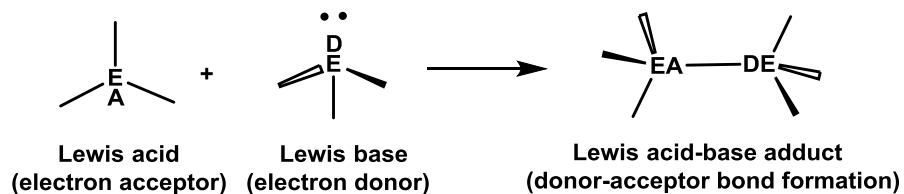


Yuanhong Ma

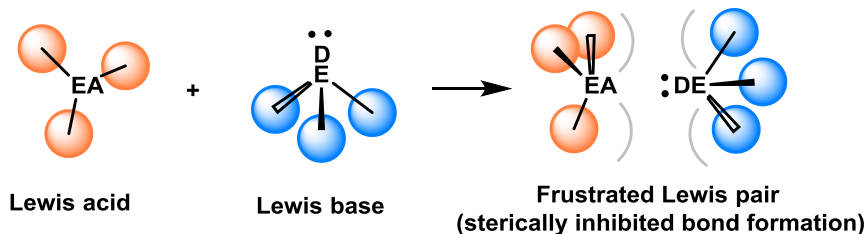
Concept

Classical Lewis acid-base chemistry

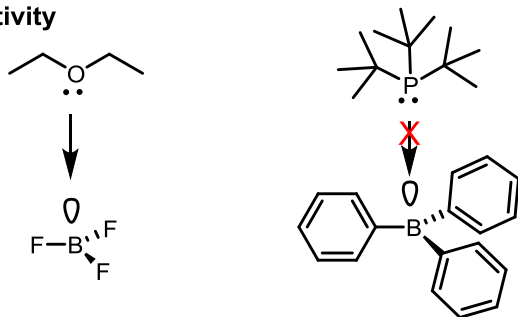


For almost 100 years, the combination of electron acceptors (Lewis acids) and electron donors (Lewis bases) has been known to give Lewis acid-base adducts that incorporate donor-acceptor bonds.

Frustrated Lewis pair chemistry



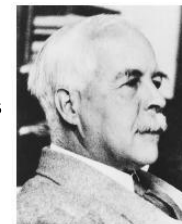
Research over the past decade has shown that the introduction of steric demands or a dissociative equilibrium provides access to free donors and acceptors, allowing them to interact with a third molecule and leading to distinct reactivity



Discovery Timeline

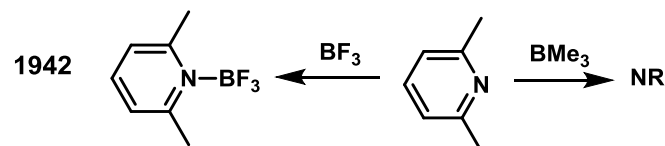
1923

Definition of Lewis acids and bases by Gilbert Lewis



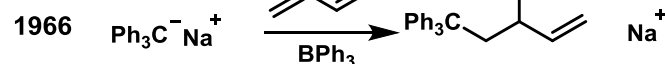
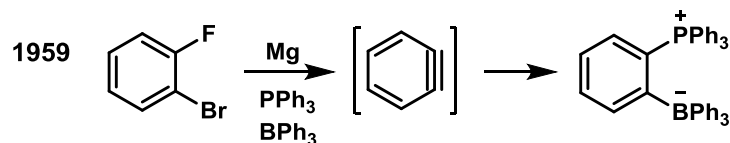
Propagation of use in organic chemistry

The acid/base reaction for the formation of adducts



Effect of steric hindrance within adduct noticed by Brown

JACS, 1942, 64, 325



Wittig, Benz and then Tochtemann noticed similar anomalies

G. Wittig, E. Benz, *Chem. Ber.* 1959, 92, 1999.

W. Tochtemann, *Angew Chem. Int. Ed. Engl.* 1966, 5, 351.

1978-1990

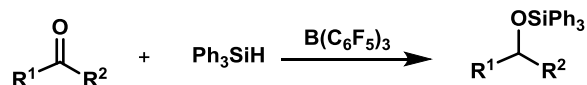
Gutmann published his analysis of the interaction of Lewis acids and bases

Gutmann, V. *The Donor-Acceptor Approach to Molecular Interactions*; Plenum Press: New York, 1978.

Discovery Timeline

1996

Piers reported first metal-free hydrosilylation of aromatic ketones

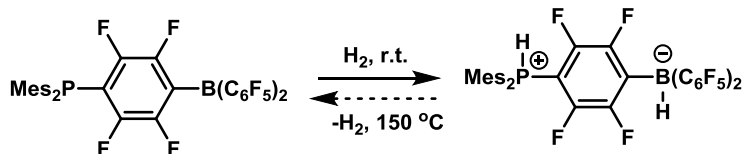


JACS, 1996, 118, 9440

2006

Stephan Douglas encounters same phenomena as Brown

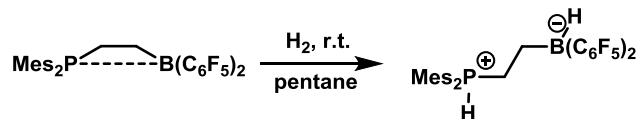
The first reversible, metal-free hydrogen activation



Science, 2006, 314, 1124

2007 Stephan formalizes the concept (*Frustrated Lewis Pairs*)
ACIE, 2007, 46, 4968

2007 Erker Reported activation of dihydrogen by intramolecular FLPs:



2018

Over the past decades rapid and great progress have been made in the field of FLPs chemistry.

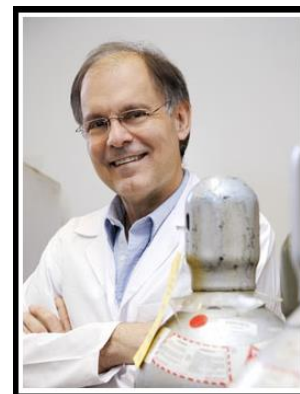
Representative players in the field

Prof Douglas W. Stephan

Ph.D 1980 (University of Western Ontario)
Postdoc 1980-1982 (Harvard, R.H. Holm)

University of Windsor
University Professor 2002-2007
Department Head 2003-2006
Professor 1992-2002
Associate Professor 1985-1992
Assistant Professor 1982-1985

University of Toronto
Professor 2008-present



Prof Gerhard Erker



Studied chemistry 1966 - 1970 (Universities Köln and Bochum)
Dr. rer. nat. 1973 (Univ. Bochum, W. R. Roth)
Postdoctoral Fellow 1974 - 75 (Princeton University, M. Jones, Jr.)
Habilitation 1981 (Univ. Bochum, Organic Chemistry)
Heisenberg-Fellow 1984 - 1985 (Max-Planck-Institut für Kohlenforschung, Mülheim)
Professor 1985 - 1990 (C3, Univ. Würzburg, Organic Chemistry)
Professor 1990 - 2015 (C4/W3, WWU Münster, Organic Chemistry)
Senior Professor 2015 - present (WWU Münster, Organic Chemistry)

To date, which aspects of applications on Frustrated Lewis Pairs have been concerned?

