Technical Information

Index

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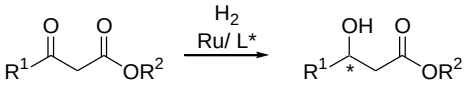
Technical Information

1. Asymmetric hydrogenation

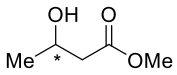
1.1. Classical Hydrogenation

1.1.1. Functionalized Ketones

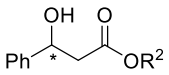
a. β-Ketoesters



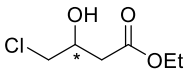
R^1 = alkyl, aryl, heteroaryl



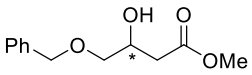
SEGPHOS® >99% ee
BINAP[1] : >99% ee



SEGPHOS® [3] 98% ee
(R^2 = Me, S/C = 10,000)
TolBINAP[3] : 87% ee
(R^2 = Et, S/C = 1,000)



SEGPHOS® [2,3] 98.5% ee
(S/C = 20,000)
TolBINAP[2,3] : 95.9% ee
(S/C = 1,000)

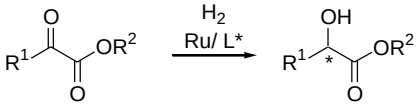


SEGPHOS® [2,3] 99.4% ee
TolBINAP[2,3] : 97.4% ee

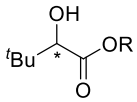
1) Noyori, R. *J. Am. Chem. Soc*. **1987**, *109*, 5856. 2) Saito, T. *Adv. Synth. Catal*. **2001**, *343*, 264. 3) Sumi, K. *Topics Organomet. Chem*. **2004**, *6*, 63. 4) JP H6-65226A, **1994**.

b. α-Ketoesters

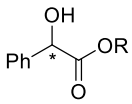
Enantioselectivities depend on the additives[3].



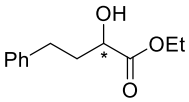
R^1 = alkyl, aryl, heteroaryl



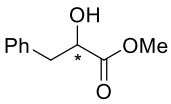
SEGPHOS® [1,2] : 98.6% ee (R = Et)
TolBINAP[2] : 84.0% ee (R = Me)



BINAP[3] : 89% ee



SEGPHOS® [1,2] :93.7% ee
(S/ C = 1,500)
BINAP[1,2] : 90.0% ee
(S/ C = 1,000)



SEGPHOS® [1] :95.9% ee

1) Saito, T. *Adv. Synth. Catal*. **2001**, *343*, 264. 2) Sumi, K. *Topics Organomet. Chem*. **2004**, *6*, 63. 3) Mashima, K. *J. Org. Chem*., **1994**, *59*, 3064.

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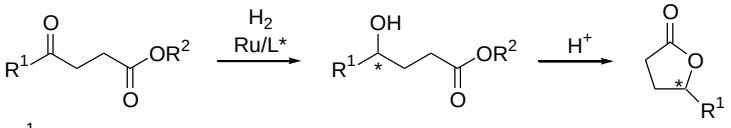
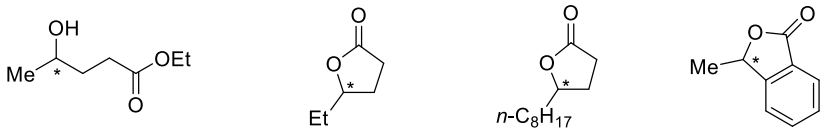
c. γ-Ketoesters



R^1 = alkyl, aryl

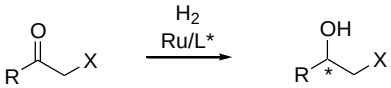


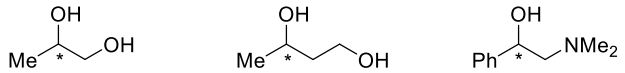
SEGPHOS® [1,2] : 99.0% ee BINAP[3] : 98% ee BINAP[3] : 98% ee BINAP[3] : 97% ee

TolBINAP [1,2] : 97.2% ee

1) Saito, T. *Adv. Synth. Catal*. **2001**, *343*, 264. 2) Sumi, K. *Topics Organomet. Chem*. **2004**, *6*, 63. 3) Noyori, R. *Tetrahedron Lett*., **1990**, *31*, 5509.

d. Hydroxyacetones and Amino ketones





L* = SEGPHOS® [1]: 98.5% ee BINAP[3] : 98% ee BINAP[3] : 96% ee

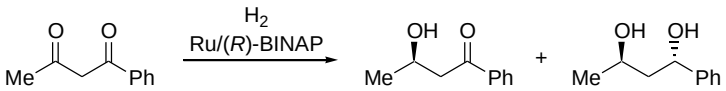
MeO-BIPHEP : 96% ee

BIPHEMP : 93% ee

BINAP : 83% ee (92% ee)[2]

