Gold(I) Catalyzed Enantioselective Reactions

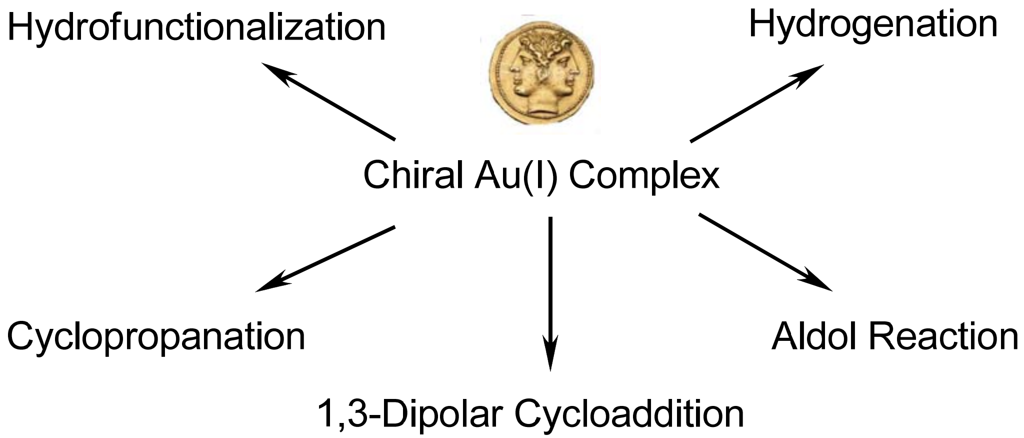
Li HUANG
Michigan State University

November 28, 2007

Outline

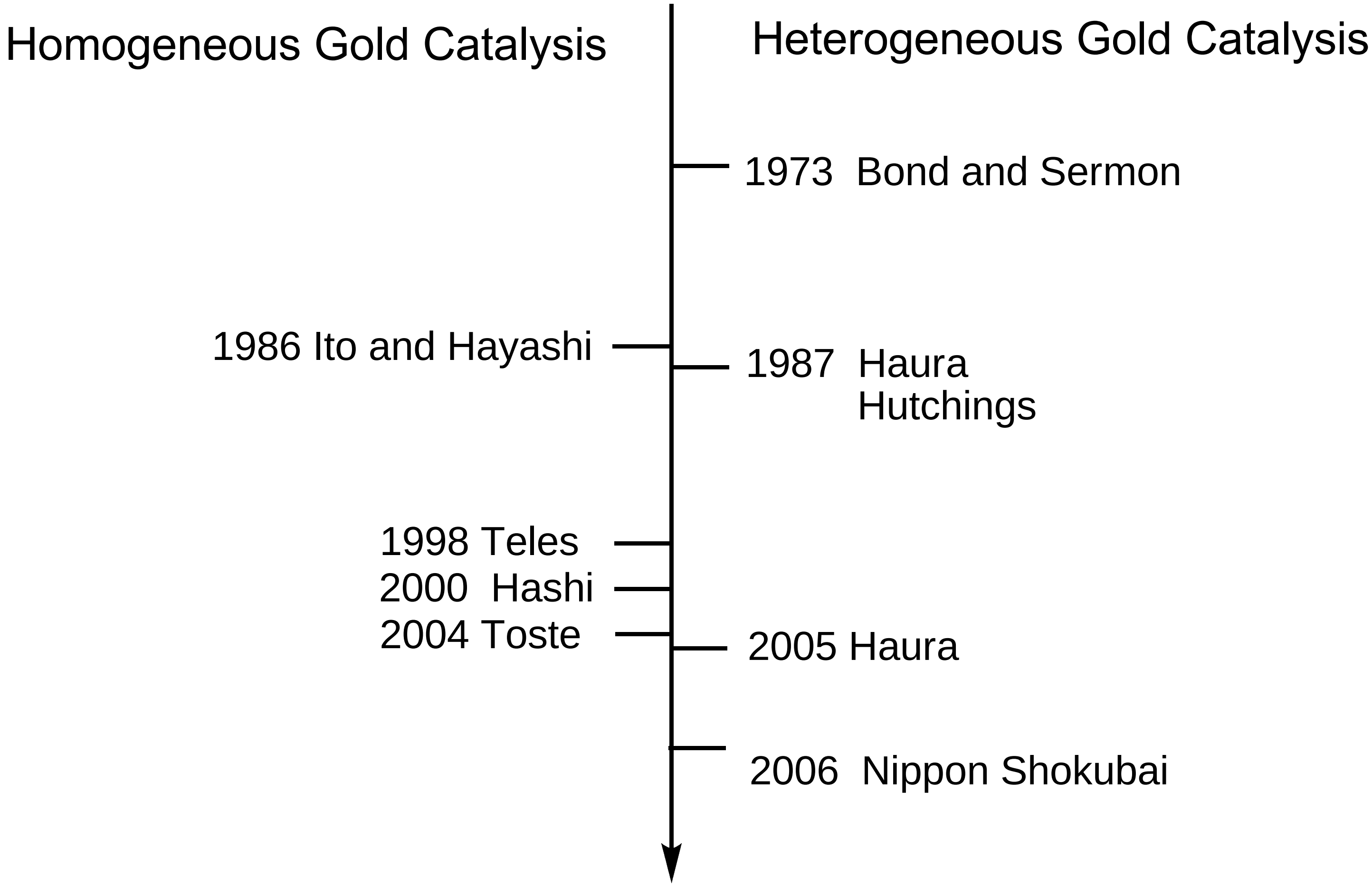
- Introduction

- Enantioselective Reactions



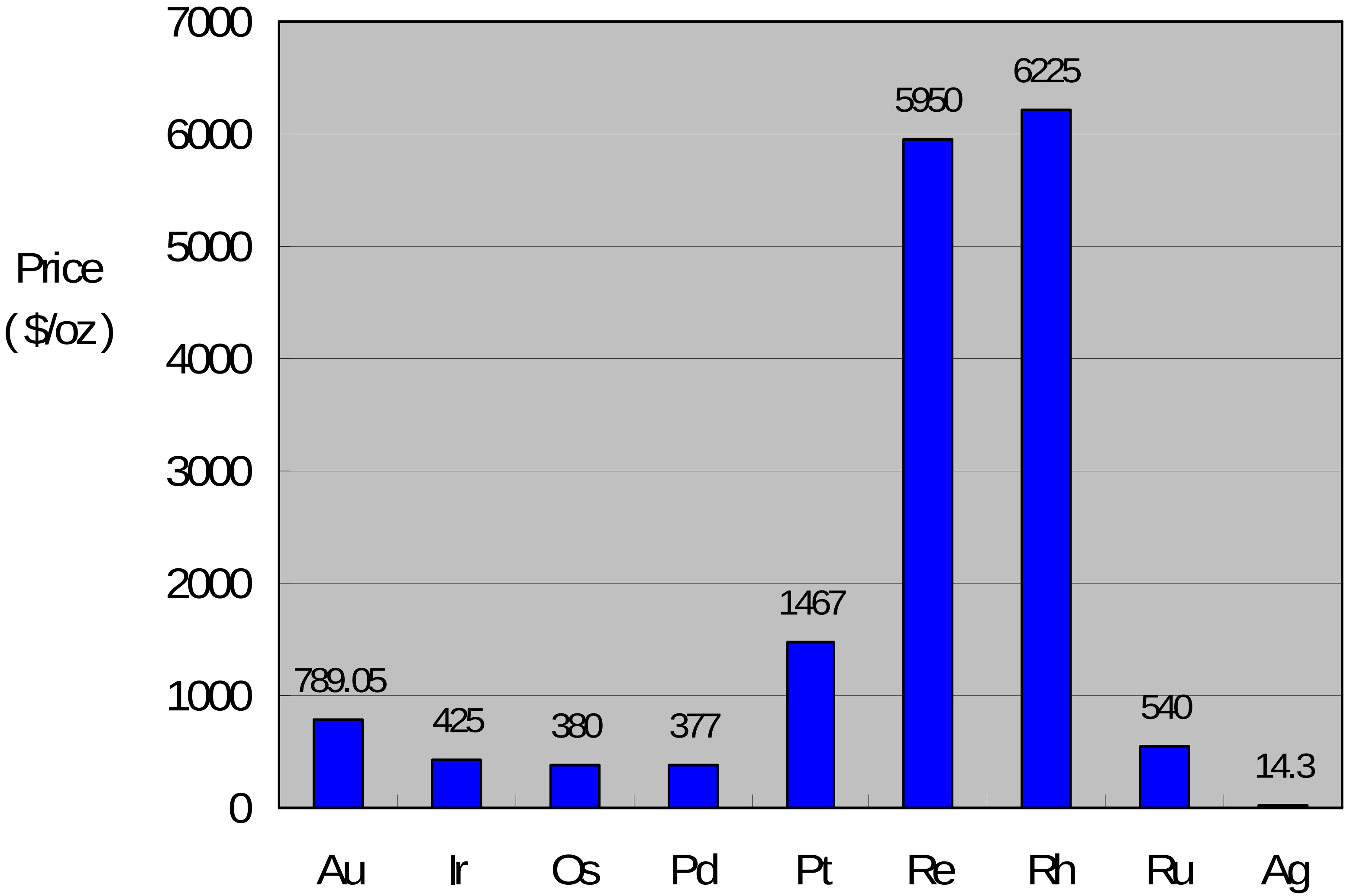
- Conclusions

History of Gold Catalysis



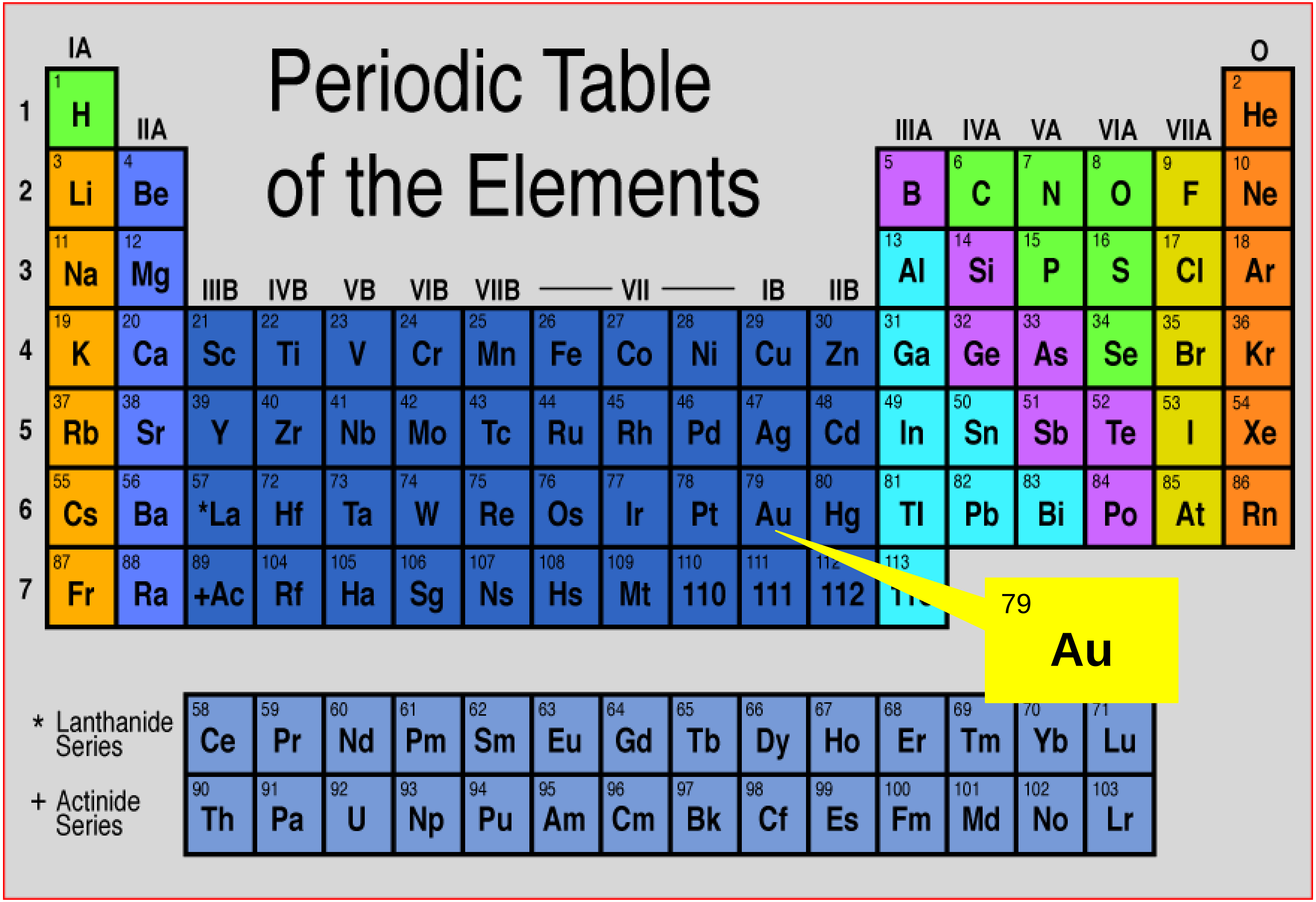
Hashmi, A.S. K.; Hutchings, G. J. *Angew. Chem. Int. Ed.* **2006**, *45*, 7896.
Burks, R. *Chem. Eng. News.* **2007**, *85*, 87.

Comparison of Metal Prices



http://www.taxfreegold.co.uk/preciousmetalpricesusdollars.html

Au in Periodic Table

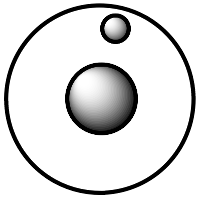


Relativistic Effects of Au

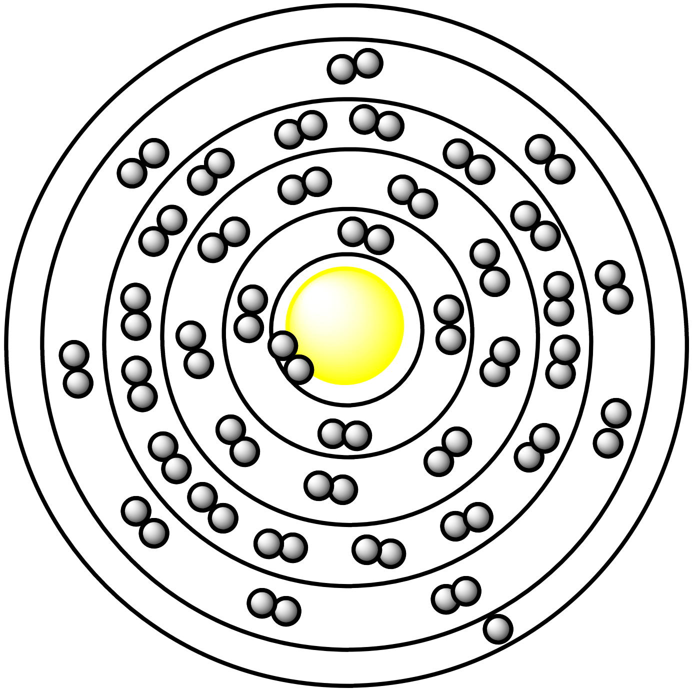
Relativistic effects
Any phenomenon resulting from the need to consider velocity as significant relative to the speed of light

Relativistic contraction of *s, p* orbitals
Relativistic expansion of *d, f* orbitals

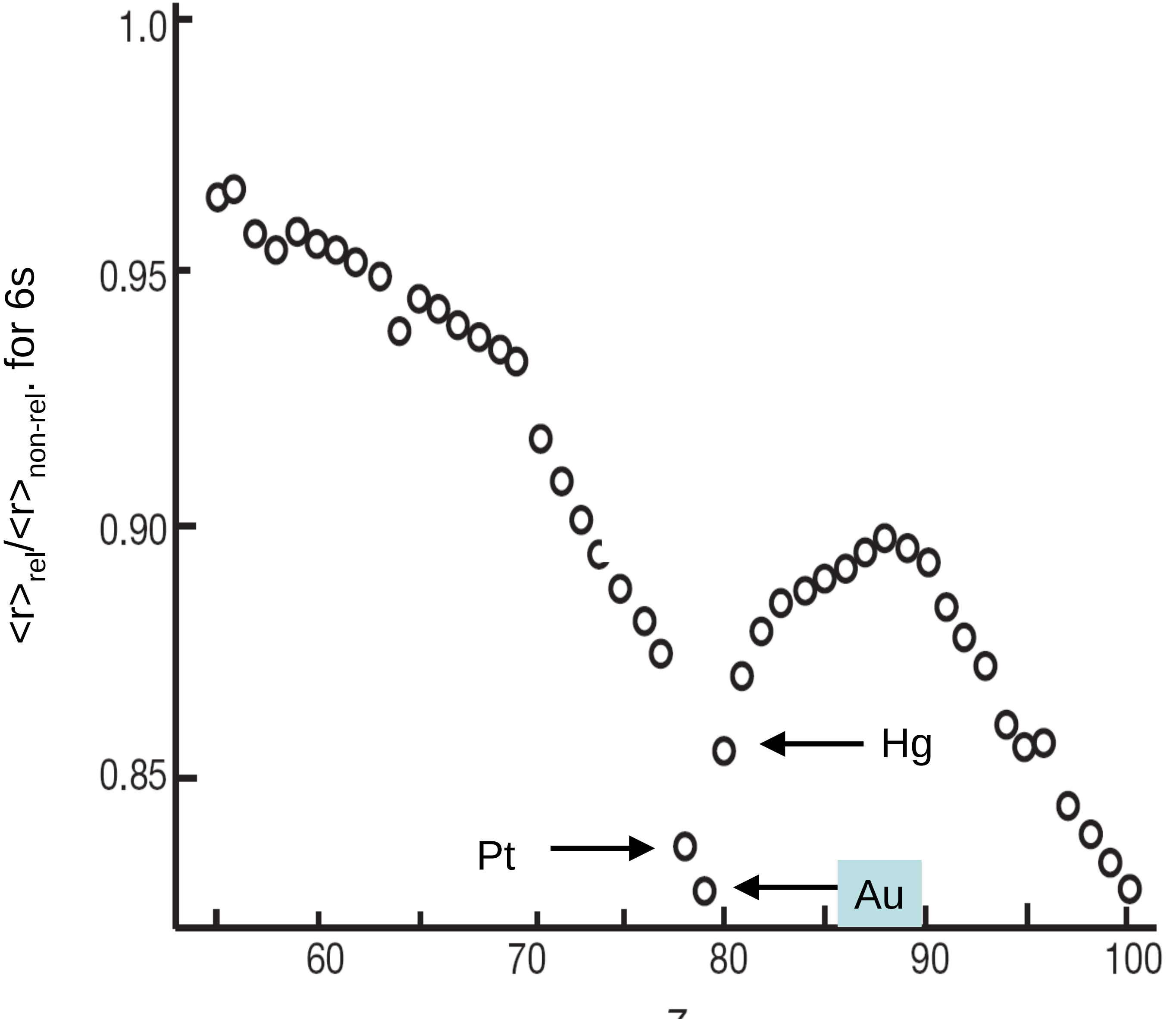
H



Au



Relativistic Effects of Au



Gorin, D. J.; Toste, F. D. *Nature*, **2007**, *446*, 395.

Consequences of Relativistic Effects

Relativistic effects

Contracted 6s orbitals

Strengthened bonds of Au-Ligands

Low LUMO

Superior Lewis Acids of Au(I) Species

Expanded 5d orbitals

Decreased electron/electron repulsion in the diffuse 5d orbital

No oxidative addition between Au(III) and Au(I)

Tolerant of oxygen

Lewis Acidity of Au(I) Species

$$Au^{\oplus} + L \longrightarrow AuL^{\oplus}$$

$$L = H_2S < CH_3CN \sim C_2H_4 \sim NH_3 \sim CH_3NC < CH_3SCH_3 < PH_3$$

R PAu(I)$^{\oplus}$

‘Soft’ Lewis Acid

Preferentially Activating π System

Gorin, D. J.; Toste, F. D. *Nature,* **2007**, *446*, 395.

Challenge in Gold(I) Catalyzed Enantioselective Reactions

Au(I) predominately adopts a linear, bicoordinate geometry.

⇓

The chiral components would be distant from the substrates.

⇓

It is hard to control the enantioselectivity.

Hamilton, G. L.; Kang, E. J.; Mba, M.; Toste, F. D. *Science,* **2007**, *317*, 496.

Methods to Generate Cationic Au Catalyst

1 $LAuCl + AgX \longrightarrow \boxed{LAuX} + AgCl$

Active species

2 $LAuCH_3 + HX \longrightarrow \boxed{LAuX} + CH_4$

Hamilton, G. L.; Kang, E. J.; Mba, M.; Toste, F. D. *Science.* **2007**, *317*, 496.

