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Asymmetric Conjugate Reduction of α,β-Unsaturated Ketones and Esters with Chiral Rhodium(2,6-bisoxazolinylphenyl) Catalysts

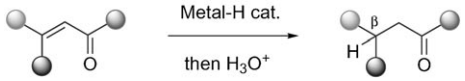
Yoshinori Kanazawa, Yasunori Tsuchiya, Kazuki Kobayashi, Takushi Shiomi, Jun-ichi Itoh, Makoto Kikuchi, Yoshihiko Yamamoto, and Hisao Nishiyama*[a]

Abstract: New asymmetric conjugate reduction of β,β-disubstituted α,β-unsaturated ketones and esters was accomplished with alkoxylhydrosilanes in the presence of chiral rhodium(2,6-bisoxazolinylphenyl) complexes in high yields and high enantioselectivity. (*E*)-4-Phenyl-3-penten-2-one and (*E*)-4-phenyl-4-isopropyl-3-penten-2-one were readily reduced at 60 °C in 95 % *ee* and 98 % *ee*, respectively, by 1 mol % of catalyst loading. $(EtO)_2MeSiH$ proved to be the best hydrogen donor of choice. *tert*-Butyl (*E*)-β-methylcinnamate and β-isopropylcinnamate could also be reduced to the corresponding dihydrocinnamate derivatives up to 98 % *ee*.

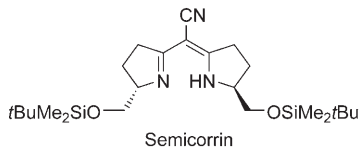
Keywords: asymmetric catalysis · conjugate reduction · hydrosilanes · oxazolines · rhodium

Introduction

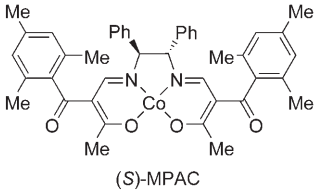
Asymmetric conjugate reduction (ACR) of β,β-disubstituted α,β-unsaturated carbonyl compounds is a very important practical synthetic method (Scheme 1), leading to a variety of optically active compounds bearing an asymmetric center at the β-position.[1] In order to resolve this issue, several chiral transition-metal catalysts in combination with hydride donors, such as borohydride or hydrosilanes, have been developed to demonstrate their high efficiency. However, the scope of metal catalysts has been limited only to cobalt and copper catalysts. The pioneering approach of ACR of α,β-unsaturated esters, carboxamides, nitriles, and sulfones, was disclosed in 1989 by Pfaltz et al. with semicorrin–cobalt catalyst and borohydride.[2] In 1998, Yamada et al. reported the aldiminate–cobalt complex (*S*)-MPAC as an efficient catalyst with modified borohydride for ACR of carboxamides.[3] Very recently, Reiser et al. reported that the azabis(oxazoline) is a superior ligand for cobalt-catalyzed ACR of esters and carboxamides.[4] On the other hand, as for copper catalysts, chiral copper–hydride species generated by reaction of CuCl/NaO*t*Bu/TolBINAP and PMHS (PMHS = polymethylhydrosiloxane) was reported by Buchwald et al. in 1999 to show higher enantioselectivity for esters, and the system was then applied to ACR giving optically active cyclopentanones, lactones, lactams, and β-azaheterocyclic acid derivatives.[5] Around the same time, Lipshutz et al. also reported that copper catalysts bearing chiral bisphosphine, JOSI-



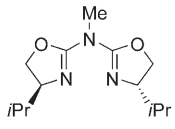
Scheme 1. Asymmetric conjugate reduction of α,β-unsaturated carbonyl compounds.



Semicorrin



(*S*)-MPAC



Azabis(oxazoline)

[a] Y. Kanazawa, Dr. Y. Tsuchiya, K. Kobayashi, T. Shiomi, Dr. J.-i. Itoh, Prof. M. Kikuchi, Prof. Y. Yamamoto, Prof. H. Nishiyama
Department of Applied Chemistry
Graduate School of Engineering, Nagoya University
Chikusa, Nagoya 464–8603 (Japan)
Fax: (+81) 52-789-3209
E-mail: hnishi@apchem.nagoya-u.ac.jp

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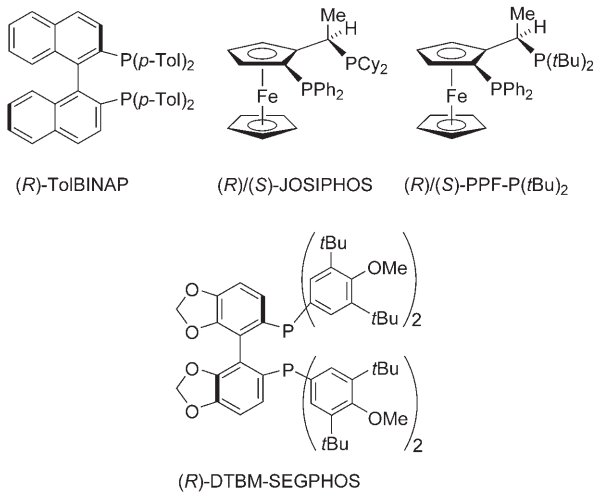
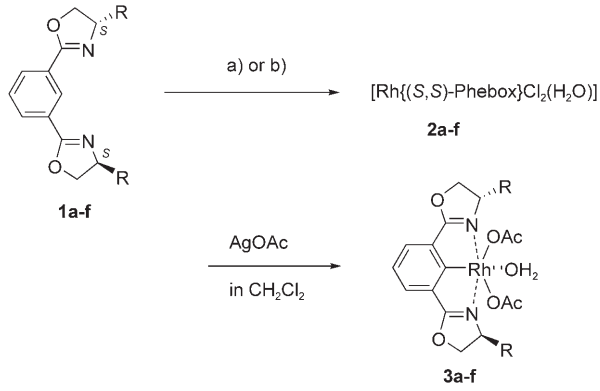




Scheme 2. a) $RhCl_3 \cdot 3H_2O$, $NaHCO_3$, in $MeOH/H_2O$, 60°; b) [{Rh(cyclooctene)$_2$Cl}$_2$], $NaHCO_3$, in $CHCl_3$, reflux; R = *i*Pr **a**, *s*Bu **b**, *i*Bu **c**, *t*Bu **d**, Bn **e**, Ph **f**.

PHOS, PPF-P(*t*-Bu)2, and DTBM-SEGPHOS, were effective toward ACR of cycloalkenones, acyclic enones, and esters.[6] In parallel, a variety of conjugate reduction systems have been also developed by using nonchiral copper catalysts.[7] More noteworthy are chiral metal-free organocatalysts for ACR of α,β-unsaturated aldehydes in the combination of dihydropyridine as a hydride donor, reported independently very recently by MacMillan et al. and List et al.[8]

We have already reported the synthesis of a chiral 2,6-bis(2-oxazolinyl)phenyl skeleton (abbreviated as Phebox) as a C_2-symmetric tridentate N-C-N ligand and its transition-metal complexes, which exhibit high potential in several high stereo- and enantioselective reactions as a new type of transition-metal Lewis acid.[9] We have recently reported that chiral Rh–Phebox catalysts show a catalytic activity for hydrosilylation of monosubstituted and α,β-disubstituted alkenes with alkoxyhydrosilanes.[10] On this basis, we considered that the asymmetric conjugate reduction of α,β-unsaturated carbonyl compounds might be accomplished in the same way by asymmetric hydrosilylation with Rh–Phebox catalysts. We report here highly efficient ACR of α,β-unsaturated ketones and esters. The case of the esters has been already reported in preliminary communication.[11]

Results and Discussion

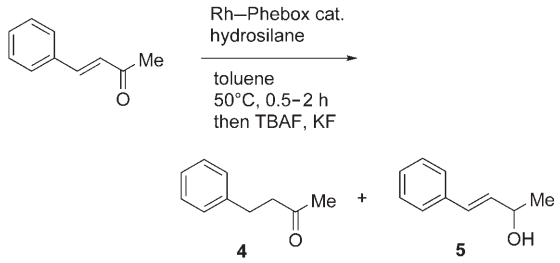
Convenient synthesis of Rh–Phebox complexes by simple C–H bond activation: The starting ligand **1** was synthesized in two steps by condensation of isophthaloyl chloride and an optically active aminoalcohol, followed by oxazoline formation with methanesulfonyl chloride and triethylamine. Heating of a mixture of the ligand, $RhCl_3(H_2O)_3$, and $NaHCO_3$ in methanol and water gave the corresponding chloride complex **2** in a moderate yield of approximately 50% (Scheme 2). As yet, we have been unable to improve this C–H bond activation process to attain high yield. As an alternative convenient synthetic method, we recently found that heating a mixture of [{Rh^{I}(cylcooctene)$_2$Cl}$_2$] and the ligand in $CHCl_3$ gave the complex **2** in a moderate yield. It was thought that coordination of the nitrogen ligand **1** to the monovalent rhodium complex accelerated oxidation by chloroform to form a $RhCl_3$–(Phebox/H, *N*,*N*-bidentate) species, which might readily cause a C–H bond cleavage giving the complex **2**. The complexes **2** were then readily converted to the corresponding acetate complexes **3** by treatment with an excess of silver acetate.

