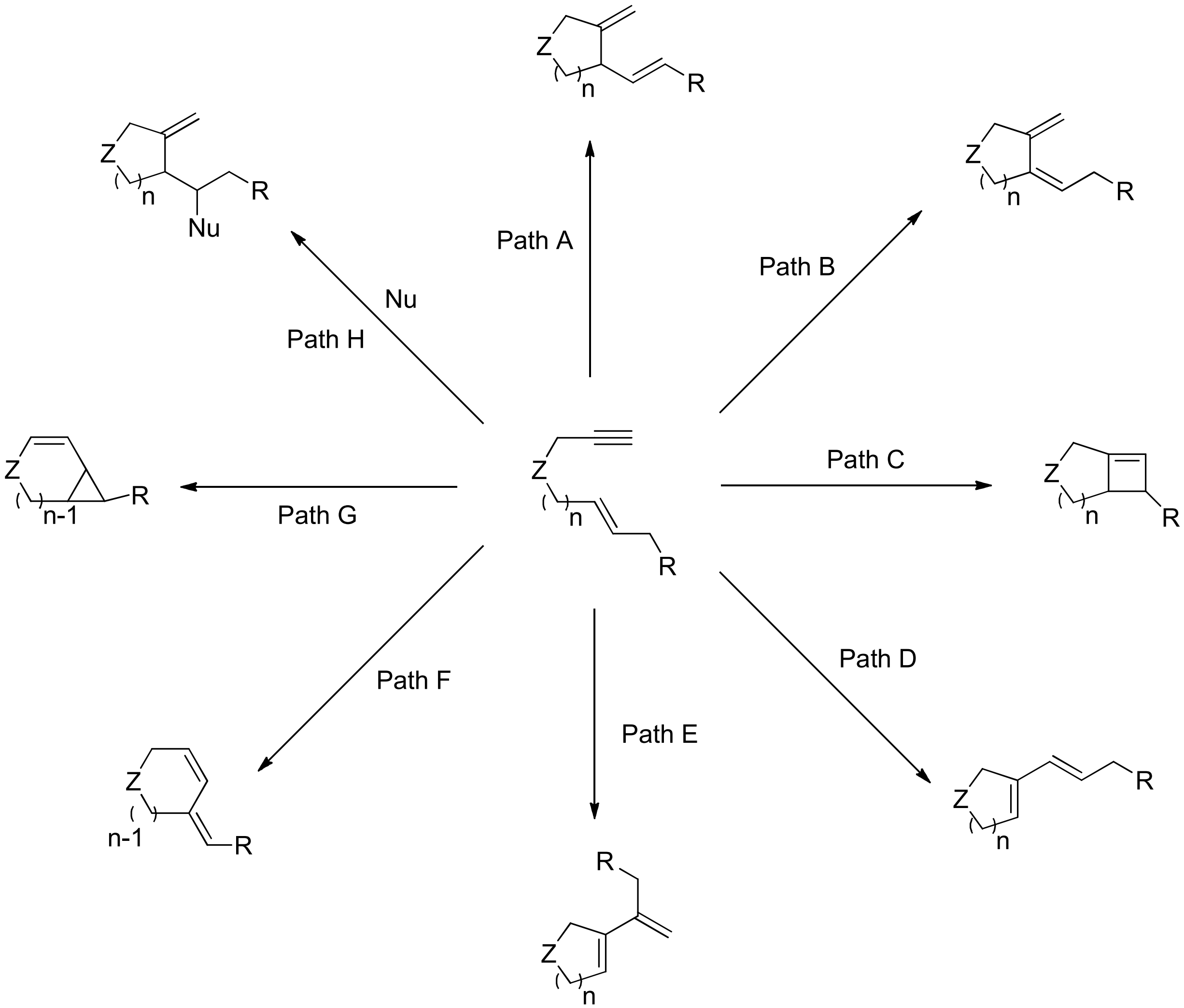
Asymmetric Enyne Cycloisomerisations

Literature Review

08/06/12

Ross Walker

Cycloisomerisation of Enynes



Aubert, C.; Buisine, O.; Malacria, M., *Chem. Rev.* **2002**, *102* (3), 813-834.
Michelet, V.; Toullec, P. Y.; Genêt, J.-P., *Angew. Chem. Int. Ed.* **2008**, *47* (23), 4268-4315.
Lee, S. I.; Chatani, N., *Chem. Commun.* **2009**, 371-384.

OVERVIEW

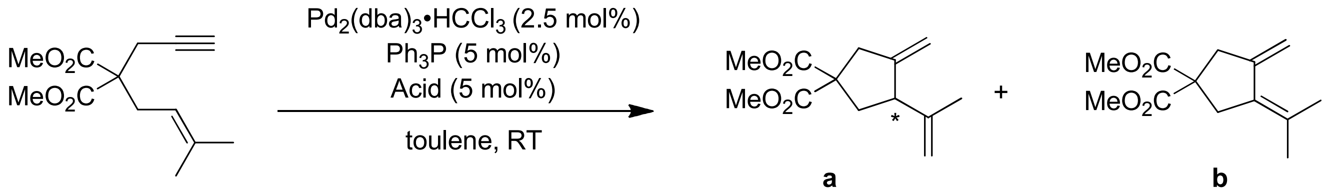
Cycloisomerisation of Enynes:

Pd, Ru, Rh, Ir, Pt, Au, Hg, Ti, Cr, Fe, Co, Ni, Cu, Ag, Ga, In

1) Enyne Rearrangements

2) Enyne Tandem Reactions

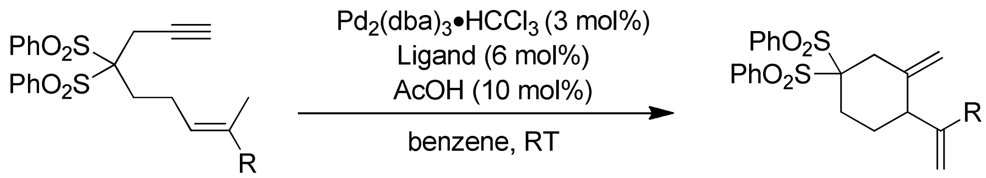
Pd-Catalysed

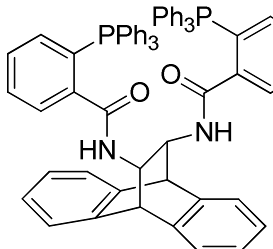


Optically Active Acids	Yield	Ratio **a:b**	**ee**
S (-)-binaphthoic	61%	3:1	33%
(+)-3*S*-methyl-2*R*-(nitromethyl)-5-oxo-3*S*-cyclopentaneacetic acid	59%	3.5:1	5-10%
(-)-2pyrrolidone-5*S*-carboxylic acid	82%	3:1	9%
S (-)-2methoxy-2-trifluoromethyl-phenylacetic acid	50%	3:1	8%
(+)-camphorcaraboxylic acid	64%	3.2:1	2-5%

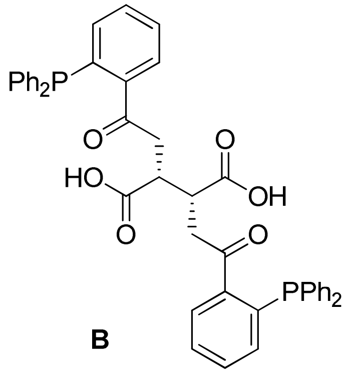
Trost, B. M.; Lee, D. C.; Rise, F., *Tetrahedron Lett.* **1989**, *30* (6), 651-654.

Pd-Catalysed





A

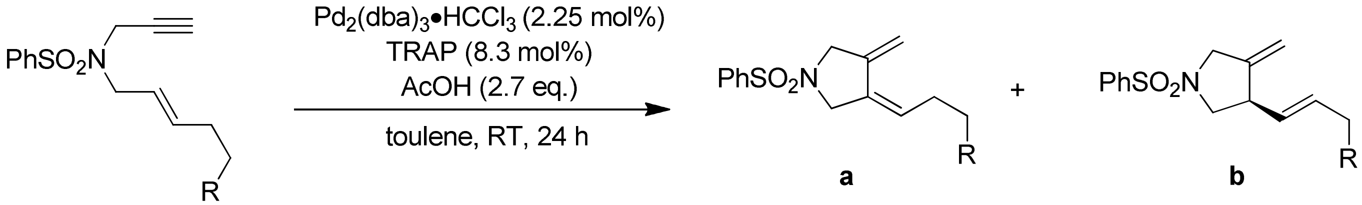


B

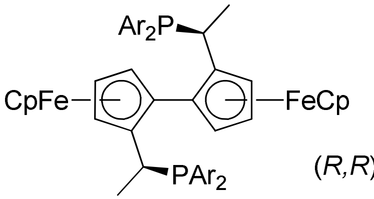
R	Ligand	ee
$(CH_2)_3O_2C(CH_2)_2CO_2H$	**A**	50%
$(CH_2)_2CO_2H$	**A**	42%
$(CH_2)_2CO_2CH_2CH_3$	**A**	24%
	B (60 °C)	33%
CO_2H	**A**	47%

Trost, B. M.; Czeskis, B. A., *Tetrahedron Lett.* **1994,** *35* (2), 211-214.

Pd-Catalysed



R = $SiMe_3$
68 % yield
a:b 1:3.5
95% ee

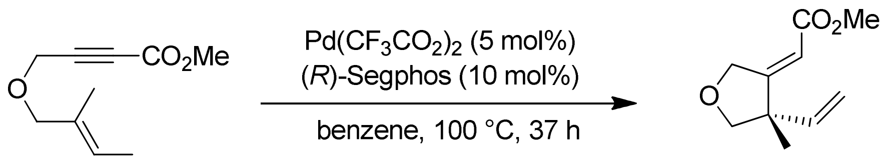


(*R*,*R*)-(*S*,*S*)-(*p*-$CF_3C_6H_4$)-trap

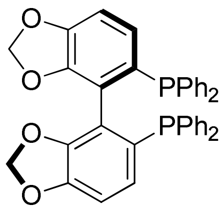
- However the chemoselectivity and substrate scope of this reaction remained very limited.
- The chiral phosphine ligand also reduces the rate of cyclisation.
- Yields 24-80 % (typically 70%), *ee* 34-95 (typically 65)

Goeke, A.; Sawamura, M.; Kuwano, R.; Ito, Y., *Angew. Chem. Int. Ed. Engl.* **1996,** *35* (6), 662-663.

Pd-Catalysed



99% yield, 99% ee

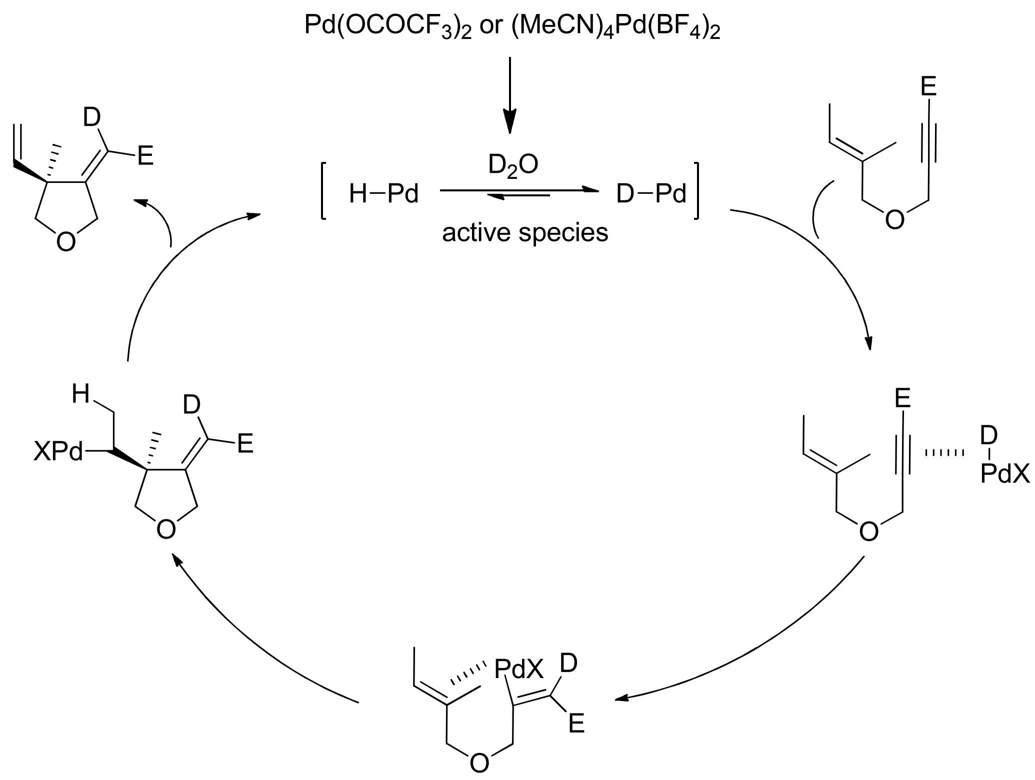


(*R*)-Segphos

Catalyst, ligand and solvent were all optimised but only with a single substrate

Hatano, M.; Terada, M.; Mikami, K., *Angew. Chem. Int. Ed.* **2001**, *40* (1), 249-253.

