Erythro-Selective Aldol Reaction of Tricarbonyl(η^6-*o*-trialkylsilylbenzaldehyde)chromium(0) Complexes with Cyclic Ketene Silyl Acetals

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The aldol reaction of tricarbonyl(*o*-trimethylsilyl (TMS)-benzaldehyde)chromium(0) complex (1a) with cyclic ketene silyl acetals (2—4) afforded the corresponding *erythro* products selectively. Changing the *ortho* TMS group to a triisopropylsilyl (TIPS) group in the complex brought about an improvement of the *erythro* selectivity in the case of the five-membered acetal (4).

Keywords stereoselective aldol reaction; *erythro* isomer; *threo* isomer; *o*-trimethylsilylbenzaldehyde–chromium complex; *o*-triisopropylsilylbenzaldehyde–chromium complex; cyclic ketene silyl acetal; boron trifluoride etherate; cerium(IV) ammonium nitrate

The stereoselective aldol reaction[1] has been well recognized as one of the most useful tools in organic synthesis. Recently we developed a highly *erythro*-selective aldol reaction[2,3] of tricarbonyl(η^6-*o*-trimethylsilylbenzaldehyde)chromium(0) complex (**1a**)[4] with cyclic silyl enol ethers. This stereoselective aldol reaction was successfully extended to an asymmetric situation[2] where a high enantiomeric excess was attained. In order to evaluate the inherent selectivity of the *o*-trimethylsilyl (TMS)-benzaldehyde–chromium complex (**1a**) in the aldol reaction, we investigated the reaction between **1a** and cyclic ketene silyl acetals (**2**—**4**). This paper describes the *erythro*-selective aldol reaction of the *o*-trialkylsilylbenzaldehyde–chromium(0) complexes (**1a**, **f**) with several cyclic ketene silyl acetals.

At the outset we chose the seven-membered ketene silyl acetal (**2**) as a nucleophile because the seven-membered silyl enol ether had previously been shown to give the highest

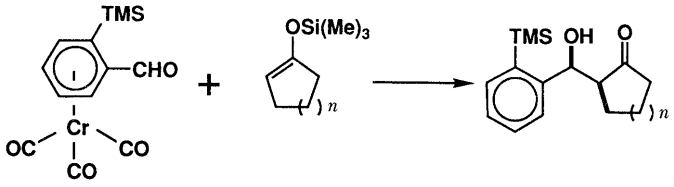
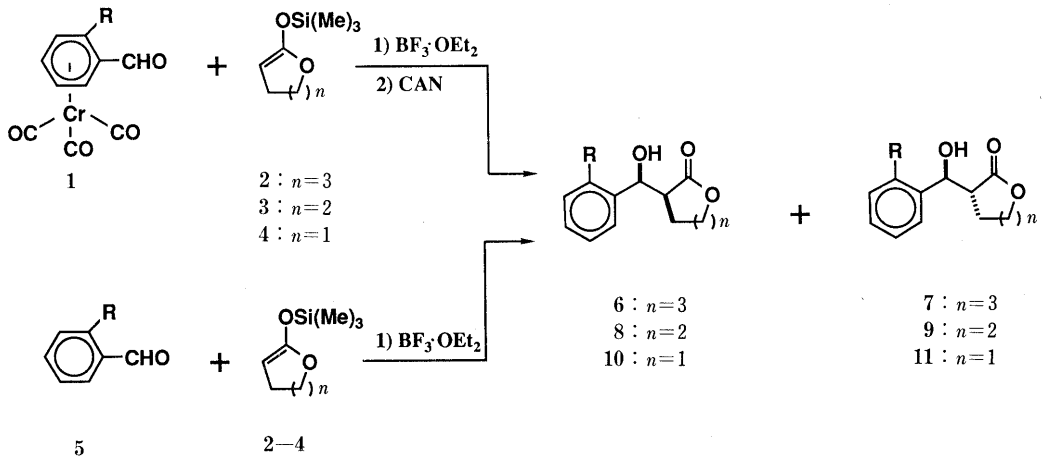