Enantioselective Reactions

Hydrofunctionalization

Hydrogenation

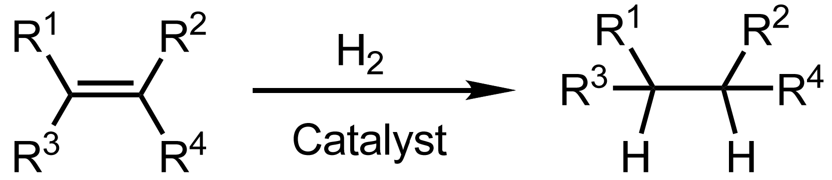
Chiral Au(I) Complex

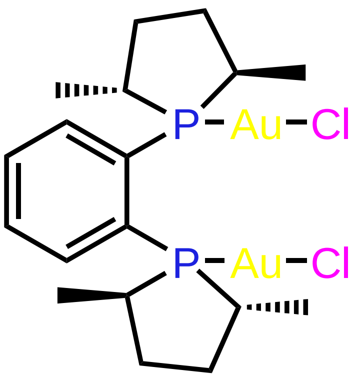
Cyclopropanation

Aldol Reaction

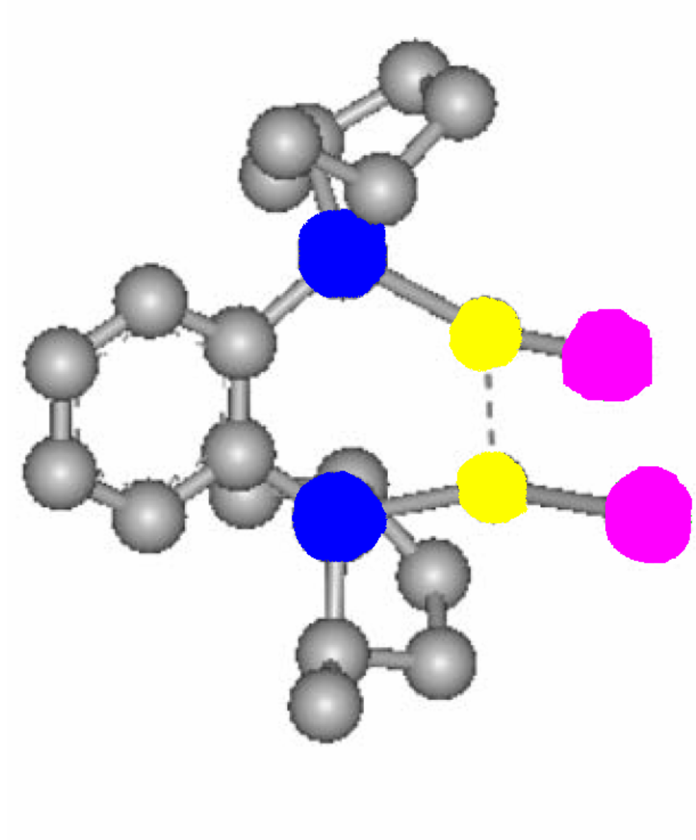
1,3-Dipolar Cycloaddition

Hydrogenation Reactions



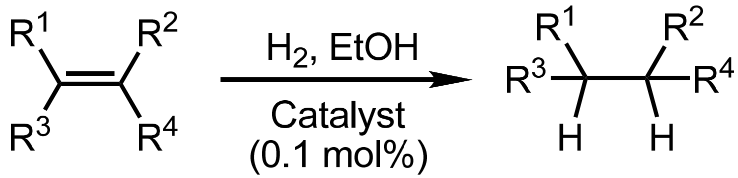


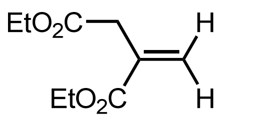
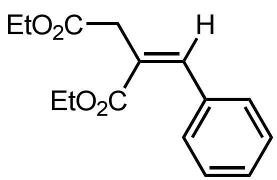
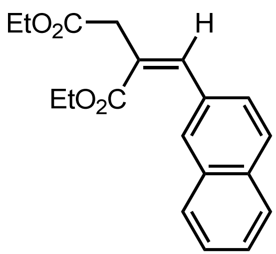
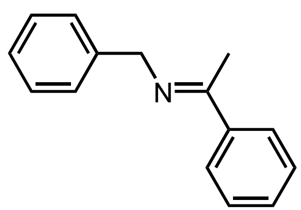
Catalyst

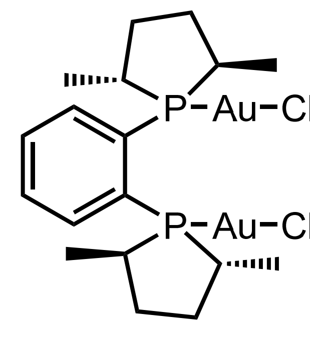


González-Arellano, C.; Corma, A.; Iglesias, M.; Sánchez, F. *Chem. Commun.* **2005**, 3451.

Hydrogenation Reactions



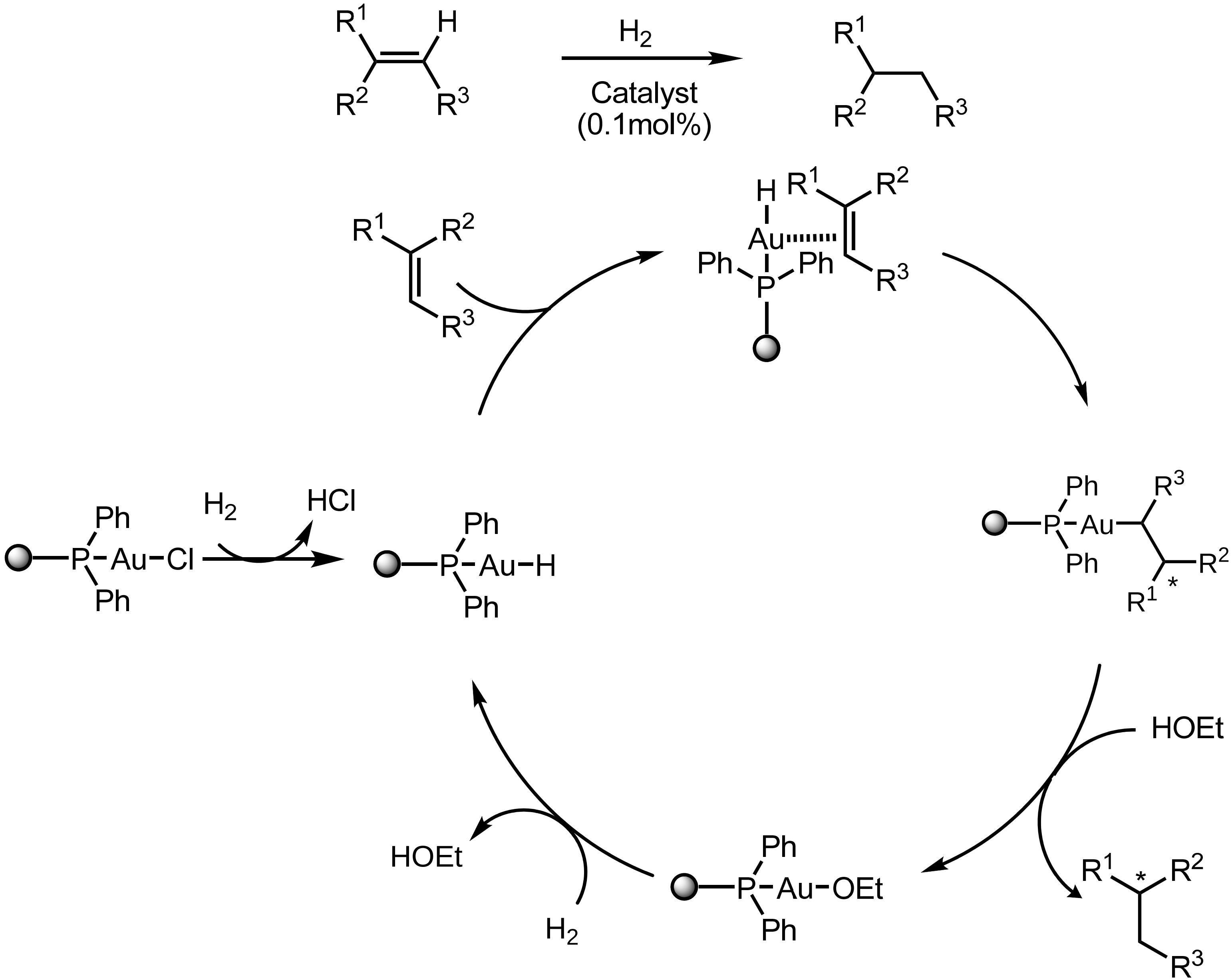
	Substrate	time (min)	*ee* (%)
1		20	20
2		50	80
3		150	95
4		~1920	75



Catalyst

González-Arellano, C.; Corma, A.; Iglesias, M.; Sánchez, F. *Chem. Commun.* **2005**, 3451.

Proposed Mechanism for Hydrogenation



González-Arellano, C.; Corma, A.; Iglesias, M.; Sánchez, F. *Chem. Commun.* **2005**, 3451.

Enantioselective Reactions

Hydrofunctionalization

Hydrogenation

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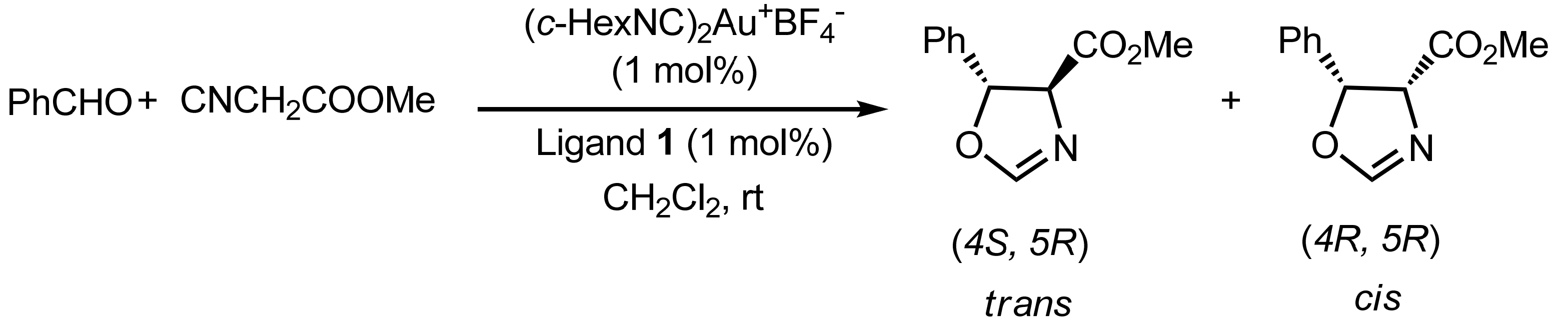
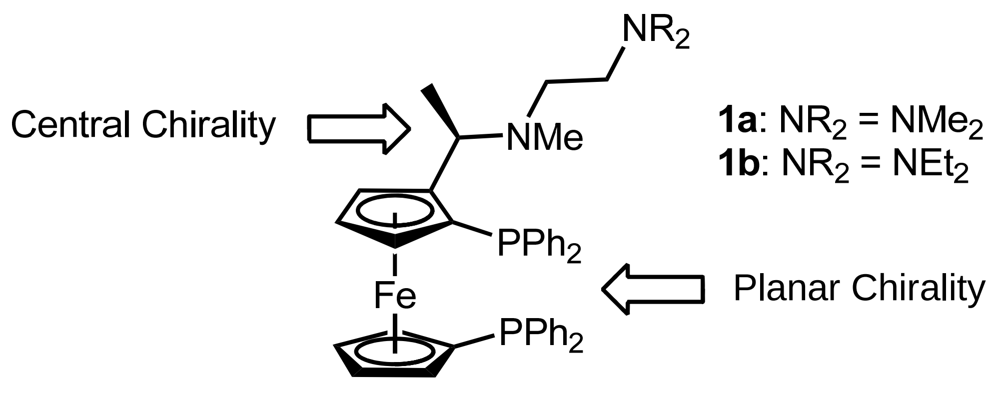
Cyclopropanation

1,3-Dipolar Cycloaddition

Aldol Reaction

Catalytic Asymmetric Aldol Reaction

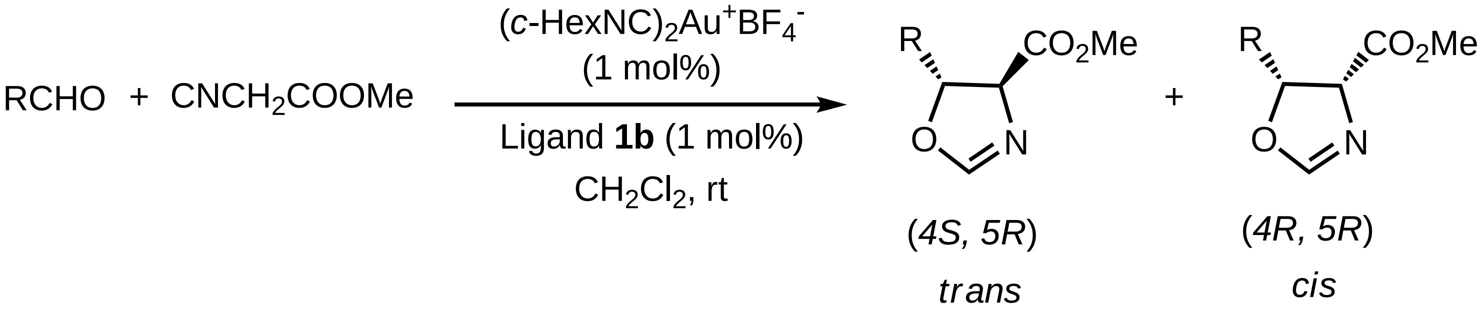


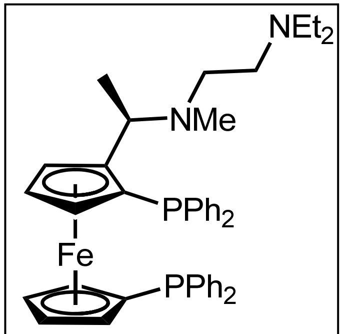


(*R*)-(*S*)-Ligand **1**

Ito, Y.; Sawamura, M.; Hayashi, T. *J. Am. Chem. Soc.* **1986**, *108*, 6405.

Aldol Reaction of Different Aldehydes



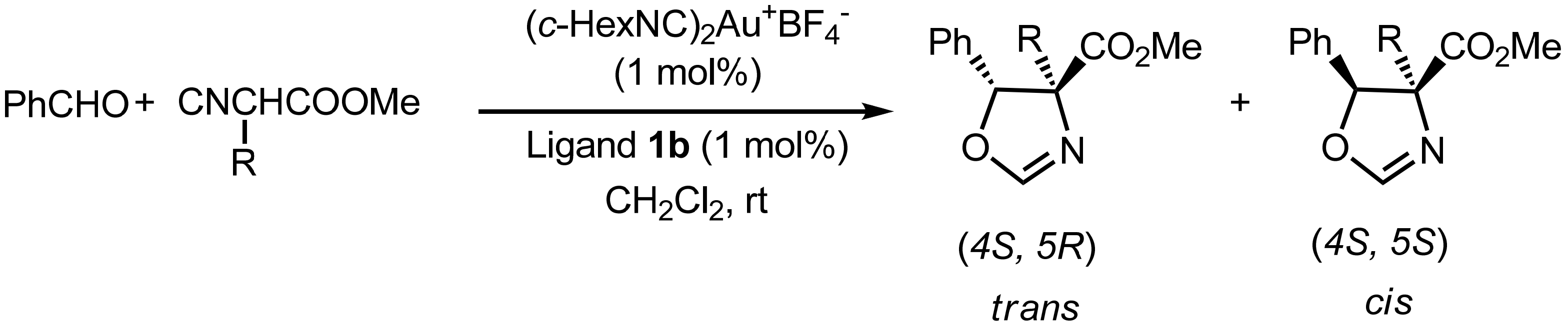


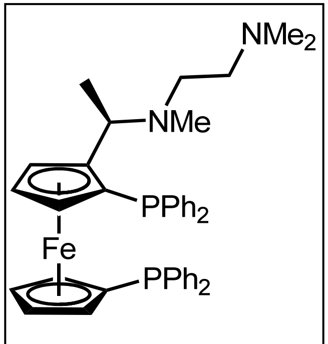
Ligand **1b**

Aldehyde	Yield (%)	*trans:cis*	ee (*trans*, %)	ee (*cis*, %)
PhCHO	98	89:11	96	49
MeCHO	100	84:16	72	44
i-PrCHO	99	98:2	92	—
c-HexCHO	95	97:3	90	—
t-BuCHO	100	100:0	97	—
(*E*)-*n*-PrCH=CHCHO	83	81:19	84	52

Ito, Y.; Sawamura, M.; Hayashi, T. *J. Am. Chem. Soc.* **1986**, *108*, 6405.

Aldol Reaction of Aldehydes with α- isocyanocarboxylates



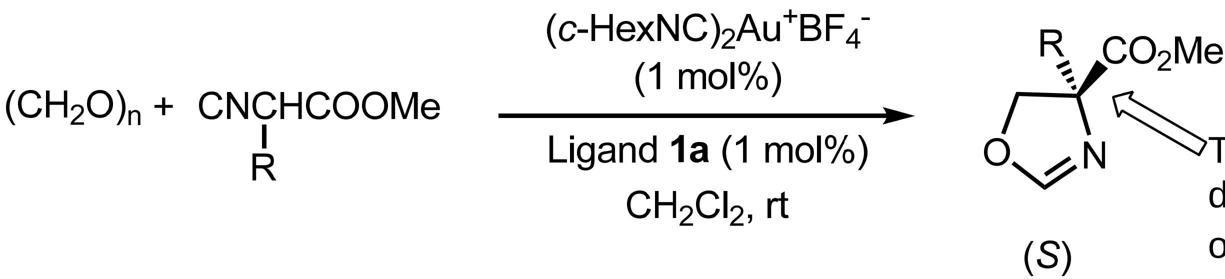


Ligand **1a**

R	Yield (%)	*trans*:*cis*	*ee* (*trans*, %)	*ee* (*cis*, %)
H	91	90:10	91	4
Me	95	82:18	92	44
i-Pr	95	50:50	88	48

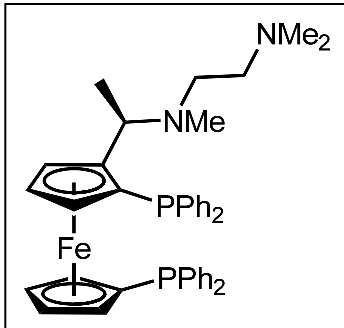
Ito, Y.; Sawamura, M.; Shirakawa, E.; Hayashizaki, K.; Hayashi, T. *Tetrahedron,* **1988**, *44*, 5253.

Aldol Reaction of Different Isocyanocarboxylates



The stereochemistry is not dependent on the steric factors but on the **electronic interactions**

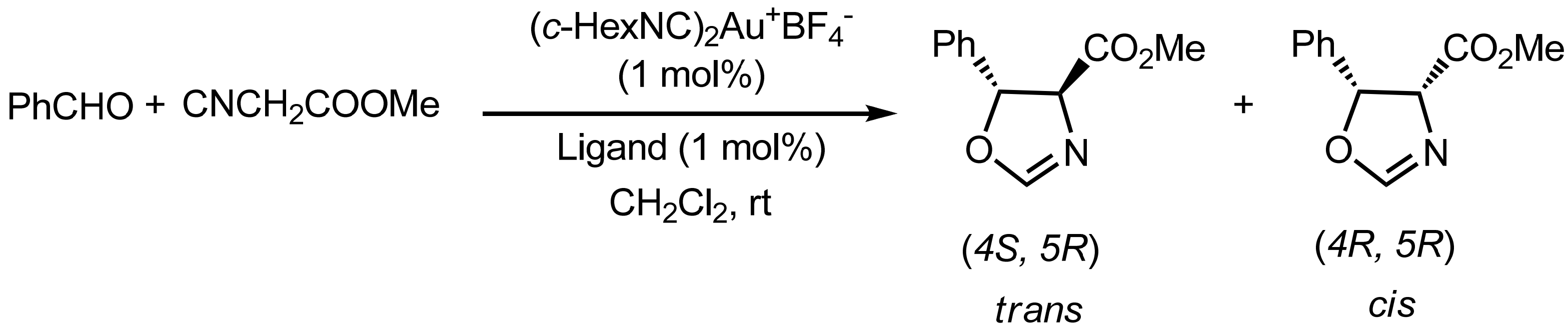
R	Yield (%)	*ee* (%)
H	99	52
Me	100	64
Et	89	70
i-Pr	99	71
Ph	75	67

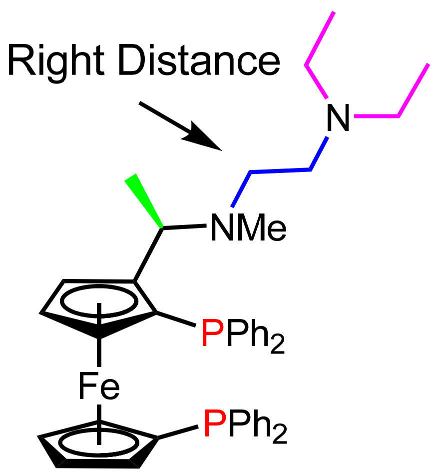


Ligand **1a**

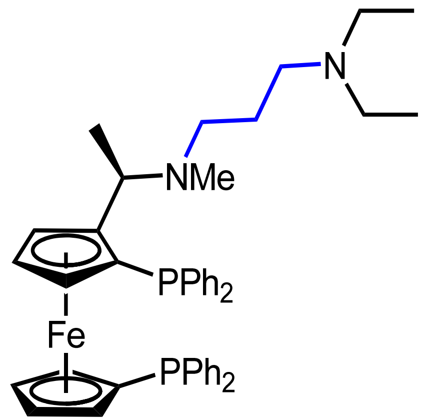
Ito, Y.; Sawamura, M.; Shirakawa, E.; Hayashizaki, K.; Hayashi, T. *Tetrahedron Lett.* **1988**, *29*, 235.

Aldol Reaction with Different Ligands

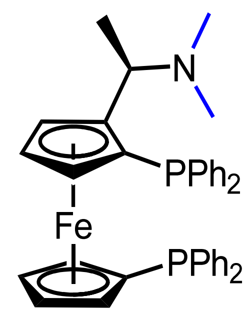




Yield: 98%
trans:*cis*: 89:11
ee (*trans*): 96%
ee (*cis*): 49%



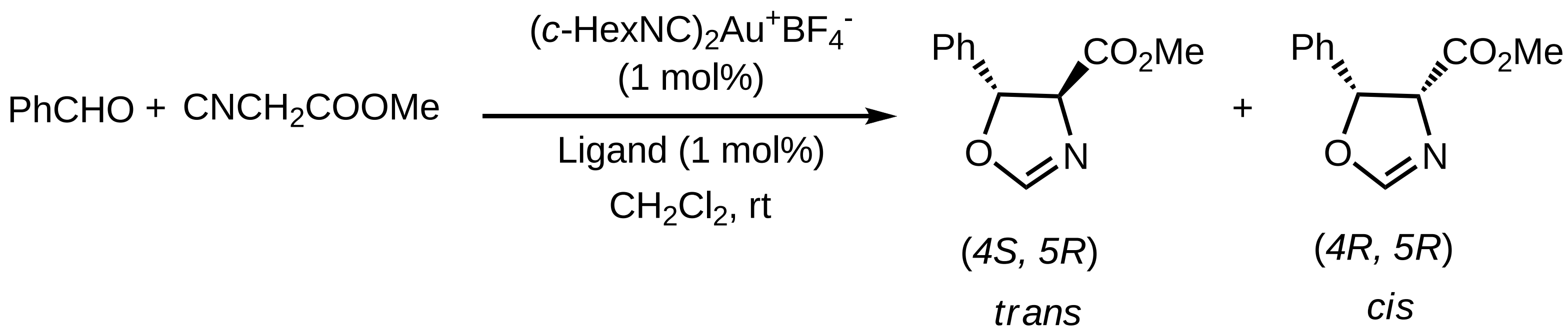
ee (*trans*): 26%

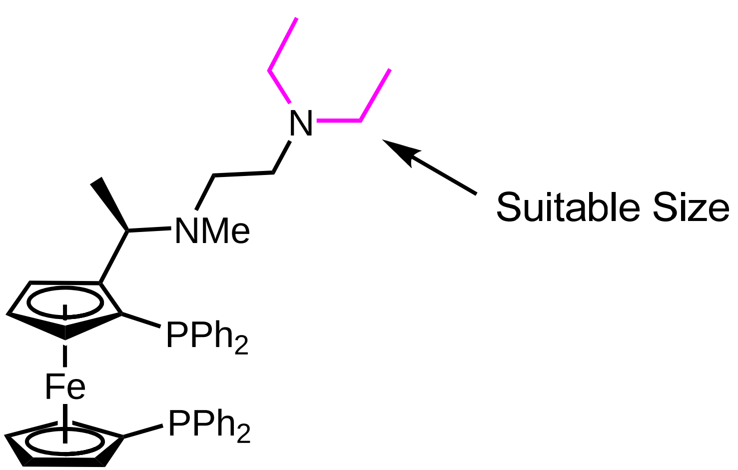


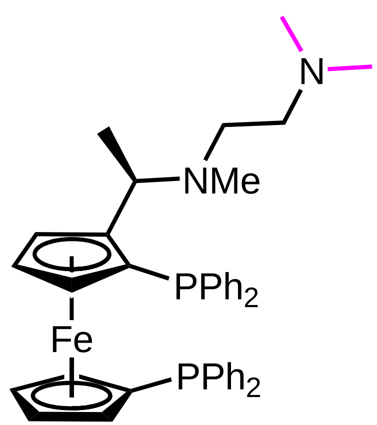
ee (*trans*): ~0%

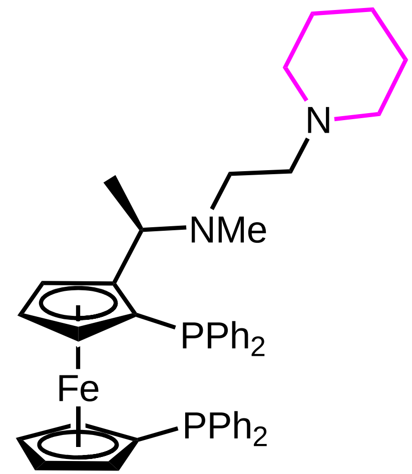
Togni, A.; Paster, S. D. *J. Org. Chem.* **1990**, *55*, 1649.

