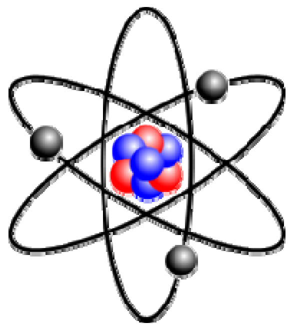
中国科学院上海有机化学研究所
Shanghai Institute of Organic Chemistry, CAS

Electron ——
A Catalyst in Organic Chemistry



Jian Rong（荣 健）

Jan 5th , 2015

The Hu Group

Outline

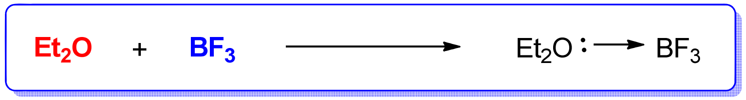
- **Introduction**
  — *Electrons in organic chemistry*
  — *Catalysts in organic chemistry*

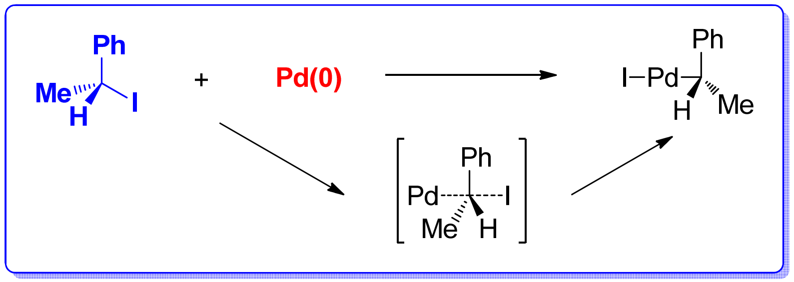
- **Electron as A Catalyst in Organic Chemistry**
  — *Acid/Base catalysis*
  — *Redox catalysis (electron/hole catalysis)*
  — *Examples of electron-catalyzed reactions*

- **Summary**

Introduction

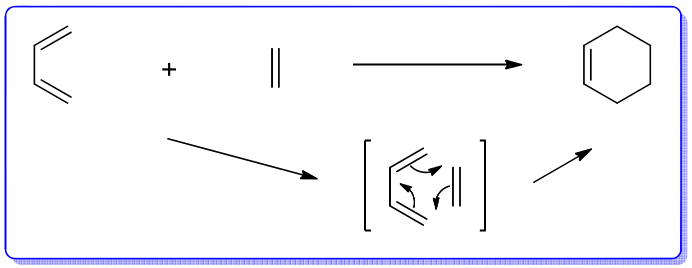
Most reactions in organic chemistry are acid-base (Lewis acid and Lewis base) reactions.





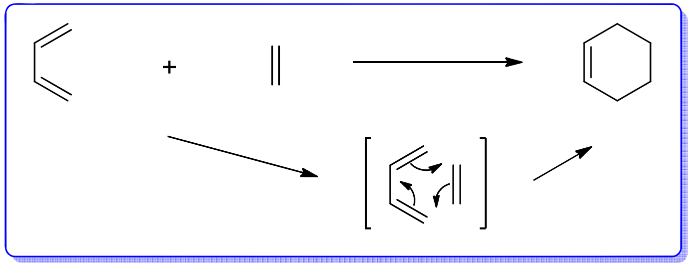
Acid (in red)
Base (in blue)

There are also exceptions: pericyclic reaction, etc.



Electrons in organic chemistry

All reactions in organic chemistry involve electrons.



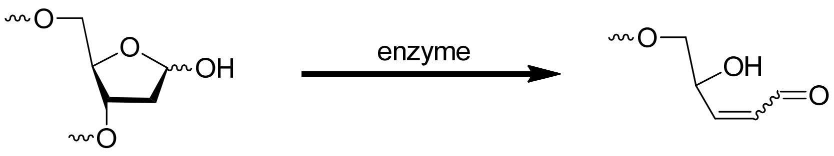
There is no exception.

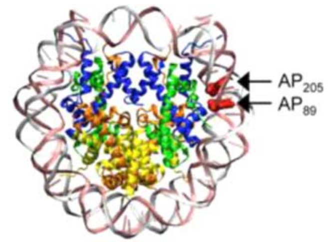
How the electron can be a catalyst in organic chemistry?

Catalysts in organic chemistry

Catalysts:

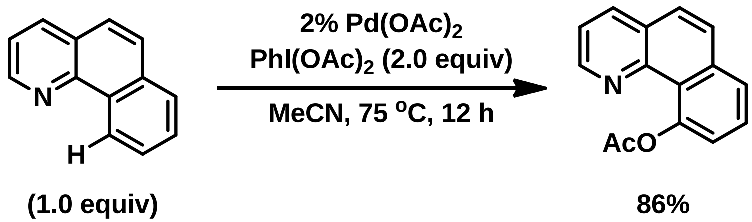
Enzymes





Zhou, C.; Sczepanski, J. T.; Greenberg, M. M. *J. Am. Chem. Soc.* **2012**, *134*, 16734.

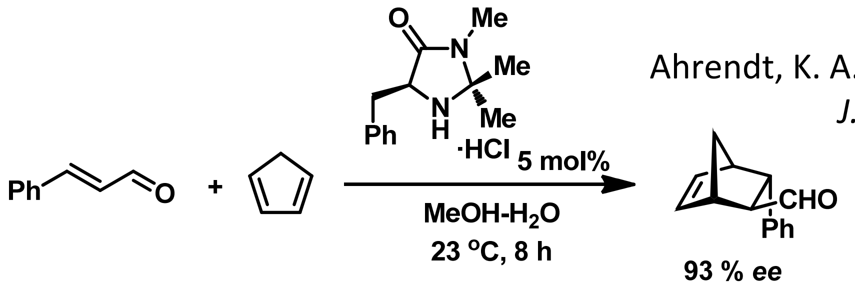
Transition metals (and complexes)



Dick, A. R.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 2300.

Organocatalysts (Lewis acids and bases etc.)

Ahrendt, K. A.; Borths, C. J. MacMillan, D. W. C. *J. Am. Chem. Soc.* **2000**, *122*, 4243.



