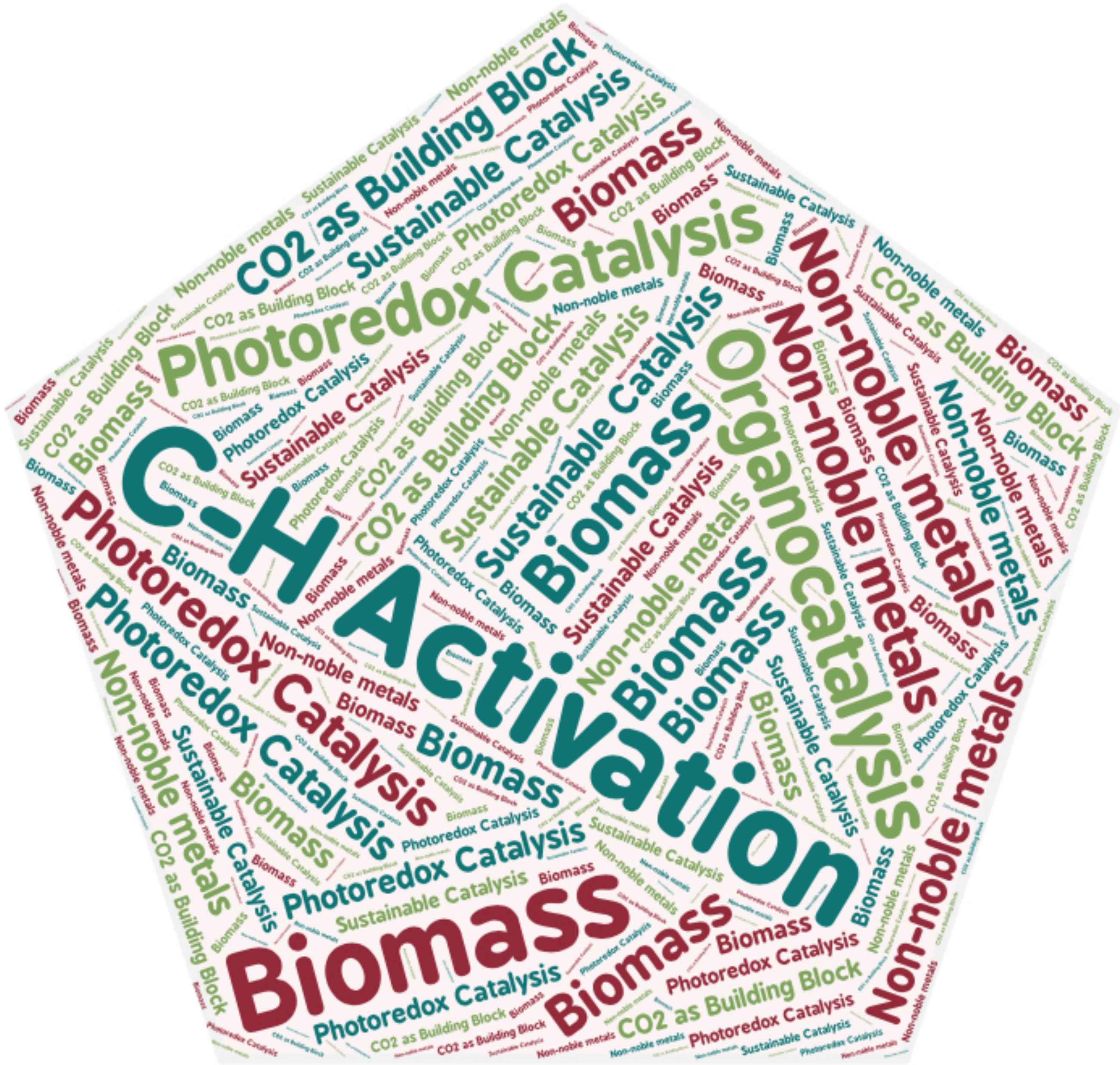
SCM1 „SYNTHESECHEMIE“
Aktuelle katalytische Synthesemethoden
Teil 2: Photoredoxkatalyse

Jun.-Prof. Dr. Ivana Fleischer

Fridays 8.15-9.45

WiSe

„Modern (Homogeneous) Catalysis?“



Outline

I. C-H Activation

II. Photoredox Catalysis

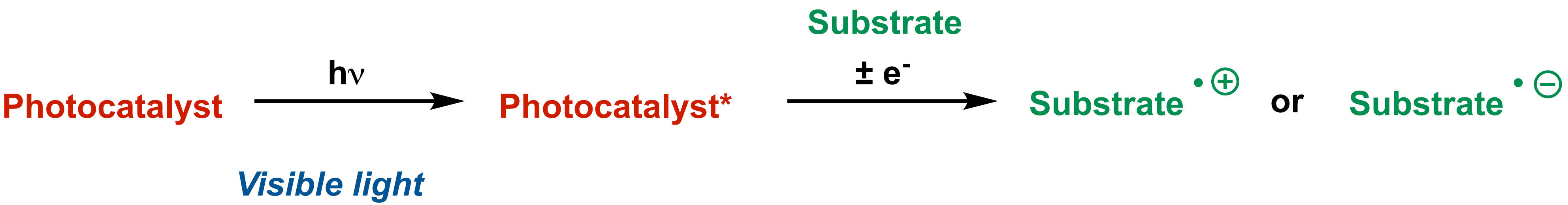
2. Introduction

- **Which reactions promoted by light do you know?**

2. Introduction

2.1. What is it?

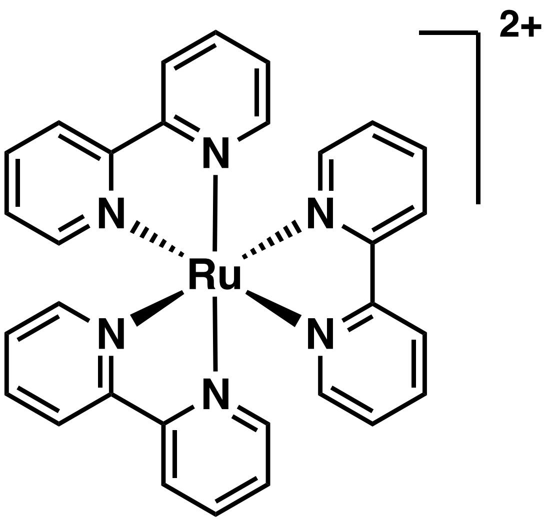
- **Photoredox catalysis:**
  - the energy of light accelerates a chemical reaction
  - the catalyst is a light-sensitive compound that after excitation mediates the transfer of electrons (SET = single electron trenasfer) between chemical compounds that otherwise would react more slowly or not at all.
  - visible light is usually used



2. Introduction

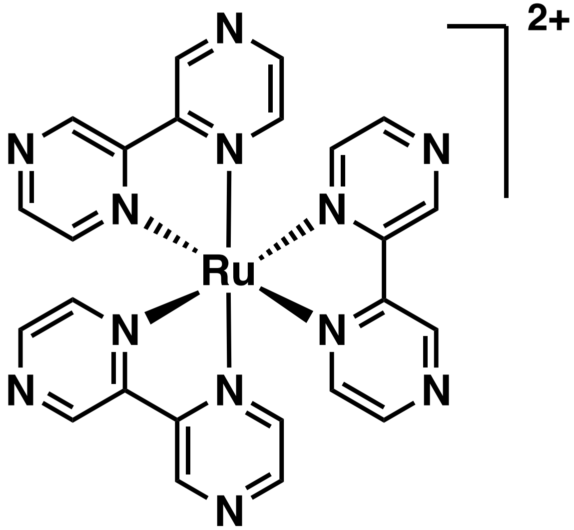
2.1. What is it?

- **Typical catalysts:**



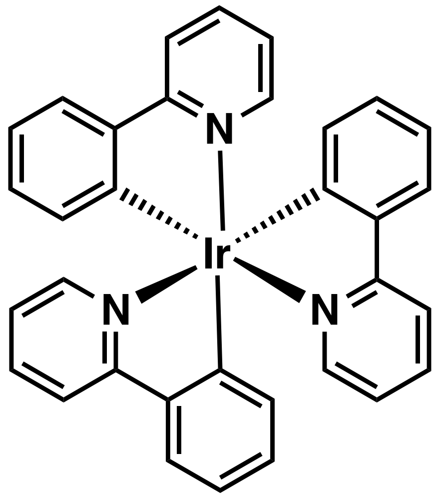
Ru(bpy)$_3$(II)

$E_{1/2}$ (M^+/M^*) = -0.81
$E_{1/2}$ (M^*/M^-) = +0.77
$E_{1/2}$ (M^+/M) = +1.29
$E_{1/2}$ (M/M^-) = -1.33



Ru(bpz)$_3$(II)

$E_{1/2}$ (M^+/M^*) = -0.26
$E_{1/2}$ (M^*/M^-) = +1.45
$E_{1/2}$ (M^+/M) = +1.86
$E_{1/2}$ (M/M^-) = -0.80



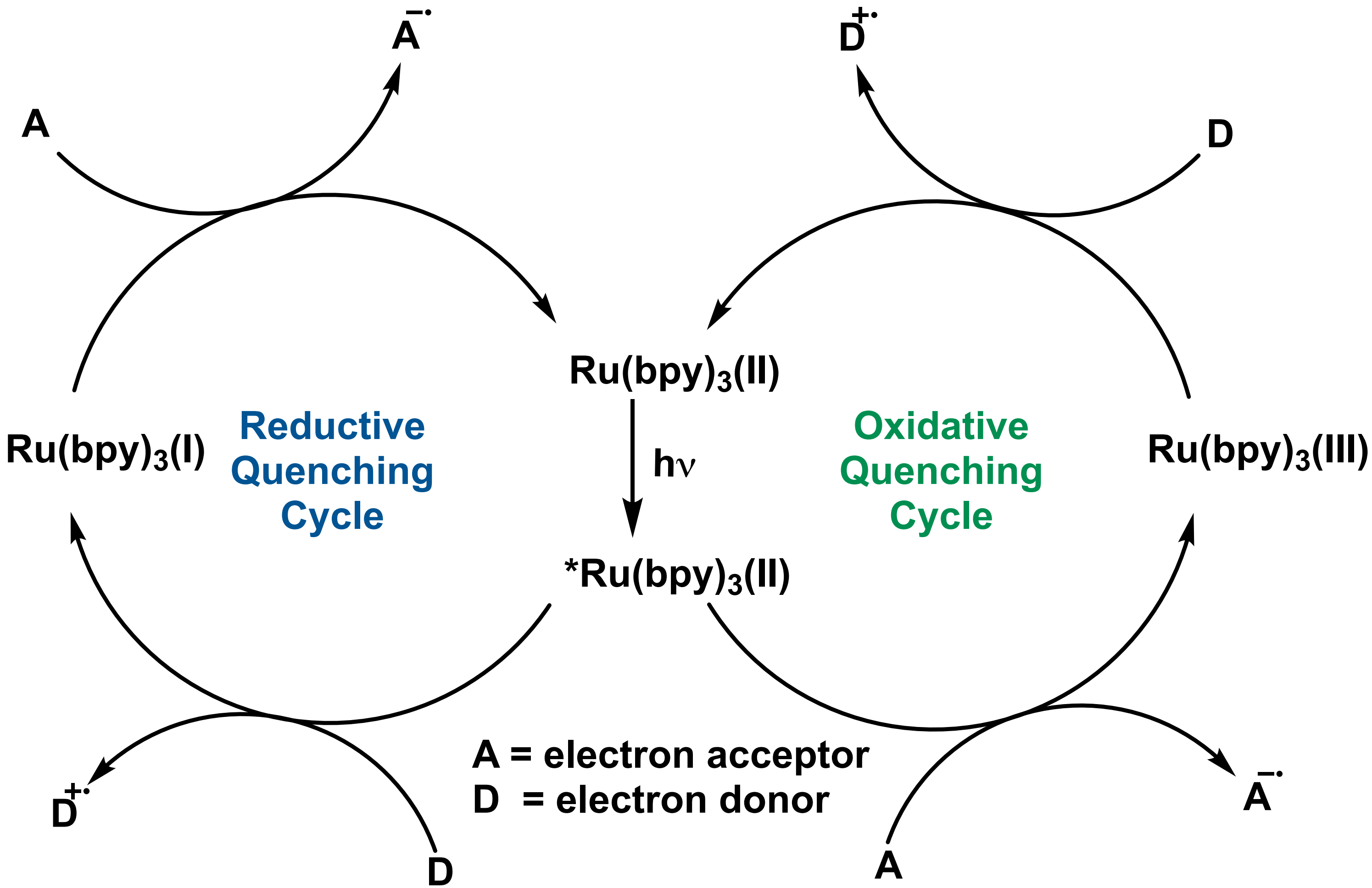
Ir(ppy)$_3$(III)

$E_{1/2}$ (M^+/M^*) = -1.73
$E_{1/2}$ (M^*/M^-) = +0.31
$E_{1/2}$ (M^+/M) = +0.77
$E_{1/2}$ (M/M^-) = -2.19

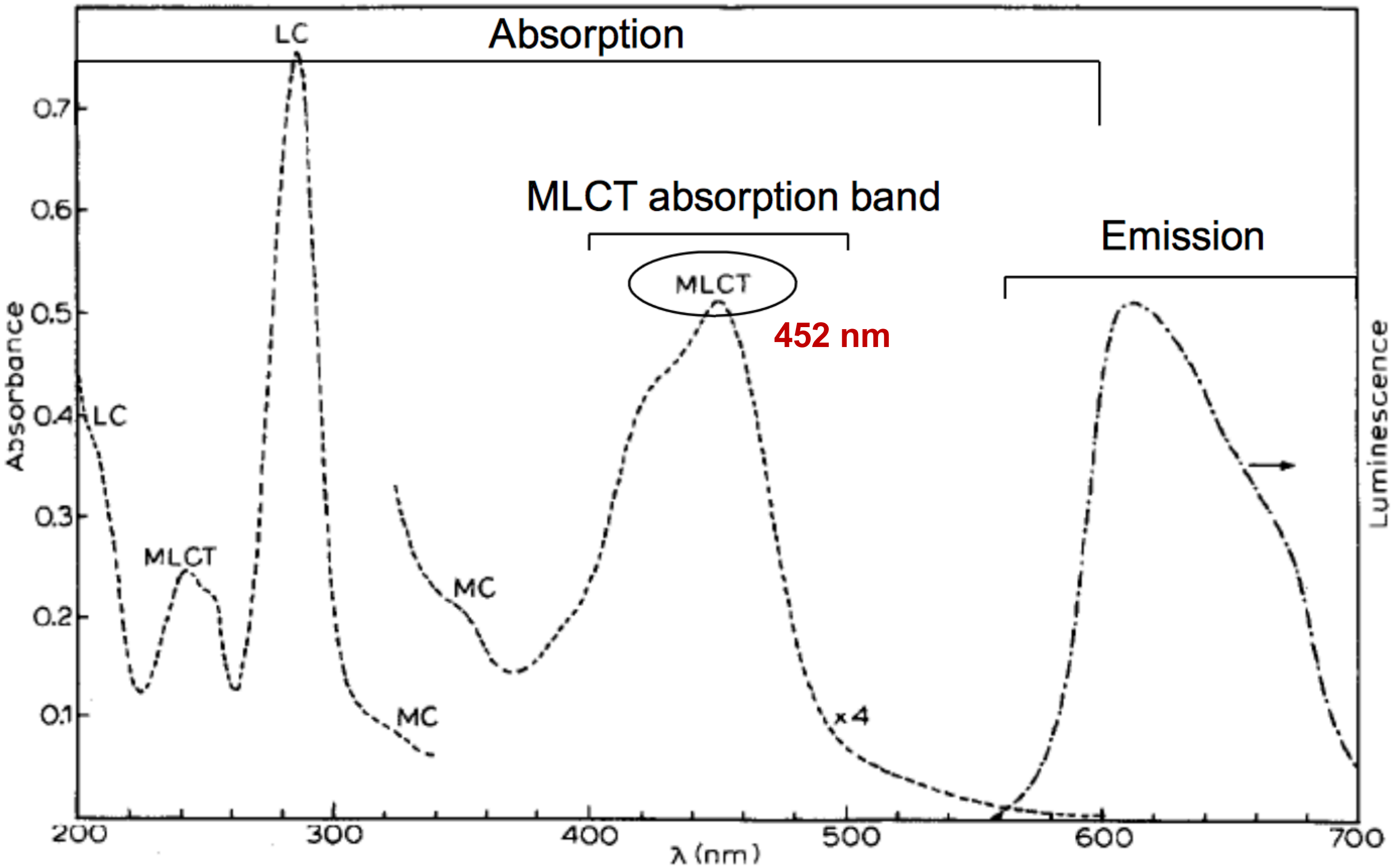
- absorption of visible light (452 nm for Ru(bpy)$_3$(II))
- stable, long lived excited state (τ = 1100 ns for Ru(bpy)$_3$(II))
- powerful oxidants and reductants in excited state

- **Redox potential: what was it again?**

- **Typical catalytic cycles:**



- **Ru(bpy)$_3$(II):**
  - absorption and emission spectrum:



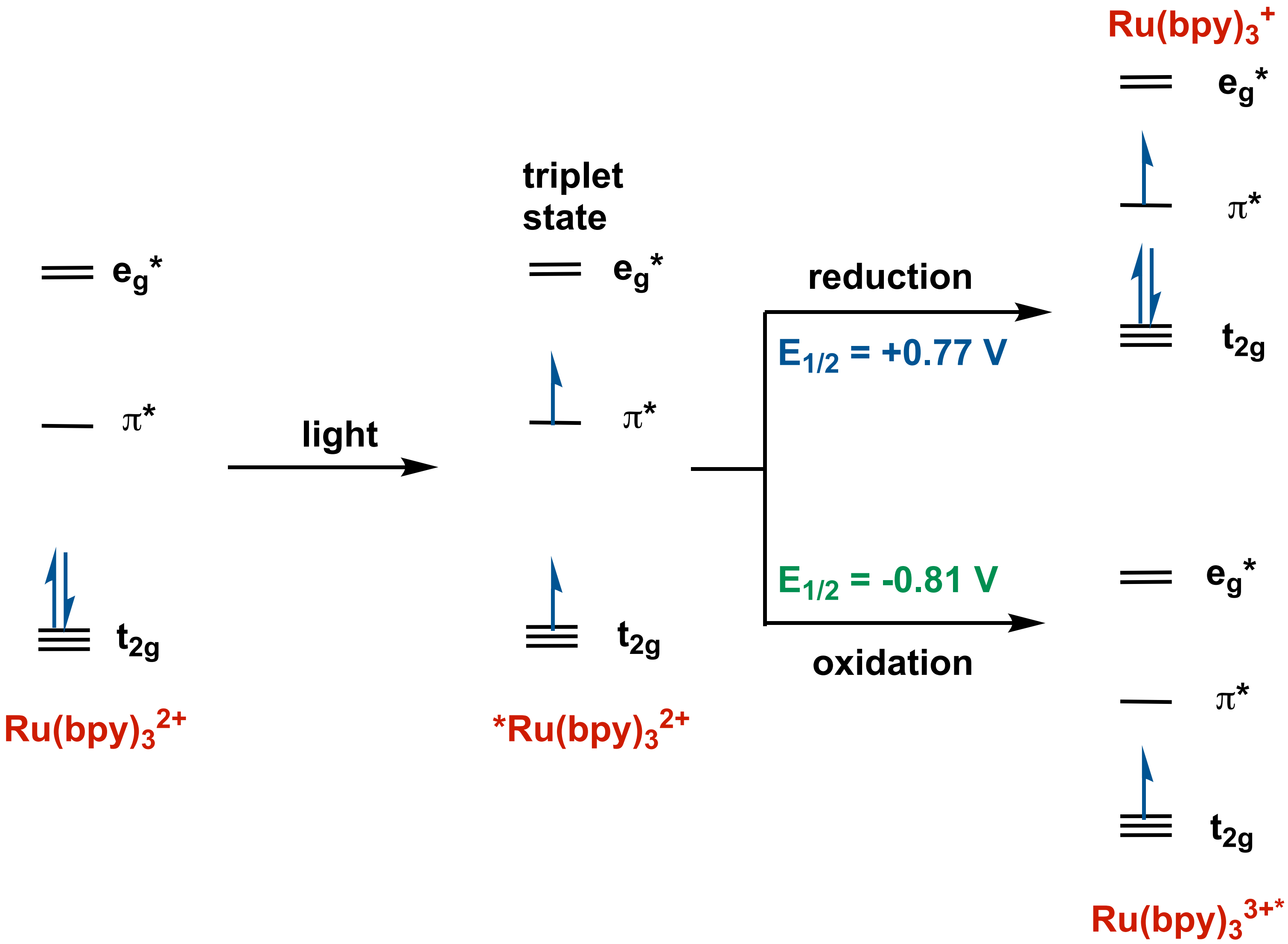
From: A.J. Bard et al., *J. Am. Chem. Soc.* **1973**, *95*, 6582.

MLCT = metal-to-ligand charge transfer

$$Ru(bpy)_3^{2+} \xrightarrow[\text{MLCT}]{h\nu} Ru(bpy)_3^{2+*}$$

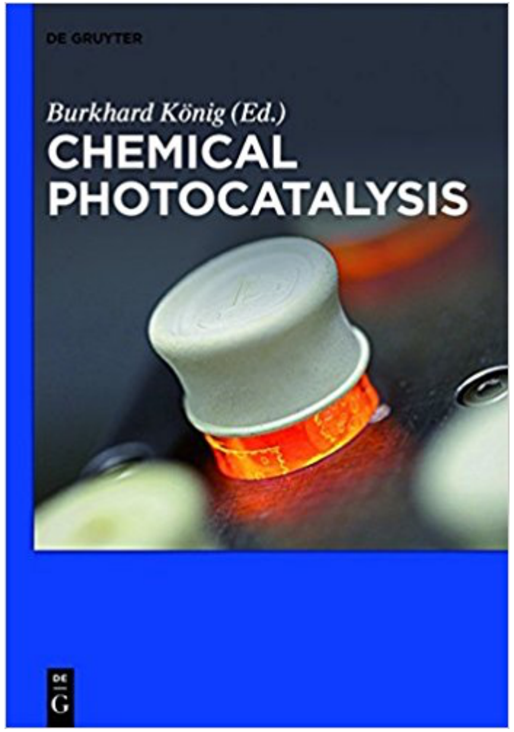
2. Introduction

- **$Ru(bpy)_3(II)$:**
  - Orbitals (simplified):



- Reviews:

(a) J. M. R. Narayanam, C. R. J. Stephenson, *Chem. Soc. Rev.* **2011**, *40*, 102-113.
(b) J. Xuan, W. J. Xiao, *Angew. Chem. Int. Ed.* **2012**, *51*, 6828-6838.
(c) C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev.* **2013**, *113*, 5322-5363.
(d) M. Reckenthaler, A. G. Griesbeck, *Adv. Synth. Catal.* **2013**, *355*, 2727-2744.
(e) D. M. Arias-Rotondo, J. K. McCusker, *Chem. Soc. Rev.* **2016**, *45*, 5803-5820.
(f) J. P. Goddard, C. Ollivier, L. Fensterbank, *Acc. Chem. Res.* **2016**, *49*, 1924-1936.
(g) M. Majek, A. Jacobi von Wangelin, *Acc. Chem. Res.* **2016**, *49*, 2316-2327.
(h) N. A. Romero, D. A. Nicewicz, *Chem. Rev.* **2016**, *116*, 10075-10166.
(i) T. P. Yoon, *Acc. Chem. Res.* **2016**, *49*, 2307-2315.



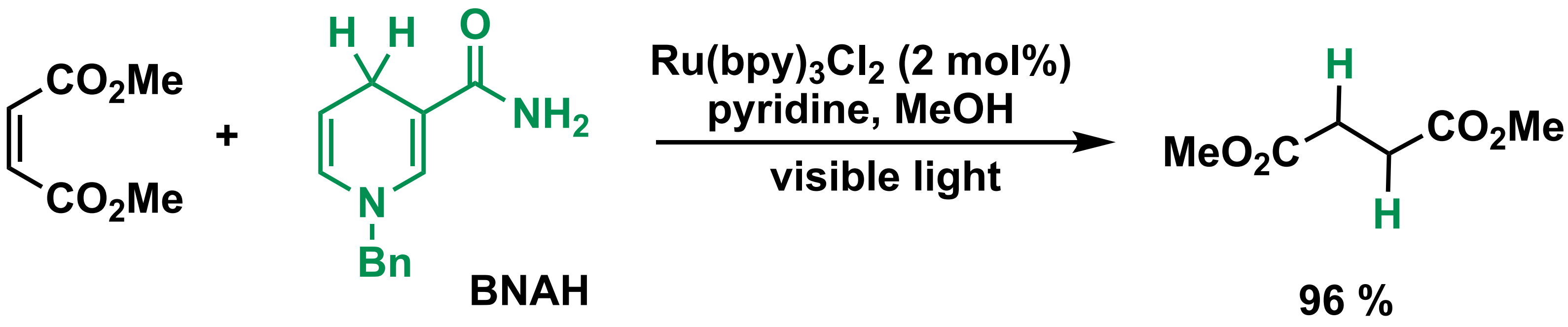
Chemical Photocatalysis

B. König (Ed.), **2013**

ISBN 978-3-11-026916-1

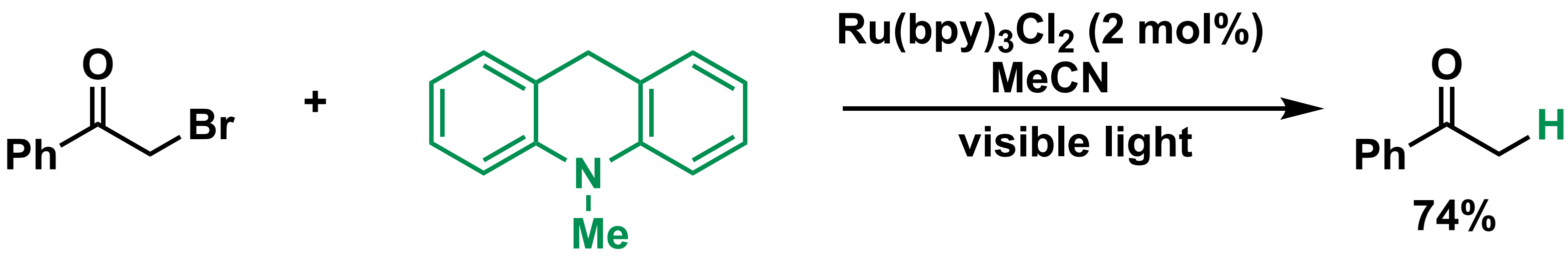
a) Early works:

Reduction of electron-deficient alkenes



C. Pac, M. Ihama, M. Yasuda, Y. Miyauchi, H. Sakurai, *J. Am. Chem. Soc.* **1981**, *103*, 6495-6497.

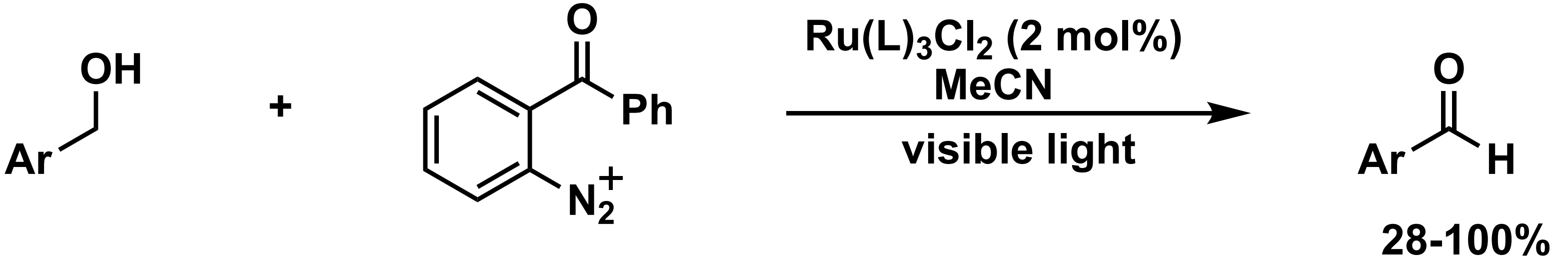
Reductive dehalogenation



S. Fukuzumi, S. Mochizuki, T. Tanaka, *J. Phys. Chem.* **1990**, *94*, 722-726.

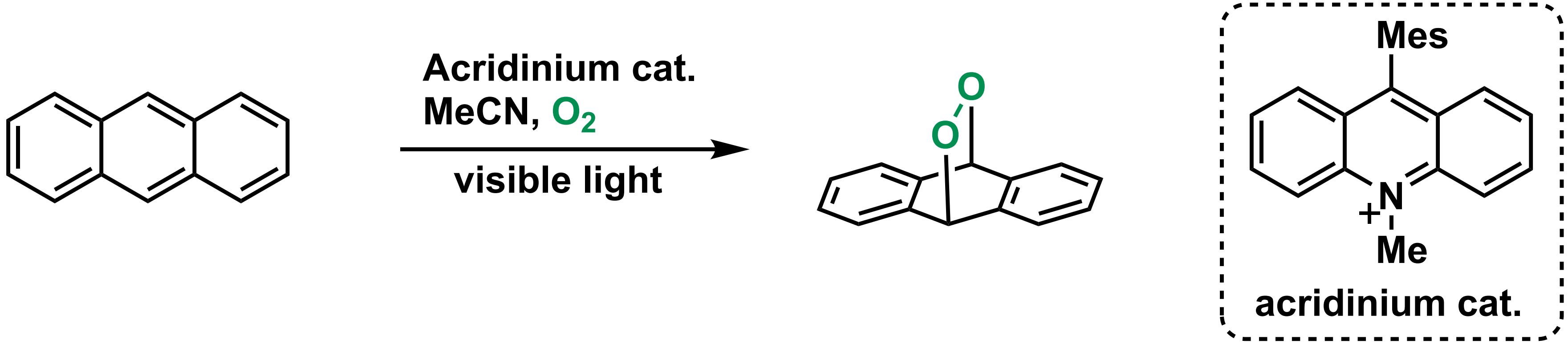
a) Early works:

Photocatalytic oxidation



H. Cano-Yelo, A. Deronzier, *Tetrahedron Lett.* **1984**, *25*, 5517-5520.

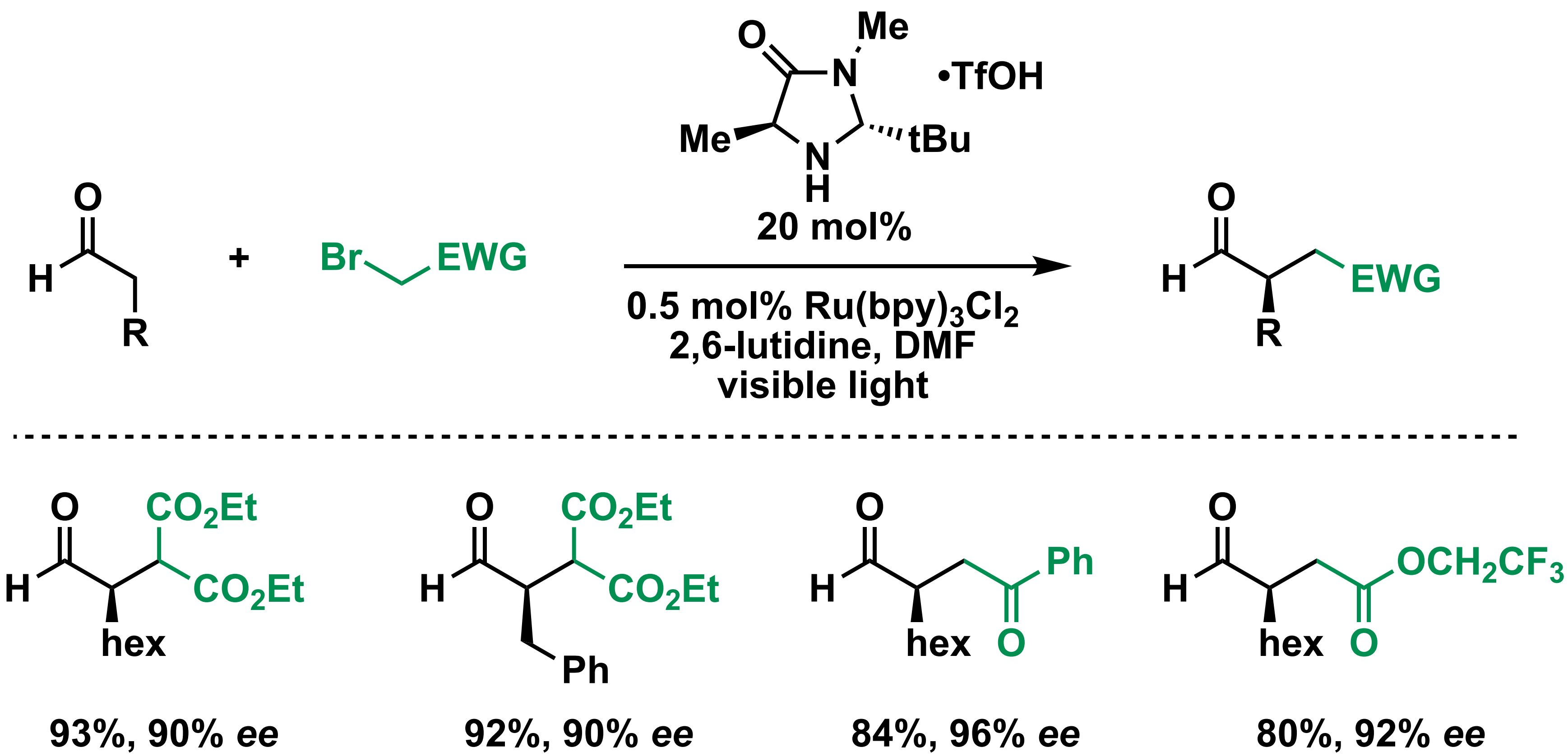
Cycloaddition of oxygen



H. Kotani, K. Ohkubo, S. Fukuzumi, *J. Am. Chem. Soc.* **2004**, *126*, 15999-16006.

b) Seminal works:

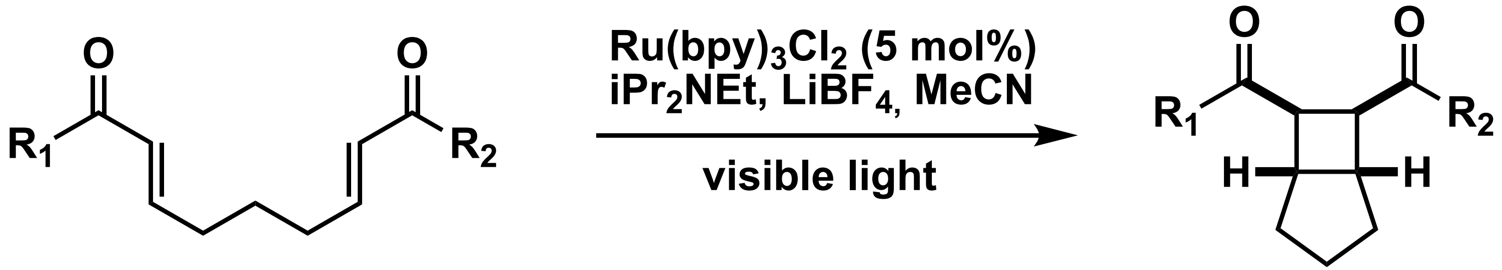
Combination of photo- and organocatalysis

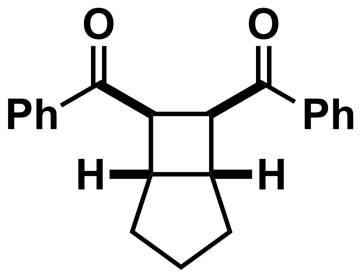


D. A. Nicewicz, D. W. C. MacMillan, *Science* **2008**, *322*, 77-80.

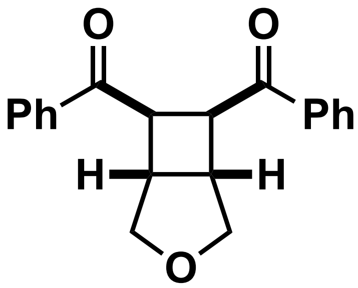
b) Seminal works:

Intramolecular [2+2] cycloaddition

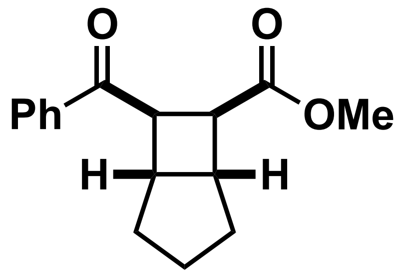




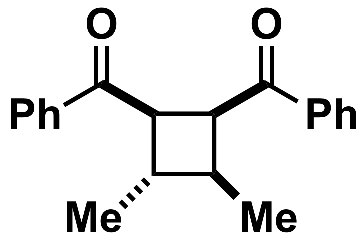
89%, >10:1 d.r.



90%, 5:1 d.r.



88%, >10:1 d.r.

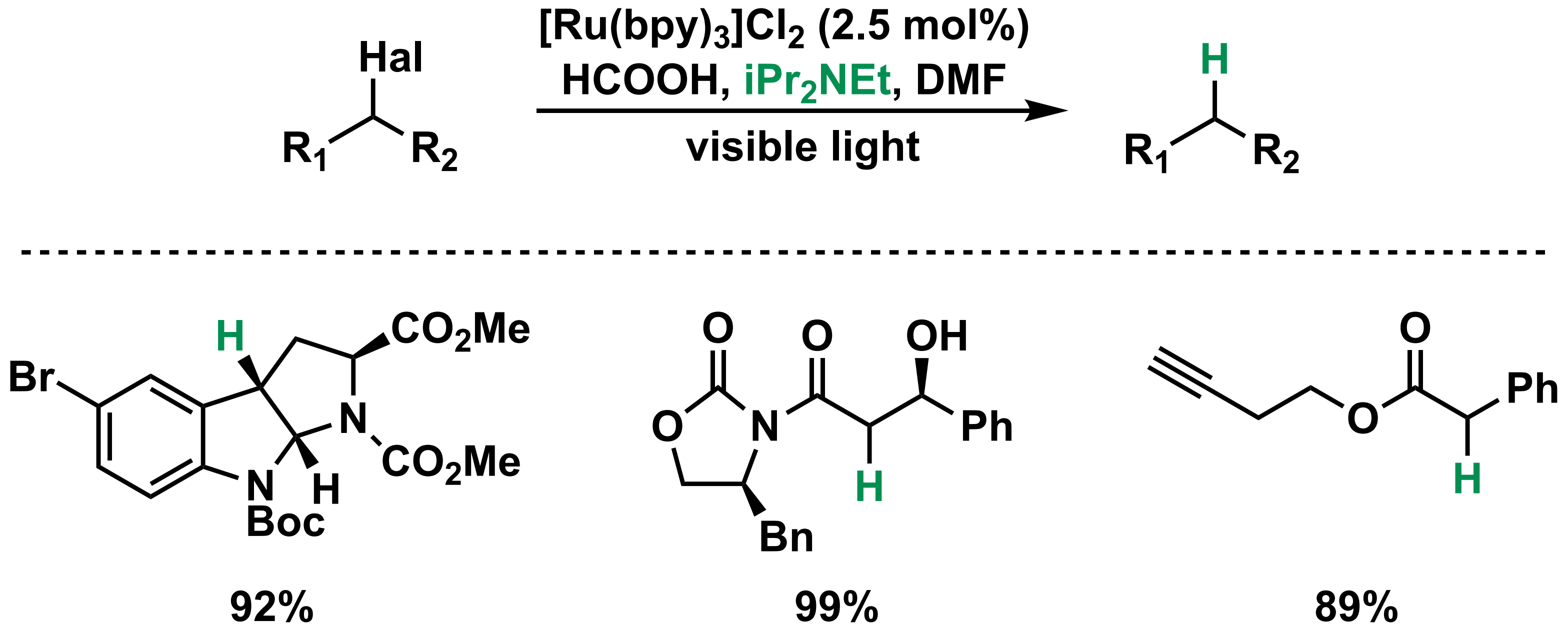


82%, >10:1 d.r.

M. A. Ischay, M. E. Anzovino, J. Du, T. P. Yoon, *J. Am. Chem. Soc.* **2008**, *130*, 12886-12887.

b) Seminal works:

Reductive dehalogenation



J. M. R. Narayanam, J. W. Tucker, C. R. J. Stephenson, *J. Am. Chem. Soc.* **2009**, *131*, 8756-8757.

D. W. C. MacMillan

T. Yoon

C. Stephenson

R. Knowles

From Germany…

B. König

T. Bach

A. Griesbeck

K. Zeitler

D. Niciewicz

P. Melchiorre

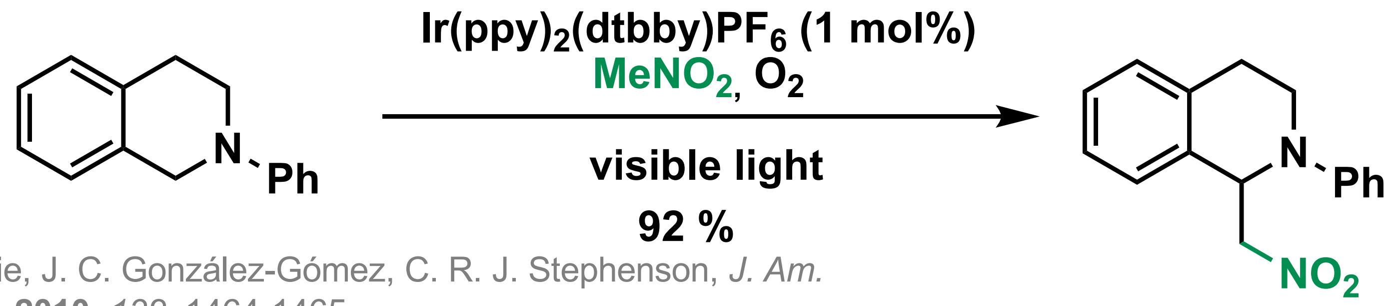
L. Fensterbank

W. Xiao

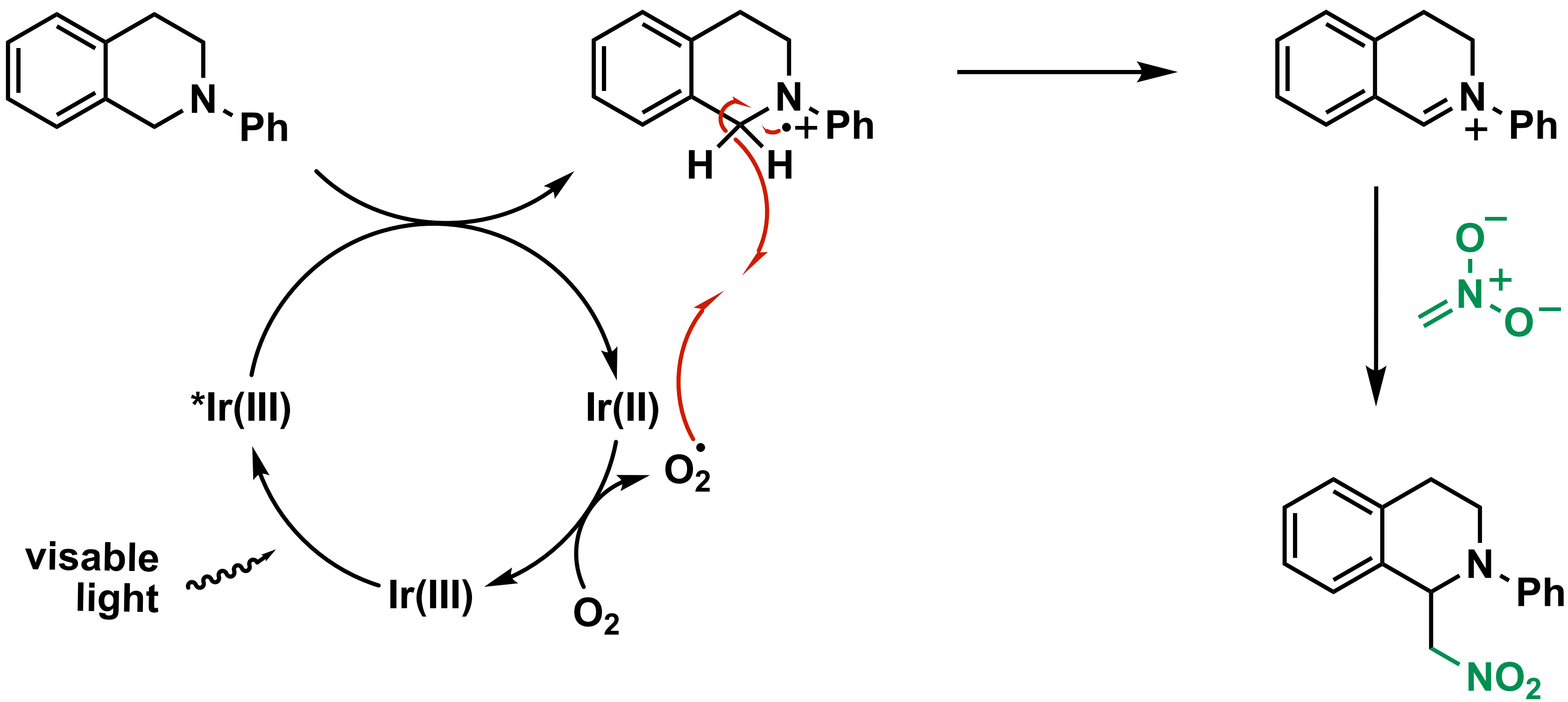
and many more ……

2.1.1. Formation and functionalization of iminium ions

Photoredox aza-Henry reaction

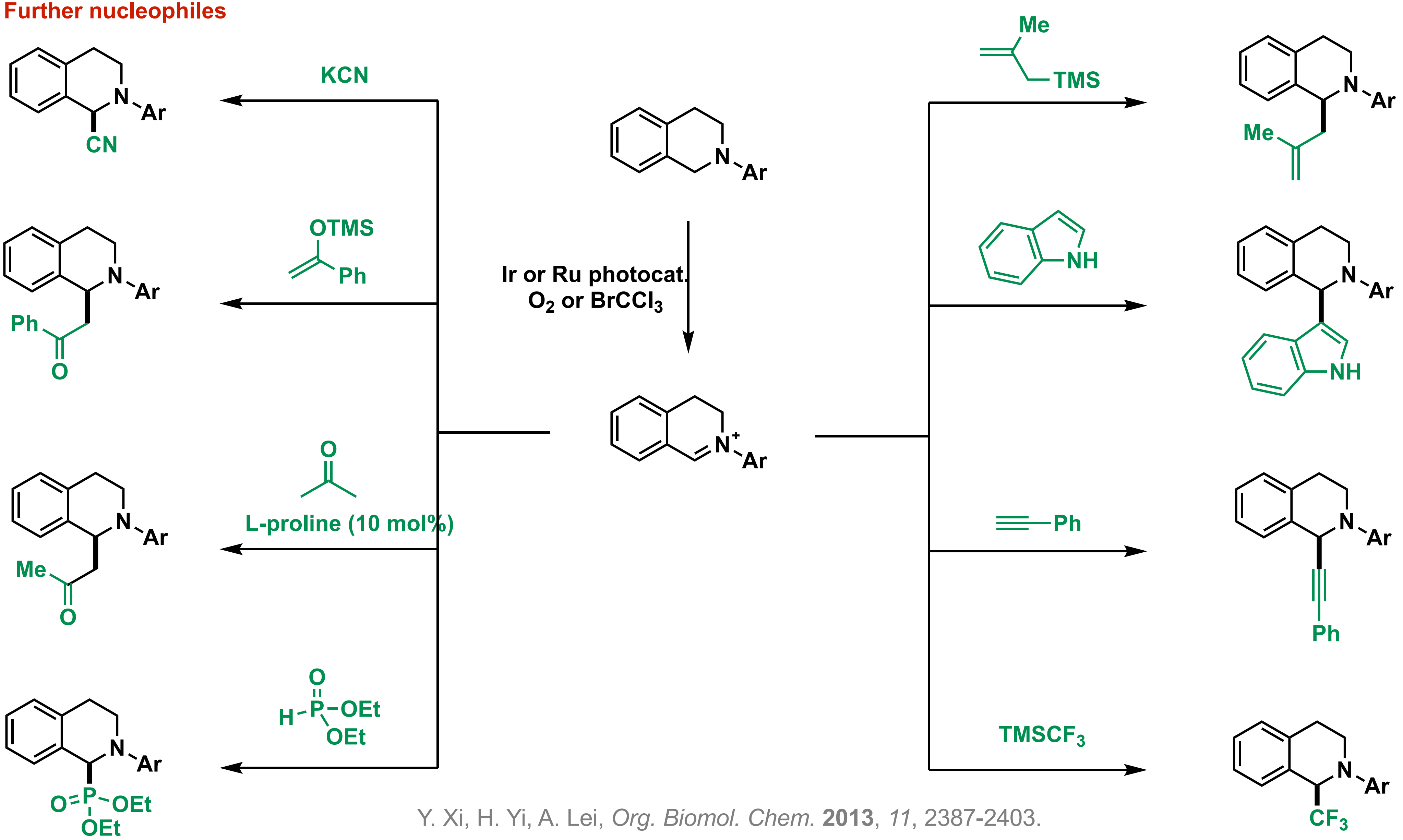


A. G. Condie, J. C. González-Gómez, C. R. J. Stephenson, *J. Am. Chem. Soc.* **2010**, *132*, 1464-1465.



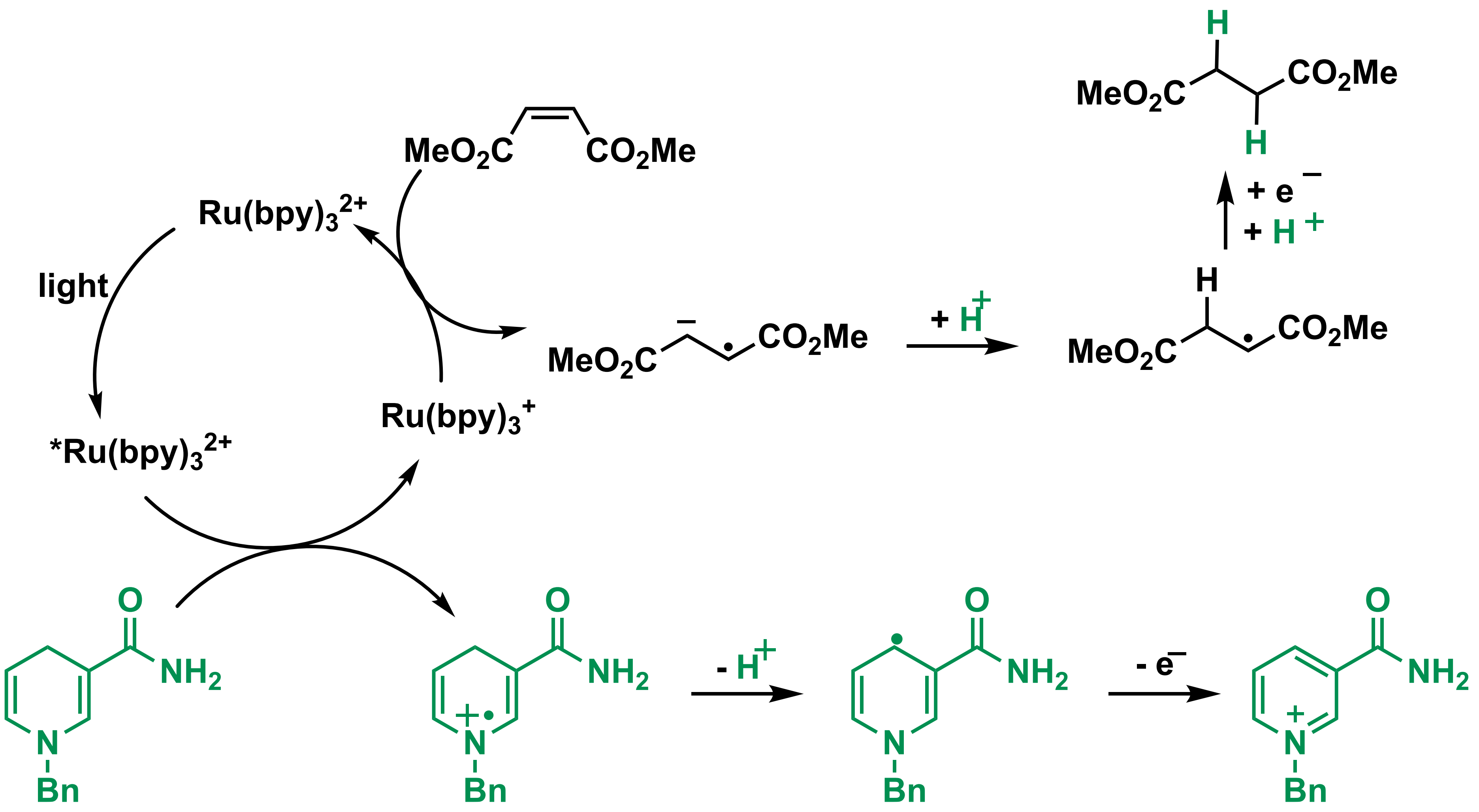
2.1.1. Formation and functionalization of iminium ions