Aldol Reaction with Different Ligands







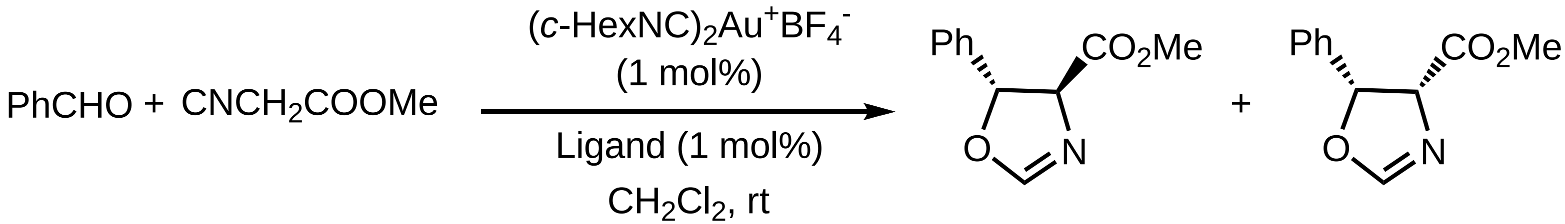


Yield: 98%
trans:*cis*: 89:11
ee (*trans*): 96%
ee (*cis*): 49%

Yield: 91%
trans:*cis*: 90:10
ee (*trans*): 94%
ee (*cis*): - 4%

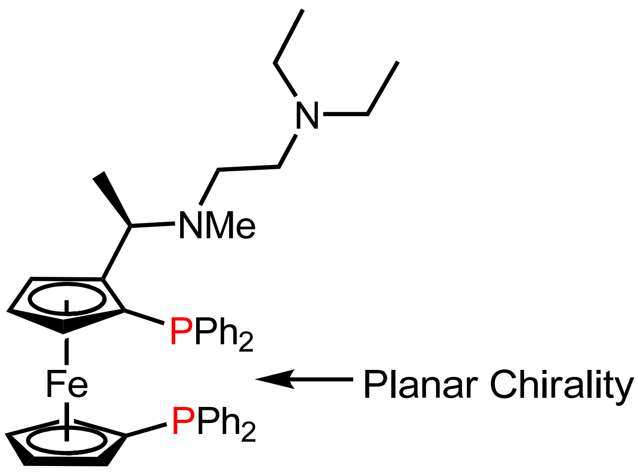
Yield: 94%
trans:*cis*: 94:6
ee (*trans*): 95%
ee (*cis*): 49%

Aldol Reaction with Different Ligands

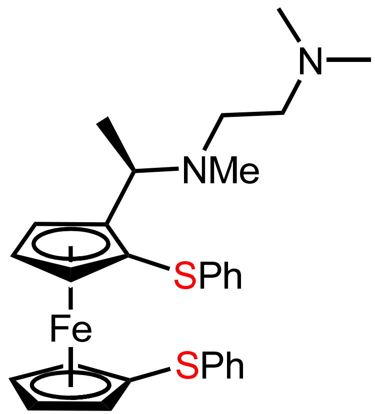


(*4S, 5R*) *trans*

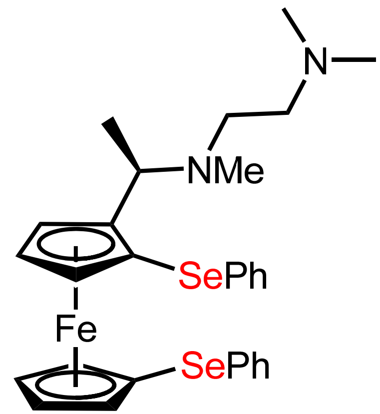
(*4R, 5R*) *cis*



Yield: 98%
trans:*cis*: 89:11
ee (*trans*): 96%
ee (*cis*): 49%

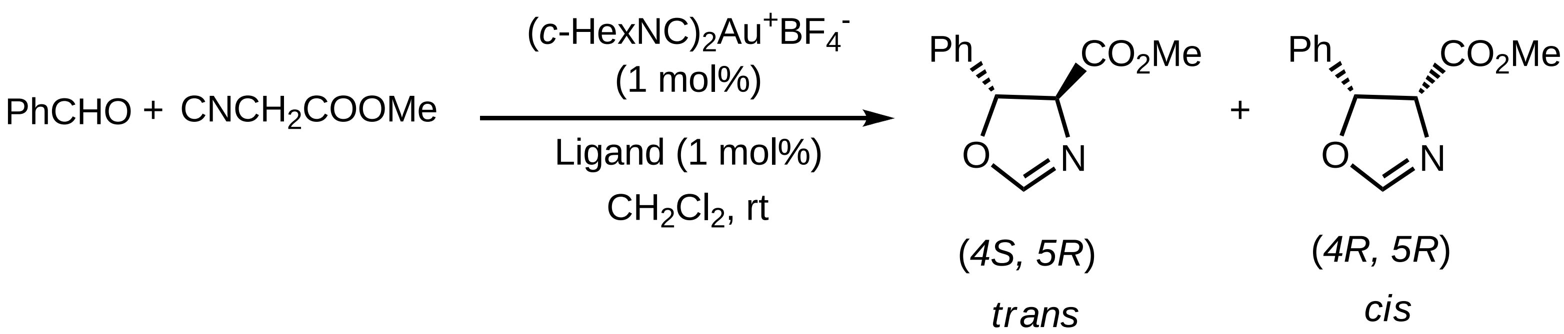


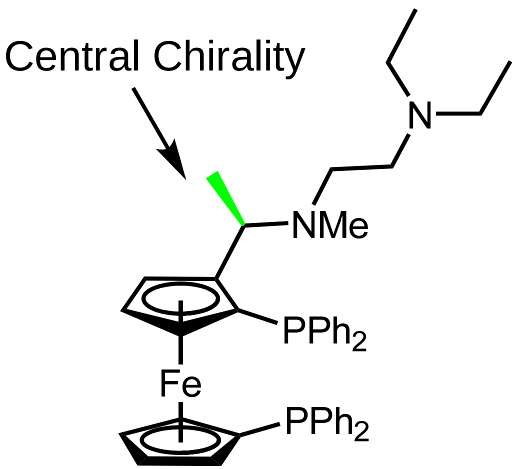
Yield: 74%
trans:*cis*: 72:28
ee (*trans*): 0%
ee (*cis*): 0%

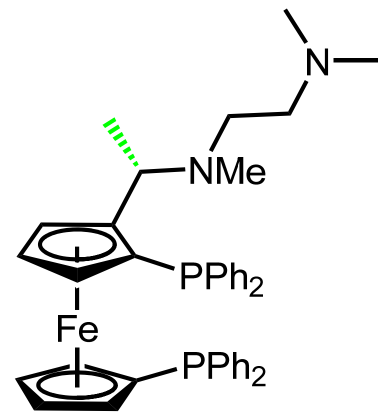


Yield: 63%
trans:*cis*: 69:31
ee (*trans*): 0%
ee (*cis*): 0%

Aldol Reaction with Different Ligands



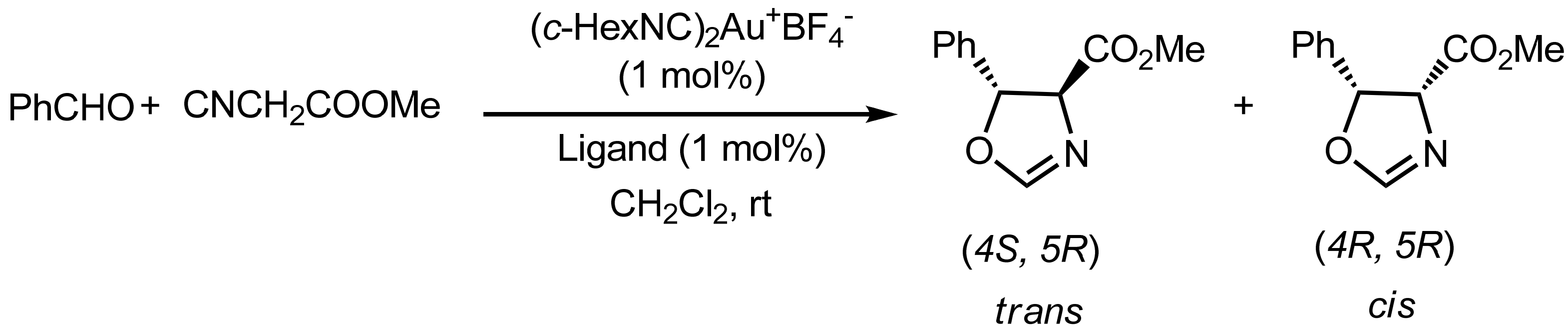


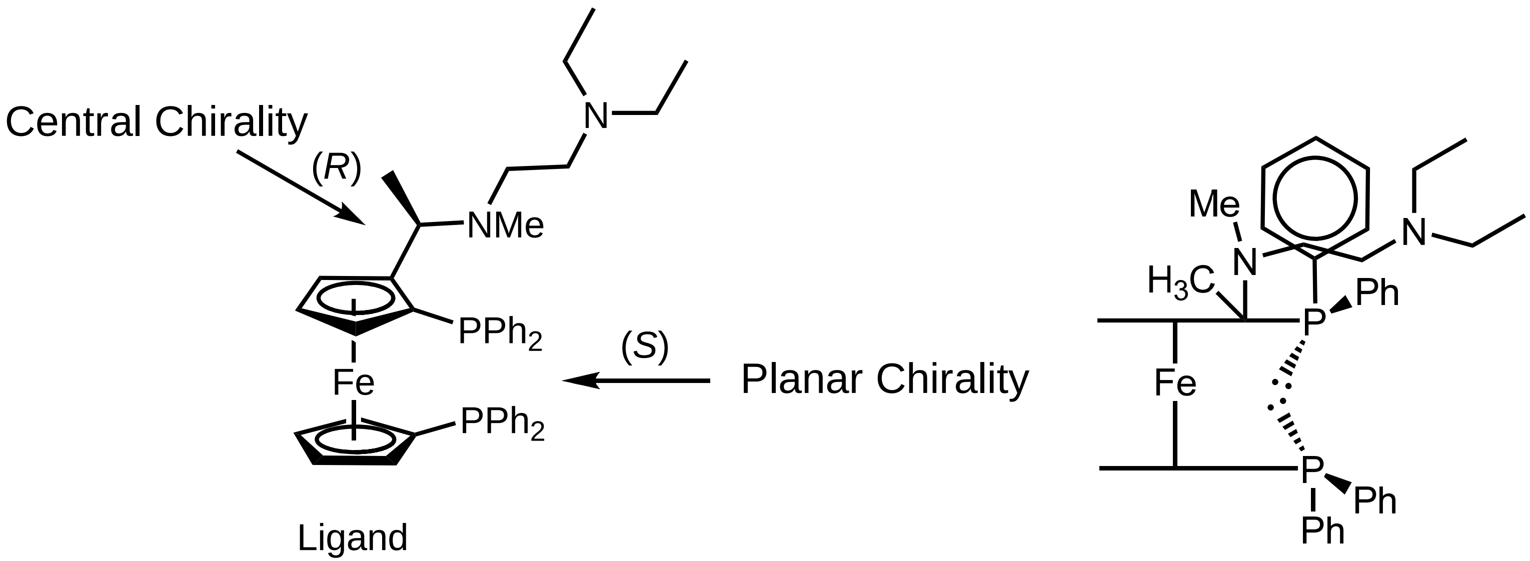


Yield: 98%
trans:*cis*: 89:11
ee (*trans*): 96%
ee (*cis*): 49%

Yield: 90%
trans:*cis*: 84:16
ee (*trans*): 41%
ee (*cis*): - 20%

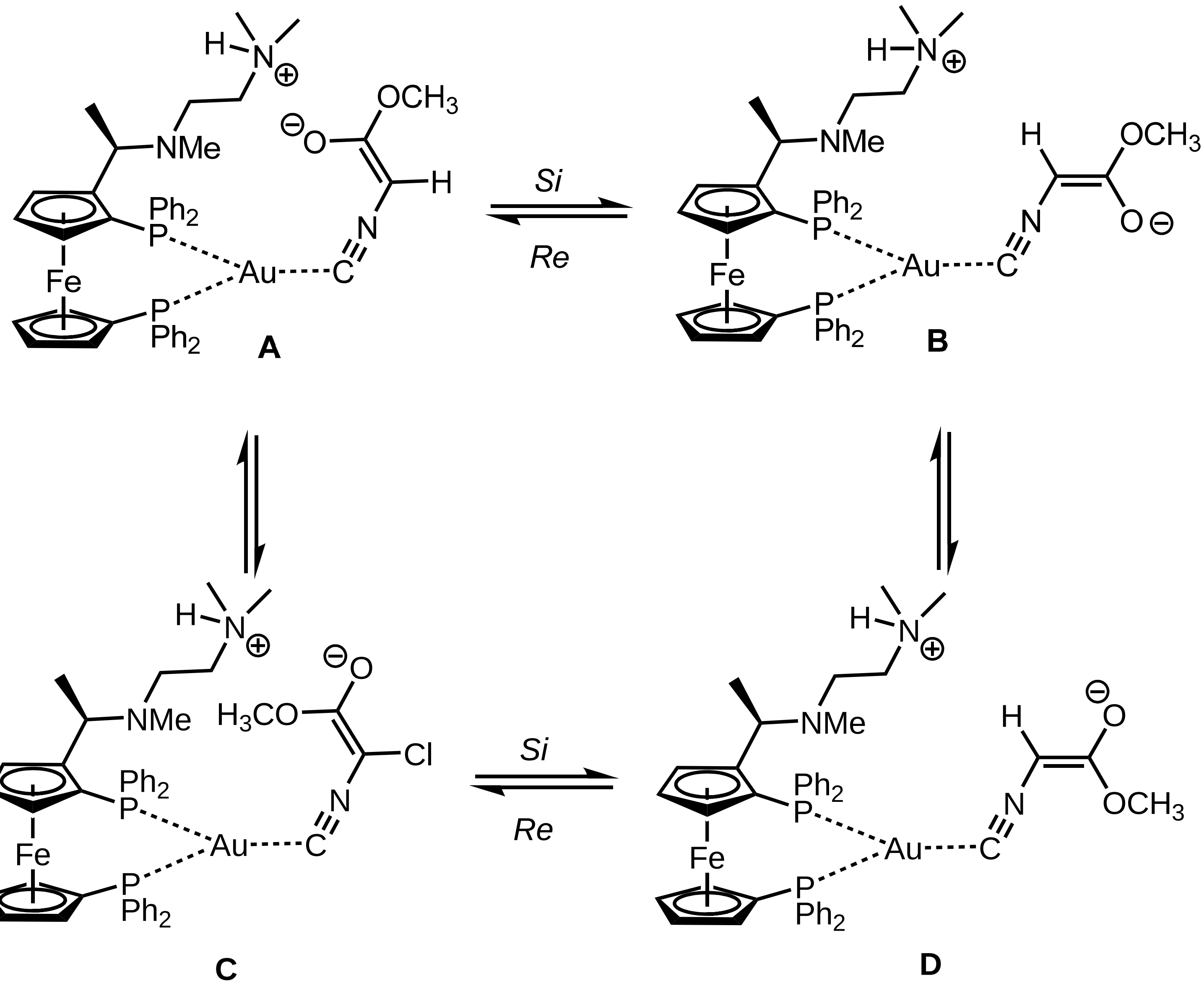
Internal Chiral Cooperativity in the Ligands





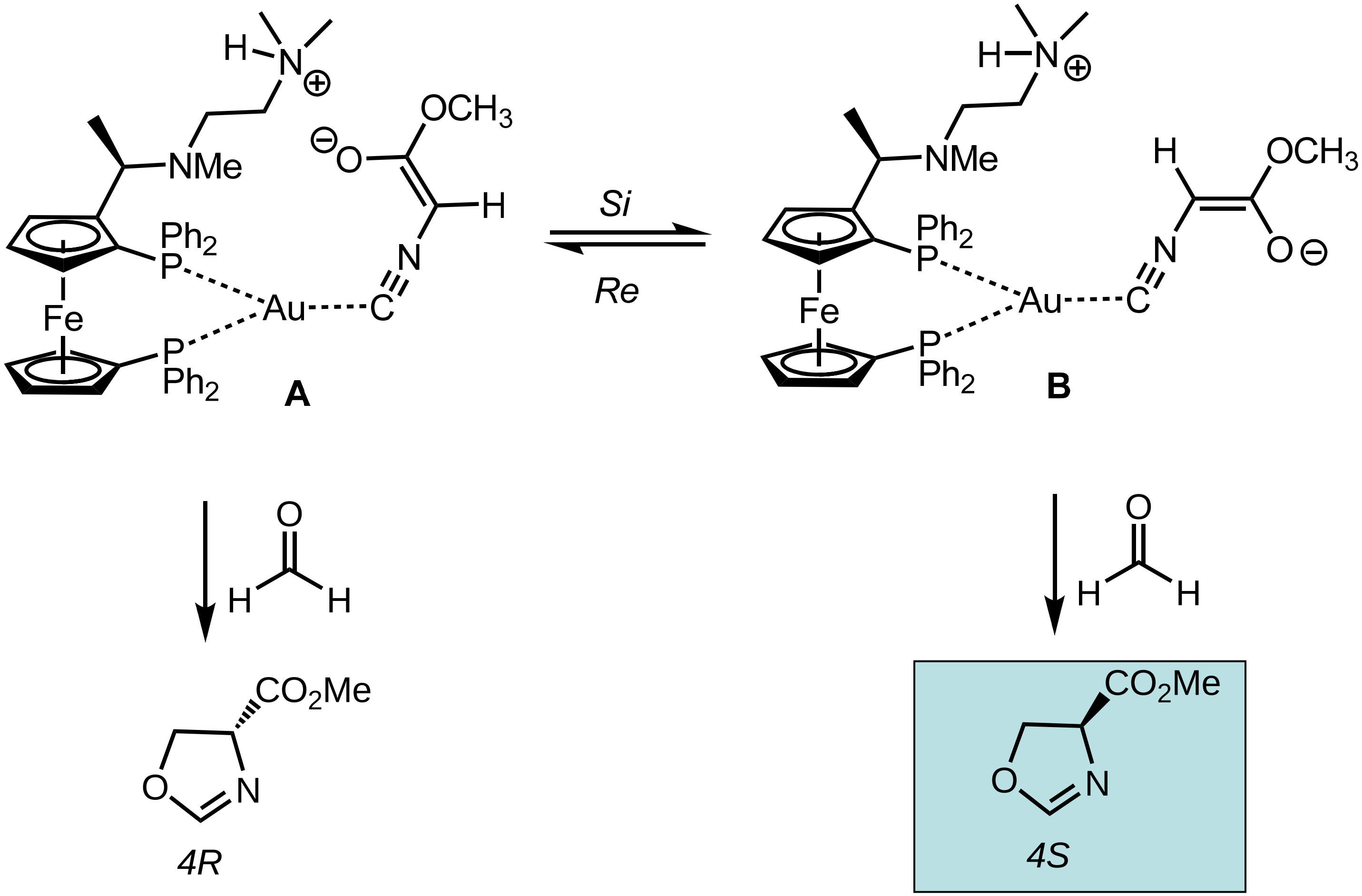
Togni, A.; Paster, S. D. *J. Org. Chem.* **1990**, *55*, 1649.