……

Catalysts in organic chemistry

The smallest catalysts are not the organocatalysts (such as *L*-proline), and they are two principal charged atomic particles: the proton (H^+) and the electron (e^-), although each particle is accompanied in solution by a counterion.

proton is small (1.0 g mol^{-1})

electron is tiny (0.55 mg mol^{-1})

For **proton as a catalyst**

Add a proton——acid catalysis

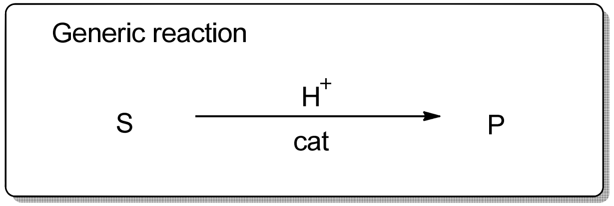
Remove a proton——base catalysis

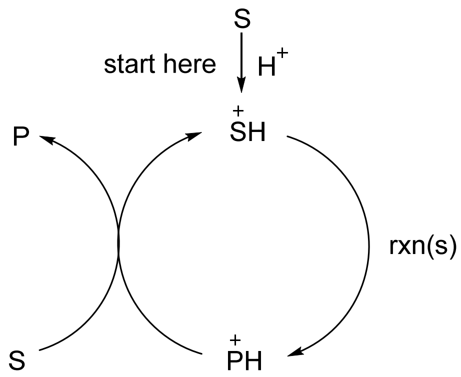
Studer, A.; Curran, D. P. *Nature Chem.* **2014**, *6*, 765.

