Well-identified Cu(III) Species in Bond Formations

MR Jan 22nd 2024

Yumeng Liao,
D2

Well-identified Cu(III) Species in Bond Formations

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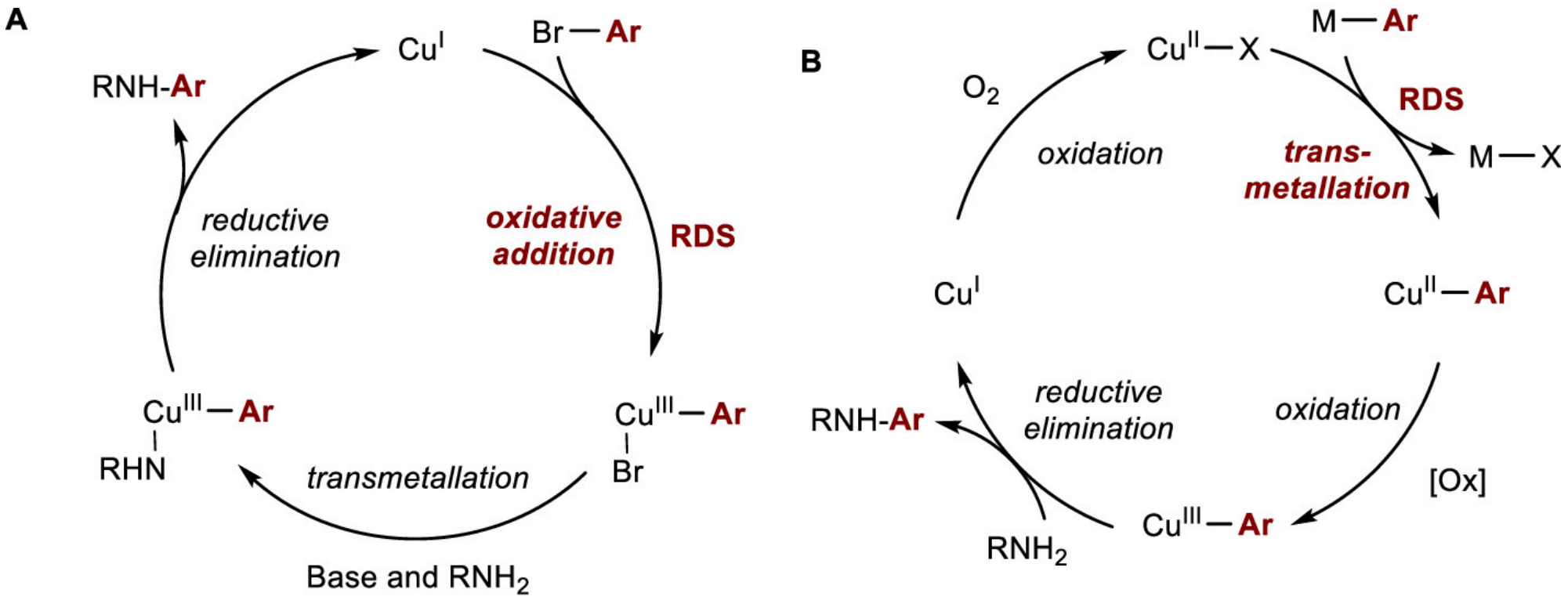
Cu(III)-mediated C–N Formation

Cu(III)-mediated C–C Formation

Cu(III)-mediated C–H Activation

Yumeng Liao,
D2

Catalytic Cycles of Cu-Catalyzed C–N Coupling Reactions



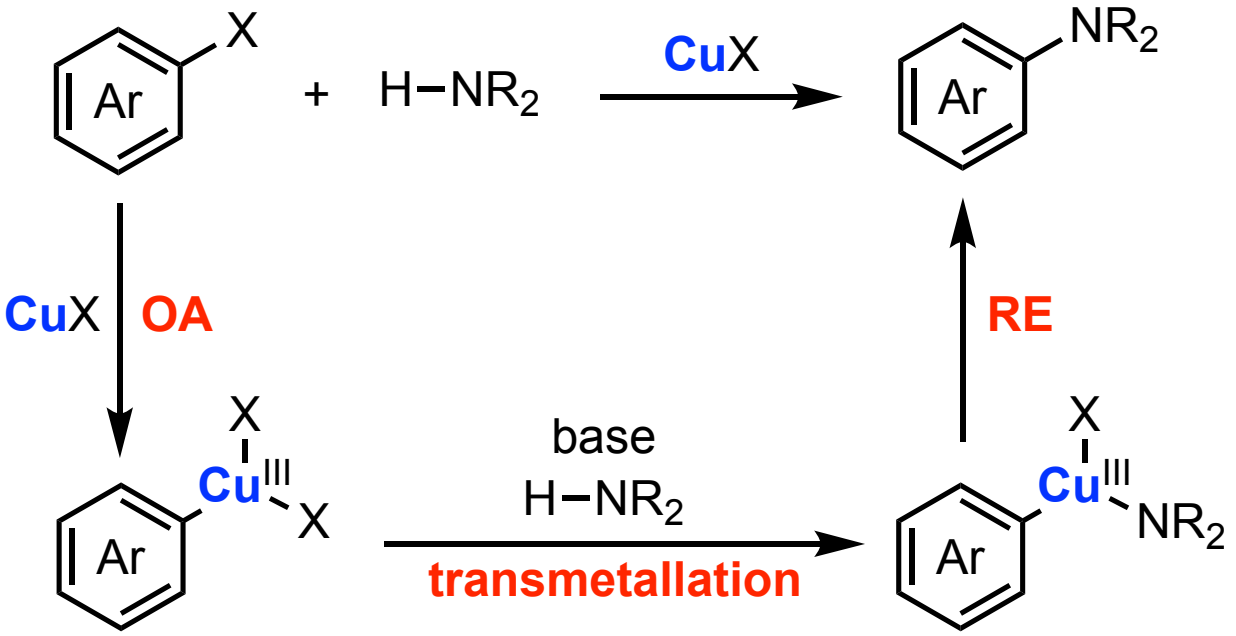
From Cu (I) cat.

From Cu (II) cat.

Cu (III) intermediates are proposed in most reports of Cu-catalyzed C–N coupling

Catalytic Cycles of Cu-Catalyzed C–N Coupling Reactions

From Cu (I) cat.

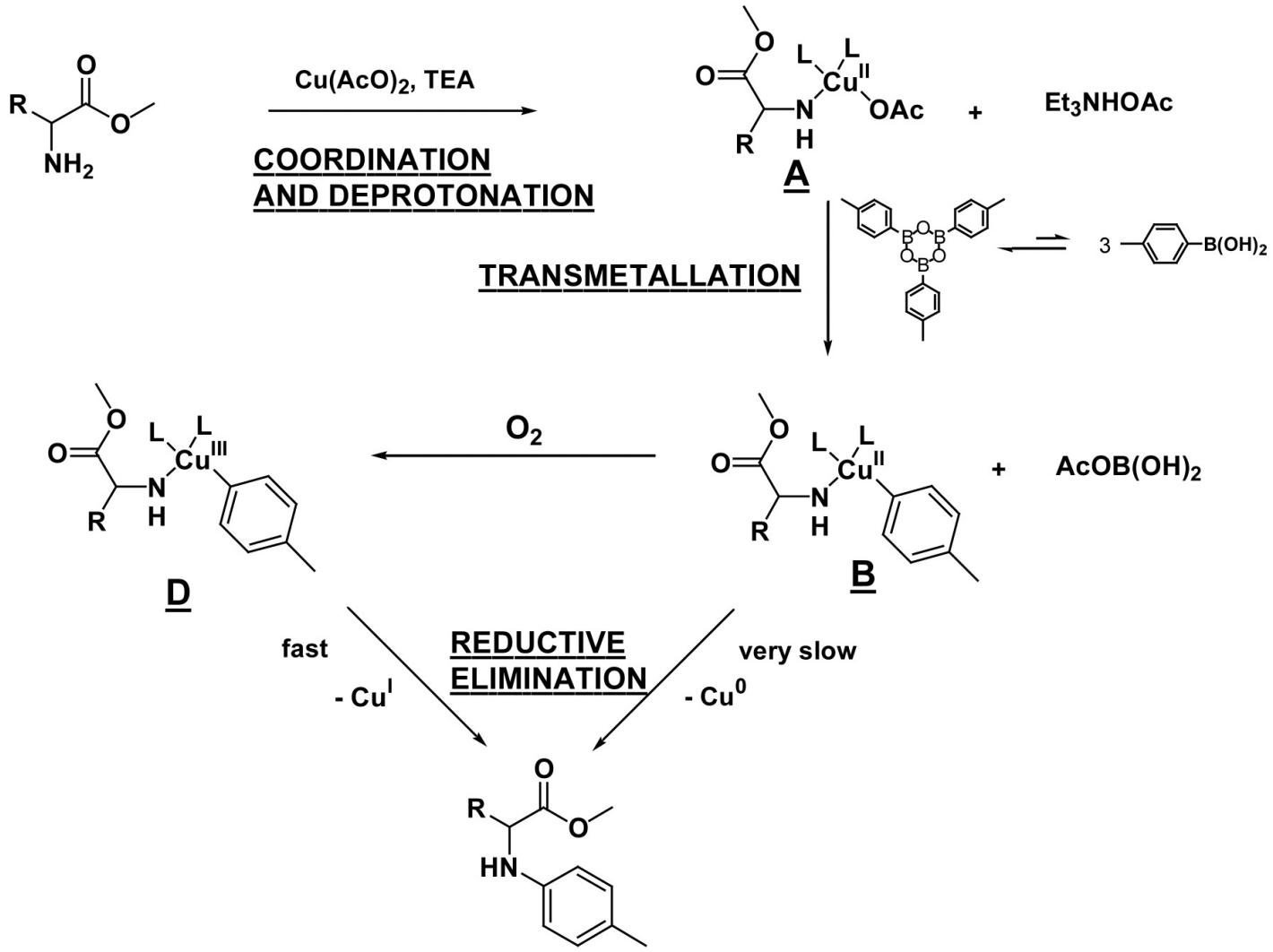


Ullmann coupling

Ullmann, F. *et al. Ber. Dtsch. Chem. Ges.* **1903**, *36*, 2382.

Catalytic Cycles of Cu-Catalyzed C–N Coupling Reactions

From Cu (II) cat.

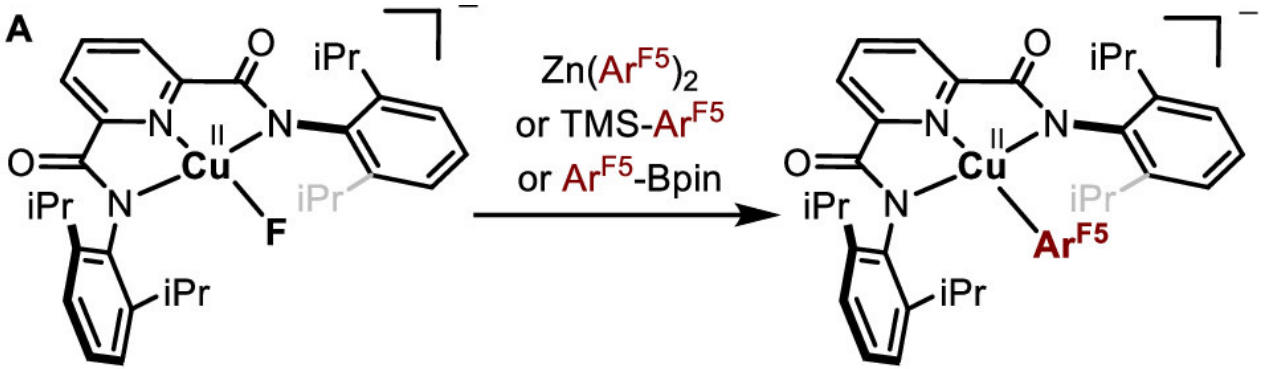


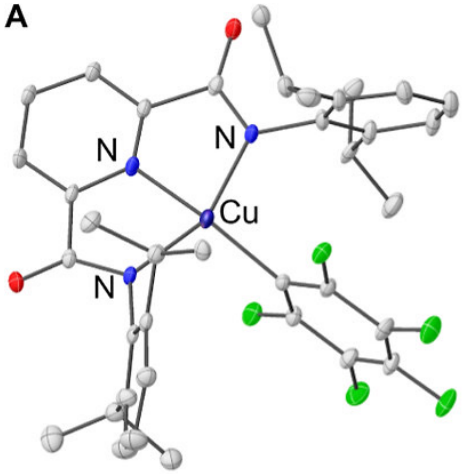
Chan-Evans-Lam coupling

Lam P. Y. S. *et al. Tetrahedron Lett.* **2003**, *44*, 1691.

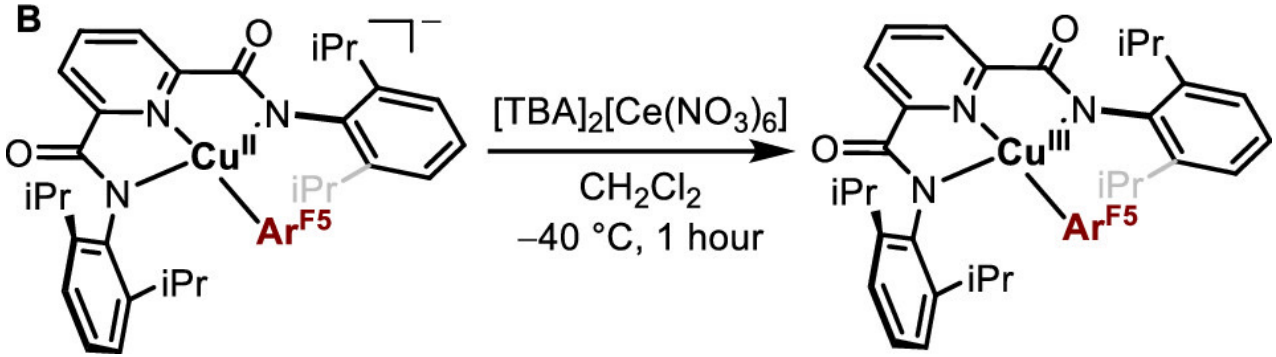
Isolated Cu(III) intermediate

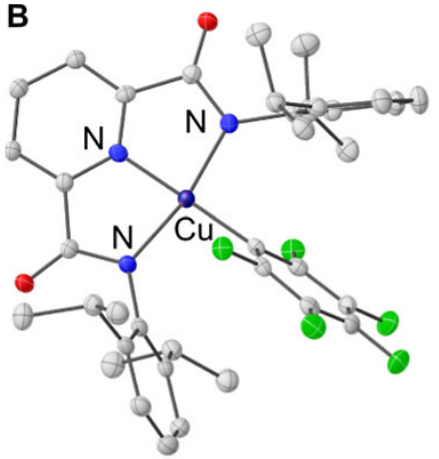
Synthesis of [TBA][L–Cu(II)–Ar^{F5}] (**A**)





Synthesis of L–Cu(III)–Ar^{F5} (**B**) from **A**

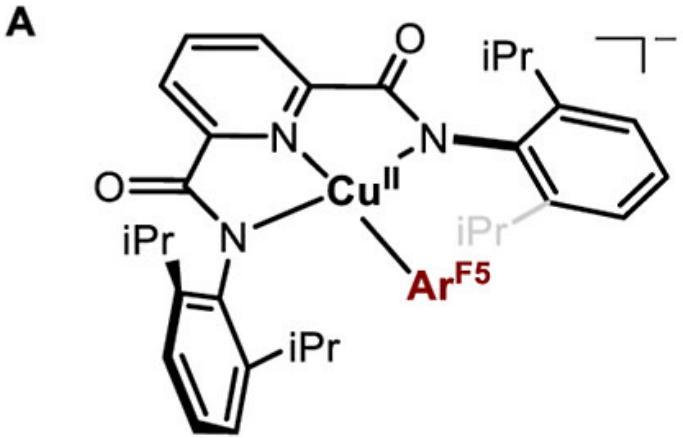




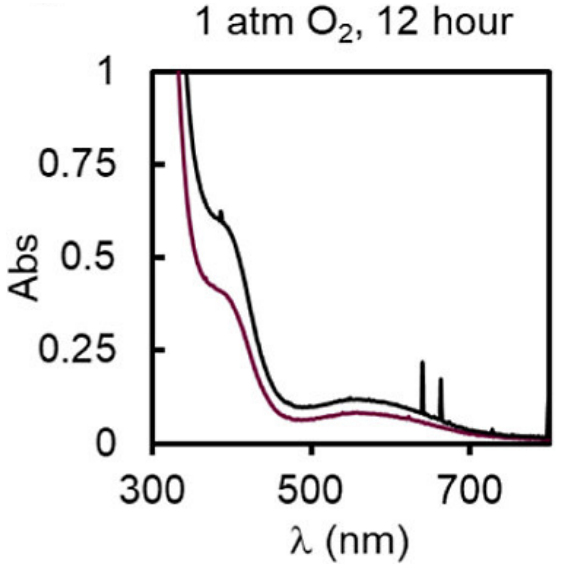
Zhang S. *et al. J. Am. Chem. Soc.* **2023**, *145*, 26810.