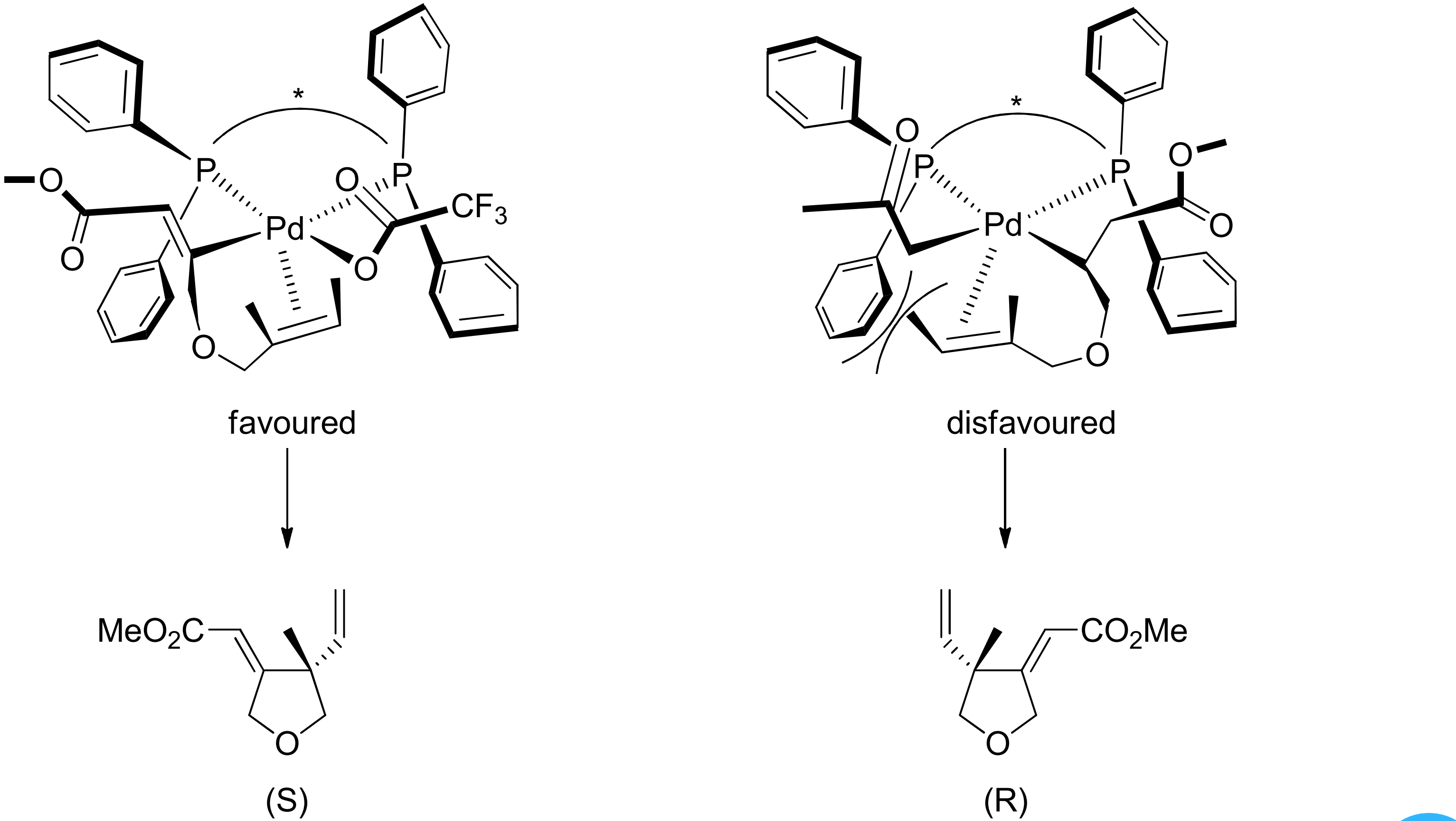
Pd-Catalysed



Hatano, M.; Terada, M.; Mikami, K., *Angew. Chem. Int. Ed.* **2001,** *40* (1), 249-253.

Pd-Catalysed

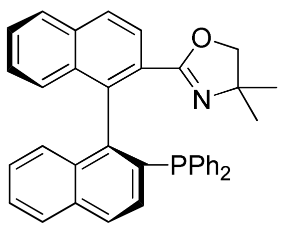
Intermediates in non-polar solvents eg. benzene



Hatano, M.; Terada, M.; Mikami, K., *Angew. Chem. Int. Ed.* **2001**, *40* (1), 249-253.

Pd-Catalysed

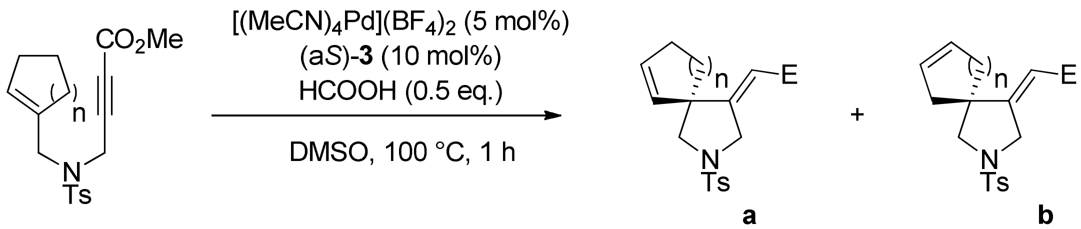
R^1=H, R^2=Me 99% yield, 93% ee
R^1=Me, R^2=H 90% yield, 66% ee

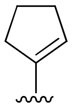
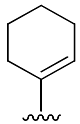
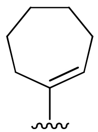
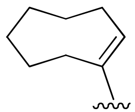
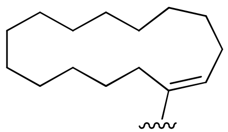


(a*S*)-**3**

Hatano, M.; Mikami, K., *Org. Biomol. Chem.* **2003**, *1* (22), 3871-3873.

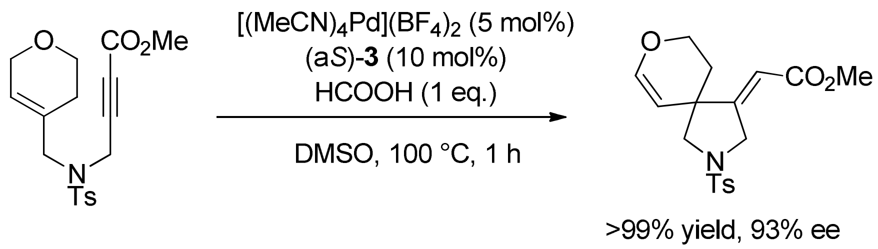
Pd-Catalysed



Substrate	% Yields (%ee)	
	a	**b**
	90(96)	9(-)
	71(84)	29(35)
	6(95)	93(95)
	25(92)	70(91)
	>95(84)	0(-)

Hatano, M.; Mikami, K., *Org. Biomol. Chem.* **2003**, *1* (22), 3871-3873.

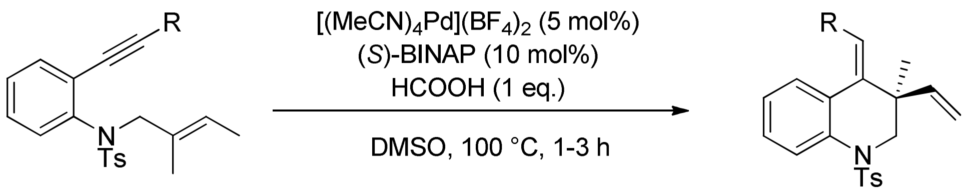
Pd-Catalysed



Hatano, M.; Mikami, K., *Org. Biomol. Chem.* **2003,** *1* (22), 3871-3873.

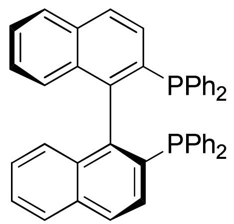
Pd-Catalysed

1,7-Enynes

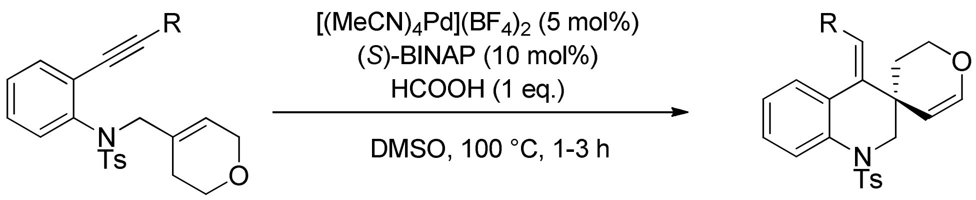


R = CO_2Me, H

99% yield, 99% ee



(*S*)-BINAP

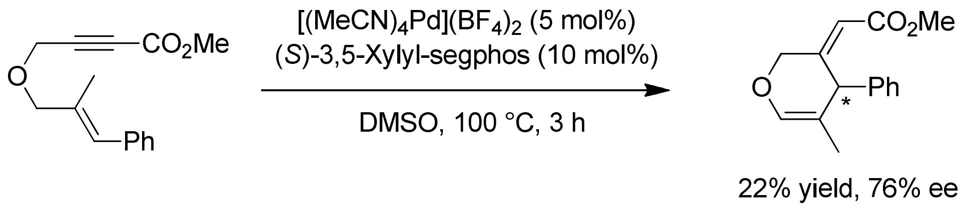


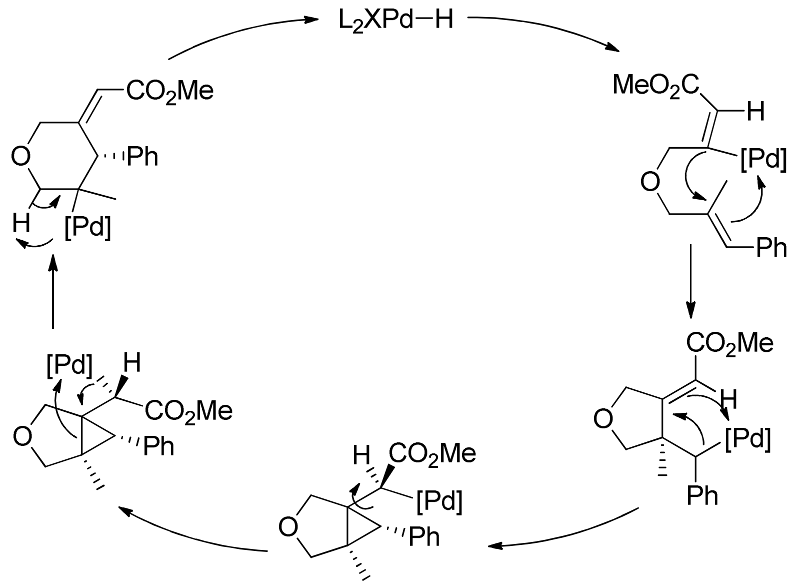
R = CO_2Me
R = H

99% yield, 99% ee
99% yield, 98% ee

Hatano, M.; Mikami, K., *J. Am. Chem. Soc.* **2003**, *125* (16), 4704-4705.

