Tetrahedron 68 (2012) 4210–4224

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Construction of quaternary carbon centers by a base-catalyzed enantioselective aldol reaction and related reactions of trimethoxysilyl enol ethers

Tomonori Ichibakase [a], Tetsuya Kaneko [a], Yuya Orito [a], Shunsuke Kotani [b], Makoto Nakajima [a,*]

[a] Graduate School of Pharmaceutical Sciences, Kumamoto University, 5-1 Oe-honmachi, Kumamoto 862-0973, Japan
[b] Priority Organization for Innovation and Excellence, Kumamoto University, 5-1 Oe-honmachi, Kumamoto 862-0973, Japan

ARTICLE INFO

Article history:
Received 25 February 2012
Received in revised form 21 March 2012
Accepted 23 March 2012
Available online 29 March 2012

Keywords:
Aldol reaction
Aldol-Tishchenko reaction
Lithium binaphtholate
Trimethoxysilyl enol ether

ABSTRACT

The aldol reactions of trimethoxysilyl enol ethers catalyzed by lithium binaphtholate were found to be powerful tools for the construction of quaternary asymmetric carbon centers. The stereoselectivities were greatly affected by the presence of water. Trimethoxysilyl enol ether derived from a cyclic ketone, such as cyclohexanone, was used as a substrate to obtain the *anti*-adduct preferentially under anhydrous conditions; by contrast, the *syn*-adduct was preferentially obtained under aqueous conditions with high stereoselectivity. The aldol-Tishchenko reaction of a trimethoxysilyl enol ether derived from acyclic ketones proceeded to give monoacyl 1,3-diol derivatives in high enantioselectivities.

1. Introduction

Quaternary asymmetric centers are found in a variety of organic compounds, including many natural and bioactive products. The efficient construction of asymmetric quaternary carbon stereocenters is a fascinating topic in organic chemistry.[1,2] Many examples of Diels–Alder reactions[3] or Michael additions[2h,4] have achieved the stereoselective formation of quaternary carbon centers; however, few examples of aldol reactions[5] for the construction of asymmetric quaternary centers have been reported.[6,7] Retro-aldol reactions readily proceed under acidic or basic conditions because aldol products with quaternary carbon atoms are sterically congested, thereby decreasing the stereoselectivity and chemical yield of the products.

The development of enantioselective aldol reactions has been led by Lewis acid-catalyzed reactions of trimethylsilyl enol ethers with carbonyl compounds, the so-called Mukaiyama aldol reaction.[8] Recently, Lewis base-catalyzed asymmetric aldol reactions[9] have attracted considerable attention because Lewis base-catalyzed aldol reactions of a trichlorosilyl enol ether give the *syn*-adduct from the *Z*-enol ether and the *anti*-adduct from the *E*-enol ether via cyclic transition state structures involving hypervalent silicates.[10] We previously described asymmetric aldol reactions of trichlorosilyl enol ethers catalyzed by chiral *N*-oxides[11] or phosphine oxides[12] as Lewis bases; however, aldol reactions of trichlorosilyl enol ether are not widely utilized in organic synthesis because trichlorosilyl enol ethers are extremely sensitive to water. We previously reported a lithium binaphtholate-catalyzed[13] asymmetric aldol reaction of trimethoxysilyl enol ethers,[14,15] which are more stable than trichlorosilyl enol ethers. Herein, we describe the enantioselective formation of quaternary carbon stereocenters utilizing base-catalyzed aldol reactions of trimethoxysilyl enol ethers.[16]

2. Results and discussion

2.1. Development of a new method for the preparation of trimethoxysilyl enol ethers

In a previous report, trimethoxysilyl enol ethers were prepared by reacting enolates with chlorotrimethoxysilane, or by reacting α,β-unsaturated ketones with trimethoxysilane in the presence of Rh(I) catalyst (Fig. 1).[14] However, the preparation of chlorotrimethoxysilane in high purity was troublesome, whereas the

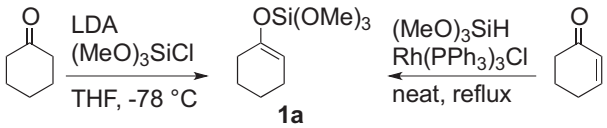


Fig. 1. Previous synthetic method for obtaining trimethoxysilyl enol ethers.

* Corresponding author. Tel.: +81 96 371 4680; fax: +81 96 362 7692; e-mail address: nakajima@gpo.kumamoto-u.ac.jp (M. Nakajima).

0040-4020/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2012.03.096

latter method was applicable to the synthesis of limited silyl enol ethers.

Therefore, we began to explore a practical and convenient method for preparing trimethoxysilyl enol ethers (Fig. 2). As an alterative silylating reagent, we focused on trimethoxysilyl triflate.[18] Trimethoxysilyl triflate is a readily available silicon source with high purity, prepared by mixing allyltrimethoxysilane and triflic acid in dichloromethane. The prepared solution of trimethoxysilyl triflate was directly added dropwise to a solution of cyclohexane and triethylamine at 0 °C. The reaction proceeded smoothly to furnish the corresponding trimethoxysilyl enol ether **1a** in high yield. We next applied this protocol to the silylation of 2-methylcyclohexanone, and trimethoxysilyl enol ethers were obtained as regioisomers, the thermodynamically stable trimethoxysilyl enol ether **1b**, and the kinetic product, trimethoxysilyl enol ether **1b′** (**1b**/**1b′**=60:40). To obtain **1b** as a single isomer, we screened reaction conditions and found that the use of tetra-*n*-butylammonium iodide as an additive in chloroform under reflux conditions improved the regioselectivity to give the desired trimethoxysilyl enol ethers **1b** (**1b**/**1b′**=>99:1). This procedure yielded the trimethoxysilyl enol ethers **1c**–**h** from the corresponding ketones in high yields and in high purity.[17] The present facile and versatile method provides access to trimethoxysilyl enol ethers with high purity. Other trimethoxysilyl enol ethers **1i**–**k** were prepared using a Rh-catalyzed conjugated reduction in the presence of trimethoxysilane.

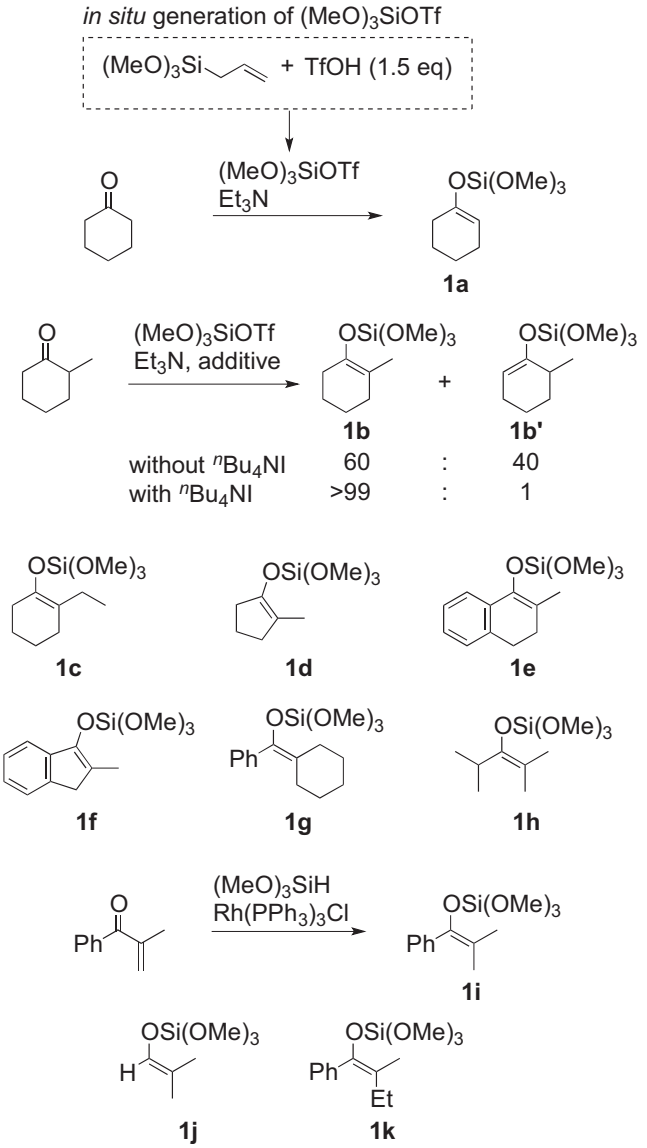


Fig. 2. Synthesis of the trimethoxysilyl enol ethers **1**.

2.2. Construction of quaternary asymmetric centers by base-catalyzed aldol reaction

2.2.1. Under anhydrous conditions. With the desired silyl enol ethers in hand, we carried out the aldol reaction of the trimethoxysilyl enol ether **1b** and the benzaldehyde **2a** in the presence of the dilithium salt of 3,3′-dibromobinaphthol (**3e**, 10 mol %) at −23 °C, according to our procedure described previously (Fig. 3).[14] The reaction proceeded smoothly, and the aqueous work-up with KF/KH_2PO_4 and silica gel column chromatography gave the mixture of *syn*-**4ba** and *anti*-**4ba** [96% yield, *syn*/*anti*=1:27, 81% ee (*anti*)].[19]

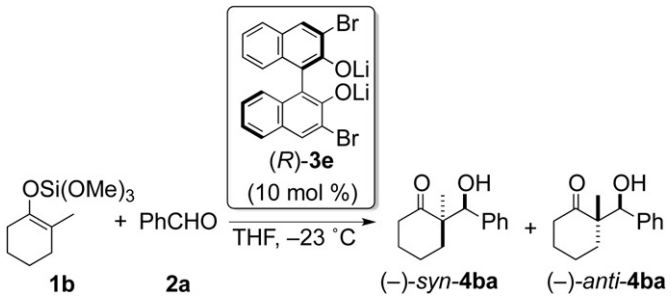


Fig. 3. Aldol reactions of trimethoxysilyl enol ether **1b** with **2a**.

Surprisingly, we found that the chemical yields and stereoselectivities of the product **4ba** were not reproducible across multiple experiments due to the retro-aldol reaction during the aqueous work-up (HCl or KF/KH_2PO_4) and silica gel column chromatography. A screen of quenching conditions revealed that the use of an aqueous solution of potassium fluoride and formic acid (KF/HCOOH) minimized the occurrence of the retro-aldol reaction. We also found that careful addition of acetic acid to the eluent suppressed the retro-aldol reaction during the silica gel column chromatography step, which isolated the aldol product **4ba**; however, to facilitate manipulation, the crude product was directly benzoylated with benzoyl chloride and isolated as the benzoate **5ba** to improve the accuracy of data collection (Fig. 4). Improvements in these isolation methods (quenching method and derivatization) increased both the yield and the stereoselectivity of the aldol products and secured reproducible results.

The relative stereochemistry (*syn* and *anti*) was assigned by comparison with the NMR data in the literature.[20] Although the absolute configurations were not determined, we confirmed that both *syn*-**4ba** and *anti*-**4ba** had the same absolute configuration at the benzylic position upon oxidation of *syn*-**4ba** and *anti*-**4ba** to **6ba** (Fig. 5).

Next, we screened the substituents at the 3,3′-positions of the catalyst **3** (Table 1). The unsubstituted binaphthol **3a** and the methyl substituted binaphtholate **3b** gave lower stereoselectivities (entries 1 and 2). The phenyl substituted binaphtholate **3c** improved the enantioselectivity but decreased the reactivity (entry 3). Among the halogen-substituted binaphtholates, **3d**–**f**, containing chloro or bromo groups, gave better yields and selectivities (entries 4 and 5). Lowering the reaction temperature to −45 °C with dilithium binaphtholate **3d** as a catalyst improved the enantioselectivities, although the reaction times were extended.

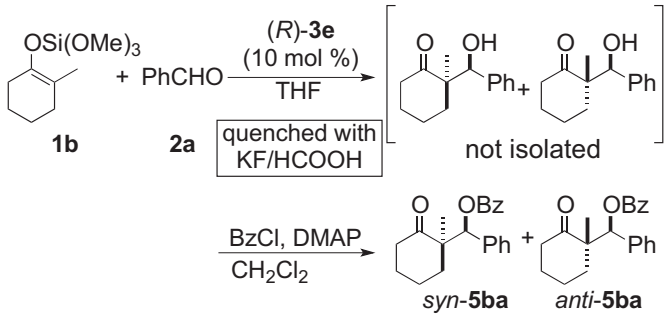


Fig. 4. Practical isolation of aldol adducts.

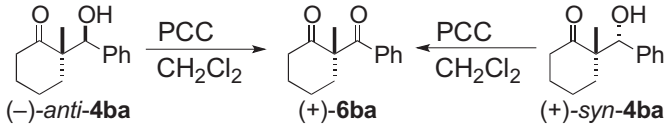
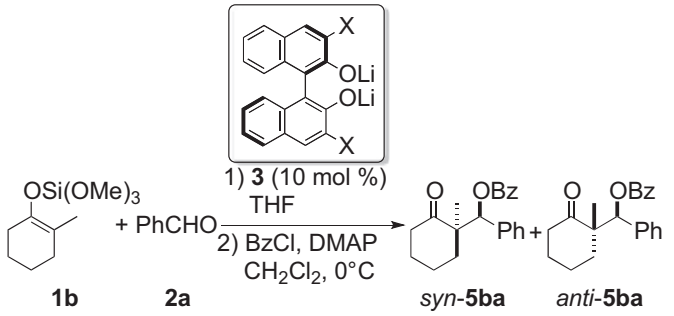


Fig. 5. Relationship between the relative configurations of the aldol adducts **4ba**.

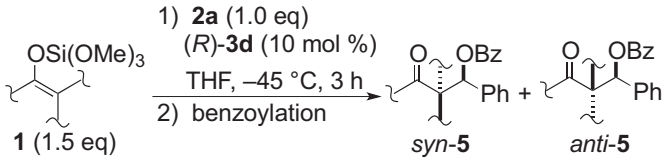
Table 1
Screening of the catalysts **3**



Entry	X (**3**)	Temp, °C	Time, h	Yield, %	*syn*/*anti*[a]	ee,[b] % (*anti*)
1	H (**3a**)	−23	0.5	98	1:17	65
2	Me (**3b**)	−23	0.5	95	1:8.7	24
3	Ph (**3c**)	−23	0.5	54	1:26	78
4	Cl (**3d**)	−23	0.5	97	1:38	86
5	Br (**3e**)	−23	0.5	97	1:27	84
6	I (**3f**)	−23	0.5	87	1:21	70
7	Cl (**3d**)	−45	3	94	1:49	87

[a] Determined by ^{1}H NMR.
[b] Determined by HPLC.

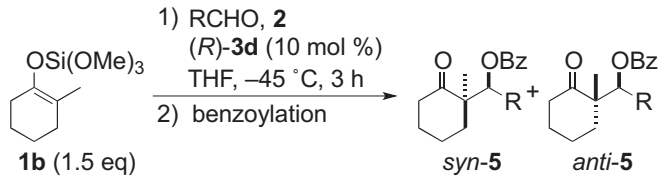
Table 2
Aldol reaction of various trimethoxysilyl enol ethers **1**



Entry	Silyl enol ether	Product	Yield, %	*syn*/*anti*[a]	ee,[b] % (*anti*)
1[c]	**1a**	**4aa**[d]	87	1:3.8	56
2	**1b**	**5ba**	94	1:49	87
3	**1c**	**5ca**	98	1:10	79
4	**1d**	**5da**[e]	98	1:1.8	83
5	**1e**	**5ea**[e,f]	91	1:1.2	42
6	**1f**	**5fa**[f]	97	2.4:1	42

[a] Determined by NMR.
[b] Determined by HPLC.
[c] −23 °C, 0.5 h.
[d] Isolated as the aldol adduct.
[e] We oxidized the hydroxyketones **4da** and **4ea** (aldol adducts before benzoylation) into the diketones (**6da** and **6ea**) and confirmed that both *syn* and *anti* adducts had the same absolute configuration at the benzylic position (see Experimental section).
[f] The relative configurations were determined by X-ray analyses of *anti*-**5ea** and *syn*-**4fa**.

Table 3
Aldol reaction of various aldehydes **2**



Entry	Aldehyde, R	Product	Yield, %	*syn*/*anti*[a]	ee,[b] % (*anti*)
1	Ph (**2a**)	**5ba**	94	1:40	81
2	4-MeOC$_6$H$_4$ (**2b**)	**5bb**	98	1:14	87
3	4-CF$_3$C$_6$H$_4$ (**2c**)	**5bc**	62	1:10	52
4	4-NO$_2$C$_6$H$_4$ (**2d**)	**5bd**	90	1:8.2	6
5	1-Naphthyl (**2e**)	**5be**	86	1:2.7	80
6	2-Naphthyl (**2f**)	**5bf**	97	1:>50	87
7	(*E*)-PhCH=CH (**2g**)	**5bg**	98	1:20	90
8[c]	PhCH$_2$CH$_2$ (**2h**)	**5bh**	64	1:2.4	68
9[c,d]	PhCH$_2$CH$_2$ (**2h**)	**5bh**	75	1:5.3	85

[a] Determined by NMR.
[b] Determined by HPLC.
[c] −23 °C, 3 h.
[d] Using (*R*)-**3e** as a catalyst.

With optimized reaction conditions in hand, we carried out the aldol reactions of trimethoxysilyl enol ethers **1a**–**f** and benzaldehyde (**2a**) (Table 2). The diastereo- and enantioselectivities were dramatically increased in the reaction of the α-methyl substituted trimethoxysilyl enol ether **1b** compared with the reaction of the trimethoxysilyl enol ether **1a** derived from cyclohexanone (entry 1 vs 2). The trimethoxysilyl enol ether **1c** bearing an ethyl group also gave good results; however the stereoselectivity was slightly reduced (entry 3). Trimethoxysilyl enol ether **1d** derived from 2-methylcyclopentanone gave a good enantioselectivity but the *syn*/*anti* ratio (diastereoselectivity) was extremely reduced (entry 4). Both the diastereo- and enantioselectivities of the reaction of **1e** were reduced (entry 5). Unexpectedly, the *syn*-adduct was predominantly produced from the trimethoxysilyl enol ether **1f** derived from 2-methylindanone, and the stereoselectivities were modest (entry 6).

