UNIVERSITÄT BERN

Merging Photoredox and Nickel Catalysis

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Group of Professor Philippe Renaud
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INTRODUCTION
Concept-Keywords

Dual

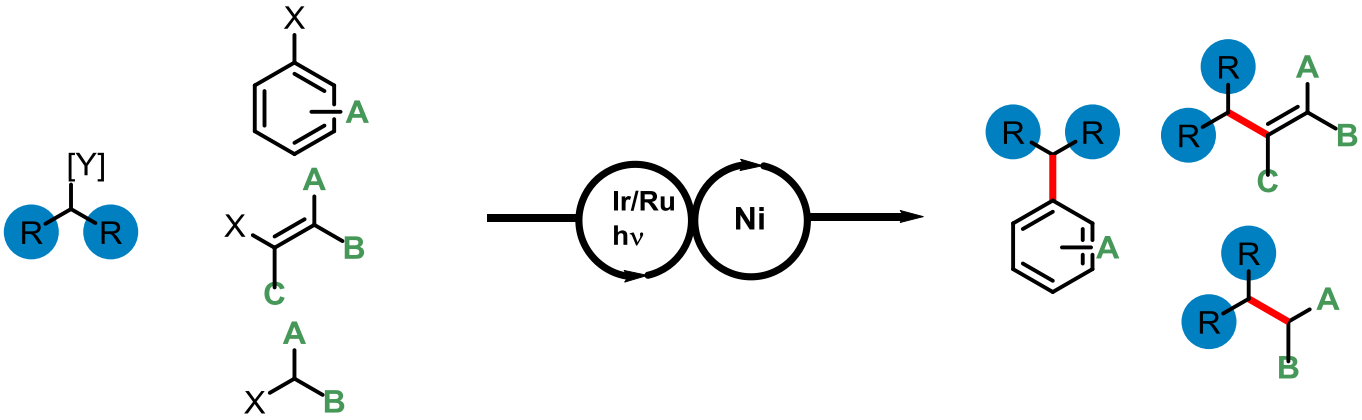
Cooperative

Tandem

Synergistic

Catalysis

Metallophotoredox



Cross-coupling

C_{sp3}-C_{sp2}

C_{sp3}-C_{sp3}

Het-C_{sp2}

Radicals

Ox/Red

Potential

SET

INTRODUCTION
Summary

- Nickel

- Photoredox Chemistry

- Formation of C-C bond
  - Scope of reactions
  - Different sources of Nucleophiles/ Radical Precursors
  - Mechanism

- Formation of C-Het bond
  - C-S, C-O, C-N, C-P

INTRODUCTION
Nickel

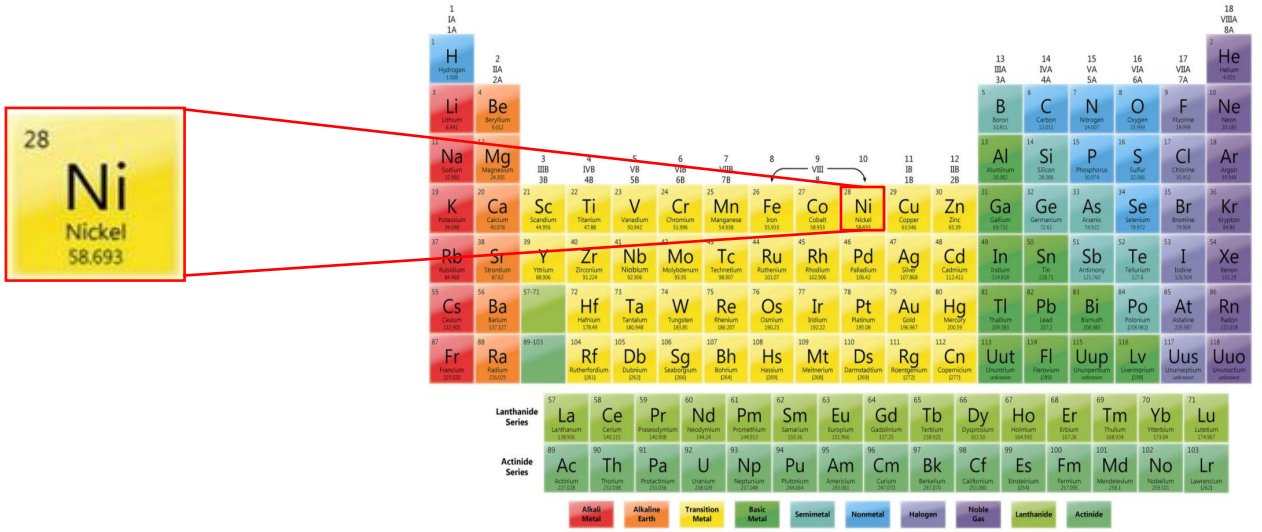
T. F. Jamison, *Nature*, **2014**, *509*, 299-309
V. P. Ananikov, *ACS Catal*., **2015**, *5*, 1964-1971

INTRODUCTION
Nickel Catalysis

“It can be compared to a spirited horse, delicate, difficult to control, and incapable of sustainable work”.
“Such a nickel can do all kinds of work and maintains its activity for a long time”.

Paul Sabatier, Nobel Prize in 1912 for the first hydrogenation of ethylene with Ni

INTRODUCTION
Nickel-features



- Belong to group 10 Metal : Above Pd and Pt
- Electropositif metal
- Small atomic radius (close to it Ligands)

T. F. Jamison, *Nature*, **2014**, *509*, 299-309
V. P. Ananikov, *ACS Catal.*, **2015**, *5*, 1964-1971

INTRODUCTION
Nickel-features

> Price

	Catalyst Precursors		
	$NiCl_2$	$PdCl_2$	$PtCl_2$
Price per 1 mmol (USD)	0.1	5.8	32.2

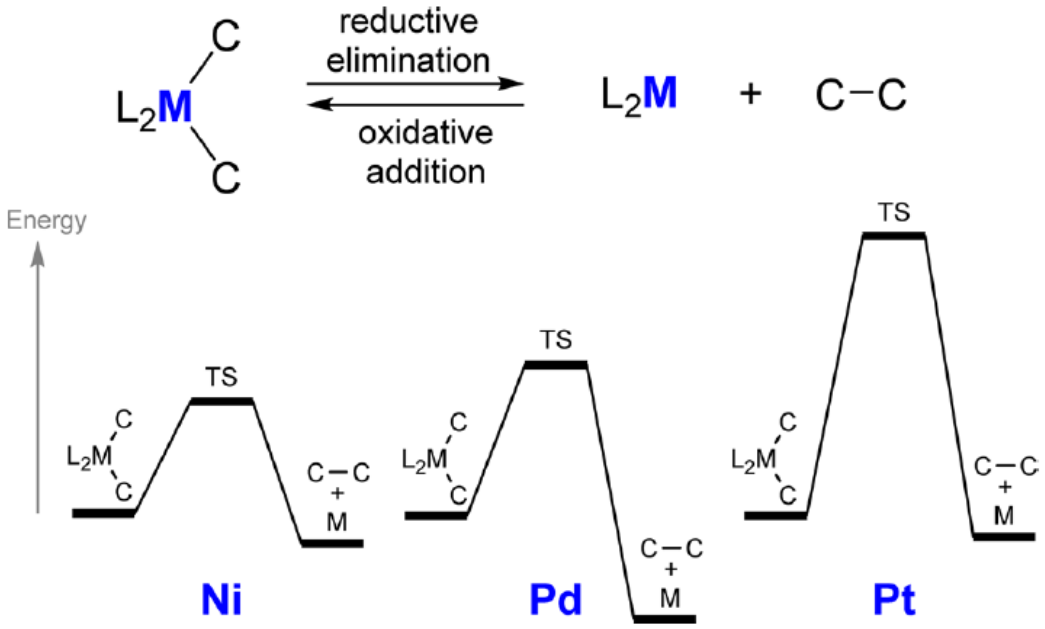
> Abundance

Fe(6.3%) >>Ni (0.0089%)>Cu (0.0068%)

> Toxicity

INTRODUCTION
Nickel vs Palladium

> C-C reductive elimination and oxidative addition

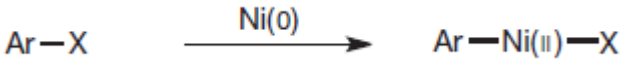


Bond	BDE, kcal/mol
CH_3-CH_3	87.4
$L_2(X)Ni(II)$-CH_3	38.0-51.1
$L_2(X)Pd(II)$-CH_3	48.3-55.2
$L_2(X)Pt(II)$-CH_3	60.8-66.5

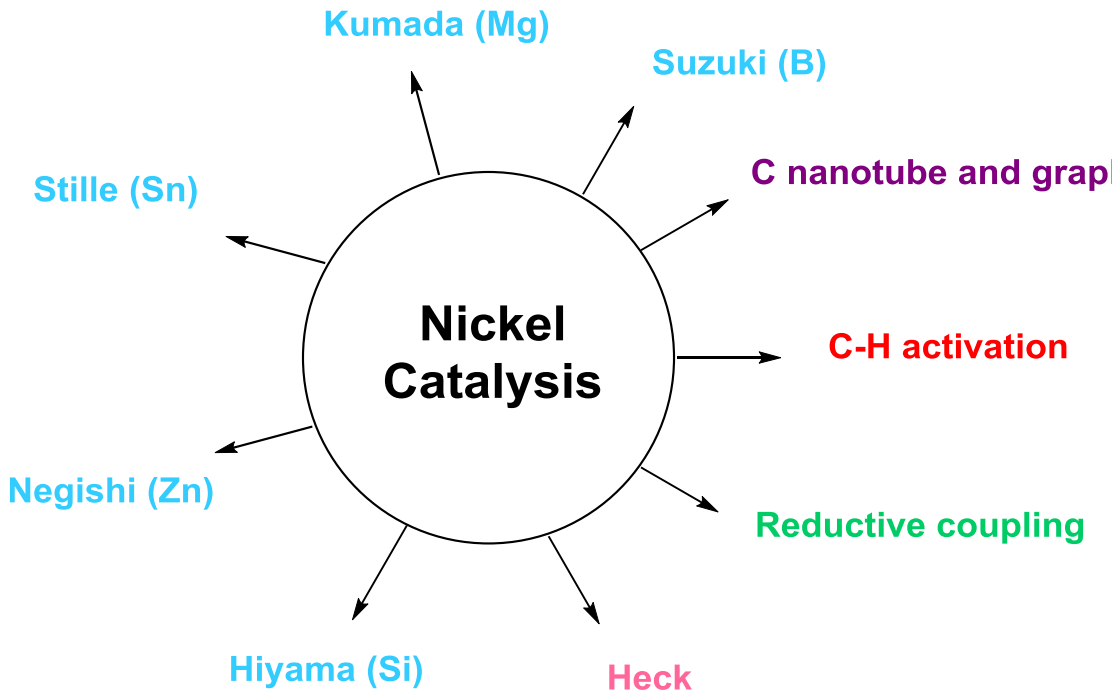
M-C	ΔE‡ (RE)	ΔE(RE)	ΔE‡ (OA)	ΔE(OA)
Ni-C	16.8	-4.1	20.9	4.1
Pd-C	24.9	-19.0	43.9	19.0
Pt-C	45.8	-3.5	49.3	3.5

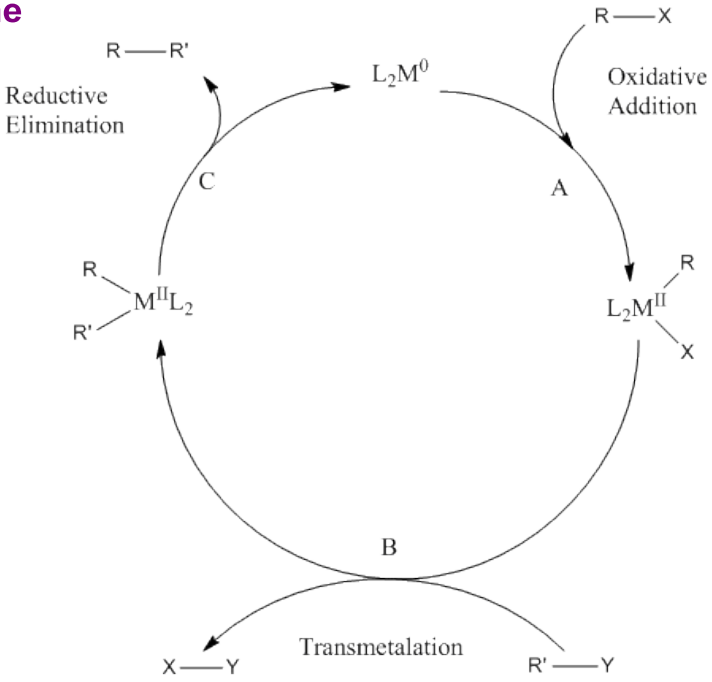
INTRODUCTION
Nickel vs Palladium

> Comparison of basic characteristics of Ni and Pd

Nickel	Palladium
–1 **0** **+1** **+2** **+3** +4	**0** +1 **+2** +3 **+4**
Smaller atomic radius	Larger atomic radius
Less electronegative	More electronegative
Facile oxidative addition	Facile β-hydride elimination
	
Radical pathways more accessible	Most often 2 e- chemistry
Cheaper	

INTRODUCTION
Nickel-Catalysis





- Oxidative addition really efficient for Csp2 centers but low rate for Csp3 centers
- Transmetallation for cross coupling slow : harsh conditions (C_{sp}> C_{sp2} > C_{sp3})
- Less β-H elimination prior to reductive elimination

INTRODUCTION
Visible light Photoredox

C.R. J. Stephenson, *J. Org. Chem*. **2012**, *77*, 1617−1622,
T. P. Yoon, *Science,* **2014,** *343, 1239176*
David. W. C MacMillab., *Chem. Rev*. **2013**, *113*, 5322−5363

INTRODUCTION
Photoredox-Principle

- *"In a general sense, this approach relies on the ability of metal complexes and organic dyes to engage in single-electrontransfer (SET) processes with organic substrates upon photoexcitation with visible light"*

  MacMillan

- Photocatalyst (PC) absorb light in the visible region of the electromagnetic spectrum to give stable, long-lived photoexcited states

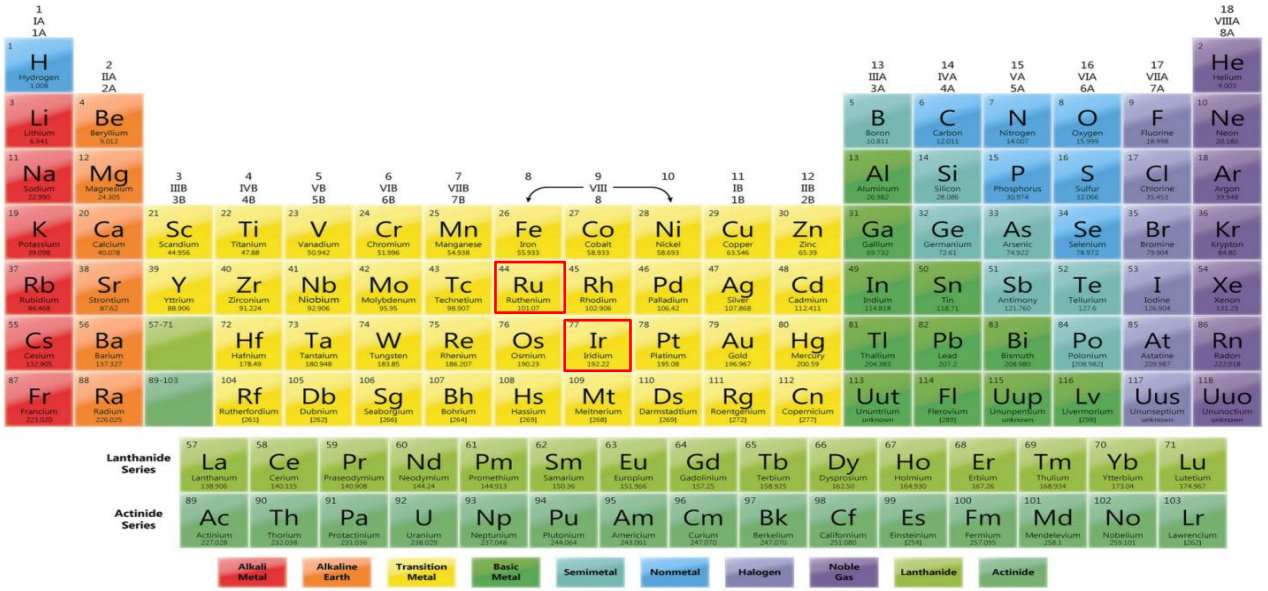
- Poor single-electron oxidants and reductants in the ground state, excitation of an electron affords excited states that are very potent SETreagents.

- Development of reactions requiring both the donation and the reception of electrons at disparate points in the reaction mechanism

- Access to radical ion intermediates with different reactivity, starting from abundant and inexpensive starting material

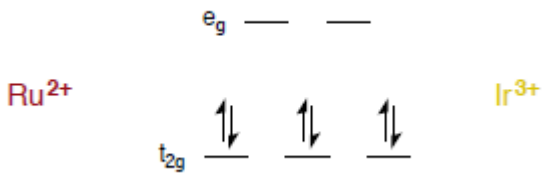
- Employ mild conditions

INTRODUCTION
Photoredox-Principle



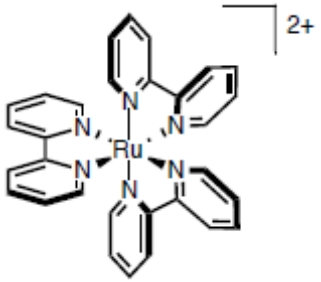
> Ru belong to group 8 (d^8) and Ir to group 9 (d^9)

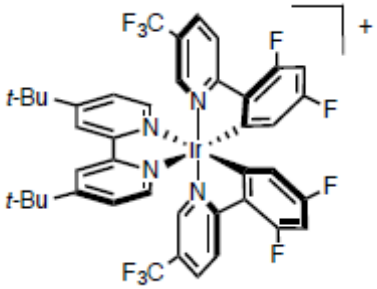
To reach low-spin d^6 state Ru^{2+} and Ir^{3+} are stable

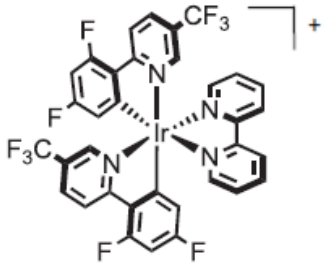


INTRODUCTION
Photoredox-Principle

> Common Transition Metal Photocatalysts







	$Ru(bpy)_3^{2+}$	$Ir[dF(CF_3)ppy)_2(dtbbpy)^+$	$Ir[dF(CF_3)ppy]_2(bpy)^+$
Reductive power	E(Ru(III)/Ru(II)*)= -0.81V Ru(III) + e- → Ru (II)*	E(Ir(IV)/Ir(III)*)= -0.88 V	E(Ir(IV)/Ir(III)*)=-0.88
Oxidative power	E(Ru(II)*/Ru(I))= +0.77V Ru(II) * + e- → Ru(I)	E(Ir(III)*/Ir(II))= +1.21V	E(Ir(III)*/Ir(II))= +1. 32 V
	Reduction and oxidation potential (vs Saturated Calomel Electrode)		
	τ=1.1 μs	τ=2.3 μs	τ=2.3 μs

> Conclusions: Excited state is a reductant and oxidant

$Ox + e^- \rightarrow Red / E$

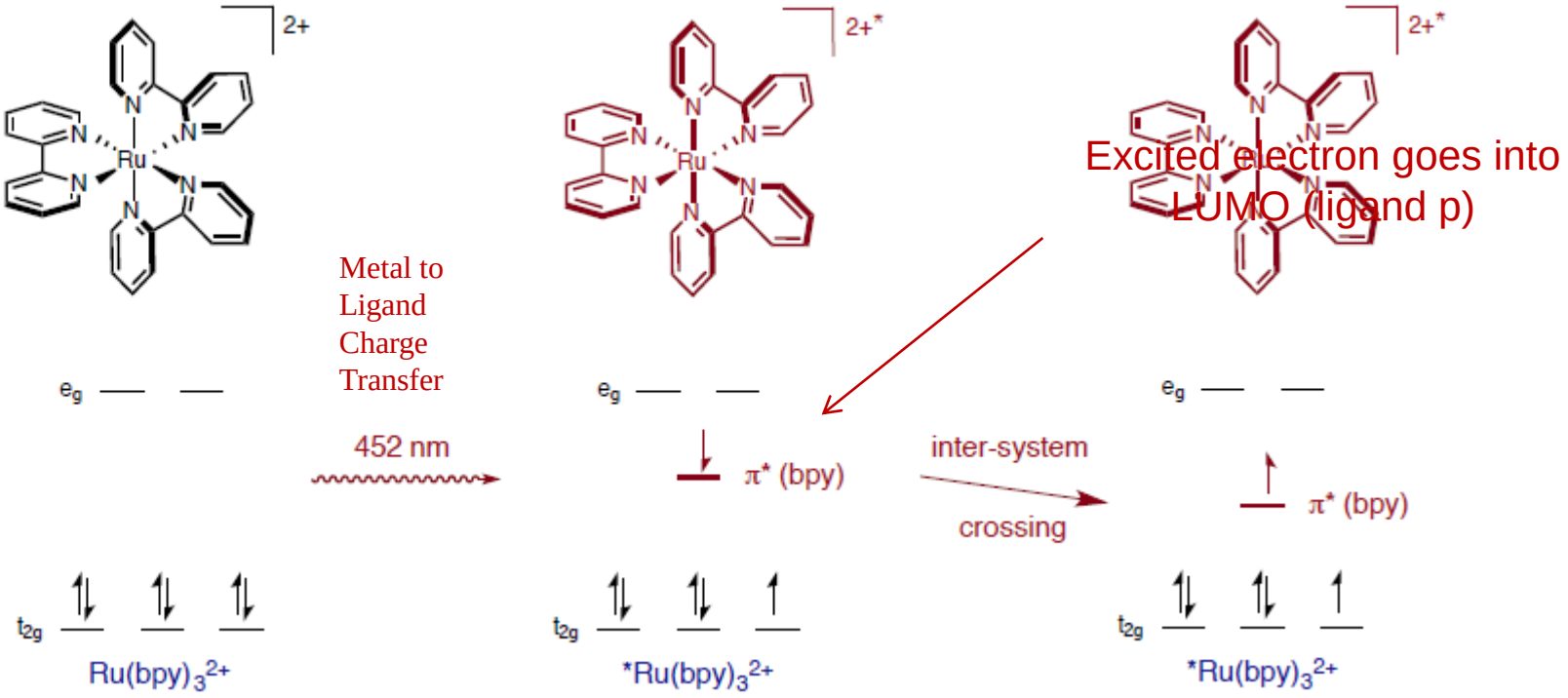
E> 0 = potent oxidant

E<0 = potent reductant

Ru cat is a **weaker oxidant, stronger reductant**

Ir cat are **similar reductant, much stronger oxidant**

INTRODUCTION
Photoredox-Principle



ground state – singlet "So"

excited state – singlet "S1", τ=100-300 fs

0 "un-spin-paired" electrons

excited state – triplet "T1", τ=1100 ns

2 "un-spin-paired" electrons
Long-lived excited state

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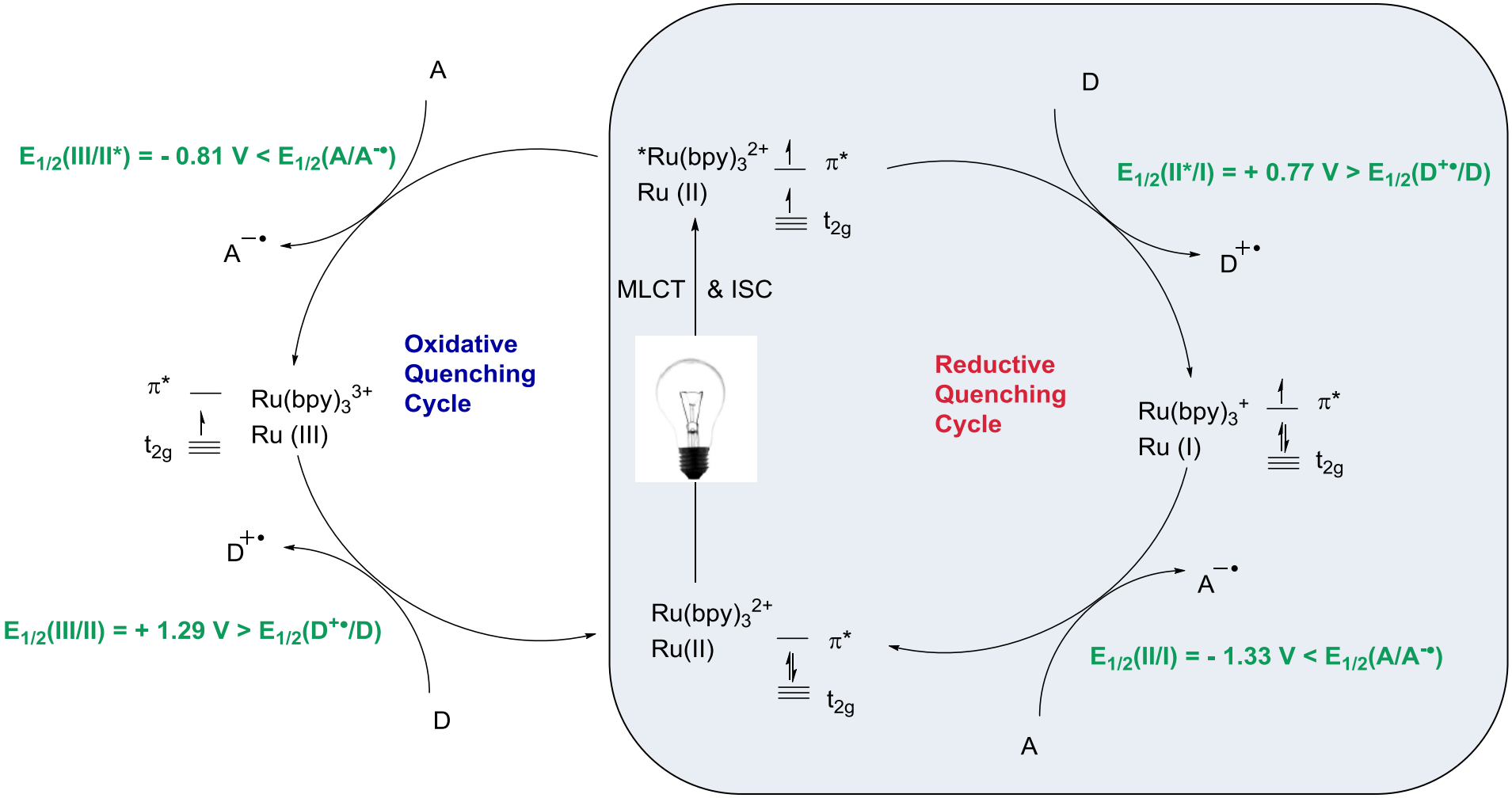
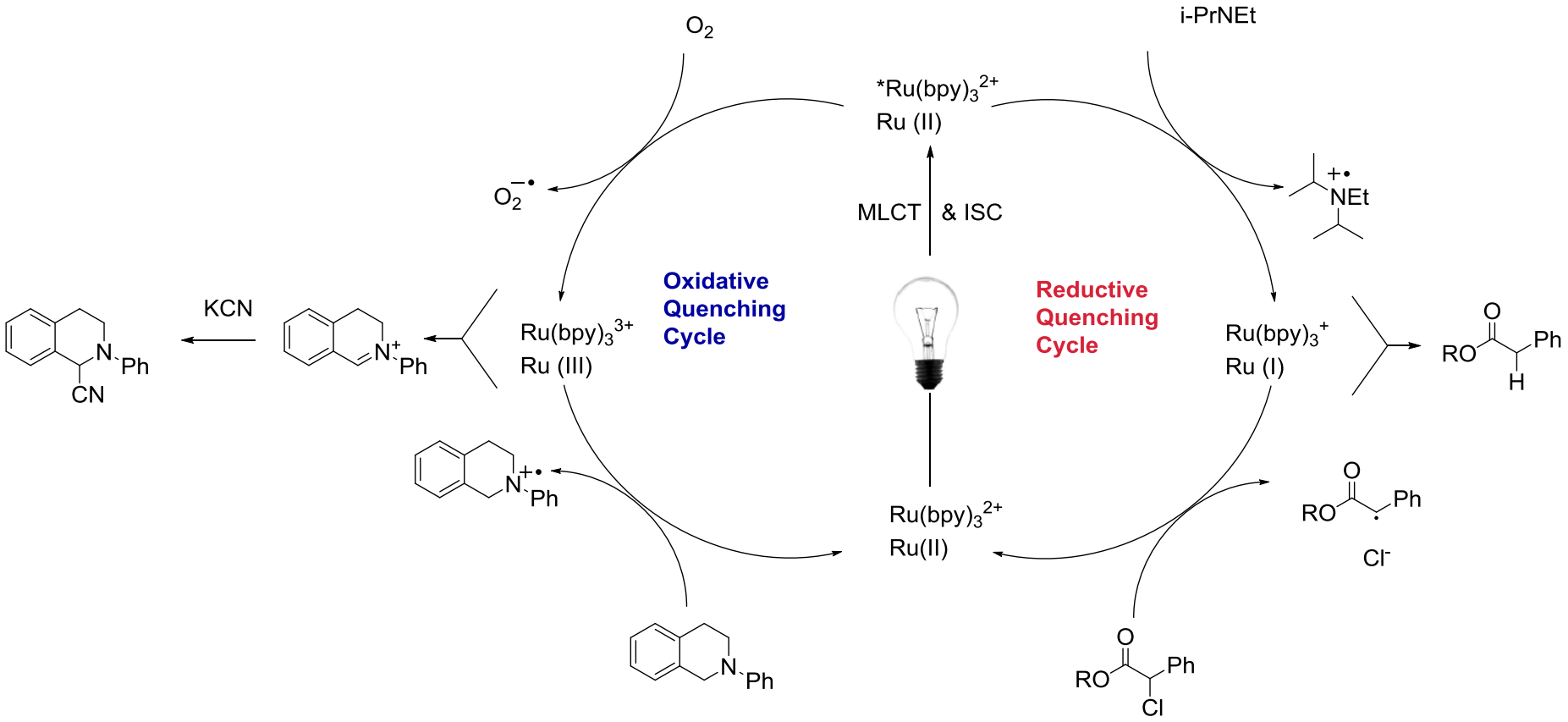
Photoredox-Principle



> An oxidant and a reductant in the same vessel!

