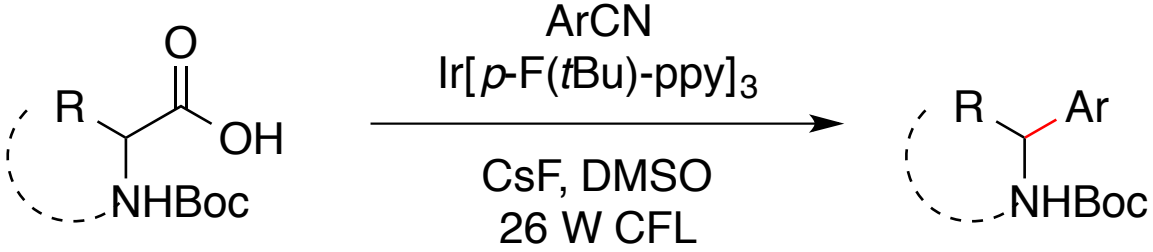
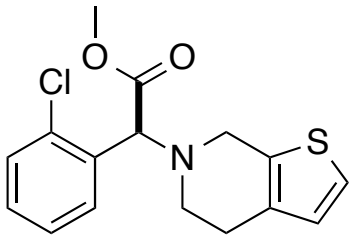
Decarboxylative Arylation of α-Amino Acids via Photoredox Catalysis



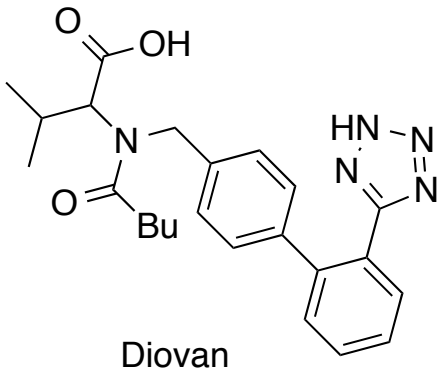
Zhiwei Zuo and David W. C. MacMillan
J. Am. Chem. Soc. ASAP, doi: 10.1021/ja501621q

