Catalytic asymmetric conjugate addition in the synthesis of β-amino acids

Literature Presentation

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12/03/2013

Asymmetric methods for the synthesis of β-amino acids

- Kinetic resolution;
- Stoichiometric use of chiral auxiliaries;
- Homologation of α-amino acids;
- Catalytic asymmetric methods.

Enantioselective Synthesis of β-amino acids, ed. E. Jurashi and V. Soloshnok, John Wiley & Sons, Inc., Hoboken,2005.

D. C. Cole, *Tetrahedron*, 1994, **50**, 9517.

G. Cardillo and C. Tomasini, *Chem. Soc. Rev*., 1996, **25**, 117.

E. Juaristi and H. Lopez-Ruiz, *Curr. Med. Chem*., 1999, **6**, 983.

D. Seebach and co-workers, *Synthesis*, 2009, 1.

G. Lalais and D. Seebach, *Biopolymers*, 2004, **76**, 206.

D. Seebach and co-workers, *Chem. Biodiversity*, 2004, **1**, 1111.

J.-A. Ma, *Angew. Chem. Int. Ed*., 2003, **42**, 4290.

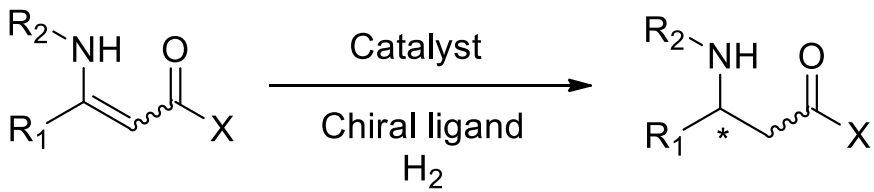
Catalytic asymmetric methods involve use of

- Transition metals;
- Organocatalysts;
- Biocatalysts.

B. L. Feringa and co-workers, *Chem. Soc. Rev*., 2010, **39**, 1656.
J.-A. Ma, *Angew. Chem. Int. Ed*., 2003, **42**, 4290.

