Article

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Lewis Base-catalyzed Enantioselective Conjugate Reduction of β,β-Disubstituted α,β-Unsaturated Ketones with Trichlorosilane: *E*/*Z* Isomerization, Regioselectivity, and Synthetic Applications

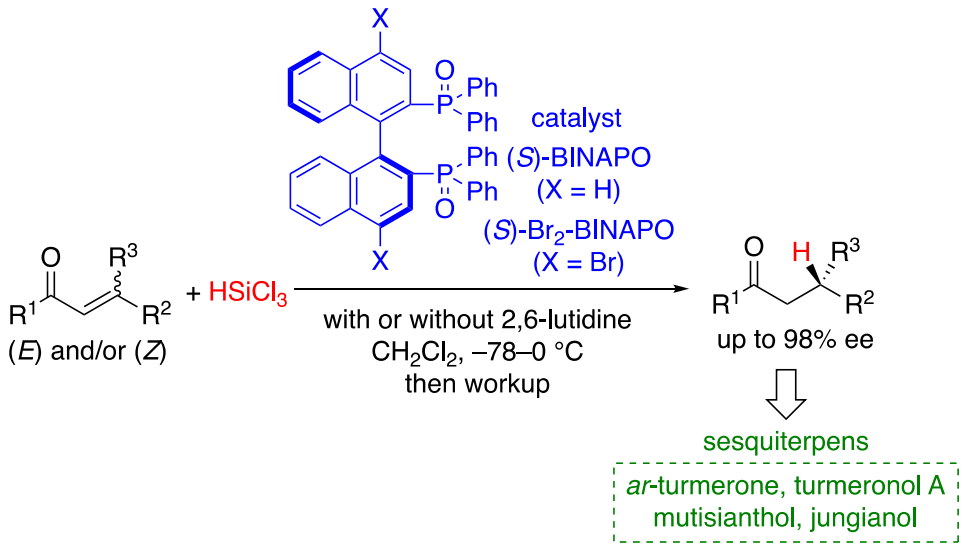
Masaharu Sugiura,,† Yasuhiko Ashikari,‡ Yuka Takahashi,‡ Koki Yamaguchi,† Shunsuke Kotani,‡*

and Makoto Nakajima‡

†Faculty of Pharmaceutical Sciences, Sojo University, 4-22-1 Ikeda, Nishi-ku, Kumamoto 860-0082, Japan

‡Graduate School of Pharmaceutical Sciences, Kumamoto University, 5-1 Oe-honmachi, Chuo-ku, Kumamoto 862-0973, Japan

TOC GRAPHIC



ABSTRACT

The chiral bisphosphine dioxide-catalyzed asymmetric conjugate reduction of acyclic β,β-disubstituted α,β-unsaturated ketones with trichlorosilane affords saturated ketones having a stereogenic carbon center at the carbonyl β-position with high enantioselectivities. Because the *E*/*Z* isomerizations of enone substrates occur concomitantly, reduction products with the same absolute configurations are obtained from either (*E*)- or (*Z*)-

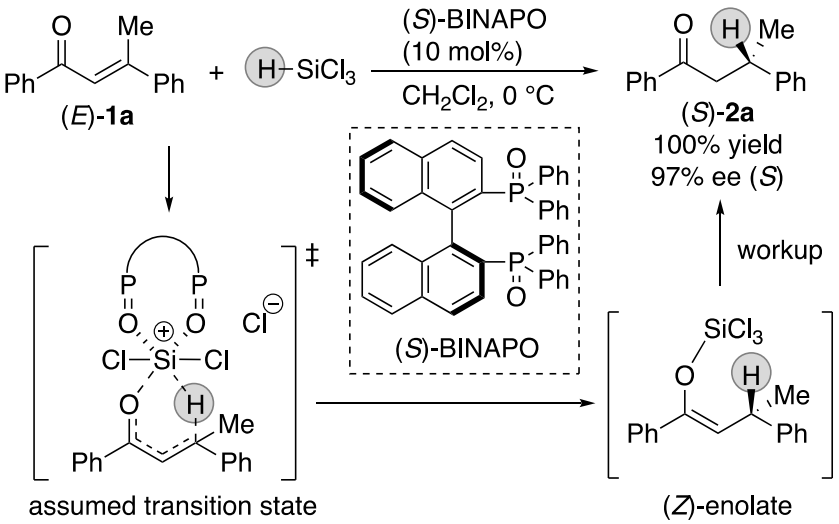
enones. Conjugate reduction is accelerated in the presence of an electron-rich aryl group at the β-position of the enone owing to its carbocation-stabilizing ability. Computational studies were also conducted in order to elucidate the origin of the observed enantioselectivity. The regio- and enantioselective reductions of dienones were realized and applied to the syntheses of *ar*-turmerone, turmeronol A, mutisianthol, and jungianol, which are optically active sesquiterpenes.

Keywords: *asymmetric catalysis, conjugate reduction, optically active sesquiterpene, phosphine oxide, trichlorosilane*

INTRODUCTION

The enantioselective conjugate reductions of β,β-disubstituted α,β-unsaturated ketones (referred to as *enones* in this article) are powerful methods for the construction of stereogenic carbon centers at carbonyl β-positions. A hydride attacks the β-carbon atom of the enone to generate an enolate intermediate, which then forms a saturated ketone with β-stereogenic center upon protonation. Although many transition metal-catalyzed methods have been developed to achieve this outcome,[1,2] organocatalytic methods, which offer several advantages such as low toxicity and high catalyst reusability, have been limited.[3,4] We reported that (*S*)-BINAP dioxide [(BINAPO)], which is a chiral Lewis base, catalyzes the enantioselective conjugate reduction of enone (*E*)-**1a** with trichlorosilane to give enantioenriched ketone **2a** with high enantioselectivity (Scheme 1).[5,6,7] A hypervalent silicon complex[8] generated from the Lewis base catalyst and trichlorosilane[9,10] has been speculated to reduce the enone to give a chiral ketone after workup. The exclusive formation of a (*Z*)-enolate intermediate was confirmed by NMR spectroscopy during the reduction of benzalacetone, suggesting that the reaction proceeds *via* a six-membered cyclic transition state. The resulting enolate intermediates were subsequently applied in enantioselective aldol reactions with aldehydes.[5,6b] Herein, we report further investigations into the conjugate reduction process. The concomitant *E/Z* isomerization of enone substrates, regioselective reduction of dienones, and applications to the syntheses of optically active sesquiterpenes are disclosed.

Scheme 1. Enantioselective Conjugate Reductions of Enones Catalyzed by a Chiral Lewis Base.



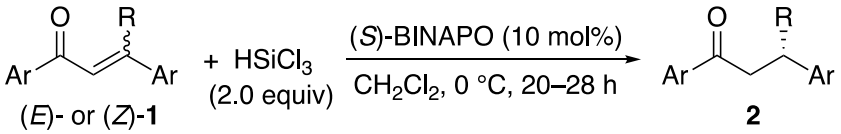
RESULTS & DISCUSSION

Reactions of 3-Alkyl-1,3-diarylprop-2-en-1-ones

To survey the substrate scope, we first investigated the reductions of several 3-alkyl-1,3-diarylprop-2-en-1-ones **1**[11] with (*S*)-BINAPO and trichlorosilane (Table 1). As shown in Scheme 1, the reaction of (*E*)-1,3-diphenylbut-2-en-1-one (**1a**) with trichlorosilane (2 equiv.) in the presence of (S)-BINAPO (10 mol%) at 0 °C for 20 h afforded (*S*)-1,3-diphenylbutan-1-one (**2a**) with high enantioselectivity (entry 1). Both electron-rich and -poor aromatic rings (enones **1b** and **1c**, respectively) were tolerated in this reaction, providing similarly high enantioselectivities as unsubstituted enone **1a** (entries 2 and 3). To compare reactivities, the reactions of **1a**–**c** were terminated after 1 h; as a result, saturated ketones **2a**–**c** were obtained in yields of 71%, 80%, and 16%, respectively. Enones with electron-rich aromatic rings tended to be reduced faster than those with electron-poor aromatic rings. This observation is discussed in more detail below (*vide infra*). Unexpectedly, the reactions of geometrical isomers (*Z*)-**1a**–**c** furnished products **2a**–**c** with the same absolute configurations and enantioselectivities (96–97% ee) as those of their (*E*)-counterparts (entries 4–6).[12,13] Similarly, the reactions of β-ethyl-substituted enones (*E*)- and (*Z*)-**1d** provided the same product, namely (*S*)-**2d**, with a slightly lower but nevertheless high enantioselectivity (93% ee) (entries 7 and 8) compared to **2a**–**c**. These results suggest that geometrical isomerization of the enone occurs concomitantly under the reaction conditions. In fact, TLC analysis of the reaction of (*Z*)-**1d** after 15 min indicated the formation of (*E*)-**1d** as the major component of the remaining enone substrate. In addition, enone **1d** was recovered in 59% yield in a 88:12 *E*/*Z* ratio when the reaction was conducted with 0.5 equivalents of trichlorosilane (entry 9). The same *E*/*Z* ratio was observed even

when the reaction was quenched after 1 h, which indicates that geometrical isomerization proceeds rapidly prior to reduction. The reaction of the β-isopropyl-substituted enone (*E*)-**1e** led to a reversal of the enantiofacial selectivity compared to the β-methyl- or -ethyl-substituted enones **1a**–**d** (entry 10). The reaction of (*Z*)-**1e** afforded a slightly higher enantioselectivity than (*E*)-**1e**, indicating a slower *E*/*Z* isomerization process and a preference for the (*Z*)-geometry during reduction (entry 11).

Table 1. Reductions of 3-Alkyl-1,3-diarylprop-2-en-1-ones.



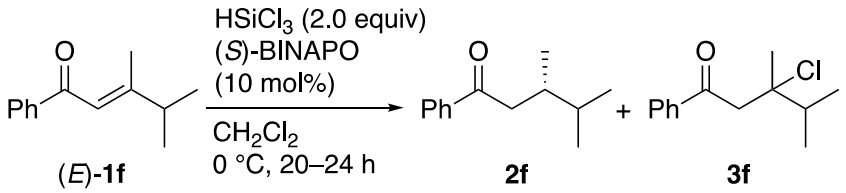
entry	enone	Ar	R	yield (%)	ee (%)
1	(*E*)-**1a**	Ph	Me	97	97 (*S*)
2	(*E*)-**1b**	*p*-$MeOC_6H_4$	Me	84	96
3	(*E*)-**1c**	*p*-ClC_6H_4	Me	87	95
4	(*Z*)-**1a**	Ph	Me	94	97 (*S*)
5	(*Z*)-**1b**	*p*-$MeOC_6H_4$	Me	84	97
6	(*Z*)-**1c**	*p*-ClC_6H_4	Me	71	96
7	(*E*)-**1d**	Ph	Et	95	93 (*S*)
8	(*Z*)-**1d**	Ph	Et	99	93 (*S*)
9[b]	(*Z*)-**1d**	Ph	Et	41	93 (*S*)
10	(*E*)-**1e**	Ph	*i*-Pr	74	47 (*S*)
11	(*Z*)-**1e**	Ph	*i*-Pr	69	60 (*S*)

[a]Unless otherwise noted, the reaction was performed using **1** (0.5 mmol), trichlorosilane (1.0 mmol), and (*S*)-BINAPO (0.05 mmol, 10 mol%) in dichloromethane (2 mL) at 0 °C for 20–28 h. [b]With $HSiCl_3$ (0.5 equiv.); **1b** (*E*/*Z* = 88:12) was recovered in 59% yield.

Reaction of β,β-Dialkyl-substituted Enone 1f

β,β-Dialkyl-substituted enone **1f** gave chlorinated product **3f** along with the desired reduced product **2f** when reacted under the same conditions as those listed in Table 1 (Scheme 2). We hypothesized that hydrogen chloride, generated *in situ* from trichlorosilane and adventitious water contamination, added to the enone.[14] Hence, 2,6-lutidine (1.0 equiv.) was added to the reaction mixture to trap the hydrogen chloride. As a consequence, formation of **3f** was completely suppressed, which led to an improved yield and selectivity for the reduced product **2f**.

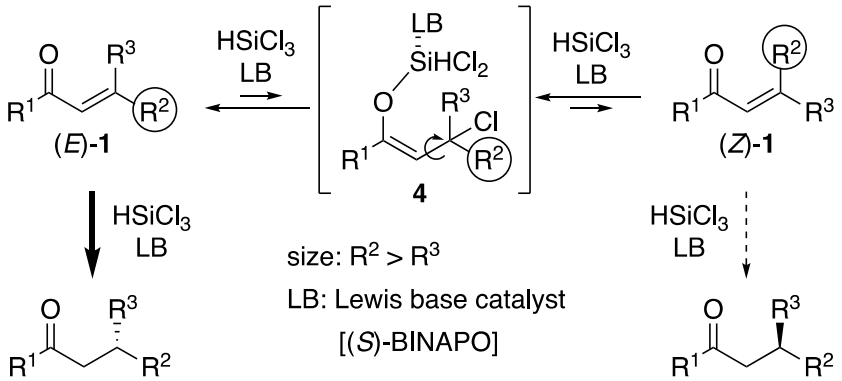
Scheme 2. The Effect of 2,6-Lutidine.



Without 2,6-lutidine	30% (55% ee)	43%
With 2,6-lutidine (1.0 equiv)	89% (68% ee)	0%

Although no chlorinated products were obtained in the reactions of β-alkyl-β-aryl-disubstituted enones **1a**–**e** (see Table 1),[15] transient enone chlorination may be responsible for the observed *E*/*Z* isomerization. Therefore, to confirm whether or not this is the case, (*E*)- and (*Z*)-**1b** were reacted in the presence of 2,6-lutidine (1 equiv.). As a result, slightly lower but nevertheless high enantioselectivities were observed (96% yield and 95% ee from (*E*)-**1b**; 85% yield and 93% ee from (*Z*)-**1b**), which indicates that *E*/*Z* isomerization is rapid at 0 °C even in the presence of 2,6-lutidine. We speculate that trichlorosilane, rather than hydrogen chloride, reversibly adds to enones **1** to form the chlorinated trichlorosilyl enol ethers **4**, which facilitates rapid *E*/*Z* isomerization (Scheme 3). To confirm if the presence of the Lewis base is required for the *E*/*Z*-isomerization, we conducted a control experiment using (*Z*)-**1d**. On treatment of (*Z*)-**1d** with trichlorosilane and 2,6-lutidine (2.0 and 1.0 equivalents, respectively) in dichloromethane at 0 °C, almost no isomerization proceeded.[16] However, on addition of (*S*)-BINAPO (10 mol%) to this mixture, a rapid *E*/*Z*-isomerization and relatively slow reduction were observed. The workup with saturated aqueous $NaHCO_3$ after 20 min at 0 °C afforded a 87:13 mixture of **1d** (*E*/*Z* = 88:12) and **2d**. This control experiment clearly shows that both the *E*/*Z*-isomerization and conjugate reduction are catalyzed by BINAPO and that the *E*/*Z*-isomerization is much faster than the conjugate reduction.

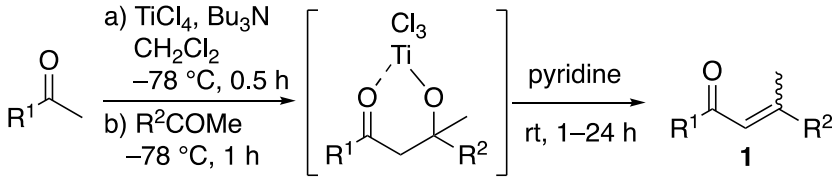
Scheme 3. Possible *E*/*Z*-Isomerization Mechanism and Preference of the (*E*)-isomer in Conjugate Reduction.



Reactions of Other Enones

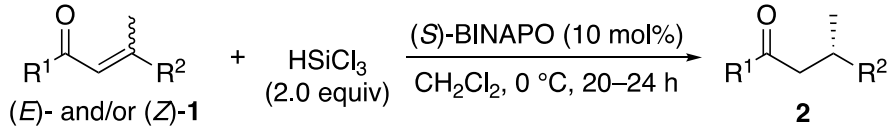
We recently reported a one-pot synthetic method for the preparation of β,β-disubstituted α,β-unsaturated ketones that uses a $TiCl_4/Bu_3N$-promoted aldol reaction between simple ketones followed by base-promoted elimination of the titanoxy group (Scheme 4).[14] Among the bases tested for promoting the elimination step, DMF, TMEDA, and pyridine gave good results. The formation of the enone products and the *E/Z* ratios are under kinetic control in the presence of pyridine (5 equiv.), but under thermodynamic control with DMF (5 equiv.) or TMEDA (1 equiv.); clearly the outcome depends on the basicity of the base and the amount used.

Scheme 4. One-pot Synthesis of Enones.



The (*S*)-BINAPO-catalyzed conjugate reductions of other enones, prepared by the above-mentioned method, were examined (Table 2). Firstly, the effect of the R^2 group was investigated when R^1 = Ph (entries 1–8), and high enantioselectivities were obtained when R^2 was an aryl group, including the 2-thienyl group (entries 1–5). 2,6-Lutidine was added to the reaction mixture to suppress undesired β-chlorination for enones bearing alkyl groups (R^2 = alkyl; see Scheme 2), with higher enantioselectivities observed for systems bearing larger alkyl groups (entries 6–8). The size of the R^2 group appears to be important and must be differentiated from that of the methyl group at the β-position. Secondly, the effect of the R^2 group was investigated when R^1 = *i*-Pr (entries 9–11). Compared to the outcomes observed when R^1 = Ph, lower reactivities and selectivities were observed when R^1 = *i*-Pr, with the R^2 group observed to play a more important role, namely, higher reactivities were observed with more electron-rich aromatic R^2 groups. Thirdly, the effect of the R^1 group was investigated when R^2 = Ph (entries 12–15). In contrast to the effect observed when the R^2 group was varied, an electron-deficient aryl group was more reactive than an electron-rich one (entries 12 and 13). In addition, smaller R^1 alkyl groups were observed to be more reactive than larger ones (entries 14, 15, and 9), while similar enantioselectivities were observed in these cases.

