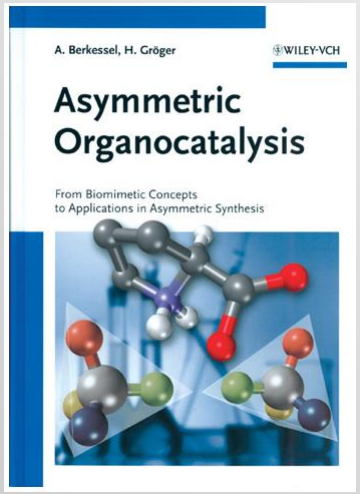
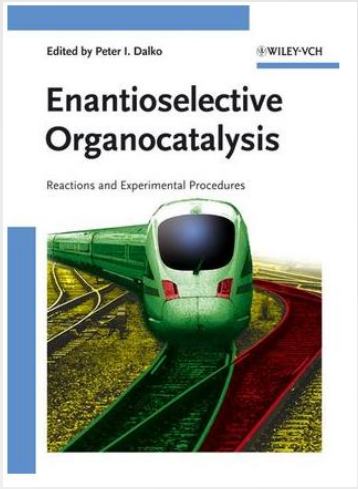
ΟΡΓΑΝΙΚΗ ΣΥΝΘΕΤΙΚΗ ΧΗΜΕΙΑ

ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ





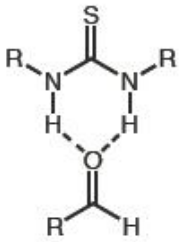
Δρ. Χριστόφορος Γ. Κόκοτος

ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

Hydrogen-Bonding Catalysis

H-bond catalysis



~30 new reactions

Jacobsen–Akiyama

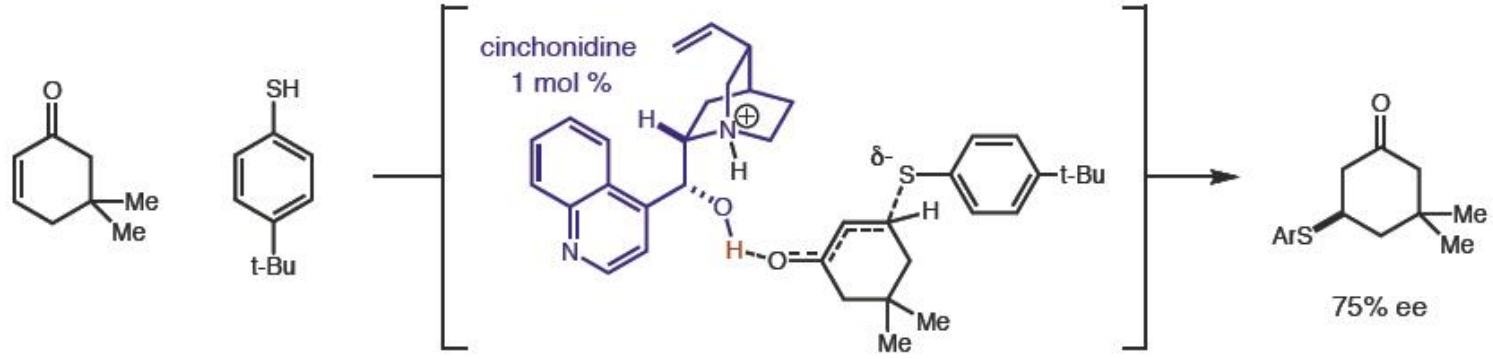
J. Am. Chem. Soc. **1981**, *103*, 417–430

Addition of Aromatic Thiols to Conjugated Cycloalkenones, Catalyzed by Chiral β-Hydroxy Amines. A Mechanistic Study on Homogeneous Catalytic Asymmetric Synthesis[1]

Henk Hiemstra and Hans Wynberg*

Contribution from the Laboratory of Organic Chemistry, The University of Groningen, Nijenborgh 16, 9747 AG Groningen, The Netherlands. *Received February 25, 1980*

■ Early examples using cinchonia alkaloidsas H-bonding catalysts



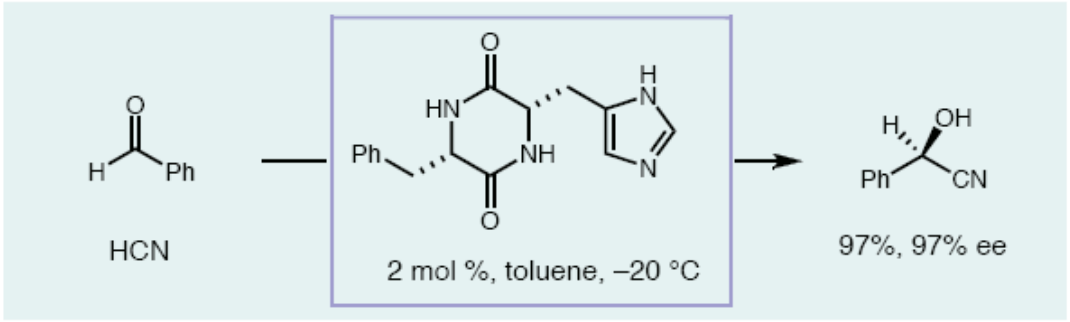
Doyle, A. G.; Jacobsen, E. N. *Chem. Rev.* **2007**, *107*, 5713. Hiemstra, H.; Wynberg, H. *J. Am. Chem. Soc.* **1981**, *103*, 417.

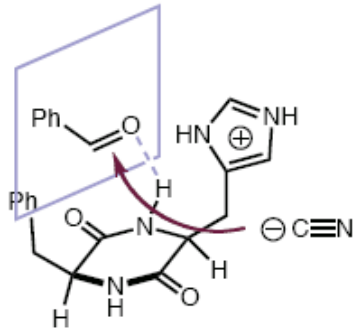
ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

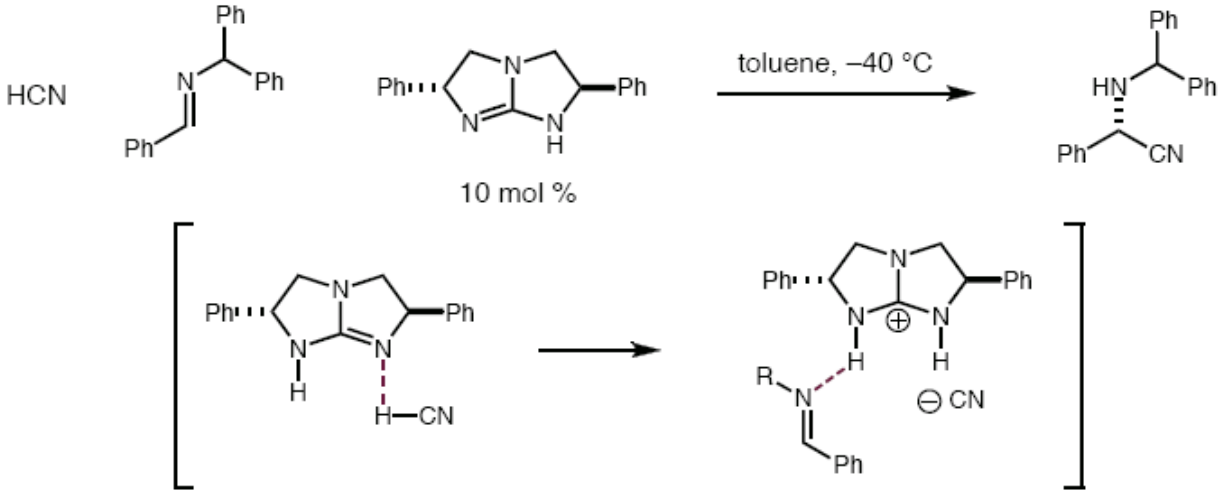
Early Examples of Hydrogen Bonding Catalysis

■ A small dipeptide was designed by Inoue to mimic oxynitrilase





■ Asymmetric Strecker reaction using Corey's guanidine H-bonding catalyst



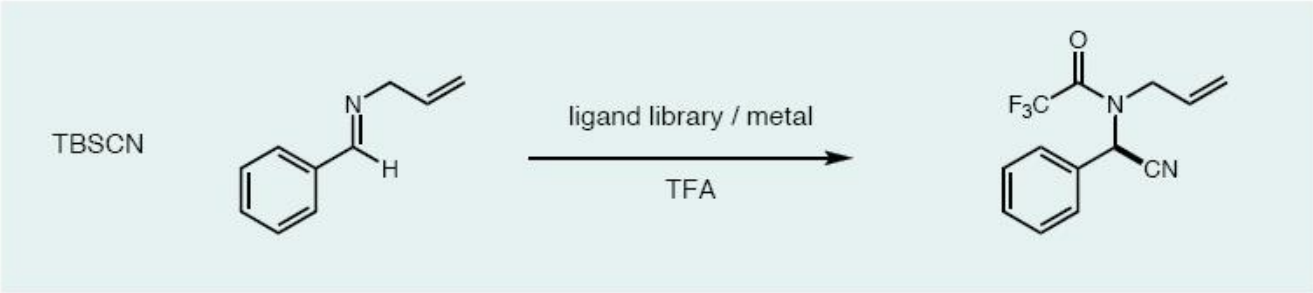
Tanaka, K.; Mori, A.; Inoue, S. *J. Org. Chem.* **1990**, *55*, 181. Grogan, M. J.; Corey, E. J. *Org. Lett.* **1999**, *1*, 157.

ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

Discovery of Acid Mediated Strecker Reactions – Jacobsen Thioureas

- Parallel synthetic ligand libraries were evaluated with various metals



Schiff Base Catalysts for the Asymmetric Strecker Reaction Identified and Optimized from Parallel Synthetic Libraries

Matthew S. Sigman and Eric N. Jacobsen*

Department of Chemistry and Chemical Biology
Harvard University, Cambridge, Massachusetts 02138

Received January 13, 1998

Sigman, M. S.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1998**, *120*, 4901.

ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

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Discovery of Acid Mediated Strecker Reactions – Jacobsen Thioureas

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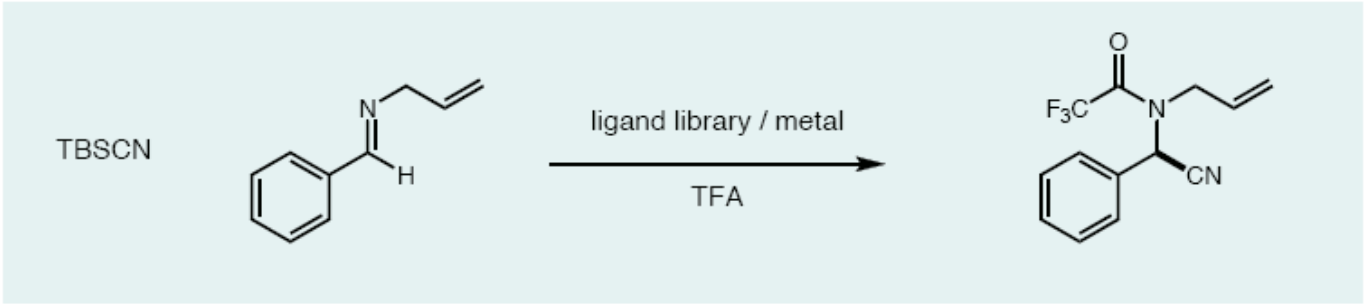
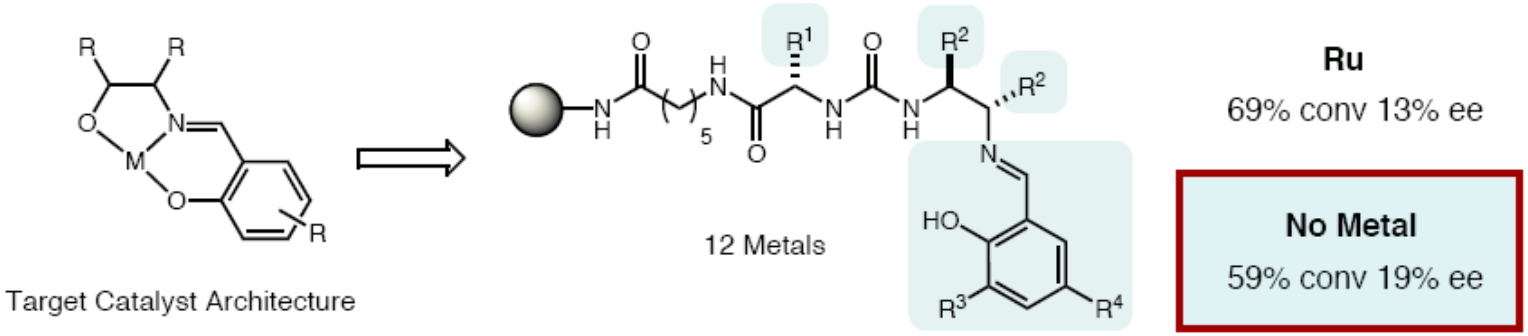


■ Modifed Schiff bases were prepared in a combinatorial fashion on a solid support



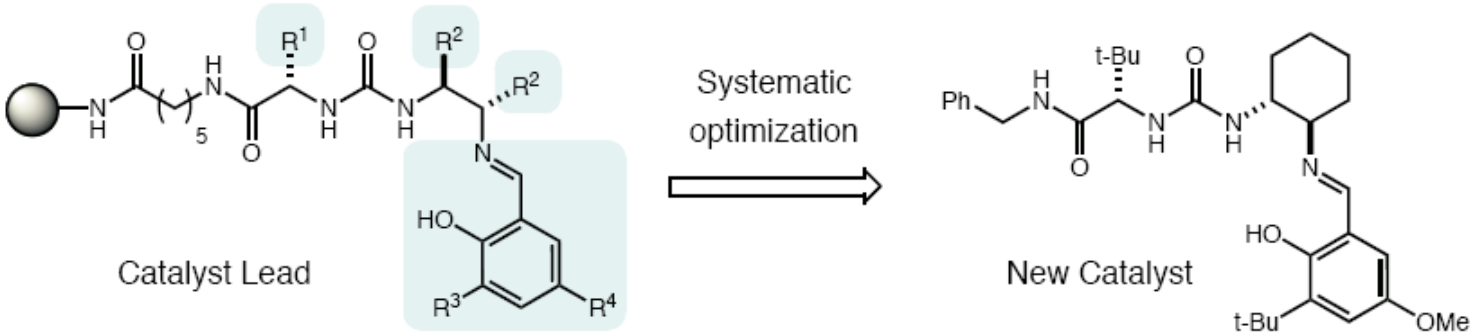
Sigman, M. S.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1998**, *120*, 4901.

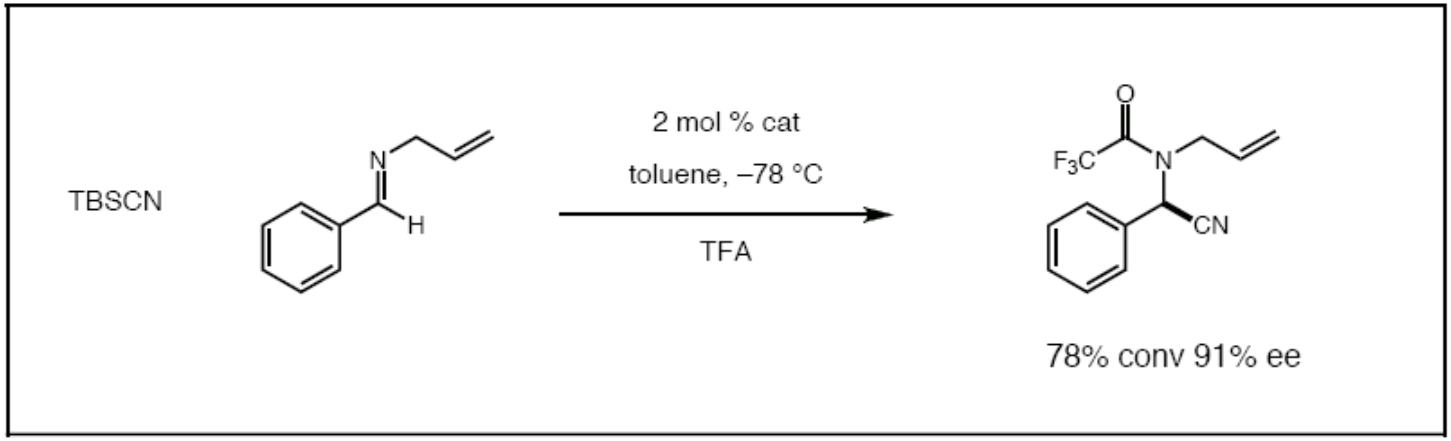
ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

Discovery of Acid Mediated Strecker Reactions – Jacobsen Thioureas

■ The structure was quickly optimized to provide an efficient Strecker catalyst



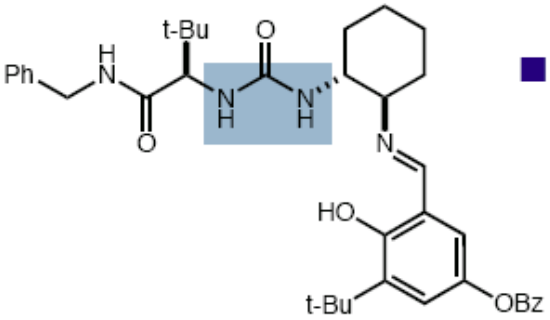


Sigman, M. S.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1998**, *120*, 4901.

ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

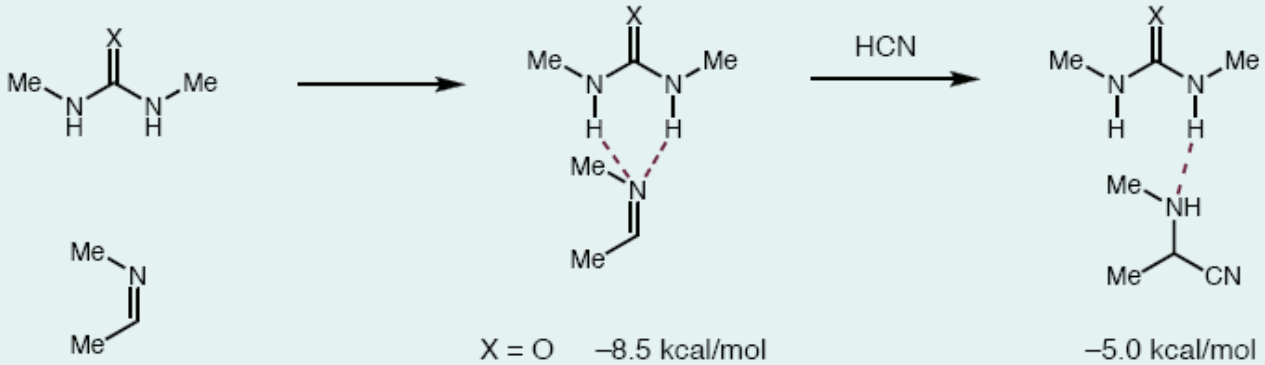
ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

How Do These New Catalysts Function?



- Knock-out studies show that the urea functional group is essential
- Hydrogen bonding established as the activation mode
- Weaker product binding enables turnover

DFT and NMR Studies:



X = O –8.5 kcal/mol –5.0 kcal/mol

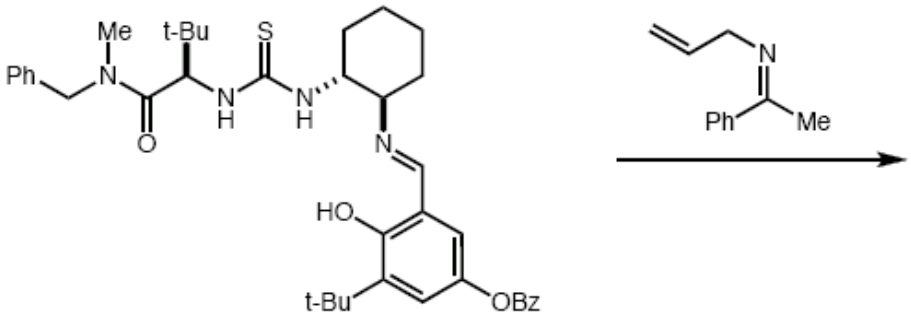
X = S –10 kcal/mol –6.3 kcal/mol

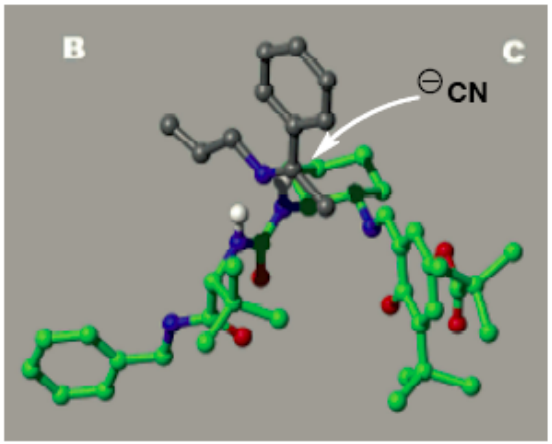
Vachal, P.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *120*, 10012.

ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

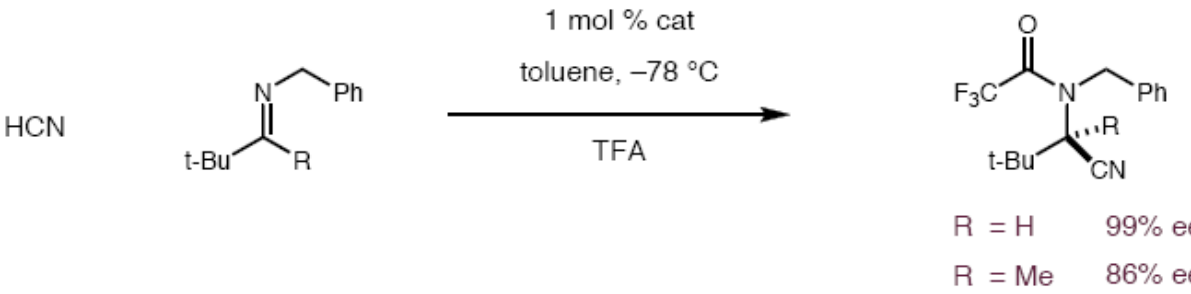
Urea Stereochemical Model





■ With a better understanding of how these catalysts work new reaction methods can be developed

Strecker reaction with aldimine or ketoimine



R = H 99% ee

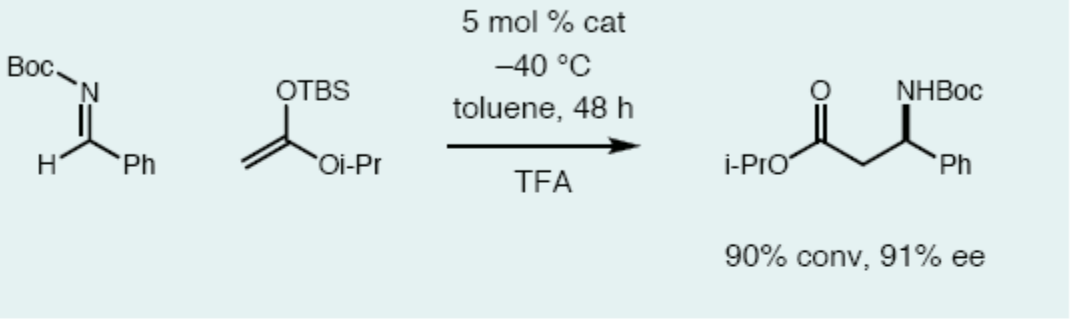
R = Me 86% ee

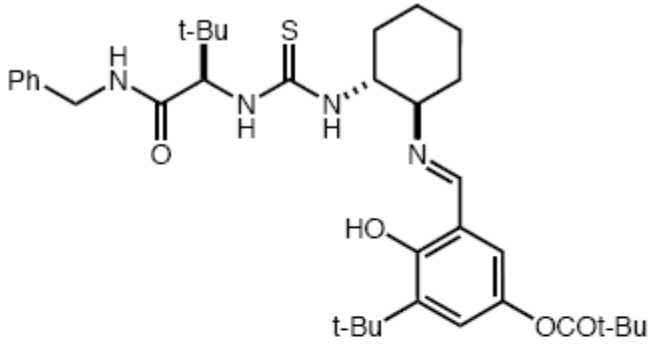
Vachal, P.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *120*, 10012.

ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

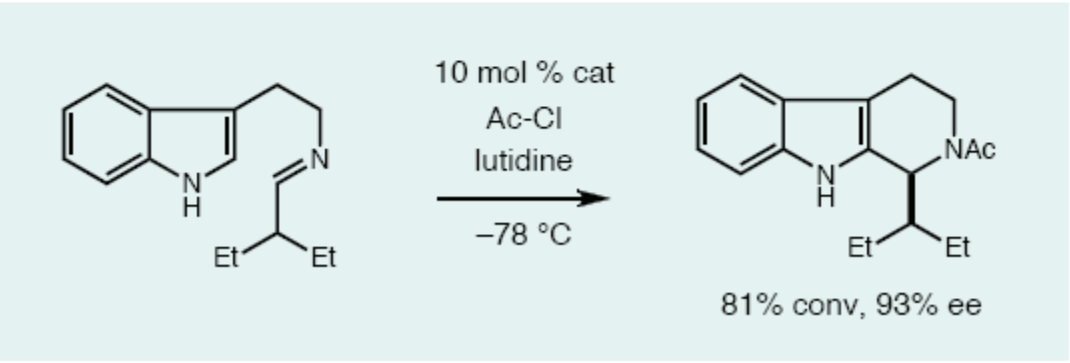
■ Enantioselective Mannich Reaction

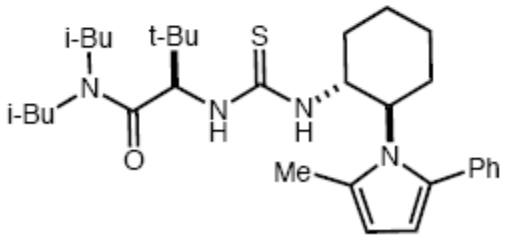




Wenzel, A. G.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 12964.

■ Enantioselective Acyl Pictet–Spengler Reaction





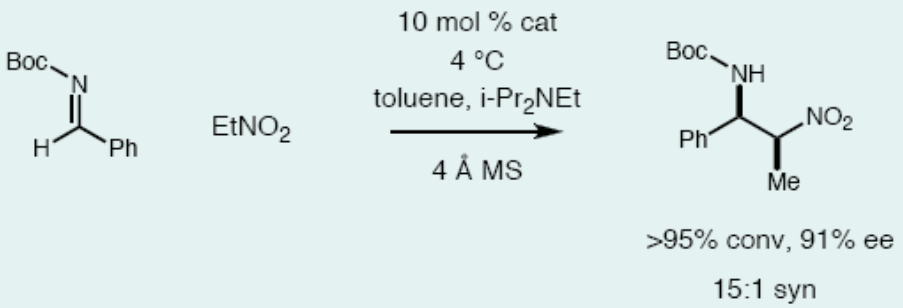
Taylor, M. S.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2004**, *126*, 10558.

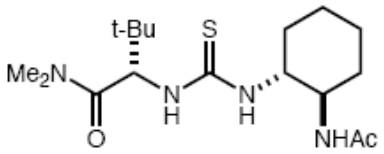
ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

Urea Catalyzed Reactions

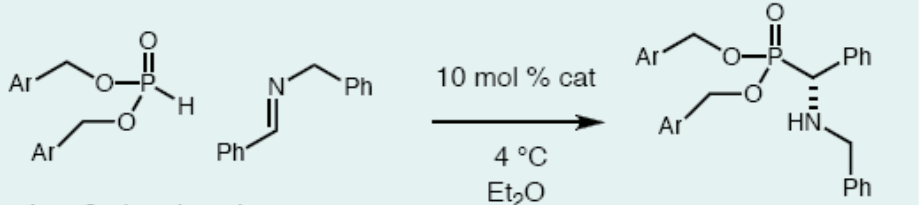
■ Enantioselective Aza-Henry Reaction

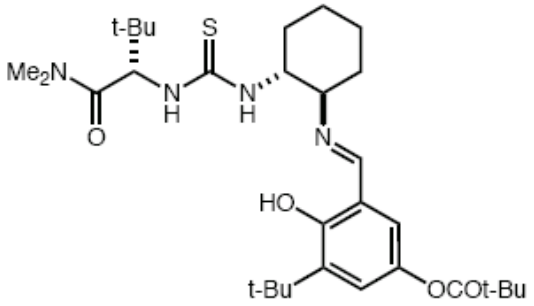




Yoon, T.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2005**, *124*, 466.

■ Enantioselective Hydrophosphorylation



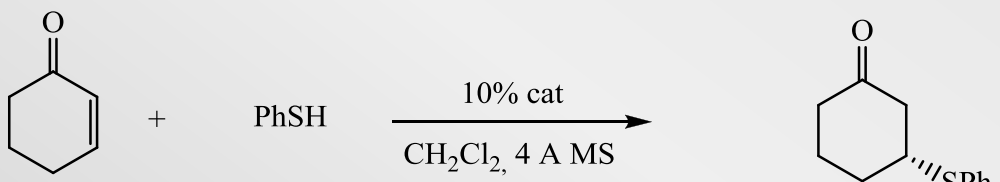


Joly, G. D.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2004**, *126*, 4102.

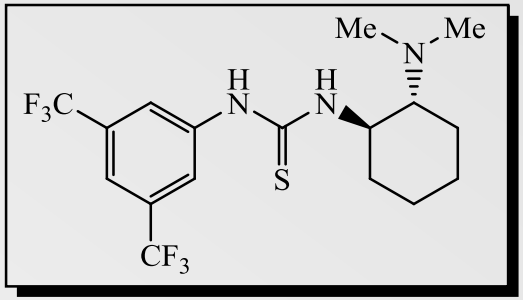
ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