INTRODUCTION
Photoredox-Principle

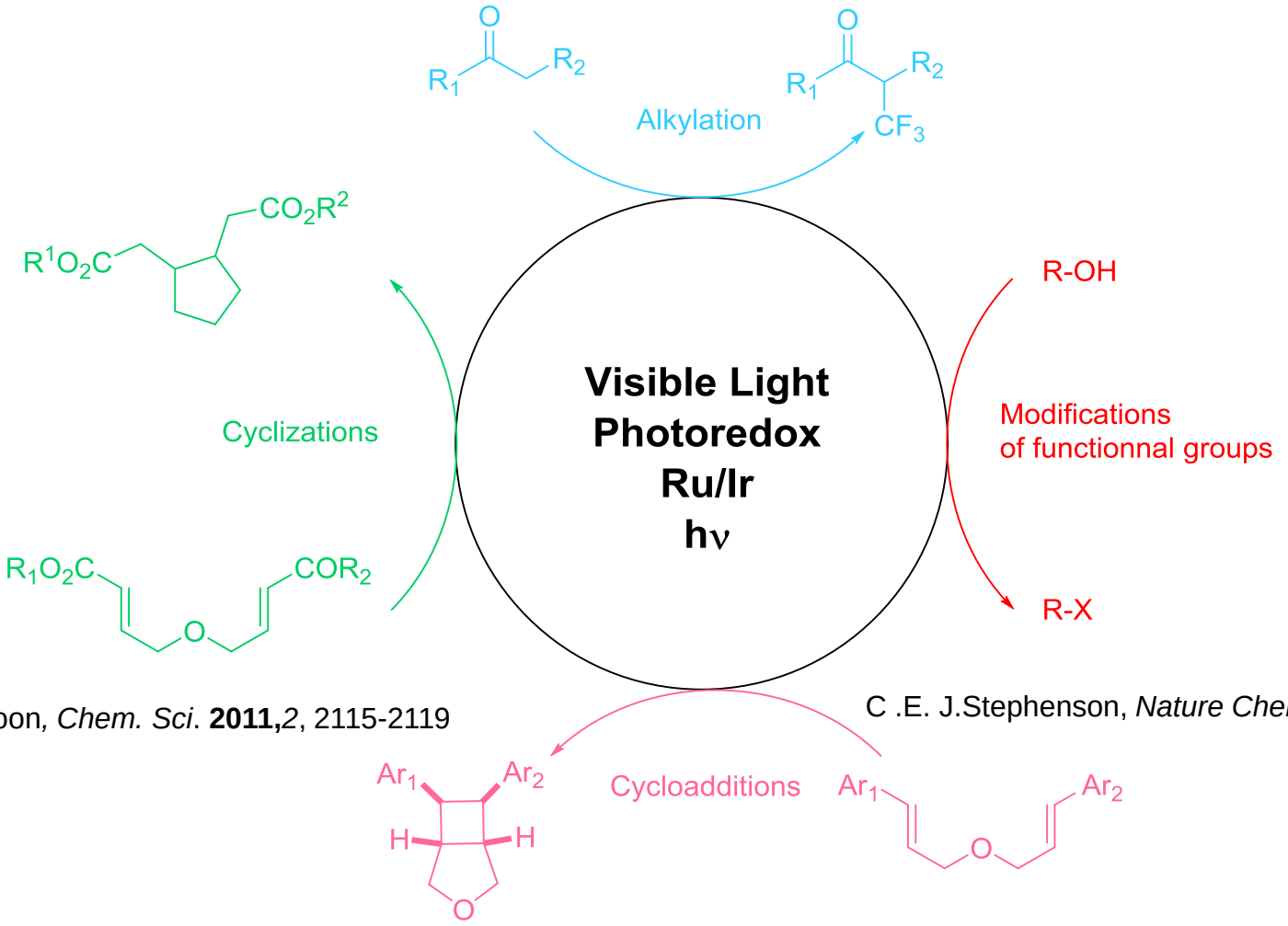


C. R. J. Stephenson, *et. al., J. Org. Chem.* **2012,** *77,* 4425

C. R. J. Stephenson. *et. al., J. Am. Chem. Soc.* **2009,** *131,* 8756

INTRODUCTION
Photoredox-Catalysis

D. W. C. Mac Millan, *JACS*, 2009, *131*, 10875



Yoon, *Chem. Sci*. **2011,***2*, 2115-2119

C .E. J.Stephenson, *Nature Chem.* **2011,** *3*, 140–145

Yoon, J. Am. Chem. Soc., **2008**, *130* ,12886–12887

INTRODUCTION
Nickel-Photoredox

Merging Nickel catalysis with Photoredox!

- Used for C_{sp3}-C_{sp2} and C_{sp3}-C_{sp3}
- Suppress Transmetallation process
- Avoid harsh conditions such as Temperature and Aq. Base
  → Tolerance of functionnal groups
- Use commercially air stable reagent

State of the Art:

- Generation of the **Radicals** previously described
- Feasability of **Radicals** addition to **TM**
- Cooperation of **TM** and **Photoredox** : Work of Glorius and Sanford
- Reported single electron potential

Sahoo, B.; Hopkinson, M. N.; Glorius, F. *J. Am. Chem. Soc*. **2013**, *135*, 5505−5508.
Ye, Y.; Sanford, M. *J. Am. Chem. Soc*. **2012**, *134*, 9034− 9037.

INTRODUCTION

Gary A. Molander

1975-1979 Ph.D with Prof. Brown
Purdue University

1979- 1980 Postdoctoral with Prof. Brown
Purdue University

1980- 1981 Postdoctoral with Prof. Trost
University of Wisconsin

1988-1999 Professor at University of Colorado
Since 1999 Professor at Pennsylvania

Research interests:
Photoredox Cross coupling, Organofluorine

David W. C. MacMillan

1991-1996 Ph.D with Prof. Overman,
University of California

1996- 1998 Postdoctoral with Prof. Evans
Harvard University

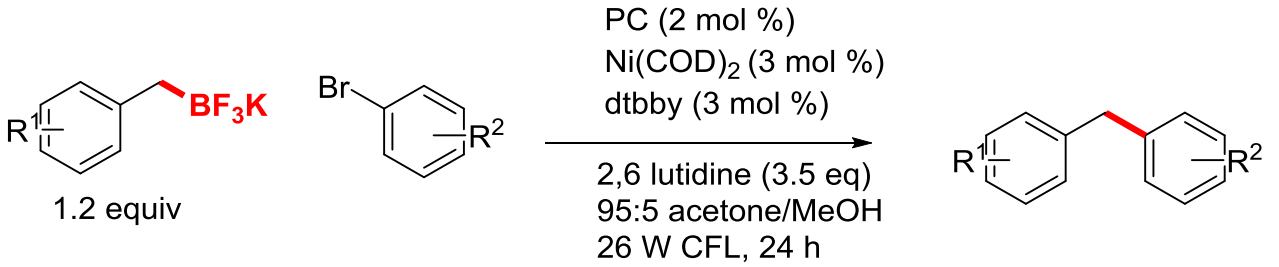
2000-2006 Professor at Caltech
Since 2006 Professor at Princeton Univeristy

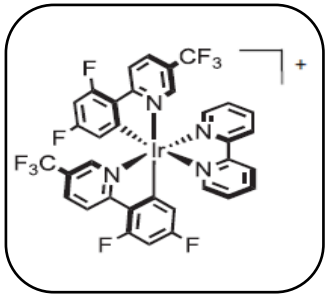
Research interests:
Enantioselective Catalysis, New Reaction Methodology, Natural Product Synthesis

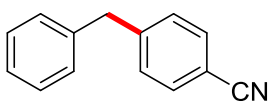
Carbon-Carbon cross coupling

C-C Coupling
Molander group

> Coupling of Benzyltrifluoroborates with Aryl halides







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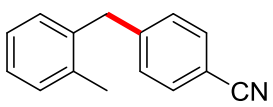

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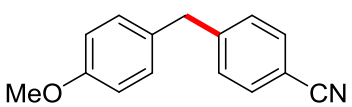

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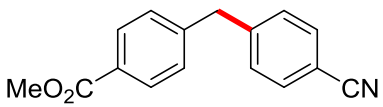

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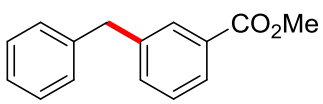

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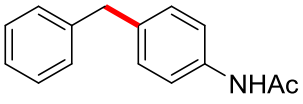

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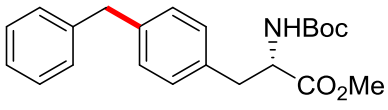

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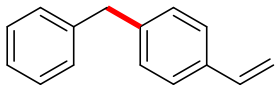

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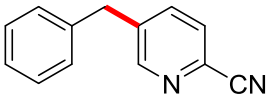

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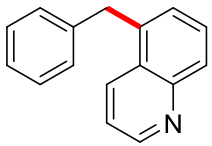

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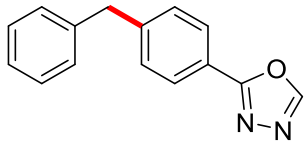

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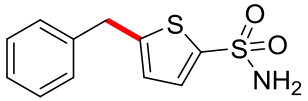


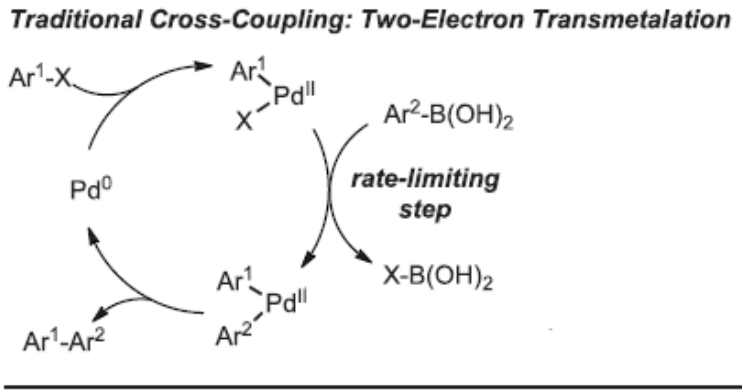
56%

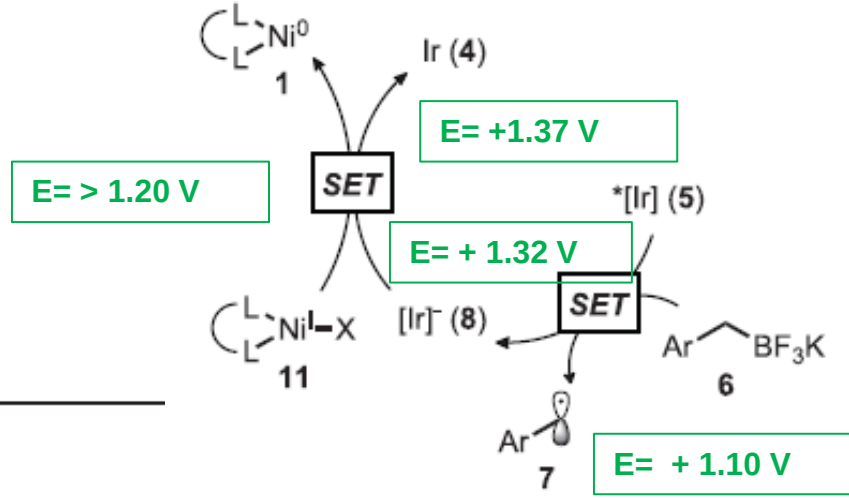
30 examples

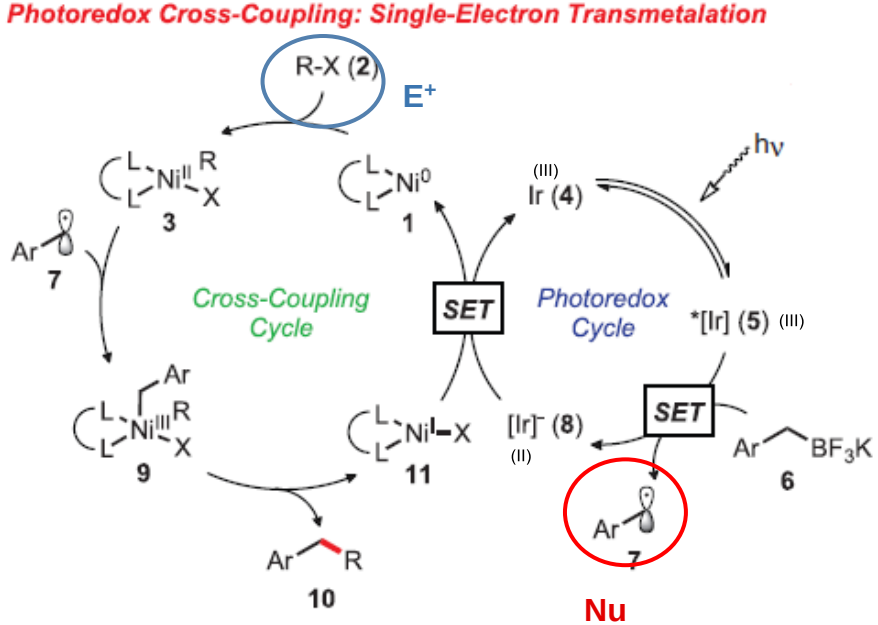
Tellis, J. C.; Primer, D. N.; Molander, G. A. *Science*, **2014**,*345*, 433

C-C Coupling
Molander group

> Mechanism, 1st assomption:



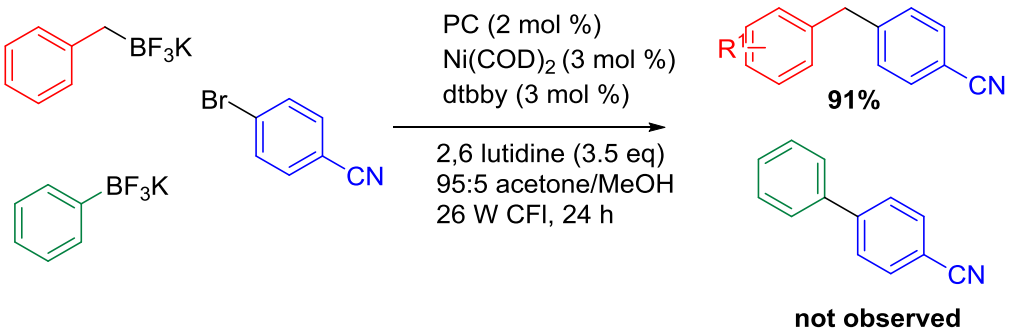




C-C Coupling
Molander group

> Control experiment without Ni, Ir,light confirmed dual catalytic nature

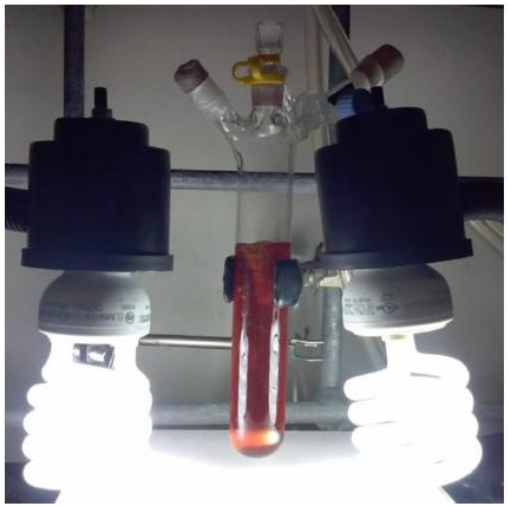
> Competition experiment



> In Practice, “operationnal simplicity”

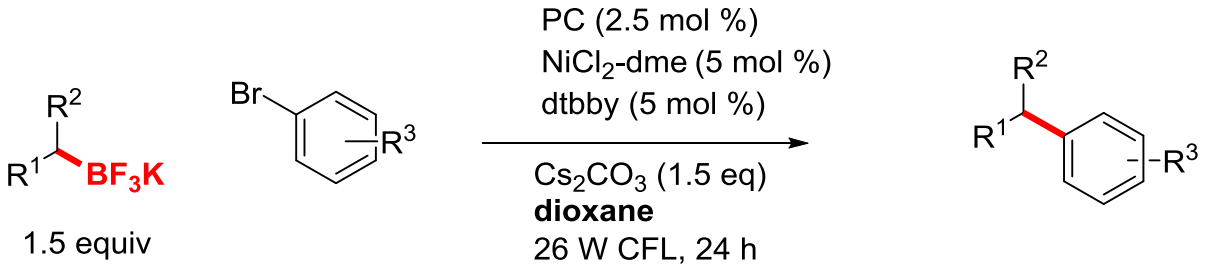
- Blue led Light, Fluorescent light bulb
- Glove box, just for Ni catalyst
- Glass vial
- Inert atmosphere

- Room temperature
- Need of homogeneous reaction mixture

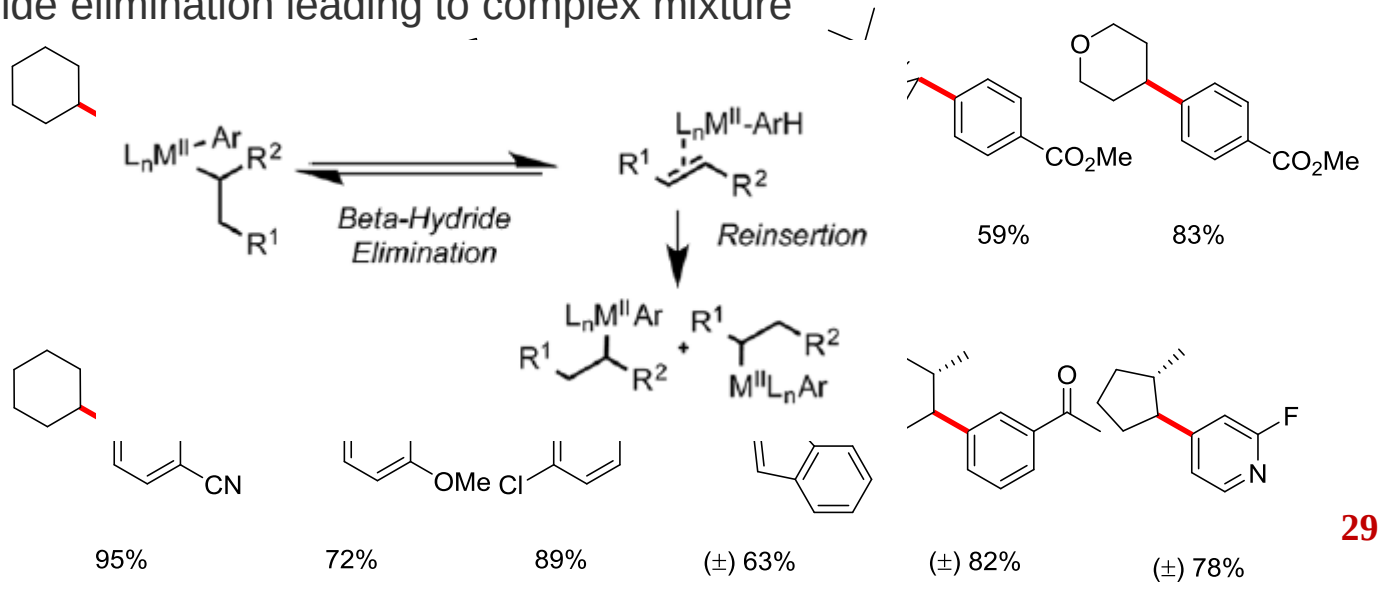


C-C Coupling
Molander group

> Challenge with Secondary unactivated alkyltrifluoroborate



- High redox pot E= 1.50 V compared to 1.10 V (E= + 1.32 V)
- No stabilization of the radical
- β-hydride elimination leading to complex mixture



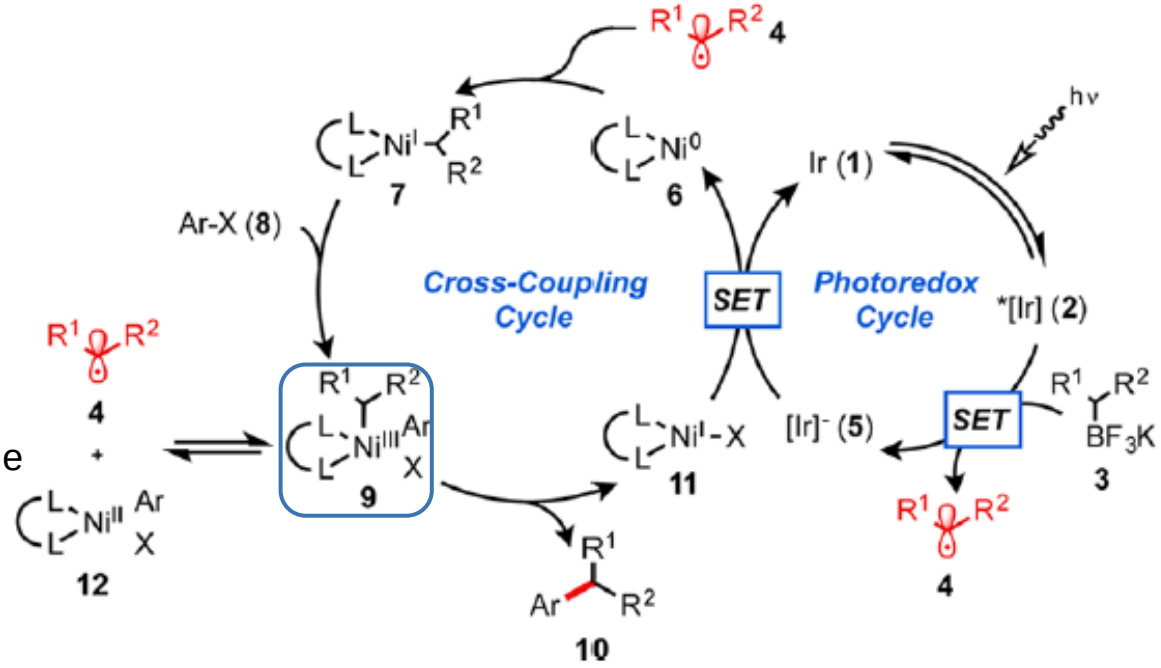
29 examples

Primer, D. N.; Karakaya, I.; Tellis, J. C.; Molander, G. A. *J. Am. Chem. Soc.*, **2015**, *137*, 2195