Michael Frasso
Current Literature
April 12, 2014

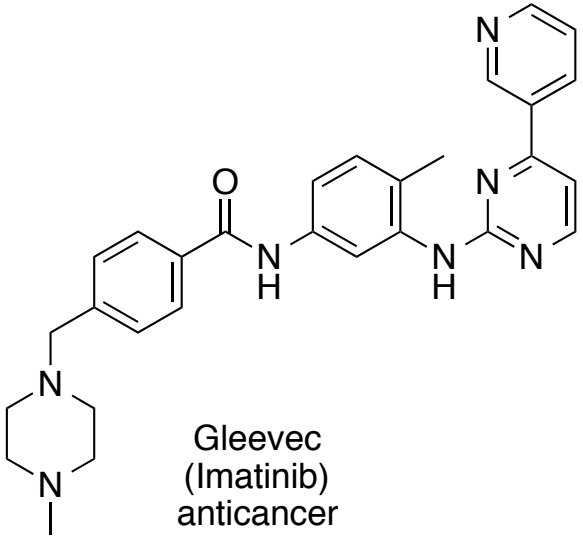
Top Selling Drugs



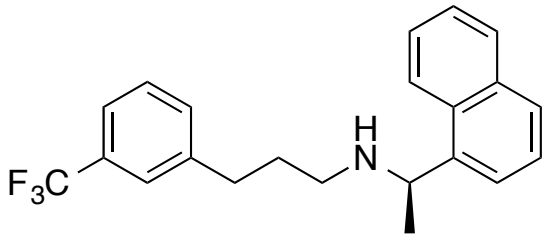
Plavtix
(Clopidogrel)
antiplatelet



Diovan
(Valsartan)
hypertension, cogestive heart failure, MI



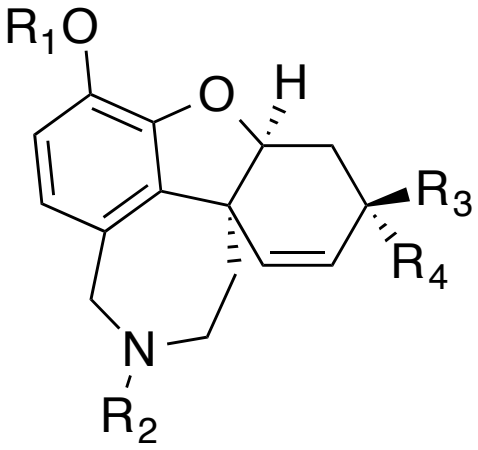
Gleevec
(Imatinib)
anticancer



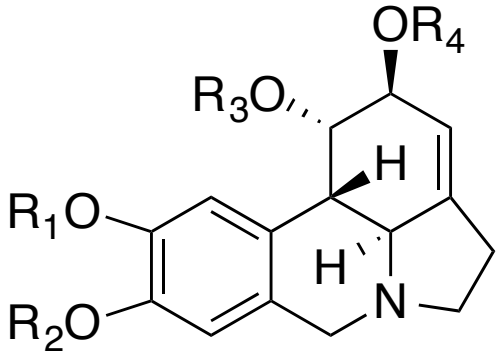
Sensipar
(Cinacalcet)
Parathyroid regulation

http://cbc.arizona.edu/njardarson/group/sites/default/files/Top200%20Pharmacetical%20Products%20by%20US%20Retail%20Sales%20in%202012_0.pdf