Further nucleophiles



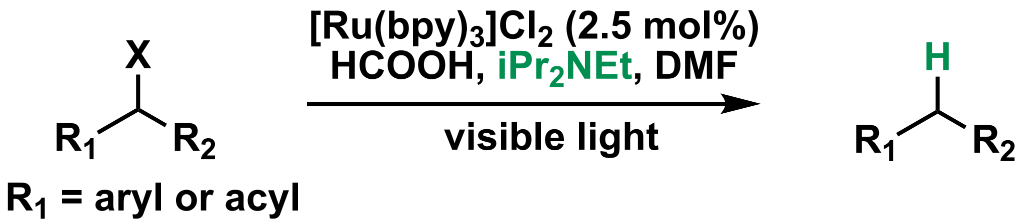
Y. Xi, H. Yi, A. Lei, *Org. Biomol. Chem.* **2013**, *11*, 2387-2403.

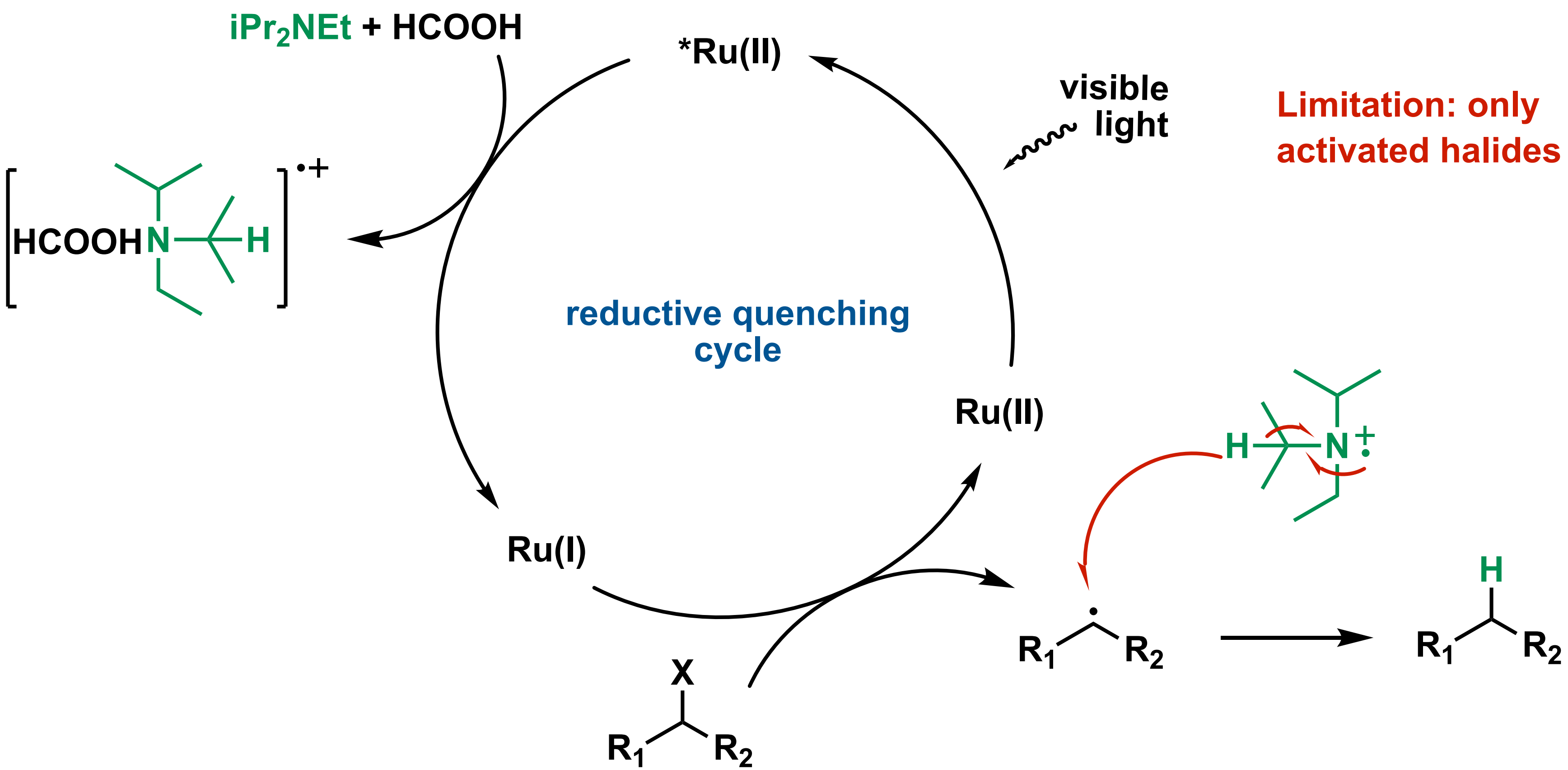
2.2.1. Alkene reduction



C. Pac, M. Ihama, M. Yasuda, Y. Miyauchi, H. Sakurai, *J. Am. Chem. Soc.* **1981**, *103*, 6495-6497.

2.2.2. Reductive dehalogenation



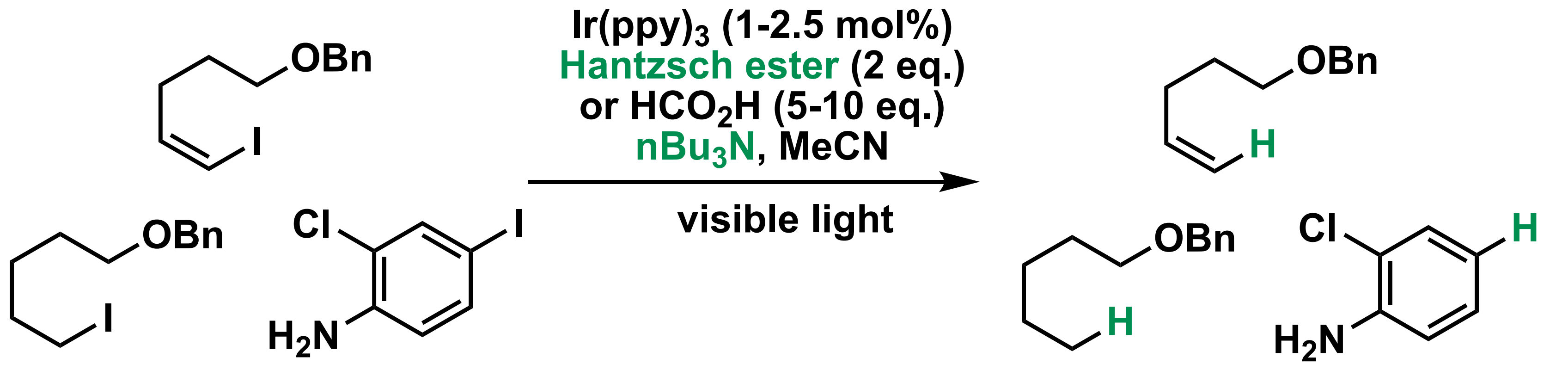


Limitation: only activated halides

J. M. R. Narayanam, J. W. Tucker, C. R. J. Stephenson, *J. Am. Chem. Soc.* **2009**, *131*, 8756-8757.

2.2.2. Reductive dehalogenation

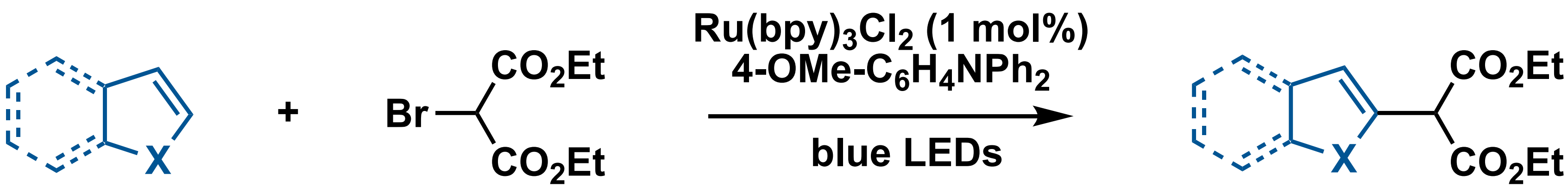
Dehalogenation of unactivated halides



Ir-catalyst has greater reduction potential!!!

J. D. Nguyen, E. M. D'Amato, J. M. R. Narayanam, C. R. J. Stephenson, *Nature Chemistry* **2012**, *4*, 854.

Combination with C-C bond formation



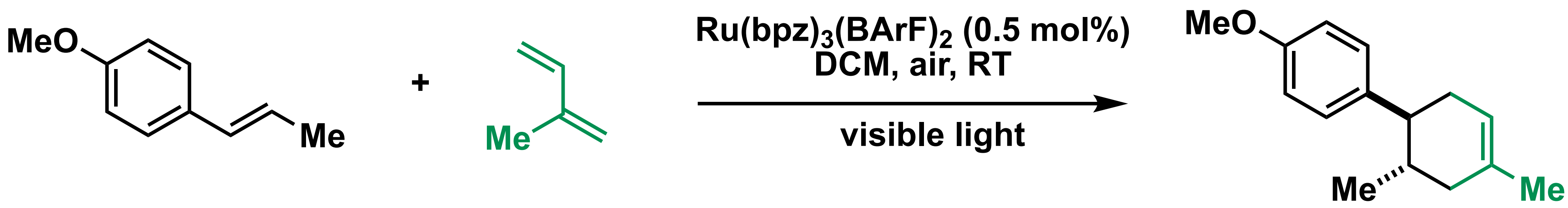
67-91%

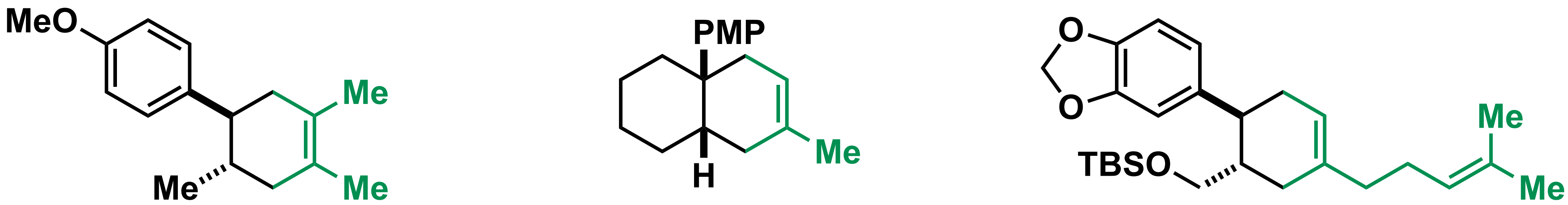
J. W. Tucker, J. M. R. Narayanam, S. W. Krabbe, C. R. J. Stephenson, *Org. Lett.* **2010**, *12*, 368-371.

- The substrates participate in both the reductive and oxidative steps of the photocatalytic cycle, with no change to the overall oxidation state from starting materials to product
- The ability to have both oxidation and reduction processes occurring simultaneously for one overall reaction can enable reaction pathways that would otherwise not be possible

2.3.1. Cycloadditions

Diels-Alder reaction: two electron-rich partners

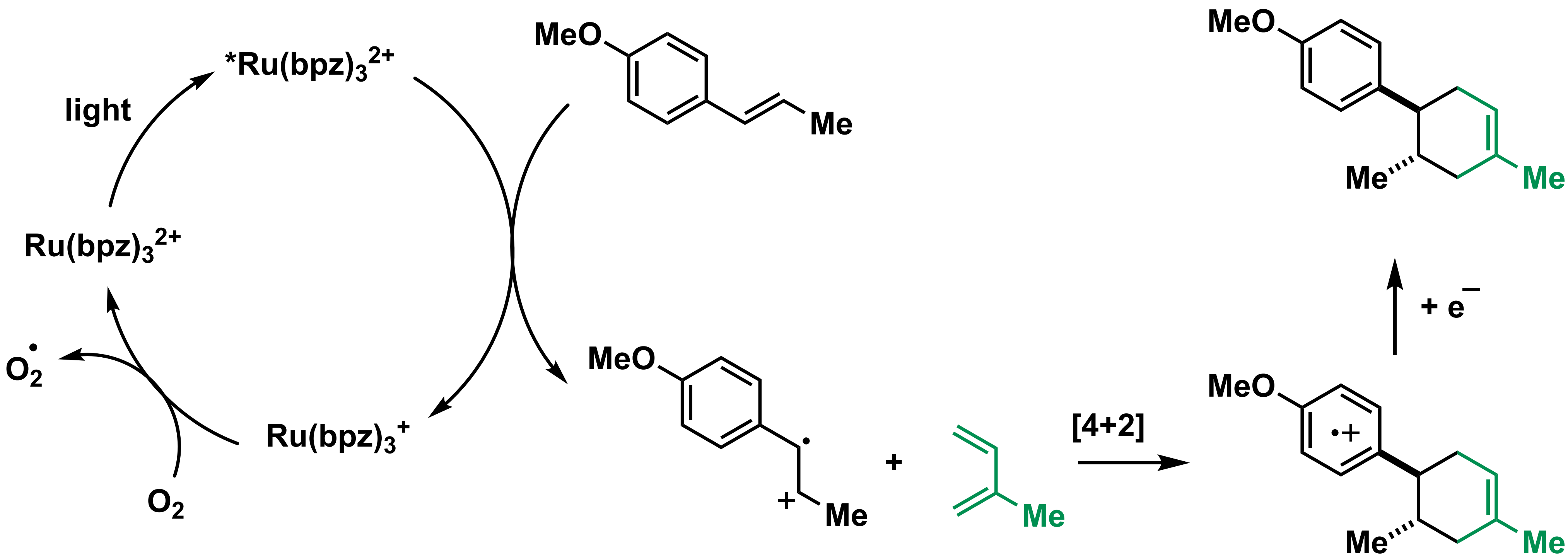




98 % | **92 %** | **80%**

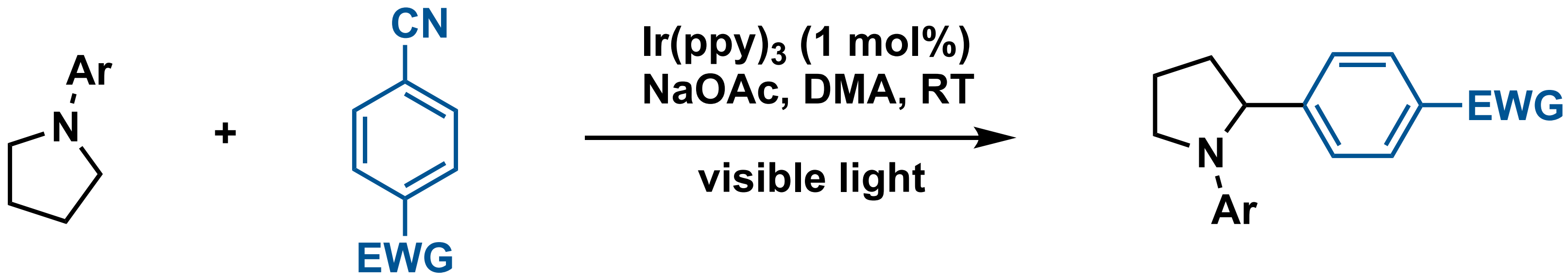
S. Lin, M. A. Ischay, C. G. Fry, T. P. Yoon, *J. Am. Chem. Soc.* **2011**, *133*, 19350-19353.