Transition State



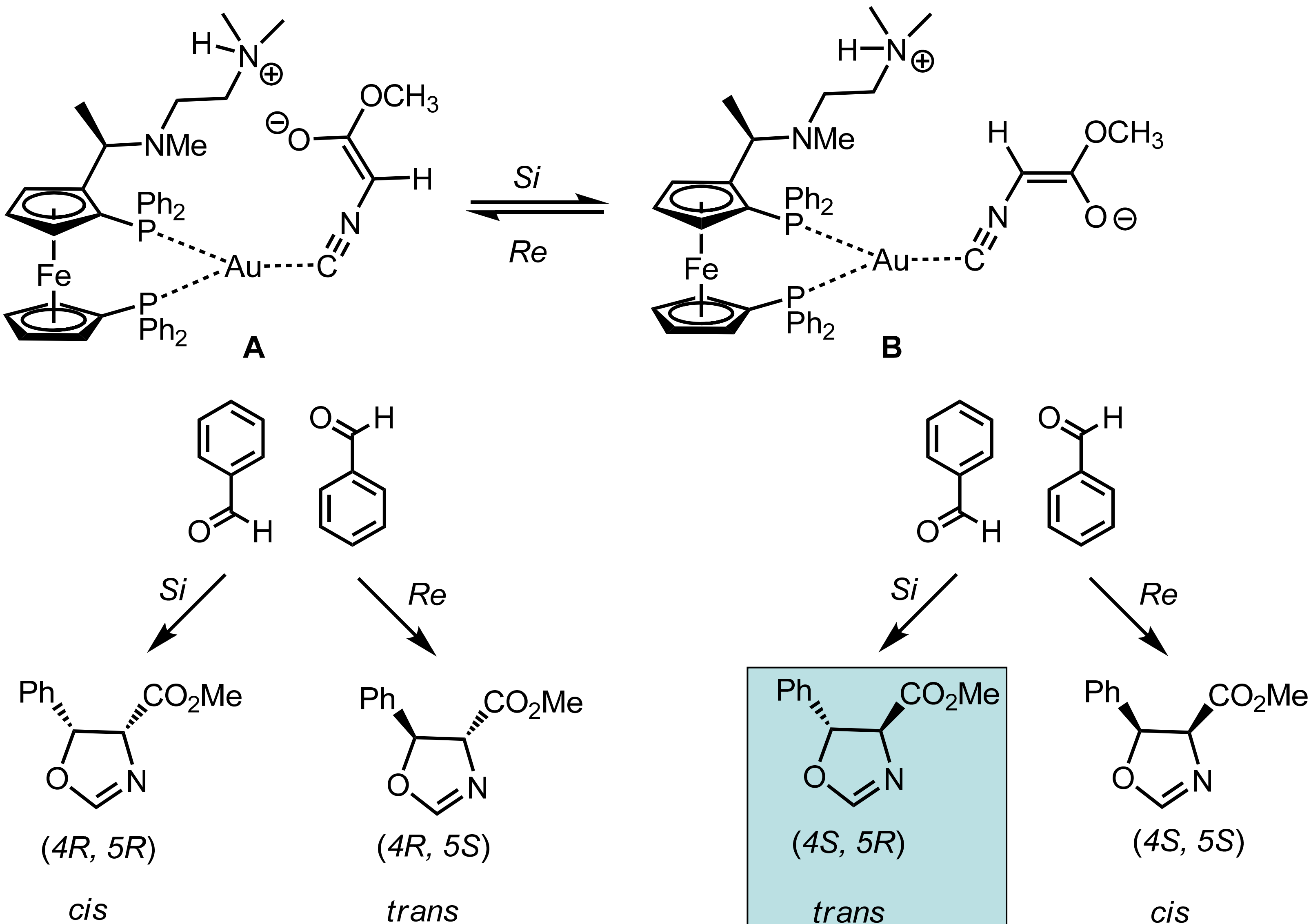
Togni, A.; Paster, S. D. *J. Org. Chem.* **1990**, *55*, 1649.

Transition State



Togni, A.; Paster, S. D. *J. Org. Chem.* **1990**, *55*, 1649.

Transition State for Aldol Reaction



Togni, A.; Paster, S. D. *J. Org. Chem.* **1990**, *55*, 1649.

Enantioselective Reactions

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Chiral Au(I) Complex

Cyclopropanation

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1,3-Dipolar Cycloaddition

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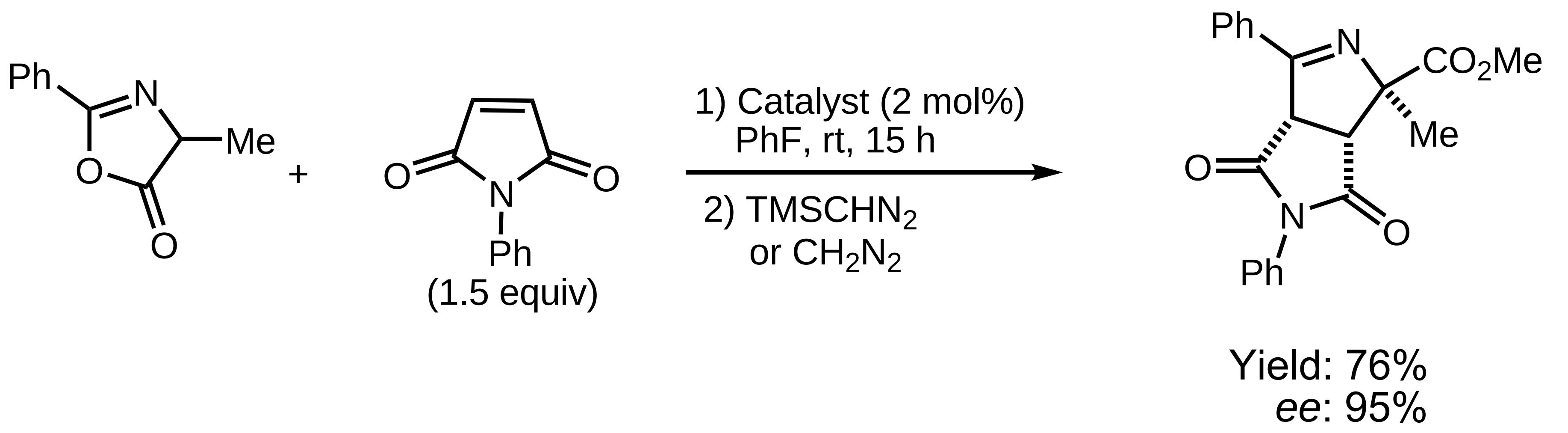
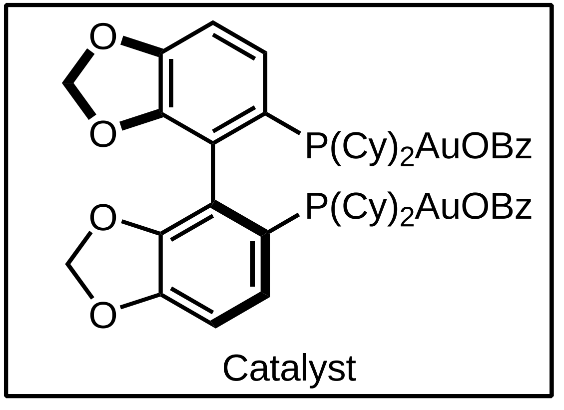
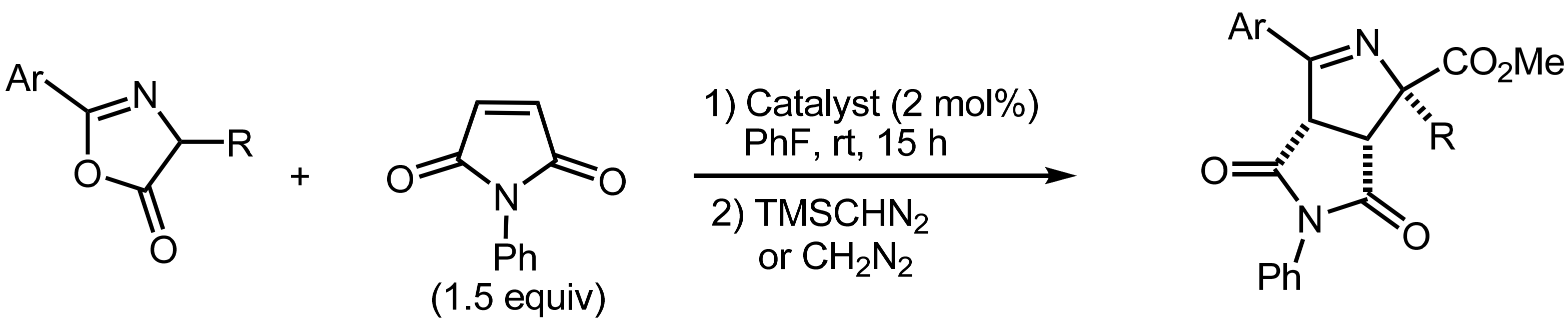


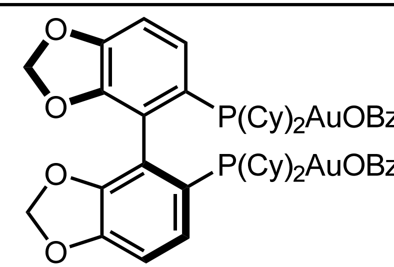


Melhado, A. D.; Luparia, M.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 12638.

Substrate Scope for Cycloaddition



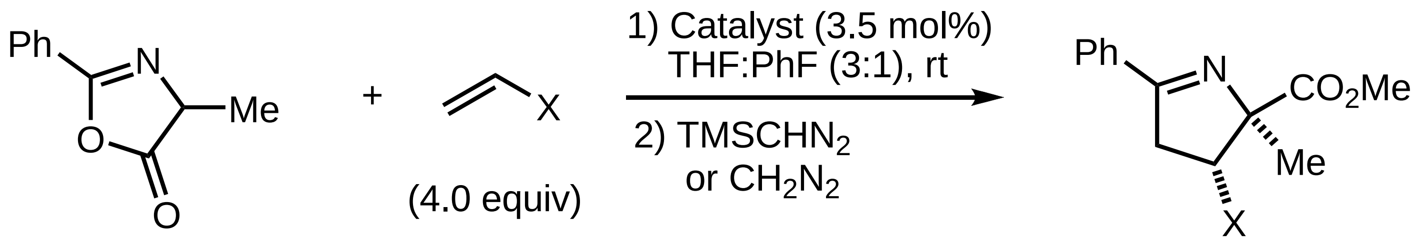
R	Ar	Yield (%)	*ee* (%)
Me	*p*-MeO-C_6H_4	77	95
Me	*p*-Br-C_6H_4	75	93
Me	*p*-Cl-C_6H_4	72	92
Me	*p*-NO_2-C_6H_4	98	91
Me	*o*-Me-C_6H_4	73	86
H	Ph	84	81
Allyl	Ph	86	87
Bn	Ph	71	68
Ph	Ph	35	78



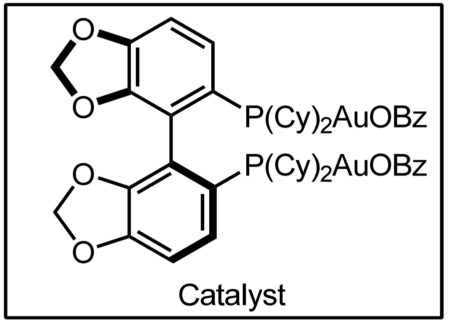
Catalyst

Melhado, A. D.; Luparia, M.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 12638.

Cycloaddition with Acyclic Alkenes

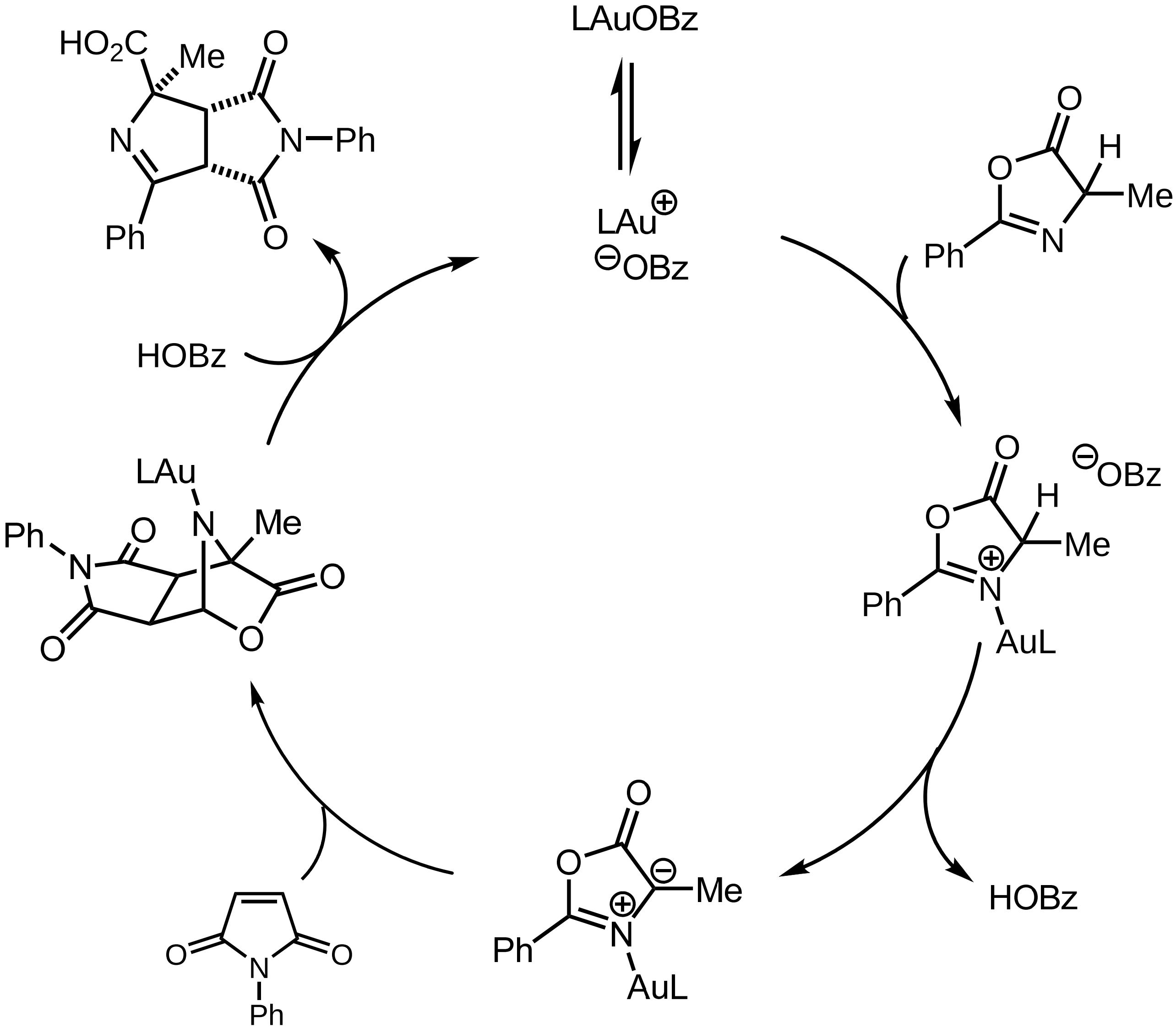


X	time (h)	Yield (%)	*ee* (%)
CO_2*t*-Bu	24	56	99
CO_2Et	14	66	90
CO_2Me	14	89	93



Melhado, A. D.; Luparia, M.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 12638.

Mechanism for 1,3-Dipolar Cycloaddtion



Melhado, A. D.; Luparia, M.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 12638.

Enantioselective Reactions

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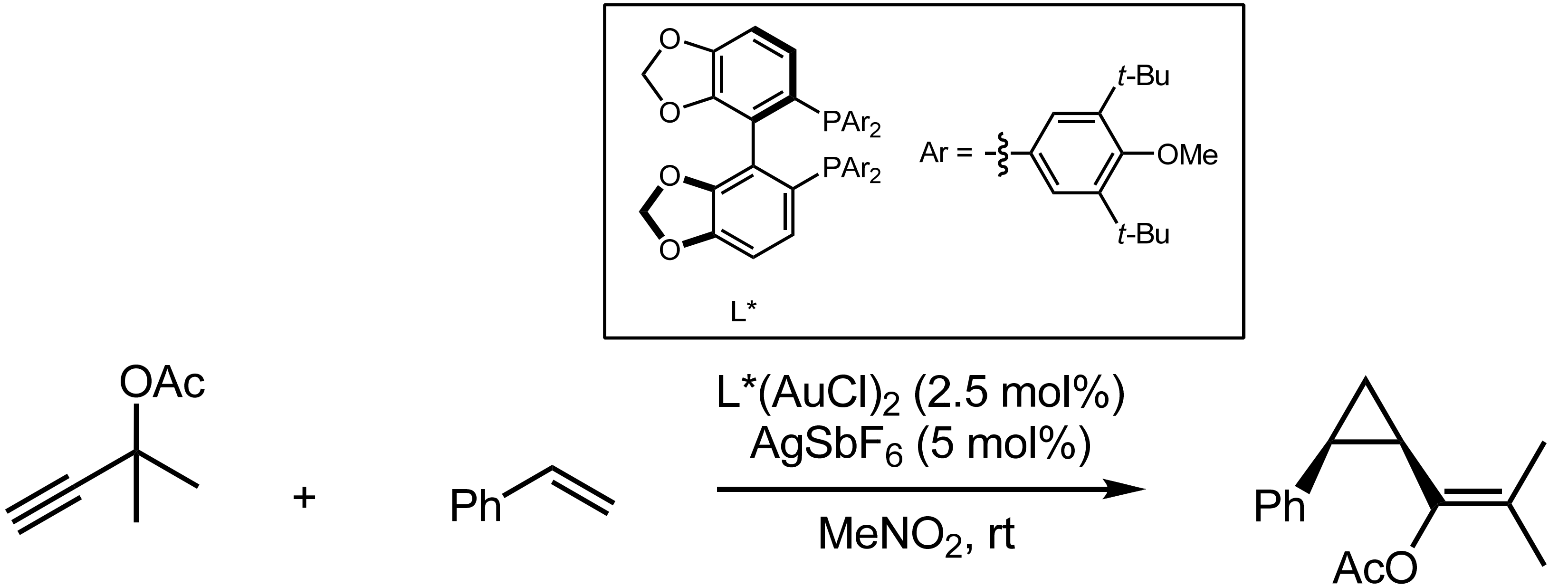
Cyclopropanation

1,3-Dipolar Cycloaddition

Aldol Reaction

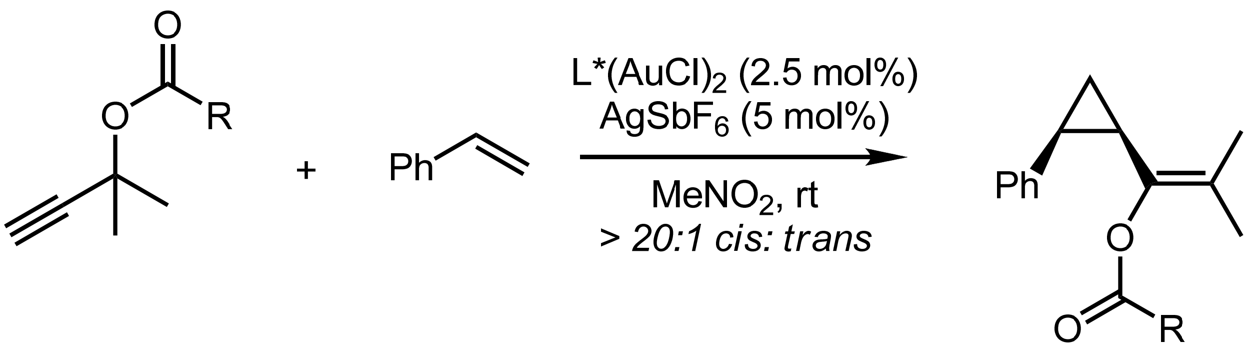
Olefin Cyclopropanation Reaction



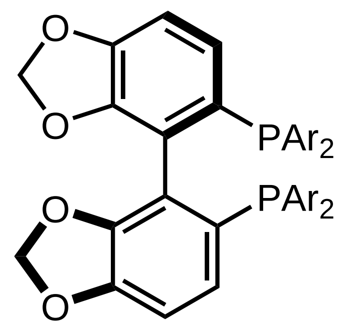
> 20:1 cis: trans

Johansson, M. J.; Gorin, D. J.; Staben, S. T. Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 18002.

Olefin Cyclopropanation



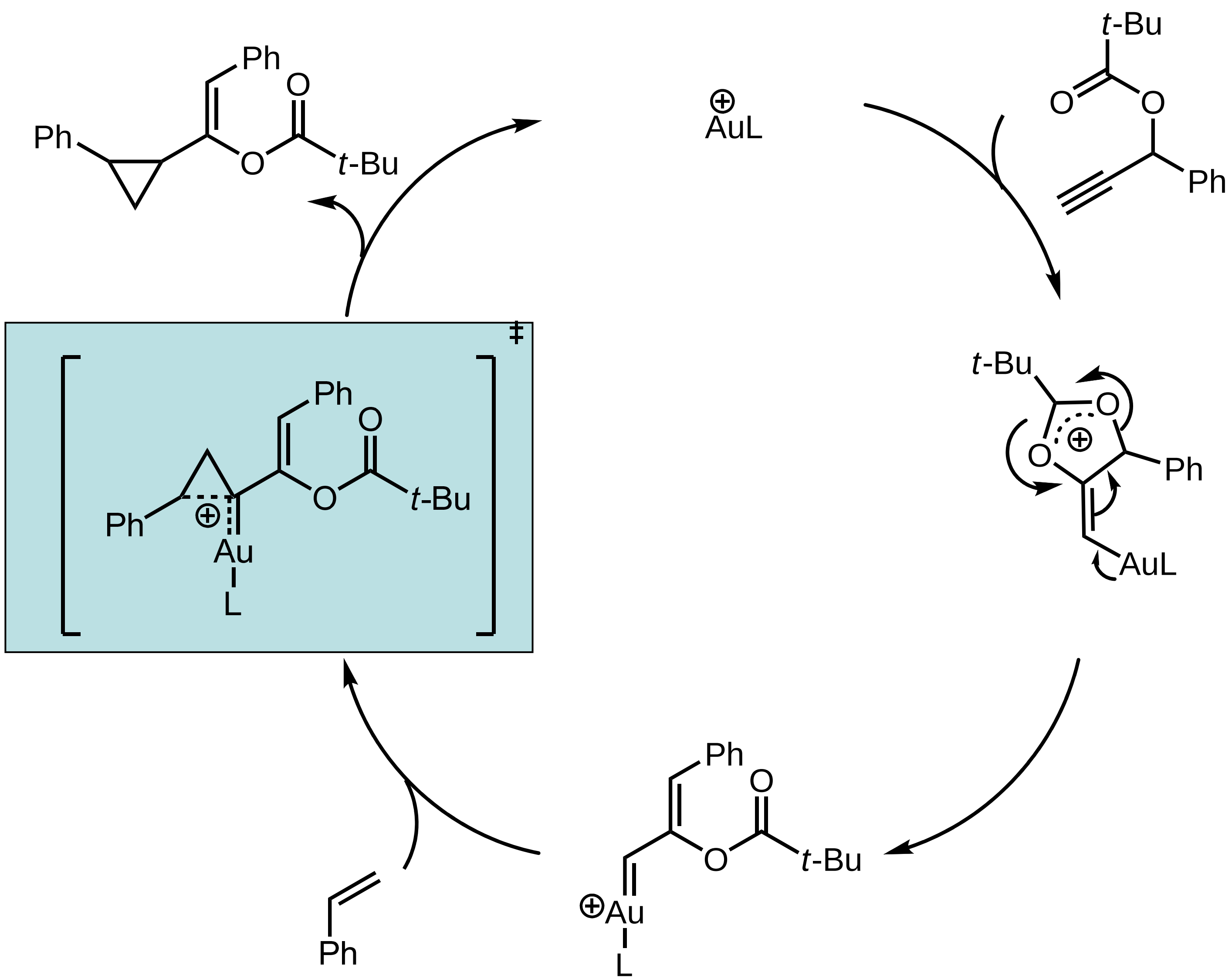
R	Yield (%)	*ee* (%)
Me	72	60
Ph	73	68
t-Bu	70	81