Metal catalysis includes

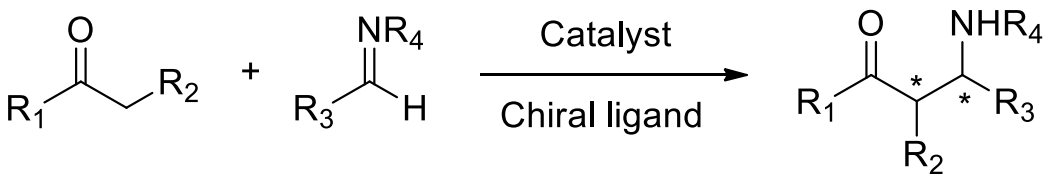
- Catalytic asymmetric hydrogenation



Catalyst: Rh, Ru, Ir

B. L. Feringa and co-workers, *Chem. Soc. Rev.*, 2010, **39**, 1656.

- Mannich reaction



Catalyst: Pd, Zn, In, La, Ni, Cu, Fe, Mg, Zr, Sc

B. L. Feringa and co-workers, *Chem. Soc. Rev.*, 2010, **39**, 1656.

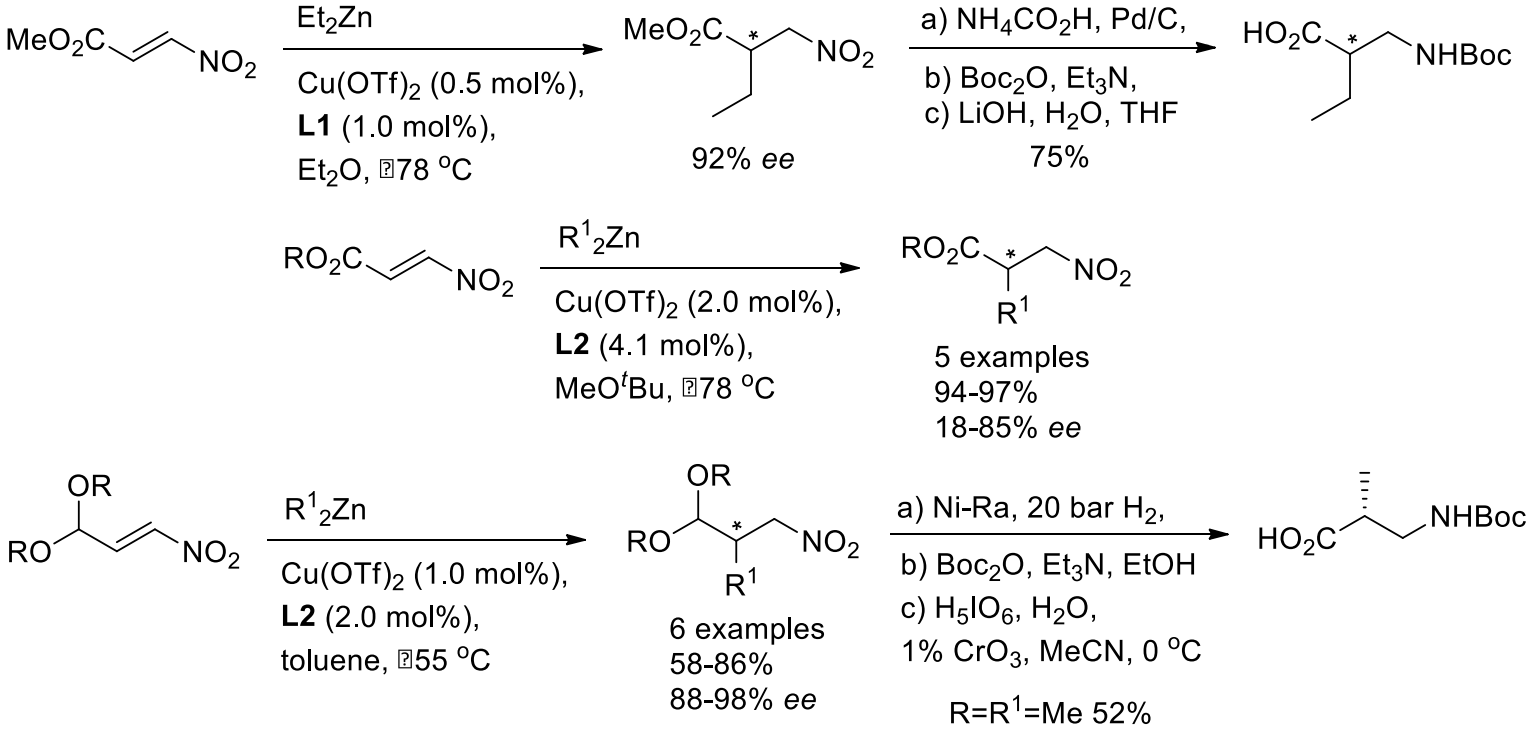
- Asymmetric conjugate addition of

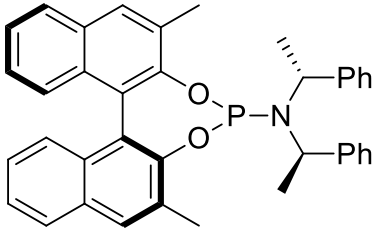
  - ✓ Carbon nucleophiles, such as organometallic reagents and Michael donors;

  - ✓ Nitrogen nucleophiles, such as aromatic amines, hydroxylamines and carbamates.

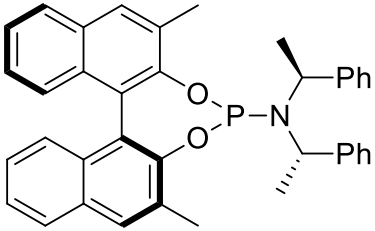
Carbon nucleophiles

- Cu-catalyzed addition of dialkylzinc reagents to 3-nitropropenoates





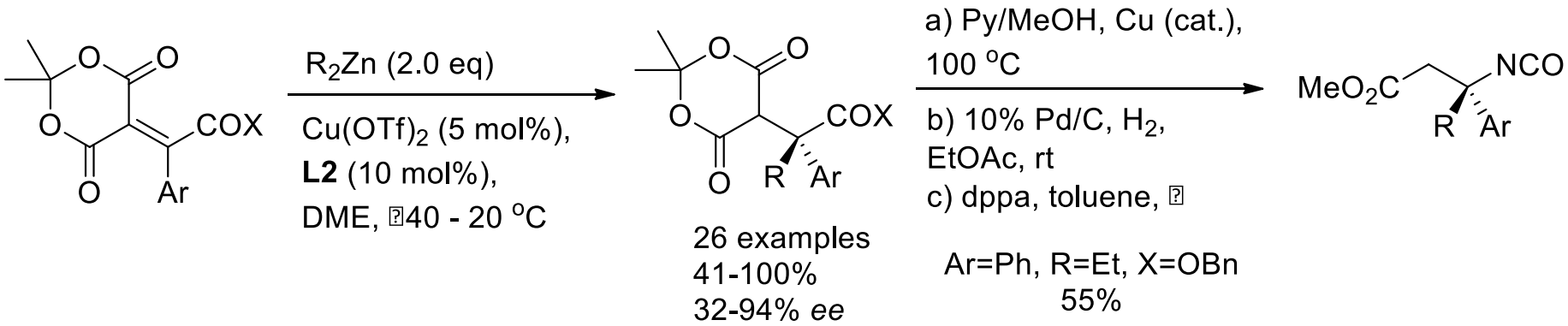
L1



L2

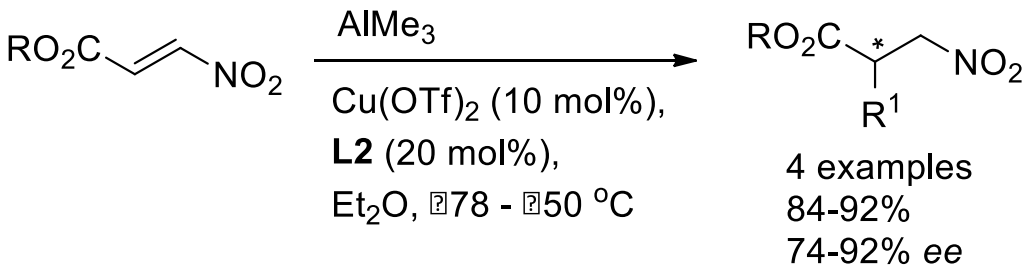
A. Rimkus and N. Sewald, *Org. Lett*., 2003, **5**, 79.
V. Wendisch and co-workers, *Tetrahedron: Asymmetry*, 2003, **14**, 189.
B. L. Feringa and co-workers, *J. Am. Chem. Soc*., 2003, **125**, 3700.

