# Optically Active Tricarbonyl[$\eta^6$-*o*-(trimethylsilyl)benzaldehyde]chromium(0) Complexes in Organic Synthesis: A Highly Anti-Selective Asymmetric Aldol Reaction with *O*-Silyl Ketene *O*,*S*-Acetals

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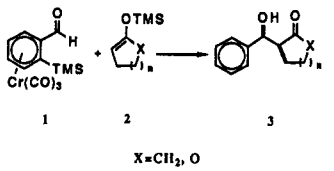
Treatment of optically pure (+)-tricarbonyl[*o*-(trimethylsilyl)benzaldehyde]chromium(0), (+)-1, with *O*-silyl ketene *O*,*S*-acetals **4c–f** afforded, after decomplexation, the (−)-*anti*-aldol products (−)-5c–f, while an antipode, (−)-1, provided the (+)-anti ones (+)-5c–f. Optical purity of these aldol products were determined to be in a range of 92 to >98% ee. The absolute configuration was established by an X-ray crystallographic analysis.

## Introduction

Tricarbonyl($\eta^6$-arene)chromium complexes[1] have been shown to be useful substrates for stereoselective carbon–carbon bond formation reactions as well as peculiar functionalization of aromatic rings that could hardly be achieved by conventional procedures. Successful application[2] of these significant properties to the synthesis of natural products and biologically active compounds were already recorded. Another synthetically important feature of these arene–chromium complexes[1] is that they have the inherently high $\pi$-facial selectivity due to complexation with chromium species and can serve as an excellent chiral auxiliary.

Recent studies from our laboratory[3] disclosed that the aldol reaction[4] of tricarbonyl[*o*-(trimethylsilyl)benzaldehyde]chromium(0) complex (1)[3,5] with cyclic *O*-silyl enol ethers 2 (X = $CH_2$)[3] proceeded in a highly stereoselective manner to afford the corresponding *syn*-aldol products 3. A high syn selectivity was also observed when cyclic *O*-silyl ketene acetals 2 (X = O)[6] were employed instead of *O*-silyl enol ethers. The above syn-selective aldol reaction was able to be extended to an asymmetric situation where a high enantiomeric excess (ee) was attained in all cases examined.[3a]

**Scheme I**




The high diastereoselectivity in the above aldol reaction of tricarbonyl[*o*-(trimethylsilyl)benzaldehyde]chromium(0) complex (1)[3,5] prompted us to investigate the aldol reaction of 1 with acyclic *O*-silyl enolic nucleophiles and explore further potentiality of 1 in the aldol chemistry.[4] In this paper we describe a highly anti-selective asymmetric aldol reaction between the chromium-complexed aldehyde 1 and *O*-silyl ketene *O*,*S*-acetals **4c–f**.

## Results and Discussion

**Aldol Reaction of Racemic 1 with Acyclic *O*-Silyl Ketene Acetals 4a,b.** Regarding (*E*)-*O*-trimethylsilyl ketene acetal **4a**[7] (*E*:*Z* = 80:20)[8] derived from ethyl propionate, the aldol reaction of racemic 1 was performed first. Treatment of 1 with (*E*)-**4a** in methylene chloride at −78 °C in the presence of titanium(IV) tetrachloride ($TiCl_4$),[9] followed by decomplexation with cerium(IV) ammonium nitrate (CAN)[10] in methanol at 0 °C, gave the aldol products as a mixture of the anti and syn isomers in a ratio of 71:29 (**5a**:**6a** = 71:29). Stereochemical assignment and ratio of each isomer were made by NMR spectral consideration based on the literature precedents.[4,11] Similar treatment of 1 with (*Z*)-**4a**[7] (*E*:*Z* = 15:85)[8] produced the anti isomer **5a** predominantly (**5a**:**6a** = 84:16). The anti isomer **5b** became a main product on exposure of 1 to (*E*)- or (*Z*)-*O*-silyl ketene acetal **4b** of ethyl butyrate.[7] These

(1) For reviews see: (a) Dickens, P. J.; Gilday, J. P.; Negri, J. T.; Widdowson, D. A. *Pure Appl. Chem.* **1990**, *62*, 575. (b) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987; p 920. (c) Pearson, A. J. *Metallo-Organic Chemistry*; John Wiley & Sons: New York, 1985; p 348. (d) Davies, S. G. *Organotransition Metal Chemistry, Application to Organic Synthesis*; Pergamon Press: Oxford, 1982. (e) Davies, R.; Kane-Maquire, L. A. P. Chromium Compounds with $\eta^2$–$\eta^8$ Carbon Ligands. In *Comprehensive Organometallic Chemistry*; Wilkinsons, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: Oxford, 1982; Vol. 3, Chapter 26–2. (f) Kundig, E. P. *Pure Appl. Chem.* **1985**, *57*, 1855. (g) Semmelhack, M. F. *Ibid.* **1981**, *53*, 2379. (h) Jaouen, G. Arene Complexes in Organic Synthesis. In *Transition Metal Organometallics in Organic Synthesis*; Alper, H., Ed.; Academic Press: New York, 1978; Vol. 2, p 65.

(2) For example see: (a) Uemura, M.; Nishimura, H.; Minami, T.; Hayashi, Y. *J. Am. Chem. Soc.* **1991**, *113*, 5402. (b) Sainsbury, M.; Williams, C. S. *Tetrahedron Lett.* **1990**, *31*, 2763. (c) Uemura, M.; Minami, T.; Hayashi, Y. *J. Chem. Soc., Chem. Commun.* **1984**, 1193. (d) Kundig, E. P.; Desobry, V.; Simmons, D. P. *J. Am. Chem. Soc.* **1983**, *105*, 6962. (e) Semmelhack, M. F.; Zask, A. *Ibid.* **1983**, *105*, 2034. (f) Semmelhack, M. F.; Yamashita, A. *Ibid.* **1980**, *102*, 5926.

(3) (a) Mukai, C.; Cho, W.-J.; Kim, I. J.; Hanaoka, M. *Tetrahedron* **1991**, *47*, 3007. (b) Mukai, C.; Cho, W.-J.; Hanaoka, M. *Tetrahedron Lett.* **1989**, *30*, 7435.

(4) For reviews see: (a) Heathcock, C. H. *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol. 3, p 111. (b) Evans, D. A.; Nelson, J. V.; Taber, T. R. *Top. Stereochem.* **1982**, *13*, 1. (c) Mukaiyama, T. *Org. React.* **1982**, *28*, 203. (d) Masamune, S.; Choy, W.; Peterson, J. S.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1. (e) Seebach, D.; Prelog, V. *Ibid.* **1982**, *21*, 654. (f) Bartlett, P. A. *Tetrahedron* **1980**, *36*, 2.

(5) Davies, S. G.; Goodfellow, C. L. *J. Chem. Soc., Perkin Trans. 1* **1990**, 393.

(6) Mukai, C.; Mihira, A.; Hanaoka, M. *Chem. Pharm. Bull.* **1991**, *39*, 2863.

(7) Chan, T. H.; Aida, T.; Lau, P. W. K.; Gorys, V.; Harpp, D. N. *Tetrahedron Lett.* **1979**, 4029.

(8) A ratio of (*E*)- and (*Z*)-isomers was determined by $^1H$ NMR spectra.

(9) Other Lewis acids for this aldol reaction was also examined, but no characteristic difference from $TiCl_4$ could be recognized.

(10) Semmelhack, M. F.; Hall, H. T., Jr.; Farina, R.; Yoshifuji, M.; Clark, G.; Bargar, T.; Hirotsu, K.; Clardy, J. *J. Am. Chem. Soc.* **1979**, *101*, 3535.

(11) The chemical shift and magnitude of vicinal coupling constant of benzylic protons in each isomer provided corroborative support for the stereochemical assignment of the aldol products. Furthermore, X-ray crystallographic analysis demonstrated those assignments unambiguously.

