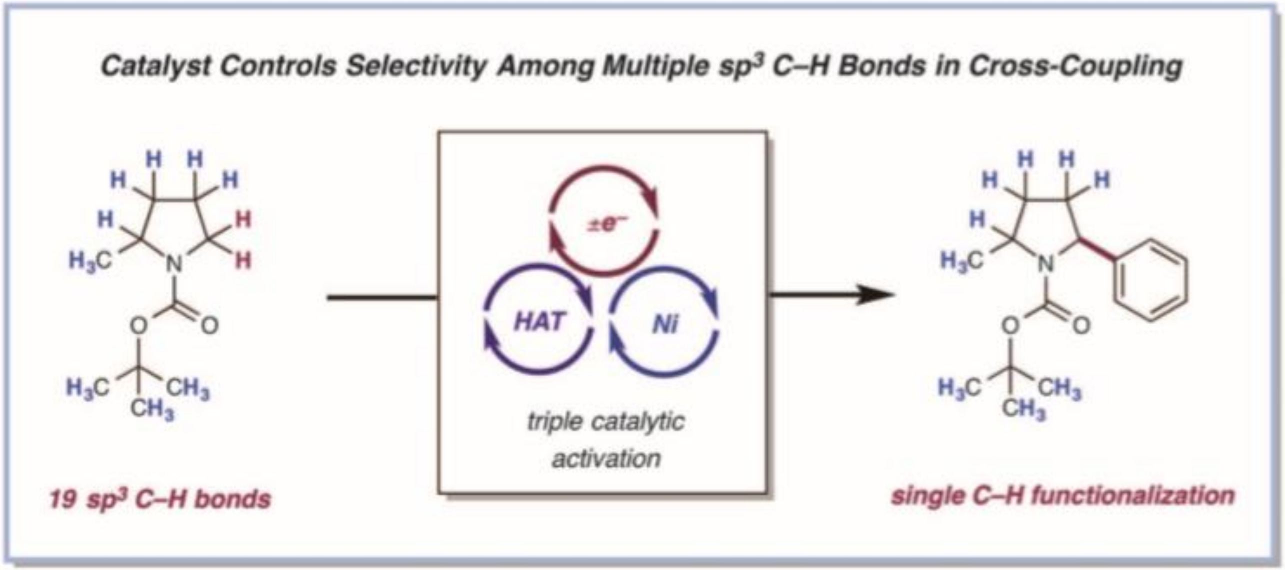
# Hybridization of Nickel Catalysis and Photoredox Catalysis

Literature seminar#1

B4 Hiromu Fuse

2017/02/04(Sat)

# Introduction




MacMillan, D. W. C. *et al*. *Science* **2016**, *352*, 1304.

- ***Novel cross coupling was reported!***
- ***Highly selective sp$^3$ C-H functionalization!***
- ***New possibility of Photoredox Catalysis!***

**What lies behind this discovery?**

# Introduction

## DAVE MACMILLAN

Dave MacMillan was born in Bellshill, Scotland and received his undergraduate degree in chemistry at the University of Glasgow, where he worked with Dr. Ernie Colvin. In 1990, he began his doctoral studies under the direction of Professor Larry Overman at the University of California, Irvine, before undertaking a postdoctoral position with Professor Dave Evans at Harvard University (1996). He began his independent career at University of California, Berkeley in July of 1998 before moving to Caltech in June of 2000 (Earle C. Anthony Chair of Organic Chemistry).

In 2006, Dave moved to the east coast of the US to take up the position of James S. McDonnell Distinguished University Professor at Princeton University and he served as Department Chair from 2010-15.

***The pioneer of Photoredox Catalysis!***

# Today’s Content

1. ***Nickel-catalyzed cross-coupling via radical pathway***
2. ***Hybrid catalysis of photoredox catalysis and nickel catalysis***
3. ***Hybrid catalysis of photoredox catalysis, nickel catalysis and HAT catalysis***

# Today's Content

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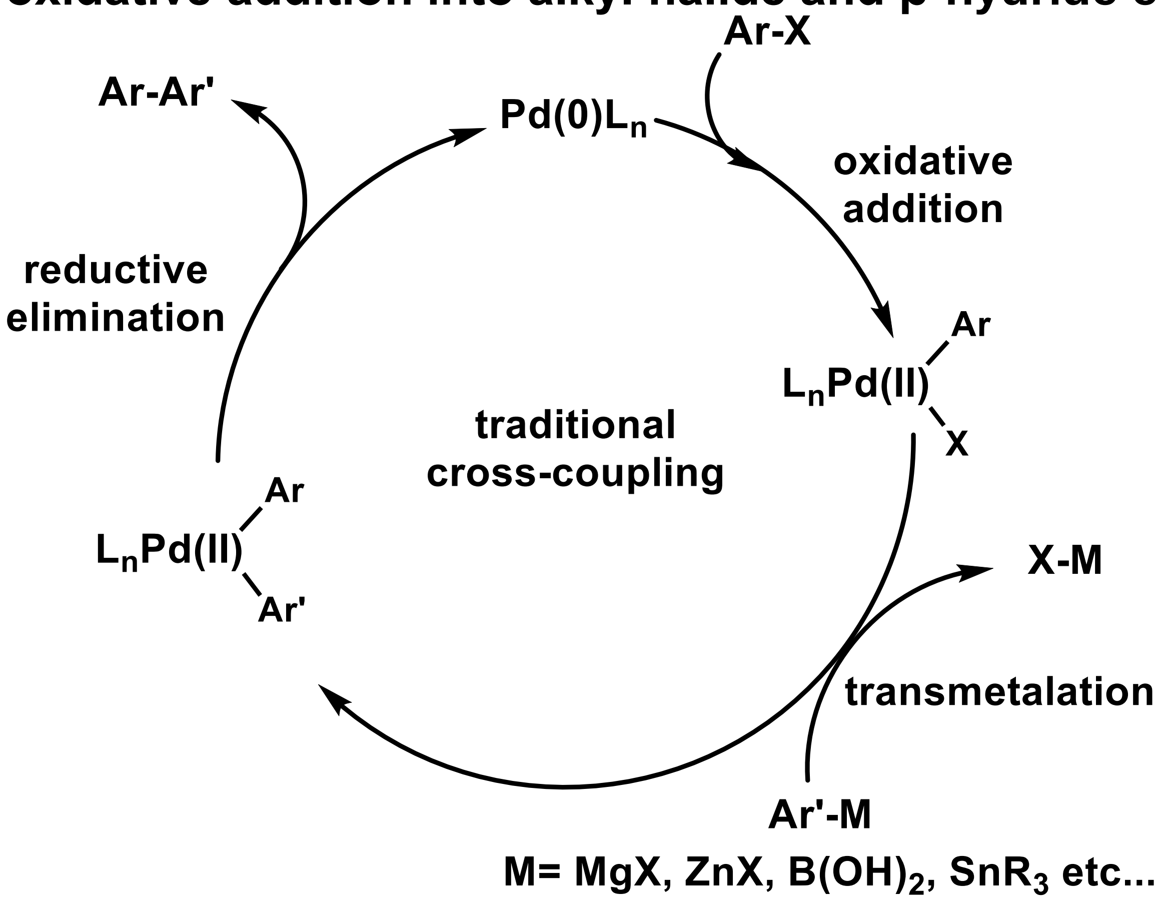
3. ***Hybrid catalysis of photoredox catalysis, nickel catalysis and HAT catalysis***

# Comparing Cross-Couplings

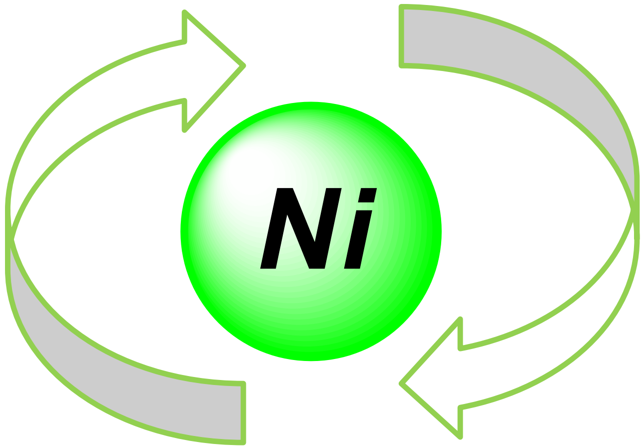
- **Traditional cross-coupling**
- **Mainly for $sp^2$-$sp^2$ bond formation**

**because of slow oxidative addition into alkyl halide and β-hydride elimination as side reaction**




**Ni catalyst has other possibility.**

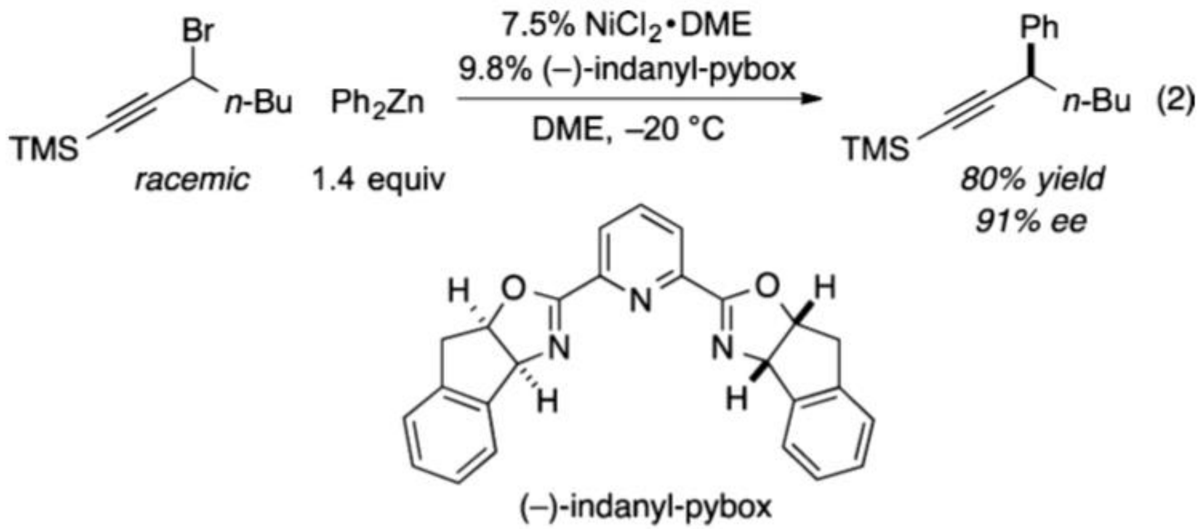
# Nickel Catalysis




| Nickel | Palladium |
|---|---|
| –1 **0 +1 +2 +3** +4 | **0** +1 **+2** +3 **+4** |
| Smaller atomic radius | Larger atomic radius |
| Less electronegative | More electronegative |
| Harder | Softer |
| Facile oxidative addition | Facile reductive elimination |
| Facile β-migratory insertion | Facile β-hydride elimination |
| Radical pathways more accessible | |

Jamison, T. F. *et al. Nature* **2014**, *509*, 299.

# Nickel-Catalyzed Cross-Coupling

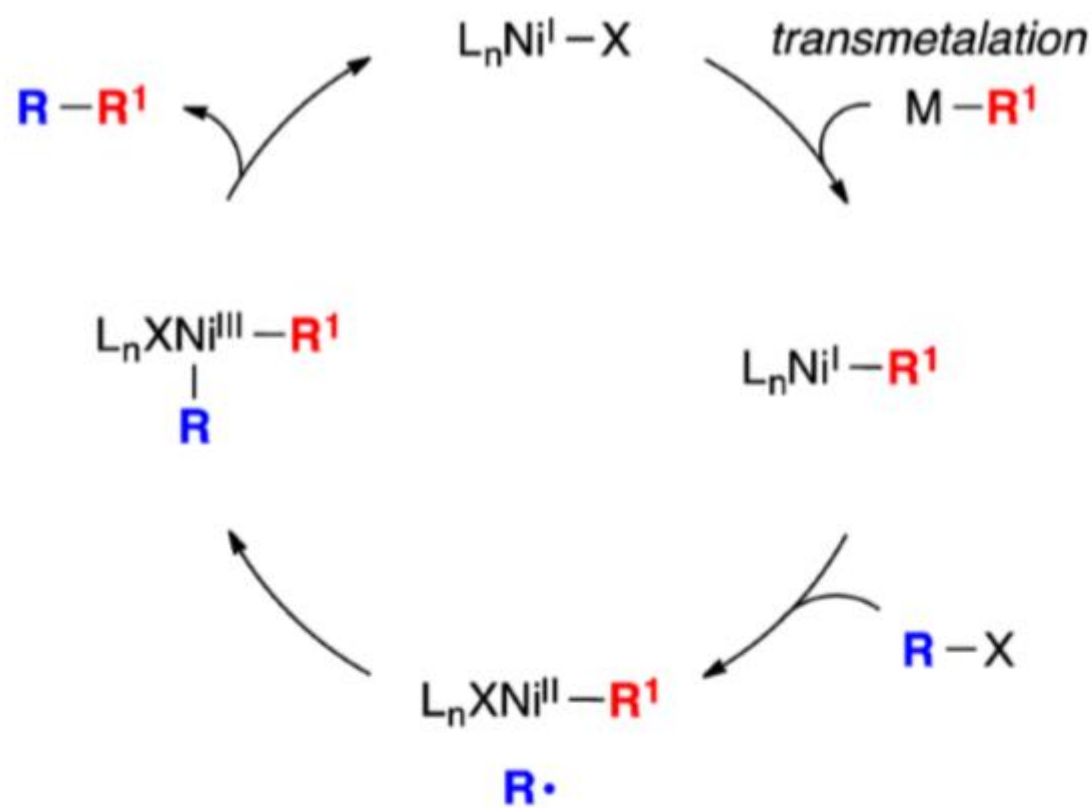



Fu, G. C. *et al. J. Am. Chem. Soc.* **2008**, *130*, 12645.

- ***$sp^3$ electrophile can be used!***
- ***enantioselective cross-coupling from a racemic compound.***

**How does this reaction proceed?**

# Firstly Proposed Cycle

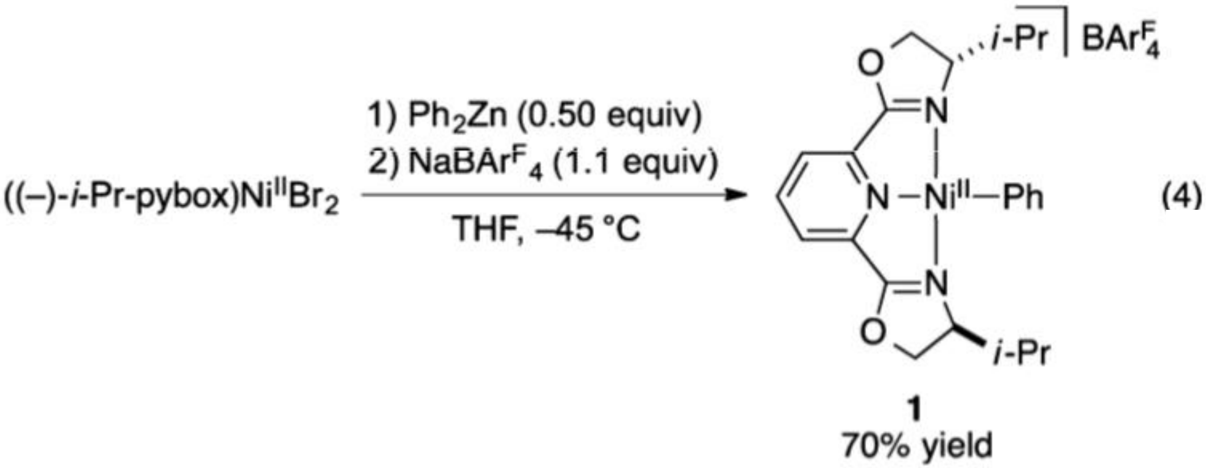



- ***Transmetalation before oxidative addition?***



Fu, G. C. *et al. J. Am. Chem. Soc.* **2014**, *136*, 16588.

# Synthesis of Nickel Complex




(BAr$^F_4$ = tetrakis(3,5-bis(trifluoromethyl)phenyl)borate)

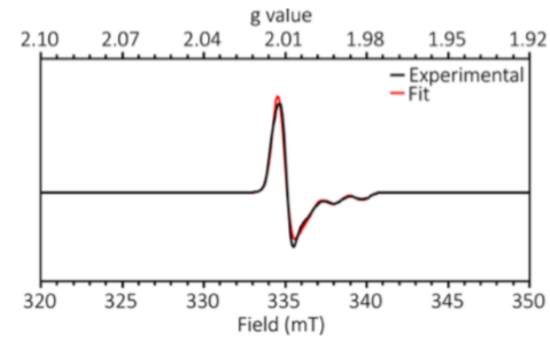
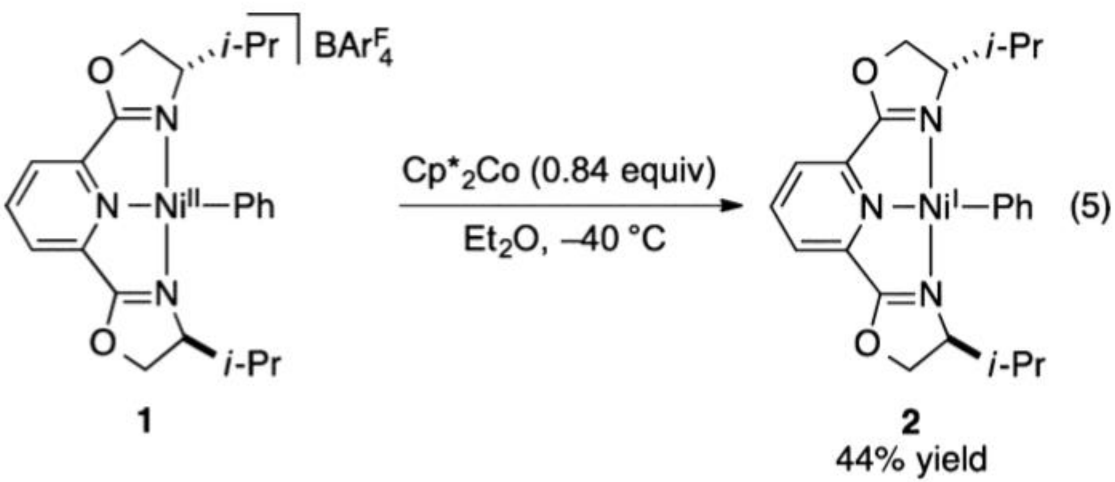



**Figure 3.** EPR spectrum of ((−)-*i*-Pr-pybox)Ni$^I$Ph (**2**; black) and corresponding fit (red). Fit parameters: $g_1$ = 2.0067, $g_2$ = 2.0075, $g_3$ = 1.9889, $^{14}$N coupling (MHz) = 0.0205, 0.0124, 47.2047, line width = 0.9929. X-band EPR spectra were collected at 77 K in a toluene glass at $\upsilon$ = 9.411 GHz at 2 mW power and a modulation amplitude of 2 G.

