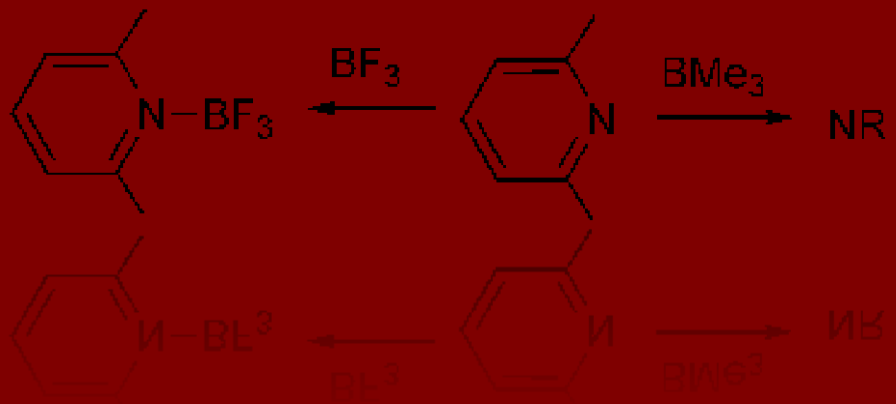


Frustrated Lewis Pairs

New Strategy for Small Molecule Activation & Catalysis

John Thompson
Dong Group Seminar
January 30th, 2013

Key Reviews:

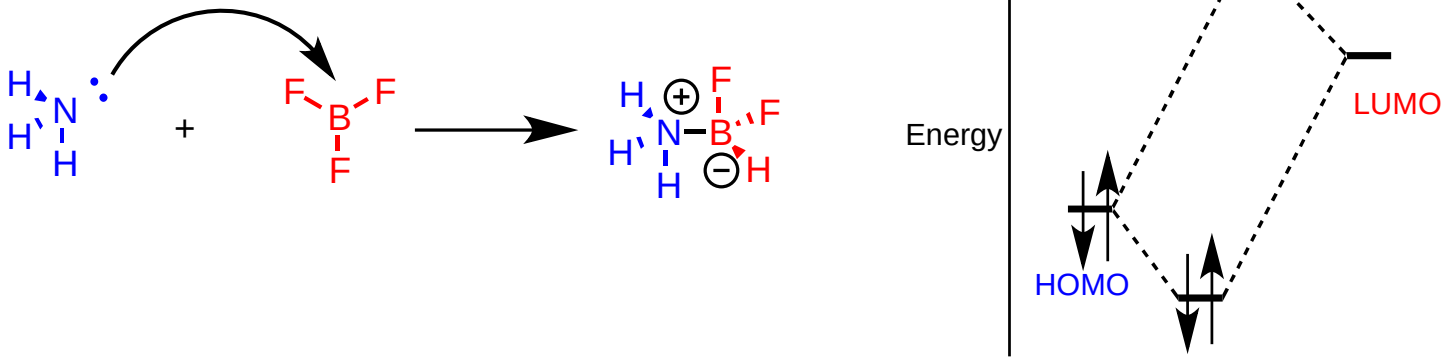
- *Dalton Trans*., **2009**, 3129.
- *Angew. Chem. Int. Ed.*, **2010**, *49*, 46.
- *Pure Appl. Chem.*, ***2012***, 84, *2203.*

Overview

- **“Frustrated Lewis Pair” (FLP)**
- **Historical Importance and Discovery**
- **H_2 activation**
- **Examples of FLPs**
- **Unusual Functional Group Reactivities**
- **Small Molecule Activation**
- **Future & Conclusion**

Acid/Base Pair History

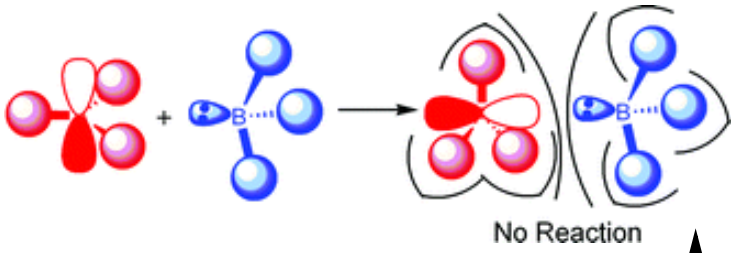
- 1923: Gilbert N. Lewis classified molecules that behave as electron-pair donors as bases and conversely electron-pair acceptor systems as acids.
  - Essential for understanding main-group and transition-metal chemistry

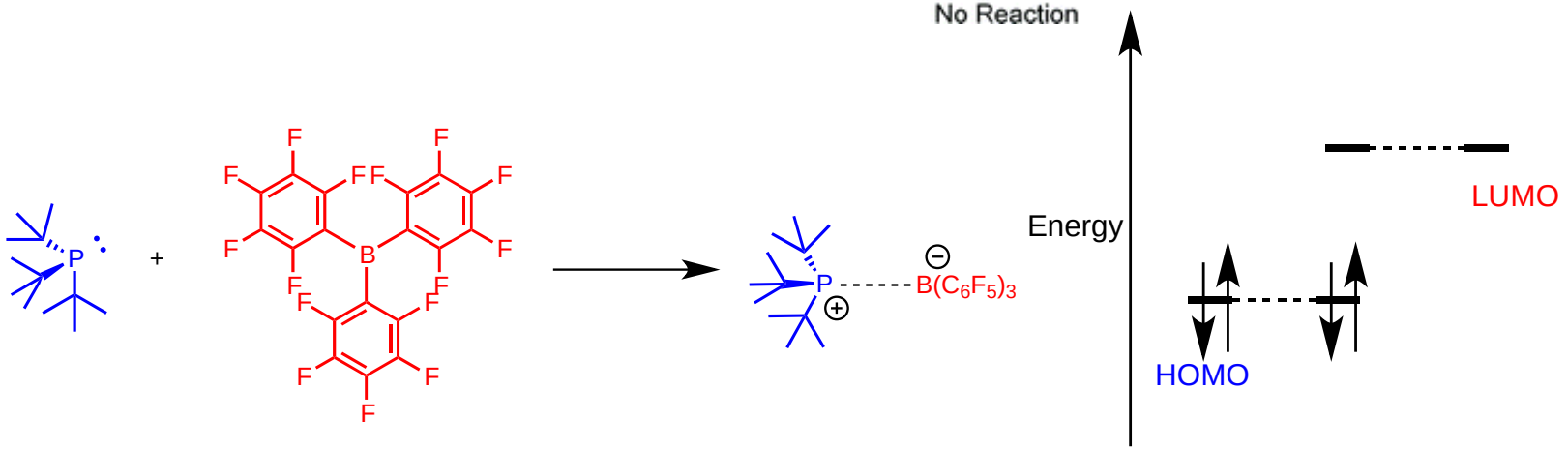


G. N. Lewis, *Valence and the Structure of Atoms and Molecules*, Chemical Catalogue Company, New York, **1923**.

So What is an FLP?

- **Frustrated Lewis Pairs** are a combination of Lewis acids and bases that are sterically precluded from forming Lewis acid–base adducts.

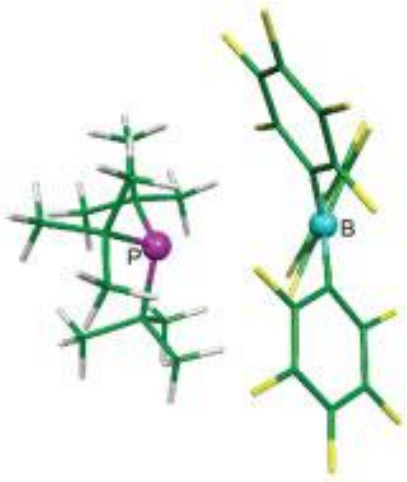




Welch, G.; San Juan, R.; Masuda, D.; Stephan, D. *Science*, **2006**, *314*, 1124.
Stephan, D. *Org. Biomol. Chem.*, **2008**, *6*, 1535.

So What is an FLP?

- **Frustrated Lewis Pairs** are a combination of Lewis acids and bases that are sterically precluded from forming Lewis acid–base adducts.
- "The last two decades has witnessed a spectacular renaissance in main group chemistry." - *Bourissou*

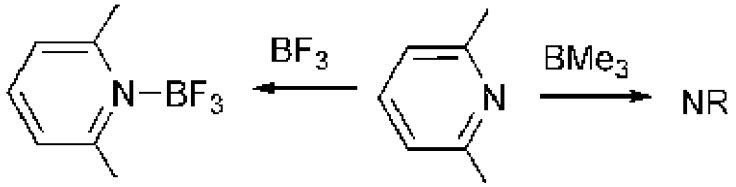


Preorganized LUMO and HOMO leads to "reactive pocket" which is the active site and leads to unique reactivity.