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**Table I. Aldol Reaction of the Chromium-Complexed Aldehyde 1 and the Uncomplexed Aldehyde 7 with O-Silyl Ketene Acetals 4**

| | | O-silyl ketene acetal 4 | | | | | |
|---|---|---|---|---|---|---|---|
| entry | aldehyde | | $R^1$ | $R^2$ | E:Z[a] | product[a] | yield[b] (%) |
| 1 | 1 | a | Me | OEt | 80:20 | **5a:6a** = 71:29 | 84 |
| 2 | 1 | a | Me | OEt | 15:85 | **5a:6a** = 84:16 | 83 |
| 3 | 1 | b | Et | OEt | 86:14 | **5b:6b** = 66:34 | 76 |
| 4 | 1 | b | Et | OEt | <2:>98 | **5b:6b** = 74:26 | 44 |
| 5 | 7 | a | Me | OEt | 80:20 | **5a:6a** = 63:37 | 88 |
| 6 | 7 | a | Me | OEt | 15:85 | **5a:6a** = 63:37 | 79 |
| 7 | 7 | b | Et | OEt | 86:14 | **5b:6b** = 66:34 | 86 |
| 8 | 7 | b | Et | OEt | <2:>98 | **5b:6b** = 65:35 | 47 |
| 9 | 1 | c | Me | $SBu^t$ | 95:5 | **5c:6c** = 93:7 | 93 |
| 10 | 1 | c | Me | $SBu^t$ | 10:90 | **5c:6c** = 96:4 | 100 |
| 11 | 1 | d | Me | SPh | 13:87 | **5d:6d** = 92:8 | 84 |
| 12 | 1 | e | Et | $SBu^t$ | 92:8 | **5e:6e** = 90:10 | 72 |
| 13 | 1 | e | Et | $SBu^t$ | 9:91 | **5e:6e** = 96:4 | 99 |
| 14 | 1 | f | Et | SPh | 27:73 | **5f:6f** = 90:10 | 93 |
| 15 | 7 | c | Me | $SBu^t$ | 95:5 | **5c:6c** = 74:26 | 94 |
| 16 | 7 | c | Me | $SBu^t$ | 10:90 | **5c:6c** = 73:27 | 72 |
| 17 | 7 | d | Me | SPh | 13:87 | **5d:6d** = 85:15 | 84 |
| 18 | 7 | e | Et | $SBu^t$ | 92:8 | **5e:6e** = 73:27 | 77 |
| 19 | 7 | e | Et | $SBu^t$ | 9:91 | **5e:6e** = 73:27 | 81 |
| 20 | 7 | f | Et | SPh | 27:73 | **5f:6f** = 79:21 | 86 |

[a] Ratios were determined from the $^1H$ NMR spectra. [b] Yield of a mixture of the anti and syn isomers 5 and 6.

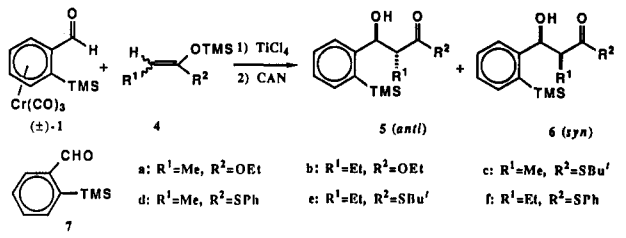
results are summarized in Table I. The anti selectivity observed in the reaction between the chromium complexed aldehyde 1 and acyclic O-silyl ketene acetals is in marked contrast to the syn selectivity[3,6] on employing cyclic O-silyl ones. The degree of the anti selectivity observed here, however, is lower than that of the syn selectivity in the case of cyclic O-silyl enolic nucleophiles.

Control experiments with o-(trimethylsilyl)benzaldehyde (7)[3] were carried out to inspect whether complexation with chromium tricarbonyl species is essential for the anti selectivity in the reaction of the complexed aldehyde 1 with 4. The aldehyde 7 was treated with 4 under the similar condition described for 1 except for exposure to CAN providing the aldol products as a mixture of 5 and 6. These results are presented in Table I. The control experiments obviously indicated that complexation with chromium is not mandatory for the anti selectivity. However, the complexation brought about very little additional selectivity compared to an uncomplexed aldehyde 7. This phenomenon was also observed in the case of acyclic O-silyl ketene O,S-acetals **4c–f** (vide infra), although the reason is so far not clear. The anti selectivity in this aldol reaction is in good accordance with the result[12] reported by Gennari in which the reaction of benzaldehyde with (E)-**4a** proceeded anti selectively.

The aldol reaction of racemic 1 with acyclic O-silyl ketene acetals **4a,b** gave the anti products **5a,b** regardless of the geometry of the starting **4a,b**. It seems to be not necessary to use chromium-complexed benzaldehyde derivatives instead of the uncomplexed ones from the points of diastereoselective view in this aldol reaction. However, tricarbonyl[o-(trimethylsilyl)benzaldehyde]chromium(0) complex (1) as a starting substrate still has a great advantage because 1 can be easily resolved into (+)- and (−)-1,[3] both of which should provide the optically active aldol condensation products in a highly enantioselective manner. The major drawback of this complex 1 in the aldol reaction with acyclic O-silyl ketene acetals is an unsatisfactory anti selectivity. Accordingly, our endeavor was focused on improvement of the degree of the anti selectivity.

(12) Palazzi, C.; Colombo, L.; Gennari, C. *Tetrahedron Lett.* **1986**, *27*, 1735.

**Scheme II**




**Aldol Reaction of Racemic 1 with Acyclic O-Silyl Ketene O,S-Acetals 4c–f.** Gennari and his co-workers[13,14] have recently reported some successful examples of the aldol reaction of various aldehydes with O-silyl ketene O,S-acetals resulting in formation of the anti isomers in a highly selective manner. We, therefore, decided to test O-silyl ketene O,S-acetals derived from S-*tert*-butyl and S-phenyl thioesters. The required (E)- and (Z)-O-silyl ketene O,S-acetals **4c–f**[13a,15] were prepared according to the procedure in the literature. In order to elucidate the relationship between the selectivity and the geometry of the starting O-silyl ketene O,S-acetals, (E)-**4c** (E:Z = 95:5)[8] and (Z)-**4c** (E:Z = 10:90)[8] were independently exposed to racemic 1 under the standard aldol condition in the presence of $TiCl_4$[9] described for **4a** to furnish the condensation products in 93% and quantitative yields, respectively. A high anti selectivity[9,16] was attained in both cases (**5c:6c** = 93:7, **5c:6c** = 96:4, respectively) irrespective of the geometry of the starting **4c** as anticipated. (Z)-O-Silyl ketene O,S-acetal, (Z)-**4d** (E:Z = 13:87),[8] derived from S-phenyl propanethiolate also effected the anti-selective aldol reaction to afford the anti isomer **5d** (anti:syn = 92:8) in 84% yield. The anti compounds **5e,f** possessing an ethyl appendage at the 2-position were selectively formed on

(13) (a) Gennari, C.; Beretta, M. G.; Bernardi, A.; Moro, G.; Scolastico, C.; Todeschini, R. *Tetrahedron* **1986**, *42*, 893. (b) Gennari, C.; Bernard, A.; Cardani, S.; Scolastico, C. *Tetrahedron Lett.* **1985**, *26*, 797.

(14) Gennari, C. Stereoselective Synthesis with Silyl Ketene Acetals and $TiCl_4$. In *Selectivities in Lewis Acid Promoted Reactions*; Schinzer, D., Ed.; Klumer Academic Publishers: London, 1989; p 53.

(15) Gennari, C.; Cozzi, P. G. *J. Org. Chem.* **1988**, *53*, 4015.

(16) When $BF_3$·$OEt_2$ was employed instead of $TiCl_4$, for instance, **5c** was again obtained in a highly anti-stereoselective manner on treatment of 1 with (E)-**4c** and (Z)-**4c** [**5c:6c** = 93:7 (96%) and **5c:6c** = 94:6 (93%), respectively].

Table II. Aldol Reaction of (+)- and (−)-1 with *O*-Silyl Ketene *O,S*-Acetal 4c–f

| entry | aldehyde | *O,S*-acetal 4c-f | $R^1$ | $R^2$ | $E:Z^a$ | isolated product[b] | $[\alpha]_D$[c] (deg) | ee[d] (%) | yield[e] (%) | anti:syn[a] |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | (+)-1 | c | Me | $SBu^t$ | >98:<2 | (−)-**5c** | −61.5[f] | 96 | 96 | 96:4 |
| 2 | (+)-1 | c | Me | $SBu^t$ | 4:96 | (−)-**5c** | −63.1 | 96 | 99 | 97:3 |
| 3 | (−)-1 | c | Me | $SBu^t$ | >98:<2 | (+)-**5c** | +63.5 | 94 | 96 | 94:6 |
| 4 | (−)-1 | c | Me | $SBu^t$ | 4:96 | (+)-**5c** | +62.7 | 92 | 94 | 95:5 |
| 5 | (+)-1 | d | Me | SPh | 13:87 | (−)-**5d** | −54.8 | 92 | 83 | 90:10 |
| 6 | (−)-1 | d | Me | SPh | 13:87 | (+)-**5d** | +52.0 | 94 | 80 | 96:4 |
| 7 | (+)-1 | e | Et | $SBu^t$ | >98:<2 | (−)-**5e** | −38.1 | 96 | 90 | 96:4 |
| 8 | (+)-1 | e | Et | $SBu^t$ | 5:95 | (−)-**5e** | −39.3 | 94 | 89 | 94:6 |
| 9 | (−)-1 | e | Et | $SBu^t$ | >98:<2 | (+)-**5e** | +37.8 | 92 | 90 | 91:9 |
| 10 | (−)-1 | e | Et | $SBu^t$ | 5:95 | (+)-**5e** | +41.3 | 92 | 91 | 92:8 |
| 11 | (+)-1 | f | Et | SPh | 22:78 | (−)-**5f** | −70.8 | >98[g] | 83 | 90:10 |
| 12 | (−)-1 | f | Et | SPh | 22:78 | (+)-**5f** | +67.6 | >98[g] | 85 | 89:11 |

[a] Ratios were determined from the $^1H$ NMR spectra. [b] The anti isomers were isolated by careful chromatography and free from contamination with the syn isomers. [c] Measured in $CHCl_3$ (*c*, 0.50). [d] Optical yields were determined by $^1H$ NMR spectra in the presence of $Eu(hfc)_3$. [e] Yield of a mixture of the anti and syn isomers. [f] Measured in $CHCl_3$ (*c*, 0.22). [g] No enantiomeric isomer could be detected.

