



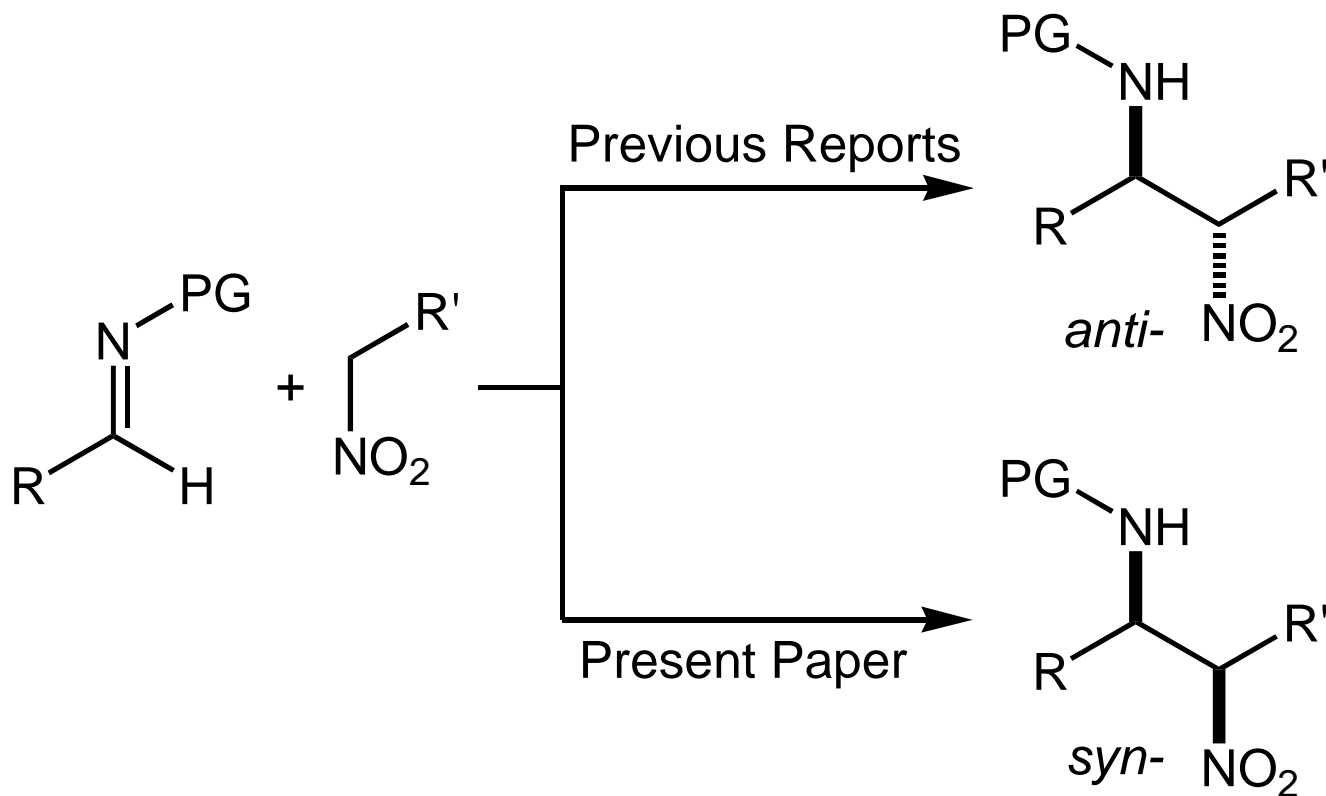
Literature Report

Heterobimetallic Cu-Sm-Schiff Base Complex Catalyzed *syn*-Selective Asymmetric *Nitro*-Mannich Reactions

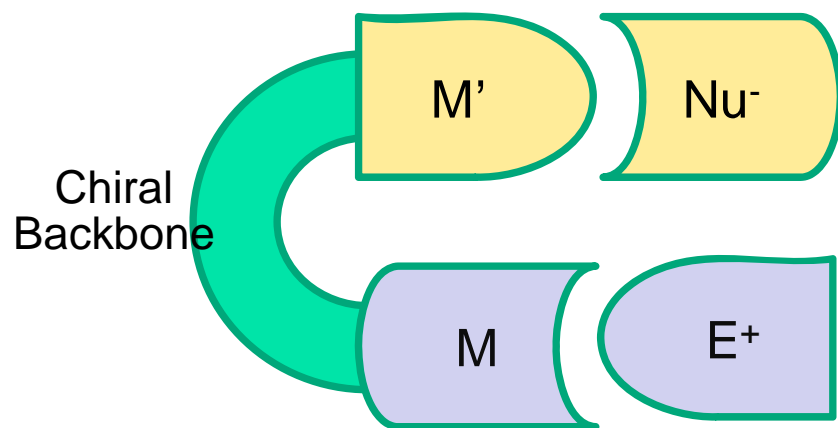
[Shibasaki, M. *et al. J. Am. Chem. Soc.* **2010**, *132*, ASAP.]

Xiao-Yu Zhou ***Checker: Duo-Sheng Wang***
13/04/2010

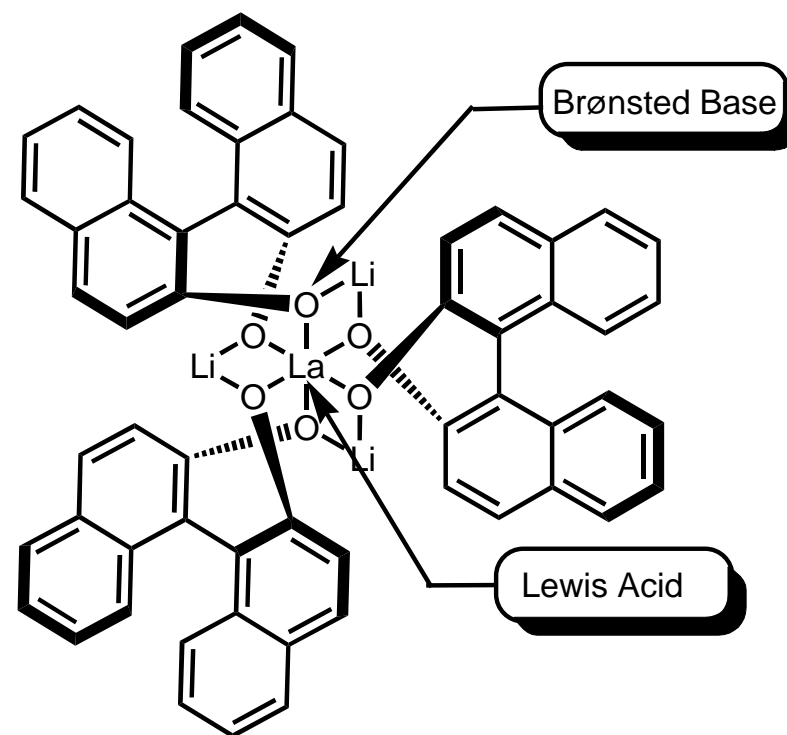
Heterobimetallic Cu-Sm-Schiff Base Complex Catalyzed *syn*-Selective Nitro-Mannich Reaction



Heterobimetallic Cu-Sm-Schiff Base Complex Catalyzed *syn*-Selective Nitro-Mannich Reaction