- Cu-catalyzed addition of dialkylzinc reagents to 2-aryl acrylates



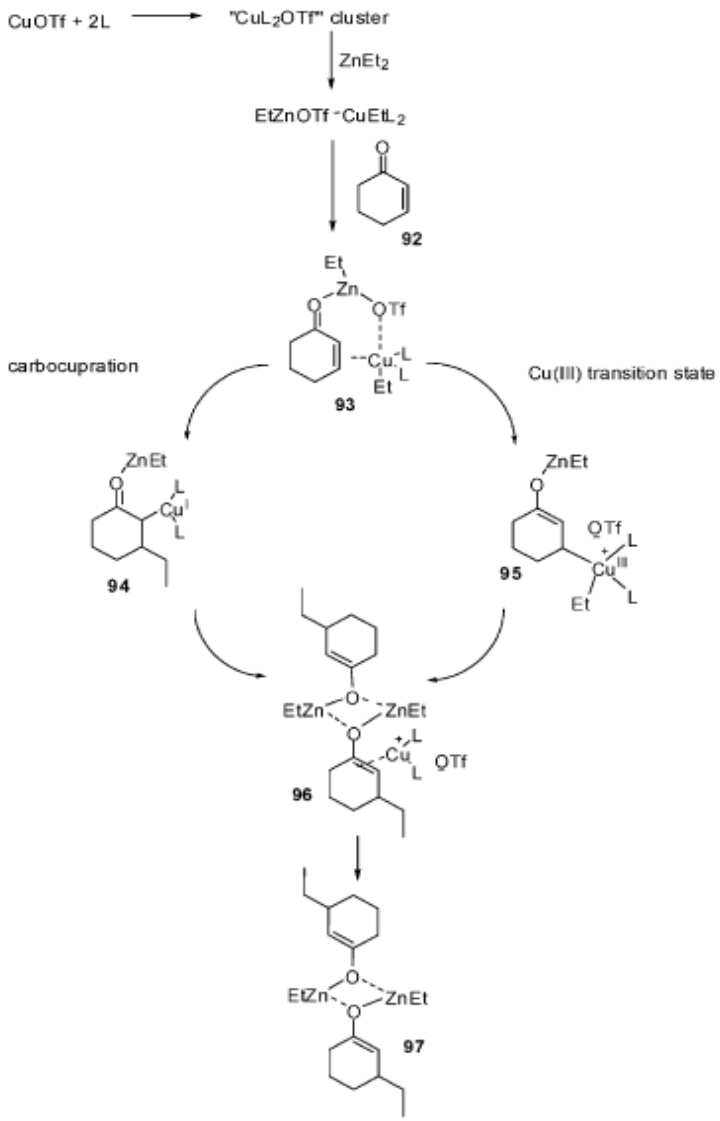
A. Wilsily and E. Fillion, *Org. Lett.*, 2008, **10**, 2801.

- Cu-catalyzed addition of trimethyl aluminium to a nitroolefin



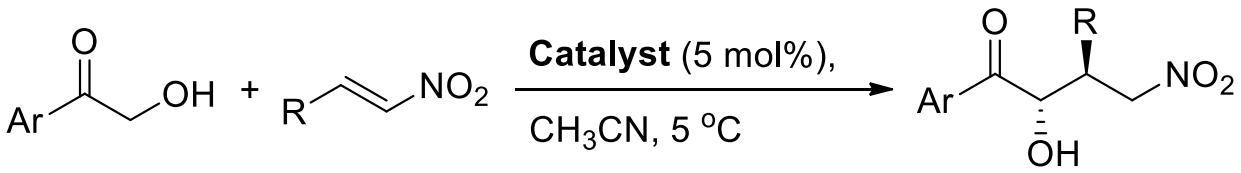
V. Wendisch and co-workers, *Tetrahedron: Asymmetry*, 2003, **14**, 3095.

Proposed catalytic cycle for Cu-catalyzed addition of dialkylzinc reagents (example on cyclohexenone)



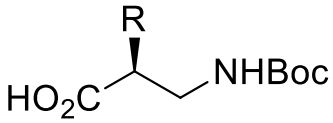
B. L. Feringa and co-workers, *Chem. Soc. Rev.*, 2009, **38**, 1039.

- Heteronuclear catalyst for the addition of α-hydroxyketones to nitroalkenes



10 examples
41-97%
76-92% *ee*

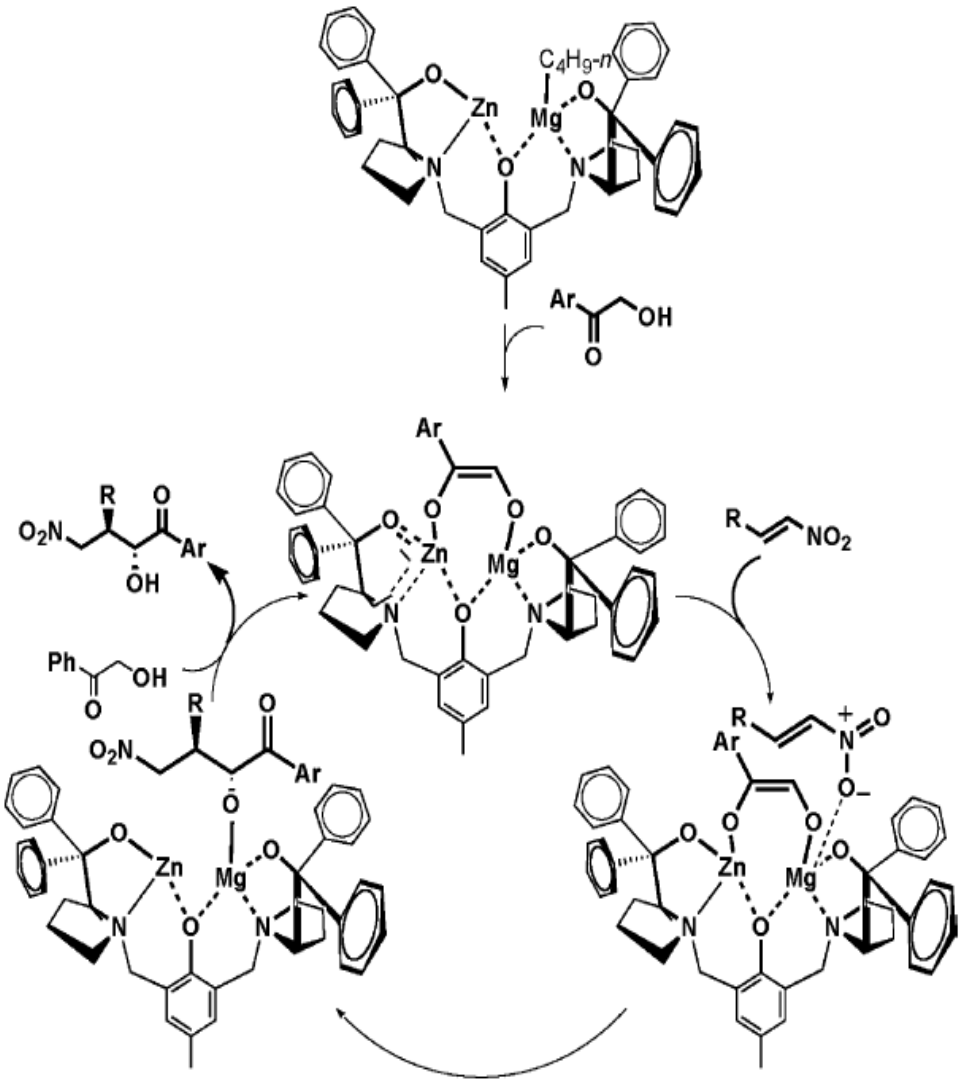
a) LAH, THF, 0 °C
b) Boc_2O, $NaHCO_3$, H_2O, EtOAc
c) $RuCl_3$ (cat.), $NaIO_4$, CCl_4, MeCN, H_2O



