

Asymmetric Aldol Additions Catalyzed by Chiral Phosphoramides: Electronic Effects of the Aldehyde Component[†]

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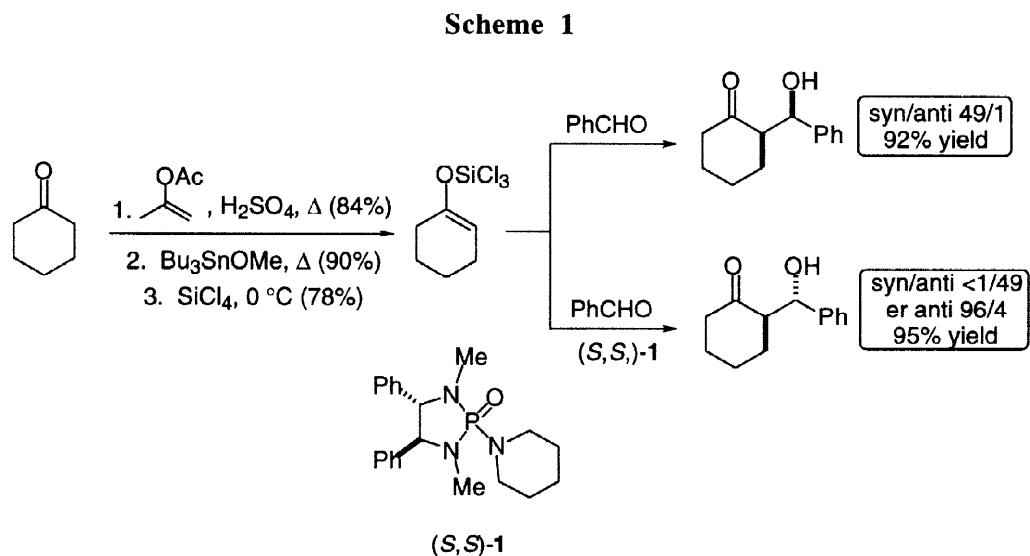
Abstract: The trichlorosilyl enolates of cyclopentanone and cycloheptanone were prepared by a mercury(II)-catalyzed metathesis from their TMS enol ethers in good yield. These enolates undergo spontaneous addition to aldehydes to provide the aldol adducts *syn*-**4**, **5a-e** in high yield and selectivity (dr 19/1 to >49/1). More electron rich aldehydes tend to be more diastereoselective. The reaction of these enolates with aldehydes is also catalyzed by the chiral phosphoramidate (*S,S*)-**1** to provide *anti*-**4**, **5a-e** in good to excellent diastereo- (dr 15/1 to 35/1) and enantioselectivity (er 84.4/15.6 to 95.9/4.1). In these cases, a trend is apparent only with sterically similar benzaldehyde derivatives. In addition, optimization studies suggest that two mechanistically distinct pathways may be operating in the catalyzed reaction. © 1998 Elsevier Science Ltd. All rights reserved.

Introduction

Catalytic, asymmetric aldol additions have come to the forefront of synthetic methodology due to both the synthetic utility of the products and the challenge of designing such a transformation.¹ There are now a number of reports concerning the addition of silyl enol ethers or silyl ketene acetals to aldehydes using chiral Lewis acids that proceed with good-to-high enantioselectivity.² These additions, however, typically suffer from lack of control of the sense of diastereoselectivity, i.e. both geometries of starting enol silane lead to the *syn* diastereomer.³ We recently disclosed a novel approach that involves the *Lewis base*-catalyzed aldol addition of chlorosilyl enolates to aldehydes.⁴ Examples with cyclohexanone- and propiophenone-derived trichlorosilyl enolates demonstrated high diastereoselectivity in additions to aldehydes in the presence of catalytic quantities of the stilbenediamine-derived phosphoramidate (*S,S*)-**1**.^{4b} Notably, the diastereoselectivity was dependent on olefin geometry, the *E*-enolate provided the *anti*-aldol product and the *Z*-enolate provided the *syn*-aldol product.⁵ This stereochemical outcome is consistent with a closed chair-like transition structure for the catalyzed reactions. Also, the trichlorosilyl enolates were highly reactive toward aldehydes without external activation; the cyclohexanone-derived enolate provided aldol adducts with high *syn*-diastereoselectivity, indicative of a closed, boat-like transition structure (Scheme 1).

Studies on silicon-substituted chlorosilyl enolates of methyl acetate revealed a distinct electronic component in the catalyzed reaction: at least three electronegative substituents on silicon were required for catalysis by HMPA.^{4c} This obtains because only these silanes are sufficiently electron deficient to accept two additional basic ligands (phosphoramidate and aldehyde). Although the selectivities overall were modest, the electronic and steric differences in the environment around the silicon center clearly manifested themselves in the overall rate and enantioselectivity of the process. To continue a systematic investigation of this fascinating aldolization reaction we began examining electronic effects of other components in the reaction, namely the acceptor aldehyde. Herein we

report out results involving trichlorosilyl enolates derived from cyclic ketones and electronically modified benzaldehydes catalyzed by (*S,S*)-1 to provide the corresponding aldol adducts.



Results and Discussion

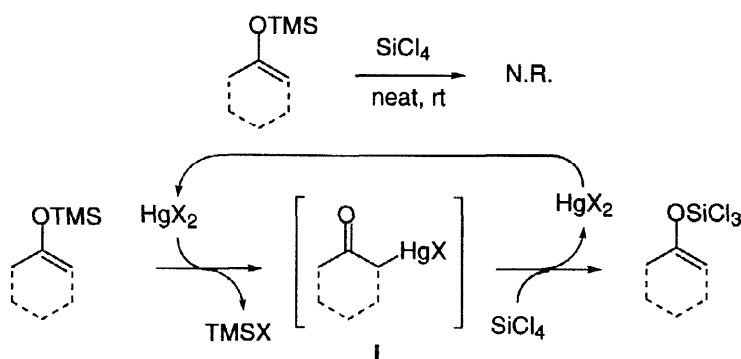
Enolate Synthesis.

Trichlorosilyl enolates have been prepared in the literature by two distinct methods. In 1968 Benkeser reported the synthesis of the trichlorosilyl enolate of acetone utilizing chloroacetone, tributylamine and trichlorosilane.⁶ We have found this to be the method of choice for preparing this enolate, though the transformation is limited due to lack of general availability of chloro ketones and other experimental difficulties. The other route involves SiCl_4 -mediated metathesis of a stannyl enolate (either *C*- or *O*-bound) to provide the trichlorosilyl enolates and tributyltin chloride as a byproduct.⁷ Although this procedure works well for a number of ketones (e.g. Scheme 1), the use of stoichiometric amounts of tin reagents is disadvantageous for both health and purification reasons. Additionally, while investigating methyl ketone substrates we encountered difficulty in preparing regiochemically pure stannyl-ketones on route to trichlorosilyl enolates.^{4d}

In light of these problems we sought a new, more general method for the preparation of trichlorosilyl enolates, preferably from trimethylsilyl enol derivatives. Initial experimentation demonstrated that under strictly anhydrous conditions, TMS enol ethers and even TMS ketene acetals were inert in the presence of SiCl_4 over days at room temperature.⁸ Consequently we explored the possibility to catalyze the exchange of silyl groups via an α -metalloketone (analogous to the stannylketones above) which could then undergo reaction with SiCl_4 to regenerate the activating metal in an overall catalytic process. Initial experiments using SnCl_4 and the TMS enol ether derived from pinacolone were encouraging, however extension to other enol systems proved problematic. Given House's early work on the formation of α -mercurioketones from TMS enol ethers and mercury(II) salts,⁹ we next attempted to catalyze the process with $\text{Hg}(\text{OAc})_2$. Gratifyingly, combination of a TMS enol ether, SiCl_4 , and catalytic quantities (1 mol %) of $\text{Hg}(\text{OAc})_2$ resulted in fast, efficient conversion to the desired trichlorosilyl enolates.^{4d} As

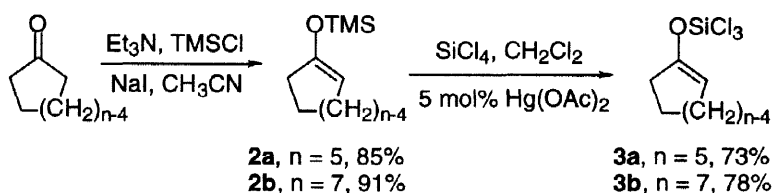
outlined in Scheme 2, we believe that the TMS enol ether undergoes C-mercuration concomitant with loss of TMSX to provide, transiently, the α -mercurio ketone **i**. The ketone then coordinates SiCl_4 to produce the trichlorosilyl enolate with the assisted loss of HgX_2 , which can then re-enter the catalytic cycle.

