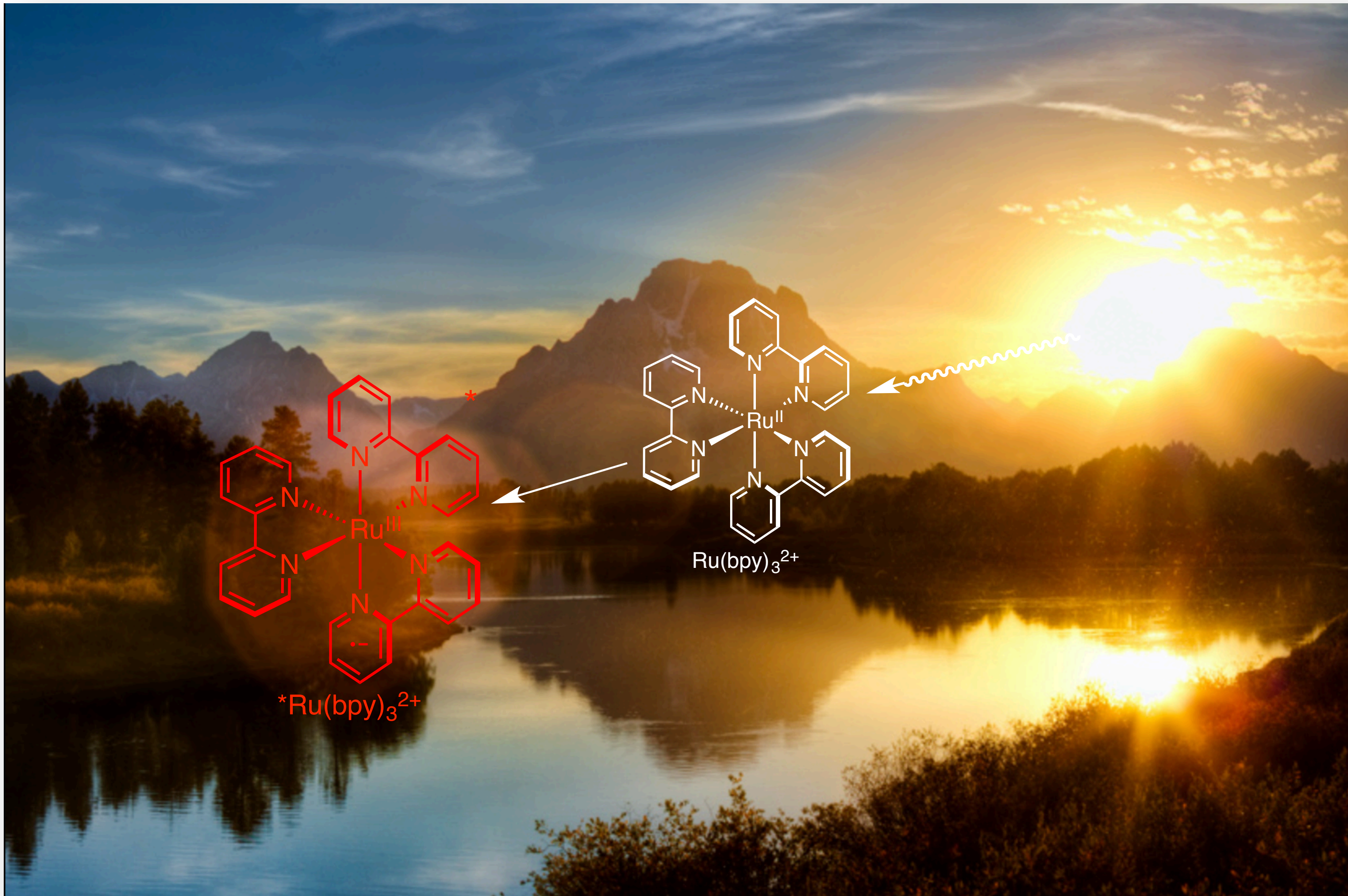
Visible Light Mediated Photoredox Catalysis

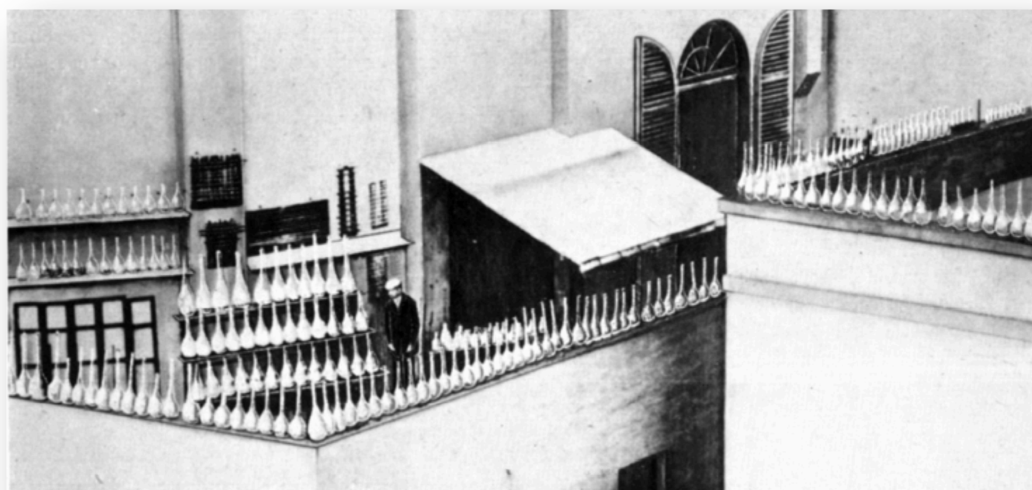


Kara George Rosenker

Frontiers of Chemistry Seminar
6 July 2013

Giacomo Ciamician:
'The Photochemistry of the Future'

"On the arid lands there will spring up industrial colonies without smoke and without smokestacks; forests of glass tubes will extend over the plains and glass buildings will rise everywhere; inside of these will take the place the photochemical processes that hitherto have been the guarded secret of the plants, but that will have been mastered by human industry which will know how to make them bear even more abundant fruit than nature, for nature is not in a hurry and mankind is. And if in a distant future the supply of coal becomes completely exhausted, civilization will not be checked by that, for life and civilization will continue as long as the sun shines!"



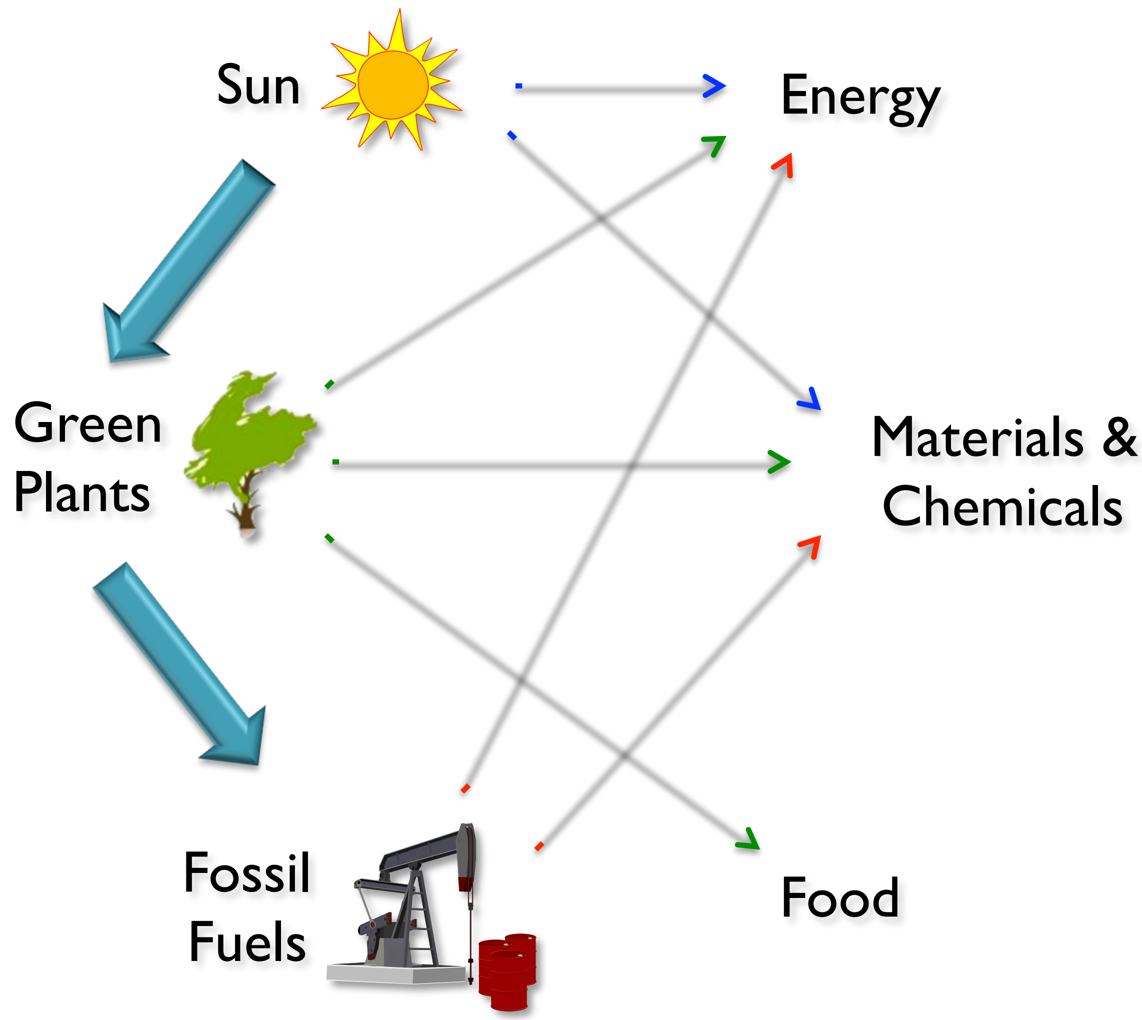
Ciamician, G. *Science* **1912**, *36*, 385.

Visible Light: Green Energy Source

Perennial

Renewable

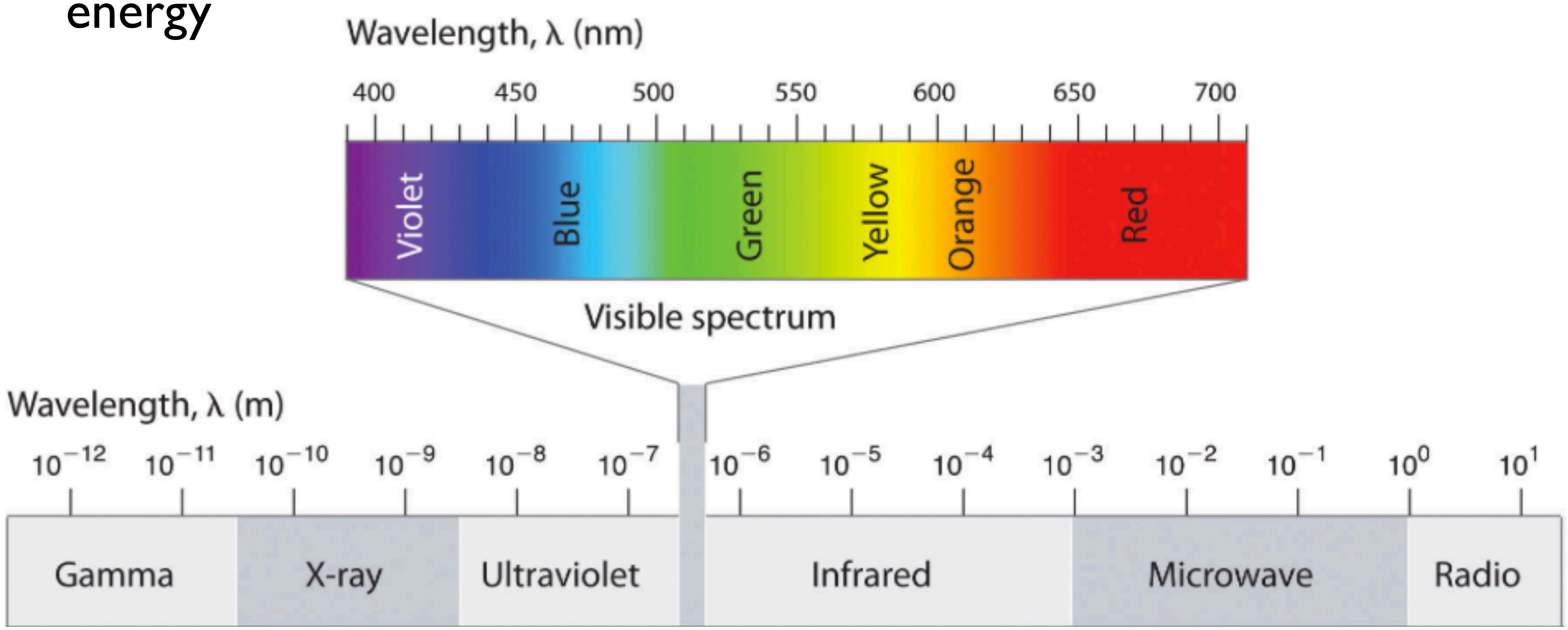
Non Renewable



Ravelli, D.; Dondi, D.; Fagnoni; M.; Albini, A. *Chem. Soc. Rev.* **2009**, *38*, 1999.

Visible Light: Green Energy Source

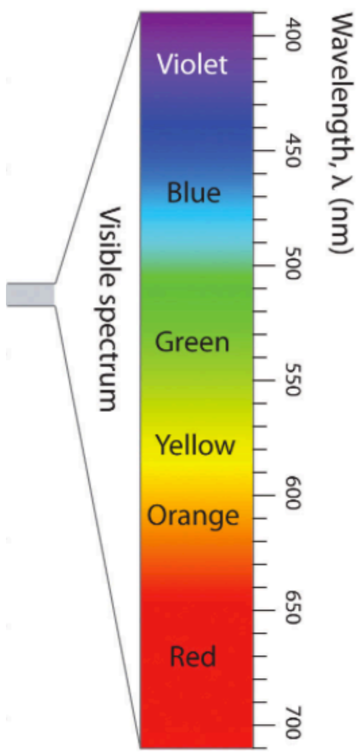
- Solar irradiation is by far the main supply of the energy on Earth and exceeds every conceivable need of mankind in the future: 25,000 – 75,000 kWh per day and hectare
  - average *annual* electricity consumption for a U.S. residential utility customer in 2011 was 11,280 kWh
- Visible light is a clean, inexpensive, and "infinitely available" source of energy



Ravelli, D.; Dondi, D.; Fagnoni; M.; Albini, A. *Chem. Soc. Rev.* **2009**, *38*, 1999.

Photochemistry in Organic Synthesis: Fundamental Impediment

- UV wavelengths are generally required in conventional organic photochemical synthesis
  - Potential for deleterious side reactions
  - Scale of the photochemical processes are constrained by the size and/or cost of photoreactor



Chromophore	λ_{max}(nm)	Chromophore	λ_{max}(nm)
C−C and C−H	<180	acetophenone	278
C−O (alcohol)	~180	naphthalene	310
C−S (alkyl sulfide)	210	anthracene	380
C−Br (alkyl bromide)	208	nitrobenzene	330
C−I (alkyl iodide)	260	C=O	280
C=C	180	N=N	350
C=C−C=C	220	$-NO_2$	270
C=C−C=C−C=C	260	N=O	660
C_6H_6	260	C=C−C=O	350
styrene	282		

Anslyn, E.V.; Dougherty, D.A. (2006) *Modern Physical Organic Chemistry.* Sausalito, CA: University Science Books.

Photochemistry in Organic Synthesis: Fundamental Impediment

- UV wavelengths are generally required in conventional organic photochemical synthesis
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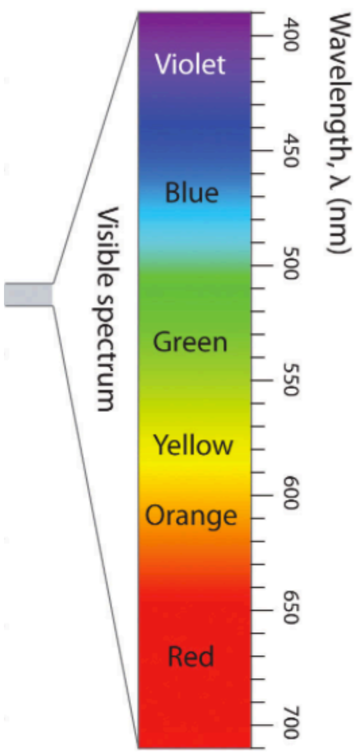


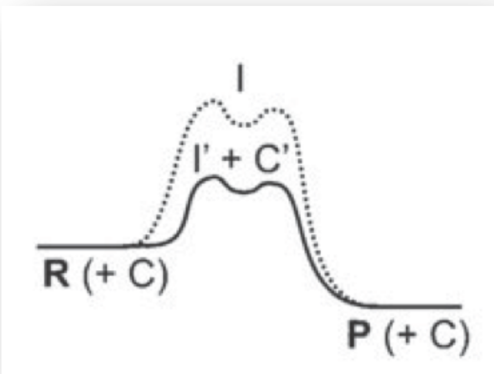
Widespread adoption of clean photochemical methods in chemical industry will require efficient photochemical reactions promoted by wavelengths of visible light.

Anslyn, E.V.; Dougherty, D.A. (2006) *Modern Physical Organic Chemistry.* Sausalito, CA: University Science Books.

Visible Light Mediated Photocatalysis

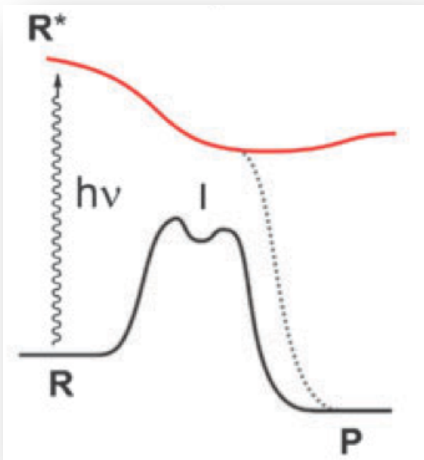
"Relies on the ability of metal complexes and organic dyes to engage in single-electron transfer (SET) processes with organic substrates upon photoexcitation with visible light"

Thermal Reaction



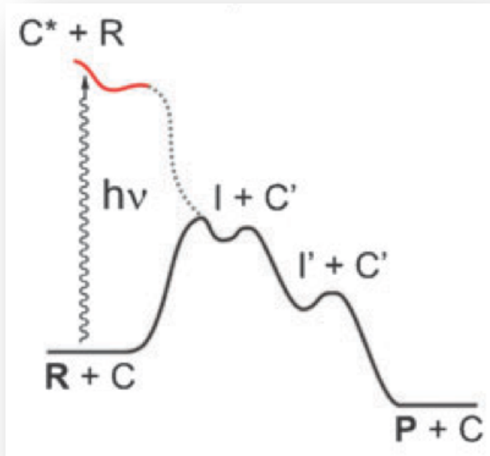
Catalyzed by **C** *via* intermdiate **I'**

Photochemical Reaction



The reaction starts from the excited state surface of reagent R*

Photocatalyzed Reaction

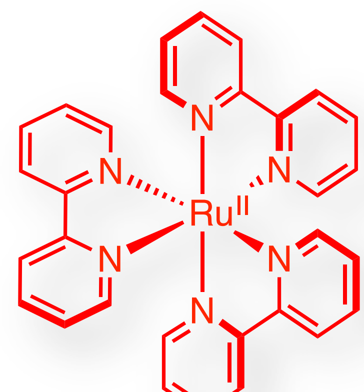


The catalyst C is active only in the excited state; the reaction of R occurs entirely on the ground state surface

Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, DOI: 10.1021/cr300503r
Ravelli, D.; Dondi, D.; Fagnoni, M.; Albini, A. *Chem. Soc. Rev.* **2009**, *38*, 1999.