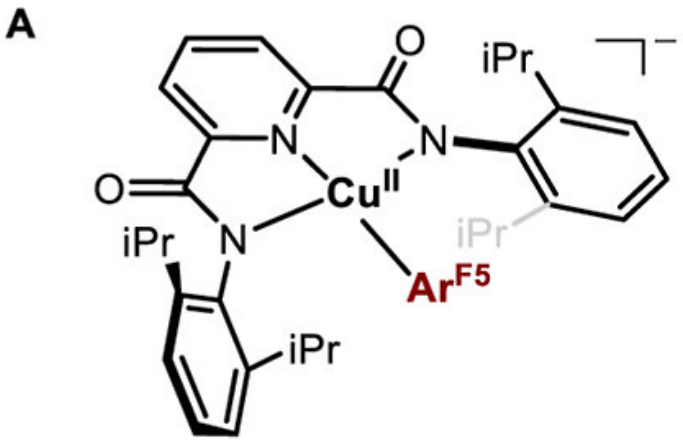
Cu(III)-Mediated C–N Formation

Oxidation of [TBA][L–Cu(II)–Ar^{F5}] (**A**)

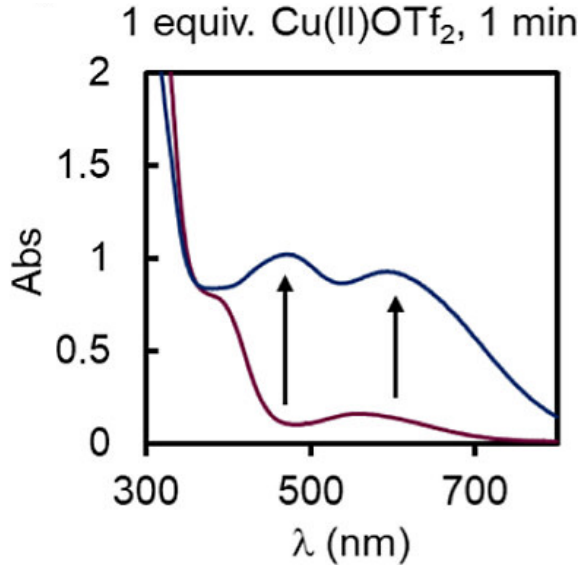


O_2 → no reaction





$Cu^{II}(OTf)_2$ → $LCu^{III}Ar^{F5}$ 60%



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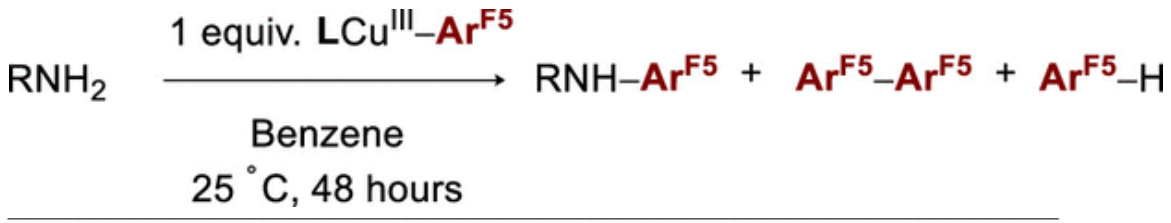
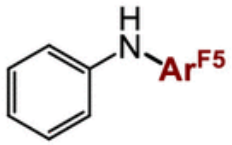
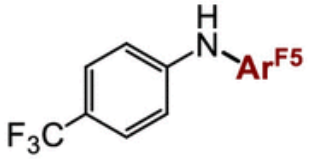
Cu(III)-Mediated C–N Formation

Arylation of Anilines by L–Cu(III)–Ar^{F5} (B)

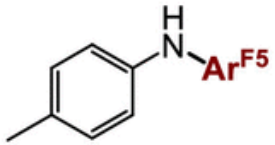




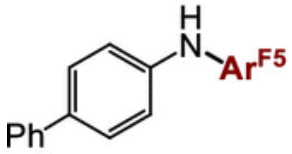
40%[a]
(35%, 5%)



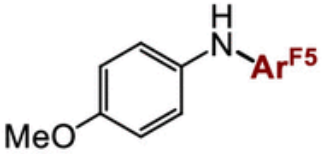
16%[b, c]
(37%, 5%)



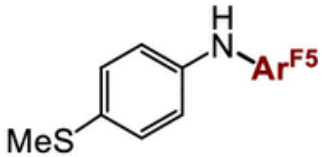
51%
(37%, 7%)



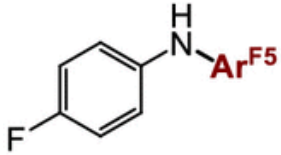
61%
(11%, 5%)



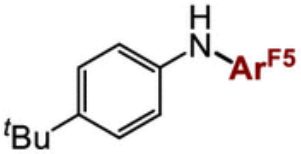
50%
(11%, 16%)



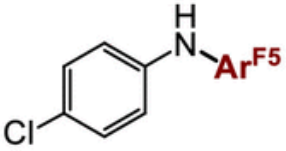
64%
(3%, 15%)



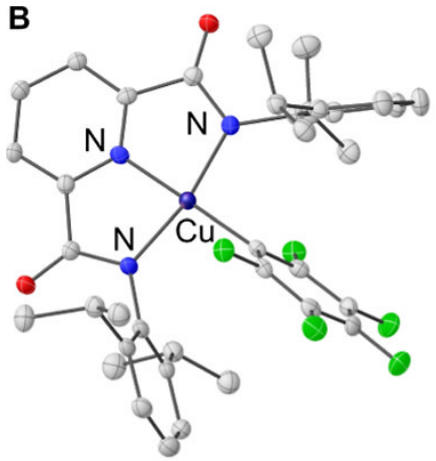
45%
(26%,5%)



46%
(36%, 9%)



50%
(45%,5%)



[a] Yields of Ar^{F5}-Ar^{F5} and Ar^{F5}-H are shown in parantheses.
[b] A significant amount of **L**Cu-Ar^{F5} remains unreacted.
[c] 10 eq of aniline substrate for 7 days

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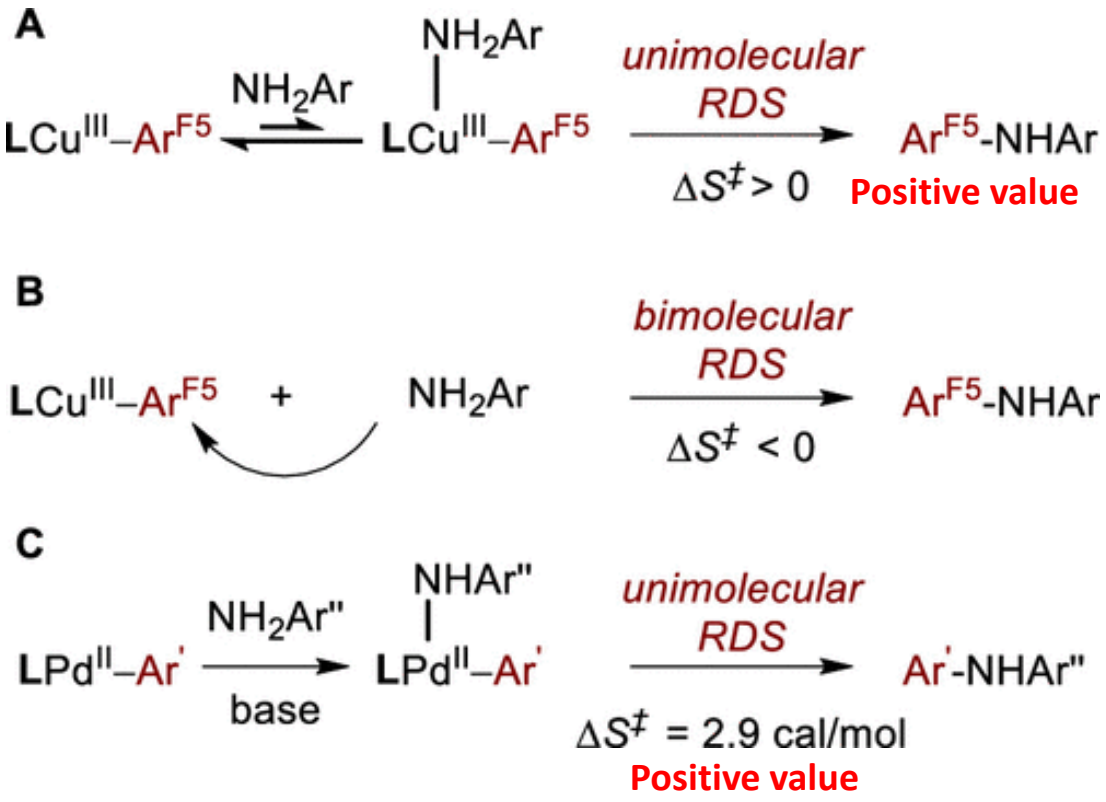
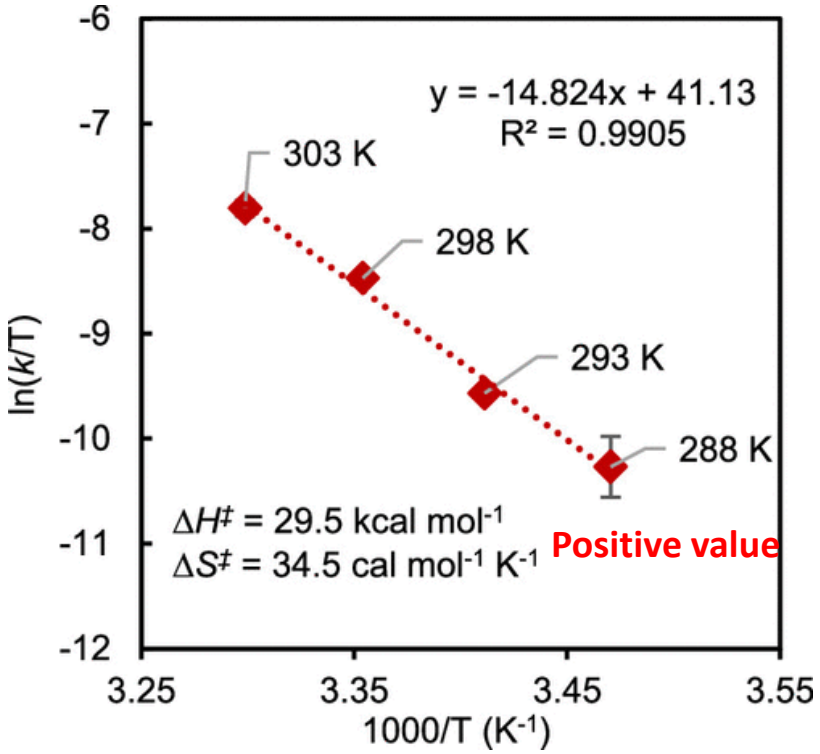
Plausible pathways



Eyring plot of **L**Cu^{III}–Ar^{F5} with 4-MeO-aniline



$$\ln\frac{k}{T} = -\frac{\Delta H^{\ddagger}}{R}\frac{1}{T} + \ln\frac{k_B}{h} + \frac{\Delta S^{\ddagger}}{R}$$

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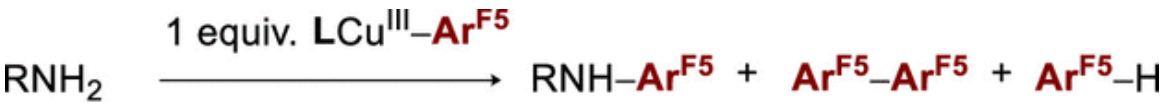
Side-reactions



A $[LCu^{II}–Ar^{F5}]^-$ —(100 equiv. H_2O)→ $Ar^{F5}–H$ 0%

B $LCu^{III}–Ar^{F5}$ —(100 equiv. H_2O)→ $Ar^{F5}–H$ 0%

Not hydrolysis

C $[LCu^{II}–Ar^{F5}]^-$ —($[Cu^{I}(MeCN)_4]^+$)→ $Ar^{F5}–H$ 20%

Cu^{I}-caused protonation

D $LCu^{III}–Ar^{F5}$ —(acetone)→ $Ar^{F5}–Ar^{F5}$ 98%

coordinative solvent caused decomposition

E $LCu^{III}–Ar^{F5}$ —($LCu^{III}–Ar$)→ $Ar^{F5}–Ar^{F5}$ 72%

Cu^{III}-caused decomposition

Homocoupling products are majority (72% + 20%)

+ Ar-Ar (20%) + $Ar^{F5}–Ar$ (5%)

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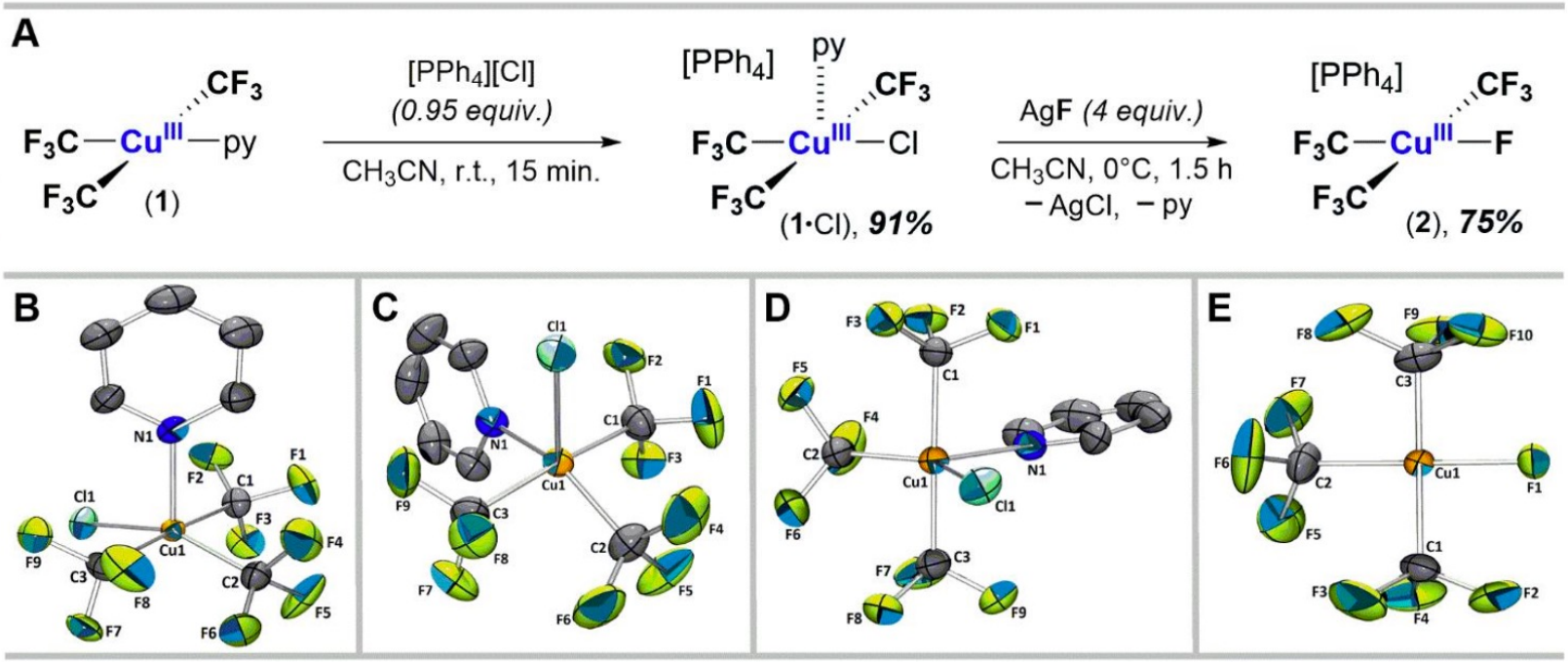
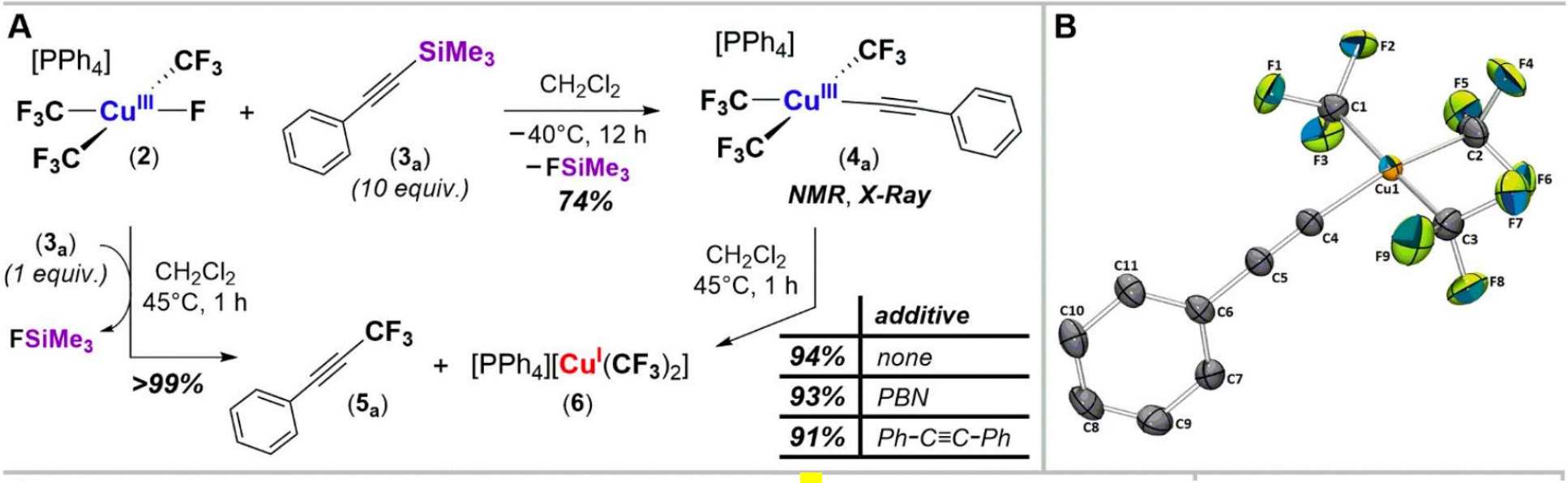
Cu(III)-Mediated C–C Formation