Scheme 2



At the outset of the current work, we attempted the same metathesis reactions on cyclic TMS enol ethers with 1 mol % $\text{Hg}(\text{OAc})_2$ only to find that metathesis was much slower than in the methyl ketone-derived systems. Increasing the mercury loading to 5 mol % did lead to complete conversion to the trichlorosilyl enolates in 22 h. Removal of the excess SiCl_4 and the TMSCl byproduct, followed by distillation, provided the trichlorosilyl enolates **3a** and **3b** in good yield and purity (Scheme 3). Both enolates were stable and could be stored for weeks at $-20\text{ }^\circ\text{C}$ under an inert atmosphere without decomposition (based on spectroscopic analysis and subsequent reactivity).

Scheme 3



Uncatalyzed Aldol Additions.

With our knowledge from previous studies that trichlorosilyl enolates derived from ketones are reactive toward aldehydes without additional activation,^{4b} uncatalyzed reactions of the enolates **3** were investigated. The cyclopentanone-derived enolate **3a** reacted with benzaldehyde smoothly in CH_2Cl_2 (0.5 M) at $0\text{ }^\circ\text{C}$ to provide the adducts (\pm)-**4** in excellent yield (Scheme 4). ^1H NMR analysis of the crude reaction mixture indicated a 22/1 syn/anti ratio.¹⁰ The high syn selectivity was presaged by our observation that Lewis acidic silyl enolates tend to react through boat-like transition structures in the absence of promoters.¹¹ We chose to study the electronic effect on diastereoselectivity of the various substituents in the benzaldehyde derivatives depicted in Figure 1. The results with the cycloheptanone-derived trichlorosilyl enolate **3b** are summarized in Table 1.

Scheme 4

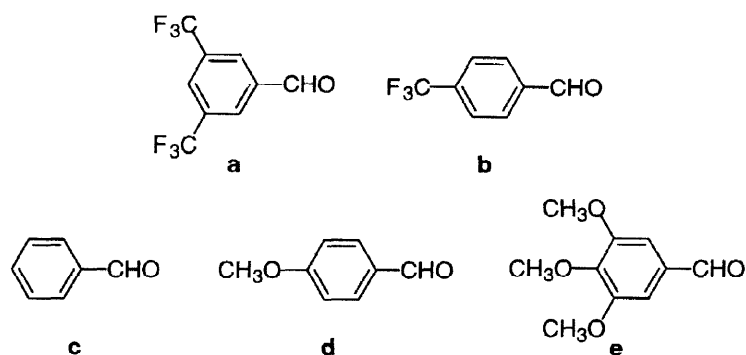
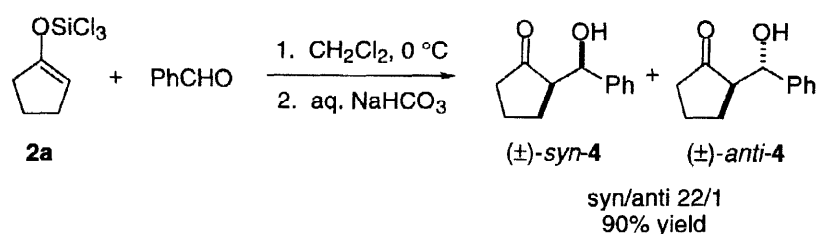
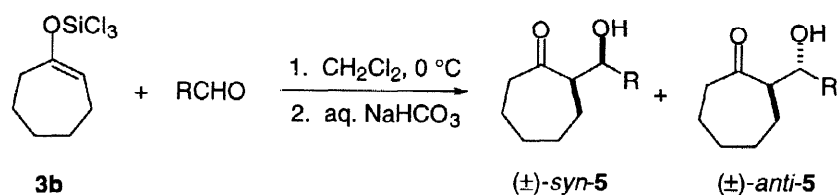


Figure 1. Benzaldehyde derivatives used in this study.

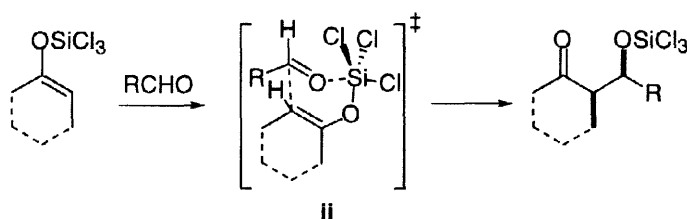
The trichlorosilyl enolate **3b** reacted cleanly and efficiently with aldehydes **a–e** in CH₂Cl₂ (0.5 M) at 0 °C to provide the aldol adducts (\pm) -**5a–e** in good to excellent yield, and high diastereoselectivity (19/1 to >49/1, as determined by ¹H NMR analysis of the crude reaction mixture), again favoring the *syn*-diastereomer.¹⁰ A modest trend is apparent, in that highly electron deficient aldehydes, e.g. **a**, are less diastereoselective than benzaldehyde (**c**) and 4-(trifluoromethyl)benzaldehyde (**b**) (Table 1, entries 1–3), while the electron rich aldehydes **d** and **e** (Table 1, entries 4,5) provided very high (>49/1) levels of diastereoselection.

We suspect that these reactions are taking place by initial aldehyde coordination to the trichlorosilyl enolate, activating *both* partners toward addition. Aldolization takes place via this pentacoordinate intermediate in a six-membered boat-like transition structure (**ii**, Scheme 5). We have previously proposed the activation of silyl enolates by aldehydes in studies concerning silacyclobutyl-derived ketene acetals^{11a} as has Myers in the reaction of a silyl-*N,O*-ketene acetal.¹² In addition, the silyl-directed aldol addition has been studied computationally by Gung and co-workers at high levels of theory (MP2/6-31G**//MP2/6-31G*).¹³ The transition structure located in this study did resemble a boat, with aldehyde and enolate occupying apical and basal positions, respectively, around a trigonal bipyramidal silicon atom (e.g. **ii**, Scheme 5). Gung's results suggest that the nucleophilicity of the enol double bond is more important than aldehyde activation for the trihydrosilyl enolate studied. This hydrosilane would be both more nucleophilic and less Lewis acidic than the trichlorosilyl enolates used in the present studies. Due to these differences we still suggest dual activation is taking place upon coordination of the aldehyde to the trichlorosilyl enolate.

Table 1. Uncatalyzed aldol additions of enolate **3b**.^a

entry	aldehyde	time, h	products	syn/anti ^b	yield, ^c %
1	a	11	5a	19/1	90
2	b	9	5b	28/1	92
3	c	10	5c	26/1	96
4	d	8	5d	>49/1	96
5	e	11	5e	>49/1	91

^a All reactions performed at 0 °C, 0.5 M in aldehyde. ^b Determined by ¹H NMR analysis. ^c Analytically pure material.

Scheme 5

The reason for the seemingly intrinsic preference for boat-like structures over chair-like structures with pentacoordinate siliconates predicted computationally by Gung (and by ourselves at semi-empirical levels^{11a}) and demonstrated for a number of enolate classes remains unclear. In his studies of zirconium enolates, Evans postulated that distortions in the six-membered transition structure relative to "typical" enolates could lead to a preference for boat-like structures.¹⁴ In addition, calculations have suggested that boron-based enolates may react through boat or twist-boat transition structures in aldol reactions.¹⁵ The energy difference between chair- and boat-like transition structures is probably small, and even subtle changes in bonding could perturb the observed selectivity. Changes in the O-M-O bond angle, the O-M bond lengths, and even the conformation (and resulting steric contribution) of "spectator" ligands bound to the metal center have all been used to rationalize the switch in preference from chair to boat in different systems.¹⁶ Clearly the factors involved in controlling the transition structure of these reactions are unclear at the present time.

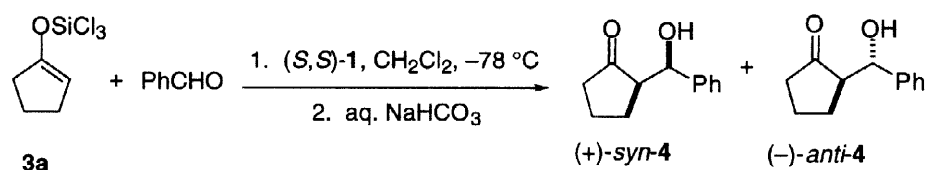
One possible explanation for the modest trend in diastereoselectivity involves the differential coordinating abilities of the aldehydes **a-e**. More electron rich aldehydes (stronger Lewis bases) presumably bind to silicon more tightly. This would lead to shorter Si-O bond lengths, perhaps accentuating any steric biases present in the competing transition structures. Experimental evidence for variable bond lengths in the complexation of

electronically distinct aldehydes is scarce, though seems intuitively reasonable. Indeed such differences need not be large when one considers the difference in $\Delta\Delta G^\ddagger$ for the production of (\pm)-**5a** and (\pm)-**5e** is roughly 0.5 kcal mol⁻¹.

Catalyzed Aldol Additions.