Visible Light Photocatalysts

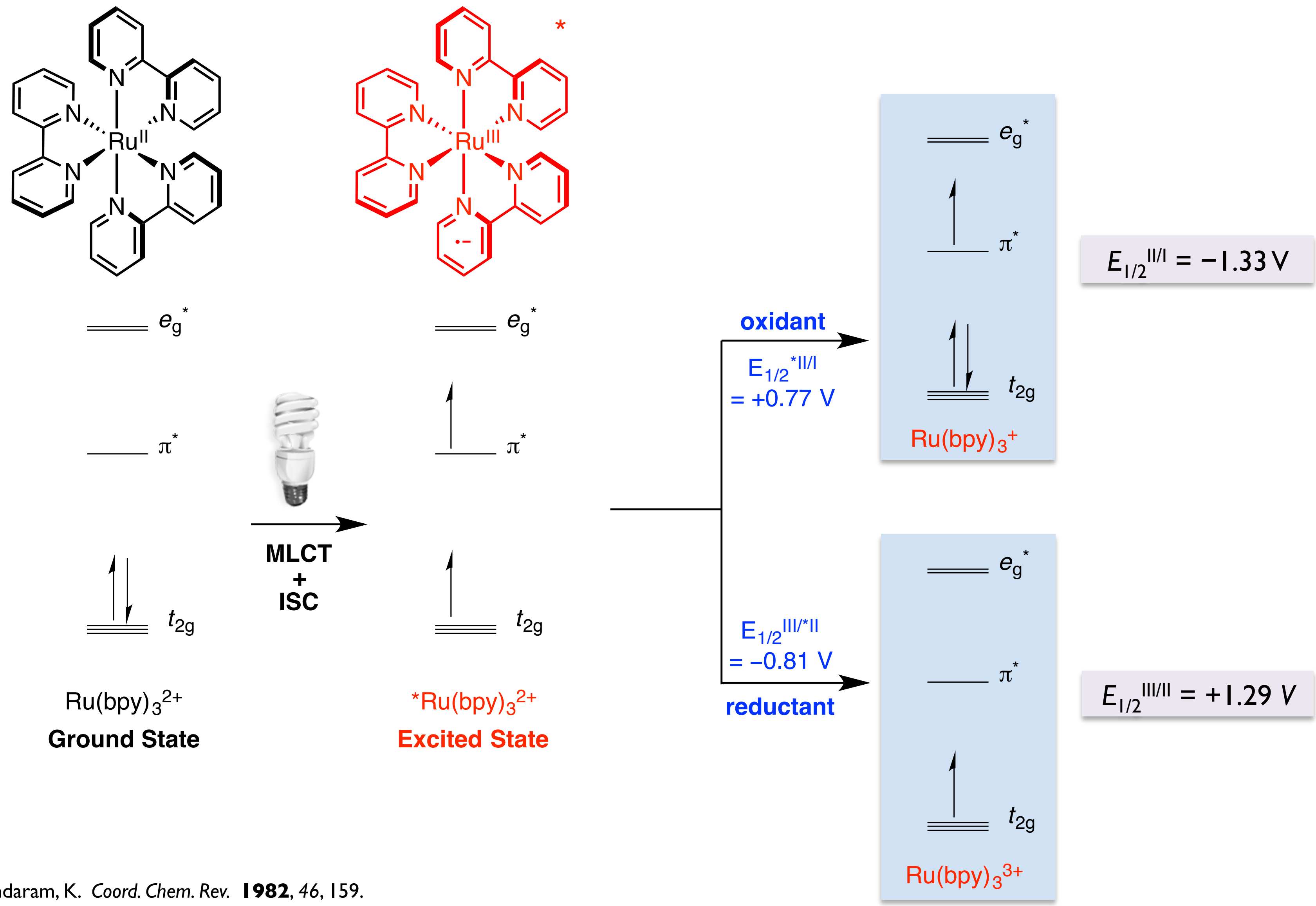
- Most commonly employed visible light photocatalysts are polypyridyl complexes of ruthenium and iridium
- Prototypical photocatalyst is $Ru(bpy)_3^{2+}$
  - Absorption at 452 nm
  - Stable, long-lived excited state (τ = 1100 ns)
  - Single electron transfer (SET) catalyst
  - Effective excited state oxidant and reductant
- Extensively used and investigated in inorganic and materials chemistry
  - splitting of water into hydrogen and oxygen
  - reduction of carbon dioxide to methane
  - initiation of polymerization reactions
  - components of dye-sensitized solar cells and light-emitting diodes
  - used in photodynamic therapy



$Ru(bpy)_3^{2+}$

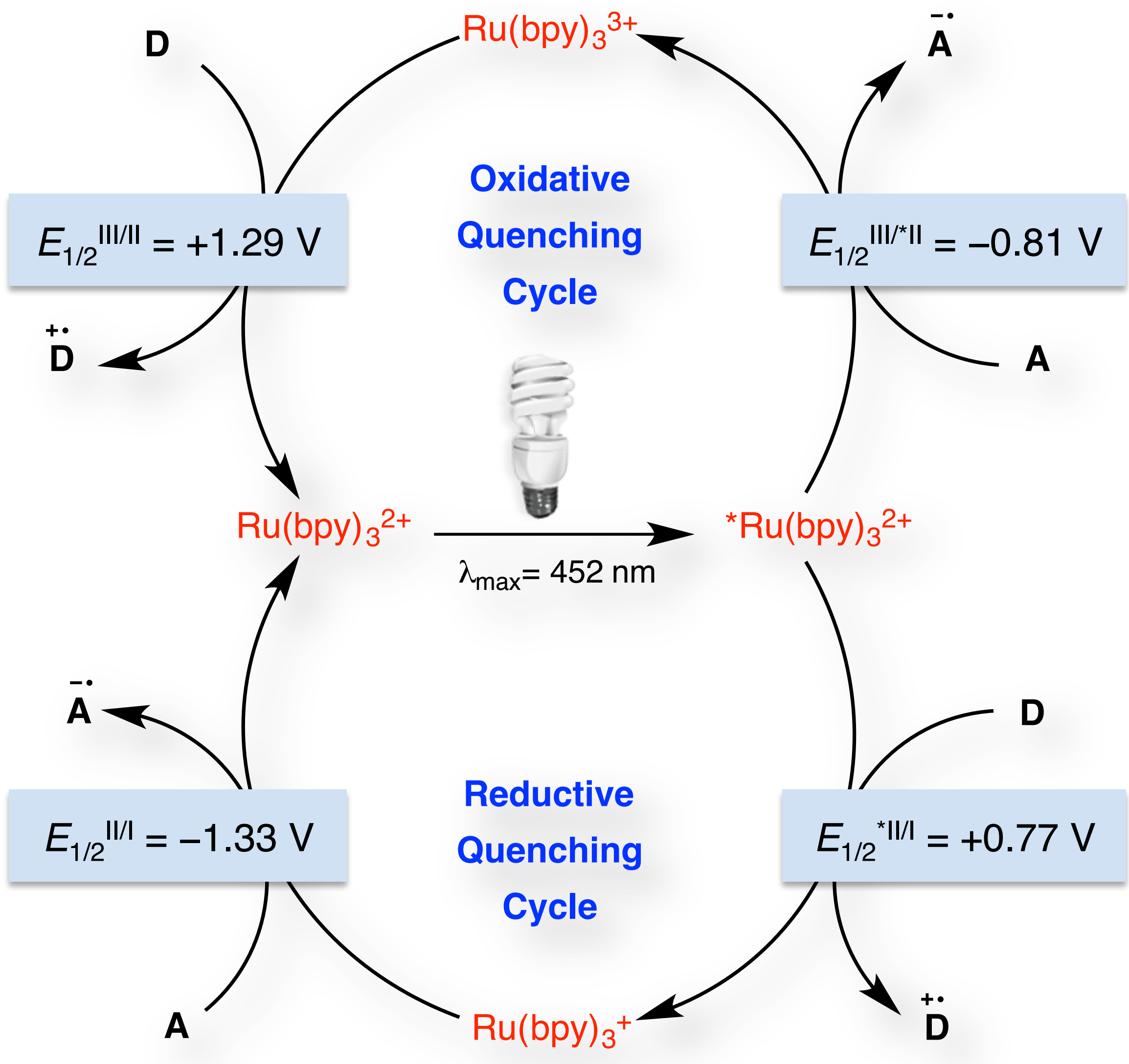
Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, DOI: 10.1021/cr300503r

Photochemistry of $Ru(bpy)_3^{2+}$: Simplified Molecular Orbital Depiction



Kalyanasundaram, K. *Coord. Chem. Rev.* **1982**, *46*, 159.
Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *ASAP*, DOI: 10.1021/cr300503r

Photochemistry of $Ru(bpy)_3^{2+}$: Oxidative and Reductive Quenching Cycle



Oxidative quenchers:

$Ar\text{-}N_2^+$	$S_2O_6^-$
$ArNO_2$	Ar_2I^+
Viologens	ArSO²-SeAr
$[Co(acac)_3]$	CBr_4
$[Co(C2O_4)_3]^{3-}$	CHI_3

Reductive quenchers:

Et_3N	Eu^{2+}
Ph_3N	$(CO_2)_2$
EDTA	xanthate
i-Pr_2NEt	ascorbate

Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *ASAP*, DOI: 10.1021/cr300503r

Photoredox Catalysis:
Applications in Organic Synthesis

- **1936** — Salts of $[Ru(bpy)_3]^{2+}$ were first reported by Burstall in 1936
- **1978** — The earliest examples of visible light photoredox catalysis in organic synthesis were net reductive reactions (Kellogg and Pac)
- **1980-2000** — Cano-Yelo and Deronzier, Willner, Tanaka; Fukuzumi, Okada, Barton, Ohkubo
- **early 2000s** — Zen, Hirao, Hasegawa, Garcia, Osawa
- **2008** — Since 2008, application of visible-light photoredox catalysis in organic synthesis experienced a remarkable acceleration (MacMillan, Stephenson, Yoon, Koike and Akita)
- **2012-2013** — Seminars by Professors Stephenson, Yoon, and Zheng at the University of Pittsburgh

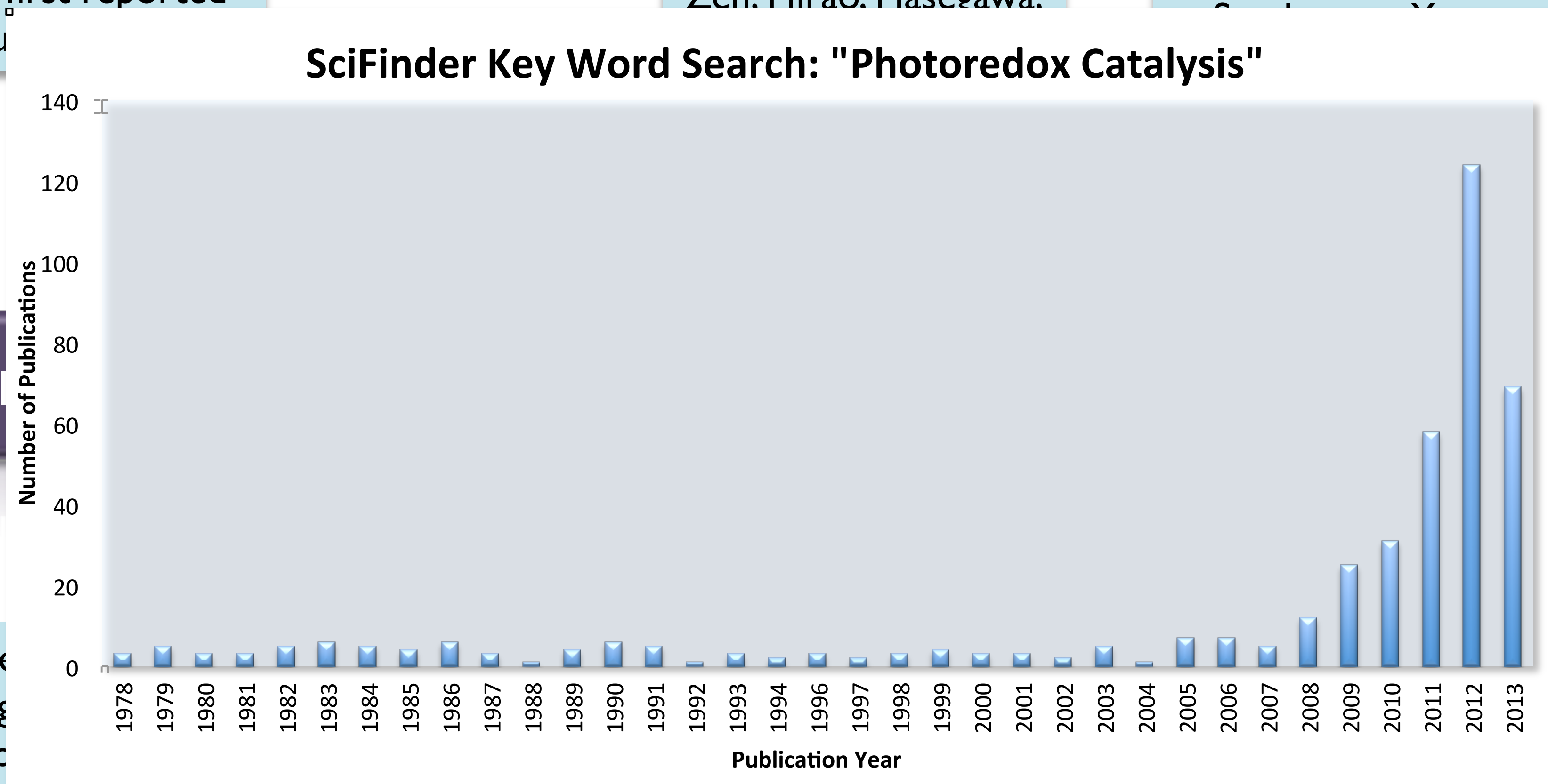
Photoredox Catalysis: Applications in Organic Synthesis

Salts of $[Ru(bpy)_3]^{2+}$ were first reported by Bu

Zen, Hirao, Hasegawa,

Seminars by Professors

of



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lig

c

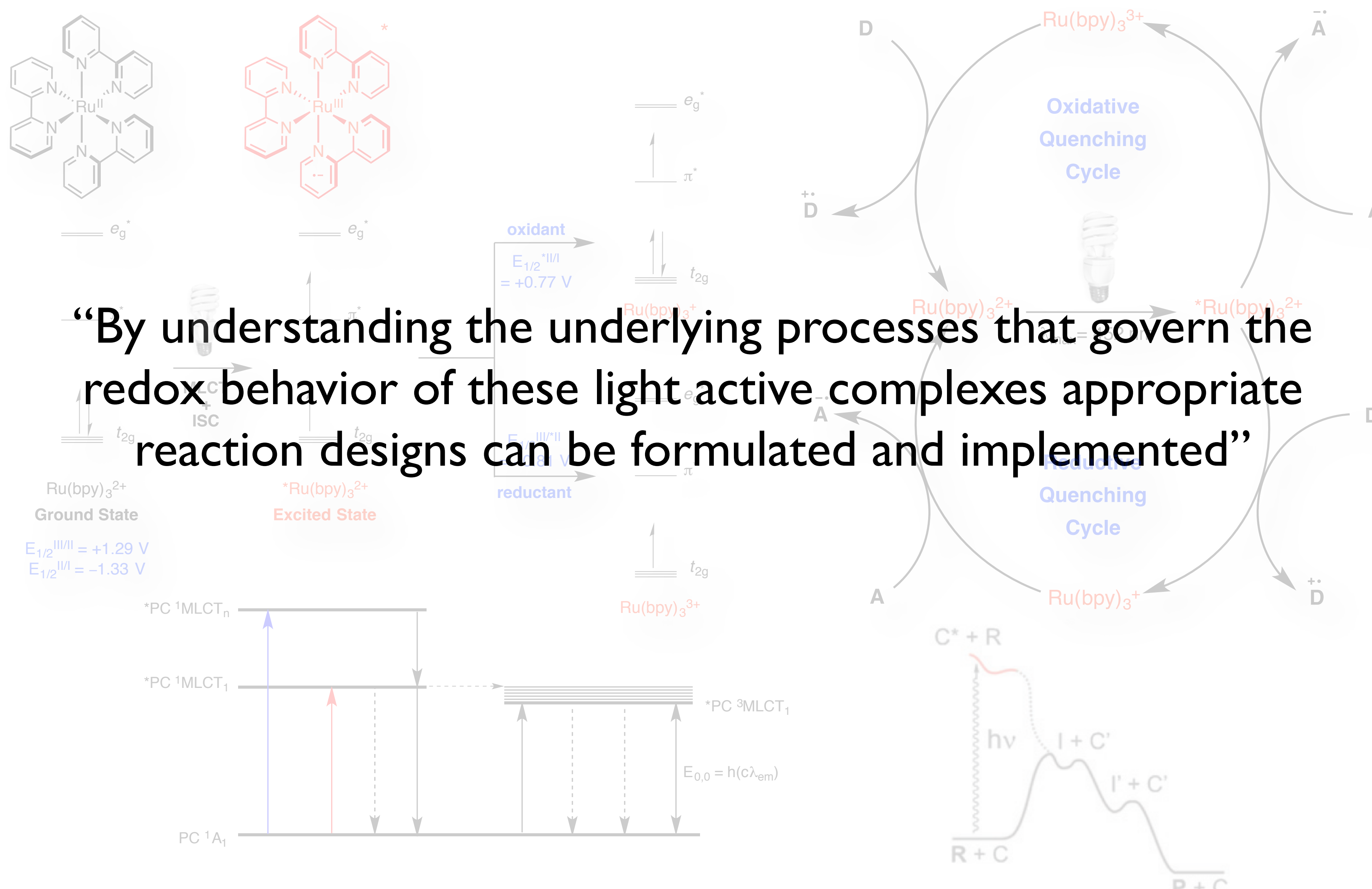
reductive reactions (Kellogg and Pac)

e-

organic synthesis experienced a remarkable acceleration (MacMillan, Stephenson, Yoon, Koike and Akita)

12

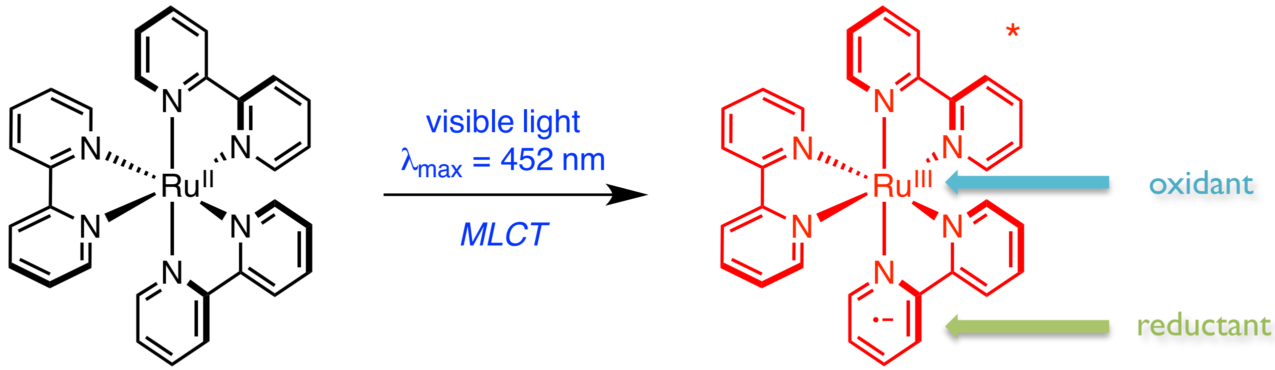
Visible Light Photocatalysis: Advancing the Field



"By understanding the underlying processes that govern the redox behavior of these light active complexes appropriate reaction designs can be formulated and implemented"

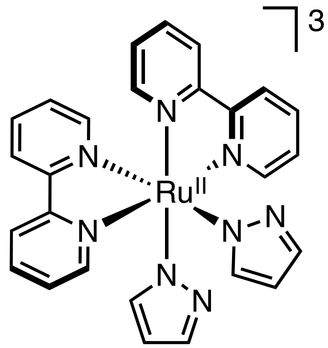
Tucker, J.W.; Stephenson, C. R. J. *J. Org. Chem.* **2012**, 77, 1617.

Photoredox Catalysis:
Ligand Effects on Ground-State Redox Properties

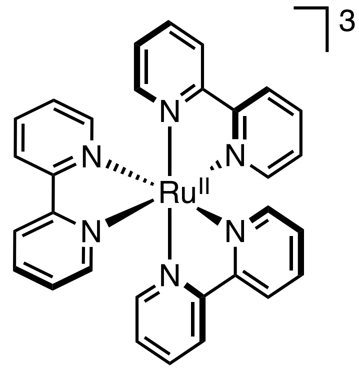


$Ru(bpy)_3^{2+}$ → $^*Ru(bpy)_3^{2+}$

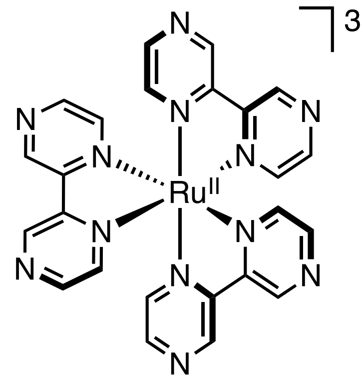
- Oxidized Complexes (Metal Centered Oxidation):



$Ru(bpy)_2(pz)_2$
E_{red} = 0.30 V



$Ru(bpy)_3$
E_{red} = 1.26 V



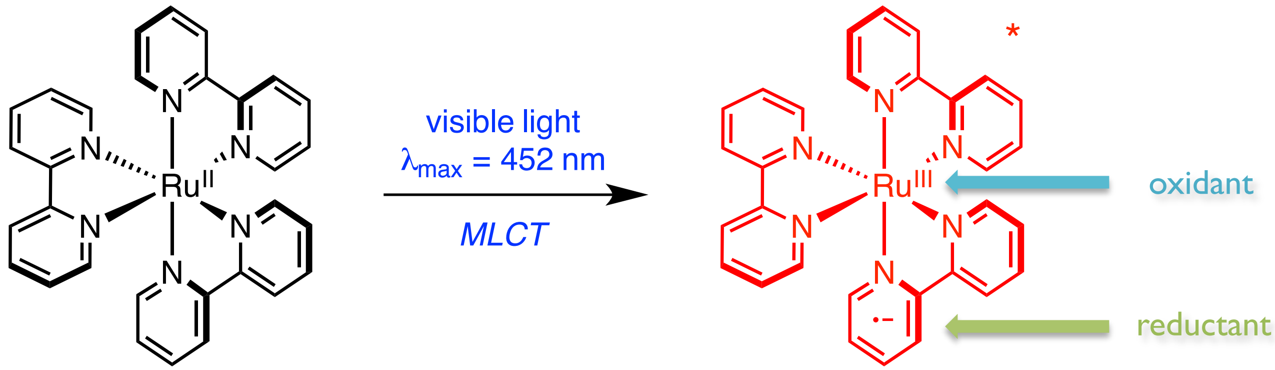
$Ru(bpz)_3$
E_{red} = 1.86 V

← electron density of metal center

oxidative power of complex →

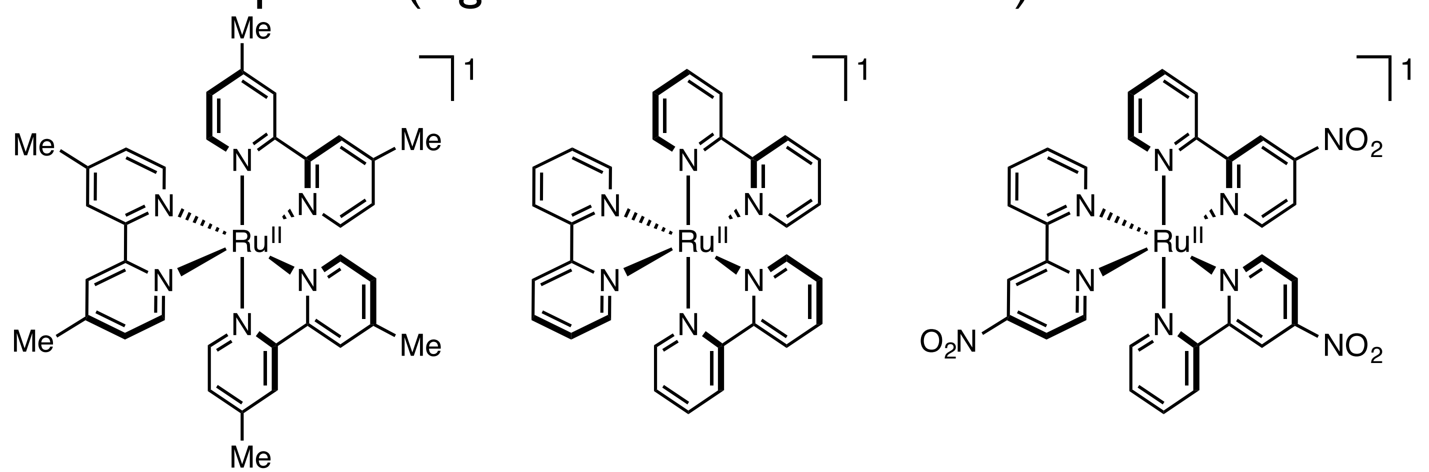
Tucker, J. W.; Stephenson, C. R. J. *J. Org. Chem.* **2012**, 77, 1617.