Next, we investigated the aldol reactions of trimethoxysilyl enol ether **1b** with various aldehydes **2a**–**h** (Table 3). Among the benzaldehyde derivatives, *p*-anisaldehyde (**2b**) bearing an electron-donating group slightly increased the enantioselectivity (entry 2). On the other hand, introduction of electron-withdrawing groups decreased the activity and stereoselectivity (entries 3 and 4). The reaction of *p*-nitrobenzaldehyde (**2d**) yielded a particularly reduced enantioselectivity (entry 4). The sterically hindered 1-naphthaldehyde (**2e**) gave a low diastereoselectivity, whereas 2-naphthaldehyde (**2f**) afforded results similar to benzaldehyde (entries 5 and 6). The reaction of *trans*-cinnamaldehyde (**2g**), a conjugated aldehyde, gave the best result (98% yield, *syn*/*anti*=1:20, 90% ee) (entry 7). The observed *anti*-selectivity was the highest yet reported for the construction of quaternary carbon centers in an enantioselective aldol reaction.[21] The aliphatic aldehydes **2h** and **2i** were less reactive, and the observed selectivities were moderate (entries 8 and 9); however, the reaction of hydrocinnamaldehyde (**2h**) in the presence of the catalyst **3e** at −23 °C improved the enantioselectivity to 85% ee (entry 9). As shown in

Table 3, the *anti*-adduct was predominantly formed from the cyclic *E*-enol ether **1b** without exception. These results suggested that the aldol reaction proceeded via a chair-like six-membered transition state, although the details remain unclear.

2.2.2. Under aqueous conditions. We previously demonstrated that the presence of water in the reaction medium greatly affects the stereoselectivity in an aldol reaction of trimethoxysilyl enol ehters.[14b] For example, the aldol reaction of **1a** under anhydrous conditions predominantly produced the *anti*-adduct with a moderate enantioselectivity. By contrast, the *syn*-adduct was predominantly obtained under aqueous conditions and the enantioselectivity of the *syn*-adduct was considerably better (Fig. 6). Therefore, we investigated the aldol reaction of the trimethoxysilyl enol ether **1b** and benzaldehyde (**2a**) in the presence of water (1.5 equiv) as an additive. As expected, the *syn*-adduct was preferentially obtained, and the enantioselectivity was greatly enhanced (Fig. 7).

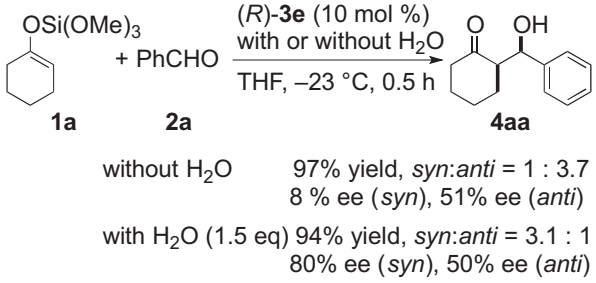


Fig. 6. Effect of water on the aldol reaction of **1a** and **2a**.

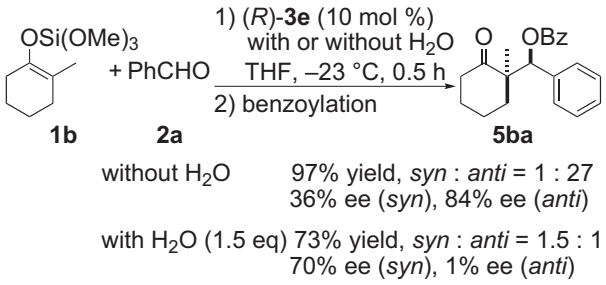


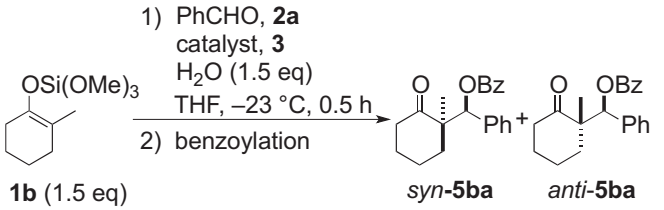
Fig. 7. Effect of water on the aldol reaction of **1b** and **2a**.

We again screened the substituents at the 3,3′-positions in binaphthol under aqueous condition (Table 4). Introduction of hydrogen, methyl, or phenyl groups in place of a halogen atom at the 3,3′-positions decreased the enantioselectivity.

The catalyst **3d** was used to investigate the aldol reaction of various trimethoxysilyl enol ethers (Table 5). The reaction of the silyl enol ether **1b** at −45 °C increased the enantioselectivity to 87% ee but the chemical yield decreased (entry 2). Trimethoxysilyl enol ether **1c** derived from 2-ethylcyclohexanone gave a stereoselectivity similar to that of **1b** (entry 3). Trimethoxysilyl enol ethers **1d** and **1e** were highly reactive, and the reactions proceeded at −45 °C (entries 4 and 5). The enol ether **1e** derived from methyltetralone gave the *anti*-adduct preferentially, although the reason for this preference was not clear. The trimethoxysilyl enol ether **1f** derived from 2-methylindanone also provided a high reactivity; therefore, the reaction temperature was decreased to −78 °C to afford a high enantioselectivity (94% ee, entry 6).

The aldol reactions of various aldehydes with the trimethoxysilyl enol ether **1f** were next investigated (Table 6). In all cases, the *syn*-adducts were preferentially obtained without exception. Cinnamaldehyde (**2g**), a linear conjugated aldehyde, gave result similar to those obtained from benzaldehyde (**2a**). Although the aliphatic aldehydes **2h**–**j** required longer reaction times, the stereoselectivities were excellent (entries 3–5). Cyclohexanecarboxaldehyde (**2i**)

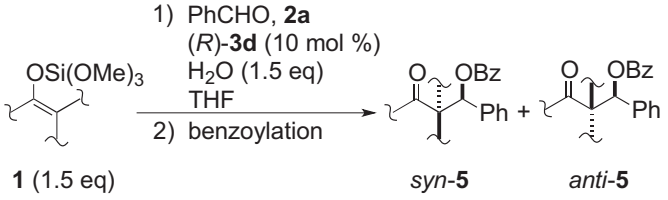
Table 4
Screening of the catalysts **3**



Entry	X (**3**)	Yield, %	*syn*/*anti*[a]	ee,[b] % (*syn*, *anti*)
1	H (**3a**)	62	1:1.6	56, 7
2	Me (**3b**)	64	1:1.1	65, 1
3	Ph (**3c**)	67	1:3.1	24, 3
4	Cl (**3d**)	72	2.3:1	81, 1
5	Br (**3e**)	73	1.5:1	70, 4

[a] Determined by NMR.
[b] Determined by HPLC.

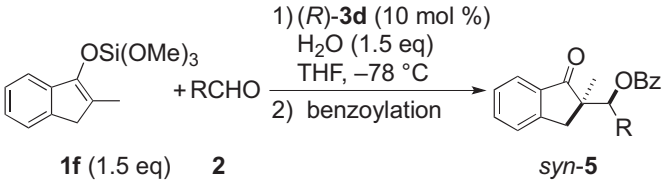
Table 5
Aldol reaction of various silyl enol ethers **1**



Entry	Silyl enol ether	Product	Conditions	Yield, %	*syn*/*anti*[a]	ee,[b] % (*syn*)
1	**1b**	**5ba**	−23 °C, 0.5 h	72	2.3:1	81
2	**1b**	**5ba**	−45 °C, 3 h	60	2.5:1	87
3	**1c**	**5ca**	−23 °C, 0.5 h	52	2.3:1	79
4	**1d**	**5da**	−45 °C, 3 h	87	1.5:1	75
5	**1e**	**5ea**	−45 °C, 3 h	83	1:5.0	85
6	**1f**	**5fa**	−78 °C, 6 h	94	6.7:1	94

[a] Determined by NMR.
[b] Determined by HPLC.

Table 6
Aldol reaction of various aldehydes **2**



Entry	R	Product	Time, h	Yield, %	*syn*/*anti*[a]	ee,[b] % (*syn*)
1	Ph (**2a**)	**5fa**	6	94	6.7:1	94
2	(*E*)-PhCH=CH (**2g**)	**5fg**	6	98	13:1	93
3	$PhCH_2CH_2$ (**2h**)	**5fh**	24	77	10:1	96
4	*c*-Hex (**2i**)	**5fi**[c]	24	95	>50:1	99
5	Me (**2j**)	**5fj**	24	62	12:1	93

[a] Determined by NMR.
[b] Determined by HPLC.
[c] Absolute configuration was determined by X-ray crystallography; see the main text.

particularly gave an extremely high *syn*/*anti* ratio with good enantioselectivity.

In a parallel experiment, the hydroxyketone **4fi** derived from the silyl enol ether **1f** and cyclohexanecarboxaldehyde (**2i**) reacted with (*S*)-camphorsulfonyl chloride to afford **7fi**, which was recrystallized from hexane and diethyl ether to give suitable crystals for X-ray analysis. X-ray analysis revealed that the absolute configuration of the hydroxyketone **4fi** was determined to be (1′*S*,2*R*) (Fig. 8).

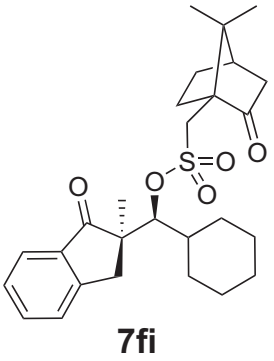


Fig. 8. Determination of the absolute configuration of **7fi**.

2.3. Base-catalyzed aldol-Tishcheko reaction of trimethoxysilyl enol ethers

The trimethoxysilyl enol ether **1i** derived from isobutyrophenone was used as a substrate under anhydrous conditions. Surprisingly, the reaction afforded a monobenzoyl 1,3-diol **8ia** (33% yield, 75% ee) accompanied by the aldol adduct **5ia** (33% yield, 33% ee). This product was an aldol-Tishchenko product formed by acetalization followed by a 1,5-hydride shift (Fig. 9).[22]

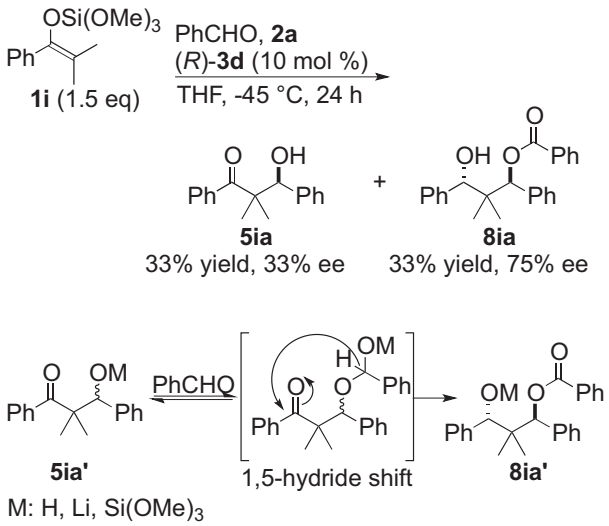
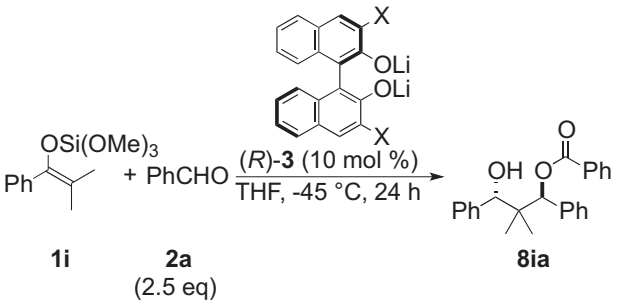


Fig. 9. Base-catalyzed aldol-Tishcheko reaction.

The enantioselective aldol-Tishchenko reaction has recently attracted interest because it forms a monoacyl-protected 1,3-diol from carbonyl equivalents.[22–24] The 1,3-*anti* configuration of the product could be explained based on the cyclic transition state of the hydride shift.[25]

Using a 2.5 mol equiv benzaldehyde (**2a**), we screened substituents on the catalyst for the enantioselective aldol-Tishchenko reaction (Table 7). The enantioselectivity was affected by the substituents at the 3,3′-positions, and the best results were obtained

Table 7
Screening of the catalysts **3**



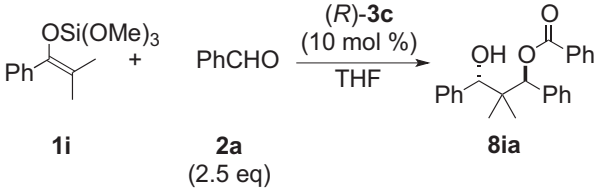
Entry	X	Yield,[a] %	ee,[b] %
1	H (**3a**)	93	56
2	Me (**3b**)	74	27
3	Ph (**3c**)	95	82
4	Cl (**3d**)	91	75
5	Br (**3e**)	89	44

[a] Isolated yield.
[b] Determined by HPLC.

using 3,3′-diphenylbinaphthol. In the above aldol reaction, the halogen-substituted catalyst appeared to give good selectivity, whereas the diphenylbinaphthol derivative (**3c**) afforded a high reactivity and selectivity in the aldol-Tishchenko reaction (entry 3).

Next, we investigated the effects of temperature on the **3c**-catalyzed reaction (Table 8). Mild conditions gave the diol **8il** in good yields and selectivity (entry 1). Lowering the temperature further improved the selectivity, and the best enantioselectivity was obtained at −23 °C (entry 4). Reactions at lower temperatures gave decreased yields and selectivities (entries 5 and 6).

Table 8
Effects of reaction temperature

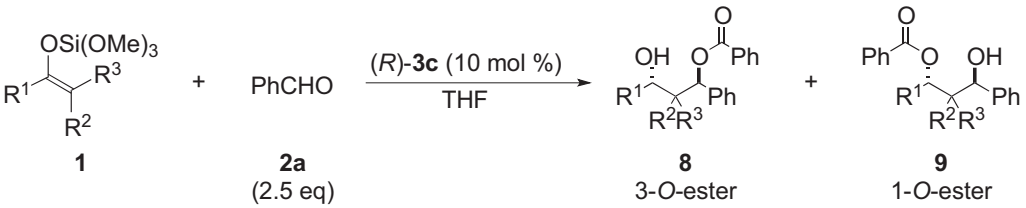


Entry	Temp, °C	Time, h	Yield,[a] %	ee,[b] %
1	rt	1	95	76
2	0	1	94	87
3	−18	3	94	86
4	−23	6	92	88
5	−45	24	95	82
6	−78	24	30	39

[a] Isolated yield.
[b] Determined by HPLC.

With the optimized reaction conditions in hand, we performed the aldol-Tishchenko reaction of various trimethoxysilyl enol ethers **1** with benzaldehyde (**2a**) (Table 9). The acyl-transferred byproducts **9** were often observed in the aldol-Tishchenko reaction.[22–25] In fact, in the reaction of the enol ether **1j** derived from the isobutyraldehyde and aldehyde **2a** yielded considerable amounts of the acyl-transferred product **9ja** (50% yield, 91% ee) with the same enantioselectivity as that of **8ja** (20% yield, 91% ee) (entry 2). The reactions of the enol ethers **1g** and **1h** with bulky substituents required higher temperatures, and the selectivities were reduced (entries 3 and 4). The trimethoxysilyl enol ether **1k** with a geometric isomer gave nearly identical results, regardless of the geometric ratio (entries 5 and 6).

Table 9
Aldol-Tishchenko reaction of various trimethoxysilyl enol ethers **1**



Entry	Silyl enol ether	Conditions	Yield,[a] %		ee,[b] %	
			3-*O*-Ester (**8**)	1-*O*-Ester (**9**)	**8**	**9**
1	**1i** (R^1=Ph, R^2=R^3=Me)	−23 °C, 6 h	92 (**8ia**)	—	88	—
2	**1j** (R^1=H, R^2=R^3=Me)	−23 °C, 24 h	20 (**8ja**)	50 (**9ja**)	91	91
3	**1g** (R^1=Ph, R^2, R^3=−$(CH_2)_5$−)	rt, 24 h	70 (**8ga**)	—	71	—
4	**1h** (R^1=^{i}Pr, R^2=R^3=Me)	rt, 24 h	10 (**8ha**)	66 (**9ha**)	60	60
5	**1k** (R^1=Ph, R^2, R^3=Et, Me) (*E*/*Z*=5.3:1)	−23 °C, 6 h	82 (**8ka**)	16 (**9ka**)	93	93
6	**1k** (R^1=Ph, R^2, R^3=Et, Me) (*E*/*Z*=1.2:1)	−23 °C, 6 h	79 (**8ka**)	16 (**9ka**)	92	92

[a] Isolated yield.
[b] Determined by HPLC.

The monoacylated products **8ka** and **9ka** are the derivatives of symmetric diol; therefore, we could not determine whether **8ka** and **9ka** were the original aldol-Tishchenko products or acyl-transferred adducts (Table 9, entries 1 and 3). This question was addressed by reacting the enol ether **1k** with 4-tolualdehyde (**2k**) to obtain a set of two diastereomers (Fig. 10). At this stage, the diastereomers could not be identified as either a set of **8kk** and **9kk** (diastereomers of the aldol-Tishchenko reaction), or a set of **8kk** and **10kk** (isomers of the acyl-transferred adducts). In the former case (**8kk** and **9kk**), the products obtained after deacylation were related to the diastereomers **11kk** and **12kk**. On the other hand, deacylation of **8kk** and **10kk** produced a single 1,3-diol (**11kk**). We next methanolyzed two diastereomers to yield two types of diols. These results suggested that the original diastereomeric mixture in the aldol-Tishchenko reaction comprised **8kk** and **9kk**, and the acyl group was not transferred in the reaction of enol ether **1k** with aldehyde **2a** or **2b**.

The enantioselective aldol-Tishchenko reactions of the trimethoxysilyl enol ether **1i** with various aldehydes **2** were next examined (Table 10). *p*-Anisaldehyde, with an electron-donating group, gave a high enantioselectivity, although the reactivity was slightly low (entry 2). On the other hand, *p*-bromobenzaldehyde **2l**, with an electron-withdrawing group, gave result similar to those of benzaldehyde (**2a**) (entry 3). Cinnamaldehyde (**2g**), a linear conjugated aldehyde, provided a high enantioselectivity but with a significant decrease in the chemical yield (entry 4). The reaction of hydrocinnamaldehyde (**2h**), a linear aliphatic aldehyde, provided a reduced enantioselectivity and chemical yield (entry 5). Cyclohexanecarboxaldehyde (**2i**) also gave the corresponding products in good yields but with low enantioselectivities (entry 6).

