Planar-Chiral Phosphine-Olefin Ligands Exploiting a (Cyclopentadienyl)manganese(I) Scaffold to Achieve High Robustness and High Enantioselectivity

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Kamikawa, K.; Tseng, Y.-Y.; Jian, J.-H.; Takahashi, T.; Ogasawara, M.
J. Am. Chem. Soc. **2017**, *139*, 1545-1553.

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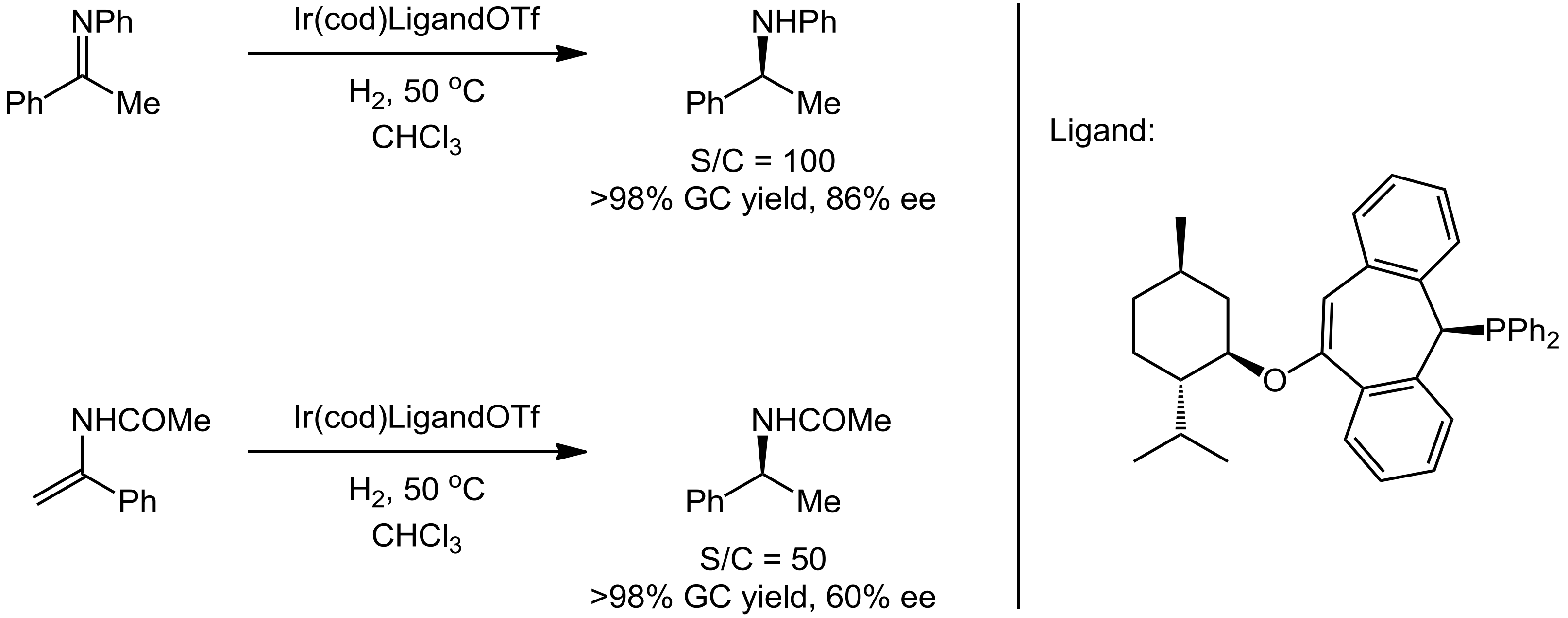
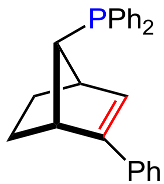
Introduction

◆ Olefins can be used as steering ligands in catalysis ... Olefins show an enormous electronic flexibility, like almost no other class of ligands, and furthermore are present as potential binding sites in many natural products not yet explored for the purposes of organometallic chemistry. A large pool of ligands with potentially better properties remains to be explored.

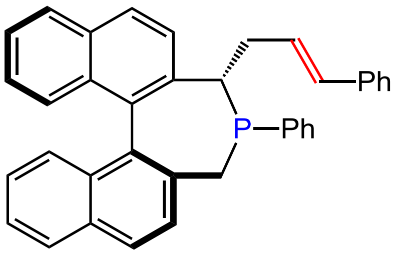


Grützmacher, H. *et al. Chem. Eur. J.* **2004**, *10,* 4198.

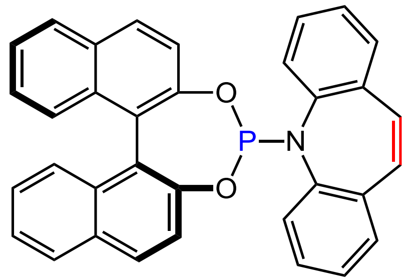
Chiral Phosphine-Olefin Ligands



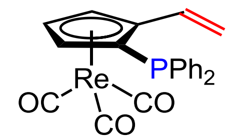
Hayashi (2005)



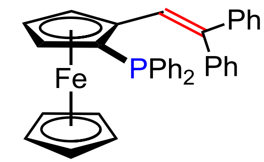
Widhalm (2006)



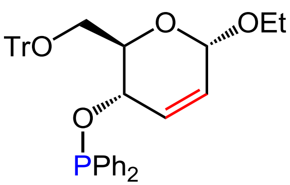
Carreira (2007)



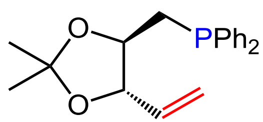
Bolm (2007)



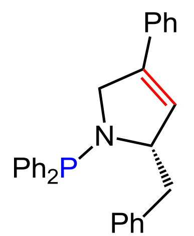
Štěpnička (2008)



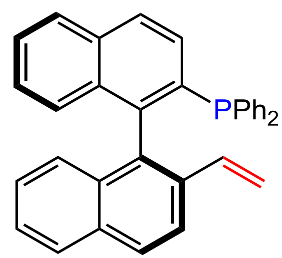
Boysen (2009)



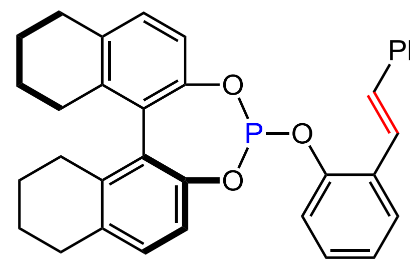
Du (2010)



Hayashi (2011)



Du (2011)