Conjugate reduction of α,β-unsaturated ketones: The conjugate reduction of α,β-unsaturated ketones commonly suffers from concurrent 1,2-reduction giving allylic alcohols. However, in 1982 Ojima et al. discovered almost complete regioselective reduction of α,β-unsaturated ketones by hydrosilylation using Wilkinson catalyst [$RhCl(Ph_3P)_3$].[12] In that system, it is important to choose a hydrosilane as a hydride donor. Use of Et_3SiH or $EtMe_2SiH$ leads to conjugate reduction (1,4-reduction) followed by hydrolysis giving ketones, whereas Ph_2SiH_2 leads exclusively to 1,2-reduction giving allylic alcohols. Keinan et al. also developed the efficient hydrosilative 1,4-reduction systems with palladium- and molybdenum-based catalytic systems, [$Pd(Ph_3P)_4$]/$ZnCl_2$/Ph_2SiH_2 and [$Mo(CO)_6$]/$PhSiH_3$, respectively.[13] Alternatively, the copper–hydride systems have recently been reported by several research groups, as mentioned above.[7]

First, we examined the reduction of benzalacetone with the Rh–Phebox catalysts **2a** and **3a** (1 mol%; Table 1). The catalytic reactions with hydrosilanes, such as $(EtO)_2MeSiH$, Et_2MeSiH, and Me_2PhSiH, proceeded smoothly at 50°C within 2 h. The acetate complex **3a** proved to be superior for 1,4-reduction to the chloride complex **2a**, giving the ketone **4** in addition to Et_2MeSiH. No asymmetric induction was observed for the 1,2-reduction product, (*E*)-4-phenyl-3-buten-2-ol (**5**), which was obtained in the case with **2a**.

As we thus found the catalytic system for the exclusive conjugate reduction, we in turn carried out an asymmetric case to adopt (*E*)-4-phenyl-3-penten-2-one (**6**) as a standard probe. The reaction of the ketone **6** (1.0 mmol) was carried out with 1 mol% of the acetate complex **3a** and 1.5 equivalents of the hydrosilanes in a toluene (1.0 mL) at 60°C (Table 2). After hydrolysis treatment, the product ketone **7**

Table 1. Conjugate reduction of benzalacetone.



Catalyst	Silane	1,4-Reduction yield of **4** [%]	1,2-Reduction yield of **5** [%]
2a	$(EtO)_2MeSiH$	72	24
2a	Et_2MeSiH	95	<1
2a	Me_2PhSiH	51	41
3a	$(EtO)_2MeSiH$	95	1
3a	Et_2MeSiH	95	<1
3a	Me_2PhSiH	97	1

Table 2. Asymmetric conjugate reduction of (*E*)-4-phenyl-3-penten-2-one (**6**).[a]

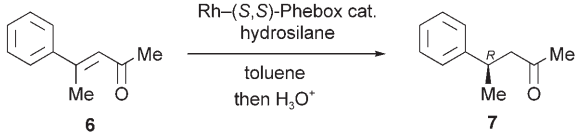
Entry	Cat.	Hydrosilane	Yield [%]	1,4/1,2	*ee* [%]
1	**3a**	$(EtO)Me_2SiH$	92	96/4	54
2	**3a**	$(EtO)_2MeSiH$	96	100/0	91
3[b]	**3a**	$(EtO)_2MeSiH$	97	100/0	95
4	**3a**	$(EtO)_3SiH$	97	100/0	93
5[b]	**3a**	$(EtO)_3SiH$	97	100/0	95
6	**3a**	$(EtO)_2PhSiH$	96	100/0	90
7	**3a**	Et_2MeSiH	94	76/24	14
8	**3a**	Me_2PhSiH	91	91/9	26
9	**3a**	$MePh_2SiH$	92	95/5	51
10[c]	**3a**	Ph_2SiH_2	92	86/14	88
11[d]	**2a**	$(EtO)_3SiH$	30	76/24	8
12[b]	**3b**	$(EtO)_2MeSiH$	92	100/0	95
13[b]	**3c**	$(EtO)_2MeSiH$	94	100/0	76
14[e]	**3d**	$(EtO)_2MeSiH$	94	85/15	1
15	**3e**	$(EtO)_2MeSiH$	93	100/0	73
16[b]	**3f**	$(EtO)_2MeSiH$	97	100/0	81
17[f]	**3a′**	$(EtO)_2MeSiH$	96	100/0	95

[a] Cat. (0.01 mmol, 1 mol%), ketone **6** (1.0 mmol), hydrosilane (1.5 mmol), toluene (1 mL), 60°C, 1 h. [b] At room temperature for 1 h. [c] 60°C, 2 h. [d] 60°C, 21 h. [e] 60°C, 5 h. [f] **3a′**, (*R*,*R*)-Phebox catalyst; the absolute configuration of the product was *S*.

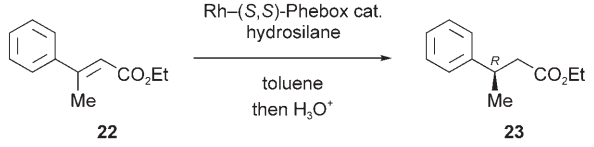
with *R* absolute configuration was isolated in high yield by column chromatography (Scheme 3). Although $(EtO)Me_2SiH$ produced a slight amount of the corresponding 1,2-reduction product, $(EtO)_2MeSiH$ and $(EtO)_3SiH$ exclusively gave the conjugate reduction product **7** in 92–97% yields (Table 2, entries 1, 2, and 4); the % *ee* reached 93% (entry 4). At room temperature, the reaction proceeded smoothly and resulted in an increase of *ee* to 95% (entries 3 and 5). Use of $(EtO)_2PhSiH$ gave 90% *ee* (entry 6). However, alkylhydrosilanes, such as Et_2MeSiH, only promoted 1,2-reduction in 5–24% and in addition to a decrease of % *ee* (entries 7–9). Surprisingly, although Ph_2SiH_2 selectively promoted 1,2-reduction with a Wilkinson catalyst, as demonstrated by Ojima et al.,[12] Rh–Phebox catalyst **3a** mainly leads to the conjugate reduction in 86% with 88% *ee* (entry 10). On the other hand, the reaction with the chloride complex **2a** and $(EtO)_3SiH$ barely proceeded even after long reaction time to give 30% yield and lower selectivity (entry 11). By using the other acetate complexes **3b–f**, the reduction proceeded smoothly to give **7** in high yield (entries 12–16). Although the case of **3d** ($R = t$Bu) did not result in asymmetric induction in the 1,4:1,2 ratio of 85:15, other catalysts gave a middle range of 73–95% *ee*. The reverse absolute configuration of the product was confirmed by use of (*R*,*R*)-Phebox skeleton (entry 17).

Next, we examined the scope of substrate ketones with the catalyst **3a** and $(EtO)_2MeSiH$ at room temperature (Table 3). With the increase in bulkiness of the ketone substituents from methyl to Et < *i*Pr < Ph, the *ee* decreased from 95 to 82% (for **9**, **11**, and **13**). When the methyl group at the β-position of **6** was changed to a bulky isopropyl group, the reduction proceeded very slowly. It took 24 h to complete the reduction of **14** at room temperature and also resulted in a drastic decrease of *ee* to 40%. However, at 60°C the catalysis proceeded smoothly for one hour to give the highest *ee* of 98% (for **15**). With a phenylethyl group at the β-position as in **17** the *ee* was 95%, but with a 4-methyl-3-pentenyl and cyclohexyl group it decreased it to 89 and 65%, respectively (for **19**, **21**). On the other hand, the reduction of (*Z*)-α,β-unsaturated ketone (*Z*)-**6** took place smoothly for 2 h to generate a reverse in the absolute configuration, but significant decrease of *ee* to 51%. In the case of (*Z*)-**17**, the *ee* was 91% with reverse absolute configuration.

Conjugate reduction of α,β-unsaturated esters: The ACR of β,β-disubstituted α,β-unsaturated esters was also conducted by the same method as described above. As a standard ester, (*E*)-ethyl 3-phenylbut-2-enoate (**22**), was chosen to be subjected to the catalysis with Rh–Phebox complexes **2a** and **3a** with several hydrosilanes (Scheme 4). Among the alkoxyhydrosilanes investigated, $(EtO)_2MeSiH$ with 1 mol% of **3a** gave **23** in the highest *ee* (97%) at 30°C (Table 4,

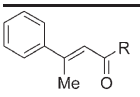
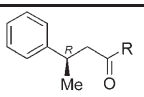
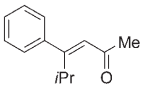
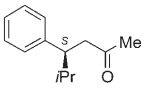
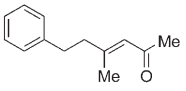
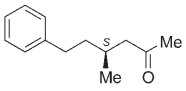
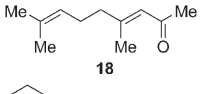
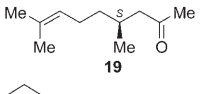
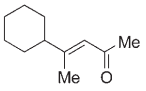
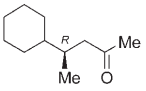
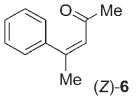
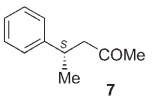
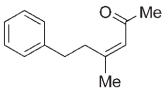
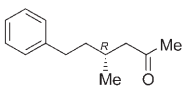


Scheme 3. Asymmetric conjugate reduction of (*E*)-4-phenyl-3-penten-2-one (**6**).



Scheme 4. Asymmetric conjugate reduction of (*E*)-ethyl 3-phenylbut-2-enoate (**22**).

Table 3. Asymmetric conjugate reduction of α,β-unsaturated ketones.[a]

Substrate	Product	Yield [%]	*ee* [%]
			
R = Et **8**	**R** = Et **9**	98	95
		96[b]	94
R = *i*Pr **10**	**R** = *i*Pr **11**	97	92
R = Ph **12**	**R** = Ph **13**	99	82
 **14**	 **15**	95[c]	40
		97[d]	98
 **16**	 **17**	97	95
 **18**	 **19**	97	89
 **20**	 **21**	94	65
 (*Z*)-**6**	 **7**	90[e]	51
 (*Z*)-**16**	 **17**	96	91

[a] Cat. **3a** (0.01 mmol, 1 mol%), ketone (1.0 mmol), $(EtO)_2MeSiH$ (1.5 mmol), toluene (1 mL), RT, 1 h. [b] $(EtO)_3SiH$ (1.5 mmol), RT, 1 h. [c] RT, 24 h. [d] 60 °C, 1 h. [e] RT, 2 h.