Table 2. Various Enone Reductions.[a]



entry	enone	R^1	R^2	product	yield (%)	ee (%)
1	(*E*)-**1a**	Ph	Ph	**2a**	97	97 (*S*)
2	(*E*)-**1g**	Ph	*p*-$MeOC_6H_4$	**2g**	99	96 (*S*)
3	(*E*)-**1h**	Ph	*p*-ClC_6H_4	**2h**	84	97 (*S*)
4	(*E*)-**1i**	Ph	2-naphthyl	**2i**	97	97 (*S*)
5	(*E*)-**1j**	Ph	2-thienyl	**2j**	80	95
6[b]	(*E*/*Z*)-**1k**[c]	Ph	*c*-Pr	**2k**	96	40
7[b]	(*E*)-**1f**	Ph	*i*-Pr	**2f**	89	68
8[d]	(*E*)-**1l**	Ph	*t*-Bu	**2l**	89	93
9	(*E*)-**1m**	*i*-Pr	Ph	**2m**	83	92 (*S*)
10	(*E*)-**1n**	*i*-Pr	*p*-$MeOC_6H_4$	**2n**	99	93 (*S*)
11	(*E*)-**1o**	*i*-Pr	*p*-ClC_6H_4	**2o**	58	90 (*S*)
12	(*E*)-**1p**	*p*-$MeOC_6H_4$	Ph	**2p**	70	97 (*S*)
13	(*E*)-**1q**	*p*-ClC_6H_4	Ph	**2q**	87	98 (*S*)
14	(*E*)-**1r**	*c*-Hex	Ph	**2r**	76	89
15	(*E*)-**1s**	*c*-Pr	Ph	**1s**	90	89

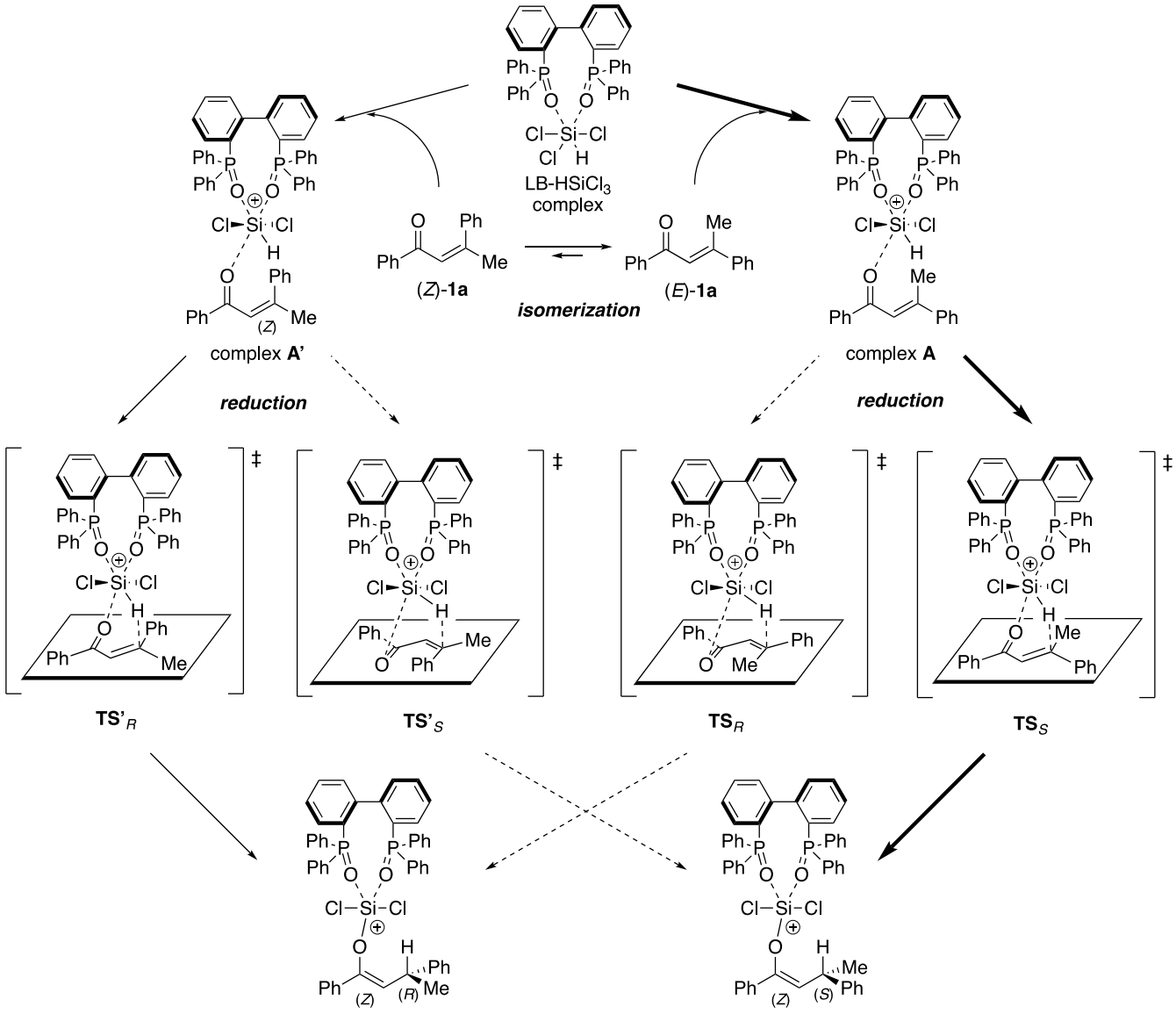
[a]Unless otherwise noted, the reaction was performed using **1** (0.5 mmol), trichlorosilane (1.0 mmol), and (*S*)-BINAPO (0.05 mmol, 10 mol %) in dichloromethane (2 mL) at 0 °C for 20–24 h. [b]With 2,6-lutidine (2.0 equiv.). [c]*E*/*Z* = 58:42. [d]At rt for 48 h.

Computational Study

We used computational methods to elucidate the origins of the observed enantioselectivities.[17] As depicted in Scheme 5, we speculate that a hexavalent silicon species (LB-$HSiCl_3$ complex), generated by bidentate coordination of the chiral bisphosphine dioxide (LB) to trichlorosilane, forms cationic complex **A** by accepting (*E*)-enone **1a** after dissociation of a chloride anion. Hydride transfer from the silicon atom to the enone β-carbon then occurs through either $\mathbf{TS}_S$ or $\mathbf{TS}_R$, which are six-membered cyclic transition states, to give the (*S*,*Z*)- or (*R*,*Z*)-silyl enol ether **B**, respectively (Scheme 5, right half). Similarly, (*Z*)-enone **1a** produces (*S*,*Z*)- or (*R*,*Z*)-silyl enol ether **B** *via* complex **A'** and cyclic transition states $\mathbf{TS'}_S$ or $\mathbf{TS'}_R$, respectively (Scheme 5, left half). These structures were first optimized, vibrational frequencies calculated, and intrinsic reaction coordinate (IRC) pathways calculated at the HF/6-31G(d) level of theory. Thermochemical properties were then calculated at the ONIOM(M06-2X/6-311++G(3df,3pd):HF/6-31G(d)) level with the ONIOM-polarizable continuum model (PCM)/X for dichloromethane applied.[18] The binaphthyl backbone of (*S*)-BINAPO was simplified to an (*S*)-configured axially chiral biphenyl unit in these calculations. The two electronegative chlorine atoms were located at the *trans* apical positions to stabilize the hypervalent three-center four-electron bonding.[8d] Figure 1 summarizes the energy profile for the overall process, as well as the optimized structures of complex **A**, $\mathbf{TS}_S$, $\mathbf{TS}_R$, complex **A'**, $\mathbf{TS'}_S$, $\mathbf{TS'}_R$, (*S*,*Z*)-**B**, and (*R*,*Z*)-**B**. The atoms treated with a high level of theory are represented as ball

and stick models, while remaining atoms are shown as a tube model. **TS**$_S$ was calculated to be the most stable among the transition states, which provides an enantioselectivity of 96.7% ee (*S*) at 0 °C assuming a Boltzmann distribution, which is in good agreement with the experimental result [97% ee (*S*) using (*S*)-BINAPO]. The side views of **TS**$_S$ and **TS**$_R$ (Figure 2) reveal steric repulsion between a phenyl group of the bisphosphine dioxide and the phenyl ketone moiety of the enone in **TS**$_R$, which is likely to be the origin of the observed enantioselectivity. In addition, there is a weak edge-to-face π-interaction[19] between the β-phenyl of the enone (ring A) and a P-phenyl of the catalyst (ring B) in **TS**$_s$ (Figure 3). The distance between the centroids of ring A and ring B is 5.35 Å. This interaction would favor the reduction of the enone having an aryl group at the β-position to give high selectivity.

Scheme 5. Assumed Mechanism.


LB-HSiCl3 complex
(Z)-1a
(E)-1a
isomerization
complex A'
complex A
reduction
reduction
TS'R
TS'S
TSR
TSS

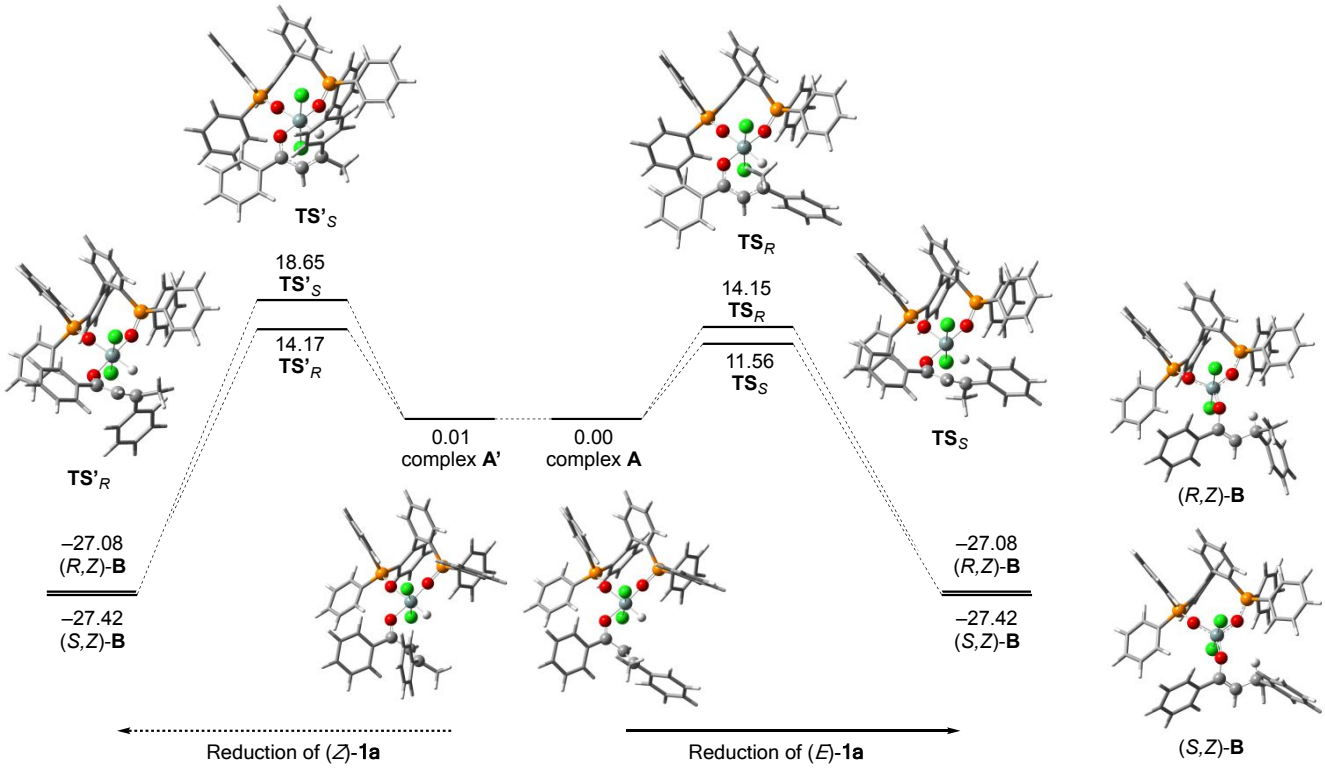


Figure 1. ONIOM(M06-2X/6-311++G(3df,3pd):HF/6-31G(d))+ONIOM-PCM/X-calculated Energy Profile in kcal/mol.

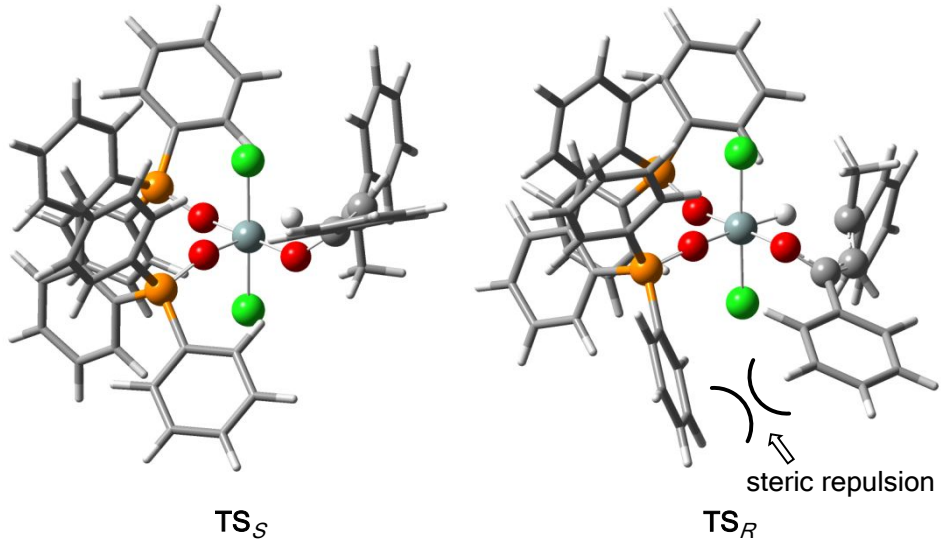


Figure 2. Side Views of $\mathbf{TS}_S$ and $\mathbf{TS}_R$.

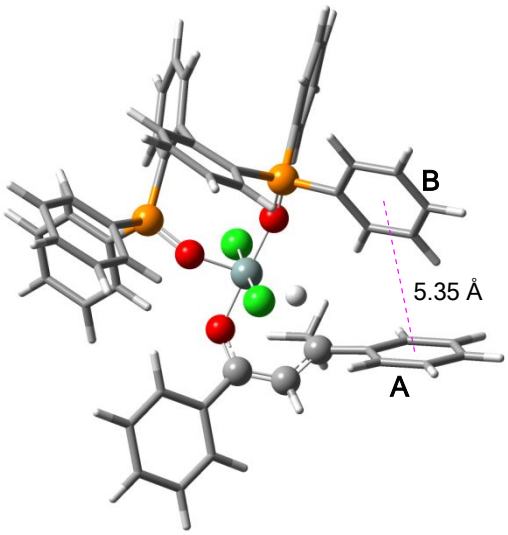
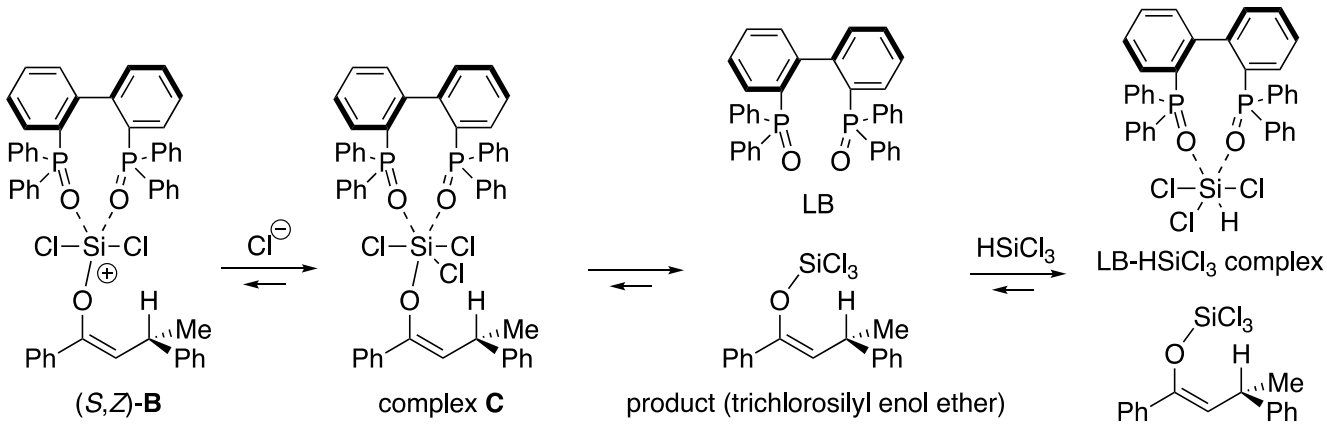


Figure 3. Edge-to-face π-Interaction in **TS**$_S$.

The Lewis base catalyst (LB, bisphosphine dioxide) would be released from product (*S,Z*)-**B** *via* formation of complex **C** by coordination of the chloride anion (Scheme 6). The released LB coordinates to $HSiCl_3$ to form the LB-$HSiCl_3$ complex, which goes on to the next catalytic cycle. The catalyst resting state would be the LB-$HSiCl_3$ complex, which was calculated to be more stable than complex **C** (see Supporting Information), presumably because $HSiCl_3$ has higher Lewis acidity than the trichlorosilyl enol ether product.

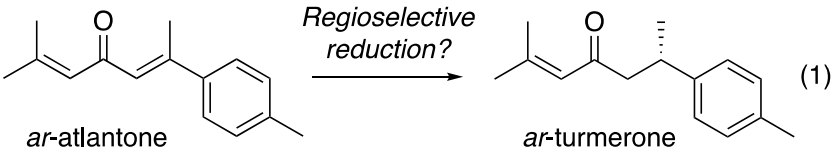


Scheme 6. Regeneration of the Lewis Base Catalyst (LB) and Formation of LB-$HSiCl_3$.

Synthesis of *ar*-Turmerone

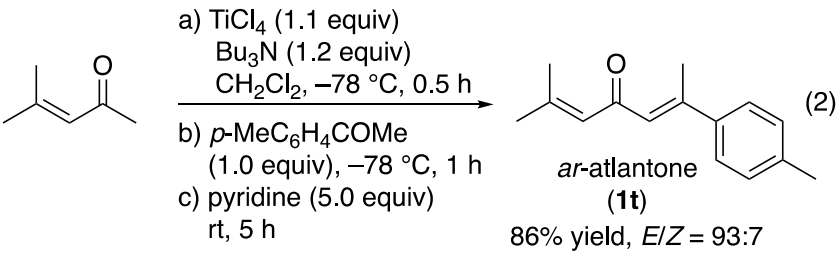
ar-Turmerone (Eq. 1) is an optically active sesquiterpene isolated from *Curcuma longa* (turmeric), with several biological properties, such as antioxidant and antitumor activities, being reported.[20] Recently, *ar*-turmerone was reported to induce neural stem cell proliferation *in vitro* and *in vivo*.[21] Due to its simple structure, many synthetic studies have been reported; in most cases these studies aimed to test new asymmetric

synthetic methods.[22] We also planned to synthesize *ar*-turmerone through the conjugate reduction of *ar*-atlantone (Eq. 1). Herewith, regioselectivity during reduction of the dienone presents an unavoidable issue. Considering the stabilizing extended conjugation of the right-hand (as drawn) β-aryl-substituted enone moiety, the left-hand β,β-dimethyl enone moiety is likely to be more reactive. However, the substituent effect noted in Table 2 suggests selectivity for the reduction of the right-hand moiety.



