The Applications of Monodentate Chiral Phosphorus Ligands in Asymmetric Catalysis

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导师：麻生明 教授
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CONTENTS

Introduction

Why do people develop the monodentate chiral ligand ?

There have been only a limited number of monodentate chiral phosphines reported in the literature and high enantioselectivity with monodentate phosphines is difficult to obtain. However, **there are many transition-metalcatalyzed reactions that do not work with chelating bidentate ligands. Efficient chiral monophosphines are clearly needed.**

-------1999, Xumu Zhang

Chelating chiral diphosphines are often used as ligands of organometallic complexes. However, **monophosphines or more generally ligands with one phosphorus linked to one or several heteroatoms, may also be useful.**

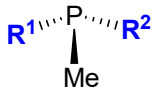
-------2000, Henri B. Kagan

Zhang, X. Enantiomer **1999**, *4*, 541.
Lagasse, F; Kagan, H. B. *Chem. Pharm. Bull.* **2000**, *48*, 315

Xumu Zhang

Henri B. Kagan

Representative of *P*-Chiral monodentate ligands

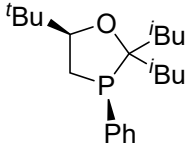


A

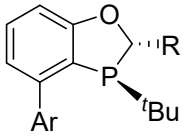
R^1 = Ph, R^2 = ^{n}Pr,
(mppp) 1967, **Korpiun and Mislow**

R^1 = Ph, R^2 = 2-$OMeC_6H_4$,
(pamp) 1967, **Korpiun and Mislow**

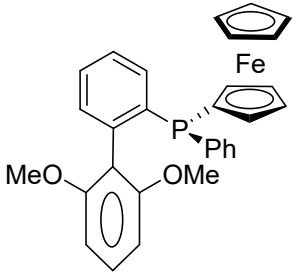
R^1 = Cy, R^2 = 2-$OMeC_6H_4$,
(camp) 1972, **Knowles**



B (*i*Bu-OxaPhos)
2011, **Morken**



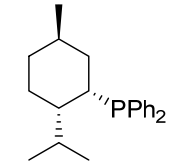
C
2010, Tang



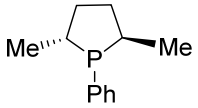
D
2013, **Han**

Korpium, O.; Mislow, K. *J. Am. Chem. Soc.* **1967**, *89*, 4784.
Knowles, W. S.; Sabacky, M. J. Vineyard B. D. *J. Chem. Soc., Chem. Commun.* **1972**, 10.
Tang, W. ; Capacci, A. G., Wei, X.; Li, W.; White, A.; Patel, N. D. Savoie, J.; Gao, J. J.; Rodriguez, S.; Qu, B.; Haddad, N.; Lu, B. Z.; Krishnamurthy, D.; Yee, N. K.; Senanayake, C. H. *Angew. Chem. Int. Ed.* **2010**, *49*, 5879.
Tang, W.; Keshipeddy, S.; Zhang, Y.; Wei, X.; Savoie, J.; Patel, N. D.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2011**, *13*, 1366.
Gao, J J.; Li,W.; Rodriguez, S.; Lu, B. Z.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2012**, *14*, 2258.
Du, K.; Guo, P.; Chen, Y.; Cao, Z.; Wang, Z.; Tang, W. *Angew. Chem. Int. Ed.* **2015**, *54*, 3033.
Schuster, C. H.; Li, B.; Morken, J. P. *Angew. Chem. Int. Ed.* **2011**, *50*, 7906.
Han, Z.; Goyal, N.; Herbage, M. A.; Sieber, J. D.; Qu, B.; Xu, Y.; Li, Z.; Reeves, J. T.; Desrosiers, J. -N.; Ma, S.; Grinberg, N.; Lee, H.; Mangunuru, H. P. R.; Zhang, Y.; Krishnamurthy, D.; Lu, B. Z.; Song, J. J.; Wang, G.; and Senanayake, C. H. *J. Am. Chem. Soc.* **2013**, *135*, 2474.

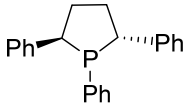
Representative of monodentate phosphorus ligands with asymmetric centers



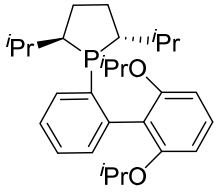
E
1971,Morrison



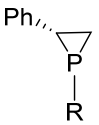
F
1991, Burk



G
1999, Fiaud

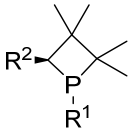


H
2012, Cramer



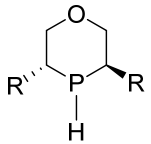
R = ^{t}Bu, (-)-menthyl

I
1993, Marinetti



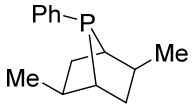
R1 = (-)-menthyl, R^2 = Bn

J
1994, Marinett

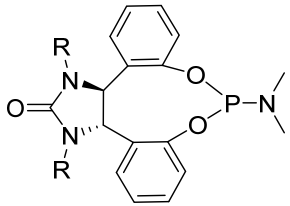


R = ^{i}Pr, Cy

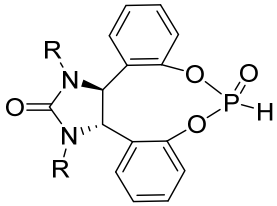
K
2002, Helmchen



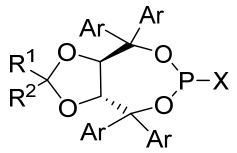
L
1997, Zhang



M (DpenPhos)
2005, Ding



N
2012, Ding

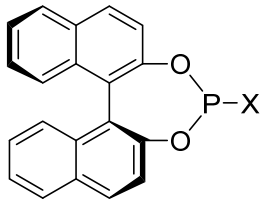


O (TADDOL-Derived)
1993, Seebach

X = C substituent: **phosphonite**
X = O substituent: **phosphite**
X = N substituent: **phosphoramidite**

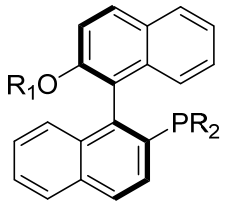
Morrison, J. D.; Burnett, R. E.; Agular, A. M.; Morrow, C, J.; Phillips, C.; *J. Am. Chem. Soc.* **1971**, *93*, 1301.
Burk, M. J.; Feaster, J. E. *Tetrahedron*: *Asymmetry.* **1991**, *2*, 569.
Guillen, F.; Fiaud, J. -C. *Tetrahedron Lett.* **1999**, *40*, 2939.
Saget, T.; Lemouzy, S. J.; Cramer, N. *Angew. Chem. Int. Ed.* **2012**, *51*, 2238.
Marinetti, A.; Mathey, F.; Ricard, L. *Organometallics*, **1993**, *12*, 1207.
Marinetti, A.; Ricard, L. *Organometallics*, **1994**, *13*, 3956.
Ostermeier, M.; Prieβ, J.; and Helmchen, G. *Angew. Chem. Int. Ed.* **2002**, *41*, 612.
Chen, Z.; Jiang, Q.; Zhu, G.; Xiao, D.; Cao, P.; Guo, C.; Zhang, X. *J. Org. Chem.* **1997**, *62*, 4521.
Liu, Y.; Ding, K. *J. Am. Chem. Soc.* **2005**, *127*, 10488.
Dong, K.; Wang, Z.; Ding, K. *J. Am. Chem. Soc.* **2012**, *134*, 12474.
Seebach, D.; Hayakawa, M.; Sakaki, J.; Schweizer, W. B. *Tetrahedron* **1993**, *49*, 1711.
Sakaki, J.; Schweizer, W. B.; Seebach, D. *Helv. Chim. Acta* **1993**, *76*, 2654.
Seebach, D.; Beck, A. K.; Heckel, A. *Angew. Chem. Int. Ed.* **2001**, *40*, 92.
Lam, H. W. *Synthesis* **2011**, *13, 2011*.

Representative of monodentate phosphorus ligands with axial chirality



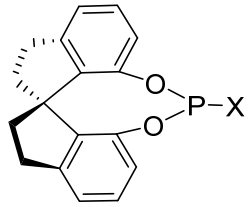
P

X = C substituent, **2000**, **Pringle**
X = O substituent, **2000**, **Reetz**
X = N substituent, **1994**, **Feringa**



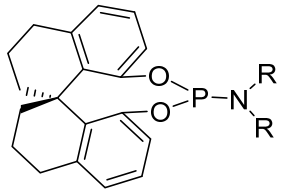
Q (MOP)

1991, Miyano



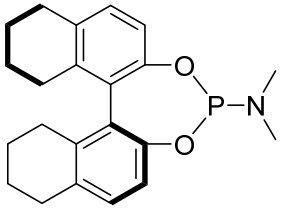
R

X = C, O, N substituent
2002, Zhou

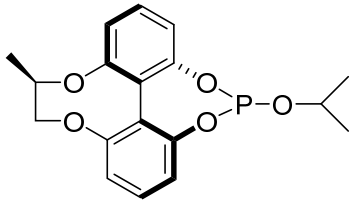


S

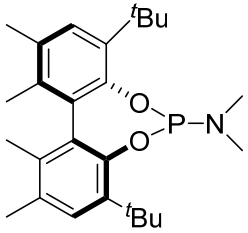
X = N substituent
2007, Zhou



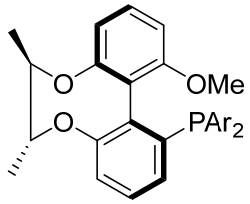
T (H_8-MonoPhos)
2002, Jiang



U
2003, Rampf



V
2004, Ojima

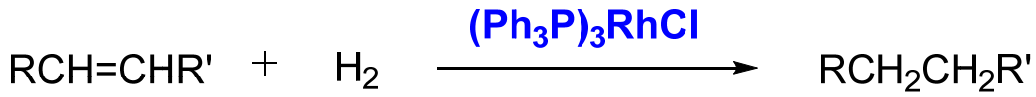


W
2012, Qiu

Claver, C.; Fernandez, E.; Gillon, A.; Hesiop, K.; Hyett, D. J.; Martorell, A.; Orpen, A. G.; Pringle, P. G. *Chem. Commun*. **2000**, 961.
Reetz, M. T.; Mehler, G. *Angew. Chem. Int. Ed*. **2000**, *39*, 3889.
Hulst, R.; De Vries, N. K.; Feringa, B. L. *Tetrahedron*: *Asymmetry* **1994**, *5*, 699.
Hattori, T.; Shijo, M.; Kumagai, S.; Miyano, S. *Chem. Express* **1991**, *6*, 335.
Hu, A. -G.; Fu, Y.; Xie, J, -H.; Zhou, H.; Wang, L, -X.; Zhou, Q. -L. *Angew. Chem. Int. Ed*. **2002**, *41*, 2348.
Huo, X, -H.; Xie, J, -H.; Wang, Q, -S.; Zhou, Q, -L. *Adv. Synth. Catal*. **2007**, *349*, 2477.
Hannen, P.; Militzer, H. -C.; Vogl, E. M.; Rampf, F. A. *Chem. Commun*. **2003**, 2210.
Hua, Z.; Vassar, V. C.; Chol, H.; Ojima, I. Proc. *Natl. Acad. Sci. USA* **2004**, *101*, 5411.
Wang, S.; Li, J.; Miao, T.; Wu, W.; Li, Q.; Zhuang, Y.; Zhou, Z.; Qiu, L. *Org. Lett*. **2012**, *14*, 1966.

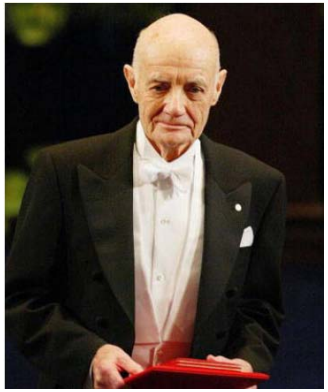
Asymmetric hydrogenation

First monodentate chiral ligand (Korpium, Mislow, Knowles)

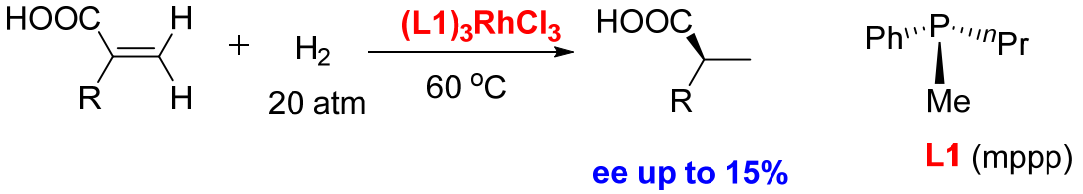


Wilkinson's catalyst: $(Ph_3P)_3RhCl$

Asymmetric version

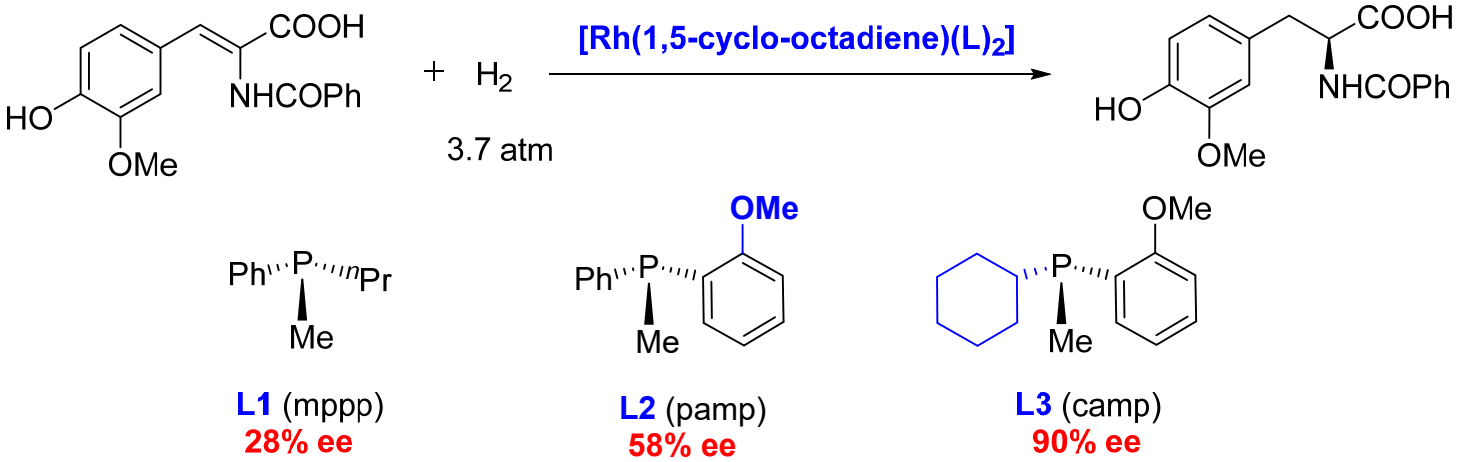


William S. Knowles

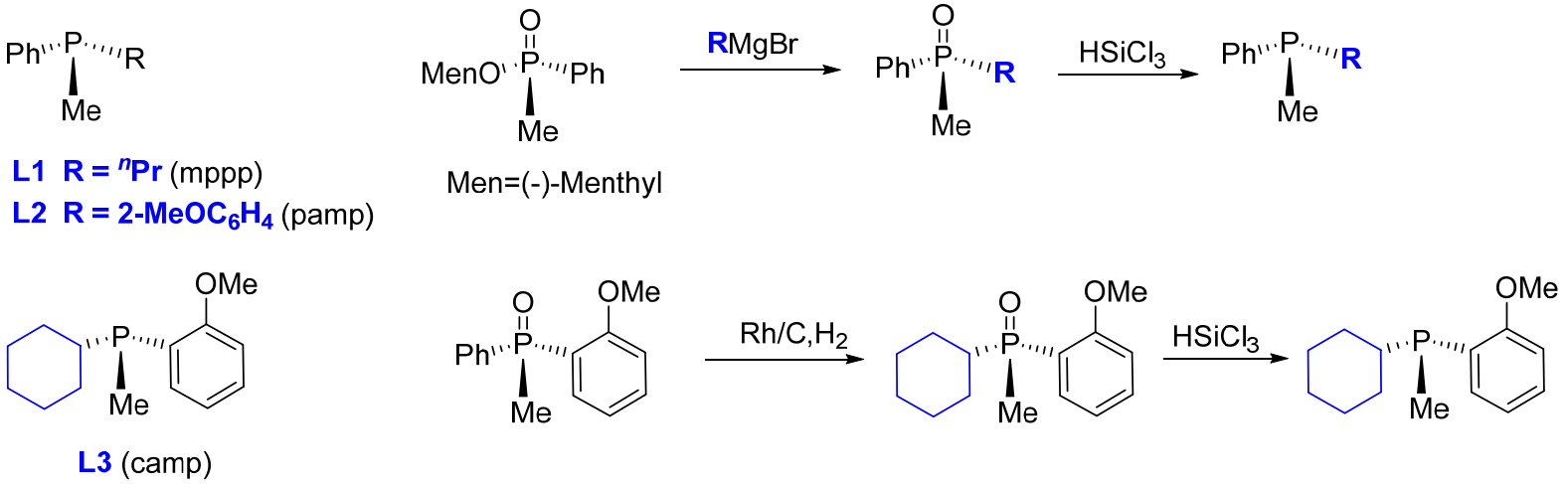


Young, J. F.; Osborn, J. A.; Jardine, F. H.; Wilkinson, G. *J. Chem. Soc., Chem. Commun.* **1965**, 131.
Korpium, O.; Mislow, K. *J. Am. Chem. Soc.* **1967**, *89*, 4784.
Knowles, W. S.; Sabacky, M. J. *J. Chem. Soc., Chem. Commun.* **1968**, 1445.

