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Chiral base-catalyzed aldol reaction of trimethoxysilyl enol ethers: effect of water as an additive on stereoselectivities

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Abstract—An aldol reaction of trimethoxysilyl enol ether catalyzed by lithium binaphtholate is described. The aldol reaction of trimethoxysilyl enol ether derived from cyclohexanone under anhydrous conditions predominantly afforded the *anti*-aldol adduct with moderate enantioselectivity, whereas the reaction under aqueous conditions predominantly resulted in the *syn*-adduct and the enantioselectivity of the *syn*-adduct was considerably improved. The best enantioselectivity was obtained in the reaction of trimethoxysilyl enol ether derived from 1-indanone with cyclohexanecarboxaldehyde (97% ee (*syn*)). This is the first example of an aldol reaction of trimethoxysilyl enol ether catalyzed by a chiral base.

1. Introduction

The asymmetric aldol reaction is well-recognized as one of the most important methods for constructing optically active β-hydroxy carbonyl compounds.[1] Recent significant developments in asymmetric aldol reactions are mostly based on the principles of conventional Mukaiyama-type catalysis, in which aldol acceptors are activated by chiral Lewis acid catalysts.[2,3] In 1996, Denmark and co-workers reported the first Lewis base-catalyzed enantioselective aldol reactions of trichlorosilyl enol ethers employing chiral phosphoramides[4] as organocatalysts, wherein the aldol donors were activated to form hypervalent silicate intermediates.[5] We have also reported asymmetric aldol reaction of trichlorosilyl enol ethers catalyzed by chiral *N*-oxides.[6] These base-catalyzed reactions afforded the corresponding adducts with high diastereo- and enantioselectivities, however, aldol reactions of trichlorosilyl enol ethers are not widely utilized in organic synthesis since the enol ethers are extremely water sensitive.

Trialkoxysilyl compounds,[7] which are more stable than its trichlorosilyl derivatives, are expected to form reactive hypervalent silicates with bases. In 2001, Yamamoto and co-workers reported an asymmetric aldol reaction of trimethoxysilyl enol ethers with high enantioselectivity wherein BINAP–silver(I) complex was employed as a Lewis acid catalyst.[7b] However, base-catalyzed aldol reactions of trimethoxysilyl enol ethers have yet to be developed, although hypervalent silicates derived from trimethoxysilyl compounds are well-investigated.[5,7c] In our pursuit to develop base-catalyzed reactions involving hypervalent silicate intermediate,[6,8] herein we describe the details of an enantioselective aldol reaction of trimethoxysilyl enol ethers catalyzed by chiral base, wherein water as an additive played a pivotal role in stereoselectivities.[9,10]

2. Results and discussion

2.1. Synthesis of trialkoxysilyl enol ethers

Trialkoxysilyl enol ethers that were sufficiently stable to survive an aqueous work-up or silica gel column chromatography were easily prepared from the corresponding enones or ketones. Starting from the corresponding conjugated enones, trimethoxysilyl enol ethers **1a** and **1b** were prepared by hydrosilylation with trimethoxysilane catalyzed by $Rh(PPh_3)_3Cl$ using a literature procedure (Eq. 1).[7b] Trimethoxysilyl enol ethers **1c**–**1g** and triethoxysilyl enol ether **1h**[17] were prepared by silylation of lithium enolates from the corresponding ketones with chlorotrimethoxysilane[11] (or chlorotriethoxysilane) in THF or silylation of ketones with iodotrimethoxysilane prepared in situ in acetonitrile in the presence of triethylamine (Eq. 2). An aqueous work-up followed by distillation in vacuo gave pure silyl enol ethers in moderate to good yields.

Keywords: Chiral catalyst; Enantioselectivity; Aldol reaction; Silyl enol ether; Binaphthol.
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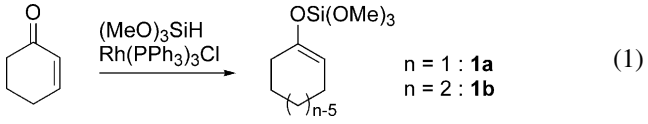

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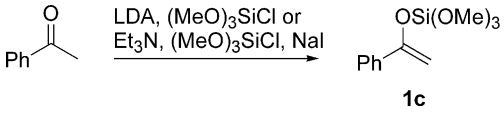

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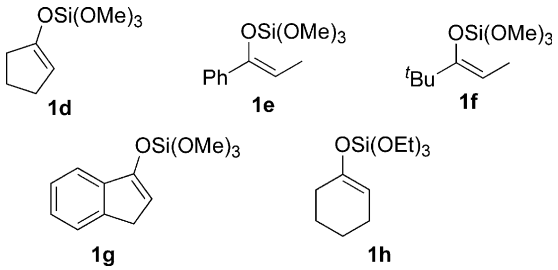
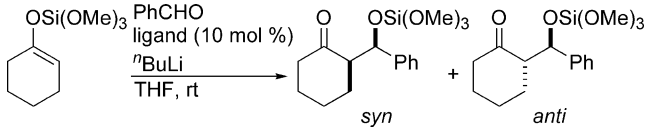


2.2. Aldol reaction of trimethoxysilyl enol ether under anhydrous condition

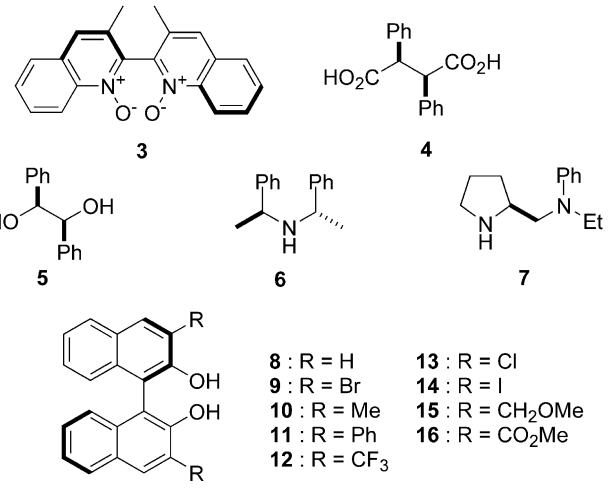
Our initial studies examined the addition of trimethoxysilyl enol ether **1a** derived from cyclohexanone with benzaldehyde using various bases (10 mol%) in THF (Table 1). Although aromatic *N*-oxides efficiently catalyzed the aldol reaction of trichlorosilyl enol ethers, *N*-oxide **3** did not afford the aldol adduct for trimethoxysilyl enol ether (entry 1). On the other hands, lithium salts of chiral alcohol **5**, amines **6**, **7**, and binaphthol **8** gave silyl ether of corresponding adduct in moderate to high yield (entries 3–6). Further catalyst screening based on binaphthol revealed that the dilithium salt of 3,3′-dibromobinaphthol **9** gave the most promising result (entry 7, 16% ee (*syn*), 12% ee (*anti*)). Decreasing the reaction temperature to −23 °C with **9** significantly improved the stereoselectivities (entry 8, *syn*/*anti* 1:3.7, 51% ee (*anti*)) without eroding the reaction rate.[12]

Table 1. Screening the catalyst



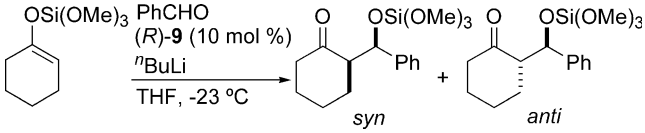
Entry	Ligand	^{n}BuLi (mol%)	Time (h)	Yield (%)[a]	*syn*:*anti*[b]	ee (%) (*syn*/*anti*)[b]
1	**3**	0	24	0		—
2	**4**	20	24	0		—
3	**5**	20	24	46	1:1.1	~0/9
4	**6**	10	5	59	1:1.5	~0/~0
5	**7**	10	0.5	59	1:1.4	~0/~0
6	**8**	20	0.5	98	1:1.3	~0/~0
7	**9**	20	0.5	83	1:1.9	16/12
8[c]	**9**	20	0.5	97	1:3.7	8/51

[a] Isolated as alcohol.
[b] Determined by HPLC analysis.
[c] At −23 °C.



Since dilithium salt and monolithium salt of **9** may form different reactive species,[7c] we then examined the stoichiometry of lithium to **9** (Table 2). Surprisingly, a slight difference in the equivalents of BuLi extensively influenced the reaction rate and stereoselectivities. Catalysts prepared with 10–14 mol% of BuLi predominantly afforded the *syn*-adduct in a moderate chemical yield with a decreased reaction rate (entries 1–3), while *anti*-adduct was predominantly formed using 16–20 mol% of BuLi (entries 4–6). Although the origin of the dramatic change in stereoselectivity is unclear, the catalyst in following studies was a dilithium salt. Screening of binaphthols revealed that dibromide **9** and dichloride **13** were superior in terms of diastereo- and enantioselectivity (Table 3).