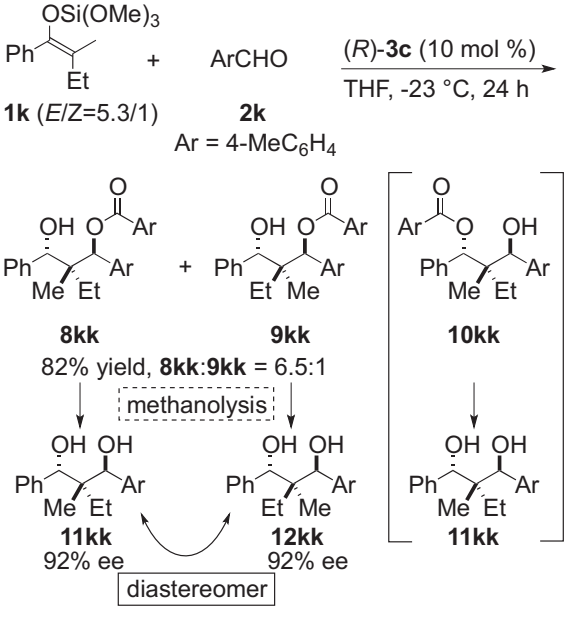
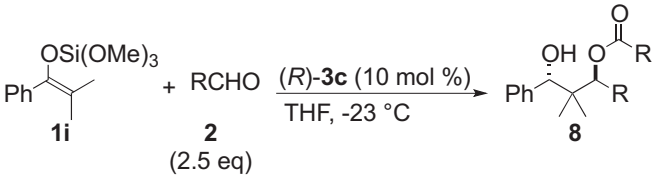


Fig. 10. Determination of the mechanism of generating the diastereomers.

Table 10
Aldol-Tishchenko reaction of various aldehydes **2**



Entry	R	Time, h	Product	Yield,[a] %	ee,[b] %
1	Ph (**2a**)	6	**8ia**	92	88
2	4-$MeOC_6H_4$ (**2b**)	24	**8ib**	80	95
3	4-BrC_6H_4 (**2l**)	6	**8il**	88	86
4	(*E*)-PhCH=CH (**2g**)	24	**8ig**	51	89
5	$PhCH_2CH_2$ (**2h**)	24	**8ih**	34	28
6	*c*-Hex (**2i**)	24	**8ii**	71	30

[a] Isolated yield.
[b] Determined by HPLC.

The reaction mechanism was investigated by carrying out the aldol-Tishchenko reaction of benzaldehyde (**2a**) with the silylated aldol adducts **13** or the aldol adduct **14** (Fig. 11). No Tishchenko adduct was obtained in the reaction of the silylated aldol adduct **13** with benzaldehyde (**2a**), whereas the aldol adduct **14** provided the corresponding 1,3-diol derivative **8ja** in high yield and enantioselectivity. These results suggested that not the silylated aldol product, but the lithiated adduct, was the active species during the aldol-Tishchenko reaction. In addition, despite the investigation of the racemate **14**, the observed yield and selectivity of **8ja** were

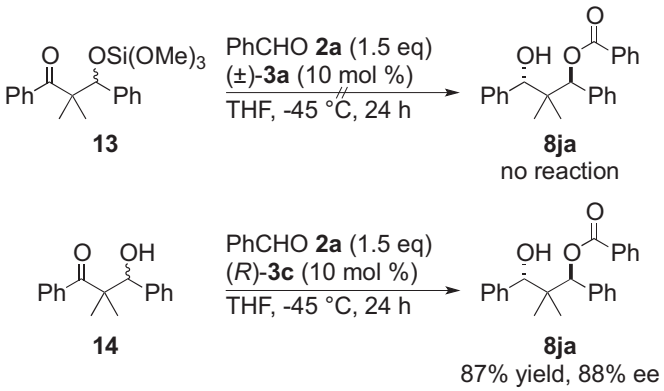


Fig. 11. Tishchenko reaction of the aldol adduct and benzaldehyde.

extremely high. This observation indicated that the aldol reaction and acetalization processes in the reaction media were reversible. Therefore, the enantioselectivity of the present reaction may be controlled via the stability of the transition state of the hydride shift (Fig. 12).[22–25] The transition state B may be more stable than C, which preferentially afforded (−)-**8ja**.

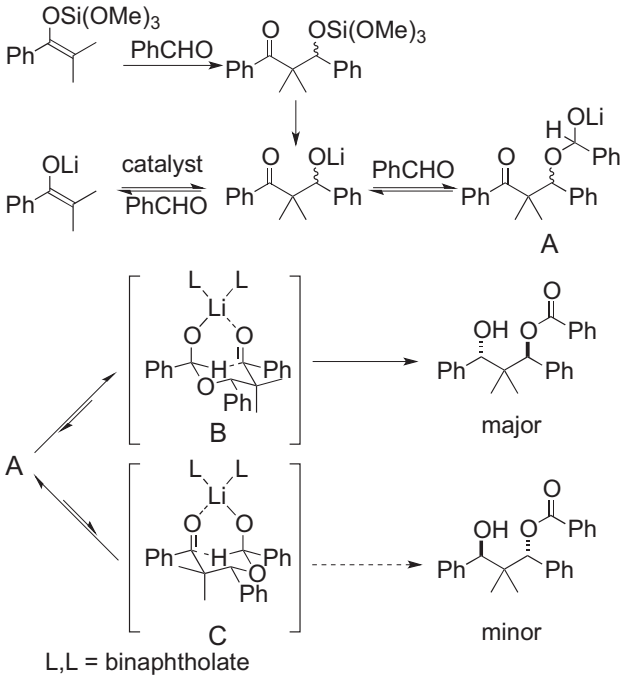


Fig. 12. Plausible reaction mechanism of the aldol-Tishchenko reaction.

3. Conclusion

We demonstrated that the aldol reaction of trimethoxysilyl enol ethers catalyzed by lithium binaphtholate provides a powerful tool for constructing quaternary asymmetric carbon centers. The stereoselectivities were greatly affected by the presence of water in the reaction mixture. The cyclic trimethoxysilyl enol ether was used as a substrate to preferentially obtain the *anti*-adduct under anhydrous conditions; the *syn*-adduct was preferentially obtained under aqueous conditions, though there are some exceptions. The trimethoxysilyl enol ether derived from the acyclic ketones reacted according to the aldol-Tishchenko reaction to give the monoacyl 1,3-diol derivatives in high enantioselectivities.

4. Experimental section

4.1. General

^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$ with JEOL AL-300 (^{1}H, 300 MHz; ^{13}C, 75 MHz) or JNM-ECX400 (^{1}H, 400 MHz; ^{13}C, 100 MHz) spectrometers. Tetramethylsilane (TMS) (δ=0 ppm) and $CDCl_3$ (δ=77.0 ppm) were served as internal standards for ^{1}H and ^{13}C NMR, respectively. Infrared spectra were recorded on JEOL JIR 6500-W. Mass spectra were measured with JEOL JMS-DX303HF mass spectrometer. Optical rotations were recorded on JASCO P-1010 polarimeter. High-pressure liquid chromatography (HPLC) was performed on JASCO P-980 and UV-1575. Thin-layer chromatography (TLC) analysis was carried out using Merck silica gel plates. Visualization was accomplished with UV light, phosphomolybdic acid, and/or anisaldehyde. Column chromatography was performed using Kanto Chemical Silica Gel 60N (spherical, neutral, 63–210 μm).

In enantioselective aldol reactions, the optical rotation data were not collected for minor diastereomers, because the quantities of the isolated minor isomers were less than few milligrams in many cases.

4.2. Preparation of trimethoxysilyl enol ethers

*4.2.1. 2-Methyl-1-(trimethoxysilyloxy)cyclohexene (**1b**). Silylation of ketone with trimethoxysilyl triflate with TBAI (procedure A)*: under an Ar atmosphere, triflic acid (6.75 g, 45 mmol, 1.5 equiv) was added to a solution of allyltrimethoxysilane (7.30 g, 45 mmol, 1.5 equiv) in $CHCl_3$ (15 mL) at 0 °C, and the mixture was stirred for 30 min at the same temperature. The resulting pale yellow solution was transferred by cannula to a mixture of 2-methylcyclohexanone (3.6 mL, 30 mmol), triethylamine (8.35 mL, 60 mmol, 2.0 equiv), and tetra-*n*-butylammonium iodide (11.1 g, 30 mmol, 1.0 equiv) in $CHCl_3$ (50 mL). The resulting mixture was heated to reflux for 3 h. After cooling to rt, the solvent was evaporated in vacuo. The residue was extracted with hexane (100 mL×2) and dried on Na_2SO_4. Purification with distillation (77–78 °C/4 mmHg) yielded **1b** (5.1 g, 73%) as a colorless oil. Bp: 77–78 °C/4 mmHg. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.53–1.69 (m, 7H), 1.94–1.98 (m, 2H), 2.12–2.16 (m, 2H), 3.63 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 15.7, 22.8, 23.6, 29.1, 30.1, 51.3, 112.0, 141.5. IR (neat): ν 2929, 2842, 1695 cm^{-1}. LR-EIMS: 232 (M^+), 217. HR-EIMS: calcd for $C_{10}H_{20}O_4Si$ 232.1131, found 232.1125.

*4.2.2. 2-Ethyl-1-(trimethoxysilyloxy)cyclohexene (**1c**). Procedure A*: a colorless oil. Bp: 102 °C/6 mmHg. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.96 (t, 3H, J=7.8 Hz), 1.54–1.58 (m, 2H), 1.64–1.70 (m, 2H), 1.95–2.10 (m, 2H), 2.12–2.19 (m, 4H), 3.61 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 12.0, 22.79, 22.81, 23.5, 27.1, 29.1, 51.1, 117.5, 141.0. IR (neat): ν 2933, 2842, 1687 cm^{-1}. LR-EIMS: 246 (M^+). HR-EIMS: calcd for $C_{11}H_{22}O_4Si$ 246.1287, found 246.1271.

*4.2.3. 2-Methyl-1-(trimethoxysilyloxy)cyclopentene (**1d**). Procedure A*: a colorless oil. Bp: 72 °C/8 mmHg. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.60 (s, 3H), 1.79–1.85 (m, 2H), 2.19–2.22 (m, 2H), 2.36–2.41 (m, 2H), 3.62 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 11.4, 19.5, 32.7, 33.5, 51.5, 113.3, 144.4. IR (neat): ν 2946, 2844, 1699 cm^{-1}. LR-EIMS: 203 ($(M-Me)^+$), 187. HR-EIMS: calcd for $C_8H_{15}O_4Si$ 203.0740, found 203.0718.

*4.2.4. 2-Methyl-1-(trimethoxysilyloxy)-3,4-dihydronaphthalene (**1e**). Silylation of ketone with trimethoxysilyl triflate without TBAI (procedure B)*: under an Ar atmosphere, triflic acid (6.75 g, 45 mmol, 1.5 equiv) was added to a solution of allyltrimethoxysilane (7.30 g, 45 mmol, 1.5 equiv) in CH_2Cl_2 (15 mL) at 0 °C, and the mixture was stirred for 30 min at the same temperature. The resulting pale yellow solution

was transferred by cannula to a mixture of 2-methyl-1-tetralone (4.8 g, 30 mmol), triethylamine (8.35 mL, 60 mmol, 2.0 equiv) in CH_2Cl_2 (50 mL). The mixture was stirred for 3 h. After warming to rt, the solvent was evaporated in vacuo. The residue was extracted with hexane (100 mL×2) and dried on Na_2SO_4. Purification with distillation yielded **1e** (5.4 g, 64%) as a colorless oil. Bp: 131 °C/5 mmHg. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.90 (s, 3H), 2.29 (t, 2H, J=7.8 Hz), 2.76 (t, 2H, J=7.8 Hz), 3.60 (s, 9H), 7.05–7.12 (m, 2H), 7.19 (dt, 1H, J=1.8, 7.8 Hz), 7.45 (d, 1H, J=7.8 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 16.7, 27.9, 29.1, 51.4, 117.1, 121.0, 126.1, 126.3, 126.6, 133.2, 135.6, 140.7. IR (neat): ν 2942, 2842, 1654, cm^{-1}. LR-EIMS: 280 (M^+), 265. HR-EIMS: calcd for $C_{14}H_{20}O_4Si$ 280.1131, found 280.1127.

*4.2.5. 2-Methyl-1-(trimethoxysilyloxy)-3H-indene (**1f**). Procedure A*: a colorless oil. Bp: 147–148 °C/4.5 mmHg. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.06 (s, 3H), 3.20 (s, 2H), 3.67 (s, 9H), 7.14 (dt, 1H, J_1=0.9, 7.3 Hz), 7.25–7.37 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 11.9, 38.6, 51.7, 117.2, 120.3, 123.5, 124.3, 126.2, 140.6, 141.8, 145.6. IR (neat): ν 2945, 2845, 1641, 1608 cm^{-1}. LR-FABMS: 289 ($M+Na^+$), 267 ($M+H^+$), 266 (M^+), 251, 235. HR-FABMS: calcd for $C_{13}H_{18}O_4Si$ 266.0974, found 266.1011.

*4.2.6. [Cyclohexylidene(trimethoxysilyloxy)methyl]benzene (**1g**). Procedure A*: a colorless oil. Bp: 160–163 °C/4.5 mmHg. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.43–1.65 (m, 6H), 2.05–2.08 (m, 2H), 2.41–2.44 (m, 2H), 3.39 (s, 9H), 7.21–7.37 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 26.5, 27.1, 27.2, 27.8, 29.7, 50.9, 121.2, 127.2, 127.6, 128.9, 137.7, 139.3. IR (neat): ν 2923, 1664, 1080 cm^{-1}. LR-EIMS: 308 (M^+), 276. HR-EIMS: calcd for $C_{16}H_{24}O_4Si$ 308.1444, found 308.1385.

*4.2.7. 2,4-Dimethyl-3-(trimethoxysilyloxy)-2-pentene (**1h**). Procedure B*: a colorless oil. Bp: 79 °C/6 mmHg. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.04 (d, 6H, J=6.9 Hz), 1.63 (s, 3H), 1.66 (s, 3H), 2.85 (hept, 1H, J=6.9 Hz), 3.62 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.7, 18.6, 19.8, 29.1, 51.5, 108.3, 147.5. IR (neat): ν 1678, 1082 cm^{-1}. LR-EIMS: 234 (M^+), 219, 202. HR-EIMS: calcd for $C_{10}H_{22}O_4Si$ 234.1287, found 234.1233.

*4.2.8. 2-Methyl-1-phenyl-1-(trimethoxysilyloxy)-1-propene (**1i**). Reductive silylation of α,β-unsaturated ketone with trimethoxysilane (procedure C)*: to an orange solution of $Rh(PPh_3)_3Cl$ (17.2 mg, 19 μmol, 0.025 mol %) in 1-phenyl-2-methyl-2-penten-1-one (10.9 g, 74 mmol) was added trimethoxysilane (11.7 g, 97 mmol, 1.3 equiv) under an Ar atmosphere at rt. After heating at 90 °C for 30 min, the reaction mixture was cooled to rt. Ice-cooled satd $NaHCO_3$ (15 mL) was added and the mixture was vigorously stirred. After removing the cloudy material by Celite filtration and washing with hexane, the combined organic layer was washed with brine, dried over Na_2SO_4, and evaporated to give the crude product as a pale yellow oil. Distillation in vacuo gave the silyl enol ether **1i** as a colorless oil (9.7 g, 49%). Bp: 124–125 °C/6 mmHg. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.64 (s, 3H), 1.86 (s, 3H), 3.40 (s, 9H), 7.19–7.26 (m, 1H), 7.28–7.39 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.8, 19.9, 51.1, 113.7, 127.5, 127.9, 129.1, 138.1, 142.0. IR (neat): ν 1686, 1092 cm^{-1}. LR-EIMS 268 (M^+), 236. HR-EIMS: calcd for $C_{13}H_{20}O_4Si$ 268.1131, found 268.1120.

*4.2.9. 2-Methyl-1-(trimethoxysilyloxy)-1-propene (**1j**). Procedure C*: a colorless oil. Bp: 90–91 °C/6 mmHg. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.55 (d, 3H, J=1.4 Hz), 1.64 (s, 3H,), 3.62 (s, 9H), 6.15 (q, 1H, J=1.4 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.5, 19.0, 51.3, 114.9, 131.5. IR (neat): ν 1687, 1097 cm^{-1}. LR-EIMS: 192 (M^+), 177, 160. HR-EIMS: calcd for $C_7H_{16}O_4Si$ 192.0818, found 192.0806.

*4.2.10. 2-Methyl-1-phenyl-1-(trimethoxysilyloxy)-1-butene (**1k**). Procedure C*: a colorless oil. Bp: 126–127 °C/6 mmHg. ^{1}H NMR ($CDCl_3$, 400 MHz): 0.98 (t, 3H, J=7.4 Hz, *E*), 1.09 (t, 3H, J=7.4 Hz, *Z*), 1.61 (s, 3H, *Z*), 1.83 (s, 3H, *E*), 1.97 (q, 2H, J=7.4 Hz, *E*), 2.31 (q, 2H, J=7.4 Hz, *Z*), 3.40 (s, 9H, *E* and *Z*), 7.23–7.38 (m, 5H, *E* and *Z*). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 11.9, 13.1, 14.5, 16.8, 24.3, 26.2, 51.0, 118.9, 119.1, 127.2, 127.4, 127.6, 127.8, 128.8, 129.0, 138.0, 138.1, 141.3, 142.0. IR (neat): ν 1678, 1093 cm^{-1}. LR-EIMS: 282 (M^+), 267, 235. HR-EIMS: calcd for $C_{14}H_{22}O_4Si$ 282.1287, found 282.1291.

4.3. Construction of quaternary asymmetric centers using base-catalyzed aldol reaction under anhydrous condition

*4.3.1. 2-(Hydroxyphenylmethyl)-2-methylcyclohexanone (**4ba**).[20] Typical procedure for the aldol reaction under anhydrous condition*: under an Ar atmosphere, *n*-BuLi (0.094 mmol, 20 mol %) in hexane (0.21 M, 0.45 mL) was added to a solution of (*R*)-3,3′-dichlorobinaphthol (16.8 mg, 0.047 mmol, 10 mol %) in THF at −45 °C, and the mixture was stirred for 5 min. Then a solution benzaldehyde **2a** in THF (1.0 M, 0.47 mL, 0.47 mmol) and silyl enol ether **1b** (0.71 mmol, 1.5 equiv) were successively added to the above mixture. After 3 h, the reaction was quenched with KF/HCOOH aq (1.5 M KF, 3.0 M HCOOH, 2 mL) and the mixture was stirred for 2 h at rt. The aqueous layer was extracted with AcOEt and the combined organic layers were successively washed with satd $NaHCO_3$ (3 mL) and brine (3 mL). Drying over Na_2SO_4 and evaporating the solvent gave the crude product, which was purified by silica gel column chromatography (SiO_2 9.0 g, CH_2Cl_2/hexane/AcOH 80:10:1, then CH_2Cl_2/AcOEt/AcOH 160:1:1, then 100:10:1) to afford the corresponding product as an oil (98 mg, 96% yield, *syn*/*anti* 1:27). The enantiomeric excess was determined to be 81% (*anti*) and 39% (*syn*) by chiral HPLC [Daicel Chiralcel OD-H, hexane/IPA=19:1, 1.0 mL/min]: t_R 10.6 min (*syn*-minor), 16.9 min (*anti*-major), 18.5 min (*syn*-major), 23.8 min (*anti*-minor).

anti-**4ba**:[20] colorless oil. $[\alpha]_D^{22}$ −40.2 (*c* 1.63, $CHCl_3$), 81% ee. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.18 (s, 3H), 1.24–1.29 (m, 1H), 1.51–1.74 (m, 4H), 2.00–2.04 (m, 1H), 2.37–2.43 (m, 1H), 2.57–2.65 (m, 1H), 3.94 (d, 1H, J=2.1 Hz), 4.97 (d, 1H, J=2.1 Hz), 7.2–7.4 (m, 5H).

syn-**4ba**:[20] colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.07 (s, 3H), 1.35–1.41 (m, 1H), 1.63–1.77 (m, 3H), 1.98–2.20 (m, 2H), 2.34–2.40 (m, 1H), 2.55–2.63 (m, 1H), 3.06 (d, 1H, J=4.0 Hz), 5.08 (d, 1H, J=4.0 Hz), 7.2–7.4 (m, 5H).