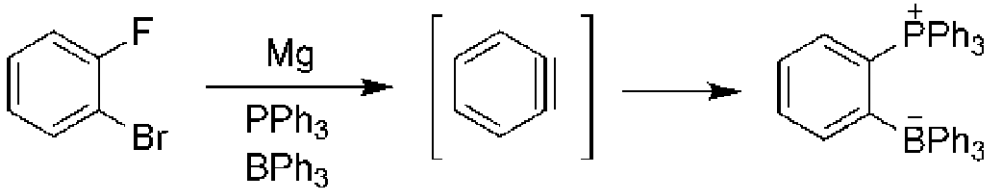
Hamza, A.; Stirling, A.; Rokob, T.; Pai, I. *Int. J. Quant. Chem.*, **2009**, *109*, 2416.

Frustrated Lewis Pair History

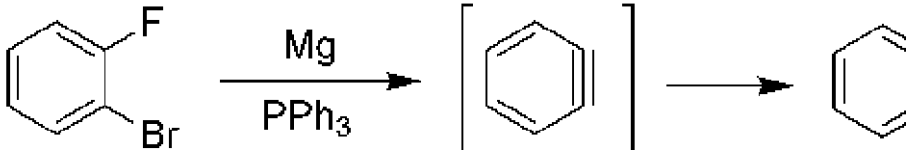
1942: Brown Lab



1959: Wittig Lab



1966: Tochtermann Lab

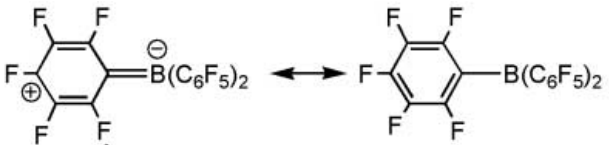


2006: Stephan Lab: exploring boranes and borane salts as activators for olefin polymerization.

H.C.Brown, H.I.Schlesinger, S.Z.Cardon, *JACS*, **1942**, *64*, 325.
G. Wittig, E. Benz, *Chem. Ber.*, **1959**, *92*, 1999.
W. Tochtermann, *Angew. Chem.*, **1966**, *78*, 355.

The Discovery

- First Reversible H_2 Activation! (Main Group Element)



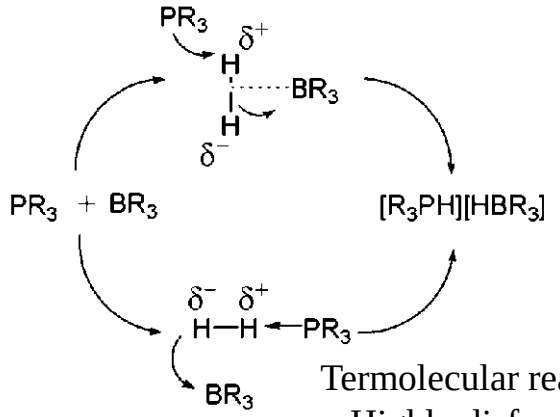
Frustrated Lewis Pair

Polarization of charge & π-stacking changed color

Welch, G.; San Juan, R.; Masuda, D.; Stephan, D. *Science*, **2006**, *314*, 1124.

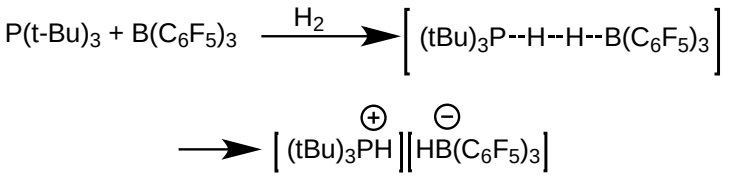
Mechanism of Activation

First Proposed Mechanisms:



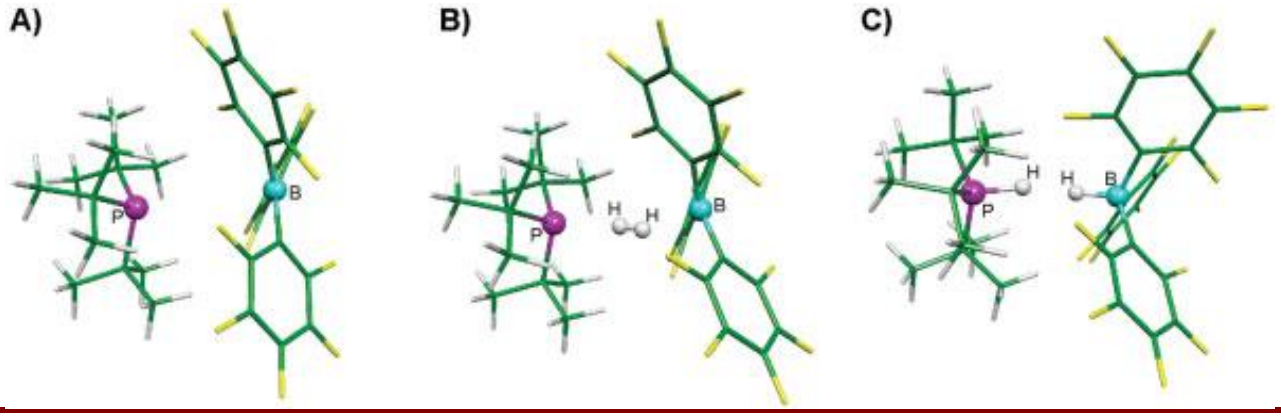
Termolecular reaction
Highly disfavored

Actual Mechanism:



Bond Cleavage/Formation is through synchronous transition state.

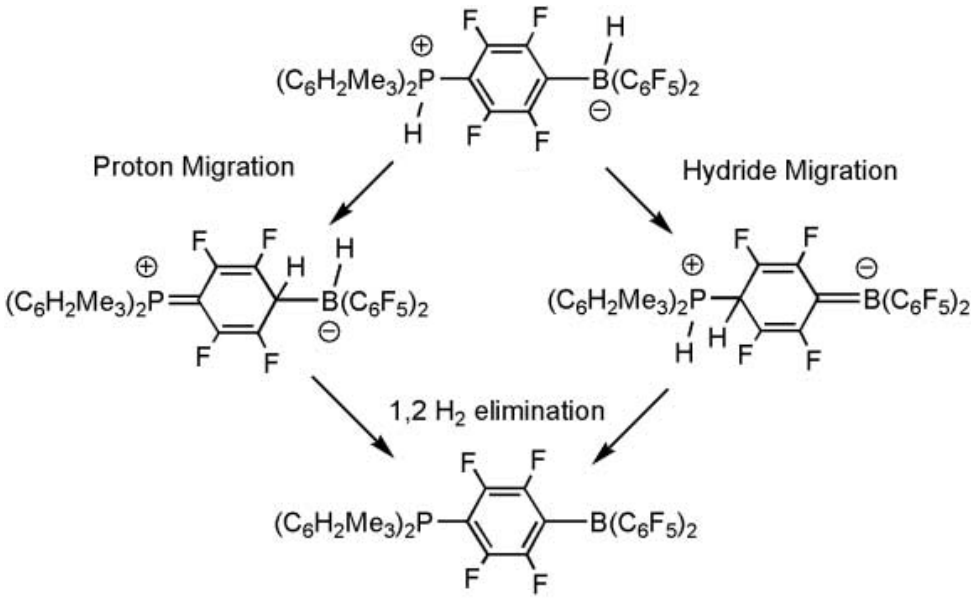
Simultaneous cleavage



Welch, G; Stephan, D. *JACS*, **2007**, *129*, 1880.
Hamza, A.; Stirling, A.; Rokob, T.; Pai, I. *Int. J. Quant. Chem.*, **2009**, *109*, 2416.

Mechanism of Release

- Hydride must migrate to carbon adjacent to either the boron or phosphine before elimination.
- Mechanism disputed, but since H_2 activation is initiated by boron (LA), microscopic reversibility should mean pathway lies toward proton migration



- Release usually requires heat to facilitate elimination.
- FLP structure plays key role.