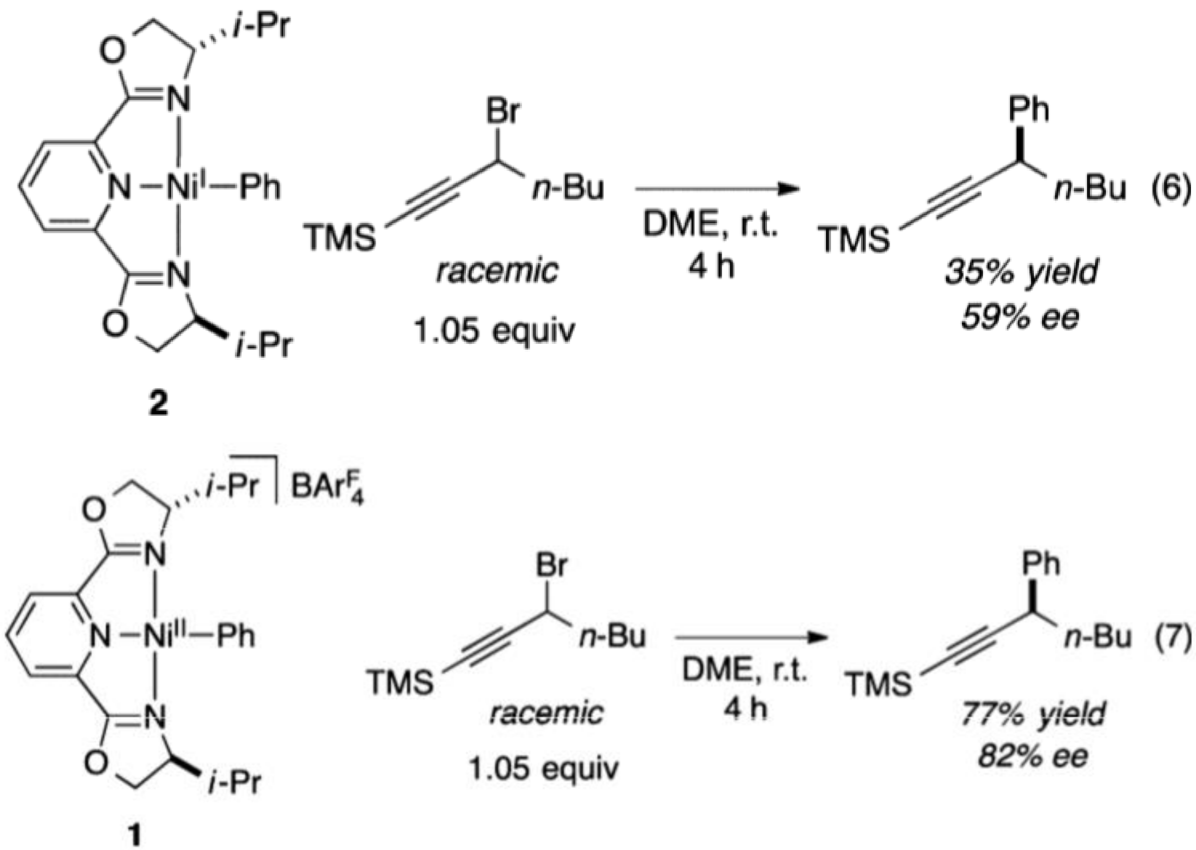



- ***Nickel(I) complex (2) was confirmed by both ESI-MS and EPR spectrum***



Fu, G. C. *et al. J. Am. Chem. Soc.* **2014**, *136*, 16588.

# Stoichiometric Reaction

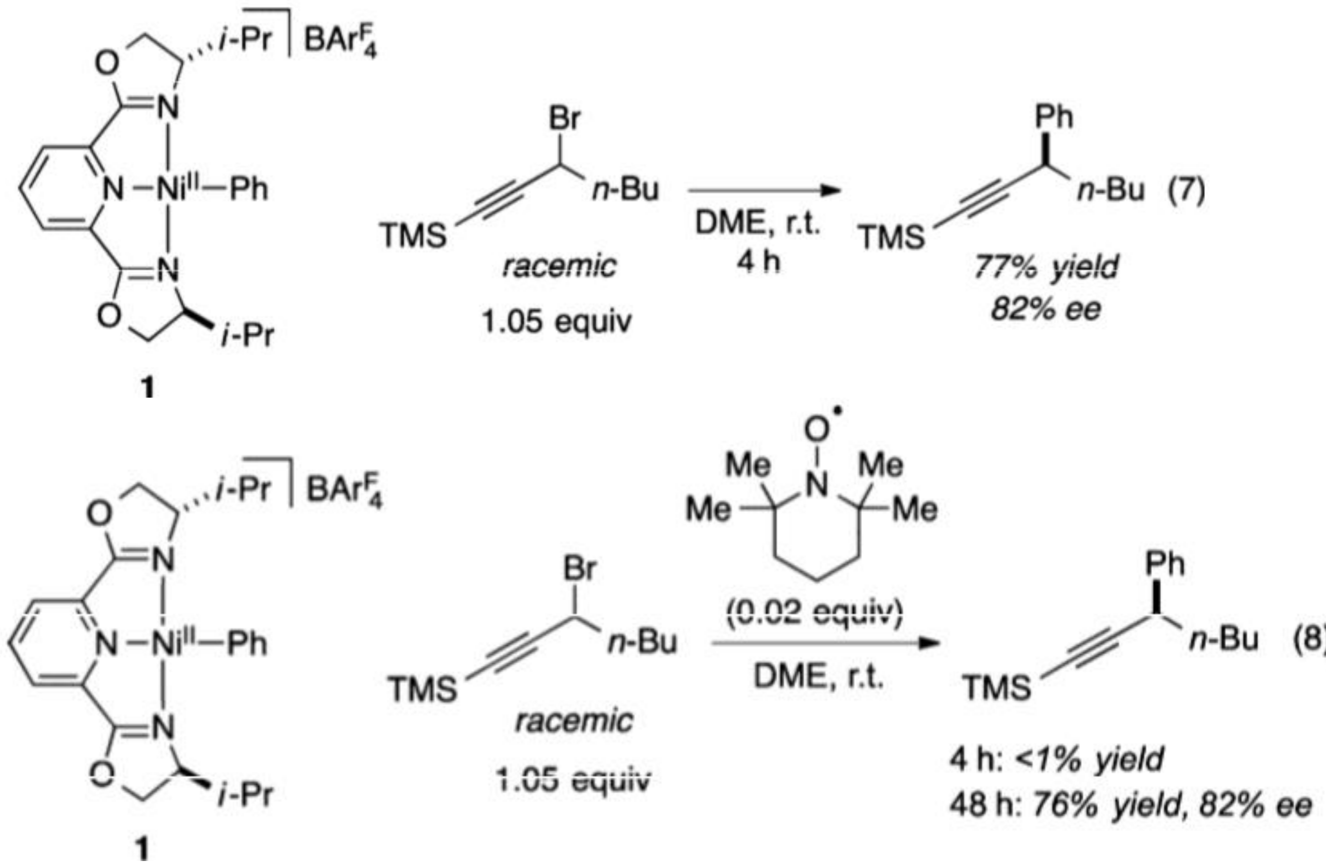



- ***Although in both cases reactions occurred, the reaction of phenylnickel(II) was more consistent with the normal reaction.***



Fu, G. C. *et al. J. Am. Chem. Soc.* **2014**, *136*, 16588.

# Oxidative Addition via Radical Pathway

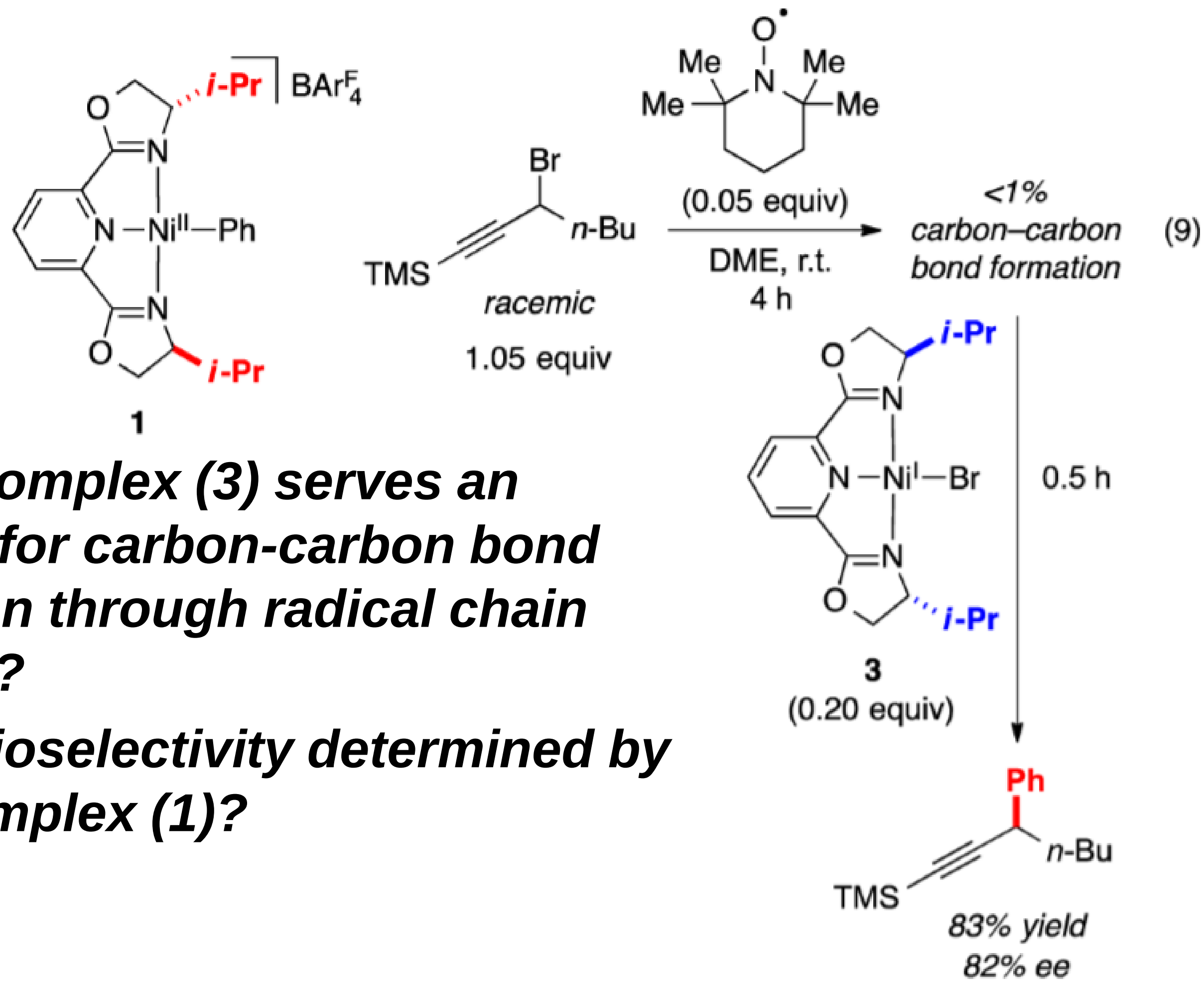



- ***TEMPO traps propargylic radical. It is confirmed by ESI-MS. (calculated for $C_{19}H_{37}NOSi+H^{+}$: 324.2717, observed: 324.2724)***



Fu, G. C. *et al. J. Am. Chem. Soc.* **2014**, *136*, 16588.

# Radical Propagation

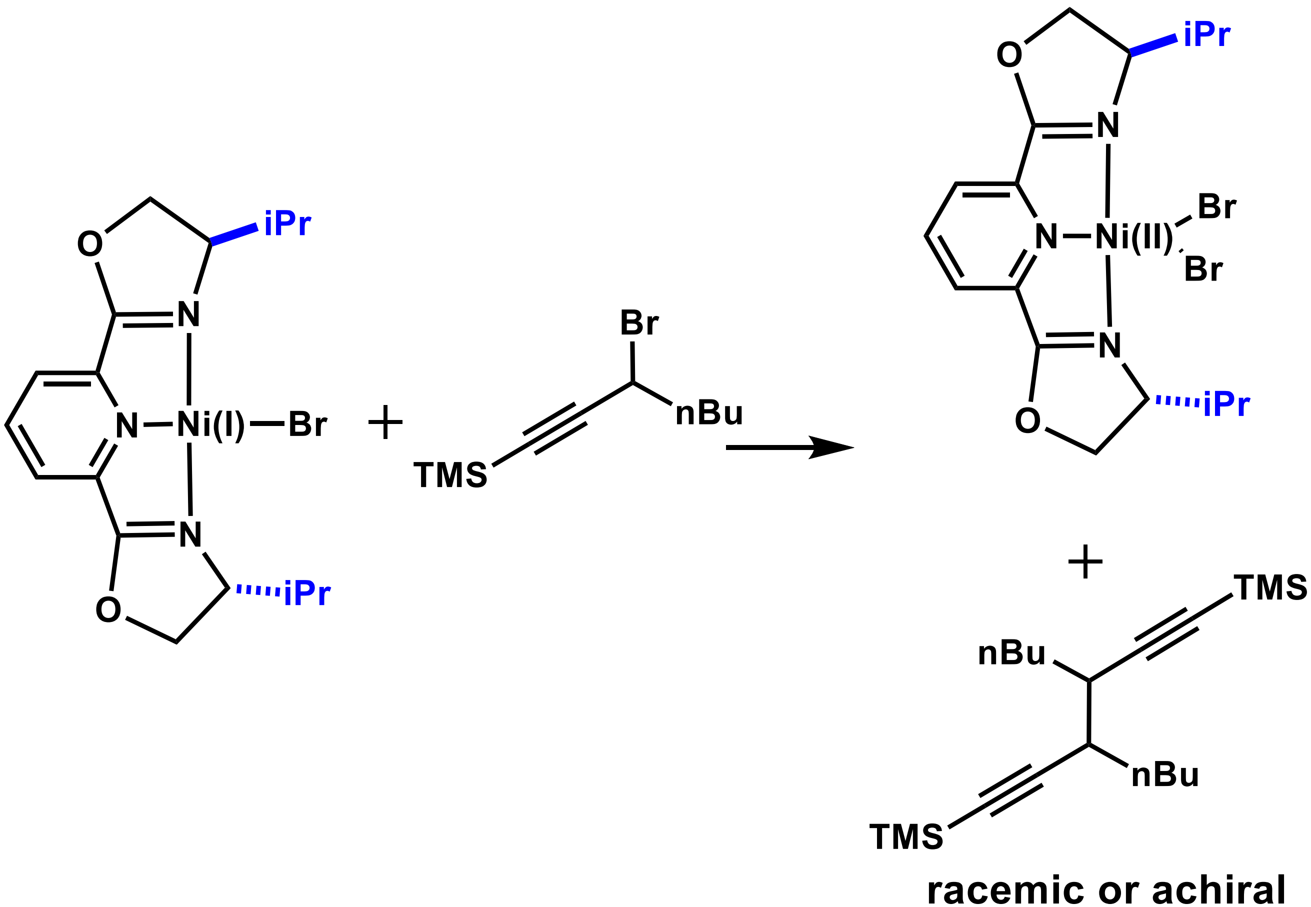



- ***Is Ni(I) complex (3) serves an initiator for carbon-carbon bond formation through radical chain process?***
- ***Is enantioselectivity determined by Ni(II) complex (1)?***



Fu, G. C. *et al. J. Am. Chem. Soc.* **2014**, *136*, 16588.

# Radical Propagation

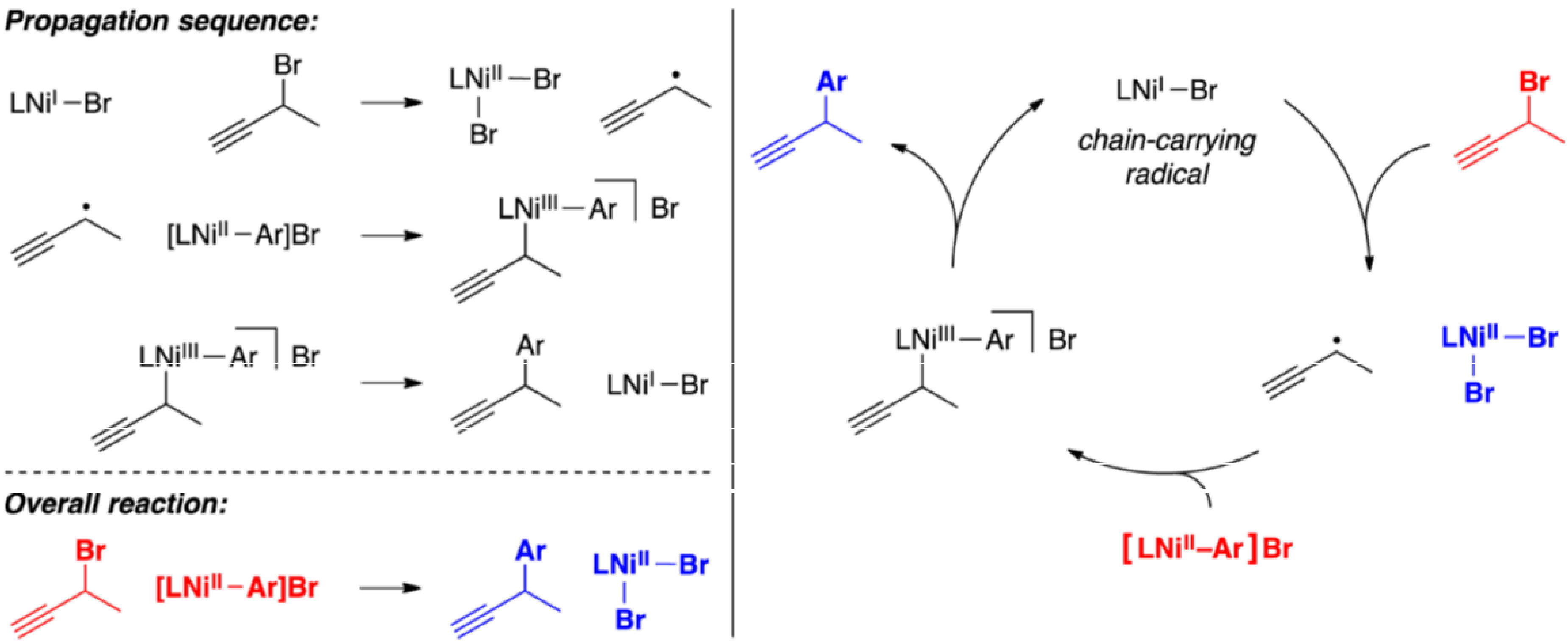



- ***((iPrPybox)Ni(I)Br) initiates radical process.***



Fu, G. C. *et al. J. Am. Chem. Soc.* **2014**, *136*, 16588.

# Radical Chain Mechanism

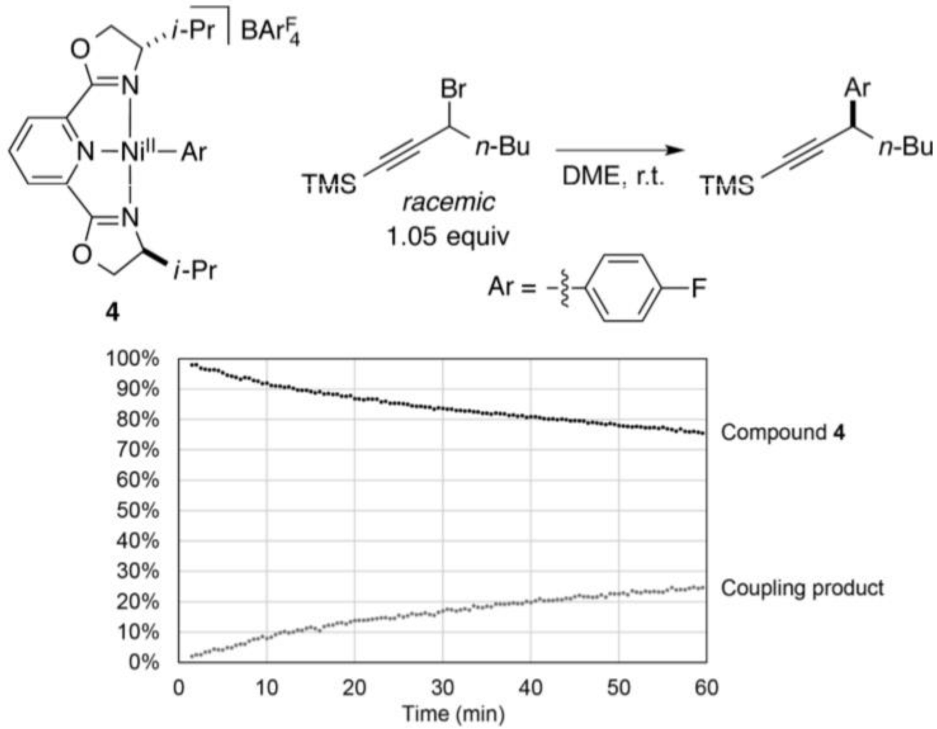



- ***Oxidative addition through bimetallic mechanism***



Fu, G. C. *et al. J. Am. Chem. Soc.* **2014**, *136*, 16588.