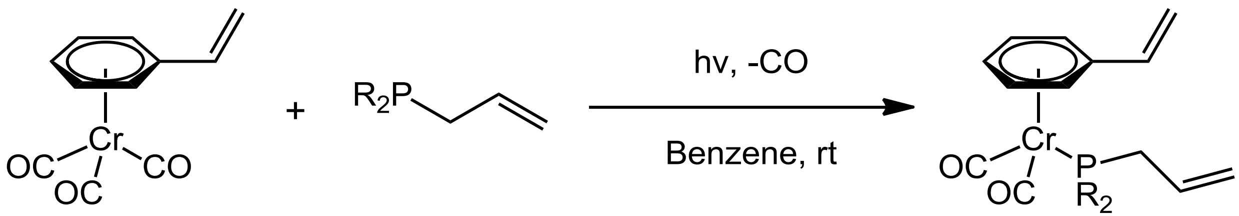


Xu (2016)

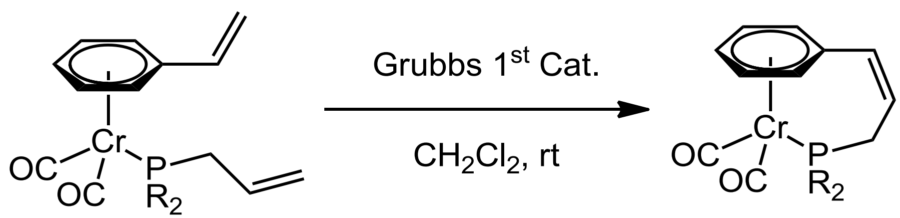
Hayashi, T. *et al. Angew. Chem. Int. Ed.* **2005**, *44*, 4611; Widhalm, M. *et al. Tetrahedron: Asymmetry* **2006**, *17*, 3084; Carreira, E. M. *et al. Angew. Chem. Int. Ed.* **2007**, *46*, 3139; Bolm, C. *et al. Synlett* **2007**, 1365; Štěpnička, P. *et al. J. Organometallic Chem.* **2008**, *693*, 446; Boysen, M. M. K. *et al. Org. Lett.* **2009**, *11*, 4212; Du, H. *et al. Org. Lett.* **2010**, *12*, 3054; Hayashi, T. *et al. Chem. Commun.* **2011**, *47*, 6123; Du, H. *et al. Org. Lett.* **2011**, *13*, 2164; Xu, M.-H. *et al. ACS Catal*. **2016**, *6*, 661.

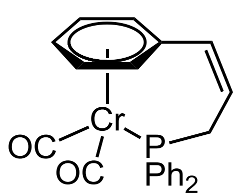
Phosphine-Chelate (π-Arene)chromium Complexes

Ru-catalyzed ring-closing metathesis:

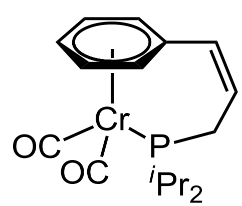


68-80% yield





93% yield

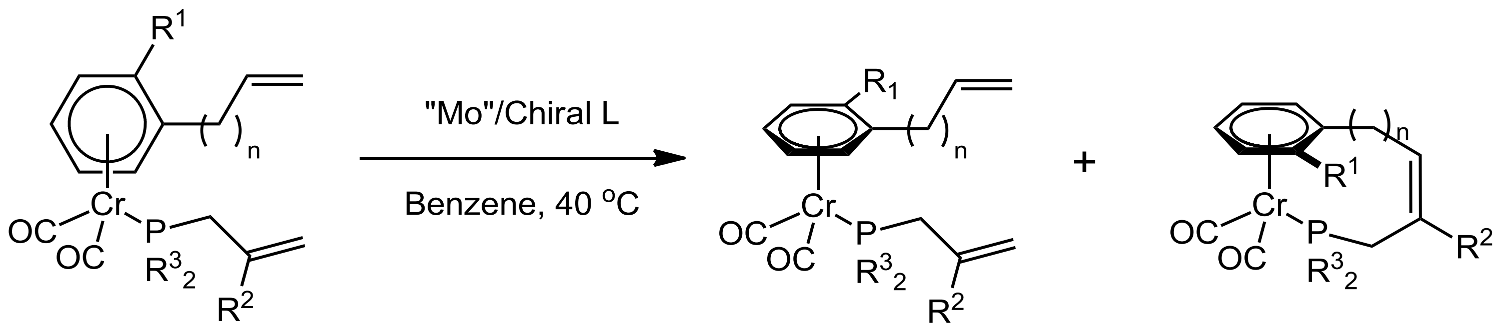


82% yield

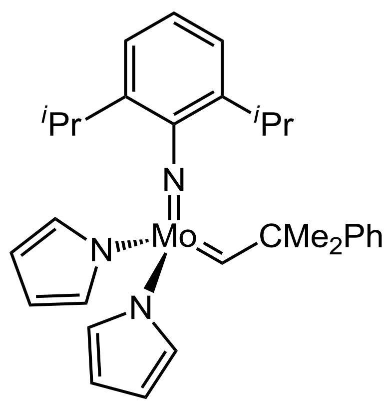
Ogasawara, M., Takahashi, T., Kamikawa, K. *et al. J. Organometallic Chem.* **2011**, *696*, 3987.

Phosphine-Chelate (π-Arene)chromium Complexes

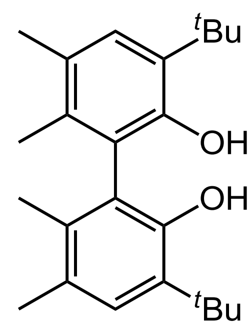
Mo-catalyzed asymmetric ring-closing metathesis:



"Mo"

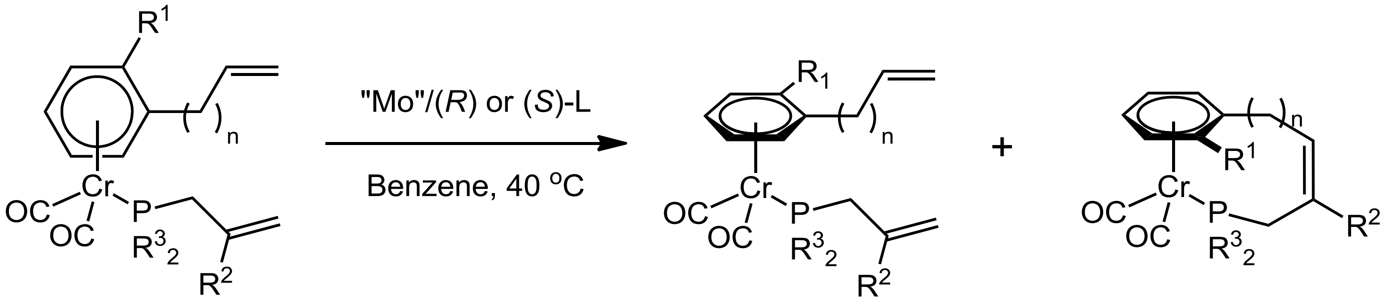


L



Ogasawara, M., Takahashi, T., Kamikawa, K. *et al. Angew. Chem. Int. Ed.* **2012**, *51*, 2951.

