Research Presentation of Ge's lab

Presenter： *Liang Lu*

Supervisor： *Jing Zhao*

Assistant Professor, Chemistry
Department of Chemistry and Chemical Biology
Indiana University Purdue University Indianapolis

Research in Ge's group :

1)Metal-catalyzed carbon-carbon and carbon-heteroatom bond formation through C-H activation

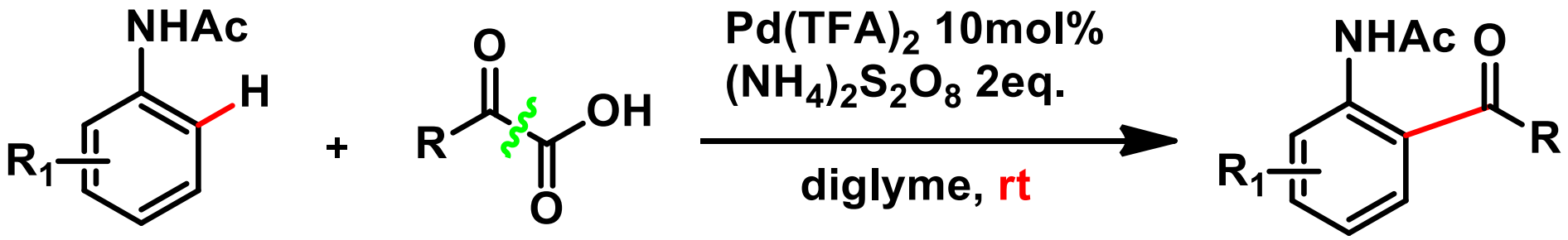
Pd **Cu** **Ni**

2)Total synthesis and structure-activity relationship studies of biologically active natural products.

Room Temperature Palladium-Catalyzed Decarboxylative *ortho*-Acylation of Acetanilides with α-Oxocarboxylic Acids

Ping Fang, Mingzong Li, and Haibo Ge*

Department of Chemistry and Chemical Biology, Indiana University Purdue University Indianapolis, Indianapolis, Indiana 46202



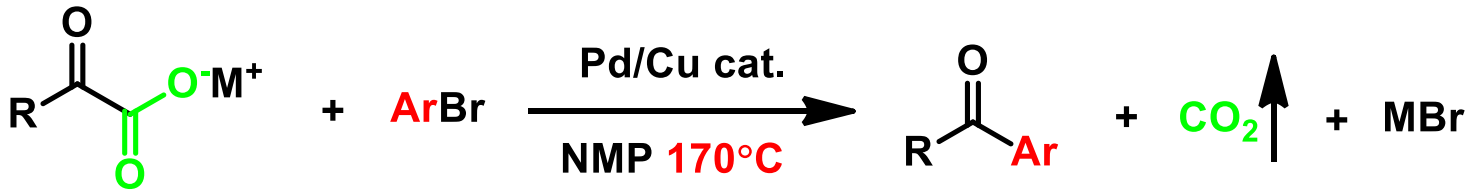
39 examples
43~96% yield

This reaction provides efficient access to *o*-acyl acetanilides *under mild conditions*

J. Am. Chem. Soc. **2010**, *132*, 11898

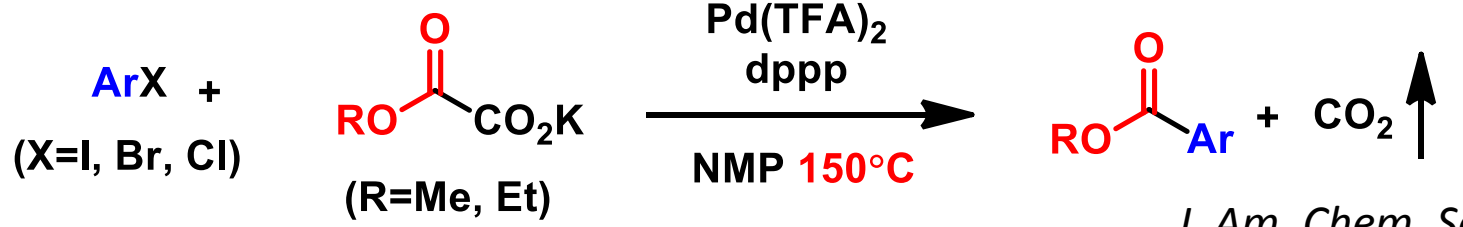
Previous work

Goossen's work



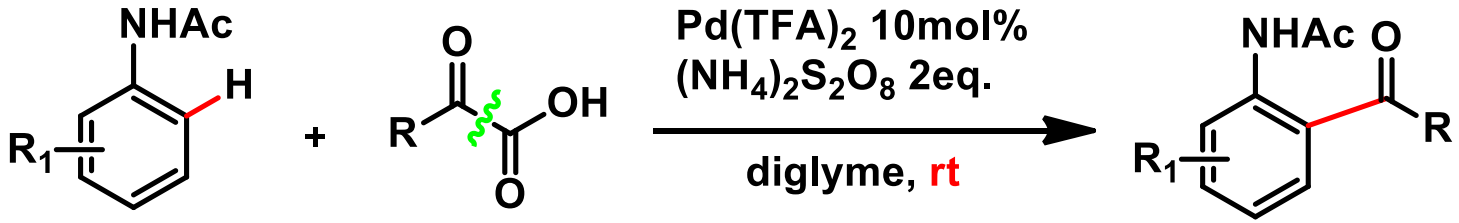
Angew. Chem., Int. Ed. **2008**, *47*, 3043.