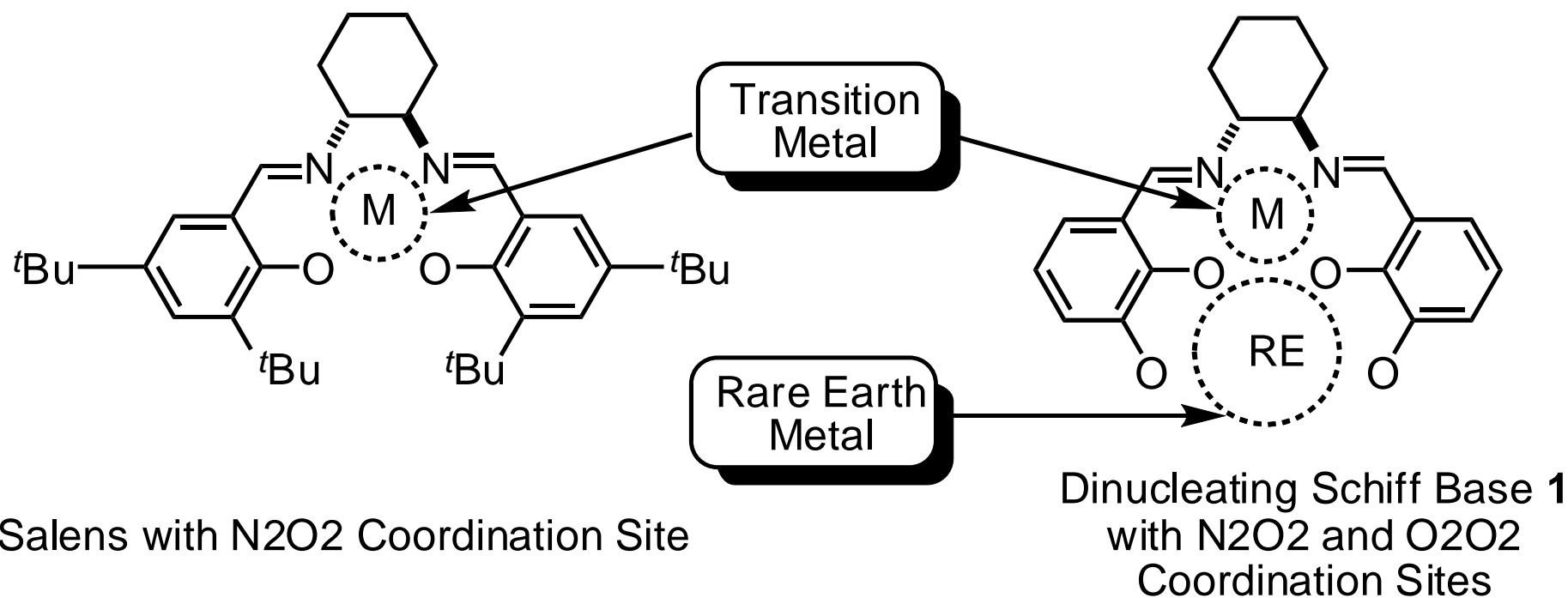
Bifunctional Chiral Catalyst



Bifunctional La/Li/BINOL Catalyst

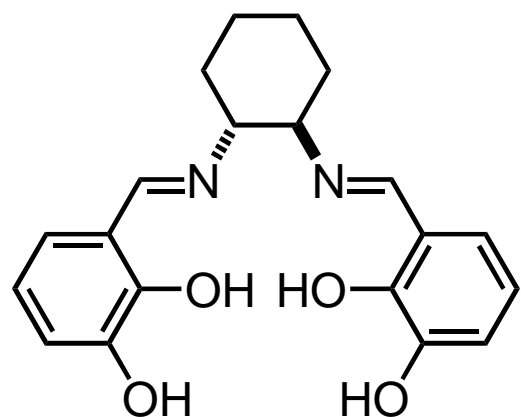
Shibasaki, M. *et al.* *J. Am. Chem. Soc.* **2010**, *132*, ASAP.

Heterobimetallic Cu-Sm-Schiff Base Complex Catalyzed *syn*-Selective Nitro-Mannich Reaction



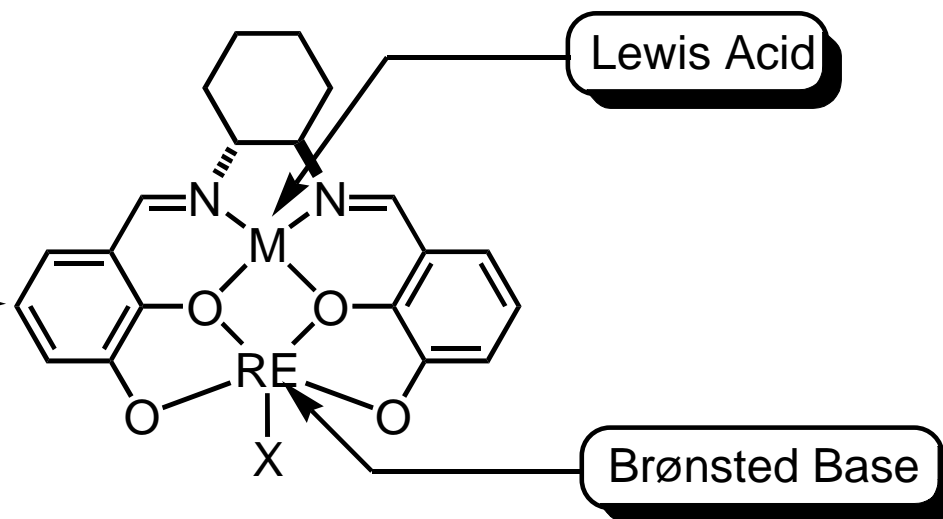
Shibasaki, M. *et al.* *J. Am. Chem. Soc.* **2010**, 132, ASAP.

Heterobimetallic Cu-Sm-Schiff Base Complex Catalyzed *syn*-Selective Nitro-Mannich Reaction