Substrate Scope

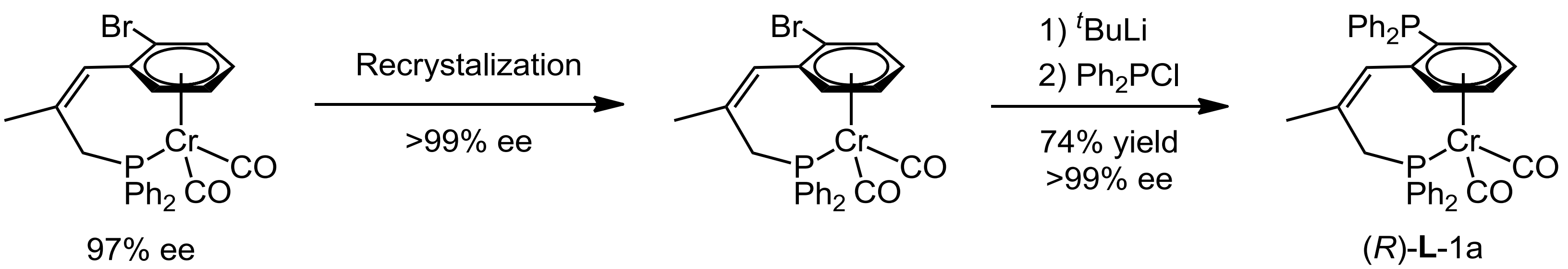


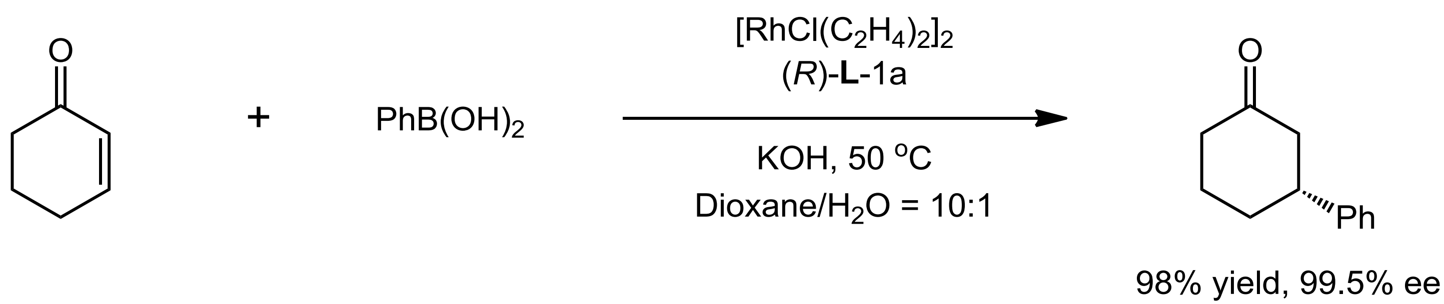
a: R^1 = Me, R^2 = Me, R^3 = Ph, n = 0
b: R^1 = Et, R^2 = Me, R^3 = Ph, n = 0
c: R^1 = Br, R^2 = Me, R^3 = Ph, n = 0
d: R^1 = Me, R^2 = Me, R^3 = ^{i}Pr, n = 0
e: R^1 = Me, R^2 = H, R^3 = Ph, n = 0
f: R^1 = Me, R^2 = Me, R^3 = Ph, n = 1

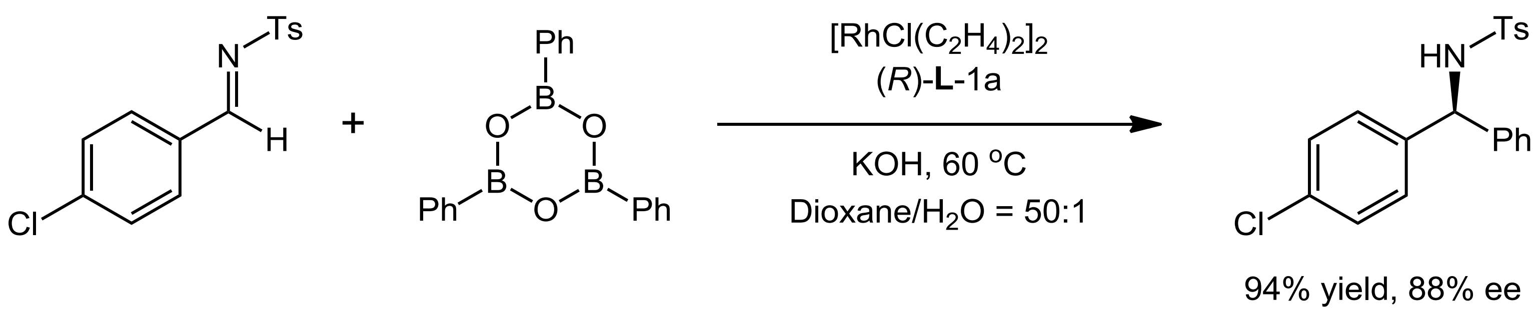
Entry	Substrates	L	Ee (yield) of recovered substrates	Ee (yield) of products	k_{rel}
1	**a**	*S*	88% (50%)	96% (44%)	114
2	**b**	*S*	63% (55%)	95% (42%)	75
3	**c**	*S*	89% (50%)	97% (47%)	198
4	**d**	*R*	98% (42%)	90% (49%)	87
5[a]	**e**	*R*	3% (69%)	14% (14%)	1.4
6	**f**	*R*	12% (55%)	45% (34%)	3

[a] 23 °C.

