Thomas Group

TEXAS A&M UNIVERSITY

Chiral Anion Chemistry

June 6th, 2023

CHEM 2122 / Group Meeting

Cheng-Chun Chen
Texas A&M University

Chiral Anion Chemistry

Important Reviews

Mahlau, M; List, B. *Angew. Chem., Int. Ed*. **2013**, *52*, 518.
Phipps, R. J.; Hamilton G. L.; Toste F. D., *Nat. Chem.,* **2012**, 4, 603.

Leading Researchers

Benjamin List
F. Dean Toste
Hisashi Yamamoto
Eric N. Jacobsen

What is chiral anion chemistry?

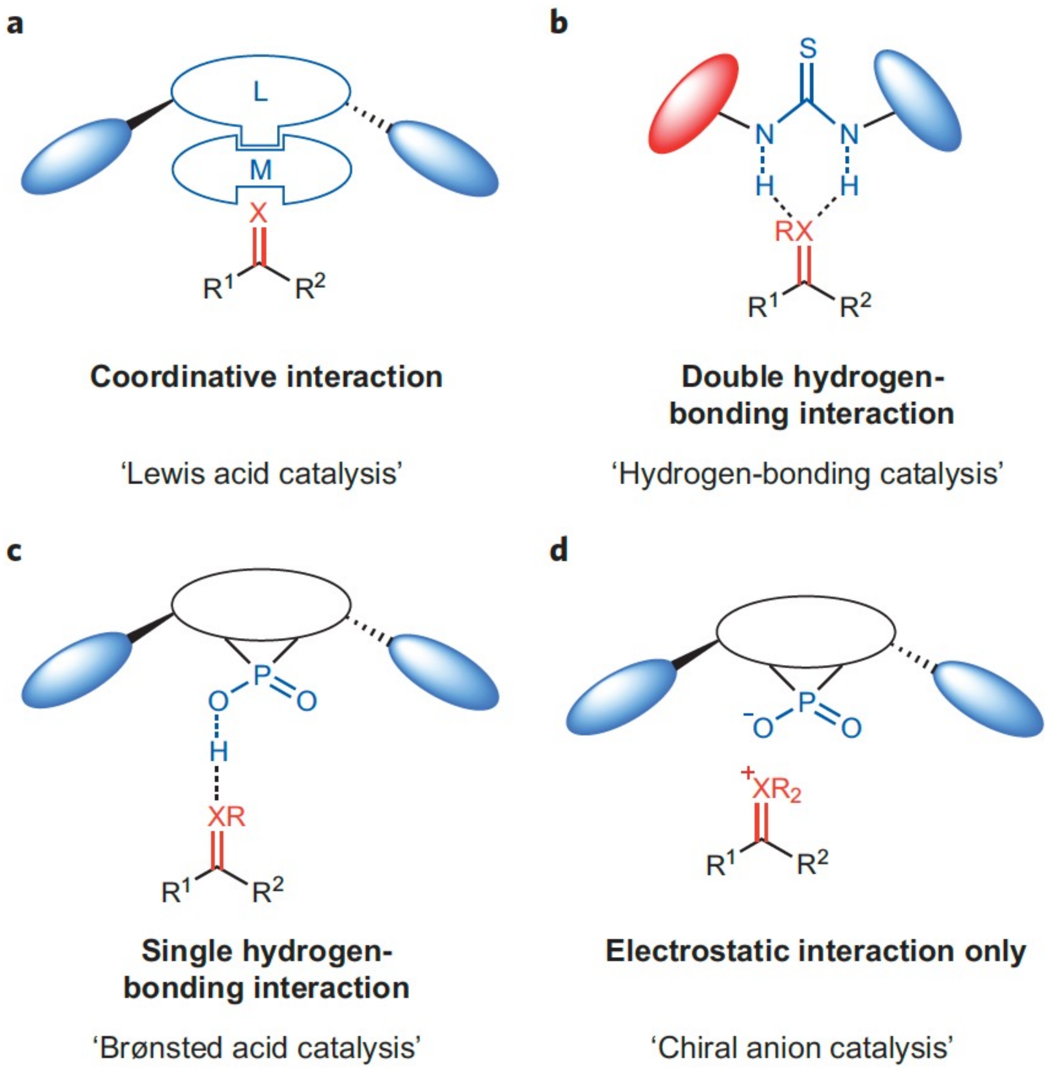
Chiral and a sufficient association

- covalent bonding
- noncovalent interactions
  (hydrogen bonding or ion pairing)

There should not be any significant covalent bonding between cation and anion during the selectivity-determining step of the catalytic cycle.

Mahlau, M; List, B. *Angew. Chem., Int. Ed*. **2013**, *52*, 518.

What is chiral anion chemistry?



Phipps, R. J.; Hamilton G. L.; Toste F. D., *Nat. Chem.*, **2012**, 4,

Development

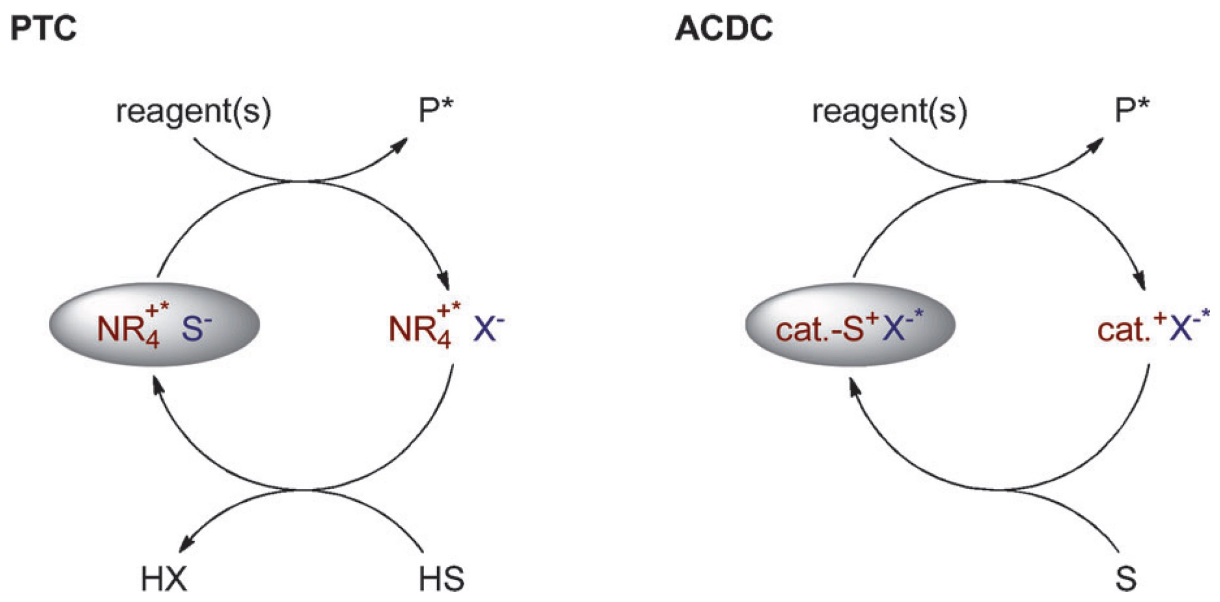
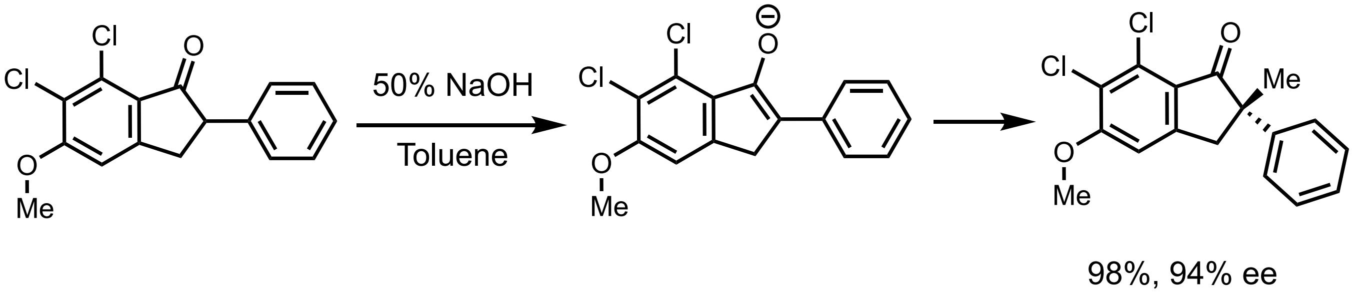


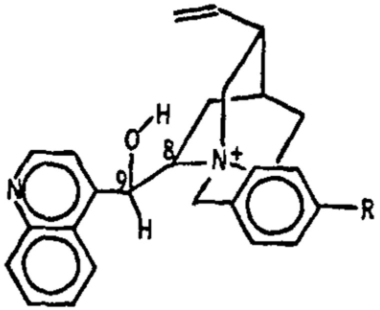
Figure 1. Schematic representation of phase-transfer catalysis with chiral countercations (PTC) and asymmetric counteranion-directed catalysis (ACDC). P = product; S = substrate; X^- = anion.

Mahlau, M; List, B. *Angew. Chem., Int. Ed.* **2013**, *52*, 518.

Development

Two-Phase (phase-transfer)

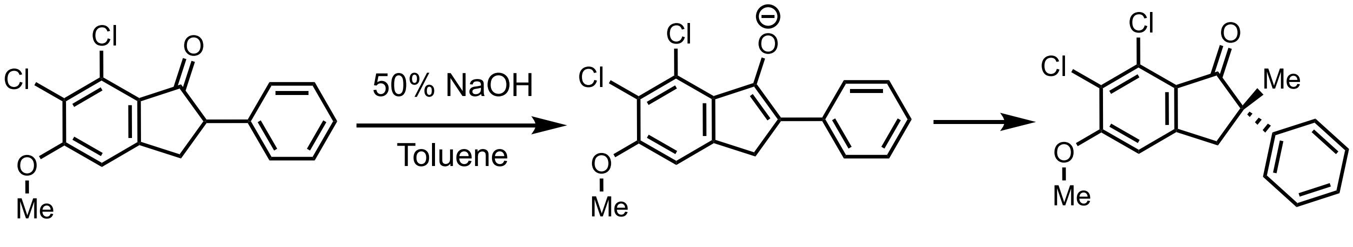




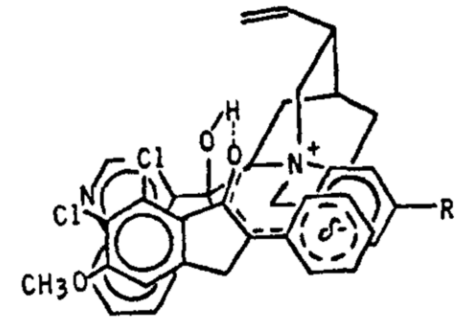
J. Am. Chem. Soc., **1984**, 106, 446.

Development

Two-Phase (phase-transfer)



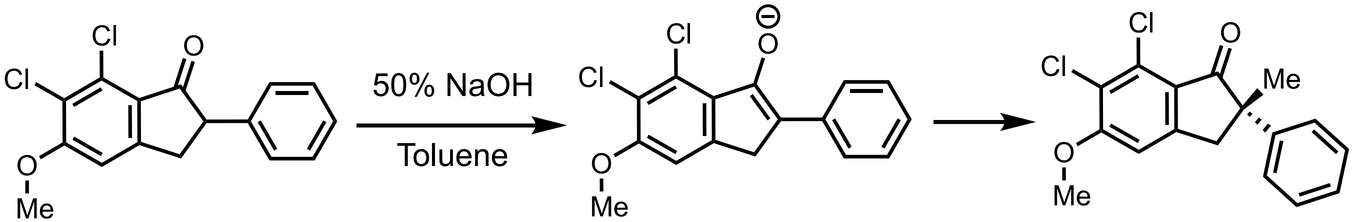
98%, 94% ee



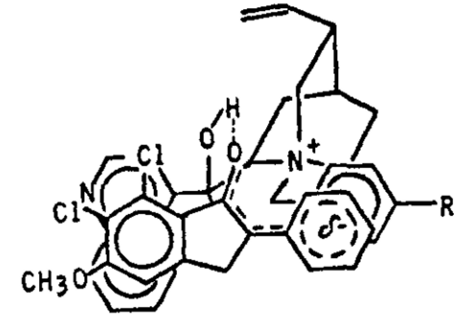
J. Am. Chem. Soc., **1984**, 106, 446.