Table 2. Effect of molar equivalent of ^{n}BuLi



Entry	^{n}BuLi (mol%)	Time (h)	Yield (%)[a]	*syn*:*anti*[b]	ee (%) (*syn*/*anti*)[b]
1	10	100	42[c]	1.8:1	27/14
2	12	30	59[c]	2.4:1	51/31
3	14	30	66[c]	2.2:1	55/38
4	16	0.5	98	1:2.7	12/50
5	18	0.5	98	1:2.8	7/47
6	20	0.5	97	1:3.7	8/51
7	22	0.5	98	1:3.5	18/49

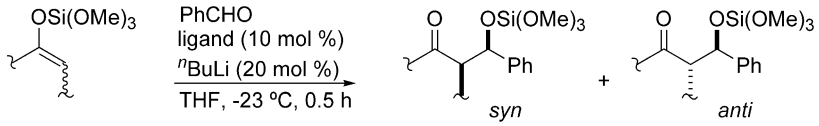
[a] Isolated as alcohol.
[b] Determined by HPLC analysis.
[c] Not completed.

Table 3. Screening binaphthol derivatives

Entry	Substituent on 3,3-positon	Yield (%)[a]	*syn*:*anti*[b]	ee (%) (*syn*/*anti*)[b]
1	Me (**10**)	91	1:1.4	14/29
2	Ph (**11**)	98	1:2.3	5/33
3	CF_3 (**12**)	98	1:2.1	24/13
4	Cl (**13**)	87	1:3.8	20/56
5	Br (**9**)	97	1:3.7	8/51
6	I (**14**)	89	1:3.7	4/31

[a] Isolated as alcohol.
[b] Determined by HPLC analysis.

Table 4. Aldol reaction of various silyl enol ethers with benzaldehyde



Entry	Ligand	Enol ether	Product	Yield (%)[a]	*syn*: *anti*[b]	ee (%) (*syn*/*anti*)[b]
1	**13**	**1a**	**2a**	87	1:3.8	20/56
2	**13**	**1b**	**2b**	91	1.4:1	39/42
3	**13**	**1c**	**2c**	98	—	50
4	**9**	**1d**	**2d**	93	3.4:1	46/30
5	**13**	**1e**	**2e**	98	1:1.7	~0/~0
6	**13**	**1f**	**2f**	87[c]	1.8:1	~0/~0

[a] Isolated as alcohol.
[b] Determined by HPLC analysis.
[c] At room temperature (45 h).

Table 5. Aldol reaction of **1a** with aldehydes catalyzed by dilithium salt of **13**

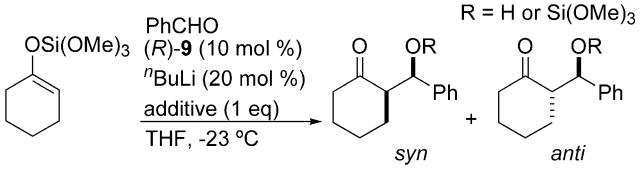
Entry	Aldehyde	Product	Time (h)	Yield (%)[a]	*syn*:*anti*[b]	ee (%) (*syn*/*anti*)[b]
1	PhCHO	**2a**	0.5	87	1:3.8	20/56
2	PhCH=CHCHO	**2h**	0.5	98	1:1.5	44/6
3	$PhCH_2CH_2CHO$	**2i**	3[c]	14	2.9:1	40/16

[a] Isolated as alcohol.
[b] Determined by HPLC analysis.
[c] Not completed.

Table 4 shows the results of the aldol reaction of trimethoxysilyl enol ethers derived from various ketones with benzaldehyde using the optimized catalyst at −23 °C. (*E*)-Enolates and enolate without substituents at the α-position afforded the corresponding aldol adducts in good to high yields, although the diastereo- and enantioselectivities were moderate (entries 1–4). On the other hand, (*Z*)-enolates gave low selectivities (entries 5 and 6), and the enolate with bulky substituent slowed the reaction rate (entry 6), probably due to steric hindrance.

The aldol reactions of other aldehydes with **1a** were investigated (Table 5). The reaction of conjugate aldehyde proceeded smoothly, but the stereoselectivity decreased (entry 2). The unconjugate aldehyde was much less reactive (entry 3), as is often observed in the base-catalyzed aldol reactions involving hypervalent silicate intermediate.

Table 6. Screening the additives



Entry	Additive	Time (h)	Yield (%)[a]	*syn*:*anti*[b]	ee (%) (*syn*/*anti*)[b]
1	None	0.5	97	1:3.7	8/51
2	EtCN	1	97	1:1.7	12/47
3	HMPA	1	91	1.1:1	9/3
4	IQNO[c]	1	80	1.1:1	30/56
5	TMEDA	5	63	1.8:1	41/32
6	$^{i}Pr_2NEt$	5	71	2.0:1	48/19
7	$^{n}PrNH_2$	2	59	1.4:1	25/16
8	NH_3	1	70	1.7:1	52/39
9	MeOH	0.5	98	1.2:1	39/40
10	H_2O	0.5	93	3.0:1	78/47

[a] Isolated as alcohol.
[b] Determined by HPLC analysis.
[c] Isoquinoline *N*-oxide.

2.3. Aldol reaction of trimethoxysilyl enol ether under aqueous condition

To enhance the stereoselectivity, we then examined the effect of the additives. As shown in Table 6, the additive structure strongly affected both diastereo- and enantioselectivities. Among various additives surveyed, water gave the best result and predominantly afforded the *syn*-adduct as the alcohol in good enantioselectivity. (entry 10).

Table 7 summarizes more detailed studies on the equivalent of water. Interestingly, the ratio of *syn* to *anti* and the enantioselectivity of *syn*-adduct increased as a function of the increasing amount of water. Equimolar amounts of water to silyl enol ether (1.5 equiv to aldehyde, i.e., 1.0 equiv to silyl enol ether) were sufficient to optimize the diastereo- and enantioselectivity (entry 5, *syn*/*anti* 3.2:1, 80% ee (*syn*), 51% ee (*anti*)), which suggests that water (or the hydroxy ion) may strongly coordinate to the silicon atom of silyl enol ether. [13,14]

Table 7. Effect of equivalent of H_2O

Entry	H_2O (equiv)	Yield (%)	*syn*:*anti*[a]	ee (%) (*syn*/*anti*)[a]
1	0	97	1:3.7	8/51
2	0.1	93	1:1.1	15/46
3	0.5	97	1.7:1	60/44
4	1.0	93	3.0:1	78/47
5	1.5	94	3.1:1	80/50

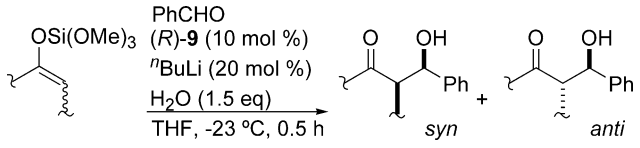
[a] Determined by HPLC analysis.

Table 8. Screening binaphthol derivatives

Entry	Substituent on 3,3′-position	Yield (%)	*syn*:*anti*[a]	ee (%) (*syn*/*anti*)[a]
1	H (**8**)	76	1.2:1	24/5
2	Me (**10**)	98	2.3:1	55/15
3	Ph (**11**)	98	2.0:1	34/5
4	CF_3 (**12**)	95	2.6:1	69/38
5	Cl (**13**)	98	3.0:1	78/48
6	Br (**9**)	94	3.1:1	80/50
7	I (**14**)	98	2.9:1	73/35
8	CH_2OMe (**15**)	98	1.6:1	14/1
9	CO_2Me (**16**)	76	1:1.1	17/46

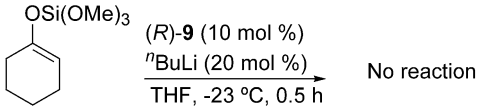
[a] Determined by HPLC analysis.

Table 9. Aldol reaction of various silyl enol ethers with benzaldehyde under hydrous condition



Entry	Silyl enol ether	Product	Yield (%)	*syn*:*anti*[a]	ee (%) (*syn*/*anti*)[a]
1	**1a**	**2a**	94	3.1:1	80/50
2	**1c**	**2c**	88	—	75
3	**1d**	**2d**	98	2.9:1	72/6
4	**1e**	**2f**	91	1.9:1	19/38
5	**1g**	**2g**	78	2.9:1	83/48
6	**1h**	**2a**	83[b]	2.9:1	77/45

[a] Determined by HPLC analysis.
[b] Eighteen hours.