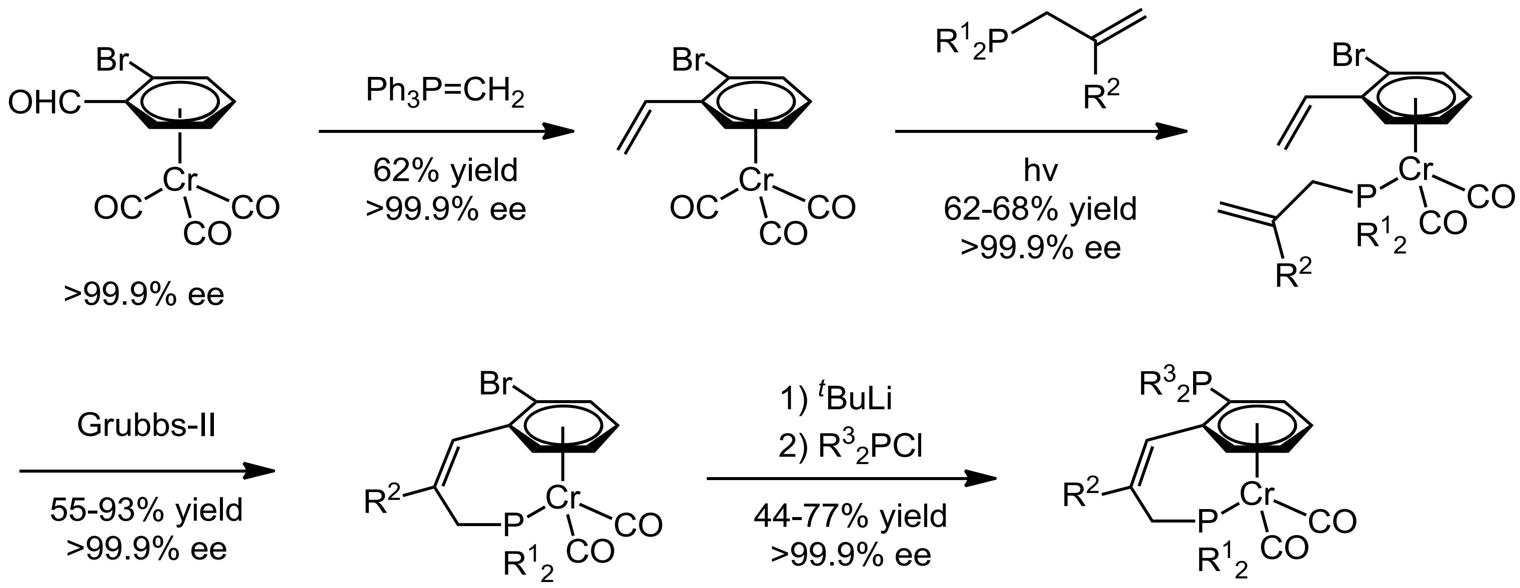
Application as the Chiral Ligands







The Improved Synthetic Route

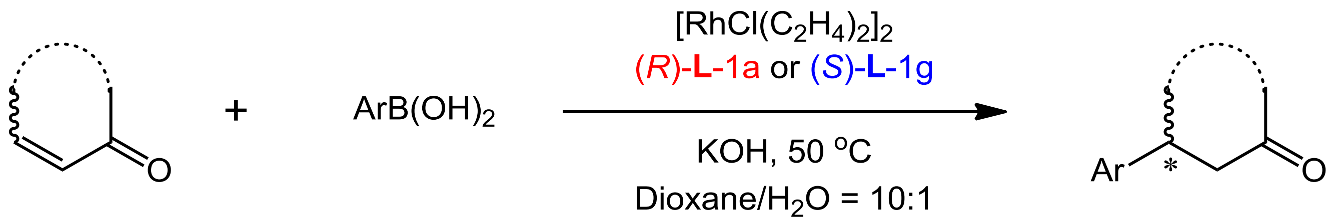


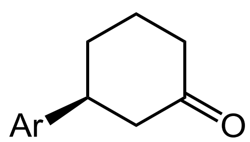
(*R*)-**L**-1a-h

L-1a: R^1 = Ph, R^2 = Me, R^3 = Ph;
L-1b: R^1 = ^{i}Pr, R^2 = Me, R^3 = Ph;
L-1c: R^1 = 3,5-Xyl, R^2 = Me, R^3 = Ph;
L-1d: R^1 = Ph, R^2 = Ph, R^3 = Ph;
L-1e: R^1 = Ph, R^2 = H, R^3 = Ph;
L-1f: R^1 = Ph, R^2 = Bn, R^3 = Ph;
L-1g: R^1 = Ph, R^2 = Me, R^3 = 3,5-Xyl;
L-1h: R^1 = Ph, R^2 = Me, R^3 = ^{i}Pr.

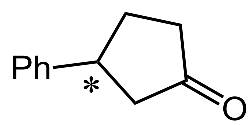
Alexakis, A. *et al. Tetrahedron: Asymmetry* **1995**, *6*, 47.
Ogasawara, M., Takahashi, T., Kamikawa, K. *et al. J. Am. Chem. Soc.* **2014**, *136*, 9377.

Rh-Catalyzed Asymmetric 1,4-Addition Reactions

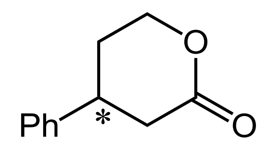




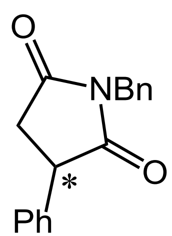
Ar = 4-$CH_3C_6H_4$, >99% yield, 98.4% ee
Ar = 4-$CF_3C_6H_4$, 95% yield, 97% ee



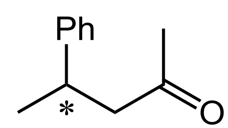
95% yield, 99.5% ee
92% yield, 99.9% ee



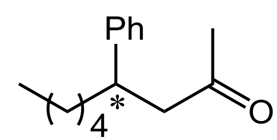
89% yield, 99.4% ee
95% yield, 99.5% ee



$[Rh(OH)(cod)]_2$, -20 °C to 0 °C
85% yield, 81% ee
83% yield, 94% ee

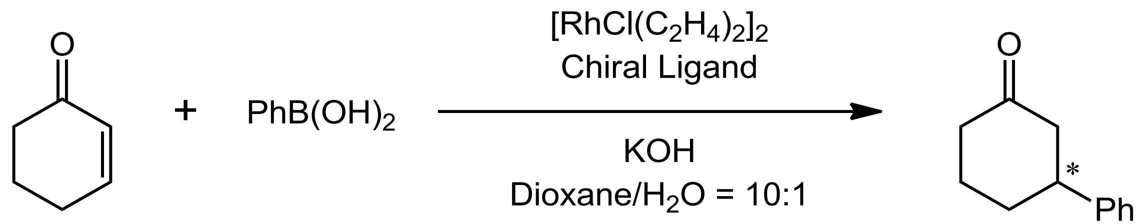


31% yield, 57% ee
34% yield, 88% ee

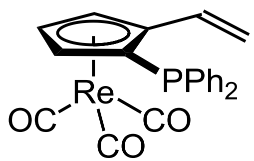


75 °C
13% yield, 58% ee
43% yield, 88% ee

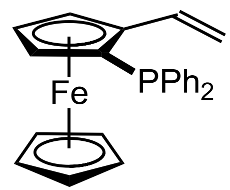
Rh-Catalyzed Asymmetric 1,4-Addition Reactions