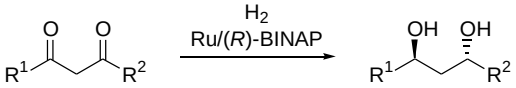
1) Saito, T. *Adv. Synth. Catal*. **2001**, *343*, 264. 2) Noyori, R. *J. Am. Chem. Soc*. **1987**, *109*, 5856. 3) Noyori, R. *J. Am. Chem. Soc*. **1988**, *110*, 629.

e. 1,3-Diketones



89%, 98% ee
(ketol : diol = 98 : 2)

Kawano, H. *J. Chem. Soc., Chem. Commun*, **1988**, 87.

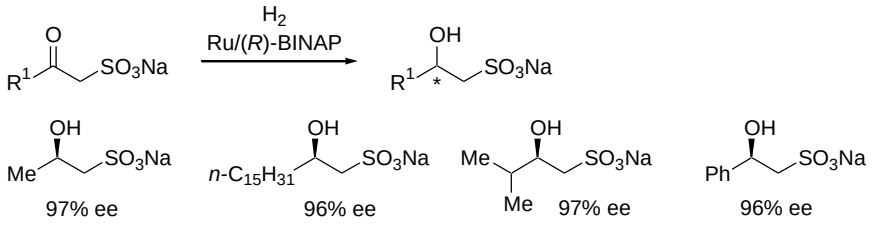


$R^1 = R^2$ = Me : 100% ee, 98% de[1]

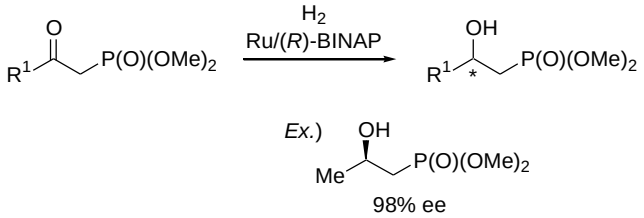
R^1 = Me, R^2 = Ph : 94% ee, 88% de[2]

1) Noyori, R. *J. Am. Chem. Soc*. **1988**, *110*, 629. 3) Kawano, H. *J. Chem. Soc., Chem. Commun*, **1988**, 87.

f. Keto sulfonates & Keto phosphonates

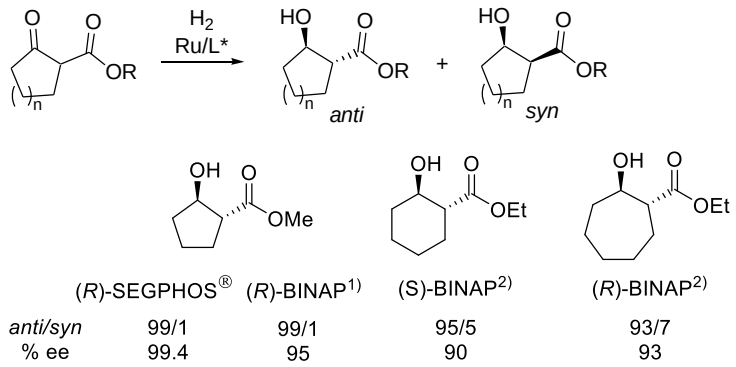


Noyori, R. *Tetrahedron* **1999**, *55*, 8769.

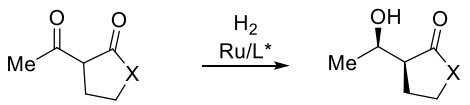


Noyori, R. *J. Am. Chem. Soc*. **1995**, *117*, 2931.

g. Dynamic Kinetic Resolution



1) Mashima, K. *J. Org. Chem*., **1994**, *159*, 3064. 2) Noyori, R. *Tetrahedron: Asymmetry*, **1990**, *31*, 1159.