Liu's work



J. Am. Chem. Soc. **2009**, *131*, 5738.

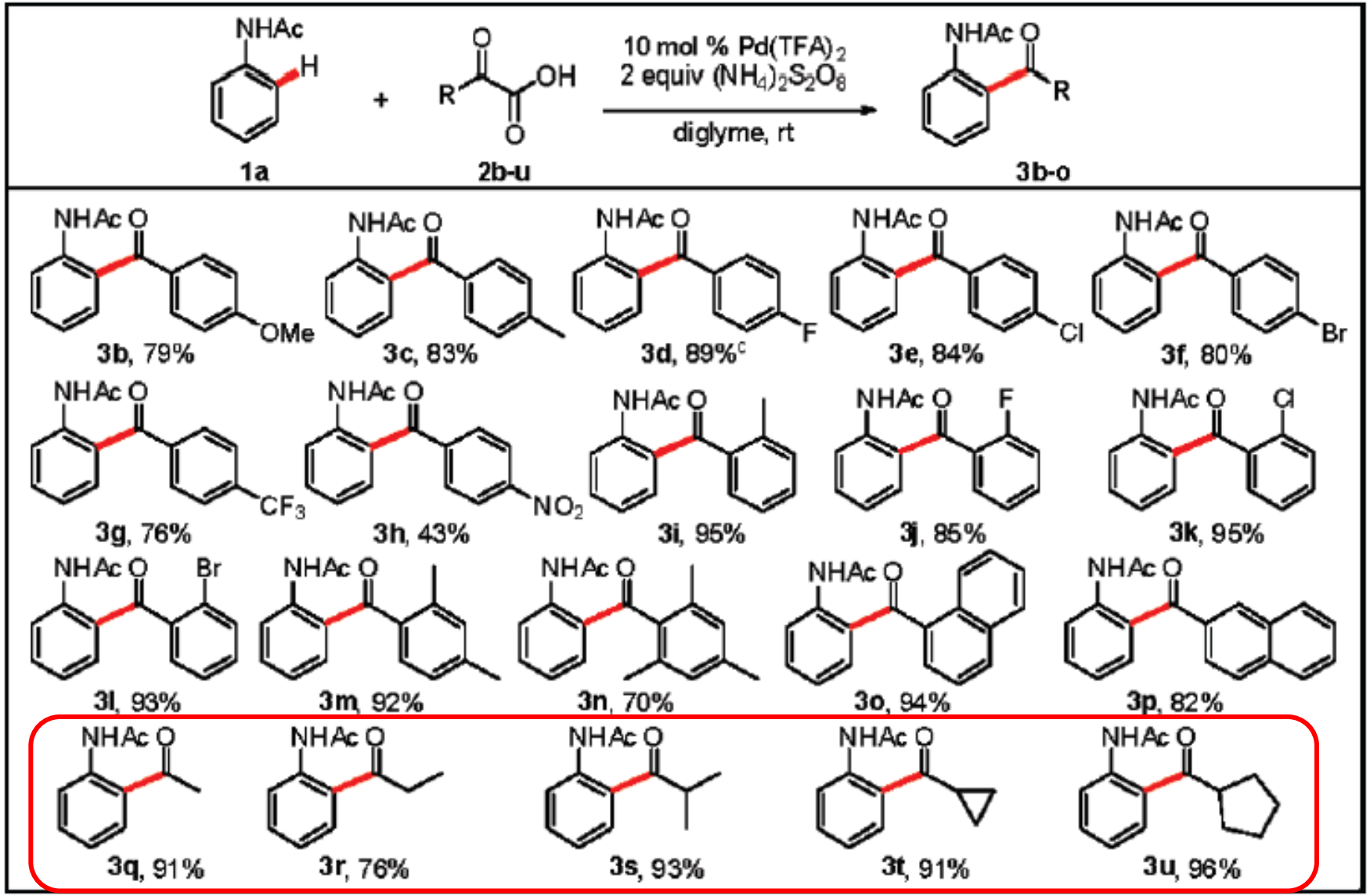
Ge's work



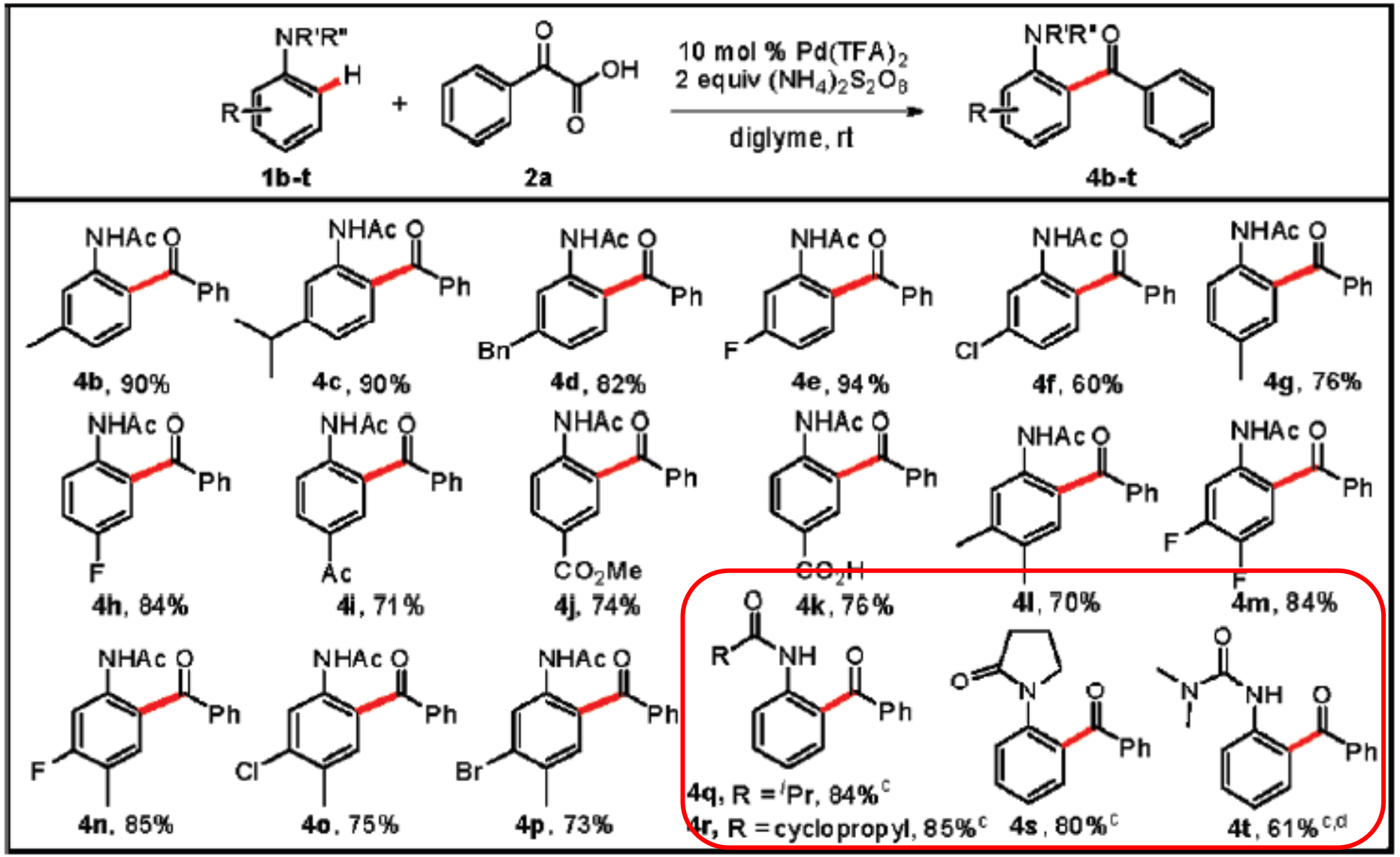
39 examples
43~96% yield

J. Am. Chem. Soc. **2010**, *132*, 11898

Scope of α-Oxocarboxylic Acids



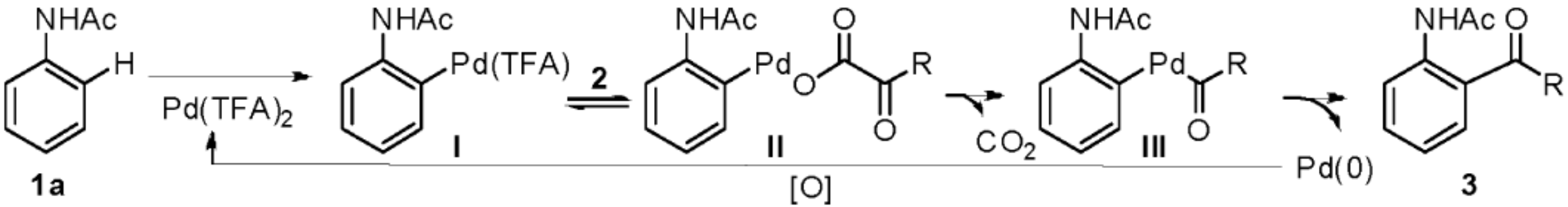
Scope of Anilides



1) *O*-substituted acetanilides **failed**

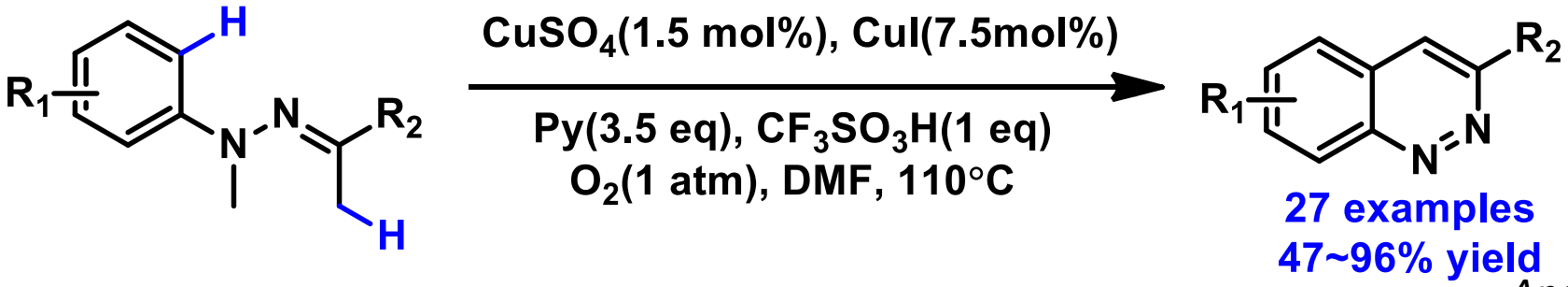
2) Acetamido group **not necessary**

Proposed Catalytic Cycle of Decarboxylative Coupling



Copper-Catalyzed Aerobic Dehydrogenative Cyclization of N-Methyl-N-phenylhydrazones: Synthesis of Cinnolines**