Acid catalysis

For **proton** as a catalyst

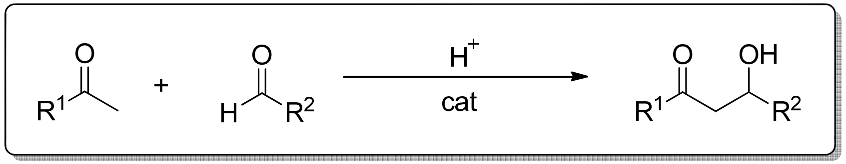
Add a proton——acid catalysis

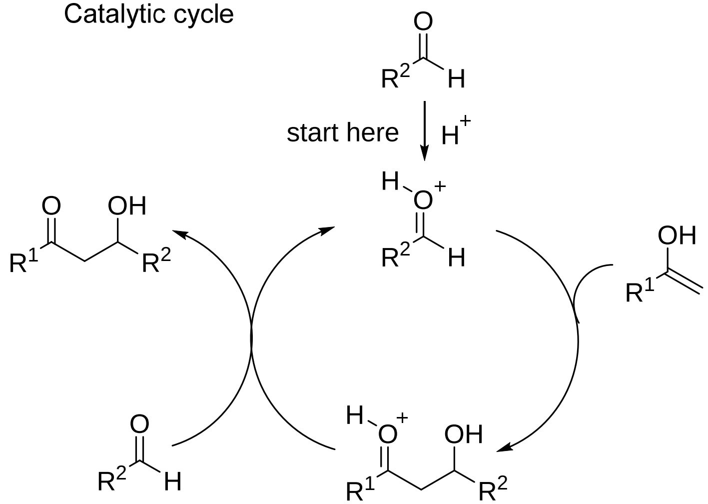




Catalytic cycle

Acid-catalyzed cross aldol reaction



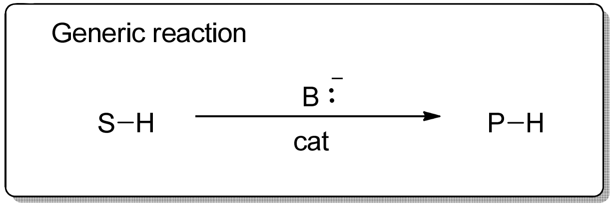


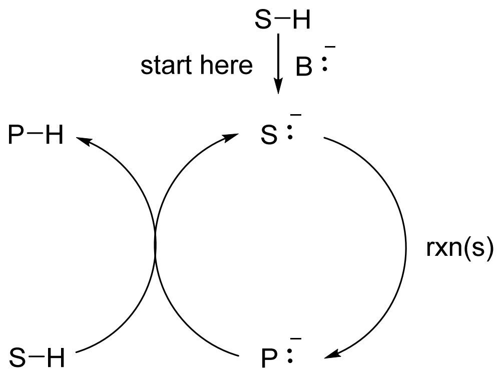
Catalytic cycle

Base catalysis

For **proton as a catalyst**

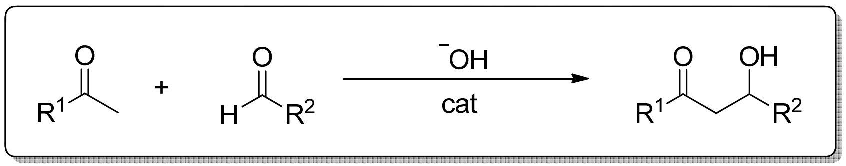
Remove a proton——base catalysis

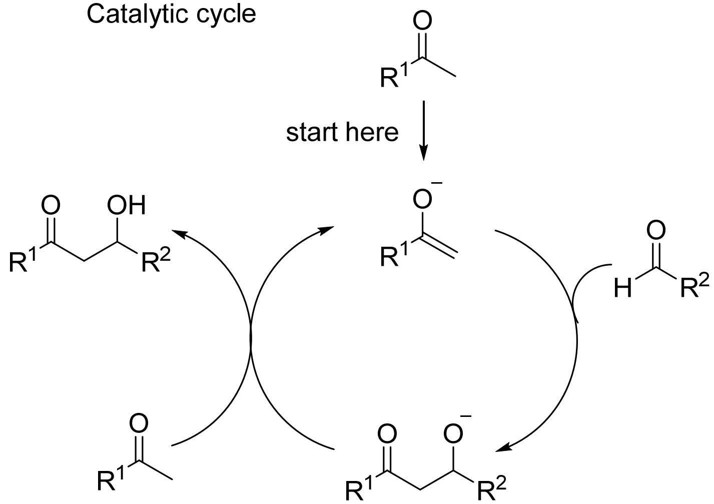




Catalytic cycle

Base-catalyzed cross aldol reaction



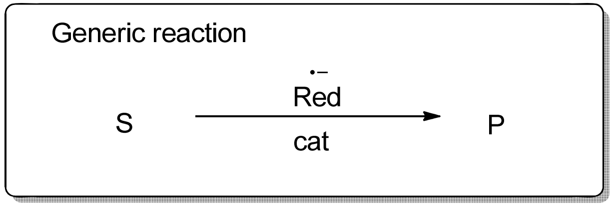


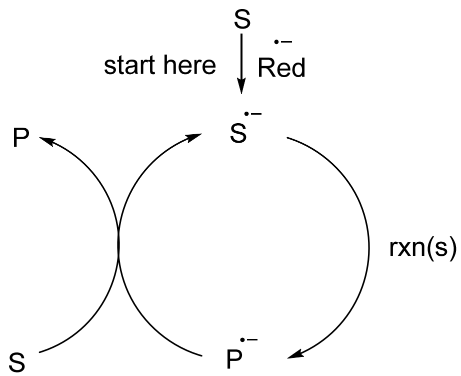
Catalytic cycle

Electron catalysis

For **electron as a catalyst**

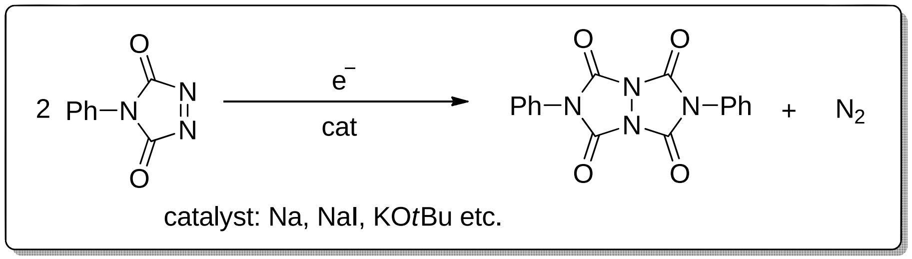
Add a electron——electron catalysis

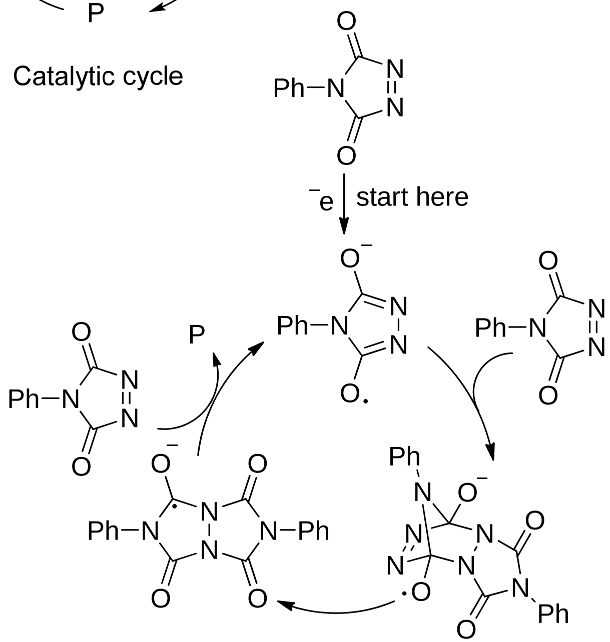




Catalytic cycle

Electron-catalyzed Diels-Alder reaction



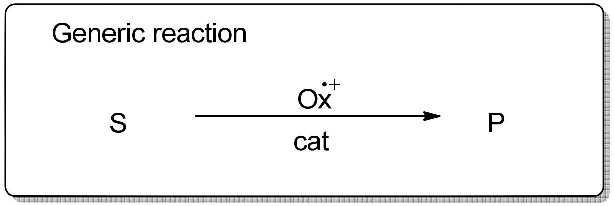


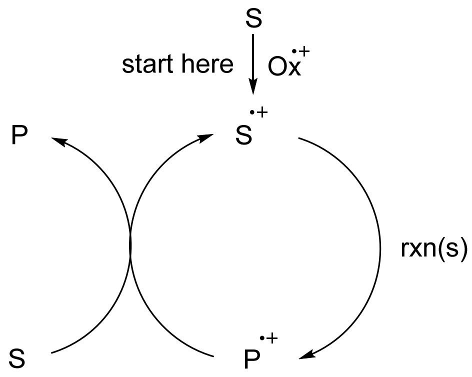
Catalytic cycle

Hole catalysis

For **electron** as a catalyst

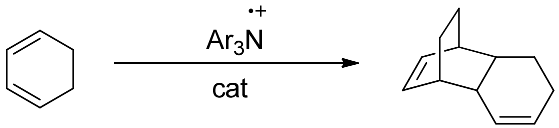
Remove a electron——hole catalysis

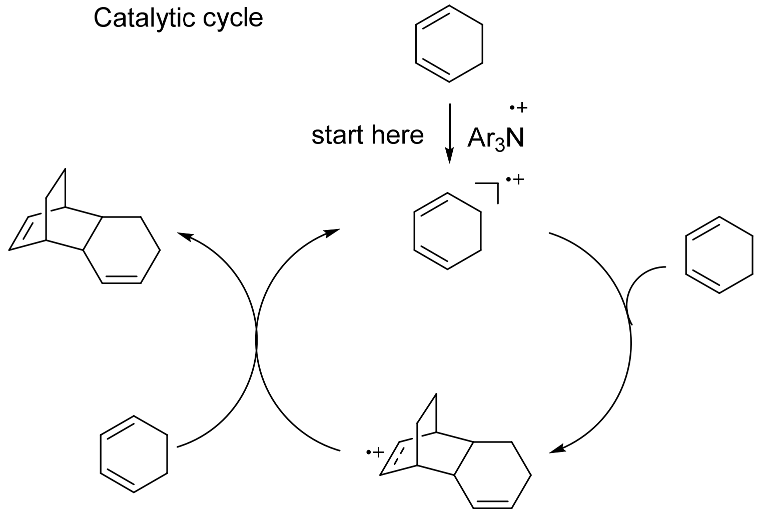




Catalytic cycle

Hole-catalyzed Diels-Alder reaction





Catalytic cycle

Redox catalysis

For **electron** as a catalyst

Add a electron——electron catalysis
Remove a electron——hole catalysis

EIC: electron-induced catalysis
ETC: electron transfer catalysis
DAISET: double activation induced by single electron transfer

Redox catalysis

Invovle reaction intermediates either one oxidation-state level above or one level below that of the substrates and products.