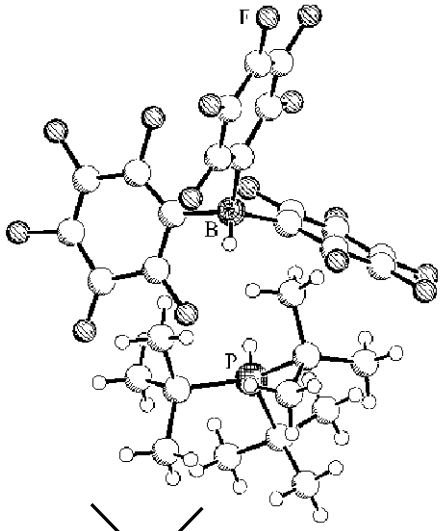
Welch, G.; San Juan, R.; Masuda, D.; Stephan, D. *Science*, **2006**, *314*, 1124.

One thing to Note

- Must balance acidity of phosphonium with hydricity of HB fragment to permit H_2 elimination and uptake.

$(C_6H_2Me_3)_3P + BPh_3$
$(C_6F_5)_3P + B(C_6F_5)_3$
$tBu_3P + BMes_3$
$Ph_3P + B(C_6F_5)_3$

$\xrightarrow[H_2]{25^oC}$ ✕



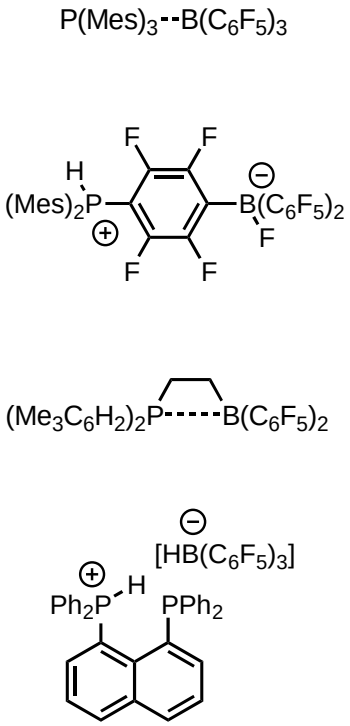
$tBu_3P + B(C_6F_5)_3 \xrightarrow[H_2]{25^oC} [tBu_3PH]^+ [HB(C_6F_5)_3]^- \xrightarrow{150^oC}$ ✕

This subject will be further discussed shortly…

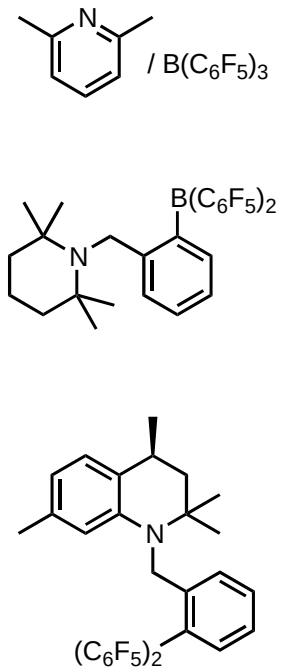
Welch, G; Stephan, D. *JACS*, **2007**, *129*, 1880.

Frustrated Lewis Pairs

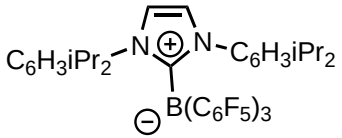
P/B Pairs



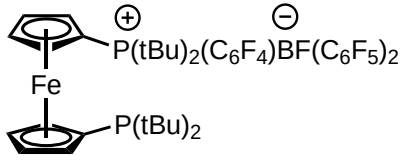
N/B Pairs



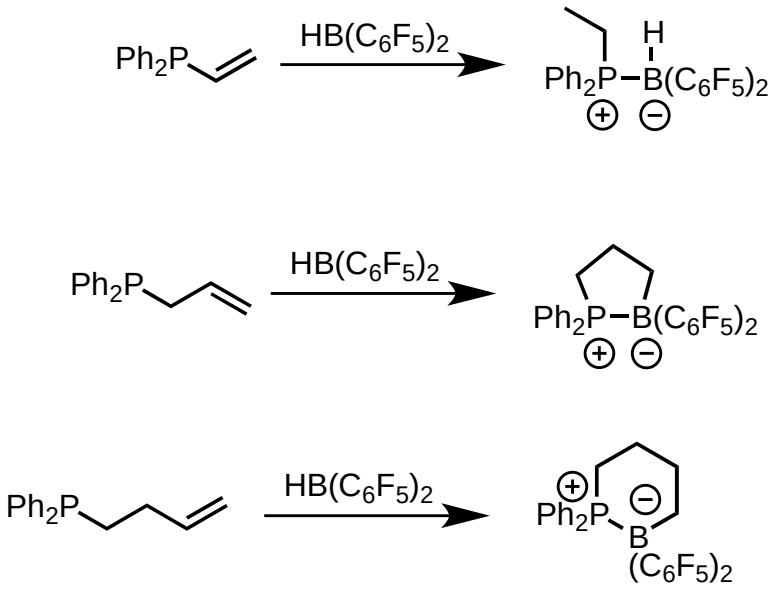
Carbene Pairs



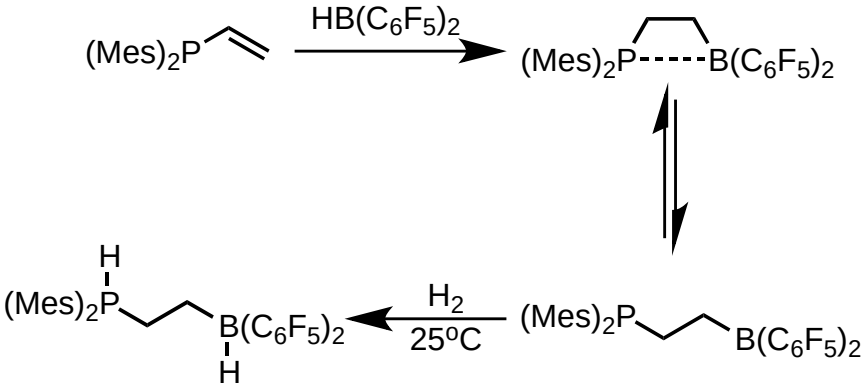
Metal Pairs



Intramolecular FLPs



"Piers' Borane"

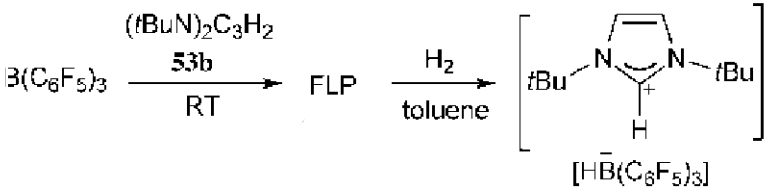


Reacts with 1.5 atm of H_2

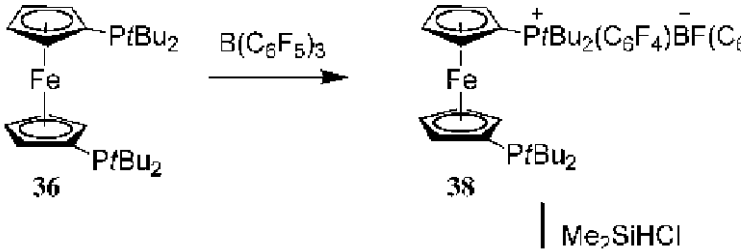
Stephan, D.; Erker G. *Angew. Chem. Int. Ed.*, **2010**, *49*, 46.
Erker *et al*. *Dalton Trans.*, **2009**, 1534.

