



北京大学
PEKING UNIVERSITY

化学生物学与生物技术学院
School of Chemical Biology & Biotechnology

Decarboxylative Arylation of α -Amino Acids via **Photoredox Catalysis**

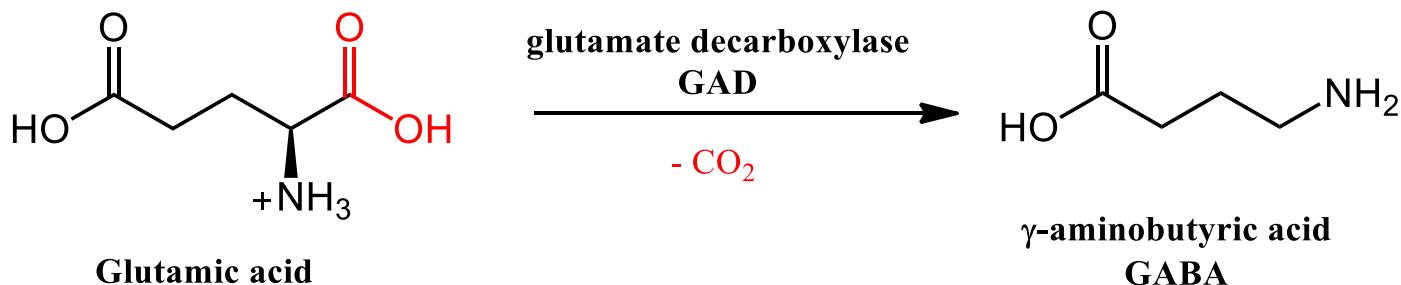
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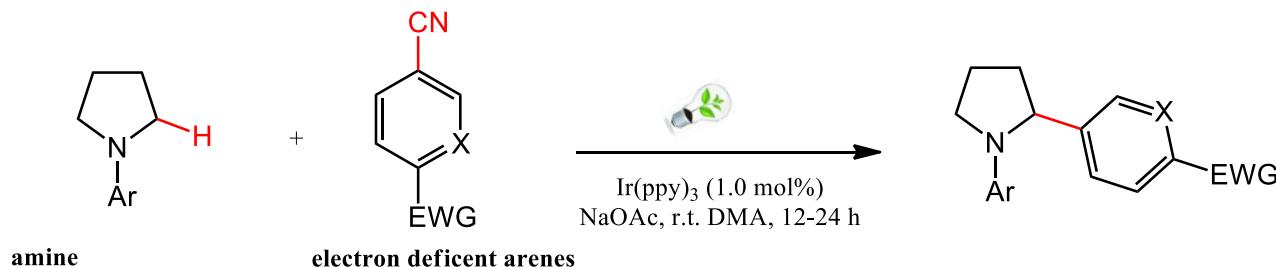
Decarboxylation

- Biochemical Precedent

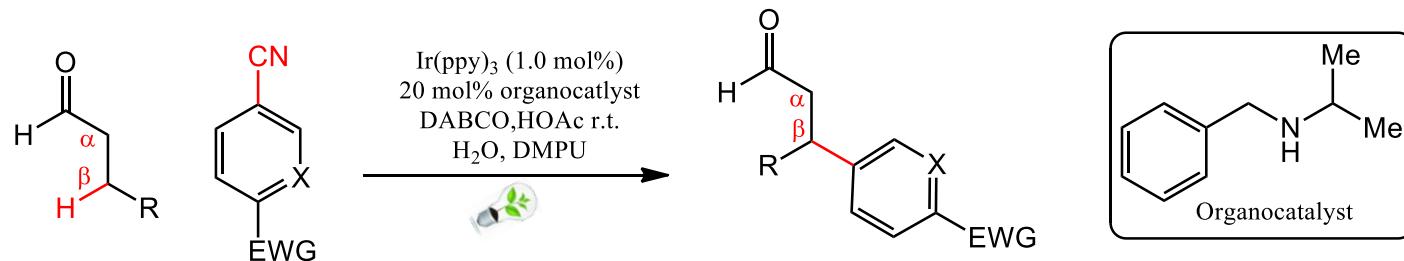


- Chemical Precedents
 - Hunsdiecker, Kolbe, Barton decarboxylation
 - Coupling reaction (Myers and Gooßen)