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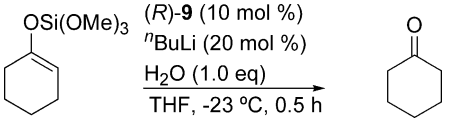

(4)

Control experiments showed that the trimethoxysilyl enol ether, which was stable under anhydrous conditions even in the presence of lithium binaphtholate, quickly decomposed into the corresponding ketone in aqueous conditions in the presence of lithium binaphtholate (Eqs. 3 and 4).[15] This suggests that the coordination of water (or hydroxy ion) to silicon atom may increase the nucleophilicity of the silicate complex to predominantly afford the *syn*-adduct via an acyclic transition state, while under anhydrous conditions the reaction may proceed via a cyclic chairlike transition state[4,5] to predominantly yield the *anti* adduct, but the details of reaction mechanism are unclear.

An evaluation of the binaphthol derivatives is shown in Table 8. Although both steric and electronic factor influenced the selectivity, binaphthols with halogen substituents at 3,3′-position gave relatively superior results. Consequently, dibromide **9** gave the best result in terms of diastereo- and enantioselectivity.

Table 9 shows the results of the aldol reactions of trimethoxysilyl enol ethers derived from various ketones and benzaldehyde under optimal conditions. In all cases, the corresponding *syn*-adducts were predominantly obtained in good to excellent yields. Enantioselectivities of (*E*)-enolates (entries 2, 3 and 5) were comparable to that of **1a** (entry 1), while (*Z*)-enolate demonstrated relatively low selectivity, similar to anhydrous conditions (entry 4). Among various silyl enol ethers, indanone derivative **1g** gave the best enantioselectivity (entry 5). Triethoxysilyl enol ether **1h**

Table 10. Aldol reaction of **1g** with various aldehydes under hydrous condition

Entry	Aldehyde	Product	Yield (%)	*syn*:*anti*[a]	ee (%) (*syn*/*anti*)[a]
1	PhCHO	**2g**	78	2.9:1	83/48
2	*p*-$MeOC_6H_4CHO$	**2j**	89	2.4:1	70/25
3	*p*-$CF_3C_6H_4CHO$	**2k**	88	2.1:1	48/39
4	PhCH=CHCHO	**2l**	98	3.4:1	73/10
5	$PhCH_2CH_2CHO$	**2m**	90	2.6:1	92/47
6	[c]HexCHO	**2n**	94	1.4:1	97/84

[a] Determined by HPLC analysis.

Table 11. Aldol reaction of **1a** with various aldehyde under hydrous condition

Entry	Aldehyde	Product	Yield (%)	*syn*:*anti*[a]	ee (%) (*syn*/*anti*)[a]
1	PhCHO	**2a**	94	3.1:1	80/50
2	1-NaphCHO	**2o**	90	1.4:1	81/65
3	2-NaphCHO	**2p**	94	1.6:1	72/45
4	PhCH=CHCHO	**2h**	96	1.4:1	75/5
5	$PhCH_2CH_2CHO$	**2i**	75	1.2:1	91/40

[a] Determined by HPLC analysis.

showed a significantly decreased reactivity, although the yield and stereoselectivities were about the same (entry 6).

Table 10 summarizes the aldol reactions of indanone derivative **1g** with various aldehydes. Introducing both electron donating/withdrawing groups decreased the enantioselectivity (entries 2 and 3). Interestingly, rather high enantioselectivities were observed in the reaction of unconjugate aldehydes (entries 5–7), which showed quite low reactivities under anhydrous conditions (Table 5, entry 3). The best enantioselectivity (97% ee) was obtained in the reaction of cyclohexenecarboxaldehyde, though the diastereoselectivity decreased (entry 6).

Table 11 shows the reaction of cyclohexanone derivative **1a** with various aldehydes. Though diastereoselectivities are not satisfactory, modest to high enantioselectivities were generally obtained. The best enantioselectivity was observed in the reaction of unconjugate aldehyde **2i** (entry 7, 91% ee). It is noteworthy that the aldol reaction of unconjugate aldehydes, which often gives inferior results under Lewis base-catalyzed condition, afforded adducts in high yield and with high enantioselectivity.

3. Conclusion

An aldol reaction of trimethoxysilyl enol ether catalyzed by lithium binaphtholate was developed, wherein water served as an additive and played a pivotal role in stereoselectivities. This is the first example of an aldol reaction of trimethoxysilyl enol ether catalyzed by a chiral base. Mechanistic studies as well as designing a new chiral catalyst to enhance the stereoselectivities are currently underway.

4. Experimental

4.1. General

Melting points were measured using a Büchi 535 melting point apparatus and were not corrected. Optical rotations were obtained on a JASCO P-1030 digital polarimeter. Infrared spectra were recorded on a JASCO FT/IR-5300. ^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL EX-270 (^{1}H, 270 MHz; ^{13}C, 68 MHz) spectrometer in deuteriochloroform. Chemical shift values are expressed in ppm relative to internal tetramethylsilane. Coupling constants (J) are reported in Hertz (Hz). NMR data are presented as follows: chemical shift, multiplicity, integration, coupling constant. Abbreviations are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Mass spectra were obtained on JEOL JMS-DX303 or JEOL FABmate. HPLC was performed on a JASCO PU-1580 with a JASCO UV-1575 (λ=254 nm) and chiral separations were performed using Daicel chiralpak or chiralcel columns (φ 0.46×25 cm). Hexane and 2-propanol for HPLC were HPLC grade and filtered and degassed before use. HPLC peaks of *syn*/*anti* isomers were assigned by the comparing to authentic samples prepared with racemic binaphthol as a catalyst. The relative configurations of new compounds were assigned based on the splitting pattern of the hydroxyl bearing methine.[4b]

Column chromatography was conducted on Silica Gel 60 N (spherical, neutral, 60–210 μm, Kanto Chemical Co.). Analytical thin-layer chromatography was carried out on Merck Kieselgel 60 F_{254} plates with visualization by ultraviolet and stains. TLC stains were prepared as follows; *p*-anisaldehyde stain: EtOH (460 mL), *p*-anisaldehyde (13 mL), AcOH (5 mL), concd H_2SO_4 (17 mL).; PMA stain: EtOH solution of phosphomolybdic acid (5% wt); PMA/H_2SO_4 stain: H_2O (400 mL), phosphoric acid (6 mL), concd H_2SO_4 (20 mL), phosphomolybdic acid (9.6 g).

Reagents and solvents were purchased and purified by standard means or used as received unless otherwise noted. Dehydrated stabilizer free THF and dichloromethane were purchased from Kanto Chemical Co., Inc. and used as received. Concentration of *n*-butyllithium was estimated by titrating with diphenylacetic acid in THF.[16]

4.2. Representative procedures for the synthesis of trimethoxysilyl enol ethers by hydrosilylation

Trimethoxysilyl enol ethers **1a** and **1b** were prepared by modifying a literature procedure.

4.2.1. 1-Trimethoxysilyloxycyclohexene (1a).[7b] To an orange solution of $Rh(PPh_3)_3Cl$ (20.5 mg, 23 μmol, 0.025 mol%) in 2-cyclohexen-1-one (8.6 g, 90 mmol) was added trimethoxysilane (14.3 g, 117 mmol, 1.3 equiv) under an argon atmosphere at room temperature. After heating at 90 °C for 30 min, the reaction mixture was cooled to room temperature. 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 (118–119 °C, 20 mmHg) gave the silyl enol ether as a colorless oil (15.1 g, 77%); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.46–1.54 (m, 2H), 1.59–1.70 (m, 2H), 1.97–2.10 (m, 2H), 3.58 (s, 9H), 5.05–5.07 (m, 1H).

4.2.2. 1-Trimethoxysilyloxycycloheptene (1b).[7b] Following the representative procedure, silyl enol ether **1b** was obtained from 2-cyclohepten-1-one (0.28 g, 2.5 mmol) as a colorless oil (0.32 g, 56%); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.47–1.81 (m, 6H), 1.91–2.02 (m, 2H), 2.28–2.32 (m, 2H), 3.58 (s, 9H), 5.21 (t, 1H, J=6.5 Hz).

4.3. Representative procedure for the synthesis of trimethoxysilyl enol ethers via enolate

4.3.1. 1-Trimethoxysilyloxy-1-phenylethylene (1c). *Method A*. To a solution of diisopropylamine (2.9 g, 28.8 mmol, 1.15 equiv) in THF (50 mL) was added *n*-butyllithium in hexane (1.6 M, 17.2 mL, 27.5 mmol, 1.1 equiv) at −78 °C. After stirring for 15 min, acetophenone (3.0 g, 25 mmol) was added dropwise to the pale yellow mixture via a cannula over a 30 min period. After stirring an additional 15 min, chlorotrimethoxysilane[11] (4.31 g, 27.5 mmol, 1.1 equiv) was added dropwise and

the entire mixture was stirred for 30 min. The mixture was evaporated and the resulting white precipitate was removed by Celite filtration and washed with hexane. Ice-cooled satd $NaHCO_3$ (30 mL) was added to the filtrate and the mixture was stirred vigorously. After removing the cloudy material by Celite filtration, the organic layer was dried over Na_2SO_4 and evaporated to give the crude product as a brown oil. Distillation in vacuo (122–124 °C, 14 mmHg) gave the silyl enol ether as a colorless oil (2.7 g, 45% yield).