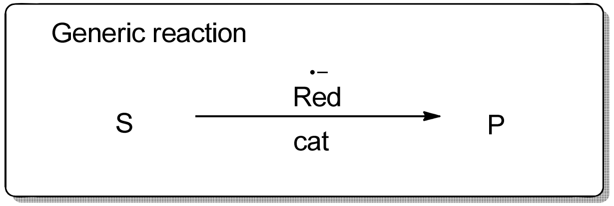
During a redox-catalyzed reaction, an electron is temporarily added or removed. The process of electron addition/removal is variously called :

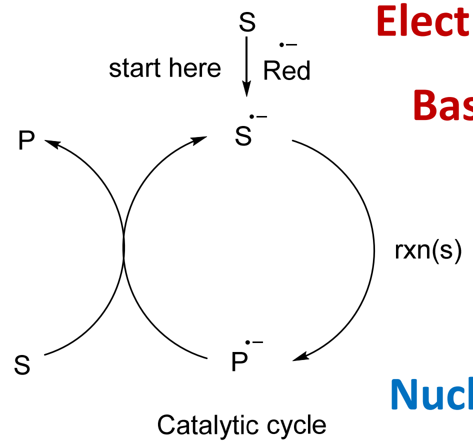
ET: electron transfer ,
SET: single-electron transfer ,
CT: charge transfer,
PET: photoinduced electron transfer

Redox catalysis

For **electron** as a catalyst

Add a electron——electron catalysis





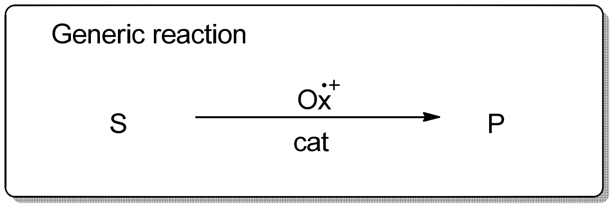
Electron-catalyzed reactions

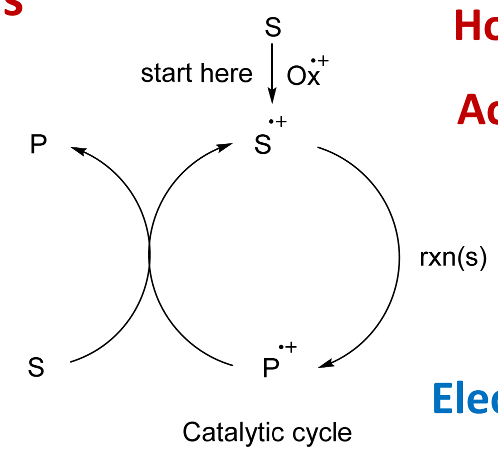
Base-catalysed reactions

Nucleophilic intermediates

For **electron** as a catalyst

Remove a electron——hole catalysis





Hole-catalyzed reactions

Acid-catalysed reactions

Electrophilic intermediates

Redox catalysis

Intermediates In Organic Synthesis

- ✓ Carbanions
- ✓ Carbocations
- ✓ Carbenes
- ✓ Neutral radicals

- ✓ Radical cations
- ✓ Radical anions

} Redox catalysis

↑

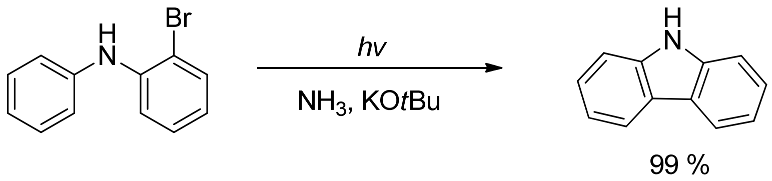
Chemical oxidation or reduction

Electrochemical processes

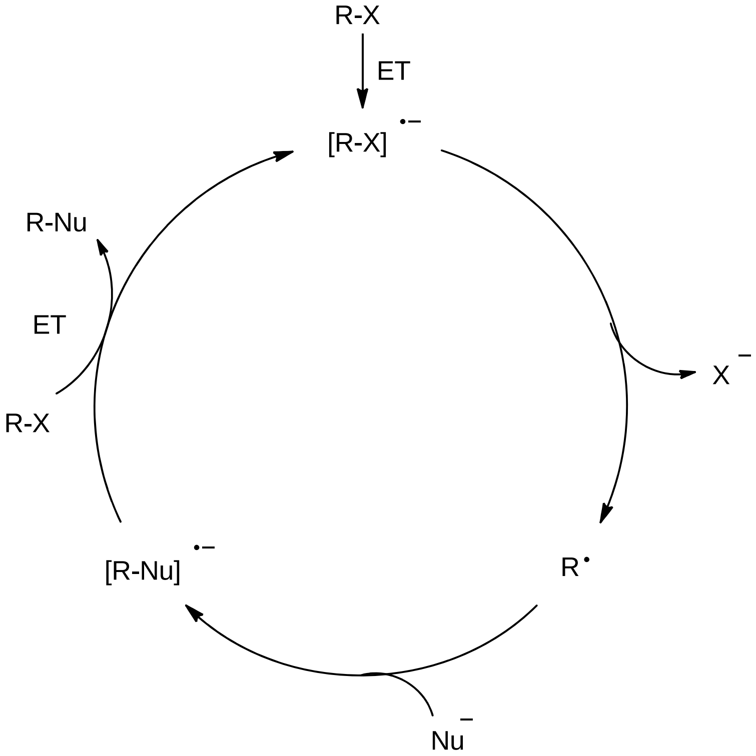
Photoinduced electron transfer (PET)

