

Using the Dial-A-Molecule Photocatalyst Library in Reaction Discovery

James Donald
University of York

Dial-A-Molecule Annual Meeting
10th July 2018
Imperial College London

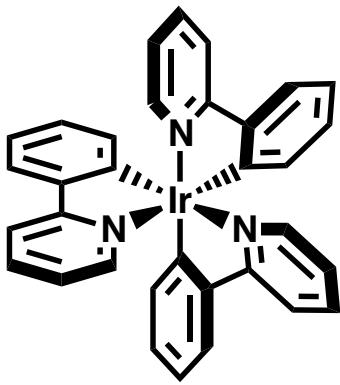


DIAL-A-MOLECULE
An EPSRC Grand Challenge Network

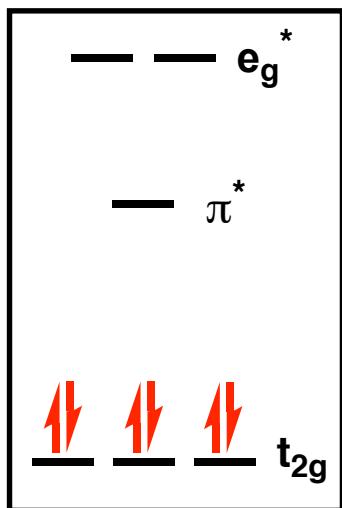
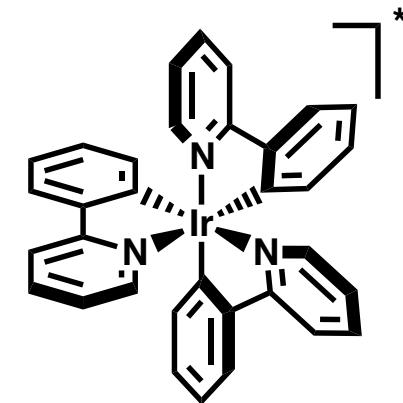


UNIVERSITY
of York

A Brief Introduction to Photoredox Catalysis



fac-Ir(ppy)₃



$\text{Ir}^{\text{III}*}$
Ground State
 S_0

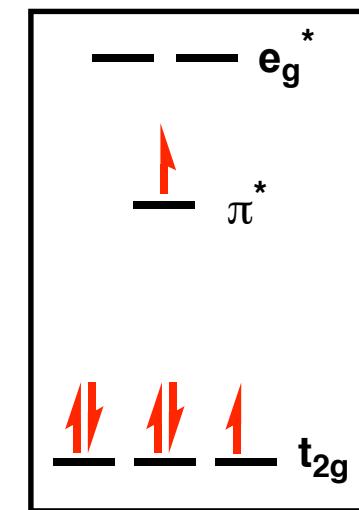
Photoexcitation $\lambda_{\text{max}} 375 \text{ nm}$



