4.6 Dual Activation on A Single Metal Center: Non-Activated Systems

4.6.1 Functionalization of Non-Activated Olefins

4.6.2 Metathesis

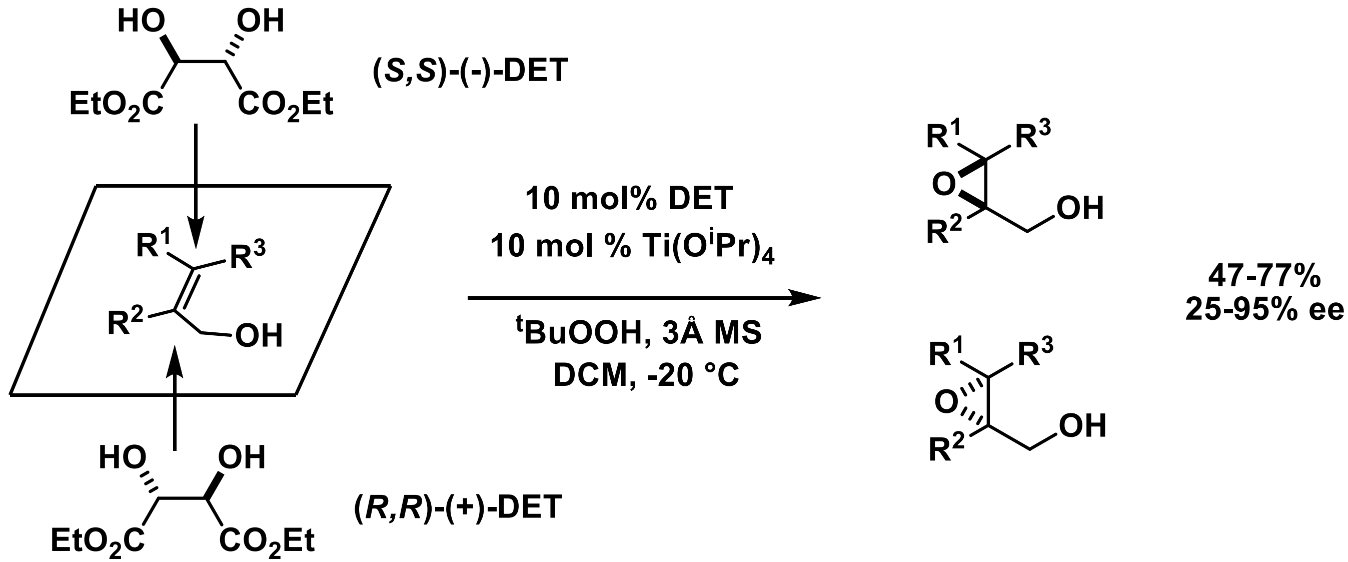
4.6.3 Cyclization and Cycloaddition Reactions

4.6.4 Cross-Coupling Reactions

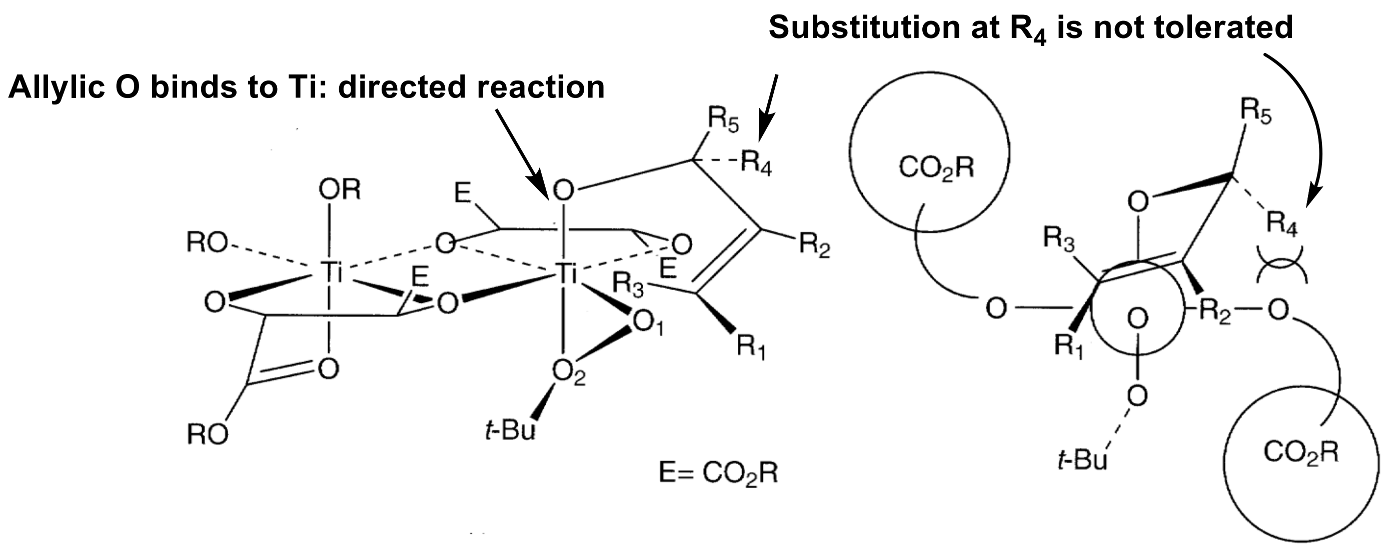
4.6.5 CH Functionalization

4.6.1.Functionalization of Olefins: Epoxidation

Sharpless Epoxidation



Model for Selectivity

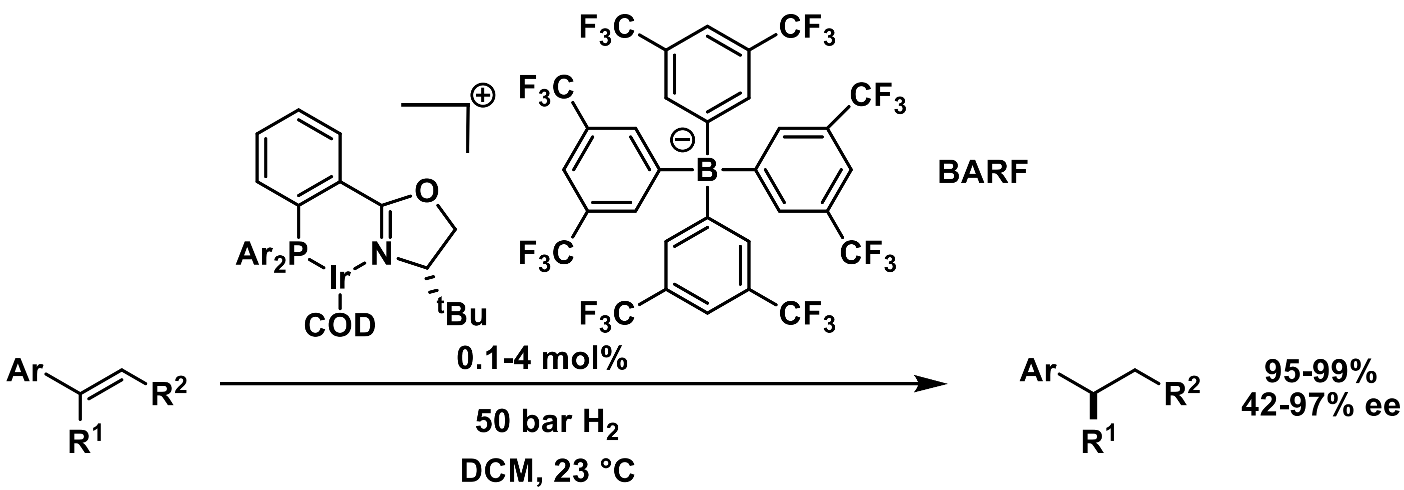


(The view down O^1-Ti bond axis)

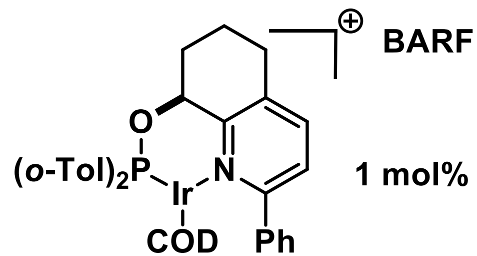
(1) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987,** *109,* 5765-5780.

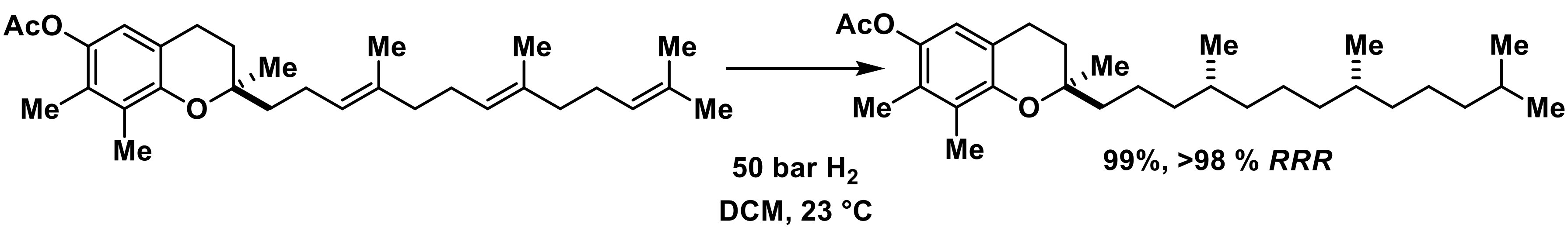
4.6.1.Functionalization of Olefins: Hydrogenation

Pfaltz: Asymmetric Hydrogenation of Non-Activated Olefins[1]



An Application: Synthesis of Tocopherol (Vitamin E) Derivatives[2]

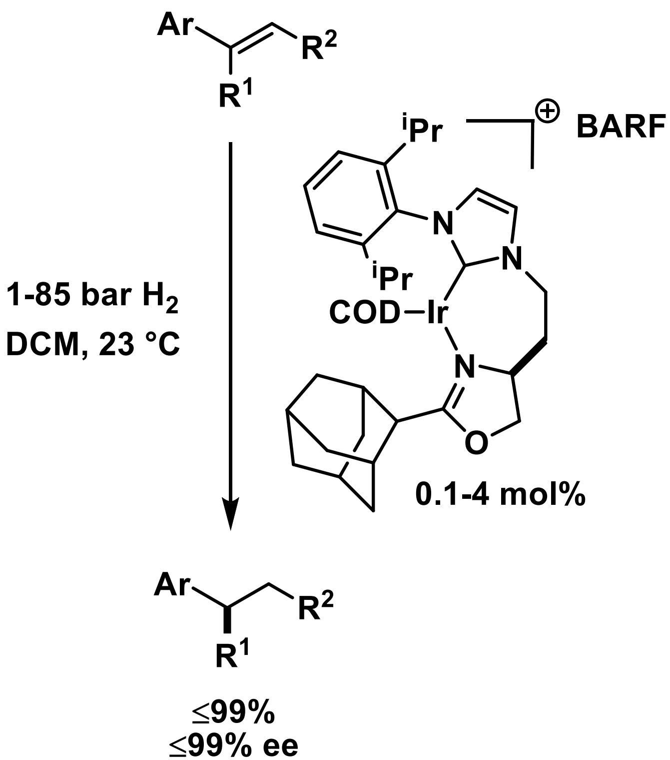




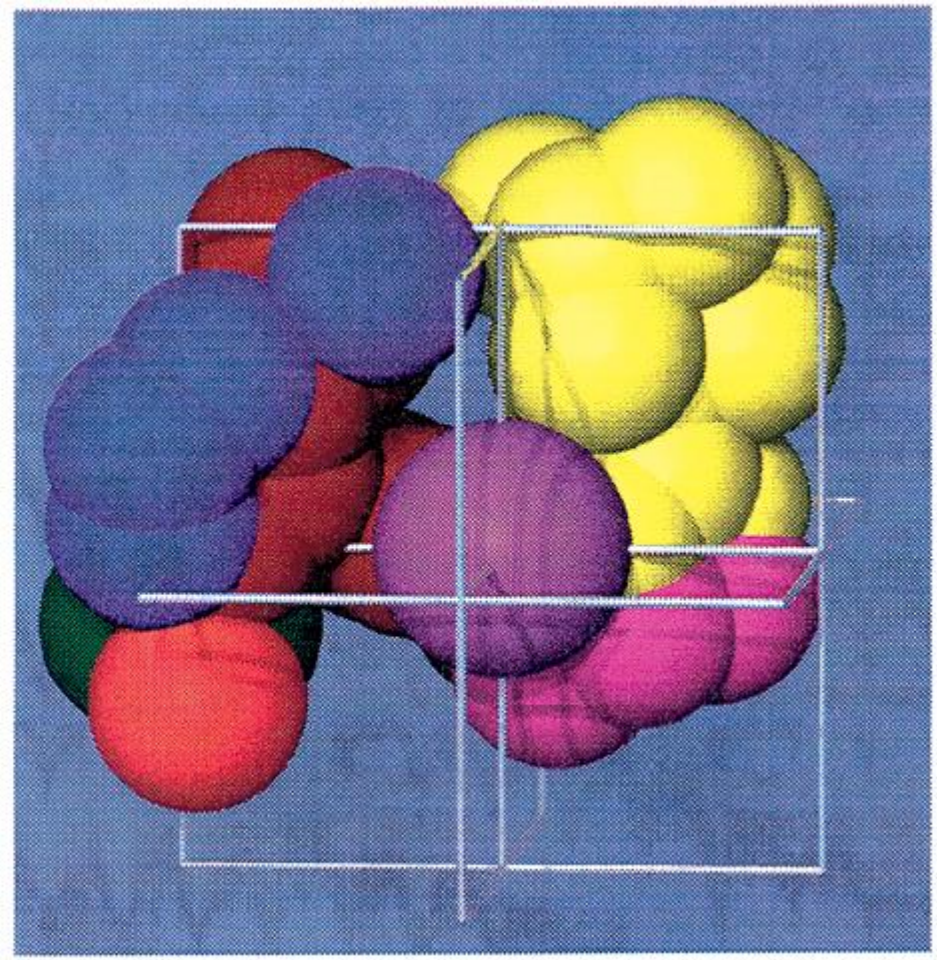
(1) Lightfoot, A.; Schnider, P.; Pfaltz, A. *Angew. Chem., Int. Ed.* **1998,** *37,* 2897-2899. (2) Bell, S.; Wustenberg, B.; Kaiser, S.; Menges, F.; Netscher, T.; Pfaltz, A. *Science* **2006,** *311,* 642-644.

4.6.1.Functionalization of Olefins: Hydrogenation

Burgess:Carbene-Oxazoline Ligands for Asymmetric Hydrogenation



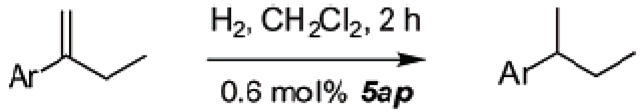
Catalyst Structure

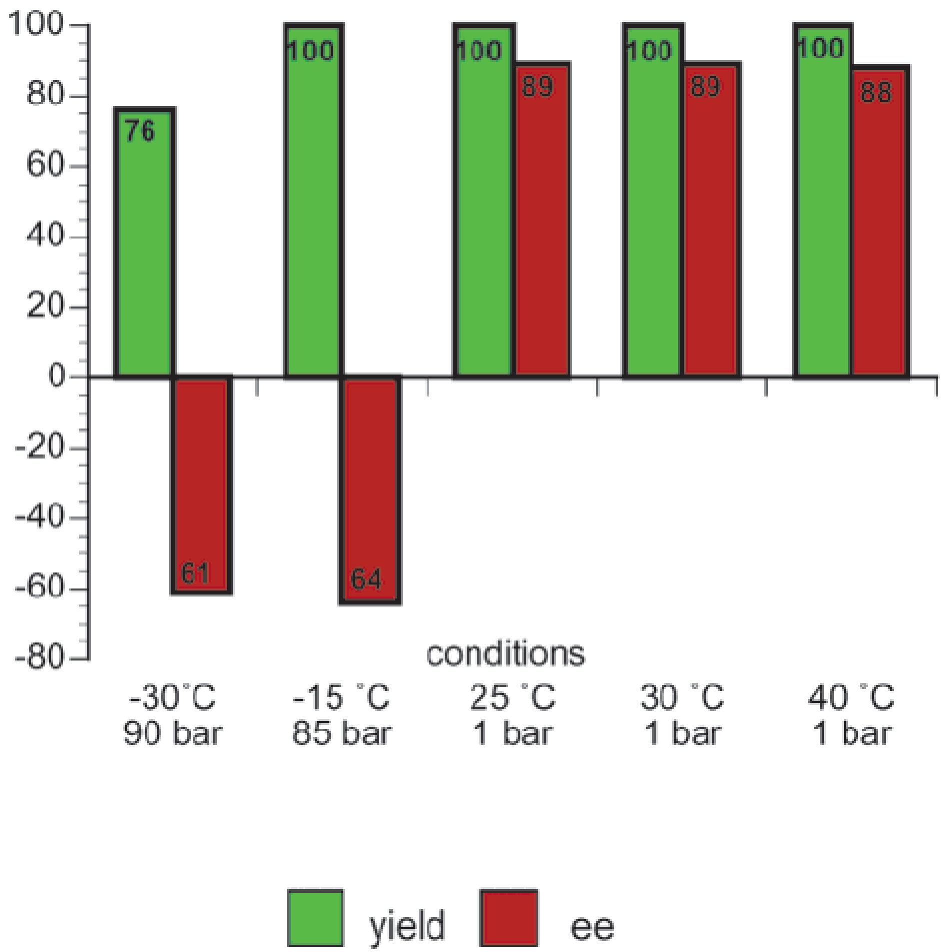


(1) Perry, M. C.; Cui, X. H.; Powell, M. T.; Hou, D. R.; Reibenspies, J. H.; Burgess, K. *J. Am. Chem. Soc.* **2003,** *125,* 113-123.

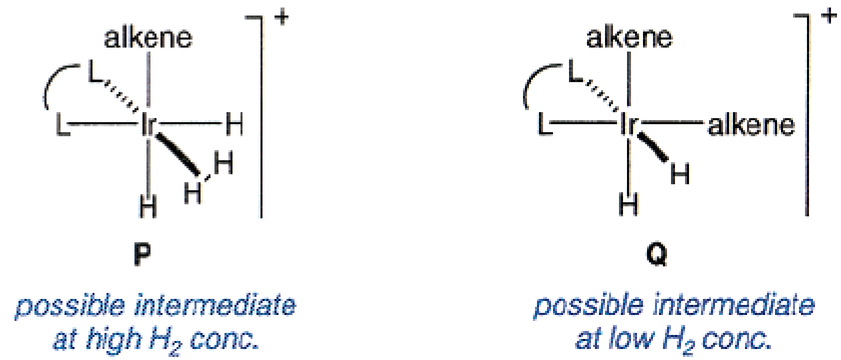
4.6.1.Functionalization of Olefins: Hydrogenation

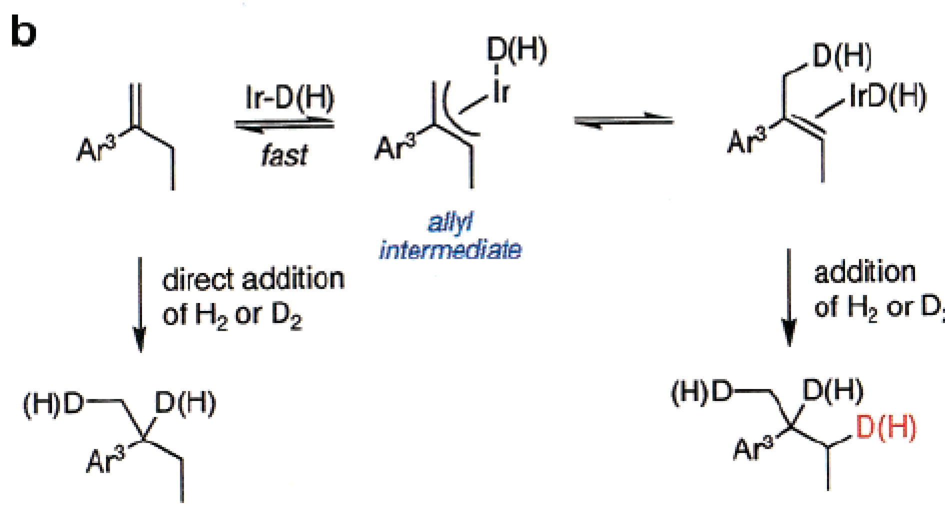
Influence of Pressure





Mechanistic Insights

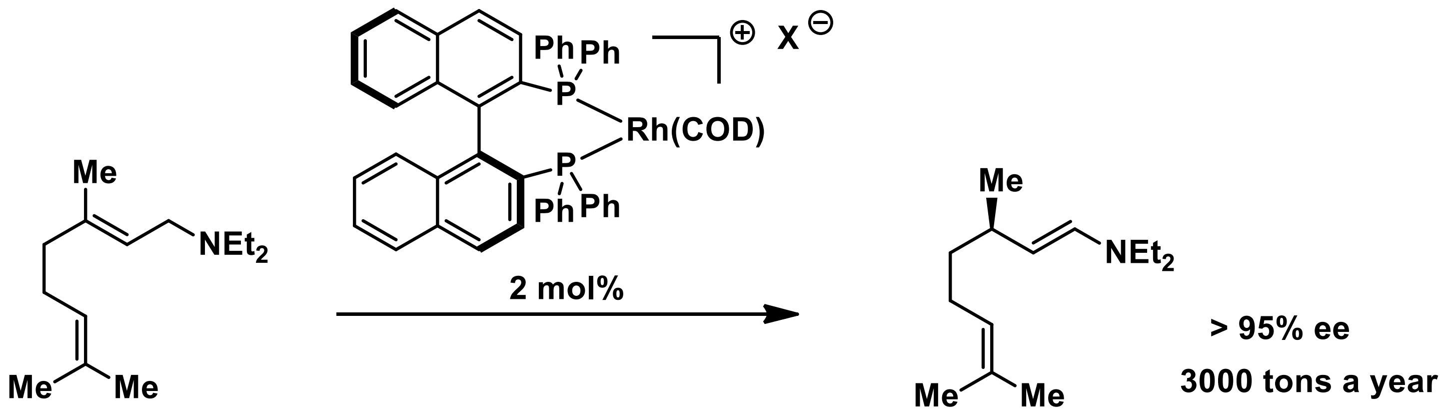




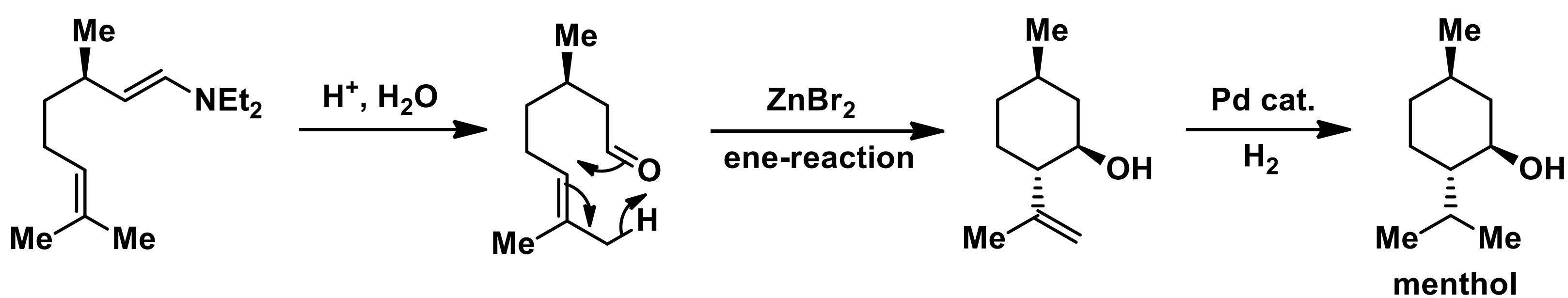
(1) Perry, M. C.; Cui, X. H.; Powell, M. T.; Hou, D. R.; Reibenspies, J. H.; Burgess, K. *J. Am. Chem. Soc.* **2003,** *125,* 113-123.

4.6.1.Functionalization of Olefins: Isomerization

Isomerization of allylamine: the Takasago process



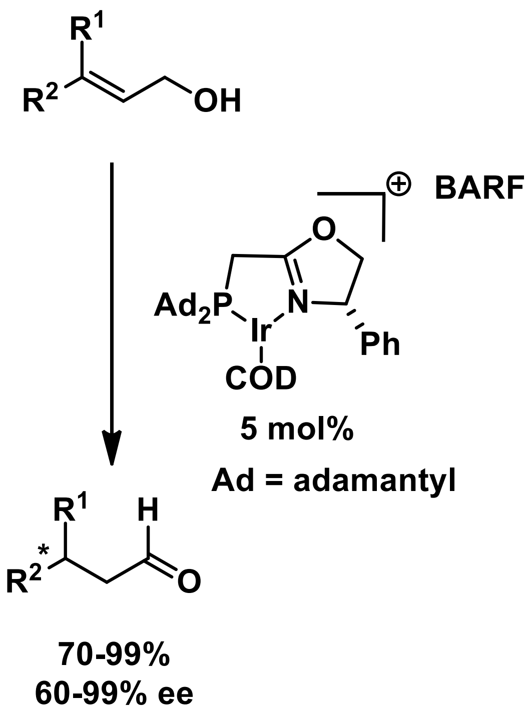
Synthesis of menthol

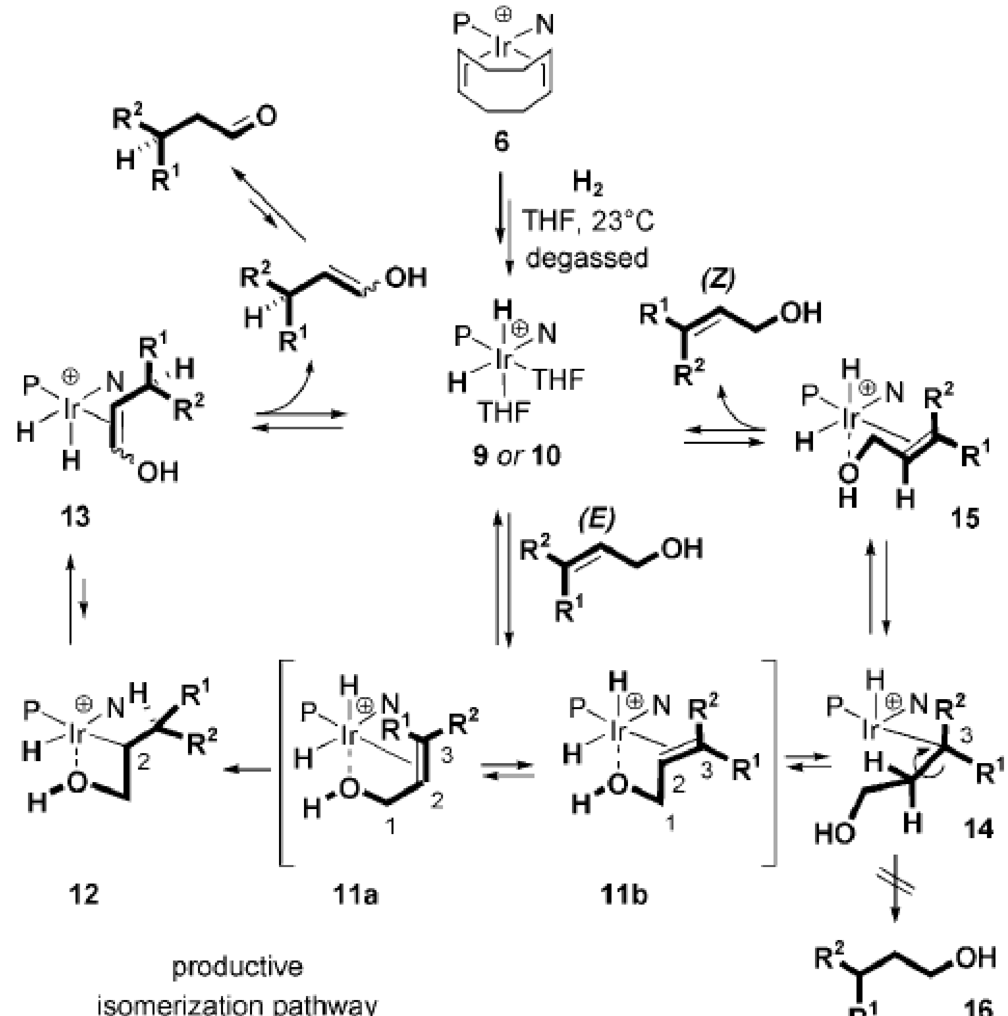


Inoue, S.; Takaya, H.; Tani, K.; Otsuka, S.; Sato, T.; Noyori, R. *J. Am. Chem. Soc.* **1990**, *112*, 4897-4905.

4.6.1.Functionalization of Olefins: Isomerization

Isomerization of allylalcohols: Mazet

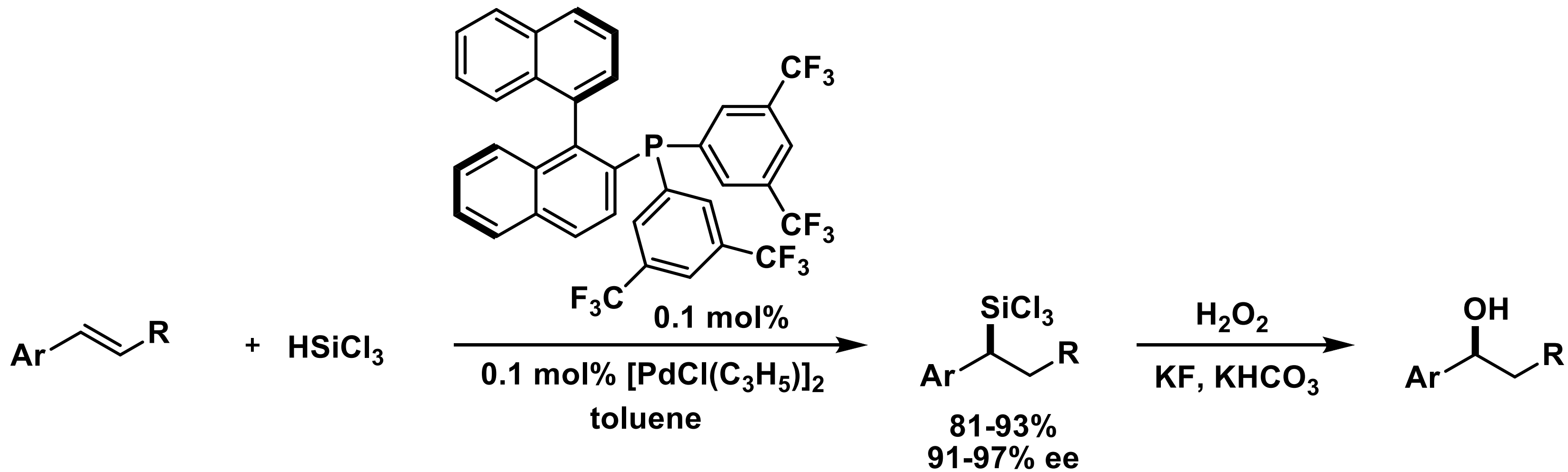




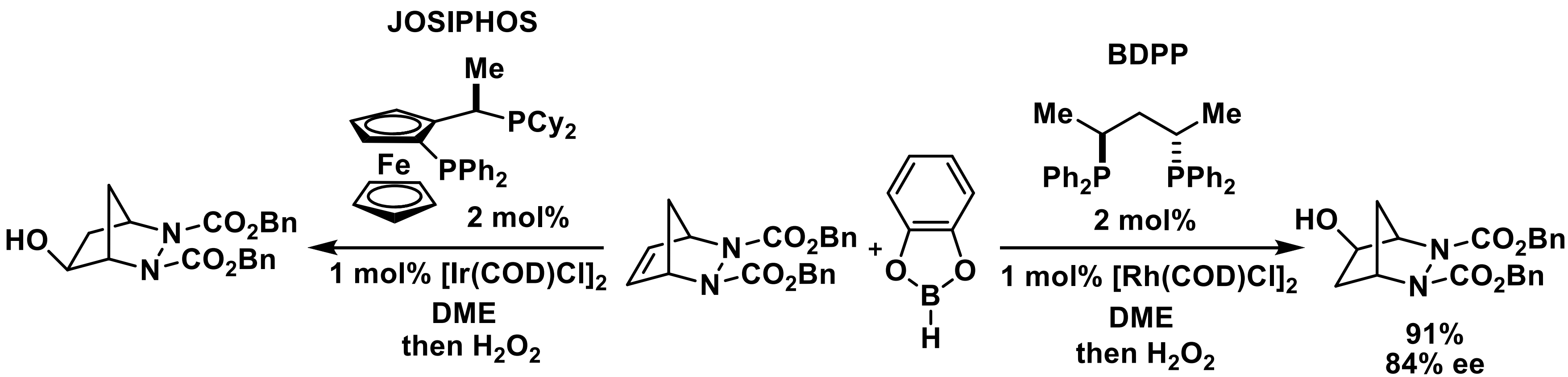
Mantilli, L.; Gerard, D.; Torche, S.; Besnard, C.; Mazet, C., *Angew. Chem., Int. Ed.* **2009**, *48*, 5143.

4.6.1.Functionalization of Olefins: Hydrosilylation/boration

Hayashi: Palladium-Catalyzed Hydrosilylation of Olefins[1]

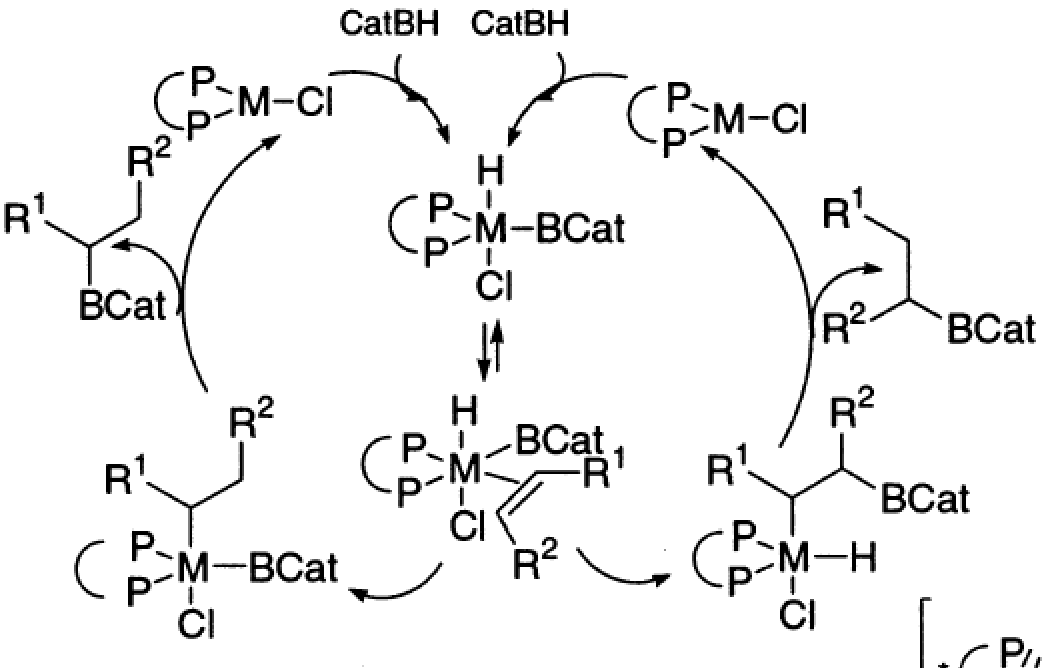


Micouin: Metal-Dependant Selectivity in Asymmetric Hydroboration[2]



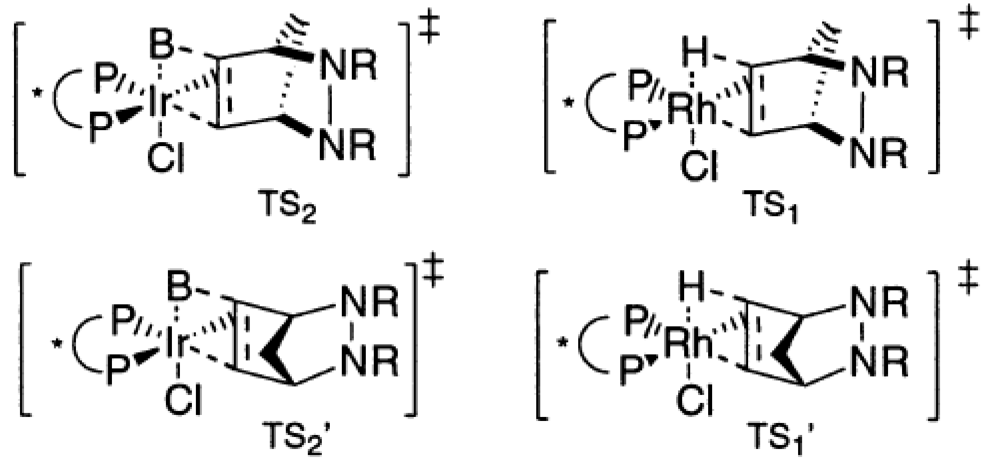
(1) Hayashi, T.; Hirate, S.; Kitayama, K.; Tsuji, H.; Torii, A.; Uozumi, Y. *J. Org. Chem.* **2001,** *66,* 1441-1449. (2) Luna, A. P.; Bonin, M.; Micouin, L.; Husson, H. P. *J. Am. Chem. Soc.* **2002,** *124,* 12098-12099.

