# *From electrocatalysis to electrophotocatalysis*

2021. 8. 28. Literature Seminar
D3 Tsukasa Shimakawa

# Contents

1. Introduction

2. Anodically coupled electrolysis -heterodifunctionalization of olefin-

nature chemistry

ARTICLES

https://doi.org/10.1038/s41557-020-0469-5

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## Dual electrocatalysis enables enantioselective hydrocyanation of conjugated alkenes

Lu Song[1], Niankai Fu[1], Brian G. Ernst[1], Wai Hang Lee[1], Michael O. Frederick[2], Robert A. DiStasio Jr.[1] and Song Lin[1]

3. New concept for reductive functionalization

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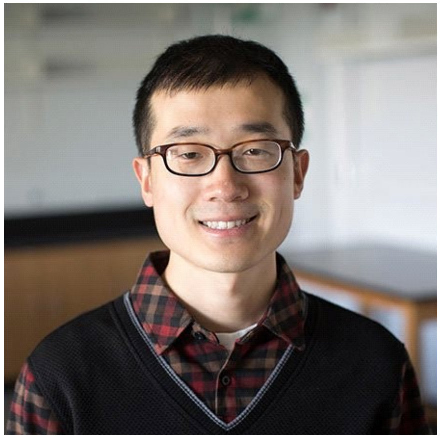
Communication

## Reductive Electrophotocatalysis: Merging Electricity and Light To Achieve Extreme Reduction Potentials

Hyunwoo Kim, Hyungjun Kim, Tristan H. Lambert,* and Song Lin*

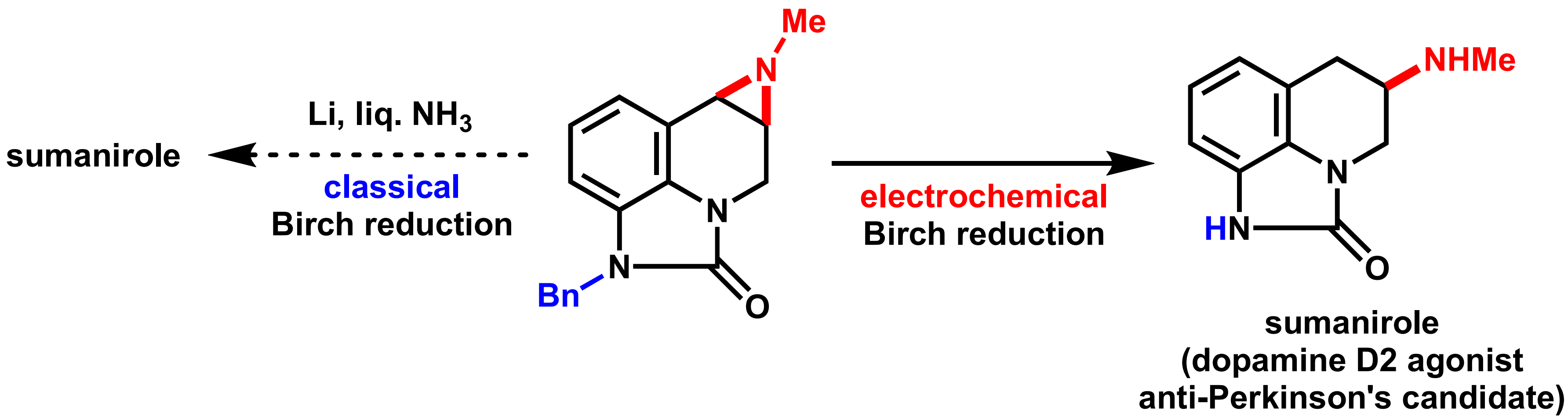
# Assistant Prof. Song Lin / Introduction



**Education and academic career**:
**2008 B.S.c @ Peking University (Prof. Zhang-Jie Shi)**
**2013 Ph. D. @ Harvard University (Prof. Eric N. Jacobsen)**
**2013-2016 Postdoc @ UC Berkeley (Prof. Christopher J. Chang)**
**2016- Assistant professor @ Cornell University**

**Research area**:
**1. Electrocatalysis 2. Electrophotocatalysis**
**3. Electroreductive chemistry 4. Radical redox relay chemistry**
**5. Polymer and materials chemistry**

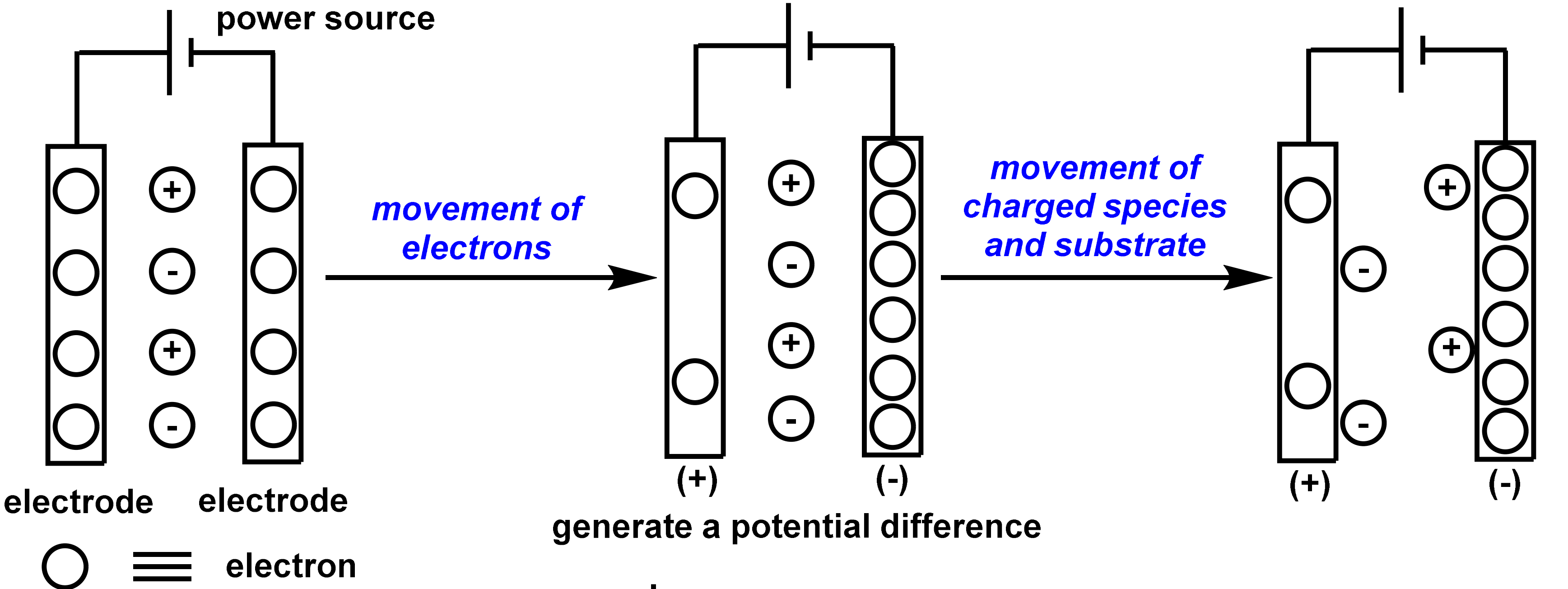
**♣replacement of classical reaction with electrochemical version**
**1. large-scale synthesis (electrochemical flow) 2. devise catalytic version of reactions**

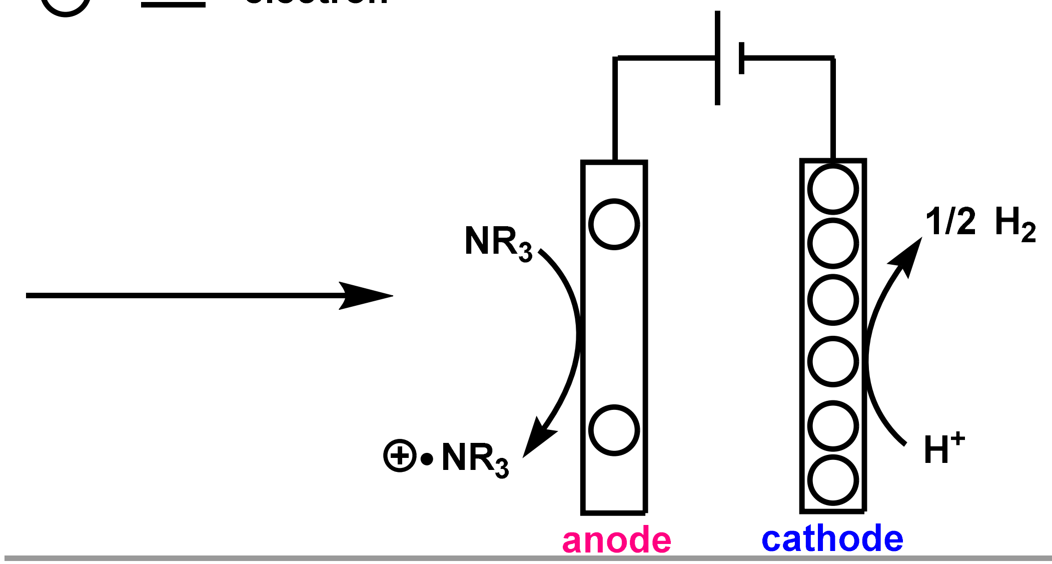



**♣ propose new concepts, development of the chemistry**

1) https://songlin.chem.cornell.edu/ 2) Baran, P. S. *et al*. *Science* **2019**, *363*, 838.

# Basics of electrochemical reaction



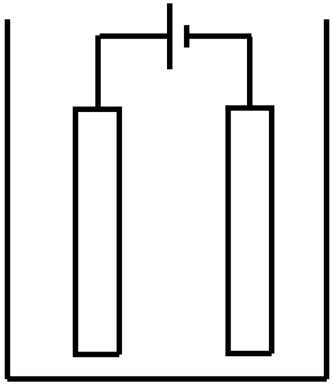

reagents or substrate are oxidized and reduced on the surface of the electrode

anode : oxidative electrode
cathode: reductive electrode

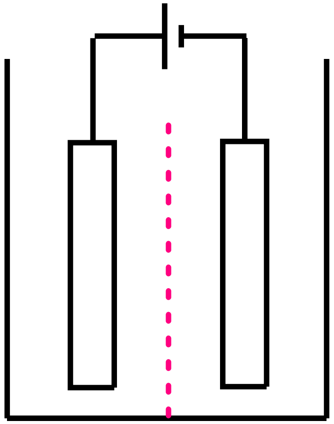
1) Kingston, C.; Palkowitz, M. D.; Takahira, Y.; Vantourout, J. C.; Peters, B. K.; Kawamata, Y.; Baran, P. S. *Acc. Chem. Res*. **2020**, *53*, 72. 2) Yan, M.; Kawamata, Y.; Baran, P. S. *Chem. Rev.* **2017**, *117*, 13230.

# Components of electrochemical reaction

undivided cell



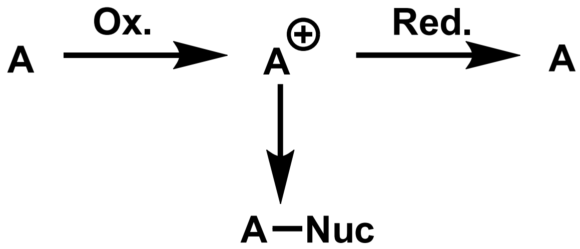
divided cell



frit or membrane

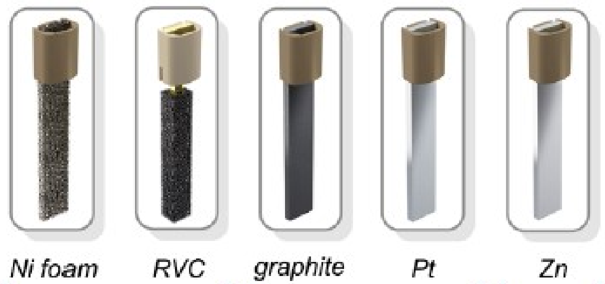
substrate, product or reagent are protected from counter electrode

eg)




**electrode**

the choice of material is important
(electron transfer occurs on the electrode surface)




sacrificial

**electrolyte**

improve the conductivity

Li or $n\mathrm{Bu_4N}$ salts (counter anion: $\mathrm{ClO_4^-}$, $\mathrm{PF_6^-}$, $\mathrm{BF_4^-}$)

electrolyte coats the eletrode surface and affects the reactivity

**mode of electrolysis**

1. constant current

potentail drifts to maintain the current

a. easier set up
b. selectivity problem (over-oxidation, reduction)

2. constant potential

current adjusts to maintain the cell potential

a. higher selectivity

← this lit. seminar

1) Kingston, C.; Palkowitz, M. D.; Takahira, Y.; Vantourout, J. C.; Peters, B. K.; Kawamata, Y.; Baran, P. S. *Acc. Chem. Res.* **2020**, *53*, 72. 2) Yan, M.; Kawamata, Y.; Baran, P. S. *Chem. Rev.* **2017**, *117*, 13230.

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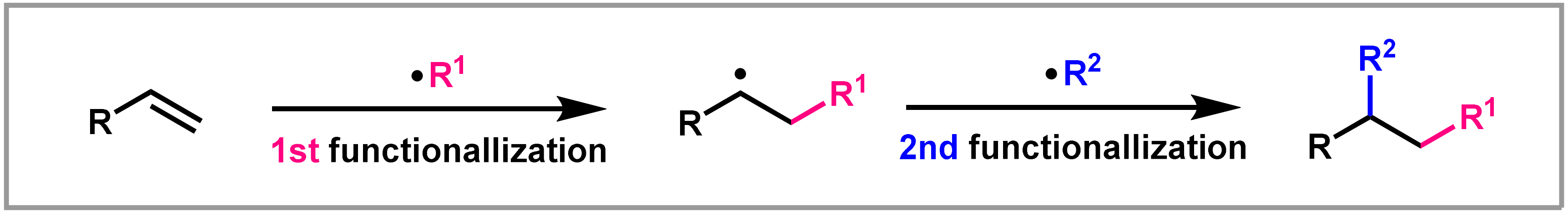
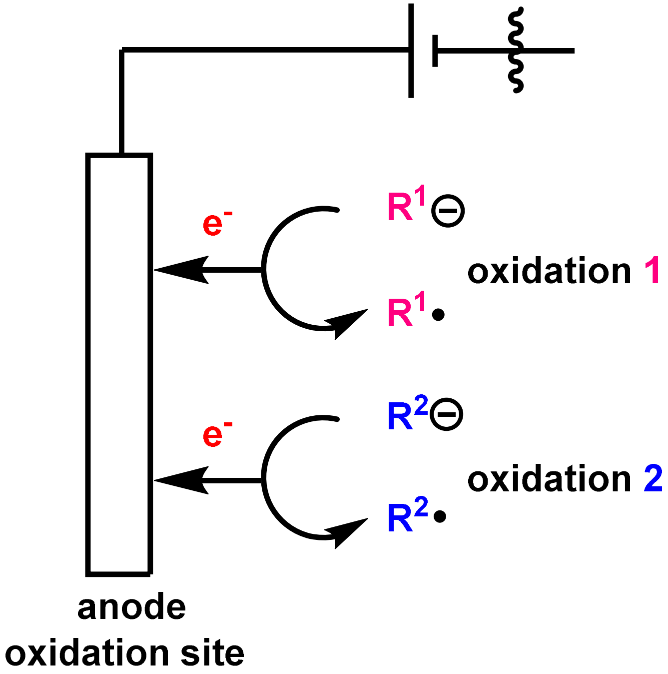
Communication

