CHEMICAL REVIEWS
Review
Cite This: *Chem. Rev.* 2018, 118, 7532–7585
pubs.acs.org/CR

Photocatalyzed arylation and alkylation of C(sp2)-H bonds

Reporter: En Li
Supervisor: *Prof.* Yong Huang
2019/02/25

北京大學 PEKING UNIVERSITY

Contents

1 *Introduction*

2 *This review*

3 *Summary and Outlook*

4 *Acknowledgement*

北京大學
PEKING UNIVERSITY

Contents

1 Introduction

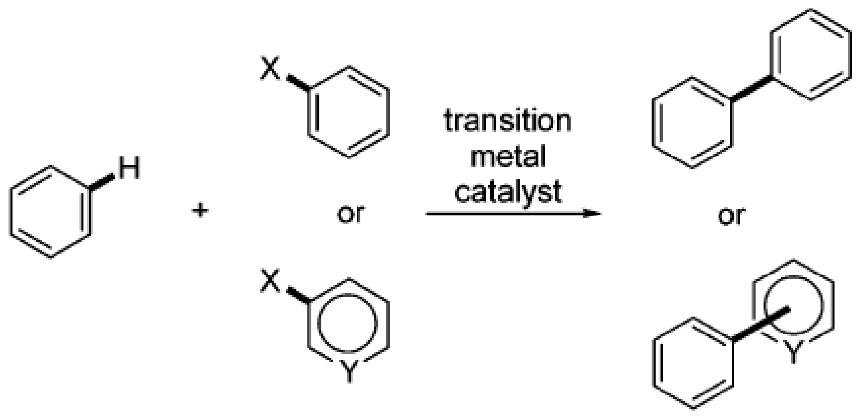
2 This review

3 Summary and Outlook

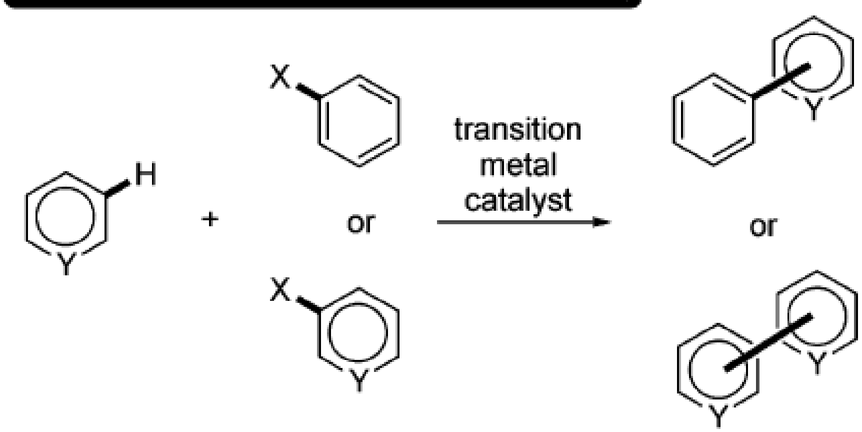
4 Acknowledgement

Transition metal-catalyzed forming C−C bonds from C(sp²)-H bonds

Direct Arylation of Aryl C-H Bonds

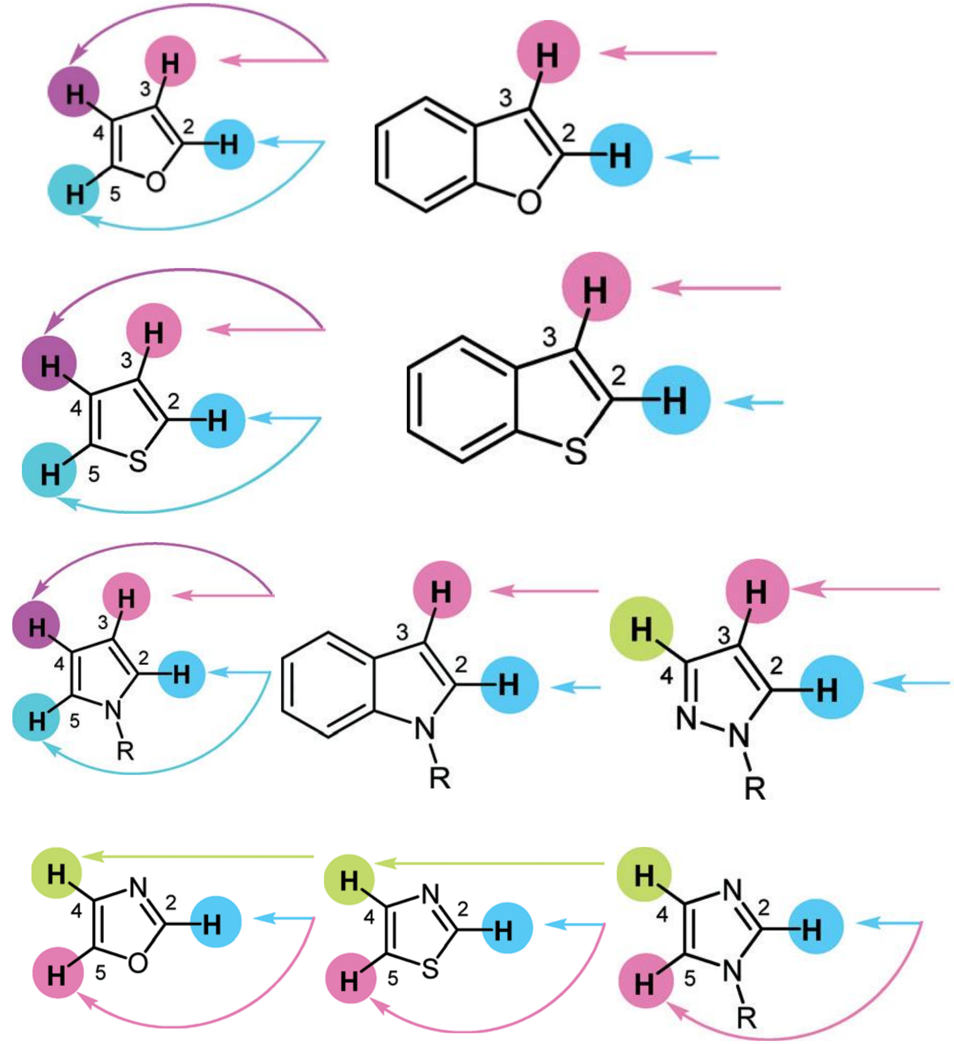


Direct Arylation of Heteroaryl C-H Bonds



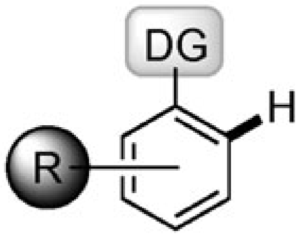
X = I, Br, Cl, OR, B, Sn

Chem. Rev. **2007**, *107*, 174– 238



Catal. Sci. Technol. **2016**, *6*, 2005– 2049

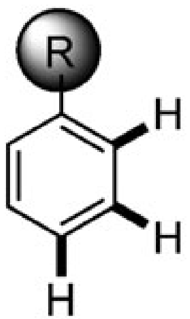
DG-assisted C–H ACTIVATION



+ *increased reactivity because of metal precoordination*
+ *high regioselectivity*

- *DG must be pre-installed and remains in the product*
- *generally limited to ortho selectivity*

C–H ACTIVATION of simple arenes



+ *no extra steps required to install and/or remove DG*
+ *possibility of meta or para selectivity*

Challenges

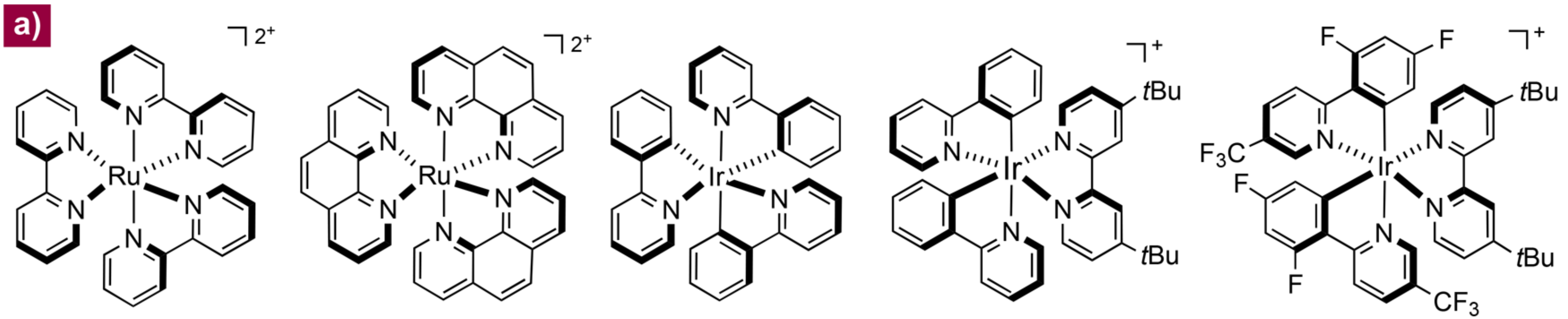
Increase of **REACTIVITY** toward transition metals

Devise new strategies to control **REGIOSELECTIVITY**

Angew. Chem., Int. Ed. **2012**, *51*, 10236– 10254

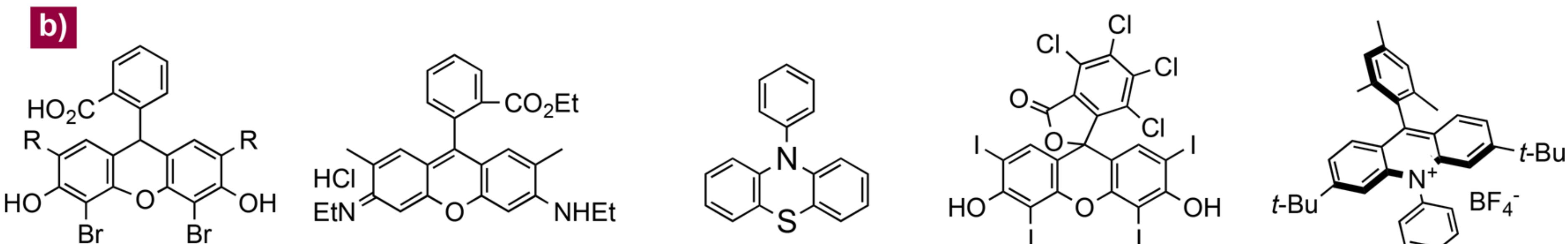
Another useful revolution in synthesis ：photoredox-initiated reactions

a)



Ru(bpy)$_3$Cl$_2$ or Ru(bpy)$_3$(PF$_6$)$_2$ | Ru(phen)$_3$Cl$_2$ or Ru(phen)$_3$(PF$_6$)$_2$ | *fac*-[Ir(ppy)$_3$] | [Ir(ppy)$_2$(dpbpy)](PF$_6$) | [Ir{dF(CF$_3$)ppy}$_2$(dtbpy)](PF$_6$)

b)



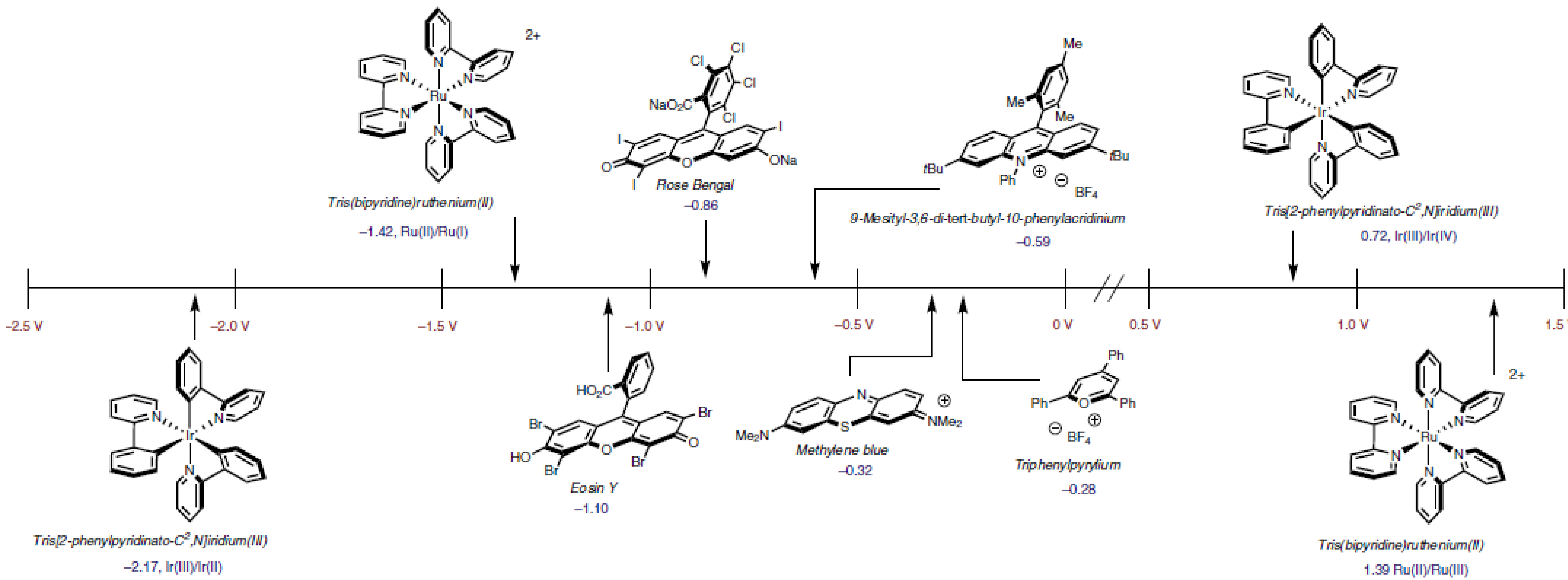
R = Br **Eosin Y**
R = NO$_2$ **Eosin B**

Rhodamine 6G (RA 6G)

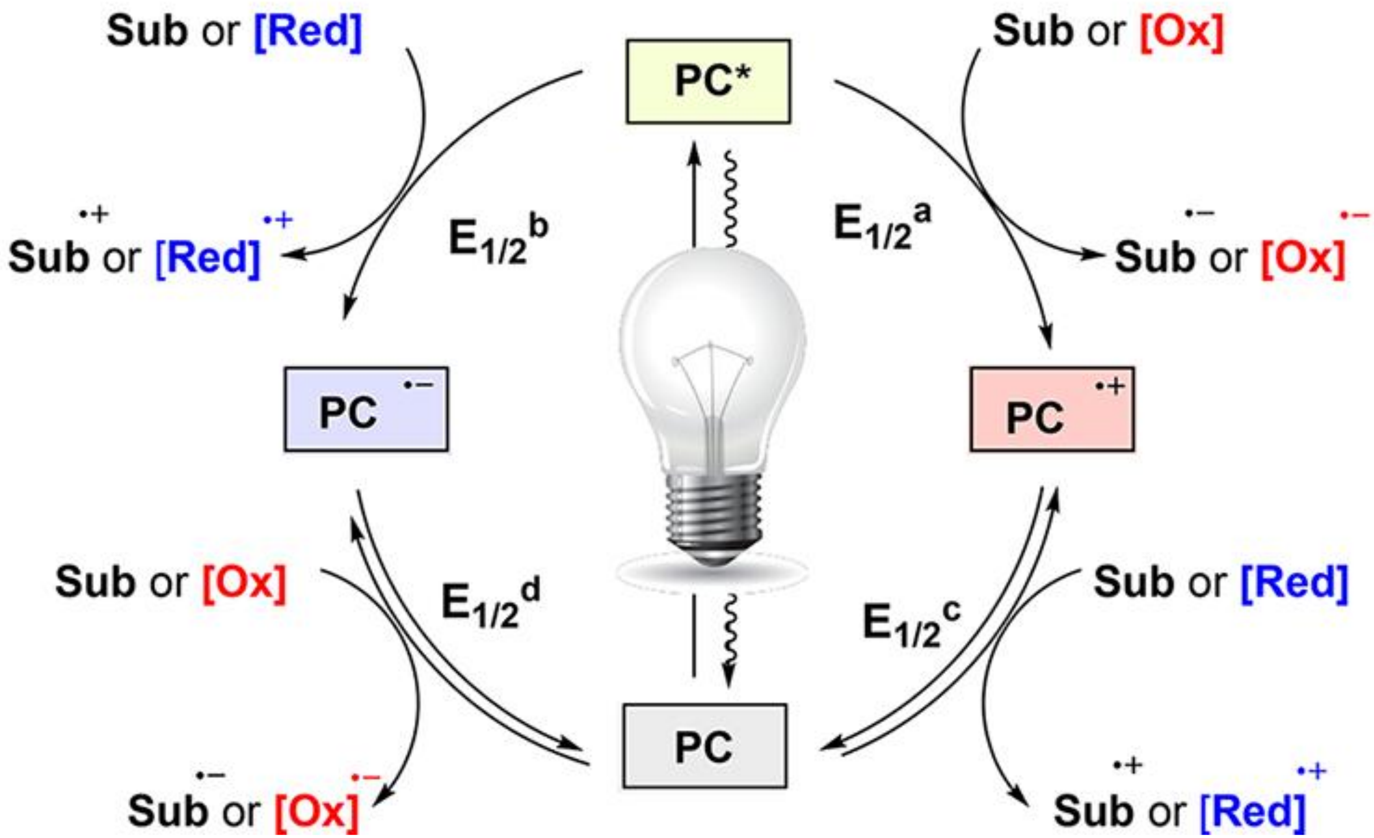
10-Phenyl phenothiazine

Rose Bengal (RB)

Mes-Acr$^+$-Ph


Tris(bipyridine)ruthenium(II)
–1.42, Ru(II)/Ru(I)
Rose Bengal
–0.86
9-Mesityl-3,6-di-tert-butyl-10-phenylacridinium
–0.59
Tris[2-phenylpyridinato-C2,N]iridium(III)
0.72, Ir(III)/Ir(IV)
-2.5 V
–2.0 V
–1.5 V
–1.0 V
–0.5 V
0 V
0.5 V
1.0 V
1.5 V
Tris[2-phenylpyridinato-C2,N]iridium(III)
–2.17, Ir(III)/Ir(II)
Eosin Y
–1.10
Methylene blue
–0.32
Triphenylpyrylium
–0.28
Tris(bipyridine)ruthenium(II)
1.39 Ru(II)/Ru(III)

a) Reductive Quenching Cycles **b) Oxidative Quenching Cycles**



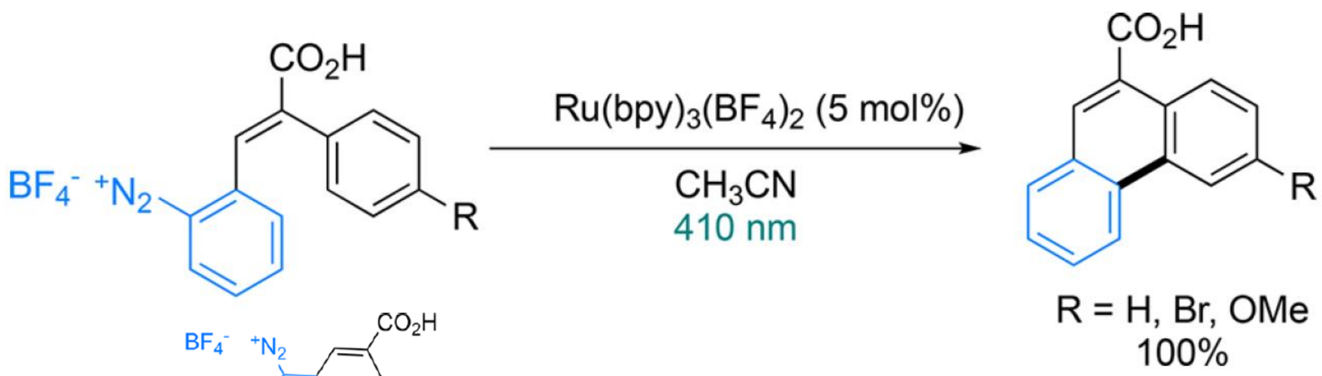
Contents

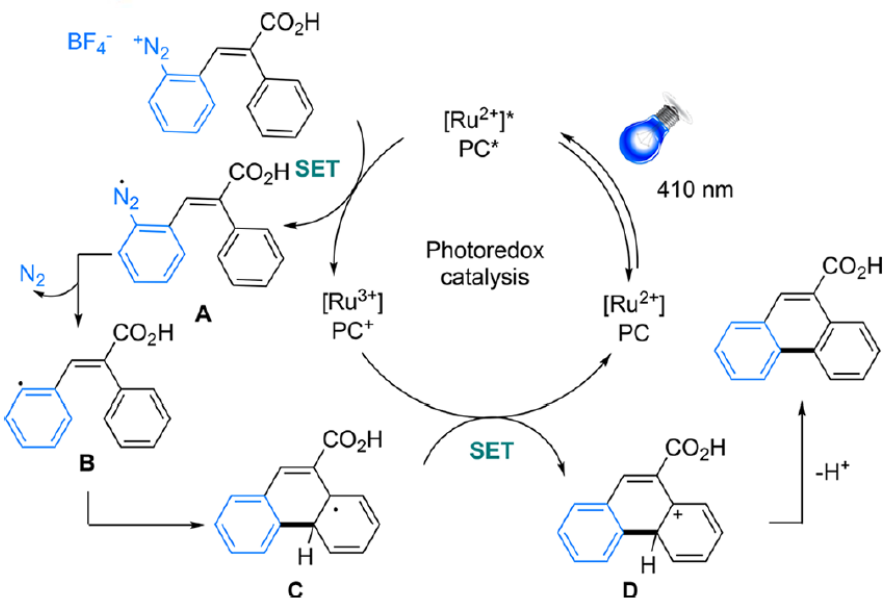
1 Introduction
2 This review
3 Summary and Outlook
4 Acknowledgement