*4.3.2. anti-2-[(Benzoyloxy)phenylmethyl]-2-methylcyclohexanone (**5ba**). Typical procedure for the preparation of benzoylated aldol adduct*: under an Ar atmosphere, *n*-BuLi (0.094 mmol, 20 mol %) in hexane (0.21 M, 0.45 mL) was added to a solution of (*R*)-3,3′-dichlorobinaphthol (16.8 mg, 0.047 mmol, 10 mol %) in THF at −45 °C, and the mixture was stirred for 5 min. Then a solution aldehyde in THF (1.0 M, 0.47 mL, 0.47 mmol) and silyl enol ether 1 (0.71 mmol, 1.5 equiv) were successively added to the above mixture. After 3 h, the reaction was quenched with KF/HCOOH aq (1.5 M KF, 3.0 M HCOOH, 2 mL) and the mixture was stirred for 2 h at rt. The aqueous layer was extracted with AcOEt and the combined organic layers were successively washed with satd $NaHCO_3$ (3 mL) and brine (3 mL). Drying over Na_2SO_4 and evaporating the solvent gave the crude product, which was dissolved in CH_2Cl_2 (2 mL). Benzoyl chloride (0.11 mL, 0.94 mmol, 2.0 equiv) and a solution of DMAP (287 mg, 2.35 mmol, 5.0 equiv) in CH_2Cl_2 (2 mL) were added to the mixture at 0 °C. After stirring for 1 h, 10% HCl aq (5 mL) was added to the mixture and the entire mixture was extracted with AcOEt (20 mL×3). The organic layer was washed with brine and dried over Na_2SO_4. After evaporating the solvent, the residue was purified by silica gel column chromatography (SiO_2 9.0 g, CH_2Cl_2/hexane=1:4 then 1:1) to afford the corresponding benzoylated product **5ba** as a colorless oil (143 mg, 94% yield, *syn*/*anti* 1:49, *anti* 87% ee). The enantiomeric excess was determined to be 87% (*anti*) and 54% (*syn*) by chiral HPLC [Daicel Chiralpak AD-H,

hexane/IPA=7:2, 1.0 mL/min]: t_R 13.2 min (*anti*-minor), 15.8 min (*syn*-major), 16.9 min (*anti*-major), 26.2 min (*syn*-minor).

anti-**5ba**: a colorless needle. $[\alpha]_D^{22}$ +102.2 (*c* 1.09, $CHCl_3$), 87% ee. Mp: 99–102 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.16 (s, 3H), 1.38–1.50 (m, 1H), 1.70–1.88 (m, 3H), 2.02–2.20 (m, 2H), 2.35–2.44 (m, 1H), 2.63–2.71 (m, 1H), 6.61 (s, 1H), 7.2–7.5 (m, 7H), 7.5–7.6 (m, 1H), 8.01 (d, 2H, *J*=8.0 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.3, 21.2, 28.0, 37.0, 38.9, 53.1, 77.1, 127.7, 128.2, 128.3, 128.6, 129.8, 130.0, 133.3, 136.5, 165.4, 212.9. IR (KBr): ν 1724, 1722 cm^{-1}. LR-EIMS: 322 (M^+), 216, 105, 77. HR-EIMS: calcd for $C_{21}H_{22}O_3$ 322.1569, found 322.1538.

*4.3.3. (+)-2-Benzoyl-2-methylcyclohexanone (**6ba**).[26] Oxidation of aldol adduct with PCC*: under an Ar atmosphere, a solution of (−)-*anti*-**4ba** (61 mg, 0.28 mmol, 81% ee), pyridinium chlorochromate (100 mg, 1.4 mmol, 5 equiv) and Celite in CH_2Cl_2 (8 mL) was stirred for 12 h. The reaction mixture was filtrated through Celite and then evaporated to give the crude product, which was purified by silica gel column chromatography (SiO_2 9.0 g, hexane/AcOEt=9:1) to afford the corresponding 1,3-diketone **6ba** as a colorless oil (48 mg, 79% yield). The enantiomeric excess was determined to be 75% by chiral HPLC [Daicel Chiralcel OJ-H, hexane/IPA=300:1, 1.0 mL/min]: t_R 12.5 min (minor), 14.8 min (major). $[\alpha]_D^{28}$ +169.2 (*c* 1.31, $CHCl_3$), 75% ee. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.40–1.49 (m, 4H), 1.67–1.84 (m, 3H), 2.00–2.16 (m, 2H), 2.40–2.43 (m, 1H), 2.80–2.84 (m, 1H), 7.38–7.85 (m, 5H).

Following the procedure for the oxidation of aldol adduct with PCC, the 1,3-diketone **6ba** was obtained from (+)-*syn*-**4ba** (61 mg, 85% ee) as a colorless oil (49 mg, 80% yield). The enantiomeric excess was determined to be 78% by chiral HPLC [Daicel Chiralcel OJ-H, hexane/IPA=300:1, 1.0 mL/min]: t_R 12.5 min (minor), 14.8 min (major). $[\alpha]_D^{28}$ +169.3 (*c* 0.56 $CHCl_3$) 78% ee.

*4.3.4. anti-2-[(Benzoyloxy)phenylmethyl]-2-ethylcyclohexanone (**5ca**).* The enantiomeric excess was determined to be 79% (*anti*) and 54% (*syn*) by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=19:1, 1.0 mL/min]: t_R 10.3 min (*anti*-minor), 12.3 min (*anti*-major), 17.1 min (*syn*-major), 38.9 min (*syn*-minor).

anti-**5ca**: a colorless needle. $[\alpha]_D^{22}$ +39.2 (*c* 0.96, $CHCl_3$) 79% ee. Mp: 102–105 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.84 (t, 3H, *J*=7.4 Hz), 1.54–1.93 (m, 7H), 2.03–2.12 (m, 1H), 2.32–2.47 (m, 2H), 6.65 (s, 1H), 7.23–7.32 (m, 3H), 7.40–7.47 (m, 4H), 7.54–7.58 (m, 1H), 8.05–8.07 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 8.3, 20.7, 25.3, 26.0, 31.4, 39.5, 56.3, 76.3, 127.77, 127.84, 128.1, 128.4, 129.6, 130.0, 133.1, 137.3, 165.2, 211.4. IR (KBr): ν 1716 cm^{-1}. LR-FABMS: 359 ($M+Na^+$), 105. HR-FABMS: calcd for $C_{22}H_{24}O_3Na$ 359.1624, found 359.1628.

*4.3.5. anti-2-[(Benzoyloxy)phenylmethyl]-2-methylcyclopentanone (**5da**).* The enantiomeric excess was determined to be 83% (*anti*) and 16% (*syn*) by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=29:1, 1.0 mL/min]: t_R 18.4 min (*anti*-minor), 26.1 min (*anti*-major), 29.3 min (*syn*-minor), 50.8 min (*syn*-major).

anti-**5da**: a colorless needle. $[\alpha]_D^{22}$ +72.3 (*c* 1.02, $CHCl_3$), 83% ee. Mp: 84–86 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.22 (s, 3H), 1.55–2.02 (m, 4H), 2.20–2.32 (m, 2H), 6.21 (s, 1H), 7.25–7.63 (m, 8H), 8.09 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.8, 20.9, 32.2, 38.6, 53.4, 78.5, 127.4, 128.1, 128.3, 128.6, 129.8, 130.2, 133.3, 137.6, 165.4, 220.2. IR (KBr): ν 1735, 1710 cm^{-1}. LR-FABMS: 331 $(M+Na)^+$, 105. HR-FABMS: calcd for $C_{20}H_{20}O_3Na$ 331.1310, found 331.1317.

*4.3.6. anti-2-(Hydroxyphenylmethyl)-2-methylcyclopentanone (**4da**).[20]* The enantiomeric excess was determined to be 62% (*anti*) and 31% (*syn*) by chiral HPLC [Daicel Chiralcel OD-H, hexane/IPA=29:1, 1.0 mL/min]: t_R 13.4 min (*anti*-major), 14.5 (*anti*-minor); [Daicel Chiralcel OD-H, hexane/IPA=49:1, 1.0 mL/min]: t_R 19.0 min (*syn*-major), 32.0 min (*syn*-minor).

anti-**4da**:[20] a colorless oil. $[\alpha]_D^{28}$ +49.1 (*c* 0.10, $CHCl_3$), 62% ee. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.06 (s, 3H), 1.41–1.47 (m, 1H), 1.76–2.02 (m, 3H), 2.19–2.28 (m, 1H), 2.40–2.48 (m, 1H), 4.10 (s, 1H), 4.81 (s, 1H), 7.26–7.36 (m, 5H).

syn-**4da**:[20] a colorless oil. $[\alpha]_D^{28}$ −2.74 (*c* 0.10, $CHCl_3$), 31% ee. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.88 (s, 3H), 1.40–1.45 (m, 1H), 1.72–1.97 (m, 2H), 2.17–2.50 (m, 3H), 4.84 (d, 1H, J=4.0 Hz,), 7.26–7.36 (m, 5H).

*4.3.7. (+)-2-Benzoyl-2-methylcyclopentanone (**6da**).[26]* Following the procedure for the oxidation of aldol adduct with PCC, the 1,3-diketone **6da** was obtained from *anti*-**4da** (62% ee) as a colorless oil (33 mg, 58% yield). The enantiomeric excess was determined to be 62% by chiral HPLC [Daicel Chiralcel OJ-H, hexane/IPA=9:1, 1.0 mL/min]: t_R 13.5 min (minor), 16.1 min (major). $[\alpha]_D^{28}$ +25.4 (*c* 0.56, $CHCl_3$), 62% ee. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.49 (s, 3H), 1.85–2.13 (m, 3H), 2.34–2.50 (m, 2H), 2.76–2.91 (m, 1H), 7.41–7.53 (m, 3H), 7.83 (d, 2H, *J*=6.8 Hz).

*4.3.8. (−)-2-Benzoyl-2-methylcyclopentanone (**6da**).[26]* Following the procedure for the oxidation of aldol adduct with PCC, the 1,3-diketone **6da** was obtained from *syn*-**4da** (31% ee) as a colorless oil (20 mg, 36% yield). The enantiomeric excess was determined to be 25% by chiral HPLC [Daicel Chiralcel OJ-H, hexane/IPA=9:1, 1.0 mL/min]: t_R 13.5 min (major), 16.1 min (minor). $[\alpha]_D^{28}$ −9.71 (*c* 1.02, $CHCl_3$), 25% ee.

*4.3.9. anti-2-[(Benzoyloxy)phenylmethyl]-2-methyl-1-tetralone (**5ea**).* The enantiomeric excess was determined to be 42% (*anti*) and 6% (*syn*) by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=19:1, 1.0 mL/min]: t_R 23.4 min (*syn*-minor), 27.7 min (*anti*-major), 37.9 min (*anti*-minor), 60.6 min (*syn*-major).

anti-**5ea**: a colorless prism. $[\alpha]_D^{26}$ +42.2 (*c* 1.05, $CHCl_3$), 42% ee. Mp: 129–131 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.39 (s, 3H), 2.11–2.19 (m, 2H), 2.99–3.10 (m, 2H), 6.66 (s, 1H), 7.15–7.31 (m, 5H), 7.37–7.60 (m, 6H), 8.00–8.15 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.0, 25.3, 30.1, 49.9, 78.3, 126.8, 127.8, 127.9, 128.1, 128.4, 128.6, 129.6, 130.2, 131.7, 133.1, 133.3, 137.5, 142.6, 165.3, 199.4. IR (KBr): ν 1700, 1681, 1598, 1581 cm^{-1}. LR-FABMS: 393 ($M+Na^+$), 105. HR-FABMS: calcd for $C_{25}H_{22}O_3Na$ 393.1467, found 393.1469. Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 868918.

*4.3.10. 2-(Hydroxyphenylmethyl)-2-methyl-1-tetralone (**4ea**).[7a,b]* The enantiomeric excess was determined to be 7% (*anti*) and 34% (*syn*) by chiral HPLC [Daicel Chiralcel OD-3, hexane/IPA=19:1, 0.5 mL/min]: t_R 26.9 min (*anti*-minor), 33.1 min (*anti*-major), 35.6 min (*syn*-major), 53.7 min (*syn*-minor).

anti-**4ea**:[7a,b] a colorless oil. $[\alpha]_D^{16}$ −6.9 (*c* 1.02, $CHCl_3$), 7% ee. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.16 (s, 3H), 1.61 (dt, 1H, *J*=3.6, 13.3 Hz), 2.42 (dt, 1H, *J*=5.0, 13.3 Hz), 2.86–3.00 (m, 2H), 14 (br s, 1H), 5.23 (d, 1H, *J*=4.6 Hz), 7.20–7.36 (m, 7H), 7.48 (dt, 1H, *J*=1.4, 7.3 Hz), 8.09 (d, 1H, *J*=7.3 Hz).

syn-**4ea**:[7a,b] a colorless oil. $[\alpha]_D^{16}$ −14.2 (*c* 1.46, $CHCl_3$), 34% ee. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.27 (s, 3H), 1.47 (ddd, 1H, *J*=3.7, 5.0, 13.3 Hz), 1.97 (dt, 1H, *J*=5.0, 13.3 Hz), 2.81–3.04 (m, 2H), 4.88 (s, 1H), 5.03 (s, 1H), 7.21–7.52 (m, 8H), 8.06 (d, 1H, *J*=1.6 Hz).

*4.3.11. (+)-2-Benzoyl-2-methy-1-tetralone (**6ea**).[27]* Following the procedure for the oxidation of aldol adduct with PCC, the 1,3-diketone **6ea** was obtained from *anti*-**4ea** (7% ee) as a colorless oil (56 mg, 76% yield). The enantiomeric excess was determined to be

6% by chiral HPLC [Daicel Chiralcel OJ-H, hexane/IPA=9:1, 1.0 mL/min]: t_R 20.3 min (minor), 36.0 min (major). $[\alpha]_D^{28}$ +1.03 (*c* 0.38, $CHCl_3$), 6% ee. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.63 (s, 3H), 2.02 (dt, 1H, *J*=5.5, 13.7 Hz), 2.83–2.90 (m, 1H), 3.05–3.13 (m, 2H), 7.26–7.35 (m, 4H), 7.45 (t, 1H, *J*=7.3 Hz), 7.5–7.53 (m, 1H), 7.73 (d, 2H, *J*=7.8 Hz), 8.06 (d, 1H, *J*=6.8 Hz).

*4.3.12. (−)-2-Benzoyl-2-methy-1-tetralone (**6ea**).*[27] Following the procedure for the oxidation of aldol adduct with PCC, the 1,3-diketone **6ea** was obtained from *syn*-**4ea** (34% ee) as a colorless oil (52 mg, 70% yield). The enantiomeric excess was determined to be 32% by chiral HPLC [Daicel Chiralcel OJ-H, hexane/IPA=9:1, 1.0 mL/min]: t_R 20.3 min (major), 36.0 min (minor). $[\alpha]_D^{28}$ −3.40 (*c* 0.46, $CHCl_3$), 32% ee.

*4.3.13. anti-2-[(Benzoyloxy)phenylmethyl]-2-methyl-1-indanone (**5fa**).* The enantiomeric excess was determined to be 42% (*anti*) and 31% (*syn*) by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=4:1, 1.0 mL/min]: t_R 15.9 min (*anti*-minor), 18.0 min (*syn*-minor), 19.8 min (*anti*-major), 54.5 min (*syn*-major).

anti-**5fa**: a colorless prism. $[\alpha]_D^{23}$ +50.4 (*c* 0.76, $CHCl_3$), 42% ee. Mp: 132–133 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.45 (s, 3H), 2.97 (d, 1H, *J*=17.4 Hz), 3.62 (d, 1H, *J*=17.4 Hz), 6.37 (s, 1H), 7.10–7.19 (m, 3H), 7.25–7.35 (m, 4H), 7.43–7.50 (m, 3H), 7.55–7.59 (m, 1H), 7.68 (d, 1H, *J*=7.8 Hz, Ar–H), 8.03 (dd, 2H, *J*=1.4, 8.2 Hz, Ar–H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 22.6, 37.1, 54.1, 79.9, 124.3, 126.4, 127.2, 127.5, 128.1, 128.6, 129.8, 130.1, 133.3, 135.1, 136.2, 137.1, 152.5, 165.4, 207.7. IR (KBr): ν 1714, 1713 cm^{-1}. LR-FABMS: 379 ($M+Na^+$), 357 ($M+H^+$), 235, 105. HR-FABMS: calcd for $C_{24}H_{21}O_3Na$ 379.1310, found 379.1332.