## Reductive Electrophotocatalysis: Merging Electricity and Light To Achieve Extreme Reduction Potentials

Hyunwoo Kim, Hyungjun Kim, Tristan H. Lambert,* and Song Lin*

# Anodically coupled electrolysis[1)]

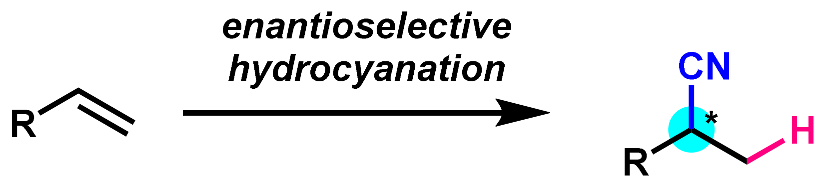



at cathode $2H^+ + 2e^- \rightarrow H_2$

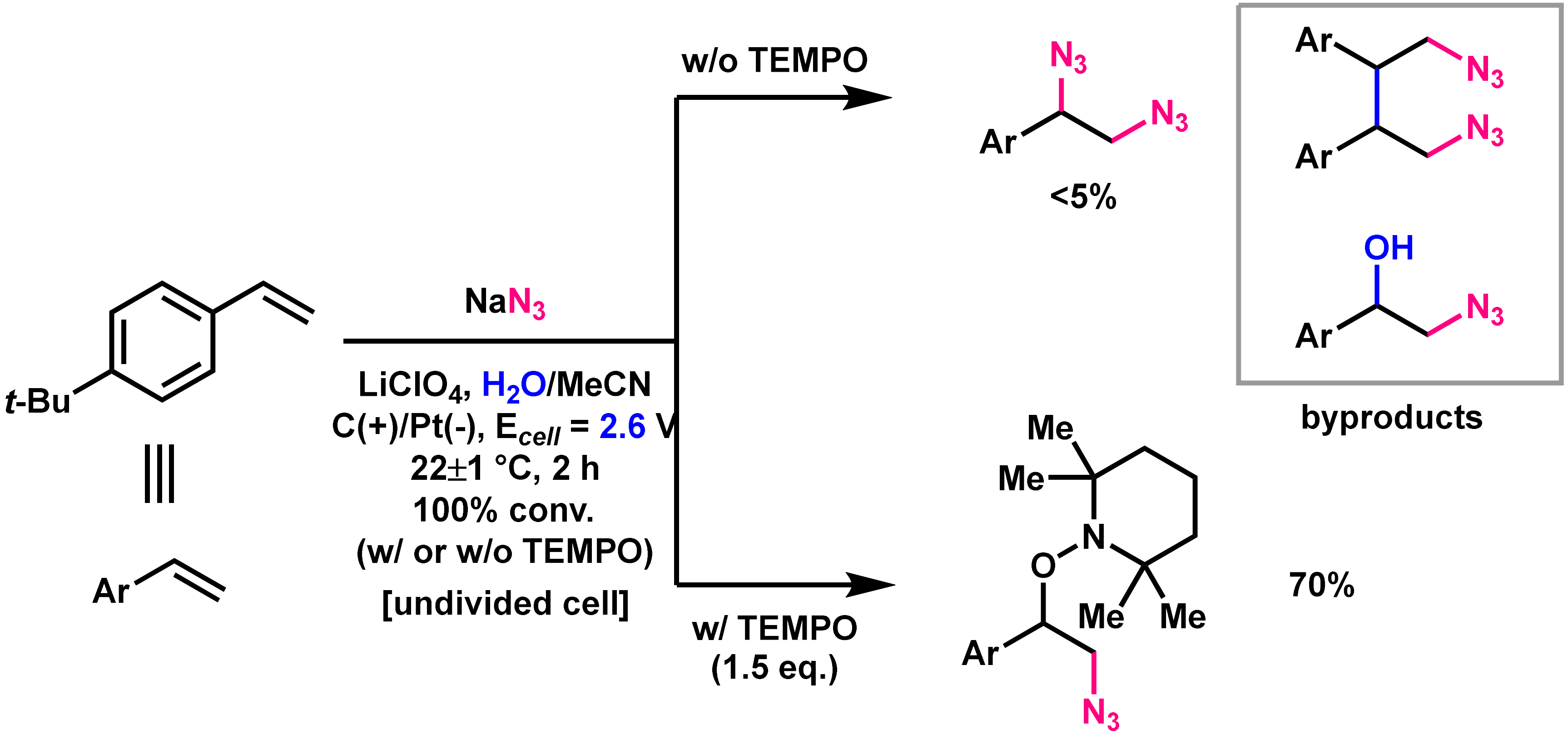
Part 1. $R^1 = R^2 = N_3$

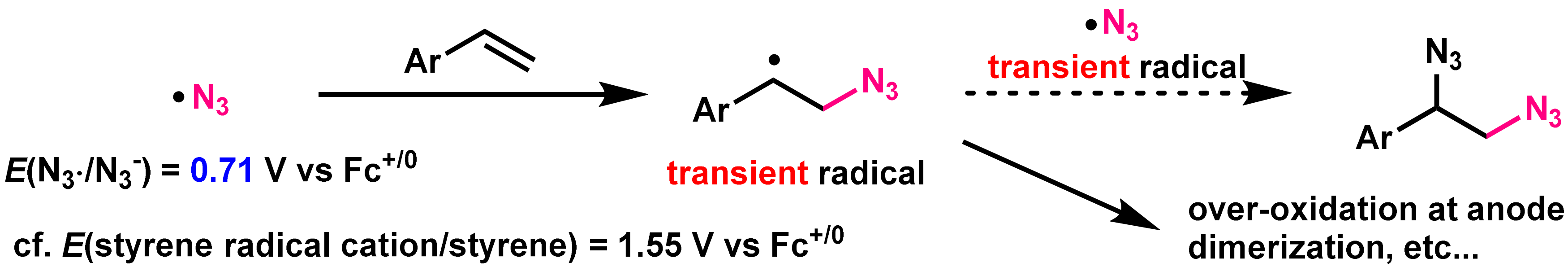

Part 2. $R^1 \neq R^2$, $R^1 = H$, $R^2 = CN$




Ye, K.-Y.; Pombar, G.; Fu, N.; Sauer, G. S.; Keresztes, I.; Lin, S. *J. Am. Chem. Soc.* **2018**, *140*, 2438.

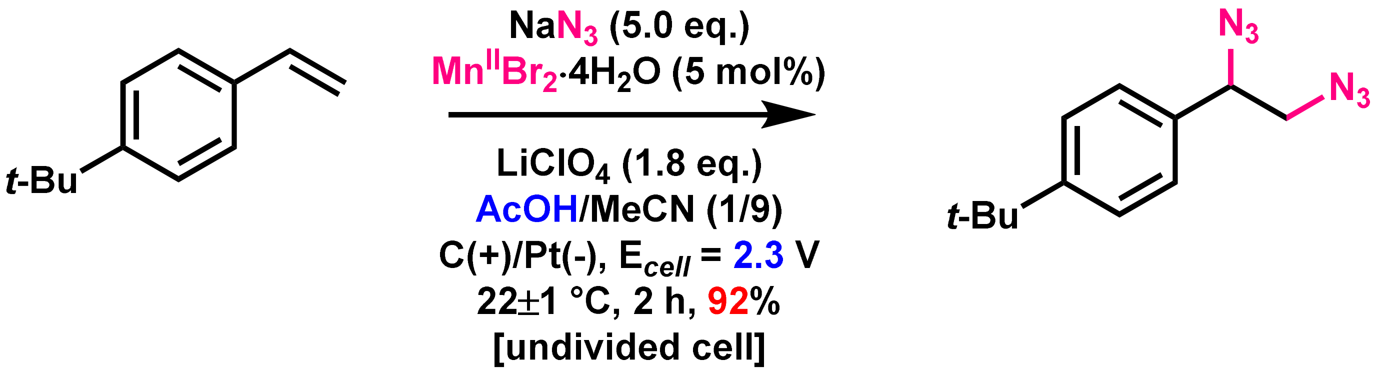
# Attempted electrochemical diazidation of olefin



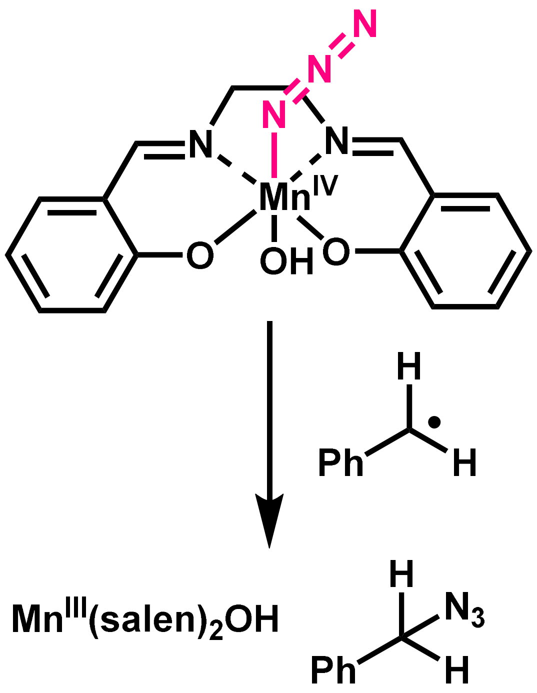



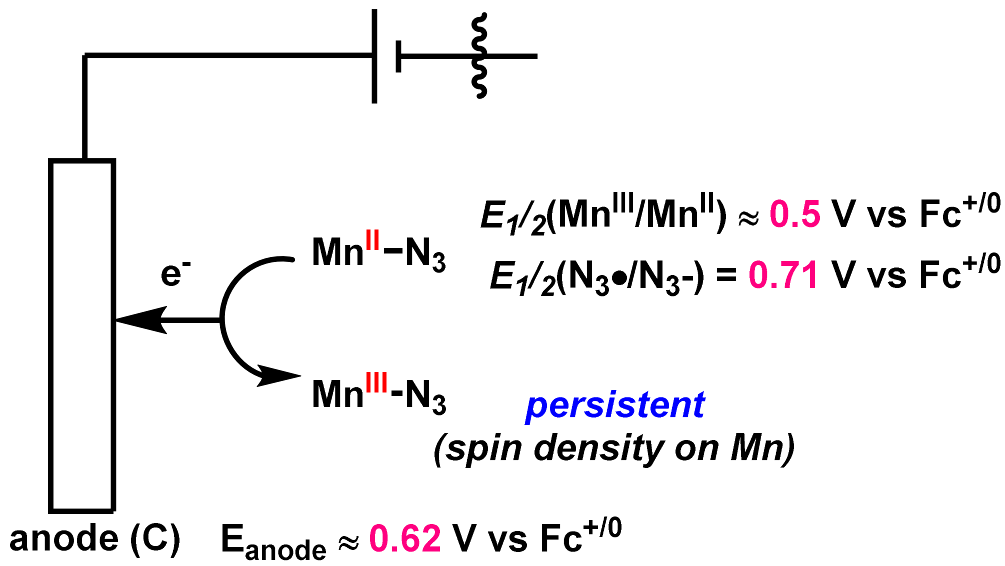

Fu, N.; Sauer, G. S.; Saha, A.; Loo, A.; Lin, S. *Science* **2017**, *357*, 575.

# Dual role of $Mn^{II}$ salt




$Mn^{IV}$ as $N_3$ transfer reagent[1)]

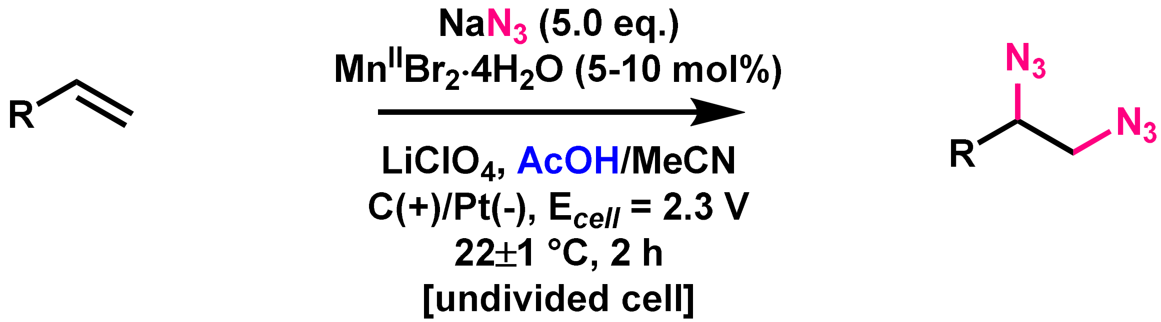


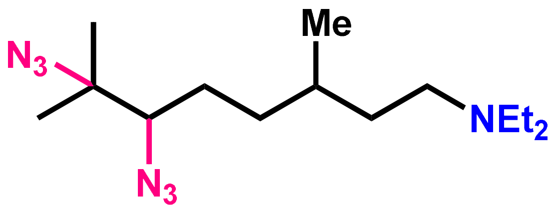

**$Mn^{II}$ salt works as**
**1. redox mediator ($Mn^{II}$-$N_3$ complex decreases the oxidation potential)**
**2. $N_3$ transfer reagent ($Mn^{III}$-$N_3$ complex showed persistent character)**

Huang, X.; Bergsten, T. M.; Groves, J. T. *J. Am. Chem. Soc.* **2015**, *137*, 5300.
Fu, N.; Sauer, G. S.; Saha, A.; Loo, A.; Lin, S. *Science* **2017**, *357*, 575.