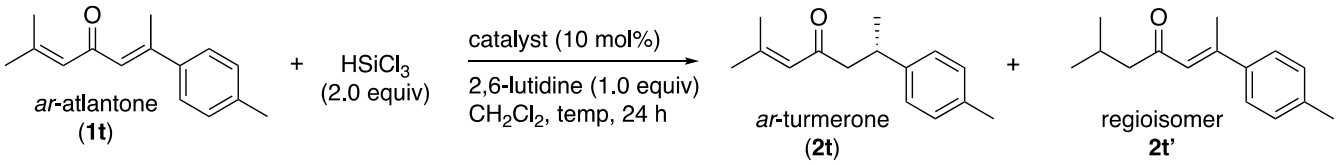
(1)

The starting material, *ar*-atlantone (**1t**) was synthesized from mesityl oxide and *p*-methylacetophenone by the one-pot enone synthetic method in 86% yield and with 93% *E*-geometry (Eq. 2),[14,23] and subjected to conjugate reduction (Table 3), with 2,6-lutidine used to prevent chlorination of the left-hand moiety. To our delight, the desired regioselectivity was observed, with *ar*-turmerone (**2t**) obtained in high yield with good enantioselectivity (entry 1). Decreasing the temperature to −40 °C improved the enantioselectivity (entry 2). We then screened a variety of chiral Lewis bases at −40 °C (entries 3–6 and Figure 4). Compared to a bulkier catalyst (xylyl-BINAPO)[24] or more Lewis basic catalysts (SEGPHOSO and *p*-tol-DIOPO[25]) (entries 3–5), 4,4'-dibromo-BINAPO (Br_2-BINAPO)[26] provided higher regio- and enantioselectivities (entry 6). Both selectivities were improved (to 99:1 regioselectivity and 92% ee) when the reaction temperature was further lowered to −78 °C using Br_2-BINAPO (entry 7). In addition, the catalyst loading could be reduced to 3 mol% without loss of reactivity or selectivity (entry 8). After the product was obtained by column chromatography on silica gel (hexane/CH_2Cl_2), the catalyst (Br_2-BINAPO) was recovered by eluting with CH_2Cl_2/MeOH and reused after recrystallization. A large-scale synthesis of *ar*-turmerone was also possible without decreasing the regio- and enantioselectivities (entry 9).



(2)

Table 3. The Synthesis of *ar*-Turmerone.[a]



entry	catalyst	temp (°C)	yield (%)	ee (%)	**2t/2t'**
1	(*S*)-BINAPO	0	93	67	94:6
2	(*S*)-BINAPO	−40	84	81	95:5
3	(*S*)-xylyl-BINAPO	−40	80	63	82:18
4	(*S*)-SEGPHOSO	−40	94	75	95:5
5	(*R,R*)-*p*-tol-DIOPO	−40	78	−55	87:13
6	(*S*)-Br_2-BINAPO	−40	94	85	97:3
7	(*S*)-Br_2-BINAPO	−78	93	92	99:1
8	(*S*)-Br_2-BINAPO[b]	−78	91	92	99:1
9[c]	(*R*)-Br_2-BINAPO	−78	85	92	99:1

[a]Unless otherwise noted, the reaction was performed using **1t** (0.1 mmol), trichlorosilane (0.2 mmol), 2,6-lutidine (0.1 mmol), and a catalyst (0.01 mmol, 10 mol%) in dichloromethane (0.4 mL) for 24 h. [b]With 3 mol% catalyst. [c]A large scale synthesis of (*R*)-*ar*-turmerone using **1t** (5.0 mmol, 1.072 g) and (*R*)-Br_2-BINAPO (3 mol%).

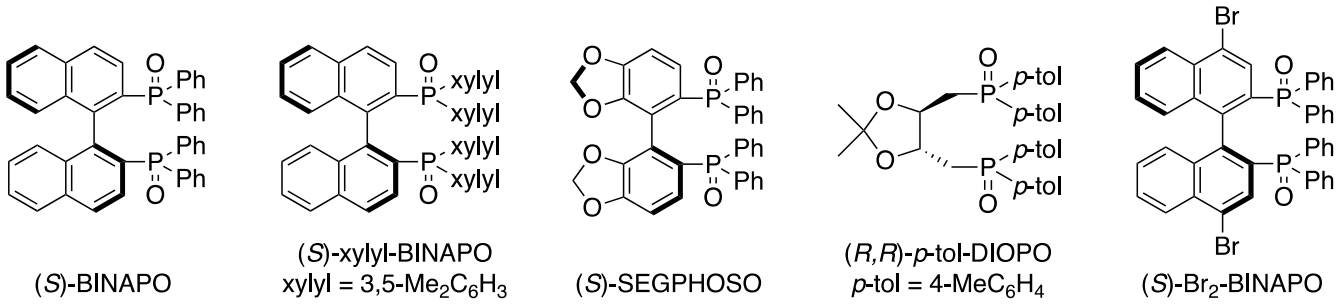


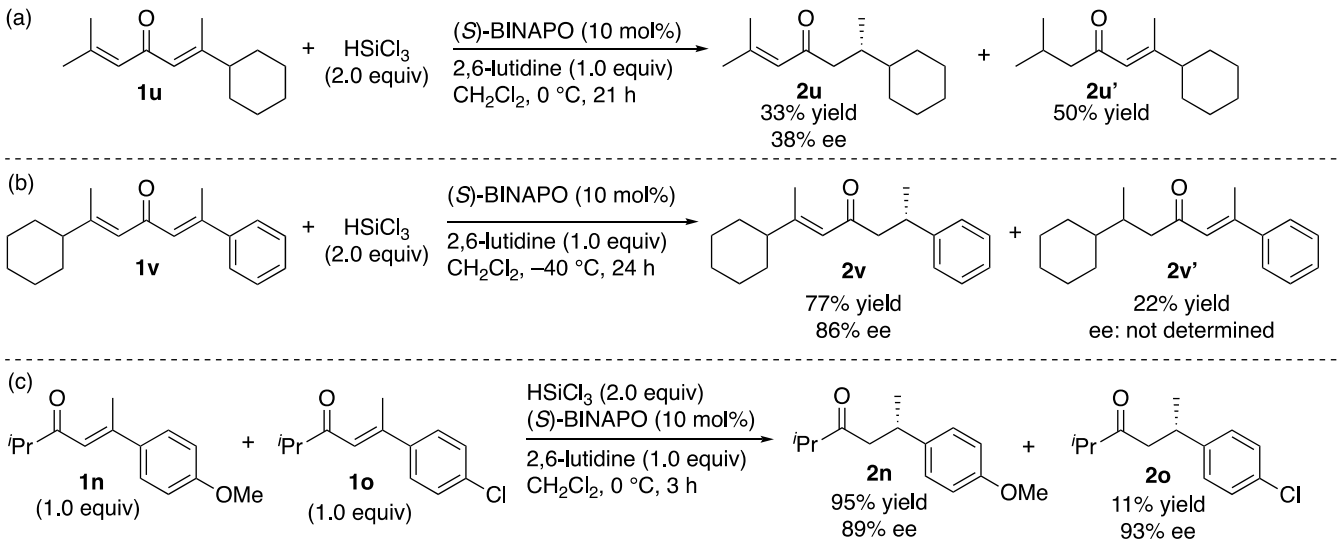
Figure 4. Chiral Lewis Bases Tested.

Origin of the Observed Regioselectivity

Several control experiments were performed in order to clarify the origin of the high regioselectivity observed in this study. Firstly, the cyclohexyl-bearing dienone **1u** was reacted instead of the *p*-tolyl-bearing **1t** in order to evaluate the steric effect of the aryl group in *ar*-atlantone (**1t**) (Scheme 7a); this reaction was conducted at 0 °C because of the low conversion observed at −40 °C. Interestingly, **1u** exhibited the reverse regioselectivity to **1t**; the sterically less-hindered side was preferentially reduced to give **2u'** as the major product. Secondly, the β-cyclohexyl-β'-phenyl-substituted enone **1v** was reduced in order to clarify the electronic role played by the aryl group (Scheme 7b); this reaction proceeded regioselectively at the phenyl-substituted terminus to give **2v** as the major product, suggesting that the electronic properties of the aryl group

controls the regioselectivity, rather than steric factors. Compared to the reduction of **1t** (Table 3, entry 2), **1v** was reduced with significantly lower regioselectivity, indicating that the steric nature of the cyclohexyl group is also influential. Finally, enones **1n** and **1o** were competitively reduced in order to evaluate the roles of electronic factors, with the methoxy-bearing ketone **2n** obtained with high chemoselectivity (Scheme 7c).

Scheme 7. Control Experiments.



These results reveal that trichlorosilane selectively attacks β-carbon atoms that are attached to carbocation-stabilizing group(s). The development of positive charge at the β-position to the carbonyl in the transition state is stabilized by an electron-rich aromatic ring, such as *p*-tolyl and *p*-anisyl, which facilitates the high regioselectivity observed during the reduction of *ar*-atlantone (Figure 5).[27] Figure 6 reveals that the ONIOM(M06-2X/6-311++G(3df,3pd):HF/6-31G(d))-calculated natural charges of selected atoms in transition state $\mathbf{TS}_S$ also support this hypothesis; positive charge is developed on carbon C3, with hydrogen H2 acting as the hydride.

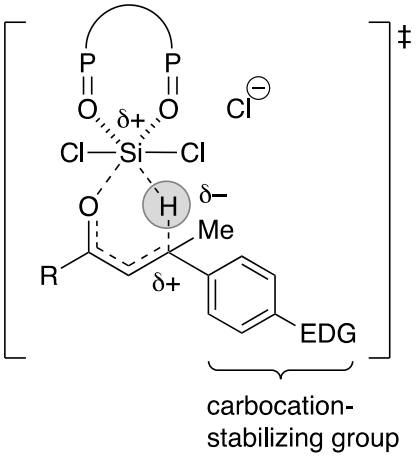
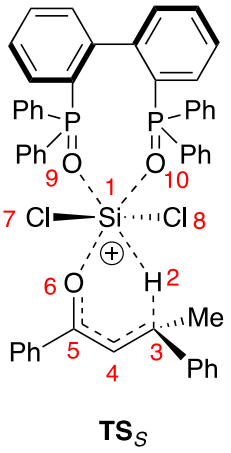


Figure 5. Stabilizing the Transition State with an Electron-rich Aromatic Ring.



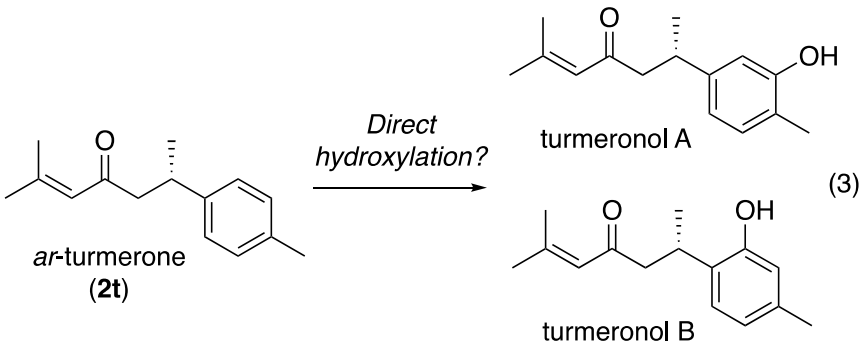
TS$_S$

atom	natural charge
Si1	+2.057
H2	–0.298
C3	+0.281
C4	–0.477
C5	+0.630
O6	–0.920
Cl7	–0.589
Cl8	–0.564
O9	–1.258
O10	–1.258

Figure 6. ONIOM(M06-2X/6-311++G(3df,3pd):HF/6-31G(d))+ONIOM-PCM/X-calculated Natural Charges of Selected Atoms in **TS**$_S$.

Syntheses of Turmeronol A, Mutisianthol, and Jungianol

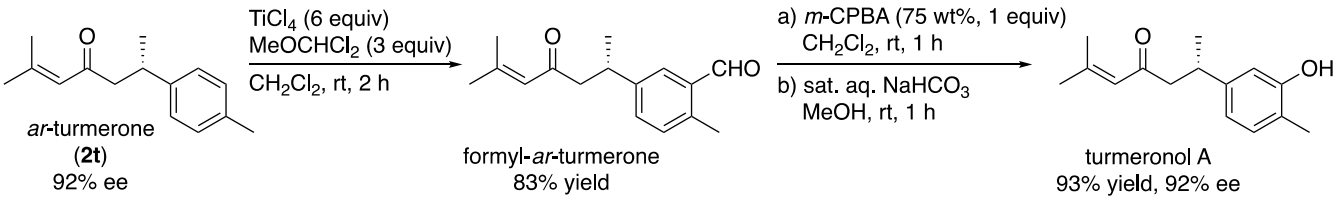
To extend the synthetic utility of the conjugate-reduction chemistry developed in this study, *ar*-turmerone was further transformed into turmeronols A and B (Eq. 3). Turmeronol A and B are also isolated from turmeric along with *ar*-turmerone, and are known to have antioxidant activities and soybean lipoxygenase inhibitory activities.[28] Despite their simple structures, only a limited number of asymmetric syntheses have been reported.[29] We planned to synthesize turmeronols A and B by the direct hydroxylation of the aromatic ring of *ar*-turmerone.



We first explored the use of Siegel's aromatic hydroxylation protocol.[30] Accordingly, *ar*-turmerone was treated with phthaloyl peroxide (2 equiv.) in hexafluoroisopropanol (HFIP) at 50 °C for 48 h. After basic hydrolysis to remove the phthaloyl group, turmeronols A and B were obtained in yields of 15% and 7%, respectively, with most of the starting material recovered. Slight modifications (changing the amount of phthaloyl peroxide (1.3-2.0), solvent (2,2,2-trifluoroethanol), temperature (40–50 °C), and time (24–72 h) were unable to improve these yields. *p*-Cymene, a simplified model compound, was quantitatively oxidized under the same conditions to give carvacrol and thymol in a 68:32 ratio (99% yield). However, the yield was reduced to 65% or 66% in the presence of mesityl oxide or acetone, respectively. These control experiments suggest that the ketone moiety may inhibit the hydroxylation reaction; this effect is larger when the ketone moiety is present in the same molecule.

We next examined a formylation/Dakin oxidation sequence (Scheme 8). Treatment of *ar*-turmerone with $TiCl_4$/$MeOCHCl_2$[31] gave 4-formyl-*ar*-turmerone as the sole regioisomer. The use of excess amounts of reagent was needed to obtain a good yield. Subsequent Dakin oxidation with *m*-CPBA[32] followed by basic hydrolysis furnished turmeronol A without loss of enantiomeric purity.

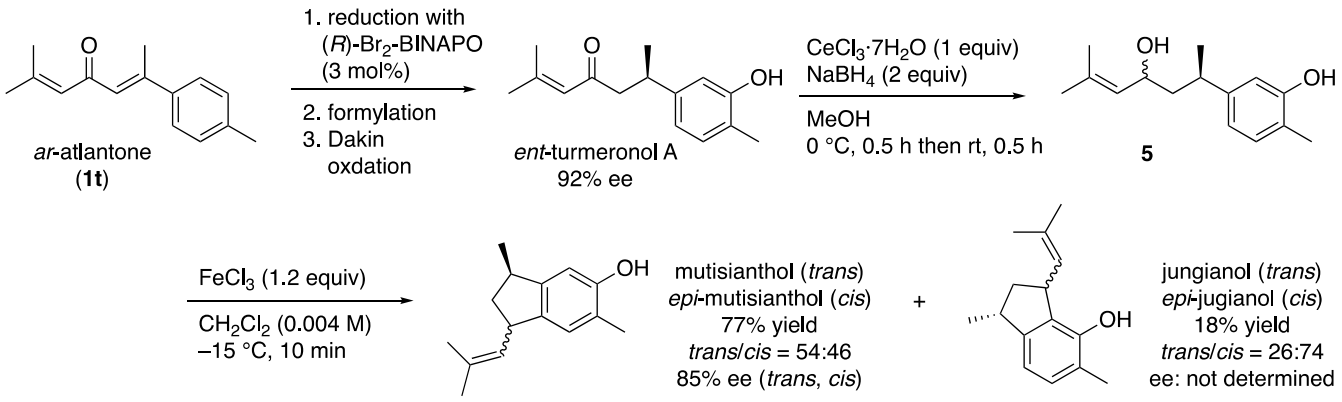
Scheme 8. Synthesis of Turmeronol A.



Mutisianthol and jungianol are phenolic sesquiterpenes isolated from *Mutisia homoeantha* and *Juniga malvaefolia*, respectively. The former is known to exhibit antitumor activity;[33] however, asymmetric syntheses

have been limited.[34] We planned to synthesize these two sesquiterpenes through sequences involving intramolecular Friedel–Crafts alkylations of the allylic alcohol derived from *ent*-turmeronol A (Scheme 9). The conjugate reduction of *ar*-atlantone with trichlorosilane and (*R*)-Br_2-BINAPO gave *ent*-*ar*-turmerone. Subsequent formylation and Dakin oxidation, as shown in Scheme 8, afforded *ent*-turmeronol A with 92% ee. Luche reduction[35] of *ent*-turmeronol A gave allylic alcohol **5** with a dr of 6:4. Treatment of the diastereomeric mixture of **5** with a low concentration of anhydrous $FeCl_3$ in dichloromethane[36] afforded mutisianthol and junginal as mixtures of epimers with a slight loss of optical purity. Although the regio- and stereoselectivities of the Friedel–Crafts cyclization reactions require improvement, a short-step synthesis of these sesquiterpenes was achieved.

Scheme 9. Synthesis of Mutisianthol and Jungianol.



CONCLUSIONS

Herein, we disclosed significant aspects of the enantioselective conjugate reductions of β,β-disubstituted α,β-unsaturated ketones with trichlorosilane catalyzed by chiral bisphosphine dioxides. These reactions were accompanied by the *E/Z* isomerization of enone substrates; consequently, reduction products of the same absolute configurations were obtained from either (*E*)- or (*Z*)-enones. This conjugate reduction is accelerated by the incorporation of an electron-rich aryl group at the β-position of the enone owing to its ability to stabilize the developing carbocation. The origin of the observed enantioselectivity is discussed on the basis of calculated transition structures. The regioselective reductions of dienones were realized and applied to the synthesis of *ar*-turmerone and other optically active sesquiterpenes.

EXPERIMENTAL SECTION

General Methods. Melting points (mp) were uncorrected. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were measured in $CDCl_3$ with 400, 500, or 600 MHz spectrometer. Tetramethylsilane (TMS) (δ = 0 ppm) and $CDCl_3$ (δ = 77.0 ppm) served as internal standards for ^{1}H and $^{13}C\{^{1}H\}$ NMR, respectively. Infrared spectra were recorded on an FT-IR spectrometer. High-resolution mass spectra were recorded on an ESI-TOFMS spectrometer or a double-focusing magnetic-sector mass analyzer operating in a FAB or EI mode. Thin-layer chromatography (TLC) was visualized with UV light, phosphomolybdic acid and/or anisaldehyde. Column chromatography was performed using silica gel (spherical, neutral, 63–210 nm). The reactions under anhydrous conditions were carried out using oven, and heating gun-dried glassware with a rubber septum and a magnetic stirring bar under argon atmosphere.

Dichloromethane was dried over 4Å MS. Titanium(IV) chloride was distilled under reduced pressure and used as a dichloromethane solution (ca. 3 M). Pyridine was distilled from CaH_2 and stored over 4Å MS. Trichlorosilane (>98%) was purchased from Tokyo Kasei Kogyo (TCI) and used as a dichloromethane solution (ca. 3 M) prepared in a screw-top test tube with PTFE-lined screw cap. (*S*)-BINAPO, (*S*)-xylyl-BINAPO, and (*S*)-SEGPHOSO were prepared by oxidation of the corresponding diphosphine with hydrogen peroxide in acetone.[37] (*R*,*R*)-*p*-tolyl-DIOPO[25] and (*S*)-Br_2-BINAPO[26] were prepared according to the literatures. Enones **1a**–**1c**,[11] **1d**–**1e**,[2g] **1f**,[14] **1l**–**1s**,[14] and *ar*-atlantone (**1t**)[14] were prepared according to the literatures. All other solvents and chemicals were purified based on standard procedures.