Visible light

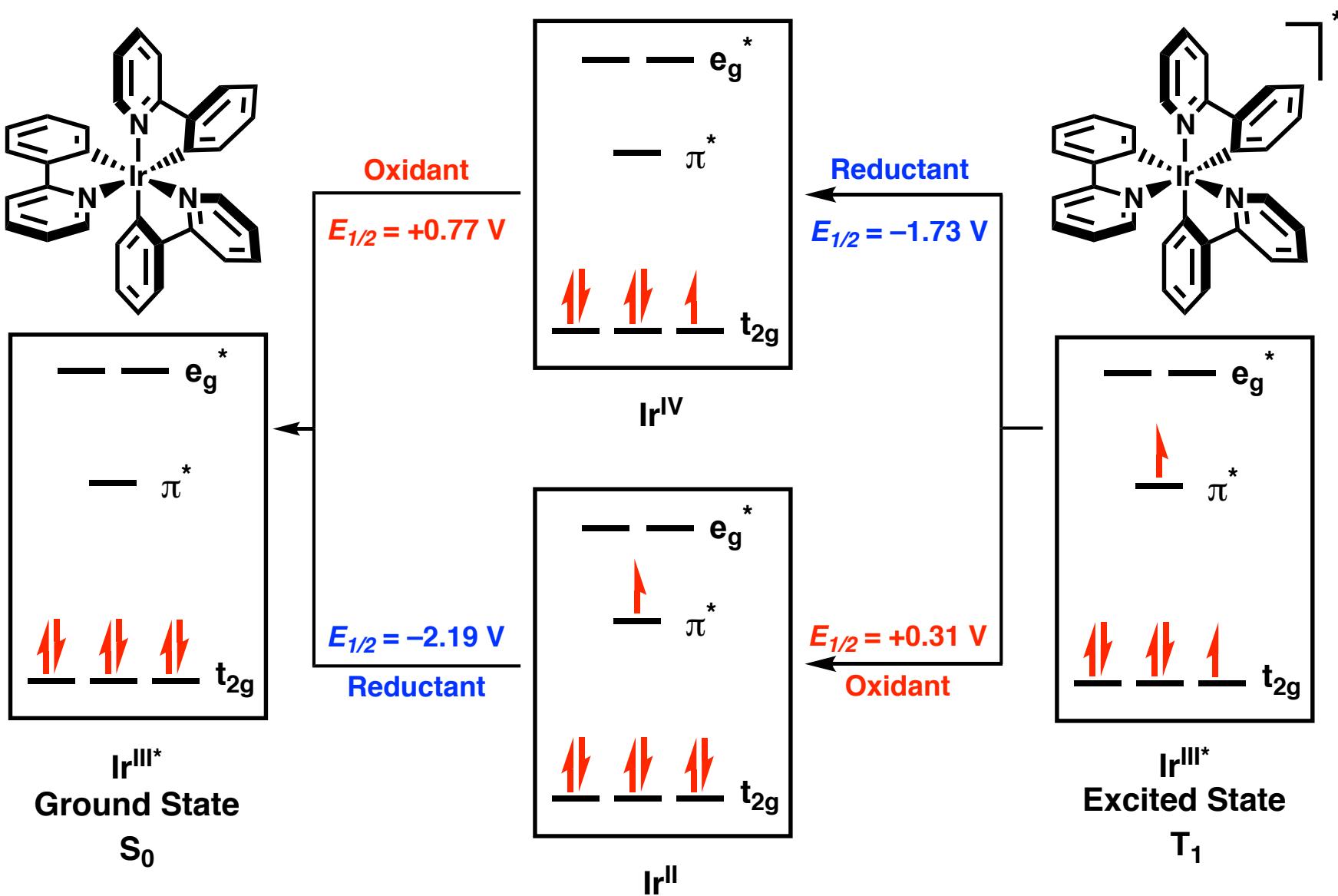
MLCT

ISC

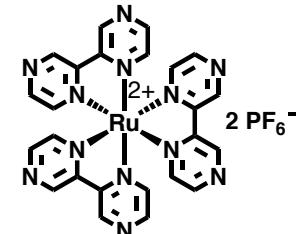
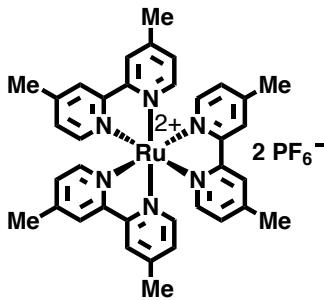
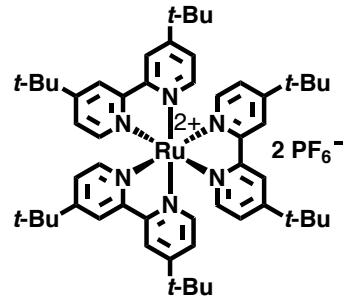
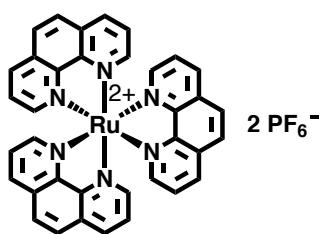
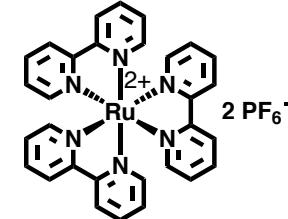
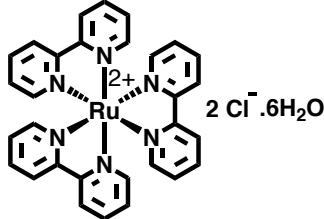
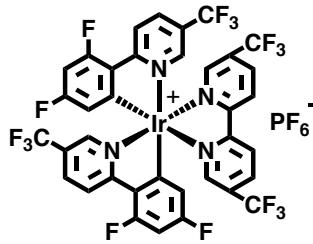
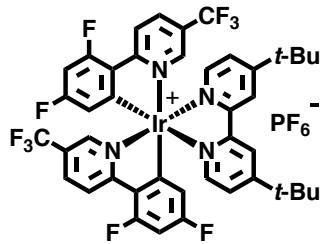
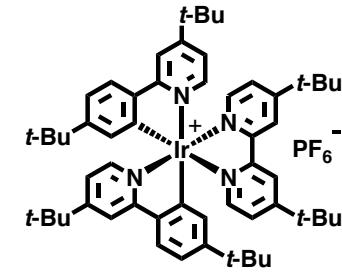
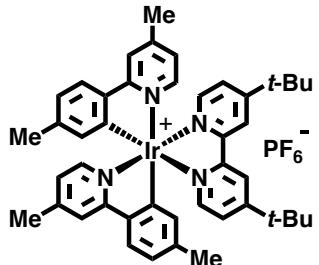
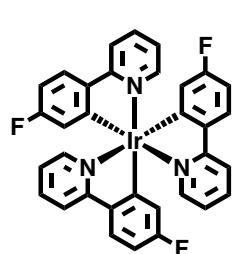
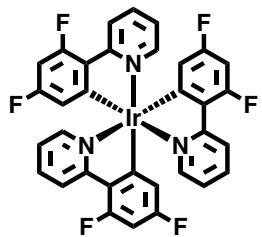
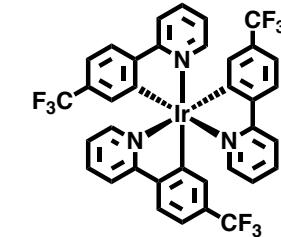
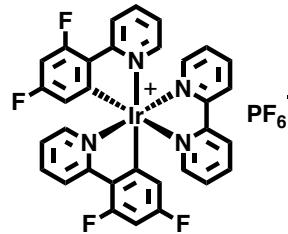
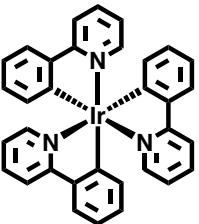
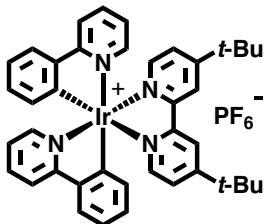
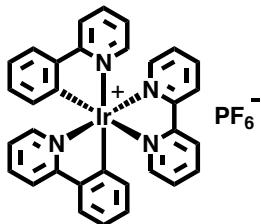


$\text{Ir}^{\text{III}*}$
Excited State
 T_1

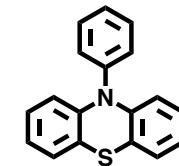
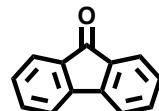
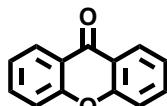
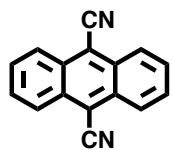
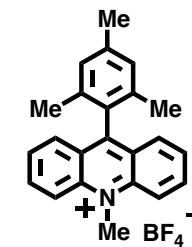
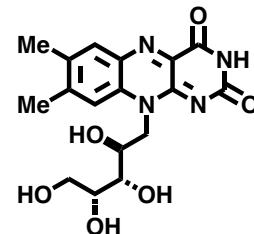
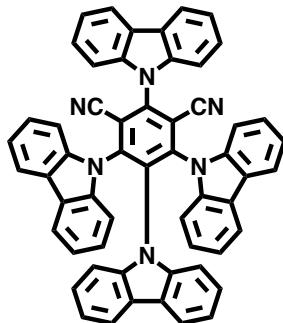
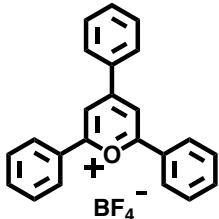
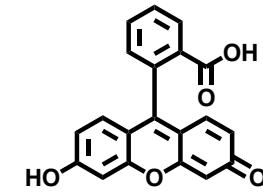
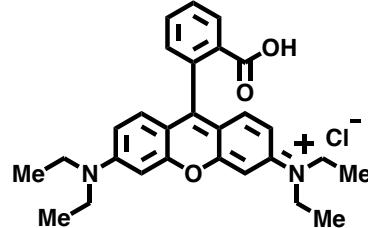
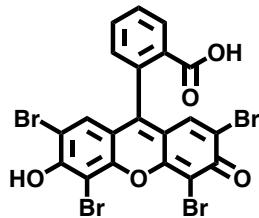
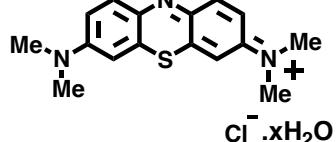
A Brief Introduction to Photoredox Catalysis