Asymmetric hydrogenation (Knowles)

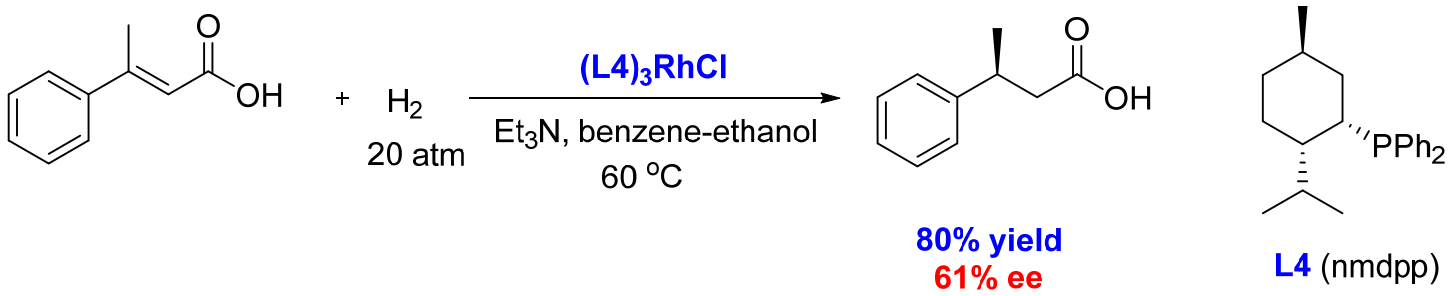


Synthesis of L1-L3

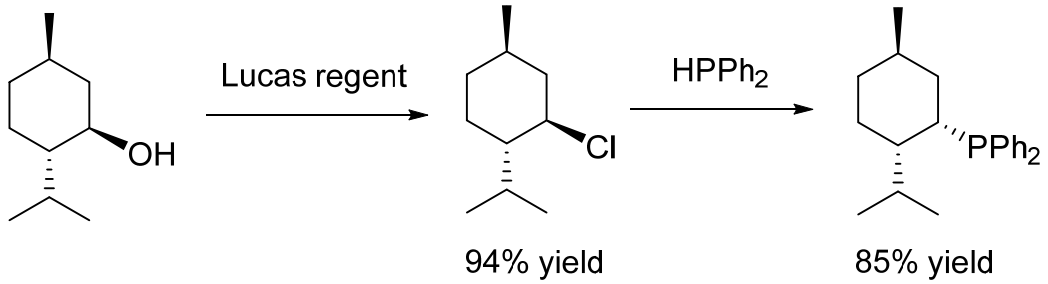


Knowles, W. S.; Sabacky, M. J. Vineyard B. D. *J. Chem. Soc., Chem. Commun.* **1972**, 10.
Korpiun, O.; Mislow, K. *J. Am. Chem. Soc.* **1967**, *89*, 4784.
Korpiun, O.; Lewis, R. A.; Chickos, J., Mislow, K. *J. Am. Chem. Soc.* **1968**, *90*, 4842.

Asymmetric hydrogenation (Morrison)

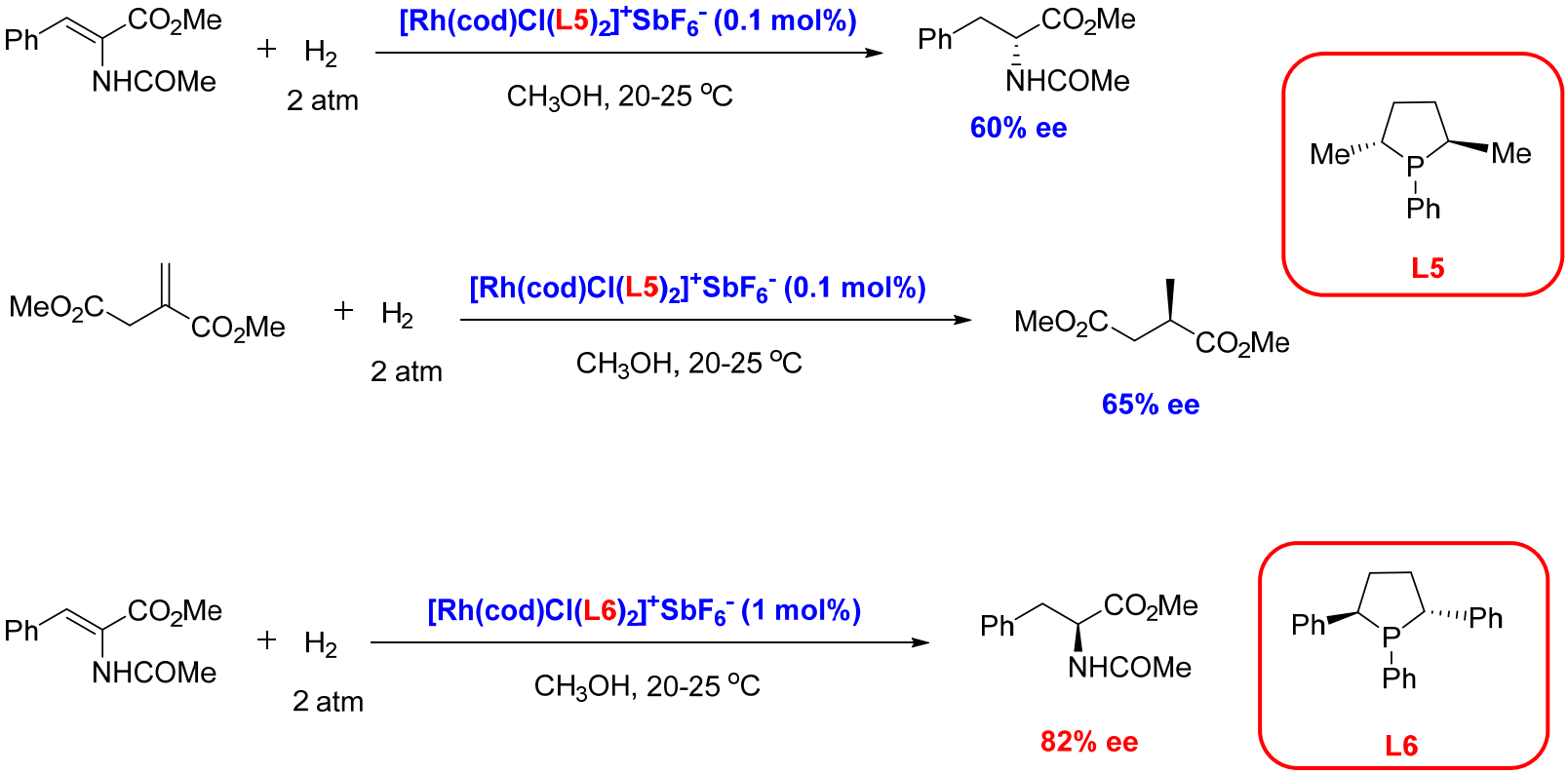


Synthesis of L4



Morrison, J. D.; Burnett, R. E.; Agular, A. M.; Morrow, C, J.; Phillips, C.; *J. Am. Chem. Soc.* **1971**, *93*, 1301.

Asymmetric hydrogenation (Burk, Fiaud)

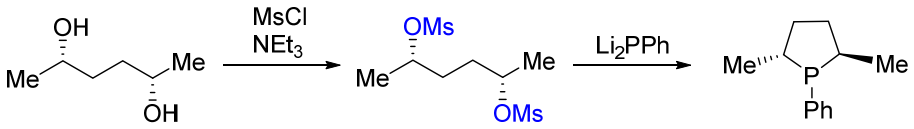


Burk, M. J.; Feaster, J. E. *Tetrahedron*: *Asymmetry.* **1991**, *2*, 569.

Guillen, F.; Fiaud, J. -C. *Tetrahedron Lett.* **1999**, *40*, 2939.

Synthesis of L5 and L6

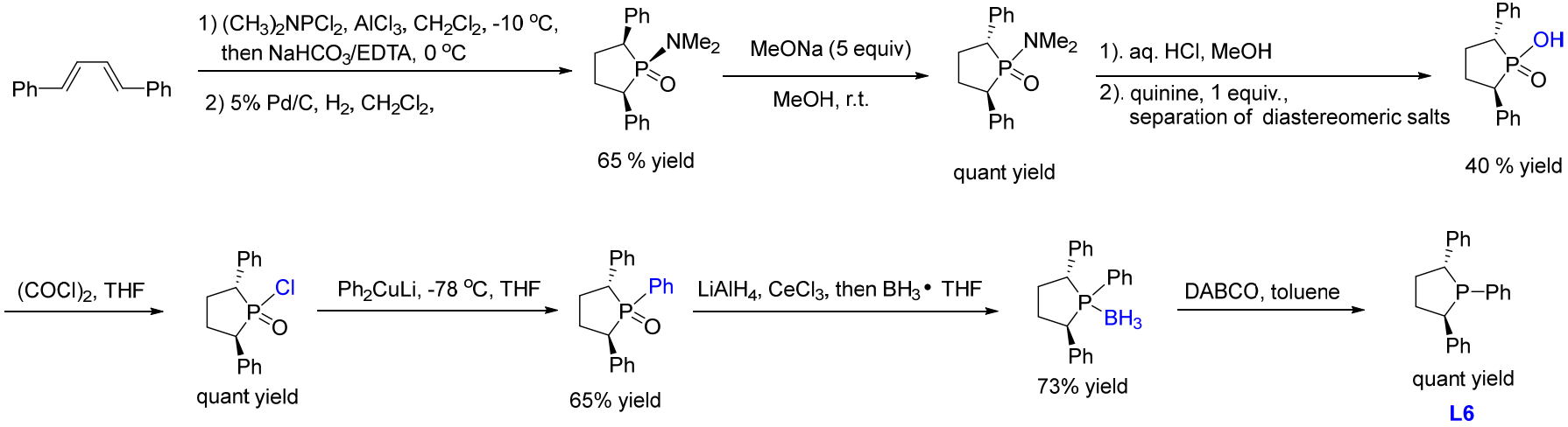
Synthesis of L5



83% yield

L5

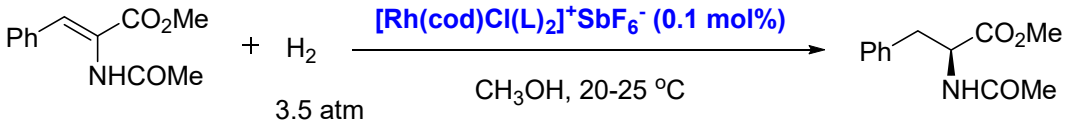
Synthesis of L6

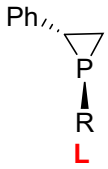


Burk, M. J.; Feaster, J. E. *Tetrahedron*: *Asymmetry*. **1991**, *2*, 569.

Guillen, F.; Fiaud, J. -C. *Tetrahedron Lett*. **1999**, *40*, 2939.

Asymmetric hydrogenation (Marinetti)

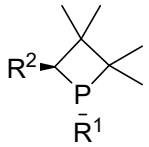




L

L7 R = ^{t}Bu 26% ee

L8 R = (-)-Menthyl 76% ee



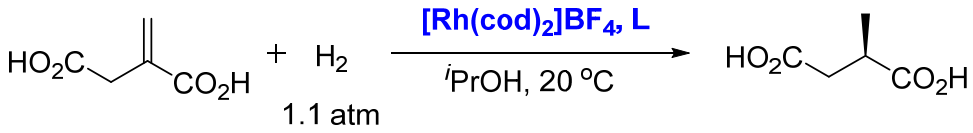
L9

R^1= (-)-Menthyl
R^2 = Bn
40% ee

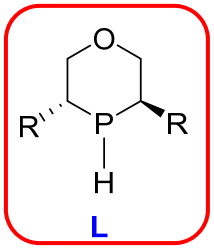
Marinetti, A.; Mathey, F.; Ricard, L. *Organometallics*, **1993**, *12*, 1207.

Marinetti, A.; Ricard, L. *Organometallics*, **1994**, *13*, 3956.

Secondary phosphanes (Helmchen)



Rh:substrate=1:500

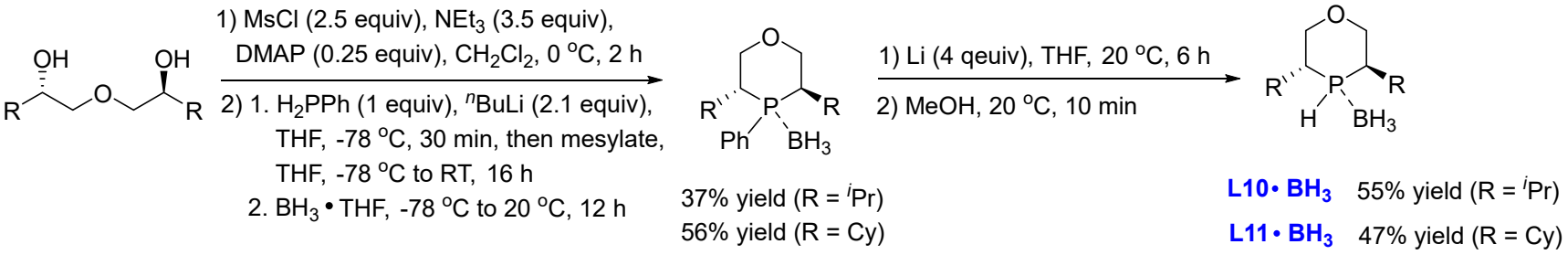


L10 R = ^{i}Pr **93 % ee**

L11 R = Cy **96 % ee**[a]

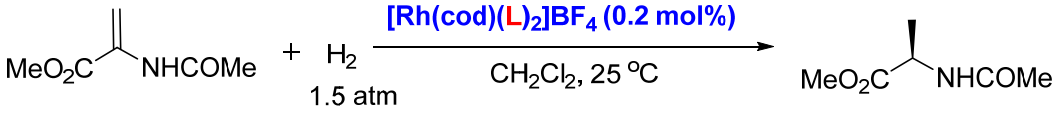
a: using *ent*-**L11** afford (s)-product

Synthesis of L10 and L11

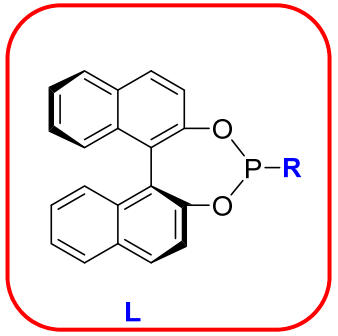


Ostermeier, M.; Prieβ, J.; and Helmchen, G. *Angew. Chem. Int. Ed.* **2002**, *41*, 612.