Development

Two-Phase (phase-transfer)

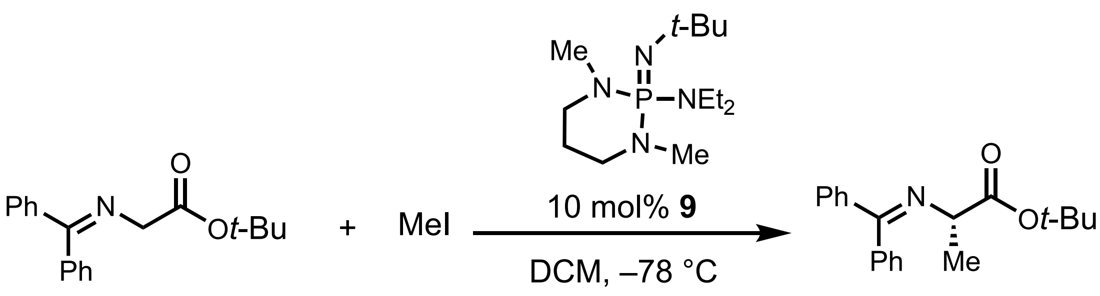


98%, 94% ee

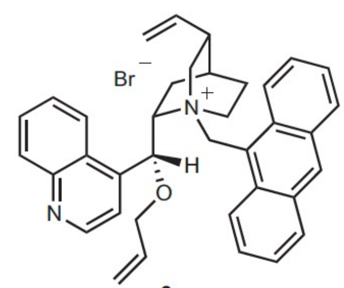


J. Am. Chem. Soc., **1984**, 106, 446.

Homogeneous



92%, 94% ee



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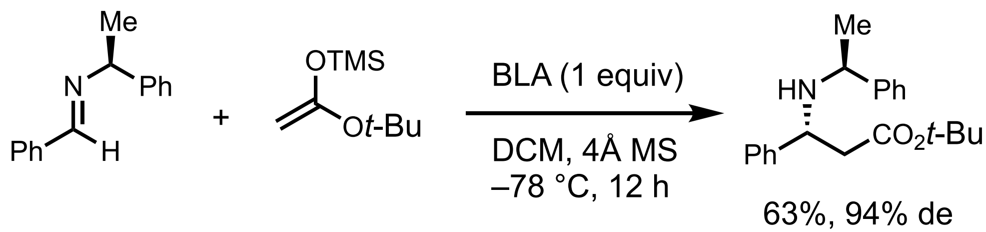
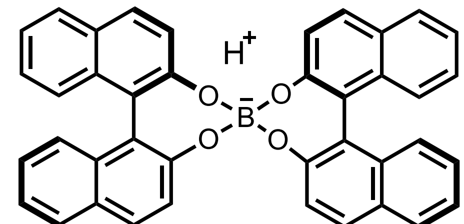
Tetrahedron Lett., **1998**, 39, 8775.

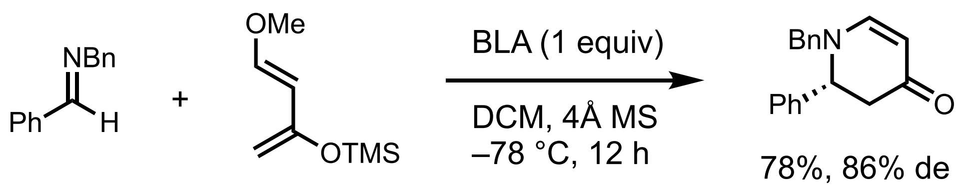
Development

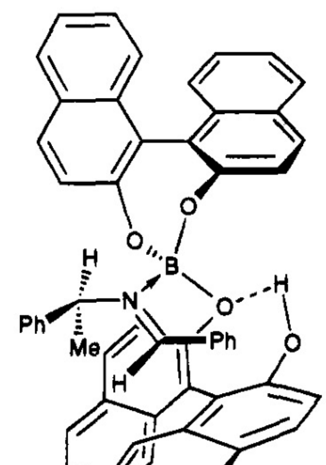
Yamamoto: Brønsted acid-assisted chiral Lewis acid (BLA).





BLA





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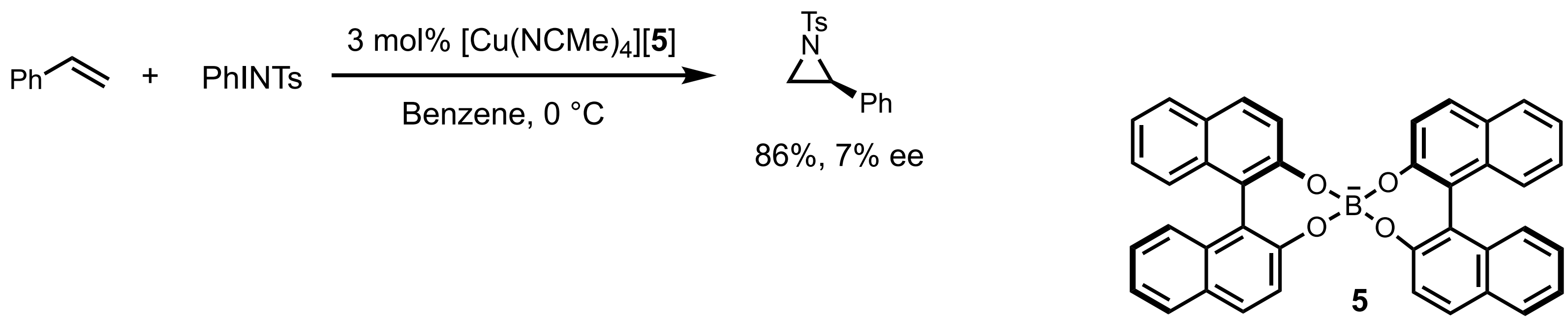
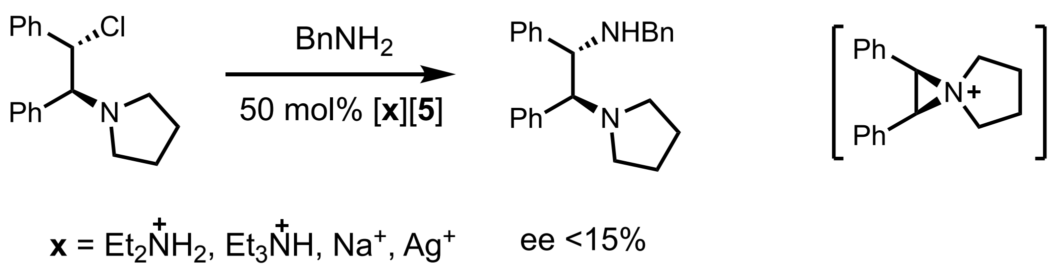
Ishihara, K., Miyata, M., Hattori, K., Tada, T. & Yamamoto, H., *J. Am. Chem. Soc.,* **1994**, *116*, 10520–10524.

Development



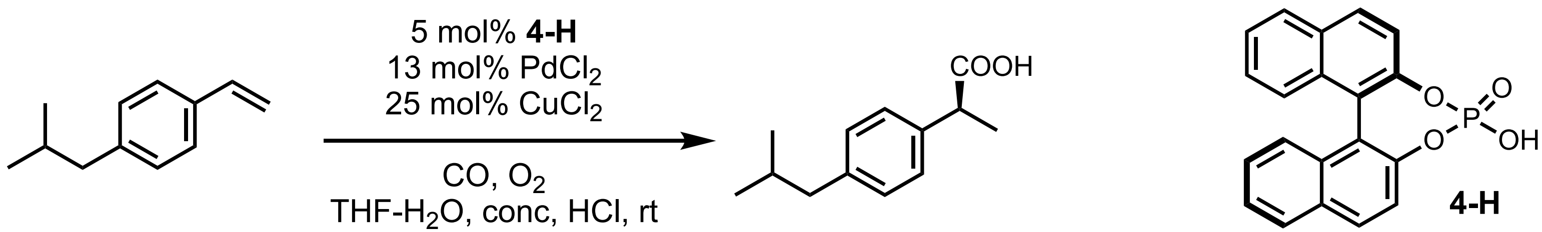
Llewellyn, D. B., Adamson, D. & Arndtsen, B. A., *Org. Lett.*, **2000**, 2, 4165.



Carter, C., Fletcher, S. & Nelson, A., *Tetrahedron*, **2003**, 14, 1995.

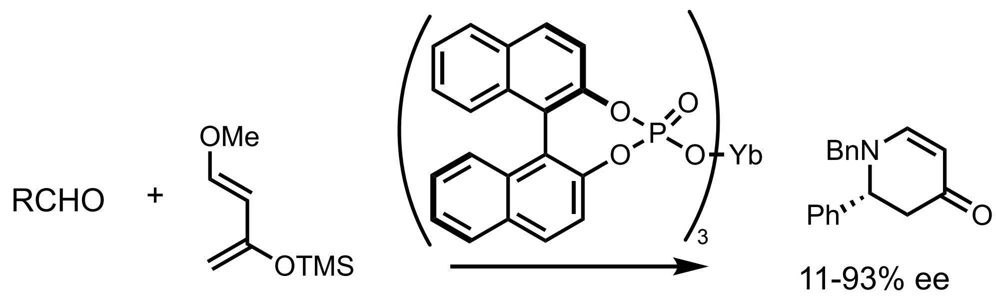
Development

BINOL-derived phosphoric acids / phosphate



Alper, H. & Hamel, N., *J. Am. Chem. Soc.,* **1990**, 112, 2803.

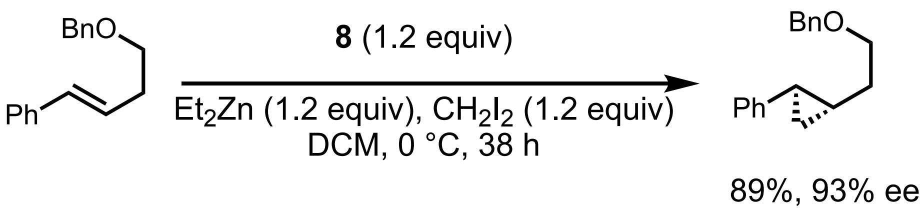
Inanaga:

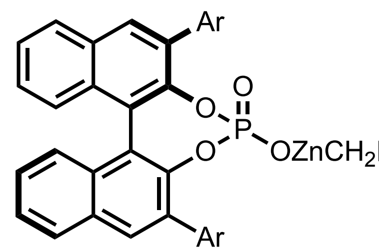


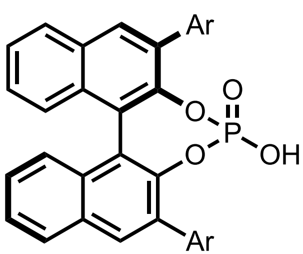
New J. Chem. **19**, 707–712 (1995). *Synlett* **1**, 79–80 (1997).

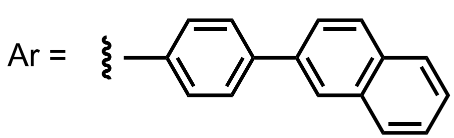
Development

Simmons–Smith cyclopropanation









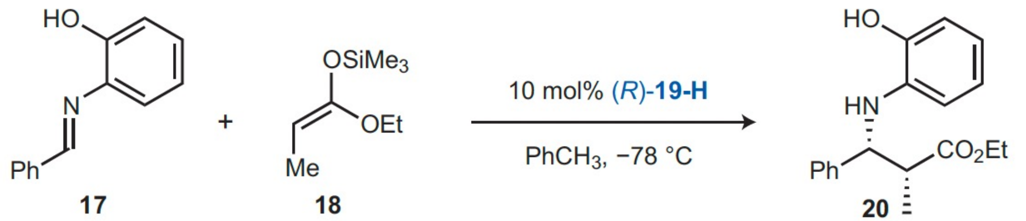
8

Discussed as a ligand

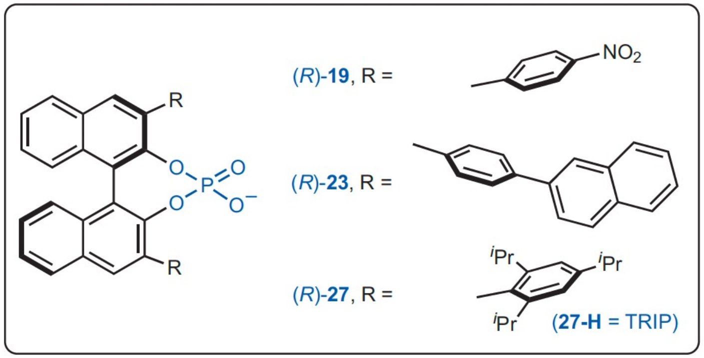
Lacasse, M. C., Poulard, C. & Charette, A. B., *J. Am. Chem. Soc.* **127**, 12440–12441 (2005).