2.1.1 Aryl diazonium salts as aryl radical precursors

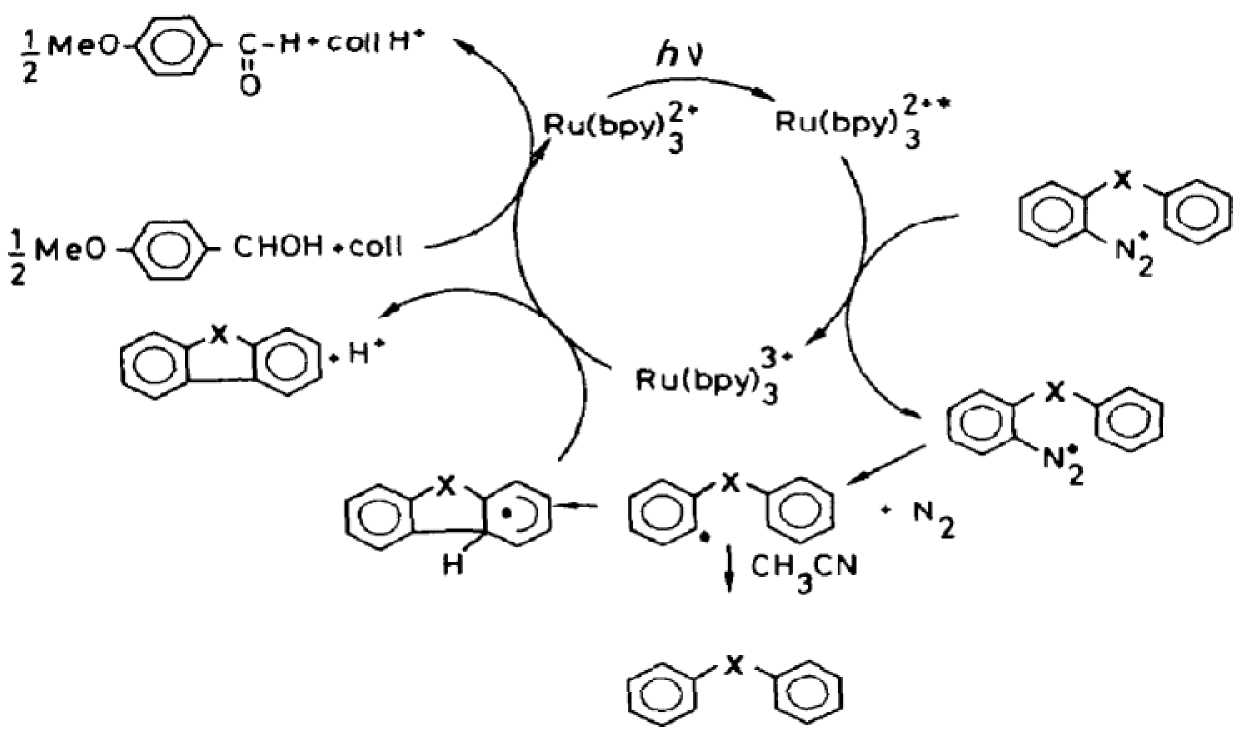
For Arylation of Arene Derivatives.

Pschorr Reaction in Phenanthrene Series by Deronzier



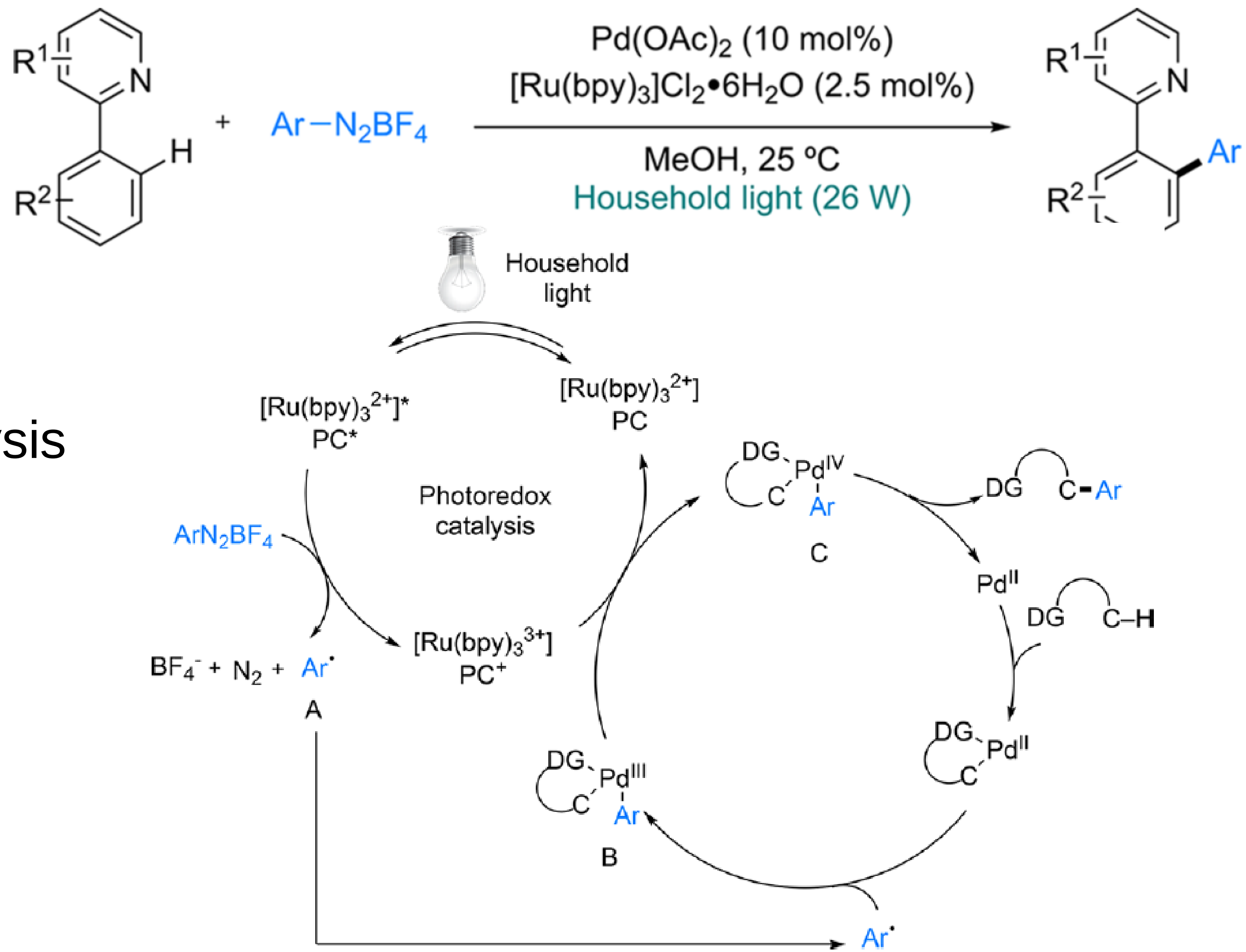



N2BF4
X
Ru(bpy)3(BF4)2 (5 mol%)
4-CH3O(C6H4)CH2OH (0.5 equiv.)
collidine (0.5 equiv.)
CH3CN
410 nm
X
X = O , 10%
X = C=O, 25%


hν
Ru(bpy)3 2+
Ru(bpy)3 2+*
Ru(bpy)3 3+
1/2 MeO
C-H + coll H+
O
1/2 MeO
CHOH + coll
X
+ H+
N2+
N2•
+ N2
CH3CN
H

Sanford

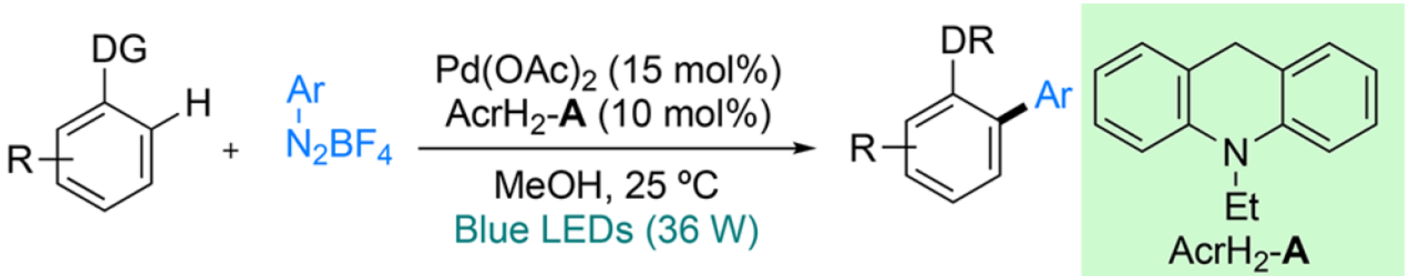
Scheme 3. Merging Pd-Catalyzed C−H Functionalization and Visible Light Photoredox Catalysis



Dual catalysis

Xu and co-workers

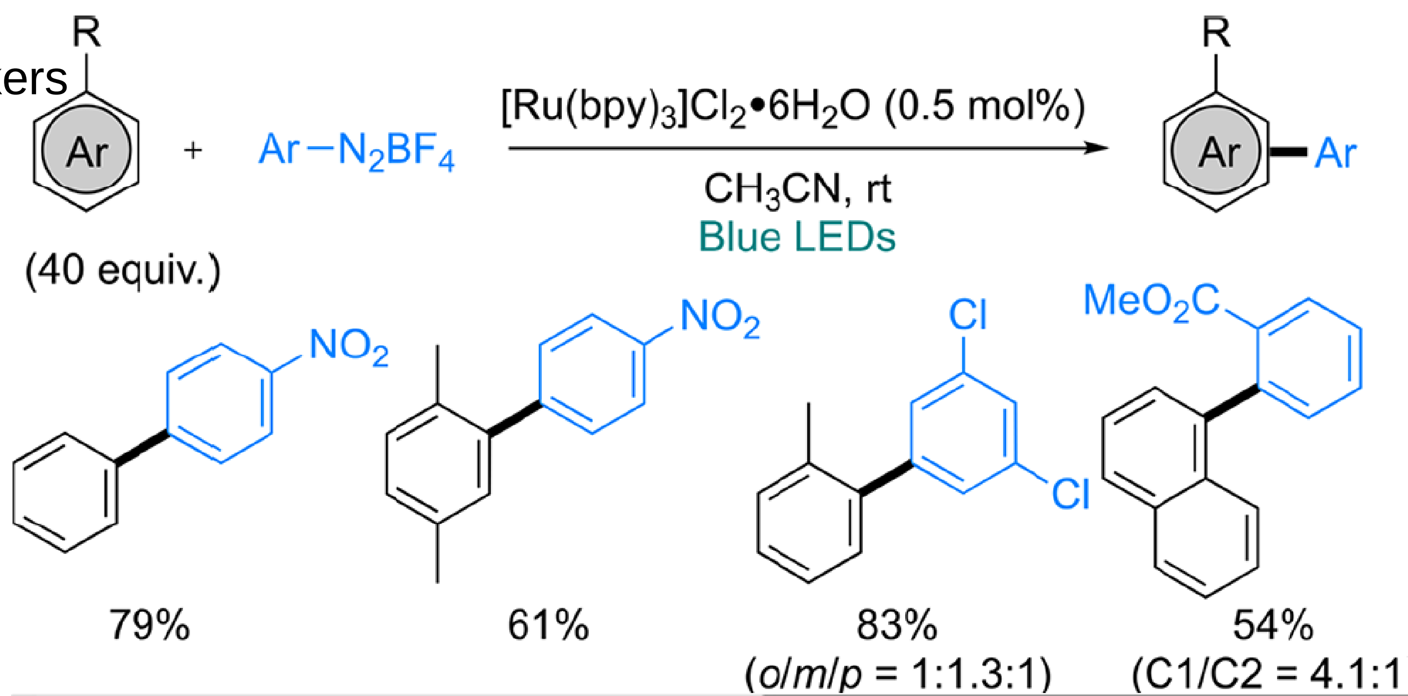
Scheme 5. Dual Catalysis $Pd(OAc)_2$/9,10-Dihydroacridine for Arylation of Acetanilides and Benzamides Using Aryldiazonium Salts



J. Org. Chem. **2017**, *82*, 3622– 3630

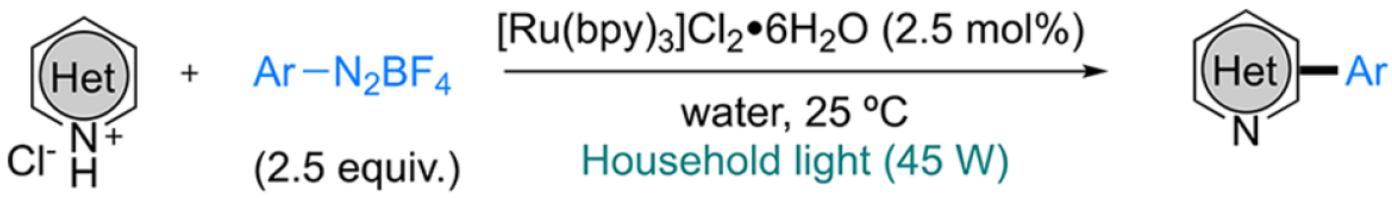
Scheme 6. Arylation of Benzene Derivatives with Aryldiazonium Salts

Malacria and co-workers

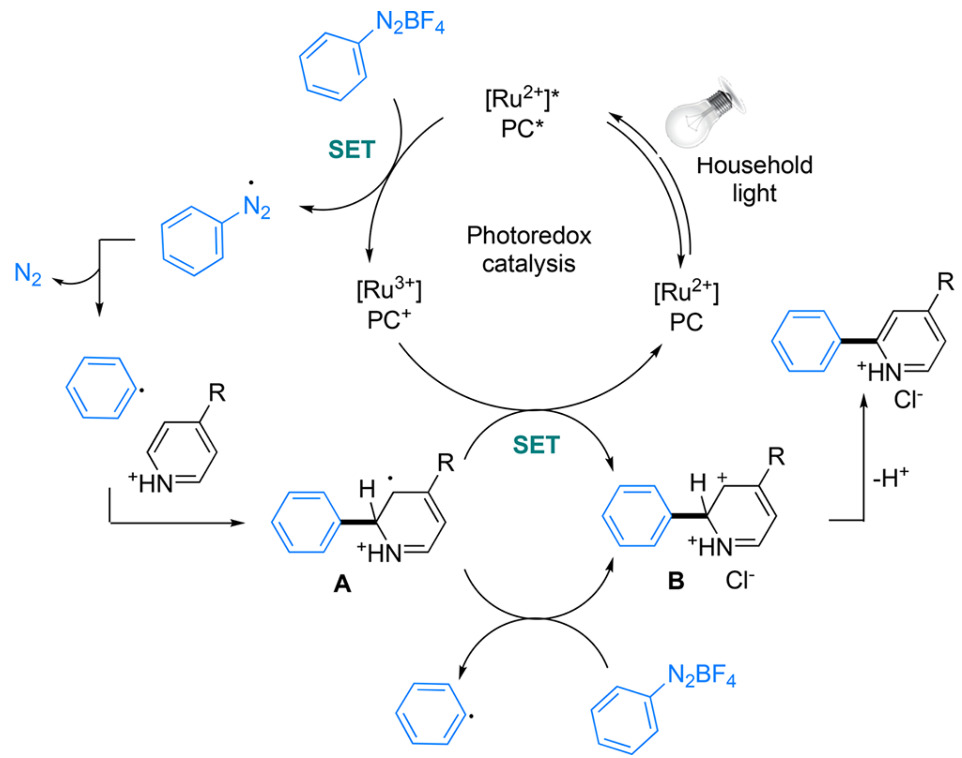


For arylation of heterocycles.