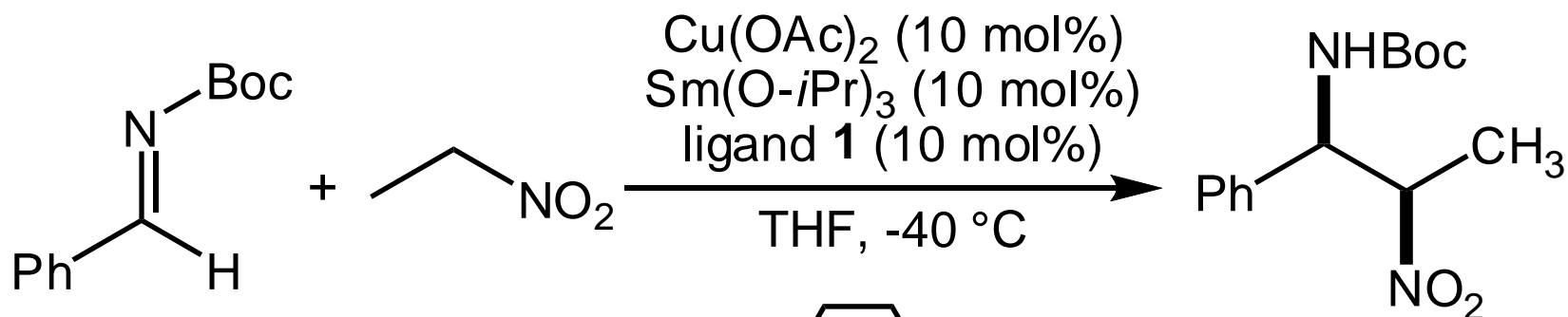
Dinucleating Schiff Base **1**

(1) M source
(2) RE source

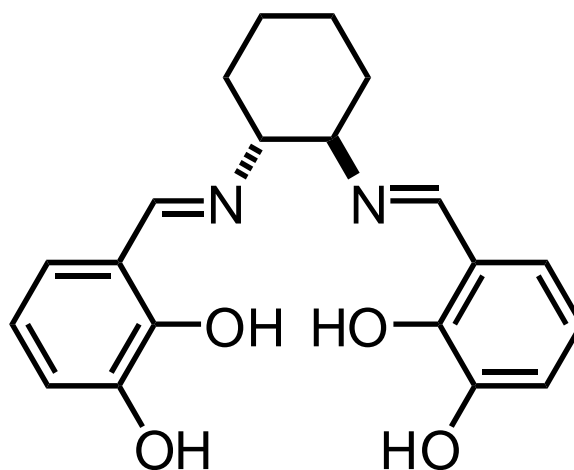


M-RE-Schiff Base **1** Complex

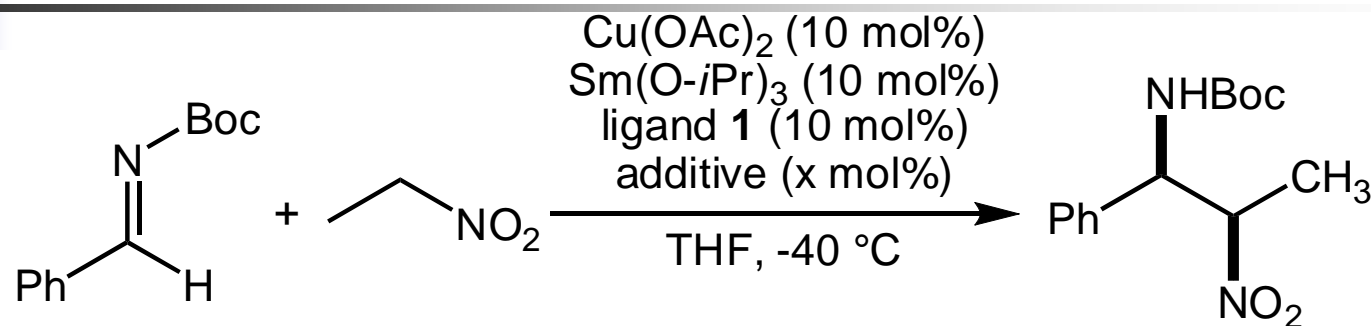
Heterobimetallic Cu-Sm-Schiff Base Complex Catalyzed *syn*-Selective Nitro-Mannich Reaction



Yield : 96%; Ee : 80%
Syn/anti: > 20:1

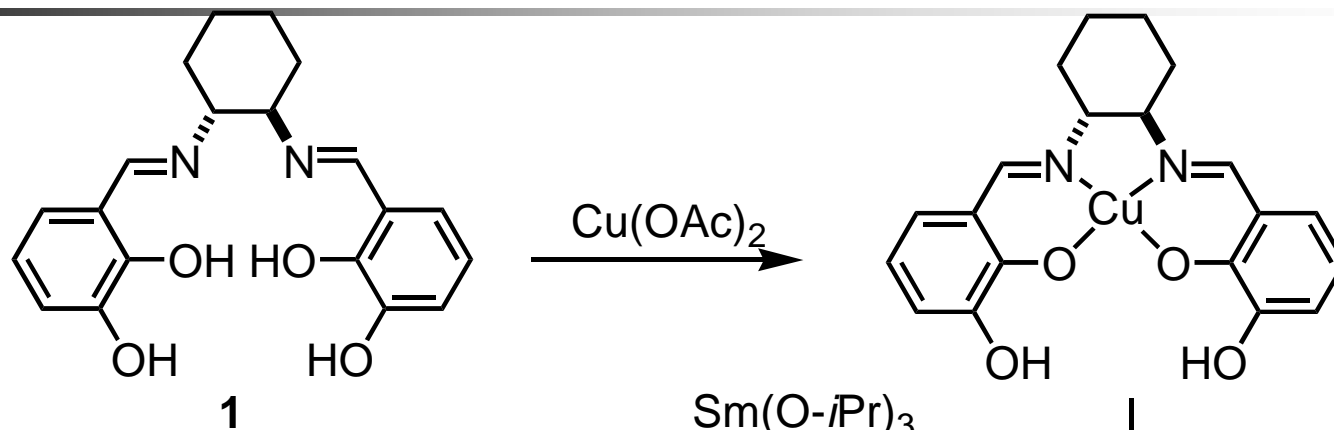


Heterobimetallic Cu-Sm-Schiff Base Complex Catalyzed *syn*-Selective Nitro-Mannich Reaction

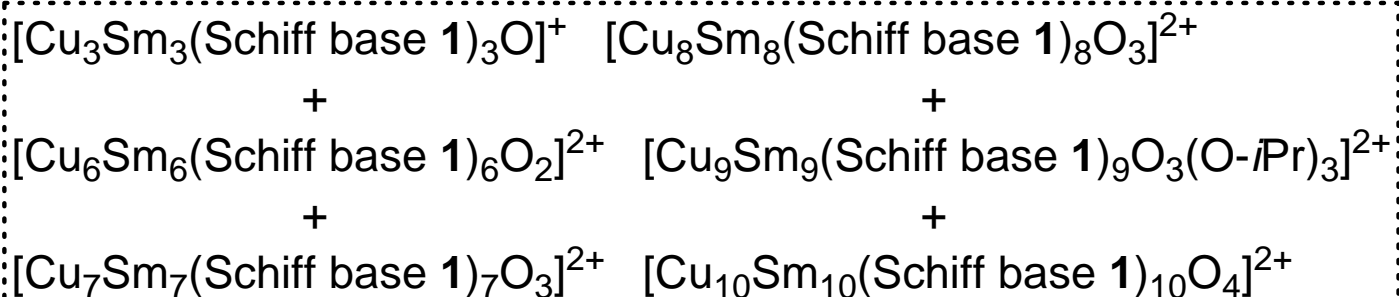


Entry	Additive(x mol%)	Yield (%)	<i>syn/anti</i>	% Ee (<i>syn</i>)
1	none	96	>20:1	80
2	DMSO (30)	94	13:1	71
3	<i>i</i> PrOH (30)	79	>20:1	62
4	<i>i</i> PrOH (100)	87	>20:1	87
5	Phenol (10)	81	>20:1	85
6	4-<i>t</i>Bu-phenol (10)	96	>20:1	94
7	4- <i>t</i> Bu-phenol (5)	88	>20:1	86
8	4- <i>t</i> Bu-phenol (15)	94	>20:1	92
9	4- <i>t</i> Bu-phenol (20)	87	>20:1	92

Heterobimetallic Cu-Sm-Schiff Base Complex Catalyzed *syn*-Selective Nitro-Mannich Reaction