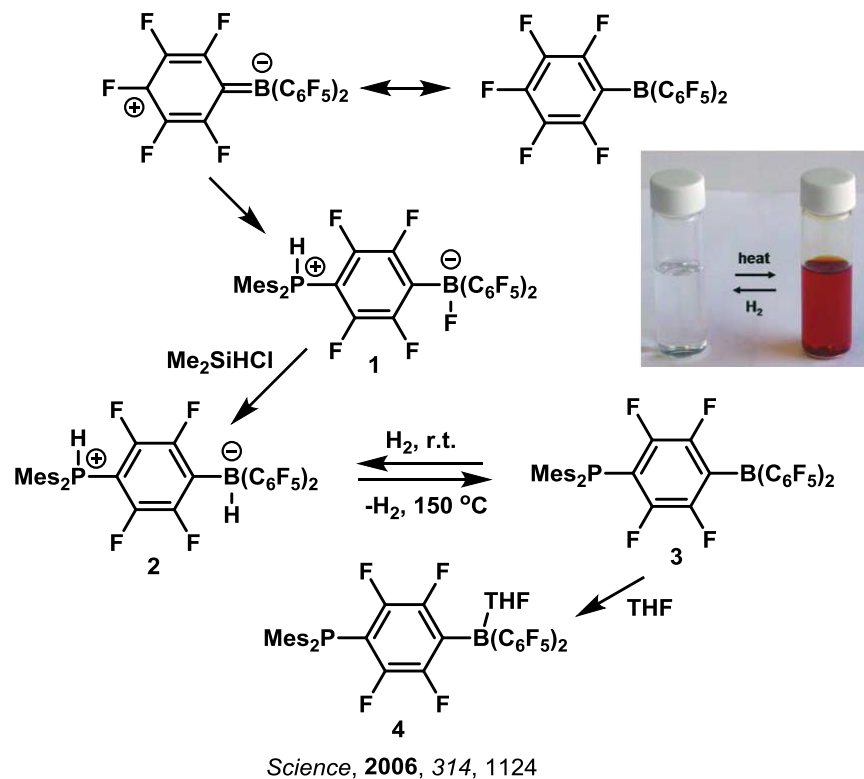
- a. Activation of H₂ and catalytic hydrogenation
- b. Small-molecule activation (CO; CO₂, SO₂, N₂O, NO etc.)
- c. Organic molecule activation (alkene, alkynes, silanes, C-H bonds etc.)
- d. Asymmetric catalysis
- e. Heterogeneous catalysis
- f. Polymers and materials
- g. Transition metal chemistry
- h. Enzyme models

Recent review: *ACIE*, **2015**, *54*, 6400; *JACS*, **2015**, *137*, 10018; *Accounts*, **2015**, *48*, 306; *Science*, **2016**, *354*, 1248; *Chem. Rec.* **2017**, *17*, 1

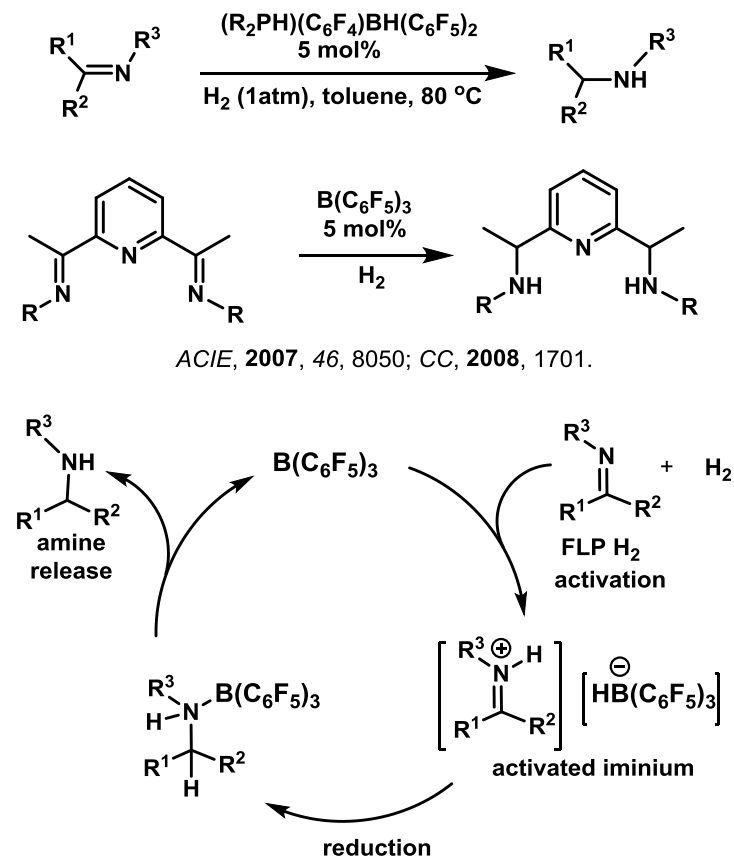
This presentation will mainly focus on homogeneous catalysis and synthesis application based on Frustrated Lewis Pairs.

1. Hydrogenation

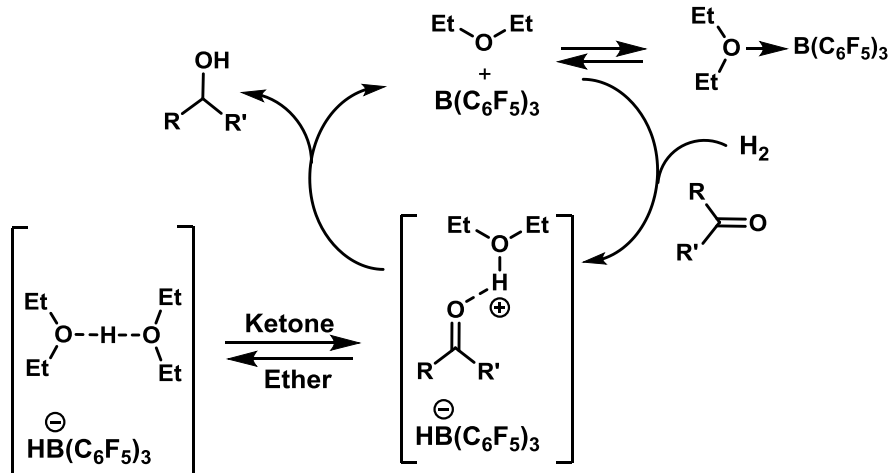
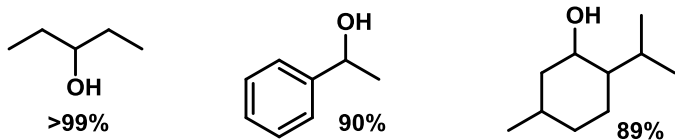
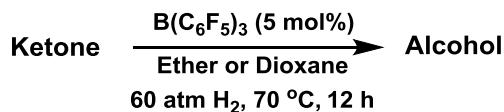
1.1 Seminal work by Stephan (H₂ activation by FLPs)