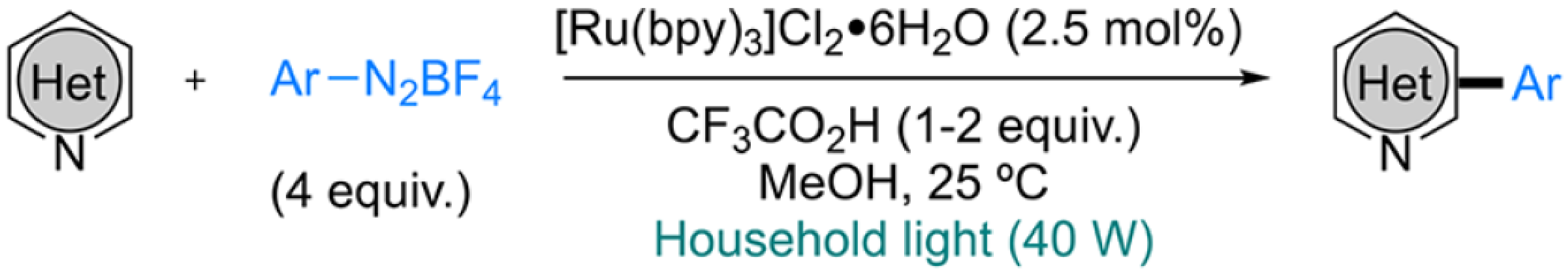
Scheme 7. Arylation of *N*-Heteroarenes with Aryldiazonium Salts[a]



Xue and coworkers



Scheme 8. Arylation of Isoquinolines with Aryldiazonium Salts

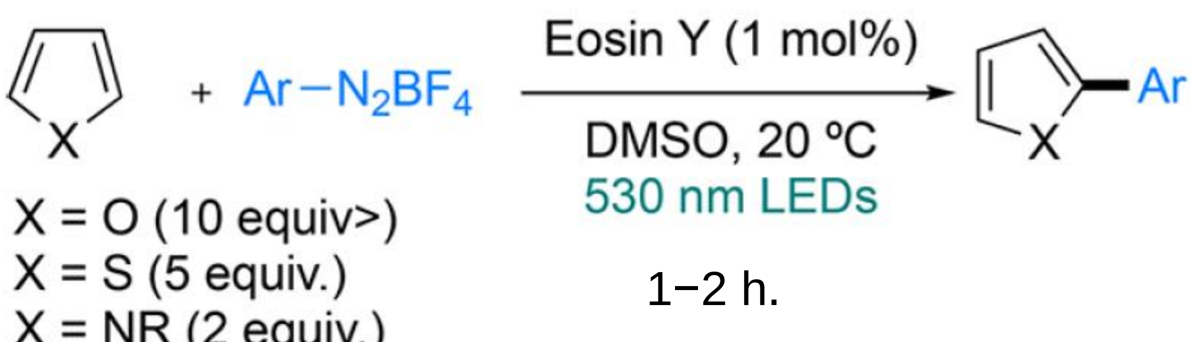


Lei and co-workers

J. Org. Chem. **2014**, *79*, 10682– 10688

Scheme 9. Metal-Free C–H Bond Arylation of Heteroarenes with Aryldiazonium Salts in the Presence of Eosin Y

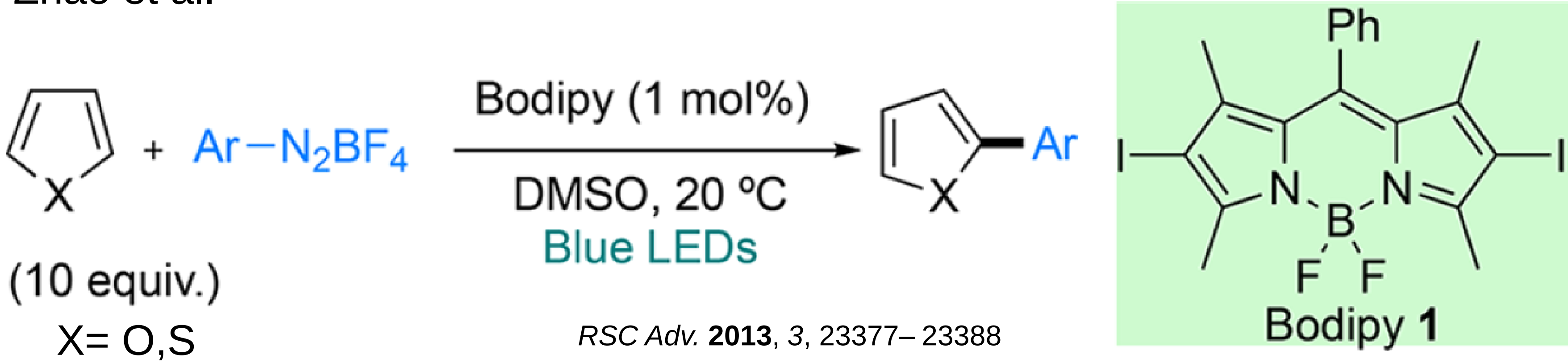
König and co-workers



J. Am. Chem. Soc. **2012**, *134*, 2958– 2961

Scheme 11. Iodo-bodipys Photoinduced C–H Bond Arylation of Heteroarenes with Aryldiazonium Salts

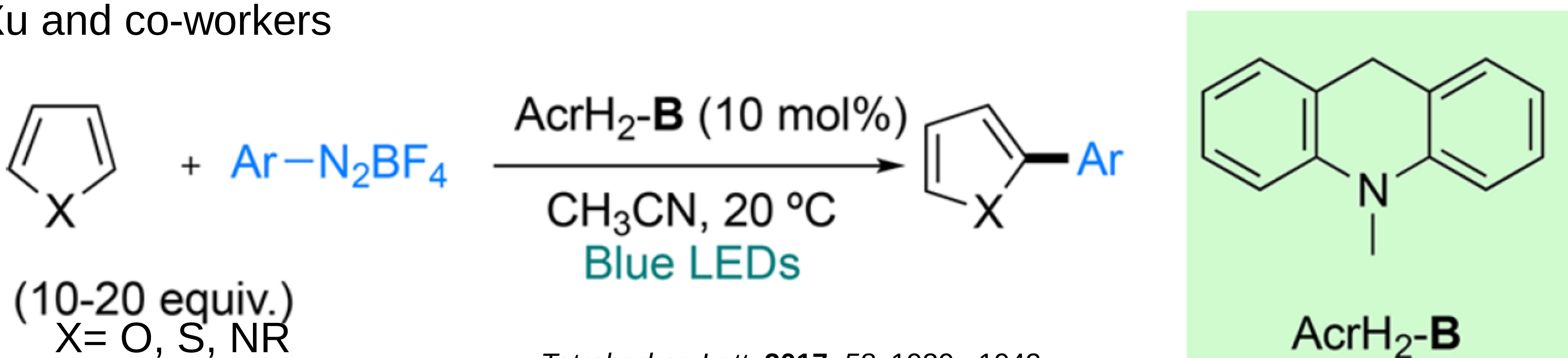
Zhao et al.



RSC Adv. **2013**, *3*, 23377– 23388

Scheme 12. 9,10-Dihydro-10-methylacridine Photoinduced C–H Bond Arylation of Heteroarenes with Aryldiazonium Salts

Xu and co-workers

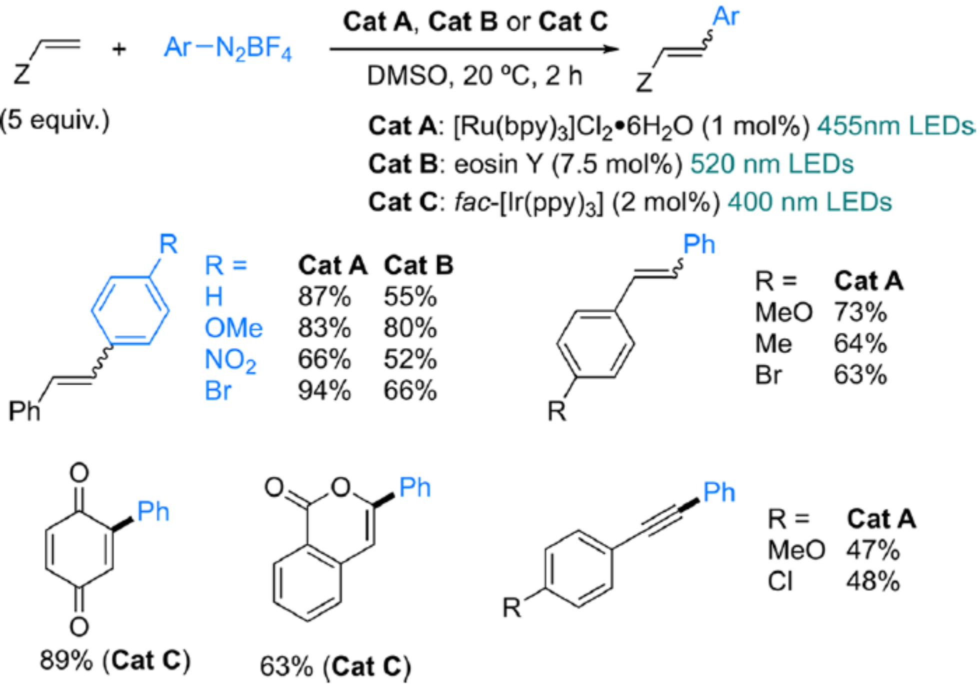


Tetrahedron Lett. **2017**, *58*, 1939– 1942

For arylation of alkenes

König and co-workers

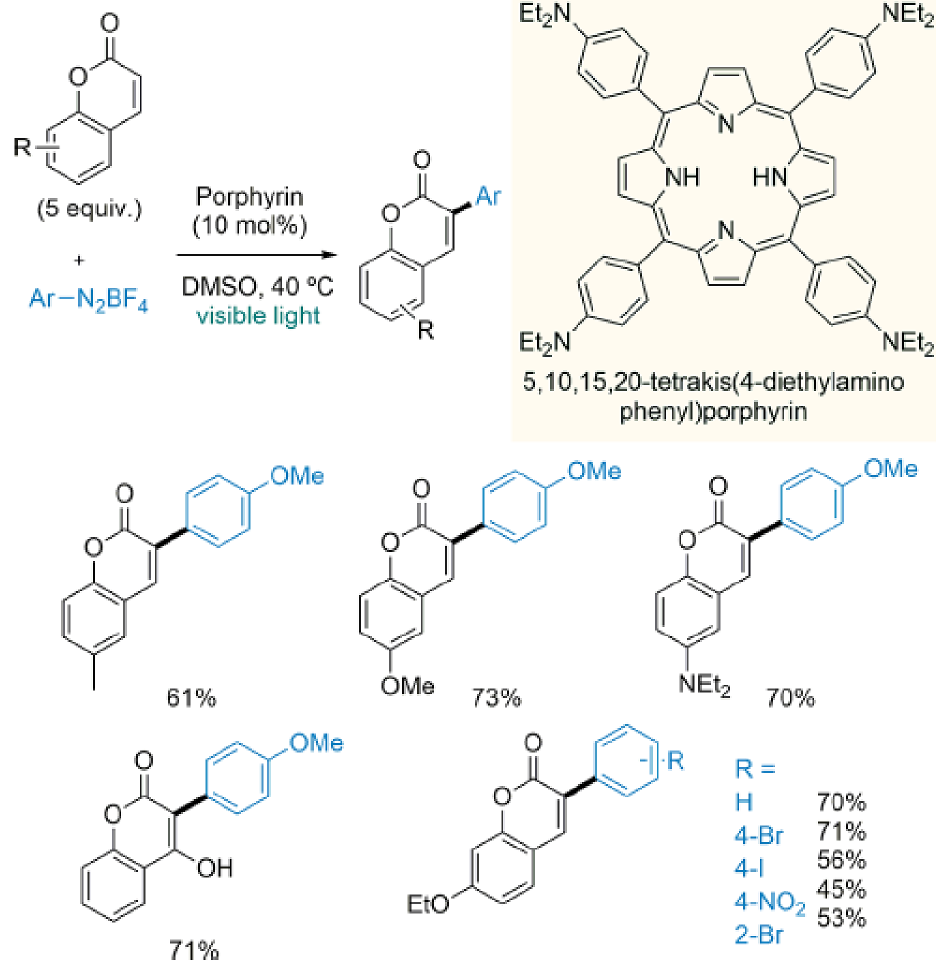
Scheme 14. Photocatalytic Arylation of Alkenes, Alkynes, and Enones with Diazonium Salts



ChemistryOpen **2012**, *1*, 130– 133

Scheme 15. Porphyrin-Induced Arylation of Coumarins with Diazonium Salts

Kanai and co-workers

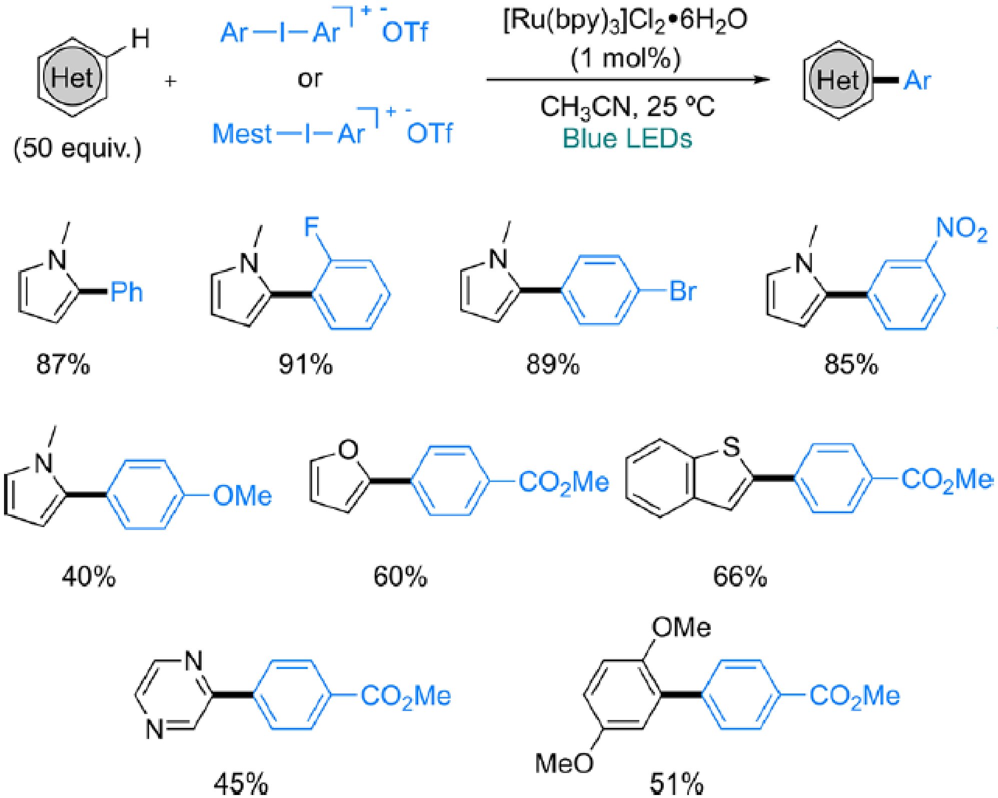


Chem. Commun. **2015**, *51*, 9718– 9721

2.1.2 Diaryliodonium Salts As Aryl Radical Precursors for Arylation of (Hetero)arenes

Xue, Xiao, and co-workers

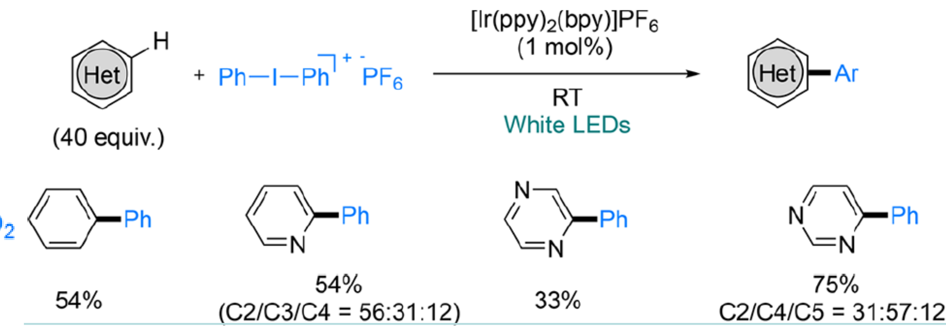
Scheme 16. Arylation of (Hetero)arenes with Diaryliodonium Salts

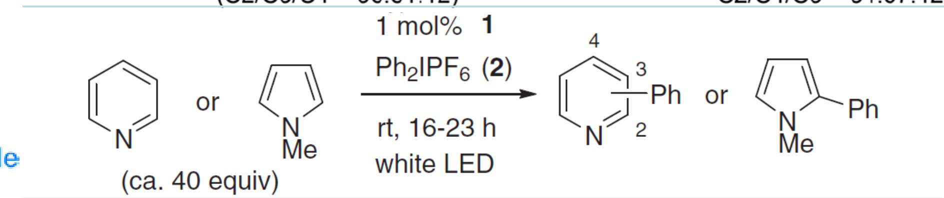


Synlett **2013**, *24*, 507– 513,

Tobisu, Chatani and co-workers

Scheme 17. Phenylation of (Hetero)arenes with Diaryliodonium Salts





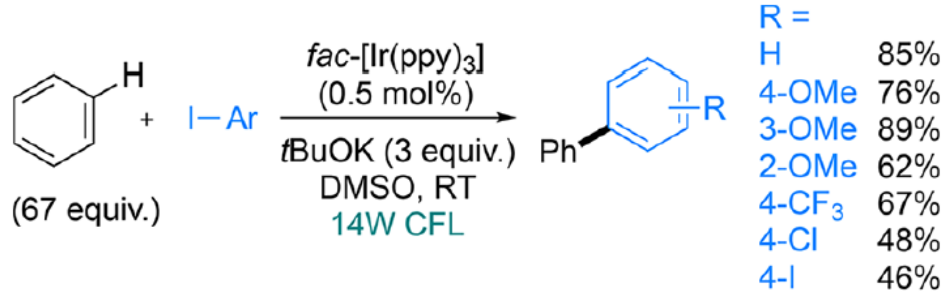
Entry	Variation from the "standard conditions"	Yield with pyridine[a]/%	Yield with pyrrole/%
1	None	57 (54:30:16)	88
2	Without **1**	9 (56:44:0)	54
3	Without LED (in dark)	0	trace
4	Under an atmosphere of air	57 (59:27:14)	75

Chem. Lett. **2013**, *42*, 1203–1205

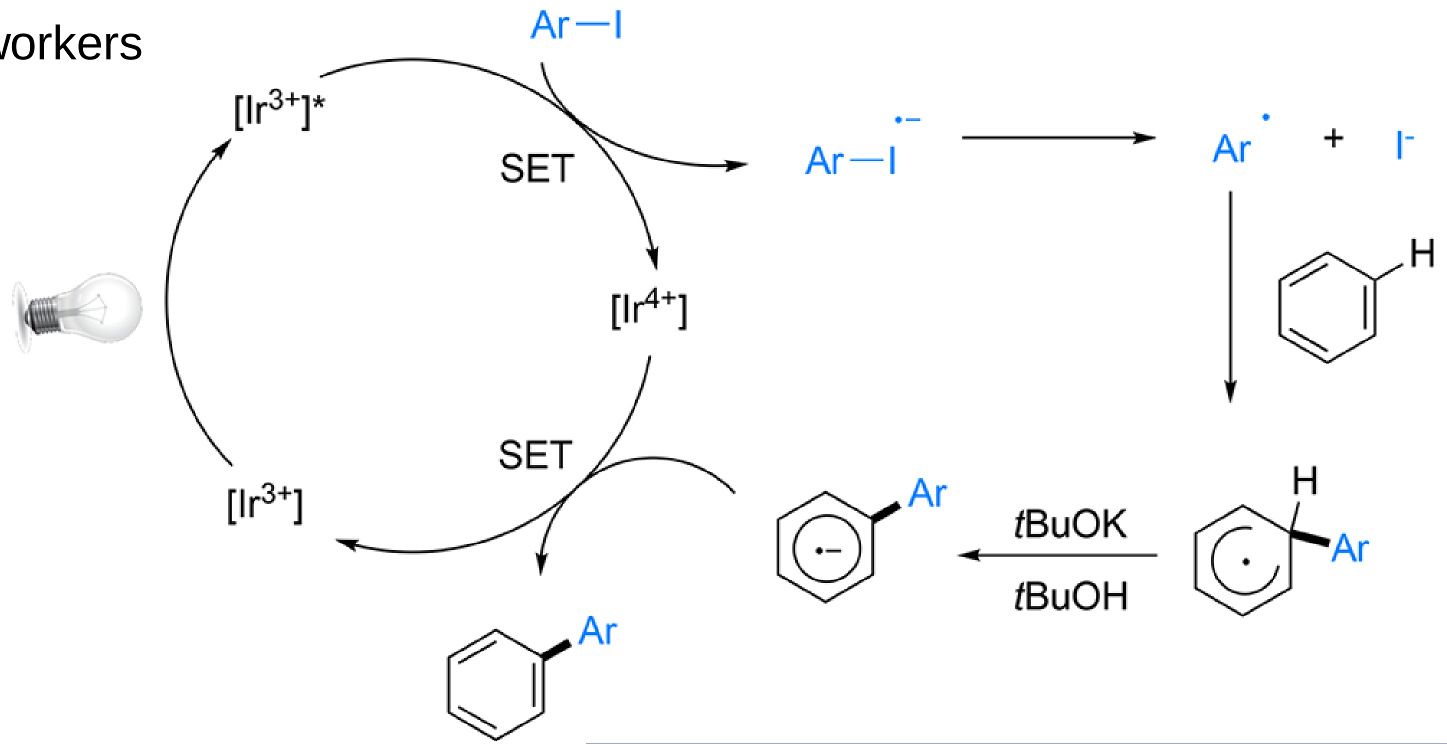
2.1.3 Aryl Halides as Aryl Radical Precursors

Scheme 18. C−H Bond Arylation of Arenes Using Aryl Halides and Ir-Photoredox Catalyst