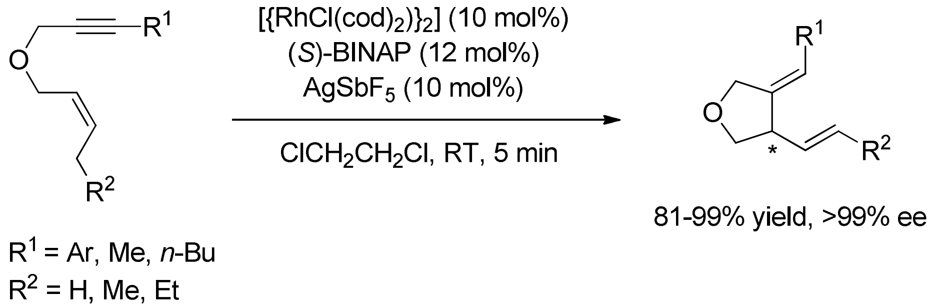
Pd-Catalysed

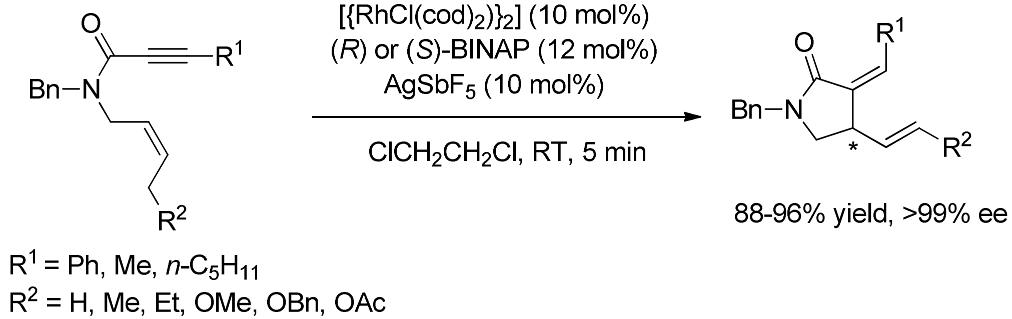




Mikami, K.; Hatano, M., *Proc. Natl. Acad. Sci. USA* **2004,** *101* (16), 5767-5769.

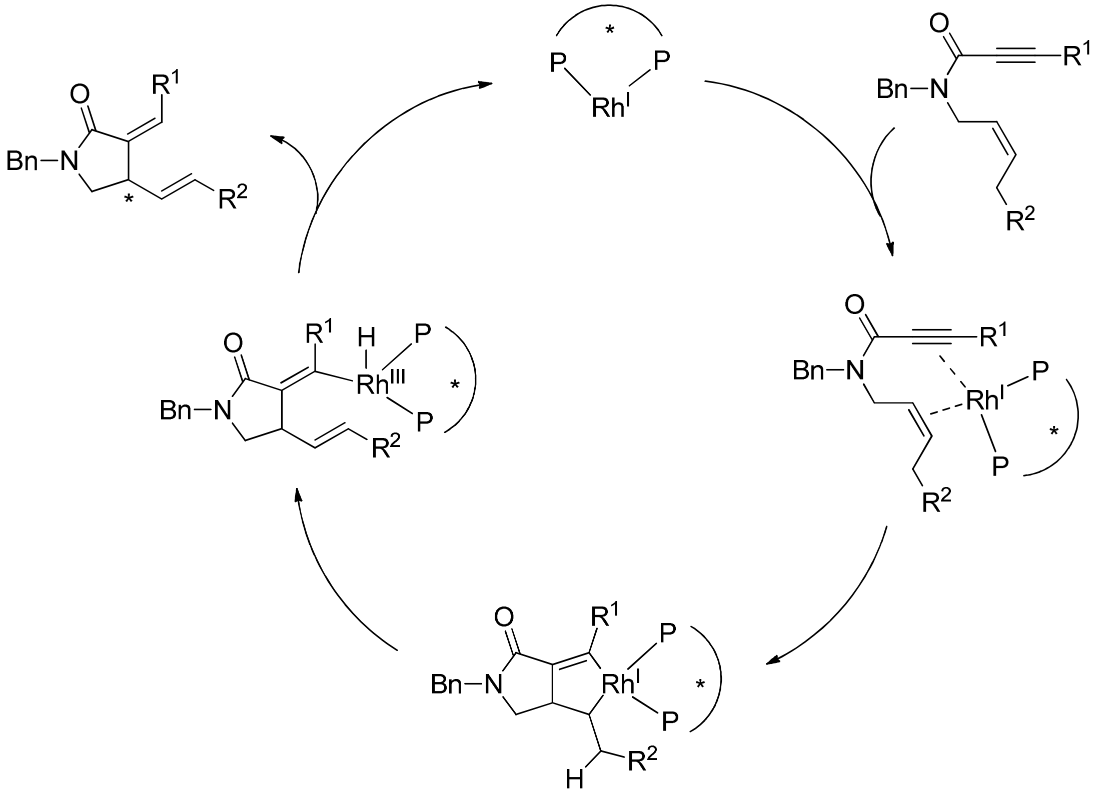
Rh-Catalysed





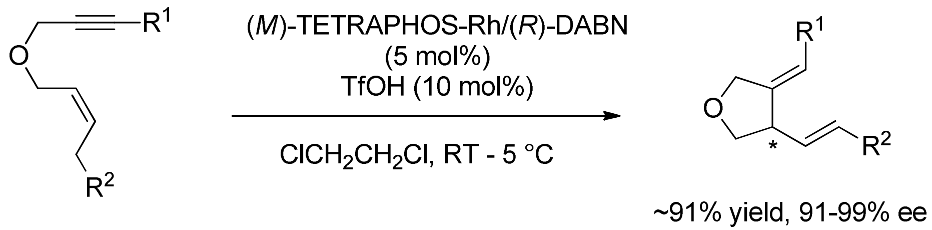
Cao, P.; Zhang, X., *Angew. Chem. Int. Ed.* **2000,** *39* (22), 4104-4106.
Lei, A.; He, M.; Wu, S.; Zhang, X., *Angew. Chem. Int. Ed.* **2002,** *114* (18), 3607-3610.
Lei, A.; Waldkirch, J. P.; He, M.; Zhang, X., *Angew. Chem. Int. Ed.* **2002,** *41* (23), 4526-4529.

Rh-Catalysed

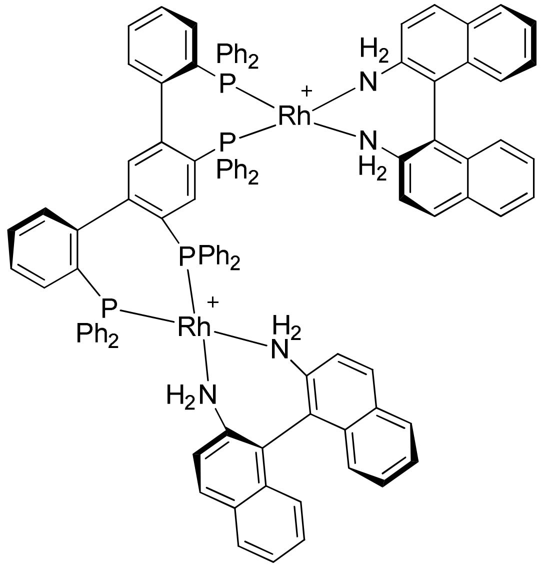


Cao, P.; Zhang, X., *Angew. Chem. Int. Ed.* **2000,** *39* (22), 4104-4106.
Lei, A.; He, M.; Wu, S.; Zhang, X., *Angew. Chem. Int. Ed.* **2002,** *114* (18), 3607-3610.
Lei, A.; Waldkirch, J. P.; He, M.; Zhang, X., *Angew. Chem. Int. Ed.* **2002,** *41* (23), 4526-4529.

Rh-Catalysed



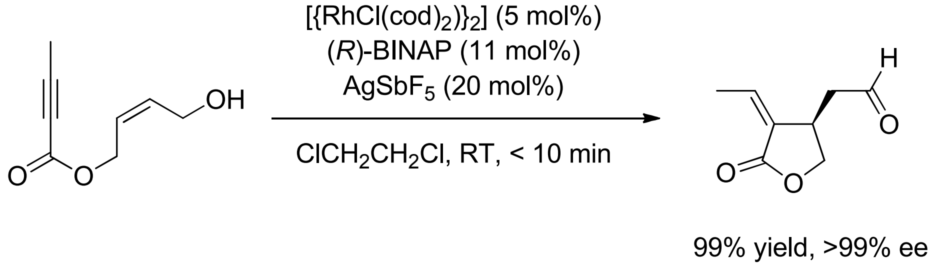
(*M*)-TETRAPHOS-Rh/(*R*)-DABN

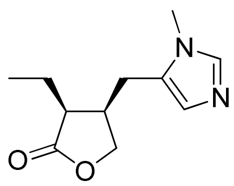


Mikami, K.; Kataoka, S.; Aikawa, K., *Org. Lett.* **2005,** *7* (26), 5777-5780.

Rh-Catalysed

Examples in Natural Product Synthesis



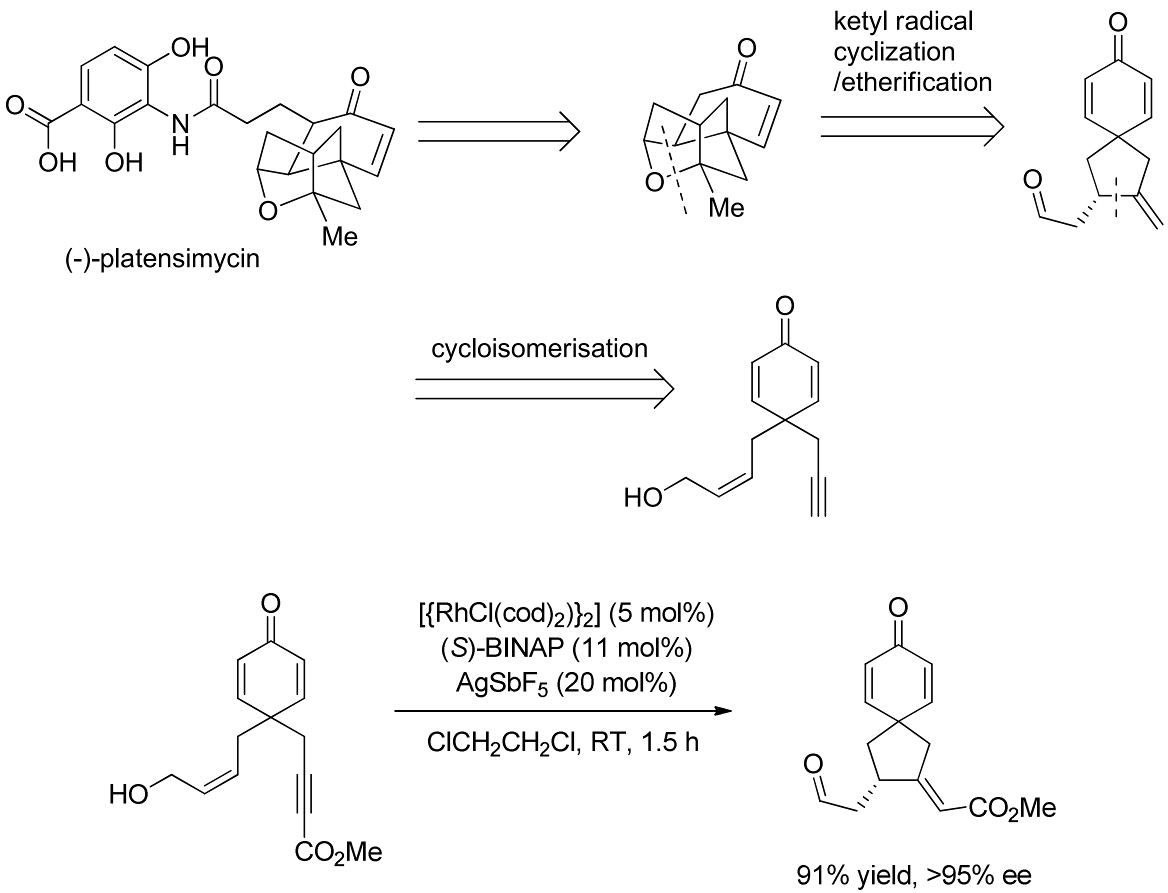


(+)-pilocarpine

Lei, A.; He, M.; Zhang, X., *J. Am. Chem. Soc.* **2002,** *124* (28), 8198-8199.
Horne, D. A.; Fugmann, B.; Yakushijin, K.; Buchi, G., *J. Org. Chem.* **1993,** *58* (1), 62-64.