On the basis of our earlier results with the trichlorosilyl enolate derived from cyclohexanone and the chiral phosphoramidate (*S,S*)-**1**^{4b} we expected both dramatic rate acceleration and high anti selectivity coupled with high enantioselectivity in the anti manifold from the corresponding cyclopentenyl and cycloheptenyl-derived enolates. Initial results with enolate **3a** were somewhat disappointing. Although there was tremendous rate acceleration (reaction time of <1 hour at -78 °C/0.1 M compared to several hours at 0 °C/0.5 M uncatalyzed), analysis of the crude reaction mixture by ¹H NMR spectroscopy indicated a syn/anti ratio of only 1/6 (Table 1). Additionally, the enantioselectivity of the reaction was markedly lower than initially hoped (er anti, 85.1/4.9). Through optimization studies we discovered that *rate of addition of aldehyde to the cold solution of enolate and catalyst was critical*. In initial experiments, aldehyde was added neat over roughly 1 minute to a cold (-78 °C) solution of enolate and catalyst (Table 2, entry 1). It was found however, that if the aldehyde was added slowly (over 45-55 minutes, in half the total reaction volume) the diastereoselectivity not only improved dramatically (Table 2, entry 2) but became more reproducible as well. Interestingly, the enantioselectivity of the process changed little with this modification, remaining modest. In both cases the aldol adducts were obtained in near quantitative yield.

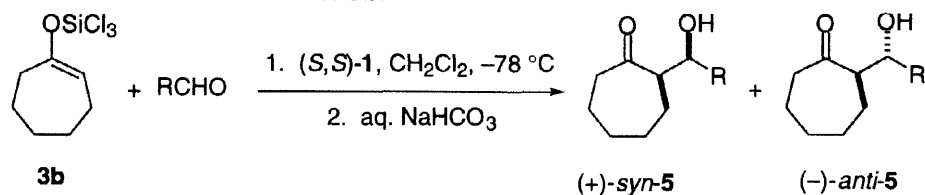
Table 2. Catalyzed aldol additions of enolate **3a** with benzaldehyde.^a



entry	addition time, min	syn/anti ^b	er syn ^{c,d}	er anti ^{c,e}	yield, ^f %
1	1	1/6	65.7/34.3	85.1/14.9	99
2	50	1/22	71.4/28.6	87.7/12.3	98

^a All reactions performed at -78 °C with 10 mol % (*S,S*)-**1**. ^b Determined by ¹H NMR analysis. ^c Determined by CSP SFC analysis. ^d Absolute configuration not established. ^e Absolute configuration assigned by analogy to (-)-*anti*-**5**. ^f Analytically pure material.

The catalyzed additions of **3b** to aldehyde benzaldehyde (**c**) also showed a significant dependence on the rate of aldehyde addition. Slow, dropwise addition again provided the highest diastereoselectivities. In these experiments, the enantiomeric composition of the anti-diastereomer remained constant. In fact, regardless of the conditions used and the *diastereoselectivity* of the reaction, the *enantiomeric* ratio of the anti-product did not change, though the enantiomeric ratio in the syn-manifold was somewhat variable. The results for enolate **3b** and aldehydes **a-e** utilizing the optimized procedure are summarized in Table 3.

Table 3. Catalyzed aldol additions of enolate **3b**.^a

entry	aldehyde	products	syn/anti ^b	er syn ^{c,d}	er anti ^{c,e}	yield, ^f %
1	a	5a	1/17	70.3/29.7	90.8/9.2	91
2	b	5b	1/15	60.5/39.5	84.4/15.6	96
3	c	5c	1/29	68.2/31.8	92.0/8.0	97
4	d	5d	1/35	61.2/38.8	95.9/4.1	97
5	e	5e	1/20	70.6/29.4	93.7/6.3	94

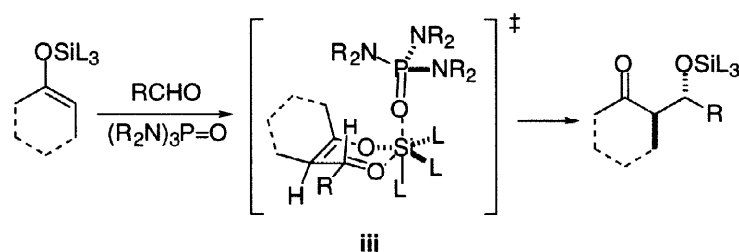
^a All reactions performed at $-78\text{ }^\circ\text{C}$ with 10 mol % *(S,S)*-**1**. ^b Determined by ^1H NMR analysis. ^c Determined by CSP SFC analysis. ^d Absolute configuration not established. ^e Absolute configuration (*2R,1'S*). ^f Analytically pure material.

All adducts were obtained in very good chemical yield, and with high diastereoselectivity favoring the anti-isomer, presumably arising from a chair-like transition structure. Noteworthy is the trend of diastereoselectivities with respect to the uncatalyzed reactions. Where steric interaction are almost certainly minimal (no 2- or 3-substituents on the aromatic ring, Table 3, entries 2-4), there is a clear trend, as before, with the more electron-rich aldehyde being the most selective. This breaks down at both ends of the spectrum (Table 3, entries 1 and 5), wherein the presence of 3-substituents on the aromatic ring may well offer a steric contribution. This is especially reasonable when one considers the crowding, even far removed from the reactive center, that would result from phosphoramidate and aldehyde simultaneously bound to silicon in a hexacoordinate array. These steric interactions, coupled with the electronic differences in aldehydes **a** and **e** could lead to the deviations from the trend.

The enantioselectivities¹⁷ for the anti-diastereomer ranged from moderate to high, again with a clear trend among aldehydes **b-d** (Table 3, entries 2-4), and then inversion of the trend at the termini (Table 3, entries 1 and 5). The same rationale may be employed here as well, the more electron-rich aldehydes forming tighter closed transition structures, and amplifying the steric differences between the diastereomeric (in the presence of *chiral* phosphoramidate) chair-like transition structures. It is interesting to note that where a trend seems to exist (entries 2-4) the enantioselectivity is much more sensitive than the diastereoselectivity to the electronic nature of the aldehyde component. This suggests that tight aldehyde coordination is more critical in discerning between the competing chair-like transition structures than between chair- and boat-like transition structures. This is not surprising as subtle differences are more likely to manifest themselves more strongly in similar (chair vs. chair) rather than dissimilar (chair vs. boat) global arrangements of the transition structure. The enantioselectivities in the syn-manifold were uniformly poor. Clearly the chiral environment provided by the phosphoramidate in the chair-like transition structure leading to the anti-isomers does not translate well to the (presumably) boat-like nature of those transition structures that operate in the syn manifold.

We view the catalyzed reactions as taking place via a hexacoordinate siliconate complex, with both aldehyde and phosphoramidate in the ligand sphere of the silicon (**iii**, Scheme 6). The origin of catalysis is presently obscure, though it could involve the intrinsic higher reactivity of hypervalent silicon.¹⁸ The apparent preference for a chair-like transition structure with hexacoordinate silicon enolates is also unclear. Interestingly, when (*S,S*)-**1** is used as the catalyst the resulting configuration of the major product obtained from 6- and 7-membered cyclic (*E*) enolates is (*2R,1'S*), whereas the propiophenone-derived (*Z*) enolate provides the (*2S,1'S*) isomer. We postulate that while the general constellation of the transition structure (i.e. hexacoordinate siliconate) is responsible for the relative induction (*diastereoselectivity*), the chirality of the catalyst controls the topicity of attack on the aldehyde or enolate (*enantioselectivity*). Thus, the products obtained from *E*- and *Z*-enolates are of opposite configuration at C(2), derived from attack on the same face of geometrically isomeric enol double bonds. The configuration of the hydroxyl-bearing center in the aldol products is found to be *S* regardless of enolate type or configuration when (*S,S*)-**1** is used as promoter. This is a consequence relative facial topicity induced by the chair-like transition structure in the octahedrally coordinated siliconate coupled with enantiofacial preference of the catalyst. In the absence of additional experimental information (e.g. on the absolute configuration of the minor components) or computational studies, specific claims about these transition structures, particularly the preference for the observed absolute configuration of the products, is impossible.

Scheme 6



The origin of the dramatic effect addition rate has on diastereoselectivity also remains unclear. However, one possibility does arise from specific trends presented above. Since the enantiomeric ratio of the anti-diastereomer does not change with diastereomeric ratio, and as the syn-diastereomer is produced in much lower enantiomeric ratio in all cases we propose that *only the anti diastereomer arises from a hexacoordinate siliconate species*. The syn product then being derived from a mechanistically distinct pathway, which is somehow disfavored by slow addition of aldehyde and inherently proceeds with poor enantioselection. The precise nature of such a second pathway is unknown at the present time. We expect that studies designed to understand this effect and the overall composition and arrangement of the transition structure will ultimately lead to better understanding and improved catalyst designs.

