

Single Electron Reduction of Aryl Halides Using Radical Anion

**2021.10.30. Literature Seminar
M2 Yuma Komori**

Contents

1. Introduction

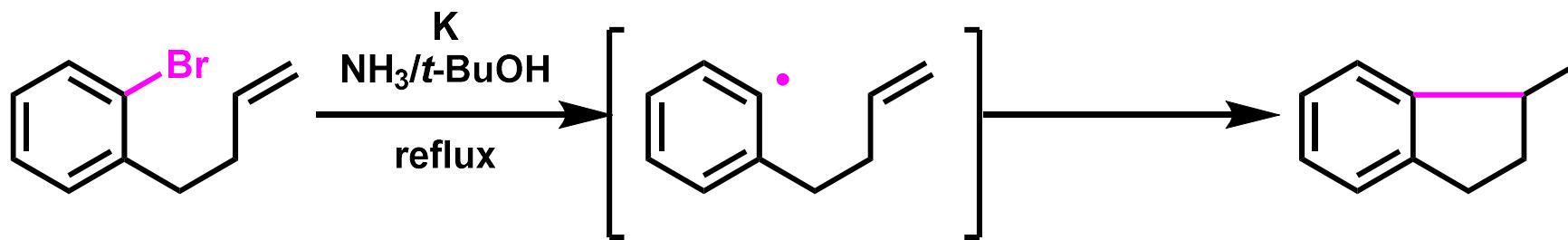
2. Reduction of Aryl Halides using Et₃N

3. Reduction of Aryl Halides using HCO₂Na

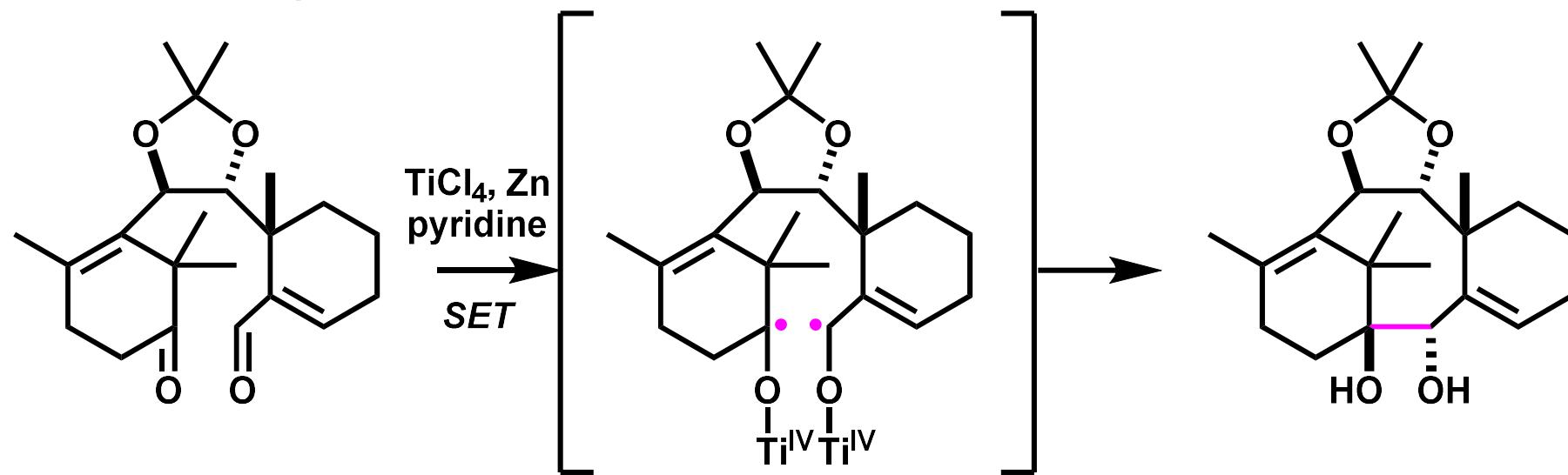
(Hendy, C. M.; Smith, G. C.; Xu, Z.; Lian, T.; Jui, N. T.
J. Am. Chem. Soc. **2021**, *143*, 8987.)

Single Electron Transfer (SET)

1. Birch reduction¹⁾



2. Pinacol coupling²⁾

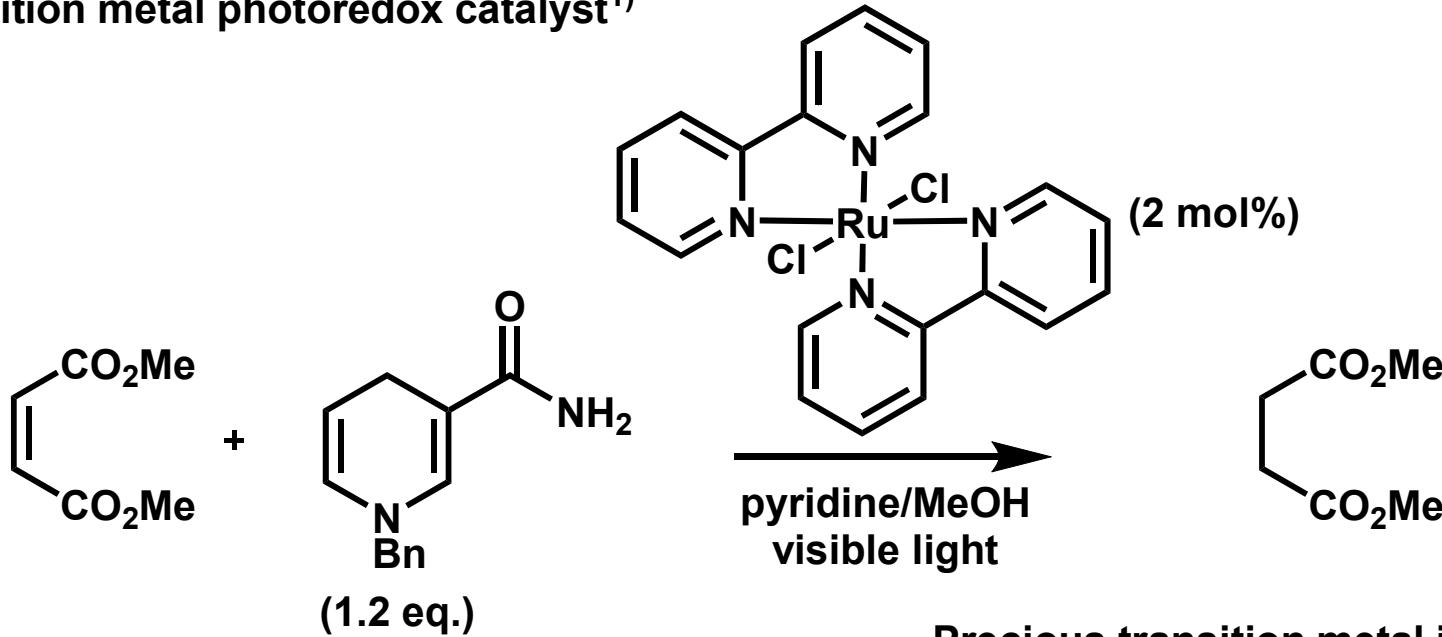


1) Meijis, G. F.; Bunnett, J. F.; Beckwith, A. L. J. *J. Am. Chem. Soc.* **1986**, *108*, 4899.

2) Imamura, Y.; Yoshioka, S.; Nagatomo, M.; Inoue, M. *Angew. Chem. Int. Ed.* **2019**, *58*, 12159.

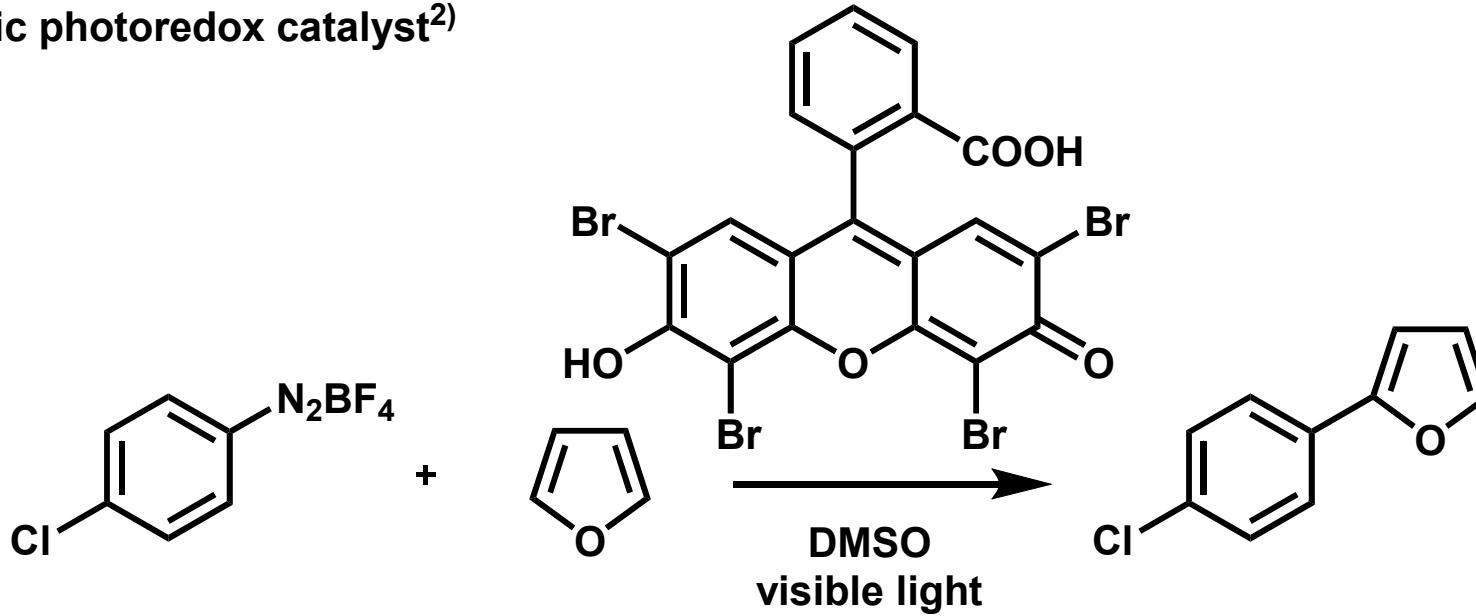
Photoredox catalyst

1. Transition metal photoredox catalyst¹⁾



Precious transition metal is necessary.

2. Organic photoredox catalyst²⁾



Reducing ability is limited.

1) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* 2013, 113, 5322.

2) Hari, D. P.; Schroll, P.; Konig, Burkhard. *J. Am. Chem. Soc.* 2012, 134, 2958.