1.2 Catalytic Hydrogenation (imines)

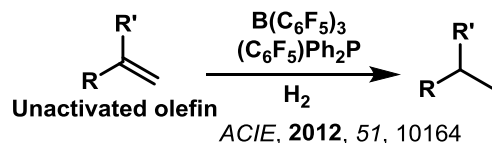


1.3 Catalytic Hydrogenation (Ketone)



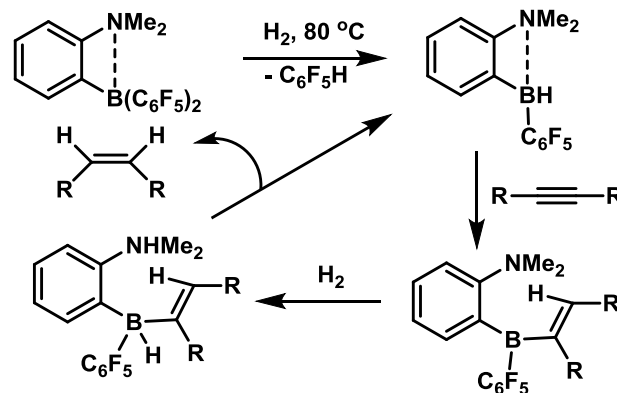
JACS, 2014, 136, 15809; *JACS*, 2014, 136, 15813

1.4 Catalytic Hydrogenation (Olefin)



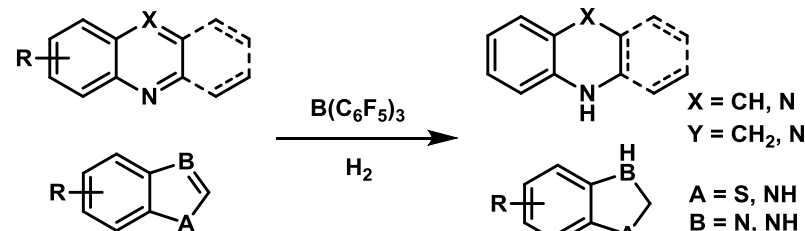
Hydrogenation of electron-poor alkene or allene, see:
ACIE, 2012, 51, 12367; *ACIE*, 2013, 52, 5876

1.5 Catalytic Hydrogenation (Alkynes)

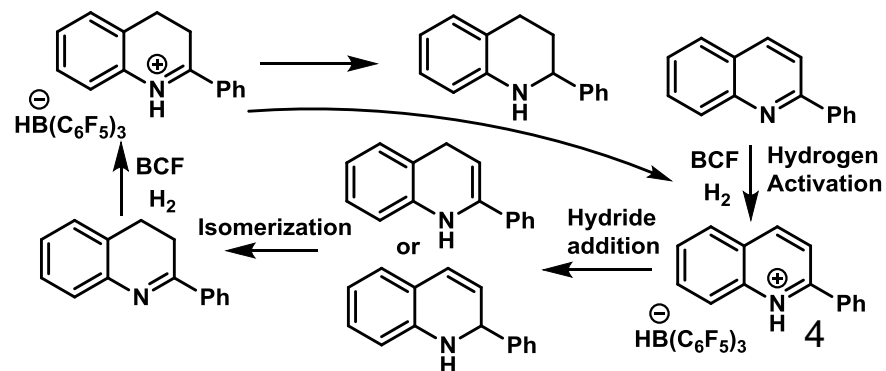


Nat. Chem. 2013, 5, 718.

1.6 Catalytic Hydrogenation (Heterocycles)



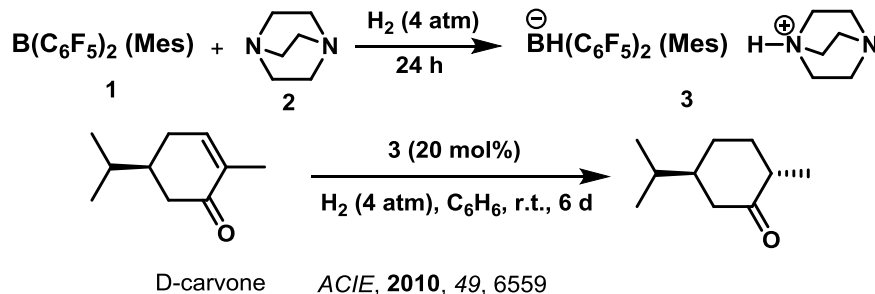
CC, 2010, 46, 4884; *IC*, 2011, 50, 12338; *CEJ*, 2012, 18, 574



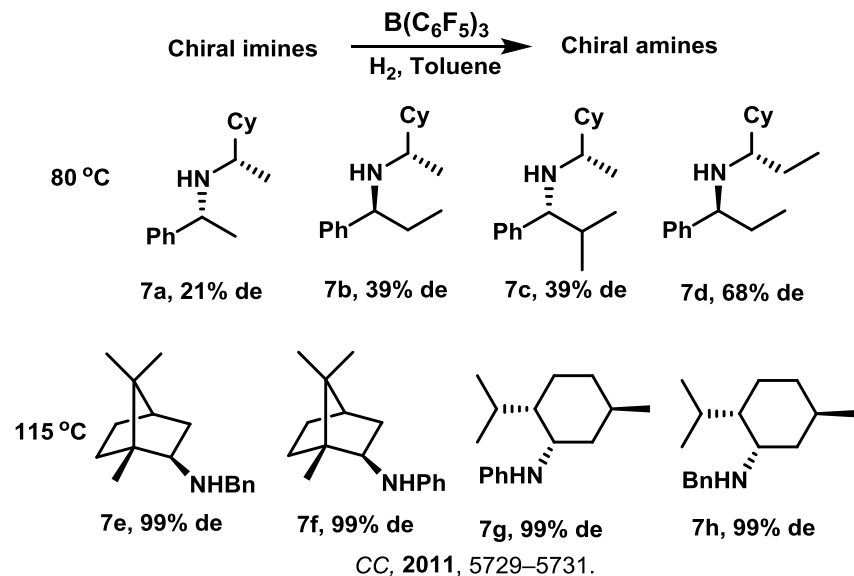
2. FLP catalyzed asymmetric hydrogenation

2.1 Substrate-controlled selectivity

In 2010, the first example of chiral substrate induced asymmetric hydrogenation catalyzed by a FLP catalyst was reported by Soós and co-workers.

