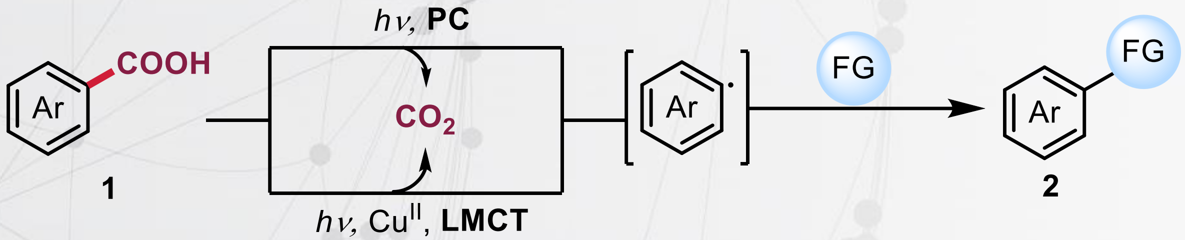
Photoinduced Radical Decarboxylative Functionalization of Aryl Carboxylic Acids



Reporter： Yibo Yu

Supervisor： Prof. Shengming Ma

2022.05.27

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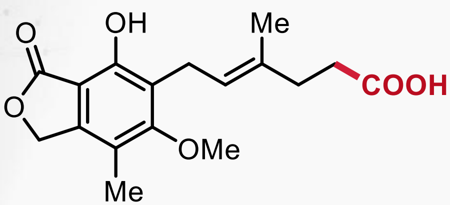
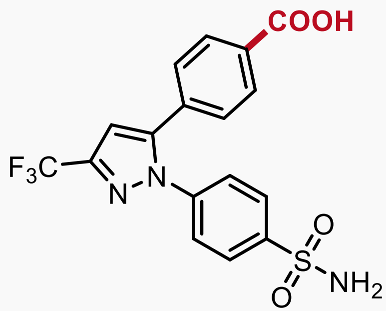
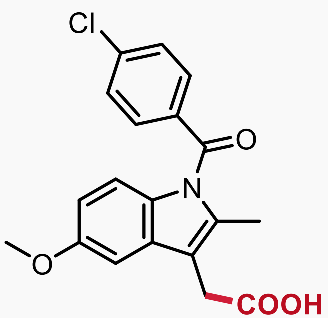
Background



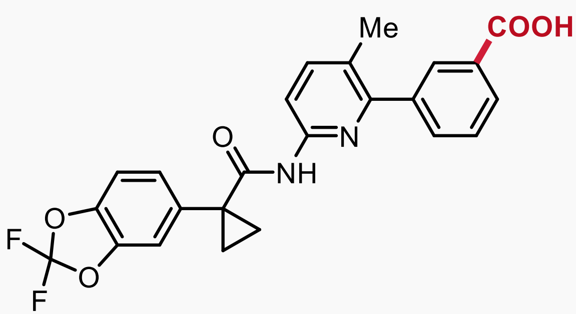
Mycophenolic acid



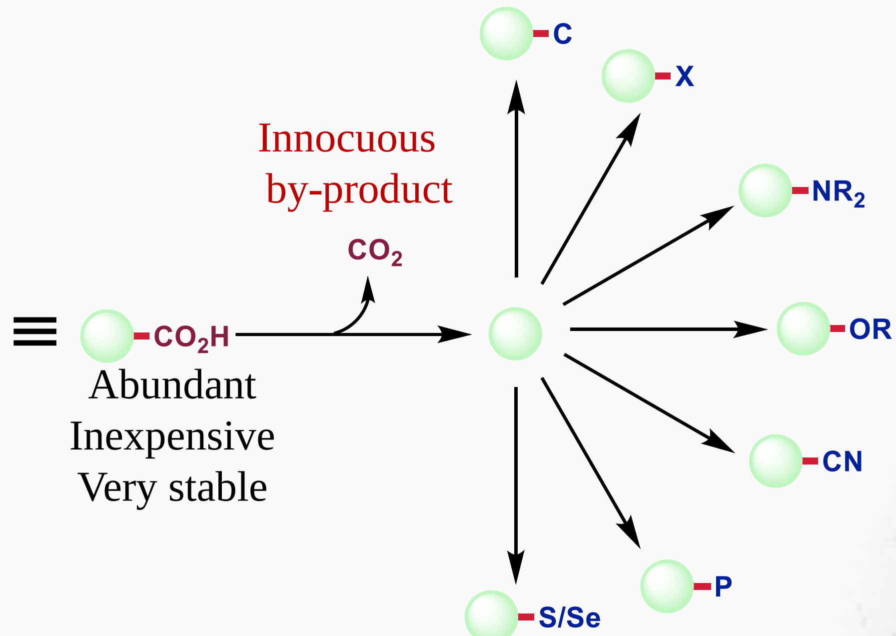
Carboxycelecoxib



Indometacin



Lumacaftor

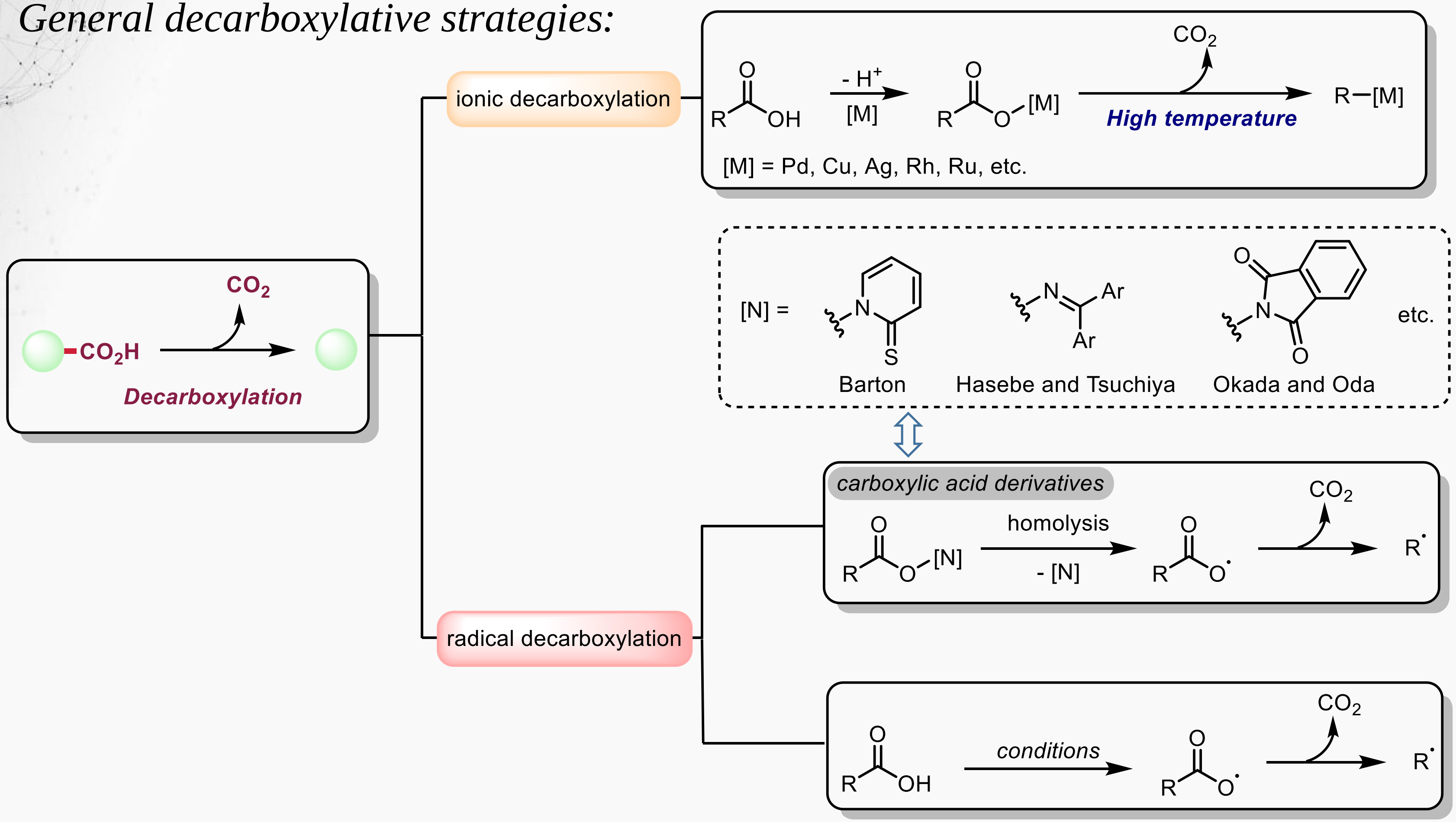


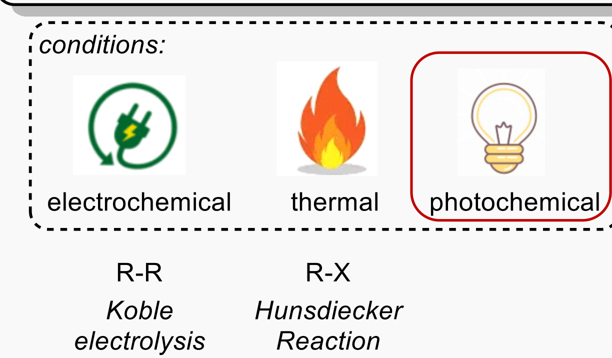
Patai, S. The chemistry of acid derivatives; wiley: New York, **1992**.
Maag, H. Prodrugs of carboxylic acids; Springer: USA, **2007**.

Goo ßen, L. J. *et al. Adv. Synth. Catal.* **2021**, *363*, 2678.
Mark Gandelman, M. *et al. Chem. Rev.* **2021**, *121*, 412.
Gevorgyan, V. *et al. Chem. Soc. Rev.*, **2021**, *50*, 2244.

Background

General decarboxylative strategies:





Nilsson, M. *et al. Acta Chem. Scand.* **1966**, *20*, 423.

Barton, D. H. R. *Tetrahedron* **1992**, *48*, 2529.

