The ice bath was then removed, and the reaction mixture was allowed to warm to room temperature and stirred for 30 min. The reaction mixture was then cooled to the temperature described in Table 1, and the aldehyde (0.192 mmol, 1.0 equiv) in 0.8 mL of CH_2Cl_2 was added dropwise via cannula over a period of about 5 min. The flask containing the aldehyde was rinsed with an additional 0.8 mL of CH_2Cl_2, which was also added to the reaction mixture via cannula. For entries 1−4 of Table 1, the reaction mixture was stirred for 6 h at −78 °C, and then slowly warmed to 0 °C over a period of about 3 h by allowing the dry ice to evaporate. As the temperature approached 0 °C, the reaction mixture was placed in an ice bath and stirred for 30 min. As for entries 5−10 of Table 1, the reaction mixture was stirred for 3 h at 0 °C. The reaction mixture was then quenched by the addition of hexanes (3 mL) and H_2O_2 (30%, 1 mL) and stirred rapidly for 10 min at room temperature. (Note that rapid stirring is required at this step. If the rate of stirring is too slow, incomplete oxidation of the borane occurs, and boron species remain in the product.) The solution was diluted with hexanes/CH_2Cl_2 (4:1, 80 mL), and the layers were separated. The organic layer was washed with distilled water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated at reduced pressure to provide an orange oil. Analysis of this material by ^{1}H NMR provided the diastereomeric ratio values given in Table 1. The products were purified by flash chromatography using neutral silica gel (1:1 hexanes/CH_2Cl_2 to 1:4 hexanes/CH_2Cl_2 depending on substrate; see general information in the Supporting Information for details regarding the use of neutral silica gel) to provide the aldol adducts as clear yellow oils. *Note that N-acyl thiazolidinethiones are sensitive to hydrolysis, and that this workup has been optimized to minimize hydrolysis and should be followed carefully in order to obtain high yields and reproducible results.*

Typical Aldol Reaction Procedure (Table 1, entry 1): To a 10 mL round-bottom flask were added *N*-acetyl thiazolidinethione **1** (54 mg, 0.250 mmol, 1.30 equiv) and CH_2Cl_2 (1.25 mL). The

flask was cooled in an ice bath, and $PhBCl_2$ (33.3 μL, 0.250 mmol, 1.30 equiv) was added dropwise to provide an orange colored solution. After stirring for 5 min, (−)-sparteine (0.115 mL, 0.500 mmol, 2.6 equiv) was added dropwise, at which point the solution turned yellow and cloudy. After stirring for about a minute, the solution became homogeneous, but remained yellow. The ice bath was then removed, and the reaction mixture was allowed to warm to room temperature and stirred for 30 min. The reaction mixture was then cooled to the temperature described in Table 1, and aldehyde **3** (48 mg, 0.192 mmol, 1.0 equiv) in 0.8 mL of CH_2Cl_2 was added dropwise via cannula over a period of about 5 min. The flask containing the aldehyde was rinsed with an additional 0.8 mL of CH_2Cl_2, which was also added to the reaction mixture via cannula. The reaction was cooled in a dry ice/acetone bath to −78 °C and stirred for 6 h and then slowly warmed to 0 °C over a period of about 3 h by allowing the dry ice to evaporate. As the temperature approached 0 °C, the reaction mixture was placed in an ice bath and stirred for 30 min. The reaction mixture was then quenched by the addition of hexanes (3 mL) and H_2O_2 (30%, 1 mL) and stirred rapidly for 10 min at room temperature. The solution was diluted with hexanes/CH_2Cl_2 (4:1, 80 mL), and the layers were separated. The organic layer was washed with distilled water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated at reduced pressure to an orange oil. Analysis of the ^{1}H NMR spectrum of the crude product revealed a diastereomeric ratio of 26:1. This material was purified by flash chromatography using neutral silica gel (1:1 hexanes/CH_2Cl_2; see general information in the Supporting Information for details regarding the use of neutral silica gel) to provide the product as a clear yellow oil (92 mg, 0.197 mmol, 79%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25 (m, 2H), 6.86 (m, 2H), 5.33 (X of ABX, 1H, J = 0.73, 8.33 Hz), 4.48 (A of AB, J = 11.08 Hz), 4.40 (B of AB, J = 11.08 Hz), 4.20 (m, 1H), 3.79 (s, 3H), 3.66 (m, 1H), 3.61 (d, OH, J = 3.02 Hz), 3.55 (A of ABX, 1H, J = 3.33, 11.80 Hz), 3.48 (A of ABX, 1H, J = 8.33, 17.49 Hz), 3.32 (B of ABX, 1H, J = 3.84, 17.49 Hz), 3.10 (B of ABX, 1H, J = 0.73, 11.80 Hz), 1.83 (m, 1H), 1.68 (m, 2H), 1.55(m, 1H), 1.33 (m, 1H), 1.00 (s, 9H), 0.90 (d, 3H, J = 3.94 Hz), 0.89 (d, 3H, J = 3.94 Hz). ^{13}C NMR (400 MHz, $CDCl_3$): δ 205.2, 172.6, 159.4, 130.8, 129.8, 114.0, 75.9, 72.3, 70.3, 66.8, 55.5, 45.6, 43.6, 41.0, 38.2, 30.7, 27.1, 24.9, 23.2, 23.1. IR (cm^{-1}): 3452, 1685, 1607, 1507, 1460. $[\alpha]_D$ = 269° (*c* 1.26, EtOH). HRMS *m*/*z* calcd for $C_{24}H_{37}NO_4S_2Na^+$, 490.2056; found, 490.2075.