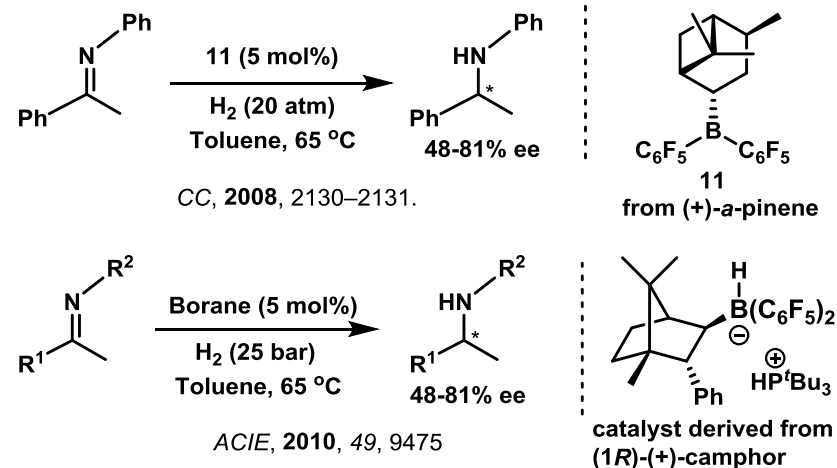


In 2011, Stephan et al. reported a highly diastereoselective catalytic hydrogenation of optically pure ketimines using 10–20 mol % $\text{B}(\text{C}_6\text{F}_5)_3$ as a catalyst.

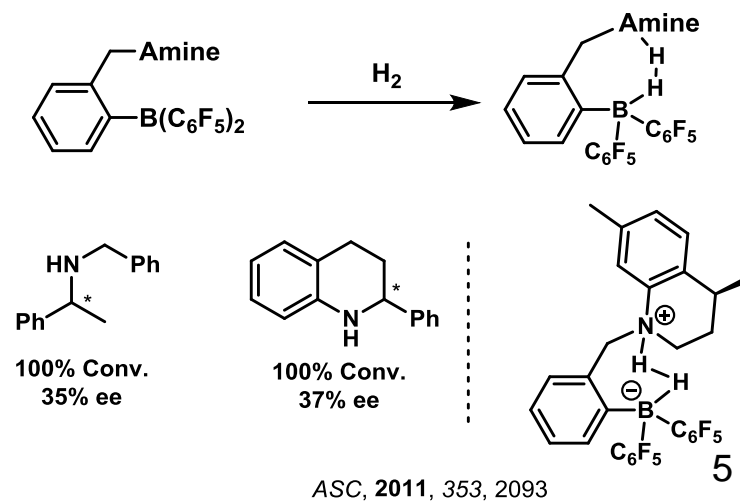


2.2 Chiral FLP catalyst controlled selectivity

In 2008, Chen and Klankermayer reported the first chiral FLP-catalyzed asymmetric hydrogenation of imine.

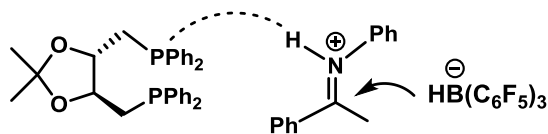
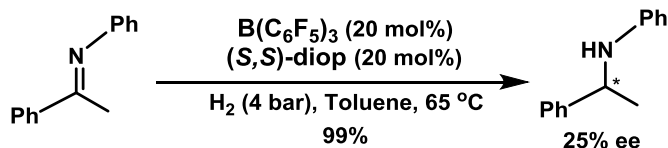


In 2011, Repo and co-workers designed a novel class of chiral intramolecular ansa-aminoborates.



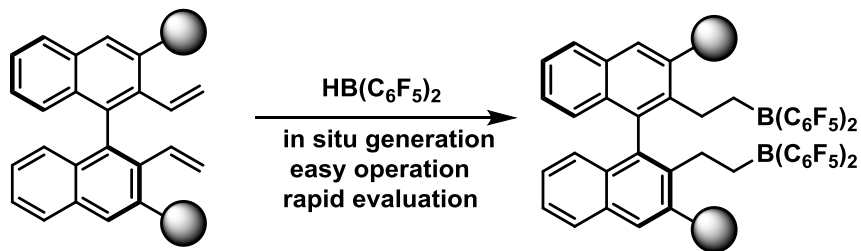
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In 2011, Stephan and co-workers employed (S,S)-diop and $B(C_6F_5)_3$ as an intermolecular FLP catalyst for the asymmetric hydrogenation of ketimine 9a to result in a promising 25% ee



Inorg. Chem., 2011, 50, 12338

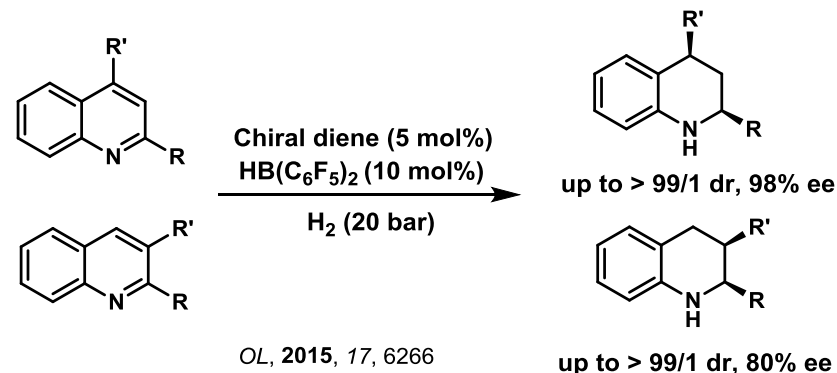
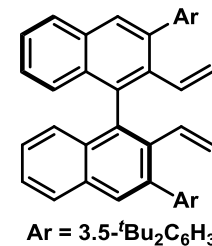
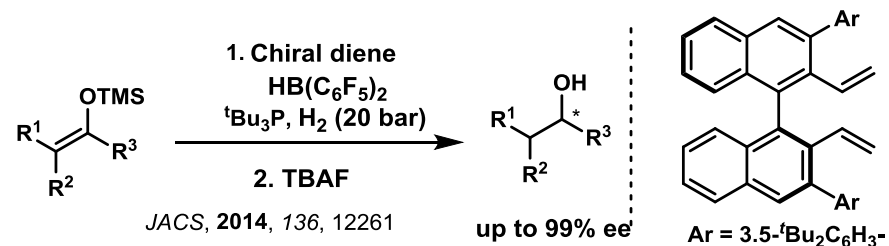
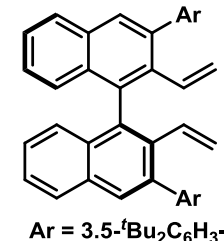
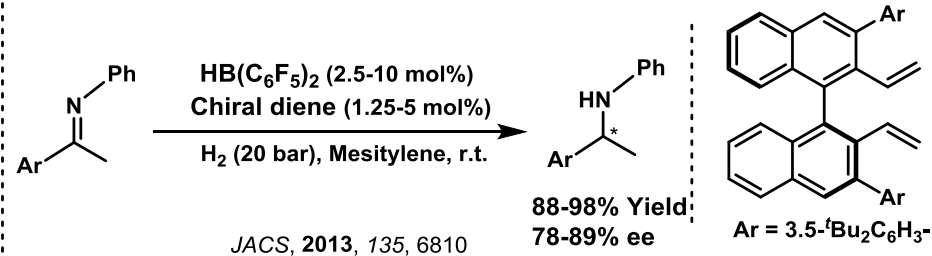
In 2013, Du et al. developed an elegant strategy for preparation of chiral borane catalyst.