Development

Akiyama:

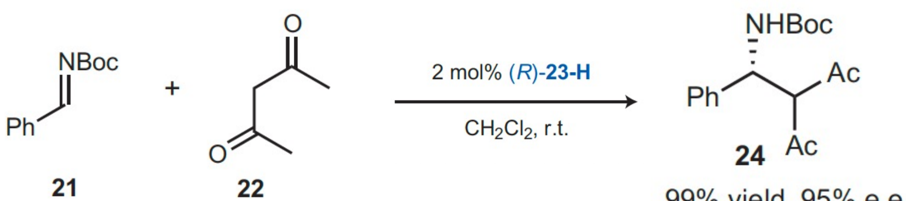


87:13 syn/anti
100% yield, 96% e.e.



Angew. Chem. Int. Ed. **43**, 1566–1568 (2004).

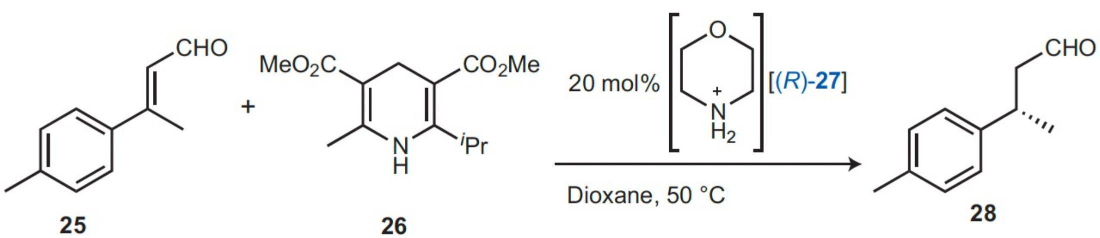
Terada:



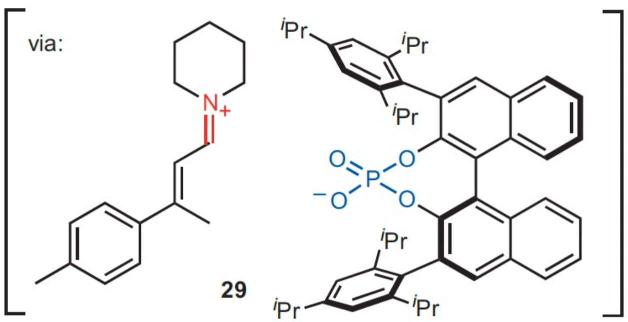
99% yield, 95% e.e.

J. Am. Chem. Soc. **126**, 5356–5357 (2004).

List:



87% yield, 96% e.e.



Mayer, S. & List, B. *Angew. Chem. Int. Ed.* 45, 4193–4195 (2006).

Outline

Organocatalysis

- Iminium + Chiral Phosphate
- aziridinium / episulfonium + Chiral Phosphate
- Lewis Acid + Chiral Phosphate
- Lewis Acid + Chiral disulfonimide
- Anion-Binding Thioureas

H-bond Doner

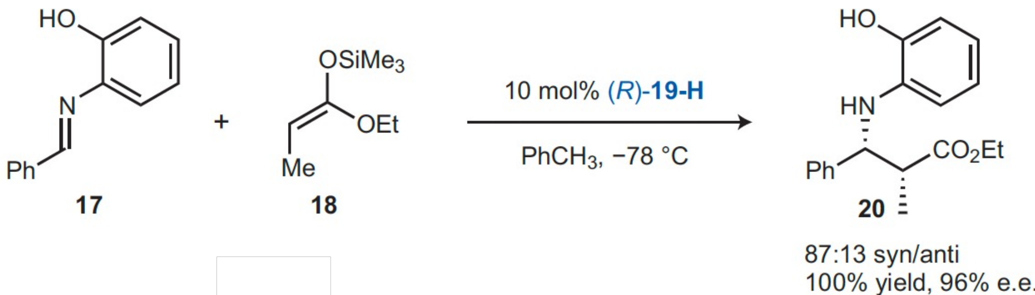
- Thiourea
- Squaramide

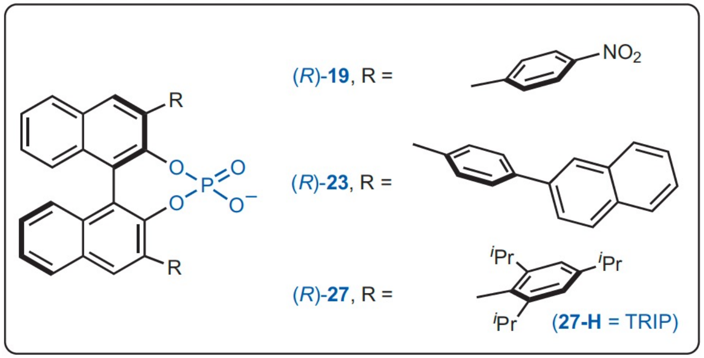
Transition-Metal Catalysis

Phase-Transfer Catalysis

Development

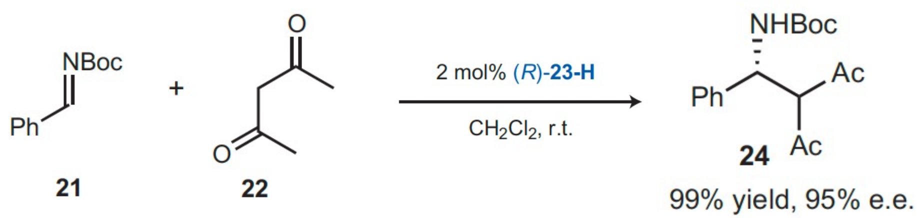
Akiyama:





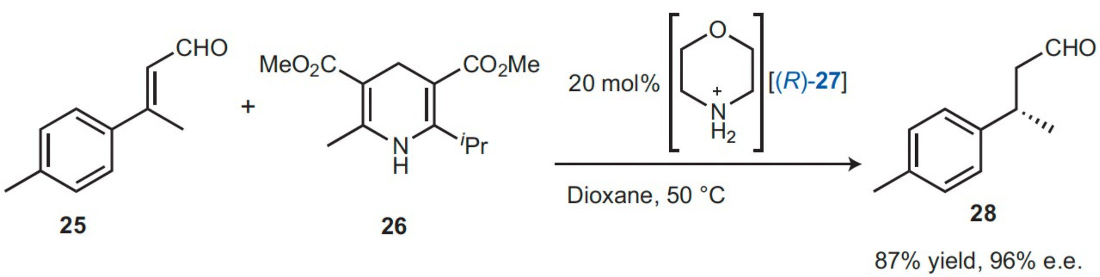
Angew. Chem. Int. Ed. **43**, 1566–1568 (2004).

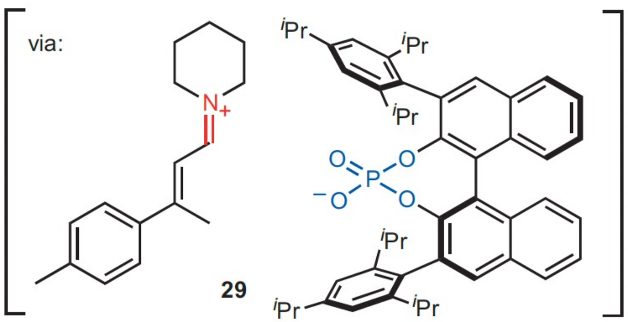
Terada:



J. Am. Chem. Soc. **126**, 5356–5357 (2004).

List:

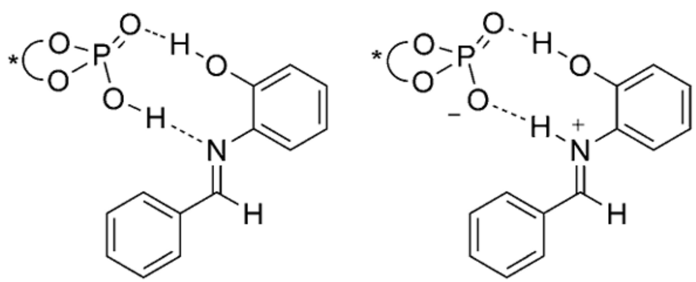




Mayer, S. & List, B. *Angew. Chem. Int. Ed.* 45, 4193–4195 (2006).

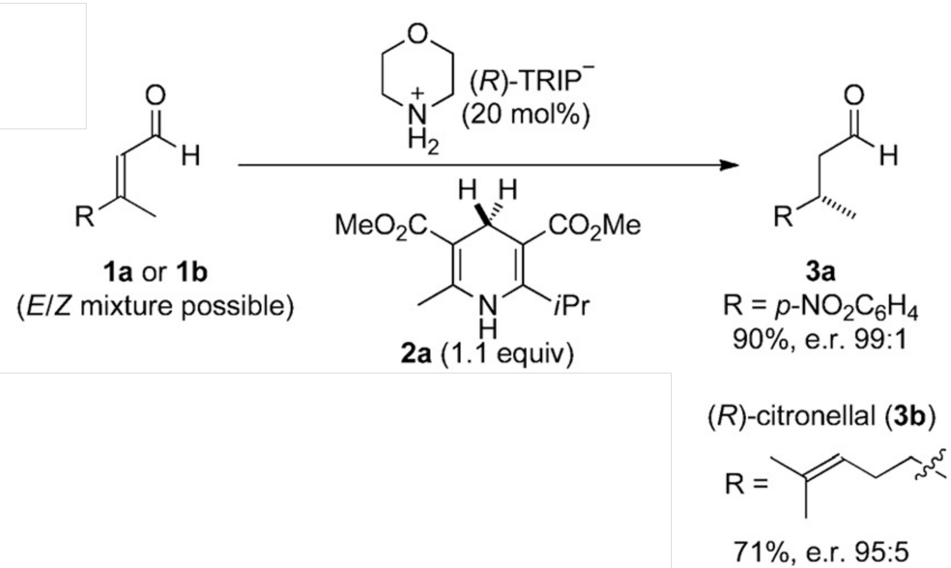
Organocatalysis: Iminium + Chiral Phosphate

The influence of the substrate or other conditions on the equilibrium between the hydrogen-bonded adduct and ion pair was also described.

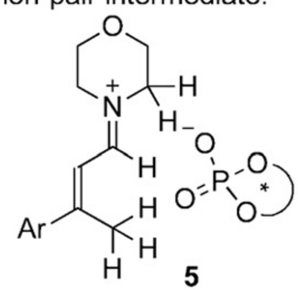


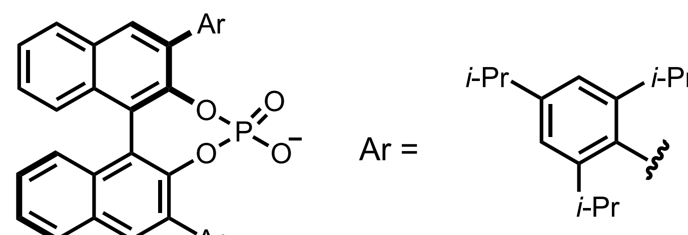
M. Fleischmann, D. Drettwan, E. Sugiono, M. Rueping, R. M. Gschwind, *Angew. Chem. Int. Ed.* **2011**, *50*, 6364–6369.