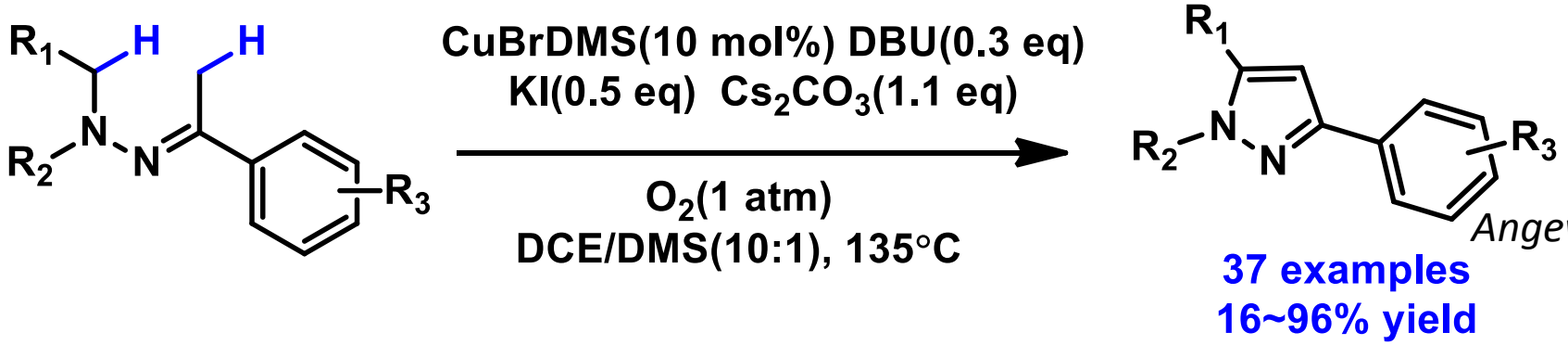
*Guangwu Zhang, Jinmin Miao, Yan Zhao, and Haibo Ge**



Angew. Chem. Int. Ed. **2012**, 51, 8318

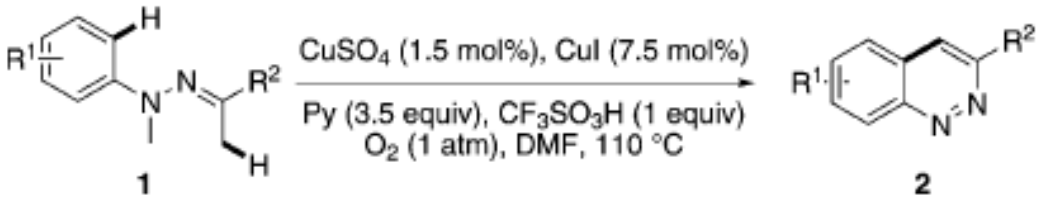
Copper-Catalyzed Aerobic Intramolecular Dehydrogenative Cyclization of N,N-Disubstituted Hydrazones through C_{sp^3}–H Functionalization**

*Guangwu Zhang, Yan Zhao, and Haibo Ge**



Angew. Chem. Int. Ed. **2013**, 52, 2559

Substrate scope



1 2

2b, 72% **2c**, 82% **2d**, 88% **2e**, 91%

2f, 92%[c] **2g**, 95%[c] **2h1+2h2**, 78% (**2h1:2h2** = 5:1)[d]

2i1+2i2, 62% (**2i1:2i2** = 2.2:1) **2j1+2j2**, 68% (**2j1:2j2** = 1.7:1)

2k, 60%[d] **2l**, 73%[c] **2m**, 88% **2n**, 76%[c]

2o, 47%[c] **2p**, 64% **2q**, 61%[d] **2r**, 77%

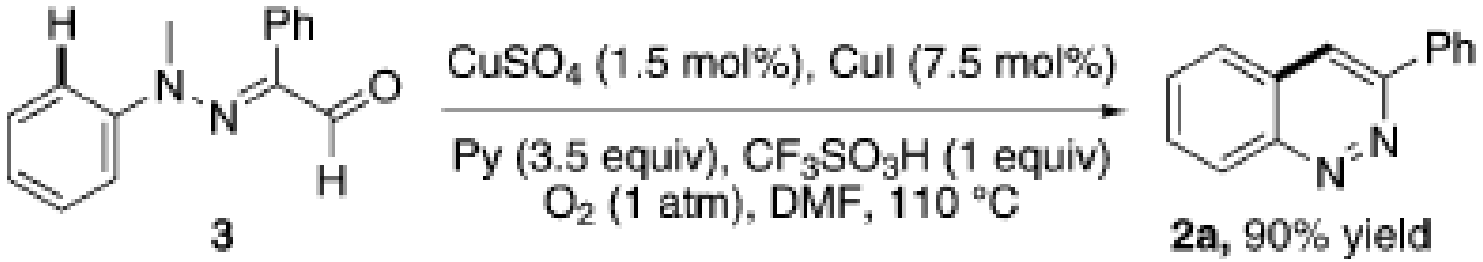
2s, 80% **2t**, 78% **2u**, 72% **2v**, 53%

2w, 75% **2x**, 61% **2y**, 90% **2z**, 82%

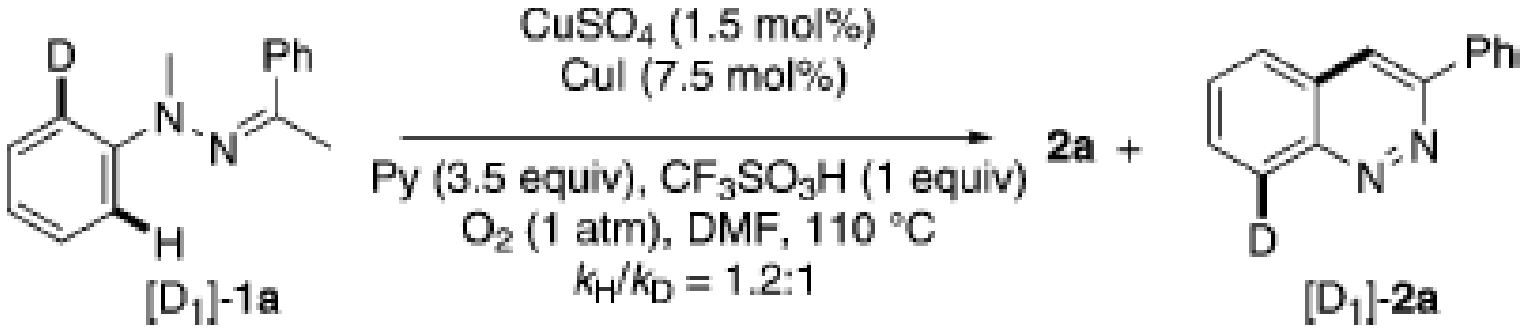
2aa, 96% **2ab**, 67%[d]

Mechanism

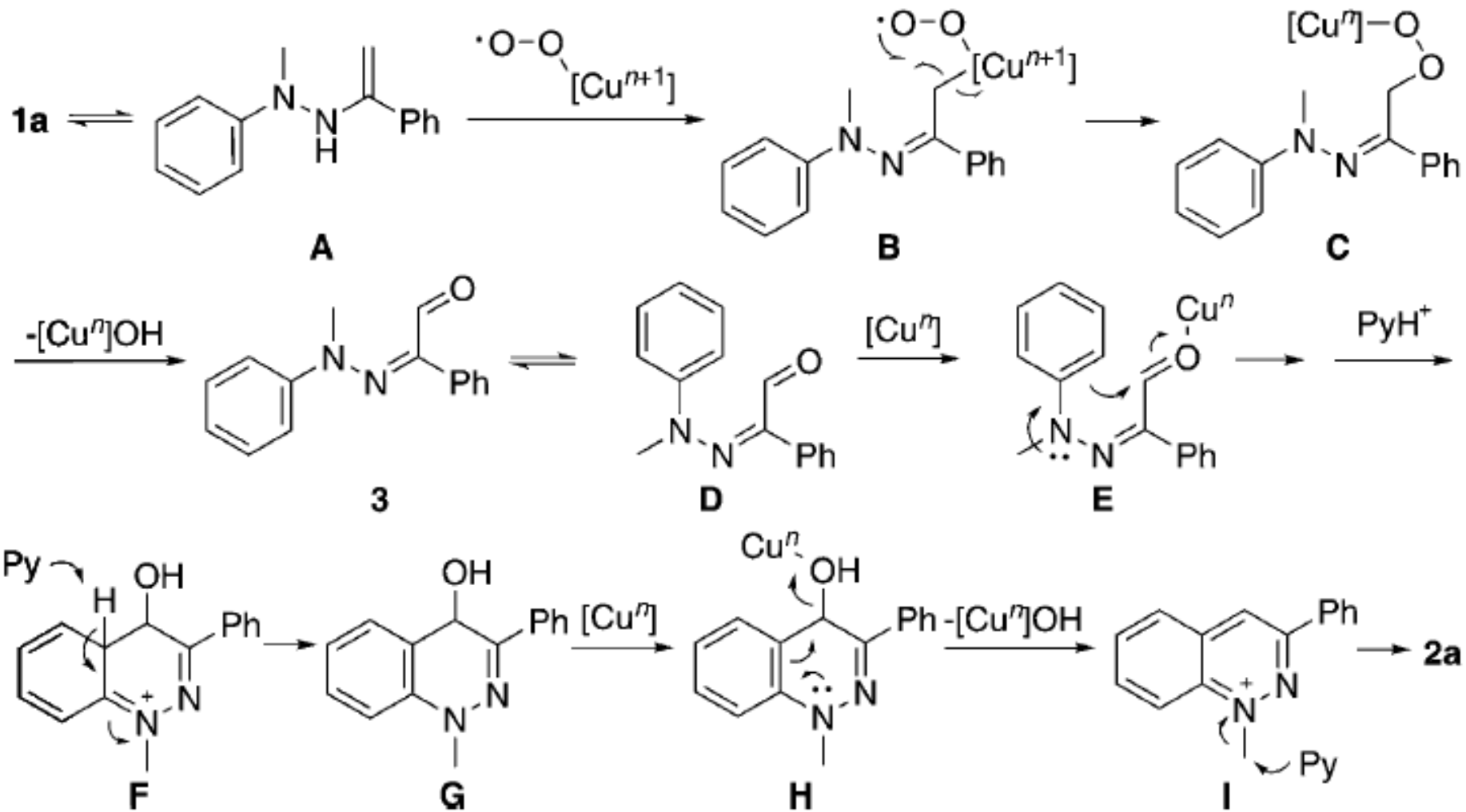
Cyclization of 2-(N-methyl-N-phenylhydrazono)-2-phenylacetaldehyde