X = NBn

DTBM-SEGPHOS® 1) : 98% ee, 98% de

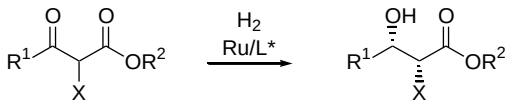
TolBINAP 2) : 88% ee, 99% de

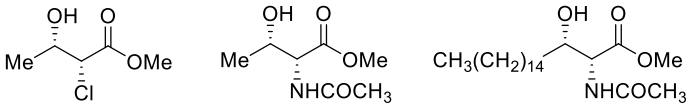
X = O

DTBM-SEGPHOS® : 99% ee, 99% de

BINAP3) : 97% ee, 98% de

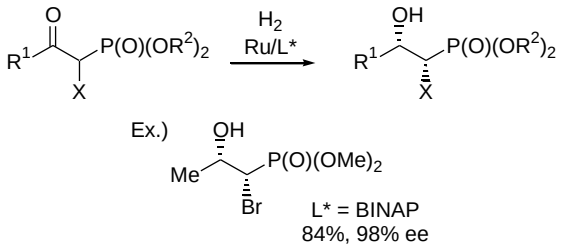
1) Sumi, K. *Topics Organomet. Chem*. **2004**, *6*, 63. 2) JPH10-204058. 3) Mashima, K. *J. Org. Chem*., **1994**, *159*, 3064.



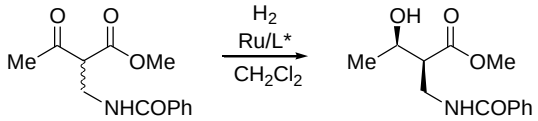


SEGPHOS® >99% ee, 97% de | DTBM-SEGPHOS® 99% ee, 98% de | DM-SEGPHOS® 98% ee, 97.5% de

Sumi, K. *Topics Organomet. Chem*. **2004**, *6*, 63.



Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 2931.



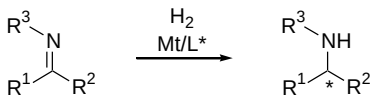
BINAP :	90% ee, 74% de	SEGPHOS® :	80% de
XylBINAP :	95% ee, 99% de	DM-SEGPHOS® :	98% ee, 94% de
DT-BINAP :	99% ee, 98% de	DTBM-SEGPHOS® * :	99% ee, 99% de

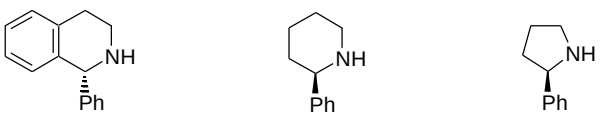
(DT = 3,5-di-^{t}Bu)

*CH_2Cl_2/MeOH (7/1) was used as solvent.

Saito, T. *Adv. Synth. Catal*. **2001**, *343*, 264.

1.1.2. Imines





Ru-(*R*)-TolBINAP[1)] 88.9% ee | Ir-(*S*)-BINAP[2)] 85% ee | Ir-(*S*)-BINAP[3)] 91% ee

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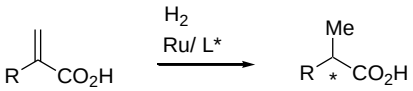
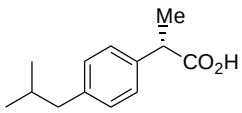
1) JP 2005-281144A, **2005**. 2) JP 2004-256460A, **2004**. 3) WO 2006/022020 A1, **2006**.

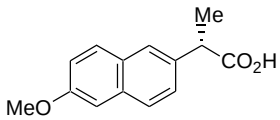
1.1.3. Olefins

a. α,β-Unsaturated carboxylic acids



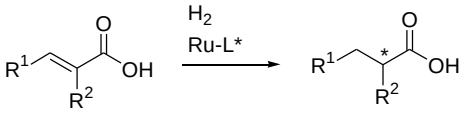


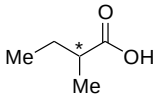
(*S*)-BINAP[1]; 97% ee



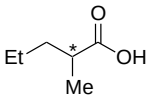
(*S*)-H8-BINAP[2,3]; 92% ee
(S/C = 5,000)

1) Noyori, R. *J. Org. Chem*. **1987**, *52*, 3174. 2) Takaya, H. *Synlett* **1994**, 501. 3) Takaya, H. *J. Org. Chem*. **1996**, *61*, 5510.

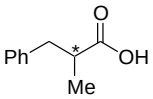




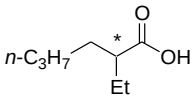
(*S*)-H_8-BINAP: 97% ee (*S*)
(*R*)-BINAP: 96% ee (*R*)



(*S*)-H_8-BINAP: 96% ee (*S*)
(*R*)-BINAP: 84% ee (*R*)



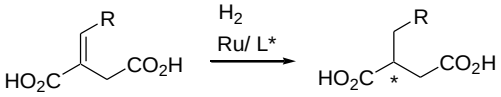
(*S*)-H_8-BINAP: 89% ee (*S*)
(*R*)-BINAP: 30% ee (*R*)

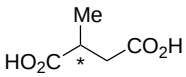


(*S*)-H_8-BINAP: 95% ee (*S*)
(*R*)-BINAP: 88% ee (*R*)