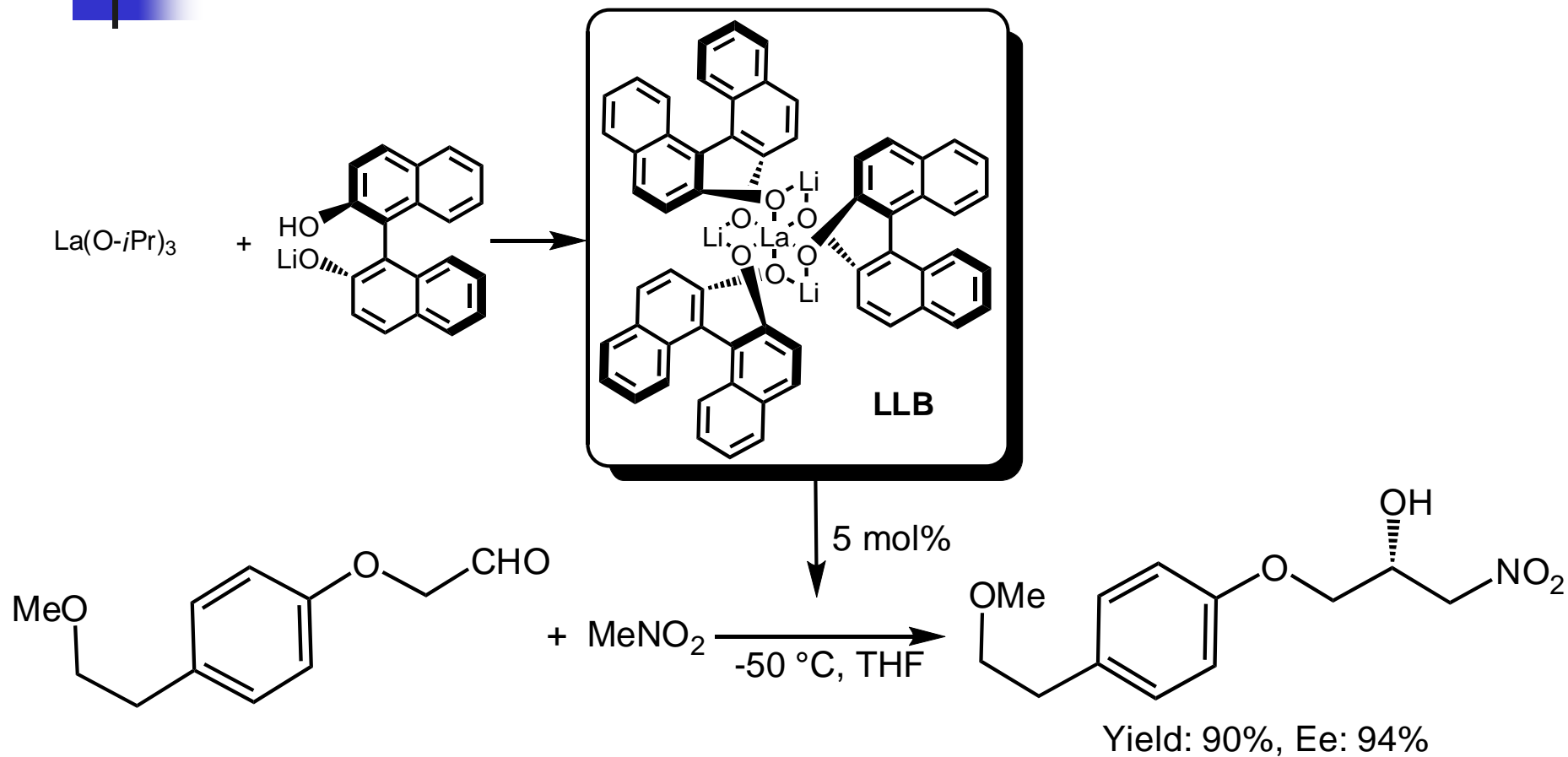
mixtures of various oligomers (observed in ESI-MS)



4-*t*Bu-phenol

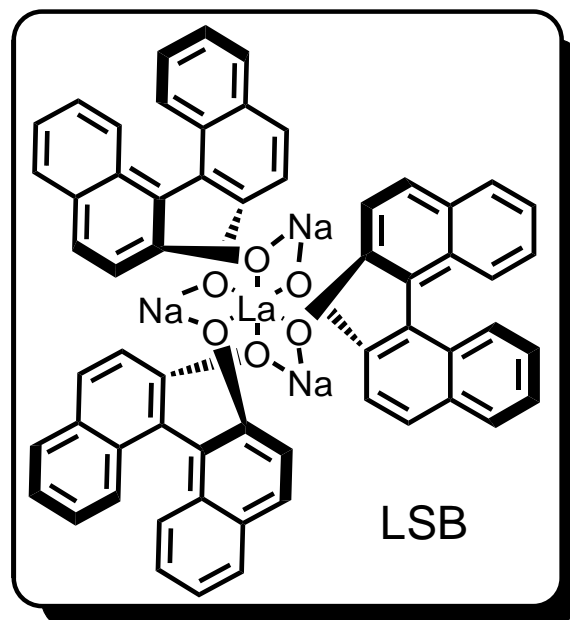
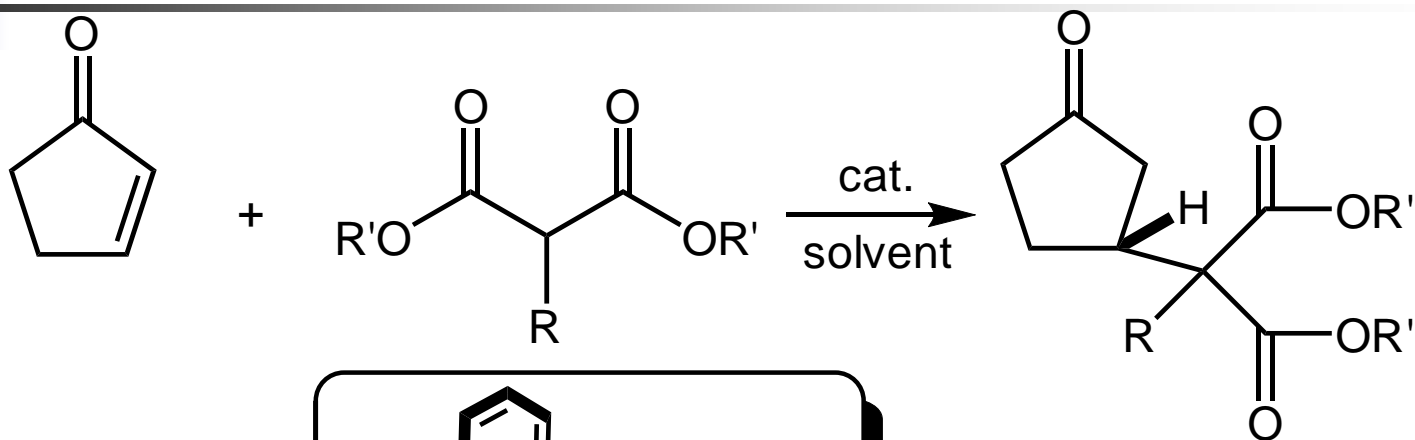
μ -oxo - μ -aryloxy-trimer (or hexamer)
 $[\text{Cu}_3\text{Sm}_3(\text{Schiff base 1})_3\text{O}(\text{O-C}_6\text{H}_4\text{-}i\text{tBu})]$

LLB Catalyzed Asymmetric Nitro-Aldol Reaction



Shibasaki, M. *et al.* *J. Am. Chem. Soc.* **1993**, *115*, 10372-10373.

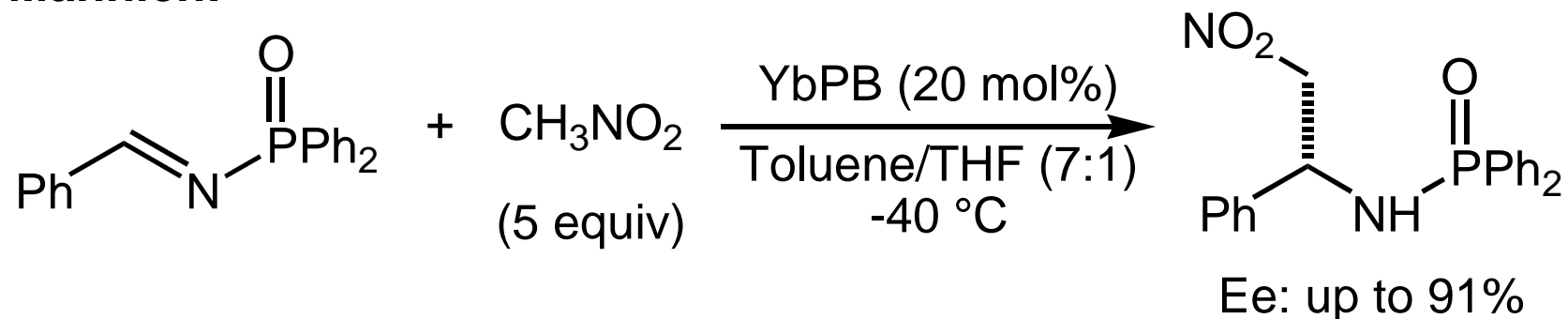
LSB Catalyzed Asymmetric Micheal Reaction