JACS, 2013, 135, 6810

The use of terminal olefins ensured the optical purity of boranes by the hydroboration with Piers borane and avoided to produce diastereoisomers for the case of internal olefins.

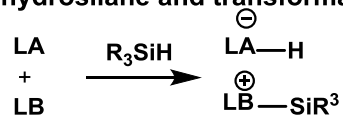
Using this catalyst, highly selective asymmetric hydrogenation of imine, silyl enol ethers and heterocycle have been achieved by Du's group.



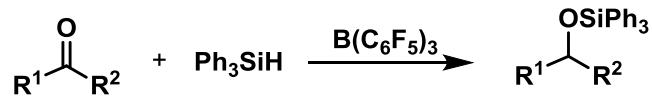
up to > 99/1 dr, 80% ee

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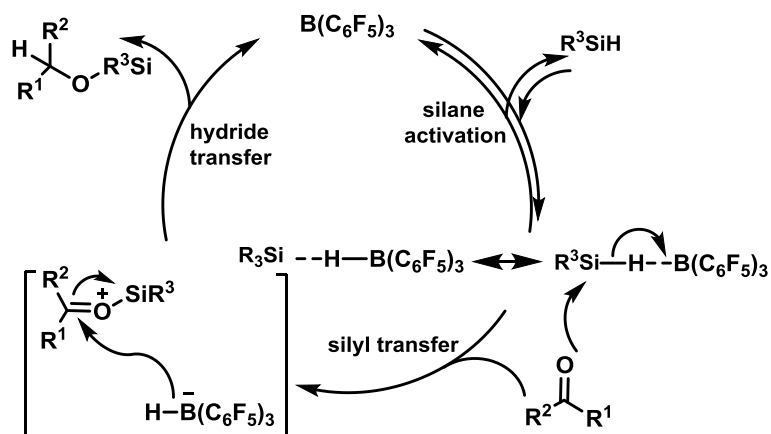
2. Activation of hydrosilane and transformations



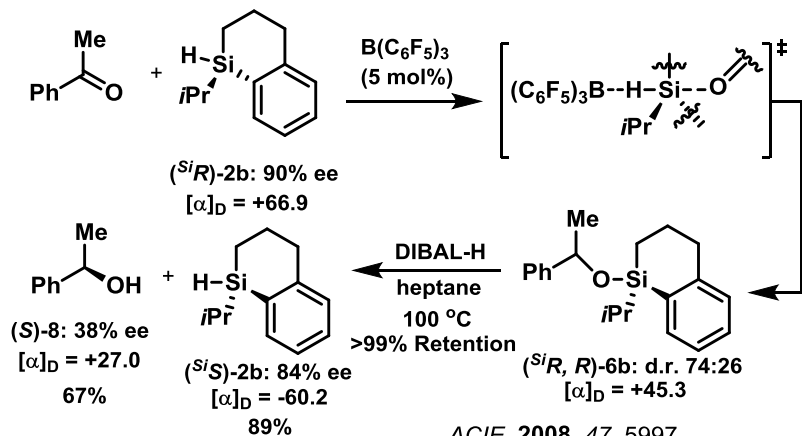
In 1996, Piers et al. reported the first metal-free hydrosilylation of ketones.



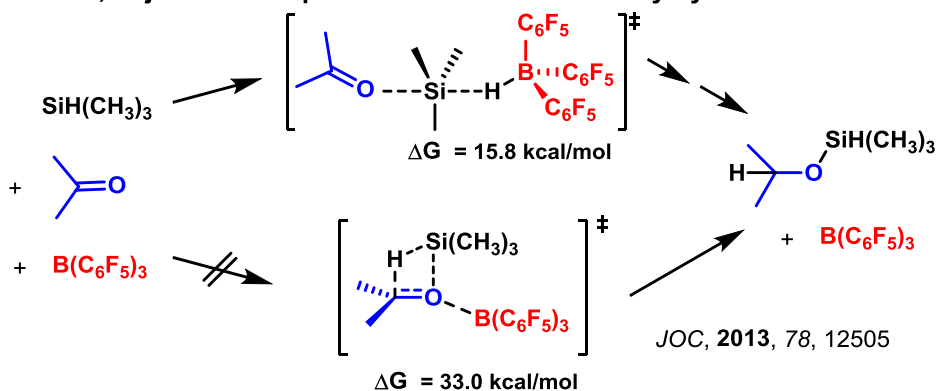
JACS, 1996, 118, 9440



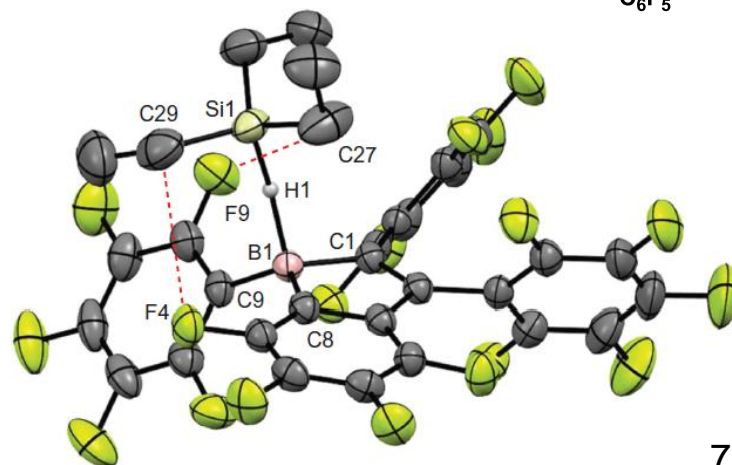
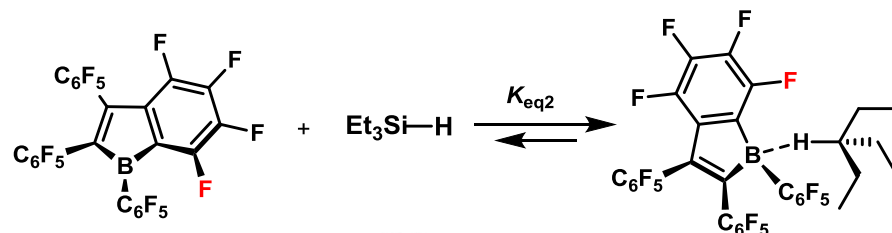
In 2008, Oestreich et al. obtained proof of an $\text{S}_{\text{N}}2$ -Si transition state employing a stereogenic silane as a stereochemical probe.



In 2013, Fujimoto et al. performed mechanism study by DFT.