Ar, R=Ph, 25% over 3 steps

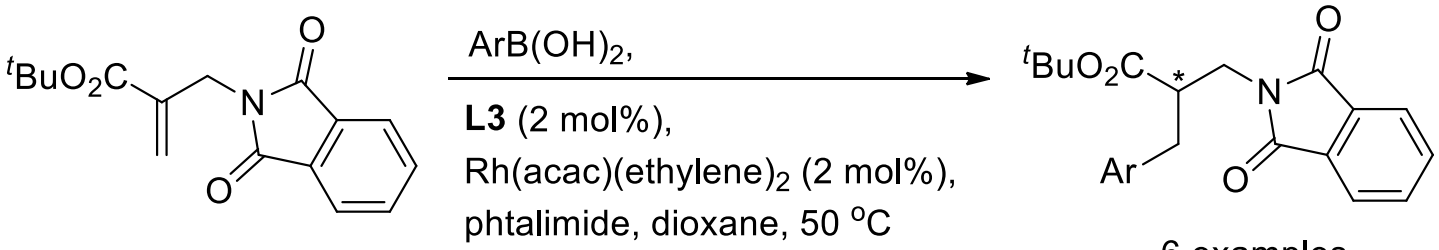
B. Trost and S. Hisaindee, *Org. Lett.*, 2006, **8**, 6003.

Proposed catalytic cycle

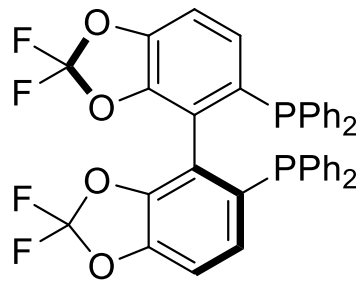


B. Trost and S. Hisaindee, *Org. Lett*., 2006, **8**, 6003.

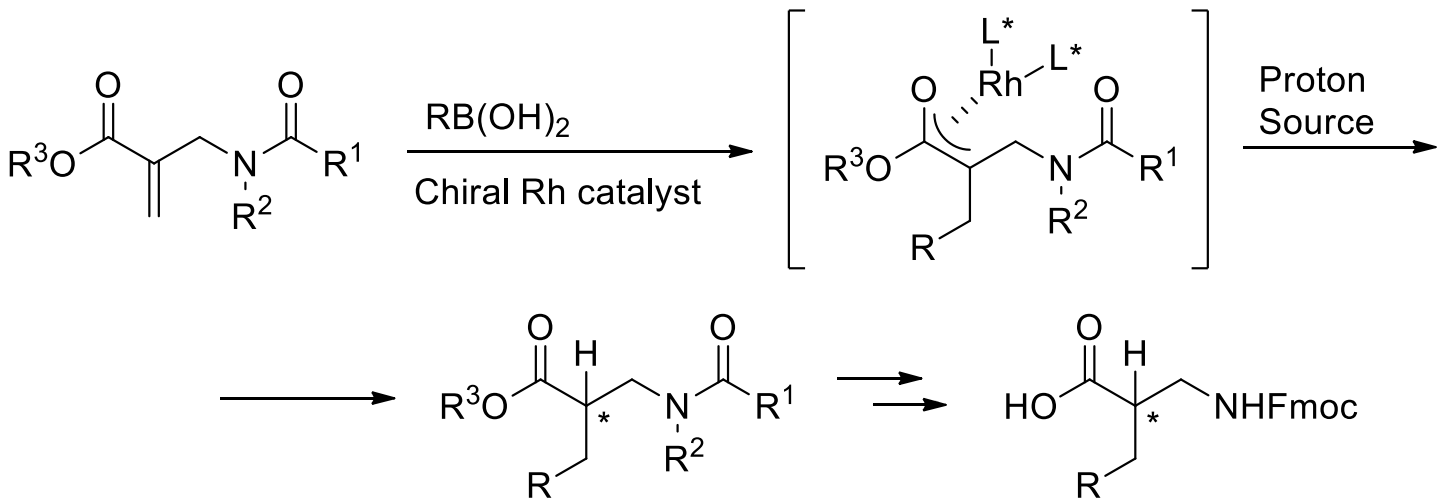
- Rh-catalyzed addition of boronic acids