# Stoichiometric Reaction




**Analyzed by 19F-NMR**

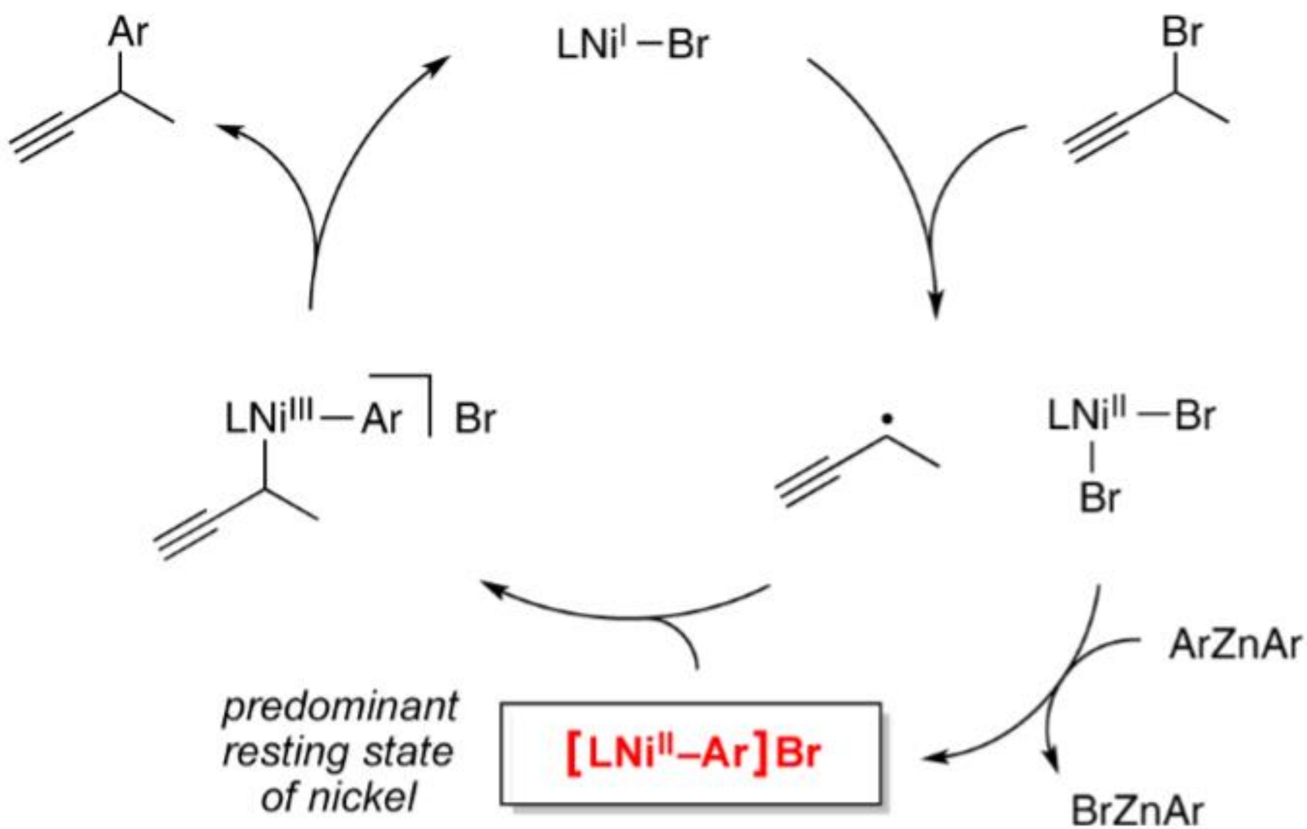
- ***When the reaction is monitored by EPR spectroscopy, no signal is observed. So, nickel(I) and nickel (III) complexes are not present in significant quantities.***

- ***The consumption of nickel(II) complex (4) directly correlates the formation of coupling product.***



Fu, G. C. *et al. J. Am. Chem. Soc.* **2014**, *136*, 16588.

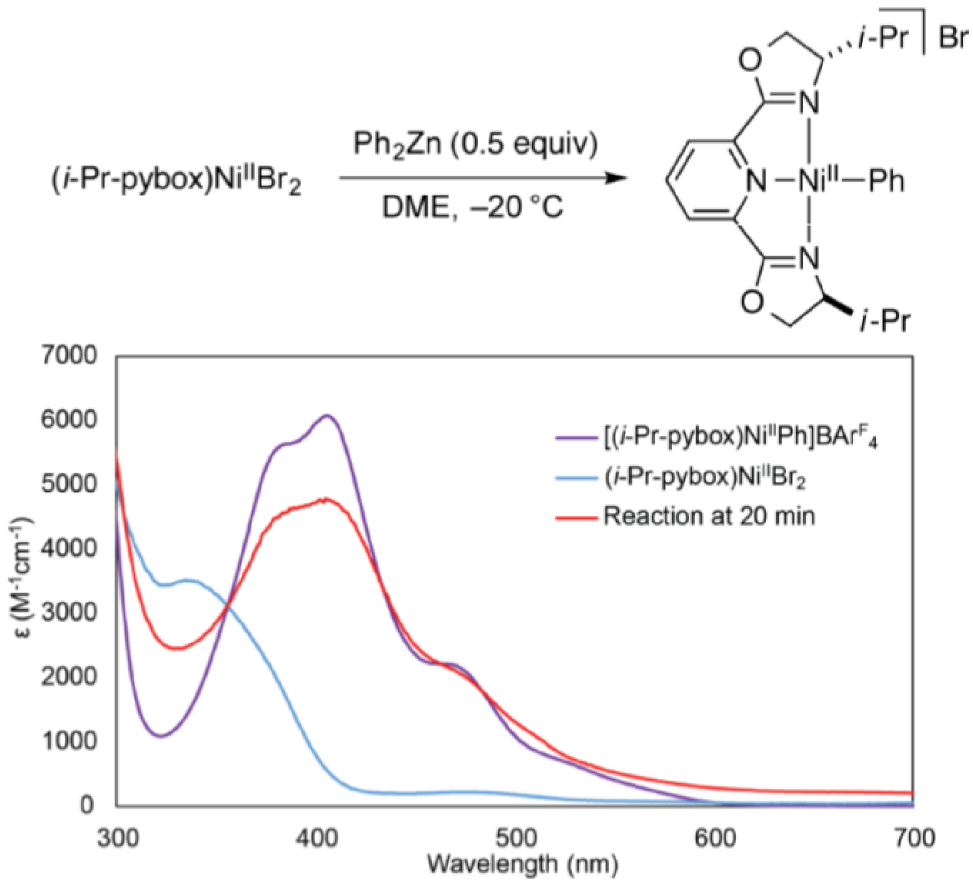
# Newly Proposed Cycle






Fu, G. C. *et al. J. Am. Chem. Soc.* **2014**, *136*, 16588.

# Confirmation of Transmetalation Step



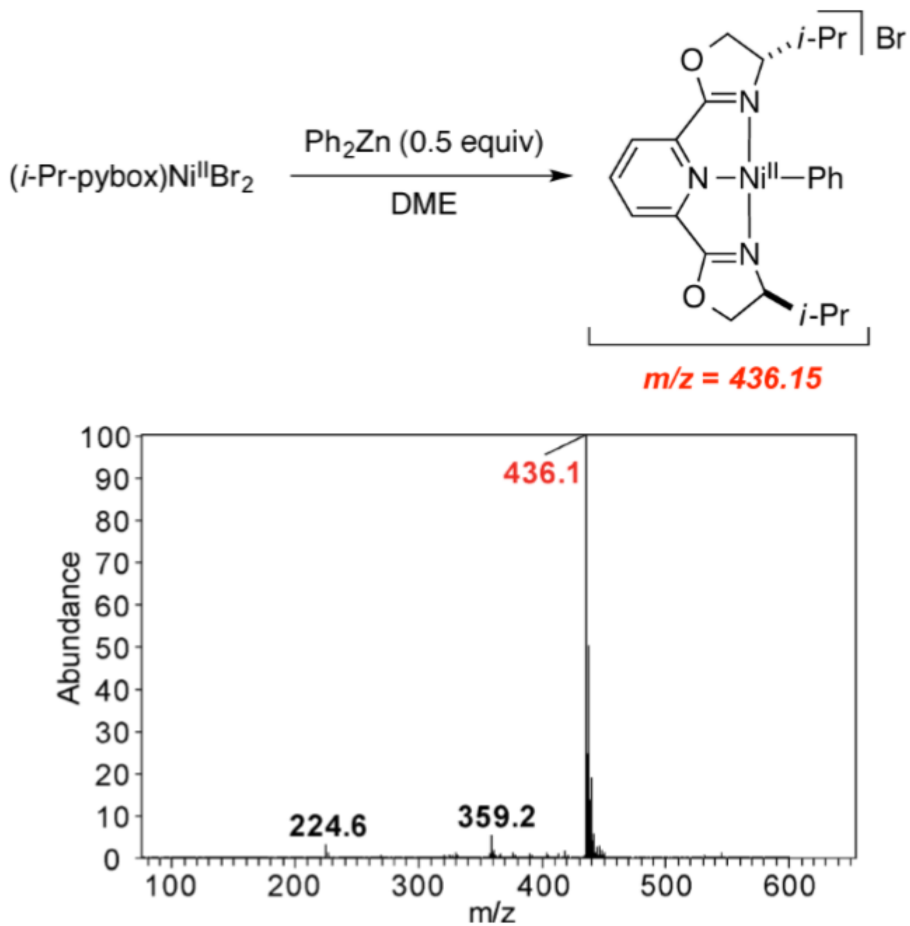

**UV-vis spectroscopy**

- ***The result suggests that transmetalation step is rational.***



Fu, G. C. *et al. J. Am. Chem. Soc.* **2014**, *136*, 16588.

# Confirmation of Transmetalation Step



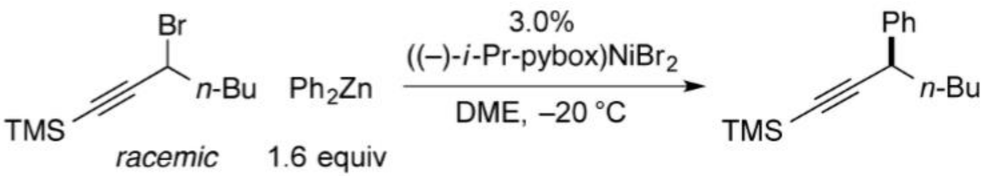

**ESI-MS**

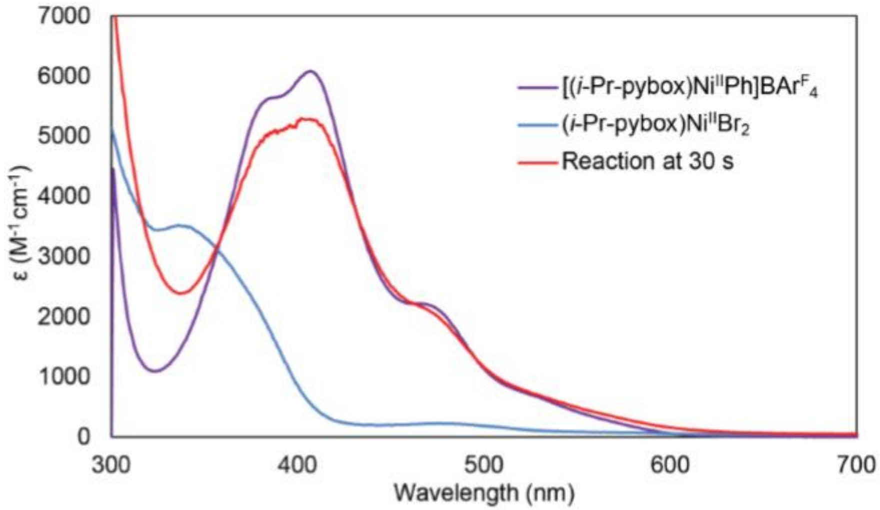
- ***ESI-MS also suggests that transmetalation step is rational.***



Fu, G. C. *et al. J. Am. Chem. Soc.* **2014**, *136*, 16588.

# Catalytic Reaction




**UV-vis spectroscopy**

- ***The result confirms rapid formation of ((iPrPybox)Ni(II)Ph)+.***
- ***When the catalytic process is analyzed by EPR spectroscopy, it is found to be EPR silent. It suggests that most of nickel complex exist as ((iPrPybox)Ni(II)Ph)+.***



Fu, G. C. *et al. J. Am. Chem. Soc.* **2014**, *136*, 16588.

# Catalytic Reaction

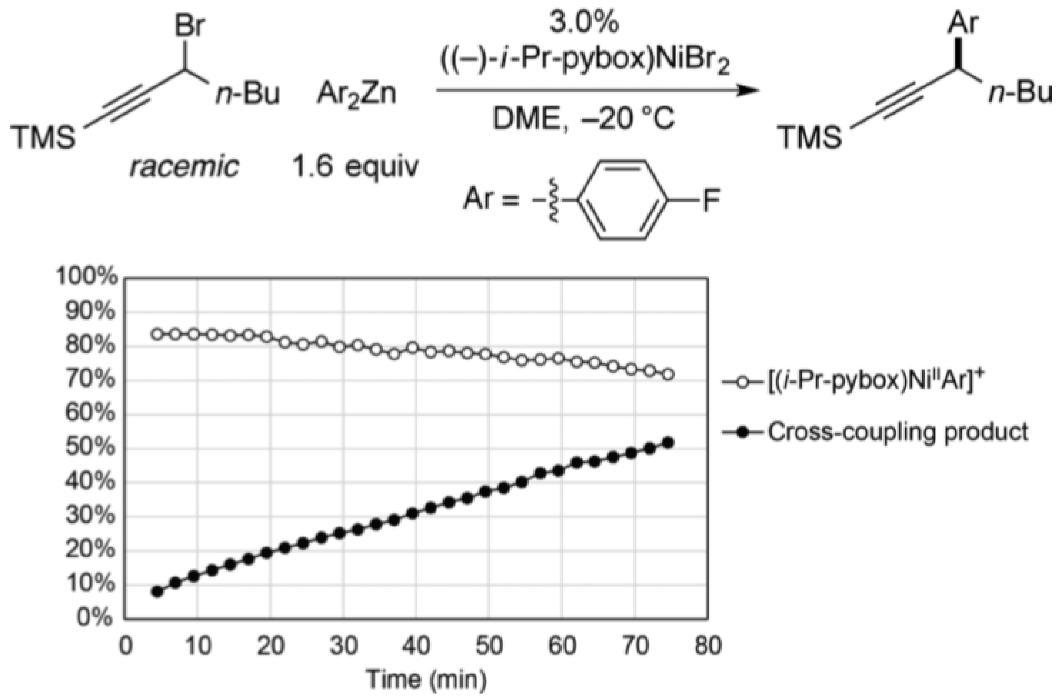



**Figure 9.** Analysis via $^{19}F$ NMR spectroscopy of a catalyzed Negishi reaction in progress: (○) $[(i\text{-Pr-pybox})Ni^{II}Ar]^+$ as a percentage of all nickel that is present; (●) yield of cross-coupling product.

- ***(iPr-pybox)Ni(II)Ar was generated more than propargylic radical, otherwise homocoupling of propargylic radical would occur.***



Fu, G. C. *et al. J. Am. Chem. Soc.* **2014**, *136*, 16588.

# Catalytic Reaction

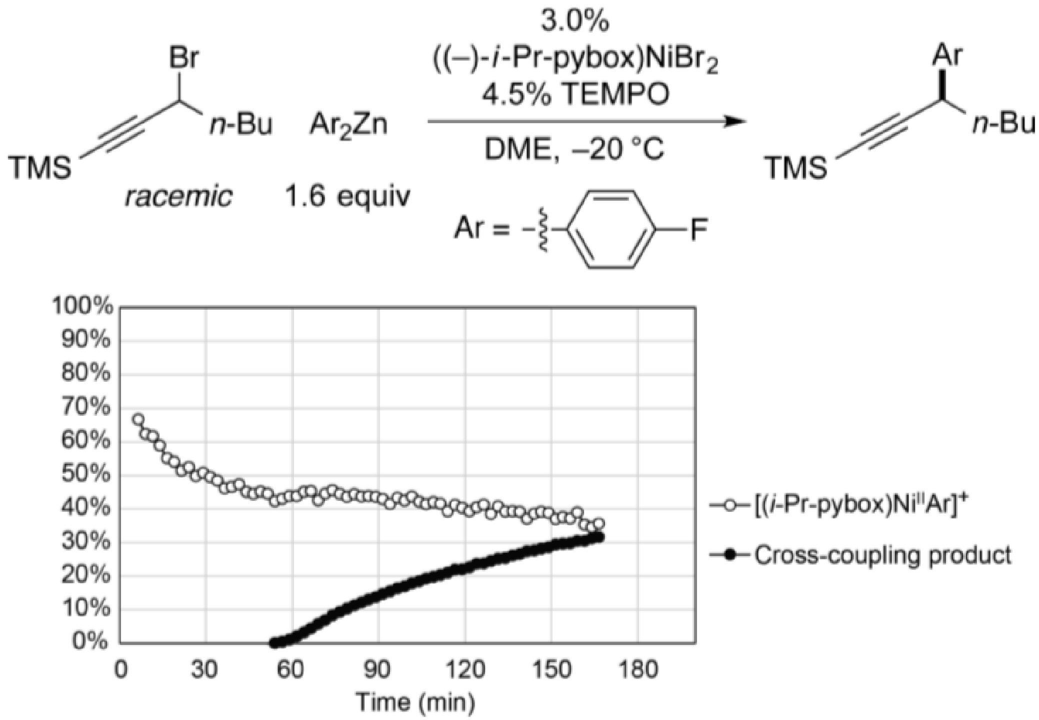


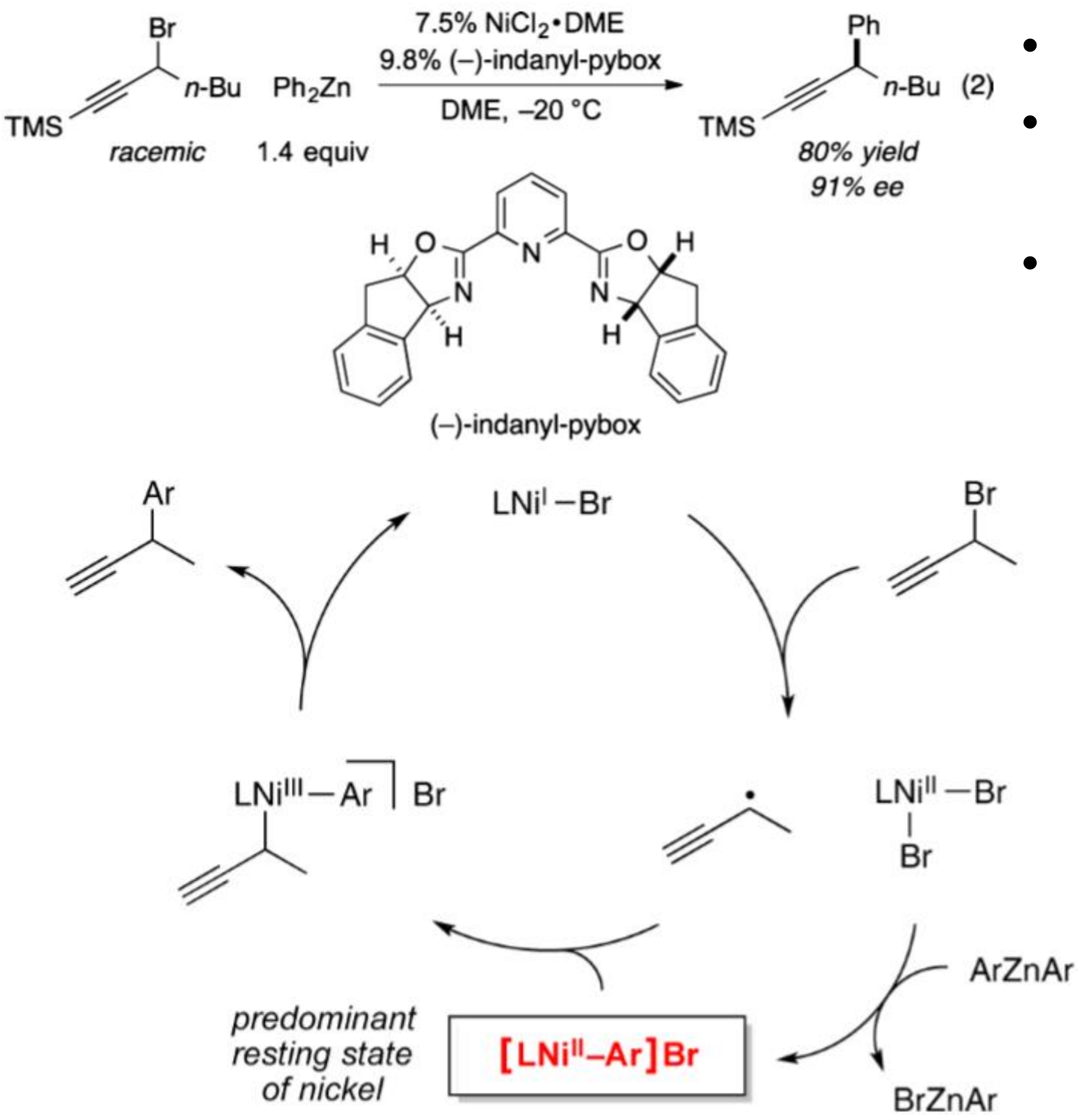

**Figure 11.** Analysis via $^{19}$F NMR spectroscopy of a catalyzed Negishi reaction in progress, in the presence of TEMPO: (○) [(*i*-Pr-pybox)Ni$^{II}$Ar]$^+$ as a percentage of all nickel that is present; (●) yield of cross-coupling product.