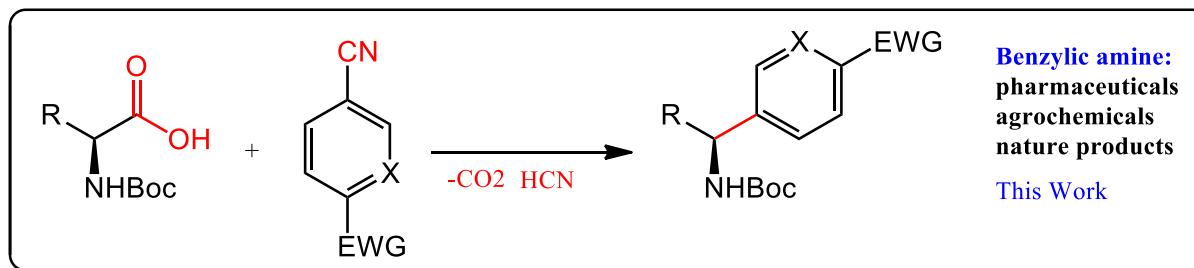
Previous Work



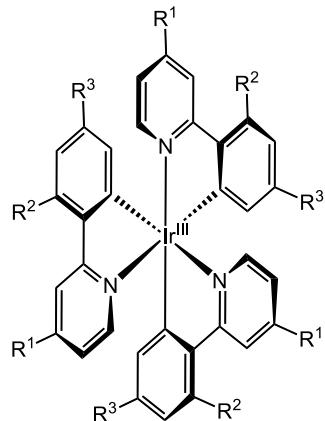
McNally, A.; Prier, C. K.; MacMillan, D. W. C. *Science* **2011**, *334*, 1114.



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



Ligand effects on ground-state redox properties of catalysts

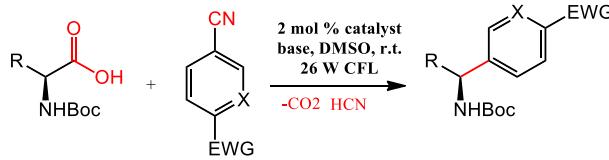


Group	Photocatalyst	$E_{1/2}^{\text{red}}[\text{Ir}^{\text{IV}}/\text{Ir}^{\text{III}}]$ vs SCE (Oxidant)	$E_{1/2}^{\text{red}}[\text{Ir}^{\text{IV}}/*\text{Ir}^{\text{III}}]$ vs SCE (Reducant)	Entry
$\text{R}^1 = \text{R}^2 = \text{R}^3 = \text{H}$	$\text{Ir}(\text{ppy})_3$	+ 0.77 V	- 1.73 V	A
$\text{R}^1 = \text{R}^2 = \text{H}, \text{R}^3 = \text{F}$	$\text{Ir}(p\text{-F-ppy})_3$	+ 0.97 V	- 1.60 V	B
$\text{R}^1 = \text{H}, \text{R}^2 = \text{R}^3 = \text{F}$	$\text{Ir}(\text{dFppy})_3$	+ 1.13 V	- 1.44 V	C
$\text{R}^1 = t\text{-Bu}, \text{R}^2 = \text{H}, \text{R}^3 = \text{F}$	$\text{Ir}[p\text{-F}(t\text{-Bu})\text{-ppy}]_3$	---	---	D
$\text{R}^1 = t\text{-Bu}, \text{R}^2 = \text{R}^3 = \text{F}$	$\text{Ir}[\text{dF}(t\text{-Bu})\text{-ppy}]_3$	---	- 1.67 V	E
	$\text{Ir}[\text{dF}(\text{CF}_3)\text{ppy}]_3(\text{dtbppy})^+$	+ 1.69 V	- 0.89 V	F

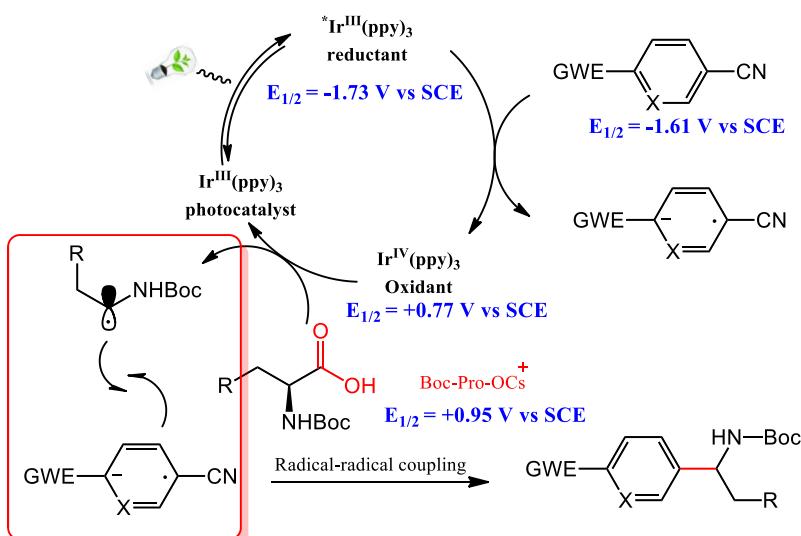
Tucker, J. W.; Stephenson, C. R. J. *J. Org. Chem.* 2012, 77, 1617.