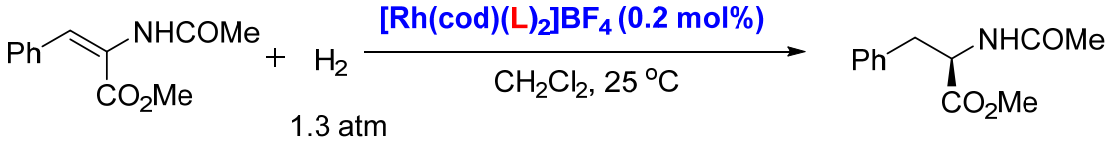
Monodentate phosphonites (Pringle, Reetz)



L12 R = ^{t}Bu **92 % ee**
2000, Pringle



L13 R = Et **-94 % ee** (using (***R***)-L)
2000, Reetz



Paul G. Pringle

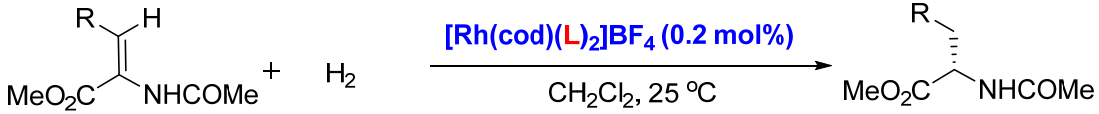
L14 R = Me **80 % ee**
2000, Pringle

Manfred T. Reetz

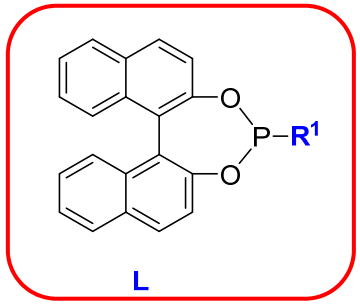
Claver, C.; Fernandez, E.; Gillon, A.; Hesiop, K.; Hyett, D. J.; Martorell, A.; Orpen, A. G.; Pringle, P. G. *Chem. Commun.* **2000**, 961.

Reetz, M. T.; Sel, l T. *Tetrahedron Lett.* **2000,** *41*, 6333.

Monodentate ligand vs *Bidentate ligand*



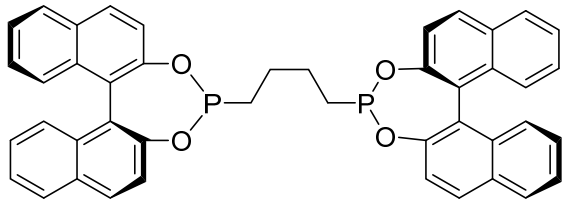
Substrate	Ligand	ee (%)
R = H	(*R*)-L13	94
R = H	L15	-90
R = Ph	(*S*)-L14	-80
R = Ph	L15	-19



L

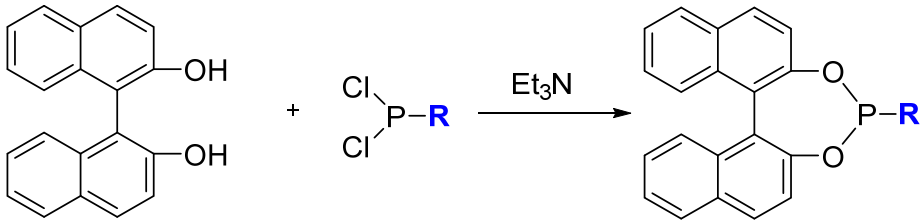
L13 R^2 = Et

L14 R^3 = Me



L15

Synthesis of L12-L14



R = ^{t}Bu

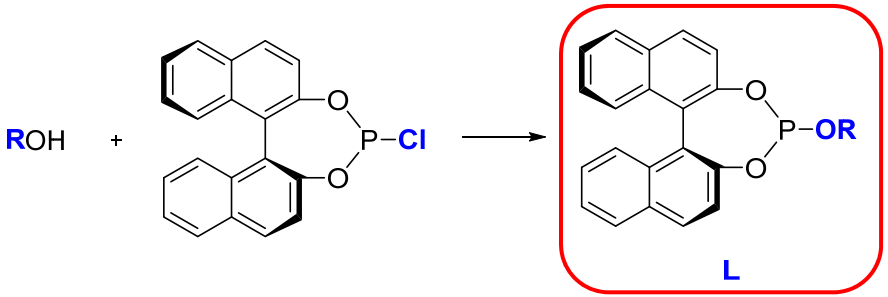
R = Et

R = Me

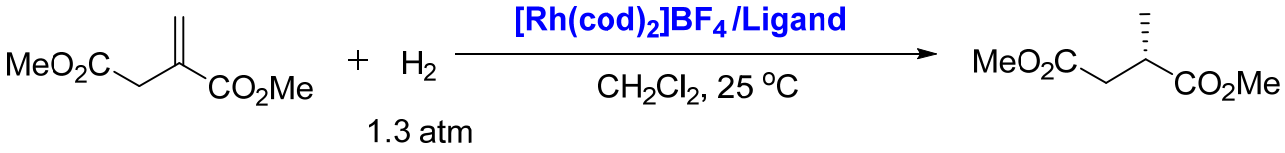
Claver, C.; Fernandez, E.; Gillon, A.; Hesiop, K.; Hyett, D. J.; Martorell, A.; Orpen, A. G.; Pringle, P. G. *Chem. Commun.* **2000**, 961.

Reetz, M. T.; Sell, T. *Tetrahedron Lett.* **2000**, *41*, 6333.

Monodentate phosphites (Reetz)



L16 R = Me
L17 R = ^{i}Pr
L18 R = C_6H_4
L19 R = 2-Br-C_6H_4

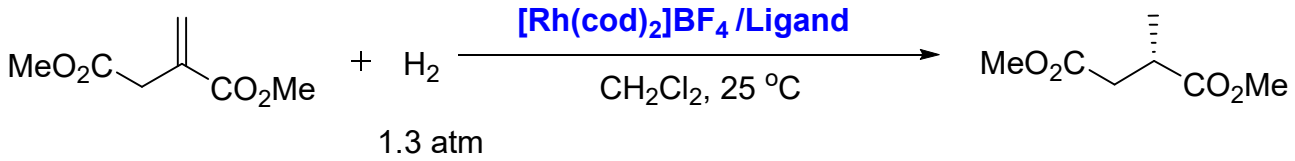


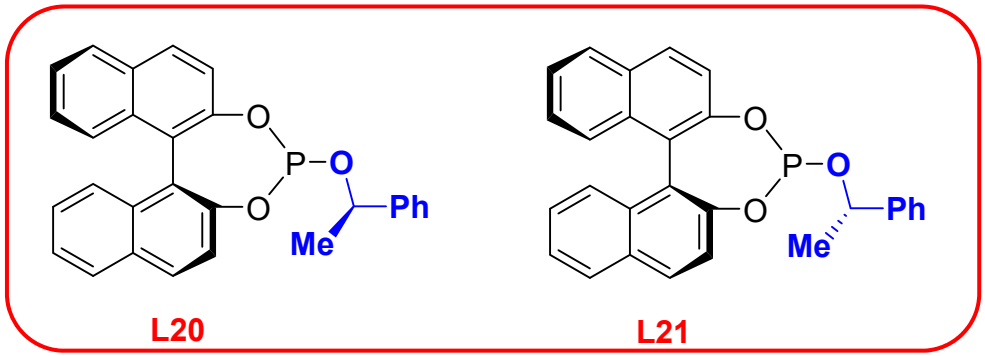
Entry	Ligand	ee (%)
1	**L16**	89.2
2	**L17**	**97.6**
3	**L18**	96.6
4	**L19**	89.8

Note: 100% conversion was observed in all case

Reetz, M. T.; Mehler, G. *Angew. Chem. Int. Ed.* **2000**, *39*, 3889.

Monodentate phosphites (Reetz)



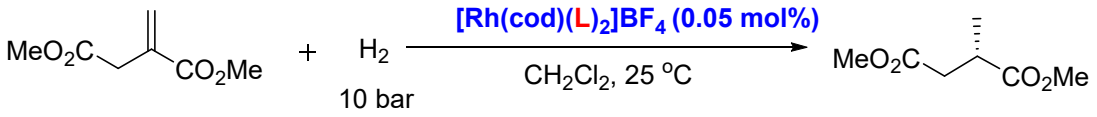


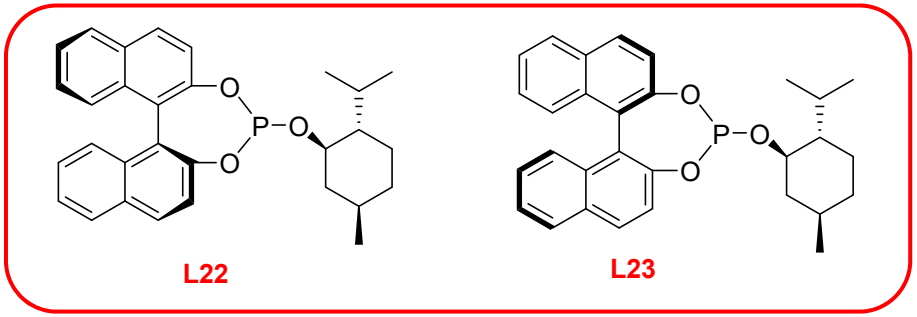
Entry	Ligand	Rh : ligand	Rh : substrate	ee (%)
1	**L20**	1 : 1	1 : 1000	99.2
2	**L21**	1 : 1	1 : 1000	98.2
3	**L20**	1 : 1	1 : 2500	99.4
4	**L20**	1 : 1	1 : 5000	99.4
5	**L20**	1 : 1	1 : 10000	96.2
6	**L20**	**1 : 2**	**1 : 1000**	**99.6**
7	**L20+L21**	**1 : 1**	**1 : 1000**	**98.8**

Note: 100% conversion was observed in all case

Reetz, M. T.; Mehler, G. *Angew. Chem. Int. Ed.* **2000**, *39*, 3889.

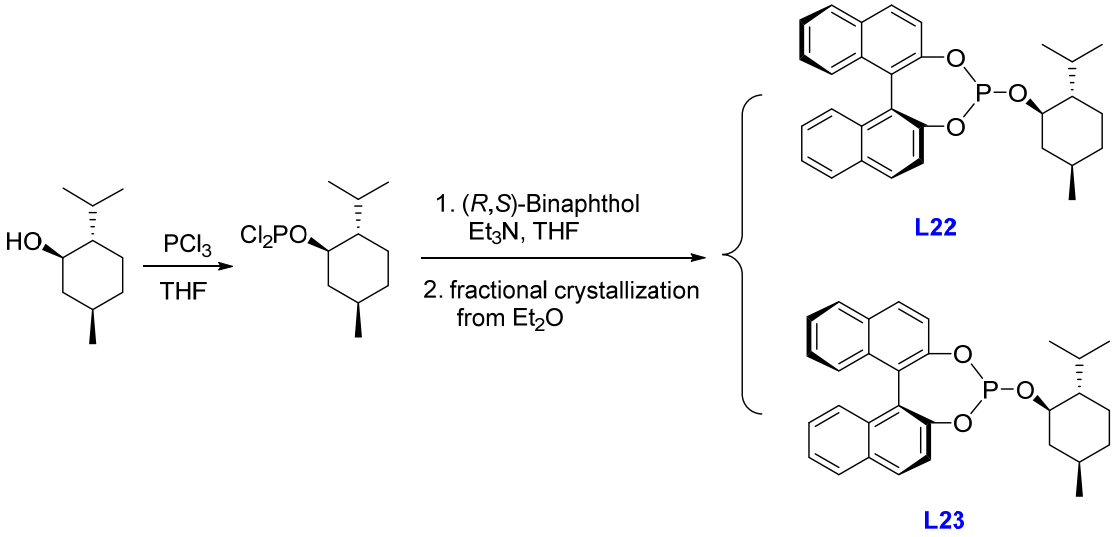
Monodentate phosphites (Xiao)





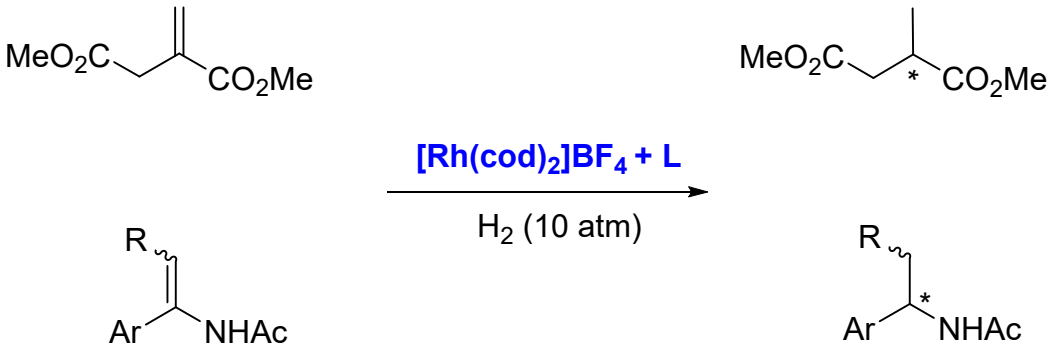
Entry	Ligand	Conversion (%)	ee% (%)
1	**L22**	100	**95.2**
2	**L23**	100	**-90.5**

Synthesis of L22 and L23

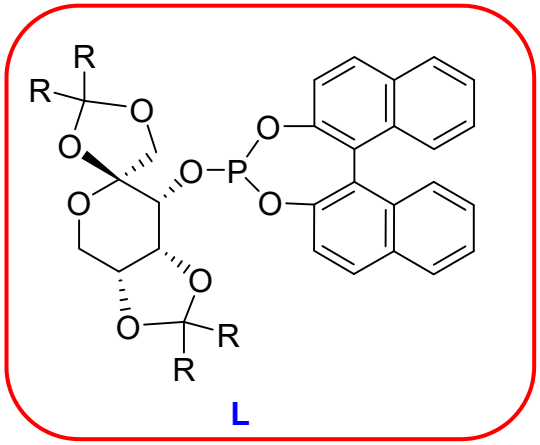


Chen, W.; Xiao, J. *Tetrahedron Lett.* **2001**, *42*, 2897.

Monodentate phosphites (Chen)



Up to 99.6% ee

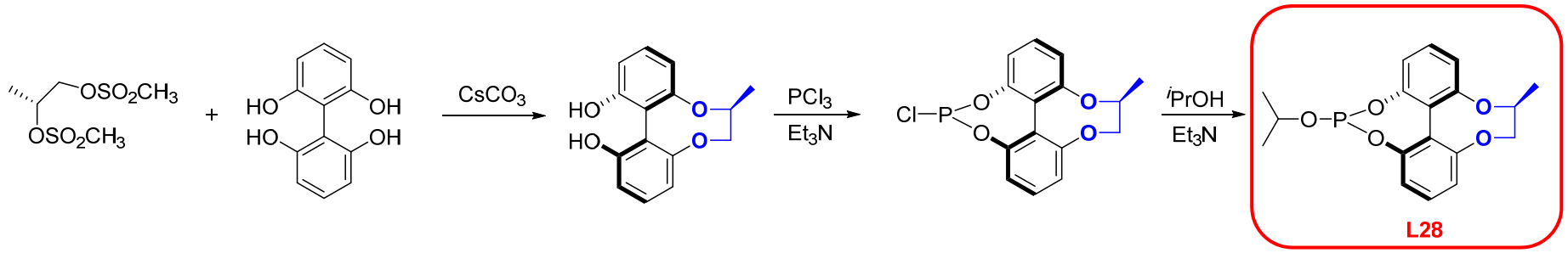


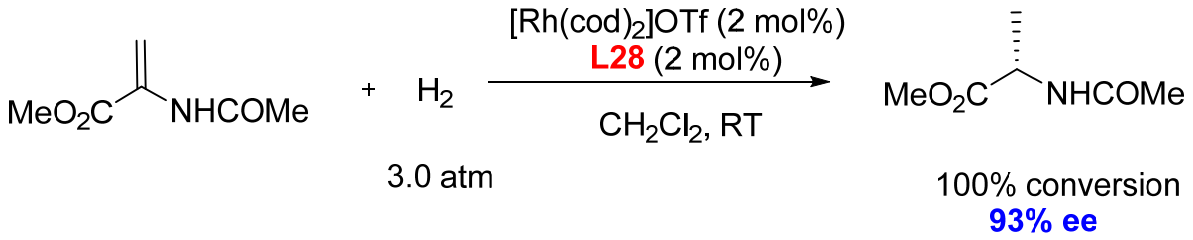
L

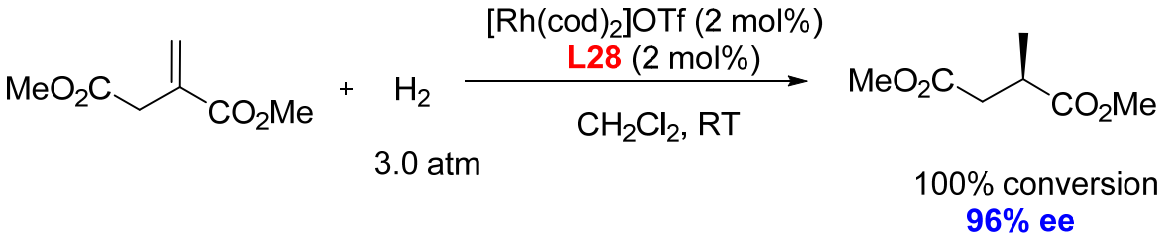
L24	R = Me, (*R*)-BINOL
L25	R = Me, (*S*)-BINOL
L26	R = -$(CH_2)_5$-, (*R*)-BINOL
L27	R = -$(CH_2)_5$-, (*S*)-BINOL

Huang, H.; Zheng, Z.; Luo, H.; Bai, C.; Hu, X.; Chen, H. *Org. Lett.* **2003**, *5*, 4137.