Method B. To a solution of anhydrous sodium iodide (8.25 g, 55 mmol, 1.1 equiv; dried over 5 mmHg, 150 °C, 6 h) in acetonitrile (60 mL) was added chlorotrimethoxysilane[11] (8.61 g, 55 mmol, 1.1 equiv) at room temperature under an argon atmosphere. After stirring for 5 min, acetophenone (6.0 g, 50 mmol) was added and the mixture was stirred for additional 5 min. Triethylamine (12.6 g, 125 mmol, 2.5 equiv) was added dropwise to the pale yellow mixture. After refluxing for 3 h, the mixture was extracted with hexane (5×80 mL). The organic layer was evaporated and the precipitates were removed by Celite filtration. Ice-cooled satd $NaHCO_3$ was added to the filtrate and the mixture was vigorously stirred. After removing the cloudy material by Celite filtration, the organic layer was dried over Na_2SO_4 and evaporated to give the crude product as a brown oil. Distillation in vacuo (108–110 °C, 9 mmHg) gave the silyl enol ether as a colorless oil (5.0 g, 42% yield).

Compound **1c**. ^{1}H NMR δ 3.62 (s, 9H, SiOC*H*$_3$), 4.72 (d, 1H, J=2.2 Hz), 5.00 (d, 1H, J=2.2 Hz), 7.34–7.28 (m, 3H), 7.65–7.60 (m, 2H); ^{13}C NMR δ 51.6, 92.0, 125.1, 128.2, 128.4, 136.3, 153.8; IR (neat) 2945, 2840, 1692, 1621, 1573, 1492, 1317, 1201, 1096, 1037, 828, 775, 743, 715 cm^{-1}; LR-EIMS 241 ((M+H)$^+$), 120, 105, 77; HR-EIMS calcd for $C_{11}H_{16}O_4Si$ 241.0896, found 241.0892.

4.3.2. (*Z*)-*tert*-butylpropenyloxytrimethoxysilane (1f).[7b] Following the representative procedure A, silyl enol ether **1f** was obtained from 2,2-dimethyl-3-pentanone (0.57 g, 5 mmol) as a colorless oil (0.87 g, 74%); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.09 (s, 9H), 1.57 (d, 3H, J=6.5 Hz), 3.68 (s, 9H), 4.64 (q, 1H, J=6.6 Hz).

4.3.3. 1-Trimethoxysilyloxycyclopentene (1d).[7b] Following the representative procedure A, silyl enol ether **1d** was obtained from cyclopentanone (2.1 g, 25 mmol) as a colorless oil (2.7 g, 53%); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.86–1.95 (m, 2H), 2.26–2.38 (m, 4H), 3.62 (s, 9H), 4.84–4.86 (m, 1H).

4.3.4. (*Z*)-trimethoxy-(1-phenylpropenyloxy)silane (1e). Following the representative procedure A, silyl enol ether **1e** was obtained from propiophenone (3.4 g, 25 mmol) as a colorless oil (1.7 g, 27%, *E*/*Z* 1:34). Bp 116 °C, 11 mmHg; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.80 (d, 3H, J=6.5 Hz), 3.49 (s, 9H), 5.37 (q, 1H, J=6.5 Hz), 7.32–7.18 (m, 3H), 7.51 (d, 2H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 148.0, 137.9, 128.2, 127.4, 125.0, 105.8, 51.4, 11.0; IR (neat) 3057, 2947, 2847, 2361, 1948, 1690, 1659, 1599, 1495, 1447, 1381, 1323, 1267, 1196, 1100, 1032 cm^{-1}; LR-EIMS 254 (M$^+$), 225 (bp), 121; HR-EIMS calcd for $C_{12}H_{17}O_4Si$ 254.0974, found 254.0966.

4.3.5. 1-Trimethoxysilyloxy-3*H*-indene (1g). Following the representative procedure A, silyl enol ether **1g** was obtained from 1-indanone (3.3 g, 25 mmol) as a colorless oil (1.7 g, 62%). Bp 125 °C, 4 mmHg; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 3.27 (d, 2H, J=2.5 Hz), 3.65 (s, 9H), 5.67 (t, 1H, J=2.5 Hz), 7.1–7.5 (m, 4H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 151.6, 142.6, 140.5, 126.0, 125.2, 123.8, 118.0, 107.3, 51.5, 33.8; IR (neat) 2948, 2847, 1605, 1578, 1366, 1181, 1082, 901, 837 cm^{-1}; LR-EIMS 252 (M$^+$), 236 (bp), 121, 91; HR-EIMS calcd for $C_{12}H_{16}O_4Si$ 252.0818, found 252.0806.

4.3.6. 1-Triethoxysilyloxycyclohexene (1h).[17] Following the representative procedure A, silyl enol ether **11** was obtained from cyclohexanone (0.98 g, 10 mmol) and chlorotriethoxysilane (2.2 g, 11 mmol) as a colorless oil (1.6 g, 62%). Bp 87–89 °C, 9 mmHg; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.22 (t, 9H, J=6.5 Hz), 1.47–1.56 (m, 2H), 1.63–1.67 (m, 2H), 1.97–2.10 (m, 4H), 3.85 (q, 6H, J=6.5 Hz), 5.07 (m, 1H).

4.4. Synthesis of 3,3′-disubstituted binaphthol derivatives

Binaphthol derivatives **10**–**16** were prepared by literature procedure.

4.4.1. (*R*)-3,3′-dimethyl-1,1′-binaphthalene-2,2′-diol (10).[18] TLC R_f=0.5 (benzene, PMA/H_2SO_4); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 2.49 (s, 6H), 5.10 (s, 2H), 7.05 (d, 2H, J=8.6 Hz), 7.20 (d, 2H, J=7.3 Hz), 7.32 (t, 2H, J=6.5 Hz), 7.79–7.81 (m, 4H); mp 199–201 °C; $[\alpha]_D$ +33.7 (*c* 1.0, $CHCl_3$); $[\alpha]_{546}$ +43.9 (*c* 1.0, $CHCl_3$).

4.4.2. (*R*)-3,3′-diphenyl-1,1′-binaphthalene-2,2′-diol (11).[19] TLC R_f=0.4 (hexane/AcOEt 4:1, UV); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 5.34 (s, 2H), 7.20–7.51 (m, 12H), 7.70–7.74 (m, 4H), 7.91 (d, 2H, J=7.8 Hz), 8.01 (s, 2H); mp 197–199 °C; $[\alpha]_D$ +104.3 (*c* 1.0, $CHCl_3$).

4.4.3. (*R*)-3,3′-dichloro-1,1′-binaphthalene-2,2′-diol (13).[20] TLC R_f=0.4 (hexane/AcOEt 4:1, UV); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 5.55 (s, 2H), 7.09 (d, 2H, J=8.4 Hz), 7.28–7.40 (m, 8H), 7.80 (d, 2H, J=8.6 Hz), 8.06 (s, 2H); mp 167–170 °C; $[\alpha]_D$ +90.3 (*c* 1.0, $CHCl_3$).

4.4.4. (*R*)-3,3′-diiodo-1,1′-binaphthalene-2,2′-diol (14).[20] TLC R_f=0.5 (hexane/AcOEt 4:1, UV); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 5.41 (s, 2H), 7.05 (d, 2H, J=8.6 Hz), 7.26–7.38 (m, 8H), 7.77 (d, 2H, J=8.6 Hz), 8.50 (s, 2H); mp>300 °C; $[\alpha]_D$ +100.9 (*c* 1.0, THF).

4.4.5. (*R*)-3,3′-bis(methoxycarbonyl)-1,1′-binaphthalene-2,2′-diol (16).[21] TLC R_f=0.4 (hexane/AcOEt 4:1, PMA/H_2SO_4); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 4.04 (s, 6H), 7.11–7.15 (m, 2H), 7.29–7.35 (m, 4H), 7.88–7.92 (m, 2H), 8.67 (s, 2H); mp 244–246 °C; $[\alpha]_D$ +170.5 (*c* 1.1, THF).

