Tetrahedron Vol. 45, No. 19, pp. 6101 to 6112, 1989
Printed in Great Britain.

0040-4020/89 $3.00+.00
Pergamon Press plc

DIASTEREOSELECTIVITY IN THE $TiCl_4$-MEDIATED ALDOL REACTION OF CYCLIC DIENYLSILYL ETHERS

Bruce A. Barner*, Yalei Liu, and Md. Abdur Rahman

Department of Chemistry, University of Wyoming, Laramie, WY 82071

(*Received in USA* 30 *May* 1989)

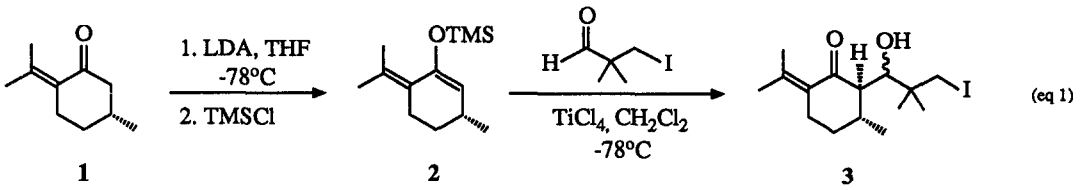
Abstract: Cyclic dienylsilyl ethers derived from α,β-unsaturated ketones undergo $TiCl_4$-catalyzed crossed aldol reactions with aldehydes, giving β'-hydroxy enone systems with good diastereoselectivity in most cases. The direction of stereocontrol (*syn* versus *anti*) in these reactions is a function of the steric demand of the aldehydic partner, favoring *syn* selectivity with sterically encumbered aldehydes.

Introduction

The aldol addition reaction has been recognized as one of the most efficient methods for stereoselective carbon-carbon bond formation in the construction of β-hydroxyketones with defined vicinal centers of asymmetry. The practicability of this process has been amplified in recent years as a result of numerous studies aimed at discerning correlations of enolate geometry, steric components and transition state structure, and the role of the enolate counterion with the stereochemical outcome of the reaction. Such conceptual advances have provided insight for the development of predictive models for stereoselection in many cases, and have been the subject of extensive review.[1] Modified aldol approaches to β-hydroxyketones have additionally played important roles in the development of transition state models, particularly in the area of enolsilanes. The seminal work of Mukaiyama[2] in the $TiCl_4$-catalyzed aldolization of ketone enolsilanes has shown that varying degrees of *anti*(threo)-selectivity generally predominate for E-enolsilanes, however many cases have been shown to be stereorandom. It is interesting to note that while numerous studies of this reaction have been performed on simple enolsilanes, the corresponding dienolsilanes, derived from α,β-unsaturated ketones, have not been systematically explored for their potential to stereoselectively produce β'-hydroxyenone systems.[3] To our knowledge, a singular report describing *anti* selectivity in the $TiCl_4$-mediated aldol reaction of a ketone dienylsilyl ether (of cyclopentenone) has recently appeared.[4]

Results and Discussion

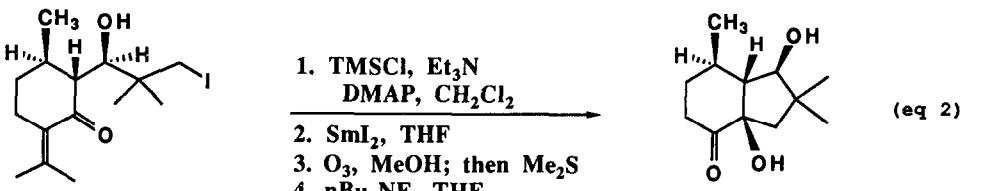
In conjunction with an ongoing program directed toward synthetic approaches to sesquiterpenoid natural products, we required a substrate of general structure **3**. Initially, there was uncertainty as to what relative configuration at the secondary hydroxyl was needed for our purposes, and we therefore sought the preparation of **3** using an aldol strategy in anticipation of obtaining sufficient quantities of both diastereomers. Preliminary studies using direct coupling of the kinetic lithium enolate of (R)-(+)-pulegone (**1**) with 3-iodo-2,2-dimethylpropanal[5] failed to produce the desired aldols. Although kinetic lithium enolates of α,β-unsaturated ketones readily alkylate, it has been observed that the corresponding aldol reactions can be problematical.[6] However, the Mukaiyama $TiCl_4$-catalyzed process as applied to the dienylsilyl ether of pulegone (**2**) and the iodopropanal gave good yields of **3** with good diastereoselection (eq 1 and Table 1).



1 2 3 (eq 1)

Significantly, only two of a possible four diastereomers were formed in this reaction, with the major product having the *syn* configuration. In light of overwhelming literature precedence for *anti* selectivity in $TiCl_4$-catalyzed aldols of E-enolsilanes, we undertook an investigation to ascertain the generality of *syn* selectivity in the $TiCl_4$-mediated aldol reaction of dienolsilanes.

Our initial course of study focused upon the derived dienylsilyl ethers of cyclic six-membered α,β-unsaturated ketones, thus guaranteeing the geometric homogeneity of the E-silyl enol ethers. Depicted in Table 1 are the results obtained in the $TiCl_4$-catalyzed reaction of four dienolsilanes with 3-iodo-2,2-dimethylpropanal. In each case, reaction occurred at -78°C within 2-3 hours in CH_2Cl_2 to provide good yields of aldol products. Consistent degrees of diastereoselectivity were obtained favoring the *syn* adduct over the *anti* product by approximately 4:1.[7] The use of etherial solvents or $TiCl(O^iPr)_3$ as catalyst failed to give acceptable yields. Verification of *syn* selectivity in these examples was provided by X-ray crystallographic analysis of derivatives of **3a** and **9a**, and subsequent ^{1}H-NMR correlations (Table 3). The major aldol product **3a** of the pulegone silylenol ether reaction was transformed into a single crystalline keto-diol **10**[8] utilizing the Molander carbocyclization procedure with SmI_2[9] (eq. 2). Figure 1 displays the ORTEP plot of **10**, clearly indicating *syn* selectivity in the initial aldol process. Unambiguous stereochemical



3a **10** (eq 2)

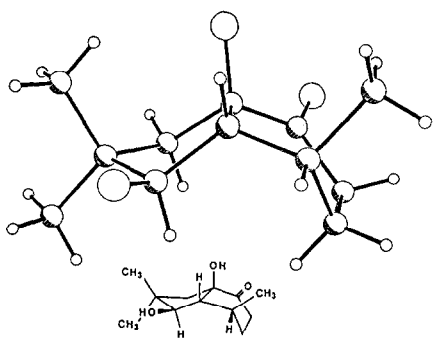


Figure 1

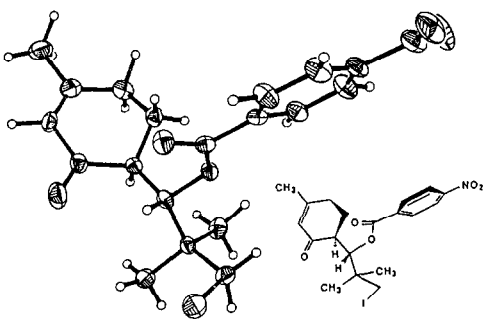
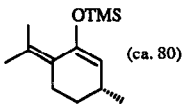
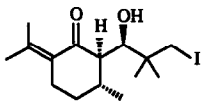
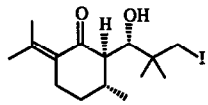
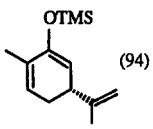
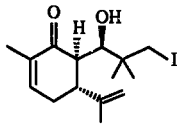
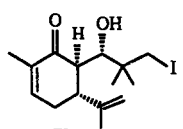
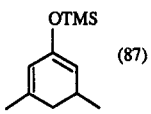
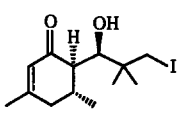
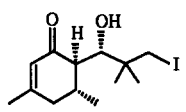
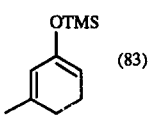
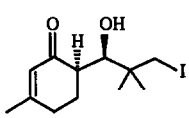
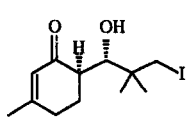