Monodentate phosphite (Rampf)

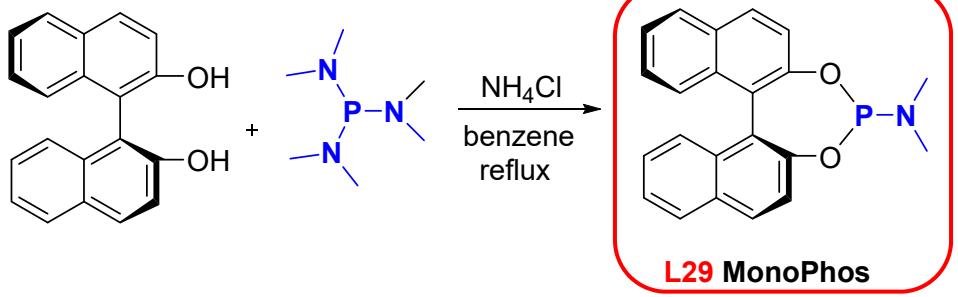






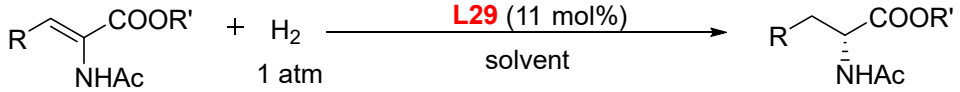
Hannen, P.; Militzer, H. -C.; Vogl, E. M.; Rampf, F. A. *Chem. Commun*. **2003**, 2210.

Monodentate phosphoramidite (Feringa)

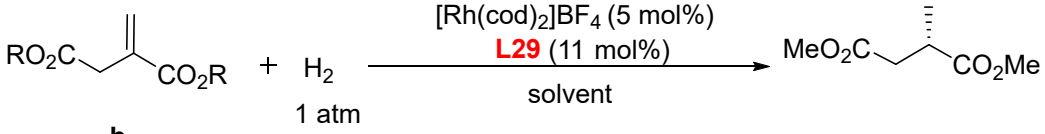


L29 MonoPhos

98% yield



a



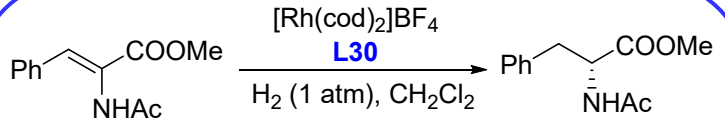
b

Selected examples:

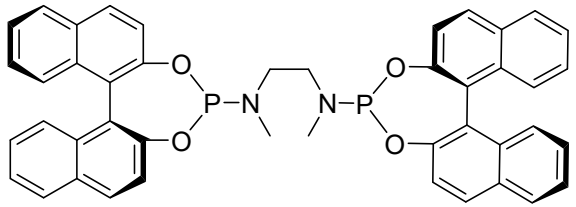
Entry	Substrate	Solvent	ee (%) 0 °C	ee (%) 25 °C
1	**a**: R = H, R' = Me	EtOAc	**99.8**	**99.6**
2	**a**: R = Ph, R' = Me	CH_2Cl_2	**97.6**	**95**
3	**a**: R = *p*-OAc-*m*-OMePh, R' = Me	CH_2Cl_2	**96.3**	**95.1**
4	**a**: R = H, R' = H	EtOAc		**98.7**
5	**a**: R = Ph, R' = H	EtOAc		**97.1**
6	**b**: R = Me	CH_2Cl_2	**94.4**	**87**
7	**b**: R = H	CH_2Cl_2		**96.6**

Note: 100% conversion was observed in all case

Ben Feringa



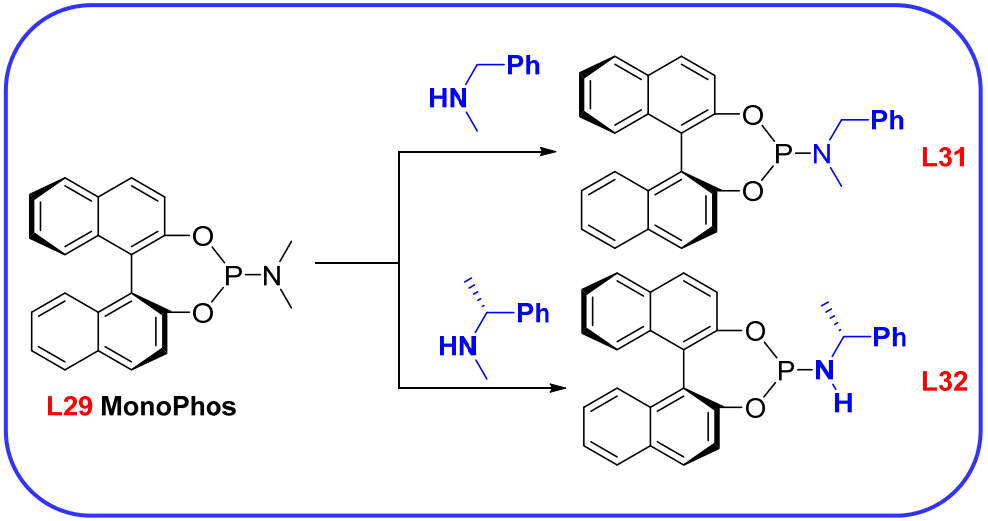
56% conversion
72% ee



L30
bidentate phosphoramidite

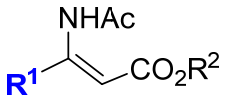
van den Berg, M.; Minnaard, A. J.; Schudde, E. P.; van Esch, J.; de Vries, A. H. M.; de Vries, J. G.; Feringa, B. L. *J. Am. Chem. Soc.* **2000**, *122*, 11539.

Monodentate phosphoramidites (Feringa)

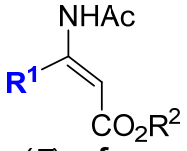


Entry	Substrate	Ligand	Solvent	ee (%)
1	(*Z*)-**a**	**L32**	^{i}PrOH	**95**
2	(*Z*)-**b**	**L32**	^{i}PrOH	**94**
3	(*Z*)-**c**	**L32**	^{i}PrOH	**94**
4	(*Z*)-**d**	**L32**	^{i}PrOH	**92**
5	(*Z*)-**e**	**L32**	^{i}PrOH	**92**
6	(*Z*)-**f**	**L32**	^{i}PrOH	**94**
7	(*E*)-**a**	**L31**	CH_2Cl_2	**99**
8	(*E*)-**b**	**L31**	CH_2Cl_2	**99**
9	(*E*)-**c**	**L31**	CH_2Cl_2	**99**
10	(*E*)-**d**	**L31**	CH_2Cl_2	**99**

Note: 100% conversion was observed in all case



(*Z*)-**a-f**

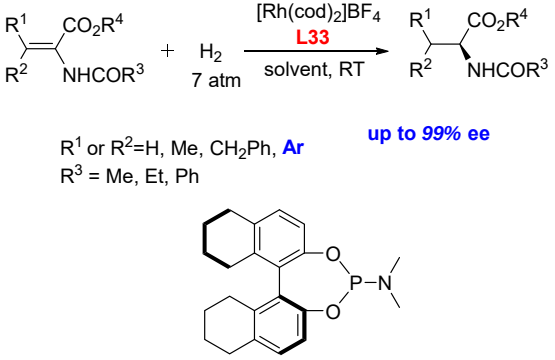


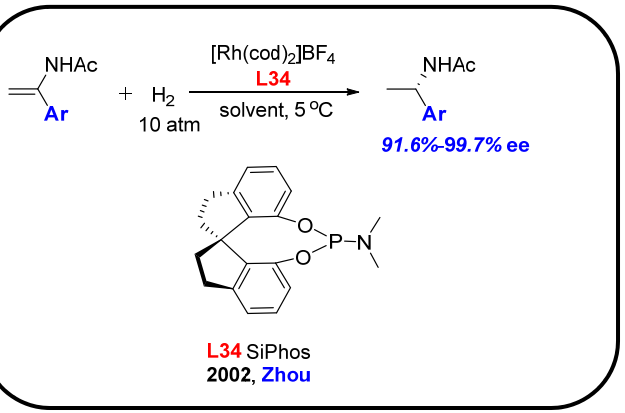
(*E*)-**a-f**

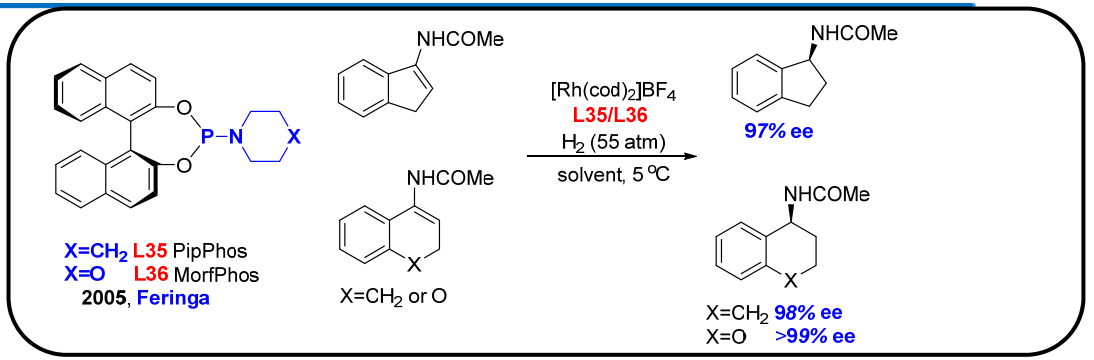
a: $R^1 = R^2 =$ **Me**
b: $R^1 =$ **Et**, $R^2 =$ Me
c: $R^1 =$ Me, $R^2 =$ Et
d: $R^1 =$ **^{i}Pr**, $R^2 =$ Et
e: $R^1 =$ **Ph**, $R^2 =$ Et
f: $R^1 =$ ***p*-F-Ph**, $R^2 =$ Me

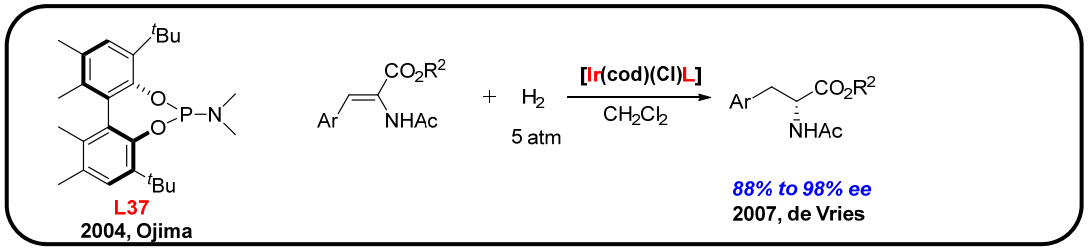
Peña, D.; Minnaard, A. J.; de Vries, J. G.; Feringa, B. L. *J. Am. Chem. Soc.* **2002**, *124*, 14552.

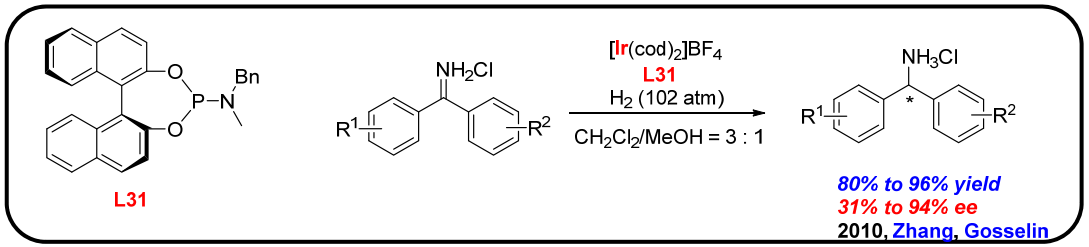
Monodentate phosphoramidites (Jiang, Zhou, Feringa, Zhang)

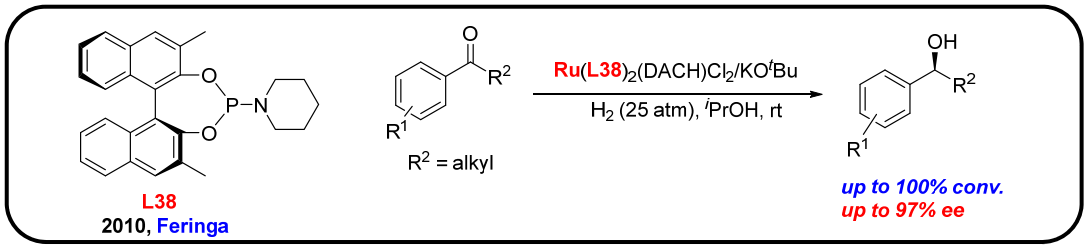






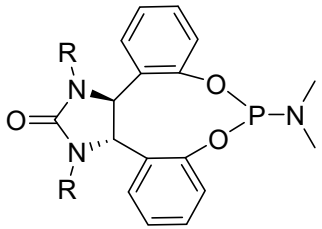






Zeng, Q.; Liu, H.; Mi, A.; Jiang, Y.; Li, X.; Choi, M. C. K. Chan. A. S. C. *Tetrahedron Lett.* **2002**, 58, 8799.
Hu, A. -G.; Fu, Y.; Xie, J, -H.; Zhou, H.; Wang, L, -X.; Zhou, Q. -L. *Angew. Chem. Int. Ed.* **2002**, *41*, 2348.
Bernsmann, H.; van den Berg, M.; Hoen, R.; Minnaard, A. J.; Mehler G.; Reetz, M. T.; De Vriex, J. G.; Feringa, B. L. *J. Org. Chem.* **2005**, *70*, 943.
Giacomina, F.; Meetsma, A.; Panella, L.; Lefort, L.; de Vries, A. H. M.; de Vries, J. G. *Angew. Chem., Int. Ed.* **2007**, *46*, 1497.
Hou, G.; Tao, R.; Sun, Y.; Zhang, X.; Gosselin, F. *J. Am. Chem. Soc.* **2010**, *132*, 2124.
Stegink, B.; van Boxtel, L.; Lefort, L.; Minnaard, A. J.; Feringa, B. L.; de Vries, J. G. *Adv. Synth. Catal.* **2010**, *352*, 2621.

