Catalytic Asymmetric Aldol Reaction of Trimethoxysilyl Enol Ethers Using 2,2′-Bis(di-*p*-tolylphosphino)-1,1′-binaphthyl·AgF Complex

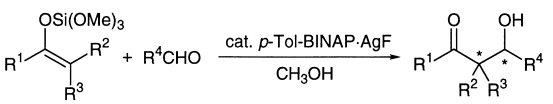
Akira Yanagisawa, Yoshinari Nakatsuka, Kenichi Asakawa, Manabu Wadamoto, Hiromi Kageyama, and Hisashi Yamamoto*

Graduate School of Engineering, Nagoya University, CREST, Japan Science and Technology Corporation (JST), Chikusa, Nagoya 464-8603

(Received March 1, 2001)

Catalytic asymmetric Mukaiyama-type aldol reaction using trimethoxysilyl enol ethers was achieved using 2,2′-bis(di-*p*-tolylphosphino)-1,1′-binaphthyl (*p*-Tol-BINAP)·AgF complex as a catalyst. The chiral silver(I) catalyst was easily generated by mixing *p*-Tol-BINAP and silver(I) fluoride in MeOH at room temperature. High *syn*- and enantioselectivities were obtained from both the *E*- and *Z*-silyl enol ethers. Use of a 1:1 mixture of MeOH and acetone as a solvent in the reaction of cyclohexanone-derived trimethoxysilyl enol ethers resulted in higher enantioselectivity.

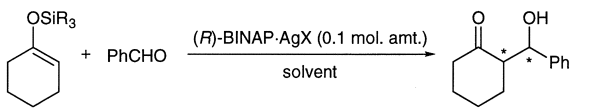
β-Hydroxy carbonyl group is an important moiety of natural products or biologically active molecules and efficient methods to construct such functional groups are strongly desired. The asymmetric Mukaiyama aldol reaction is a beneficial route to optically active β-hydroxy carbonyl compounds.[1] Numerous chiral Lewis acid catalysts have been designed and applied to the reaction of trialkylsilyl enol ethers or ketene trialkylsilyl acetals with carbonyl compounds,[1,2] however, the majority are the main-group metal (B, Zn, Sn, etc.) compounds or first row-transition metal (Ti, Cu, etc.) compounds, and there are few examples of second or third row-transition metal compounds.[3,4] We have previously shown that BINAP·AgOTf complex is a good chiral catalyst for asymmetric allylation of aldehydes with allylic trialkyltin compounds[5] and asymmetric aldol reaction of tributyltin enolates,[6] however, these reactions have the disadvantage of requiring the use of toxic trialkyltin compounds. To solve this problem, we developed a catalytic asymmetric Sakurai–Hosomi allylation reaction by 2,2′-bis(di-*p*-tolylphosphino)-1,1′-binaphthyl (*p*-Tol-BINAP)·AgF complex using less toxic allylic trimethoxysilanes instead of allylic tin compounds.[7] We report here an application of this catalytic system to the aldol process: *p*-Tol-BINAP·AgF-catalyzed asymmetric condensation of trimethoxysilyl enol ethers with aldehydes (Eq. 1).[8]



(1)

Results and Discussion

We initially attempted the addition of trimethylsilyl enol ethers to aldehydes in the presence of BINAP·AgOTf as a chiral catalyst, however, the desired product was obtained only in low yield. Yamagishi and co-workers independently examined the BINAP·Ag(I)-catalyzed asymmetric Mukaiyama aldol reaction using trimethylsilyl enol ethers and found that the reaction was accelerated by BINAP·$AgPF_6$ in DMF containing a small amount of water to give the aldol product with high enantioselectivity.[9] In contrast, we examined diverse combinations of BINAP·Ag(I) catalysts and silyl enol ethers and found that high enantioselectivity and chemical yields were obtained in the BINAP·AgF-catalyzed aldol reaction of trimethoxysilyl enol ethers in methanol. For example, when trimethoxysilyl enol ether of cyclohexanone was treated with benzaldehyde, the reaction proceeded smoothly at −78 °C and *syn*(R^*, R^*)-aldol adduct was obtained diastereoselectively with 71% ee (Eq. 2). Both trimethoxysilyl enol ethers and BINAP·AgF are necessary for this aldol reaction; if BINAP·AgOTf is used instead, the racemic aldol product is obtained in only 3% yield. When trimethylsilyl enol ether of cyclohexanone was added to benzaldehyde under the influence of BINAP·AgF catalyst, yield and diastereo- and enantioselectivities decreased.

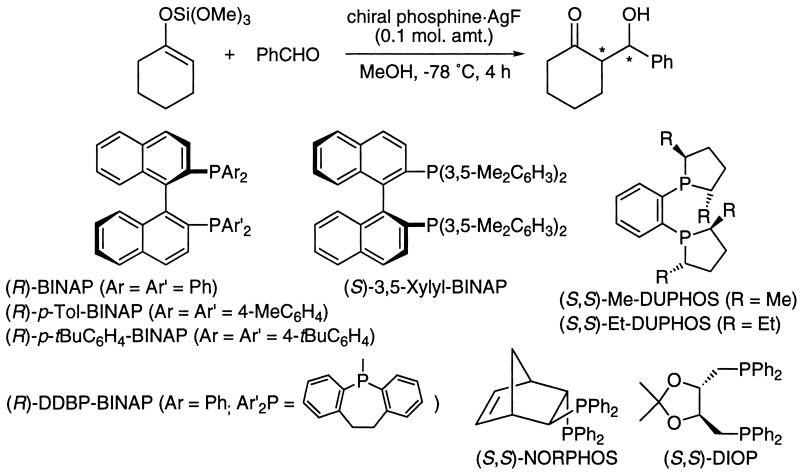


(2)

R	X	Solvent	Conditions	Yield/%	*syn* (% ee)/*anti* (% ee)
OMe	F	MeOH	-78 °C, 3 h	64	71 (71)/29 (40)
OMe	OTf	THF	-78 °C ~ r.t., 75 h	3	35 (<1)/65 (<1)
Me	F	MeOH	-78 ~ -20 °C, 6 h	48	44 (28)/56 (62)

Using various BINAP derivatives and other chiral phosphines, we studied the enantioselectivity of this process; yields, *syn*(R^*, R^*)/*anti*(R^*, S^*) ratios, and enantiomeric excesses of the products obtained by the reaction of cyclohexanone-derived trimethoxysilyl enol ether with benzaldehyde under the influence of 0.1 molar amount of various chiral phosphine–AgF complexes in MeOH are shown in Table 1. Among the BINAP derivatives examined, (*R*)-*p*-Tol-BINAP[10] was found to provide the most satisfactory result (entry 3). Use of (*R*)-*p*-*t*BuC_6H_4-BINAP[10] resulted in a higher yield with slight-