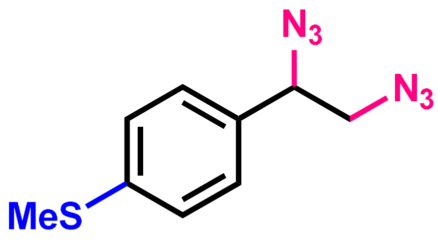
# Effect of terminal reductant



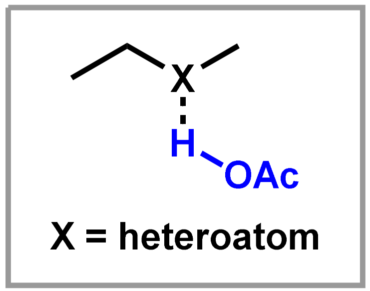

1. substrate with oxidation labile functional group



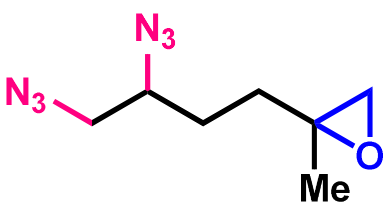

69%



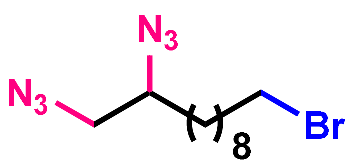

82%



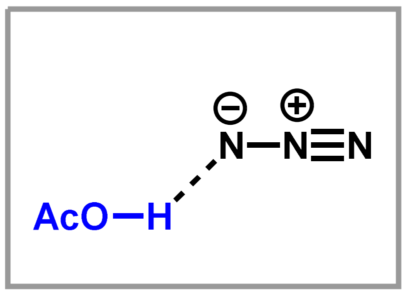

2. substrate with nucleophile labile functional group




72%
(reaction temp: 40 °C)

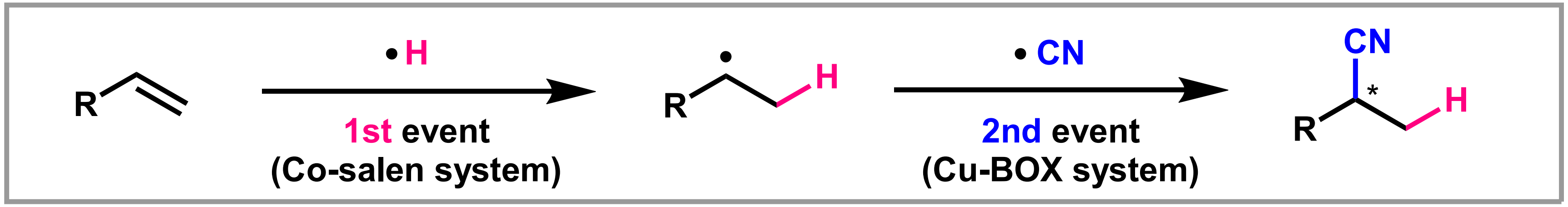


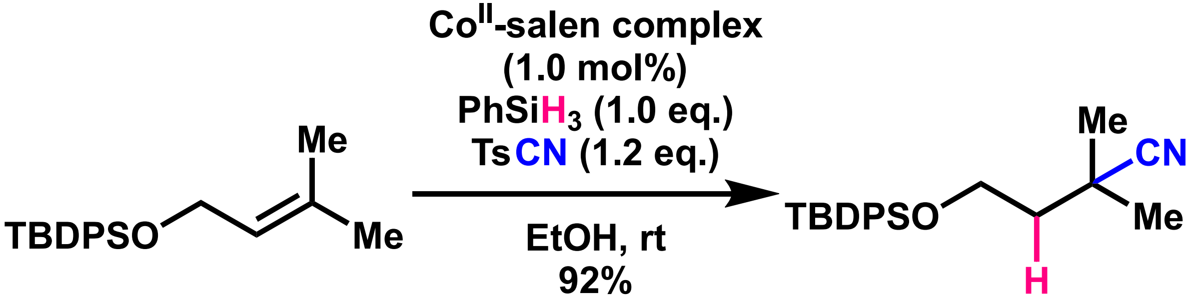

79%

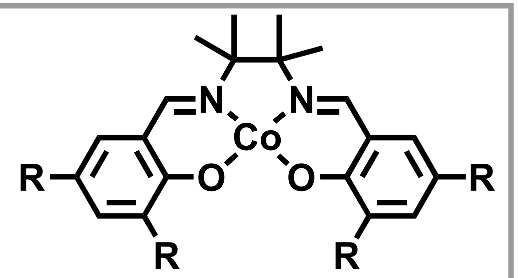



Fu, N.; Sauer, G. S.; Saha, A.; Loo, A.; Lin, S. *Science* **2017**, *357*, 575.

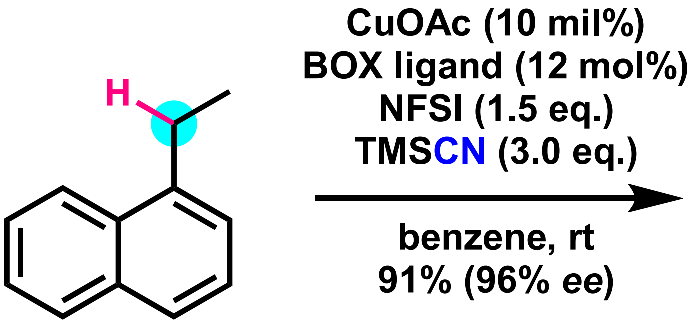
# Dual electrocatalysis approach

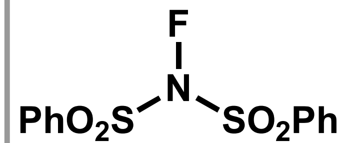


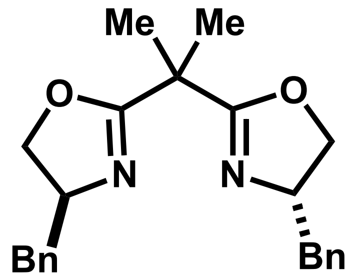



Co-salen catalyst (R = *t*-Bu)



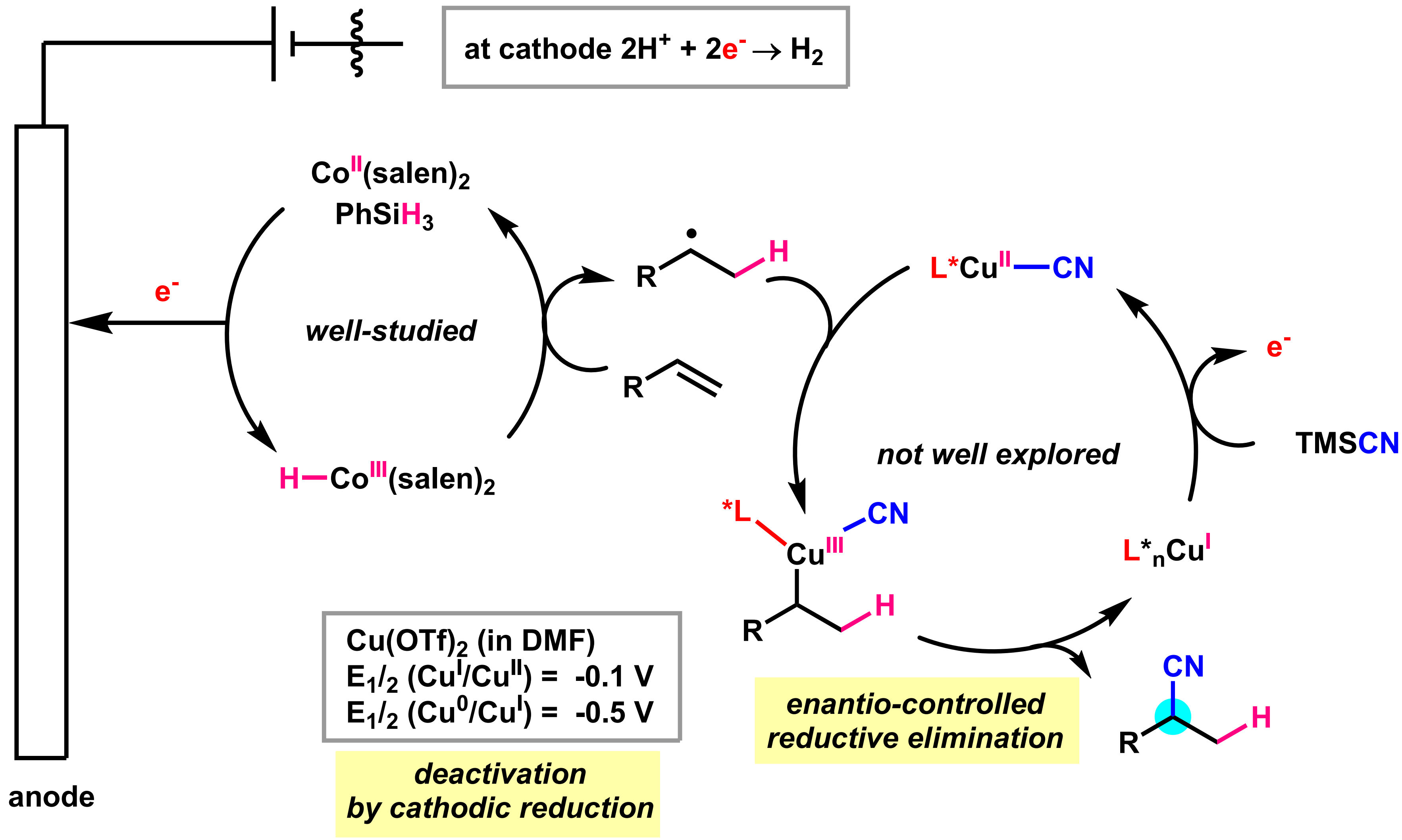
NFSI
(HAT reagent)



chiral BOX ligand

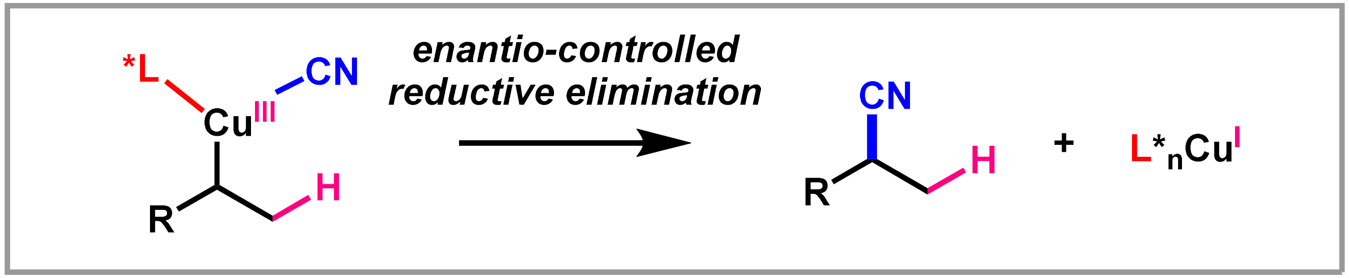

1) Gaspar, B.; Carreira, E. M. *Angew. Chem., Int. Ed*. **2007**, *46*, 4519.
2) Zhang, W.; Wang, F.; McCann, S. D.; Wang, D.; Chen, P.; Stahl, S. S.; Liu, G. *Science* **2016**, *353*, 1014.

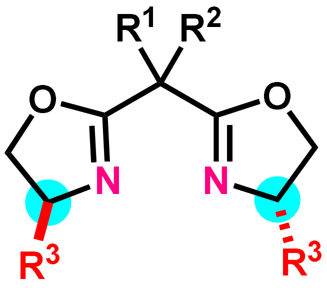
# Initial reaction design



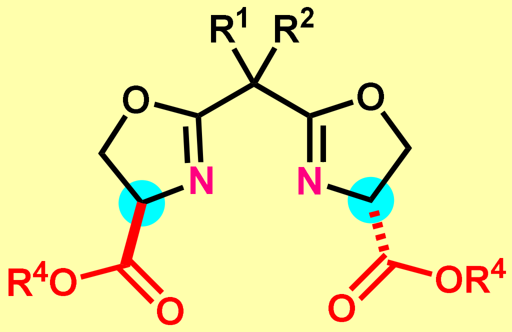

1) Eichhorn, E.; Rieker, A.; Speisesr, B. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1215.
2) Song, L.; Fu, N.; Ernst, B. G.; Lee, W. H.; Frederick, M. O.; DiStasio Jr. R. A.; Lin, S. *Nat. Chem.* **2020**, *12*, 747.

# sBOX ligand -Initial ligand design-

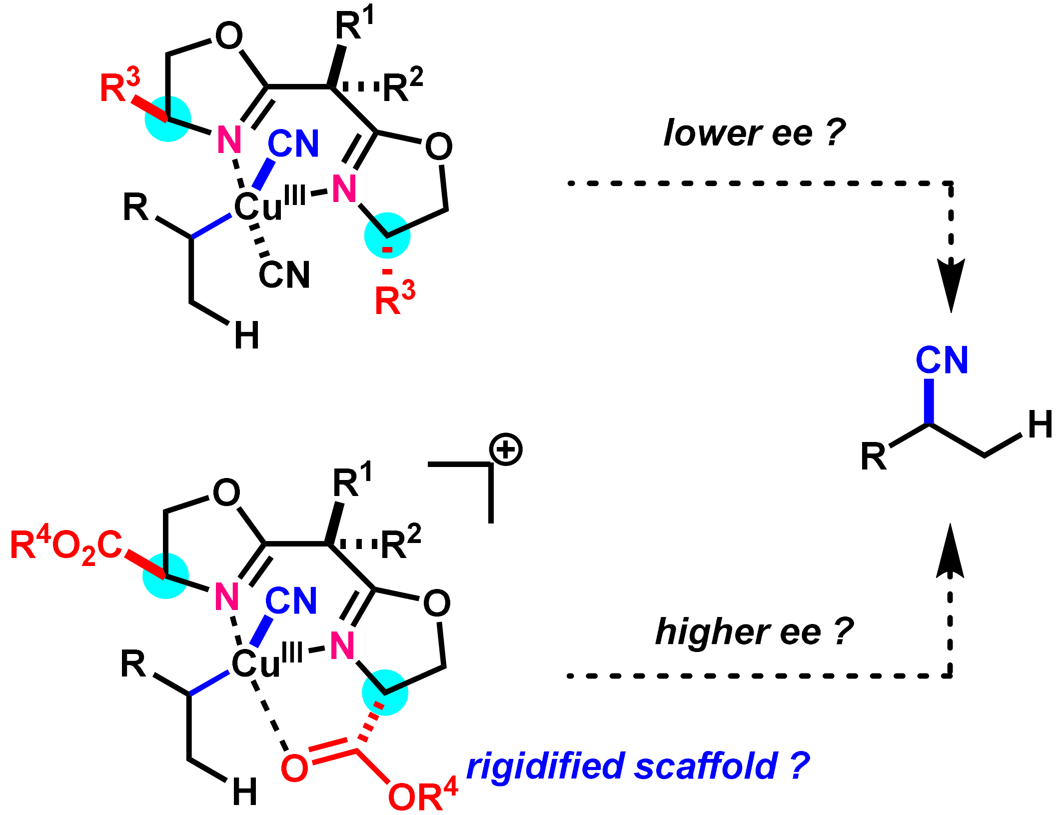



classical BOX ligand[1)]
$R^3$ = alkyl, aryl
(steric control sites)

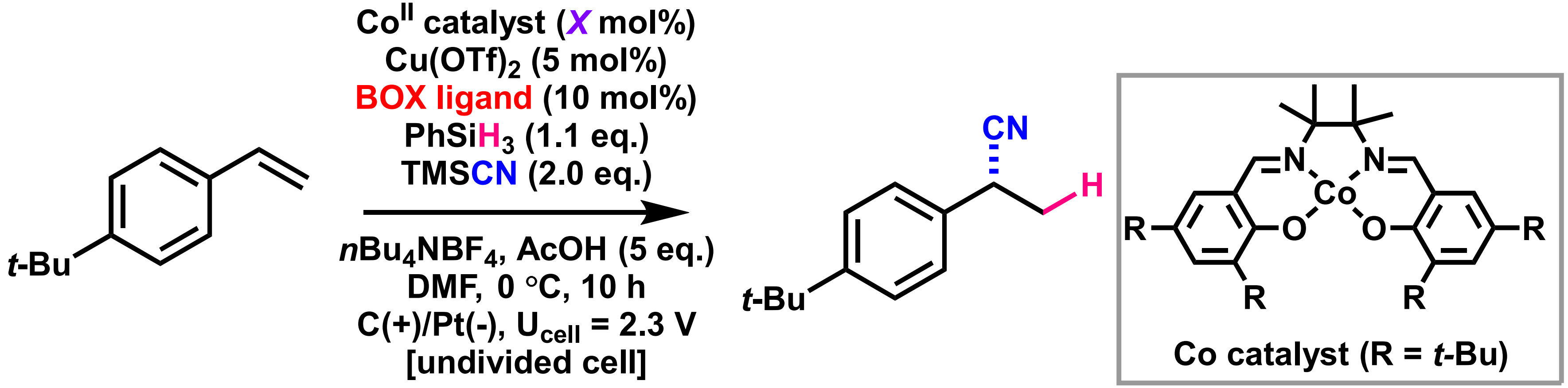


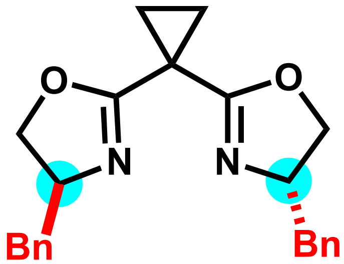

sBOX (serine derived BOX) ligand[3)]



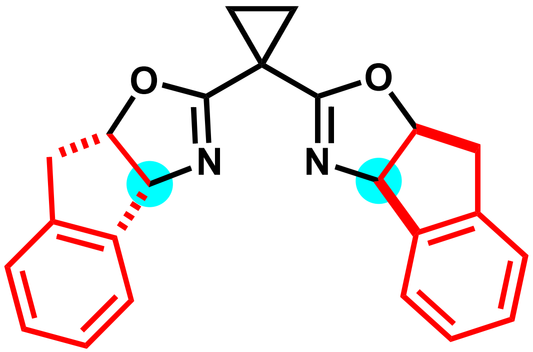

1) Lowenthal, R. E.; Abiko, A.; Masamune, S. *Tetrahedron Lett.* **1990**, *31*, 6005.
2) Zhang, W.; Wang, F.; McCann, S. D.; Wang, D.; Chen, P.; Stahl, S. S.; Liu, G. *Science* **2016**, *353*, 1014.
3) Fu, N.; Song, L.; Liu, J.; Shen, Y.; Siu, C. J.; Lin, S. *J. Am. Chem. Soc.* **2019**, *141*, 14480.