Photoredox Catalysis: Ligand Effects on Ground-State Redox Properties



$Ru(bpy)_3^{2+}$ → $^*Ru(bpy)_3^{2+}$

- Reduced Complexes (Ligand Centered Reduction):



Ru(dmb)$_3$	Ru(bpy)$_3$	*mer*-Ru(4-O$_2$N-bpy)$_3$
E_{red} = -1.45 V	E_{red} = -1.35 V	E_{red} = -0.63 V

← electron density of ligand

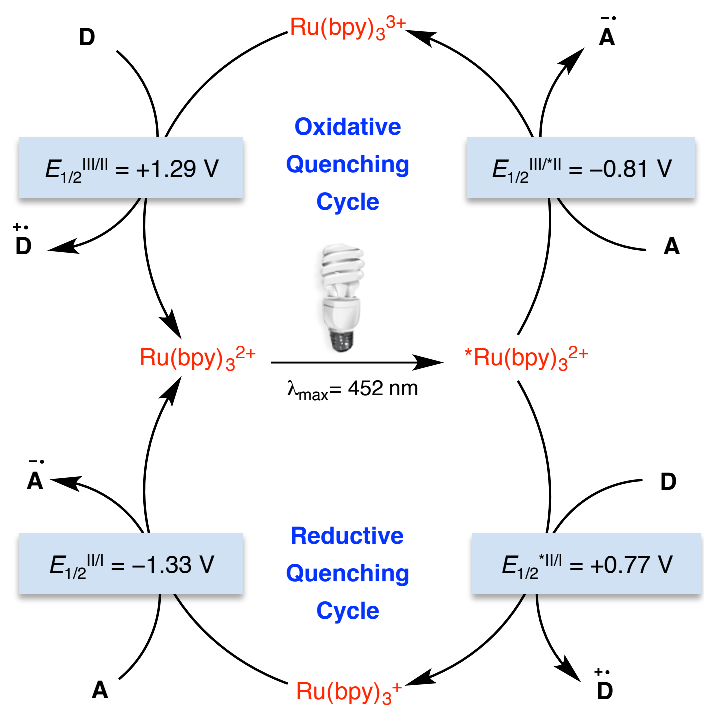
← reductive power of complex

Tucker, J. W.; Stephenson, C. R. J. *J. Org. Chem.* **2012**, 77, 1617.

Photoredox Catalysis: Common Catalysts

- General rule:
  - electron-donating substituents on the ligands render the complex more strongly reducing
  - electron-withdrawing substituents render the complex more strongly oxidizing

Photocatalyst	$E_{1/2}$ (M^+/M^*)	$E_{1/2}$ (M^*/M^-)	$E_{1/2}$ (M^+/M)	$E_{1/2}$ (M/M^-)
$Ru(bpm)_3^{2+}$	−0.21	+0.99	+1.69	−0.91
$Ru(bpz)_3^{2+}$	−0.26	+1.45	+1.86	−0.80
$Ru(bpy)_3^{2+}$	−0.81	+0.77	+1.29	−1.33
$Ru(phen)_3^{2+}$	−0.87	+0.82	+1.26	−1.36
$Ir[dF(CF_3)ppy]_2(dtbbpy)^+$	−0.89	+1.21	+1.69	−1.37
$Ir(ppy)_2(dtbbpy)^+$	−0.96	+0.66	+1.21	−1.51
$Cu(dap)^+$	−1.43		+0.62	
fac-$Ir(ppy)_3$	−1.73	+0.31	+0.77	−2.19



Prier, C. K.; Rankic, D.A.; MacMillan, D.W. C. *Chem. Rev.* **2013**, *ASAP*, DOI: 10.1021/cr300503r

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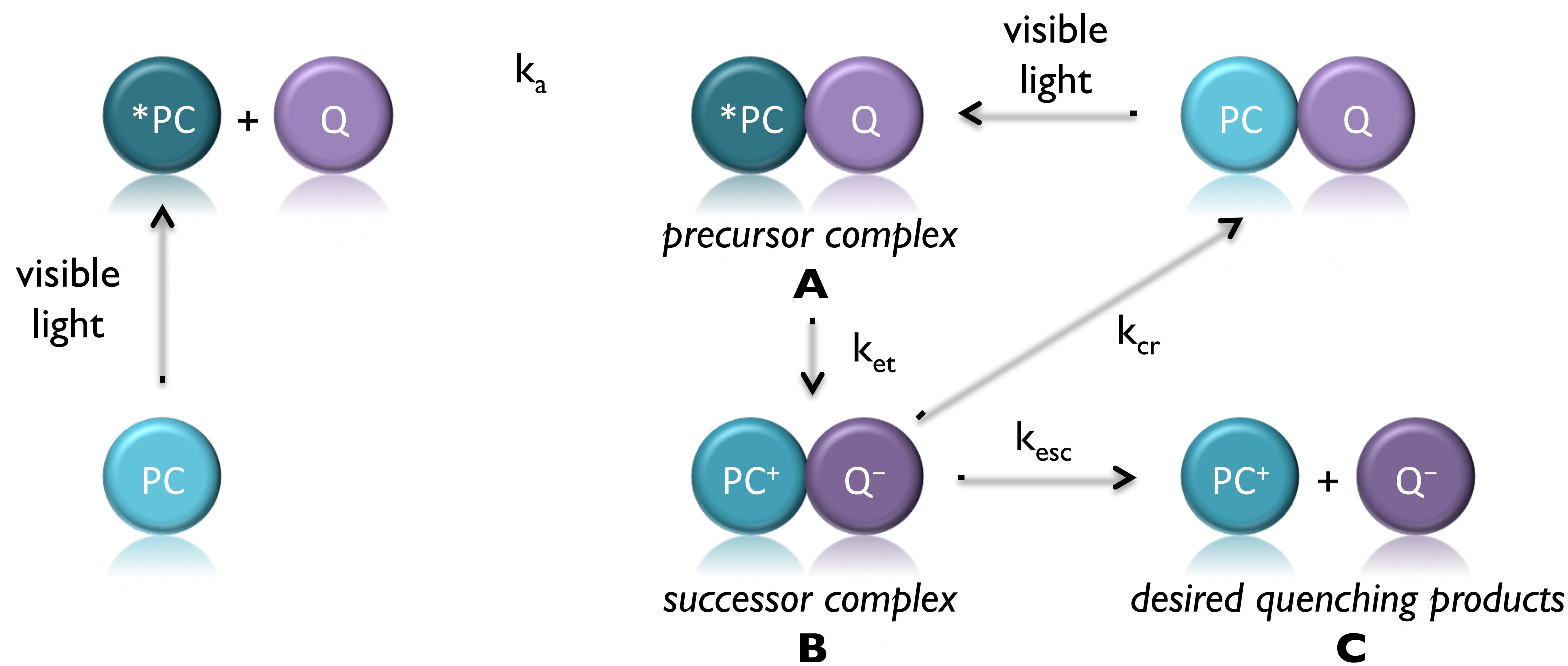
  - electron-withdrawing substituents render the complex more strongly oxidizing

Photocatalyst	$E_{1/2}$ (M^+/M^*)	$E_{1/2}$ (M^*/M^-)	$E_{1/2}$ (M^+/M)	$E_{1/2}$ (M/M^-)	Excited-state lifetime τ (ns)	Excitation λ_{max} (nm)	Emission λ_{max} (nm)
$Ru(bpm)_3^{2+}$	−0.21	+0.99	+1.69	−0.91	131	454	639
$Ru(bpz)_3^{2+}$	−0.26	+1.45	+1.86	−0.80	740	443	591
$Ru(bpy)_3^{2+}$	−0.81	+0.77	+1.29	−1.33	1100	452	615
$Ru(phen)_3^{2+}$	−0.87	+0.82	+1.26	−1.36	500	422	610
$Ir[dF(CF_3)ppy]_2(dtbbpy)^+$	−0.89	+1.21	+1.69	−1.37	2300	380	470
$Ir(ppy)_2(dtbbpy)^+$	−0.96	+0.66	+1.21	−1.51	557		581
$Cu(dap)^+$	−1.43		+0.62		270		670
fac-$Ir(ppy)_3$	−1.73	+0.31	+0.77	−2.19	1900	375	494

Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *ASAP*, DOI: 10.1021/cr300503r

Photoredox Catalysis: Kinetic Parameters

- For any closed photoredox catalytic cycle there are at least two outer-sphere electron transfer processes that must occur:
  1) an electron transfer to quench the excited state
  2) a subsequent electron transfer to regenerate the ground-state catalyst
- Electron transfer process for oxidative quenching:



Tucker, J. W.; Stephenson, C. R. J. *J. Org. Chem.* **2012**, 77, 1617.

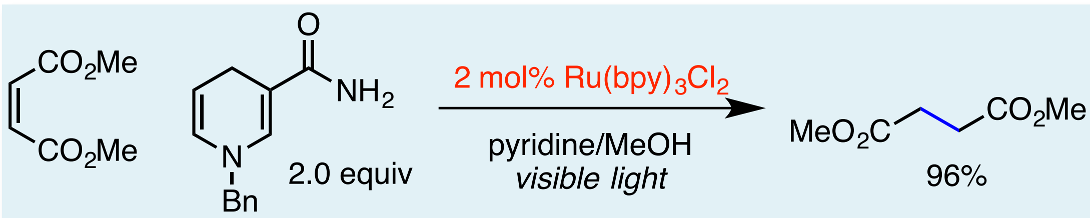
Visible Light Photoredox Catalysis: Applications in Organic Synthesis

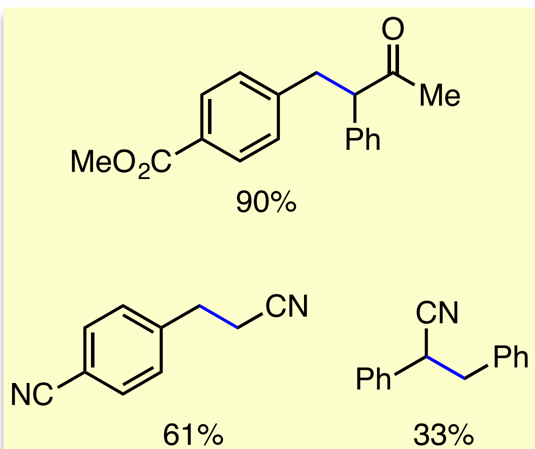
- Net Reductive Reactions
- Net Oxidative Reactions
- Redox Neutral Reactions
- Energy Transfer Reactions

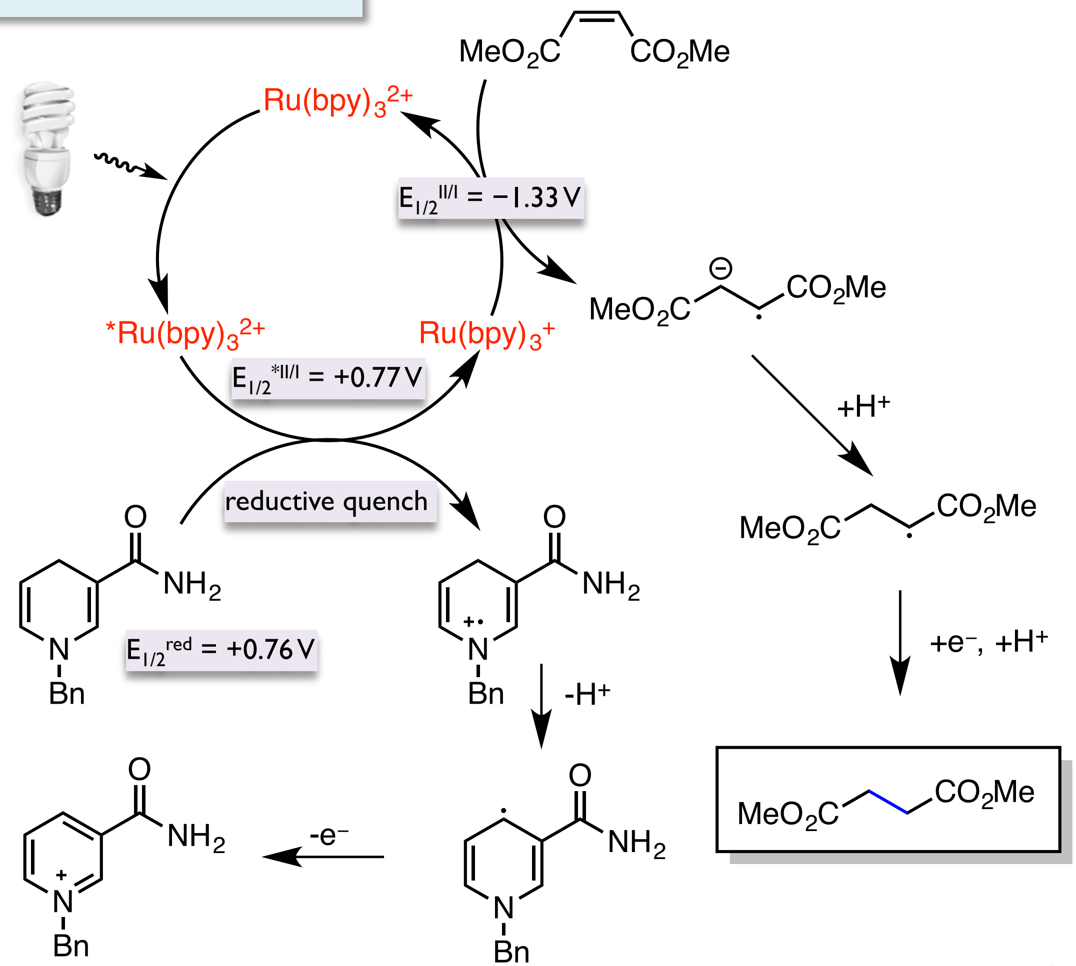
Visible Light Photoredox Catalysis: Applications in Organic Synthesis

- Net Reductive Reactions
  - Reduction of Electron-Poor Olefins
  - Reductive dehalogenation
  - Reductive Cleavage of Sulfonium and Sulfonyl Groups
  - Nitrogen Functional Group Reductions
  - Radical Cyclizations
  - Reductive Epoxide and Aziridine Opening
  - Reduction-Labile Protecting Groups

Net Reductive Reactions: Reduction of Electron Poor Olefins

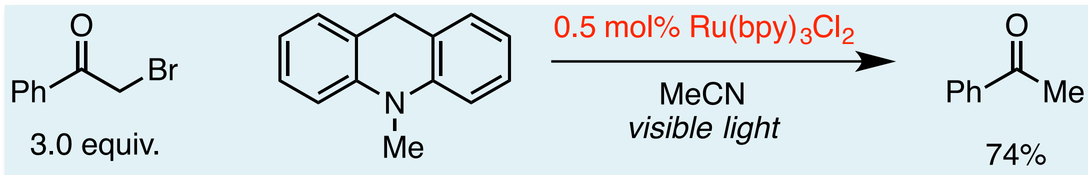


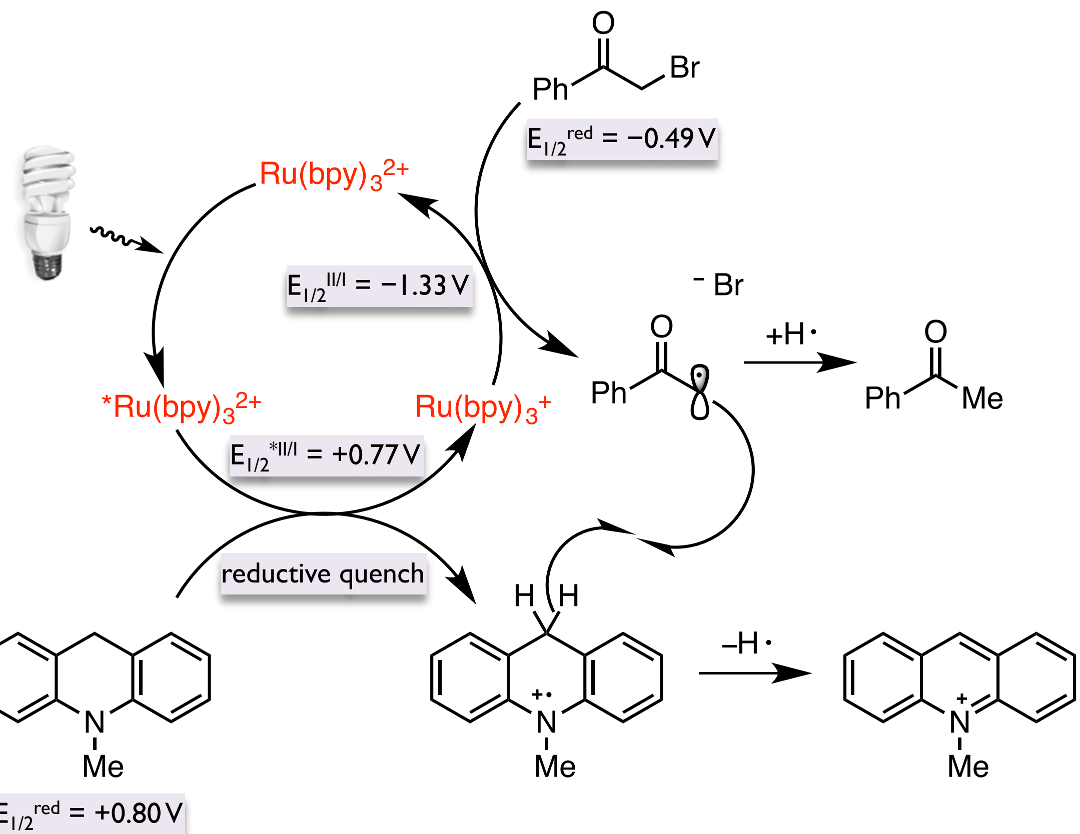




Pac, C.; Ihama, M.; Yasuda, M.; Miyauchi, Y.; Sakurai, H. *J. Am. Chem. Soc.* **1981**, *103*, 6495.

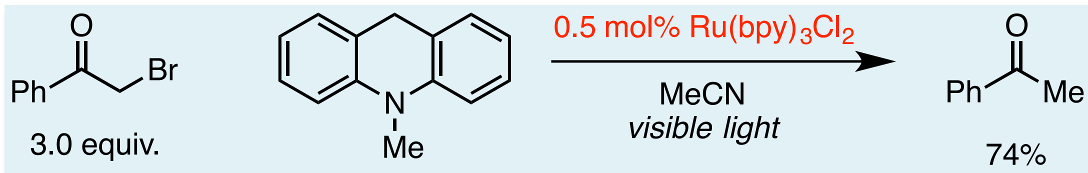
Net Reductive Reactions: Reductive Dehalogenation



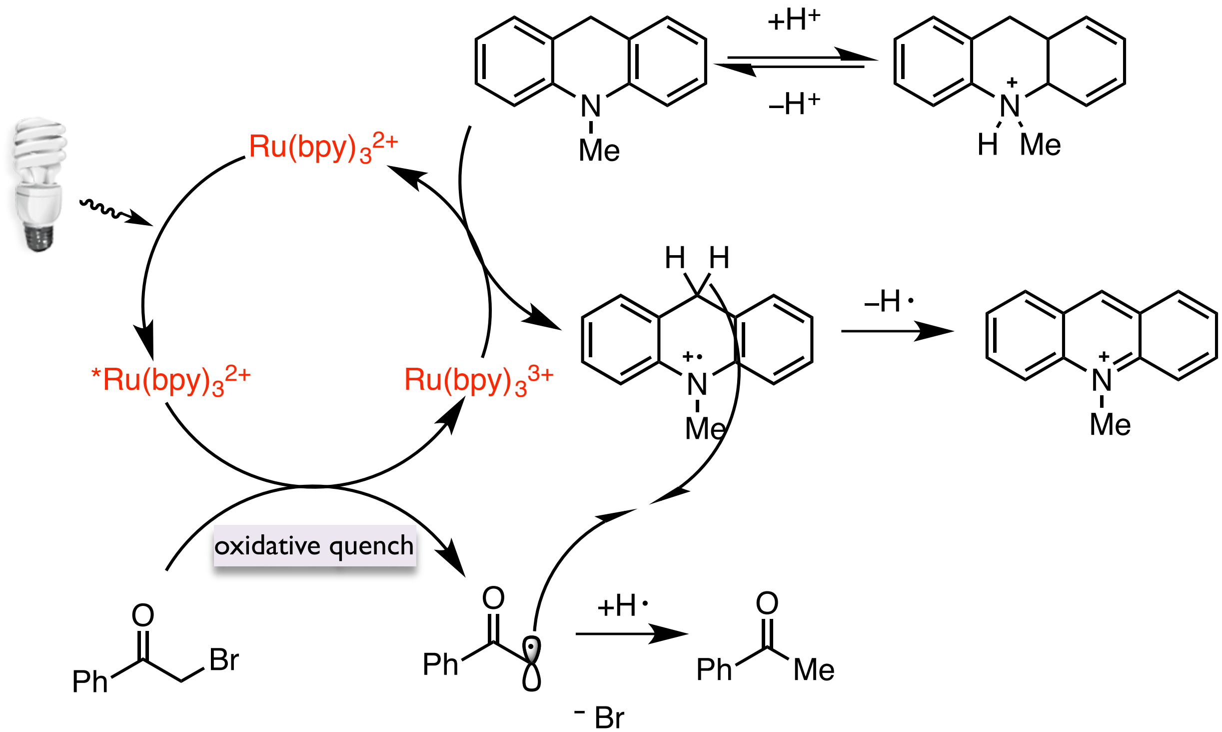


Fukuzumi, S.; Muchizuki, S.; Tanaka, T. *J. Phys. Chem.* **1990**, *94*, 722.
Fukuzumi, S.; Koumitsu, S.; Hironaka, K.; Tanaka, T. *J. Am. Chem. Soc.* **1987**, *109*, 305.
Tanner, D. D.; Singh, H. K. *J. Org. Chem.* **1986**, *51*, 5182.