Examples of electron-catalyzed reactions

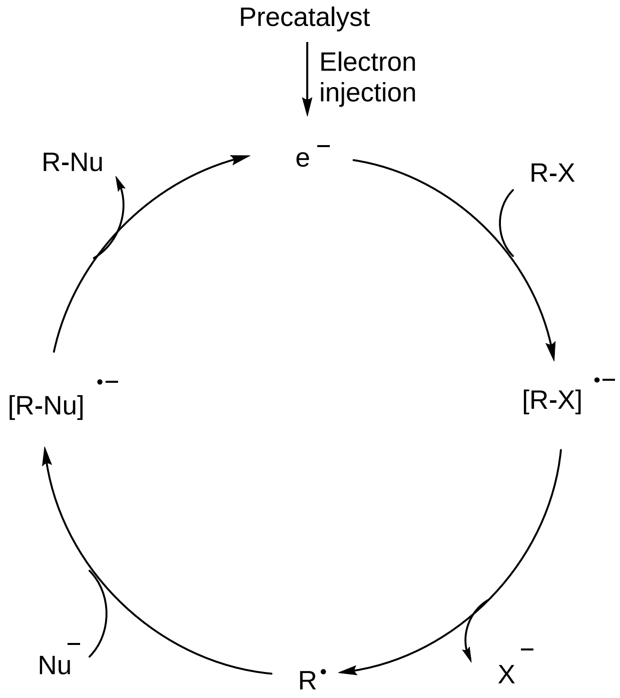
Monomolecular radical nucleophilic substitution reaction (S_{RN1}-chemistry)



Classic view of the S_{RN1}-mechanism



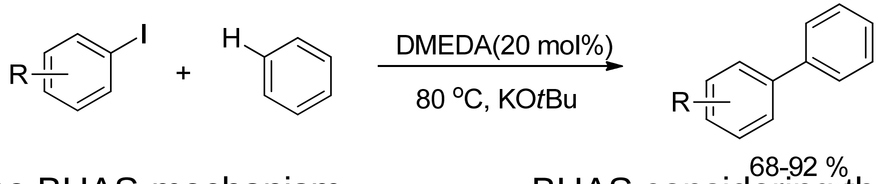
S_{RN1}-process considering the electron as a catalyst



Budén, M. E., Vaillard, V. A., Martin, S. E. & Rossi, R. A. *J. Org. Chem*. **2009**, *74*, 4490.

Examples of electron-catalyzed reactions

Base-promoted homolytic aromatic substitution (BHAS)

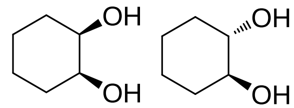


other catalysts:

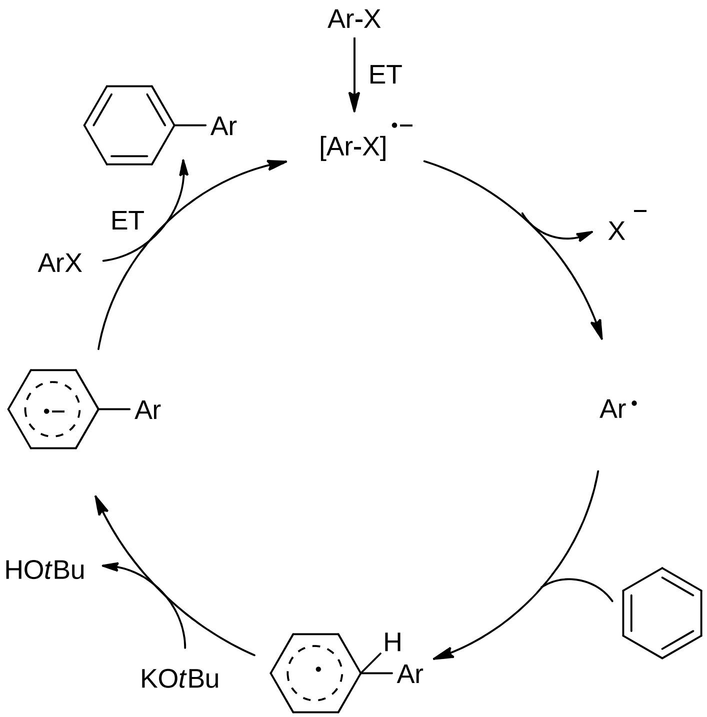
L-proline

$NH_2CH_2CH_2NH_2$

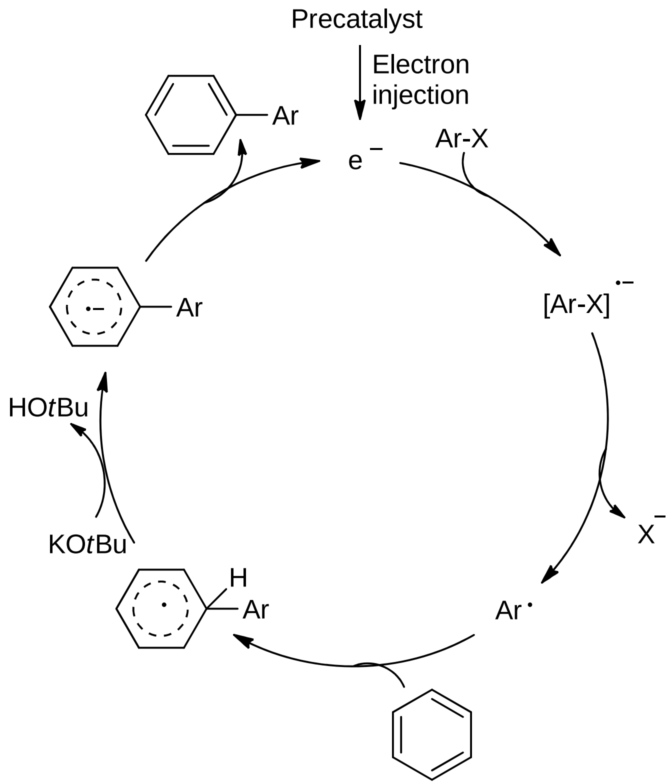
$NH_2CH_2CH_2OH$



Classic view of the BHAS-mechanism



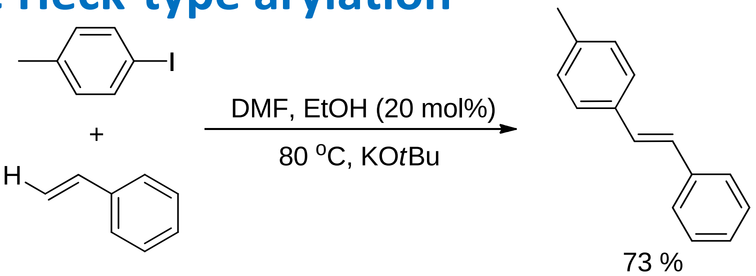
BHAS considering the electron as a catalyst