# Screening of BOX ligands

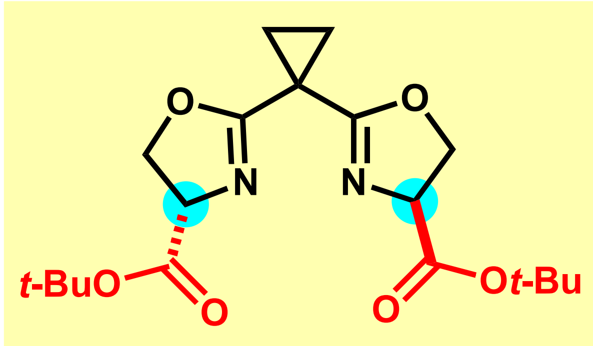



*X* = 0.5
46% yield
-50% *ee*




*X* = 0.5
73% yield
72% *ee*



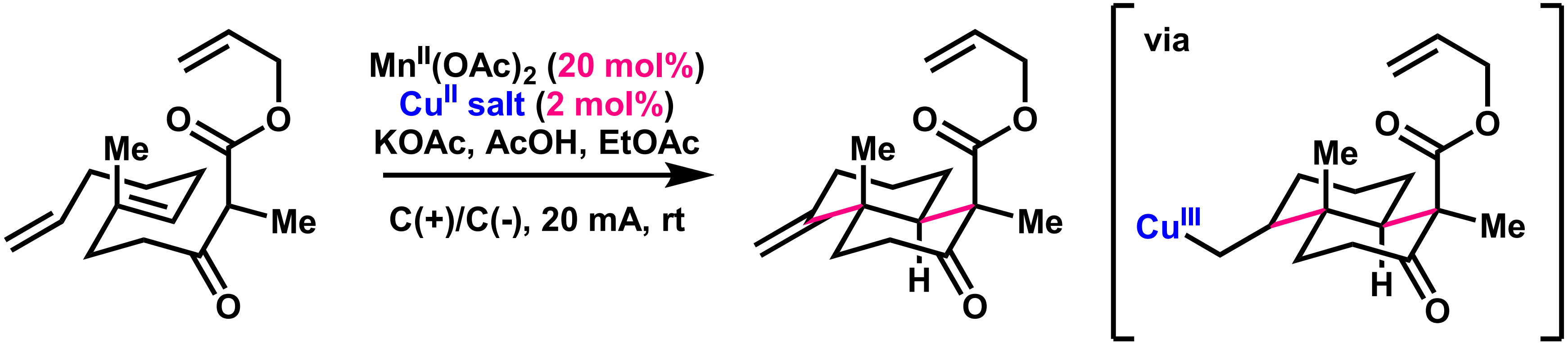

*X* = 0.5
79% yield
91% *ee*

( *X* = 2
37% yield
84% *ee* )

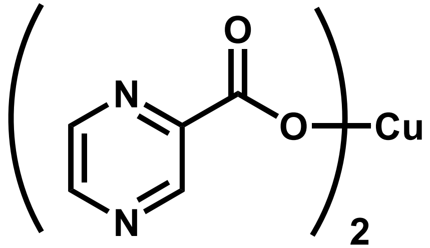
1. sBOX ligand showed better ee.
2. balancing the rate of MHAT and cyanation events was important


Song, L.; Fu, N.; Ernst, B. G.; Lee, W. H.; Frederick, M. O.; DiStasio Jr. R. A.; Lin, S.
*Nat. Chem.* **2020**, *12*, 747.

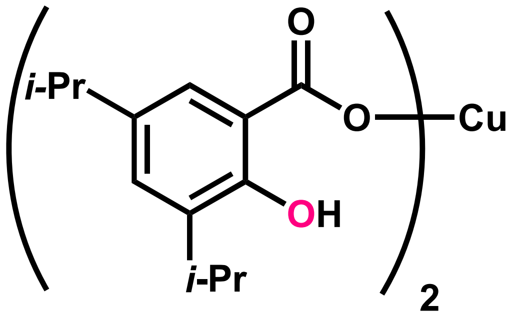
# Electrochemical radical polycyclization




| entry | $Cu^{II}$ salt | results |
|---|---|---|
| 1 | $Cu(OAc)_2$ | 20% |
| 2 | $Cu(pyrazineCO_2)_2$ | 22%<br>27% rcv. |
| 3 | $Cu(sal)_2$ | 30% |



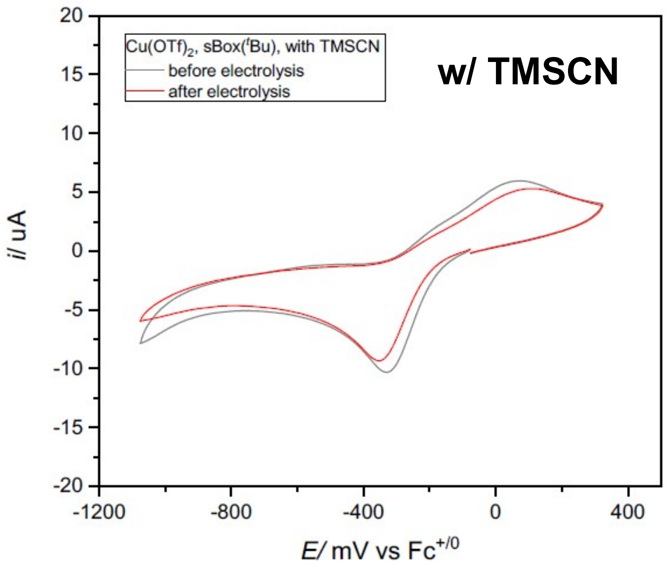

$Cu(pyrazineCO_2)_2$

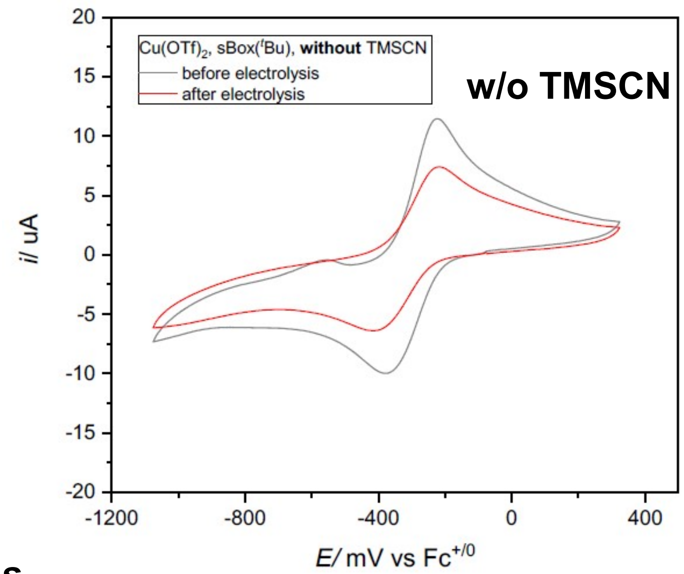



$Cu(sal)_2$

Merchant, R. R.; Oberg, K. M.; Lin, Y.; Novak, A. J. E.; Felding, J.; Baran, P. S.
*J. Am. Chem. Soc.* **2018**, *140*, 7462.

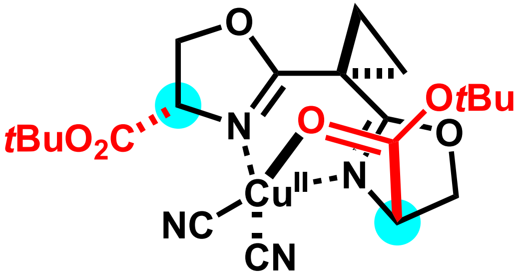
# Cathodic reduction tolerant Cu$^{II}$ species



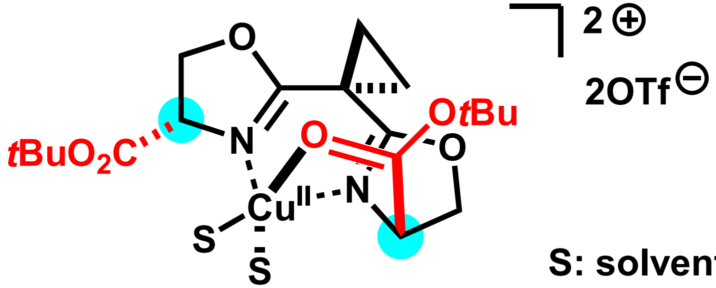




***conditions***
**Pt working electrode**
***n*$Bu_4NBF_4$ (0.20 M in DMF), $Cu(OTf)_2$ (2.5 mM)**
**sBOX(*t*Bu) (5 mM), HOAc (250 mM)**
**w/ or w/oTMSCN (100 mM)**

**<proposed>**




**<proposed>**

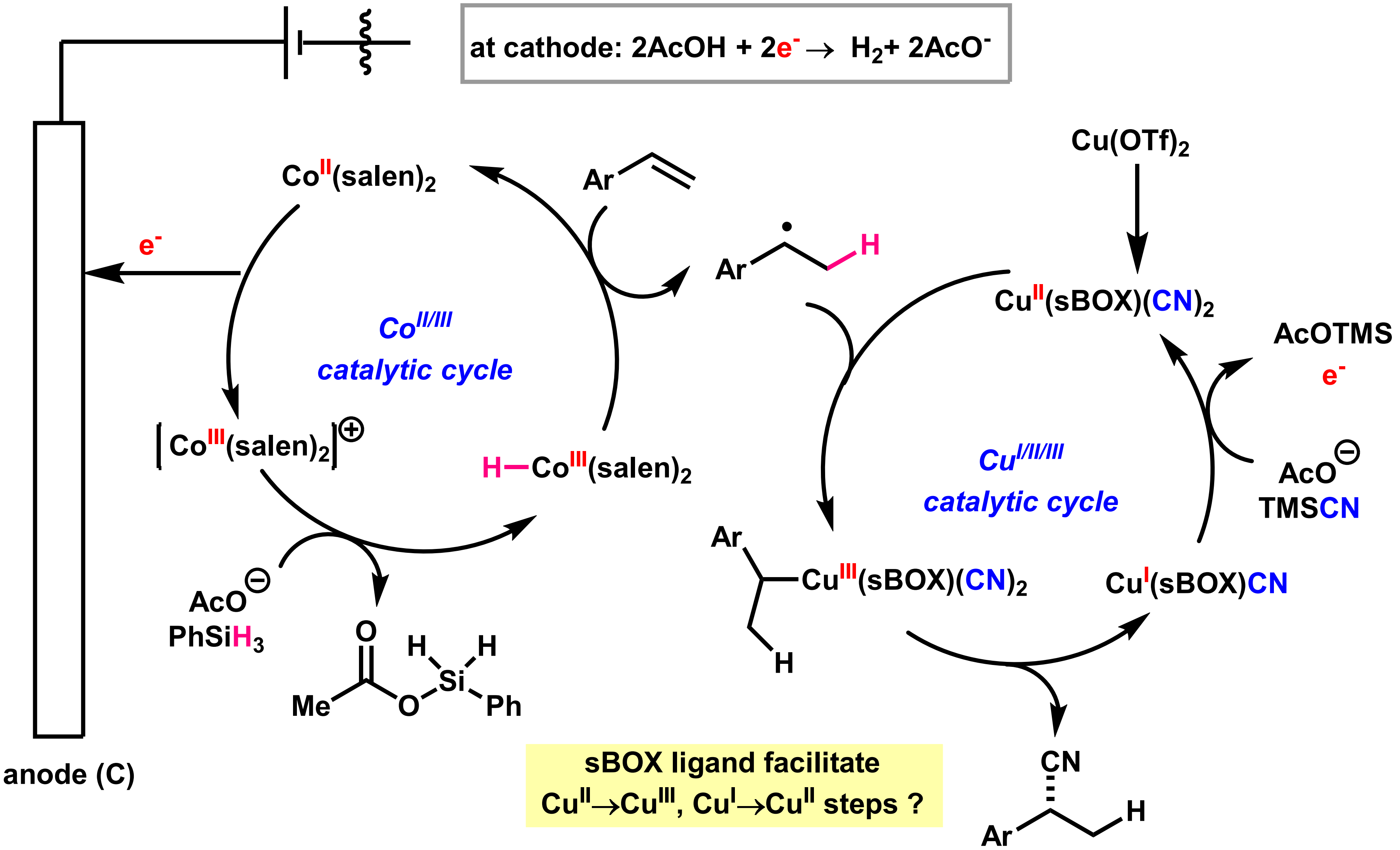



**S: solvent (DMF or AcOH)**

**Cu, sBOX ligand,and TMSCN formed new Cu$^{II}$ species, which is tolerate for cathocic reduction.**


Song, L.; Fu, N.; Ernst, B. G.; Lee, W. H.; Frederick, M. O.; DiStasio Jr. R. A.; Lin, S. *Nat. Chem.* **2020**, *12*, 747.