Chart 1

erythro selectivity in our aldol reaction.[2,3] The aldol reaction was carried out as follows. A mixture of the complex (**1a**) and the acetal (**2**) in dry methylene chloride was treated with boron trifluoride etherate ($BF_3 \cdot OEt_2$) under a nitrogen atmosphere at $-78\,^{\circ}C$. After usual work-up, the residue was exposed to cerium(IV) ammonium nitrate (CAN)[5] in methanol at $0\,^{\circ}C$ to give the aldol condensation products in 72% yield. This adduct was found to be made up of the *erythro* and *threo* isomers (**6a** and **7a**) in a ratio of 90 : 10 by careful examination of its proton magnetic resonance (^{1}H-NMR) spectrum. Stereochemical assignment of the *erythro* and *threo* isomers was also made by consideration of the chemical shifts as well as coupling constants of benzylic protons on the basis of the literature precedents.[1] The signal of the benzylic proton of the *erythro* isomer (**6a**) appeared at δ 5.48 ppm as a doublet ($J = 1.5$ Hz), whereas that of the *threo* isomer (**7a**) appeared at δ 5.21 ppm as a doublet of doublets ($J = 9.3$, 3.4 Hz). Thus, the *erythro* isomer (**6a**) was obtained in a highly selective manner. This result was in line with the expectation based on our earlier results[2,3] with cyclic silyl enol ethers.

The *o*-ethylbenzaldehyde–chromium(0) complex (**1b**), however, showed only a good *erythro* selectivity (*erythro* : *threo* = 76 : 24) under identical reaction conditions. This observation was in sharp contrast to the case of the reaction[2,3] between **1b** and 1-trimethylsilyloxycyclohe-



a : R=TMS b : R=Et c : R=Me d : R=OMe e : R=H f : R=TIPS

Chart 2

ptene, where the corresponding *erythro* isomer was exclusively formed. Other *ortho* substituents such as methyl and methoxy groups in the chromium complex exhibited much less selectivity, as anticipated.[2] Interestingly, the benzaldehyde–chromium complex (**1e**) provided the *threo* isomer predominantly, although the selectivity is rather low. The results obtained are summarized in Table I. Control experiments using the *ortho* substituted benzaldehydes (**5**) afforded the aldol products nonselectively (Table II) except for **5e**, which showed a moderate *threo* selectivity, as the complex (**1e**) did. This *threo*-selective reaction of **5e** is understandable based on the moderate *threo* selectivity observed in the reaction of **5e**[1,6] with trimethylsilyloxycyclohexene.

Since the *o*-TMS-benzaldehyde–chromium complex (**1a**) was found to provide the highest selectivity, we next examined the aldol reaction of **1a** with the six- and five-membered ketene silyl acetals (**3** and **4**). Upon treatment with **3** under conditions similar to those described for **2**, **1a** yielded a mixture of **8a** and **9a** in a ratio of 87 : 13, the *erythro* selectivity of which is in good agreement with that observed for **2**. However, it disappointingly became manifest that contracting the ring size from six to five enormously decreased the *erythro* selectivity. Indeed **1a** furnished a mixture of **10a** and **11a** in a ratio of 66 : 34 when exposed to **4** (Table I). The uncomplexed aldehyde (**5a**) did not exhibit any selectivity in the aldol reaction (Table II). To sum up these results, the aldol reaction of **1a** with cyclic ketene silyl acetals afforded the *erythro* isomer in a stereoselective manner, but the selectivity is generally lower than that obtained from the reaction between **1a** and cyclic silyl enol ethers.

We previously explained a high *erythro* selectivity obtained from the reaction of **1a** with cyclic silyl enol ethers in terms of an acyclic transition state[2] where the *ortho* TMS group in the complex plays an important role in producing the high selectivity. In the favorable transition states (A_1 and B_1), the smallest substituent, the hydrogen on the double bond of the silyl enol ether was placed in the most sterically demanding position to minimize the nonbonding interaction with the bulky *ortho* TMS moiety. When cyclic ketene silyl acetals (Chart 3, X = O: **2**—**4**) were employed instead of cyclic silyl enol ethers (X = CH_2), there was another significant interaction to be considered. Namely unfavorable dipole–dipole interaction between the ethereal oxygen of the acetals and the aldehyde oxygen might exist in the transition states (A_1 and B_1). This interaction seems not to be serious in other staggered transition states (A_2, A_3, B_2, and B_3). Therefore, the reaction might be able to proceed *via* other transition states besides A_1, resulting in a decrease of the *erythro* selectivity. The above analysis can also be applied to interpret the low *erythro* selectivity of **4** in comparison with that of **2** and **3**. Molecular model examination indicated that the dipole–dipole interaction is much severer in the case of the five-membered acetal (**4**) than in seven- and six-membered ones (**2** and **3**). If the *ortho* silyl group in the complex is sterically large enough to prevent an approach of substituents other than the smallest one, hydrogen, on the double bond of the cyclic acetal, steric factors will override electronic factors and again favor the transition state (A_1) leading to the *erythro* isomer. On the basis of the above consideration, we pursued the reaction of the chromium complex having the triisopropylsilyl (TIPS)