6 examples
16-95%
63-95% *ee*

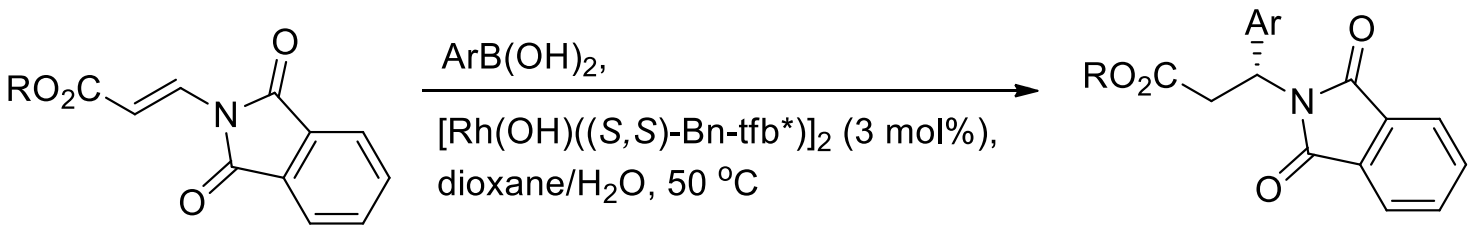


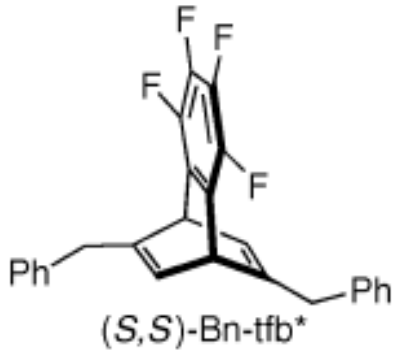
L3



M. P. Sibi and co-workers, *Org. Lett.*, 2005, **7**, 2571.

- Rh-catalyzed addition of boronic acids

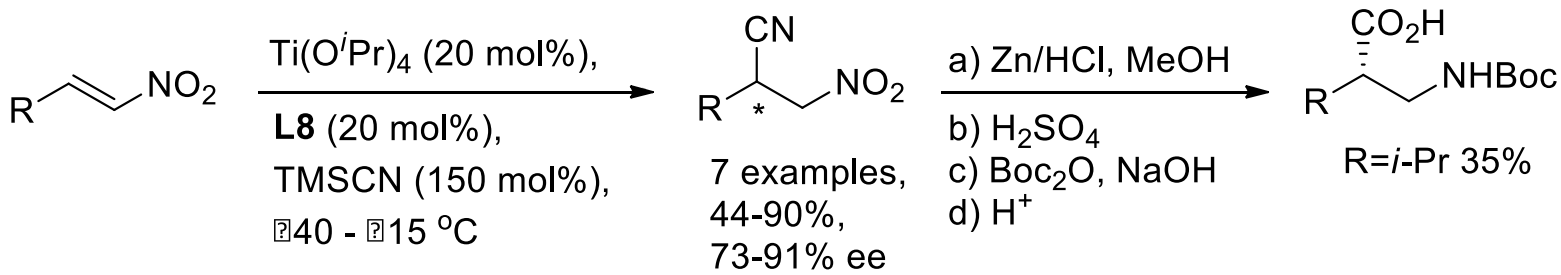


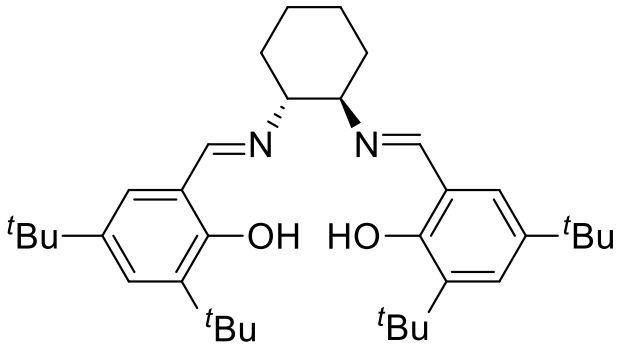


14 examples
81-99%
93-99% *ee*

T. Hayashi and co-workers, *J. Am. Chem. Soc.*, 2010, **132**, 464.

- Ti-catalyzed cyanation of nitroalkenes



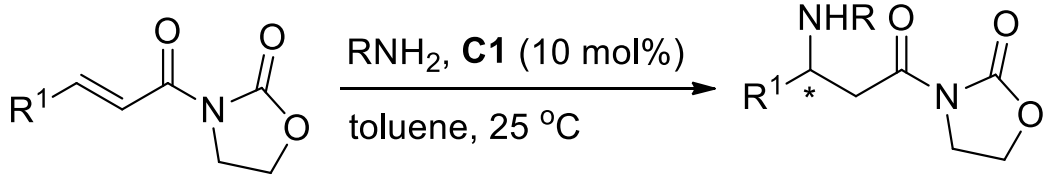


L8

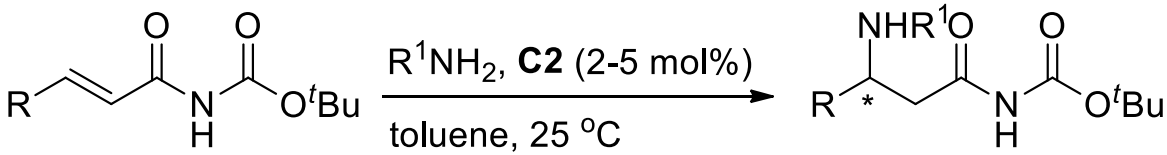
R. Wang and co-workers, *Org. Biomol. Chem.*, 2012, **10**, 83.