- ***In the presence of TEMPO, (iPr-pybox)Ni(II)Ar was consumed, and cross-coupling product was not observed.***



Fu, G. C. *et al. J. Am. Chem. Soc.* **2014**, *136*, 16588.

# Nickel-Catalyzed Cross-Coupling




- ***$sp^3$-$sp^2$ cross-coupling!***
- ***Nickel(II) can intercept radical species!***
- ***However, nucleophile is limited, and it sometimes diminishes functional group tolerance.***



Fu, G. C. *et al. J. Am. Chem. Soc.* **2014**, *136*, 16588.

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1. ***Nickel-catalyzed cross-coupling via radical pathway***
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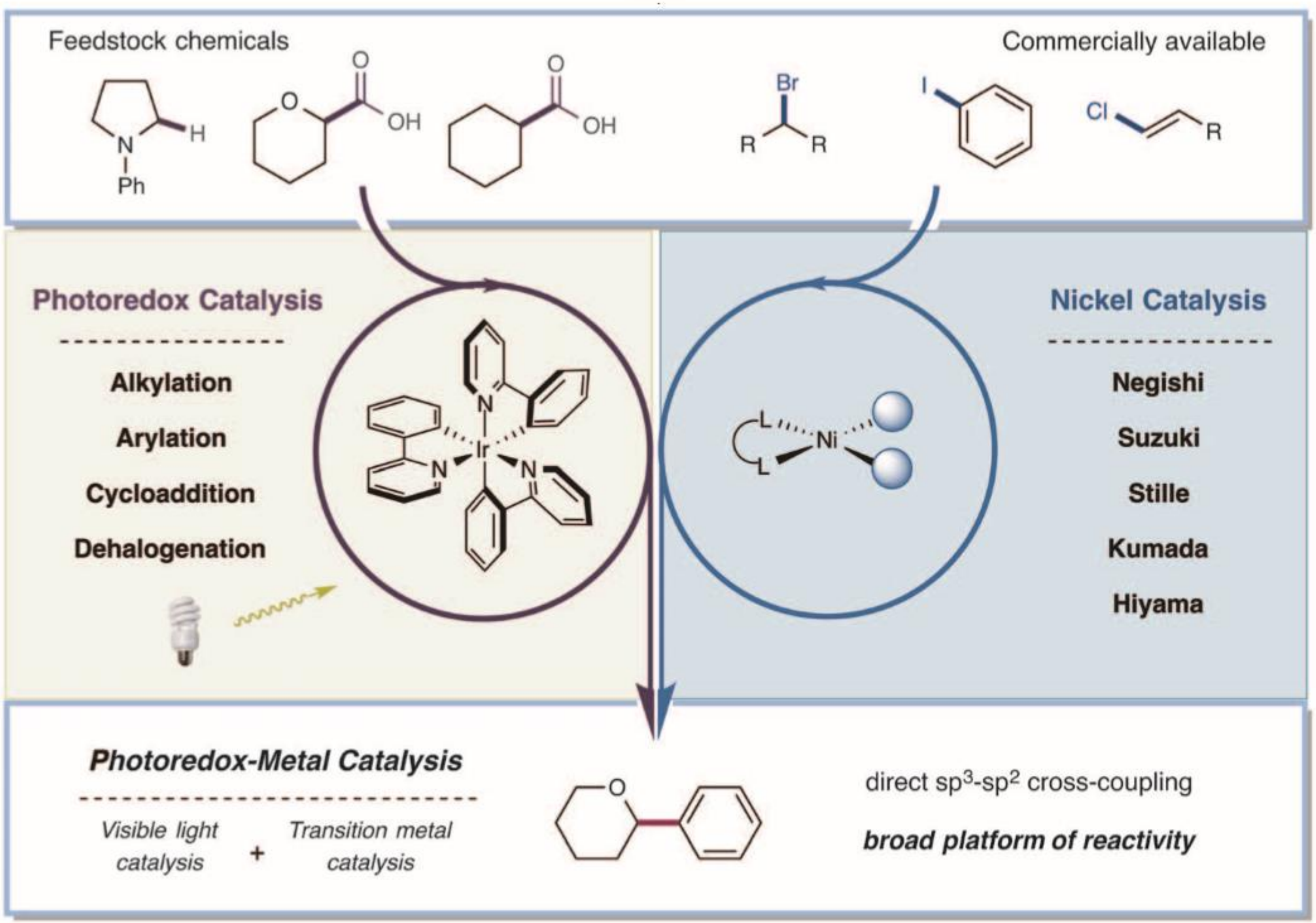
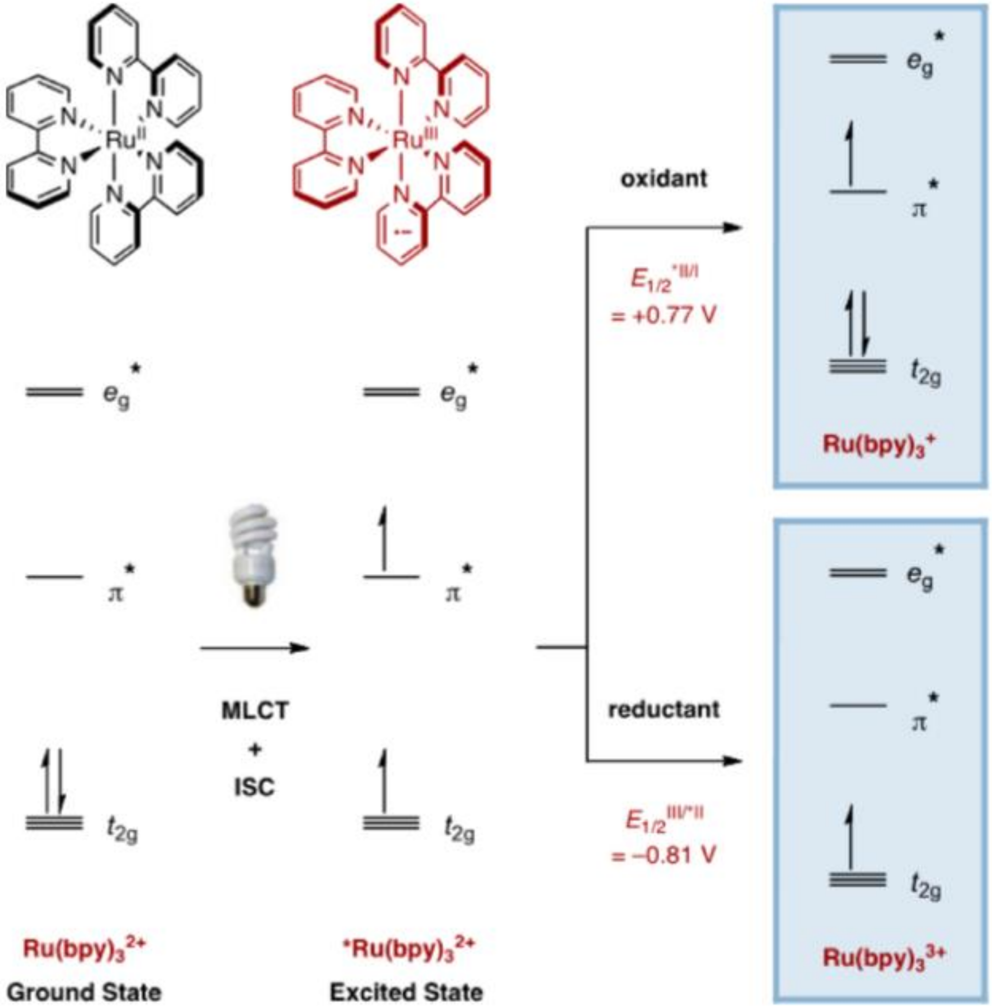
# Hybrid Catalysis of Photoredox Catalysis and Nickel Catalysis






Doyle, A. G.; MacMillan, D. W. C. *et al*. *Science* **2014**, *345*, 437.

# Photoredox Catalysis



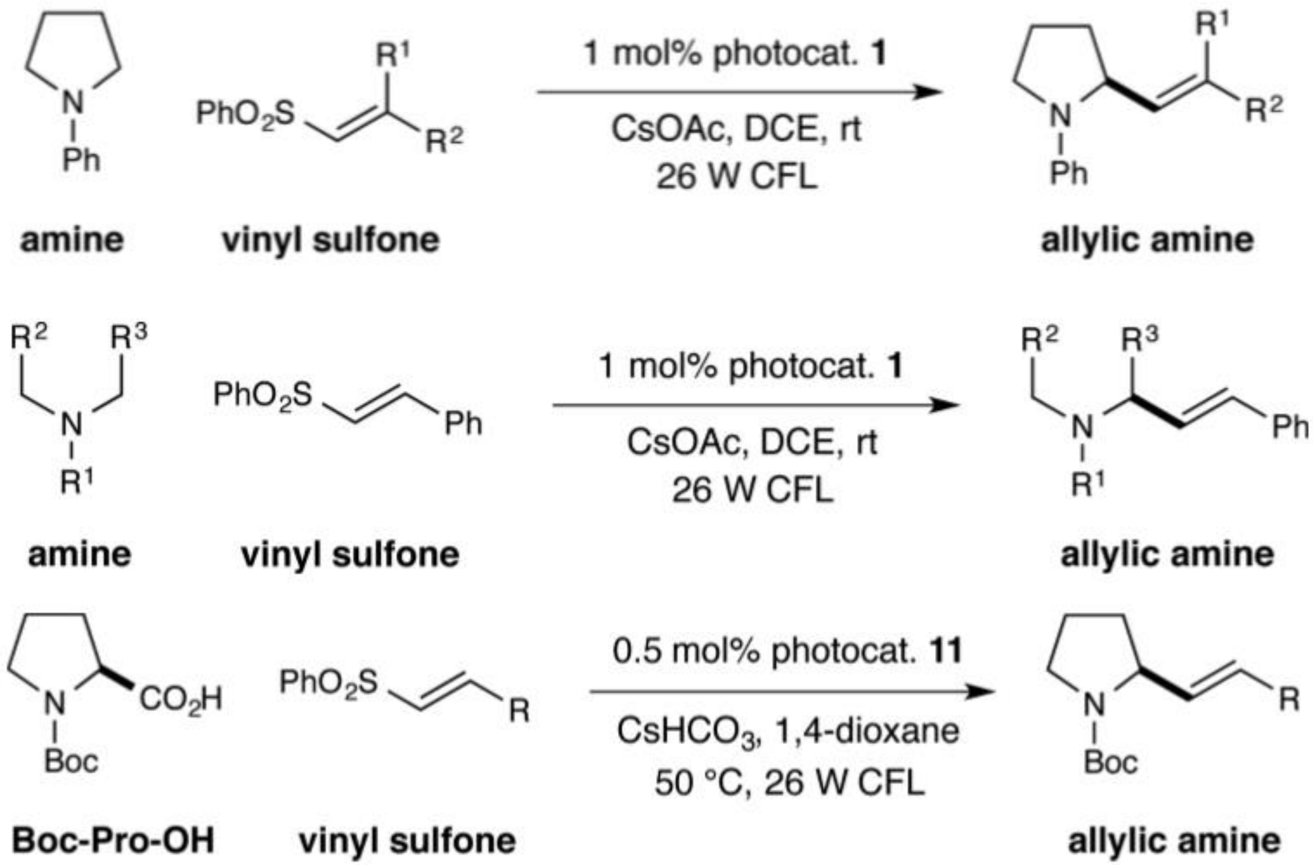

- ***MLCT and ISC give long-lived triplet photoexcited state.***
- ***Photoredox catalyst can work as both strong oxidant and strong reductant.***

**MLCT: metal to ligand charge transfer**
**ISC: intersystem crossing**



MacMillan, D. W. C. *et al*. *Chem. Rev.* **2013**, *113*, 5322.

# Photoredox-Catalyzed Reaction

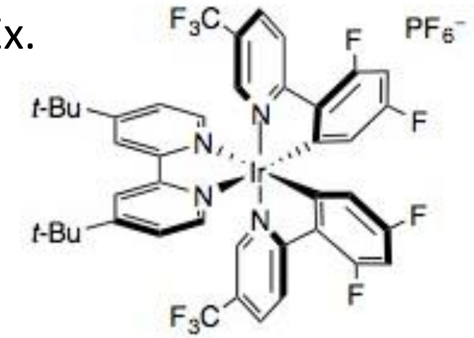


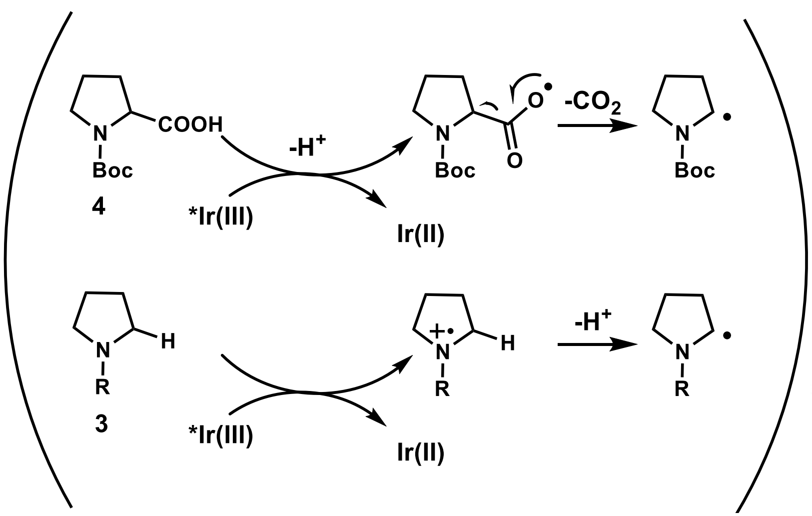


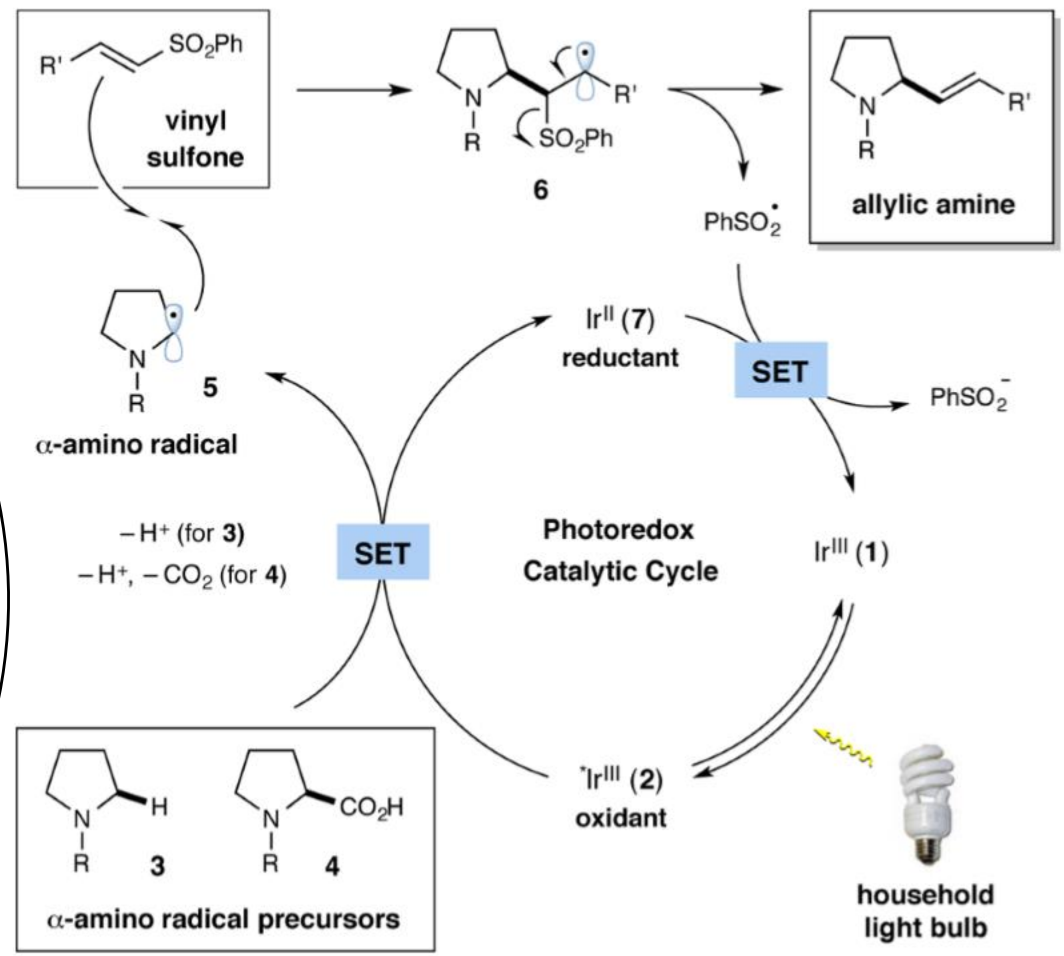

MacMillan, D. W. C. *et al*. *J. Am. Chem. Soc.* **2014**, *136*, 11602.

# Photoredox-Catalyzed Reaction

Ex.



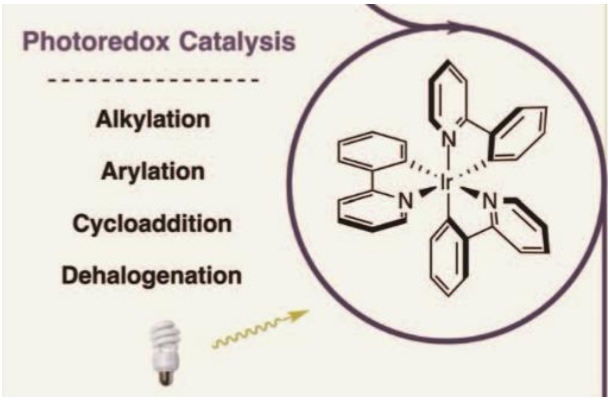



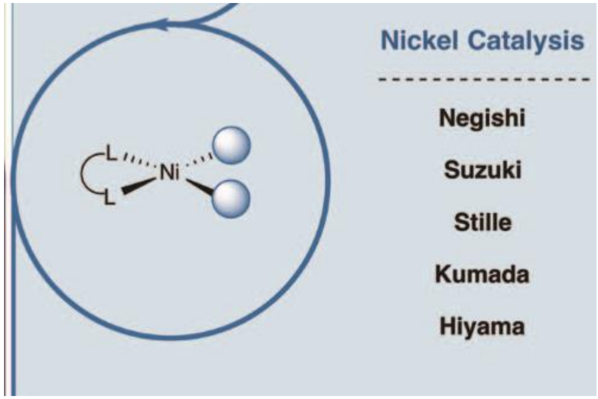




- ***Photoredox catalysis can generate carbon-centered radical.***

MacMillan, D. W. C. *et al*. *J. Am. Chem. Soc.* **2014**, *136*, 11602.