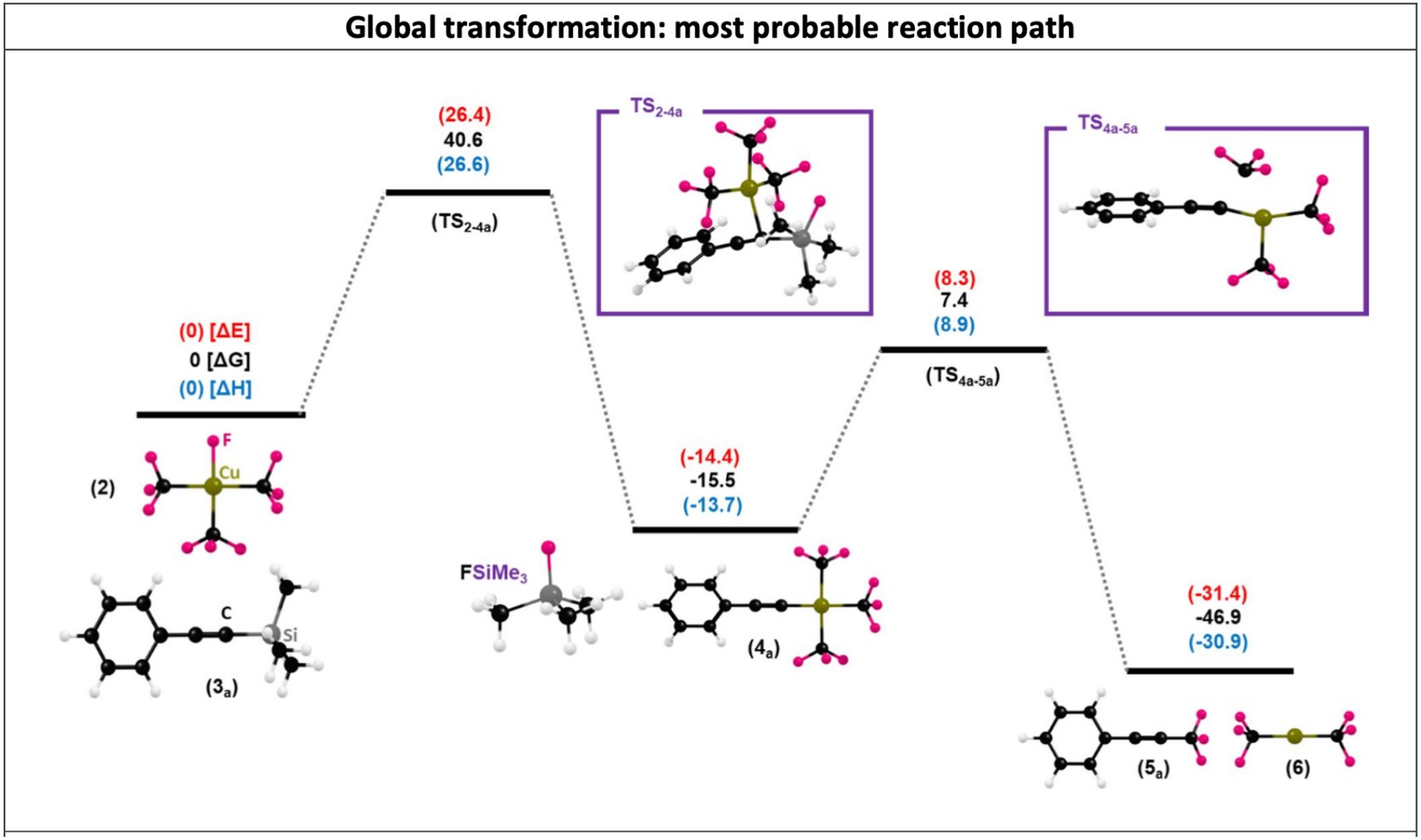
Alkyne trifluoromethylation





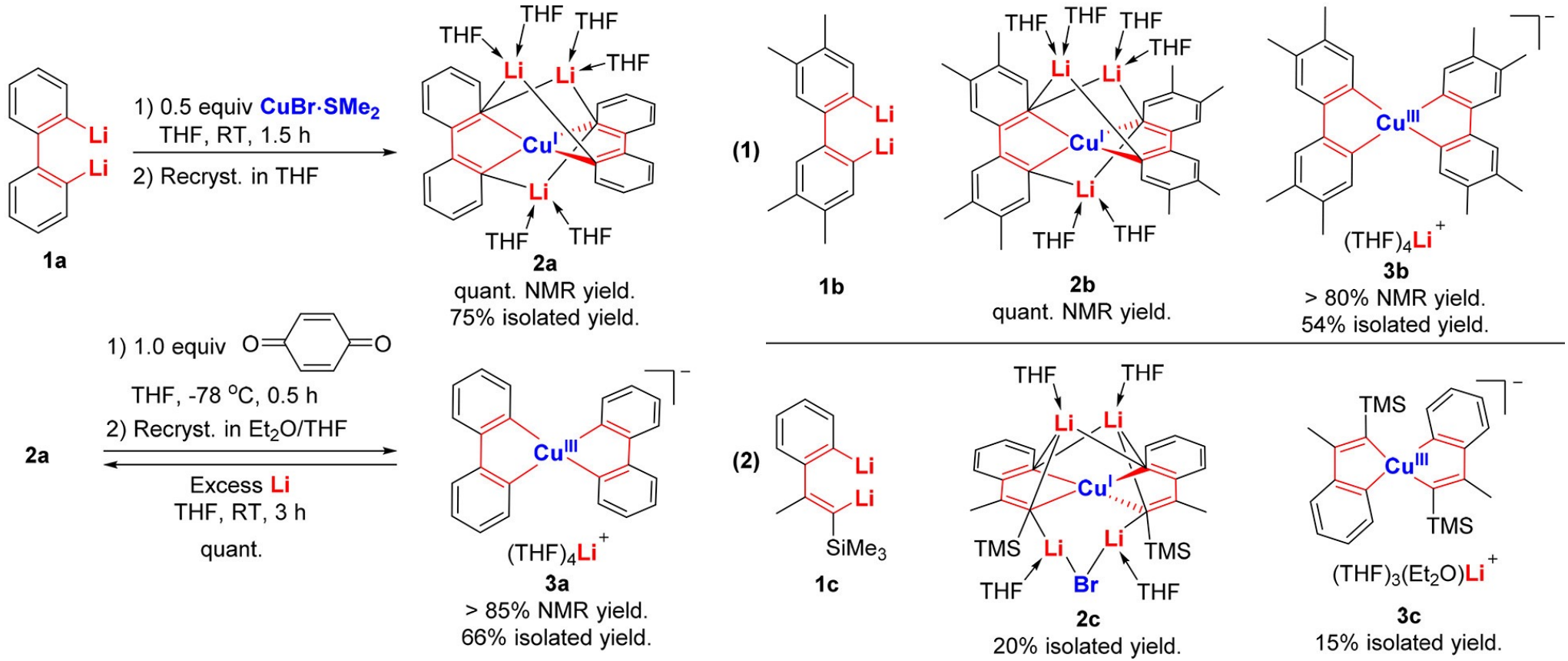
Nebra N. *et al. Angew. Chem. Int. Ed.* **2023**, e202319412.

Most Feasible Pathway (by DFT)



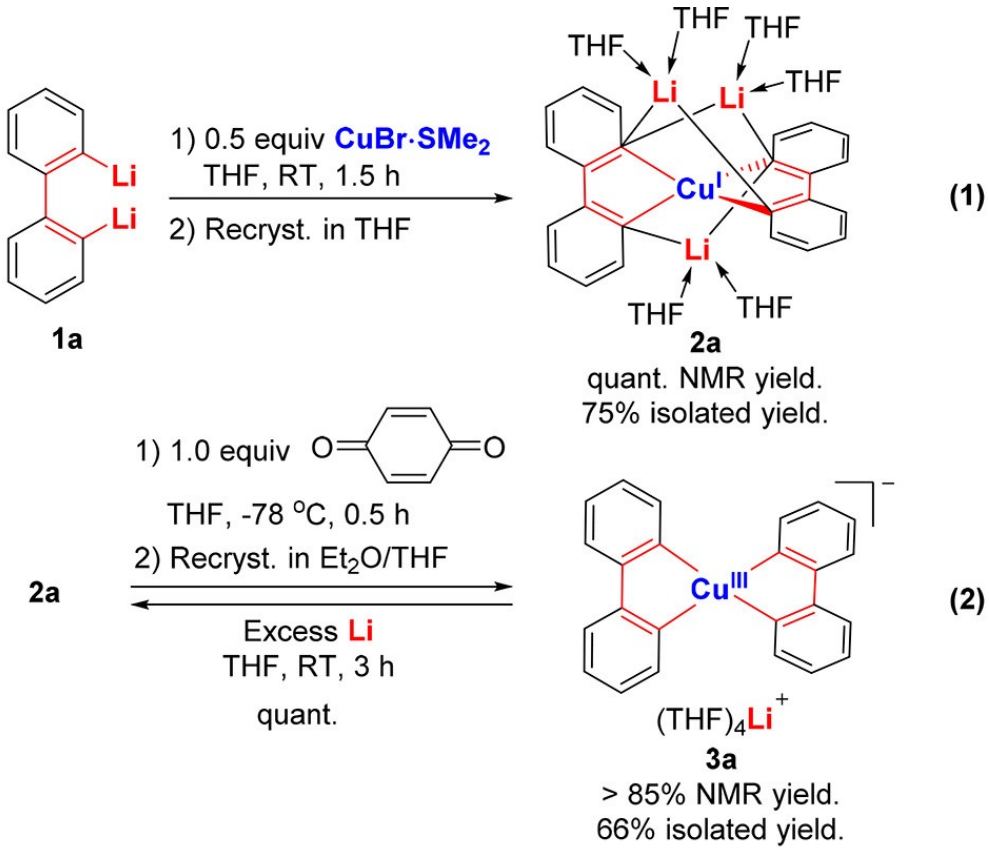
Nebra N. *et al. Angew. Chem. Int. Ed.* **2023**, e202319412.

Synthesis of organocopper(III) spiro complexes

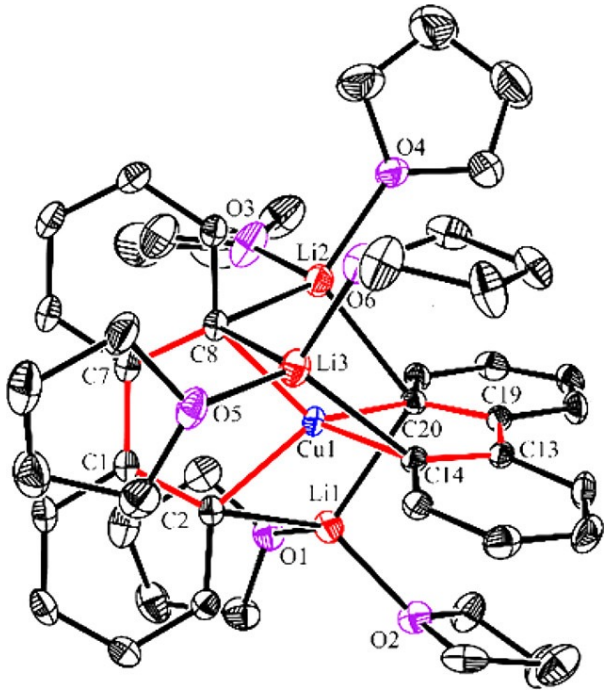


Xi Z. *et al. J. Am. Chem. Soc.* **2017**, *139*, 13688.

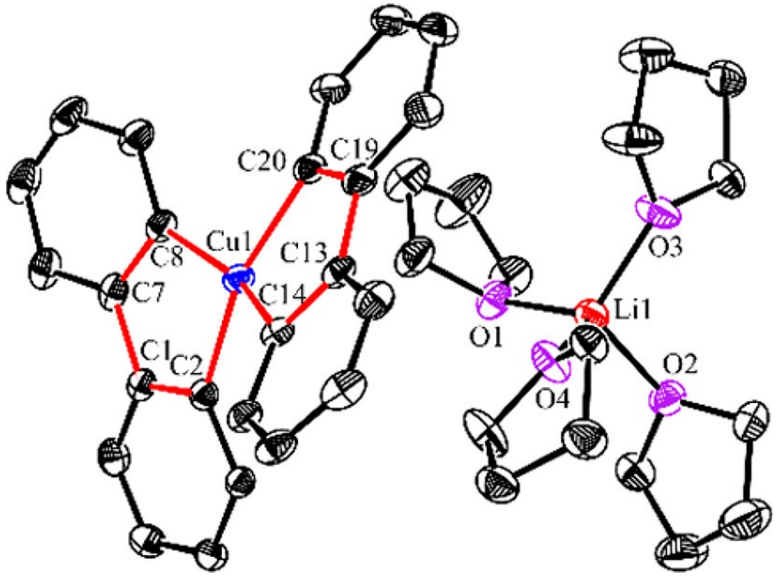
Synthesis of organocopper(III) spiro complexes



(1)

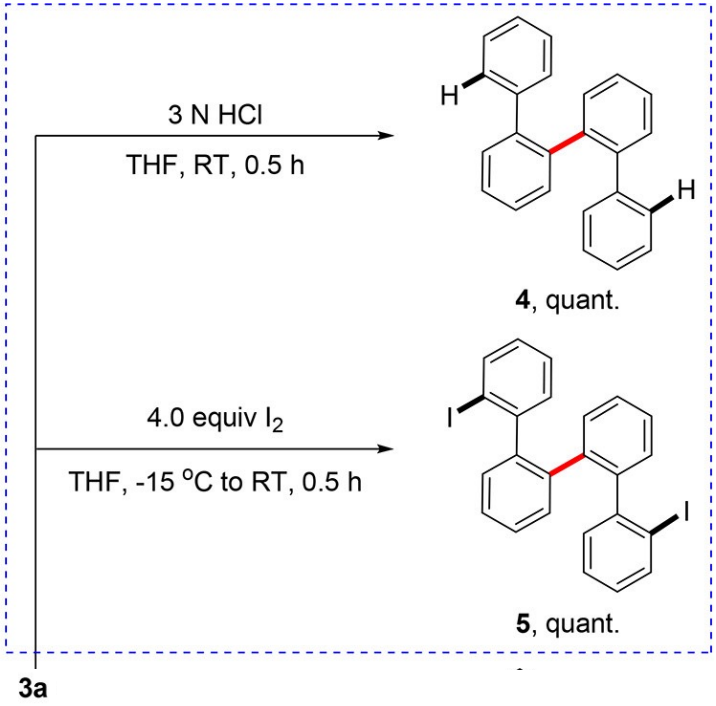


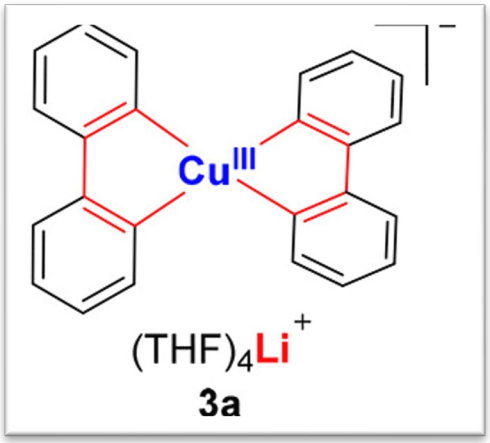
(2)