4.4.6. (*R*)-3,3′-bis(trifluoromethyl)-1,1′-binaphthalene-2,2′-diol (12).[22] To a double-necked 20 mL round-bottomed flask equipped with a magnetic stirring bar, septum, and dry-ice condenser containing activated cadmium (675 mg,

6 mmol) was added DMF (2.5 mL) under argon atmosphere. Dibromodifluoromethane (0.28 mL, 3 mmol) was added to the mixture at 0 °C and the entire mixture was immediately warmed to room temperature. After stirring for 2 h, the suspension was filtered with glass filter under argon pressure and the precipitate was washed with DMF (0.5 mL). To the resulting brown solution, HMPA (3.0 mL) was added followed by cuprous bromide (215 mg, 1.5 mmol) in one portion at 0 °C. After stirring for a few minutes, 3,3′-diiodo-2,2′-bis(methoxymethoxy)-1,1′-binaphthyl (62.6 mg, 0.1 mmol), which was prepared by the literature procedure[20] was added in one portion and then the reaction mixture was heated at 70 °C for 6 h. Benzene (10 mL) and H_2O (5 mL) were added to the reaction mixture and the mixture was vigorously stirred at room temperature for 12 h. After removing the precipitate by Celite filtration, the organic layer was washed with H_2O and brine, dried over Na_2SO_4, and evaporated. The brown residue was purified with silica gel column chromatography (hexane/benzene, 1:1). Dichloromethane (2 mL), methanol (2 mL), and concd HCl (0.3 mL) were added to the resulting yellow oil and the mixture was stirred overnight at room temperature. Then the organic layer was washed with satd $NaHCO_3$ and brine, dried over Na_2SO_4, and evaporated. Purification with silica gel column chromatography (hexane/AcOEt, 20:1) afforded 3,3′-bis(trifluoromethyl)-1,1′-binaphthalene-2,2′-diol (34.0 mg, 81% yield) as pale yellow prisms. TLC $R_f=0.4$ (hexane/AcOEt 8:1, UV); ^{1}H NMR δ 5.35 (br, 2H), 7.10 (d, 2H, $J=7.3$ Hz), 7.44 (m, 4H), 7.86 (d, 2H, $J=7.3$ Hz), 8.36 (s, 2H); IR (KBr) 3549, 3063, 1630, 1332, 1207, 1155 cm^{-1}; $[\alpha]_D^{23}$ +657 (*c* 1.01, THF); mp 235–237 °C; LR-FABMS 422 (M^+); 154, 136; HR-FABMS calcd 422.0742 found 422.0752; Anal. Calcd for $C_{22}H_{12}F_6O_2$: C, 62.57; H, 2.86 found C, 62.18; H, 2.96.

4.4.7. (*R*)-3,3′-bis(methoxymethyl)-1,1′-binaphthalene-2,2′-diol (16). To a 20 mL round-bottomed flask equipped with magnetic stirring bar containing sodium hydride (65%, 57 mg, 1.5 mmol, 2.4 equiv) and THF (5 mL) was added THF (5 mL) solution of (*R*)-3,3′-bis(hydroxymethyl)-2,2′-bis(methoxymethoxy)-1,1′-binaphthyl (277 mg, 0.64 mmol) prepared by the literature procedure[23] via a cannula. After stirring for 1 h, methyl iodide (0.25 mL, 4.0 mmol, 6.3 equiv) was added to the resulting yellow solution, which was then stirred additional 2 days. After the reaction was completed, water (10 mL) was added to the mixture and the entire mixture was extracted with AcOEt (3×50 mL). The organic layer was washed with brine, dried over Na_2SO_4, and evaporated to give (*R*)-3,3′-bis(methoxymethyl)-2,2′-bis(methoxymethoxy)-1,1′-binaphthyl as a yellow oil (288 mg, 98% (crude)). Dichloromethane (5 mL) was added to this crude product, followed by concd HCl aq (0.3 mL), and the solution was stirred for 2 h at room temperature. The reaction mixture was neutralized with satd $NaHCO_3$ and extracted with AcOEt (3×50 mL). The organic layer was washed with brine, dried over Na_2SO_4, and evaporated. The resulting yellow oil was purified with silica gel column chromatography (12 g SiO_2, CH_2Cl_2/AcOEt 100:1→20:1). Recrystalization of resulting yellow solid (hexane/AcOEt 4:1) gave 3,3′-bis(methoxymethyl)-1,1′-binaphthalene-2,2′-diol as colorless prisms (1st crop, 90.2 mg, 38%) and pale yellow prisms (2nd crop, 55.4 mg, 23%). TLC $R_f=0.25$ (hexane/AcOEt 1:1, UV); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 3.51 (s, 3H), 4.84 (dd, 2H, $J=12.7$, 16.4 Hz), 7.11 (d, 1H, $J=8.4$ Hz), 7.2–7.4 (m, 2H), 7.82 (s, 1H), 7.85 (s, 1H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 58.5, 72.5, 113.9, 123.8, 124.5, 125.5, 126.8, 128.1, 128.5, 128.8, 133.5, 151.3; IR (KBr) 3526, 3294, 1626, 1504, 1392, 1194, 1107, 922 cm^{-1}; mp 143–144 °C; $[\alpha]_D$ +20.2 (*c* 0.78, $CHCl_3$); LR-FABMS 374 (M^+); HR-FABMS calcd 374.1518 found 374.1505; Anal. Calcd for $C_{24}H_{22}O_4$: C, 76.99; H, 5.92 found C, 77.20; H, 6.02.

4.5. General procedure for the aldol reaction of trimthoxysilyl enol ethers under anhydrous conditions

To a stirred solution of (*R*)-3,3′-dibromo-1,1′-binaphthalene-2,2′-diol **9** (21.0 mg, 0.047 mmol, 0.1 equiv) in THF (3 mL) was added *n*-butyllithium in hexane (0.16 M, 0.6 mL, 0.094 mmol, 0.2 equiv) at −23 °C, and the resulting yellow mixture was stirred for a few minutes. Then a solution aldehyde in THF (1.0 M, 0.47 mL, 0.47 mmol) and trimethoxysilyl enol ether (0.70 mmol, 1.5 equiv) were added. The mixture was stirred for 0.5 h at the same temperature and the reaction was quenched with KF/KH_2PO_4 aq (15% KF, 10% KH_2PO_4 solution, 2 mL). The entire mixture was stirred for an additional 2 h and the mixture was diluted with AcOEt (10 mL). The organic layer was washed three times with brine, dried over Na_2SO_4, and then evaporated. The crude product was purified by silica gel column chromatography (9.0 g SiO_2, CH_2Cl_2/hexane 8:1, then CH_2Cl_2/AcOEt 160:1→10:1) to give the corresponding aldol adduct as a *syn*/*anti* mixture. The enantiomeric excess of the adduct was determined by chiral HPLC.

4.5.1. 2-(Hydroxyphenylmethyl)cyclohexanone (2a).[7b] Following the general procedure, the aldol adduct **2a** was obtained from silyl enol ether **1a** and benzaldehyde as a colorless oil (93.4 mg, 97%, *syn*/*anti* 1:3.7, *syn* 8% ee, *anti* 51% ee). TLC $R_f=0.35$ (*syn*), 0.30 (*anti*) (hexane/AcOEt 4:1, *p*-anisaldehyde); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.4–1.9 (m, 8H), 2.0–2.1 (m, 4H), 2.3–2.7 (m, 4H), 2.99 (d, 1H, $J=2.7$ Hz), 3.93 (m, 1H), 4.79 (d, 1H, $J=8.9$ Hz), 5.40 (d, 1H, $J=2.7$ Hz), 7.2–7.4 (m, 10H); HPLC (Daicel chiralcel OD-H, hexane/IPA 19:1, 1.0 mL/min): t_R 9.4 (*syn*-minor, 2*S*, 1′*S*), 10.6 (*syn*-major, 2*R*, 1′*R*), 12.5 (*anti*-major, 2*S*, 1′*R*), 18.5 min (*anti*-minor, 2*R*, 1′*S*).

4.5.2. 2-(Hydroxyphenylmethyl)cycloheptanone (2b).[7b] Following the general procedure, the aldol adduct **2b** was obtained from silyl enol ether **1b** and benzaldehyde as a colorless oil (93.0 mg, 91%, *syn*/*anti* 1.4:1, *syn* 39% ee, *anti* 42% ee). TLC $R_f=0.5$ (hexane/AcOEt 4:1, *p*-anisaldehyde); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.2–1.9 (m, 14H), 2.4–2.7 (m, 4H), 2.85 (m, 1H), 3.00 (m, 1H), 3.3–3.5 (m, 2H), 4.82 (d, 1H, $J=8.4$ Hz), 5.19 (d, 1H, $J=2.7$ Hz), 7.2–7.5 (m, 10H); HPLC (Daicel chiralpak AD-H, hexane/IPA 19:1, 1.0 mL/min): t_R 11.8 (*syn*-major), 13.4 (*syn*-minor), 20.2 (*anti*-minor), 23.5 min (*anti*-major).