Table 1. Asymmetric Aldol Reaction of Cyclohexanone-Derived Trimethoxysilyl Enol Ether with Benzaldehyde Catalyzed by Various Chiral Phosphine·AgF Complexes[a)]

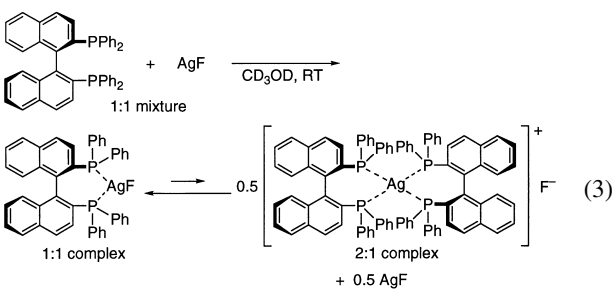


Entry	Chiral phosphine	Yield/%[b)]	*syn*(R^*, R^*)/*anti*(R^*, S^*)[c)]	ee%[d)]
1[e)]	(*R*)-BINAP	64	71/29	71
2[f)]	(*S*)-3,5-Xylyl-BINAP	30	59/41	15[g)]
3	(*R*)-*p*-Tol-BINAP	78	84/16	87
4	(*R*)-*p*-*t*BuC_6H_4-BINAP	87	70/30	90
5	(*R*)-DDBP-BINAP	32	50/50	12[h)]
6	(*S*,*S*)-Me-DUPHOS	73	73/27	57
7	(*S*,*S*)-Et-DUPHOS	93	86/14	72
8	(*S*,*S*)-DIOP	59	48/52	3[i)]
9	(*S*,*S*)-NORPHOS	40	51/49	12[j)]

a) Unless otherwise specified, the reaction was carried out using chiral phosphine·AgF (0.1 mol amt.), cyclohexanone-derived trimethoxysilyl enol ether (1 mol amt.) and benzaldehyde (1 mol amt.) in MeOH at −78 °C for 4 h. b) Isolated yield. c) Determined by ^{1}H NMR analysis. d) The value corresponds to the major diastereomer. Determined by HPLC analysis (Chiralcel OD-H, Daicel Chemical Industries, Ltd.). e) The reaction was performed for 3 h. f) The reaction was performed at −78 °C for 1 h, then at −40 °C for 1 h, and finally at −20 °C for 3 h. g) The *anti* isomer: 15% ee. h) The value corresponds to the *syn* isomer. The *anti* isomer; 8% ee. i) The *syn* isomer: 4% ee. j) The *anti* isomer: 9% ee.

ly better ee, although the *syn*(R^*, R^*)/*anti*(R^*, S^*) ratio was lower (entry 4). Me- and Et-DUPHOS also showed moderate enantioselectivities (entries 6 and 7), but other representative chiral phosphines were less effective.

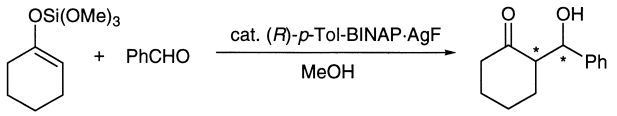
Although the mechanism of the present catalytic reaction is not clear, the BINAP·AgF complex is believed to act as a chiral Lewis acid catalyst rather than a silver enolate, judging from the following NMR results. When trimethoxysilyl enol ether of cyclohexanone was treated with a 1:1 mixture of (*R*)-BINAP·AgF complex and DMF in CD_3OD at room temperature, no peaks of the silyl enol ether were observed and a set of new peaks assignable to 1-cyclohexenyl group appeared, whereas peaks of $(MeO)_3SiF$ and cyclohexanone were not seen at all. These observations are a positive proof that none of the silver enolate was generated. Furthermore, we found that, when (*R*)-BINAP was mixed with an equimolar amount of AgF in CD_3OD at room temperature, a significant amount of 2:1 complex [FAB- and ESI-MS: *m*/*z* 1353 (M^+ − F)] was produced, accompanied by a 1:1 complex (Eq. 3).[11] The 2:1 complex showed no reactivity in the present aldol reaction. Various ratios of the mixture in CD_3OD were measured by ^{1}H NMR and a 0.6:1 mixture was found to give the desired 1:1 complex without formation of the 2:1 complex. The formation of the undesired 2:1 complex is also avoidable by introducing a bulky substituent at the *para*-position of phenyl groups of BINAP. Indeed, (*R*)-*p*-Tol-BINAP and (*R*)-*p*-*t*BuC_6H_4-BINAP afforded higher chemical yields than did (*R*)-BINAP (compare entries 1, 3, and 4 in Table 1).



(3)

The optimum reaction conditions of *p*-Tol-BINAP·AgF-catalyzed asymmetric Mukaiyama aldol reaction are shown in Table 2. We attempted to reduce the amount of catalyst and found that the reaction proceeded in high yield without loss of enantioselectivity, even when only 0.03 molar amount of *p*-

Table 2. The Optimum Reaction Conditions of *p*-Tol-BINAP·AgF-Catalyzed Asymmetric Aldol Reaction of Cyclohexanone-Derived Trimethoxysilyl Enol Ether with Benzaldehyde[a)]



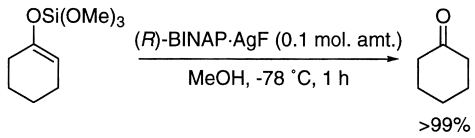
Entry	(*R*)-*p*-BINAP mol amt.	AgF mol amt.	Conditions[b)]	Yield/%[c)]	*syn*/*anti*[d)]	ee%[e)]
1	0.1	0.1	A	78	84/16	87
2	0.05	0.05	A	36	82/18	89
3	0.03	0.03	B	56	69/31	82
4	0.03	0.05	C	83	75/25	88
5	0.012	0.02	C	53	74/26	85
6	0.006	0.01	C	16	55/45	55[f)]

a) Unless otherwise noted, the reaction was carried out using (*R*)-*p*-Tol-BINAP (specified amt.), AgF (specified amt.), cyclohexanone-derived trimethoxysilyl enol ether (1 mol amt.) and benzaldehyde (1 mol amt.) in MeOH. b) Condition A: at −78 °C for 4 h. Condition B: at −78 °C for 2 h and then at −40 °C for 4 h. Condition C: at −78 °C for 4 h and then at −40 °C for 4 h. c) Isolated yield. d) Determined by ^{1}H NMR analysis. *syn* = (R^*, R^*); *anti* = (R^*, S^*). e) The value corresponds to the *syn* isomer. Determined by HPLC analysis (Chiralcel OD-H, Daicel Chemical Industries, Ltd.). f) The *anti* isomer: 10% ee.