Rh-Catalysed

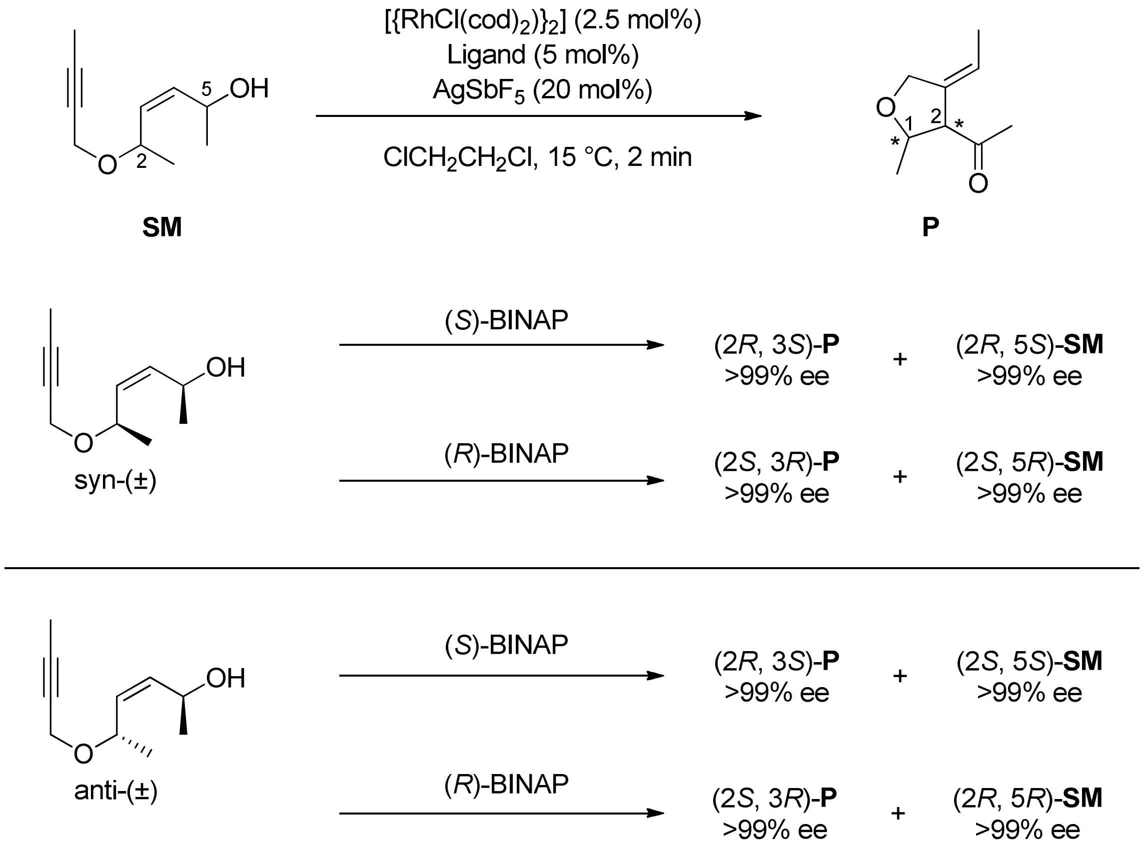
Examples in Natural Product Synthesis



Nicolaou, K. C.; Edmonds, D. J.; Li, A.; Tria, G. S., *Angew. Chem. Int. Ed.* **2007,** *46* (21), 3942-3945.

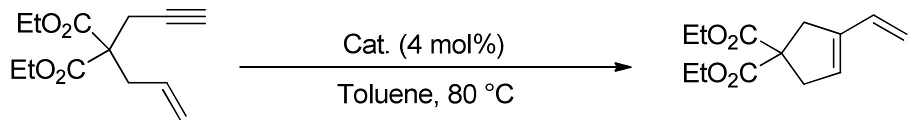
Rh-Catalysed

Kinetic Resolution

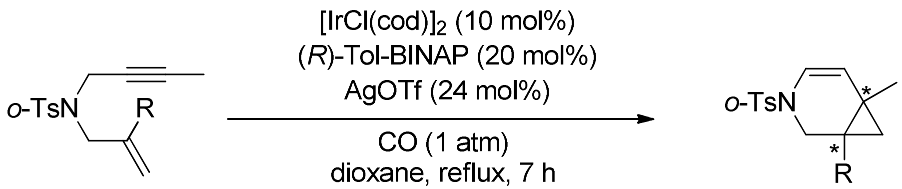


Lei, A.; He, M.; Zhang, X., *J. Am. Chem. Soc.* **2003**, *125* (38), 11472-11473.

Ir-Catalysed



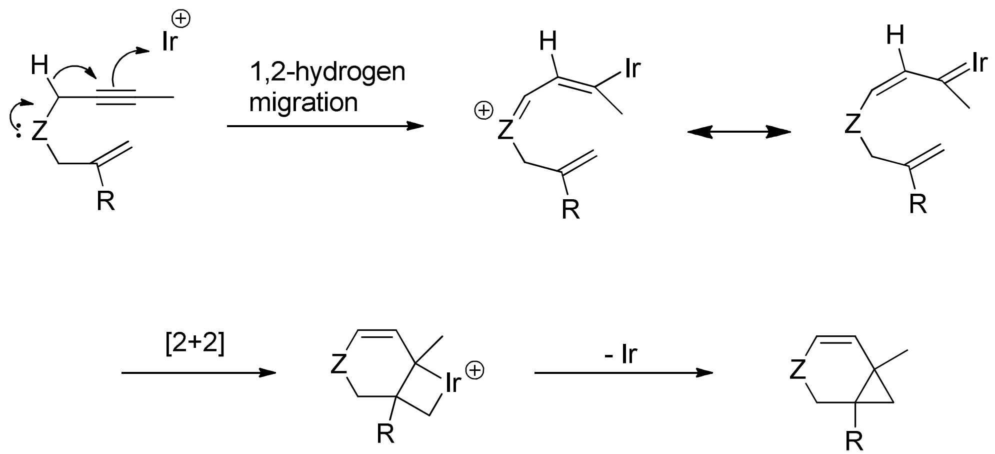
$[IrCl(CO)_3]_n$	CO	2 d	5%
$[IrCl(CO)_3]_n$	N_2	20 h	59%
$[IrCl(cod)]_2$	CO	12 h	51%
$[IrCl(cod)]_2$	N_2	6 h	0%



R = 4-ClPh
71% yield, 74% ee

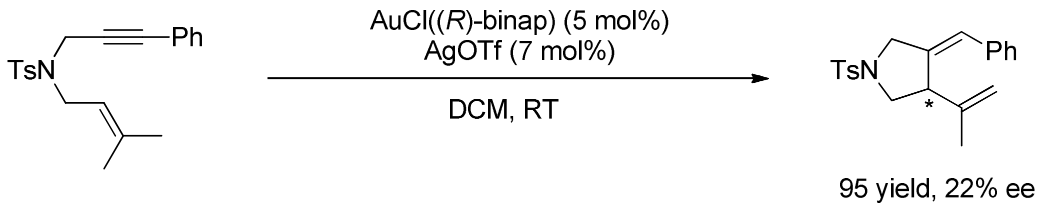
Chatani, N.; Inoue, H.; Morimoto, T.; Muto, T.; Murai, S., *J. Org. Chem.* **2001,** *66* (12), 4433-4436.
Shibata, T.; Kobayashi, Y.; Maekawa, S.; Toshida, N.; Takagi, K., *Tetrahedron* **2005,** *61* (38), 9018-9024.

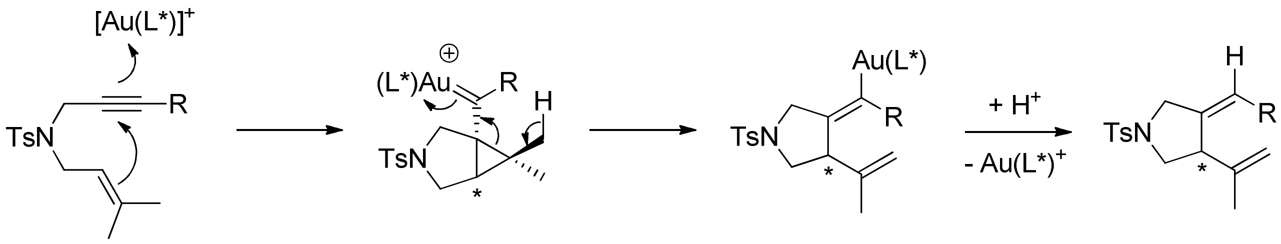
Ir-Catalysed



Shibata, T.; Kobayashi, Y.; Maekawa, S.; Toshida, N.; Takagi, K., *Tetrahedron* **2005,** *61* (38), 9018-9024.

Au-Catalysed





Lee, S. I.; Kim, S. M.; Kim, S. Y.; Chung, Y. K., *Synlett* **2006**, (14), 2256,2260.

Overview

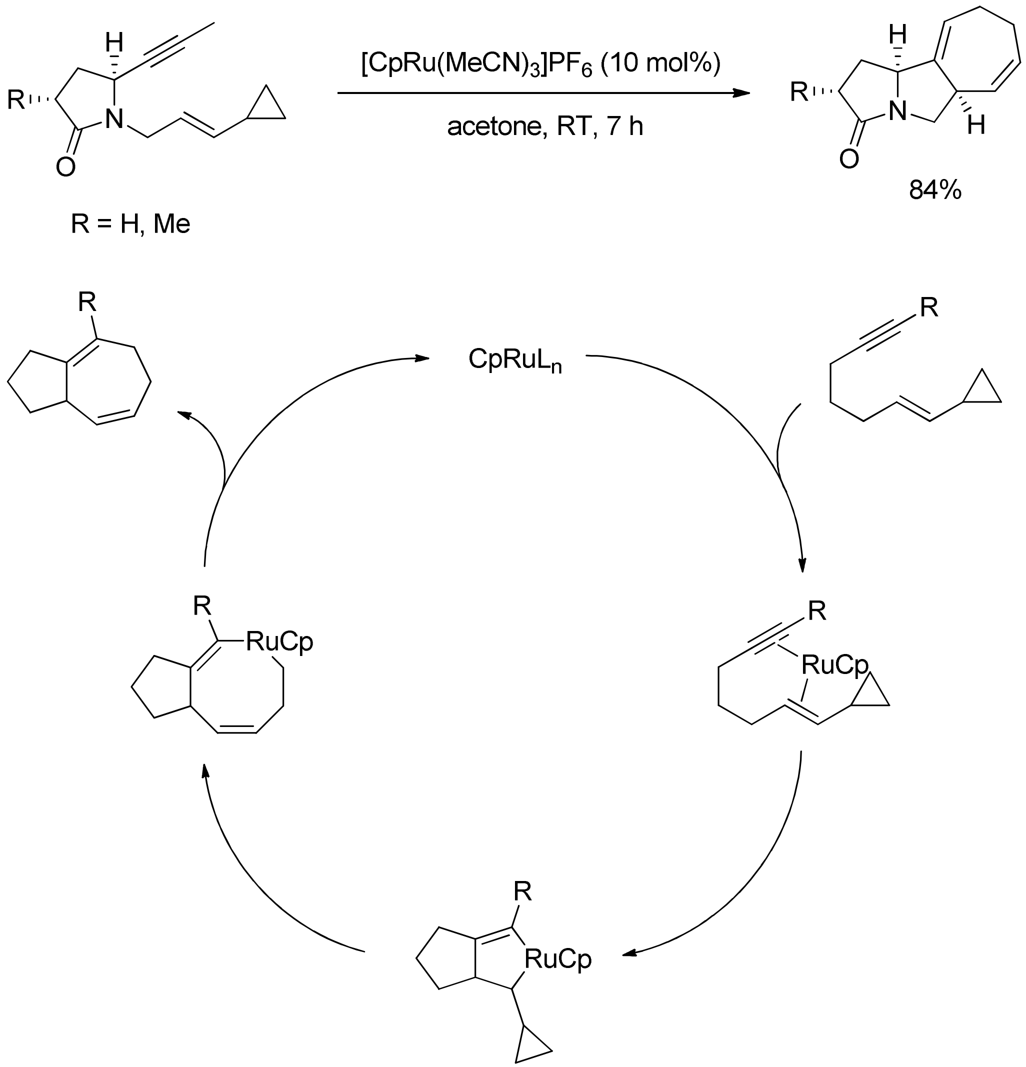
Cycloisomerisation of Enynes:

Pd, Ru, Rh, Ir, Pt, Au, Hg, Ti, Cr, Fe, Co, Ni, Cu, Ag, Ga, In

1) Enyne Rearrangements

2) Enyne Tandem Reactions

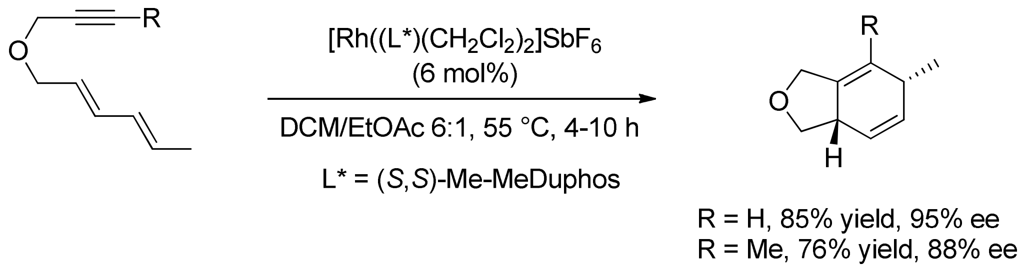
Ru-Catalysed (substrate control)



Trost, B. M.; Toste, F. D.; Shen, H., *J. Am. Chem. Soc.* **2000,** *122* (10), 2379-2380.
Trost, B. M.; Shen, H. C., *Org. Lett.* **2000,** *2* (16), 2523-2525.
Trost, B. M.; Shen, H. C., *Angew. Chem. Int. Ed.* **2001,** *40* (12), 2313-2316.