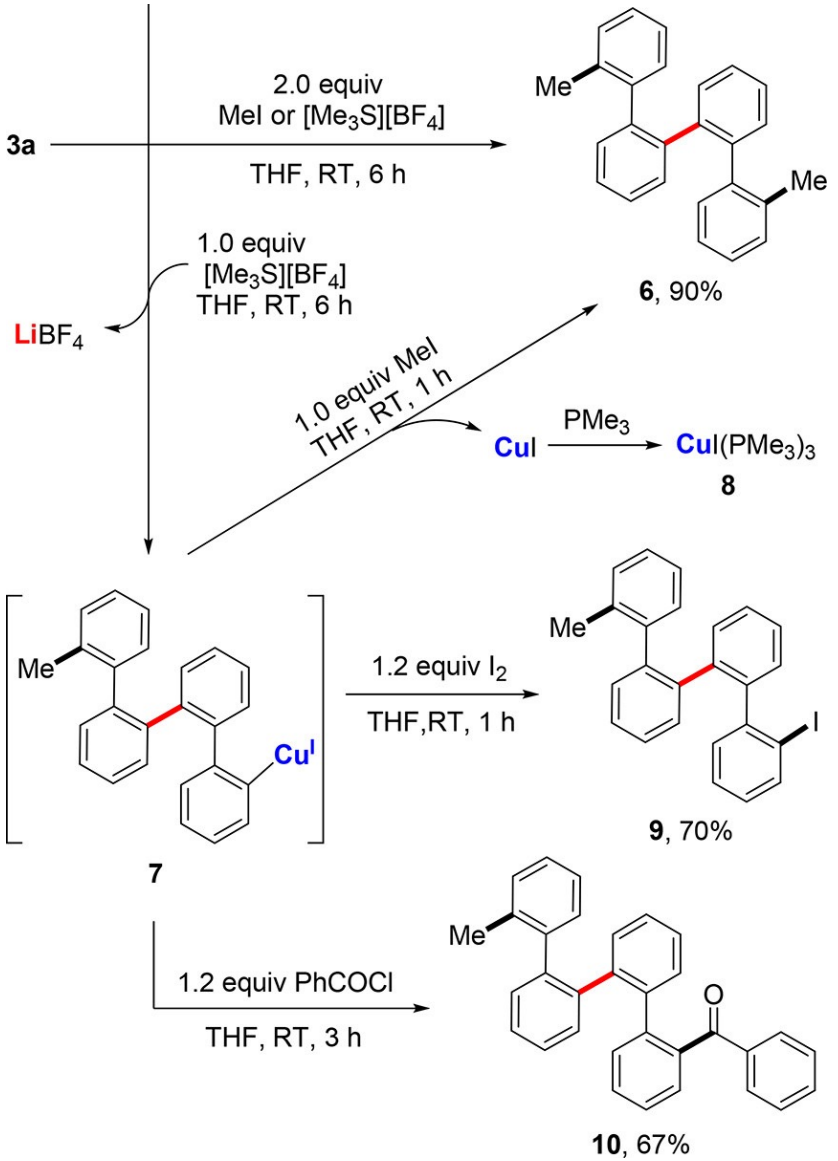


Xi Z. *et al. J. Am. Chem. Soc.* **2017**, *139*, 13688.

Reductive elimination study of **3a**



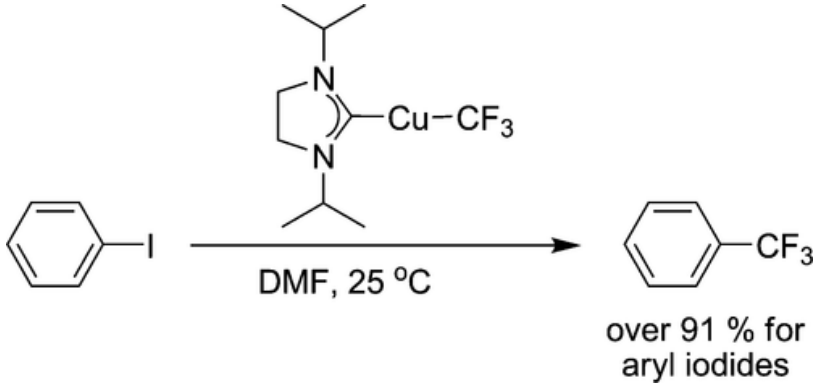




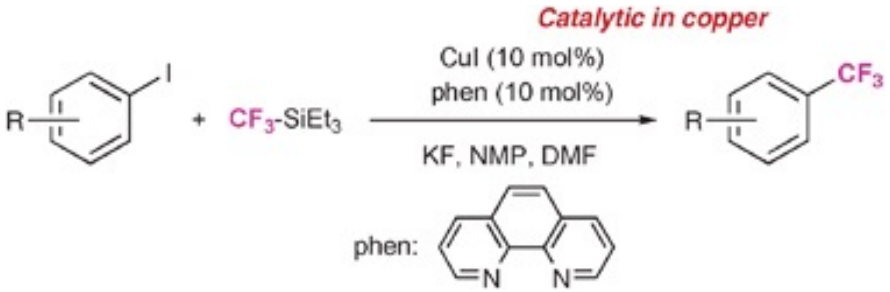
Xi Z. *et al. J. Am. Chem. Soc.* **2017**, *139*, 13688.

Arene trifluoromethylation

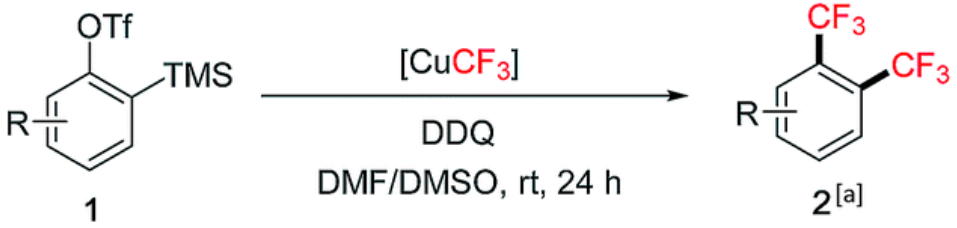
Type I: from ArX



Viciv D. A. *et al. Chem. Sci.* **2008**, *130*, 8600.



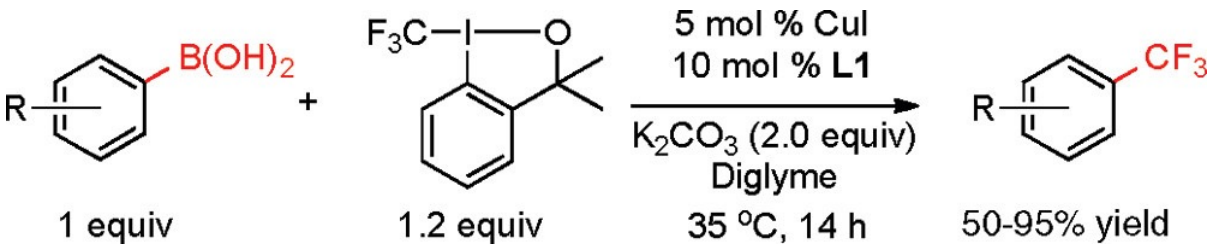
Amii H. *et al. Chem. Commun.* **2009**, 1909.



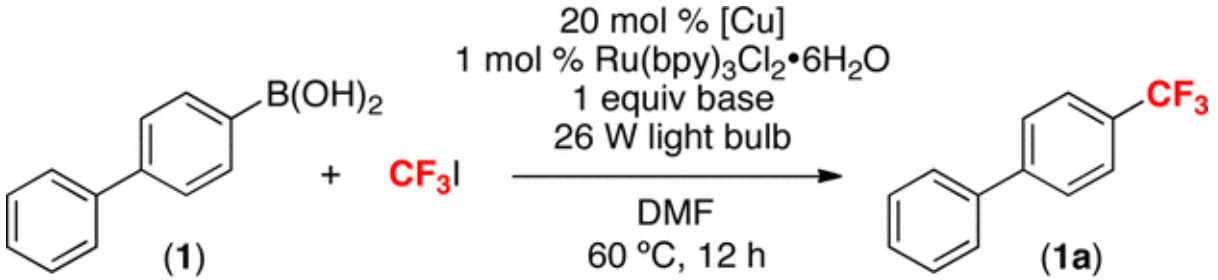
Tsui G. C. *et al. Chem. Sci.* **2018**, *9*, 8871.

Arene trifluoromethylation

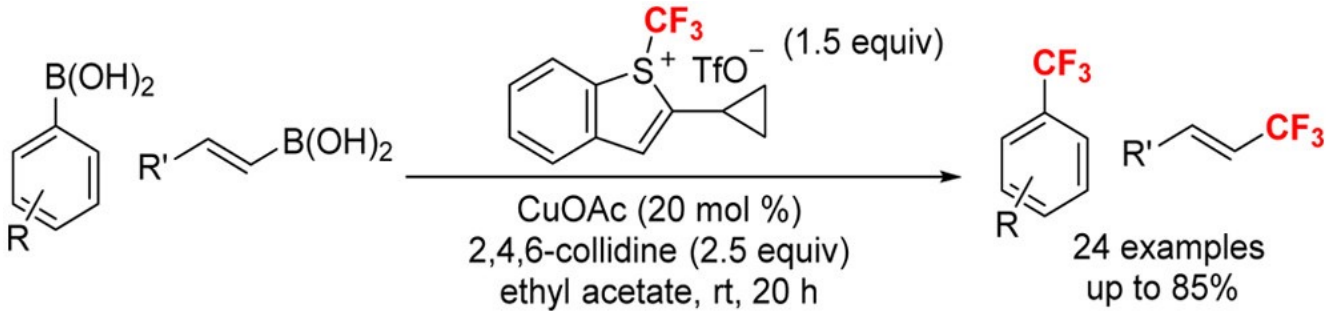
Type II: from $ArB(OH)_2$



Shen Q. *et al. Org. Lett.* **2011**, *13*, 2342.



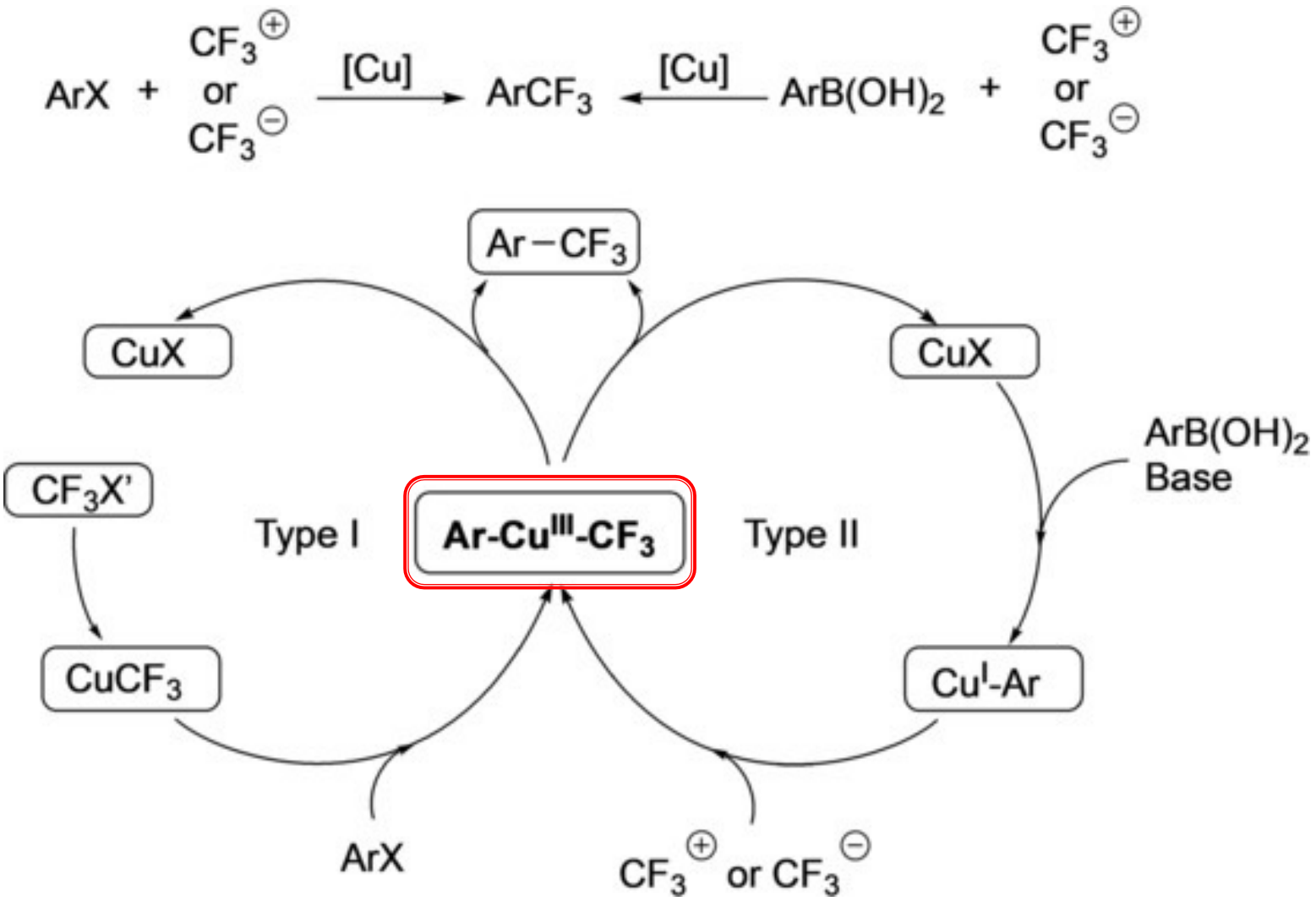
Sanford M. *et al. J. Am. Chem. Soc.* **2012**, *134*, 9034.



Shibata N. *et al. Org. Lett.* **2015**, *17*, 1632.

Arene trifluoromethylation

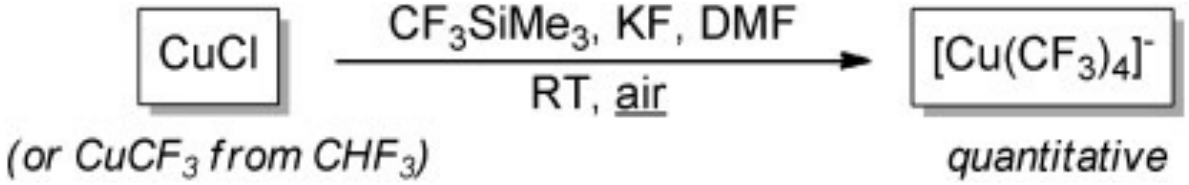
Two types of Cu-mediated arene trifluoromethylation

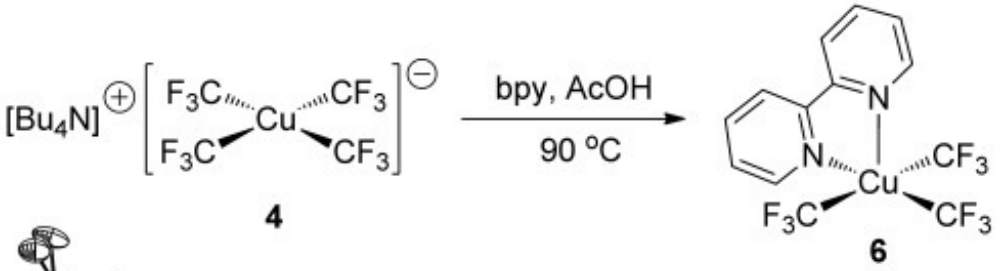


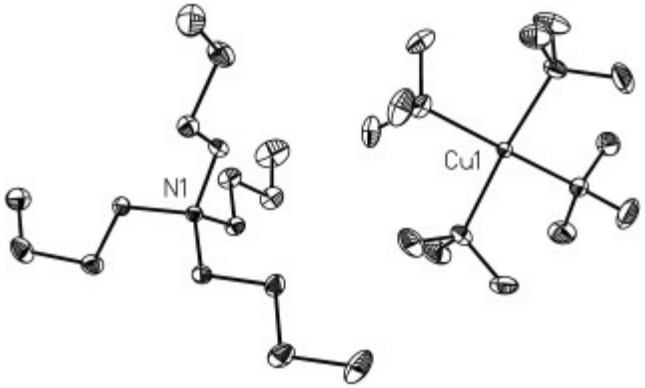
Shen Q. *et al. Angew. Chem. Int. Ed.* **2019**, *58*, 8510.