Contents

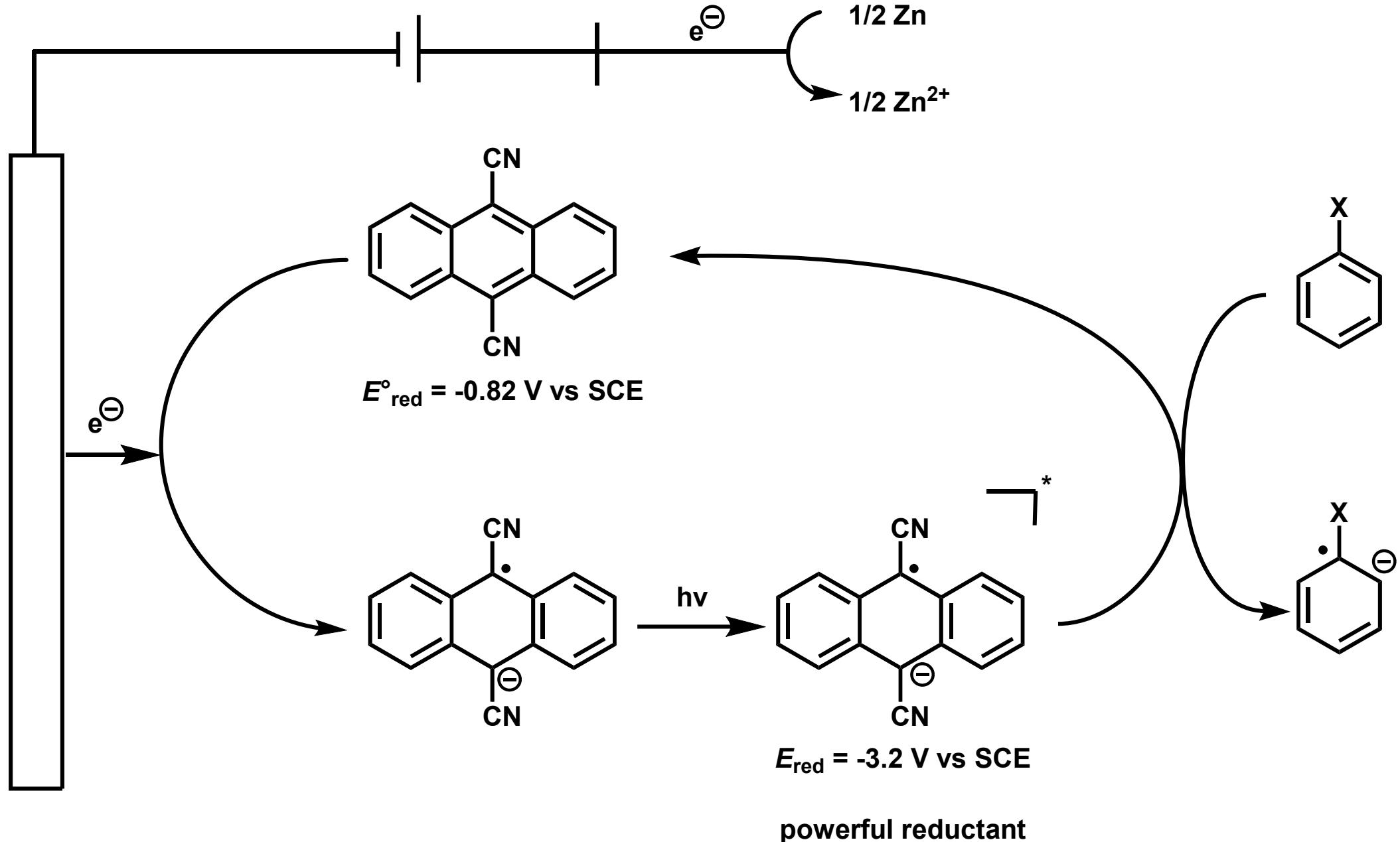
1. Introduction

2. Reduction of Aryl Halides using Et₃N

3. Reduction of Aryl Halides using HCO₂Na

(Hendy, C. M.; Smith, G. C.; Xu, Z.; Lian, T.; Jui, N. T.
J. Am. Chem. Soc. 2021, 143, 8987.)

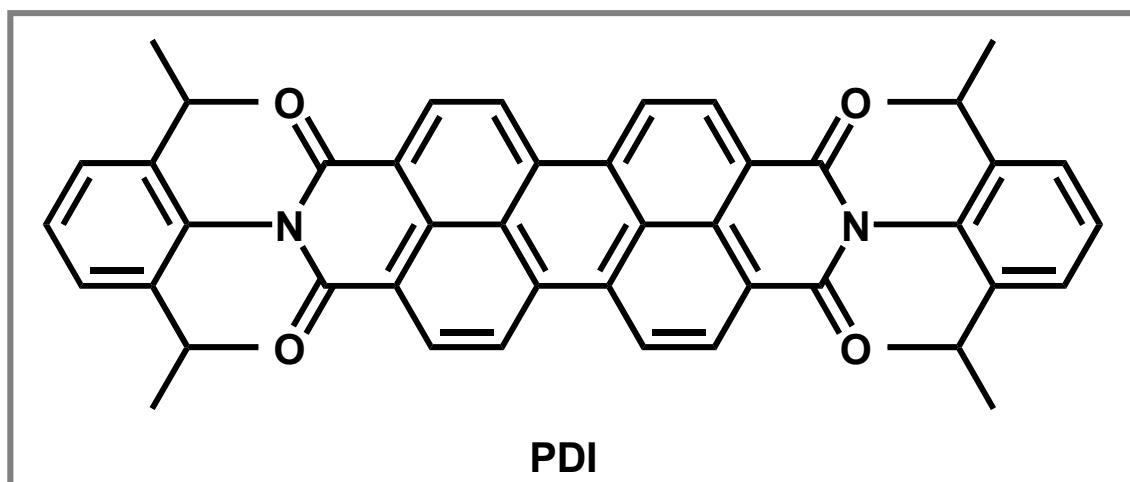
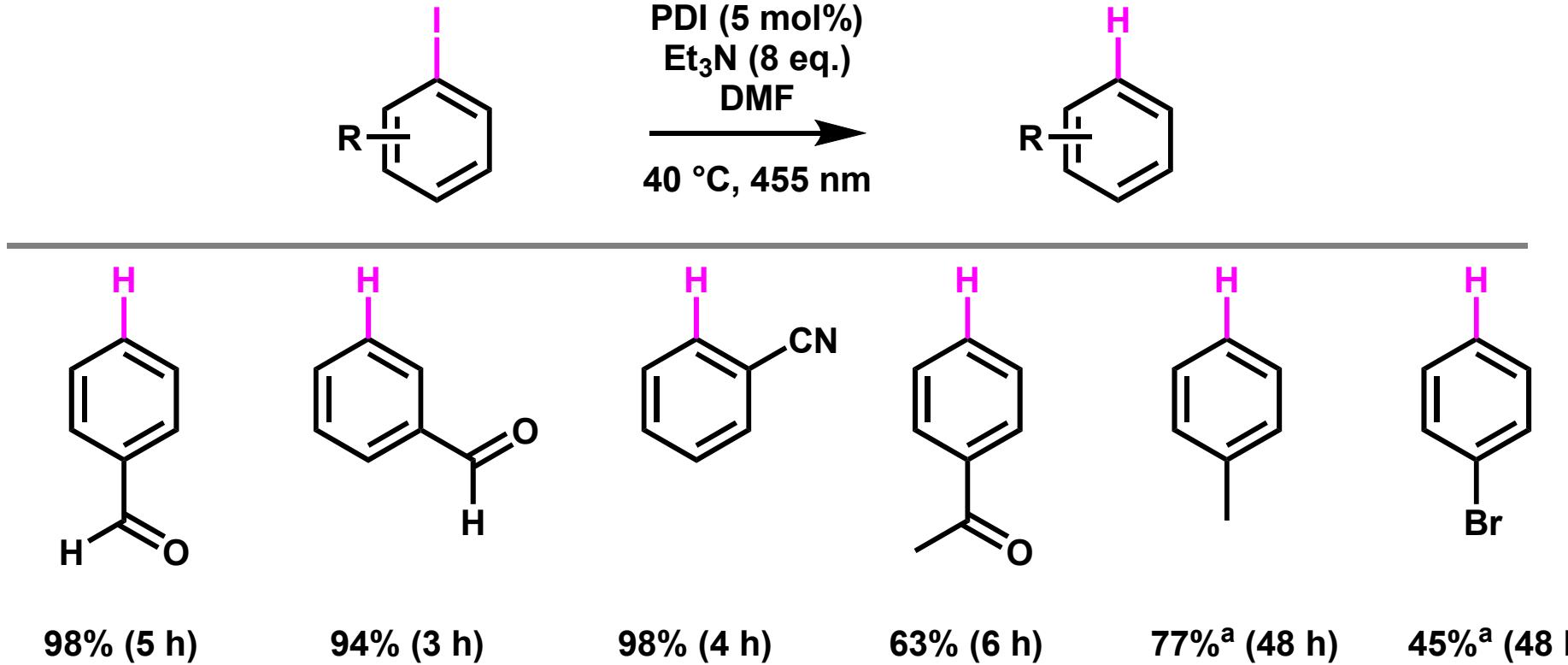
Radical Anion



Difficult to control

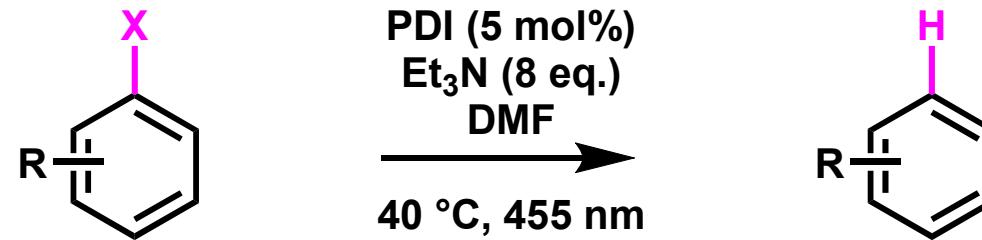
For details, please see 210828_LS_Tsukasa_Shimakawa

Photocatalytic Reduction

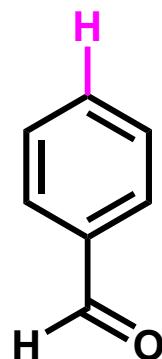


^aPDI (10 mol%), Et₃N (16 eq.)