Dial-A-Molecule Funded Photoredox Catalyst Library



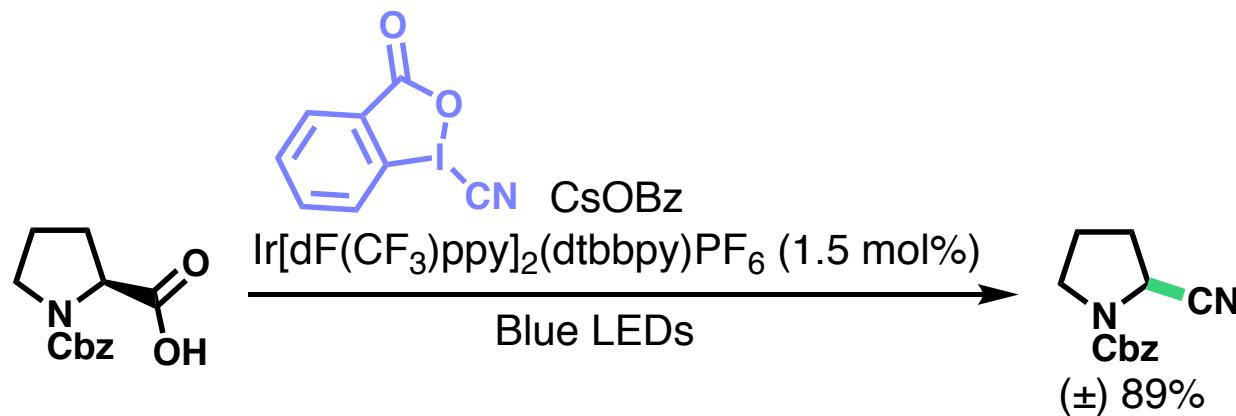
Dial-A-Molecule Funded Photoredox Catalyst Library



Developing a Radical Cyanomethylation Reaction



D. H. R. Barton, et al.
Tetrahedron, 1992, **48**, 2613

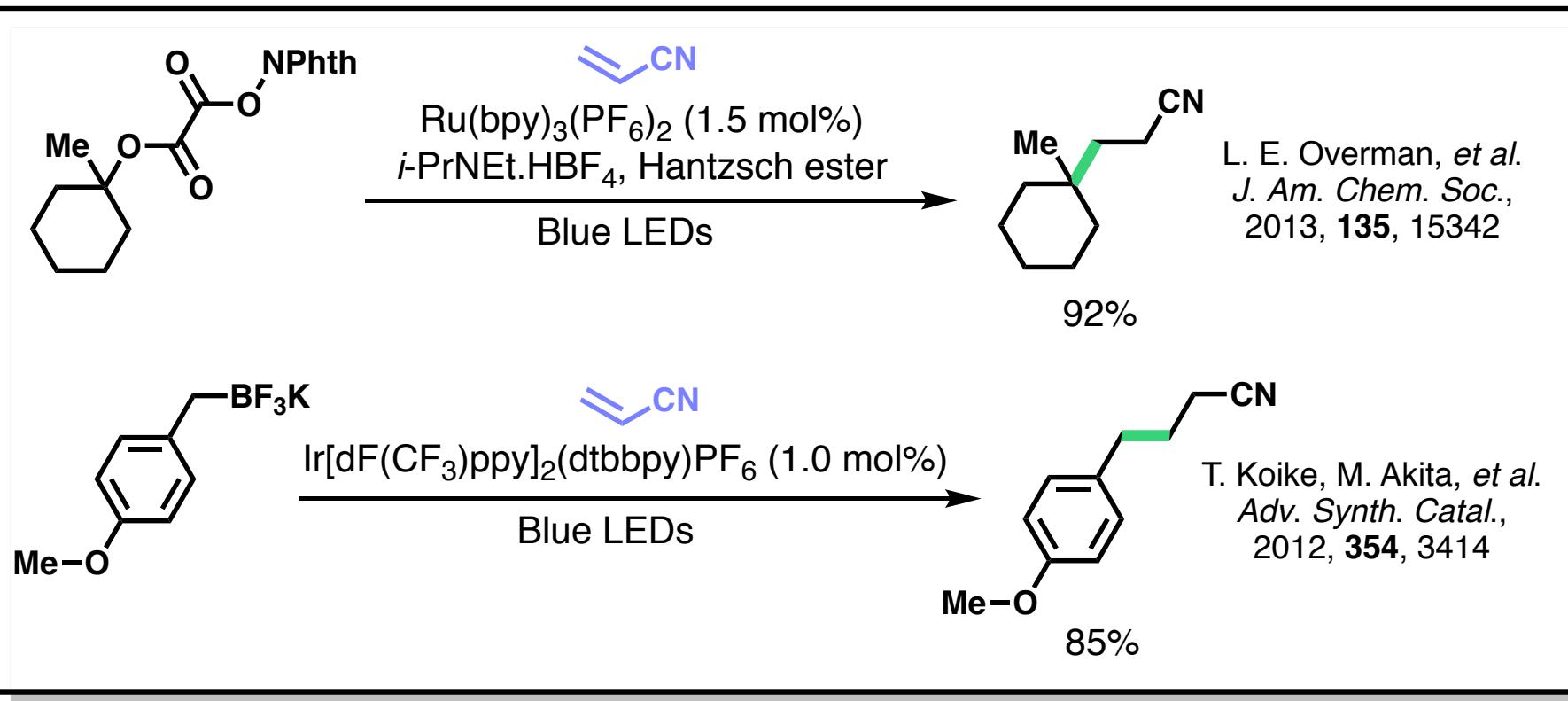


J. Waser, et al.
Chem. Sci., 2017, **8**, 1790

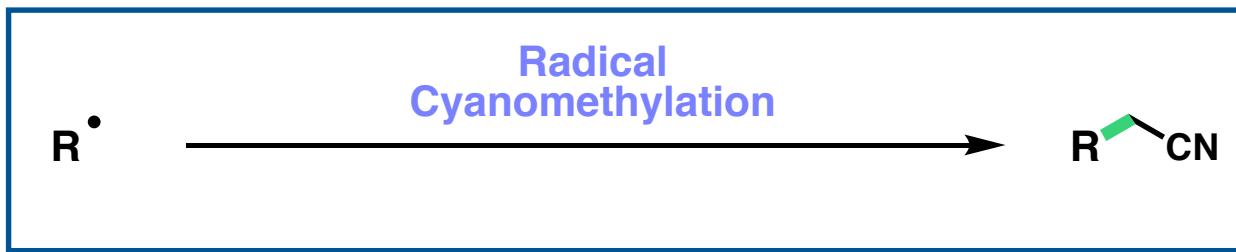


Z. Lin, G. Liu, et al.
J. Am. Chem. Soc., 2017, **139**, 15632

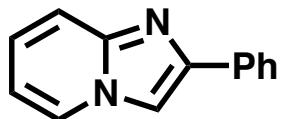
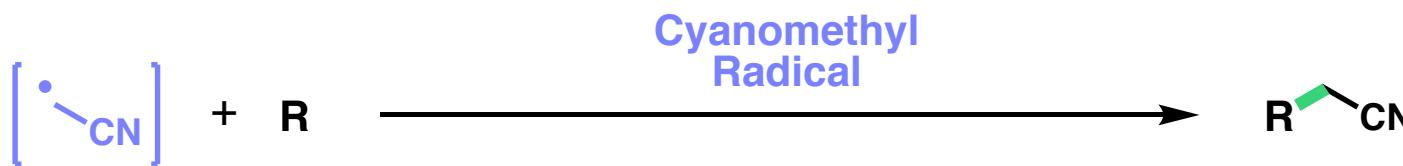
Developing a Radical Cyanomethylation Reaction