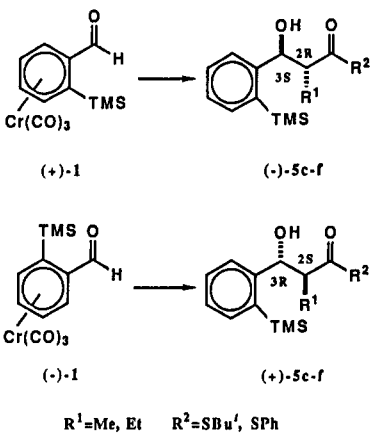
treatment of 1 with **4e,f** regardless of their geometry (Scheme II, Table I).

Satisfactory anti selectivity as well as chemical yields were realized by changing *O*-silyl ketene acetals to their *O,S* congeners (Table I). An uncomplexed aldehyde **7** was submitted to the reaction of **4c–f** as control experiments (Table I) providing the anti isomers as **4a,b** did (vide supra). It should be noted that chromium-complexed aldehyde **1** is superior to the uncomplexed one **7** with respect to the anti selectivity. Since we could develop a highly anti-selective aldol reaction mediated by chromium complexation, the next phase of our research is now faced to extension of this reaction to asymmetric situation.

**Asymmetric Aldol Reaction of (+)- and (−)-1 with *O*-Silyl Ketene *O,S*-Acetals.** Optically pure (+)- and (−)-aldehydes were easily obtained according to our previous report.[3a] (+)-Aldehyde (+)-1[3a,5] was treated with (*E*)-**4c** (*E:Z* = >98:<2)[8] in methylene chloride at −78 °C in the presence of Lewis acid to leave the aldol products with a chromium moiety which were subsequently decomplexed with CAN[10] in methanol at 0 °C to give a mixture of the anti and syn isomers in 96% yield in a ratio of 96:4. A careful column chromatography of the mixture afforded (−)-*anti*-**5c** [$[\alpha]_D$ −61.5° (*c*, 0.50), $CHCl_3$] which was completely free from the syn isomer. Optical purity of (−)-*anti*-**5c**, thus obtained, was determined to be 96% ee by $^1H$ NMR spectrum using a shift reagent, tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]europium(III) [$Eu(hfc)_3$]. Similarly, (*Z*)-**4c** (*E:Z* = 4:96) afforded (−)-*anti*-**5c** with 96% ee on exposure to (+)-1. On the other hand, treatment of (−)-aldehyde (−)-1[3a,5] with (*E*)- and (*Z*)-**4c** provided an antipode, (+)-*anti*-**5c** with high ee in both cases as shown in Table II. Other *O*-silyl ketene *O,S*-acetals **4d–f** also gave, upon treatment with (+)- and (−)-1, (−)-**5d–f** and (+)-**5d–f**, respectively, in a highly enantioselective manner (Table II).

We considered an X-ray crystallographic analysis of a suitable aldol condensation product having chromium moiety in order to establish the absolute configuration of these *anti*-aldol products and get some information about reaction mechanism. Reaction of racemic 1 with (*Z*)-**4e** (*E:Z* = 5:95) under the standard conditions yielded the anti product having a chromium moiety along with a small amount of the syn product. Chromatographic separation of the mixture left the pure anti isomer **8** which was recrystallized from ether/*n*-hexane to afford a yellow cubic crystals suitable for an X-ray analysis. An X-ray analysis of racemic **8** disclosed the relative stereochemistry of the stereogenic centers on the 2 and 3 positions and the benzene ring to be 2*R**,3*S**,1′*S** as depicted in Figure 1. The X-ray analysis of **8** established the absolute stereochemistry of (−)-*anti*-**5** to be 2*R*,3*S*, while an antipode, (+)-*anti*-**5** has 2*S*,3*R* configuration because the absolute configuration of the starting (+)- and (−)-1 have already

Scheme III



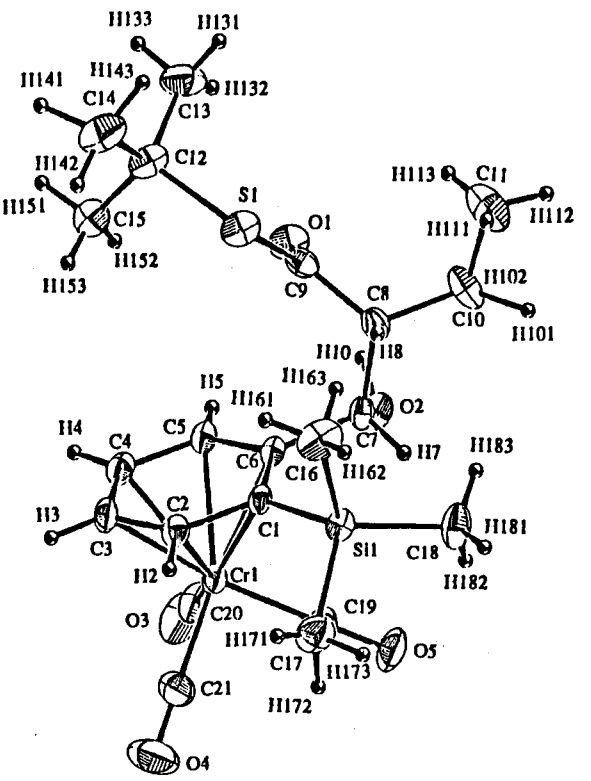
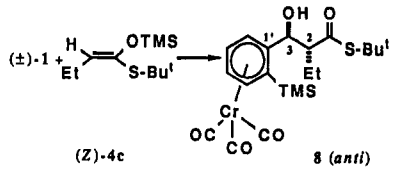




Figure 1. Perspective ORTEP drawing of compound 8.

**Scheme IV**




been unambiguously determined.[3a]

The reaction mechanism of this anti-selective aldol reaction has not yet been elucidated. We previously reported a highly syn-selective aldol reaction between 1 and cyclic O-silyl enolic nucleophiles 2, the mechanism of which could be tentatively rationalized in terms of acyclic synclinal transition states where the o-TMS group of the complex 1 plays a crucial role to govern the diastereoselectivity. In the case of acyclic O-silyl ketene O,S-acetals **4c–f**, the above explanation can not be simply applied any longer for understanding the anti selectivity. Judging from the result of an X-ray analysis of 8, however, there are still two assumptions that deserve to be considered: the first one is that 1 would exist in the most preferred conformer in which the oxygen of the aldehyde is forced to direct far from the TMS group to avoid an unfavorable steric interaction, and the second is that trajectory of the approach of nucleophiles 4 to the electrophilic center, the aldehyde moiety, must be from opposite face occupied with chromium complexation.

On the basis of these assumptions and the reaction mechanism proposed by Heathcock[17b] and Gennari,[13b,14] we interpreted the high anti selectivity observed in the reaction of 1 with **4c–f** in terms of intermediacy of acyclic staggered transition states with the antiperiplanar conformation as shown in Figure 2. The transition states A(*E*) and A(*Z*) leading to the anti isomers may have only an unfavorable nonbonding gauche interaction between the alkyl side chain of the nucleophiles and aromatic moiety. On the other hand, the transition states S(*E*) and S(*Z*) would suffer the serious interaction between the aromatic ring of 1 and O-silyl group or the substituent on the sulfur atom.[13] In addition, Lewis acid coordinated with the oxygen of the aldehyde[17] may increase the instability of the transition states S(*E*) and S(*Z*) in comparison with A(*E*) and A(*Z*). As mentioned earlier, a slightly higher anti selectivity was constantly recognized in utility of the chromium-complexed aldehyde 1 compared to the uncomplexed aldehyde 7. This tendency can be explained, by neither the only aforementioned mechanism nor the difference[18] for the degree of selectivity between O-silyl ketene acetals **4a,b** and O-silyl ketene O,S-acetals **4c–f**. Consequently, it is obvious that the above mechanism is not enough yet for understanding real process of this aldol reaction.