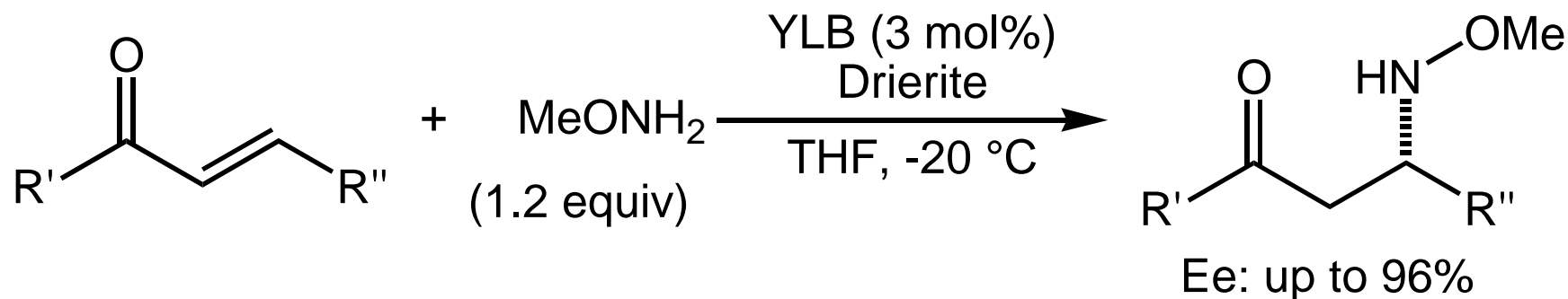
Yield: up to 98%
Ee: up to 92%

REMB-Catalyzed Asymmetric *Nitro-Mannich* and *Aza-Micheal* Reactions

Nitro-Mannich:

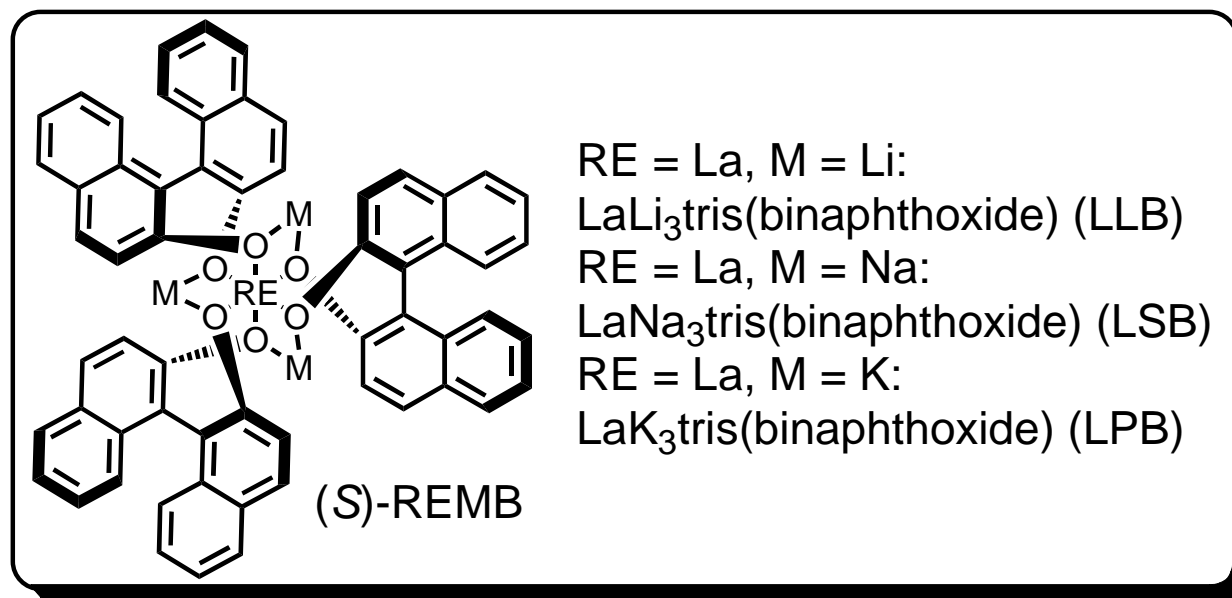
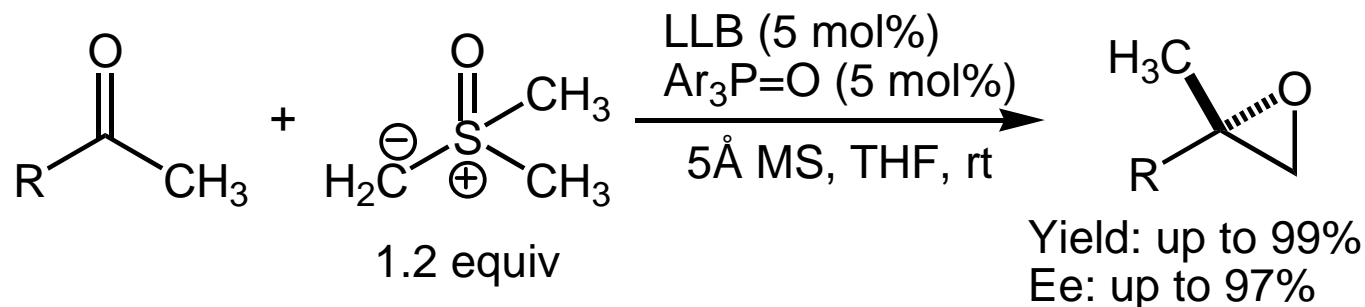


Aza-Micheal:



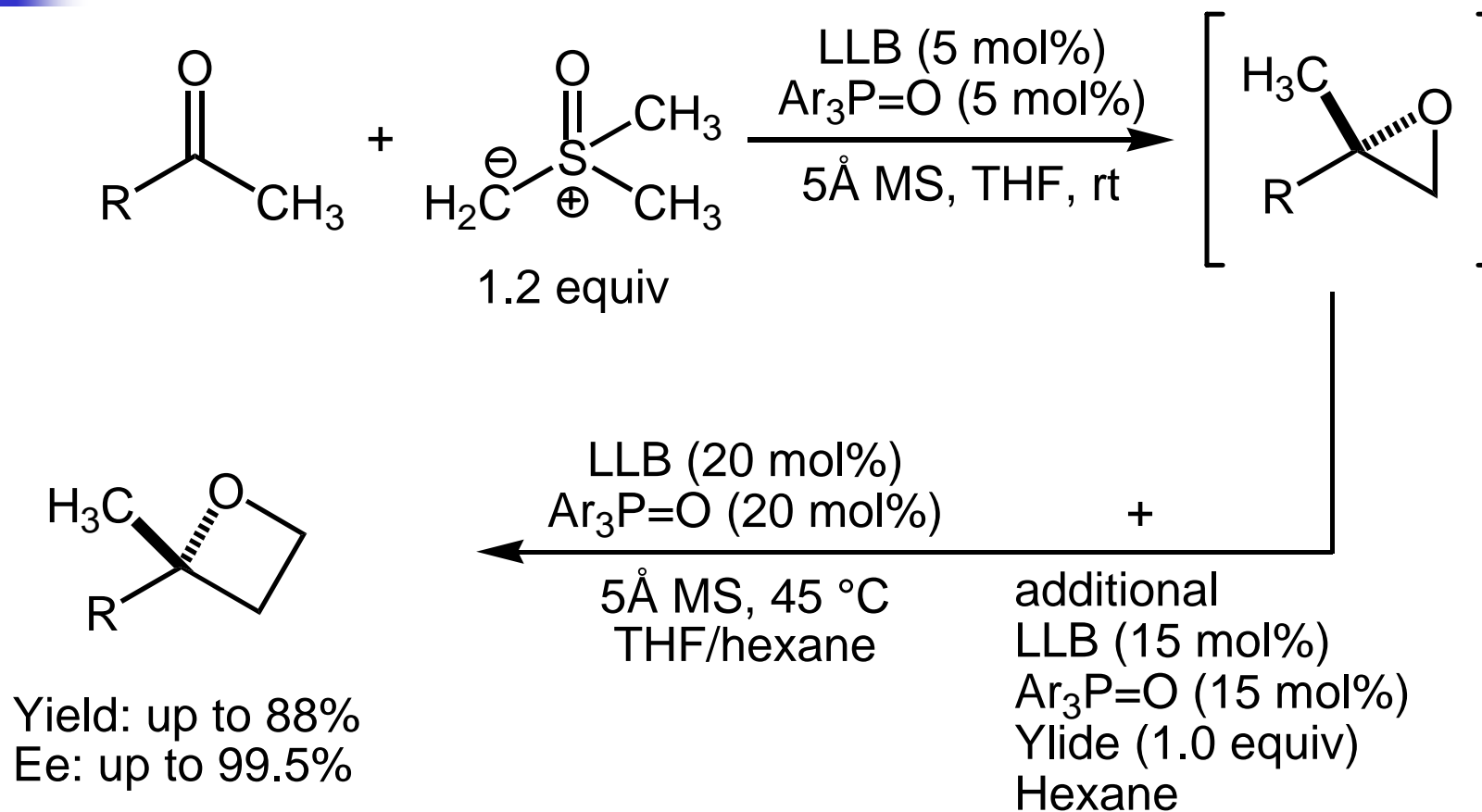
Shibasaki, M. *et al.* *Angew. Chem. Int. Ed.* **1999**, 38, 3504-3506.
Shibasaki, M. *et al.* *J. Am. Chem. Soc.* **2005**, 127, 13419-13427.