C-C Coupling
Molander group

- Mechanism, New hypothesis

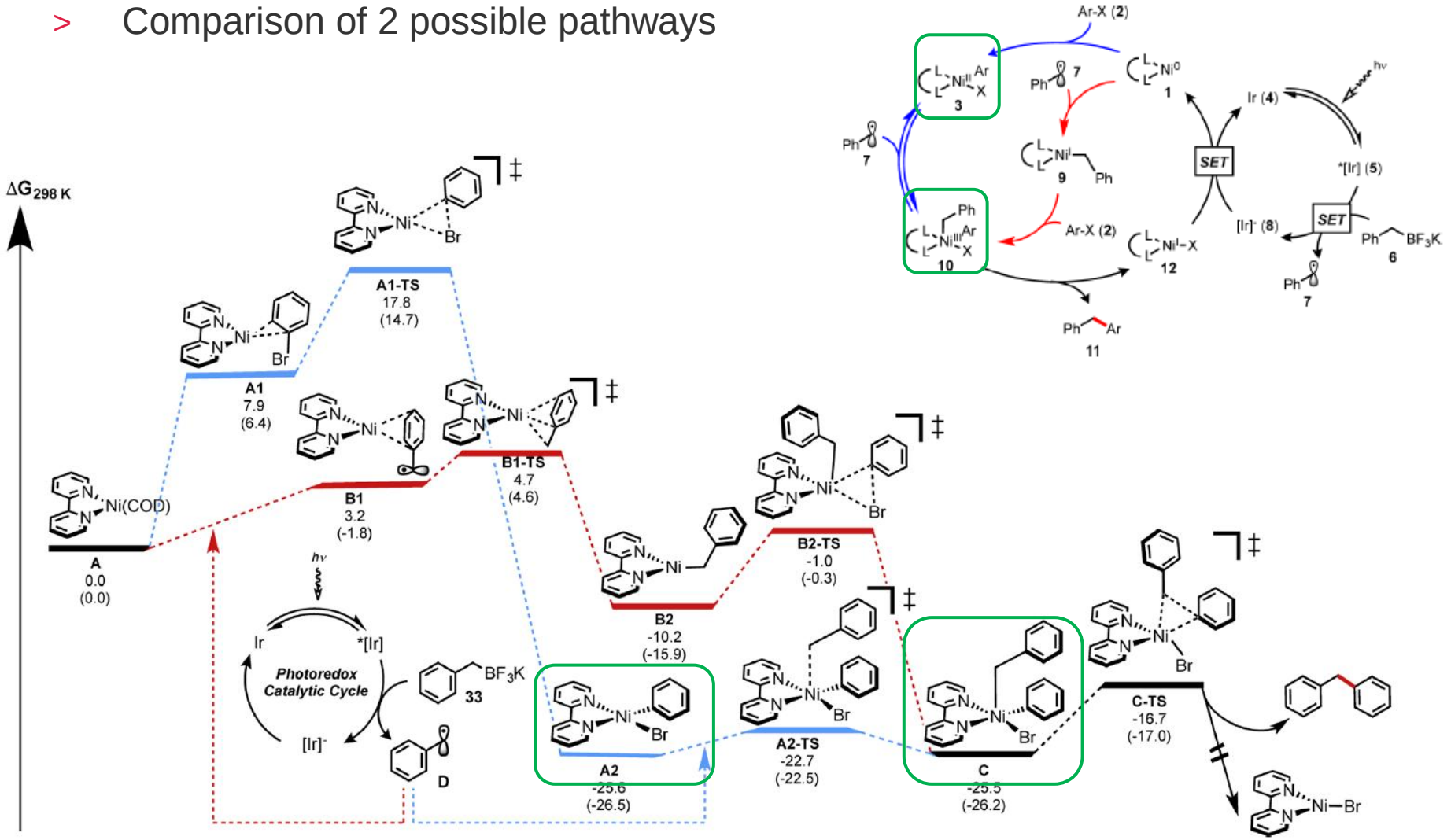
Reversible and rapid homolitycleavage of Ni-C



- Radical addition to Ni(0) prior to oxidative addition: low barrier
- Common intermediate **9** anyway

C-C Coupling
Molander group

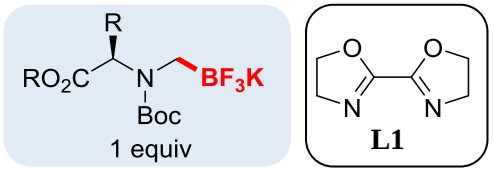
> Comparison of 2 possible pathways



Gutierrez, O.; Tellis, J. C.; Primer, D. N.; Molander, G. A.; Kozlowski, M. C. *J. Am. Chem. Soc.*, **2015**, *137*, 4896

C-C Coupling
Molander group

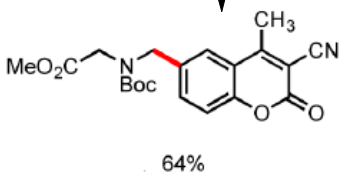
> Extension of the Scope



E_{red}= 1.01 V

(Het)Ar-Br (1 equiv)
PC (2 mol %)
$Ni(NO_3)_2.6H_2O$ (5 mol %)
L_1 (10 mol %)

K_2HPO_4 (3 equiv)
EtOAc
26 W CFL, 5-8 h



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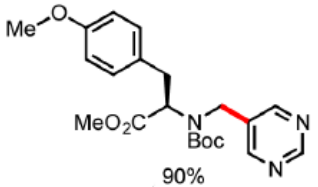

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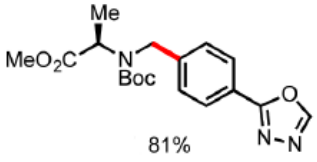
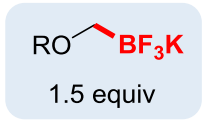


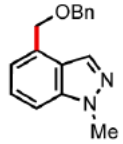
81%



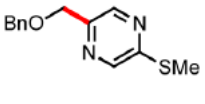
E_{red}= 1.11 V

(Het)Ar-Br (1 equiv)
PC (2 mol %)
$NiCl_2.dme$ (3 mol %)
dtbbpy (3mol %)

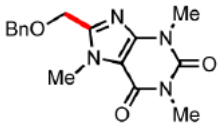
K_2HPO_4 (3 equiv)
Dioxame/DMA (5:1)
2 x 26 W CFL, 24 h



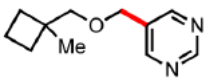
73%



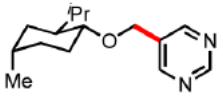
84%



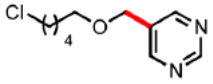
58, 93%



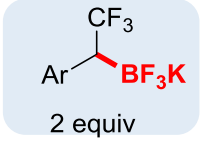
74%



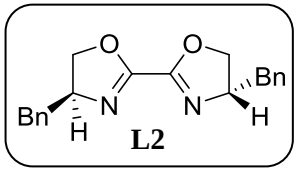
60, 63%



79%

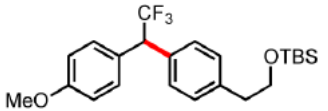


E_{red}= 1.17 V

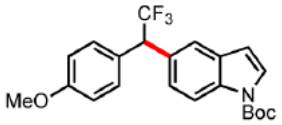


(Het)Ar-Br (1 equiv)
PC (3 mol %)
$NiBr_2.dme$ (5 mol %)
L_2 (7.5 mol %)

Cs_2CO_3(4 equiv)
KF (1 equiv)
Dioxame
2 x 26 W CFL, 48 h



64%



56%

32%

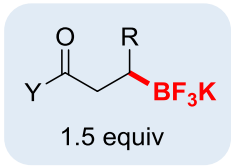
31 examples

40 examples

18 examples

1) El Khatib, M.; Serafim, R. A. M.; Molander, G. A. *Angew. Chem. Int. Ed.*, **2016**, *55*, 254 2) Karakaya, I.; Primer, D. N.; Molander, G. A. *Org. Lett.*,**2015**, *17*, 3294 3) Ryu, D.; Primer, D. N.; Tellis, J. C.; Molander, G. A. *Chem. Eur. J.* , **2016**, *22*, 120

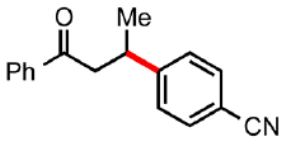
C-C Coupling
Molander group



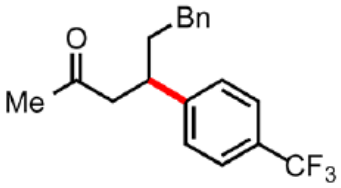
1.5 equiv

(Het)Ar-Br (1 equiv)
PC (2.5 mol %)
$NiCl_2$.dme (2.5 mol %)
dtbbpy (2.5 mol %)

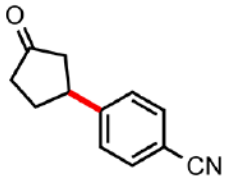
Cs_2CO_3(0.5 equiv)
2,6-lutidine (0.5 equiv)
Dioxane
26 W CFL, 30 h



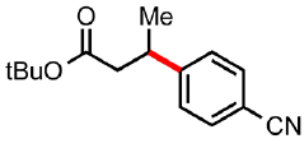
(50%)



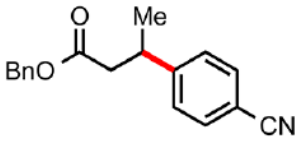
(88%[a])



(79%)

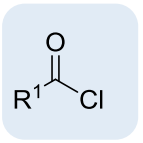


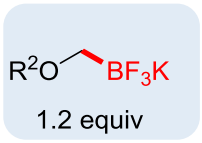
(87%)



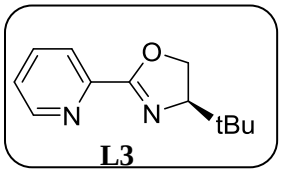
(84%[a])

19 examples

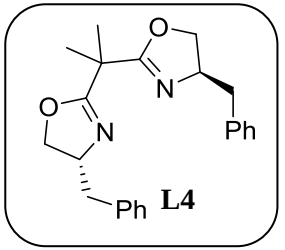




1.2 equiv



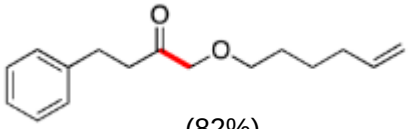
L3



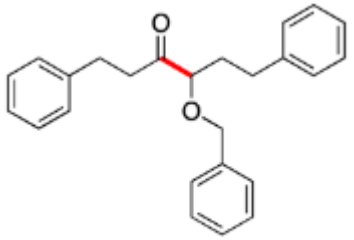
L4

PC (2 mol %)
$NiCl_2$.dme (4 mol %)
L (4 mol %)

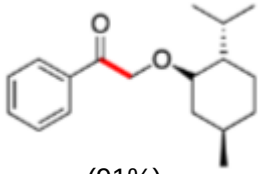
Cs_2CO_3(1 equiv)
THF
26 W CFL, 24 h



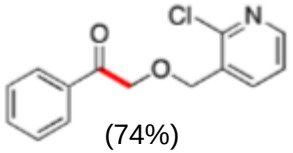
(82%)



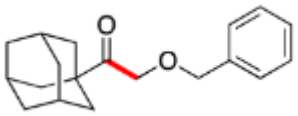
64:36 er,[b] (91% yield, 81:19 er)[c]



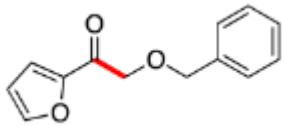
(91%)



(74%)



(85%)



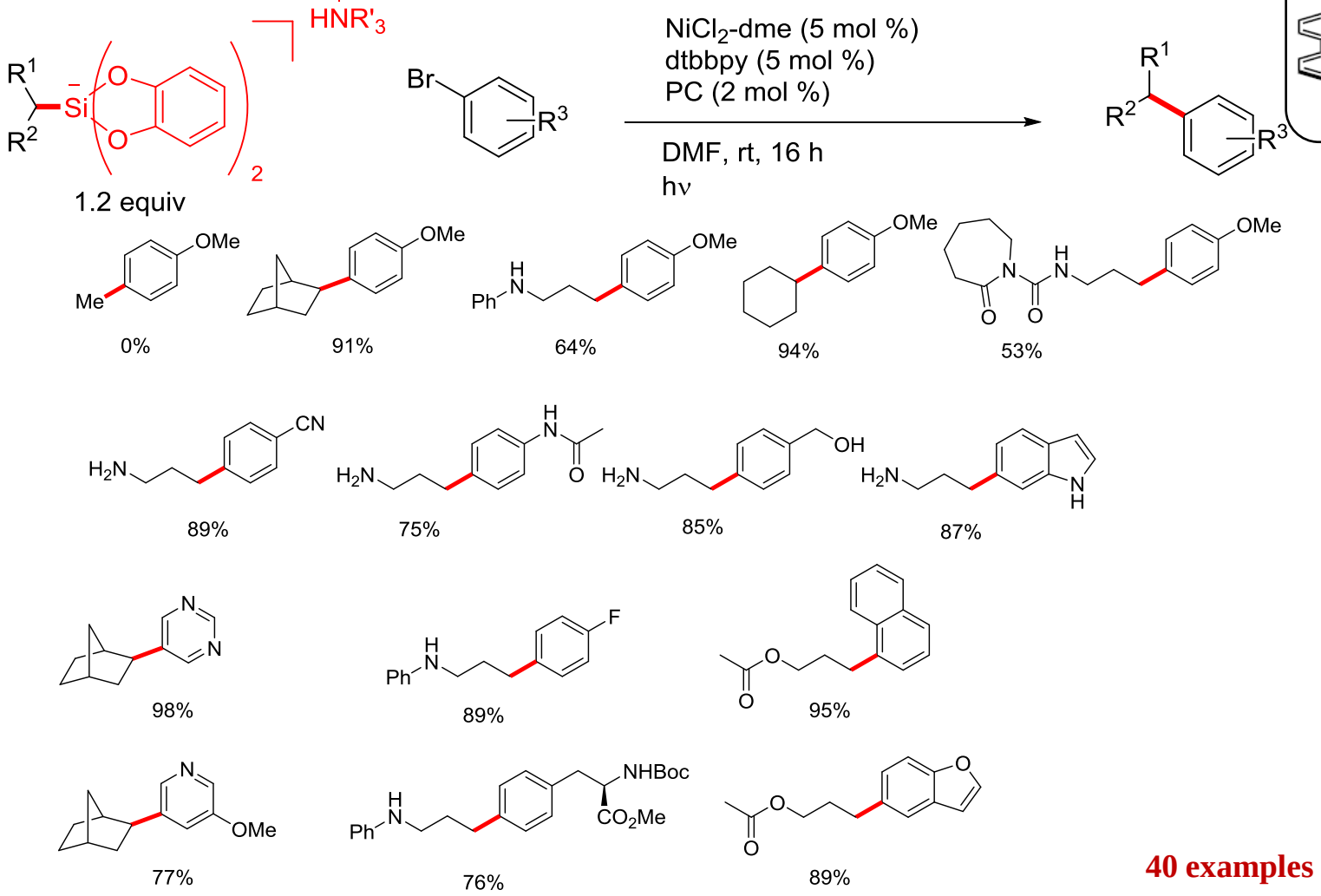
(36%)

27 examples

Tellis, J. C.; Amani, J.; Molander, G. A. *Org. Lett.*, **2016**, *18*2572
Amani, J.; Sodagar, E.; Molander, G. A. *Org. Lett.*, **2016**,*18*, 732

C-C Coupling
Molander group

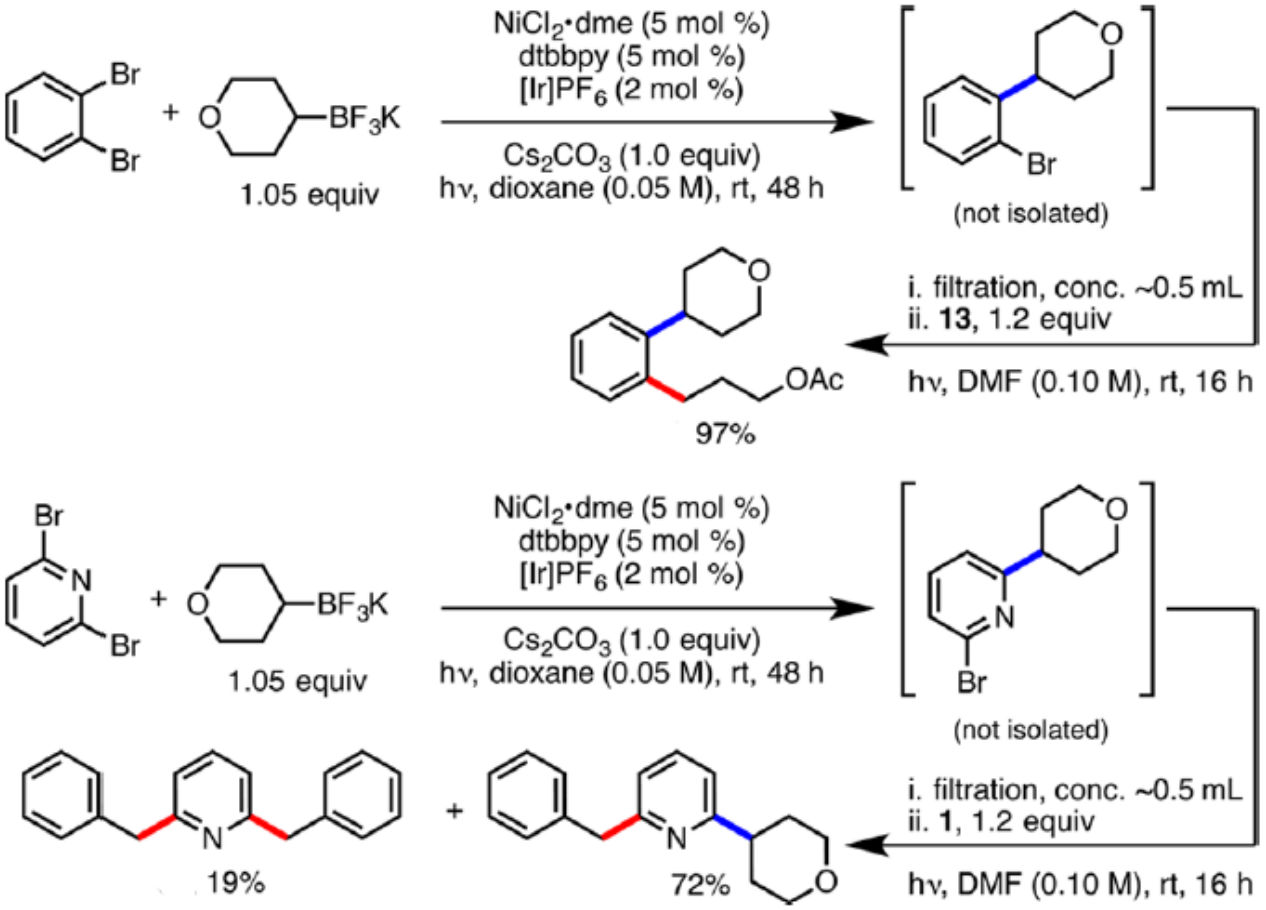
> Cross coupling using Alkylsilicates as radical precursor



40 examples

Jouffroy, M.; Primer, D. N.; Molander, G. A. *J. Am. Chem. Soc.*, **2016**, *138*, 475

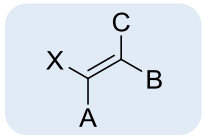
C-C Coupling
Molander group

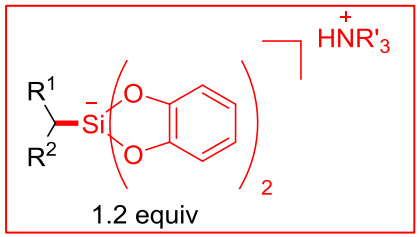


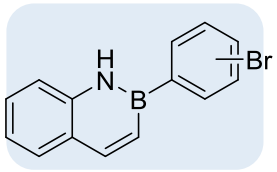
Jouffroy, M.; Primer, D. N.; Molander, G. A. *J. Am. Chem. Soc.*, **2016**, *138*, 475

C-C Coupling
Molander group

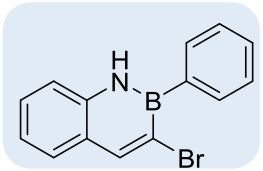
> Extension of the Scope





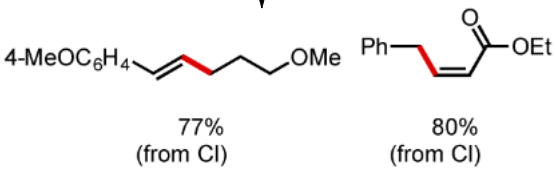


or



PC (2 mol %)
$NiCl_2$-dme (5 mol %)
dtbbpy (5 mol %)

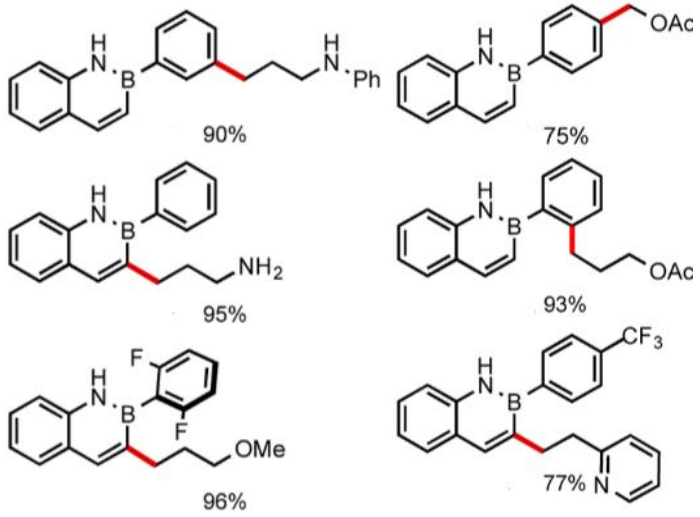
DMF, rt, 16 h
hν



38 examples

PC (2 mol %)
$NiCl_2$-dme (5 mol %)
dtbbpy (5 mol %)