Table 4. Asymmetric conjugate reduction of (*E*)-ethyl 3-phenylbut-2-enoate (**22**).[a]

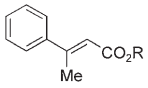
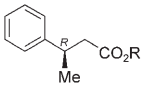
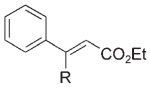
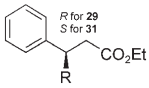
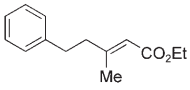
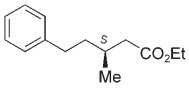
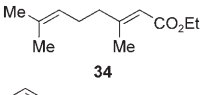
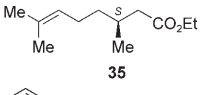
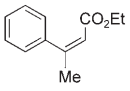
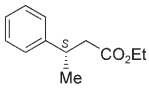
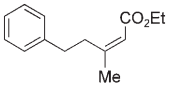
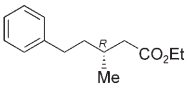
Entry	Cat.	Hydrosilane	*T* [°C]/*t* [h]	Yield [%]	*ee* [%]
1	**3a**	$(EtO)Me_2SiH$	60/3	94	86
2	**3a**	$(EtO)_2MeSiH$	60/1	96	96
3	**3a**	$(EtO)_2MeSiH$	30/1	97	97
4[b]	**3a**	$(EtO)_2MeSiH$	60/24	89	94
5	**2a**	$(EtO)_2MeSiH$	60/5	95	95
6	**2a**	$(EtO)_2MeSiH$	40/24	99	95
7[c]	**2a**	$(EtO)_2MeSiH$	60/2	97	95
8	**3a**	$(EtO)_3SiH$	60/0.5	95	93
9	**2a**	Et_2MeSiH	80/12	30	15
10	**2a**	Me_2PhSiH	80/24	55	64
11	**2e**	$(EtO)_2MeSiH$	60/2	96	69

[a] Cat. (0.01 mmol), **22** (1.0 mmol), hydrosilane (1.5 mmol), toluene (1 mL). [b] **22** (5.0 mmol). [c] $AgBF_4$ (0.02 mmol).

entry 3). Even with decrease of the catalyst loading to 0.2 mol%, the *ee* was only slightly decreased to 94% (entry 4). The chloride catalyst **2a** and the cationic complex were also effective and gave 95% *ee* (entries 6, 7). However, the combination of **2a** and alkylhydrosilanes is not preferable due to decrease of the yields and *ee*, even at higher temperature 80 °C (entries 9, 10). The benzyl catalyst **2e** decreased the *ee* to 69% (entry 11).

Similarly, the substrate scope of the esters was demonstrated with the catalyst **3a** and $(EtO)_2MeSiH$ (Table 5). In most cases, the reactions were retarded at 30 °C. Therefore, the reactions were carried out at 60 °C. The bulky ester moieties such as *i*Pr and *t*Bu slightly increased the *ee* up to 98% (for **25**, **27**), and the β-substituents Et and *i*Pr also increased the *ee* to 98% (for **29**, **31**). However, alkyl substituents for **32** and **34** decreased the *ee* to 91–93% (for **33**, **35**), whereas the reduction of the isomers (*Z*)-**22** and (*Z*)-**32** resulted in reverse of absolute configuration with decrease of *ee*. In the case of (*Z*)-**22**, rapid isomerization from *Z* to *E* was observed during the reaction by an NMR experiment. The isomerization can explain the decrease in *ee*. In this context, Buchwald et al. attained high *ee* for the reduction of (*Z*)-**22** in 92% *ee* with a copper–BINAP catalyst.[5e]

Table 5. Asymmetric conjugate reduction of α,β-unsaturated esters.[a]

Substrate	*T* [°C]/*t* [h]	Product	Yield [%]	*ee* [%]
				
R = *i*Pr **24**	60/1	**R** = *i*Pr **25**	98[b]	97
R = *t*Bu **26**	60/1	**R** = *t*Bu **27**	99	98[b]
				
R = Et **28**	60/1	**R** = Et **29**	99	96
R = *i*Pr **30**	60/0.5	**R** = *i*Pr **31**	97	98
 **32**	60/1	 **33**	96	96
	40/1		91[b]	93
 **34**	60/0.5	 **35**	96	92
 (*Z*)-**22**	60/19	 **23**	81	43
 (*Z*)-**32**	60/1	 **33**	86	81

[a] Cat. **3a** (0.01 mmol, 1 mol%), ester (1.0 mmol), $(EtO)_2MeSiH$ (1.5 mmol), toluene (1 mL). [b] Data were corrected from those previously reported in reference [11].

Limitations of substrate scope: We have examined a variety of β,β-disubstituted α,β-unsaturated carbonyl compounds. In conclusion, cyclic ketones and lactones could not be smoothly reduced under the same standard conditions at room temperature to 60 °C, as described above.

Structure of the catalyst: The molecular structure of **3a** could be analyzed by X-ray crystallography to show its C_2-symmetric form (Figure 1). The Phebox skeleton meridio-

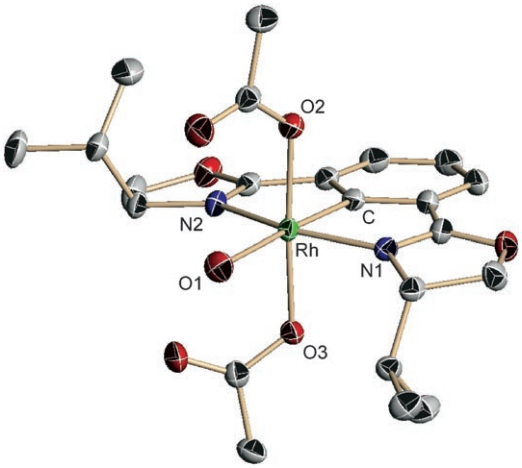


Figure 1. Molecular structure of complex **3a**. Selected bond lengths [Å] and angles [°]: Rh–C 1.9234(18), Rh–N1 2.0579(16), Rh–N2 2.0877(17), Rh–O1 2.2317(15), Rh–O2 2.0473(14), Rh–O3 2.0265 (13); C-Rh-O1 176.06(7), C-Rh-O2 87.29(7), C-Rh-O3 90.26(6), C-Rh-N1 79.50(7), C-Rh-N2 87.73(6), N1-Rh-N2 158.36(7).

nally binds to the rhodium atom with an Rh–C bond lengths of 1.92 Å and Rh–N bond lengths of 2.05 and 2.09 Å. The bond angle of N-Rh-N is 158.36°. The bond length of Rh–$O1_{aqua}$1 is 2.23 Å. These data are similar to those for the chloride complex **2e**, previously reported.[9d]

Stereochemical course of the asymmetric induction: We present here a hypothetical mechanism and stereochemical course of the reaction: the starting rhodium(III) complex is reduced by an excess of the hydrosilane to the corresponding rhodium(I) species, which react with the hydrosilane to form the [(hydrido)(silyl)rhodium(III)Phebox] species as a catalyst. The α,β-unsaturated carbonyl compound approaches to the active intermediate, the Rh–H species **I** (Figure 2). The hydride attack to the β-carbon atom gives

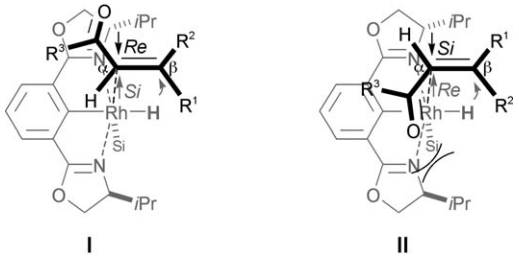


Figure 2. Hypothetical stereochemical course.

the *R* absolute configuration. The reductive elimination with the silyl group via the Rh–O enolate produces the silylenol ether or the ketene silylacetal, which is then converted to the reduction product by hydrolysis. The absolute *S* configuration from the (*Z*)-carbonyl compound can also be explained by the structure **I**. Therefore, the absolute configuration observed is based on selective coordination of the *Si*-face of the α-carbon atom to the rhodium metal and subsequent hydride attack on the β-carbon atom. The *Re*-face coordination illustrated in structure **II** is disfavored by steric repulsion between the carbonyl group and the isopropyl group on the ligand.

Conclusion

We have found that chiral rhodium(bisoxazolinylphenyl) complexes can act as potent catalysts for the asymmetric conjugate reduction of acyclic β,β-disubstituted α,β-unsaturated ketones and esters with diethoxymethylsilane in high enantioselectivity. This reaction will provide a potential route to bioactive chiral carbonyl compounds with a β-asymmetric center.

Experimental Section

General: Column chromatography was performed with a silica gel column (Merck Silica gel 60) and ethyl acetate/hexane as eluent, unless otherwise mentioned. ^{1}H and ^{13}C NMR spectra were obtained at 25 °C on a Varian Mercury 300 spectrometer. ^{1}H NMR chemical shifts are reported in δ units, in ppm relative to the singlet at 7.26 ppm for chloroform. ^{13}C NMR spectra are reported in terms of chemical shift (δ, ppm) relative to the triplet at $\delta = 77.0$ ppm for $CDCl_3$ as an internal standard. Infrared spectra were recorded on a JASCO FT/IR-230 spectrometer. Absolute toluene and hydrosilanes were purchased from TCI. The substrate ketones **6**, **8**, **10**, **12**, **14**, **16**, **18**, and **20**, were prepared from the corresponding esters via Weinreb's amide and subsequent alkylation; see Supporting Information. The substrate esters **22**, **24**, **26**, **28**, **30**, **32**, and **34** were prepared by the Horner–Wadsworth–Emmons reaction according to a previously reported procedure; see Supporting Information.[2b,5a,7j] The ester **22** can also be purchased from Aldrich.