## Conclusion

A highly anti- and enantioselective aldol reaction of chromium-complexed chiral aldehyde with acyclic O-silyl ketene O,S-acetals has been developed. The high anti selectivity is not affected by variation of the geometry and a substituent of the starting O-silyl ketene O,S-acetals. In light of the fact that the TMS group can be easily removed by usual manner, this aldol reaction would provide a new type of asymmetric aldol reaction mediated by arene–chromium complexation. Further investigation from a mechanistic point of view as well as utility of the chromium complex 1 is in progress.

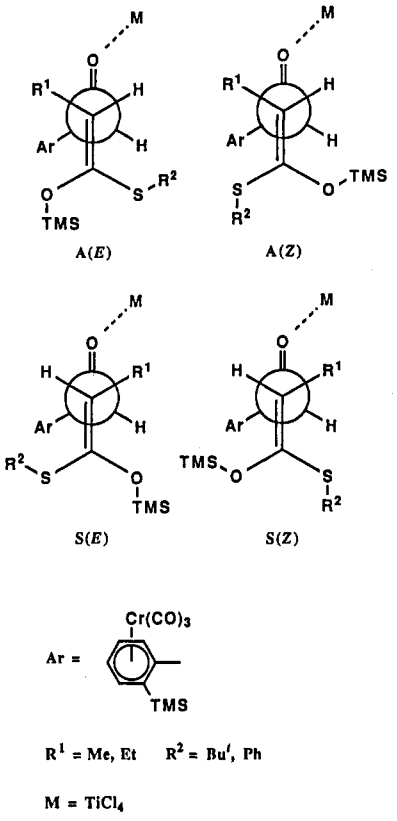



**Figure 2.**

## Experimental Section

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectra were measured with a JASCO-102 spectrometer in $CHCl_3$, mass spectra (MS) and high-resolution mass spectra (HRMS) with a Hitachi M-80 mass spectrometer, optical rotations with a JASCO DIP-181 digital polarimeter, $^1H$ NMR spectra with JEOL JNM-GX 400 and 500 spectrometers in $CDCl_3$ using tetramethylsilane as an internal standard, and $^{13}C$ NMR spectra with a JEOL EX-270 in $CDCl_3$ with $CDCl_3$ (77.00 ppm) as an internal reference. $CH_2Cl_2$ was freshly distilled from $CaH_2$ prior to use. Aldol reactions were carried out in oven-dried glassware under an inert atmosphere of nitrogen. Silica gel (silica gel 60, 230–400 mesh, Nacalai Tesque) was used for chromatography. Organic extracts were dried over anhydrous $Na_2SO_4$. The starting O-silyl ketene acetals **4a,b**[12] and O-silyl ketene O,S-acetals **4c–f**[13a,15] were prepared according to the literature.

**General Procedure for the Aldol Reaction of Chromium-Complexed Aldehyde 1 with O-Silyl Ketene Acetals and O-Silyl Ketene O,S-Acetals 4.** To a solution of the complex 1 (1.0 equiv) and a silyl ketene acetal 4 (1.1–2.0 equiv) in dry $CH_2Cl_2$ (5 mL) was added dropwise a solution of $TiCl_4$ in dry $CH_2Cl_2$ (1 M solution, 1.2–2.0 equiv) at −78 °C. The reaction mixture was stirred at −78 °C for 30 min to 1 h. The reaction was monitored by TLC and quenched by addition of saturated $NH_4Cl$ solution (0.5 mL) at the same temperature. The reaction mixture was gradually warmed to room temperature, washed with $H_2O$ and brine, dried, and concentrated. The residue was then dissolved in MeOH (5 mL), to which CAN (3.0 equiv) was added portionwise at 0 °C. The reaction mixture was stirred until the decomplexation of the chromium moiety was completed (monitored by TLC, 10–20 min). MeOH was evaporated off, and the residue was taken up in $CH_2Cl_2$, which was washed with $H_2O$ and brine, dried, and concentrated to dryness. Chromatography of

(17) Heathcock, C. H.; Davidsen, S. K.; Hug, K. T.; Flippin, L. A. *J. Org. Chem.* **1986**, *51*, 3027. (b) Heathcock, C. H.; Hug, K. T.; Flippin, L. A. *Tetrahedron Lett.* **1984**, *24*, 5973. (c) Reetz, M. T.; Hullmann, M.; Massa, W.; Berger, S.; Rademacher, P.; Heymanns, P. *J. Am. Chem. Soc.* **1986**, *108*, 2405.

(18) Gennari[14] interpreted this difference in terms of the electronical difference between thiolesters and esters, the former of which have more similar properties to those of the corresponding ketones than the latter.

the residue with $CH_2Cl_2$/*n*-hexane (1/1) afforded the corresponding aldol products as a mixture of the anti (5) and syn (6) isomers.

**Ethyl (2*R**,3*S**)- and (2*R**,3*R**)-3-Hydroxy-2-methyl-3-[2-(trimethylsilyl)phenyl]propionate (5a and 6a).** The aldehyde 1 (39.5 mg, 0.13 mmol) and (*E*)-**4a** (30.5 mg, 0.18 mmol) were treated with $TiCl_4$ (0.18 mmol) and CAN (210 mg, 0.38 mmol) to afford a mixture of **5a** and **6a** (30 mg, 84%, **5a**:**6a** = 71:29). Careful chromatography was repeated several times to provide **5a** and **5b** in pure form. **5a**: colorless crystals, mp 52.5–53 °C (benzene/*n*-hexane); MS *m*/*z* 280 ($M^+$, 0.3), 265 (18), 163 (100); IR 3600 (OH), 1730 (CO) $cm^{-1}$; $^1H$ NMR $\delta$ 7.53–7.29 (m, 4 H, aromatic H), 5.08 (dd, 1 H, *J* = 9.2 and 3.3 Hz, benzylic H), 4.23 (q, 2 H, *J* = 7.3 Hz, $OCH_2CH_3$), 2.98 (dq, 1 H, *J* = 9.2 and 7.3 Hz, CHCO), 2.80 (d, 1 H, *J* = 3.3 Hz, OH), 1.30 (t, 3 H, *J* = 7.3 Hz, $CH_3$), 0.94 (d, 3 H, *J* = 7.3 Hz, $CH_3$), 0.38 (s, 9 H, TMS); $^{13}C$ NMR $\delta$ 176.00, 146.52, 139.25, 134.56, 129.81, 127.39, 125.70, 74.83, 60.70, 46.87, 14.67, 14.09, 0.92; HRMS calcd for $C_{15}H_{24}O_3Si$ 280.1493, found 280.1499. Anal. Calcd for $C_{15}H_{24}O_3Si$: C, 64.24; H, 8.63. Found: C, 64.40; H, 8.68. **6a**: a colorless oil; MS *m*/*z* 280 ($M^+$, 1.2), 265 (26), 163 (100); IR 3550 (OH), 1720 (CO) $cm^{-1}$; $^1H$ NMR $\delta$ 7.58 (d, 1 H, *J* = 7.8 Hz, aromatic H), 7.52 (d, 1 H, *J* = 7.8 Hz, aromatic H), 7.34 (t, 1 H, *J* = 7.8 Hz, aromatic H), 7.27 (t, 1 H, *J* = 7.8 Hz, aromatic H), 5.34 (d, 1 H, *J* = 4.3 Hz, benzylic H), 4.19–4.08 (m, 2 H, $OCH_2CH_3$), 2.79–2.75 (m, 1 H, CHCO), 1.24 (d, 3 H, *J* = 7.3 Hz, $CH_3$), 1.19 (t, 3 H, *J* = 7.3 Hz, $CH_3$), 0.37 (s, 9 H, TMS); $^{13}C$ NMR $\delta$ 175.83, 146.76, 137.45, 134.77, 129.00, 127.10, 126.45, 72.90, 60.63, 45.73, 14.04, 10.80, 0.88; HRMS calcd for $C_{15}H_{24}O_3Si$ 280.1493, found 280.1527. Treatment of 1 (31 mg, 0.10 mmol) with (*Z*)-**4a** (24 mg, 0.14 mmol) in the presence of $TiCl_4$ (0.14 mmol) gave, after decomplexation with CAN (164 mg, 0.30 mmol), a mixture of **5a** and **6a** (23 mg, 83%, **5a**:**6a** = 84:16).