General Procedure A: One-pot Synthesis of β,β-Disubstituted Enone.[14] To a stirred solution of a ketone (aldol donor, 1.0 mmol) in CH_2Cl_2 (2.0 mL) cooled at –78 °C in a dry ice bath are successively added $TiCl_4$ (ca. 3 M in CH_2Cl_2, 1.1 mmol) and Bu_3N (0.29 mL, 1.2 mmol). After 30 min, another ketone (aldol acceptor, 1.0 mmol) is added to the mixture at –78 °C. After 1 h, formation of the aldol product is detected by TLC analysis. Then pyridine (0.40 mL, 5.0 mmol) is added at –78 °C and the dry ice bath is removed. After being stirred at rt for the indicated time, the reaction mixture is diluted with Et_2O (5 mL) and hexane (5 mL). The mixture was filtered through a Celite pad with Et_2O and the filtrate was concentrated. The residue is purified by column chromatography on silica gel (hexane/AcOEt) to give enone **1**. In most cases, the geometrical isomers are separable.

3-(4-Methoxyphenyl)-1-phenylbut-2-en-1-one (1g).[38] According to General Procedure A, the reaction of acetophenone (120.2 mg) and *p*-methoxyacetophenone (150.1 mg) at rt for 2 h gave enone **1g** as yellow oil (134.5 mg, 53%, *E*/*Z* = 90:10). (*E*)-isomer: TLC R_f 0.44 (hexane/AcOEt = 7:1, stained red-orange with anisaldehyde). ^{1}H NMR (400 MHz) δ 2.60 (s, 3H), 3.86 (s, 3H), 6.94 (d, *J* = 8.4 Hz, 2H), 7.16 (s, 1H), 7.47 (apparent t, *J* = 7.3 Hz, 2H), 7.52-7.58 (m, 3H), 7.99 (apparent d, *J* = 7.6 Hz, 2H). (*Z*)-isomer: TLC R_f 0.36 (hexane/AcOEt = 7:1, stained red-orange with anisaldehyde). ^{1}H NMR (400 MHz) representative signals: δ 2.29 (d, *J* =1.4 Hz, 3H), 3.75 (s, 3H), 6.62 (q, *J* = 1.4 Hz, 1H).

3-(4-Chlorophenyl)-1-phenylbut-2-en-1-one (1h).[38,39] According to General Procedure A, the reaction of acetophenone (120.2 mg) and *p*-chloroacetophenone (154.6 mg) at rt for 2 h gave **1h** as yellow oil (218.2 mg, 85%, *E*/*Z* = 82:18). (*E*)-isomer: TLC R_f 0.61 (hexane/AcOEt = 7:1, stained yellow-green with anisaldehyde). ^{1}H NMR (400 MHz) δ 2.57 (d, *J* = 1.4 Hz, 3H), 7.14 (q, *J* = 1.4 Hz, 1H), 7.39 (apparent d, *J* = 8.2 Hz, 2H), 7.46-7.53 (m, 4H), 7.57 (apparent t, *J* = 7.3 Hz, 1H), 7.98 (apparent d, *J* = 6.8 Hz, 2H). (*Z*)-isomer: TLC R_f 0.50 (hexane/AcOEt = 7:1, stained yellow-green with anisaldehyde). ^{1}H NMR (400 MHz) representative signals: δ 2.29 (d, *J* =1.4 Hz, 3H), 6.74 (q, *J* = 1.4 Hz, 1H).

3-(Naphthalen-2-yl)-1-phenylbut-2-en-1-one (1i).[39] According to general procedure A, the reaction of acetophenone (120.2 mg) and 2'-acetonaphthone (170.2 mg) at rt for 2 h gave **1i** as yellow oil (178.2 mg, 65%, *E*/*Z* = 79:21). (*E*)-isomer: TLC R_f 0.56 (hexane/AcOEt = 10:1, stained red-purple with anisaldehyde). ^{1}H NMR (400 MHz) δ 2.71 (d, *J* = 1.4 Hz, 3H), 7.32 (q, *J* = 1.4 Hz, 1H), 7.44-7.60 (m, 5H), 7.71 (dd, *J* = 8.7, 1.4 Hz, 1H), 7.84-7.93 (m, 3H), 8.00-8.06 (m, 3H). (*Z*)-isomer: TLC R_f 0.44 (hexane/AcOEt = 10:1, stained dark green with anisaldehyde). ^{1}H NMR (400 MHz) representative signals: δ 2.40 (d, *J* =1.4 Hz, 3H), 6.80 (q, *J* = 1.4 Hz, 1H).

1-Phenyl 3-(thiophen-2-yl)but-2-en-1-one (1j).[38] According to General Procedure A, the reaction of acetophenone (134.1 mg) and 2-acetylthiophene (129.8 mg) at rt for 2 h gave **1j** as yellow oil (147.8 mg, 51%, *E*/*Z* = 94:6). (*E*)-isomer: TLC R_f 0.44 (hexane/AcOEt = 10:1, stained dark green with anisaldehyde). ^{1}H NMR (500 MHz) δ 2.66 (d, *J* = 1.4 Hz, 3H), 7.10 (t, *J* = 4.3 Hz, 1H), 7.33 (q, *J* = 1.4 Hz, 1H), 7.38 (d, *J* = 5.2 Hz, 1H), 7.43 (d, *J* = 3.6 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.56 (t, *J* = 6.9 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 2H). (*Z*)-isomer: TLC R_f 0.39

(hexane/AcOEt = 10:1, stained dark green with anisaldehyde). ^{1}H NMR (500 MHz) representative signals: δ 2.41 (d, *J* = 1.4 Hz, 3H), 6.57 (q, *J* = 1.4 Hz, 1H).

3-Cyclopropyl-1-phenylbut-2-en-1-one (1k).[40] According to General Procedure A, the reaction of acetophenone (237.6 mg) and cyclopropyl methyl ketone (176.0 mg) at rt for 1 h gave enone **1k** as yellow oil (348.7 mg, 94%, *E*/*Z* = 58:42). *E*/*Z* mixture: TLC R_f 0.58 (hexane/AcOEt = 7:1, stained purple with anisaldehyde). ^{1}H NMR (400 MHz) δ 0.76-0.94 (m, 4H), 1.66 (d, *J* = 1.4 Hz, 1.26H (*Z*)), 1.67 (tt, *J* = 8.2, 5.0Hz, 0.58H (*E*)), 2.02 (d, *J* = 1.4 Hz, 1.74H (*E*)), 3.26 (tt, *J* = 8.2, 5.0 Hz, 0.42H (*Z*)), 6.79 (brs, 0.42H (*Z*)), 6.82 (brs, 0.58H (*E*)), 7.42−7.54 (m, 3H), 7.91-7.96 (m, 2H).

2-Cyclohexyl-6-methylhepta-2,5-dien-4-one (1u). According to General Procedure A, the reaction of mesityl oxide (94.1 mg) and cyclohexyl methyl ketone (126.2 mg) at rt for 1 h gave dienone **1u** as yellow oil (159.6 mg, 81%, *E*/*Z* = 88:12). (*E*)-isomer: TLC: R_f 0.49 (hexane/AcOEt = 10:1, stained purple with anisaldehyde). IR (ATR) 2925, 1672, 1621, 1604, 1446, 1380, 1215, 1108, 871 cm^{-1}. ^{1}H NMR (400 MHz) δ 1.10-1.36 (m, 5H), 1.65-1.85 (m, 5H), 1.88 (d, *J* = 1.4 Hz, 3H), 1.95 (tt, *J* = 7.4, 3.2 Hz, 1H), 2.14 (d, *J* = 1.4 Hz, 3H), 2.16 (d, *J* = 1.4 Hz, 3H), 6.02 (brs, 3H), 6.08 (brs, 3H). ^{13}C{^{1}H} NMR (100 MHz) δ 17.7, 20.5, 26.1, 26.4, 27.7, 31.4, 49.0, 123.8, 126.5, 153.9, 162.8, 192.3. (*Z*)-isomer: TLC R_f 0.51 (hexane/AcOEt = 10:1, stained dark green with anisaldehyde). ^{1}H NMR (400 MHz) δ 1.08-1.47 (m, 7H), 1.56-1.65 (m, 2H), 1.65-1.78 (m, 3H), 1.80 (s, 3H), 1.88 (s, 3H), 2.17 (s, 3H), 3.56-3.66 (m, 1H) 5.94 (s, 1H), 6.05 (s, 1H). ^{13}C{^{1}H} NMR (100 MHz) δ 20.5, 21.0, 26.2, 27.8, 29.7, 30.9, 40.1, 125.9, 126.4, 154.0, 162.9, 191.3. HRMS (EI+) Calcd for $C_{14}H_{22}O$ (M^+) 206.1671, found 206.1671.

2-Cyclohexyl-6-phenylhepta-2,5-dien-4-one (1v). According to General Procedure A, the reaction of (*E*)-4-phenylpent-3-en-2-one (80.1 mg)[41] and cyclohexyl methyl ketone (63.1 mg) at rt for 1 h gave dienone **1v** as yellow oil (112.2 mg, 84%, *E*/*Z* = 87:13). (*E*,*E*)-isomer: TLC: R_f 0.67 (hexane/AcOEt = 7:1, stained purple with anisaldehyde). IR (ATR) 2924, 2851, 1663, 1606, 1445, 1104, 879, 759, 695. ^{1}H NMR (400 MHz) δ 1.10-1.36 (m, 5H), 1.64-1.88 (m, 5H), 1.95-2.03 (m, 1H), 2.19 (d, *J* = 1.4 Hz, 3H), 2.56 (d, *J* = 1.4 Hz 3H), 6.17 (brs, 1H), 6.51 (brs, 1H), 7.32-7.40 (m, 3H), 7.46-7.52 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz) δ 17.9, 18.1, 26.1, 26.4, 31.4, 49.0, 124.2, 126.4, 127.2, 128.4, 128.7, 142.9, 152.8, 163.6, 192.3. HRMS (EI+) Calcd for $C_{19}H_{24}O$ (M^+) 268.1827, found 268.1815.

General Procedure B: Asymmetric Conjugate Reduction of Enone. Trichlorosilane (ca. 3.00 M CH_2Cl_2; 1 mmol) is added to a stirred solution of (*S*)-BINAPO (32.7 mg, 10 mol %), enone **1** (0.5 mmol), and 2,6-lutidine (0.5 mmol, in the cases of β,β-dialkyl-α,β-unsaturated ketones) in CH_2Cl_2 (2 mL) at 0 °C or rt. The mixture is stirred at that temperature for the indicated time. The reaction is quenched with saturated $NaHCO_3$ (5 mL). The mixture was stirred for 1 h at rt, filtered through a Celite pad, and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and evaporated. The residue was purified by silica gel column chromatography (hexane/CH_2Cl_2 or hexane/AcOEt) to give saturated ketone **2**. For the reduction of β,β-dialkyl enones, 2,6-lutidine (0.5 mmol) is added to prevent unwanted chloride addition.

(*S*)-1,3-Diphenylbutan-1-one (2a).[42] According to General Procedure B, the reaction of enone (*E*)-**1a** as colorless needles (111.8 mg) and trichlorosilane (1.57 M CH_2Cl_2; 0.64 mL) with (*S*)-BINAPO (32.4 mg) in CH_2Cl_2 (2 mL) at 0 °C for 20 h gave (*S*)-**2a** (109.7 mg, 97% yield, 97% ee). TLC: R_f 0.33 (hexane/CH_2Cl_2 = 1:1, stained purple with anisaldehyde). Mp: 50–51 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (d, *J* = 6.8 Hz, 3H), 3.18 (dd, *J* = 8.4, 16.8 Hz, 3H), 3.30 (dd, *J* = 6.0, 16.8 Hz, 3H), 3.51 (ddq, *J* = 6.0, 6.8, 8.4 Hz, 3H), 7.16-7.34 (m, 5H), 7.38-7.57 (m, 3H), 7.88-7.98 (m, 2H). HPLC (a combination of Chiralpak AD-H and AS-H, hexane/2-propanol = 9:1, 1.0 mL/min, 254 nm) t_R = 14.4 min (*S*), 15.8 min (*R*). $[\alpha]^{23}_D$ +14.7 (c 1.005, CCl_4) for 97% ee (*S*) [lit.[2h] $[\alpha]^{25}_D$ –13.5 (c 1.00, CCl_4) for 82% ee (*R*)].

1,3-Bis(4-methoxyphenyl)butan-1-one (2b).[43] According to General Procedure B, the reaction of enone (*E*)-**1b** (141.5 mg) and trichlorosilane (2.98 M, 0.34 mL) with (*S*)-BINAPO (32.9 mg) in CH_2Cl_2 (2 mL) at 0 °C for 20 h gave (*S*)-**2b** as colorless needles (119.8 mg, 84% yield, 97% ee). Mp 92-93 °C. IR (KBr, cm^{-1}) 2962, 1674, 1601, 1514, 1250, 1176, 1030, 816. TLC R_f 0.08 (hexane/CH_2Cl_2 = 1:1, stained red-purple with anisaldehyde). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (d, *J* = 6.9 Hz, 3H), 3.09 (dd, *J* = 16.0, 8.3 Hz, 1H), 3.20 (dd, *J* = 16.0, 6.0 Hz, 1H), 3.44 (ddq, *J* = 8.3, 6.0, 6.9 Hz, 1H), 3.78 (s, 3H), 3.86 (s, 3H), 6.84 (apparent d, *J* = 8.7 Hz, 2H), 6.91 (apparent d, *J* = 8.7 Hz, 2H), 7.91 (apparent d, *J* = 8.7 Hz, 2H). HPLC (a combination of CHIRALPAK AD and AS-H, hexane/2-propanol= 9:1, flow rate 1.0 mL/min, UV detection at 254 nm) t_R = 23.1 min (*S*), 30.0 min (*R*). $[\alpha]^{31}_D$ –1.6 (c 1.005, $CHCl_3$) for 96% ee.

1,3-Bis(4-chlorophenyl)butan-1-one (2c).[44] According to General Procedure B, the reaction of enone **1c** (146.0 mg) and trichlorosilane (2.98 M, 0.34 mL) with (*S*)-BINAPO (32.9 mg) at 0 °C for 24 h gave **2c** as colorless needles (128.5 mg, 87%, 96% ee). TLC R_f 0.42 (hexane/CH_2Cl_2 = 1:1, stained purple with anisaldehyde). Mp: 58–59 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (d, *J* = 6.9 Hz, 3H), 3.13 (dd, *J* = 16.9, 7.6 Hz, 1H), 3.23 (dd, *J* = 16.9, 6.4 Hz, 1H), 3.47 (ddq, *J* = 7.6, 6.4, 6.9, 1H), 7.19 (apparent d, *J* = 8.7 Hz, 2H), 7.26 (apparent d, *J* = 8.7 Hz, 2H), 7.41 (apparent d, *J* = 8.7 Hz, 2H), 7.84 (apparent d, *J* = 8.7 Hz, 2H). HPLC (a combination of Chiralpak AD-H and AS-H, hexane/2-propanol = 9/1, flow rate 1.0 mL/min, UV detection at 254 nm) t_R = 11.3 min (*S*), 12.8 min (*R*). $[\alpha]^{28}_D$ –11.4 (c 1.085, $CHCl_3$) for 95% ee.

(*S*)-1,3-Diphenylpentan-1-one (2d).[2h] According to General Procedure B, the reaction of enone (*E*)-**1d** (117.1 mg) and trichlorosilane (2.89 M, 0.35 mL) with (*S*)-BINAPO (32.2 mg) in CH_2Cl_2 (2 mL) at 0 °C for 22 h gave **2d** as colorless needles (112.7 mg, 95% yield, 93% ee (*S*)).

According to General Procedure B, the reaction of enone (*Z*)-**1d** (117.8 mg) and trichlorosilane (2.89 M, 0.35 mL) with (*S*)-BINAPO (32.8 mg) in CH_2Cl_2 (2 mL) at 0 °C for 22h gave **2d** as colorless needles (117.9 mg, 99% yield, 93% ee (*S*)). TLC R_f 0.31 (hexane/CH_2Cl_2 = 1:1, stained yellow with anisaldehyde). Mp: 45–46 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.80 (t, *J* = 7.2 Hz, 3H), 1.59-1.71 (m, 1H), 1.73-1.85 (m, 1H), 3.19-3.34 (m, 3H), 7.15-7.34 (m, 5H), 7.43 (apparent t, *J* = 7.6 Hz, 2H), 7.53 (apparent t, *J* = 7.6 Hz, 1H), 7.92 (apparent d, *J* = 7.6 Hz, 2H). HPLC (a combination of CHIRALPAK AY-3, hexane/2-propanol= 19/1, flow rate 1.0 mL/min, UV detection at 254 nm) t_R = 7.3 min (*S*), 10.8 min (*R*). $[\alpha]^{20}_D$ +14.0 (c 1.320, EtOH) for 93% ee (*S*) [lit.[45] $[\alpha]^{25}_D$ –4.3 (c 1.35, EtOH) for 80% ee (*R*)].

(*S*)-4-Methyl-1,3-diphenylpentan-1-one (2e).[2h] According to General Procedure B, the reaction of enone (*E*)-**1e** (124.9 mg, 0.5 mmol) and trichlorosilane (2.89 M, 0.35 mL) with (*S*)-BINAPO (32.6 mg, 0.05 mmol) in CH_2Cl_2 (2 mL) at 0 °C for 28 h gave **2e** as colorless needles (92.8 mg, 74% yield, 47% ee). TLC R_f 0.28 (hexane/CH_2Cl_2 = 1:1, stained yellow with anisaldehyde). Mp: 40–43 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.79 (d, *J* = 6.9 Hz, 3H), 0.98 (d, , *J* = 6.9 Hz 3H) , 1.88-2.00 (m, 1H), 3.17 (dt, *J* = 7.3, 6.9 Hz, 1H), 3.36 (d, *J* = 7.3 Hz 2H), 7.12-7.20 (m, 3H), 7.20-7.28 (m, 2H), 7.41 (apparent t, *J* = 7.6 Hz, 2H), 7.52 (apparent t, *J* = 7.3 Hz, 1H), 7.87 (apparent d, *J* = 8.2 Hz, 2H). HPLC (a combination of CHIRALPAK AD-H, hexane/2-propanol= 49/1, flow rate 1.0 mL/min, UV detection

at 254 nm) t_R = 8.8 min (*R*), 10.6 min (*S*). $[\alpha]^{20}_D$ –8.2 (c 1.015, CCl_4) for 47% ee (*S*). [lit.[46] $[\alpha]^{22}_D$ +13.2 (c 2.591, CCl_4) for 71% ee (*R*)].

3,4-Dimethyl-1-phenylpentan-1-one (2f).[47] According to General Procedure B, the reaction of enone **1f** (57.3 mg), 2,6-lutidine (35 μL) and trichlorosilane (2.77 M, 0.22 mL) with (*S*)-BINAPO (20.3 mg) at 0 °C for 26 h gave **2f** as colorless oil (50.7 mg, 89% yield, 68% ee). TLC R_f 0.42 (hexane/CH_2Cl_2 = 1:1, stained purple with anisaldehyde). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (d, *J* = 6.9 Hz, 3H), 0.90 (d, *J* = 6.9 Hz, 3H), 0.92 (d, *J* = 6.9 Hz, 3H), 1.61-1.71 (m, 1H), 2.04-2.16 (m, 1H), 2.71 (dd, *J* = 15.6 , 9.2 Hz, 1H), 2.99 (dd, *J* = 15.6, 4.6 Hz, 1H), 7.46 (apparent t, *J* = 8.0 Hz, 2H), 7.56 (apparent t, *J* = 7.4 Hz, 1H), 7.95 (apparent d, *J* = 8.0 Hz, 2H). HPLC (Chiralpak AY-H, hexane/2-propanol = 49:1, flow rate 1.0 mL/min, UV detection at 220 nm) t_R = 5.5 min (*S*), 6.0 min (*R*). $[\alpha]^{19}_D$ –17.7 (c 0.80, $CHCl_3$) for 58% ee.