*4.3.14. syn-2-(Hydroxyphenylmethyl)-2-methyl-1-indanone (**4fa**).*[28] Under an Ar atmosphere, H_2O in THF (2.8 M, 0.26 mL, 0.71 mmol, 1.5 equiv) and *n*-BuLi (0.094 mmol, 20 mol %) in hexane (0.21 M, 0.45 mL) were added to a solution of (±)-binaphthol (13.5 mg, 0.047 mmol, 10 mol %) in THF at −23 °C, and the mixture was stirred for 5 min. Then a solution benzaldehyde **2a** in THF (1.0 M, 0.47 mL, 0.47 mmol) and silyl enol ether **1e** (0.71 mmol, 1.5 equiv) were successively added to the above mixture. After 3 h, the reaction was quenched with KF/HCOOH aq (1.5 M KF, 3.0 M HCOOH, 2 mL) and the mixture was stirred for 2 h at rt. The aqueous layer was extracted with AcOEt and the combined organic layers were successively washed with satd $NaHCO_3$ (3 mL) and brine (3 mL). Drying over Na_2SO_4 and evaporating the solvent gave the crude product, which was purified by silica gel column chromatography (SiO_2 9.0 g, CH_2Cl_2/hexane 8:1, then CH_2Cl_2/AcOEt 160:1, then 10:1) and crystallized from hexane/AcOEt to give *syn*-**4fa** (38 mg, 32% yield). Mp: 105–106 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.09 (s, 3H), 2.27 (d, 1H, *J*=4.1 Hz), 2.52 (d, 1H, *J*=17.0 Hz), 3.71 (d, 1H, *J*=17.0 Hz), 5.14 (d, 1H, *J*=4.1 Hz), 7.30–7.43 (m, 7H), 7.56–7.63 (m, 1H), 7.78–7.82 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 22.9, 35.0, 54.6, 77.2, 124.2, 126.6, 127.2, 127.3, 127.9, 128.1, 135.0, 135.7, 141.0, 153.6, 211.0. IR ($CHCl_3$): ν 3604, 1709 cm^{-1}. LR-FABMS: 275 ($M+Na^+$), 235. HR-FABMS: calcd for $C_{17}H_{16}O_2Na$ 275.1048, found 275.1054.Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 868917.

*4.3.15. 2-[(Benzoyloxy)(p-methoxyphenyl)methyl]-2-methylcyclohexanone (**5bb**).* The enantiomeric excess was determined to be 81% (*anti*) and 78% (*syn*) by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=6:1, 1.0 mL/min]: t_R 11.1 min (*anti*-minor), 15.7 min (*anti*-major), 24.0 min (*syn*-minor), 28.5 min (*syn*-major).

anti-**5bb**: a colorless prism. $[\alpha]_D^{20}$ +80.8 (*c* 0.98, $CHCl_3$), 81% ee. Mp: 86–88 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.16 (s, 3H), 1.39–1.49 (m, 1H), 1.67–1.85 (m, 3H), 2.01–2.14 (m, 2H), 2.35–2.43 (m, 1H), 2.60–2.72 (m, 1H), 3.78 (s, 3H), 6.56 (s, 1H), 6.85–6.88 (m, 2H), 7.30–7.55 (m, 5H), 8.01–8.03 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.3, 21.2, 27.9, 37.0, 38.9, 53.3, 55.3, 76.7, 113.9, 128.6, 128.9, 129.8, 130.0, 133.3, 159.5, 165.4, 213.2. IR (KBr): ν 1714 cm^{-1}. LR-FABMS: 375 ($M+Na^+$), 231, 105. HR-FABMS: calcd for $C_{22}H_{24}O_4Na$ 375.1573, found 375.1582.

syn-**5bb**: a colorless prism. Mp: 135–137 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.08 (s, 3H), 1.60–1.98 (m, 5H), 2.27–2.39 (m, 1H), 2.50–2.55 (m, 2H), 3.76 (s, 3H), 6.43 (s, 1H), 6.80–6.83 (m, 2H), 7.22–7.25 (m, 2H), 7.41–7.45 (m, 2H), 7.53–7.57 (m, 1H), 8.03 (d, 2H, *J*=6.8 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.7, 20.8, 26.5, 33.3, 39.6, 52.9, 55.3, 77.0, 113.5, 128.5, 128.9, 129.1, 129.7, 130.5, 133.0, 159.3, 165.1, 212.5. IR (KBr): ν 1720, 1705 cm^{-1}. LR-FABMS: 375 ($M+Na^+$), 231, 105. HR-FABMS: calcd for $C_{22}H_{24}O_4Na$ 375.1573, found 375.1596.

*4.3.16. 2-[(Benzoyloxy)(p-trifluoromethylphenyl) methyl]-2-methylcyclohexanone (**5bc**).* The enantiomeric excess was determined to be 52% (*anti*) and 27% (*syn*) by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=9:1, 1.0 mL/min]: t_R 7.3 min (*anti*-minor), 12.1 min (*anti*-major), 17.9 min (*syn*-minor), 24.1 min (*syn*-major).

anti-**5bc**: a colorless prism. $[\alpha]_D^{20}$ +54.6 (*c* 0.95, $CHCl_3$), 52% ee. Mp: 131–134 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.19 (s, 3H), 1.46–1.58 (m, 1H), 1.75–1.88 (m, 3H), 1.95–2.10 (m, 2H), 2.38–2.49 (m, 1H), 2.55–2.64 (m, 1H), 6.60 (s, 1H), 7.43–7.60 (m, 8H), 8.01 (d, 2H, *J*=7.3 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.5, 21.1, 27.7, 36.4, 38.8, 52.9, 76.6, 123.9 (q, J=270.8 Hz), 125.1 (q, *J*=2.9 Hz), 128.1, 128.6, 129.6, 129.8, 130.3 (q, *J*=32.4 Hz), 133.5, 140.8, 165.3, 212.1. IR (KBr): ν 1727, 1706 cm^{-1}. LR-FABMS: 413 ($M+Na)^+$, 105. HR-FABMS: calcd for $C_{22}H_{21}O_3F_3Na$ 413.1341, found 413.1346.

syn-**5bc**: a colorless prism. Mp: 132–135 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.10 (s, 3H), 1.61–2.04 (m, 5H), 2.30–2.42 (m, 1H), 2.51–2.57 (m, 2H), 6.51 (s, 1H), 7.44–7.60 (m, 7H), 8.02 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.7, 20.8, 26.4, 33.0, 39.3, 52.5, 76.8, 124.0 (q, *J*=270.8 Hz), 125.0 (q, *J*=3.8 Hz), 128.1, 128.6, 129.7, 130.0, 130.2 (q, *J*=32.4 Hz), 133.3, 141.3, 165.0, 211.7. IR (KBr): ν 1722, 1706 cm^{-1}. LR-FABMS: 413 ($M+Na^+$). HR-FABMS: calcd for $C_{22}H_{21}O_3F_3Na$ 413.1341, found 413.1347.

*4.3.17. 2-[(Benzoyloxy)(p-nitrophenyl)methyl]-2-methylcyclohexanone (**5bd**).* The enantiomeric excess was determined to be 6% (*anti*) and 4% (*syn*) by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=9:1, 1.0 mL/min]: t_R 19.6 min (*anti*-minor), 23.6 min (*syn*-major), 36.6 min (*anti*-major), 64.5 min (*syn*-minor).

anti-**5bd**: a viscous colorless oil. $[\alpha]_D^{20}$ +10.1 (*c* 0.99, $CHCl_3$), 6% ee. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.21 (s, 3H), 1.55–2.08 (m, 6H), 2.42–2.60 (m, 2H), 6.59 (s, 1H), 7.41–7.62 (m, 5H), 8.01 (d, 2H, *J*=7.3 Hz), 8.19 (d, 2H, *J*=8.7 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.9, 21.0, 27.5, 36.1, 38.8, 52.9, 76.6, 123.4, 128.6, 128.7, 129.4, 129.8, 133.7, 144.3, 147.7, 165.3, 211.8. IR (KBr): ν 1722, 1712 cm^{-1}. LR-FABMS: 390 ($M+Na^+$), 176, 149. HR-FABMS: calcd for $C_{21}H_{21}NO_5Na$ 390.1318, found 390.1322.

syn-**5bd**: a colorless prism. Mp: 136–138 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.13 (s, 3H), 1.57–2.07 (m, 5H), 2.28–2.41 (m, 1H), 2.47–2.63 (m, 2H), 6.51 (s, 1H), 7.40–7.62 (m, 5H), 8.02 (d, 2H, *J*=8.7 Hz), 8.16 (d, 2H, *J*=8.7 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.7, 20.8, 26.4, 33.1, 39.2, 52.4, 76.7, 123.3, 128.6, 128.7, 129.7, 130.3, 133.5, 144.8, 147.7, 165.0, 211.4. IR (KBr): ν 1724, 1706 cm^{-1}. LR-FABMS: 390 ($M+Na^+$). HR-FABMS: calcd for $C_{21}H_{21}NO_5Na$ 390.1318, found 390.1334.

*4.3.18. 2-[(Benzoyloxy)(1-naphthyl)methyl]-2-methylcyclohexanone (**5be**).* The enantiomeric excess was determined to be 80% (*anti*) and 14% (*syn*) by chiral HPLC [Daicel Chiralpak AD-H, hexane/

IPA=19:1, 1.0 mL/min]: t_R 49.0 min (*anti*-minor), 52.2 min (*anti*-major), 61.4 min (*syn*-minor), 88.7 min (*syn*-major).

anti-**5be**: a colorless prism. $[\alpha]_D^{20}$ +193.4 (*c* 1.22, $CHCl_3$), 80% ee. Mp: 47–49 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.21–1.35 (m, 2H), 1.38 (s, 3H), 1.66–2.02 (m, 5H), 2.54–2.58 (m, 2H), 7.32–7.67 (m, 8H), 7.76–7.90 (m, 2H), 7.97–8.08 (m, 2H), 8.42 (d, 1H, *J*=8.0 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.9, 21.5, 27.9, 37.2, 39.4, 53.6, 73.2, 124.0, 125.7, 126.4, 127.0, 127.8, 128.5, 129.0, 129.1, 129.8, 132.0, 133.2, 133.4, 165.5, 213.0. IR (KBr): ν 1716 cm^{-1}. LR-FABMS: 395 ($M+Na^+$), 251, 105. HR-FABMS: calcd for $C_{25}H_{24}O_3Na$ 395.1623, found 395.1626.

syn-**5be**: a colorless prism. Mp: 56–58 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ 0.98 (s, 3H), 1.68–1.95 (m, 5H), 2.03–2.08 (m, 1H), 2.45–2.60 (m, 2H), 7.38–7.58 (m, 8H), 7.78 (d, 1H, *J*=8.2 Hz), 7.83 (d, 1H, *J*=7.3 Hz), 8.01–8.03 (m, 2H), 8.40 (d, 1H, *J*=8.2 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.6, 21.6, 25.7, 31.4, 38.9, 53.0, 72.5, 123.8, 124.7, 125.5, 125.7, 126.3, 128.3, 128.6, 128.8, 129.5, 130.4, 132.1, 132.8, 133.4, 133.5, 164.9, 212.4. IR (KBr): ν 1722 cm^{-1}. LR-FABMS: 395 ($M+Na^+$). HR-FABMS: calcd for $C_{25}H_{24}O_3Na$ 395.1623, found 395.1628.

*4.3.19. 2-[(Benzoyloxy)(2-naphthyl)methyl]-2-methylcyclohexanone (**5bf**).* The enantiomeric excess was determined to be 87% (*anti*) and 23% (*syn*) by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=9:1, 1.0 mL/min]: t_R 14.7 min (*anti*-minor), 18.4 min (*anti*-major), 22.9 min (*syn*), 39.0 min (*syn*).

anti-**5bf**: a colorless prism. $[\alpha]_D^{20}$ +140.3 (*c* 1.02, $CHCl_3$), 87% ee. Mp 115–118 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.24 (s, 3H), 1.45–1.57 (m, 1H), 1.68–1.96 (m, 3H), 2.01–2.24 (m, 2H), 2.40–2.52 (m, 1H), 2.64–2.76 (m, 1H), 6.78 (s, 1H), 7.41–7.62 (m, 6H), 7.76–7.89 (m, 4H), 8.05–8.14 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.5, 21.3, 28.0, 37.0, 38.9, 53.4, 77.4, 125.4, 126.4, 127.0, 127.8, 127.9, 128.2, 128.6, 129.9, 130.0, 132.9, 133.2, 133.4, 134.2, 165.5, 212.9. IR (KBr): ν 1724, 1709 cm^{-1}. LR-FABMS: 395 ($M+Na^+$), 251, 105. HR-FABMS: calcd for $C_{25}H_{24}O_3Na$ 395.1623, found 395.1624.

syn-**5bf**: a colorless prism. Mp: 151–153 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.14 (s, 3H), 1.63–2.05 (m, 5H), 2.37–2.59 (m, 3H), 6.64 (s, 1H), 7.42–7.58 (m, 5H, Ar-H), 7.75–7.85 (m, 4H), 8.06 (d, 2H, *J*=6.7 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.8, 21.0, 26.4, 33.2, 39.5, 52.9, 77.8, 125.6, 126.19, 126.23, 127.0, 127.7, 128.2, 128.5, 129.7, 130.4, 132.9, 133.1, 134.6, 165.1, 212.3. IR (KBr): ν 1724, 1704, 1600 cm^{-1} LR-FABMS: 395 ($M+Na^+$), 105. HR-FABMS: calcd for $C_{25}H_{24}O_3Na$ 395.1623, found 395.1620.

*4.3.20. 2-[1-(Benzoyloxy)-3-phenyl-2-propenyl]-2-methylcyclohexanone (**5bg**).* The enantiomeric excess was determined to be 90% (*anti*) and 42% (*syn*) by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=19:1, 1.0 mL/min]: t_R 15.4 min (*anti*-major), 17.2 min (*syn*-major), 21.1 min (*anti*-minor), 26.9 min (*syn*-minor).

anti-**5bg**: a colorless prism. $[\alpha]_D^{20}$ +91.8 (*c* 0.97, $CHCl_3$), 90% ee. Mp: 76–78 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.30 (s, 3H), 1.58–2.07 (m, 6H), 2.35–2.43 (m, 1H), 2.58–2.67 (m, 1H), 6.18–6.30 (m, 2H), 6.77 (d, 1H, *J*=15.6 Hz), 7.23–7.57 (m, 8H), 8.01 (d, 2H, *J*=7.3 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.8, 20.9, 27.6, 36.6, 38.9, 52.7, 77.3, 123.1, 126.8, 127.2, 128.3, 128.5, 128.7, 128.8, 129.8, 130.1, 133.2, 135.1, 136.1, 165.6, 213.0. IR (KBr): ν 1706, 1600 cm^{-1}. LR-FABMS: 371 ($M+Na^+$), 227, 105. HR-FABMS: calcd for $C_{23}H_{24}O_3Na$ 371.1623, found 371.1634.

syn-**5bg**: a colorless prism. Mp: 141–144 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.25 (s, 3H), 1.66–1.82 (m, 2H), 1.85–1.95 (m, 3H), 2.10–2.22 (m, 1H), 2.40–2.52 (m, 2H), 6.14–6.23 (m, 2H), 6.70 (dd, 1H, *J*=5.5, 20 Hz), 7.16–7.60 (m, 8H), 8.05 (d, 2H, *J*=7.4 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 19.6, 20.9, 27.1, 35.0, 39.7, 53.0, 76.0, 123.2, 126.8, 128.2, 128.5, 128.6, 129.7, 130.3, 133.2, 134.8, 136.2, 165.4, 212.4. IR (KBr): ν 1714, 1270 cm^{-1}. LR-FABMS: 371 ($M+Na^+$), 227, 105. HR-FABMS: calcd for $C_{23}H_{24}O_3Na$ 371.1623, found 371.1639.

*4.3.21. 2-[1-(Benzoyloxy)-3-phenylpropyl]-2-methylcyclohexanone (**5bh**).* The enantiomeric excess was determined to be 85% (*anti*) and 70% (*syn*) by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=19:1, 1.0 mL/min]: t_R 9.7 min (*syn*-major), 14.4 min (*anti*-major), 16.3 min (*syn*-minor), 19.6 min (*anti*-minor).

anti-**5bh**: a colorless prism. $[\alpha]_D^{20}$ +21.9 (*c* 1.06, $CHCl_3$), 85% ee. Mp: 75–78 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.18 (s, 3H), 1.57–1.77 (m, 4H), 1.82–2.05 (m, 4H), 2.27–2.39 (m, 1H), 2.58–2.73 (m, 3H), 5,85 (m, 1H), 7.14–7.28 (m, 5H), 7.39–7.46 (m, 2H), 7.54–7.61 (m, 1H), 8.02 (d, 2H, *J*=8.6 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 19.0, 20.7, 27.2, 32.1, 32.8, 36.0, 38.9, 52.9, 76.2, 126.2, 128.5, 129.9, 130.1, 133.2, 141.6, 166.4, 213.5. IR (KBr) ν 2939, 1712 cm^{-1} LR-FABMS: 351 ($M+H^+$). HR-FABMS: calcd for $C_{23}H_{27}O_3$ 351.1960, found 351.1994.

syn-**5bh**: a viscous colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.19 (s, 3H), 1.42–1.51 (m, 1H), 1.54–1.78 (m, 3H), 1.86–2.18 (m, 5H), 2.28–2.38 (m, 1H), 2.56–2.75 (m, 2H), 5.80 (dd, 1H, *J*=10.5, 1.4 Hz), 7.12–7.26 (m, 5H), 7.42–7.51 (m, 2H), 7.56–7.62 (m, 1H), 8.04–8.12 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.6, 20.8, 28.0, 32.6, 37.0, 39.9, 53.9, 73.7, 126.1, 128.4, 128.58, 128.61, 129.9, 130.0, 133.3, 141.3, 166.3, 213.5. IR (KBr): ν 2933, 1716, 1714 cm^{-1}. LR-FABMS: 373 ($M+Na^+$). HR-FABMS: calcd for $C_{23}H_{26}O_3Na$ 373.1780, found 373.1788.

4.4. Construction of quaternary asymmetric centers using base-catalyzed aldol reaction under aqueous condition

*4.4.1. syn-2-[(Benzoyloxy)phenylmethyl]-2-methylcyclohexanone (**5ba**). Typical procedure for the aldol reaction under aqueous condition*: under an Ar atmosphere, H_2O in THF (2.8 M, 0.26 mL, 0.71 mmol, 1.5 equiv) and *n*-BuLi (0.094 mmol, 20 mol %) in hexane (0.21 M, 0.45 mL) were added to a solution of (*R*)-3,3′-dichlorobinaphthol (16.8 mg, 0.047 mmol, 10 mol %) in THF at −23 °C, and the mixture was stirred for 5 min. Then a solution aldehyde **2a** in THF (1.0 M, 0.47 mL, 0.47 mmol) and silyl enol ether **1b** (0.71 mmol, 1.5 equiv) were successively added to the above mixture. After 3 h, the reaction was quenched with KF/HCOOH aq (1.5 M KF, 3.0 M HCOOH, 2 mL) and the mixture was stirred for 2 h at rt. The aqueous layer was extracted with AcOEt and the combined organic layers were successively washed with satd $NaHCO_3$ (3 mL) and brine (3 mL). Drying over Na_2SO_4 and evaporating the solvent gave the crude product, which was dissolved in CH_2Cl_2 (2 mL). Benzoyl chloride (0.11 mL, 0.94 mmol, 2.0 equiv) and a solution of DMAP (287 mg, 2.35 mmol, 5.0 equiv) in CH_2Cl_2 (2 mL) were added to the mixture at 0 °C. After stirring for 1 h, 10% HCl aq (5 mL) was added to the mixture and the entire mixture was extracted with AcOEt (20 mL×3). The organic layer was washed with brine and dried over Na_2SO_4. After evaporating the solvent, the residue was purified by silica gel column chromatography (SiO_2 9.0 g, CH_2Cl_2/hexane=1:4 then 1:1) to afford the corresponding benzoylated product **5ba** as a colorless oil (109 mg, 72% yield, *syn*/*anti* 2.3:1). The enantiomeric excess was determined to be 81% (*syn*) and 1% (*anti*) by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=7:2, 1.0 mL/min]: t_R 13.4 min (*anti*-minor), 16.2 min (*syn*-major), 17.2 min (*anti*-major), 27.1 min (*syn*-minor).

syn-**5ba**: a colorless needle. $[\alpha]_D^{21}$ −90.4 (*c* 1.08, $CHCl_3$), 81% ee. Mp: 115–117 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.09 (s, 3H), 1.55–1.79 (m, 2H), 1.80–2.03 (m, 3H), 2.32–2.40 (m, 1H), 2.45–2.58 (m, 2H), 6.49 (s, 1H), 7.22–7.35 (m, 5H), 7.42–7.46 (m, 2H), 7.54–7.58 (m, 1H), 8.04 (d, 2H, *J*=6.9 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.76, 20.79, 26.5, 33.2, 39.5, 52.8, 77.5, 127.7, 128.0, 128.5, 129.7, 130.4, 133.1, 137.1, 165.0, 212.3. IR (KBr): ν 1722, 1704 cm^{-1}. LR-EIMS: 322 (M^+), 216, 105, 77. HR-EIMS: calcd for $C_{21}H_{22}O_3$ 322.1569, found 322.1547.