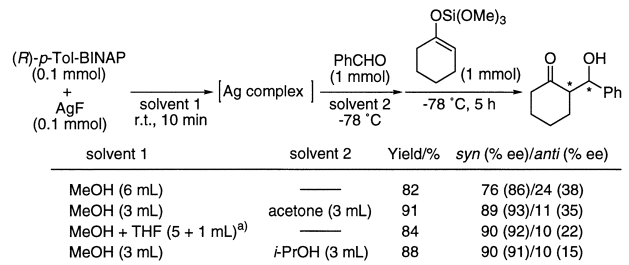
Tol-BINAP and 0.05 molar amount of AgF were present (entry 4). However, less than 0.01 molar amount of these catalysts decreased the enantioselectivity and the yield to a great extent (entry 6).

Table 3 summarizes the results obtained for the reaction of (*E*)- and (*Z*)-silyl enol ethers with various aldehydes under the influence of 0.1 molar amount of (*R*)-*p*-Tol-BINAP·AgF in MeOH. All the reactions of cyclohexanone-derived (*E*)-trimethoxysilyl enol ether resulted in remarkable *syn*(R^*, R^*)- and enantioselectivities not only with aromatic aldehydes but also with an α,β-unsaturated aldehyde (entries 1–3, and 5), with the exception of 1-naphthaldehyde, which gave the *anti*(R^*, S^*) product selectively (entry 4). In the reaction with cinnamaldehyde, only a 1,2-adduct was observed (entry 5). Aliphatic aldehydes were inactive under the standard reaction conditions. For example, the reaction with hydrocinnamaldehyde gave the aldol product in less than 1% yield at −78 °C for 4 h (entry 6). Ketone showed no reactivity even at room temperature (entry 7). (*E*)-Trimethoxysilyl enol ethers of cyclopentanone and cycloheptanone also underwent the *syn*(R^*, R^*)- and enantioselective aldol reaction (entries 8 and 9), while the former afforded the product in low yield because of the simultaneous methanolysis of the silyl enol ether by the silver catalyst leading to cyclopentanone (entry 8). In contrast, *t*-butyl ethyl ketone-derived (*Z*)-silyl enol ether gave the *syn* product almost exclusively with high enantioselectivity up to 97% ee in combination with various aromatic aldehydes (entries 10–12). Hydrocinnamaldehyde, however, did not react at all with the (*Z*)-silyl enol ether (entry 13).

We further studied the solvent effect on the aldol reaction of trimethoxysilyl enol ether of cyclohexanone to improve the chemical yield and diastereo- and enantioselectivities. MeOH plays an important role as solvent which can dissolve AgF and BINAP·AgF or *p*-Tol-BINAP·AgF complex; however, it also causes undesired hydrolysis of the silyl enol ether in the presence of the silver(I) catalyst even at −78 °C (Eq. 4). Thus, we tested various mixed solvents consisting of MeOH and another solvent to suppress the hydrolysis. As a consequence, acetone, THF, and *i*-PrOH were found to be effective as the second solvent for the aldol reaction, with a 1:1 mixture of MeOH and acetone in particular providing the highest yield and ee (Eq. 5). These three mixed solvents indicate even higher *syn*(R^*, R^*)/*anti*(R^*, S^*) ratio than does MeOH alone. These remarkable solvent effects are probably due to changes in proportion of the two in situ generated silver(I) complexes shown in Eq. 3.



(4)



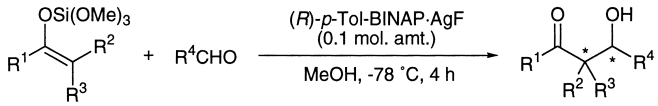
solvent 1	solvent 2	Yield/%	*syn* (% ee)/*anti* (% ee)
MeOH (6 mL)	——	82	76 (86)/24 (38)
MeOH (3 mL)	acetone (3 mL)	91	89 (93)/11 (35)
MeOH + THF (5 + 1 mL)[a)]	——	84	90 (92)/10 (22)
MeOH (3 mL)	*i*-PrOH (3 mL)	88	90 (91)/10 (15)

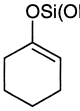
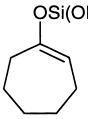
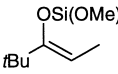
a) (*R*)-*p*-Tol-BINAP·AgF complex was prepared in a mixture of two solvents.

(5)

From the aforementioned NMR results and the facts that AgF clearly activated trimethoxysilyl enol ethers (Eq. 2) and that these ethers reacted with aldehydes *syn*-selectively regardless of the *E*/*Z* stereochemistry in the presence of BINAP·AgF catalyst, the cyclic transition-state structures **A** and **B** shown in Fig. 1 can be viewed as possible models for the aldol reaction. In these assemblies, the BINAP·AgF complex acts as a chiral Lewis acid and coordinates to both an aldehyde and a silyl enol

Table 3. Diastereo- and Enantioselective Aldol Reaction of Trimethoxysilyl Enol Ethers with Aldehydes Catalyzed by (*R*)-*p*-Tol-BINAP·AgF Complex[a)]



Entry	Silyl enol ether	Carbonyl compound	Yield/%[b)]	*syn/anti*[c)]	ee%[d)]
1		PhCHO	78	84/16	87
2		4-$MeOC_6H_4CHO$	86	75/25	92
3		4-BrC_6H_4CHO	87	76/24	90
4		1-naphthyl-CHO	68	27/73	76[e)]
5		(*E*)-PhCH=CHCHO	81	81/19	68
6		$Ph(CH_2)_2CHO$	< 1	—	—
7[f)]		PhCOMe	< 1	—	—
8[g)]		PhCHO	18	75/25	52
9		PhCHO	67	81/19	78
10[h)]		PhCHO	84	$> 99/1$	97
11[h)]		4-$MeOC_6H_4CHO$	76	$> 99/1$	96
12[h)]		1-naphthyl-CHO	63	94/6	95
13[h)]		$Ph(CH_2)_2CHO$	< 1	—	—

a) Unless otherwise noted, the reaction was carried out using (*R*)-*p*-Tol-BINAP·AgF (0.1 mol amt.), trimethoxysilyl enol ether (1 mol amt.), and aldehyde (1 mol amt.) in MeOH at −78 °C for 4 h. b) Isolated yield. c) Determined by ^{1}H NMR analysis. For entries 1–9: *syn* = (R^*, R^*); *anti* = (R^*, S^*). d) The value corresponds to the major diastereomer. Determined by HPLC analysis (Chiralcel OB-H, OD-H, or Chiralpak AD, Daicel Chemical Industries, Ltd.). e) The *syn* isomer: 70% ee. f) The reaction was performed at −40 °C for 30 min, −20 °C for 1 h, 0 °C for 1 h, and finally at 20 °C for 12 h. g) The reaction was performed for 5 h. h) The reaction was performed at −78 °C for 2 h, then at −40 °C for 2 h, and finally at −20 °C for 2 h.

