Truong N. Nguyen

Asymmetric Organocatalysis

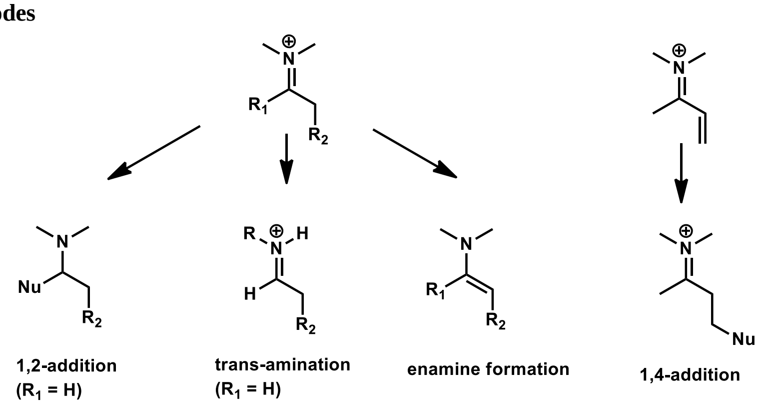
Contents

Organocatalysis: "The catalysis with small molecules, where an inorganic element is not a part of the active principle"

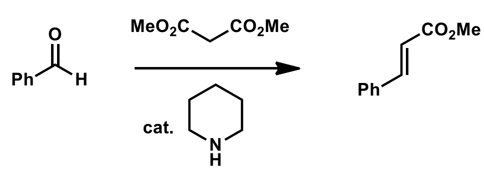
I. Lewis bases

1. Iminium catalysis

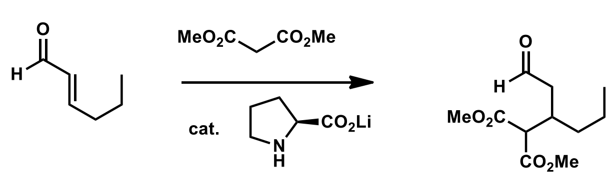
- **Activation modes**



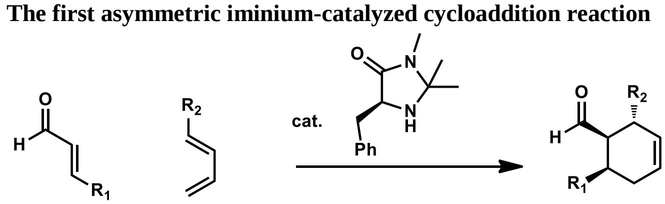
- **1894 – Knoevenagel condensation**



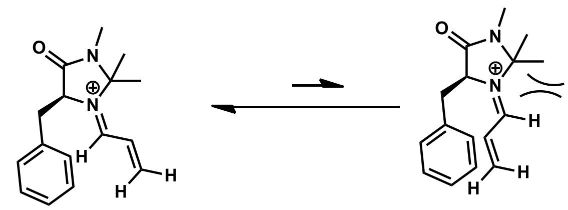
- **1991 – Yamaguchi**



- **2000 – MacMillan. The first asymmetric iminium-catalyzed cycloaddition reaction**

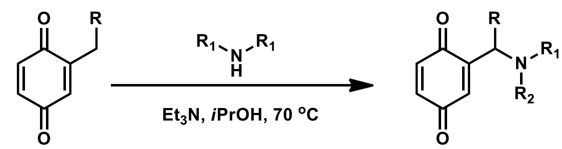


MacMillan, *J. Am. Chem. Soc*. **2000**, *122*, 4243



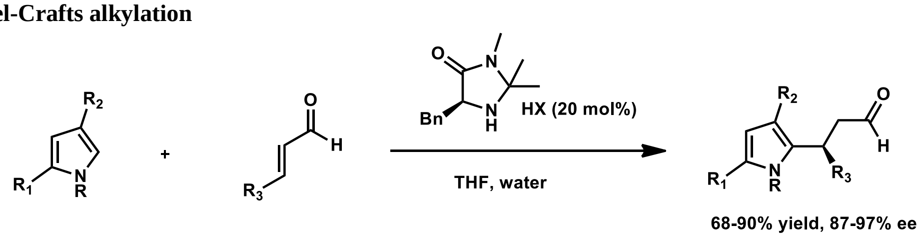
- selective (*E*)-iminium isomer formation to avoid geminal methyl substituents
- favor *si*-face due to the effective shield of benzyl group