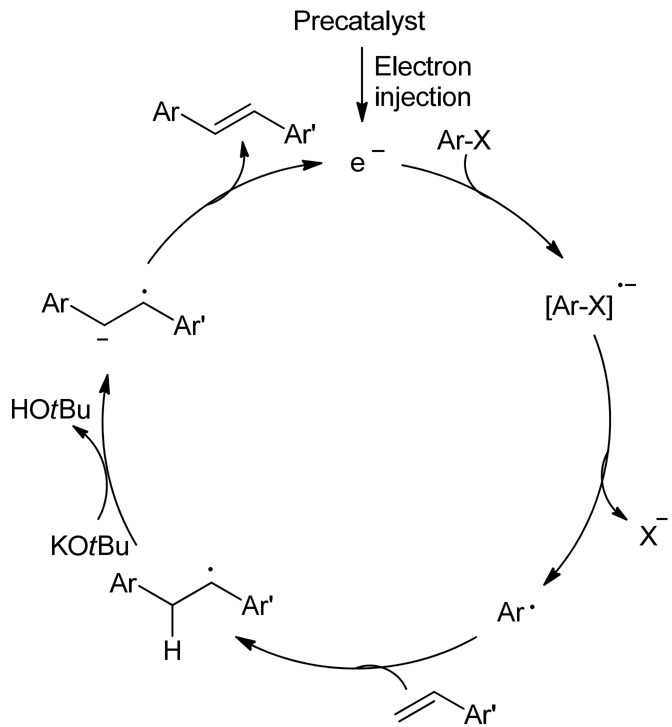
Liu, W.; Cao, H.; Zhang, H.; Chung, K, K.; He, C.; Wang, H.; Kwang, F. Y.; Lei, A. *J. Am. Chem. Soc*. **2010,** *132*, 16737.

Examples of electron-catalyzed reactions

Transition-metal-free Heck-type arylation



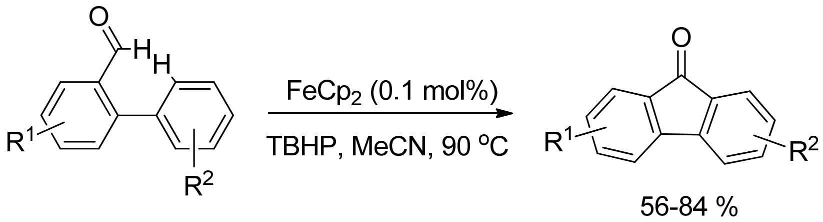
Heck-type arylation considering the electron as a catalyst



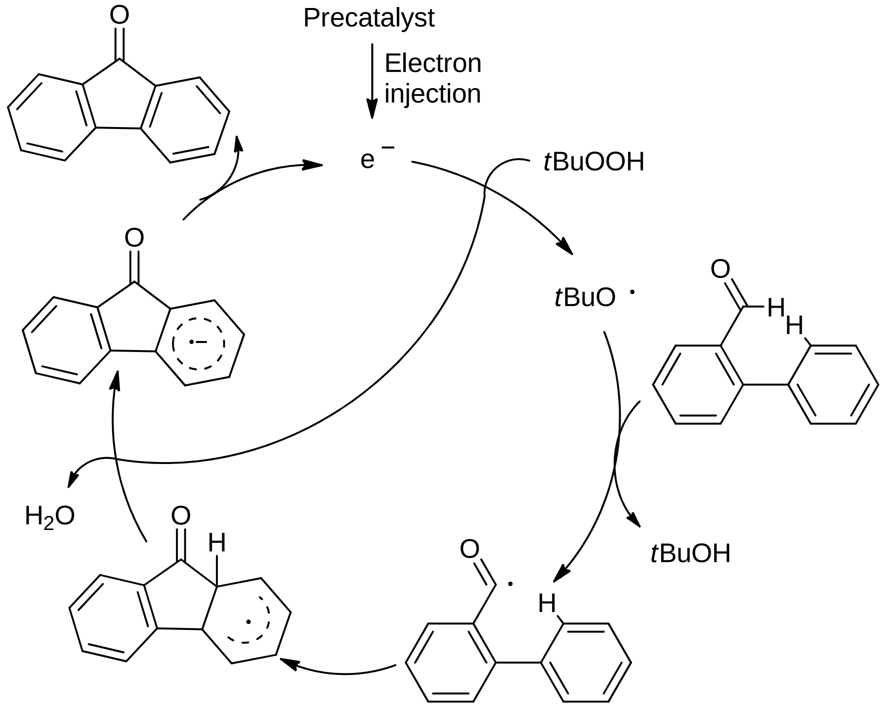
Shirakawa, E., Zhang, X. & Hayashi, T. *Angew. Chem. Int. Ed*. **2011,** *50*, 4671