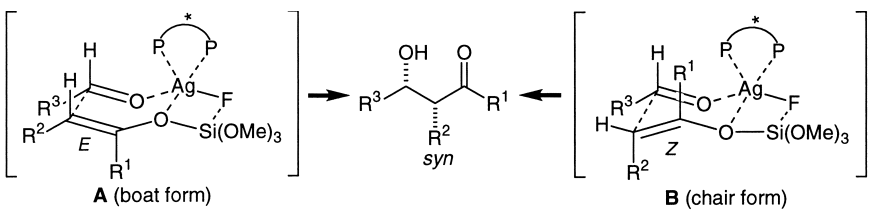


Fig. 1. Probable cyclic transition-state structures.

ether to give a six-membered cyclic structure, which is further stabilized by the adjacent four-membered ring made by AgF and trimethoxysiloxy group.[12] Thus, from the *E*-enol ether, the *syn*-aldol adduct can be selectively obtained via a boat-like transition-state structure **A**, whereas model **B** having a chair conformation resulting from the *Z*-enol ether leads to the *syn* product. These models are different from those proposed for asymmetric allylation by allylic trimethoxysilanes[7] which are proposed to advance via six-membered cyclic transition-state structures involving a BINAP-coordinated allylic silver. The difference in structure is probably dependent on whether or not the transmetallation to allylic silvers or silver enolates occurs before the reaction with aldehydes.

Conclusion

We have described a novel example of asymmetric Mukaiyama aldol reaction of trimethoxysilyl enol ethers catalyzed by *p*-Tol-BINAP·AgF complex. The main features of this process are: (1) the procedure can be carried out with no difficulty using readily available chemicals and can furnish a variety of optically active β-hydroxy ketones with high enantioselectivity up to 97% ee; (2) remarkable *syn* selectivity is observed for the reaction irrespective of the *E*/*Z* stereochemistry of the silyl enol ethers; (3) this process is environmentally

friendlier because less toxic trimethoxysilyl enol ether and MeOH solvent are used. Further work is now in progress on the catalytic aldol reaction and the detailed reaction mechanism.

Experimental

General. Analytical TLC was done on E. Merck precoated (0.25 mm) silica gel 60 F_{254} plates. Column chromatography was conducted using silica gel 60 (E. Merck 9385, 230–400 mesh). Infrared (IR) spectra were recorded on a Shimadzu FTIR-8100 spectrometer. ^{1}H NMR spectra were measured on a Varian Gemini-300 (300 MHz) spectrometer. Chemical shifts of ^{1}H NMR spectra were reported relative to tetramethylsilane (δ 0) or chloroform (δ 7.26). Splitting patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. ^{13}C NMR spectra were measured on a Varian Gemini-300 (75 MHz) spectrometer. Chemical shifts of ^{13}C NMR spectra were reported relative to $CDCl_3$ (δ 77.0). Analytical high-performance liquid chromatography (HPLC) was done with a Shimadzu 10A instrument using a chiral column (4.6 mm × 25 cm, Daicel CHIRALCEL OB-H, OD-H, or CHIRALPAK AD). Optical rotation was measured on a JASCO DIP-1000 polarimeter.

All experiments were carried out in an atmosphere of standard grade argon gas (oxygen < 10 ppm) and exclusion of direct light. Dry THF was used as purchased from Wako Pure Chemical (dehydrated, > 99.5%, water: < 0.005%). MeOH and *i*-PrOH were purified by distillation over Mg turnings. Acetone was purified by distillation over molecular sieves 4A. Silver fluoride (99.9+%) and silver triflate (99+%) were used as purchased from Aldrich. (*R*)-BINAP (guaranteed reagent) was used as purchased from Nacalai Tesque. (*R*)-*p*-Tol-BINAP and (*S*)-3,5-Xylyl-BINAP[13] were donated by the Takasago International Corporation. (*R*)-*p*-*t*BuC_6H_4-BINAP was prepared according to the reported procedure.[10] (*S*,*S*)-Me-DUPHOS [(+)-1,2-bis((2*S*,5*S*)-2,5-dimethylphospholano)benzene], (*S*,*S*)-Et-DUPHOS [(+)-1,2-bis((2*S*,5*S*)-2,5-diethylphospholano)benzene], (*S*,*S*)-DIOP [(4*S*,5*S*)-(+)-2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane], and (*S*,*S*)-NORPHOS [(2*S*,3*S*)-(+)-2,3-bis(diphenylphosphino)bicyclo[2.2.1]hept-5-ene] were used as purchased from STREM. (*R*)-DDBP-BINAP, 10,11-dihydro-5*H*-dibenzo[*b*,*f*]phosphepine derivative of (*R*)-BINAP, was prepared by a palladium-catalyzed coupling reaction [$Pd(OAc)_2$ (0.1 mol amt.), dppb (1,4-bis(diphenylphosphino)butane, 0.1 mol amt.), DMSO, 100 °C, > 99% yield][14] between ditriflate of (*R*)-1,1′-bi-2-naphthol[14b,15] and 10,11-dihydro-5*H*-dibenzo[*b*,*f*]phosphepine 5-oxide (2 mol amt.)[16] followed by a three-step sequence:[14b,17] (1) deoxygenation of the resulting monosubstituted product with trichlorosilane (Et_3N, toluene, 100 °C, 69% yield), (2) substitution of the second triflate by diphenylphosphine oxide (2 mol amt.) in the presence of $NiCl_2$(dppe) [dppe = 1,2-bis(diphenylphosphino)ethane, 0.025 mol amt.], DABCO (1,4-diazabicyclo[2.2.2]octane, 4 mol amt.) in DMF (58% yield), and (3) deoxygenation with trichlorosilane (Et_3N, toluene, 100 °C, 50% yield). Spectral data of (*R*)-DDBP-BINAP: TLC R_f 0.32 (1:10 ethyl acetate/hexane); IR ($CHCl_3$) 3058, 3015, 1507, 1474, 1435, 1225, 1208, 818, 793 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.98–3.30 (m, 4H, 2 CH_2), 6.68 (t, 1H, J = 7.4 Hz, aromatic), 6.75–7.21 (m, 20H, aromatic), 7.29–7.44 (m, 4H, aromatic), 7.50 (dd, 1H, J = 8.5, 3.6 Hz, aromatic), 7.75 (d, 1H, J = 8.0 Hz, aromatic), 7.81 (d, 1H, J = 8.5 Hz, aromatic), 7.89 (d, 1H, J = 8.2 Hz, aromatic), 7.95 (d, 1H, J = 8.5 Hz, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$, main peaks) δ 34.1, 34.8, 125.2, 125.3, 125.6, 125.7, 126.2, 126.4, 126.9, 127.4, 127.7, 127.9, 128.1, 128.3, 128.4, 128.5, 128.6, 129.2, 129.7, 130.9, 132.6, 132.9, 133.2, 133.7, 134.2, 134.5; $[\alpha]_D^{29}$ +41.3° (*c* 0.5, C_6H_6). Aldehydes were purified by distillation before use. Trimethoxysilyl enol ethers of cyclohexanone and cycloheptanone were prepared by 1,4-hydrosilylation of the corresponding 2-cycloalken-1-one with $(MeO)_3SiH$ catalyzed by $(Ph_3P)_3RhCl$ or $(Ph_3P)_4RhH$.[18] Trimethoxysilyl enol ethers of *t*-butyl ethyl ketone and cyclopentanone were prepared by treating the ketones with LDA in ether followed by silylation with $(MeO)_3SiCl$.[19] Trimethylsilyl enol ether of cyclohexanone was prepared by treating the ketone with LDA in ether followed by silylation with Me_3SiCl. These silyl enol ethers were purified by distillation before use. Other chemicals were used as purchased.