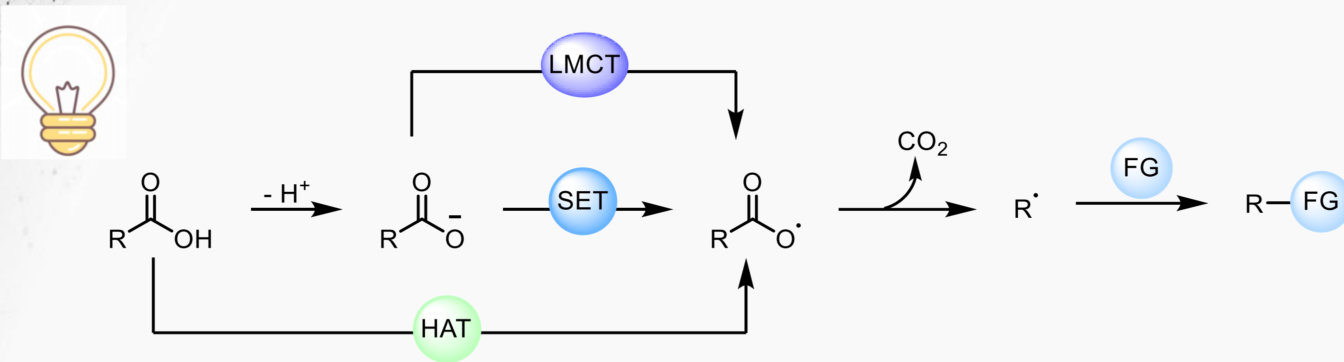
Kolbe, H. *Justus Liebigs Ann. Chem.* **1848**, *64*, 339.

Hunsdiecker H. *et al. Ber. Dtsch. Chem. Ges. B* **1942**, *75*, 291.

Libman, J. *J. Am. Chem. Soc.* **1975**, *97*, 4139.

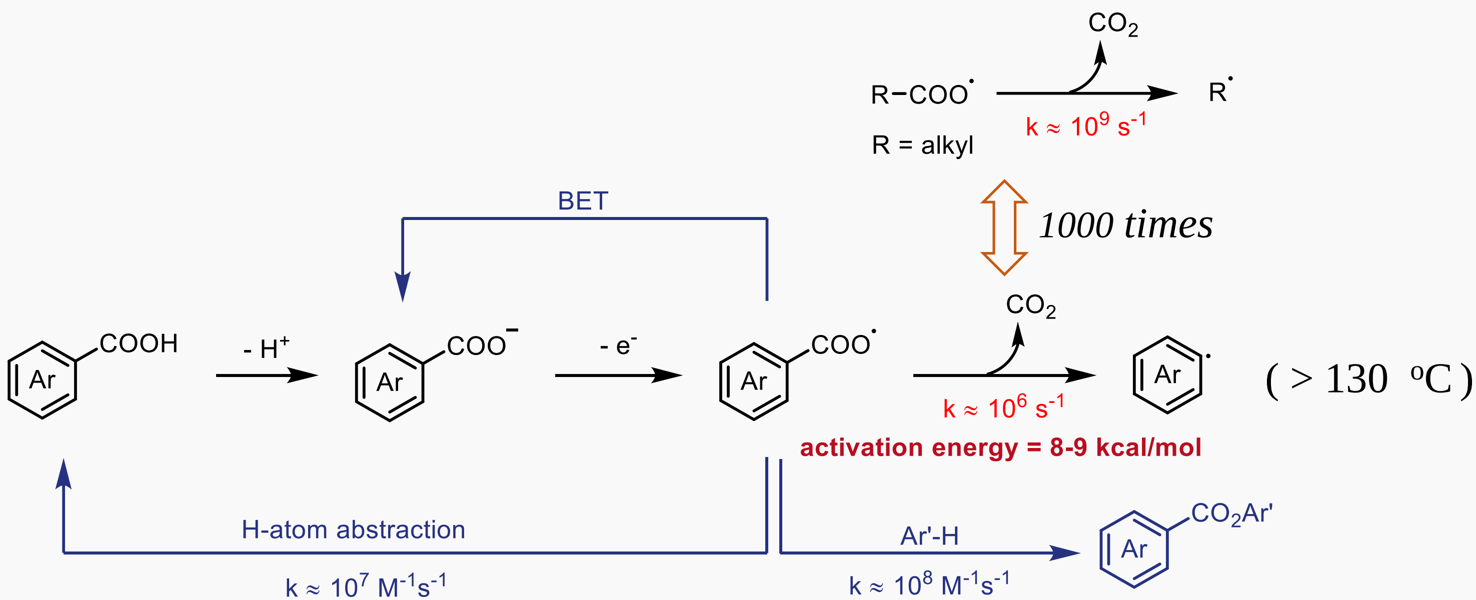
Background

Photodecarboxylative functionalization



R = alkyl, *well-developed*

R= aryl, *rarely-reported*



Challenge: competitive transformations

Fu, H. *et al. Asian J. Org. Chem.* **2017**, *6*, 368.
König, B. *et al. Green Chem.* **2018**, *20*, 323.
Ingold, K. U. *et al. J. Am. Chem. Soc.* **1988**, *110*, 2886.
Barton, D. H. R. *et al. Tetrahedron* **1987**, *43*, 4321.

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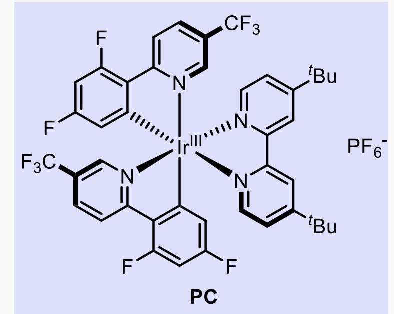
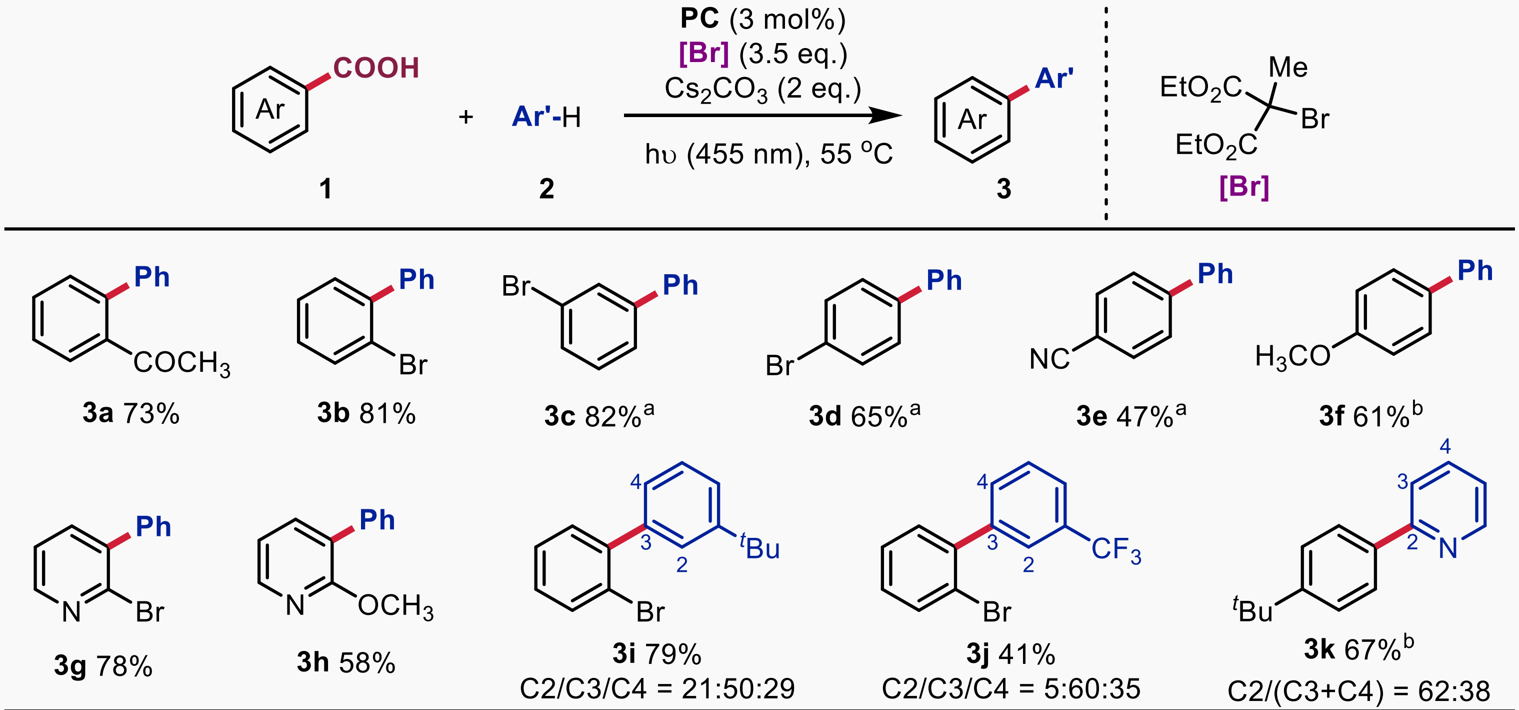
via SET