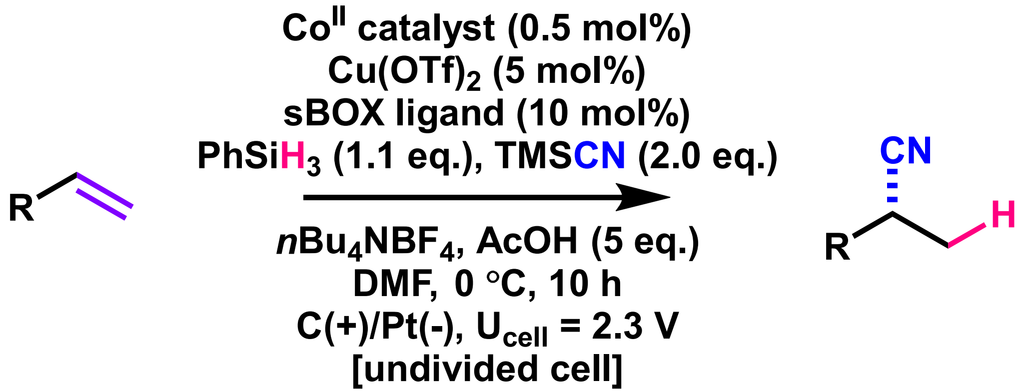
# Possible reaction mechanism

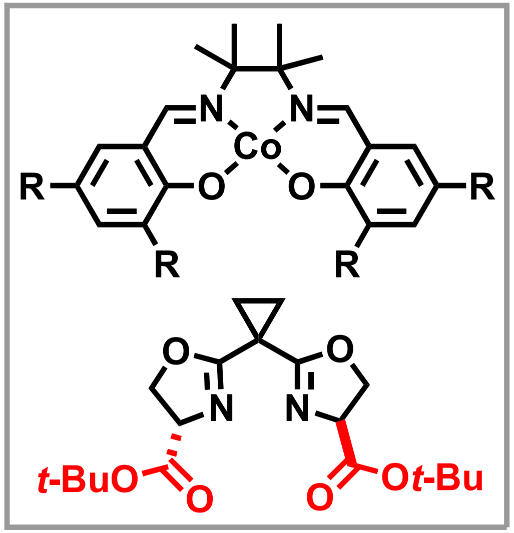



sBOX ligand facilitate
$Cu^{II} \rightarrow Cu^{III}$, $Cu^{I} \rightarrow Cu^{II}$ steps ?

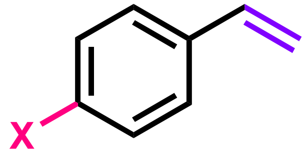
Kim, H.; Kim, H.; Lambert, T. H.; Lin, S. *J. Am. Chem. Soc.* **2020**, *142*, 2087.
Stoll, E. L.; Tongue, T.; Andrews, K. G.; Valette, D.; Hirst, D. J.; Denton, R. M. *Chem. Sci*. **2020**, *11*, 9494.
Wang, P.-Z.; Gao, Y.; Chen, J.; Huan, X.-D.; Xiao, W.-J.; Chen, J.-R. *Nat. Commun.* **2021**, *12*, 1.

# Substrate scope

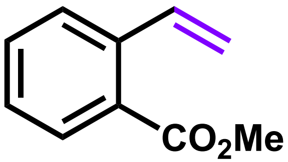


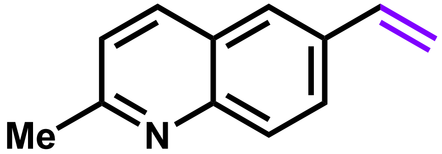

**1. terminal olefin**



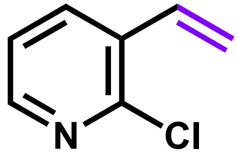

X = H, 76%, 84% *ee*
X = Br, 69%, 84% *ee*
X = SMe, 69%, 86% *ee*




79%, 85% *ee*

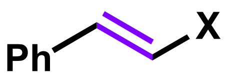



74%, 92% *ee*

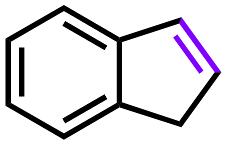



78%, 85% *ee*

**2. Internal olefin**

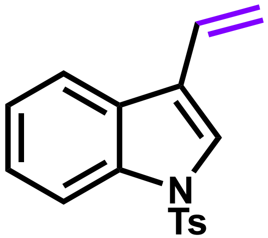



X = $CO_2Me$, 82%, 94% *ee*
X = OAc, 69%, 90% *ee*
X = Bpin, 71%, 95% *ee*



65%, 85% *ee*

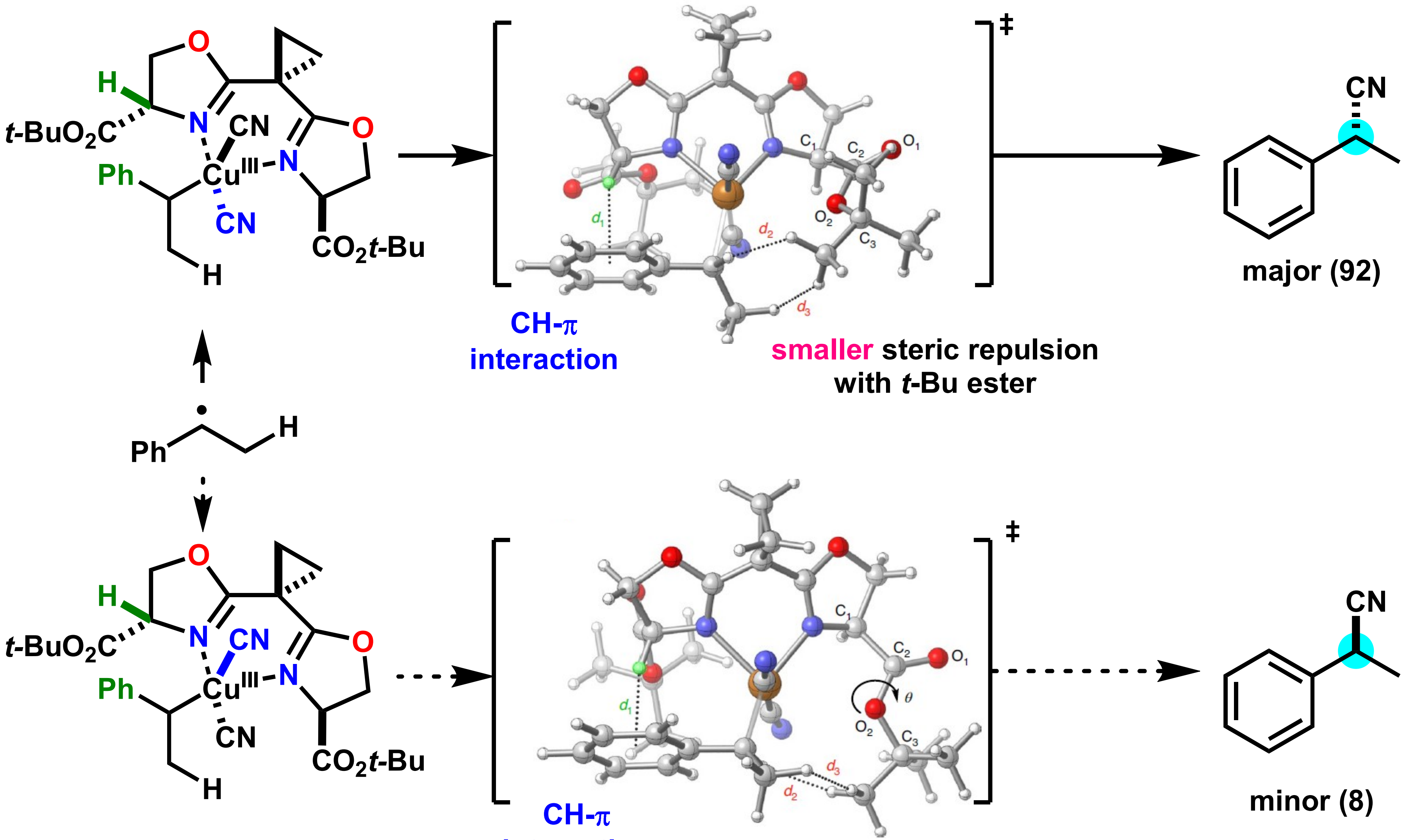
**3. Oxidation labile substrate**




11%, n.d.% *ee*, ($U_{cell}$ = 2.3 V)
71%, 87% *ee* ($U_{cell}$ = 1.8 V)


Song, L.; Fu, N.; Ernst, B. G.; Lee, W. H.; Frederick, M. O.; DiStasio Jr. R. A.; Lin, S. *Nat. Chem.* **2020**, *12*, 747.

# Explanation for enantioselectivity

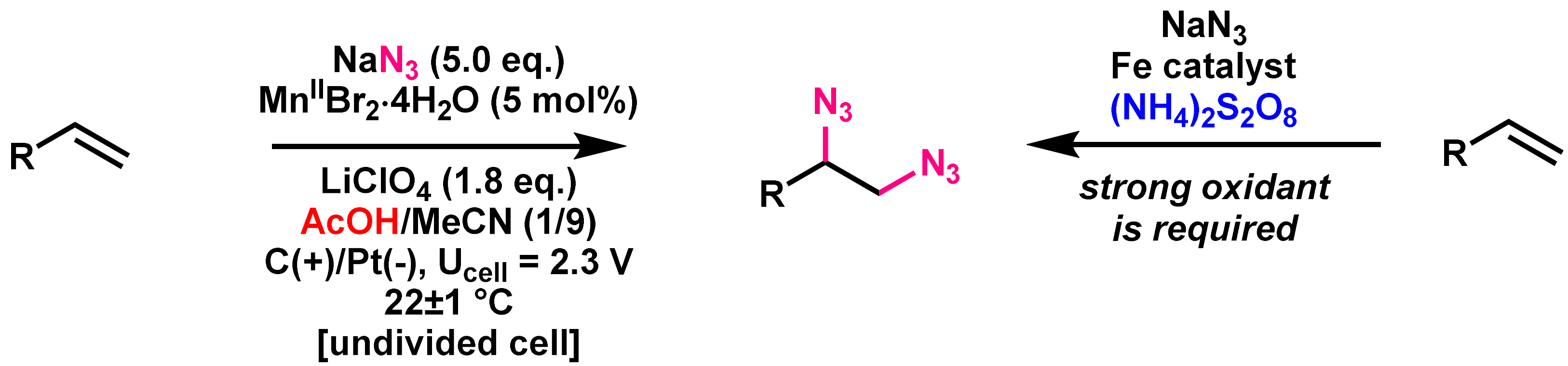



1. electron rich aromatic ring
2. internal olefin

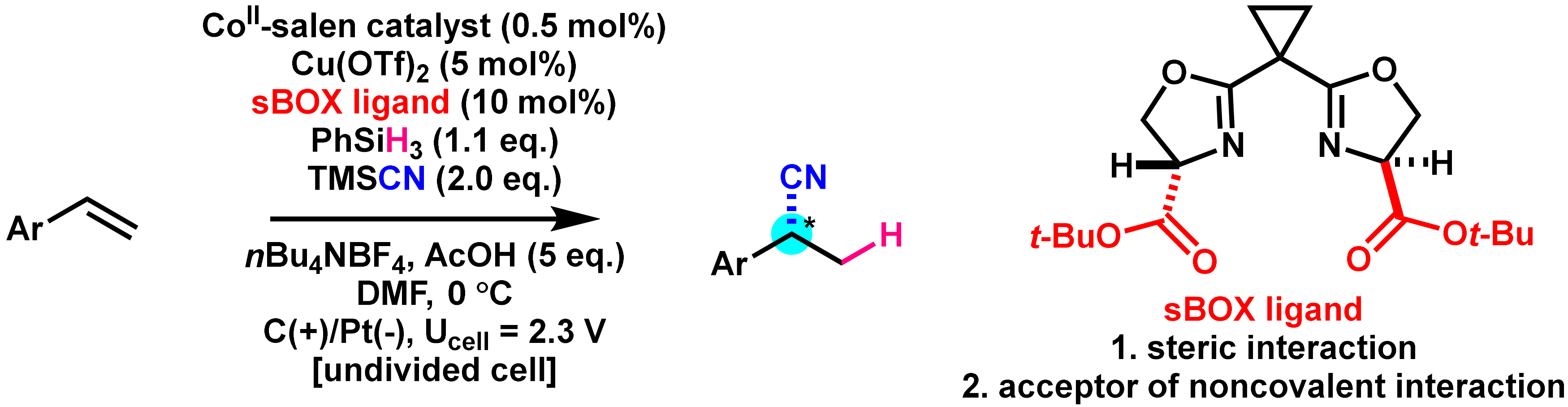
ωB97X-D/6-31G(d) level of theory


Song, L.; Fu, N.; Ernst, B. G.; Lee, W. H.; Frederick, M. O.; DiStasio Jr. R. A.; Lin, S.
*Nat. Chem.* **2020**, *12*, 747.

# Summary (1) -anodically coupled electrolysis-




1. terminal reductant AcOH expanded the substrate scope
2. $Mn^{II}$ salt electrocataysis offered milder reaction conditions




1. application of redox labile $Cu^{II}$ catalysis in electrochemical reaction
2. further development of classical BOX ligand


1) Fu, N.; Sauer, G. S.; Saha, A.; Loo, A.; Lin, S. *Science* **2017**, *357*, 575.
2) Song, L.; Fu, N.; Ernst, B. G.; Lee, W. H.; Frederick, M. O.; DiStasio Jr. R. A.; Lin, S. *Nat. Chem.* **2020**, *12*, 747.