Monodentate phosphoramidites (Ding)

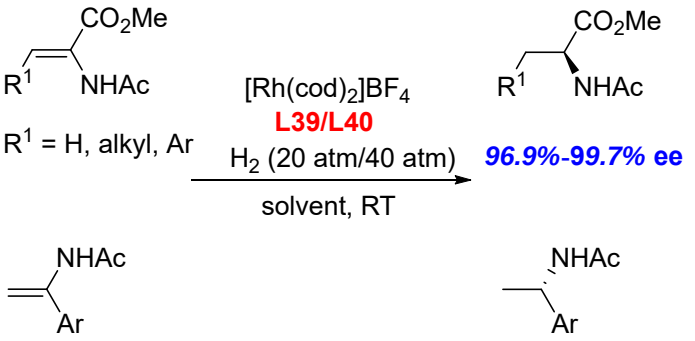


DpenPhos

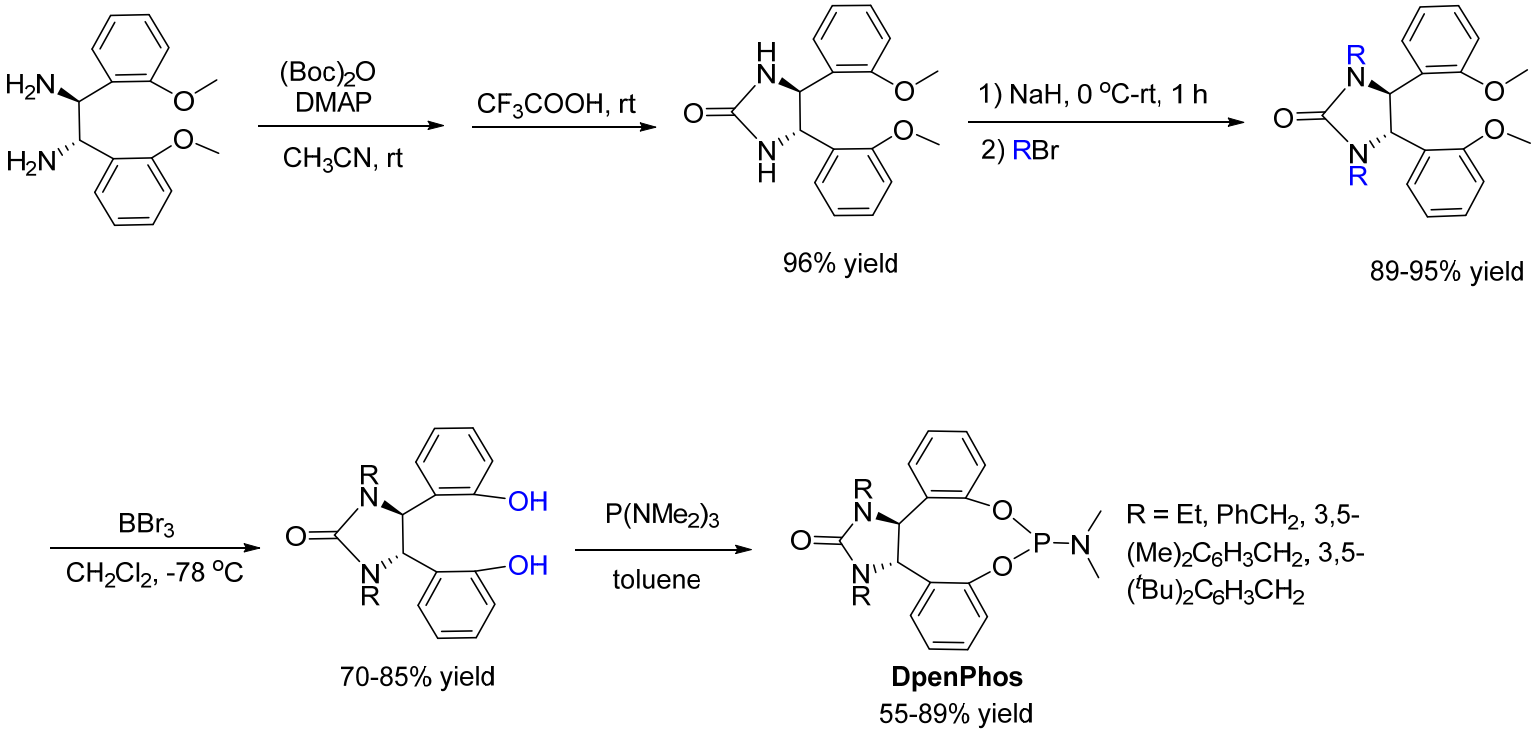
R = $PhCH_2$ **L39**

R = 3,5-(^{t}Bu)$_2$C$_6$H$_3$CH$_2$ **L40**

Ding, 2005

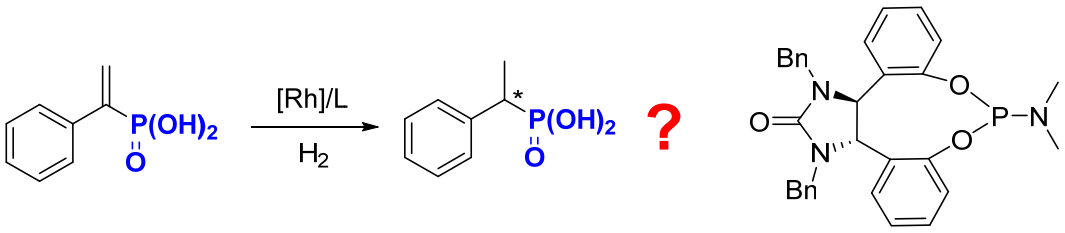


Synthesis of L39 and L40 (Dpenphos)



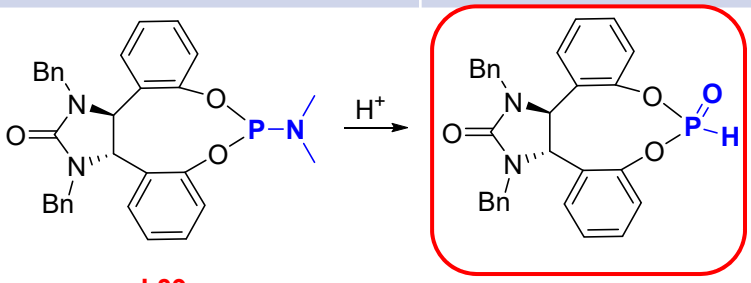
Liu, Y.; Ding, K. *J. Am. Chem. Soc.* **2005**, *127*, 10488.

Monodentate secondary phosphine oxide (Ding)



L39

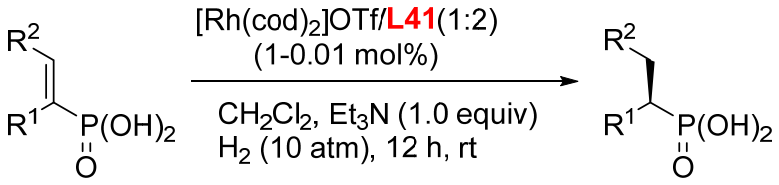
sequence of operations	results
Normal, in the absence of Et_3N	10% conv, 67% ee (*R*)
Substrate was first reacted with 1 equiv Et_3N, the resultant salt was added to the Rh catalyst prepared with L39.	<5% conv, ee ND
Substrate was first mixed with Rh catalyst prepared with the L39 in CH_2Cl_2 and stirred for 10 min, then the 1 equiv of Et_3N was introduced into the reaction system.	>99% conv, >99% ee (*R*)



L39

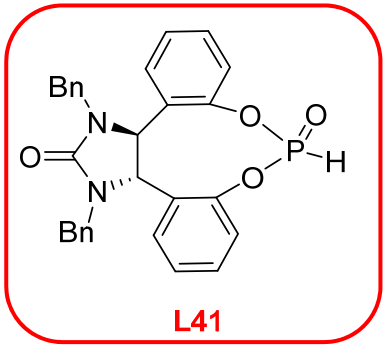
Dong, K.; Wang, Z.; Ding, K. *J. Am. Chem. Soc.* **2012**, *134*, 12474.

Monodentate secondary phosphine oxide (Ding)



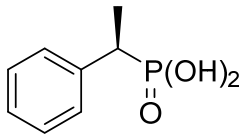
1a-e

2a-e

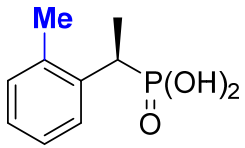


L41

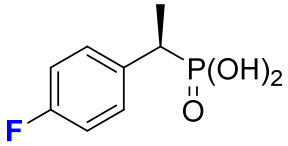
Selected example



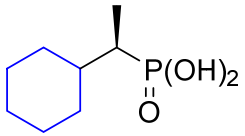
2a
>99% ee



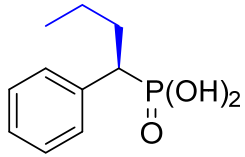
2b
>99% ee



2c
99% ee



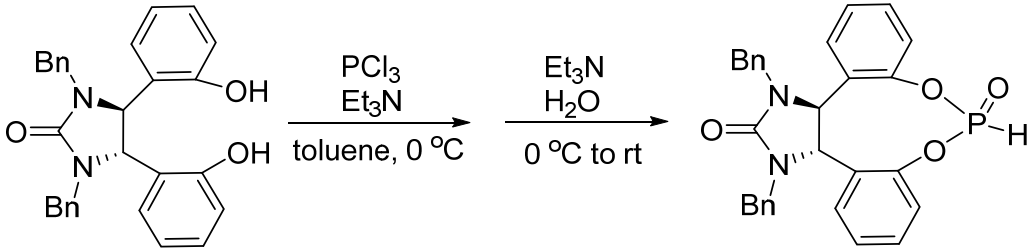
2d
>99% ee



2e
>99% ee

Note: 100% conversion was observed in all case

Synthesis of L41

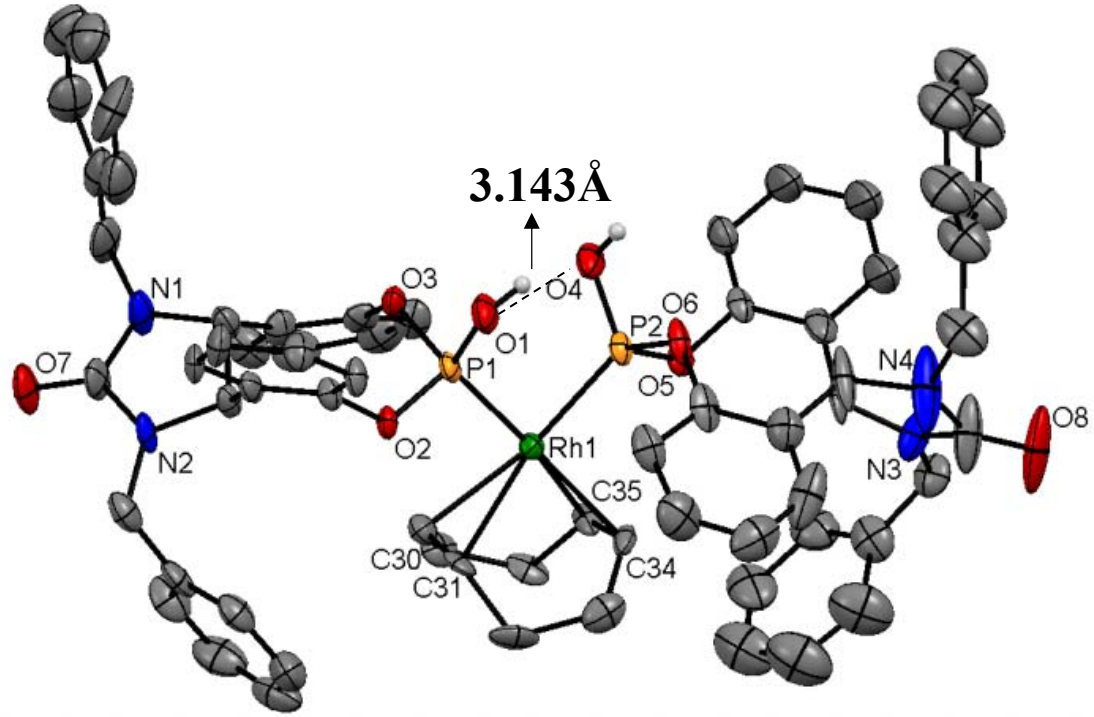


L41

Dong, K.; Wang, Z.; Ding, K. *J. Am. Chem. Soc.* **2012**, *134*, 12474.

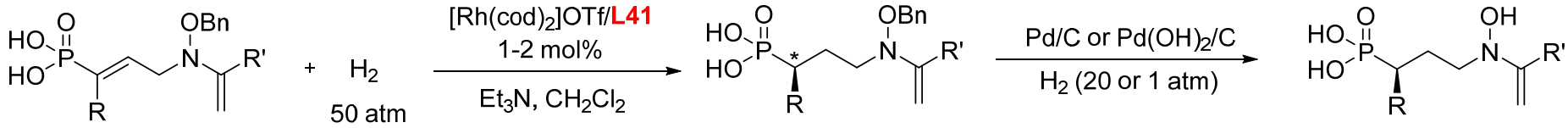
Monodentate secondary phosphine oxide (Ding)

X-ray crystal structure of complex [Rh(cod){(S,S)-L41}$_2$]OTf



The distance of O(1)···O(4) is 3.143 Å, indicating the existence of intermolecular H-bonding between the OH groups of the two ligands

Synthesis of Fosmidomycin Analogues



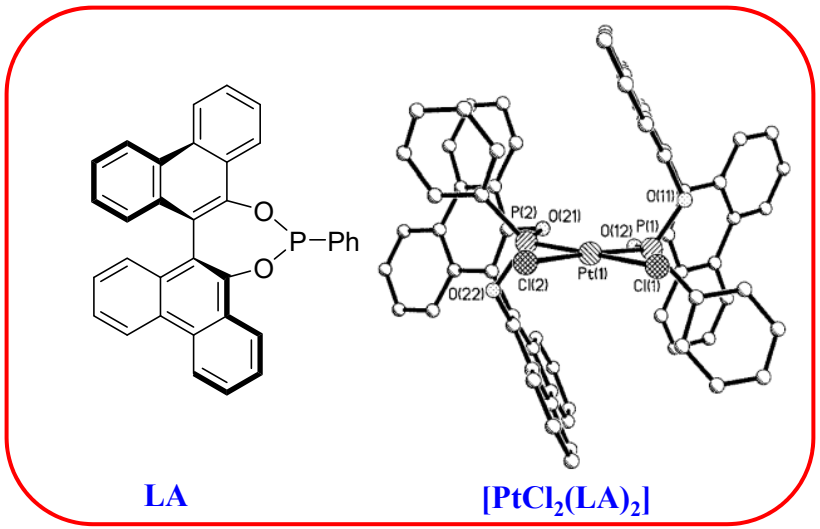
R = Ph, R' = CH_3

99% ee

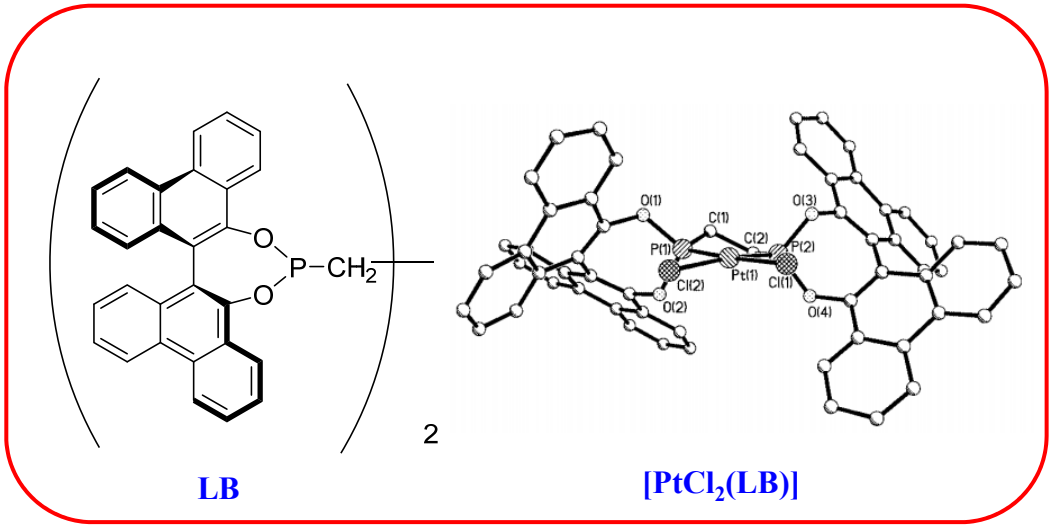
95% yield (2 step)

Dong, K.; Wang, Z.; Ding, K. *J. Am. Chem. Soc.* **2012**, *134*, 12474.

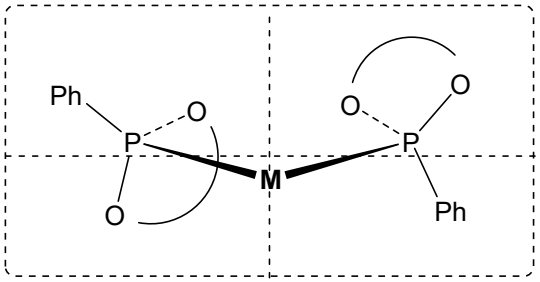
The difference between monodentate ligands and bidentate ligands as complexes

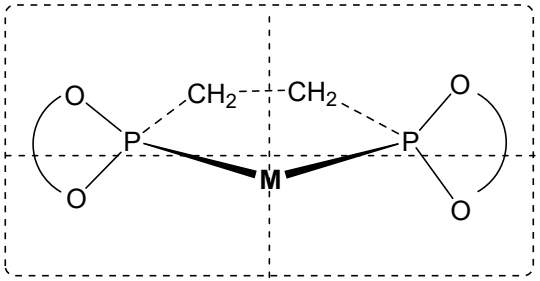


LA [$PtCl_2(LA)_2$]



LB [$PtCl_2(LB)$]



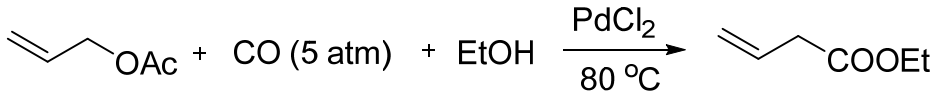


(i) rotation about the M–P bond in monodentate phosphonites is prevented;
(ii) a different rotamer from that in the chelate analogues is favoured;
(iii) the favoured rotamer causes more effective chiral induction in the hydogenation catalyses.