*4.4.2. syn-2-[(Benzoyloxy)phenylmethyl]-2-ethylcyclohexanone (**5ca**).* The enantiomeric excess was determined to be 79% (*syn*) and 19% (*anti*) by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=19:1, 1.0 mL/min]: t_R 10.3 min (*anti*-minor), 12.3 min (*anti*-major), 17.1 min (*syn*-major), 38.9 min (*syn*-minor).

syn-**5ca**: a colorless needle. $[\alpha]_D^{22}$ −116.6 (*c* 1.05, $CHCl_3$), 75% ee. Mp: 165–168 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.89 (t, 3H, *J*=7.6 Hz), 1.25–1.34 (m, 1H), 1.69–1.91 (m, 5H), 1.99–2.02 (m, 1H), 2.33–2.47 (m, 3H), 6.56 (s, 1H), 7.24–7.56 (m, 8H), 8.01 (d, 1H, *J*=7.2 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 8.4, 20.8, 25.7, 26.0, 30.9, 40.2, 55.8, 75.7, 127.6, 127.91, 127.92, 128.3, 129.5, 130.5, 132.8, 137.1, 164.9, 211.1. IR (KBr): ν 1724, 1702 cm^{-1}. LR-EIMS: 336 (M^+), 105, 77. HR-EIMS: calcd for $C_{22}H_{24}O_3$ 336.1725, found 336.1701.

*4.4.3. syn-2-[(Benzoyloxy)phenylmethyl]-2-methylcyclopentanone (**5da**).* The enantiomeric excess was determined to be 75% (*syn*) and 42% (*anti*) by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=29:1, 1.0 mL/min]: t_R 18.4 min (*anti*-minor), 26.1 min (*anti*-major), 29.3 min (*syn*-major), 50.8 min (*syn*-minor).

syn-**5da**: a colorless needle. $[\alpha]_D^{22}$ +12.9 (*c* 1.01, $CHCl_3$), 75% ee. Mp: 111–114 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.95 (s, 3H), 1.63–1.71 (m, 1H), 1.77–1.91 (m, 1H), 2.05–2.13 (m, 1H), 2.20–2.31 (m, 1H), 2.40–2.49 (m, 1H), 2.62–2.71 (m, 1H), 6.05 (s, 1H), 7.25–7.60 (m, 8H), 7.95–8.02 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.7, 20.4, 31.2, 38.6, 53.0, 78.9, 127.5, 128.27, 128.31, 128.5, 129.6, 130.3, 133.1, 137.7, 164.8, 220.3. IR (KBr): ν 1735, 1720, 1600, 1583 cm^{-1}. LR-FABMS: 331 $(M+Na)^+$. HR-FABMS: calcd for $C_{20}H_{20}O_3Na$ 331.1310, found 331.1315.

*4.4.4. syn-2-[(Benzoyloxy)phenylmethyl]-2-methyl-1-tetralone (**5ea**).* The enantiomeric excess was determined to be 85% (*syn*) and 72% (*anti*) by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=19:1, 1.0 mL/min]: t_R 23.4 min (*syn*-major), 27.7 min (*anti*-minor), 36.6 min (*anti*-major), 62.3 min (*syn*-minor).

syn-**5ea**: a colorless prism. $[\alpha]_D^{22}$ −88.1 (*c* 1.02, $CHCl_3$), 85% ee. Mp: 158–160 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.17 (s, 3H), 1.88–1.97 (m, 1H), 2.58–2.70 (m, 1H), 2.96–3.17 (m, 2H), 6.57 (s, 1H), 7.20–7.56 (m, 11H), 7.88 (d, 2H, *J*=7.2 Hz), 8.06 (d, 1H, *J*=7.0 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 19.5, 25.0, 28.8, 49.1, 78.7, 126.8, 127.6, 127.9, 128.0, 128.3, 128.7, 129.5, 130.1, 131.9, 132.8, 133.4, 136.8, 143.1, 164.9, 199.4. IR (KBr): ν 1726, 1673 cm^{-1}. LR-FABMS: 393 ($M+Na^+$), 105. HR-FABMS: calcd for $C_{25}H_{22}O_3Na$ 393.1467, found 393.1474.

*4.4.5. syn-2-[(Benzoyloxy)phenylmethyl]-2-methyl-1-indanone (**5fa**).* The enantiomeric excess was determined to be 94% (*syn*) and 35% (*anti*) by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=4:1, 1.0 mL/min]: t_R 15.9 min (*anti*-minor), 18.0 min (*syn*-major), 19.8 min (*anti*-major), 54.5 min (*syn*-minor).

syn-**5fa**: a colorless prism. $[\alpha]_D^{28}$ −45.8 (*c* 1.18, $CHCl_3$), 94% ee. Mp: 103–104 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.18 (s, 3H, $-CH_3$), 2.73 (d, 1H, *J*=17.0 Hz), 3.91 (d, 1H, *J*=17.0 Hz), 6.26 (s, 1H), 7.24 (t, 2H, *J*=7.8 Hz), 7.29–7.47 (m, 7H), 7.55 (d, 1H, *J*=7.8 Hz), 7.61–7.68 (m, 3H), 7.77 (d, 1H, *J*=7.8 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 22.3, 36.0, 53.6, 79.8, 124.6, 126.7, 127.3, 127.7, 128.34, 128.39, 128.43, 129.5, 130.0, 133.0, 135.2, 135.8, 137.5, 152.9, 164.7, 208.4. IR (neat): ν 1716 cm^{-1}. LR-FABMS: 357 ($M+H^+$), 235, 105. HR-FABMS: calcd for $C_{24}H_{21}O_3$ 357.1491, found 357.1510.

*4.4.6. 2-[1-(Benzoyloxy)-3-phenyl-2-propenyl]-2-methyl-1-indanone (**5fg**).* The enantiomeric excess was determined to be 93% (*syn*) and 79% (*anti*) by chiral HPLC, after hydrogenation of double bond [Daicel Chiralpak AD-H+Chiralcel OD-H, hexane/IPA=19:1, 1.0 mL/min]: t_R 27.7 min (*anti*-major), 30.2 min (*anti*-minor), 33.4 min (*syn*-minor), 35.3 min (*syn*-major).

anti-**5fg**: a colorless needle. Mp: 71–72 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.39 (s, 3H), 3.02 (d, 1H, *J*=17.4 Hz), 3.48 (d, 1H, *J*=17.4 Hz), 5.90 (dd, 1H, *J*=7.8, 0.9 Hz), 6.30 (dd, 1H, *J*=16.0, 7.8 Hz), 6.73 (d, 1H, *J*=16.0 Hz), 7.19–7.29 (m, 5H), 7.34–7.43 (m, 4H), 7.49–7.53 (m, 1H), 7.58 (dt, 1H, *J*=0.9, 7.6 Hz), 7.81–7.82 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.9, 38.4, 53.0, 79.8, 123.4, 124.4, 126.5, 126.9, 127.7, 128.11, 128.5, 128.6, 129.7, 130.1, 133.2, 135.1, 135.2, 136.2, 136.5, 152.8, 165.6, 207.9. IR (neat): ν 1709, 1259 cm^{-1}. LR-FABMS: 405 ($M+Na^+$), 261, 105. HR-FABMS: calcd for $C_{26}H_{22}O_3Na$ 405.1467, found 405.1492.

syn-**5fg**: a colorless needle. $[\alpha]_D^{26}$ +17.0 (*c* 1.03, $CHCl_3$), 93% ee. Mp: 155–166 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.31 (s, 3H), 2.97 (d, 1H, *J*=17.0 Hz), 3.72 (d, 1H, *J*=17.0 Hz), 5.91 (dd, 1H, *J*=7.8, 0.9 Hz), 6.27 (dd, 1H, *J*=16.0, 7.8 Hz), 6.85 (d, 1H, *J*=16.0), 7.21–7.44 (m, 9H), 7.55–7.59 (m, 3H), 7.66 (dt, 1H, *J*=0.9, 7.6 Hz), 7.74 (d, 1H, J=7.8 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.5, 36.7, 52.9, 78.8, 123.4, 124.6, 126.6, 126.9, 127.7, 128.28, 128.34, 128.7, 129.5, 130.1, 132.9, 135.2, 135.8, 136.0, 136.1, 152.9, 164.9, 208.2. IR (neat): ν 1713, 1705 cm^{-1}. LR-FABMS: 405 ($M+Na^+$), 261, 55 (bp). HR-FABMS: calcd for $C_{26}H_{22}O_3Na$ 405.1467, found 405.1476.

*4.4.7. 2-[1-(Benzoyloxy)-3-phenylpropyl]-2-methyl-1-indanone (**5fh**).* The enantiomeric excess was determined to be 96% (*syn*) and 69% (*anti*) by chiral HPLC [Daicel Chiralpak AD-H+Chiralcel OD-H, hexane/IPA=19:1, 1.0 mL/min]: t_R 27.7 min (*anti*-major), 30.8 min (*anti*-minor), 32.9 min (*syn*-minor), 36.0 min (*syn*-major).

anti-**5fh**: a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.31 (s, 3H), 1.77–1.87 (m, 1H), 1.95–2.06 (m, 1H), 2.57–2.65 (m, 2H), 2.90 (d, 1H, *J*=17.4 Hz), 3.47 (d, 1H, *J*=17.4 Hz), 5.62 (dd, 1H, *J*=10.5, 2.3 Hz), 7.07–7.13 (m, 3H), 7.18–7.21 (m, 2H), 7.35–7.43 (m, 4H), 7.53–7.58 (m, 2H), 7.78 (d, 1H, *J*=7.8 Hz), 7.91–7.94 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 22.4, 32.67, 32.70, 38.0, 53.2, 78.3, 124.5, 126.0, 126.6, 127.7, 128.41, 128.45, 128.5, 129.8, 130.0, 133.2, 135.3, 136.3, 141.4, 152.8, 166.4, 208.2. IR (neat): ν 1709 cm^{-1}. LR-FABMS: 407 ($M+Na^+$), 385, 263. HR-FABMS: calcd for $C_{26}H_{24}O_3Na$ 407.1623, found 407.1645.

syn-**5fh**: a colorless needle. $[\alpha]_D^{28}$ +16.1 (*c* 0.98, $CHCl_3$), 96% ee. Mp: 106–107 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.31 (s, 3H), 1.92–2.09 (m, 1H), 2.18–2.29 (m, 1H), 2.69–2.79 (m, 2H), 2.93 (d, 1H, *J*=17.4 Hz), 3.54 (d, 1H, *J*=17.4 Hz), 5.62 (dd, 1H, *J*=10.0, 2.8 Hz), 7.15–7.22 (m, 3H), 7.25–7.35 (m, 5H), 7.45–7.54 (m, 2H), 7.61 (dt, 1H, *J*=0.9, 7.8 Hz), 7.69 (d, 1H, *J*=7.8 Hz), 7.77–7.79 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.0, 32.7, 33.0, 37.6, 53.3, 77.1, 124.6, 126.1, 126.6, 127.7, 128.4, 128.5, 128.6, 129.7, 130.0, 133.0, 135.2, 135.9, 141.6, 152.6, 165.9, 208.2. IR (KBr): ν 1720 cm^{-1}. LR-FABMS: 385 ($(M+H)^+$), 313, 263, 154, 105. HR-FABMS: calcd for $C_{26}H_{25}O_3$ 385.1804, found 385.1801.

*4.4.8. (1′S,2R)-2-[(Benzoyloxy)(cyclohexyl)methyl]-2-methyl-1-indanone (**5fi**).* The enantiomeric excess was determined to be 99% (*syn*) and 86% (*anti*) by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=19:1, 1.0 mL/min]: t_R 25.6 min (*syn*-major), 27.0 min (*anti*-major), 31.0 min (*syn*-minor), 33.9 min (*anti*-minor).

anti-**5fi**: a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.00–1.14 (m, 5H), 1.26 (s, 3H), 1.38–1.76 (m, 6H), 2.88 (d, 1H, *J*=17.4 Hz), 3.56 (d, 1H, *J*=17.4 Hz), 5.47 (d, 1H, *J*=6.4 Hz), 7.37–7.47 (m, 4H), 7.54–7.62 (m, 2H), 7.80 (d, 1H, *J*=7.8 Hz), 8.04 (dd, 2H, *J*=0.9, 8.5 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 24.2, 26.0, 26.1, 26.3, 29.0, 31.5, 37.5, 40.5, 53.4, 81.5, 124.6, 126.8, 127.7, 128.5, 129.8, 130.2, 133.1, 135.1, 136.0, 152.4, 166.2, 208.0. IR (neat): ν 1718, 1704 cm^{-1}. LR-FABMS: 363 ($M+H^+$), 241, 105. HR-FABMS: calcd for $C_{24}H_{27}O_3$ 363.1960, found 363.1972.

syn-**5fi**: a colorless prism. $[\alpha]_D^{28}$ +29.1 (*c* 1.09, $CHCl_3$), 99% ee. Mp: 69–70 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.00–1.35 (m, 8H), 1.57–1.95 (m, 6H), 2.96 (d, 1H, *J*=17.0 Hz), 3.70 (d, 1H, *J*=17 Hz), 5.51 (d, 1H, *J*=2.8 Hz), 7.20–7.28 (m, 3H), 7.35–7.42 (m, 1H), 7.45–7.56 (m, 2H), 7.62–7.66 (m, 1H), 7.67–7.72 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.8, 26.1, 26.48, 26.55, 27.9, 31.9, 37.9, 39.8, 53.3, 80.0, 124.6, 126.5, 127.5, 128.3, 129.6, 130.1, 132.8, 135.0, 135.3, 153.0, 165.5, 208.8. IR (neat): ν 1712, 1705 cm^{-1}. LR-FABMS: 363 ($M+H^+$),

241, 159, 105. HR-FABMS: calcd for $C_{24}H_{27}O_3$ 363.1960, found 363.1952.

*4.4.9. 2-[1-(Benzoyloxy)ethyl]-2-methyl-1-indanone (**5fj**).* The enantiomeric excess was determined to be 93% (*syn*) and 64% (*anti*) by chiral HPLC [Daicel Chiralcel OD-H, hexane/IPA=69:1, 1.0 mL/min]: t_R 15.2 min (*anti*-minor), 16.8 min (*anti*-major), 22.4 min (*syn*-minor), 23.9 min (*syn*-major).

anti-**5fj**: a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.28 (d, 1H, J=6.4 Hz), 1.36 (s, 3H), 2.96 (d, 1H, J=17.4 Hz), 3.44 (d, 1H, J=17.4 Hz), 5.41 (q, 1H, J=6.4 Hz), 7.34–7.62 (m, 6H), 7.80–7.82 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 15.5, 21.9, 38.0, 52.6, 75.7, 124.3, 126.4, 127.5, 128.3, 129.5, 130.2, 132.9, 135.0, 136.5, 152.9, 165.8, 208.1. IR (neat): ν 1716 cm^{-1}. LR-FABMS: 317 (M+Na$^+$). HR-FABMS: calcd for $C_{19}H_{18}O_3Na$ 317.1154, found 317.1169.

syn-**5fj**: a colorless needle. $[\alpha]_D^{30}$ +33.1 (*c* 1.38, $CHCl_3$), 93% ee. Mp: 63–64 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.28 (s, 3H), 1.45 (d, 3H, J=6.4 Hz), 2.93 (d, 1H, J=17.0 Hz), 3.57 (d, 1H, J=17.0 Hz), 5.40 (q, 1H, J=6.4 Hz), 7.21–7.26 (m, 2H), 7.34–7.45 (m, 2H), 7.52–7.58 (m, 3H), 7.62–7.66 (m, 1H), 7.70–7.72 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 15.4, 20.6, 36.6, 52.8, 74.7, 124.3, 126.4, 127.4, 128.1, 129.2, 130.2, 132.6, 134.9, 135.9, 152.6, 165.2, 208.3. IR (neat): ν 1720 cm^{-1}. LR-FABMS: 295 (M+H$^+$), 173, 105. HR-FABMS: calcd for $C_{19}H_{19}O_3$ (M+H$^+$) 295.1334, found 295.1381.