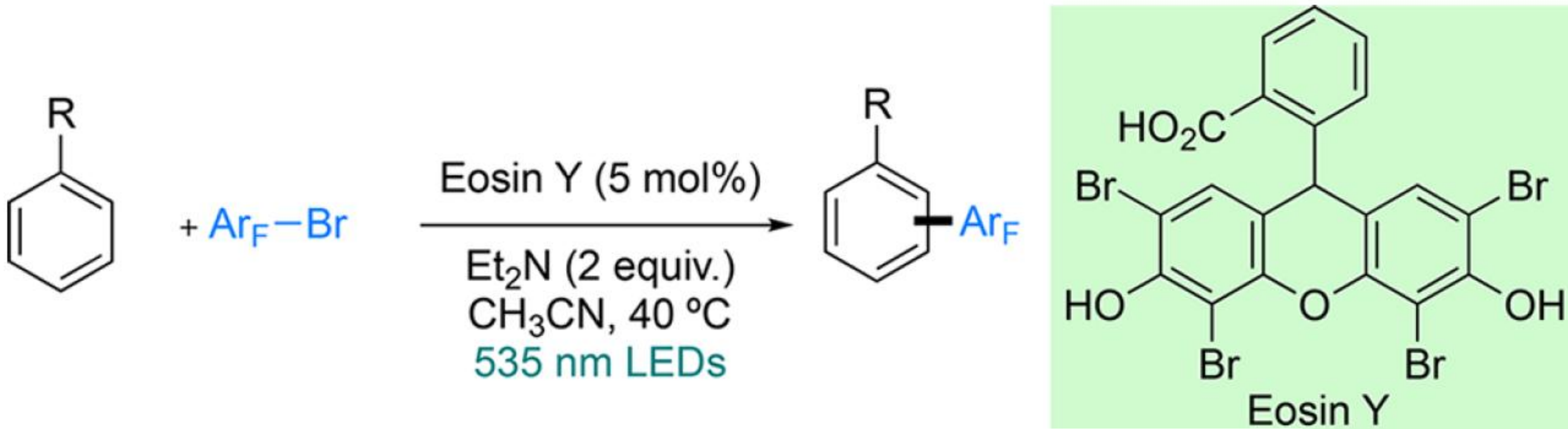
For Arylation of Arenes



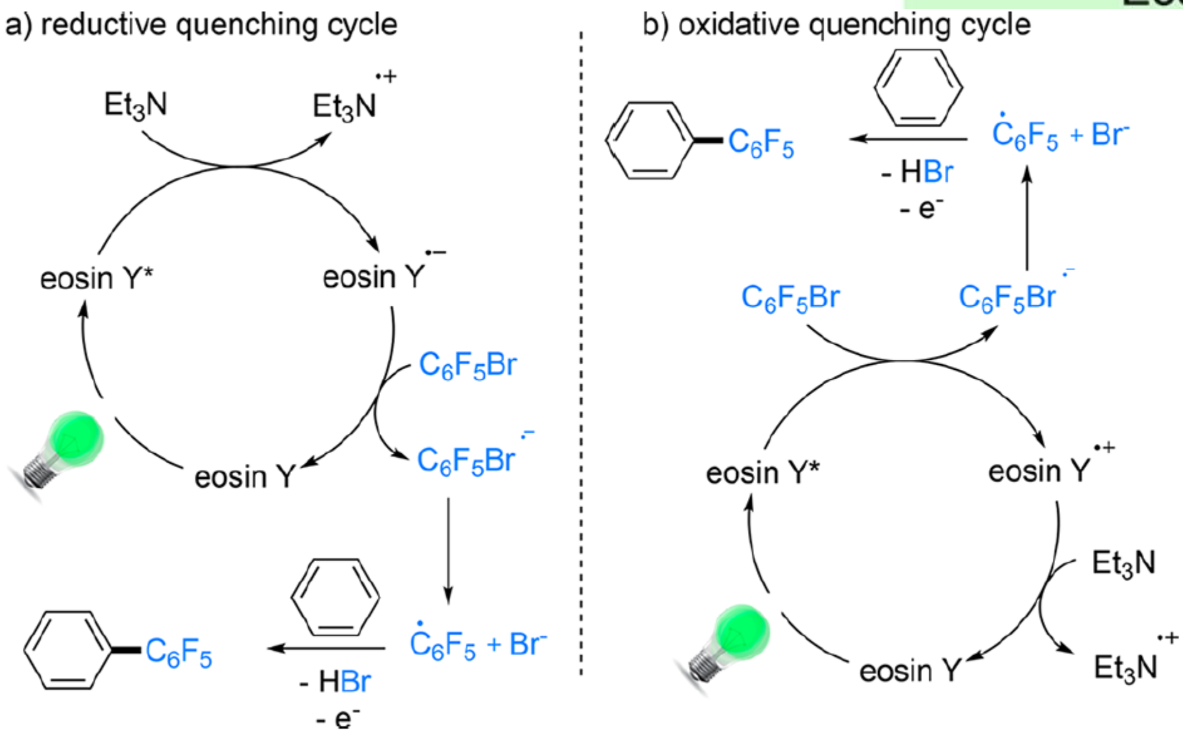
Li and co-workers



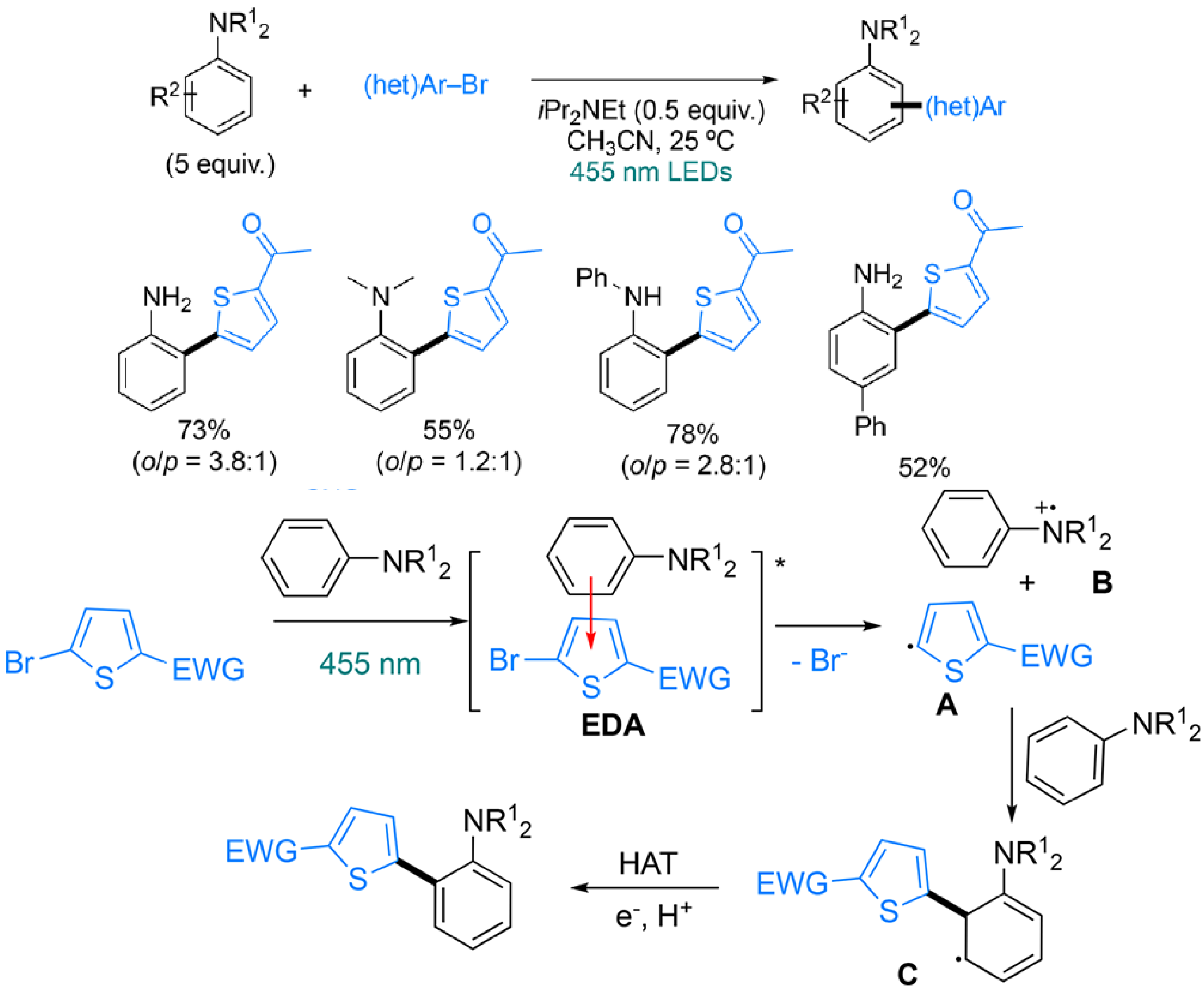
Scheme 19. Organic Photoredox Catalyst for the Perfluoroarylation of (Hetero)arene Derivatives



König



Scheme 20. Arylation of Anilines via EDA Complex



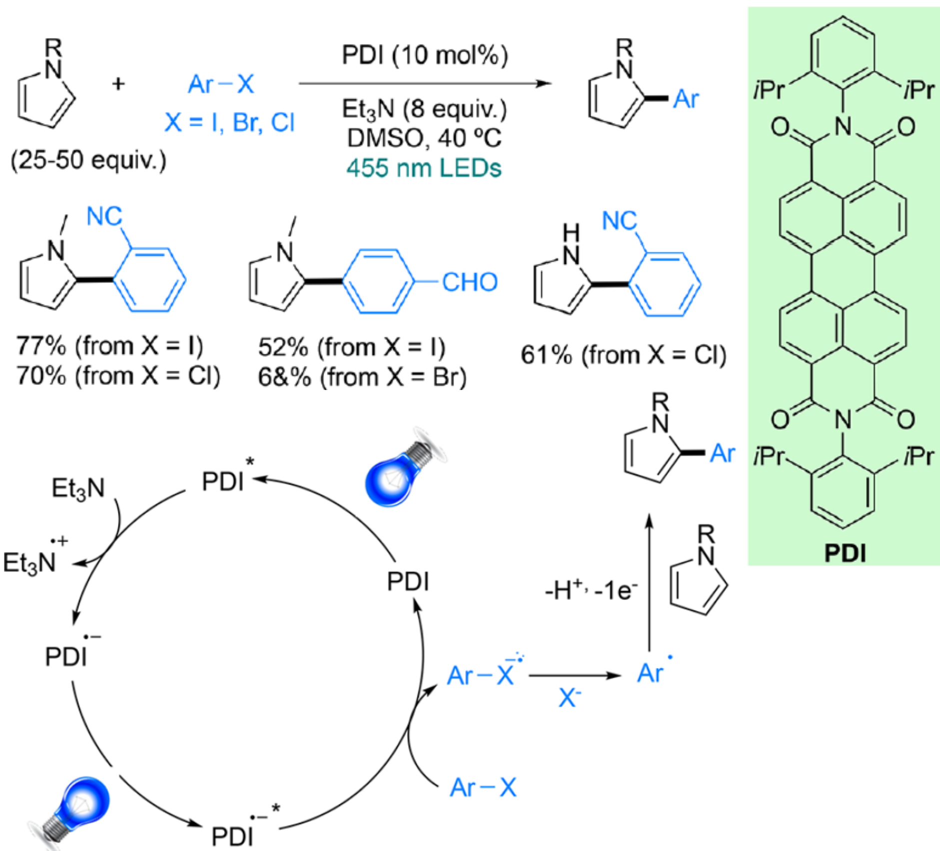
König and co-workers

Org. Lett. **2017**, *19*, 5976– 5979

For arylation of heteroarenes

König and co-workers

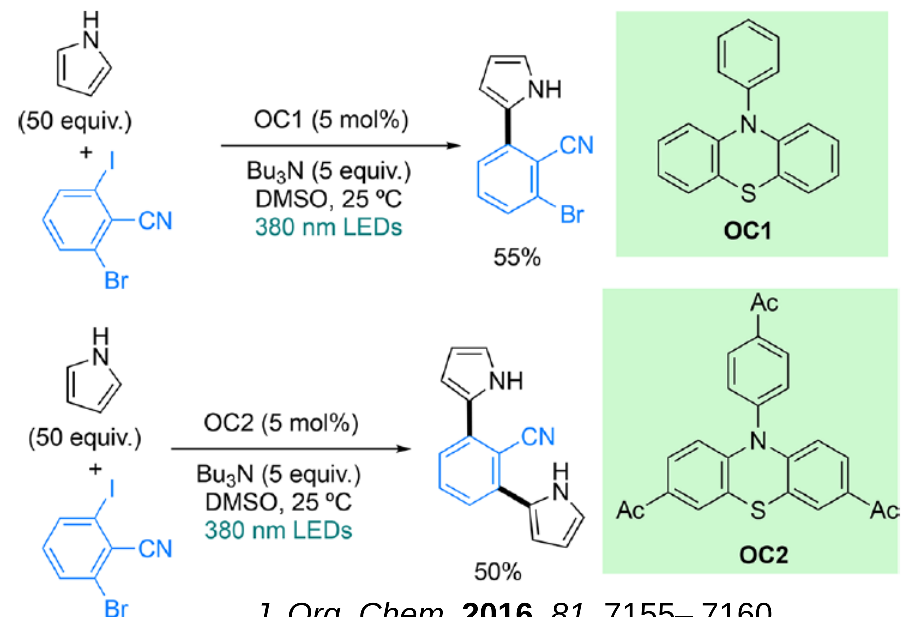
Scheme 21. C−H Bond Arylation of Pyrroles with Aryl Halides Using *N,N*-Bis(2,6-diisopropylphenyl)perylene-3,4,9,10-bis(dicarboximide) (PDI) as Organic Photoredox Catalyst



Science **2014**, *346*, 725– 728

Hawker, Alaniz,

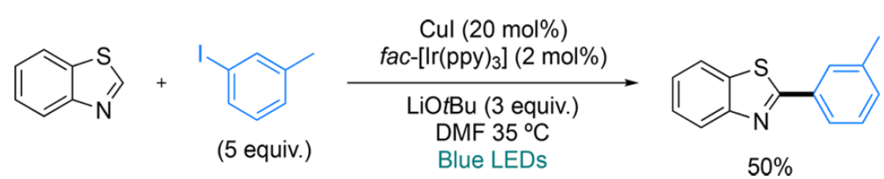
Scheme 25. 10-Phenylphenothiazine as Organic Photoredox Catalyst for C−H Bond Arylation of Pyrroles



J. Org. Chem. **2016**, *81*, 7155– 7160

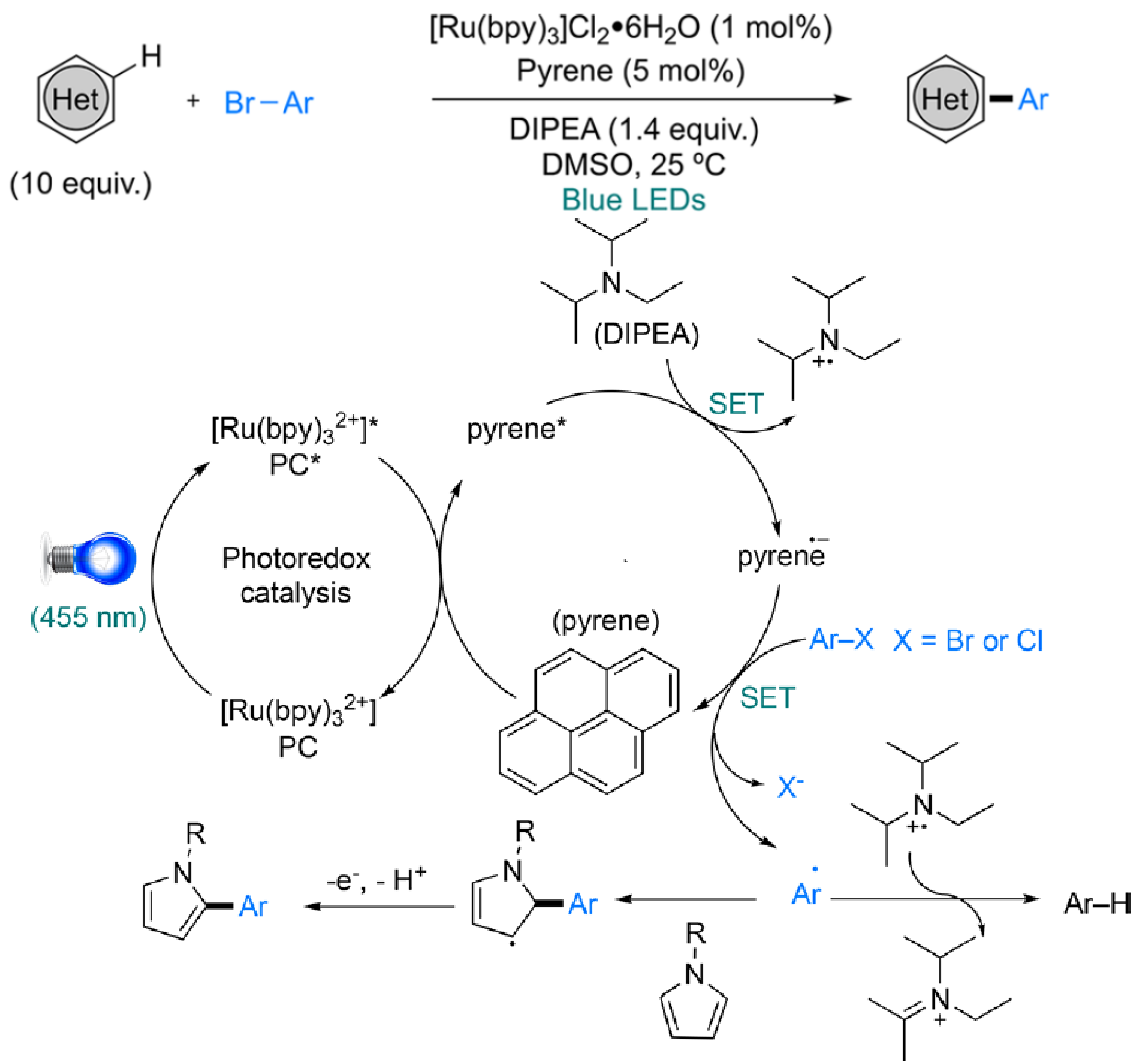
Ackermann

Scheme 27. Arylation of Thiazole with Aryl Iodide Using Ir/Cu Dual Catalytic System



König and co-workers

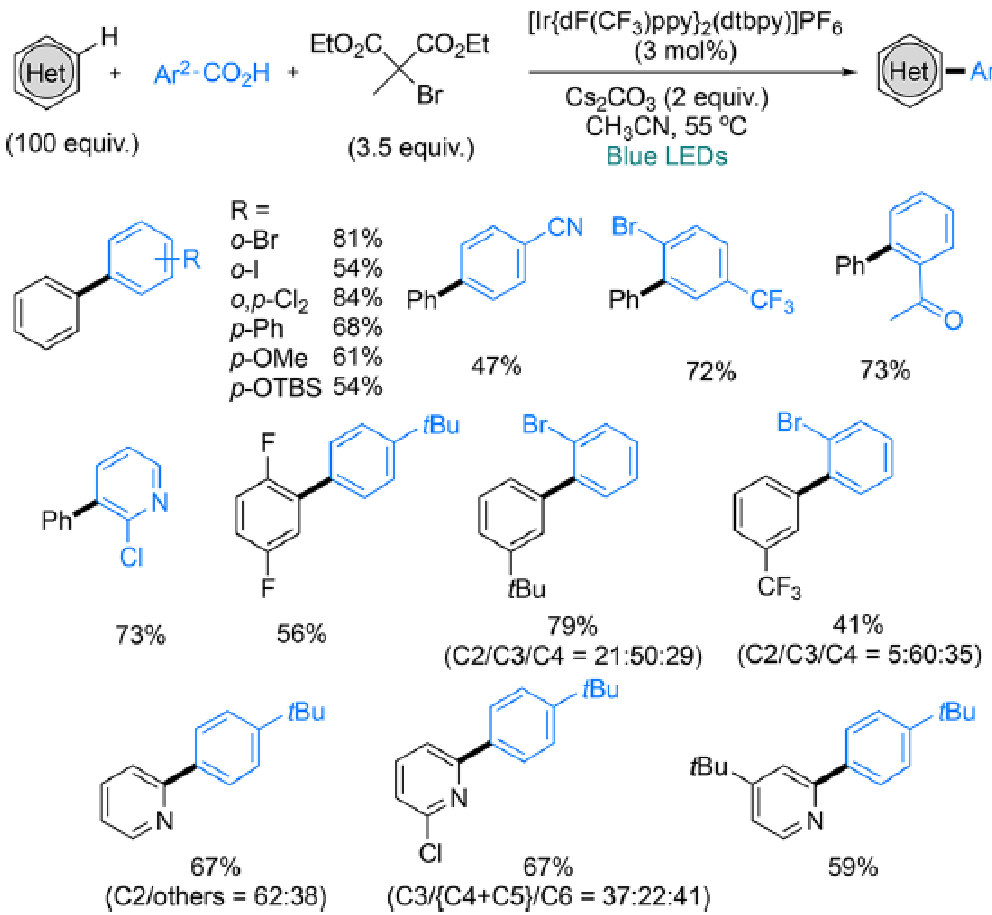
Scheme 28. Arylation of (Hetero)arenes Using Aryl Bromides and Chlorides[a]