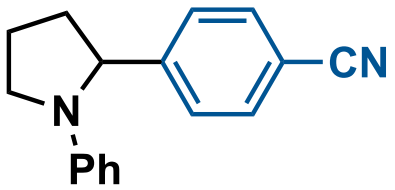
2.3.1. Cycloadditions



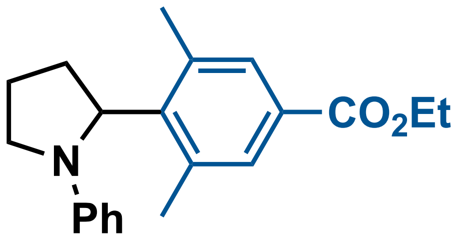
S. Lin, M. A. Ischay, C. G. Fry, T. P. Yoon, *J. Am. Chem. Soc.* **2011**, *133*, 19350-19353.

2.3.2. C-H arylation of amines

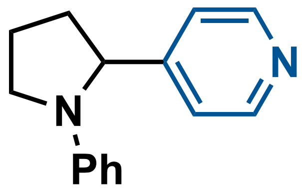




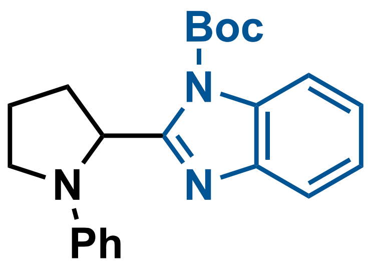
96 %



54 %



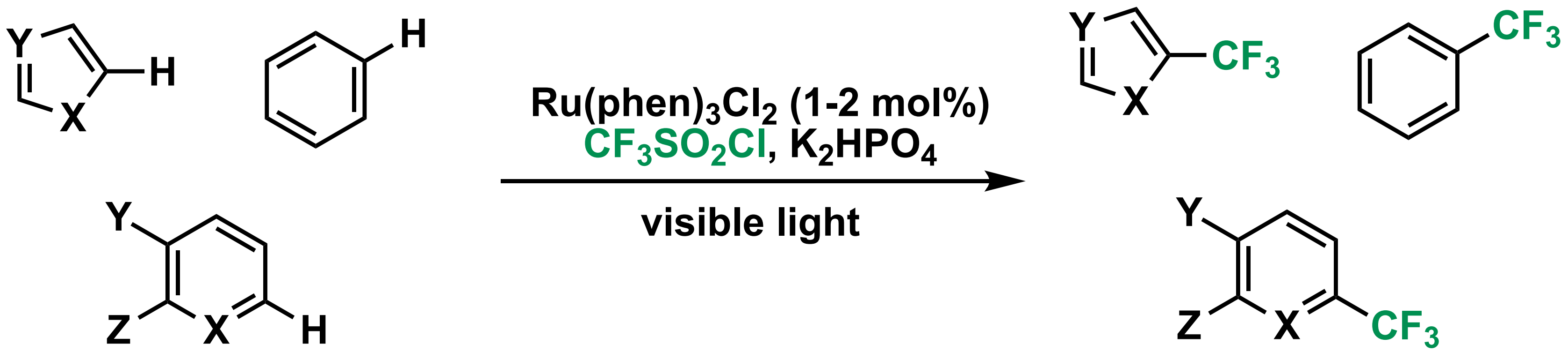
72 %



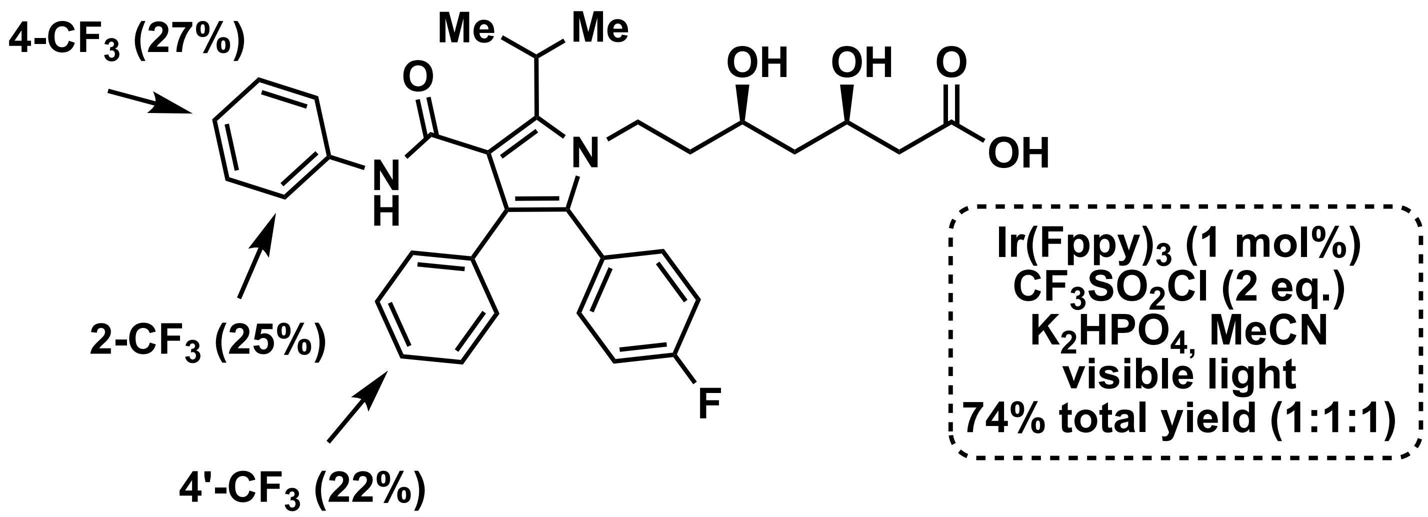
92 %

A. McNally, C. K. Prier, D. W. C. MacMillan, *Science* **2011**, *334*, 1114-1117.

2.3.3. Trifluoromethylation

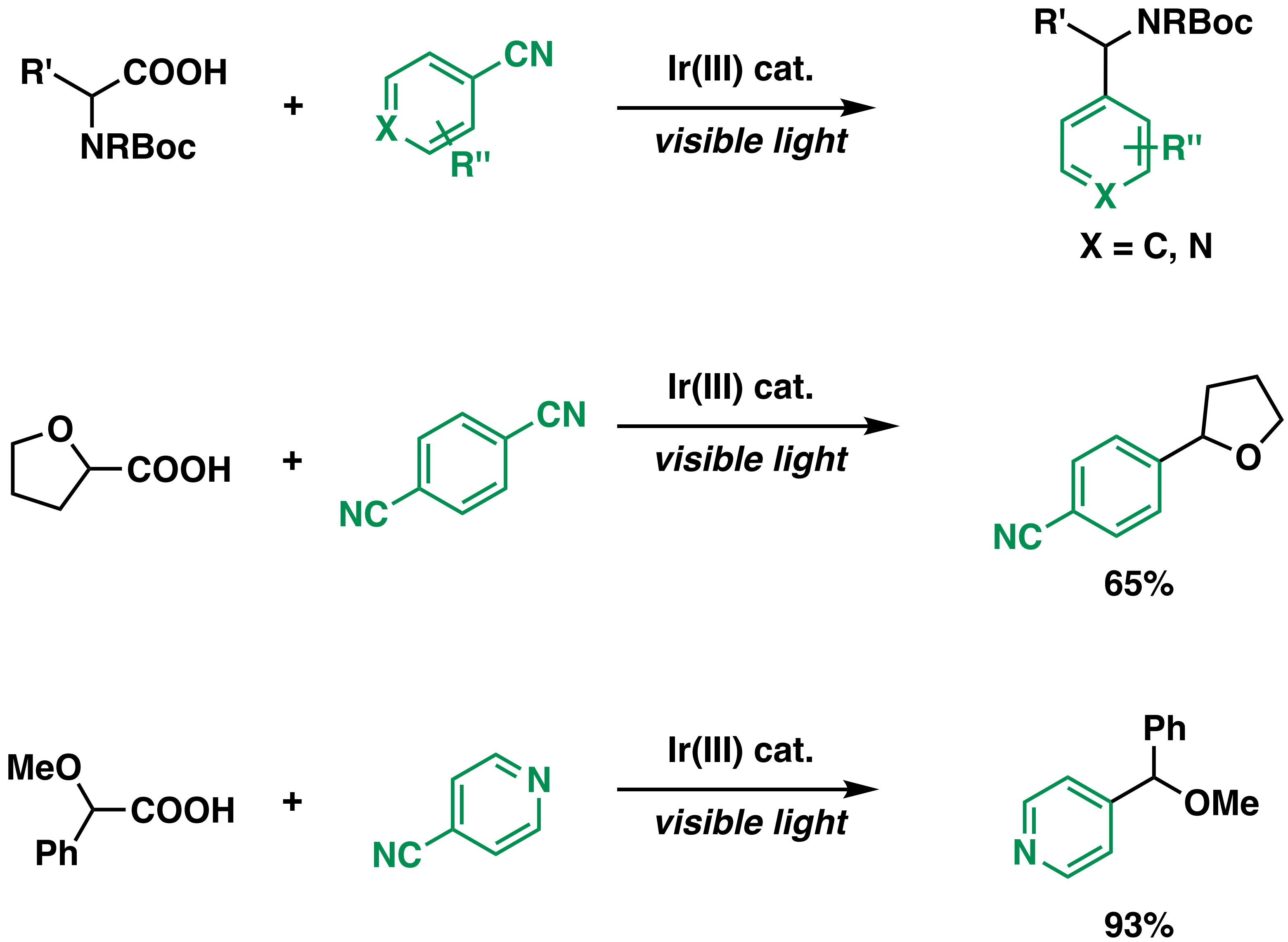


Trimethylfluoronation of Lipitor



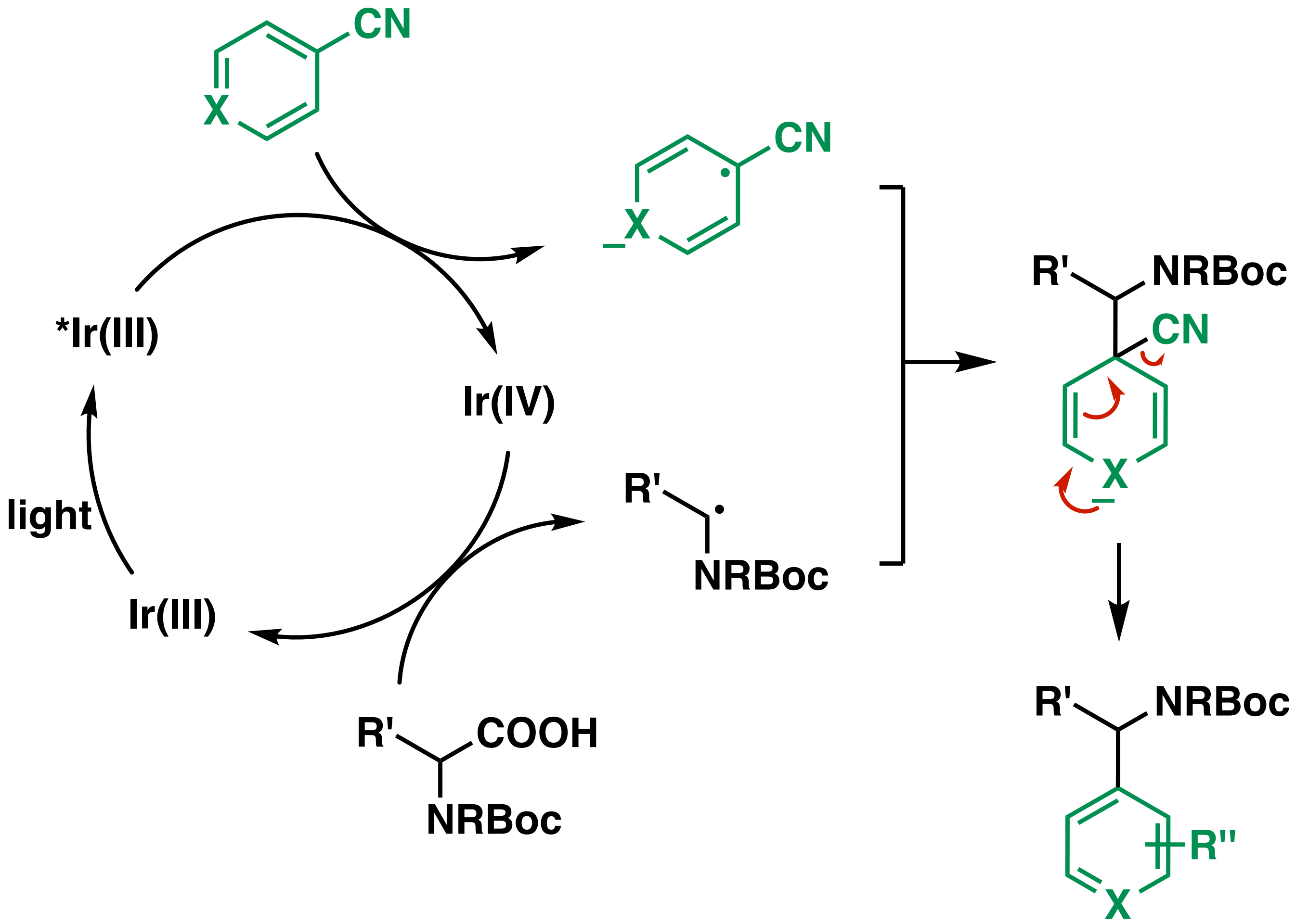
D. A. Nagib, D. W. C. MacMillan, *Nature* **2011**, *480*, 224.

2.3.4. Decarboxylative couplings



Z. Zuo, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2014**, *136*, 5257-5260.

2.3.4. Decarboxylative couplings

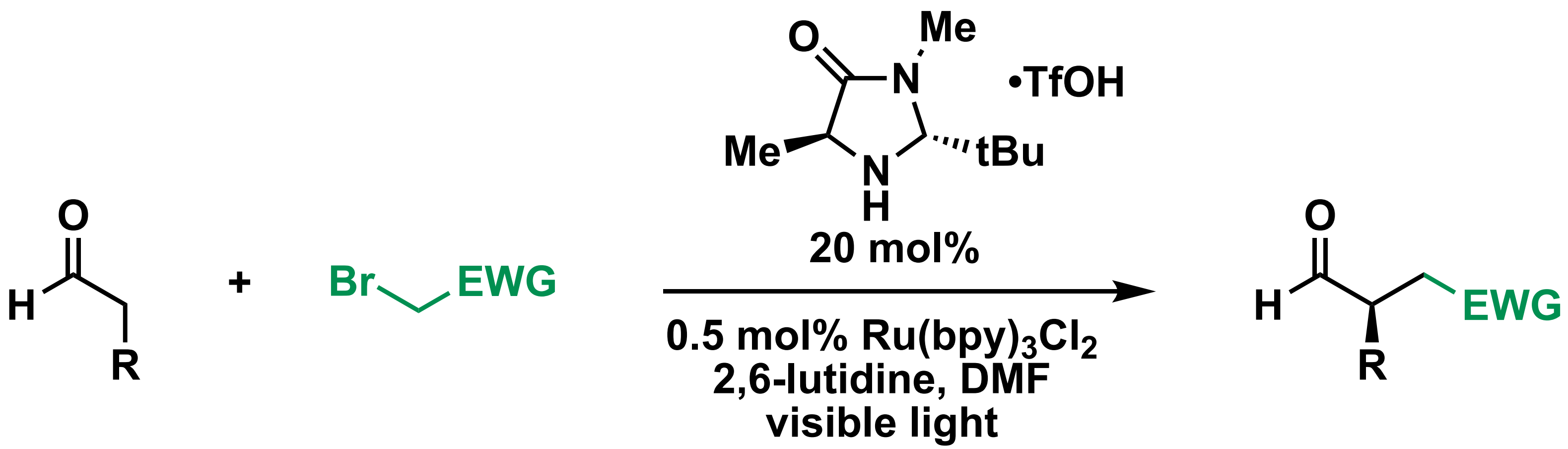


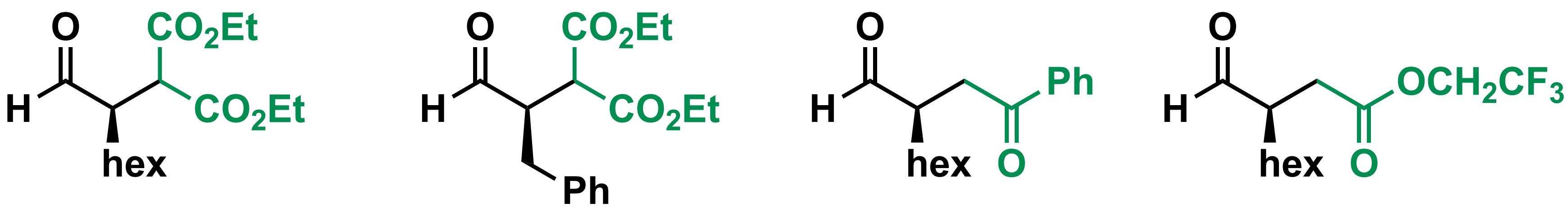
Z. Zuo, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2014**, *136*, 5257-5260.