# Working Hypothesis



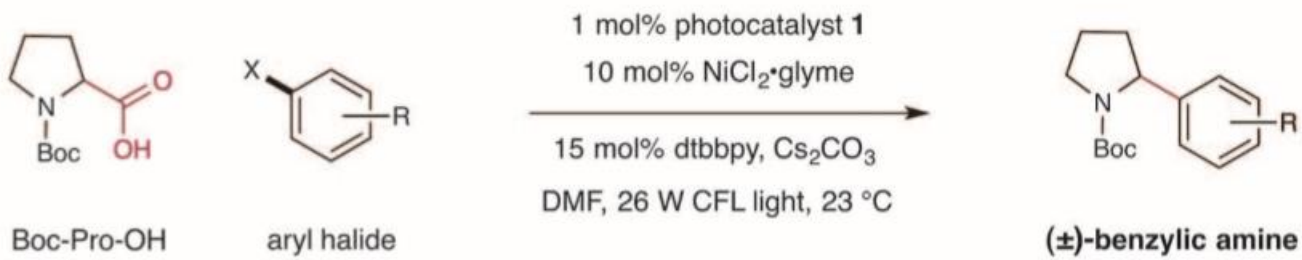



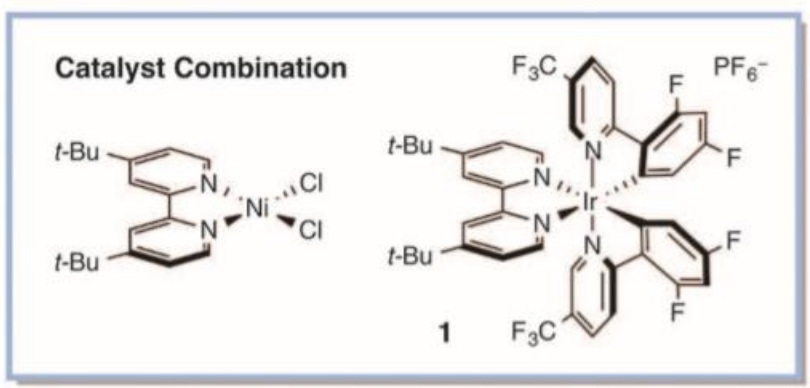

- ***Generate carbon-centered radical***
- ***However, electrophile is limited such as vinyl sulfone, or cyanoarene.***

- ***C-C bond formation via radical pathway***
- ***However, nucleophile is limited such as organo-boron, organo-zinc, organo-stannanes, or Grignard reagents.***

**Ni catalyst can intercept radical species generated by photoredox catalyst and catalyze cross-coupling?**

# Hybrid Catalysis of Photoredox Catalysis and Nickel Catalysis

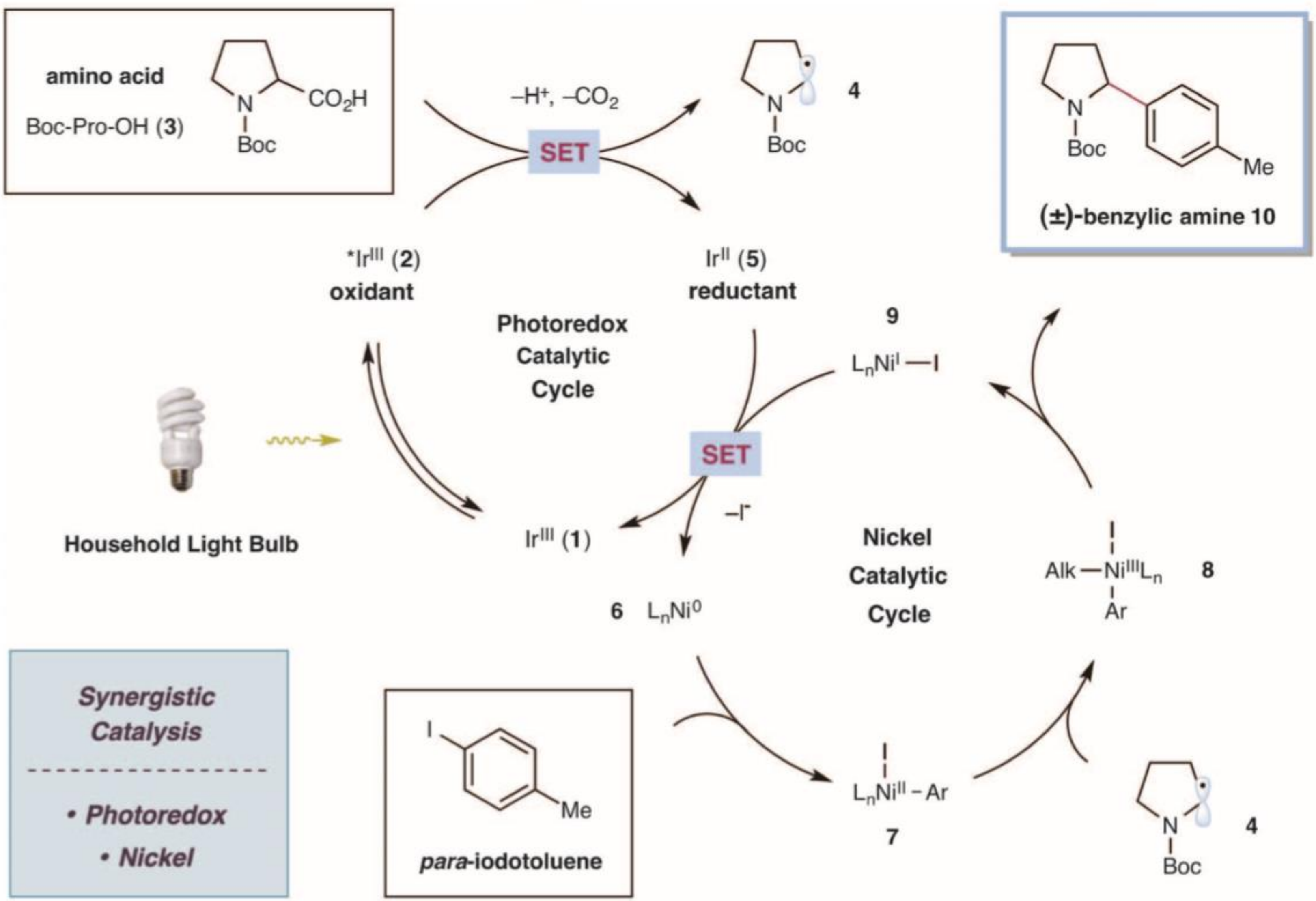





Doyle, A. G.; MacMillan, D. W. C. *et al*. *Science* **2014**, *345*, 437.

# Proposed Catalytic Cycle

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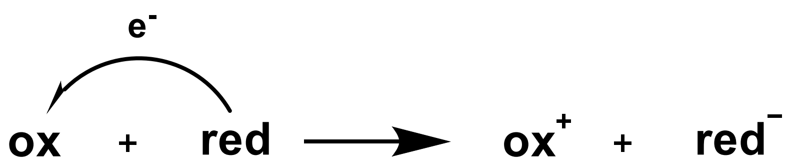
# $E_{1/2}$ (Half-Wave Potential)



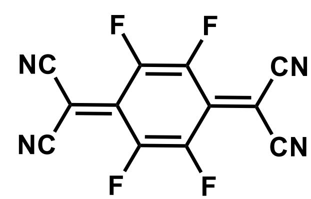

- **$E_{1/2}$…The tool for discussion about whether single electron transfer proceeds or not**

  **red → $red^{+}$ + $e^{-}$ …largely negative $E_{1/2}$ = strong reductant**

  **ex. $Cp_2Co$ ($E_{1/2}$= -1.16 V)**

  **ox + $e^{-}$ → $ox^{-}$ …largely positive $E_{1/2}$ = strong oxidant**

  **ex. TCNQ-F4 ($E_{1/2}$= +0.61 V)**



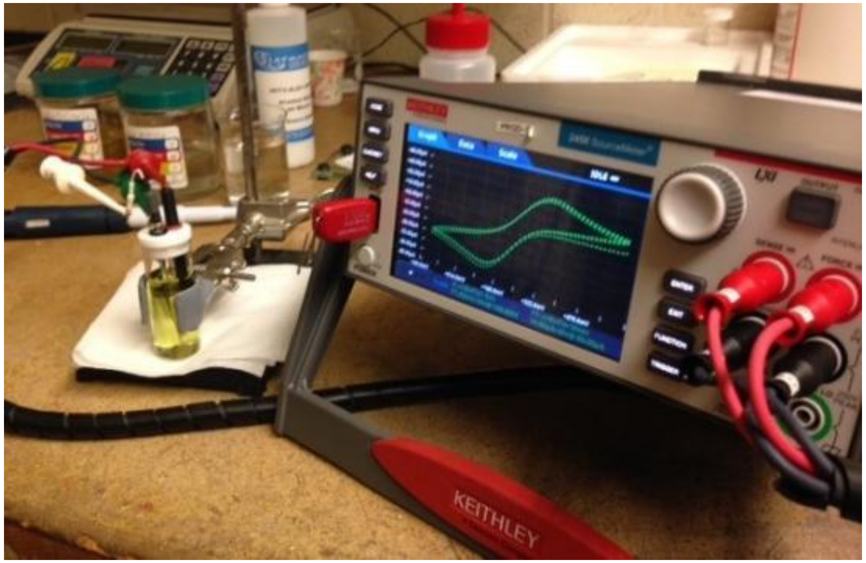

**TCNQ-$F_4$**

- **$E_{1/2}$ (oxidant) - $E_{1/2}$ (reductant)**

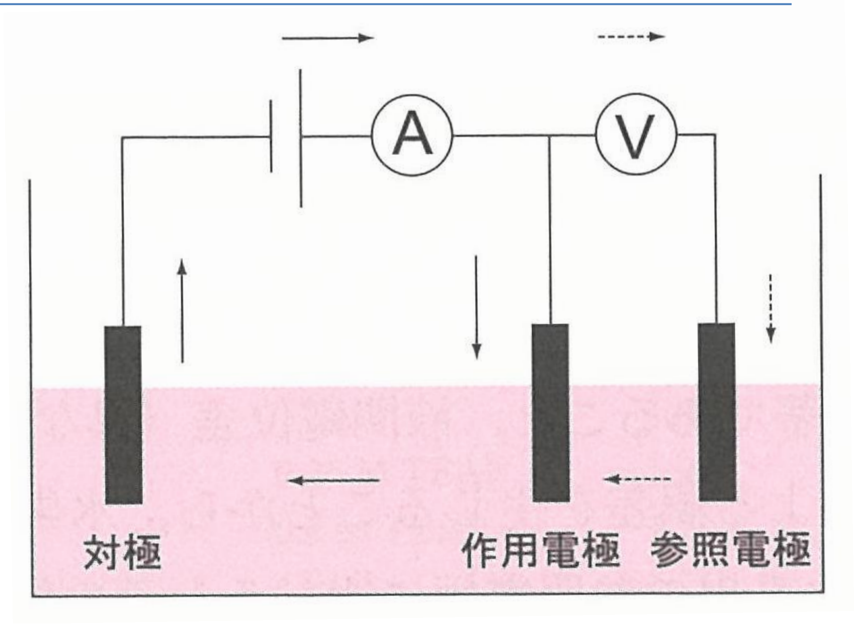
  **>0…reaction proceeds (single electron transfer can proceed)**

  **<0…reaction does not proceed (single electron transfer cannot)**

# How to determine $E_{1/2}$? -Cyclic Voltammetry-



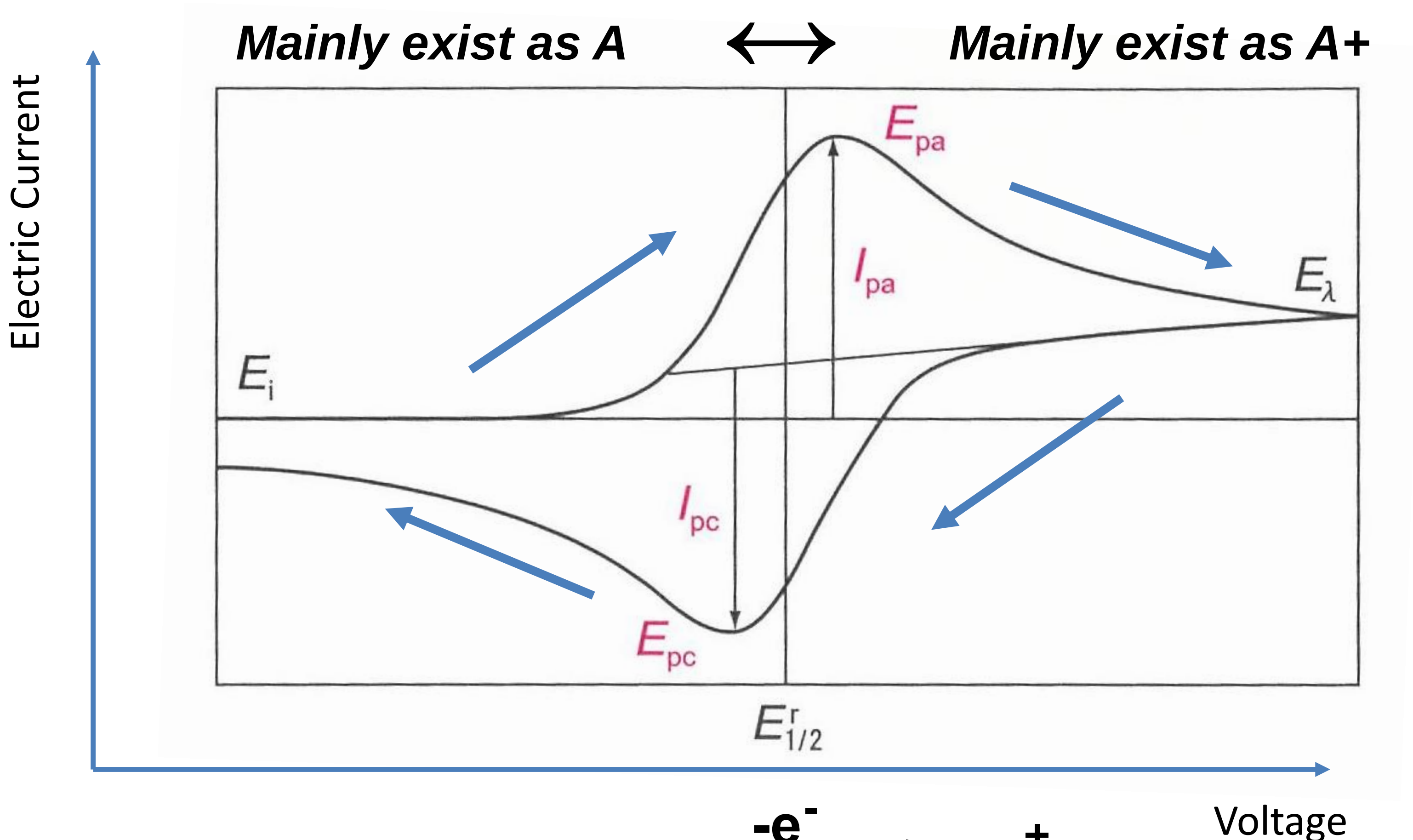

http://www.tek.com/blog/performing-cyclic-voltammetry

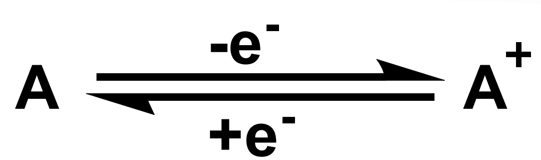



金属錯体の電子移動と電気化学
（錯体化学選書）

- ***The experiment to measure $E_{1/2}$***
- ***In this experiment, voltage is changed in certain rate in solvent which contains electrolyte.***

# How to determine $E_{1/2}$? -Cyclic Voltammetry-

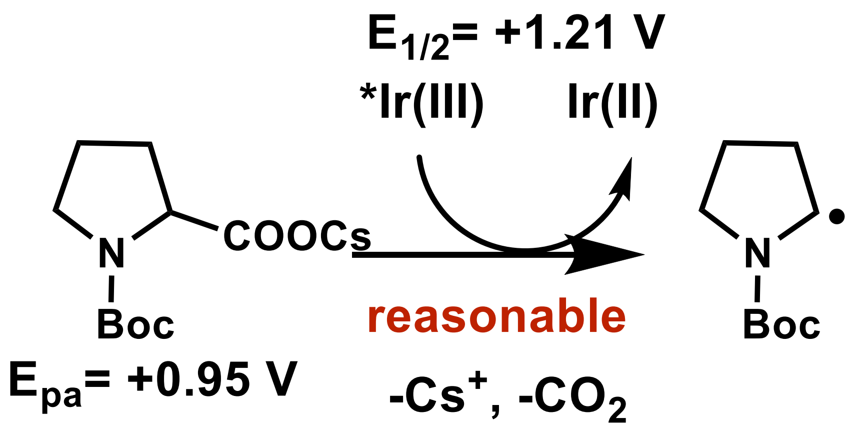


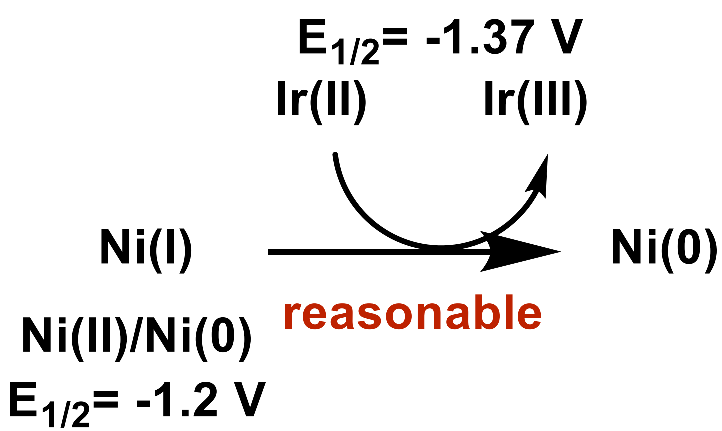




- ***Cyclic Voltammetry reveals $E_{1/2}$***
- ***$E_{1/2} = (E_{pc}+E_{pa})/2$***

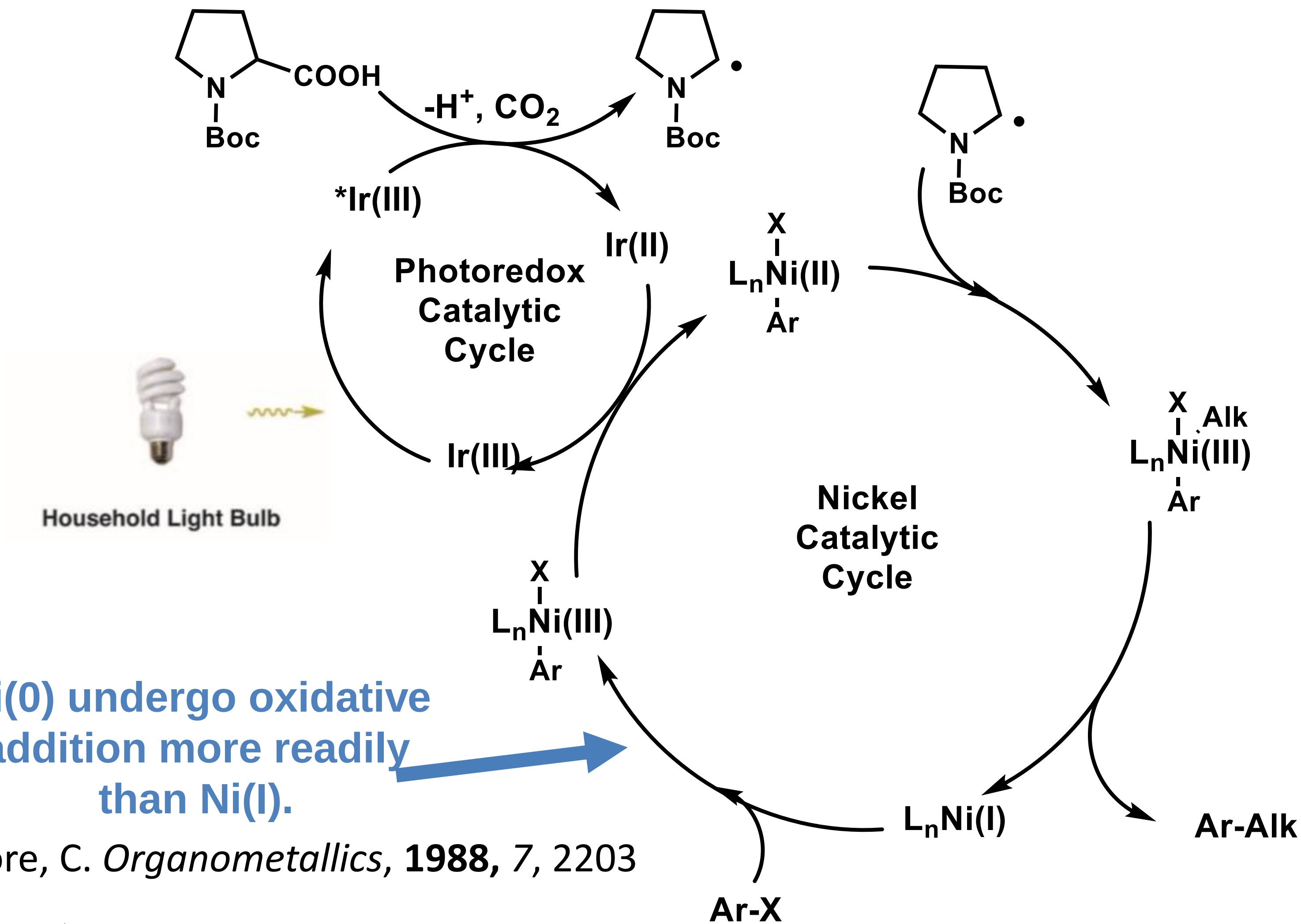
金属錯体の電子移動と電気化学（錯体化学選書）

# Reaction proceeds or not?



# Other Possibility




Ni(0) undergo oxidative addition more readily than Ni(I).