L*

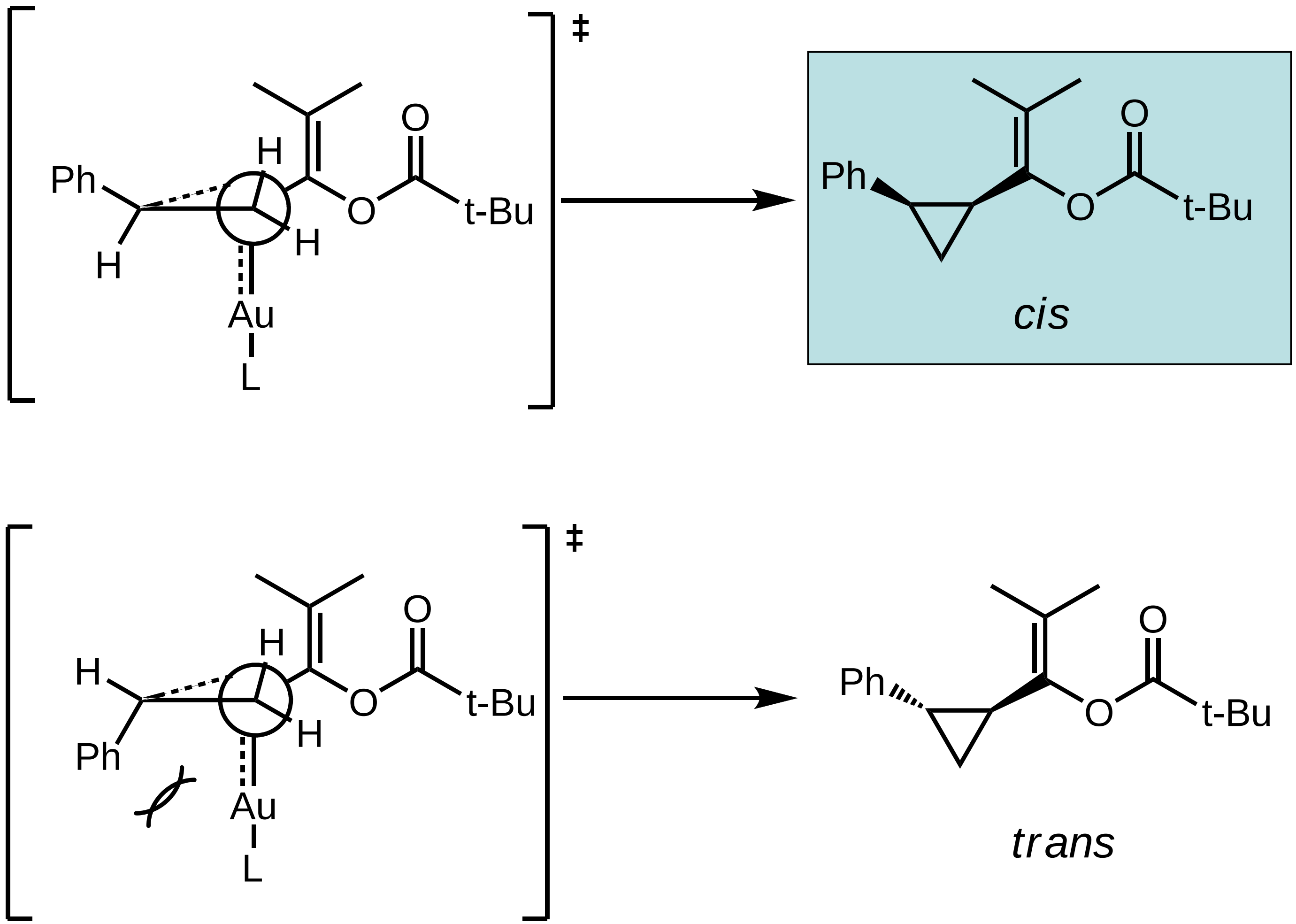
Johansson, M. J.; Gorin, D. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 18002.

Mechanism for Cyclopropanation



Johansson, M. J.; Gorin, D. J.; Staben, S.T.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 18002.

Mechanism for Diastereoselectivity



Johansson, M. J.; Gorin, D. J.; Staben, S. T.; Toste, F.D. *J. Am. Chem. Soc.* **2005**, *127*, 18002.

Enantioselective Reactions

Hydrofunctionalization

Hydrogenation

Chiral Au(I) Complex

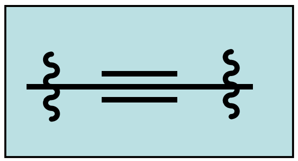
Cyclopropanation

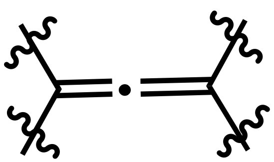
Aldol Reaction

1,3-Dipolar Cycloaddition

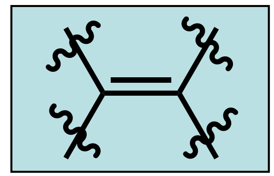
Classification for Intramolecular Hydrofunctionalization

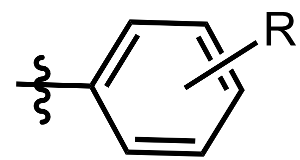
Funtional Groups 1





Functional Groups 2



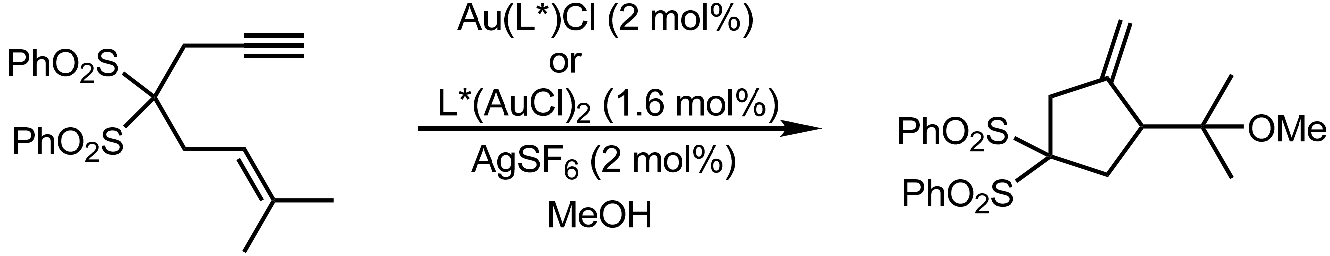


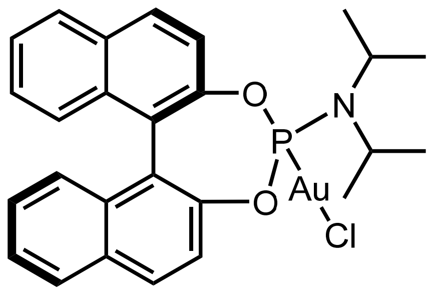
—OH

—COOH

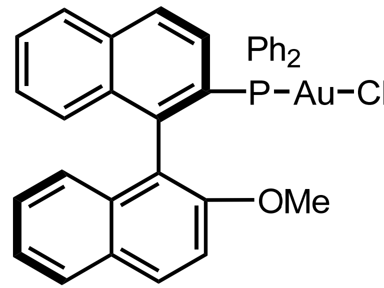
—NHR

Catalysts for Cyclization of Enynes

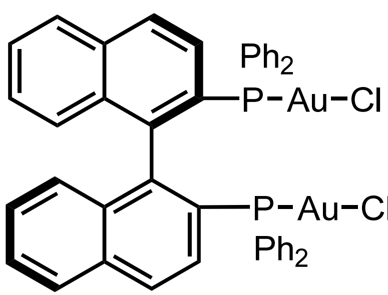




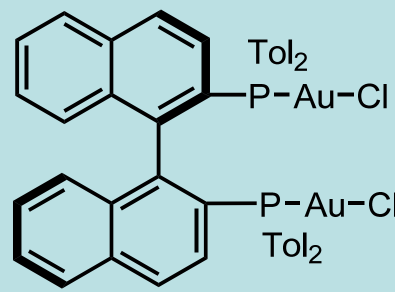
Yield: 60%
ee: <2%



Yield: 94%
ee: <2%



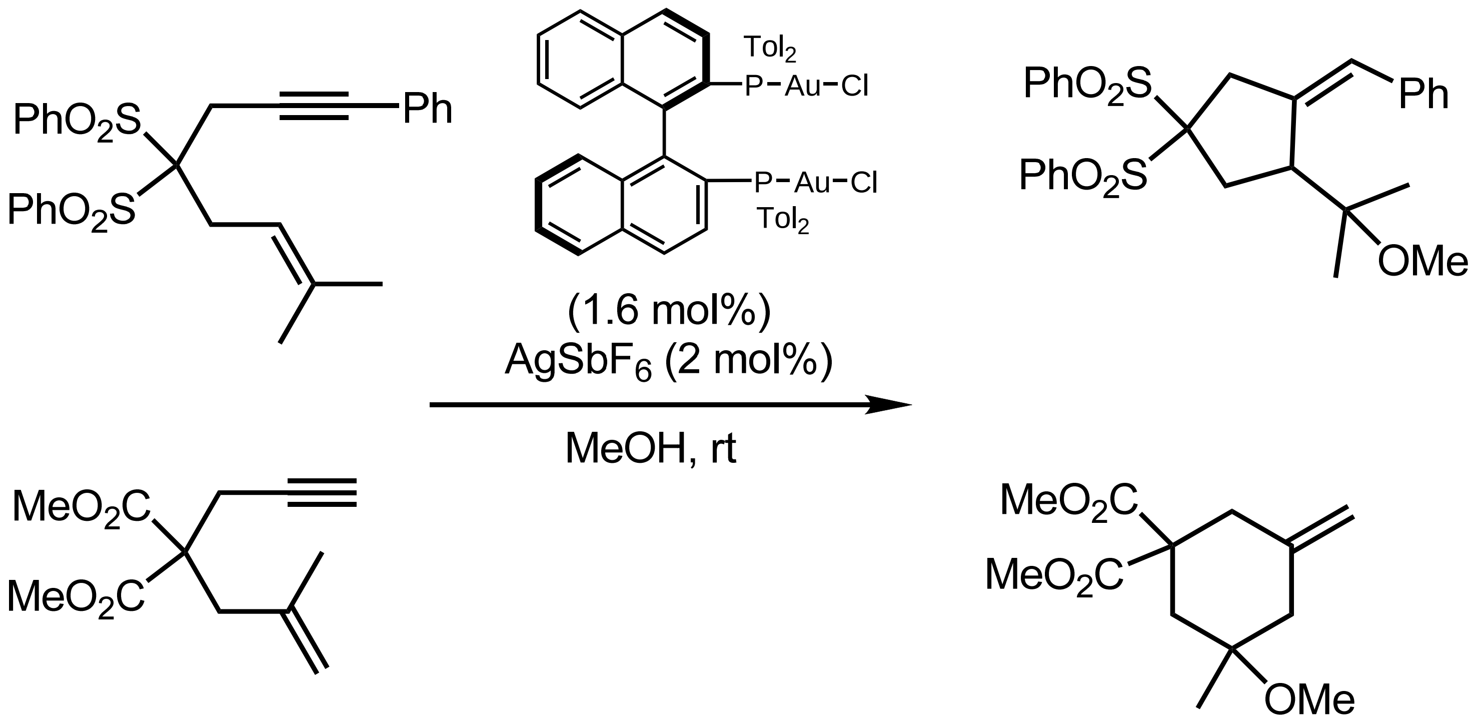
Yield: 98%
ee: -39%



Yield: 93%
ee: -43%

Muñoz, M. P.; Adrio, J.; Carretero, J. C.; Echavarren, A. M. *Organometallics*, **2005**, *24*, 1293.

Regioselectivity for Cyclization

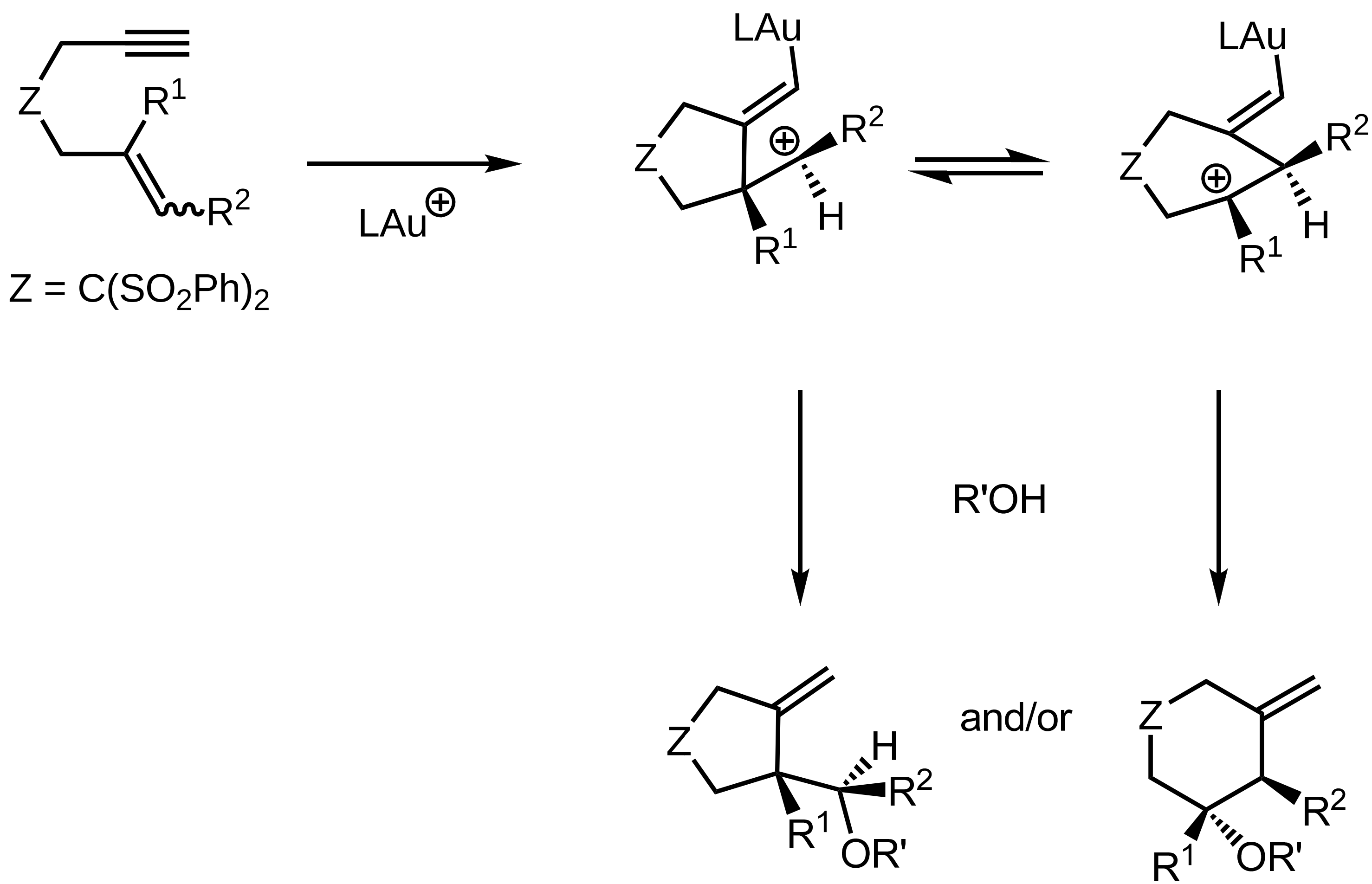


Yield: 52%
ee: 94%

Yield: 41%
ee: 30%

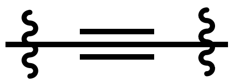
Muñoz, M. P.; Adrio, J.; Carretero, J. C.; Echavarren, A. M. *Organometallics*, **2005**, *24*, 1293.

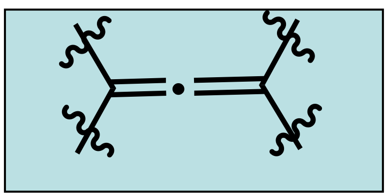
Mechanism for the Formation of Products



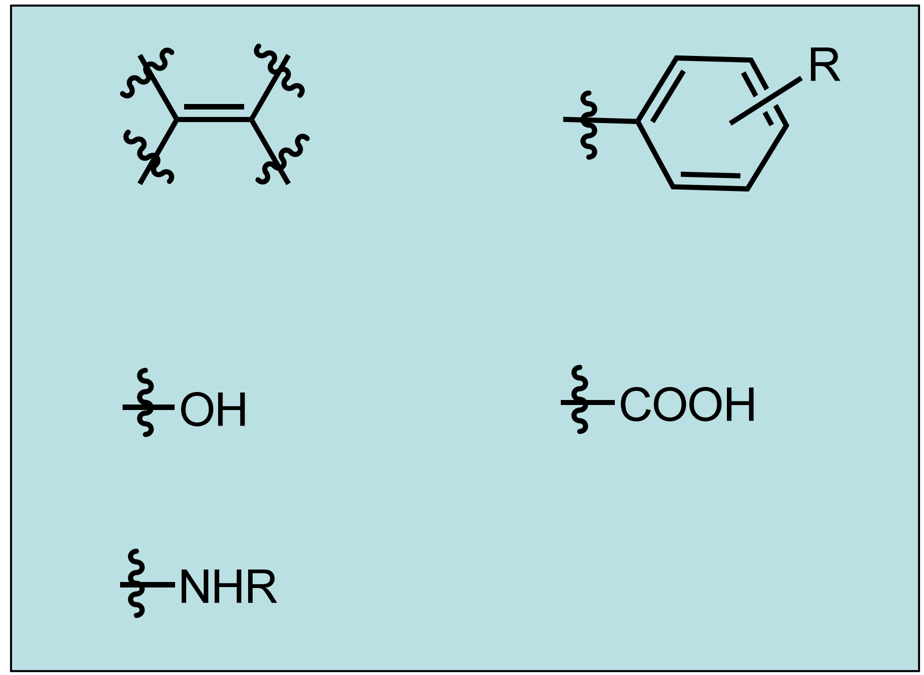
Classification for Intramolecular Hydrofunctionalization

