

Experimental Section

Representative experimental procedure: VO(OiPr)₃ (5 μ L, 20 μ mol) and hydroxamic acid (26.6 mg, 60 μ mol) were dissolved in toluene (1 mL), stirred for 1 hour, and cooled to 0°C. Cumene hydroperoxide (275 μ L, 1.5 mmol) and 3-(1-naphthyl)-3-buten-1-ol (**2j**) (198 mg, 1.0 mmol) were added at 0°C. The reaction mixture was stirred for 10 h, then trimethylphosphite (177 μ L, 1.5 mmol) was added at that temperature. The mixture was allowed to reach room temperature, then it was extracted with ethyl acetate, dried over sodium sulfate, and evaporated. The crude product was purified by column chromatography on a silica gel (eluent ethyl acetate/hexane, 1:1) to give 3,4-epoxy-3-(1-naphthyl)-1-butanol in 42% yield with 91% ee. ¹H NMR (300 MHz, CDCl₃, 25°C, TMS): δ = 8.13 (d, J = 8.0 Hz, 1H; Ar-H), 7.90 (d, J = 8.0 Hz, 1H; Ar-H), 7.83 (d, J = 8.0 Hz, 1H; Ar-H), 7.50 (m, 4H; Ar-H), 3.71 (m, 2H; CH₂OH), 3.35 (d, J = 6.0 Hz, 1H; OCH₂), 3.00 (d, J = 6.0 Hz, 1H; OCH₂), 2.45 (m, 1H; CCH₂CH₂), 2.29 (m, 1H; CCH₂CH₂), 1.69 ppm (br, 1H; OH). HPLC analysis (column: OD-H, Daisel): retention times 44.9 (main peak) and 68.1 min (minor peak) using hexane/2-propanol (40:1) as the eluent at a flow rate of 1.0 mL min⁻¹. For the epoxy alcohols **3a–e**, a saturated aqueous solution of sodium sulfite instead of trimethylphosphite was used for quenching the reaction.

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- [15] **9**: [α]_D²⁵ = –54.9 (c = 1.27 in ethanol);^[13d] ¹³C NMR (300 MHz, CDCl₃, 25°C, TMS): δ = 133.9, 131.3, 124.6, 120.6, 74.1, 42.9, 40.1, 31.0, 26.9, 25.6, 23.3, 23.2, 23.0, 22.0, 17.6 ppm.
- [16] **9'**: [α]_D²⁵ = –61.4 (c = 1.70 in ethanol), –69 (c = 1.3 in ethanol);^[13d] ¹³C NMR (300 MHz, CDCl₃, 25°C, TMS): δ = 133.9, 131.8, 124.7, 120.9, 74.4, 43.4, 39.4, 31.1, 26.2, 25.8, 24.1, 24.0, 23.5, 22.4, 17.8 ppm.

Catalytic Asymmetric Hydrogenation

Phospholane–Oxazoline Ligands for Ir-Catalyzed Asymmetric Hydrogenation**

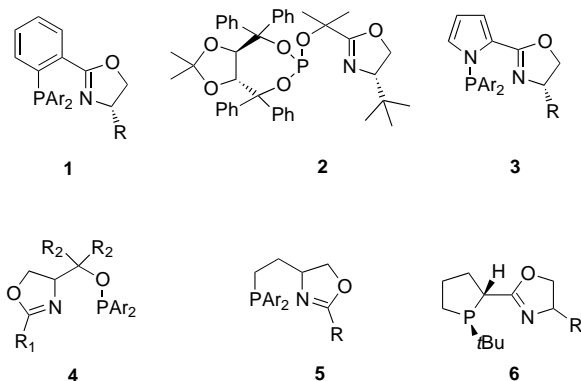
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Although a lot of progress has been made in Rh- or Ru-catalyzed asymmetric hydrogenation, Ir-catalyzed asymmetric hydrogenation is relatively unexplored.^[1] Pfaltz and co-workers first reported several Ir-phosphino-oxazoline complexes as catalysts for asymmetric hydrogenation. With leading efforts by Pfaltz and co-workers,^[2] and Burgess and