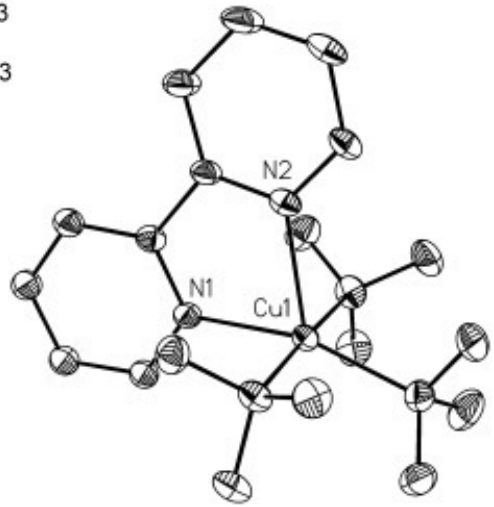
Arene trifluoromethylation

Synthesis of [(bpy)Cu^{III}(CF$_3$)$_3$] precursor





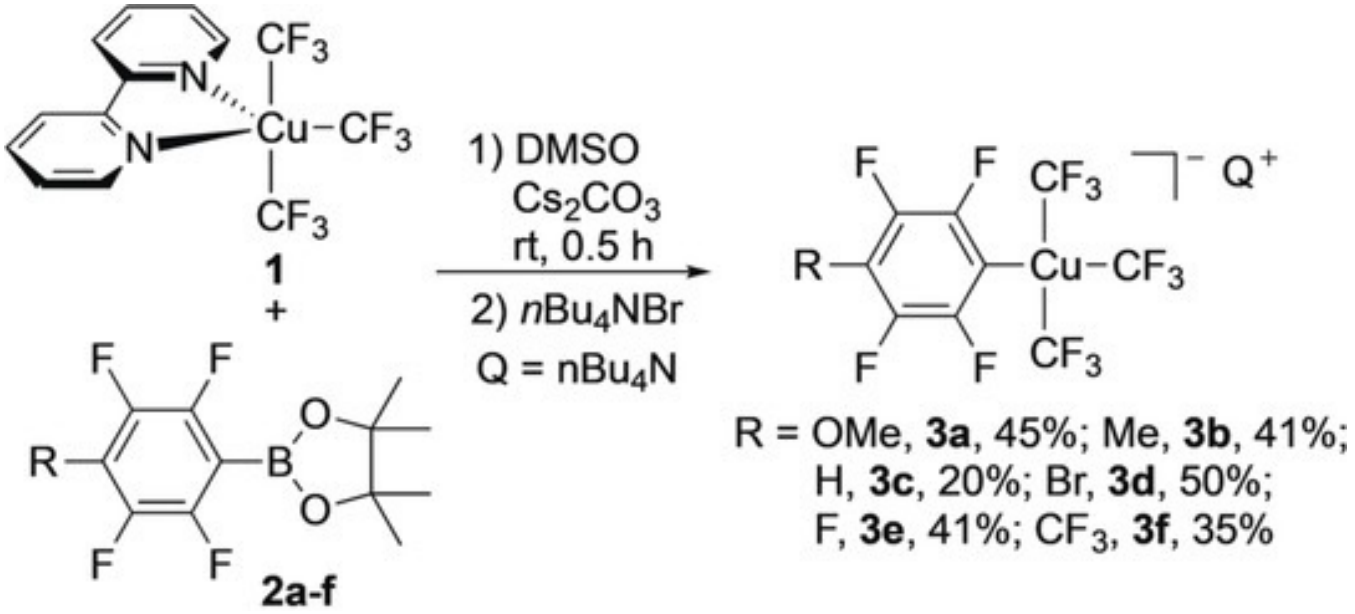




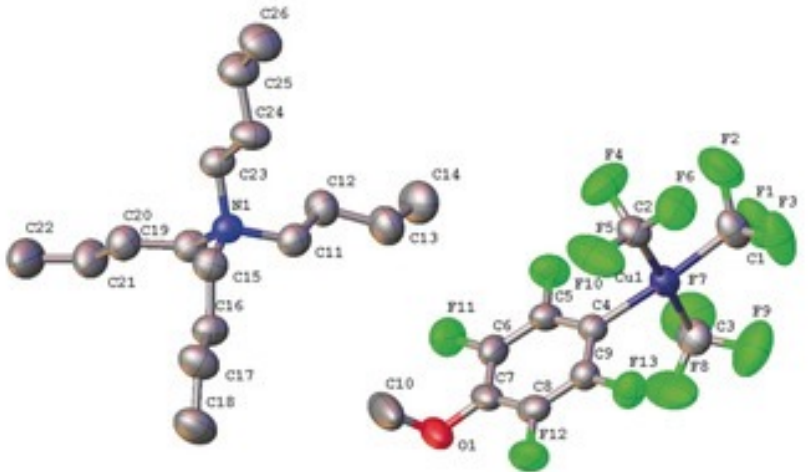
Grushin V. V. *et al. Angew. Chem. Int. Ed.* **2015**, *54*, 2745

Arene trifluoromethylation

Synthesis of [nBu$_4$N][Cu^{III}(Ar)(CF$_3$)$_3$]



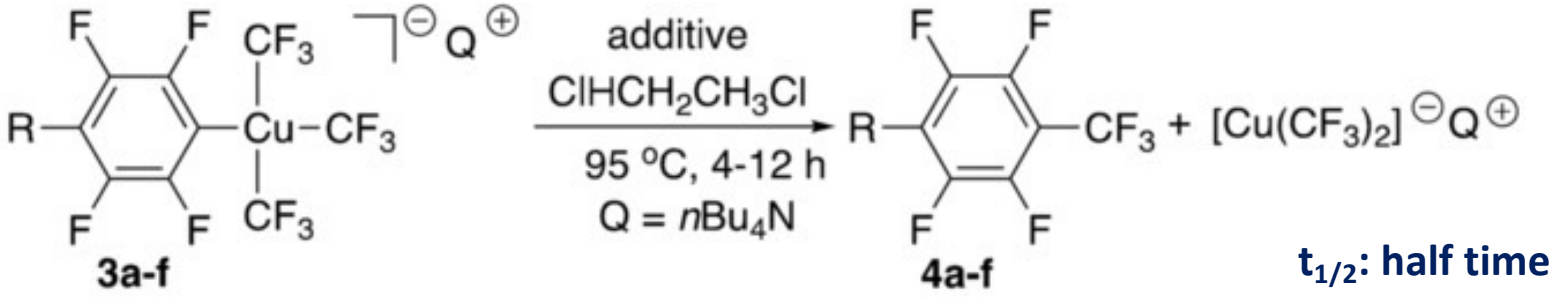
R = OMe, **3a**, 45%; Me, **3b**, 41%;
H, **3c**, 20%; Br, **3d**, 50%;
F, **3e**, 41%; CF_3, **3f**, 35%



Shen Q. *et al. Angew. Chem. Int. Ed.* **2019**, *58*, 8510.

Arene trifluoromethylation

Study on reductive elimination



$t_{1/2}$: half time

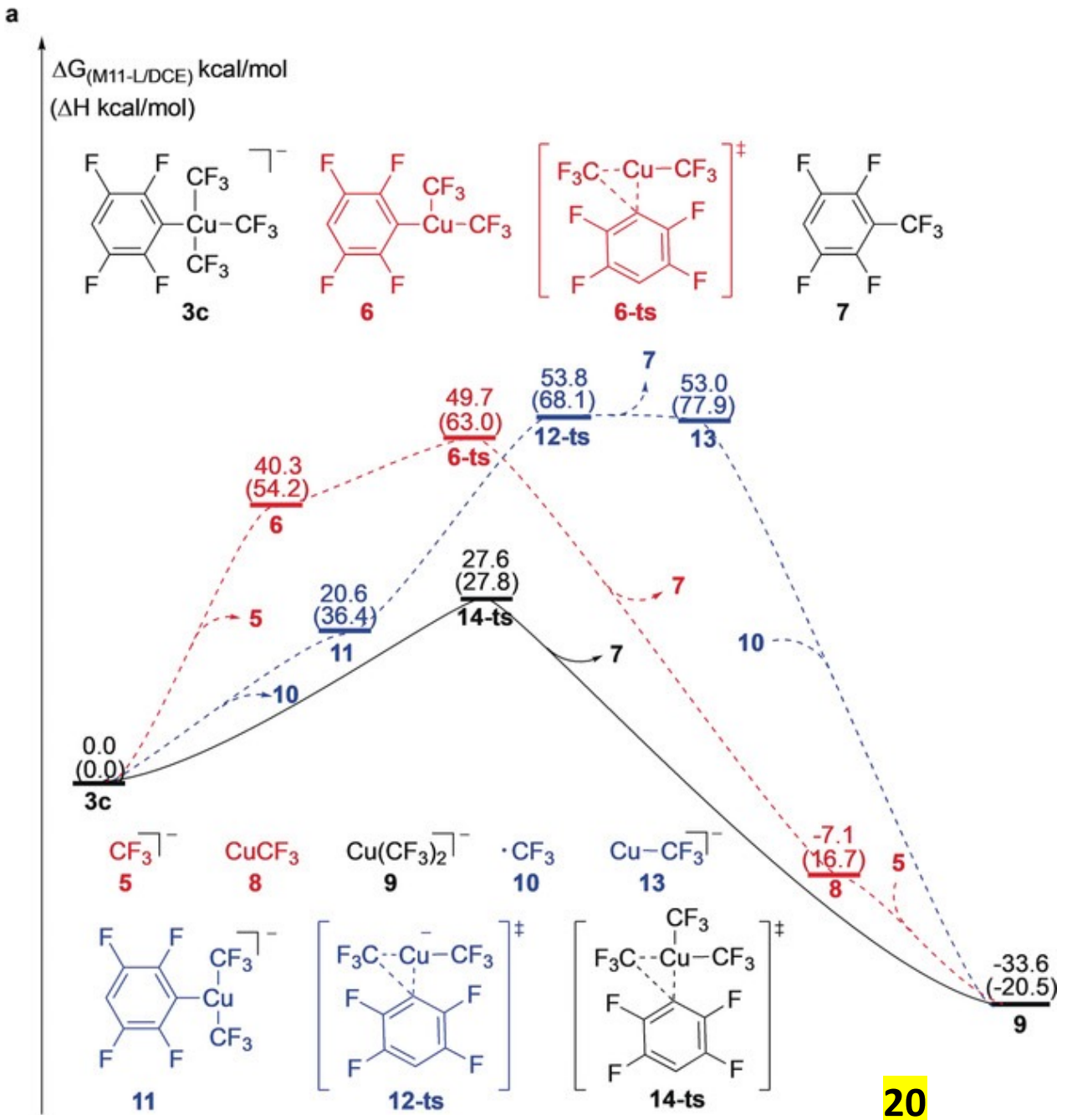
entry	R	complex **3**	additive	yield (%)	$t_{1/2}$ (min)
1	OMe	**3a**	-	99%	25.3
2	OMe	**3a**	TEMPO	79%	-
3	OMe	**3a**	1,4-dinitrobenzene	81%	-
4	Me	**3b**	-	97%	18.3
5	H	**3c**	-	95%	31.5
6	Br	**3d**	-	82%	46.7
7	F	**3e**	-	90%	53.5
8	CF_3	**3f**	-	86%	61.6

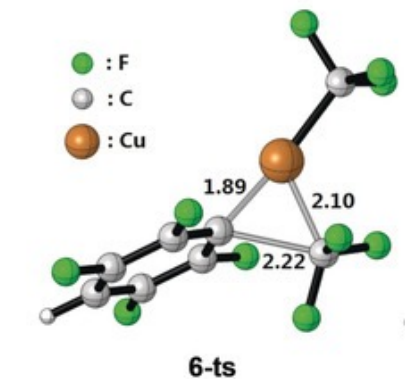
Entries 2-3: radical inhibitor didn't significantly decrease the yield

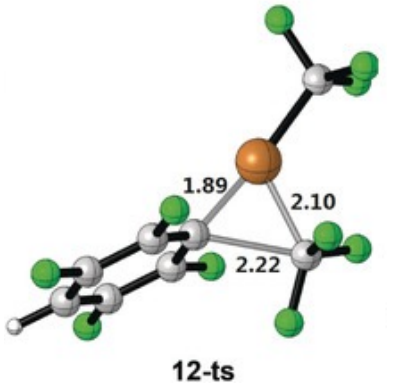
Shen Q. *et al. Angew. Chem. Int. Ed.* **2019**, *58*, 8510.

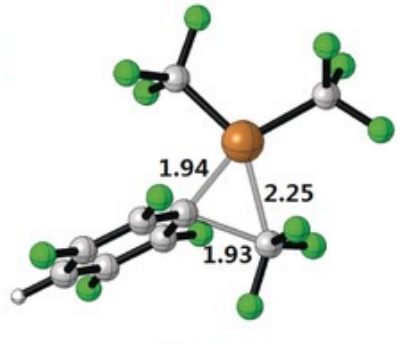
Cu(III)-Mediated C–C Formation

Computational study on reductive elimination







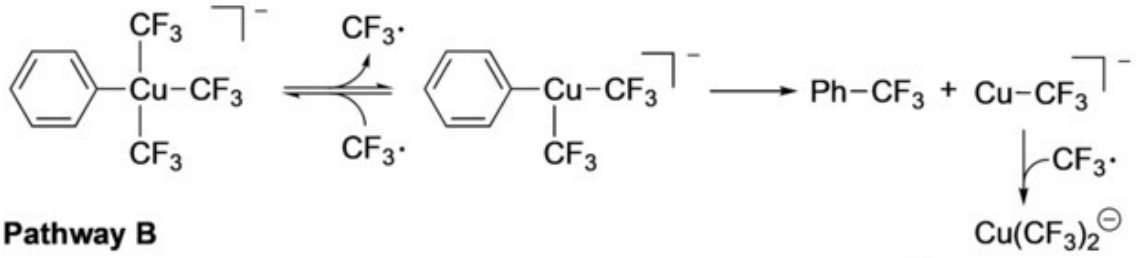


Shen Q. *et al. Angew. Chem. Int. Ed.* **2019**, *58*, 8510.

Plausible pathways

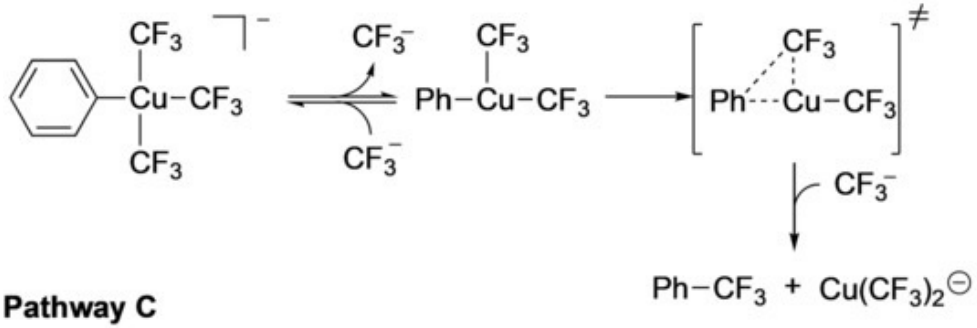
Study on reductive elimination

Pathway A



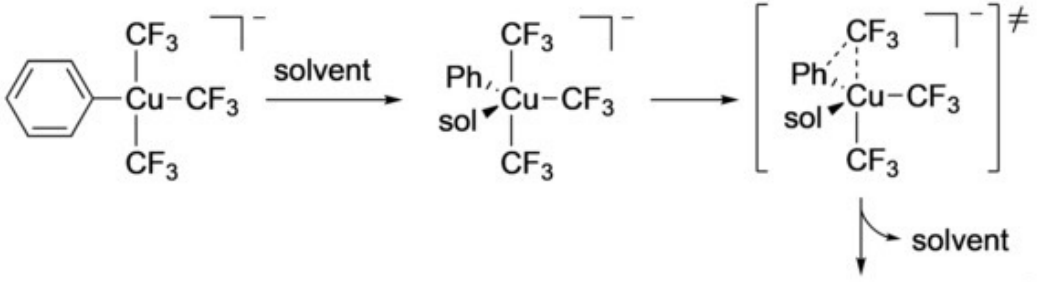
Ruled Out
Higher barrier in DFT calculation
radical inhibitor didn't significantly decrease the yield

Pathway B



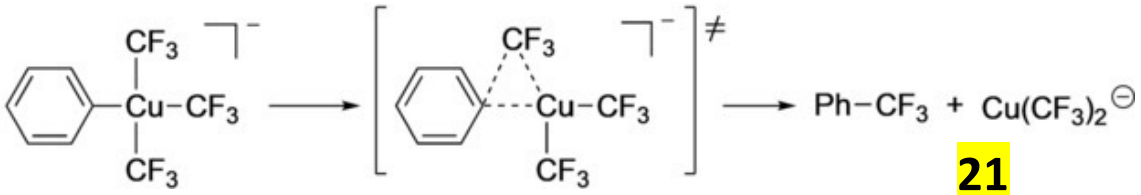
Ruled Out
Higher barrier in DFT calculation

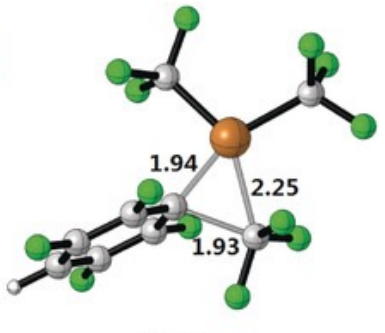
Pathway C



Ruled Out
No obvious change with various solvents.