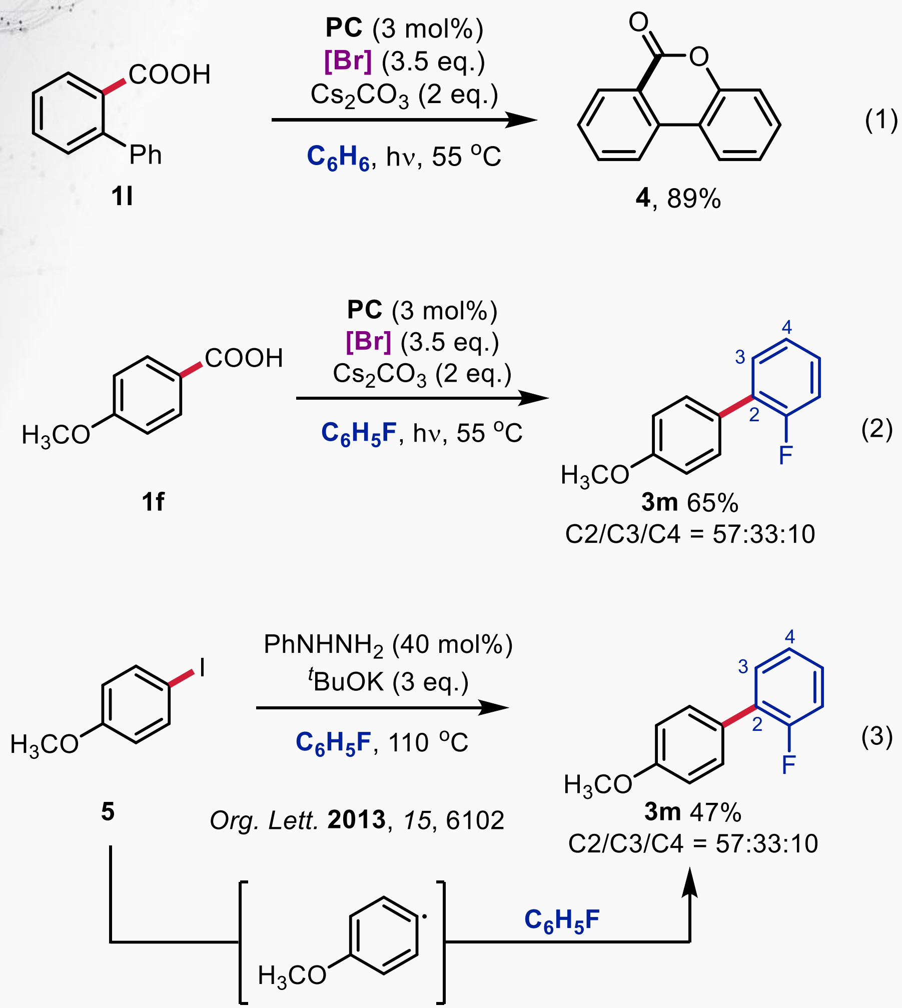


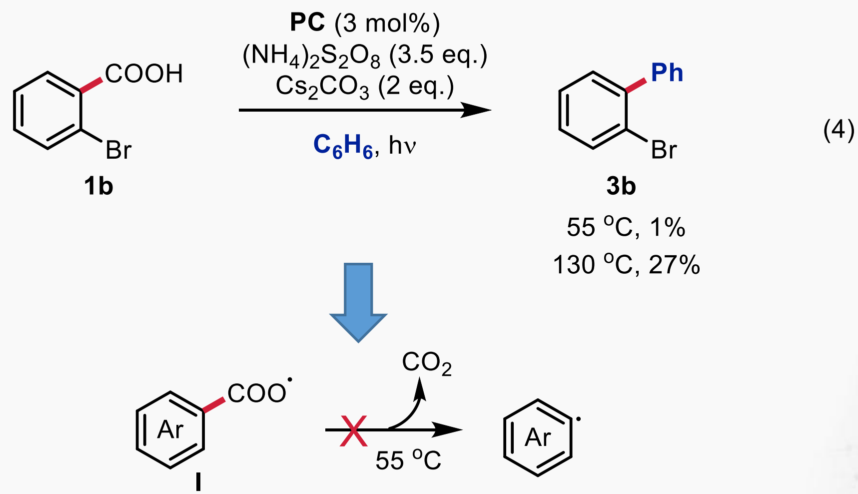
[a] 80 °C; [b] 2.0 eq. [Br] was used

Glorius, F. *et al. Chem. Sci.* **2017**, *8*, 3618.

via SET

Mechanistic studies:





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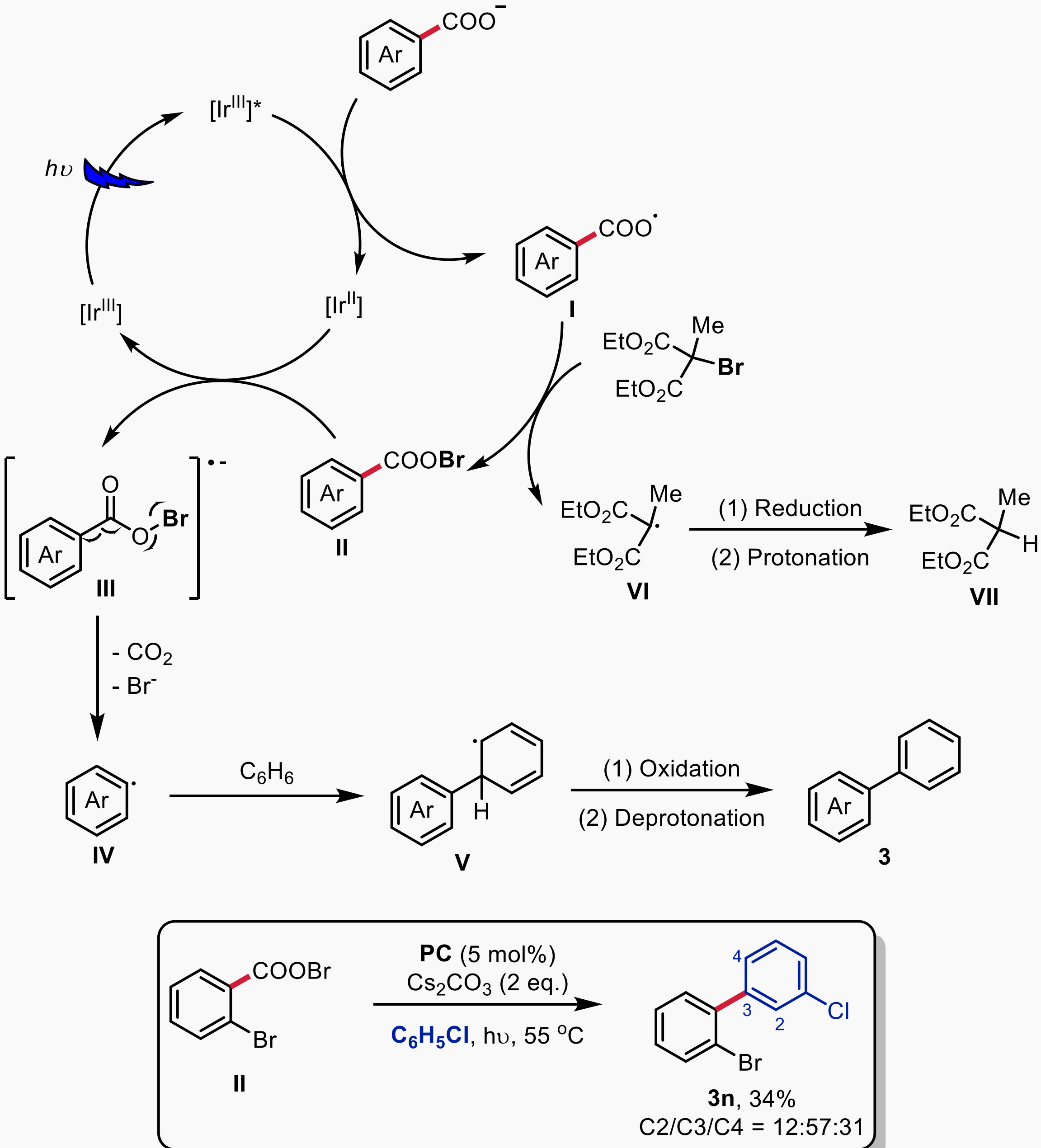
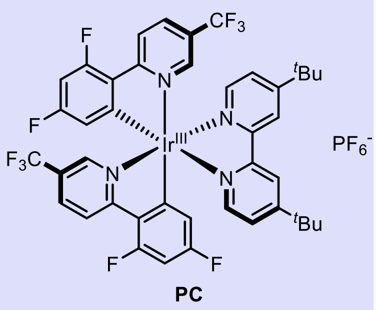
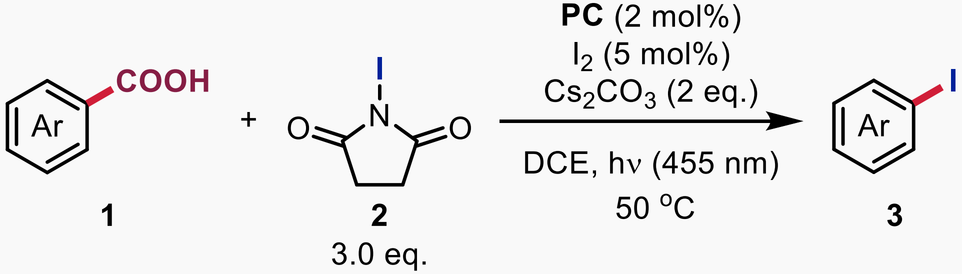
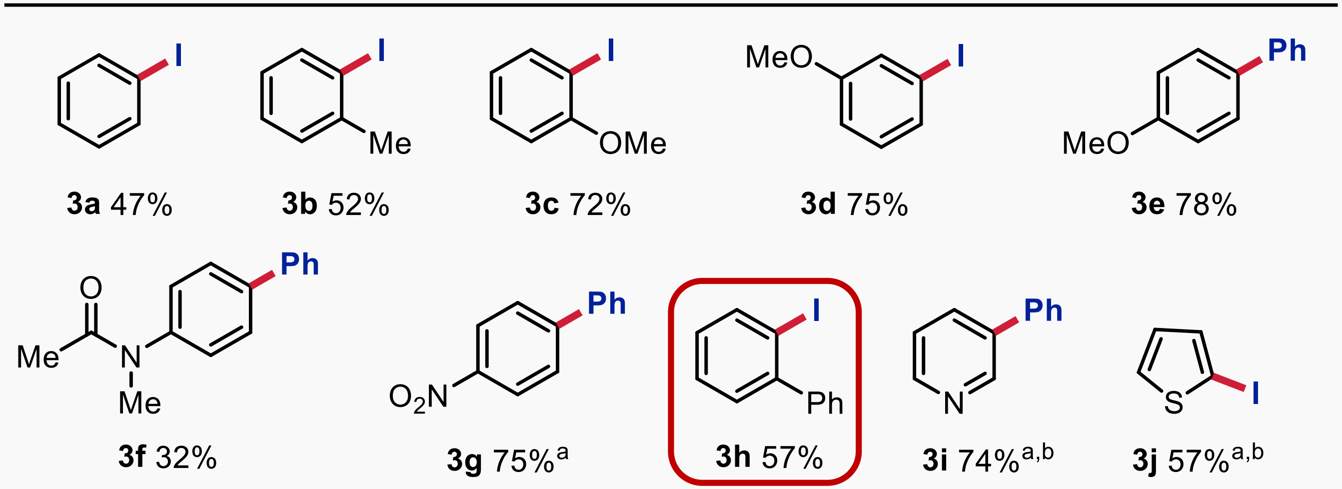


Glorius, F. *et al. Chem. Sci.* **2017**, *8*, 3618.