A Mechanistic Proposal for the Reversal of Selectivity[1]



M-H insertion

M-B insertion



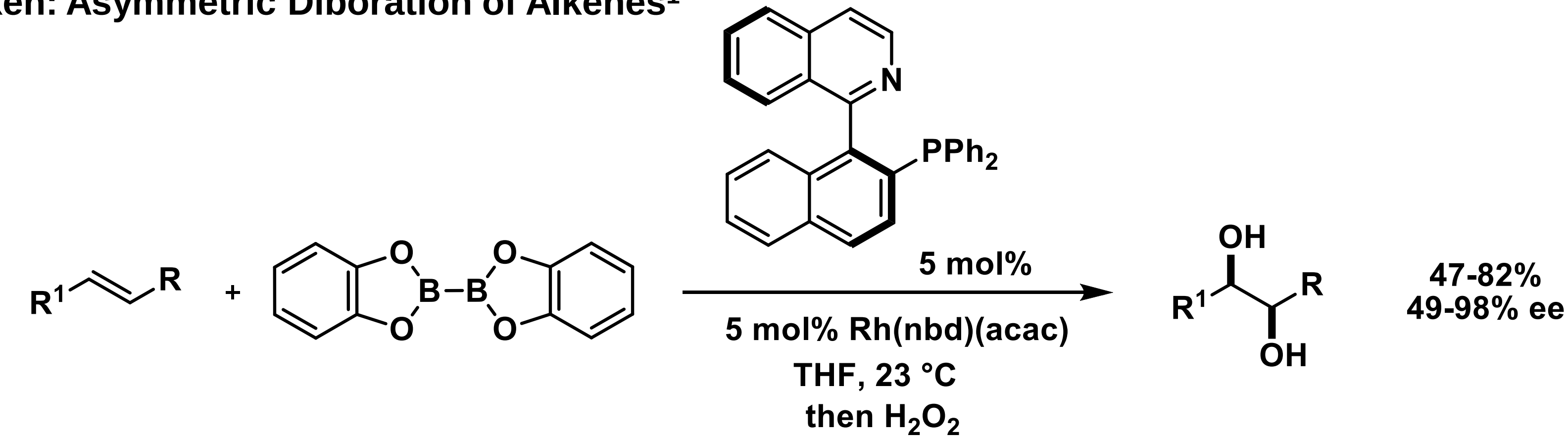
M-B insertion

M-H insertion

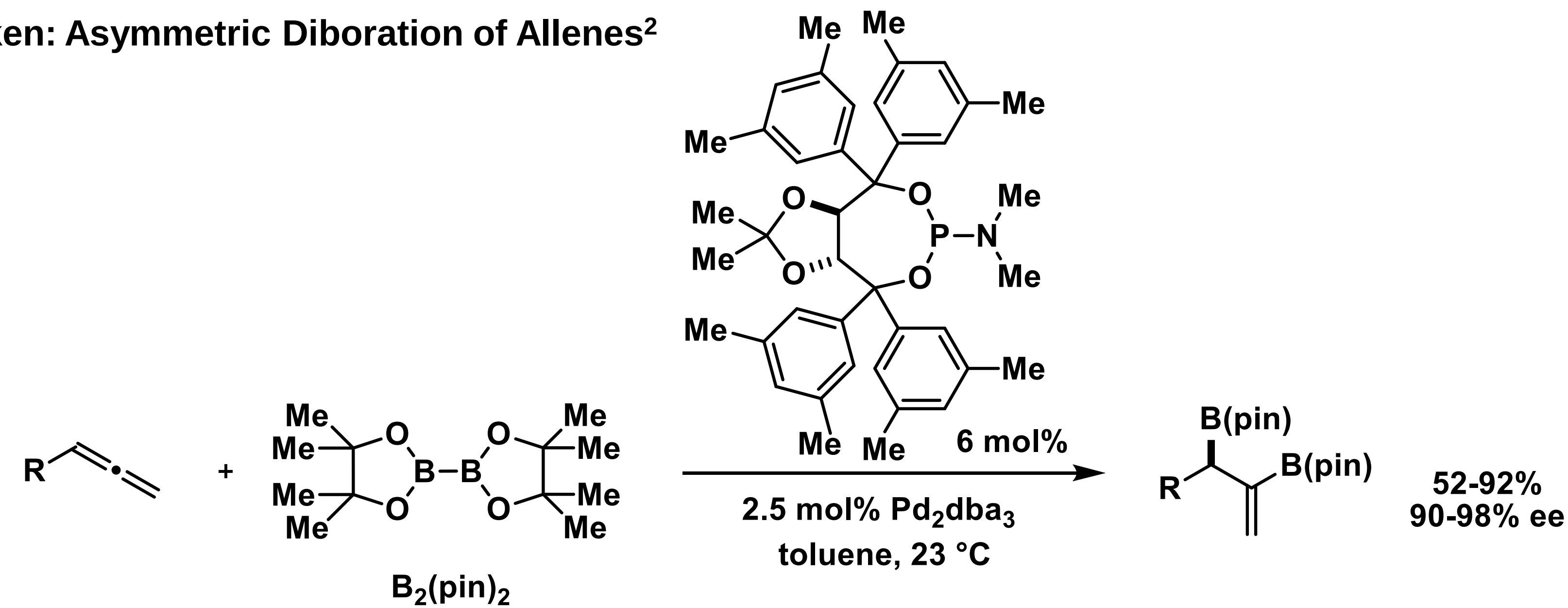
(1) Luna, A. P.; Bonin, M.; Micouin, L.; Husson, H. P. *J. Am. Chem. Soc.* **2002,** *124,* 12098-12099.

4.6.1.Functionalization of Olefins: Diboration

Morken: Asymmetric Diboration of Alkenes[1]



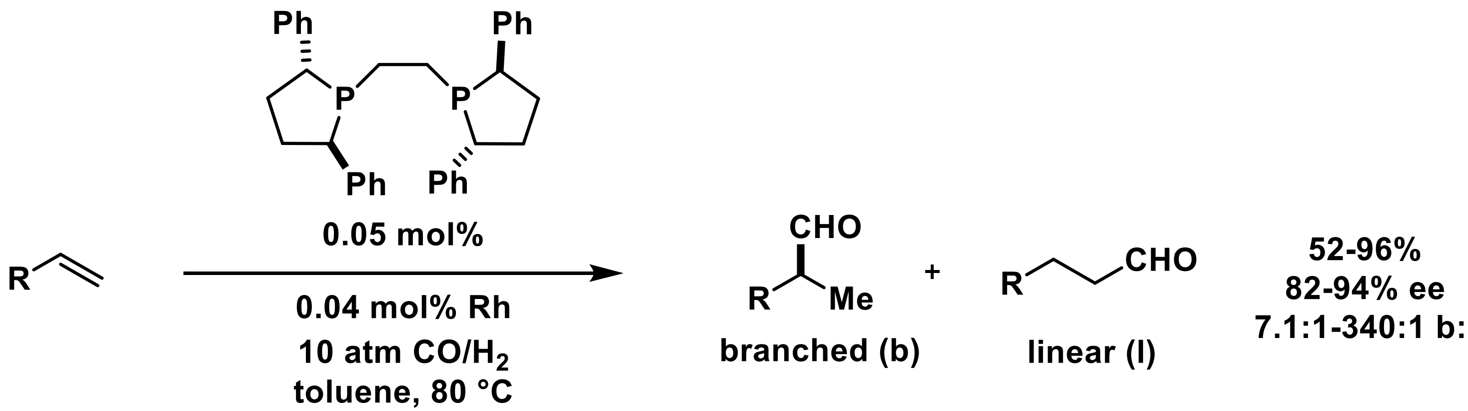
Morken: Asymmetric Diboration of Allenes[2]



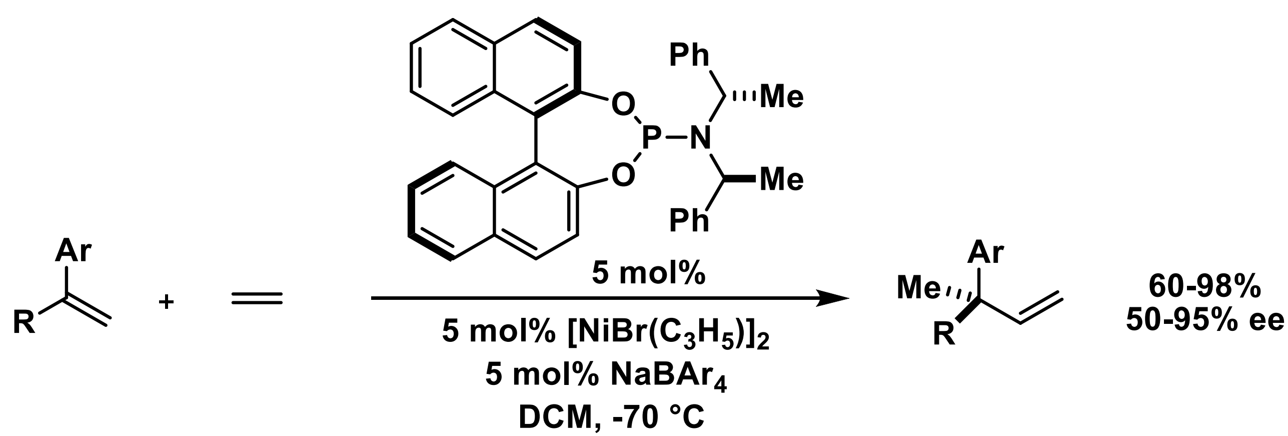
(1) Trudeau, S.; Morgan, J. B.; Shrestha, M.; Morken, J. P. *J. Org. Chem.* **2005,** *70,* 9538-9544. (2) Burks, H. E.; Liu, S. B.; Morken, J. P. *J. Am. Chem. Soc.* **2007,** *129,* 8766-8773.

4.6.1.Functionalization of Olefins: Hydroformyl/vinylation

Klosin: Asymmetric Hydroformylation[1]



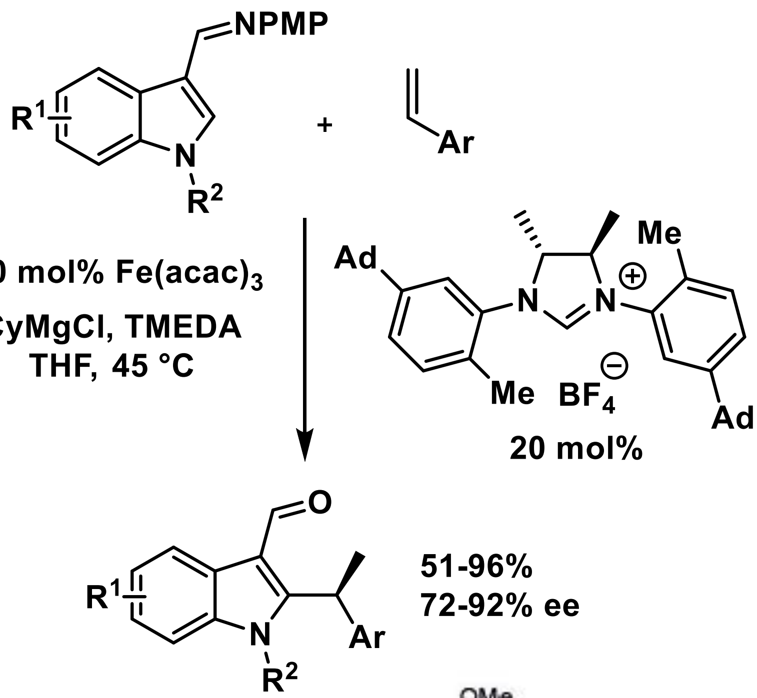
Rajanbabu: Asymmetric Hydrovinylation[2]

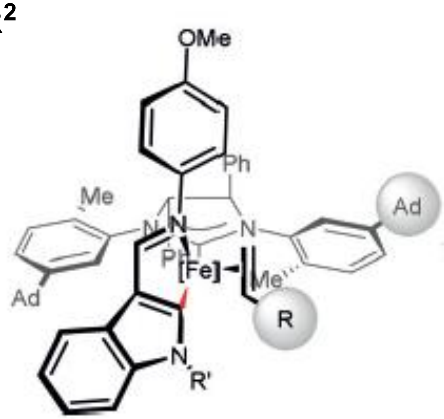


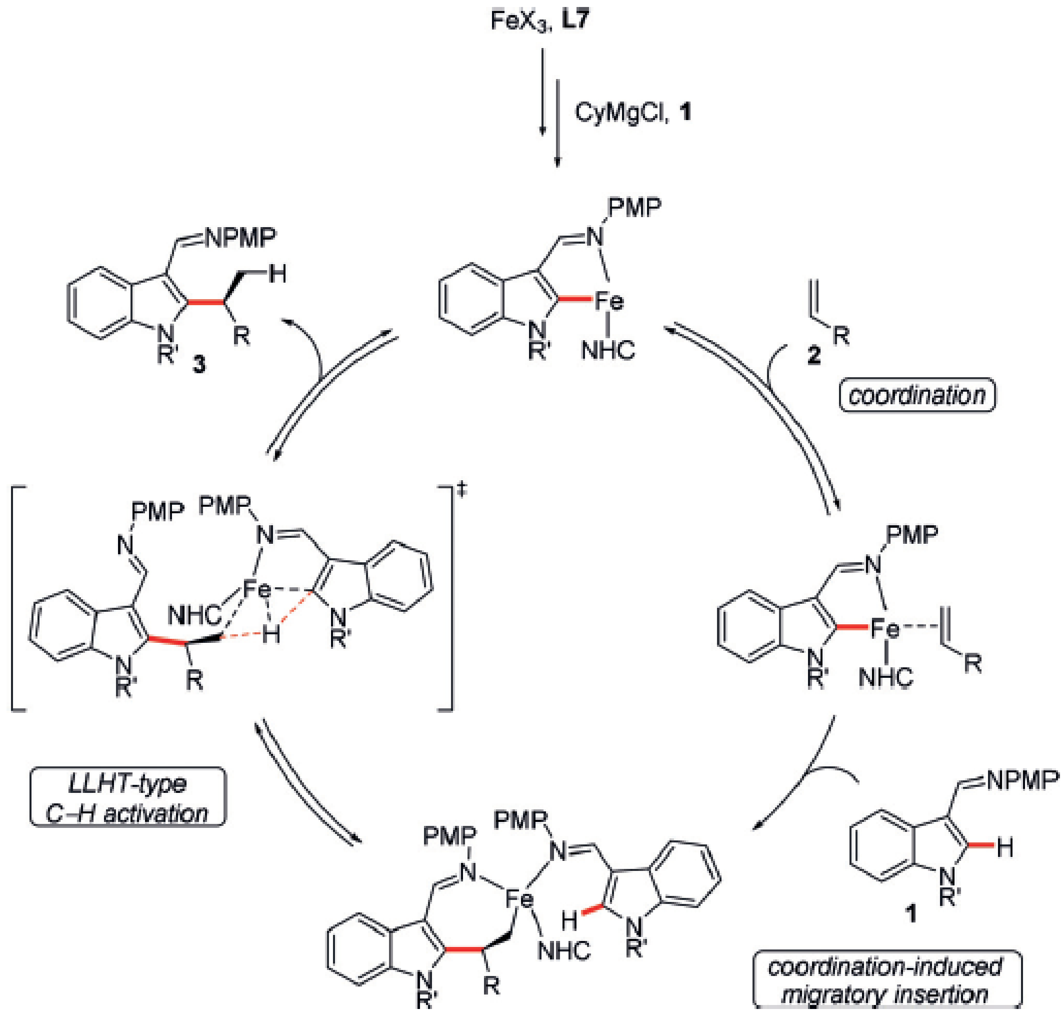
(1) Axtell, A. T.; Cobley, C. J.; Klosin, J.; Whiteker, G. T.; Zanotti-Gerosa, A.; Abboud, K. A. *Angew. Chem., Int. Ed.* **2005,** *44,* 5834-5838. (2) Zhang, A. B.; RajanBabu, T. V. *J. Am. Chem. Soc.* **2006,** *128,* 5620-5621.

4.6.1.Functionalization of Olefins: Hydroarylation

Ackermann: Iron-catalyzed hydroarylation of alkenes with indoles



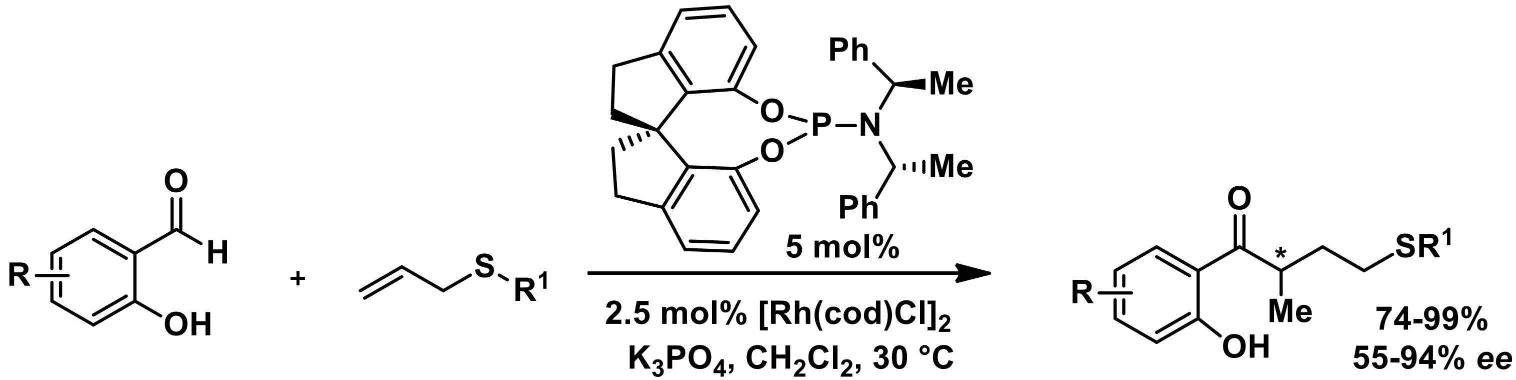




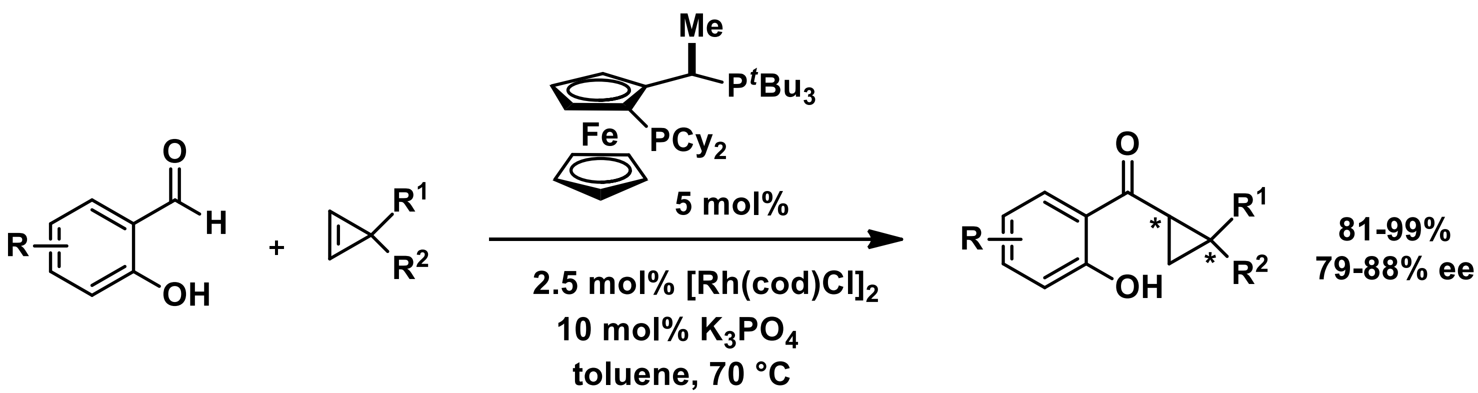
Loup, J.; Zell, D.; Oliveira, J. C. A.; Keil, H.; Stalke, D.; Ackermann, L., *Angew. Chem., Int. Ed.* **2017,** *56*, 14197-14201.

4.6.1.Functionalization of Olefins: Hydroacylation

Dong: Asymmetric hydroacylation based on directing group[1]



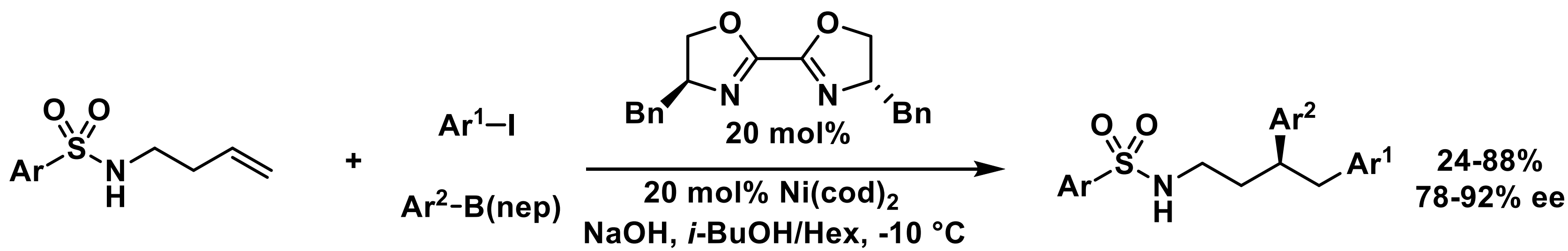
Dong: Asymmetric hydroacylation based on ring strain[2]



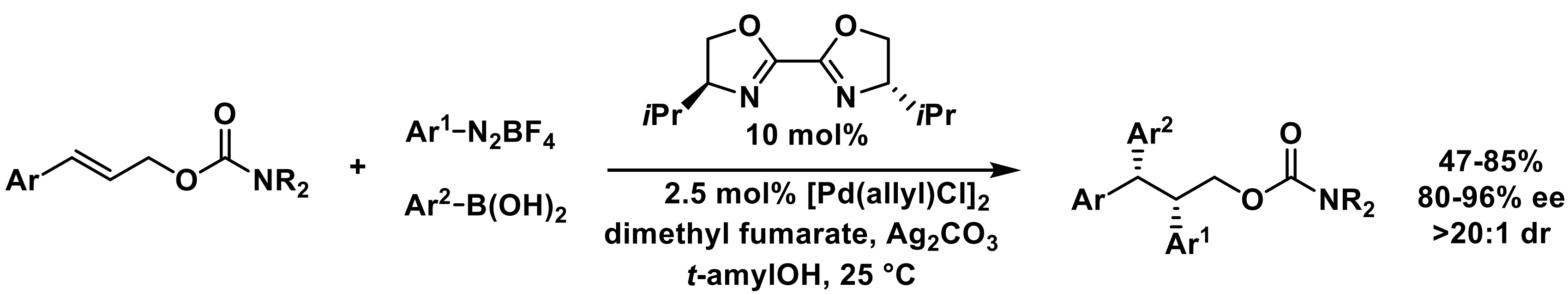
(1) Coulter, M. M.; Kou, K. G. M.; Galligan, B.; Dong, V. M., *J. Am. Chem. Soc.* **2010**, *132*, 16330. (2) Phan, D. H. T.; Kou, K. G. M.; Dong, V. M., *J. Am. Chem. Soc.* **2010**, *132*, 16354.

4.6.1.Functionalization of Olefins: Diarylation

Engle: Ni Catalyzed diarylation[1]

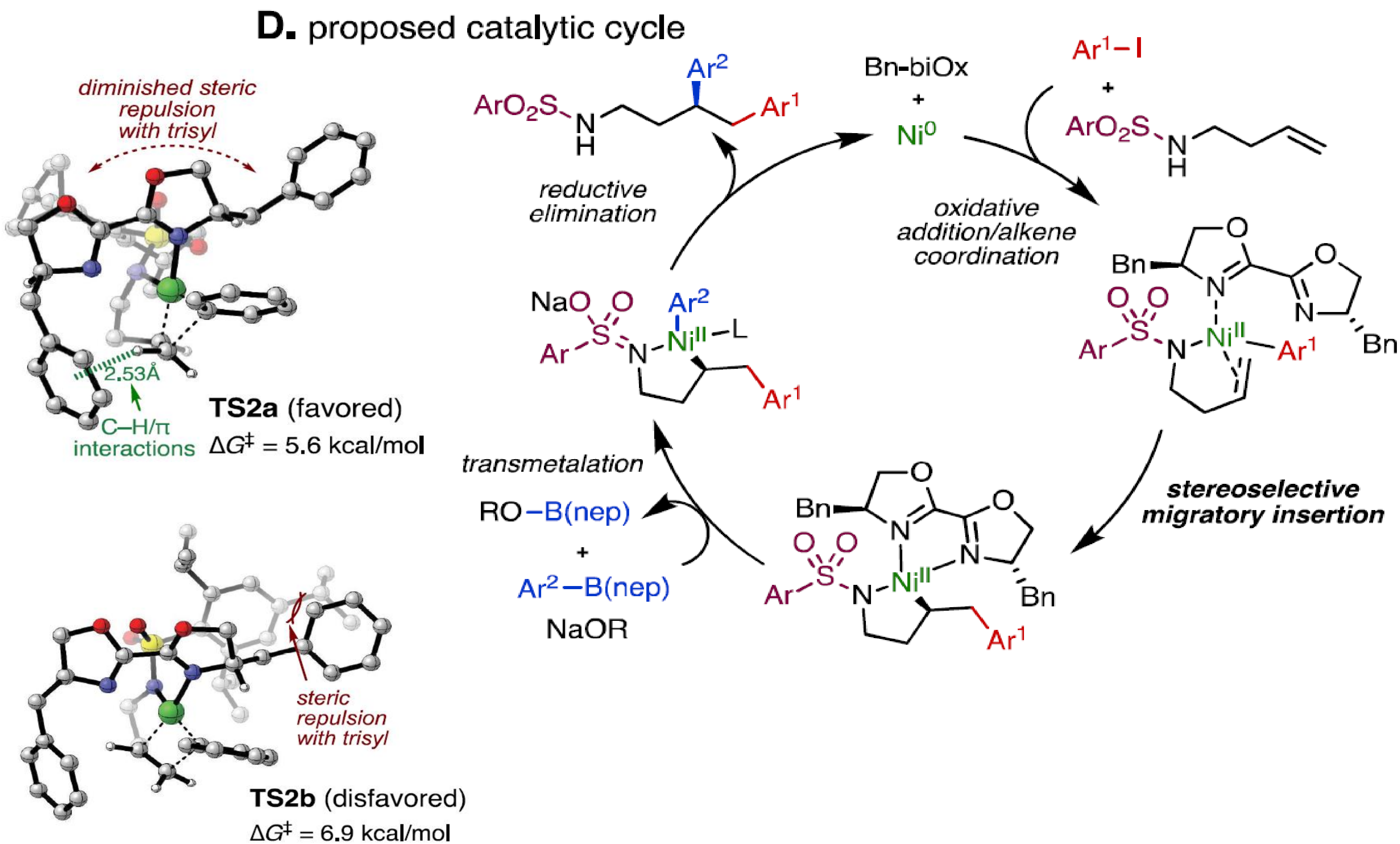


Cheng: Pd-Catalyzed diarylation[2]



(1) Apolinar, O.; Kang, T.; Alturaifi, T. M.; Bedekar, P. G.; Rubel, C. Z.; Derosa, J.; Sanchez, B. B.; Wong, Q. N.; Sturgell, E. J.; Chen, J. S.; Wisniewski, S. R.; Liu, P.; Engle, K. M. *J. Am. Chem. Soc.* **2022**, *144*, 19337-19343. (2) Xi, Y.; Huang, W.; Wang, C.; Ding, H.; Xia, T.; Wu, L.; Fang, K.; Qu, J.; Chen, Y. *J. Am. Chem. Soc.* **2022**, *144*, 8389-8398.

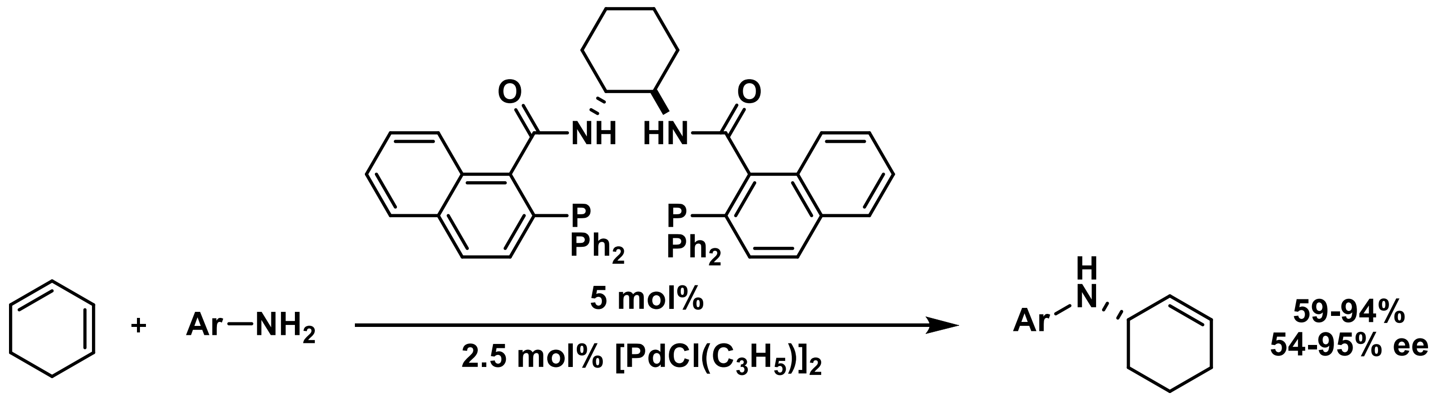
4.6.1.Functionalization of Olefins: Diarylation



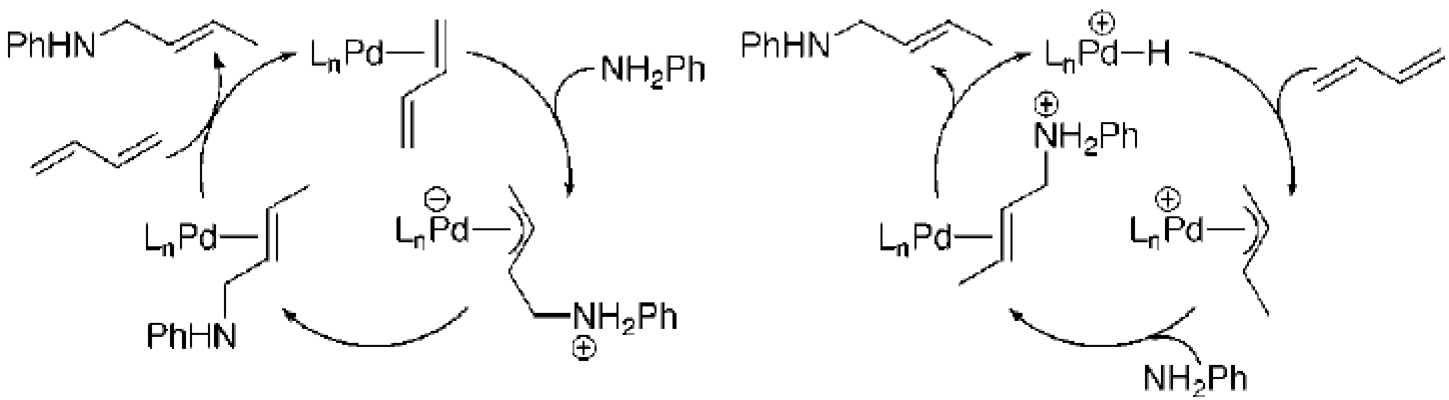
Apolinar, O.; Kang, T.; Alturaifi, T. M.; Bedekar, P. G.; Rubel, C. Z.; Derosa, J.; Sanchez, B. B.; Wong, Q. N.; Sturgell, E. J.; Chen, J. S.; Wisniewski, S. R.; Liu, P.; Engle, K. M. *J. Am. Chem. Soc.* **2022**, *144*, 19337-19343.

4.6.1.Functionalization of Olefins: Hydroamination

Hartwig: Asymmetric Hydroamination of Dienes[1]



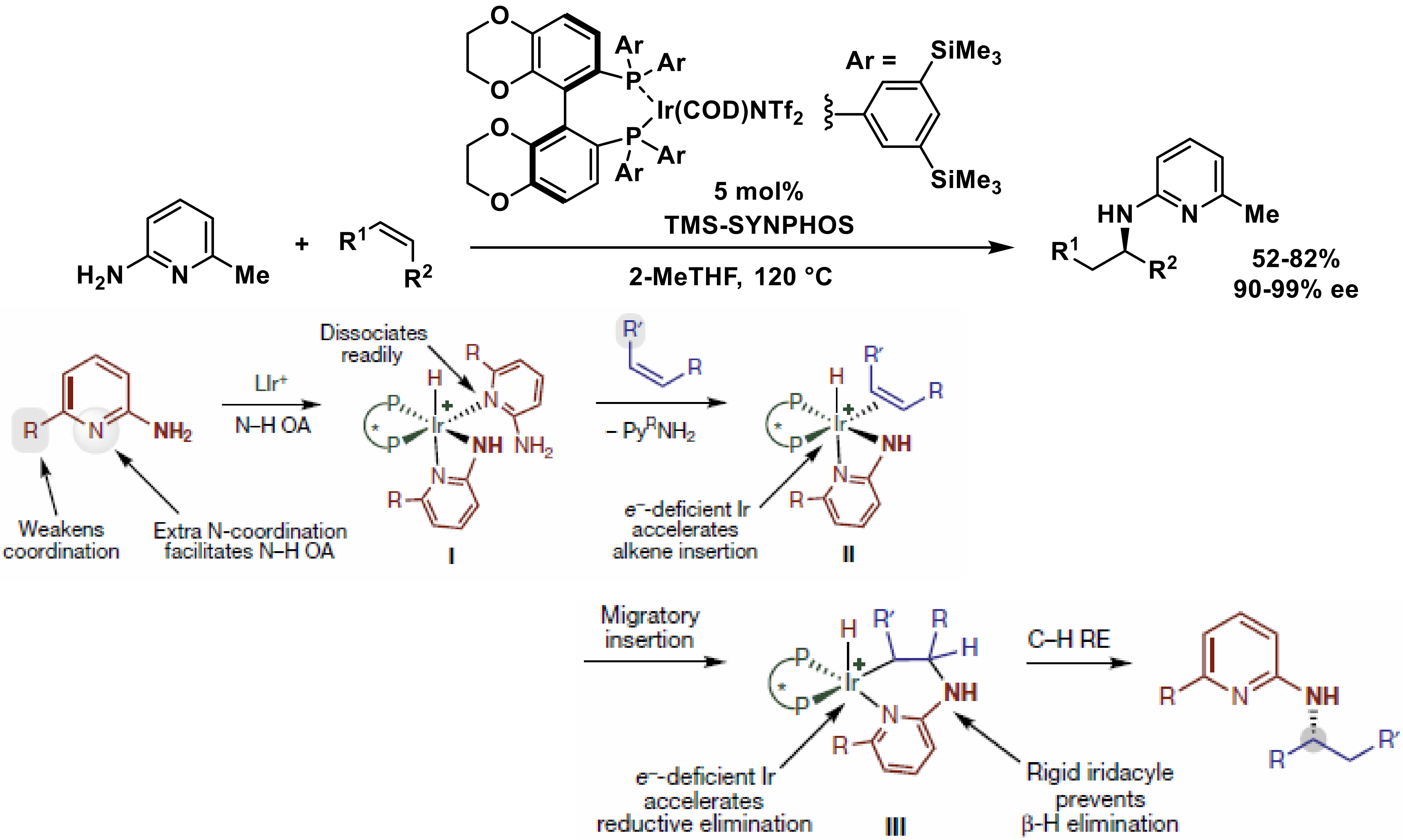
Possible Mechanisms



(1) Lober, O.; Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2001,** *123,* 4366-4367.

4.6.1.Functionalization of Olefins: Hydroamination

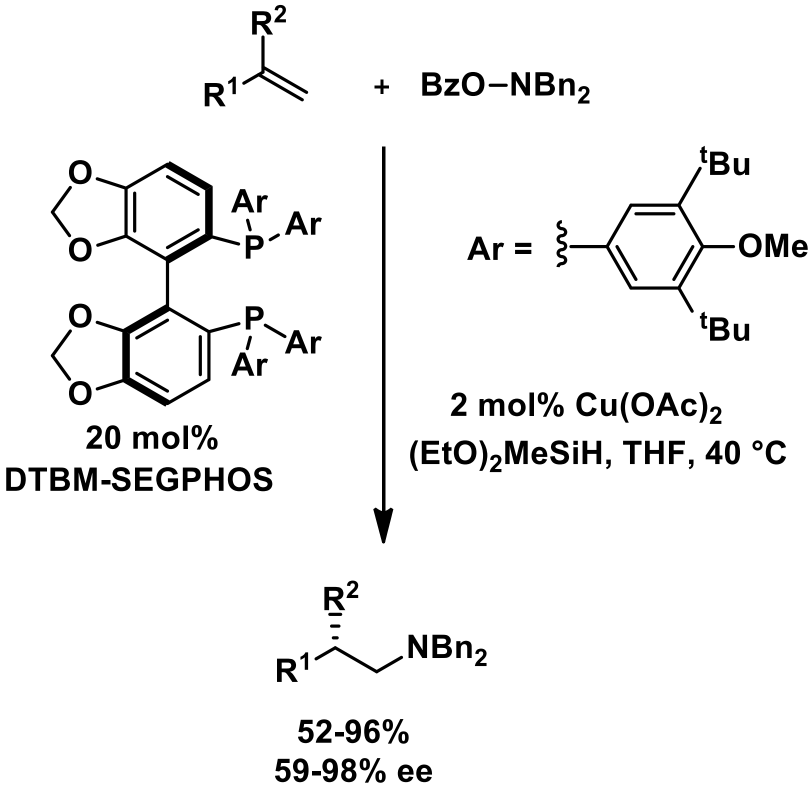
Hartwig: 20 years later non-activated alkenes[1]

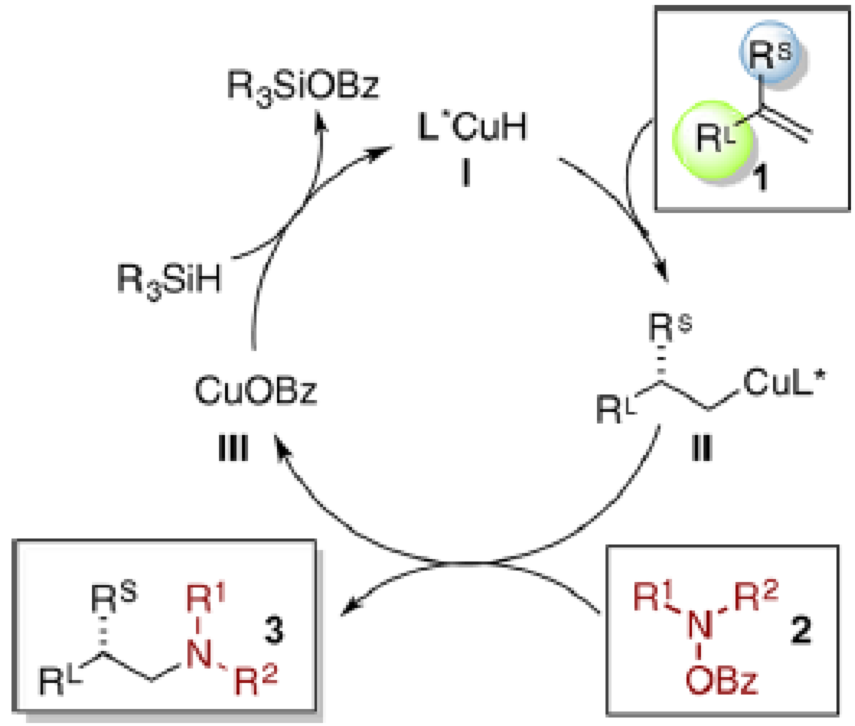


(1) Xi, Y.; Ma, S.; Hartwig, J. F. *Nature* **2020**, *588*, 254.