DMF, rt, 16 h
hν

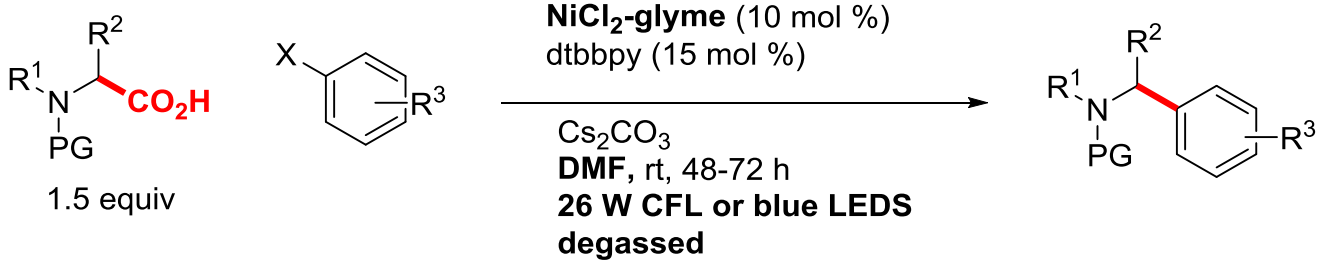


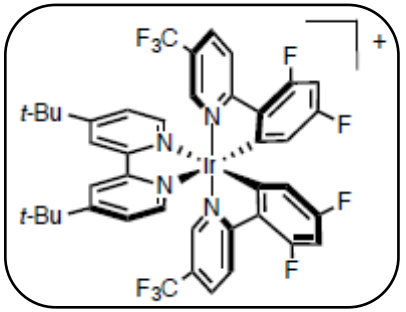
30 examples

> See also work oh L. Fensterbank, C. Ollivier and J-P. Goddard

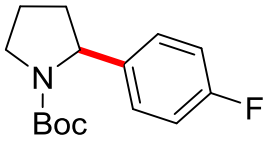
C-C Coupling
MacMillan group

> Coupling of α-amino acids with aryl halides

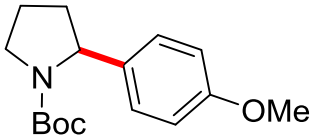




X=I

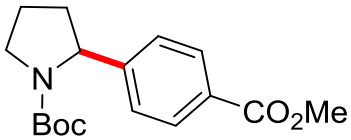


65%

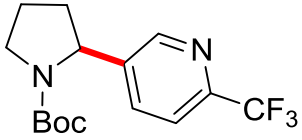


74%

X=Br

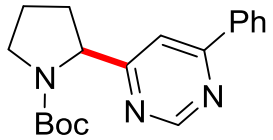


90%



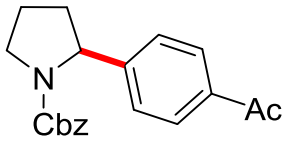
82%

X=Cl

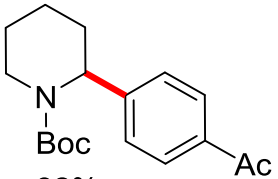


65%

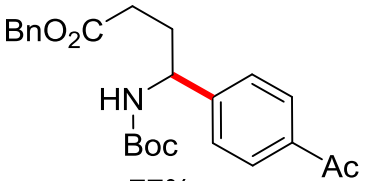
X=Br



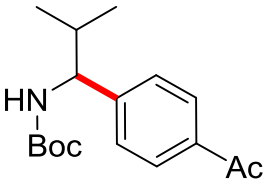
93%



82%

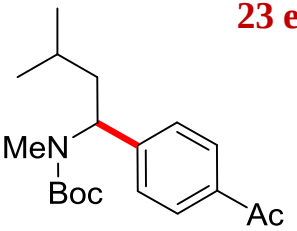


77%



72%

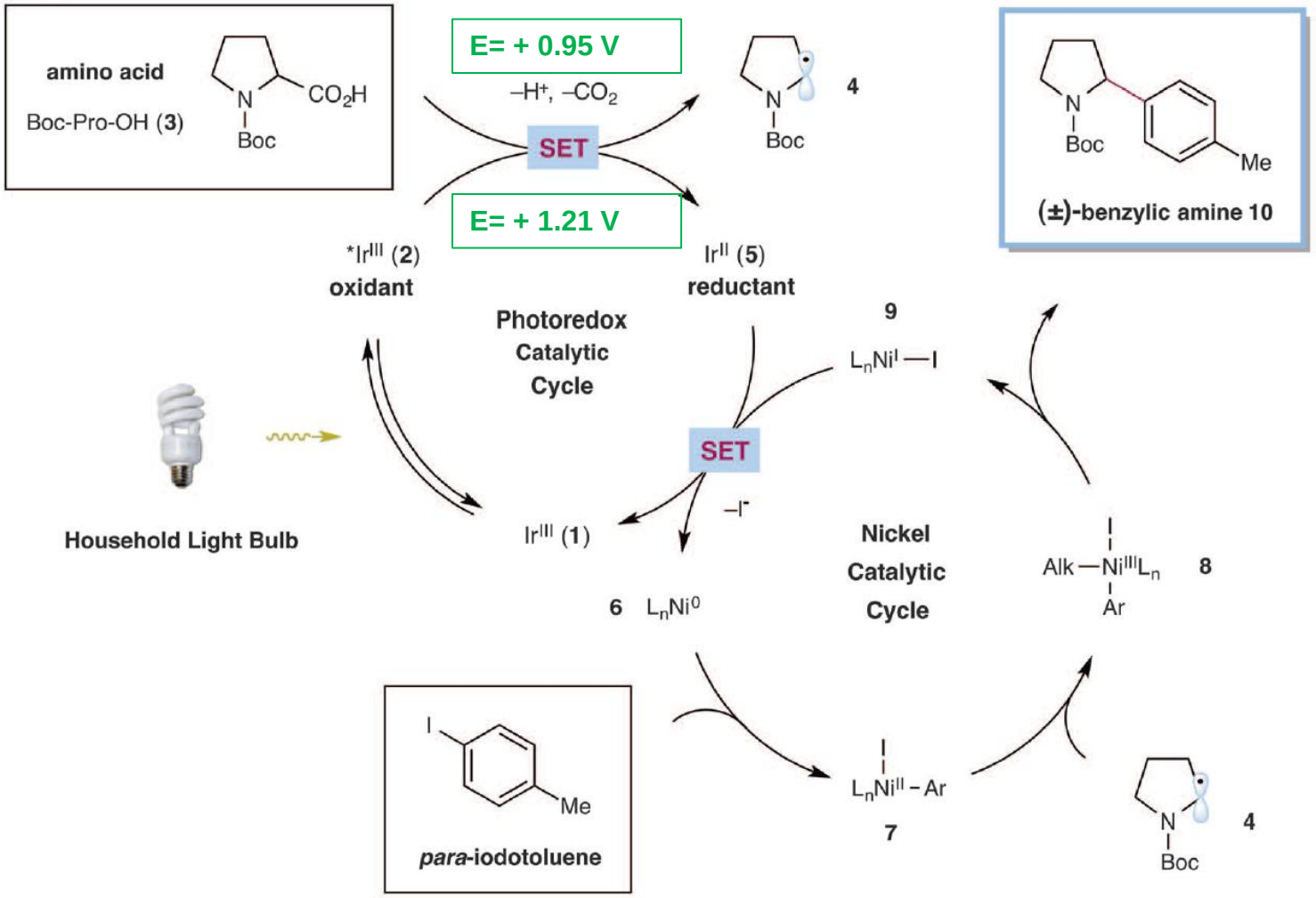
23 examples



92%

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

C-C Coupling
MacMillan group



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

C-C Coupling
MacMillan group

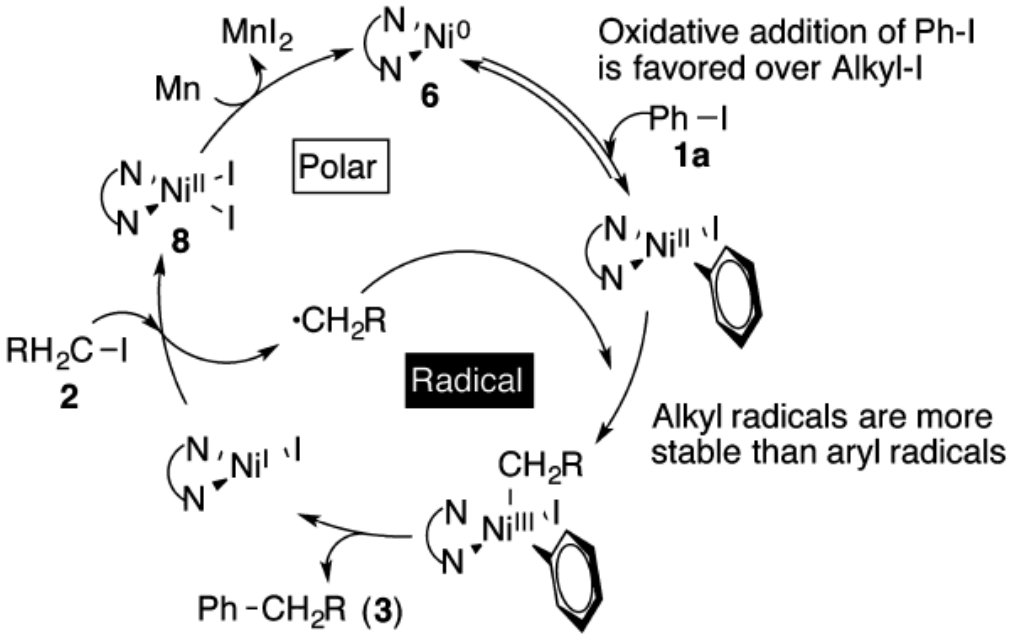
> Proof to support the mechanism

- Oxidative addition of ArBr faster on Ni(0) than on Ni(I) : Cyclic voltammetry

$$\mathrm{PhBr + Ni^0(dppe) \xrightarrow{step\ 1} PhNi^{II}Br(dppe)} \qquad k_1 = 1.1 \times 10^5\ \mathrm{M^{-1}\ s^{-1}}$$

$$\mathrm{PhBr + PhNi^{I}(dppe) \xrightarrow{step\ 3} Ph_2Ni^{III}Br(dppe)} \qquad k_3 = 960\ \mathrm{M^{-1}\ s^{-1}}$$

- Rapid reaction between Ni(II) and sp3 radical in the competition between aryl-X and alkyl X oxidative insertion

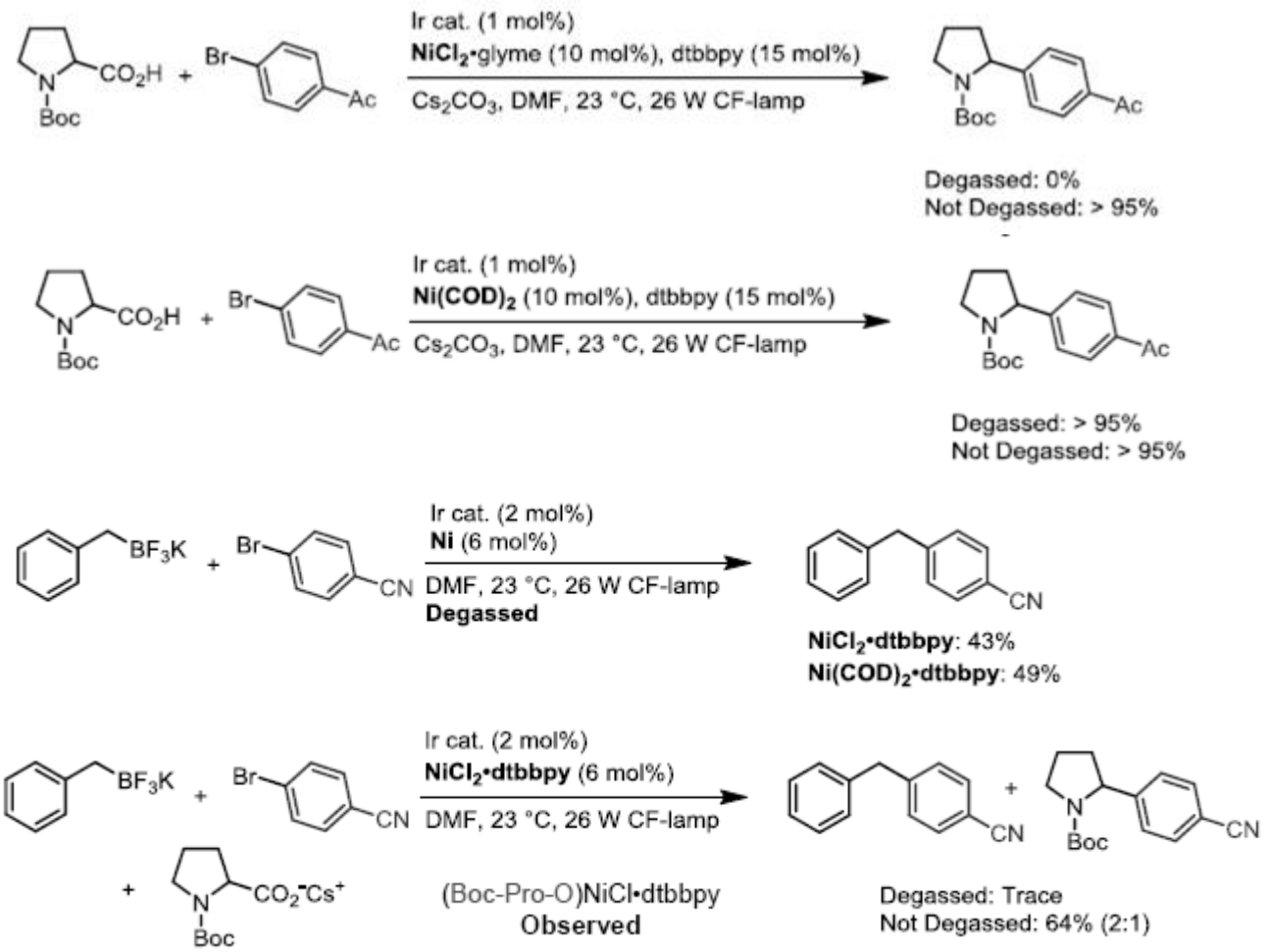


C. Amatore, A. Jutand, *Organometallics* **1988**, *7*, 2203–2214

S. Biswas, D. J. Weix *J. Am. Chem. Soc*. **2013**, *135*, 16192−16197

C-C Coupling
MacMillan group

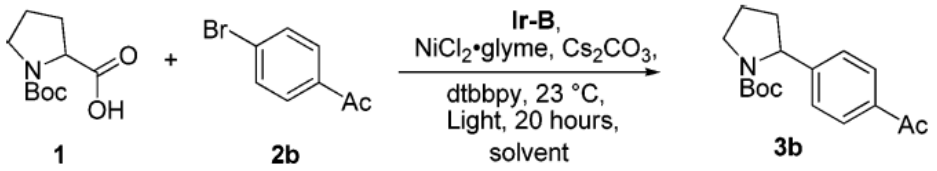
> Effect of Oxygen, solvent and light



M. S. Oderinde, A.Varela-Alvarez, B. Aquila, D. W. Robbins,J. W. Johannes, *J. Org. Chem*. **2015**, *80*, 7642−7651

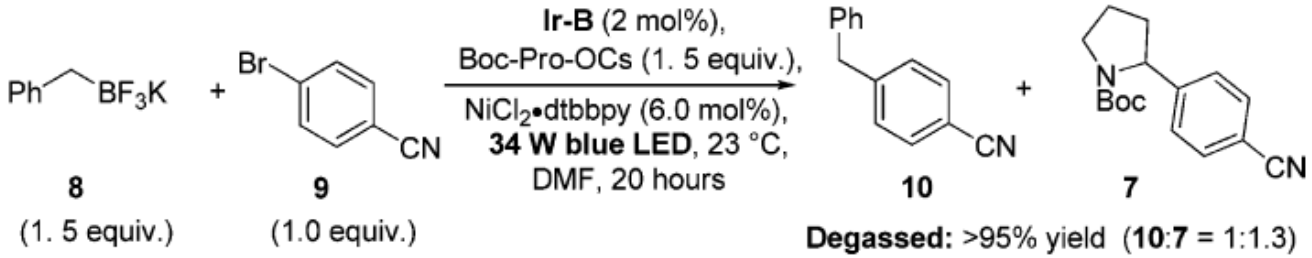
C-C Coupling
MacMillan group

> Effect of Oxygen, solvent and light



1 2b 3b

entry	light source	solvent	reaction mixture	% yield[b,c]
1	26 W CF lamp	DMF	degassed	0
2	26 W CF lamp	MeCN	degassed	68
3	26 W CF lamp	MeCN/DMF (4:1)	degassed	90
4	34 W blue LEDs	DMF	degassed	>95[d]



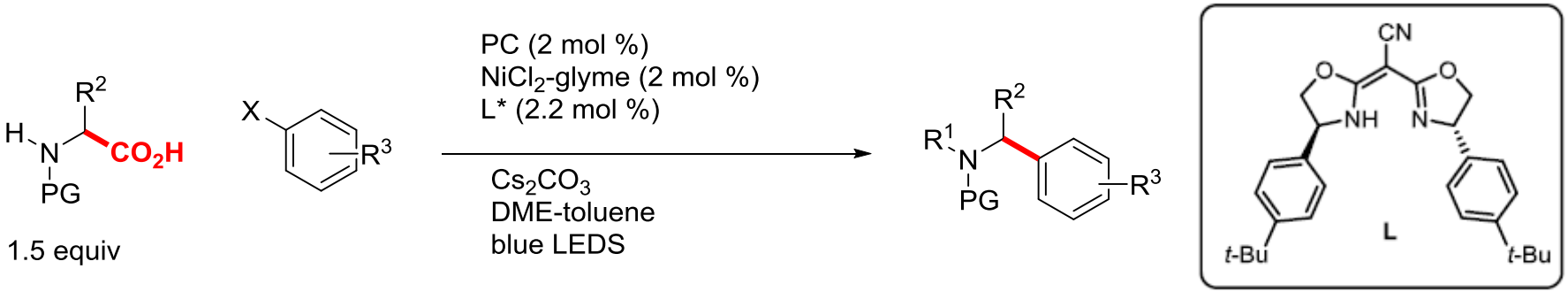
8 (1. 5 equiv.) **9** (1.0 equiv.) **10** **7**

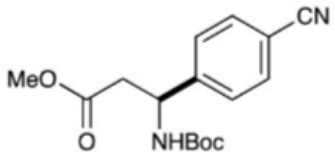
Degassed: >95% yield (**10**:**7** = 1:1.3)

M. S. Oderinde, A.Varela-Alvarez, B. Aquila, D. W. Robbins,J. W. Johannes, *J. Org. Chem.* **2015**, *80*, 7642−7651

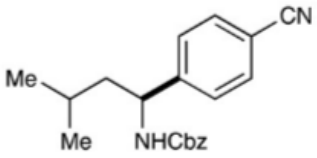
C-C Coupling
MacMillan group

> Asymmetric decarboxylation for enantioenriched benzyilic amines

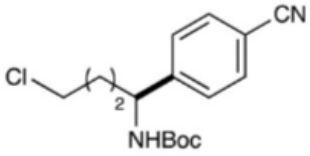




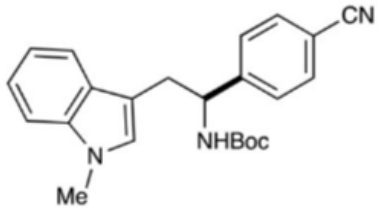
80% yield, 82% ee



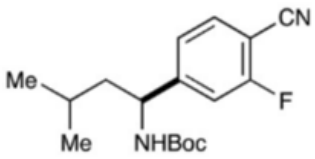
45% yield, 88% ee



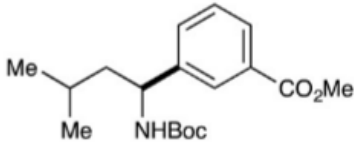
71% yield, 85% ee



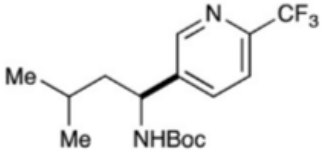
51% yield, 84% ee[c]



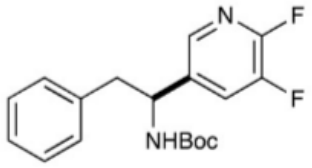
76% yield, 91% ee



73% yield, 91% ee[b]



73% yield, 92% ee



47% yield, 90% ee[d]

24 examples

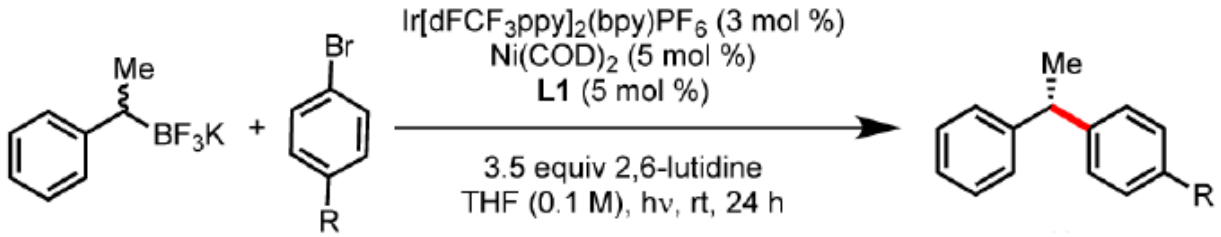
Z. Zuo, H. Cong, W, Li, J. Choi, G. C. Fu, D. W. C. MacMillan *J. Am. Chem. Soc*, **2016**, 138, 1832-1835

C-C Coupling
MacMillan group

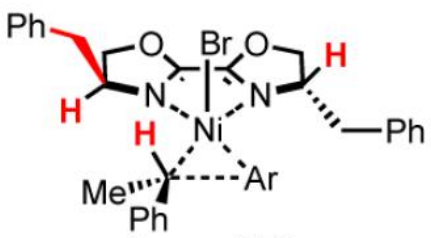
> Explanation

- MacMillan : facial selectivity in the addition of a prochiral radical to Ni(II) followed by stereoretentive reductive elimination

- Molander : equilibrium Ni(III)/Ni(II). So two equilibrating diastereomeric Ni(III)
  Faster elimination of 1 give the major enantiomer

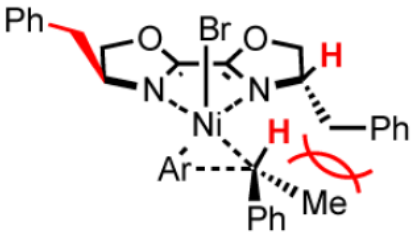


Major Product



favored-TS

Minor Product

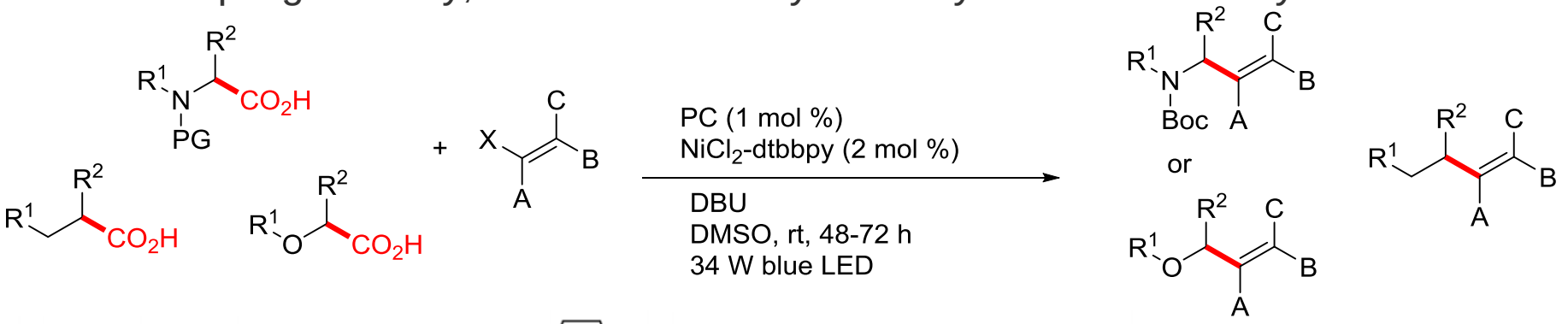


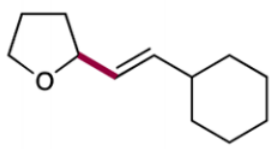
disfavored-TS

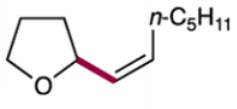
Z. Zuo, H. Cong, W, Li, J. Choi, G. C. Fu, D. W. C. MacMillan *J. Am. Chem. Soc*, **2016**, 138, 1832-1835

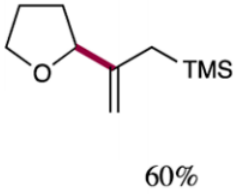
C-C Coupling
MacMillan group

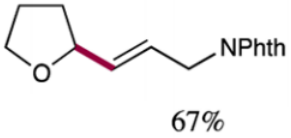
> Coupling of α-oxy, α-amino and alkyl carboxylic acids with Vinyl halides

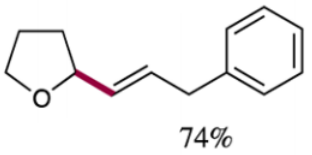


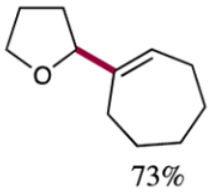

90%

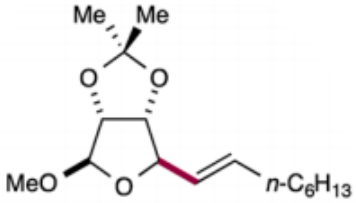

84%

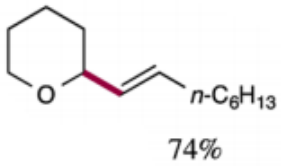

60%

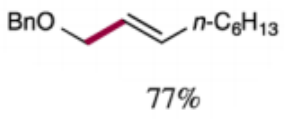

67%

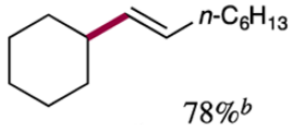

74%

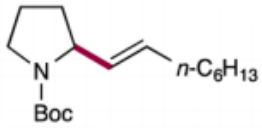

73%


89% (18:1 dr)


74%


77%


78%[b]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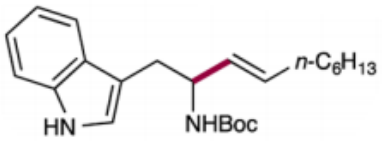
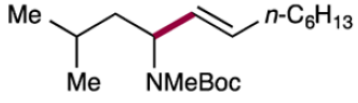
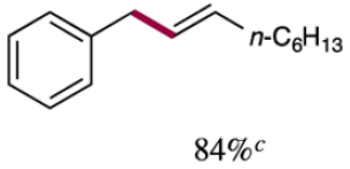

79%


89%

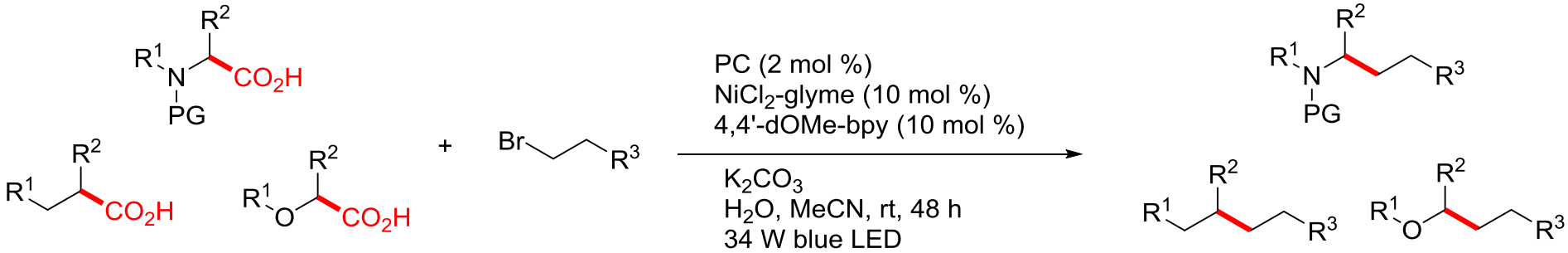

84%[c]

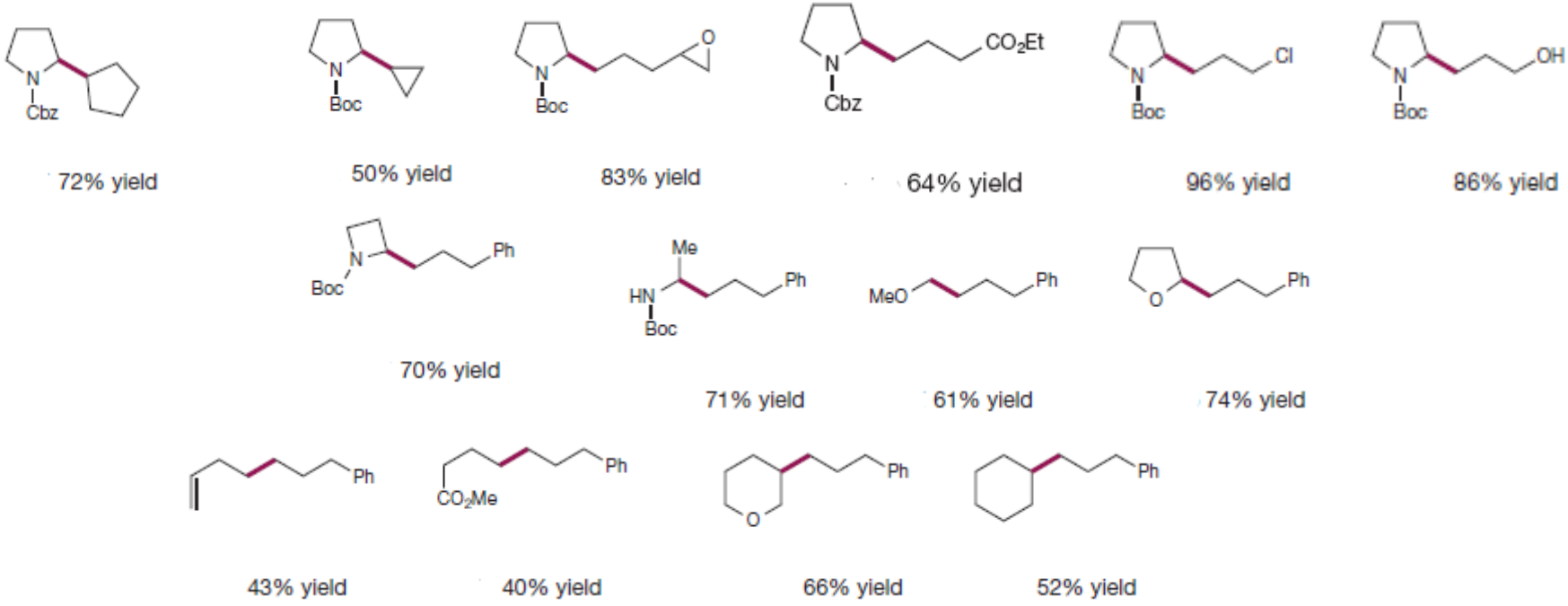
22 examples

A. Noble, S. J. McCarver, D. W. C. MacMillan, *J. Am. Chem. Soc.*, **2015,** *137*, 624-627

C-C Coupling
MacMillan group

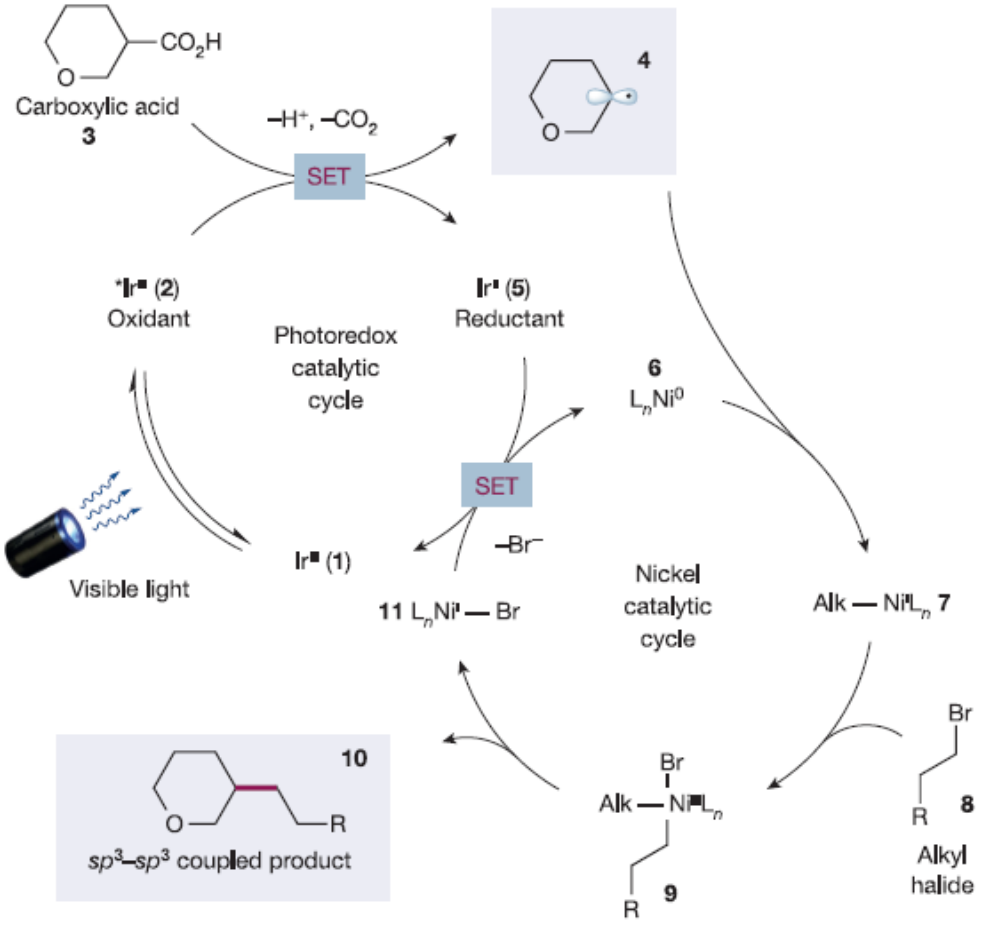
> Coupling of α-oxy, α-amino and alkyl carboxylic acids acids with Alkyl halides