- **Amine benzylation**



Clift, *Org. Lett.* **2016**, *18*, 3446

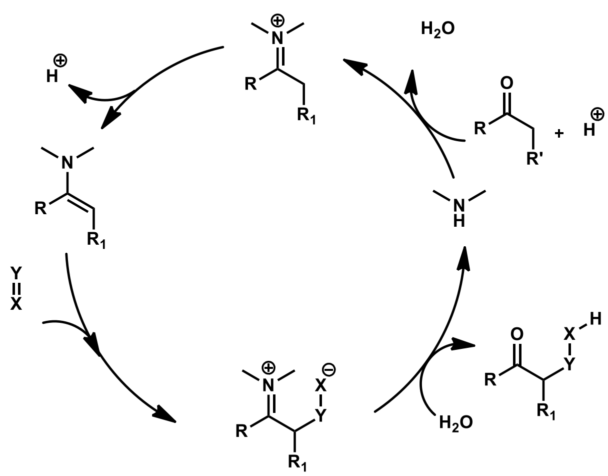
- **Friedel-Crafts alkylation**



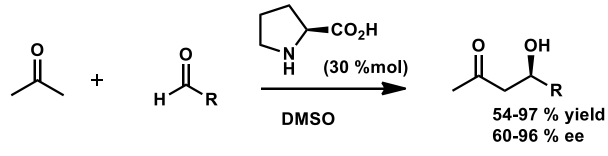
MacMillan, *J. Am. Chem. Soc*. **2001**, *123*, 4370

2. Enamine catalysis

- **Activation mode**

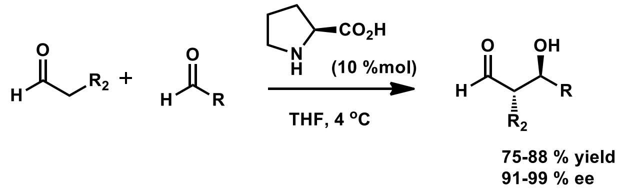


- **Ketone – Aldehyde Aldol**



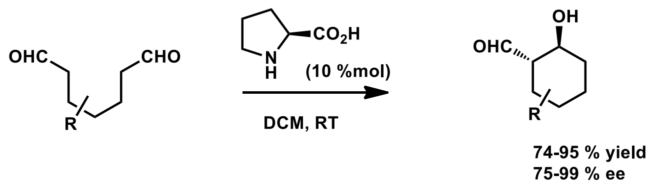
List, *J. Am. Chem. Soc*. **2002**, *124*, 2395

- **Aldehyde Cross - Aldol**



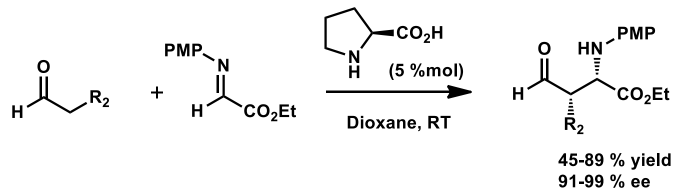
MacMillan, *J. Am. Chem. Soc*. **2002**, *124*, 6798