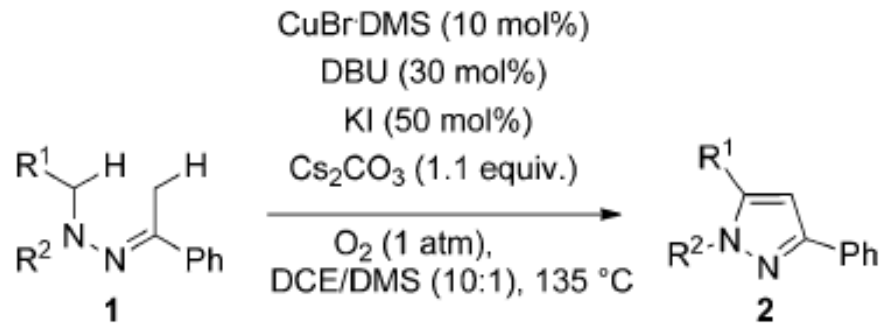
Deuterium-labeling experiments

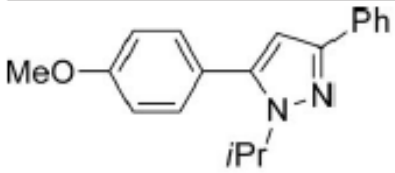


Proposed reaction mechanism.

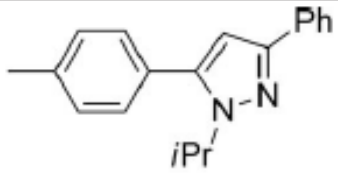


Scope: N substituents

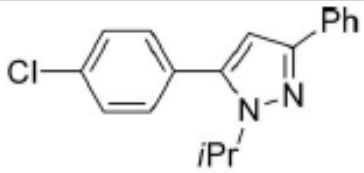




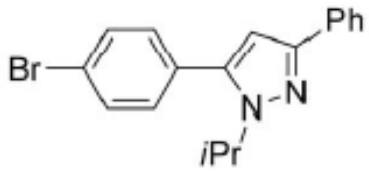
2b: 70%



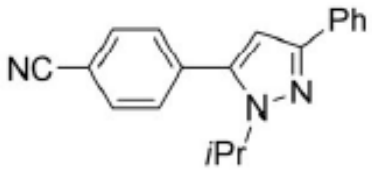
2c: 82%



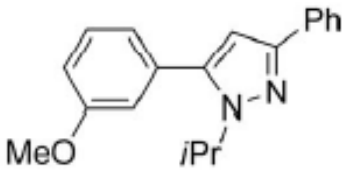
2d: 80%



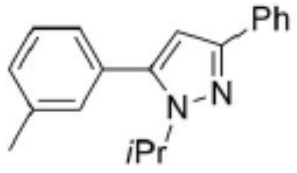
2e: 81%



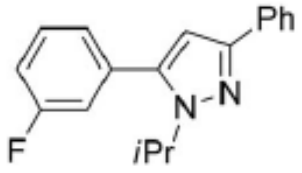
2f: 71%



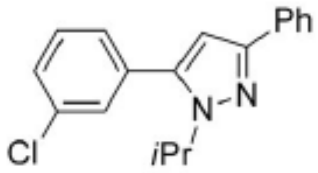
2g: 62%



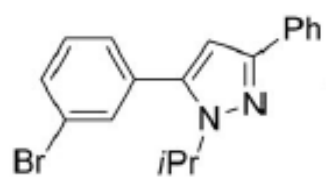
2h: 66%



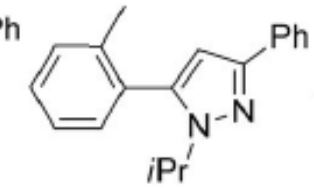
2i: 70%



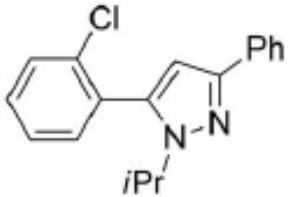
2j: 72%



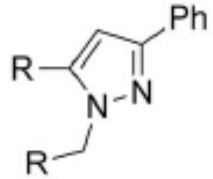
2k: 72%



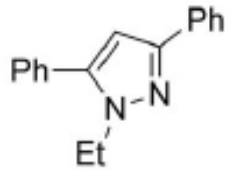
2l: 86%



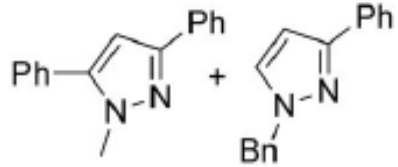
2m: 80%



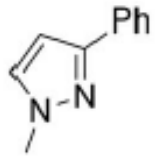
2na: R = Ph, 79%
2nb: R = 4-MeC$_6$H$_4$, 80%
2nc: R = 4-ClC$_6$H$_4$,78%
2nd: R = 2-MeC$_6$H$_4$, 82%