Funtional Groups 1

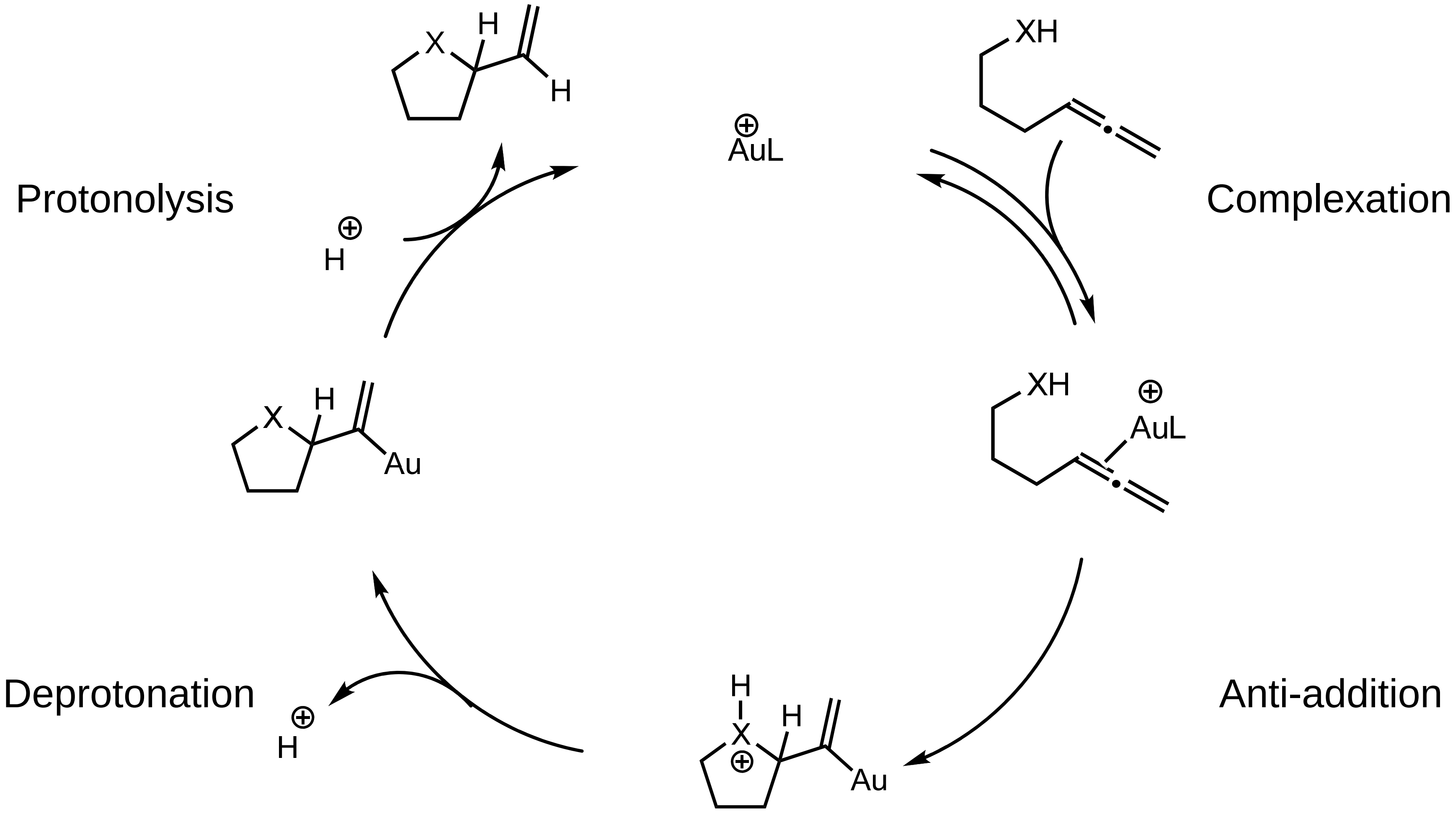




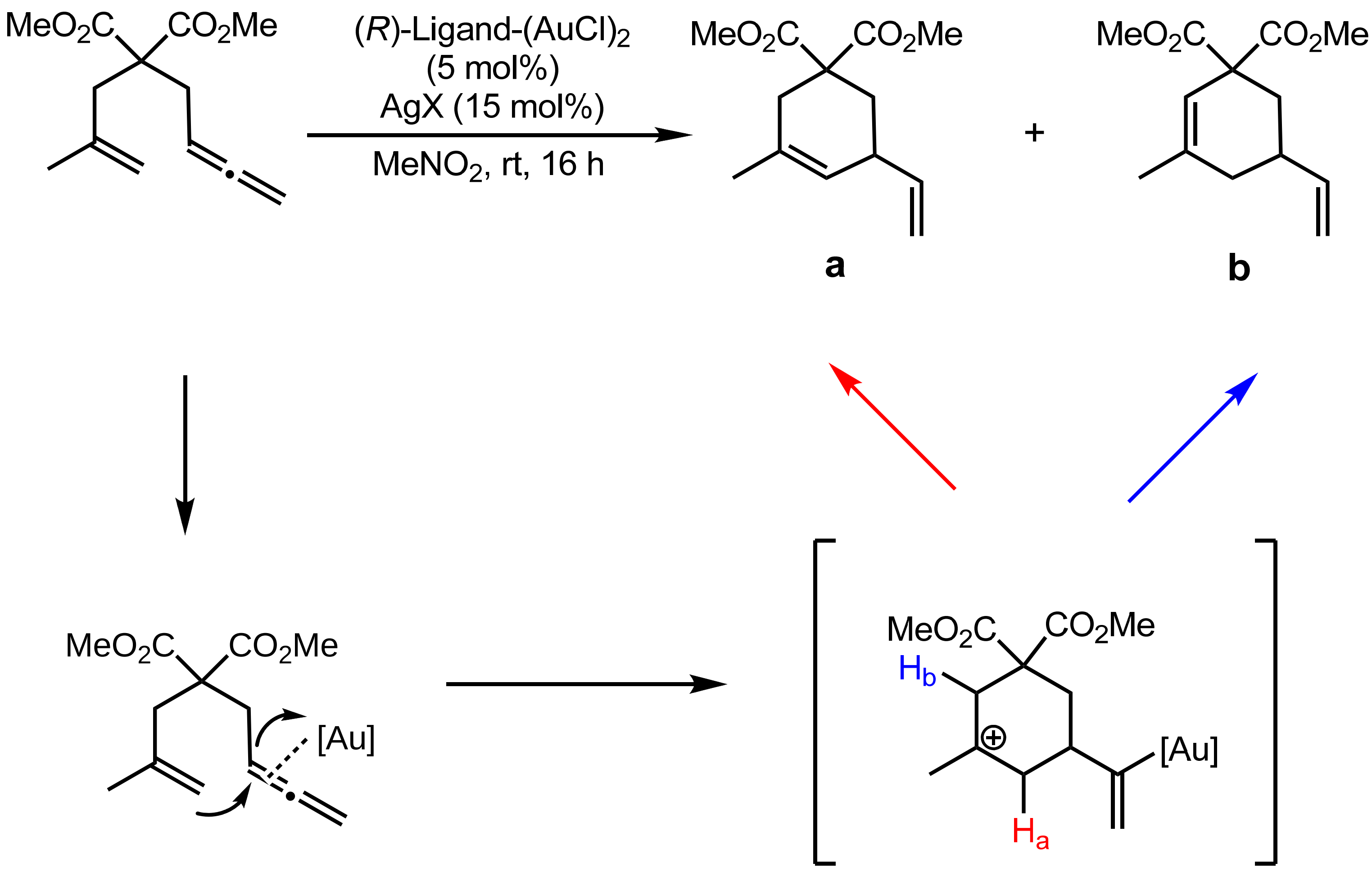
Functional Groups 2



General Mechanism for Hydrofunctionalization of Allenes

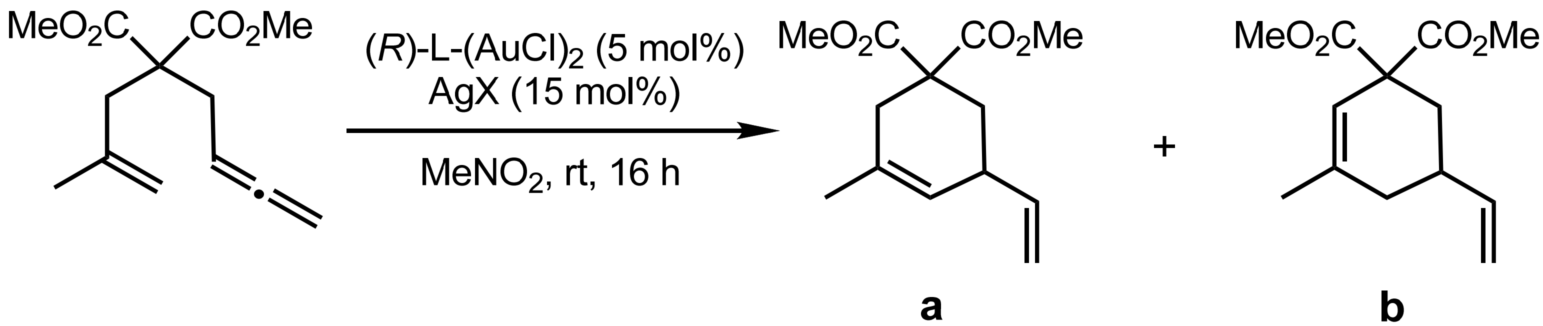


Hydroalkylation of Allenes

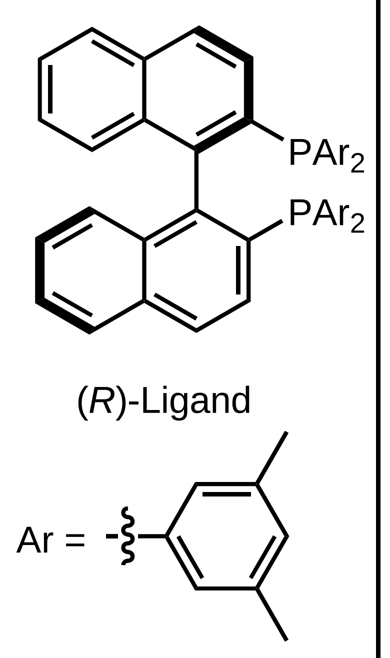


Tarselli, M. A.; Chianese, A. R.; Lee, S. J.; Gagné, M. R. *Angew. Chem. Int. Ed.* **2007**, *46*, 6670.

Counterion Effect in the Reaction

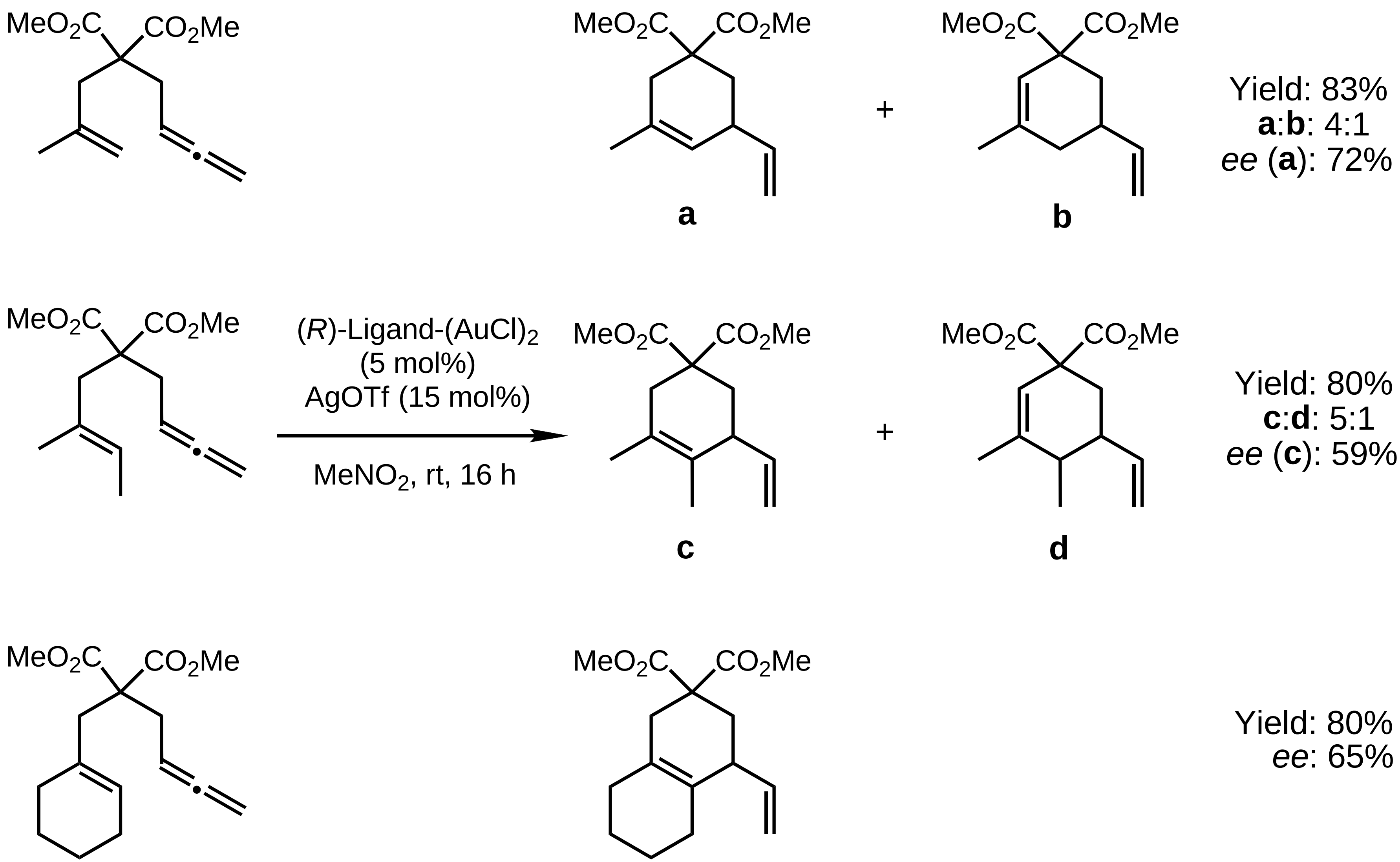


AgX	a:b	*ee* (a, %)
$AgNTf_2$	4:1	65
$AgSbF_6$	4:3	57
AgOTs	10:1	50
$AgPF_6$	9:1	65
AgOTf	4:1	72



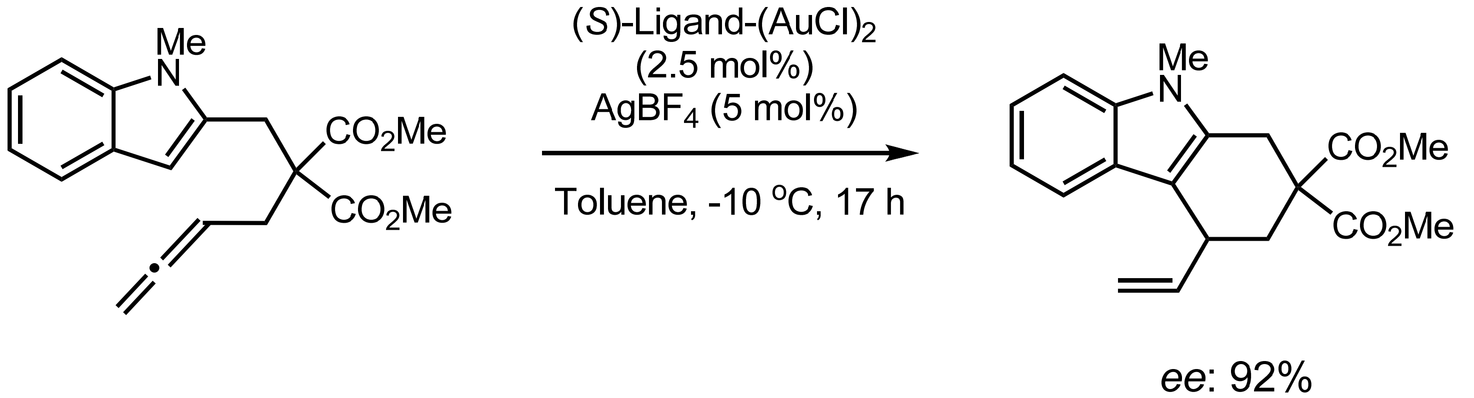
Tarselli, M. A.; Chianese, A. R.; Lee, S. J.; Gagné, M. R. *Angew. Chem. Int. Ed.* **2007**, *46*, 6670.

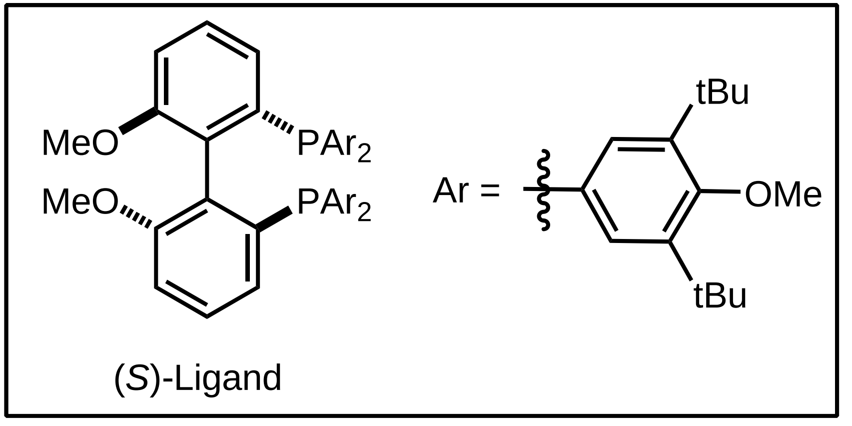
Substrate Scope for Hydroalkylation



Tarselli, M. A.; Chianese, A. R.; Lee, S. J.; Gagné, M. R. *Angew. Chem. Int. Ed.* **2007**, *46*, 6670.

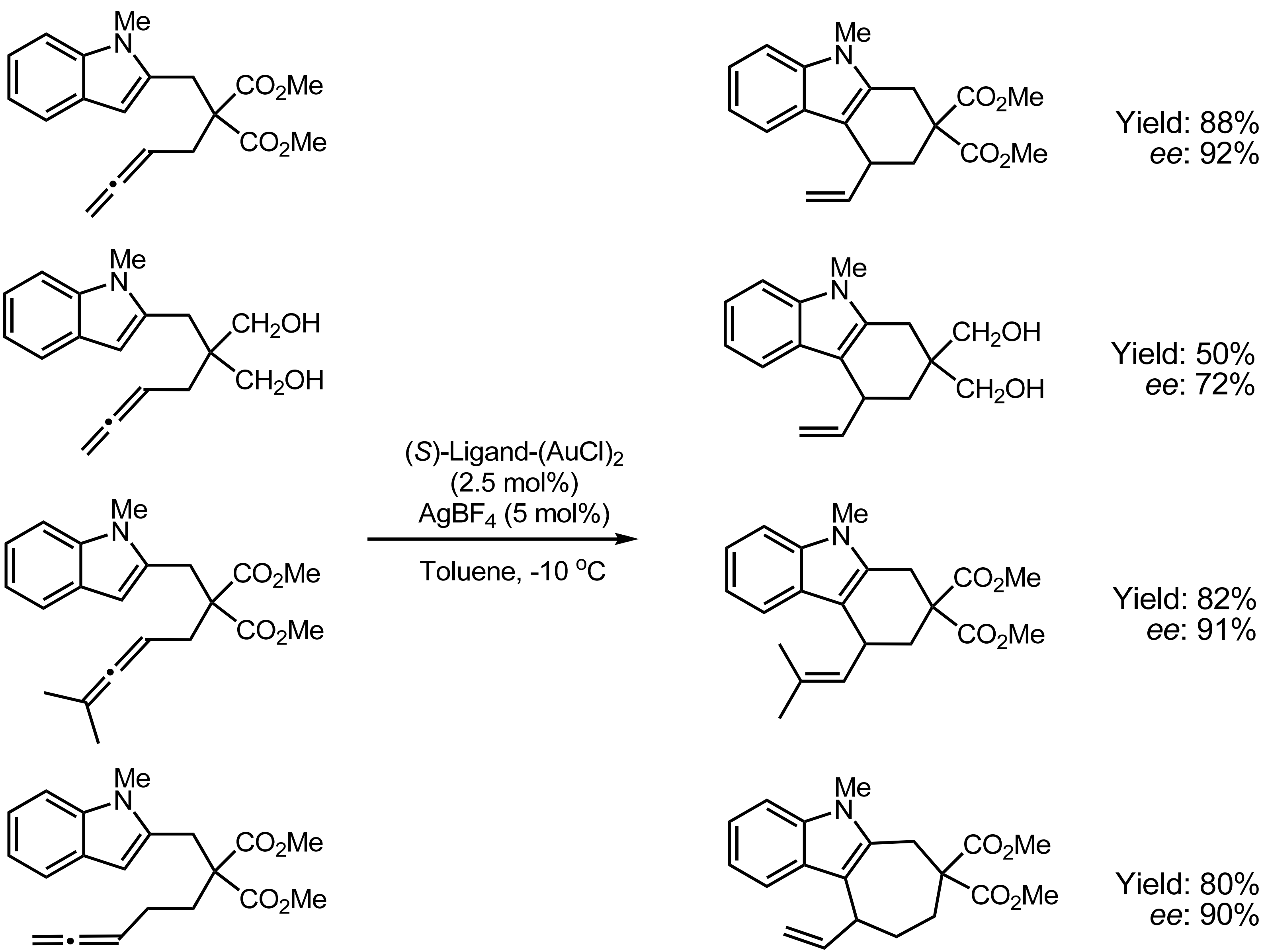
Hydroarylation of Allenes





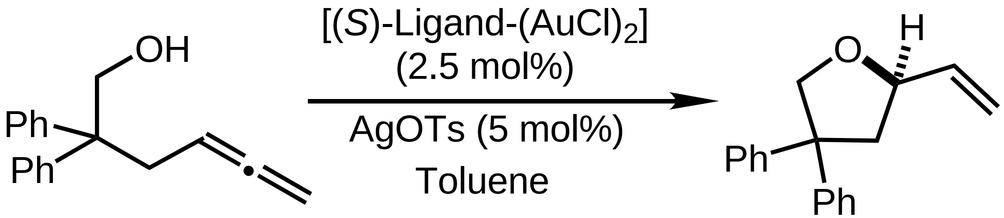
Liu, C.; Widenhoefer, R. A. *Org. Lett.* **2007**, *9*, 1935.

Substrate Scope for Hydroarylation

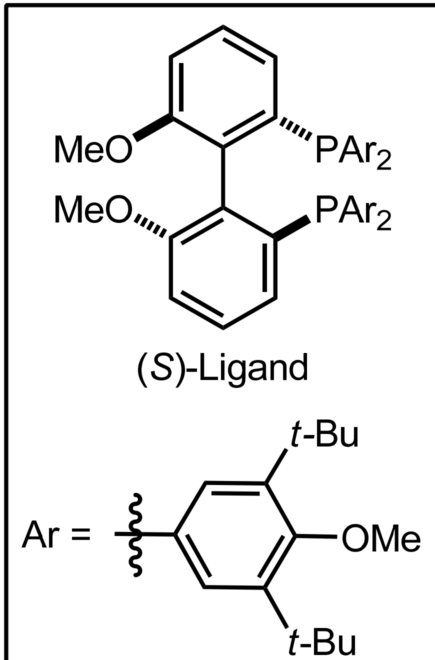


Liu, C.; Widenhoefer, R. A. *Org. Lett.* **2007**, *9*, 1935.

Intramolecular Hydroalkoxylation



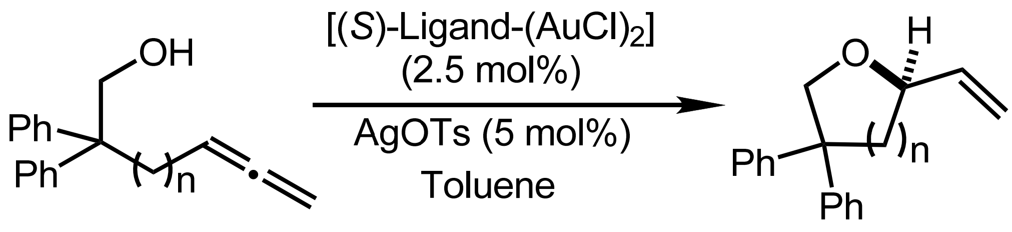
1 **2**

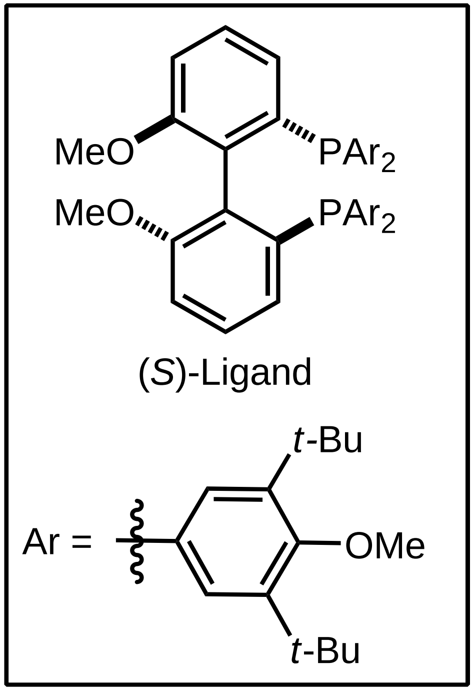


Conc. 1 (mM)	T (°C)	t (*h*)	Yield (%)	*ee* (%)
125	25	< 0.1	73	86
13	25	4	73	90
13	-20	61	73	93
63	-20	18	76	93

Zhang, Z.; Widenhoefer, R.A. *Angew. Chem. Int. Ed.* **2007**, *46*, 283.