3-(4-Methoxyphenyl)-1-phenylbutan-1-one (2g).[22g] According to General Procedure B, the reaction of enone **1g** (50.5 mg) and trichlorosilane (3.19 M, 0.13 mL) with (*S*)-BINAPO (13.1 mg) at 0 °C for 24 h gave **2g** as colorless oil (50.3 mg, 99%, 96% ee). TLC R_f 0.14 (hexane/CH_2Cl_2 = 1:1, stained purple with anisaldehyde). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (d, *J* = 6.9 Hz, 3H), 3.15 (dd, *J* = 16.3, 8.2 Hz, 1H), 3.24 (dd, *J* = 16.3, 6.0 Hz, 1H), 3.45 (ddq, *J* = 8.2, 6.0, 6.9 Hz,, 1H), 3.78 (s, 3H), 6.84 (apparent d, *J* = 8.5 Hz, 2H), 7.19 (apparent d, *J* = 8.5 Hz, 2H), 7.44 (apparent t, *J* = 7.8 Hz, 2H), 7.54 (apparent t, *J* = 7.4 Hz, 1H), 7.92 (apparent d, *J* = 7.3 Hz, 2H). HPLC (a combination of Chiralpak AD-H and AS-H, hexane/2-propanol = 9:1, flow rate 1.0 mL/min, UV detection at 220 nm) t_R = 14.9 min (*S*), 16.8 min (*R*). $[\alpha]^{20}_D$ +6.6 (c 1.01, $CHCl_3$) for 92% ee (*S*) [lit.[18d] $[\alpha]^{31.4}_D$ –6.87 (c 1.39, $CHCl_3$) for >98% ee (*R*)].

3-(4-Chlorophenyl)-1-phenylbutan-1-one (2h).[22g,42,48] According to the typical procedure B, the reaction of enone **1h** (64.2 mg) and trichlorosilane (3.12 M, 0.19 mL) with (*S*)-BINAPO (19.4 mg) at 0 °C for 24 h gave **2h** as colorless oil (54.5 mg, 84%, 97% ee). TLC R_f 0.33 (hexane/CH_2Cl_2 = 1:1, stained orange with anisaldehyde). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (d, *J* = 6.9 Hz, 3H), 3.19 (dd, *J* = 16.5, 7.8 Hz, 1H), 3.24 (dd, *J* = 16.5, 6.4 Hz, 1H), 3.49 (ddq, *J* = 7.8, 6.4, 6.9 Hz, 1H), 7.20 (apparent d, *J* = 8.5 Hz, 2H), 7.26 (apparent d, *J* = 8.5 Hz, 2H), 7.45 (apparent t, *J* = 7.8 Hz, 1H), 7.56 (apparent t, *J* = 7.3 Hz, 1H), 7.91 (apparent d, *J* = 8.5 Hz, 2H). HPLC (Chiralpak AD-H, hexane/2-propanol = 19:1, flow rate 1.0 mL/min, UV detection at 254 nm) t_R = 5.7 min (*S*), 6.9 min (*R*).

$[\alpha]^{21}_{D}$ –1.5 (c 0.59, $CHCl_3$) for 97% ee [lit.[18d] $[\alpha]^{24.0}_{D}$ +1.76 (c 1.30, $CHCl_3$) for 95% ee].

3-(Naphthalen-2-yl)-1-phenylbutan-1-one (2i).[49] According to General Procedure B, the reaction of enone **1i** (38.7 mg) and trichlorosilane (2.88 M, 0.10 mL) with (*S*)-BINAPO (9.1 mg) at 0 °C for 20 h gave **2i** as colorless needles (37.3 mg, 97%, 97% ee). TLC R_f 0.28 (hexane/CH_2Cl_2 = 1:1, stained purple with anisaldehyde). Mp: 59–61 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (d, *J* = 6.8 Hz, 3H), 3.28 (dd, *J* = 16.5, 8.2 Hz, 1H), 3.41 (dd, *J* = 16.8, 5.6 Hz, 1H), 3.69 (ddq, *J* = 8.2, 5.6, 6.8 Hz, 1H), 7.39-7.49 (m, 5H), 7.55 (apparent t, *J* = 7.3 Hz, 1H), 7.70 (brs, 1H), 7.70-7.83 (m, 3H), 7.95 (apparent d, *J* = 7.6 Hz, 2H). HPLC (a combination of Chiralpak AD-H and AS-H, hexane/2-propanol = 39:1, flow rate 1.0 mL/min, UV detection at 254 nm) t_R = 8.0 min (*S*), 9.3min (*R*). $[\alpha]^{20}_{D}$ +7.1 (c 1.02, $CHCl_3$) for 97% ee.

3-(2-Thienyl)-1-phenylbutan-1-one (2j).[50] According to General Procedure B, the reaction of enone **1j** as yellow oil (67.6 mg, 0.3 mmol) and trichlorosilane (2.91 M, 0.21 mL) with (*S*)-BINAPO (19.8 mg, 0.03 mmol) in CH_2Cl_2 (1.2 mL) at 0 °C for 20 h gave **2j** (55.1 mg, 80% yield, 95% ee). TLC R_f 0.33 (hexane/CH_2Cl_2 = 1:1, stained blue-green with anisaldehyde). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42 (d, *J* = 6.9 Hz, 3H), 3.20 (dd, *J* = 16.7, 8.0 Hz, 1H), 3.37 (dd, *J* = 16.7, 5.7 Hz, 1H), 3.85 (ddq, *J* = 8.0, 5.7, 6.9, 1H), 6.87 (d, *J* = 3.7 Hz, 1H), 6.92 (dd, *J* = 5.0, 3.8 Hz, 1H), 7.13 (brd, *J* = 5.0 Hz, 1H), 7.46 (apparent t, *J* = 7.8 Hz, 2H), 7.56 (apparent t, *J* = 7.3 Hz, 1H), 7.95 (apparent d, *J* = 7.3 Hz, 2H). HPLC (a combination of CHIRALPAK AD-H and AS-H, hexane/2-propanol= 39:1, flow rate 1.0 mL/min, UV detection at 254 nm) t_R = 5.4 min (*S*), 5.9 min (*R*). $[\alpha]^{20}_{D}$ +7.7 (c 1.09, EtOH) for 95% ee.

3-Cyclopropyl-1-phenylbutan-1-one (2k). According to General Procedure B, the reaction of enone **1k** (18.6 mg), 2,6-lutidine (12 μL) and trichlorosilane (3.19 M, 0.06 mL) with (*S*)-BINAPO (6.5 mg) at 0 °C for 24 h gave **2k** as colorless oil (18.0 mg, 96% yield, 40% ee). TLC R_f 0.42 (hexane/CH_2Cl_2 = 1:1, stained purple with anisaldehyde). IR (ATR) 2959, 1682, 1448, 1279, 1171, 1010, 753, 689 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.04-0.17 (m, 2H), 0.33-0.50 (m, 2H), 0.59-0.70 (m, 1H), 1.05 (d, *J* = 6.9 Hz, 3H), 1.33-1.48 (m, 1H), 2.92 (dd, *J* = 15.6, 8.2 Hz, 1H), 3.10 (dd, *J* = 15.6, 5.5 Hz, 1H), 7.46 (apparent t, *J* = 7.8 Hz, 2H), 7.55 (apparent t, *J* = 7.1 Hz, 1H), 7.96 (apparent d, *J* = 7.8 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz) δ 3.9, 4.4, 18.2, 20.1, 35.8, 46.1, 128.1, 128.5, 132.8, 137.5, 200.4. HRMS (ESI+) Calcd for $C_{13}H_{16}NaO$ ($M+Na^+$) 211.1093 found 211.1094. HPLC (Chiralpak AY-H, hexane/2-propanol = 49:1, flow rate 1.0 mL/min, UV detection at 220 nm) t_R = 11.9 min (*S*), 12.6 min (*R*). $[\alpha]^{21}_{D}$ –3.2 (c

1.38, $CHCl_3$) for 40% ee.

4,4-Dimethyl-1,3-diphenylpentan-1-one (2l). According to General Procedure B, the reaction of enone **1l** (20.6 mg), 2,6-lutidine (12 μL) and trichlorosilane (3.19 M, 0.063 mL) with (*S*)-BINAPO (6.6 mg) at rt for 48 h gave **2l** as colorless oil (18.5 mg, 89% yield, 93% ee). TLC R_f 0.17 (hexane/CH_2Cl_2 = 2:1, stained blue with anisaldehyde). IR (ATR) 2959, 1683, 1448, 1365, 1288, 1214, 1178, 750, 689 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (d, *J* = 6.9 Hz, 3H), 0.94 (s, 9H), 2.02 (ddq, *J* = 10.5, 2.8, 6.9 Hz, 1H), 2.64 (dd, *J* = 15.6, 10.5 Hz, 1H), 3.10 (dd, *J* = 15.6, 2.8 Hz, 1H), 7.46 (apparent t, *J* = 7.6 Hz, 2H), 7.56 (apparent t, *J* = 7.3 Hz, 1H), 7.95 (apparent d, *J* = 7.3 Hz, 2H). $^{13}C\{^1H\}$ NMR (100 MHz) δ 15.1, 27.3, 33.0, 39.1, 41.5, 128.1, 128.5, 132.8, 137.5, 201.2. HRMS (EI+) Calcd for $C_{14}H_{20}O$ (M^+) 204.1514, found 204.1520. HPLC (Chiralpak AY-H, hexane/2-propanol = 49:1, flow rate 1.0 mL/min, UV detection at 220 nm) t_R = 5.7 min (*S*), 6.4 min (*R*). $[\alpha]^{17}_D$ –42.3 (c 1.71, $CHCl_3$) for 93% ee (*S*).

2-Methyl-5-phenylhexan-3-one (2m).[51] According to General Procedure B, the reaction of enone **1m** (37.6 mg) and trichlorosilane (3.13 M, 0.13 mL) with (*S*)-BINAPO (13.2 mg) at 0 °C for 24 h gave **2m** as colorless oil (31.6 mg, 83%, 92% ee). TLC R_f 0.54 (hexane/Et_2O = 6:1, stained purple with anisaldehyde). ^1H NMR (400 MHz, $CDCl_3$) δ 0.98 (d, *J* = 6.9 Hz, 3H), 1.04 (d, *J* = 6.9 Hz, 3H), 1.25 (d, *J* = 6.9 Hz, 3H), 2.48 (sept, *J* = 6.9 Hz, 1H), 2.67 (dd, *J* = 16.5, 8.2 Hz, 1H), 2.75 (dd, *J* = 16.5, 6.0 Hz, 1H), 3.34 (ddq, *J* = 8.2, 6.0, 6.9 Hz, 1H), 7.16-7.23 (m, 3H), 7.25-7.32 (m, 2H). HPLC (Chiralpak AD-H, hexane/2-propanol = 49:1, flow rate 1.0 mL/min, UV detection at 254 nm) t_R = 4.3 min (*S*), 4.6 min (*R*). $[\alpha]^{20}_D$ +30.5 (c 1.00, $CHCl_3$) for 92% ee (*S*) [lit.[47] $[\alpha]^{25}_D$ +19.7 (c 1.00, $CHCl_3$) for 65% ee (*S*)].

5-(4-Methoxyphenyl)-2-methylhexan-3-one (2n). According to General Procedure B, the reaction of enone **1n** (43.7 mg) and trichlorosilane (3.19 M, 0.13 mL) with (*S*)-BINAPO (13.1 mg) at 0 °C for 20 h gave **2n** as colorless oil (43.6 mg, 99%, 93% ee). TLC R_f 0.16 (hexane/CH_2Cl_2 = 1:1, stained red-purple with anisaldehyde). IR (ATR) 2965, 1708, 1512, 1244, 1034, 828, 551 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ 0.97 (d, *J* = 6.9 Hz, 3H), 1.03 (d, *J* = 6.9 Hz, 3H), 1.22 (d, *J* = 6.9 Hz, 3H), 2.47 (sept, *J* = 6.9 Hz, 1H), 2.63 (dd, *J* = 16.5, 7.8 Hz, 1H), 2.72 (dd, *J* = 16.5, 6.4 Hz, 1H), 3.29 (ddq, *J* = 7.8, 6.0, 6.9 Hz, 1H), 3.78 (s, 3H), 6.83 (apparent d, *J* = 8.7 Hz, 2H), 7.13 (apparent d, *J* = 8.7 Hz, 2H). $^{13}C\{^1H\}$ NMR (100 MHz) δ 17.8, 17.9, 21.9, 34.4, 41.2, 49.1, 55.1, 113.7, 127.6, 138.5, 157.8, 213.6. LRMS (FAB+, $CHCl_3$+NBA) *m/z* 220 (M + H^+, 45), 135 ($CH_3CH^+C_6H_4OMe$, 100). HRMS (FAB+, $CHCl_3$+NBA)

Calcd for $C_{14}H_{20}O_2$ (M + H^+) 220.1463, found 220.1460. HPLC (Chiralpak AD-H, hexane/2-propanol = 49:1, flow rate 1.0 mL/min, UV detection at 220 nm) t_R = 5.9 min (*S*), 6.7 min (*R*). $[\alpha]^{23}_D$ +31.8 (c 1.00, $CHCl_3$) for 92% ee.

5-(4-Chlorophenyl)-2-methylhexan-3-one (2o). According to General Procedure B, the reaction of enone **1o** (44.5 mg) and trichlorosilane (3.19 M, 0.13 mL) with (*S*)-BINAPO (13.1 mg) at 0 °C for 24 h gave **2o** as colorless oil (26.0 mg, 58%, 93% ee). TLC R_f 0.29 (hexane/CH_2Cl_2 = 1:1, stained purple with anisaldehyde). IR (ATR) 2968, 1710, 1683, 1601, 1492, 1093, 1011, 823, 534 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.98 (d, *J* = 6.9 Hz, 3H), 1.04 (d, *J* = 6.9 Hz, 3H), 1.23 (d, *J* = 6.9 Hz, 3H), 2.48 (sept, *J* = 6.9 Hz, 1H), 2.65 (dd, *J* = 16.5, 7.6 Hz, 1H), 2.73 (dd, *J* = 16.5, 6.9 Hz, 1H), 3.33 (ddq, *J* = 7.6, 6.9, 6.9 Hz, 1H), 7.15 (apparent d, *J* = 8.2 Hz, 2H), 7.25 (apparent d, *J* = 8.2 Hz, 2H). $^{13}C\{^1H\}$ NMR (100 MHz) δ 17.8, 18.0, 21.8, 34.5, 41.3, 48.7, 128.2, 128.5, 131.8, 144.9, 213.1. HRMS (ESI+) Calcd for $C_{13}H_{17}ClNaO$ ($M+Na^+$) 247.0860 found 247.0860. HPLC (Chiralpak AD-H, hexane/2-propanol = 49:1, flow rate 1.0 mL/min, UV detection at 220 nm) t_R = 4.6 min (*S*), 5.1 min (*R*). $[\alpha]^{18}_D$ +33.2 (c 1.00, $CHCl_3$) for 93% ee.

1-(4-Methoxyphenyl)-3-phenylbutan-1-one (2p).[48,52] According to General Procedure B, the reaction of enone **1p** (19.0 mg) and trichlorosilane (3.19 M, 0.05 mL) with (*S*)-BINAPO (4.9 mg) at 0 °C for 24 h gave **2p** as colorless oil (13.3 mg, 70%, 97% ee). TLC R_f 0.11 (hexane/CH_2Cl_2 = 1:1, stained brown with anisaldehyde). ^1H NMR (400 MHz, $CDCl_3$) δ 1.33 (d, *J* = 6.9 Hz, 3H), 3.13 (dd, *J* = 16.0, 8.5 Hz, 1H), 3.23 (dd, *J* = 16.0, 5.5 Hz, 1H), 3.49 (ddq, *J* = 8.5, 5.5, 6.9 Hz, 1H), 3.86 (s, 3H), 6.91 (apparent d, *J* = 8.9 Hz, 2H), 7.17-7.34 (m, 5H), 7.92 (apparent d, *J* = 8.9 Hz, 2H). HPLC (Chiralpak AS-H, hexane/2-propanol = 9/1, flow rate 1.0 mL/min, UV detection at 254 nm) t_R = 8.2 min (*S*), 9.0 min (*R*). $[\alpha]^{21}_D$ –8.8 (c 1.02, $CHCl_3$) for 97% ee.

1-(4-chlorophenyl)-3-phenylbutan-1-one (2q).[48] According to General Procedure B, the reaction of enone **1q** (13.9 mg) and trichlorosilane (3.19 M, 0.03 mL) with (*S*)-BINAPO (3.5 mg) at 0 °C for 24 h gave **2q** as colorless oil (12.2 mg, 87%, 98% ee). TLC R_f 0.31 (hexane/CH_2Cl_2 = 1:1, stained brown with anisaldehyde). ^1H NMR (400 MHz, $CDCl_3$) δ 1.34 (d, *J* = 6.9 Hz, 3H), 3.15 (dd, *J* = 16.5, 8.2 Hz, 1H), 3.27 (dd, *J* = 16.5, 6.0 Hz, 1H), 3.48 (ddq, *J* = 8.2, 6.0, 6.9 Hz, 1H), 7.17-7.34 (m, 5H), 7.41 (apparent d, *J* = 8.7 Hz, 2H), 7.86 (apparent d, *J* = 8.7 Hz, 2H). HPLC (a combination of Chiralpak AD-H and AS-H, hexane/2-propanol = 39:1, flow rate 1.0 mL/min, UV detection at 254 nm) t_R = 5.2 min (*S*), 5.6 min (*R*). $[\alpha]^{29}_D$ –5.5 (c 1.15, $CHCl_3$) for 98% ee.

1-Cyclohexyl-3-phenylbutan-1-one (2r). According to General Procedure B, the reaction of enone **1r** (10.4 mg) and trichlorosilane (3.12 M, 0.03 mL) with (*S*)-BINAPO (3.0 mg) at 0 °C for 24 h gave **2r** as colorless oil (8.1 mg, 76%, 89% ee). IR (ATR) 2919, 2853, 1705, 1348, 762, 698 cm^{-1}. TLC R_f 0.26 (hexane/CH_2Cl_2 = 1:1, stained light blue with anisaldehyde). ^1H NMR (400 MHz, $CDCl_3$) δ 1.12-1.45 (m, 6H), 1.24 (d, *J* = 6.9 Hz, 3H), 1.58-1.85 (m, 4H), 2.17-2.27 (m, 1H) 2.66 (dd, *J* = 16.5, 8.2 Hz, 1H), 2.69 (dd, *J* = 16.5, 6.4 Hz, 1H), 3.33 (ddq, *J* = 8.2, 6.4, 6.9 Hz, 1H), 7.15-7.23 (m, 3H), 7.25-7.31 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz) δ 21.8, 25.7, 25.8, 28.1, 28.3, 35.1, 49.1, 51.2, 126.2, 126.8, 128.4, 146.6, 210.1. HRMS (ESI+) Calcd for $C_{16}H_{22}NaO$ ($M+Na^+$) 253.1563 found 253.1558. HPLC (Chiralpak AD-H, hexane/2-propanol = 49:1, flow rate 1.0 mL/min, UV detection at 220 nm) t_R = 5.3 min (*S*), 5.7 min (*R*). $[\alpha]^{22}_D$ +22.9 (c 1.00, $CHCl_3$) for 89% ee.