Examples of electron-catalyzed reactions

Cross-dehydrogenative coupling reaction



Cross-dehydrogenative coupling reactions considering the electron as a catalyst



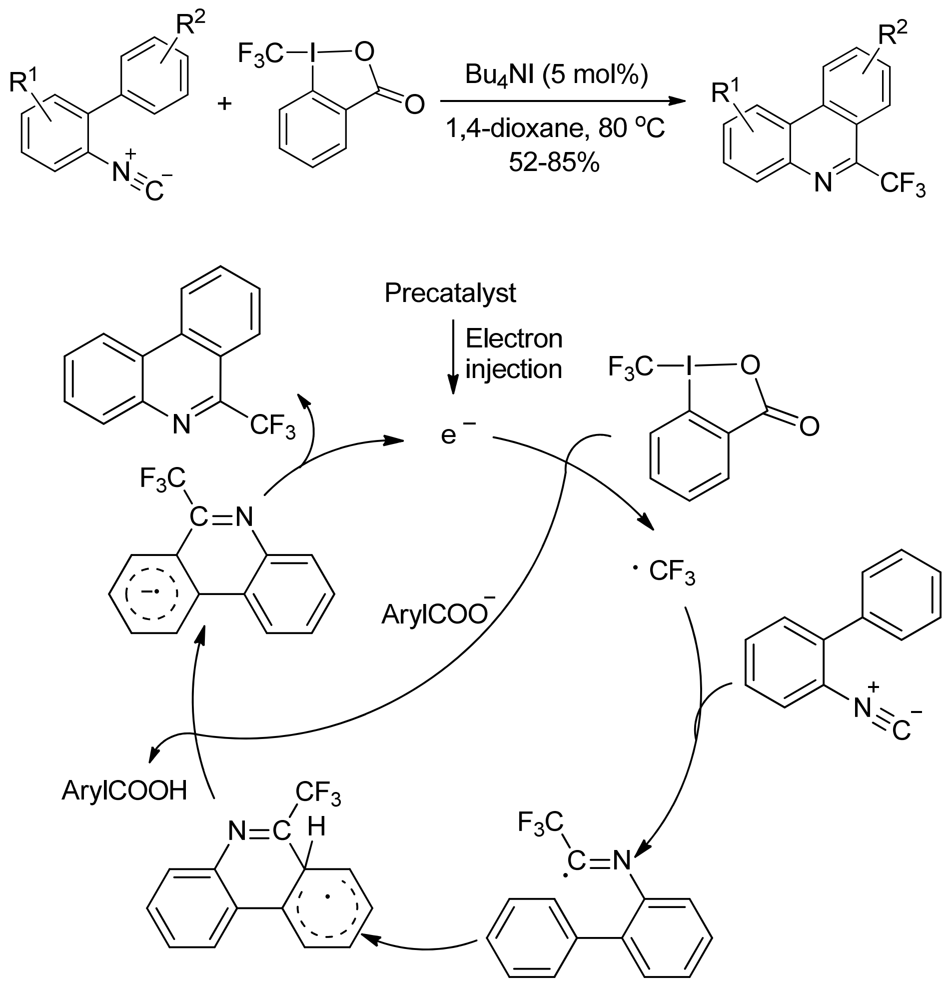
other catalysts:

$FeCl_2$	$FeSO_4$
$Fe(OAc)_2$	CuI
Bu_4NI	DMEDA
TMEDA	

Wertz, S., Leifert, D. & Studer, A. *Org. Lett*. **2013,** *15*, 928.

Examples of electron-catalyzed reactions

Arene trifluoromethylation



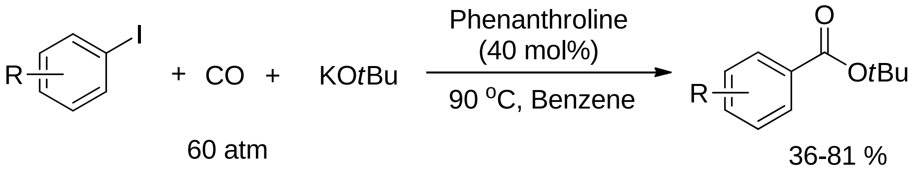
other catalysts:

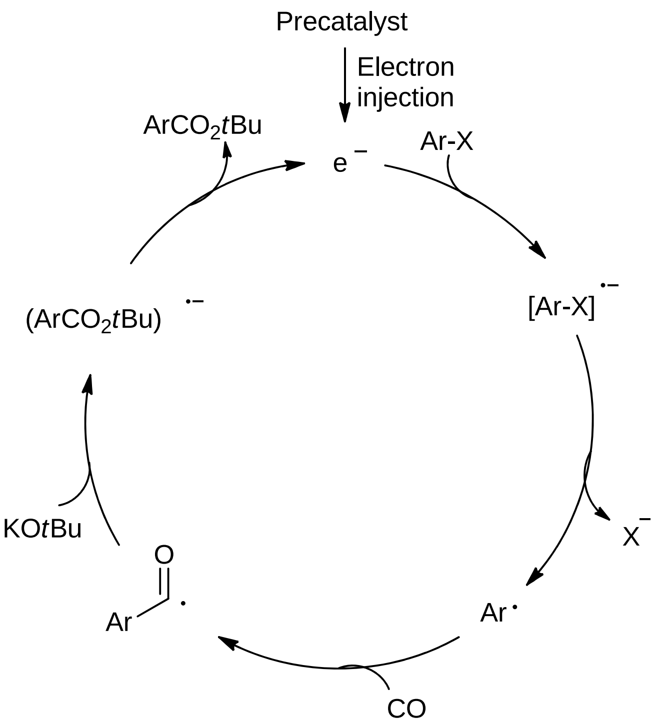
$FeCl_2$	$FeBr_2$
FeI_2	$Fe(aca)_2$
CuOAc	$NiCl_2$
$CoCl_2$	Bu_4NBr

Zhang, B., Mück-Lichtenfeld, C., Daniliuc, C. G. & Studer, A. *Angew. Chem. Int. Ed.* **2013,** *52*, 10792.