Intramolecular Hydroalkoxylation

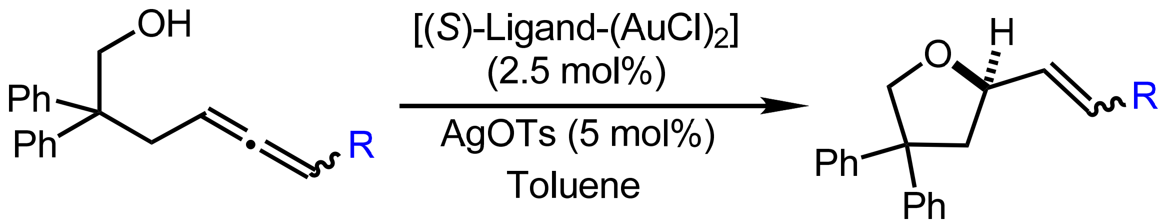


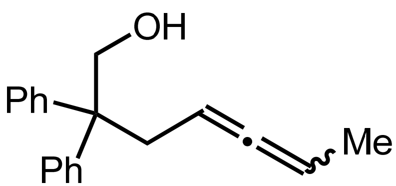
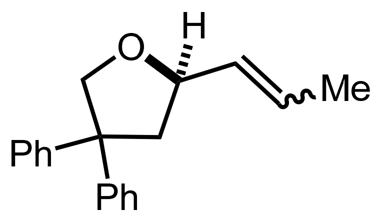
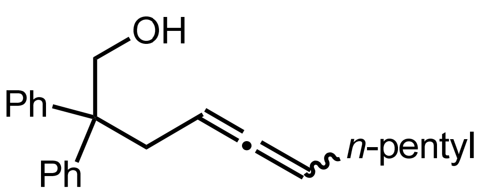
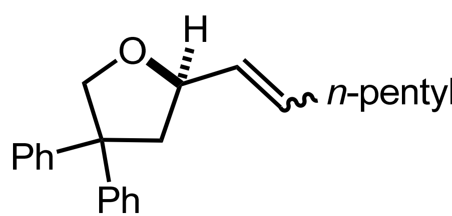
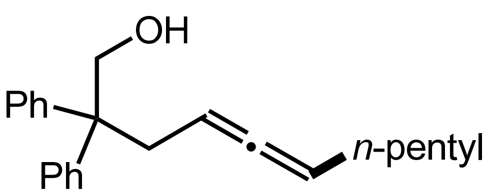
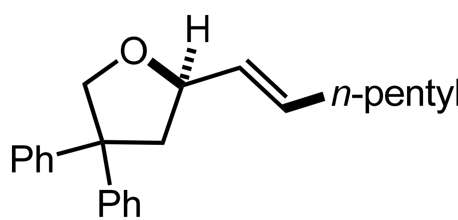


n	**Yield (%)**	***ee* (%)**
1	67	93
2	96	88

Zhang, Z.; Widenhoefer, R.A. *Angew. Chem. Int. Ed.* **2007**, *46*, 283.

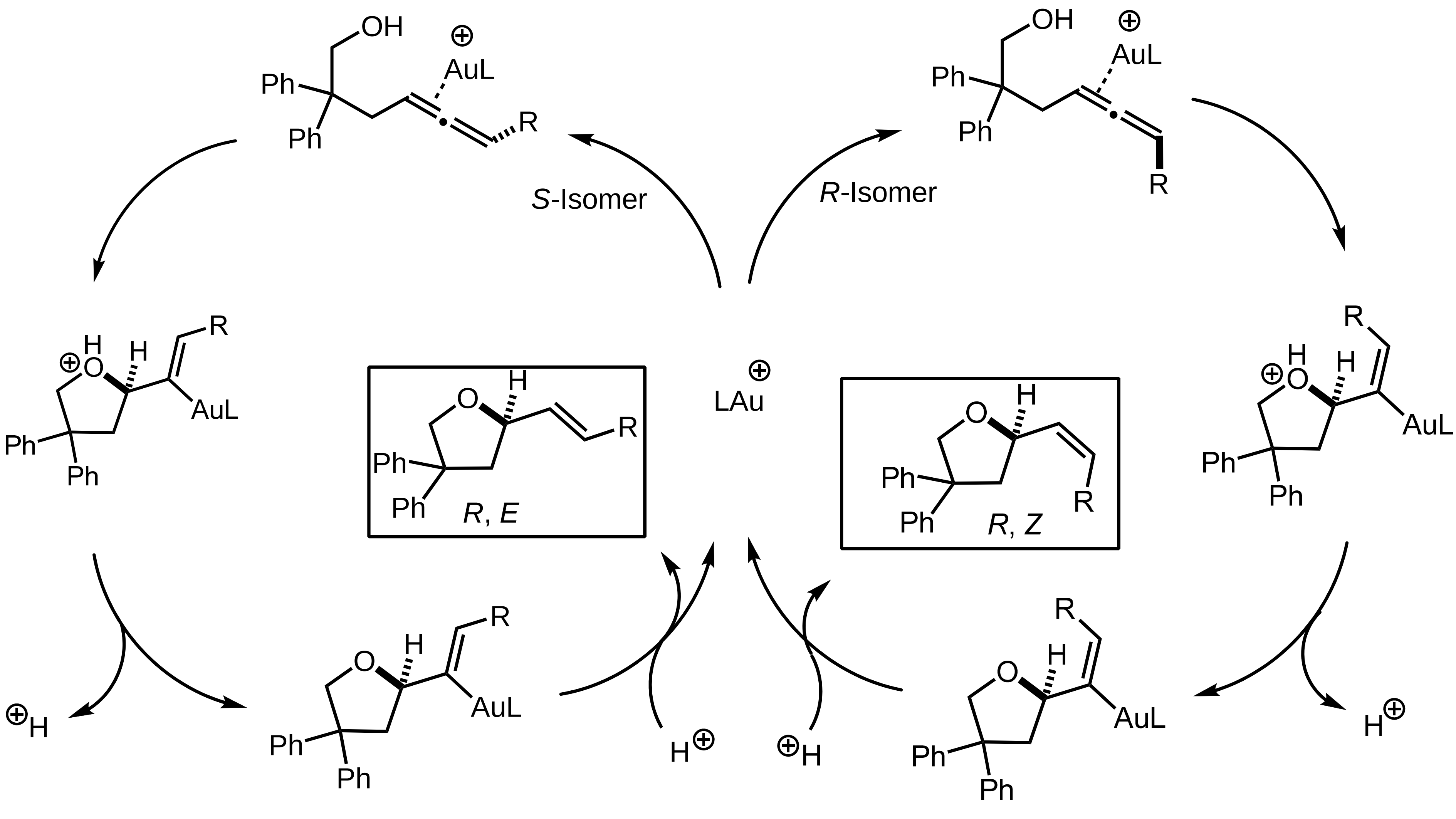
Intramolecular Hydroalkoxylation



Substrate	Product	Z:E	Yield (%)	ee (%)
		1:1	96	97/99
		1:1	94	>95/>95
		>20:1	88	>95

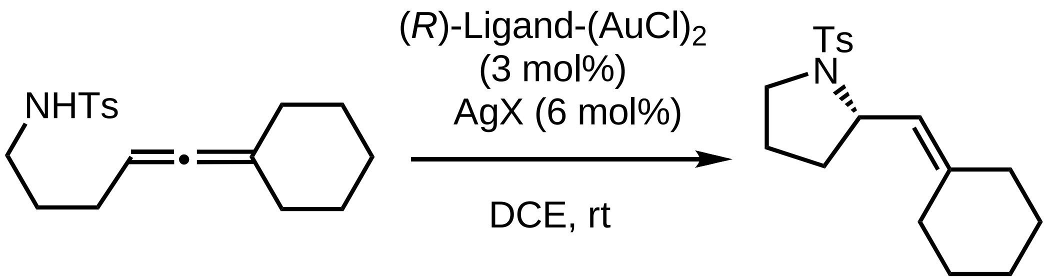
Zhang, Z.; Widenhoefer, R.A. *Angew. Chem. Int. Ed.* **2007**, *46*, 283.

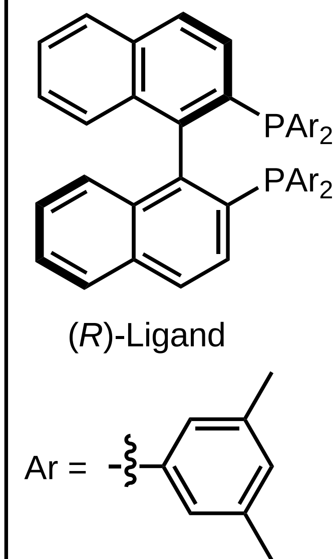
Proposed Mechanism

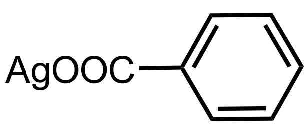
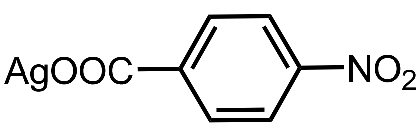


Zhang, Z.; Widenhoefer, R.A. *Angew. Chem. Int. Ed.* **2007**, *46*, 283.

Counteranion Effect in Hydroamination

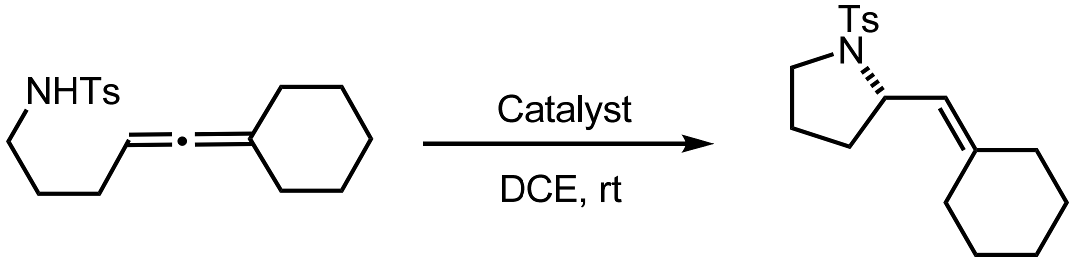


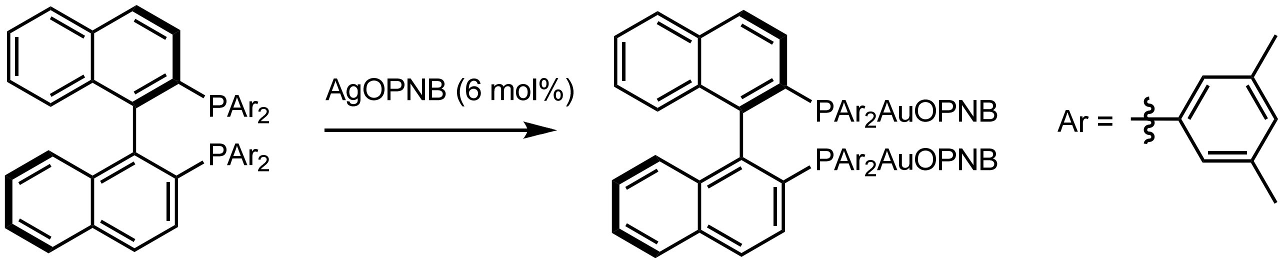


AgX	Time (h)	Yield (%)	*ee* (%)
$AgBF_4$	0.5	82	1
	24	27	98
	24	76	98

LaLonde, R. L.; Sherry, B. D.; Kang, E. J.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 2452.

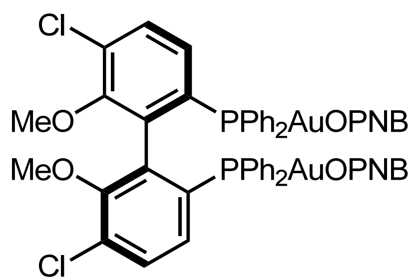
Intramolecular Hydroamination





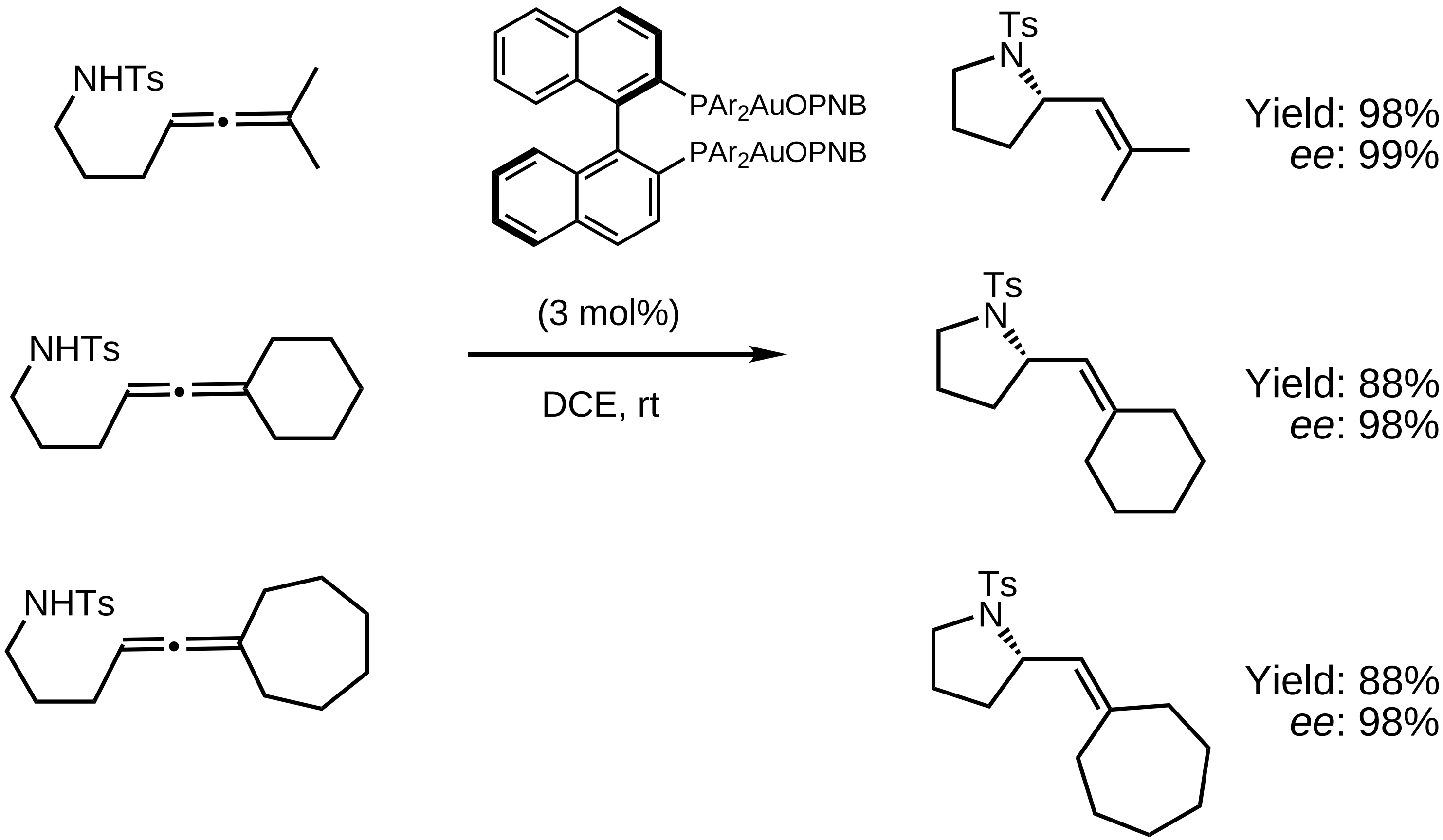
(3 mol%)

(*R*)-**1**

	time (h)	Yield (%)	*ee* (%)
in situ generated catalyst	24	76	98
isolated catalyst	17	88	98
 (*R*)-**2**	15	85	97

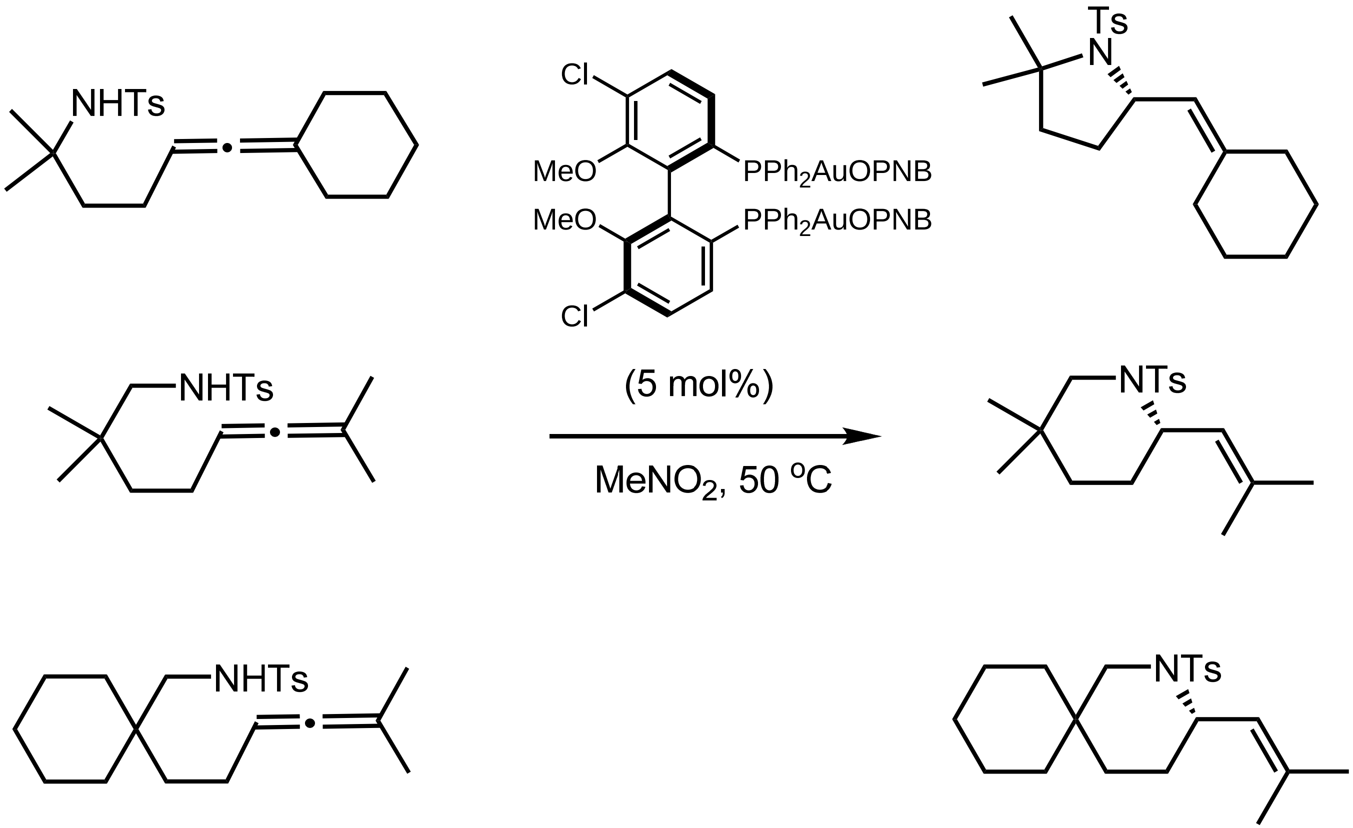
LaLonde, R. L.; Sherry, B. D.; Kang, E. J.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 2452.

Substrate Scope for Hydroamination



LaLonde, R. L.; Sherry, B. D.; Kang, E. J.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 2452.

Substrate Scope for Hydroamination



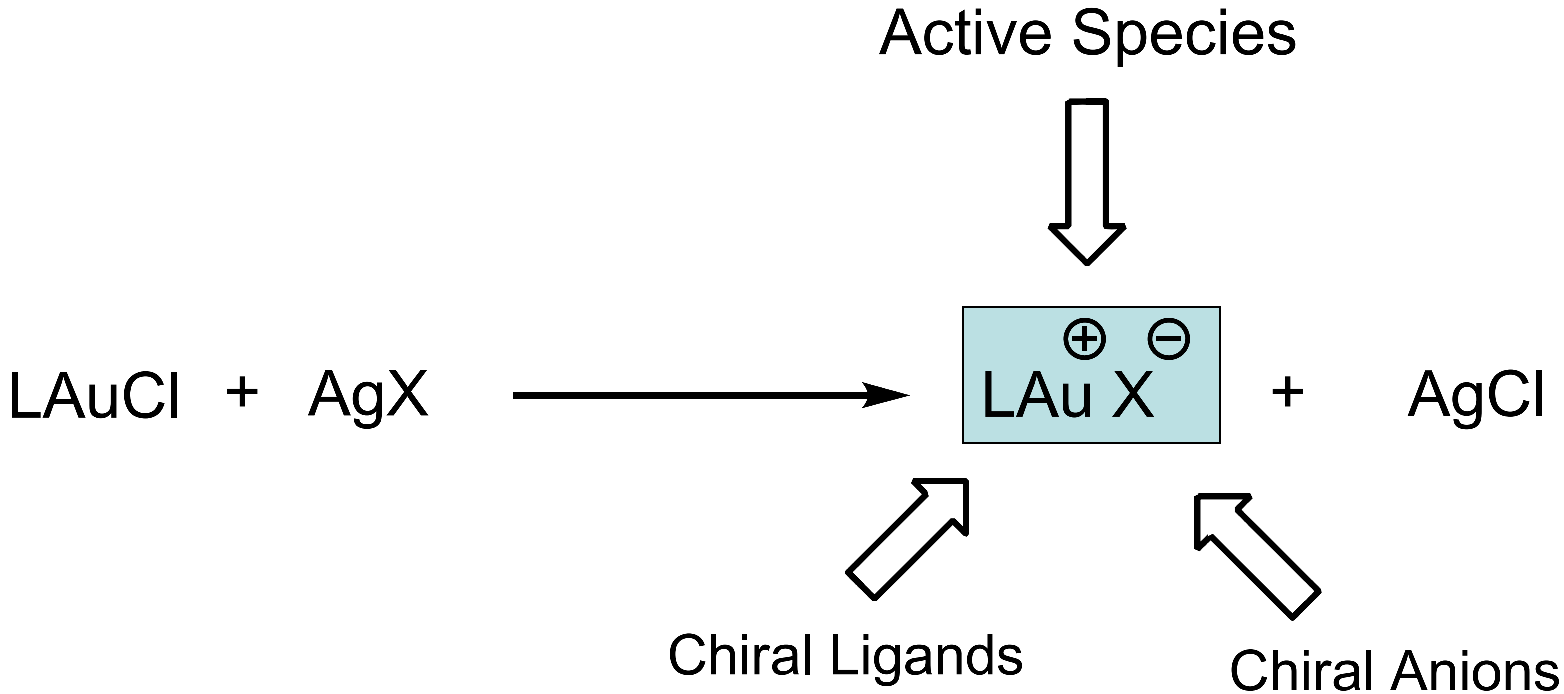
Yield: 76%
ee: 96%

Yield: 70%
ee: 98%

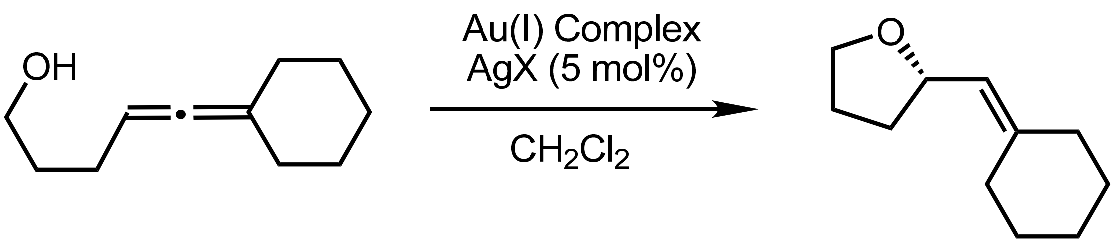
Yield: 66%
ee: 97%

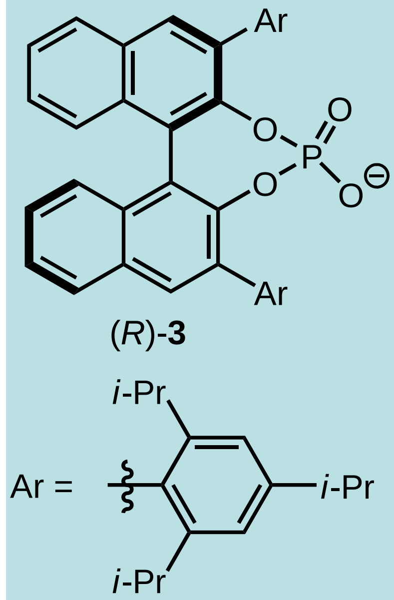
LaLonde, R. L.; Sherry, B. D.; Kang, E. J.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 2452.