Typical Aldol Reaction Procedure (Table 1, entry 6): To a 10 mL round-bottom flask were added *N*-acetyl thiazolidinethione **2** (83 mg, 0.250 mmol, 1.30 equiv) and CH_2Cl_2 (1.25 mL). The flask was cooled in an ice bath, and $PhBCl_2$ (33.3 μL, 0.250 mmol, 1.30 equiv) was added dropwise to provide an orange colored solution. After stirring for 5 min, (−)-sparteine (0.115 mL, 0.500 mmol, 2.6 equiv) was added dropwise, at which point the solution turned yellow and cloudy. After stirring for about a minute, the solution became homogeneous, but remained yellow. The ice bath was then removed, and the reaction mixture was allowed to warm to room temperature and stirred for 30 min. The reaction mixture was then cooled back to 0 °C in an ice bath, and aldehyde **5** (50 mg, 0.192 mmol, 1.0 equiv) in 0.8 mL of CH_2Cl_2 was added dropwise via cannula over a period of about 5 min. The flask containing the aldehyde was rinsed with an additional 0.8 mL of CH_2Cl_2, which was also added to the reaction mixture via cannula, and the reaction was allowed to stir for 3 h at 0 °C. The reaction was then quenched by the addition of hexanes (3 mL) and H_2O_2 (30%, 1 mL) and stirred rapidly for 10 min at room temperature. The solution was diluted with hexanes/CH_2Cl_2 (4:1, 80 mL), and the layers were separated. The organic layer was washed with water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated at reduced pressure to provide an orange oil. Analysis of the ^{1}H NMR spectrum of the crude product revealed a diastereomeric ratio of 4.5:1. This material was purified by flash chromatography using neutral silica gel (1:1 hexanes/CH_2Cl_2; see general information for details regarding the use of neutral silica gel) to provide the product as clear yellow oil (89 mg, 0.15 mmol, 60%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.35 (X of ABX, 1H, J = 1.28, 8.05 Hz), 4.06 (m, 1H), 4.04 (m, 1H), 3.96 (d, OH, J = 3.67 Hz), 3.51 (A of ABX, 1H, J = 3.02, 16.94 Hz), 3.47 (A of ABX, 1H, J = 7.96, 11.35 Hz), 3.43 (B of ABX, 1H, J = 8.97, 16.94 Hz), 3.41 (B of ABX, 1H, J = 1.28, 11.35 Hz), 1.70 (m, 1H), 1.60 (m, 1H), 1.40 (m, 2H), 1.30 (s, 3H), 1.29 (s, 3H), 0.96 (t, 9H, J = 8.05 Hz), 0.94 (t, 9H, J = 7.78 Hz), 0.90 (d, 3H, J = 6.59 Hz), 0.88 (d, 3H, J = 6.59 Hz), 0.80 (d, 3H, J = 7.05 Hz), 0.62 (q, 6H, J = 7.78 Hz), 0.60 (q, 6H, J = 8.05 Hz). ^{13}C NMR (400 MHz, $CDCl_3$): δ 205.7, 173.0, 77.0, 72.8, 72.4, 70.6, 44.3, 43.0, 42.4, 30.3, 28.6, 26.6, 24.9, 23.3, 23.2, 11.5, 7.5, 7.3, 7.0, 5.5. IR (cm^{-1}): 3425, 1678. $[\alpha]_D$ = −216° (*c* 0.98, EtOH). HRMS *m*/*z* calcd for $C_{28}H_{57}NO_4S_2Si_2Na^+$, 614.3159; found, 614.3154.

Acknowledgment. We wish to thank Professor Andrew Phillips for helpful discussions. This work was supported by the National Institutes of Health (GM48498). NMR instrumentation used in this work was supported in part by the National Science Foundation CRIF program (CHE-0131003).

Supporting Information Available: Experimental procedures for the synthesis of aldehydes **3**, **5**, and **6**, and for conducting aldol reactions, and spectral data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0605694