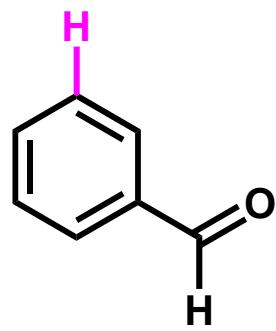
Substrate Scope



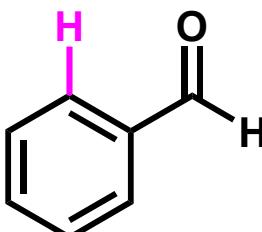
X = Br



98% (3 h)

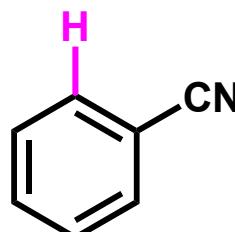


35% (48 h)

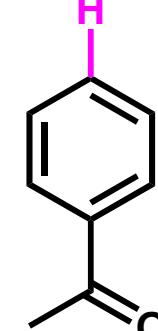


86% (5 h)

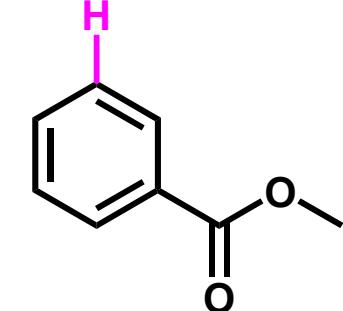
X = Cl



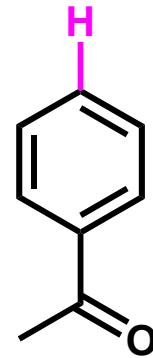
90% (8 h)



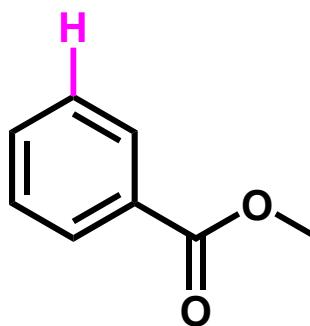
70%^a (48 h)



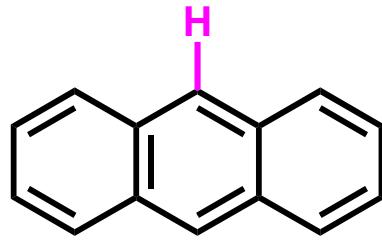
52%^a (48 h)



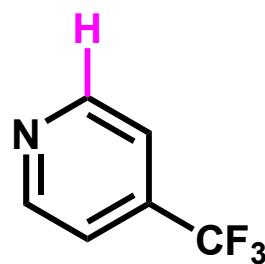
82% (4 h)



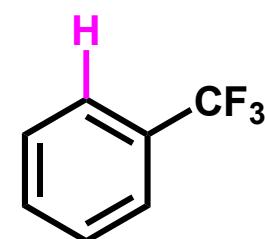
77% (4 h)



45% (2 h)



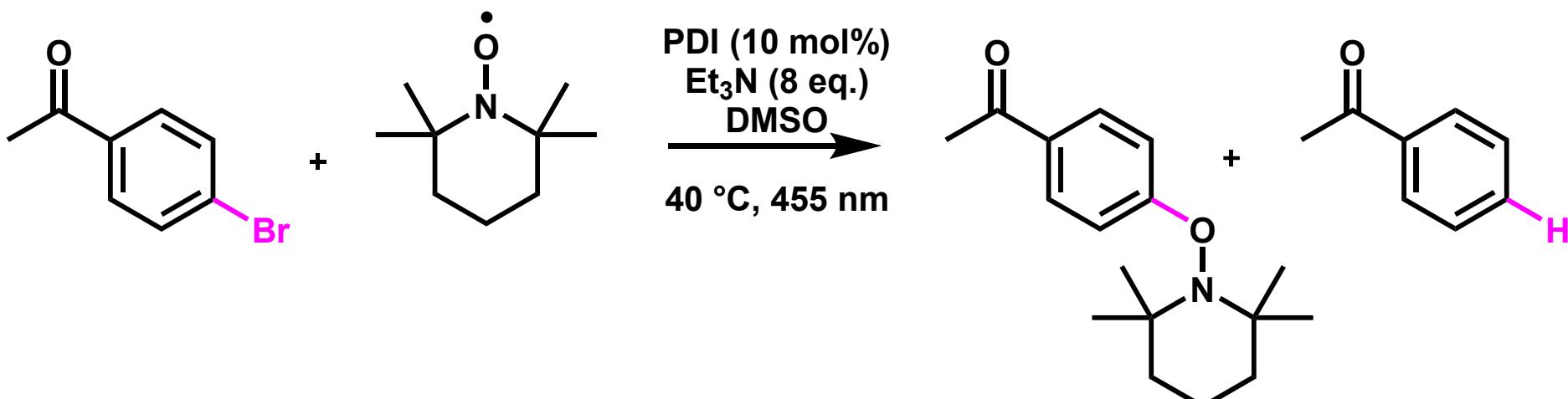
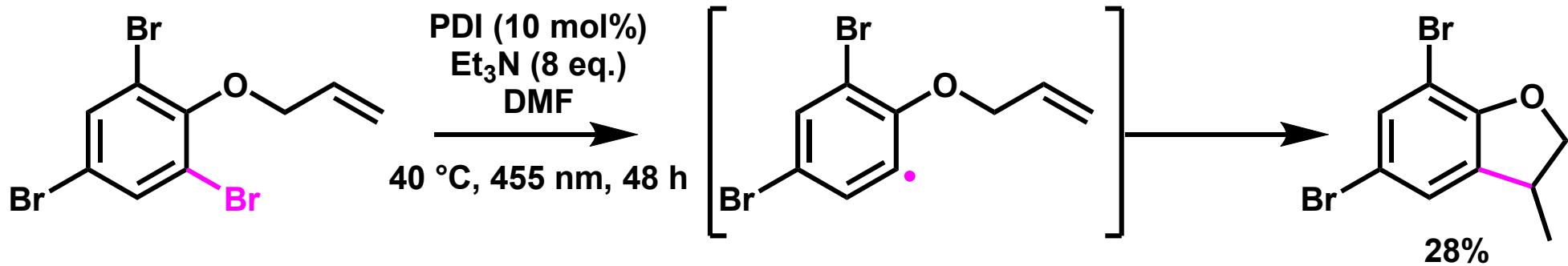
91% (16 h)



64%^a (46 h)

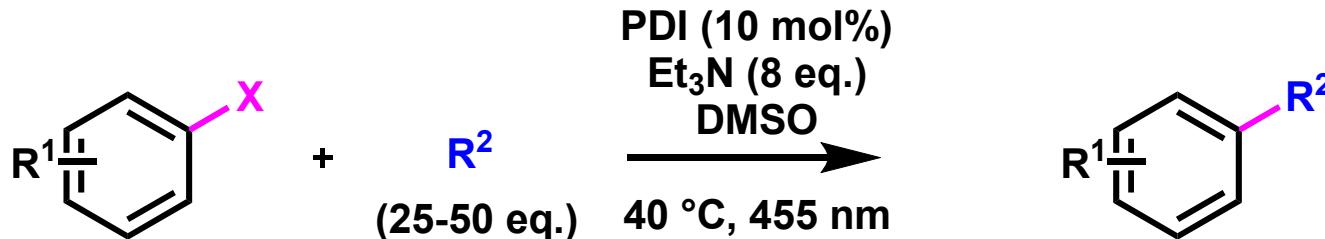
^aPDI (10 mol%), Et₃N (16 eq.)

Radical Experiment

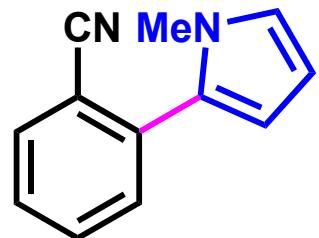


HRMS analysis

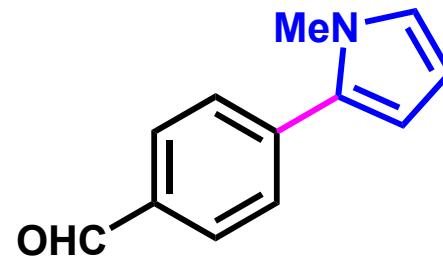
Aryl Radical Addition



X = I

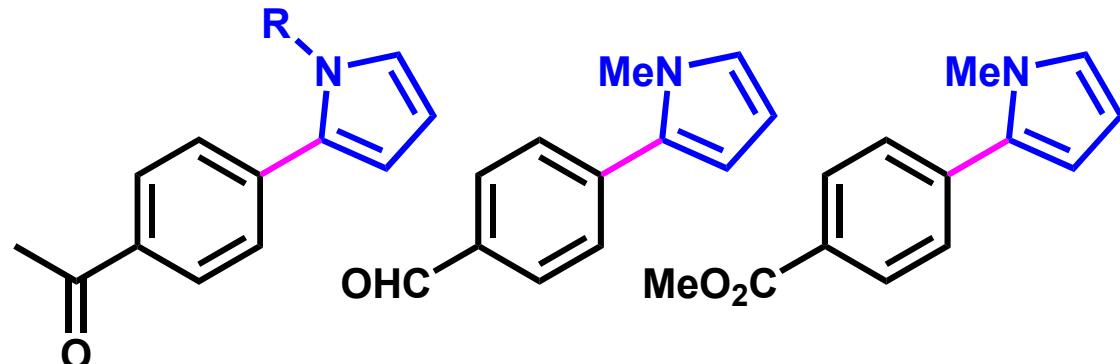


72% (22 h)

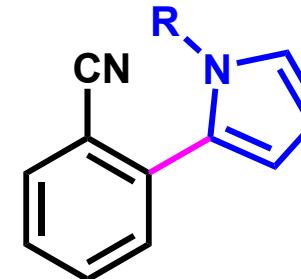


52% (24 h)

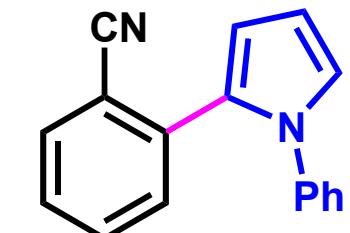
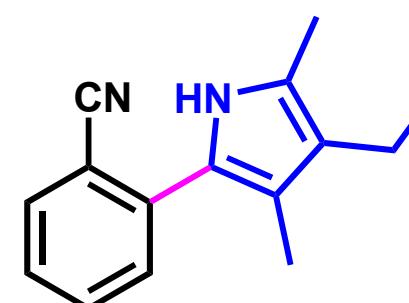
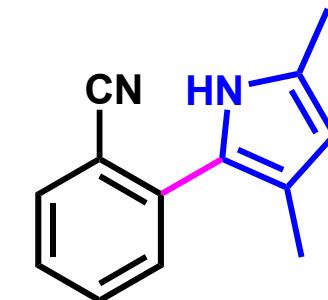
X = Br



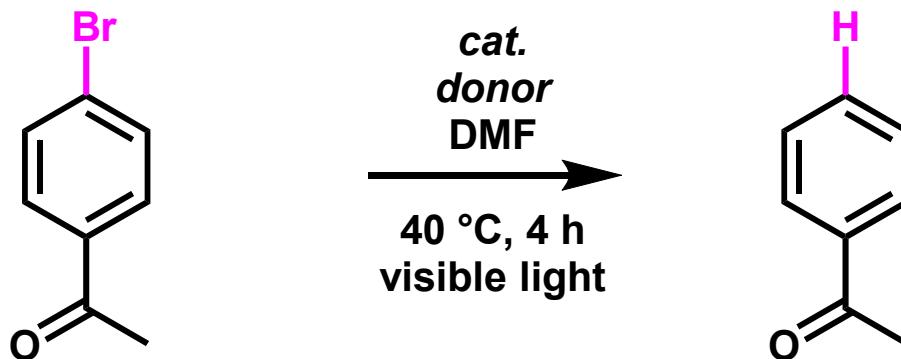
X = Cl



R = Me: 70% (12 h)
R = H: 61% (16 h)