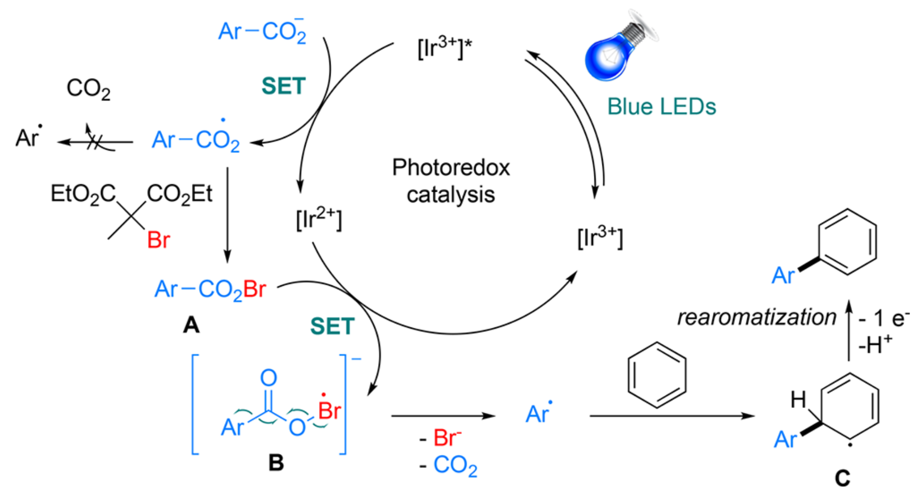
2.1.4 Aryl Carboxylic Acids as Aryl Radical Precursors for Arylation of Heteroarenes and Arenes

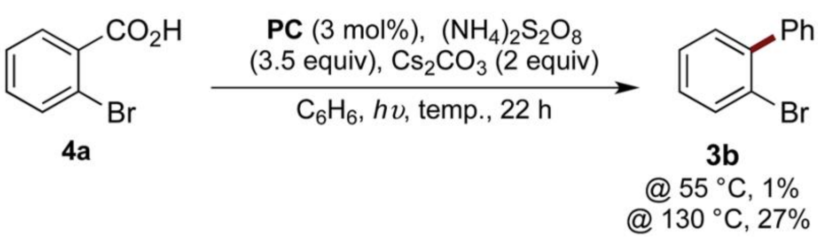
Glorius and co-workers

Scheme 29. Arylation of (Hetero)arenes with Aryl Carboxylic Acids



Mechanism

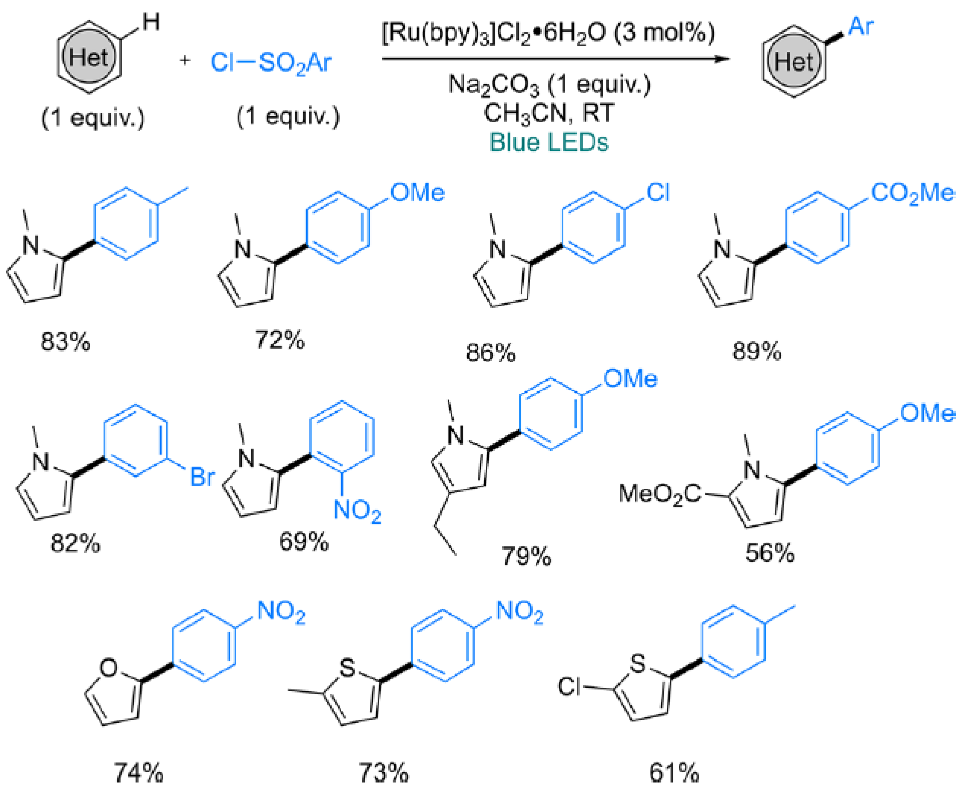


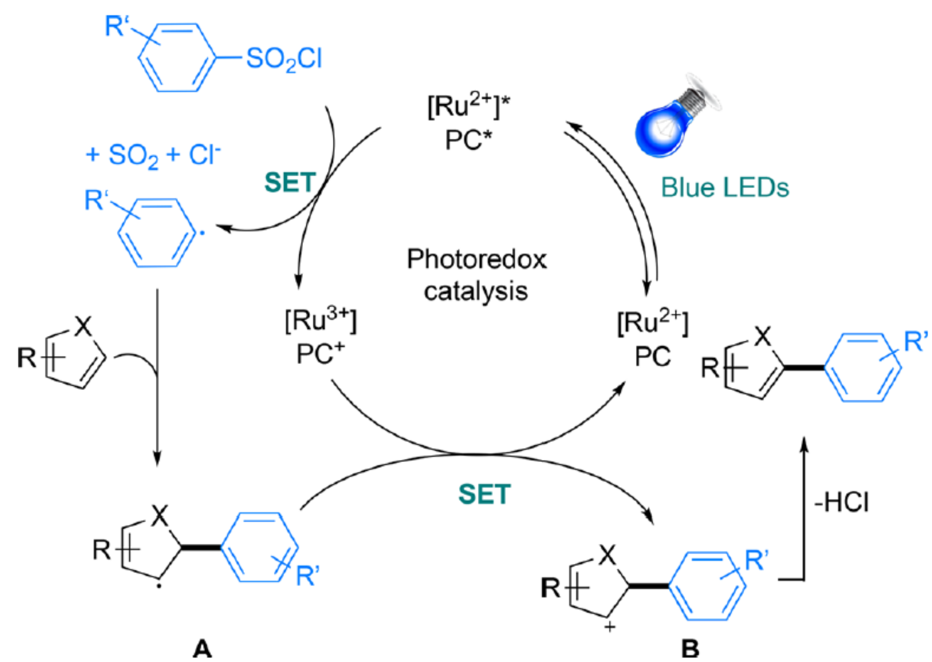


2.1.5 *Benzenesulfonyl Chlorides as Aryl Radical Precursors for Arylation of Heteroarenes*

Natarajan et al.

Scheme 30. Arylation of Heteroarenes with Arenesulfonyl Chlorides



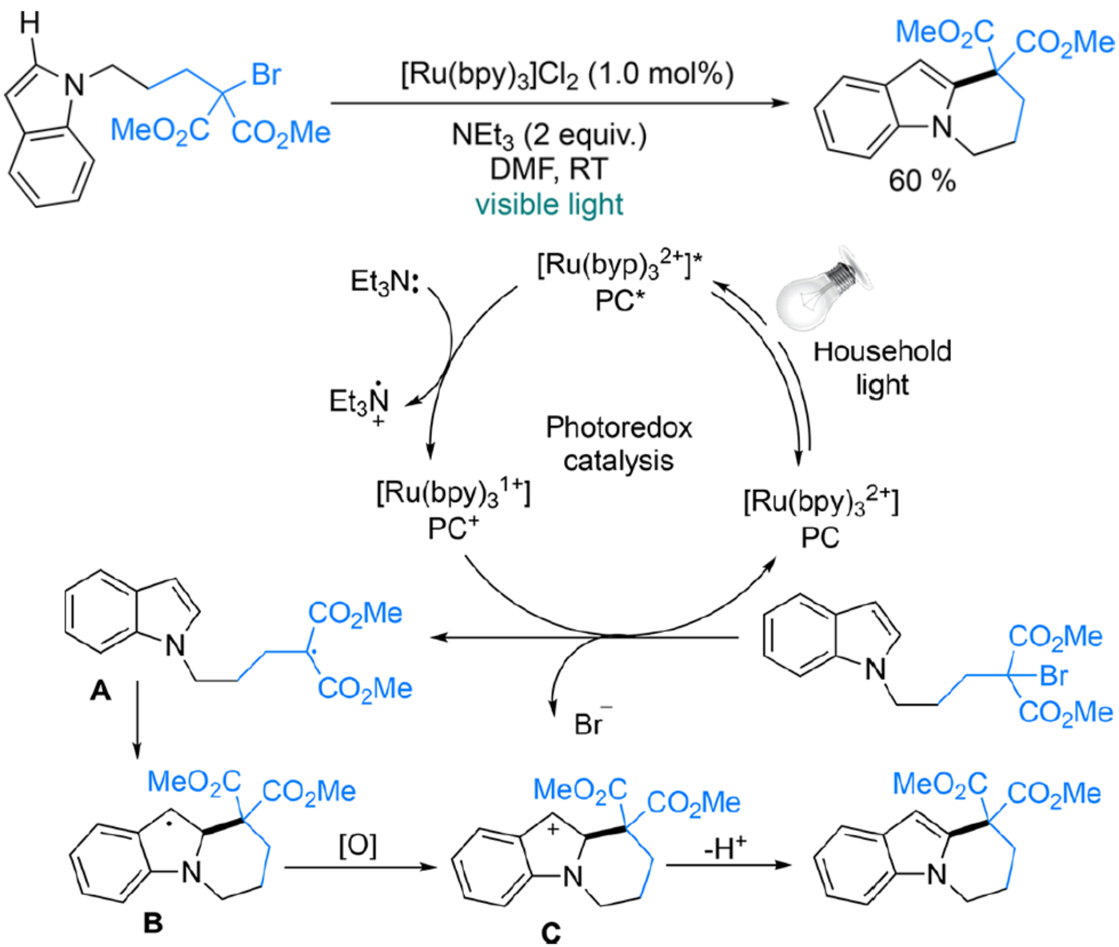


2.2.1 Alkyl bromides as alkyl radical precursors

For intramolecular alkylation of heteroarenes.

Scheme 63. Photoredox-Catalyzed *Intramolecular* Alkylation of Indoles and Pyrroles

Stephenson et al.

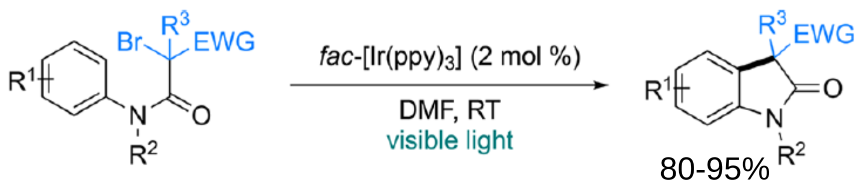


Org. Lett. **2010**, *12*, 368– 371

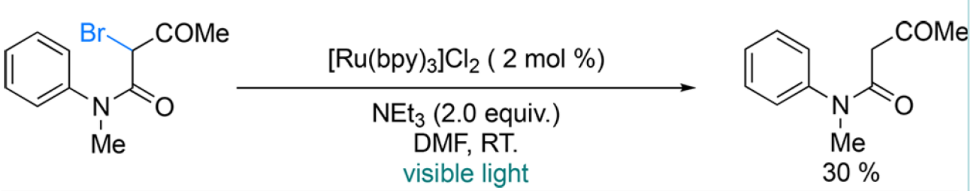
For intramolecular alkylation of arenes.

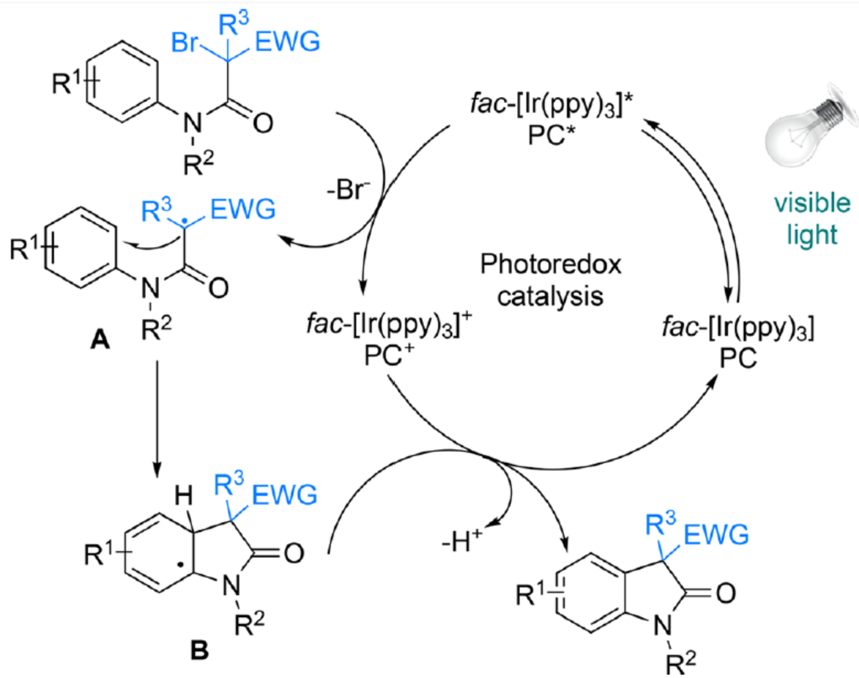
Wei Yu

Scheme 65. Synthesis of 3,3-Disubstituted Oxindoles from 2-Bromoanilides



Scheme 66. Reduction of 2-Bromoanilide by $Ru(bpy)_3^{2+}$/ NEt_3

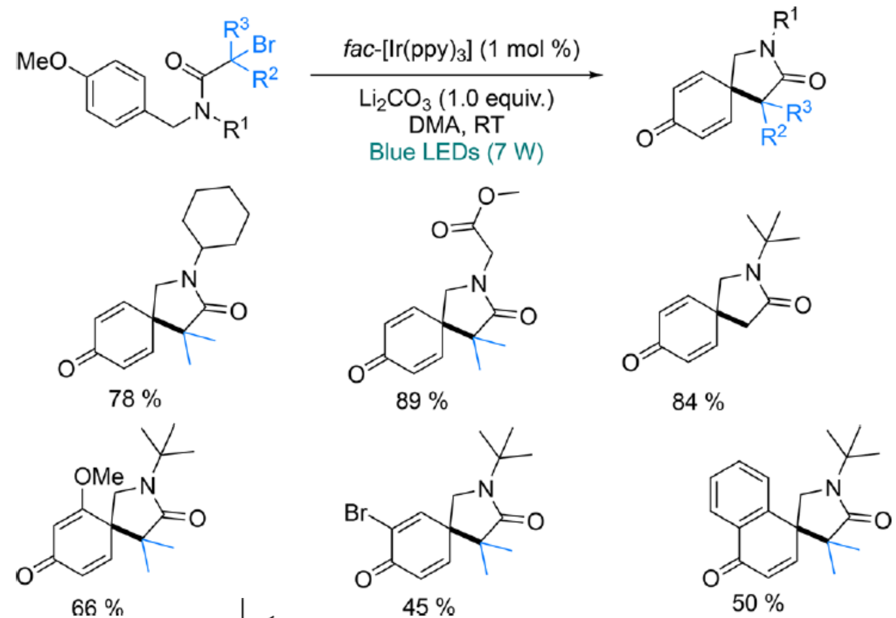


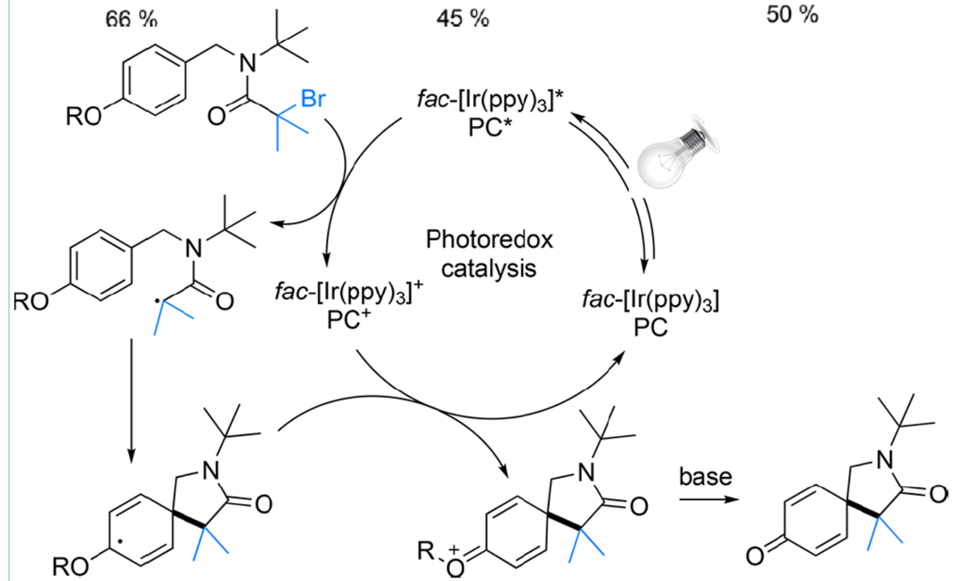


Org. Biomol. Chem. **2012**, *10*, 498– 501

Zhang et al.