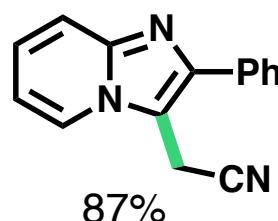
Developing a Radical Cyanomethylation Reaction



Developing a Radical Cyanomethylation Reaction

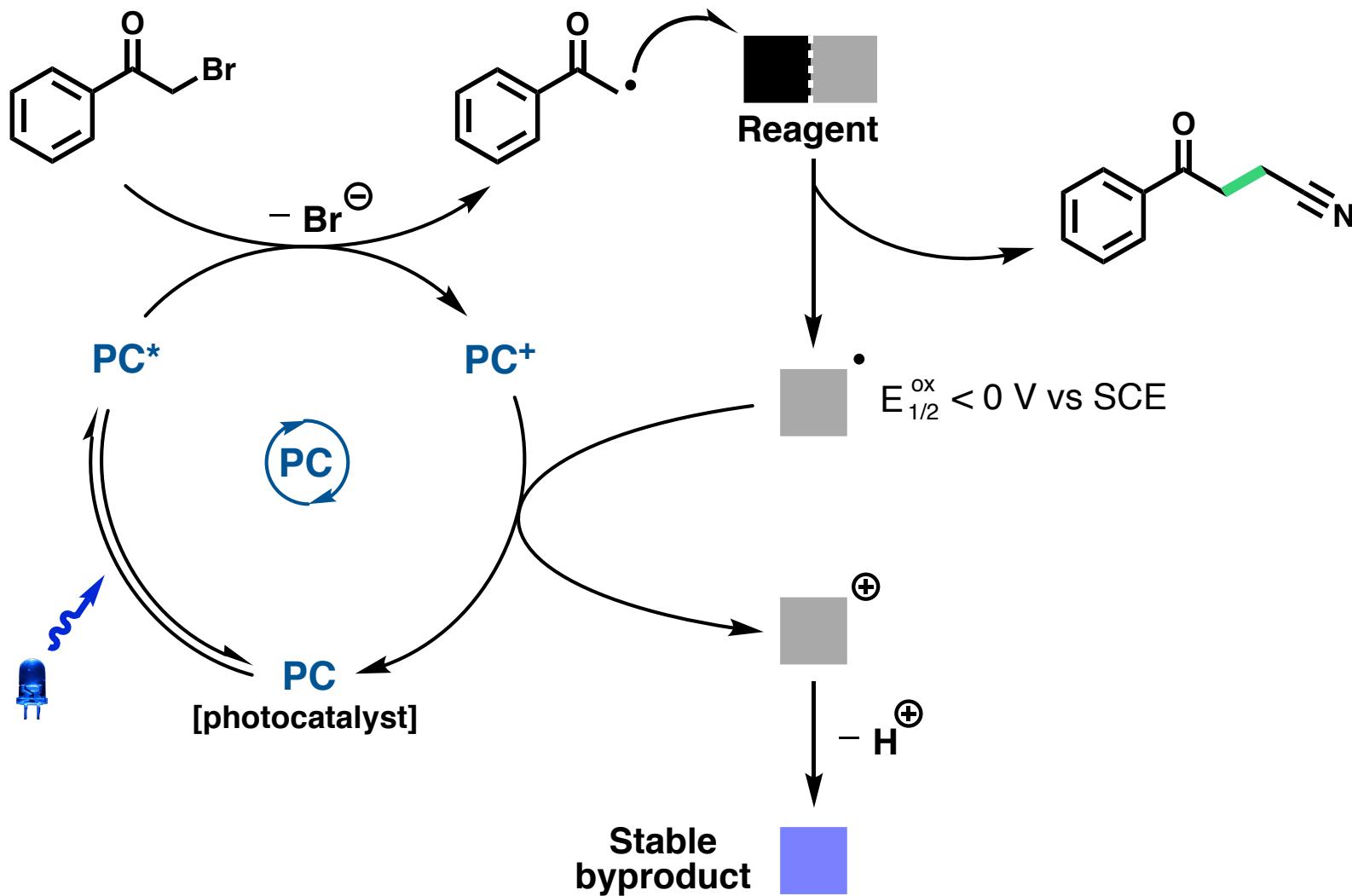


$\text{Br}-\text{CH}_2-\text{CN}$ NaHCO_3
 $\text{Ir}(\text{ppy})_3$ (2.0 mol%)
Blue LEDs