Organocatalysis: Iminium + Chiral Phosphate



chiral ion-pair intermediate:

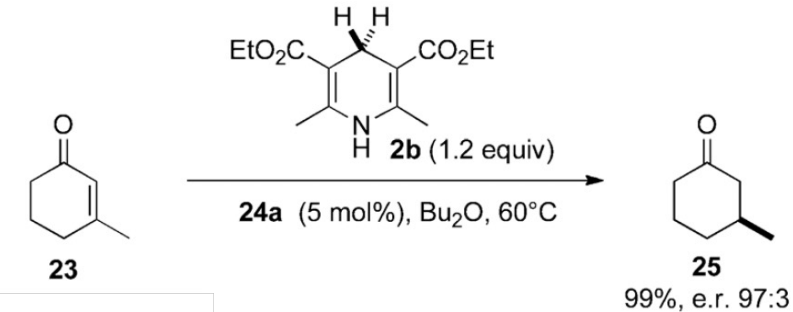


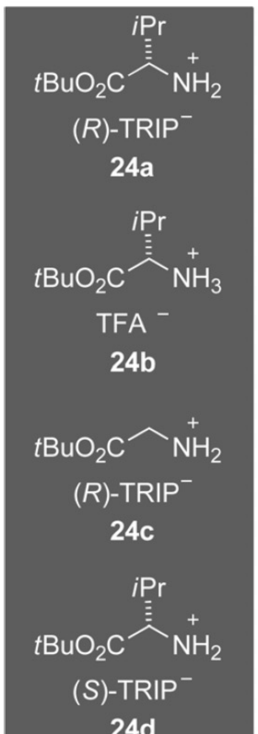


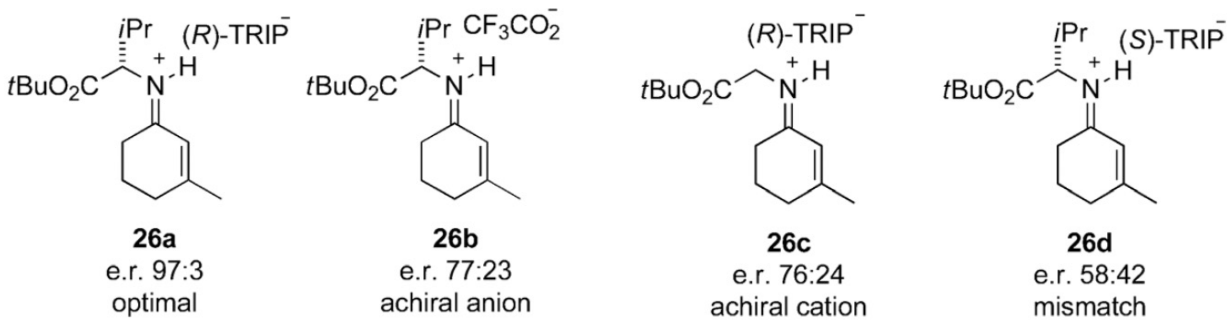
(R)-TRIP⁻

Mayer, S. & List, B. *Angew. Chem. Int. Ed. 45*, 4193–4195 (**2006**).

Organocatalysis: Iminium + Chiral Phosphate

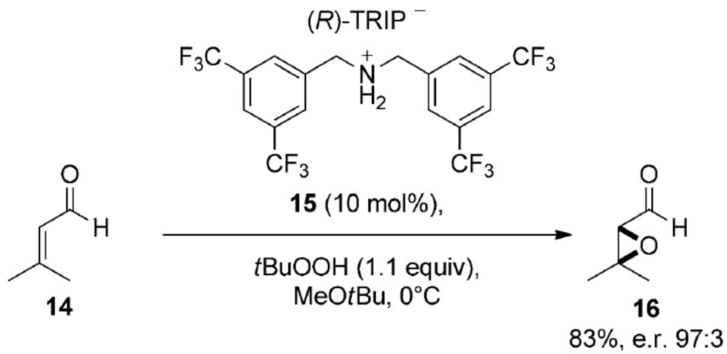


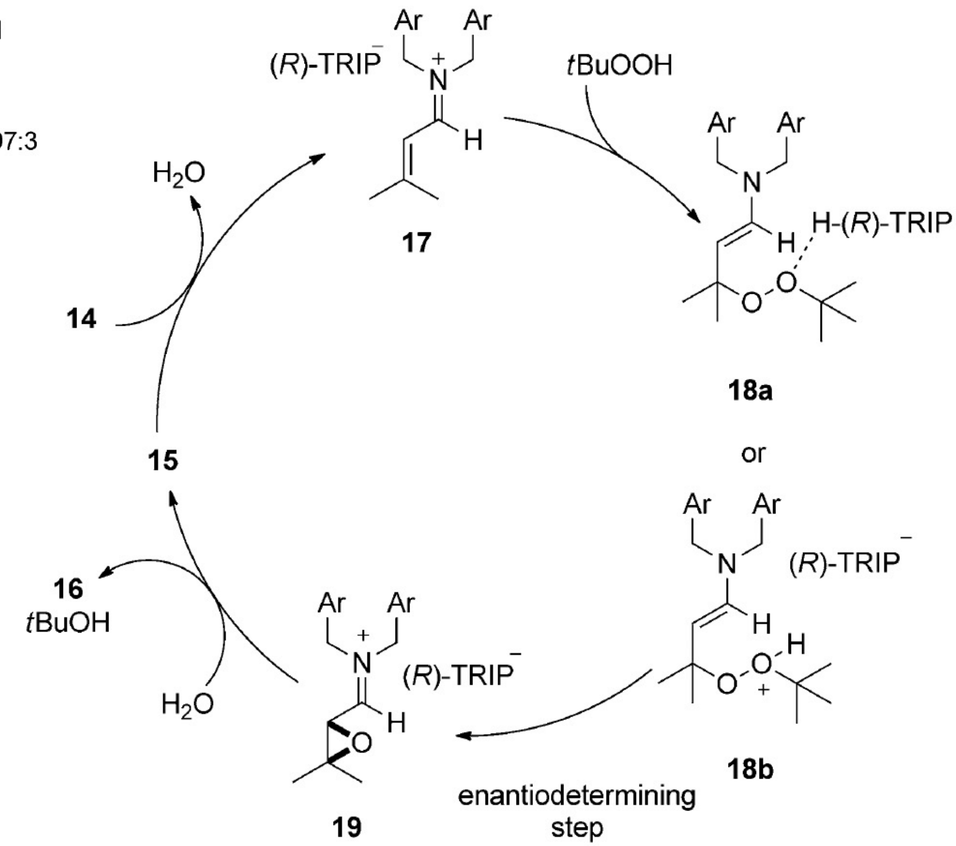




N. J. A. Martin, B. List, *J. Am. Chem. Soc*. **2006**, *128*, 13368– 13369.

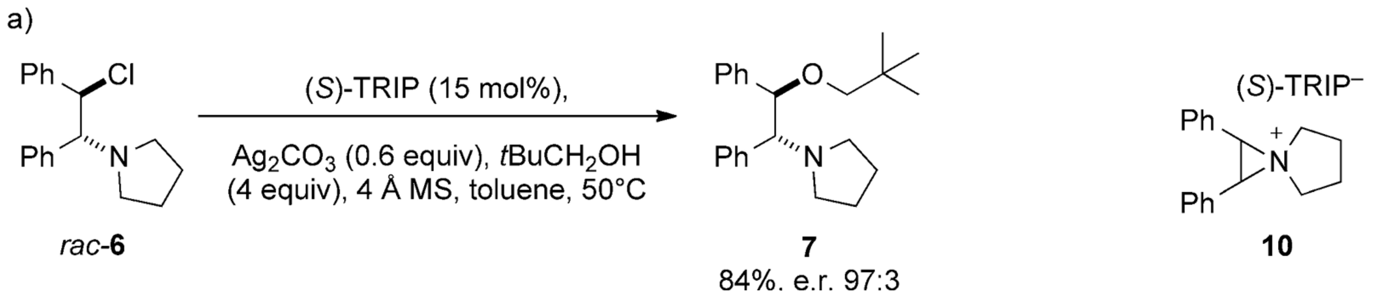
Organocatalysis: Iminium + Chiral Phosphate

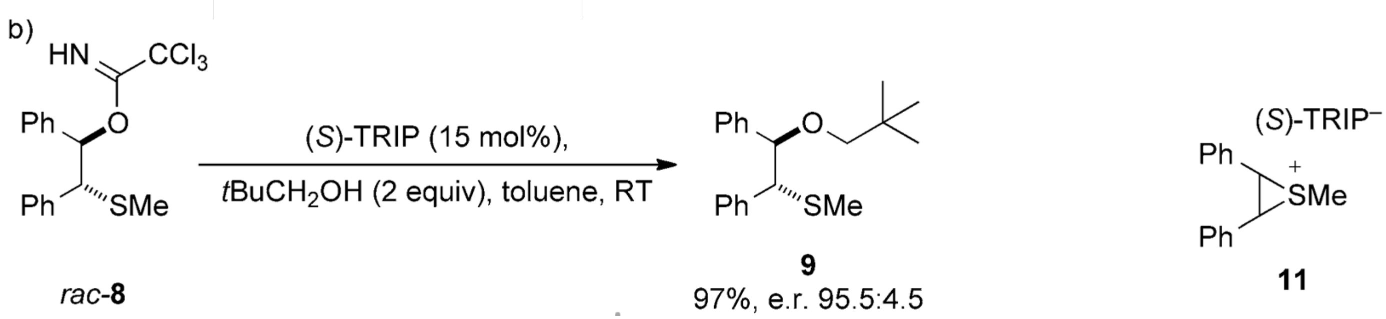




X. Wang, B. List, *Angew. Chem. Int. Ed.* **2008**, *47*, 1119– 1122.

Organocatalysis: aziridinium / episulfonium + Chiral Phosphate





G. L. Hamilton, T. Kanai, F. D. Toste, *J. Am. Chem. Soc.* **2008**, *130*, 14984– 14986.

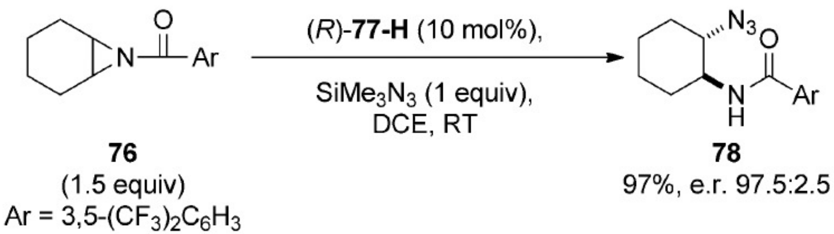
Organocatalysis: Lewis Acid + Chiral Phosphate

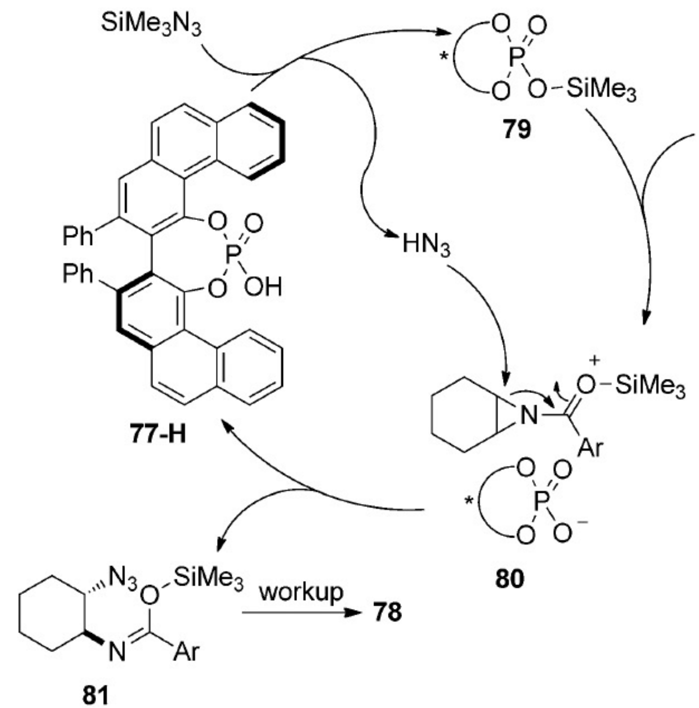
A major limitation of asymmetric Brønsted acid catalysis has been the need for rather electrophilic substrates, such as imines.

The development of catalysts of higher acidity than phosphoric acid diesters has received considerable attention to allow for less-activated substrates, such as ketones.

Mahlau, M; List, B. *Angew. Chem., Int. Ed*. **2013**, *52*, 518.