Nitrogen nucleophiles

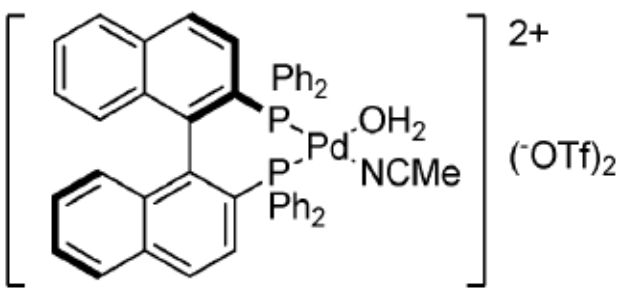
- Addition of aromatic amines to α,β-unsaturated oxazolidinones and imides



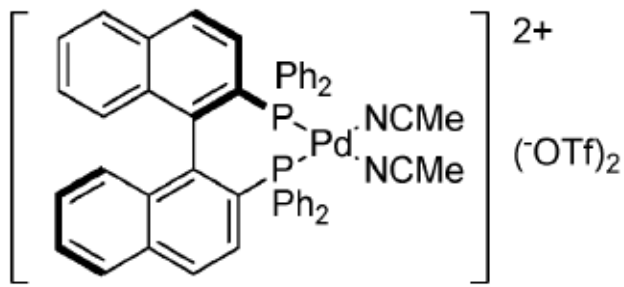
11 examples
52-96%
3-93% *ee*



12 examples
82-99%
16-99% *ee*



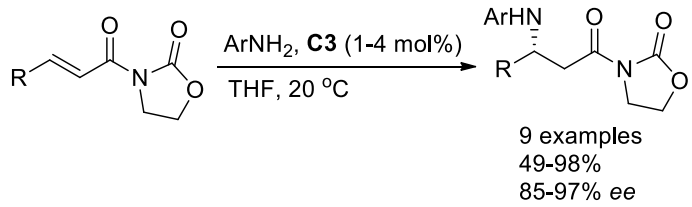
C1

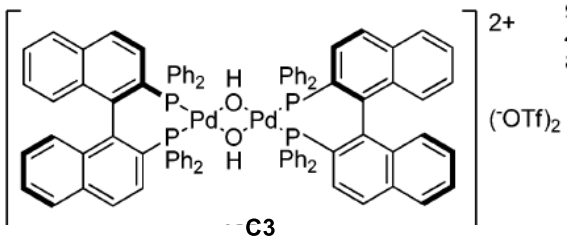


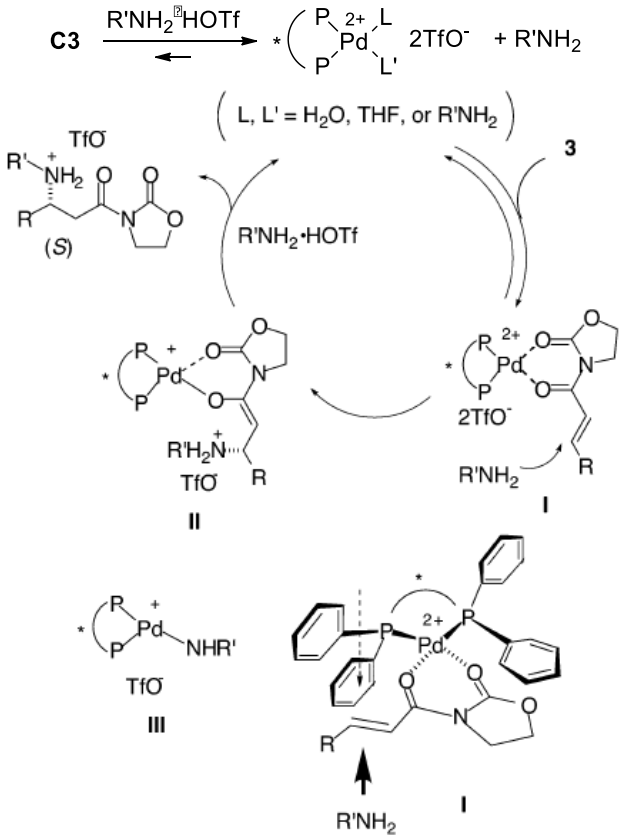
C2

K. Li and K. K. Hii, *Chem. Comm.*, 2003, 1132.
K. K. Hii and co-workers, *Eur. J. Org. Chem.*, 2004, 959.
K. K. Hii and co-workers, *Adv. Synth. Catal.*, 2006, **348**, 587.

- Addition of aromatic amines to α,β-unsaturated oxazolidinones and imides

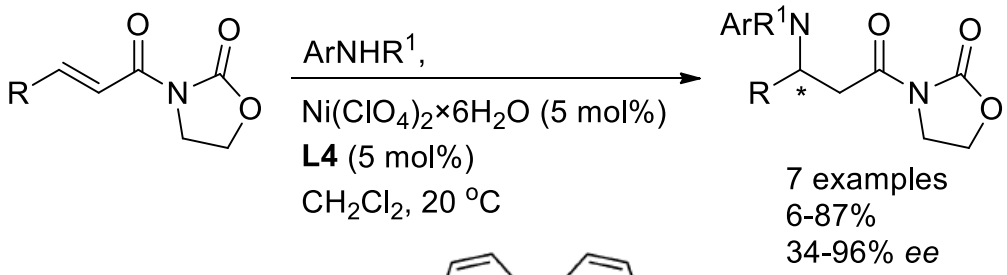


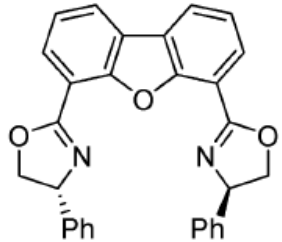




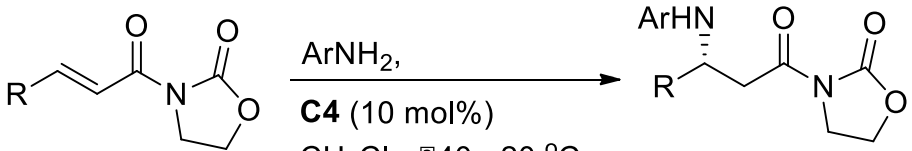
M. Sodeoka and co-workers,
Org. Lett., 2004, **6**, 1861