**Ethyl (2*R**,3*S**)- and (2*R**,3*R**)-2-Ethyl-3-hydroxy-3-[2-(trimethylsilyl)phenyl]propionate (5b and 6b).** The aldehyde 1 (47.5 mg, 0.15 mmol) and (*E*)-**4b** (36 mg, 0.19 mmol) were treated with $TiCl_4$ (0.19 mmol) and CAN (258 mg, 0.47 mmol) to afford a mixture of **5b** and **6b** (40 mg, 76%, **5b**:**6b** = 66:34). Careful chromatography was repeated several times to provide **5b** and **6b** in pure form. **5b**: a colorless oil; MS *m*/*z* 294 ($M^+$, 0.5), 279 (21), 163 (100), 116 (31), 101 (18); IR 3600 (OH), 1725 (CO) $cm^{-1}$; $^1H$ NMR $\delta$ 7.52–7.25 (m, 4 H, aromatic H), 5.07 (dd, 1 H, *J* = 4.6 and 8.9 Hz, benzylic H), 4.27–4.16 (m, 2 H, $OCH_2CH_3$), 2.83–2.77 (m, 1 H, CHCO), 2.69 (d, 1 H, *J* = 4.6 Hz, OH), 1.65–1.48 (m, 1 H, $CH_2CH_3$), 1.28 (t, 3 H, *J* = 7.2 Hz, $CH_3$), 1.23–1.09 (m, 1 H, $CH_2CH_3$), 0.82 (t, 3 H, *J* = 7.5 Hz, $CH_3$), 0.38 (s, 9 H, TMS); $^{13}C$ NMR $\delta$ 175.33, 147.13, 139.14, 134.70, 129.81, 127.44, 125.55, 74.63, 60.56, 54.99, 23.11, 14.25, 12.04, 0.94; HRMS calcd for $C_{16}H_{26}O_3Si$ 294.1649, found 294.1642. Anal. Calcd for $C_{16}H_{26}O_3Si$: C, 65.26; H, 8.90. Found: C, 65.20; H, 8.91. **6b**: a colorless oil; MS *m*/*z* 294 ($M^+$, 3.8), 279 (90), 249 (13), 179 (14), 163 (97), 131 (15), 116 (100), 101 (34); IR 3600 (OH), 1725 (CO) $cm^{-1}$; $^1H$ NMR $\delta$ 7.57 (d, 1 H, *J* = 7.9 Hz, aromatic H), 7.50 (d, 1 H, *J* = 7.9 Hz, aromatic H), 7.38 (t, 1 H, *J* = 7.9 Hz, aromatic H), 7.26 (t, 1 H, *J* = 7.9 Hz, aromatic H), 5.11 (d, 1 H, *J* = 6.1 Hz, benzylic H), 4.06–3.97 (m, 2 H, $OCH_2CH_3$), 2.78–2.70 (m, 1 H, CHCO), 2.55 (br s, 1 H, OH), 1.87–1.79 (m, 2 H, $CH_2CH_3$), 1.06 (t, 3 H, *J* = 7.2 Hz, $CH_3$), 0.91 (t, 3 H, *J* = 7.5 Hz, $CH_3$), 0.37 (s, 9 H, TMS); $^{13}C$ NMR $\delta$ 174.74, 146.72, 138.19, 134.81, 129.15, 127.26, 126.38, 73.24, 60.27, 53.49, 20.69, 14.00, 11.84, 0.90; HRMS calcd for $C_{16}H_{26}O_3Si$ 294.1649, found 294.1624. Treatment of 1 (107 mg, 0.34 mmol) with (*Z*)-**4b** (95 mg, 0.51 mmol) in the presence of $TiCl_4$ (0.51 mmol) gave, after decomplexation with CAN (566 mg, 1.03 mmol), a mixture of **5b** and **6b** (66 mg, 66%, **5b**:**6b** = 74:26).

***S*-*tert*-Butyl (2*R**,3*S**)- and (2*R**,3*R**)-3-Hydroxy-2-methyl-3-[2-(trimethylsilyl)phenyl]propanethioate (5c and 6c).** The aldehyde 1 (62 mg, 0.20 mmol) and (*E*)-**4c** (66 mg, 0.30 mmol) were treated with $TiCl_4$ (0.30 mmol) and CAN (331 mg, 0.60 mmol) to afford a mixture of **5c** and **6c** (60 mg, 93%, **5c**:**6c** = 93:7). Careful chromatography was repeated several times to provide **5c** and **6c** in pure form. **5c**: a colorless oil; MS *m*/*z* 324 ($M^+$, 0.1), 309 (2.9), 235 (29), 175 (16), 163 (99), 146 (100), 117 (14), 90 (99); IR 3550 (OH), 1670 (CO) $cm^{-1}$; $^1H$ NMR $\delta$ 7.51 (d, 1 H, *J* = 7.8 Hz, aromatic H), 7.44 (d, 1 H, *J* = 7.8 Hz, aromatic H), 7.40 (t, 1 H, *J* = 7.8 Hz, aromatic H), 7.28 (t, 1 H, *J* = 7.8 Hz, aromatic H), 5.11 (d, 1 H, *J* = 8.3 Hz, benzylic H), 3.05 (quin-like, 1 H, *J* = 8.3 Hz, CHCO), 2.61 (br s, 1 H, OH), 1.42 (s, 9 H, *t*-Bu), 0.93 (d, 3 H, *J* = 7.3 Hz, $CH_3$), 0.38 (s, 9 H, TMS); $^{13}C$ NMR $\delta$ 204.35, 146.83, 138.97, 134.57, 129.81, 127.42, 125.89, 74.95, 55.47, 48.29, 29.76, 16.22, 1.01. Anal. Calcd for $C_{17}H_{28}O_2SSi$: C, 62.91; H, 8.70. Found: c, 62.66; H, 9.08. **6c**: colorless crystals, mp 74–74.5 °C (AcOEt/*n*-hexane); MS *m*/*z* 324 ($M^+$, 0.1), 309 (1.6), 235 (9.4), 190 (13), 163 (100), 146 (70), 90 (41); IR 3400 (OH), 1655 (CO) $cm^{-1}$; $^1H$ NMR $\delta$ 7.58 (d, 1 H, *J* = 7.8 Hz, aromatic H), 7.51 (d, 1 H, *J* = 7.8 Hz, aromatic H), 7.38 (t, 1 H, *J* = 7.8 Hz, aromatic H), 7.25 (t, 1 H, *J* = 7.8 Hz, aromatic H), 5.33 (t, 1 H, *J* = 2.4 Hz, benzylic H), 2.99 (d, 1 H, *J* = 2.4 Hz, OH), 2.82–2.76 (m, 1 H, CHCO), 1.44 (s, 9 H, *t*-Bu), 1.23 (d, 3 H, *J* = 7.3 Hz, $CH_3$), 0.36 (s, 9 H, TMS); $^{13}C$ NMR $\delta$ 205.57, 146.42, 137.22, 134.72, 128.90, 126.99, 126.76, 72.56, 53.98, 48.30, 29.69, 11.66, 1.06. Anal. Calcd for $C_{17}H_{28}O_2SSi$: C, 62.91; H, 8.70. Found: C, 63.25; H, 8.40. Treatment of 1 (75.5 mg, 0.24 mmol) with (*Z*)-**4c** (80 mg, 0.37 mmol) in the presence of $TiCl_4$ (0.30 mmol) gave, after decomplexation with CAN (397 mg, 0.72 mmol), a mixture of **5c** and **6c** (77.5 mg, 100%, **9a**:**10a** = 96:4).

***S*-Phenyl (2*R**,3*S**)- and (2*R**,3*R**)-3-Hydroxy-2-methyl-3-[2-(trimethylsilyl)phenyl]propanethioate (5d and 6d).** The aldehyde 1 (69 mg, 0.22 mmol) and (*Z*)-**4d** (63.5 mg, 0.27 mmol) were treated with $TiCl_4$ (0.27 mmol) and CAN (368 mg, 0.67 mmol) to afford a mixture of **5d** and **6d** (63.5 mg, 84%, **5d**:**6d** = 92:8). Careful chromatography was repeated several times to provide **5d** and **6d** in pure form. **5d**: colorless crystals, mp 94.5–95 °C (AcOEt/*n*-hexane); MS *m*/*z* 344 ($M^+$, 0.5), 235 (91), 163 (100), 145 (41), 110 (33); IR 3375 (OH), 1695 (CO) $cm^{-1}$; $^1H$ NMR $\delta$ 7.56–7.24 (m, 9 H, aromatic H), 5.20 (d, 1 H, *J* = 8.9 Hz, benzylic H), 3.33–3.29 (m, 1 H, CHCO), 2.41 (br s, 1 H, OH), 1.02 (d, 3 H, *J* = 7.3 Hz, $CH_3$), 0.37 (s, 9 H, TMS); $^{13}C$ NMR $\delta$ 201.83, 146.43, 139.32, 134.74, 134.52, 129.99, 129.49, 129.22, 127.67, 127.44, 125.86, 75.02, 55.08, 15.73, 0.97; HRMS calcd for $C_{19}H_{24}O_2SSi$ 344.1264, found 344.1235. **6d**: a colorless oil; MS *m*/*z* 344 ($M^+$, 0.3), 235 (36), 163 (100), 145 (17), 110 (28); IR 3550 (OH), 1680 (CO) $cm^{-1}$; $^1H$ NMR $\delta$ 7.62–7.29 (m, 9 H, aromatic H), 5.40 (br s, 1 H, benzylic H), 3.07–3.02 (m, 1 H, CHCO), 2.73 (br s, 1 H, OH), 1.37 (d, 3 H, *J* = 7.3 Hz, $CH_3$), 0.37 (s, 9 H, TMS); $^{13}C$ NMR $\delta$ 202.42, 146.24, 137.38, 134.86, 134.52, 129.56, 129.22, 129.04, 127.22, 126.69, 72.63, 53.93, 11.75, 1.05; HRMS calcd for $C_{19}H_{24}O_2SSi$ 344.1264, found 344.1262.