Other H_2 Activation Systems

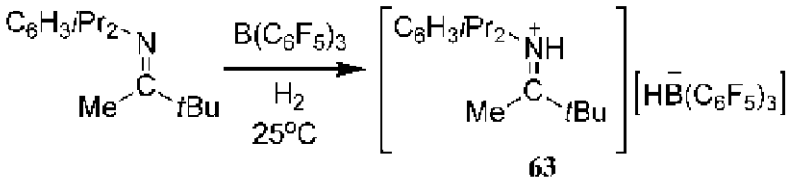
Carbenes



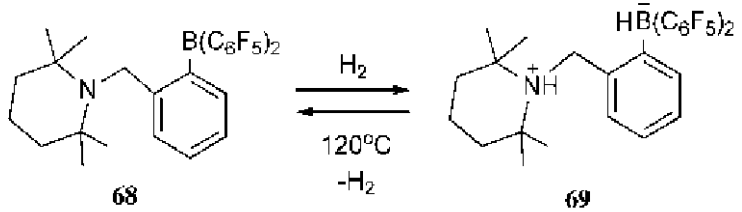
Phosphinometallocnes



Imines

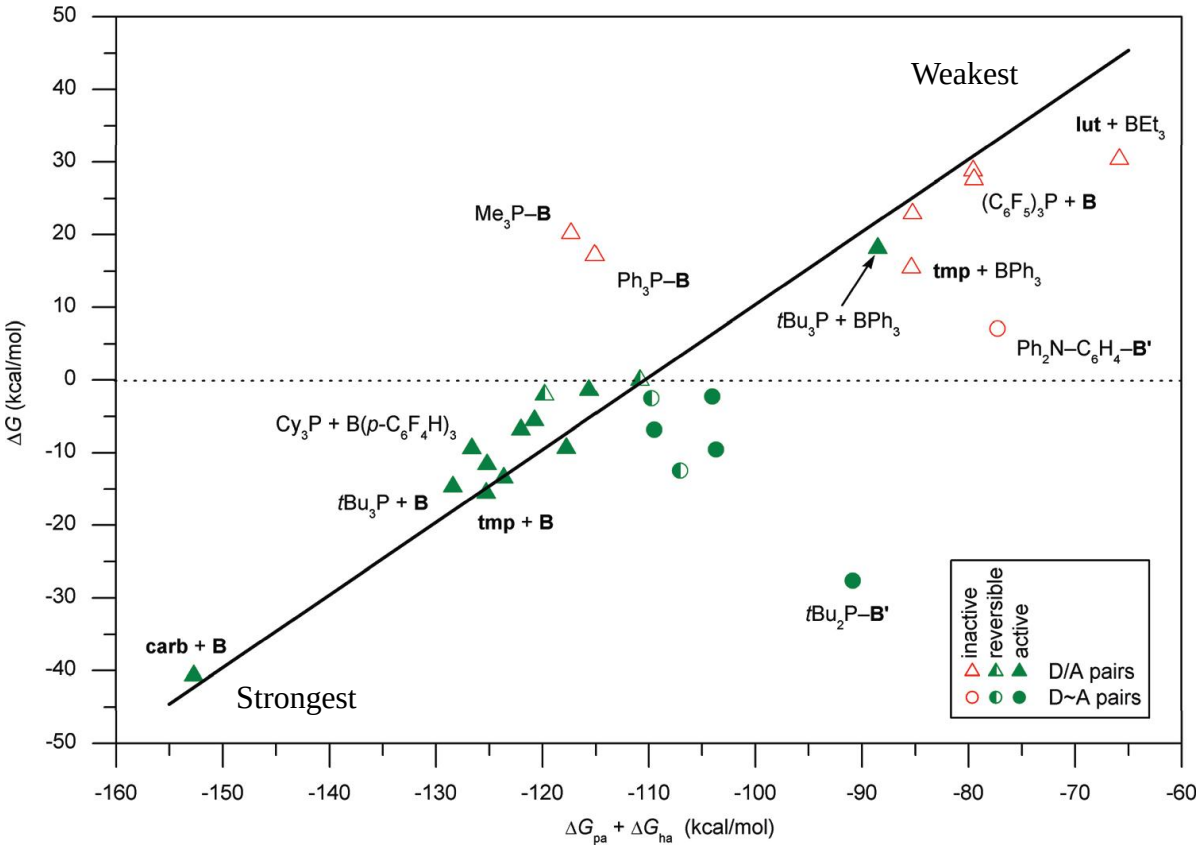


Amines



Stephan, D.; Erker G. *Angew. Chem. Int. Ed.*, **2010**, *49*, 46.

Final thoughts on H_2 Activation



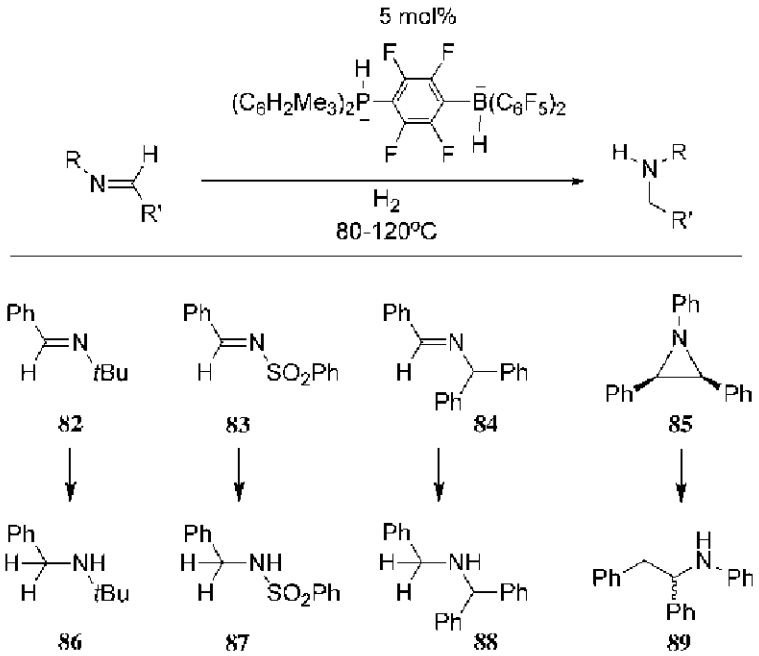
Acid/Base Pair Strength

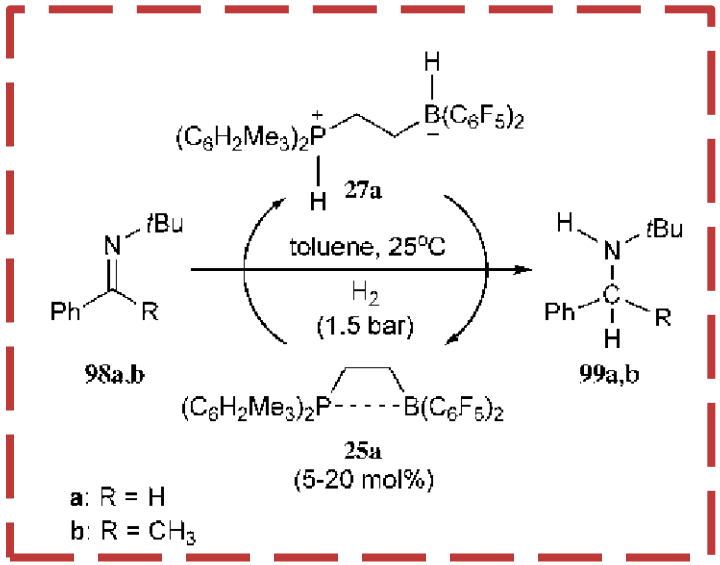
1. Key step: H-H heterolytic cleavage (103 kcal).
2. Strength of acid/base pairs directly correlates to thermodynamic interactions.
3. Linked Pairs: less entropic activation cost leads to reversibility.
   - Can utilize less acid/basic pairs
4. Kinetic roles have yet to be fulfilled.
5. tBu_3-BPh_3 is statistical anomaly.

Rokob, T.; Hamza, A.; Papai, I. *JACS*, **2007**, *131*, 10701.