Claver, C.; Fernandez, E.; Gillon, A.; Hesiop, K.; Hyett, D. J.; Martorell, A.; Orpen, A. G.; Pringle, P. G. *Chem. Commun.* **2000**, 961.

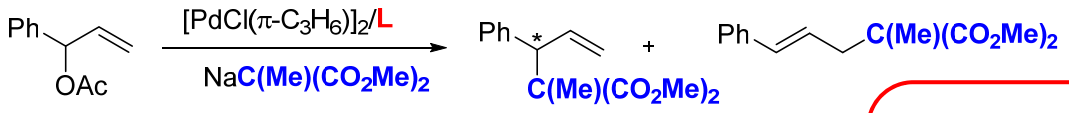
Allyic substitution

Pd-Catalyzed (Tsuji, Hayashi)

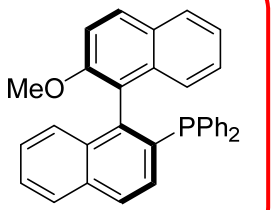


80% yield

1964, Tsuji



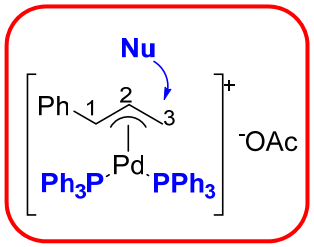
Entry	L	yield (%) a+b	Ratio a:b	ee (%) of 2
1	dppe	92	7:93	-
2	PPh_3	99	15:85	-
3	(R)-MeO-MOP	97	82:18	86

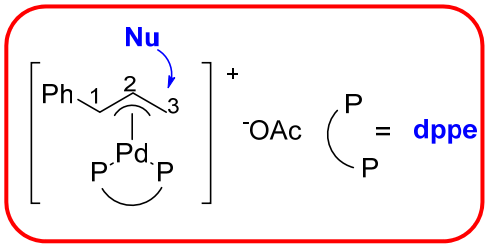


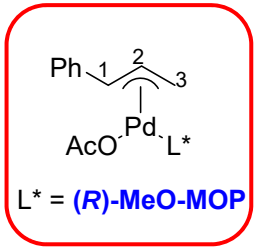
L42 (*R*)-MeO-MOP

1991, Hayashi

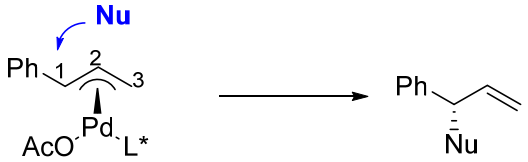
Tamio Hayashi







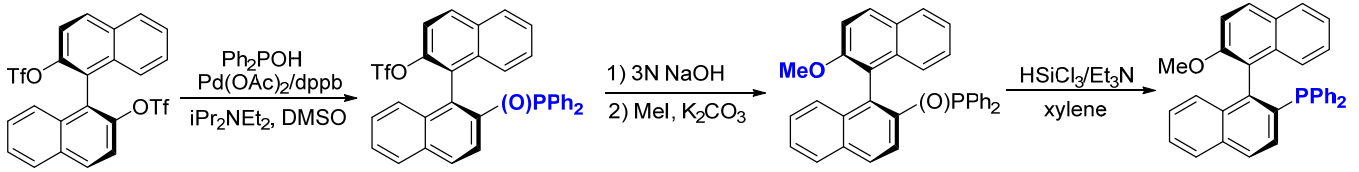
L* = (*R*)-MeO-MOP



trans effect

characterized by ^{31}P and ^{1}H NMR

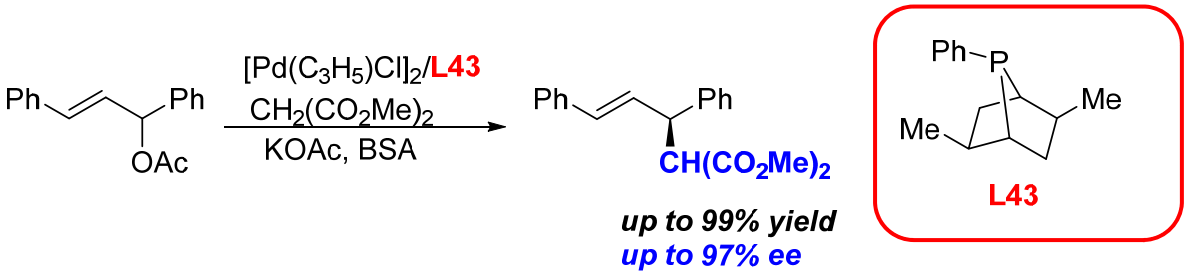
Synthesis of L42



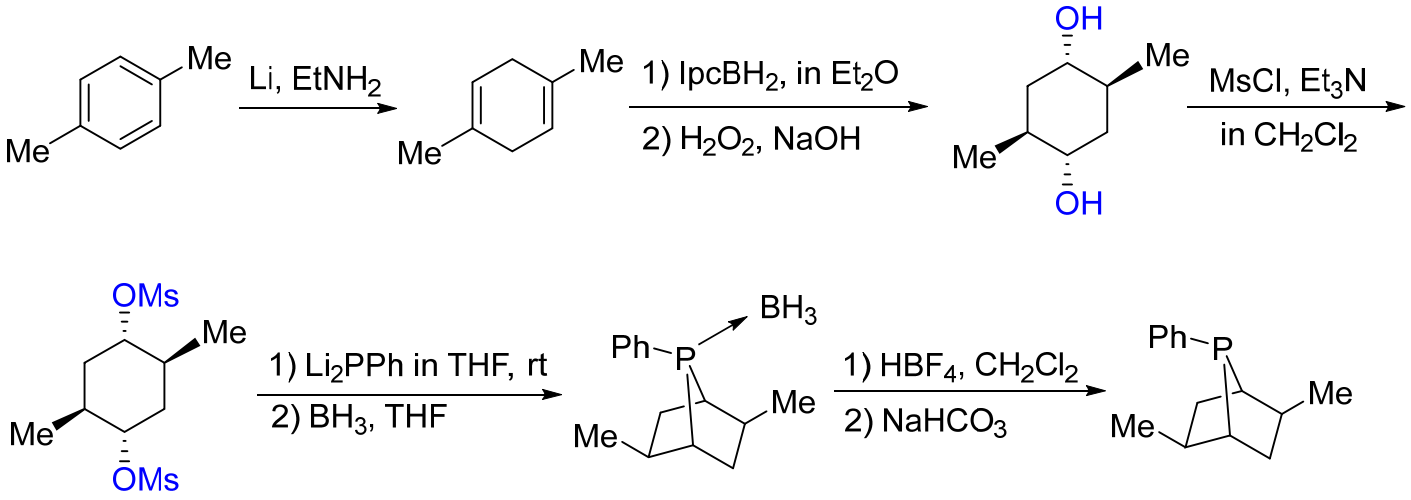
L42 (*R*)-MeO-MOP

Tsuji, J.; Kiji, J.; Imamura , J.; Morikawa, M. *J. Am. Chem. Soc.* **1964**, *86*, 4350.
Hayashi, T.; Kawatsura, M.; Uozumi, Y. *Chem. Commun.* **1997**, 561−562.
Uozumi, Y.; Hayashi, T. *J. Am. Chem. Soc.* **1991**, *113*, 9887.
Hattori, T.; Shijo, M.; Kumagai, S.; Miyano, S. *Chem. Express* **1991**, *6*, 335.

Pd-Catalyzed (Zhang)



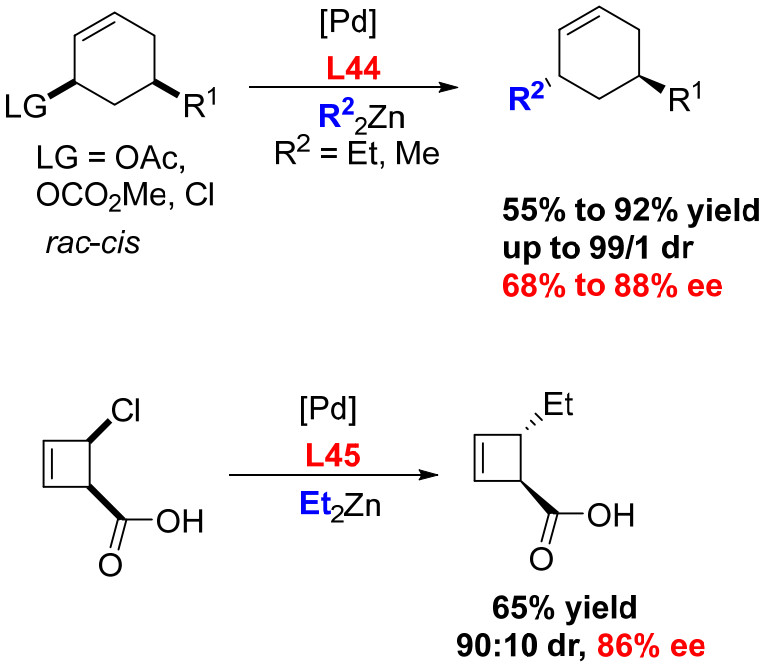
Synthesis of L43

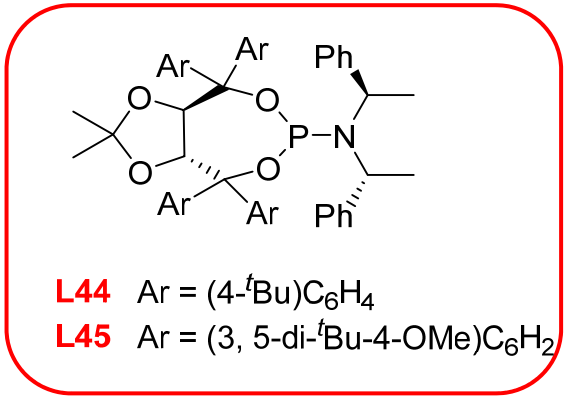


Chen, Z.; Jiang, Q.; Zhu, G.; Xiao, D.; Cao, P.; Guo, C.; Zhang, X. *J. Org. Chem.* **1997**, *62*, 4521.

Pd-Catalyzed (Maulide)

TADDOL-derived phosphoramidites

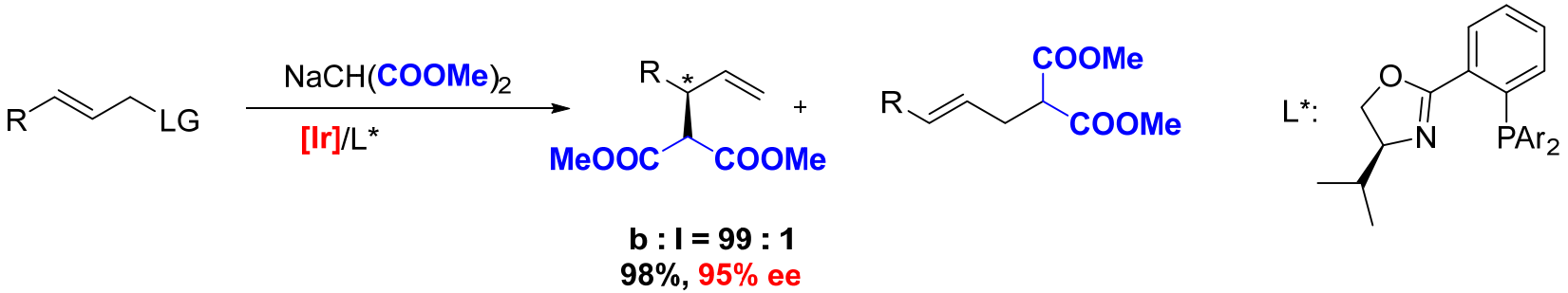




Misale, A.; Niyomchon, S.; Luparia, M.; Maulide, N. *Angew. Chem. Int. Ed.* **2014**, *53*, 7068.

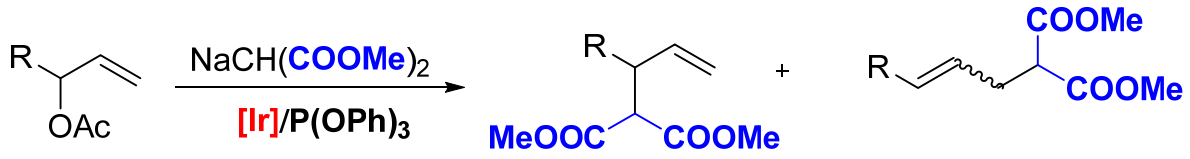
Ir-Catalyzed (Helmchen, Takeuchi)

Precedents for Ir-Catalyzed allyic substitution



b : l = 99 : 1
98%, 95% ee

1997, Helmchen

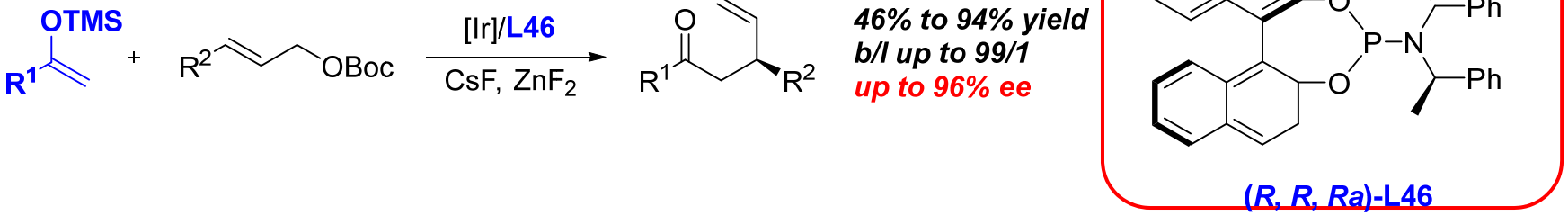


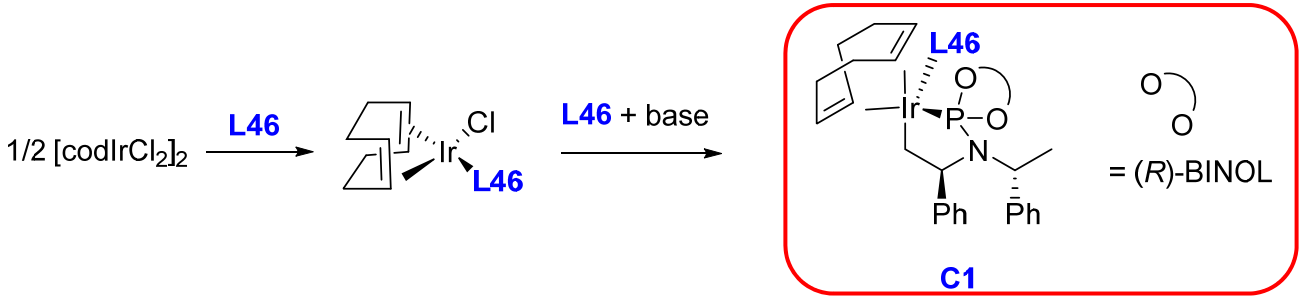
b : l = 99 : 1
91%

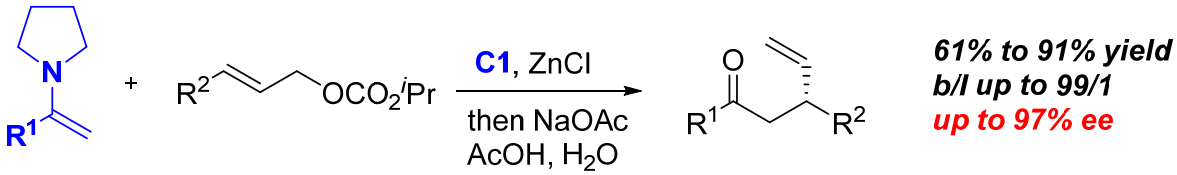
1998, Takeuchi

Janssen, J. P.; and Helmchen, G. *Tetrahedron Lett.* 1**997**, *38*, 8025.
Takeuchi, R.; and Kashio, M. *J. Am. Chem. Soc.* **1998**, *120*, 8647.