Scheme 68. Visible Light Assisted Synthesis of 2-Azaspiro[4.5]decanes



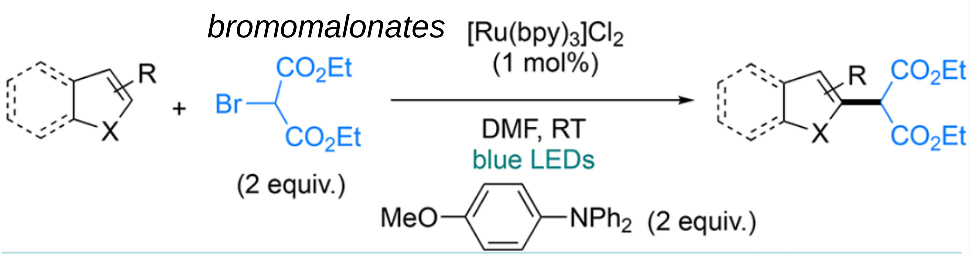


Chem. Commun. **2016**, *52*, 3709– 3712

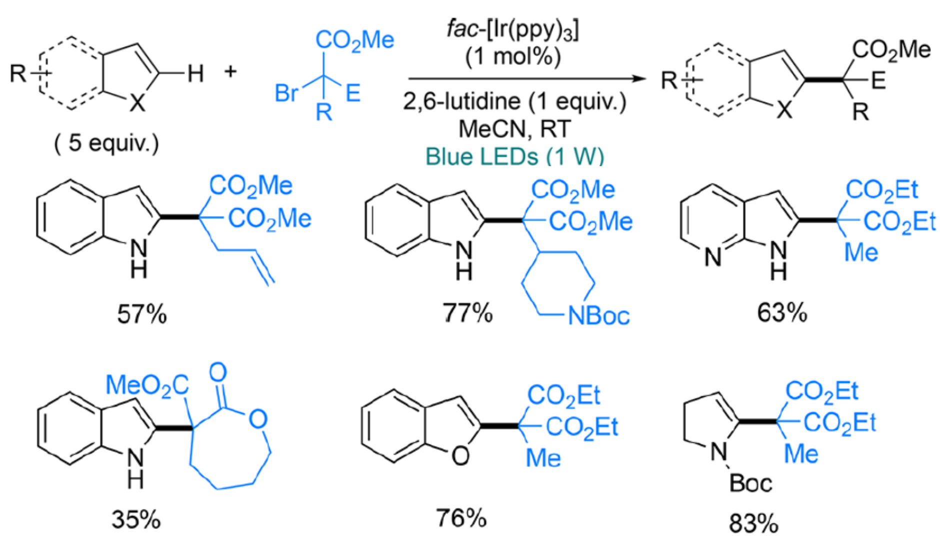
For Intermolecular Alkylation of Heteroarenes

Stephenson

Scheme 69. Photocatalyzed *Intermolecular* Radical C−H Functionalization of Heteroaromatics

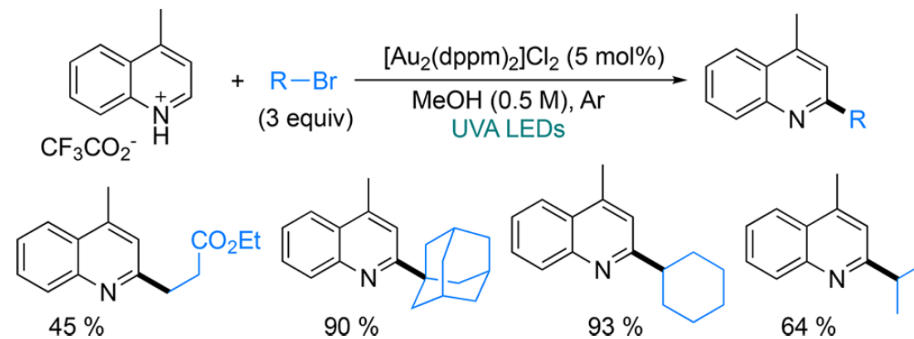


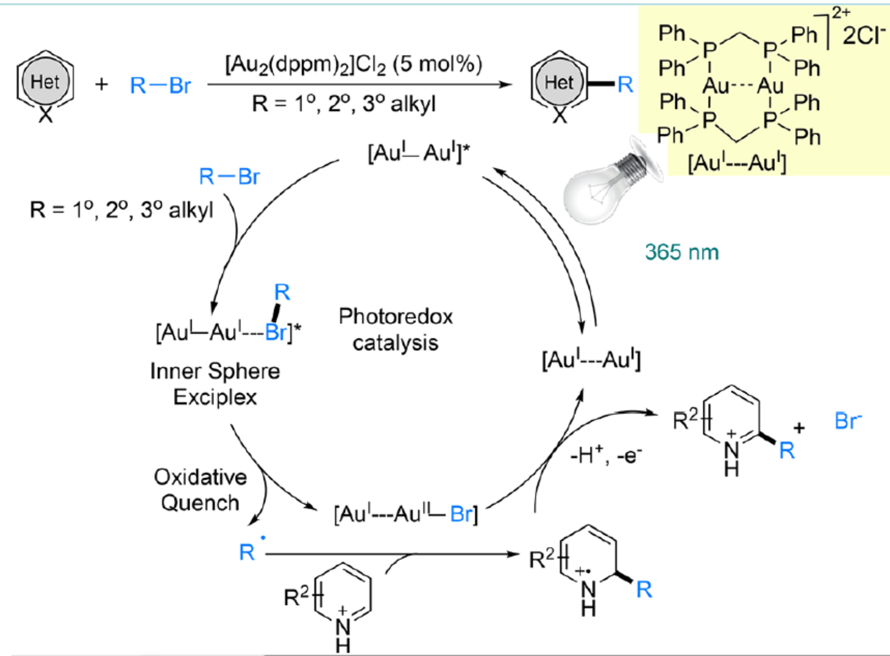
Scheme 72. Coupling of Substituted Bromomalonates with N, O, and S-Heterocycles



Barriault et al.

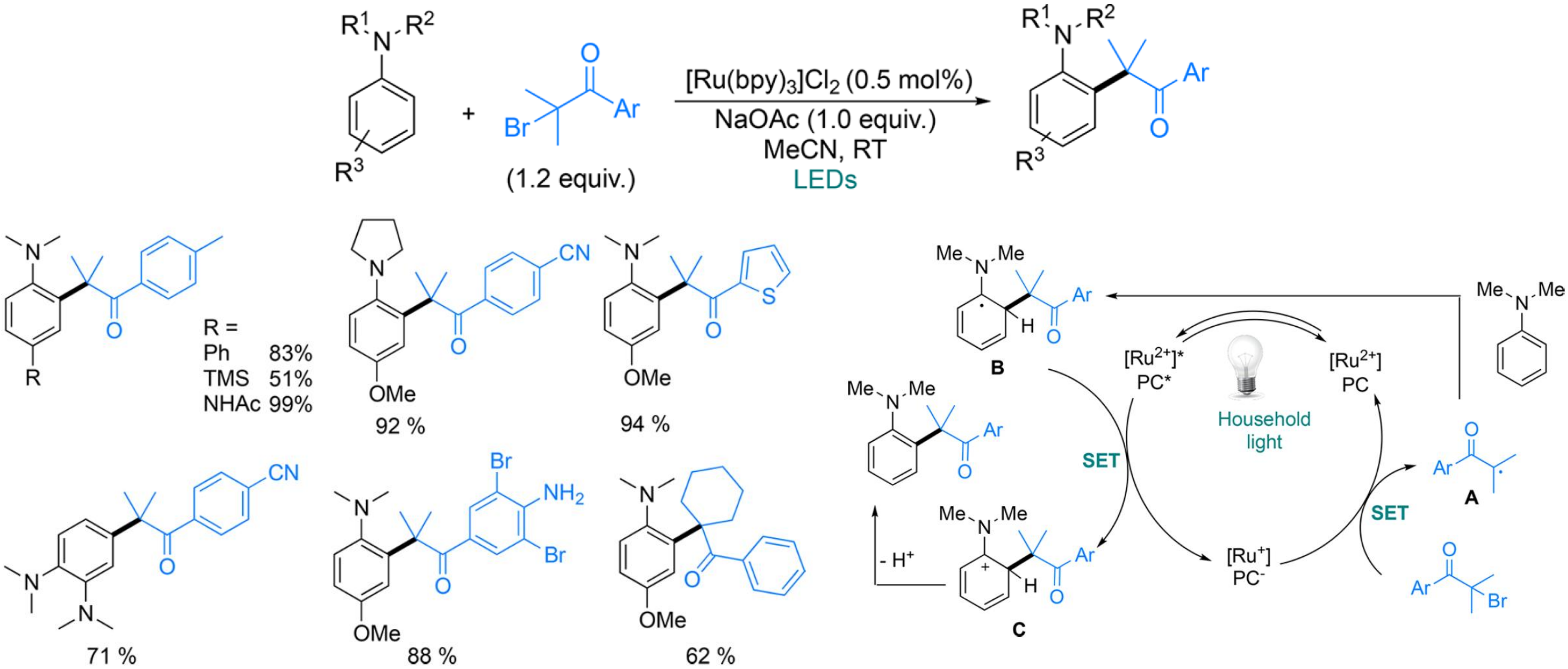
Scheme 74. Examples of Alkylation of Lepidine with Bromoalkanes





Cheng et al.

Scheme 77. Regioselective Alkylation of Aniline with α-Bromoketones

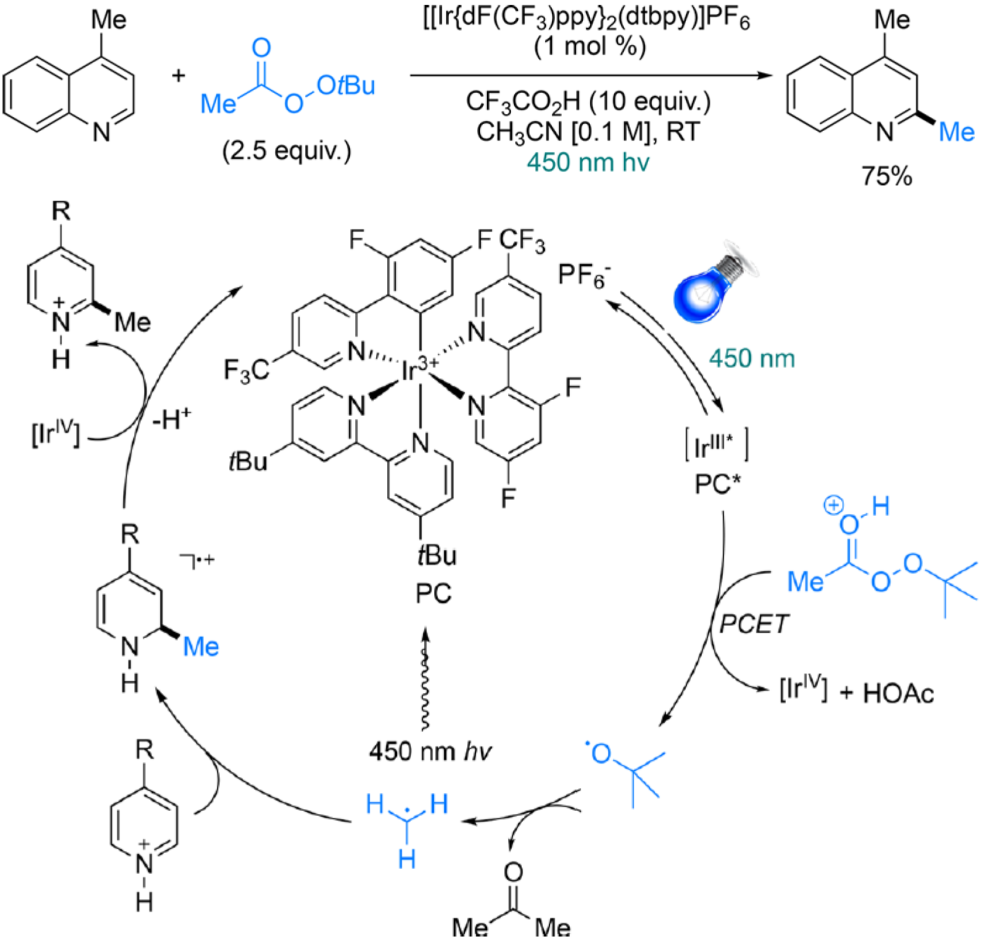


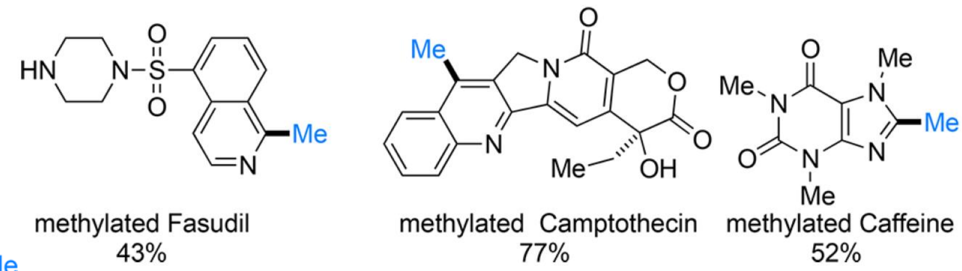
Org. Lett. **2016**, *18*, 4538– 4541

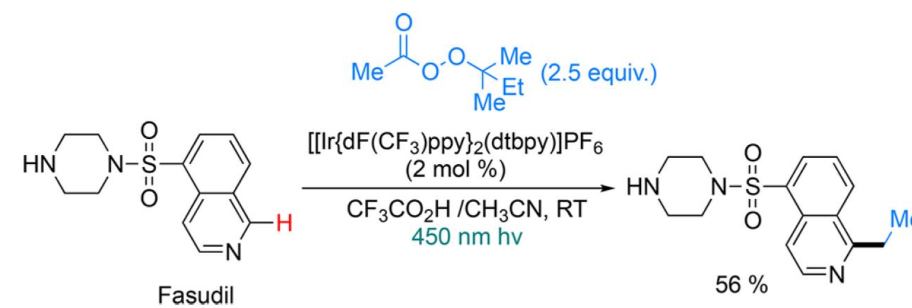
2.2.2 Alkylation of pyridine derivatives using alkylperoxides as alkyl radical precursors

DiRocco et al

Scheme 78. Methylation of *N*-Heterocycle with *tert*-Butylperacetate Using Iridium(III) Photoredox Catalyst

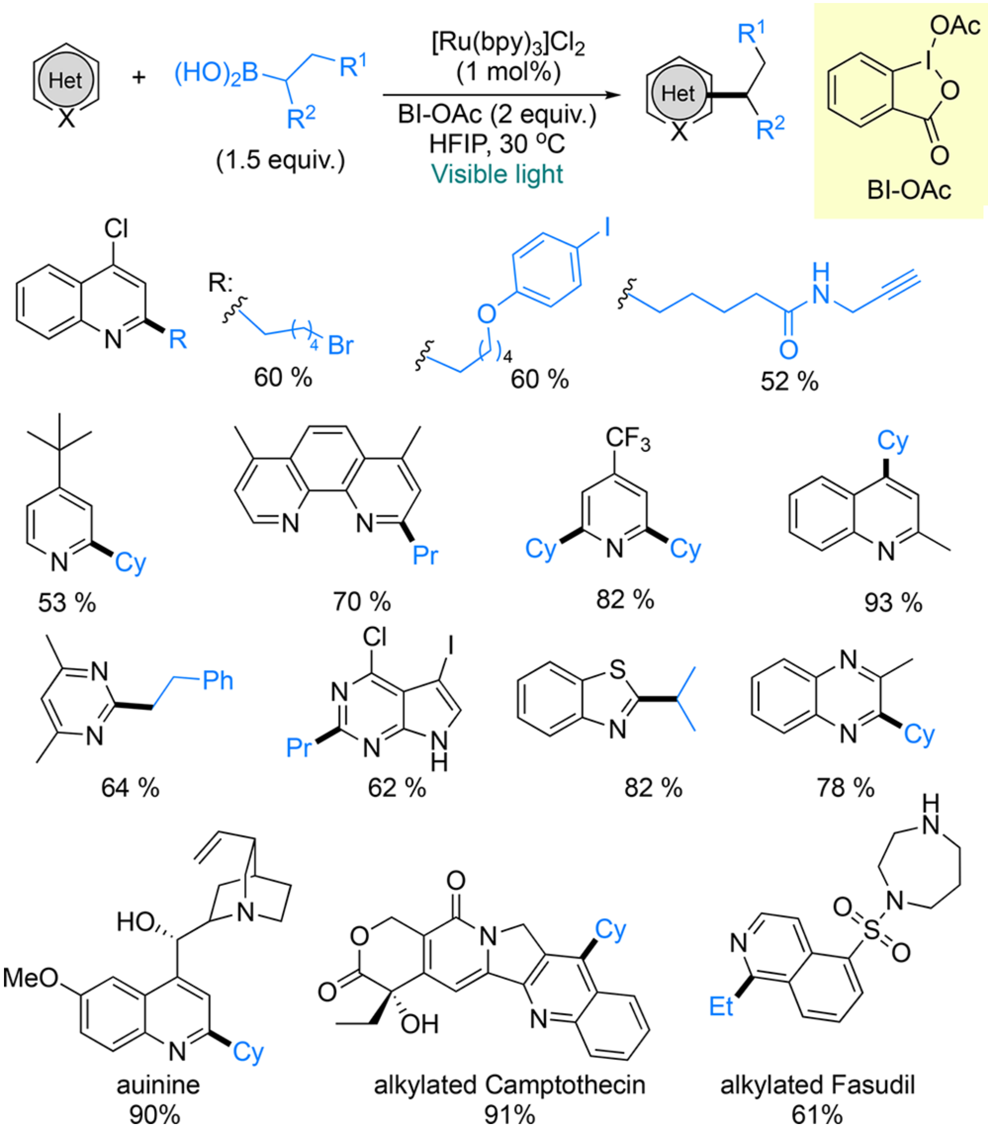




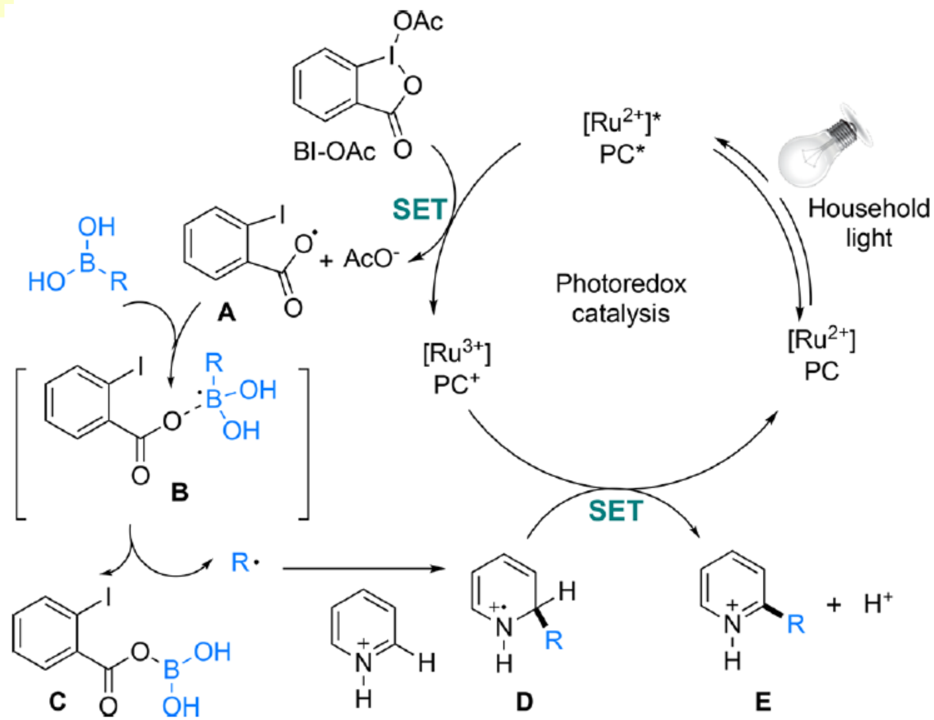


Angew. Chem., Int. Ed. **2014**, *53*, 4802–4806

2.2.3 Alkylation of pyridine derivatives and other heterocycles using alkylboronic acids as alkyl radical precursors



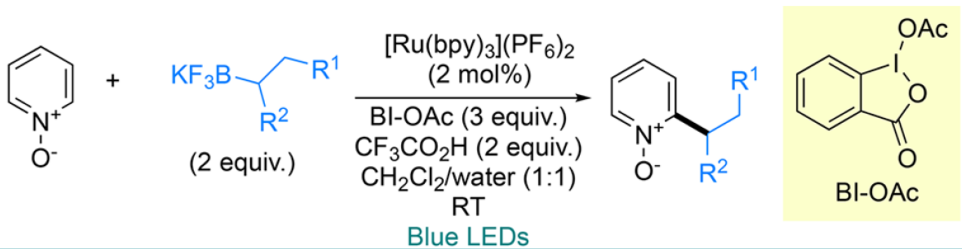
Liu and Chen



Chem. Sci. **2016**, *7*, 6407–6412

Dai, Xu, and co-workers

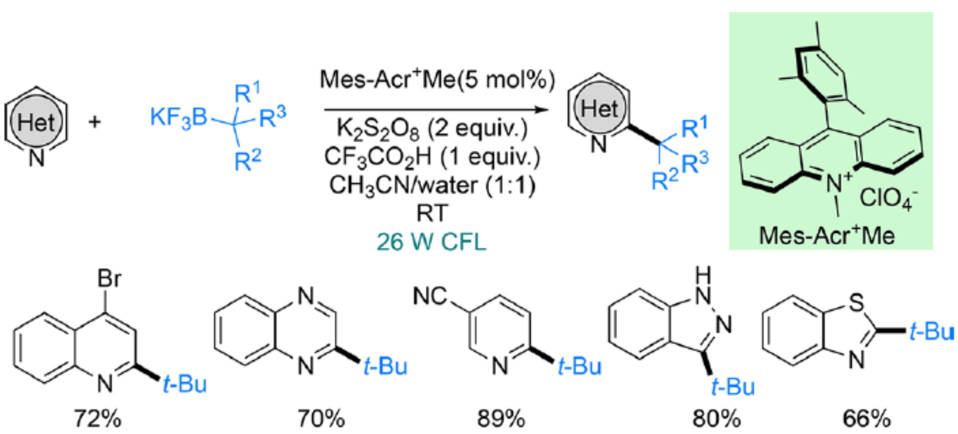
Scheme 82. Alkylation of *N*-Heteroarenes Using Potassium Alkyltrifluoroborates and Ru-Photoredox Catalysts