Figure 2

Table 1. Aldol Reaction of Siloxydienes with 3-Iodo-2,2-dimethylpropanal. [a]

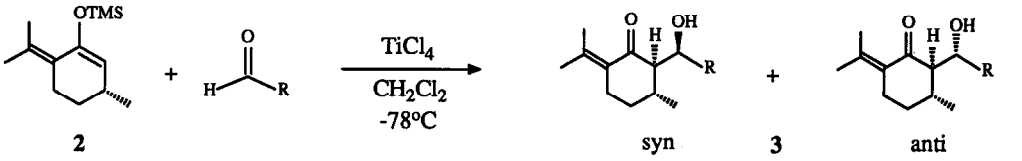
Entry	Siloxydiene[b]	Products syn	Products anti	Ratio[c] syn/anti	%Yield[d]
1	 (ca. 80) **2**	 **3a**	 **3b**	80 : 20	72
2	 (94) **4**	 **5a**	 **5b**	83 : 17	76
3[e]	 (87) **6**	 **7a**	 **7b**	72 : 28	80
4[e]	 (83) **8**	 **9a**	 **9b**	78 : 22	70

a. Vacuum distilled prior to use, see Ref. 5. b. Prepared from the corresponding enones in the yields shown in parentheses: i. LDA, THF, -78°C; ii. TMSCl, -78°C. Vacuum distilled prior to use. c. Ratios determined by ^{1}H-NMR (270 MHz) integration and HPLC analysis of the corresponding acetates. d. Purified yields following silica gel chromatography. e. Only one enantiomer depicted.

assignments of **9a,b** (Entry 4) were not possible by ^{1}H-NMR analysis, and a crystalline derivative (pNO_2-benzoate) of the major aldol product **9a** was prepared. X-ray crystallographic analysis of this derivative[10] established *syn* selectivity in this example (Figure 2). That *syn* selectivity in Entry 4 is maintained indicates that the C-6 substituent of the dienylsilyl ether plays little or no role in directing the stereochemical outcome at the secondary hydroxyl.

Having established that *syn* selectivity predominates in these reactions with the iodopropanal, we sought to examine the scope of the *syn*-selective aldol as applied to various aldehydes possessing decreasing degrees of steric demand. These studies were initiated in anticipation of identifying the fundamental factors controlling stereoselectivity in this process. The dienylsilyl ether of pulegone, **2**, was chosen as being representative, and Table 2 lists the results obtained upon its reaction with various aldehydes under the Mukaiyama conditions. Again, good yields of aldol products were obtained, however varying degrees of stereoselectivity were observed as a function of the steric demand imparted by the aldehydic partner. With large 'R' groups of the aldehyde (Entries 1 and 2), *syn* selectivity predominated in accord with the results in Table 1. With decreasing size of 'R', *syn/anti* crossover occurred to give good *anti* selectivity with smaller aldehydes (Entries 5 and 6). The pivital point in the *syn*→*anti* crossover was apparent between

Table 2. $TiCl_4$-Mediated Aldol Reactions of the Dienylsilyl Ether of (R)-(+)-Pulegone.



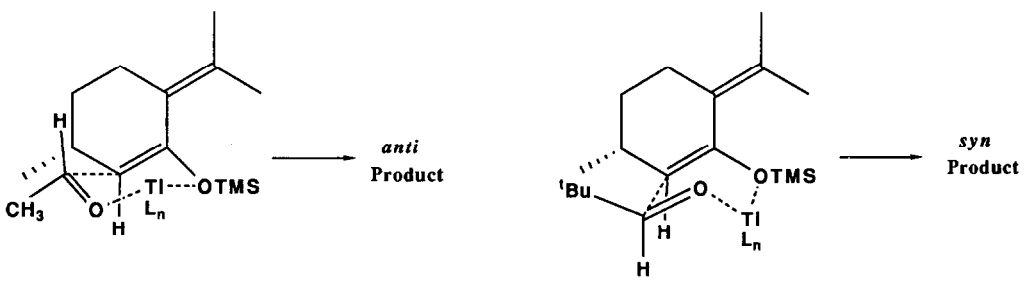
2 3

Entry	Aldehyde[a]		Ratio[b] syn/anti	%Yield[c]
1	R = -$C(CH_3)_2CH_2I$	3a:b	80 : 20	72
2	R = -$C(CH_3)_3$	3c:d	81 : 19	75
3	R = -$CH(CH_3)_2$	3e:f	56 : 44	70
4	R = -CH_2CH_3	3g:h	40 : 60	71
5	R = -CH_3	3i:j	26 : 74	80
6	R = -Ph	3k:l	30 : 70	63

a. Distilled prior to use except for acetaldehyde. b. Ratios were determined by ^{1}H-NMR (270 MHz) integration and/or HPLC analysis of the corresponding acetates. c. Purified yields following silica gel chromatography.

isobutyraldehyde and propanal, which were both stereorandom. All stereochemical assignments were ascertained by examination of extensive single frequency decoupled ^{1}H-NMR spectra (Table 3).

Assessment of the results in this investigation lead to the conclusion that steric demand of the aldehyde plays a critical role in determining the direction of stereoselectivity in the $TiCl_4$-catalyzed aldol reaction of dienylsilyl ethers. Our interpretation of the stereochemical outcome of this process favors the "closed" or chelated transition state model as first proposed by Zimmerman and Traxler,[11] and later refined by Evans.[12] With smaller 'R' groups present in the aldehyde portion, the transition state structure can adequately be represented as a chair form, with the 'R' group occupying an equatorial position (Figure 3). This mode of

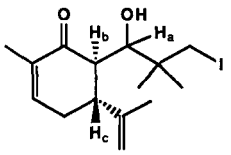
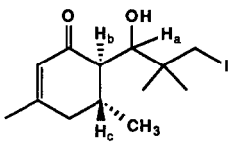
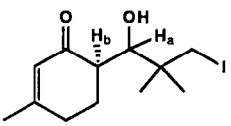
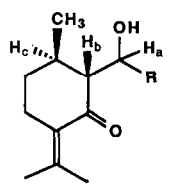


Chair Transition State
Small 'R' of Aldehyde

Boat Transition State
Large 'R' of Aldehyde

Figure 3

Table 3. Chemical Shifts and ^{1}H-NMR Coupling Constants.[a]