- **Συζυγής προσθήκη θειολών σε α,β-ακόρεστες καρβονυλικές ενώσεις**

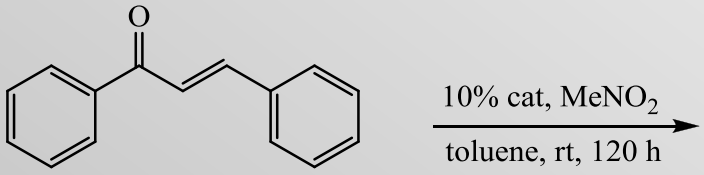


97 yield, 85% ee

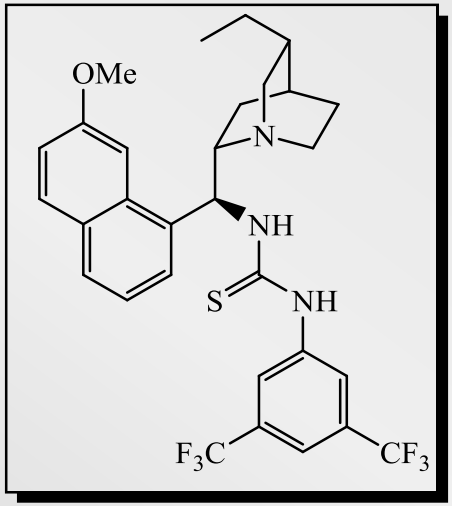


Chen et al, Synlett, **2005**, 603

- **Συζυγής προσθήκη νιτροαλκανίων**



94% yield, 96% ee

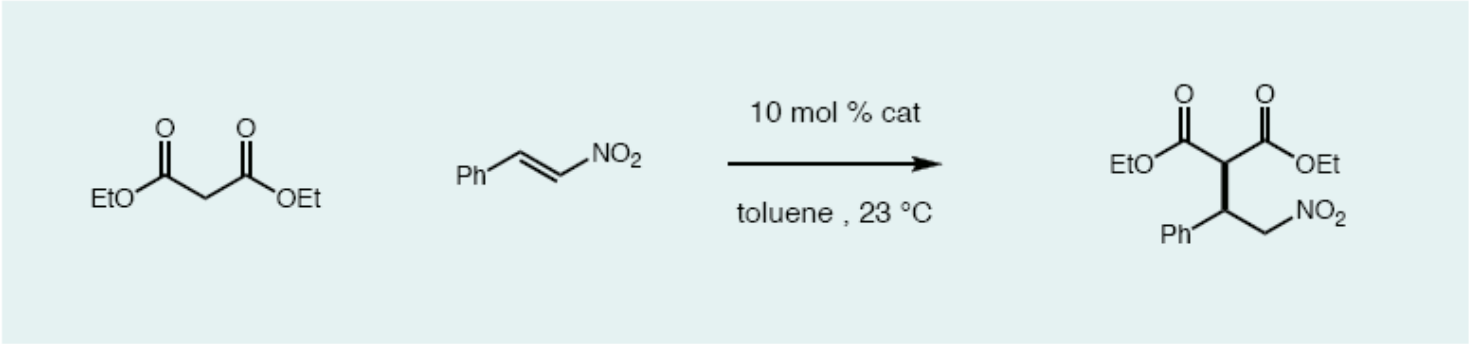


Soos et al, Org. Lett., **2005**, *7*, 1967

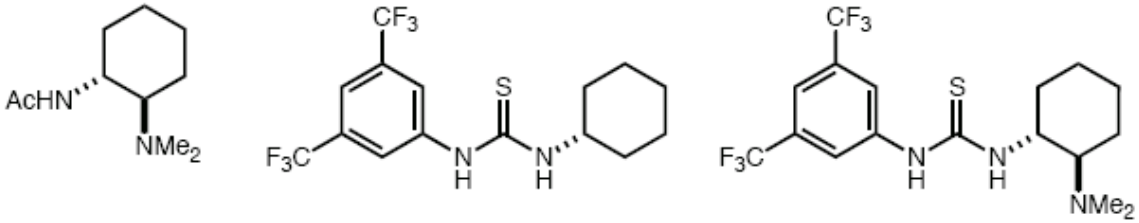
ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

■ Enantioselective Michael Addition



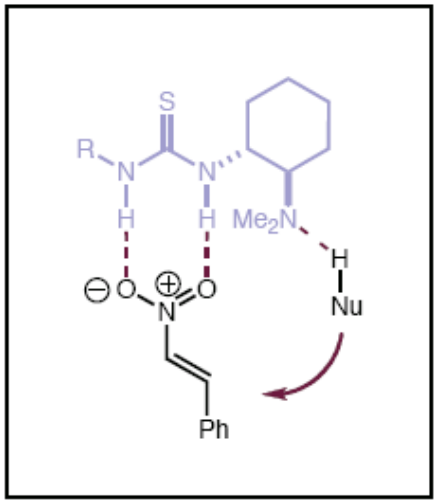
■ Both thiourea and tertiary amine are needed



14%, 35% ee

57%, 0% ee

86%, 93% ee

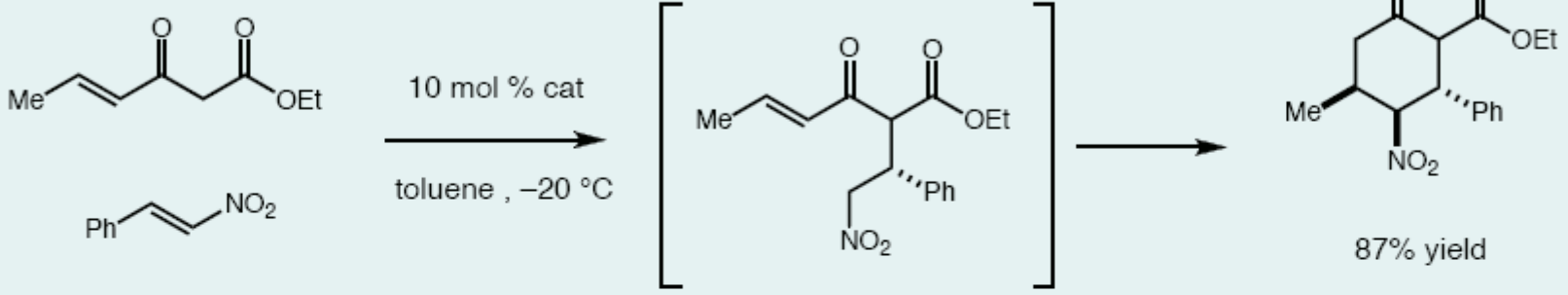


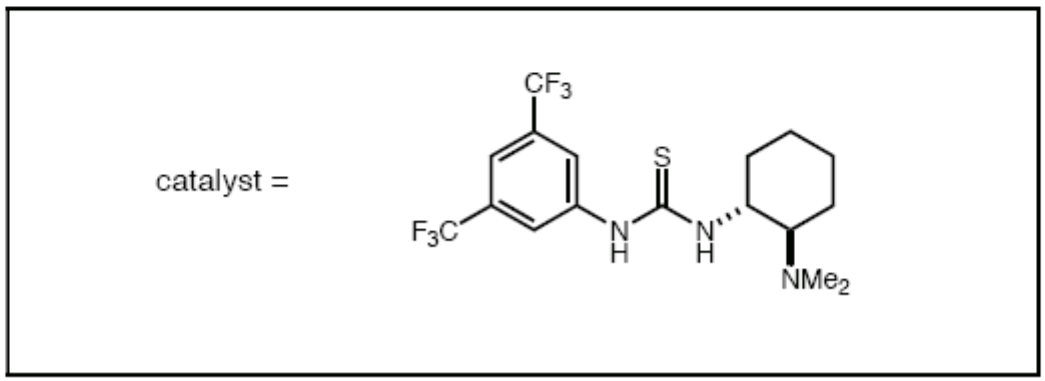
Okino, T.; Hoashi, Y.; Takemoto, Y. *J. Am. Chem. Soc.* **2003**, *128*, 12672.

ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

■ Enantioselective Double Michael Addition



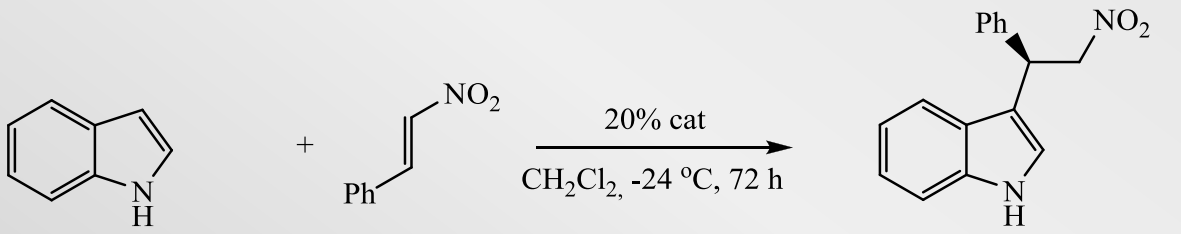


Hoashi, Y.; Yabuta, T.; Takemoto, Y. *Tettrahdron Lett.* **2003**, *45*, 9185.

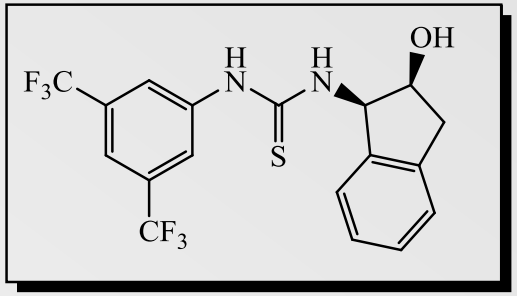
ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

- **Προσθήκη ινδολίων σε νιτροαλκένια**

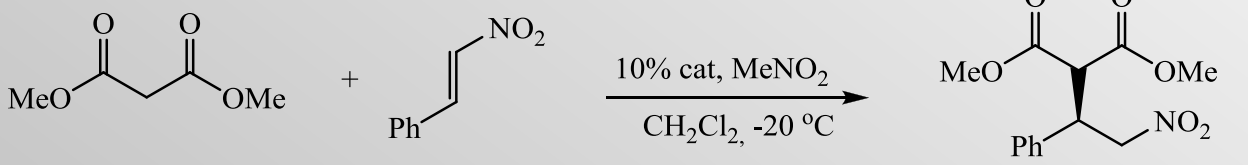


78 yield, 85% ee

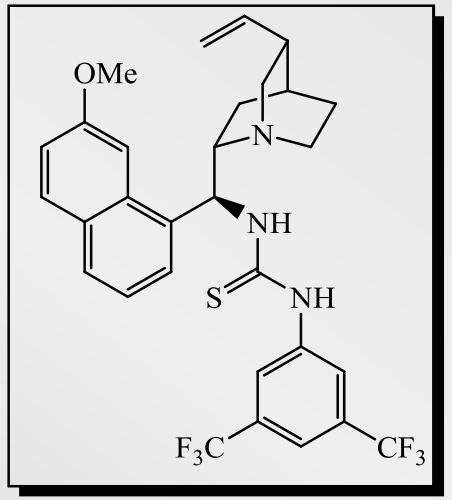


Ricci et al, Angew. Chem. Int. Ed., **2005**, *44*, 6576

- **Προσθήκη δικαρβονυλικών ενώσεων σε νιτροαλκένια**



95% yield, 94% ee

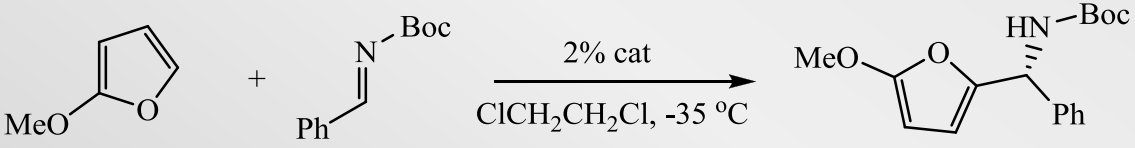


Dixon et al, Chem. Commun., **2005**, 4481

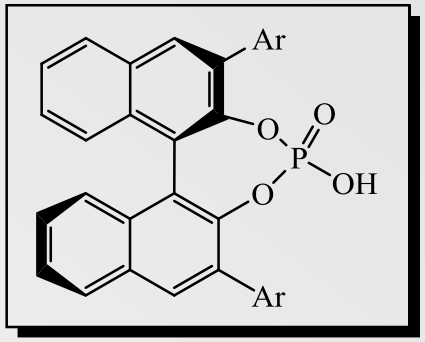
ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