2.4.1. Enamine catalysis

a) α-Functionalization

Combination of photo- and organocatalysis



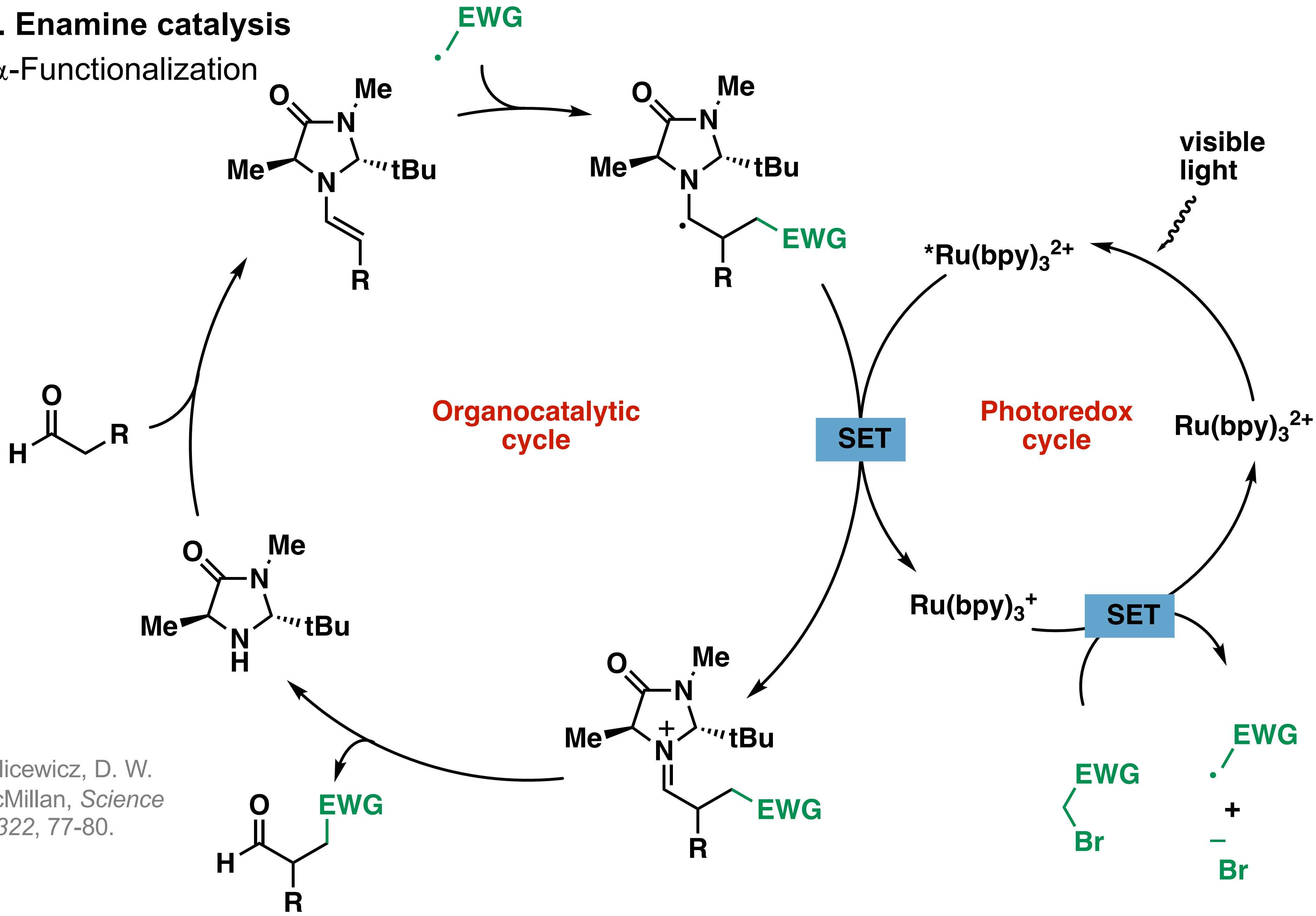


93%, 90% *ee*	92%, 90% *ee*	84%, 96% *ee*	80%, 92% *ee*

D. A. Nicewicz, D. W. C. MacMillan, *Science* **2008**, *322*, 77-80.

2.4.1. Enamine catalysis

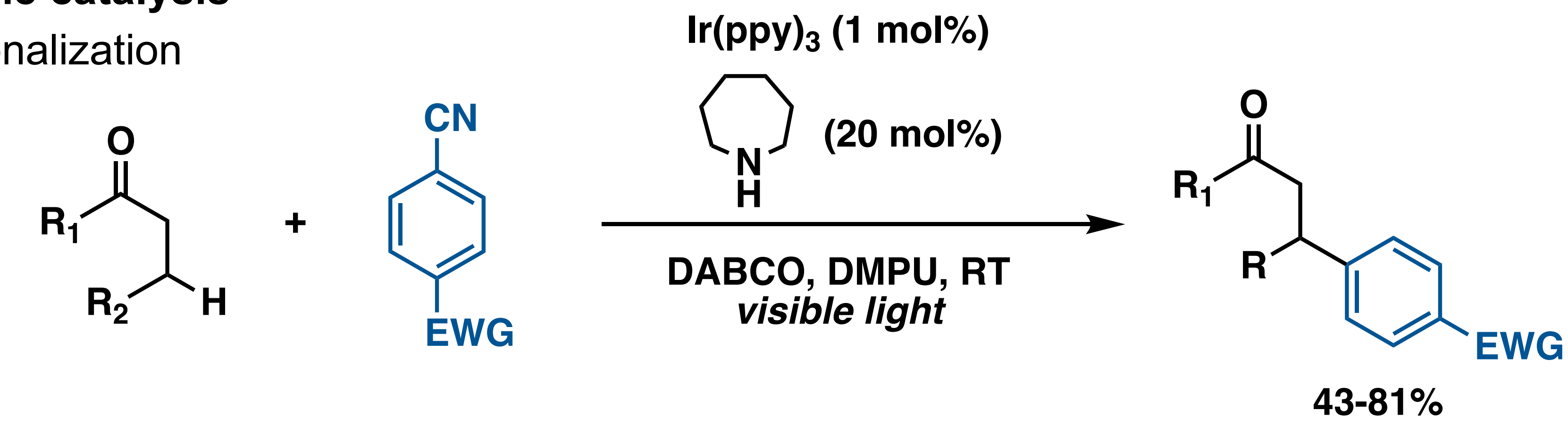
a) α-Functionalization

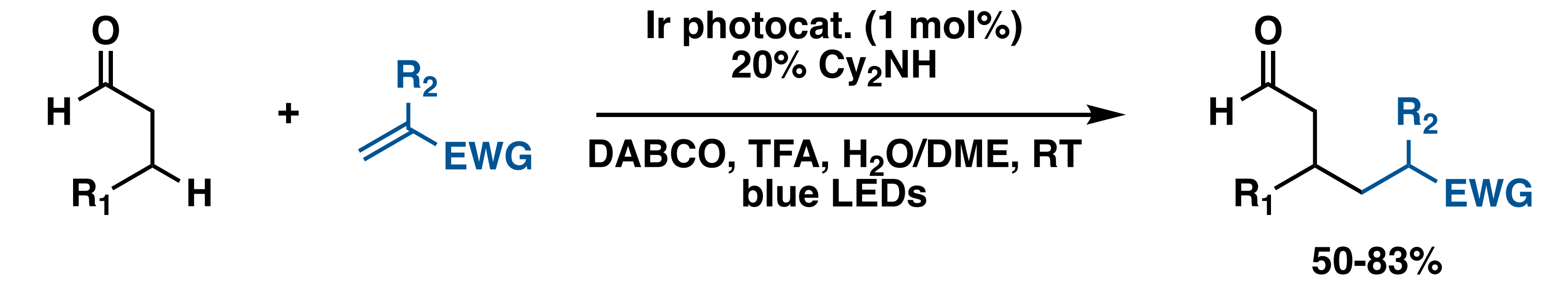


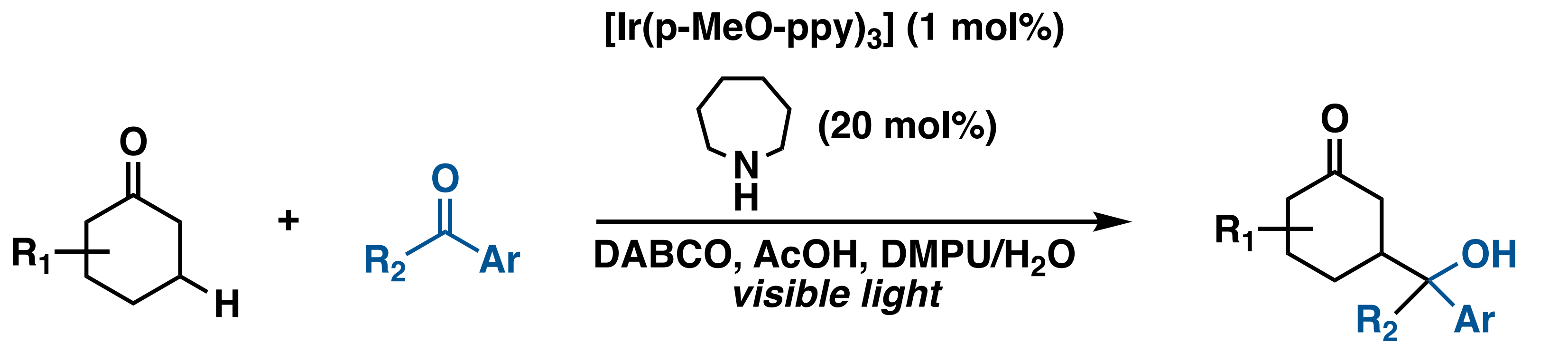
D. A. Nicewicz, D. W. C. MacMillan, *Science* **2008**, *322*, 77-80.