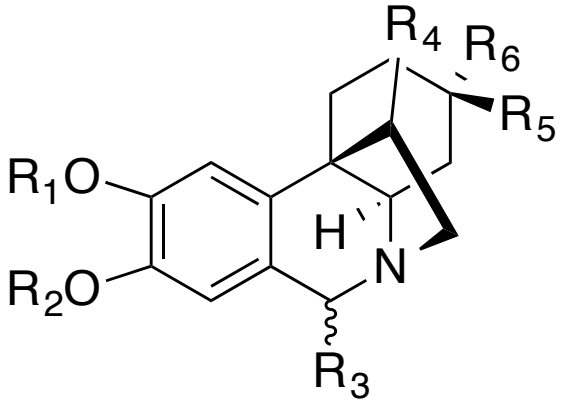
Amaryllidaceae Alkaloids



Galanthamine-type



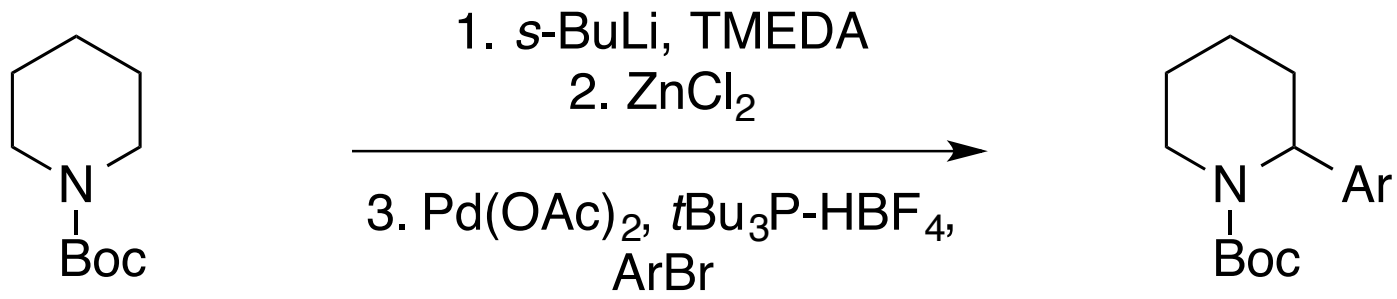
Lycorine-type

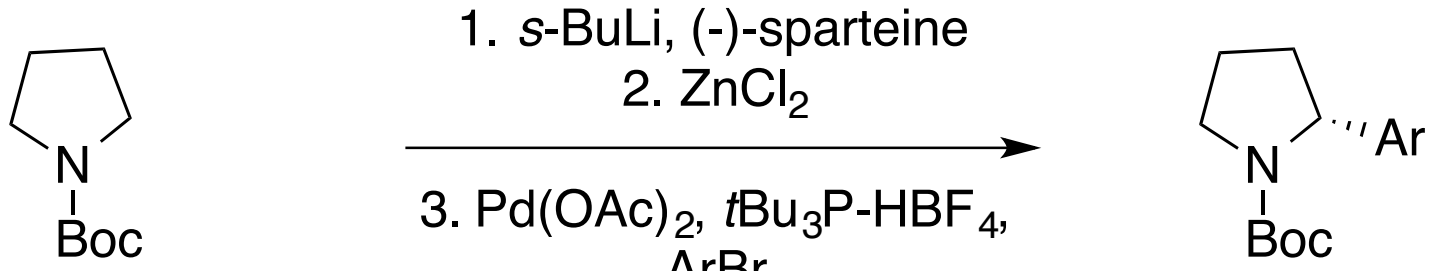


Crinine-type

Nat. Prod. Rep. **2007**, *24*, 886-905

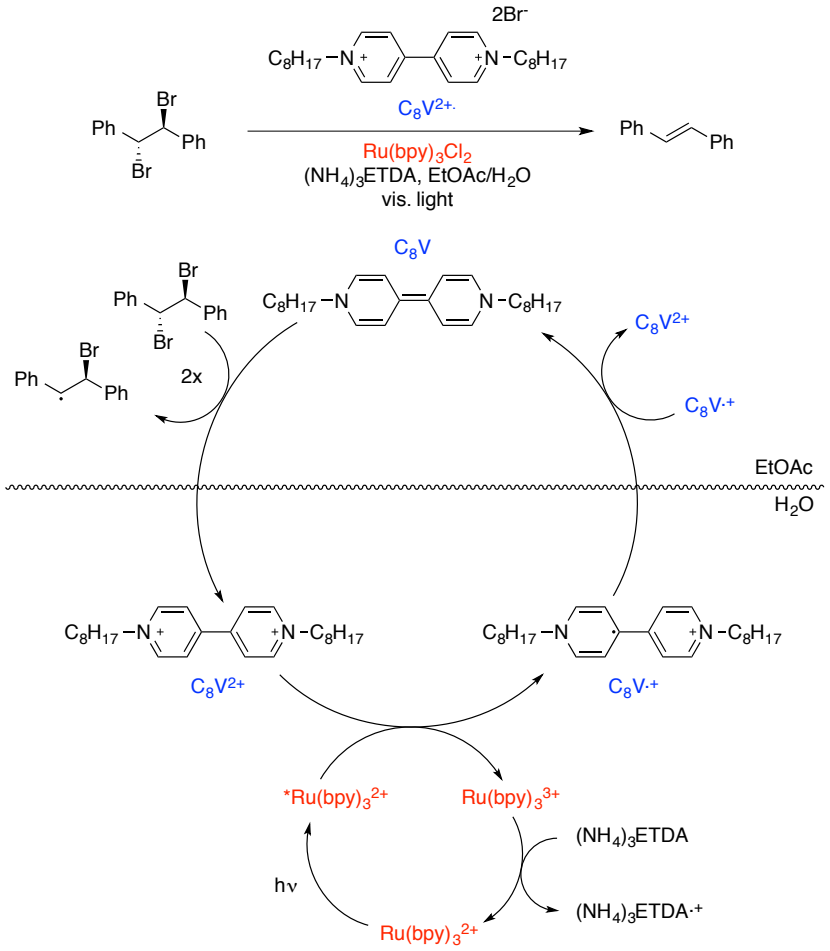
Previous Methods





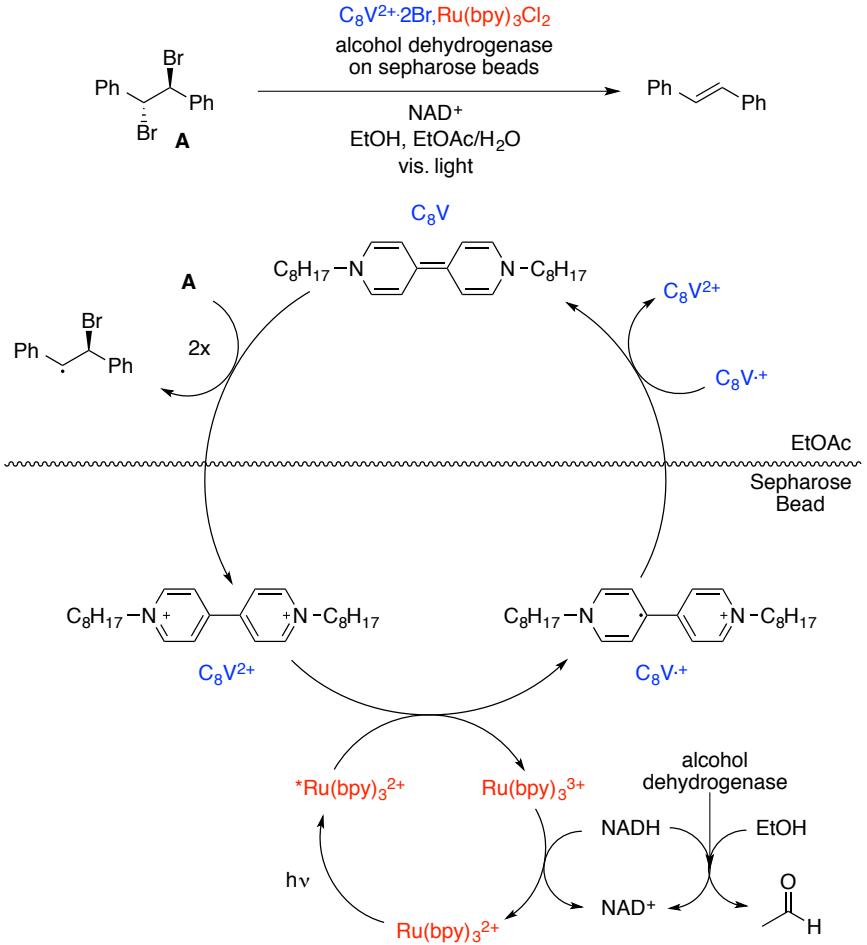
Org. Lett. **2008**,*10*, 3923-3925
J. Am. Chem. Soc. **2006**, *128*, 3538-3539