- **Enolexo Aldolization**

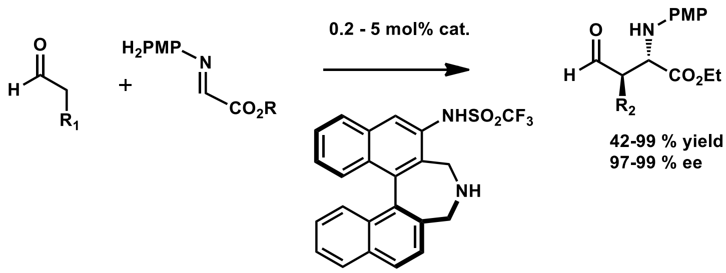


List, *Angew. Chem. Int. Ed.* **2003**, *42,* 2785

- **Mannich reaction**

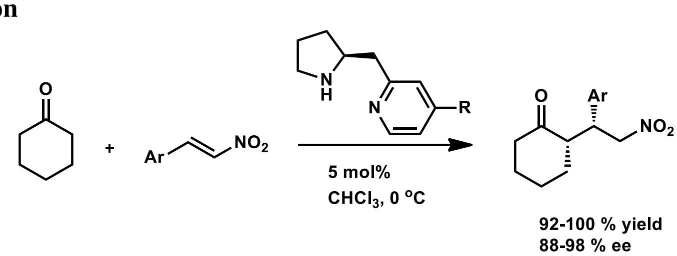


Barbas III, *J. Org. Chem.* **2003**, *68*, 9624

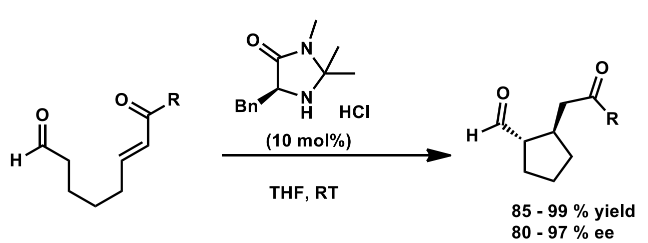


Maruoka, *J. Am. Chem. Soc*. **2005**, *127*, 6798

- **Michael Addition**

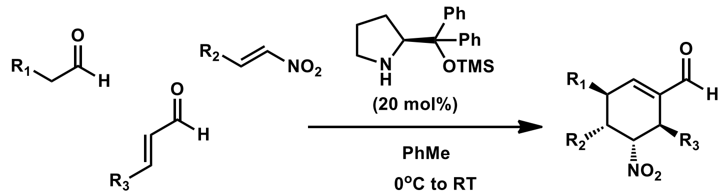


Kotsuki, *J. Am. Chem. Soc*. **2004**, *126*, 9558



List, *Angew. Chem. Int. Ed.* **2004**, *43*, 3958

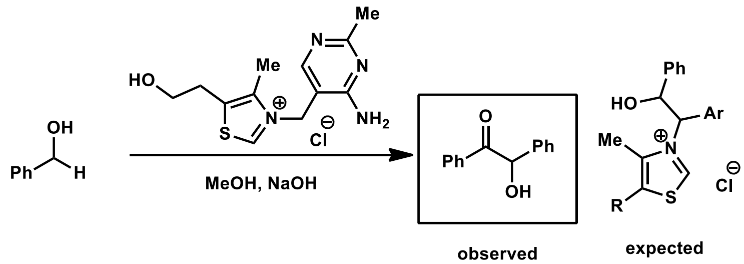
- **Three-component domino reaction**



Enders, *Nature*, **2006**, *441*, 861

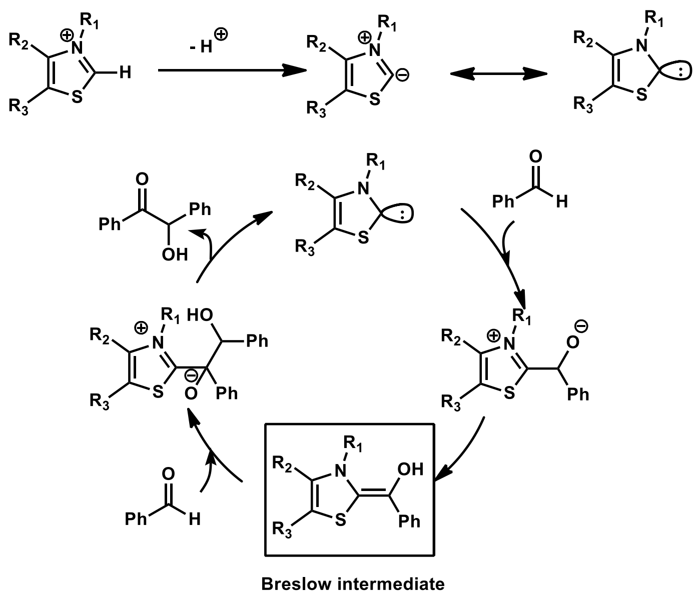
3. NHC-catalyst

- **1948 – Ugai**



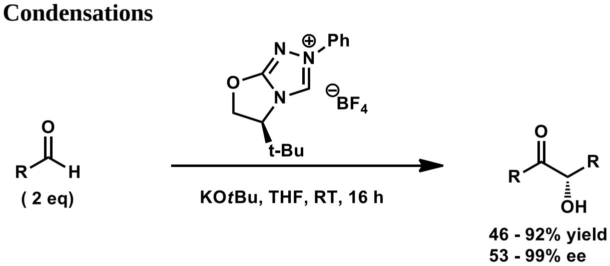
Ugai, *J. Pham. Soc. Jpn.* **1943**, *63*, 296

- **1958 - Breslow**



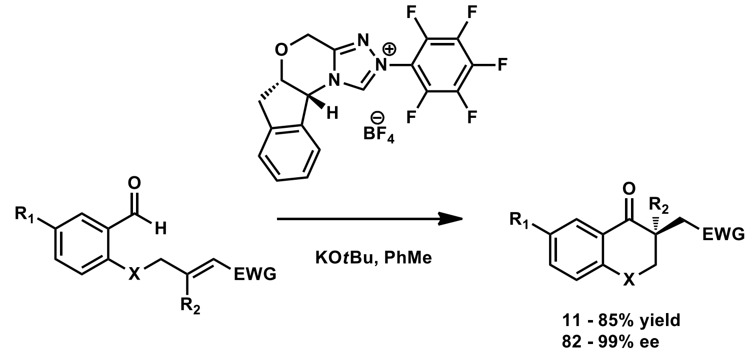
Breslow, *J. Am. Chem. Soc*. **1958**, *80*, 3719

- **Asymmetric Benzoin Condensations**



Enders, *Angew. Chem. Int. Ed.* **2002**, *41*, 1743

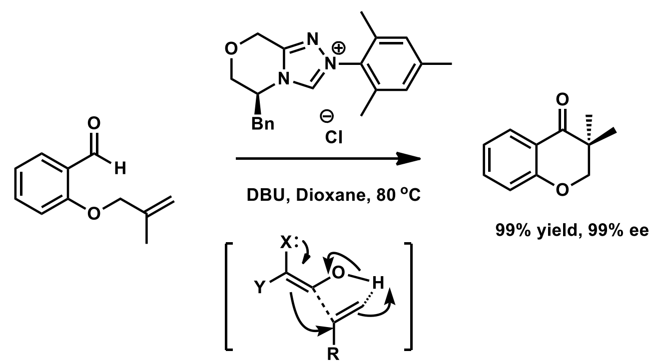
- **Stetter reaction**



Rovis, *J. Am. Chem. Soc*. **2004**, *126*, 8876

General method for asymmetric intermolecular Stetter reaction has not been developed!!!