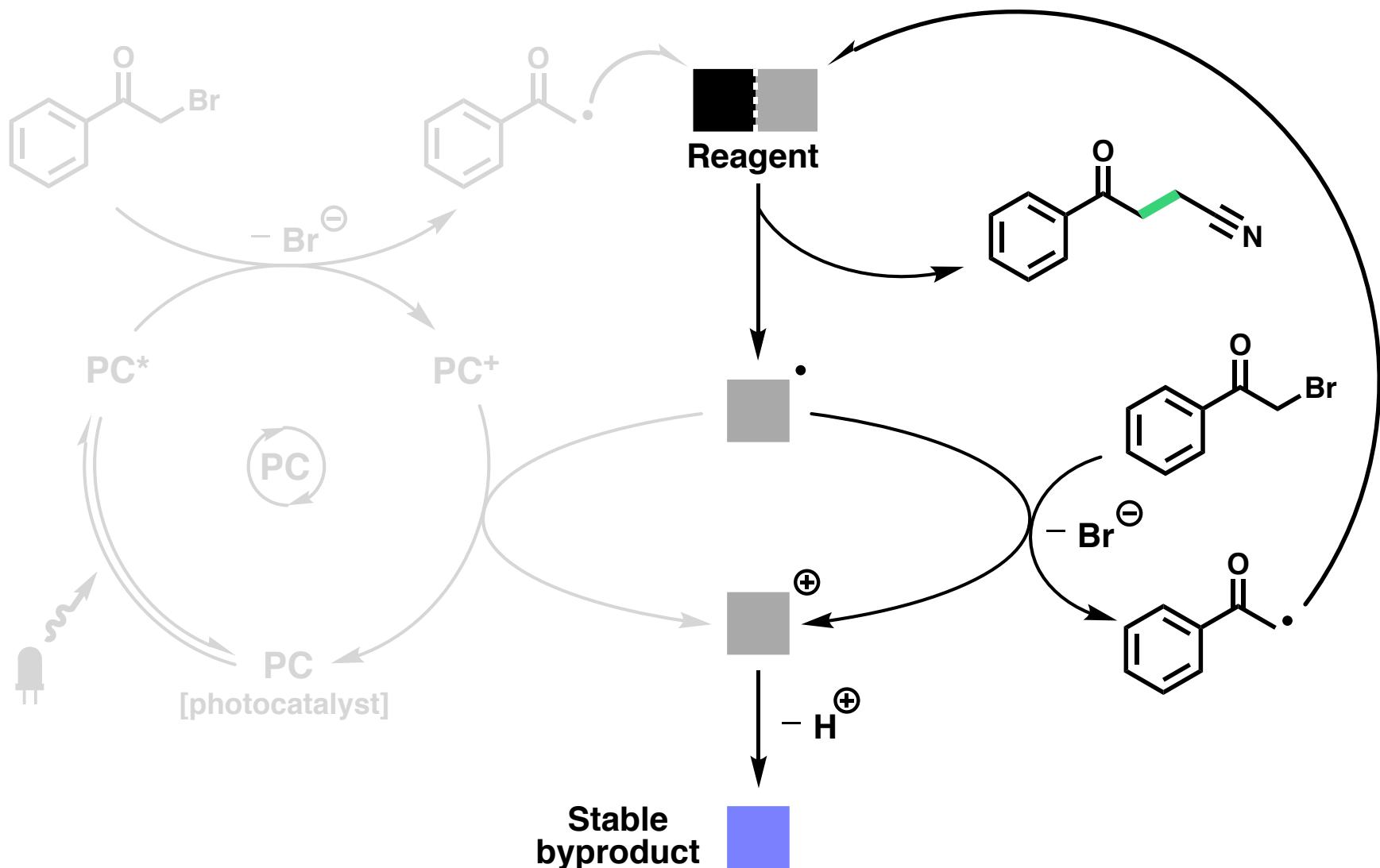


P. Liu, P. Sun, et al.
J. Org. Chem.,
2017, **82**, 5391

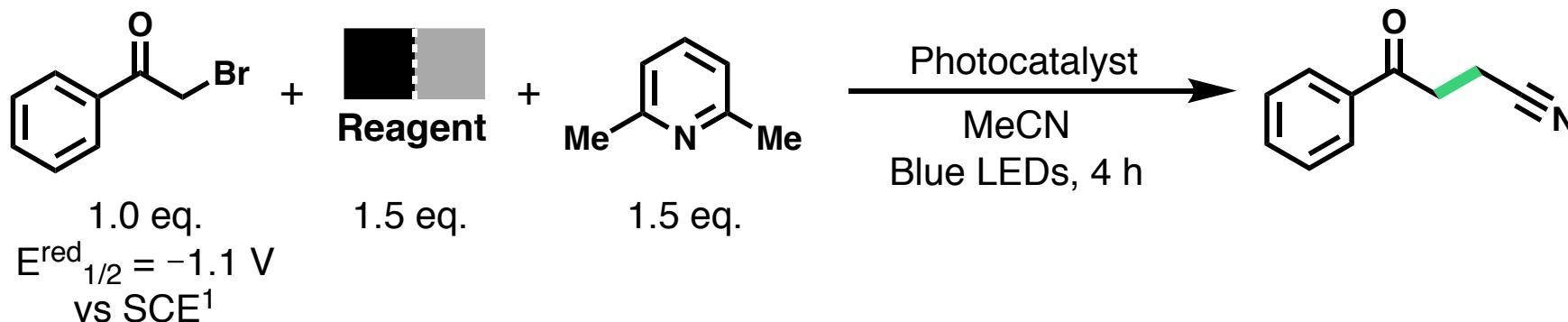
Proposed Photoredox Catalytic Cycle for Radical Cyanomethylation



Possible Chain for Radical Cyanomethylation



Photoredox Catalyst Screen for Radical Cyanomethylation

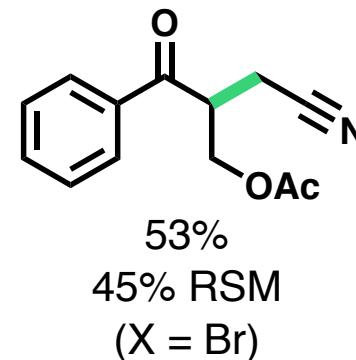
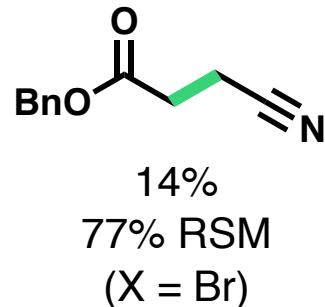
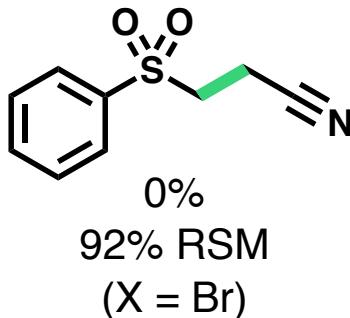
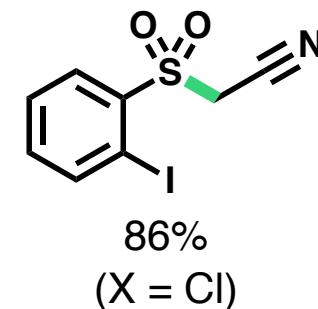
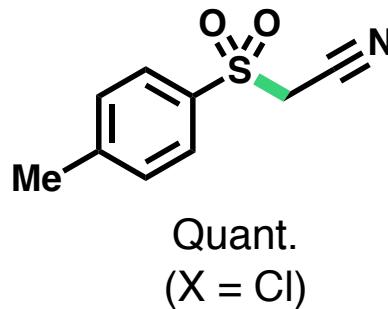
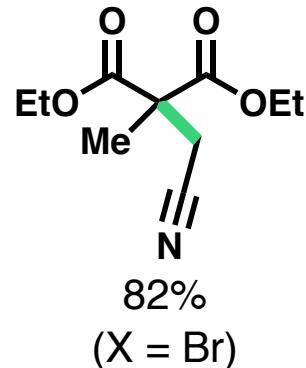
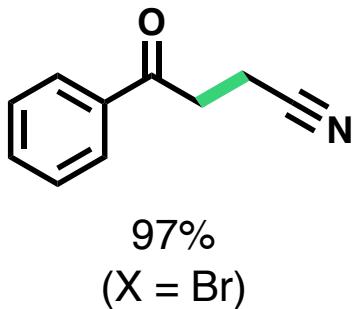
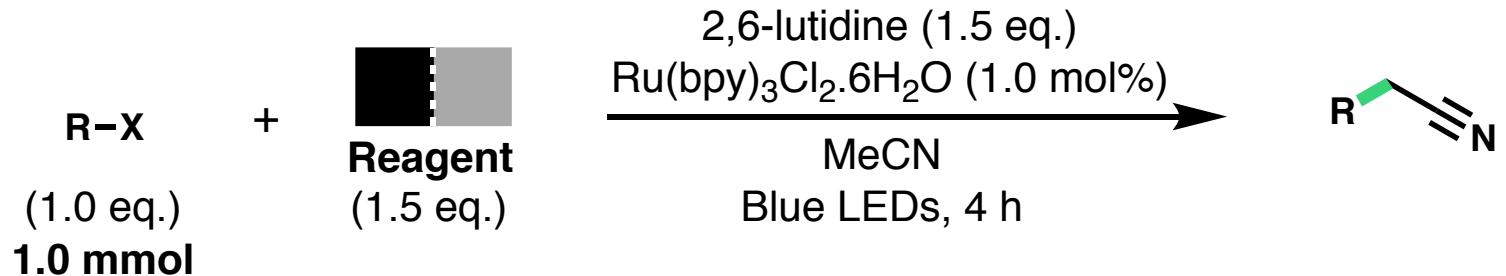