Pathway D





14-ts

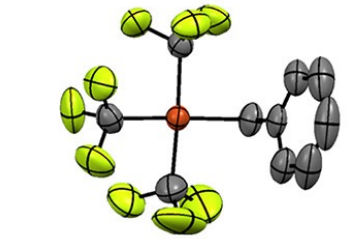
Shen Q. *et al. Angew. Chem. Int. Ed.* **2019**, *58*, 8510.

Cu(III)-Mediated C–C Formation

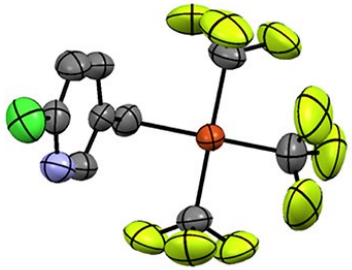
Alkane trifluoromethylation

Synthesis of $[(alkyl)Cu^{III}(CF_3)_3]^-$

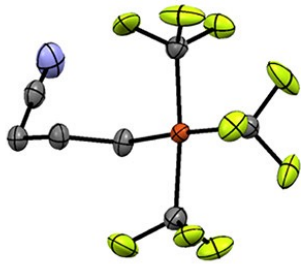
Well-identified
(XRD confirmed)



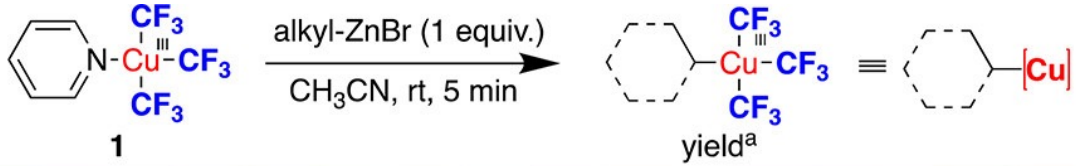
1a

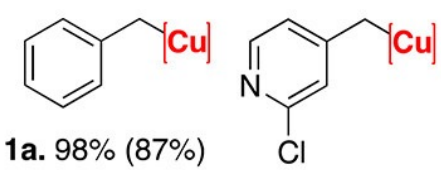


1b



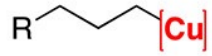
1c



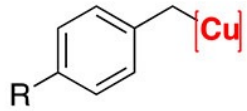


1a. 98% (87%)

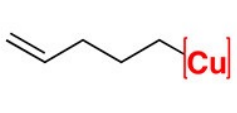
1b. 99% (91%)



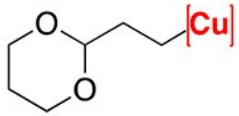
1c. R = CN, 97% (84%)
1d. R = Me, 98% (86%)
1e. R = OAc, 97% (79%)
1f. R = CH_2Cl 98% (85%)



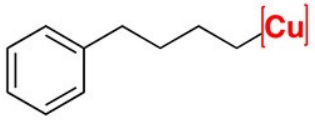
1g. R = OMe, 99% (84%)
1h. R = F, 99% (75%)
1i. R = Cl, 99% (84%)
1j. R = Me, 97% (91%)



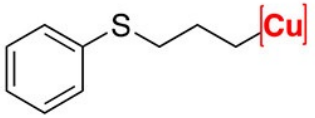
1k. 97% (84%)



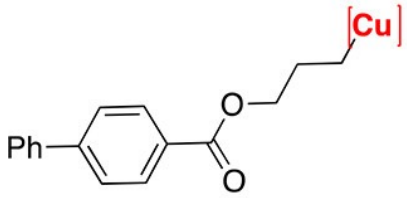
1l. 92% (76%)



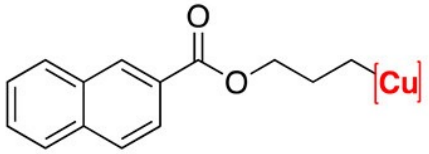
1m. 99% (94%)



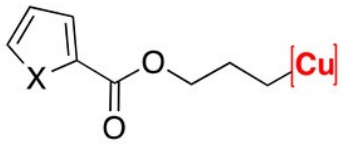
1n. 99% (87%)



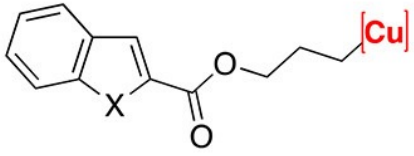
1o. 99% (92%)



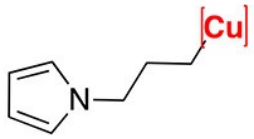
1p. 98% (88%)



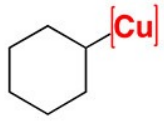
1q. X = NMe 97% (85%)
1r. X = S 98% (89%)
1s. X = O 99% (91%)



1t. X = NMe 99% (87%)
1u. X = O 98% (79%)



1v. 97% (88%)



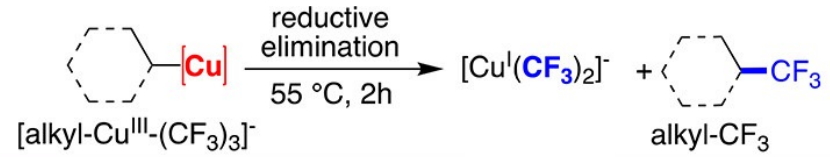
1w. 91%

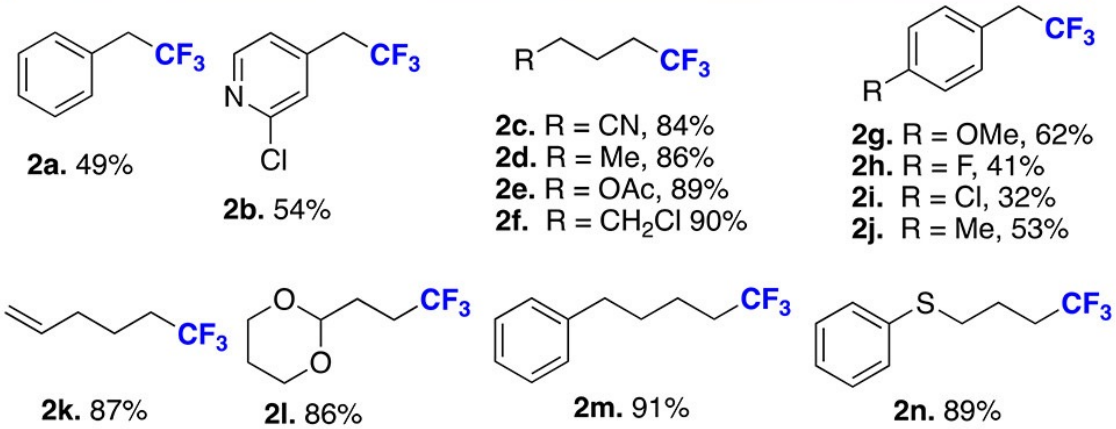
1x. 0%

Liu W. *et al. J. Am. Chem. Soc.* **2019**, *141*, 3153.

Alkane trifluoromethylation

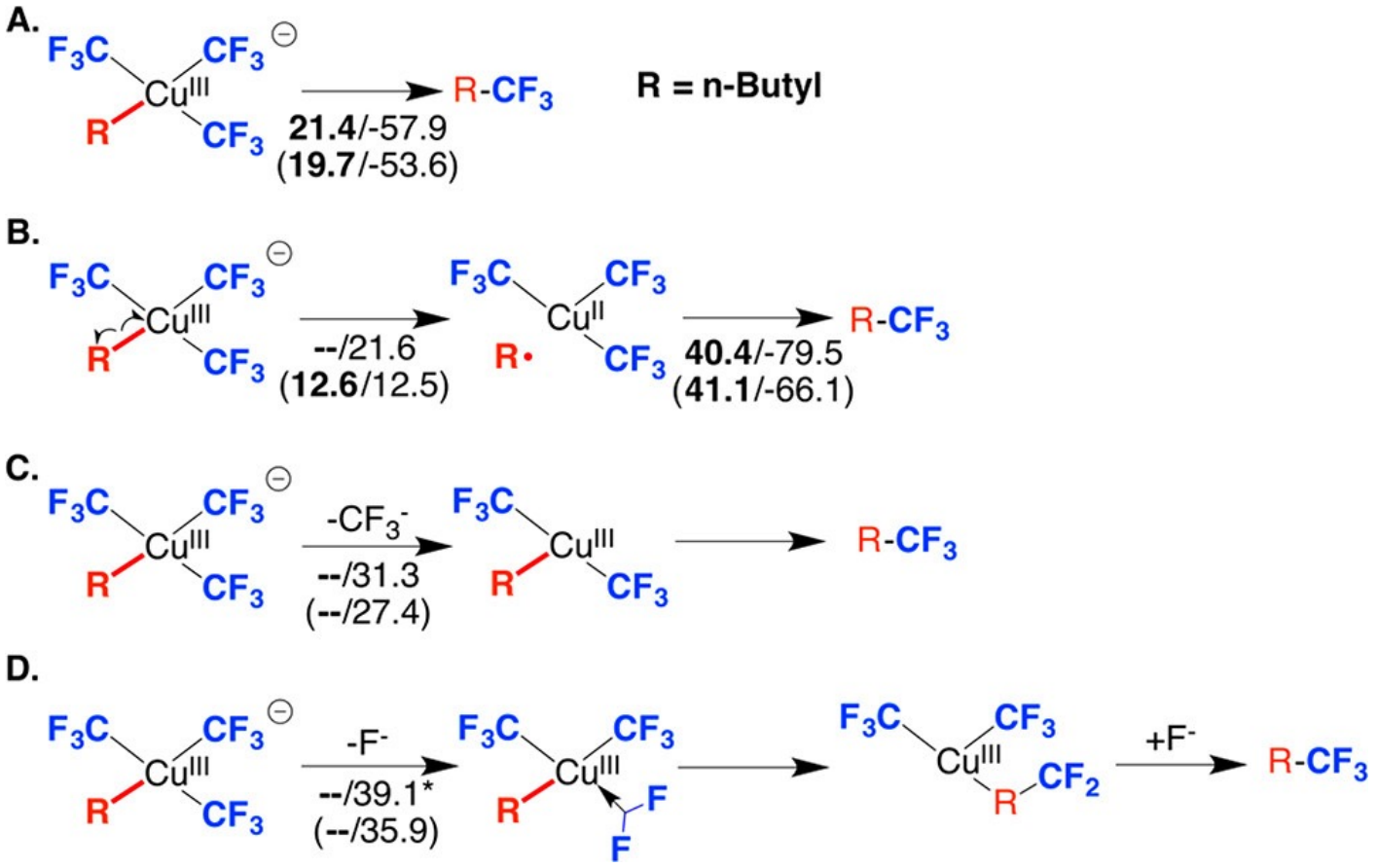
Reductive elimination of $[(alkyl)Cu^{III}(CF_3)_3]^-$





Liu W. *et al. J. Am. Chem. Soc.* **2019**, *141*, 3153.

Plausible pathways suggested by DFT calculation

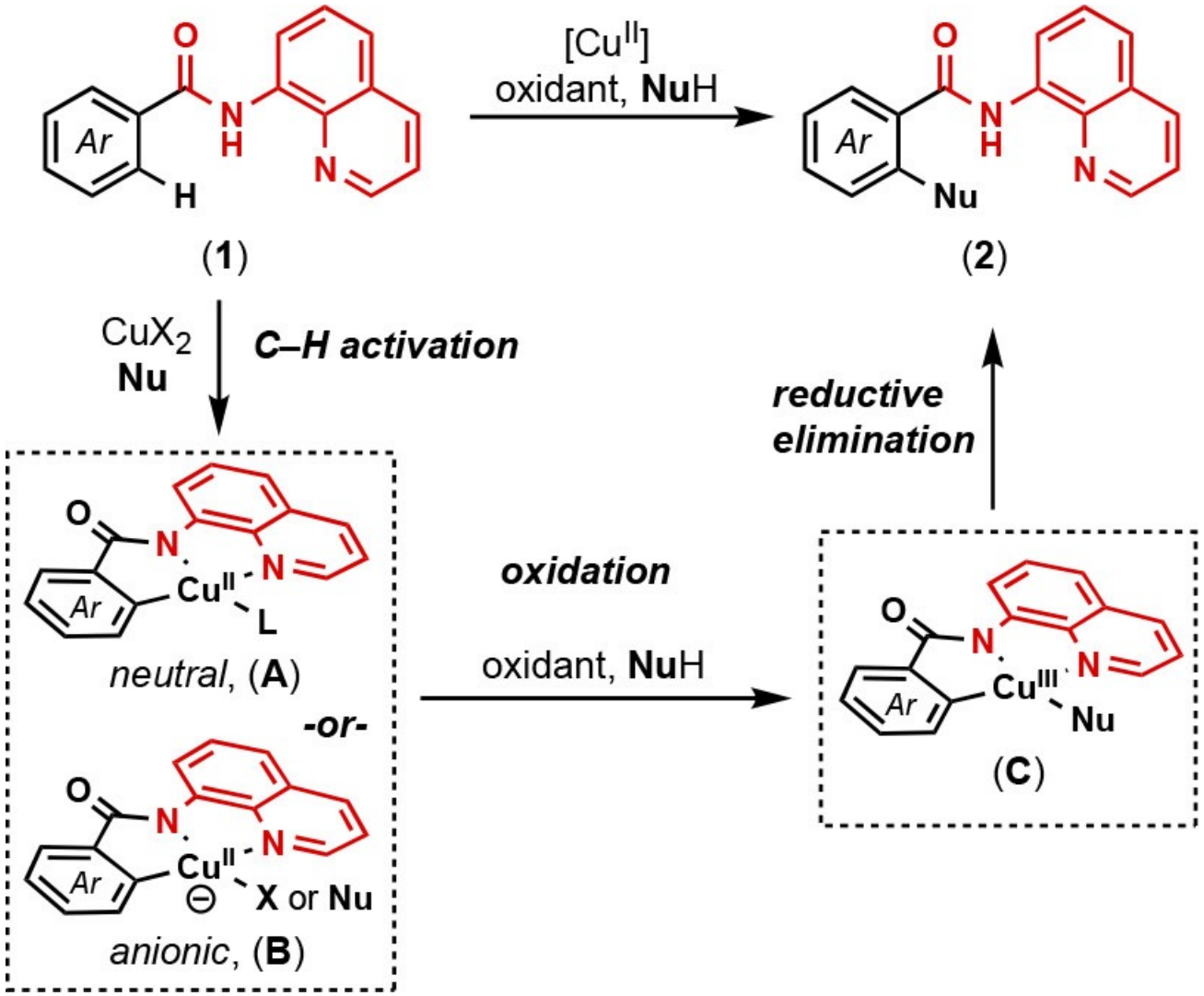


Numbers in **bold style** are $H^{\ddagger}$ values, whereas those in plain style are ΔH values.

Liu W. *et al. J. Am. Chem. Soc.* **2019**, *141*, 3153.

Cu(III)-Mediated C–H Activation

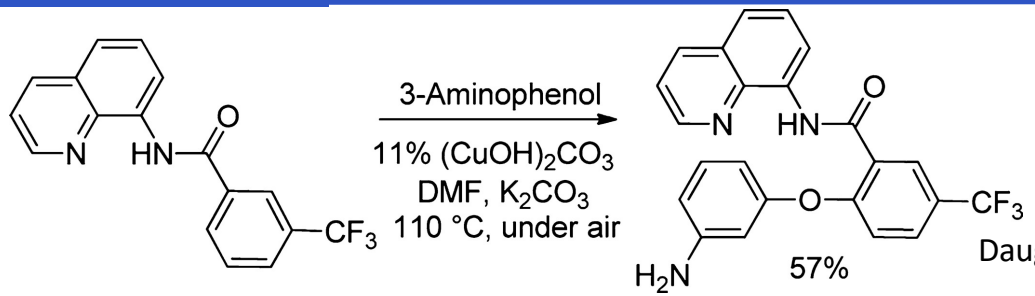
Proposed intermediates in Cu-mediated C–H activation



Sanford M. *et al. J. Am. Chem. Soc.* **2023**, *145*, 18253.