In 2014, Piers et al. obtained crucial X-ray crystallography structure of borane-silane adduct and demonstrates conclusively the role of this species in metal-free 'frustrated-Lewis-pair' hydrosilylation reactions.

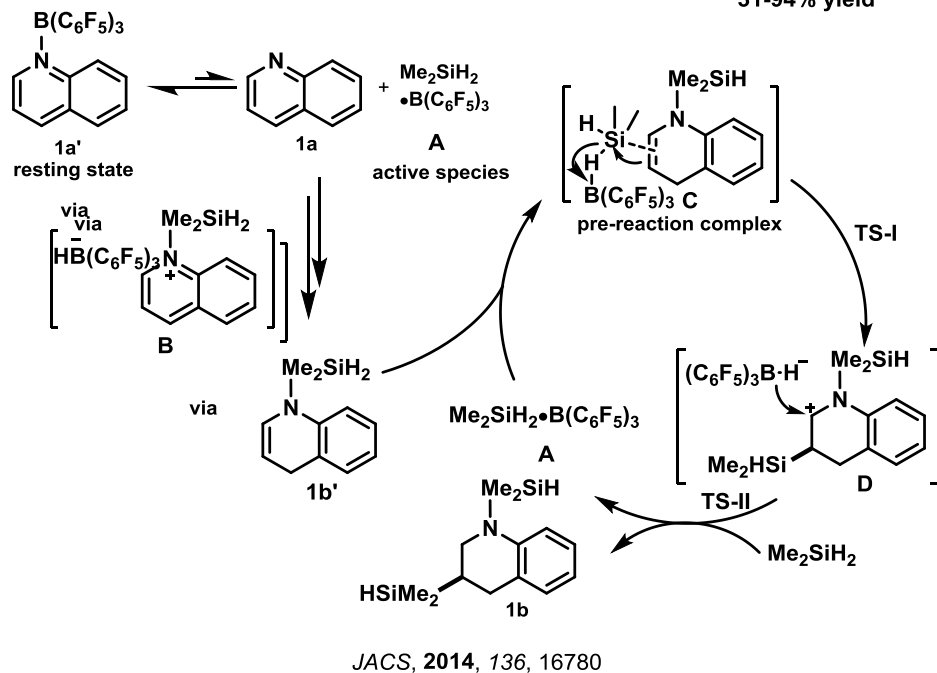
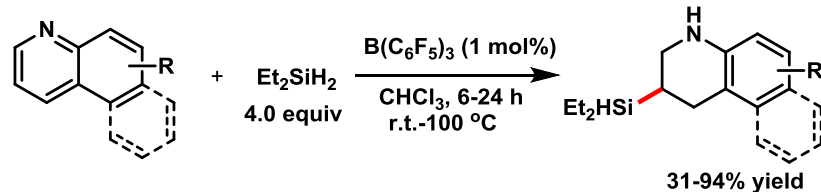


Nat. Chem., 2014, 6, 983

Yuanhong Ma

2. Activation of hydrosilane and transformations

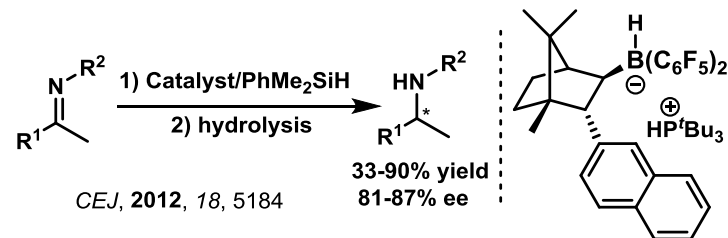
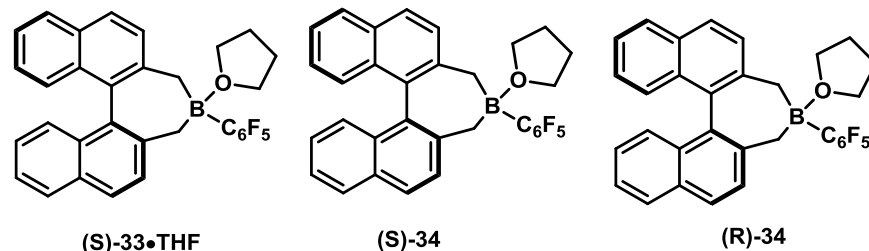
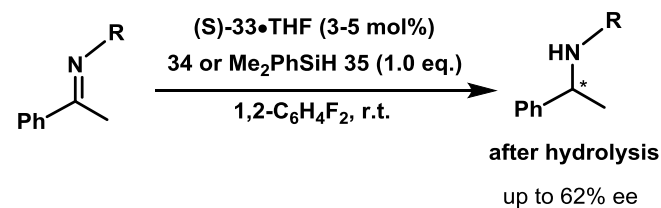
In 2014, Chang et al. reported silylative reduction of Quinolines.



Besides these, silylative reduction of pyridines, imines, amides and nitriles also have been reported.

see : JACS, 2013, 135, 17537; CC, 2014, 50, 9349; JACS, 2015, 137, 15176; JOC, 2015, 80, 7281; CC, 2016, 52, 12195; OBC, 2016, 14, 5774.

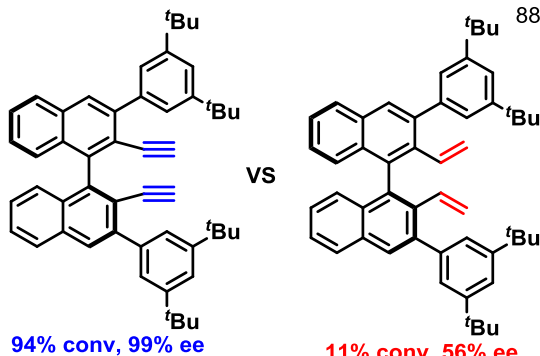
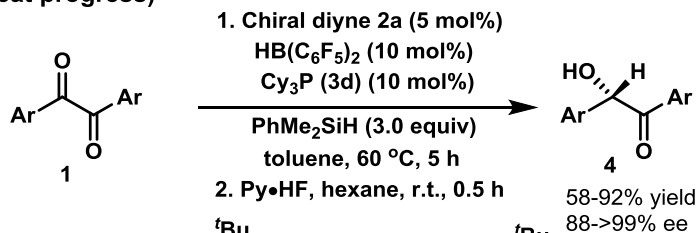
In 2012, Klankermayer et al. reported the first chiral FLP-catalyzed silylative reduction of imines.


 In 2012, Mewald and Oestreich demonstrated an axially chiral C₆F₅-substituted borane. With this catalyst, a phenyl-substituted imine could be reduced to amine with low to moderate ee value.


CEJ, 2012, 18, 14079; JACS, 2013, 135, 17537.