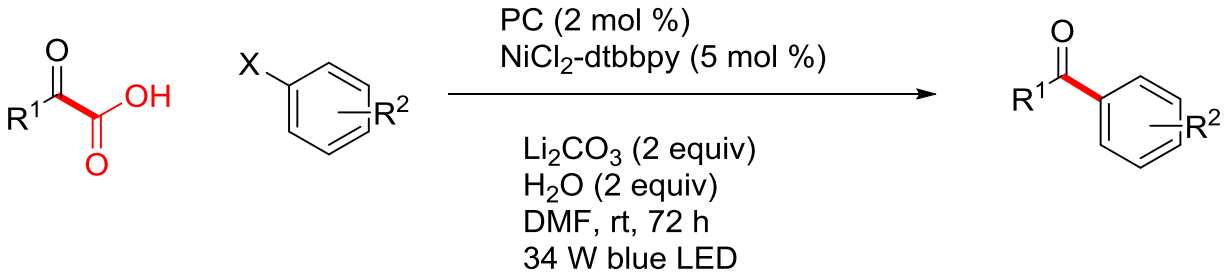
C-C Coupling
MacMillan group

> Proposed mechanism

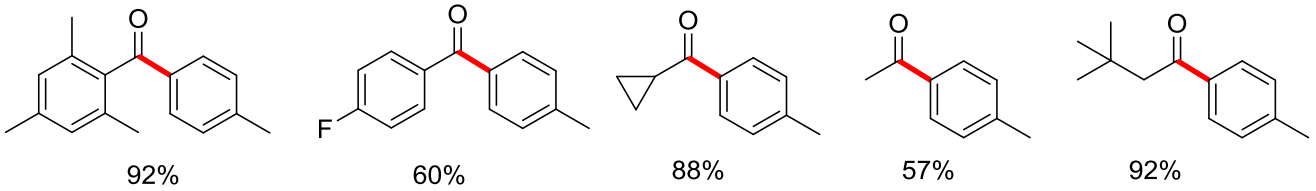


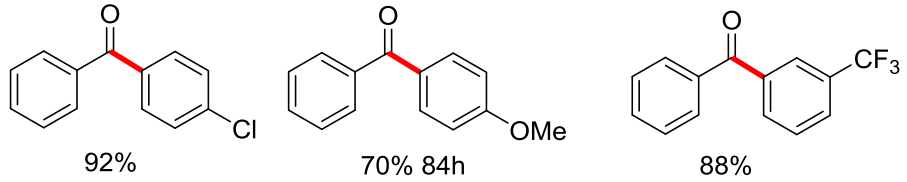
C-C Coupling
MacMillan group

> Coupling of keto acids with Aryl halides

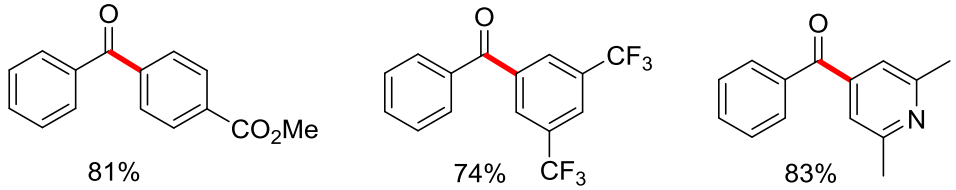


X=I





X=Br

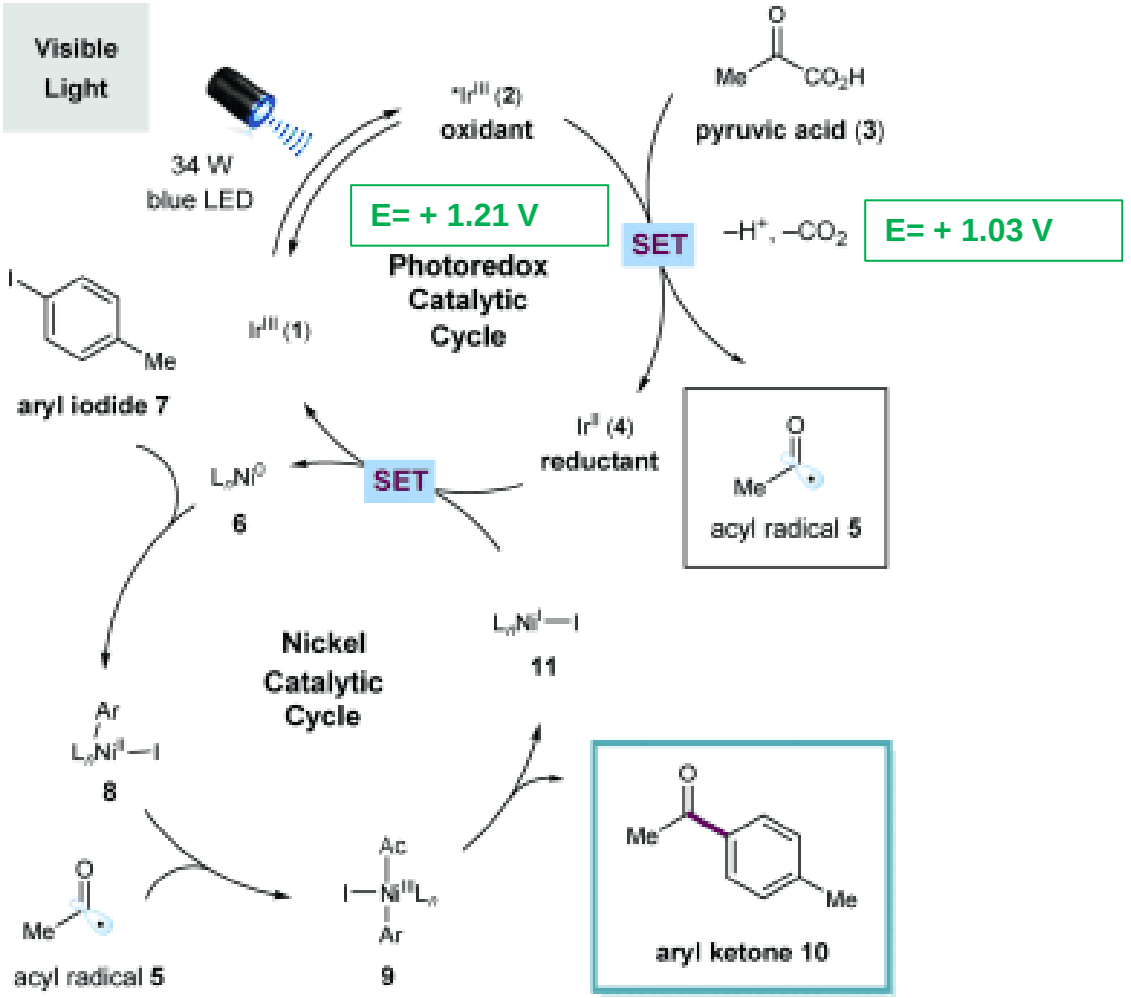


26 examples

L. Chu, J. M. Lipshultz, D. W. C. MacMillan , *Angew. Chem. Int. Ed.*,**2015,** *54*, 7929-7933

C-C Coupling
MacMillan group

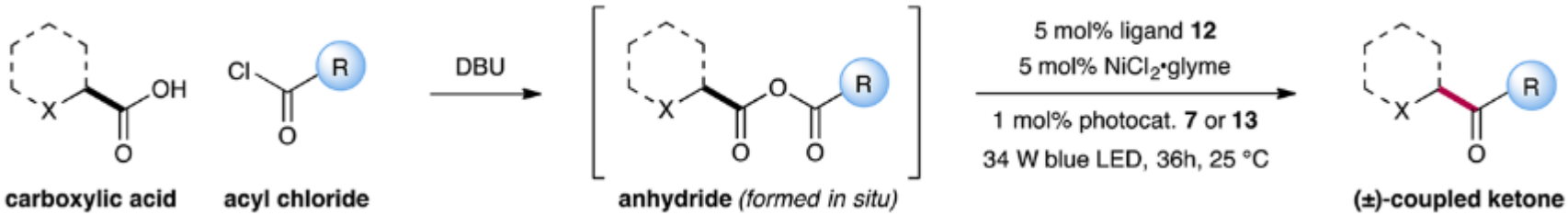
> Proposed mechanism

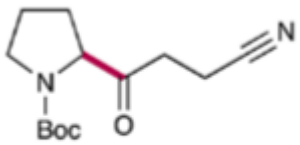


L. Chu, J. M. Lipshultz, D. W. C. MacMillan , *Angew. Chem. Int. Ed.*,**2015,** *54*, 7929-7933

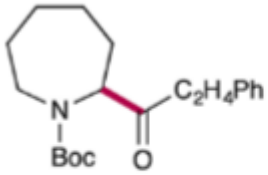
C-C Coupling
MacMillan group

> Coupling of Fragments from Anhydrides via CO_2 extrusion-recombination

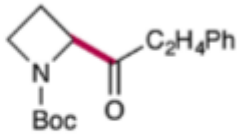




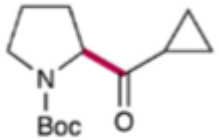
83% yield



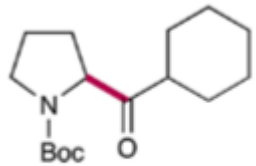
69% yield



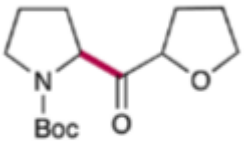
40% yield



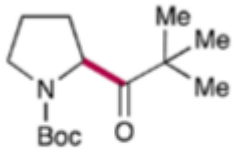
71% yield



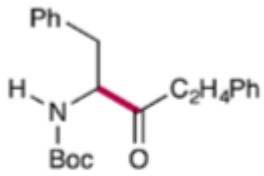
82% yield



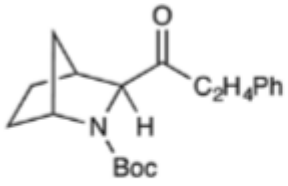
65% yield



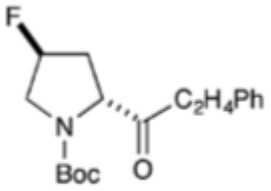
32% yield



55% yield



70% yield[a] (>20:1 dr)



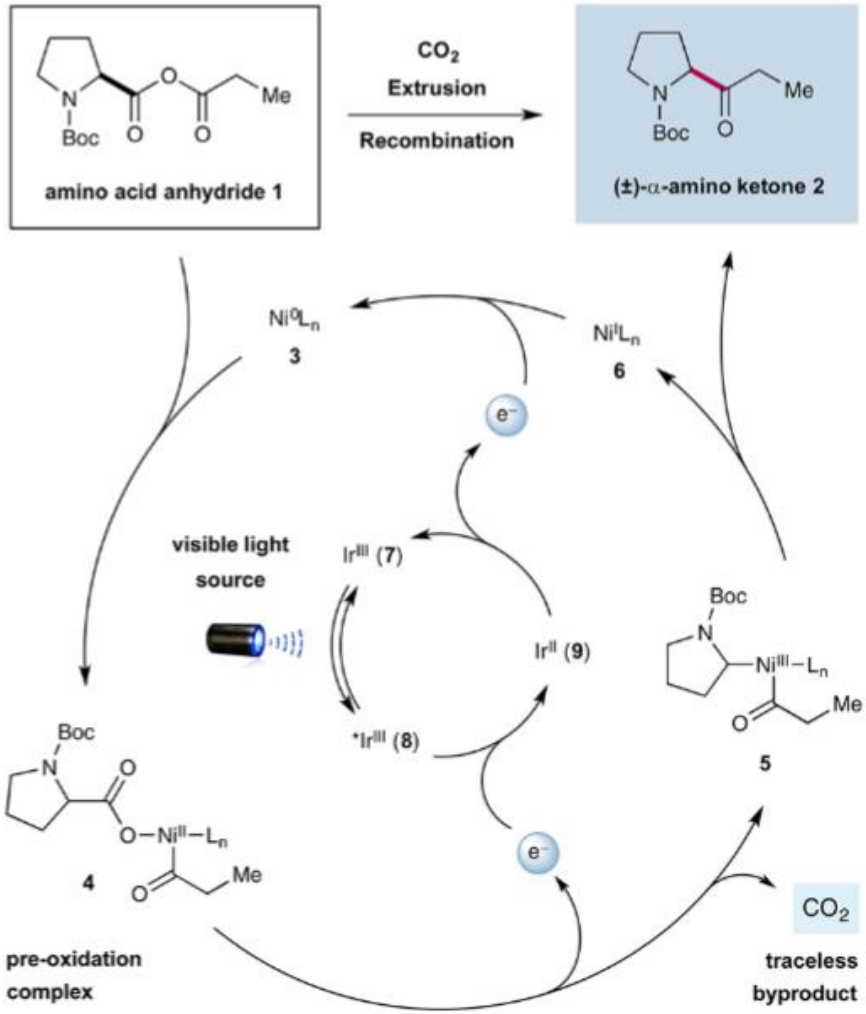
82% yield[a] (8:1 dr)

30 examples

C. C. Le, D. W. C. MacMillan. *J. Am. Chem. Soc.* **2015**, *137*, 11938-11941

C-C Coupling
MacMillan group

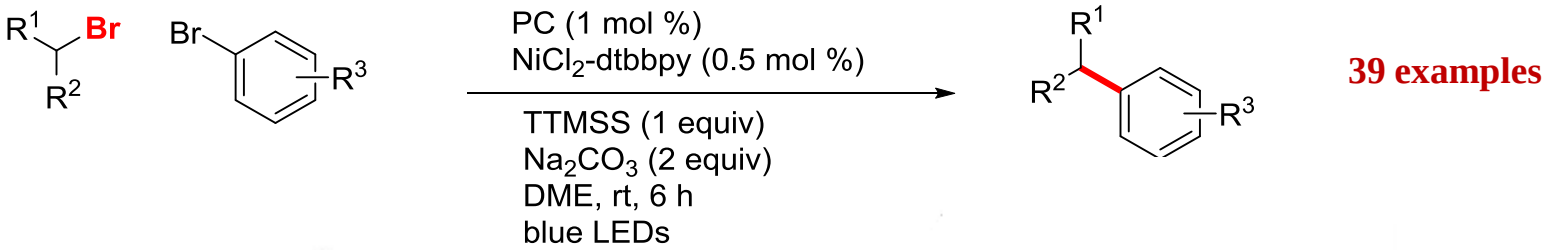
> Proposed mechanism



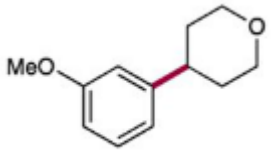
C. C. Le, D. W. C. MacMillan. *J. Am. Chem. Soc.* **2015**, *137*, 11938-11941

C-C Coupling
MacMillan group

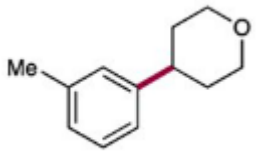
> Coupling of Alkyl halides with Aryl halide



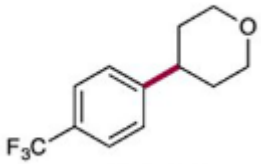
39 examples



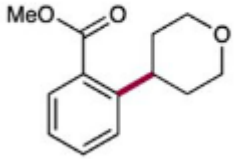
82% yield



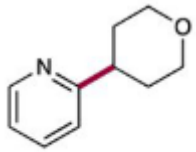
80% yield



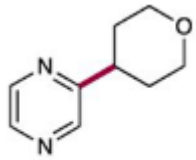
78% yield



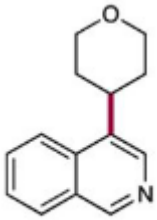
63% yield[b]



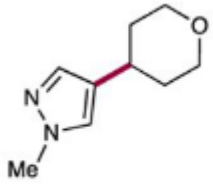
50% yield



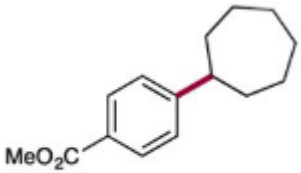
50% yield



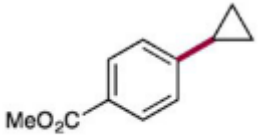
78% yield[f]



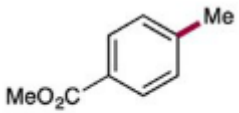
66% yield[e]



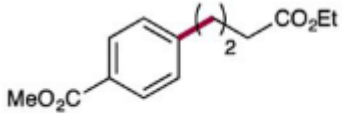
66% yield



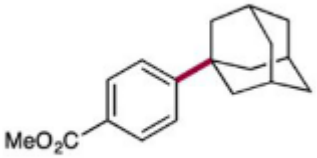
32% yield



62% yield[h]



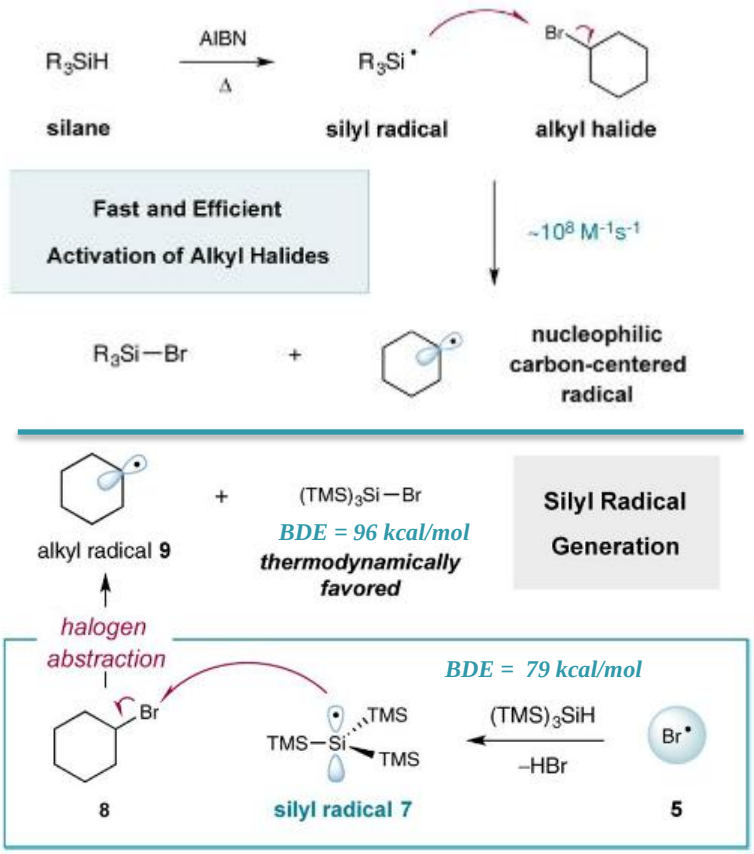
92% yield

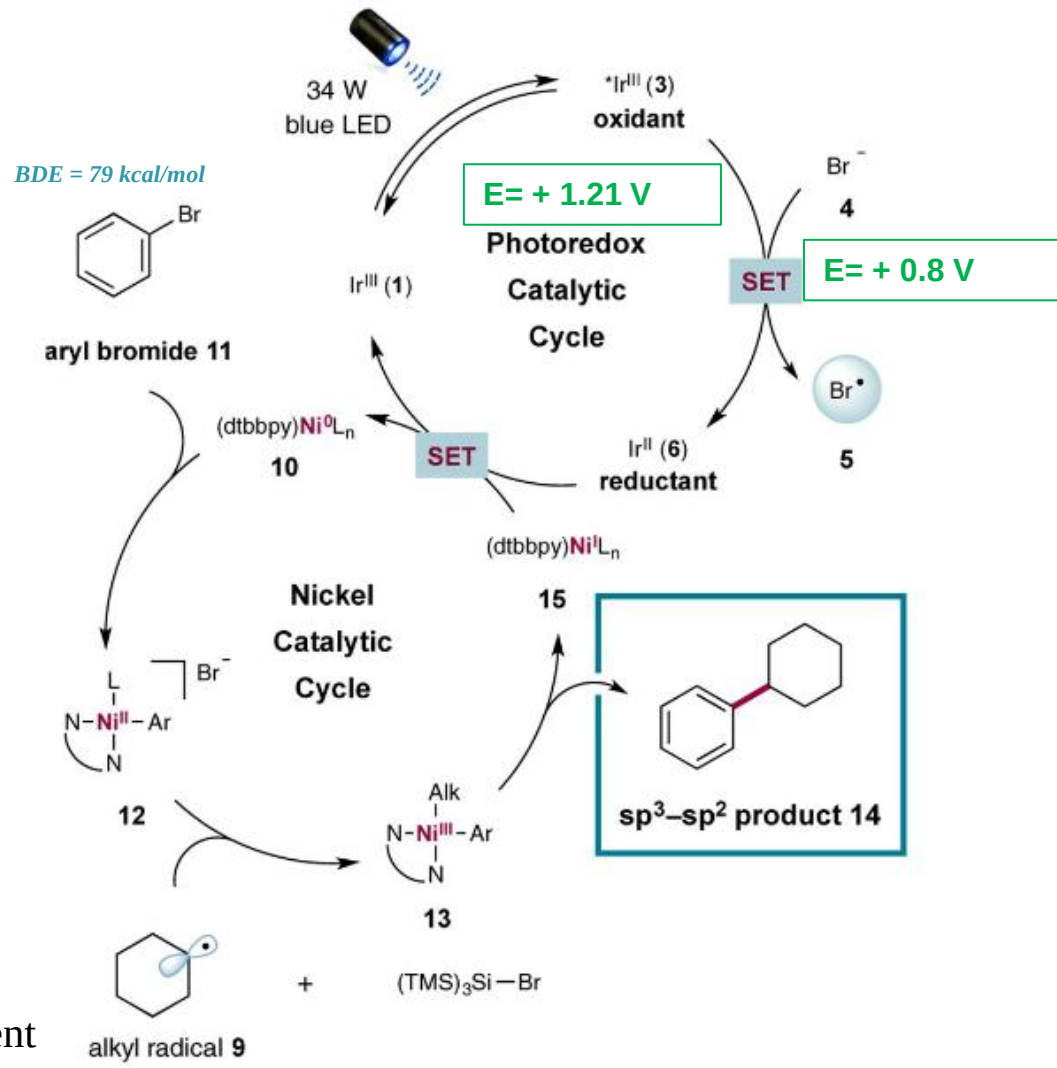


62% yield[e,i,k]

C. C. Le, D. W. C. MacMillan. *J. Am. Chem. Soc.* **2015**, *137*, 11938-11941

C-C Coupling
MacMillan group



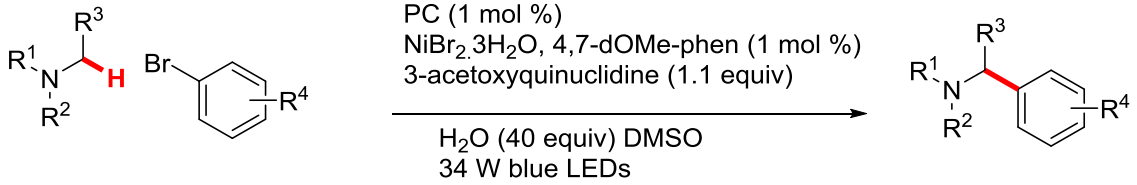


Other reductants and other silanes less/not efficient
Et_3SiH (91 kcal/mol) Ph_3SiH (84 kcal/mol)

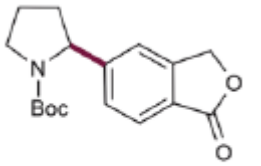
C. C. Le, D. W. C. MacMillan. *J. Am. Chem. Soc.* **2015**, *137*, 11938-11941
Chatgilialoglu, C. *Acc. Chem. Res*. **1992**, *25*, 188

C-C Coupling
MacMillan group

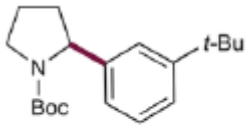
> Coupling of amine with aryl halide via HAT



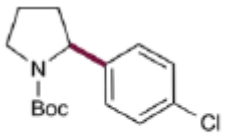
35 examples



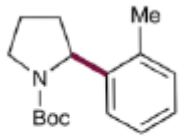
76% yield



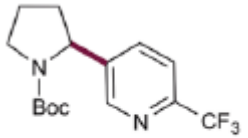
79% yield



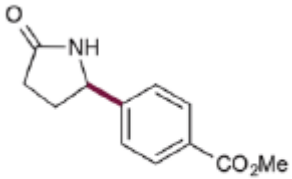
70% yield



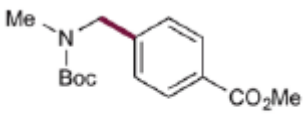
70% yield



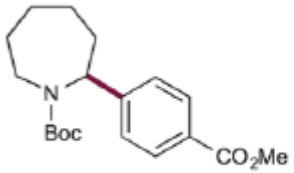
81% yield



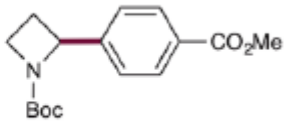
69% yield



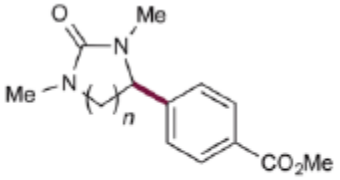
44 65% yield



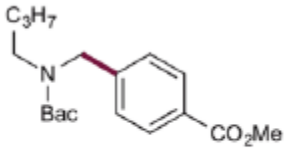
69% yield



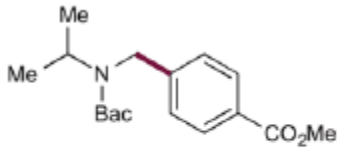
58% yield



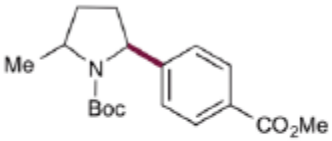
n = 1 84% yield, 3:1 r.r.†
n = 2 71% yield, 1:1 r.r.†