Imine Hydrogenation

- Non-metal catalyzed hydrogenations

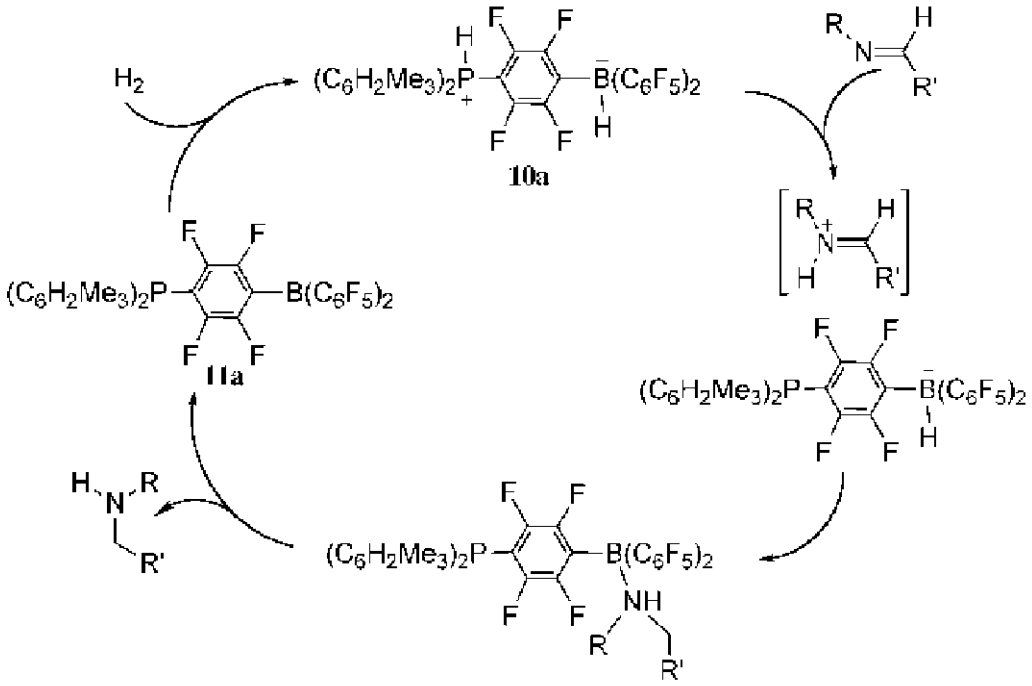




Chase, P.; Welch, G.; Jurca, T.; Stephan, D. *Angew. Chem. Int. Ed.*, **2007**, *119*, 8196.

Hydrogenation Mechanism

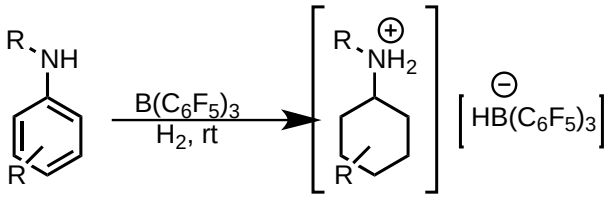
- Living Mechanism
  - >99% yield after 5 turnovers



Chase, P.; Welch, G.; Jurca, T.; Stephan, D. *Angew. Chem. Int. Ed.*, **2007**, *119*, 8196.

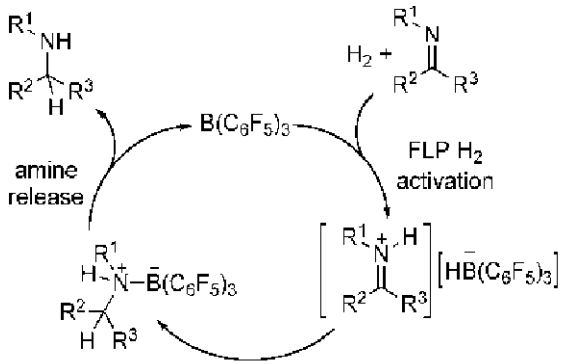
Catalytic Hydrogenation

- Also works for:
  - Enamines, Silylenol ethers, Nitriles, and Aldehydes (stoichiometrically)
- Aromatic Reduction (stoichiometric)



JACS, **2012**, *134*, 4088.

- Substrates can act as bases

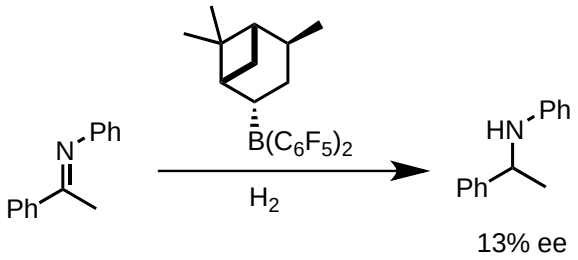


Lower yielding reaction due to imine being a poor base

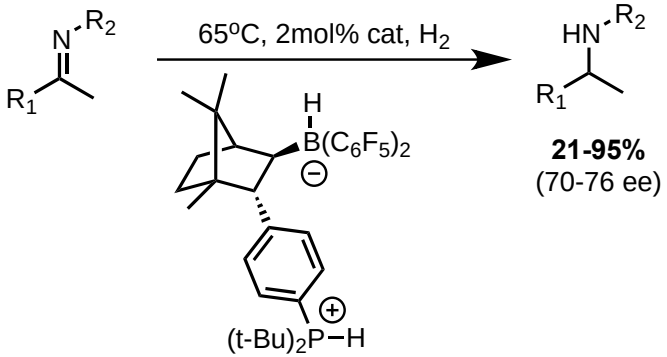
Stephan, D.; Erker G. *Angew. Chem. Int. Ed.*, **2010**, *49*, 46.
Chase, P.; Welch, G.; Jurca, T.; Stephan, D. *Chem. Commun.*, **2008**, 1701.

Chiral Hydrogenation

- Chiral Borane



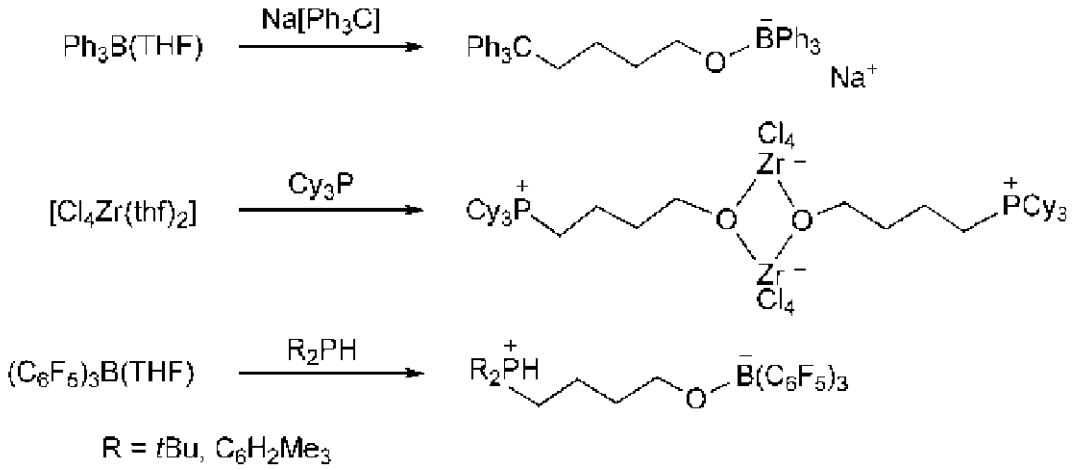
- Chiral FLP



Ghattas, G.; Chen, D.; Pan, F.; Klankermayer, J. *Dalton. Trans.*, **2012**, *41*, 9026.

Small Molecule Activation

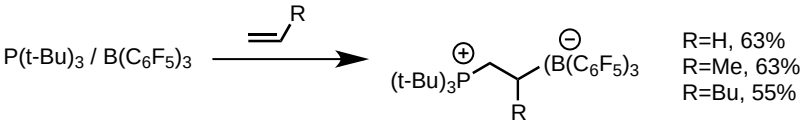
- FLPs retain same reactivity patterns as their individual lewis acid and base components.
- Add cooperatively to substrates
- Initial Discovery: 1950 – THF Ring Opening

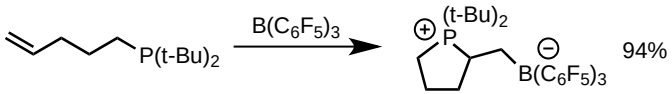


Breen, T.; Stephan, D. *Inorg. Chem.*, **1992**, *31*, 4019.