Net Reductive Reactions: Reductive Dehalogenation



- Addition of acid ($HClO_4$) results in a switch from reductive to oxidative quenching



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Fukuzumi, S.; Koumitsu, S.; Hironaka, K.; Tnaaka, T. *J. Am. Chem. Soc.* **1987**, *109*, 305.
Tanner, D. D.; Singh, H. K. *J. Org. Chem.* **1986**, *51*, 5182.

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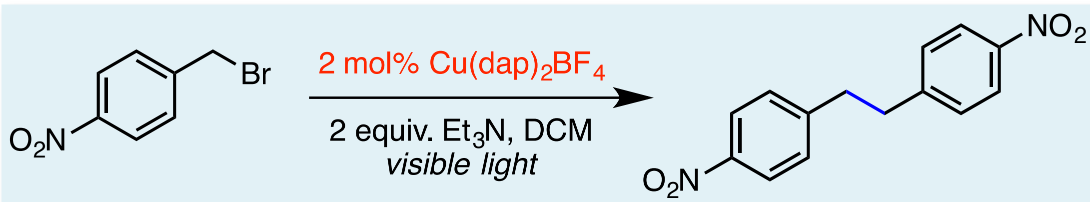
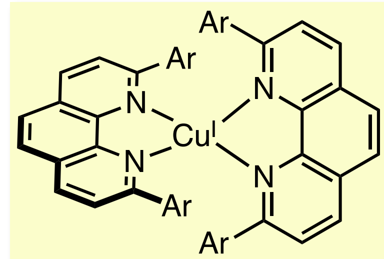
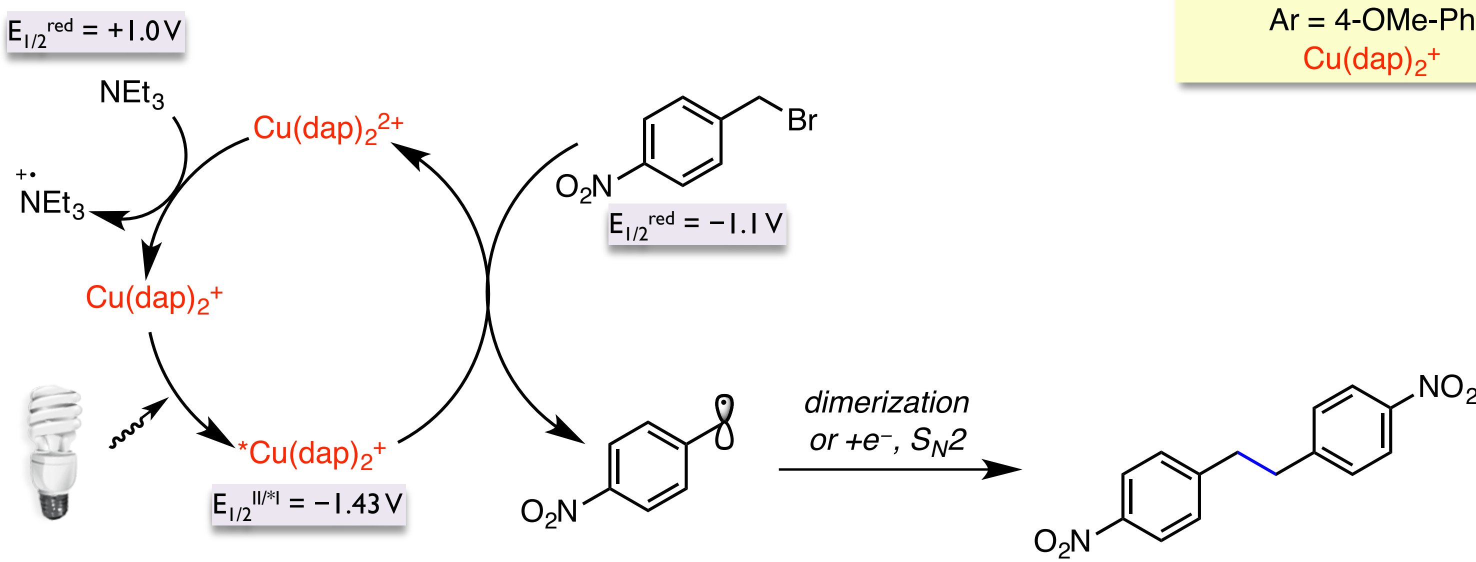




Ar = 4-OMe-Ph

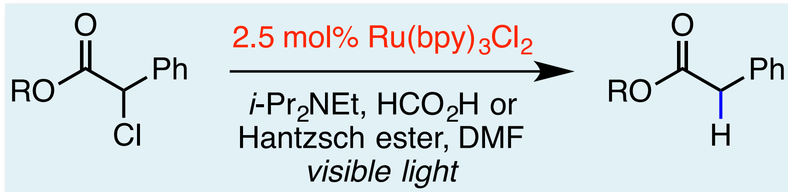
$Cu(dap)_2^+$

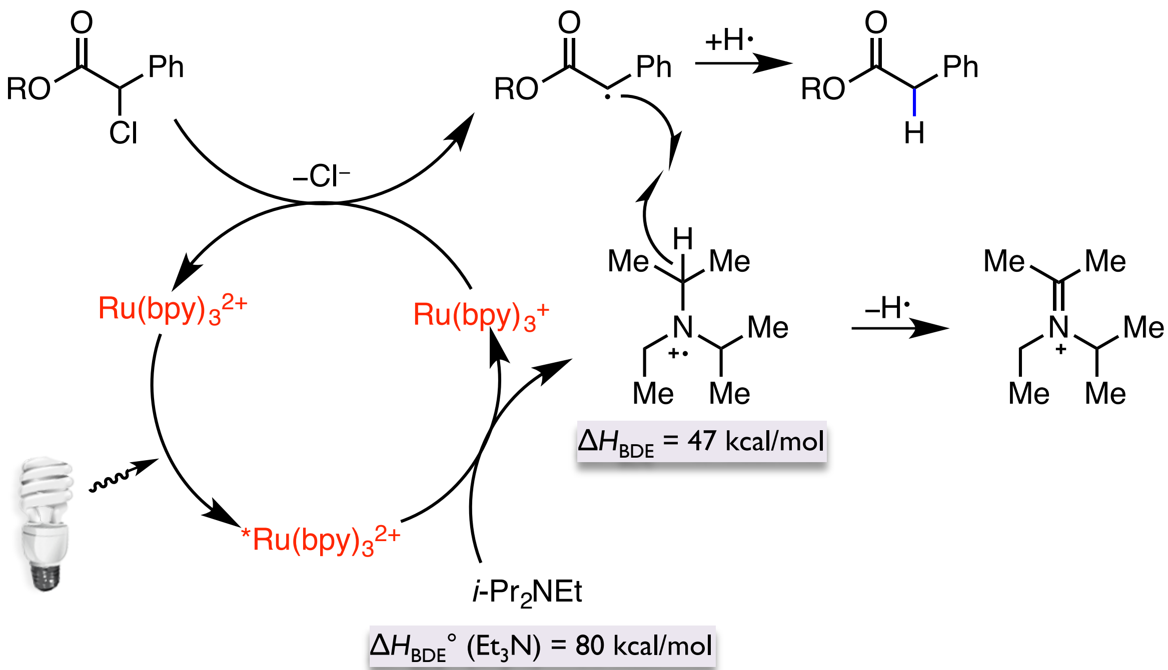


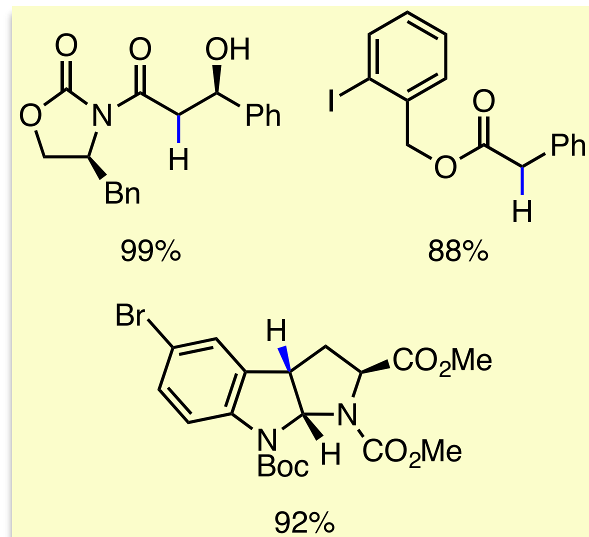
- $Cu(dap)_2^+$ is substantially more reducing than $Ru(bpy)_3^{2+}$ and can perform the reduction directly from its photoexcited state

Kern, J.-M.; Sauvage, J.-P. *J. Am. Chem. Soc., Chem. Commun.* **1987**, 546.

Net Reductive Reactions: Reductive Dehalogenation





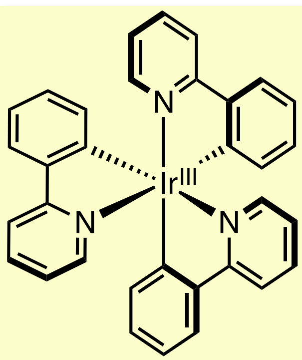


- Selective for the dehalogenation of alkyl bromides and chlorides α-to electron-withdrawing groups over vinyl iodides and aryl bromides and iodides
- Tolerant of protecting groups (silyl ethers and carbamates)

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

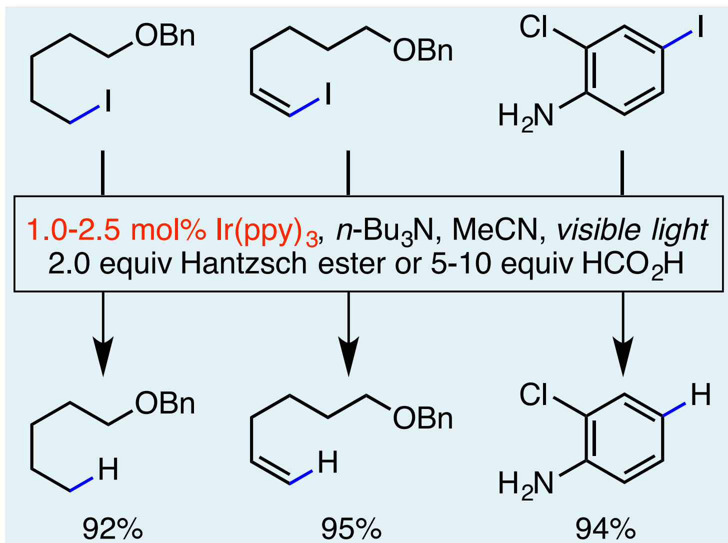
Net Reductive Reactions: Reductive Dehalogenation

- Limitation of reduction dehalogenation with $Ru(bpy)^{2+}$ is the requirement for activated halides
- The reductive dehalogenation of alkyl, alkenyl, and aryl iodides can be achieved using iridium photocatalyst *fac*-$Ir(ppy)_3$
- Allows for the selective dehalogenation of aryl iodides in the presence of aryl bromides and chlorides



fac-$Ir(ppy)_3$

$E_{1/2}^{IV/*III} = -1.73$ V

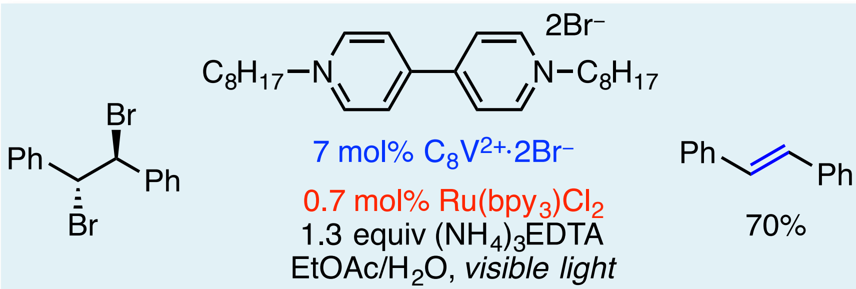


$E_{1/2}^{red}$ (ethyl iodide) = −1.67 V

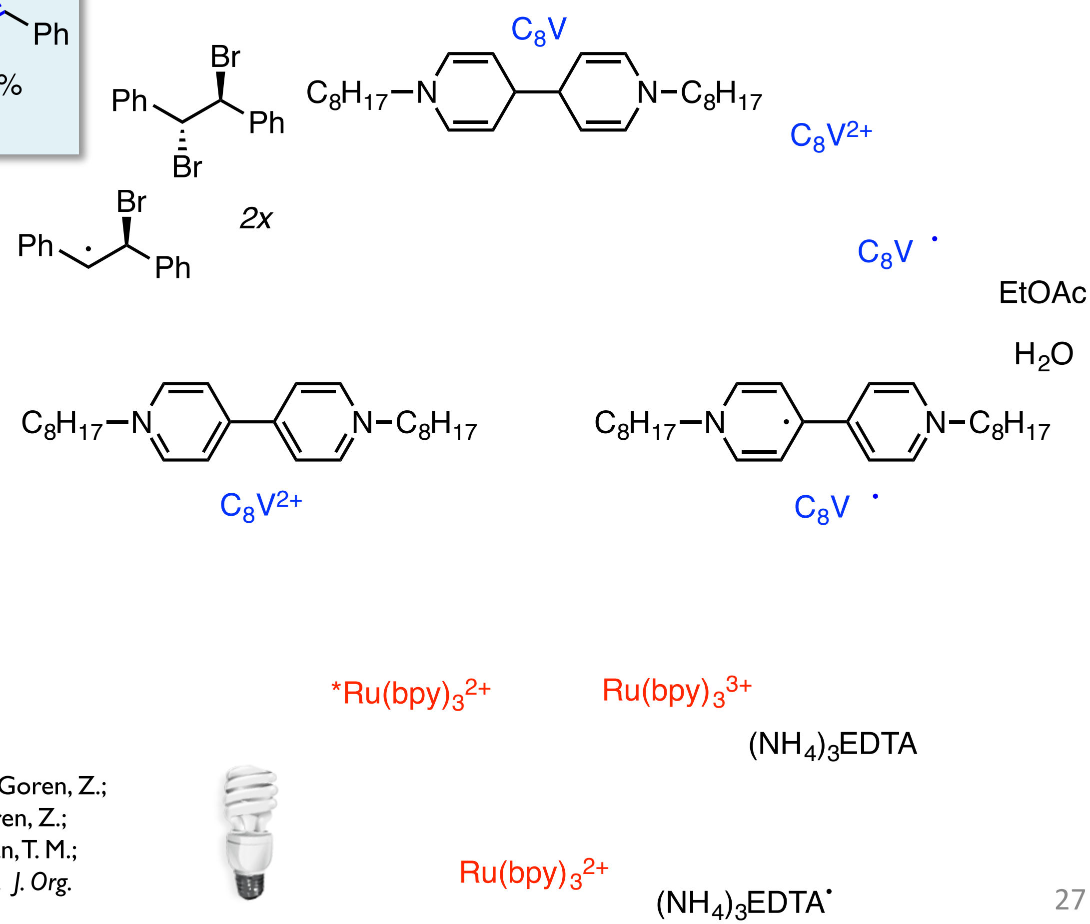
Nguyen, J. D.; D'Amato, E. M.; Narayanam, J. M. R.; Stephenson, C. R. J. *Nature Chem.* **2012**, *4*, 854.

Net Reductive Reactions: Reductive Dehalogenation

- Reduction of *vic*-dibromides via photoredox and viologen catalysis in a biphasic system



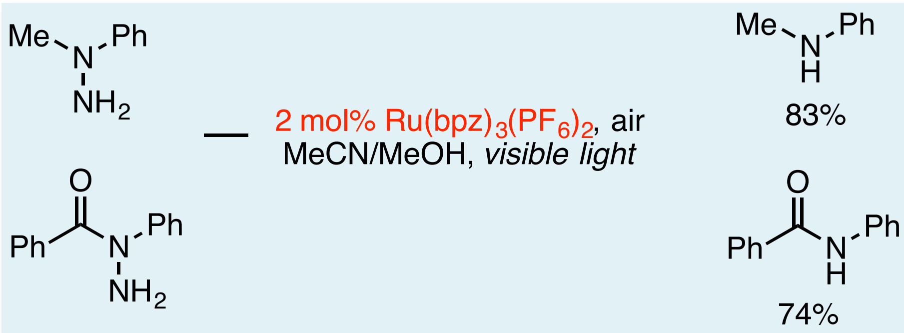
When reaction mixture is monophasic, the cis isomer forms as the reaction progresses via energy transfer from photocatalyst

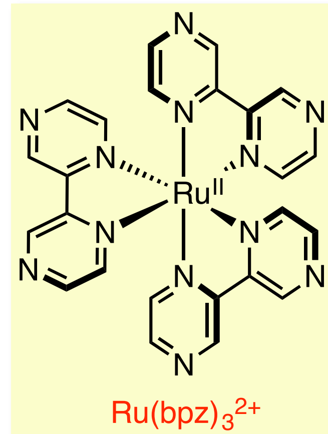


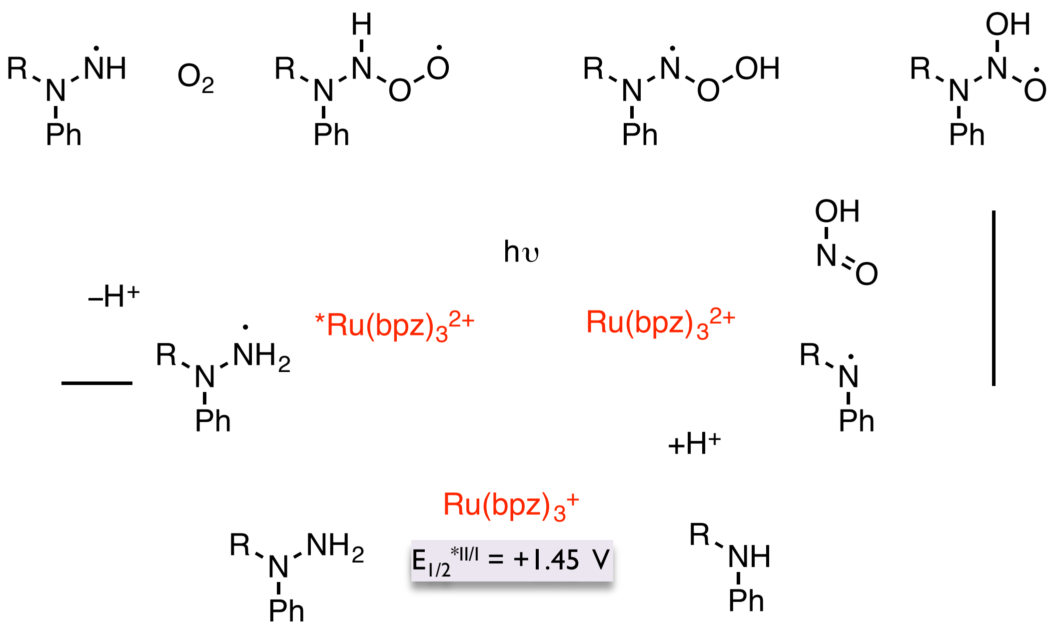
(a) Goren, Z.; Willner, I. *J. Am. Chem. Soc.* **1983**, *105*, 7764. (b) Maidan, R.; Goren, Z.; Becker, J. Y.; Willner, I. *J. Am. Chem. Soc.* **1984**, *106*, 6217. (c) Willner, I.; Goren, Z.; Mandler, D.; Maidan, R.; Degani, Y. *J. Photochem.* **1985**, *28*, 215. (d) Bockman, T. M.; Kochi, J. K. *J. Org. Chem.* **1990**, *55*, 4127. (e) Willner, I.; Tsfania, T.; Eichen, Y. *J. Org. Chem.* **1990**, *55*, 2656.

Net Reductive Reactions: Nitrogen Functional Group Reductions

- Reduction of hydrazides and hydrazines





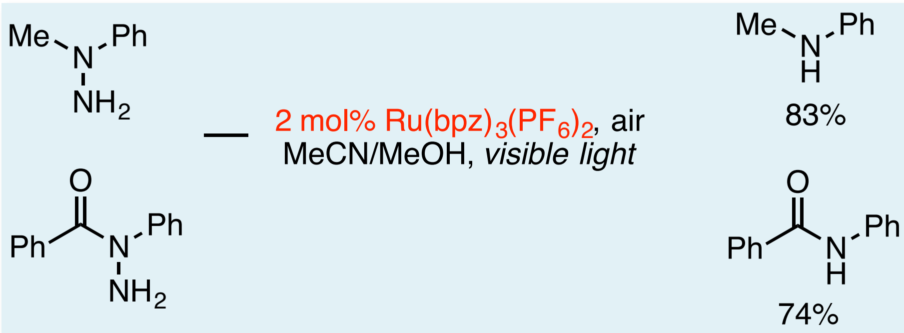


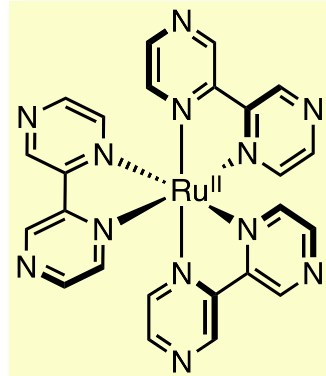
NH_2 group required and tri- or tetra-substituted hydrazines do not give the products of N-N bond cleavage

Zhu, M.; Zheng, N. *Synthesis* **2011**, *14*, 2223.