1-Cyclopropyl-3-phenylbutan-1-one (2s). According to General Procedure B, the reaction of enone **1s** (70.5 mg) and trichlorosilane (3.12 M, 0.24 mL) with (*S*)-BINAPO (24.9 mg) at 0 °C for 24 h gave **2s** as colorless oil (64.4 mg, 90%, 89% ee). TLC R_f 0.53 (hexane/AcOEt = 10:1, stained black with anisaldehyde). IR (ATR) 2963, 1695, 1384, 1073, 1010, 762, 699 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.74-0.86 (m, 2H), 0.91-1.01 (m, 2H), 1.28 (d, *J* = 6.9 Hz, 3H), 1.83-1.90 (m, 1H), 2.77 (dd, *J* = 16.0, 8.2 Hz, 1H), 2.87 (dd, *J* = 16.0, 6.4 Hz, 1H), 3.35 (ddq, *J* = 8.2, 6.4, 6.9 Hz, 1H), 7.15-7.33 (m, 5H). $^{13}C\{^1H\}$ NMR (100 MHz) δ 10.6, 10.7, 20.9, 21.9, 35.6, 51.9, 126.2, 126.8, 128.4, 146.3, 209.9. HRMS (ESI+) Calcd for $C_{13}H_{16}NaO$ ($M+Na^+$) 211.1093 found 211.1093. HPLC (Chiralpak AD-H, hexane/2-propanol = 49:1, flow rate 1.0 mL/min, UV detection at 220 nm) t_R = 5.4 min (*S*), 5.8 min (*R*). $[\alpha]^{21}_D$ +44.8 (c 1.00, $CHCl_3$) for 89% ee.

Asymmetric Conjugate Reduction of *ar*-Atlantone to *ar*-Turmerone. To a stirred solution of (*S*)-4,4'-Br_2-BINAPO (24.4 mg, 0.03 mmol), *ar*-atlantone (**1t**) (214.3 mg, 1.0 mmol) and 2,6-lutidine (0.12 mL, 1.0 mmol) in CH_2Cl_2 (4.0 mL) was added trichlorosilane (3.19 M CH_2Cl_2; 0.63 mL) at –78 °C. The mixture was stirred at –78 °C for 24 h. The reaction was quenched with saturated $NaHCO_3$ (5 mL). The mixture was stirred for 1 h at rt, filtered through a Celite pad and extracted with AcOEt (3 × 20 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and evaporated. The residue was purified by silica gel column chromatography (hexane/CH_2Cl_2 = 1:3) to give (*S*)-*ar*-turmerone (**2t**) (197.0 mg, 91% yield, 92% ee, **2t**:**2t'** = 99:1).

The reaction of *ar*-atlantone (**1t**) (1.072 g, 5 mmol) with (*R*)-4,4'-Br_2-BINAPO (121.9 mg, 0.03 equiv), 2,6-

lutidine (0.58 mL) and trichlorosilane (3.12 M CH_2Cl_2; 3.13 mL) gave (*R*)-*ar*-turmerone (**2t**) as yellow oil (918.6 mg, 85%, 92% ee, **2t**:**2t'** = 98:2).

After the product was obtained by column chromatography on silica gel, the catalyst (Br_2-BINAPO) was recovered quantitatively by eluting with CH_2Cl_2/MeOH (10:1) and reused after recrystallization.[26]

***ar*-Turmerone (2t).**[22] TLC: R_f 0.45 (hexane/CH_2Cl_2 = 1:1, stained black with anisaldehyde); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (d, *J* = 6.8 Hz, 3H), 1.86 (d, *J* = 0.9 Hz, 3H), 2.11 (d, *J* = 1.4 Hz, 3H), 2.31 (s, 3H), 2.61 (dd, *J* = 15.6, 8.3 Hz, 1H), 2.71 (dd, *J* = 15.6, 6.0 Hz, 1H), 3.29 (ddq, *J* = 8.3, 6.0, 6.8 Hz, 1H), 6.03 (sept, *J* = 1.4 Hz, 1H), 7.07-7.13 (m, 4H). HPLC (Chiralpak AD-3, hexane/2-propanol = 29:1, 1.0 mL/min, 220 nm) t_R = 4.5 min (*S*), 5.0 min (*R*). $[\alpha]^{24}_D$ +56.4 (c 1.00, $CHCl_3$) for 92% ee (*S*). With (*R*)-4,4'-Br_2-BINAPO instead of (*S*)-catalyst: $[\alpha]^{22}_D$ –56.4 (c 1.00, $CHCl_3$) for 92% ee (*R*) [lit.[18f] $[\alpha]^{22}_D$ –60.6 (c 1.00, $CHCl_3$) for 98% ee (*R*)].

(*E*)-6-Methyl-2-(*p*-tolyl)hept-2-en-4-one (2t').[53] TLC: R_f 0.48 (hexane/CH_2Cl_2 = 1:1, stained dark green with anisaldehyde). ^{1}H NMR (500 MHz) δ 0.96 (d, *J* = 6.3 Hz, 6H), 2.14-2.25 (m, 1H), 2.37 (s, 3H), 2.40 (d, *J* = 6.9 Hz, 2H), 2.53 (d, *J* = 1.4 Hz, 3H), 6.49 (d, *J* = 1.4 Hz, 1H), 7.18 (apparent d, *J* = 8.1 Hz, 2H), 7.39 (apparent d, *J* = 8.1 Hz, 2H). ^{13}C{^{1}H} NMR (125 MHz) δ 18.2, 21.2, 22.7, 25.3, 53.9, 123.8, 126.3, 129.2, 139.2, 139.6, 153.5, 201.5. HRMS (ESI+) Calcd for $C_{15}H_{20}NaO$ ($M+Na^+$) 239.1406 found 239.1404.

Control Experiment 1: Regioselective Reduction of Dienone 1u. According to General Procedure B, the reaction of **1u** (20.6 mg, 0.10 mmol), $HSiCl_3$ (3.33 M CH_2Cl_2; 0.06 mL), 2,6-lutidine (12 μL, 0.10 mmol), and (*S*)-BINAPO (6.5 mg, 0.01 mmol) at 0 °C for 21 h gave **2u** as colorless oil (6.8 mg, 33% yield, 38% ee) and **2u'** as colorless oil (10.4 mg, 50% yield).

(*S*)-6-Cyclohexyl-2-methylhept-2-en-4-one (2u). TLC: R_f 0.52 (hexane/ CH_2Cl_2 = 1:1, stained yellow with anisaldehyde). IR (ATR) 2924, 2852, 1686, 1615, 1448, 1378 cm^{-1}. ^{1}H NMR (400 MHz) δ 0.84 (d, *J* = 6.9 Hz, 3H), 0.89-1.31 (m, 5H), 1.58-1.68 (m, 3H), 1.68-1.78 (m, 2H), 1.88 (s, 3H), 1.84-1.96 (m, 1H), 2.14 (s, 3H), 2.15 (dd, *J* = 15.1, 9.2 Hz, 1H), 2.44 (dd, *J* = 15.1, 4.8 Hz, 3H), 6.06 (s, 1H). ^{13}C{^{1}H} NMR (100 MHz) δ 16.6, 20.6, 26.6, 26.7, 27.6, 29.1, 30.4, 34.7, 42.9, 49.1, 124.2, 154.2, 201.7. LRMS (EI+) *m/z* 208 (M^+, 9), 125 (Me_2C=CHCOCHC^+Me, 51), 98 (Me_2C=CHC(OH^+)C=CH_2, 99), 83 (Me_2C=$CHCO^+$, 100). HRMS (ESI+) Calcd for $C_{14}H_{24}NaO$ ($M+Na^+$) 231.1719

found 231.1717. HPLC (Chiralpak AY-H, hexane/2-propanol= 99:1, 1.0 mL/min, 254 nm) t_R = 5.7 min (*S*), 6.1 min (*R*). $[\alpha]^{20}_D$ +8.3 (c 0.31, $CHCl_3$) for 86% ee (*S*).

(*E*)-2-Cyclohexyl-6-methylhept-2-en-4-one (2u').[54] TLC: R_f 0.45 (hexane/CH_2Cl_2 = 1:1, stained red with anisaldehyde). ^{1}H NMR (400 MHz) δ 0.92 (d, *J* = 6.7 Hz, 6H), 1.11-1.36 (m, 5H), 1.66-1.84 (m, 5H), 1.94 (tt, *J* = 11.0, 3.2 Hz, 11 H), 2.06-2.18 (m, 1H), 2.10 (d, *J* = 0.9 Hz, 3H), 2.29 (d, *J* = 6.9 Hz, 2H), 6.03 (s, 1H). ^{13}C{^{1}H} NMR (100 MHz) δ 17.8, 22.7, 25.2, 26.1, 26.4, 31.4, 48.9, 53.6, 121.8, 163.0, 201.9.

Control Experiment 2: Regioselective Reduction of Dienone 1v. According to General Procedure B, the reaction of **1v** (17.1 mg, 0.064 mmol), $HSiCl_3$ (2.64 M CH_2Cl_2; 0.05 mL), 2,6-lutidine (7.4 μL, 0.064 mmol), and (*S*)-BINAPO (4.2 mg, 0.0064 mmol) at –40 °C for 24 h gave **2v** as yellow oil (13.3 mg, 77% yield, 86% ee) and **2v'** as yellow oil (3.8 mg, 22% yield).

(*S*,*E*)-2-Cyclohexyl-6-phenylhept-2-en-4-one (2v). TLC: R_f 0.45 (hexane/CH_2Cl_2 = 1:1, stained red with anisaldehyde). IR (ATR) 2924, 2852, 1731, 1686, 1608, 1450, 1261, 1119, 1073, 1014, 762, 699 cm^{-1}. ^{1}H NMR (400 MHz) δ 1.08-1.35 (m, 5H), 1.27 (d, *J* = 6.9 Hz, 3H), 1.63-1.83 (m, 5H), 1.91 (tt, *J* = 11.4, 2.8 Hz, 1H), 2.06 (s, 3H), 2.65 (dd, 1H, *J* = 15.6, 8.2 Hz), 2.74 (dd, 1H, *J* = 15.6, 6.2 Hz), 3.31 (ddq, *J* = 18.2, 6.2, 6.9 Hz, 1H), 5.97 (s, 1H), 7.15-7.32 (m, 5H). ^{13}C{^{1}H} NMR (100 MHz) δ 17.9, 22.0, 26.1, 26.3, 31.3, 35.9, 48.9, 52.8, 121.7, 126.1, 126.8, 128.4, 146.7, 163.5, 200.5. HRMS (ESI+) Calcd for $C_{19}H_{26}NaO$ ($M+Na^+$) 293.1876 found 293.1869. HPLC (Chiralpak AD-3, hexane/2-propanol = 29:1, 1.0 mL/min, 220 nm) t_R = 10.8 min (*S*), 11.8 min (*R*). $[\alpha]^{22}_D$ +32.5 (c 0.57, $CHCl_3$) for 86% ee (*S*).

(*E*)-6-Cyclohexyl-2-phenylhept-2-en-4-one (2v'). TLC: R_f 0.48 (hexane/CH_2Cl_2 = 1:1, stained yellow with anisaldehyde). IR (ATR) 2922, 2851, 1682, 1599, 1447, 1376, 1056, 756, 696 cm^{-1}. ^{1}H NMR (400 MHz) δ 0.88 (d, *J* = 6.9 Hz, 3H), 0.93-1.33 (m, 5H), 1.60-1.80 (m, 5H), 1.91-2.03 (m, 1H), 2.29 (dd, *J* = 15.1, 9.2 Hz, 1H), 2.55 (d, *J* = 1.4 Hz, 1H), 2.61 (dd, *J* = 15.1, 4.9 Hz, 1H), 6.49 (q, *J* = 1.4 Hz, 1H), 7.35-7.42 (m, 3H), 7.46-7.51 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz) δ 16.7, 18.3, 26.6, 26.7, 26.8, 29.1, 30.4, 34.9, 42.9, 49.7, 124.7, 126.5, 128.5, 129.0, 142.7, 153.3, 202.1. LRMS (EI+) *m/z* 270 (M^+, 2), 187 ($MeCH^+CH_2COCH$=CMePh, 13), 160 (CH_2=C(O^+H)CH=CMePh, 59), 145 ($^+$COCH=CMePh, 100). HRMS (EI+) Calcd for $C_{19}H_{26}O$ (M^+) 270.1984, found 270.1987. The enantiomeric excess

was not determined.

Control Experiment 3: Competitive Reaction between Enones 1n and 1o. According to General Procedure B, a mixture of **1n** (18.1 mg, 0.083 mmol) and **1o** (18.5 mg, 0.083 mmol) was treated with $HSiCl_3$ (3.33 M CH_2Cl_2; 0.05 mL), 2,6-lutidine (9.6 μL, 0.083 mmol), and (*S*)-BINAPO (5.4 mg, 0.0083 mmol) at 0 °C for 3 h. Ketone **2n** (17.4 mg, 95% yield, 89% ee) and ketone **2o** (2.1 mg, 11% yield, 93% ee) were obtained.

Synthesis of Turmeronol A and B. (a) *Via* direct oxidation of (*S*)-*ar*-turmerone. To a solution of *ar*-turmerone (**2t**) (28.2 mg, 0.13 mmol) in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) (0.52 mL) was added phthaloyl peroxide (27.9 mg, 0.17 mmol) at rt. After being heated at 50 °C for 48 h, the mixture was cooled, concentrated, diluted with MeOH (3 mL), and treated with saturated aqueous $NaHCO_3$ solution (0.2 mL). After being stirred for 2 h, the reaction mixture was treated with phosphate buffer (5 mL, pH 7.0) and extracted with AcOEt (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography on silica gel (hexane/CH_2Cl_2 = 3:1) to give (*S*)-turmeronol A as yellow oil (4.6 mg, 15% yield) and (*S*)-turmeronol B as yellow oil (2.2 mg, 7% yield).

(*S*)-Turmeronol A.[29a] TLC: R_f 0.30 (hexane/CH_2Cl_2 = 1:1, stained black with anisaldehyde). ^{1}H NMR (400 MHz) δ 1.22 (d, *J* = 6.8 Hz, 3H), 1.86 (d, *J* = 1.2 Hz, 3H), 2.11 (d, *J* = 1.2 Hz, 3H), 2.20 (s, 3H), 2.59 (dd, *J* = 16.0, 8.2 Hz, 1H), 2.72 (dd, *J* = 16.0, 6.1 Hz, 1H), 3.25 (ddq, *J* = 8.2, 6.1, 6.8 Hz, 1H), 4.67 (brs, 1H), 6.02 (sept, *J* = 1.4 Hz, 1H), 6.66 (d, *J* = 1.8 Hz, 1H), 6.70 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.03 (d, *J* = 7.8 Hz, 1H).

(*S*)-Turmeronol B.[29b] TLC: R_f 0.42 (hexane/CH_2Cl_2 = 1:1, stained purple with anisaldehyde). ^{1}H NMR (400 MHz) δ 1.29 (d, *J* = 7.1 Hz, 3H), 1.85 (d, *J* = 1.2 Hz, 3H), 2.11 (d, *J* = 1.2 Hz, 3H), 2.25 (s, 3H), 2.80 (d, *J* = 6.6 Hz, 2H), 3.48-3.69 (m, 1H), 6.00 (m, 1H), 6.72 (d, *J* = 7.6 Hz, 1H), 6.74 (s, 1H), 7.02 (d, *J* = 7.6 Hz, 1H), 8.13 (s, 1H).

(b) Via formylation of *ar*-turmerone and Dakin oxidation. To a solution of *ar*-turmerone (**2t**) (140.0 mg, 0.65 mmol) in CH_2Cl_2 (2.7 mL) were added $TiCl_4$ (4.30 M in CH_2Cl_2, 0.91 mL, 3.9 mmol) and dichloromethyl methyl ether (0.18 mL, 2.1 mmol) at 0 °C. The mixture was warmed to rt and stirred for 2 h. After addition of

iced water (10 mL), the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography (hexane/CH_2Cl_2 = 2:1) to give formyl-*ar*-turmerone (131.8 mg, 83% yield). IR (ATR) 2927, 1686, 1617, 1447, 1380, 1119, 1019, 833 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 1.27 (d, *J* = 6.9 Hz, 3H), 1.86 (s, 3H), 2.10 (s, 3H), 2.63 (s, 3H), 2.67 (dd, *J* = 16.0, 7.8 Hz, 1H), 2.73 (dd, *J* = 16.0, 6.4 Hz, 1H), 3.38 (m, 1H), 6.03 (brs, 1H), 7.18 (d, *J* = 7.8 Hz, 2H), 7.35 (dd, *J* = 7.8, 2.1 Hz, 2H), 7.65 (d, *J* = 2.1 Hz, 1H), 10.26 (s, 1H). $^{13}C\{^1H\}$ NMR (100 MHz) δ 19.0, 20.8, 21.9, 27.7, 34.9, 52.1, 123.9, 129.8, 131.9, 132.6, 134.1, 138.4, 144.9, 155.7, 192.8, 199.2. LRMS (FAB+, $CHCl_3$+NBA) *m/z* 245 ($M+H^+$, 5), 147 (CH_3CH^+Ar, 19), 83 ($Me_2C{=}CHCH_2^+$, 57). HRMS (FAB+, $CHCl_3$+NBA) Calcd for $C_{16}H_{21}O_2$ ($M+H^+$) 245.1542, found 245.1536.

To a solution of formyl-*ar*-turmerone (13.0 mg, 0.05 mmol) in CH_2Cl_2 (0.08 mL) was added *m*CPBA (75 wt%, 13.5 mg, 0.06 mmol) at 0 °C. After being stirred for 1 h, the reaction mixture was treated with MeOH (0.31 mL) and saturated $NaHCO_3$ (0.29 mL). After 1 h, the mixture was concentrated and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography on silica gel (hexane/AcOEt = 4:1) to give turmernol A (11.4 mg, 93% yield, 92% ee). HPLC (Chiralcel OB-H, hexane/2-propanol = 97:3, 0.7 mL/min, 254 nm) t_R = 27.4 min (*S*), 37.4 min (*R*). $[\alpha]^{20}_D$ +57.8 (c 1.00, $CHCl_3$) for 92% ee (*S*). $[\alpha]^{20}_D$ +57.4 (c 1.00, $CHCl_3$) for 92% ee (*R*). [lit.[25b] $[\alpha]^{21}_D$ +62.3 (c 0.43, $CHCl_3$) for 99% ee (*S*)].

Synthesis of Mutisianthol and Jungianol.