4.6.1.Functionalization of Olefins: Hydroamination

Buchwald: Hydroamination with Hydroxylamines and Silanes[1]

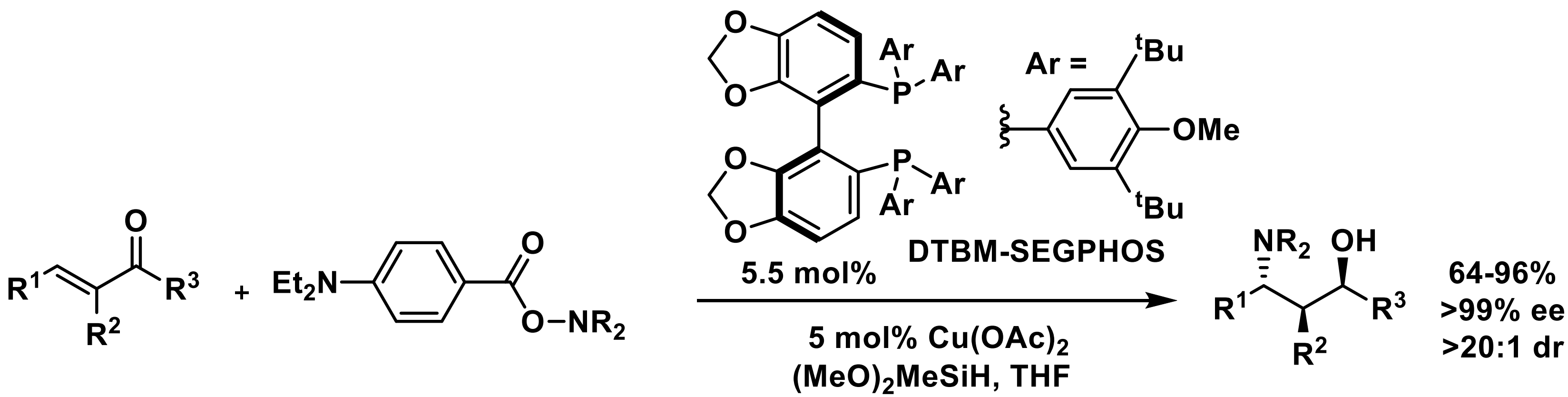




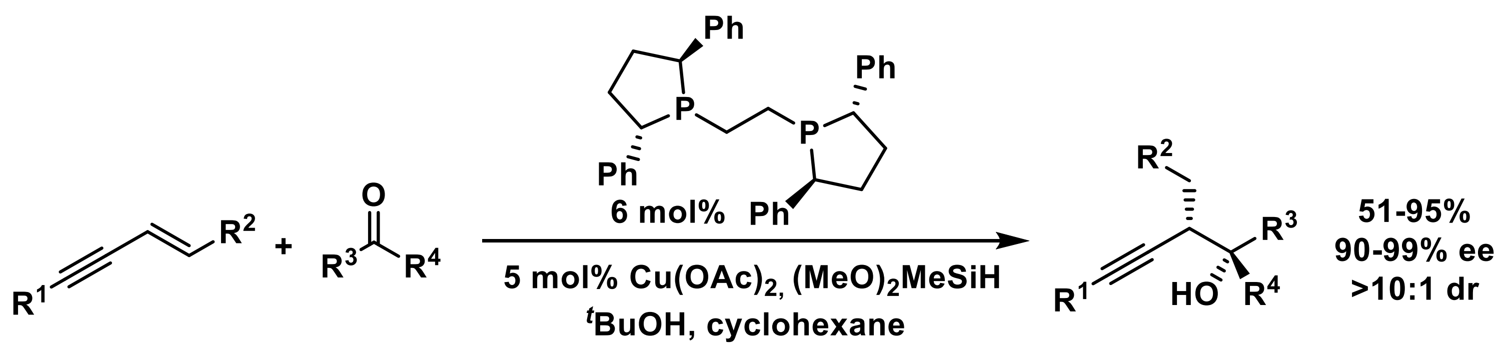
(1) Zhu, S.; Buchwald, S. L. *J. Am. Chem. Soc.* **2014**, *136*, 15913.

4.6.1.Functionalization of Olefins: Hydroamination/ Ketones

Buchwald: Stereodivergent synthesis of aminoalcohols[1]



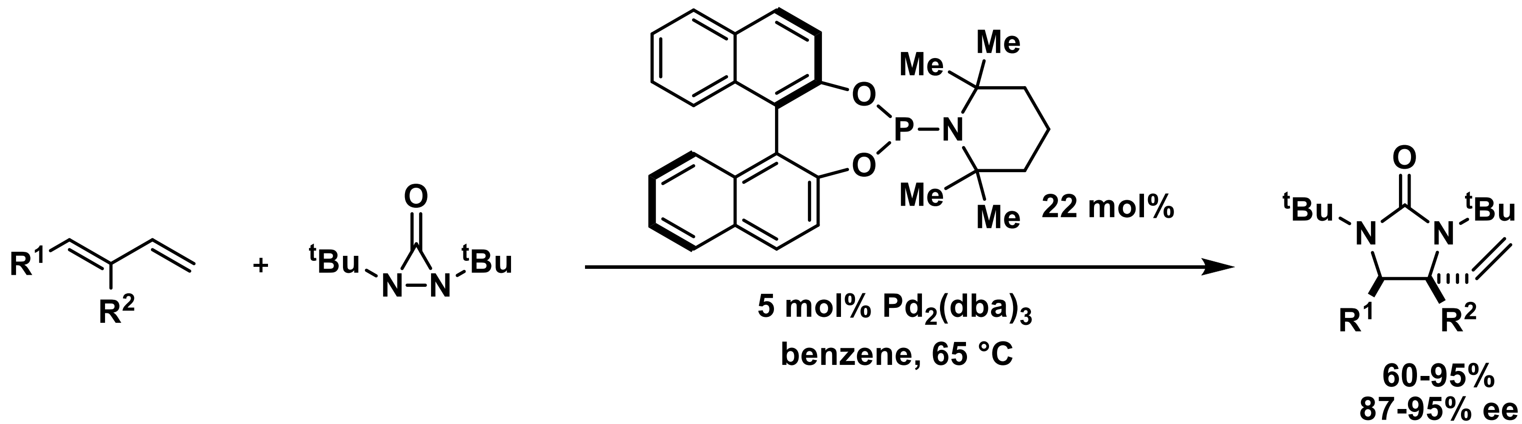
Buchwald: Addition to ketones[2]



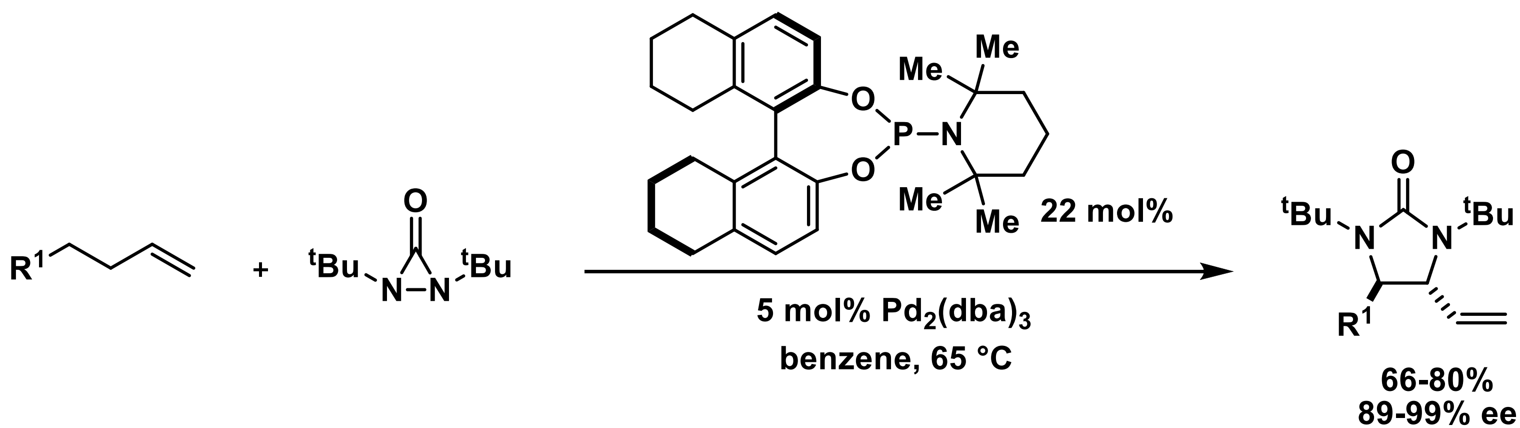
(1) Shi, S. L.; Wong, Z. L.; Buchwald, S. L. *Nature* **2016**, *532*, 353-356. (2) Yang, Y.; Perry, I. B.; Lu, G.; Liu, P.; Buchwald, S. L. *Science* **2016**, *353*, 144-150.

4.6.1.Functionalization of Olefins: Diamination

Shi: Asymmetric Diamination of Dienes[1]



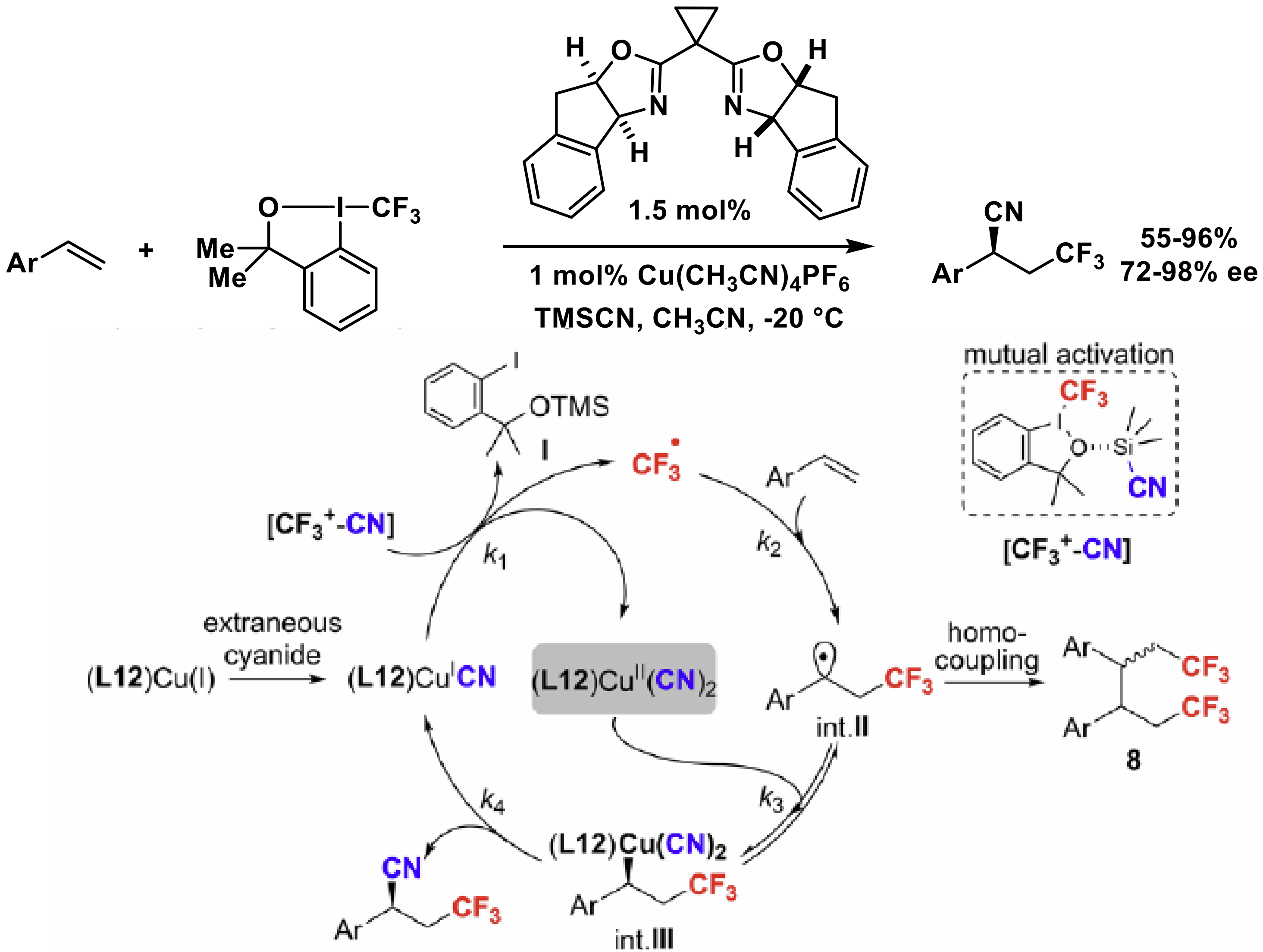
Shi: Asymmetric C-H Diamination of Terminal Olefins[2]



(1) Du, H. F.; Yuan, W. C.; Zhao, B. G.; Shi, Y. *J. Am. Chem. Soc.* **2007,** *129,* 11688-11689. (2) Du, H. F.; Zhao, B. G.; Shi, Y. *J. Am. Chem. Soc.* **2008,** *130,* 8590-8591.

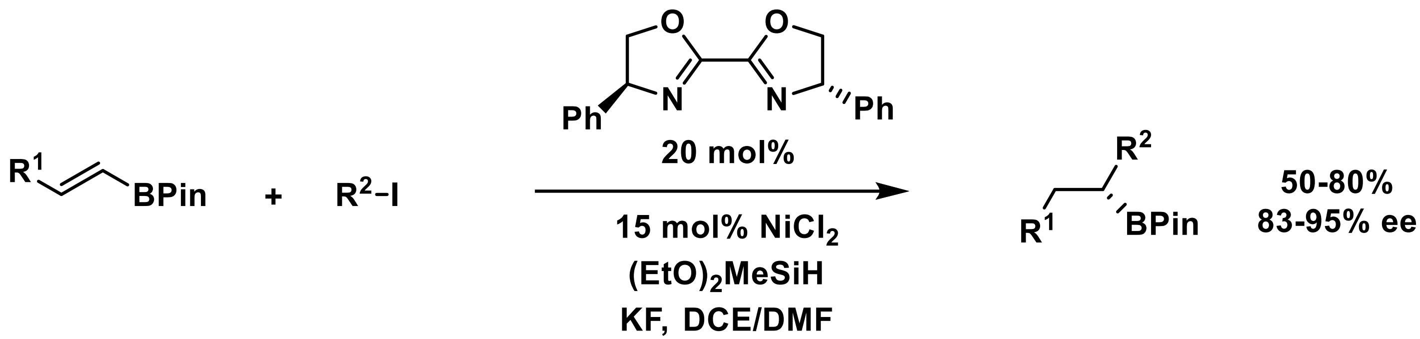
4.6.1.Functionalization of Olefins: Radicals

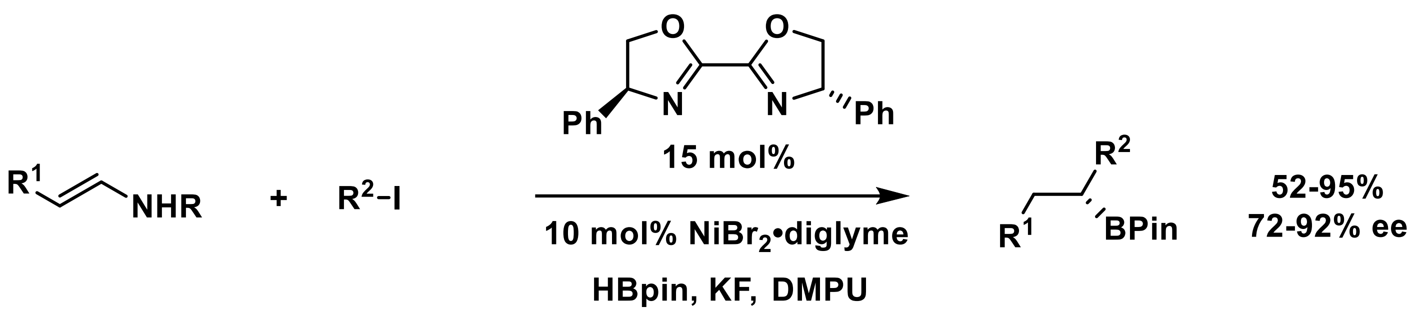
Guosheng Liu: Trifluoromethylcyanation of alkenes via radicals[1]



Wang, F.; Wang, D.; Wan, X.; Wu, L.; Chen, P.; Liu, G., *J. Am. Chem. Soc.* **2016**, *138*, 15547-15550.

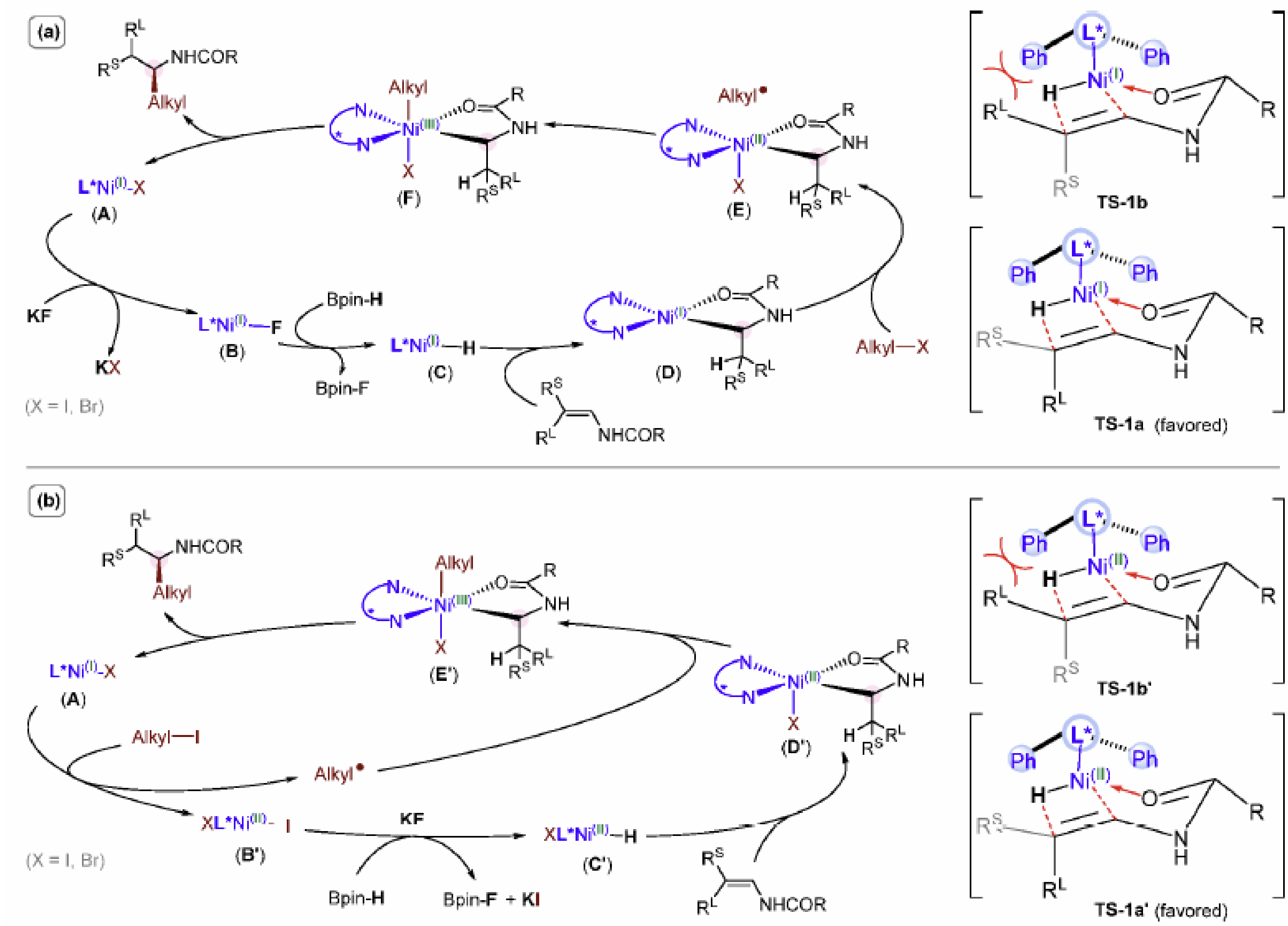
Xile Hu: Nickel-catalyzed hydroalkylation of vinyl boronic esters[1] and enamides[2]





(1) Bera, S.; Mao, R.; Hu, X. *Nat. Chem.* **2021**, *13*, 270. (2) Qian, D.; Bera, S.; Hu, X. *J. Am. Chem. Soc.* **2021**, *143*, 1959.

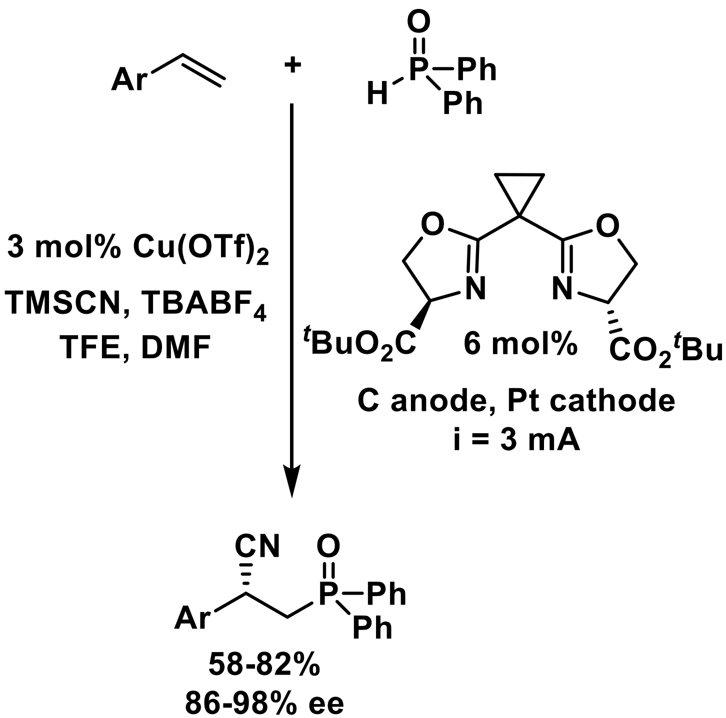
4.6.1.Functionalization of Olefins: Radicals

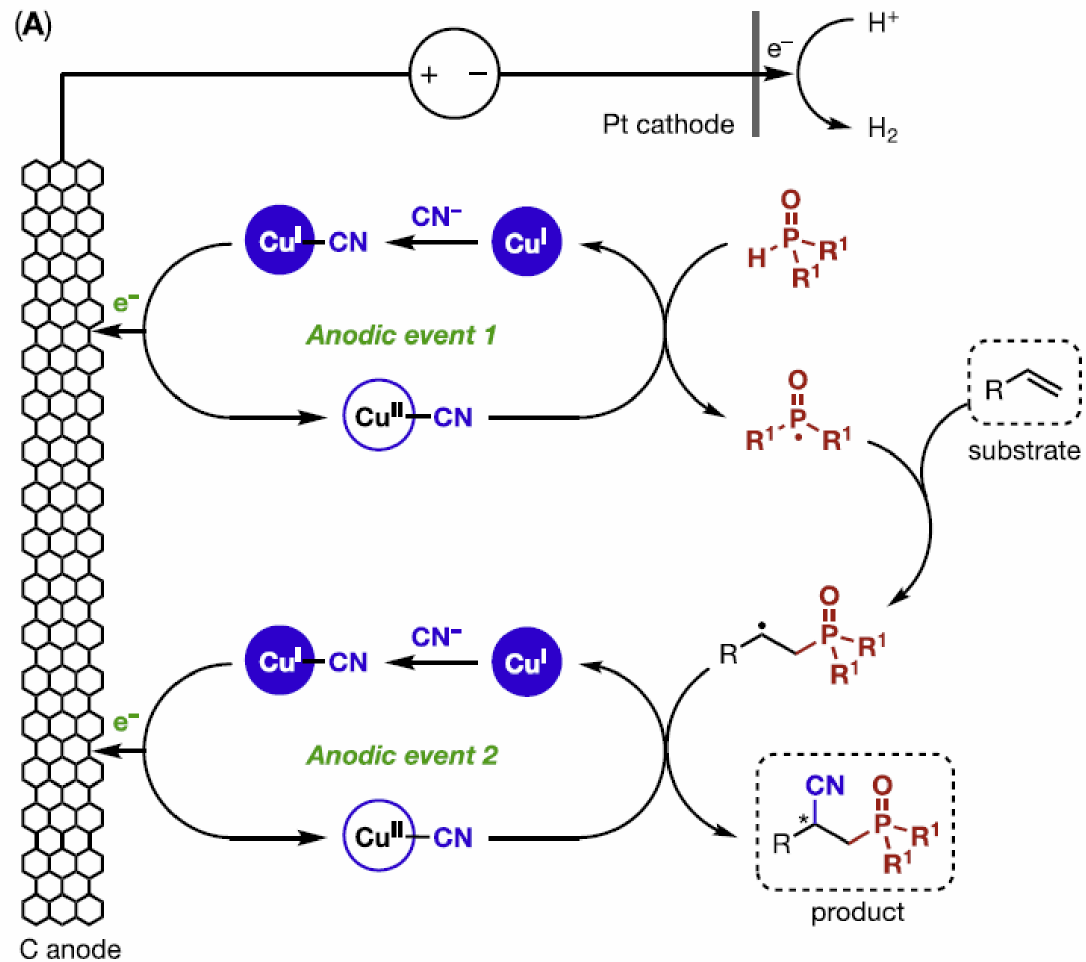


(1) Bera, S.; Mao, R.; Hu, X. *Nat. Chem.* **2021**, *13*, 270. (2) Qian, D.; Bera, S.; Hu, X. *J. Am. Chem. Soc.* **2021**, *143*, 1959.

4.6.1.Functionalization of Olefins: Radicals

Song Lin: generation of radicals via electrochemistry[1]

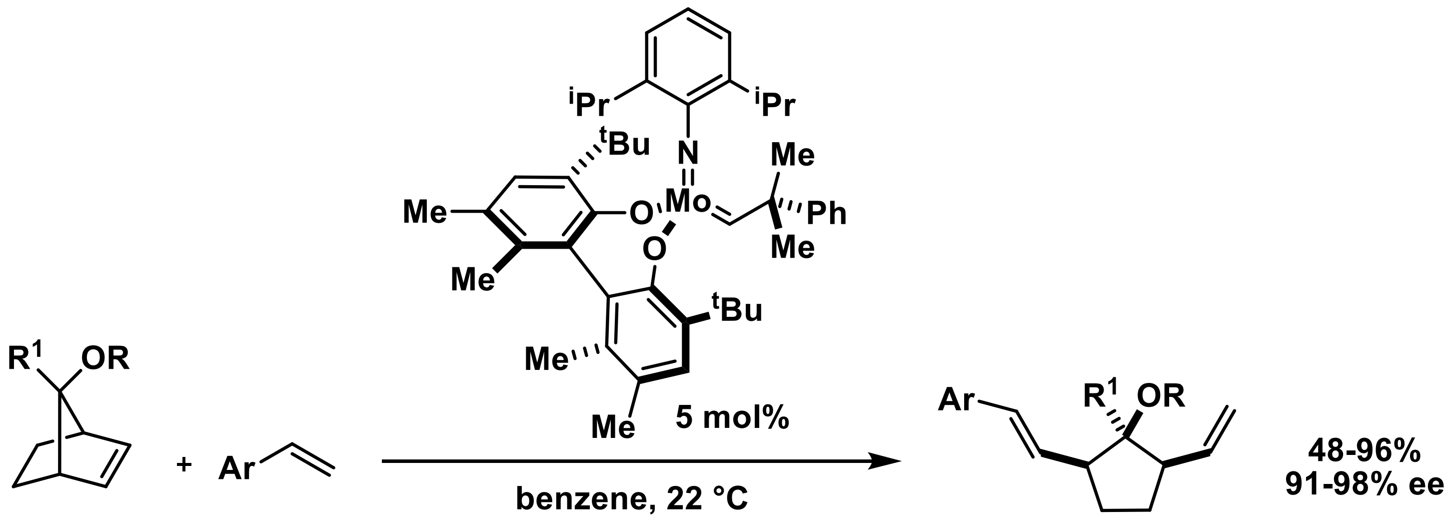




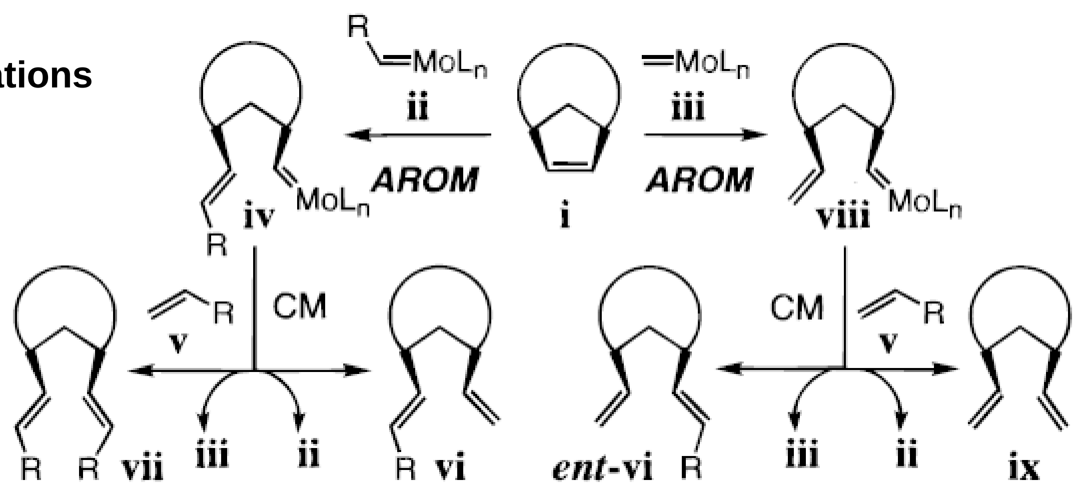
Fu, N. K.; Song, L.; Liu, J. J.; Shen, Y. F.; Siu, J. C.; Lin, S., *J. Am. Chem. Soc.* **2019**, *141*, 14480-14485.

4.6.2 Metathesis: Mo Catalysts

Schrock-Hoveyda: Ring-Opening –Cross Metathesis with Chiral Mo Catalysts (AROM/CM)



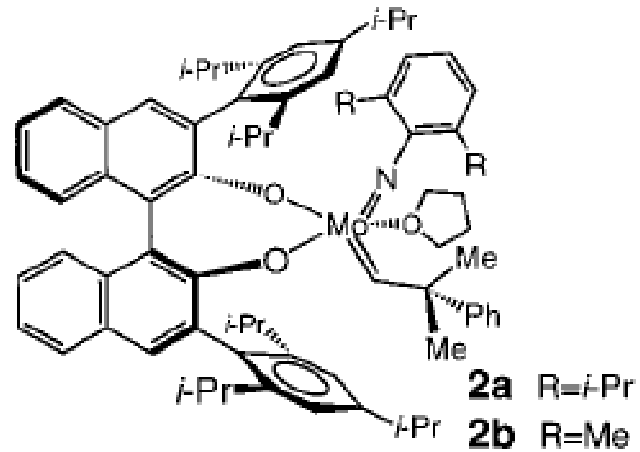
Mechanistic Considerations

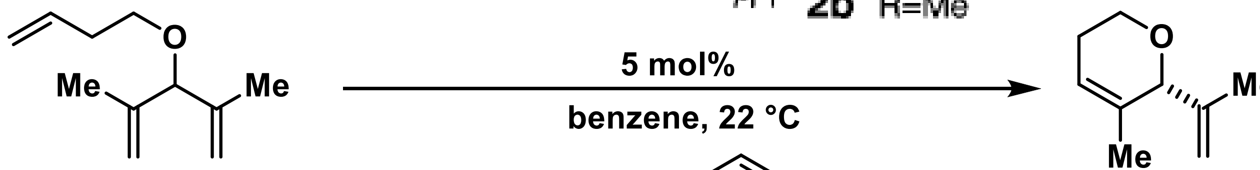


(1) La, D. S.; Ford, J. G.; Sattely, E. S.; Bonitatebus, P. J.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999,** *121,* 11603-11604. (1) La, D. S.; Sattely, E. S.; Ford, J. G.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2001,** *123,* 7767-7778.

4.6.2 Metathesis: Mo Catalysts

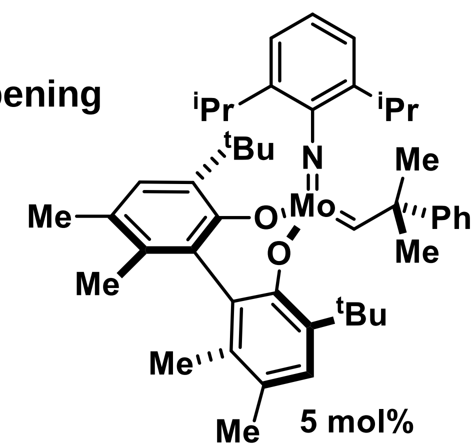
Schrock-Hoveyda: Asymmetric Ring-Closing Metathesis (RCM)

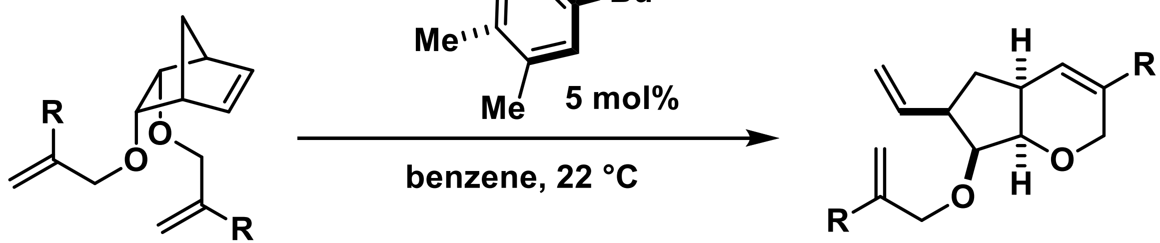




86%
99% ee

Schrock-Hoveyda: Asymmetric Ring-Opening -Ring Closing Metathesis (AROM-RCM)



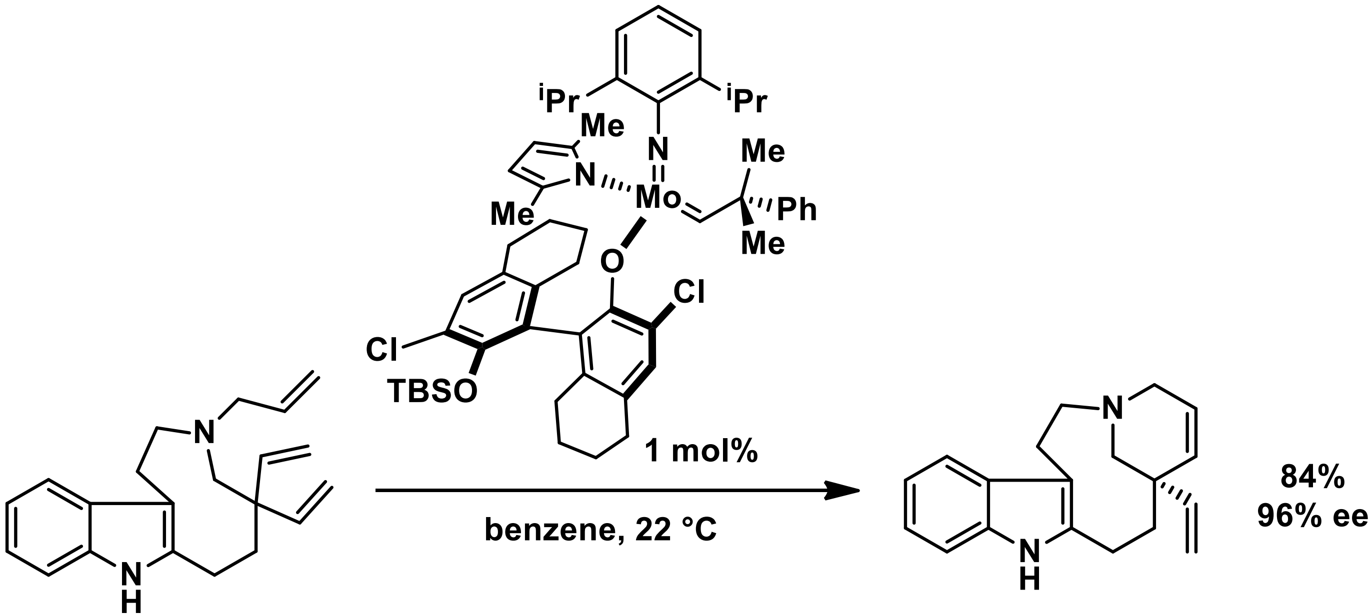


76-84%
98% ee

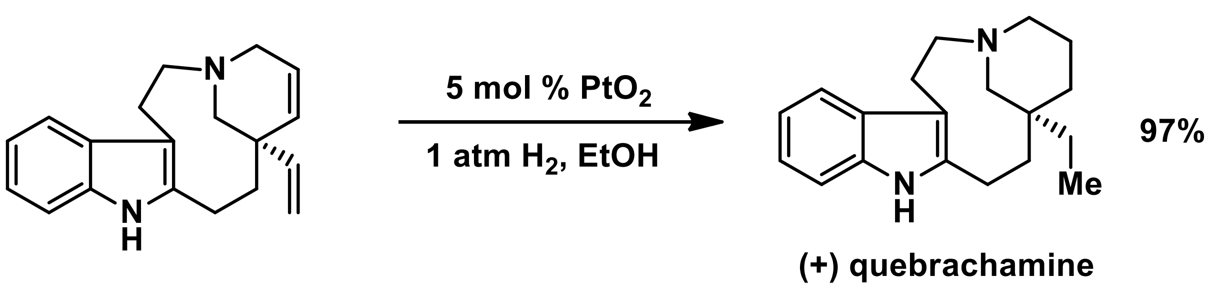
(1) Zhu, S. S.; Cefalo, D. R.; La, D. S.; Jamieson, J. Y.; Davis, W. M.; Hoveyda, A. H.; Schrock, R. R. *J. Am. Chem. Soc.* **1999,** *121,* 8251-8259. (2) Weatherhead, G. S.; Ford, J. G.; Alexanian, E. J.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000,** *122,* 1828-1829.