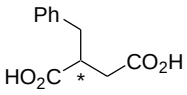
1) Zhang, X. *Synlett* **1994**, 501. 2) Uemura, T. *J. Org. Chem*. **1996**, *61*, 5510. 3) Kumobayashi, H. *Synlett* **2001**, 1055.

b. Itaconic acid delivatives





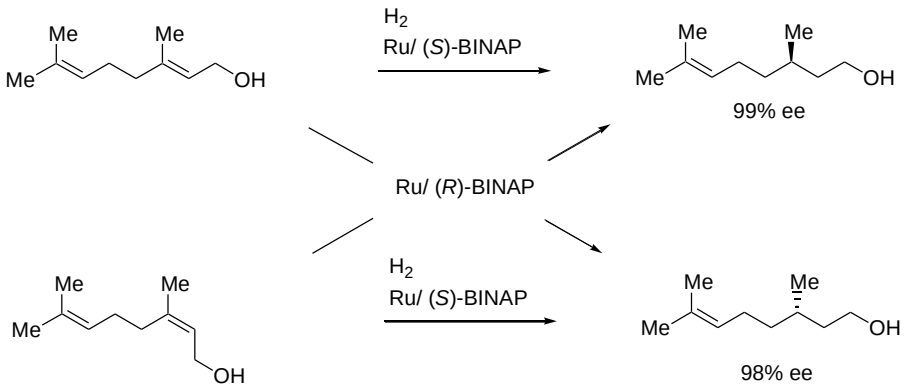
BINAP
88% ee



BINAP
90% ee

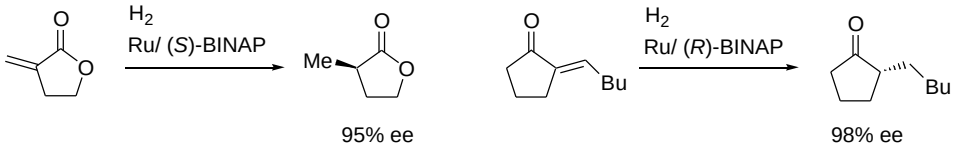
1) Ikariya, T. *J. Chem. Soc., Chem. Commn*. **1985**, 922. 2) Kumobayashi, H. *J. Chem. Soc., Perkin Trans.* I **1989**, 1571. 3) Kumobayashi, H. *Tetrahedron, Lett*., **1987**, *28*, 1905. 4) Uchida, Y. *J. Chem. Soc., Perkin Trans.* I **1990**, 1441.

c. Allyl alcohols



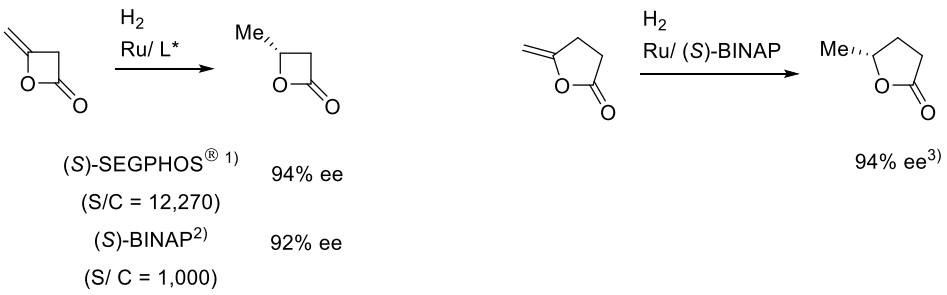
Takaya, H. *J. Am. Chem. Soc*. **1987**, *109*, 1596.

d. α,β-Unsaturated lactones & ketones



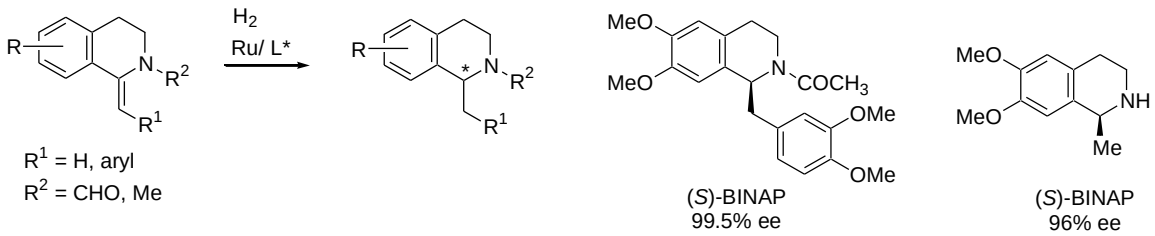
1) Ohta, T. *J. Org. Chem*. **1995**, *60*, 357. 2) Ohta, T. *Tetrahedron Lett*., **1992**, *33,* 635.