Entry	Syn Product			Anti Product		
	δHa	Ja,b(Hz)	Jb,c(Hz)	δHa	Ja,b(Hz)	Jb,c(Hz)
	3.82	7.3	2.9	3.76	0	11.4
	3.80	7.0	2.9	3.84	0	9.5
	4.52	2.2	_	4.22	2.2	_
						
R = -C(CH$_3$)$_2$CH$_2$I	4.10	5.1	5.1	3.63	0	8.8
R = -C(CH$_3$)$_3$	3.79	4.8	4.8	3.34	0	8.8
R = -CH(CH$_3$)$_2$	3.72	5.1	7.0	3.30	4.4	8.1
R = -CH$_2$CH$_3$	3.67	4.0	9.5	3.60	3.5	8.1
R = -CH$_3$	3.96	4.0	9.9	3.90	5.1	7.7
R = -Ph	5.08	4.6	8.4	4.76	7.7	5.9

a. Coupling constants determined by extensive homonuclear ^{1}H-NMR decoupling.

addition would result in the formation of the *anti* product, as is typically observed with E-enolsilanes. With increasing size of 'R', as in 3-iodo-2,2-dimethylpropanal and pivaldehyde, steric interaction of 'R' with the C-6 ring position of the relatively planar dienylsilyl ether is postulated to result in a preference for a boat (or twist-boat) transition state, leading to the observed *syn* product. In this mode it is speculated that the eclipsing of the large 'R' group with the C-6 ring position is more favorable than the buttressing interaction of 'R' with ligands about titanium. One cannot, however, rule out the option of an "open" transition state leading to the *syn* product.

In summary, $TiCl_4$-catalyzed aldol reactions of dienylsilyl ethers occur readily to give good yields of β'-hydroxy enone systems with consistently good degrees of stereoselectivity with aldehydes possessing either large or small degrees of steric demand. Our studies have additionally shown that the direction of stereocontrol is a function of the steric demand of the reacting aldehyde. Further progress in this area will be reported in due course.

Experimental Section

General Procedures. ^{1}H-NMR spectra were recorded on a JEOL FX-270 spectrometer at 269.7 MHz. All spectra were taken in $CDCl_3$ and chemical shifts are reported in δ (in parts per million) downfield from internal standard, tetramethylsilane. ^{13}C-NMR spectra were recorded on the same instrument at 67.8 MHz. All spectra were measured in $CDCl_3$ and chemical shifts are reported in δ (in parts per million) using the residual solvent triplet as internal reference (δ 77.00). Infrared spectra were recorded on a Mattson Cygnus 100 FT-IR spectrometer. High resolution mass spectra were obtained on a VG ZAB 1F mass spectrometer at 70 eV (EI). Thin layer chromatography was performed on Merck silica gel F-254 analytical plates, and flash chromatography was accomplished as described by Still[13] using Merck silica gel 60 (230-400 mesh). HPLC was performed on a Hewlett Packard 1090 L liquid chromatograph using a 4x25 mm, 5-μm Zorbax Sil (DuPont) column with 5-10% ethyl acetate in hexanes. Crystal structures were obtained on a Nicolet R3mN automated X-ray diffractometer at -130°C.

Materials. Tetrahydrofuran (Burdick and Jackson, HPLC grade) and diethyl ether (J.T. Baker) were freshly distilled from sodium benzophenone ketyl under argon. Methylene chloride and ethyl acetate (J.T. Baker) were distilled from CaH_2. All liquid reagents were dried (CaH_2) and distilled under an argon atmosphere prior to use, with the exception of titanium tetrachloride (Aldrich) which was used as received. SmI_2[14] and 3-iodo-2,2-dimethylpropanal[5] were prepared according to literature procedures. All $TiCl_4$ reactions and all LDA deprotonations were carried out under a positive pressure of argon in glassware flame-dried under a stream of argon.

General Procedure for the Preparation of Dienolsilanes.

To a flame-dried 250 mL round-bottom flask fitted with a magnetic stirring bar, rubber septum, and connected to an argon source were added dry tetrahydrofuran (100 mL) and freshly distilled diisopropylamine (5.67 mL, 43.8 mmol). The flask and contents were cooled to -78°C in a dry ice-acetone bath and over a period of 5 min n-BuLi (24.7 mL, 39.4 mmol/hexane) was added by syringe with continuous stirring. After 20 min, freshly distilled R-(+)-pulegone (Aldrich) (5.0 g, 32.8 mmol) was added neat over 5 min. The bright yellow solution was stirred at -78°C for 30 min, then freshly distilled chlorotrimethylsilane (7.91 ml, 62.4 mmol) was added rapidly by a syringe. The resulting slurry was stirred for an additional 2 hr at -78°C. The reaction

mixture was quenched with brine (20 mL) at -78°C and then extracted with n-pentane (3x150 mL). The combined organic extract was washed with brine (3x20 mL) and dried over anhydrous Na_2SO_4. Filtration and concentration *in vacuo* gave the crude oil which was distilled (Kugelrohr) at reduced pressure, providing 6.78 g (92%) of dienylsilyl ether **2**, bp 89°C (2 mm Hg) as a colorless oil. The material so obtained was contaminated with ca. 10-15% of the dienylsilyl ether derived from LDA deprotonation at the terminus (-CH_3) of the enone system, as evidenced by the appearance of a doublet at δ 4.85 (=CH_2) and a singlet at δ 1.90 (vinyl methyl) in the ^{1}H-NMR spectrum. Further purification was not attempted, and this material was used in subsequent reactions. The analogous contaminants were not observed in the other three dienylsilyl ethers. IR (film) 3050-2850, 1660, 1635, 1255, 1180 cm^{-1}. ^{1}H-NMR δ 4.78 (d, 1H, J = 2.6 Hz), 2.48 (m, 1H), 2.32 (m, 1H), 2.1 (m, 1H), 1.98 (s, 3H), 1.71 (s, 3H), 1.15 (m, 1H), 0.97 (d, 3H, J = 7.3 Hz), 0.18 (s, 9H).

Dienylsilyl ether of R-(-)-carvone (4). IR (film) 3100-2820, 1662, 1655 (sh), 1646 (sh), 1595, 1250, 1208, 1180 cm^{-1}. ^{1}H-NMR δ 5.57 (brS, 1H), 4.79 (s, 2H), 4.73 (s, 1H), 3.03 (m, 1H), 2.15 (m, 2H), 1.74 (s, 3H), 1.71 (s, 3H), 0.22 (s, 9H).

Dienylsilyl ether of 3,5-dimethyl-2-cyclohexenone (6). IR (film) 3070-2810, 1661, 1609, 1224, 1120 cm^{-1}. ^{1}H-NMR δ 5.42 (s, 1H), 4.62 (brS, 1H), 2.49 (m, 1H), 2.10 (dd, 1H, J = 16.6, 8.2 Hz), 1.84-1.73 (m, 1H), 1.77 (s, 3H), 0.98 (d, 3H, J = 7.0 Hz), 0.18 (s, 9H).