- **Aza-Friedel-Crafts σε αλδιμίνες**

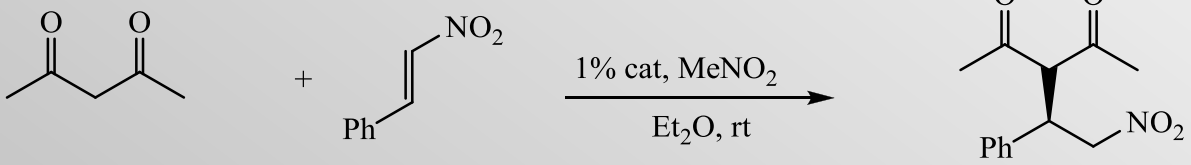


95% yield, 97% ee

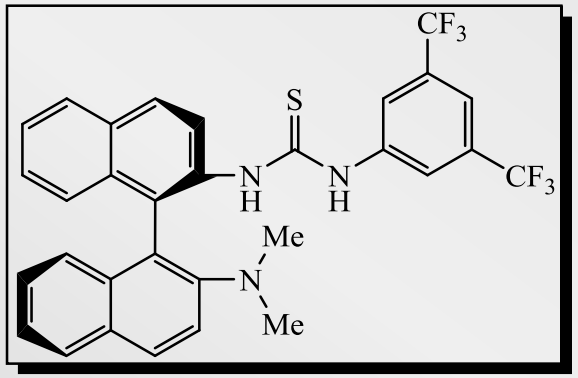


Terada et al, J. Am. Chem. Soc., **2004**, *126*, 11804

- **Προσθήκη δικαρβονυλικών ενώσεων σε νιτροαλκένια**



87 yield, 55% ee



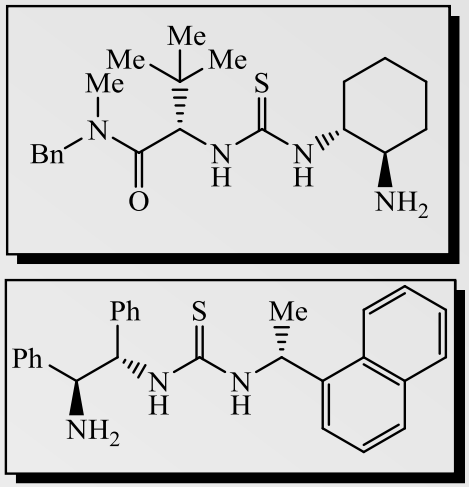
Wang et al, Org. Lett., **2005**, *7*, 4713

ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

■ **Αντίδραση Michael ακετόνης με νιτροαλκένια**

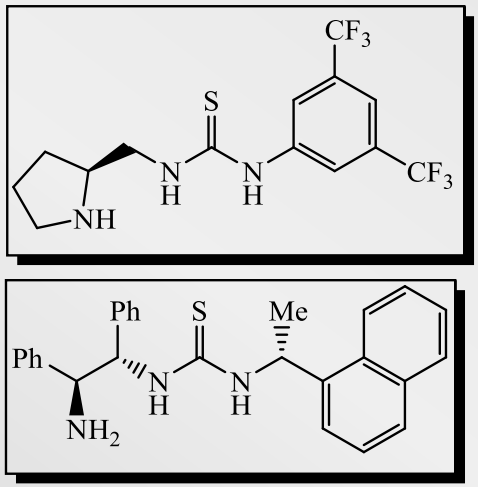
Jacobsen: 93% yield, 99% ee
Tsogoeva: 100% yield, 91% ee



Jacobsen et al, J. Am. Chem. Soc., **2006**, *128*, 7170
Tsogoeva et al, Chem. Commun., **2006**, 1451

■ **Αντίδραση Michael κυκλοεξανόνης με νιτροαλκένια**

Tang: 93% yield, 96:4 dr, 90% ee
Tsogoeva: 82% yield, 80:20 dr, 96% ee

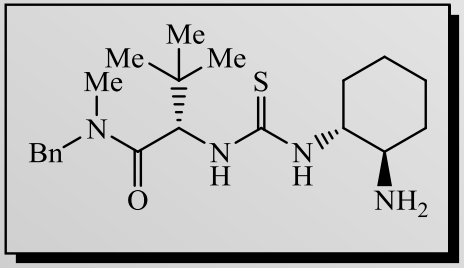


Tang et al, Org. Lett., **2006**, *8*, 2559
Tsogoeva et al, Chem. Commun., **2006**, 1451

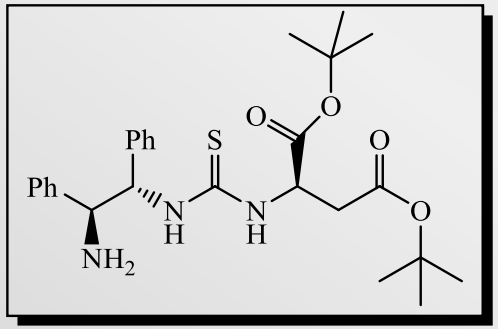
ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

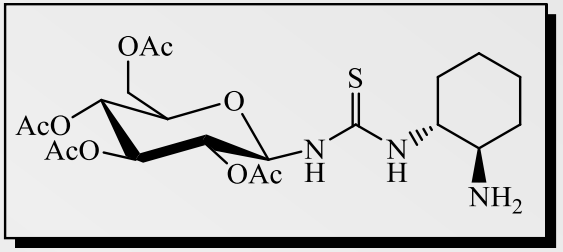
«Δύσκολη» αντίδραση Michael ακετοφαινόνης με νιτροαλκένια



83% yield, 99% ee



68-98 % yield, 95-99% ee



65% yield, 98% ee

Jacobsen et al, J. Am. Chem. Soc., **2006**, *128*, 7170

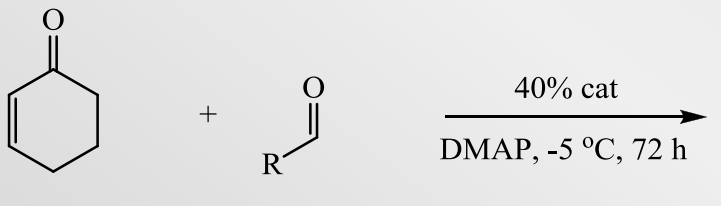
Ma et al, Org. Lett., **2007**, *9*, 923

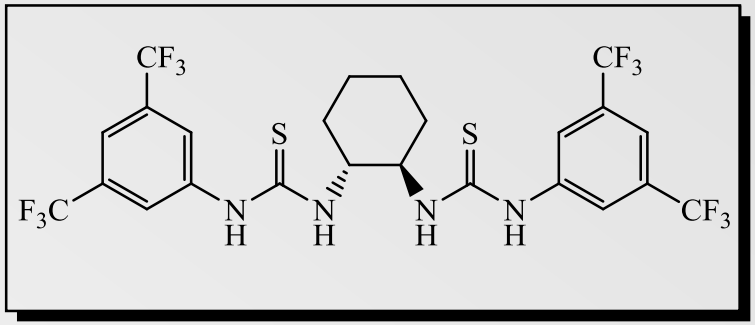
Kokotos et al, Adv. Synth. Catal., **2009**, *351*, 1355

ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

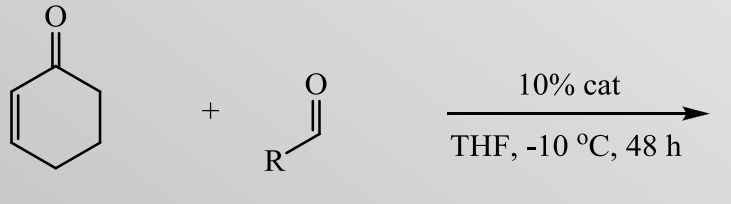
- **Αντίδραση Morita Baylis-Hillman**

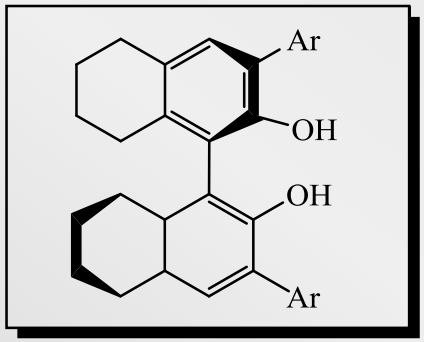




63-99% yield, 33-90% ee

Nagasawa et al, Tetrahedron Lett., **2004**, *45*, 5589





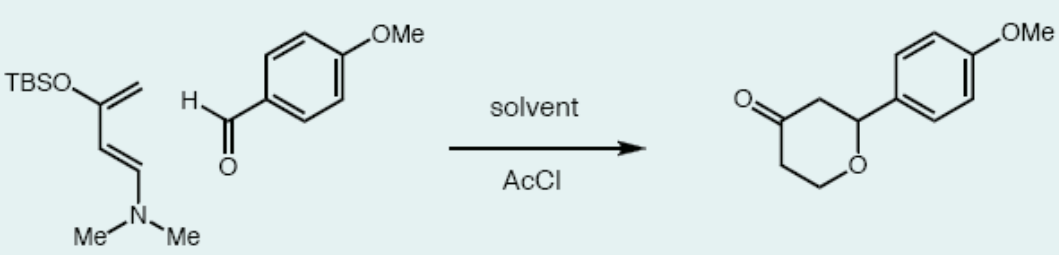
40-88% yield, 67-96% ee

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

ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

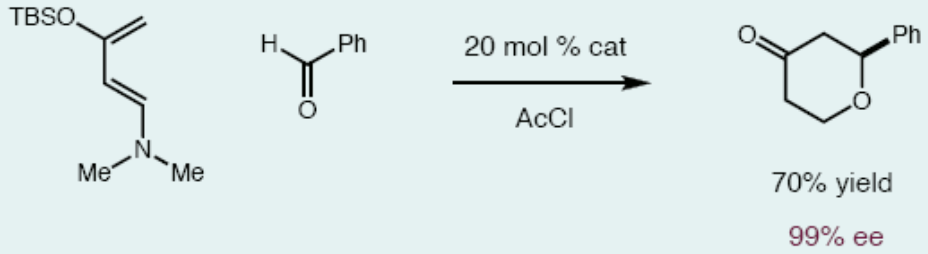
Rawal's Discovery of H-Bonding Catalyzed Diels–Alder

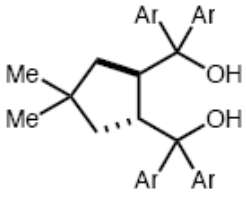


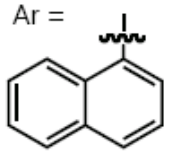
solvent	k_{rel}
THF	1
Benzene	1.3
t-BuOH	280
i-PrOH	630

Huang, Y.; Rawal, V. H. *J. Am. Chem. Soc.* **2002**, *124*, 9662.