4.6.2 Metathesis: Mo Catalysts

Schrock-Hoveyda: Asymmetric Ring-Closing Metathesis (RCM) with chiral center on Mo



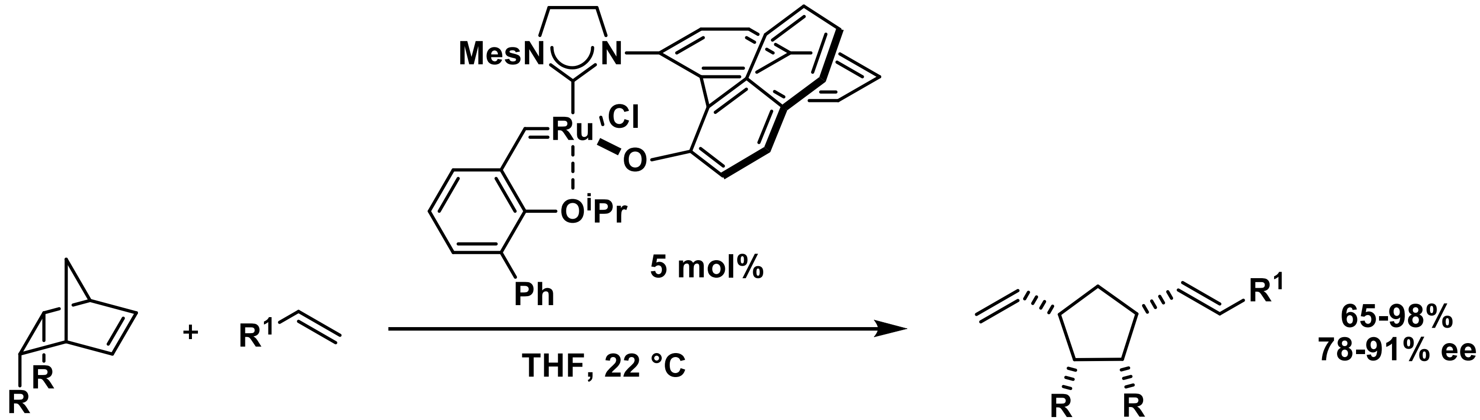
Application: synthesis of quebrachamine



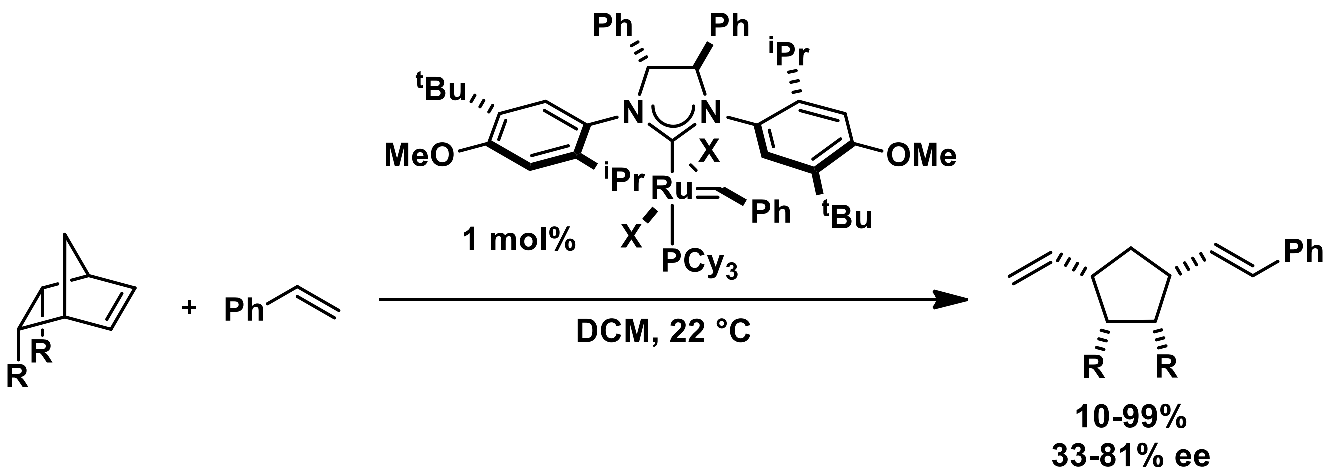
(1) Malcolmson, S. J.; Meek, S. J.; Sattely, E. S.; Schrock, R. R.; Hoveyda, A. H. *Nature* **2008**, *456*, 933-937.

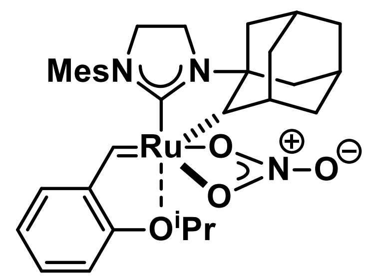
4.6.2 Metathesis: Ru Catalysts

Hoveyda: Ru Catalyst for AROM/CM[1]



Grubbs: Ru Catalyst for AROM/CM[2]



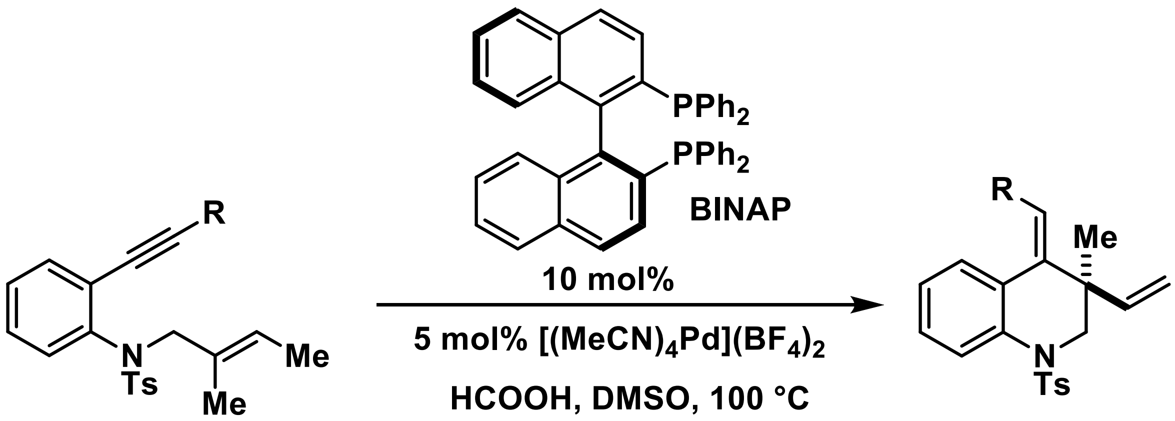


Improved chiral at Ru catalyst[3]

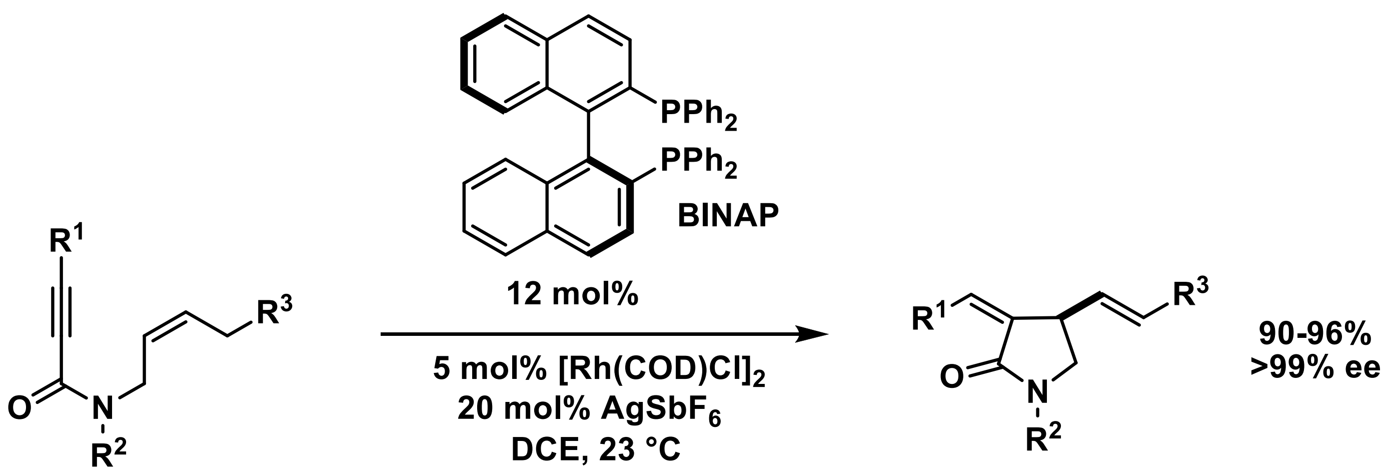
(1) Van Veldhuizen, J. J.; Gillingham, D. G.; Garber, S. B.; Kataoka, O.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2003,** *125,* 12502. (2) Berlin, J. M.; Goldberg, S. D.; Grubbs, R. H. *Angew. Chem., Int. Ed.* **2006,** *45,* 7591. (3) Hartung, J.; Dornan, P. K.; Grubbs, R. H. *J. Am. Chem. Soc.* **2014**, *136*, 13029.

4.6.3 Cyclization Reactions with Alkynes

Mikami: Pd-Catalyzed Alder-Ene Cyclization[1]



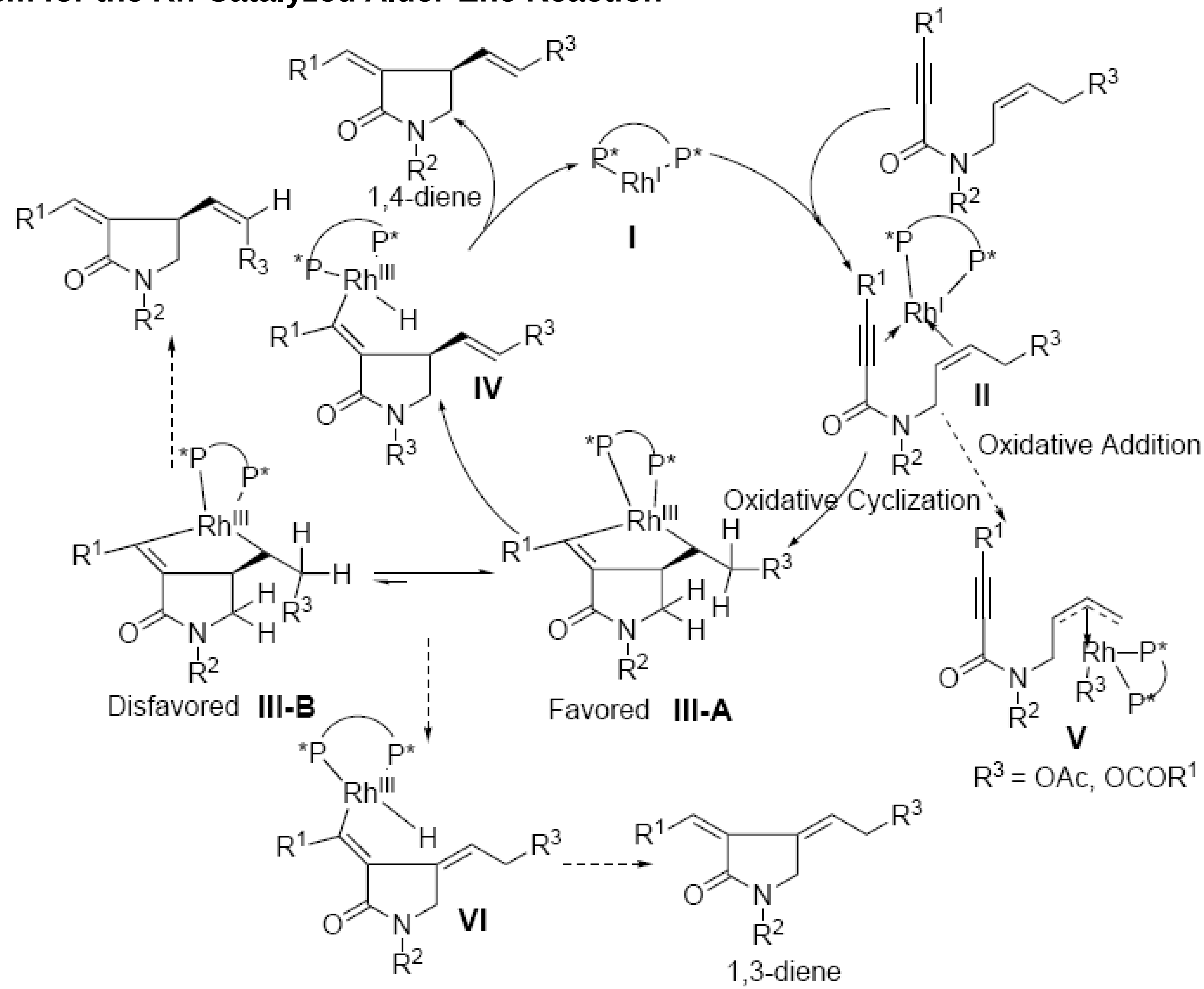
Zhang: Pd-Catalyzed Alder-Ene Cyclization[2]



(1) Hatano, M.; Mikami, K. *J. Am. Chem. Soc.* **2003,** *125,* 4704-4705. (2) Lei, A. W.; Waldkirch, J. P.; He, M. S.; Zhang, X. M. *Angew. Chem., Int. Ed.* **2002,** *41,* 4526-4529.

4.6.3 Cyclization Reactions with Alkynes

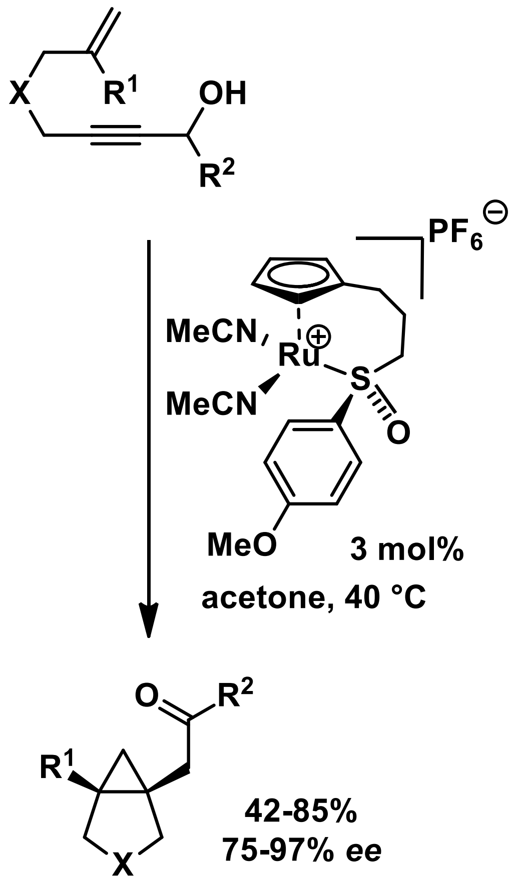
Mechanism for the Rh-Catalyzed Alder-Ene Reaction[1]

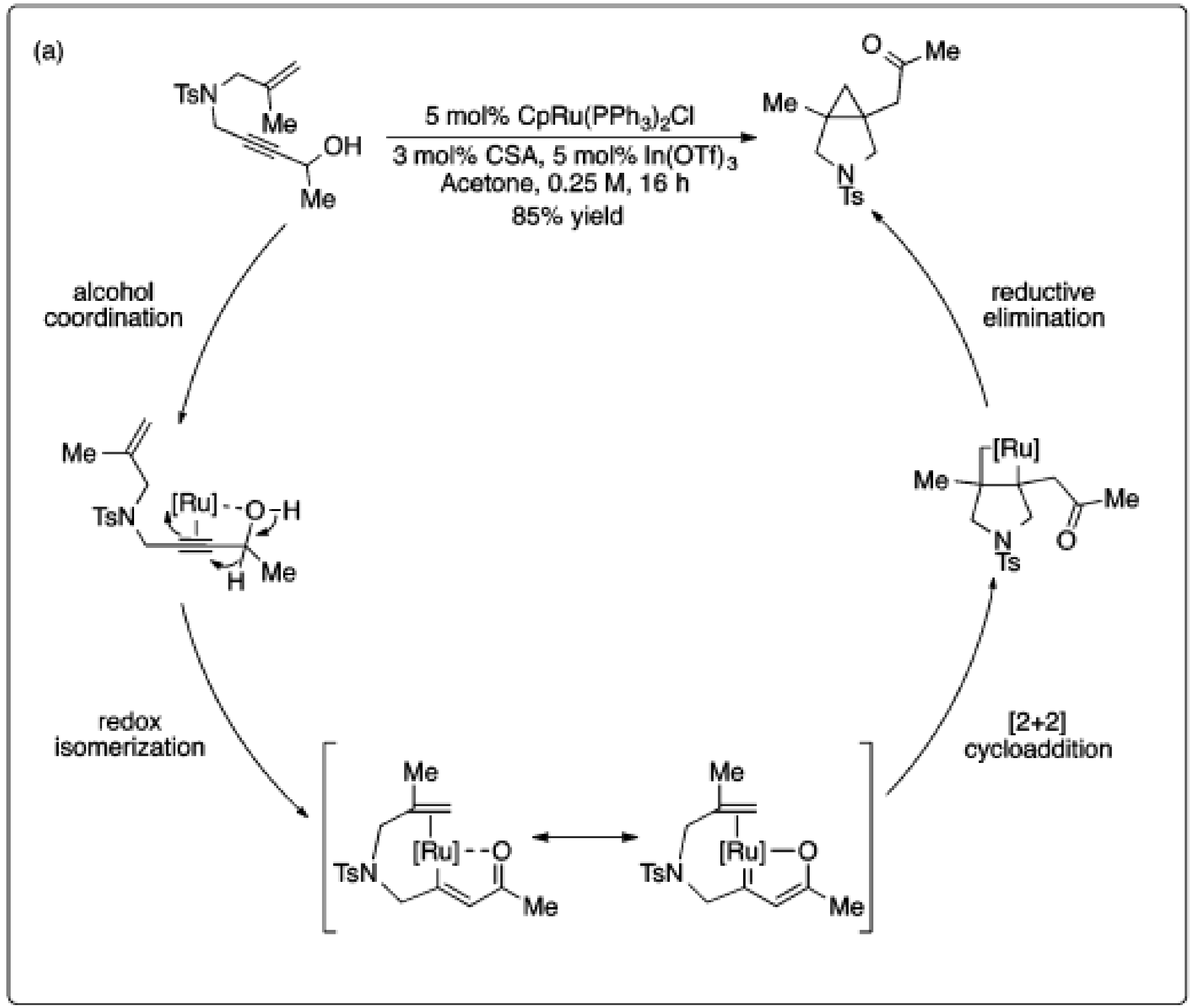


(1) Lei, A. W.; Waldkirch, J. P.; He, M. S.; Zhang, X. M. *Angew. Chem., Int. Ed.* **2002,** *41,* 4526-4529.

4.6.3 Cyclization Reactions with Alkynes

Trost: Ruthenium-Catalyzed Cycloisomerization Reaction[1]

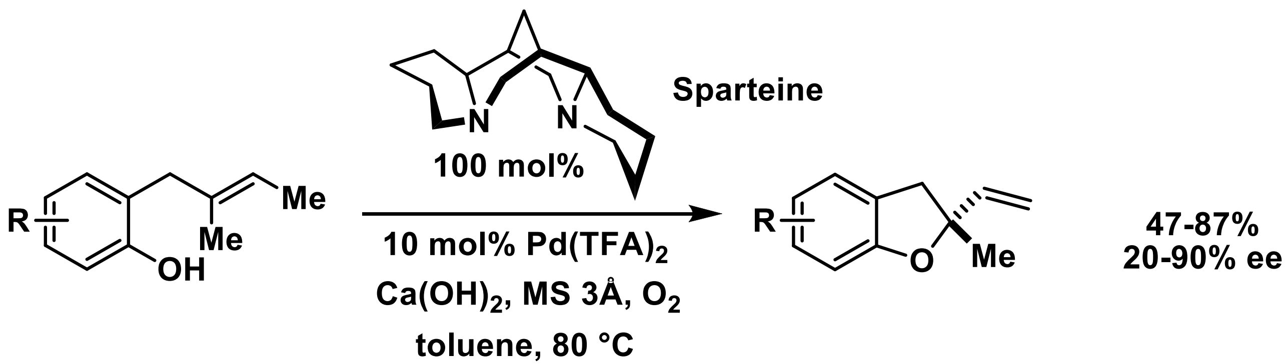




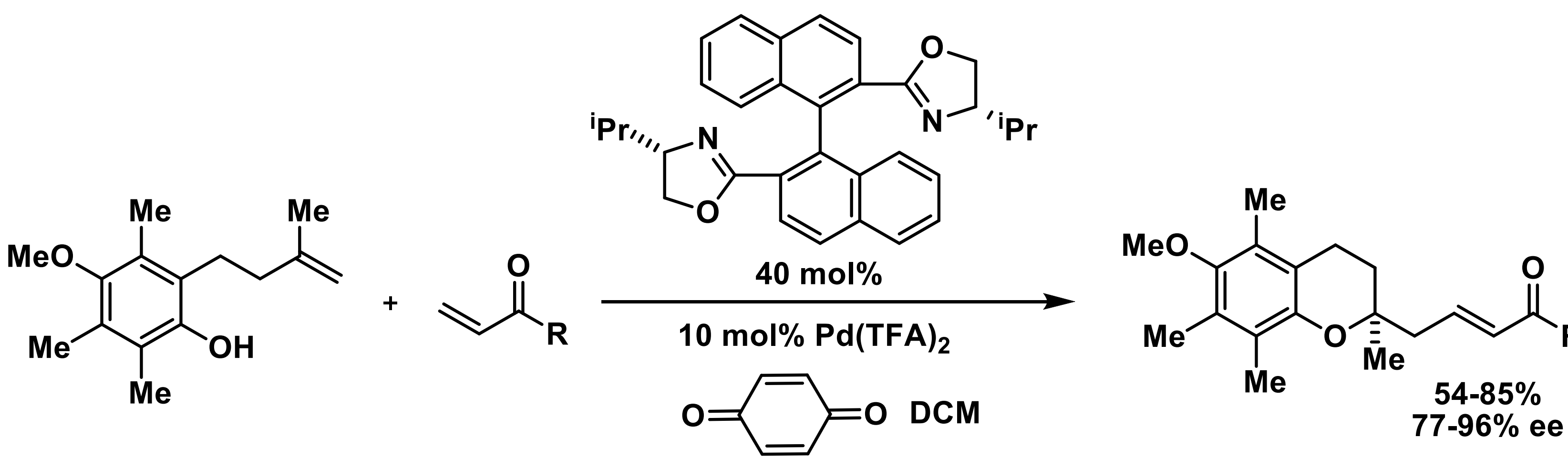
(1) Trost, B. M.; Ryan, M. C.; Rao, M.; Markovic, T. Z. *J. Am. Chem. Soc.* **2014**, *136*, 17422.

4.6.3 Cyclization Reactions with Alkenes

Stoltz: Wacker-Type Oxidative Cyclization[1]



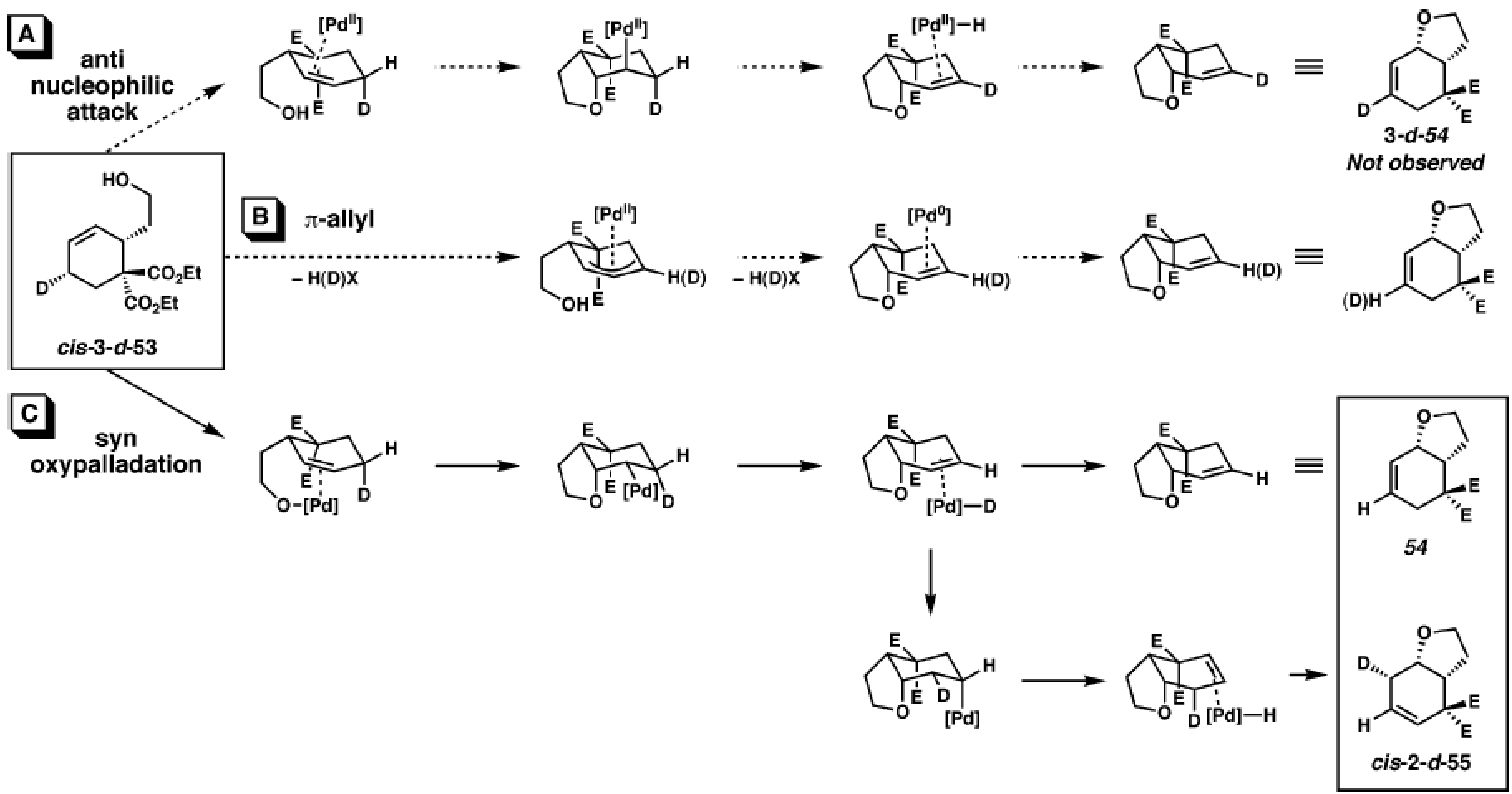
Tietze: Tandem Wacker-Cyclization Heck Coupling[1]



(1) Trend, R. M.; Ramtohul, Y. K.; Stoltz, B. M. *J. Am. Chem. Soc.* **2005,** *127,* 17778-17788. (1) Tietze, L. F.; Sommer, K. M.; Zinngrebe, J.; Stecker, F. *Angew. Chem., Int. Ed.* **2005,** *44,* 257-259.

4.6.3 Cyclization Reactions with Alkenes

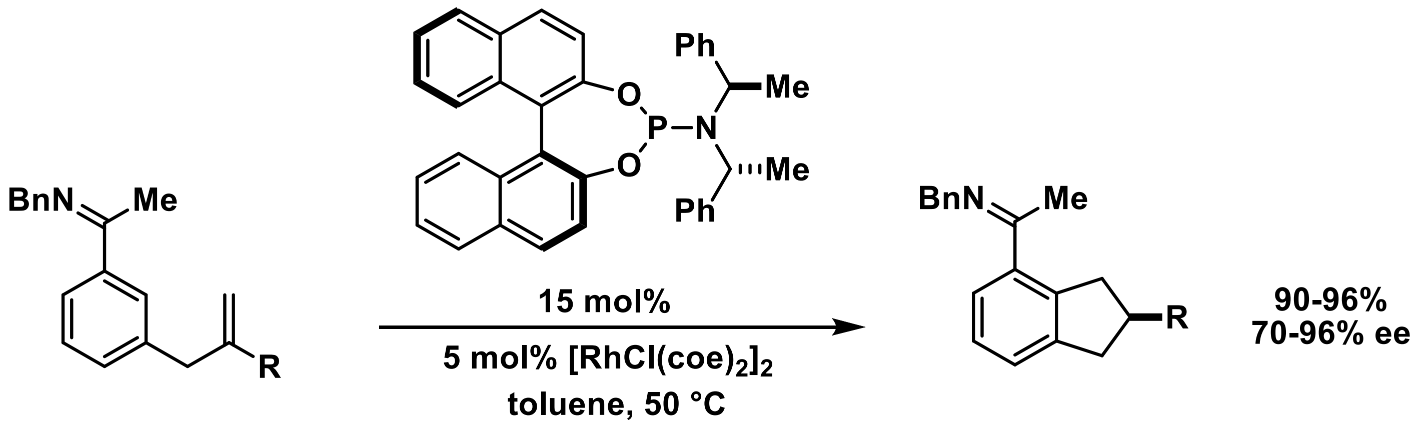
Stoltz: Deuterium-Labeling Gives Insights into the Reaction Mechanism[1]



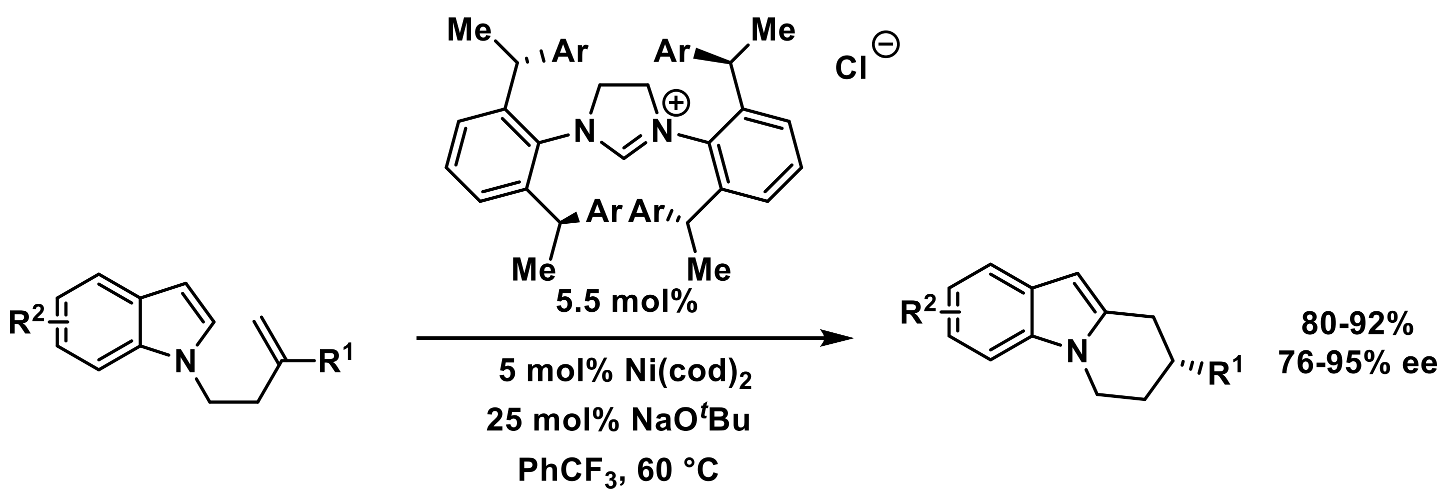
(1) Trend, R. M.; Ramtohul, Y. K.; Stoltz, B. M. *J. Am. Chem. Soc.* **2005,** *127,* 17778-17788.

4.6.3 Cyclization Reactions with Alkenes

Bergman-Ellman: Rh-Catalyzed cyclization initiated by C-H activation[1]



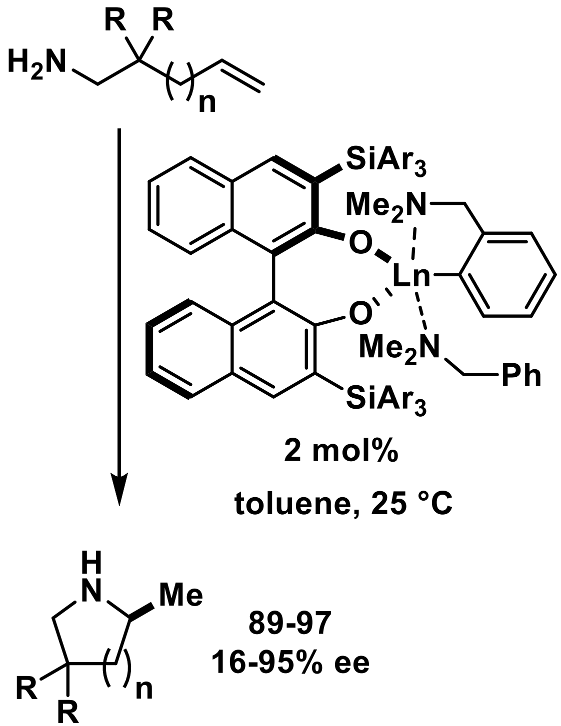
Cramer: Ni-Catalyzed cyclization with chiral carbene ligands[2]

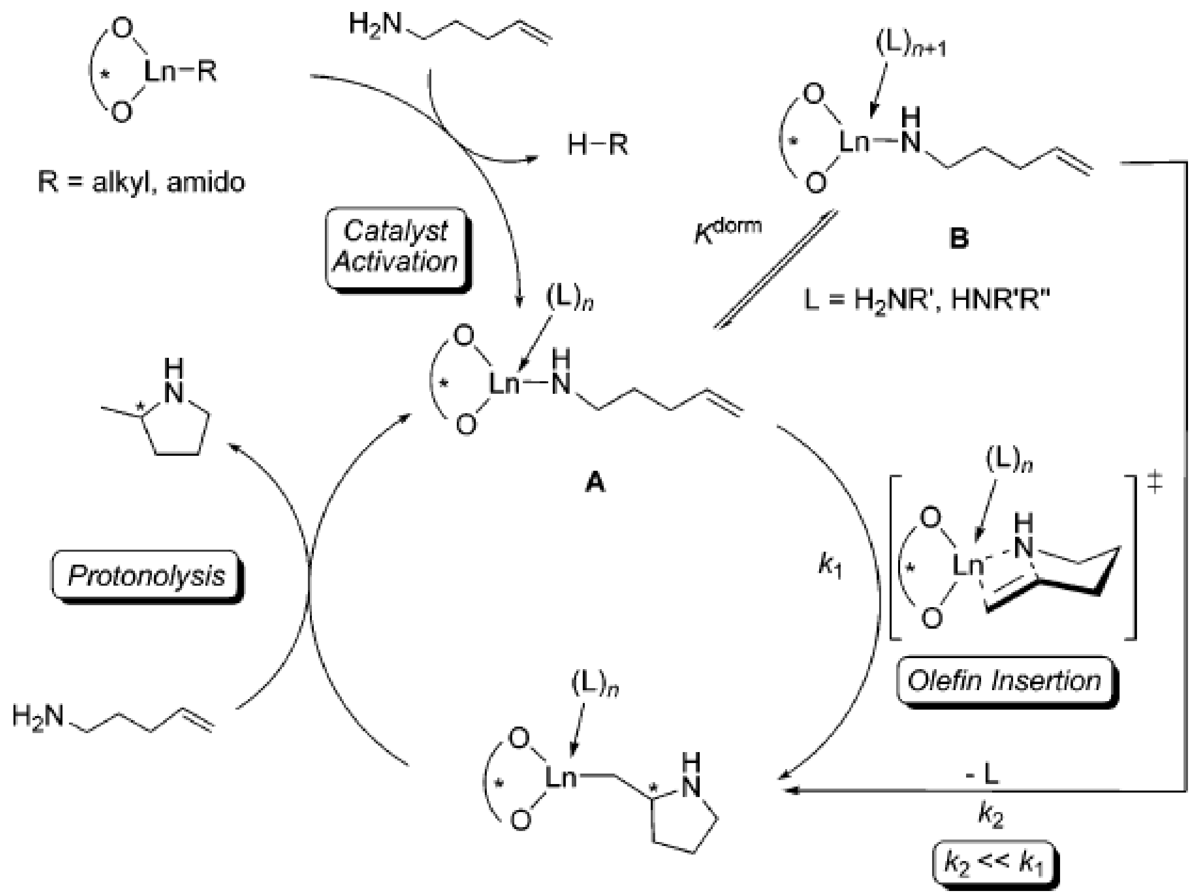


(1) Thalji, R. K.; Ellman, J. A.; Bergman, R. G. *J. Am. Chem. Soc.* **2004,** *126,* 7192-7193. (2) Diesel, J.; Grosheva, D.; Kodama, S.; Cramer, N., Angew. Chem., Int. Ed. **2019**, *58*, 11044-11048.

4.6.3 Cyclization Reactions with Alkenes

Hultsch: Intramolecular Hydroamination of Alkenes

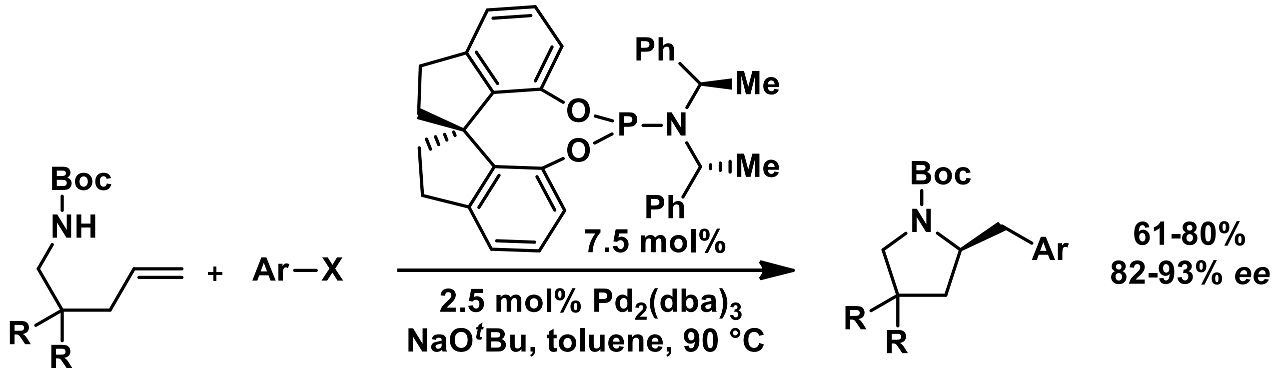


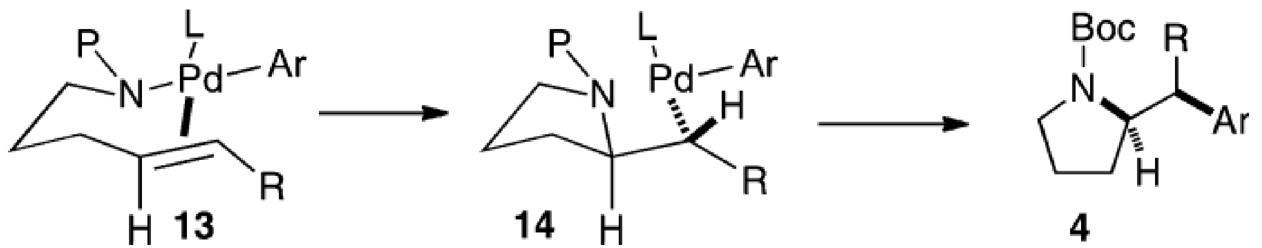


(1) Gribkov, D. V.; Hultzsch, K. C.; Hampel, F. **2006,** *128,* 3748-3759.