2.4.1. Enamine catalysis

b) β-Functionalization





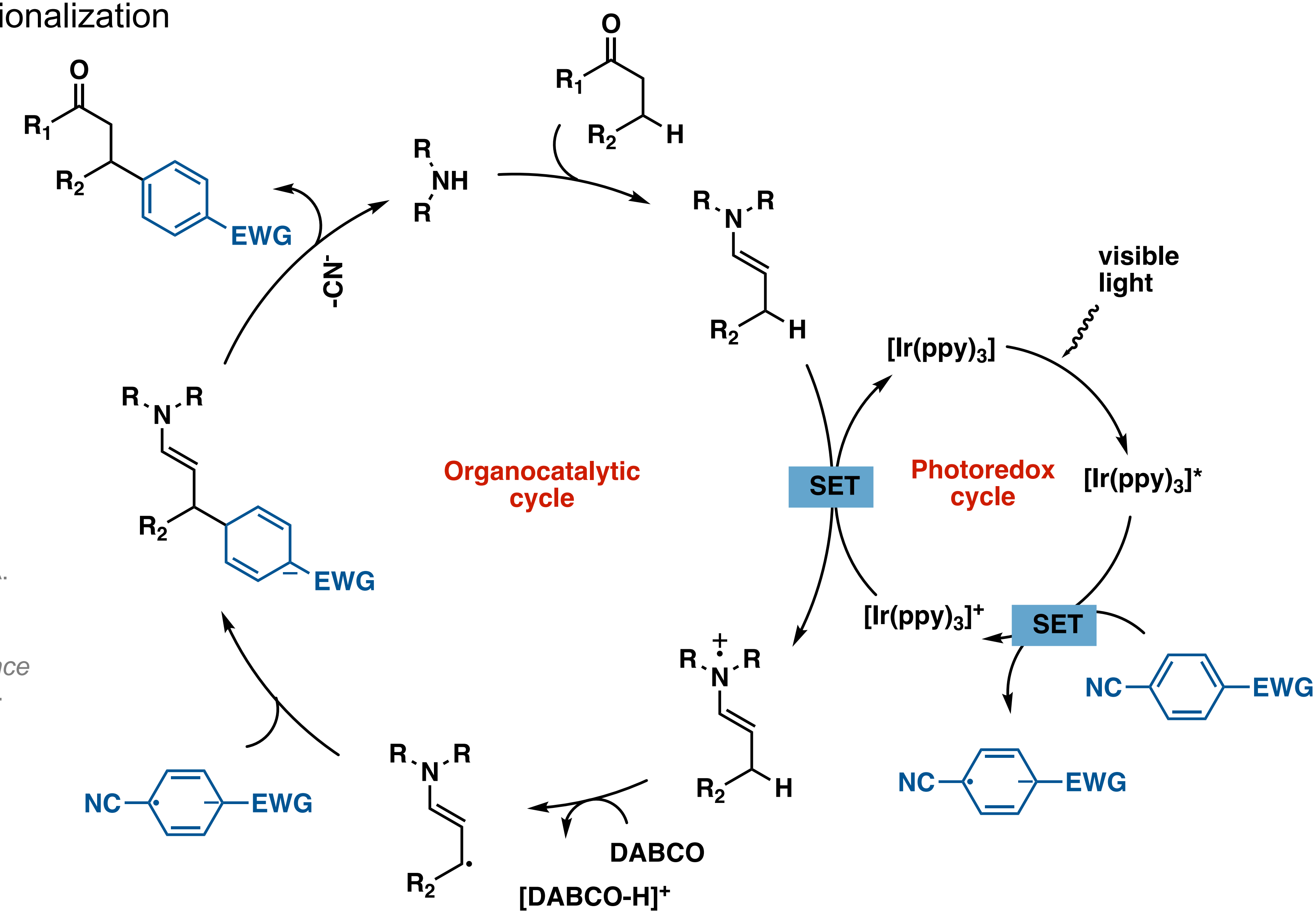


M. T. Pirnot, D. A. Rankic, D. B. C. Martin, D. W. C. MacMillan, *Science* **2013**, *339*, 1593-1596.

43-61%

2.4.1. Enamine catalysis

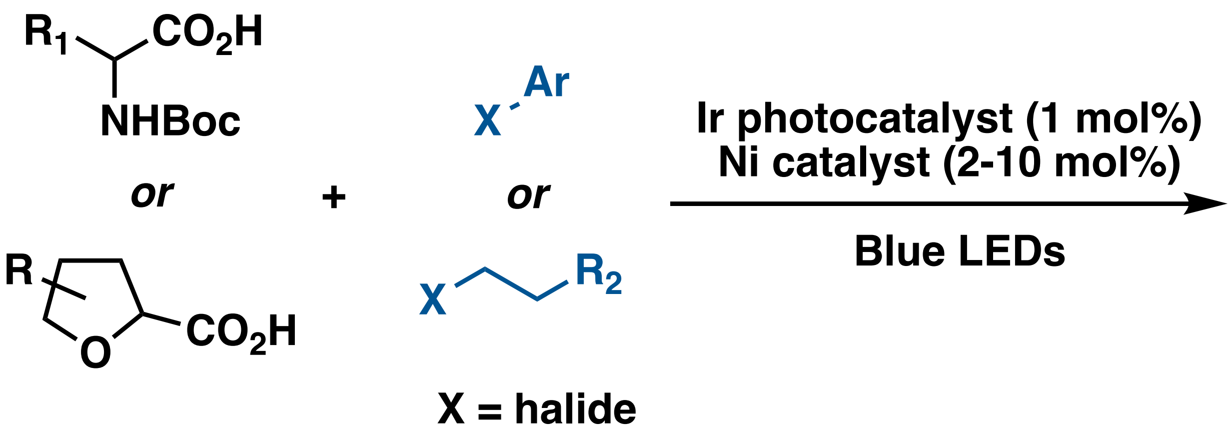
b) β-Functionalization



M. T. Pirnot, D. A. Rankic, D. B. C. Martin, D. W. C. MacMillan, *Science* **2013**, *339*, 1593-1596.

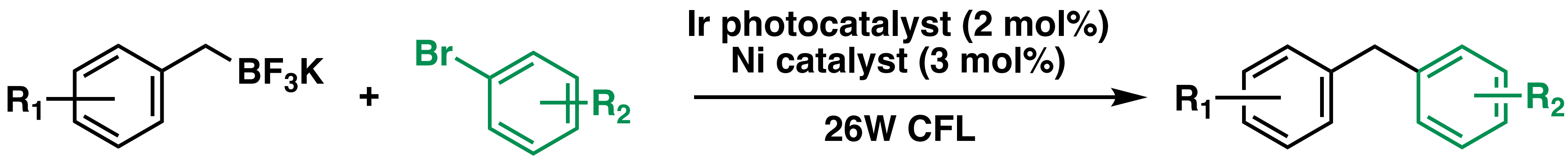
2.4.2. Metal catalysis

Cross-coupling of amines with halides



Z. Zuo, D. T. Ahneman, L. Chu, J. A. Terrett, A. G. Doyle, D. W. C. MacMillan, *Science* **2014**, *345*, 437-440.

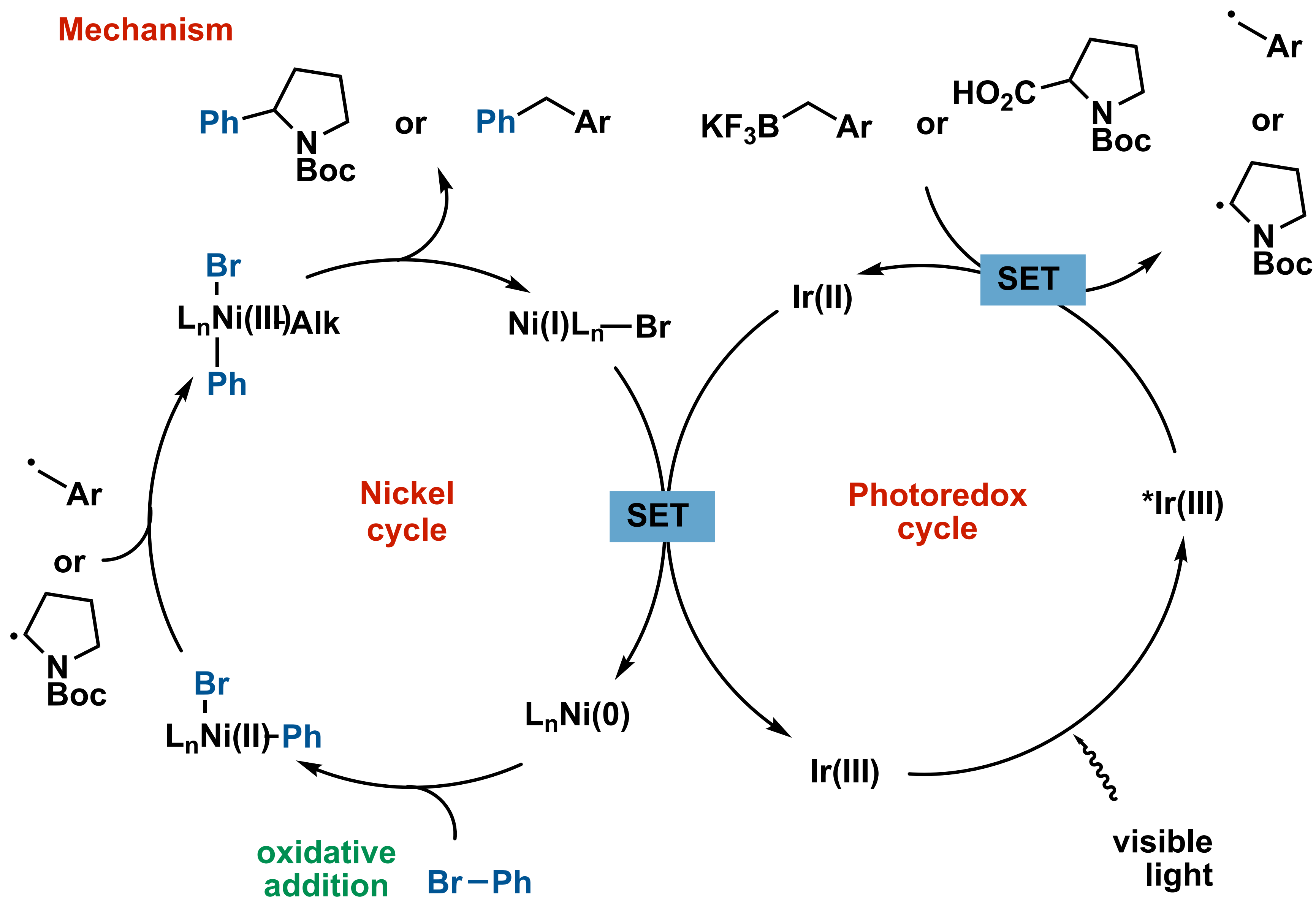
Cross-coupling of boronates with halides



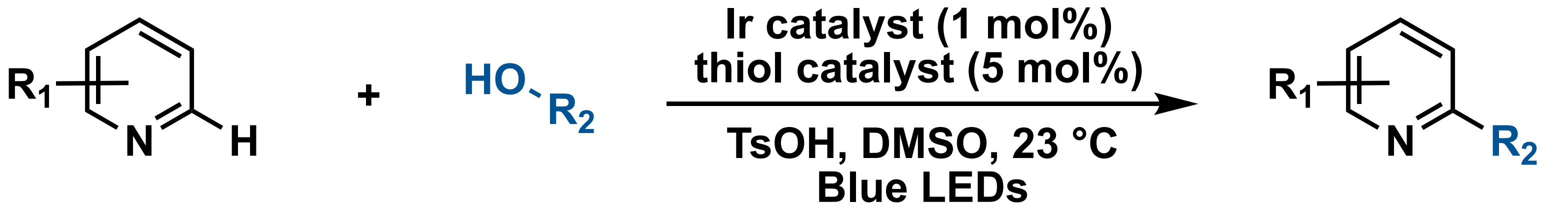
J. C. Tellis, D. N. Primer, G. A. Molander, *Science* **2014**, *345*, 433-436.

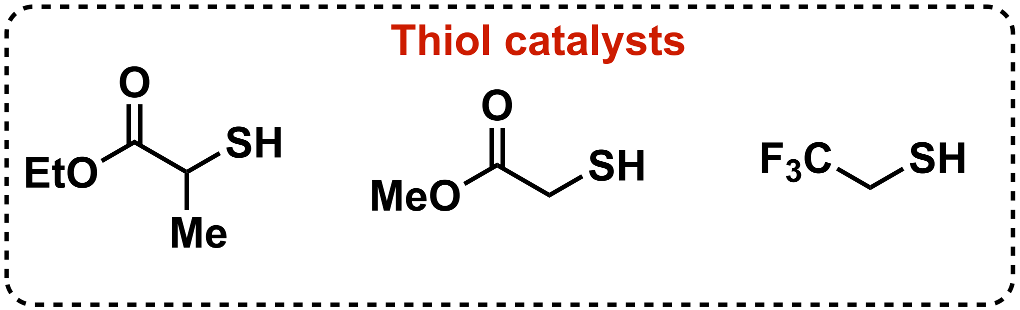
2.4.2. Metal catalysis

Mechanism



2.4.3. Hydrogen atom transfer catalysis

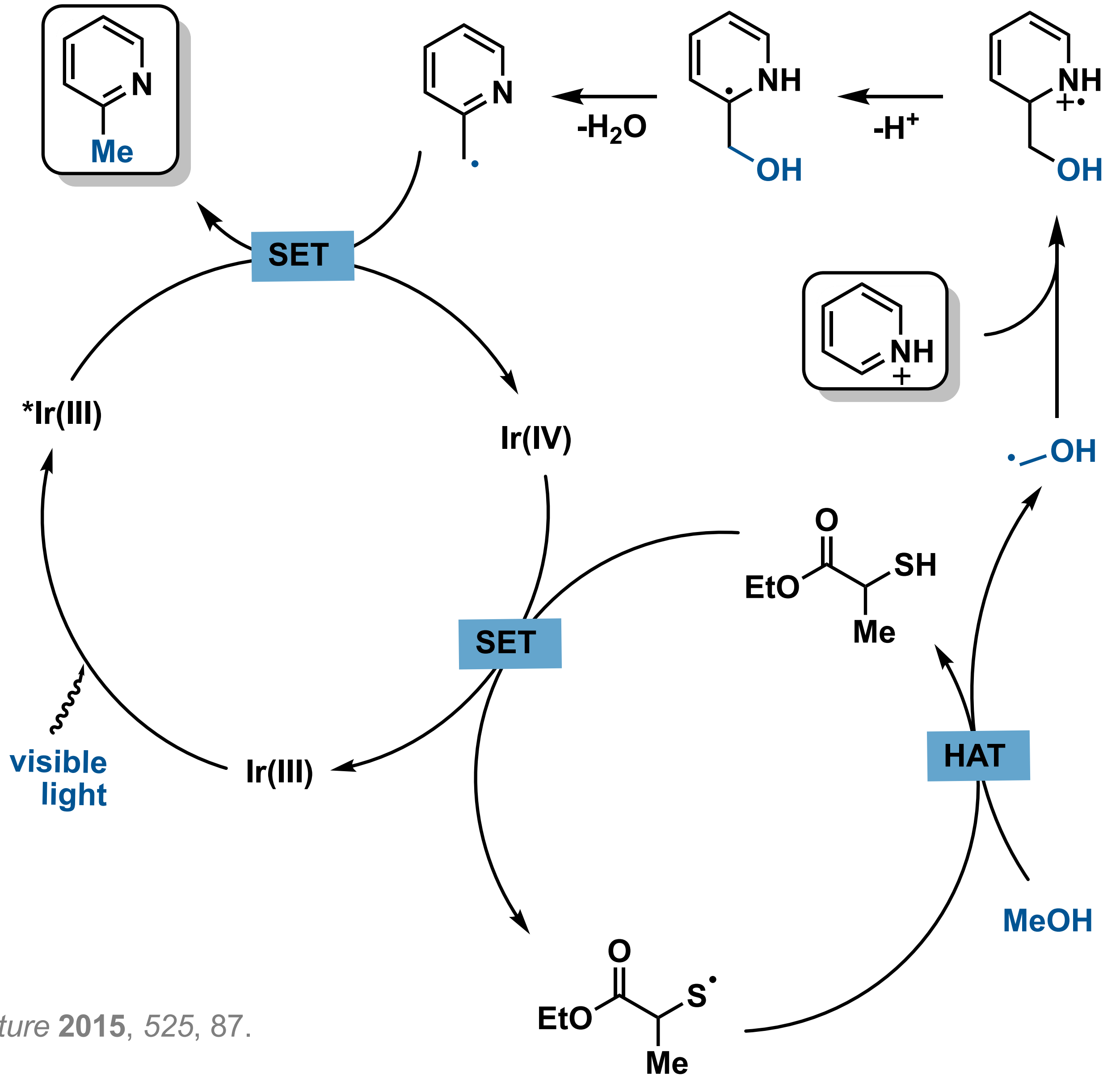




J. Jin, D. W. C. MacMillan, *Nature* **2015**, *525*, 87.

2.4.3. Hydrogen atom transfer catalysis

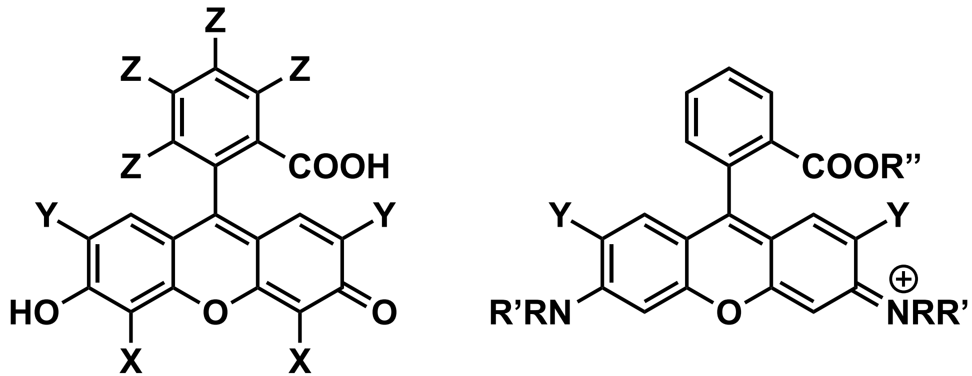
For methylation of pyridine:



J. Jin, D. W. C. MacMillan, *Nature* **2015**, *525*, 87.

- Excellent review on this topic: N. A. Romero, D. A. Nicewicz, *Chem. Rev.* **2016**, *116*, 10075-10166.
- Often cheaper and better available then metal-based catalysts
- Good properties (see review above)

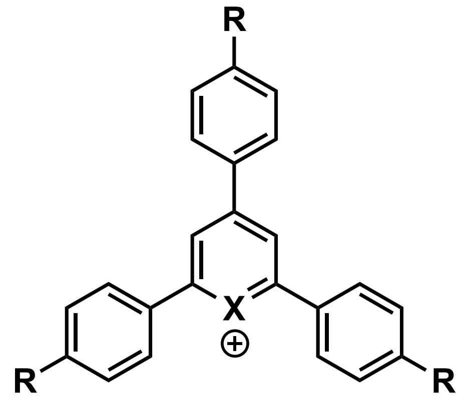
XANTHENES



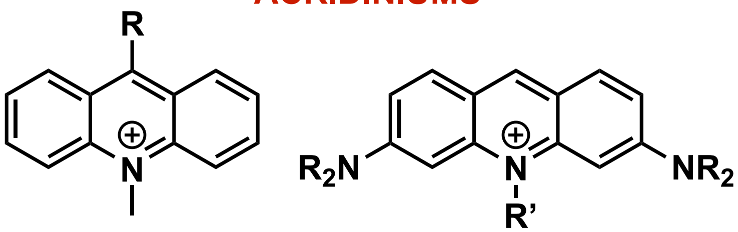
X, Y, Z = H Fluorescein
X, Y = Br, Z = H Eosin Y
X, Y = I, Z = Cl Rose Bengal

Y, R`` = H, R, R' = Et Rhodamine B
Y = Me, R' = H, R, R'' = Et Rhodamine 6G

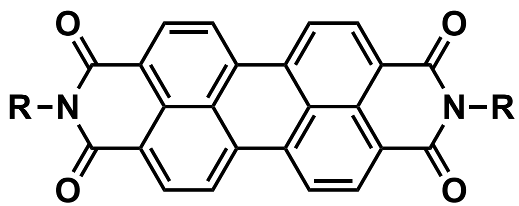
PYRYLIUMS



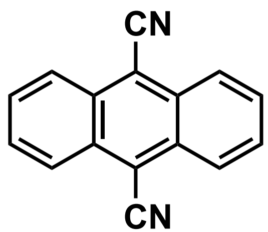
ACRIDINIUMS



PERYLENES

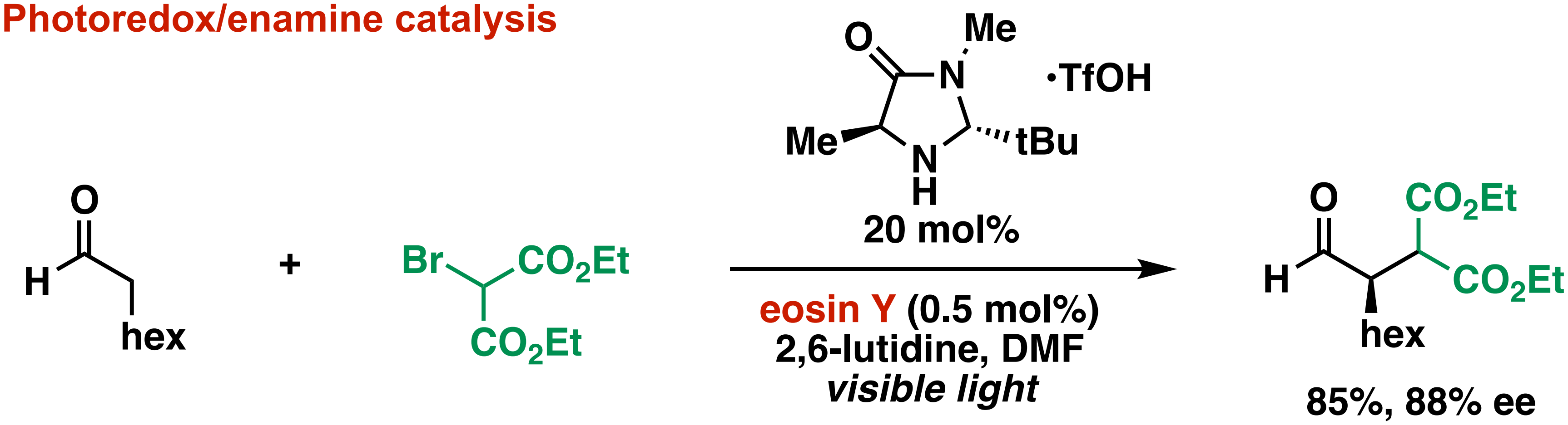


CYANOARENES



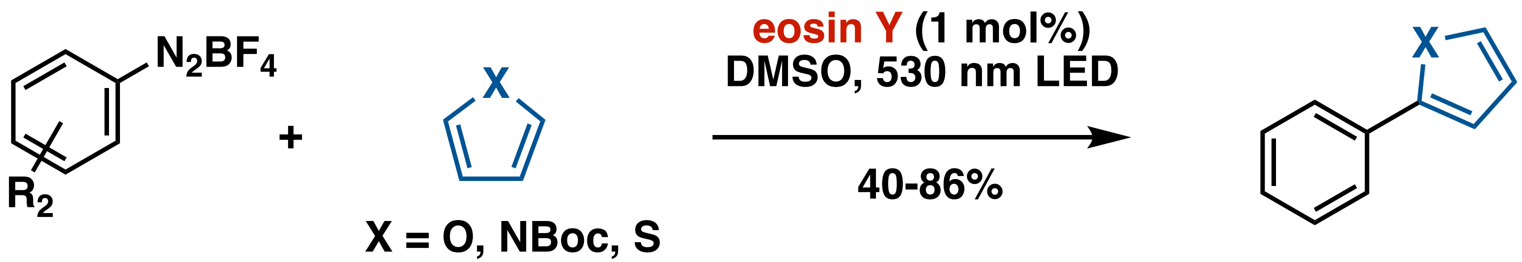
3.2.1. With Eosin Y

Photoredox/enamine catalysis



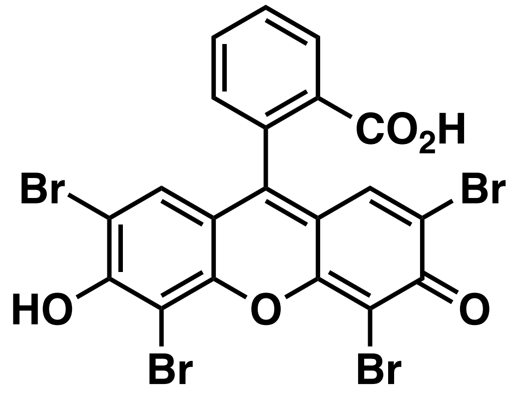
M. Neumann, S. Füldner, B. König, K. Zeitler, *Angew. Chem. Int. Ed.* **2011**, *50*, 951-954.