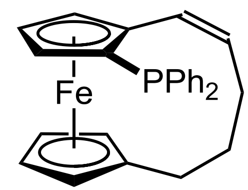
100 °C



86% yield, 71% ee

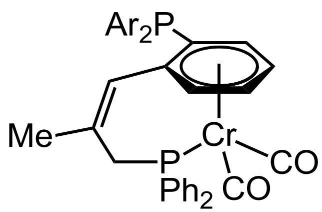


82% yield, 58% ee

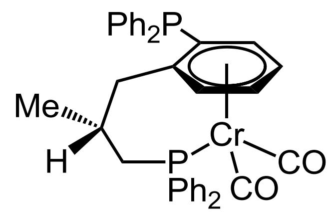


77% yield, 86% ee

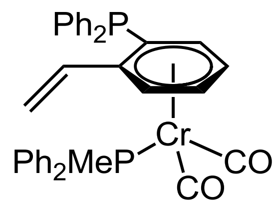
50 °C



Ar = Ph, 99% yield, 98% ee
Ar = 3,5-Xyl, 98% yield, 99.6% ee

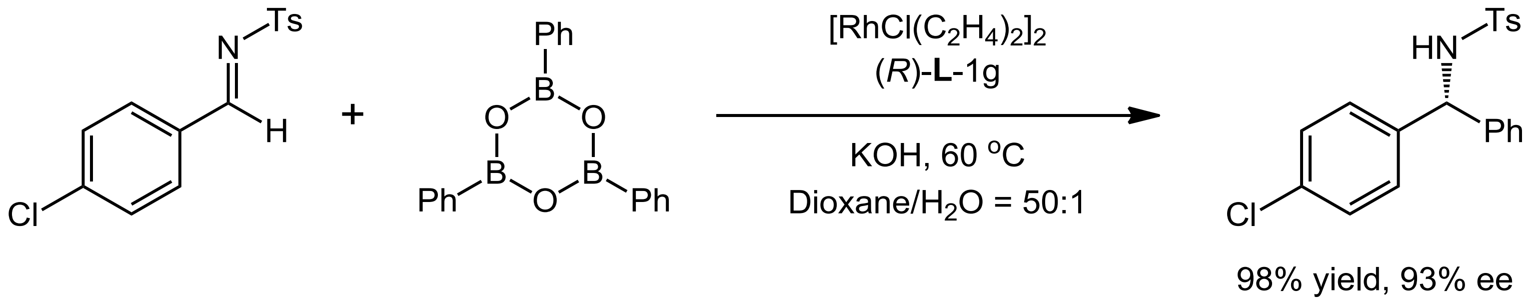


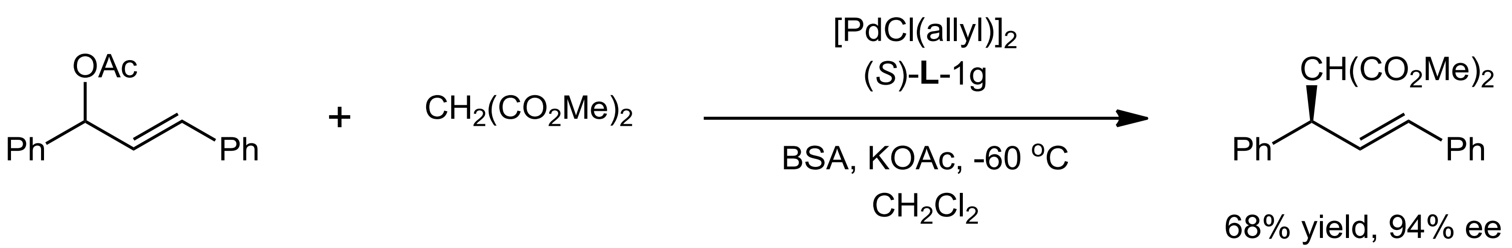
27% yield, <1% ee



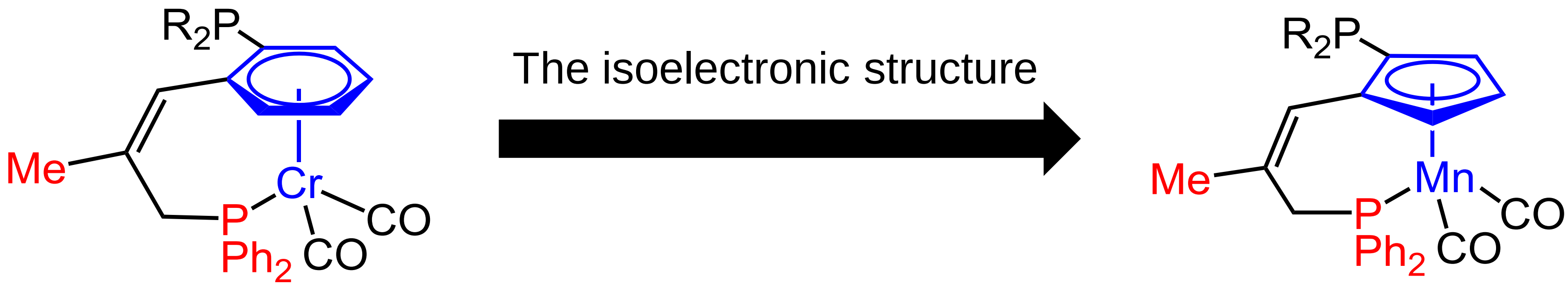
47% yield, 59% ee

Other Application as the Chiral Ligands





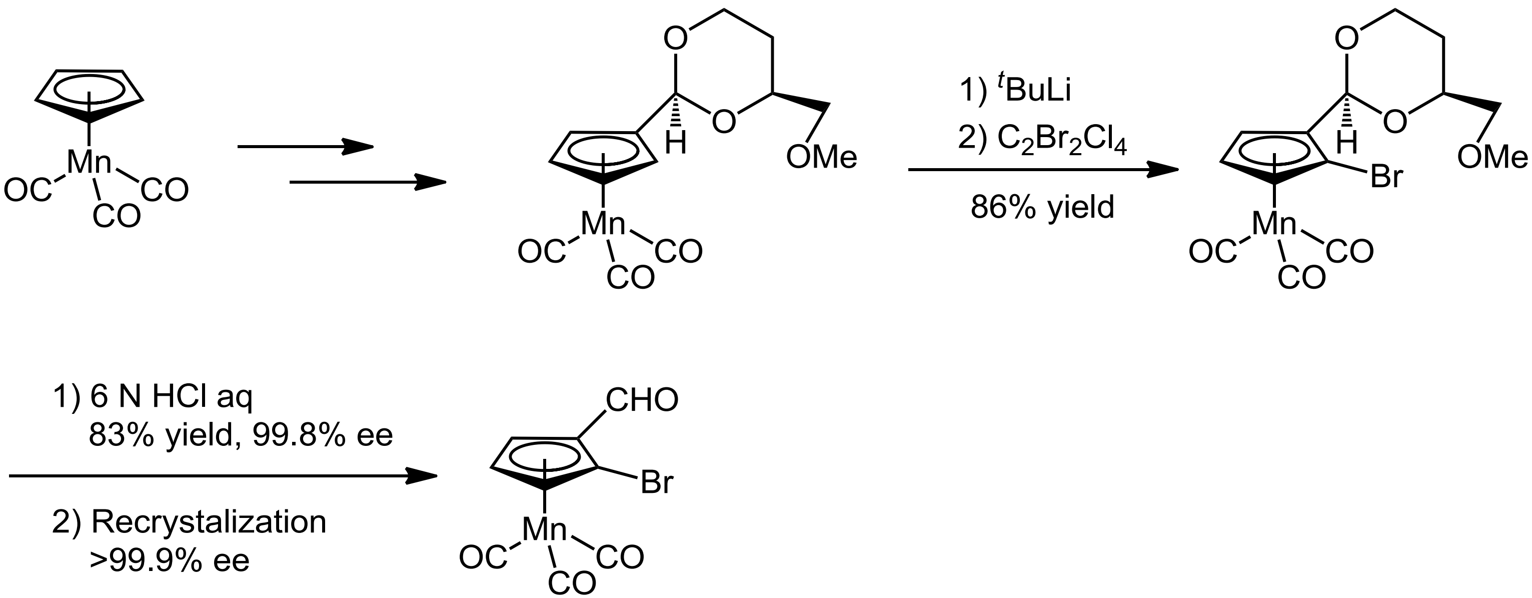