Summary

We have demonstrated that the mercury-catalyzed metathesis from TMS enol ethers to trichlorosilyl enolates serves admirably for cyclic ketone substrates. In turn, these enolates react spontaneously with aldehydes to provide

aldol adducts in excellent yield with high syn diastereoselectivity, presumably via a boat-like transition structure organized around a trigonal bipyramidal, pentacoordinate siliconate. Additionally, more electron-rich aldehydes provide higher diastereoselectivity in these uncatalyzed aldol additions. Aldol additions of trichlorosilyl enolates are also catalyzed by the chiral phosphoramidate (*S,S*)-**1** to provide aldol adducts in excellent yield, now with high anti-diastereoselectivity and moderate-to-high enantioselectivity in the anti manifold, derived from a chair-like transition structure organized around an octahedral, hexacoordinate siliconate. A trend similar to that found in the uncatalyzed pathway seems to hold true for sterically similar aldehydes (**b-d**), that is, more electron rich aldehydes lead to higher diastereo- and enantioselectivities. However, both of these trends fail when 3-substituted aldehydes are employed, perhaps due to combined electronic and steric effects. We have discovered that slow addition of aldehyde is crucial for high diastereoselectivity in the catalyzed reaction. This may be due to a second, poorly enantioselective, highly syn-selective pathway being operative in the catalyzed reaction. Studies to investigate this phenomenon, in addition to extension to other enolate types and catalyst design are currently underway and will be reported in due course.

Experimental

General Information. ^1H NMR spectra and ^{13}C NMR spectra were recorded on Varian Unity 500 or Varian Inova 500 (500 MHz, ^1H ; 126 MHz, ^{13}C) spectrometers. Spectra are referenced to residual chloroform (δ 7.26 ppm, ^1H ; δ 77.0 ppm, ^{13}C) or tetramethylsilane (δ 0 ppm, ^1H ; ^{13}C) in CDCl_3 unless otherwise stated. ^{19}F NMR spectra were obtained on a Varian Unity 400 (376 MHz) and referenced to hexafluorobenzene (δ -162.0 ppm). Chemical shifts are reported in ppm (δ); multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), pent (pentet), m (multiplet) and br (broad). Coupling constants, *J*, are reported in Hertz. Mass spectrometry was performed by the University of Illinois Mass Spectrometry Center. Electron impact (EI) spectra were performed on a VG 70-VSE spectrometer. Data are reported in the form of *m/z* (intensity relative to base peak = 100). Infrared spectra (IR) were recorded on a Mattson Galaxy 5020 spectrophotometer. Peaks are reported in cm^{-1} with indicated relative intensities: s (strong, 67-100%); m (medium, 34-66%); w (weak, 0-33%). Optical rotations were obtained on a Jasco DIP-360 digital polarimeter and are reported as follows: $[\alpha]_D^T$ temperature (T), concentration (*c* = g/100 mL) and solvent. Elemental analyses were performed by the University of Illinois Microanalytical Service Laboratory.

All reactions were performed in oven and/or flame dried glassware under an atmosphere of dry argon. Dichloromethane (CH_2Cl_2) was distilled from P_2O_5 , SiCl_4 was heated to reflux for 2-4 h then distilled immediately before use. Commercial reagents were purified by distillation or recrystallization prior to use. Analytical thin-layer chromatography was performed on Merck silica gel plates with QF-254 indicator. Analytical supercritical fluid chromatography (SFC) was performed on a Berger Instruments packed-column SFC with built-in photometric detector (λ = 220 nm) using Daicel Chiralpak AD, Chiralpak AS and Regis (*R,R*)-Whelk-O1 columns. Preparative HPLC was performed with a Ranin Dynamax pumping system on a Regis 10 μm SiO_2 2.11 \times 25 cm column. Melting points (mp) were determined in vacuum-sealed capillaries on a Thomas-Hoover apparatus and are corrected.

Starting Materials. [(Cyclopentenyl)oxy]trimethylsilane (**2a**) and [(cycloheptenyl)oxy]trimethylsilane (**2b**) were prepared by the method of Kochi,¹⁹ (*S,S*)-**1** was prepared as previously reported.^{4a}

Trichloro[(cyclopentenyl)oxy]silane (3a). Silicon tetrachloride (9.30 mL, 81.2 mmol, 2.0 equiv) was added quickly to a suspension of $\text{Hg}(\text{OAc})_2$ (600.0 mg, 2.0 mmol, 0.05 equiv) in CH_2Cl_2 (40 mL). During the addition the mercury salt dissolved. [(Cyclopentenyl)oxy]trimethylsilane (**2a**) (6.35 g, 40.6 mmol) was then added to the solution dropwise over 10 min and the solution was stirred at rt for an additional 10 h. During this

time the reaction mixture became somewhat cloudy. Removal of an aliquot and ^1H NMR analysis indicated that the reaction was complete. The mixture was concentrated at reduced pressure (150 mmHg) and the resulting oil was distilled twice through a 7.5 cm Vigreux column to give 6.43 g (73%) of the trichlorosilyl enolate **3a** as a clear, colorless oil: bp 45–46 °C (7 mmHg); ^1H NMR (500 MHz) 5.10 (pent, $J = 2.0$, 1 H), 2.44–2.40 (m, 2 H), 2.36–2.31 (m, 2 H), 1.98–1.90 (m, 2 H); ^{13}C NMR (126 MHz) 150.75, 108.38, 32.14, 28.30, 20.99; MS (EI, 70 eV) 222 (3), 220 (5), 218 (11), 216 (18), 55 (100); IR (neat) 1657 (s). Anal. Calcd for $\text{C}_5\text{H}_7\text{Cl}_3\text{OSi}$ (217.55): C, 27.60; H, 3.24; Cl, 48.89. Found: C, 27.61; H, 3.35; Cl, 48.60.

Trichloro[(cycloheptenyl)oxy]silane (3b). Silicon tetrachloride (19.20 mL, 168.0 mmol, 2.0 equiv) was added quickly to a suspension of $\text{Hg}(\text{OAc})_2$ (1.30 g, 4.2 mmol, 0.05 equiv) in CH_2Cl_2 (85 mL). During the addition the mercury salt dissolved. [(Cycloheptenyl)oxy]trimethylsilane (**2b**) (15.50 g, 84.1 mmol) was then added to the solution dropwise over 10 min and the solution was stirred at rt for an additional 11 h. During this time the reaction mixture became somewhat cloudy. Removal of an aliquot and ^1H NMR analysis indicated that the reaction was complete. The mixture was concentrated at reduced pressure (150 mmHg) and the resulting oil was distilled twice through a 7.5 cm Vigreux column to give 16.12 g (78%) of the trichlorosilyl enolate **3b** as a clear, colorless oil: bp 84–85 °C (10 mmHg); ^1H NMR (500 MHz) 5.44 (t, $J = 6.5$, 1 H), 2.38–2.35 (m, 2 H), 2.05 (br q, $J = 4.9$), 1.73–1.55 (m, 6 H); ^{13}C NMR (126 MHz) 152.80, 113.78, 34.16, 30.68, 27.06, 24.93, 24.75; MS (EI, 70 eV) 247 (2), 245 (2), 55 (100); IR (neat) 1673 (s). Anal. Calcd for $\text{C}_7\text{H}_{11}\text{Cl}_3\text{OSi}$ (245.61): C, 34.23; H, 4.51; Cl, 43.30. Found: C, 34.05; H, 4.67; Cl, 43.48.

(2*R,1'*R*')-2-(Hydroxy(phenyl)methyl)cyclopentanone ((±)-*syn*-4). General Procedure I: Uncatalyzed Aldol Additions of Trichlorosilyl Enolates.** Benzaldehyde (**c**) (203 μL , 2.0 mmol) was added dropwise over 2 min to a solution of enolate **3a** (478 mg, 2.2 mmol, 1.1 equiv) in CH_2Cl_2 (4.0 mL) at 0 °C. The mixture was stirred at 0 °C for 10 h then was poured into cold (0 °C) sat. aq. NaHCO_3 solution and was stirred for 15 min. The two-phase mixture was filtered through Celite, then the phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 \times 50 mL). The organic phases were combined, dried over Na_2SO_4 , filtered and concentrated. ^1H NMR analysis (500 MHz) of the crude material indicated a *syn*/*anti* ratio of 19/1. The crude material was purified by column chromatography (SiO_2 , hexane/EtOAc, 4/1) to give an oil which was crystallized from EtOAc/hexane to afford 343.0 mg (90%) of (±)-*syn*-4 as white needles. Data for (±)-*syn*-4: mp 59–60 °C (EtOAc/hexane); ^1H NMR (500 MHz) 7.36–7.31 (m, 4 H), 7.29–7.25 (m, 1 H), 5.31 (br s, 1 H), 2.49–2.44 (m, 1 H), 2.39–2.33 (m, 1 H), 2.18–2.10 (m, 1 H), 2.06–1.94 (m, 2 H), 1.86–1.80 (m, 1 H), 1.74–1.64 (m, 1 H); ^{13}C NMR (126 MHz) 220.50, 142.72, 128.36, 127.32, 125.55, 71.51, 56.09, 39.16, 22.72, 20.43; MS (EI, 70 eV) 190 (7), 84 (100); IR (CHCl_3) 1731 (s); TLC R_f 0.35 (hexane/EtOAc, 3/1). Anal. Calcd for $\text{C}_{12}\text{H}_{14}\text{O}_2$ (190.24): C, 75.76; H, 7.42. Found: C, 75.82; H, 7.50.