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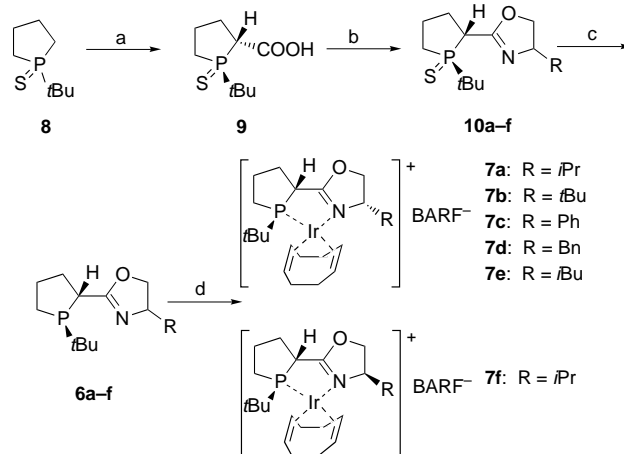
co-workers,^[3] Ir-catalyzed asymmetric hydrogenation has been realized for some functionalized and nonfunctionalized olefins. However, since Ir-catalyzed asymmetric hydrogenation is still highly substrate dependent, the development of new efficient chiral ligands for Ir-catalyzed hydrogenation is a continuing challenge. Herein we report a new class of chiral N,P ligands, the phospholane-oxazolines **6** (Scheme 1), for Ir-catalyzed asymmetric hydrogenation. Excellent enantioselectivities have been obtained in hydrogenation of methylstilbene derivatives and β -methylcinammic esters.



Scheme 1. N,P Ligands for enantioselective Ir-catalyzed hydrogenation.

After the development of phosphino-oxazoline ligands (PHOX, **1**) for Ir-catalyzed asymmetric hydrogenation,^[2a] Pfaltz and others have continued their efforts for the search of new efficient N,P ligands (Scheme 1). Various N,P ligands such as TADDOL-phosphite-oxazoline (**2**),^[2b] PyrPHOX (**3**),^[2d] and phosphinite-oxazoline (**4**),^[2e,f,g] were subsequently developed by Pfaltz and co-workers. Burgess and co-workers also reported JM-Phos (**5**)^[3a,b] and imidazolylidene-oxazoline.^[3c] These ligands expanded the reaction scope of Ir-catalyzed asymmetric hydrogenation. The closely related Crabtree's catalyst, $[\text{Ir}(\text{cod})(\text{Py})\text{PCy}_3]\text{PF}_6$ (cod = 1,5-cyclooctadiene, Py = pyridine, Cy = cyclohexyl), is an efficient achiral catalyst for the hydrogenation of tri- or tetrasubstituted olefins.^[4] Since an electron-rich phosphane PCy_3 is used in this system, we aimed to develop a new class of chiral N,P ligands **6** with an electron-rich phosphorus center to match the electronic properties of Crabtree's catalyst. It is noteworthy that these phospholane-oxazoline ligands not only have a stereogenic center in the oxazoline ring but also at the phosphorus center.^[5] The structure of **6** is modular since the oxazoline ring can vary with an array of R groups.

We reported the synthesis of an efficient chiral bisphospholane ligand, TangPhos, from 1-*tert*-butyl-phospholane 1-sulfide **8** in only three steps.^[6] Phospholane-oxazolines **6** can also be synthesized easily from **8** in four steps (Scheme 2). Selective deprotonation of **8** by *n*-butyllithium in the presence of (–)-sparteine^[7] followed by reaction with CO_2 provided acid **9** with 72 % *ee*.^[8,9] Recrystallization of the acid from ethanol yielded the enantiomerically pure **9** in 40 % yield.^[15] The absolute configuration of **9** was confirmed by its X-ray structure analysis.^[10] The condensation of **9** with chiral amino

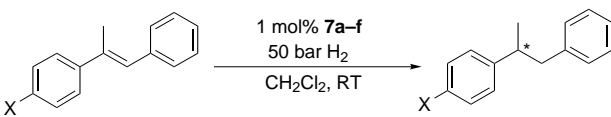


Scheme 2. Synthesis of phospholane-oxazoline ligands **6**. a) *n*BuLi, (–)-sparteine, CO_2 , -78°C , recrystallization, 71 % *ee* \rightarrow 100 % *ee*, 40 %; b) 1. amino alcohol, EDC, HOBT, DMF, 70°C ; 2. MsCl , CH_2Cl_2 , 70–80 %; c) Raney Ni, CH_3CN , 80–95 %; d) $[\text{Ir}(\text{cod})\text{Cl}]_2$, NaBARF, 50–70 %. EDC = *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride, HOBT = 1-hydroxybenzotriazole, cod = 1,5-cyclooctadiene, BARF = tetrakis[3,5-bis(trifluoromethyl)phenyl]borate, MsCl = methanesulfonyl chloride.