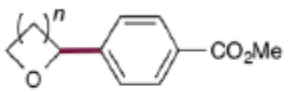
78% yield
4:1 r.r.‡



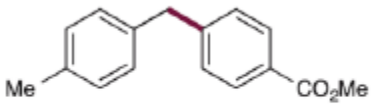
82% yield
single regioisomer



62% yield, 1:1 d.r.
single regioisomer



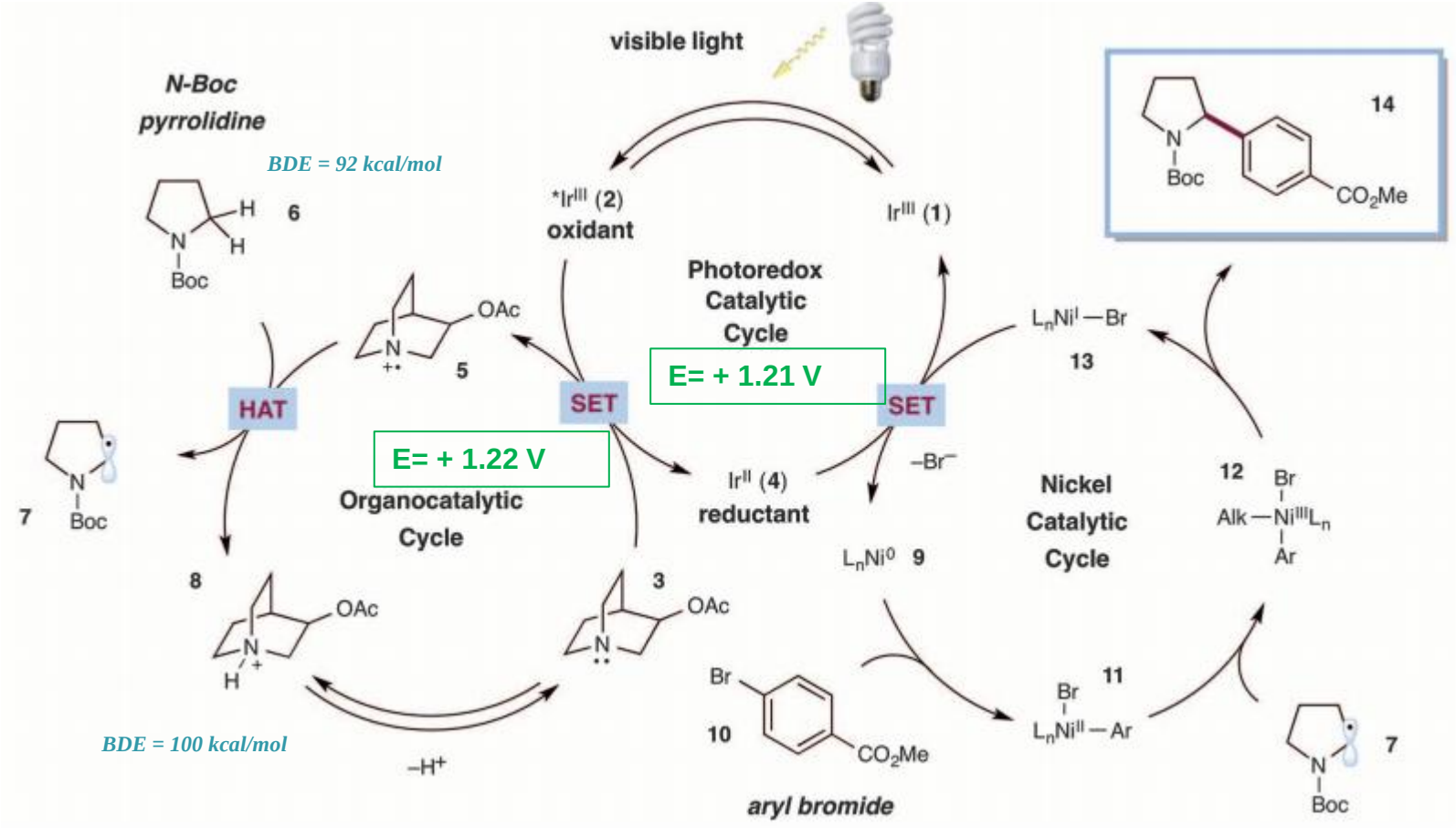
n = 2 76% yield
n = 1 53% yield



54% yield§

M. H. Shaw, V. W. Shurtleff, J. A, Terrett, J. D. Cuthbertson, D. W. C. MacMillan, *Science*,**2016,** *352*, 1304-1308

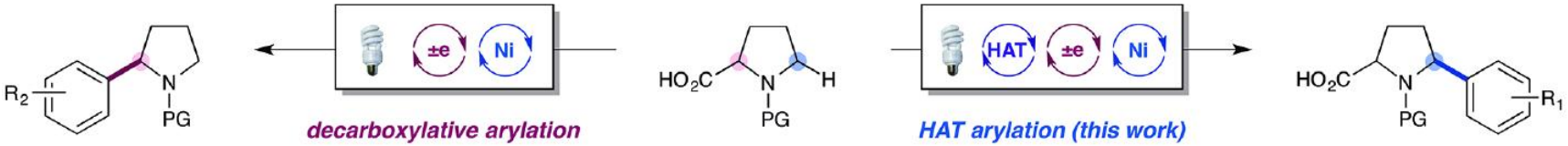
C-C Coupling
MacMillan group

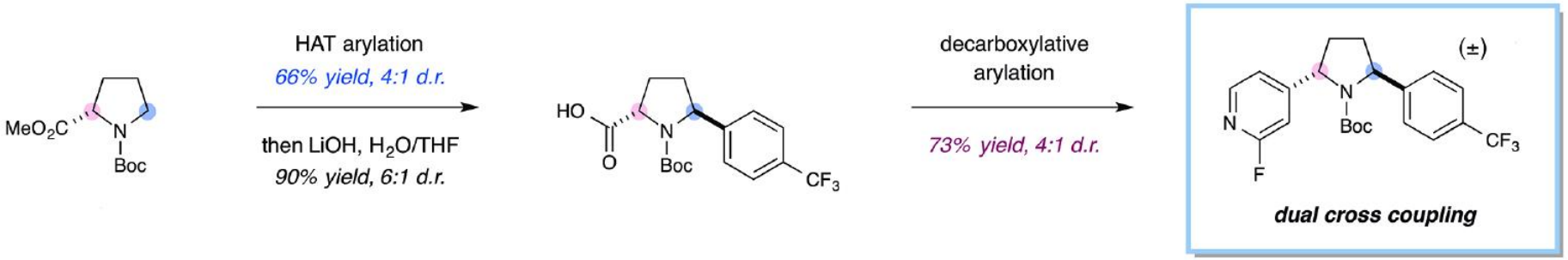


M. H. Shaw, V. W. Shurtleff, J. A, Terrett, J. D. Cuthbertson, D. W. C. MacMillan, *Science*,**2016,** *352*, 1304-1308

C-C Coupling
MacMillan group

> Useful application



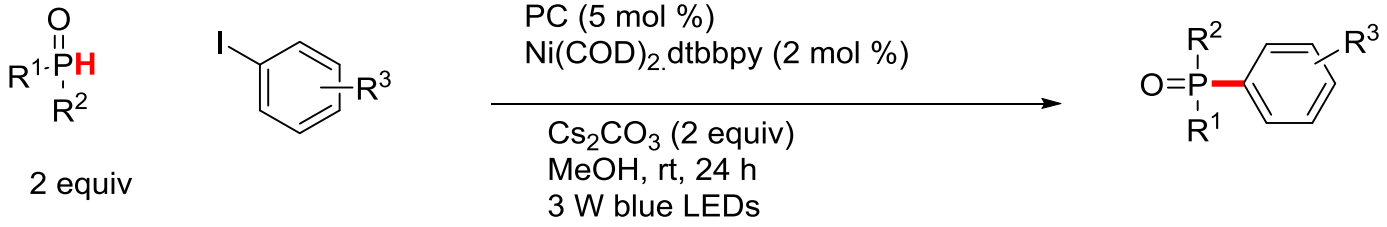


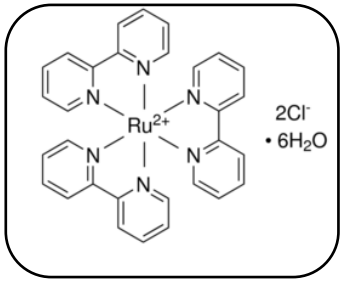
M. H. Shaw, V. W. Shurtleff, J. A, Terrett, J. D. Cuthbertson, D. W. C. MacMillan, *Science*,**2016,** *352*, 1304-1308

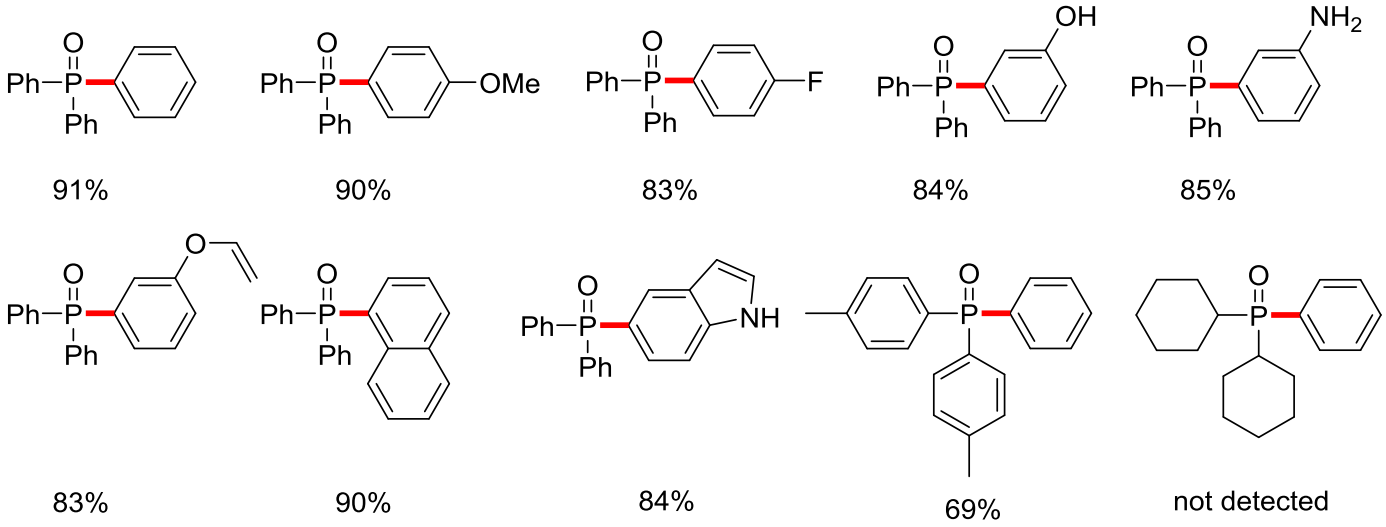
Carbon-Heteroatom cross coupling

C-P coupling

> Coupling of phosphine with Aryl halide





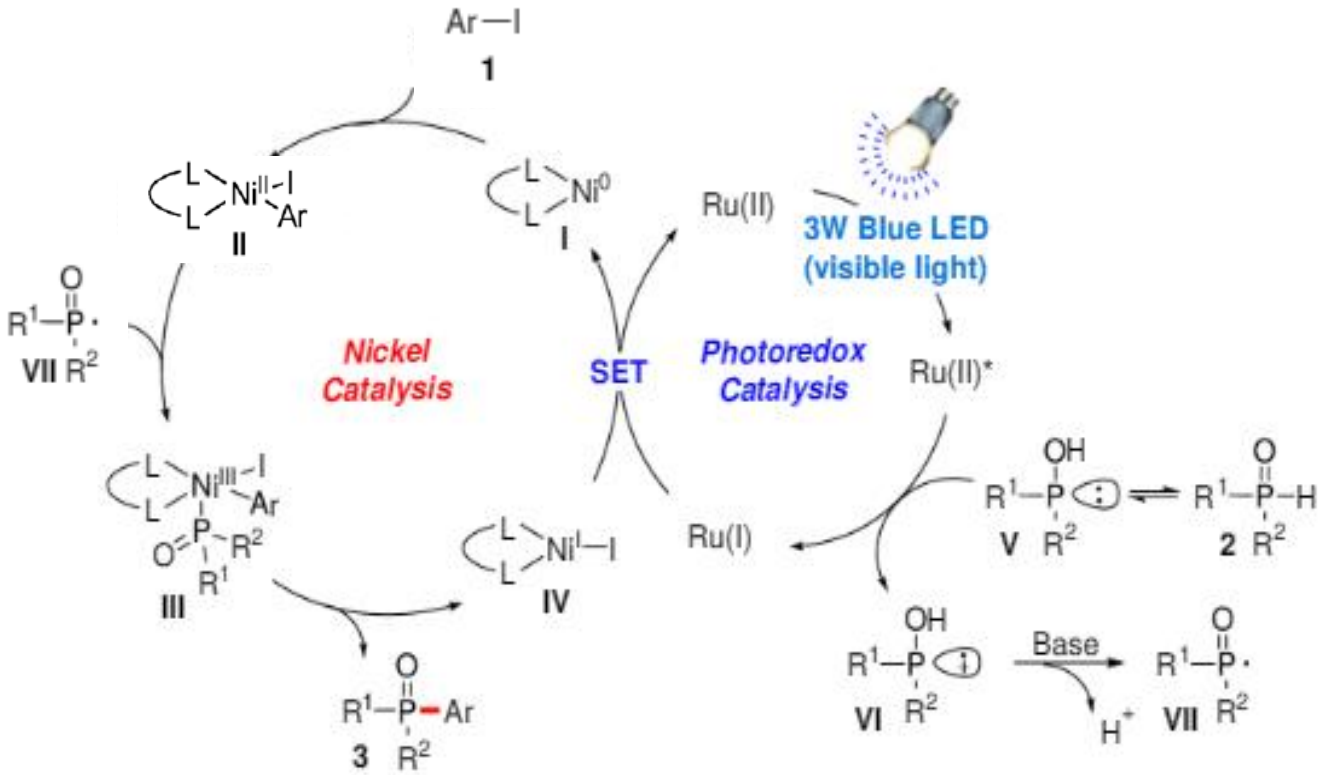


15 examples

Xuan, J.; Zeng, T.-T.; Chen, J.-R.; Lu, L.-Q.; Xiao, W.-J. *Chem. Eur. J.* **2015**, *21*, 4962.

C-P coupling

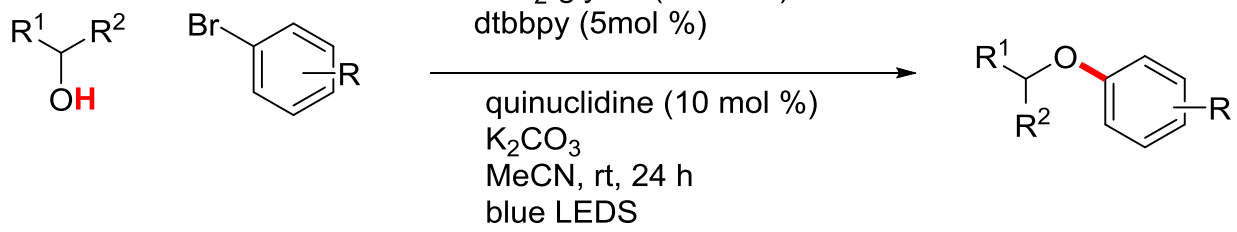
> Proposed mechanism

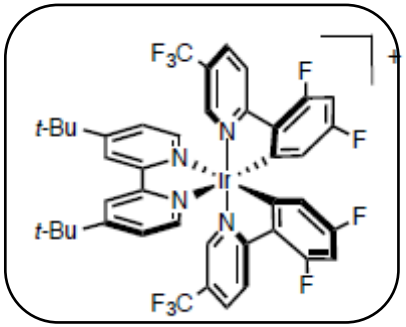


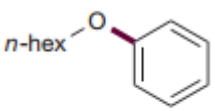
Xuan, J.; Zeng, T.-T.; Chen, J.-R.; Lu, L.-Q.; Xiao, W.-J. *Chem. Eur. J.* **2015**, *21*, 4962.

C-O coupling

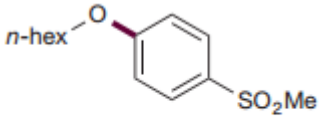
> Coupling of alcohol with aryl halide



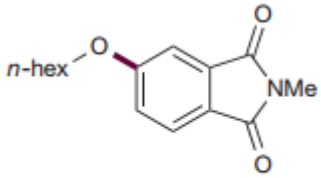




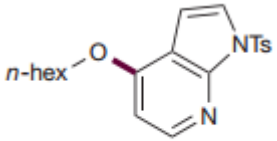
68% yield



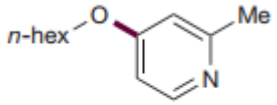
93% yield



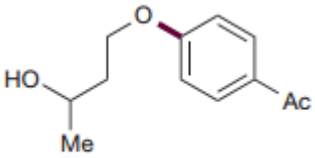
92% yield



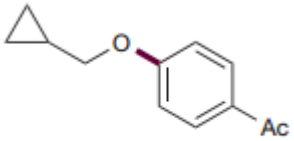
88% yield



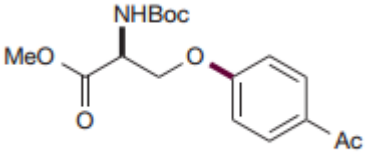
91% yield



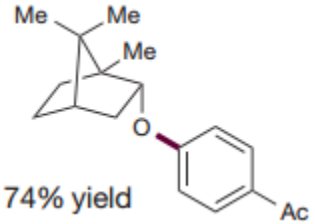
71% yield, 6:1 rr



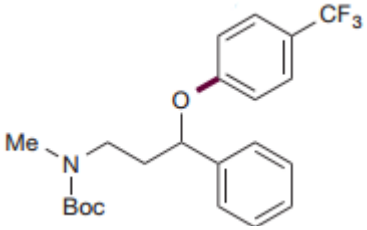
82% yield



78% vield

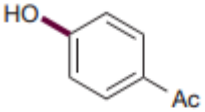


74% yield

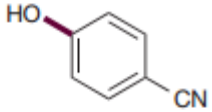


82% yield

Water



65% yield



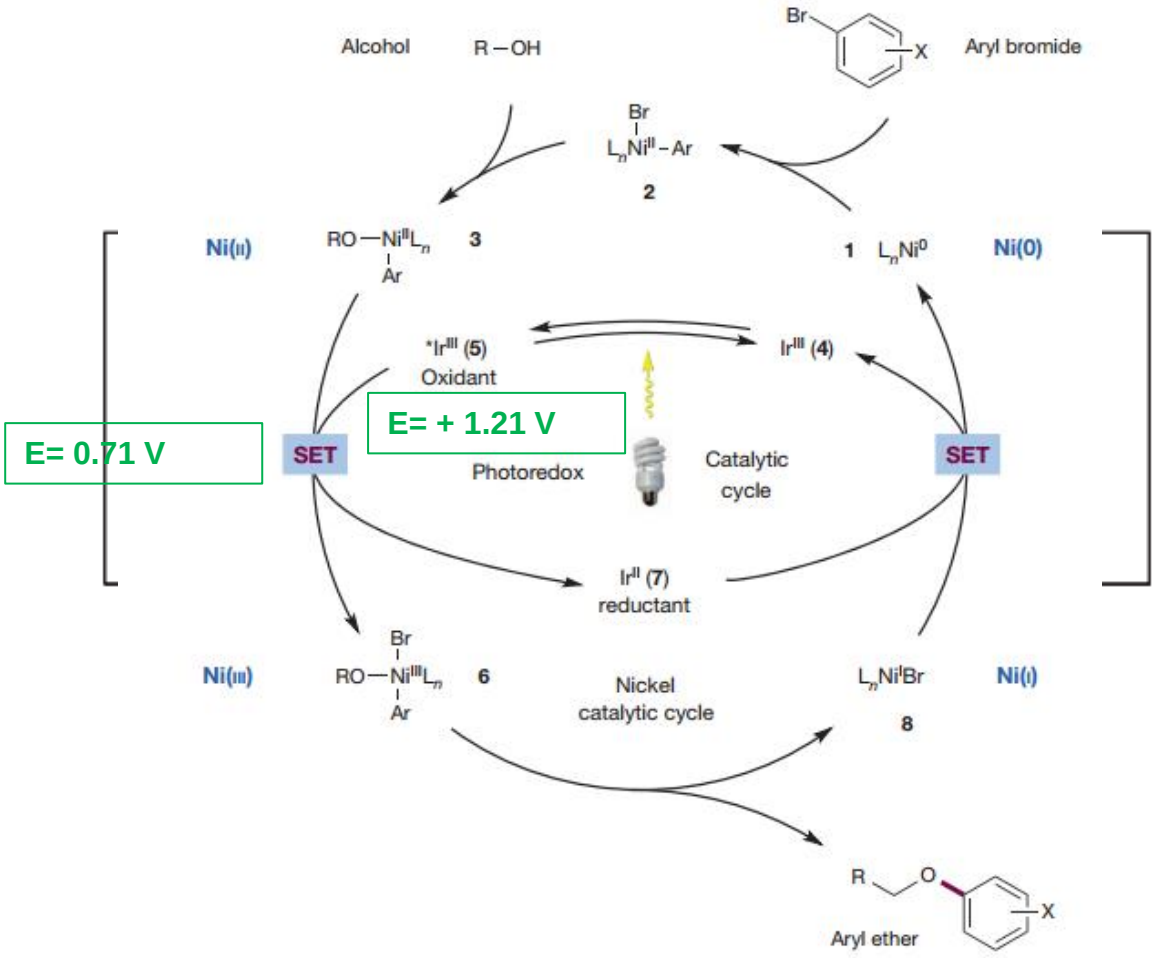
62% yield

36 examples

J. A. Terrett, J. D. Cuthbertson, V. W. Shurtleff, D. W. C. MacMillan, *Nature*,**2015,** *524*, 330-334

C-O coupling

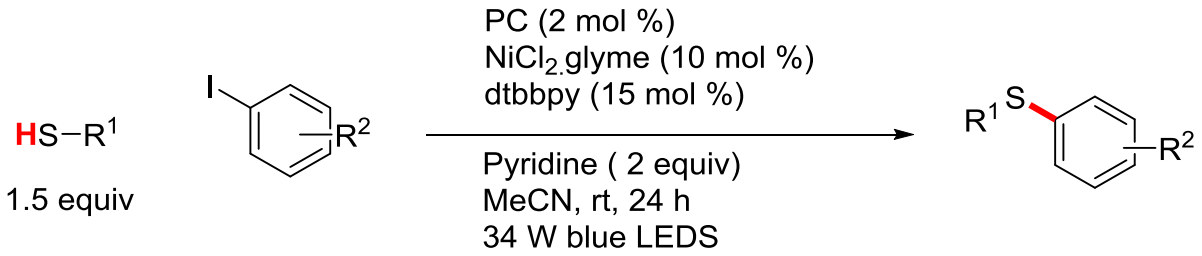
> Challenge and proposed mechanism

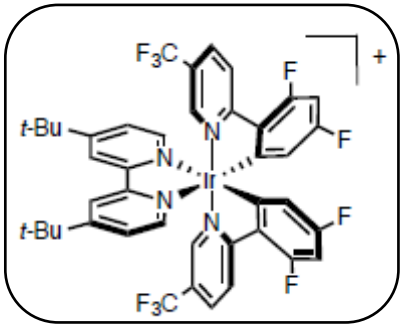


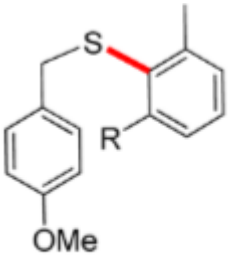
J. A. Terrett, J. D. Cuthbertson, V. W. Shurtleff, D. W. C. MacMillan, *Nature*,**2015,** *524*, 330-334

C-S coupling

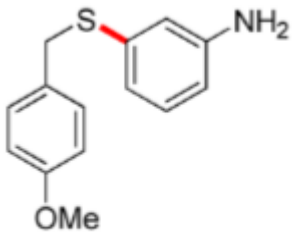
> Coupling of Thiols with aryl halide



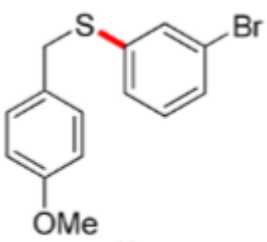




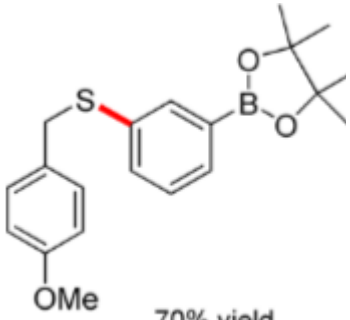
3e; R= H, 40% yield
3f; R= Me, 0% yield



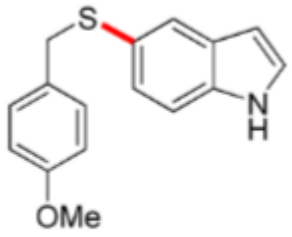
93% yield



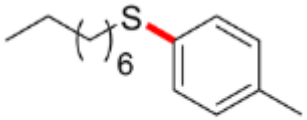
96% yield



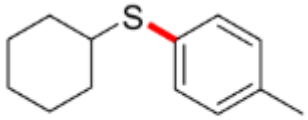
70% yield



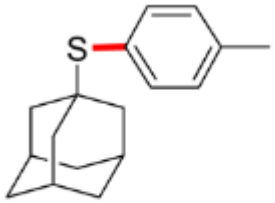
97% yield



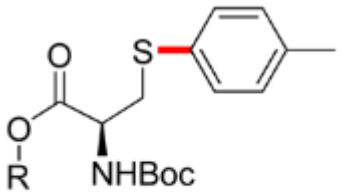
95% yield



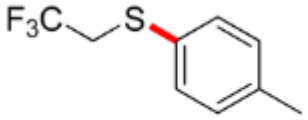
88% yield



30% yield



R = Me, 92% yield
R = H, 85% yield[b]