Organocatalysis: Lewis Acid + Chiral Phosphate

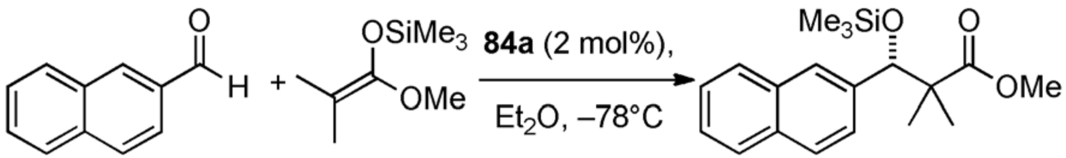




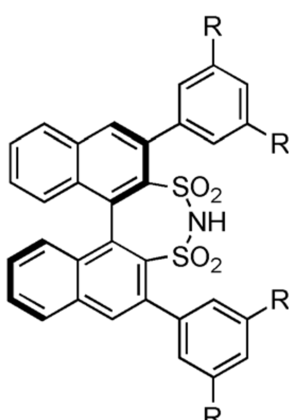
E. B. Rowland, G. B. Rowland, E. Rivera-Otero, J. C. Antilla, *J. Am. Chem. Soc.* 2007, **129**, 12084– 12085

Organocatalysis: Lewis Acid + Chiral disulfonimide

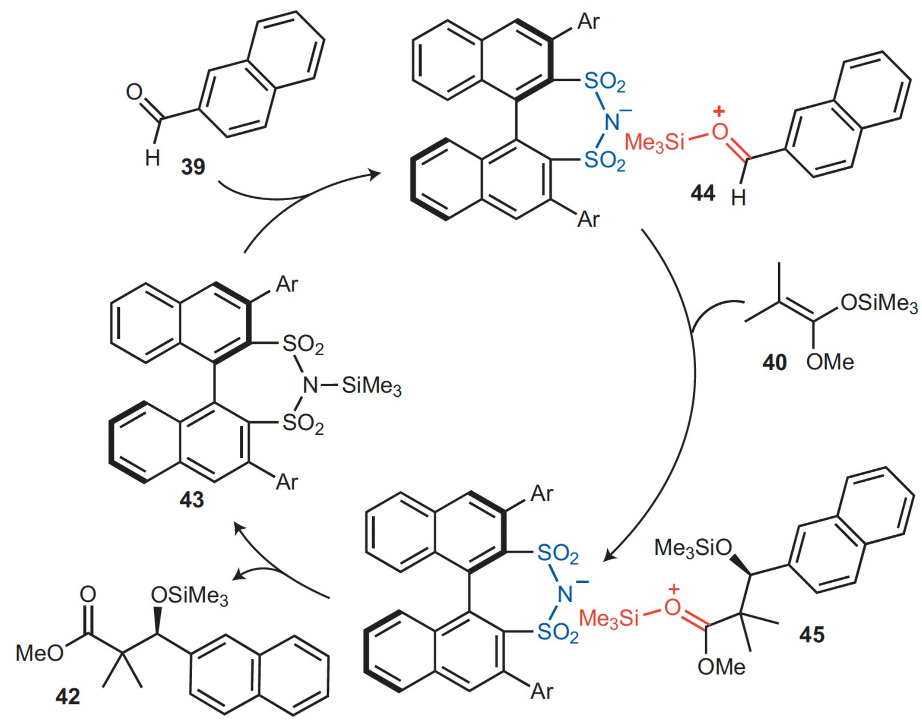
Mukaiyama-aldol reaction



82 — **83** (1.3 equiv.) — **85** 98%, e.r. 97:3



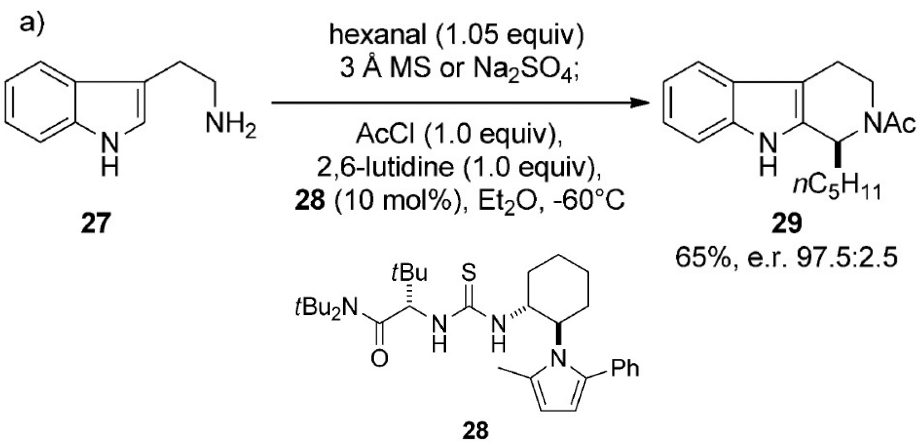
84a: R = CF_3
84b: R = $CF(CF_3)_2$

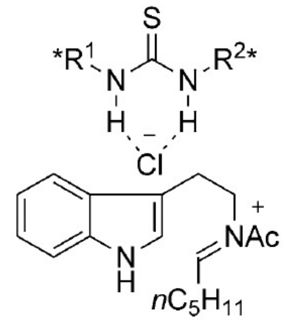


S. C. Pan, B. List, *Chem. Asian J.* 2008, **3**, 430– 437

H-bond Doner: Thiourea

Pictet–Spengler Reaction





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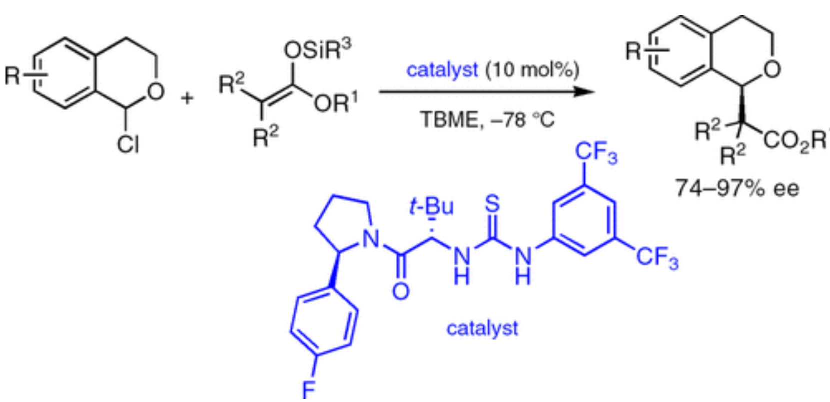
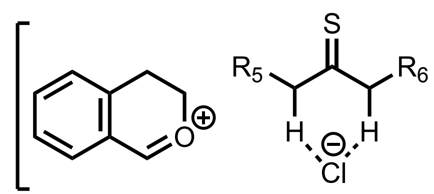
M. S. Taylor, E. N. Jacobsen, *J. Am. Chem. Soc.* **2004**, *126*, 10558– 10559.

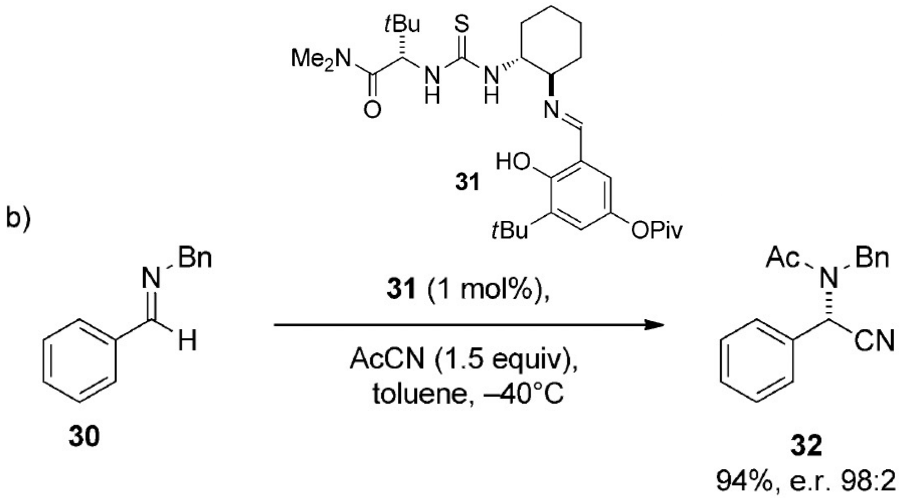


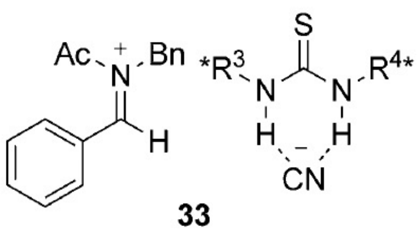


Sarah E. Reisman, Abigail G. Doyle, and Eric N. Jacobsen, *J. Am. Chem. Soc.* **2008**, 130, 23, 7198–7199

H-bond Doner: Thiourea

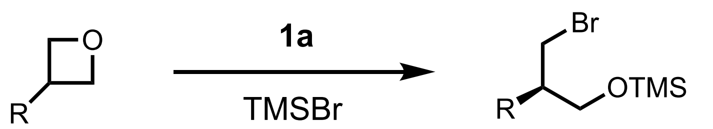
Acyl-Strecker Reaction



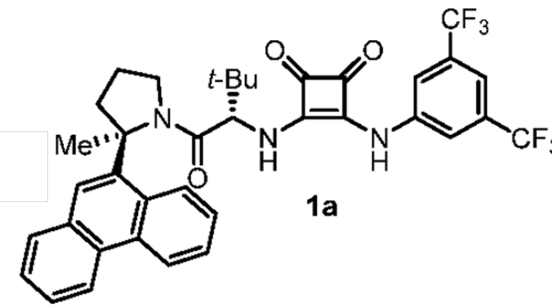


S. C. Pan, J. Zhou, B. List., *Angew. Chem. Int. Ed.* **2007**, *46,* 612– 614.

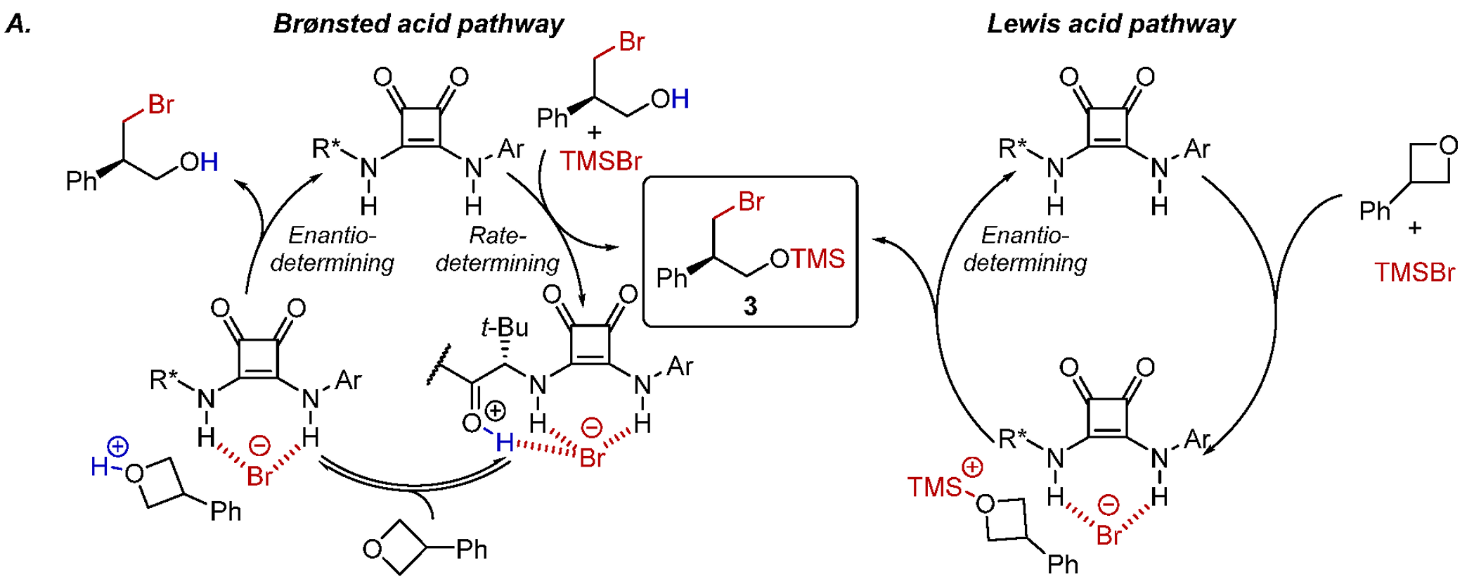
H-bond Doner: Squaramide



83-95%, 85-99% ee



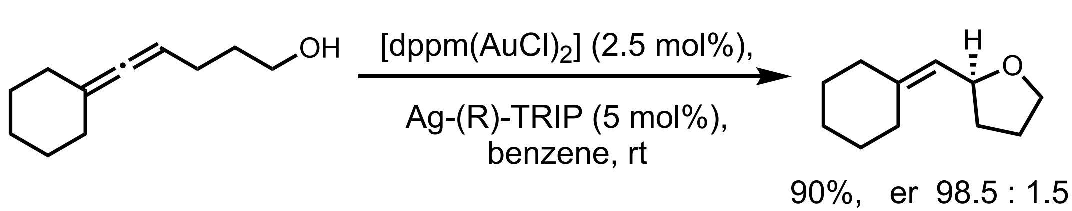
1a

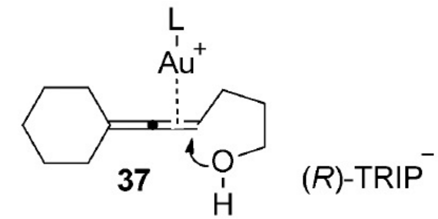


Daniel A. Strassfeld, Russell F. Algera, Zachary K. Wickens, and Eric N. Jacobsen, *J. Am. Chem. Soc.* **2021**, 143, 25, 9585–9594