- **Hydroacylation of Unactivated Double Bonds**

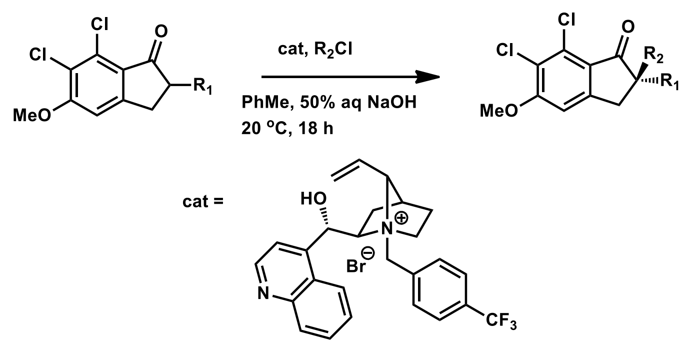


Glorius, *Angew. Chem. Int. Ed.* **2011**, *50*, 4983

II. Lewis bases

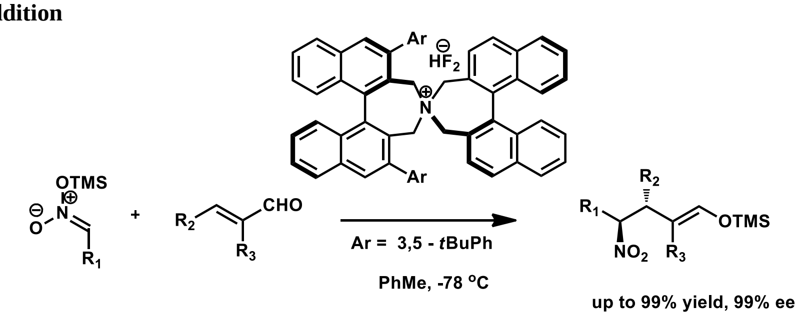
1. Phase transfer catalysis

- **Alkylation**

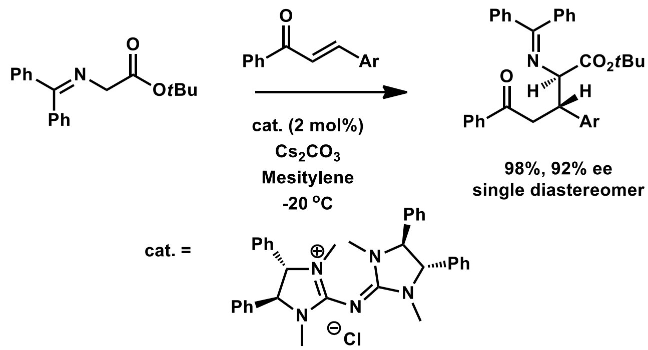


Dolling, *J. Am. Chem. Soc*. **1984**, *126*, 446

- **Michael Addition**

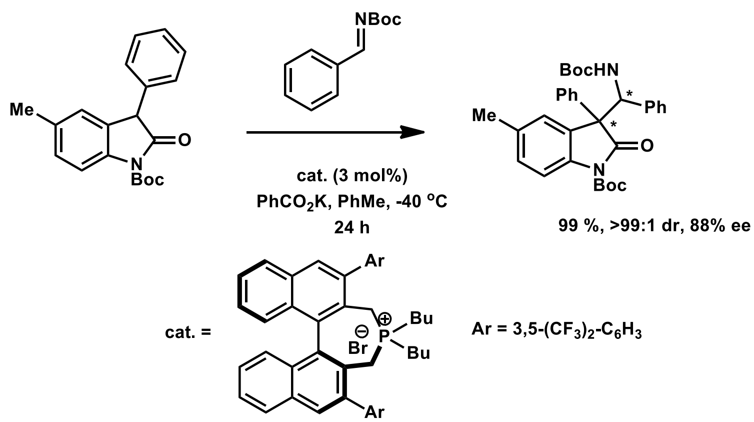


Maruoka, *J. Am. Chem. Soc*. **2003**, *125*, 9022



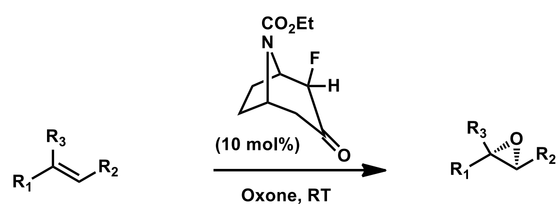
Tan, *J. Am. Chem. Soc*. **2011**, *133*, 2828