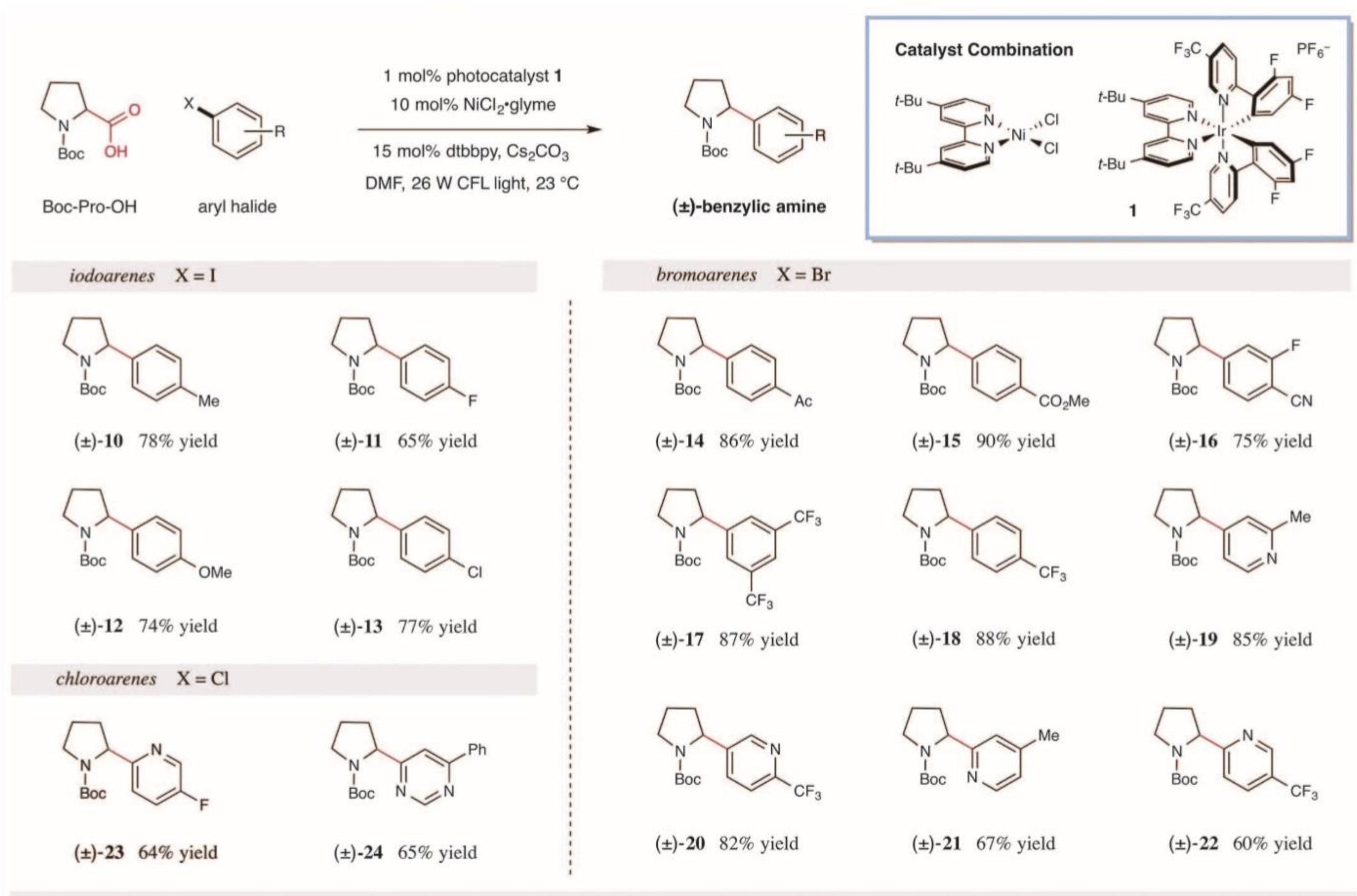
Amatore, C. *Organometallics*, **1988,** *7*, 2203

So proposed as previous slide



Doyle, A. G.; MacMillan, D. W. C. *et al. Science* **2014**, *345*, 437.

# Substrate Scope

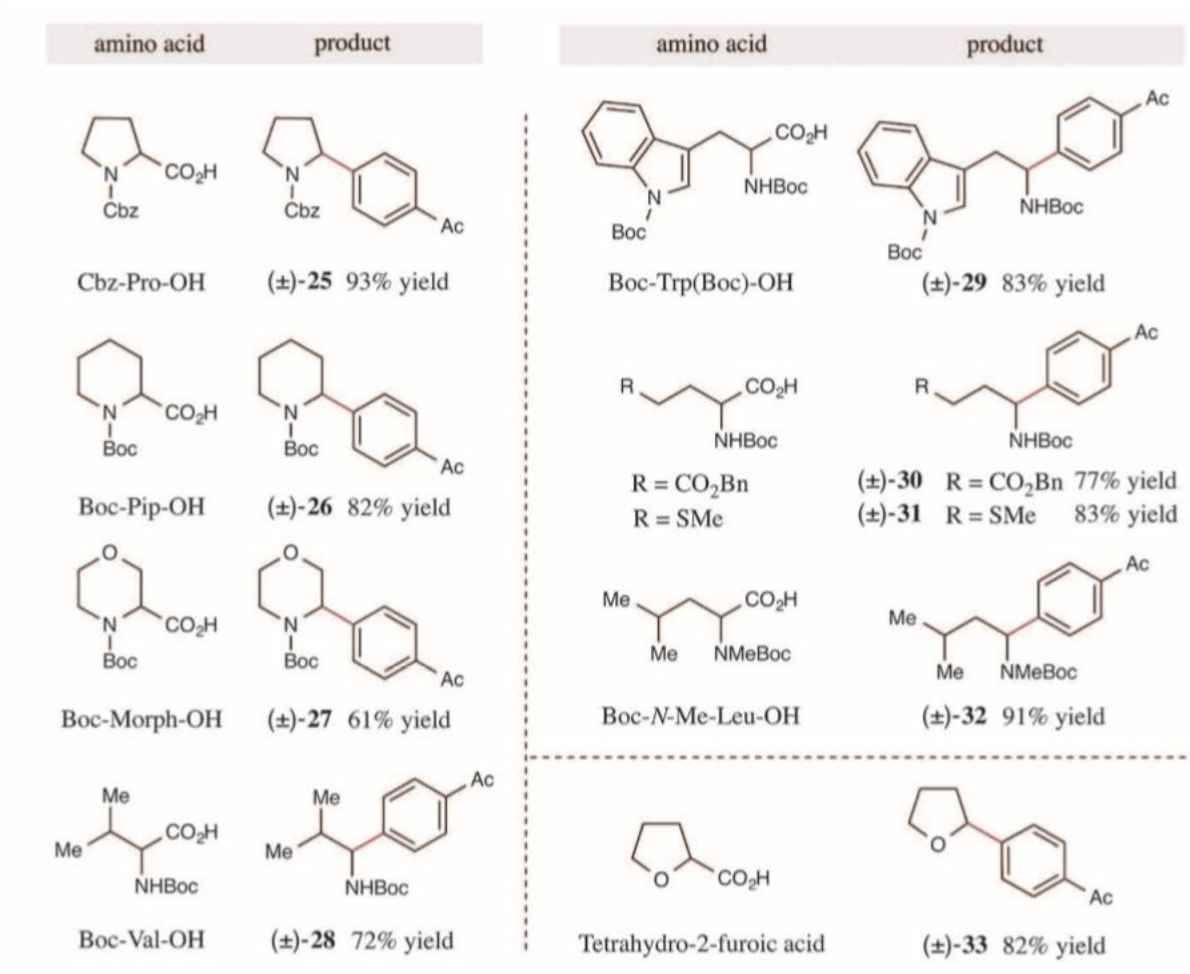



- ***N-Heterocycles also work as electrophile.***



Doyle, A. G.; MacMillan, D. W. C. *et al*. *Science* **2014**, *345*, 437.

# Substrate Scope

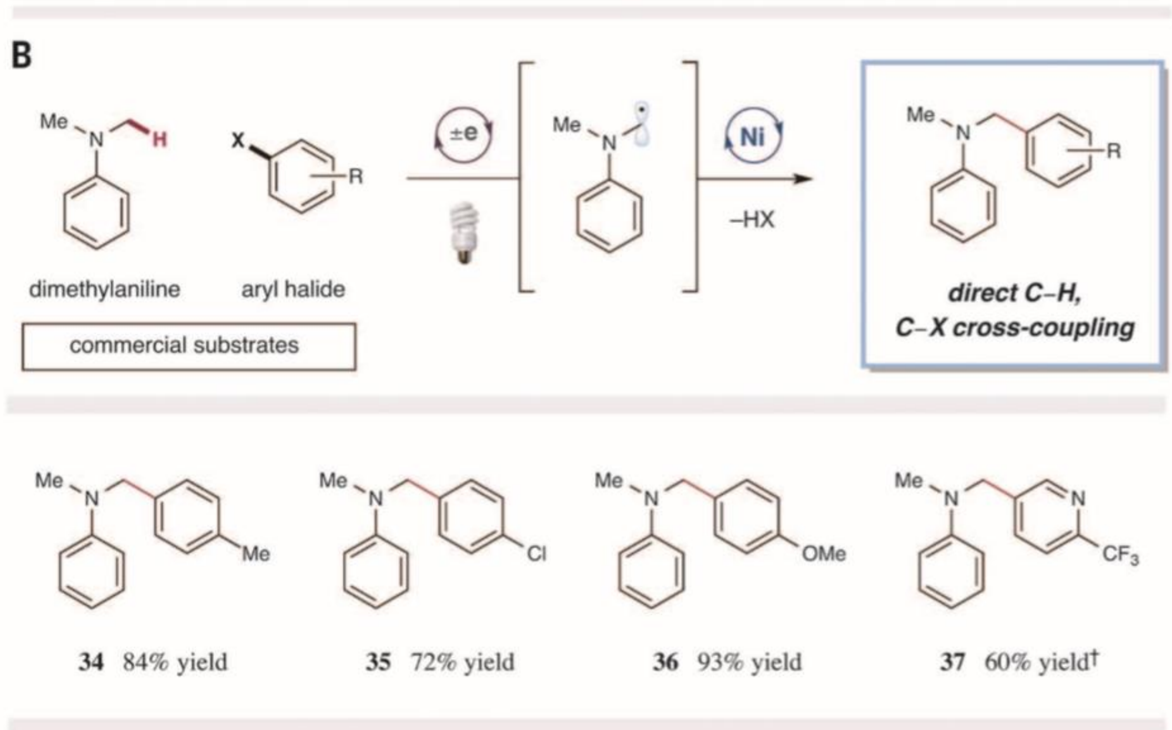



- ***Thioether can tolerate reaction conditions.***



Doyle, A. G.; MacMillan, D. W. C. *et al*. *Science* **2014**, *345*, 437.

# Substrate Scope



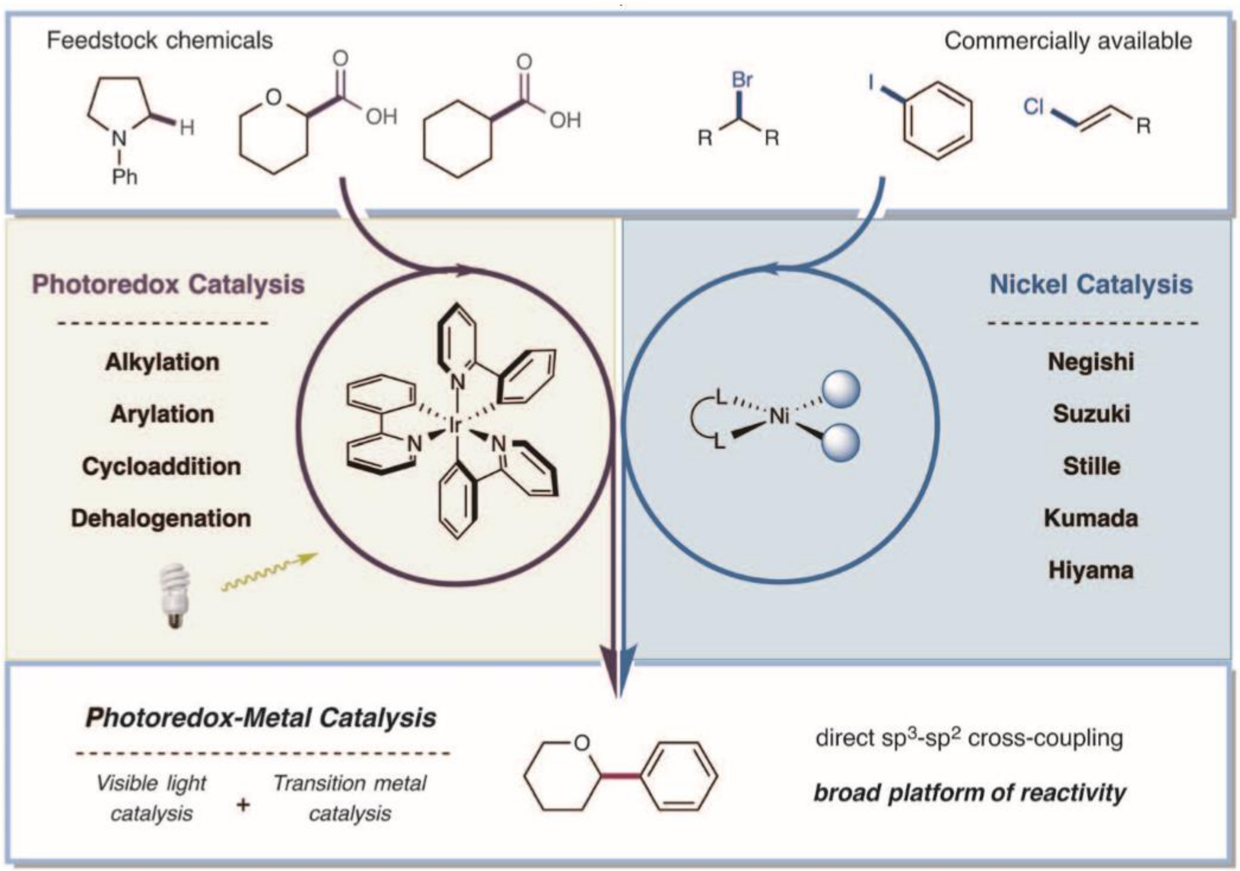

KOH is used as base.

- ***Direct C-H functionalization was also achieved in case of aniline derivatives.***



Doyle, A. G.; MacMillan, D. W. C. *et al*. *Science* **2014**, *345*, 437.

# Hybrid Catalysis of Photoredox catalysis and Nickel Catalysis




- ***sp*$^3$*-sp*$^2$ *bond formation via feedstock chemicals!***
- ***However, nucleophile was limited. (only easy to abstract one electron (ex. sp*$^3$ *C-COOH))***

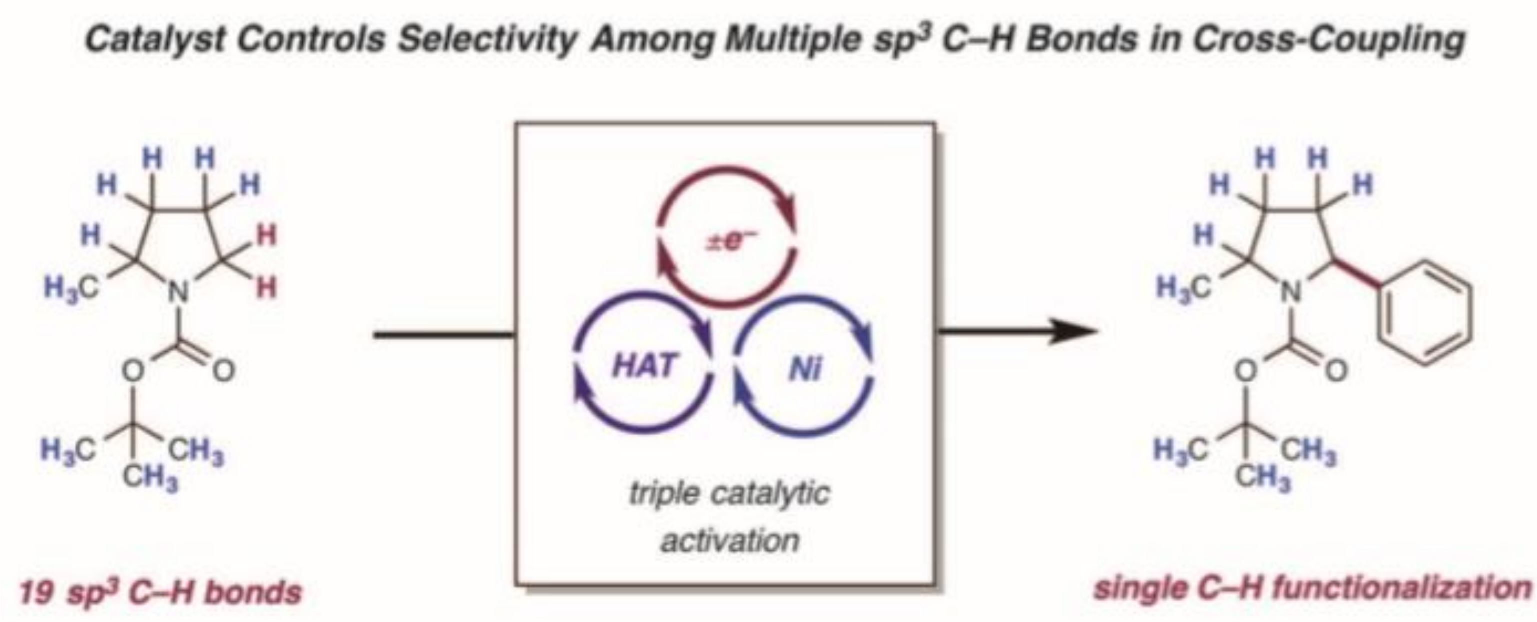


Doyle, A. G.; MacMillan, D. W. C. *et al*. *Science* **2014**, *345*, 437.

# Today's Content

1. ***Nickel-catalyzed cross-coupling via radical pathway***
2. ***Hybrid catalysis of photoredox catalysis and nickel catalysis***
3. ***Hybrid catalysis of photoredox catalysis, nickel catalysis and HAT catalysis***

# Ternary Catalysis



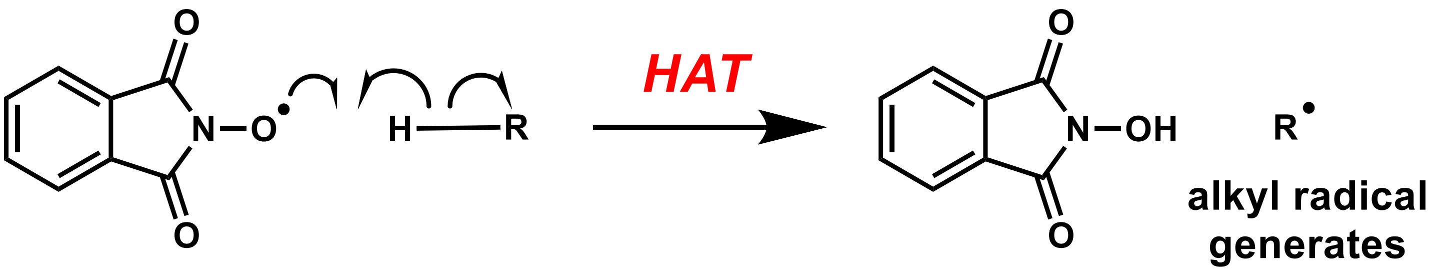



MacMillan, D. W. C. *et al*. *Science* **2016**, *352*, 1304.

# HAT Process

- ***HAT (Hydrogen Atom Transfer) process is effective way to access radical intermediates.***

***ex.***




Ishii, Y. *et al. J. Org. Chem.* **1995**, *60*, 3934.