REMB-Catalyzed Addition of Sulfur Ylide to Ketones



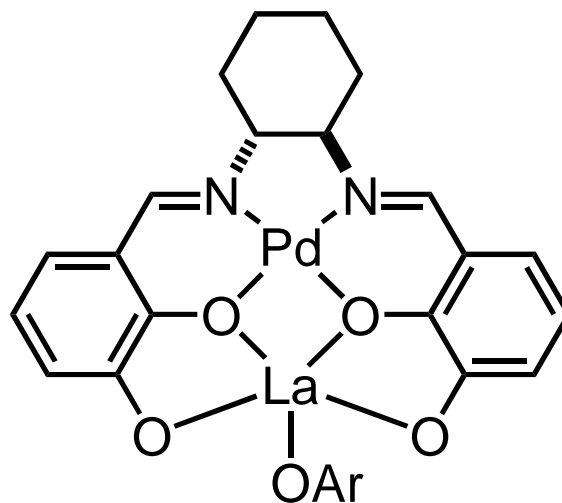
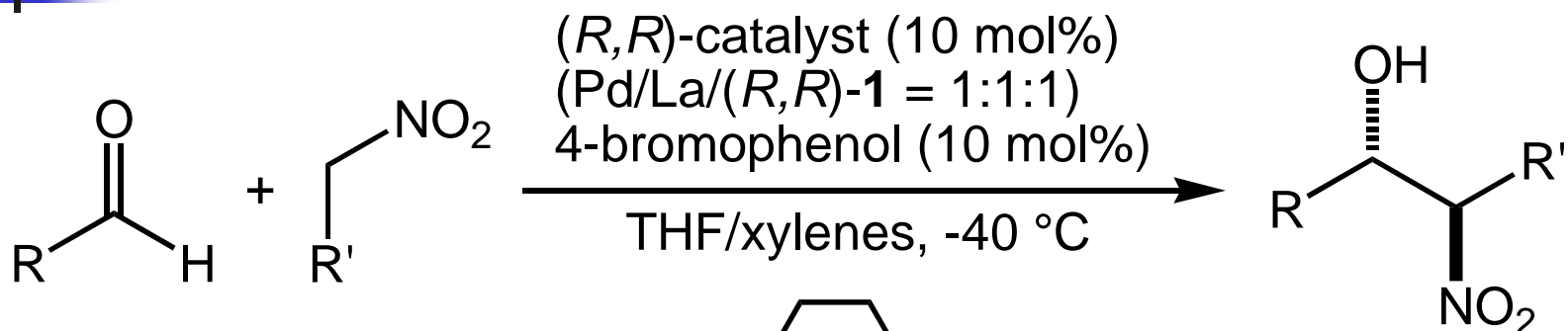
Shibasaki, M. *et al.* *J. Am. Chem. Soc.* **2008**, *130*, 10078-10079.

REMB-Catalyzed One-Pot Sequential Addition of Sulfur Ylide to Ketones



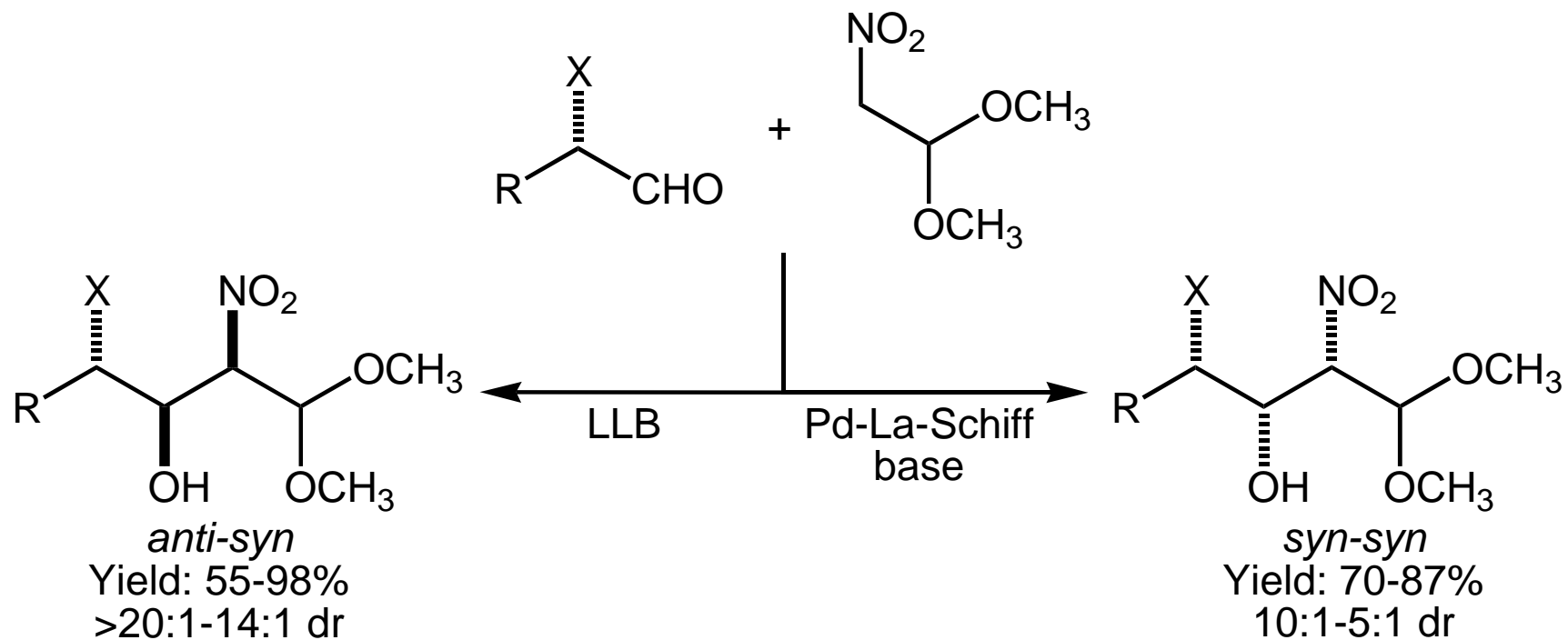
Shibasaki, M. *et al. Angew. Chem. Int. Ed.* **2009**, *48*, 1677-1680.