Table I. Aldol Reaction of Chromium-Complexes (**1**) with Cyclic Ketene Silyl Acetals (**2**—**4**)

Entry	Aldehyde	R	Ketene silyl acetal	Product[a]	Yield[b] (%)
1	**1a**	TMS	**2**	**6a** : **7a** = 90 : 10	72
2	**1b**	Et	**2**	**6b** : **7b** = 76 : 24	87
3	**1c**	Me	**2**	**6c** : **7c** = 66 : 34	98
4	**1d**	OMe	**2**	**6d** : **7d** = 53 : 47	62
5	**1e**	H	**2**	**6e** : **7e** = 33 : 67	63
6	**1a**	TMS	**3**	**8a** : **9a** = 87 : 13	61
7	**1a**	TMS	**4**	**10a** : **11a** = 66 : 34	91
8	**1f**	TIPS	**4**	**10f** : **11f** = 85 : 15	98
9	**1f**	TIPS	**3**	**8f** : **9f** = 83 : 17	85
10	**1f**	TIPS	**2**	**6f** : **7f** = 67 : 33	100

a) Ratios were determined from the 400-MHz ^{1}H-NMR spectra. *b*) Yield of a mixture of *erythro* and *threo* isomers.

Table II. Aldol Reaction of *o*-Substituted Benzaldehydes (**5**) with Cyclic Ketene Silyl Acetals (**2**—**4**)

Entry	Aldehyde	R	Ketene silyl acetal	Product[a]	Yield[b] (%)
1	**5a**	TMS	**2**	**6a** : **7a** = 47 : 53	99
2	**5b**	Et	**2**	**6b** : **7b** = 55 : 45	70
3	**5c**	Me	**2**	**6c** : **7c** = 47 : 53	94
4	**5d**	OMe	**2**	**6d** : **7d** = 54 : 46	88
5	**5e**	H	**2**	**6e** : **7e** = 22 : 78	99
6	**5a**	TMS	**3**	**8a** : **9a** = 42 : 58	66
7	**5a**	TMS	**4**	**10a** : **11a** = 47 : 53	85
8	**5f**	TIPS	**4**	**10f** : **11f** = 70 : 30	99
9	**5f**	TIPS	**3**	**8f** : **9f** = 84 : 16	98
10	**5f**	TIPS	**2**	**6f** : **7f** = 76 : 24	98

a) Ratios were determined from the 400-MHz ^{1}H-NMR spectra. *b*) Yield of a mixture of *erythro* and *threo* isomers.

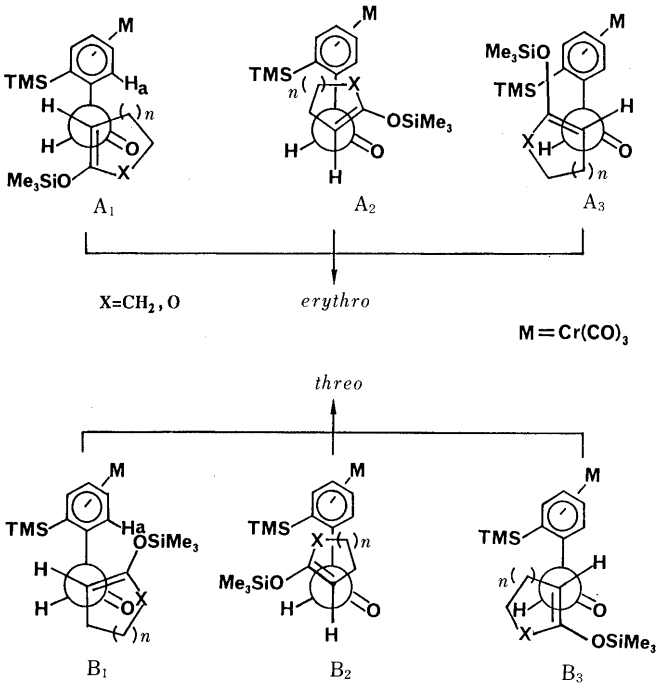


Chart 3

group at the *ortho* position.