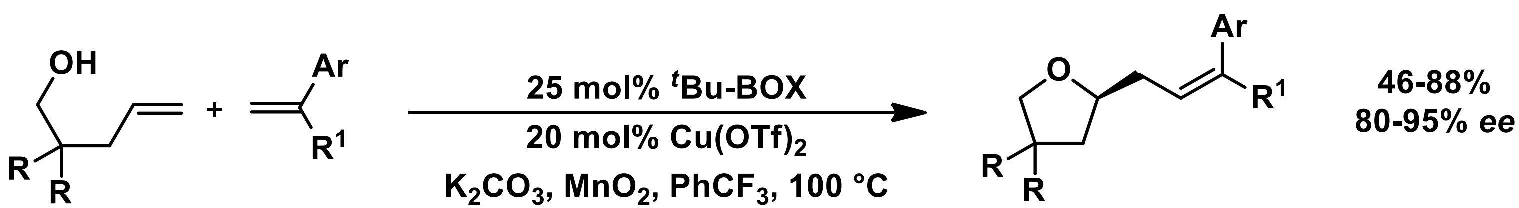
4.6.3 Cyclization Reactions with Alkenes

Wolfe: Asymmetric Carboamination with Pd catalysts[1]





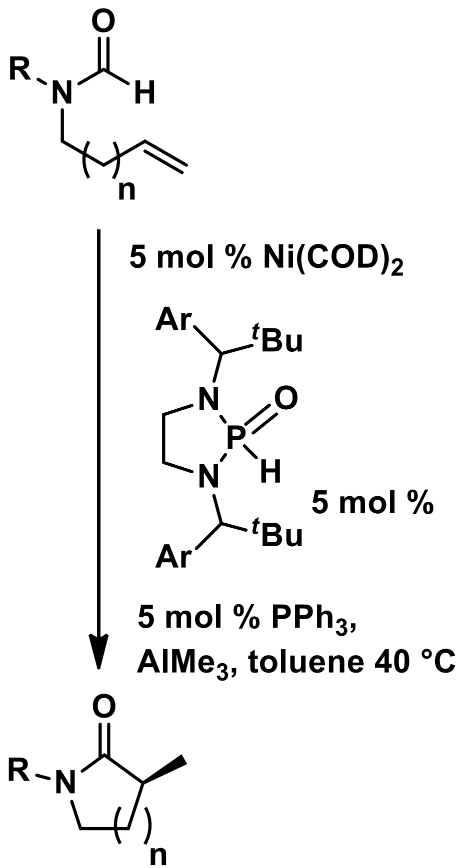
Chemler: Asymmetric Carbooxygenation with Cu catalysts[2]



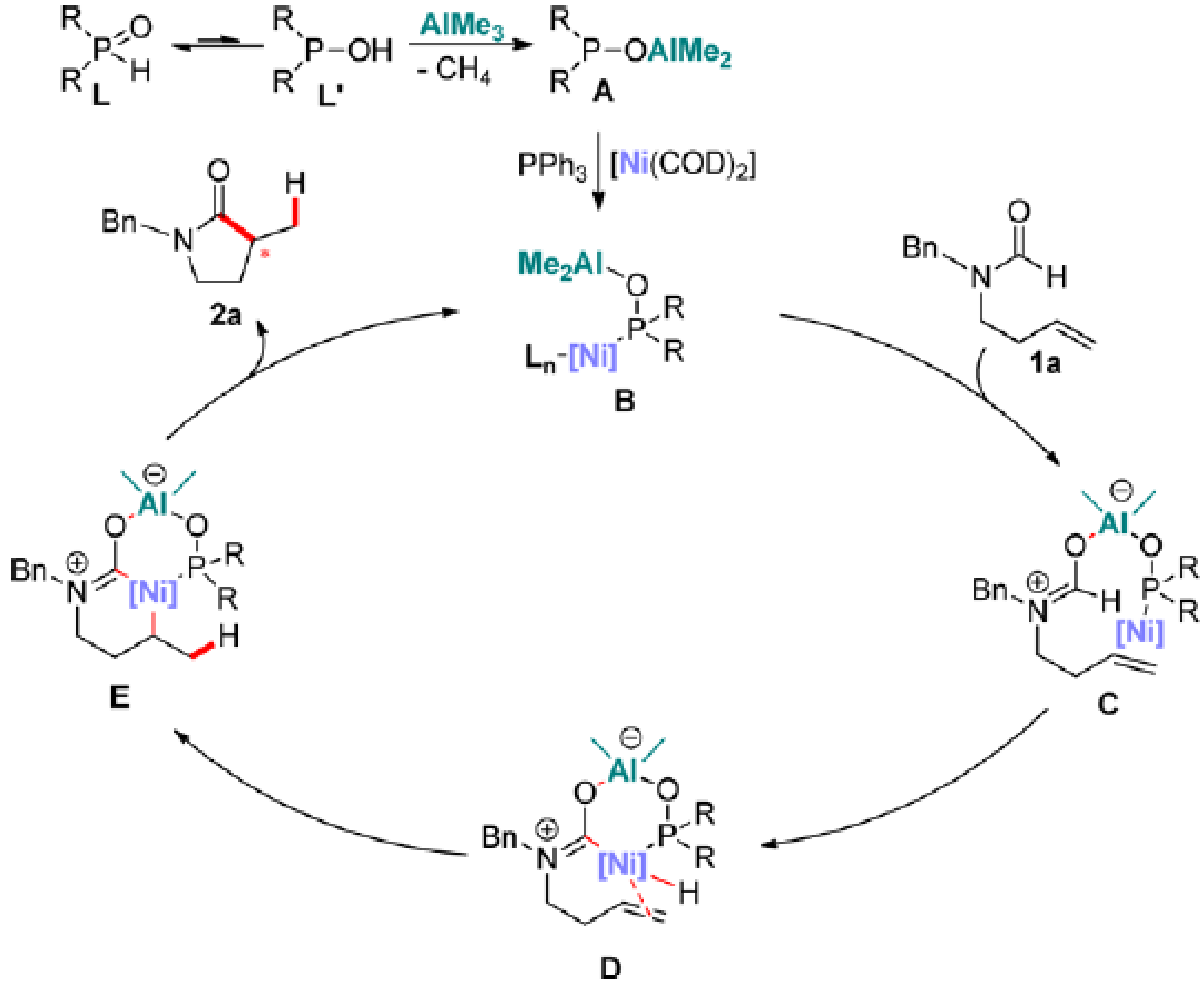
(1) Mai, D. N.; Wolfe, J. P., *J. Am. Chem. Soc.* **2010**, *132*, 12157. (2) Bovino, M. T.; Liwosz, T. W.; Kendel, N. E.; Miller, Y.; Tyminska, N.; Zurek, E.; Chemler, S. R. *Angew. Chem., Int. Ed.* **2014**, *53*, 6383.

4.6.3 Cyclization Reactions: Hydrocarbamoylation

Cramer: Nickel-catalyzed hydrocarbamoylation of olefins with new phosphine oxide ligand[1]



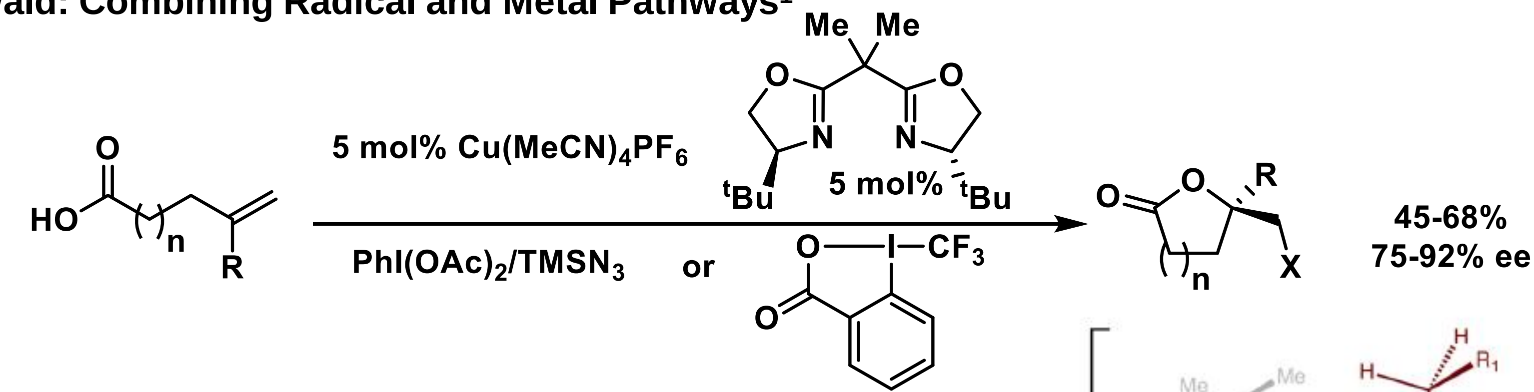
46-98%
80-95% *ee*

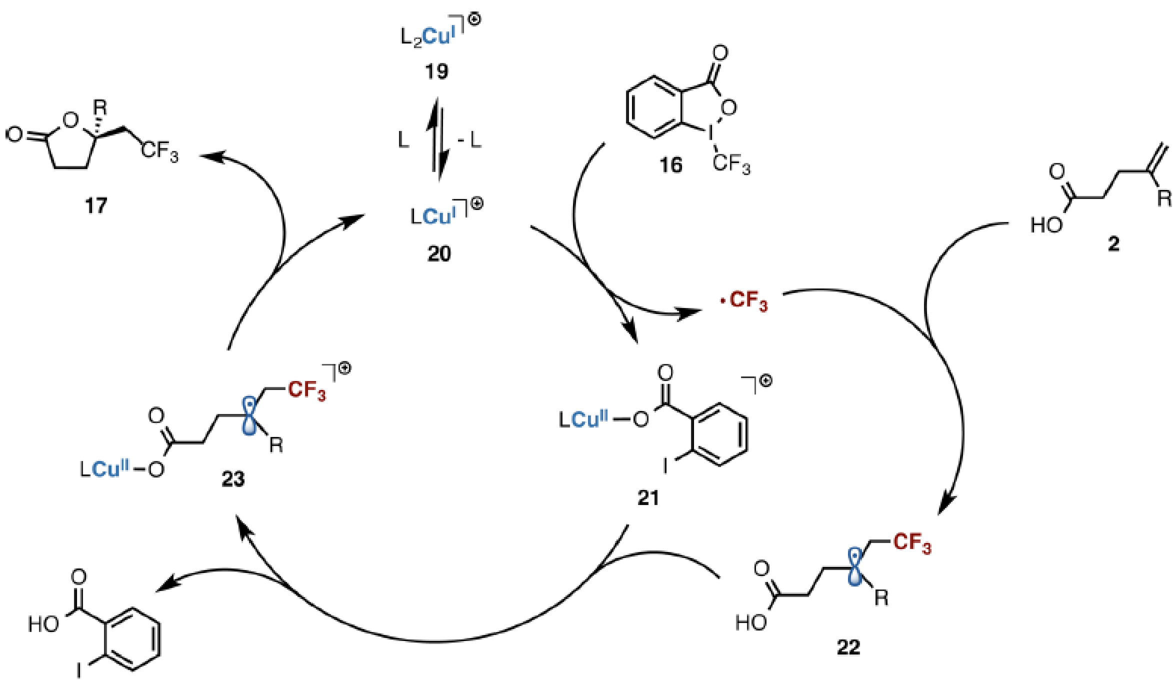


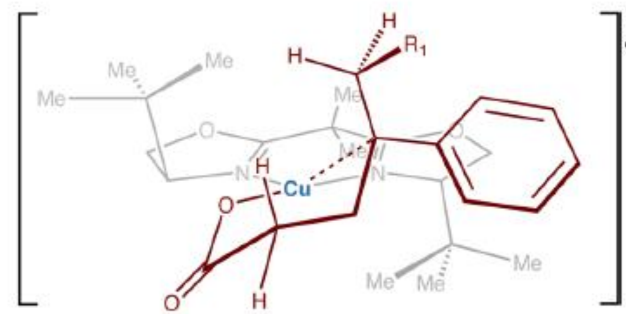
(1) Donets, P. A.; Cramer, N. *J. Am. Chem. Soc.* **2013**, *135*, 11772.

4.6.3. Cyclization Reactions: via radicals

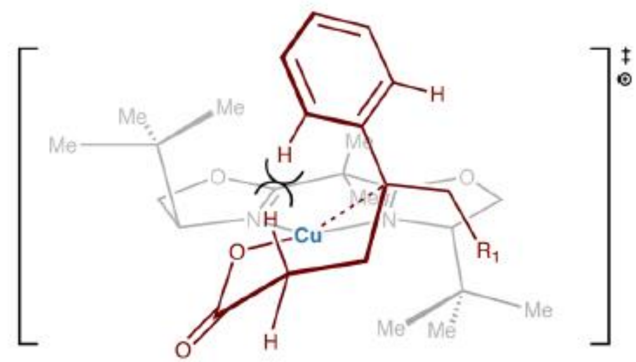
Buchwald: Combining Radical and Metal Pathways[1]







favored TS, leads to II

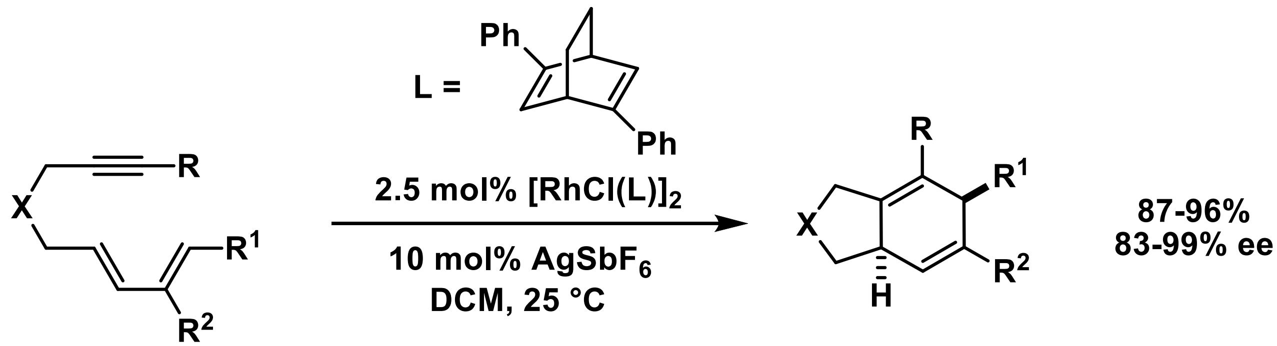


disfavored TS, leads to III

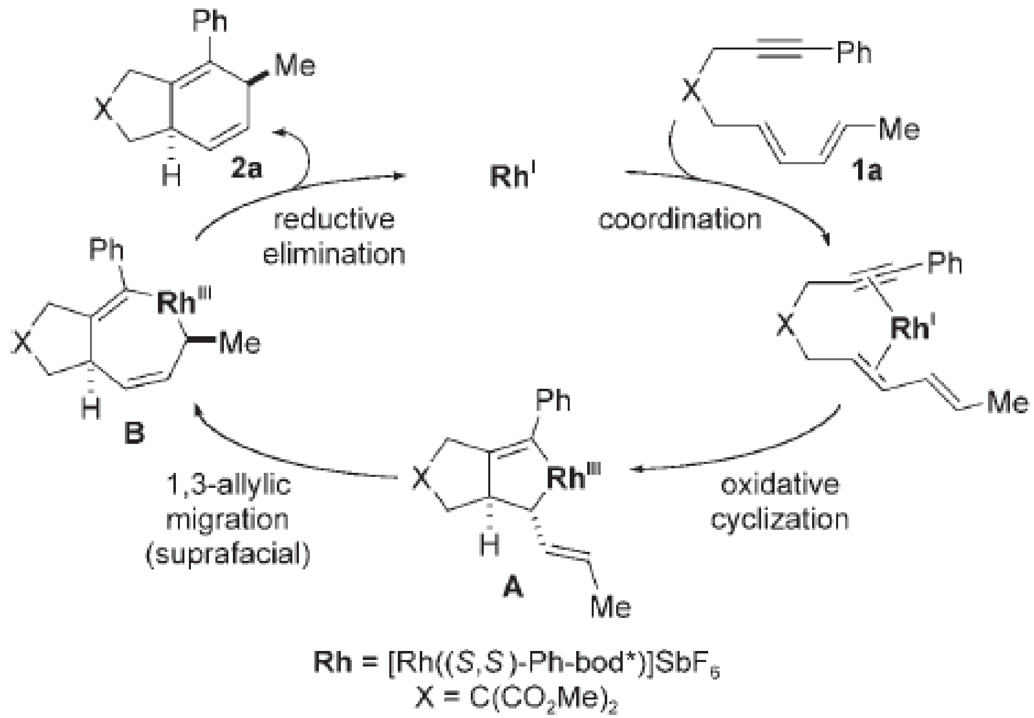
(1) Zhu, R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2015**, *137*, 8069.

4.6.3 Cycloaddition Reactions

Hayashi: [4+2] Intramolecular Cycloaddition Reaction of Alkynes and Dienes



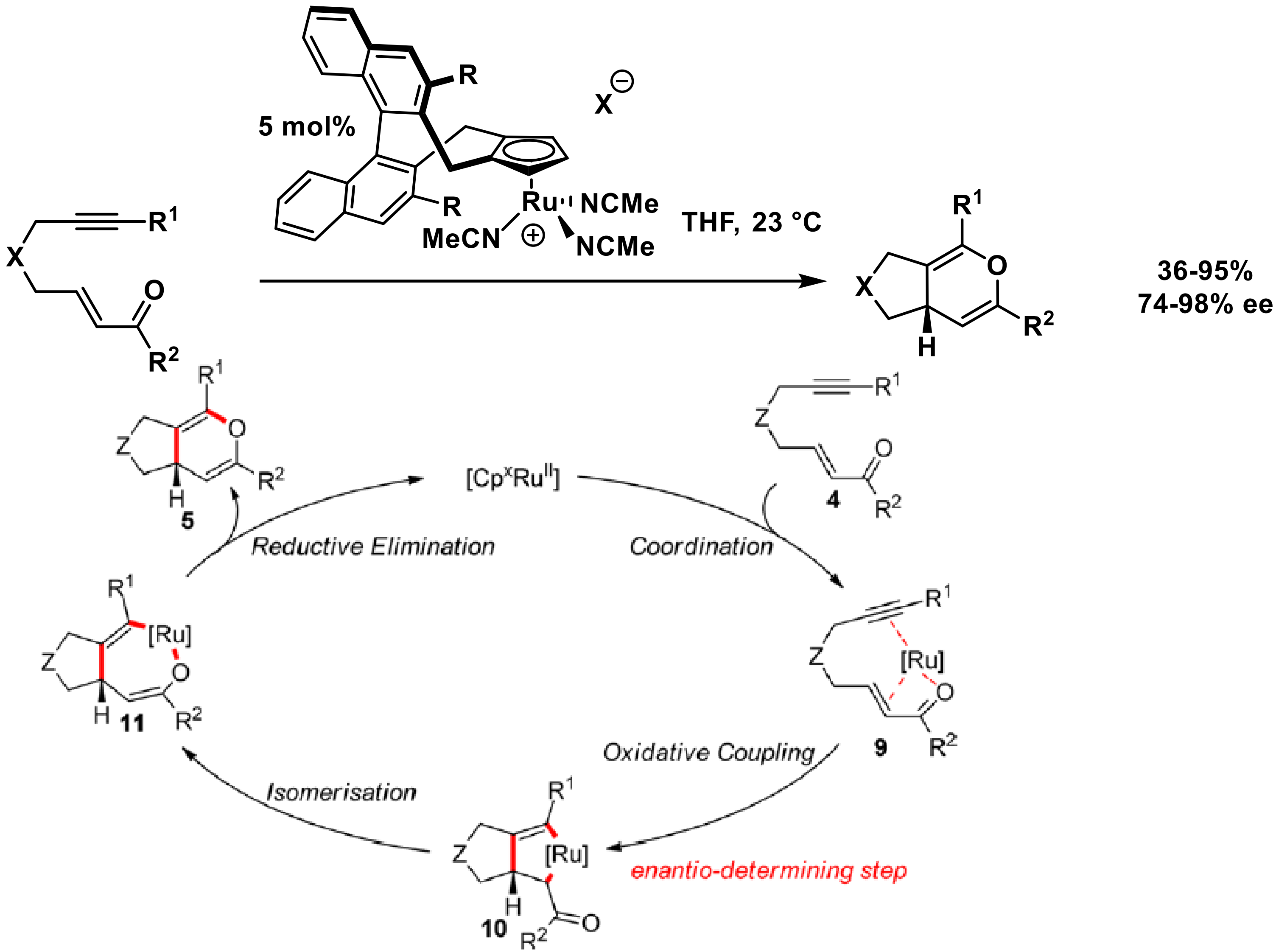
Mechanism



(1) Shintani, R.; Sannohe, Y.; Tsuji, T.; Hayashi, T. *Angew. Chem., Int. Ed.* **2007,** *46,* 7277-7280.

4.6.3 Cycloaddition Reactions

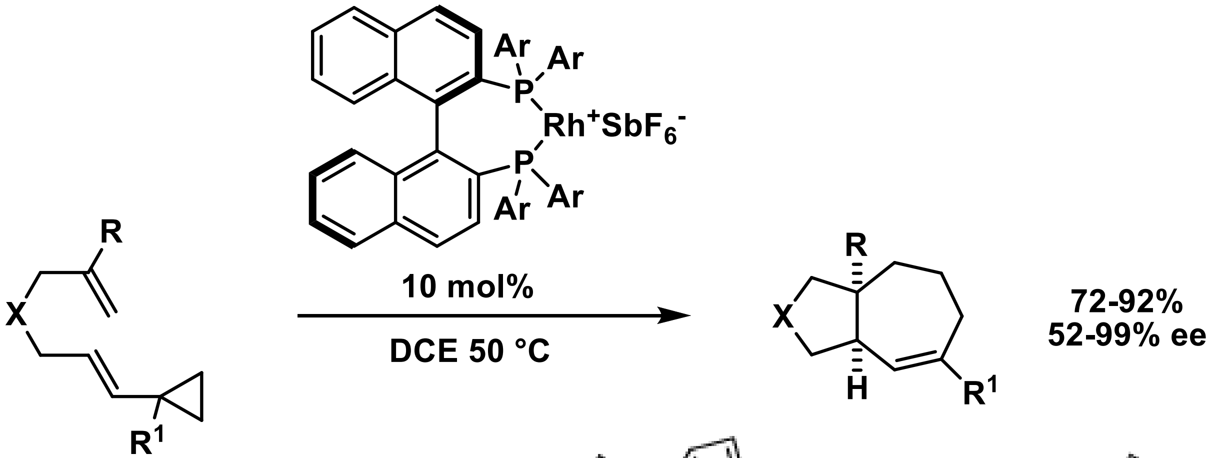
Cramer: Ruthenium-Catalyzed Annulation with Chiral CP ligand[1]



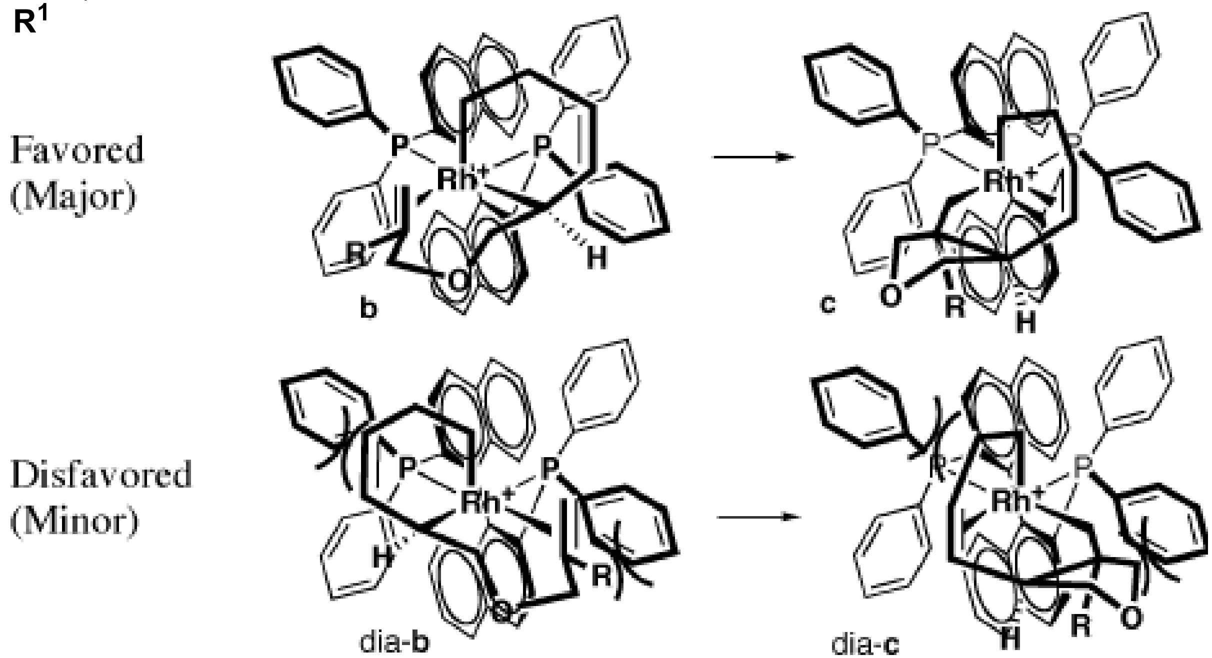
(1) Kossler, D.; Cramer, N. *J. Am. Chem. Soc.* **2015**, *137*, 12478.

4.6.3 Cycloaddition Reactions

Wender: [5+2] Intramolecular Cycloaddition of Vinylcyclopropanes and Alkenes



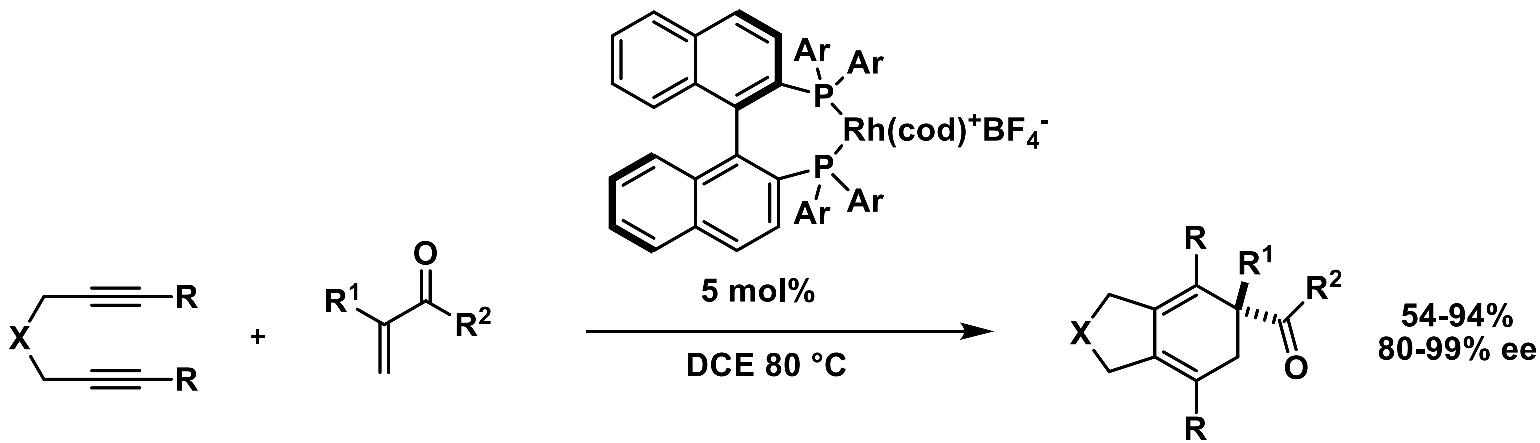
Model for Selectivity



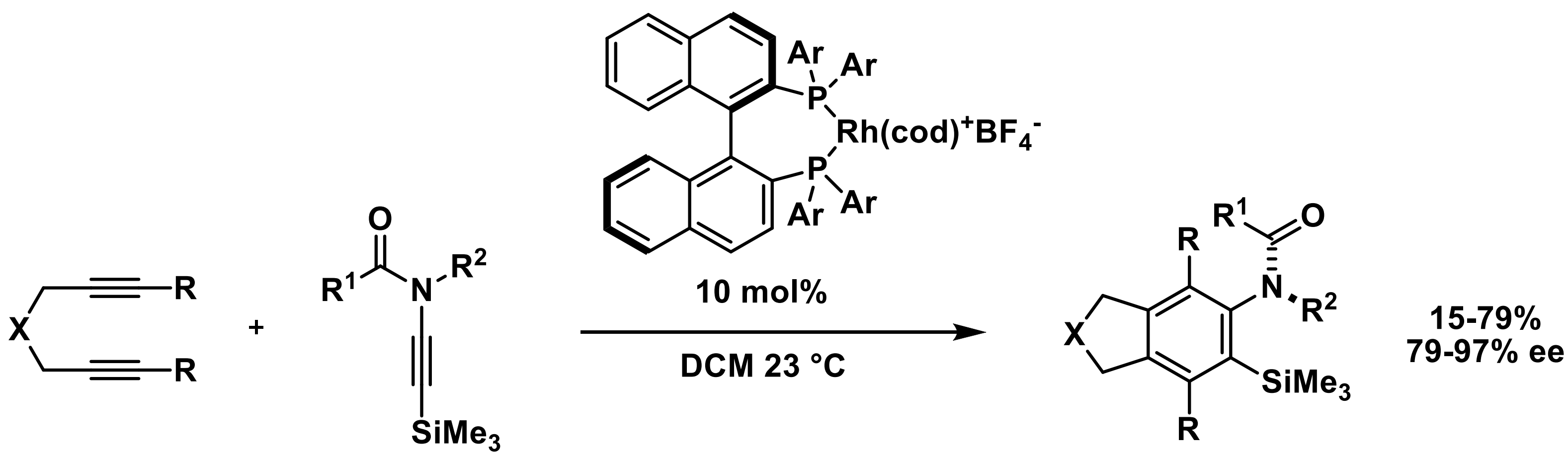
(1) Wender, P. A.; Haustedt, L. O.; Lim, J.; Love, J. A.; Williams, T. J.; Yoon, J. Y. *J. Am. Chem. Soc.* **2006,** *128,* 6302-6303.

4.6.3 Cycloaddition Reactions

Shibata: Asymmetric [2+2+2] Cycloaddition – Alkyne, Alkyne, Alkene[1]



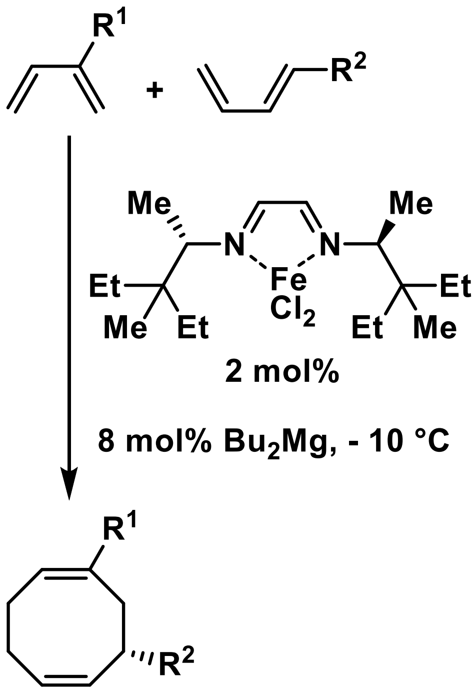
Tanaka: Asymmetric Trimerization of Alkynes for the Synthesis of Axially Chiral Anilides[2]

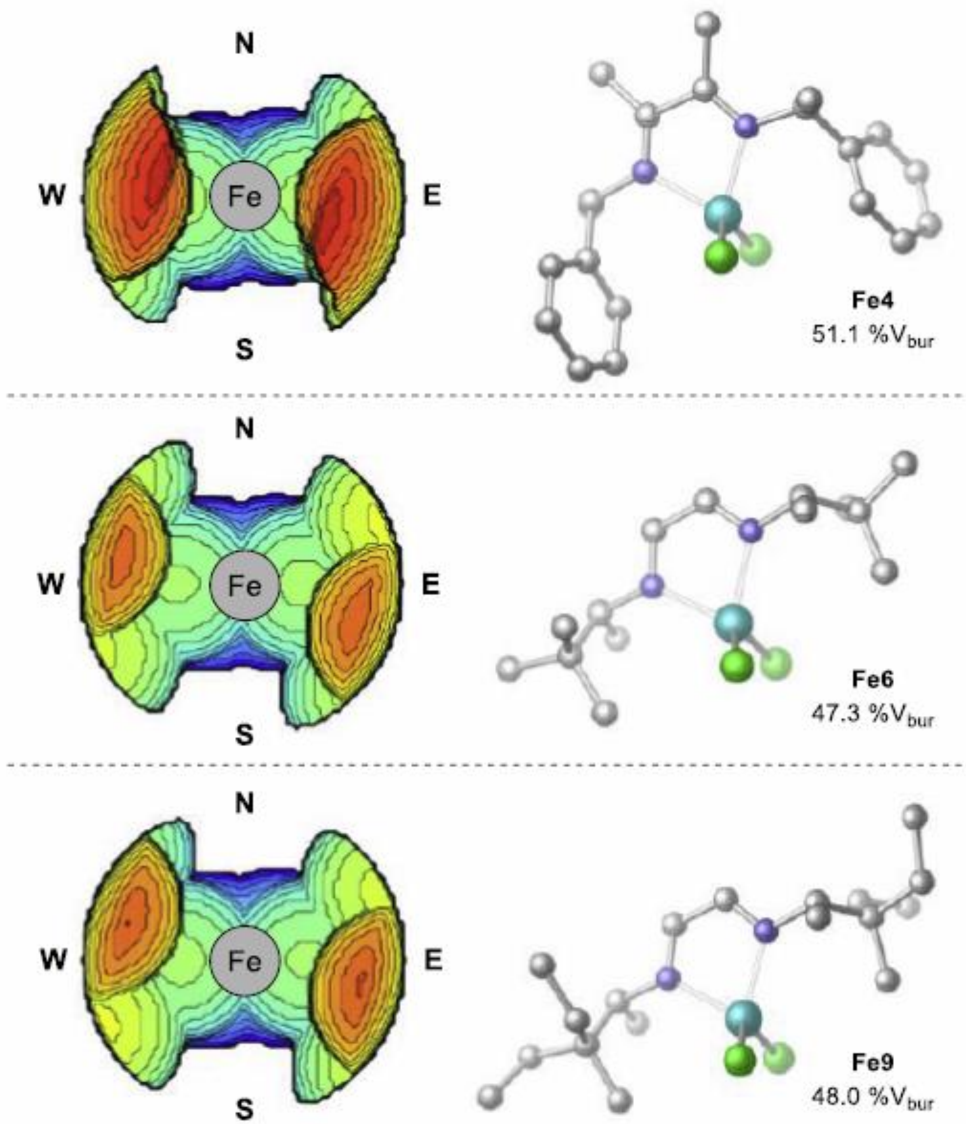


(1) Tsuchikama, K.; Kuwata, Y.; Shibata, T. *J. Am. Chem. Soc.* **2006,** *128,* 13686-13687. (1) Tanaka, K.; Takeishi, K.; Noguchi, K. *J. Am. Chem. Soc.* **2006,** *128,* 4586-4587.

4.6.3 Cycloaddition Reactions

Cramer: [4+4] with iron catalysis[1]

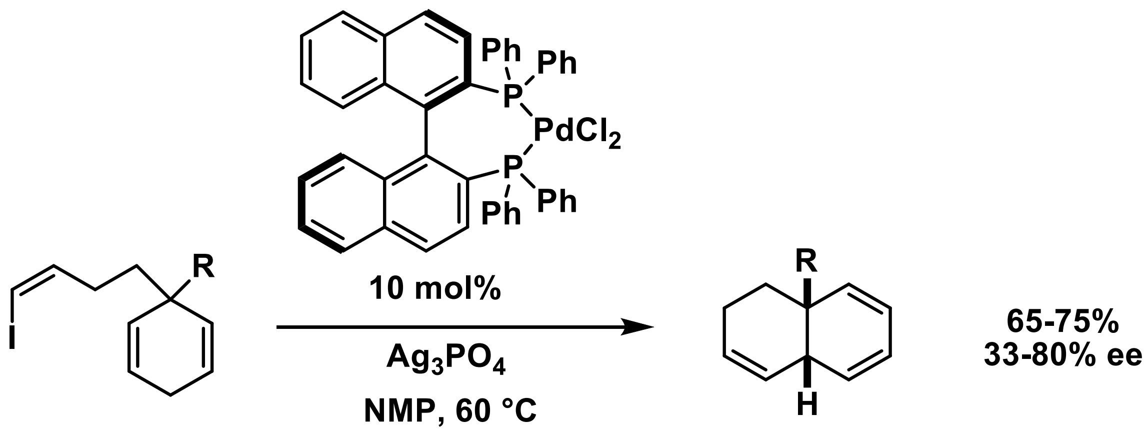




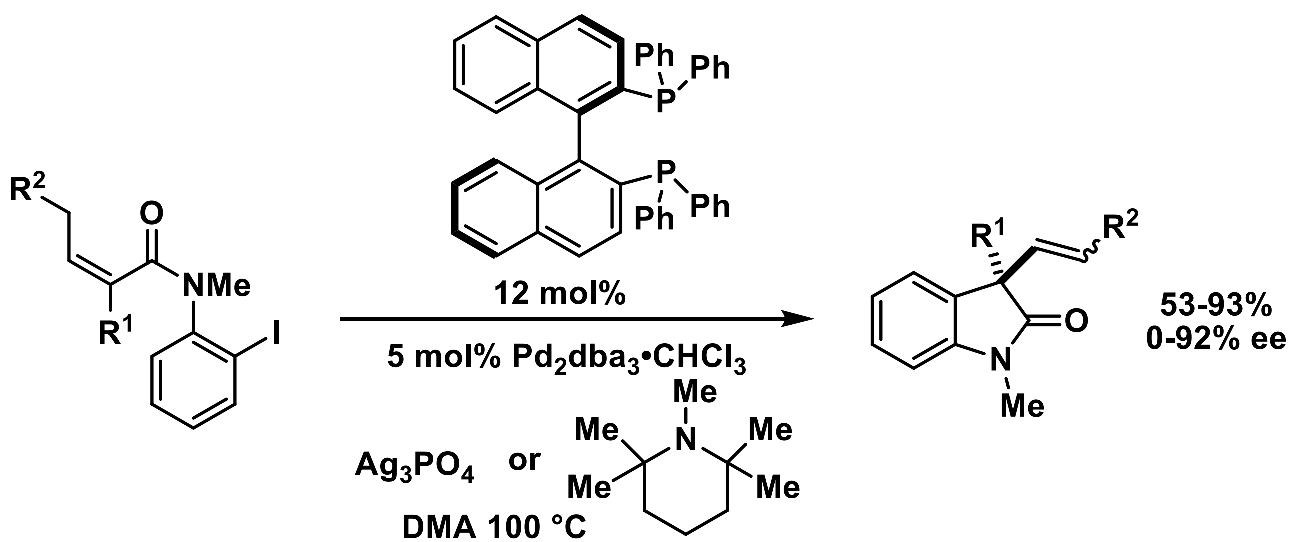
(1) Braconi, E.; Götzinger, A. C.; Cramer, N. *J. Am. Chem. Soc.* **2020**, *142*, 19819.