Heterobimetallic Pd-La-Schiff Base Complex Catalyzed *anti*-Selective Nitro-Aldol Reaction



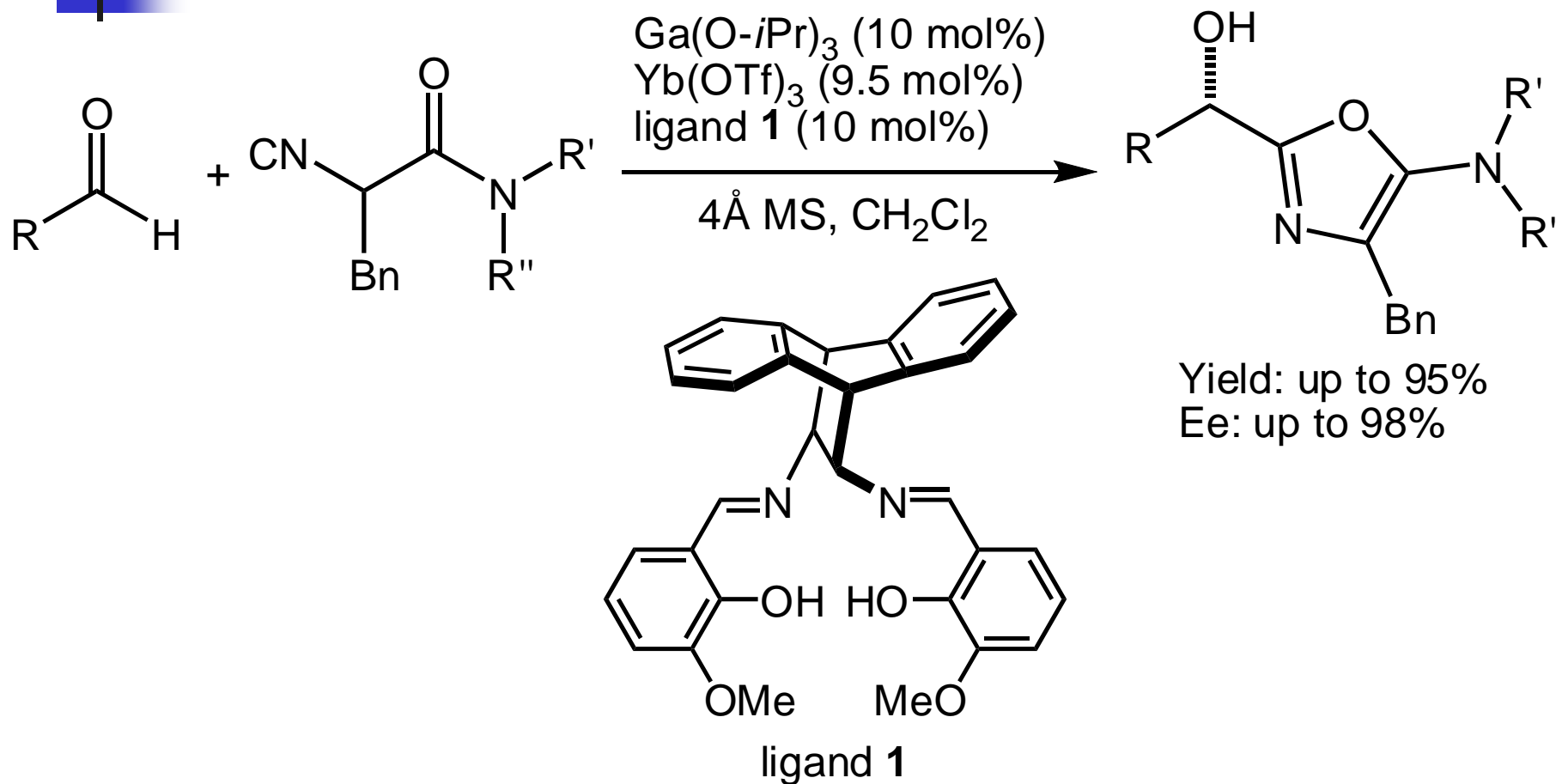
Yield: up to 92%
Anti/syn: up to 22:1
Ee: up to 92%

LLB and Heterobimetallic Pd-La-Schiff Base Complex Catalyzed *Nitro-Aldol* Reaction



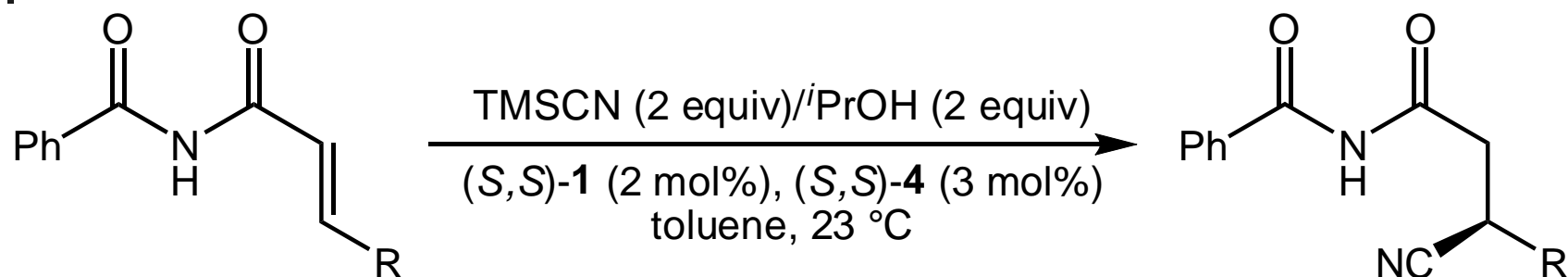
Shibasaki, M. *et al. Org. Lett.* **2008**, *10*, 2231-2234.

Heterobimetallic Ga-Yb-Schiff Base Complex Catalyzed α -Addition of Isocyanides to Aldehydes

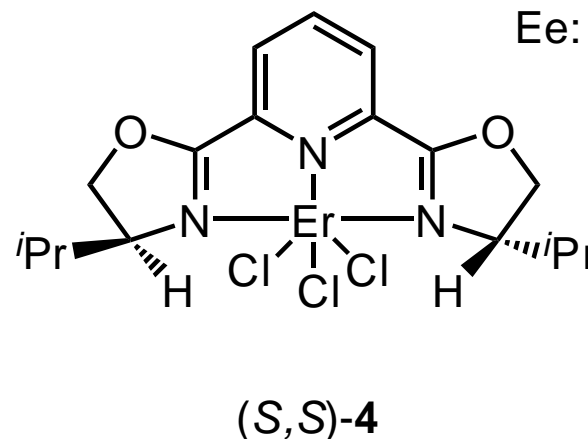
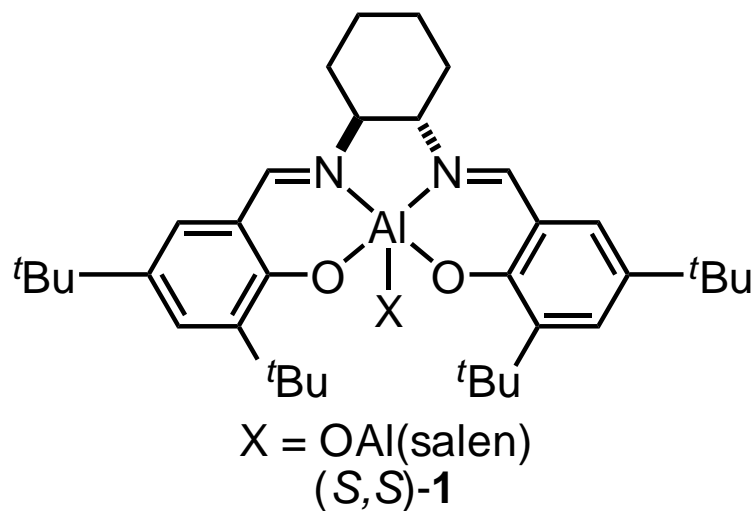


Shibasaki, M. *et al.* *J. Am. Chem. Soc.* **2009**, 131, 8384-8385.