Preparation of [(*S*,*S*)-Phebox-*i*Pr]H (1a): A solution of isophthaloyl dichloride (1.02 g, 5.0 mmol) in dichloromethane (20 mL) was slowly added to a solution of L-valinol (1.03 g, 10.0 mmol) and triethylamine (7.6 g, 75 mmol) in dichloromethane (40 mL) at 0 °C. The mixture was stirred at room temperature for 1 h. Formation of the intermediate diamide–dialcohol was monitored by TLC examination; $R_f = 0.4$ (ethyl acetate/methanol = 10:1). Then, methanesulfonyl chloride (1.26 g, 11 mmol) was added at 0 °C, and the mixture was stirred at room temperature for 5 h. Formation of the product **1a** was monitored by TLC examination; $R_f = 0.8$ (ethyl acetate/hexane = 3:1). At 0 °C, aqueous potassium carbonate (1 N, ca. 30 mL) was added and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine, was dried over magnesium sulfate, and was concentrated. The crude product was purified by column chromatography to give **1a** in 87% yield (1.30 g, 4.33 mmol) as a colorless solid. For full analytical data for **1a** and an alternative synthetic route to **1a**, see a procedure reported by Bolm et al.[14]

The preparation procedures of **1b**, **1c**, **1d**, **1e**, and **1f** were similar to that of **1a**.

[(*S*,*S*)-Phebox-*s*Bu]H (1b): Yield: 82% (1.35 g) from L-isoleucinol (1.17 g, 10 mmol) and isophthaloyl dichloride (1.0 g, 5.0 mmol). For full analytical data for **1b**, see reference [14].

[(*S*,*S*)-Phebox-*i*Bu]H (1c): Yield: 84% (1.38 g) from L-leucinol (1.17 g, 10 mmol) and isophthaloyl dichloride (1.0 g, 5.0 mmol); colorless solid: m.p. 47–48 °C; $[\alpha]_D^{25} = -107.0°$ ($c = 1.03$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta =$ 8.47 (t, $J = 1.5$ Hz, 1H), 8.04 (dd, $J = 7.8$, 1.5 Hz, 2H), 7.36 (t, $J = 7.8$ Hz, 1H), 4.51 (dd, $J = 9.3$, 7.8 Hz, 2H), 4.28–4.38 (m, 2H), 3.99 (t, $J = 7.8$ Hz, 2H), 1.76–1.90 (m, 2H), 1.66–1.75 (m, 2H), 1.32 (m, 2H), 0.98 (d, $J =$ 6.6 Hz, 6H), 0.96 ppm (d, $J = 6.6$ Hz, 6H); ^{13}C NMR ($CDCl_3$): $\delta = 22.71$, 22.81, 25.41, 45.52, 65.11, 73.08, 127.8, 128.0, 128.1, 130.5, 163.3 ppm; IR

(KBr disk): $\tilde{\nu}$ = 1652, 1574 cm^{-1}; elemental analysis calcd (%) for $C_{20}H_{28}N_2O_2$ (328.45): C 73.14, H 8.59, N 8.53; found: C 73.25, H 9.02, N 8.61.

[(*S*,*S*)-Phebox-*t*Bu]H (1d): Yield: 81% (1.34 g) from L-*tert*-leucinol (1.17 g, 10 mmol) and isophthaloyl dichloride (1.0 g, 5.0 mmol); colorless solid: m.p. 123–124°C; $[\alpha]_D^{26} = -123.9°$ (c = 1.01 in $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ = 8.51 (t, J = 1.8 Hz, 1H), 8.06 (dd, J = 7.8, 1.8 Hz, 2H), 7.44 (t, J = 7.8 Hz, 1H), 4.35 (dd, J = 10.2, 8.7 Hz, 2H), 4.24 (dd, J = 8.7, 7.8 Hz, 2H), 4.06 (dd, J = 10.2, 7.8 Hz, 2H), 0.95 ppm (s, 18H); ^{13}C NMR ($CDCl_3$): δ = 25.94, 34.11, 68.79, 76.29, 127.9, 128.1, 128.2, 130.7, 162.4 ppm; IR (KBr disk): $\tilde{\nu}$ = 1653, 1587 cm^{-1}; elemental analysis calcd (%) for $C_{20}H_{28}N_2O_2$ (328.45): C 73.14, H 8.59, N 8.53; found: C 73.16, H 9.08, N 8.44.

[(*S*,*S*)-Phebox-Bn]H (1e): Yield: 81% (1.60 g) from L-phenylalaninol (1.51 g, 10 mmol) and isophthaloyl dichloride (1.0 g, 5.0 mmol); colorless solid: m.p. 106–107°C; $[\alpha]_D^{26} = -4.8°$ (c = 0.99 in $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ = 8.50 (t, J = 1.8 Hz, 1H), 8.09 (dd, J = 7.8, 1.8 Hz, 2H), 7.47 (t, J = 7.8 Hz, 1H), 7.20–7.34 (m, 10H), 4.60 (m, 2H), 4.36 (dd, J = 9.6, 8.4 Hz, 2H), 4.15 (dd, J = 8.4, 7.5 Hz, 2H), 3.25 (dd, J = 13.8, 5.1 Hz, 2H), 2.74 ppm (dd, J = 13.8, 9.0 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 41.71, 67.85, 71.85, 126.3, 127.9, 128.2, 128.3, 129.0, 130.8, 137.6, 163.0 ppm; IR (KBr disk): $\tilde{\nu}$ = 1649, 1575 cm^{-1}; elemental analysis calcd (%) for $C_{26}H_{24}N_2O_2$ (396.48): C 78.76, H 6.10, N 7.07; found: C 78.86, H 6.20, N 6.87.

[(*S*,*S*)-Phebox-Ph]H (1f): Yield: 80% (1.48 g) from (*S*)-2-phenylglycinol (1.37 g, 10 mmol) and isophthaloyl dichloride (1.0 g, 5.0 mmol); colorless solid: m.p. 120–124°C; $[\alpha]_D^{25} = -74.4°$ (c = 1.04 in $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ = 8.69 (t, J = 1.5 Hz, 1H), 8.20 (dd, J = 7.8, 1.5 Hz, 2H), 7.53 (t, J = 7.8 Hz, 1H), 7.27–7.40 (m, 10H), 5.41 (dd, J = 10.2, 8.4 Hz, 2H), 4.82 (dd, J = 10.2, 8.1 Hz, 2H), 4.30 ppm (dd, J = 8.4, 8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 70.16, 74.94, 126.6, 127.5, 127.8, 128.4, 128.5, 128.6, 131.2, 142.0, 163.9 ppm; IR (KBr disk): $\tilde{\nu}$ = 1649, 1575 cm^{-1}; elemental analysis calcd (%) for $C_{24}H_{20}N_2O_2$ (368.43): C 78.24, H 5.47, N 7.60; found: C 78.10, H 5.69, N 7.52.

Simple preparation of [Rh{(*S*,*S*)-Phebox-*i*Pr}Cl$_2$]·H$_2$O (2a): $RhCl_3 \cdot 3H_2O$ (579 mg, 2.2 mmol), the ligand **1a** (600 mg, 2.0 mmol), sodium bicarbonate (168 mg, 2.0 mmol) were placed in a flask. After addition of methanol (20 mL) and water (1 mL), the mixture was heated at 60°C for 5 h. The concentrated residue was purified by silica-gel chromatography with ethyl acetate/hexane (2:1 to 1:1) as eluent to give **2a** in 56% yield (549 mg, 1.12 mmol). As an alternative method, [{Rh(cyclooctene)$_2$Cl}$_2$] was used in place of $RhCl_3 \cdot 3H_2O$. The mixture of the rhodium complex (180 mg, 0.25 mmol) and ligand **1a** (150 mg, 0.50 mmol) was heated at 60°C for 6 h in a $CHCl_3$ (10 mL). After chromatography, complex **2a** was obtained in 46% (113 mg, 0.23 mmol). Full characterization data of **2a** and the alternative preparation methods with Phebox-SnMe$_3$ were reported in reference [9d].

The preparation procedures of **2b** (541 mg, 52%), **2c** (554 mg, 53%), **2d** (246 mg, 24%), **2e** (608 mg, 52%), and **2f** (557 mg, 50%) were similar to that of **2a**. For full analytical data for **2d**, **2e**, and **2f**, see reference [9d].

[Rh{(*S*,*S*)-Phebox-*s*Bu}Cl$_2$]·H$_2$O (2b): Pale yellow solid: m.p. 268°C (decomp); ^{1}H NMR ($CDCl_3$): δ = 7.58 (d, J = 7.8 Hz, 2H), 7.28 (t, J = 7.8 Hz, 1H), 4.75 (dd, J = 10.2, 9.0 Hz, 2H), 4.68 (dd, J = 9.0, 7.2 Hz, 2H), 4.36 (ddd, J = 10.2, 7.2, 3.0 Hz, 2H), 2.15–2.23 (m, 2H), 1.94 (s, 2H), 1.17–1.43 (m, 4H), 0.99 (dd, J = 7.5, 7.2 Hz, 6H), 0.90 ppm (d, J = 6.6 Hz, 6H); ^{13}C NMR ($CDCl_3$): δ = 12.09, 12.60, 27.02, 35.95, 65.94, 71.09, 123.1, 127.8, 131.4, 170.6, 180.1 ppm (d, $J_{Rh\text{-}C}$ = 23.9 Hz); IR (KBr disk): $\tilde{\nu}$ = 1617, 1481 cm^{-1}; elemental analysis calcd (%) for $C_{20}H_{29}Cl_2N_2O_3Rh$ (519.27): C 46.26, H 5.63, N 5.39; found: C 46.21, H 5.92, N 5.15.