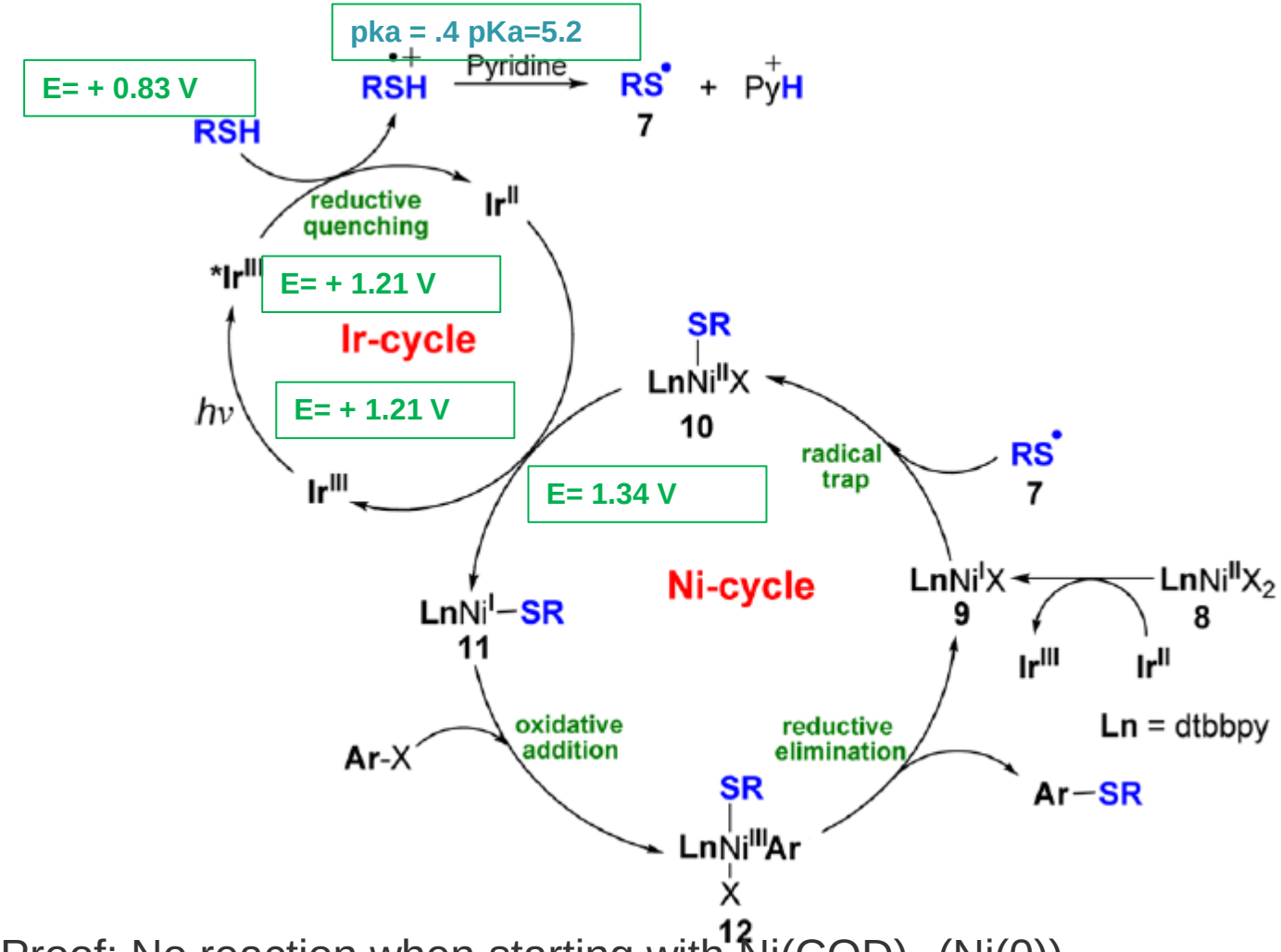
92% yield

29 examples

M. S. Oderinde, M. Frenette, B.Aquila, D.W. Robbins, and J. W. Johannes. *J. Am. Chem. Soc.* **2016**, *138*, 1760−1763

C-S coupling

- Proposed mechanism

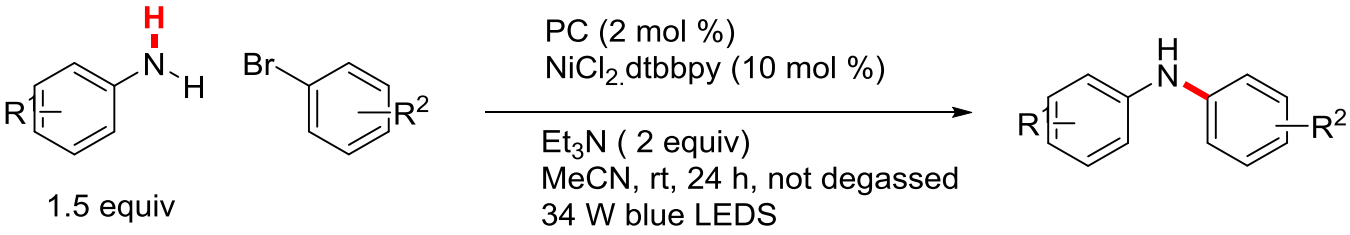


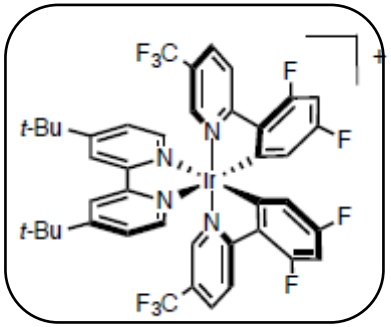
- Proof: No reaction when starting with $Ni(COD)_2$ (Ni(0))

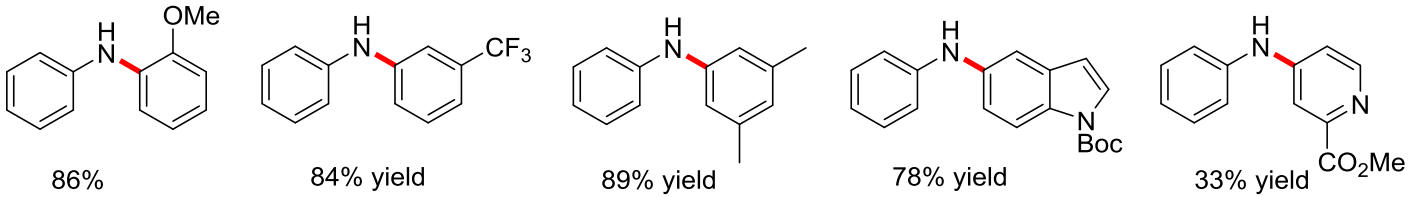
M. S. Oderinde, M. Frenette, B.Aquila, D.W. Robbins, and J. W. Johannes. *J. Am. Chem. Soc.* **2016**, *138*, 1760−1763

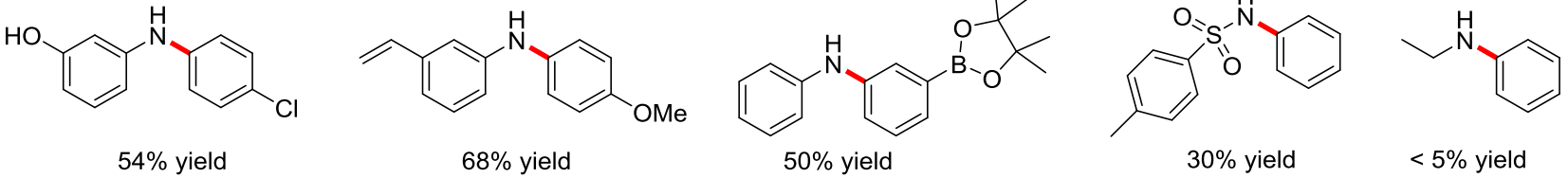
C-N coupling

> Coupling of amines with aryl halide





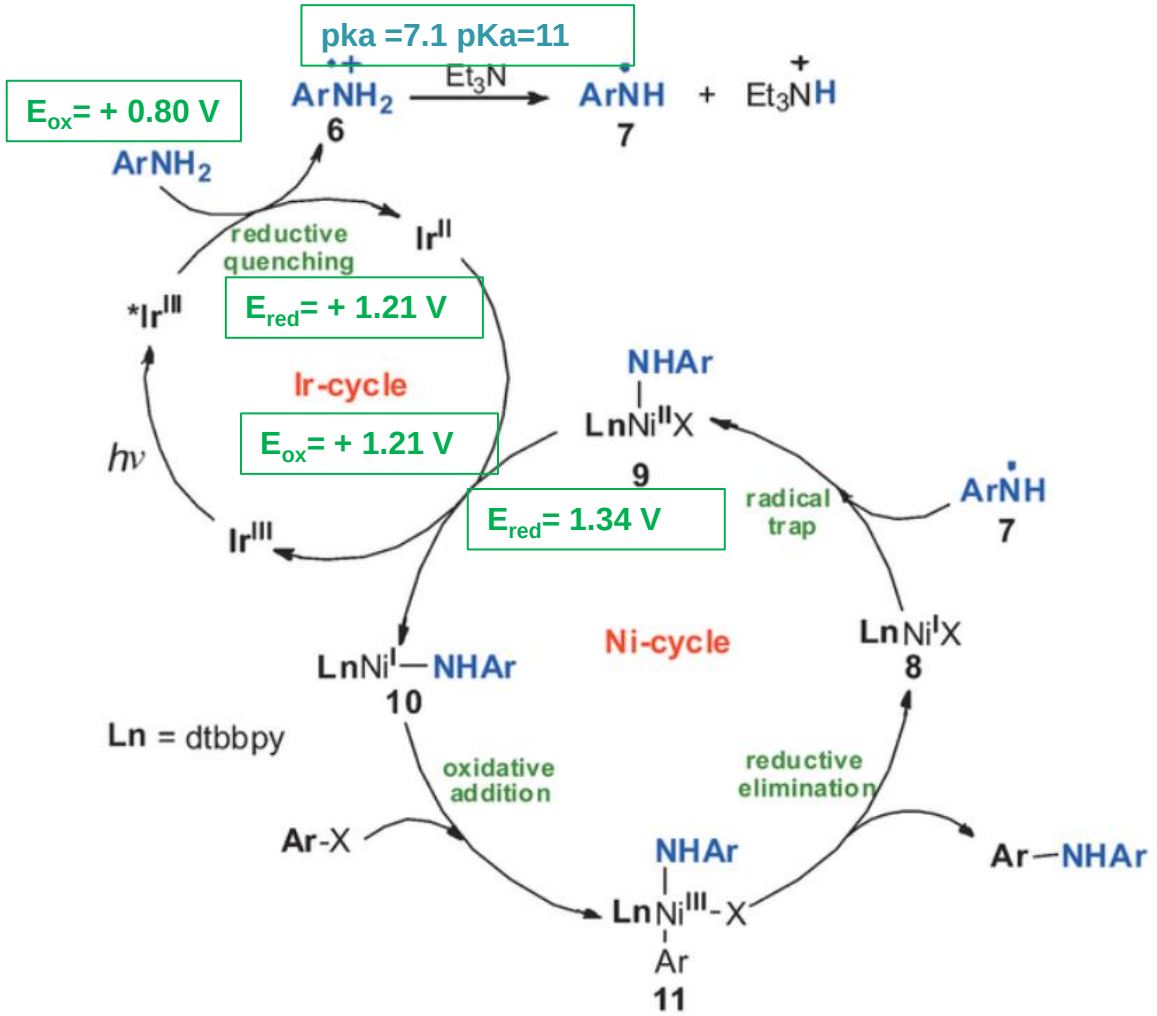




31 examples

M. S. Oderinde, N.H. Jones, A. Juneau, M. Frenette, B.Aquila, S.Tentarelli, D.W. Robbins, and J. W. Johannes. *Angew. Chem.* **2016**, *128*, 1–6

C-N coupling



M. S. Oderinde, N.H. Jones, A. Juneau, M. Frenette, B.Aquila, S.Tentarelli, D.W. Robbins, and J. W. Johannes. *Angew. Chem.* **2016**, *128*, 1–6

Conclusion

- Efficient method using mild conditions

- Wide scope of substrate (commercially available)
  - Functionnal group tolerance
  - Good yield
  - Enantioselective methode

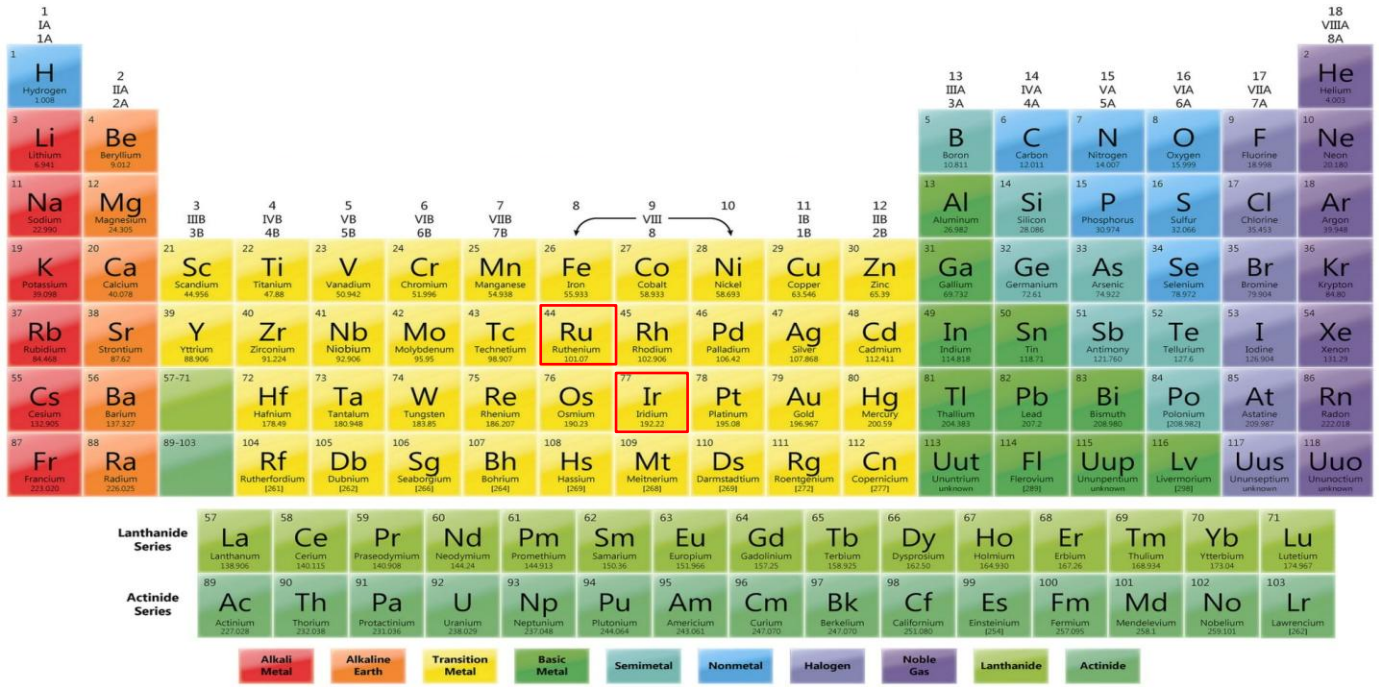
- Applicable on Carbon centered and heteroatom

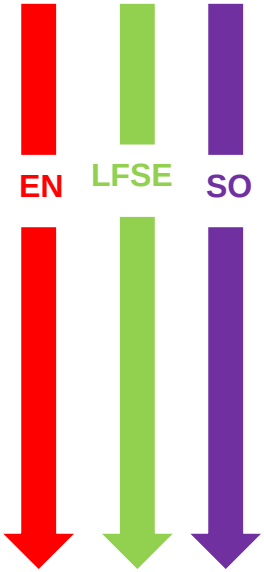
- C_{sp3}-C_{sp2} and C_{sp3}-C_{sp3}

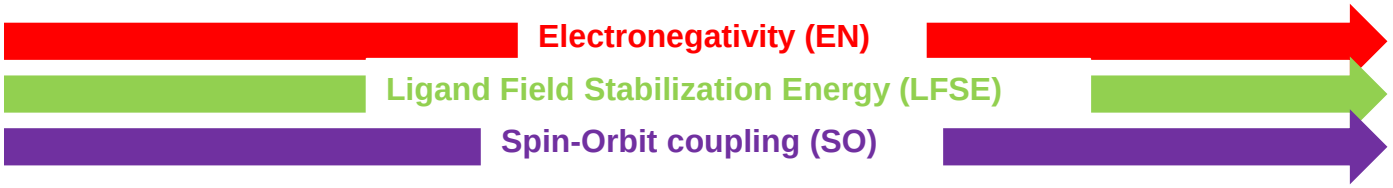
- Mechanism still discussed

Thank you for your attention

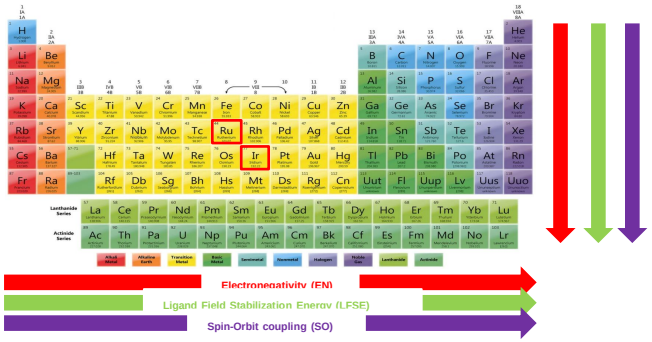
INTRODUCTION
Photoredox-Principle

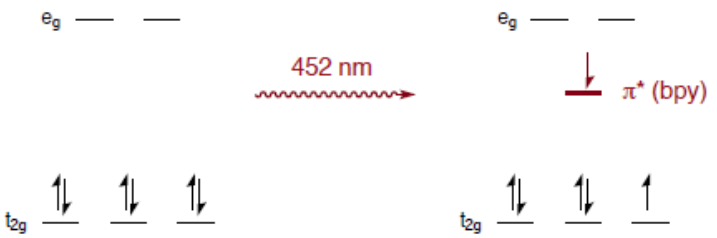






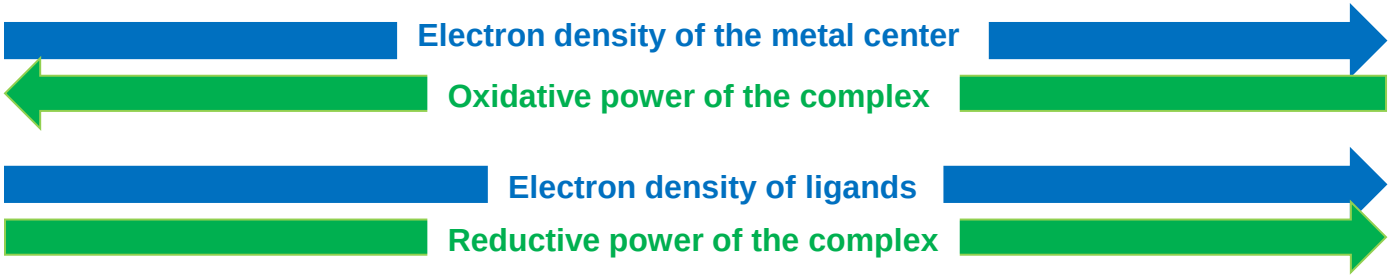
INTRODUCTION
Photoredox-Principle





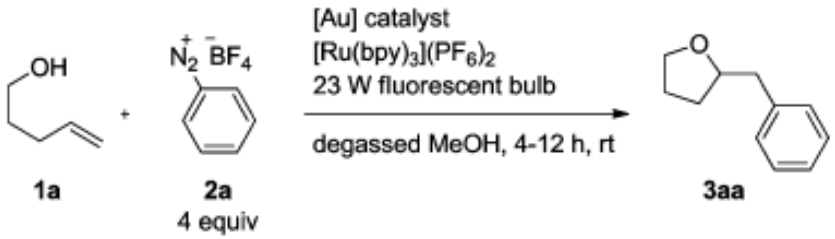
- [Ru]$^{2+}$ complexes are more electron-rich than the corresponding [Ir]$^{3+}$
- LFSE ↗ HOMO-LUMO gap ↗ Energy light for excitation ↗ Difference between reduction and oxidation potentials ↗
- [Ir]$^{3+}$ is a better oxidant than [Ru]$^{2+}$ (higher OS to be d6 more electron poor)

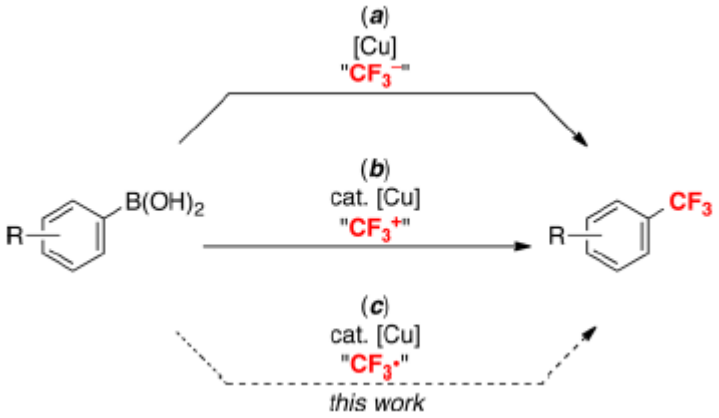
- Importance of the Ligand

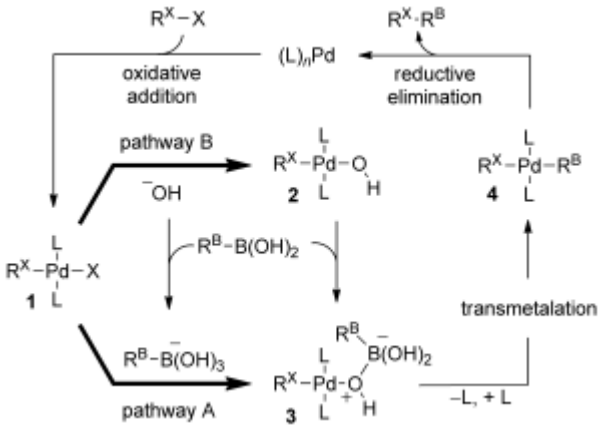


Glorius-Sanford

> Diapositive 19

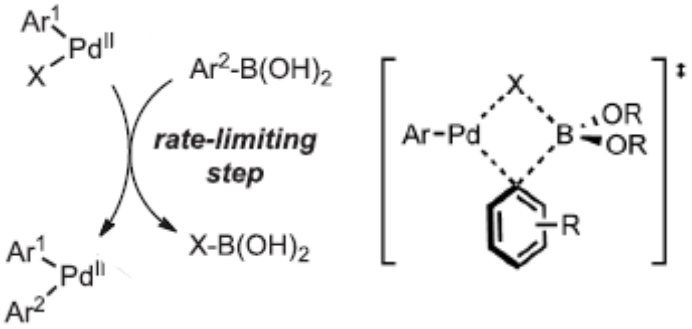





R^X–X
oxidative addition
(L)nPd
R^X–R^B
reductive elimination
pathway B
⁻OH
2
4
R^B–B(OH)2
1
transmetalation
R^B–B(OH)3
pathway A
3
–L, + L

C-C Coupling
Molander group

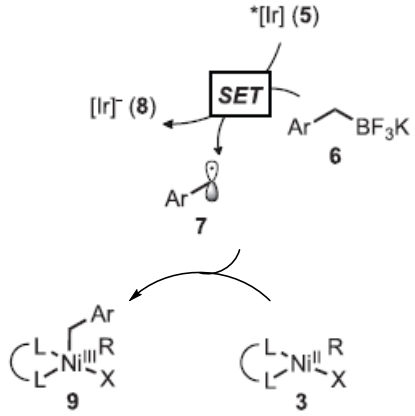
Two-Electron Transmetalation



- High activation energy
- Rate limiting step for most Cross coupling reaction
- Requires stoichiometric base, high T
- Transmetalation rate:

  $C_{sp} > C_{sp2} > C_{sp3}$

Single-Electron Transmetalation



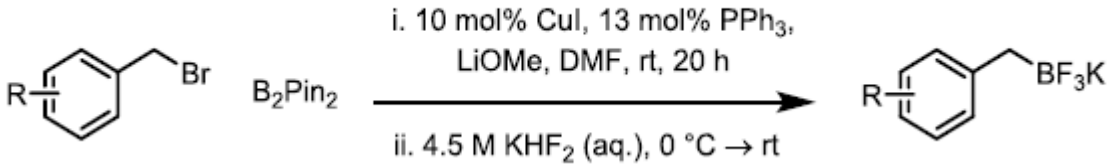
- Low activation energy
- Reactivity dictated by measurable redox potentials
- Requires no base or heat
- Transmetalation rate:

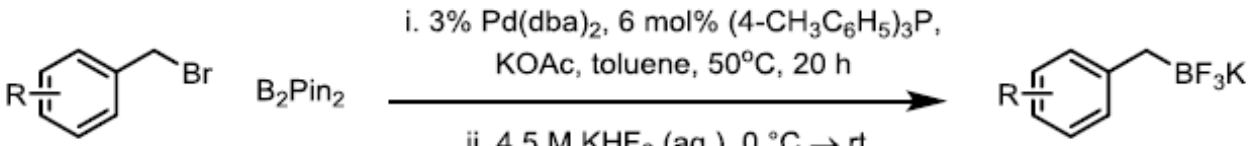
  $C_{sp3} > C_{sp2} > C_{sp}$

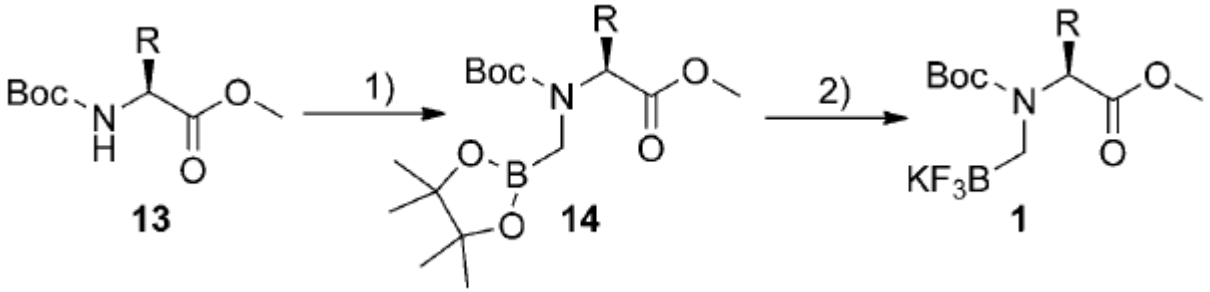
Also C-centered radical stability!