Allyic alkylation with TMS enolates and enamines (Ir Catalyzed, Hartwig)



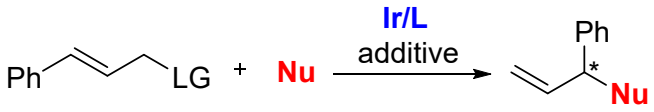


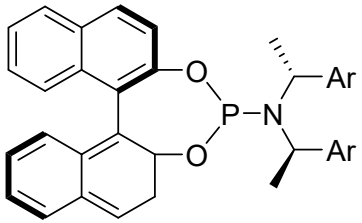


John F. Hartwig

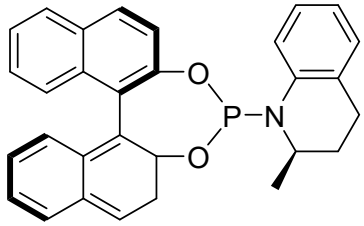
Graening, T.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 17192.
Kiener, C. A.; Shu, C.; Incarvito, C.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 14272.
Weix, D. J.; Hartwig, J. F. *J. Am. Chem. Soc.* **2007**, *129*, 7720.

Allyic substitution with prochiral nucleophiles (Hartwig, Stoltz)

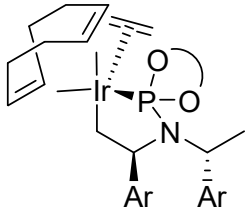




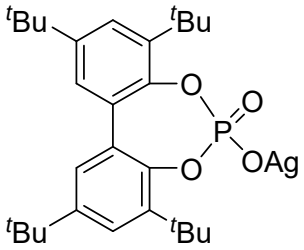
L47 Ar = 2-OMeC$_6$H$_4$



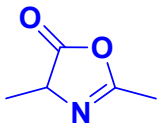
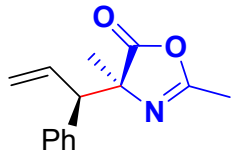
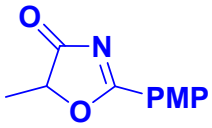
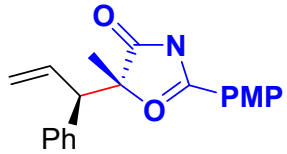
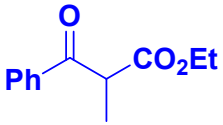
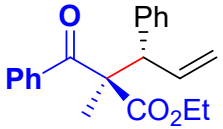
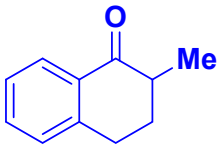
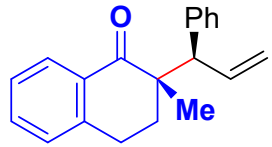
L48



C2 Ar = 2-OMeC$_6$H$_4$
C3 Ar = 2-Naphthyl

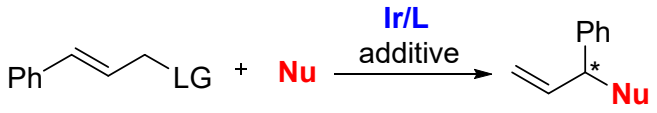


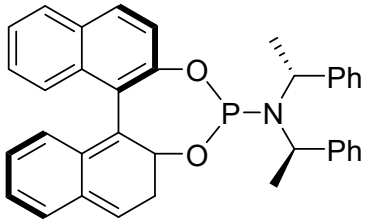
A

Entry	Nu	Ligand /catalyst	Additive /Base	Major Product
1		**L47**	A	 **dr > 20 : 1** **87%, 98% ee**
2		**C2**	Et_2Zn	 **dr = 12 : 1** **86%, 99% ee**
3		**L48**	TBD LiO^{t}Bu	 **b : l = 93 : 7** **dr > 12 : 1** **97%, 98% ee**
4		**C3**	Ba(O^{t}Bu)$_2$	 **b : l = 93 : 7** **dr = 10 : 1** **81%, 98% ee**

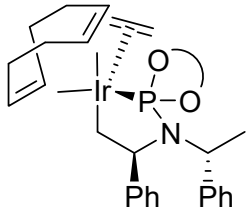
Chen,W.; Hartwig, J. F. *J. Am. Chem. Soc.* **2013**, *135*, 2068.
Chen, W.; Hartwig, J. F. *J. Am. Chem. Soc.* **2014**, *136*, 377.
Liu, W. B.; Reeves, C. M.; Stoltz, B. M. *J. Am. Chem. Soc.* **2013**, *135*, 17298.
Chen, W.; Chen, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2014**, *136*, 15825.

Allyic amination, etherification, sulfonation (Hartwig)

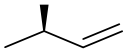
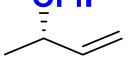
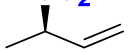




L46

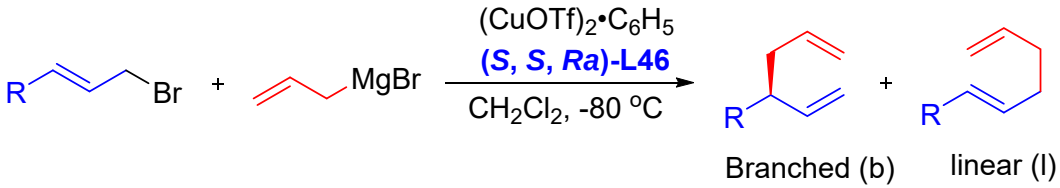


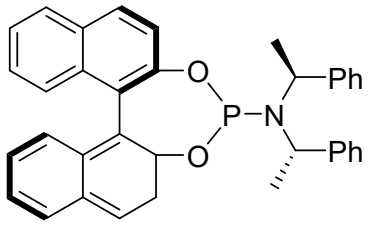
C4

Entry	Nu	Ligand /catalyst	results	Major product
1	$BnNH_2$	L46	b : l = 98 : 2 84%, 95% ee	NHBn 
2	PhONa	L46	b : l = 97 : 3 76%, 84% ee	OPh 
3	$PhSO_2Na$	C4	b : l = 97 : 3 94%, 91% ee	SO_2Ph 

Ohmura, T.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 15164.
López, F.; Ohmura, T.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 3426
Ueda, M.; Hartwig, J. F. *Org. Lett.* **2010**, *12*, 92.

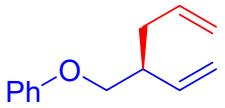
Cu-Catalyzed (Feringa)



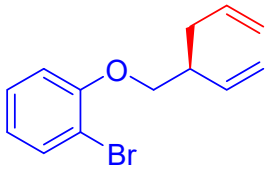


(*S*, *S*, *Ra*)-L46

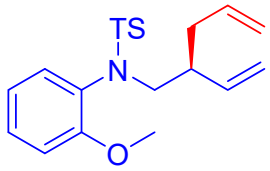
Selected examples



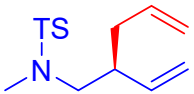
87%
b/l 70 : 30
90% ee



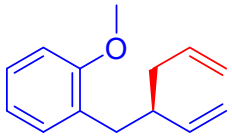
71%
b/l 77 : 23
94% ee



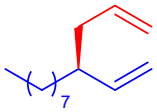
87%
b/l 91 : 9
94% ee



81%
b/l 74 : 26
92% ee



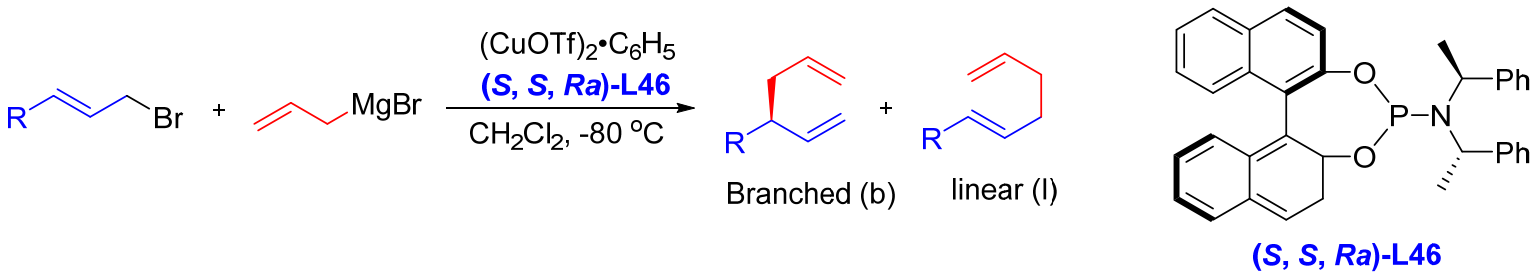
81%
b/l 85 : 15
82% ee



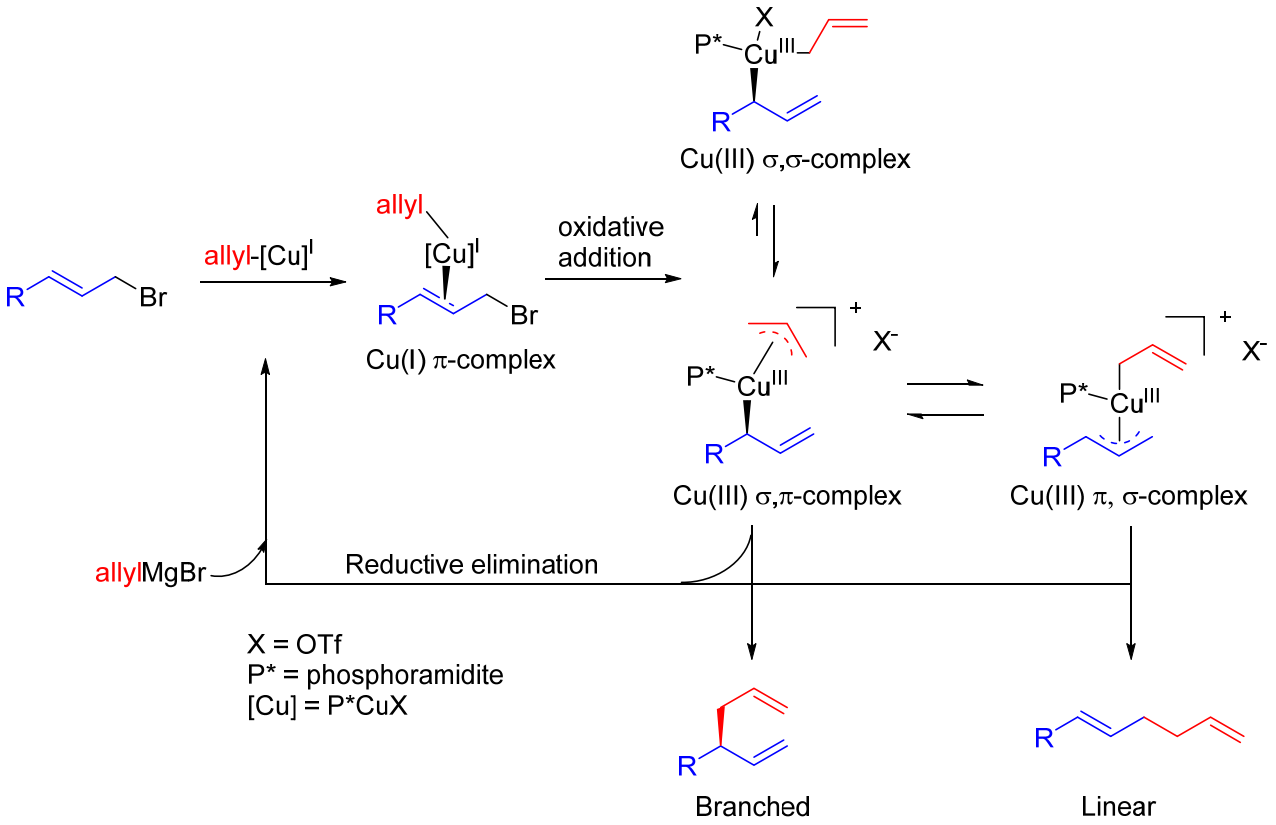
91%
b/l 88 : 12
94% ee

Hornillos, V.; Pérez, M.; Fañanás-Mastral, M.; Feringa, B. L. *J. Am. Chem. Soc.* **2013**, *135*, 2140.

Cu-Catalyzed (Feringa)



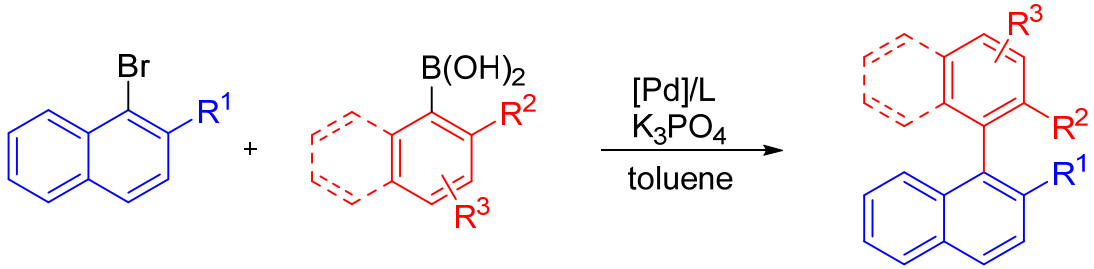
Proposed mechanism



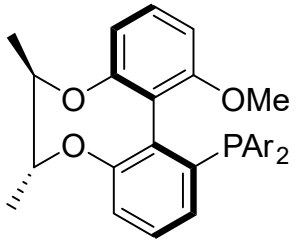
Hornillos, V.; Pérez, M.; Fañanás-Mastral, M.; Feringa, B. L. *J. Am. Chem. Soc.* **2013**, *135*, 2140.

Suzuki-Miyaura cross-coupling

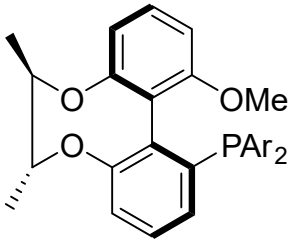
Suzuki-Miyaura cross-couplings with various functional group (Qiu)



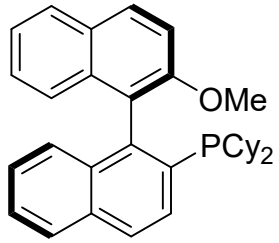
Liqin Qiu



2012, **Qiu**
Ar = (3, 5-di-^{t}Bu)C_6H_3
(*R*, *R*, *Sa*)-L49
R^1 = $PO(OEt)_2$
20 °C - 60 °C
62% to 98% yield
78% to 97% ee



2014, **Qiu**
Ar = (3, 5-di-^{t}Bu)C_6H_3
(*R*, *R*, *Sa*)-L49
R^1 = $PO(Ar^2)_2$
30 °C or 50 °C
90% to 99% yield
45% to 87% ee



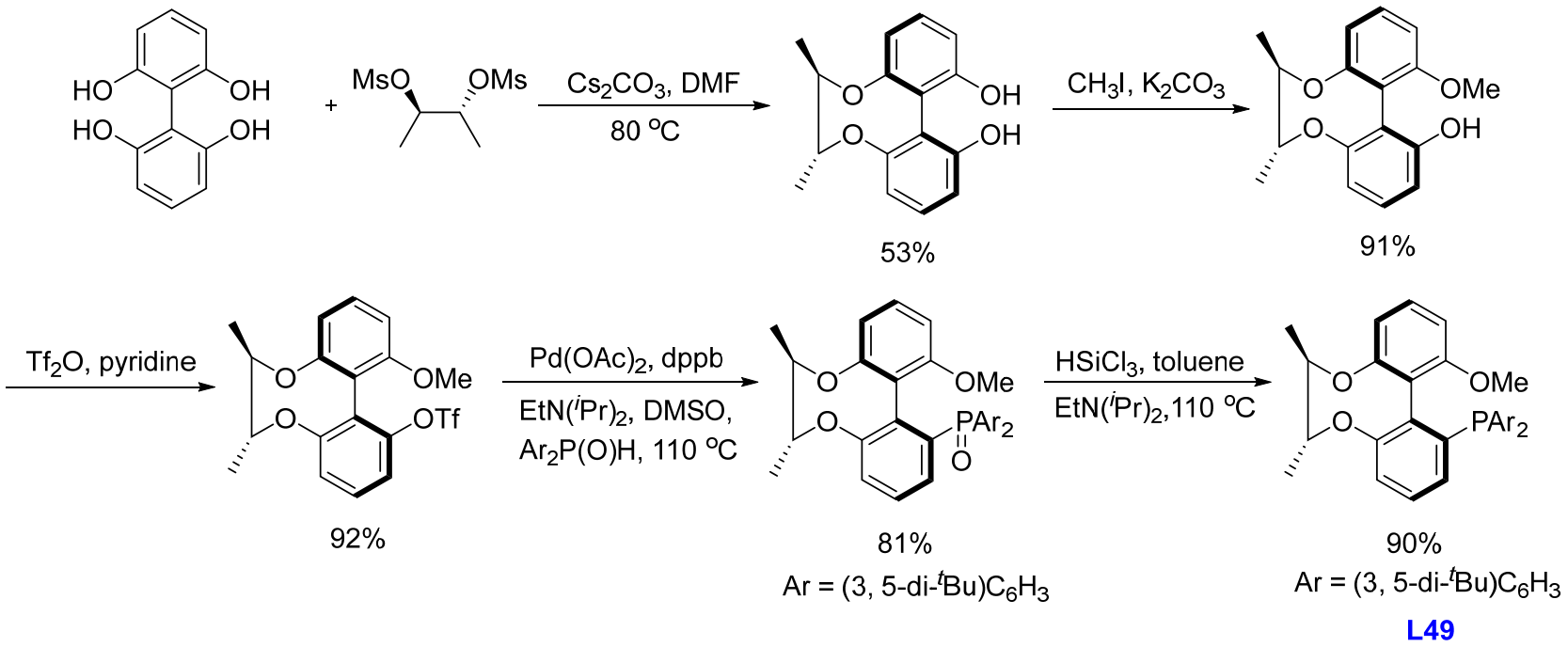
2013, Qiu
L50 (*R*)-Cy-MOP
R^2 = CHO
50 °C or 80 °C
34% to 97% yield
86% to 97% ee

Wang, S.; Li, J.; Miao, T.; Wu, W.; Li, Q.; Zhuang, Y.; Zhou, Z.; Qiu, L. *Org. Lett.* **2012**, *14*, 1966.