➢ **Mannich reaction**

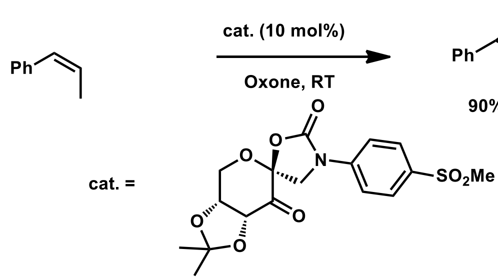


Maruoka, *Angew. Chem. Int. Ed.* **2009**, *48*, 4559

2. Ketone catalyzed epoxidation

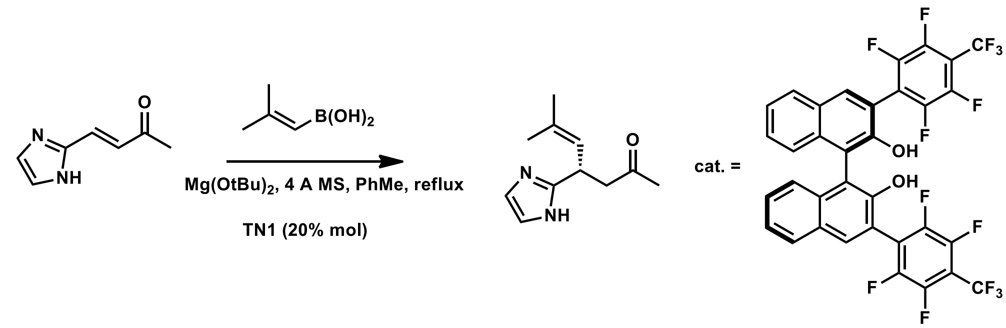


Armstrong, *J. Org. Chem.* **2002**, *67*, 8610

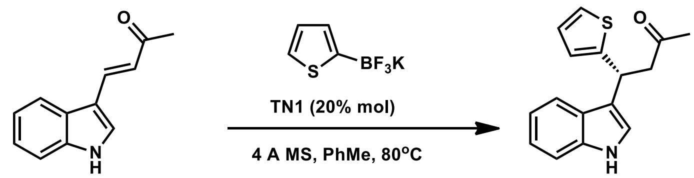


Shi, *Org. Lett.* **2003**, *5*, 293 (**Shi epoxidation**)

3. BINOL catalyzed conjugate addition

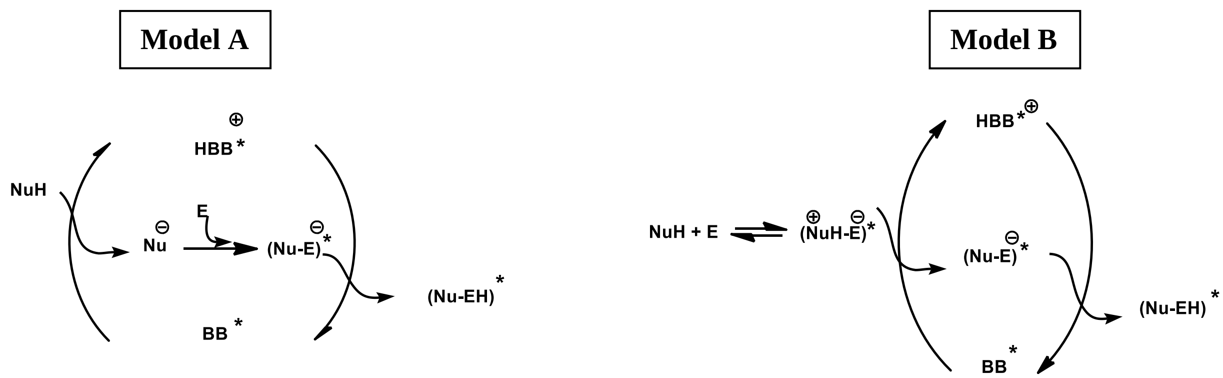


May, *Org. Lett.* **2012**, *14*, 6104



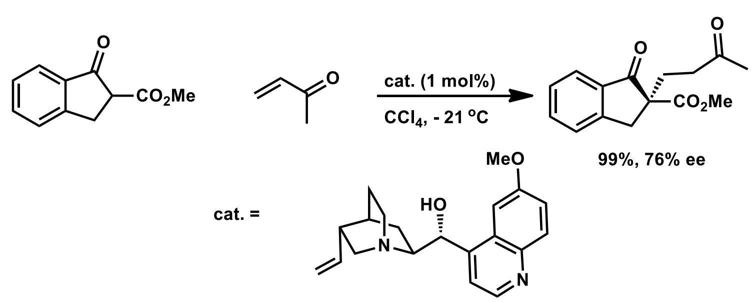
May, *Angew. Chem. Int. Ed.* **2015**, *54*, 9931