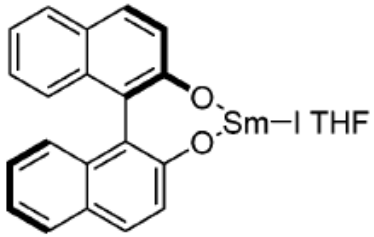
- Addition of aromatic amines to α,β-unsaturated oxazolidinones and imides





L4



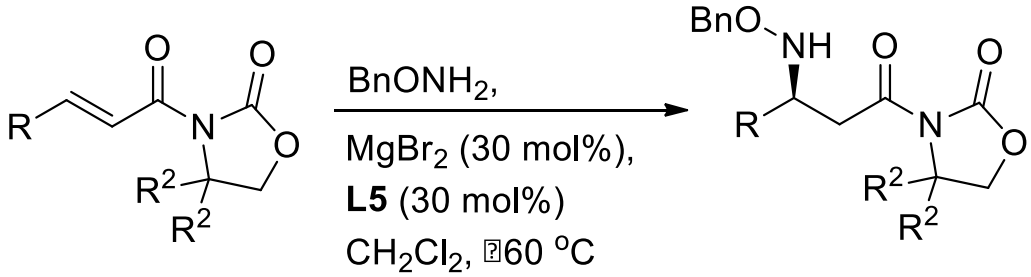


C4

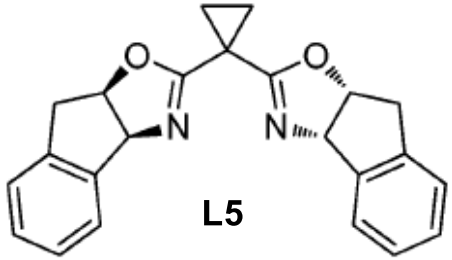
K. A. Jorgensen and co-workers, *Chem. Comm.*, 2001, 1240.

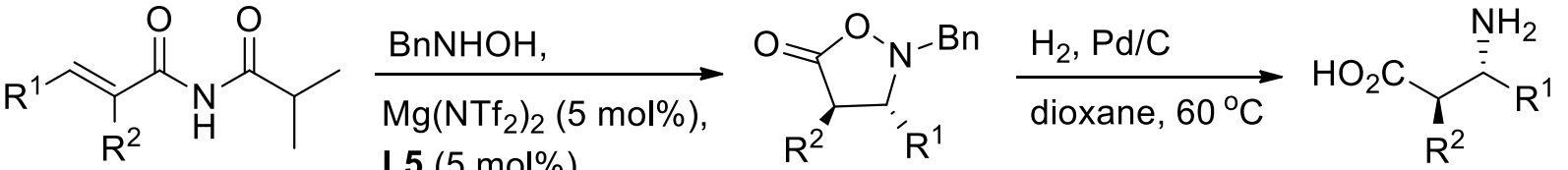
J. Collin and co-workers, *Eur. J. Org. Chem..*, 2008, 532.

- Addition of hydroxylamines to α,β-unsaturated oxazolidinones and imides



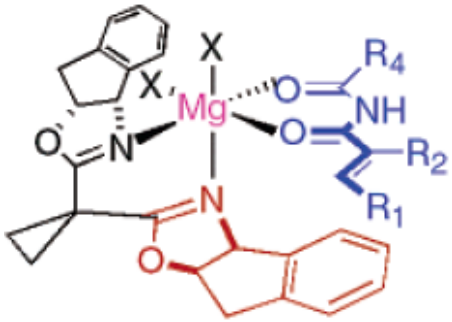
5 examples
66-87%
26-81% *ee*





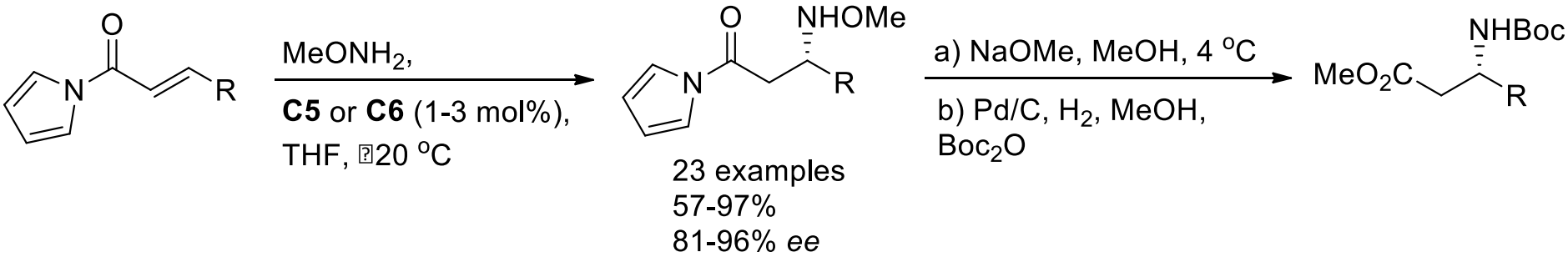
12 examples
28-95%
93-99% *de*
60-96% *ee*