[Rh{(*S*,*S*)-Phebox-*i*Bu}Cl$_2$]·H$_2$O (2c): Pale yellow solid: m.p. 287°C (decomp); ^{1}H NMR ($CDCl_3$): δ = 7.58 (d, J = 7.8 Hz, 2H), 7.30 (t, J = 7.8 Hz, 1H), 4.91–4.97 (m, 2H), 4.51–4.57 (m, 2H), 4.28–4.38 (m, 2H), 2.65 (brs, 2H), 2.06–2.15 (m, 2H), 1.51–1.72 (m, 4H), 1.00 (d, J = 6.6 Hz, 6H), 0.99 ppm (d, J = 6.6 Hz, 6H); ^{13}C NMR ($CDCl_3$): δ = 21.68, 23.80, 25.76, 43.12, 61.43, 76.19, 123.6, 128.1, 131.1, 170.0, 177.4 ppm (d, $J_{Rh\text{-}C}$ = 26.2 Hz); IR (KBr disk): $\tilde{\nu}$ = 1615, 1478 cm^{-1}; elemental analysis calcd (%) for $C_{20}H_{29}Cl_2N_2O_3Rh$ (519.27): C 46.26, H 5.63, N 5.39; found: C 46.38, H 5.56, N 5.35.

Preparation of [Rh{(*S*,*S*)-Phebox-*i*Pr}(OAc)$_2$]·H$_2$O (3a): A mixture of **2a** (246 mg, 0.50 mmol) and silver acetate (334 mg, 2.0 mmol) in dichloromethane (15 mL) was stirred for 15 h at room temperature. The concentrated residue was purified by silica-gel chromatography with ethyl acetate/methanol as eluent to give **3a** (232 mg, 0.43 mmol) in 86% yield as a yellowish-orange solid. M.p. 235°C (decomp); ^{1}H NMR ($CDCl_3$): δ = 7.43 (d, J = 7.2 Hz, 2H), 7.30 (t, J = 7.2 Hz, 1H), 5.08 (brs, 2H), 4.60–4.80 (m, 4H), 4.38 (m, 2H), 2.50 (m, 2H), 1.71 (s, 6H), 0.97 (d, J = 7.2 Hz, 6H), 0.75 ppm (d, J = 7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$): δ = 14.79, 19.13, 23.42, 29.50, 67.72, 71.27, 122.9, 127.5, 131.5, 171.3, 182.3 ppm (d, $J_{Rh\text{-}C}$ = 25.7 Hz); IR (KBr disk): $\tilde{\nu}$ = 1615, 1395 cm^{-1}; elemental analysis calcd (%) for $C_{22}H_{31}N_2O_7Rh$ (538.40): C 49.08, H 5.80, N 5.20; found: C 49.22, H 5.79, N 5.14.

The preparation procedures of **3b**, **3c**, **3d**, **3e**, and **3f** were similar to that of **3a**.

[Rh{(*S*,*S*)-Phebox-*s*Bu}(OAc)$_2$]·H$_2$O (3b): Yield: 80% (227 mg); yellow solid: m.p. 193°C (decomp); ^{1}H NMR ($CDCl_3$): δ = 7.58 (d, J = 7.5 Hz, 2H), 7.31 (t, J = 7.5 Hz, 1H), 4.71 (dd, J = 10.2, 8.7 Hz, 2H), 4.64 (dd, J = 8.7, 6.6 Hz, 2H), 4.45–4.51 (m, 2H), 3.03 (brs, 2H), 2.24–2.37 (m, 2H), 1.29–1.45 (m, 2H), 1.13–1.27 (m, 2H), 1.01 (t, J = 7.5 Hz, 6H), 0.68 ppm (d, J = 6.9 Hz, 6H); ^{13}C NMR ($CDCl_3$): δ = 11.81, 12.03, 23.97, 26.73, 35.90, 66.44, 71.00, 123.0, 127.3, 131.6, 171.6, 182.0, 188.8 ppm (d, $J_{Rh\text{-}C}$ = 23.9 Hz); IR (KBr disk): $\tilde{\nu}$ = 1614, 1483 cm^{-1}; elemental analysis calcd (%) for $C_{24}H_{35}N_2O_7Rh$ (566.45): C 50.89, H 6.23, N 4.95; found: C 50.84, H 6.38, N 4.85.

[Rh{(*S*,*S*)-Phebox-*i*Bu}(OAc)$_2$]·H$_2$O (3c): Yield: 85% (242 mg); yellow solid: m.p. 147°C (decomp); ^{1}H NMR ($CDCl_3$): δ = 7.57 (d, J = 7.5 Hz, 2H), 7.27 (t, J = 7.5 Hz, 1H), 6.12 (brs, 2H), 4.92 (dd, J = 9.0, 8.1 Hz, 2H), 4.50 (dd, J = 8.1, 7.8 Hz, 2H), 4.34–4.44 (m, 2H), 2.16 (m, 2H), 1.70 (m, 2H), 1.69 (s, 6H), 1.31 (m, 2H), 1.00 ppm (d, J = 6.6 Hz, 6H); ^{13}C NMR ($CDCl_3$): δ = 21.89, 23.58, 23.70, 25.52, 43.38, 61.59, 76.42, 122.9, 127.3, 131.8, 171.2, 182.0, 188.5 ppm (d, $J_{Rh\text{-}C}$ = 24.5 Hz); IR (KBr disk): $\tilde{\nu}$ = 1611, 1479 cm^{-1}; elemental analysis calcd (%) for $C_{24}H_{35}N_2O_7Rh$ (566.45): C 50.89, H 6.23, N 4.95; found: C 50.79, H 6.50, N 4.81.

[Rh{(*S*,*S*)-Phebox-*t*Bu}(OAc)$_2$]·H$_2$O (3d): Yield: 85% (241 mg); yellow solid: m.p. 283°C (decomp); ^{1}H NMR ($CDCl_3$): δ = 7.57 (d, J = 7.5 Hz, 2H), 7.28 (t, J = 7.5 Hz, 1H), 4.65–4.76 (m, 4H), 4.10 (dd, J = 9.9, 7.5 Hz, 2H), 3.11 (brs, 2H), 1.77 (s, 6H), 1.07 ppm (s, 18H); ^{13}C NMR ($CDCl_3$): δ = 23.32, 25.94, 34.12, 72.21, 72.36, 122.9, 128.0, 131.4, 171.8, 181.7, 185.2 ppm (d, $J_{Rh\text{-}C}$ = 27.3 Hz); IR (KBr disk): $\tilde{\nu}$ = 1615, 1490, 1401 cm^{-1}; elemental analysis calcd (%) for $C_{24}H_{35}N_2O_7Rh$ (566.45): C 50.89, H 6.23, N 4.95; found: C 51.05, H 6.24, N 4.78.

Rh[(*S*,*S*)-Phebox-*bn*](OAc)$_2$(H$_2$O) (3e); 82% yield (261 mg); yellow solid: mp. 104°C (dec); ^{1}H NMR ($CDCl_3$): δ = 7.62 (d, J = 7.8 Hz, 2H), 7.22–7.35 (m, 11H), 6.19 (brs, 2H), 4.54–4.76 (m, 6H), 3.69 (dd, J = 13.5, 3.0 Hz, 2H), 2.62 (dd, J = 13.5, 9.3 Hz, 2H), 1.72 (s, 6H) ppm; ^{13}C NMR ($CDCl_3$): δ = 24.05, 40.03, 63.99, 75.27, 123.2, 126.7, 127.7, 128.7, 129.2, 131.7, 136.8, 172.2, 182.3, 188.8 (d, $J_{Rh\text{-}C}$ = 23.9 Hz); IR (KBr disk): $\tilde{\nu}$ = 1610, 1488, 1393 cm^{-1}; elemental analysis calcd (%) for $C_{30}H_{31}N_2O_7Rh$ (634.48): C 56.79, H 4.92, N 4.42; found: C 57.05, H 4.94, N 4.14.

[Rh{(*S*,*S*)-Phebox-Ph}(OAc)$_2$](H$_2$O) (3f): Yield: 81% (244 mg); yellow solid: m.p. 301°C (decomp); ^{1}H NMR ($CDCl_3$): δ = 7.69 (d, J = 7.5 Hz, 2H), 7.36 (t, J = 7.5 Hz, 1H), 7.28–7.37 (m, 10H), 5.39 (dd, J = 10.2, 7.8 Hz, 2H), 5.16 (dd, J = 10.2, 9.0 Hz, 2H), 4.78 (dd, J = 9.0, 7.8 Hz, 2H), 4.73 (brs, 2H), 1.44 ppm (s, 6H); ^{13}C NMR ($CDCl_3$): δ = 23.60, 66.67, 78.32, 123.0, 127.8, 128.3, 128.5, 131.6, 138.6, 172.2, 181.0, 189.8 ppm (d, $J_{Rh\text{-}C}$ = 24.5 Hz); IR (KBr disk): $\tilde{\nu}$ = 1613, 1487, 1394 cm^{-1}; elemental analysis calcd (%) for $C_{28}H_{27}N_2O_7Rh$ (606.43): C 55.46, H 4.49, N 4.62; found: C 55.41, H 4.43, N 4.27.