Typical Experimental Procedure for Asymmetric Aldol Reaction of Trimethoxysilyl Enol Ethers with Aldehydes Catalyzed by (*R*)-*p*-Tol-BINAP·AgF Complex: Synthesis of 2-(Hydroxyphenylmethyl)cyclohexanone (Entry 3 in Table 1, Entry 1 in Table 2, Entry 1 in Table 3).[20] A mixture of AgF (13.0 mg, 0.102 mmol) and (*R*)-*p*-Tol-BINAP (67.9 mg, 0.100 mmol) was dissolved in dry MeOH (6 mL) under argon atmosphere and with direct light excluded, and stirred at 20 °C for 10 min. To the resulting solution was added dropwise benzaldehyde (100 μL, 0.98 mmol) and (1-cyclohexenyloxy)trimethoxysilane (220.4 mg, 1.01 mmol) successively at −78 °C. The mixture was stirred for 4 h at this temperature and then treated with brine (2 mL) and solid KF (ca. 1 g) at ambient temperature for 30 min. The resulting precipitate was filtered off by a glass filter funnel filled with Celite® and silica gel. The filtrate was dried over Na_2SO_4 and concentrated in vacuo after filtration. The residual crude product was purified by column chromatography on silica gel (1:5 ethyl acetate/hexane as the eluant) to afford a mixture of the aldol adducts (156.5 mg, 78% yield) as white solids. The *syn*(R^*, R^*)/*anti*(R^*, S^*) ratio was determined to be 84/16 by ^{1}H NMR analysis. The enantioselectivities of the *syn* and *anti* isomers were determined to be 87% ee and 48% ee, respectively, by HPLC analysis using a chiral column (Chiralcel OD-H, Daicel Chemical Industries, Ltd., hexane/*i*-PrOH = 9/1, flow rate = 0.5 mL min^{-1}): $t_{syn\text{-}minor}$ = 13.4 min (2*S*,1′*S*), $t_{syn\text{-}major}$ = 14.5 min (2*R*,1′*R*), $t_{anti\text{-}major}$ = 16.1 min (2*S*,1′*R*), $t_{anti\text{-}minor}$ = 22.2 min (2*R*,1′*S*). The absolute configurations of all stereoisomers were unambiguously established by Denmark and co-workers.[20d] Specific rotation of the *syn* isomer (87% ee): $[\alpha]_D^{25}$ +109.5° (*c* 1.0, $CHCl_3$); elemental analysis calcd for $C_{13}H_{16}O_2$: C 76.44, H 7.90%; found: C 76.10, H 8.23%. Specific rotation of the *anti* isomer (48% ee): $[\alpha]_D^{25}$ +13.6° (*c* 1.0, $CHCl_3$); elemental analysis calcd for $C_{13}H_{16}O_2$: C 76.44, H 7.90%; found: C 76.35, H 7.96%. Other spectral data (TLC, IR, ^{1}H NMR, and ^{13}C NMR) of the *syn* and *anti* isomers indicated good agreement with reported data.[6b,20]

2-[Hydroxy(4-methoxyphenyl)methyl]cyclohexanone (Entry 2 in Table 3).[21] The *syn*(R^*, R^*)/*anti*(R^*, S^*) ratio was determined to be 75/25 by ^{1}H NMR analysis. Specific rotation of the *syn* isomer (white solids, 92% ee): $[\alpha]_D^{30}$ +97.7° (*c* 1.0, $CHCl_3$); elemental analysis calcd for $C_{14}H_{18}O_3$: C 71.77, H 7.74%; found: C 71.61, H 7.78%. The enantioselectivity was determined to be 92% ee by HPLC analysis using a chiral column (Chiralcel OD-H, Daicel Chemical Industries, Ltd., hexane/*i*-PrOH = 20/1, flow rate = 0.25 mL min^{-1}): t_{major} = 52.4 min, t_{minor} = 58.5 min. Spectral data of the *anti* isomer (white solids, 40% ee): TLC R_f 0.12 (1:3 ethyl acetate/hexane); IR (KBr) 3700–3250, 2932, 1705, 1686, 1516, 1250, 1173, 1129, 1028, 830 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.23–1.33 (m, 1H, one proton of CH_2), 1.48–1.81

(m, 4H, 2 CH_2), 2.04–2.12 (m, 1H, one proton of CH_2), 2.30–2.41 (m, 1H, one proton of CH_2), 2.44–2.52 (m, 1H, one proton of CH_2), 2.55–2.64 (m, 1H, CH), 3.80 (s, 3H, CH_3), 3.94 (d, 1H, J = 2.5 Hz, OH), 4.74 (dd, 1H, J = 1.9, 8.8 Hz, C*H*(OH)), 6.88 (d, 2H, J = 8.5 Hz, aromatic), 7.24 (d, 2H, J = 8.8 Hz, aromatic); $[\alpha]_D^{32}$ +15.4° (*c* 1.0, $CHCl_3$); elemental analysis calcd for $C_{14}H_{18}O_3$: C 71.77, H 7.74%; found: C 71.70, H 7.86%. The enantioselectivity was determined to be 40% ee by HPLC analysis using a chiral column (Chiralcel OD-H, Daicel Chemical Industries, Ltd., hexane/*i*-PrOH = 20/1, flow rate = 1.0 mL min^{-1}): t_{major} = 15.2 min, t_{minor} = 20.0 min. Spectral data (TLC, IR, ^1H NMR, and ^{13}C NMR) of the *syn* and *anti* isomers indicated good agreement with reported data.[21]