Control Experiments



| entry | cat. (mol%) | donor | conditions | yield |
|-------|-------------|---------------------------|--------------|-----------|
| 1 | 5 | Et ₃ N (8 eq.) | DMF, 455 nm | 82% |
| 2 | 5 | Et ₃ N (8 eq.) | DMF, Dark | 0% |
| 3 | - | - | DMF, 455 nm | 0% |
| 4 | 5 | - | DMF, 455 nm | 14% (ca.) |
| 5 | - | Et ₃ N (8 eq.) | DMF, 455 nm | 0% |
| 6 | 5 | Et ₃ N (2 eq.) | DMF, 455 nm | 33% |
| 7 | 5 | Et ₃ N (4 eq.) | DMF, 455 nm | 43% |
| 8 | 5 | Et ₃ N (8 eq.) | DMSO, 455 nm | 47% |

Generation of Radical Anion

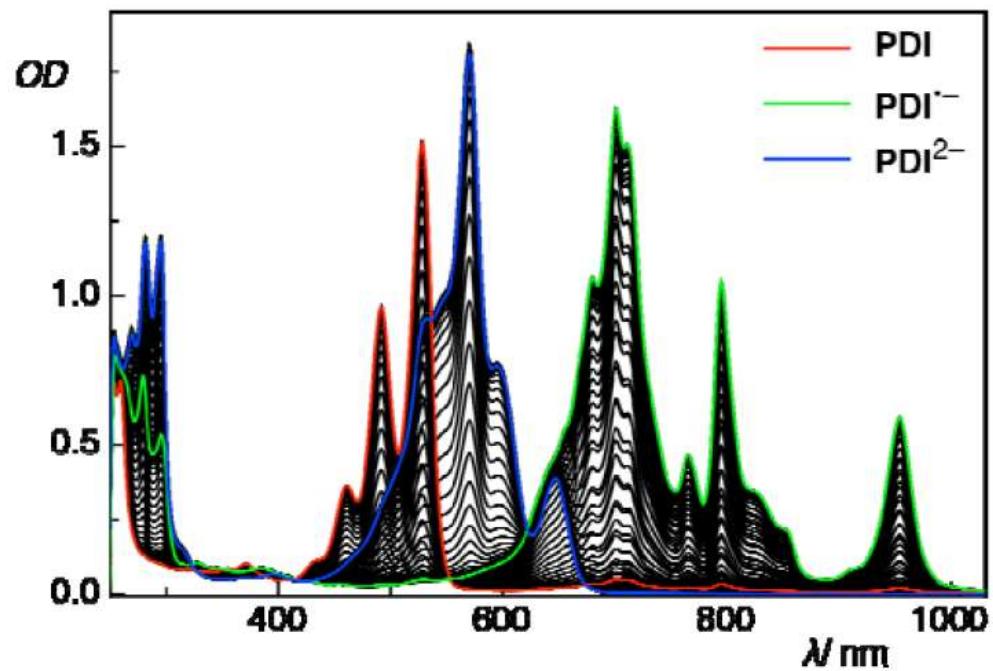


Fig.1 Spectroelectrochemical analysis of PDI in DMF

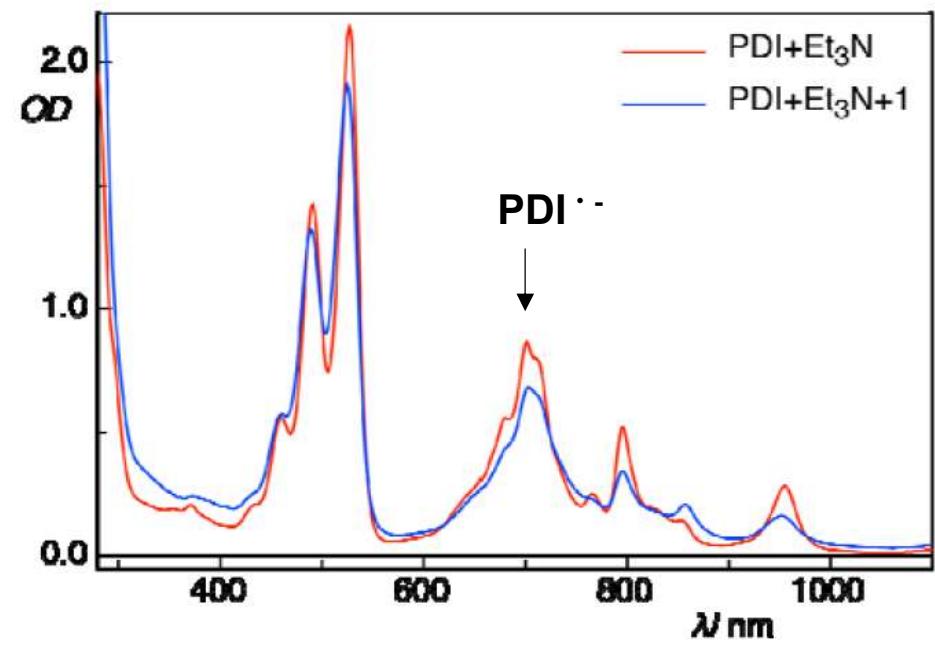
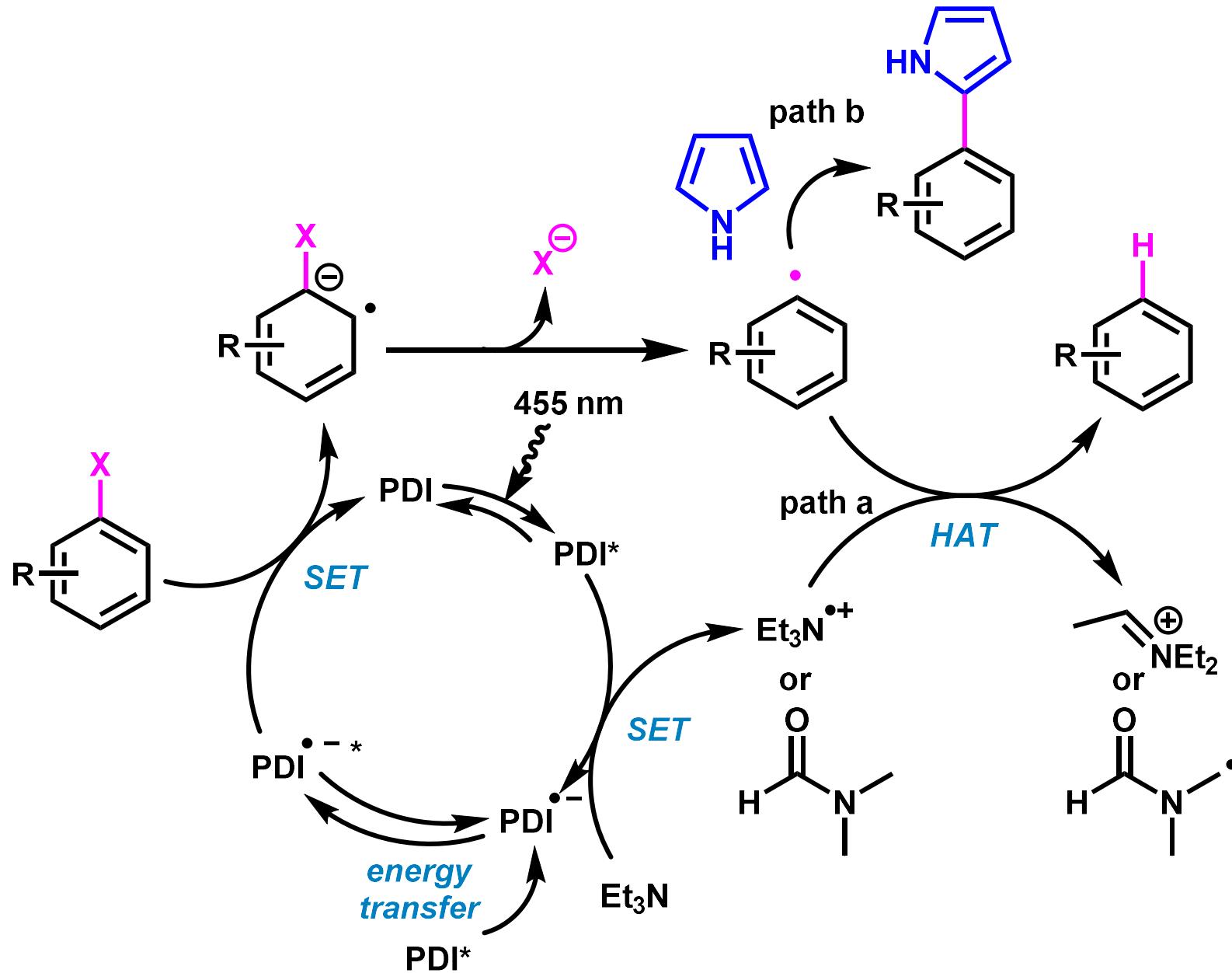