Conjugate reduction of α,β-unsaturated ketones

Reduction of benzalacetone (Table 1): Hydrosilane (1.5 mmol) was slowly added to a mixture of benzalacetone (146 mg, 1.0 mmol) and the catalyst **2a** (4.9 mg, 0.01 mmol) or **3a** (5.4 mg, 0.01 mmol) in toluene (1.0 mL) at 50°C. The mixture was stirred for 0.5–2 h, and the solvent was removed under reduced pressure. THF (1 mL), MeOH (1 mL), KF (116 mg, 2.0 mmol), and tetrabutylammonium fluoride (TBAF, 0.3 mmol)

in THF (0.3 mL) were added to the residueat 0 °C. The mixture was stirred for 1 h. After extraction with ethyl acetate and concentration, the residue was purified by silica-gel chromatography with ethyl acetate/hexane to give a mixture of 4-phenyl-2-butanone (**4**) and (*E*)-4-phenyl-3-buten-2-ol (**5**). The ratio of **4** and **5** was determined by ^{1}H NMR spectroscopy; ($CDCl_3$): $\delta = 2.14$ (s, CH_3 for **4**), 1.38 ppm (d, CH_3 for **5**).

Reduction of (*E*)-4-phenyl-3-penten-2-one (6) (Table 2, entry 3): Diethoxymethylsilane (201 mg, 1.5 mmol) was slowly added by a syringe to a mixture of compound **6** (160 mg, 1.0 mmol) and the catalyst **3a** (5.4 mg, 0.01 mmol) in toluene (1.0 mL) at room temperature. The mixture was stirred for 1 h and the solvent was removed under reduced pressure. The residue was treated with hydrochloric acid (4 N, 1 mL), MeOH (1 mL), and THF (1 mL) at 0 °C for 1 h. After extraction with ethyl acetate and concentration, the residue was purified by silica-gel chromatography with ethyl acetate/hexane to give the product (*R*)-4-phenyl-2-pentanone (**7**; 97 %, 158 mg, 0.97 mmol) as colorless oil. The *ee* was determined by chiral HPLC analysis [DAICEL CHIRALCEL OJ-H column, 0.5 mL min^{-1}, *i*PrOH/hexane 1:99, $R_t = 26.8$ min (minor), 29.2 min (major)]: 95 % *ee* for *R*; $[\alpha]_D^{20} = -40.8°$ ($c = 1.0$ in $CHCl_3$); lit.[15a] $[\alpha]_D^{20} = +40°$ ($c = 0.5$ in $CHCl_3$) for *S*; lit.[15b] $[\alpha]_D^{20} = +38.8°$ ($c = 0.4$ in $CHCl_3$), 97 % *ee* for *S*. Spectroscopic data were consistent with previously reported data in reference [15a].

For other entries in Table 2, the procedures were the same as described above for entry 3; scale and conditions were described in the footnote of Table 2.

Reduction of other α,β-unsaturated ketones (1.0 mmol) listed in Table 3: The reactions were performed by the same procedure described above for entry 3 in Table 2 for **6**.

(*R*)-5-Phenyl-3-hexanone (9):[16] Yield: 98 % (172 mg, 0.98 mmol), colorless oil. No 1,2-reduction product was obtained. DAICEL CHIRALCEL AD-H column, 0.5 mL min^{-1}, *i*PrOH/hexane 1:99, $R_t = 9.6$ min (minor), 10.4 min (major), 95 % *ee* for *R*; $[\alpha]_D^{25} = -49.5°$ ($c = 1.0$ in $CHCl_3$); lit.[16] $[\alpha]_D^{22} = -56.4°$ ($c = 1.0$ in benzene) for *R*. NMR and IR spectroscopic data were consistent with that previously reported.[16]

(*R*)-2-Methyl-5-phenyl-3-hexanone (11):[17] 97 % (185 mg, 0.97 mmol), colorless oil. No 1,2-reduction product was obtained. DAICEL CHIRALCEL AD-H column, 0.5 mL min^{-1}., *i*-PrOH/hexane (1:99), $R_t = 8.9$ min. (minor), 9.8 min. (major), 92 % *ee* for *R* (by analogy to **9**); $[\alpha]_D^{21} = -30.5°$ ($c = 1.0$ in $CHCl_3$). Neither spectroscopic data nor $[\alpha]_D$ data were found in reference [17]. ^{1}H NMR ($CDCl_3$): $\delta = 7.26$–7.32 (m, 2H), 7.16–7.23 (m, 3H), 3.35 (m, 1H), 2.76 (dd, $J = 16.5$, 6.6 Hz, 1H), 2.67 (dd, $J = 16.5$, 8.1 Hz, 1H), 2.48 (m, 1H), 1.26 (d, $J = 6.9$ Hz, 3H), 1.04 (d, $J = 6.9$ Hz, 3H), 0.98 ppm (d, $J = 6.9$ Hz, 3H); ^{13}C NMR ($CDCl_3$): $\delta = 17.92$, 18.10, 21.86, 35.24, 41.31, 48.95, 126.1, 126.7, 128.3, 146.4, 213.2 ppm; IR (KBr, film): $\tilde{\nu} = 1712$ cm^{-1}; elemental analysis calcd (%) for $C_{13}H_{18}O$ (190.28): C 82.06, H 9.53; found: C 81.88, H 9.71.

(*R*)-1,3-Diphenyl-1-butanone (13):[18] Yield: 99 % (222 mg, 0.99 mmol), colorless oil. No 1,2-reduction product was obtained. DAICEL CHIRALCEL AD-H column. 0.5 mL min^{-1}, *i*PrOH/hexane 1:30, $R_t = 12.6$ min (minor), 14.9 min (major), 82 % *ee* for *R*; $[\alpha]_D^{25} = -13.5°$ ($c = 1.0$ in CCl_4); lit.[19a] $[\alpha]_D^{24} = -13°$ ($c = 1.02$ in CCl_4), 75 % *ee* for *R*; lit.[19b] $[\alpha]_D^{25} = +12.6°$ ($c = 2.62$ in CCl_4) for *S*; lit.[19c] $[\alpha]_D^{20} = -14.8°$ ($c = 1.2$ in CCl_4) for *R*. Spectroscopic data of NMR and IR were consistent with previously reported data.[18]

(*S*)-5-Methyl-4-phenyl-2-hexanone (15):[20,21] Yield: 97 % (185 mg, 0.97 mmol), colorless oil. No 1,2-reduction product was obtained. DAICEL CHIRALCEL OJ-H column, 0.5 mL min^{-1}, *i*PrOH/hexane 1:99, $R_t = 18.9$ min (minor), 23.6 min (major), 98 % *ee* for *S*;[22] $[\alpha]_D^{24} = -38.9°$ ($c = 0.97$ in $CHCl_3$); lit.[20] $[\alpha]_D^{20} = -33°$ ($c = 1.12$ in $CHCl_3$). NMR data were consistent with previously reported data.[20]

(*S*)-4-Methyl-6-phenyl-2-hexanone (17)[23]: Yield: 97 % (185 mg, 0.97 mmol), colorless oil. No 1,2-reduction product was obtained. DAICEL CHIRALPAK AD-H column, 1.0 mL min^{-1}, *i*PrOH/hexane 0.5:99.5, $R_t = 16.1$ min (major), 23.4 min (minor), 95 % *ee* for *S*; $[\alpha]_D^{22} = -21.7°$ ($c = 1.0$ in $CHCl_3$); lit.[23] minus specific rotation for *S*. Spectroscopic date were consistent with previously reported data.[23]

(*S*)-4,8-Dimethyl-7-nonen-2-one (19):[24] Yield: 97 % (164 mg, 0.97 mmol), colorless oil. No 1,2-reudction product was obtained. GLPC, Alltech Chiraldex G-TA (60 kPa, 80 °C), $R_t = 56.5$ min (minor), 57.7 min (major), 89 % *ee* for *S*; $[\alpha]_D^{22} = -13.8°$ ($c = 1.03$ in $CHCl_3$); lit.[24a] $[\alpha]_D^{20} = +9.44°$ ($c = 2.50$ in $CHCl_3$) for *R*; lit.[24b] $[\alpha]_D^{24} = -10.7°$ ($c = 1.00$ in EtOH) for *S*. NMR and IR spectra were consistent with previously reported data.[24]

(*R*)-4-Cyclohexyl-2-pentanone (21):[25] Yield: 94 % (158 mg, 0.94 mmol), colorless oil. No 1,2-reduction product was obtained. DAICEL CHIRALPAK AS-H column, 0.5 mL min^{-1}, *i*PrOH/hexane 1:99, $R_t = 11.5$ min (minor), 12.3 min (major), 65 % *ee* for *R*; $[\alpha]_D^{25} = -4.37°$ ($c = 1.06$ in $CHCl_3$), according to Science Finder, (*S*)-(+); lit.[25] $[\alpha]_D^{24} = +5.4°$ ($c = 1.03$ in C_6H_6). Spectroscopic data were consistent with previously reported data.[25]

(*S*)-4-Phenyl-2-pentanone (7) from (*Z*)-6: Yield: 90 % (147 mg, 0.90 mmol), colorless oil; 51 % *ee* for *S*; $[\alpha]_D^{27} = +21.3°$ ($c = 1.0$ in $CHCl_3$).

(*R*)-4-Methyl-6-phenyl-2-hexanone (17) from (*Z*)-16: Yield: 96 % (182 mg, 0.96 mmol), colorless oil; 91 % *ee* for *R*; $[\alpha]_D^{28} = +20.8°$ ($c = 1.0$ in $CHCl_3$).

Conjugate reduction of α,β-unsaturated esters

Reduction of (*E*)-ethyl 3-phenylbut-2-enoate (22) (Table 4, entry 2): Diethoxymethylsilane (201 mg, 1.5 mmol) was slowly added to a mixture of the ester **22** (190 mg, 1.0 mmol) and the catalyst **3a** (5.4 mg, 0.01 mmol) in toluene (1.0 mL) at 60 °C. The mixture was stirred for 1 h and then treated with hydrochloric acid (1*N*, 1 mL). After extraction with ethyl acetate and concentration, the residue was purified by silica-gel chromatography with ethyl acetate/hexane to give the product, ethyl (*R*)-3-phenylbutanoate (**23**; 184 mg, 96 %, 0.96 mmol) as a colorless oil. The *ee* was determined by chiral HPLC analysis [DAICEL CHRALCEL OB column, 0.5 mL min^{-1}, *i*PrOH/hexane 1:99, $R_t = 14.1$ min (major), 16.8 min (minor)], 95.9 % *ee* for *R*; $[\alpha]_D^{26} = -24.7°$ ($c = 1.12$ in $CHCl_3$); lit.[4a] $[\alpha]_D^{25} = +19°$ ($c = 1.1$ in $CHCl_3$), 90 % *ee* for *R*. NMR spectra were consistent with previously reported data.[4,5a,7j]

Reduction of other α,β-unsaturated esters (1.0 mmol) listed in Table 5. The reactions were performed by the same procedure as above described for **22**.