(2*R,1'*R*')-2-[Hydroxy-(3,5-bis(trifluoromethyl)phenyl)methyl]cycloheptanone ((±)-*syn*-5a).** Following General Procedure I, enolate **3b** (420 μL , 2.2 mmol, 1.1 equiv), and 3,5-bis(trifluoromethyl)benzaldehyde (**a**) (330 μL , 2.0 mmol) were stirred in CH_2Cl_2 (4 mL) for 11 h at 0 °C. Workup provided the crude aldolates in a 19/1 *syn*/*anti* ratio. The crude product was purified by column chromatography (SiO_2 , hexane/EtOAc, 7/1) to give 21.0 mg of (±)-*anti*-5a as a clear oil and 618.0 mg (90% total) of (±)-*syn*-5a as a thick oil which slowly solidified on standing. Data for (±)-*syn*-5a: ^1H NMR (500 MHz) 7.82 (br s, 2 H), 7.79 (br s, 1 H), 5.32 (br s, 1 H), 3.66 (d, $J = 3.9$, 1 H), 2.87 (dt, $J_d = 10.5$, $J_t = 3.7$, 1 H), 2.70–2.63 (m, 1 H), 2.50 (ddd, $J = 15.6$, 11.7, 3.9, 1 H), 1.93–1.80 (m, 3 H), 1.74–1.64 (m, 1 H), 1.60–1.54 (m, 1 H), 1.51–1.43 (m, 1 H), 1.33–1.23 (m, 2 H); ^{13}C NMR (126 MHz) 217.49, 144.69, 131.55 (q, $J = 33.1$), 126.17, 123.33 (q, $J = 272.4$), 121.18 (sept, $J = 3.7$), 71.96, 56.87, 43.81, 29.05, 28.89, 23.66, 23.42; ^{19}F NMR (376 MHz) –63.00; MS (EI, 70 eV) 354 (8), 112 (100); IR (CHCl_3) 1688 (s); TLC R_f 0.66 (hexane/EtOAc, 3/1). Anal. Calcd for $\text{C}_{16}\text{H}_{16}\text{F}_6\text{O}_2$ (354.34): C, 54.25; H, 4.55; F, 32.16. Found: C, 54.13; H, 4.40; F, 32.09.

(2*R,1'*R*')-2-[Hydroxy-(4-(trifluoromethyl)phenyl)methyl]cycloheptanone ((±)-*syn*-5b).** Following General Procedure I, enolate **3b** (420 μL , 2.2 mmol, 1.1 equiv), and 4-(trifluoromethyl)benzaldehyde (**b**) (273 μL , 2.0 mmol) were stirred in CH_2Cl_2 (4 mL) for 9 h at 0 °C. Workup provided the crude aldolates in a 28/1 *syn*/*anti* ratio. The crude product was purified by column chromatography (SiO_2 , hexane/EtOAc, 4/1) to give 15.1 mg of (±)-*anti*-5b as a clear oil and 541.1 mg of (±)-*syn*-5b as an oil which was crystallized from

EtOAc/hexane to give 510.0 mg (92% total) of (\pm)-*syn*-**5b** as white needles. Data for (\pm)-*syn*-**5b**: mp 60–61 °C (EtOAc/hexane); ^1H NMR (500 MHz) 7.61 (d, $J = 8.1$, 2 H), 7.46 (d, $J = 8.0$, 2 H), 5.25 (br s, 1 H), 3.50 (d, $J = 2.2$, 1 H), 2.85 (dt, $J_{\text{d}} = 10.8$, $J_{\text{t}} = 2.7$, 1 H), 2.65–2.57 (m, 1 H), 2.47 (ddd, $J = 15.8$, 12.0, 3.7, 1 H), 1.91–1.79 (m, 3 H), 1.70–1.60 (m, 2 H), 1.50–1.41 (m, 1 H), 1.31–1.19 (m, 2 H); ^{13}C NMR (126 MHz) 217.87, 145.97, 129.34 (q, $J = 32.2$), 126.22, 125.16 (q, $J = 3.7$), 72.61, 57.26, 43.90, 29.11, 29.02, 23.90, 23.58; ^{19}F NMR (376 MHz) –62.68; MS (EI, 70 eV) 286 (6), 112 (100); IR (CHCl₃) 1686 (s); TLC R_f 0.34 (hexane/EtOAc, 3/1). Anal. Calcd for C₁₅H₁₇F₃O₂ (286.27): C, 62.93; H, 5.99; F, 19.91. Found: C, 63.14; H, 5.97; F, 19.72.

(2*R,1'*R**)-2-(Hydroxy(phenyl)methyl)cycloheptanone ((\pm)-*syn*-**5c**)**. Following General Procedure I, enolate **3b** (420 μL , 2.2 mmol, 1.1 equiv), and benzaldehyde (**c**) (203 μL , 2.0 mmol) were stirred in CH₂Cl₂ (4 mL) for 10 h at 0 °C. Workup provided the crude aldolates in a 26/1 *syn*/*anti* ratio. The crude product was purified by column chromatography (SiO₂, hexane/EtOAc, 6/1) to give 14.3 mg of (\pm)-*anti*-**5c** as a clear oil and 420.0 mg of (\pm)-*syn*-**5c** as an oil which was crystallized from EtOAc/hexane to give 405.0 mg (96% total) of (\pm)-*syn*-**5c** as a white solid. Data for (\pm)-*syn*-**5c**: mp 80–81 °C (EtOAc/hexane); ^1H NMR (500 MHz) 7.37–7.31 (m, 4 H), 7.27–7.24 (m, 1 H), 5.18 (d, $J = 2.7$, 1 H), 3.35 (br s, 1 H), 2.84 (dt, $J_{\text{d}} = 11.0$, $J_{\text{t}} = 3.0$, 1 H), 2.61–2.54 (m, 1 H), 2.45 (ddd, $J = 15.7$, 12.0, 3.7, 1 H), 1.91–1.80 (m, 3 H), 1.79–1.73 (m, 1 H), 1.65–1.56 (m, 1 H), 1.51–1.43 (m, 1 H), 1.31–1.19 (m, 2 H); ^{13}C NMR (126 MHz) 218.15, 141.93, 128.16, 127.08, 125.84, 73.32, 57.75, 43.95, 29.13, 29.07, 24.09, 23.78; MS (EI, 70 eV) 218 (8), 112 (100); IR (CHCl₃) 1686 (s); TLC R_f 0.56 (hexane/EtOAc, 3/1). Anal. Calcd for C₁₄H₁₈O₂ (218.30): C, 77.03; H, 8.31. Found: C, 77.13; H, 8.23.

(2*R,1'*R**)-2-[Hydroxy-(4-methoxyphenyl)methyl]cycloheptanone ((\pm)-*syn*-**5d**)**. Following General Procedure I, enolate **3b** (420 μL , 2.2 mmol, 1.1 equiv), and 4-methoxybenzaldehyde (**d**) (243 μL , 2.0 mmol) were stirred in CH₂Cl₂ (4 mL) for 8 h at 0 °C. Workup provided the crude aldolates in a >50/1 *syn*/*anti* ratio. The crude product was purified by column chromatography (SiO₂, hexane/EtOAc, 4/1) to give 7.1 mg of (\pm)-*anti*-**5d** as a clear oil and 481.6 mg of (\pm)-*syn*-**5d** as an oil which was crystallized from EtOAc/hexane to give 467.3 mg (96% total) of (\pm)-*syn*-**5d** as white crystals. Data for (\pm)-*syn*-**5d**: mp 69–70 °C (EtOAc/hexane); ^1H NMR (500 MHz) 7.24 (d, $J = 8.5$, 2 H), 6.88 (d, $J = 8.7$, 2 H), 5.11 (d, $J = 2.9$, 1 H), 3.81 (s, 3 H), 3.28 (br s, 1 H), 2.80 (dt, $J_{\text{d}} = 11.0$, $J_{\text{t}} = 3.2$, 1 H), 2.58–2.52 (m, 1 H), 2.43 (ddd, $J = 15.6$, 12.0, 3.9, 1 H), 1.90–1.76 (m, 4 H), 1.64–1.54 (m, 1 H), 1.50–1.40 (m, 1 H), 1.30–1.20 (m, 2 H); ^{13}C NMR (126 MHz) 218.23, 158.69, 134.06, 127.02, 113.59, 73.12, 57.87, 55.22, 44.00, 29.16, 29.07, 24.36, 23.80; MS (EI, 70 eV) 248 (7), 137 (100); IR (CHCl₃) 1686; TLC R_f 0.33 (hexane/EtOAc, 3/1). Anal. Calcd for C₁₅H₂₀O₃ (248.32): C, 72.55; H, 8.12. Found: C, 72.66; H, 8.20.