Dienylsilyl ether of 3-methyl-2-cyclohexenone (8). ^{1}H-NMR δ 5.44 (s, 1H), 4.72 (brS, 1H), 2.18 (m, 2H), 2.02 (m, 2H), 1.78 (s, 3H), 0.18 (s, 9H).

General Procedure for the $TiCl_4$-catalyzed Preparation of Aldols.

To a flame-dried 250 mL round-bottom flask fitted with a magnetic stirring bar, rubber septum, and connected to an argon source were added dry methylene chloride (100 mL) and freshly prepared and distilled 3-iodo-2,2-dimethylpropanal (3.00 g, 14.2 mmol). The flask and contents were cooled to -78°C in a dry ice-acetone bath and the dienylsilyl ether (**2**) of pulegone (4.29 g, 19.1 mmol) and titanium tetrachloride (2.79 mL, 25.4 mmol) in 5 mL dry methylene chloride were added separately by syringe with continuous stirring. After 2 hr at -78°C, the reaction mixture was quenched with saturated sodium bicarbonate solution (20 mL). The resulting solution was extracted with methylene chloride (3x100 mL), and the combined extract was dried over anhydrous sodium sulfate. Filtration and concentration *in vacuo* gave the crude product which was flash-chromatographed on a small pad of silica gel (hexane/EtOAc 7:3) providing 3.72 g (72%) of a mixture of two aldol isomers, **3a** and **3b**. An aliquot of this mixture was derivatized (*vide infra*) as the trimethylsilyl ether (or acetates) for ^{1}H-NMR and/or HPLC analysis of the mixture composition. The aldols were separated by careful flash chromatography (hexane/EtOAc 7:3) or by preparative TLC (3% EtOAc/hexane) to provide pure samples.

General Procedure for the Preparation of Trimethylsilyl Ethers of Aldol Products

To a 0°C solution of the isomeric aldol mixture (1.0 mmol) in methylene chloride (10 mL) under argon was added dried (CaH_2) and distilled triethylamine (1.2 mmol) and 4-N,N-dimethylaminopyridine (0.1 mmol), followed by dried (CaH_2) and distilled chlorotrimethylsilane (2.0 mmol) with continuous stirring. After 3 hr at 0°C, the reaction mixture was poured into cold water (3 mL) and extracted with methylene chloride (3x5 mL). The combined extract was washed once with water (3 mL) and then with brine (3 mL), and was dried over anhydrous sodium sulfate. Filtration and concentration afforded the crude product, which was flash-filtered through a small bed of silica gel (hexane/EtOAc 95:5) giving trimethylsilyl ethers suitable for ^{1}H-NMR analysis.

General Procedure for the Preparation of Acetates of Aldol Products

To a 0°C solution of the isomeric aldol mixture (1.0 mmol) in methylene chloride (10 mL) under argon was added dried (CaH_2) and distilled triethylamine (1.5 mmol) and 4-N,N-dimethylaminopyridine (0.1 mmol), followed by acetic anhydride (2.5 mmol) with continuous stirring. After 3 hr at 0°C, the reaction mixture was warmed to ambient temperature (22°C) and stirred for 12 hr. The reaction mixture was diluted with methylene chloride (30 mL) and washed with 10% HCl (10 mL) followed by saturated sodium bicarbonate solution (10 mL) and finally water (10 mL). The organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*, giving the crude acetates. Following flash-filtration through a small pad of silica gel (hexane/EtOAc 4:1), the isomeric composition of the mixture was determined by ^{1}H-NMR and/or HPLC analysis.

Syn Aldol 3a. IR (film) 3475, 1669, 1614 cm^{-1}. ^{1}H-NMR δ 4.10 (dd, 1H, J = 5.1, 6.6 Hz), 3.50 (d, 1H, J = 10.3 Hz), 3.15 (d, 1H, J = 10.3 Hz), 2.6 (m, 1H), 2.45 (d, 1H, J = 6.6 Hz), 2.4 (m, 1H), 2.30 (dd, 1H, J = 5.1, 5.1), 1.96 (s, 3H), 1.78 (s, 3H), 1.9 (m, 1H), 1.4 (m, 1H), 1.11 (d, 3H, J = 7.3 Hz), 1.06 (s, 3H), 0.99 (s, 3H). ^{13}C-NMR δ 207.4, 142.9, 132.1, 74.4, 58.8, 38.9, 30.9, 29.4, 26.6, 25.5, 23.6, 22.7, 22.1, 21.8, 21.0.

Trimethylsilyl Ether of 3a. IR (film) 1688, 1613, 1210 cm^{-1}. ^{1}H-NMR δ 4.49 (d, 1H, J = 3.7 Hz), 3.26 (d, 1H, J = 10.3 Hz), 3.19 (d, 1H, J = 9.5 Hz), 2.6 (m, 1H), 2.3 (m, 1H), 2.14 (m, 1H), 2.12 (d, 1H, J = 6.6 Hz), 1.87 (s, 3H), 1.7 (m, 1H), 1.73 (s, 3H), 1.5 (m, 1H), 1.10 (d, 3H, J = 6.6 Hz), 0.94 (s, 6H), 0.10 (s, 9H).

Anti Aldol 3b. ^{1}H-NMR δ 4.64 (d, 1H, J = 10.3 Hz), 3.64 (d, 1H, J = 10.3 Hz), 3.48 (d, 1H, J = 9.5 Hz), 3.15 (d, 1H, J = 9.5 Hz), 2.6 (m, 1H), 2.4 (m, 1H), 2.3 (m, 1H), 2.16 (d, 1H, J = 8.8 Hz), 1.86 (s, 3H), 1.73 (s, 3H), 1.8 (m, 1H), 1.5 (m, 1H), 1.11 (d, 3H, J = 6.6 Hz), 1.01 (s, 3H), 0.96 (s, 3H). ^{13}C-NMR δ 210.3, 139.3, 134.9, 54.9, 39.4, 36.0, 31.3, 27.2, 26.0, 23.6, 23.0, 21.6, 21.1, 20.5.

Trimethylsilyl Ether of 3b. ^{1}H-NMR δ 4.35 (d, 1H, J = 8.8 Hz), 3.33 (d, 1H, J = 9.5 Hz), 3.24 (d, 1H, J = 9.5 Hz), 2.7 (m, 1H), 2.4 (m, 1H), 2.3 (m, 1H), 1.93 (s, 3H), 1.7 (m, 1H), 1.68 (s, 3H), 1.2 (m, 1H), 1.08 (d, 3H, J = 6.6 Hz), 0.98 (s, 3H), 0.87 (s, 3H), 0.21 (s, 9H).

Syn Aldol 5a. ^{1}H-NMR δ 6.60 (m, 1H), 4.81 (s, 1H), 4.68 (s, 1H), 3.82 (dd, 1H, J = 7.3, 7.3 Hz), 3.45 (d, 1H, J = 9.5 Hz), 3.15 (m, 1H), 3.08 (d, 1H, J = 9.5 Hz), 2.72 (m, 1H), 2.4-2.3 (m, 1H), 2.72 (dd, 1H, J = 7.3, 2.9 Hz), 2.21 (d, 1H, J = 7.3 Hz), 1.75 (s, 3H), 1.73 (s, 3H), 1.10 (s, 3H), 0.96 (s, 3H).