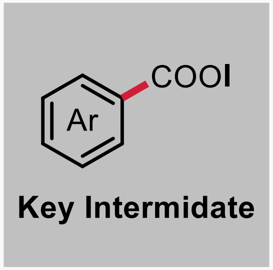
via SET





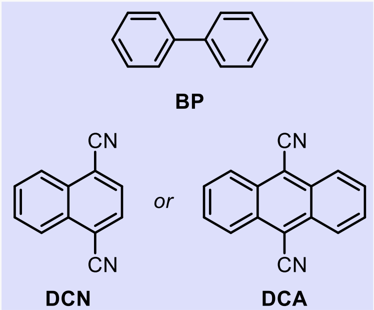


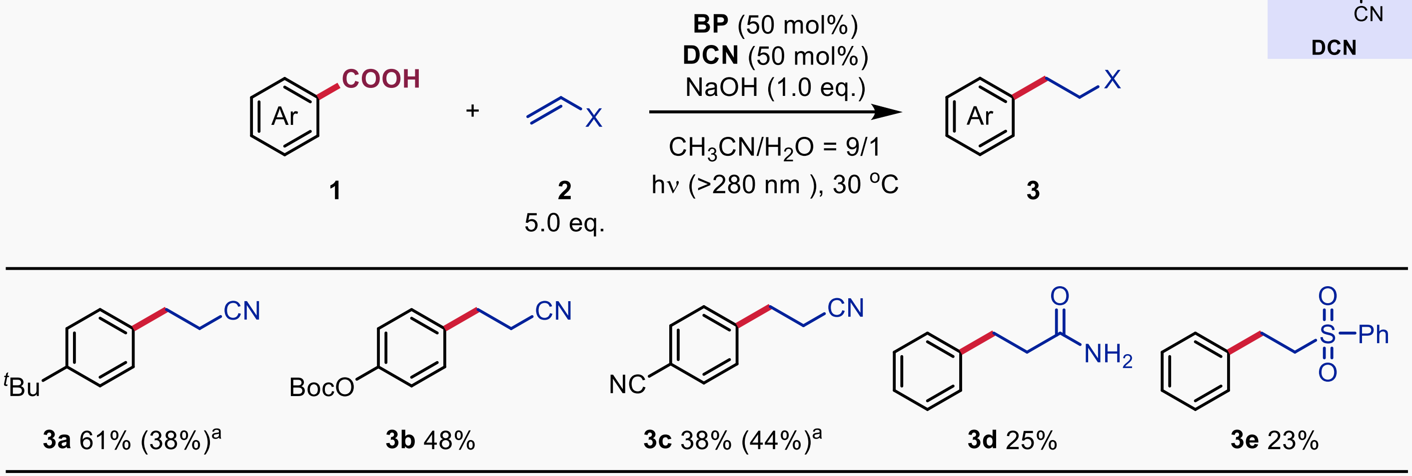
[a] NIS (5.0 eq.), I_2 (20 mol%); [b] CH_3CN as solvent



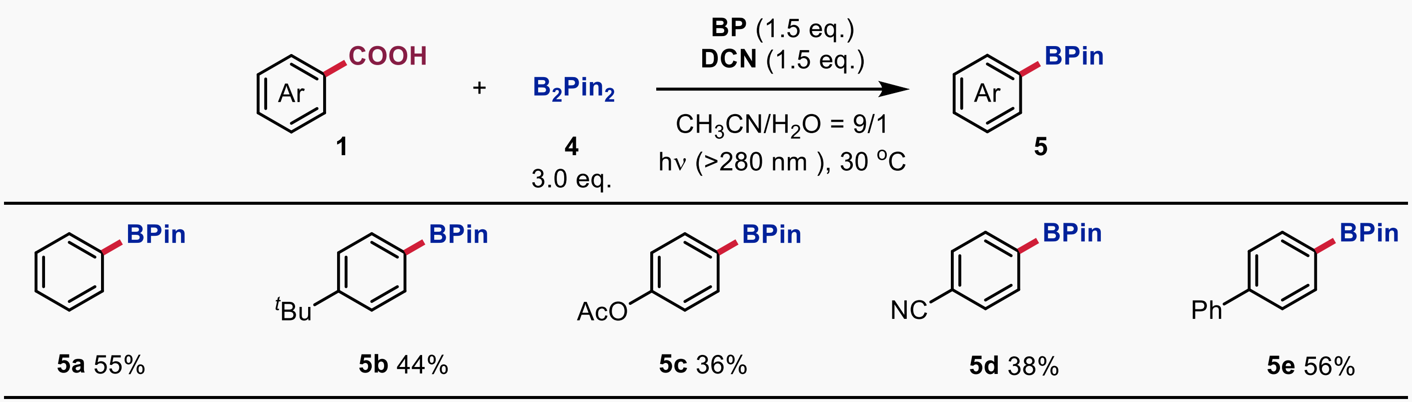
Fu, H. *et al. Synlett* **2018**, *29*, 1572.

via SET



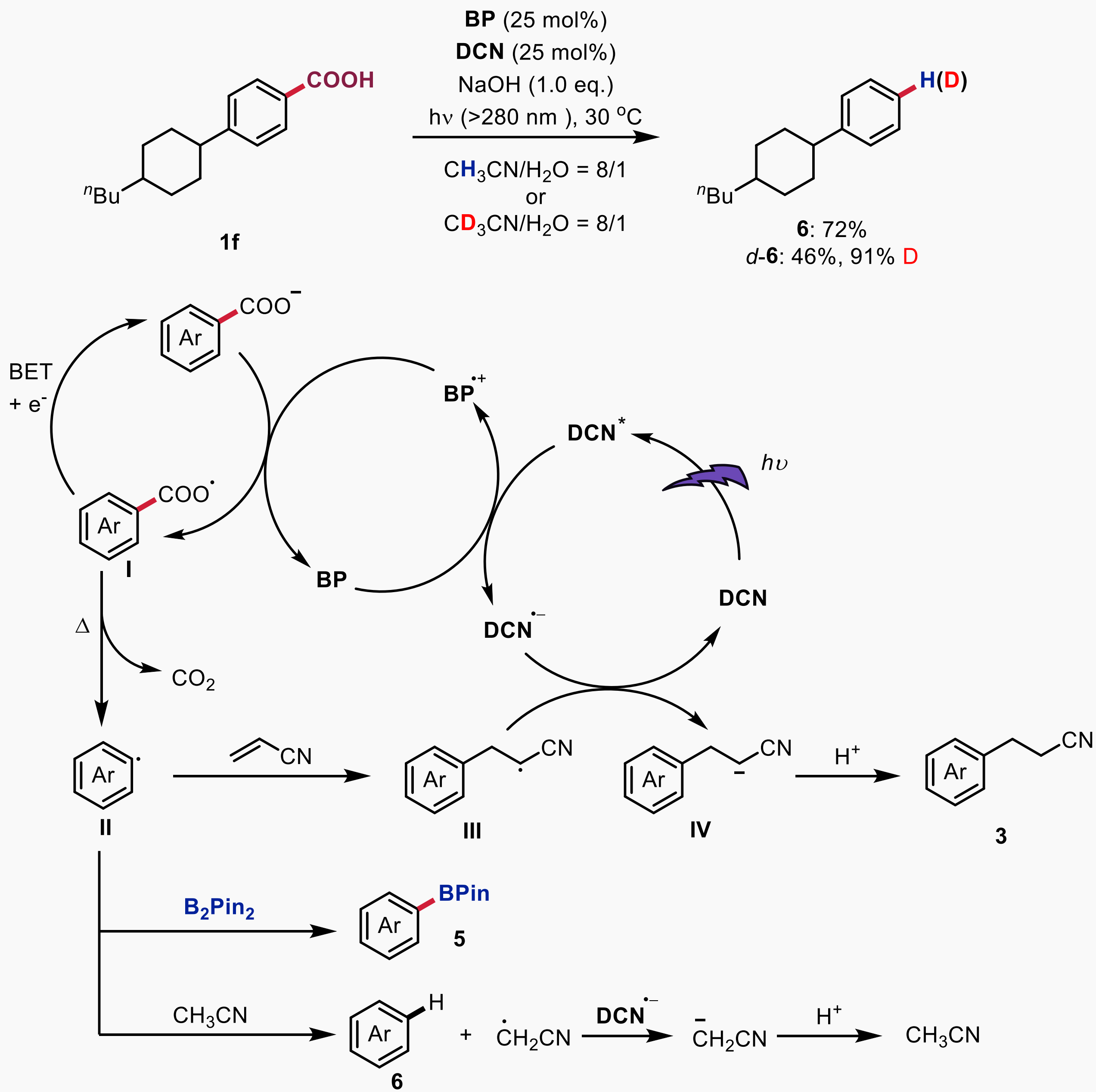


[a] BP (40 mol%), DCA (40 mol%),hυ (405 nm)



Yoshimi, Y. *et al. J. Org. Chem.* **2020**, *85*, 5362.

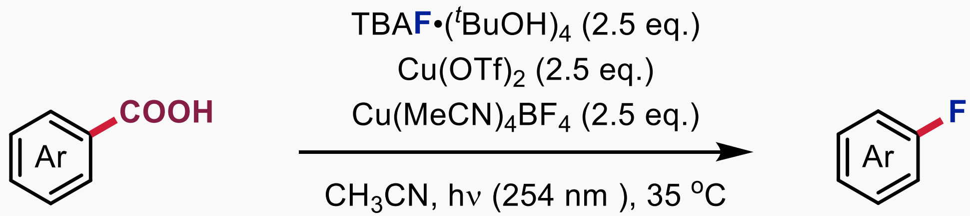
via SET



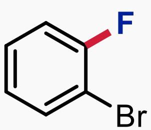
Yoshimi, Y. *et al. J. Org. Chem.* **2020**, *85*, 5362.