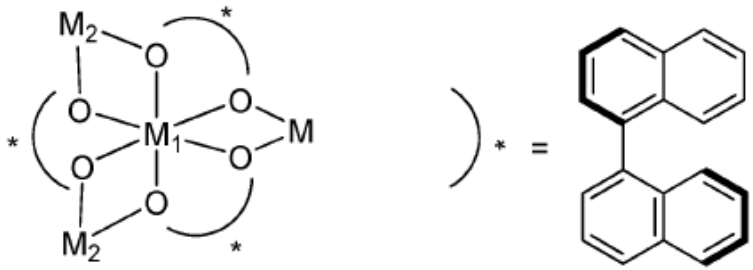
R^1=R^2=Me 90%



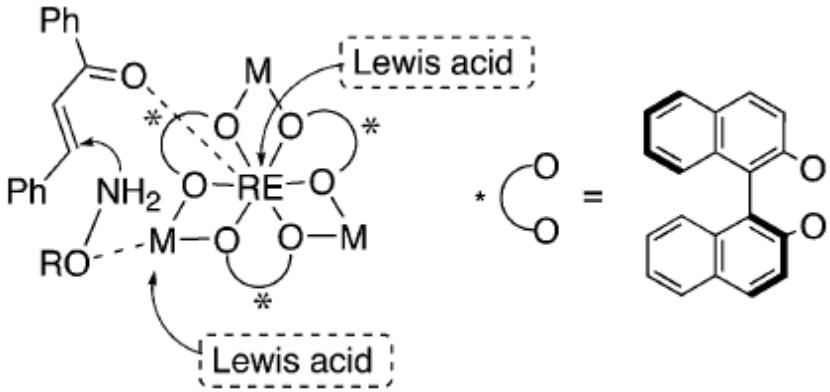
M. P. Sibi and co-workers, *Tetrahedron*, **58**, 2002, 8357.
M. P. Sibi and co-workers, *J. Am. Chem. Soc.*, **125**, 2003, 11796.

- Addition of hydroxylamines to α,β-unsaturated oxazolidinones and imides



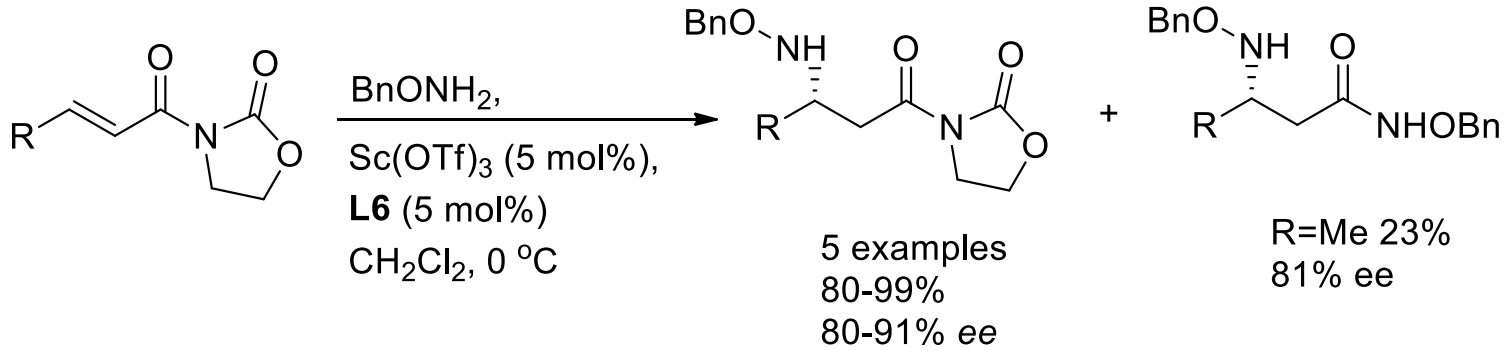


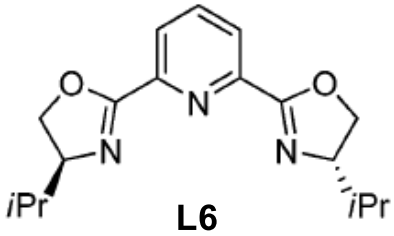
C5: M_1 (rare earth metal)=Y, M_2=Li
C6: M_1 (rare earth metal)=Dy, M_2=Li



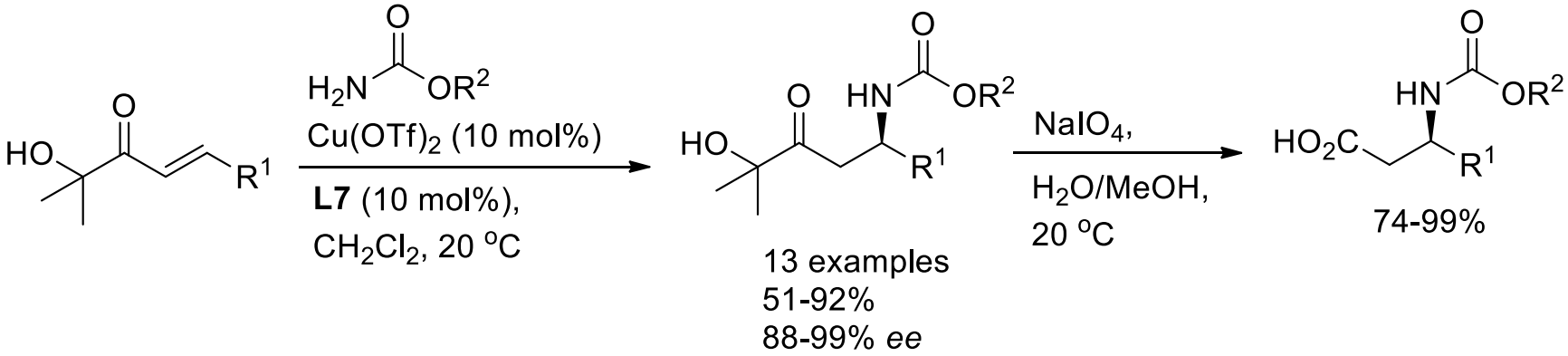
M. Shibasaki and co-workers, *J. Am. Chem. Soc.*, 2005, **127**, 13419.

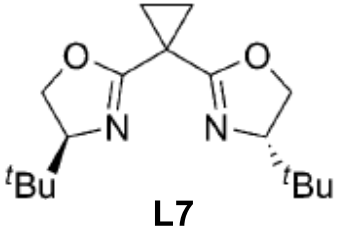
- Addition of hydroxylamines and carbamates to α,β-unsaturated oxazolidinones and imides





S. I. Fukuzawa and co-workers, *Synlett*, 2006, **7**, 1023.





C. Palomo and co-workers, *J. Am. Chem. Soc.*, 2004, **126**, 9188