Trimethylsilyl Ether of 5a. IR (film) 1700, 1662, 1569, 1251 cm^{-1}. ^{1}H-NMR δ 6.6 (m, 1H), 4.77 (s, 1H), 4.62 (s, 1H), 4.03 (d, 1H, J = 4.4 Hz), 3.27 (d, 1H, J = 9.9 Hz), 3.20 (d, 1H, J = 9.5 Hz), 3.08 (m, 1H), 2.9-2.7 (m, 1H), 2.64 (dd, 1H, J = 4.4, 1.5 Hz), 2.4-2.2 (m, 1H), 1.77 (s, 3H), 1.70 (s, 3H), 1.07 (s, 3H), 1.05 (s, 3H). MS (70 eV), m/z (rel intensity) 434 (2.4), 306 (8), 285 (31), 252 (25), 251 (100), 222 (15), 207 (32), 181 (12), 169 (36), 165 (11), 162 (11), 161 (100), 143 (30), 135 (20), 133 (17), 105 (14), 91 (27). Exact mass calcd for $C_{18}H_{31}IO_2Si$: 434.1137. Found: 434.1125.

Acetate of 5a. ^{1}H-NMR δ 6.5 (m, 1H), 5.23 (d, 1H, J = 3.7 Hz), 4.79 (s, 1H), 4.66 (s, 1H), 3.30 (d, 1H, J = 10.2 Hz), 3.15 (d, 1H, J = 10.2 Hz), 2.9 (m, 1H), 2.85 (m, 1H), 2.7 (m, 1H), 2.4-2.3 (m, 1H), 1.92 (s, 3H), 1.71 (s, 6H), 1.07 (s, 6H).

Anti Aldol 5b. ^{1}H-NMR δ 6.65 (m, 1H), 4.97 (s, 1H), 4.94 (s, 1H), 3.76 (d, 1H, J = 9.2 Hz), 3.52 (d, 1H, J = 9.5 Hz), 3.42 (d, 1H, J = 9.2 Hz), 3.17 (d, 1H, J = 9.5 Hz), 2.9 (m, 1H), 2.62 (d, 1H, J = 11.0 Hz), 2.5-2.4 (m, 2H), 1.75 (s, 3H), 1.74 (s, 3H), 1.08 (s, 3H), 1.00 (s, 3H).

Syn Aldol 7a. ^{1}H-NMR δ 5.85 (s, 1H), 3.80 (dd, 1H, J = 7.0, 7.0 Hz), 3.45 (d, 1H, J = 9.5 Hz), 3.09 (d, 1H, J = 9.5 Hz), 2.75 (m, 1H), 2.7 (m, 1H), 2.28 (dd, 1H, J = 7.0, 2.9 Hz), 2.20 (d, 1H, J = 7.0 Hz), 1.94 (s, 3H),

1.15 (m, 1H), 1.10 (s, 3H), 1.03 (d, 3H, J = 7.3 Hz), 0.99 (s, 3H).

Trimethylsilyl Ether of 7a. IR (film) 1659, 1252, 1110 cm^{-1}. ^{1}H-NMR δ 5.86 (s, 1H), 4.26 (d, 1H, J = 2.3 Hz), 3.24 (d, 1H, J = 9.9 Hz), 3.19 (d, 1H, J = 9.9 Hz), 2.54 (dd, 1H, J = 4.6, 17.8 Hz), 2.35 (m, 1H), 2.07 (dd, 1H, J = 2.7, 5.6 Hz), 1.88 (s, 3H), 1.2 (m, 1H), 1.08 (d, 3H, J = 6.6 Hz), 0.99 (s, 6H), 0.08 (s, 9H).

Acetate of 7a. IR (film) 1738, 1656, 1385, 1245 cm^{-1}. ^{1}H-NMR δ 5.89 (s, 1H), 5.28 (d, 1H, J = 8.1 Hz), 3.27 (d, 1H, J = 10.2 Hz), 3.21 (d, 1H, J = 10.2 Hz), 2.72 (m, 1H), 2.36 (dd, 1H, J = 8.1, 4.0 Hz), 2.15 (m, 1H), 2.06 (s, 3H), 1.90 (s, 3H), 1.3 (m, 1H), 1.07 (s, 3H), 1.06 (d, 3H, J = 7.3 Hz), 1.02 (s, 3H). MS (70 eV), m/z (rel intensity) 378 (0.2), 335 (35), 195 (20), 192 (15), 191 (100), 167 (23), 154 (11), 153 (89), 150 (12), 149 (50), 135 (17), 129 (17), 124 (16), 123 (35), 109 (28), 107 (15). Exact mass calcd for $C_{15}H_{23}IO_3$: 378.0691. Found: 378.0688.

Anti Aldol 7b. ^{1}H-NMR δ 5.85 (s, 1H), 3.84 (d, 1H, J = 11.0 Hz), 3.53 (d, 1H, J = 9.5 Hz), 3.51 (d, 1H, J = 11.0 Hz), 3.12 (d, 1H, J = 9.5 Hz), 2.49 (dd, 1H, J = 18.3, 4.4 Hz), 2.3 (m, 1H), 2.22 (d, 1H, J = 9.5 Hz), 2.2-2.1 (m, 1H), 1.95 (s, 3H), 1.13 (d, 3H, J = 6.6 Hz), 1.08 (s, 3H), 1.01 (s, 3H).

Syn Aldol 9a. IR (film) 3457, 1698 (sh), 1662, 1382, 1211 cm^{-1}. ^{1}H-NMR δ 5.91 (s, 1H), 4.50 (dd, 1H, J = 5.1, 2.2 Hz), 3.43 (d, 1H, J = 9.5 Hz), 3.22 (d, 1H, J = 9.5 Hz), 2.43 (ddd, 1H, J = 2.2, 12.5, 5.1 Hz), 2.3 (m, 2H), 2.2-2.0 (m, 2H), 1.98 (d, 1H, J = 5.1 Hz), 1.95 (s, 3H), 1.12 (s, 3H), 1.03 (s, 3H).

Acetate of 9a. IR (film) 1754, 1668, 1370, 1240, 1130, 1000 cm^{-1}. ^{1}H-NMR δ 5.92 (s, 1H), 5.50 (d, 1H, J = 3.7 Hz), 3.28 (d, 1H, J = 8.8 Hz), 3.21 (d, 1H, J = 8.8 Hz), 2.7 (m, 1H), 2.4-2.3 (m, 2H), 2.04 (s, 3H), 1.95 (m, 1H), 1.92 (s, 3H), 1.66 (m, 1H), 1.05 (s, 3H), 1.03 (s, 3H).

para-Nitrobenzoate of 9a (11). Syn aldol **9a** was derivatized as the corresponding para-nitrobenzoate in 90% yield according to the general procedure for acetate formation, utilizing para-nitrobenzoyl chloride in place of acetic anhydride. This material was recrystallized from 10% ethyl acetate in hexane, giving colorless needles, mp 142-142°C, used for X-ray crystallographic analysis. IR (solid film) 1725, 1670, 1526, 1274 cm^{-1}. ^{1}H-NMR δ 8.31 (d, 2H, J = 8.8 Hz), 8.18 (d, 2H, J = 8.8 Hz), 5.98 (s, 1H), 5.89 (d, 1H, J = 2.9 Hz), 3.34 (d, 1H, J = 9.3 Hz), 3.27 (d, 1H, J = 9.3 Hz), 2.52 (m, 1H), 2.4 (m, 2H), 2.12 (m, 1H), 1.94 (s, 3H), 1.72 (m, 1H), 1.20 (s, 3H), 1.15 (s, 3H).