Rh-Catalysed

Formal [4+2] cycloaddition

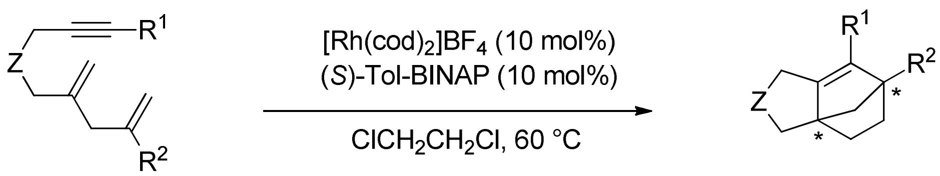


Gilbertson, S. R.; Hoge, G. S.; Genov, D. G., *J. Org. Chem.* **1998,** *63* (26), 10077-10080.

Rh-Catalysed

Formal [2+2+2] cycloaddition

a) 1,4-Diene-ynes



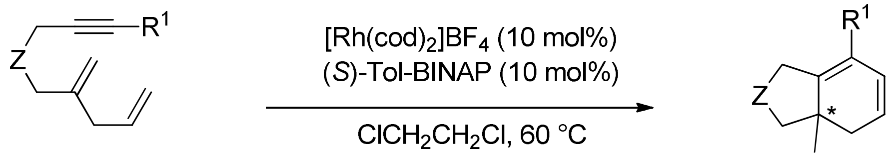
Z	R^1	R^2	Time/h	Yield	ee
NTs	$BnOCH_2$	Me	48	83%	88%
NTs	H	Me	6	83%	93%
NTs	H	Ph	6	72%	91%
$C(CO_2Bn)_2$	H	Me	48	76%	93%

Shibata, T.; Tahara, Y.-k., *J. Am. Chem. Soc.* 2006, *128* (36), 11766-11767.

Rh-Catalysed

Formal [2+2+2] cycloaddition

a) 1,4-Diene-ynes



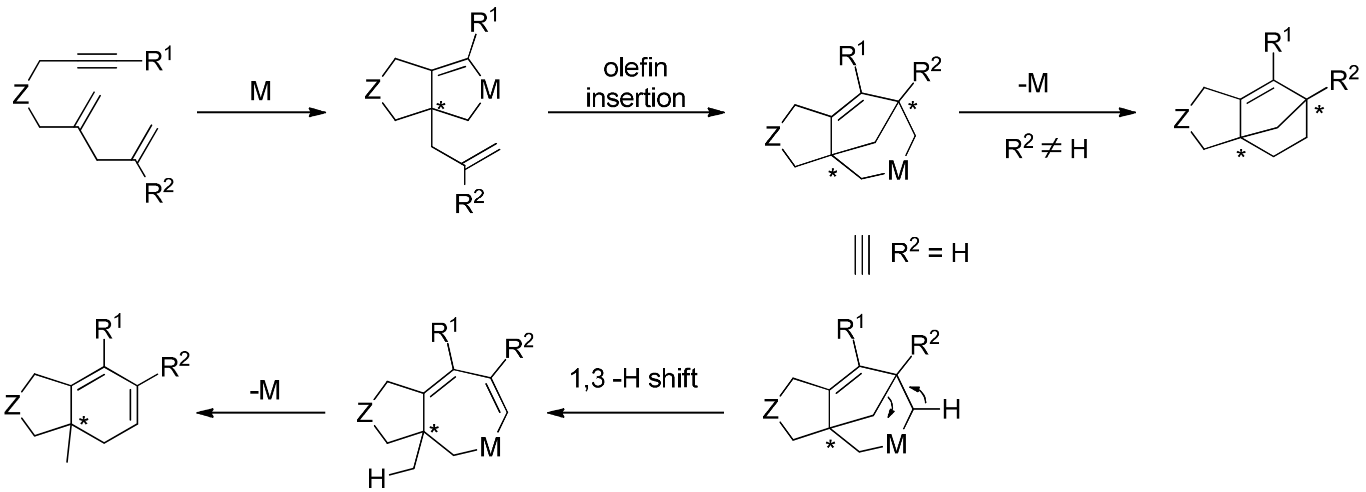
Z	R^1	Time/h	Yield	ee
NTs	$BnOCH_2$	12	91%	99%
NTs	H	12	79%	99%
$C(CO_2Bn)_2$	H	6	80%	90%
O	Ph	48	55%	92%
O	$Ph(CH_2)_3$	6	64%	94%

Shibata, T.; Tahara, Y.-k., *J. Am. Chem. Soc.* 2006, *128* (36), 11766-11767.

Rh-Catalysed

Formal [2+2+2] cycloaddition

a) 1,4-Diene-ynes

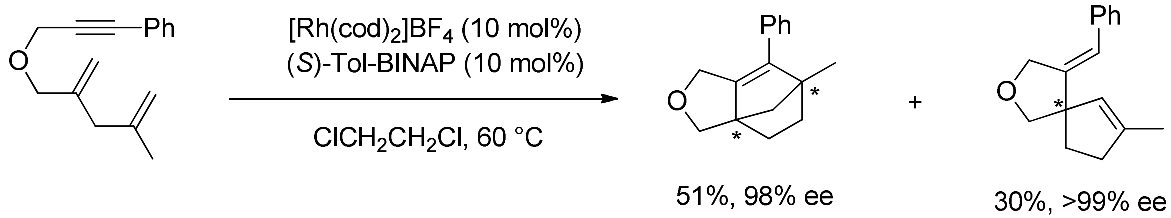


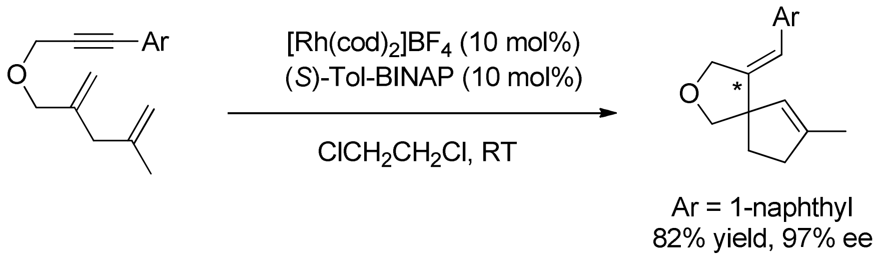
Shibata, T.; Tahara, Y.-k., *J. Am. Chem. Soc.* **2006**, *128* (36), 11766-11767.

Rh-Catalysed

Formal [2+2+2] cycloaddition

a) 1,4-Diene-ynes



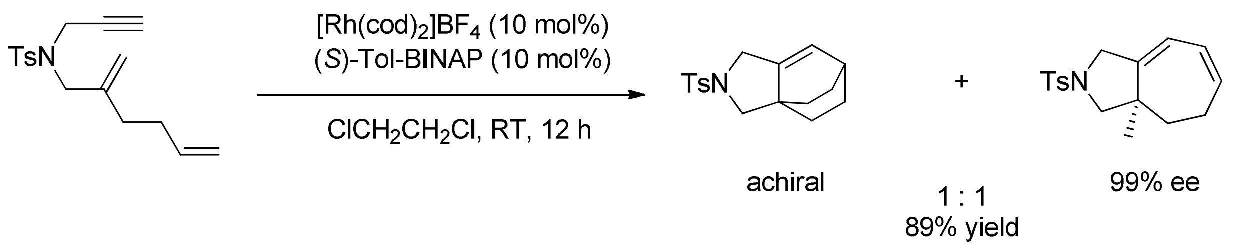


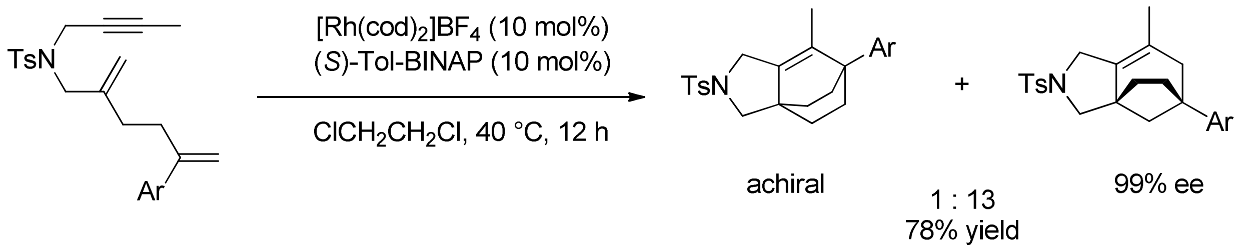
Shibata, T.; Tahara, Y.-k.; Tamura, K.; Endo, K., *J. Am. Chem. Soc.* **2008**, *130* (11), 3451-3457.

Rh-Catalysed

Formal [2+2+2] cycloaddition

a) 1,5-Diene-ynes



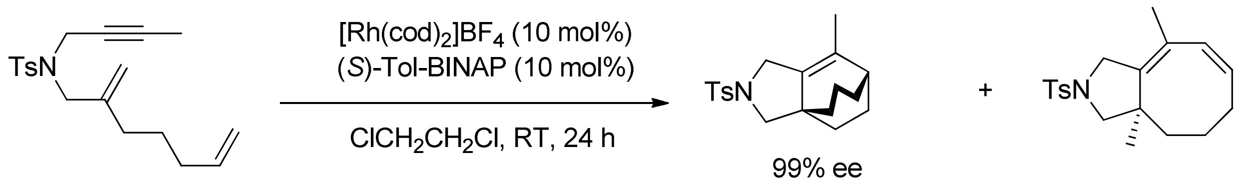


Shibata, T.; Tahara, Y.-k.; Tamura, K.; Endo, K., *J. Am. Chem. Soc.* **2008,** *130* (11), 3451-3457.