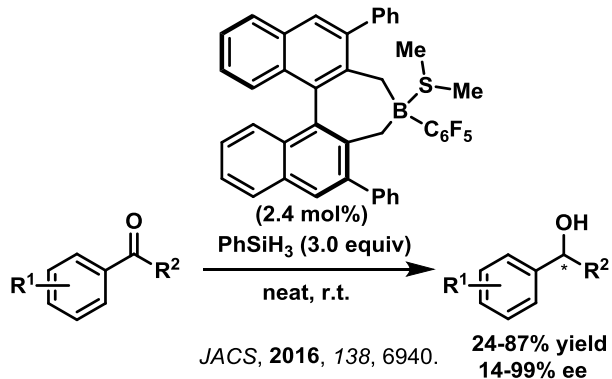
2. Activation of hydrosilane and transformations

In 2016, Du et al. reported chiral FLPs-catalyzed highly enantioselective hydrosilylations of 1,2-dicarbonyl compounds. (great progress)



JACS, 2016, 138, 810.

In 2016, Oestreich et al. realized the first asymmetric piers hydrosilylation. (simple ketone)

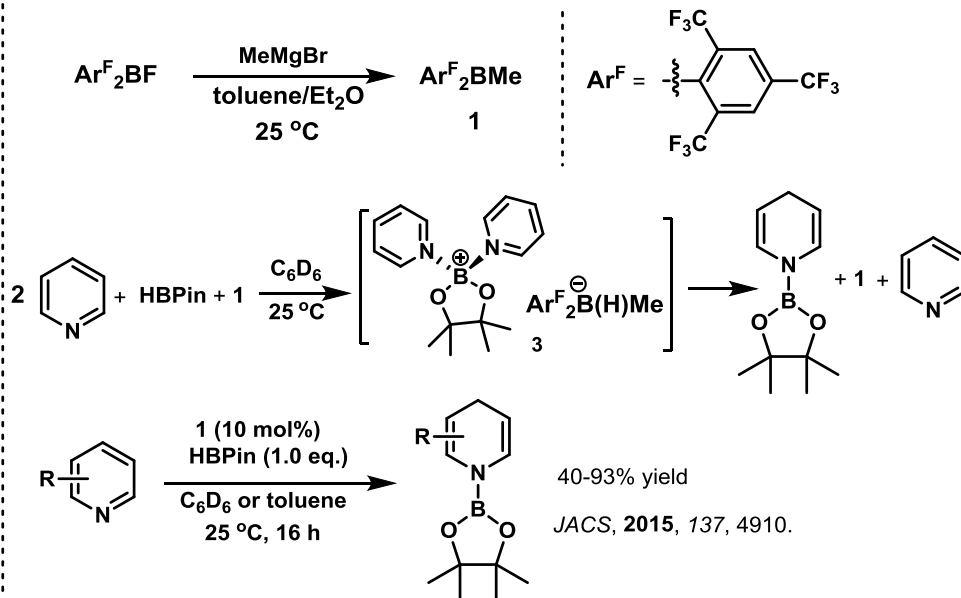


JACS, 2016, 138, 6940.

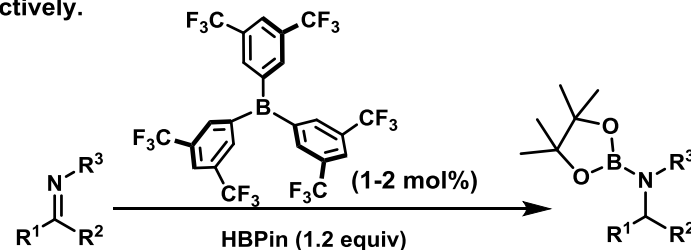
3. Activation of borane and transformations

In 2015, Wang et al. reported 1,4-Hydroboration of Pyridines via FLP

The reduction of unsubstituted pyridine with FLPs has not been achieved. This could be due to the lack of steric protection around the nitrogen atom of pyridine, which can coordinate to the Lewis acid of FLPs and deactivate the catalysts.



In 2017, Oestreich and Melen reported borylative reduction of imine, respectively.

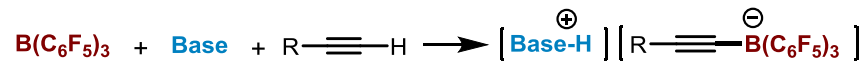


OM, 2017, 36, 2381; CEJ, 2017, 23, 10997

4. Activation of C-H bond and transformations

4.1 Examples on stoichiometric C-H bonds activation

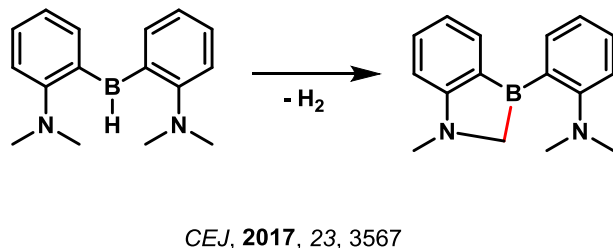
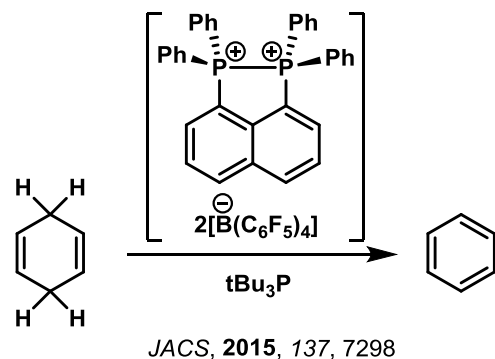
In 2009, Stephan et al. reported the stoichiometric cleavage of a terminal Csp-H bond by a mixture of P(*t*Bu)₃ and B(C₆F₅)₃.