Net Reductive Reactions: Nitrogen Functional Group Reductions

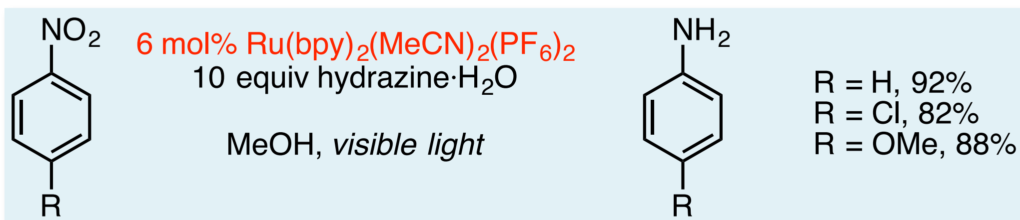
- Reduction of hydrazides and hydrazines



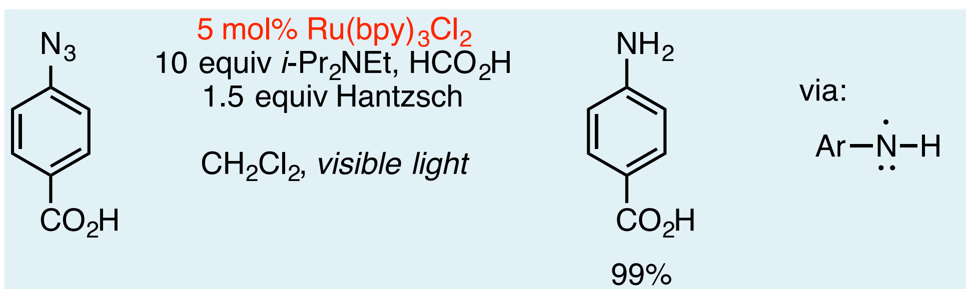


$Ru(bpz)_3^{2+}$

- Reduction of nitrobenzenes to anilines



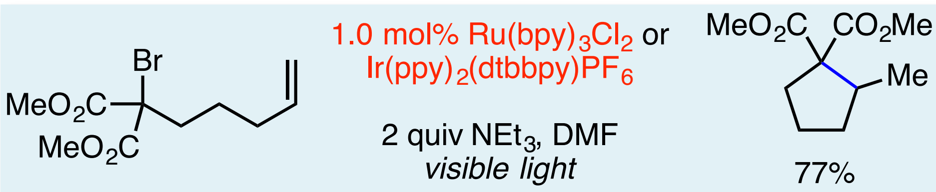
- Reduction of azides to amines

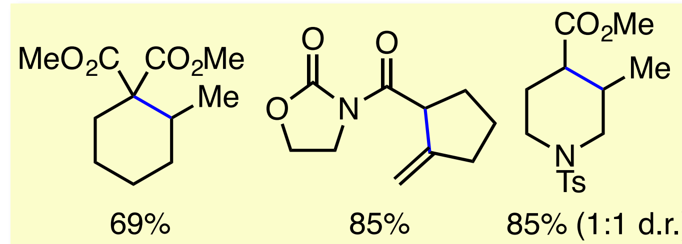


(a) Hirao, T.; Shiori, J.; Okahata, N. *Bull. Chem. Soc. Jpn.* **2004**, 77, 1763. (b)Chen, Y.; Kamlet, A. S.; Steinman, J. B.; Liu, D. R. *Nat. Chem.* **2011**, *3*, 146.

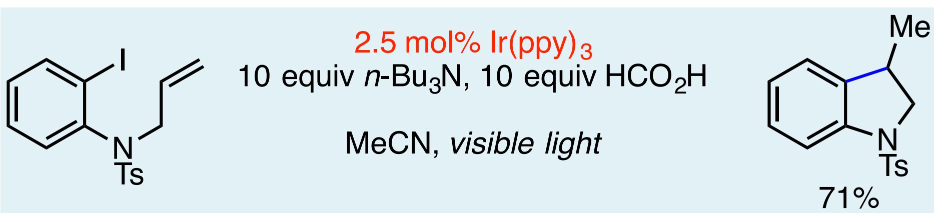
Net Reductive Reactions: Radical Cyclizations

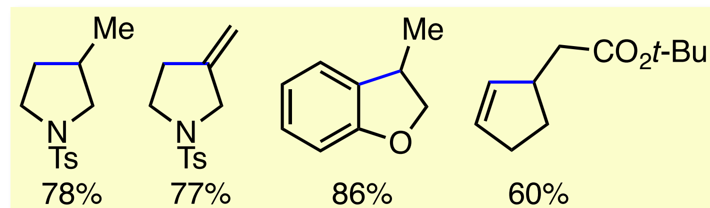
- Photoredox-catalyzed reductive radical cyclization



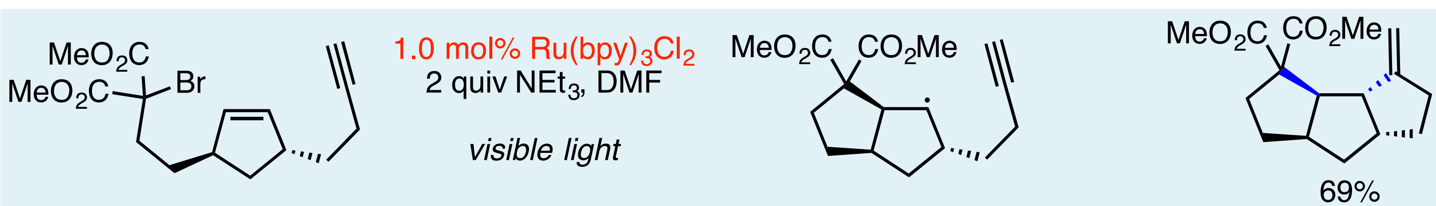


- Radical cyclizations of alkyl, alkenyl, and aryl iodides





- Cascade photoredox cyclization reactions



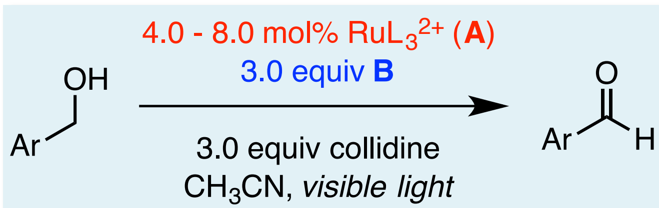
(a) Tucker, J. W.; Nguyen, J. D.; Narayanam, J. M. R.; Krabbe, S. W.; Stephenson, C. R. J. *Chem Comm.* **2010**, *46*, 4985. (b) Kim, H.; Lee, C. *Angew. Chem., Int. Ed.* **2012**, *51*, 12303. (c) Tucker, J. W.; Stephenson, C. R. J. *Org. Lett.* **2011**, *13*, 5468.

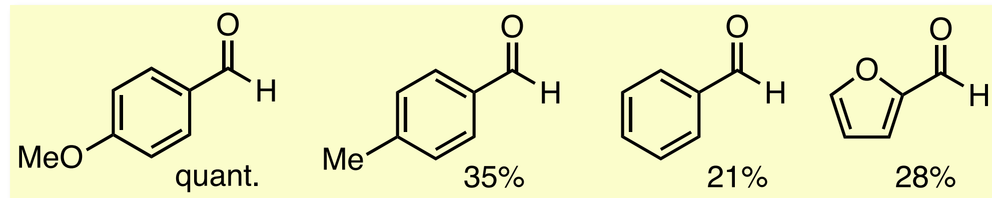
Visible Light Photoredox Catalysis: Applications in Organic Synthesis

- Net Oxidative Reactions
  - Functional Group Oxidations
  - Oxidative Removal of the PMB Group
  - Oxidative Biaryl Coupling
  - Oxidative Generation of Iminium Ions
  - Azomethine Ylide [3+2] Cycloadditions
  - Cyclizations of Aminium Radical Cations

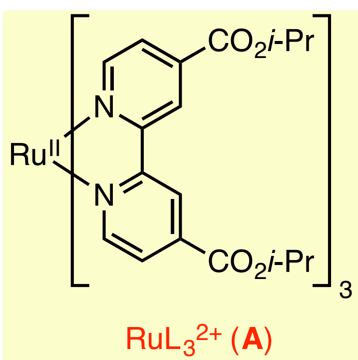
Net Oxidative Reactions: Functional Group Oxidations

- Oxidation of benzylic alcohols to aldehydes

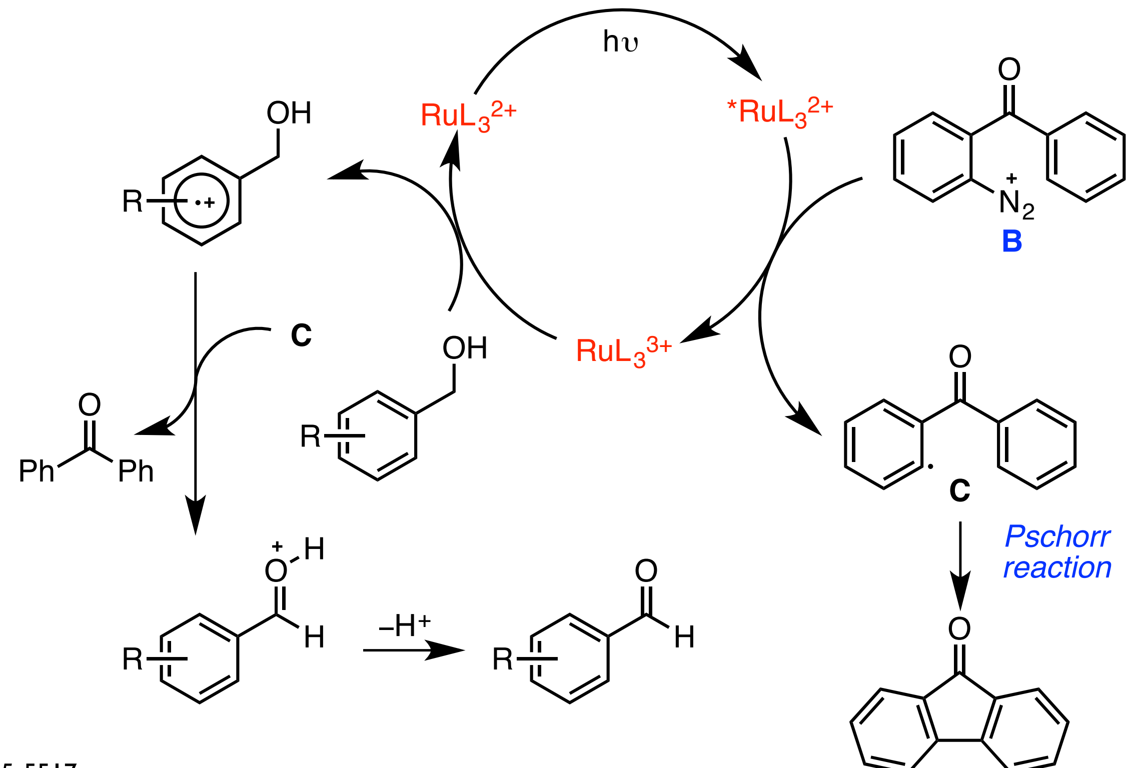




$E_{1/2}^{red}$ (OH) = +1.52 V $E_{1/2}^{red}$ (OH) = +1.89 V $E_{1/2}^{red}$ (OH) = +2.19 V



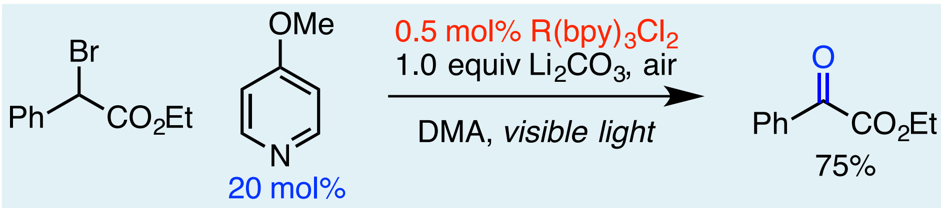
$E_{1/2}^{III/II}$ = +1.59 V

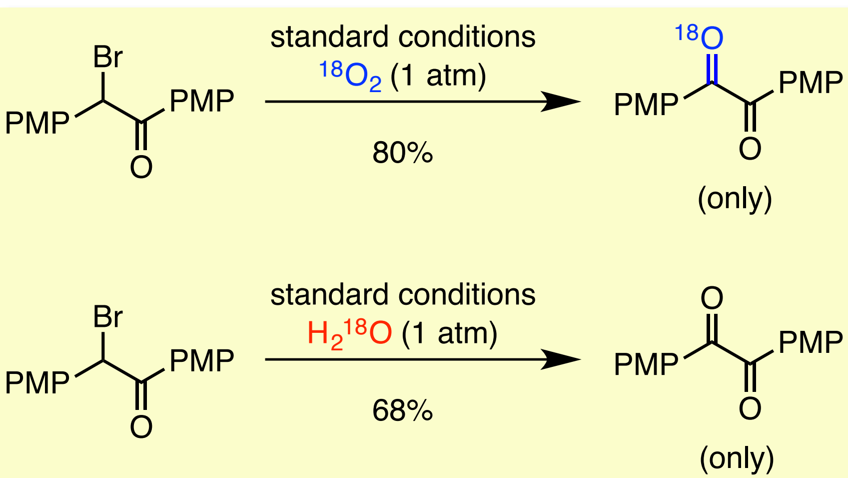


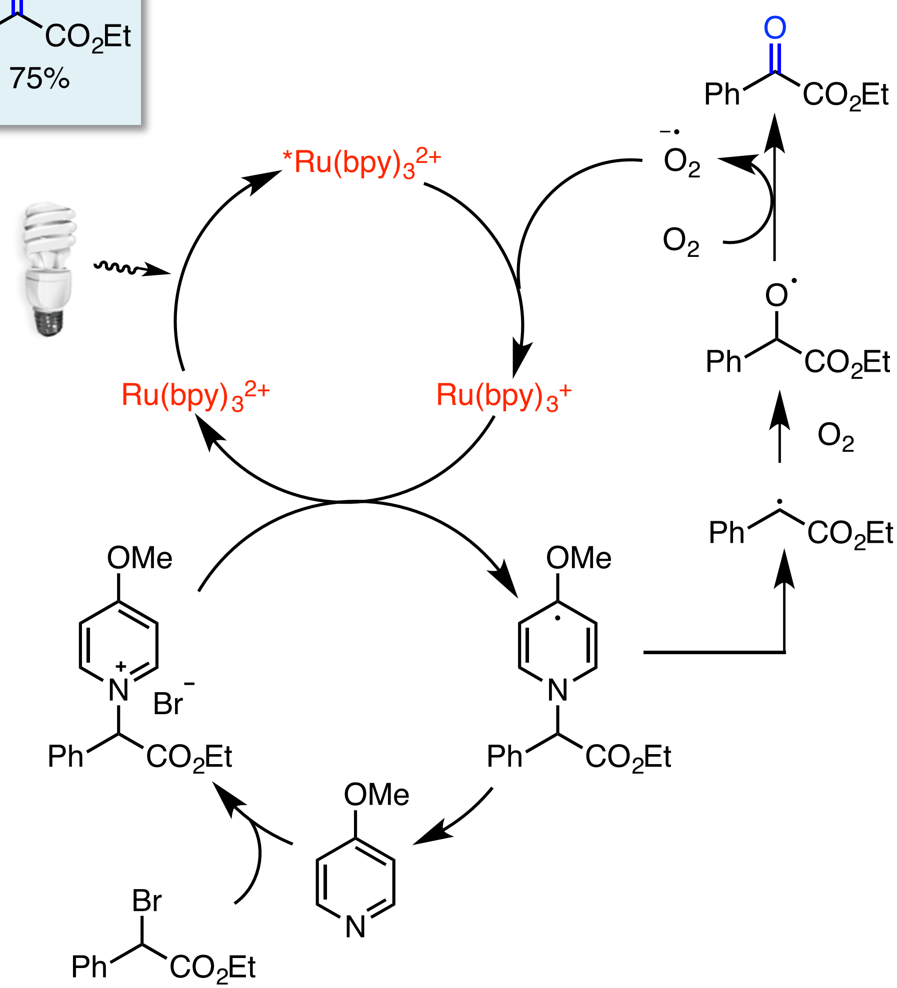
Cano-Yelo, H.; Deronzier, A. *Tetrahedron Lett.* **1984**, *25*, 5517.

Net Oxidative Reactions: Functional Group Oxidations

- Photoredox oxidation of α-haloester to α-ketoesters



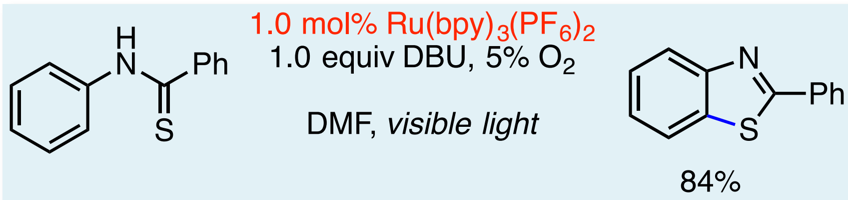


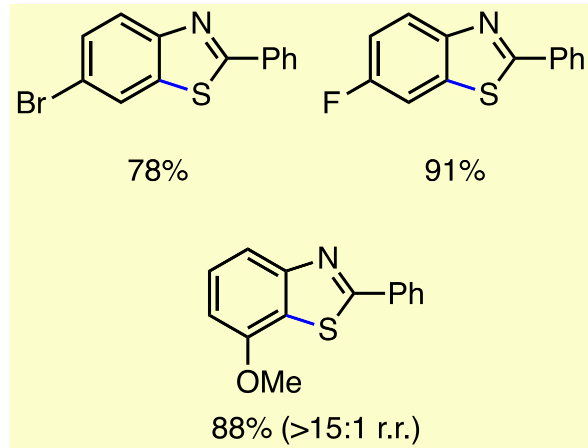


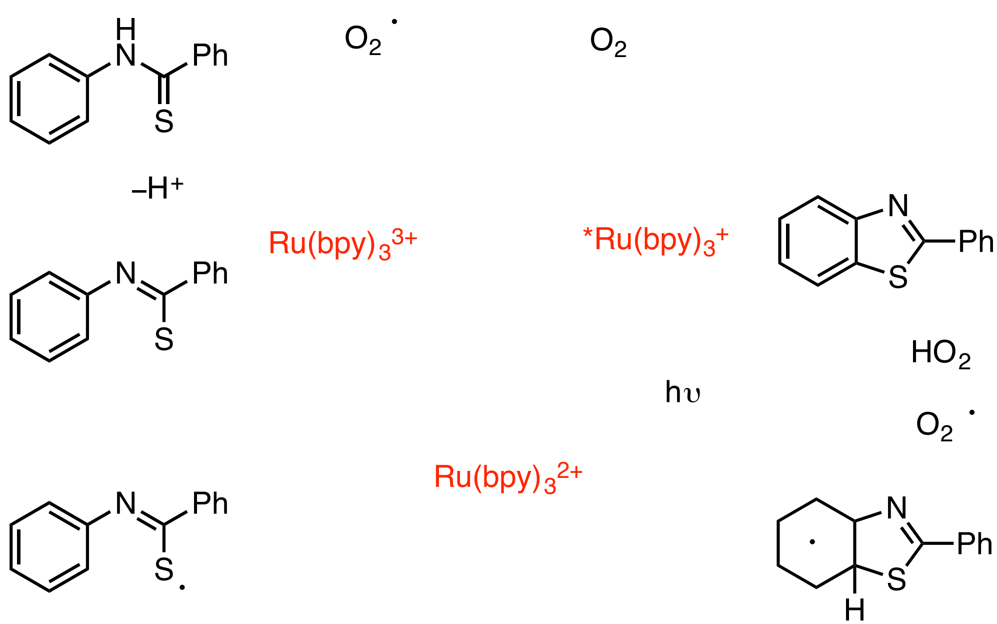
Su, Y.; Zhang, L.; Jioa, N. *Org. Lett.* **2011**, *13*, 2168.
Recupero, f.; Punta, C. *Chem. Rev.* **2007**, *107*, 3800.

Net Oxidative Reactions: Functional Group Oxidations

- Oxidative conversion of thiobenzamides to benzothiazoles





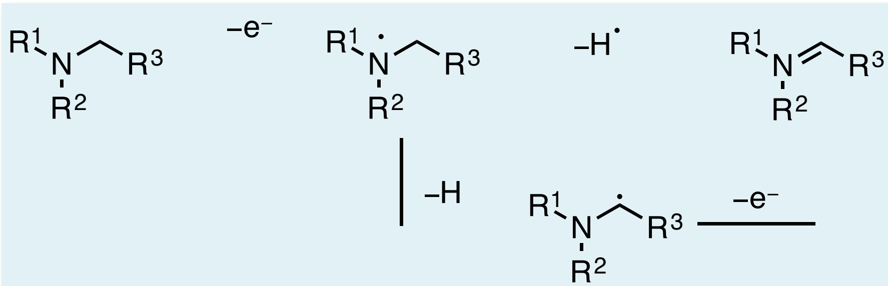


High regioselectivity for addition *ortho* to a functional group

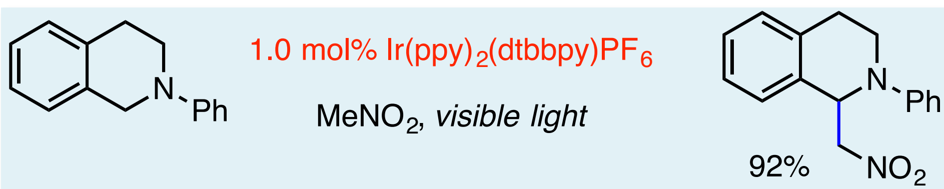
Cheng, Y.; Yang, J.; Qu, Y.; Li, P. *Org. Lett.* **2012**, *14*, 98.