Design the New Phosphine-Olefin Ligands



- **Retain** the key structural motifs:
  - ✓ The bridging structure between the π-arene and the chromium-bound phosphine
  - ✓ A methyl group on the olefin unit

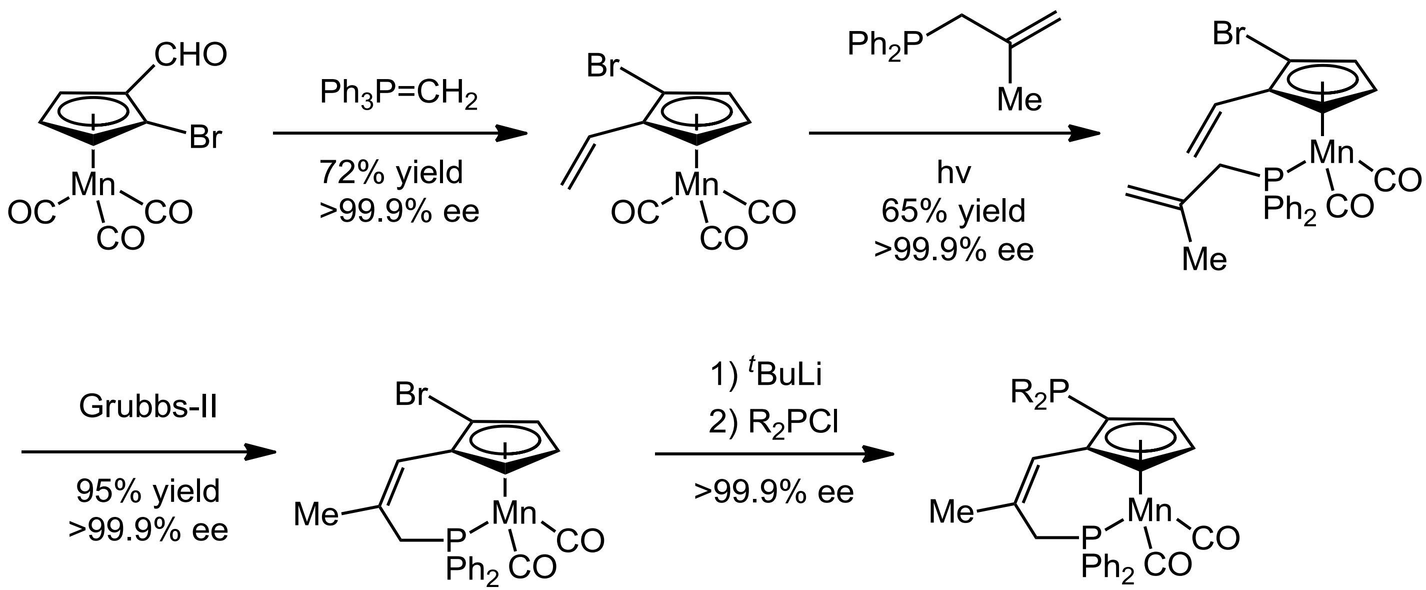
- **Replace** the photo- and oxygen-sensitive (π-arene)chromium(0) moiety
  - ✓ The partially ionic metal/π-ligand interaction
  - ✓ The different phosphine-olefin bite angles

(Cyclopentadienyl)manganese(I)-Based Ligands



Jaouen, G. *et al. J. Organometallic Chem.* **2004**, *689*, 4872.