***S*-*tert*-Butyl (2*R**,3*S**)- and (2*R**,3*R**)-2-Ethyl-3-hydroxy-3-[2-(trimethylsilyl)phenyl]propanethioate (5e and 6e).** The aldehyde 1 (51 mg, 0.16 mmol) and (*E*)-**4e** (46 mg, 0.20 mmol) were treated with $TiCl_4$ (0.20 mmol) and CAN (273 mg, 0.50 mmol) to afford a mixture of **5e** and **6e** (39 mg, 72%, **5e**:**6e** = 90:10). Careful chromatography was repeated several times to provide **5e** and **6e** in pure form. **5e**: a colorless oil; MS *m*/*z* 338 ($M^+$, 0.08), 323 (1.7), 249 (35), 163 (100), 160 (55), 131 (24), 104 (41); IR 3600 (OH), 1670 (CO) $cm^{-1}$; $^1H$ NMR $\delta$ 7.51 (d, 1 H, *J* = 7.8 Hz, aromatic H), 7.44 (d, 1 H, *J* = 7.8 Hz, aromatic H), 7.40 (t, 1 H, *J* = 7.8 Hz, aromatic H), 7.28 (t, 1 H, *J* = 7.8 Hz, aromatic H), 5.07 (dd, 1 H, *J* = 4.3 and 8.2 Hz, benzylic H), 2.87–2.82 (m, 1 H, CHCO), 2.52 (d, 1 H, *J* = 4.3 Hz, OH), 1.68–1.59 (m, 1 H, $CH_2CH_3$), 1.49 (s, 9 H, *t*-Bu), 1.18–1.10 (m, 1 H, $CH_2CH_3$), 0.86 (t, 3 H, *J* = 7.3 Hz, $CH_3$), 0.38 (s, 9 H, TMS); $^{13}C$ NMR $\delta$ 204.00, 147.35, 138.76, 134.66, 127.49, 127.42, 125.91, 75.06, 63.04, 48.66, 29.72, 23.81, 12.08, 1.04. Anal. Calcd for $C_{18}H_{30}O_2SSi$: C, 63.85; H, 8.93. Found: C, 63.56; H, 9.31. **6e**: a colorless oil; MS *m*/*z* 338 ($M^+$, 0.06), 323 (1.4), 249 (13), 163 (100), 160 (42), 131 (13), 104 (31); IR 3375 (OH), 1660 (CO) $cm^{-1}$; $^1H$ NMR $\delta$ 7.58 (d, 1 H, *J* = 7.8 Hz, aromatic H), 7.50 (d, 1 H, *J* = 7.8 Hz, aromatic H), 7.38 (t, 1 H, *J* = 7.8 Hz, aromatic H), 7.27 (t, 1 H, *J* = 7.8 Hz, aromatic H), 5.21 (dd, 1 H, *J* = 2.2 and 5.5 Hz, benzylic H), 2.87–2.82 (m, 1 H, CHCO), 2.75 (d, 1 H, *J* = 2.2 Hz, OH), 1.96–1.82 (m, 2 H, $CH_2CH_3$), 1.42 (s, 9 H, *t*-Bu), 1.00 (t, 3 H, *J* = 7.5 Hz, $CH_3$), 0.45 (s, 9 H, TMS); $^{13}C$ NMR $\delta$ 203.99, 146.33, 138.02, 134.79, 128.97, 127.15, 127.04, 73.30, 61.35, 48.47, 29.54, 20.81, 11.93, 1.15. Anal. Calcd for $C_{18}H_{30}O_2SSi$: C, 63.85; H, 8.93. Found: C, 63.88; H, 9.32. Treatment of 1 (85.5 mg, 0.27 mmol) with (*Z*)-**4e** (80.5 mg, 0.35 mmol) in the presence of $TiCl_4$ (0.35 mmol) gave, after decomplexation with CAN (449 mg, 0.82 mmol), a mixture of **5e** and **6e** (90.5 mg, 99%, **5e**:**6e** = 96:4).

***S*-Phenyl (2*R**,3*S**)- and (2*R**,3*R**)-2-Ethyl-3-hydroxy-3-[2-(trimethylsilyl)phenyl]propanethioate (5f and 6f).** The aldehyde 1 (65 mg, 0.21 mmol) and (*E*)-**4f** (77 mg, 0.31 mmol)

were treated with $TiCl_4$ (0.31 mmol) and CAN (344 mg, 0.63 mmol) to afford a mixture of **5f** and **6f** (69 mg, 93%, **5f**:**6f** = 90:10). Careful chromatography was repeated several times to provide **5f** and **6f** in pure form. **5f**: colorless crystals, mp 85–85.5 °C (AcOEt/*n*-hexane); MS *m*/*z* 358 ($M^+$, 0.2), 249 (62), 163 (100), 131 (23), 110 (23); IR 3400 (OH), 1685 (CO) $cm^{-1}$; $^1H$ NMR δ 7.54–7.25 (m, 9 H, aromatic H), 5.17 (dd, 1 H, *J* = 4.3 and 8.6 Hz, benzylic H), 3.15–3.09 (m, 1 H, CHCO), 2.31 (d, 1 H, *J* = 4.3 Hz, OH), 1.68–1.60 (m, 1 H, $CH_2CH_3$), 1.24–1.16 (m, 1 H, $CH_2CH_3$), 0.94 (t, 3 H, *J* = 7.5 Hz, $CH_3$), 0.39 (s, 9 H, TMS); $^{13}C$ NMR δ 201.44, 146.92, 139.07, 134.77, 134.39, 129.90, 129.47, 129.18, 127.71, 127.62, 125.79, 75.01, 62.59, 23.78, 12.17, 0.96; HRMS calcd for $C_{20}H_{26}O_2SSi$ 358.1422, found 358.1472. Anal. Calcd for $C_{20}H_{26}O_2SSi$: C, 66.99; H, 7.31. Found: C, 67.28; H, 7.64. **6f**: a colorless oil; MS *m*/*z* 358 ($M^+$, 0.4), 249 (73), 163 (100), 131 (22), 110 (29); IR 3600 (OH), 1690 (CO) $cm^{-1}$; $^1H$ NMR 7.63 (d, 1 H, *J* = 7.8 Hz, aromatic H), 7.54 (d, 1 H, *J* = 7.8 Hz, aromatic H), 7.42 (t, 1 H, *J* = 7.8 Hz, aromatic H), 7.36–7.35 (m, 3 H, aromatic H), 7.30 (t, 1 H, *J* = 7.8 Hz, aromatic H), 7.21–7.19 (m, 2 H, aromatic H), 5.21 (d, 1 H, *J* = 5.9 Hz, benzylic H), 3.05 (q-like, 1 H, *J* = 5.9 Hz, CHCO), 2.50 (br s, 1 H, OH), 1.97–1.90 (m, 2 H, $CH_2CH_3$), 1.04 (t, 3 H, *J* = 7.5 Hz, $CH_3$), 0.38 (s, 9 H, TMS); $^{13}C$ NMR δ 200.63, 146.20, 138.28, 134.95, 134.29, 129.43, 129.11, 127.39, 126.83, 73.16, 61.31, 21.33, 11.92, 1.12; HRMS calcd for $C_{20}H_{26}O_2SSi$ 358.1422, found 358.1425.