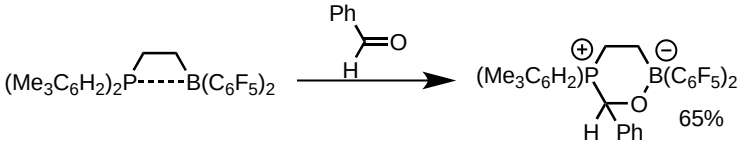
Unsaturated Hydrocarbons

- Alkenes

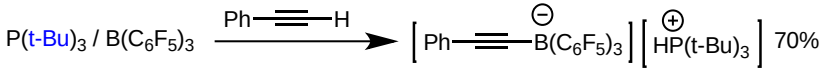




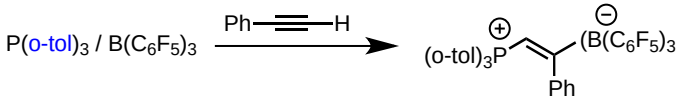
- Carbonyls



- Alkynes



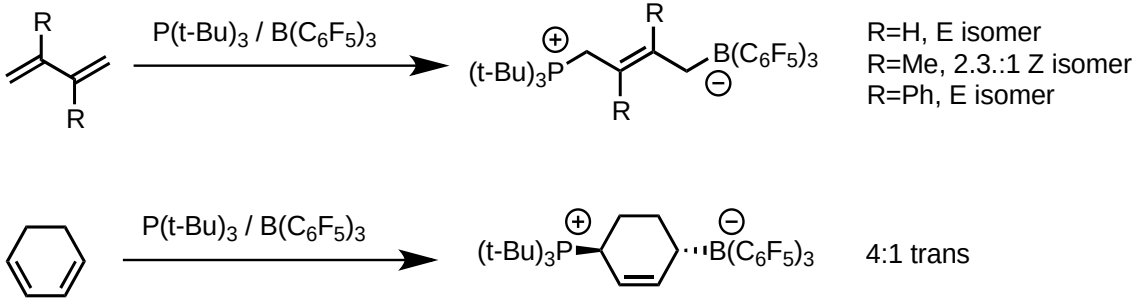
- Acidic proton causes deprotonation
- Steric bulk inhibits addition.



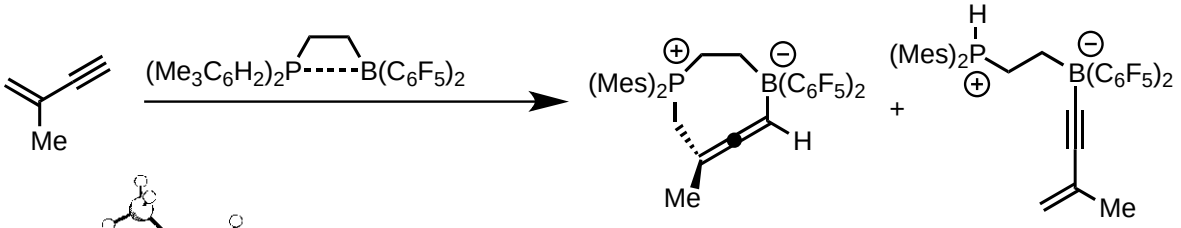
- Using decreased lewis basicity promoted addition product
- Sterics reduced.

Unsaturated Hydrocarbons

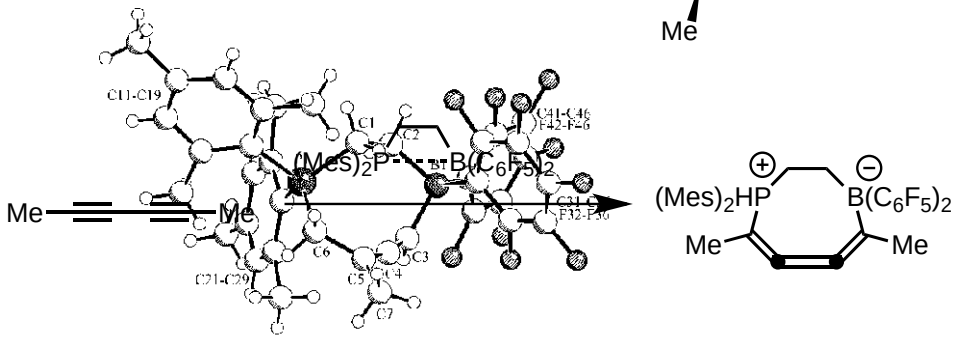
- Dienes



- Enynes



- Diynes

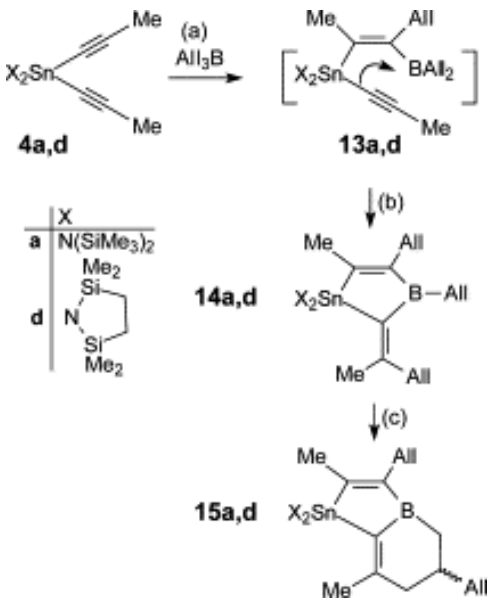


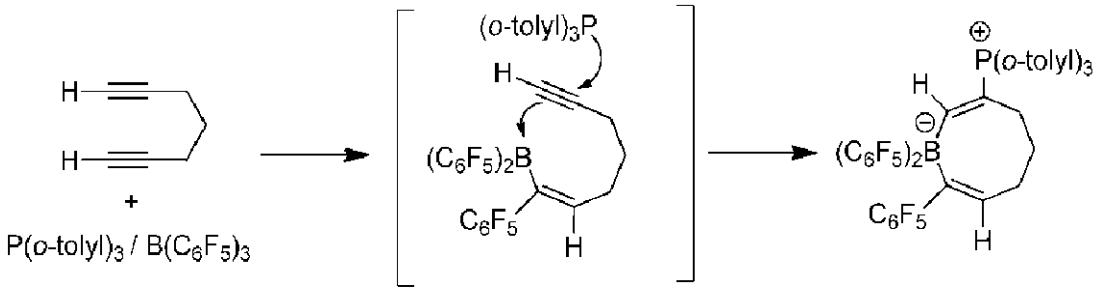
Ulrich, M.; Seto, K.; Lough, A.; Stephan, D. *Chem. Comm.*, **2009**, *2335*.

Momming, C.; Wibbeling, B.; Frohlich, R.; Schirmer, B, Grimme, S.; Ecker, G. *Angew. Chem. Int. Ed.*, **2010**, *49*, 2414.

1,1-Carboboration

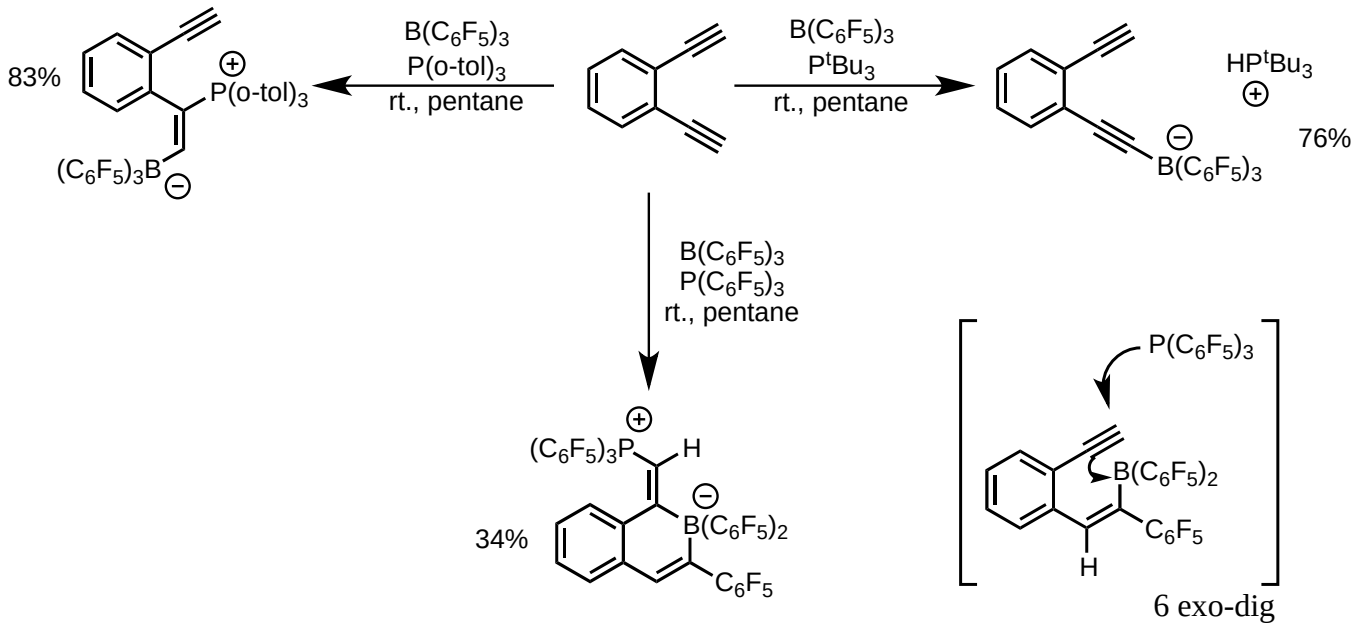
- Wrackmeyer Reaction
  - Historically shown with Si, Sn, or Pb alkynes
  - Strong electrophillic borane promoted cyclization over depronation or 1,2 addition
- FLP Chemistry
  - Use diynes to promote 1,1-carboboration





Wrackmeyer, B.; Pedall, A.; Milus, W.; Tok, O.; Bubnov, Y. *J. Org. Chem.*, **2002**, *649*, 232.
Chen, C.; Frohlich, R.; Kehr, G.; Erker, G. *Chem. Commun.*, **2010**, *46*, 3580.