Diaryl coupling



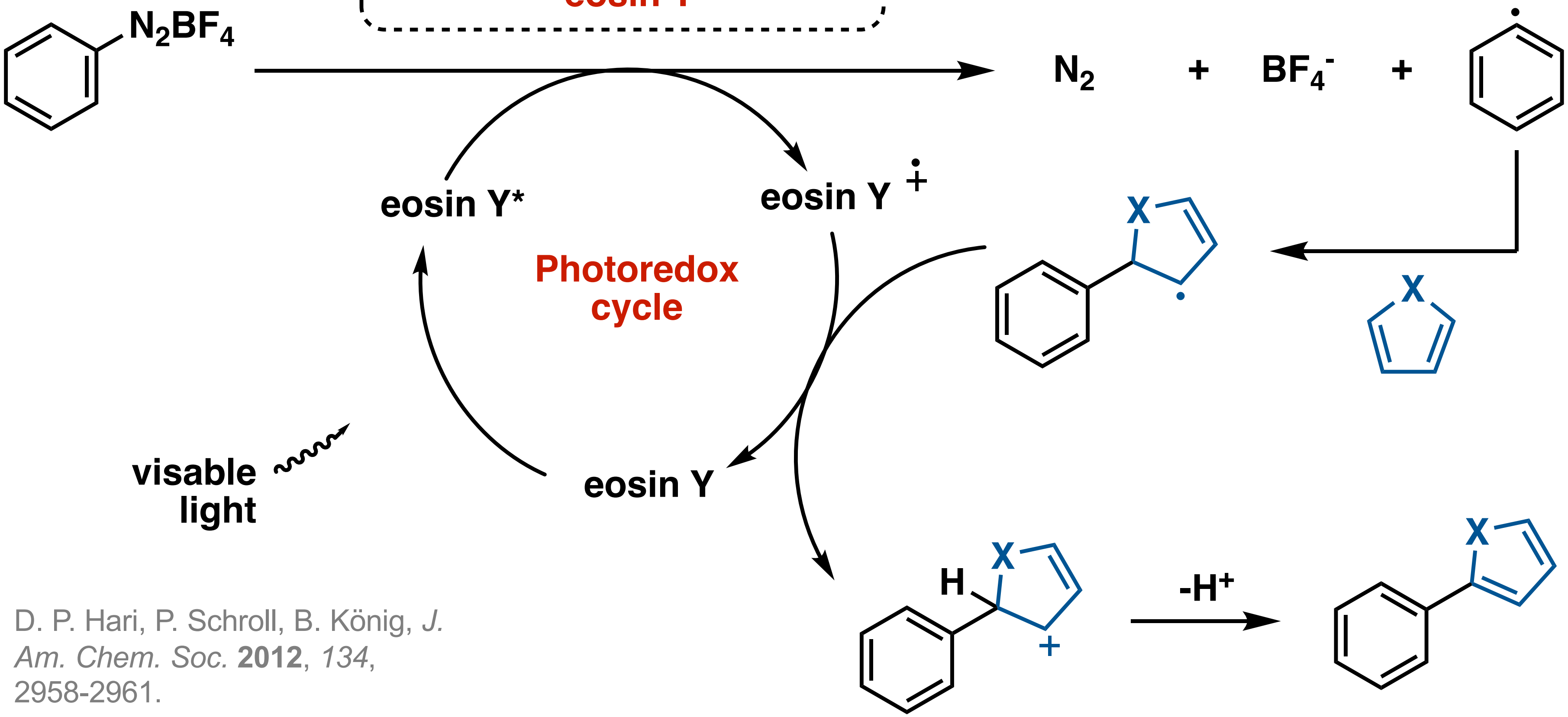
D. P. Hari, P. Schroll, B. König, *J. Am. Chem. Soc.* **2012**, *134*, 2958-2961.

3.2.1. With Eosin Y



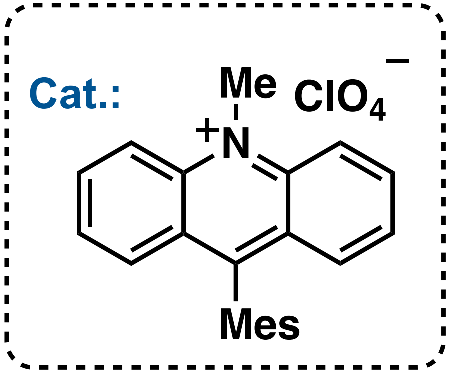
eosin Y

Mechanism

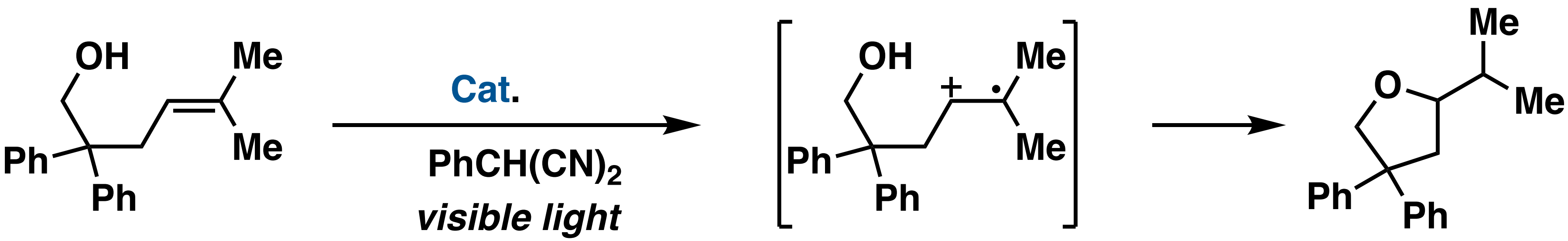


D. P. Hari, P. Schroll, B. König, *J. Am. Chem. Soc.* **2012**, *134*, 2958-2961.

3.2.2. With Acridinium Salts



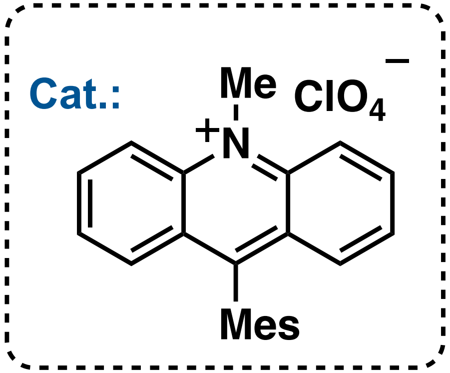
Intramolecular hydroetherification



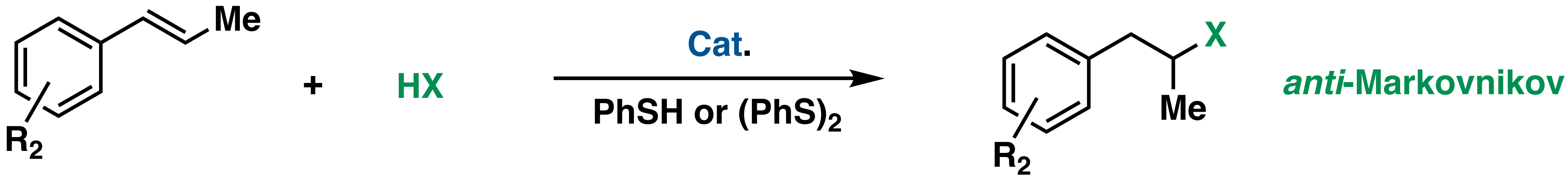
***anti*-Markovnikov product**

D. S. Hamilton, D. A. Nicewicz, *J. Am. Chem. Soc.* **2012**, *134*, 18577-18580.

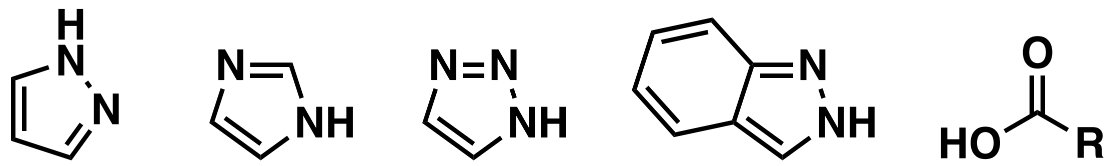
3.2.2. With Acridinium Salts



Intermolecular hydrofunctionalization



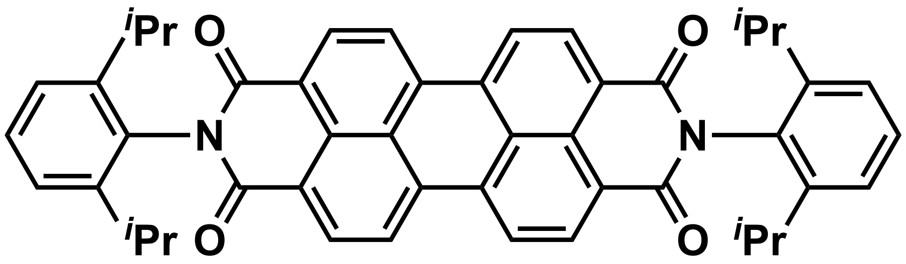
HX = HF, HCl, HR_2PO_4, $HRSO_3$



A. J. Perkowski, D. A. Nicewicz, *J. Am. Chem. Soc.* **2013**, *135*, 10334-10337; N. A. Romero, D. A. Nicewicz, *J. Am. Chem. Soc.* **2014**, *136*, 17024-17035; T. M. Nguyen, N. Manohar, D. A. Nicewicz, *Angew. Chem. Int. Ed.* **2014**, *53*, 6198-6201.

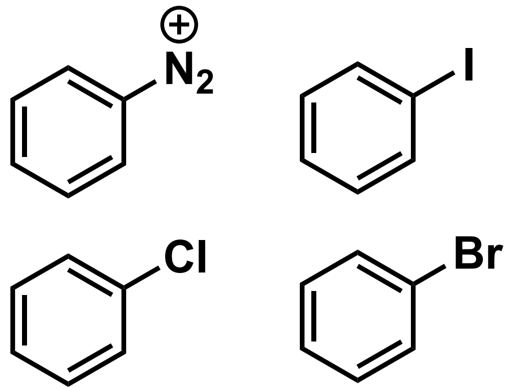
3.2.3. With Perylenes

CATALYST: PDI



Challenge:

- **aryl radical generation: only from electron-poor substrates:**
- **common photocatalysts cannot provide enough energy for:**

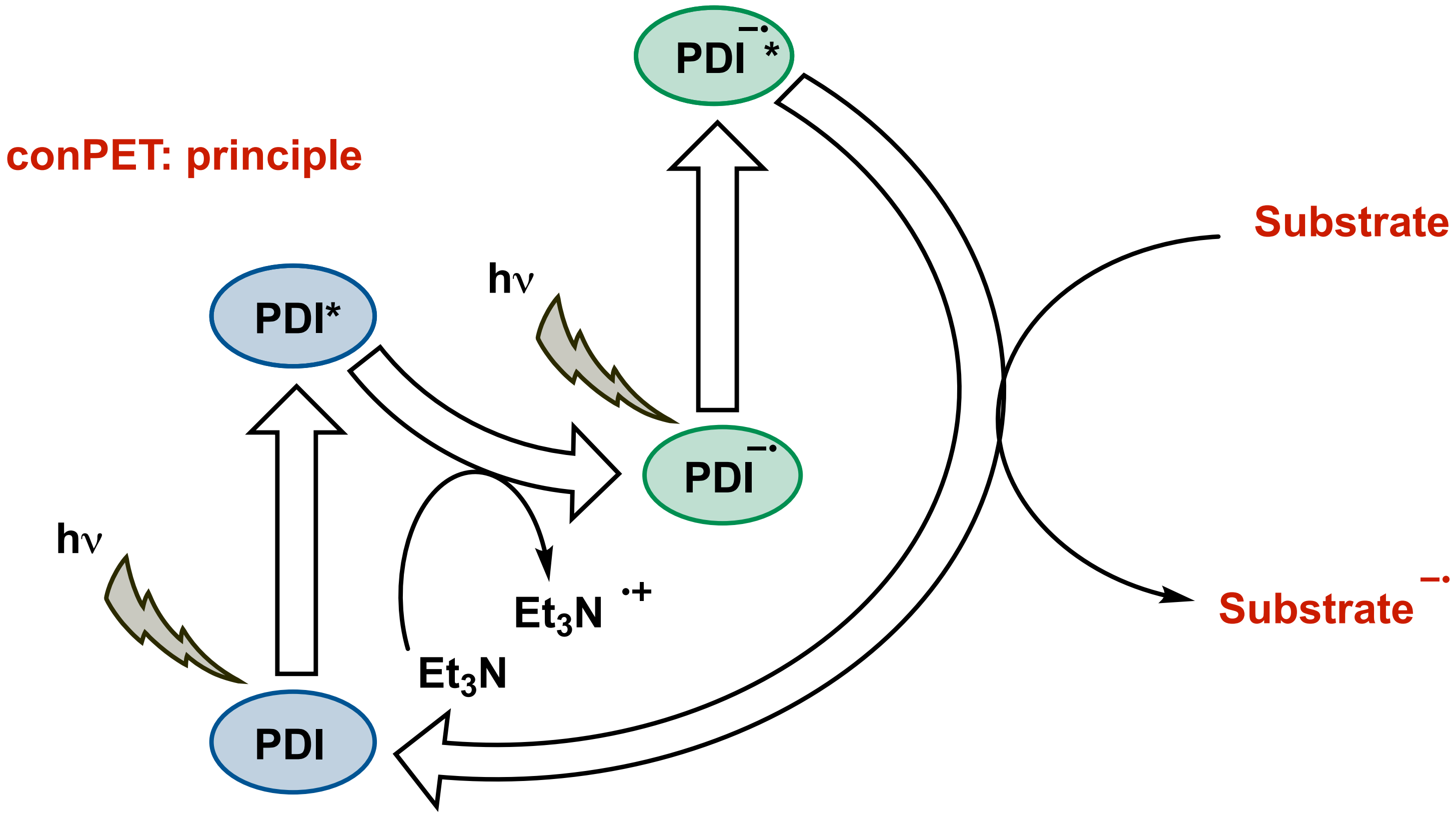


Solution:

- **consecutive photoelectron transfer: conPET = two excitations of the catalyst**

I. Ghosh, T. Ghosh, J. I. Bardagi, B. König, *Science* **2014**, *346*, 725-728.

3.2.3. With Perylenes

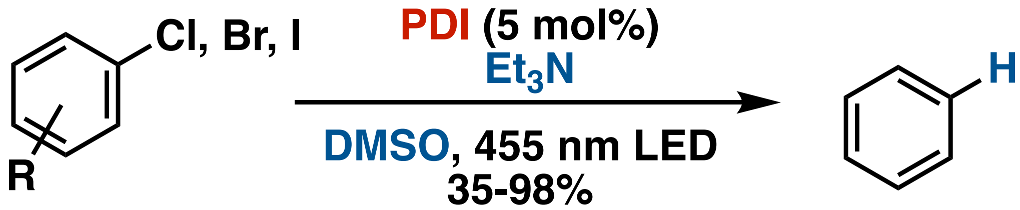


I. Ghosh, T. Ghosh, J. I. Bardagi, B. König, *Science* **2014**, *346*, 725-728.

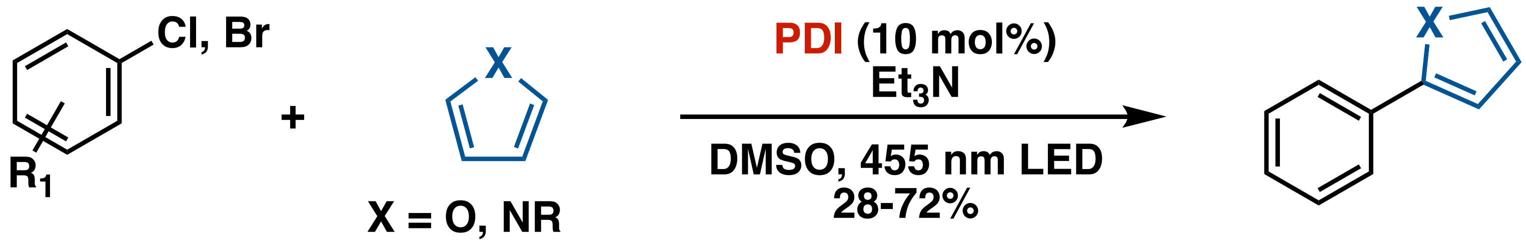
3.2.3. With Perylenes

- Applications:

Photoreduction



Arylation



I. Ghosh, T. Ghosh, J. I. Bardagi, B. König, *Science* **2014**, *346*, 725-728.

4. Total Syntheses