Biphasic Viologen/Photoredox Catalysis



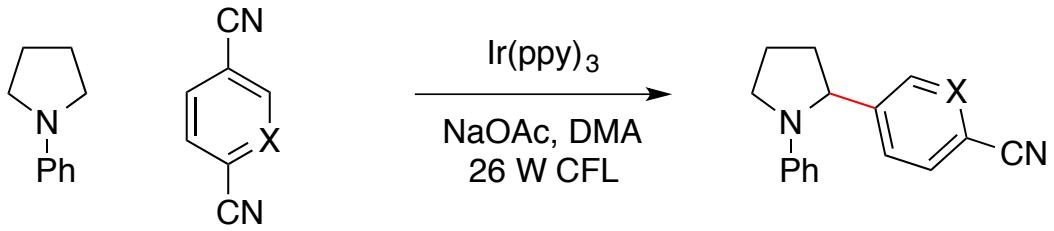
J. Org. Chem. **1983**,*105*, 7764-7765

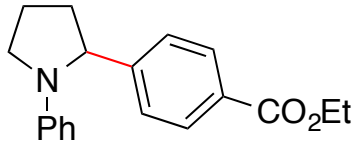
Dual Enzymatic/Photoredox Catalysis



J. Am. Chem. Soc. **1986**,*108*, 1080-1082

Inspiration for Current Work





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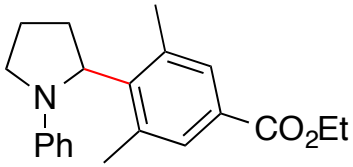

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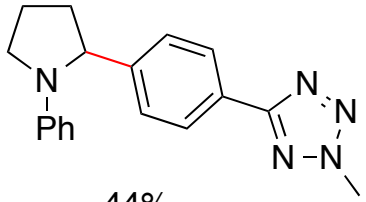

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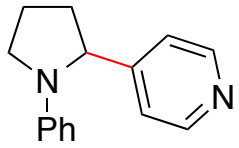

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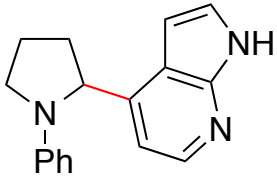

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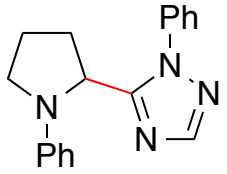