# Contents

1. Introduction

2. Anodically coupled electrolysis -heterodifunctionalization of olefin-

nature chemistry ARTICLES
https://doi.org/10.1038/s41557-020-0469-5

Check for updates

**Dual electrocatalysis enables enantioselective hydrocyanation of conjugated alkenes**

Lu Song[1], Niankai Fu[1], Brian G. Ernst[1], Wai Hang Lee[1], Michael O. Frederick[2], Robert A. DiStasio Jr.[1] and Song Lin[1]

3. New concept for reductive functionalization

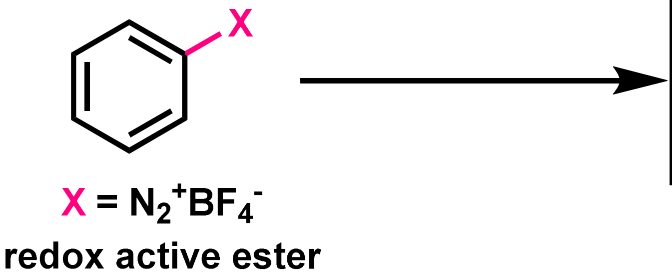
JACS JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

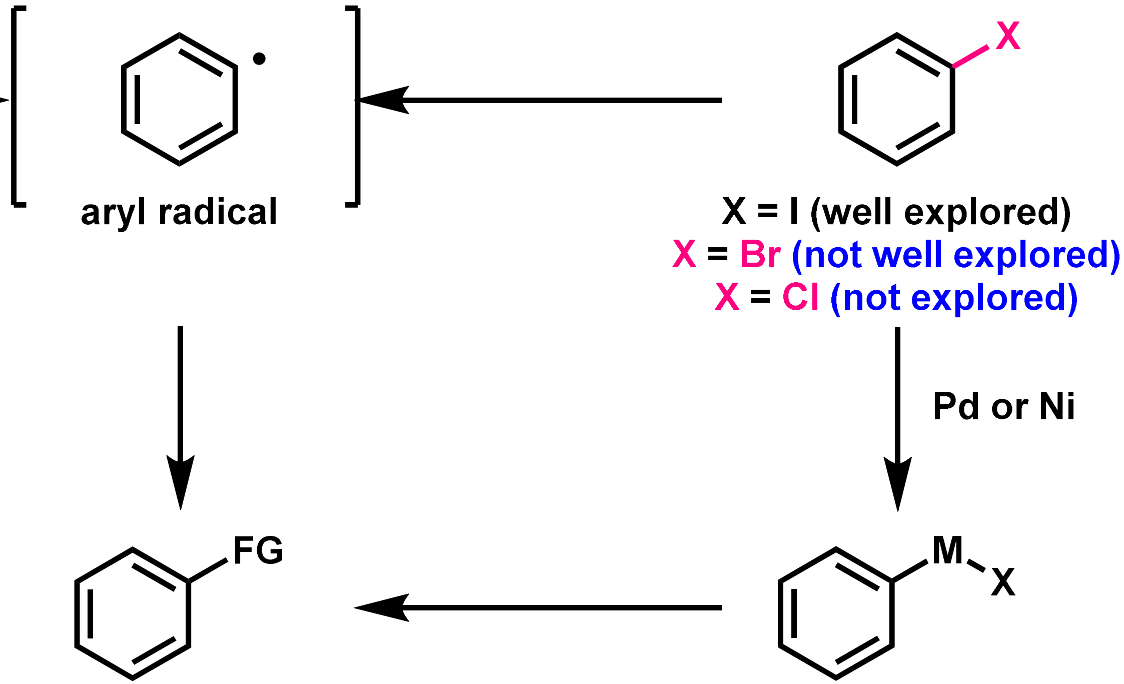
pubs.acs.org/JACS Communication

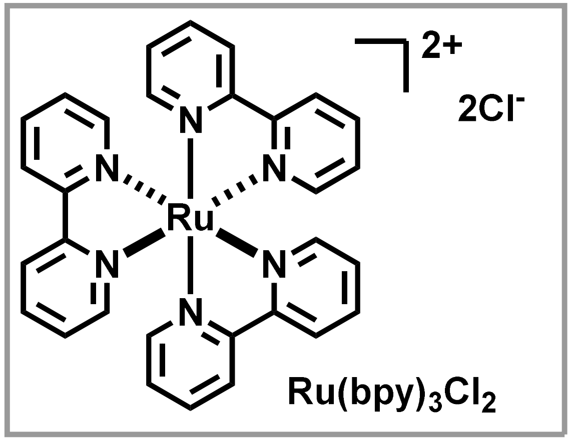
**Reductive Electrophotocatalysis: Merging Electricity and Light To Achieve Extreme Reduction Potentials**

Hyunwoo Kim, Hyungjun Kim, Tristan H. Lambert,* and Song Lin*

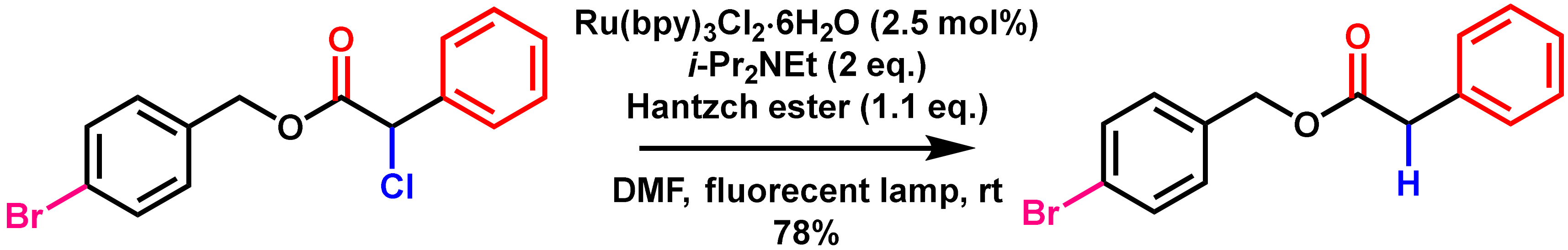
# SET induced reductive functionalization



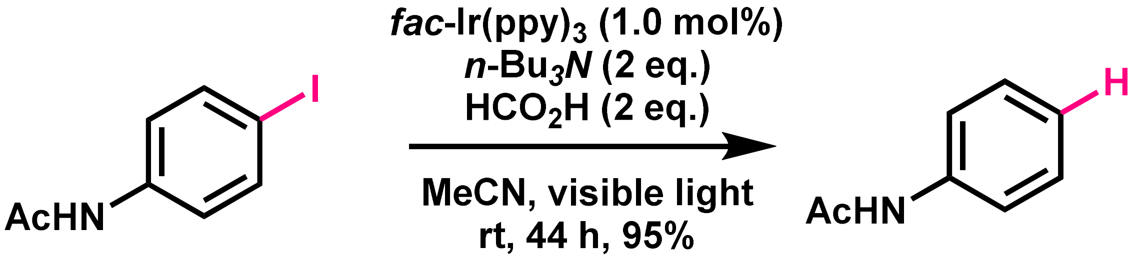




with **Lewis basic** functional group,
Pd or Ni catalyzed reaction semms to be ineffective

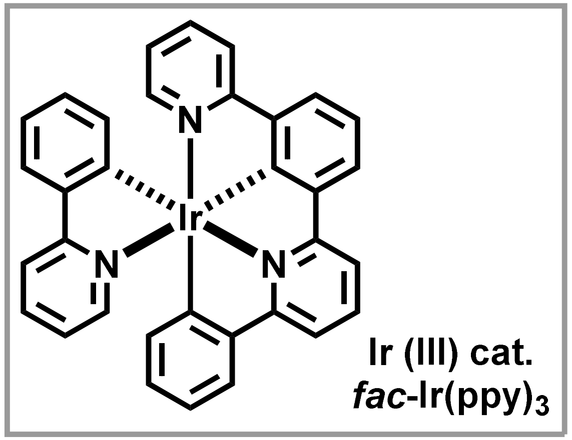


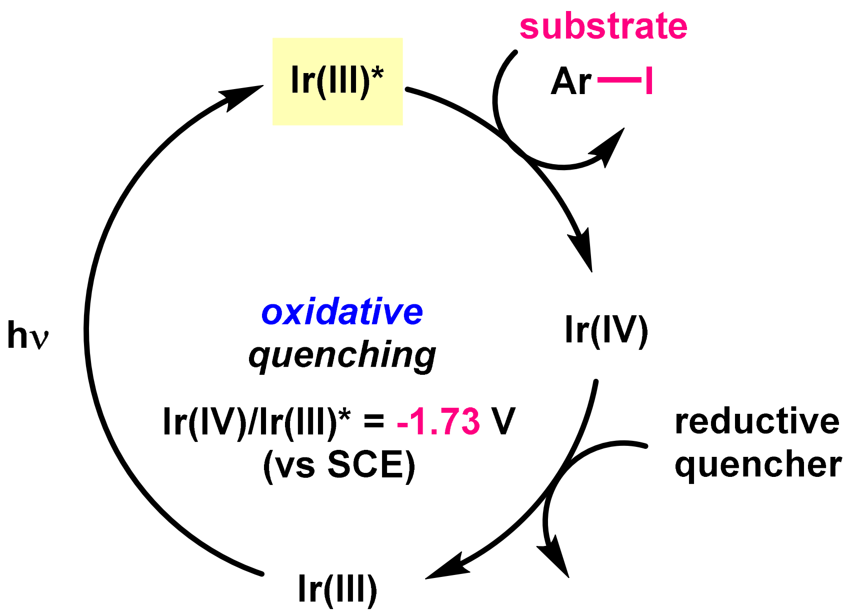

Narayanam, J. M. R.; Trucker, J. W.; Stephenson, C. R. J. *J. Am. Chem. Soc.* **2009**, *131*, 8756.

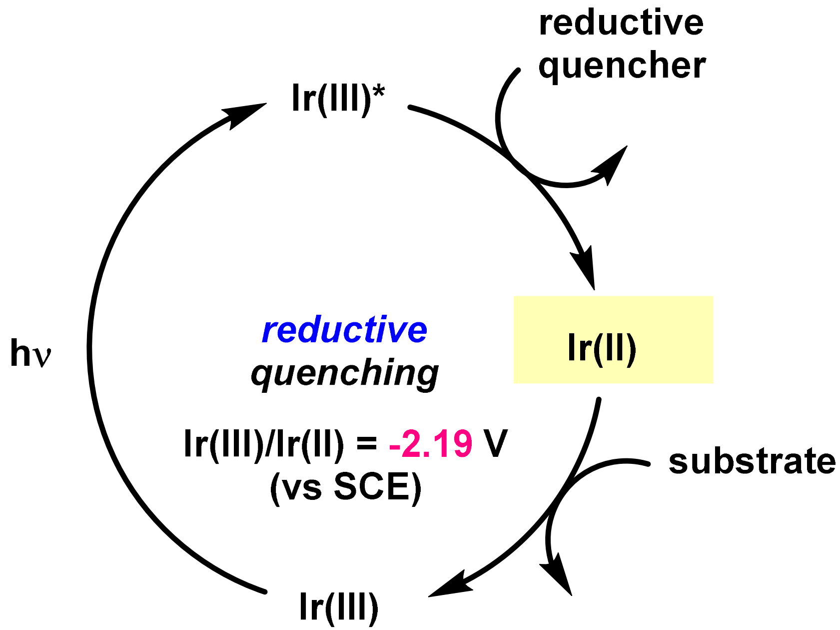
# Modification of photocatalysis




*oxidative quenching cycle*

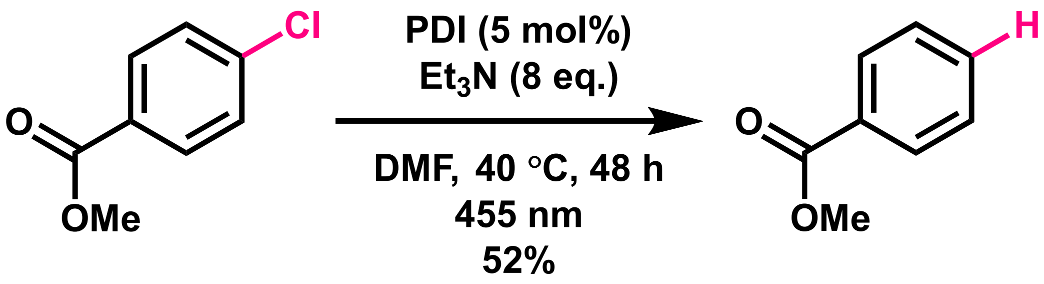


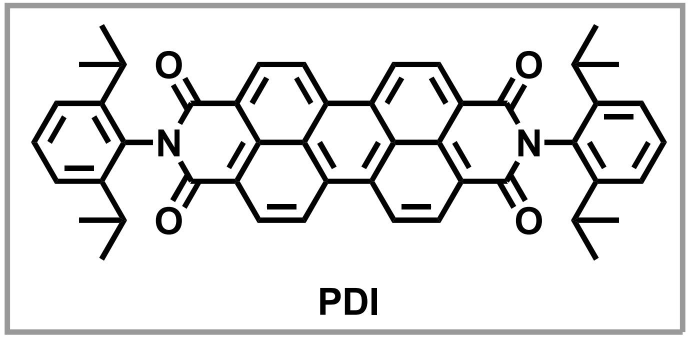



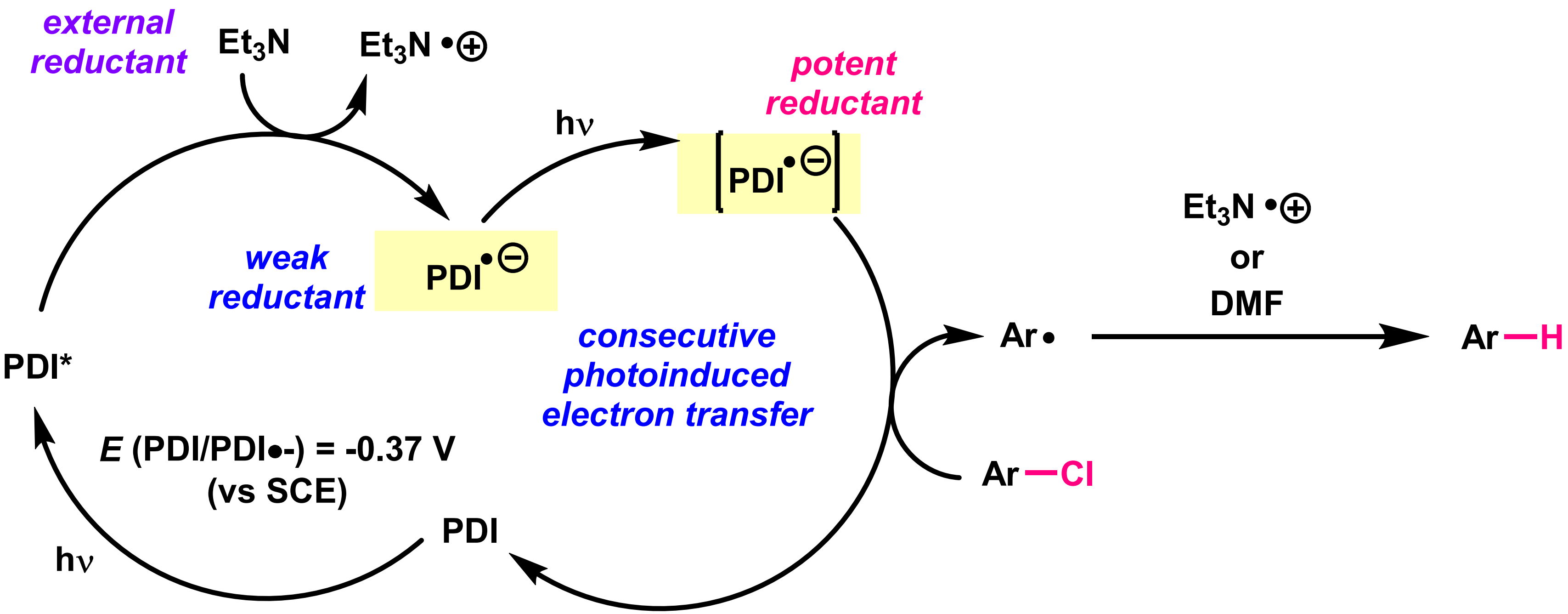




Nguyen, J. D.; D'Amato, E. M.; Narayanam, J. M. R.; Stephenson, C. R. J. *Nat. Chem.* **2012**, *4*, 854.