The required *o*-TIPS-benzaldehyde–chromium complex (**1f**) was prepared according to the literature.[7] We first performed the aldol reaction of **1f** with the five-membered acetal (**4**) under the standard conditions to give the aldol adducts in 98% yield. The ratio of the *erythro* and *threo* isomers was determined to be 85 : 15. The *erythro* selectivity was greatly improved in comparison with the *o*-TMS-benzaldehyde derivative (**1a**) (*erythro* : *threo* = 66 : 34). A six-membered acetal (**3**) also showed a high *erythro* selectivity (*erythro* : *threo* = 83 : 17). However, the seven-membered acetal (**2**), the best nucleophile for *erythro* selectivity in the reaction of **1a**, produced a mixture of the *erythro* and *threo* isomers, the ratio of which was found to be only 67 : 33 (Table I). The *erythro* selectivity observed here was much lower than that of the *o*-TMS derivative (**1a**). In addition, control experiments using *o*-TIPS-benzaldehyde (**5f**) consistently provided a good *erythro* selectivity as shown in Table II.

We could not interpret all of these results in terms of only the aforementioned mechanism. However, we found that a high *erythro* selectivity could be achieved by appropriate choice of the *ortho* trialkylsilyl group (TMS or TIPS) in the chromium complex.

Experimental

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectra were measured with a JASCO A-102 spectrometer in $CHCl_3$, mass spectra (MS) with a Hitachi M-80 mass spectrometer, and ^{1}H-NMR spectra with a JEOL JNM-GX 400 spectrometer in $CDCl_3$. Silica gel (Silica gel 60, 230—400 mesh, Nacalai Tesque) was used for chromatography. All reactions were carried out under a nitrogen atmosphere. Organic extracts were dried over anhydrous Na_2SO_4. The starting chromium complexes (**1a**,[2] **b**,[2] **c**,[8] **d**,[8] **e**,[8] **f**[7]) were prepared according to the literature.

General Procedure for the Aldol Reaction of the Chromium Complexes (1) with Cyclic Ketene Silyl Acetals (2—4) A solution of $BF_3 \cdot OEt_2$ in dry CH_2Cl_2 (1 M solution, 1.2—2.0 eq) was slowly added to a solution of one of the complexes (**1**, 1.0 eq) and a ketene silyl acetal (**2**—**4**, 1.1—2.0 eq) in dry CH_2Cl_2 (5 ml) at −78 °C. The reaction mixture was stirred at the same temperature for 30 min—3 h. The reaction was monitored by thin-layer chromatography (TLC) and quenched by addition of saturated NH_4Cl solution (0.5 ml). The reaction mixture was washed with H_2O and brine, dried, and concentrated. The residue was then dissolved in MeOH (5 ml). CAN (3.0 eq) was added portionwise to the stirred MeOH solution at −20 °C. Stirring was continued until the decomplexation was completed (monitored by TLC, 10—20 min). MeOH was evaporated off and the residue was taken up in CH_2Cl_2. The CH_2Cl_2 solution was washed with H_2O and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–AcOEt (10 : 1—4 : 1) afforded the corresponding aldol product as a mixture of the *erythro* (**6**, **8**, **10**) and *threo* (**7**, **9**, **11**) isomers.

(*R,*R**)- and (*R**,*S**)-2-[Hydroxy(2-trimethylsilylphenyl)methyl]-6-hexanolide (6a and 7a)** The aldehyde (**1a**) (53 mg, 0.17 mmol) and **2** (40 mg, 0.21 mmol) were treated with a solution of $BF_3 \cdot OEt_2$ in dry CH_2Cl_2 (0.25 ml) and then with CAN (283 mg, 0.52 mmol) to afford a mixture of **6a** and **7a** (36 mg, 90%, **6a** : **7a** = 90 : 10). Careful chromatography was repeated several times to provide **6a** and **7a** in pure form. **6a**: A colorless solid, mp 97—97.5 °C (AcOEt–hexane). IR ν_{max} cm^{-1}: 3550 (OH), 1710 (C=O). ^{1}H-NMR δ: 7.61—7.28 (4H, m, aromatic H), 5.48 (1H, d, J = 1.5 Hz, benzylic H), 4.35—4.10 (m, 2H), 3.44 (1H, br s, OH), 2.76—2.74 (1H, m), 2.09—1.28 (6H, m), 0.32 (9H, s, TMS). MS m/z (%): 292 (M^+, 0.38), 163 (100). *Anal.* Calcd for $C_{16}H_{24}O_3Si$: C, 65.71; H, 8.27. Found: C, 65.67; H, 8.49. **7a**: A colorless solid, mp 142—143 °C (AcOEt–hexane). IR ν_{max} cm^{-1}: 3550 (OH), 1715 (C=O). ^{1}H-NMR δ: 7.54—7.29 (4H, m, aromatic H), 5.21 (1H, dd, J = 9.3, 3.4 Hz, benzylic H), 4.38—4.36 (2H, m), 3.54 (1H, d, J = 3.4 Hz, OH), 3.17—3.14 (1H, m), 1.94—1.31 (6H, m), 0.37 (9H, s, TMS). MS m/z (%): 292 (M^+, 0.16), 163 (100). *Anal.* Calcd for $C_{16}H_{24}O_3Si$: C, 65.71; H, 8.27. Found: C, 65.46; H, 8.51.