(2*R,1'*R**)-2-[Hydroxy-(3,4,5-trimethoxyphenyl)methyl]cycloheptanone ((\pm)-*syn*-**5e**)**. Following General Procedure I, enolate **3b** (420 μL , 2.2 mmol, 1.1 equiv), and 3,4,5-trimethoxybenzaldehyde (**e**) (392 mg, 2.0 mmol) were stirred in CH₂Cl₂ (4 mL) for 11 h at 0 °C. Workup provided the crude aldolates in a >50/1 *syn*/*anti* ratio. The crude product was purified by column chromatography (SiO₂, hexane/EtOAc, 2/1) to give 8.1 mg of (\pm)-*anti*-**5e** as a clear oil and 553.3 mg (91% total) of (\pm)-*syn*-**5e** as a thick oil which slowly solidified on standing. Data for (\pm)-*syn*-**5e**: ^1H NMR (500 MHz) 6.52 (s, 2 H), 5.08 (t, $J = 3.0$, 1 H), 3.84 (s, 6 H), 3.81 (s, 3 H), 3.79 (d, $J = 1.3$, 1 H), 2.75 (dt, $J_{\text{d}} = 11.0$, $J_{\text{t}} = 3.1$, 1 H), 2.58–2.52 (m, 1 H), 2.46 (ddd, $J = 15.4$, 11.9, 3.7, 1 H), 1.90–1.80 (m, 3 H), 1.79–1.72 (m, 1 H), 1.63–1.52 (m, 1 H), 1.50–1.42 (m, 1 H), 1.31–1.19 (m, 2 H); ^{13}C NMR (126 MHz) 218.12, 153.03, 137.75, 136.74, 102.72, 73.44, 60.74, 57.94, 56.04, 43.96, 29.17, 28.99, 24.08, 23.83; MS (EI, 70 eV) 308 (19), 196 (100); IR (CHCl₃) 1686 (m); TLC R_f 0.11 (hexane/EtOAc, 3/1). Anal. Calcd for C₁₇H₂₄O₅ (308.37) C, 66.21; H, 7.84. Found: C, 66.30; H, 7.92.

(+)-(2*R*,1'*S*)-2-(Hydroxy(phenyl)methyl)cyclopentanone ((+)-*anti*-4**)**. **General Procedure II: Aldol Additions of Trichlorosilyl Enolates Catalyzed by (*S,S*)-1**. Catalyst (*S,S*)-**1** (74 mg, 0.2 mmol, 0.1 equiv) was dried under vacuum (0.05 mmHg) for 12 h at rt, CH₂Cl₂ (10 mL) was added and the solution was cooled to –75 °C (internal). Trichlorosilyl enolate **3a** (478 mg, 2.2 mmol, 1.1 equiv) was added dropwise over 2 min. A solution of benzaldehyde (**c**) (203 μL , 2.0 mmol) in CH₂Cl₂ (10 mL) was then added to the first solution, dropwise, via cannula over 50 min. During the addition the temperature remained at –75 °C. The reaction mixture was stirred at –75 °C for 30 min, then it was quickly poured into cold (0 °C) sat. aq. NaHCO₃ solution and

the slurry was stirred for 15 min. The two-phase mixture was filtered through Celite, the phases separated, and the aqueous phase was extracted with CH_2Cl_2 (3×50 mL). The organic phases were combined, dried Na_2SO_4 , filtered and concentrated. The syn/anti ratio was determined by ^1H NMR (500 MHz) analysis to be 1/22. The crude material was purified by column chromatography (SiO_2 , hexane/EtOAc, 4/1) to give 372.4 mg (98%) of an analytically pure mixture of diastereomers as a clear, colorless oil. A pure sample of (+)-*anti*-4 was obtained by preparative HPLC (hexane/EtOAc, 19/1). Data for (+)-*anti*-4: ^1H NMR (500 MHz) 7.36–7.26 (m, 5 H), 4.71 (d, $J = 9.0$, 1 H), 4.54 (s, 1 H), 2.47–2.37 (m, 2 H), 2.29–2.20 (m, 1 H), 2.00–1.92 (m, 1 H), 1.78–1.67 (m, 2 H), 1.55–1.45 (m, 1 H); ^{13}C NMR (126 MHz) 223.11, 141.41, 128.42, 127.98, 126.54, 75.18, 55.29, 38.70, 26.95, 20.35; MS (EI, 70 eV) 190 (6), 84 (100); IR (neat) 1710 (s); TLC R_f 0.35 (hexane/EtOAc, 3/1); $[\alpha]_D^{21} +37.1^\circ$ ($c = 1.16$, CHCl_3); SFC t_R (2*R*,1'*S*)-4, 4.08 min (87.7%); t_R (2*S*,1'*R*)-4, 4.59 min (12.3%) (Chiralpak AS, 150 bar, 40 °C, 3% CH_3OH in CO_2 , 2.5 mL min^{-1}). Anal. Calcd for $\text{C}_{12}\text{H}_{14}\text{O}_2$ (190.24): C, 75.76; H, 7.42. Found: C, 75.87; H, 7.55. Data for *syn*-4: SFC t_R *syn*-4', 5.97 min (28.6%); t_R *syn*-4, 11.08 min (71.4%) (Chiralpak AS, 150 bar, 40 °C, 3% CH_3OH in CO_2 , 2.5 mL min^{-1}).

(+)-(2*R*,1'*S*)-2-[Hydroxy-(3,5-bis(trifluoromethyl)phenyl)methyl]cycloheptanone ((+)-*anti*-5a). Following General Procedure II, 3,5-bis(trifluoromethyl)benzaldehyde (**a**) (330 μL , 2.0 mmol) in CH_2Cl_2 (10 mL) was added over 50 min to a cold (-75 °C) solution of (*S,S*)-**1** (74 mg, 0.2 mmol, 0.1 equiv) and enolate **3b** (420 μL , 2.2 mmol, 1.1 equiv) in CH_2Cl_2 (10 mL). Workup provided the crude aldolates in a 1/17 syn/anti ratio. The crude product was purified by column chromatography (SiO_2 , hexane/EtOAc, 7/1) to give 33.2 mg of (–)-*syn* **5a** as a clear oil and 614.4 mg (91% total) of (+)-*anti*-**5a** as a clear, thick oil. Data for (+)-*anti*-**5a**: ^1H NMR (500 MHz) 7.81 (s, 3 H), 4.93 (dd, $J = 7.6$, 4.9, 1 H), 3.79 (d, $J = 4.9$, 1 H), 3.01–2.95 (m, 1 H), 2.61–2.55 (m, 1 H), 2.49 (ddd, $J = 15.4$, 11.2, 4.2, 1 H), 1.93–1.64 (m, 4 H), 1.60–1.54 (m, 1 H), 1.44–1.24 (m, 3 H); ^{13}C NMR (126 MHz) 216.89, 144.55, 131.68 (q, $J = 33.1$), 127.16, 123.25 (q, $J = 273.4$), 121.81, 74.59, 57.78, 44.06, 28.55, 28.08, 23.36; ^{19}F NMR (376 MHz) -63.03 ; MS (EI, 70 eV) 354 (2), 112 (100); IR (CHCl_3) 1690 (m); TLC R_f 0.45 (hexane/EtOAc, 3/1); $[\alpha]_D^{21} +8.9^\circ$ ($c = 3.13$, CHCl_3); SFC t_R (2*R*,1'*S*)-**5a**, 3.72 (90.8%); t_R (2*S*,1'*R*)-**5a**, 8.42 min (9.2%) (Whelk-O1, 150 bar, -10 °C, 1% CH_3OH in CO_2 , 2.5 mL min^{-1}). Anal. Calcd for $\text{C}_{16}\text{H}_{16}\text{F}_6\text{O}_2$ (354.24): C, 54.25; H, 4.55; F, 32.16. Found: C, 54.06; H, 4.50; F, 32.05. Data for (–)-*syn*-**5a**: $[\alpha]_D^{21} -36.8^\circ$ ($c = 1.32$, CHCl_3); t_R (–)-**5a**, 4.06 min (70.3%); t_R (+)-**5a**, 4.63 min (29.7%) (Whelk-O1, 150 bar, 0 °C, 0.5% CH_3OH in CO_2 , 3.0 mL min^{-1}).