e. Diketene & Methylene-γ-butyrolactone



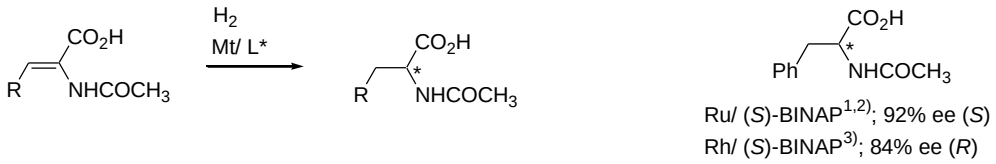
1) US 006043380A, **1999**. 2) Takaya, H. *J. Chem. Soc. Chem. Commun*. **1992**. 3) Ohta, T. *J. Org. Chem*. **1995**, *60*, 357.

f. Enamide



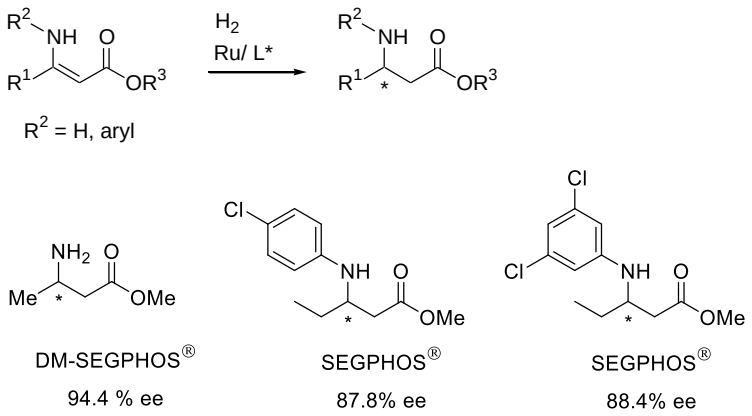
1) Takaya, H. *J. Am. Chem. Soc*. **1986**, *108*, 7117.

g. Dehydro amino acids



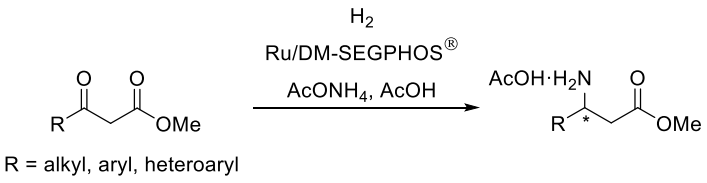
1) Ikariya, T. *J. Chem. Soc., Chem. Commn*. I **1985**, 922. 2) *J. Chem. Soc., Perkin Trans.* I **1989**, 1571. 3) Noyori, R. *J. Am. Chem. Soc*. **1980**, *102,* 7932.

h. Enamino esters



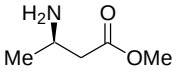
1) US 2004/0023344 A1, **2003**. 2) US 2006/122225 A1, **2006**.

1.2. Direct Reductive Amination of *β*-ketoesters

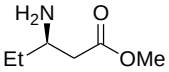


Technical Information

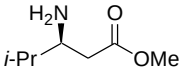
- Product List as AcOH salt -



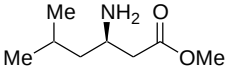
92.9% ee



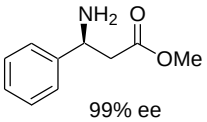
98% ee



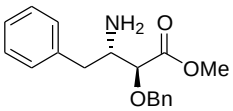
99% ee



98% ee



99% ee



anti/ syn = 86/ 14

99% ee (*anti*)
95% ee (*syn*)

1) WO 2005/028419 A3, 2004. 2) *Acc. Chem. Res.*; **2007**,40, 1385.

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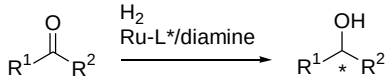
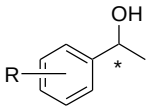
1.3. $RuCl_2$(diphosphine)(diamine) catalyzed hydrogenation

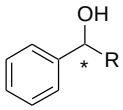
a. Aryl alkyl ketones & heteroaryl alkyl ketones