(*R,*R**)- and (*R**,*S**)-2-[(2-Ethylphenyl)hydroxymethyl]-6-hexanolide (6b and 7b)** The aldehyde (**1b**) (57 mg, 0.21 mmol) and **2** (79 mg, 0.43 mmol) were treated with a solution of $BF_3 \cdot OEt_2$ in dry CH_2Cl_2 (0.42 ml) and then with CAN (346 mg, 0.63 mmol) to afford a mixture of **6b** and **7b** (46 mg, 87%, **6b** : **7b** = 76 : 24). Careful chromatography was repeated several times to provide **6b** and **7b** in pure form. **6b**: Colorless plates, mp 84—84.5 °C (AcOEt–hexane). IR ν_{max} cm^{-1}: 3400 (OH), 1710 (C=O). ^{1}H-NMR δ: 7.71—7.11 (4H, m, aromatic H), 5.49 (1H, br s, benzylic H), 4.25—3.96 (2H, m), 2.86—2.20 (4H, m), 1.97—1.04 (6H, m), 1.24 (3H, t, J = 7.6 Hz, $CH_2C\underline{H}_3$). MS m/z (%): 248 (M^+, 0.46), 114 (100). *Anal.* Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.53; H, 8.49. **7b**: A colorless solid, mp 97.5—99 °C (AcOEt–hexane). IR ν_{max} cm^{-1}: 3400 (OH), 1710 (C=O). ^{1}H-NMR δ: 7.54—7.06 (4H, m, aromatic H), 5.24 (1H, d, J = 9.3 Hz, benzylic H), 4.31—4.18 (2H, m), 3.17—2.20 (4H, m), 2.01—1.04 (6H, m), 1.24 (3H, t, J = 7.6 Hz, $CH_2C\underline{H}_3$). MS m/z (%): 248 (M^+, 0.27), 114 (100). *Anal.* Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.24; H, 8.46.

(*R,*R**)- and (*R**,*S**)-2-[Hydroxy(2-methylphenyl)methyl]-6-hexanolide (6c and 7c)** The aldehyde (**1c**) (149 mg, 0.58 mmol) and **2** (164 mg, 0.88 mmol) were treated with a solution of $BF_3 \cdot OEt_2$ in dry CH_2Cl_2 (1.2 ml) and then with CAN (958 mg, 1.75 mmol) to afford a mixture of **6c** and **7c** (133 mg, 98%, **6c** : **7c** = 66 : 34). Careful chromatography was repeated several times to provide **6c** and **7c** in pure form. **6c**: Colorless pillars, mp 92.5—93 °C (AcOEt–hexane). IR ν_{max} cm^{-1}: 3550 (OH), 1710 (C=O). ^{1}H-NMR δ: 7.58—7.14 (4H, m, aromatic H), 5.43 (1H, br s, benzylic H), 4.37—4.15 (2H, m), 3.58 (1H, d, J = 2.8 Hz, OH), 2.76—2.74 (1H, m), 2.29 (3H, s, CH_3), 1.99—1.24 (6H, m). MS m/z (%): 234 (M^+, 6.9), 114 (100). *Anal.* Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.85; H, 8.00. **7c**: A colorless solid, mp 131.5—132.5 °C (AcOEt–hexane). IR ν_{max} cm^{-1}: 3400 (OH), 1715 (C=O). ^{1}H-NMR δ: 7.41—7.18 (4H, m, aromatic H), 5.19 (1H, d, J = 10.5 Hz, benzylic H), 4.36—3.33 (2H, m), 3.60 (1H, br s, OH), 3.03—3.02 (1H, m), 2.39 (3H, s, CH_3), 1.90—1.44 (6H, m). MS m/z (%): 234 (M^+, 1.3), 114 (100). *Anal.* Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.50; H, 7.88.