Photocatalyst (1.0 mol %)	$E_{1/2}^{n+1/n^*}$ (V vs SCE) ²	Remaining Reagent (%)	Yield of Product (%) [*]
Ir(ppy) ₃	-1.73	41	98
Ir(ppy) ₂ dtbbppyPF ₆	-0.96	27	97
Ru(bpy) ₃ Cl ₂ .6H ₂ O	-0.81	38	93
Ir[dF(CF ₃)ppy] ₂ d(CF ₃)bpyPF ₆	-0.69	43	76
Ru(bpz) ₃ (PF ₆) ₂	-0.26	116	14
—	—	113	0

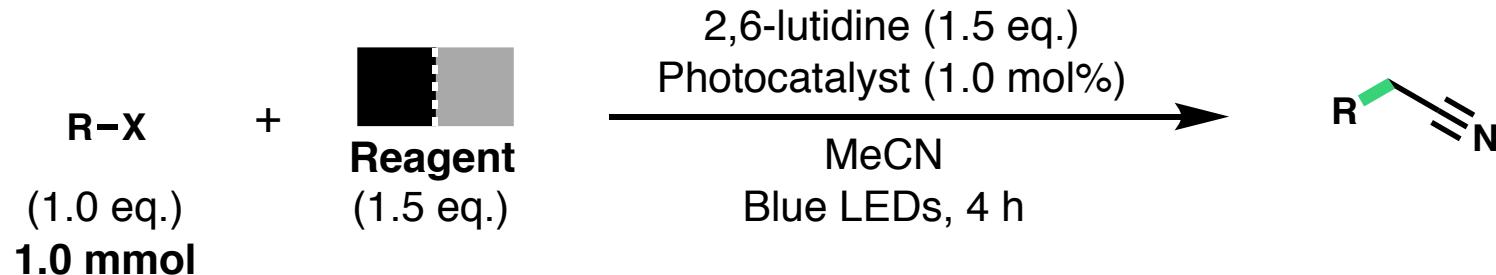
*Determined by ¹H NMR Analysis

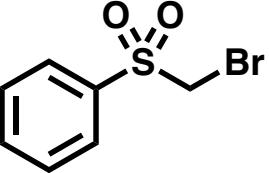
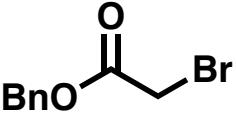
- D. W. C. MacMillan *et al.* *J. Am. Chem. Soc.* 2018, **140**, 3322
- J. Weaver *et al.* *Org. Process. Res. Dev.*, 2016, **20**, 1156

Halide Substrate Scope in Radical Cyanomethylation



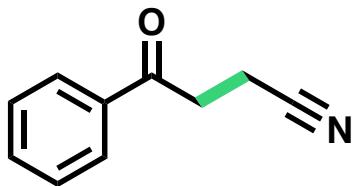
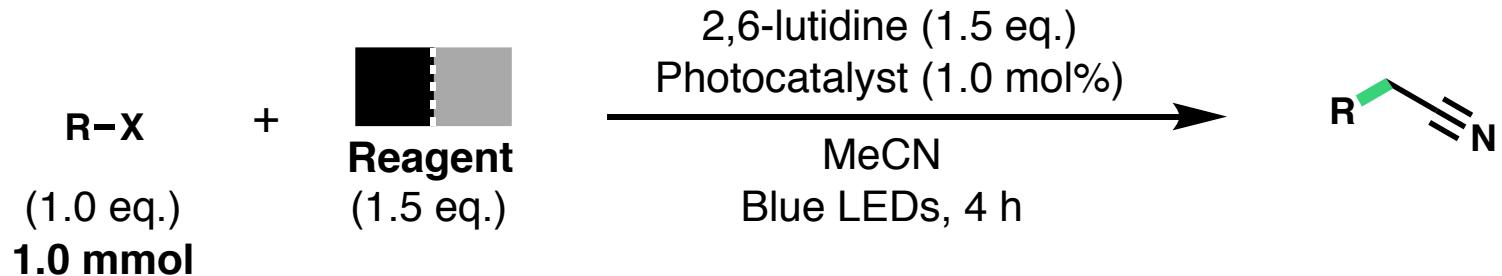
Halide Substrate Scope in Radical Cyanomethylation



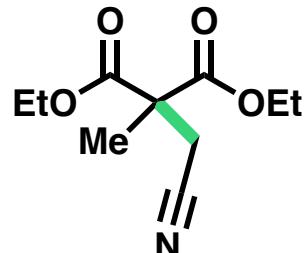
	$\text{Ru(bpy)}_3\text{Cl}_2\cdot 6\text{H}_2\text{O}$ $E_{1/2}^{\text{PC+}/\text{PC}^*} = -0.81 \text{ V}$ 4 h	$\text{Ir(ppy)}_2\text{dtbbppyPF}_6$ $E_{1/2}^{\text{PC+}/\text{PC}^*} = -0.96 \text{ V}$ 4 h	Ir(ppy)_3 $E_{1/2}^{\text{PC+}/\text{PC}^*} = -1.73 \text{ V}$ 4 h 24 h
	0% Prod. 92% S.M.	17% Prod.* 75% S.M.	65% Prod.* 26% S.M. 85% Prod.* 0% S.M.
	14% Prod. 77% S.M.	57% Prod.* 28% S.M.	84% Prod.* 3% S.M. — —