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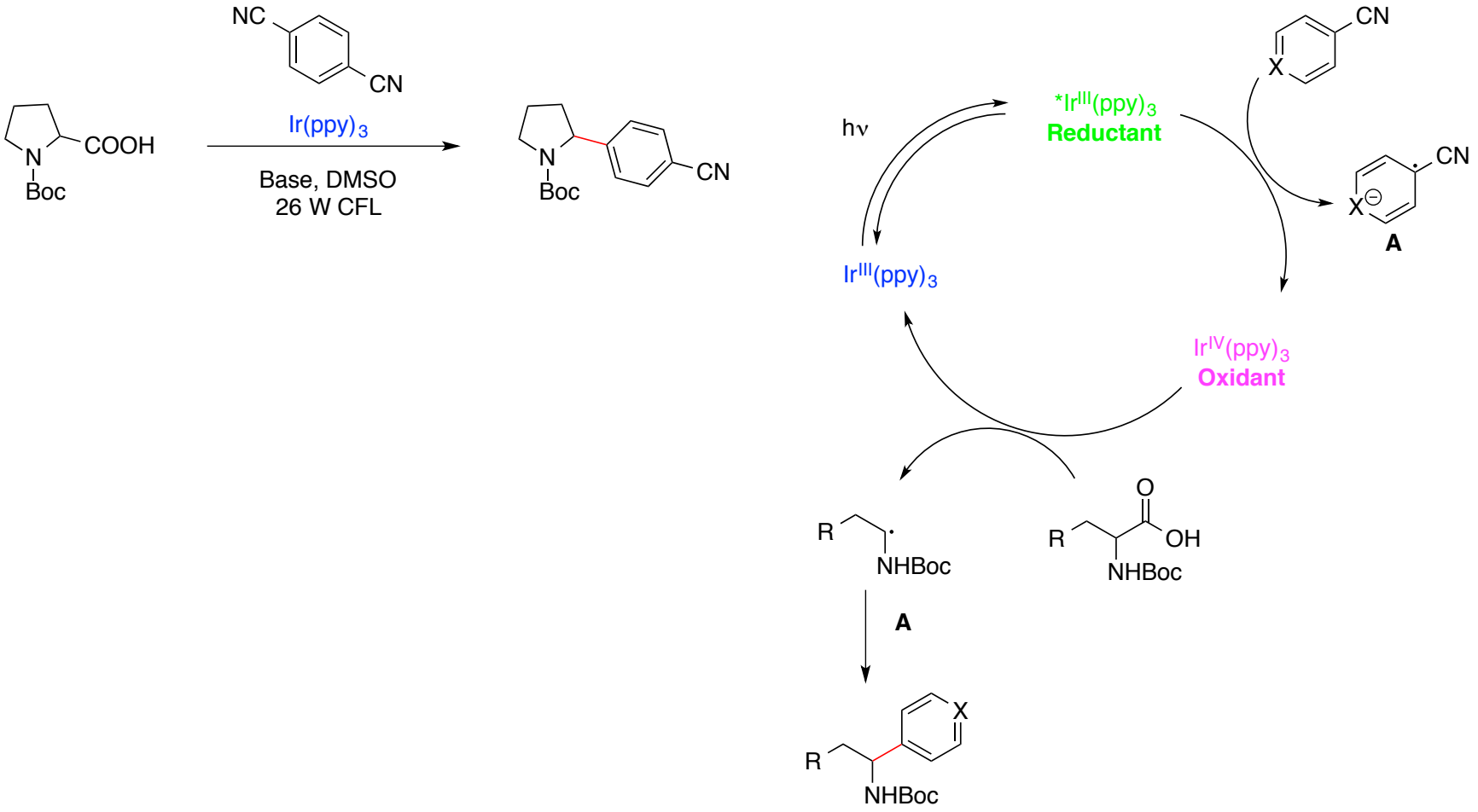
Science **2011**, *334*, 1114-1117

Proposed Mechanism



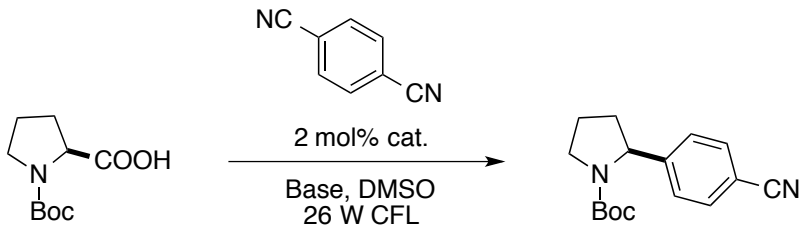
J. Am. Chem. Soc. **ASAP**, doi: 10.1021/ja501621q

General Comments

- Redox properties of Ir^{3+} described primarily as metal oxidation, ligand reduction
- As ligands becomes more electron donating, complex becomes more reducing
- As ligands become more electron withdrawing, complex becomes more oxidizing