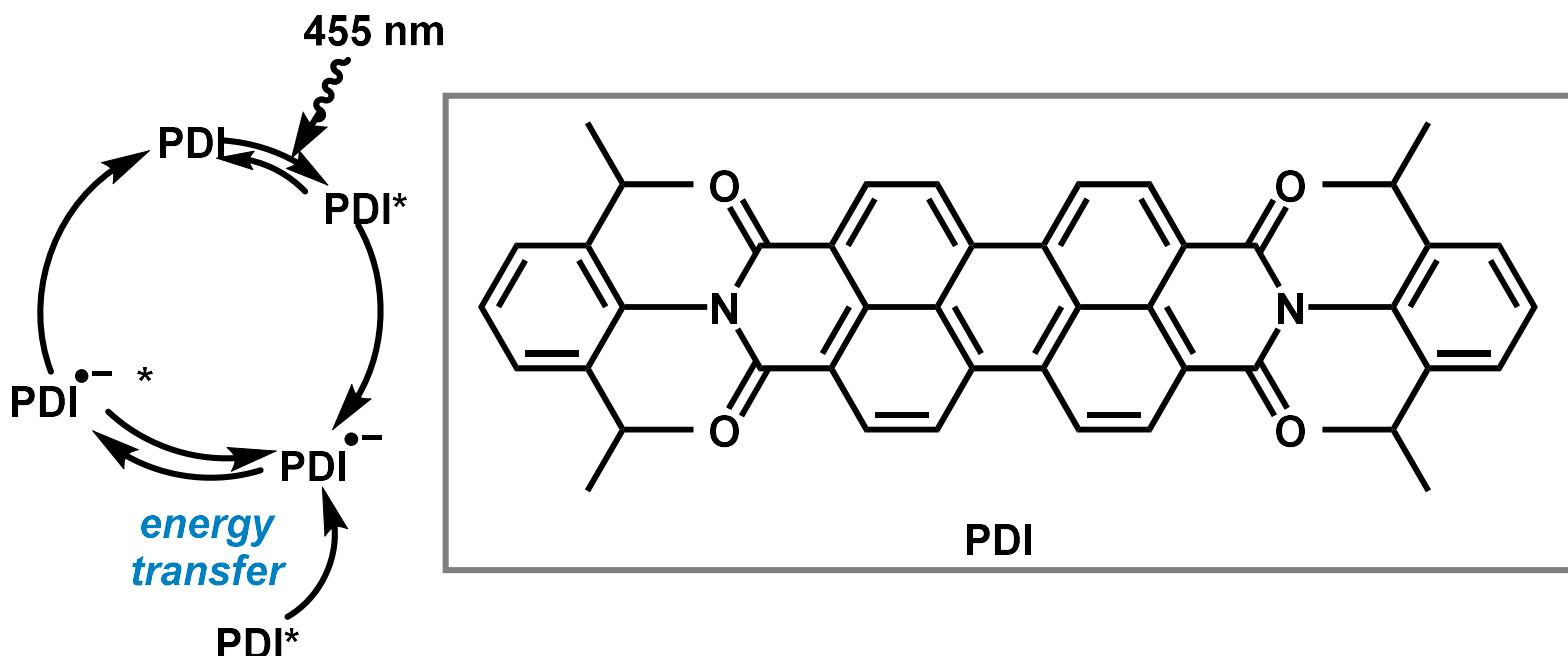
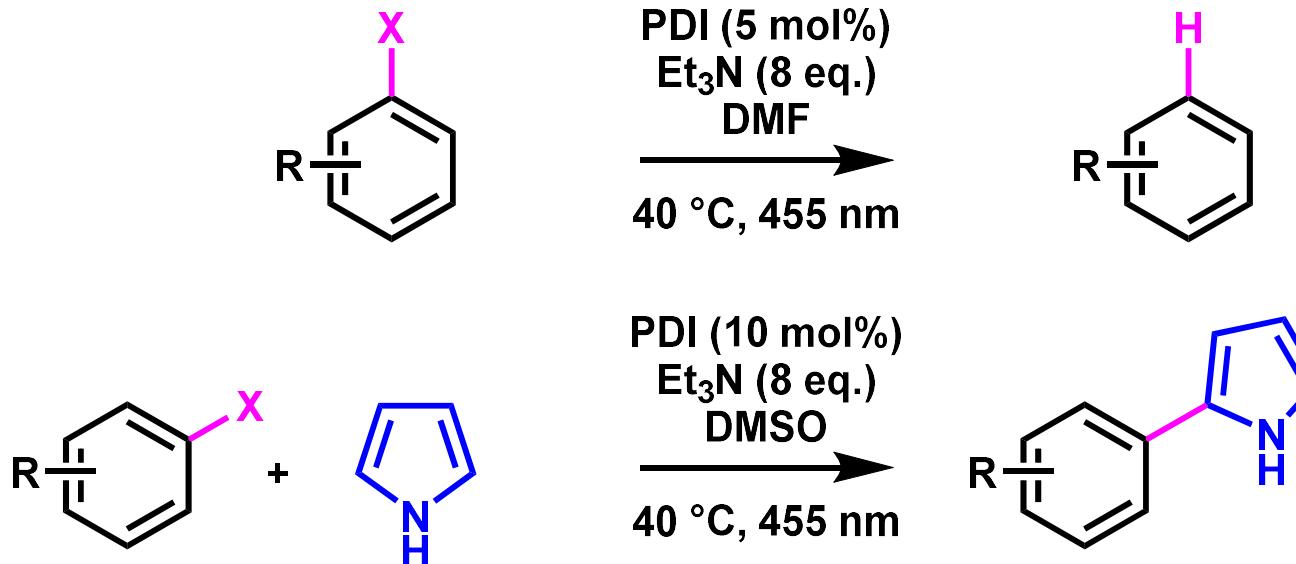
Fig.2 Formation of the PDI radical anion upon photoexcitation ($\lambda_{\text{Ex}} = 455 \text{ nm}$)

1: 4'-bromoacetophenone

Proposed Mechanism



Short Summary



Second excitation of PDI radical anion makes catalyst more powerful reductant.

Contents

1. Introduction

2. Reduction of Aryl Halides using Et₃N

3. Reduction of Aryl Halides using HCO₂Na

(Hendy, C. M.; Smith, G. C.; Xu, Z.; Lian, T.; Jui, N. T.
J. Am. Chem. Soc. **2021**, *143*, 8987.)

Associate Prof. Nathan T. Jui

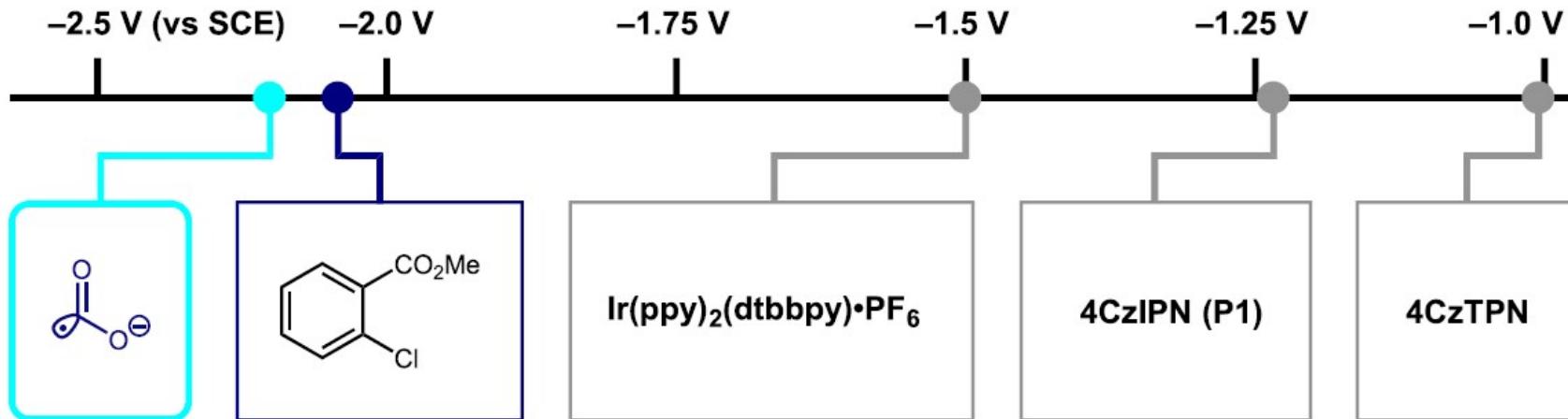


**-2008 B.S. @Colorado State University
2008-2013 Ph.D @Princeton University (Prof. MacMillan)
2013-2014 Postdoc. @Massachusetts Institute of Technology
(Prof. Buchwald)**
**2014- @Emory University
2020- Associate Professor @Emory University**

Research topics

- Nitrogen heterocycle functionalization with catalytic method**
- Development of small modulators of Liver Receptor Homologue-1 (LRH1)**