Anti Aldol 9b. ^{1}H-NMR δ 6.76 (s, 1H), 4.22 (dd, 1H, J = 4.8, 2.2 Hz), 3.44 (d, 1H, J = 9.5 Hz), 3.18 (d, 1H, J = 9.5 Hz), 2.41 (d, 1H, J = 4.8 Hz), 2.3-2.2 (m, 2H), 2.2-2.0 (m, 2H), 1.90 (s, 3H), 1.7 (m, 1H), 1.09 (s, 3H), 0.99 (s, 3H).

Syn Aldol 3c. IR (film) 3468, 1673, 1641, 1615, 1366, 1288 cm^{-1}. ^{1}H-NMR δ 3.79 (dd, 1H, J = 6.6, 4.8 Hz), 2.6-2.5 (m, 2H), 2.4 (m, 1H), 2.31 (dd, 1H, J = 4.8, 4.8 Hz), 2.18 (d, 1H, J = 6.6 Hz), 1.94 (s, 3H), 1.9-1.8 (m, 1H), 1.77 (s, 3H), 1.4 (m, 1H), 1.10 (d, 3H, J = 7.0 Hz), 0.93 (s, 9H). MS (70 eV), m/z (rel intensity), 238 (6), 220 (6), 205 (14), 181 (45), 163 (20), 153 (22), 152 (78), 138 (14), 137 (100), 135 (33), 123 (14), 121 (12), 109 (50), 107 (15), 97 (17), 95 (30), 93 (22), 91 (14). Exact mass calcd for $C_{15}H_{26}O_2$: 238.1933. Found: 238.1967.

Acetate of 3c. IR (film) 1738, 1665, 1372, 1240 cm^{-1}. ^{1}H-NMR δ 5.17 (d, 1H, J = 5.9 Hz), 2.5-2.4 (m, 2H), 2.33 (dd, 1H, J = 5.9, 4.4 Hz), 2.1-2.0 (m, 1H), 2.03 (s, 3H), 1.90 (s, 3H), 1.8-1.7 (m, 1H), 1.72 (s, 3H), 1.4-1.3 (m, 1H), 1.05 (d, 3H, J = 7.3 Hz), 0.88 (s, 9H).

Anti Aldol 3d. ^{1}H-NMR δ 4.44 (d, 1H, J = 10.6 Hz, -OH), 3.34 (d, 1H, J = 10.6 Hz), 2.6 (m, 1H), 2.4-2.2 (m, 2H), 2.20 (d, 1H, J = 8.8 Hz), 1.9-1.8 (m, 1H), 1.88 (s, 3H), 1.74 (s, 3H), 1.5 (m, 1H), 1.3 (m, 1H), 1.09 (d, 3H, J = 6.2 Hz), 0.91 (s, 9H).

Syn Aldol 3e. ^{1}H-NMR δ 3.72 (m, 1H), 2.81 (d, 1H, J = 7.0 Hz, -OH), 2.5 (m, 2H), 2.29 (dd, 1H, J = 7.0, 5.1 Hz), 2.2-2.1 (m, 1H), 1.96 (s, 3H), 1.9-1.6 (m, 2H), 1.77 (s, 3H), 1.4 (m, 1H), 1.06 (d, 3H, J = 6.6 Hz), 0.93 (d, 3H, J = 7.0 Hz), 0.89 (d, 3H, J = 6.6 Hz).

Acetate of 3e. IR (film) 1740, 1678, 1618, 1372, 1239 cm^{-1}. ^{1}H-NMR δ 4.93 (dd, 1H, J = 7.7, 4.2 Hz), 2.5-2.4 (m, 2H), 2.3 (m, 1H), 2.28 (dd, 1H, J = 7.7, 4.2 Hz), 1.95 (s, 3H), 1.90 (s, 3H), 1.8-1.6 (m, 2H), 1.73 (s, 3H), 1.03 (d, 3H, J = 6.5 Hz), 0.95 (d, 3H, J = 7.0 Hz), 0.84 (d, 3H, J = 7.0 Hz). MS (70 eV), m/z (rel intensity) 266 (0.4), 207 (20), 206 (95), 192 (20), 191 (100), 181 (15), 163 (39), 152 (45), 151 (16), 150 (13), 149 (18), 138 (34), 137 (87), 135 (25), 129 (28), 123 (22), 122 (29), 121 (17), 118 (14), 110 (11), 109 (80), 107 (35), 105 (11), 97 (12), 95 (21), 93 (22), 91 (20). Exact mass calcd for $C_{16}H_{26}O_3$: 266.1882. Found: 266.1896.

Anti Aldol 3f. ^{1}H-NMR δ 3.3 (m, 1H), 2.7-2.5 (m, 2H), 2.53 (d, 1H, J = 9.5 Hz, -OH), 2.4 (m, 1H), 2.2-2.1 (m, 1H), 2.20 (dd, 1H, J = 8.1, 4.0 Hz), 2.0 (m, 1H), 1.89 (s, 3H), 1.8 (m, 1H), 1.74 (s, 3H), 1.06 (d, 3H, J = 6.6 Hz), 0.97 (d, 3H, J = 6.6 Hz), 0.89 (d, 3H, J = 6.6 Hz).

Acetate of 3f. ^{1}H-NMR δ 5.10 (dd, 1H, J = 8.1, 4.8 Hz), 2.6-2.3 (m, 3H), 2.43 (dd, 1H, J = 8.1, 4.0 Hz), 2.04 (s, 3H), 1.89 (s, 3H), 1.76 (s, 3H), 1.7-1.6 (m, 1H), 1.4-1.2 (m, 2H), 1.03 (d, 3H, J = 6.5 Hz), 0.92 (d, 3H, J = 7.0 Hz), 0.87 (d, 3H, J = 7.0 Hz).

Syn Aldol 3g. IR (film) 3472, 1672, 1616, 1376, 1289 cm^{-1}. ^{1}H-NMR δ 3.67 (m, 1H), 3.41 (d, 1H, J = 9.5 Hz, -OH), 2.6-2.5 (m, 1H), 2.4 (m, 1H), 2.26 (dd, 1H, J = 9.5, 4.0 Hz), 2.01 (s, 3H), 1.9-1.7 (m, 2H), 1.79 (s, 3H), 1.45 (m, 1H), 1.4-1.2 (m, 2H), 1.04 (d, 3H, J = 6.5 Hz), 0.99 (t, 3H, J = 7.3 Hz).

Acetate of 3g. IR (film) 1739, 1679, 1617, 1372, 1234 cm^{-1}. ^{1}H-NMR δ 5.12 (m, 1H), 2.4 (m, 2H), 2.31 (dd, 1H, J = 7.0, 4.8 Hz), 2.02 (s, 3H), 1.87 (s, 3H), 1.8-1.6 (m, 2H), 1.73 (s, 3H), 1.5 (m, 1H), 1.4-1.2 (m, 2H), 1.03 (d, 3H, J = 7.0 Hz), 0.85 (d, 3H, J = 7.3 Hz).