- Observed that the hetero Diels–Alder reaction is accelerated in alcohol solvent
- This observation was turned into an asymmetric reaction using a chiral H-donor catalyst







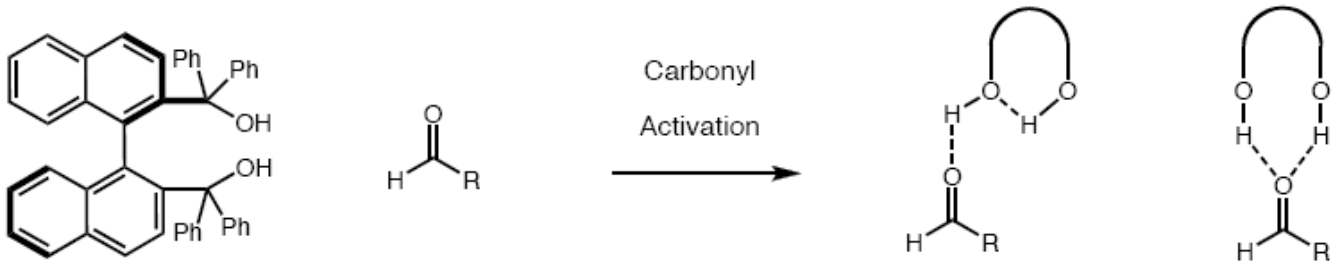
Huang, Y.; Unni, A. K.; Thadani, A. N.; Rawal, V. H. *Nature* **2003**, *424*, 146.

ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

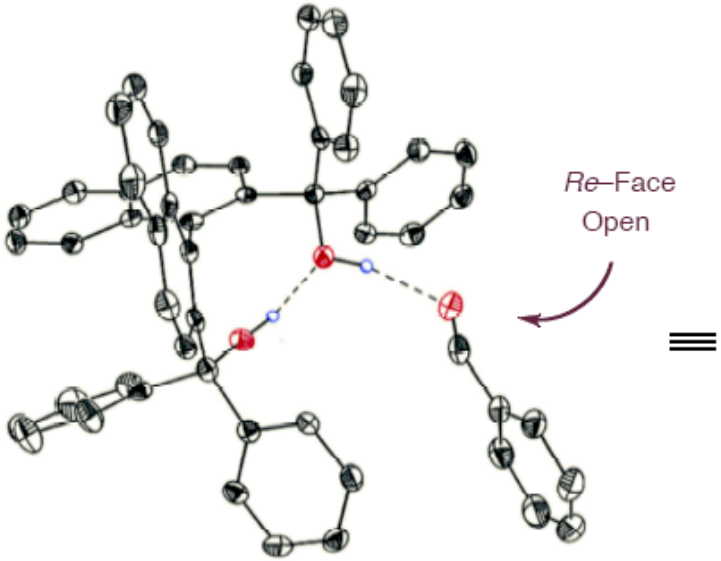
ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

Mechanism of Rawal's H-Bonding Diels–Alder Reaction

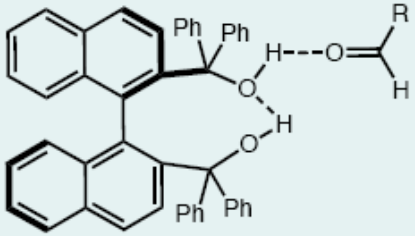
■ Is single or double point activation in operation?



Single or Double–point activation



≡



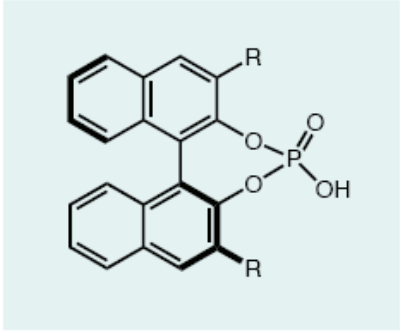
Single–Point Activation

Unni, A. K.; Takenaka, N.; Yamamoto, H.; Rawal, V. H. *J. Am. Chem. Soc.* **2005**, *127*, 1336.

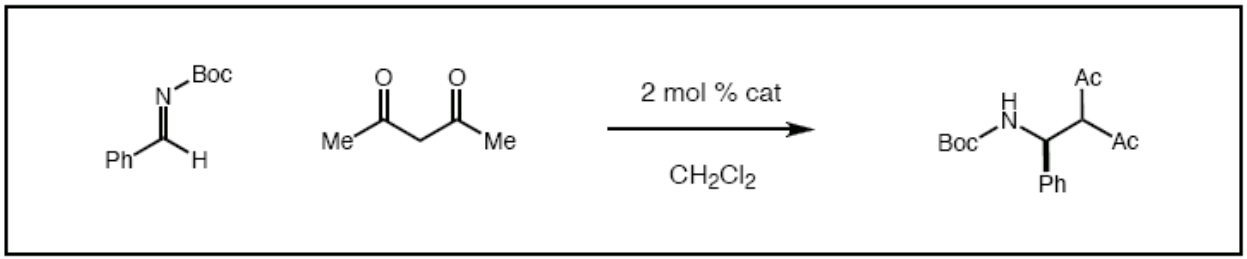
ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

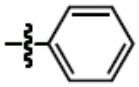
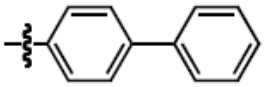
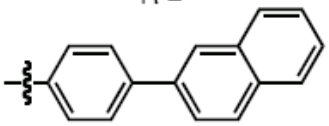
ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

Chiral Phosphoric Acids



- Long used for chiral resolutions
- Used as a ligand for Lewis acid catalysis
- 2004 Terada and Akiyama use as Brønsted acid catalyst
- Size of R group very important for enantioselectivity



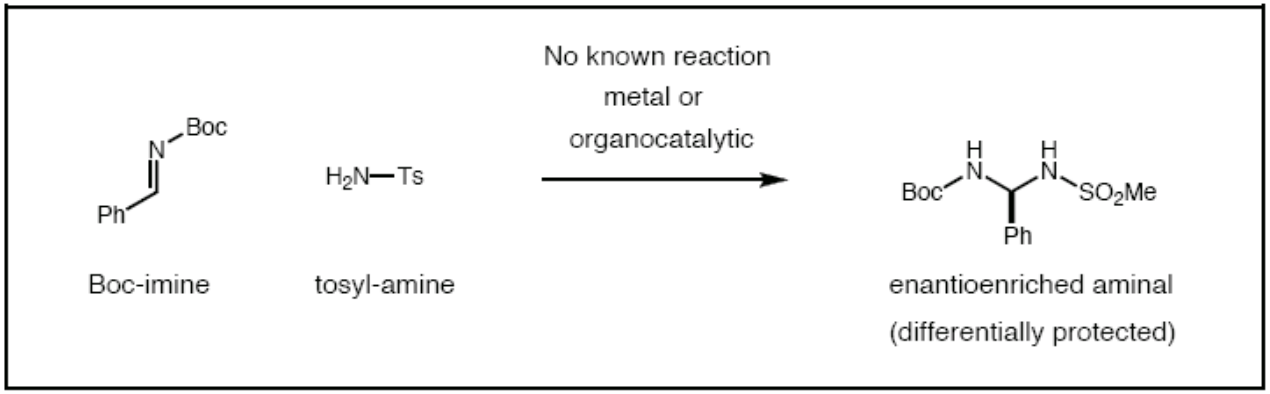
R =	R =	R =	R =
H			
92% yield 12% ee	95% yield 56% ee	88% yield 90% ee	99% yield 95% ee

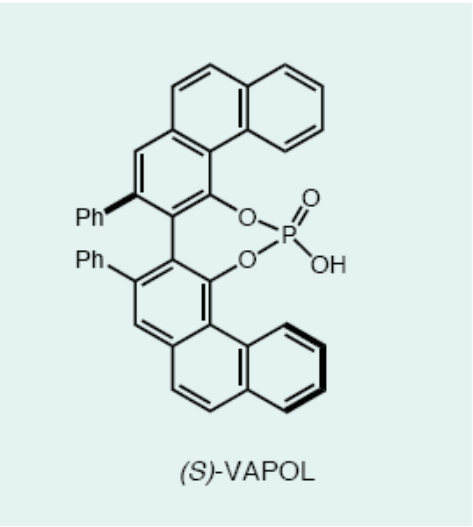
Akiyama, T.; Itoh, K.; Yokota, K.; Fuchibe, K. *Angew Chem. Int. Ed.* **2004**, *43*, 1566.
Uraguchi, D.; Terada, M. *J. Am. Chem. Soc.* **2004**, *126*, 5356.

ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

New Reactivity – Imine Amination





5 mol % cat

Et_2O, 1 h, 21 °C

86% yield

93% ee

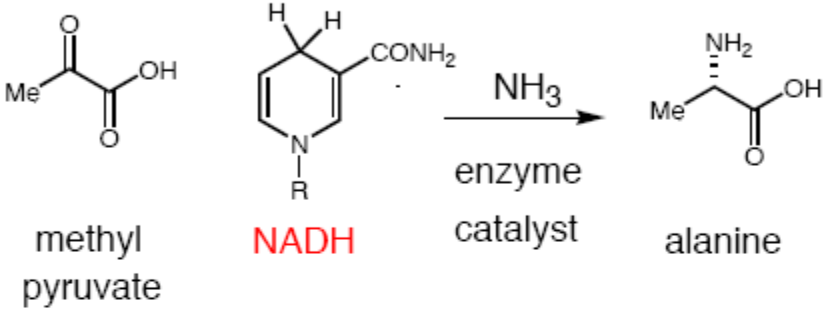
Rowlan, G. B.; Zang, H.; Rowland, E. B.; Chennamadhavuni, S.; Wang, Y.; Antilla, J. C. *J. Am. Chem. Soc.* **2005**, *127*, 15696.

ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

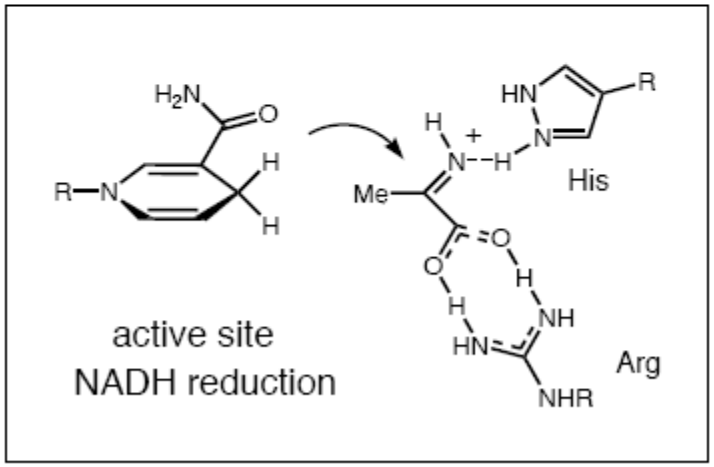
Organic Catalyzed Reductions in Biological Systems

■ NADH: Natures Reduction (Hydrogenation) Reagent (Coenzyme)



methyl pyruvate — NADH — alanine

alanine transferase



active site NADH reduction

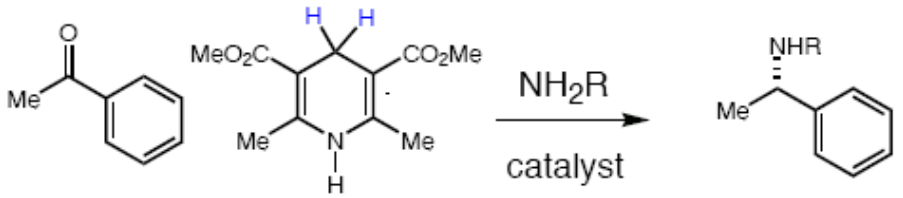
Selective reduction of pyruvate imines to create amino acids

ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

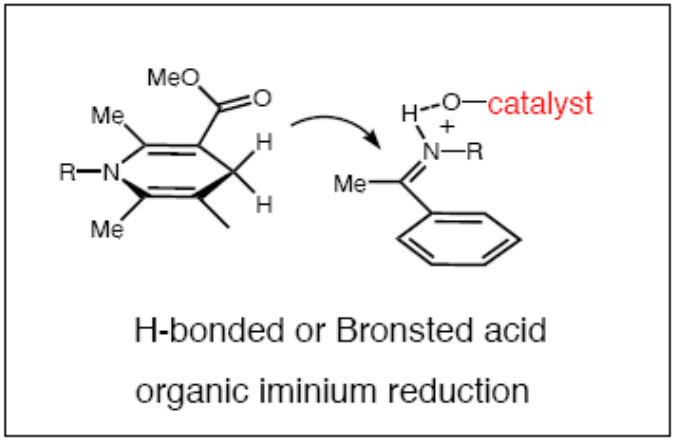
ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

Organic Catalyzed Reductions in Laboratory Systems

■ Hantzsch ester as a useful surrogate for NADH reductions in the lab

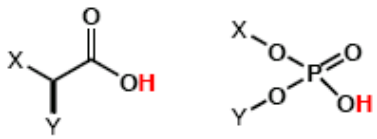


acetophenone NADH analog phenylethyl amine



H-bonded or Bronsted acid organic iminium reduction

catalyst



simple carboxylic or phosphonic acids

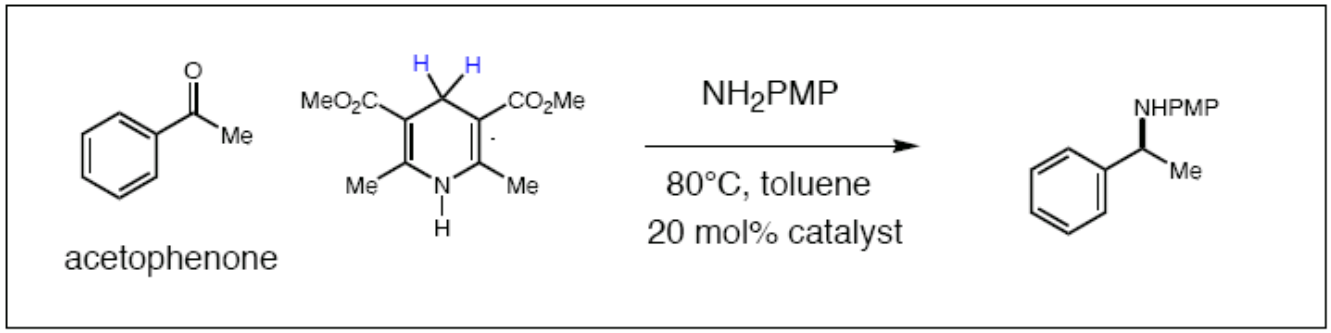
Can we translate a biochemical concept to a laboratory reaction

Can we develop a useful transformation on the basis of established Bronsted acid catalysts

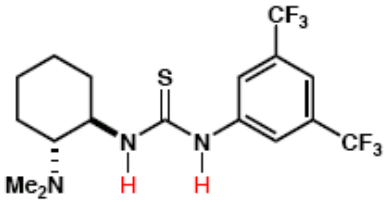
ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

Organocatalysis and the advent of Bronsted Acid/H-bonded catalysis

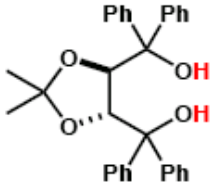


■ Pioneers



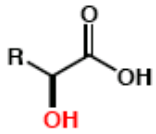
Jacobsen

No reaction



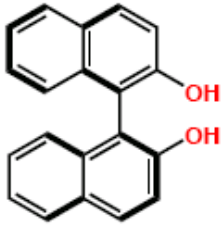
Rawal

No reaction



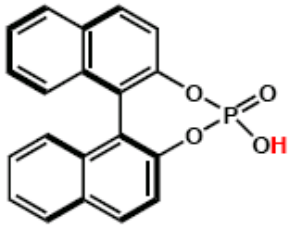
Yamamoto

No reaction



Schaus

No reaction



Akiyama, Terada

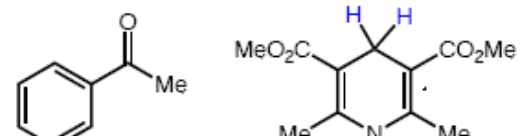
43% yield

7%ee

ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

Attempts to develop a Bronsted Acid Catalyst for Reductive Amination

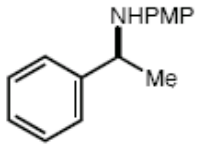


acetophenone

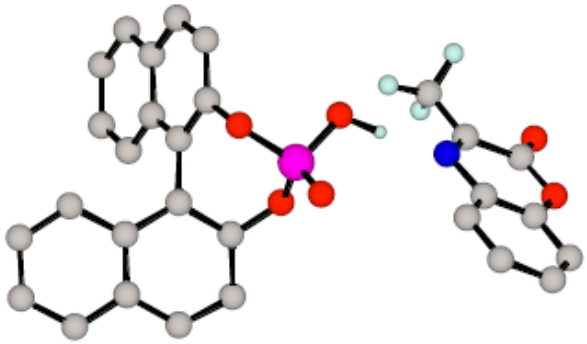
NH_2PMP

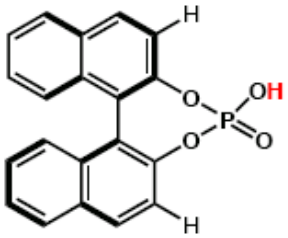
80°C, toluene

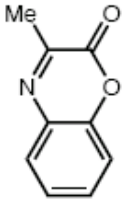
20 mol% catalyst

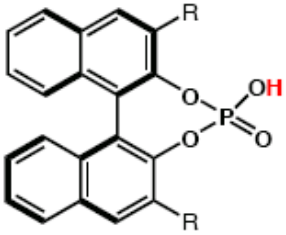


7% ee









R	Yield	%ee
H	43	7
$Ph(NO_2)_2$	45	16
$Ph(CF_3)_2$	39	65
2-Nap	56	40
Ph_3Si	90	85

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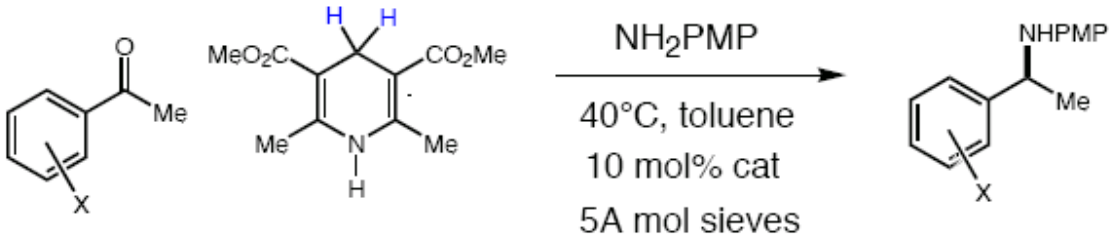
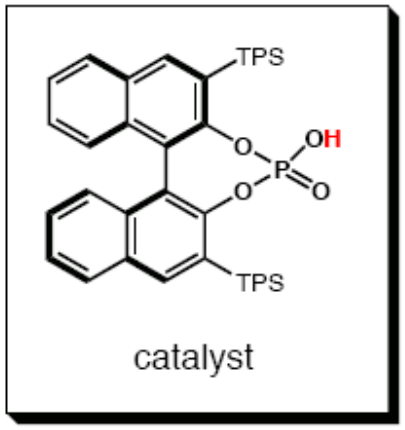
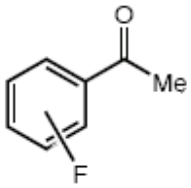
The scope of the reductive amination with respect to aryl ketones

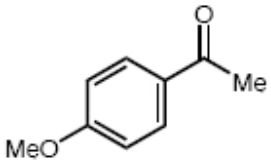




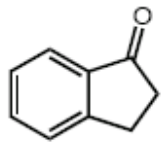
■ Scope of the ketone component



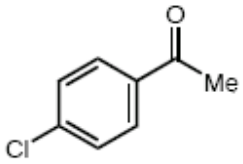
(o) 83% ee
(m) 95% ee
(p) 94% ee
60-85% yield



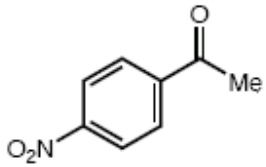
90% ee
77% yield



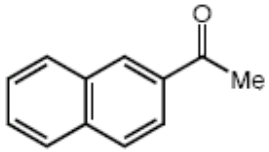
85% ee
75% yield



95% ee
75% yield



95% ee
71% yield



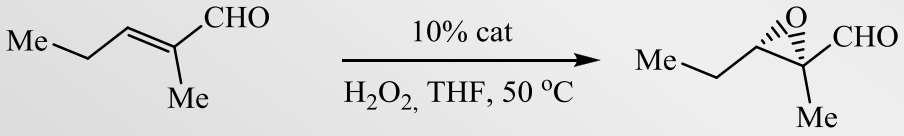
96% ee
73% yield

■ Are there other systems that are successful in this transformation?