Rh-Catalysed

Formal [2+2+2] cycloaddition

a) 1,6-Diene-ynes

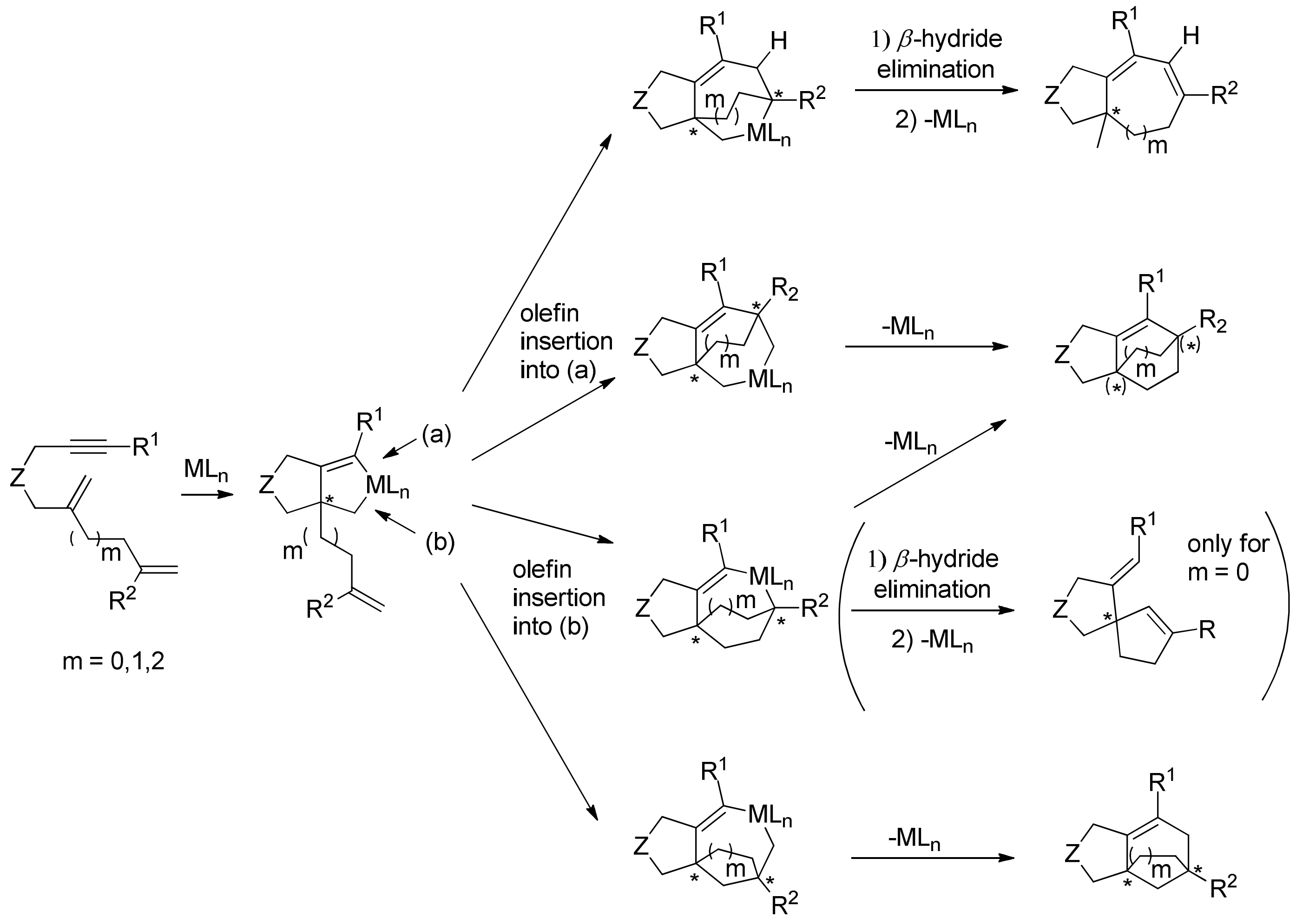


Ar = 2-PhC_6H_4
13 : 1
78% yield

Shibata, T.; Tahara, Y.-k.; Tamura, K.; Endo, K., *J. Am. Chem. Soc.* **2008**, *130* (11), 3451-3457.

Rh-Catalysed

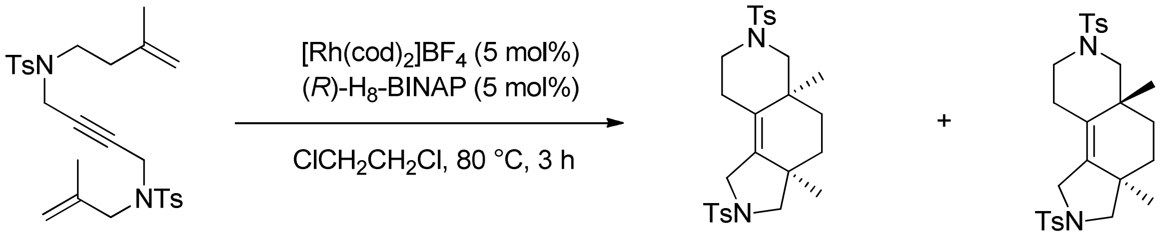
Formal [2+2+2] cycloaddition



Shibata, T.; Tahara, Y.-k.; Tamura, K.; Endo, K., *J. Am. Chem. Soc.* **2008,** *130* (11), 3451-3457.

Rh-Catalysed

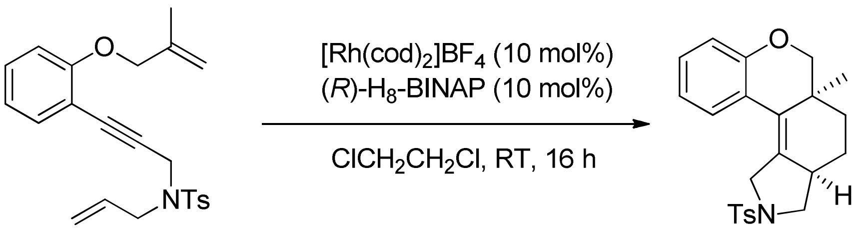
Formal [2+2+2] cycloaddition



4% ee

99% ee

99% yield
1 : 2.4

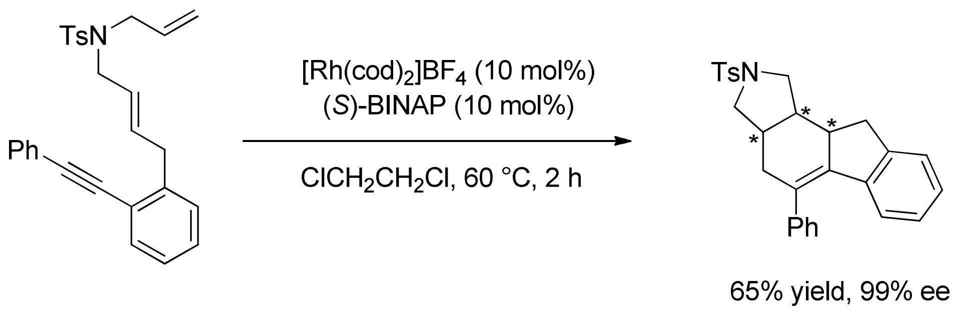


89% yield, 98% ee

Tanaka, K.; Nishida, G.; Sagae, H.; Hirano, M., *Synlett* **2007**, (09), 1426,1430.
Sagae, H.; Noguchi, K.; Hirano, M.; Tanaka, K., *Chem. Commun.* **2008**, (32), 3804-3806.

Rh-Catalysed

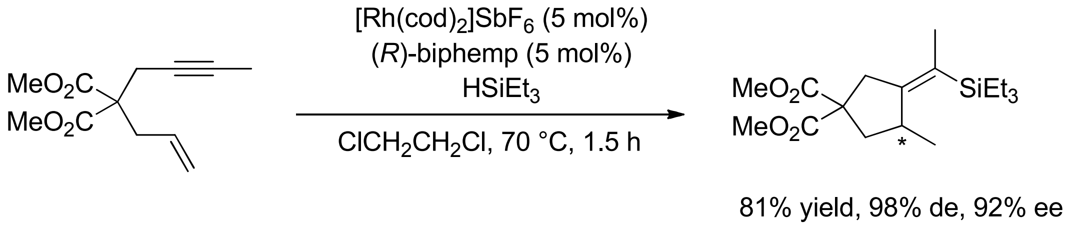
Formal [2+2+2] cycloaddition

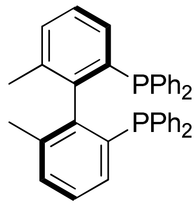


Shibata, T.; Otomo, M.; Endo, K., *Synlett* **2010**, (8), 1235,1238.

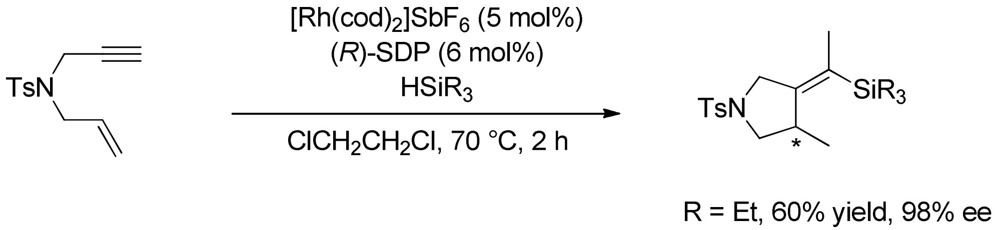
Rh-Catalysed

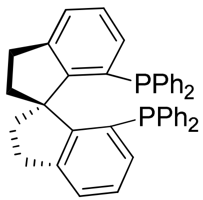
Hydrosilylation/Cyclisation





(*R*)-biphemp



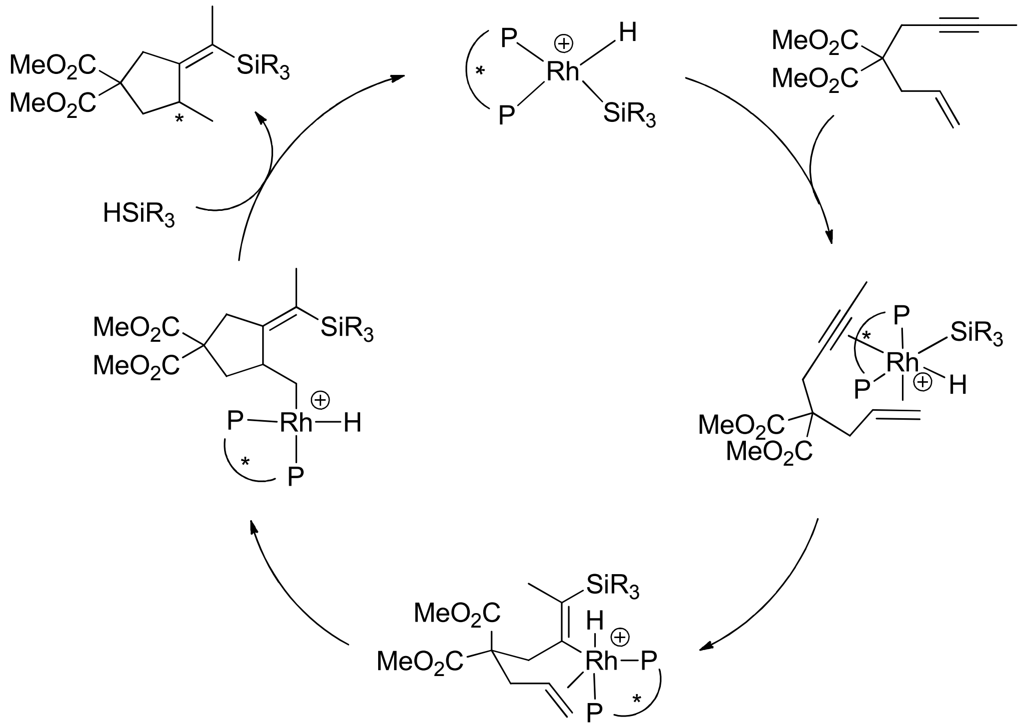


(*R*)-SDP

Chakrapani, H.; Liu, C.; Widenhoefer, R. A., *Org. Lett.* **2003**, *5* (2), 157-159.
Fan, B.-M.; Xie, J.-H.; Li, S.; Wang, L.-X.; Zhou, Q.-L., *Angew. Chem. Int. Ed.* **2007**, *46* (8), 1275-1277.