alcohols by using EDC/HOBT as the reagents proceeded smoothly to yield the coupling products, which were subsequently treated with MsCl to form the oxazoline compounds **10**. Desulfurization of **10** using Raney Ni^[11] provided a set of phospholane-oxazoline ligands **6** in excellent yields. The corresponding iridium complexes **7a–f** were synthesized in good yields according to standard procedures.^[2a] Although the iridium complexes **7a–f** are slightly air-sensitive, they can be stored under nitrogen for a long period of time without deterioration. To investigate the influence of the relative configuration of the chirality in the oxazoline ring, and the chiralities in the phospholane ring, two diastereomeric ligands **6a** and **6f** ($\text{R} = i\text{Pr}$) were synthesized. A series of ligands **6a–f** were also synthesized to study the influence of R in the oxazoline ring.

To test the effectiveness of the new chiral N,P ligands, iridium complexes **7a–f** were used as catalysts for asymmetric hydrogenation of methylstilbene derivatives.^[12] The hydrogenations were carried out at room temperature under 50 bar of pressure using CH_2Cl_2 as the solvent. All the reactions proceeded to completion in the presence of 1 mol % of an iridium complex. The diastereomeric complexes **7a** and **7f** led to hydrogenation products with different configuration (Table 1), which indicated that the chirality in the oxazoline ring of the ligand determined the configuration of the product. Iridium complex **7a** was favored over **7b** for the reaction, as a higher *ee* value (91 %) was obtained (Table 1, entries 1 and 6). Among the Ir complexes with different steric bulk (**7a–e**, Table 1, entries 1–5), the highest *ee* value (95 %) was obtained with **7c**, which has a phenyl group on the oxazoline ring. The enantiomeric excess of the product is comparable to those reported by Pfaltz et al.^[2a] with an Ir–PHOX system. With **7c** as the catalyst, another two substituted methylstilbene deriva-

Table 1: Ir-catalyzed asymmetric hydrogenation of methylstilbene derivatives.



Entry ^[a]	Substrate	X	Catalyst	ee [%] ^[b]	Config. ^[c]
1	8	H	7a	91	R
2	8	H	7b	81	R
3	8	H	7c	95	R
4	8	H	7d	89	R
5	8	H	7e	75	R
6	8	H	7f	77	S
7	9	OMe	7c	91	R
8	10	Cl	7c	90	R

[a] See Supporting Information for experimental details. [b] The enantiomeric excesses were determined by chiral HPLC (Chiralcel OJH). [c] The absolute configuration was assigned by comparison of the observed optical rotation with reported data.

tives were also subjected to hydrogenation and ee values over 90 % were obtained (entry 7 and 8).

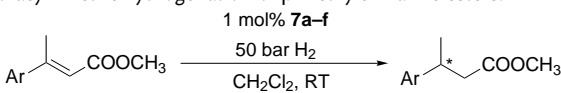
Asymmetric hydrogenation of β -methylcinnamic esters can directly form chiral 3-arylbutyric esters. The reduction products of 3-arylbutyric esters (i.e. chiral 3-arylbutanols) are important intermediates for the synthesis of aromatic sesquiterpenes of the bisabolane family.^[13] Pfaltz and co-workers applied the iridium phosphinite–oxazoline system to the asymmetric hydrogenation of ethyl β -methylcinnamate ester and obtained the desired product in 94 % ee.^[2f] We used the iridium complexes **7a–f** for hydrogenation of (*E*)- β -methylcinnamic esters, which can be easily synthesized by using the Heck reaction from aryl halides and crotonic esters.^[14] Methyl (*E*)- β -methylcinnamate was selected as the substrate to screen different iridium catalysts (Table 2, entries 1–6). The

two diastereomeric catalysts **7a** and **7f** (R = *i*Pr) led to products with different configurations (Table 2, entries 1 and 6). The highest enantiomeric excess (98 %) was obtained when **7c** was used as the catalyst (Table 2, entry 3). We therefore used **7c** as the catalyst for hydrogenation of a series of substituted (*E*)- β -methylcinnamic esters. A variety of chiral 3-arylbutyric esters were thus obtained in excellent enantiomeric excesses (95–99 %) regardless of the substitution pattern on the phenyl ring (Table 2, entries 7–12). The electronic properties of the substrates did not have a significant influence on the enantioselectivities. Substrates with a 2-naphthyl group and a 1-naphthyl group also gave high ee values (Table 2, entries 13, 14). To our knowledge, these are highest enantioselectivities to date for asymmetric hydrogenation of β -methylcinnamic esters. Asymmetric hydrogenation of a (*Z*)- β -methylcinnamic ester led to a product with a different configuration, and a lower enantiomeric excess was obtained (entries 8 and 15).