(*R,*R**)- and (*R**,*S**)-2-[Hydroxy(2-methoxyphenyl)methyl]-6-hexanolide (6d and 7d)** The aldehyde (**1d**) (138 mg, 0.51 mmol) and **2** (113 mg, 0.61 mmol) were treated with a solution of $BF_3 \cdot OEt_2$ in dry CH_2Cl_2 (0.76 ml) and then with CAN (834 mg, 1.52 mmol) to afford a mixture of **6d** and **7d** (78 mg, 62%, **6d** : **7d** = 53 : 47). Careful chromatography was repeated several times to provide **6d** and **7d** in pure form. **6d**: Colorless pillars, mp 125—125.5 °C (AcOEt–hexane). IR ν_{max} cm^{-1}: 3550 (OH), 1710 (C=O). ^{1}H-NMR δ: 7.57—6.86 (4H, m, aromatic H), 5.46 (1H, br s, benzylic H), 4.34—4.18 (2H, m), 3.83 (3H, s, OMe), 3.78 (1H, d, J = 3.1 Hz, OH), 3.04—3.01 (1H, m), 1.89—1.23 (6H, m). MS m/z (%): 250 (M^+, 13.3), 137 (100). *Anal.* Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.00; H, 7.38. **7d**: A pale yellow solid, mp 79.5—80 °C (AcOEt–hexane). IR ν_{max} cm^{-1} 3400 (OH), 1715 (C=O). ^{1}H-NMR: δ: 7.52—6.83 (4H, m, aromatic H), 5.26 (1H, d, J = 7.1 Hz, benzylic H), 4.41—4.01 (3H, m), 3.84 (3H, s, OMe), 3.21—2.89 (1H, m), 2.15—1.10 (6H, m). MS m/z (%): 250 (M^+, 9.1), 137 (100). *Anal.* Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 66.97; H, 7.43.

(*R,*R**)- and (*R**,*S**)-2-(1-Hydroxy-1-phenylmethyl)-6-hexanolide (6e and 7e)** The aldehyde (**1e**) (169 mg, 0.70 mmol) and **2** (158 mg, 0.85 mmol) were treated with a solution of $BF_3 \cdot OEt_2$ in dry CH_2Cl_2 (1.05 ml) and then with CAN (1.15 g, 2.10 mmol) to afford a mixture of **6e** and **7e** (96 mg, 63%, **6e** : **7e** = 33 : 67). Careful chromatography was repeated several times to provide **6e** and **7e** in pure form. **6e**: Colorless needles, mp 100—101.5 °C (AcOEt–hexane). IR ν_{max} cm^{-1}: 3550 (OH), 1710 (C=O). ^{1}H-NMR δ: 7.38—7.27 (5H, m, aromatic H), 5.29 (1H, br s, benzylic H), 4.38—4.21 (2H, m), 3.70 (1H, d, J = 2.7 Hz, OH), 2.86—2.83 (1H, m), 1.92—1.25 (6H, m). MS m/z (%): 220 (M^+, 7.3), 114 (100). *Anal.* Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.82; H, 7.40. **7e**: Colorless plates, mp 166.5—167 °C (AcOEt–hexane). IR ν_{max} cm^{-1}: 3500 (OH), 1710 (C=O). ^{1}H-NMR δ: 7.38—7.30 (5H, m, aromatic H), 4.84 (1H, dd, J = 8.6, 4.0 Hz, benzylic H), 4.37—4.29 (2H, m), 3.76 (1H, d, J = 4.0 Hz, OH), 2.96 (1H, dt, J = 8.6, 1.8 Hz), 1.94—1.26 (6H, m). MS m/z (%): 220 (M^+, 9.3), 114 (100). *Anal.* Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.75; H, 7.36.