Base = *t*Bu₃P, PhNMe₂, 2,6-lutidine, 2,2,6,6-tetramethylpiperidine

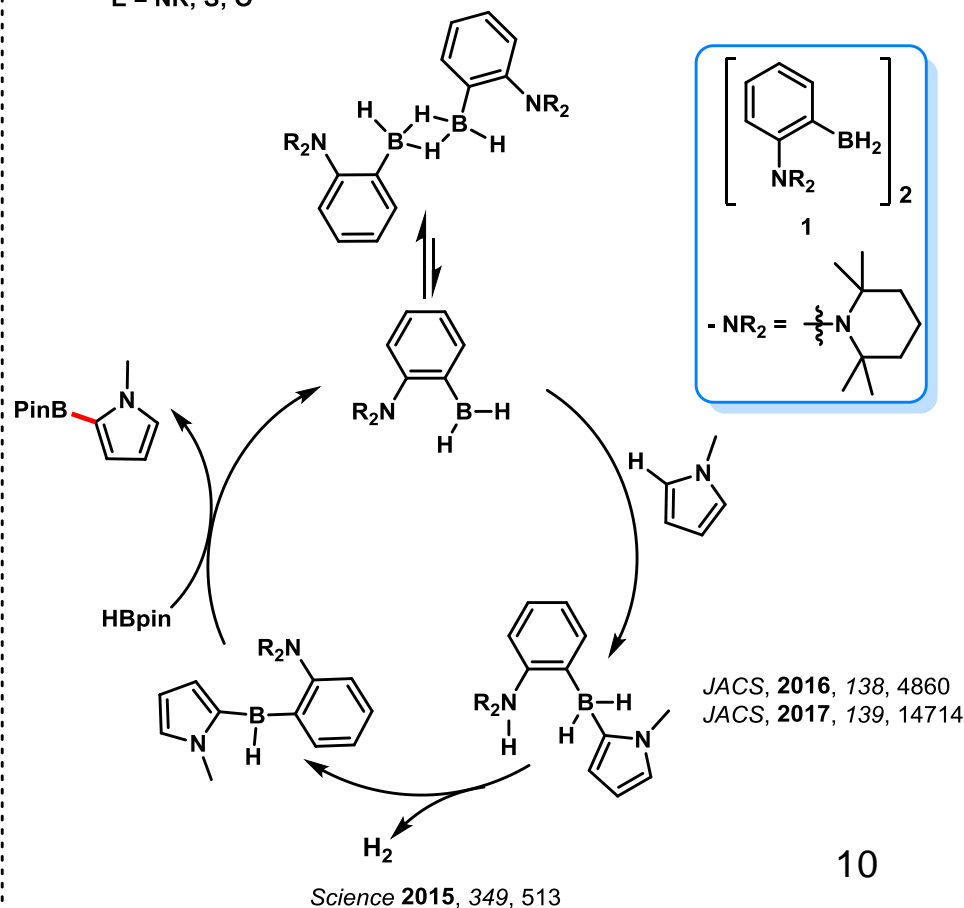
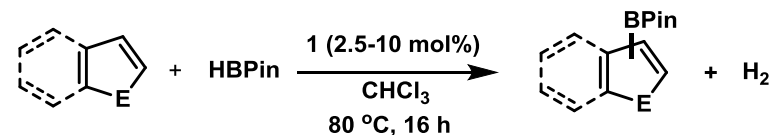
JACS 2009, 131, 8396; OM, 2010, 29, 125;
OM, 2012, 31, 2367; ACIE, 2016, 55, 14146

C(Sp³)-H bond



4.2 FLP-catalyzed C-H bonds activation and borylation

In 2015, Fontaine et al. reported C-H bond borylation of heteroarenes via FLP catalysis. It represents the first example of FLP-catalyzed C-H bond activation.

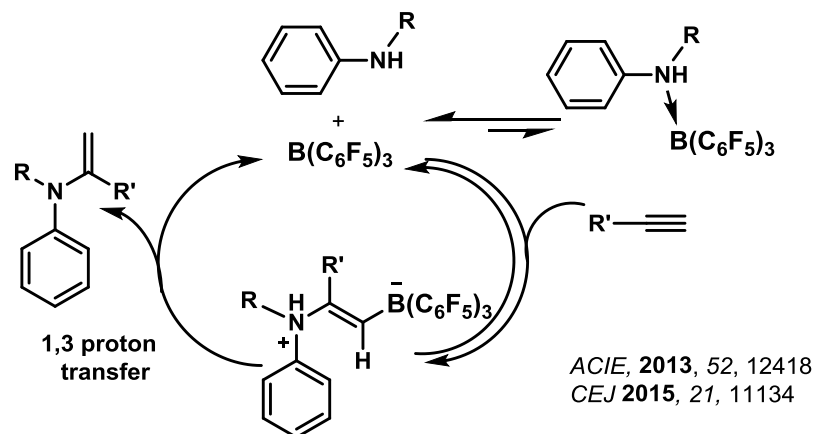
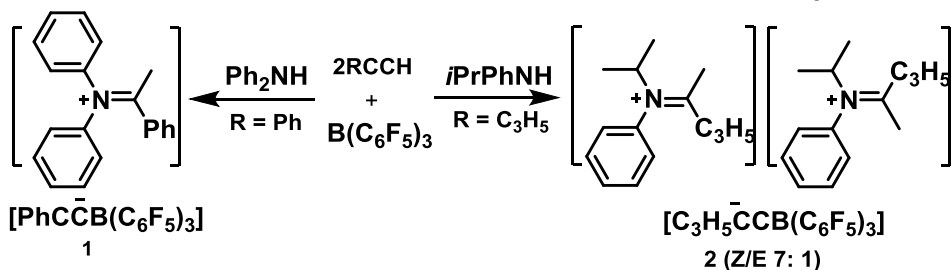
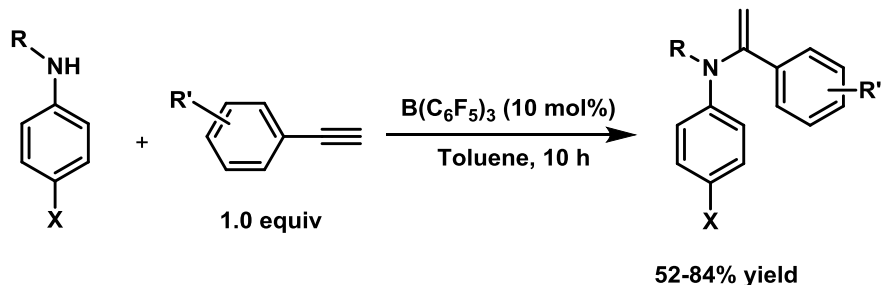


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5. Other catalytic transformation

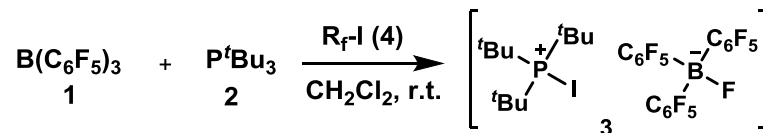
5.1 Hydroamination

In 2013, Stephan et al. reported Frustrated Lewis Pair catalyzed hydroamination of terminal alkynes

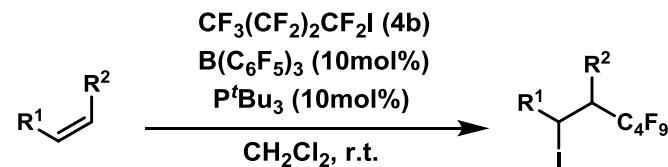


5.2 Difunctionalization of Alkenes

In 2016, Czekelius et al. reported perfluoroalkylation of alkenes by Frustrated Lewis Pairs



Entry	R_f-I	Time	Yield (%)
1	F_3C-I (4a)	20 min	65
2	C_4F_9-I (4b)	24 h	62
3	$C_8F_{17}-I$ (4c)	24 h	54
4	$C_4F_9-CF_2-I$ (4d)	20 min	85
5	$C_6F_{11}-I$ (4e)	60 min	75
6	$C_6F_5CF_2-I$ (4f)	30 min	70



CEJ 2016, 22, 17177

6. Outlooks

Catalytic C-H bond functionalization

Functionalization of carbon carbon multiple bonds

Asymmetric catalytic transformation

Catalytic usage of CO_2 , CO etc.