# Polar Effect of HAT Process

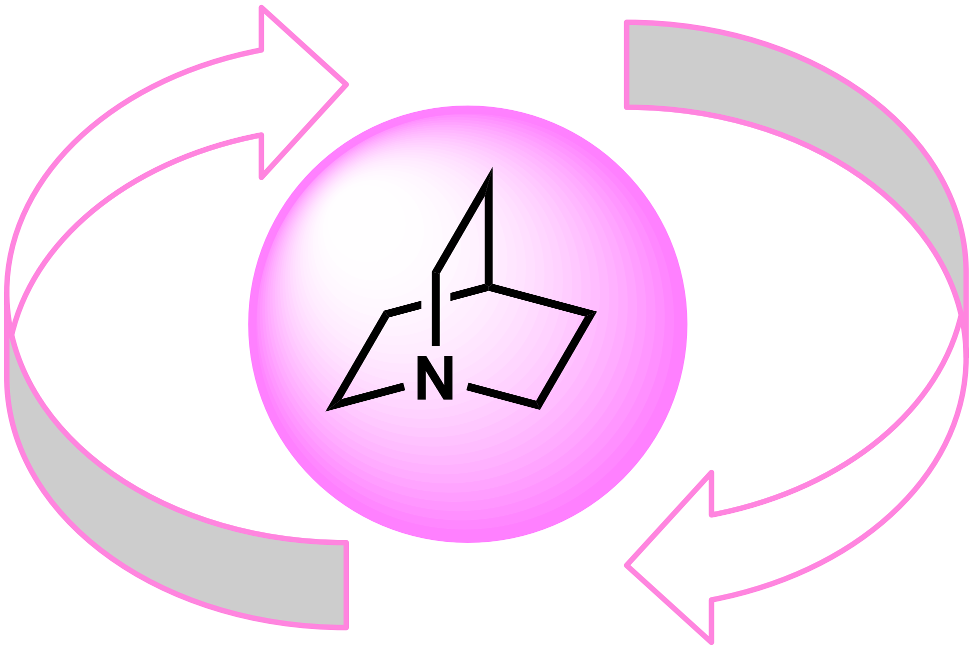
- ***Although BDE is important, polar effect is also important.***

| | | | | |
|---|---|---|---|---|
| **El·** | **+ H–Nuc** | **→ El–H** | **+Nuc·** | } favored |
| **Nuc·** | **+ H–El** | **→ Nuc–H** | **+El·** | |
| **El1·** | **+ H–El2** | **→ El1–H** | **+El2·** | } disfavored |
| **Nuc1·** | **+ H–Nuc2** | **→ Nuc1–H** | **+Nuc2·** | |

**El·: elecrophilic radical**
**Nuc·: nucleophilic radical**

Roberts, B. P. *Chem. Soc. Rev.* **1999**, *28*, 25.

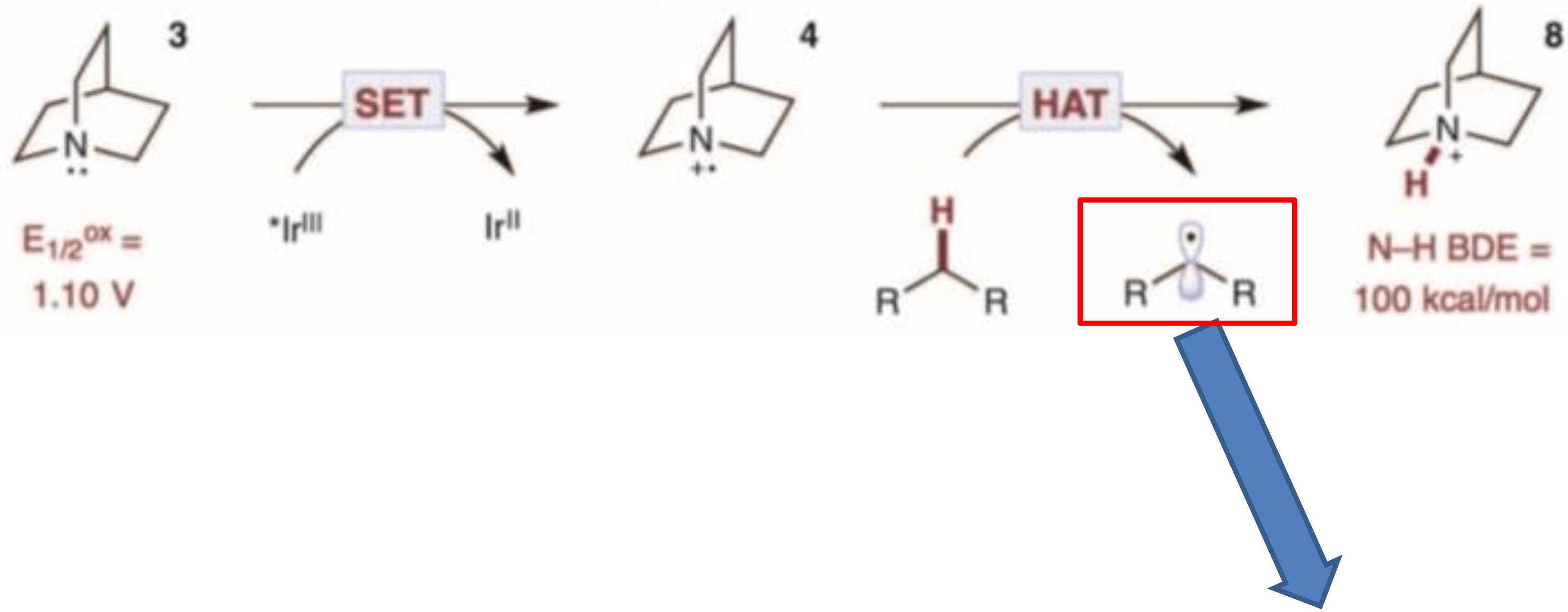
# Quinuclidine as HAT Catalyst




- ***Strong BDE (H-N$^+$ BDE= 100 kcal/mol vs S-H BDE= 87 kcal/mol)***
- ***Amine radical cation could abstract hydridic C-H bond***
- ***Rigid bicyclic structure prevents α-deprotonation***

MacMillan, D. W. C. *et al*. *Science* **2015**, *349*, 1532.

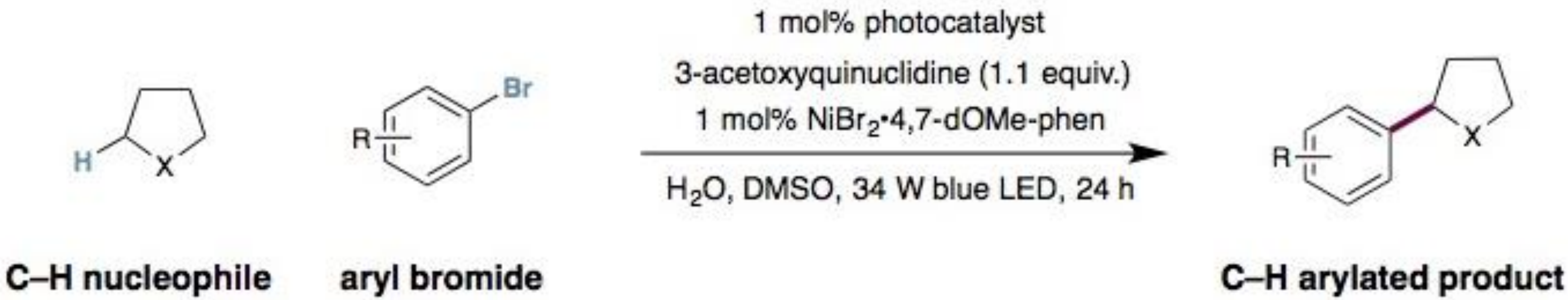
# Working Hypothesis

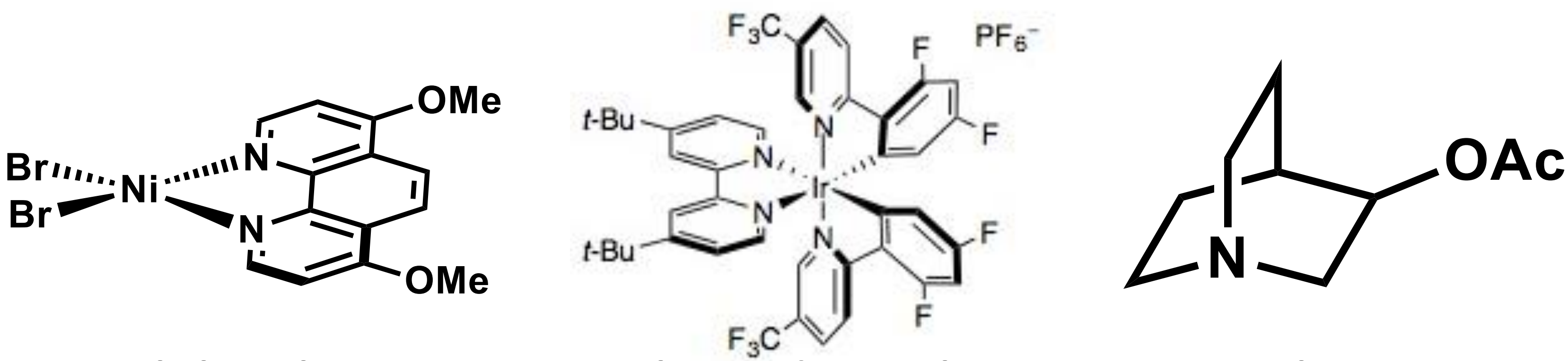



**Nickel catalyst might intercept radical species like this?**

MacMillan, D. W. C. *et al*. *Science* **2015**, *349*, 1532.

# Ternary Catalysis




Nickel catalyst

Photoredox catalyst

HAT catalyst



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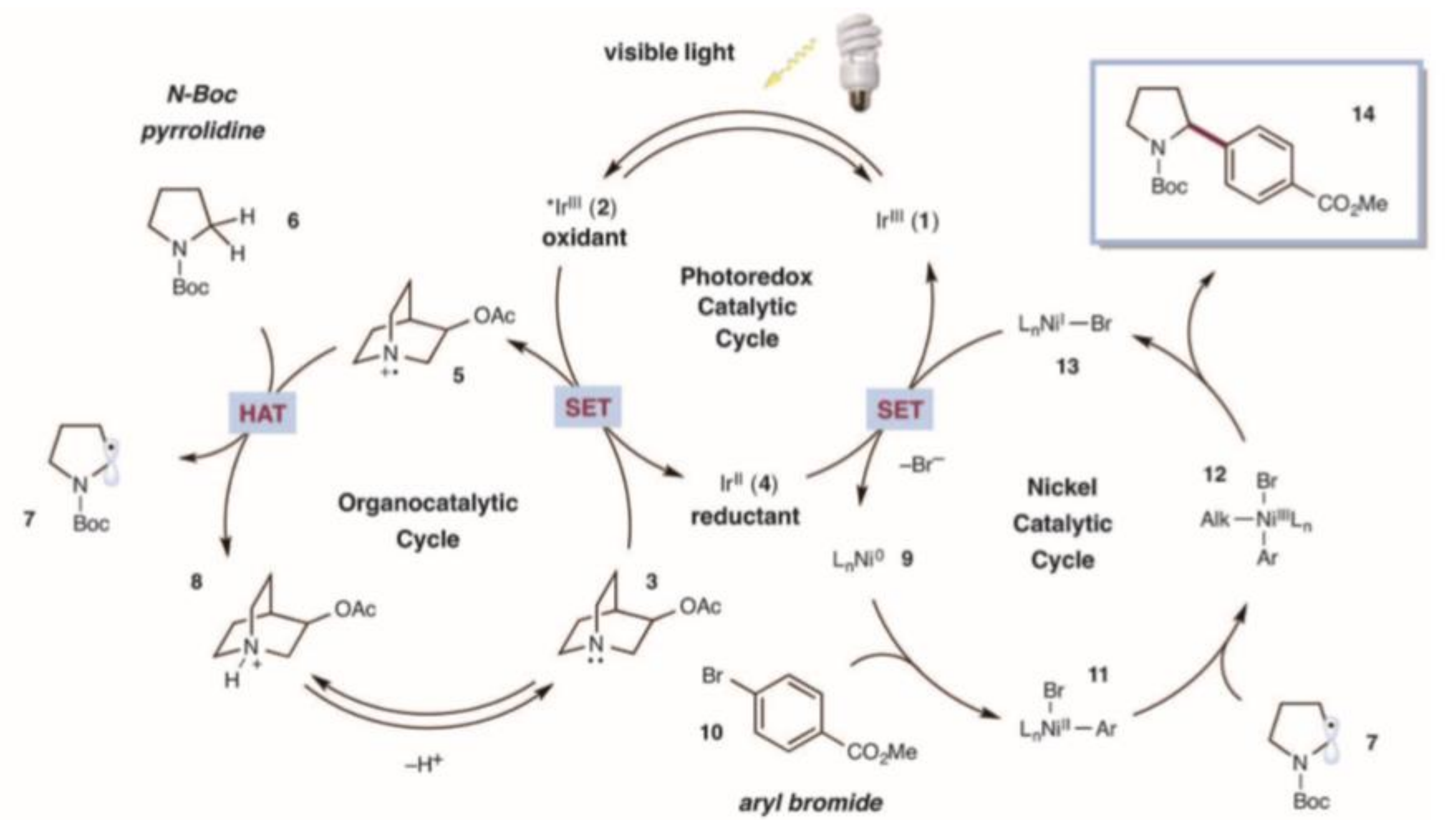
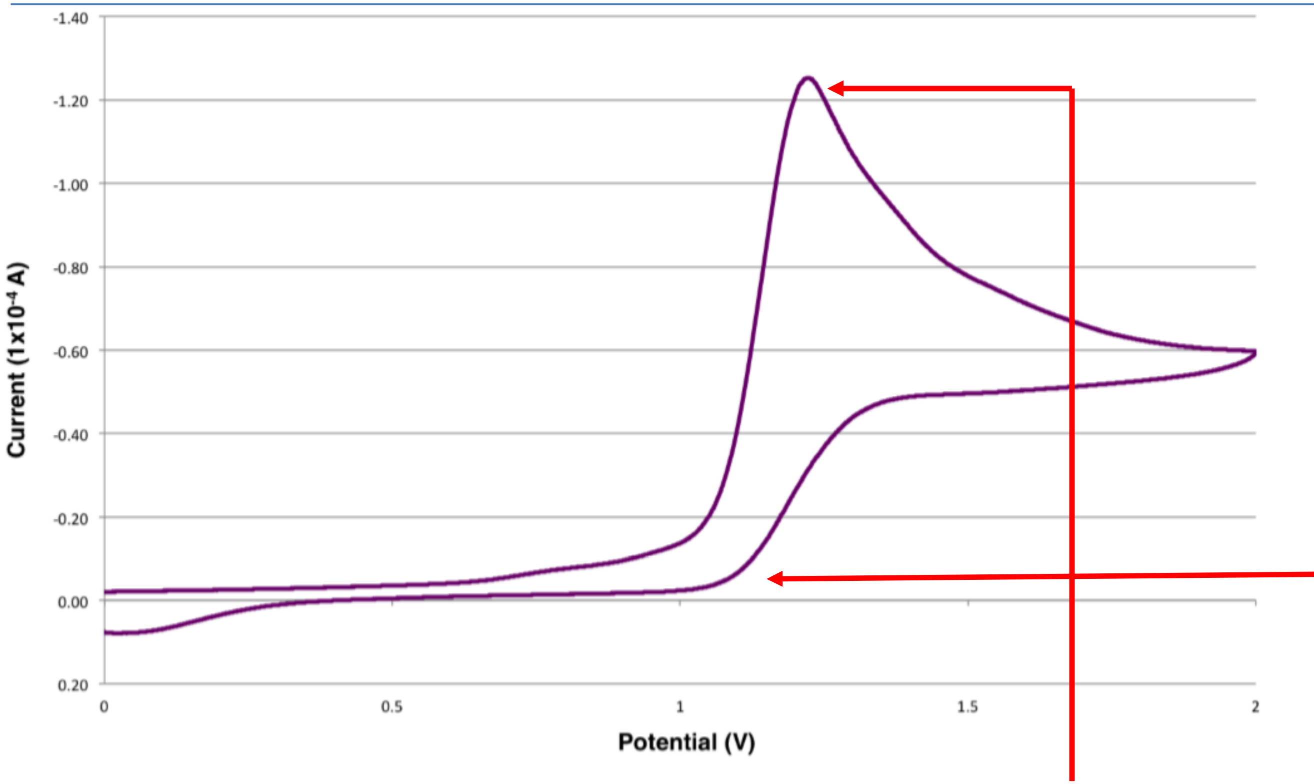
# Proposed Catalytic Cycle






MacMillan, D. W. C. *et al*. *Science* **2016**, *352*, 1304.

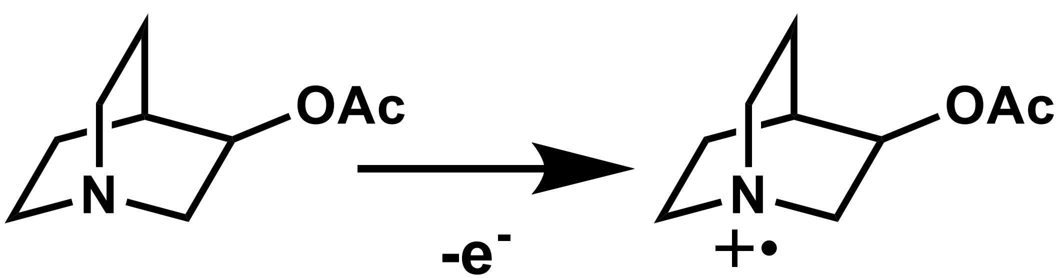
# Cyclic Voltammetry




***$E_{pc}$ could not be confirmed maybe because of decomposition or side reaction.***

***Irreversible oxidation event at +1.22 V vs SCE in MeCN***

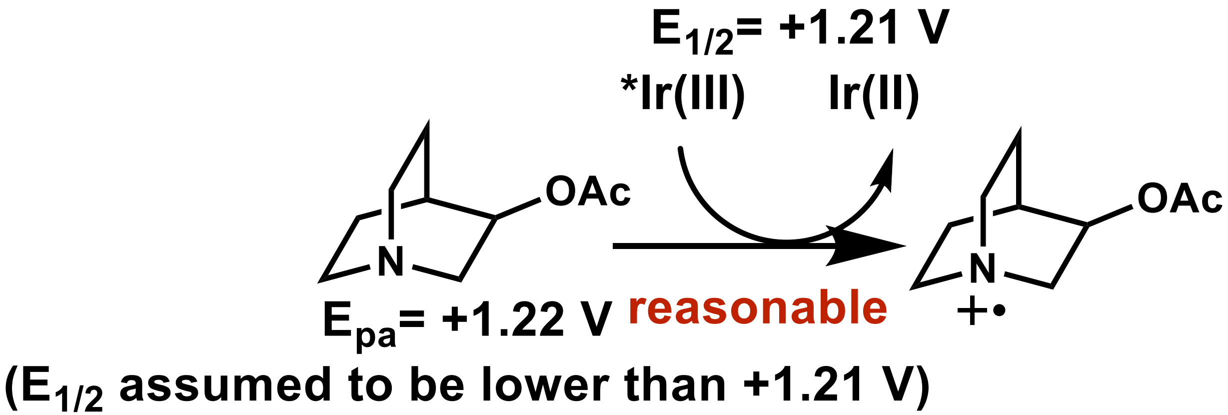
***So, $E_{pa}$= +1.22 V***

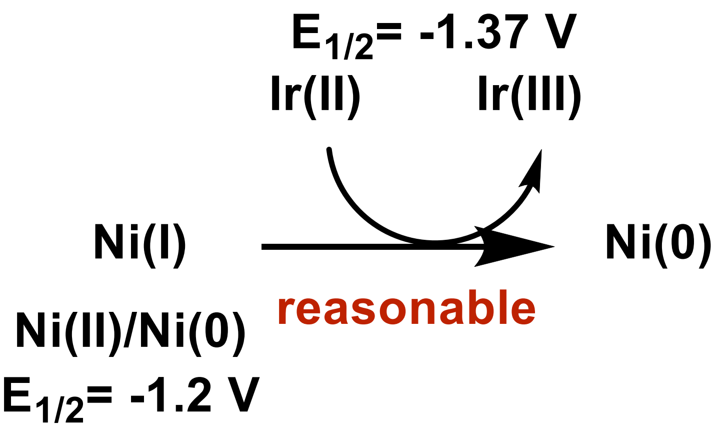


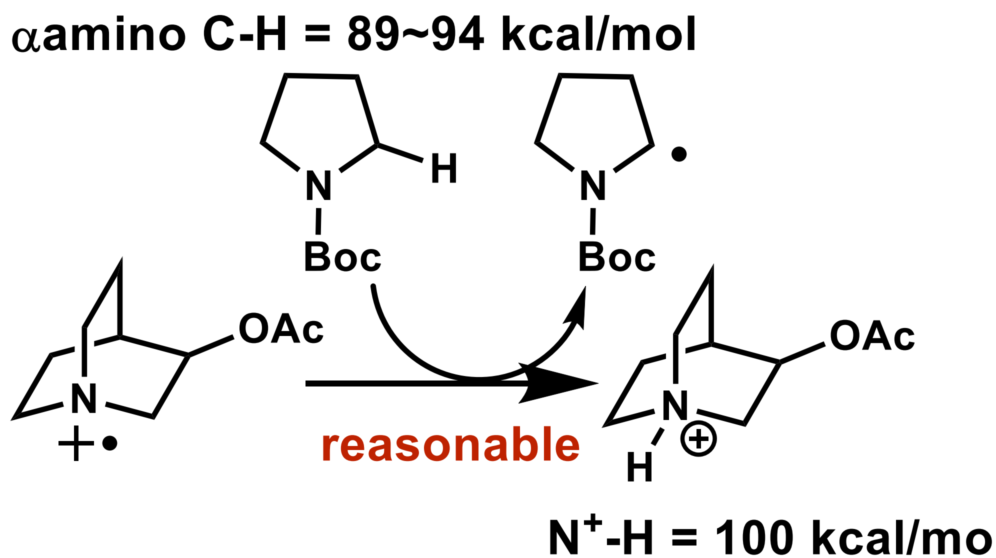



MacMillan, D. W. C. *et al*. *Science* **2016**, *352*, 1304.