**General Procedure for the Aldol Reaction of *o*-(Trimethylsilyl)benzaldehyde 7 with *O*-Silyl Ketene Acetals and *O*-Silyl Ketene *O*,*S*-Acetals 4.** To a solution of **7** (1.0 equiv) and a silyl ketene acetal **4** (1.1–2.0 equiv) in dry $CH_2Cl_2$ (5 mL) was added dropwise a solution of $TiCl_4$ in dry $CH_2Cl_2$ (1 M solution, 1.2–2.0 equiv) at −78 °C. The reaction mixture was stirred for 30 min to 2 h at the same temperature. The reaction was monitored by TLC and quenched by addition of saturated $NH_4Cl$ solution (0.5 mL). The reaction mixture was then warmed to room temperature, washed with $H_2O$ and brine, dried, and concentrated to dryness. Chromatography of the residue gave the aldol products. The results are summarized in Table II.

**Asymmetric Aldol Reaction of (+)- and (−)-1 with *O*-Silyl Ketene *O*,*S*-Acetals 4c–f.** Asymmetric aldol reaction of (+)- and (−)-1 with **4c–f** were performed as described for the racemates.

***S*-*tert*-Butyl (−)-(2*R*,3*S*)-3-Hydroxy-2-methyl-3-[2-(trimethylsilyl)phenyl]propanethioate [(−)-5c].** The aldehyde (+)-1 (41 mg, 0.13 mmol) was treated with (*E*)-**4c** (39.5 mg, 0.16 mmol) to yield a mixture of the anti and syn isomers (40.5 mg, 96%, anti:syn = 96:4). Careful chromatography afforded (−)-**5c**: a colorless oil; $[\alpha]^{26}_D$ −61.5° (*c*, 0.22, $CHCl_3$) (96% ee); HRMS calcd for $C_{17}H_{28}O_2SSi$ 324.1577, found 324.1538. Anal. Calcd for $C_{17}H_{28}O_2SSi$: C, 62.91; H, 8.70. Found: C, 63.01; H, 8.75. Similar treatment of (+)-1 (41 mg, 0.13 mmol) with (*Z*)-**4c** (39.5 mg, 0.16 mmol) gave (−)-**5c** [$[\alpha]^{26}_D$ −63.1° (*c*, 0.50, $CHCl_3$) (96% ee)] after careful chromatography of a mixture of the anti and syn isomers (42 mg, 99%, anti:syn = 97:3).

***S*-*tert*-Butyl (+)-(2*S*,3*R*)-3-Hydroxy-2-methyl-3-[2-(trimethylsilyl)phenyl]propanethioate [(+)-5c].** The aldehyde (−)-1 (42 mg, 0.13 mmol) was treated with (*E*)-**4c** (59 mg, 0.27 mmol) to yield a mixture of the anti and syn isomers (40 mg, 95%, anti:syn = 94:6). Careful chromatography afforded (+)-**5c**: a colorless oil; $[\alpha]^{23}_D$ +63.5° (*c*, 0.50, $CHCl_3$) (94% ee). Anal. Calcd for $C_{17}H_{28}O_2SSi$: C, 62.91; H, 8.70. Found: C, 63.15; H, 8.88. Similar treatment of (−)-1 (46.5 mg, 0.15 mmol) with (*Z*)-**4c** (42.5 mg, 0.19 mmol) gave (+)-**5c** [$[\alpha]^{26}_D$ +62.7° (*c*, 0.50, $CHCl_3$) (92% ee)] after careful chromatography of a mixture of the anti and syn isomers (46 mg, 94%, anti:syn = 95:5).

***S*-Phenyl (−)-(2*R*,3*S*)-3-Hydroxy-2-methyl-3-[2-(trimethylsilyl)phenyl]propanethioate [(−)-5d].** The aldehyde (+)-1 (55 mg, 0.18 mmol) was treated with (*Z*)-**4d** (50.5 mg, 0.21 mmol) to yield a mixture of the anti and syn isomers (50 mg, 83%, anti:syn = 90:10). Careful chromatography afforded (−)-**5d**: a colorless oil; $[\alpha]^{27}_D$ −54.8° (*c*, 0.50, $CHCl_3$) (92% ee); HRMS calcd for $C_{19}H_{24}O_2SSi$ 344.1265, found 344.1290.

***S*-Phenyl (+)-(2*S*,3*R*)-3-Hydroxy-2-methyl-3-[2-(trimethylsilyl)phenyl]propanethioate [(+)-5d].** The aldehyde (−)-1 (56.5 mg, 0.18 mmol) was treated with (*Z*)-**4d** (51.5 mg, 0.22 mmol) to yield a mixture of the anti and syn isomers (51.5 mg, 80%, anti:syn = 96:4). Careful chromatography afforded (+)-**5d**: colorless crystals, mp 92–92.5 °C (AcOEt/*n*-hexane); $[\alpha]^{27}_D$ +52.0° (*c*, 0.50, $CHCl_3$) (94% ee). Anal. Calcd for $C_{19}H_{24}O_2SSi$: C, 66.23; H, 7.02. Found: C, 65.89; H, 7.08.

***S*-*tert*-Butyl (−)-(2*R*,3*S*)-2-Ethyl-3-hydroxy-3-[2-(trimethylsilyl)phenyl]propanethioate [(−)-5e].** The aldehyde (+)-1 (52 mg, 0.17 mmol) was treated with (*E*)-**4e** (49 mg, 0.21 mmol) to yield a mixture of the anti and syn isomers (52 mg, 90%, anti:syn = 96:4). Careful chromatography afforded (−)-**5e**: a colorless oil; $[\alpha]^{27}_D$ −38.1° (*c*, 0.50, $CHCl_3$) (96% ee). Anal. Calcd for $C_{18}H_{30}O_2SSi$: C, 63.85; H, 8.93. Found: C, 63.74; H, 8.99. Similar treatment of (+)-1 (54 mg, 0.18 mmol) with (*Z*)-**4e** (53 mg, 0.22 mmol) gave (−)-**5e** [$[\alpha]^{27}_D$ −39.3° (*c*, 0.50, $CHCl_3$) (94% ee)] after careful chromatography of a mixture of the anti and syn isomers (54 mg, 89%, anti:syn = 94:6).

***S*-*tert*-Butyl (+)-(2*S*,3*R*)-2-Ethyl-3-hydroxy-3-[2-(trimethylsilyl)phenyl]propanethioate [(+)-5e].** The aldehyde (−)-1 (54 mg, 0.18 mmol) was treated with (*E*)-**4e** (49 mg, 0.21 mmol) to yield a mixture of the anti and syn isomers (52 mg, 90%, anti:syn = 91:9). Careful chromatography afforded (+)-**5e**: a colorless oil; $[\alpha]^{27}_D$ +37.8° (*c*, 0.50, $CHCl_3$) (92% ee). Anal. Calcd for $C_{18}H_{30}O_2SSi$: C, 63.85; H, 8.93. Found: C, 63.84; H, 8.91. Similar treatment of (−)-1 (55 mg, 0.18 mmol) with (*Z*)-**4e** (51.5 mg, 0.22 mmol) gave (+)-**5e** [$[\alpha]^{27}_D$ +41.3° (*c*, 0.50, $CHCl_3$) (92% ee)] after careful chromatography of a mixture of the anti and syn isomers (55.5 mg, 91%, anti:syn = 92:8).

***S*-Phenyl (−)-(2*R*,3*S*)-2-Ethyl-3-hydroxy-3-[2-(trimethylsilyl)phenyl]propanethioate [(−)-5f].** The aldehyde (+)-1 (66 mg, 0.21 mmol) was treated with (*Z*)-**4f** (86.5 mg, 0.34 mmol) to yield a mixture of the anti and syn isomers (62 mg, 83%, anti:syn = 90:10). Careful chromatography afforded (−)-**5f**: colorless crystals, mp 84.5–85 °C (AcOEt/*n*-hexane); $[\alpha]^{27}_D$ −70.8° (*c*, 0.50, $CHCl_3$) (>98% ee). Anal. Calcd for $C_{20}H_{26}O_2SSi$: C, 69.99; H, 7.31. Found: C, 66.85; H, 7.35.

***S*-Phenyl (+)-(2*S*,3*R*)-2-Ethyl-3-hydroxy-3-[2-(trimethylsilyl)phenyl]propanethioate [(+)-5f].** The aldehyde (−)-1 (45 mg, 0.14 mmol) was treated with (*Z*)-**4f** (57.5 mg, 0.21 mmol) to yield a mixture of the anti and syn isomers (43 mg, 89%, anti:syn = 89:11). Careful chromatography afforded (+)-**5f**: colorless crystals, mp 84–84.5 °C (AcOEt/*n*-hexane); $[\alpha]^{27}_D$ +67.6° (*c*, 0.50, $CHCl_3$) (>98% ee). Anal. Calcd for $C_{20}H_{26}O_2SSi$: C, 69.99; H, 7.31. Found: C, 66.69; H, 7.31.