Zhou, Y.; Zhang, X.; Liang, H.; Cao, Z.; Zhao, X.; He, Y.; Wang, S.; Pang, J.; Zhou, Z.; Ke, Z.; Qiu, L. *ACS Catal.* **2014**, *4*, 1390.

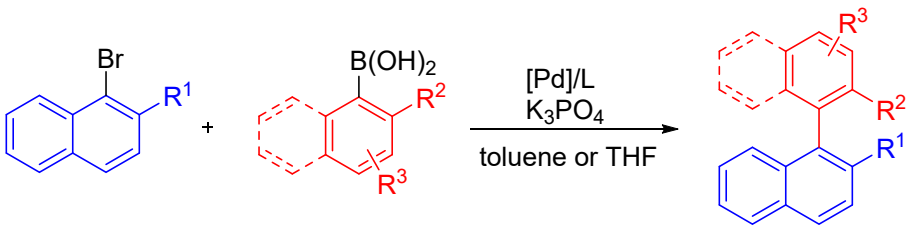
Zhou, Y.; Wang, S.; Wu, W.; Li, Q.; He, Y.; Zhuang, Y.; Li, L.; Pang, J.; Zhou, Z.; Qiu, L. *Org. Lett.* **2013**, *15*, 5508.

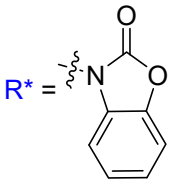
Synthesis of L49

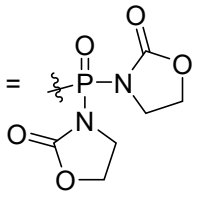


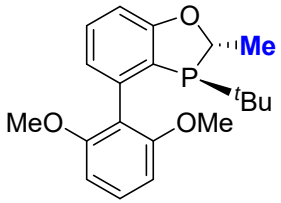
Wang, S.; Li, J.; Miao, T.; Wu, W.; Li, Q.; Zhuang, Y.; Zhou, Z.; Qiu, L. *Org. Lett.* **2012**, *14*, 1966.

Suzuki-Miyaura cross-couplings with various functional group (Qiu)

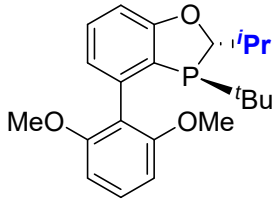


R* = 

BOP = 



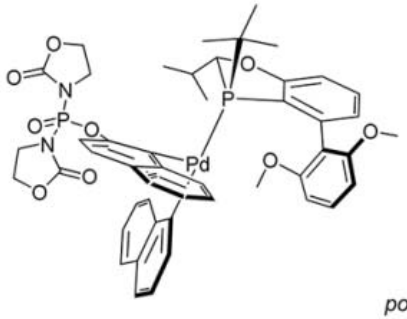
2012, Tang
L51
R^1 = COR*
rt or 65 °C
85% to 96% yield
64% to 96% ee

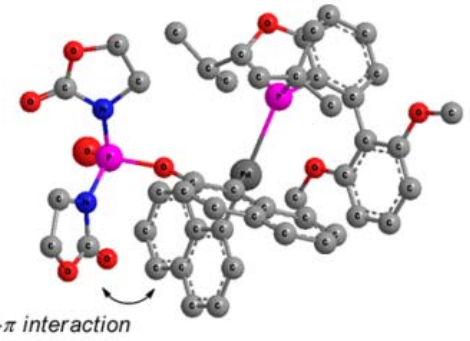


2014, Tang
L52
R^1 = OBOP
rt
91% to 96% yield
90% to 99% ee

Wenjun Tang

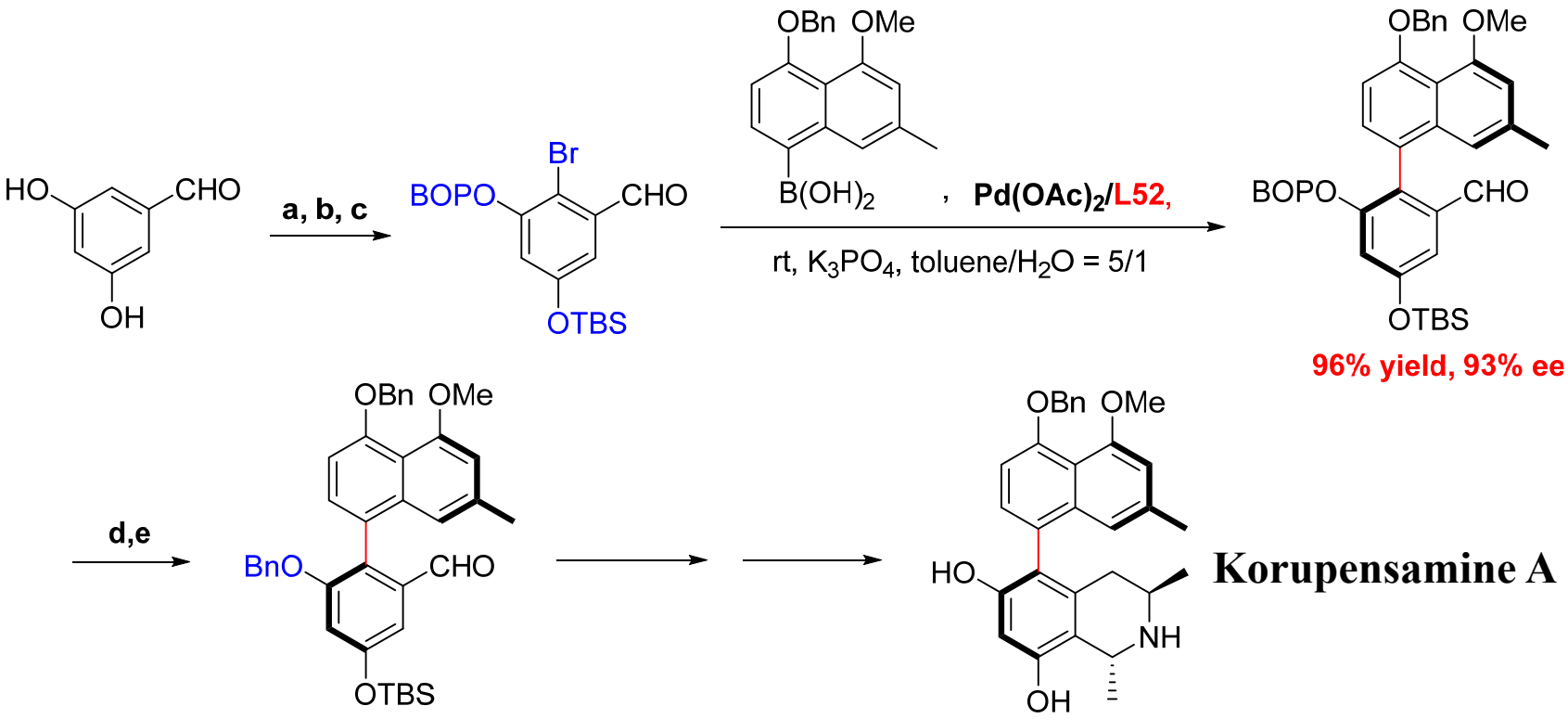
A proposed model of Pd(II)-L52 catalyst during the reductive elimination step (polar - π interation):





Tang, W.; Patel, N. D.; Xu, G.; Xu, X.; Savoie, J.; Ma, S.; Hao, M. -H.; Keshipeddy, S.; Capacci, A. G.; Wei, X.; Zhang, Y.; Gao, J .J.; Li, W.; Rodriguez, S.; Lu, B. Z.; Yee, N. K.; Senanayake, C. H. *Org. Lett*. **2012**, *14*, 2258.
Xu, G.; Fu, W.; Liu, G.; Senanayake, C. H.; Tang, W. *J. Am. Chem. Soc*. **2014**, *136*, 570.

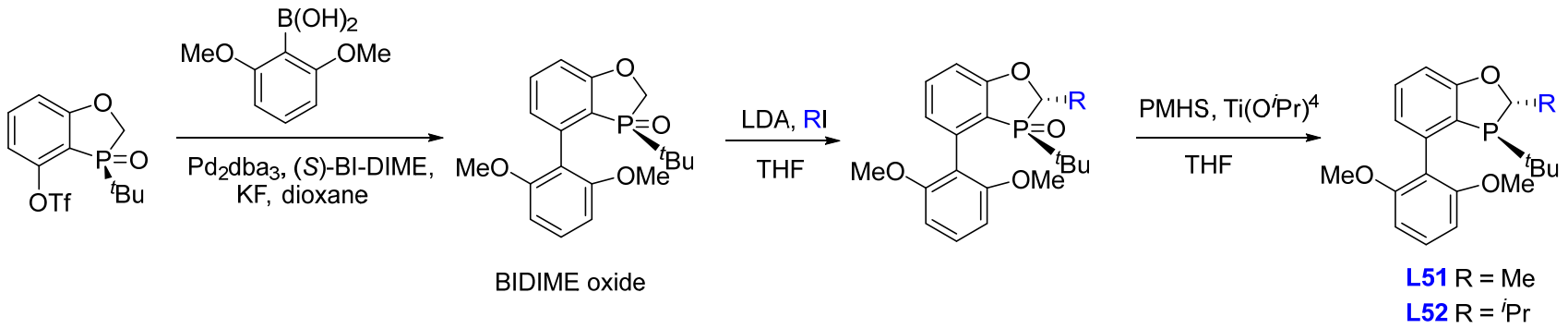
The application of Suzuki-Miyaura cross-coupling in synthesis of Korupensamine A



a: TBSCl, TEA, DCM, -78 °C to rt, 59%
b: NBS, DCM, -15 °C, 86%
c: BOPCl, TEA, DCM, 98%
d: NaOH, MeOH, 97%
e: BnBr, K_2CO_3, DMF, 95%

Xu, G.; Fu, W.; Liu, G.; Senanayake, C. H.; Tang, W. *J. Am. Chem. Soc.* **2014**, *136*, 570.

Synthesis of L51-L52

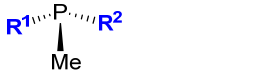


Tang, W.; Patel, N. D.; Xu, G.; Xu, X.;Savoie, J.; Ma, S.; Hao, M. -H.; Keshipeddy, S.; Capacci, A. G.; Wei, X.; Zhang, Y.; Gao, J .J.; Li, W.; Rodriguez, S.; Lu, B. Z.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2012**, *14*, 2258.
Xu, G.; Fu, W.; Liu, G.; Senanayake, C. H.; Tang, W. *J. Am. Chem. Soc.* **2014**, *136*, 570.

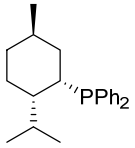
Summary and outlook

Summary

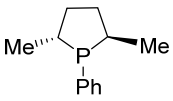
In asymmetric hydrogenation



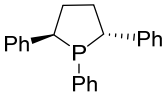
L1 R^1 = Ph, R^2 = ^{n}Pr,
L2 R^1= Ph, R^2 = 2-OMeC_6H_4,
L3 R^1 = Cy, R^2 = 2-OMeC_6H_4,



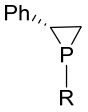
L4



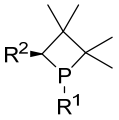
L5



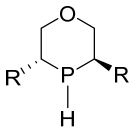
L6



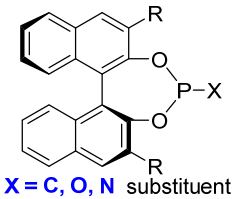
R = ^{t}Bu, (-)-menthyl
L7-L8



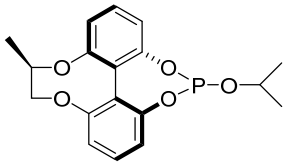
R1 = (-)-menthyl, R^2 = Bn
L9



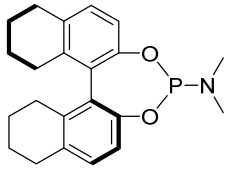
R = ^{i}Pr, Cy
L10-L11



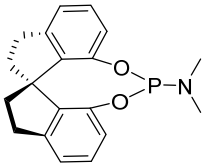
X = C, O, N substituent
L12-L14, L16-L27, L29, L31-L32, L35-L36, L38



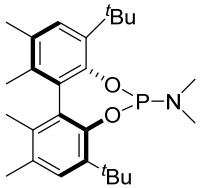
L28



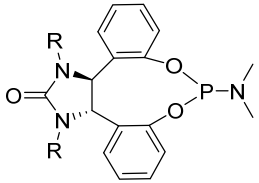
L33 (H_8-MonoPhos)



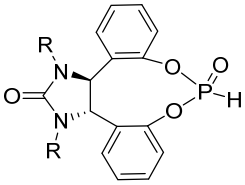
L34



L37



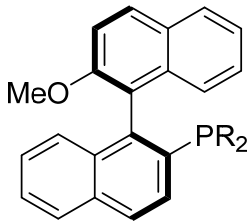
L39-L40 (DpenPhos)



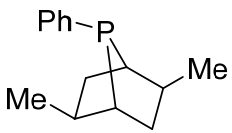
L41

Summary

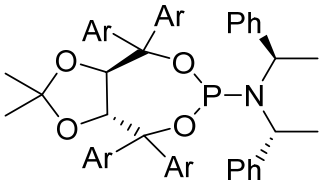
In asymmetric Allyic substitution:



L42 (MeO-MOP)

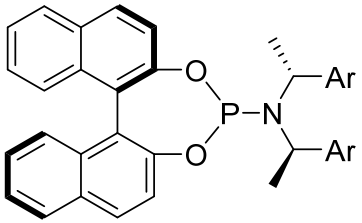


L43



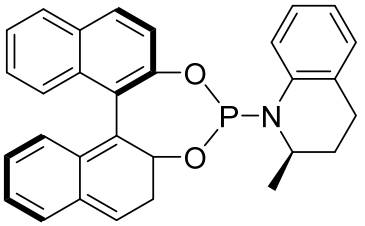
Ar = (4-^{t}Bu)C_6H_4, (3, 5-di-^{t}Bu-4-OMe)C_6H_2

L44-L45



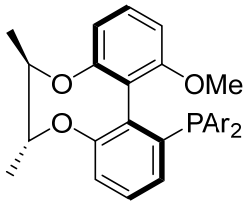
Ar = Ph, 2-OMeC_6H_4

L46-L47



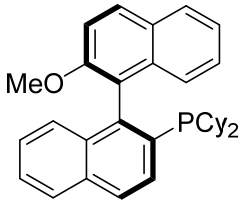
L48

In Suzuki-Miyaura cross-coupling

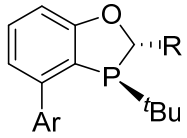


Ar = 3,5 - ^{t}Bu$_2C_6H_3$

L49



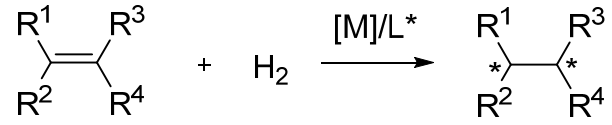
L50 (Cy-MOP)



L51-L52

Outlook

Hydrogenation of tetrasubstituted alkenes



$R^1 \neq R^2 \neq H$

$R^3 \neq R^4 \neq H$

THANK YOU!