Chirality in Active Species



Chiral Anion Directed Hydroalkoxylation

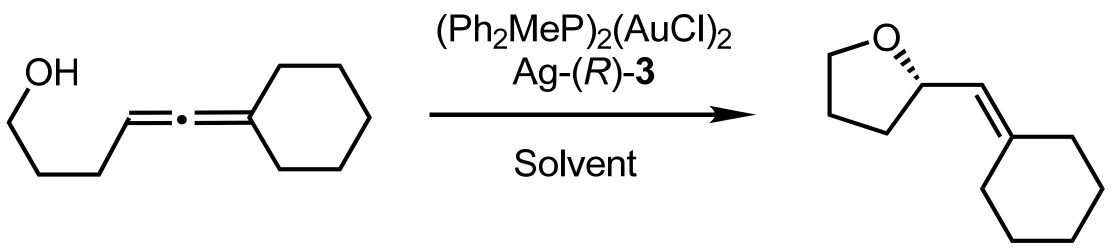


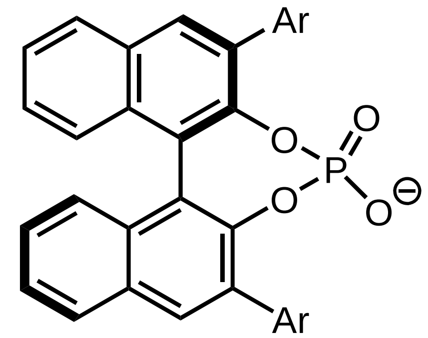


Au(I) Complex	X	Yield (%)	*ee* (%)
Ph_3PAuCl (5 mol%)	(*R*)-**3**	89	48
$(Ph_2MeP)_2(AuCl)_2$ (2.5 mol%)	(*R*)-**3**	76	65

Hamilton, G. L.; Kang, E. J.; Mba, M.; Toste, F. D. *Science*, **2007**, *317*, 496.

Screening for Solvents



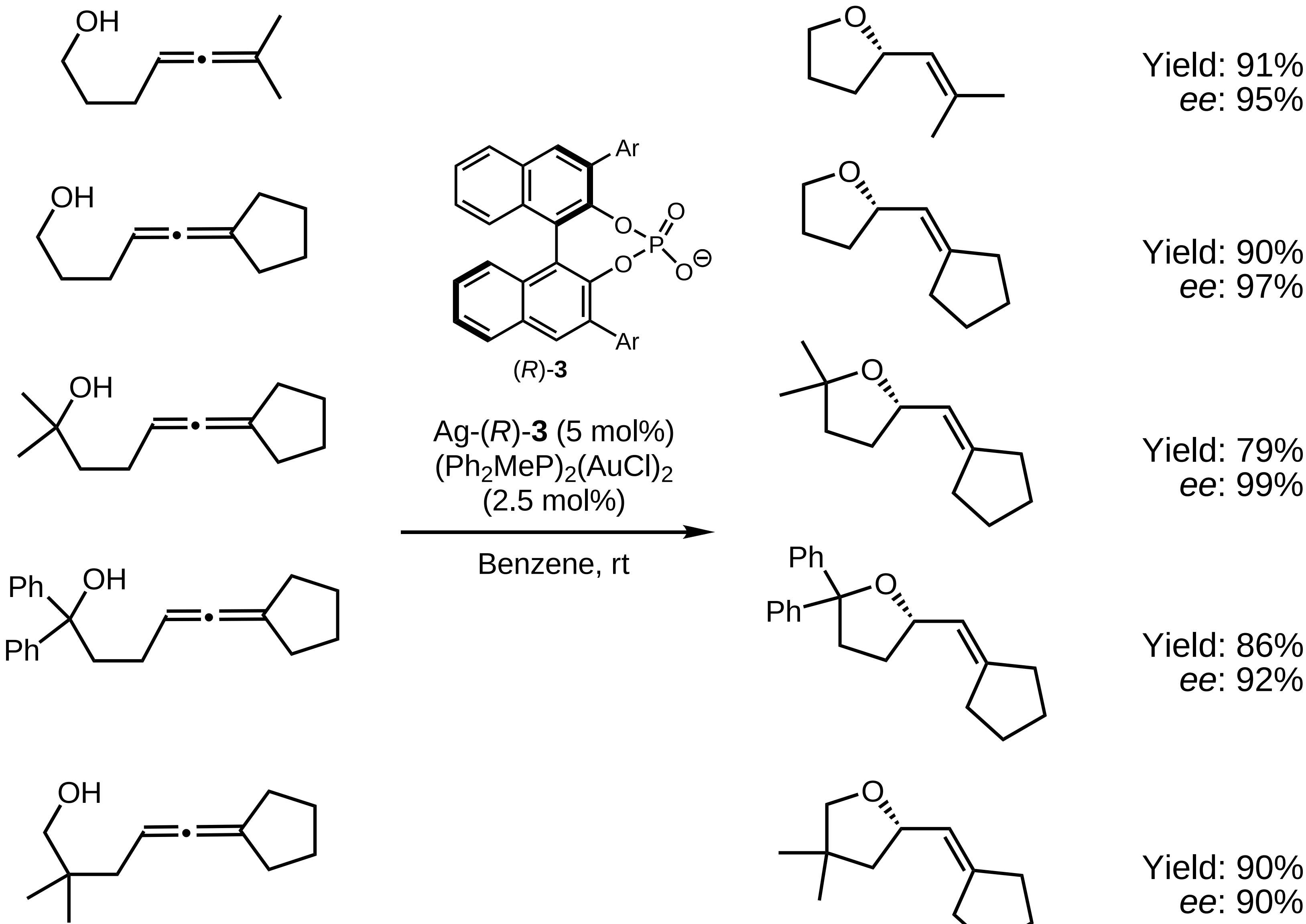


(*R*)-**3**

Solvent	Yield (%)	ee (%)
Nitromethane	60	18
Acetone	71	37
Dichloromethane	76	65
Tetrahydrofuran	83	76
Benzene	90	97

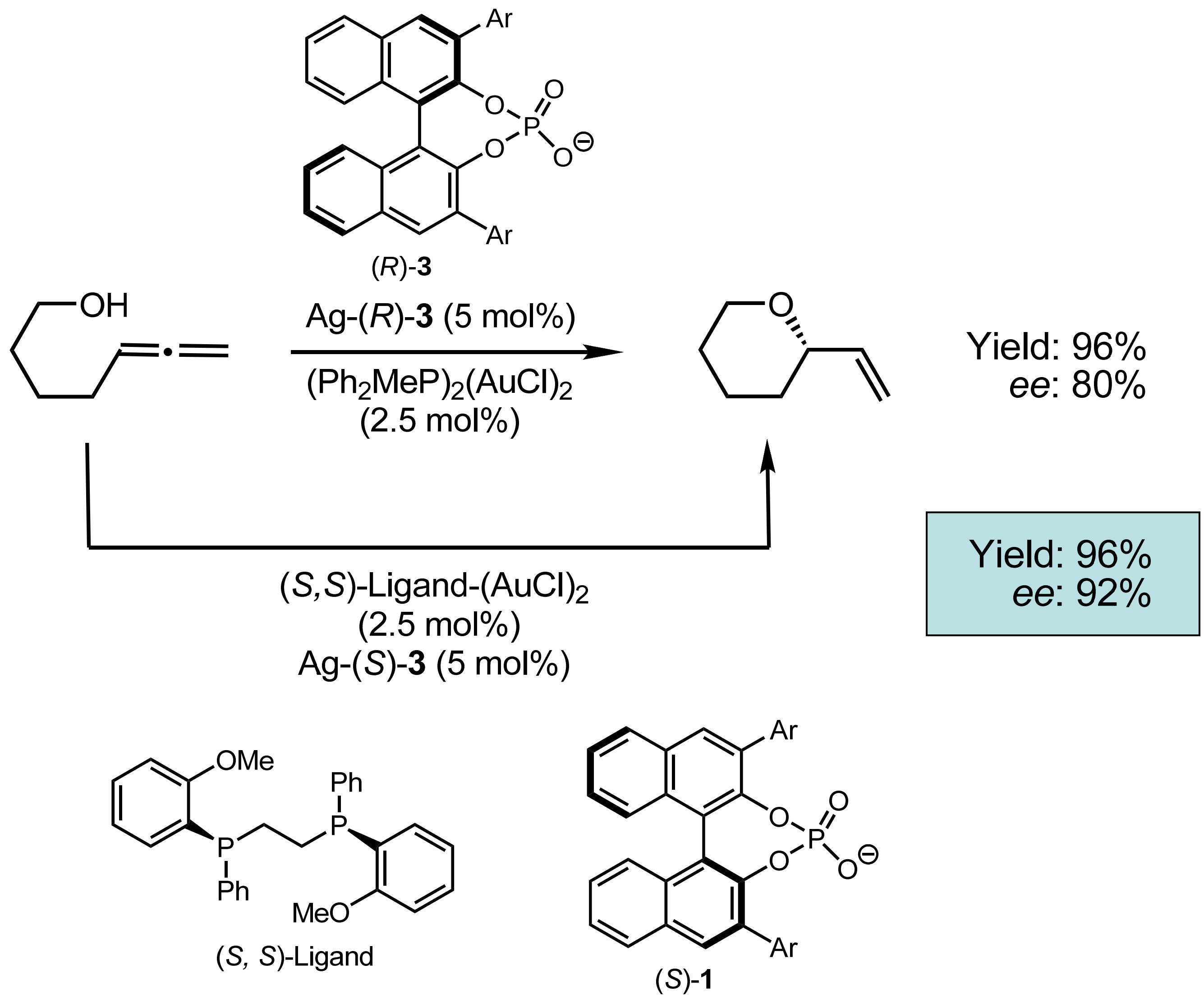
Hamilton, G. L.; Kang, E. J.; Mba, M.; Toste, F. D. *Science*, **2007**, *317*, 496.

Substrate Scope for Hydroalkoxylation



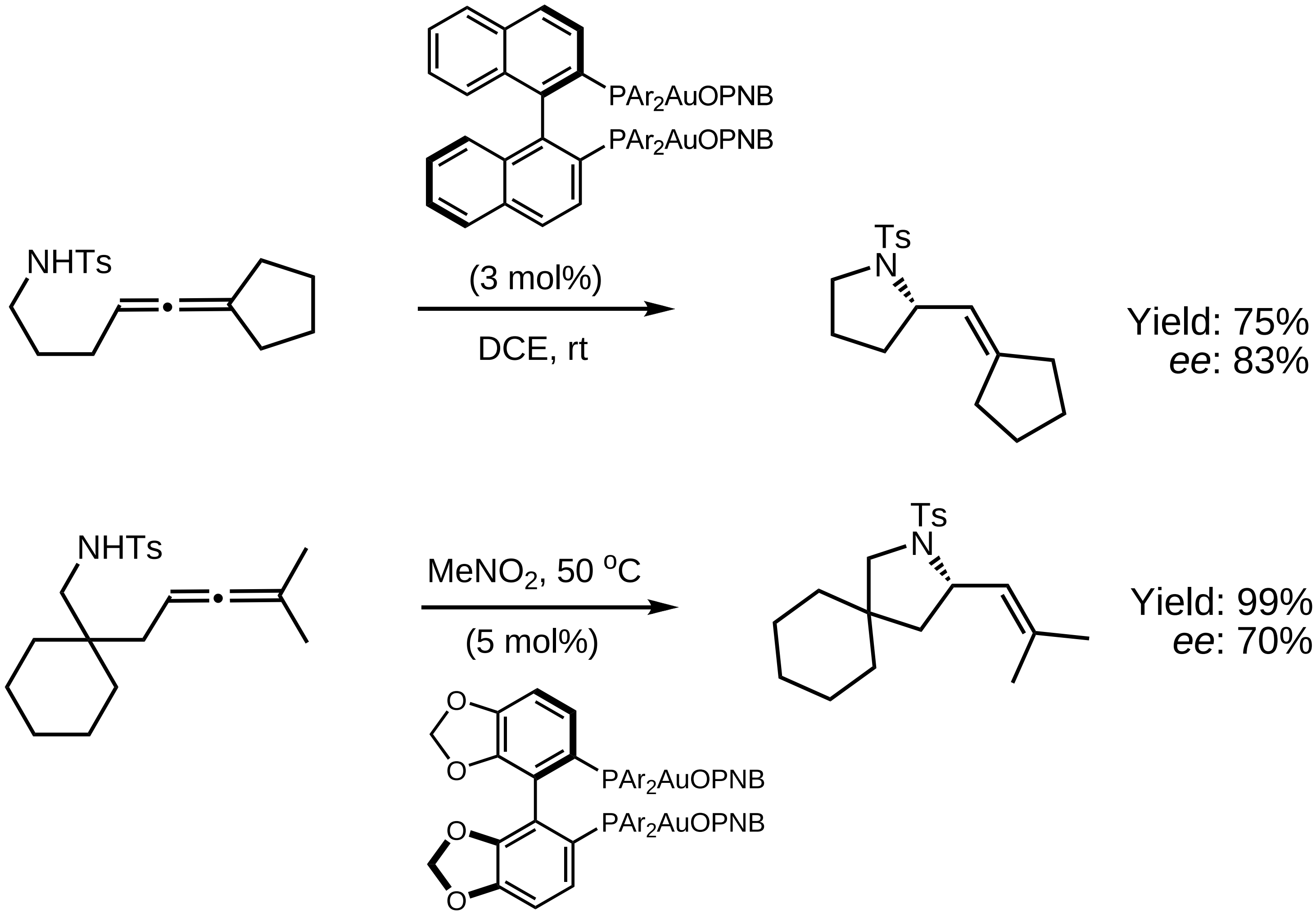
Hamilton, G. L.; Kang, E. J.; Mba, M.; Toste, F. D. *Science*, **2007**, *317*, 496.

Matched Case for Hydroalkoxylation



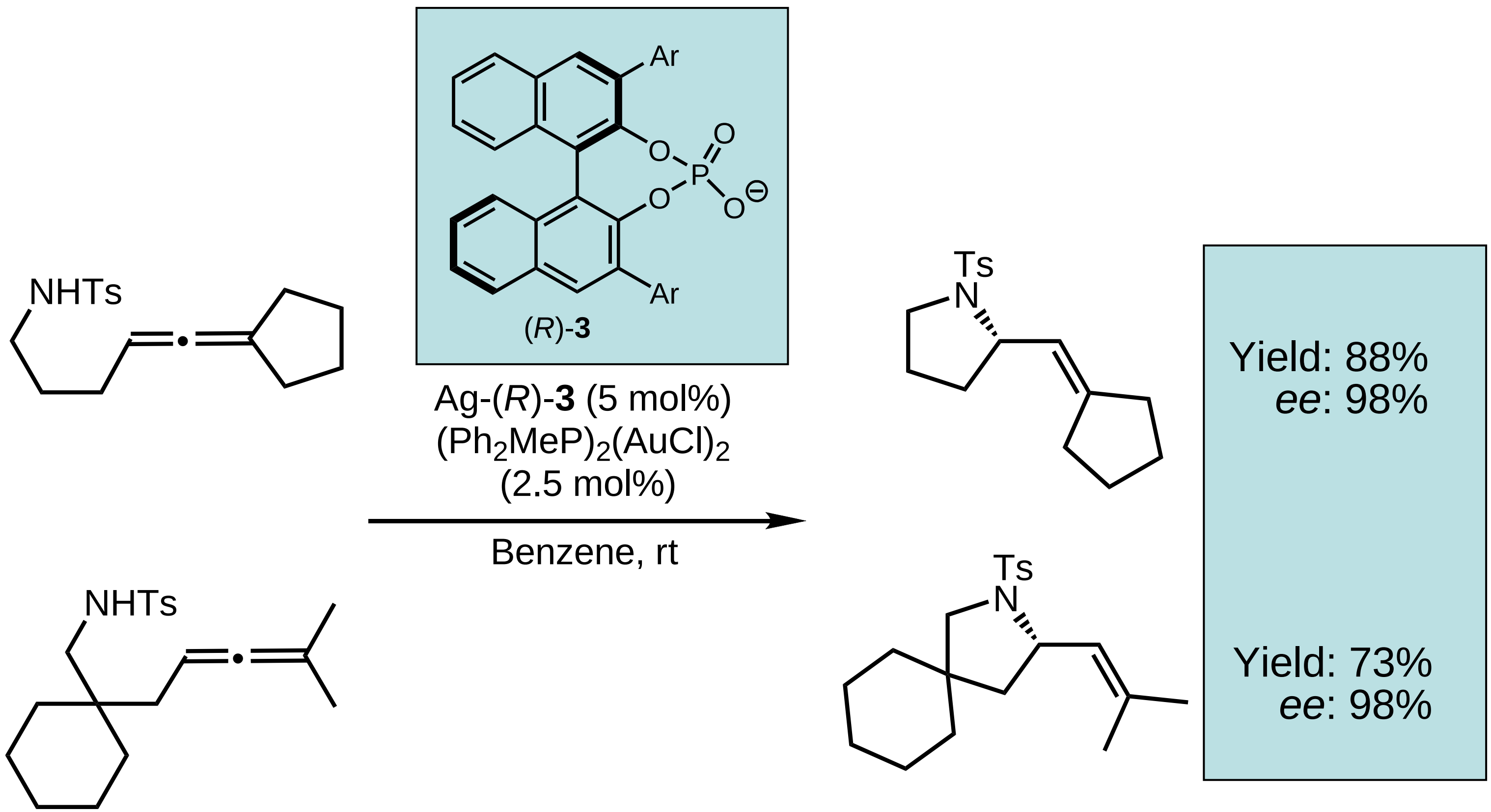
Hamilton, G. L.; Kang, E. J.; Mba, M.; Toste, F. D. *Science*, **2007**, *317*, 496.

Hydroamination Using Chiral Ligands



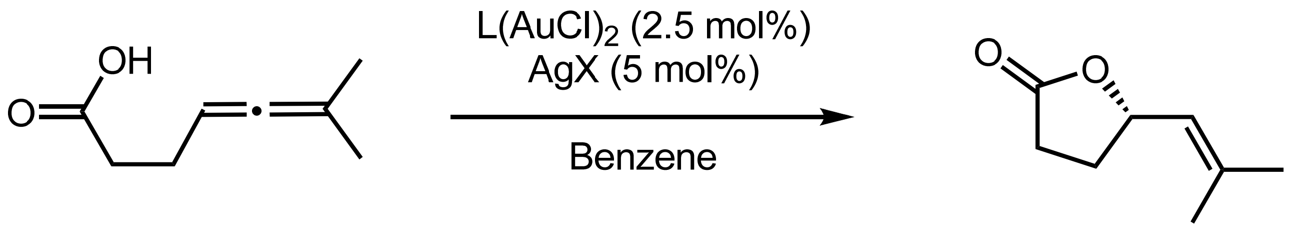
LaLonde, R. L.; Sherry, B. D.; Kang, E. J.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 2452.

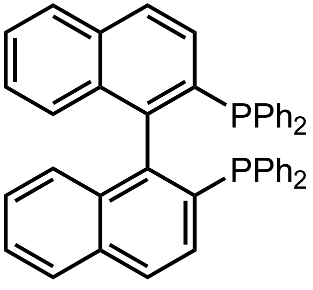
Hydroamination Using Chiral Counterion



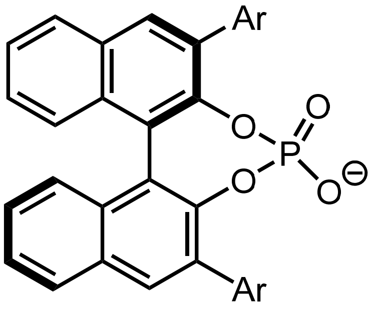
Hamilton, G. L.; Kang, E. J.; Mba, M.; Toste, F. D. *Science*, **2007**, *317*, 496.

Matched and Mismatched Case in Hydrocarboxylation





4



(*R*)-**3**

L	X	Yield (%)	ee (%)
(*R*)-**4**	4-(NO_2)-C_6H_3-$COO^{\ominus}$	80	-38
$(Ph_2MeP)_2$	(*R*)-**3**	89	12
(*S*)-**4**	(*R*)-**3**	88	82
(*R*)-**4**	(*R*)-**3**	91	-3

Hamilton, G. L.; Kang, E. J.; Mba, M.; Toste, F. D. *Science*, **2007**, *317*, 496.

Potentials of Chiral Counterion Strategy

Metal Cationic Catalyst

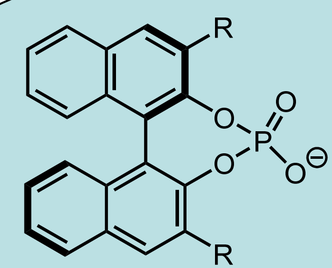
Ti^{4+} Al^{3+} Mg^{2+}

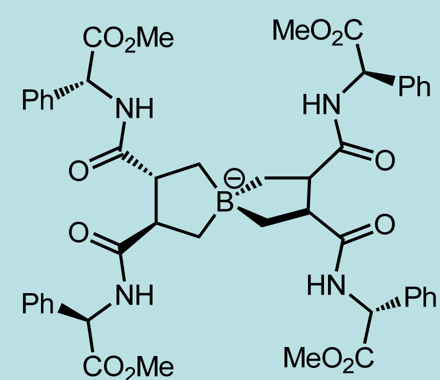
Cs^{+} Zn^{2+} Cu^{+}

Ni^{2+} Pt^{2+} Ag^{+}

....

Chiral Anions





Conclusions

- Gold(I) catalysts are superb Lewis acids for activation of alkynes.
- Several enantioselective reactions catalyzed by gold(I) catalysts have been reported.

In the future,

- More enantioselective reactions could be found to be catalyzed by gold(I) species.
- Work should be done in understanding the mechanism of the enantioselective reaction.

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