Controlling FLP Reactivity

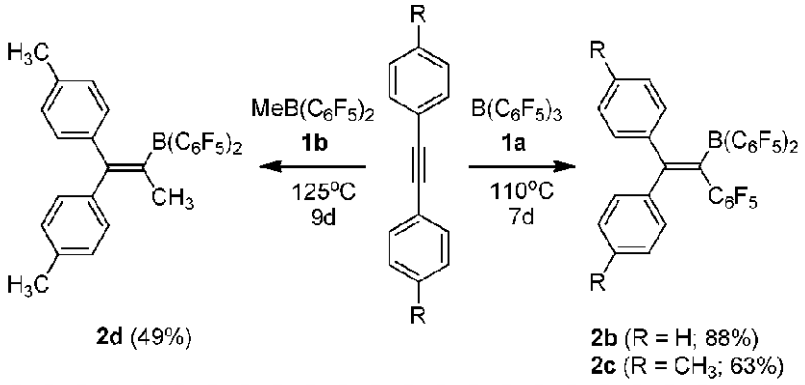


- Need very lewis acidic boron for reaction
- Varrying phosphane lewis basicity/sterics causes different reactivity patterns
- 1,1-Carboboration is fast

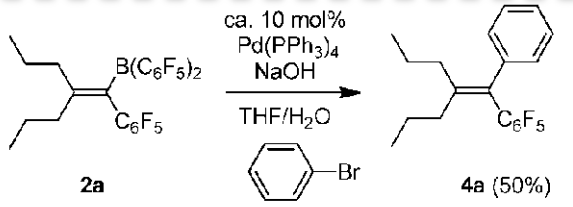
Liedtke, R.; Frohlich, R.; Kehr, G.; Erker, G. *Organometallics*, **2011**, *30*, 5222.

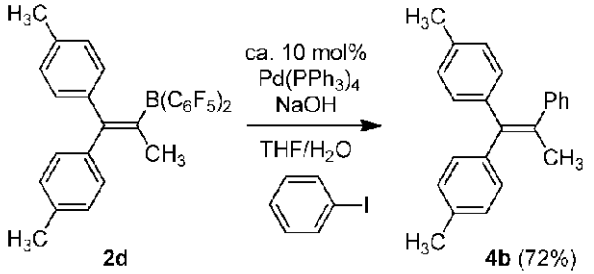
C-C Activation

- Selective migration in 1,1-carboboration
- Simple conditions
  to break the C-C bond



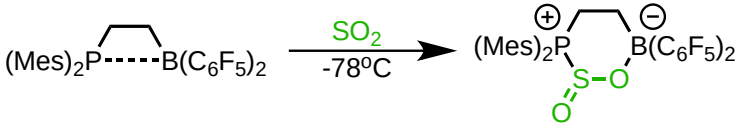
- Suzuki-Miyaura coupling
- Pd-catalyzed arylation



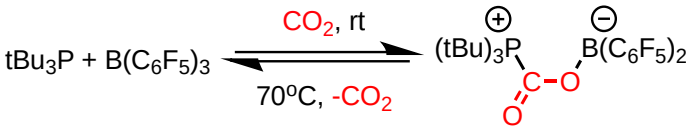


Chen, C.; Kehr, G.; Frohlich, R.; Erker, G. *JACS*, **2010**, *132*, 13594.

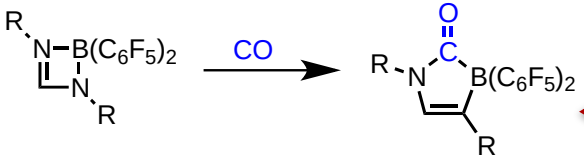
Activation of Small Molecules



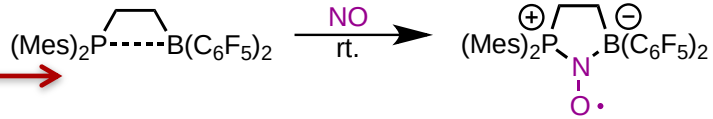
Chem. Sci., **2013**, *4*, 213.



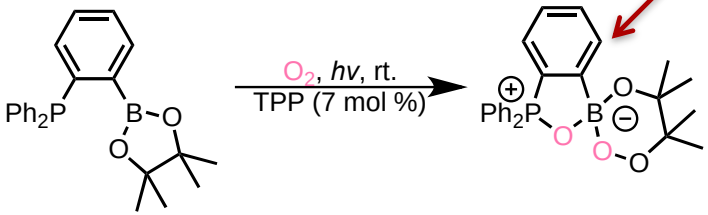
Angew. Chem. Int. Ed., **2009**, *498*, 66436.



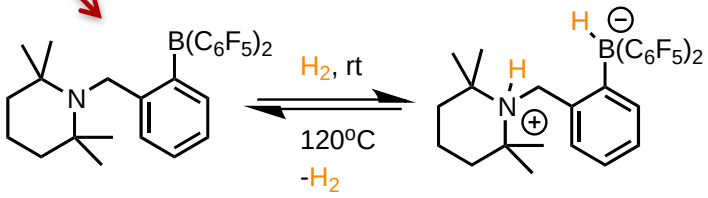
JACS, **2010**, *132*, 13559.



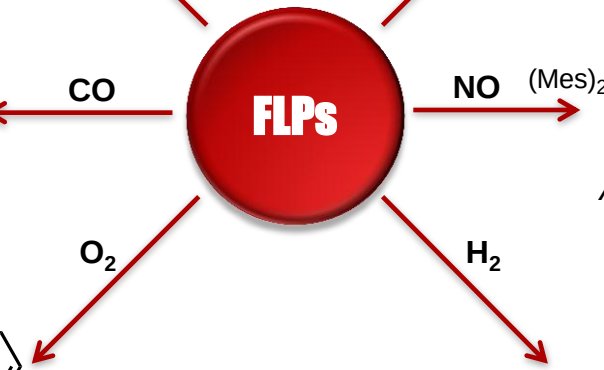
Angew. Chem. Int. Ed., **2011**, *50*, 7576.



Angew. Chem. Int. Ed., **2010**, *49*, 6186.



JACS, **2008**, *130*, 14117.



And more to be discovered...

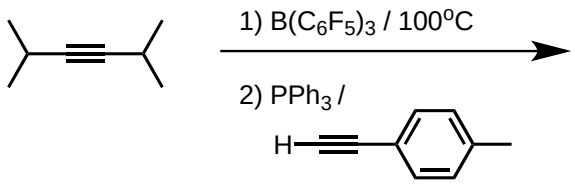
Conclusion

- FLP reactivity presents a unique way to form new C-C bonds.
    - May find use in future synthetic methods
- FLP catalytic reduction offers a very appealing and cost-effective method.
    - Asymmetric catalysis is key
- Reversible activation of gases offers new pathway for gas storage
    - Not answer due to each FLP activating 1 molecule of gas
    - Future applications in MOF or materials chemistry
- Could be useful for new ligand development in organometallic chemistry

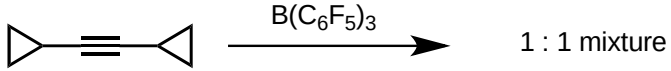
Questions?