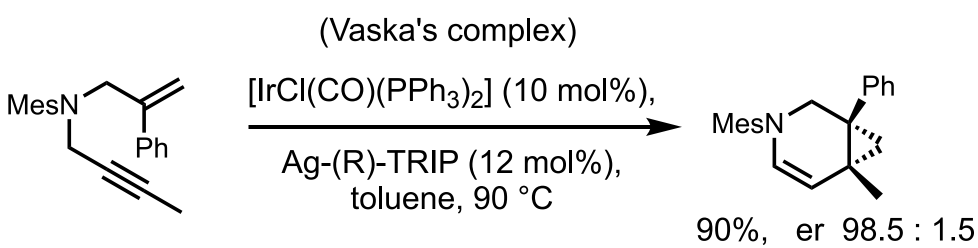
Transition-Metal Catalysis

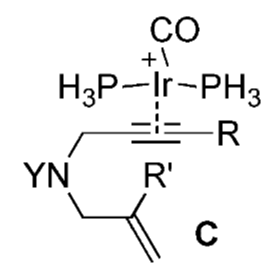
Au[I] catalysis proceeds via dicoordinated species





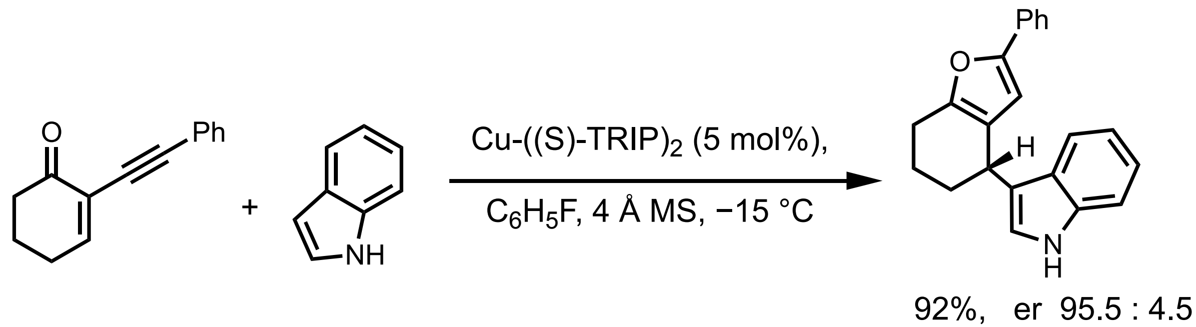
G. L. Hamilton, E. J. Kang, M. Mba, F. D. Toste, *Science* **2007**, *317*, 496– 499.



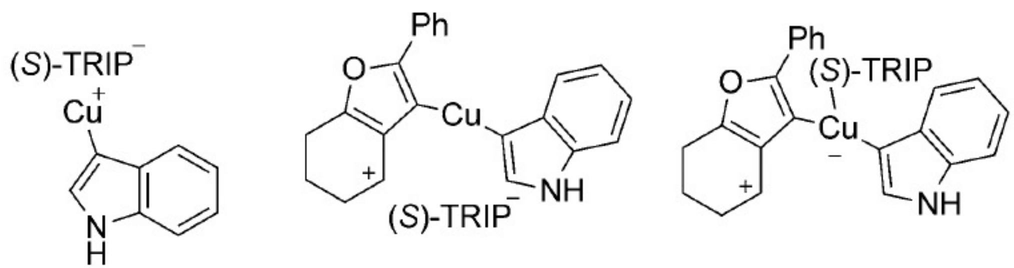


M. Barbazanges, M. Augé, J. Moussa, H. Amouri, C. Aubert, C. Desmartes, L. Fensterbank, V. Gandon, M. Malacria, C. Ollivier, *Chem. Eur. J.* **2011**, *17*, 13789– 13794

Transition-Metal Catalysis



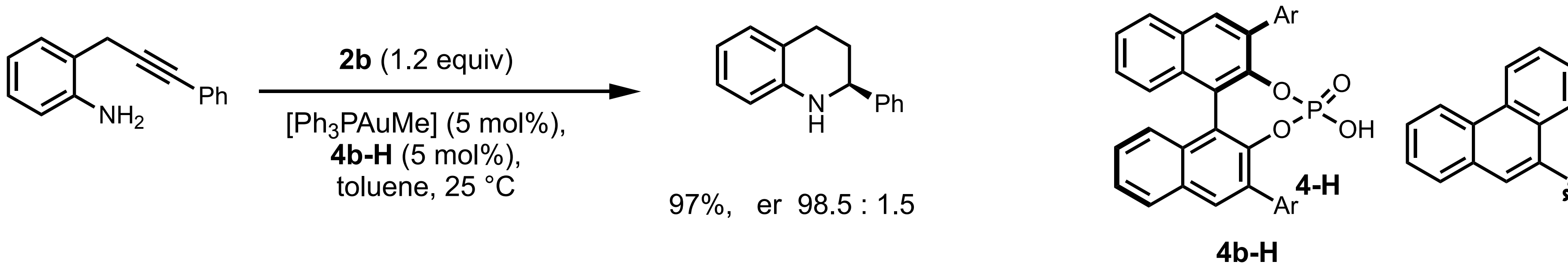
active catalyst: chiral intermediate:



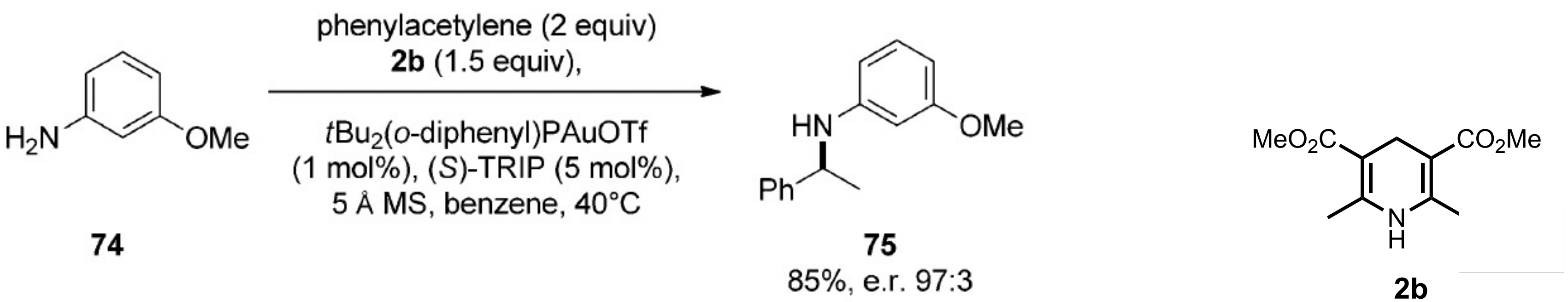
58 **59a** **59b**

V. Rauniyar, Z. J. Wang, H. E. Burks, F. D. Toste, *J. Am. Chem. Soc*. **2011**, *133*, 8486– 8489

Transition-Metal Catalysis

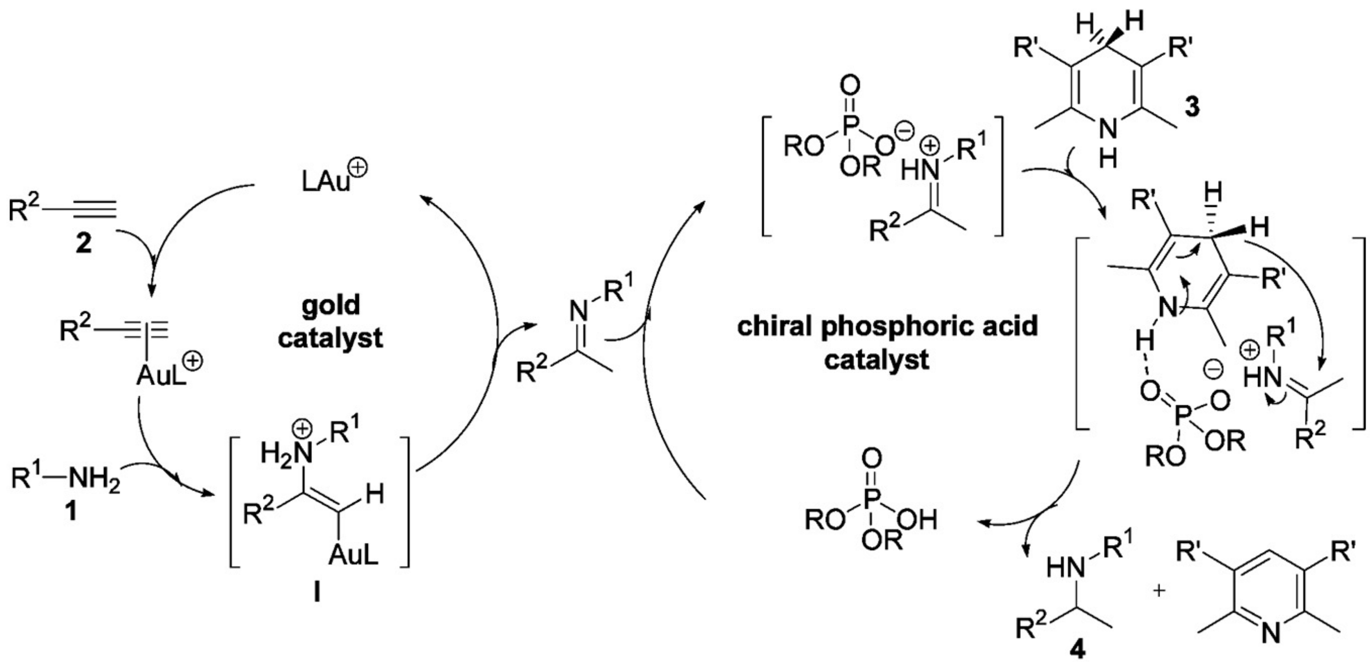


Z.-Y. Han, H. Xiao, X.-H. Chen, L.-Z. Gong, *J. Am. Chem. Soc.* 2009, **131**, 9182– 9183.



X.-Y. Liu, C.-M. Che, *Org. Lett.* 2009, **11**, 4204– 4207.

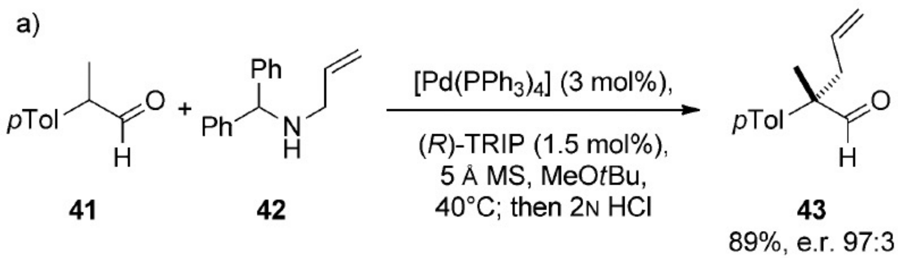
Transition-Metal Catalysis



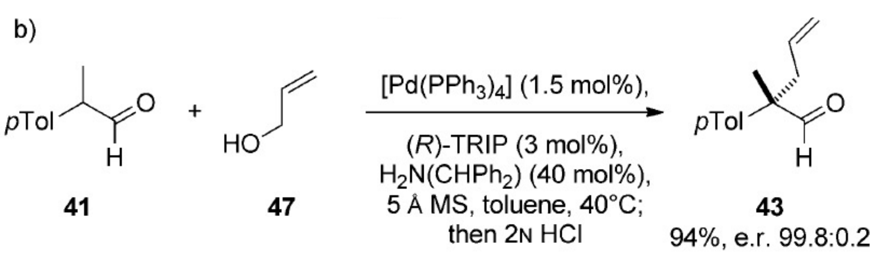
X.-Y. Liu, C.-M. Che, *Org. Lett.* 2009, **11**, 4204– 4207.