(Cyclopentadienyl)manganese(I)-Based Ligands

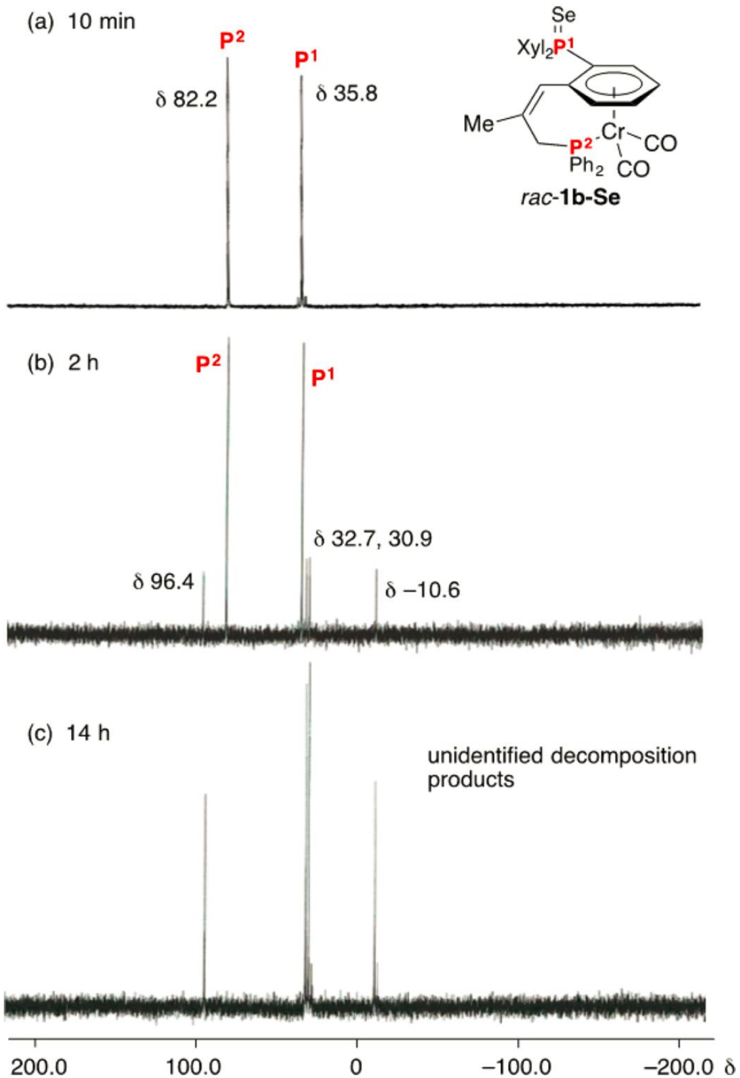


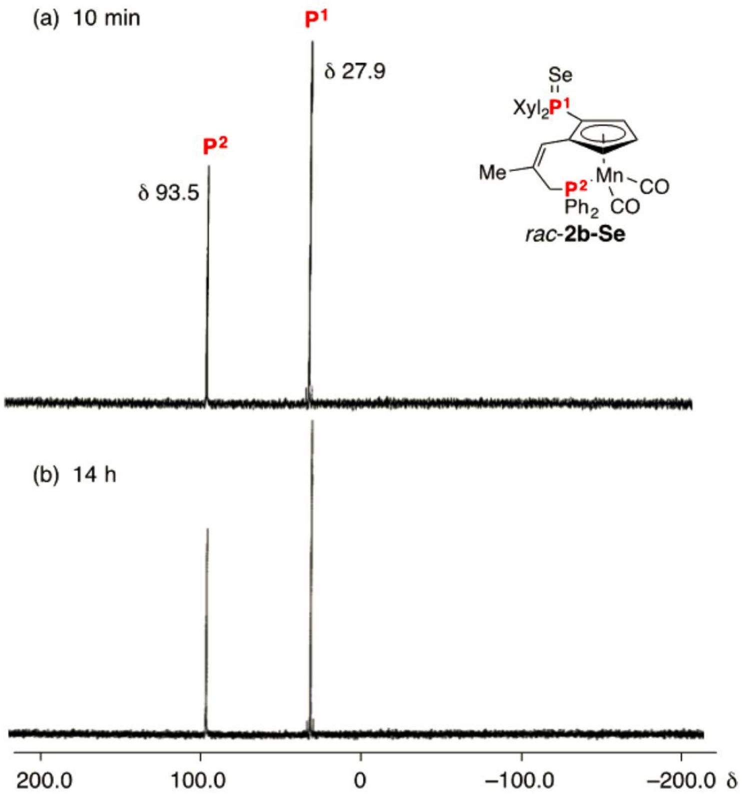
(*S*)-**L**-2a-d

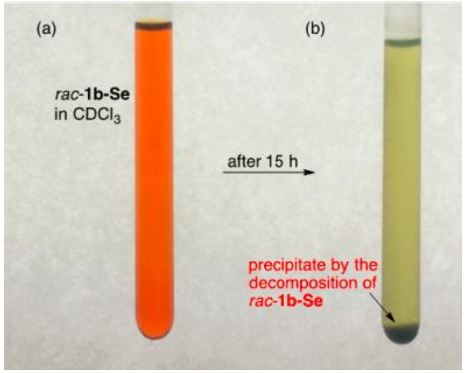
L-2a: R = Ph, 86% yield
L-2b: R = 3,5-$(CH_3)_2$-C_6H_3, 76% yield
L-2c: R = 3,5-$(CF_3)_2$-C_6H_3, 82% yield
L-2d: R = 3,5-$(^t Bu)_2$-4-$MeOC_6H_2$, 61% yield

Kamikawa, K., Ogasawara, M. *et al. J. Am. Chem. Soc.* **2017**, *139*, 1545.

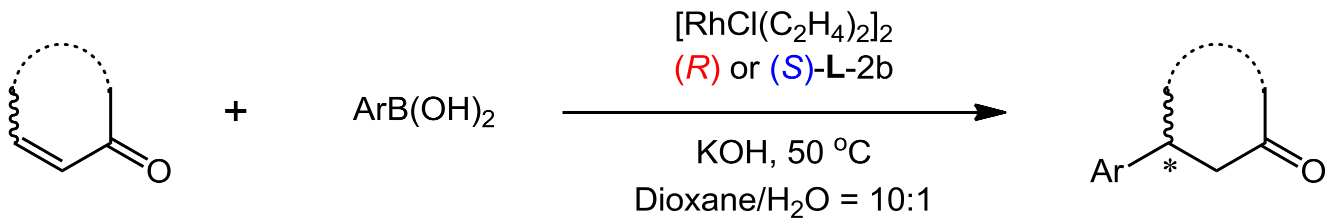
Comparison of Air-Oxidation Tolerance

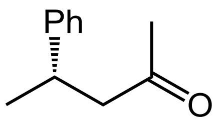




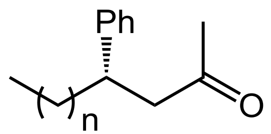


Rh-Catalyzed Asymmetric 1,4-Addition Reactions

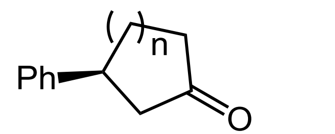




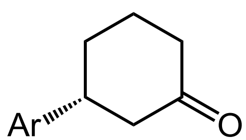
99% yield, 98% ee



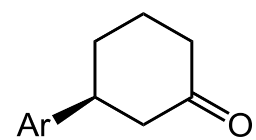
n = 2, 92% yield, 98.9% ee
n = 4, 77% yield, 99.8% ee
n = 5, 43% yield, 99.7% ee



n = 1, 99% yield, 99.6% ee
n = 3, 99% yield, 99.9% ee

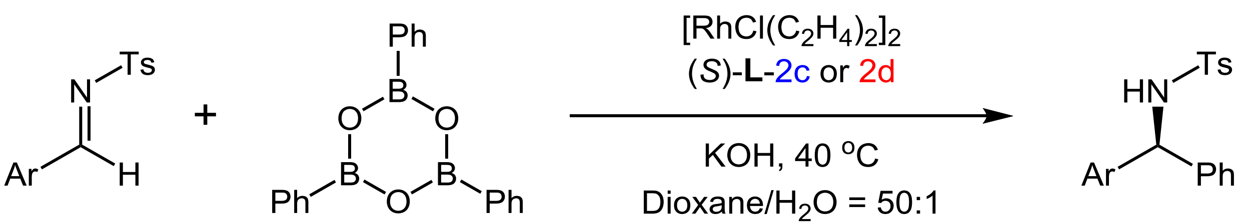


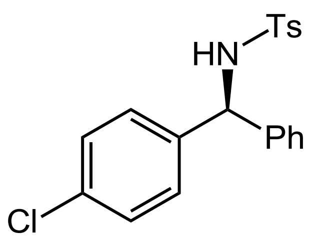
Ar = 4-$MeOC_6H_4$, 99% yield, 99.8% ee
Ar = 4-MeC_6H_4, 99% yield, 99.9% ee