2-[(4-Bromophenyl)hydroxymethyl]cyclohexanone (Entry 3 in Table 3).[21c,22] The *syn*(*R**, *R**)/*anti*(*R**, *S**) ratio was determined to be 76/24 by ^1H NMR analysis. Specific rotation of the *syn* isomer (white solids, 90% ee): $[\alpha]_D^{29}$ +80.9° (*c* 1.0, $CHCl_3$); elemental analysis calcd for $C_{13}H_{15}O_2Br$: C 55.14, H 5.34%; found: C 55.04, H 5.39%. The enantioselectivity was determined to be 90% ee by HPLC analysis using a chiral column (Chiralcel OD-H, Daicel Chemical Industries, Ltd., hexane/*i*-PrOH = 40/1, flow rate = 0.5 mL min^{-1}): t_{major} = 46.8 min, t_{minor} = 61.4 min. Spectral data of the *anti* isomer (white solids, 66% ee): TLC R_f 0.21 (1:3 ethyl acetate/hexane); IR (KBr) 3700–3150, 2930, 2857, 1690, 1541, 1509, 1127, 1069, 1053, 1009, 826 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.19–1.36 (m, 1H, one proton of CH_2), 1.47–1.83 (m, 4H, 2 CH_2), 2.07–2.14 (m, 1H, one proton of CH_2), 2.30–2.41 (m, 1H, one proton of CH_2), 2.46–2.60 (m, 2H, one proton of CH_2 and CH), 3.99 (d, 1H, J = 2.5 Hz, OH), 4.75 (dd, 1H, J = 1.9, 8.8 Hz, C*H*(OH)), 7.20 (d, 2H, J = 8.5 Hz, aromatic), 7.47 (d, 2 H, J = 8.5 Hz, aromatic); $[\alpha]_D^{32}$ +16.8° (*c* 1.0, $CHCl_3$); elemental analysis calcd for $C_{13}H_{15}O_2Br$: C 55.14, H 5.34%; found: C 55.07, H 5.41%. The enantioselectivity was determined to be 66% ee by HPLC analysis using a chiral column (Chiralcel OB-H, Daicel Chemical Industries, Ltd., hexane/*i*-PrOH = 40/1, flow rate = 0.5 mL min^{-1}): t_{major} = 43.4 min, t_{minor} = 52.4 min. Spectral data (TLC, IR, ^1H NMR, and ^{13}C NMR) of the *syn* and *anti* isomers indicated good agreement with reported data.[21c,22]

2-[(1-Naphthyl)hydroxymethyl]cyclohexanone (Entry 4 in Table 3).[20c,20d] The *syn*(*R**, *R**)/*anti*(*R**, *S**) ratio was determined to be 27/73 by ^1H NMR analysis. The enantioselectivities of the *syn* and *anti* isomers were determined to be 70% ee and 76% ee, respectively, by HPLC analysis using a chiral column (Chiralcel OD-H, Daicel Chemical Industries, Ltd., hexane/*i*-PrOH = 9/1, flow rate = 0.5 mL min^{-1}): $t_{syn\text{-}minor}$ = 18.4 min, $t_{syn\text{-}major}$ = 23.7 min, $t_{anti\text{-}minor}$ = 43.2 min (2*R*,1′*S*), $t_{anti\text{-}major}$ = 45.2 min (2*S*,1′*R*). The absolute configurations of the *anti* isomers were assigned by Denmark and co-workers.[20c,20d] Specific rotation of the *syn* isomer (70% ee): $[\alpha]_D^{27}$ +90.5° (*c* 1.0, $CHCl_3$); elemental analysis calcd for $C_{17}H_{18}O_2$: C 80.28, H 7.13%; found: C 80.27, H 7.27%. Specific rotation of the *anti* isomer (76% ee): $[\alpha]_D^{31}$ +6.9° (*c* 1.0, $CHCl_3$); elemental analysis calcd for $C_{17}H_{18}O_2$: C 80.28, H 7.13%; found: C 80.29, H 7.31%. Other spectral data (TLC, IR, ^1H NMR, and ^{13}C NMR) of the *syn* and *anti* isomers indicated good agreement with reported data.[20c,20d]

2-[(*E*)-1-Hydroxy-3-phenyl-2-propenyl]cyclohexanone (Entry 5 in Table 3).[6b,20b–20d] The *syn*(*R**, *R**)/*anti*(*R**, *S**) ratio was determined to be 81/19 by ^1H NMR analysis. The enantioselectivities of the *syn* and *anti* isomers were determined to be 68% ee and 44% ee, respectively, by HPLC analysis using a chiral column (Chiralpak AD, Daicel Chemical Industries, Ltd., hexane/*i*-PrOH = 40/1, flow rate = 0.5 mL min^{-1}): $t_{syn\text{-}major}$ = 58.8 min, $t_{syn\text{-}minor}$ = 72.4 min, $t_{anti\text{-}major}$ = 78.8 min (2*S*,1′*R*), $t_{anti\text{-}minor}$ = 89.3 min (2*R*,1′*S*). The absolute configurations of the *anti* isomers were assigned by Denmark and co-workers.[20b–20d] Specific rotation of the *syn* isomer (68% ee): $[\alpha]_D^{27}$ +55.2° (*c* 1.0, $CHCl_3$); elemental analysis calcd for $C_{15}H_{18}O_2$: C 78.23, H 7.88%; found: C 78.12, H 8.12%. Specific rotation of the *anti* isomer (44% ee): $[\alpha]_D^{27}$ −14.0° (*c* 0.5, $CHCl_3$); elemental analysis calcd for $C_{15}H_{18}O_2$: C 78.23, H 7.88%; found: C 78.22, H 8.14%. Other spectral data (TLC, IR, ^1H NMR, and ^{13}C NMR) of the *syn* and *anti* isomers indicated good agreement with reported data.[6b,20b–20d]

2-(Hydroxyphenylmethyl)cyclopentanone (Entry 8 in Table 3).[6a,20a,23] The *syn*(*R**, *R**)/*anti*(*R**, *S**) ratio was determined to be 75/25 by ^1H NMR analysis. The enantioselectivities of the *syn* and *anti* isomers were determined to be 52% ee and 2% ee, respectively, by HPLC analysis using a chiral column (Chiralcel OD-H, Daicel Chemical Industries, Ltd., hexane/*i*-PrOH = 9/1, flow rate = 0.5 mL min^{-1}): $t_{syn\text{-}major}$ = 15.0 min, $t_{syn\text{-}minor}$ = 17.4 min, $t_{anti\text{-}major}$ = 21.1 min (2*S*,1′*R*), $t_{anti\text{-}minor}$ = 24.0 min (2*R*,1′*S*). The absolute configurations of the *anti* isomers were assigned by Denmark and co-workers.[23] Spectral data (TLC, IR, ^1H NMR, and ^{13}C NMR) of the *syn* and *anti* isomers indicated good agreement with reported data.[6a,20a,23]

2-(Hydroxyphenylmethyl)cycloheptanone (Entry 9 in Table 3).[23] The *syn*(*R**, *R**)/*anti*(*R**, *S**) ratio was determined to be 81/19 by ^1H NMR analysis. The enantioselectivity of the *syn* isomer was determined to be 78% ee by HPLC analysis using a chiral column (Chiralcel OD-H, Daicel Chemical Industries, Ltd., hexane/*i*-PrOH = 40/1, flow rate = 0.5 mL min^{-1}): $t_{syn\text{-}minor}$ = 26.1 min, $t_{syn\text{-}major}$ = 31.2 min, t_{anti} = 37.7 min (2*S*,1′*R* + 2*R*,1′*S*). The enantioselectivity of the *anti* isomer could not be determined. The absolute configurations of the *anti* isomers were unambiguously established by Denmark and co-workers.[23] Specific rotation of the *syn* isomer (78% ee): $[\alpha]_D^{28}$ +99.3° (*c* 1.0, $CHCl_3$). Other spectral data (TLC, IR, ^1H NMR, and ^{13}C NMR) of the *syn* and *anti* isomers indicated good agreement with reported data.[23]