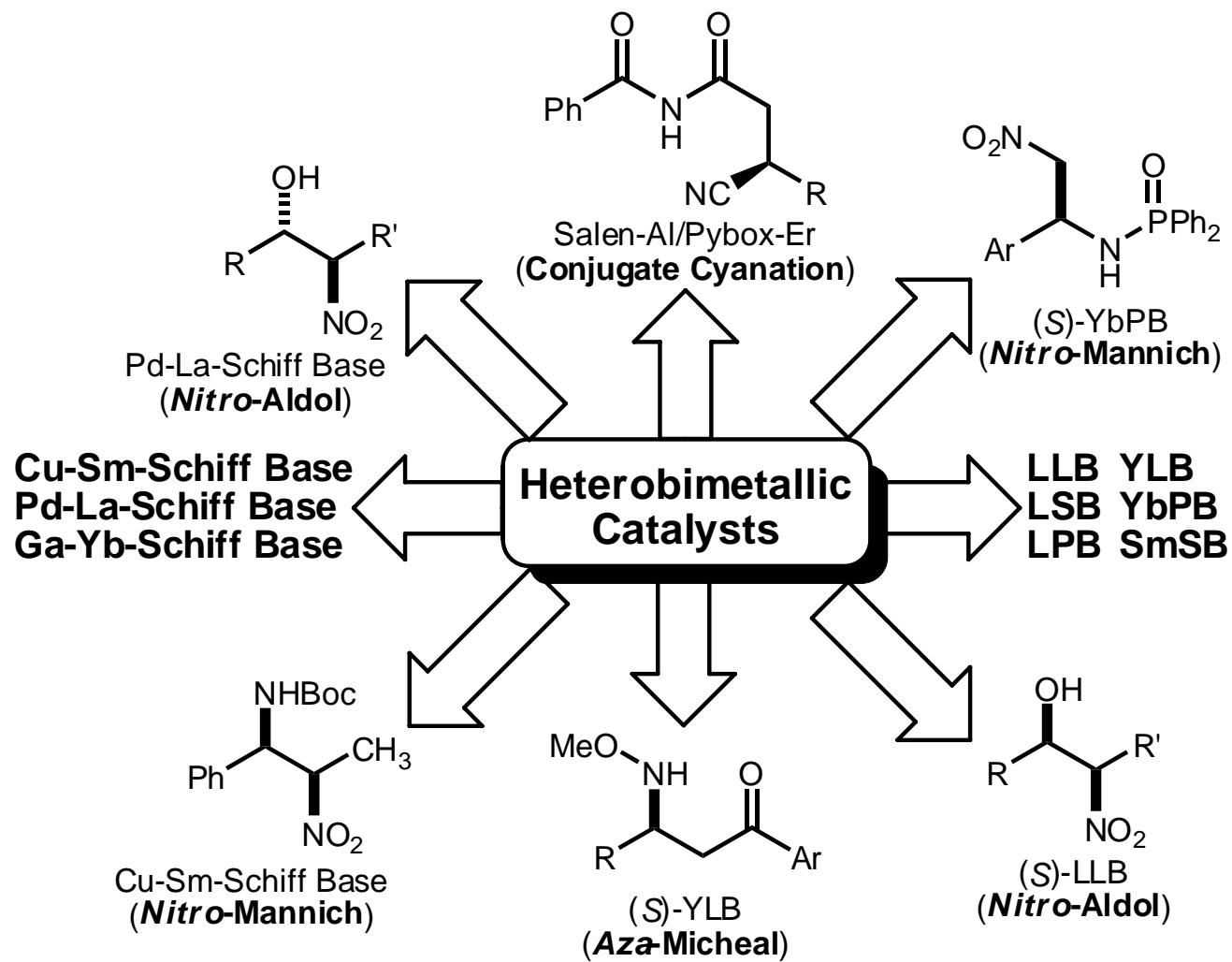
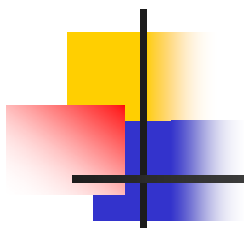
Cooperative Dual Catalysis: Salen-Al/Pybox-Er Catalyzed conjugate Cyanation of Unsaturated Imides

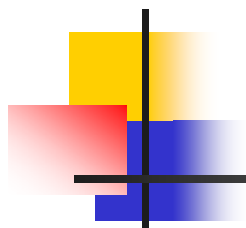


Yield: up to 94%
Ee: up to 97%

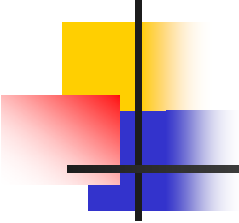


Jacobsen, E. N. *et al.* *J. Am. Chem. Soc.* **2004**, *126*, 9928-9929.
Jacobsen, E. N. *et al.* *Angew. Chem. Int. Ed.* **2008**, *47*, 1762-1765.

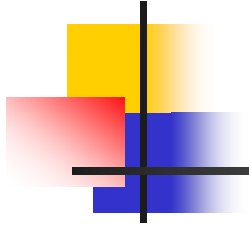




Catalytic asymmetric processes are potentially more economical and environmentally benign than those using stoichiometric amounts of chiral reagents. To develop asymmetric catalysts that exhibit high activity, high stereoselectivity, and broad substrate generality, investigators often employ the concept of bifunctional asymmetric catalysis with both metallic catalysts and organocatalysts. Dual activation of nucleophiles and electrophiles is key to developing bifunctional catalysts. Since our first report on a lanthanum/lithium/binolate heterobimetallic complex in the early 1990s, our group has been intensively working on the heterobimetallic Lewis acid/Brønsted base bifunctional catalysis of rare earth metal/alkali metal using BINOL and its derivatives as ligands. When designing bifunctional asymmetric catalysts, the construction of a suitable chiral environment for each targeted reaction is important. Optimization of enantioselectivity and reactivity requires a strategy for constructing a flexible and diverse chiral environment. To broaden the scope of heterobimetallic bifunctional rare earth metal asymmetric catalysis, it is desirable to develop a heterobimetallic system without using BINOLs or alkali metals. We believe that a new metal combination will lead to the new catalytic activity and selectivity.



We developed a new heterobimetallic transition metal/rare earth metal system with a dinucleating Schiff base **1**. A mixture of $\text{Cu}(\text{OAc})_2/\text{Sm}(\text{O-}i\text{Pr})_3/\text{Schiff base } \mathbf{1}$ complex with an achiral phenol additive was partially successful for achieving a syn-selective catalytic asymmetric nitro-Mannich reaction. The substrate generality of the first-generation system remained problematic. After mechanistic studies on the catalyst prepared from $\text{Sm}(\text{O-}i\text{Pr})_3$, we reoptimized the catalyst preparation method, and the second-generation catalyst derived from $\text{Sm}_5\text{O}(\text{O-}i\text{Pr})_{13}$ showed broader substrate generality as well as higher reactivity and stereoselectivity compared to $\text{Sm}(\text{O-}i\text{Pr})_3$. The optimal system with $\text{Sm}_5\text{O}(\text{O-}i\text{Pr})_{13}$ was applicable to various aromatic, heteroaromatic, and isomerizable aliphatic *N*-Boc imines, giving products in 66-99% ee and *syn/anti* = (>20:1-13:1). Further studies to apply the heterobimetallic transition metal/rare earth metal catalysts with dinucleating Schiff bases **1** to other asymmetric reactions, especially ones in which the rare earth metal/alkali metal/BINOL systems were not suitable, are ongoing.



THANKS!