*Determined by ^1H NMR Analysis

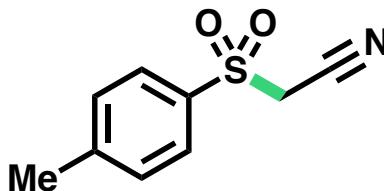
Halide Substrate Scope in Radical Cyanomethylation



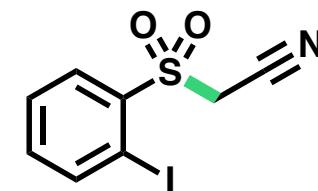
97%
[Ru]
(X = Br)



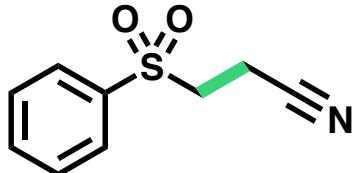
82%
[Ru]
(X = Br)



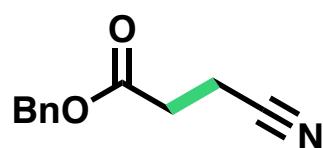
Quant.
[Ru]
(X = Cl)



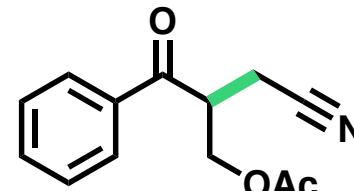
86%
[Ru]
(X = Cl)



80%
[Ir] (24 h)
(X = Br)

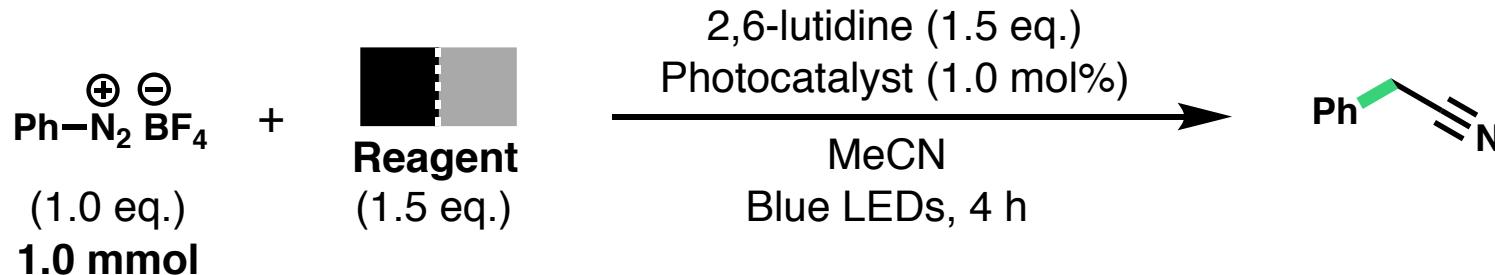


94%
[Ir]
(X = Br)



88%
[Ir]
(X = Br)

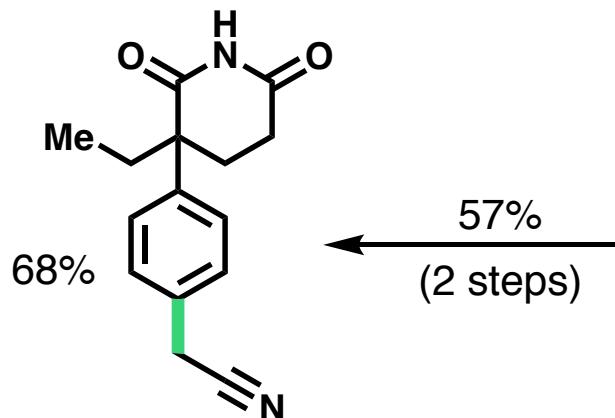
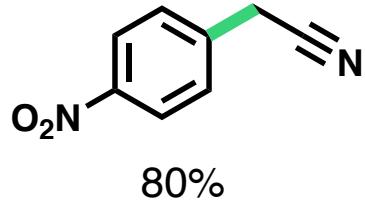
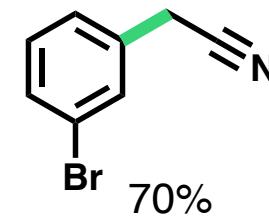
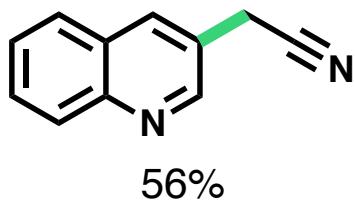
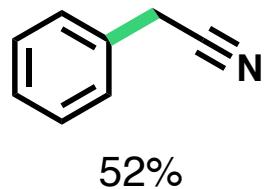
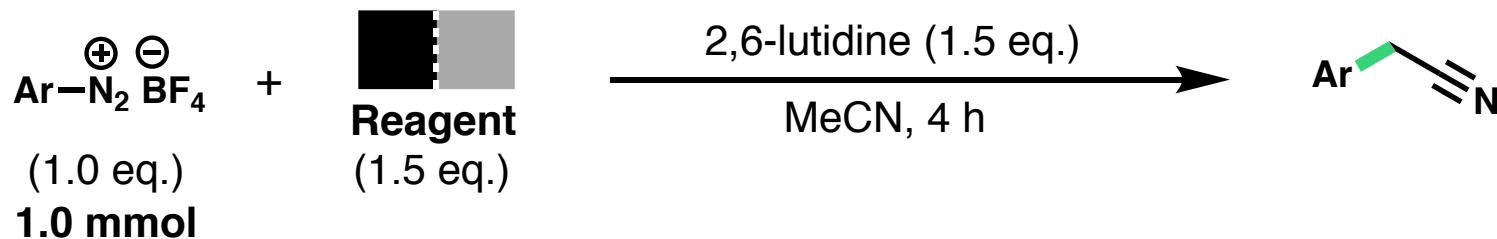
Diazonium Substrate Scope in Radical Cyanomethylation



Photocatalyst (1.0 mol %)	Remaining Reagent (%)	Yield of Product (%) [*]
Ru(bpy) ₃ Cl ₂ .6H ₂ O	55	56
4CzIPN	54	55
None (fume hood light)	70	52
None (dark)	64	51
Blue LEDs (no base or PC)	0	7