1-Hydroxy-2,4,4-trimethyl-1-phenyl-3-pentanone (Entry 10 in Table 3).[6a,24] The *syn*/*anti* ratio was determined to be > 99/1 by ^1H NMR analysis. The enantioselectivity of the *syn* isomer was determined to be 97% ee by HPLC analysis using a chiral column (Chiralcel OD-H, Daicel Chemical Industries, Ltd., hexane/*i*-PrOH = 40/1, flow rate = 0.5 mL min^{-1}): $t_{syn\text{-}minor}$ = 17.1 min, $t_{syn\text{-}major}$ = 18.0 min. Specific rotation of the *syn* isomer (95% ee): $[\alpha]_D^{30}$ −67.1° (*c* 1.3, $CHCl_3$). Other spectral data (IR and ^1H NMR) of the *syn* isomer indicated good agreement with reported data.[6a,24]

1-Hydroxy-1-(4-methoxyphenyl)-2,4,4-trimethyl-3-pentanone (Entry 11 in Table 3).[24c,25] The *syn*/*anti* ratio was determined to be > 99/1 by ^1H NMR analysis. The enantioselectivity of the *syn* isomer was determined to be 96% ee by HPLC analysis using a chiral column (Chiralcel OD-H, Daicel Chemical Industries, Ltd., hexane/*i*-PrOH = 40/1, flow rate = 0.5 mL min^{-1}): $t_{syn\text{-}major}$ = 22.0 min, $t_{syn\text{-}minor}$ = 24.0 min. Satisfactory spectral data (TLC, IR, ^1H NMR, and ^{13}C NMR) were obtained for the *syn* isomer.[24c,25]

1-Hydroxy-2,4,4-trimethyl-1-(1-naphthyl)-3-pentanone (Entry 12 in Table 3).[24a,24b] The *syn*/*anti* ratio was determined to be 94/6 by ^1H NMR analysis. The enantioselectivity of the *syn* isomer was determined to be 95% ee by HPLC analysis using a chiral column (Chiralcel OD-H, Daicel Chemical Industries, Ltd., hexane/*i*-PrOH = 20/1, flow rate = 1.0 mL min^{-1}): $t_{syn\text{-}minor}$ = 7.9 min, $t_{syn\text{-}major}$ = 22.8 min. Spectral data (IR and ^1H NMR) of the *syn* isomer indicated good agreement with reported data.[24a,24b]

We thank Takasago International Corporation for its generous gift of (*R*)-*p*-Tol-BINAP and (*S*)-3,5-Xylyl-BINAP. A. Yanagisawa also acknowledges financial support from the Naito Foundation and the Takeda Science Foundation.

References

1 Review: C. Gennari, "Comprehensive Organic Synthesis," ed by B. M. Trost, I. Fleming, and C. H. Heathcock, Pergamon, Oxford (1991), Vol. 2, p. 629.

2 Reviews for catalytic asymmetric aldol reactions using silyl enol ethers or ketene silyl acetals: a) T. Bach, *Angew. Chem. Int. Ed. Engl.*, **33**, 417 (1994). b) T. K. Hollis and B. Bosnich, *J. Am. Chem. Soc.*, **117**, 4570 (1995). c) M. Braun, "Houben–Weyl: Methods of Organic Chemistry," ed by G. Helmchen, R. W. Hoffmann, J. Mulzer, and E. Schaumann, Georg Thieme Verlag, Stuttgart (1995), Vol. E21, p 1730. d) S. G. Nelson, *Tetrahedron: Asymmetry*, **9**, 357 (1998). e) H. Gröger, E. M. Vogl, and M. Shibasaki, *Chem. Eur. J.*, **4**, 1137 (1998). f) R. Mahrwald, *Chem. Rev.*, **99**, 1095 (1999). g) P. Arya, and H. Qin, *Tetrahedron*, **56**, 917 (2000). h) T. D. Machajewski, and C.-H. Wong, *Angew. Chem. Int. Ed. Engl.*, **39**, 1353 (2000). Reviews for chiral Lewis base-catalyzed asymmetric aldol reactions using trichlorosilyl enol ethers: i) S. E. Denmark, R. A. Stavenger, X. Su, K.-T. Wong, and Y. Nishigaichi, *Pure Appl. Chem.*, **70**, 1469 (1998). j) S. E. Denmark and R. A. Stavenger, *Acc. Chem. Res.*, **33**, 432 (2000).

3 Chiral rhodium catalysts: a) M. T. Reetz, and A. E. Vougioukas, *Tetrahedron Lett.*, **28**, 793 (1987). Chiral palladium catalysts: b) M. Sodeoka, K. Ohrai, and M. Shibasaki, *J. Org. Chem.*, **60**, 2648 (1995). c) M. Sodeoka, R. Tokunoh, F. Miyazaki, E. Hagiwara, and M. Shibasaki, *Synlett*, **1997**, 463. d) M. Sodeoka, and M. Shibasaki, *Pure Appl. Chem.*, **70**, 414 (1998). e) A. Fujii and M. Sodeoka, *Tetrahedron Lett.*, **40**, 8011 (1999). See also: f) E. Hagiwara, A. Fujii, and M. Sodeoka, *J. Am. Chem. Soc.*, **120**, 2474 (1998). g) A. Fujii, E. Hagiwara, and M. Sodeoka, *J. Am. Chem. Soc.*, **121**, 5450 (1999). Chiral platinum catalysts: h) O. Fujimura, *J. Am. Chem. Soc.*, **120**, 10032 (1998).

4 Recent examples of direct catalytic asymmetric aldol reactions of aldehydes with unmodified ketones are also noteworthy: a) Y. M. A. Yamada, N. Yoshikawa, H. Sasai, and M. Shibasaki, *Angew. Chem. Int. Ed. Engl.*, **36**, 1871 (1997). b) Y. M. A. Yamada and M. Shibasaki, *Tetrahedron Lett.*, **39**, 5561 (1998). c) N. Yoshikawa, Y. M. A. Yamada, J. Das, H. Sasai, and M. Shibasaki, *J. Am. Chem. Soc.*, **121**, 4168 (1999). d) B. List, R. A. Lerner, and C. F. Barbas III, *J. Am. Chem. Soc.*, **122**, 2395 (2000). e) W. Notz, and B. List, *J. Am. Chem. Soc.*, **122**, 7386 (2000).