(+)-(2*R*,1'*S*)-2-[Hydroxy-(4-(trifluoromethyl)phenyl)methyl]cycloheptanone ((+)-*anti*-5b). Following General Procedure II, 4-(trifluoromethyl)benzaldehyde (**b**) (273 μL , 2.0 mmol) in CH_2Cl_2 (10 mL) was added over 55 min to a cold (-75 °C) solution of (*S,S*)-**1** (74 mg, 0.2 mmol, 0.1 equiv) and enolate **3b** (420 μL , 2.2 mmol, 1.1 equiv) in CH_2Cl_2 (10 mL). Workup provided the crude aldolates in a 1/15 syn/anti ratio. The crude product was purified by column chromatography (SiO_2 , hexane/EtOAc, 5/1) to give 33.1 mg of (–)-*syn*-**5b** as a clear oil and 515.0 mg (96% total) of (+)-*anti*-**5b** as a white solid. Data for (+)-*anti*-**5b**: ^1H NMR: (500 MHz) 7.61 (d, $J = 8.3$, 2 H), 7.46 (d, $J = 8.1$, 2 H), 4.87 (dd, $J = 7.8$, 4.6, 1 H), 3.61 (d, $J = 4.4$, 1 H), 3.00–2.95 (m, 1 H), 2.59–2.52 (m, 1 H), 2.48 (ddd, $J = 15.6$, 11.2, 4.4, 1 H), 1.90–1.82 (m, 2 H), 1.80–1.65 (m, 2 H), 1.60–1.54 (m, 1 H), 1.40–1.24 (m, 3 H); ^{13}C NMR (126 MHz) 217.20, 145.97, 129.87 (q, $J = 33.1$), 127.30, 125.40 (q, $J = 3.7$), 124.08 (q, $J = 271.6$), 74.97, 57.97, 44.08, 28.65, 28.61, 28.11, 23.47; ^{19}F NMR (376 MHz) -62.80 ; MS (EI, 70 eV) 286 (2); 112 (100); IR (CHCl_3) 1688 (s); TLC R_f 0.28 (hexane/EtOAc, 3/1); $[\alpha]_D^{21} +7.2^\circ$ ($c = 1.71$, CHCl_3); SFC t_R (2*R*,1'*S*)-**5b**, 2.17 min (84.4%); t_R (2*S*,1'*R*)-**5b**, 3.00 min (15.6%) (Chiralpak AD, 150 bar, 40 °C, 10% CH_3OH in CO_2 , 3.0 mL min^{-1}). Anal. Calcd for $\text{C}_{15}\text{H}_{17}\text{F}_3\text{O}_2$ (286.27): C, 62.93; H, 5.99; F, 19.91. Found: C, 63.12; H, 6.02; F, 20.16. Data for (–)-*syn*-**5b**: $[\alpha]_D^{21} -20.0^\circ$ ($c = 0.21$, CHCl_3); SFC t_R (+)-**5b**, 1.72 min (39.5%); t_R (–)-**5b**, 1.97 min (60.5%) (Chiralpak AD, 150 bar, 40 °C, 10% CH_3OH in CO_2 , 3.0 mL min^{-1}).

(+)-(2*R*,1'*S*)-2-(Hydroxy(phenyl)methyl)cycloheptanone ((+)-*anti*-5c). Following General Procedure II, benzaldehyde (**c**) (203 μL , 2.0 mmol) in CH_2Cl_2 (10 mL) was added over 50 min to a cold (-75 °C) solution of (*S,S*)-**1** (74 mg, 0.2 mmol, 0.1 equiv) and enolate **3b** (420 μL , 2.2 mmol, 1.1 equiv) in CH_2Cl_2 (10 mL). Workup provided the crude aldolates in a 1/29 syn/anti ratio. The crude product was purified by column chromatography (SiO_2 , hexane/EtOAc, 6/1) to give 13.0 mg of (–)-*syn*-**5c** as a clear oil and 411.0 mg (97% total)

of (+)-*anti*-**5c** as a clear oil. Data for (+)-*anti*-**5c**: $^1\text{H NMR}$ (500 MHz) 7.37–7.27 (m, 5 H), 4.81 (d, $J = 8.3$, 1 H), 3.39 (br s, 1 H), 2.99 (ddd, $J = 10.3$, 8.3, 3.4, 1 H), 2.60–2.54 (m, 1 H), 2.48 (ddd, $J = 15.6$, 11.2, 4.2, 1 H), 1.90–1.82 (m, 2 H), 1.77–1.65 (m, 2 H), 1.56–1.50 (m, 1 H), 1.35–1.23 (m, 3 H); $^{13}\text{C NMR}$ (126 MHz) 217.30, 141.65, 128.42, 127.85, 126.99, 75.32, 58.31, 43.90, 28.68, 28.53, 27.97, 23.59; MS (EI, 70 eV) 218 (6), 112 (100); IR (neat) 1698 (s); TLC R_f 0.34 (hexane/EtOAc, 3/1); $[\alpha]_D^{21} +11.8^\circ$ ($c = 0.82$, CHCl_3); SFC t_R (2*S*,1'*R*)-**5c**, 3.95 min (8.0%); t_R (2*R*,1'*S*)-**5c**, 4.46 min (92.0%) (Chiralpak AS, 150 bar, 40 °C, 6% CH_3OH in CO_2 , 2.5 mL min $^{-1}$). Anal. Calcd for $\text{C}_{14}\text{H}_{18}\text{O}_2$ (218.30): C, 77.03; H, 8.31. Found: C, 77.01; H, 8.36. Data for (–)-*syn*-**5c**: $[\alpha]_D^{21} -47.7^\circ$ ($c = 0.31$, CHCl_3); SFC t_R (+)-**5c**, 3.84 min (31.8%); t_R (–)-**5c**, 4.99 min (68.2%) (Chiralpak AS, 150 bar, 40 °C, 6% CH_3OH in CO_2 , 2.5 mL min $^{-1}$).

(+)-(2*R*,1'*S*)-2-[Hydroxy-(4-methoxyphenyl)methyl]cycloheptanone ((+)-*anti*-**5d**). Following General Procedure II, 4-methoxybenzaldehyde (**d**) (243 μL , 2.0 mmol) in CH_2Cl_2 (10 mL) was added over 45 min to a cold (–75 °C) solution of (*S,S*)-**1** (74 mg, 0.2 mmol, 0.1 equiv) and enolate **3b** (420 μL , 2.2 mmol, 1.1 equiv) in CH_2Cl_2 (10 mL). Workup provided the crude aldolates in a 1/35 *syn/anti* ratio. The crude product was purified by column chromatography (SiO_2 , hexane/EtOAc, 4/1) to give 9.5 mg of (–)-*syn*-**5d** as a clear oil and 474.0 mg (97% total) of (+)-*anti*-**5d** as a white solid. Data for (+)-*anti*-**5d**: $^1\text{H NMR}$ (500 MHz) 7.26 (d, $J = 8.3$, 2 H), 6.88 (d, $J = 8.1$, 2 H), 4.77 (d, $J = 8.5$, 1 H), 3.81 (s, 3 H), 3.28 (br s, 1 H), 2.95 (ddd, $J = 11.3$, 9.5, 3.4, 1 H), 2.61–2.55 (m, 1 H), 2.49 (ddd, $J = 15.4$, 11.2, 3.7, 1 H), 1.90–1.82 (m, 2 H), 1.75–1.65 (m, 2 H), 1.55–1.49 (m, 1 H), 1.36–1.20 (m, 3 H); $^{13}\text{C NMR}$ (126 MHz) 217.33, 159.21, 133.77, 128.16, 113.79, 74.77, 58.51, 55.21, 43.85, 28.75, 28.52, 27.92, 23.63; MS (EI, 70 eV) 248 (6), 137 (100); IR (CHCl_3) 1687 (s); TLC R_f 0.17 (hexane/EtOAc, 3/1); $[\alpha]_D^{21} +2.2^\circ$ ($c = 1.90$, CHCl_3); SFC t_R (2*S*,1'*R*)-**5d**, 9.73 min (4.1%); t_R (2*R*,1'*S*)-**5d**, 10.70 min (95.9%) (Chiralpak AS, 150 bar, 40 °C, 6% CH_3OH in CO_2 , 2.5 mL min $^{-1}$). Anal. Calcd for $\text{C}_{15}\text{H}_{20}\text{O}_3$ (248.32): C, 72.55; H, 8.12. Found: C, 72.45; H, 8.03. Data for (–)-*syn*-**5d**: $[\alpha]_D^{21} -23.1^\circ$ ($c = 0.65$, CHCl_3); SFC t_R (+)-**5d**, 5.97 min (38.8%); t_R (–)-**5d**, 7.99 min (61.2%) (Chiralpak AA, 150 bar, 40 °C, 6% CH_3OH in CO_2 , 2.5 mL min $^{-1}$).