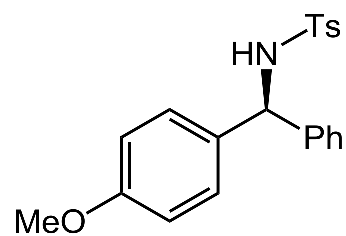
Ar = 2-$MeOC_6H_4$, 99% yield, 99.9% ee
Ar = 4-$CF_3C_6H_4$, 99% yield, 99.2% ee
Ar = 4-FC_6H_4, 99% yield, 99.6% ee

Rh-Catalyzed Asymmetric 1,2-Addition Reactions

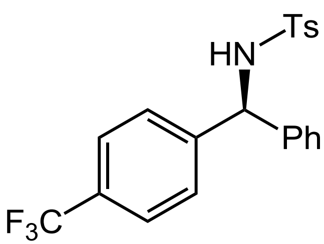




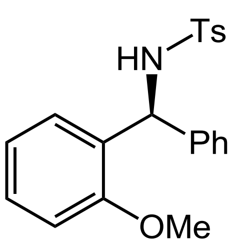
62% yield, 99.6% ee
92% yield, 99.2% ee



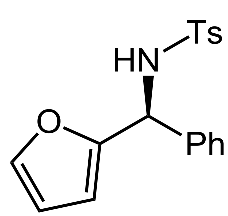
99% yield, 99.9% ee
99% yield, 99.6% ee



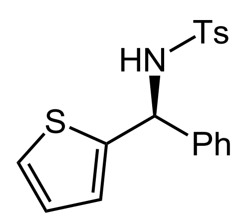
88% yield, 99.8% ee
96% yield, 99.6% ee



99% yield, 99.9% ee
99% yield, 99.0% ee



99% yield, 99.8% ee
97% yield, 99.8% ee

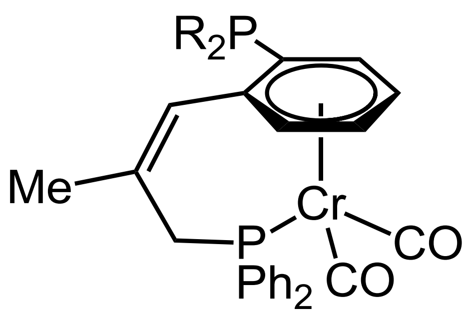


99% yield, 99.9% ee
89% yield, 99.7% ee

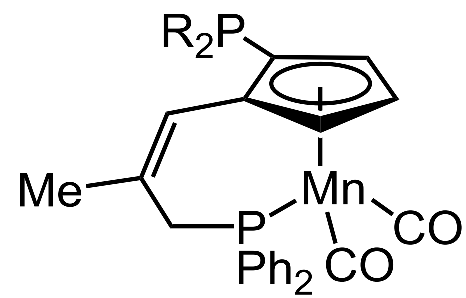
Summary

- The (π-Arene)chromium scaffold
- The (Cyclopentadienyl)manganese(I) scaffold

1st Generation P-olefin Ligands



2nd Generation P-olefin Ligands



- Instability toward air-oxidation especially in a solution state
- Insufficient enantioselectivities and reactivities with acyclic enones

- Stability toward air-oxidation in a solution state
- Excellent enantioselectivities and reactivities

The First Paragraph

Enantioselective reactions catalyzed by chiral transition-metal complexes are very powerful methods to supply various chiral building blocks in modern organic synthesis. The most common method for chiral modification of transition-metal catalysts is introduction of appropriate chiral ligands onto a metal center, and thus, design and synthesis of new chiral ligands, which could provide high activity and high enantioselectivity for the metal catalysts, has been a central subject in the development of asymmetric reactions. Chiral phosphines are arguably the chiral ligands most extensively studied for transition-metal-catalyzed asymmetric reactions. Meanwhile, conceptually novel chiral dienes have been elaborated over the past decade and have demonstrated to be superior to traditional chiral phosphines in various rhodium and iridium-catalyzed asymmetric reactions.

The First Paragraph

While chiral diene ligands enable construction of an effective chiral environment around the metal center, their coordination to a transition metal is generally weaker than that of phosphorus-based ligands, which diminish their applicability in transition-metal catalysis. Recently, chiral phosphine-olefin ligands have emerged as a new promising class of ligands, whose structural motifs can be regarded as a hybrid of classical chiral phosphines and chiral dienes.

The Last Paragraph

A new family of chiral phosphine-olefin bidentate ligands, whose chirality is based on a planar-chiral (η^5-cyclopentadienyl)manganese(I) dicarbonyl scaffold, has been developed. Ligand **2** shows better robustness as well as higher enantioselectivity over homologous (η^6-arene)chromium(0)-based planar-chiral phosphine-olefin ligand **1**. We have developed a general and enantiospecific synthetic method of **2** that can be conducted in a macroscale with ease. As the chelate coordination of **2** to a rhodium(I) cation constructs an effective chiral environment at the rhodium(I) center, the rhodium complexes of 2 display excellent catalytic performances in the various asymmetric reactions with arylboron nucleophiles.

The Last Paragraph

Ligand **2b**, which has a bis(3,5-dimethylphenyl)-phosphino group on the cyclopentadienyl ring, shows very high enantioselectivity in the rhodium-catalyzed asymmetric 1,4-addition reactions of arylboronic acids to various cyclic and acyclic enones to give the corresponding arylation products in up to 99.9% ee. Ligands **2c** (with bis[3,5-bis(trifluoromethyl)-phenyl]phosphino group) and **2d** (with bis(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphino group) are suited for rhodium catalyzed asymmetric 1,2-addition reactions of arylboron nucleophiles to imines or aldehydes showing up to 99.9% ee selectivity.