5 a) A. Yanagisawa, H. Nakashima, A. Ishiba, and H. Yamamoto, *J. Am. Chem. Soc.*, **118**, 4723 (1996). b) A.Yanagisawa, A. Ishiba, H. Nakashima, and H. Yamamoto, *Synlett*, **1997**, 88. c) A. Yanagisawa, Y. Nakatsuka, H. Nakashima, and H. Yamamoto, *Synlett,* **1997**, 933. d) A. Yanagisawa, H. Nakashima, Y. Nakatsuka, A. Ishiba, and H. Yamamoto, *Bull. Chem. Soc. Jpn.*, in press.

6 a) A. Yanagisawa, Y. Matsumoto, H. Nakashima, K. Asakawa, and H. Yamamoto, *J. Am. Chem. Soc.*, **119**, 9319 (1997). b) A. Yanagisawa, Y. Matsumoto, K. Asakawa, and H. Yamamoto, *J. Am. Chem. Soc.*, **121**, 892 (1999).

7 A. Yanagisawa, H. Kageyama, Y. Nakatsuka, K. Asakawa, Y. Matsumoto, and H. Yamamoto, *Angew. Chem. Int. Ed.*, **38**, 3701 (1999).

8 A preliminary communication of this work has been published: A. Yanagisawa, Y. Nakatsuka, K. Asakawa, H. Kageyama, and H. Yamamoto, *Synlett*, **2001**, 69.

9 a) M. Ohkouchi, M. Yamaguchi, and T. Yamagishi, *Enantiomer*, **5**, 71 (2000). b) M. Ohkouchi, D. Masui, M. Yamaguchi, and T. Yamagishi, *J. Mol. Catalysis A: Chemical*, in press.

10 H. Takaya, K. Mashima, K. Koyano, M. Yagi, H. Kumobayashi, T. Taketomi, S. Akutagawa, and R. Noyori, *J. Org. Chem.*, **51**, 629 (1986). (*R*)- and (*S*)-*p*-Tol-BINAP are commercially available (AZmax).

11 Neutral silver(I) complexes such as $(R_3P)_3AgF$ are also conceivable alternatives for the 2:1 complex, see: E. L. Muetterties and C. W. Alegranti, *J. Am. Chem. Soc.*, **94**, 6386 (1972). A competing side reaction ($2\ AgF + R_3P \rightarrow 2\ Ag + R_3PF_2$) reported in the literature could not be observed in our reactions.

12 Bottoni, Tagliavini, and coworkers have suggested similar eight-membered cyclic transition-state models for BF_3-promoted addition of allylsilanes to aldehydes: A. Bottoni, A. L. Costa, D. D. Tommaso, I. Rossi, and E. Tagliavini, *J. Am. Chem. Soc.*, **119**, 12131 (1997).

13 K. Mashima, K. Kusano, N. Sato, Y. Matsumura, K. Nozaki, H. Kumobayashi, N. Sayo, Y. Hori, T. Ishizaki, S. Akutagawa, and H. Takaya, *J. Org. Chem.*, **59**, 3064 (1994).

14 a) L. Kurz, G. Lee, D. Morgans, Jr., M. J. Waldyke, and T. Ward, *Tetrahedron Lett.*, **31**, 6321 (1990). b) Y. Uozumi, A. Tanahashi, S.-Y. Lee, and T. Hayashi, *J. Org. Chem.*, **58**, 1945 (1993).

15 D. Cai, J. F. Payack, D. R. Bender, D. L. Hughes, T. R. Verhoeven, and P. J. Reider, *Org. Synth.*, **76**, 6 (1999).

16 a) S. Warren and P. Wyatt, *J. Chem. Soc., Perkin Trans. 1*, **1998**, 249. See also: b) J. L. Suggs and L. D. Freedman, *J. Org. Chem.*, **17**, 2566 (1971). 10,11-dihydro-5*H*-dibenzo[*b*,*f*]phosphepine can be readily transformed into the corresponding oxide by oxidation with air in ether.

17 a) S. Gladiali, S. Pulacchini, D. Fabbri, M. Manassero, and M. Sansoni, *Tetrahedron: Asymmetry*, **9**, 391 (1998). b) S. Y. Cho and M. Shibasaki, *Tetrahedron Lett.*, **39**, 1773 (1998). c) S. Gladiali, A. Dore, D. Fabbri, S. Medici, G. Pirri, and S. Pulacchini, *Eur. J. Org. Chem.*, 2861 (2001).

18 a) I. Ojima and T. Kogure, *Organometallics*, **1**, 1390 (1982). b) G. Z. Zheng and T. H. Chan, *Organometallics*, **14**, 70 (1995).

19 a) D. F. Peppard, W. G. Brown, and W. C. Johnson, *J. Am. Chem. Soc.*, **68**, 70 (1946). b) K. Moedritzer and J. R. Van Wazer, *Inorg. Chem.*, **3**, 268 (1964).

20 a) E. Juaristi, A. K. Beck, J. Hansen, T. Matt, T. Mukhopadhyay, M. Simson, and D. Seebach, *Synthesis*, **1993**, 1271. b) S. E. Denmark, S. B. D. Winter, X. Su, and K.-T. Wong, *J. Am. Chem. Soc.*, **118**, 7404 (1996). c) S. E. Denmark, K.-T. Wong, and R. A. Stavenger, *J. Am. Chem. Soc.*, **119**, 2333 (1997). d) S. E. Denmark, R. A. Stavenger, K.-T. Wong, and X. Su, *J. Am. Chem. Soc.*, **121**, 4982 (1999).

21 a) E. Nakamura, M. Shimizu, I. Kuwajima, J. Sakata, K. Yokoyama, and R. Noyori, *J. Org. Chem.*, **48**, 932 (1983). b) S. Kobayashi and I. Hachiya, *J. Org. Chem.*, **59**, 3590 (1994). c) A. Yanagisawa, K. Asakawa, and H. Yamamoto, *Chirality*, **12**, 421 (2000).

22 Y.-Z. Huang, C. Chen, and Y. Shen, *J. Chem. Soc. Perkin Trans. I*, **1988**, 2855.

23 S. E. Denmark, R. A. Stavenger, and K.-T. Wong, *Tetrahedron*, **54**, 10389 (1998).

24 a) A. Ando and T. Shioiri, *Tetrahedron*, **45**, 4969 (1989).

b) A. Ando, T. Tatematsu, and T. Shioiri, *Chem. Pharm. Bull.*, **39**, 1967 (1991). c) C. H. Heathcock, C. T. Buse, W. A. Kleschick, M. C. Pirrung, J. E. Sohn, and J. Lampe, *J. Org. Chem.*, **45**, 1066 (1980).

25 a) C. H. Heathcock, M. C. Pirrung, and J. E. Sohn, *J. Org. Chem.*, **44**, 4294 (1979). b) T. Mukaiyama, N. Iwasawa, R. W. Stevens, and T. Haga, *Tetrahedron*, **40**, 1381 (1984).