In conclusion, we have developed a new class of phospholane–oxazoline ligands for Ir-catalyzed asymmetric hydrogenation. Excellent reactivities and enantioselectivities were obtained in the hydrogenation of methylstilbene derivatives and (*E*)- β -methylcinnamic esters. Since the phospholane–oxazoline ligands can be easily synthesized, these ligands are promising for the synthesis of chiral arenes and 3-arylbutyric esters.^[15]

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Table 2: Ir-catalyzed asymmetric hydrogenation of β -methylcinnamic esters.



Entry ^[a]	Substrate	Ar	Catalyst	ee [%] ^[b]	Config. ^[c]
1	11	Ph	7a	94	R
2	11	Ph	7b	91	R
3	11	Ph	7c	98	R
4	11	Ph	7d	92	R
5	11	Ph	7e	95	R
6	11	Ph	7f	93	S
7	12	<i>p</i> -F-C ₆ H ₄	7c	95	R
8	13	<i>p</i> -Cl-C ₆ H ₄	7c	98	R
9	14	<i>p</i> -CH ₃ -C ₆ H ₄	7c	97	R
10	15	<i>p</i> -OCF ₃ -C ₆ H ₄	7c	97	R
11	16	<i>p</i> -OCH ₃ -C ₆ H ₄	7c	97	R
12	17	<i>m</i> -CH ₃ -C ₆ H ₄	7c	99	R
13	18	1-naphthyl	7c	98	R
14	19	2-naphthyl	7c	95	R
15	(<i>Z</i>)- 13	<i>p</i> -Cl-C ₆ H ₄	7c	80	S

[a] See Supporting Information for experimental details. [b] The enantiomeric excesses were determined by chiral HPLC (Chiralcel OJH) or chiral GC (Chiralselect 1000). [c] The absolute configurations were assigned by comparison of the observed optical rotation with reported data or by analogy.

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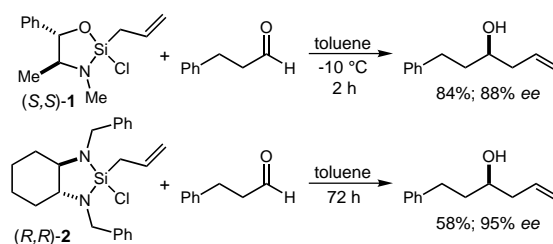
Allylation of Aldehydes

A Highly Practical and Enantioselective Reagent for the Allylation of Aldehydes**

Katsumi Kubota and James L. Leighton*

Owing mainly to the prevalence of secondary alcohols in bioactive natural products, chemists have developed many moderately to highly enantioselective chiral reagents^[1] and catalytic systems^[2] for the allylation of aldehydes. In terms of practical utility, an ideal reagent should 1. be readily prepared in both enantiomeric forms, 2. be a stable/storable solid that can be prepared in bulk and employed at will by using only trivial procedures, 3. possess a good safety profile both for the user and environmentally, and 4. be generally effective in terms of both efficiency and enantioselectivity. Herein we report a new reagent that almost completely satisfies all of these conditions.

Based on our discovery that silicon—constrained in a five-membered ring by 1,2-diols, 1,2-aminoalcohols and 1,2-diamines—possesses Lewis acidity sufficient for clean, uncatalyzed allylation of aldehydes, we recently described the pseudoeephedrine-derived strained silacycle **1** as a reagent for the enantioselective allylation of aldehydes (Scheme 1).^[3] Whereas this reagent is trivially prepared and employed, and the enantioselectivities for aliphatic aldehydes are good (87–89% *ee*, typically), they are unacceptably low for aromatic and conjugated aldehydes (60–81% *ee*, typically). This reagent thus falls short of ideal mainly in terms of condition 4 (see above). Also reported were preliminary data regarding reagent **2**, which was found to provide improved enantioselectivity, but also low reactivity. We therefore initiated a full investigation into the potential of the diamine-based system.



Scheme 1. Reagents for asymmetric allylation.

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