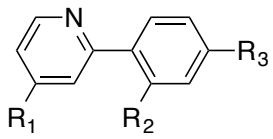
J. Org. Chem. **2012**, *77*, 1617-1622

Conditions Screen



Entry	Catalyst	Base	% yield
1	$Ir(ppy)_3$	K_2HPO_4	12
2	$Ir(p\text{-F-ppy})_3$	K_2HPO_4	58
3	$Ir(dFppy)_3$	K_2HPO_4	54
4	$Ir[dF(CF_3)ppy]_2(dtbbpy)_2$	K_2HPO_4	trace
5	$Ir[p\text{-F}(t\text{Bu})\text{-ppy}]_3$	K_2HPO_4	73
6	$Ir[dF(t\text{Bu})\text{-ppy}]_3$	K_2HPO_4	68
7	$Ir[p\text{-F}(t\text{Bu})\text{-ppy}]_3$	CsF	83
8*	$Ir[p\text{-F}(t\text{Bu})\text{-ppy}]_3$	CsF	0
9	none	CsF	0
10	$Ir[p\text{-F}(t\text{Bu})\text{-ppy}]_3$	none	trace

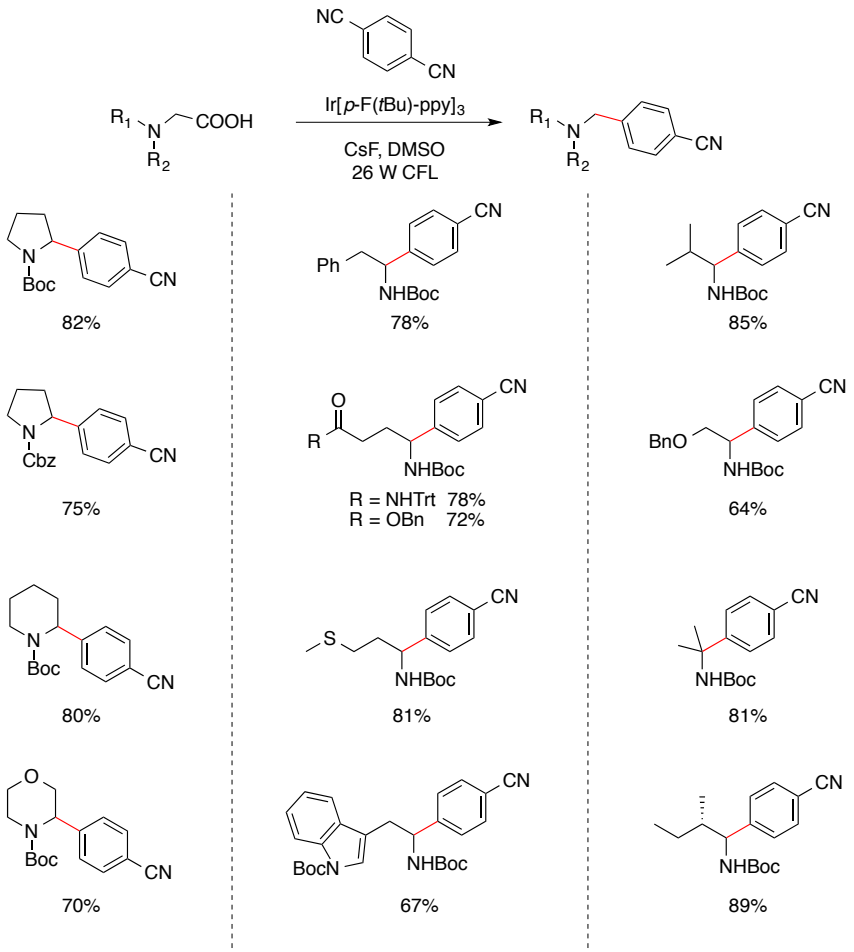
*no visible light



R_1, R_2, R_3	Catalyst
$R_1 = R_2 = R_3 = H$	$Ir(ppy)_3$
$R_1 = H$, $R_2 = R_3 = F$	$Ir(dFppy)_3$
$R_1 = R_2 = H$, $R_3 = F$	$Ir(p\text{-F-ppy})_3$
$R_1 = t\text{Bu}$ $R_2 = R_3 = F$	$Ir[dF(t\text{Bu})\text{-ppy}]_3$
$R_1 = t\text{Bu}$, $R_2 = H$, $R_3 = F$	$Ir[p\text{-F}(t\text{Bu})\text{-ppy}]_3$