III. Brønsted Bases (BB)

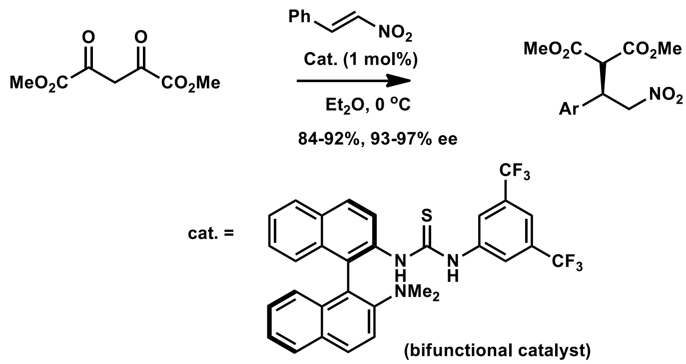


Early (A) and late (B) participation of a chiral BB catalyst

- **Michael addition**

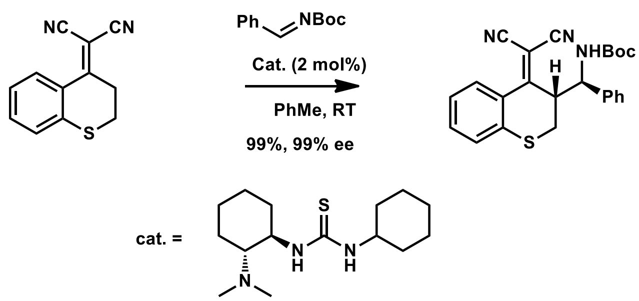


Wynberg, *J. Org. Chem.* **1979**, *44*, 2238



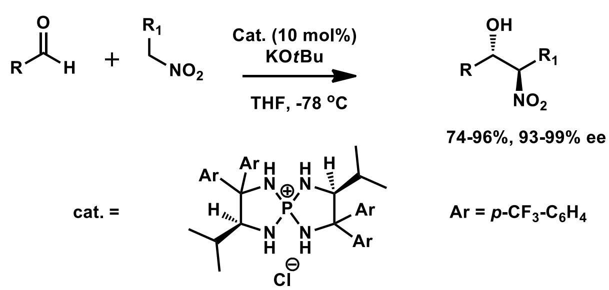
Wang, *Org. Lett.* **2005**, *7*, 4713

- **Mannich reaction**



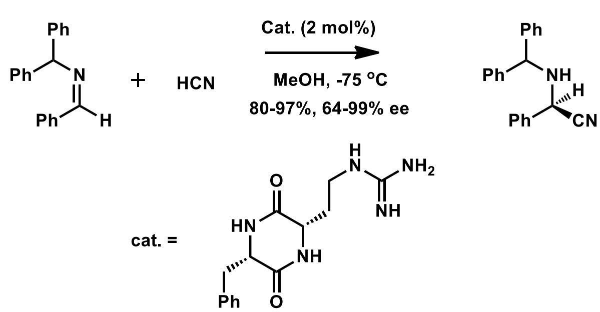
Chen, *J. Am. Chem. Soc*. **2007**, *129*, 1878

- **Henry reaction**



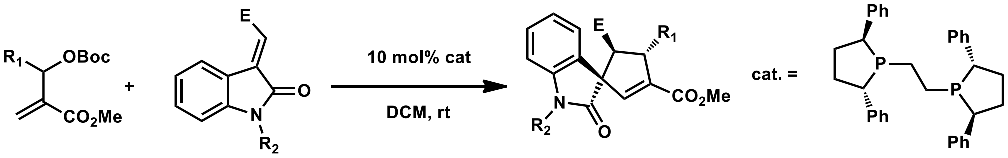
Ooi, *J. Am. Chem. Soc*. **2007**, *129*, 12392

- **Strecker reaction**



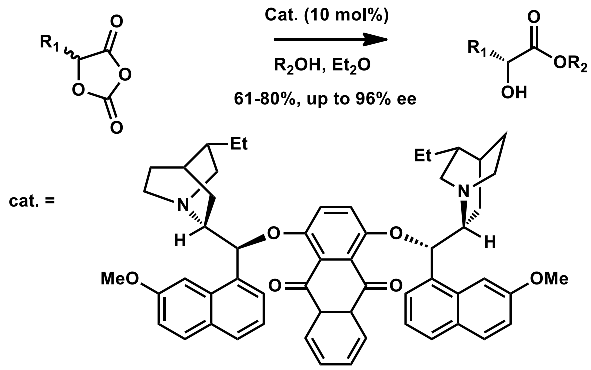
Lipton, *J. Am. Chem. Soc*. **1996**, *118*, 4910