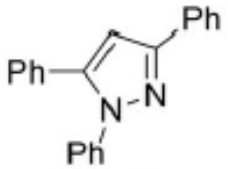
2o: 45%



2pa: 39% **2pb**: 22%

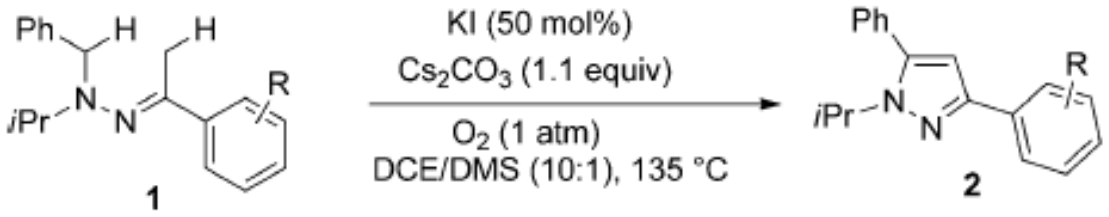


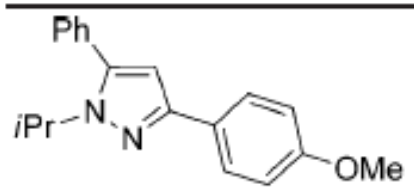
2q: 68%

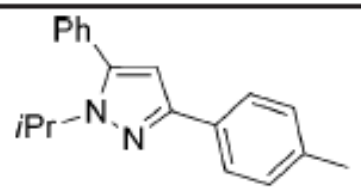


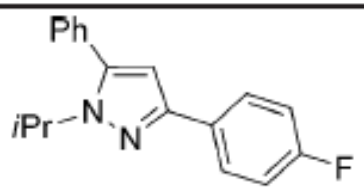
2r: 66%

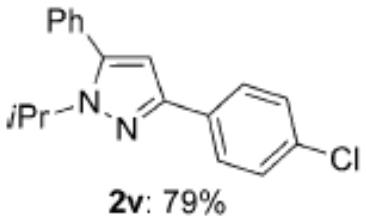
Scope: Imine moiety

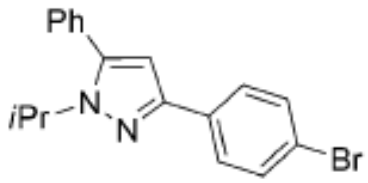


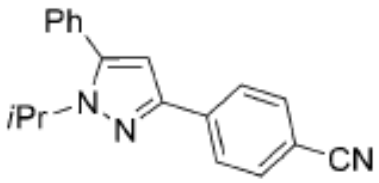


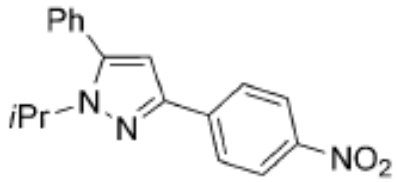


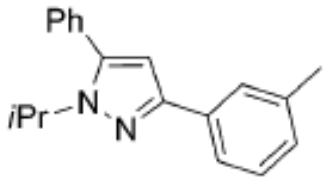


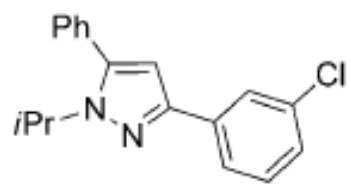


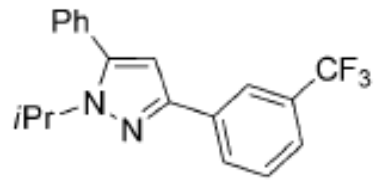


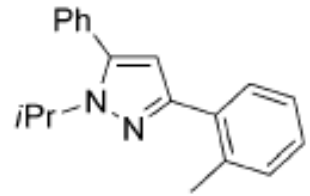


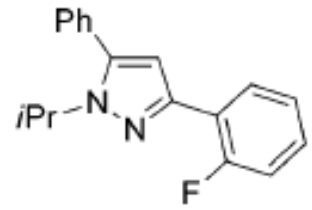


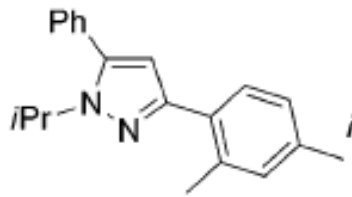


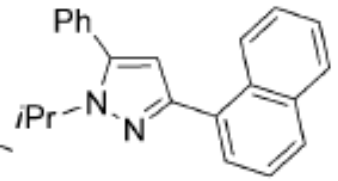


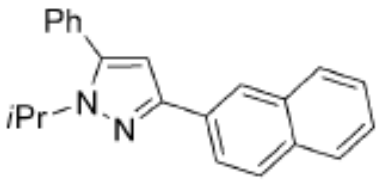