Isopropyl (*R*)-3-phenylbutanoate (25): Yield: 98 % (203 mg, 0.98 mmol), colorless oil. Chiral HPLC analysis: DAICEL CHRALCEL OB column, 0.2 mL min^{-1}, *i*PrOH/hexane 2:98, $R_t = 22.8$ min (major), 25.2 min (minor), 97 % *ee* for *R*. $[\alpha]_D^{26} = -29.0°$ ($c = 1.1$ in $CHCl_3$). ^{1}H NMR ($CDCl_3$): $\delta = 7.17$–7.31 (m, 5H), 4.95 (sept, $J = 3.3$ Hz, 1H), 3.27 (ddq, $J = 15.3$, 15.0, 7.2 Hz, 1H), 2.58 (dd, $J = 15.3$, 7.2 Hz, 1H), 2.51 (dd, $J = 15.0$, 7.2 Hz, 1H), 1.30 (d, $J = 7.2$ Hz, 3H), 1.17 (d, $J = 6.3$ Hz, 3H), 1.12 ppm (d, $J = 6.3$ Hz, 3H); ^{13}C NMR ($CDCl_3$): $\delta = 17.40$, 17.48, 17.54, 32.33, 38.96, 60.71, 63.11, 121.8, 122.3, 123.9, 141.2, 167.3 ppm; IR (KBr, film): $\tilde{\nu} = 1730$ cm^{-1}; elemental analysis calcd (%) for $C_{13}H_{18}O_2$ (206.28): C 75.69, H, 8.80; found: C 75.46, H 8.82.

***tert*-Butyl (*R*)-3-phenylbutanoate (27)**: 217 mg (99 %, 0.99 mmol), colorless oil. Chiral HPLC analysis: DAICEL CHRALCEL OD-H column, 0.3 mL min^{-1}, *i*PrOH/hexane 1:99, $R_t = 15.3$ min (major), 16.5 min (minor), 98 % *ee* for *R*. $[\alpha]_D^{26} = -20.6°$ ($c = 1.2$ in $CHCl_3$). ^{1}H NMR ($CDCl_3$): $\delta = 7.16$–7.31 (m, 5H), 3.22 (ddq, $J = 15.3$, 15.0, 7.2 Hz, 1H), 2.53 (dd, $J = 15.3$, 7.2 Hz, 1H), 2.46 (dd, $J = 15.0$, 7.2 Hz, 1H), 1.35 (s, 9H), 1.29 ppm (d, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$): $\delta = 17.60$, 23.67, 32.47, 39.82, 75.80, 121.8, 122.4, 123.9, 141.4, 167.2 ppm; elemental analysis calcd (%) for $C_{14}H_{20}O_2$ (220.31): C 76.33, H, 9.15; found: C 76.31, H 9.26.

Ethyl (*R*)-3-phenylpentanoate (29): Yield: 99 % (206 mg, 0.99 mmol), colorless oil. Chiral HPLC analysis: DAICEL CHRALCEL OJ-H column, 0.7 mL min^{-1}, *i*PrOH/hexane 1:99, $R_t = 15.5$ min (major), 12.5 min (minor), 97 % *ee* for *R*; $[\alpha]_D^{26} = -18.3°$ ($c = 1.1$ in $CHCl_3$); lit.[5a] $[\alpha]_D^{25} = +18°$ ($c = 1.1$ in $CHCl_3$), 90 % *ee* for *S*. NMR spectra were consistent with previously reported data.[5a]

Ethyl (*S*)-4-methyl-3-phenylpentanoate (31): Yield: 97 % (213 mg, 0.97 mmol), colorless oil. Chiral GC analysis: Alltec Chiraldex G-TA, 105 °C, 60 kPa, $R_t = 63.6$ min (minor), 65.3 min (minor), 98 % *ee* for *S*; $[\alpha]_D^{26} = -25.4°$ ($c = 1.0$ in $CHCl_3$). The ester **31** was converted to the corresponding aldehyde by reduction with DIBAL. The aldehyde showed

minus rotation; lit.[26], $[\alpha]_D^{26} = -23.1°$ ($c = 0.94$ in C_6H_6) for (3*S*)-(−)-4-methyl-3-phenylpentanal. ^{1}H NMR($CDCl_3$): $\delta = 7.13$–7.29 (m, 5H), 3.96 (q, $J = 7.2$ Hz, 2H), 2.84–2.92 (m, 1H), 2.77 (dd, $J = 15.0$, 5.4 Hz, 1H), 2.58 (dd, $J = 14.7$, 9.9 Hz, 1H), 1.86 (dsep, $J = 6.6$, 6.6 Hz, 1H), 1.06 (t, $J = 7.2$ Hz, 3H), 0.95 (d, $J = 6.9$ Hz, 3H), 0.76 ppm (d, $J = 6.9$ Hz, 3H); ^{13}C NMR($CDCl_3$): $\delta = 14.1$, 20.4, 20.7, 33.2, 38.7, 49.0, 60.1, 126.1, 127.9, 128.1, 142.7, 172.6 ppm; IR (KBr, film): $\tilde{\nu} = 1735\ cm^{-1}$; elemental analysis calcd (%) for $C_{14}H_{20}O_2$ (220.31): C 76.33, H 9.15; found: C 76.10, H 9.29. For preparation of the starting substrate **30**, see reference [27].

Ethyl (*S*)-3-methyl-5-phenylpentanoate (33): At 60 °C; yield: 96% (211 mg, 0.96 mmol), colorless oil. Chiral HPLC analysis: DAICEL CHIRALCEL OJ-H column, 0.5 mL min^{-1}, EtOH/hexane (3:97), R_t = 10.1 min (minor), 10.6 min (major), 91% *ee* for *S*; $[\alpha]_D^{26} = -13.0°$ ($c = 1.0$ in $CHCl_3$); lit.[5a] $[\alpha]_D^{25} = +12°$ ($c = 1.0$ in $CHCl_3$), 84% *ee* for *R*. NMR spectra were consistent with previously reported data.[4,5a]

Ethyl (*S*)-3,7-dimethyloct-6-enoate (35): Yield: 96% (190.2 mg, 0.96 mmol), colorless oil. Chiral GC analysis: Alltech CHIRALDEX G-TA, $R_t = 75.9$ min (minor), 78.5 min (major), 92% *ee* for *S*; $[\alpha]_D^{28} = -3.82°$ ($c = 1.0$ in $CHCl_3$); lit.[5a] $[\alpha]_D^{25} = +4.6°$ ($c = 1.1$ in $CHCl_3$), 86% *ee* for *R*. NMR spectra were consistent with previously reported data.[4,5a]

X-ray crystallographic determination: Single crystals suitable for X-ray analysis were obtained by recrystallization from diethyl ether/hexane at room temperature. A crystal was mounted on a quartz fiber, and diffraction data were collected in θ ranges at 173 K with a Brucker SMART APEX CCD diffractometer with graphite-monochromated $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å). An empirical absorption correction was applied by using SADABS. The structure was solved by direct methods and refined by full-matrix least-squares on F^2 by using SHELXTL.[28] All non-hydrogen atoms were refined with anisotropic displacement parameters. Refinement details: empirical formula; $C_{22}H_{31}N_2O_7Rh$; $M_r = 538.40$; crystal system: monoclinic; space group: $P2_1$; $a = 8.7699(5)$, $b = 15.5207(9)$, $c = 9.5423(6)$ Å, $\alpha = 90°$, $\beta = 115.5730(10)°$, $\gamma = 90°$, $V = 1171.61(12)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.526$ Mg m^{-3}, $\mu = 0.773$ mm^{-1}, $F(000) = 556$, crystal size = $0.1 \times 0.3 \times 0.5$ mm^3, θ range = 2.37–29.15°; index ranges: $-12 \le h \le 11$, $-19 \le k \le 21$, $-8 \le l \le 13$; reflections collected 9075, independent reflections 5490 [R(int) = 0.0181]; completeness $\theta = 29.15°$, 98.9%; max/min transmission 1.000000/0.811634; data/restraints/parameters 5490/1/300; goodness-of-fit on F^2 1.085; final R indices [$I > 2\sigma(I)$]: $R1 = 0.0206$, $wR2 = 0.0557$; R indices (all data): $R1 = 0.0208$, $wR2 = 0.0559$; absolute structure parameter −0.001(16); largest diff. peak/hole 0.491/−0.684 e Å^{-3}. CCDC-248010 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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[1] a) J. D. Connolly, R. A. Hill, *Dictionary of Terpenoids, Vol. 1*, Chapman and Hall, London, **1991**, p. 476; for examples: b) V. K. Honwad, A. S. Rao, *Tetrahedron* **1964**, *20*, 2921; c) T. Sakai, Y. Hirose, *Chem. Lett.* **1973**, 491; d) J. F. Austin, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2002**, *124*, 1172; e) W. C. Black, C. Bayly, M. Belley, C. C. Chan, S. Charleson, D. Denis, J. Y. Gauthier, R. Gordon, D. Guay, S. Kargman, C. K. Lau, Y. Leblac, J. Mancini, M. Ouellet, D. Percival, P. Roy, K. Skorey, P. Tagari, P. Vickers, W. Wong, L. Xu, P. Prasit, *Bioorg. Med. Chem. Lett.* **1996**, *6*, 725.