4.6.4 Cross-Coupling Reactions: Heck

Shibasaki: The First Asymmetric Heck Cyclization Reaction[1]



Overman: Asymmetric Heck Cyclization for the Synthesis of Oxindoles[2]

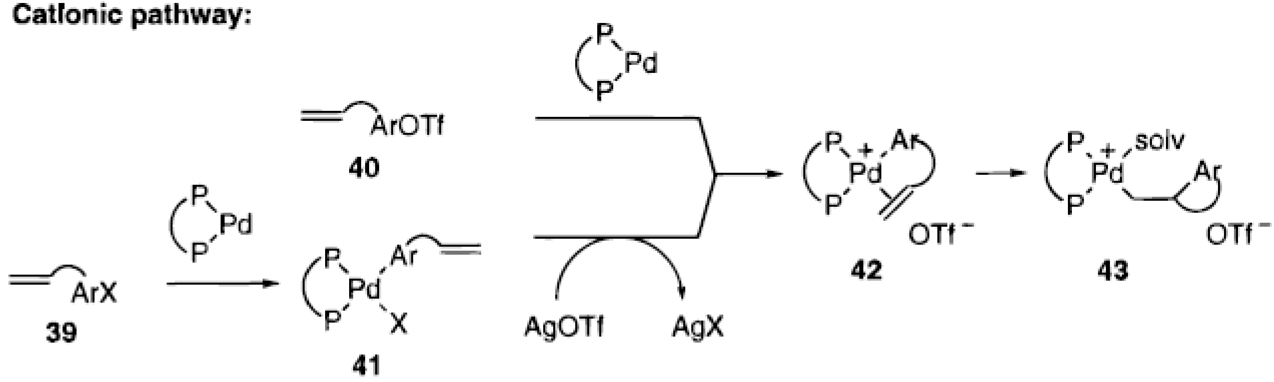


(1) Sato, Y.; Nukui, S.; Sodeoka, M.; Shibasaki, M. *Tetrahedron* **1994,** *50,* 371-382. (2) Ashimori, A.; Bachand, B.; Calter, M. A.; Govek, S. P.; Overman, L. E.; Poon, D. J. *J. Am. Chem. Soc.* **1998,** *120,* 6488-6499. (3) Ashimori, A.; Bachand, B.; Overman, L. E.; Poon, D. J. *J. Am. Chem. Soc.* **1998,** *120,* 6477-6487.

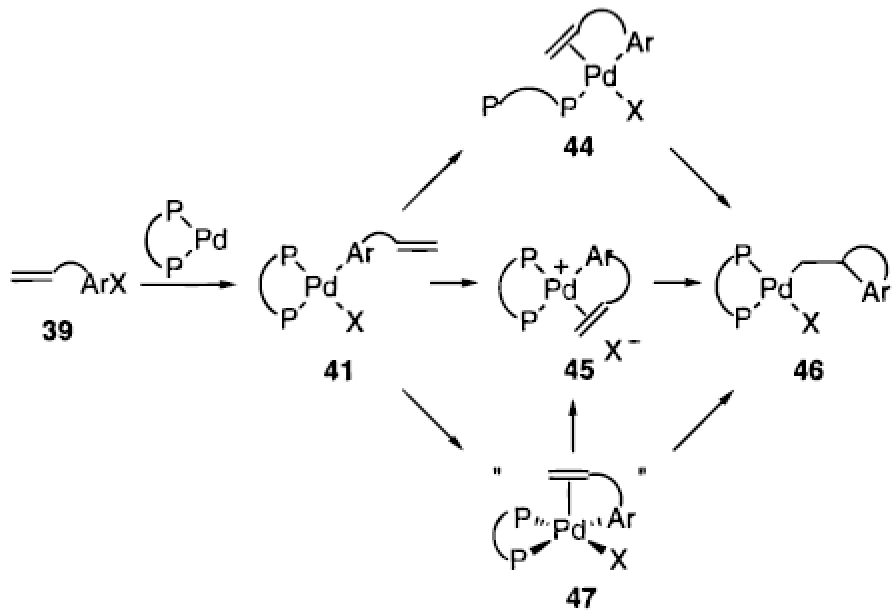
4.6.4 Cross-Coupling Reactions: Heck

The Two Possible Mechanism for the Heck Cyclization[1]

Cationic pathway:



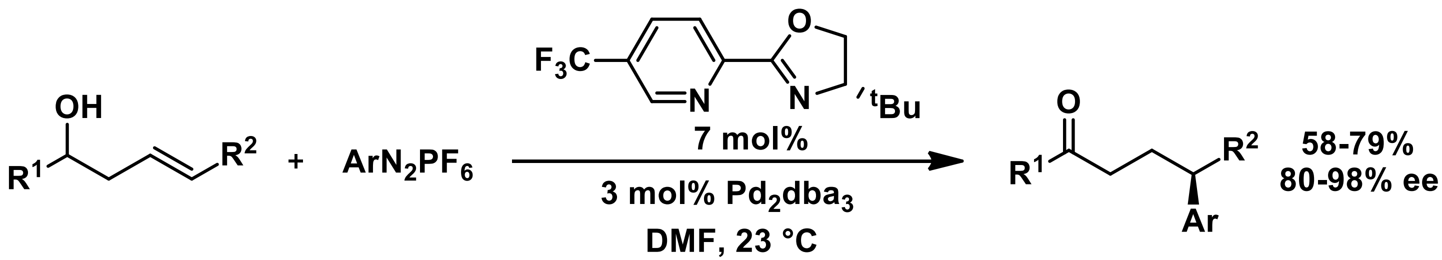
Neutral pathway:

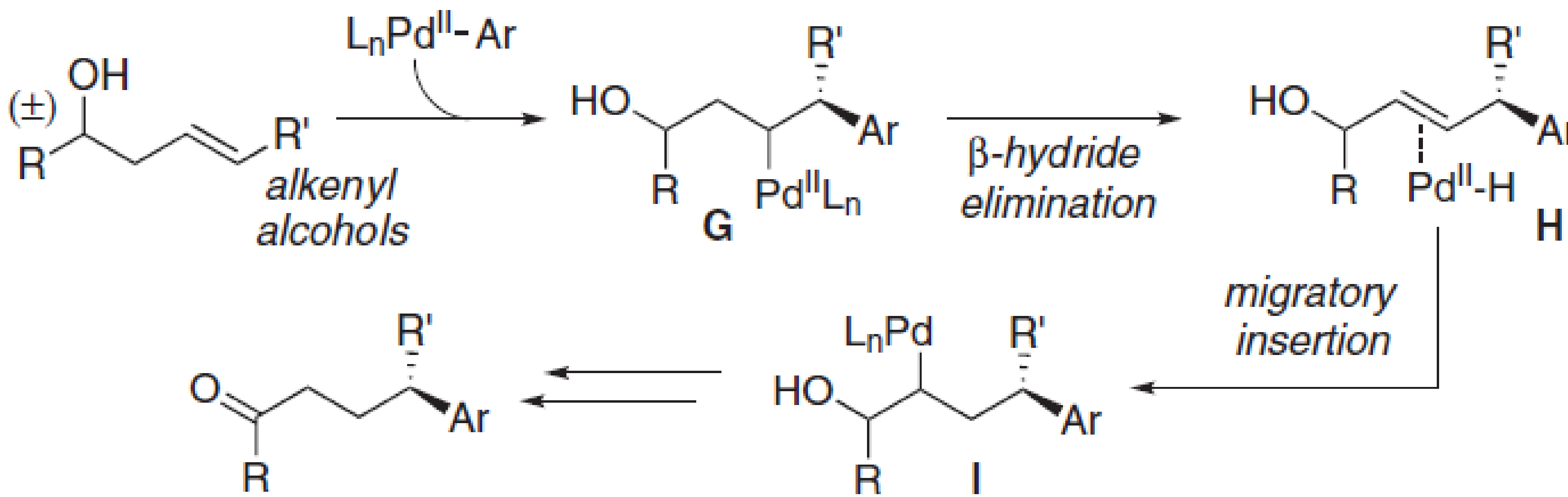


(1) Ashimori, A.; Bachand, B.; Calter, M. A.; Govek, S. P.; Overman, L. E.; Poon, D. J. *J. Am. Chem. Soc.* **1998,** *120,* 6488-6499.

4.6.4 Cross-Coupling Reactions: Heck

Sigman: Enantioselective Heck arylation

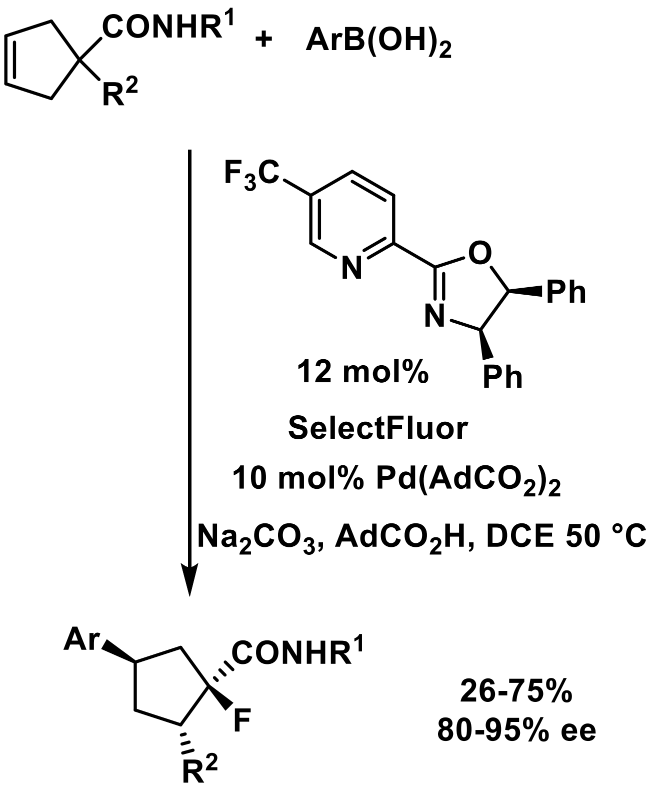


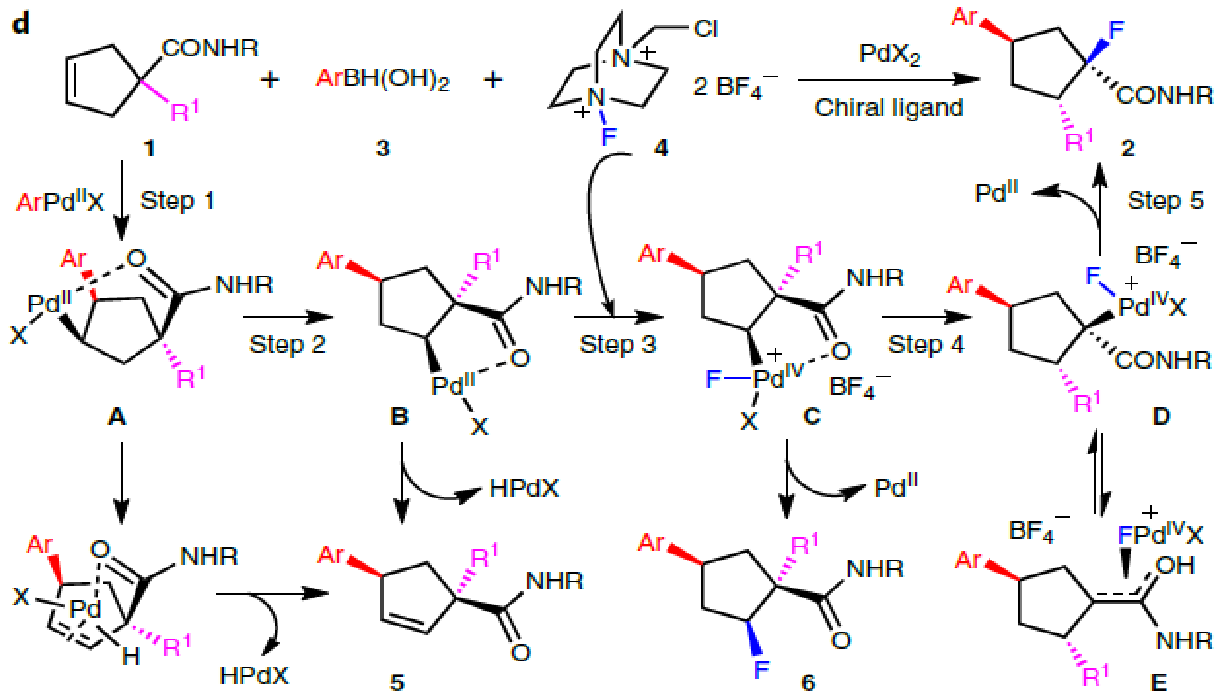


(1) Werner, E. W.; Mei, T. S.; Burckle, A. J.; Sigman, M. S. *Science* **2012**, *338*, 1455. (2) Mei, T. S.; Patel, H. H.; Sigman, M. S. *Nature* **2014**, *508*, 340.

4.6.4 Cross-Coupling Reactions: Dyotropic Rearrangements

Zhu: dyotropic rearrangement of carbon and palladium[1]

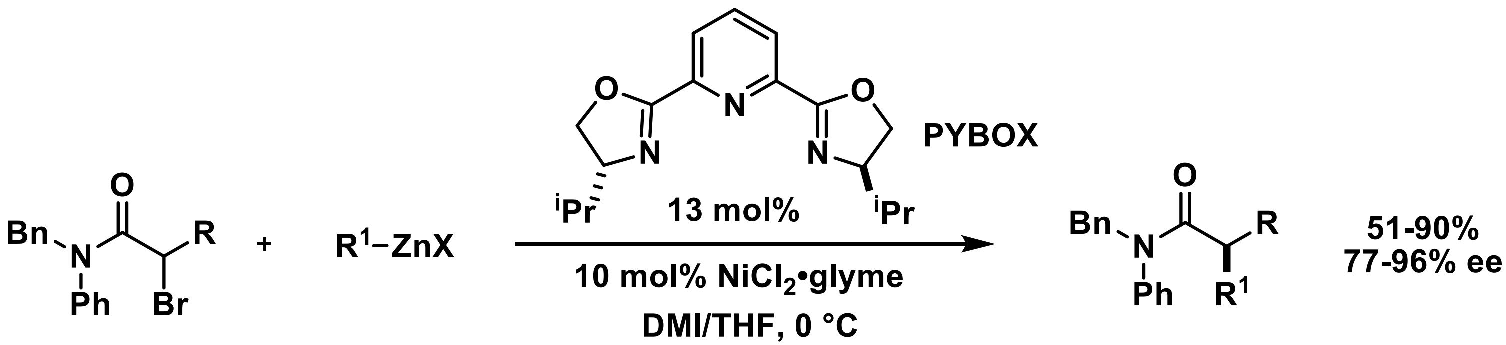




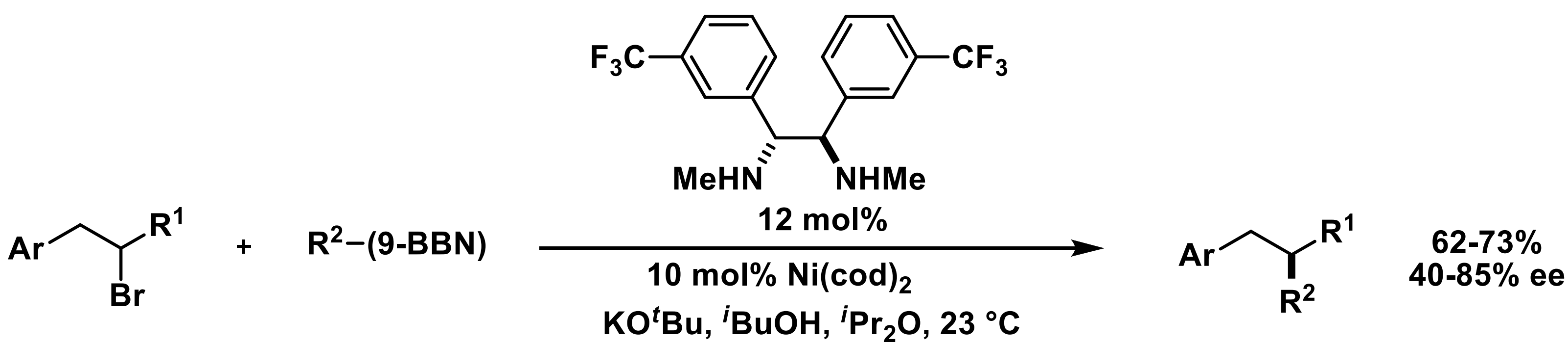
(1) Cao, J.; Wu, H.; Wang, Q.; Zhu, J. *Nat. Chem.* **2021**, *13*, 671-676.

4.6.4 Cross-Coupling Reactions: Negishi and Suzuki

Fu: Asymmetric Negishi Coupling of α-Bromo Amides[1]



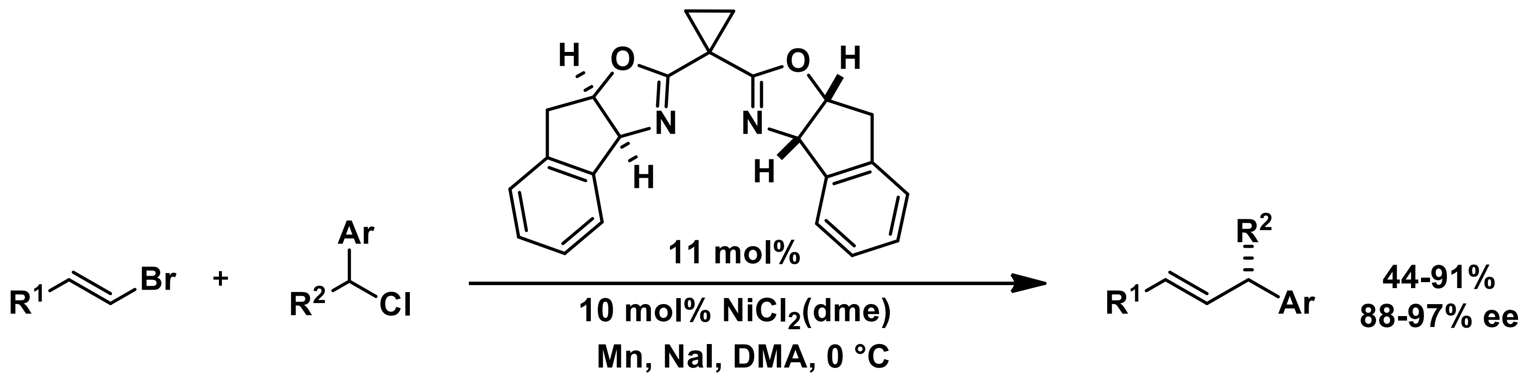
Fu: Asymmetric Asymmetric Suzuki Coupling of Homobenzylic Bromides[2]



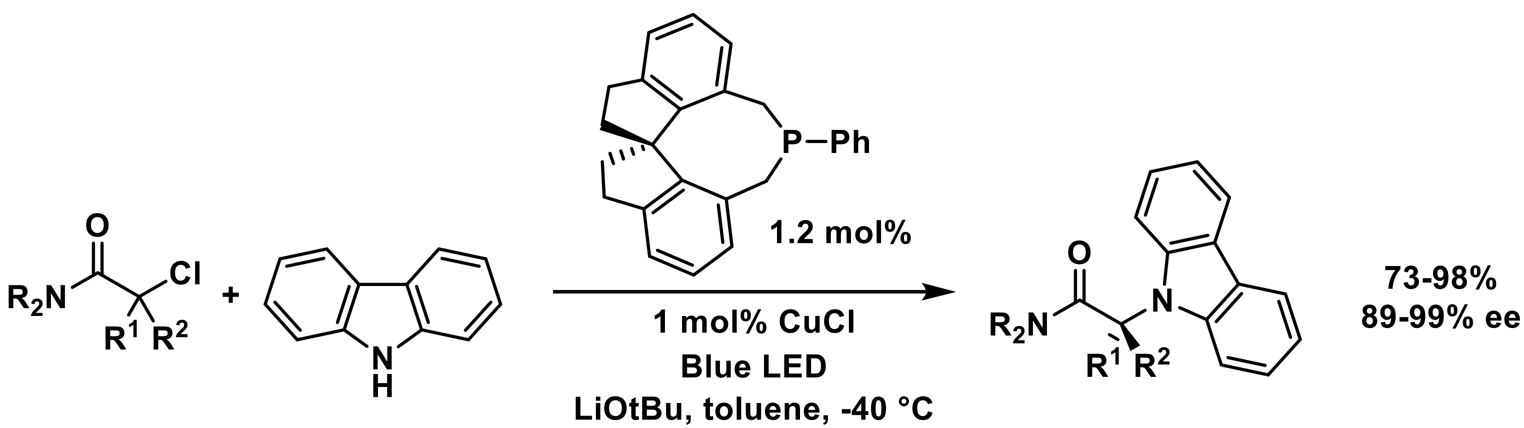
(1) Fischer, C.; Fu, G. C. *J. Am. Chem. Soc.* **2005,** *127,* 4594-4595. (2) Saito, B.; Fu, G. C. *J. Am. Chem. Soc.* **2008**, *130*, 6694.

4.6.4 Cross-Coupling Reactions: Reductive and C-N

Reisman: Reductive Cross-Coupling[2]



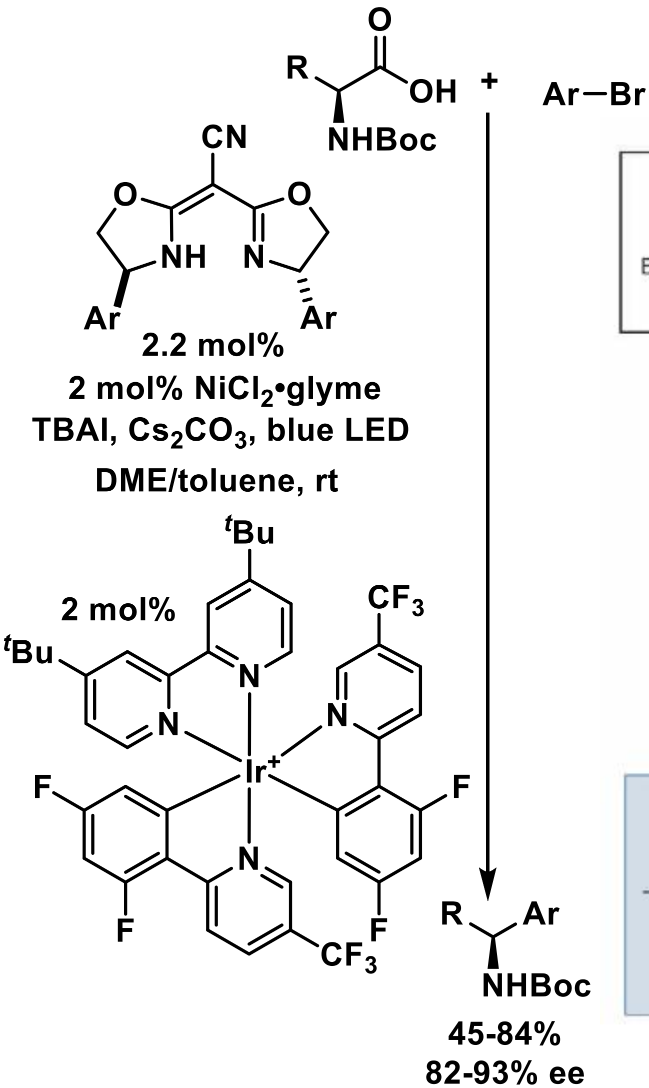
Fu/Peters: C-N Coupling Combining Nickel and Photoredox Catalysis[2]

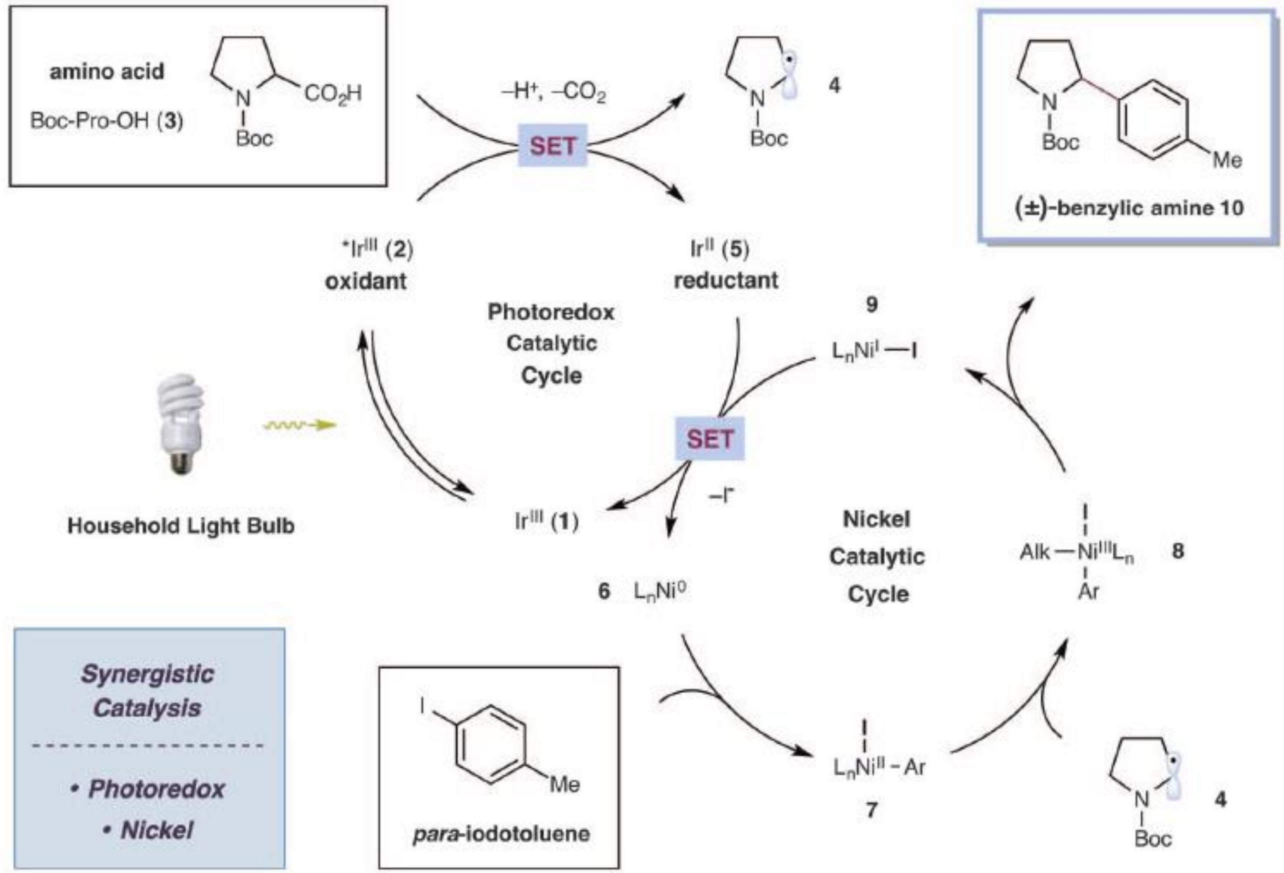


(1) Cherney, A. H.; Reisman, S. E. *J. Am. Chem. Soc.* **2014**, *136*, 14365. (2) Kainz, Q. M.; Matier, C. D.; Bartoszewicz, A.; Zultanski, S. L.; Peters, J. C.; Fu, G. C. *Science* **2016**, *351*, 681-684.

4.6.4 Cross-Coupling Reactions: Decarboxylative/Photoredox

MacMillan: Combining Decarboxylative Photoredox and Nickel Catalysis

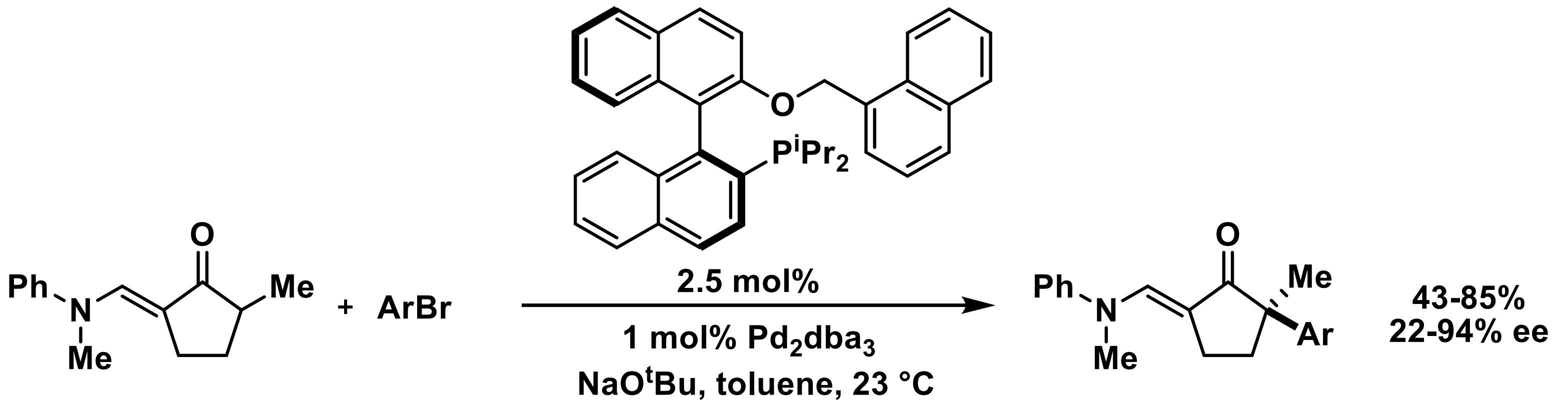




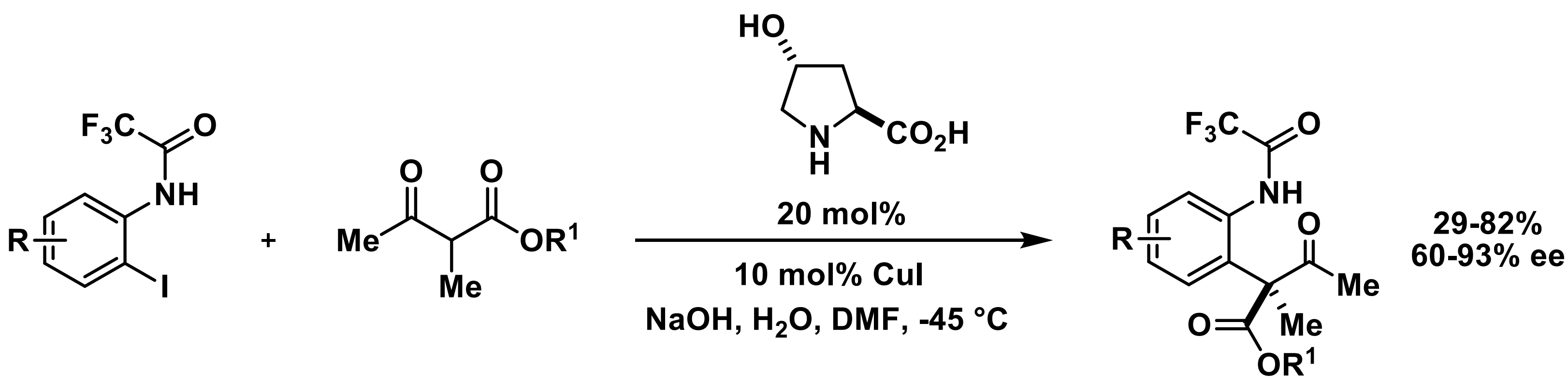
(1) Zuo, Z.; Ahneman, D. T.; Chu, L.; Terrett, J. A.; Doyle, A. G.; MacMillan, D. W. C. *Science* **2014,** *345*, 437-440. (2) Zuo, Z. W.; Gong, H.; Li, W.; Choi, J.; Fu, G. C.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2016,** *138*, 1832-1835.

4.6.4 Cross-Coupling Reactions: Arylation of Ketones

Buchwald: Asymmetric α-Arylation of Ketones[1]



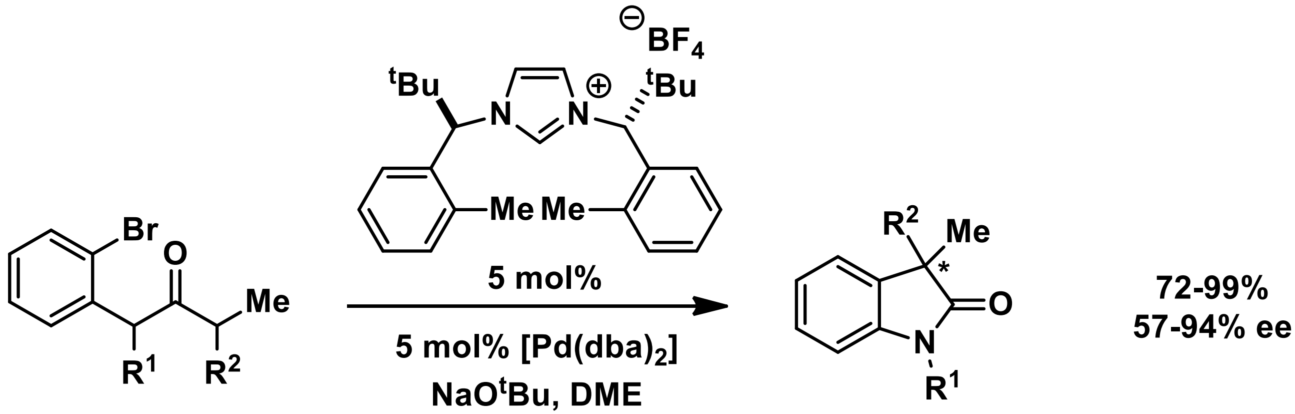
Ma: Cu-Catalyzed Arylation of β-Ketoesters[2]



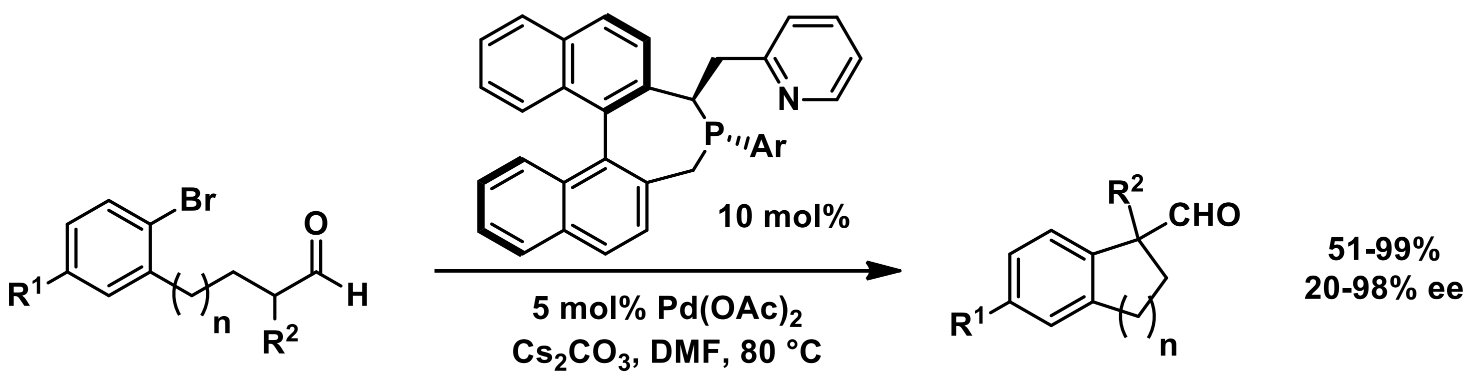
(1) Hamada, T.; Chieffi, A.; Ahman, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 1261-1268. (2) Xie, X. A.; Chen, Y.; Ma, D. W. *J. Am. Chem. Soc.* **2006**, *128,* 16050-16051.

4.6.4 Cross-Coupling Reactions: Arylation of Carbonyls

Kundig: Intramolecular Arylation of Ketones using Carbene Ligands[1]



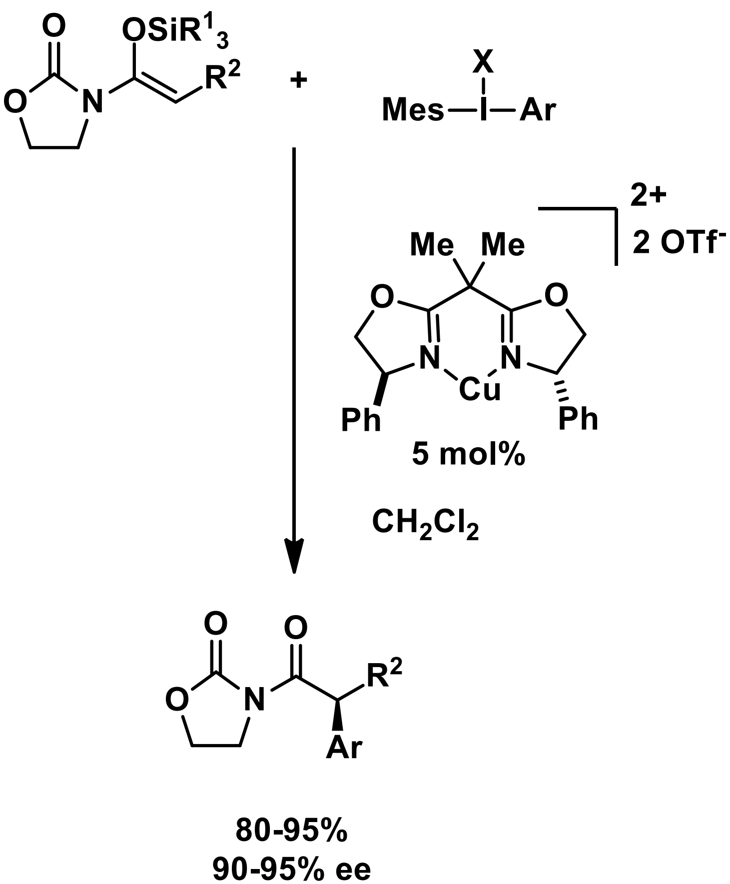
Mazet: Intramolecular Arylation of Aldehydes[2]

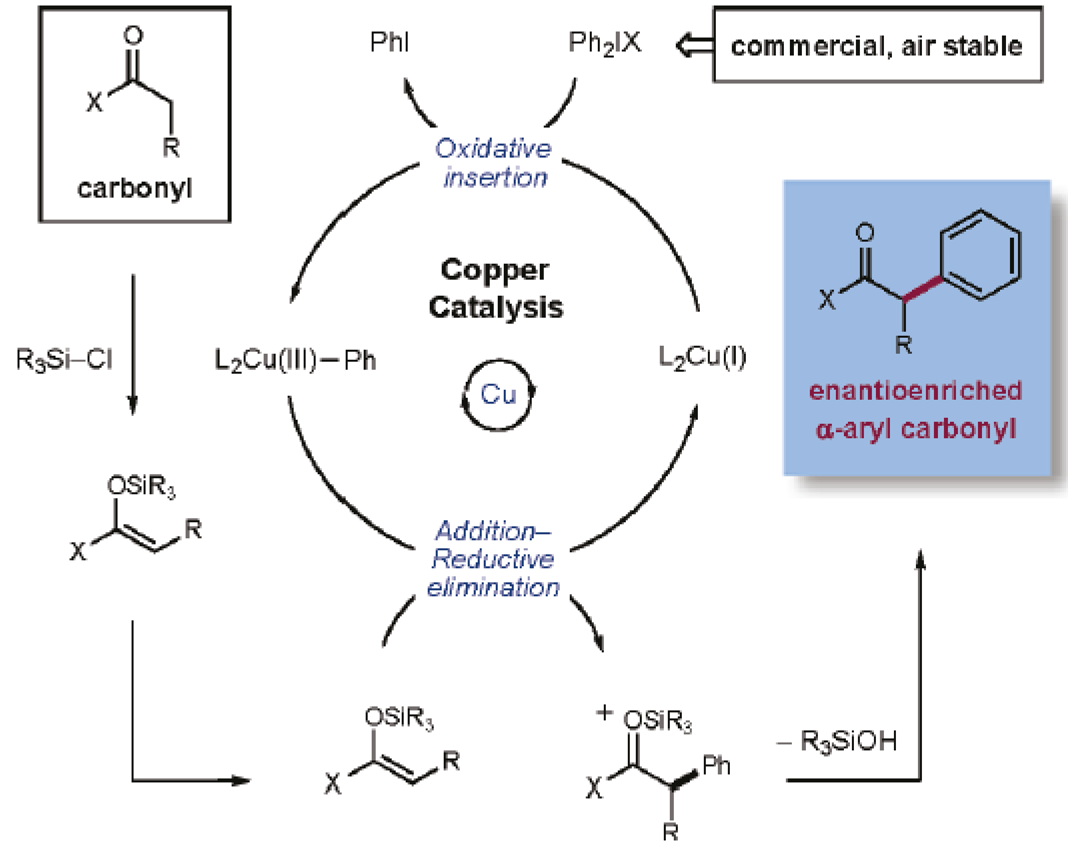


(1) Kundig, E. P.; Seidel, T. M.; Jia, Y. X.; Bernardinelli, G. *Angew. Chem., Int. Ed.* **2007,** *46,* 8484. (2) Nareddy, P.; Mantilli, L.; Guenee, L.; Mazet, C. *Angew. Chem., Int. Ed.* **2012,** *51*, 3826.