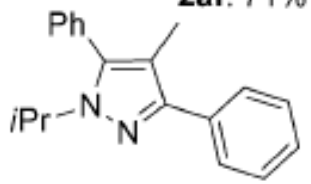


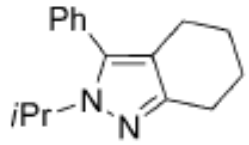




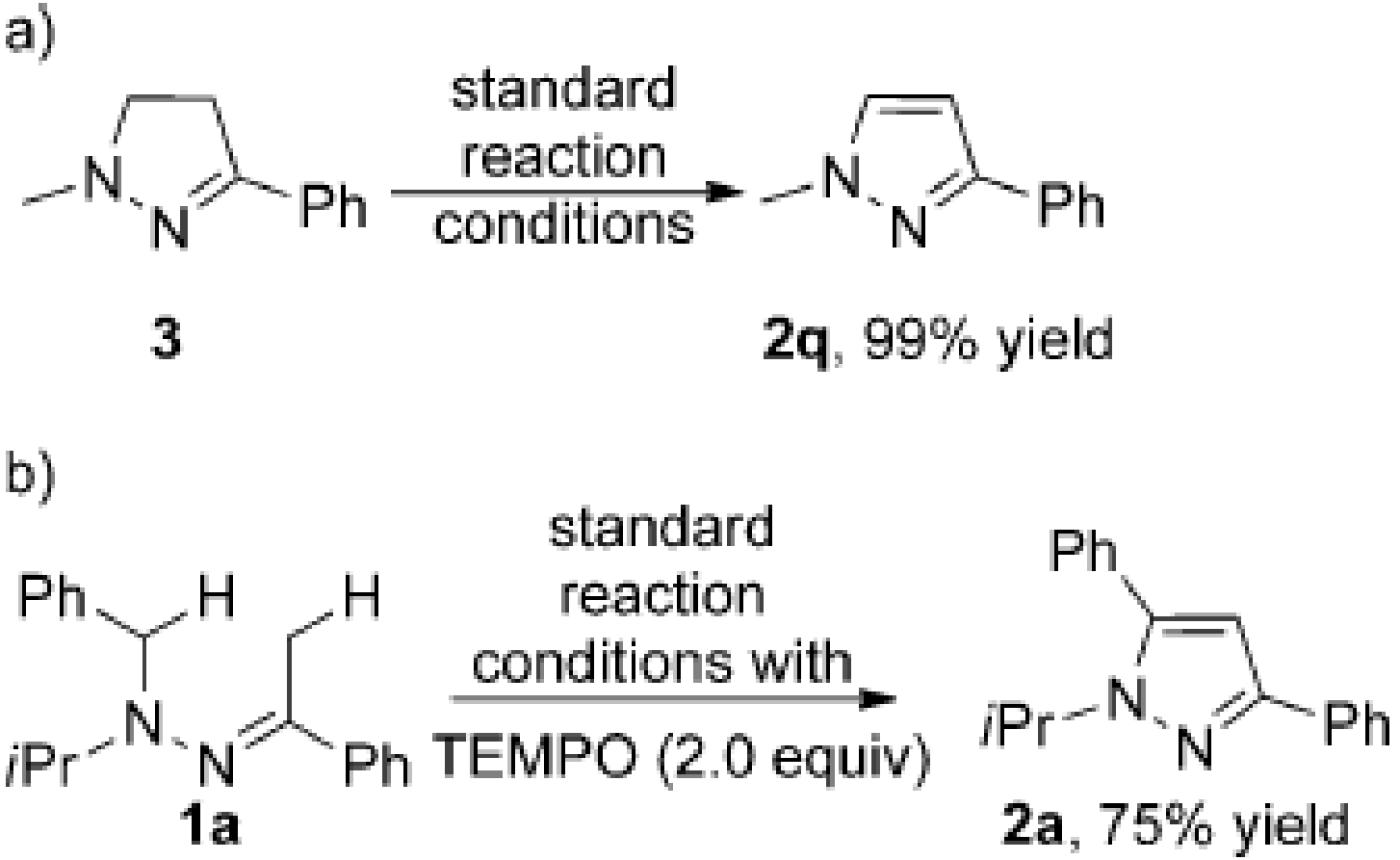






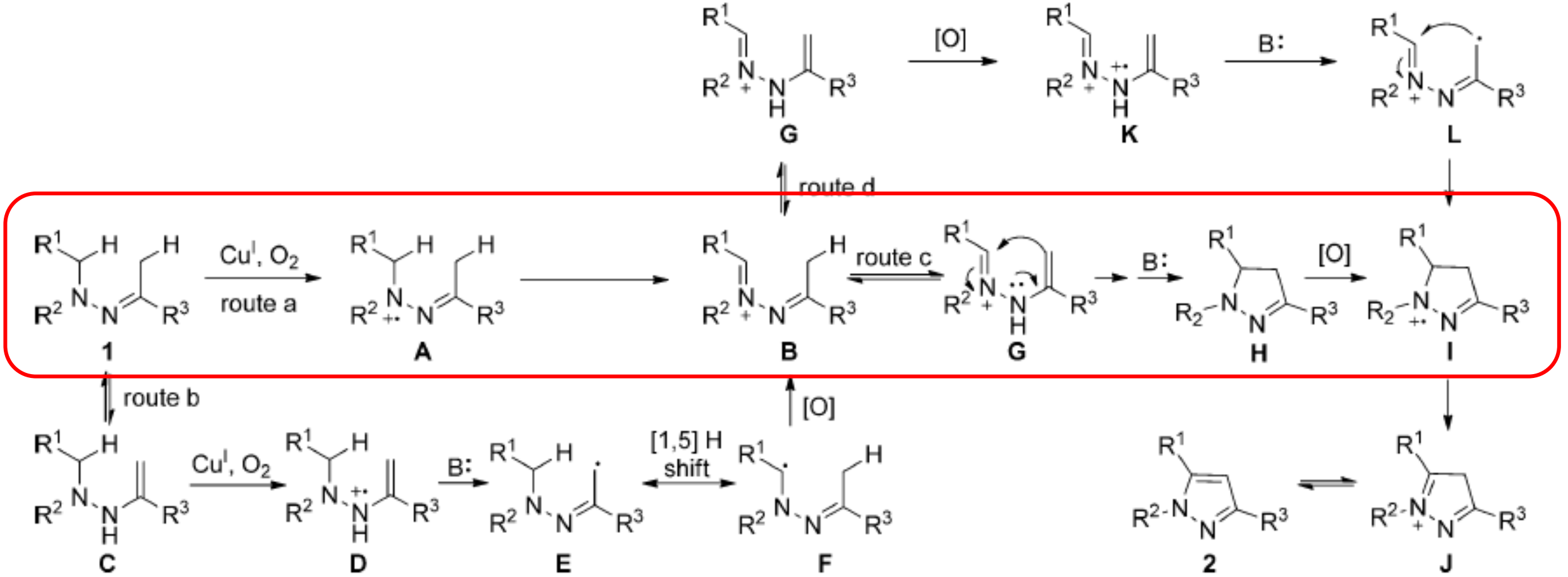


Mechanism



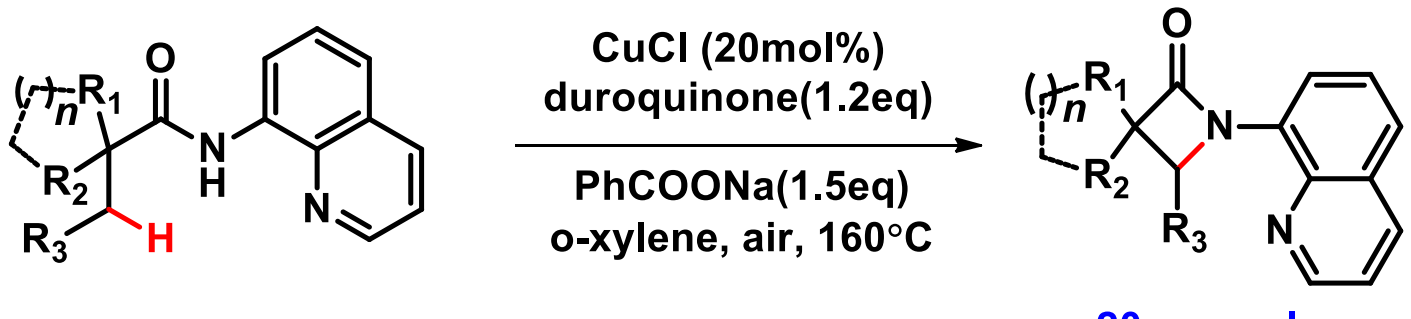
Excess TEMPO has no apparent effect on this intramolecular cyclization reaction

Plausible reaction mechanism



Copper-Catalyzed Site-Selective Intramolecular Amidation of Unactivated C(sp^3)–H Bonds**

*Xuesong Wu, Yan Zhao, Guangwu Zhang, and Haibo Ge**

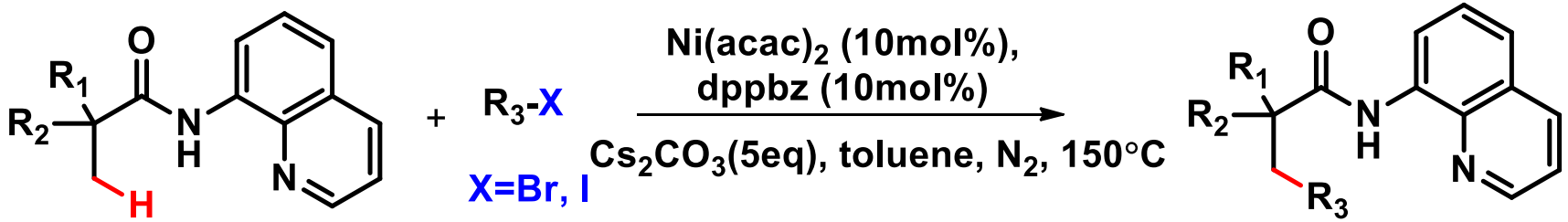


20 examples
69~94% yield

Angew. Chem. Int. Ed. **2014**, 53, 3706

Nickel-Catalyzed Site-Selective Alkylation of Unactivated C(sp^3)–H Bonds

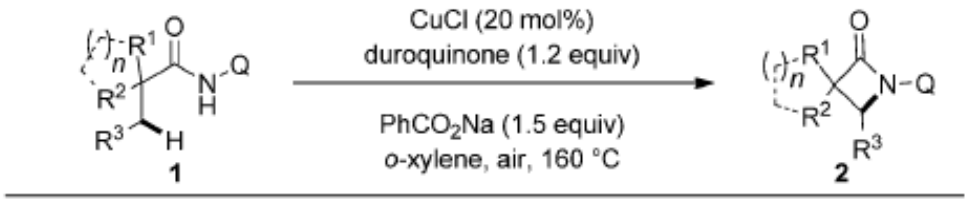
Xuesong Wu,[†] Yan Zhao,[†] and Haibo Ge*[,†,‡,§]