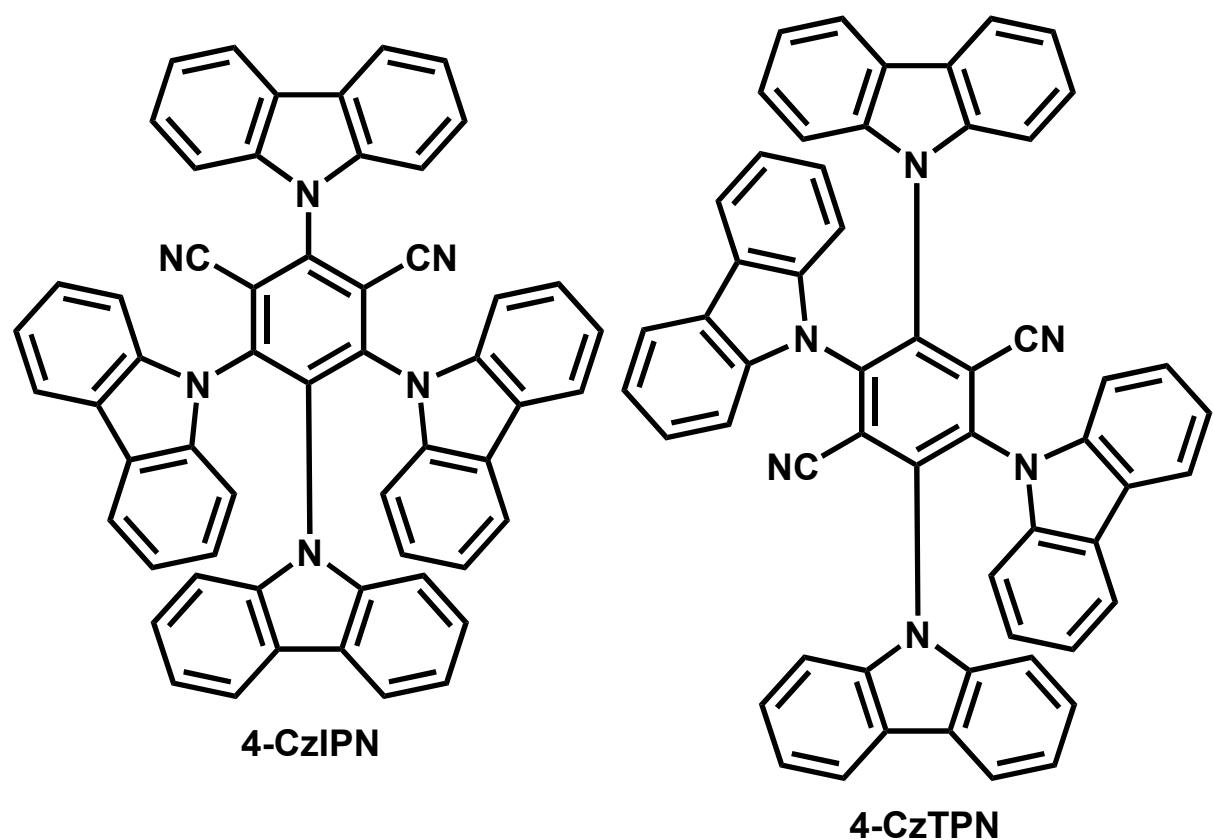
Carbon Dioxide Anion Radical



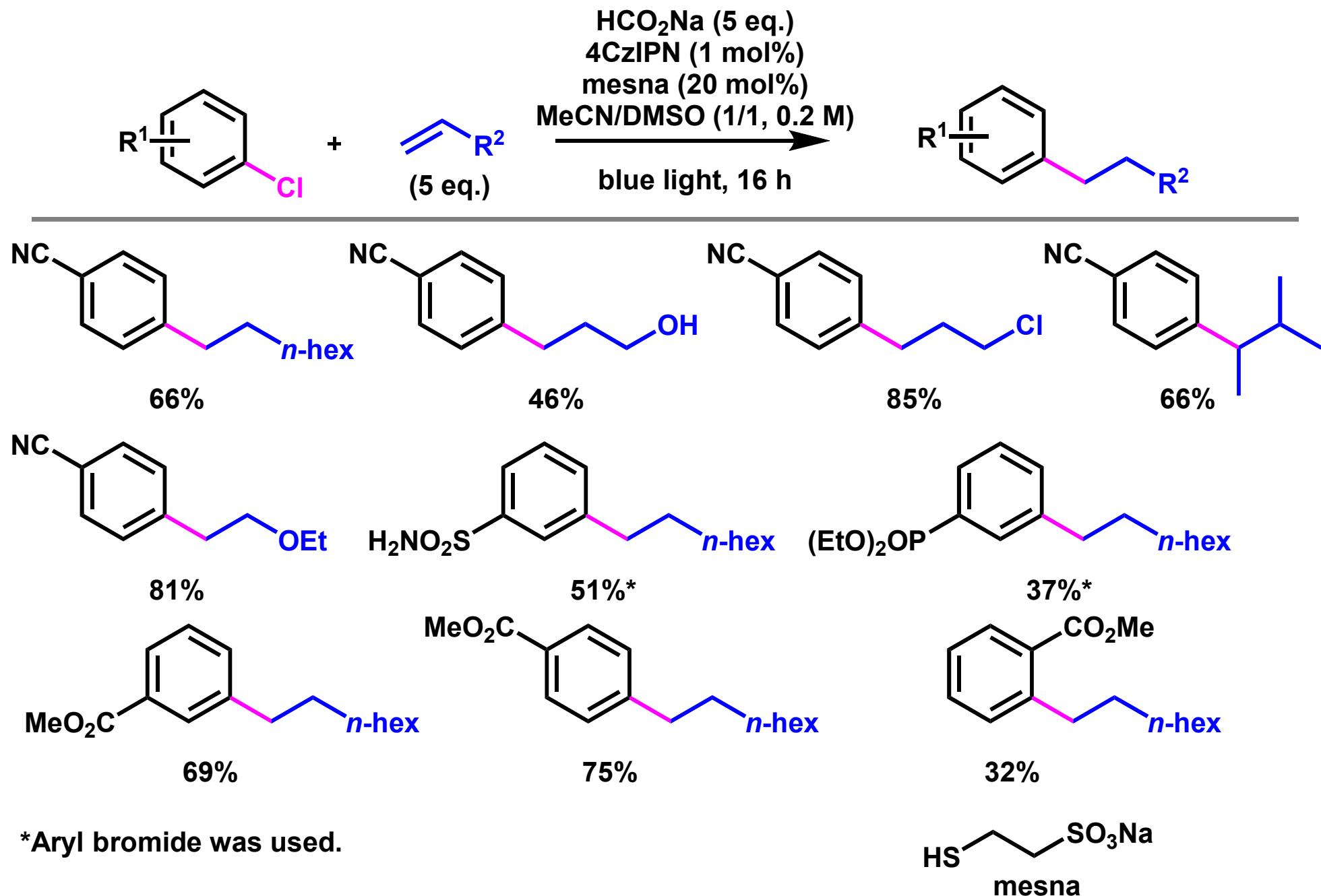
Powerful reductant

Difficult to access

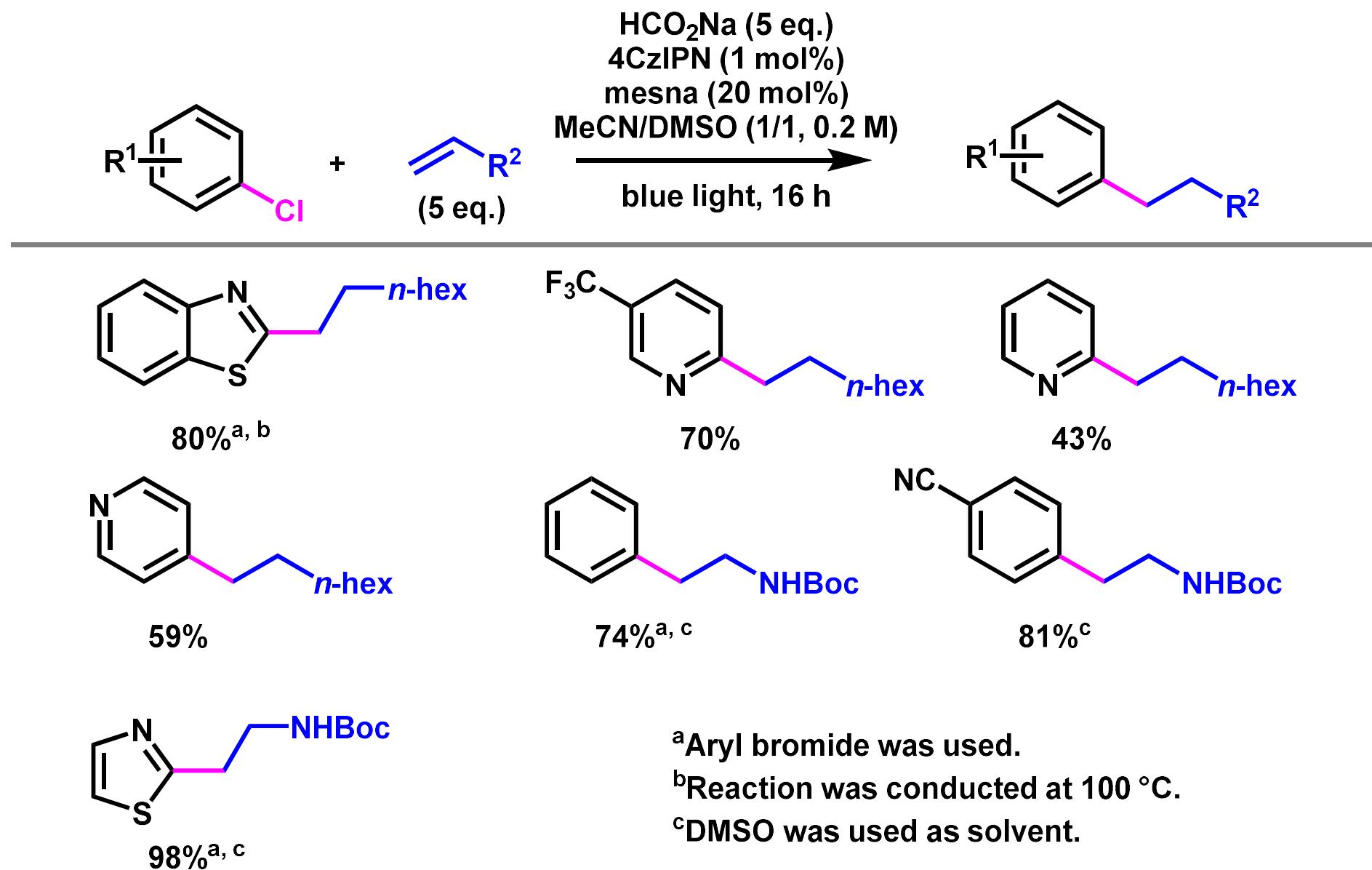
- Electrochemical reduction of CO_2
- Reduction of CO_2 using more reductive reagents



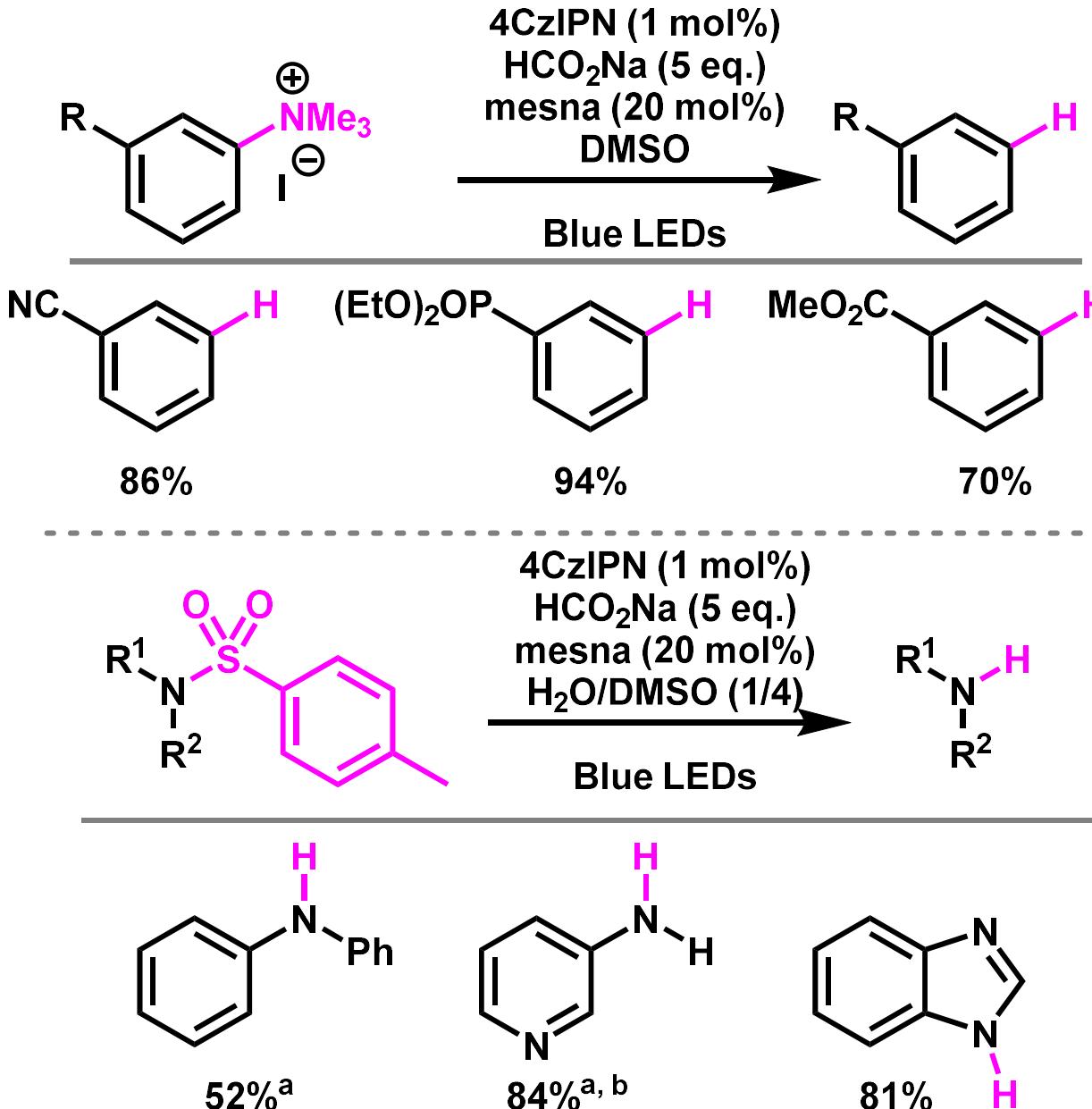
Substrate Scope(1)



Substrate Scope(2)