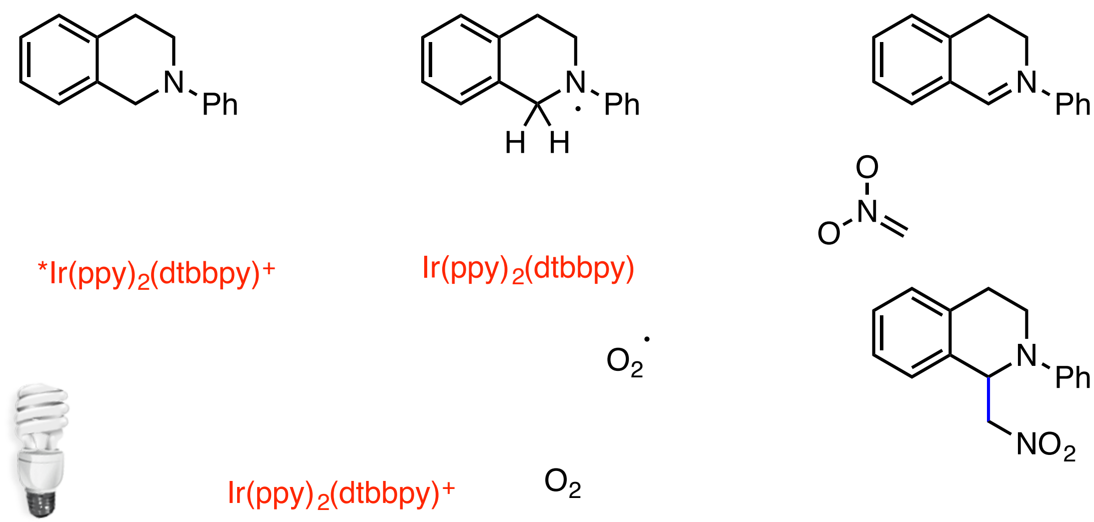
Net Oxidative Reactions:
Oxidative Generation of Iminium Ions

- Pathways of amine oxidation to iminium ions



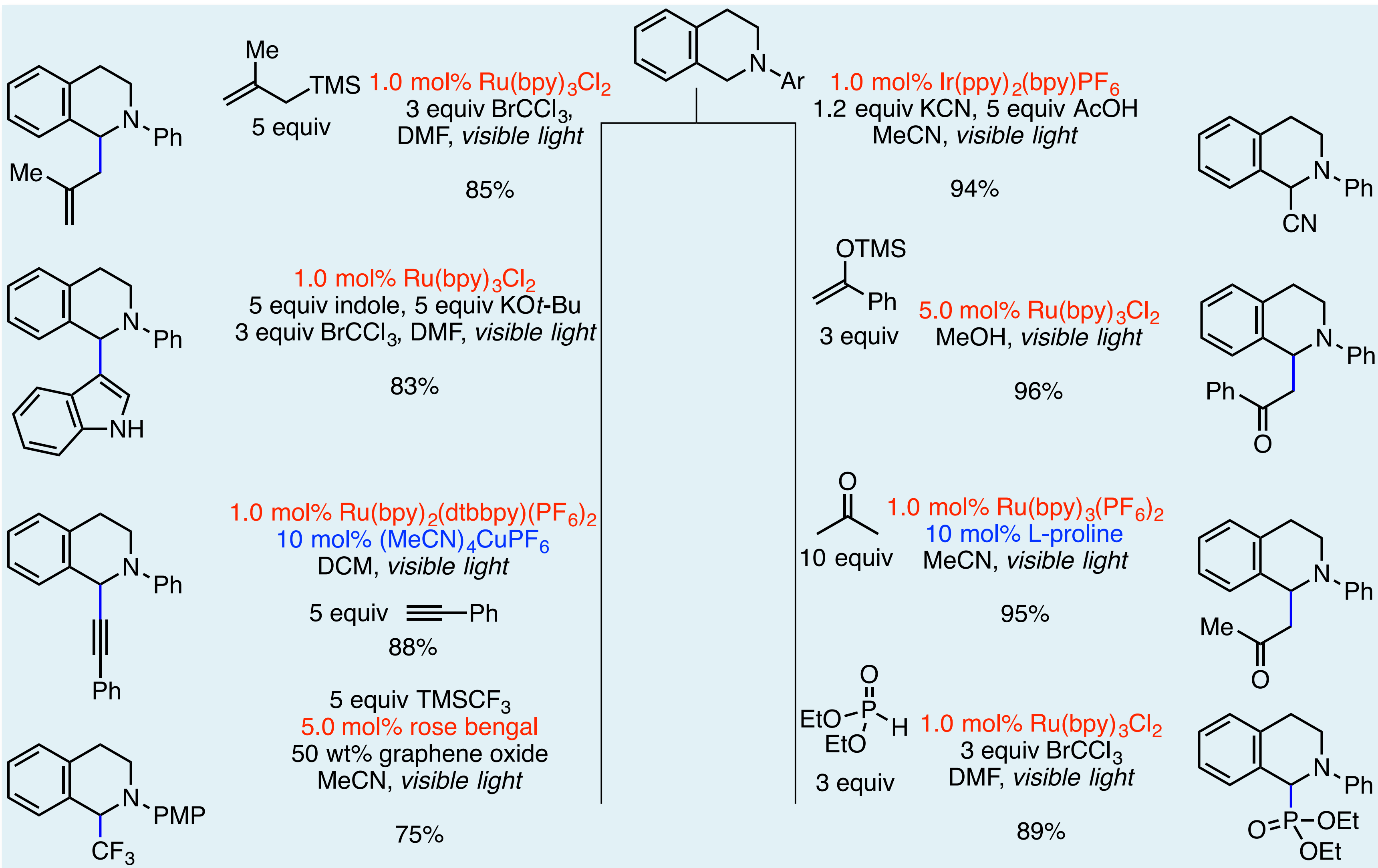
- Photoredox aza-Henry reaction via iminium intermediate





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

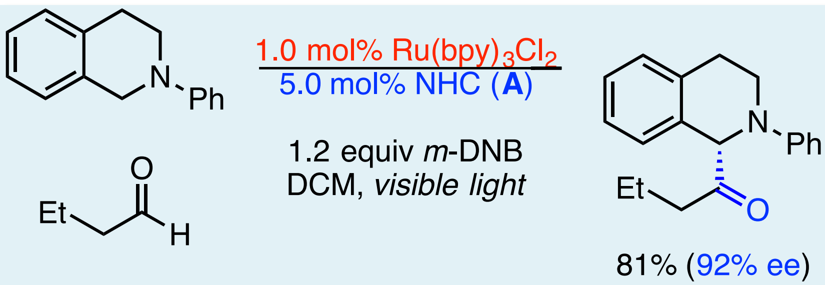
Net Oxidative Reactions:
Oxidative Generation of Iminium Ions

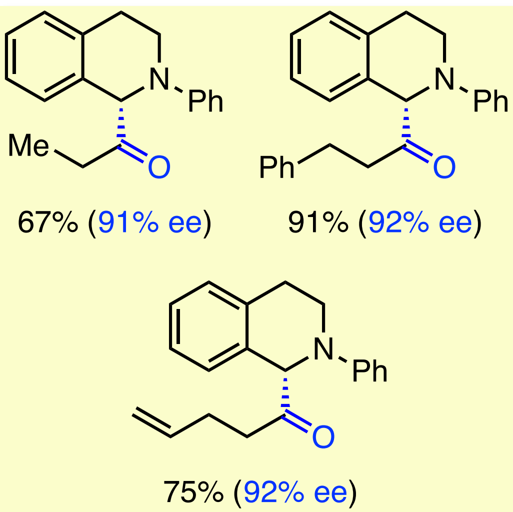


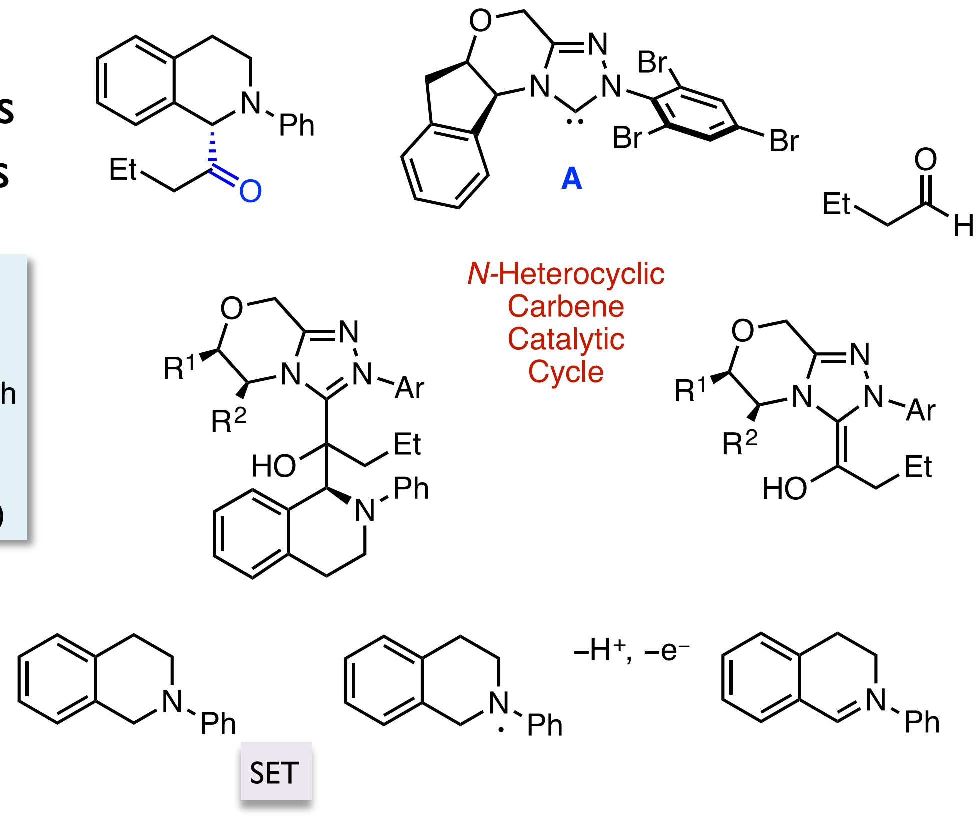
(a) Rueping, M.; Zhu, S.; Koenigs, R. M. *Chem. Commun.* **2011**, *47*, 12709. (b) Zhao, G.; Yang, C.; Guo, L.; Sun, H.; Chen, C.; Xia, W. *Chem. Commun.* **2012**, *48*, 2337. Rueping, M.; Vila, C.; Koenigs, R. M.; Poscharny, K.; Fabry, D. C. *Chem. Commun.* **2011**, *47*, 2360. (d) Rueping, M.; Zhu, S.; Koenigs, R. M. *Chem. Commun.* **2011**, *47*, 8679. (e) Freeman, D. B.; Furst, L.; Condie, A. G.; Stephenson, C. R. *J. Org. Lett.* **2012**, *14*, 94. (f) Rueping, M.; Koenigs, R. M.; Poscharny, K.; Fabry, D. C.; Leonori, D.; Vila, C. *Chem.-Eur. J.* **2012**, *18*, 5170. (g) Pan, Y.; Wang, S.; Kee, C. W.; Dubuisson, E.; Yang, Y.; Loh, K. P.; Tan, C.-H. *Green Chem.* **2011**, *13*, 3341. (h) Fu, W.; Guo, W.; Zou, G.; Xu, C. *J. Fluorine Chem.* **2012**, *140*, 88.

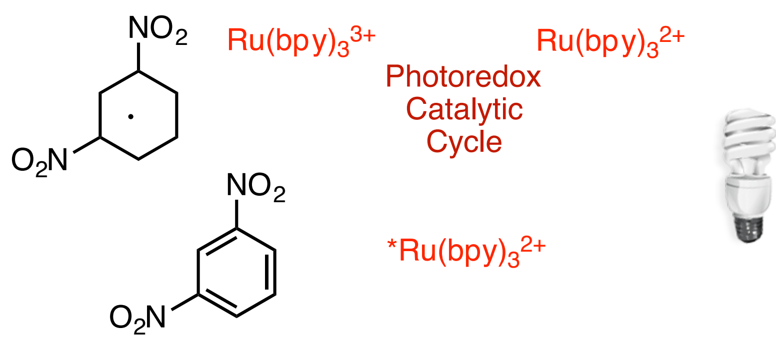
Net Oxidative Reactions:
Oxidative Generation of Iminium Ions

α-Acylation of amines:
Rovis's merger of photoredox catalysis with *N*-hetereocyclic carbene catalysis





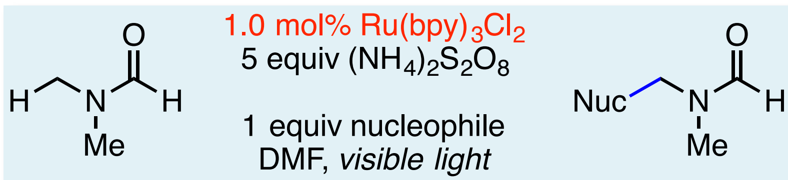


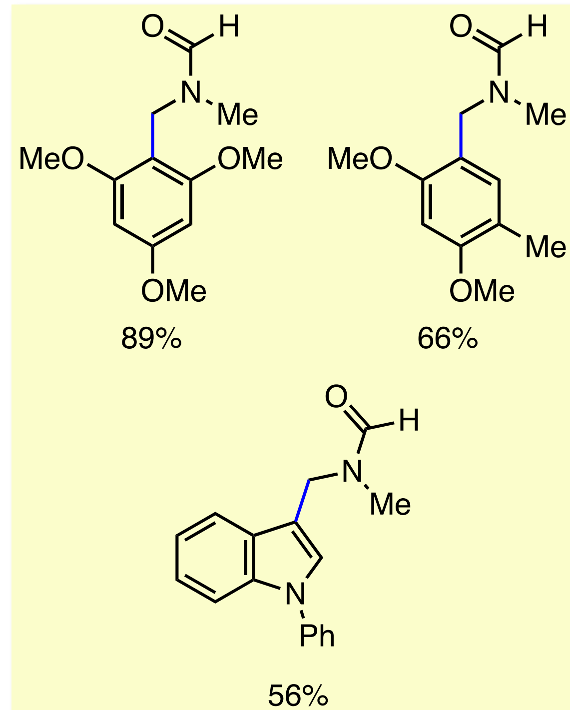


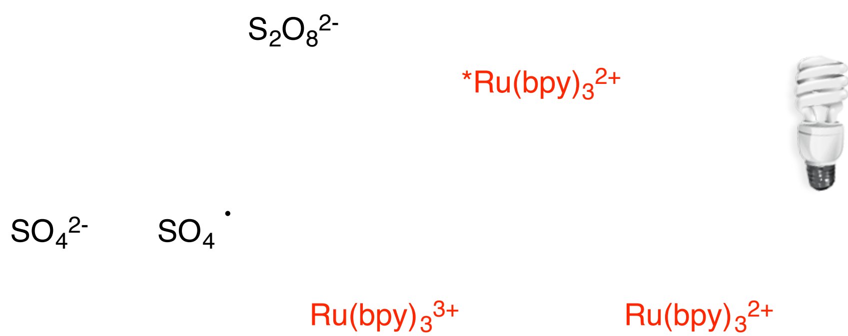
DiRocco, D. A.; Rovis, T. J. *J. Am. Chem. Soc.* **2012**, *134*, 8094.

Net Oxidative Reactions:
Oxidative Generation of Iminium Ions

- α-Arylation of amides via hydrogen atom abstraction
  - DMF: $E_{1/2}^{red}$ = +2.3 V vs. Et_3N: $E_{1/2}^{red}$ = +1.0 V







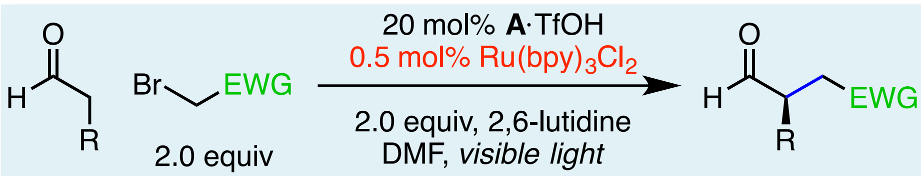
Dai, C.; Meschini, F.; Narayanam, J. M. R.; Stephenson, C. R. J. *J. Org. Chem.* **2012**, 77, 4425.

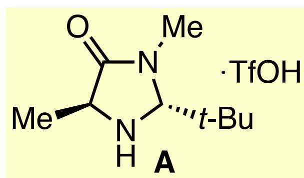
Visible Light Photoredox Catalysis: Applications in Organic Synthesis

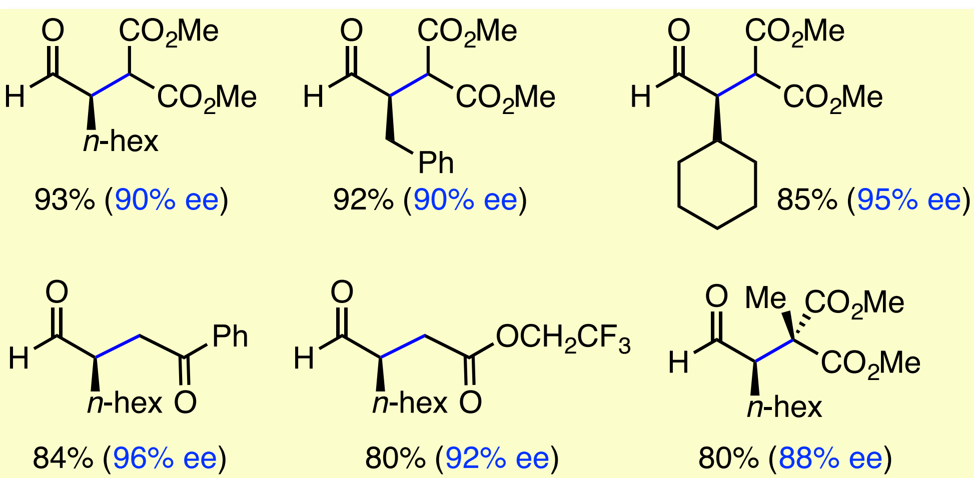
- Redox Neutral Reactions
  - Atom Transfer Radical Addition
  - Photoredox Organocatalysis
  - Radical Additions to Arenes
    - Arylation of Arenes: Diazonium Salts
    - Alkylation of Arenes
    - Trifluoromethylation of Arenes
    - Oxygenation of Arenes
  - Radical Additions to Other π Nucleophiles
  - Reactions of Enamine Radical Cations
  - [2 + 2] Cycloadditions
  - [4 + 2] and [2 + 2 + 2] Cycloadditions
  - [3 + 2] Cycloadditions: Cyclopropane Ring-Opening
  - Radical Conjugate Addition Reactions
  - α-Arylation of Amines
  - Hydrothiolation
  - Generation of the Vilsmeier-Haack Reagent

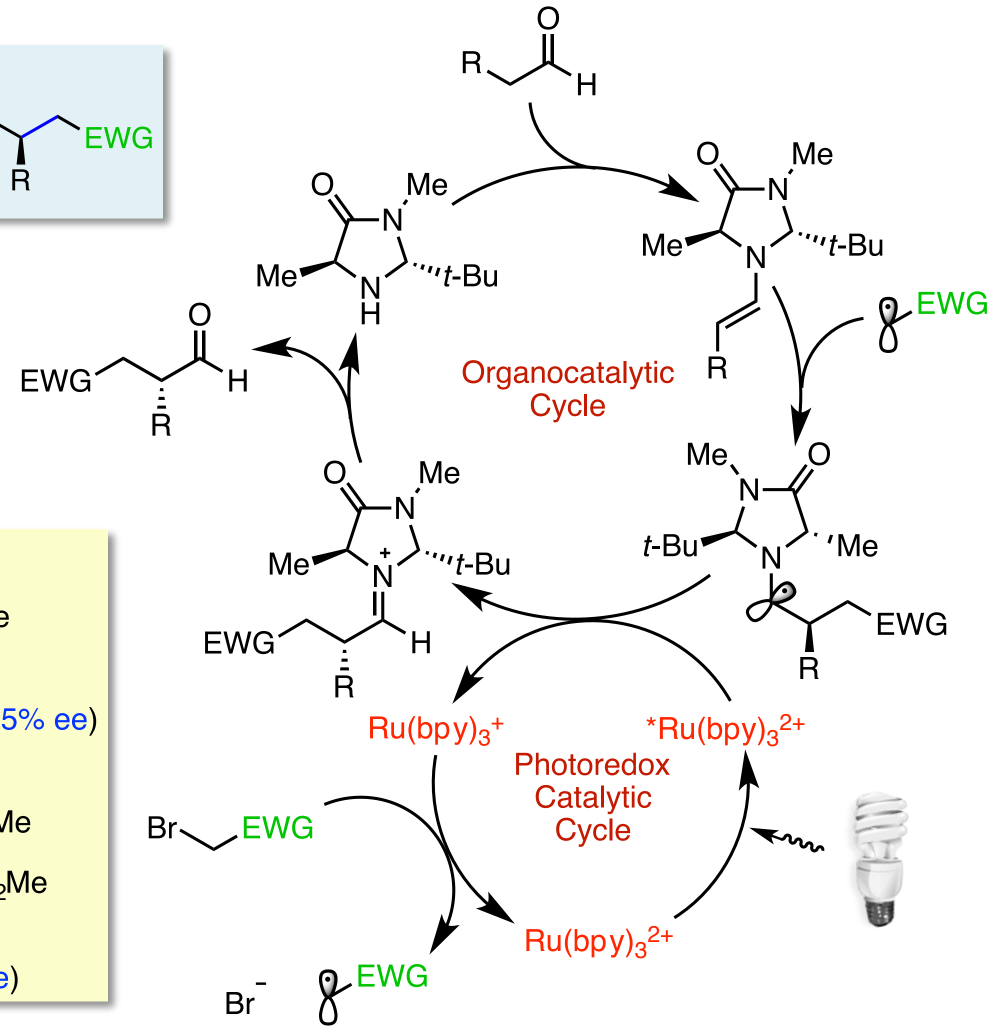
Redox Neutral Reactions: Photoredox Organocatalysis

- Merger of photoredox catalysis and enamine catalysis: asymmetric α-alkylation of aldehydes





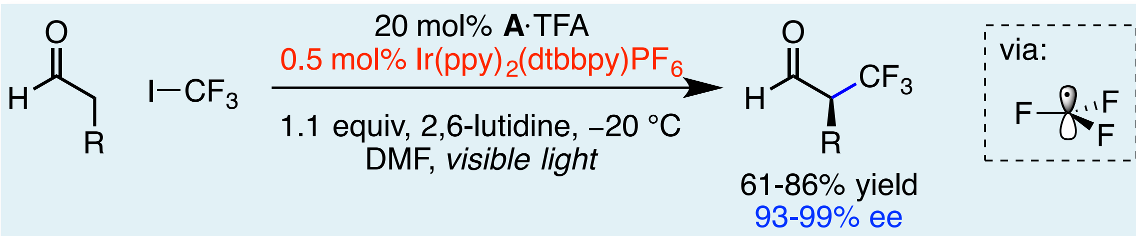


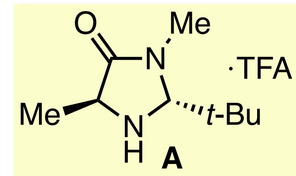


(a) MacMillan, D.W. C. *Nature* **2008**, *455*, 304. (b) Mukherjee, S.; Yang, J. W.; Hoffmann, S.; List, B. *Chem. Rev.* **2007**, *107*, 5471.