[2] a) U. Leutenegger, A. Madin, A. Pfaltz, *Angew. Chem.* **1989**, *101*, 61; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 60; b) M. Misun, A. Pfaltz, *Helv. Chim. Acta* **1996**, *79*, 961; c) P. von Matt, A. Pfaltz, *Tetrahedron: Asymmetry* **1991**, *2*, 691.

[3] a) T. Yamada, Y. Ohtsuka, T. Ikeno, *Chem. Lett.* **1998**, 1129; b) Y. Ohtsuka, T. Ikeno, T. Yamada, *Tetrahedron: Asymmetry* **2003**, *14*, 967.

[4] C. Geiger, P. Kreitmeier, O. Reiser, *Adv. Synth. Catal.* **2005**, *347*, 249.

[5] a) D. H. Appella, Y. Moritani, R. Shintani, E. M. Ferreira, S. L. Buchwald, *J. Am. Chem. Soc.* **1999**, *121*, 9473; b) Y. Moritani, D. H. Appella, V. Jurkauskas, S. L. Buchwald, *J. Am. Chem. Soc.* **2000**, *122*, 6797; c) J. Yun, S. L. Buchwald, *Org. Lett.* **2001**, *3*, 1129; d) G. Hughes, M. Kimura, S. L. Buchwald, *J. Am. Chem. Soc.* **2003**, *125*, 11253; e) M. P. Rainka, Y. Aye, S. L. Buchwald, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5821.

[6] a) B. H. Lipshutz, J. M. Servesko, *Angew. Chem.* **2003**, *115*, 4937–4940; *Angew. Chem. Int. Ed.* **2003**, *42*, 4789; b) B. H. Lipshutz, J. M. Servesko, T. B. Petersen, P. Papa, A. A. Lover, *Org. Lett.* **2004**, *6*, 1273; c) B. H. Lipshutz, J. M. Servesko, B. R. Taft, *J. Am. Chem. Soc.* **2004**, *126*, 8352.

[7] a) W. S. Mahoney, D. M. Brestensky, J. M. Stryker, *J. Am. Chem. Soc.* **1988**, *110*, 291; b) W. S. Mahoney, J. M. Stryker, *J. Am. Chem. Soc.* **1989**, *111*, 8818; c) D. M. Brestensky, J. M. Stryker, *Tetrahedron Lett.* **1989**, *30*, 5677; d) T. M. Koenig, J. F. Daeuble, D. M. Brestensky, J. M. Stryker, *Tetrahedron Lett.* **1990**, *31*, 3237; further extension: e) A. Mori, A. Fujita, Y. Nishihara, T. Hiyama, *Chem. Commun.* **1997**, 2159; f) H. Ito, T. Ishizuka, K. Arimoto, K. Miura, A. Hosomi, *Tetrahedron Lett.* **1997**, *38*, 8887; g) B. H. Lipshutz, J. Keith, P. Papa, R. Vivian, *Tetrahedron Lett.* **1998**, *39*, 4627; h) A. Mori, A. Fujita, H. Kajiro, Y. Nishihara, T. Hiyama, T. *Tetrahedron* **1999**, *55*, 4573; i) B. H. Lipshutz, W. Chrisman, K. Noson, P. Papa, J. A. Scalfani, R. W. Vivian, J. M. Keith, *Tetrahedron* **2000**, *56*, 2779; j) P. Chiu, C.-P. Szeto, Z. Geng, K.-F. Cheng, *Org. Lett.* **2001**, *3*, 1901; k) V. Jurkauskas, J. P. Sadighi, S. L. Buchwald, *Org. Lett.* **2003**, *5*, 2417; chiral Cu-catalyzed hydrosilylation of nitroalkenes, see: l) C. Czekelius, E. M. Carreira, *Angew. Chem.* **2003**, *115*, 4941–4943; *Angew. Chem. Int. Ed.* **2003**, *42*, 4793; m) C. Czekelius, E. M. Carreira, *Org. Lett.* **2004**, *6*, 4575; n) Chu nitro cyclization, copper-catalyzed conjugate reduction of α,β-unsaturated nitriles, see: o) D. Kim, B.-M Park, J. Yun, *Chem. Commun.* **2005**, 1755.

[8] a) J. W. Yang, M. T. H. Fonseca, B. List, *Angew. Chem.* **2004**, *116*, 6829; *Angew. Chem. Int. Ed.* **2004**, *43*, 6660; b) J. W. Yang, M. T. H. Fonseca, N. Vignola, B. List, *Angew. Chem.* **2005**, *117*, 110; *Angew. Chem. Int. Ed.* **2005**, *44*, 108; c) S. G. Ouellet, J. B. Tuttle, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2005**, *127*, 32.

[9] a) Y. Motoyama, N. Makihara, Y. Mikami, K. Aoki, H. Nishiyama, *Chem. Lett.* **1997**, 951; b) Y. Motoyama, H. Narusawa, H. Nishiyama, *Chem. Commun.* **1999**, 131; c) Y. Motoyama, Y. Koga, H. Nishiyama, *Tetrahedron* **2001**, *57*, 853; d) Y. Motoyama, M. Okano, H. Narusawa, N. Makihara, K. Aoki, H. Nishiyama, *Organometallics* **2001**, *20*, 1580; e) Y. Motoyama, K. Shimozono, K. Aoki, H. Nishiyama, *Organometallics* **2002**, *21*, 1684; f) Y. Motoyama, Y. Koga, K. Kobayashi, K. Aoki, H. Nishiyama, *Chem. Eur. J.* **2002**, *8*, 2968; g) Y. Motoyama, H. Nishiyama, *Synlett* **2003**, 1883. For polymer supported Rh-Phebox: h) A. Weissberg, M. Portnoy, *Chem. Commun.* **2003**, 1538. For Pd- and Pt-Phebox complexes: i) Y. Motoyama, Y. Mikami, H. Kawakami, K. Aoki, H. Nishiyama, *Organometallics* **1999**, *18*, 3584; j) Y. Motoyama, H. Kawakami, K. Shimozono, K. Aoki, H. Nishiyama, *Organometallics* **2002**, *21*, 3408. As a review: k) Y. Motoyama, H. Nishiyama in *Latest Frontiers of Organic Synthesis* (Ed.: Y. Kobayashi), Research Signpost, **2002**, p. 1.

[10] Y. Tsuchiya, H. Uchimura, K. Kobayashi, H. Nishiyama, *Synlett* **2004**, 2099.

[11] Y. Tsuchiya, Y.Kanazawa, T. Shiomi, K. Kobayashi, H. Nishiyama, *Synlett* **2004**, 2493.

[12] I. Ojima, T. Kogure, *Organometallics* **1982**, *1*, 1390.

[13] a) E. Keinan, N. Greenspoon, *J. Am. Chem. Soc.* **1986**, *108*, 7314; b) E. Keinan, D. Perez, *J. Org. Chem.* **1987**, *52*, 2576.

[14] C. Bolm, K. Weickhardt, M. Zehnder, T. Ranff, *Chem. Ber.* **1991**, *124*, 1173.

[15] a) L. F. Tietze, B. Weigand, L. Völkel, C. Wulff, C. Bittner, *Chem. Eur. J.* **2001**, *7*, 161; b) F. López, S. R. Harutyunyan, A. J. Minnaard, B. L. Feringa, *J. Am. Chem. Soc.* **2004**, *126*, 12784.

[16] H. Ahlbrecht, H. Sommer, *Chem. Ber.* **1990**, *123*, 829.
[17] M. van Klaveren, F. Lambert, D. J. F. Eijkelkamp, D. M. Grove, G. van Koten, *Tetrahedron Lett.* **1994**, *35*, 6135.
[18] S. Oi, M. Moro, H. Ito, Y. Honma, S. Miyano, Y. Inoue, *Tetrahedron* **2002**, *58*, 91.
[19] a) S. Oi, A. Taira, Y. Honma, Y. Inoue, *Org. Lett.* **2003**, *5*, 97; b) M. Kanai, K. Koga, K. Tomioka, *Tetrahedron Lett.* **1992**, *33*, 7193; c) H. Tatemitsu, F. Ogura, Y. Nakagawa, M. Nakagawa, K. Naemura, M. Nakazaki, *Bull. Chem. Soc. Jpn.* **1975**, *48*, 2473.
[20] Y. Takaya, M. Ogasawara, T. Hayashi, M. Sakai, N. Miyaura, *J. Am. Chem. Soc.* **1998**, *120*, 5579.
[21] M. T. Reetz, D. Moulin, A. Gosberg, *Org. Lett.* **2001**, *3*, 4083.
[22] R. Shintani, N. Tokunaga, H. Doi, T. Hayashi, *J. Am. Chem. Soc.* **2004**, *126*, 6240.
[23] A. Fischli, D. Süss, *Helv. Chim. Acta* **1979**, *62*, 2361.
[24] a) B. K. Shull, M. Koreeda, *J. Org. Chem.* **1990**, *55*, 2249; b) T. Yamamoto, H. Ujihara, S. Watanabe, M. Harada, H. Matsuda, T. Hagiwara, *Tetrahedron* **2003**, *59*, 517.
[25] P. K. Fraser, S. Woodward, *Chem. Eur. J.* **2003**, *9*, 776.
[26] H. Ahlbrecht, S. Enders, L. Santowski, G. Zimmermann, *Chem. Ber.* **1989**, *122*, 1995.
[27] K. Tanaka, G. C. Fu, *J. Org. Chem.* **2001**, *66*, 8177.
[28] G. M. Sheldrick, SHELXTL 5.1, Bruker AXS Inc., Madison, Wisconsin, **1997**.

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