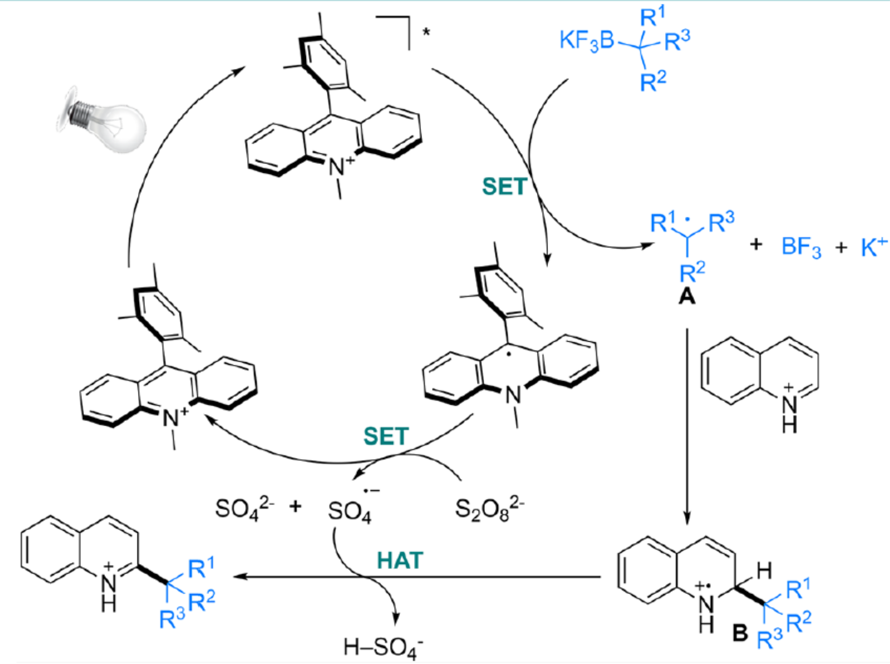


J. Org. Chem. **2017**, *82*, 2059– 2066

Molander and co-workers

Scheme 83. Alkylation of *N*-Heteroarenes Using Potassium Alkyltrifluoroborates and Fukuzumi's Organic Photoredox Catalyst

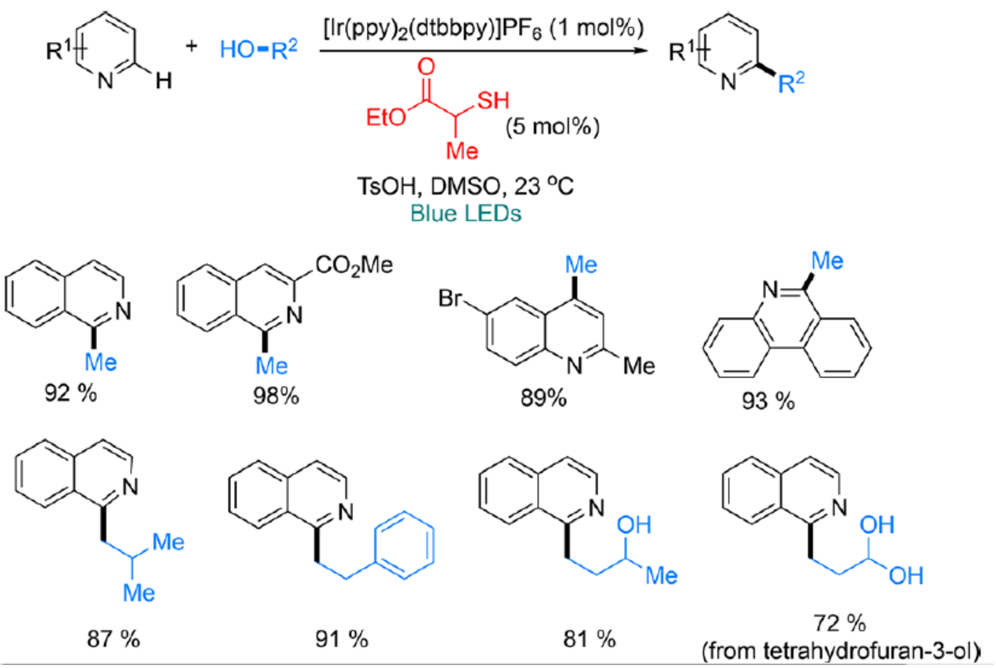




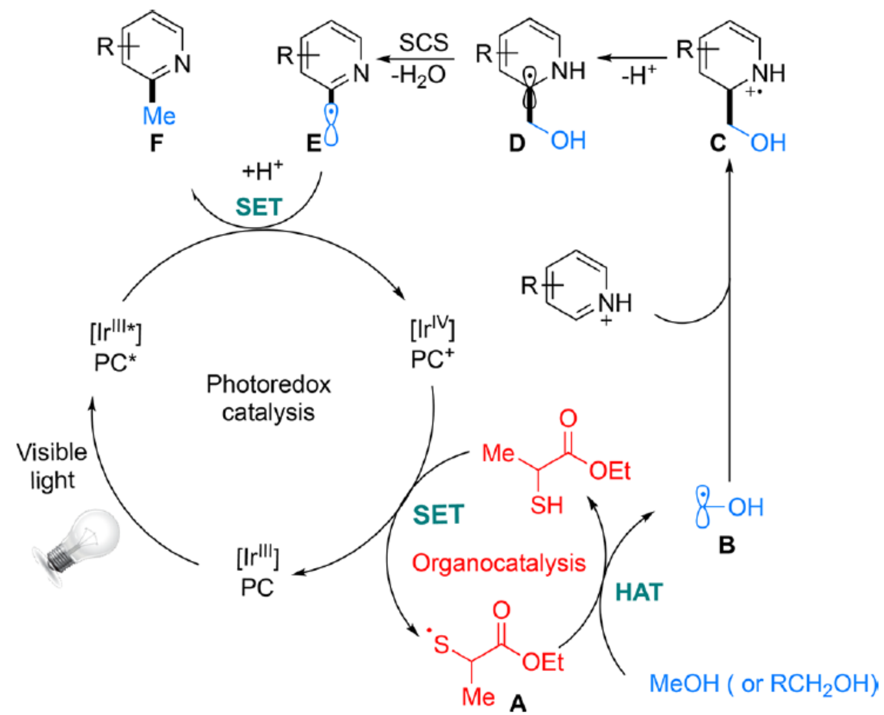
2.2.5. Alkylation of pyridine derivatives using methanol and alcohols as methyl and alkyl radical precursors

MacMillan

Scheme 84. Alkylation of Heteroaromatic C−H Bonds with Alcohols via the Dual Photoredox Organocatalytic Platform



spin-center shift

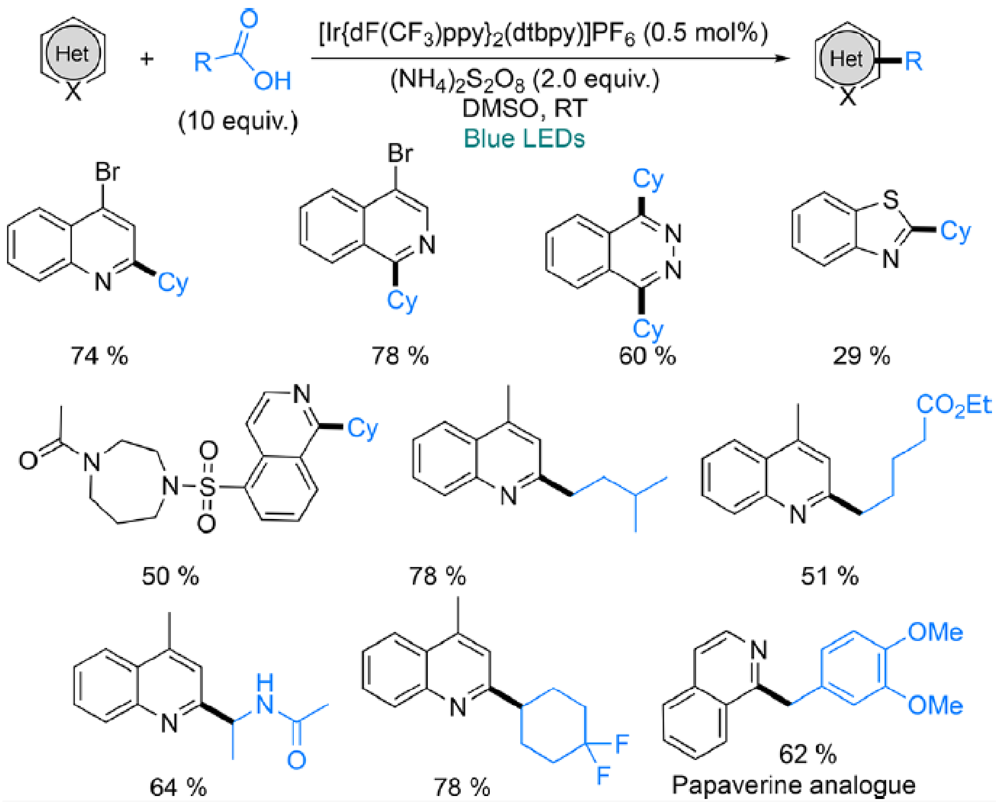


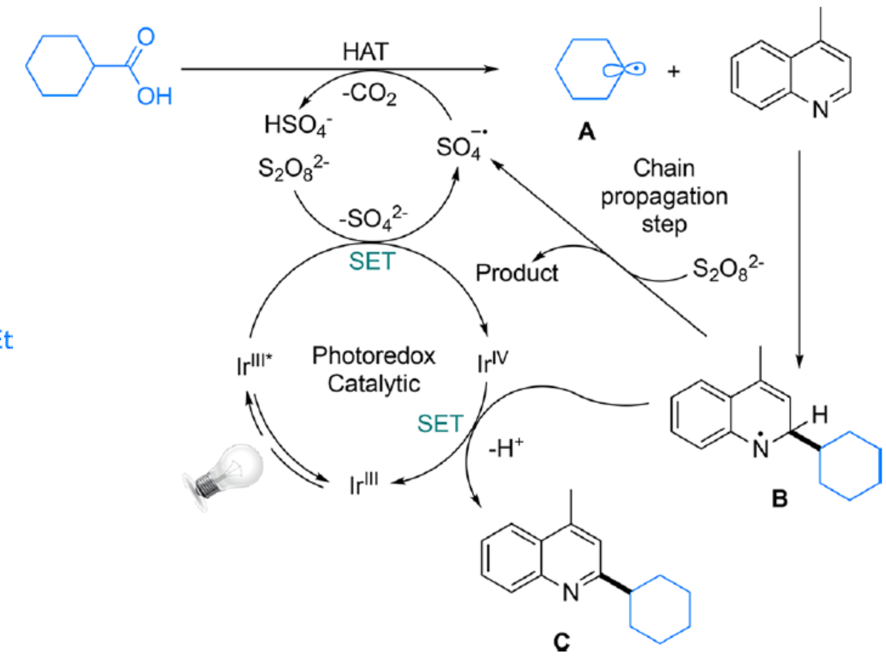
Nature **2015**, *525*, 87– 90

2.2.6. Alkylation of pyridine derivatives using alkylcarboxylic acid derivatives as alkyl radical precursors

Glorius

Scheme 86. Alkylation of *N*-Heteroarenes with Radical Generated from Carboxylic Acids



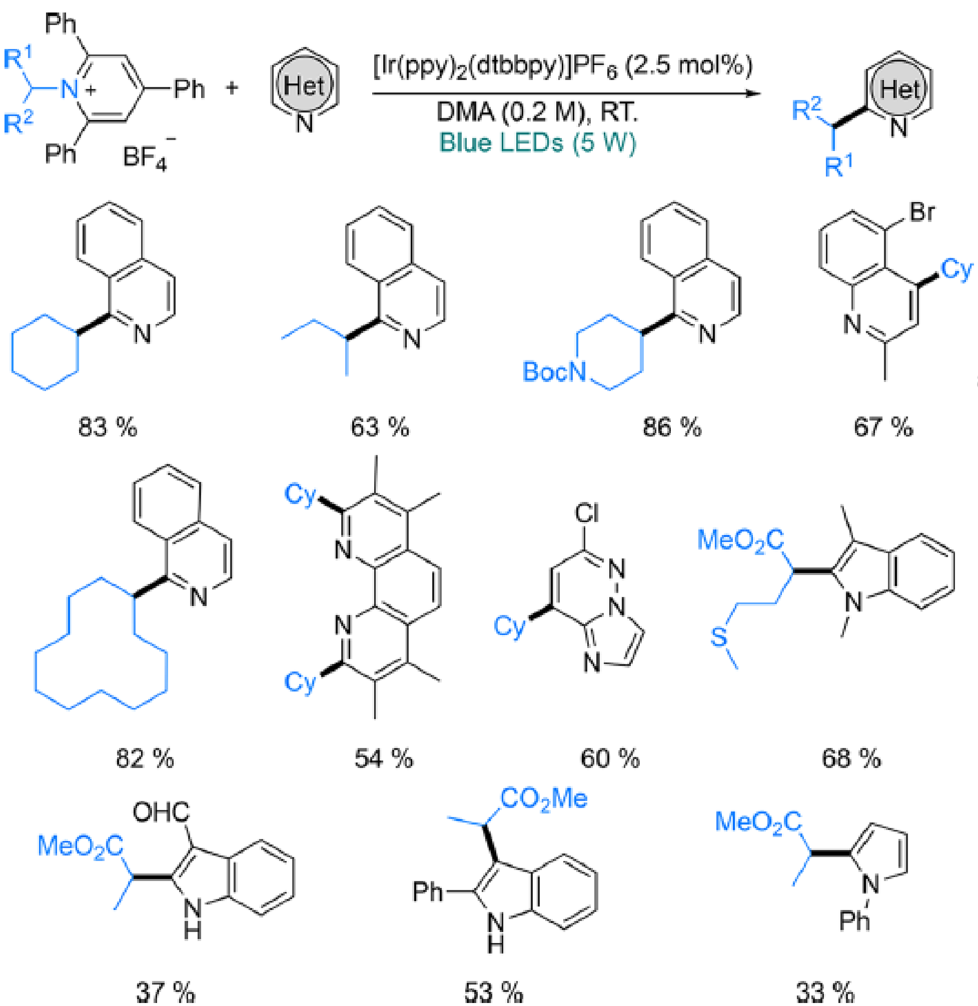


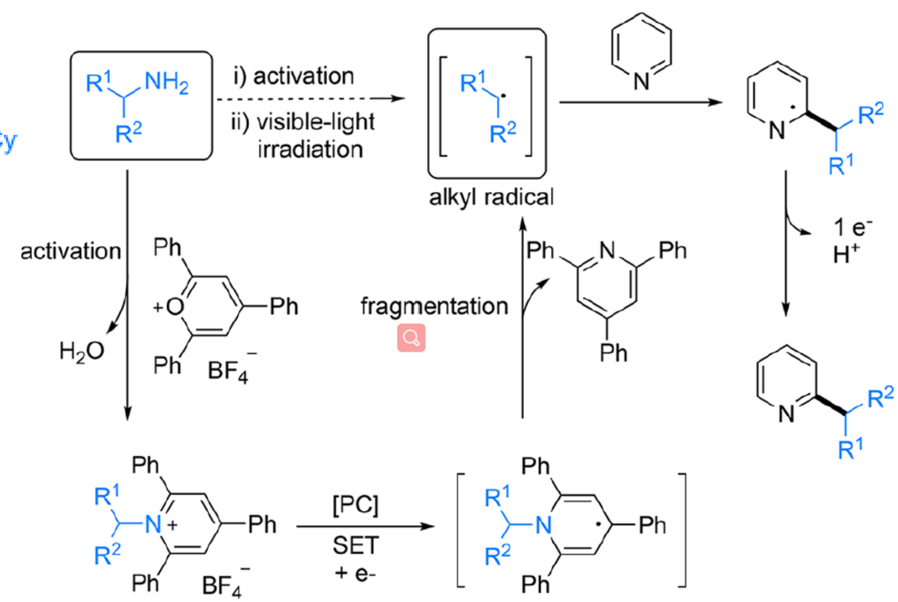
ACS Catal. **2017**, *7*, 4057– 4061

2.2.7. Alkylation of pyridine derivatives and five-Membered heterocycles using primary amines and amino acids as alkyl radical precursors

Glorius

Scheme 88. Examples of Alkylation of N-Heteroarenes with Radical from Primary Amines and Amino Acids via Katritzky Salts

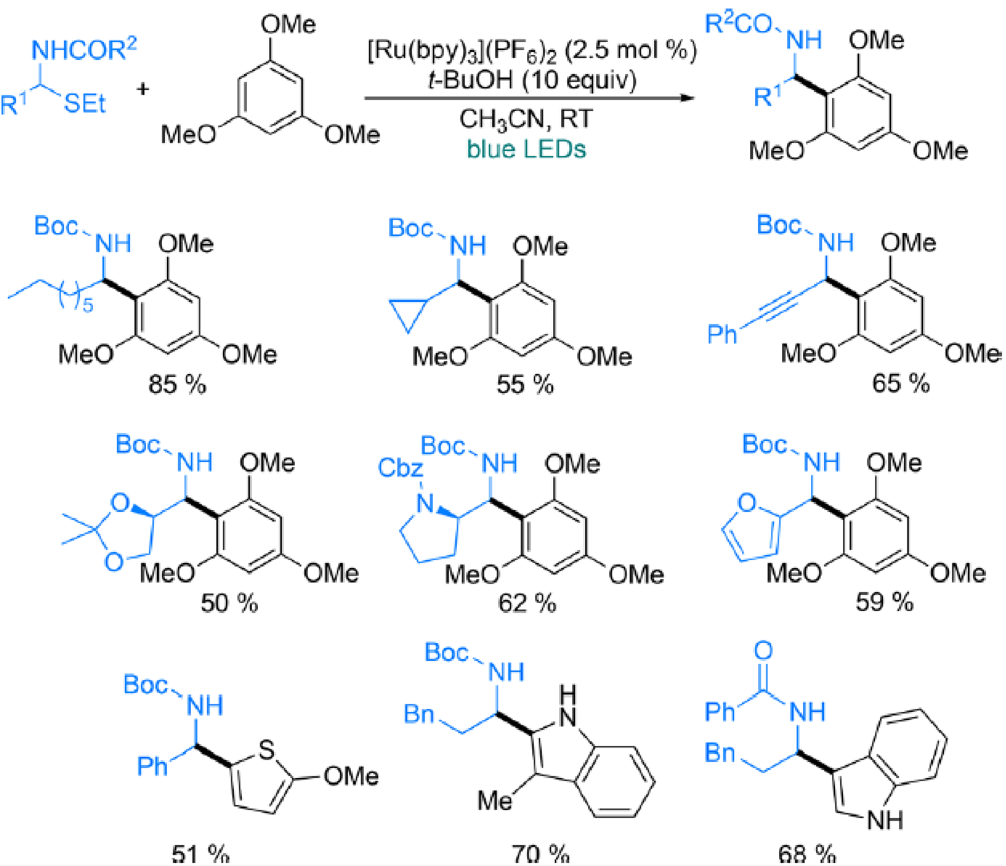


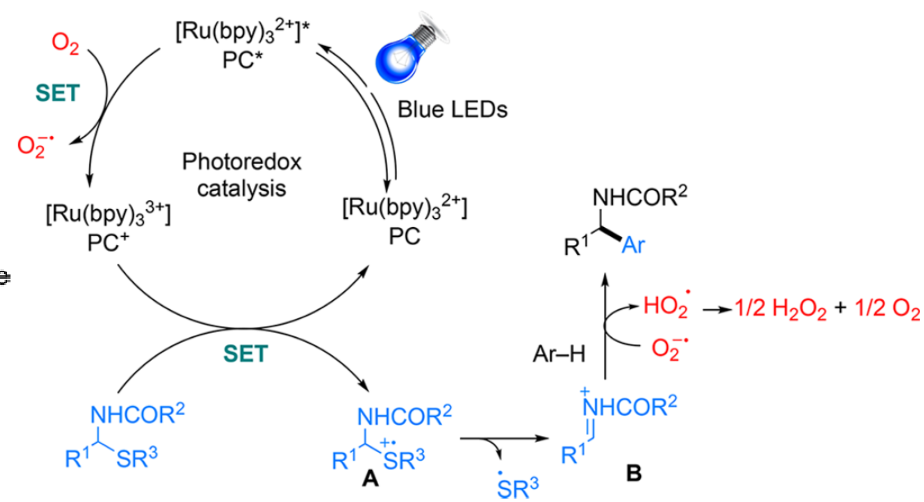


Angew. Chem., Int. Ed. **2017**, *56*, 12336– 12339

Masson et al

Scheme 89. Photoredox-Catalyzed Aza- Friedel–Crafts Reaction of α-Amidosulfide Derivatives with Trimethoxybenzene and Heterocycles