Anti Aldol 3h. ^{1}H-NMR δ 3.60 (m, 1H), 2.6 (m, 1H), 2.58 (d, 1H, J = 8.4 Hz, -OH), 2.4-2.3 (m, 1H), 2.1 (m, 1H), 2.04 (dd, 1H, J = 8.1, 3.3 Hz), 1.90 (s, 3H), 1.8 (m, 1H), 1.75 (s, 3H), 1.7-1.5 (m, 2H), 1.4 (m, 1H), 1.08 (d, 3H, J = 6.6 Hz), 0.98 (t, 3H, J = 7.5 Hz).

Acetate of 3h. ^{1}H-NMR δ 5.12 (m, 1H), 2.4 (m, 2H), 2.21 (dd, 1H, J = 7.7, 4.8 Hz), 1.95 (s, 3H), 1.87 (s, 3H), 1.8-1.6 (m, 2H), 1.71 (s, 3H), 1.5 (m, 1H), 1.4-1.2 (m, 2H), 1.03 (d, 3H, J = 6.5 Hz), 0.87 (t, 3H, J = 7.3 Hz).

Syn Aldol 3i. IR (film) 3450, 1673, 1616, 1376, 1291 cm^{-1}. ^{1}H-NMR δ 3.93 (m, 1H), 3.85 (d, 1H, J = 9.9 Hz, -OH), 2.6 (m, 1H), 2.4-2.3 (m, 1H), 2.23 (dd, 1H, J = 10.3, 4.0 Hz), 2.02 (s, 3H), 1.9-1.7 (m, 2H), 1.79 (s, 3H), 1.3 (m, 1H), 1.16 (d, 3H, J = 6.2 Hz), 1.04 (d, 3H, J = 6.6 Hz).

Acetate of 3i. IR (film) 1740, 1683, 1618, 1373, 1242 cm^{-1}. ^{1}H-NMR δ 5.18 (m, 1H), 2.5-2.4 (m, 2H), 2.27 (dd, 1H, J = 7.7, 5.1 Hz), 2.04 (s, 3H), 1.91 (s, 3H), 1.9-1.7 (m, 2H), 1.76 (s, 3H), 1.35 (m, 1H), 1.18 (d, 3H, J = 6.2 Hz), 1.07 (d, 3H, J = 7.0 Hz).

Anti Aldol 3j. ^{1}H-NMR δ 3.92 (m, 1H), 2.82 (d, 1H, J = 7.3 Hz, -OH), 2.6 (m, 1H), 2.4 (m, 1H), 1.97 (dd, 1H, J = 7.7, 4.9 Hz), 1.92 (s, 3H), 1.8-1.6 (m, 2H), 1.75 (s, 3H), 1.4 (m, 1H), 1.32 (d, 3H, J = 6.2 Hz), 1.10 (d, 3H, J = 6.6 Hz).

Acetate of 3j. ^{1}H-NMR δ 5.22 (m, 1H), 2.5-2.4 (m, 2H), 2.22 (dd, 1H, J = 7.0, 5.9 Hz), 1.97 (s, 3H), 1.88 (s, 3H), 1.8-1.7 (m, 2H), 1.4-1.3 (m, 1H), 1.29 (d, 3H, J = 6.2 Hz), 1.07 (d, 3H, J = 7.0 Hz). MS (70 eV), m/z (rel intensity) 238 (0.4), 179 (24), 178(100), 163 (78), 149 (19), 137 (29), 136 (24), 135 (39), 131 (12), 123 (22), 122 (49), 121 (47), 109 (40), 108 (18), 107 (57), 105 (11), 97 (11), 96 (11), 95 (32), 93 (28), 91 (18). Exact mass calcd for $C_{14}H_{22}O_3$: 238.1569. Found: 238.1548.

Syn Aldol 3k. ^{1}H-NMR δ 7.4-7.2 (m, 5H), 5.08 (dd, 1H, J = 7.0, 4.6 Hz), 4.28 (d, 1H, J = 7.0 Hz, -OH), 2.5 (m, 2H), 2.48 (dd, 1H, J = 8.4, 4.6 Hz), 2.2 (m, 1H), 1.99 (s, 3H), 1.8 (m, 1H), 1.71 (s, 3H), 1.35 (m, 1H), 0.92 (d, 3H, J = 7.0 Hz).

Acetate of 3k. ^{1}H-NMR δ 7.4-7.2 (m, 5H), 6.13 (d, 1H, J = 7.3 Hz), 2.66 (dd, 1H, J = 7.1, 4.8 Hz), 2.6-2.4 (m, 2H), 2.2 (m, 1H), 2.05 (s, 3H), 2.0-1.9 (m, 1H), 1.74 (s, 3H), 1.7 (m, 1H), 1.63 (s, 3H), 1.4-1.3 (m, 1H), 0.87 (d, 3H, J = 7.0 Hz).

Anti Aldol 3l. ^{1}H-NMR δ 7.4-7.2 (m, 5H), 4.77 (dd, 1H, J = 7.7, 4.8 Hz), 3.51 (d, 1H, J = 4.8 Hz, -OH), 2.6-2.5 (m, 2H), 2.43 (dd, 1H, J = 7.7, 5.9 Hz), 1.94 (s, 3H), 1.9-1.7 (m, 2H), 1.79 (s, 3H), 1.4 (m, 1H), 0.77 (d, 3H, J = 6.6 Hz).

Acetate of 3l. IR (film) 1744, 1688, 1628, 1496, 1372, 1231, 765, 700 cm^{-1}. ^{1}H-NMR δ 7.4-7.2 (m, 5H), 5.93 (d, 1H, J = 10.3 Hz), 2.68 (dd, 1H, J = 10.3, 3.7 Hz), 2.6 (m, 1H), 2.4 (m, 1H), 1.97 (s, 3H), 1.9-1.7 (m, 2H), 1.86 (s, 3H), 1.77 (s, 3H), 1.4-1.3 (m, 1H), 0.85 (d, 3H, J = 7.0 Hz). MS (70 eV), m/z (rel intensity) 300 (0.3), 241 (16), 240 (93), 239 (54), 238 (19), 225 (15), 198 (12), 197 (27), 191 (14), 178 (13), 169 (12), 156 (12), 155 (44), 152 (11), 149 (12), 141 (15), 137 (24), 131 (23), 130 (11), 129 (44), 128 (22), 122 (26), 121 (13), 119 (10), 118 (100), 115 (28), 109 (10), 107 (20), 105 (35), 93 (12), 91 (72). Exact mass calcd for $C_{19}H_{24}O_3$: 300.1725. Found: 300.1696.