CONTENT >>

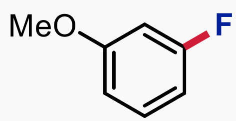
via LMCT



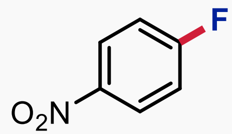
1 **3**



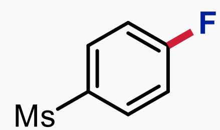
3a 83%



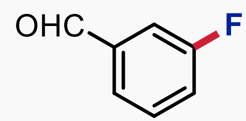
3b 60%



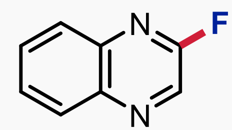
3c 72%



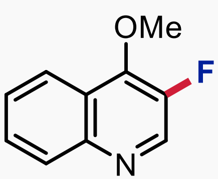
3d 71%



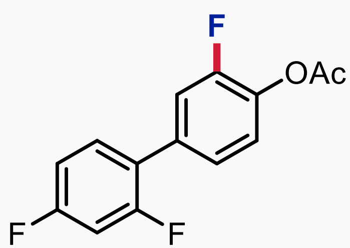
3e 64%



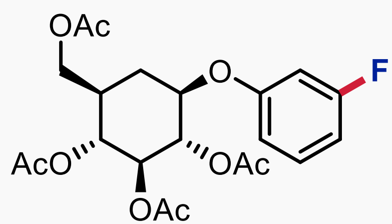
3f 74%



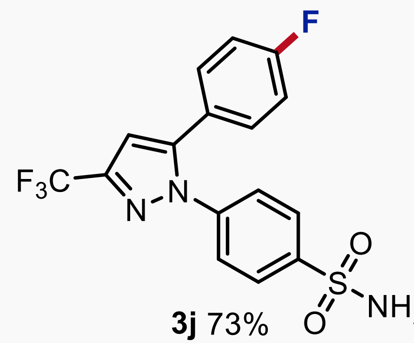
3g 68%
from *O*-metylkynurenic acid



3h 36%
from diflusinal acetate



3i 66%
D-glucose derivative

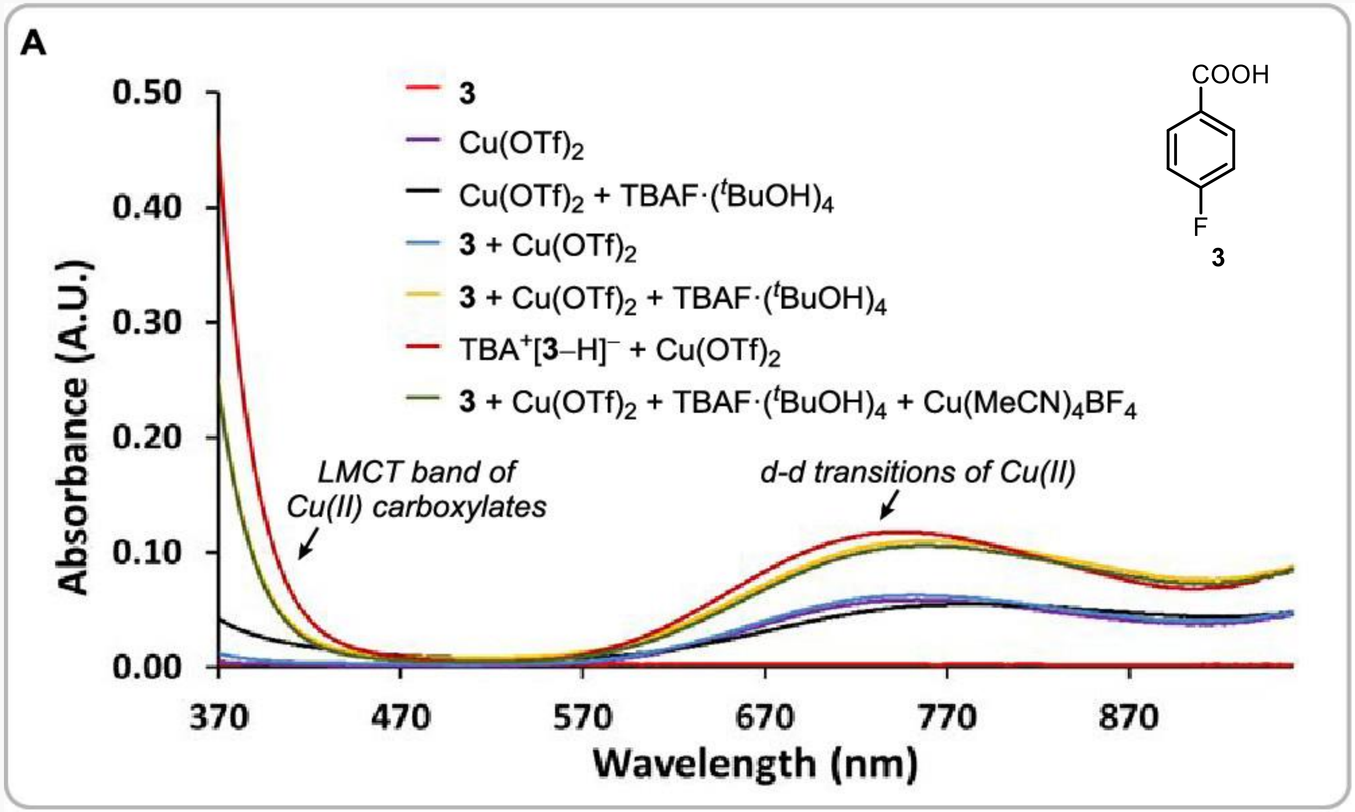


3j 73%
Mavacoxib

Ritter, T. *et al. J. Am. Chem. Soc.* **2021**, *143*, 5349.

via LMCT

Mechanistic studies:

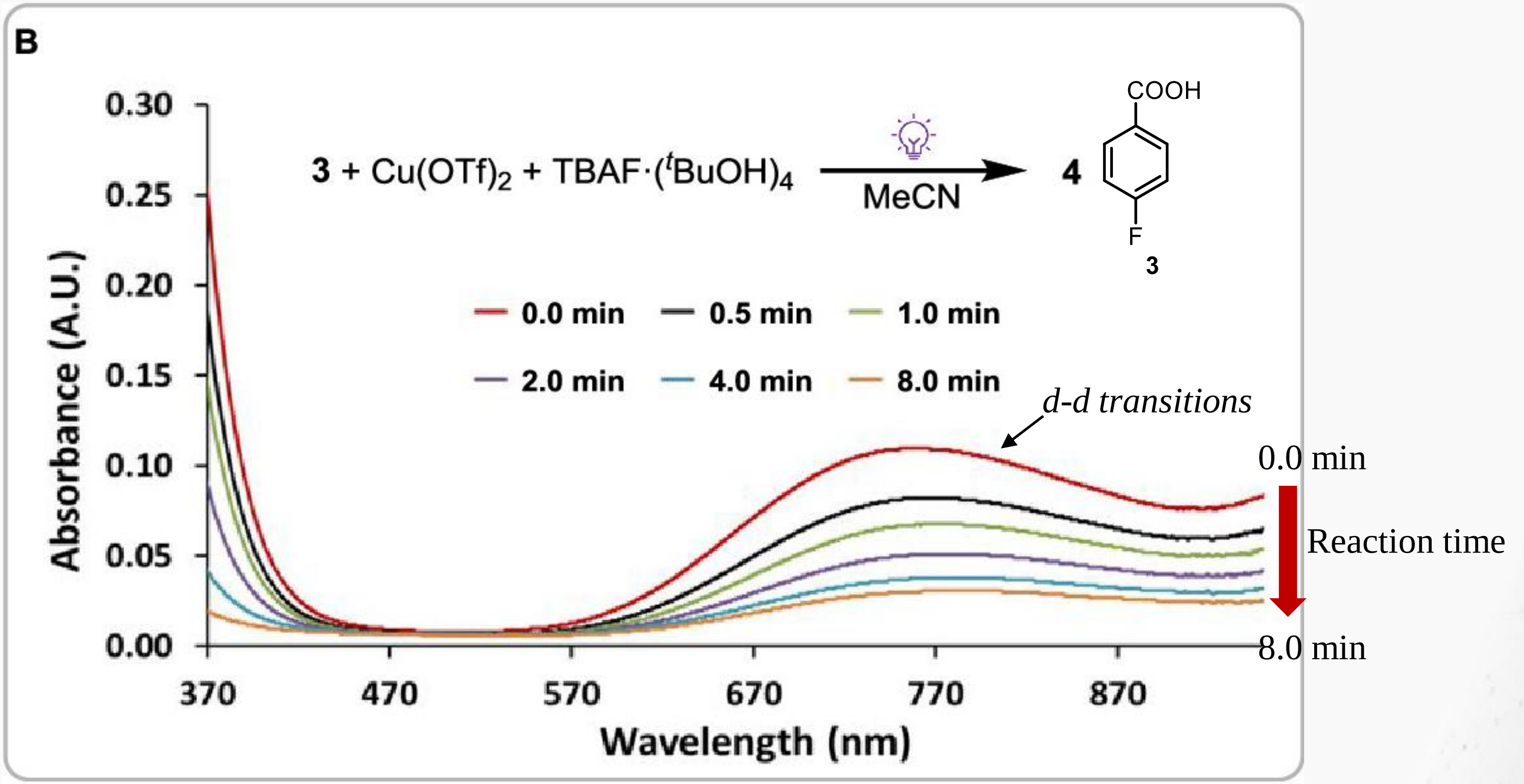


(A) UV−vis absorption spectra of reaction components

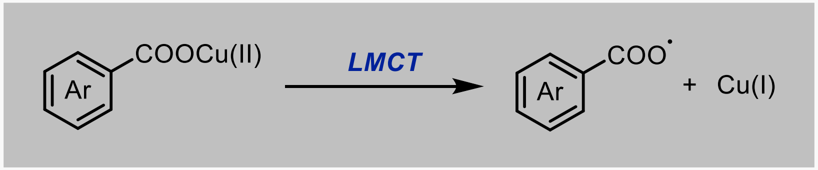
Ritter, T. *et al. J. Am. Chem. Soc.* **2021**, *143*, 5349.

via LMCT

Mechanistic studies:



(B) UV−vis spectral changes under purple LED irradiation (0−8 min)

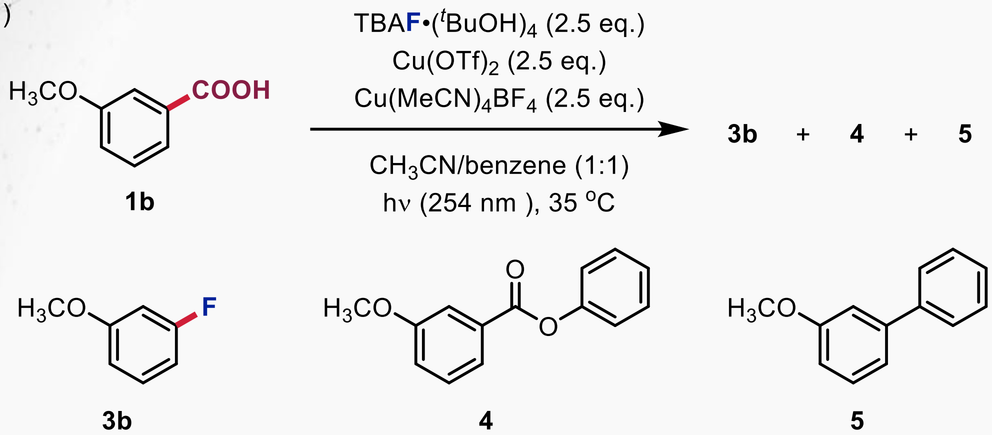


Ritter, T. *et al. J. Am. Chem. Soc.* **2021**, *143*, 5349.

via LMCT

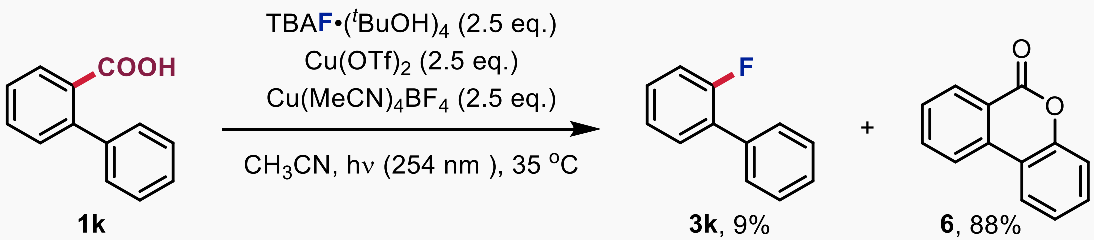
Mechanistic studies:

(1)

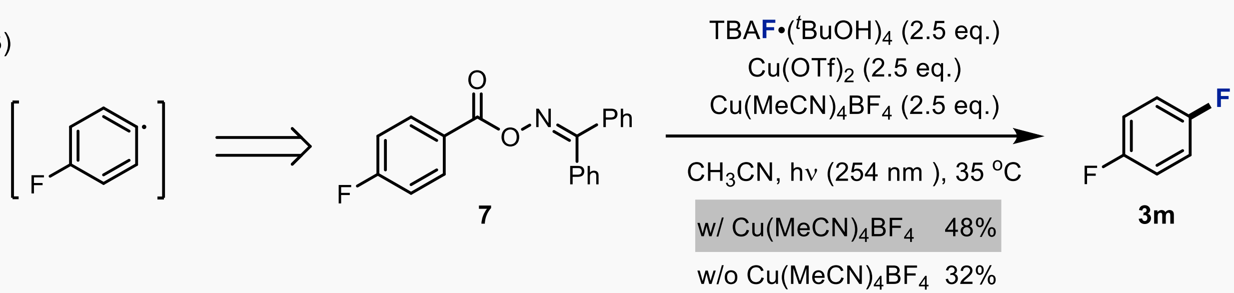


reaction condition	yield (%)		
	3b	**4**	**5**
w/ Cu(MeCN)$_4$BF$_4$	36	14	4
w/o Cu(MeCN)$_4$BF$_4$	25	21	9

(2)

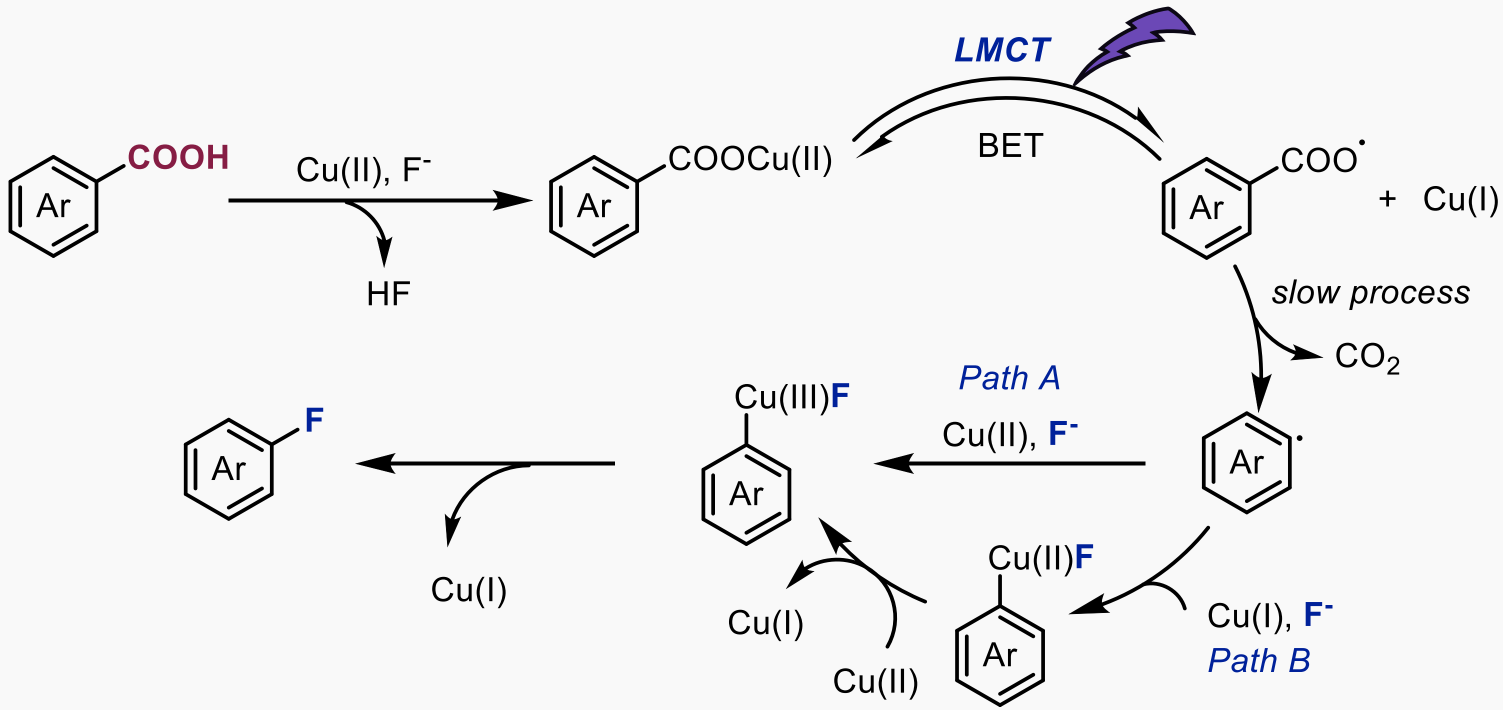


(3)



Ritter, T. *et al. J. Am. Chem. Soc.* **2021**, *143*, 5349.

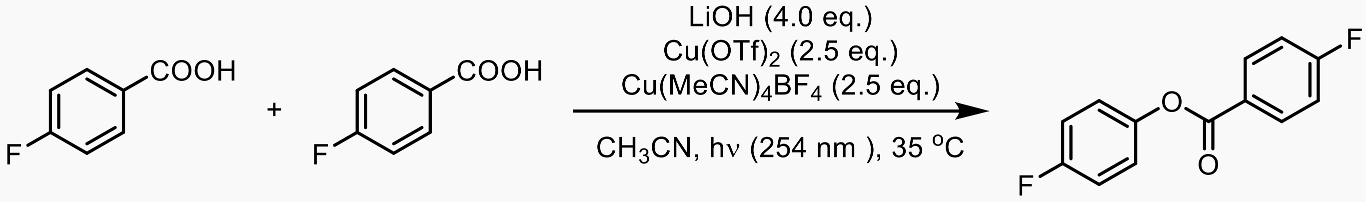
via LMCT



Ritter, T. *et al. J. Am. Chem. Soc.* **2021**, *143*, 5349.