4.5.3. 2-(Hydroxyphenylmethyl)cyclopentanone (2d).[7b] Following the general procedure, the aldol adduct **2d** was obtained from silyl enol ether **1d** and benzaldehyde as a colorless oil (83.0 mg, 93%, *syn*/*anti* 3.4:1, *syn* 46% ee, *anti* 30% ee). TLC $R_f=0.4$ (hexane/AcOEt 4:1,

p-anisaldehyde); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.6–2.5 (m, 14H), 4.69 (d, 1H, J=9.5 Hz), 5.29 (t, 1H, J=4.0 Hz), 7.2–7.4 (m, 10H); HPLC (Daicel chiralcel OD-H, hexane/IPA 9:1, 1.0 mL/min): t_R 7.9 (*syn*-minor), 9.5 (*syn*-major), 11.5 (*anti*-minor, 2*S*, 1′*R*), 13.7 min (*anti*-major, 2*R*, 1′*S*).

4.5.4. 3-Hydroxy-1,3-diphenyl-1-propanone (2c).[24] Following the general procedure, the aldol adduct **2c** was obtained from silyl enol ether **1c** and benzaldehyde as a colorless oil (98.0 mg, 92%, 50% ee). TLC R_f=0.25 (hexane/AcOEt 4:1, UV); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 3.38 (d, 2H, J=6.1 Hz), 5.36 (t, 1H, J=6.1 Hz), 7.3–7.6 (m, 8H), 7.9–8.0 (m, 2H); HPLC (Daicel chiralcel OB-H, hexane/IPA 9:1, 1.0 mL/min) t_R 17.8 min (major, *R*), 25.8 min (minor, *S*).

4.5.5. 3-Hydroxy-2-methyl-1,3-diphenyl-1-propanone (2e).[4b] Following the general procedure, the aldol adduct **2e** was obtained from silyl enol ether **1e** and benzaldehyde as a colorless oil (111 mg, 98%, *syn*/*anti* 1:1.7, *syn* ~0% ee, *anti* ~0% ee). TLC R_f=0.20 (hexane/AcOEt 4:1, *p*-anisaldehyde); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.06 (d, 3H, J=7.3 Hz), 1.18 (d, 3H, J=7.3 Hz), 2.94 (d, 1H, J=4.6 Hz), 3.7–3.9 (m, 3H), 4.95 (m, 1H), 5.23 (s, 1H), 7.2–7.6 (m, 17H), 7.9–8.0 (m, 3H); HPLC (Daicel chiralcel OD-H, hexane/IPA 19:1, 1.0 mL/min): t_R 10.5 (*syn*), 12.3 (*syn*), 15.2 (*anti*), 16.9 min (*anti*).

4.5.6. 1-Hydroxy-2,4,4-trimethyl-1-phenylpentan-3-one (2f).[7b] Following the general procedure, the aldol adduct **2f** was obtained from silyl enol ether **1f** and benzaldehyde as a colorless oil (91.0 mg, 87%, *syn*/*anti* 1.8:1, *syn* ~0% ee, *anti* ~0% ee). TLC R_f=0.4 (hexane/AcOEt 4:1, KI/I_2 aq, H_2SO_4); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 0.9–1.1 (m, 24H), 3.1–3.4 (m, 3H), 3.5–3.6 (m, 1H), 4.75 (d, 1H, J=7.3 Hz), 5.23 (d, 1H, J=4.1 Hz), 7.1–7.4 (m, 10H); HPLC (Daicel chiralpak AD-H, hexane/IPA 40:1, 1.0 mL/min): t_R 11.1 (*syn*), 11.7 (*syn*), 12.8 (*anti*), 15.1 min (*anti*).

4.5.7. 2-(1-Hydroxy-3-phenyl-2-propenyl)cyclohexanone (2h).[4b] Following the general procedure, the aldol adduct **2h** was obtained from silyl enol ether **1a** and cinnamaldehyde as a colorless oil (106 mg, 98%, *syn*/*anti* 1:1.5, *syn* 44% ee, *anti* 6% ee). TLC R_f=0.4 (hexane/AcOEt 4:1, UV); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.3–1.8 (m, 8H), 1.8–1.9 (m, 2H), 2.0–2.2 (m, 2H), 2.3–2.6 (m, 6H), 4.43 (t, 1H, J=8.1 Hz), 4.77 (m, 1H), 6.1–6.3 (m, 2H), 6.5–6.7 (m, 2H), 7.1–7.4 (m, 10H); HPLC (Daicel chiralcel AD-H, hexane/IPA 19:1, 1mL/min) t_R 32.8 (*syn*-major), 40.0 (*syn*-minor), 44.3 (*anti*-minor), 53.1 min (*anti*-major).

4.5.8. 2-(1-Hydroxy-3-phenylpropyl)cyclohexanone (2i).[4b] Following the general procedure, the aldol adduct **2i** was obtained from silyl enol ether **1a** and hydrocinnamaldehyde as a colorless oil (15 mg, 14%, *syn*/*anti* 2.9:1, *syn* 40% ee, *anti* 16% ee). TLC R_f=0.35 (hexane/AcOEt 4:1, *p*-anisaldehyde); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.5–1.9 (m, 12H), 2.0–2.2 (m, 4H), 2.3–2.5 (m, 4H), 2.5–2.7 (m, 3H), 2.8–3.0 (m, 2H), 3.51 (m, 1H), 3.73 (m, 1H), 4.10 (m, 1H), 7.1–7.3 (m, 10H, Ar-H); HPLC (Daicel chiralcel OJ-H, hexane/IPA 40:1, 1.0 mL/min): t_R 16.1 (*syn*-major), 20.5 (*syn*-minor), 23.2 (*anti*-major), 24.8 min (*anti*-minor).

4.6. The general procedure for the aldol reaction of trimethoxysilyl enol ethers under aqueous conditions. To a stirred solution of (*R*)-3,3′-dibromo-1,1′-binaphthalene-2,2′-diol **9** (21.0 mg, 0.047 mmol, 0.1 equiv) in THF (3 mL) was added H_2O in THF (2.8 M, 0.25 mL, 0.70 mmol, 1.5 equiv) and *n*-butyllithium in hexane (0.16 M, 0.6 mL, 0.094 mmol, 0.2 equiv) at −23 °C. The resulting yellow mixture was stirred for a few minutes and then a solution of aldehyde in THF (1.0 M, 0.5 mL, 0.47 mmol) and trimethoxysilyl enol ether (0.70 mmol, 1.5 equiv) were added. The mixture was stirred for 0.5 h at the same temperature and the reaction was quenched with KF/KH_2PO_4 aq (15% KF, 10% KH_2PO_4 solution, 2 mL). The mixture was diluted with AcOEt (10 mL) and washed three times with brine. The organic layer was dried over Na_2SO_4 and then evaporated. The crude product was purified by silica gel column chromatography (CH_2Cl_2/hexane 8:1, then CH_2Cl_2/AcOEt 160:1→10:1) to give the corresponding aldol adduct as a *syn*/*anti* mixture. The enantiomeric excess of the adduct was determined by chiral HPLC.

4.6.1. 2-(Hydroxyphenylmethyl)cyclohexanone (2a).[7b] Following the general procedure, the aldol adduct **2a** was obtained from silyl enol ether **1a** and benzaldehyde as a colorless oil (89.2 mg, 93%, *syn*/*anti* 3.1:1, *syn* 80% ee, *anti* 50% ee). TLC R_f=0.35 (*syn*), 0.30 (*anti*) (hexane/AcOEt 4:1, *p*-anisaldehyde); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.4–1.9 (m, 8H), 2.0–2.1 (m, 4H), 2.3–2.7 (m, 4H), 2.99 (d, 1H, J=2.7 Hz), 3.93 (m, 1H), 4.79 (d, 1H, J=8.9 Hz), 5.40 (d, 1H, J=2.7 Hz), 7.2–7.4 (m, 10H); HPLC (Daicel chiralcel OD-H, hexane/IPA 19:1, 1.0 mL/min): t_R 9.4 (*syn*-minor, 2*S*, 1′*S*), 10.6 (*syn*-major, 2*R*, 1′*R*), 12.5 (*anti*-major, 2*S*, 1′*R*), 18.5 min (*anti*-minor, 2*R*, 1′*S*).

4.6.2. 2-(Hydroxyphenylmethyl)cyclopentanone (2d).[7b] Following the general procedure, the aldol adduct **2d** was obtained from silyl enol ether **1d** and benzaldehyde as a colorless oil (88 mg, 98%, *syn*/*anti* 2.9:1, *syn* 72% ee, *anti* 6% ee). TLC R_f=0.4 (hexane/AcOEt 4:1, *p*-anisaldehyde); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.6–2.5 (m, 14H), 4.69 (d, 1H, J=9.5 Hz), 5.29 (t, 1H, J=4.0 Hz), 7.2–7.4 (m, 10H); HPLC (Daicel chiralcel OD-H, hexane/IPA 9:1, 1.0 mL/min): t_R 7.9 (*syn*-minor), 9.5 (*syn*-major), 11.5 (*anti*-minor, 2*S*, 1′*R*), 13.7 min (*anti*-major, 2*R*, 1′*S*).