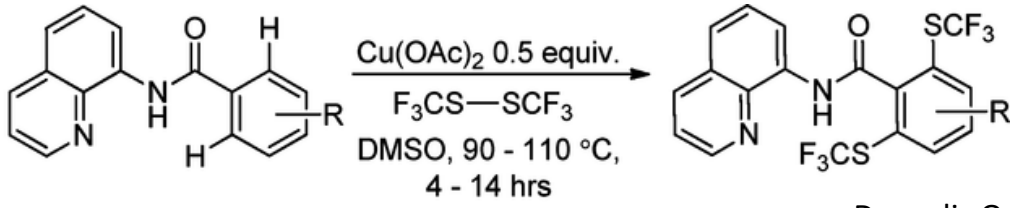
Applications on functionalization

C–H etherification



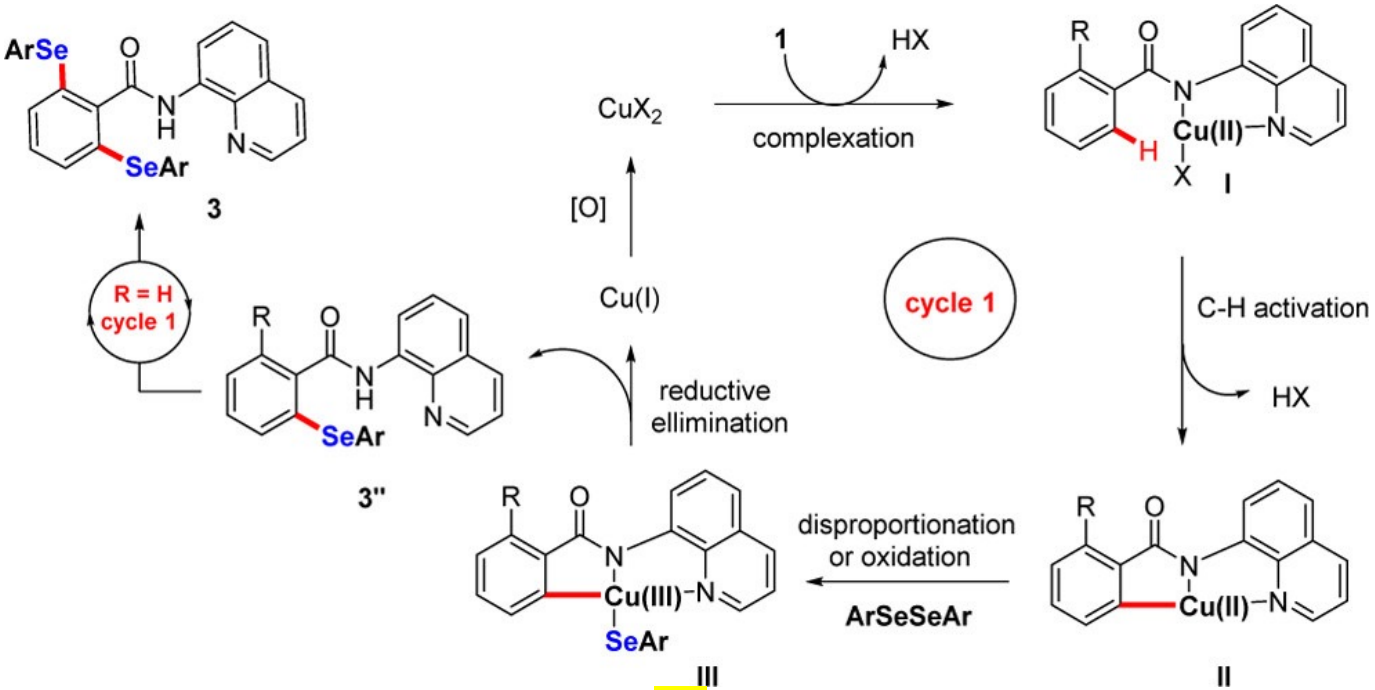
Daugulis O. *et al Org. Lett.* **2013**, *15*, 5842.

C–H sulfenylation



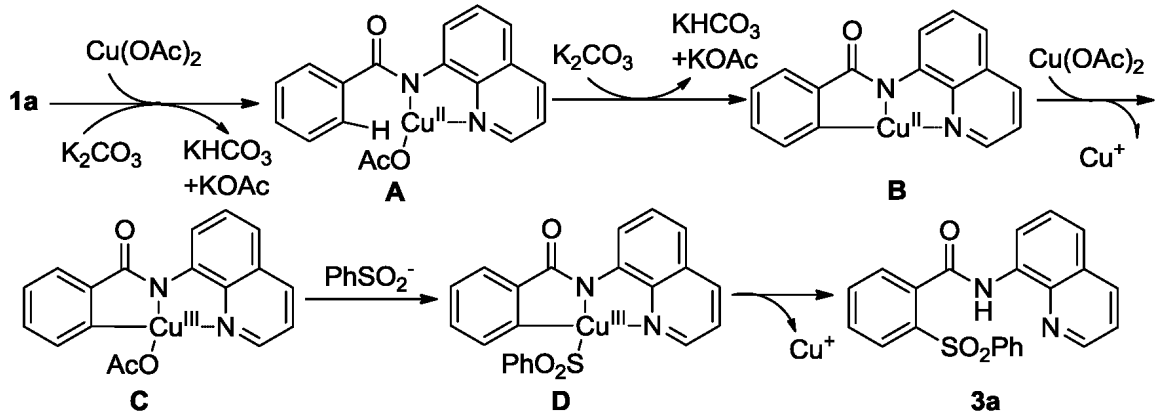
Daugulis O. *et al J. Am. Chem. Soc.* **2012**, *134*, 18237.

C–H selenylation



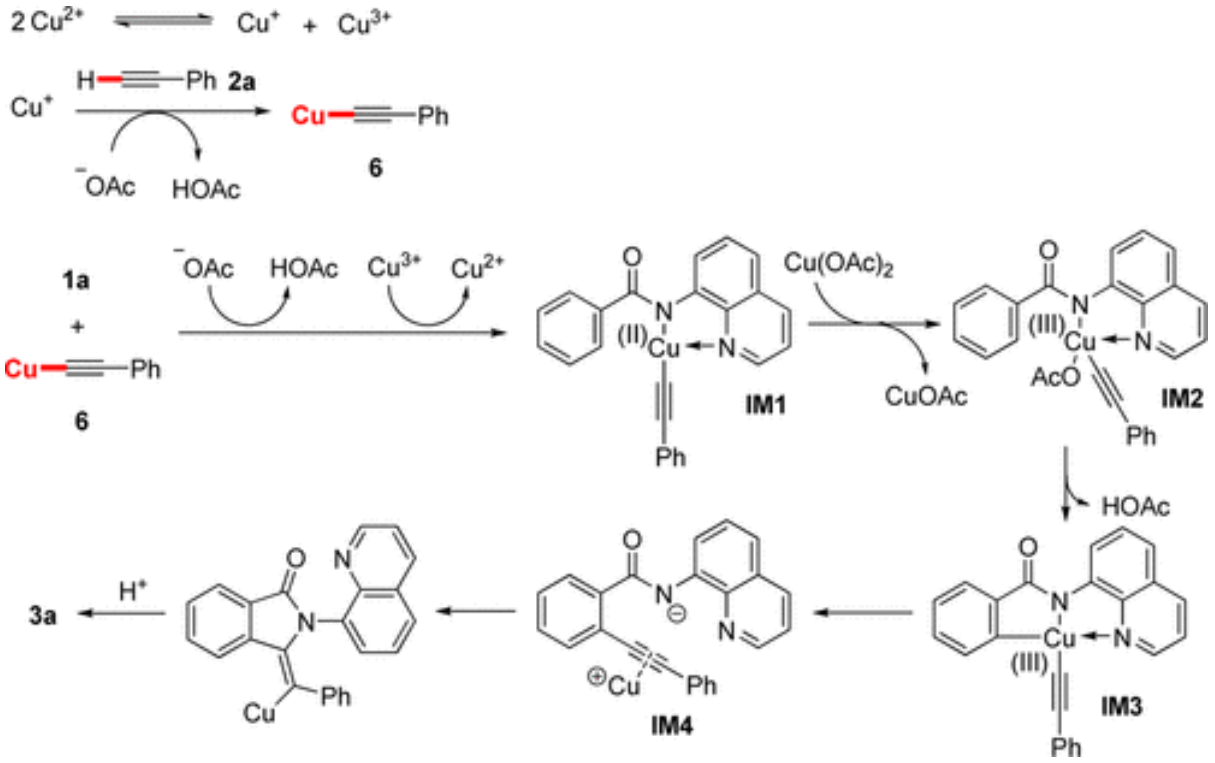
Baidya M. *et al. Org. Lett.* **2016**, *18*, 3202

C–H sulfonylation



Tan Z. *et al Chem. Commun.* **2015**, *51*, 6418.

C–H Alkynylation

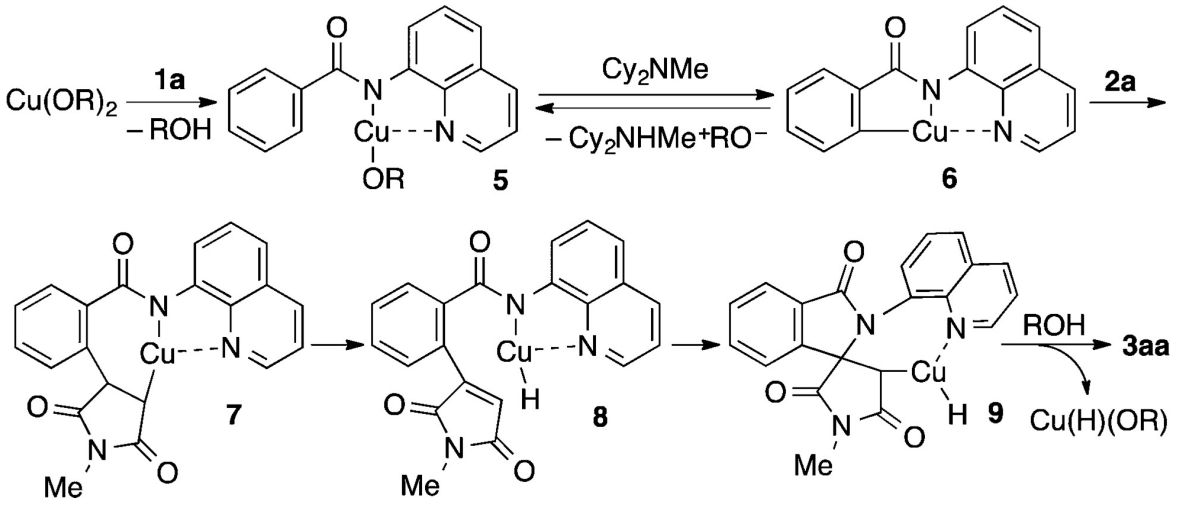


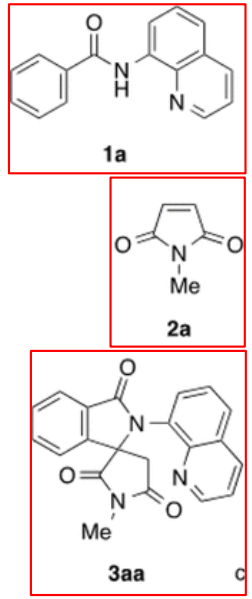
You J. *et al. Org. Lett.* **2014**, *16*, 2884.

Cu(III)-Mediated C–H Activation

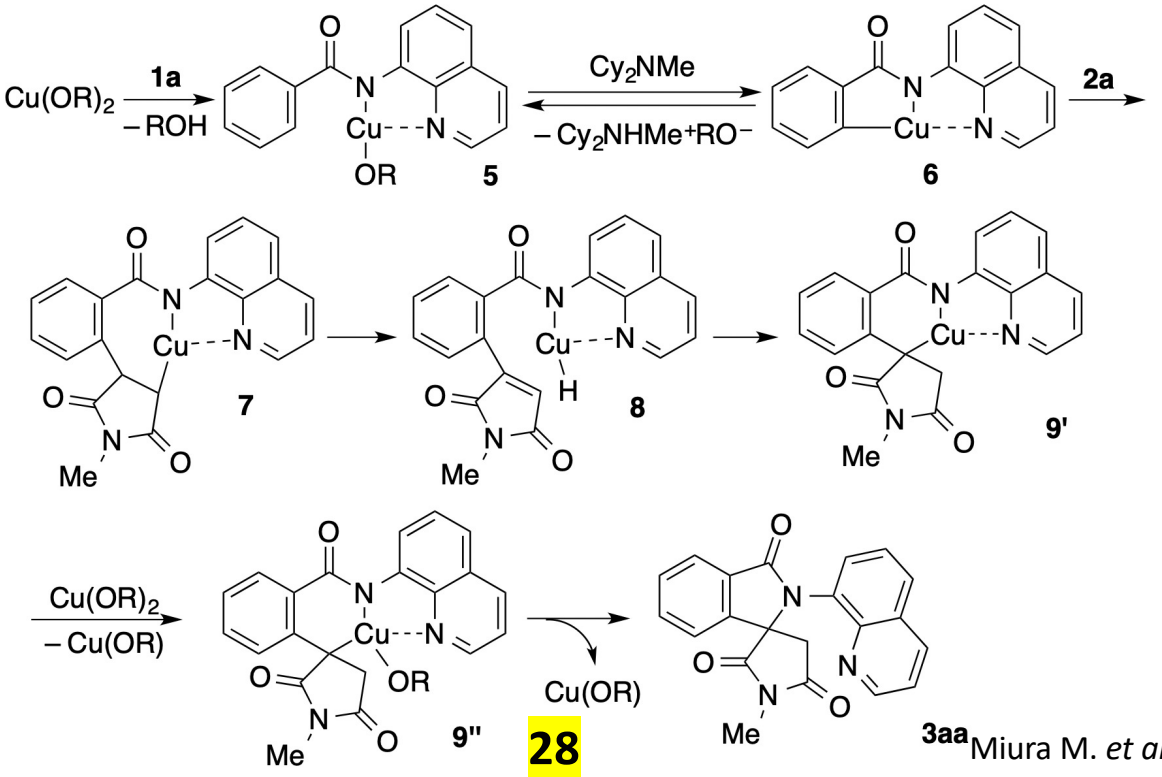
Oxidative coupling via C–H cleavage

Cu(II)-mediated pathway



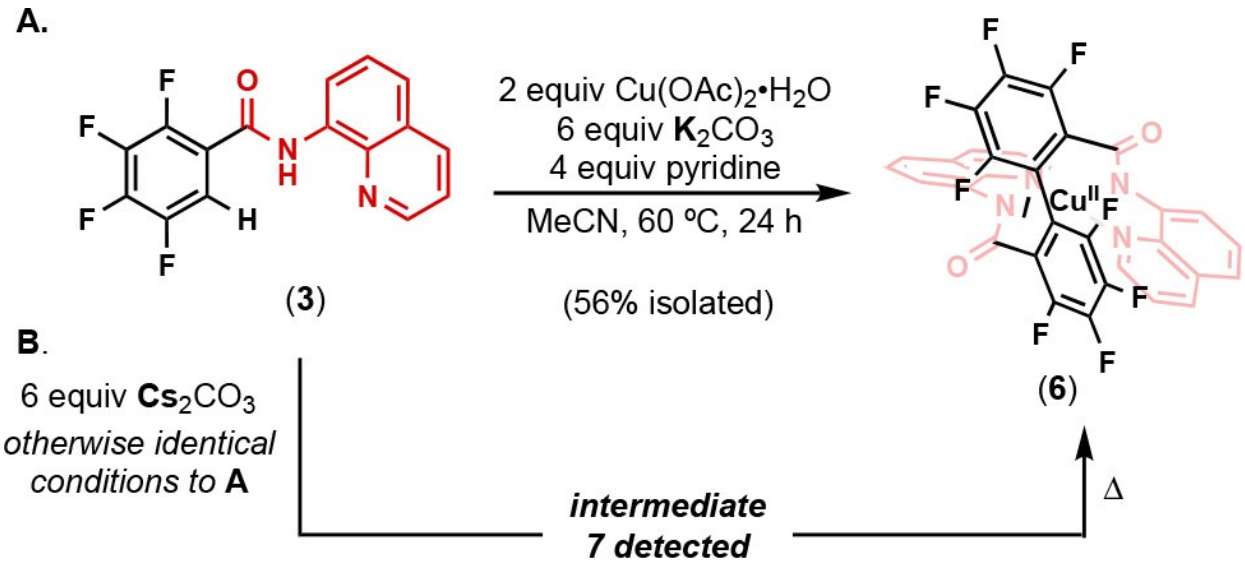


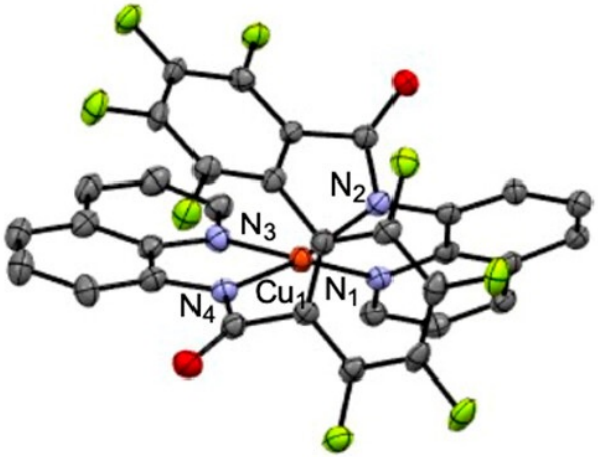
Cu(III)-mediated pathway

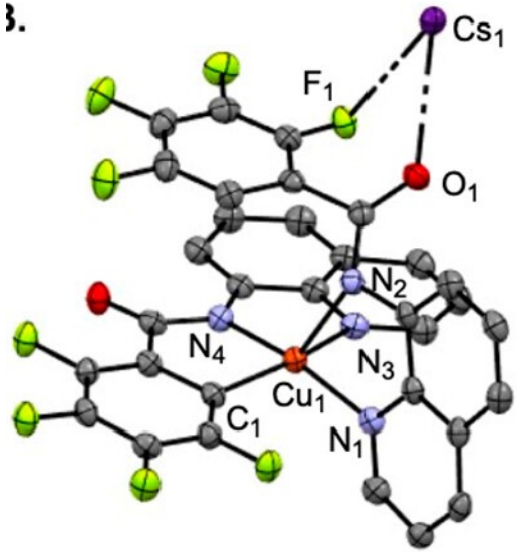


3aa Miura M. *et al. Org. Lett.* **2015**, *17*, 4034.