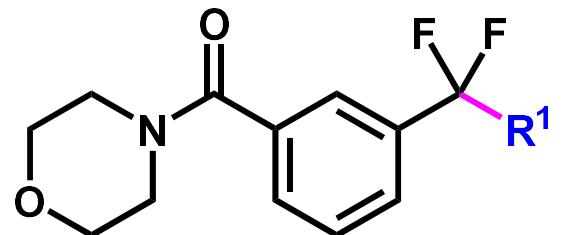
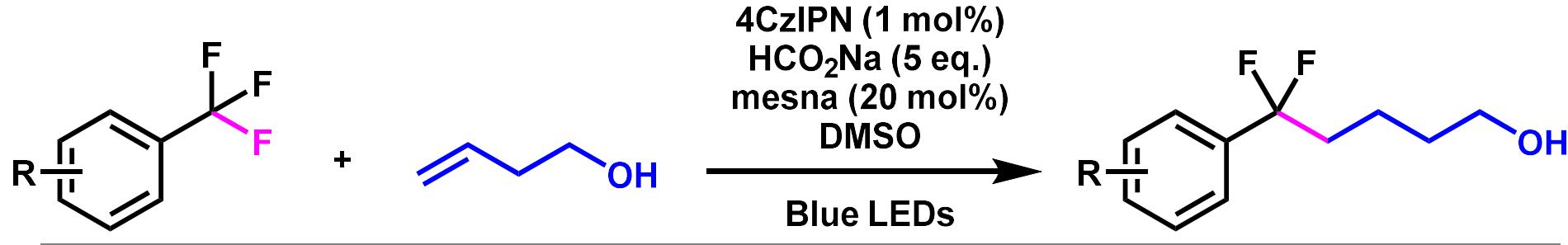
Single Electron Reduction (1)



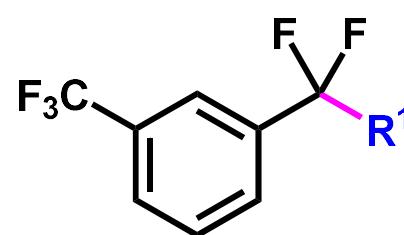
^aReaction was conducted at 100 °C.

^bDMSO was used as solvent.

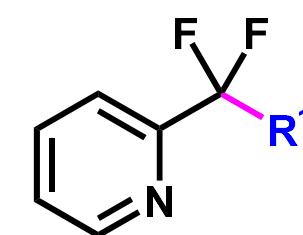
Single Electron Reduction (2)



59%



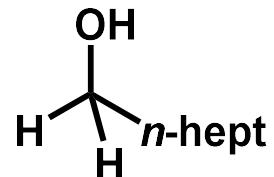
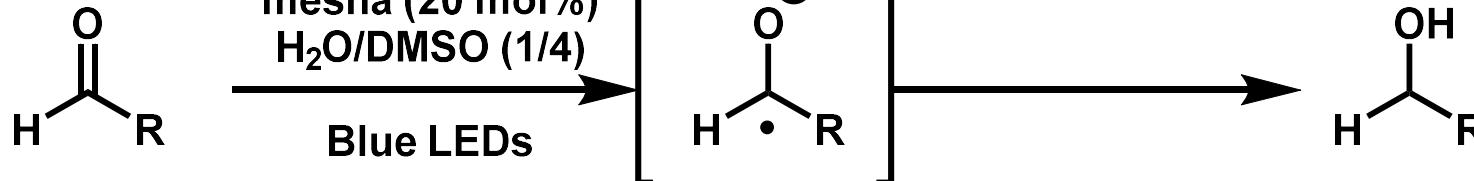
50%



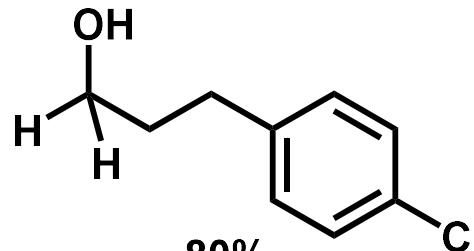
30%^a

^aReaction was conducted at 100 °C.

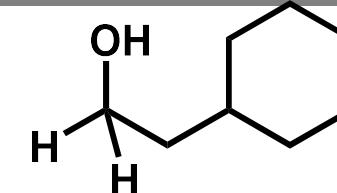
R1 = 



87%

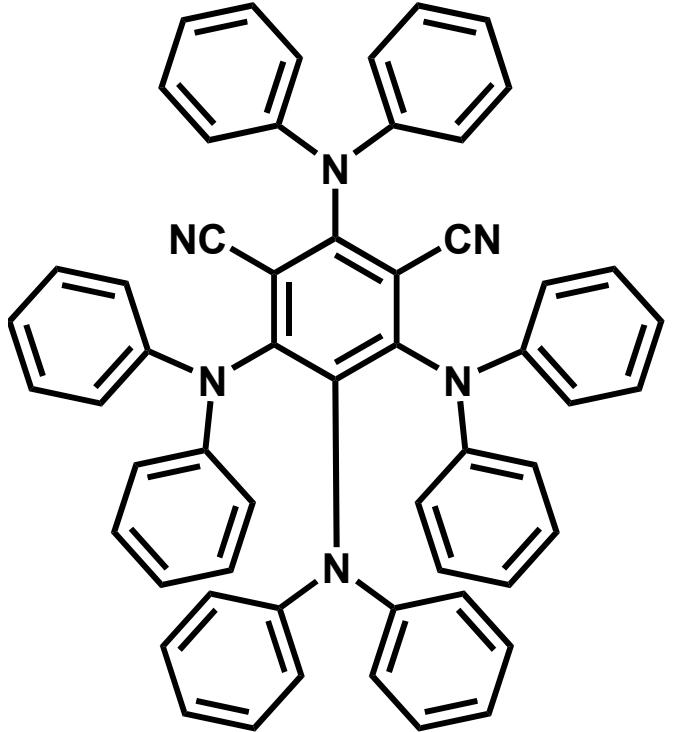


80%

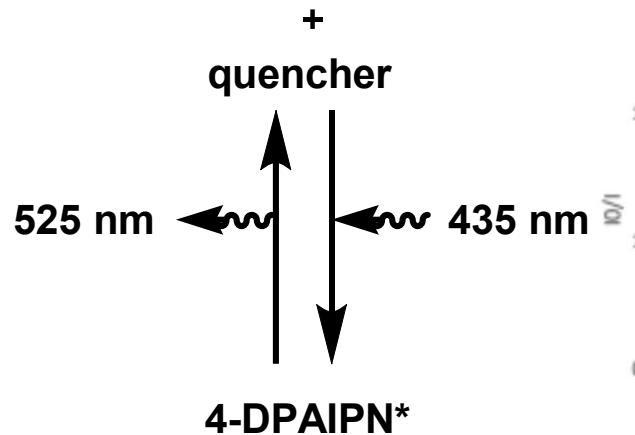


70%

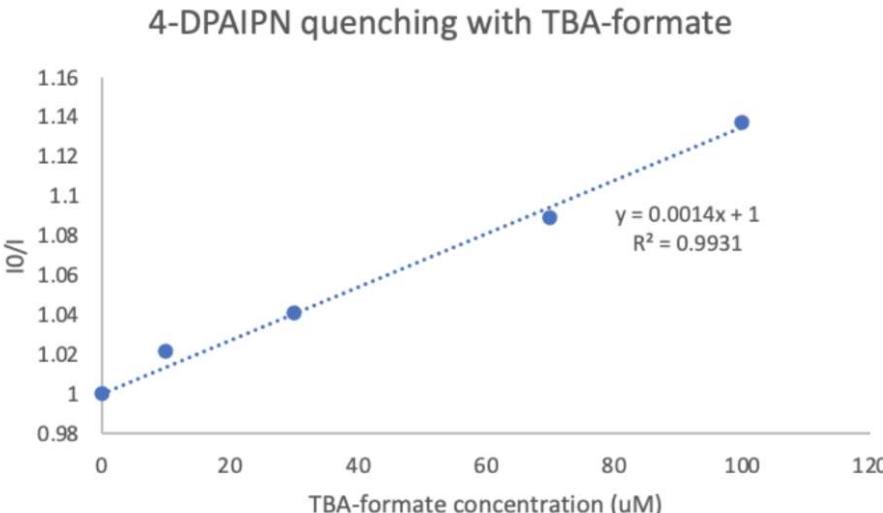
Stern-Volmer Quenching Study



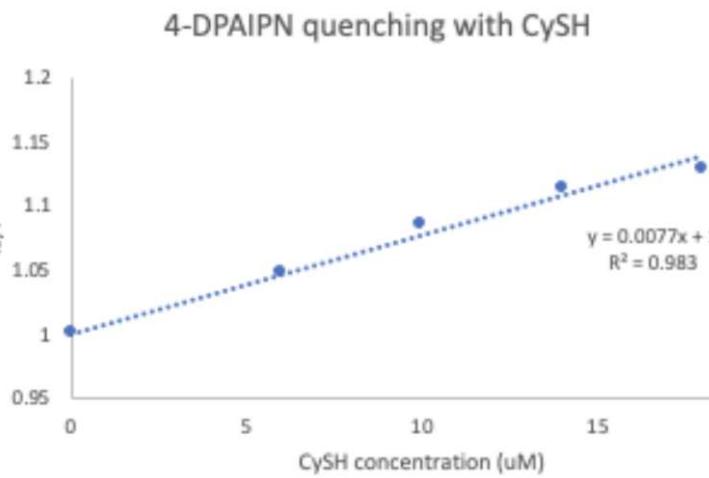
4-DPAIPN (25 μM in DMSO)



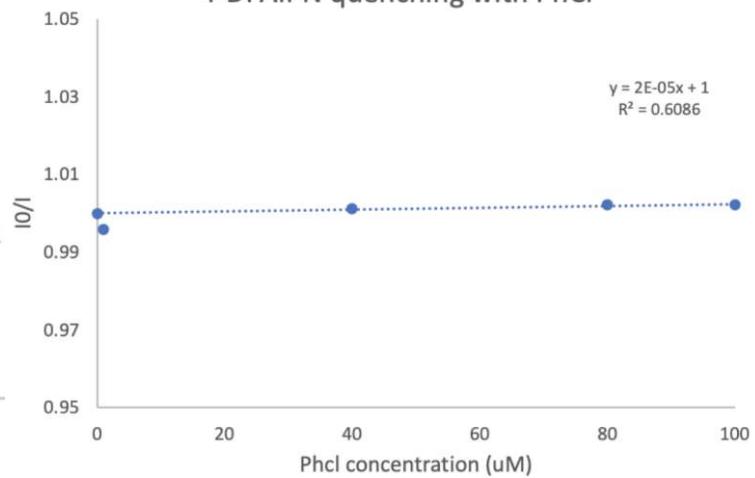
I_0 : emission intensity without quencher
 I : emission intensity (variable)