- **MBH reaction**



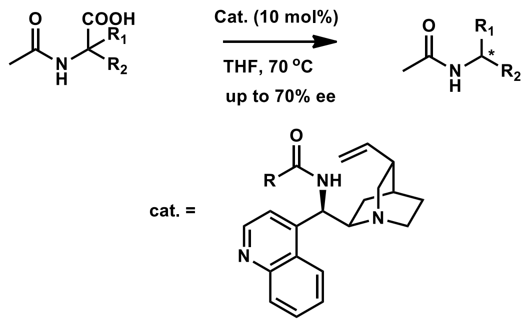
Barbas III, *J. Am. Chem. Soc*. **2011**,133, 4672

- **Kinetic resolution**



Deng, *J. Am. Chem. Soc*. **2002**, *124*, 2870

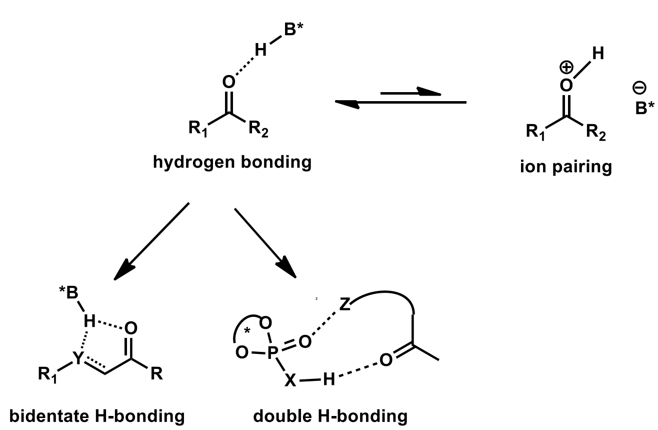
- **Desymmetrization**



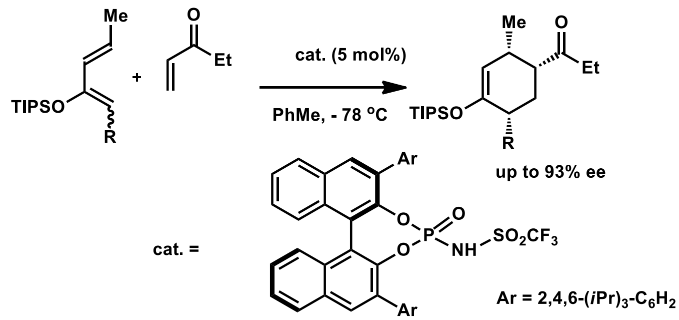
Baur, *Eur. J. Org. Chem*. **2003**, 2854

IV. Brønsted acids

- **Activation modes**

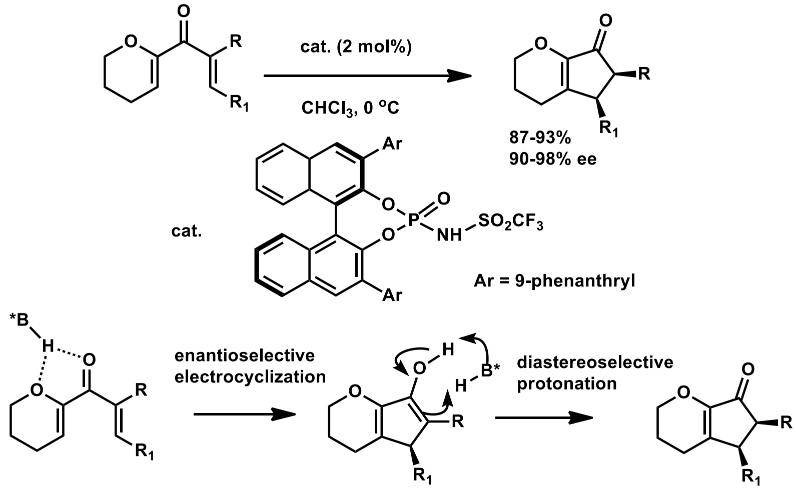


- **Diels –Alder reaction**



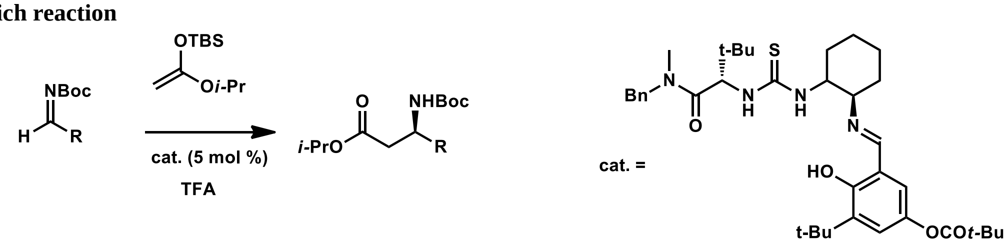
Yamamoto, *J. Am. Chem. Soc*. **2006**, *128*, 9626