Examples of electron-catalyzed reactions

Alkoxycarbonylation of aryl halides

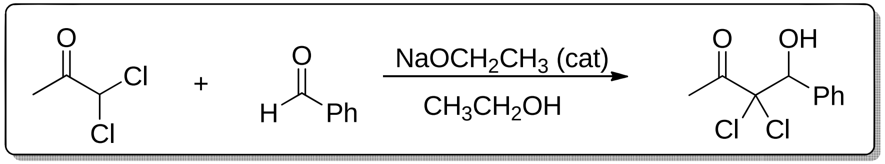


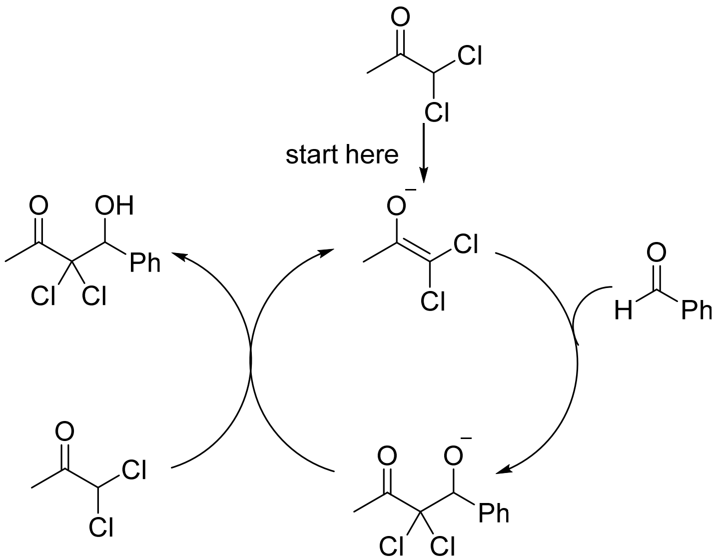


Zhang, H.; Shi, R.; Ding, A.; Lu, L.; Chen, B.; Lei, A. *Angew. Chem. Int. Ed*. **2012.** *51*, 12542.

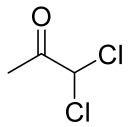
pK_a to acid / base reactions

Acid-catalyzed cross aldol reaction





Catalytic cycle



	(substrate)	CH_3CH_2OH	PhOH
pK_a:	14.9	15.9	10.0

pK_a of CH_3CH_2OH > pK_a of Substrate

↑ conjugated acid of the base

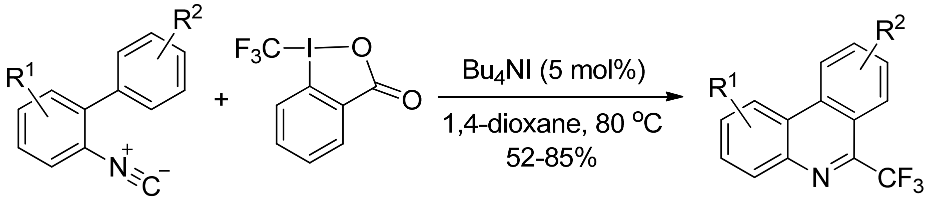
pK_a of PhOH < pK_a of Substrate

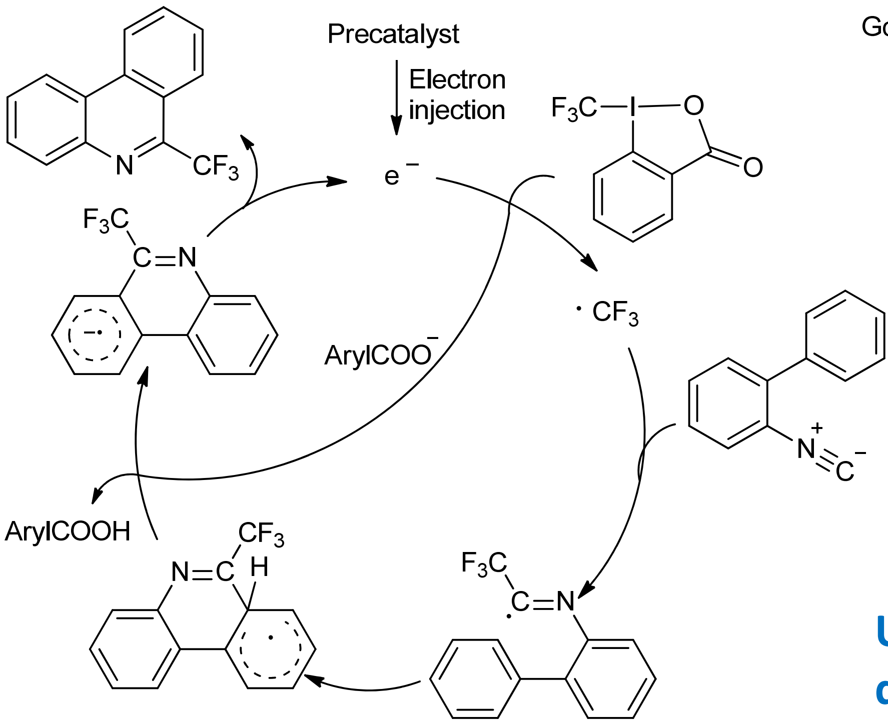
Understand the existing reactions and design new reactions by pK_a.

CH_3CH_2OH (not PhOH) can be the solvent of this reaction. (pK_a rules is not considered!)

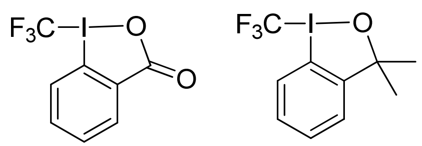
Redox potentials are to redox catalysis

Arene trifluoromethylation





reduction potential



	Togni reagent I	Togni reagent II
Gouverneur, V. *OL*, **2013**, *15*, 1250.	-0.68 V	
Akita, M. *ACIE*, **2012**, *51*, 9567.	-0.75 V	-1.49 V

$E(Fe^{2+}/Fe^{3+}) = -0.77$ V

other catalysts:

$FeCl_2$	$FeBr_2$
FeI_2	$Fe(aca)_2$
CuOAc	$NiCl_2$
$CoCl_2$	Bu_4NBr

other catalysts:

$FeCl_2$ $FeBr_2$ FeI_2 $Fe(aca)_2$	→	Professor A
CuOAc	→	Professor B
$NiCl_2$	→	Professor C
$CoCl_2$	→	Professor D

Understand the existing reactions and design new reactions by Redox potentials .

Zhang, B., Mück-Lichtenfeld, C., Daniliuc, C. G. & Studer, A. *Angew. Chem. Int. Ed.* **2013,** *52*, 10792.

Summary

1. The observation that many different 'catalysts' work for the same reaction may be a clue to electron-catalyzed reactions.

2. Redox potentials are to redox catalysis what pK_a is to acid/base catalysis.

3. The unifying concept of 'the electron as a catalyst' provides a framework to identify relationships between existing reactions, to solve problems with inefficient reactions, and to design new reactions and sequences of reactions.

Thanks for your attention!