Design

Conditions Screening



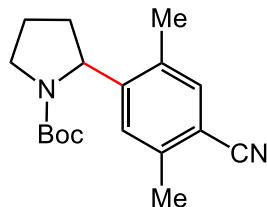
entry	photocatalyst	base	% yield ^a
1	$\text{Ir}(\text{ppy})_3$	K_2HPO_4	12
2	$\text{Ir}(p\text{-F-ppy})_3$	K_2HPO_4	58
3	$\text{Ir}(\text{dFppy})_3$	K_2HPO_4	54
4	$\text{Ir}[\text{dF}(\text{CF}_3)\text{ppy}]_2(\text{dtbppy})$	K_2HPO_4	trace
5	$\text{Ir}[p\text{-F}(t\text{-Bu})\text{-ppy}]_3$	K_2HPO_4	73
6	$\text{Ir}[\text{dF}(t\text{-Bu})\text{-ppy}]_3$	K_2HPO_4	68
7	$\text{Ir}[p\text{-F}(t\text{-Bu})\text{-ppy}]_3$	CsF	83
8 ^b	$\text{Ir}[p\text{-F}(t\text{-Bu})\text{-ppy}]_3$	CsF	0
9	none	CsF	0
10	$\text{Ir}[p\text{-F}(t\text{-Bu})\text{-ppy}]_3$	none	trace



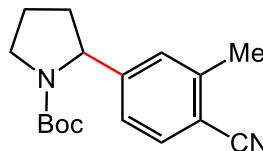
α -Amino Acid Scope

amino acid	product	amino acid	product	amino acid	product
Boc-Pro-OH	(\pm)-8 82% yield	Boc-Phe-OH	(\pm)-12 78% yield	Boc-Val-OH	(\pm)-17 85% yield
Cbz-Pro-OH	(\pm)-9 75% yield	R = NHTrt R = OBn	(\pm)-13 R = NHTrt 78% yield (\pm)-14 R = OBn 72% yield	O-Bn	(\pm)-18 64% yield
Boc-Pip-OH	(\pm)-10 86% yield	Boc-Met-OH	(\pm)-15 81% yield	Boc-Aib-OH	(\pm)-19 81% yield
Boc-Morph-OH	(\pm)-11 70% yield	Boc-Trp(Boc)-OH	(\pm)-16 67% yield ^c	Boc-Ile-OH	20 89% yield ^d

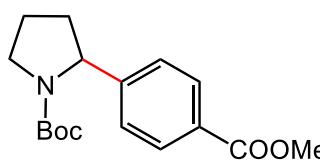
Aromatic Scope



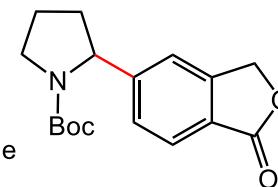
2a 85% yield



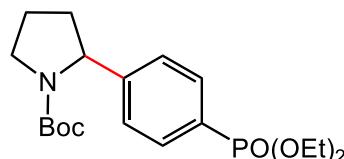
2b 77% yield



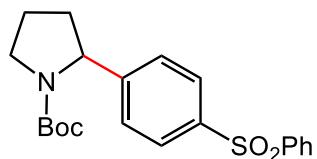
2c 52% yield



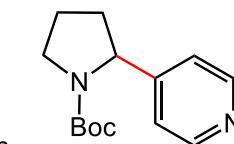
2d 70% yield



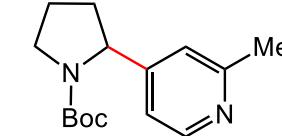
2e 65% yield



2f 64% yield

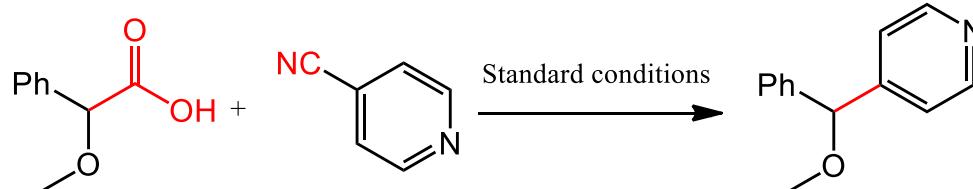
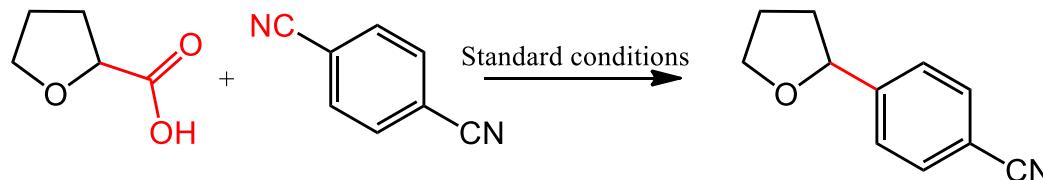


2g 73% yield



2h 83% yield

Another Two Examples



Summary

- Ligand effects are important for Photo-catalyzed reactions.
- The substrates are limited in electron-deficient aromatic compounds.