(+)-(2*R*,1'*S*)-2-[Hydroxy-(3,4,5-trimethoxyphenyl)methyl]cycloheptanone ((+)-*anti*-**5e**). Following General Procedure II, 3,4,5-trimethoxybenzaldehyde (**e**) (392 mg, 2.0 mmol) in CH_2Cl_2 (10 mL) was added over 50 min to a cold (–75 °C) solution of (*S,S*)-**1** (74 mg, 0.2 mmol, 0.1 equiv) and enolate **3b** (420 μL , 2.2 mmol, 1.1 equiv) in CH_2Cl_2 (10 mL). Workup provided the crude aldolates in a 1/20 *syn/anti* ratio. The crude product was purified by column chromatography (SiO_2 , hexane/EtOAc, 2/1) to give 24.3 mg of (–)-*syn*-**5e** as a clear oil and 551.0 mg (94% total) of (+)-*anti*-**5e** as a clear, thick oil. Data for (+)-*anti*-**5e**: $^1\text{H NMR}$ (500 MHz) 6.56 (s, 2 H), 4.74 (dd, $J = 8.6$, 3.8, 1 H), 3.87 (s, 6 H), 3.84 (s, 3 H), 3.37 (d, $J = 3.7$, 1 H), 2.94 (ddd, $J = 10.4$, 8.4, 3.3, 1 H), 2.62–2.56 (m, 1 H), 2.50 (ddd, $J = 15.6$, 11.2, 4.2, 1 H), 1.91–1.83 (m, 2 H), 1.80–1.67 (m, 2 H), 1.60–1.54 (m, 1 H), 1.40–1.24 (m, 3 H); $^{13}\text{C NMR}$ (126 MHz) 217.29, 153.20, 137.47, 137.27, 103.89, 75.54, 60.76, 58.44, 56.08, 43.86, 28.76, 28.57, 27.89, 23.65; MS (EI, 70 eV) 308 (13), 196 (100); IR (CHCl_3) 1688 (s); TLC R_f 0.054 (hexane/EtOAc, 3/1); $[\alpha]_D^{21} +12.6^\circ$ ($c = 1.02$, CHCl_3); SFC t_R (2*S*,1'*R*)-**5e**, 2.93 min (6.3%); t_R (2*R*,1'*S*)-**5e**, 3.44 min (93.7%) (Chiralpak AS, 150 bar, 40 °C, 7% CH_3OH in CO_2 , 3.0 mL min $^{-1}$). Anal. Calcd for $\text{C}_{17}\text{H}_{24}\text{O}_5$ (308.37): C, 66.21; H, 7.84. Found: C, 66.03; H, 7.82. Data for (–)-*syn*-**5e**: $[\alpha]_D^{21} -27.2^\circ$ ($c = 0.81$, CHCl_3); SFC t_R (+)-**5e**, 3.01 min (29.4%); t_R (–)-**5e**, 3.61 min (70.6%) (Chiralpak AS, 150 bar, 40 °C, 7% CH_3OH in CO_2 , 3.0 mL min $^{-1}$).

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References

† The Chemistry of Trichlorosilyl Enolates. 5.

(1) For reviews on catalytic asymmetric aldol additions, see (a) Bach, T. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 417. (b) Franklin, A. S.; Paterson, I. *Contemporary Org. Syn.* **1994**, *1*, 317–416. (c) Braun, M.; Sacha, H. *J. Prakt. Chem.* **1993**, *335*, 653–668. (d) Sawamura, M.; Ito, Y. In *Catalytic Asymmetric Synthesis*, Ojima, I., Ed.; VCH: New York, 1993; pp 367–388. (e) Yamamoto, H.; Maruoka, K.; Ishihara, K. *J. Synth. Org.*

Jpn. **1994**, 52, 912. (f) Braun, M. In *Stereoselective Synthesis, Methods of Organic Chemistry (Houben-Weyl)*; Edition E21; Helmchen, G.; Hoffman, R.; Mulzer, J.; Schaumann, E. Eds.; Thieme: Stuttgart, 1996; Vol. 3; pp 1730-1736.

(2) For leading references on catalytic asymmetric aldol additions see: (a) Sodeoka, M.; Tokunoh, R.; Miyazaki, F.; Hagiwara, E.; Shibasaki, M. *Synlett* **1997**, 463. (b) Yamada, Y. M. A.; Yoshikawa, N.; Sasai, H.; Shibasaki, M. *Angew. Chem., Int. Ed. Engl.* **1997**, 36, 1871. See also refs 4b and 5.

(3) For examples of primarily anti-selective catalytic asymmetric aldol additions, see: (a) Evans, D. A.; MacMillan, D. W. C.; Campos, K. R. *J. Am. Chem. Soc.* **1997**, 119, 10859. (b) Kobayashi, S.; Horibe, M.; Hachiya, I. *Tetrahedron Lett.* **1995**, 36, 3173.

(4) (a) Denmark, S. E.; Winter, S. B. D.; Su, X.; Wong, K.-T. *J. Am. Chem. Soc.* **1996**, 118, 7404. (b) Denmark, S. E.; Wong, K.-T.; Stavenger, R. A. *J. Am. Chem. Soc.* **1997**, 119, 2333. (c) Denmark, S. E.; Winter, S. B. D. *Synlett* **1997**, 1087. (d) Denmark, S. E.; Stavenger, R. A.; Wong, K.-T. *J. Org. Chem.* **1998**, 63, 0000.

(5) Recently Yamamoto has described a silver(I)-catalyzed aldol addition of stannyl enolates to aldehydes which also correlates starting enolate geometry and the major diastereomer: Yanagisawa, A.; Matsumoto, Y.; Nakashima, H.; Asakawa, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1997**, 119, 9319.

(6) Benkeser, R. A.; Smith, W. E. *J. Am. Chem. Soc.* **1968**, 90, 5307.

(7) (a) Burlachenko, G. S.; Khasapov, B. N.; Petrovskaya, L. I.; Baukov, Yu. I.; Lutsenko, I. F.; *J. Gen. Chem. USSR (Engl. Transl.)* **1966**, 36, 532. (b) Ponomarev, S. V.; Baukov, Yu. I.; Dudukina, O. V.; Petrosyan, I. V.; Petrovskaya, L. I. *J. Gen. Chem. USSR (Engl. Transl.)* **1967**, 37, 2092.

(8) For a review of the conversion of TMS enol ethers to reactive enolates see: Kuwajima, I.; Nakamura, E. *Acc. Chem. Res.* **1985**, 18, 181.

(9) House, H. O.; Auerbach, R. A.; Gall, M.; Pect, N. P. *J. Org. Chem.* **1973**, 38, 514.

(10) The relative configuration was established on the basis of the splitting pattern and resonance frequency of the hydroxyl bearing methine. The proton appears as a broad singlet in the syn-isomer and as a doublet or doublet of doublets in the anti-isomer. In addition, this proton in the anti-isomer appears 0.4-0.7 ppm upfield of the syn-isomer.

(11) (a) Denmark, S. E.; Griedel, B. D.; Coe, D. M.; Schnute, M. E. *J. Am. Chem. Soc.* **1994**, 116, 7026. (b) See also ref. 4b.

(12) (a) Myers, A. G.; Widdowson K. L. *J. Am. Chem. Soc.* **1990**, 112, 9672. (b) Myers, A. G.; Widdowson, K. L.; Kukkola, P. J. *J. Am. Chem. Soc.* **1992**, 114, 2765.

(13) Gung, B. W.; Zhu, Z.; Fouch, R. A. *J. Org. Chem.* **1995**, 60, 2860.

(14) Evans, D. A.; McGee, L. R. *Tetrahedron Lett.* **1980**, 21, 3975.

(15) Enol borates: (a) Hoffmann, R. W.; Ditrich, K.; Froech, S.; Cremer, D. *Tetrahedron* **1985**, 41, 5517. (b) Gennari, C.; Todeschini, R.; Beretta, M. G.; Favini, G.; Scolastico, C.; *J. Org. Chem.* **1986**, 51, 612. Enol boronates see: (c) Li, Y.; Paddon-Row, M. N.; Houk, K. N. *J. Org. Chem.* **1990**, 55, 481.

(16) (a) Nakamura, E.; Kuwajima, I. *Tetrahedron Lett.* **1983**, 24, 3343. (b) Evans, D. A.; Nelson, J. V.; Taber, T. R. in *Topics in Stereochemistry*; Allinger, N. L.; Eliel, E. L.; Wilen, S. H., Eds.; Wiley Interscience: New York, 1982; Vol. 13, p1. See also refs. 8 and 16.

(17) The absolute configuration of the (–)-anti-5c was determined to be (2R,1'S) by X-ray crystallographic analysis of the corresponding 4-bromobenzoate. The absolute configurations of the other anti diastereomers are assigned by analogy. The absolute configurations of the syn diastereomers were not established.

(18) For a review on the reactivity of hypervalent silicon species see: Chuit, C.; Corriu, R. J. P.; Reye, C.; Young, J. C. *Chem. Rev.* **1993**, 93, 1371.

(19) Bockman, T. M.; Shukla, D.; Kochi, J. K. *J. Chem. Soc., Perkin Trans. 2* **1996**, 1623.