R^1 = aryl, heteroaryl
R^2 = alkyl

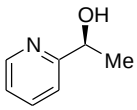


R =
H: 99% ee
2-Cl: % ee
4-OMe: > 99.9% ee
4-CF_3: 99.6% ee

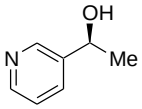


R =
Et: 99% ee
cyclo-C_3H_5: 99.7% ee
CF_3: 96% ee

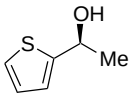
(*S*)-XylBINAP/ (*S*)-DAIPEN



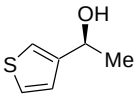
96% ee



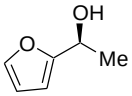
99.6% ee



99% ee



99.7% ee

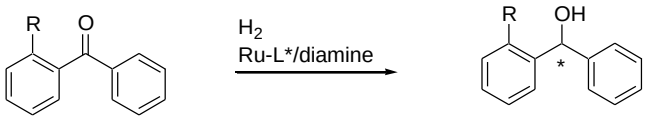


99% ee

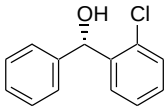
(*R*)-XylBINAP/ (*R*)-DAIPEN

1) Noyori, R. *J. Am. Chem. Soc*. **1998**, *120*, 13529. 2) Noyori, R. *Org. Lett*. **2000**, *2*, 1749.

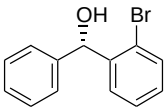
b. Aryl aryl ketones



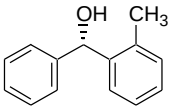
(*S*)-XylBINAP/ (*S*)-DAIPEN



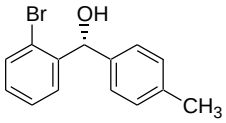
97% ee



96% ee



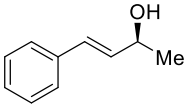
93% ee



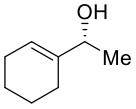
98% ee

Noyori, R. *Org. Lett*., **2000**, *2*, 659.

c. Others

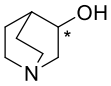


97% ee



>99% ee

(*S*)-XylBINAP/ (*S*)-DAIPEN[1)]



DM-SEGPHOS® / DAIPEN[2)]; 90.5% ee
XylBINAP/ DAIPEN[2)]; 74.5% ee

1) Noyori, R. *J. Am. Chem. Soc*. **1998**, *120*, 13529. 2) US 2006041722, **2006**.

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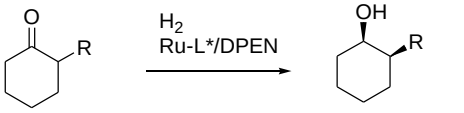
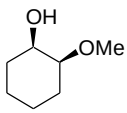
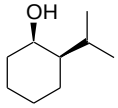
d. Dynamic Kinetic Resolution





99% ee
99% de

(*S*)-XylBINAP/
(*S*,*S*)-DPEN

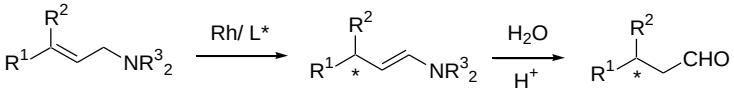


93% ee
99.6% de

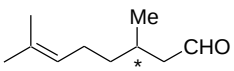
(*S*)-XylBINAP/
(*S*,*S*)-DPEN

1) Matsumoto, T. *Tetrahedron Lett*. **1999**, *40*, 5043. 2) Noyori, R. *J. Org. Chem*. **1996**, *61*, 4872.

2. Asymmetric Isomerization

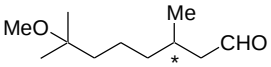


L*; BINAP or TolBINAP

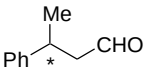


> 98% ee
(S/C = 400,000)

in l-Menthol process



> 98% ee

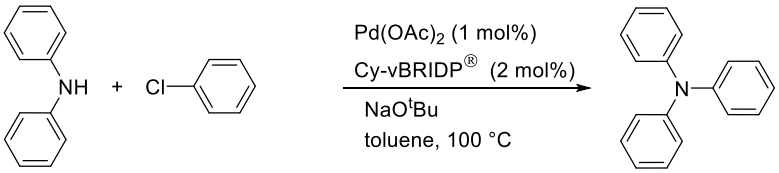


95% ee

Akutagawa, S. *Tetrahedron Lett*. **1985**, *26*, 5153.

3. Monophosphine Ligands for Pd Catalyzed Coupling Reactions

3.1. Buchwald-Hartwig Reaction



95%

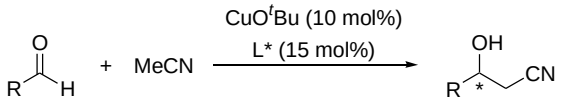
Suzuki, K.; Hori, Y.; Nishikawa, T.; Kobayashi, T. *Adv. Synth. Catal.* **2007**, *349*, 2089.