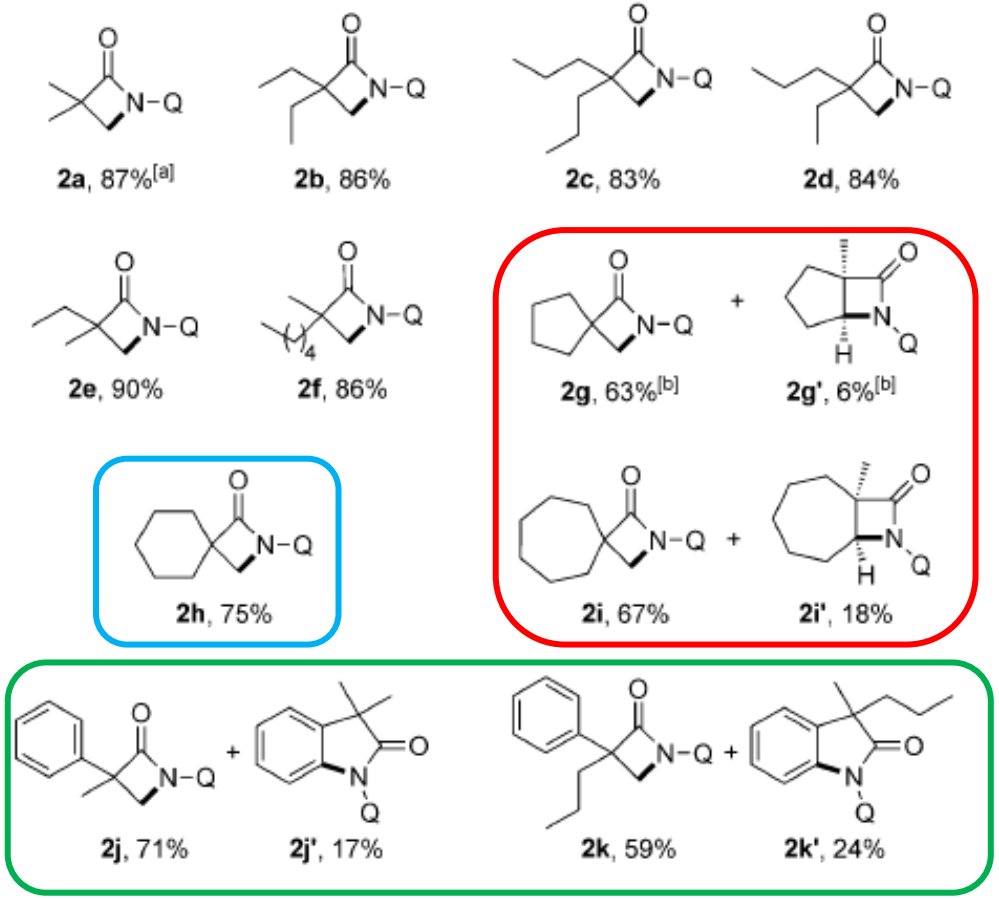


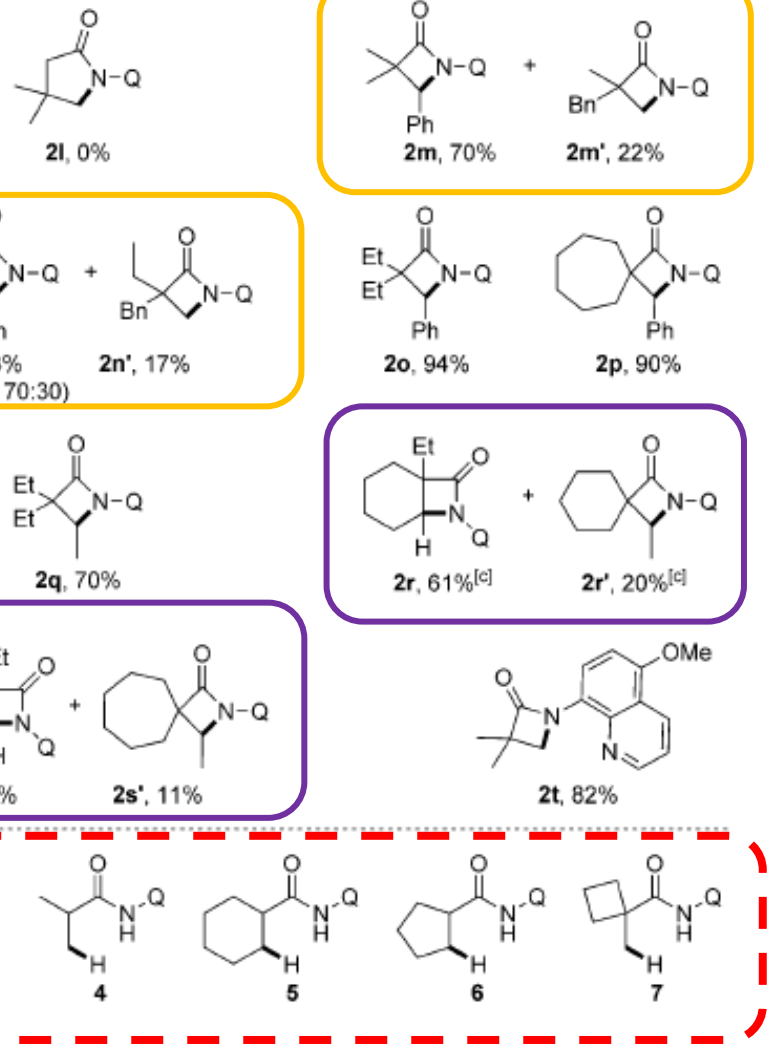
32 examples
8~91% yield

J. Am. Chem. Soc. **2014,** 136, 1789

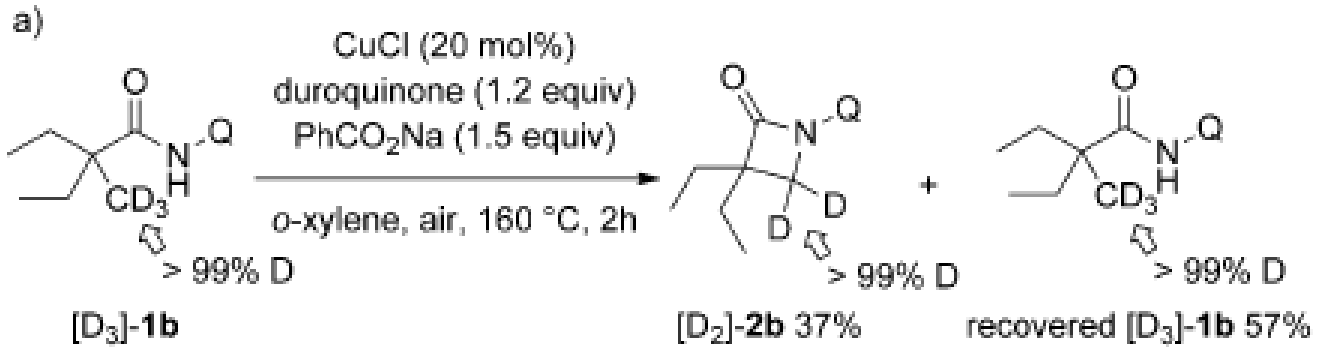
Direct amidation on sp^3-carbon atoms



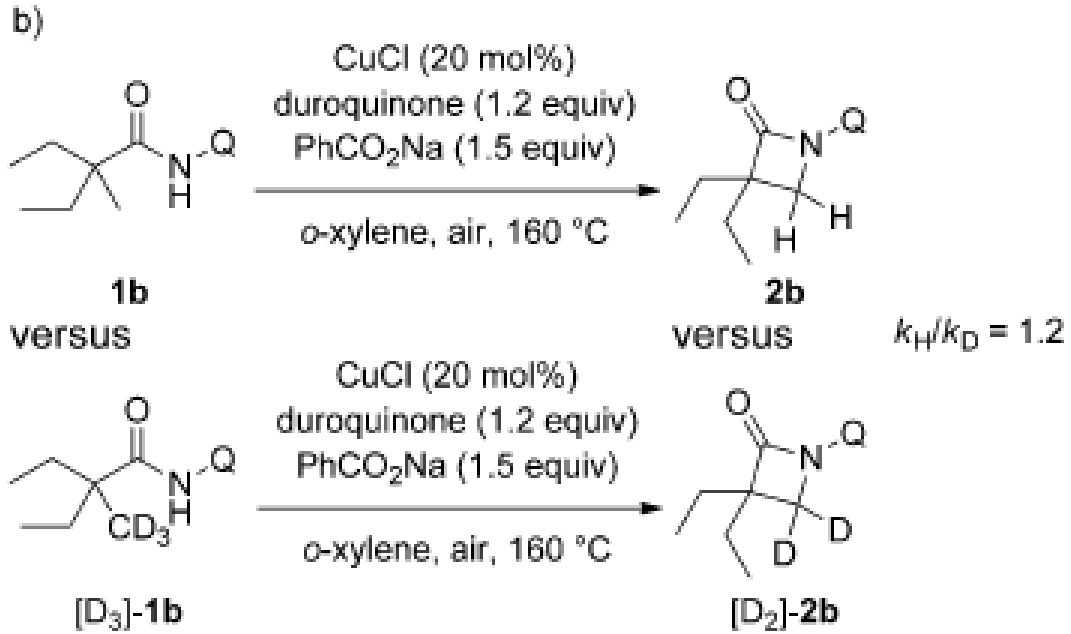




Deuterium-labeling experiments

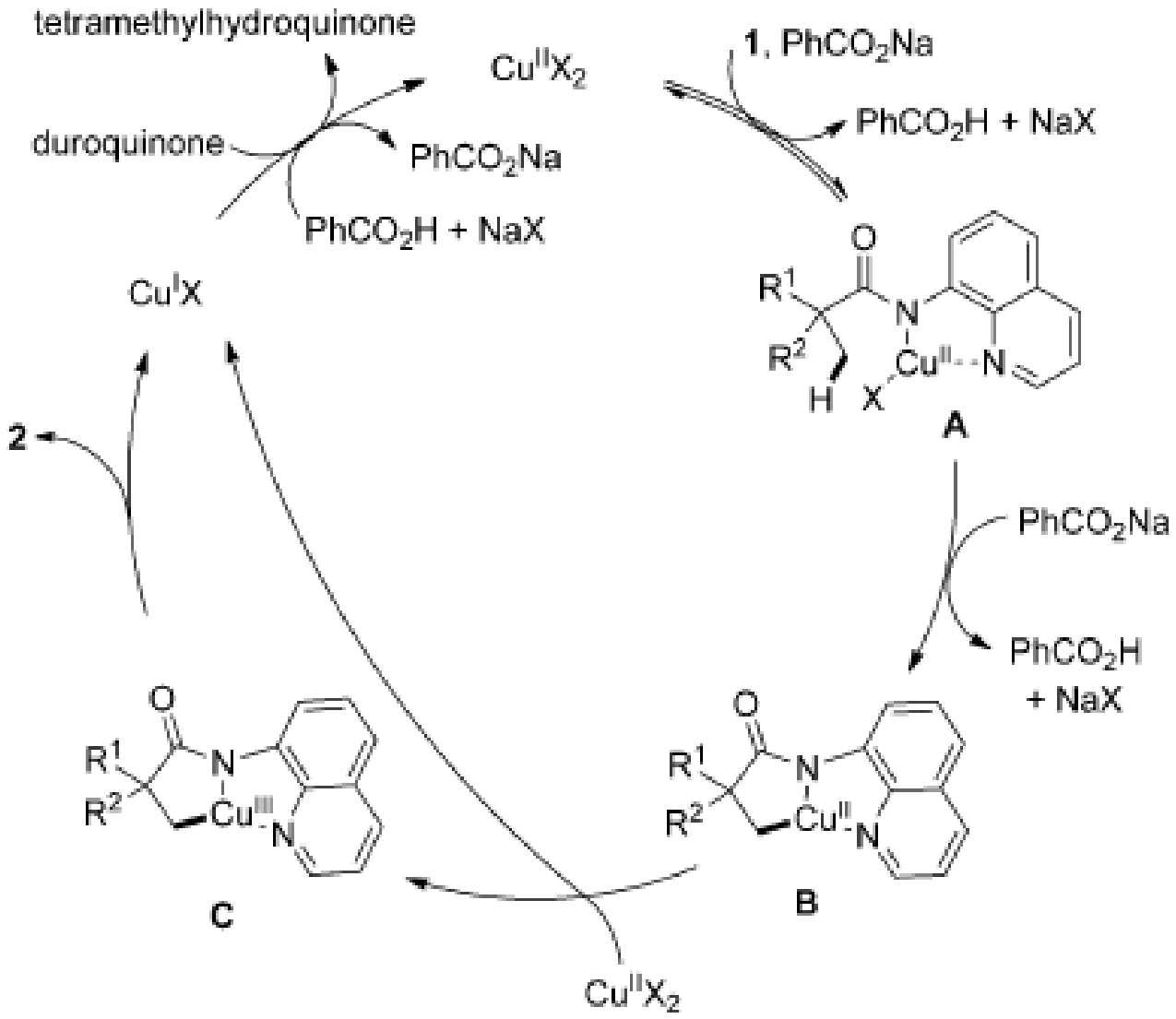