Complementary pattern : offer a way for Csp2-Csp3

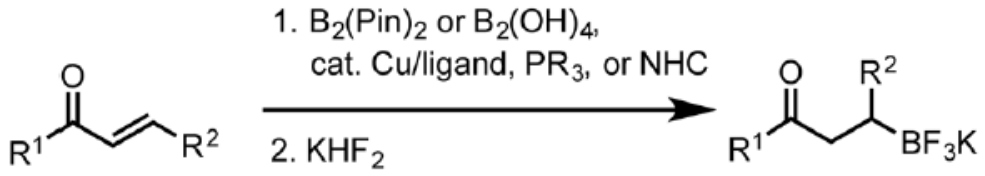
Preparation of reagents

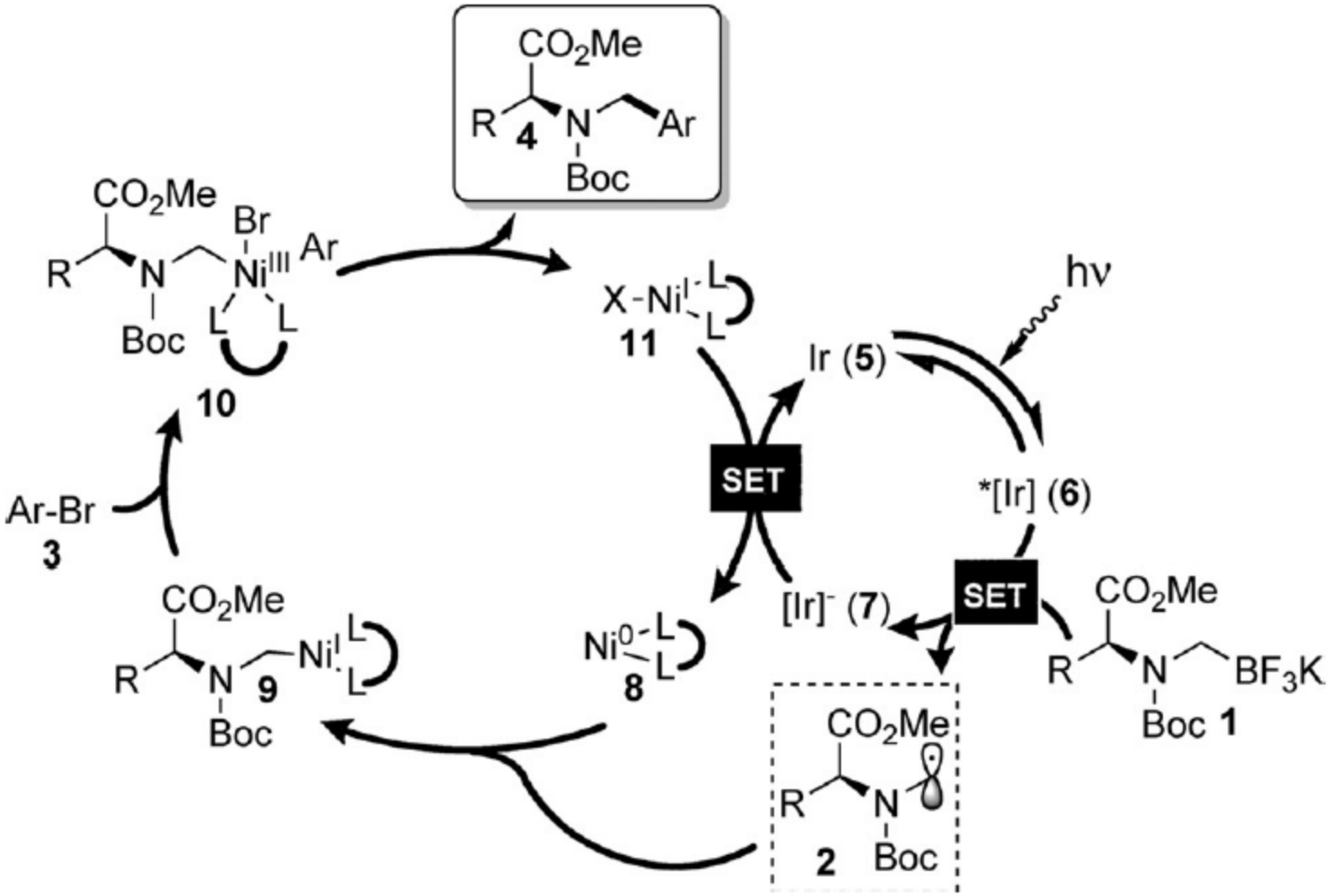


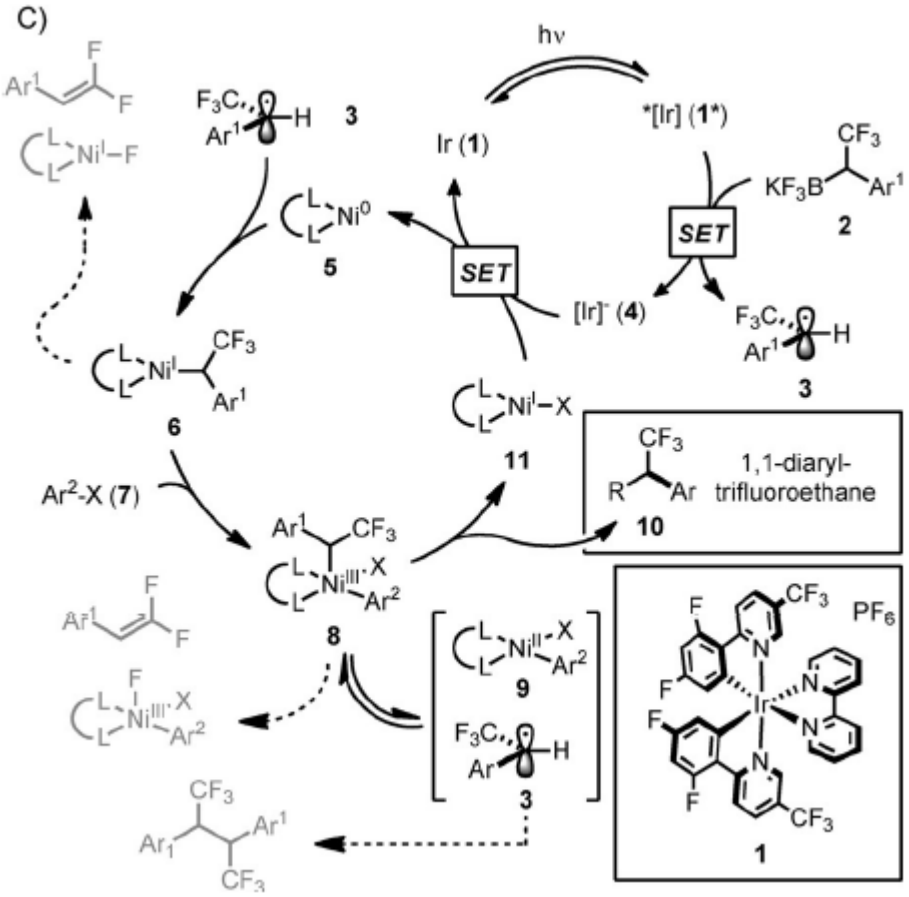


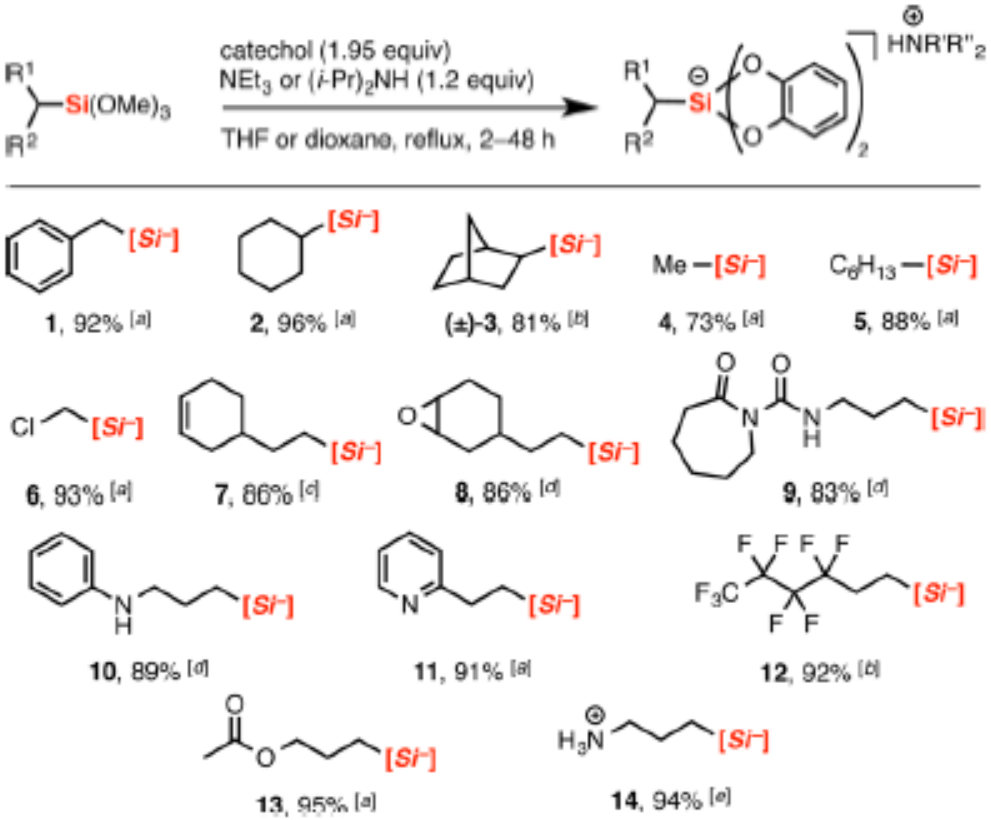


(A) Synthesis of β-trifluoroboratocarbonyl compounds

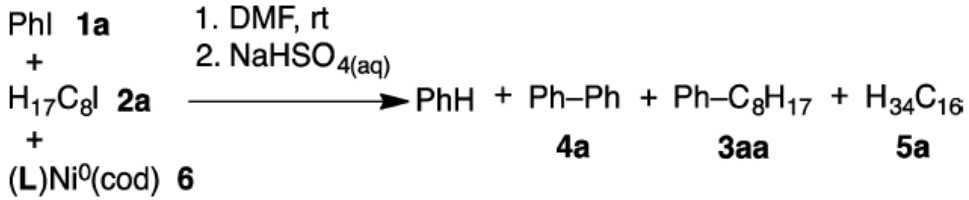



CO2Me
R
4
N
Ar
Boc
CO2Me
Br
R
N
NiIII
Ar
Boc
L
L
10
X-NiI
L
L
11
hν
Ir (5)
SET
*[Ir] (6)
Ar-Br
3
SET
CO2Me
R
N
BF3K
Boc 1
[Ir]- (7)
CO2Me
R
N
NiI
L
L
9
Boc
Ni0
L
L
8
CO2Me
R
N
2
Boc

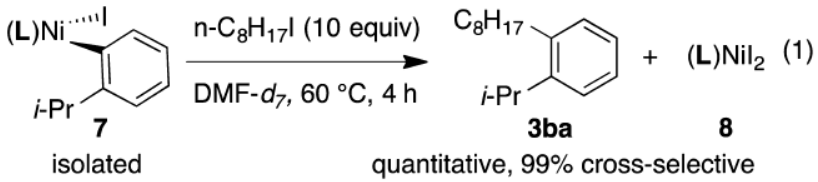

C)
hν
Ir (1)
[Ir] (1)
SET
SET
[Ir]⁻ (4)
3
5
2
6
11
10
1,1-diaryl-
trifluoroethane
Ar²-X (7)
8
9
3
1

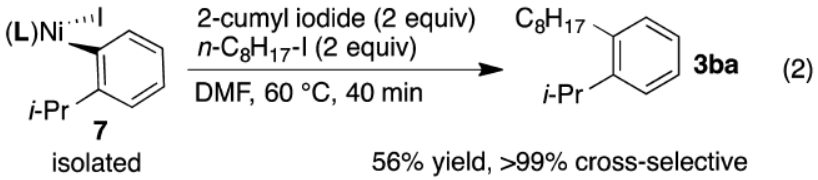

catechol (1.95 equiv)
NEt3 or (i-Pr)2NH (1.2 equiv)
THF or dioxane, reflux, 2–48 h
HNR'R''2
1, 92% [a]
2, 96% [a]
(±)-3, 81% [b]
4, 73% [a]
5, 88% [a]
6, 93% [a]
7, 86% [c]
8, 86% [d]
9, 83% [d]
10, 89% [d]
11, 91% [a]
12, 92% [b]
13, 95% [a]
14, 94% [e]

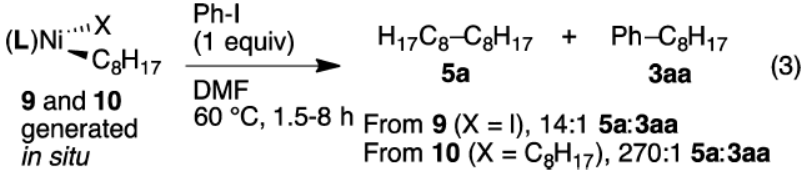
C-C Coupling
MacMillan group

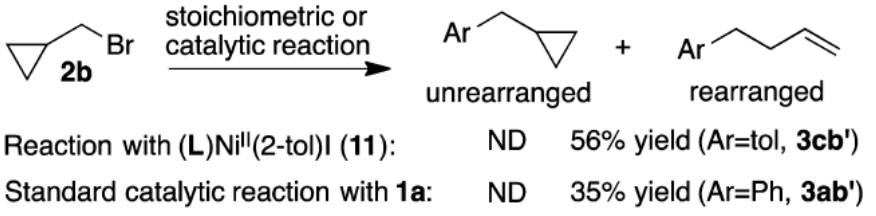


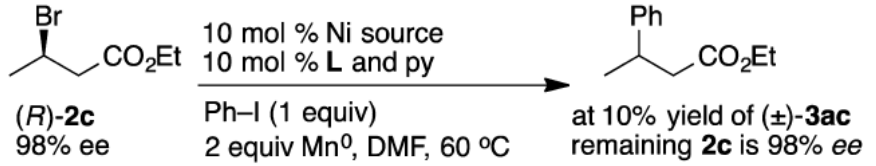
substrate	total conv (%)[b]	yield (%)[c] alkyl-H or Ph-H	4a	3aa	5a
Ph-I	89	49	21	13	NA
$H_{17}C_8$-I	19	0	NA	51	45

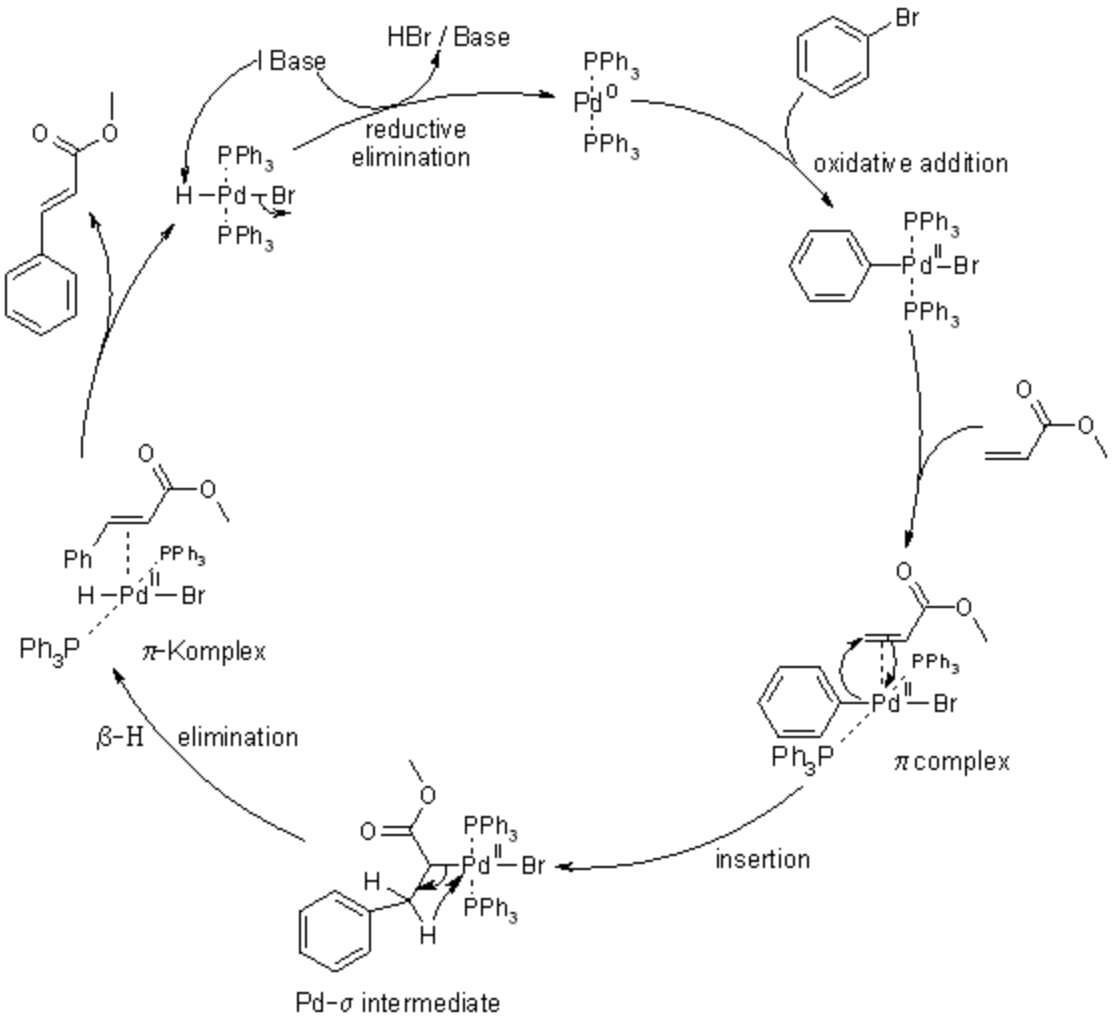






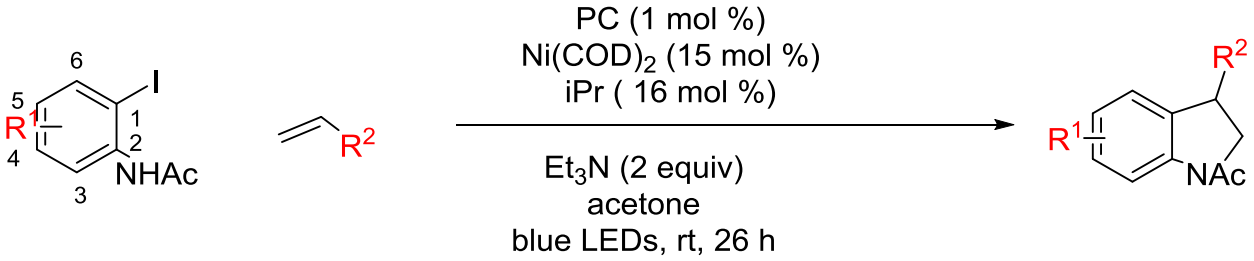


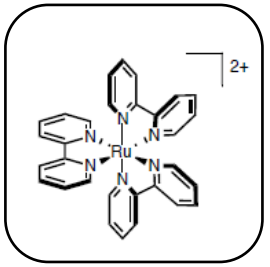


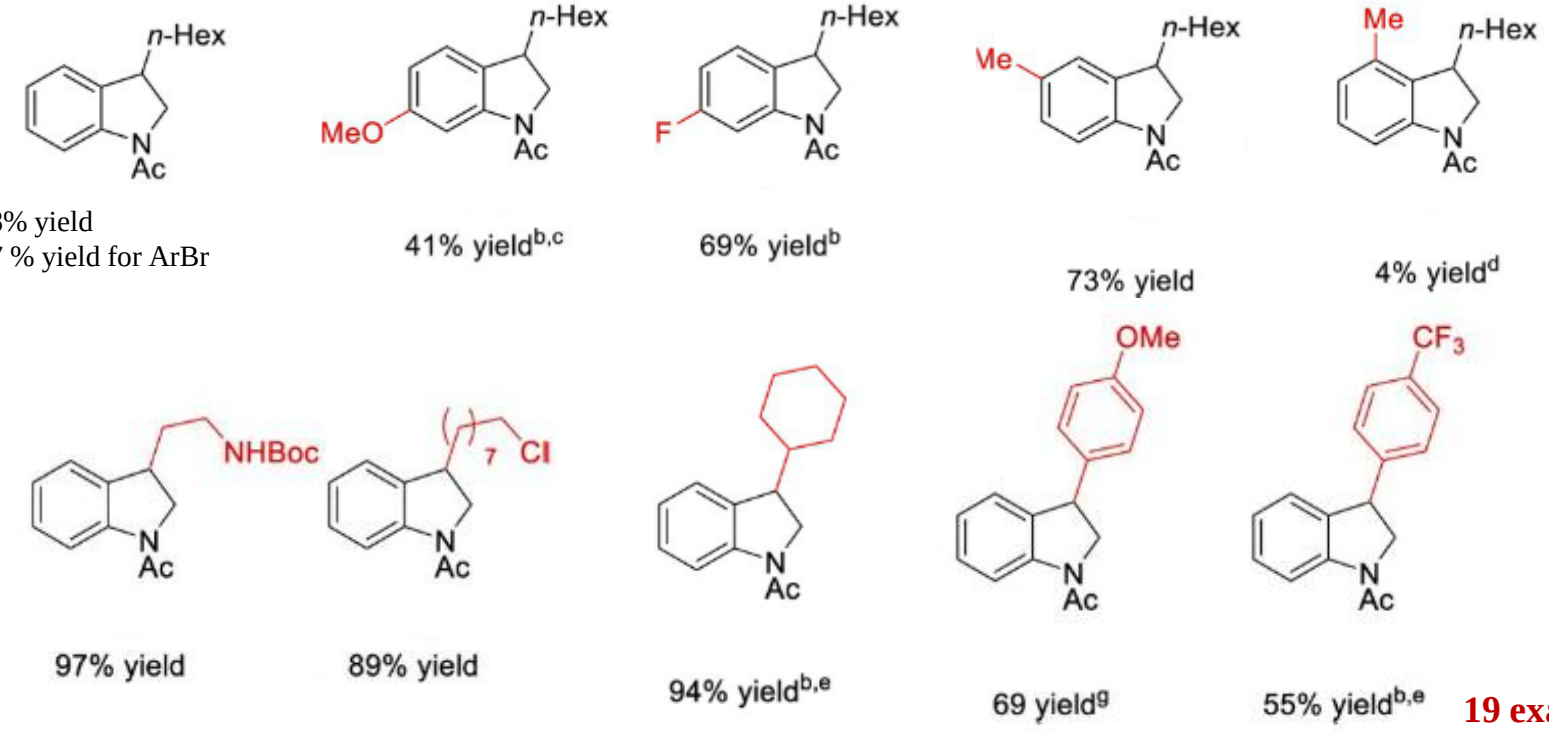

HBr / Base
I Base
reductive elimination
oxidative addition
insertion
β-H elimination
π-Komplex
π complex
Pd-σ intermediate

C-N Coupling

> Coupling of alkene with aryl to form Indoline







88% yield
27 % yield for ArBr

41% yield[b,c]

69% yield[b]

73% yield

4% yield[d]

97% yield

89% yield

94% yield[b,e]

69 yield[g]

55% yield[b,e]

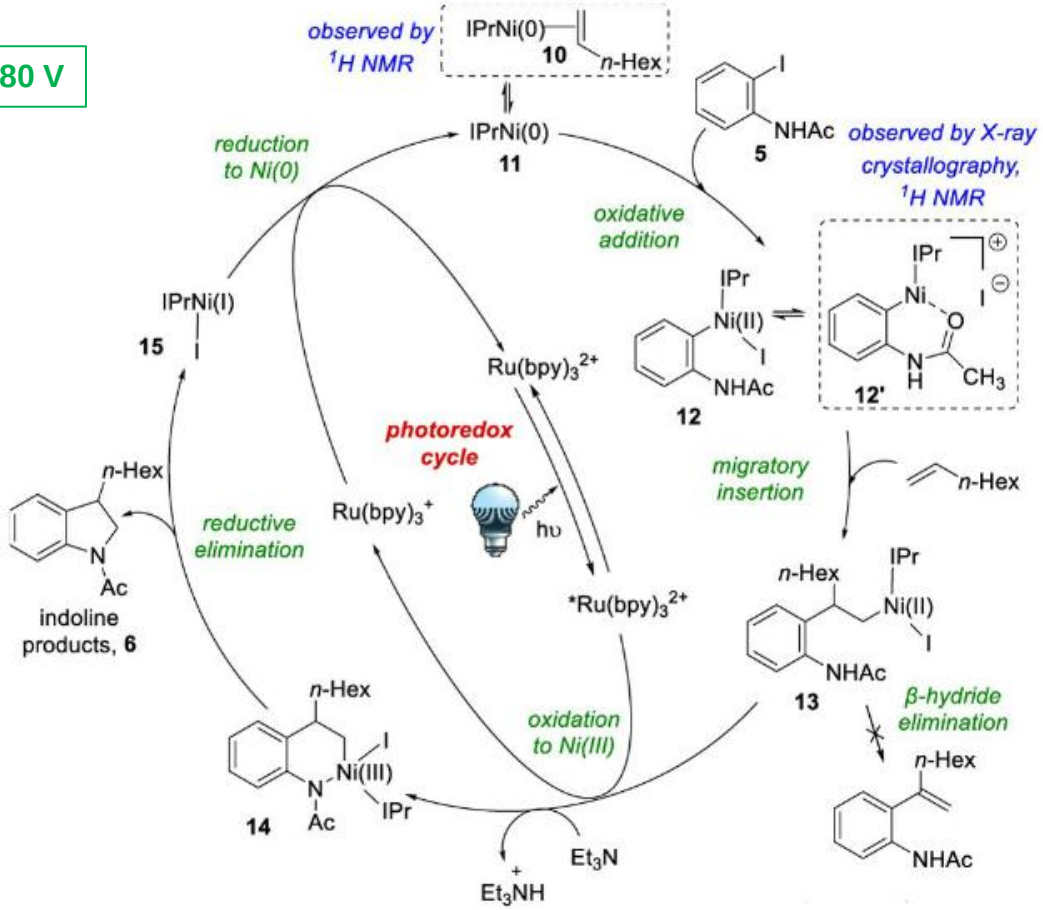
19 examples

A. Z. Tasker, T. F. Jamison, *J. Am. Chem. Soc.* **2015**, *137*, 9531−9534

C-N Coupling

> Proposed mechanism

E_{ox}= + 0.80 V



C-N Coupling

> Proposed mechanism