**(2*R**,3*S**,1′*S**)-Tricarbonyl[*S*-*tert*-butyl 2-ethyl-3-hydroxy-3-[2-(trimethylsilyl)phenyl]propanethioate]chromium(0) (8).** To a solution of (±)-1 (121.5 mg, 0.39 mmol) and (*Z*)-**4e** (111.5 mg, 0.48 mmol, *E*:*Z* = 5:95) in dry $CH_2Cl_2$ (8 mL) was added dropwise a solution of $TiCl_4$ in dry $CH_2Cl_2$ (1 M solution, 0.48 mL) at −78 °C. After being stirred for 30 min at the same temperature, the reaction mixture was quenched by addition of saturated $NH_4Cl$ solution (1.5 mL), and the reaction mixture was gradually warmed up to room temperature. $H_2O$ (2 mL) was added to the reaction mixture, and the $CH_2Cl_2$ layer was separated. The $H_2O$ layer was extracted with $CH_2Cl_2$. The combined $CH_2Cl_2$ layers were washed with $H_2O$ and brine, dried, and concentrated to dryness. The residue was recrystallized from *n*-hexane/diethyl ether to give pure **8** (116 mg, 65%) as yellow cubic crystals, mp 117–118 °C; MS *m*/*z* 474 ($M^+$, 0.1), 314 (8.8), 230 (35), 163 (100), 126 (24), 90 (15); IR 1975, 1900 (CO), 1645 (CO) $cm^{-1}$; $^1H$ NMR δ 5.58 (t, 1 H, *J* = 6.4 Hz, aromatic H), 5.44 (d, 1 H, *J* = 6.4 Hz, aromatic H), 5.23 (d, 1 H, *J* = 6.4 Hz, aromatic H), 5.15 (t, 1 H, *J* = 6.4 Hz, aromatic H), 4.68 (dd, 1 H, *J* = 4.4 and 6.8 Hz, benzylic H), 3.31 (d, 1 H, *J* = 6.8 Hz, OH), 2.61 (dt-like, 1 H, *J* = 10.3 and 4.4 Hz, CHCO), 2.02–1.93 (m, 1 H, $CH_2CH_3$), 1.62–1.53 (m, 1 H, $CH_2CH_3$), 1.41 (s, 9 H, *t*-Bu), 0.99 (t, 3 H, *J* = 7.3 Hz, $CH_3$), 0.42 (s, 9 H, TMS); $^{13}C$ NMR δ 232.90, 203.68, 121.83, 100.05, 96.68, 94.68, 90.41, 87.48, 72.81, 62.27, 49.24, 29.45, 24.37, 12.13, 1.31; HRMS calcd for $C_{21}H_{30}CrO_5SSi$ 474.0987, found 474.0989. Anal. Calcd for $C_{21}H_{30}CrO_5SSi$: C, 53.14; H, 6.37. Found: C, 53.58; H, 6.46. This aldol product **8** (30 mg, 0.06 mmol) was converted into **5e** (21 mg, 99%) by treatment with CAN (108 mg, 0.18 mmol) in MeOH (5 mL) at −20 °C.

**X-ray Analysis of 8.** Crystal data: $C_{21}H_{30}CrO_5SSi$, M = 474.61, monoclinic, *a* = 11.009 (4) Å, *b* = 19.763 (9) Å, *c* = 12.147 (3) Å, β = 111.07 (2)°, *V* = 2466 (2) $Å^3$, *Z* = 4, $D_c$ = 1.28 $g/cm^3$, space group $P2_1/n$, μ = ($MoK_\alpha$) = 6.06 $cm^{-1}$. A yellow cubic crystal, ca. 0.50 × 0.50 × 0.50 mm, was mounted on a glass fiber. All measurements were made on a Rigaku AFC5R diffractometer. The cell dimensions and intensities were refined by the least-

squares method, using 25 reflections measured on the diffractometer with graphite-monochromated Mo-$K_\alpha$ radiation with $\omega$-scan mode for $2\theta$ less than 55°. The structure was solved by direct method (MITHRIL method[19]). The non-hydrogen atoms were refined anisotropically and the hydrogens isotropically. The final cycle of full-matrix least-squares refinement was based on 2731 observed reflections [$I > 3.00\sigma(I)$]. The final $R$ value was 0.051.

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**Supplementary Material Available:** $^{13}C$ NMR spectra for compounds **5d**, **6a**, **6b**, **6d**, **6f**, and **8**, the $^1H$ NMR spectrum of (−)-**5d**, and tables of bond angles and distances for **8** (12 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

# Ab Initio Study of the Conrotatory Ring Opening of Phospha- and Azacyclobutenes. 2. Diphospha- and Diazacyclobutenes

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The thermally allowed conrotatory ring opening of 1,2-dihydro-1,3-diphosphate (**1**), *trans*- and *cis*-1,2-dihydro-1,2-diphosphete (**2** and **3**), 1,2-dihydro-1,3-diazete (**4**), and *trans*- and *cis*-1,2-dihydro-1,2-diazete (**5** and **6**) is examined using ab initio calculations. The rings, transition structures, and products were fully optimized at HF/6-31G* with single-point energy calculations performed at MP2. The opening of the dihydrodiphosphetes is endothermic while the opening of the dihydrodiazetes is exothermic. The calculated activation barrier for the opening of **3** and **6** is 19.78 and 24.58 kcal mol$^{-1}$, respectively. The ring opening of **1**, **2**, **4**, and **5** can occur via two diastereomeric pathways. Inward rotation of the heteroatom lone pair is favored for all four compounds. The lower barriers are: 28.78 kcal mol$^{-1}$ for **1**, 18.00 kcal mol$^{-1}$ for **2**, 27.82 kcal mol$^{-1}$ for **4**, and 22.95 kcal mol$^{-1}$ for **5**. The structural and energetic differences and trends among these compounds are interpreted in terms of ring strain and orbital interactions.

Electrocyclic ring openings of small rings, particularly four-membered rings, have been of significant interest for their synthetic utility and for the theoretical insight they provide about the nature of pericyclic reaction mechanisms.[1,2] The ring opening of heterosubstituted cyclobutenes allows synthetic access to heterosubstituted butadienes. The heteroatom also affords an additional test of the validity of the Woodward–Hoffman rules of electrocyclic reactions and the ability to explore substituent effects on reaction and activation energies.

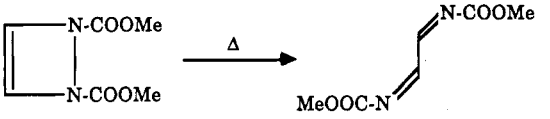
In our previous paper,[3] we examined the ring opening of monoaza- and monophosphacyclobutenes. The MP2/6-31G*//HF/6-31G* activation barriers and the reaction energies for the ring opening of 1,2-dihydrophosphete, 3,4-dihydrophosphete, 1,2-dihydroazete, and 3,4-dihydroazete are listed in Table I. For comparison, the ring opening of cyclobutene is 11.4 kcal mol$^{-1}$ exothermic[4] with a barrier[5,6] of 32.9 kcal mol$^{-1}$. Substitution with phosphorus leads to an endothermic ring opening, since phosphorus can readily accommodate the bond angles of small rings, while the opening of the azetes is exothermic. The activation barrier for the azetes and 3,4-dihydrophosphete are comparable to cyclobutene, but the opening of 1,2-dihydrophosphete is much smaller. There is also a strong preference in both systems for inward rotation of the heteroatom lone pair, which was explained in terms of favorable interactions of the lone pair with the $\sigma^*$ orbital of the breaking ring bond. These results suggest that the phosphetes may readily undergo ring opening reactions, particularly when substituted with groups that will stabilize the phosphabutadienes.

**Table I. Reaction and Activation Energies (kcal mol$^{-1}$) at MP2/6-31G*//HF/6-31G* for the Ring Opening of Cyclobutene and the Dihydroazetes and Dihydrophosphetes**[a]

| reactant | product | $E_a$ | $\Delta E$ |
|---|---|---|---|
| cyclobutene | $H_2C{=}CHCH{=}CH_2$ | 37.36 | −4.96 |
| 1,2-dihydrophosphete | anti-HP=CHCH=$CH_2$ | 24.59 | 0.94 |
| | syn-HP=CHCH=$CH_2$ | 29.56 | 0.99 |
| 3,4-dihydrophosphete | $H_2C{=}PCH{=}CH_2$ | 40.76 | 8.41 |
| 1,2-dihydroazete | anti-HN=CHCH=$CH_2$ | 29.76 | −18.00 |
| | syn-HN=CHCH=$CH_2$ | 37.51 | −17.36 |
| 3,4-dihydroazete | $H_2C{=}NCH{=}CH_2$ | 37.08 | −1.03 |

[a] See ref 3.

**Scheme I**




We turn our attention here to the dihydrodiazetes and dihydrodiphosphetes. There have been only three reports[7-9] of the preparation of substituted 1,2-dihydro-

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