Rh-Catalysed

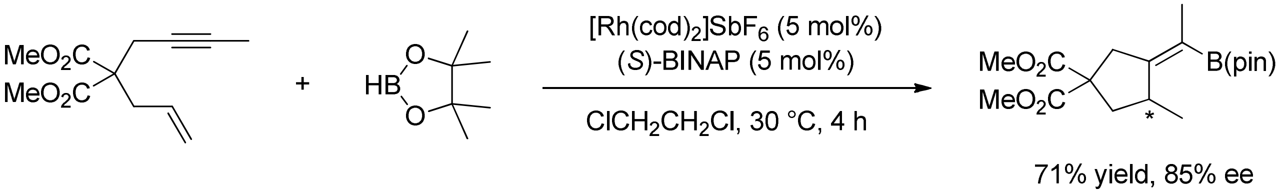
Hydrosilylation/Cyclisation

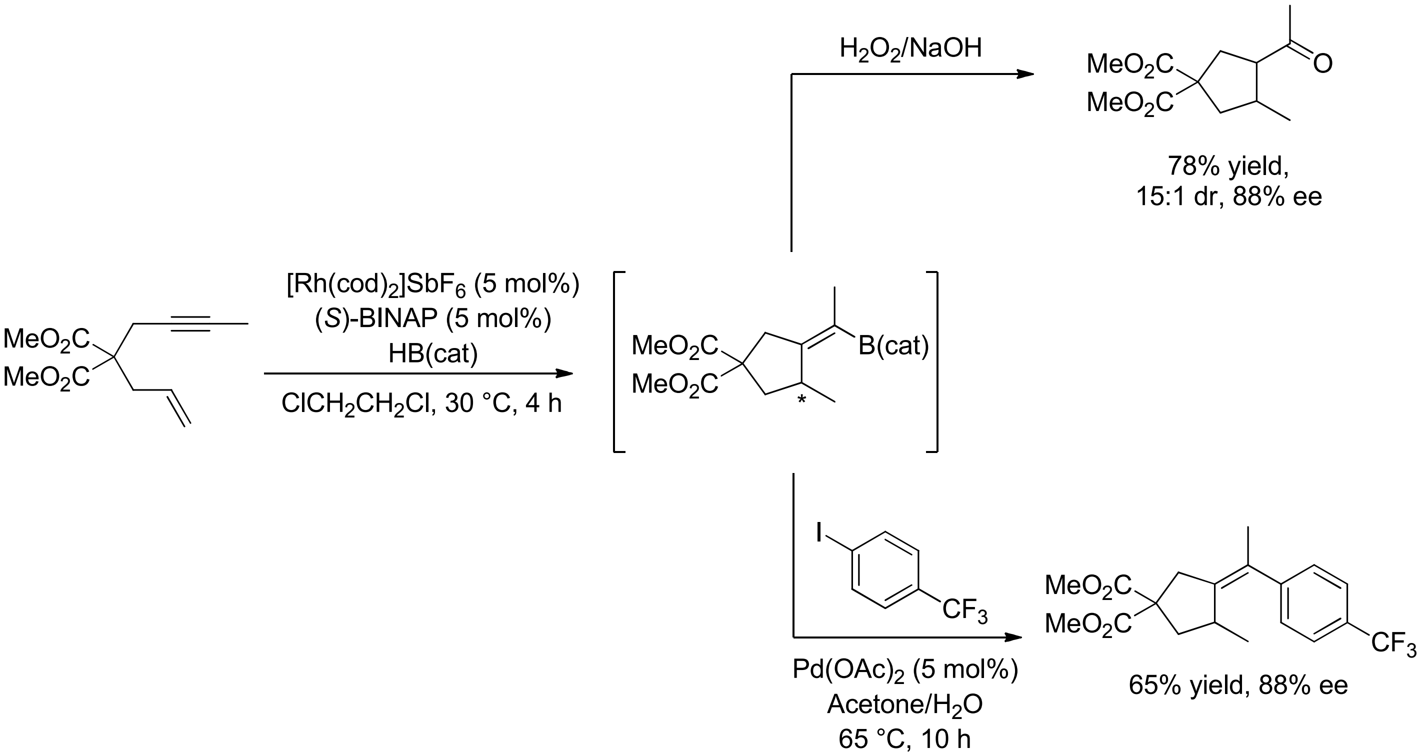


Chakrapani, H.; Liu, C.; Widenhoefer, R. A., *Org. Lett.* **2003,** *5* (2), 157-159.
Fan, B.-M.; Xie, J.-H.; Li, S.; Wang, L.-X.; Zhou, Q.-L., *Angew. Chem. Int. Ed.* **2007**, *46* (8), 1275-1277.

Rh-Catalysed

Hydroboration/Cyclisation

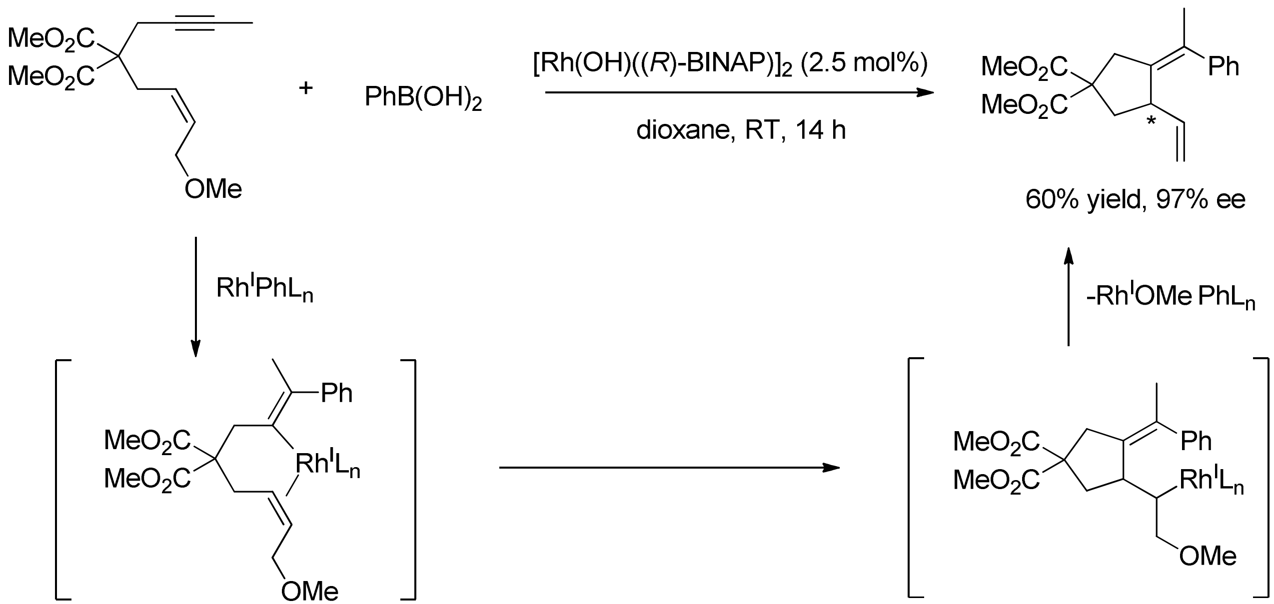




Kinder, R. E.; Widenhoefer, R. A., *Org. Lett.* **2006**, *8* (10), 1967-1969.

Rh-Catalysed

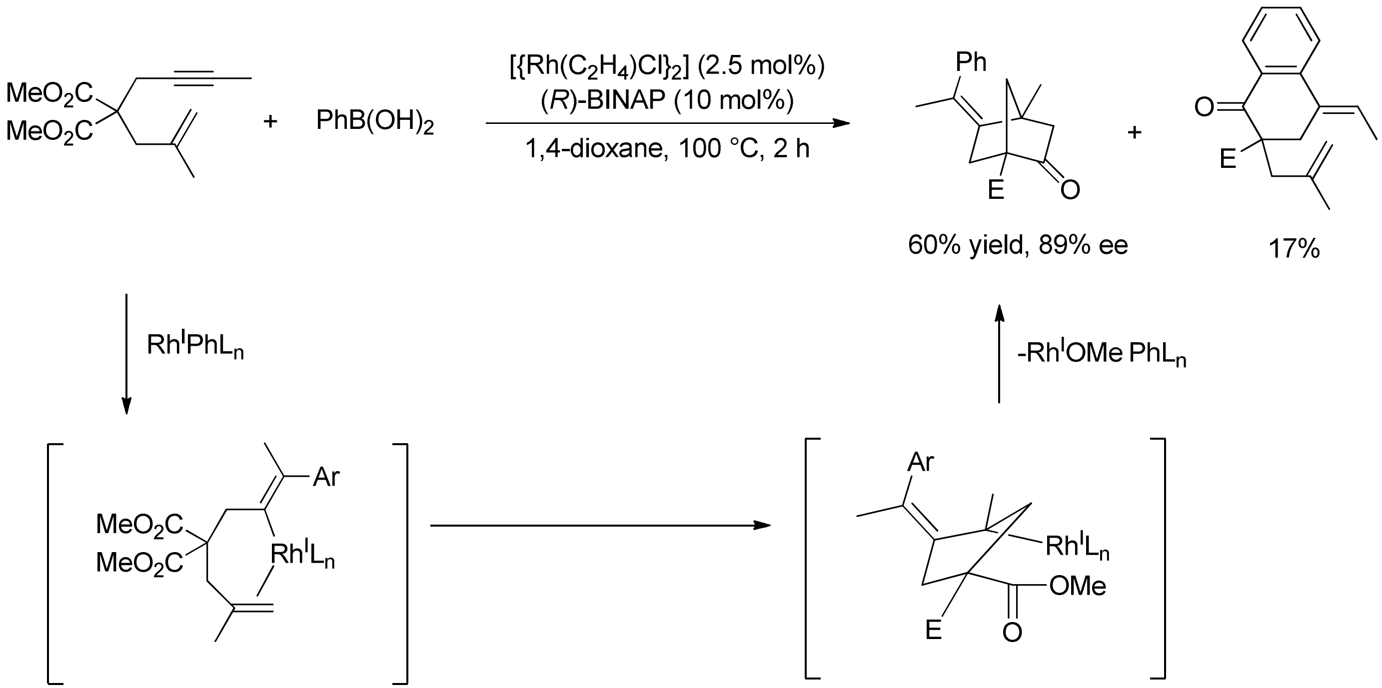
Tandem addition of boronic acids



Miura, T.; Shimada, M.; Murakami, M., *J. Am. Chem. Soc.* **2005**, *127* (4), 1094-1095.

Rh-Catalysed

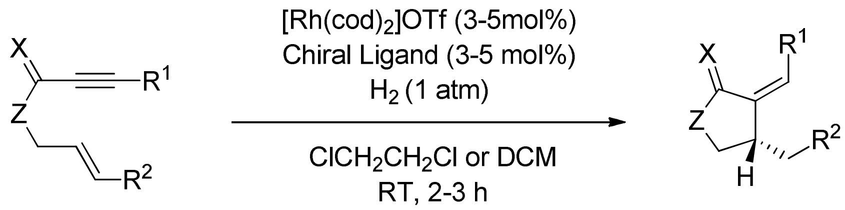
Tandem addition of boronic acids

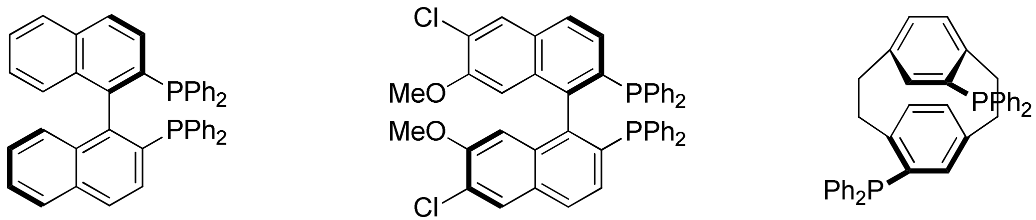


Miura, T.; Sasaki, T.; Nakazawa, H.; Murakami, M., *J. Am. Chem. Soc.* **2005,** *127* (5), 1390-1391.