Transition-Metal Catalysis

Enantioselective Tsuji–Trost α-allylations of α-branched aldehydes



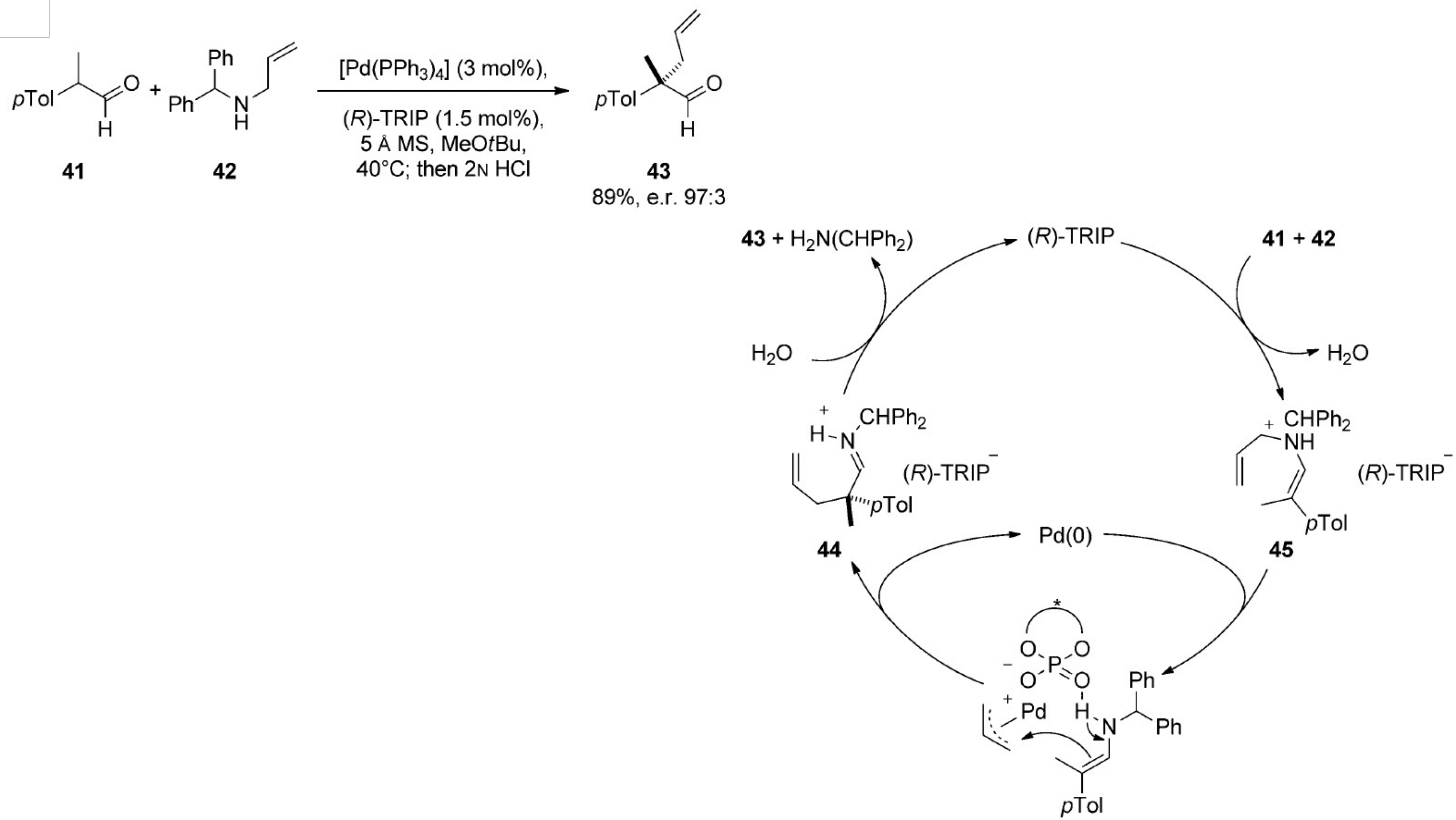
S. Mukherjee, B. List, *J. Am. Chem. Soc.* **2007**, *129*, 11336– 11337



G. Jiang, B. List, *Angew. Chem. Int. Ed.* **2011**, *50*, 9471– 9474.

Transition-Metal Catalysis

Enantioselective Tsuji–Trost α-allylations of α-branched aldehydes



S. Mukherjee, B. List, *J. Am. Chem. Soc.* **2007**, *129*, 11336– 11337.

Transition-Metal Catalysis

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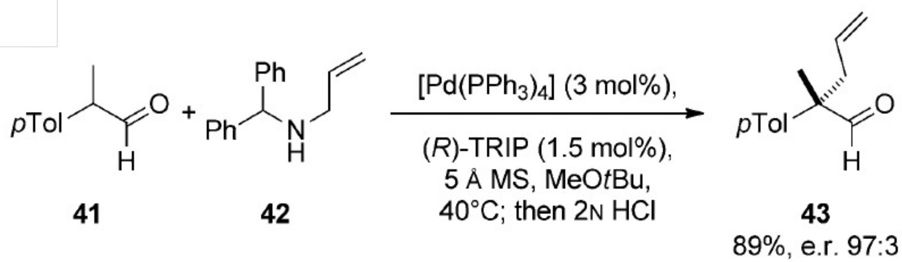
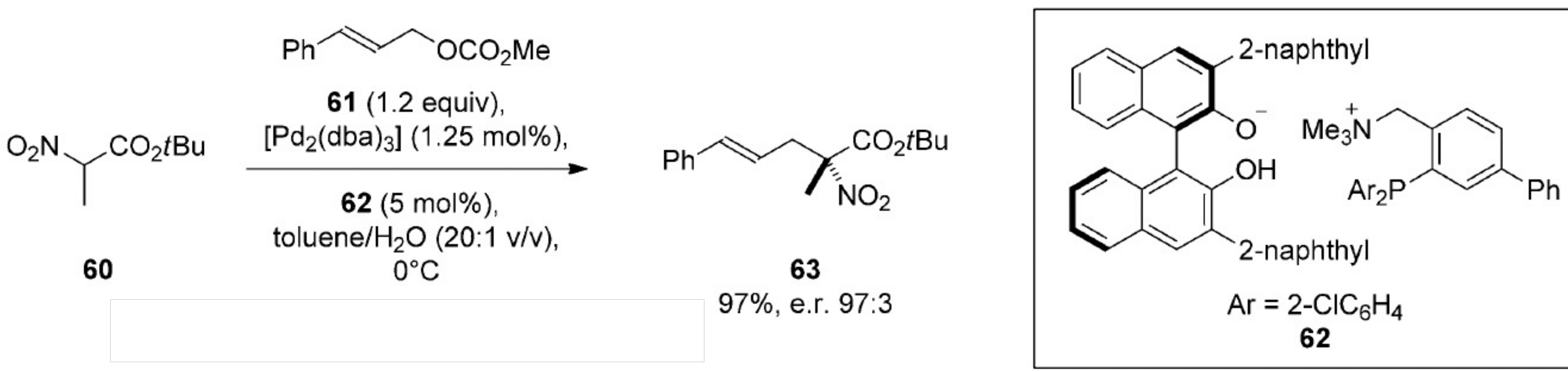


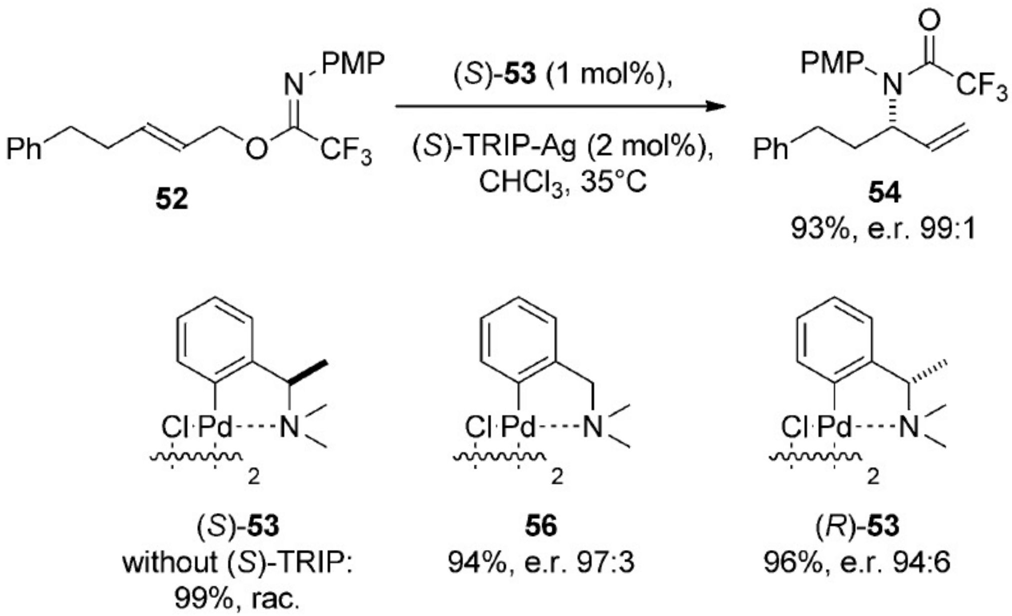
S. Mukherjee, B. List, *J. Am. Chem. Soc.* **2007**, *129*, 11336– 11337.

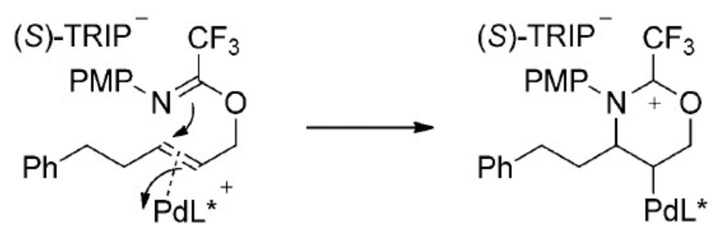


K. Ohmatsu, M. Ito, T. Kunieda, T. Ooi, *Nat. Chem.* **2012**, *4*, 473– 477.

Transition-Metal Catalysis

Overman Rearrangment:

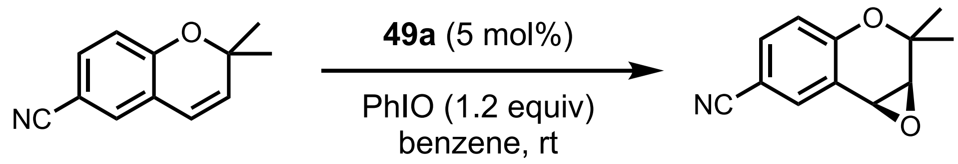




G. Jiang, R. Halder, Y. Fang, B. List, *Angew. Chem., Int. Ed.* **2011**, *50*, 9752.

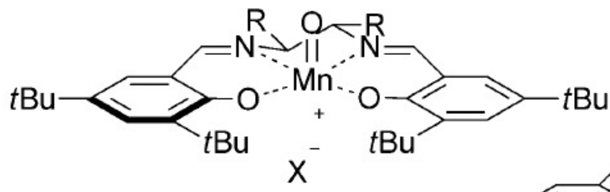
Transition-Metal Catalysis

Jacobsen–Katsuki epoxidation

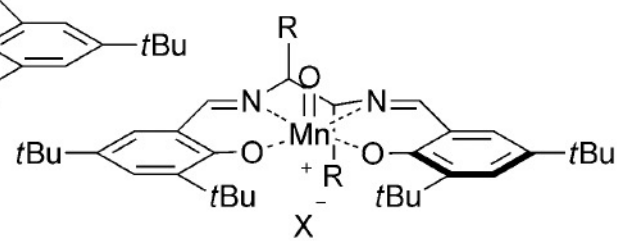


98%, er 97 : 3

chiral conformations of Mn^{III}-salen complexes:

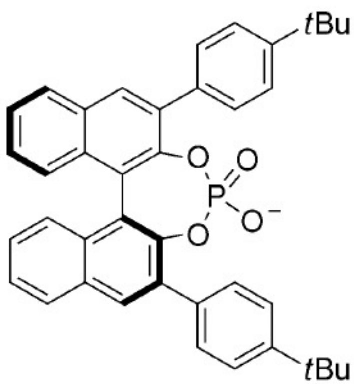


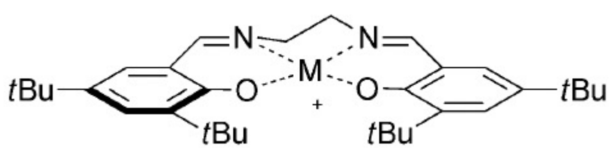
51a



51b

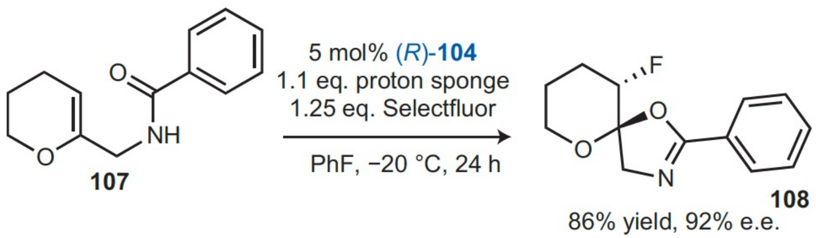
ACDC catalyst:

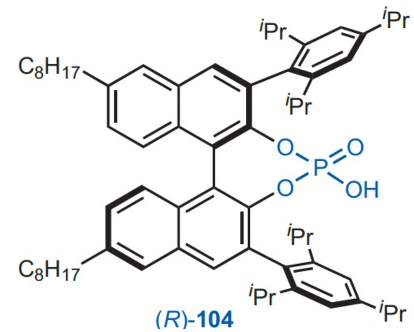


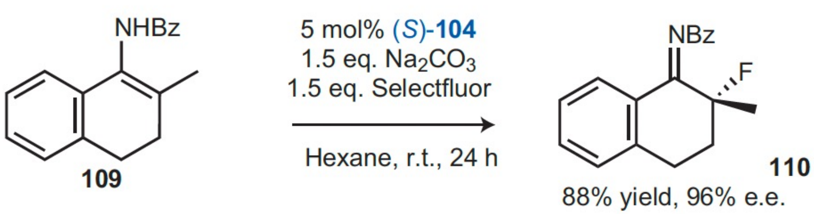


49a (M = Mn) epoxidation catalyst
49b (M = Fe) sulfoxidation catalyst

Transition-Metal Catalysis

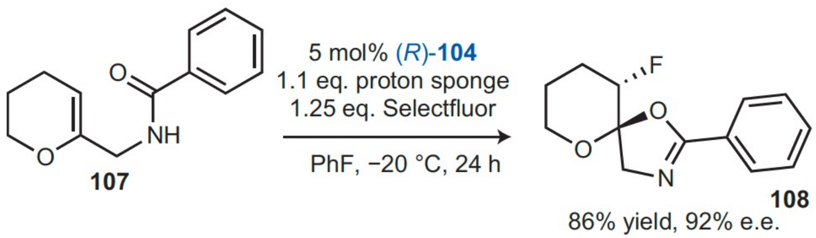


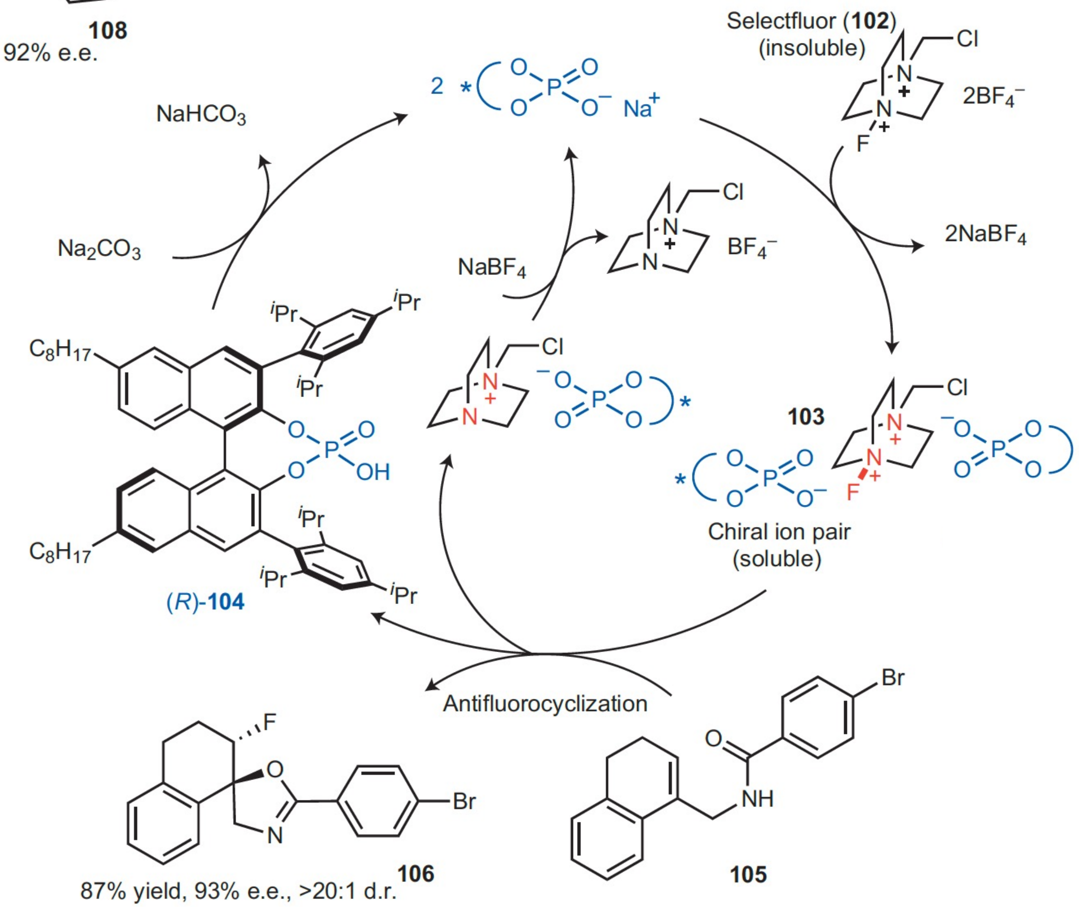




Robert J. Phipps, Kenichi Hiramatsu, and F. Dean Toste, *J. Am. Chem. Soc.* **2012**, 134, 20, 8376–8379

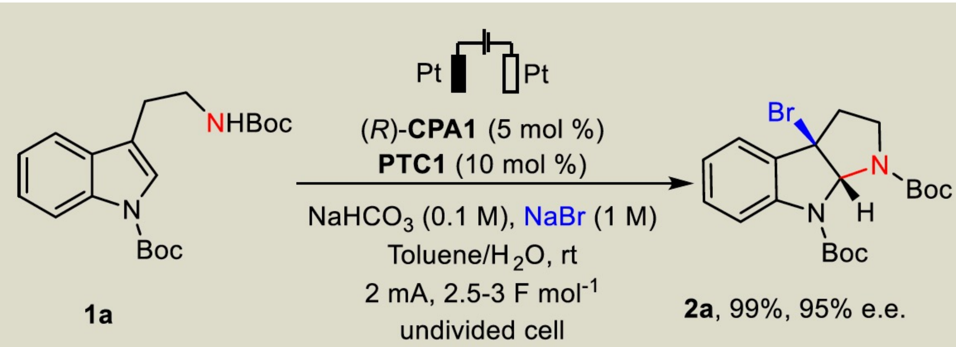
Transition-Metal Catalysis

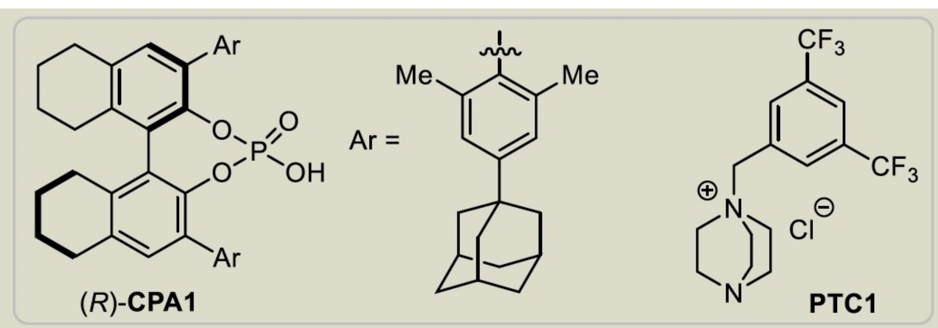


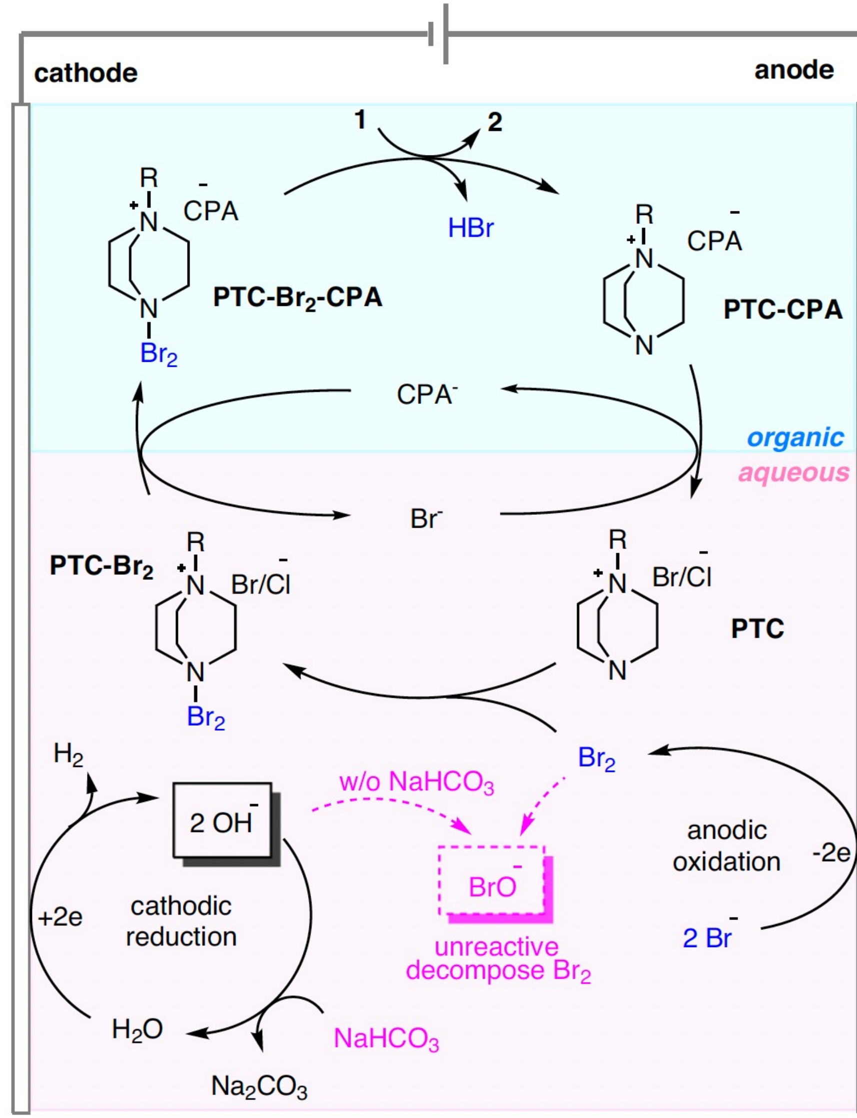


Robert J. Phipps, Kenichi Hiramatsu, and F. Dean Toste, *J. Am. Chem. Soc.* **2012**, 134, 20, 8376–8379

Phase-Transfer Catalysis







Tan, X., Wang, Q., Sun, J. *Nat Commun* **14**, 357 (2023)