# Reaction proceeds or not?



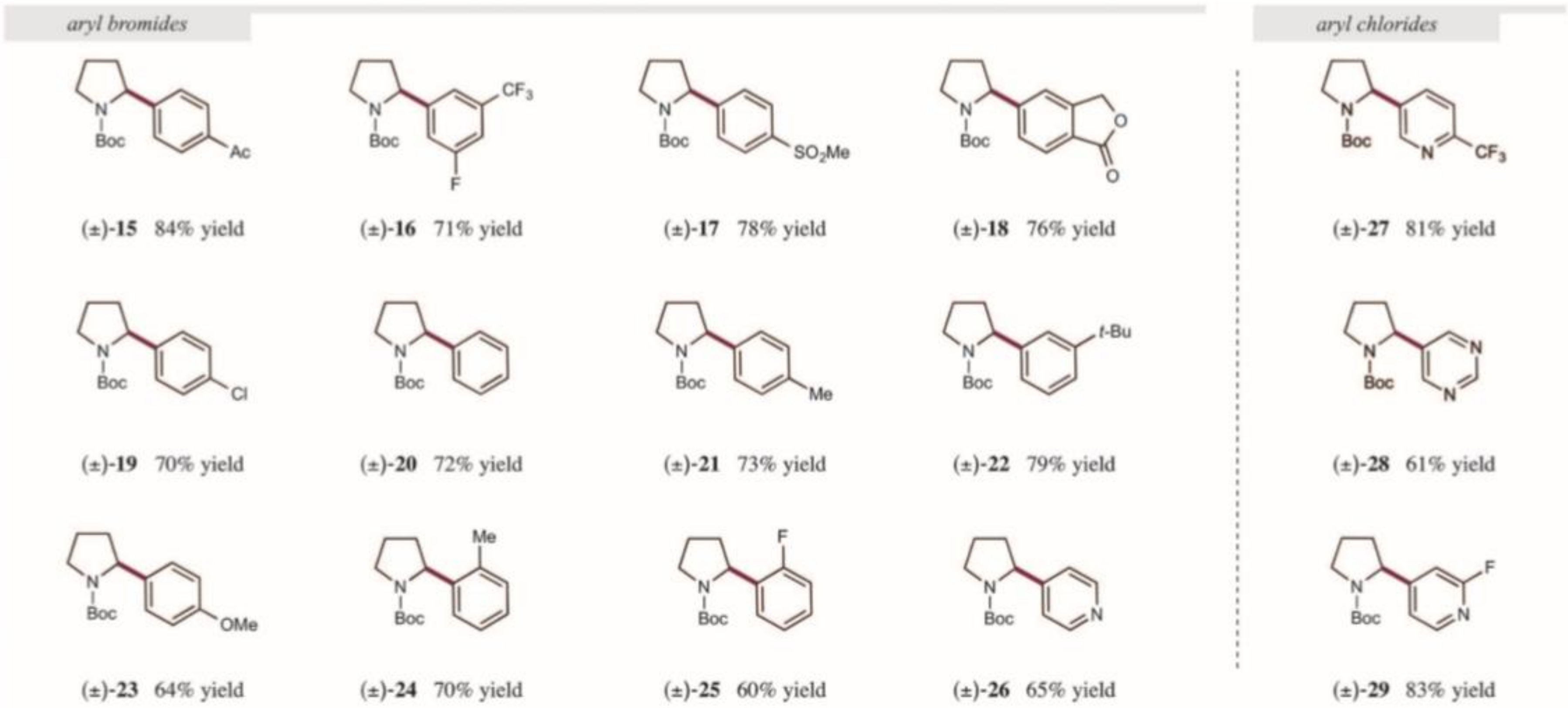






MacMillan, D. W. C. *et al. Science* **2016**, *352*, 1304.

# Substrate Scope

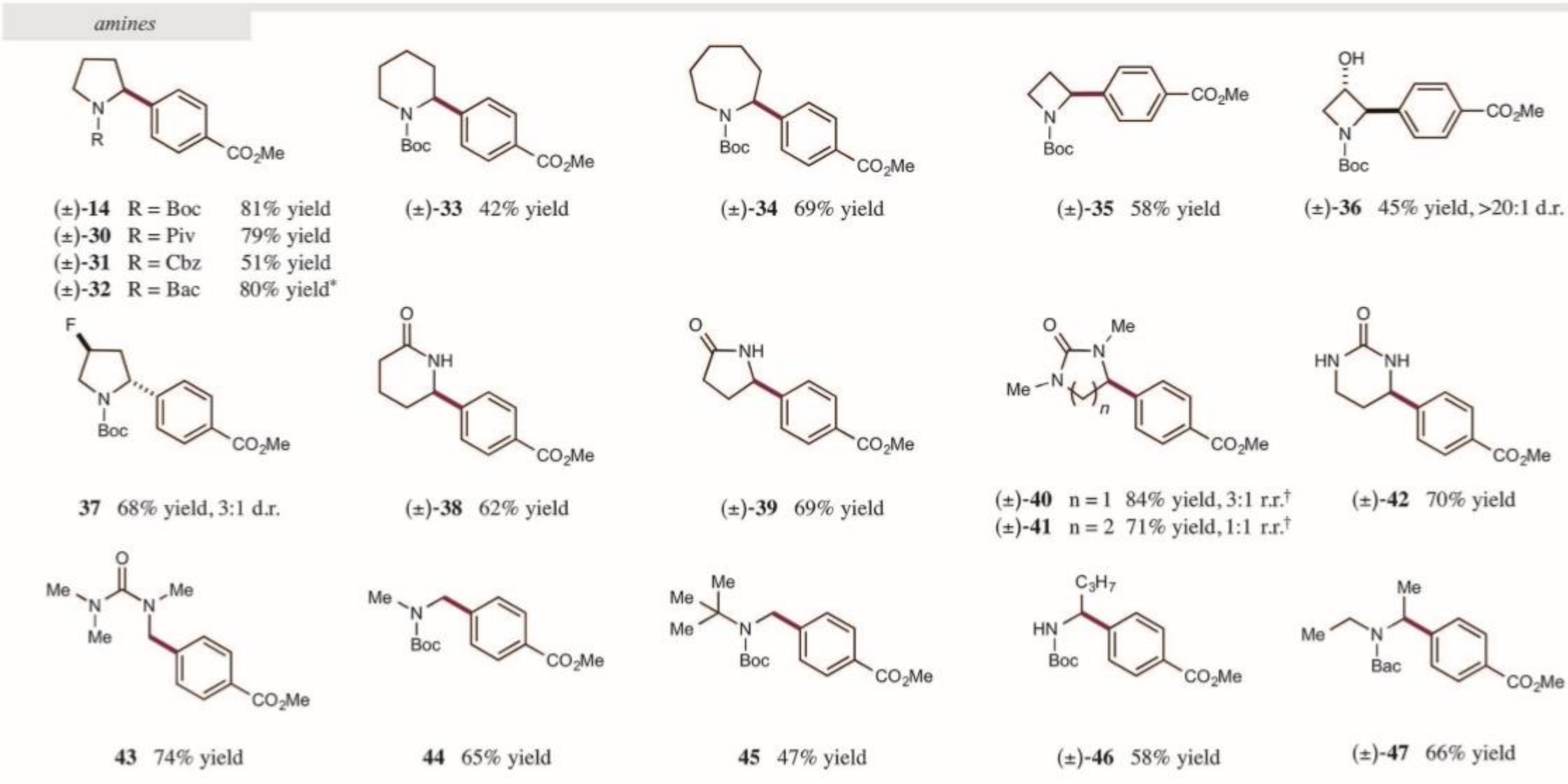



- ***N-Heterocycles also can tolerate reaction conditions.***



MacMillan, D. W. C. *et al*. *Science* **2016**, *352*, 1304.

# Substrate Scope




- ***Fluorine and hydroxyl group could tolerate reaction condition.***



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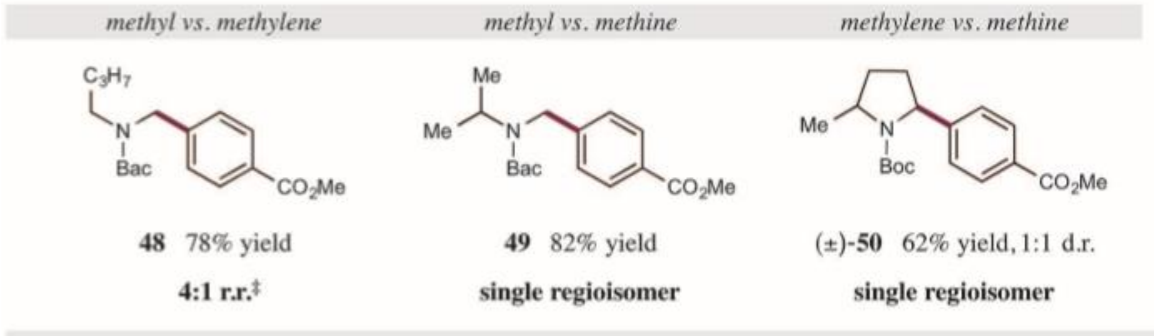
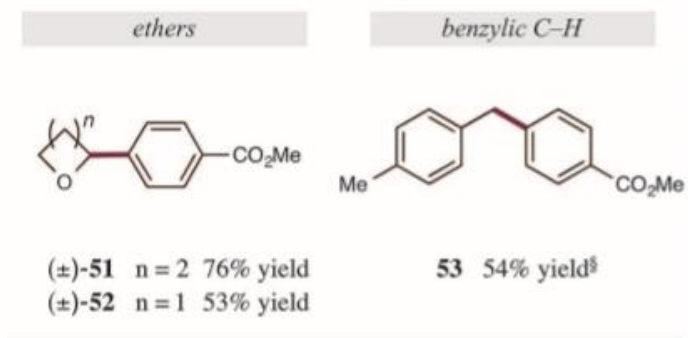
# Substrate Scope




- ***Regioselectivity is unique about unsymmetrical amine. Maybe, it is highly influenced by kinetics.***
- ***α-Oxy $sp^3$ C-H bond and benzylic C-H bond are also functionalized.***



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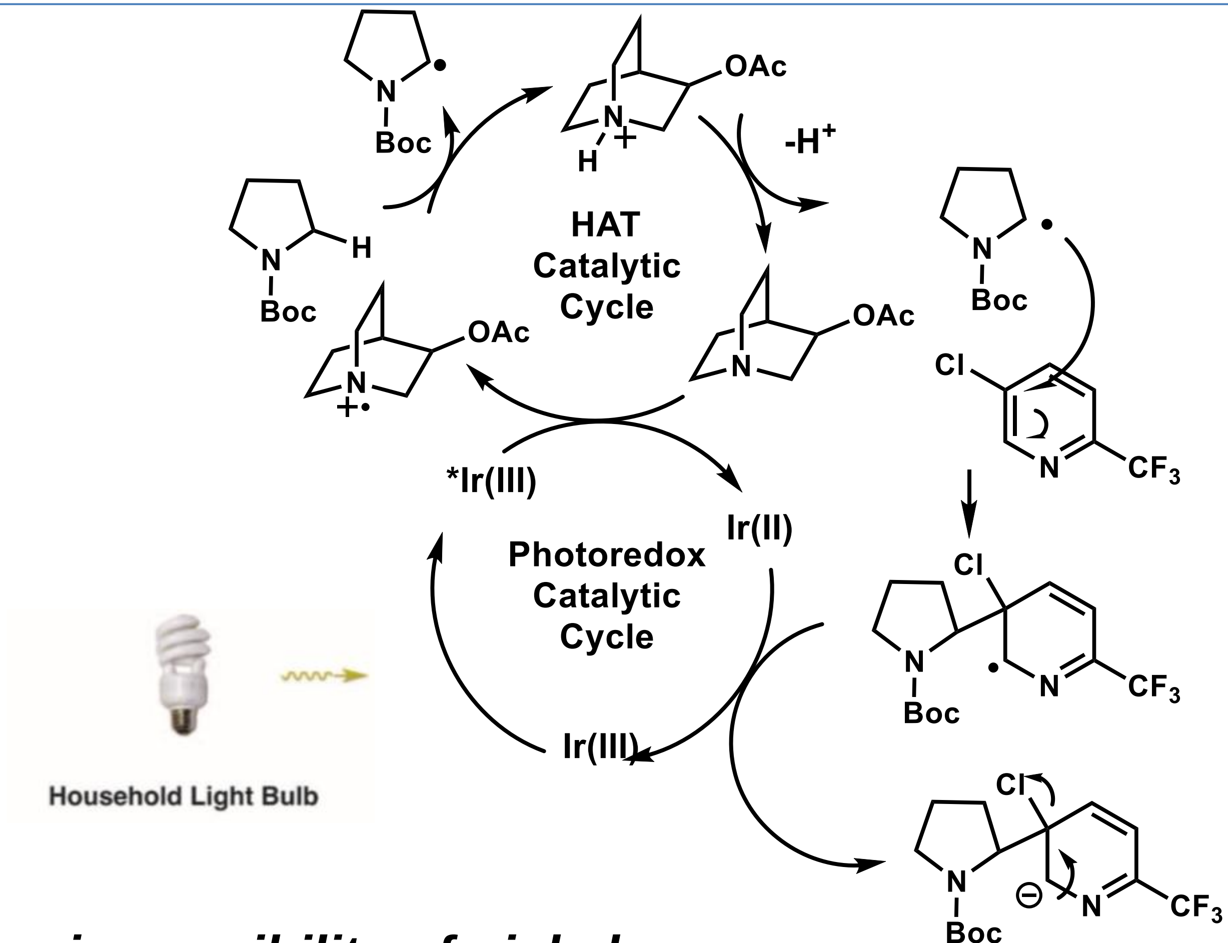
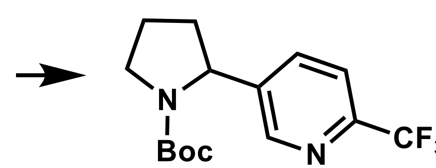
# Other Possibility




- ***There is possibility of nickel-uncatalyzed cycle like this***



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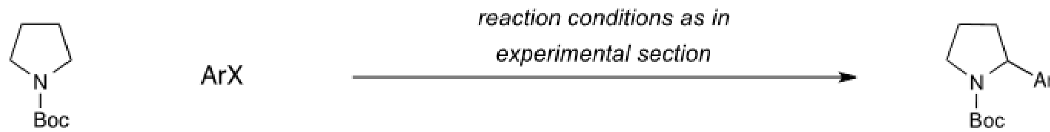
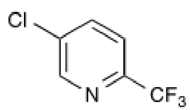
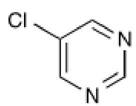
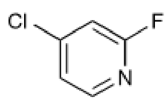
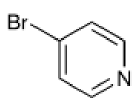
# Control Experiment




| ArX | Control experiment | Product yield* |
|---|---|---|
|  | with $NiBr_2$·4,7-dOMe-phen | 81% |
| | without $NiBr_2$·4,7-dOMe-phen | 0% |
|  | with $NiBr_2$·4,7-dOMe-phen | 61% |
| | without $NiBr_2$·4,7-dOMe-phen | 0% |
|  | with $NiBr_2$·4,7-dOMe-phen | 86% |
| | without $NiBr_2$·4,7-dOMe-phen | 0% |
|  | with $NiBr_2$·4,7-dOMe-phen | 66% |
| | without $NiBr_2$·4,7-dOMe-phen | 0% |

**Control experiment for N-Heterocycles as electrophiles was performed**

**Deny nickel-uncatalyzed cycle**



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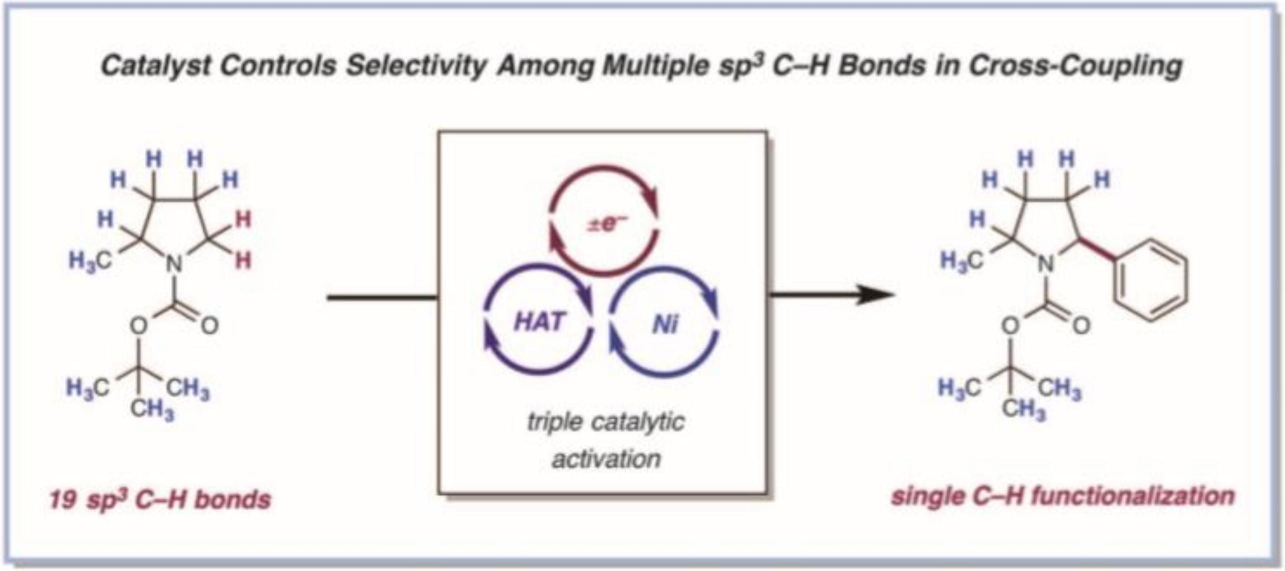
# Ternary Catalysis




- ***Selective functionalization of sp$^3$ C-H bond which is most abundant structure on the organic compounds.***



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# Conclusion

1. ***Nickel-catalyzed cross-coupling via radical pathway***
   - ***$sp^3$-$sp^2$ bond formation via radical pathway***
2. ***Hybrid catalysis of photoredox catalysis and nickel catalysis***
   - ***$sp^3$-$sp^2$ bond formation with simple and readily available organic molecules as nucleophile***
3. ***Hybrid catalysis of photoredox catalysis, nickel catalysis and HAT catalysis***
   - ***$sp^3$-$sp^2$ bond formation with $sp^3$ C-H bond as nucleophile***