4.6.3. 3-Hydroxy-1,3-diphenyl-1-propanone (2c).[24] Following the general procedure, the aldol adduct **2c** was obtained from silyl enol ether **1c** and benzaldehyde as a colorless oil (94 mg, 88%, 75% ee). TLC R_f=0.25 (hexane/AcOEt 4:1, UV); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 3.38 (d, 2H, J=6.1 Hz), 5.36 (t, 1H, J=6.1 Hz), 7.3–7.6 (m, 8H), 7.9–8.0 (m, 2H); HPLC (Daicel chiralcel OB-H, hexane/IPA 9:1, 1.0 mL/min) t_R 17.8 min (major, *R*), 25.8 min (minor, *S*).

4.6.4. 3-Hydroxy-2-methyl-1,3-diphenyl-1-propanone (2e).[4b] Following the general procedure, the aldol adduct **2e** was obtained from silyl enol ether **1e** and benzaldehyde as a colorless oil (103 mg, 91%, *syn*/*anti* 1.9:1, *syn* 19% ee, *anti* 38% ee). TLC R_f=0.20 (hexane/AcOEt 4:1, *p*-anisaldehyde); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.06 (d, 3H, J=7.3 Hz), 1.18 (d, 3H, J=7.3 Hz), 2.94 (d, 1H, J=4.6 Hz), 3.7–3.9 (m, 3H), 4.95 (m, 1H), 5.23 (s, 1H), 7.2–7.6

(m, 17H), 7.9–8.0 (m, 3H); HPLC (Daicel chiralcel OD-H, hexane/IPA 19:1, 1.0 mL/min): t_R 10.5 (*syn*-major), 12.3 (*syn*-minor), 15.2 (*anti*-minor), 16.9 min (*anti*-major).

4.6.5. 2,3-Dihydro-2-(hydroxyphenylmethyl)-1*H*-inden-1-one (2g).[25] Following the general procedure, the aldol adduct **2g** was obtained from silyl enol ether **1g** and benzaldehyde as a colorless oil (88 mg, 78%, *syn*/*anti* 2.9:1, *syn* 83% ee, *anti* 48% ee). TLC R_f=0.35 (hexane/AcOEt 4:1, UV); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 2.24 (d, 1H, J= 4.9 Hz), 2.67 (m, 1H), 2.8–3.1 (m, 3H), 3.25 (dd, 1H, J= 4.0, 16.7 Hz), 4.78 (d, 1H, J=9.5 Hz), 5.59 (m, 1H), 7.2–7.4 (m, 14H), 7.5–7.6 (m, 2H), 7.6–7.8 (m, 2H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 26.6, 54.7, 71.9, 124.1, 126.5, 127.0, 128.5, 135.5, 137.0, 142.6, 154.8, 207.3 (*syn*); 29.8, 53.1, 75.6, 124.1, 126.5, 127.2, 128.4, 134.9, 136.4, 141.3, 154.0, 209.6 (*anti*); $[\alpha]_D^{25}$ +108 (*c* 1.0, $CHCl_3$); IR (KBr) 3553, 3449, 3055, 2910, 1703, 1605, 1462, 1449, 1329, 1294, 1280, 1095, 765 cm^{-1}; LR-EIMS 238 (M^+), 219, 132; HR-EIMS calcd for $C_{16}H_{14}O_2$ 238.0994 found 238.0990; HPLC (Daicel chiralpak AS-H, hexane/IPA 9:1, 1.0 mL/min): t_R 15.4 (*anti*-minor), 16.9 (*anti*-major), 22.1 (*syn*-minor), 34.2 min (*syn*-major).

4.6.6. 2,3-Dihydro-2-[hydroxy-(4-methoxyphenyl)-methyl]-1*H*-inden-1-one (2j). Following the general procedure, the aldol adduct **2j** was obtained from silyl enol ether **1g** and *p*-anisaldehyde as a colorless oil (113 mg, 89%, *syn*/*anti* 2.4:1, *syn* 70% ee, *anti* 25% ee). TLC R_f=0.3 (hexane/AcOEt 4:1, UV); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 2.6–2.7 (m, 1H), 2.8–3.0 (m, 4H), 3.2–3.3 (m, 1H), 3.77 (s, 6H), 4.78 (d, 1H, J=19.1 Hz), 5.51 (s, 1H), 6.8–6.9 (m, 4H), 7.3–7.8 (m, 12H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 26.7, 29.8, 53.1, 54.7, 55.1, 71.4, 75.0, 76.6, 113.6, 113.8, 123.7, 124.0, 126.4, 126.5, 126.6, 127.1, 127.5, 128.1, 133.4, 134.8, 135.3, 136.2, 136.9, 153.9, 154.8, 158.6, 159.3, 207.5, 209.6 (*syn*/*anti* mixture); $[\alpha]_D^{25}$ +143 (*c* 1.2, $CHCl_3$); IR (KBr) 3493, 1692, 1609, 1512, 1298, 1256, 1092, 1028, 853 cm^{-1}; LR-EIMS 268 (M^+), 132; HR-EIMS calcd for $C_{17}H_{16}O_3$ 268.1099 found 268.1102; HPLC (Daicel chiralpak AS-H, hexane/IPA 3:1, 1.0 mL/min): t_R 10.2 (*anti*-minor), 13.7 (*anti*-major), 17.6 (*syn*-major), 30.2 min (*syn*-minor).

4.6.7. 2,3-Dihydro-2-[hydroxy-(4-trifluoromethyl-phenyl)methyl]-1*H*-inden-1-one (2k). Following the general procedure, the aldol adduct **2k** was obtained from silyl enol ether **1g** and *p*-(trifluoromethyl)benzaldehyde as a colorless oil (128 mg, 88%, *syn*/*anti* 2.1:1, *syn* 48% ee, *anti* 39% ee). TLC R_f=0.4 (hexane/AcOEt 4:1, UV); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 2.4–2.7 (m, 1H), 2.7–3.3 (m, 7H), 4.89 (d, 1H, J=8.9 Hz), 5.67 (br s, 1H), 7.3–7.8 (m, 16H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 26.5, 29.6, 53.0, 54.7, 71.1, 75.1, 122.3, 123.9, 124.2, 125.3, 125.4, 125.5, 125.6, 125.7, 125.8, 126.5, 126.6, 127.3, 127.4, 127.9, 129.3, 129.7, 130.2, 130.6, 135.2, 135.7, 136.1, 136.8, 145.2, 146.8, 153.7, 154.7, 207.0, 209.1 (*syn*/*anti* mixture); $[\alpha]_D^{25}$ +40.1 (*c* 1.0, $CHCl_3$); IR (KBr) 3433, 1693, 1604, 1467, 1413, 1325, 1298, 1163, 1109, 1064, 1016 cm^{-1}; LR-EIMS 306 (M^+), 288, 173, 132 (bp); HR-EIMS calcd for $C_{17}H_{13}O_2F_3$ 306.0868 found 306.0858; HPLC (Daicel chiralpak AS-H, hexane/IPA 9:1, 1.0 mL/min): t_R 12.5 (*anti*-minor), 14.5 (*anti*-major), 15.6 (*syn*-major), 22.2 min (*syn*-minor).

4.6.8. 2,3-Dihydro-2-(1-hydroxy-3-phenyl-2-propen-yl)-1*H*-inden-1-one (2l). Following the general procedure, the aldol adduct **2l** was obtained from silyl enol ether **1g** and cinnamaldehyde as a colorless oil (122 mg, 98%, *syn*/*anti* 3.4:1, *syn* 73% ee, *anti* 10% ee). TLC R_f=0.2 (hexane/AcOEt 4:1, UV); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 2.8–3.0 (m, 2H), 3.1–3.3 (m, 4H), 4.52 (t, 1H, J=6.5 Hz), 5.02 (m, 1H), 6.2–6.3 (m, 2H), 6.7–6.8 (m, 2H), 7.2–7.8 (m, 18H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 27.3, 29.6, 52.0, 52.6, 71.6, 74.0, 123.8, 124.1, 126.4, 126.5, 126.6, 127.3, 127.6, 127.7, 127.8, 128.5, 128.7, 129.4, 131.0, 132.2, 135.0, 135.4, 136.3, 136.3, 136.4, 137.0, 154.0, 154.8, 207.8, 209.0 (*syn*/*anti* mixture); $[\alpha]_D^{25}$ +82.2 (*c* 0.96, $CHCl_3$); IR (KBr) 3478, 1698, 1605, 1464, 1329, 1296, 1205, 963, 765, 705 cm^{-1}; LR-EIMS 264 (M^+), 246, 132; HR-EIMS calcd for $C_{18}H_{16}O_2$ 264.1150 found 264.1158; HPLC (Daicel chiralpak AS-H, hexane/IPA 9:1, 1.0 mL/min): t_R 22.1 (*anti*-major), 26.8 (*anti*-minor), 31.8 (*syn*-minor), 37.2 min (*syn*-major).