3.2. Suzuki-Miyaura Reaction

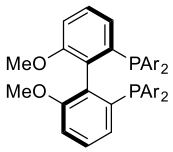
Suzuki, K.; Hori, Y.; Kobayashi, T. *Synlett.* **2007** 20, 3206.

4. Other Reactions

4.1. Cyanomethylation



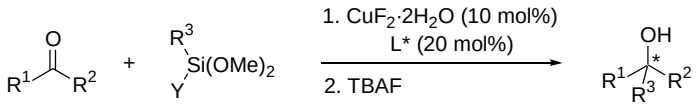
	R = *n*-Hex
L* = (*R*)-DTBM-SEGPHOS® :	84%, 58% ee
(*R*)-DTBM-SEGPHOS® (at rt) :	72%, 74% ee
(*S*)-TolBINAP :	21%, 16% ee
(*R*,*R*)-Ph-BPE :	32%, 0% ee
(*R*,*S*)-Josiphos :	18%, 6% ee
(*R*)-SEGPHOS® :	18%, 8% ee
(*R*)-Tuned-BIPHEP :	40%, 75% ee

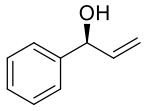


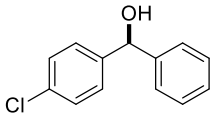
(*R*)-Tuned-BIPHEP
Ar = 4-^{i}PrO-3,5-(^{i}Pr)$_2$-C_6H_2

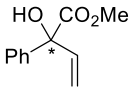
Shibasaki, M. *Org. Lett.* **2005**, *7,* 3757.

4.2. Vinylation & Phenylation









L* = **(*R*)-DTBM-SEGPHOS®** :	99%, 94%*ee	(*R*)-DTBM-SEGPHOS®	DTBM-SEGPHOS®
(*R*)-TolBINAP :	47%, 61% ee	92% ee	76%, 84% ee
(*R*,*R*)-CHIRAPHOS :	24%, 7% ee		
(*R*,*R*)-Et-DuPHOS :	51%, 38% ee		
(S,S)-*i*-Pr-DuPHOS :	87%, 64% ee		

* $CuF_2 \cdot 2H_2O$ (3 mol%), DTBM-SEGPHOS® (6 mol%)

Shibasaki, M. *J. Am. Chem. Soc.* **2005**, *127,* 4138.

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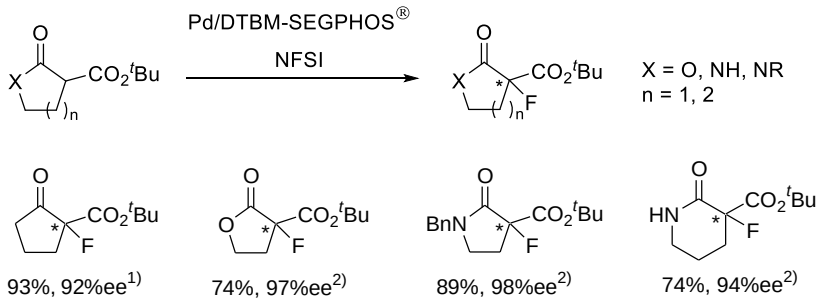
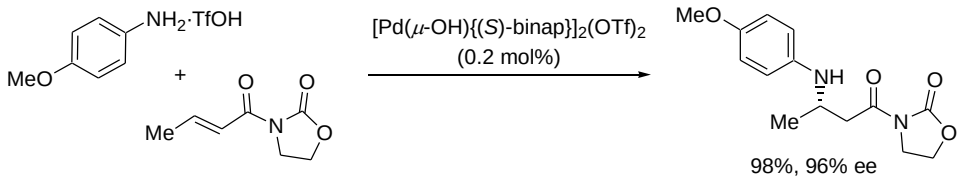
4.3. Fluorination



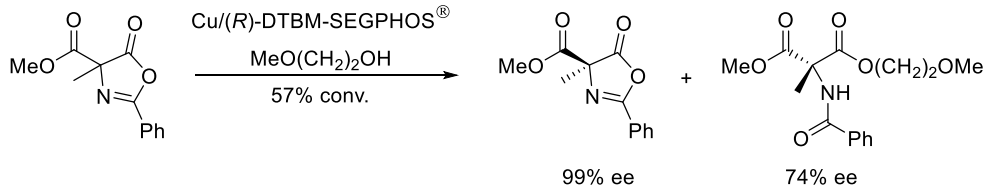
1) Sodeoka, M. *J. Am. Chem. Soc.* **2002**, *124*, 14530. 2) Sodeoka, M. *J. Org. Chem*. **2007**, *72*, 246.