Questions

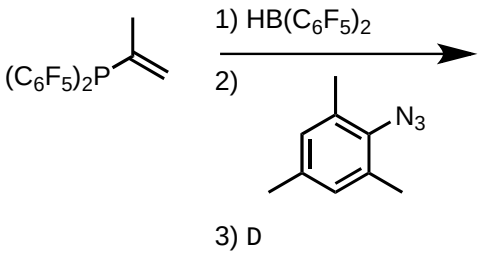
- 1)



- 2)

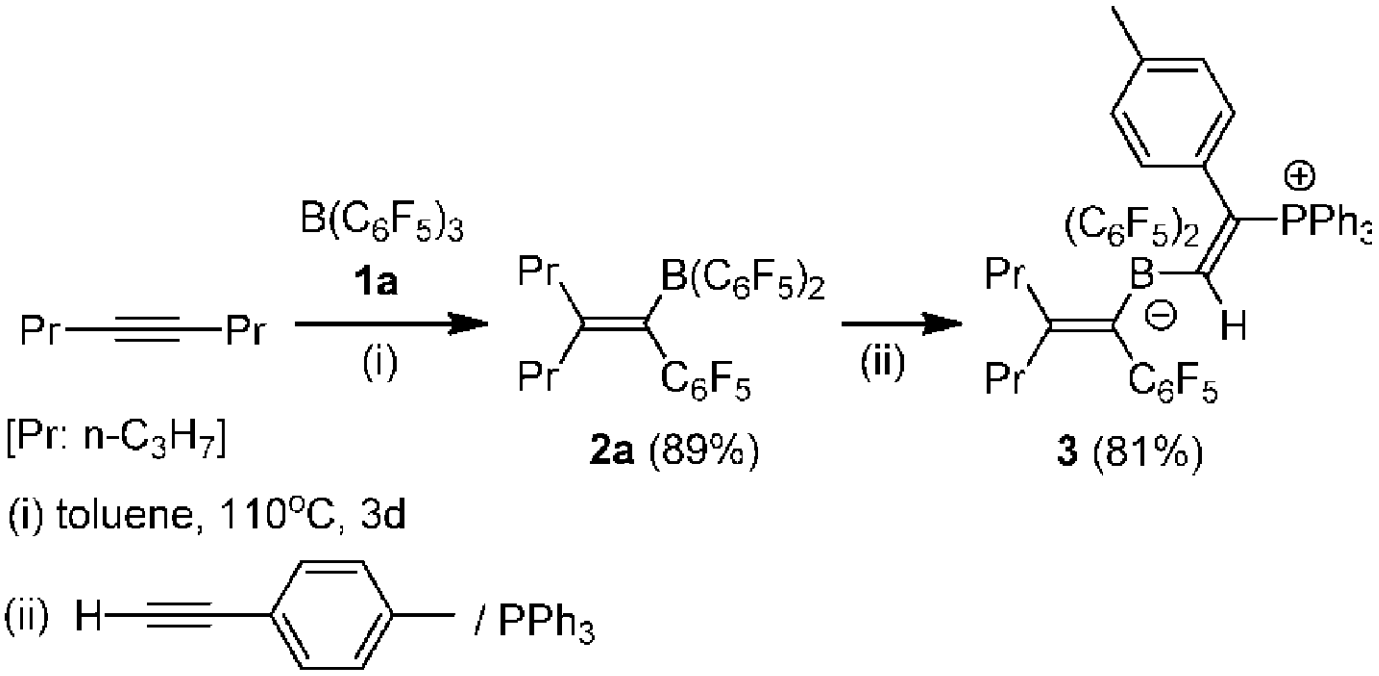


- 3)



FLP Reactions

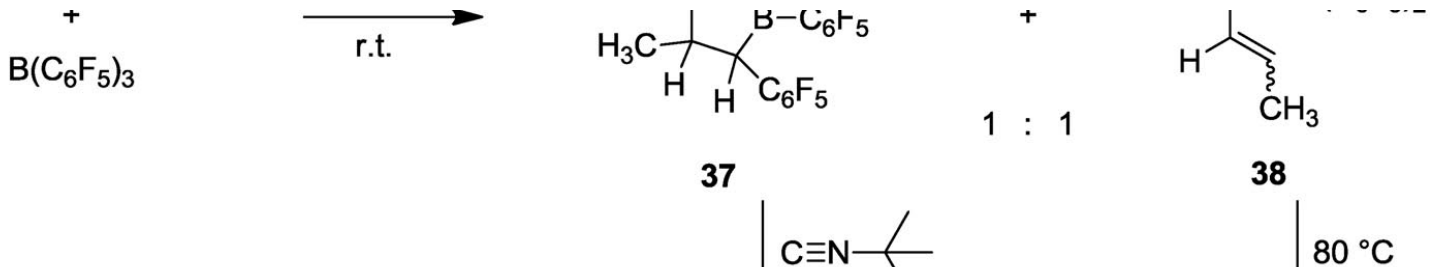
- Question 1



Chen, C.; Kehr, G.; Frohlich, R.; Erker, G. *JACS*, **2010**, *132*, 13594.

1,1-Carboboration

- Question 2



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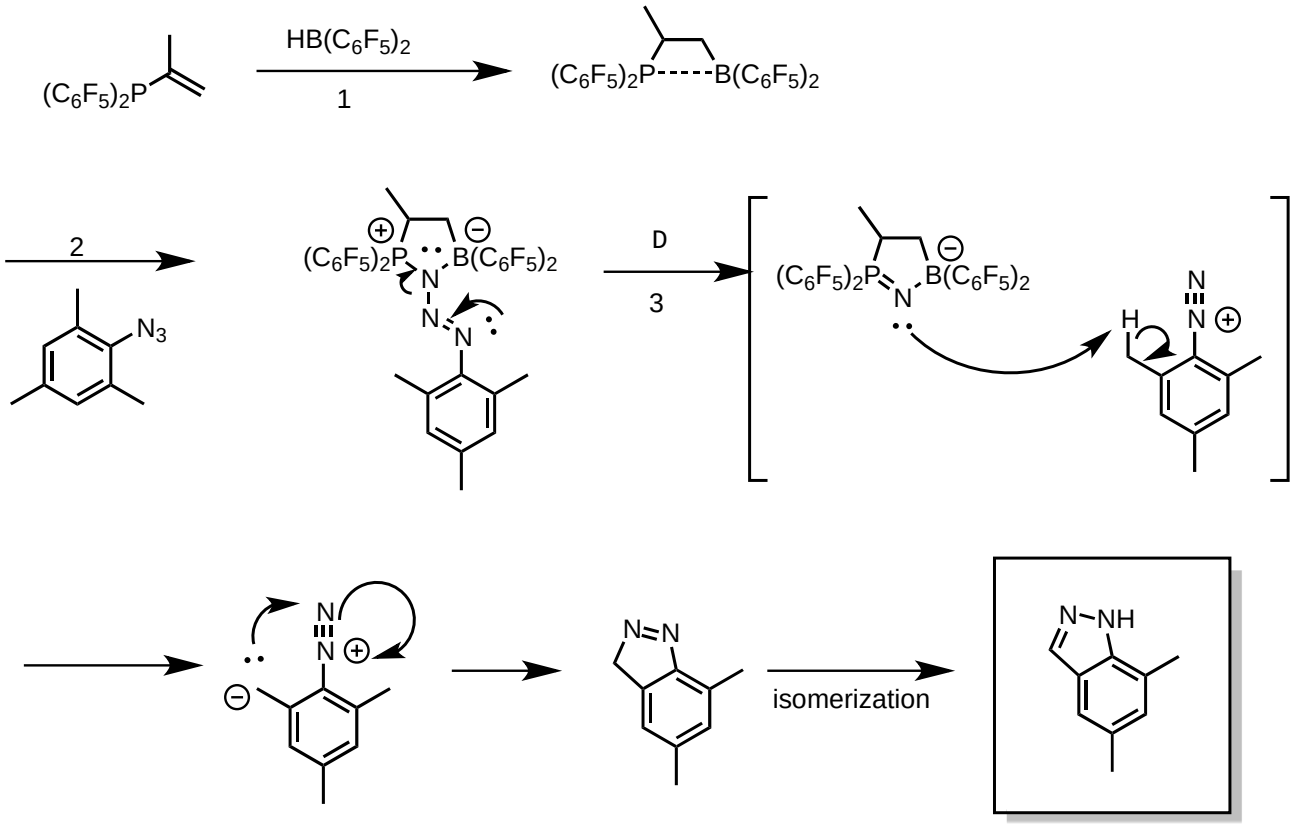
Staudinger Reaction

- Question 3



Chem. Commun., **2012**, *48*, 11739.