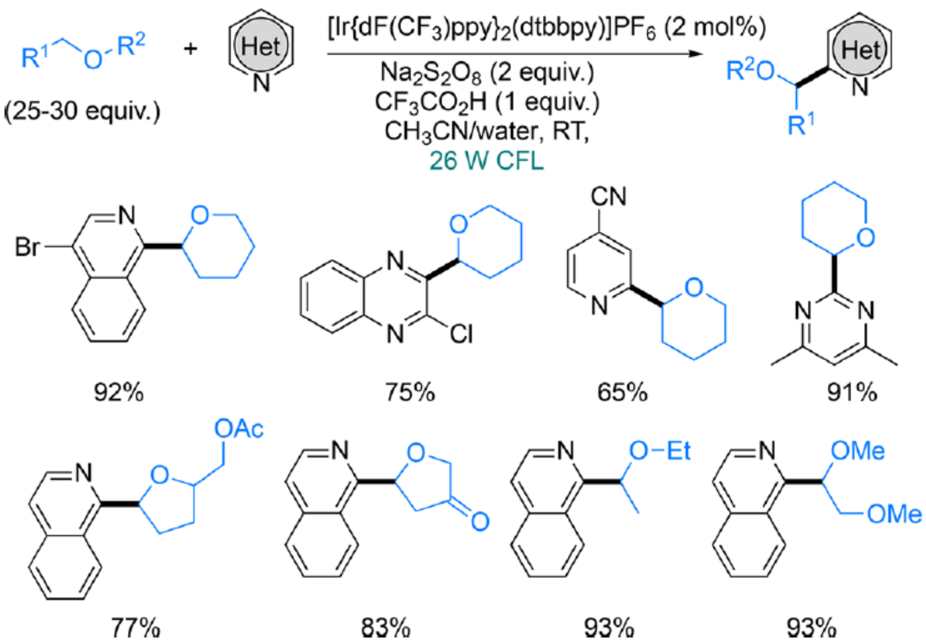


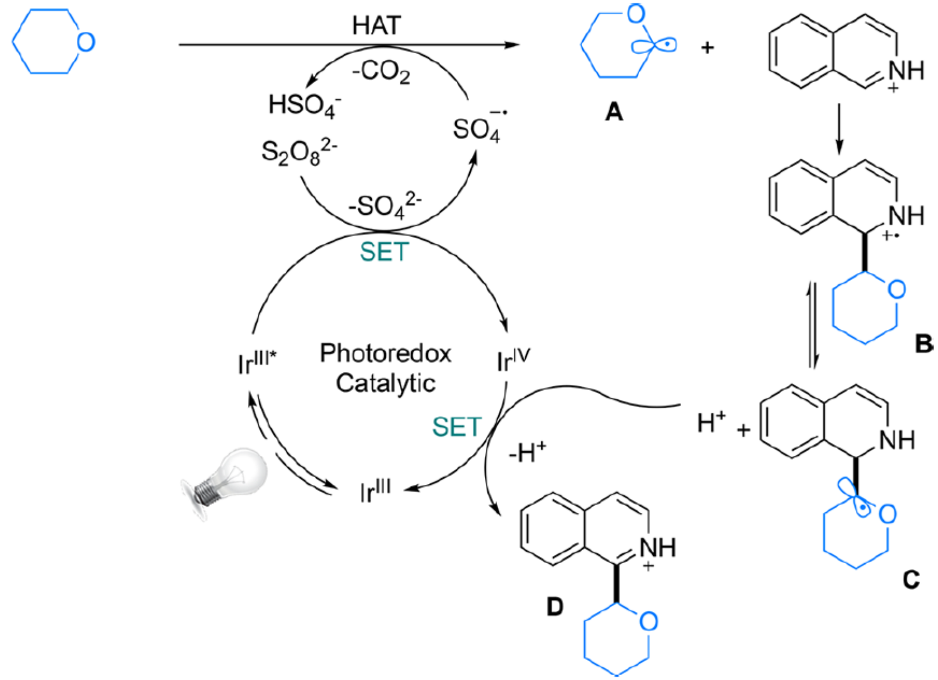
Org. Lett. **2016**, *18*, 1478– 1481

2.2.9. Alkylation of pyridine and pyrimidine derivatives through the generation of α-oxyalkyl radicals from photoredox catalysis of dialkyl ethers

MacMillan

Scheme 90. Photoredox-Catalyzed C−H Bond Arylation of Pyridines Derivatives from Ethers





Angew. Chem., Int. Ed. **2015**, *54*, 1565– 1569

北京大學
PEKING UNIVERSITY

Contents

1 Introduction

2 This review

3 Summary and Outlook

4 Acknowledgement

3. Summary and Outlook

1. Aryl radicals have been shown to be generated from aryl diazonium salts, diaryliodonium salts , and aryl halides, aryl carboxylic Acids, benzenesulfonyl chlorides.

2. Alkyl radicals have been shown to be generated from alkyl bromides, organic peroxides, alkylboronic acids, and hypervalent iodine, methanol and alcohols, carboxylic acids, and primary amines.

3. Cyclizations and multicomponent reactions provide alternative avenues to exploit the robustness of photochemical transformations.

4. Photoredox C−H bond functionalizations of arenes often lead to a mixture of regioisomers and the reactions are limited to only electron-rich arenes, as electron-poor arenes have never been successfully employed yet.

北京大學 PEKING UNIVERSITY

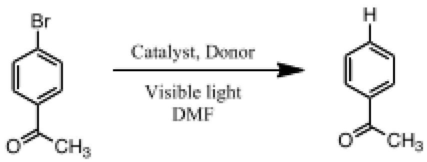
4. Acknowledgement

Thank *Prof.* Yong Huang;

Thank *Dr.* Chen;

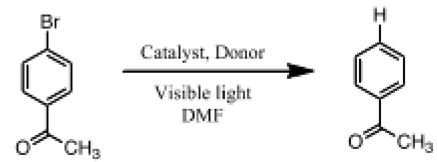
Thank all of you being here.

Table S1. Control experiments and optimization of photoreduction reaction condition



Entry	Catalyst/ mol %	Donor (equiv)	Reaction condition*	Time/ h	Yield/ %†
Control experiments					
1	5	Et_3N (8)	DMF, 40 °C, 455 nm, N_2	4	82
2	5	Et_3N (8)	DMF, 40 °C, Dark, N_2	4	0‡
3	–	–	DMF, 40 °C, 455 nm, N_2	4	0‡
4	5	–	DMF, 40 °C, 455 nm, N_2	4	ca. 14
5	–	Et_3N (8)	DMF, 40 °C, 455 nm, N_2	4	0‡
6	5	Et_3N (8)	DMF, 40 °C, 455 nm, Air	4	ca. 5
7§	5	Et_3N (8)	DMF, 40 °C, 455 nm, N_2	2	54
8 ǁ	5	Et_3N (8)	DMF, 40 °C, 455 nm, N_2	4	70
9¶	5	Et_3N (8)	DMF, 40 °C, Dark, N_2	4	0‡
10	5	$(Et_4N)_2S_2O_4$	DMF, 40 °C, Dark, N_2	4	0‡
11¶	15	Et_3N (12)	DMF, 40 °C, Dark, N_2	4	0‡

Table S1 (cont.). Control experiments and optimization of photoreduction reaction condition



Entry	Catalyst/ mol %	Donor (equiv)	Reaction condition*	Time/ h	Yield/ %†
Optimization of reaction condition					
12	5	Et_3N (2)	DMF, 40 °C, 455 nm, N_2	4	33
13	5	Et_3N (4)	DMF, 40 °C, 455 nm, N_2	4	43
14#	5	Et_3N (8)	DMF, 40 °C, 455 nm, N_2	4	38
15#	5	Et_3N (8)	DMF, 40 °C, 455 nm, N_2	8	78
16	5	Et_3N (8)	DMSO, 40 °C, 455 nm, N_2	4	47
17	5	Et_3N (8)	DMSO, 40 °C, 455 nm, N_2	8	69

*The reaction was performed with 4′-bromoacetophenone; †From GC analysis with respect to an internal standard; ‡The yield, if any, is too low to quantify accurately; §The reaction was stopped after 2h and kept under dark; ||The radical anion of **PDI** was generated upon irradiation (λ_{Ex} = 455 nm) in the presence of Et_3N and then 4′-bromoacetophenone was added and irradiated continuously; ¶The radical anion of **PDI** was generated upon irradiation (λ_{Ex} = 455 nm) in the presence of Et_3N and then 4′-bromoacetophenone was added and kept under dark; #Reaction was performed with a commercially available catalyst: *N,N′*-bis(3-pentyl)perylene-3,4,9,10-bis(dicarboximide) (see **Fig. S2** for the chemical structure).

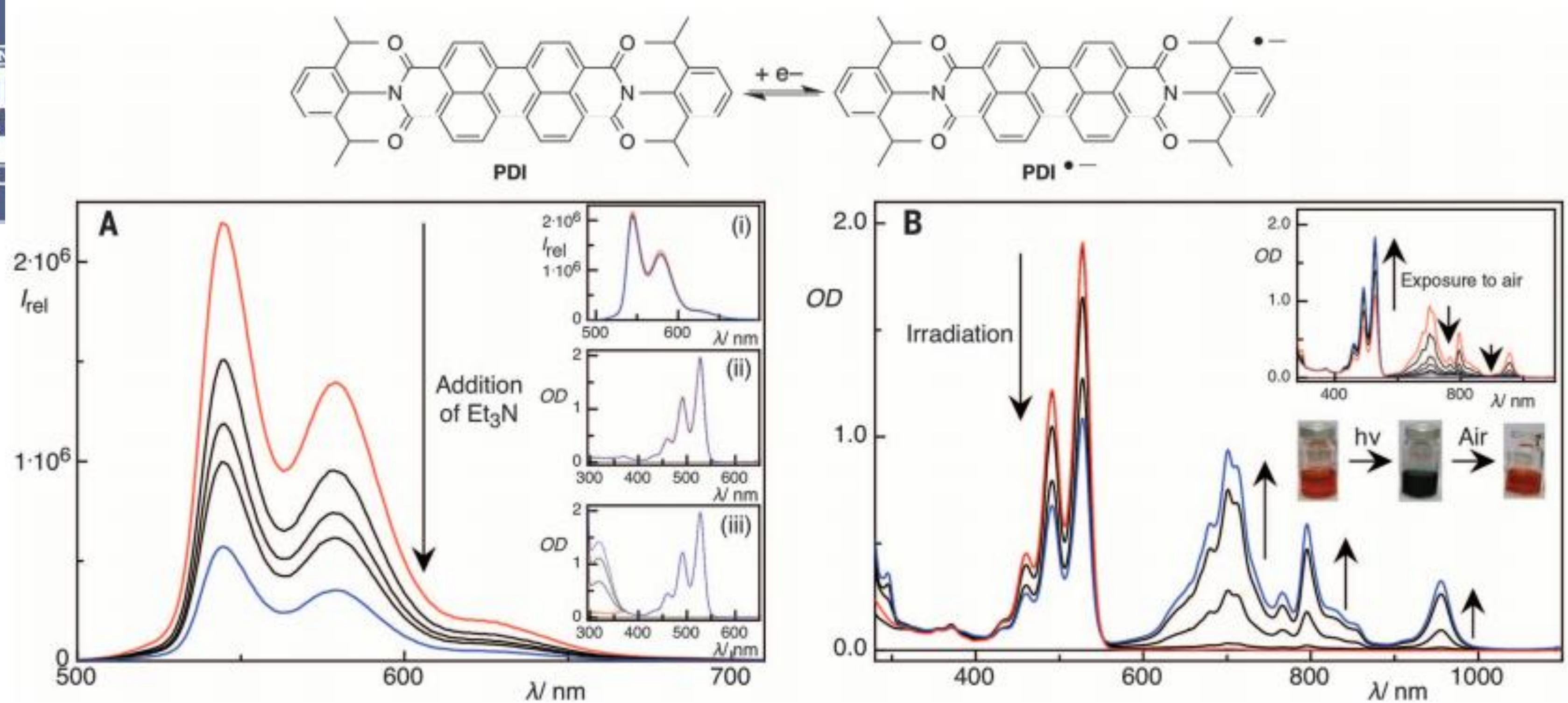
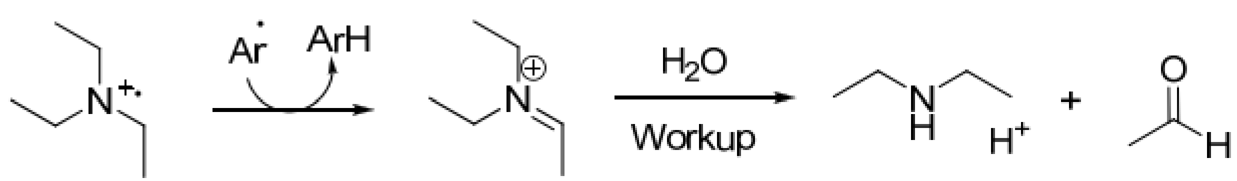
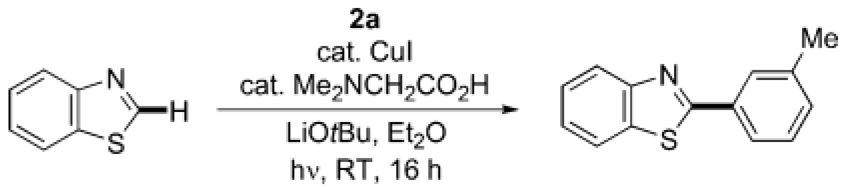


Fig. 1. Chemical structure of the photocatalyst PDI, one electron reduction of PDI to its radical anion, and effects of Et_3N and 4′-bromoacetophenone on its photophysical properties. (**A**) Changes in the fluorescence spectra (in this case, intensity; λ_{Ex} = 455 nm) of PDI upon successive addition of Et_3N in DMF. In the insets, changes in the fluorescence spectra of PDI upon addition of (i) 4′-bromoacetophenone, and changes in the absorption spectra of PDI upon addition of (ii) Et_3N, and (iii) 4′-bromoacetophenone are shown. (**B**) Formation of the PDI radical anion ($PDI^{•-}$) upon photoexcitation (λ_{Ex} = 455 nm) of PDI in the presence of Et_3N. In the inset, regeneration of neutral PDI from $PDI^{•-}$ upon exposure to air is shown (see also fig. S5).



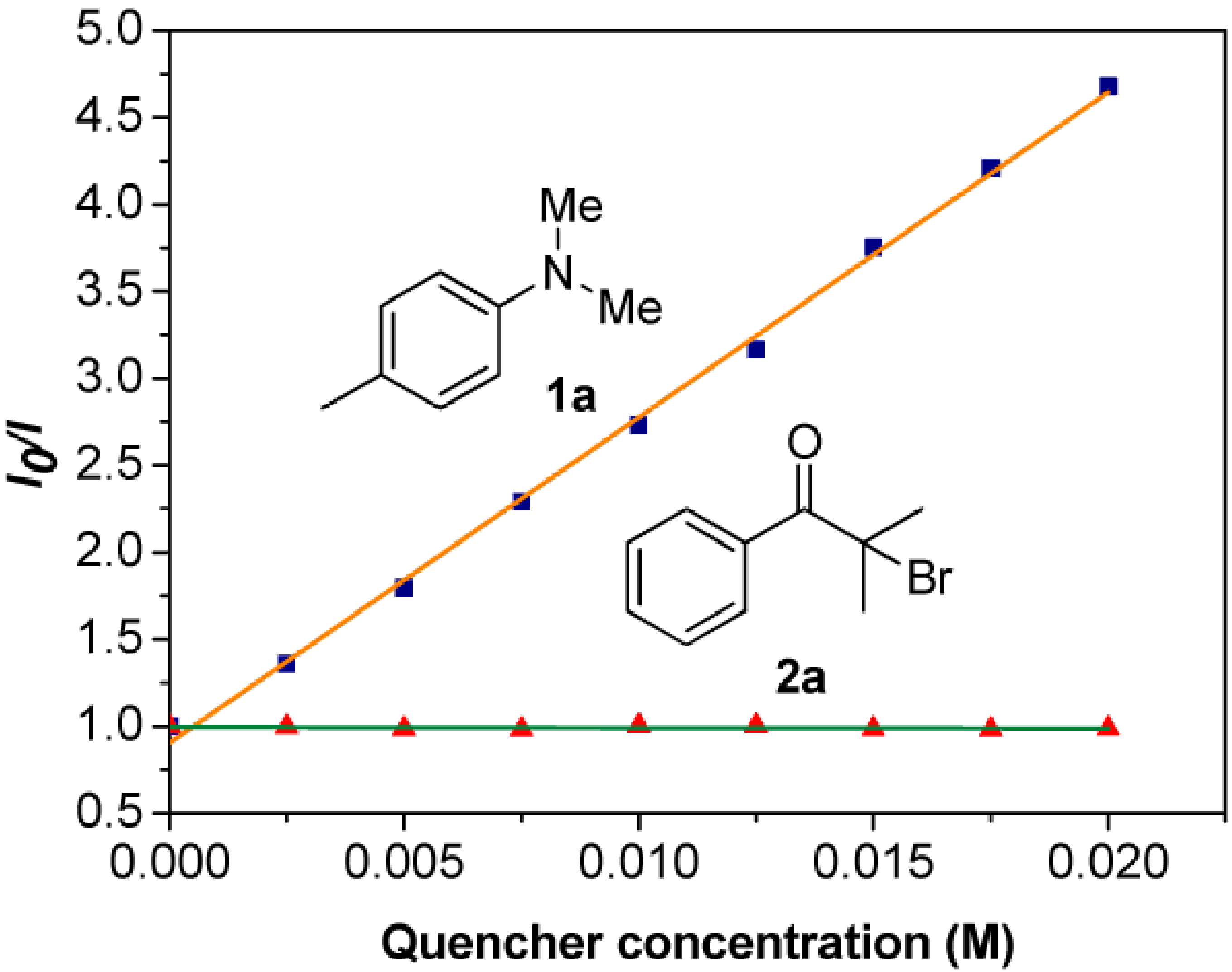
The presence of diethylamine in the reaction mixture, resulting from the proposed hydrogen abstraction of aryl radicals from the triethylamine radical cation, was confirmed by GC–MS analysis



1a **3aa**

standard conditions:	73%
galvinoxyl (1 equiv):	44%
galvinoxyl (3 equiv):	0%

Scheme 6. Probing an SET-type mechanism.



5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
I_0/I
Me
N
Me
1a
O
Br
2a
0.000
0.005
0.010
0.015
0.020
Quencher concentration (M)