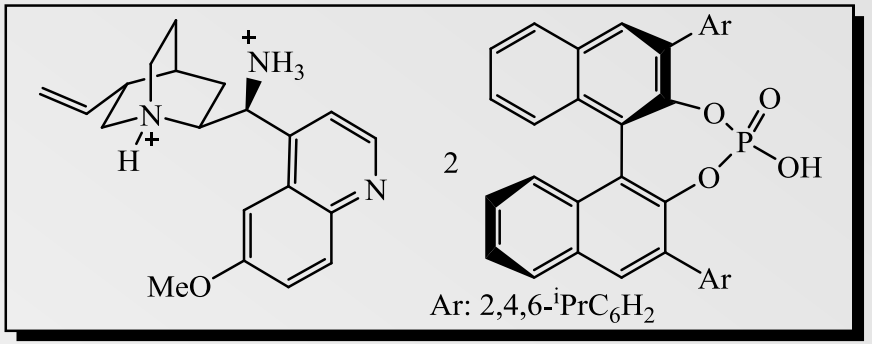
ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

- **Εποξείδωση τρι-υποκατεστημένων α,β-ακόρεστων αλδεϋδών**

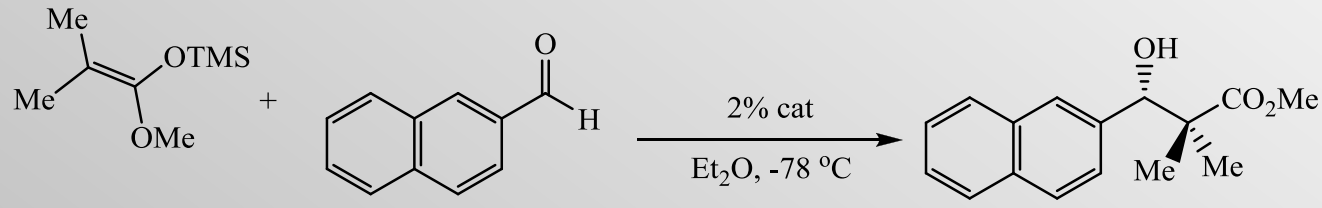


100% conversion, 92:8 de, 97% ee

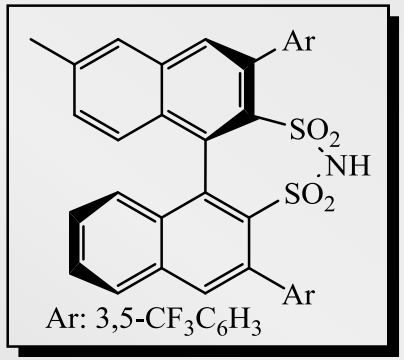


List et al, J. Am. Chem. Soc., **2010**, *132*, 10227

- **Τύπου Mukaiyama αλδολική αντίδραση**



98 yield, 94% ee



List et al, Angew. Chem. Int. Ed., **2009**, *48*, 4363

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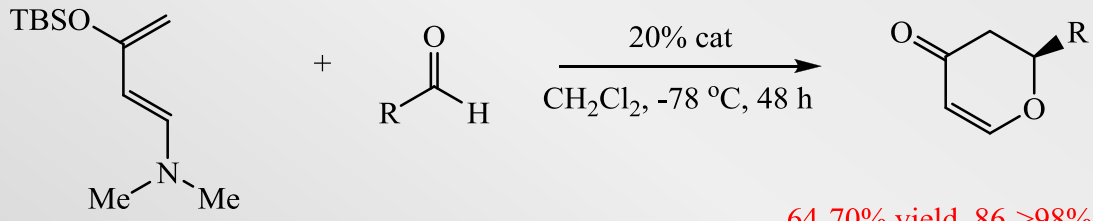
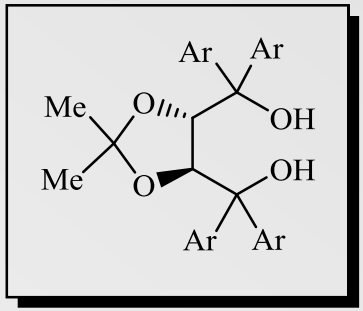
ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

- **Αντίδραση Diels-Alder**

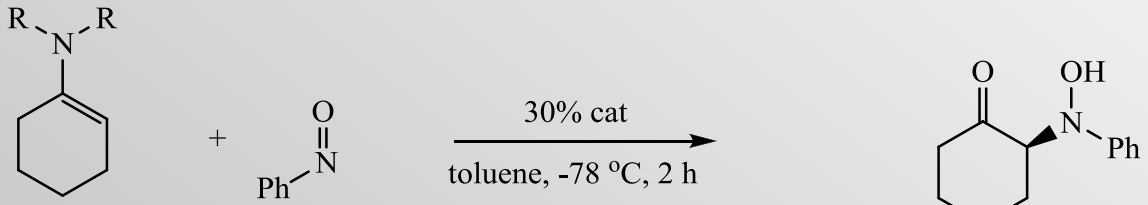


64-70% yield, 86->98% ee

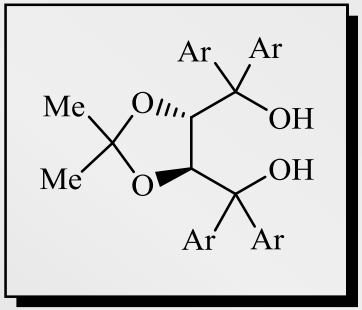


Ding et al, Chem. Eur. J., **2004**, *10*, 5964

- **Αντίδραση με νιτροσοβενζόλιο: Ν-εκλεκτικότητα και όχι Ο-εκλεκτικότητα!!!!!!**



81% yield, 83% ee

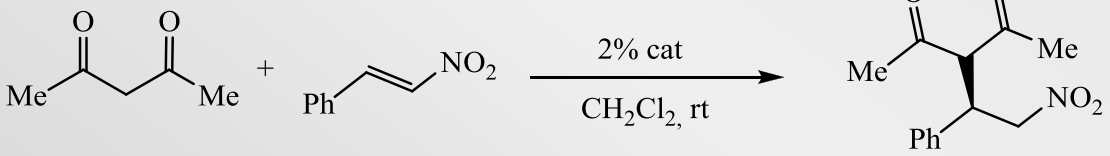


Yamamoto et al, J. Am. Chem. Soc., **2005**, *127*, 1080

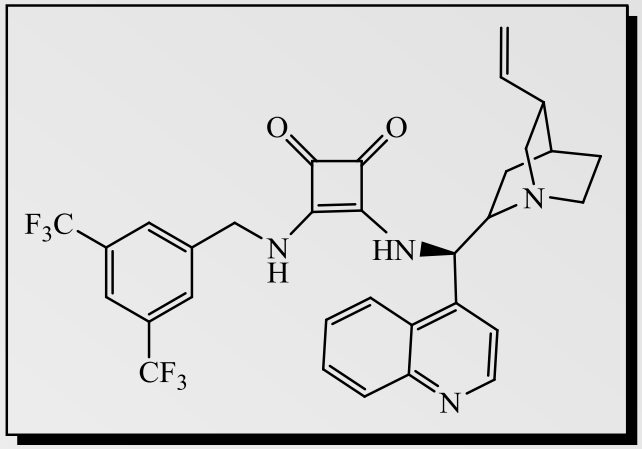
ΤΡΟΠΟΙ ΕΝΕΡΓΟΠΟΙΗΣΗΣ ΣΤΗΝ ΟΡΓΑΝΟΚΑΤΑΛΥΣΗ

ΕΝΕΡΓΟΠΟΙΗΣΗ ΜΕΣΩ ΔΕΣΜΩΝ ΥΔΡΟΓΟΝΟΥ

- **Σκουαραμίδια ως αντικαταστάτες θειουριών**

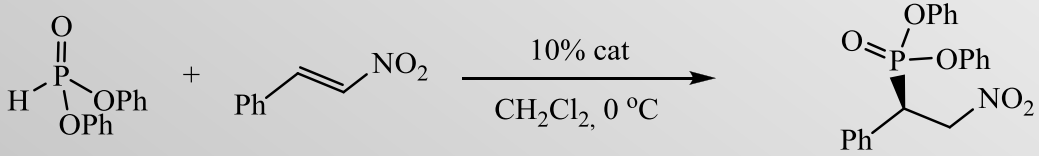


98% yield, >99% ee

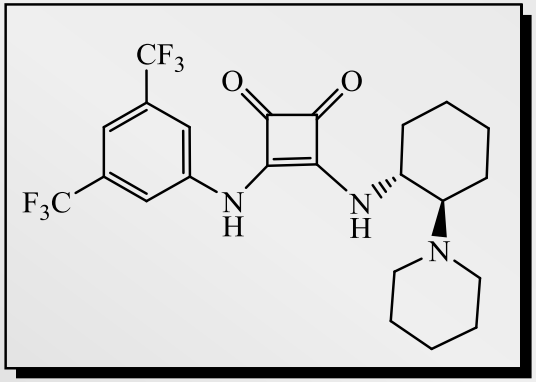


Rawal et al, J. Am. Chem. Soc., **2008**, *130*, 14416

- **Σκουαραμίδια ως αντικαταστάτες θειουριών**



95% yield, 97% ee



Rawal et al, Angew. Chem. Int. Ed., **2010**, *49*, 153