4.6.4 Cross-Coupling Reactions: Arylation of Enols

Gaunt and MacMillan: Cu-Catalyzed arylation of silyl enol ether with aryl iodonium salts[1,2]

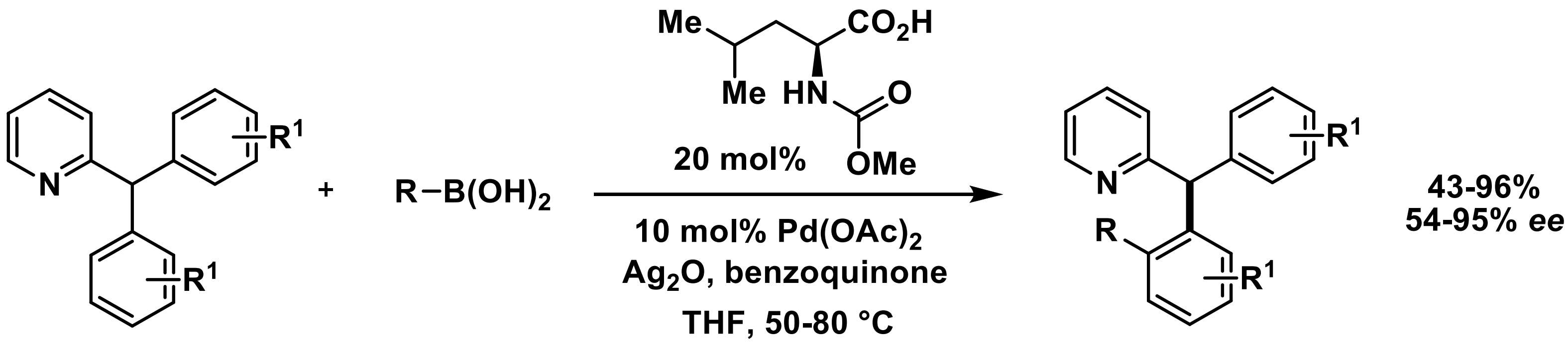




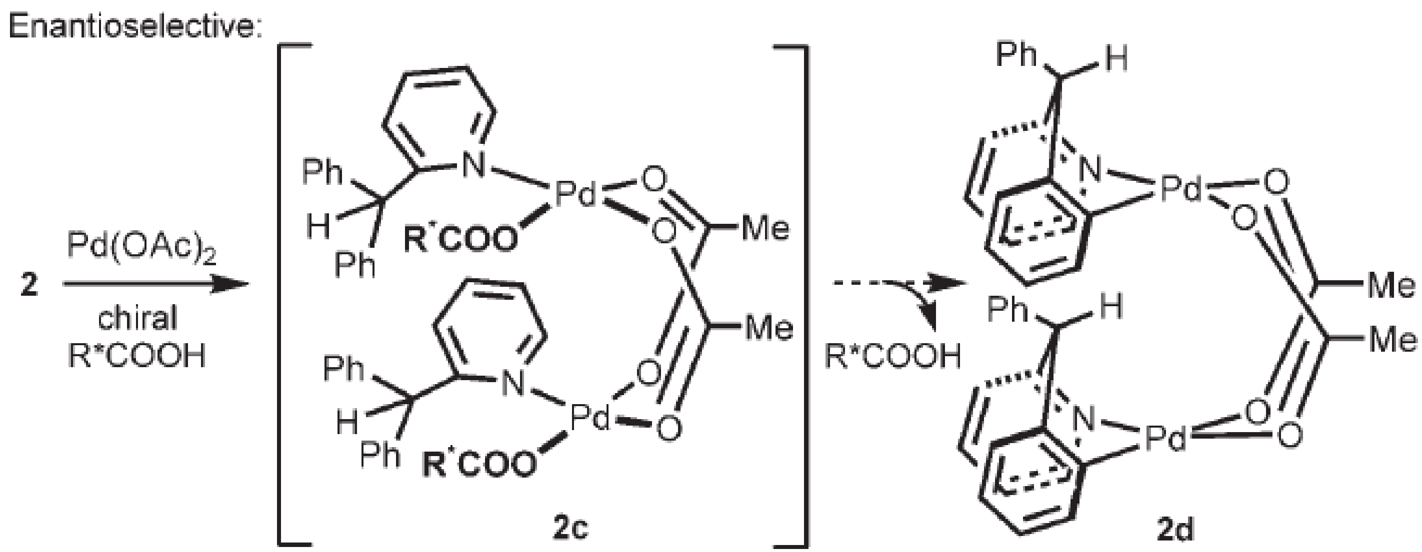
(1) Bigot, A.; Williamson, A. E.; Gaunt, M. J. *J. Am. Chem. Soc.* **2011,** *133*, 13778. (2) Harvey, J. S.; Simonovich, S. P.; Jamison, C. R.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2011,** *133*, 13782.

4.6.5 CH Functionalization: SP2 C-H activation

Yu: Enantioselective C-H Activation[1]



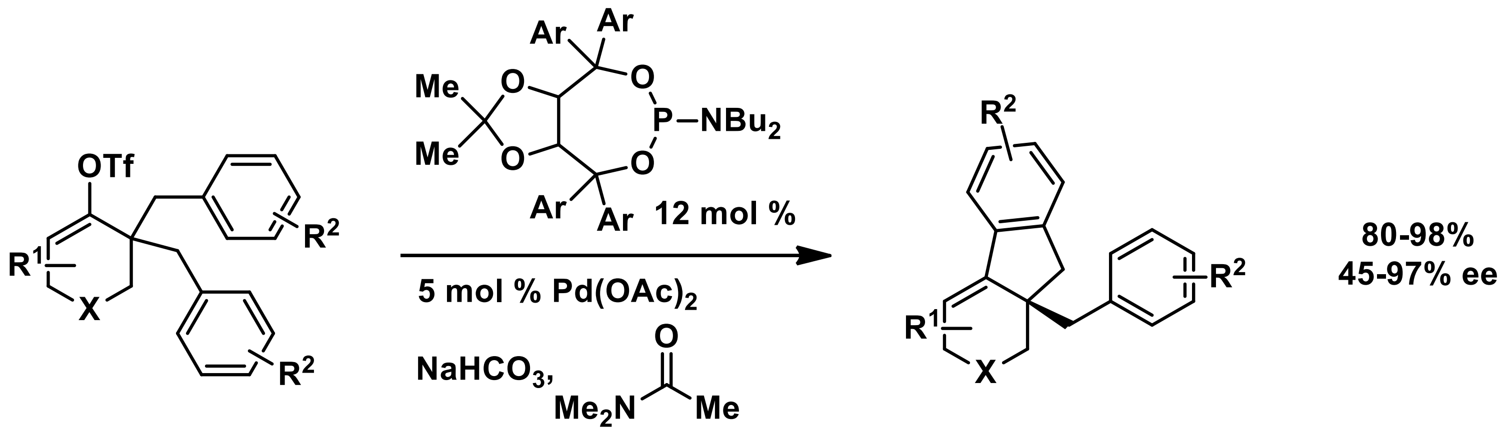
Working Model



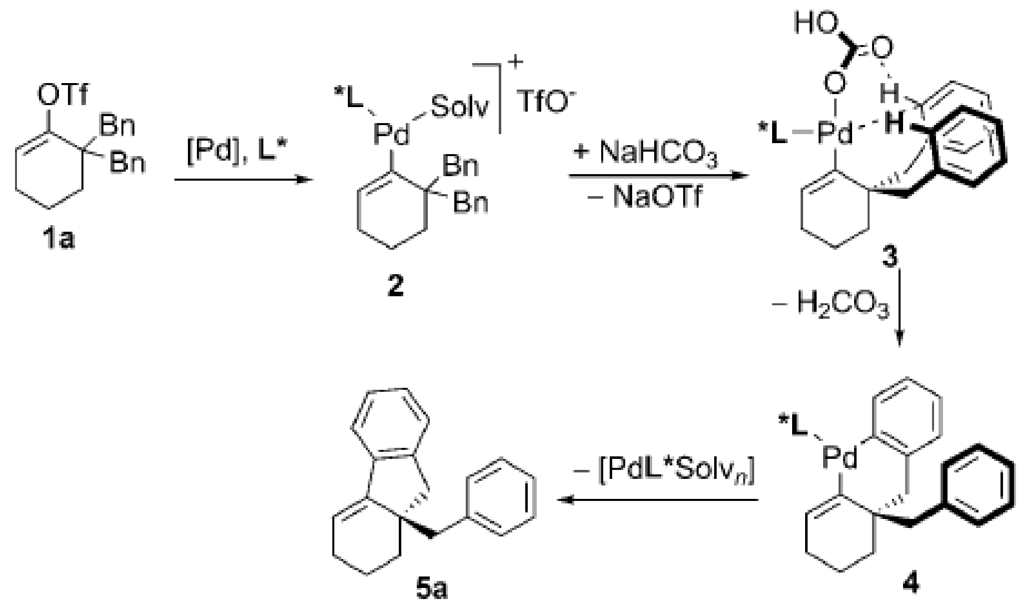
(1) Shi, B. F.; Maugel, N.; Zhang, Y. H.; Yu, J. Q. *Angew. Chem., Int. Ed.* **2008**, *47*, 4882.

4.6.5 CH Functionalization: SP^2 C-H activation

Cramer: Enantioselective C-H Activation[1]



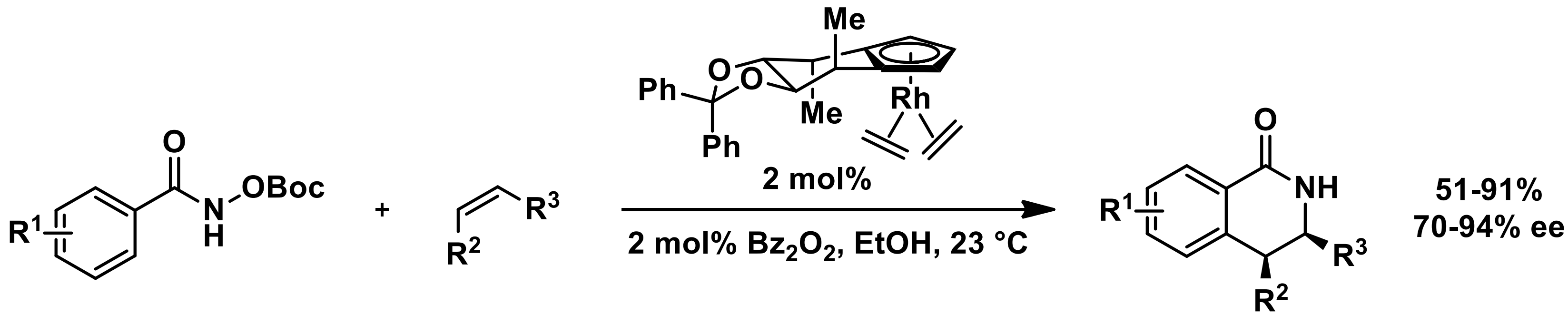
Working Model



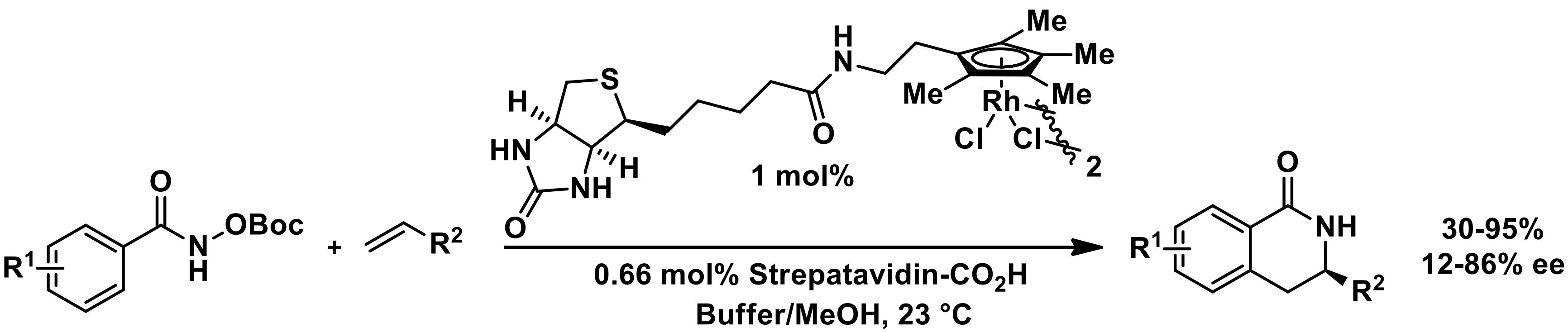
(1) Albicker, M. R.; Cramer, N. *Angew. Chem., Int. Ed.* **2009**, *48*, 9139.

4.6.5 CH Functionalization: SP^2 C-H activation

Cramer: The first truly efficient chiral Cp ligand for C-H activation cyclization[1]



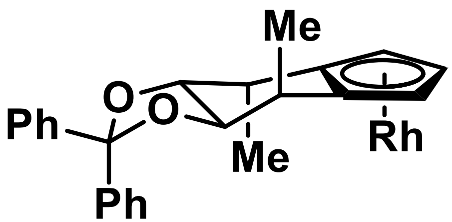
Rovis/Ward: An alternative combining transition metals and enzymes[2]

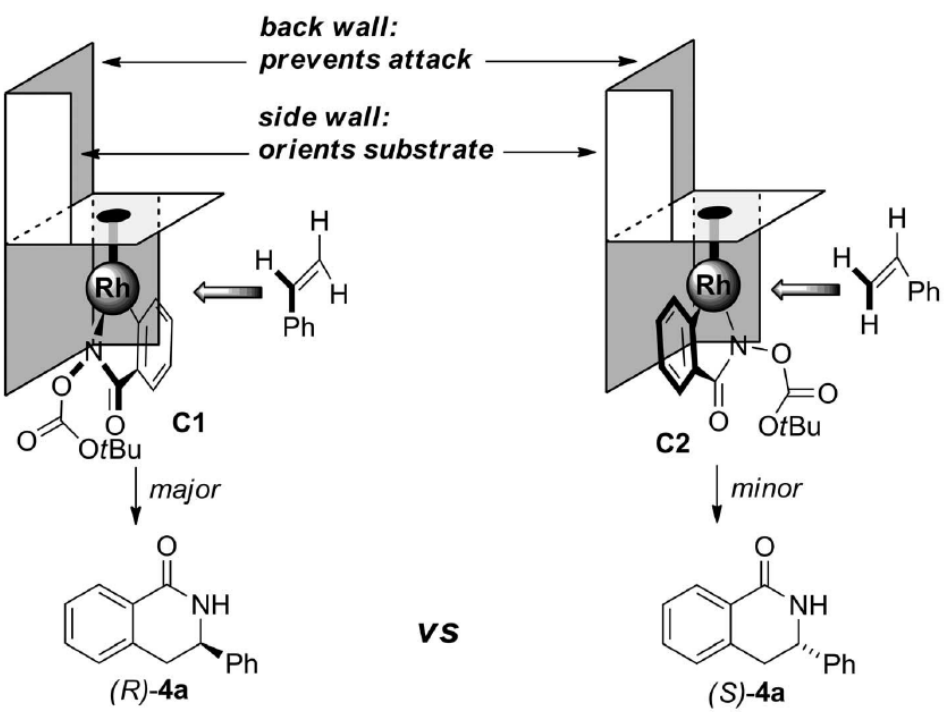


(1) Ye, B. H.; Cramer, N. *Science* **2012**, *338*, 504. (2) Hyster, T. K.; Knorr, L.; Ward, T. R.; Rovis, T. *Science* **2012**, *338*, 500.

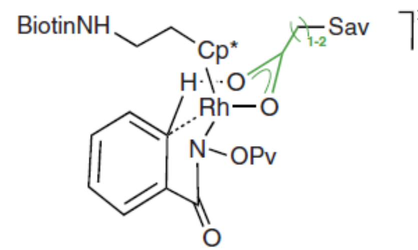
4.6.5 CH Functionalization: SP^2 C-H activation

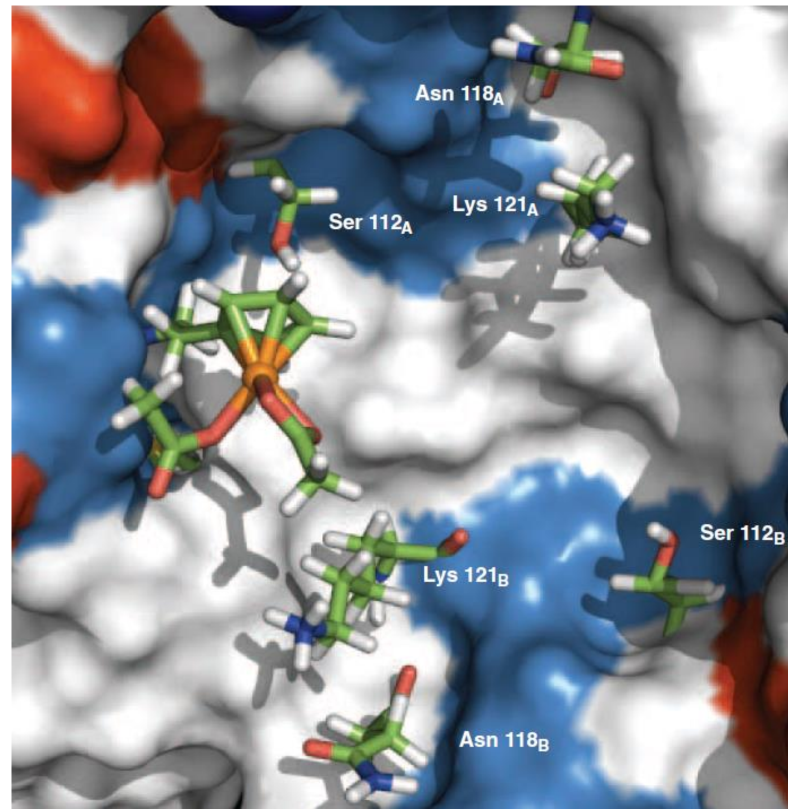
Cramer[1]





Rovis/Ward[2]

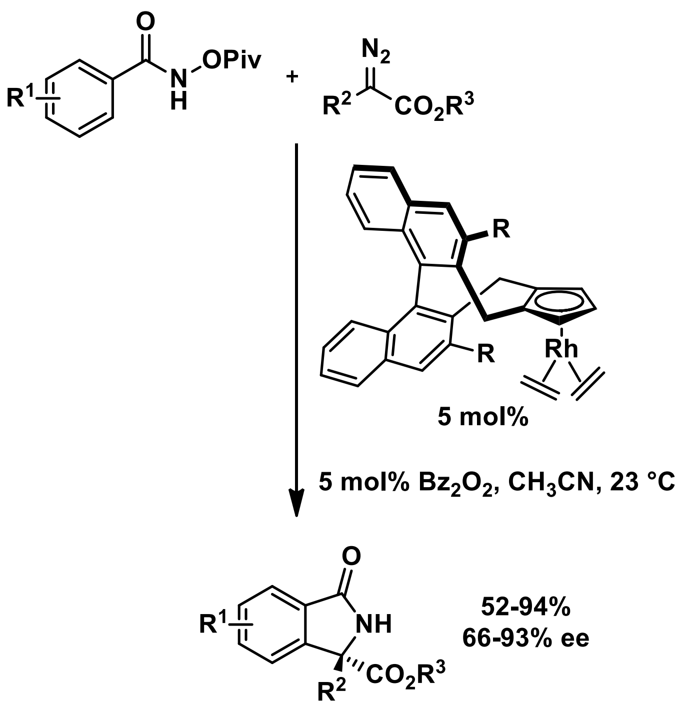


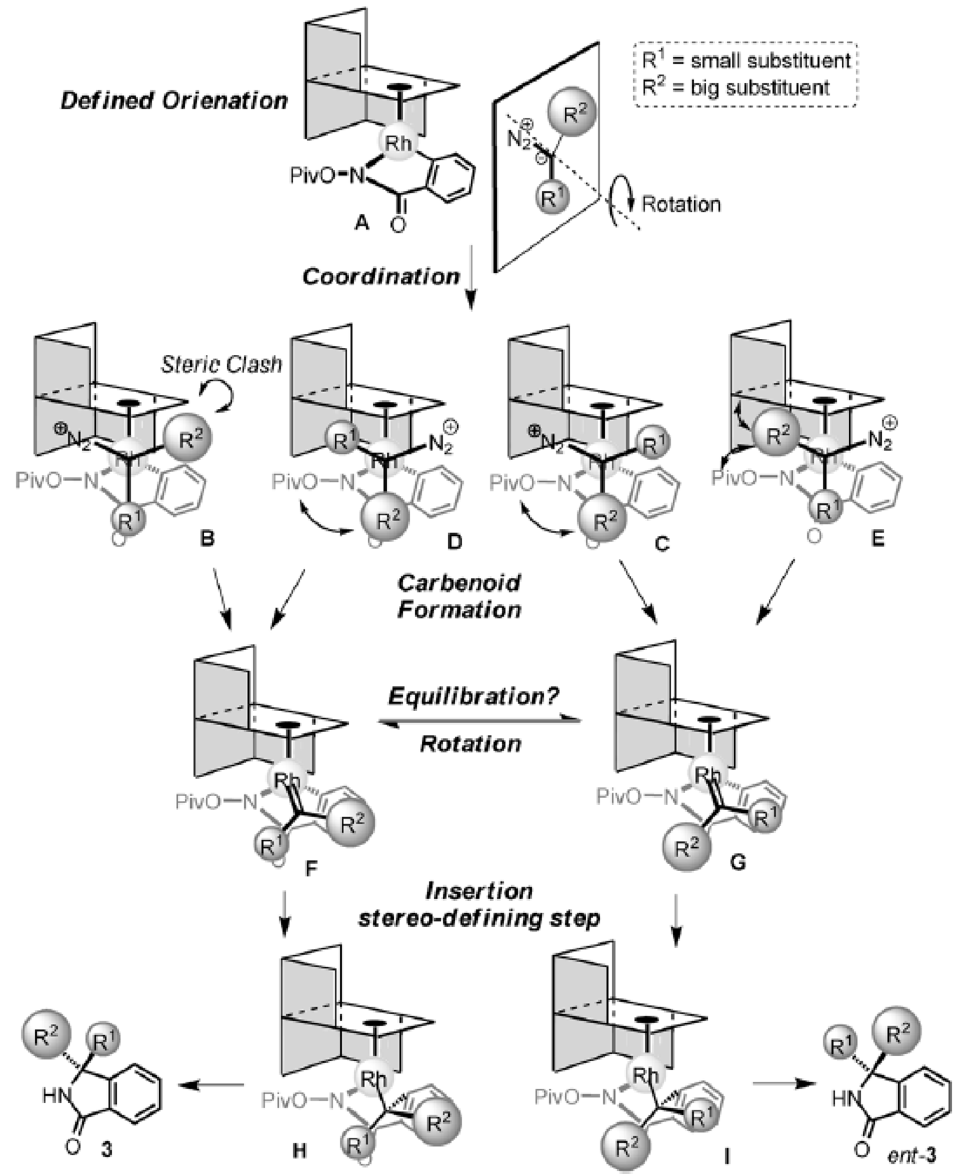


(1) Ye, B. H.; Cramer, N. *Science* **2012**, *338*, 504. (2) Hyster, T. K.; Knorr, L.; Ward, T. R.; Rovis, T. *Science* **2012**, *338*, 500.

4.6.5 CH Functionalization: SP^2 C-H activation

Cramer: C-H Functionalization with Binaphthyl-Based CP ligands[1]

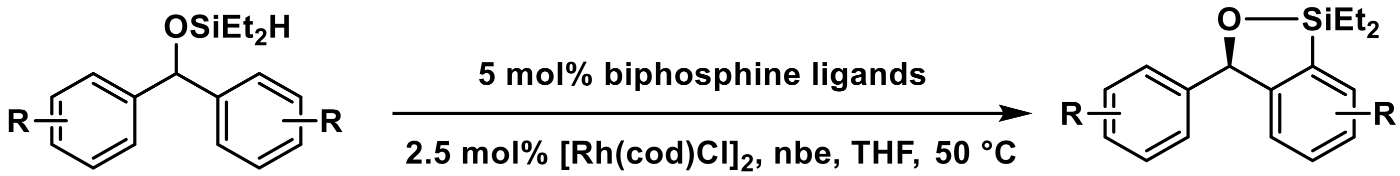




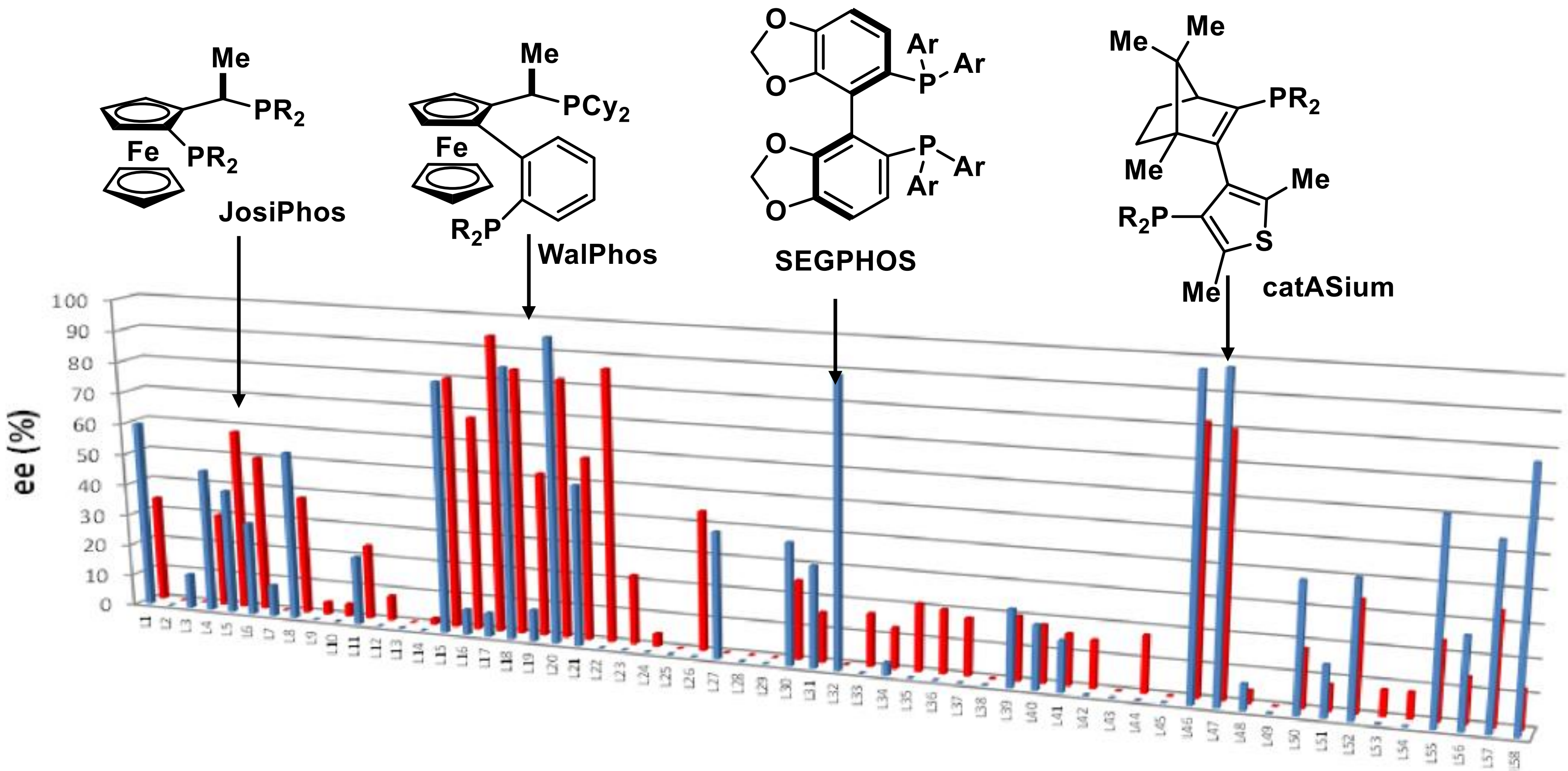
(1) Ye, B.; Cramer, N. *Angew. Chem., Int. Ed.* **2014**, *53*, 7896.

4.6.5 CH Functionalization: SP^2 C-H activation

Hartwig: Desymmetrization via C-H silylation[1]



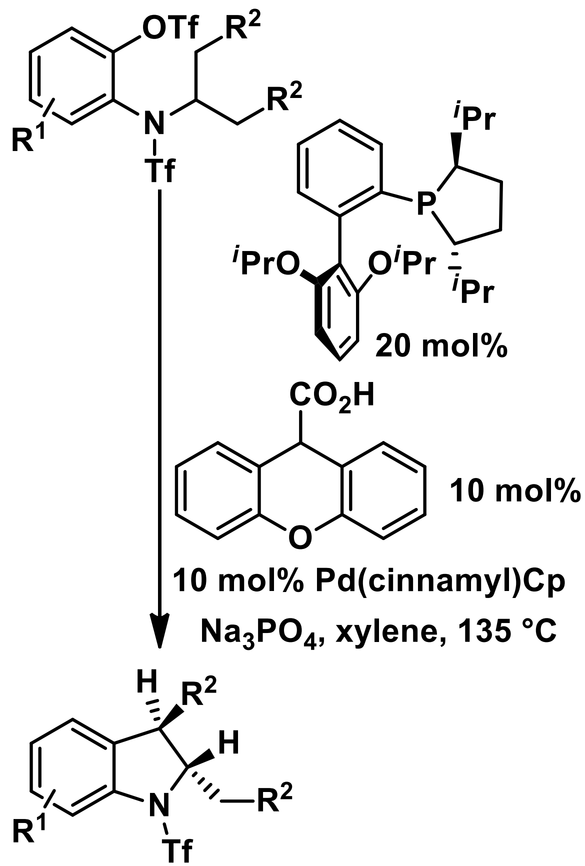
54-90%
81-99% *ee*

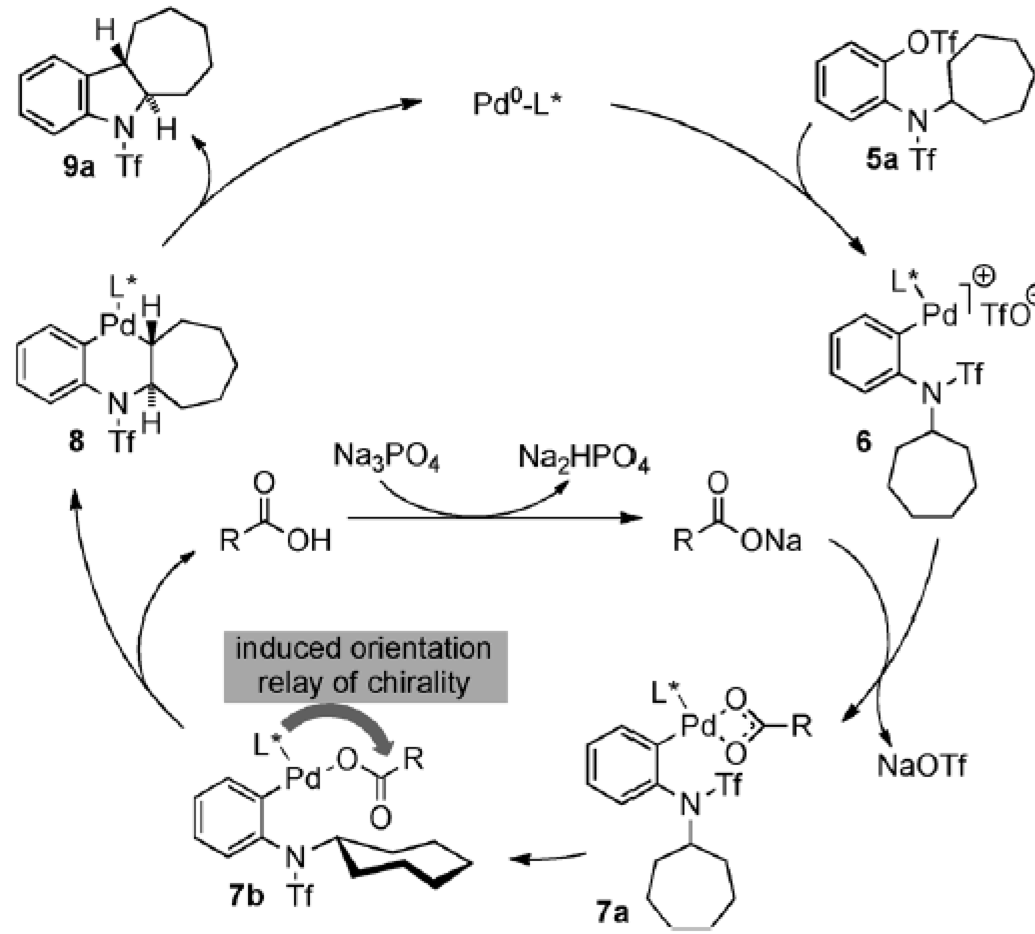


(1) Lee, T.; Wilson, T. W.; Berg, R.; Ryberg, P.; Hartwig, J. F. *J. Am. Chem. Soc.* **2015**, *137*, 6742.

4.6.5 CH Functionalization : SP^3 C-H activation

Cramer: Enantioselective C-H Activation of SP^3 bonds[1]

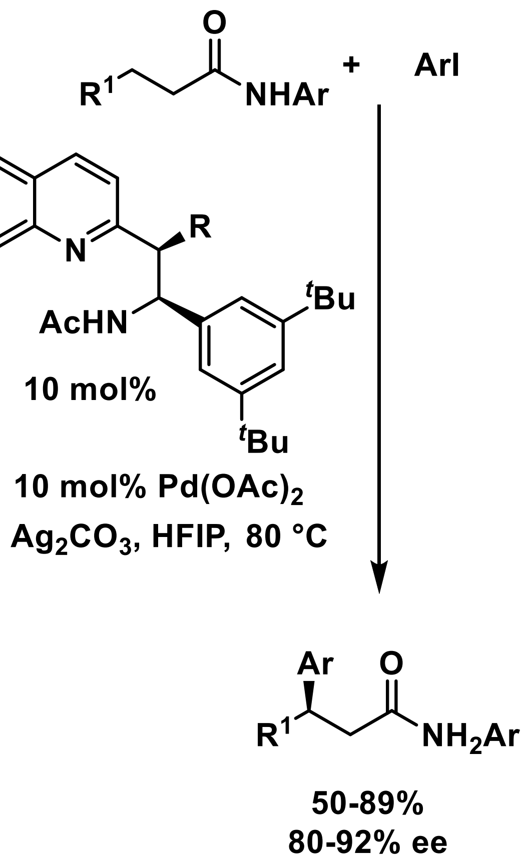


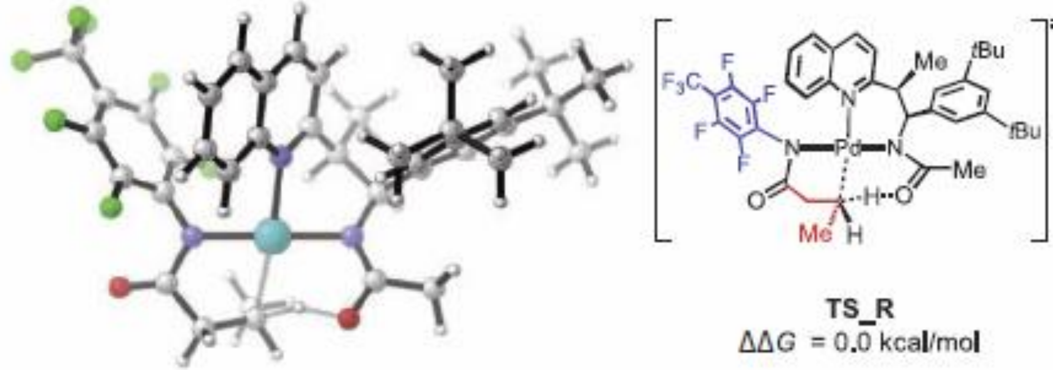


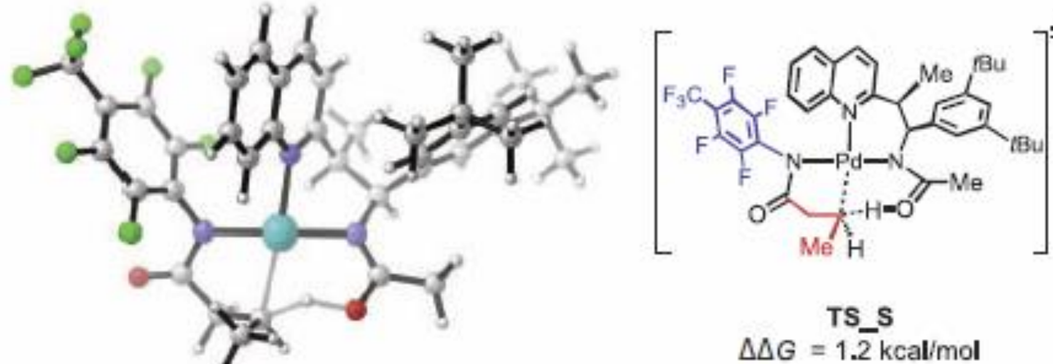
(1) Saget, T.; Lemouzy, S. J.; Cramer, N. *Angew. Chem., Int. Ed.* **2012,** *51*, 2238.