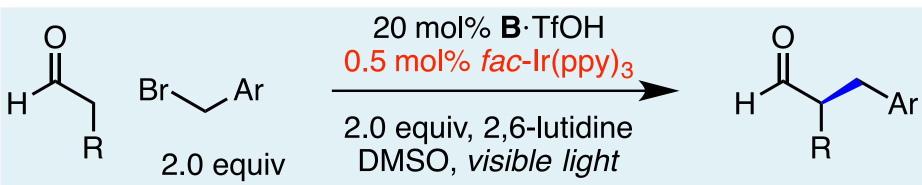
Redox Neutral Reactions: Photoredox Organocatalysis

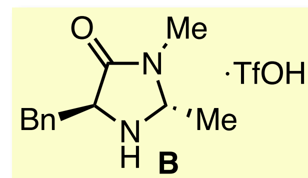
- α-Trifluoromethylation of aldehydes

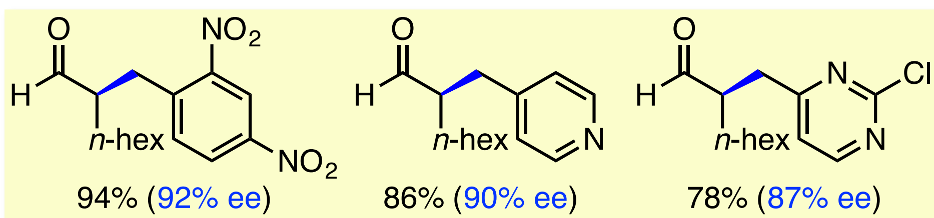




- α-Benzylation of aldehydes via photoredox organocatalysis



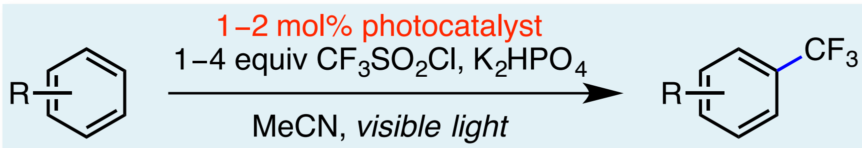


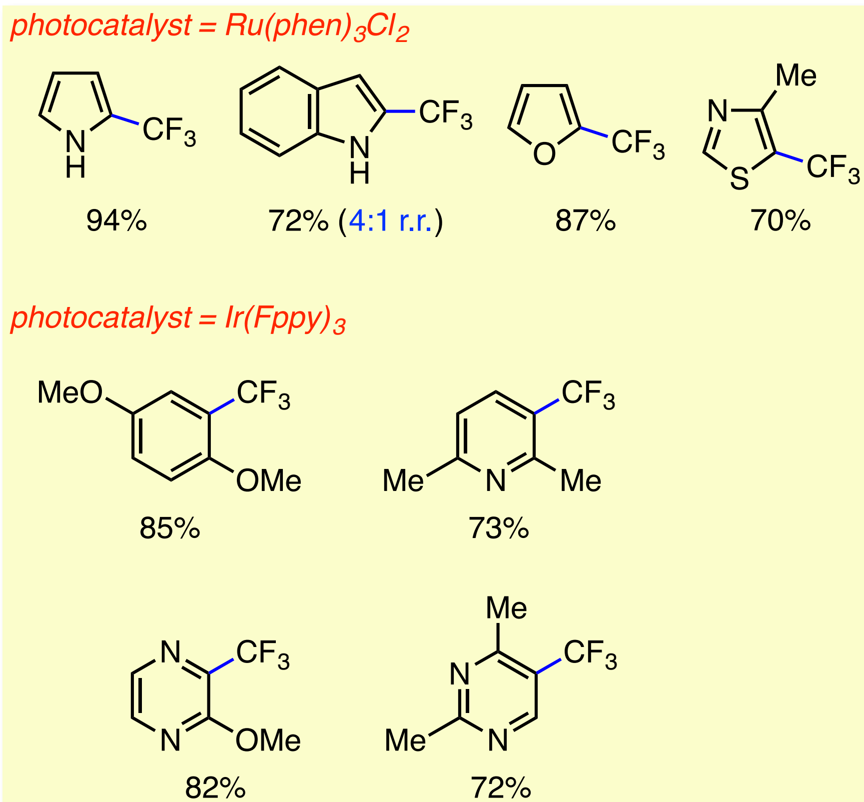


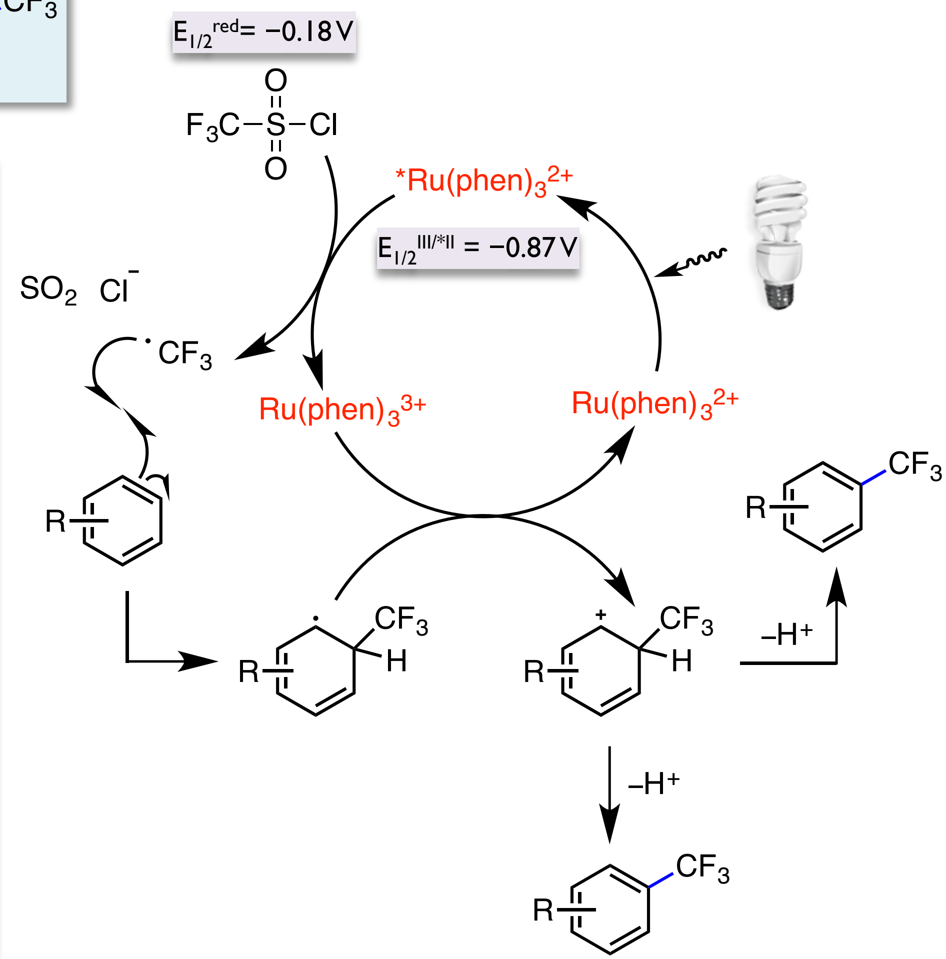
Nagib, D. A.; Scott, M. E.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2009**, *131*, 10875.
Shih, H.-W.; Vander Wal M. N.; Grange, R. L.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2010**, *132*, 13600.

Redox Neutral Reactions: Trifluromethylation of Arenes

- Photoredox arene and heteroarene trifluoromethylation



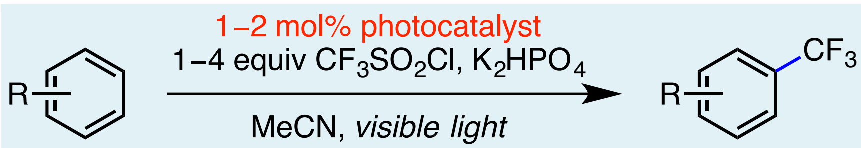


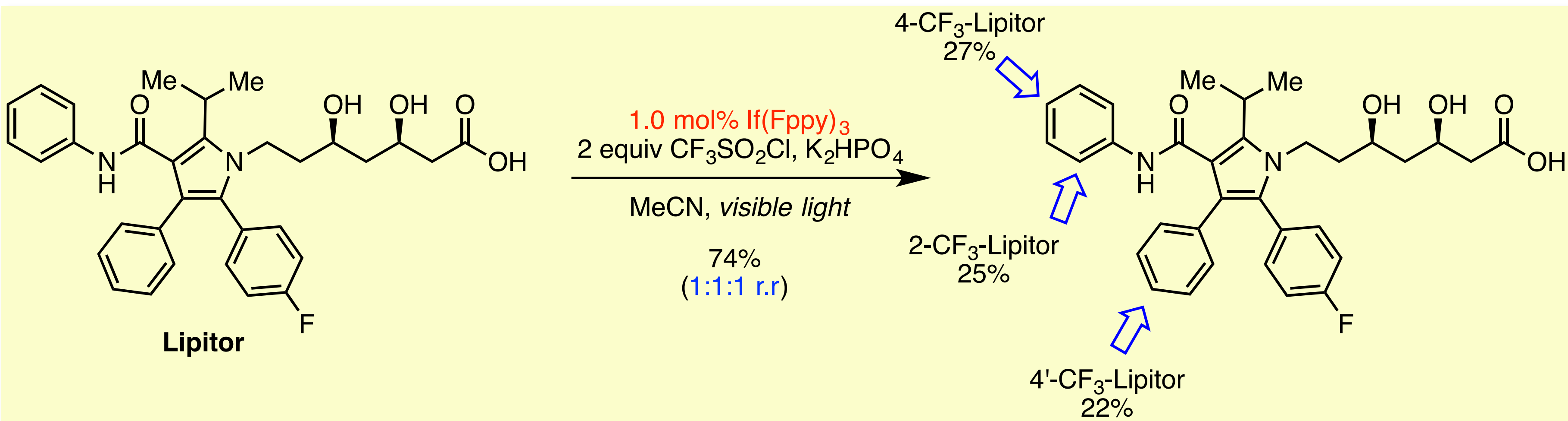


Nagib, D.A.; MacMillan, D.W. *Nature* **2011**, *480*, 224.

Redox Neutral Reactions: Triflurometylation of Arenes

- Photoredox arene and heteroarene trifluoromethylation

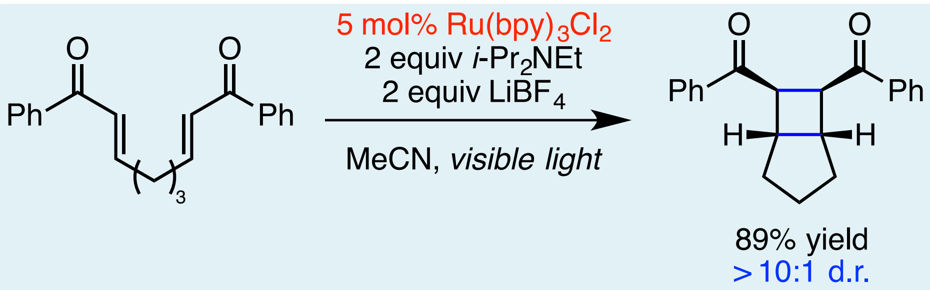


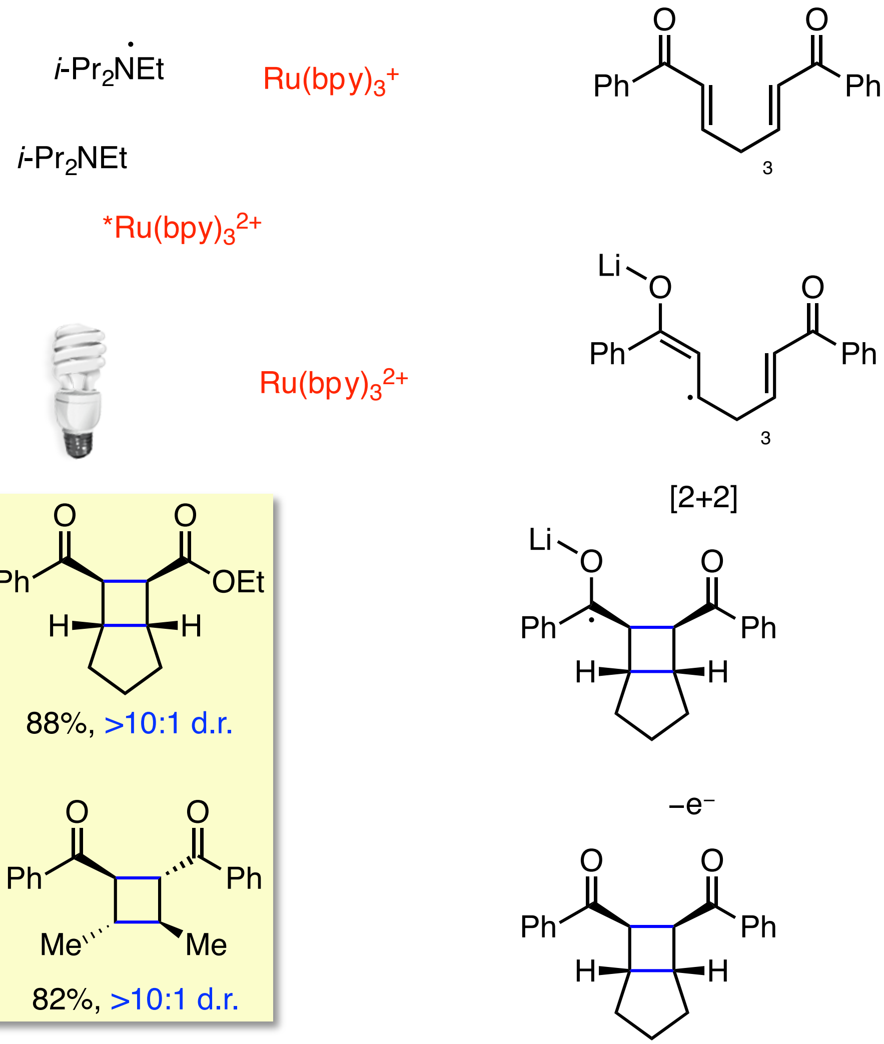


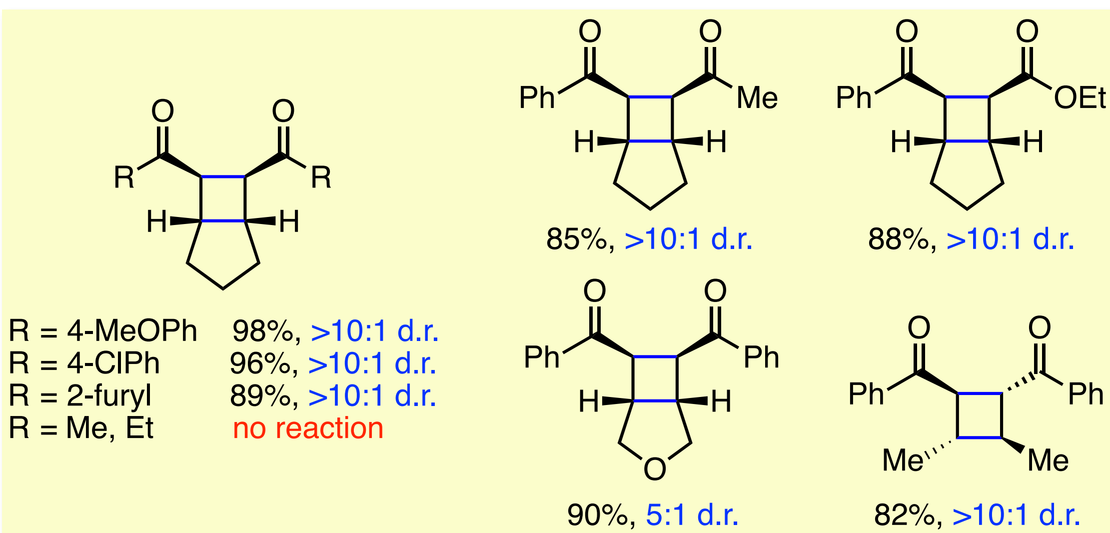
Nagib, D.A.; MacMillan, D.W. *Nature* **2011**, *480*, 224.

Redox Neutral Reactions: [2+2] Cycloadditions

- Photoredox eneone [2+2] cycloaddition



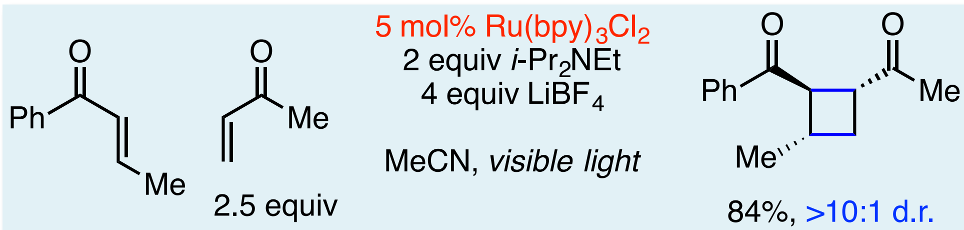


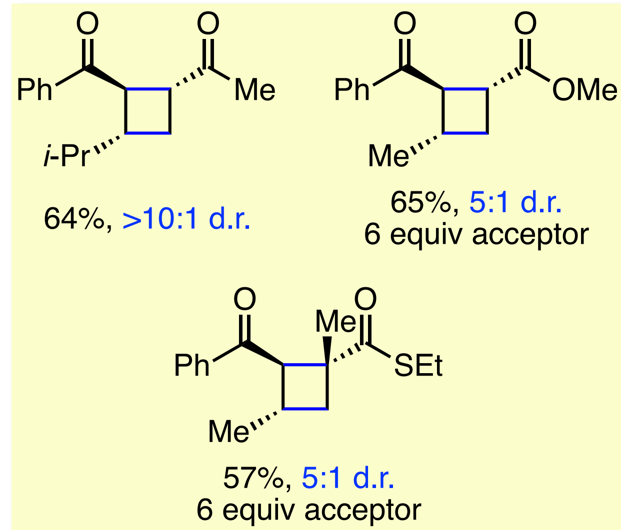


Ischay, M. A.; Anzovino, M. E.; Du, J.; Yoon, T. P. *J. Am. Chem. Soc.* **2008**, *130*, 12886.