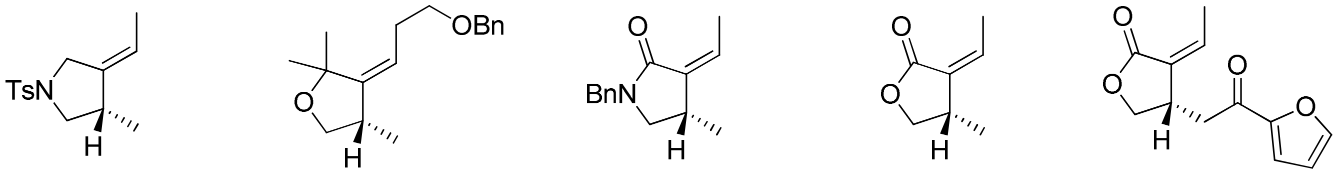
Rh-Catalysed

Reductive cyclisation





(*R*)-BINAP (*R*)-Cl, MeO-BINAP (*R*)-phanephos

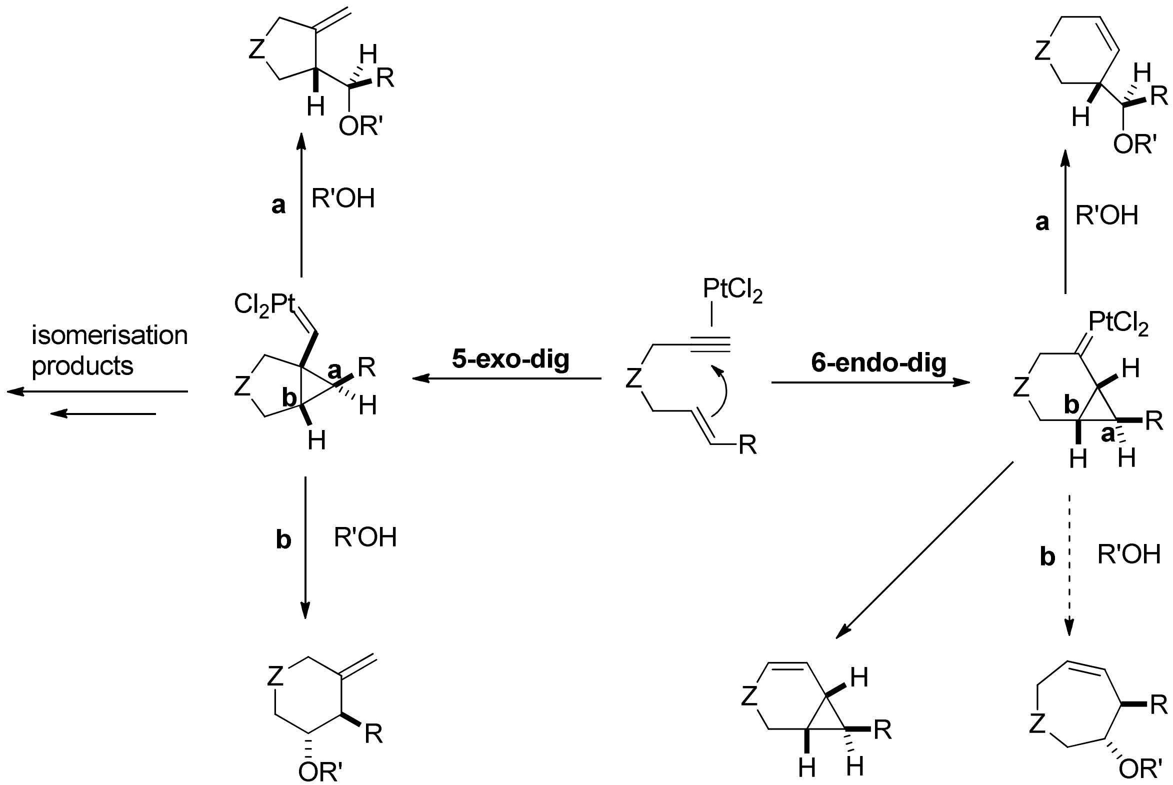


(*R*)-BINAP	(*R*)-Cl,MeO-BINAP	(*R*)-phanephos	(*R*)-phanephos	(*R*)-BINAP
69% yield, 94% ee	82% yield, 98% ee	73% yield, 91% ee	73% yield, 94% ee	72% yield, 96% ee

Jang, H.-Y.; Krische, M. J., *J. Am. Chem. Soc.* **2004,** *126* (25), 7875-7880.
Jang, H.-Y.; Hughes, F. W.; Gong, H.; Zhang, J.; Brodbelt, J. S.; Krische, M. J., *J. Am. Chem. Soc.* **2005,** *127* (17), 6174-6175.

Pt-Catalysed

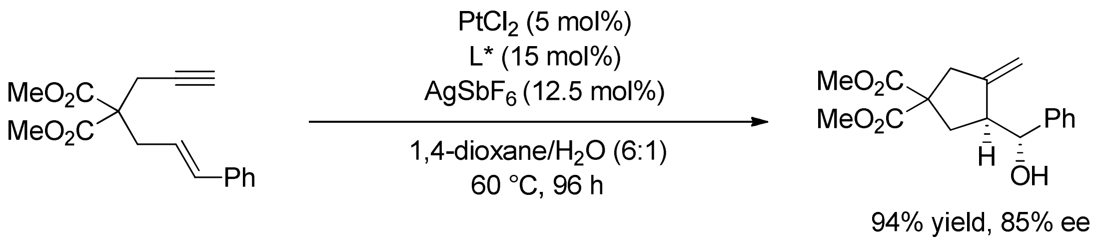
Trapping platinumcarbene intermediates

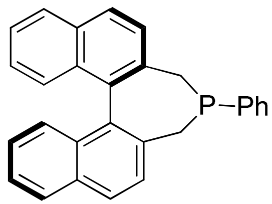


Méndez, M.; Muñoz, M. P.; Echavarren, A. M., *J. Am. Chem. Soc.* **2000**, *122* (46), 11549-11550.
Nevado, C.; Cárdenas, D. J.; Echavarren, A. M., *Chem. Eur. J.* **2003**, *9* (11), 2627-2635.

Pt-Catalysed

Trapping platinumcarbene intermediates



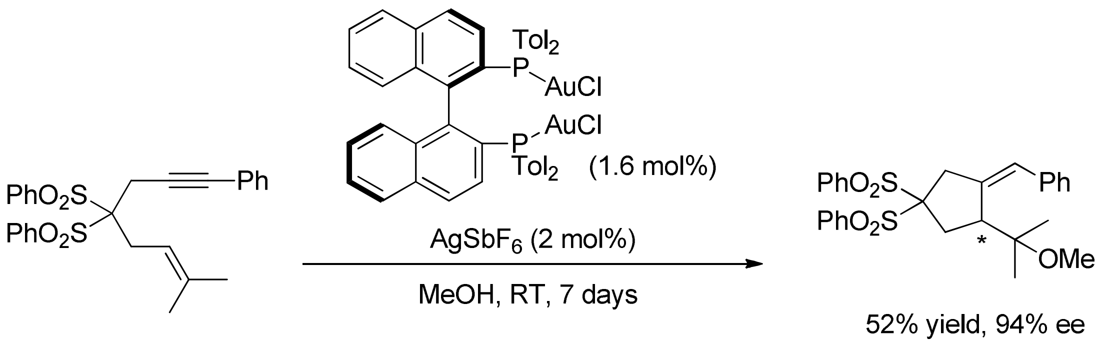


L* = (*R*)-Ph-binepine

Charruault, L.; Michelet, V.; Taras, R.; Gladiali, S.; Genet, J.-P., *Chem. Commun.* **2004**, (7), 850-851.

Au-Catalysed

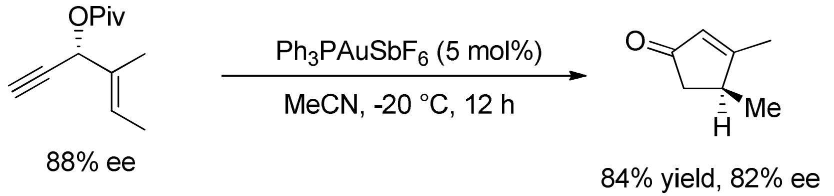
Trapping goldcarbene intermediates

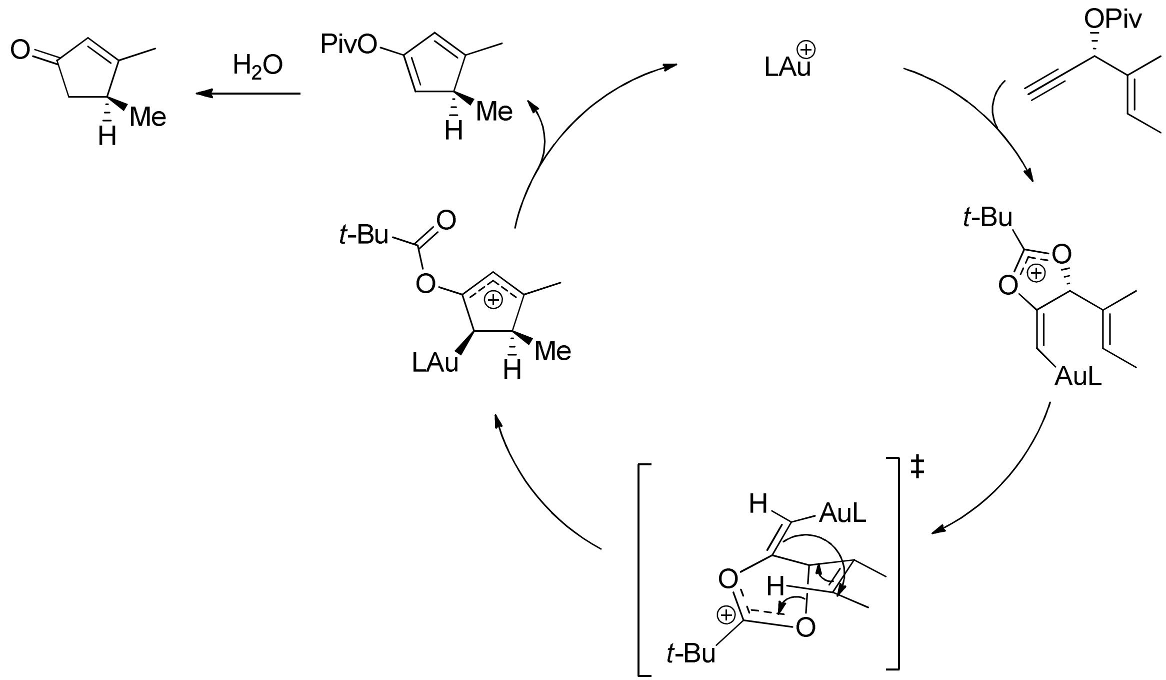


Muñoz, M. P.; Adrio, J.; Carretero, J. C.; Echavarren, A. M., *Organometallics* **2005,** *24* (6), 1293-1300.

Au-Catalysed (substrate control)

Enantioselective Cyclopentenone Synthesis

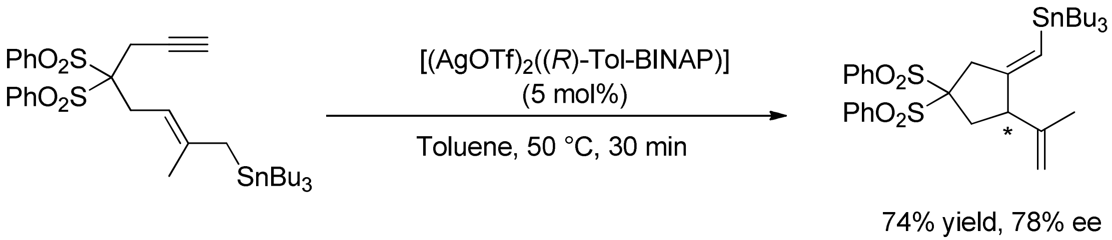


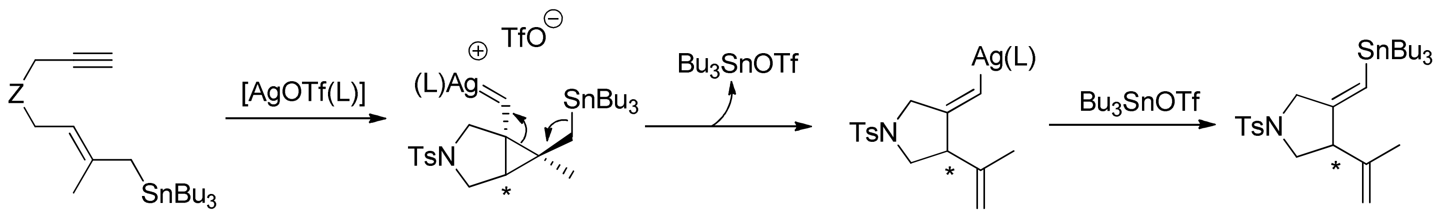


Shi, X.; Gorin, D. J.; Toste, F. D., *J. Am. Chem. Soc.* **2005,** *127* (16), 5802-5803.
Faza, O. N.; López, C. S.; Álvarez, R.; de Lera, A. R., *J. Am. Chem. Soc.* **2006,** *128* (7), 2434-2437.

Ag-Catalysed

Intramolecular Carbostannylation





Porcel, S.; Echavarren, A. M., *Angew. Chem. Int. Ed.* **2007**, *46* (15), 2672-2676.

CONCLUSIONS

- There is great potential for the use of chiral ligands to affect asymmetric induction in cycloisomerisation and tandem addition/cycloisomerisation reactions.
- In particular, chiral diphosphine ligands have in the past proved effective.
- However, the substrate scope and general applicability of most current asymmetric catalysis systems remains low.
- There is therefore still great need to develop new protocols in the area of asymmetric cycloisomerisation reactions.