# Consecutive photoinduced electron transfer



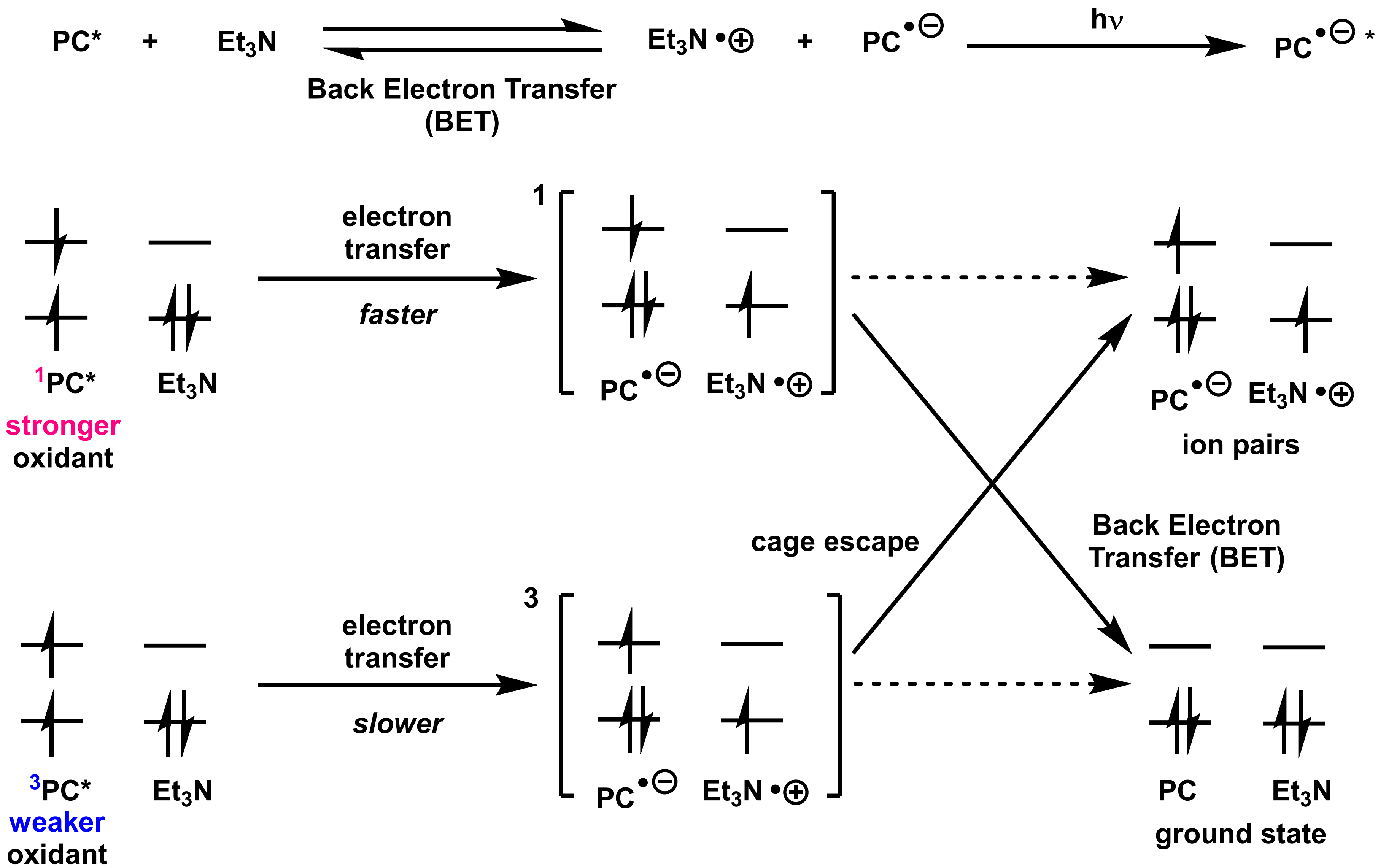




**Electron transfer between excitated state PC (PC*) and external reductant limits its application**

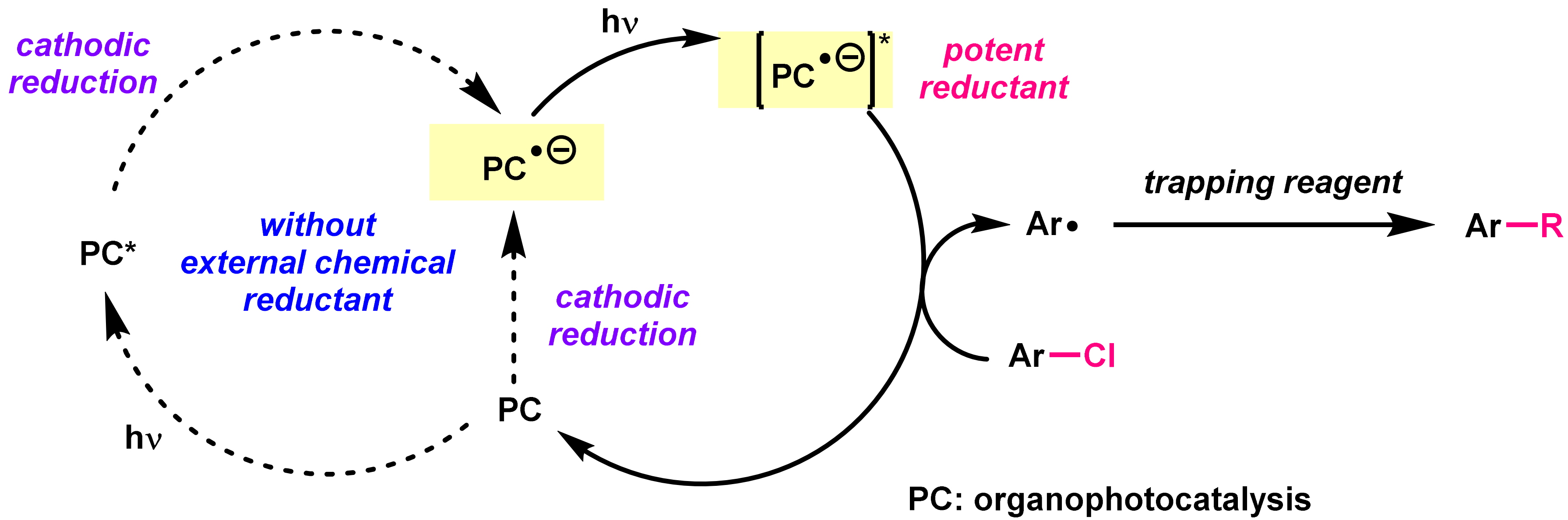
Ghosh, I.; Chosh, T.; Bardagi, J. I.; König, B. *Science* **2014**, *346*, 725.

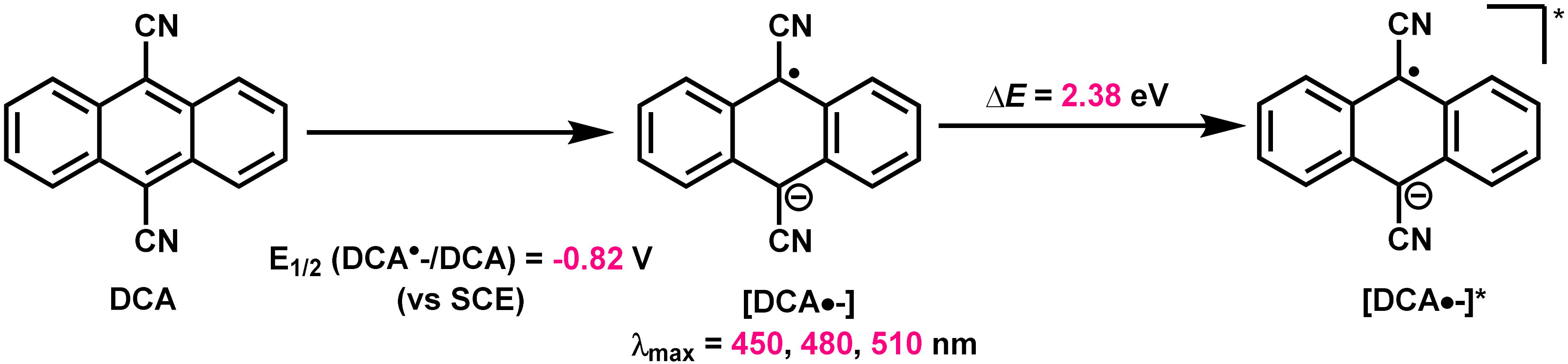
# BET from organophotocatalysis




Romero, N. A.; Nicewicz, D. A. *Chem. Rev.* **2016**, *116*, 10075.

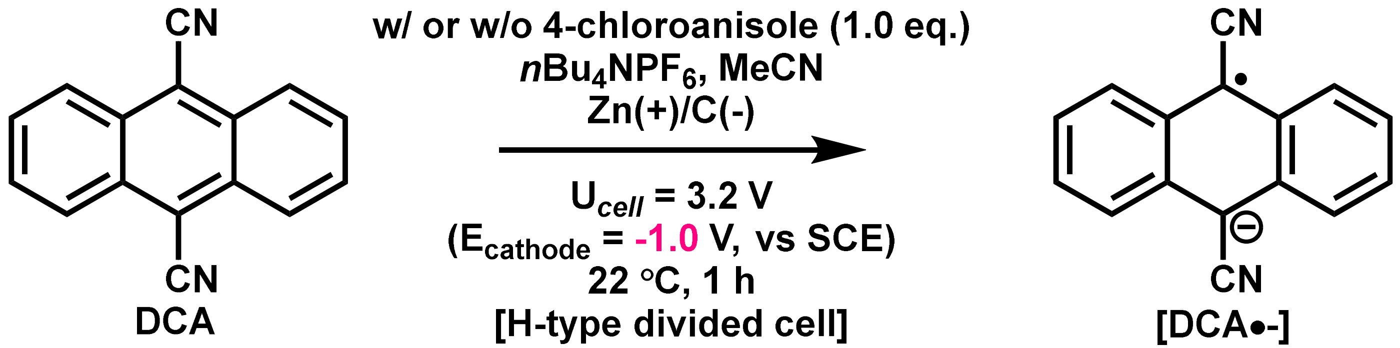
# Electrophotocatalytic approach




Kim, H.; Kim, H.; Lambert, T. H.; Lin, S. *J. Am. Chem. Soc.* **2020**, *142*, 2087.
Eriksen, J.; Lund, H.; Nyvad, A. I. *Acta. Chem. Scand.* **1983**, *37*, 459.

# Electrochemical formation of DCA radical anion




$E_{1/2}$ (DCA$^{\bullet}$-/DCA) = -0.82 V (vs SCE)

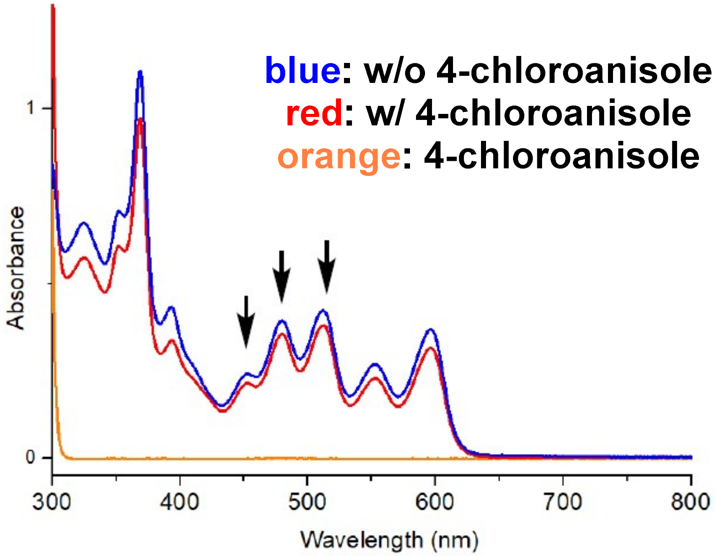



**Figure 1. UV-vis spectrum of cathode solution after the electrolysis**

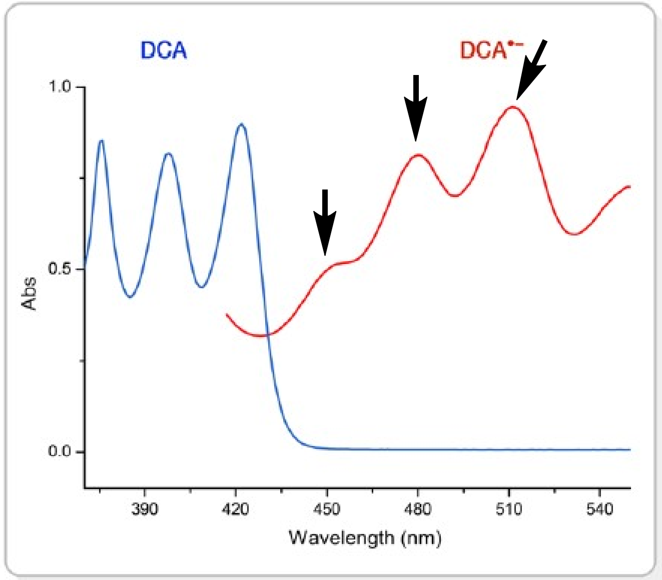
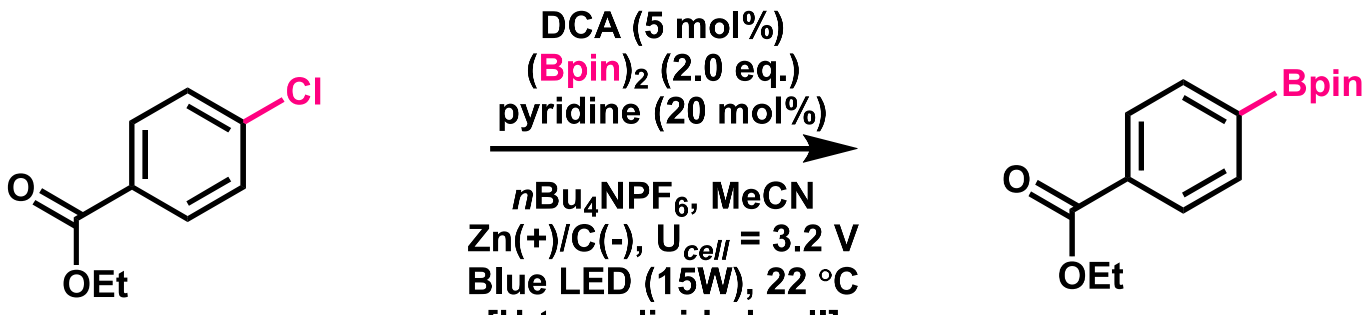



**Figure 2. UV-vis spectrum of DCA and DCA radical anion**

**DCA radical anion is electronically generated without the formation of EDA complex**

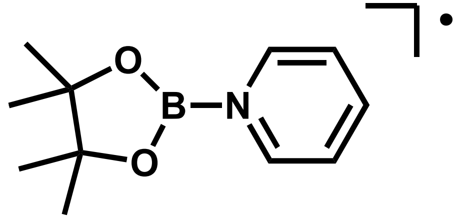
Kim, H.; Kim, H.; Lambert, T. H.; Lin, S. *J. Am. Chem. Soc.* **2020**, *142*, 2087.