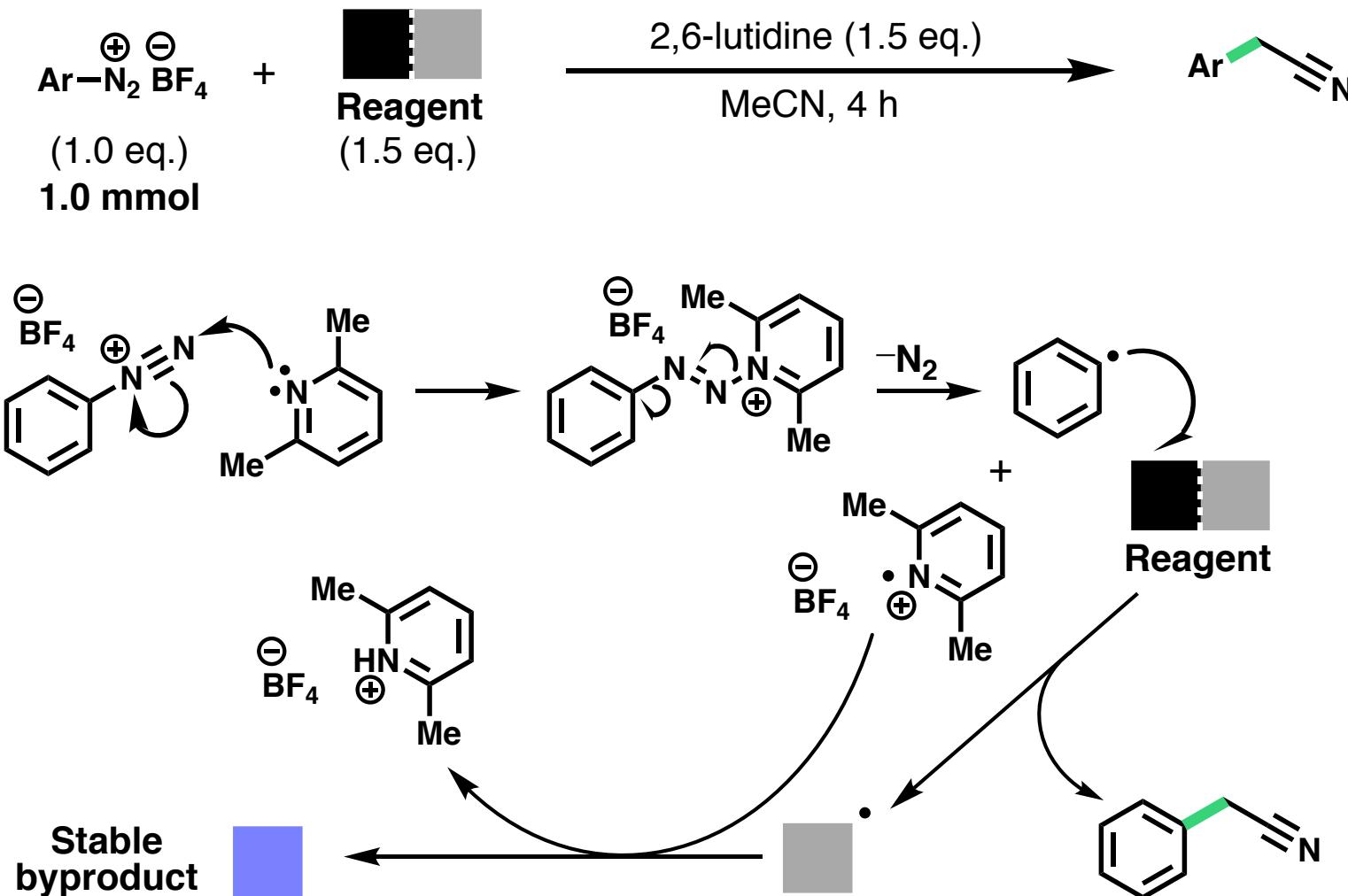
*Determined by ¹H NMR Analysis

Diazonium Substrate Scope in Radical Cyanomethylation



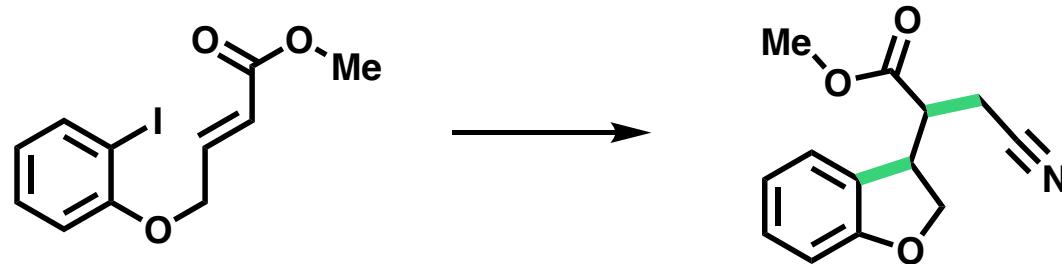
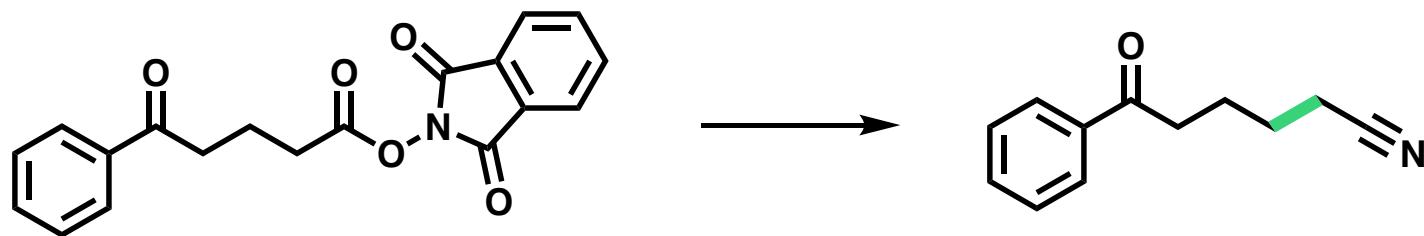
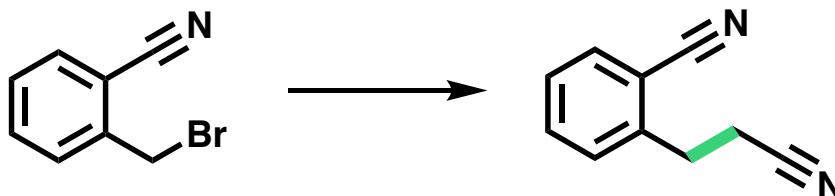
Aminoglutethimide

Proposed Mechanism for Aryl Cyanomethylation



R. A. Abramovitch and J. G. Saha, *Tetrahedron*, 1965, **21**, 3297
M. Tanaka *et al.* *J. Chem. Soc. Perkin Trans. 1*, 1994, 283

Future Work



We Want to Share the Photocatalyst Library

University of York

**Dr James Donald
Dr Will Unsworth
Prof. Richard Taylor
Prof. Peter O'Brien**

University of Lancaster

Dr Susannah Coote

Durham University

Dr Paul McGonigal

Acknowledgements



University of York



UNIVERSITY
of York

Prof. Richard Taylor

Dr Will Unsworth

Funding

Dial-A-Molecule

EPSRC

Elsevier



DIAL-A-MOLECULE

An EPSRC Grand Challenge Network

EPSRC

Engineering and Physical Sciences
Research Council