(a) Luche reduction of *ent*-turmeronol A. To a solution of turmeronol A (29.3 mg, 0.13 mmol) in MeOH (0.33 mL) were added $CeCl_3 \cdot 7H_2O$ (48.4 mg, 0.13 mmol) and $NaBH_4$ (4.9 mg, 0.13 mmol) at 0 °C. After being stirred at 0 °C for 30 min, the reaction mixture was treated with additional $NaBH_4$ (4.9 mg, 0.13 mmol) and stirred at rt for 30 min. The reaction was quenched with saturated NH_4Cl (2 mL) and the mixture was extracted with AcOEt (3 × 20 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and evaporated. The residue was purified by silica gel column chromatography (hexane/AcOEt = 5:1) to give allylic alcohol **5** (29.6 mg, 97% yield, dr = 64:36). TLC: R_f 0.30 (hexane/CH_2Cl_2 = 1:1, stained black with anisaldehyde). ^1H NMR (400 MHz) δ 1.20 (d, *J* = 6.9 Hz, 1.08H), 1.22 (d, *J* = 6.9 Hz, 1.92H), 1.53 (s, 1.08H), 1.54 (s, 1.92H), 1.57-1.84 (m, 3.36H), 1.67 (s, 1.08H), 1.72 (s, 1.92H), 1.88-1.98 (m, 0.64H), 2.20 (s, 1.92H), 2.21 (s, 1.08H), 2.60-

2.73(m, 0.64H), 2.75-2.87 (m, 0.36H), 4.14-4.28 (m, 1H), 5.19-5.47 (br, 1H), 6.59-6.65 (m, 1.64H), 6.69 (dd, *J* = 7.8, 1.7 Hz, 0.36H), 7.01 (d, *J* = 7.8 Hz, 0.64H), 7.03 (d, *J* = 7.8 Hz, 0.36H). HRMS (ESI+) Calcd for $C_{15}H_{22}NaO_2$ ($M+Na^+$) 257.1512 found 257.1513.

(b) Intramolecular Friedel-Crafts cyclization of allylic alcohol. To a solution of allylic alcohol **3** (14.0 mg, 0.06 mmol) in CH_2Cl_2 (19.8 mL) was added anhydrous $FeCl_3$ (11.4 mg, 0.07 mmol) at –15 °C. The mixture was stirred at that temperature for 10 min and treated with saturated $NaHCO_3$ (10 mL). The mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and evaporated. The residue was purified by column chromatography on silica gel (hexane/AcOEt = 8:1) to give mutisianthol and *epi*-mutisianthol (10.0 mg, 77% yield, *trans*/*cis* = 54:46, 92% ee), and jungianol and *epi*-jungianol (2.3 mg, 18% yield, *trans*/*cis* = 26:74).

Mutisianthol.[33,34d] TLC: R_f 0.41 (hexane/AcOEt = 5:1, stained black with anisaldehyde). ^{1}H NMR (400 MHz) δ 1.20 (d, *J* = 6.8 Hz, 1.62H, *trans*), 1.28 (d, *J* = 6.8 Hz, 1.38H, *cis*), 1.74 (d, *J* = 0.9 Hz, 1.62H, *trans*), 1.76 (s, 1.38H, *cis*), 1.78 (d, *J* = 0.9 Hz, 1.62H, *trans*), 1.80 (s, 1.38H, *cis*), 1.86-2.00 (m, 0.54H, *trans*), 2.21 (s, 1.62H, *trans*), 2.22 (s, 1.38H, *cis*), 2.39-2.47 (m, 0.46H, *cis*), 2.99-3.08 (m, 0.46H, *cis*), 3.16-3.24 (m, 0.54H, *trans*), 3.75-3.84 (m, 0.46H, *cis*), 3.93-4.01 (m, 0.54H, *trans*), 4.57 (brs, 1H), 5.07-5.14 (m, 1H), 6.62 (s, 1H), 6.78 (s, 0.46H, *cis*), 6.81 (s, 0.54H, *trans*). HPLC (Chiralpak IA-3, hexane/2-propanol = 29:1, 1.0 mL/min, 220 nm) t_R = 10.0 min (*major*, *trans*), 15.4 min (*major*, *cis*), 16.6 min (*minor*, *cis*), 26.9 min (*minor*, *trans*).

Jungianol.[34g] TLC: R_f 0.45 (hexane/AcOEt = 5:1, stained stain light red with anisaldehyde). ^{1}H NMR (400 MHz) δ 1.19 (d, *J* = 7.2 Hz, 0.78H, *trans*), 1.30 (d, *J* = 6.8 Hz, 2.22H, *cis*), 1.80 (d, *J* = 0.9 Hz, 0.78H, *trans*), 1.82 (d, *J* = 0.9 Hz, 2.22H, *cis*), 1.87 (d, *J* = 0.9 Hz, 3H), 1.92-2.08 (m, 0.26H, *trans*), 2.19 (s, 3H), 2.38-2.47 (m, 0.74H, *cis*), 3.02-3.11 (m, 0.74H, *cis*), 3.21-3.30 (m, 0.26H, *trans*), 3.95-4.05 (m, 0.74H, *cis*), 4.13-4.23 (m, 0.26H, *trans*), 5.29 (brd, *J* = 9.0 Hz, 0.26H, *trans*), 5.34 (brd, *J* = 9.8 Hz, 0.74H, *cis*), 5.60 (brs, 0.26H, *trans*), 5.94 (brs, 0.74H, *cis*), 6.67 (d, *J* = 7.3 Hz, 0.74H, *cis*), 6.68 (d, *J* = 7.3 Hz, 0.26H, *trans*), 6.96 (d, *J* = 7.3 Hz, 0.26H, *trans*), 6.98 (d, *J* = 7.3 Hz, 0.74H, *cis*).

ASSOCIATED CONTENT

Supporting Information

^{1}H and $^{13}C\{^{1}H\}$ NMR spectra, HPLC traces of optically active compounds, and computational methods with the full Gaussian 09 reference, including optimized geometries (Cartesian coordinates), energies, and the number of imaginary frequencies of all stationary points (PDF). This Supporting Information is available free of charge on the ACS Publications website at DOI:

AUTHOR INFORMATION

Corresponding Author

msugiura@ph.sojo-u.ac.jp

Author Contributions

All authors have given approval to the final version of the manuscript.

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REFERENCES

REFERENCES

(1) For reviews on transition metal-catalyzed asymmetric conjugate reduction of enones, see: (a) Pfaltz, A. Chiral Semicorrins and Related Nitrogen Heterocycles as Ligands in Asymmetric Catalysis. *Acc. Chem. Res*. **1993**, *26*, 339–345. (b) Deutsch, C.; Krause, N.; Lipshutz, B. H. CuH-Catalyzed Reactions. *Chem. Rev.* **2008,** *108*, 2916–2927.

(2) For representative examples of transition metal-catalyzed asymmetric conjugate reduction of α,β-

unsaturated carbonyl compounds, see: (a) Leutenegger, U.; Madin, A.; Pfaltz, A. Enantioselective Reduction of α,β-Unsaturated Carboxylates with $NaBH_4$ and Catalytic Amounts of Chiral Cobalt Semicorrin Complexes. *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 60–61. (b) Yamada, T.; Ohtsuka, Y.; Ikeno, T. Enantioselective Borohydride 1,4-Reduction of α,β-Unsaturated Carboxamides Using Optically Active Cobalt(II) Complex Catalysts. *Chem. Lett.* **1998,** *27*, 1129–1130. (c) Appella, D. H.; Moritani, Y.; Shintani, R.; Ferreira, E.; Buchwald, S. L. Asymmetric Conjugate Reduction of α,β-Unsaturated Esters Using a Chiral Phosphine-Copper Catalyst. *J. Am. Chem. Soc*. **1999**, *121*, 9473–9474. (d) Lipshutz, B. H.; Servesko, J. M. CuH-Catalyzed Asymmetric Conjugate Reductions of Acyclic Enones. *Angew. Chem. Int. Ed.* **2003,** *42*, 4789–4792. (e) Lipshutz, B. H.; Servesko, J. M.; Petersen, T. B.; Papa, P. P.; Lover, A. A. Asymmetric 1,4-Reductions of Hindered β-Substituted Cycloalkenones Using Catalytic SEGPHOS-Ligated CuH. *Org. Lett.* **2004,** *6*, 1273–1275. (f) Kanazawa, Y.; Tsuchiya, Y.; Kobayashi, K.; Shiomi, T.; Itoh, J.; Kikuchi, M.; Yamamoto, Y.; Nishiyama, H. Asymmetric Conjugate Reduction of α,β-Unsaturated Ketones and Esters with Chiral Rhodium(2,6-bisoxazolinylphenyl) Catalysts. *Chem. Eur. J.* **2005,** *12*, 63–71. (g) Tsuchiya, Y.; Hamashima, Y.; Sodeoka, M. A New Entry to Pd-H Chemistry: Catalytic Asymmetric Conjugate Reduction of Enones with EtOH and a Highly Enantioselective Synthesis of Warfarin. *Org*. *Lett*. **2006,** *8*, 4851–4854. (h) Lu, S. M.; Bolm, C. Highly Chemo- and Enantioselective Hydrogenation of Linear α,β-Unsaturated Ketones. *Chem. Eur. J.* **2008,** *14*, 7513–7516.

(3) For reviews on organocatalysts: (a) Dalko, P. I.; Moisan, L. Enantioselective Organocatalysis. *Angew. Chem. Int. Ed*. **2001**, *40*, 3726–3748. (b) Dalko, P. I.; Moisan, L. In the Golden Age of Organocatalysis. *Angew. Chem. Int. Ed.* **2004**, *43*, 5138–5175.

(4) For asymmetric conjugate reduction by organocatalysts, see: (a) Martin, N. J.; List, B. Highly Enantioselective Transfer Hydrogenation of α,β-Unsaturated Ketones. *J. Am. Chem. Soc.* **2006,** *128*, 13368–13369. (b) Tuttle, J. B.; Ouellet, S. G.; MacMillan, D. W. Organocatalytic Transfer Hydrogenation of Cyclic Enones. *J. Am. Chem. Soc.* **2006,** *128*, 12662–12663. (c) Ouellet, S. G.; Walji, A. M.; MacMillan, D. W. Enantioselective Organocatalytic Transfer Hydrogenation Reactions Using Hantzsch Esters. *Acc. Chem. Res.* **2007,** *40*, 1327–1339.

(5) For the preliminary communication, see: Sugiura, M.; Sato, N.; Kotani, S.; Nakajima, M. Lewis Base-catalyzed Conjugate Reduction and Reductive Aldol Reaction of α,β-Unsaturated Ketones Using

Trichlorosilane. *Chem. Commun.* **2008**, 4309–4311.

(6) For Lewis base-catalyzed conjugate reduction and reductive aldol reaction with trichlorosilane, see: (a) Sugiura, M.; Kumahara, M.; Nakajima, M. Asymmetric Synthesis of 4*H*-1,3-Oxazines: Enantioselective Reductive Cyclization of *N*-Acylated β-Amino Enones with Tichlorosilane Catalyzed by Chiral Lewis Bases. *Chem. Commun.* **2009**, 3585–3587. (b) Sugiura, M.; Sato, N.; Sonoda, Y.; Kotani, S.; Nakajima, M. Diastereo- and Enantioselective Reductive Aldol Reaction with Trichlorosilane Using Chiral Lewis Bases as Organocatalysts. *Chem. Asian J.* **2010**, *5*, 478–481. (c) Han, Z. S.; Zhang, L.; Xu, Y.; Sieber, J. D.; Marsini, M. A.; Li, Z.; Reeves, J. T.; Fandrick, K. R.; Patel, N. D.; Desrosiers, J. N.; Qu, B.; Chen, A.; Rudzinski, D. M.; Samankumara, L. P.; Ma, S.; Grinberg, N.; Roschangar, F.; Yee, N. K.; Wang, G.; Song, J. J.; Senanayake, C. H. Efficient Asymmetric Synthesis of Structurally Diverse P-Stereogenic Phosphinamides for Catalyst Design. *Angew. Chem. Int. Ed.* **2015,** *54*, 5474–5477. (d) Yang, H.; Weng, G.; Fang, D.; Peng, C.; Zhang, Y.; Zhang, X.; Wang, Z. Enantioselective Conjugate Hydrosilylation of α,β-Unsaturated Ketones. *RSC Adv.* **2019**, *9*, 11627-11633.

(7) For the use of (*S*)-BINAPO or related chiral Lewis base catalysts in our laboratory, see: (a) Kotani, S.; Sugiura, M.; Nakajima, M. Enantioselective Aldol Reactions Catalyzed by Chiral Phosphine Oxides. *Chem. Rec.* **2013**, *13*, 362–370. (b) Kotani, S.; Ito, M.; Nozaki, H.; Sugiura, M.; Ogasawara, M.; Nakajima, M. Enantioselective Morita–Baylis–Hillman Reaction Catalyzed by a Chiral Phosphine Oxide. *Tetrahedron Lett.* **2013**, *54*, 6430–6433. (c) Kotani, S.; Hanamure, T.; Nozaki, H.; Sugiura, M.; Nakajima, M. Enantioselective Chlorinative Aldol Reaction of α-Substituted Acroleins Catalyzed by Chiral Phosphine Oxides. *Tetrahedron: Asymmetry* **2017**, *28*, 282–287. See also ref. 8d.

(8) For reviews on Lewis base catalysts for activation of chlorosilane reagents, see: (a) Oestreich, M.; Rendler, S. Hypervalent Silicon as a Reactive Site in Selective Bond-Forming Processes. *Synthesis* **2005**, 1727–1747. (b) Orito, Y.; Nakajima, M. Lewis Base-catalyzed Asymmetric Reactions Involving Hypervalent Silicate Intermediates. *Synthesis* **2006**, 1391–1401. (c) Benaglia, M.; Guizzetti, S.; Pignataro, L. Stereoselective Reactions Involving Hypervalent Silicate Complexes. *Coord. Chem. Rev.* **2008**, *252*, 492–512. (d) Denmark, S. E.; Beutner, G. L. Lewis Base Catalysis in Organic Synthesis. *Angew. Chem. Int. Ed.* **2008**, *47*, 1560–1638. (e) Ayad, T.; Gernet, A.; Pirat, J.-L.; Virieux, D. Enantioselective Reactions Catalyzed by Phosphine Oxides. *Tetrahedron* **2019**, *75*, 4385–4418.

(9) For reviews on Lewis base-catalyzed stereoselective reduction with trichlorosilane, see: (a) Rossi, S.; Benaglia, M.; Massolo, E.; Raimondi, L. Organocatalytic Strategies for Enantioselective Metal-free Reductions. *Catal. Sci. Technol.* **2014,** *4*, 2708–2723. (b) Jones, S.; Warner, C. J. Trichlorosilane Mediated Asymmetric Reductions of the C=N bond. *Org Biomol Chem* **2012,** *10*, 2189–2200. (c) Guizzetti, S.; Benaglia, M. Trichlorosilane-Mediated Stereoselective Reduction of C=N Bonds. *Eur. J. Org. Chem.* **2010**, 5529–5541.

(10) For selected examples of enantioselective reduction of C=N or C=O bonds with trichlorosilane, see: (a) Iwasaki, F.; Onomura, O.; Mishima, K.; Maki, T.; Matsumura, Y. Catalytic Activation of Trichlorosilane for Efficient and Stereoselective Reduction of Ketones. *Tetrahedron Lett.* **1999**, *40*, 7507–7511. (b) Matsumura, Y.; Ogura, K.; Kouchi, Y.; Iwasaki, F.; Onomura, O. New Efficient Organic Activators for Highly Enantioselective Reduction of Aromatic Ketones by Trichlorosilane. *Org. Lett.* **2006**, *8*, 3789–3792. (c) Malkov, A. V.; Stončius, S.; Vranková, K.; Arndt, M.; Kočovský, P. Dynamic Kinetic Resolution in the Asymmetric Synthesis of β-Amino Acids by Organocatalytic Reduction of Enamines with Trichlorosilane. *Chem. Eur. J.* **2008**, *14*, 8082–8085. (d) Wang, Z.; Ye, X.; Wei, S.; Wu, P.; Zhang, A.; Sun, J. A Highly Enantioselective Lewis Basic Organocatalyst for Reduction of *N*-Aryl Imines with Unprecedented Substrate Spectrum. *Org. Lett.* **2006**, *8*, 999–1001. (e) Ye, J.; Wang, C.; Chen, L.; Wu, X.; Zhou, L.; Sun, J. Chiral Lewis Base-Catalyzed, Enantioselective Reduction of Unprotected β-Enamino Esters with Trichlorosilane. *Adv. Synth. Catal.* **2016**, *358*, 1042–1047. (f) Genoni, A.; Benaglia, M.; Mattiolo, E.; Rossi, S.; Raimondi, L.; Barrulas, P. C., Burke, A. J. Synthesis of an Advanced Precursor of Rivastigmine: Cinchona-derived Quaternary Ammonium Salts as Organocatalysts for Stereoselective Imine Reductions. *Tetrahedron Lett.* **2015**, *56*, 5752–5756. (g) Li, A. T.; Torri, F.; Adams, H.; Jones, S. Mechanistic Investigations of the Asymmetric Hydrosilylation of Ketimines with Trichlorosilane Reveals a Dual Activation Model and an Organocatalyst with Enhanced Efficiency. *Org. Biomol. Chem.* **2017**, *15*, 2422–2435. (h) Chelouan, A.; Recio, R.; Borrego, L. G.; Álvarez, E.; Khiar, N.; Fernández, I. Sulfinamide Phosphinates as Chiral Catalysts for the Enantioselective Organocatalytic Reduction of Imines. *Org. Lett.* **2016**, *18*, 3258–3261. (i) Wagner, C.; Kotthaus, A. F.; Kirsch, S. F. The Asymmetric Reduction of Imidazolinones with Trichlorosilane. *Chem. Commun.* **2017**, *53*, 4513–4516.

(11) Enones were synthesized by the self-condensation of acetophenone derivatives, see: Yatluk, Y. G.;

Sosnovskikh, V. Y.; Suvorov, A. L. Condensation of Ketones in the Presence of Titanium Alkoxides. *Russ. J. Org. Chem.* **2004**, *40*, 763–765.

(12) Reversal of product absolute configuration was generally observed during enantioselective conjugate reductions of enones, see: refs. 2d, 2f, and 2h.

(13) Products with the same absolute configurations are obtained from *E/Z* mixtures of acrylates during the asymmetric hydrogenations of β-(acylamino)acrylates, see: (a) Zhou, Y.-G.; Tang, W.; Wang, W.-B.; Li, W.; Zhang, X. Highly Effective Chiral Ortho-Substituted BINAPO Ligands (o-BINAPO): Applications in Ru-Catalyzed Asymmetric Hydrogenations of β-Aryl-Substituted β-(Acylamino)acrylates and β-Keto Esters. *J. Am. Chem. Soc.* **2002**, *124*, 4952−4953. (b) Tang, W.; Zhang, X. Highly Efficient Synthesis of Chiral β-Amino Acid Derivatives via Asymmetric Hydrogenation. *Org. Lett.* **2002**, *4*, 4159−4161. (c) Fu, Y.; Guo, X.-X.; Zhu, S.-F.; Hu, A.-G.; Xie, J.-H.; Zhou, Q.-L. Rhodium-Catalyzed Asymmetric Hydrogenation of Functionalized Olefins Using Monodentate Spiro Phosphoramidite Ligands. *J. Org. Chem.* **2004**, *69*, 4648−4655.

(14) We have already reported that hydrogen chloride promotes *E*/*Z*-isomerization of β,β-disubstituted enones, see: Sugiura, M.; Ashikari, Y.; Nakajima, M. One-Pot Synthesis of β,β-Disubstituted α,β-Unsaturated Carbonyl Compounds. *J. Org. Chem.* **2015**, *80*, 8830–8835.

(15) Because enones having an aromatic ring at the β-position are stabilized by the long conjugation between the α,β-unsaturated ketone moiety and the aromatic ring, addition of hydrogen chloride to the enone moiety would be energetically disfavored. We reported Lewis base-catalyzed domino chlorination/aldol reactions of enones or ynones with aldehydes, see: refs. 7b, 7c, and 25.

(16) A slight *Z* to *E* isomerization was observed only in the early stage of the reaction, presumably due to the adventitiously generated hydrogen chloride, see ref. 14.