Preparation of Keto-diol 10. A flame-dried 100 mL flask under argon was charged with 1.30 g (8.65 mmol) of samarium metal (-40 mesh) and dry tetrahydrofuran (17 mL). Diiodomethane (2.21 g, 8.24 mmol) was added dropwise by syringe, and the resulting green slurry was stirred at ambient temperature for 1 hr, producing a deep-blue solution (SmI_2). A solution of the trimethylsilyl ether of syn aldol 3a (1.80 g, 4.12 mmol) in tetrahydrofuran (16 mL) was added over a period of 5 min, and stirring was continued for 3 hr. The reaction was quenched with saturated ammonium chloride solution (20 mL) and the product extracted into diethylether (3x40 mL). The extract was washed with brine (20 mL) and dried over anhydrous sodium sulfate. Following filtration and concentration *in vacuo*, the crude product was flash chromatographed on silica gel (hexane/EtOAc, 95:5) giving 1.23 g (96%) of cyclized material. IR (film) 3504, 1680, 1461, 1369, 1250, 1100 cm^{-1}. ^{1}H-NMR δ 4.23 (s, 1H, -OH), 3.80 (s, 1H), 2.6 (m, 1H), 2.1-2.0 (m, 1H), 1.94 (s, 3H), 1.9-1.7 (m, 2H), 1.64 (s, 3H), 1.6 (m, 1H), 1.5 (m, 2H), 1.3 (m, 1H), 1.10 (s, 3H), 1.06 (s, 3H), 0.98 (d, 3H, J = 6.6 Hz), 0.10 (s, 9H). ^{13}C-NMR δ 132.0, 127.4, 84.9, 84.8, 66.4, 53.6, 41.1, 33.1, 32.1, 31.8, 27.3, 27.2, 22.9, 22.4, 20.6, 0.1.

A flame-dried 50 mL flask under argon was charged with the above cyclization product (200 mg, 0.64 mmol) and absolute methanol (20 mL), and was cooled to -78°C in a dry-ice acetone bath. Ozone was bubbled gently with the solution until a slightly blue color persisted (0.5 hr), and argon was passed into the solution to remove excess ozone. Dimethylsulfide (0.5 mL) was added, and the solution was stirred at -78°C for 20 min then warmed gradually to ambient temperature (~ 1 hr). The volume of the solution was reduced *in vacuo* and the residue was taken up in methylene chloride (60 mL). After washing with water (3 x 15 mL), the solution was dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The residue was chromatographed on silica gel (hexane/EtOAc 95:5) giving 164 mg (90%) of the ketone. IR (film) 3483, 1706, 1465, 1366, 1250, 1120 cm^{-1}. ^{1}H-NMR δ 3.81 (s, 1H, -OH), 3.73 (d, 1H, J = 5.2 Hz), 2.5-2.4 (m, 2H), 2.15-2.0 (m, 2H), 1.79 (d, 1H, J = 13.9 Hz), 1.75 (m, 1H), 1.6 (m, 1H), 1.55 (d, 1H, J = 13.9 Hz), 1.10 (s, 3H), 1.06 (s, 3H), 1.01 (d, 3H, J = 6.6 Hz), 0.99 (s, 9H). ^{13}C-NMR δ 213.4, 85.8, 82.7, 65.0, 51.0, 42.4, 34.0, 31.1, 30.2, 29.5, 24.0, 19.9, 0.1.

To a 0°C solution of the above ketone (400 mg, 1.41 mmol) in dry tetrahydrofuran (8 mL) was added a

1.0 M THF-solution of tetrabutylammonium fluoride (1.71 mL, 1.71 mmol) with stirring. After 2 hr at 0°C, the reaction was concentrated *in vacuo*, and the residue was flash-chromatographed on silica gel (hexane/EtOAc 7:3), giving 262 mg (88%) of keto-diol **10**. This material was recrystallized from hexane/EtOAc 14:5, giving colorless needles, mp 150-154°C, suitable for X-ray crystallographic analysis. IR ($CHCl_3$) 3500, 1705, 1222, 1208, 1042 cm^{-1}. ^{1}H-NMR δ 3.97 (s, 1H, -OH), 3.78 (d, 1H, J = 11.7 Hz), 2.78 (d, 1H, J = 11.7 Hz, -OH), 2.6-2.4 (m, 2H), 2.04 (d, 1H, J = 13.9 Hz), 2.0-1.9 (m, 1H), 1.7 (m, 1H), 1.6-1.4 (m, 2H), 1.20 (s, 3H), 1.2 (m, 1H), 1.19 (s, 3H), 1.08 (d, 3H, J = 6.6 Hz). ^{13}C-NMR δ 212.9, 86.4, 85.2, 68.4, 52.5, 42.9, 36.2, 34.5, 32.5, 32.2, 26.0, 19.2.

Acknowledgement. We are grateful to the following agencies for generous support of this work: National Science Foundation (EPSCoR RII-8610680); Atlantic Richfield Foundation Grant of Research Corporation; American Cancer Society (IN-160A); and the University of Wyoming College of Arts and Sciences (BRG-767). We thank Professor Oren P. Anderson (Colorado State University) for performing the X-ray structural determination of **10**, and Professor James Panek (Boston University) for helpful discussion.

References and Notes

1. Heathcock, C. H. in *"Asymmetric Synthesis"*; Morrison, J. D., Ed.; Academic Press: Orlando, 1984; Vol. 3, Chapter 2.
2. Mukaiyama, T.; Banno, K.; Narasaka, K. *J. Am. Chem. Soc.* (1974), **96**, 7503.
3. For a recent report of *syn* selectivity in titanium and zirconium dienolate aldol reactions, see: Panek, J. S.; Bula, O. A. *Tetrahedron Lett.* (1988), **29**, 1661.
4. Brown, D. W.; Campbell, M. M.; Taylor, A. P.; Zhang, X. *Tetrahedron Lett.* (1987), **28**, 985. In this report, *anti* selectivity predominated in all cases studied.
5. Koreeda, M.; Mislankar, S. G. *J. Am. Chem. Soc.* (1983), **105**, 7203.
6. Torii, S.; Inokuchi, T.; Ogawa, H. *Bull. Chem. Soc. Jpn.* (1979), **52**, 1233. We note here that pulegone and the aldehyde were the predominant compounds present in the ^{1}H-NMR of the crude reaction mixture, presumably the result of retroaldolization.
7. All compounds exhibited spectral characteristics consistent with their assigned structures. Isomeric ratios were determined by ^{1}H-NMR integration and in some cases, HPLC analysis. We note here the somewhat labile nature of the aldol products which could be chromatographed (SiO_2), but which underwent retroaldolization upon prolonged standing. It was thus expedient to prepare the corresponding acetates of trimethylsilyl ethers. Examples 2 and 3 of Table 1 displayed traces of a third minor component (<5%), the structures of which have yet to be determined.
8. Details of this structure are given as supplementary materials.
9. Molander, G. A.; Etter, J. B. *Tetrahedron Lett.* (1984), **25**, 3281.
10. For complete details of this structure see: Corbin, K. M.; Lynn, M. H.; Barner, B. A.; Hodgson, D. J. *Acta Crystallographica, Section C*, (1989), in press.
11. Zimmerman, H. E.; Traxler, M. D. *J. Am. Chem. Soc.* (1957), **79**, 1920.
12. Evans, D. A.; Nelson, J. V.; Taber, T. R. *Top Stereochem.* (1982), **13**, 1.
13. Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* (1978), **43**, 2923.
14. Molander, G. A.; Hahn, G. *J. Org. Chem.* (1986), **51**, 1135. We used CH_2I_2 in place of ICH_2CH_2I.