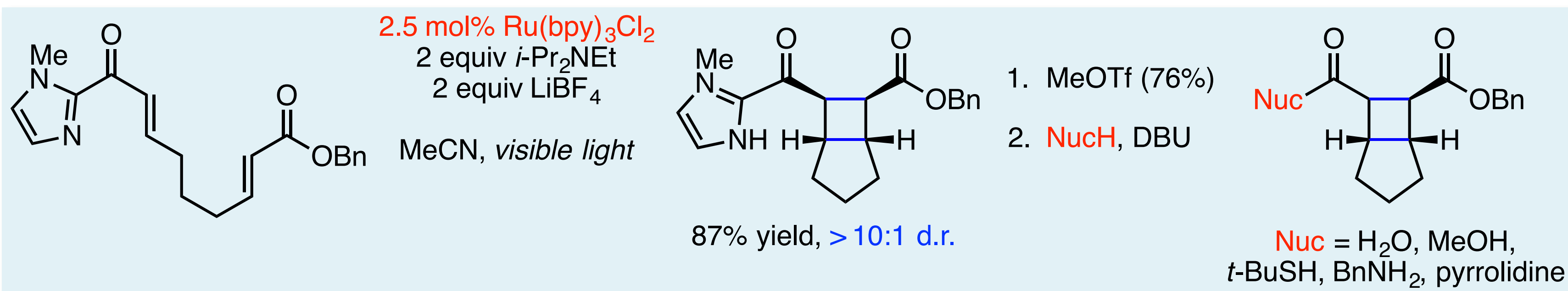
Redox Neutral Reactions: [2+2] Cycloadditions

- Crossed intermolecular [2+2] cycloaddition





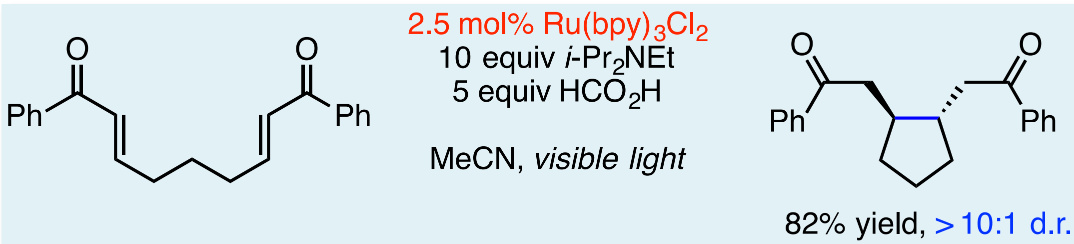
- Use of the *N*-methylimidazolyl group as a redox auxiliary

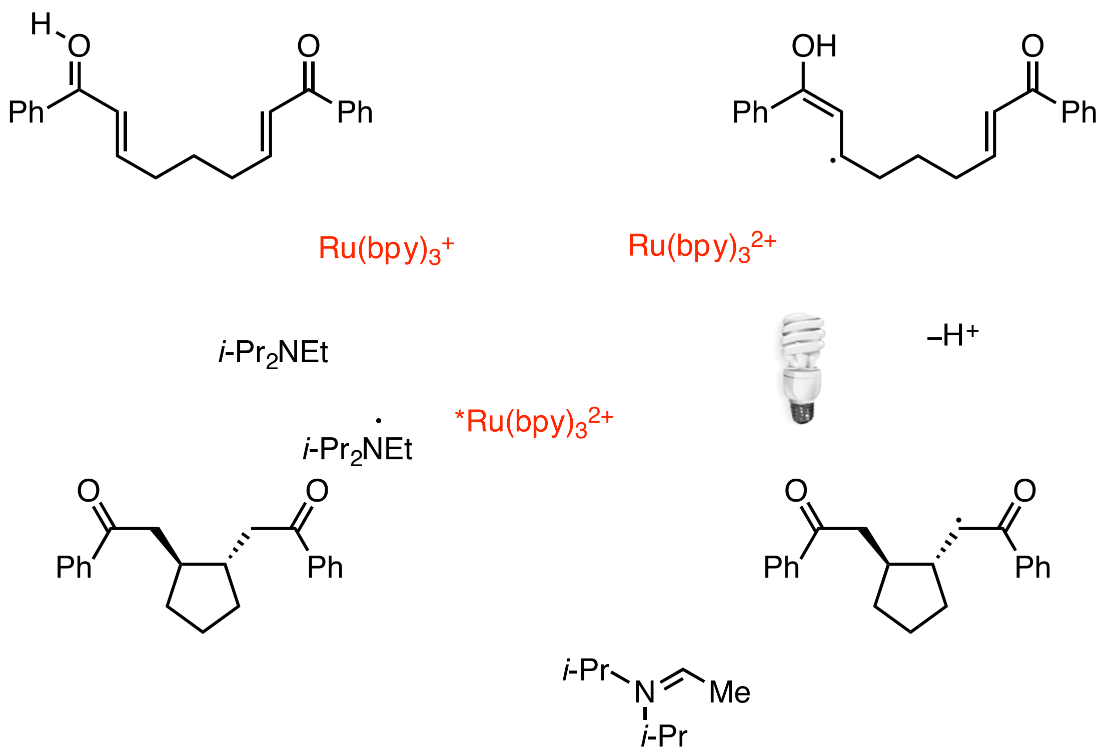


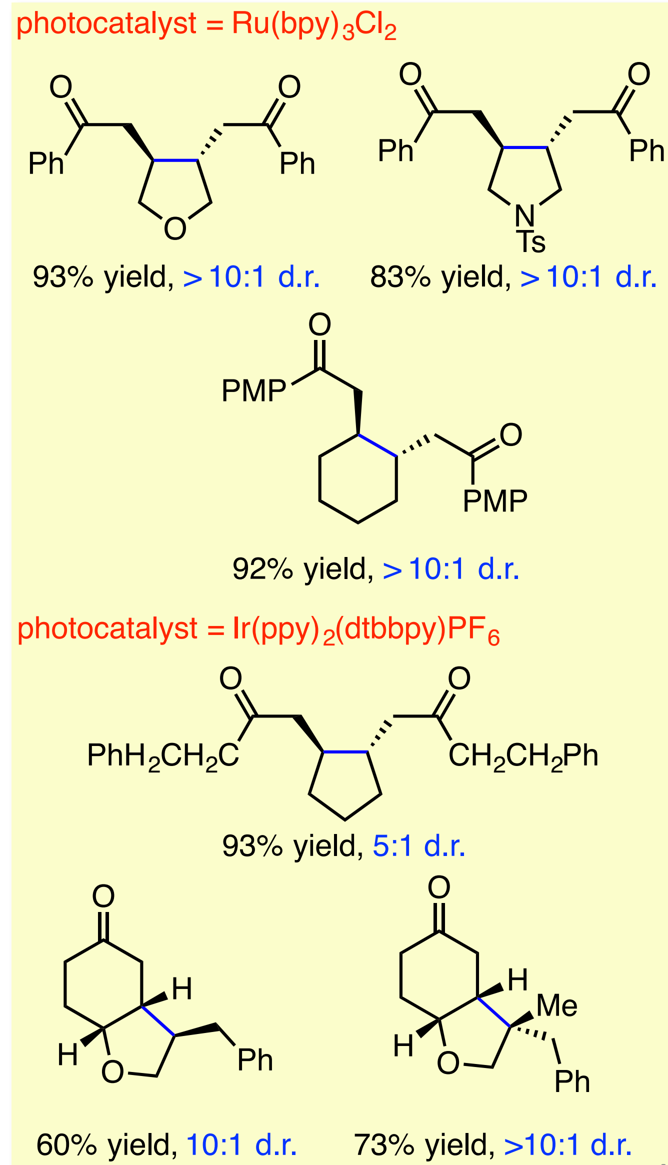
Du, J.; Yoon, T. P. *J. Am. Chem. Soc.* **2009**, *131*, 14604.
Tyson, E. L.; Farney, E. P.; Yoon, T. P. *Org. Lett.* **2012**, *14*, 1110.

Redox Neutral Reactions: [2+2] Cycloadditions

- Phtoredox reductive cyclization of bis(enones)



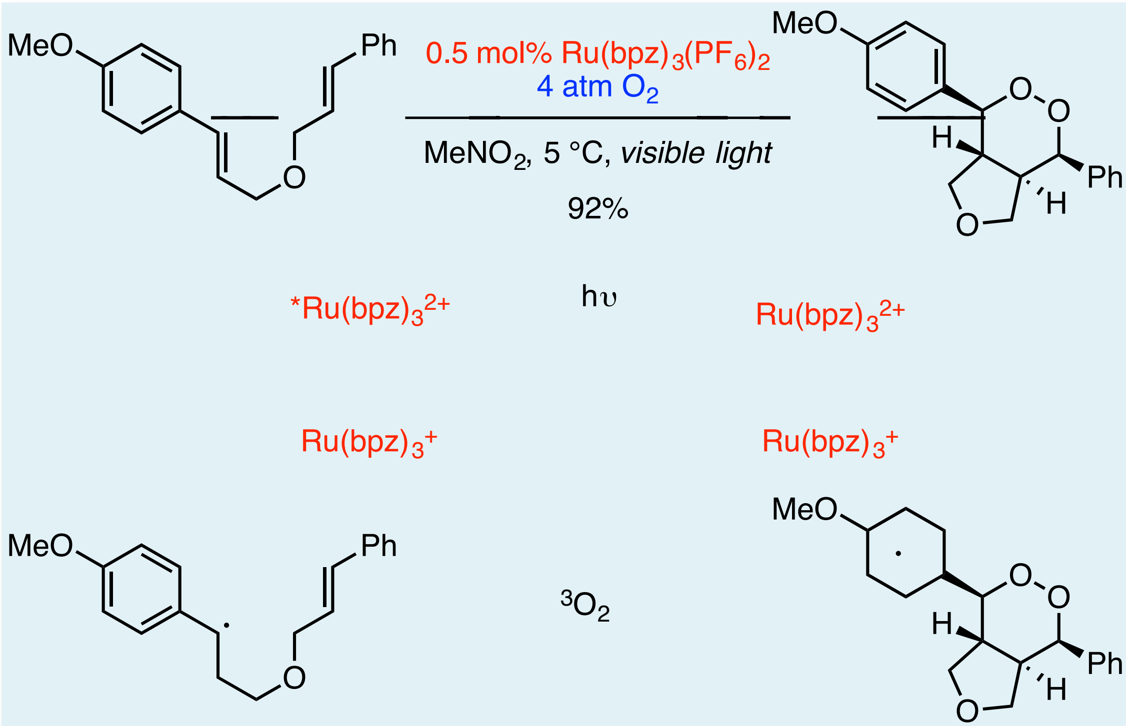




Du, J.; Espelt, L. R.; Guzei, I. A.; Yoon, T. P. *Chem. Sci.* **2011**, 2, 2115.

Redox Neutral Reactions: [2+2+2] Cycloadditions

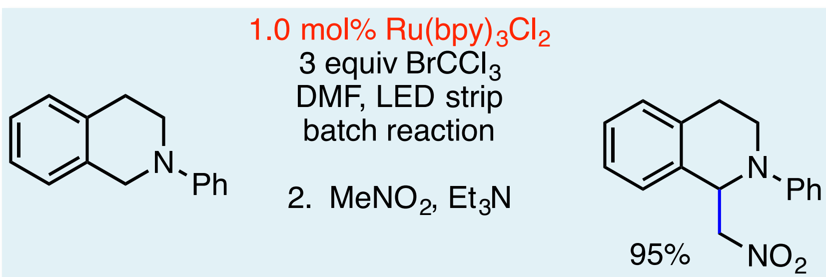
- Synthesis of endoperoxides via [2+2+2] cycloaddition of bis(styrenes) with molecular oxygen



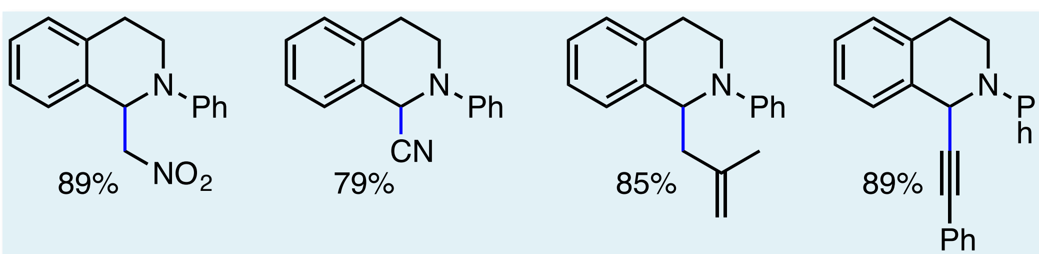
Parrish, J. D.; Ischay, M. A.; Lu, Z.; Guo, S.; Peters, N. R.; Yoon, T. P. *Org. Lett.* **2012**, *14*, 1640.

Visible Light Photocatalysis: Flow

- Stephenson and co-workers observed that large-scale reactions were often slower than those conducted on a larger scale
- Beer-Lambert Law
  - A = εlc
- Flow reactor
  - Direct irradiation, unlimited reacation scale, short reaction times



Batch reaction time for iminium formation:
3 h - 0.081 mmol h^{-1}

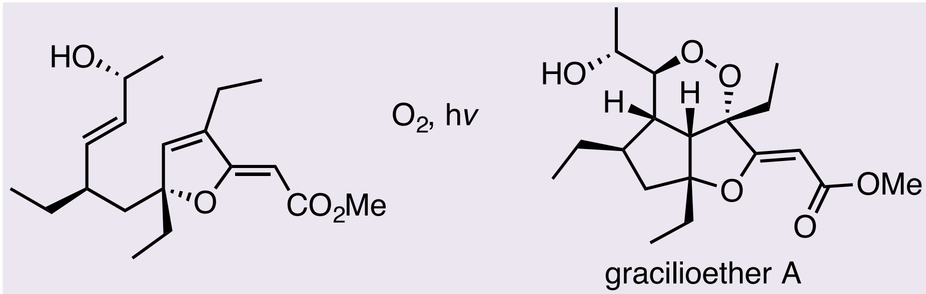


t_r for iminium formation in flow:
0.5 min – 5.75 mmol h^{-1}
(with a 479 μL reactor)

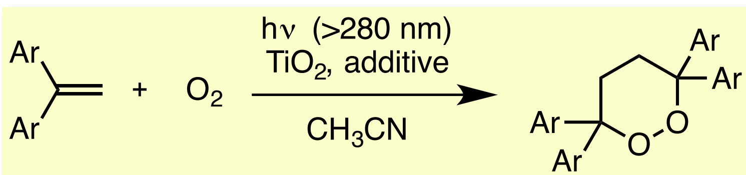
Condie, A. G.; González-Gómez, J. C.; Stephenson, C. R. J. *J. Am. Chem. Soc.* **2010**, *132*, 1464.
Tucker, J. W.; Zhang, Y.; Jamison, T. F.; Stephenson, C. R. J. *Angew. Chem. Int. Ed.* **2012**, *51*, 4144.

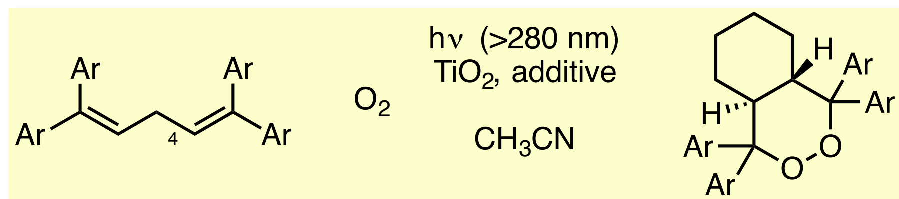
Visible Light Photocatalysis: Advancing the Field

- MOM – October 2011



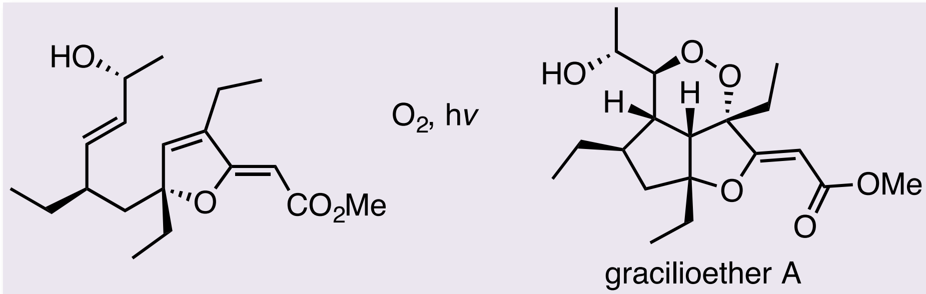
- Precedent?



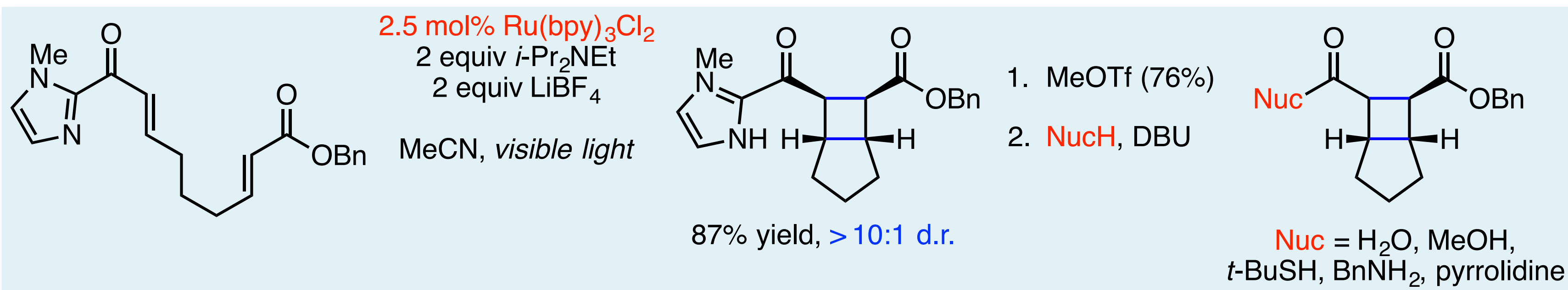


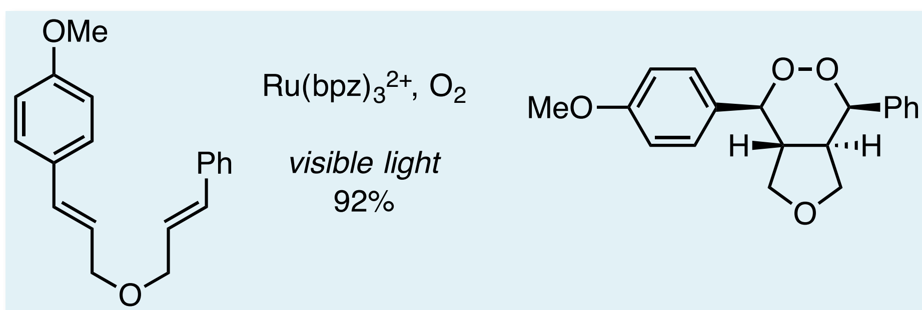
Visible Light Photocatalysis: Advancing the Field

- MOM – October 2011



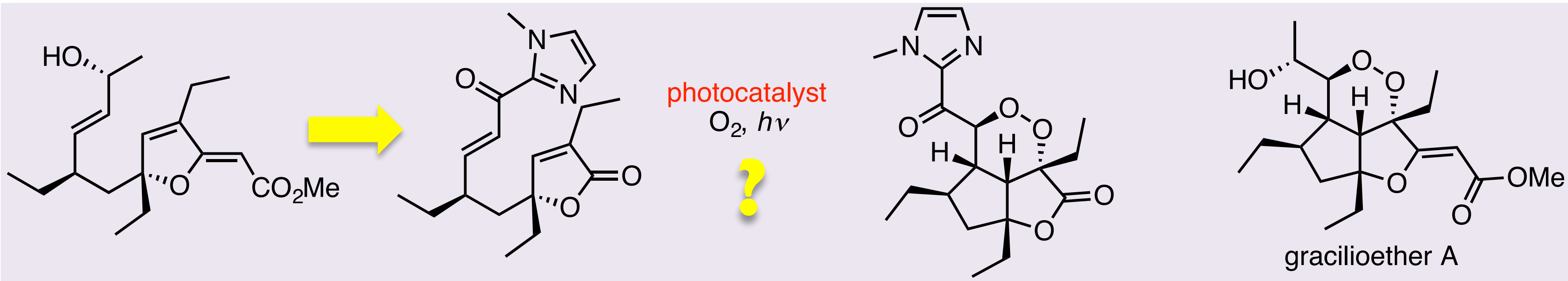
- Visible Light Photoredox Catalysis?



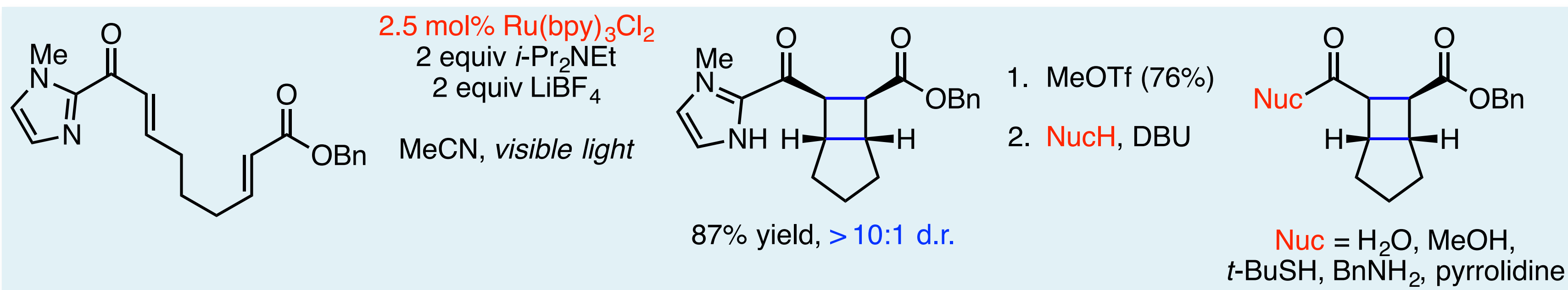


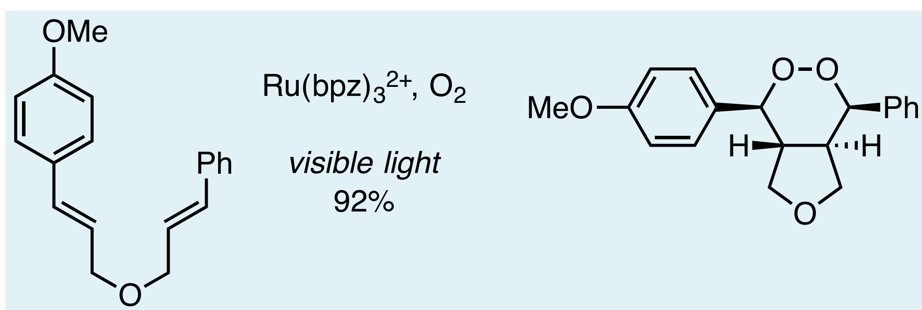
Visible Light Photocatalysis: Advancing the Field

- MOM – Revised



- Visible Light Photoredox Catalysis?





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Visible Light Photocatalysis: Advancing the Field

- Need for environmentally responsible chemical processes
  - Inexpensive, abundant, and non-toxic first-row transition metal elements
- Ideally no sacrificial donor/acceptor
  - Rely on tertiary amine and halogen compounds for reaction initiation
- Asymmetric transformations
  - Radical intermediates generated via photoredox catalysis are rarely utilized in enantioselective bond-forming reactions
- Long-term goal will be utilization of large-scale photochemical processes in commercial applications
  - Must not remain an academic exercise

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- Wipf group members past & present
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