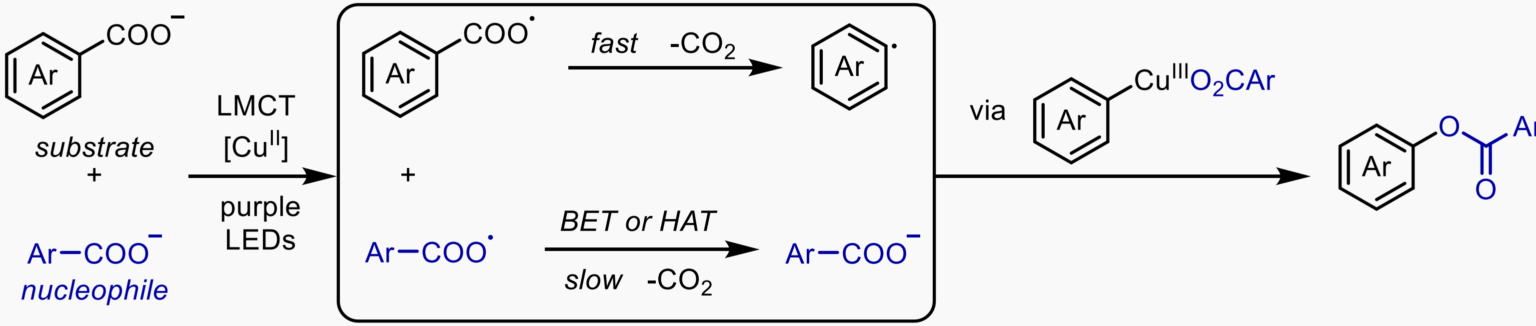
via LMCT

A

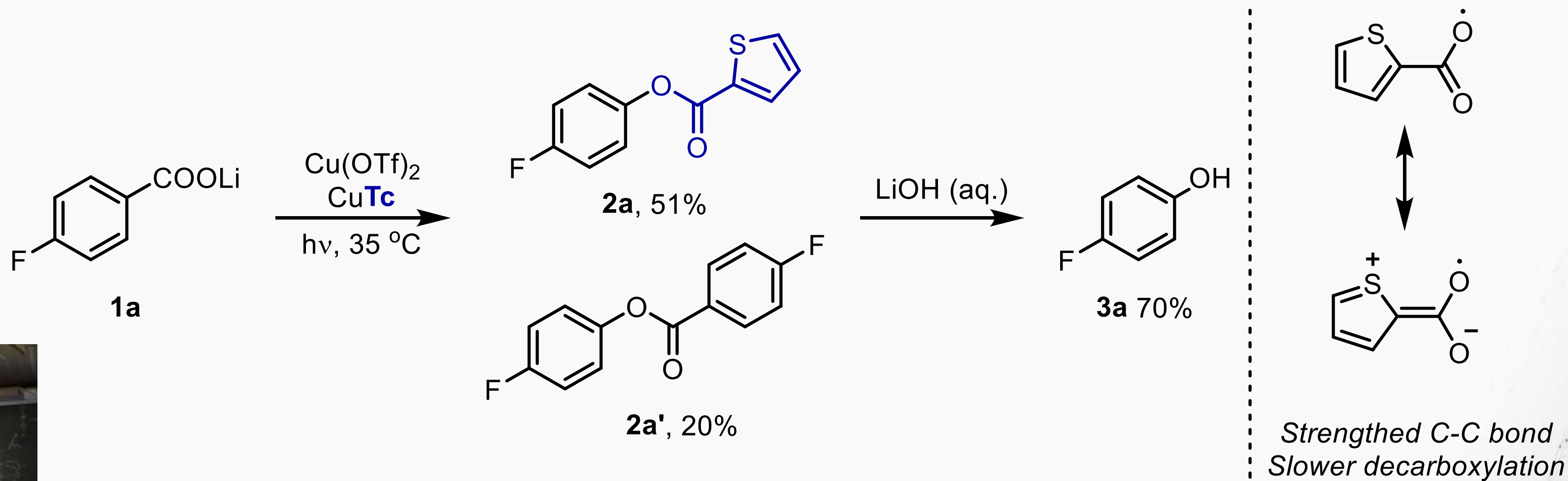


98%

B

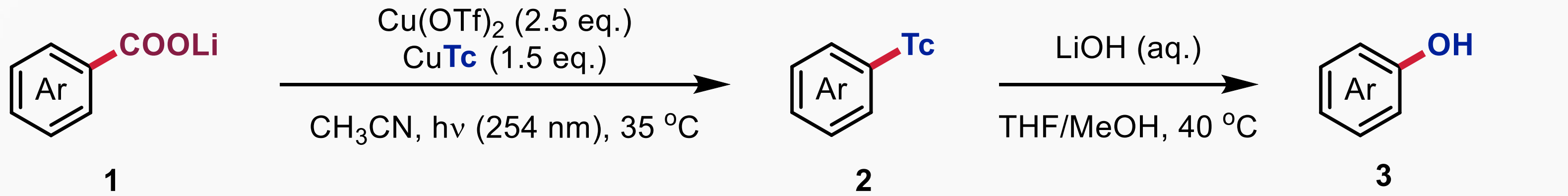


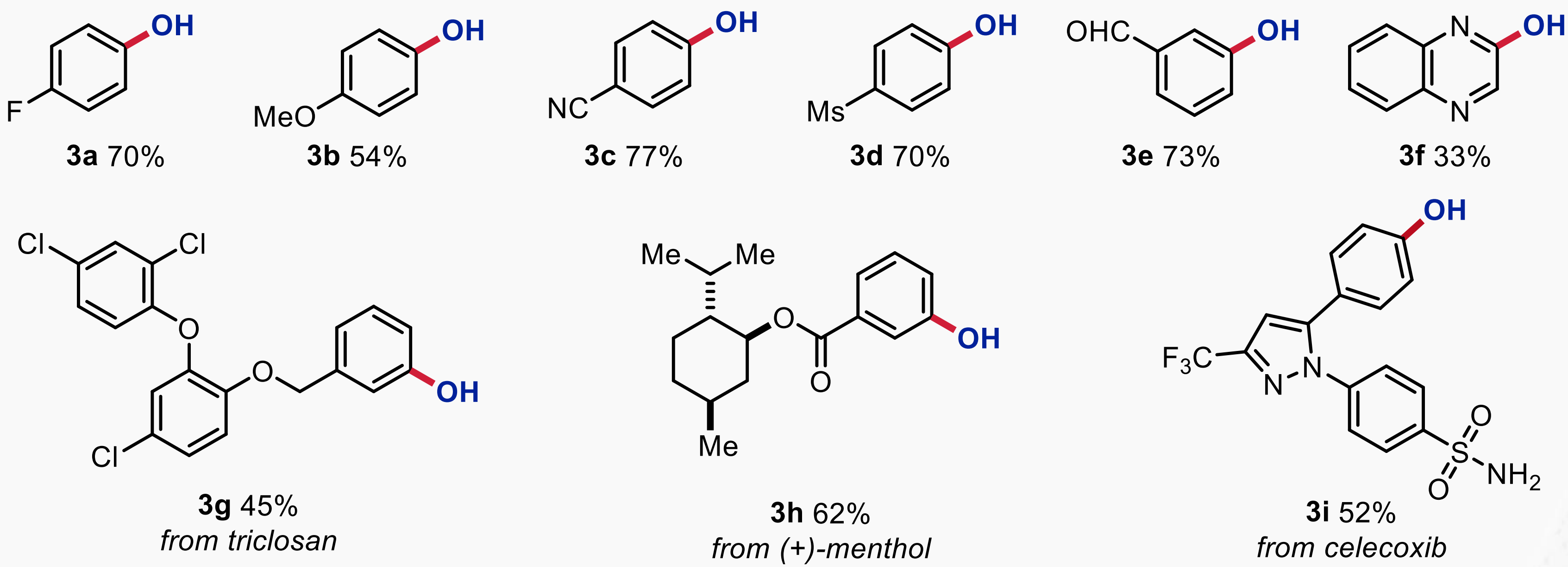
C



Ritter, T. *et al. Angew. Chem. Int. Ed.* **2021**, *60*, 24012.

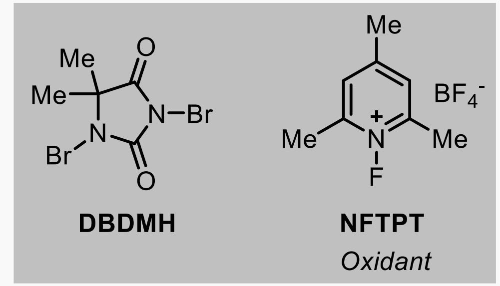
via LMCT

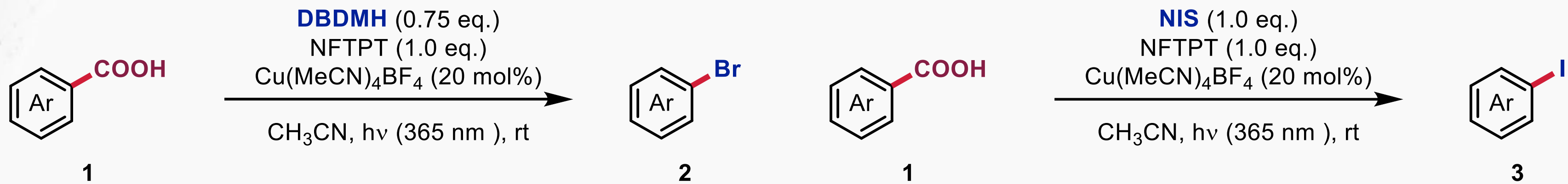


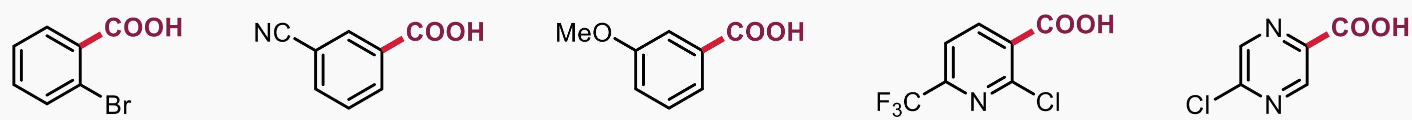


Ritter, T. *et al. Angew. Chem. Int. Ed.* **2021**, *60*, 24012.

via LMCT





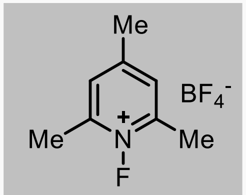


Bromination	**2a** 83%[a]	**2b** 75%	**2c** 40%[a]	**2d** 70%	**2e** 56%
Iodination	**3a** 60%	**3b** 67%	**3c** 67%	**3d** 56%	**3e** 32%

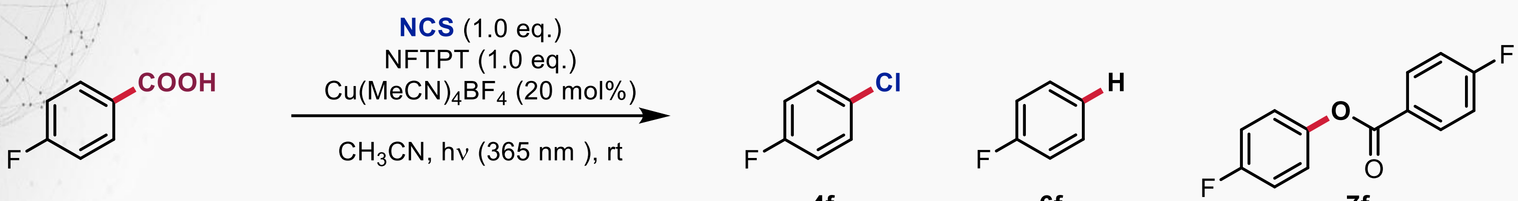
[a] $BrCCl_3$ (3.0 eq.) was used instead of DBDMH

MacMillan, D. W. C. *et al. J. Am. Chem. Soc.* **2022**, *144*, 8296.

via LMCT



NFTPT
Oxidant



1f **4f** 15% yield **6f** 18% yield **7f** 24% yield

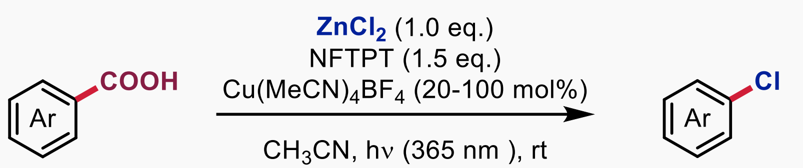
BDE of NXS:

N-Cl: 72.9 kcal/mol

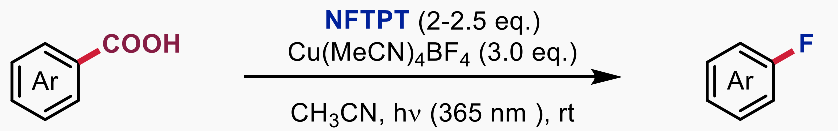
N-Br: 65.9 kcal/mol

N-I: 57.7 kcal/mol

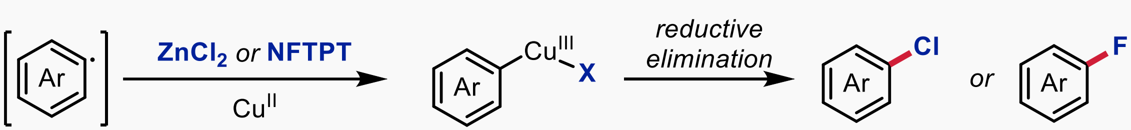
Low efficiency of chlorine atom transfer