- **Nazarov cyclization**

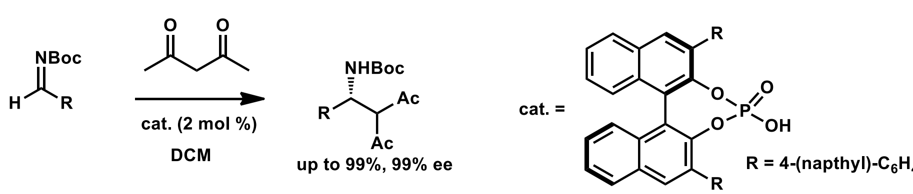


Rueping, *Angew. Chem. Int. Ed.* **2007**, *46*, 2097

- **Mannich reaction**

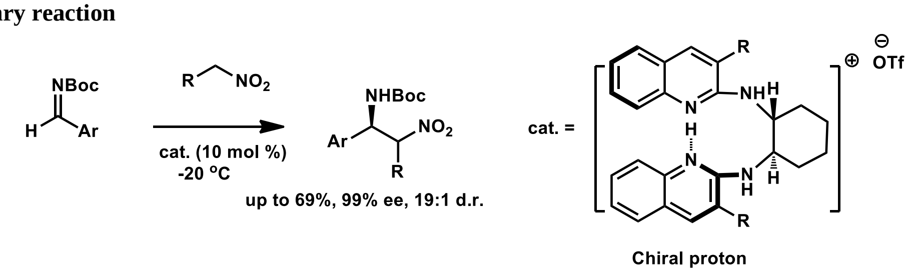


Jacobsen, *J. Am. Chem. Soc*. **2002**, *124*, 12964



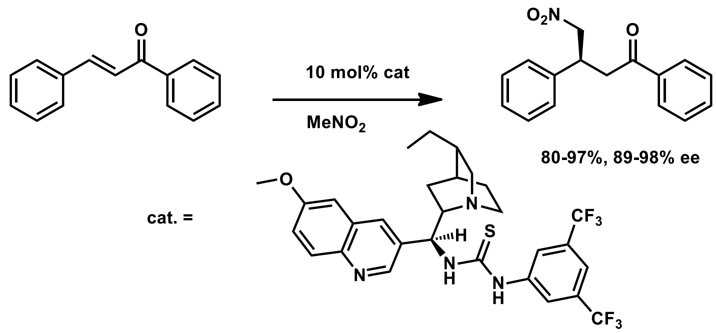
Terada, *J. Am. Chem. Soc*. **2004**, *126*, 5356

- **Aza-Henry reaction**



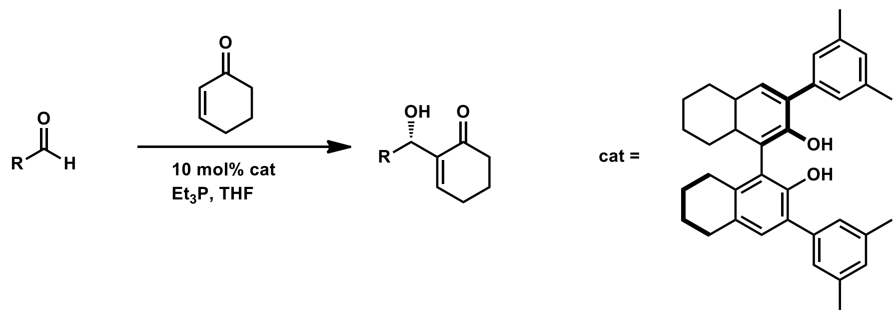
Johnson, *J. Am. Chem. Soc*. **2004**, *126*, 3418

➢ **Michael addition**



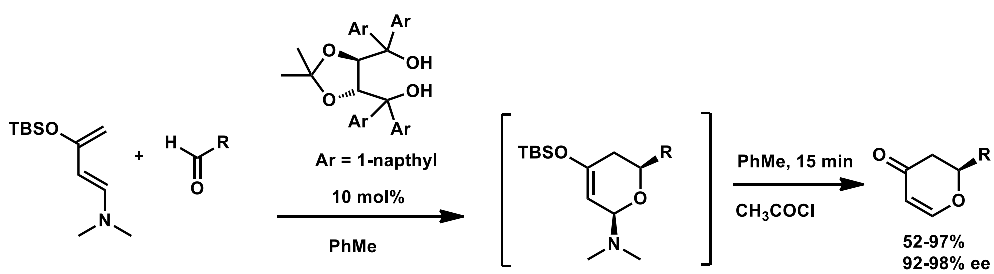
Soos, *Org. Lett.* **2005**, *7*, 1967

➢ **Morita-Baylis-Hillman reaction**



Schaus, *J. Am. Chem. Soc*. **2003**, *125*, 12094

➢ C**ycloaddition**



Rawal, *Nature* **2003**, *424*, 146

References: Claudio, *Chem. Soc. Rev*., **2009**, *38*, 632
Rueping, *Chem. Soc. Rev*., **2011**, *40*, 4539
Handout: "Asymmetric Organocatalytic Transformation", Stoltz/Reisman Group
Hand out: "Organocatalysis: Almost everything you wanted to know, but never asked", Wipf Group
Handout: "NHC organocatalysis" MacMillan group

The end