Synthesis of [TBA][L–Cu(II)–Ar^{F5}] (**A**)







[TBA][L–Cu(II)–Ar^{F5}] (**A**)

Sanford M. *et al. J. Am. Chem. Soc.* **2023**, *145*, 18253.

Cu(III)-Mediated C–H Activation

Conversion of **7** to **6**

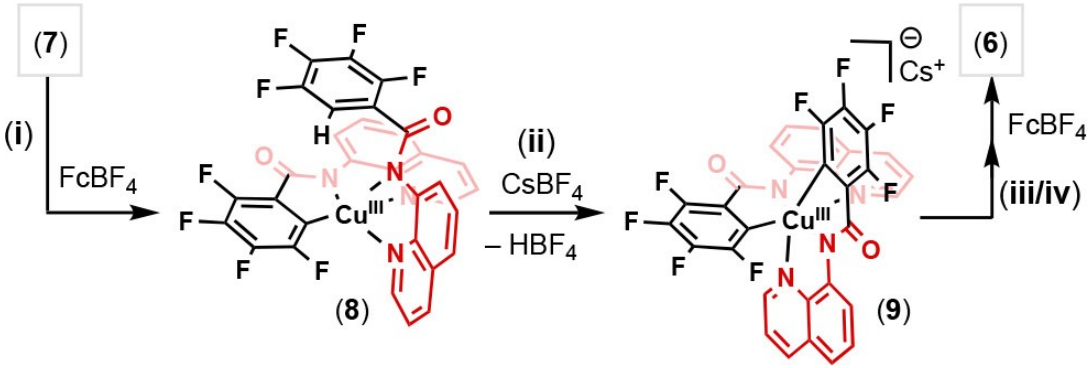
Oxidatively induced conversion

$$7 \xrightarrow[\text{conditions}]{\text{2 equiv oxidant}} 6$$

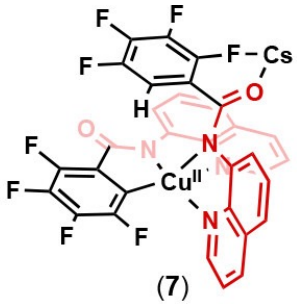
entry	oxidant	conditions	yield **6** (%)[a]
1	$FcBF_4$	25 °C, <5 min	90
2	$AgBF_4$	25 °C, <5 min	97
3	$Cu_2(OAc)_4(py)_2$	60 °C, 24 h	97

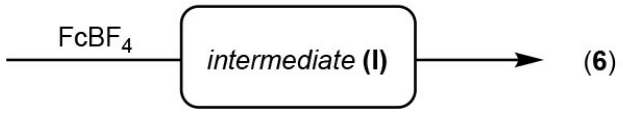
[a]Yields were determined by ^{19}F NMR spectroscopy based on an internal standard.

Plausible pathway

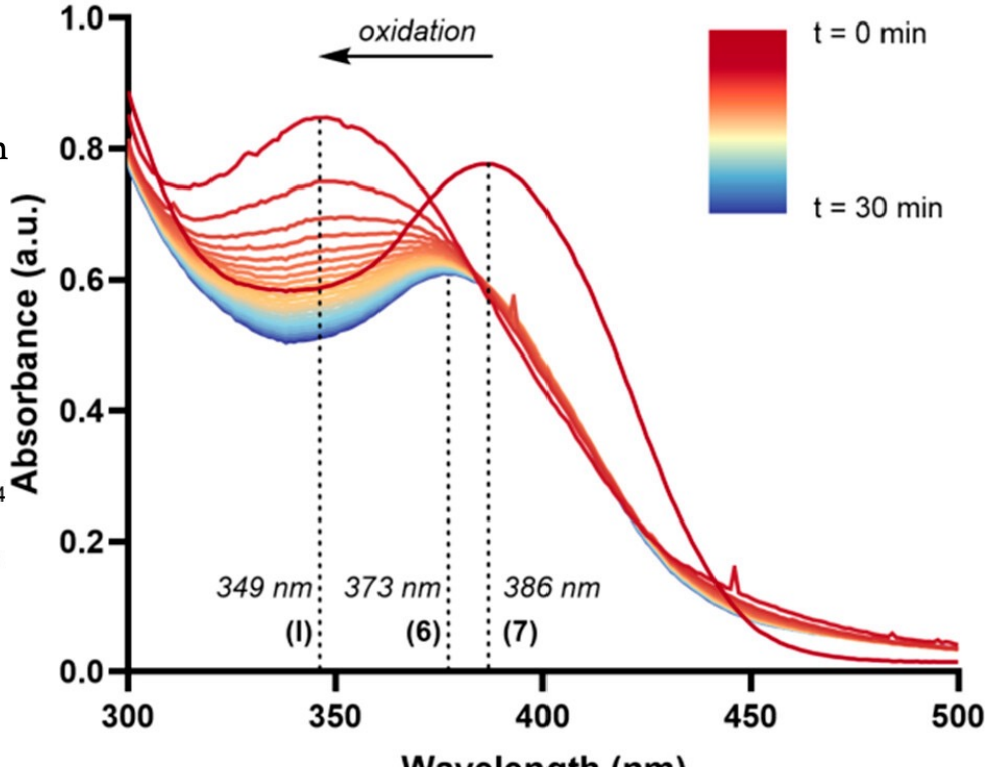


Assignment of intermediate **I** to be **8**





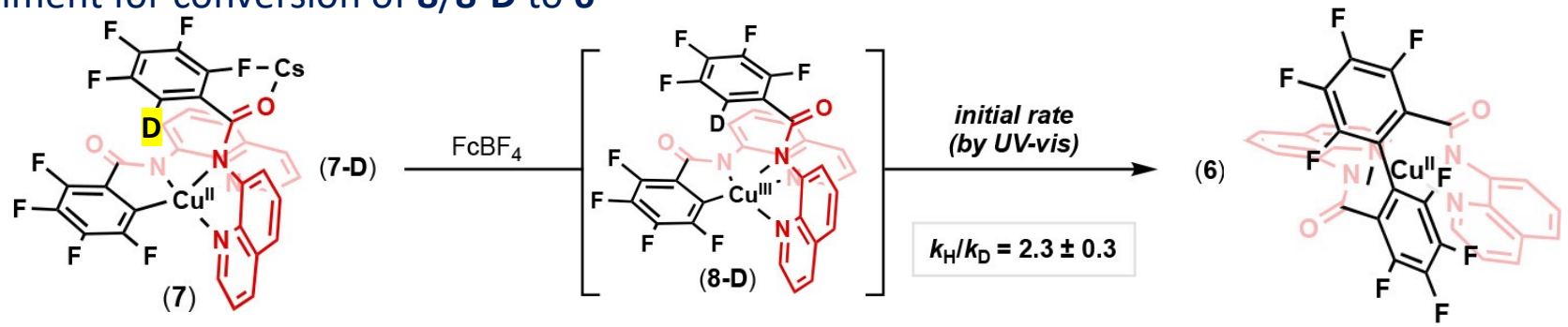
- λ_{max} = 349 nm (**UV-vis**)
- diamagnetic (**^{19}F, ^{1}H NMR**)
- 7 resonances integrating to 8F (**^{19}F NMR**)
- C–H at 6.75 ppm (**^{1}H NMR**)
- ***assigned as Cu^{III} complex 8***



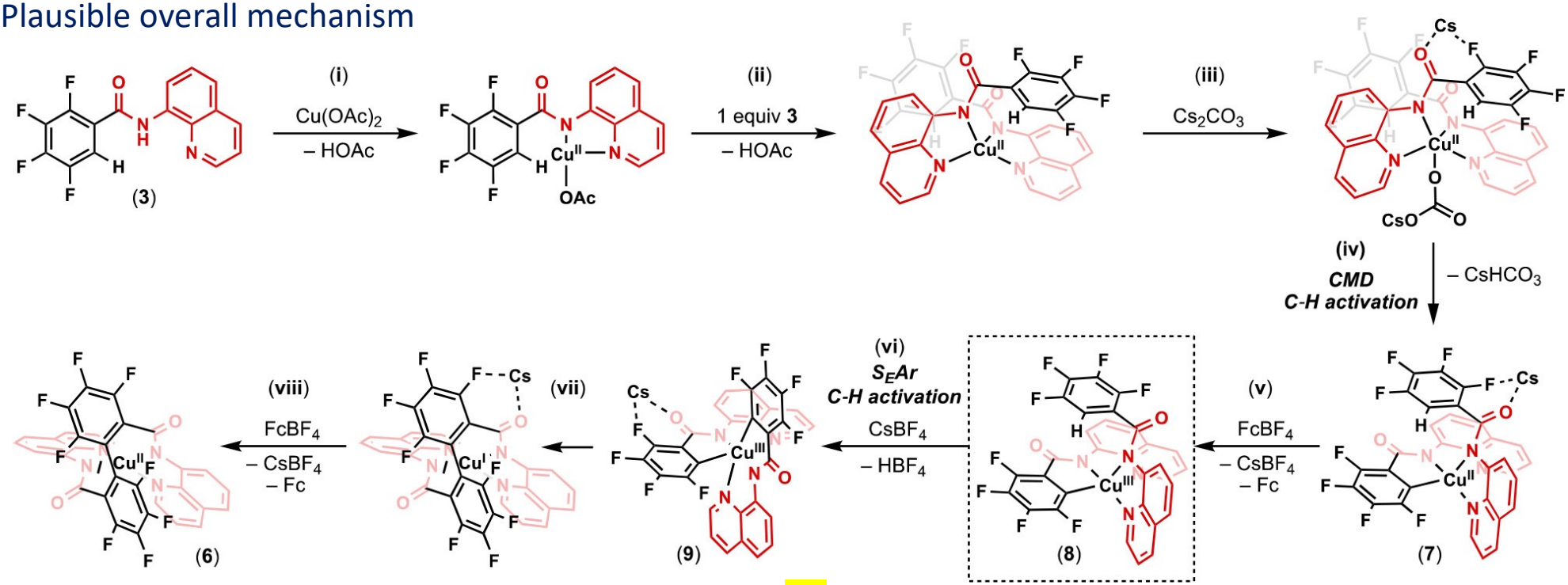
Sanford M. *et al. J. Am. Chem. Soc.* **2023**, *145*, 18253.

Cu(III)-Mediated C–H Activation

KIE experiment for conversion of **8**/**8-D** to **6**



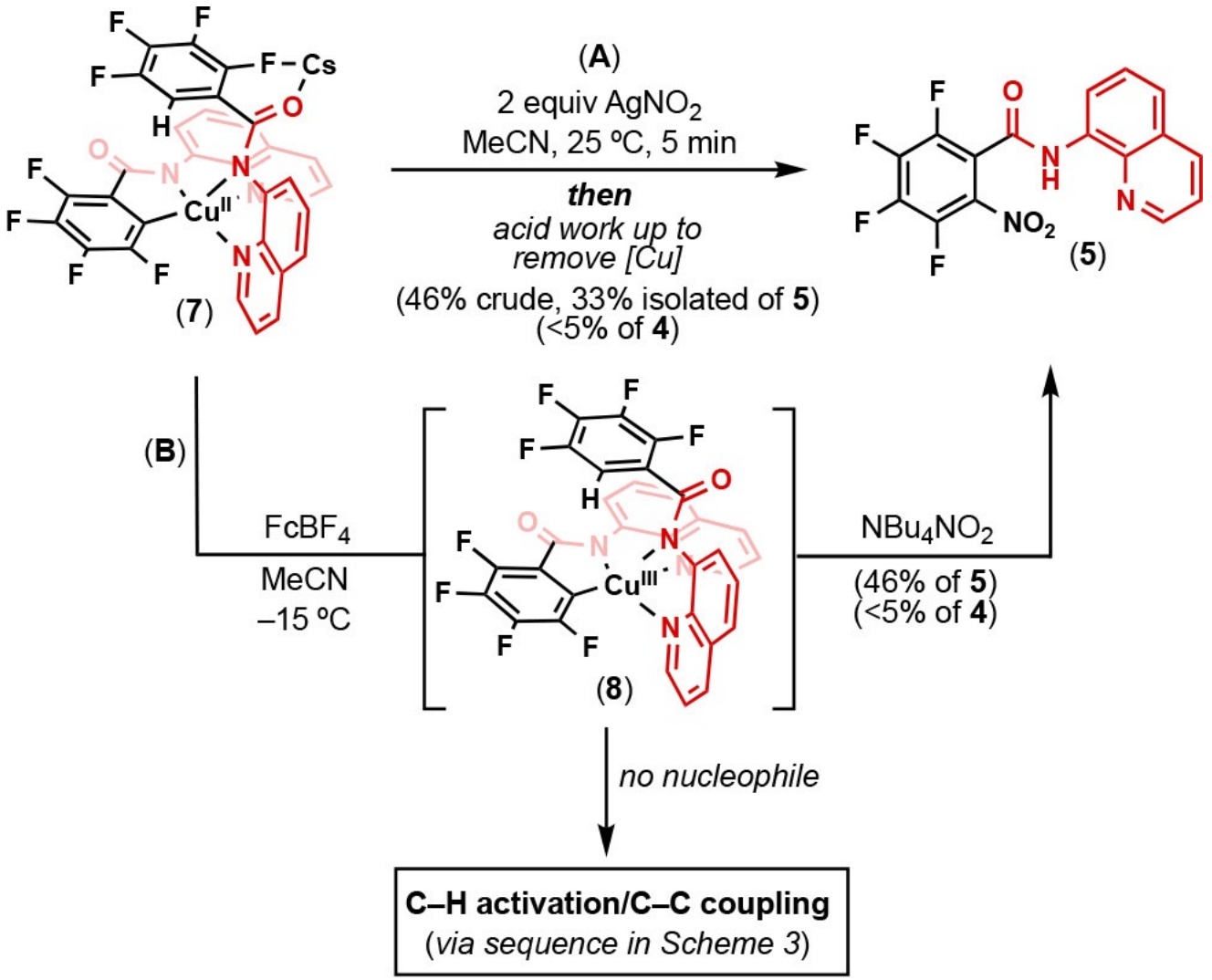
Plausible overall mechanism



Sanford M. *et al. J. Am. Chem. Soc.* **2023**, *145*, 18253.

Cu(III)-Mediated C–H Activation

If introduce a nucleophile…



Sanford M. *et al. J. Am. Chem. Soc.* **2023**, *145*, 18253.

Summary Well-identified Cu(III) intermediates in bond formations

Frequently proposed, but rarely identified

Chemistry of Cu(III) in organic reactions is intriguing but rarely deeply investigated, mainly being proposed in catalytic cycles.

To have crystallographically or spectroscopically confirmed Cu(III) intermediate, and experimentally confirmed reactivity, would further establish the role of Cu(III) in organic synthesis.

For more info. ……

Recommend review article:

> Casitas A., Ribas X. The role of organometallic copper(III) complexes in homogeneous catalysis. *Chem. Sci.* **2013**, *4*, 2301.

> Liu H., Shen Q., Well-defined organometallic Copper(III) complexes: Preparation, characterization and reactivity. *Coord. Chem. Rev.* **2021**, *442*, 213923.

THANK YOU FOR YOUR PATIENCE!!!