4.4. Aza-Michael addition



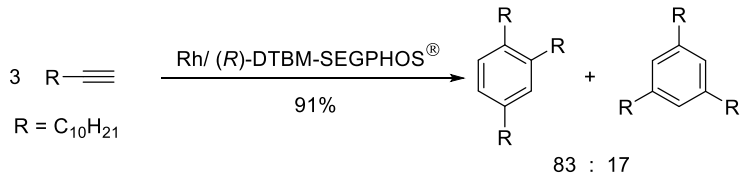
Sodeoka, M. *Org. Lett.* **2004**, *6,* 1861.

4.5. Asymmetric alcoholysis of azlactones



Tokunaga, M. *J. Am. Chem. Soc.* **2006**, *128*, 4481.

4.6. Cyclotrimerization of terminal alkynes



1) Tanaka, K. *Org. Lett*. **2003**, *5*, 4697. 2) Tanaka, K. *Chem. Eur. J*. **2005**, *11*, 1145.

5. Publications

(1) "Asymmetric synthesis by metal BINAP catalysts"
Akutagawa, S. *Applied Catalysis A: General* **1995**, *128*, 171–207.
doi: 10.1016/0926-860X(95)00097-6

(2) "Industrial application of asymmetric reactions catalyzed by BINAP-metal complexes"
Kumobayashi, H. *Recl. Trav. Chim. Pays-Bas* **1996**, *115*, 201–210.
doi: 10.1002/recl.19961150403

(3) "Rhodium/Ruthenium Applications"
Sumi, K; Kumobayashi, H. In *Organometallics in Process Chemistry (Topics in Organometallic Chemistry. Vol 6)*, Ed.; Larsen, R. D., Eds., Springer: Berlin, **2004**; p. 63-95.
doi: 10.1007/b11768

(4) "Recent advances in biaryl-type bisphosphine ligands"
Shimizu, H.; Nagasaki, I.; Saito, T. *Tetrahedron* **2005,** *61* (23), 5405-5432.
doi: 10.1016/j.tet.2005.03.022

(5) "Developments in Asymmetric Hydrogenation from an Industrial Perspective"
Shimizu, H.; Nagasaki, I.; Matsumura, K.; Sayo, N.; Saito, T. *Acc. Chem. Res.* **2007,** *40*, 1385-1393.
doi: 10.1021/ar700101x

(6) "Chiral Ligands & Their Complexes"
Kuriyama, W.; Sayo, N.; Saito, T. *The Strem Chemiker* **2007**, *23*, 1.
http://www.strem.com/uploads/resources/documents/chemiker23.pdf

(7) "Axial Chiral Diphosphines: Atropisomeric Biaryl Diphosphine Ligands"
Shimizu, H.; Nagasaki, I.; Sayo, N.; Saito, T. In *Phosphorus Ligands in Asymmetric Catalysis: Synthesis and Applications*. Ed. Bȯrner,A. Eds.; Wiley-VCH: Weinheim, **2008**, Vol. 1, p. 207.
ChemInform, **2009**, 40(43), nopage.
doi: 10.1002/chin.200942246

(8) "(*R*)- and(*S*)-(4,4'-bi-1,3-benzodioxol)-5,5'-diyl-bis(bis 3,5-di-tert–butyl-4-methoxyphenyl)phosphin"
Saito, T. In *e-EROS Encyclopedia of Reagents for Organic Synthesis*, **2009** (accessed 27 March 2009).
doi: 10.1002/047084289X.rn00766

(9) "Eliminating Barriers in Large-Scale Asymmetric Synthesis."
Shimizu, H.; Sayo, N.; Saito, T. In *Asymmetric Catalysis on Industrial Scale.* 2nd Ed; Blaser, H.-U.; Federsel, H.-J. Eds.; Wiley-VCH: Weinheim, **2010,** Chapter 12; p. 207–218.
doi: 10.1002/9783527630639.ch12

(10) "Industrial Application of the Asymmetric Reduction of C=O and C=N Bonds, including Enamides and Enamines"
Shimizu, H.; S. Komiya; Nagasaki, I. In *Comprehensive Chirality*. Ed. Yamamoto,H.; Carreira, E. Eds.; Elsevier: Oxford, 9, **2012**, 83–103.
doi: 10.1016/B978-0-08-095167-6.00905-8

(11) "Development of New Phosphine Ligands (BRIDPs) for Efficient Palladium-Catalyzed Coupling Reactions and Their Application to Industrial Processes"
Suzuki, K.; Hori. Y.; Nakayama,Y.; Kobayashi, T. *J. Synth. Org. Chem., Jpn.* **2011**, 69, 1231.
doi: 10.5059/yukigoseikyokaishi.69.1231

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