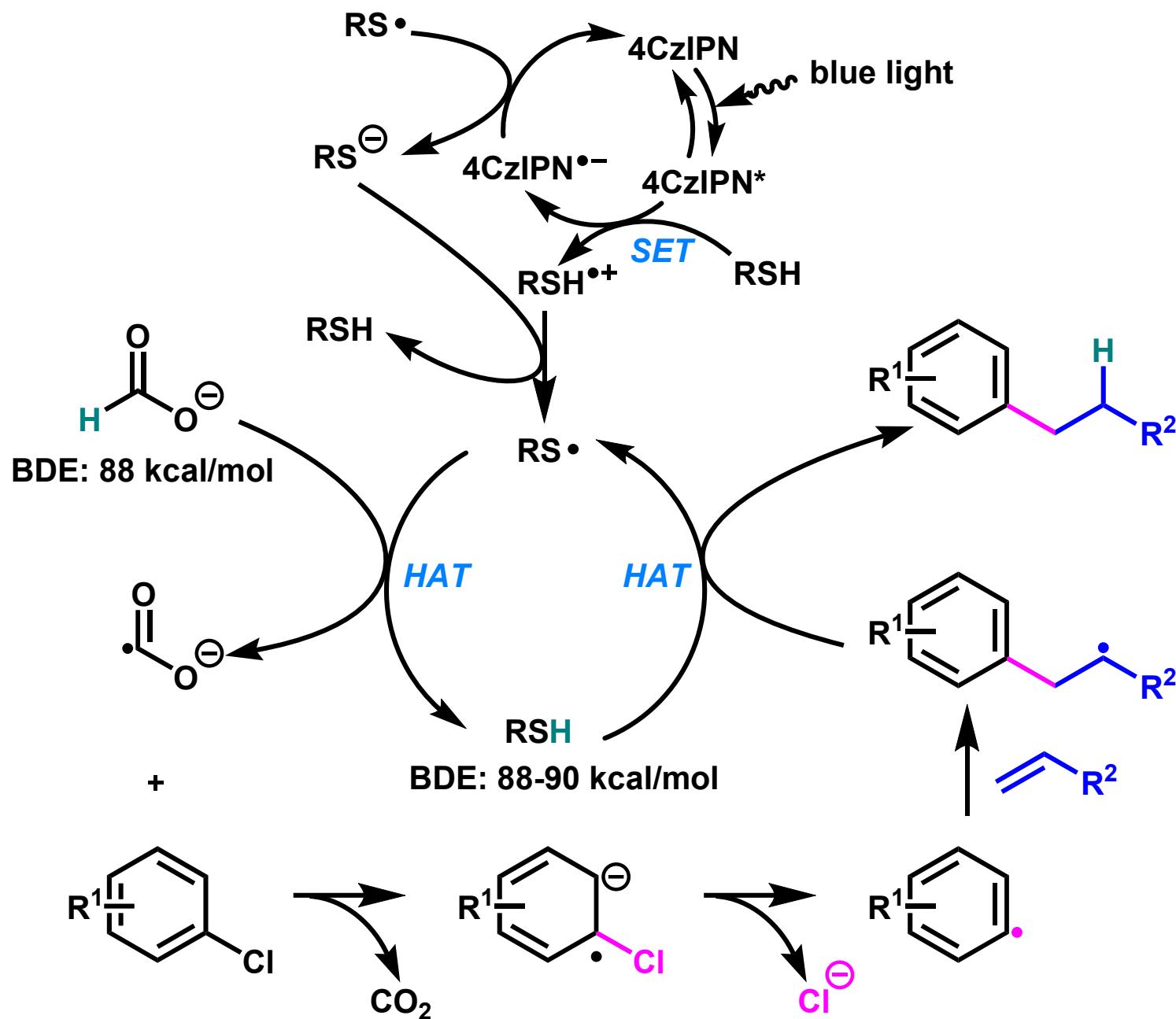
4-DPAIPN quenching with CySH



4-DPAIPN quenching with PhCl

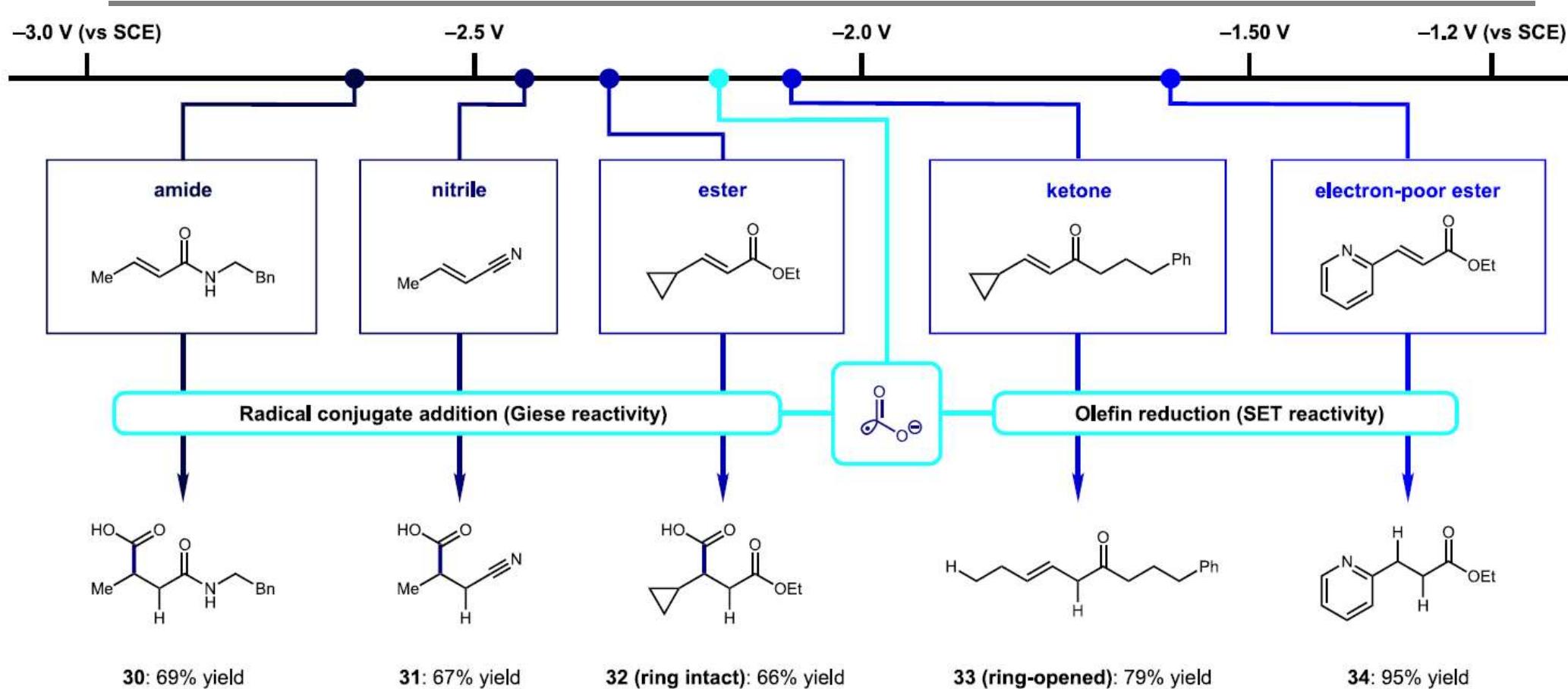
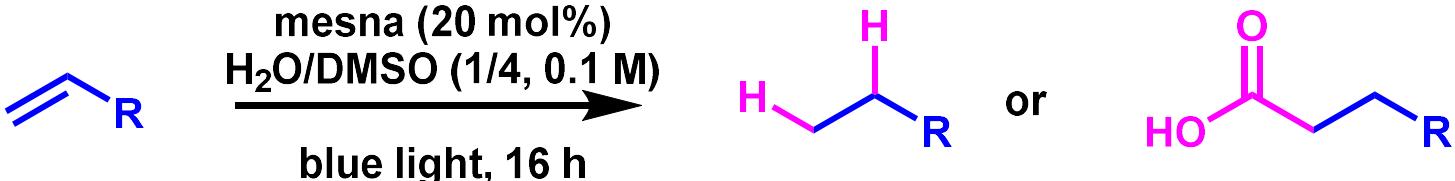


Proposed Mechanism



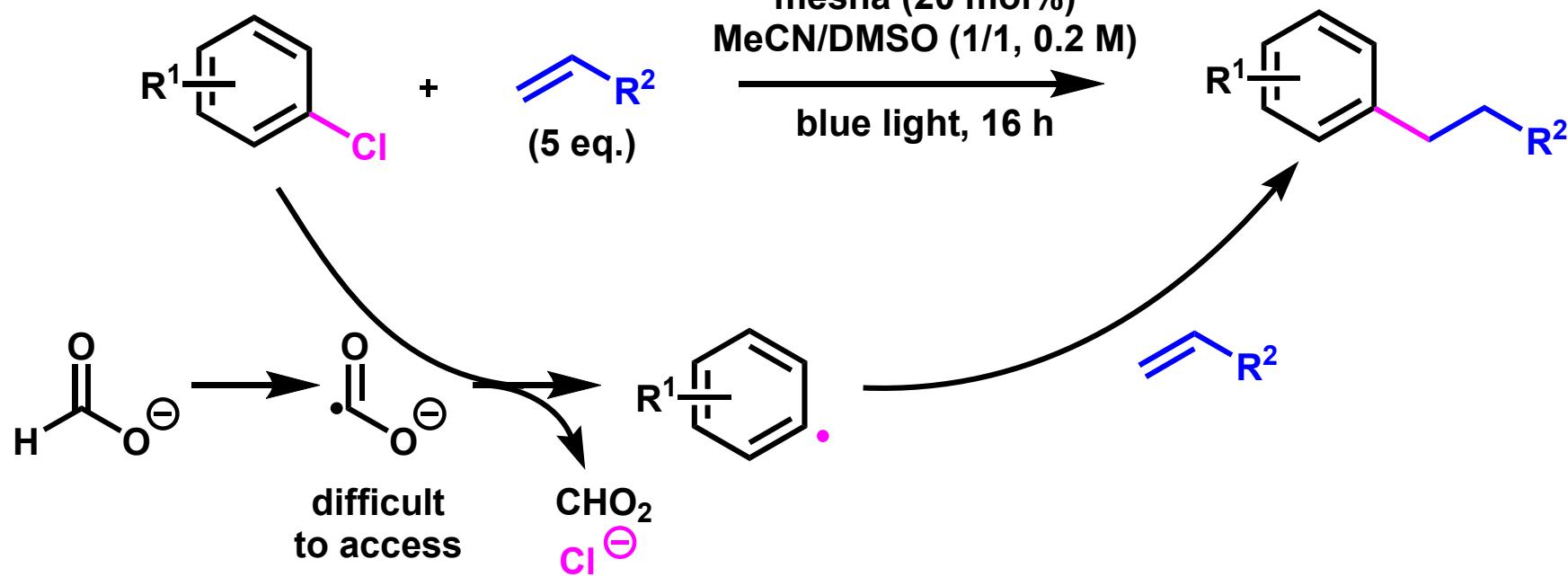
Carbon Dioxide Radical Anion as C1 unit

4CzIPN (1 mol%)
 HCO_2Na (5 eq.)
 HCO_2H (5 eq.)
mesna (20 mol%)
 $\text{H}_2\text{O}/\text{DMSO}$ (1/4, 0.1 M)
blue light, 16 h



Summary

As powerful reductant



As C1 unit