1 **4** 46-98% yield

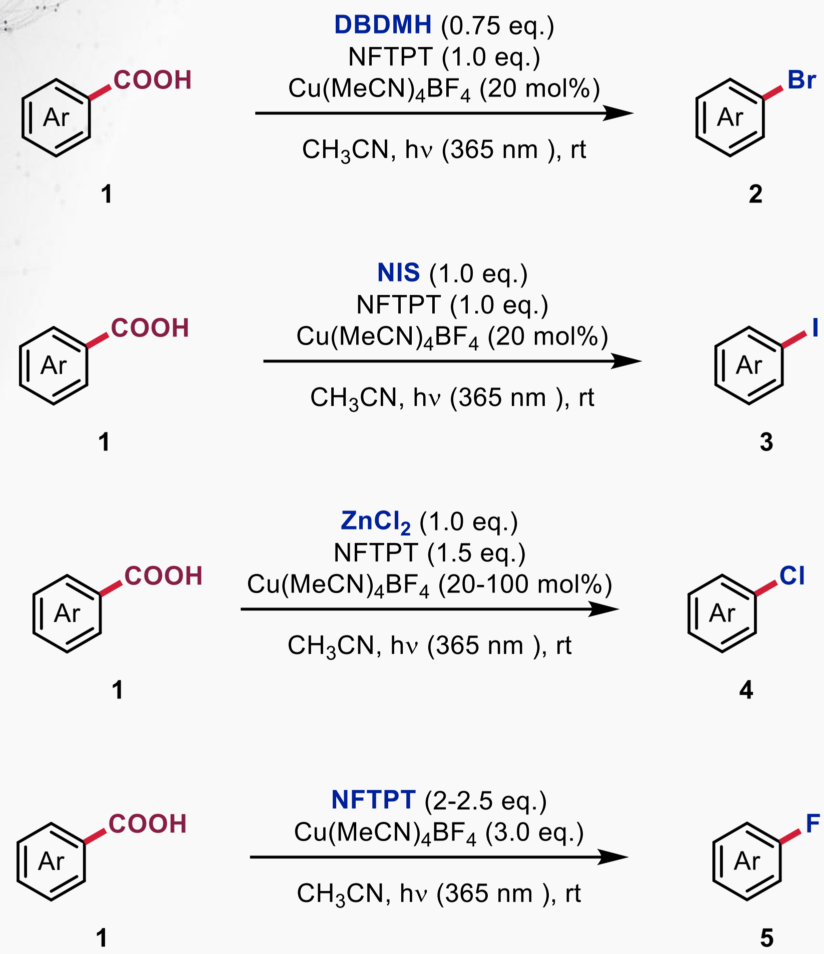


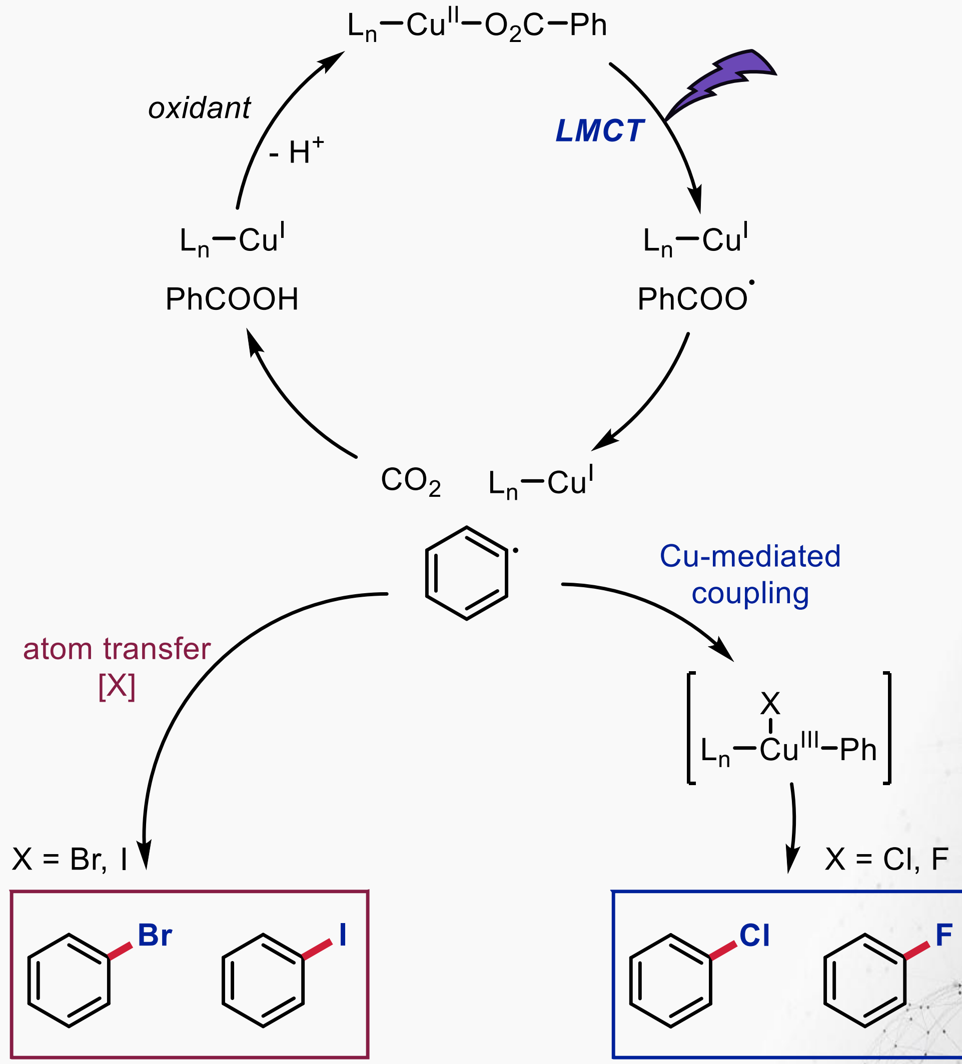
1 *Decarboxylative Fluorination* **5** 40-81% yield



MacMillan, D. W. C. *et al. J. Am. Chem. Soc.* **2022**, *144*, 8296.

via LMCT





MacMillan, D. W. C. *et al.* *J. Am. Chem. Soc.* **2022**, *144*, 8296.

CONTENT >>

01 /

Background

02 /

2.1 *via* SET

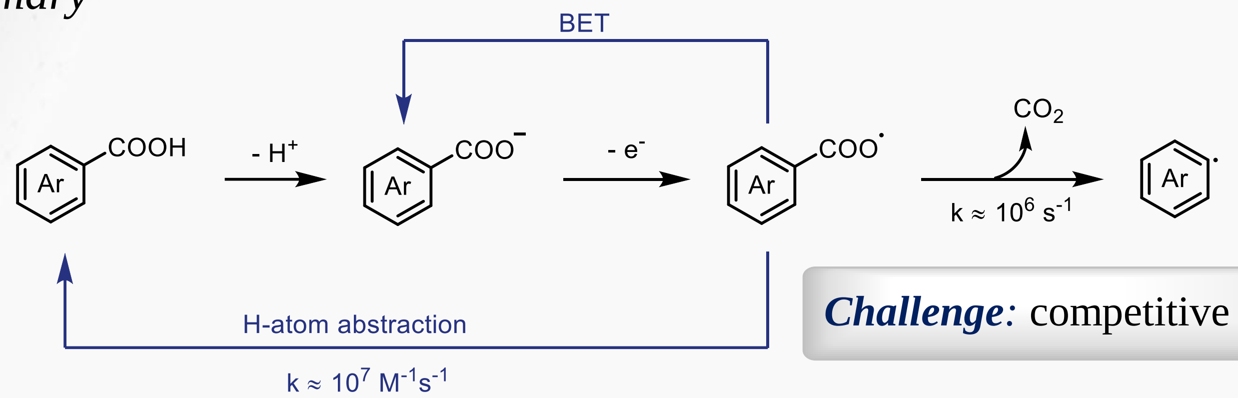
2.2 *via* LMCT

03 /

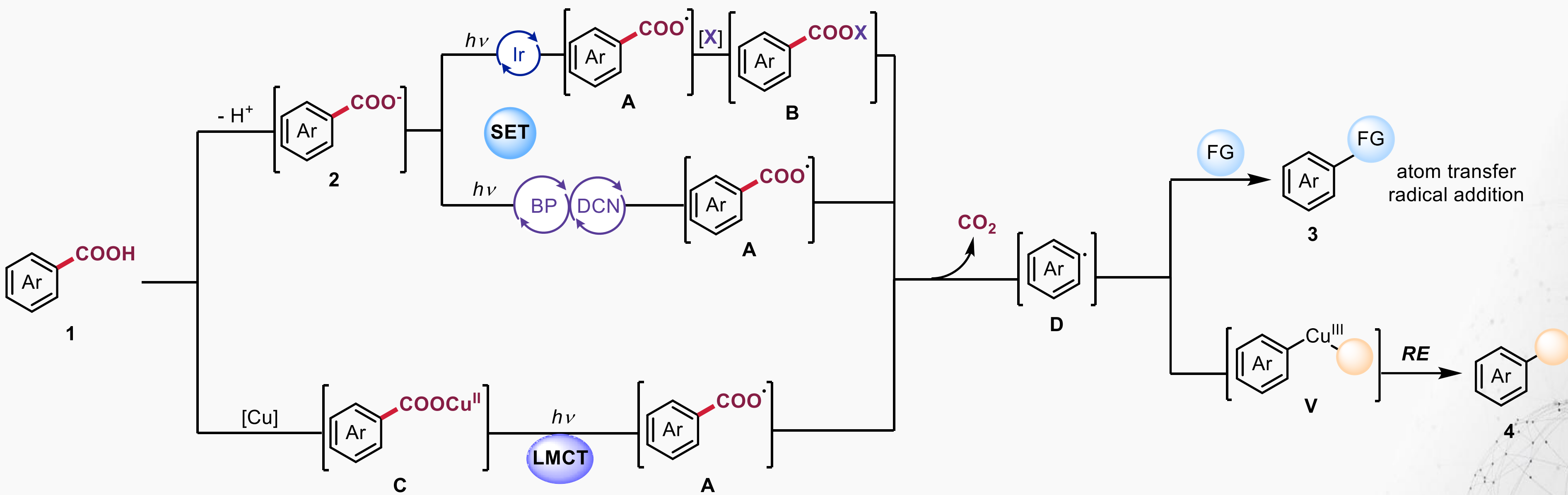
Summary and outlook

Summary and outlook

Summary



Challenge: competitive transformations

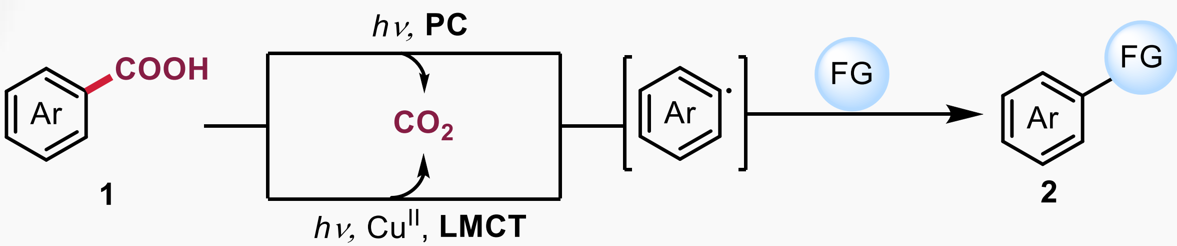


Summary and outlook

Outlook

Development of inexpensive photocatalysts and HAT

Expensive photocatalysts and excessive bases



Limited substrate scope

Poor regioselectivity

The use of stoichiometric Cu

Extended substrate scope

C-C, C- N, C-O, C-X,
C-B, C-P, C-S *etc.*

Controllably regioselectivity

Catalytic decarboxylation

Greener oxidant

Thanks for your attention