(*R,*R**)- and (*R**,*S**)-2-[Hydroxy(2-trimethylsilylphenyl)methyl]-5-pentanolide (8a and 9a)** The aldehyde (**1a**) (50 mg, 0.16 mmol) and **3** (56 mg, 0.32 mmol) were treated with a solution of $BF_3 \cdot OEt_2$ in dry CH_2Cl_2 (0.32 ml) and then with CAN (270 mg, 0.49 mmol) to afford a mixture of **8a** and **9a** (27 mg, 61%, **8a** : **9a** = 87 : 13), a colorless solid, mp 120.5—122 °C (AcOEt–hexane). IR ν_{max} cm^{-1}: 3400 (OH), 1730 (C=O). ^{1}H-NMR δ: 7.59—7.26 (4H, m, aromatic H), 5.82 (87/100 × 1H, t, J = 2.8 Hz, benzylic H), 5.09 (13/100 × 1H, dd, J = 9.5, 1.5 Hz), 4.61—4.27 (2H, m),

3.07—2.63 (2H, m), 2.08—1.53 (4H, m), 0.39 (9H, s, TMS). *Anal.* Calcd for $C_{15}H_{22}O_3Si$: C, 64.71; H, 7.96. Found: C, 64.54; H, 8.16.

(*R,*R**)- and (*R**,*S**)-2-[Hydroxy(2-trimethylsilylphenyl)methyl]-4-butanolide (10a and 11a)** The aldehyde (**1a**) (63 mg, 0.20 mmol) and **4** (63 mg, 0.40 mmol) were treated with a solution of $BF_3 \cdot OEt_2$ in dry CH_2Cl_2 (0.40 ml) and then with CAN (340 mg, 0.62 mmol) to afford a mixture of **10a** and **11a** (48 mg, 91%, **10a**:**11a**=66:34), colorless plates, mp 134.5—135.5 °C (AcOEt–hexane). IR ν_{max} cm^{-1}: 3400 (OH), 1770, 1760 (C=O). ^{1}H-NMR δ: 7.58—7.26 (4H, m, aromatic H), 5.64 (66/100×1H, d, J=1.8 Hz, benzylic H), 5.00 (34/100×1H, d, J=9.8 Hz, benzylic H), 4.44—4.11 (2H, m), 3.19—2.66 (2H, m), 2.13—1.74 (2H, m), 0.39 (66/100×9H, s, TMS), 0.37 (34/100×9H, s, TMS). *Anal.* Calcd for $C_{14}H_{20}O_3Si$: C, 63.59; H, 7.62. Found: C, 63.52; H, 7.81.

(*R,*R**)- and (*R**,*S**)-2-[Hydroxy(2-triisopropylsilylphenyl)methyl]-6-hexanolide (6f and 7f)** The aldehyde (**1f**) (106 mg, 0.27 mmol) and **2** (74 mg, 0.40 mmol) were treated with a solution of $BF_3 \cdot OEt_2$ in dry CH_2Cl_2 (0.40 ml) and then with CAN (447 mg, 0.81 mmol) to afford a mixture of **6f** and **7f** (100 mg, quantitative, **6f**:**7f**=67:33). Careful chromatography was repeated several times to provide **6f** and **7f** in pure form. **6f**: A colorless solid, mp 83.5—84.5 °C (AcOEt—hexane). IR ν_{max} cm^{-1}: 3380 (OH), 1715 (C=O). ^{1}H-NMR δ: 7.69—7.26 (4H, m, aromatic H), 5.41 (1H, br s, benzylic H), 4.34—4.05 (2H, m), 3.49 (1H, d, J=2.7 Hz, OH), 2.73—2.70 (1H, m), 2.25—1.24 (9H, m), 1.14 (9H, d, J=7.5 Hz, CHC$\underline{H}_3$), 1.08 (9H, d, J=7.5 Hz, CHC$\underline{H}_3$). Chemical ionization MS m/z (%): 377 (M^++1, 0.1), 41 (100). *Anal.* Calcd for $C_{22}H_{36}O_3Si$: C, 70.16; H, 9.63. Found: C, 69.77; H, 10.01. **7f**: A colorless solid, mp 138.5—139 °C (AcOEt–hexane). IR ν_{max} cm^{-1}: 3400 (OH), 1715 (C=O). ^{1}H-NMR δ: 7.60—7.26 (4H, m, aromatic H), 5.16 (1H, dd, J=9.2, 3.6 Hz, benzylic H), 4.42—4.33 (2H, m), 3.37 (1H, d, J=3.6 Hz, OH), 3.20—3.15 (1H, m), 1.94—1.27 (9H, m), 1.16 (9H, d, J=7.3 Hz, CHC$\underline{H}_3$), 1.14 (9H, d, J=7.3 Hz, CHC$\underline{H}_3$). Chemical ionization MS m/z (%): 377 (M^++1, 0.2), 41 (100). *Anal.* Calcd for $C_{22}H_{36}O_3Si \cdot H_2O$: C, 69.79; H, 10.12. Found: C, 69.65; H, 10.26.