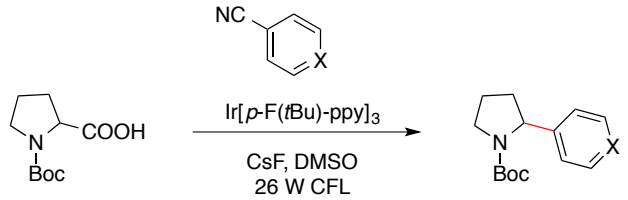
J. Am. Chem. Soc. **ASAP**, doi: 10.1021/ja501621q

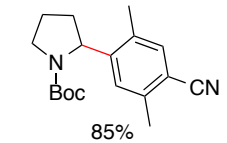
Amino Acid Scope



J. Am. Chem. Soc. **ASAP**, doi: 10.1021/ja501621q

Cyanoarene Scope





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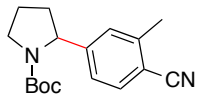

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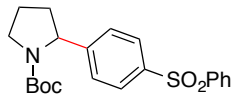

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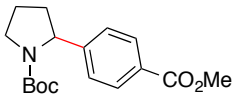

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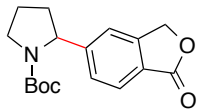

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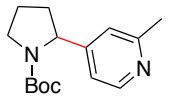

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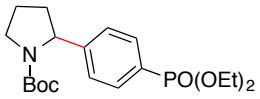

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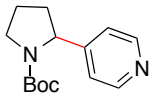

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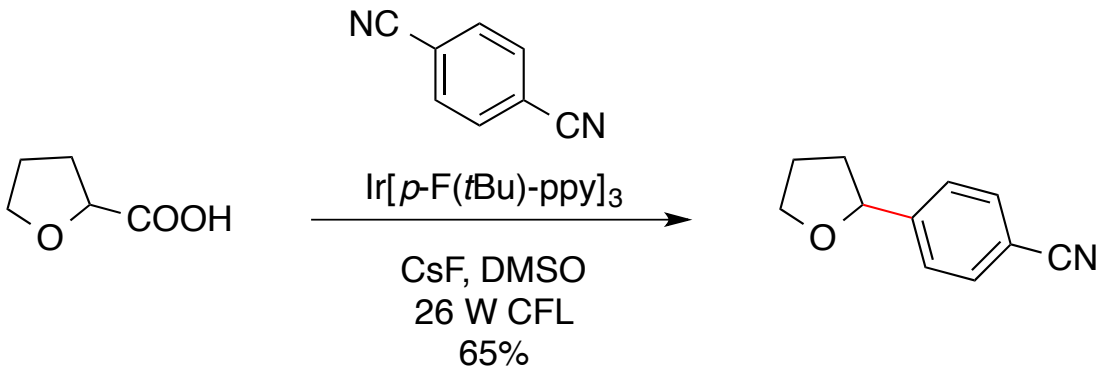
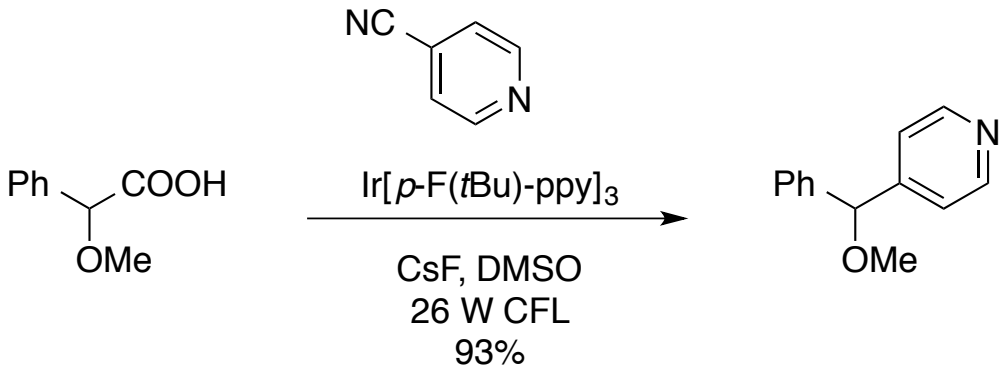
J. Am. Chem. Soc. **ASAP**, doi: 10.1021/ja501621q

α-Arylation of Ethers





J. Am. Chem. Soc. **ASAP**, doi: 10.1021/ja501621q

Issues to Address

- Currently not scalable
  - Reactions performed on 0.4 mmol scale, 0.02 M, 48 h reaction times
- No stereocontrol