*4.4.10. (1′S,2R)-2-{[(1S)-10-Camphorsulfonyloxy] (cyclohexyl)methyl}-2-methyl-1-indanone (**7fi**).* Under an Ar atmosphere, H_2O in THF (2.8 M, 0.26 mL, 0.71 mmol, 1.5 equiv) and *n*-BuLi (0.094 mmol, 20 mol %) in hexane (0.21 M, 0.45 mL) were added to a solution of (*R*)-3,3′-dichlorobinaphthol **2d** (16.8 mg, 0.047 mmol, 10 mol %) in THF at −23 °C, and the mixture was stirred for 5 min. Then a solution cyclohexanecarboxaldehyde **2i** in THF (1.0 M, 0.52 mL, 0.47 mmol) and silyl enol ether **1f** (0.71 mmol, 1.5 equiv) were successively added to the above mixture. After 3 h, the reaction was quenched with KF/HCOOH aq (1.5 M KF, 3.0 M HCOOH, 2 mL) and the mixture was stirred for 2 h at rt. The aqueous layer was extracted with AcOEt and the combined organic layers were successively washed with satd $NaHCO_3$ (3 mL) and brine (3 mL). Drying over Na_2SO_4 and evaporating the solvent gave the crude product, which was dissolved in CH_2Cl_2 (2 mL). 10-*S*-Camphorsulfonyl chloride (354 mg, 0.94 mmol, 2.0 equiv) and a solution of DMAP (287 mg, 2.35 mmol, 5.0 equiv) in CH_2Cl_2 (2 mL) were added to the mixture at 0 °C. After stirring for 1 h, 10% HCl aq (5 mL) was added to the mixture and the entire mixture was extracted with AcOEt (20 mL×3). The organic layer was washed with brine and dried over Na_2SO_4. After evaporating the solvent, the residue was purified by silica gel column chromatography (SiO_2 9.0 g, CH_2Cl_2/hexane=1:4 then 1:1) to afford the corresponding product as an colorless prism. $[\alpha]_D^{22}$ +61.0 (*c* 1.60, $CHCl_3$). Mp: 110–111 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.70 (s, 3H), 1.07 (s, 3H), 1.12–1.85 (m, 17H), 1.95–2.05 (m, 2H), 2.23–2.29 (m, 1H), 2.35–2.42 (m, 1H), 2.54 (d, 1H, J=14.7 Hz), 2.92 (d, 2H, J=14.7 Hz), 3.63 (d, 1H, J=17.0 Hz), 5.11 (d, 1H, J=2.3 Hz), 7.37 (t, 1H, J=7.3 Hz), 7.50 (d, 1H, J=7.8 Hz), 7.64 (t, 1H, J=7.3 Hz), 7.74 (d, 1H, J=7.8 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 19.3, 19.7, 22.1, 24.4, 25.7, 26.3, 26.4, 26.8, 27.3, 31.3, 37.1, 39.5, 42.3, 42.4, 47.7, 47.8, 53.4, 57.6, 89.5, 124.3, 126.8, 127.7, 134.5, 135.6, 153.3, 209.2, 214.0. IR ($CHCl_3$) ν 1745, 1709, 1360, 1171, 769 cm^{-1}. LR-FABMS: 495 (M+Na$^+$). HR-FABMS: calcd for $C_{27}H_{36}O_5SNa$ 495.2181, found 495.2178. Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 868919.

4.5. Base-catalyzed aldol-Tishchenko reaction of trimethoxysilyl enol ethers

*4.5.1. anti-3-Hydroxy-2,2-dimethyl-1,3-diphenypropyl benzoate 3-Benzoyloxy-2,2-dimethyl-1,3-diphenylpropan-1-ol (**8ia**).*[29] *Typical procedure for the aldol-Tishchenko reaction:* under an Ar atmosphere, *n*-BuLi (0.094 mmol, 20 mol %) in hexane (0.21 M, 0.45 mL) was added to a solution of (*R*)-3,3′-diphenylbinaphthol (20.7 mg, 0.047 mmol, 10 mol %) in THF at −23 °C, and the mixture was stirred for 5 min. Then an aldehyde (1.18 mmol, 2.5 equiv) and silyl enol ether **1** (0.47 mmol) were successively added to the above mixture. After 6 h, the reaction was quenched with KF/HCOOH aq (1.5 M KF, 3.0 M HCOOH, 2 mL) and the mixture was stirred for 2 h at rt. The aqueous layer was extracted with AcOEt and the combined organic layers were successively washed with satd $NaHCO_3$ (3 mL) and brine (3 mL). Drying over Na_2SO_4 and evaporating the solvent gave the crude product, which was purified by silica gel column chromatography (SiO_2 9.0 g, CH_2Cl_2/hexane=1:1) to afford the product (156 mg, 92% yield) as a colorless needle. The enantiomeric excess was determined to be 88% by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=4:1, 1.0 mL/min]: t_R 10.2 min (major), 27.4 min (minor). $[\alpha]_D^{30}$ −30.4 (*c* 1.06, $CHCl_3$), 88% ee. Mp: 128–129 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.80 (s, 3H), 0.87 (s, 3H), 3.01 (br s, 1H), 4.74 (s, 1H), 6.37 (s, 1H), 7.19–7.57 (m, 13H), 8.11–8.13 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.9, 19.2, 42.9, 76.9, 80.0, 127.2, 127.4, 127.68, 127.71, 128.09, 128.14, 128.5, 129.6, 130.2, 133.1, 137.9, 141.1, 166.0. IR ($CHCl_3$) ν 1720 cm^{-1}. LR-FABMS: 383 (M+Na$^+$), 176, 105. HR-FABMS: calcd for $C_{24}H_{24}O_3Na$ 383.1623, found 383.1627.

*4.5.2. anti-3-Hydroxy-2,2-dimethyl-1-phenylpropyl benzoate (**8ja**).* The enantiomeric excess was determined to be 91% by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=9:1, 1.0 mL/min]: t_R 10.8 min (major), 17.7 min (minor). A colorless oil. $[\alpha]_D^{32}$ −43.7 (*c* 0.77, $CHCl_3$), 91% ee. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.97 (s, 3H), 1.00 (s, 3H), 2.31 (br s, 1H), 3.32 (d, 1H, J=11.5 Hz), 3.53 (d, 1H, J=11.5 Hz), 6.06 (s, 1H), 7.26–7.37 (m, 3H), 7.41–7.49 (m, 4H), 7.56–7.60 (m, 1H), 8.08–8.11 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 19.5, 21.5, 40.4, 69.1, 79.4, 127.8, 127.9, 128.5, 129.7, 130.1, 133.2, 137.6, 166.2. IR ($CHCl_3$): ν 3506, 1718 cm^{-1}. LR-FABMS: 307 (M+Na$^+$), 105. HR-FABMS: calcd for $C_{18}H_{20}O_3Na$ 307.1310, found 307.1325.

*4.5.3. anti-3-Hydroxy-2,2-dimethyl-3-phenylpropyl benzoate (**9ja**).*[24] The enantiomeric excess was determined to be 91% by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=9:1, 1.0 mL/min]: t_R 9.6 min (major), 14.6 min (minor). A colorless prism. $[\alpha]_D^{30}$ −23.1 (*c* 1.13, $CHCl_3$), 91% ee. Mp: 73–74 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.97 (s, 3H), 1.04 (s, 3H), 2.38 (br s, 1H), 4.02 (d, 1H, J=11.0 Hz), 4.43 (d, 1H, J=11.0 Hz), 4.69 (s, 1H), 7.25–7.48 (m, 7H), 7.56–7.60 (m, 1H), 8.04–8.06 (m, 2H).

*4.5.4. anti-{1-[(Hydroxyl)(phenyl)methyl]cyclohexyl}(phenyl)methyl benzoate (**8ga**).* The enantiomeric excess was determined to be 71% by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=9:1, 1.0 mL/min]: t_R 18.8 min (major), 21.3 min (minor). A colorless needle. $[\alpha]_D^{32}$ −22.3 (*c* 1.15, $CHCl_3$), 71% ee. Mp: 159–160 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.07–1.70 (m, 8H), 1.75–1.95 (m, 2H), 3.42 (br s, 1H), 4.85 (s, 1H), 6.43 (s, 1H), 7.18–7.62 (m, 13H), 8.05–8.13 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.7, 21.2, 25.8, 26.1, 29.3, 44.1, 77.0, 78.8, 127.3, 127.5, 127.6, 128.0, 128.1, 128.3, 128.7, 129.5, 130.0, 133.3, 137.3, 140.7, 164.9. IR ($CHCl_3$): ν 3589, 1724 cm^{-1}. LR-FABMS: 423 (M+Na$^+$), 105. HR-FABMS: calcd for $C_{27}H_{28}O_3Na$ 423.1936, found 423.1972.

*4.5.5. anti-3-Hydroxy-2,2,4-trimethyl-1-phenylpentyl benzoate (**8ha**).* The enantiomeric excess was determined to be 60% by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=9:1, 1.0 mL/min]: t_R 10.2 min (major), 15.2 min (minor). A colorless oil. $[\alpha]_D^{32}$ −34.1 (*c* 1.12, $CHCl_3$), 60% ee. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.89 (s, 3H), 1.05 (d, 3H, J=6.9 Hz), 1.07 (d, 3H, J=6.9 Hz), 1.14 (s, 3H), 1.95–2.05 (m, 1H), 2.34 (br s, 1H), 3.41 (s, 1H), 6.15 (s, 1H), 7.25–7.60 (m, 8H), 8.05–8.13 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.1, 19.3, 24.0, 28.8, 43.3, 78.2,

81.0, 127.8, 128.2, 128.5, 129.7, 130.3, 133.2, 137.9, 166.0. IR ($CHCl_3$): ν 3514, 1720 cm^{-1}. LR-FABMS: 349 ($M+Na^+$), 105. HR-FABMS: calcd for $C_{21}H_{26}O_3Na$ 349.1780, found 349.1834.

*4.5.6. anti-3-Hydroxy-2,2-dimethyl-1-(methylethyl)-3-phenylpropyl benzoate (**9ha**).* The enantiomeric excess was determined to be 60% by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=9:1, 1.0 mL/min]: t_R 7.4 min (major), 14.5 min (minor). A colorless oil. $[\alpha]_D^{30}$ +7.6 (*c* 1.12, $CHCl_3$), 60% ee. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.88 (s, 3H), 0.96 (s, 3H), 1.07 (d, 3H, *J*=6.9 Hz), 1.09 (d, 3H, *J*=6.9 Hz), 2.18–2.31 (m, 1H), 3.29 (d, 1H, *J*=2.7 Hz), 4.48 (d, 1H, *J*=1.8 Hz), 5.34 (d, 1H, *J*=2.7 Hz), 7.16–7.30 (m, 5H), 7.45–7.52 (m, 2H), 7.58–7.65 (m, 1H), 8.08–8.25 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.6, 18.2, 20.1, 23.5, 28.9, 43.3, 77.1, 81.7, 127.1, 127.3, 128.3, 128.5, 129.8, 133.2, 140.6, 167.4. IR ($CHCl_3$): ν 3493, 1697 cm^{-1}. LR-FABMS: 349 ($M+Na^+$), 309, 105 (bp). HR-FABMS: calcd for $C_{21}H_{26}O_3Na$ 349.1780, found 349.1779.

*4.5.7. 2-(Hydroxyphenylmethyl)-2-methyl-1-phenylbutyl benzoate (**8ka** and **9ka**).* The enantiomeric excess was determined to be **8ka** 93% and **9ka** 93% by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=9:1, 1.0 mL/min]: t_R 13.4 min (**8ka,** major), 16.9 min (**9ka**, major), 24.9 min (**8ka**, minor), 82.0 min (**9ka**, minor).

Compound **8ka**: a colorless needle. $[\alpha]_D^{30}$ −28.4 (*c* 1.25, $CHCl_3$), 93% ee. Mp: 96–97 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.84 (s, 3H), 0.84 (t, 3*H*, *J*=6.7 Hz), 1.26–1.37 (m, 1H), 1.85–1.95 (m, 1H), 3.25 (br s, 1H), 4.80 (s, 1H), 6.18 (s, 1H), 7.15–7.35 (m, 8H), 7.42–7.51 (m, 4H), 7.53–7.60 (m, 1H), 8.05–8.10 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 7.9, 19.3, 23.3, 44.6, 77.9, 80.6, 127.2, 127.5, 127.97, 128.02, 128.1, 128.5, 129.5, 130.0, 133.2, 137.5, 141.0, 165.2. IR ($CHCl_3$) ν 3591, 1724 cm^{-1}. LR-FABMS: 397 ($M+Na^+$), 105. HR-FABMS: calcd for $C_{25}H_{26}O_3Na$ 397.1779, found 397.1786.

Compound **9ka**: a colorless needle. $[\alpha]_D^{30}$ −24.2 (*c* 0.89, $CHCl_3$), 93% ee. Mp 139–140 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.92 (s, 3H), 1.00 (t, 3H, *J*=7.4 Hz), 1.22–1.37 (m, 1H), 1.51–1.65 (m, 1H), 3.00 (br s, 1H), 4.86 (s, 1H), 6.19 (s, 1H), 7.22–7.31 (m, 8H), 7.38–7.42 (m, 2H), 7.45–7.51 (m, 2H), 7.55–7.60 (m, 1H), 8.12–8.15 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 8.8, 17.5, 25.7, 45.1, 76.8, 81.3, 127.5, 127.7, 127.8, 127.93, 127.95, 128.03, 128.6, 129.7, 130.2, 133.2, 137.8, 141.1, 165.5. IR ($CHCl_3$): ν 3602, 1722 cm^{-1}. LR-FABMS: 397 ($M+Na^+$), 105. HR-FABMS: calcd for $C_{25}H_{26}O_3Na$ 397.1779, found 397.1779.

*4.5.8. 2-(Hydroxyphenylmethyl)-2-methyl-1-(p-methylphenyl)butyl p-methylbenzoate (**8kk** and **9kk**).* Compound **8kk**: a colorless prism. $[\alpha]_D^{24}$ −36.7 (*c* 1.39, $CHCl_3$), 92% ee. Mp: 116–117 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.81 (s, 3H), 0.84 (t, 3H, *J*=7.3 Hz), 1.26–1.35 (m, 1H), 1.84–1.93 (m, 1H), 2.31 (s, 3H), 2.38 (s, 3H), 3.45 (br s, 1H), 4.80 (s, 1H), 6.13 (s, 1H), 7.13–7.28 (m, 9H), 7.36 (d, 2H, *J*=7.8 Hz), 7.95 (d, 2H, *J*=8.2 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 7.8, 19.4, 21.0, 21.5, 23.1, 44.4, 77.8, 80.5, 127.1, 127.2, 127.4, 127.8, 128.1, 128.7, 129.2, 129.5, 134.4, 137.6, 140.9, 143.9, 165.1. IR ($CHCl_3$): ν 3581, 1722 cm^{-1}. LR-FABMS: 425 ($M+Na^+$), 119. HR-FABMS: calcd for $C_{27}H_{30}O_3Na$ 425.2093, found 425.2093.

Compound **9kk**: a colorless prism. $[\alpha]_D^{25}$ −31.3 (*c* 0.89, $CHCl_3$), 92% ee. Mp: 140–141 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.91 (s, 3H), 0.99 (t, 3H, *J*=7.4 Hz), 1.24–1.33 (m, 1H), 1.50–1.60 (m, 1H), 2.31 (s, 3H), 2.43 (s, 3H), 3.19 (br s, 1H), 4.84 (s, 1H), 6.12 (s, 1H), 7.11–7.31 (m, 11H), 8.00–8.02 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 8.7, 17.4, 21.1, 21.7, 25.7, 45.0, 76.9, 81.2, 127.4, 127.7, 127.8, 127.9, 128.0, 128.7, 129.3, 129.7, 134.8, 137.5, 141.1, 144.0, 165.5. IR ($CHCl_3$): ν 3583, 1720 cm^{-1}. LR-FABMS: 425 ($M+Na^+$), 119. HR-FABMS: calcd for $C_{27}H_{30}O_3Na$ 425.2093, found 425.2109.

*4.5.9. 2-Ethyl-2-methyl-3-(p-methylphenyl)-1-phenyl-propane-1,3-diol (**11kk** and **12kk**). Hydrolysis of monoester*: 1,3-diol monoester **8kk** was dissolved in MeOH (2 mL) and treated with NaOMe (0.05 mmol, 11 mol %) in MeOH (0.5 M, 0.1 mL). After 3 h, the mixture was diluted with AcOEt (20 mL), and washed with water (5 mL). The aqueous layer was extracted twice with AcOEt (10 mL×2) and the combined organic layers were washed with brine (10 mL) and dried over Na_2SO_4. After concentration in vacuo, the residue was purified by column chromatography (SiO_2, hexane/AcOEt=4:1) to gave diol **11kk** (74 mg, 81%) as a colorless oil. The enantiomeric excess was determined to be 92% by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=19:1, 1.0 mL/min]: t_R 24.9 min (major), 27.7 min (minor). $[\alpha]_D^{18}$ −5.1 (*c* 1.22, $CHCl_3$), 92% ee. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.64 (s, 3H), 0.87 (t, 3H, *J*=7.3 Hz), 1.02–1.11 (m, 1H), 1.80–1.89 (m, 1H), 2.36 (s, 3H), 3.96 (d, 1H, *J*=4.1 Hz), 4.34 (d, 1H, *J*=2.3 Hz), 4.60 (d, 1H, *J*=4.1 Hz), 4.62 (d, 1H, *J*=2.3 Hz), 7.12 (d, 2H, *J*=8.2 Hz), 7.19–7.24 (m, 7H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 7.4, 19.3, 21.1, 23.5, 43.2, 79.0, 79.3, 127.1, 127.4, 127.9, 128.0, 128.4, 137.0, 138.0, 141.1. IR ($CHCl_3$): ν 3602, 3467 cm^{-1}. LR-FABMS: 307 ($M+Na^+$). HR-FABMS: calcd for $C_{19}H_{24}O_2Na$ 307.1674, found 307.1670.

Compound **12kk**: the enantiomeric excess was determined to be 92% by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=19:1, 1.0 mL/min]: t_R 23.3 min (major), 29.6 min (minor). A colorless oil. $[\alpha]_D^{19}$ −2.8 (*c* 1.05, $CHCl_3$), 92% ee. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.67 (s, 3H), 0.90 (t, 3H, *J*=7.3 Hz), 1.05–1.14 (m, 1H), 1.82–1.91 (m, 1H), 2.32 (s, 3H), 3.86 (br s, 1H), 4.09 (br s, 1H), 4.63 (s, 1H), 4.67 (d, 1H, *J*=4.1 Hz), 7.06–7.36 (m, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 7.5, 19.3, 21.0, 23.7, 43.3, 79.1, 79.5, 127.4, 127.7, 127.8, 128.0, 128.2, 136.9, 138.0, 141.3. IR ($CHCl_3$): ν 3602, 3477 cm^{-1}. LR-FABMS: 307 ($M+Na^+$). HR-FABMS: calcd for $C_{19}H_{24}O_2Na$, 307.1674, found 307.1673.

*4.5.10. anti-3-Hydroxy-2,2-dimethyl-1-(p-methoxyphenyl)-3-phenylpropyl p-methoxybenzoate (**8ib**).* The enantiomeric excess was determined to be 95% by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=1L1, 1.0 mL/min]: t_R 11.1 min (major), 48.5 min (minor). A colorless needle. $[\alpha]_D^{30}$ −37.1 (*c* 1.45, $CHCl_3$), 95% ee. Mp: 126–127 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.79 (s, 3H), 0.84 (s, 3H), 3.21 (d, *J*=3.2 Hz), 3.75 (s, 3H), 3.83 (s, 3H), 4.70 (d, *J*=2.8 Hz, 1H), 6.29 (s, 1H), 6.84–6.89 (m, 2H), 6.94–6.99 (m, 2H), 7.2–7.5 (m, 7H), 8.05–8.10 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.0, 19.4, 43.1, 55.2, 55.5, 77.5, 79.7, 113.3, 113.9, 122.7, 127.3, 127.5, 128.2, 129.4, 130.3, 131.8, 141.3, 159.1, 163.7, 166.0. IR ($CHCl_3$) ν 3493, 1709 cm^{-1}. LR-FABMS: 443 ($M+Na^+$), 163, 135. HR-FABMS: calcd for $C_{26}H_{28}O_5Na$ 443.1834, found 443.1823.