4.6.9. 2,3-Dihydro-2-(1-hydroxy-3-phenylpropyl)-1*H*-inden-1-one (2m). Following the general procedure, the aldol adduct **2m** was obtained from silyl enol ether **1g** and hydrocinnamaldehyde as a colorless oil (113 mg, 90%, *syn*/*anti* 2.6:1, *syn* 92% ee, *anti* 47% ee). TLC R_f=0.3 (hexane/AcOEt 4:1, UV); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.7–2.0 (m, 4H), 2.4–2.9 (m, 8H), 3.1–3.3 (m, 2H), 3.84 (m, 1H), 4.38 (m, 1H), 7.1–7.7 (m, 18H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 27.2, 29.6, 29.7, 31.3, 32.4, 36.6, 37.3, 51.9, 53.1, 70.2, 71.7, 123.6, 123.9, 125.8, 125.9, 126.4, 126.5, 127.2, 127.6, 128.3, 128.4, 128.5, 128.7, 134.9, 135.3, 136.4, 137.0, 141.7, 142.0, 153.7, 154.7, 208.4, 209.9 (*syn*/*anti* mixture); $[\alpha]_D^{25}$ +39.6 (*c* 0.93, $CHCl_3$); IR (KBr) 3486, 1698, 1605, 1464, 1329, 1296, 1209, 1039, 770 cm^{-1}; LR-EIMS 266 (M^+), 248, 161, 132; HR-EIMS calcd for $C_{18}H_{18}O_2$ 266.1306 found 266.1299; HPLC (Daicel chiralpak AS-H, hexane/IPA 9:1, 1.0 mL/min) t_R 15.4 (*anti*-minor), 16.9 (*anti*-major), 22.1 (*syn*-minor), 34.2 min (*syn*-major).

4.6.10. 2,3-Dihydro-2-(hydroxycyclohexylmethyl)-1*H*-inden-1-one (2n). Following the general procedure, the aldol adduct **2n** was obtained from silyl enol ether **1g** and hydrocinnamaldehyde as a colorless oil (109 mg, 94%, *syn*/*anti* 1.4:1, *syn* 97% ee, *anti* 84% ee). TLC R_f=0.4 (hexane/AcOEt 4:1, UV); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 0.9–1.4 (m, 8H), 1.5–1.9 (m, 12H), 2.0–2.1 (m, 2H), 2.8–2.9 (m, 2H), 3.0–3.3 (m, 3H), 3.66 (d, 1H, J=9.2 Hz), 4.10 (d, 1H, J= 7.3 Hz), 4.2–4.3 (m, 1H), 7.3–7.8 (m, 8H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 25.6, 25.8, 26.1, 26.2, 26.4, 26.6, 26.7, 29.3, 29.5, 29.8, 30.1, 41.5, 41.9, 49.3, 50.8, 74.9, 76.4, 123.5, 123.8, 126.4, 126.5, 127.0, 127.5, 134.7, 135.2, 136.5, 137.2, 153.8, 154.9, 209.0, 211.0 (*syn*/*anti* mixture); $[\alpha]_D^{25}$ +46.8 (*c* 1.2, $CHCl_3$); IR (KBr) 3409, 2924, 2847, 1678, 1605, 1466, 1296, 1084, 1024, 960 cm^{-1}; LR-EIMS 244 (M^+), 161, 132; HR-EIMS calcd for $C_{16}H_{20}O_2$ 244.1463 found 244.1455; HPLC (Daicel chiralpak AD-H, hexane/IPA 19:1, 1.0 mL/min): t_R 15.4 (*anti*-minor), 19.4 (*anti*-major), 22.4 (*syn*-major), 28.4 min (*syn*-minor).

4.6.11. 2-(Hydroxy-1-naphthalenylmethyl)cyclohexanone (2o).[7b] Following the general procedure, the aldol adduct **2o** was obtained from silyl enol ether **1a** and 1-naphthaldehyde as a colorless oil (108 mg, 90%, *syn*/*anti*

1.4:1, *syn* 81% ee, *anti* 65% ee). TLC R_f=0.35 (*syn*), 0.30 (*anti*) (hexane/AcOEt 4:1, *p*-anisaldehyde); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.3–1.9 (m, 8H), 2.0–2.2 (m, 4H), 2.3–2.6 (m, 4H), 2.77 (m, 1H), 2.97 (m, 1H), 3.08 (d, 1H, J=3.3 Hz), 4.11 (d, 1H, J=3.3 Hz), 5.57 (m, 1H), 6.24 (br s, 1H), 7.4–7.6 (m, 7H), 7.7–7.9 (m, 6H), 8.25 (m, 1H); HPLC (Daicel chiralcel OD-H, hexane/IPA 40:1, 0.7 mL/min): t_R 19.0 (*syn*-minor), 26.3 (*syn*-major), 44.2 (*anti*-minor), 52.7 min (*anti*-major).

4.6.12. 2-(Hydroxy-2-naphthalenylmethyl)cyclohexanone (2p).[26] Following the general procedure, the aldol adduct **2p** was obtained from silyl enol ether **1a** and 2-naphthaldehyde as a colorless oil (113 mg, 94%, *syn*/*anti* 1.6:1, *syn* 72% ee, *anti* 45% ee). TLC R_f=0.30 (*syn*), 0.25 (*anti*) (hexane/AcOEt 4:1, *p*-anisaldehyde); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.3–1.8 (m, 8H), 2.0–2.2 (m, 4H), 2.3–2.6 (m, 4H), 2.7–2.8 (m, 2H), 3.13 (d, 1H, J=3.3 Hz), 4.03 (d, 1H, J=3.0 Hz), 4.95 (m, 1H), 5.56 (br s, 1H), 7.36 (d, 1H, J=8.7 Hz), 7.4–7.5 (m, 5H), 7.75 (m, 1H), 7.8–7.9 (m, 7H); HPLC (Daicel chiralcel OD-H, hexane/IPA 9:1, 1.0 mL/min): t_R 9.0 (*syn*-minor), 9.7 (*syn*-major), 11.0 (*anti*-minor), 13.5 min (*anti*-major).

4.6.13. 2-(1-Hydroxy-3-phenyl-2-propenyl)cyclohexanone (2h).[4b] Following the general procedure, the aldol adduct **2h** was obtained from silyl enol ether **1a** and cinnamaldehyde as a colorless oil (104 mg, 95%, *syn*/*anti* 1.4:1, *syn* 75% ee, *anti* 5% ee). TLC R_f=0.4 (hexane/AcOEt 4:1, UV); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.3–1.8 (m, 8H), 1.8–1.9 (m, 2H), 2.0–2.2 (m, 2H), 2.3–2.6 (m, 6H), 4.43 (t, 1H, J=8.1 Hz), 4.77 (m, 1H), 6.1–6.3 (m, 2H), 6.5–6.7 (m, 2H), 7.1–7.4 (m, 10H); HPLC (Daicel chiralpak AD-H, hexane/IPA 19:1, 1.0 mL/min) t_R 32.8 (*syn*-major), 40.0 (*syn*-minor), 44.3 (*anti*-minor), 53.1 min (*anti*-major).

4.6.14. 2-(1-Hydroxy-3-phenylpropyl)cyclohexanone (2i).[4b] Following the general procedure, the aldol adduct **2i** was obtained from silyl enol ether **1a** and hydrocinnamaldehyde as a colorless oil (83 mg, 75%, *syn*/*anti* 1.2:1, *syn* 92% ee, *anti* 40% ee). TLC R_f=0.35 (hexane/AcOEt 4:1, *p*-anisaldehyde); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.5–1.9 (m, 12H), 2.0–2.2 (m, 4H), 2.3–2.5 (m, 4H), 2.5–2.7 (m, 3H), 2.8–3.0 (m, 2H), 3.51 (m, 1H), 3.73 (m, 1H), 4.10 (m, 1H), 7.1–7.3 (m, 10H); HPLC (Daicel chiralcel OJ-H, hexane/IPA 40:1, 1.0 mL/min): t_R 16.1 (*syn*-major), 20.5 (*syn*-minor), 23.2 (*anti*-major), 24.8 min (*anti*-minor).

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(*anti*); K: 12 h, 66% yield, *syn*/*anti* 1:1.5, <10% ee (*syn*), 28% ee (*anti*); Rb: no reaction).
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