(*R,*R**)- and (*R**,*S**)-2-[Hydroxy(2-triisopropylsilylphenyl)methyl]-5-pentanolide (8f and 9f)** The aldehyde (**1f**) (65 mg, 0.16 mmol) and **3** (42 mg, 0.24 mmol) were treated with a solution of $BF_3 \cdot OEt_2$ in dry CH_2Cl_2 (0.24 ml) and then with CAN (274 mg, 0.50 mmol) to afford a mixture of **8f** and **9f** (50 mg, 85%, **8f**:**9f**=83:17), a colorless solid, mp 124—125 °C (AcOEt–hexane). IR ν_{max} cm^{-1}: 3430 (OH), 1725 (C=O). ^{1}H-NMR δ: 7.62—7.25 (4H, m, aromatic H), 5.71 (83/100×1H, br s, benzylic H), 5.00 (17/100×1H, d, J=9.1 Hz, benzylic H), 4.43—4.19 (2H, m), 2.99—2.62 (2H, m), 2.16—1.23 (7H, m), 1.19—1.11 (18H, m, CHC$\underline{H}_3$). Chemical ionization MS m/z (%): 363 (M^++1, 0.5), 41 (100).

(*R,*R**)- and (*R**,*S**)-2-[Hydroxy(2-triisopropylsilylphenyl)methyl]-4-butanolide (10f and 11f)** The aldehyde (**1f**) (60 mg, 0.15 mmol) and **4** (35 mg, 0.22 mmol) were treated with a solution of $BF_3 \cdot OEt_2$ in dry CH_2Cl_2 (0.23 mmol) and then with CAN (250 mg, 0.46 mmol) to afford a mixture of **10f** and **11f** (52 mg, 98%, **10f**:**11f**=85:15). Careful chromatography was repeated several times to provide **10f** and **11f** in pure form. **10f**: A colorless solid, mp 124—124.5 °C (AcOEt–hexane). IR ν_{max} cm^{-1}: 3375 (OH), 1770 (C=O). ^{1}H-NMR δ: 7.58—7.27 (4H, m, aromatic H), 5.54 (1H, br s, benzylic H), 4.45—4.11 (2H, m), 2.86—2.12 (3H, m), 2.21 (1H, d, J=3.7 Hz, OH), 1.68—1.48 (3H, m, C$\underline{H}$CH$_3$), 1.17 (9H, d, J=7.3 Hz, CHC$\underline{H}_3$), 1.12 (9H, d, J=7.3 Hz, CHC$\underline{H}_3$). Chemical ionization MS m/z (%): 349 (M^++1, 4.3), 87 (100). *Anal.* Calcd for $C_{20}H_{32}O_3Si$: C, 68.92; H, 9.25. Found: C, 68.45; H, 9.60. **11f**: A colorless solid, mp 99—101 °C (AcOEt–hexane). IR ν_{max} cm^{-1}: 3500 (OH), 1755 (C=O). ^{1}H-NMR δ: 7.58—7.29 (4H, m, aromatic H), 4.92 (1H, dd, J=9.2, 1.5 Hz, benzylic H), 4.36—4.16 (2H, m), 4.33 (1H, d, J=1.5 Hz, OH), 3.24—3.17 (1H, dt, J=9.2, 11.6 Hz), 2.03—1.75 (2H, m), 1.50—1.40 (3H, m, C$\underline{H}$CH$_3$), 1.14 (9H, d, J=7.3 Hz, CHC$\underline{H}_3$), 1.12 (9H, d, J=7.3 Hz, CHC$\underline{H}_3$). Chemical ionization MS m/z (%): 349 (M^++1, 1.3), 87 (100). *Anal.* Calcd for $C_{20}H_{32}O_3Si$: C, 68.92; H, 9.25. Found: C, 68.68; H, 9.60.

General Procedure for the Aldol Reaction of *o*-Substituted Benzaldehydes (5) with Cyclic Ketene Silyl Acetals (2—4) A solution of $BF_3 \cdot OEt_2$ in dry CH_2Cl_2 (1 M solution, 1.2—2.0 eq) was slowly added to a solution of **5** (1.0 eq) and a ketene silyl acetal (**2**—**4**, 1.2—2.0 eq) in dry CH_2Cl_2 (5 ml) at −78 °C. The reaction mixture was stirred for 30 min—3 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 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.

References and Notes

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