*4.5.11. anti-1-(p-Bromophenyl)-3-hydroxy-2,2-dimethyl-3-phenylpropyl p-bromobenzoate (**8ik**).* The enantiomeric excess was determined to be 86% by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=1:1, 1.0 mL/min]: t_R 9.3 min (major), 55.2 min (minor). A colorless needle. $[\alpha]_D^{30}$ −55.8 (*c* 1.22, $CHCl_3$), 86% ee. Mp: 167–168 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.76 (s, 3H), 0.85 (s, 3H), 2.79 (br s, 1H), 4.72 (s, 1H), 6.28 (s, 1H), 7.20–7.35 (m, 7H), 7.42–7.47 (m, 2H), 7.60–7.63 (m, 2H), 7.90–7.95 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 18.0, 19.1, 42.9, 77.2, 79.6, 122.0, 127.6, 127.7, 128.2, 128.6, 129.1, 129.9, 131.1, 131.2, 132.0, 137.1, 141.2, 165.2. IR ($CHCl_3$): ν 3608, 3514, 1720 cm^{-1}. LR-FABMS: 543, 541, 539 ($M+Na^+$). HR-FABMS: calcd for $C_{24}H_{22}Br_2O_3Na$ 538.9834, found 538.9836.

*4.5.12. anti-(E)-5-Hydroxy-4,4-dimethyl-1,5-diphenyl-1-pentenyl 3-O-trans-cinnamate (**8ig**).* The enantiomeric excess was determined to be 89% by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=2:1, 1.0 mL/min]: t_R 10.1 min (major), 75.1 min (minor). A colorless oil. $[\alpha]_D^{33}$ −38.6 (*c* 1.35, $CHCl_3$), 89% ee. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.90 (s, 3H), 0.94 (s, 3H), 3.10 (br s, 1H), 4.63 (s, 1H), 5.84 (d, 1H, *J*=7.8 Hz), 6.32 (dd, 1H, *J*=7.8, 16.0 Hz), 6.54 (d, 1H, *J*=16.0 Hz), 6.72 (d, 1H, *J*=16.0 Hz), 7.23–7.43 (m, 13H), 7.56–7.58 (m, 2H), 7.77 (d, 1H, *J*=16.0 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.6, 19.7, 42.7, 76.9, 79.2,

117.7, 124.4, 126.6, 127.3, 127.5, 128.0, 128.1, 128.2, 128.6, 128.9, 130.5, 134.3, 134.6, 136.4, 140.8, 145.7, 166.8. IR ($CHCl_3$) ν 3491, 1709, 1172 cm^{-1}. LR-FABMS: 435 ($M+Na^+$), 413, 131, 107. HR-FABMS: calcd for $C_{28}H_{38}O_3Na$ 435.1936, found 435.1966.

*4.5.13. anti-1-Hydroxy-2,2-dimethyl-1,5-diphenylpentanyl 3-O-hydrocinnamate (**8ih**).* The enantiomeric excess was determined to be 28% by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=9:1, 1.0 mL/min]: t_R 13.5 min (minor), 17.1 min (major). A colorless oil. $[\alpha]_D^{32}$ +3.9 (*c* 1.36, $CHCl_3$), 28% ee. ^1H NMR ($CDCl_3$, 400 MHz) δ 0.65 (s, 3H), 0.78 (s, 3H), 1.84–1.97 (m, 2H), 2.47–2.59 (m, 2H), 2.73–2.79 (m, 2H), 3.02 (t, 2H, *J*=7.4 Hz), 3.20 (d, 1H, *J*=3.6 Hz), 4.21 (d, 1H, *J*=4.1 Hz), 5.18 (dd, 1H, *J*=4.1, 9.2 Hz), 7.13–7.30 (m, 15H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 19.3, 30.9, 31.7, 33.0, 35.8, 42.1, 76.5, 78.7, 126.0, 126.5, 127.1, 127.3, 128.2, 128.3, 128.36, 128.42, 128.6, 140.2, 140.4, 141.5, 174.1. IR: ($CHCl_3$) ν 3502, 1713 cm^{-1}. LR-FABMS: 439 ($M+Na^+$), 413, 176, 91, 23. HR-FABMS: calcd for $C_{28}H_{32}O_3Na$ 439.2249, found 439.2291.

*4.5.14. anti-1-Cyclohexyl-3-hydroxy-2,2-dimethyl-3-phenylpropyl cyclohexanecarboxylate (**8ii**).* The enantiomeric excess was determined to be 30% by chiral HPLC [Daicel Chiralpak AD-H, hexane/IPA=29:1, 1.0 mL/min]: t_R 10.3 min (minor), 13.1 min (major). A colorless prism. $[\alpha]_D^{30}$ +1.2 (*c* 1.03, $CHCl_3$), 30% ee. Mp: 87–88 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ 0.76 (s, 3H), 0.88 (s, 3H), 1.05–1.43 (m, 8H), 1.45–1.90 (m, 11H), 1.95–2.05 (m, 2H), 2.39–2.49 (m, 1H), 3.25 (d, *J*=2.8 Hz, 1H), 4.44 (d, *J*=1.8 Hz), 4.92 (q, *J*=2.8 Hz, 1H), 7.22–7.30 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.5, 20.4, 25.4, 25.5, 25.7, 26.1, 26.4, 26.6, 28.5, 29.3, 29.4, 33.9, 38.5, 42.9, 43.7, 77.0, 81.4, 127.1, 127.3, 128.2, 140.7, 176.6. IR ($CHCl_3$) ν 3500, 1705 cm^{-1}. LR-FABMS: 395 ($M+Na^+$), 355, 83. HR-FABMS: calcd for $C_{24}H_{36}O_3Na$ 395.2562, found 395.2539.

References and notes

1. Herein a 'quaternary carbon atom' means a carbon atom singly bonded to four other carbon atoms.
2. For reviews on the construction of quaternary asymmetric carbon, see: (a) Fuji, K. *Chem. Rev.* **1993**, *93*, 2037–2066; (b) Corey, E. J.; Guzman-Perez, A. *Angew. Chem., Int. Ed.* **1998**, *37*, 388–401; (c) Denissova, I.; Barriault, L. *Tetrahedron* **2003**, *59*, 10105–10146; (d) Douglas, C. J.; Overman, L. E. *Pure Appl. Chem.* **2004**, *101*, 5363–5367; (e) Peterson, E. A.; Overman, L. E. *Pure Appl. Chem.* **2004**, *101*, 11943–11948; (f) Christpher, J. D.; Overman, L. E. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5363–5367; (g) Trost, B. M.; Jiang, C. *Synthesis* **2006**, 369–396; (h) Bella, M.; Gasperi, T. *Synthesis* **2009**, 1583–1614; (i) Das, J. P.; Marek, I. *Chem. Commun.* **2011**, 4593–4623.
3. For reviews on Diels–Alder reactions, see: (a) Shen, J.; Tan, C.-H. *Org. Biomol. Chem.* **2007**, *6*, 3229–3236; (b) Reymond, S.; Cossy, J. *Chem. Rev.* **2008**, *108*, 5359–5406; (c) Tadano, K. *Eur. J. Org. Chem.* **2009**, 4381–4394.
4. For reviews on Michael additions, see: (a) Christffers, J. *Chem.—Eur. J.* **2003**, *9*, 4862–4867; (b) Jautze, S.; Peters, R. *Synthesis* **2010**, 365–388.
5. For reviews on enantioselective aldol reaction, see: (a) Nelson, S. G. *Tetrahedron: Asymmetry* **1998**, *9*, 357–389; (b) Gröger, H.; Vogl, E. M.; Shibasaki, M. *Chem.—Eur. J.* **1998**, *4*, 1137–1141; (c) Mahrwald, R. *Chem. Rev.* **1999**, *99*, 1095–1120; (d) Machajewski, T. D.; Wong, C.-H. *Angew. Chem., Int. Ed.* **2000**, *39*, 1352–1374.
6. For recent reviews, see: Schetter, B.; Mahrwald, R. In *Quaternary Stereocenters: Challenges and Solutions for Organic Synthesis*; Christoffers, J., Baro, A., Eds.; Wiley-VCH: Weinheim, Germany, 2005; pp 51–81.
7. (a) Ando, A.; Miura, T.; Tatematsu, T.; Shioiri, T. *Tetrahedron Lett.* **1993**, *34*, 1507–1510; (b) Shioiri, T.; Bohsako, A.; Ando, A. *Heterocycles* **1996**, *42*, 93–97; (c) Mase, N.; Tanaka, F.; Barbas, C. F., III. *Angew. Chem., Int. Ed.* **2004**, *43*, 2420–2423; (d) Ishikawa, S.; Hamada, T.; Manabe, K.; Kobayashi, S. *J. Am. Chem. Soc.* **2004**, *126*, 12236–12237; (e) Kobayashi, S.; Ogino, T.; Shimizu, H.; Ishikawa, S.; Hamada, T.; Manabe, K. *Org. Lett.* **2005**, *7*, 4729–4731; (f) Denmark, S. E.; Wilson, T. W.; Burk, M. T.; Heemstra, J. R. J. *J. Am. Chem. Soc.* **2007**, *129*, 14864–14865; (g) Markert, M.; Scheffler, U.; Mahrward, R. *J. Am. Chem. Soc.* **2009**, *131*, 16642–16643.
8. Carreira, E. M. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999; Vol. 3, pp 997–1065.
9. (a) Denmark, S. E.; Winter, S. B. D.; Su, X.; Wong, K.-T. *J. Am. Chem. Soc.* **1996**, *118*, 7404–7405; (b) Denmark, S. E.; Wong, K.-T.; Stavenger, R. A. *J. Am. Chem. Soc.* **1997**, *119*, 2333–2334; (c) Denmark, S. E.; Stavenger, R. A.; Wong, K.-T. *J. Org. Chem.* **1998**, *63*, 918–919; (d) Denmark, S. E.; Stavenger, R. A.; Su, X.; Wong, K.-T.; Nishigaichi, Y. *Pure Appl. Chem.* **1998**, *70*, 1469–1476; (e) Denmark, S. E.; Stavenger, R. A.; Wong, K.-T. *Tetrahedron* **1998**, *54*, 10389–10402; (f) Denmark, S. E.; Stavenger, R. A. *J. Org. Chem.* **1998**, *63*, 9524–9527; (g) Denmark, S. E.; Su, X.; Nishigaichi, Y. *J. Am. Chem. Soc.* **1998**, *120*, 12990–12991; (h) Denmark, S. E.; Stavenger, R. A.; Wong, K.-T.; Su, X. *J. Am. Chem. Soc.* **1999**, *121*, 4982–4991; (i) Denmark, S. E.; Pham, S. M. *Helv. Chim. Acta* **2000**, *83*, 1846–1853; (j) Denmark, S. E.; Stavenger, R. A. *J. Am. Chem. Soc.* **2000**, *122*, 8837–8847; (k) Denmark, S. E.; Stavenger, R. A. *Acc. Chem. Res.* **2000**, *33*, 432–440; (l) Denmark, S. E.; Ghosh, S. K. *Angew. Chem., Int. Ed.* **2001**, *40*, 4759–4762; (m) Denmark, S. E.; Pham, S. M. *J. Org. Chem.* **2003**, *68*, 5045–5055.
10. (a) Rendler, S.; Oestreich, M. *Synthesis* **2005**, 1727–1736; (b) Orito, Y.; Nakajima, M. *Synthesis* **2006**, 1391–1401; (c) Denmark, S. E.; Beutner, G. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 1560–1638.
11. (a) Nakajima, M.; Yokota, T.; Saito, M.; Hashimoto, S. *Tetrahedron Lett.* **2004**, *45*, 61–64.
12. (a) Kotani, S.; Hashimoto, S.; Nakajima, M. *Synlett* **2006**, 1116–1118; (b) Kotani, S.; Hashimoto, S.; Nakajima, M. *Tetrahedron* **2007**, *63*, 3122–3132.
13. (a) Tanaka, K.; Ueda, T.; Ichibakase, T.; Nakajima, M. *Tetrahedron Lett.* **2010**, *51*, 2168–2169; (b) Ueda, T.; Tanaka, K.; Ichibakase, T.; Orito, Y.; Nakajima, M. *Tetrahedron* **2010**, *66*, 7726–7731.
14. (a) Nakajima, M.; Orito, Y.; Ishizuka, T.; Hashimoto, S. *Org. Lett.* **2004**, *6*, 3763–3765; (b) Orito, Y.; Hashimoto, S.; Ishizuka, T.; Nakajima, M. *Tetrahedron* **2006**, *62*, 390–400.
15. For acid-catalyzed aldol reaction of trimethoxysilyl enol ethers, see: (a) Yanagisawa, A.; Nakatsuka, Y.; Asakawa, K.; Wadamoto, M.; Kageyama, H.; Yamamoto, H. *Synlett* **2001**, 69–72; (b) Yanagisawa, A.; Nakatsuka, Y.; Asakawa, K.; Wadamoto, M.; Kageyama, H.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **2001**, 1477–1481; (c) Wadamoto, M.; Ozasa, N.; Yanagisawa, A.; Yamamoto, H. *J. Org. Chem.* **2003**, *68*, 5593–5601.
16. A part of this work was reported as a communication Ichibakase, T.; Orito, Y.; Nakajima, M. *Tetrahedron Lett.* **2008**, *49*, 4427–4429.
17. Enol ether **1b**–**1d**, **1f**, and **1g** were prepared in chloroform under reflux condition. Enol ethers **1e** and **1h** were prepared in dichloromethane at 0 °C.
18. (a) Uhlig, W. *J. Organomet. Chem.* **1993**, *452*, 29–32; (b) Uhlig, W. *Chem. Ber.* **1996**, *129*, 733–739.
19. Although *syn* or *anti* may be not truly accurate terms to indicate the stereochemistry of the successive stereogenic centers including the quaternary carbon centers, herein we use these terms for convenience in order to discuss the relationship of the stereochemistries between enol ethers and aldol adducts.
20. (a) Mahrwald, R.; Schetter, B. *Org. Lett.* **2006**, *8*, 281–284; (b) Schetter, B.; Ziemer, B.; Schnakenburg, G.; Mahrwald, R. *J. Org. Chem.* **2008**, *73*, 813–819.
21. To the best of our knowledge, the best *syn*/*anti* ratio for constructing quaternary carbon centers by an enantioselective aldol reaction reported to date is 1:6 Wang, W.; Li, H.; Wang, J. *Tetrahedron Lett.* **2005**, *46*, 5077–5079.
22. Reviews on the enantioselective aldol-Tishchenko reactions, see: (a) Mahrward, R. *Curr. Org. Chem.* **2003**, *7*, 1713–1723; (b) Mlynarski, J. *Eur. J. Org. Chem.* **2006**, 4779–4786.
23. (a) Loog, O.; Maeorg, U. *Tetrahedron: Asymmetry* **1999**, *10*, 2411–2415; (b) Mascarenhas, C. M.; Miller, S. P.; White, P. S.; Morken, J. P. *Angew. Chem., Int. Ed.* **2001**, *40*, 601–603; (c) Gnanadesikan, V.; Horiuchi, Y.; Ohshima, T.; Shibasaki, M. *J. Am. Chem. Soc.* **2004**, *126*, 7782–7783; (d) Horiuchi, Y.; Gnanadesikan, V.; Ohshima, T.; Masu, H.; Katagiri, K.; Sei, Y.; Yamaguchi, K.; Shibasaki, M. *Chem.—Eur. J.* **2005**, *11*, 5195–5204; (e) Mlynarski, J.; Mitura, M. *Tetrahedron Lett.* **2004**, *45*, 7549–7552; (f) Mlynarski, J.; Jankowska, J.; Rakiel, B. *Chem. Commun.* **2005**, 4854–4856; (g) Mlynarski, J.; Jankowska, J.; Rakiel, B. *Tetrahedron: Asymmetry* **2005**, *16*, 1521–1526; (h) Mlynarski, J.; Rakiel, B.; Stodulski, M.; Suszczynska, A.; Frelek, J. *Chem.—Eur. J.* **2006**, *12*, 8158–8167; (i) Rohr, K.; Herre, R.; Mahrwald, R. *Org. Lett.* **2005**, *7*, 4499–4501; (j) Rohr, K.; Herre, R.; Mahrwald, R. *J. Org. Chem.* **2009**, *74*, 3744–3749.
24. (a) Ichibakase, T.; Nakajima, M. *Org. Lett.* **2011**, *13*, 1579–1581; (b) Ichibakase, T.; Nakatsu, M.; Nakajima, M. *Molecules* **2011**, *16*, 5008–5019.
25. Mechanistic studies of the aldol-Tishchenko reaction: (a) Evans, D. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1990**, *112*, 6447–6449; (b) Burkhardt, E. R.; Bergman, R. G.; Heathcock, C. H. *Organometallics* **1990**, *9*, 30–44; (c) Mahrwald, R.; Costisella, B. *Synthesis* **1996**, 1087–1089; (d) Bodnar, P. M.; Shaw, J. T.; Woerpel, K. A. *J. Org. Chem.* **1997**, *62*, 5674–5675; (e) Abu-Hasanayn, F.; Streitwieser, A. *J. Org. Chem.* **1998**, *63*, 2954–2960; (f) Lu, L.; Chang, H.-Y.; Fang, J.-M. *J. Org. Chem.* **1999**, *64*, 843–853; (g) Mascarenhas, C. M.; Duffey, M. O.; Liu, S.-Y.; Morken, J. P. *Org. Lett.* **1999**, *1*, 1427–1429; (h) Markert, M.; Mahrwald, R. *Synthesis* **2004**, 1429–1433.
26. Nishimura, Y.; Miyake, Y.; Amemiya, R.; Yamaguchi, M. *Org. Lett.* **2006**, *8*, 5077–5080.
27. Hasegawa, T.; Nishimura, M.; Kodama, Y.; Yoshioka, M. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 935–937.
28. Cheon, C. H.; Yamamoto, H. *Tetrahedron* **2010**, *66*, 4257–4264.
29. Patit, M. N.; Gonnade, R. G.; Joshi, N. N. *Tetrahedron* **2010**, *66*, 5036–5041.