4.6.5 CH Functionalization : SP^3 C-H activation

Yu: Enantioselective C-H Activation of SP^3 bonds[1]



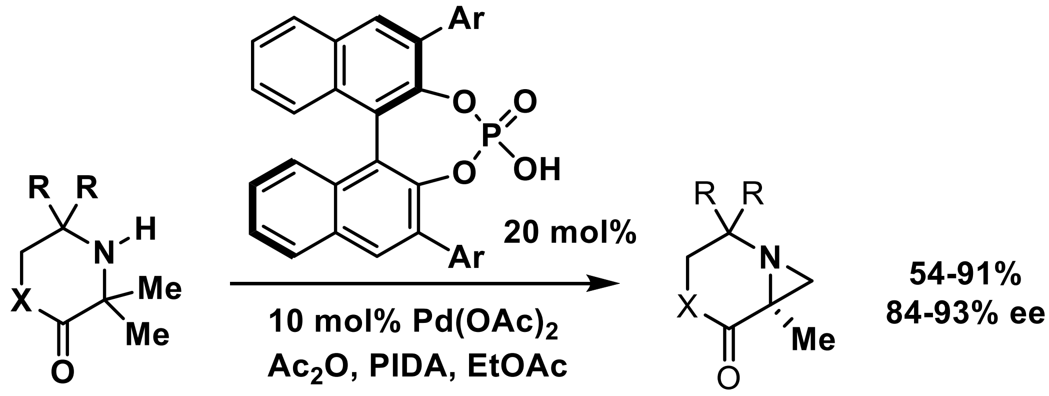


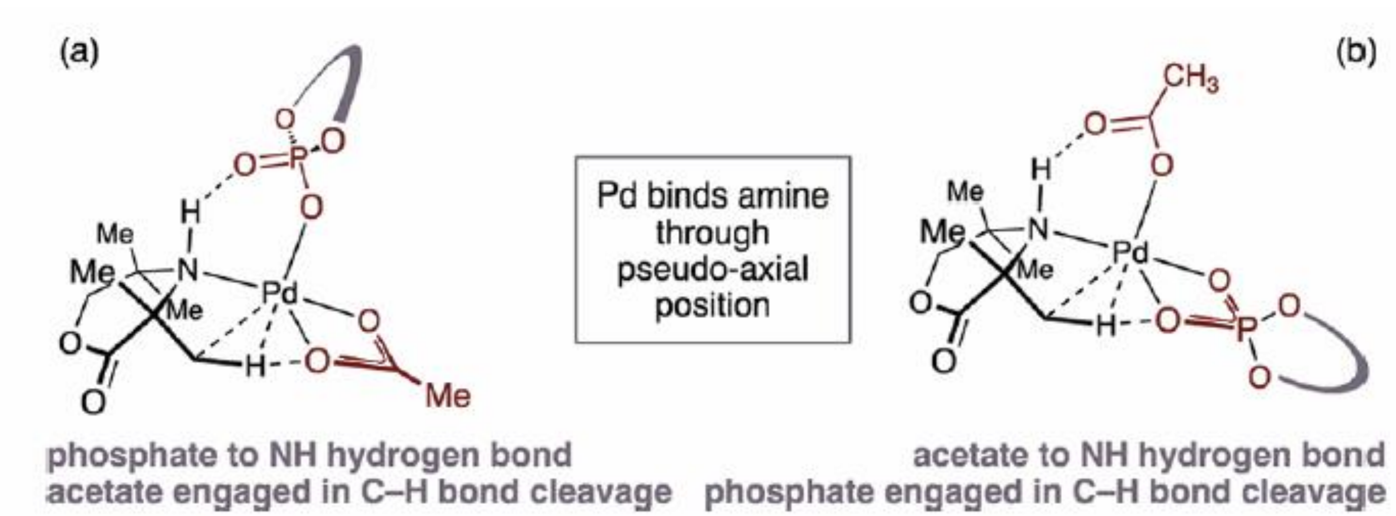


(1) Chen, G.; Gong, W.; Zhuang, Z.; Andra, M. S.; Chen, Y. Q.; Hong, X.; Yang, Y. F.; Liu, T.; Houk, K. N.; Yu, J. Q. *Science* **2016,** *353*, 1023-1027.

4.6.5 CH Functionalization : SP3 C-H activation

Gaunt: Enantioselective C-H Activation of SP3 bonds[1]

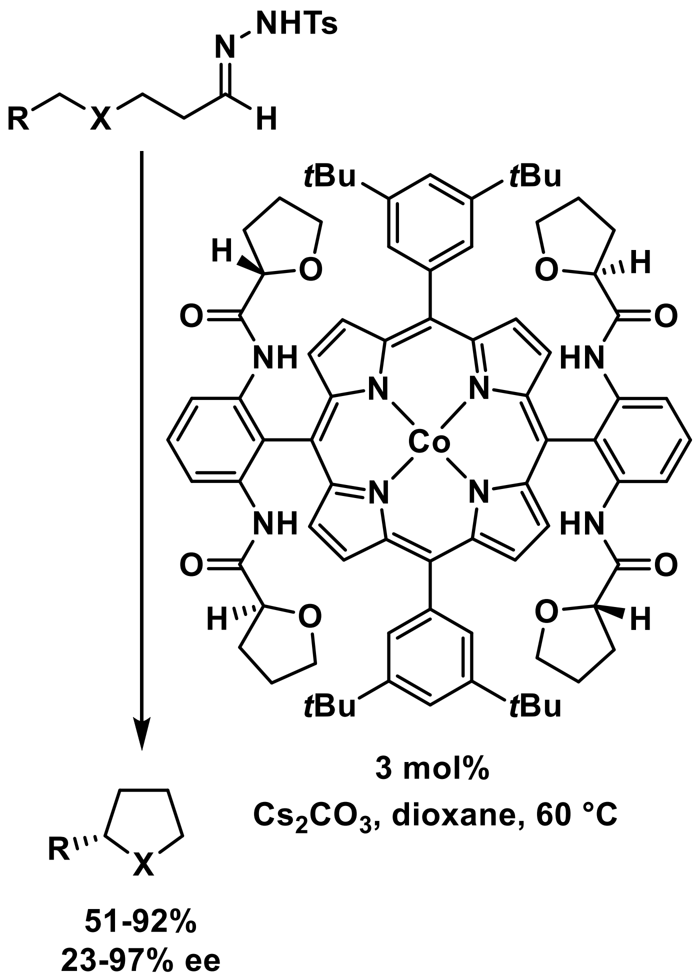


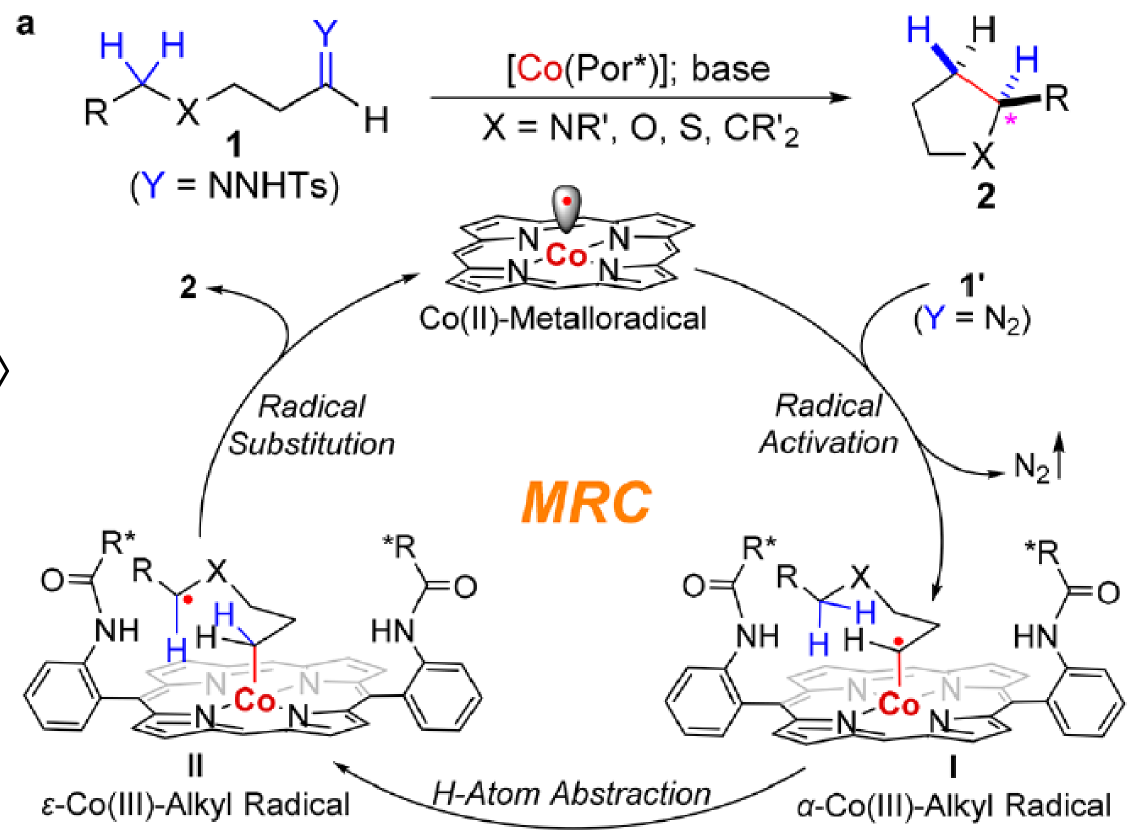


(1) Smalley, A. P.; Cuthbertson, J. D.; Gaunt, M. J. *J. Am. Chem. Soc.* **2017**, *139*, 1412-1415.

4.6.5 CH Functionalization : via Radicals

Zhang: HAT for enantioselective radical cyclization

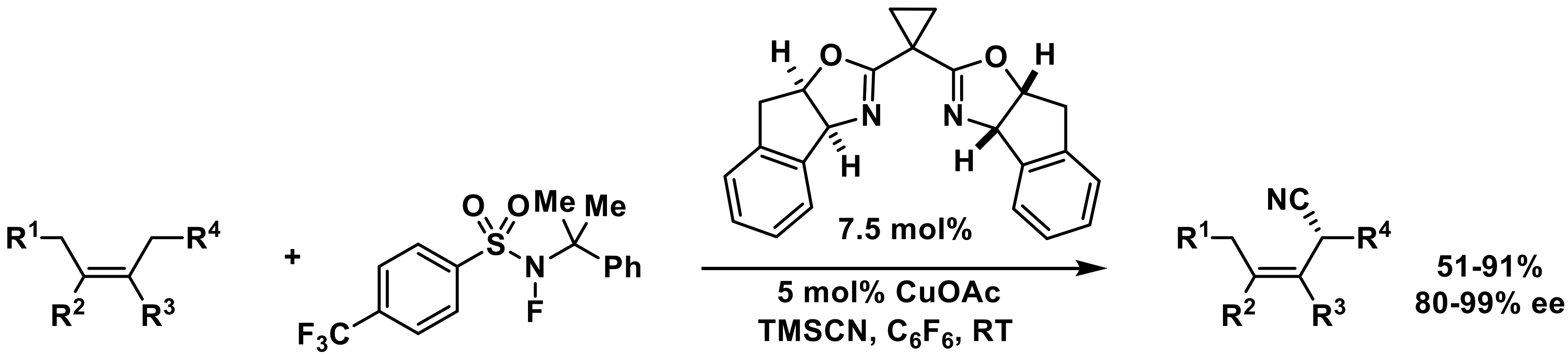


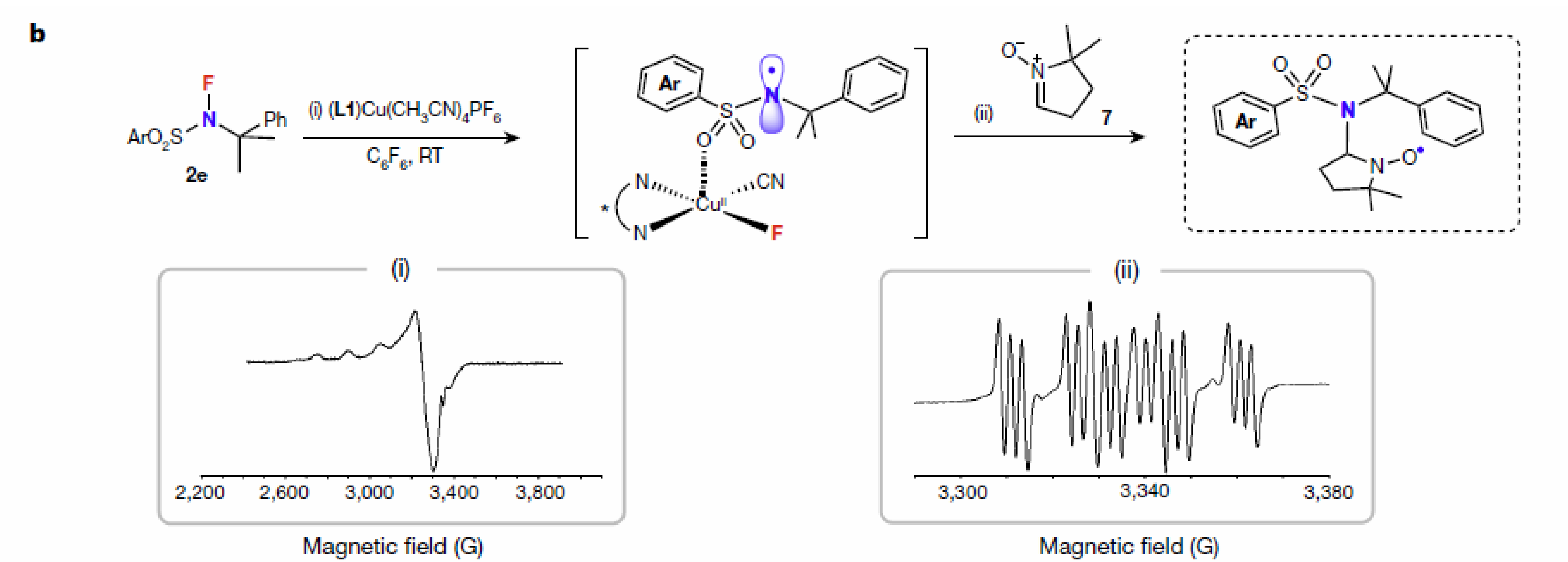


Wang, Y.; Wen, X.; Cui, X.; Zhang, X. P. *J. Am. Chem. Soc.* **2018**, *140*, 4792-4796.

4.6.5 CH Functionalization: via Radicals

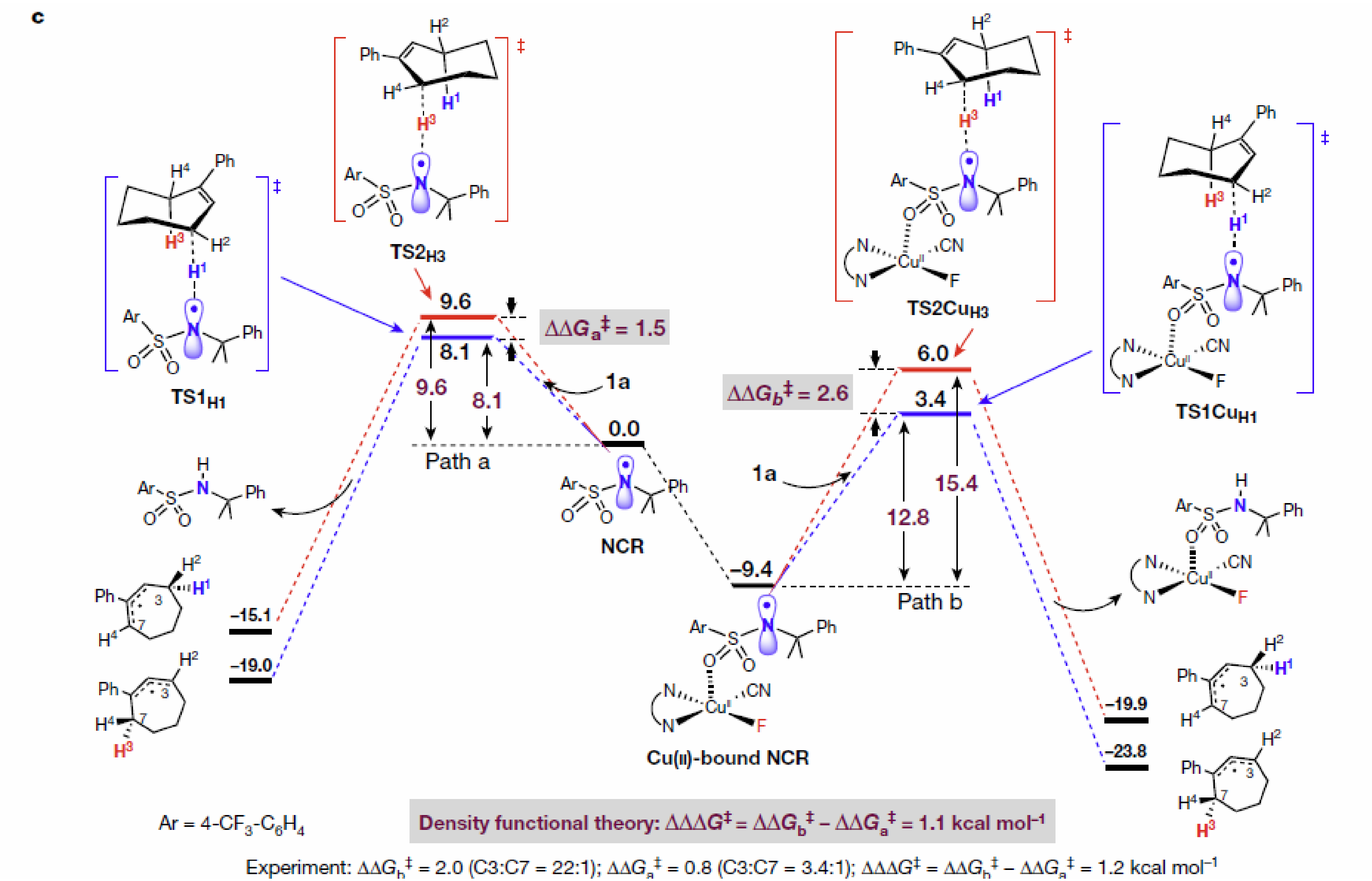
Guosheng Liu: Controling both regio- and enantio-selectivity for allylic cyanation





Li, J. Y.; Zhang, Z. H.; Wu, L. Q.; Zhang, W.; Chen, P. H.; Lin, Z. Y.; Liu, G. S., *Nature* **2019**, *574*, 516.

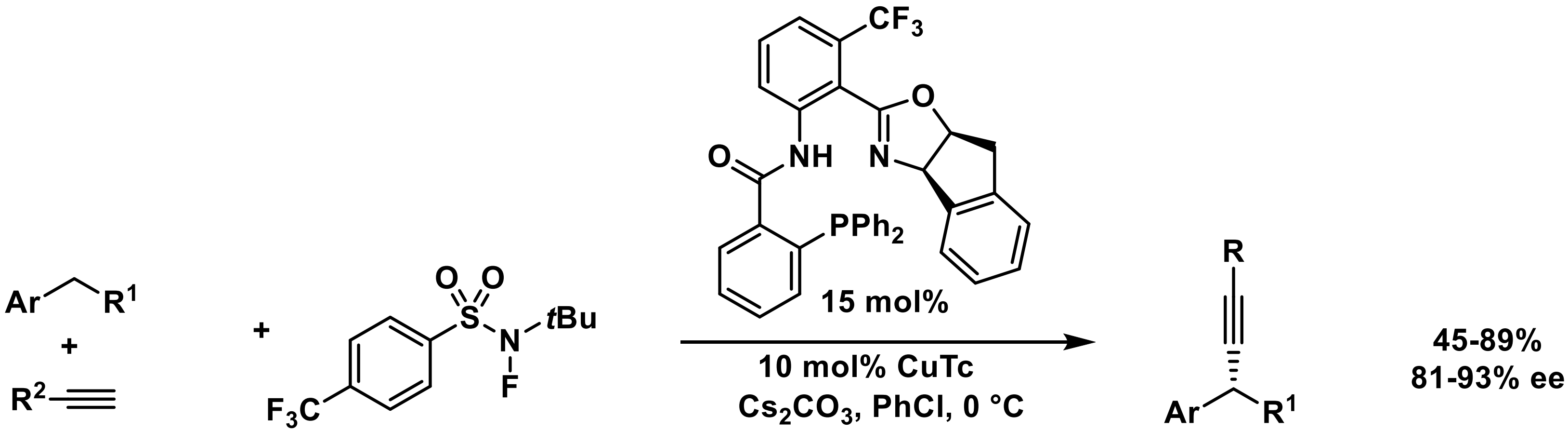
4.6.5 CH Functionalization: via Radicals



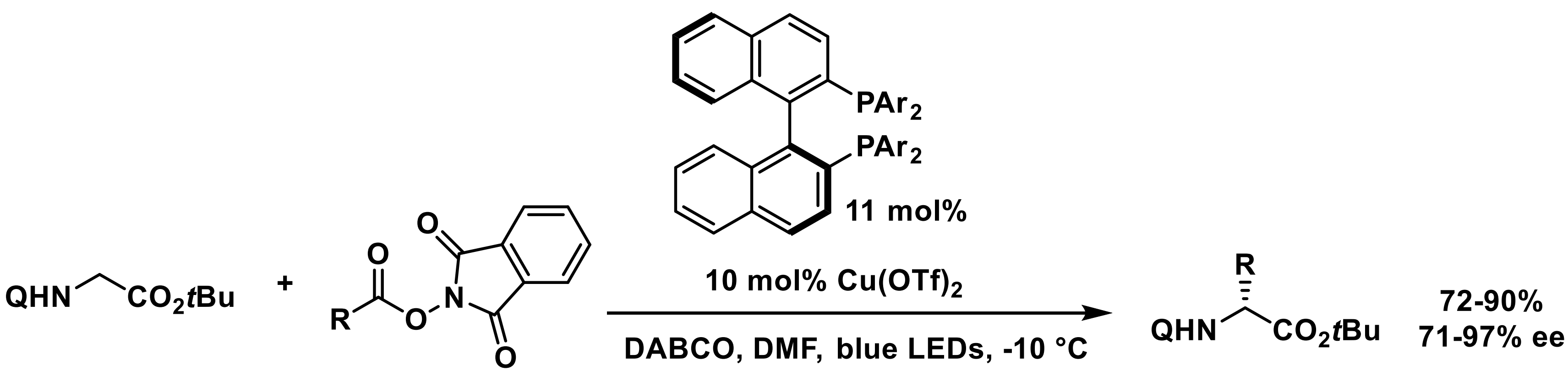
Li, J. Y.; Zhang, Z. H.; Wu, L. Q.; Zhang, W.; Chen, P. H.; Lin, Z. Y.; Liu, G. S., *Nature* **2019**, *574*, 516.

4.6.5 CH Functionalization: via Radicals

Xin-Yuan Liu: Enantioselective CH alkynylation[1]

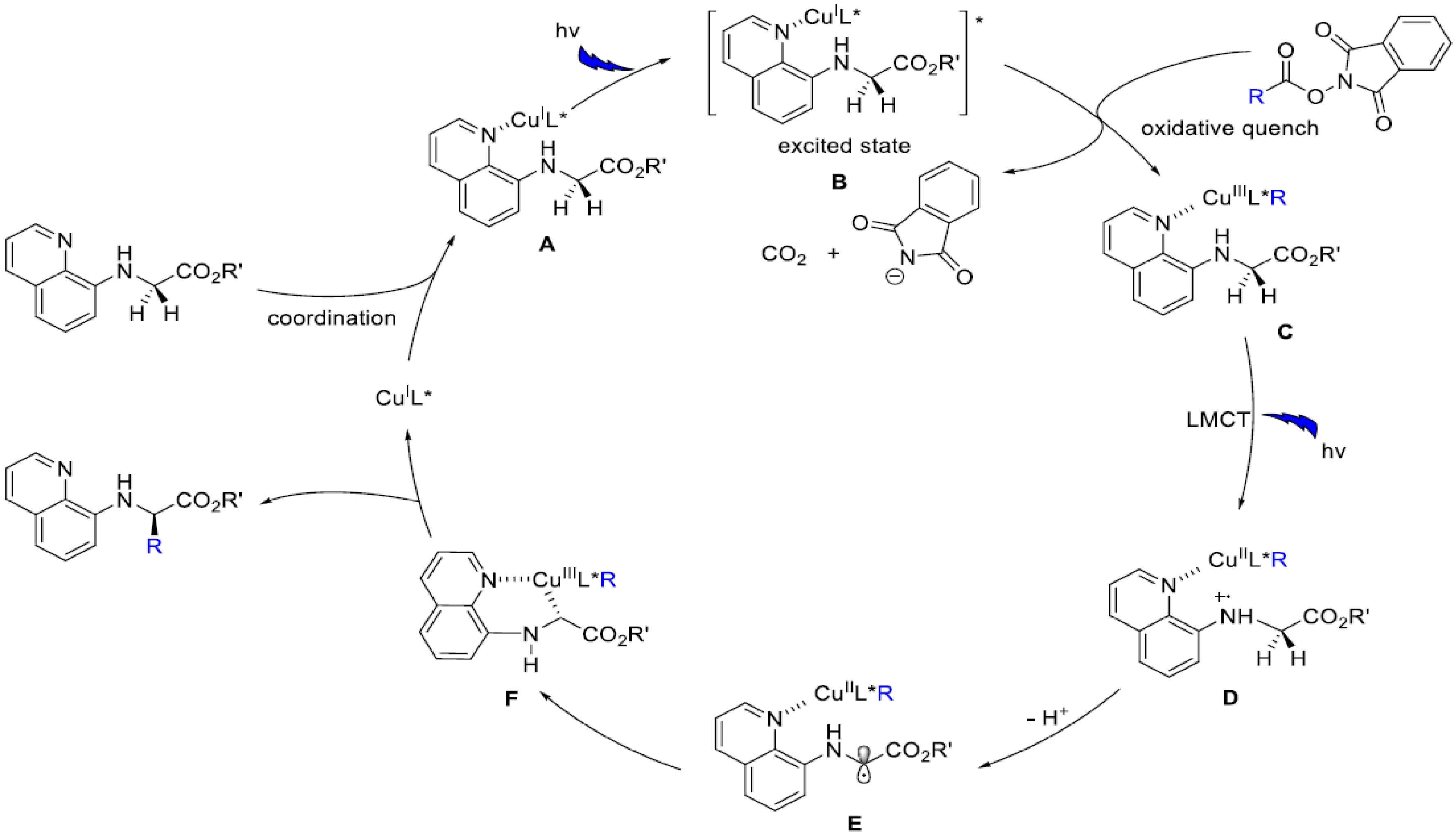


Zhaoqing Xu: Enantioselective CH alkylation using visible light[2]



(1) Liu, L.; Guo, K.-X.; Tian, Y.; Yang, C.-J.; Gu, Q.-S.; Li, Z.-L.; Ye, L.; Liu, X.-Y. *Angew. Chem., Int. Ed.* **2021**, *60*, 26710-26717. (2) Qi, R.; Wang, C.; Huo, Y.; Chai, H.; Wang, H.; Ma, Z.; Liu, L.; Wang, R.; Xu, Z. *J. Am. Chem. Soc.* **2021**, *143*, 12777-12783.

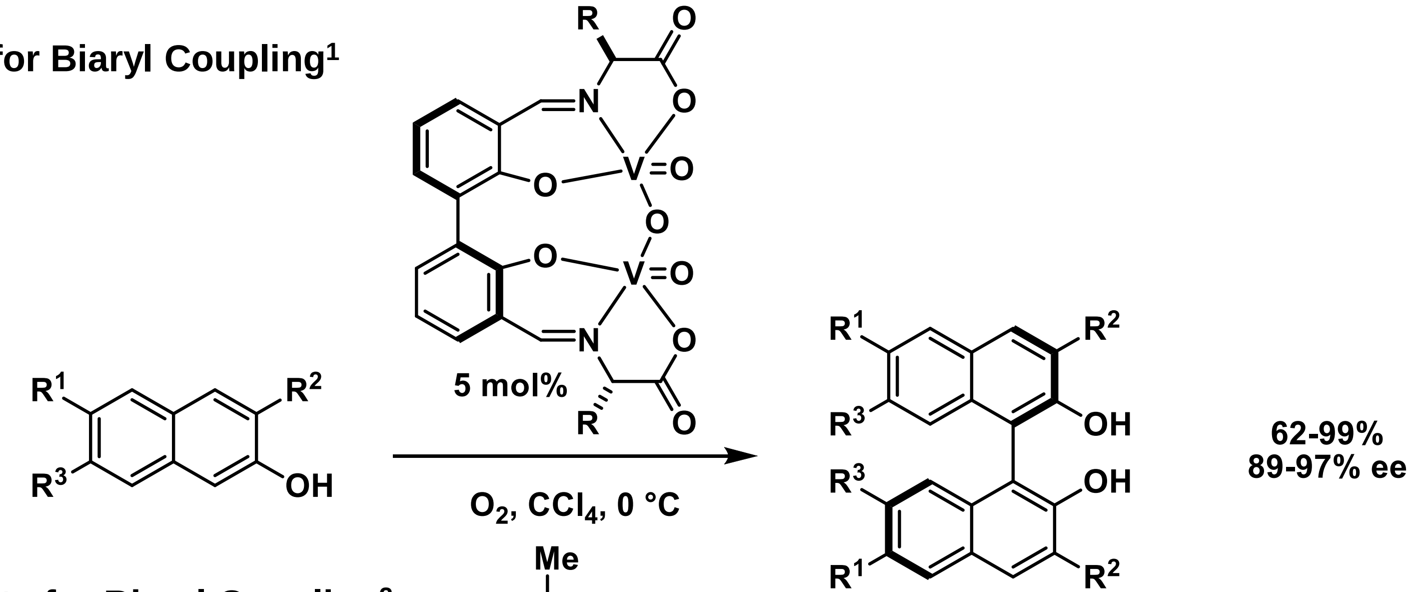
4.6.5 CH Functionalization: via Radicals



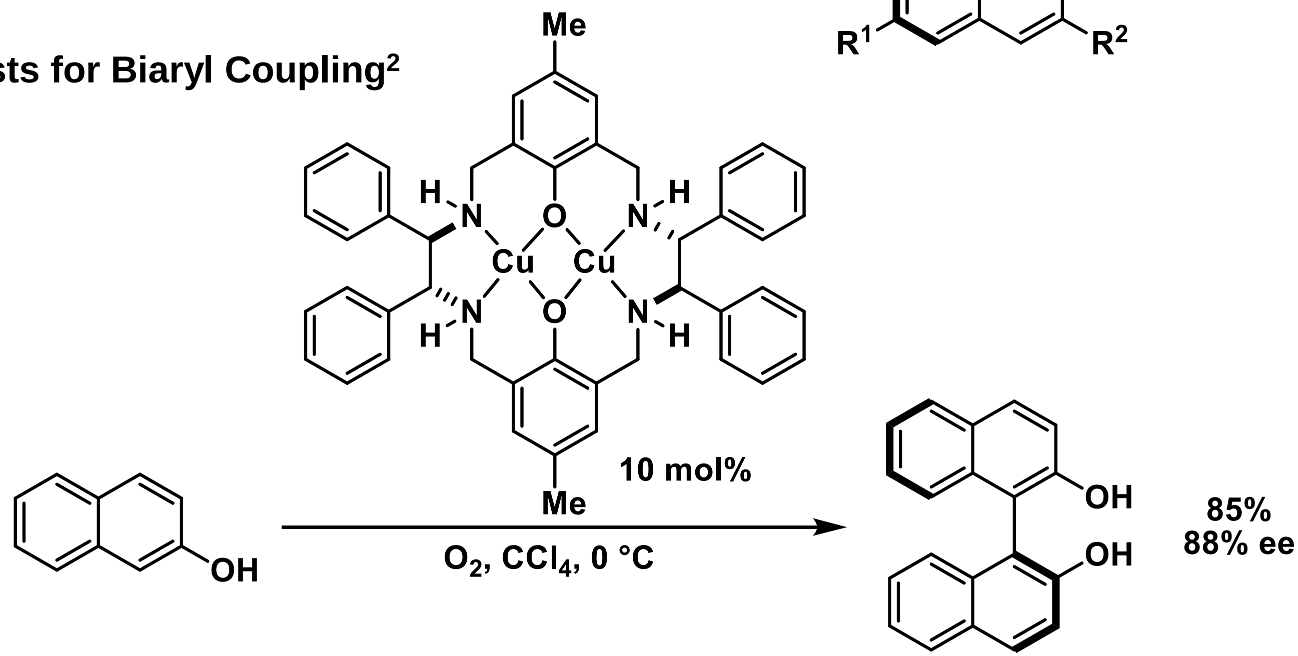
Qi, R.; Wang, C.; Huo, Y.; Chai, H.; Wang, H.; Ma, Z.; Liu, L.; Wang, R.; Xu, Z. *J. Am. Chem. Soc.* **2021**, *143*, 12777-12783.

4.6.5 CH Functionalization: Oxidative Biaryl Coupling

Gong: Bis-V Catalysts for Biaryl Coupling[1]



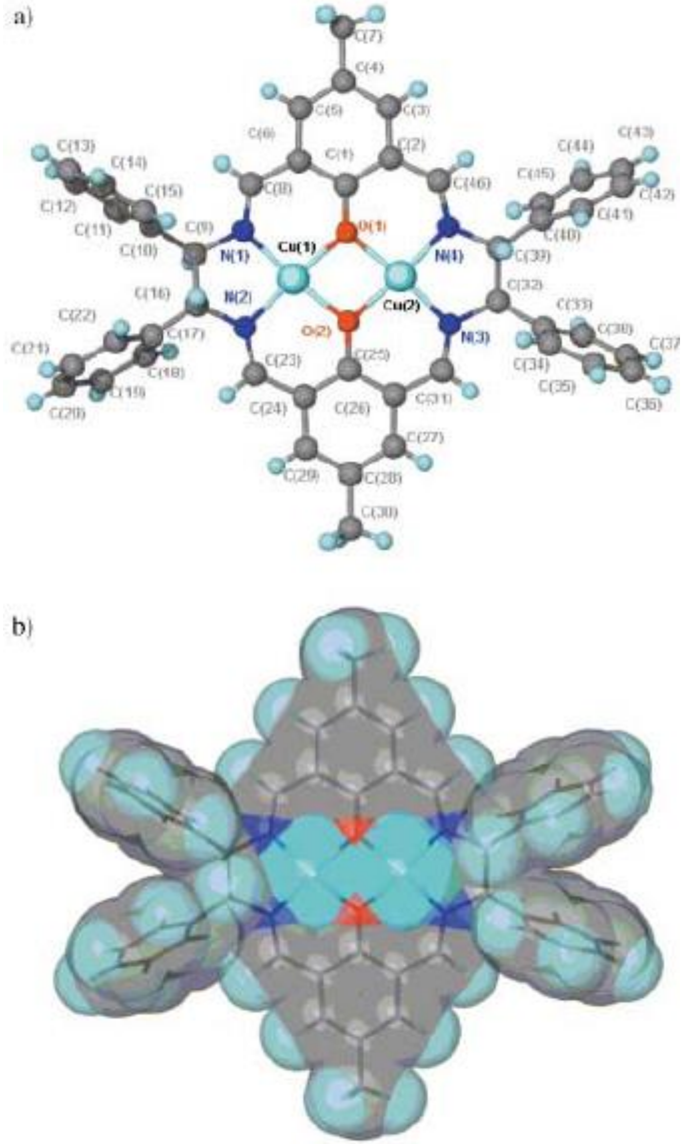
Martell: Bis-Cu Catalysts for Biaryl Coupling[2]

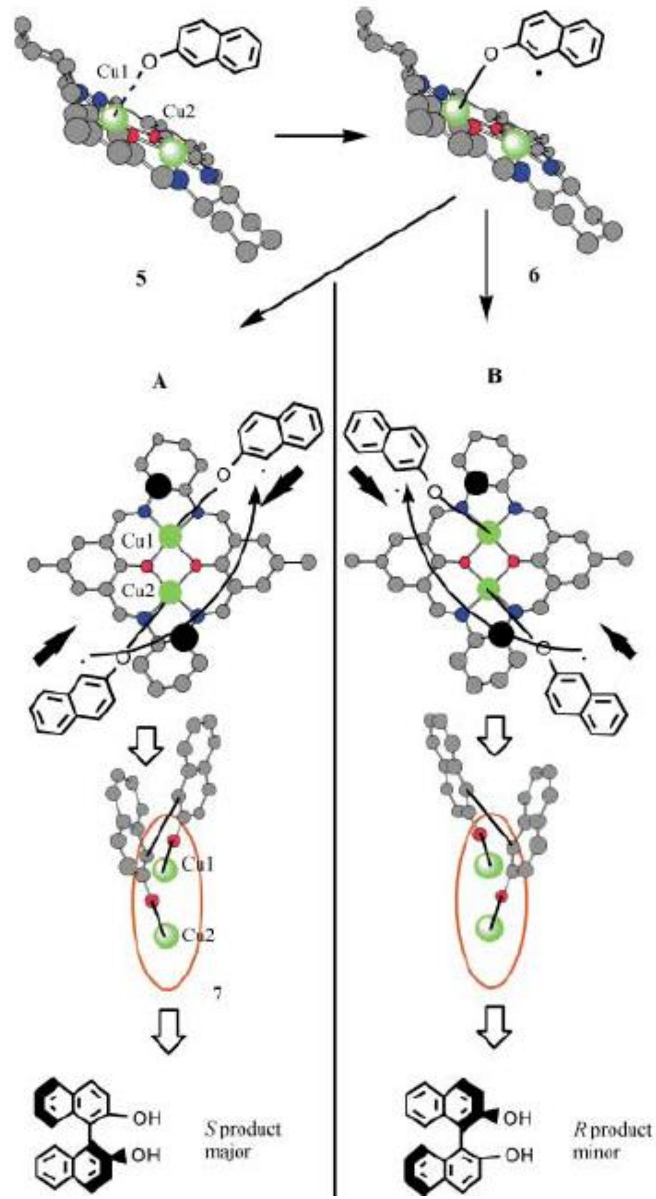


(1) Luo, Z. B.; Liu, Q. Z.; Gong, L. Z.; Cui, X.; Mi, A. Q.; Jiang, Y. Z. *Angew. Chem., Int. Ed.* **2002,** *41,* 4532-4535. (2) Gao, J.; Reibenspies, J. H.; Martell, A. E. *Angew. Chem., Int. Ed.* **2003,** *42,* 6008-6012.

4.6.5 CH Functionalization: Oxidative Biaryl Coupling

Structure of Catalyst and Mechanism





(1) Gao, J.; Reibenspies, J. H.; Martell, A. E. *Angew. Chem., Int. Ed.* **2003,** *42,* 6008-6012.