(17) For related computational studies on the reactions of trichlorosilane, see: (a) Bonsignore, M.; Benaglia, M.; Raimondi, L.; Orlandi, M.; Celentano, G. Enantioselective Reduction of Ketoimines Promoted by Easily Available (*S*)-Proline Derivatives. *Beilstein J. Org. Chem.* **2013**, *9*, 633–640. (b) Orlandi, M.; Benaglia, M.; Tosi, F.; Annunziata, R.; Cozzi, F. $HSiCl_3$-mediated Reduction of Nitro-Derivatives to Amines: Is Tertiary Amine-Stabilized $SiCl_2$ the Actual Reducing Species? *J. Org. Chem.* **2016**, *81*, 3037−3041.

(18) For a review on the ONIOM method, see: Chung, L. W.; Sameera, W. M. C.; Ramozzi, R.; Page, A. J.;

Hatanaka, M.; Petrova, G. P.; Harris, T. V.; Li, X.; Ke, Z.; Liu, F.; Li, H.-B.; Ding, L.; Morokuma, K. The ONIOM Method and Its Applications. *Chem. Rev.* **2015**, *115*, 5678–5796.

(19) For edge-to-face interaction, see: (a) Neel, A. J.; Hilton, M. J.; Sigman, M. S.; Toste, F. D. Exploiting non-covalent π interactions for catalyst design. *Nature* **2017**, *543*, 637–646. (b) Jennings, W. B.; Farrell, B. M.; Malone, J. F. Attractive Intramolecular Edge-to-Face Aromatic Interactions in Flexible Organic Molecules. *Acc. Chem. Res.* **2001**, *34*, 885–894. (c) Gardarsson, H.; Schweizer, W. B.; Trapp, N.; Diederich, F. Structures and Properties of Molecular Torsion Balances to Decipher the Nature of Substituent Effects on the Aromatic Edge-to-Face Interaction. *Chem. Eur. J.* **2014**, *20*, 4608–4616. (d) Paliwal, S.; Geib, S.; Wilcox, C. S. Molecular Torsion Balance for Weak Molecular Recognition Forces. Effects of "Tilted-T" Edge-to-Face Aromatic Interactions on Conformational Selection and Solid-State Structure. *J. Am. Chem. Soc.* **1994**, *116*, 4497–4497.

(20) (a) Lee, Y. Activation of Apoptotic Protein in U937 Cells by a Component of Turmeric Oil. *BMB Rep.* **2009**, *42*, 96–100. (b) Park, S. Y.; Jin, M. L.; Kim, Y. H.; Kim, Y.; Lee, S. J. Anti-inflammatory Effects of Aromatic-turmerone through Blocking of NF-κB, JNK, and p38 MAPK Signaling Pathways in Amyloid β-Stimulated Microglia. *Int. Immunopharmacol.* **2012,** *14*, 13–20. (c) Park, S. Y.; Kim, Y. H.; Kim, Y.; Lee, S. J. Aromatic-Turmerone Attenuates Invasion and Expression of MMP-9 and COX-2 Through Inhibition of NF-κB Activation in TPA-Induced Breast Cancer Cells. *J. Cell. Biochem.* **2012**, *113*, 3653. (d) Park, S. Y.; Kim, Y. H.; Kim, Y.; Lee, S. J. Aromatic-turmerone's Anti-inflammatory Effects in Microglial Cells Are Mediated by Protein Kinase A and Heme Oxygenase-1 Signaling. *Neurochem. Int.* **2012,** *61*, 767–777. (e) Mythri, R. B.; Bharath, M. M. Curcumin: A Potential Neuroprotective Agent in Parkinson's Disease. *Curr. Pharm. Des.* **2012**, *18*, 91–99. See also: (f) Esatbeyoglu, T.; Huebbe, P.; Ernst, I. M.; Chin, D.; Wagner, A. E.; Rimbach, G. Curcumin—From Molecule to Biological Function. *Angew. Chem. Int. Ed.* **2012,** *51*, 5308–5332.

(21) Hucklenbroich, J.; Klein, R.; Neumaier, B.; Graf, R.; Fink, G. R.; Schroeter, M.; Rueger, M. A. Aromatic-turmerone Induces Neural Stem Cell Proliferation *In Vitro* and *In Vivo*. *Stem. Cell. Res. Ther.* **2014,** *5*, 100.

(22) For selected examples of asymmetric synthesis of *ar*-turmerone, see: (a) Meyers, A. I.; Smith, R. K. A Total Asymmetric Synthesis of (+)-*ar*-Turmerone. *Tetrahedron Lett.* **1979**, *20*, 2749–2752. (b) Li, A.; Yue, G.; Li, Y.; Pan, X.; Yang, T.-K. Total Asymmetric Synthesis of (7*S*,9*R*)-(+)-Bisacumol. *Tetrahedron: Asymmetry* **2003**, *14*, 75–78. (c) Zhang, A.; RajanBabu, T. V. Chiral Benzyl Centers through Asymmetric Catalysis. A

Three-step Synthesis of (*R*)-(–)-α-Curcumene via Asymmetric Hydrovinylation. *Org. Lett.* **2004**, *6*, 3159–3161. (d) Mori, K. Synthesis of (*R*)-*ar*-Turmerone and Its Conversion to (*R*)-*ar*-Himachalene, a Pheromone Component of the Flea Beetle: (*R*)-*ar*-Himachalene is Dextrorotatory in hexane, while Levorotatory in Chloroform. *Tetrahedron: Asymmetry* **2005**, *16*, 685–692. (e) Nave, S.; Sonawane, R. P.; Elford, T. G.; Aggarwal, V. K. Protodeboronation of Tertiary Boronic Esters: Asymmetric Synthesis of Tertiary Alkyl Stereogenic Centers. *J. Am. Chem. Soc.* **2010**, *132,* 17096–17098. (f) Afewerki, A.; Breistein, P.; Pirttila, K.; Deiana, L.; Dziedzic, P.; Ibrahem, I.; Cordova, A. Catalytic Enantioselective β-Alkylation of α,β-Unsaturated Aldehydes by Combination of Transition-Metal- and Aminocatalysis: Total Synthesis of Bisabolane Sesquiterpenes. *Chem. Eur. J.* **2011**, *17*, 8784–8788. (g) Endo, K.; Hamada, D.; Yakeishi, S.; Shibata, T. Effect of Multinuclear Copper/Aluminum Complexes in Highly Asymmetric Conjugate Addition of Trimethylaluminum to Acyclic Enones. *Angew. Chem. Int. Ed.* **2013**, *52*, 606–610. (h) Mao, J.; Liu, F.; Wang, M.; Lin, W.; Zheng, B.; Liu, S.; Zhong, J.; Bian, Q.; Walsh, P. J. Cobalt–Bisoxazoline-catalyzed Asymmetric Kumada Cross-Coupling of Racemic α-Bromo Esters with Aryl Grignard Reagents. *J. Am. Chem. Soc.,* **2014**, *136,* 17662–17668. (i) Drissi-Amraoui, S.; Morin, M. S. T.; Crevisy, C.; Basle, O.; Marcia de Figueiredo, R.; Mauduit, M.; Campagne, J.-M. Copper-Catalyzed Asymmetric Conjugate Addition of Dimethylzinc to Acyl-*N*-methylimidazole Michael Acceptors: a Powerful Synthetic Platform. *Angew. Chem. Int. Ed.* **2015**, *54*, 11830–11834.

(23) For an alternative synthesis of *ar*-atlantone, see: Sakai, T.; Miyata, K.; Ishikawa, M.; Takeda, A. A Novel Synthetic Method of Dihydro-4-pyrone Derivatives and Its Application to the Syntheses of *ar*-Atlantone and (±)-*ar*-Turmerone. *Tetrahedron Lett.* **1985**, *26*, 4727–4730.

(24) Hayashi, T.; Senda, T.; Takaya, Y.; Ogasawara, M. Rhodium-catalyzed Asymmetric 1,4-Addition to 1-Alkenylphosphonates. *J. Am. Chem. Soc.* **1999**, *121*, 11591–11592.

(25) Ohmaru, Y.; Sato, N.; Mizutani, M.; Kotani, S.; Sugiura, M.; Nakajima, M. Synthesis of Aryl Group-modified DIOP Dioxides (Ar-DIOPOs) and Their Application as Modular Lewis Base Catalysts. *Org. Biomol. Chem.* **2012**, *10*, 4562–4570.

(26) (a) Kant, M.; Bischoff, S.; Siefken, R.; Gründemann, E.; Köckritz, A. Synthesis and Characterization of 4- and 4,4'-Phosphorylated 2,2'-Bis(diphenylphosphanyl)-1,1'-binaphthyls. *Eur. J. Org. Chem.* **2001,** 477–481. (b) Dayoub, W.; Favre-Reguillon, A.; Berthod, M.; Jeanneau, E.; Mignani, G.; Lemaire, M. An Improved and

Safer Synthesis of (*R*)- and (*S*)-4,4'-Diaminomethyl-BINAP. *Eur. J. Org. Chem.* **2012,** 3074–3078.

(27) A similar tendency was observed in BINOL-catalyzed conjugate addition of boronates to enones, see: Nguyen, T. S.; Yang, M. S.; May, J. A. Experimental Mechanistic Insight into the BINOL-catalyzed Enantioselective Conjugate Addition of Boronates to Enones. *Tetrahedron Lett.* **2015**, *56*, 3337–3341.

(28) (a) Imai, S.; Morikiyo, M.; Furihata, K.; Hayakawa, Y.; Seto, H. Turmeronol A and Turmeronol B, New Inhibitors of Soybean Lipoxygenase. *Agric. Biol. Chem.* **1990**, *54*, 2367–2371. (b) Khan, M. G. U.; Nahar, K.; Rahman, M. S.; Hasan, C. M.; Rashid, M. A. Phytochemical and Biological Investigations of *Curcuma longa. Dhaka Univ. J. Pharm. Sci.*, **2008**, *8*, 39–45.

(29) (a) Serra, S. Lipase-mediated Resolution of Substituted 2-Aryl-propanols: Application to the Enantioselective Synthesis of Phenolic Sesquiterpenes. *Tetrahedron: Asymmetry* **2011**, *22*, 619–628. (b) Tanaka, K.; Nuruzzaman, M.; Yoshida, M.; Asakawa, N.; Yang, X.-S.; Tsubaki, K.; Fuji, K. Use of 1,1'-Binaphthalene-8,8'-diol as a Chiral Auxiliary for Asymmetric Michael Addition. Application to the Syntheses of Turmeronol A and B. *Chem. Pharm. Bull.*, **1999**, *47*, 1053–1055.

(30) Yuan, C.; Liang, Y.; Hernandez, T.; Berriochoa, A.; Houk, K. N.; Siegel, D. Metal-free Oxidation of Aromatic Carbon–Hydrogen Bonds through a Reverse-rebound Mechanism. *Nature* **2013**, *499*, 192–196.

(31) Rieche, A.; Gross, H.; Höft, E. Aromatic Aldehyde. Mesitaldehyde. *Org. Synth.* **1967**, *49*, 1.

(32) Mandal, S.; Mukhopadhyay, A.; Moorthy, J. N. Photochromism of Acetyl-Cyclophanochromene: Intriguing Stabilization of Photogenerated Colored *o*-Quinonoid Intermediates. *Eur. J. Org. Chem.* **2015**, 1403–1408.

(33) Bianco, G. G.; Ferraz, H. M. C.; Costa, A. M.; Costa-Lotufo, L. V.; Pessoa, C.; de Moraes, M. O.; Schrems, M. G.; Pfalts, A.; Silva, Jr., L. F. (+)- and (–)-Mutisianthol: First Total Synthesis, Absolute Configuration, and Antitumor Activity. *J. Org. Chem.* **2009**, *74*, 2561–2566.

(34) For synthesis of racemic mutisianthol, see: (a) Ho, T.-L.; Lee, K.-Y.; Chen, C.-K. Structural Amendment and Stereoselective Synthesis of Mutisianthol. *J. Org. Chem.* **1997**, *62*, 3365–3369. (b) Ferraz, H. M. C.; Aguilar, A. M.; Silva, Jr., L. F. A Diastereoselective Total Synthesis of the Sesquiterpene (±)-Mutisianthol. *Tetrahedron* **2003**, *59*, 5817–5821. (c) Dethe, D. H.; Boda, R.; Murhade, G. M. Lewis Acid Catalyzed Nazarov Type Cyclization for the Synthesis of a Substituted Indane Framework: Total Synthesis of (±)-Mutisianthol. *Org. Chem. Front.* **2015**, *2*, 645–648. (d) Bhorkade, S. B.; Gavhane, K. B.; Shinde, V. S. Total Synthesis of (±) Mutisianthol and (±) *epi*-Mutisianthol via Intramolecular Oxidative Heck Cyclization

Approach *Tetrahedron* **2016**, *72*, 1954–1959. For synthesis of enantimerically enriched mutisianthol, see ref. 33. For synthesis of racemic jungianol, see: (e) Hashmi, A. S. K.; Ding, L.; Bats, J. W.; Fischer, P.; Frey, W. Gold Catalysis: Efficient Synthesis and Structural Assignment of Jungianol and *epi*-Jungianol. *Chem. Eur. J.* **2003**, *9*, 4339–4345. (f) Dethe, D. H.; Murhade, G. M. $FeCl_3$ Catalyzed Prins-type Cyclization for the Synthesis of Highly Substituted Indenes: Application to the Total Synthesis of (±)-Jungianol and *epi*-Jungianol. *Org. Lett.* **2013**, *15*, 429–431. (g) Dethe, D. H.; Murhade, G. M.; Ghosh, S. $FeCl_3$-catalyzed Intramolecular Michael Reaction of Styrenes for the Synthesis of Highly Substituted Indenes. *J. Org. Chem.* **2015**, *80*, 8367–8376.

(35) Luche, J.-L. Lanthanides in Organic Chemistry. 1. Selective 1,2 Reductions of Conjugated Ketones. *J. Am. Chem. Soc.* **1978**, *100*, 2226–2227.

(36) Yu, W.; Hjerrild, P.; Overgaard, J.; Poulsen, T. B. A Concise Route to the Strongylophorines. *Angew. Chem. Int. Ed.* **2016**, *55*, 8294–8298. See also refs. 34f and 34g.

(37) Kotani, S.; Hashimoto, S.; Nakajima, M. Chiral Phosphine Oxide BINAPO as a Lewis Base Catalyst for Asymmetric Allylation and Aldol Reaction of Trichlorosilyl Compounds, *Tetrahedron*, **2007**, *63*, 3122–3132.

(38) Park, Y.; Min, J.; Eom, D.; Lee, P. H. Synthesis of Acyl Alkenylindium Reagents and Their Application in the Synthesis of (*Z*)-α,β-Unsaturated Ketones via Palladium-Catalyzed Cross-Coupling Reaction. *Org. Lett.* **2015**, *17*, 3934–3937.

(39) Nishikawa, Y.; Yamamoto, H. Iron-Catalyzed Asymmetric Epoxidation of β,β-Disubstituted Enones. *J. Am. Chem. Soc.* **2011**, *133*, 8432–8435.

(40) Ibuka, T.; Tabushi, E.; Yasuda, M. Highly Regio-and Stereoselective 1, 4-Addition Reaction of β-Cyclopropyl- α,β-enones with Organocopper (I)-Aluminum Trichloride. *Chem. Pharm. Bull.* **1983**, *31*, 128–134.

(41) (*E*)-4-Phenylpent-3-en-2-one was prepared in two steps *via* $InCl_3$-catalyzed addition of ethyl acetylacetonate to phenylacetylene followed by decarbonylation (Krapcho reaction), see: (a) Zhang, J.; Blazecka, P. G.; Angell, P.; Lovdahl, M.; Curran, T. T. Indium (III) Mediated Markovnikov Addition of Malonates and β-Ketoesters to Terminal Alkynes and the Formation of Knoevenagel Condensation Products. *Tetrahedron*, **2005**, *61*, 7807–7813. (b) Chowdhury, R.; Ghosh, S. K. Enantioselective Route to β-

Silyl- δ-keto Esters by Organocatalyzed Regioselective Michael Addition of Methyl Ketones to a (Silylmethylene)malonate and Their Use in Natural Product Synthesis. *Synthesis*, **2011**, 1936–1945.

(42) Denmark, S. E.; Amishiro, N. Palladium-catalyzed Conjugate Addition of Organosiloxanes to α,β-Unsaturated Carbonyl Compounds and Nitroalkenes. *J. Org. Chem.* **2003**, *68*, 6997–7003.

(43) Makarov, I. S.; Madsen, R. Ruthenium-catalyzed Self-coupling of Primary and Secondary Alcohols with theLiberation of Dihydrogen. *J. Org. Chem.* **2013**, *78*, 6593–6598.

(44) Matsumoto, S.; Koitabashi, S.; Otani, Y.; Akazome, M. HI Gas as a Reagent for α-Alkylation Reaction with Two Ketone Molecules. *Tetrahedron Lett.* **2015**, *56*, 4320–4323.

(45) Isleyen, A.; Dogan, Ö. Application of Ferrocenyl Substituted Aziridinylmethanols (FAM) as Chiral Ligands in Enantioselective Conjugate Addition of Diethylzinc to Enones. *Tetrahedron: Asymmetry* **2007**, *18*, 679–684.

(46) Abbrecht, H.; Sommer, H. Chirale Homoenolat-Äquivalente, III Asymmetrische Synthese 3-Substituierter 3-Phenylketone über Metallierte SMP-Allylamine. *Chem. Ber.* **1990**, *123*, 829–836.

(47) Huffman, J. W.; Starnes, J. J. Friedel-Crafts Reaction of 3, 4, 4-Trimethylbutyrolactone and Benzene. *J. Org. Chem.* **1972**, *37*, 487–490.

(48) Umeda, R.; Takahashi, Y.; Nishiyama, Y. Rhenium Complex-catalyzed Coupling Reaction of Enol Acetates with Alcohols. *Tetrahedron Lett.* **2014**, *55*, 6113–6116.

(49) Matsuda, T.; Makino, M.; Murakami, M. Addition/Ring-Opening Reaction of Organoboronic Acids to Cyclobutanones Catalyzed by Rhodium(I)/P(*t*-Bu)$_3$ Complex. *Bull. Chem. Soc. Jpn.* **2005**, *78*, 1528–1533.

(50) Nishimoto, Y.; Onishi, Y.; Yasuda, M.; Baba, A. α-Alkylation of Carbonyl Compounds by Direct Addition of Alcohols to Enol Acetates. *Angew. Chem. Int. Ed.* **2009**, *48*, 9131–9134.

(51) Inagaki, T.; Phong, L. T.; Furuta, A.; Ito, J.; Nishiyama, H. Iron- and Cobalt-catalyzed Asymmetric Hydrosilylation of Ketones and Enones with Bis (oxazolinylphenyl)amine Ligands. *Chem. Eur. J.* **2010**, *16*, 3090–3096.

(52) Kalutharage, N.; Yi, C. S. Deaminative and Decarboxylative Catalytic Alkylation of Amino Acids with Ketones. *Angew. Chem. Int. Ed,* **2013**, *52*, 13651–13655.

(53) Kashima, C.; Yamamoto, Y. The Regioselective Amino-exchange Reaction of β-Amino Conjugated Enones. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1735–1737.

(54) Young, S. T.; Turner, J. R.; Tarbell, D. S. Synthetic Studies in the Fumagillin Series. *J. Org. Chem.* **1963**, *28*, 928–932.