# Optimization of reductive radical borylation




$E_{red}$ = -2.04 V
(vs SCE)

| entry | varidation | results |
|---|---|---|
| 1 | none | 88% |
| 2 | no electrolysis | <5% |
| 3 | no light | <5% |
| 4 | no DCA | <5% |
| 5 | no pyridine | 58% |
| 6 | undivided cell | 37% |

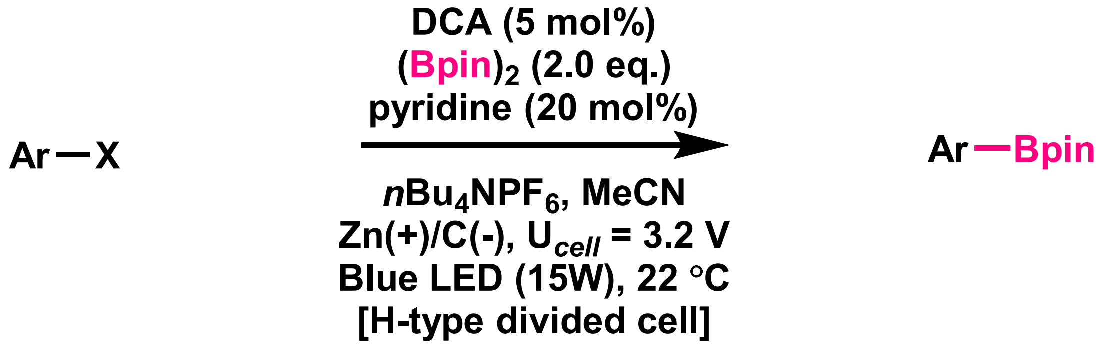


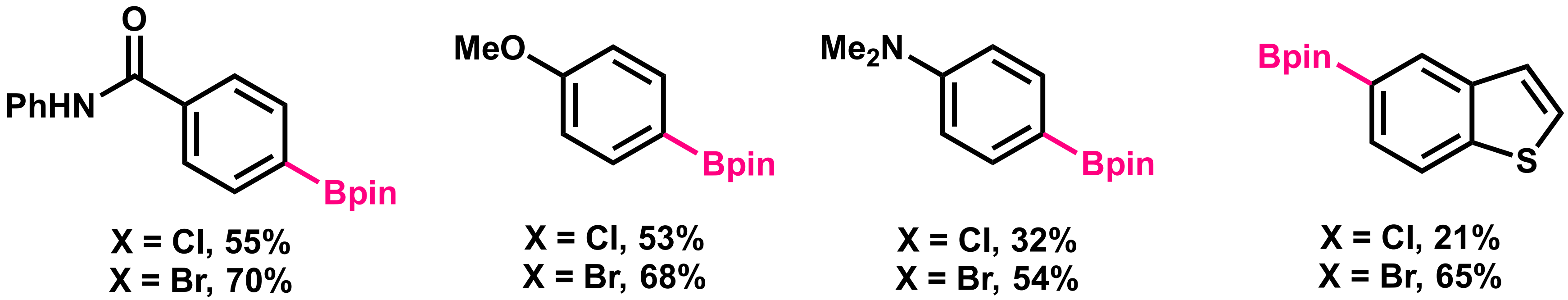

**A**
**stabilized boryl radical**

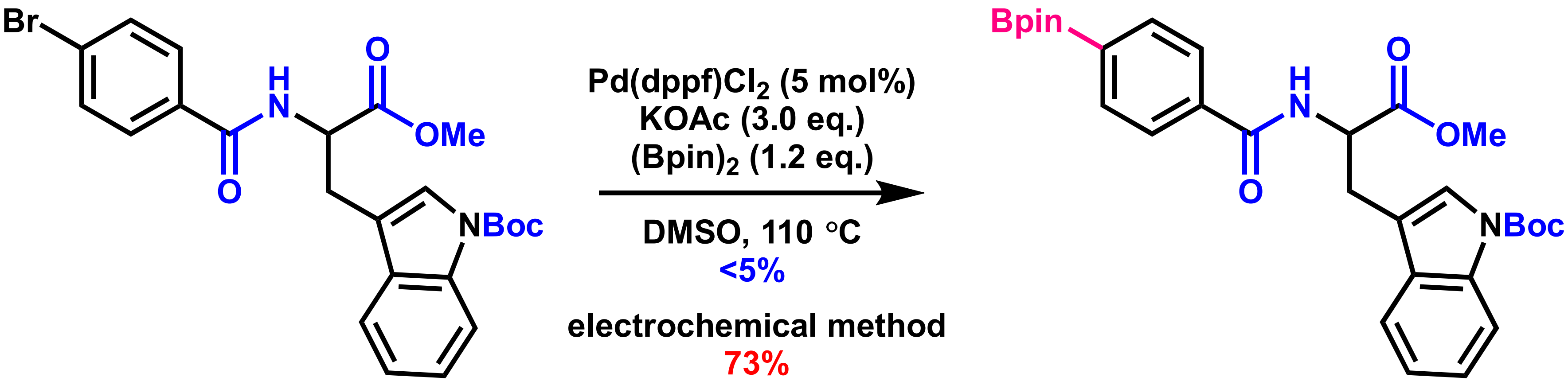
**$Zn \rightarrow Zn^{2+} \rightarrow Zn$**
**(Zn bridge formation)**

Kim, H.; Kim, H.; Lambert, T. H.; Lin, S. *J. Am. Chem. Soc.* **2020**, *142*, 2087.
Wang, G.; Zhang, H.; Zhao, J.; Li, W.; Cao, L.; Zhu, C.; Li, S. *Angew. Chem., Int. Ed.* **2016**, *55*, 5985.

# Substrate scope (1)

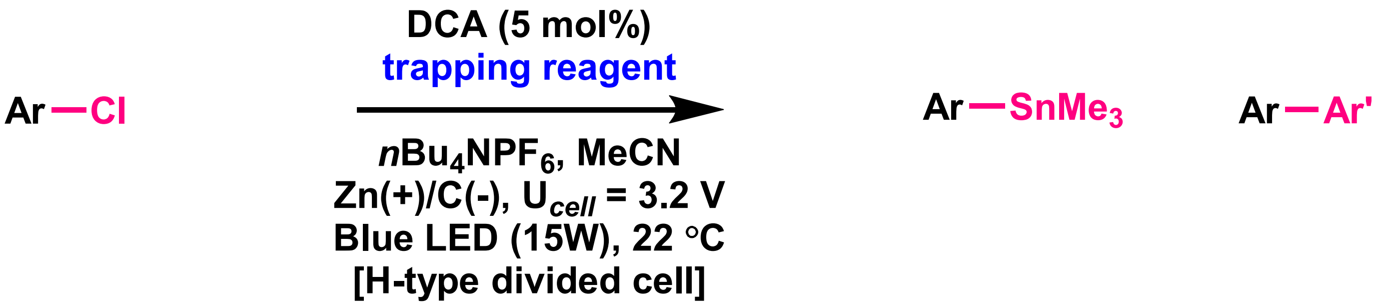


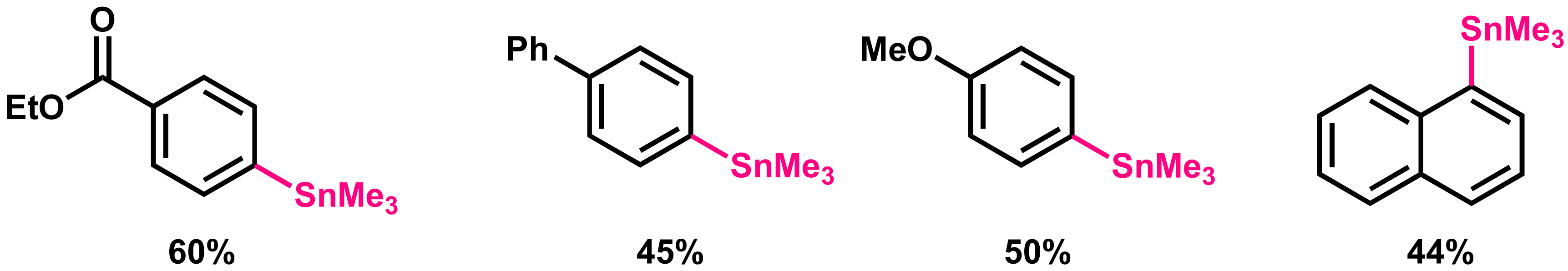




Kim, H.; Kim, H.; Lambert, T. H.; Lin, S. *J. Am. Chem. Soc.* **2020**, *142*, 2087.

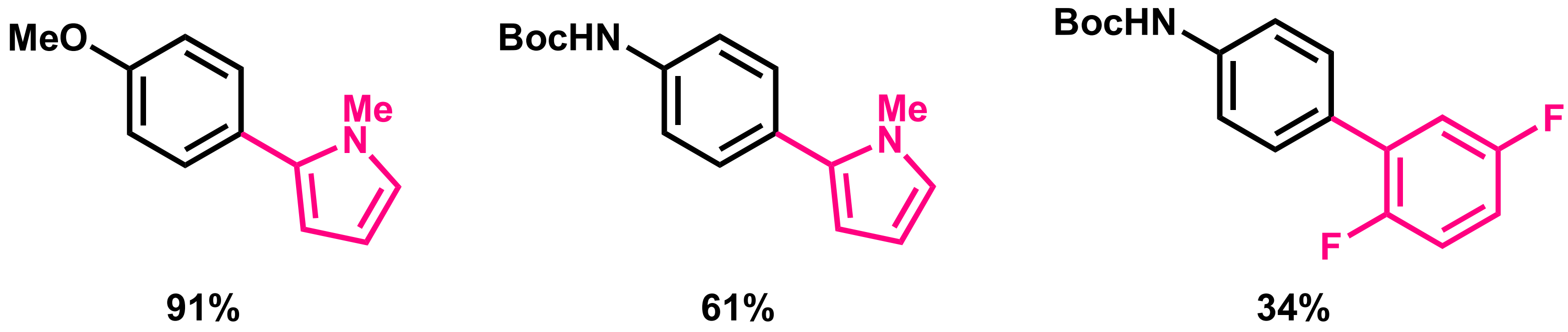
# Substrate scope (2)




trapping reagent : $(Me_3Sn)_2$ (2.0 eq.)

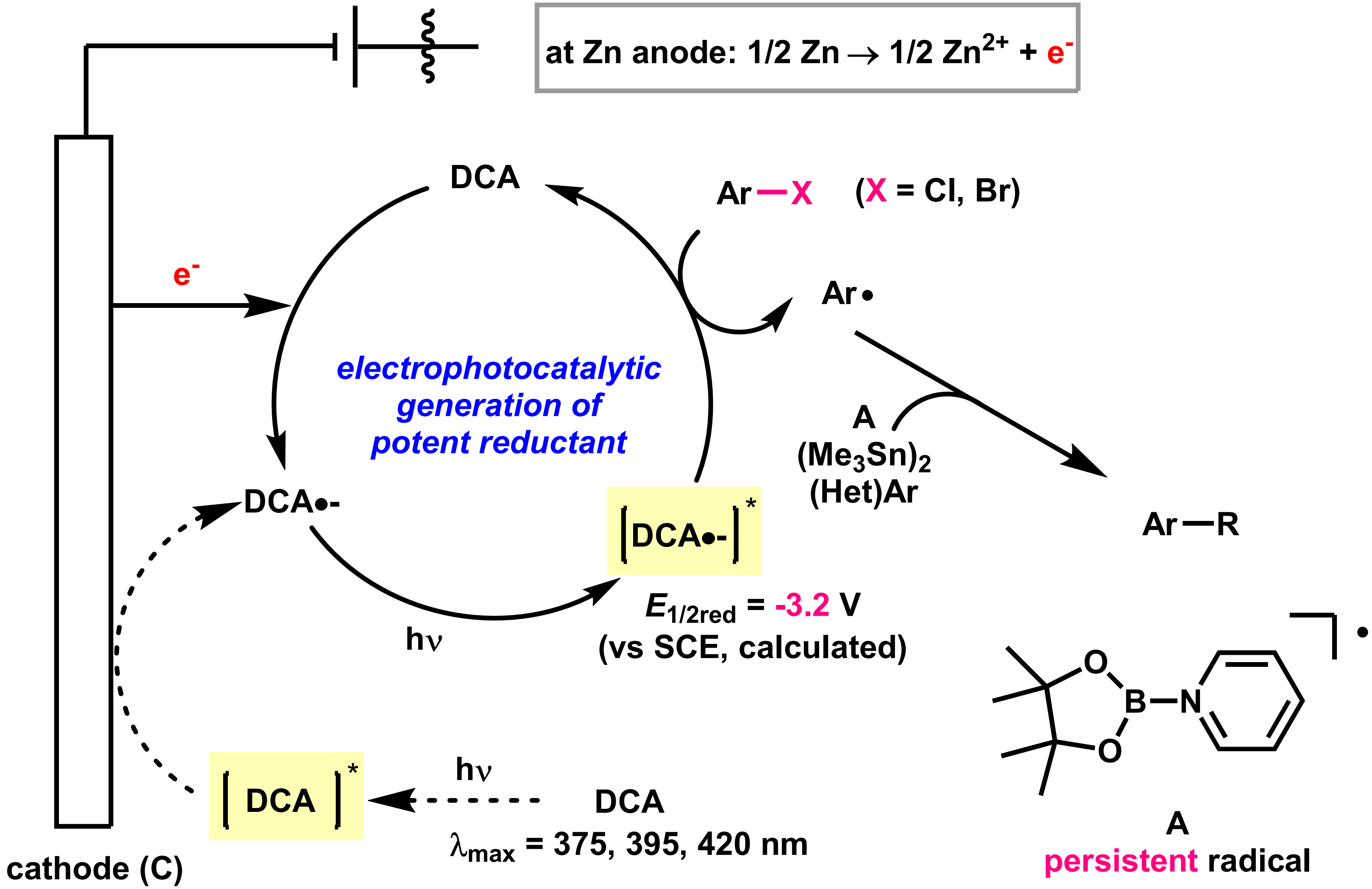



trapping reagent : (Het)Ar (20 eq.)



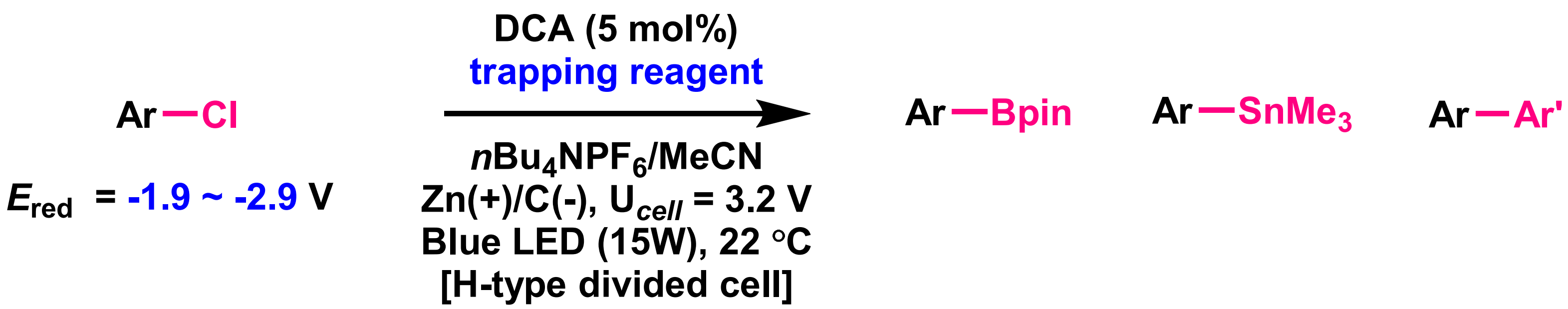

Kim, H.; Kim, H.; Lambert, T. H.; Lin, S. *J. Am. Chem. Soc.* **2020**, *142*, 2087.

# Reaction mechanism




Kim, H.; Kim, H.; Lambert, T. H.; Lin, S. *J. Am. Chem. Soc.* **2020**, *142*, 2087.

# Summary (2) -Electrophotocatalysis-




**1. Electrophotocatalytic generation of potent reductant ($E_{red}$ = -3.2 V)**

**2. compatible with Lewis basic functional group**

**many research groups adapted these strategies**

***modification of external reductant & organophotocatalysis***

**Zickens (2020, 2021)**
**Wu (2021)**

Kim, H.; Kim, H.; Lambert, T. H.; Lin, S. *J. Am. Chem. Soc.* **2020**, *142*, 2087.