There was no apparent H–D exchange in this process

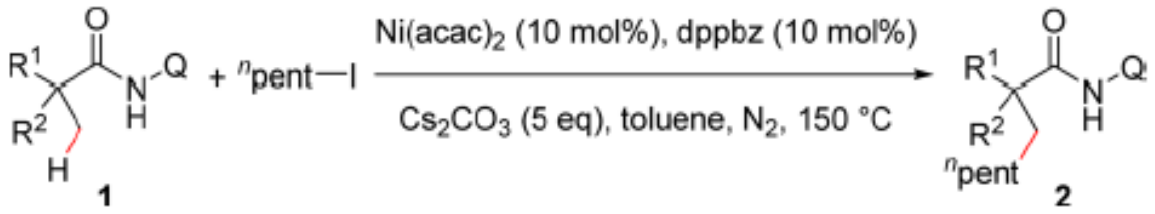


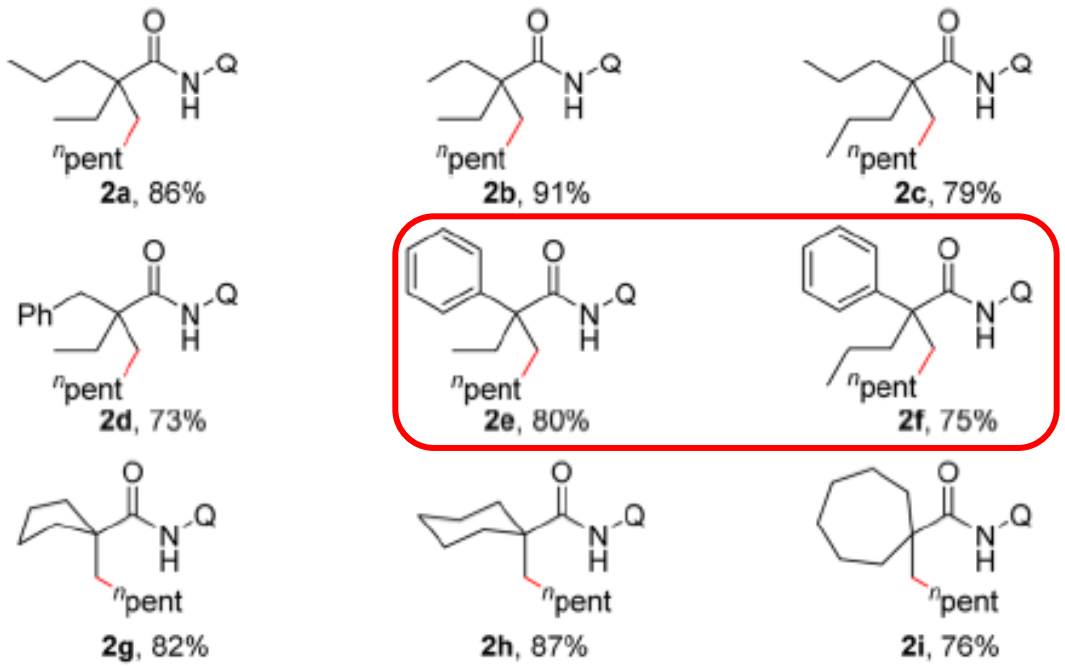
The sp^3 C-H bond cleavage should not be the rate-limiting step in this catalytic process

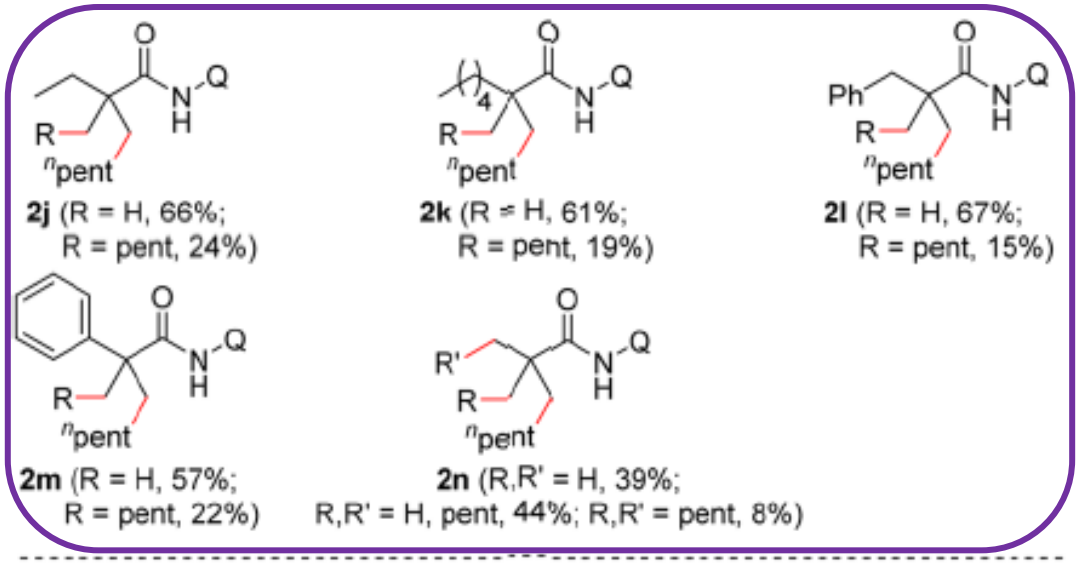
Plausible reaction mechanism

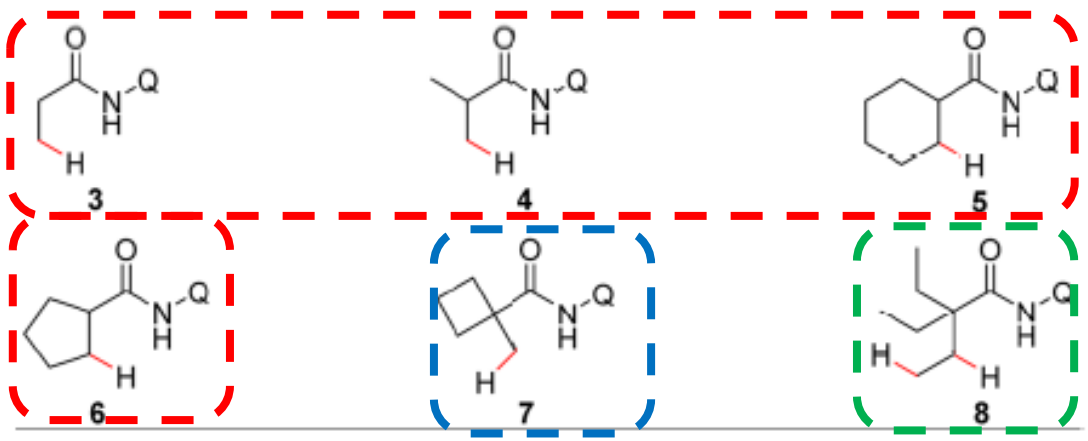


Scope of Aliphatic Amides

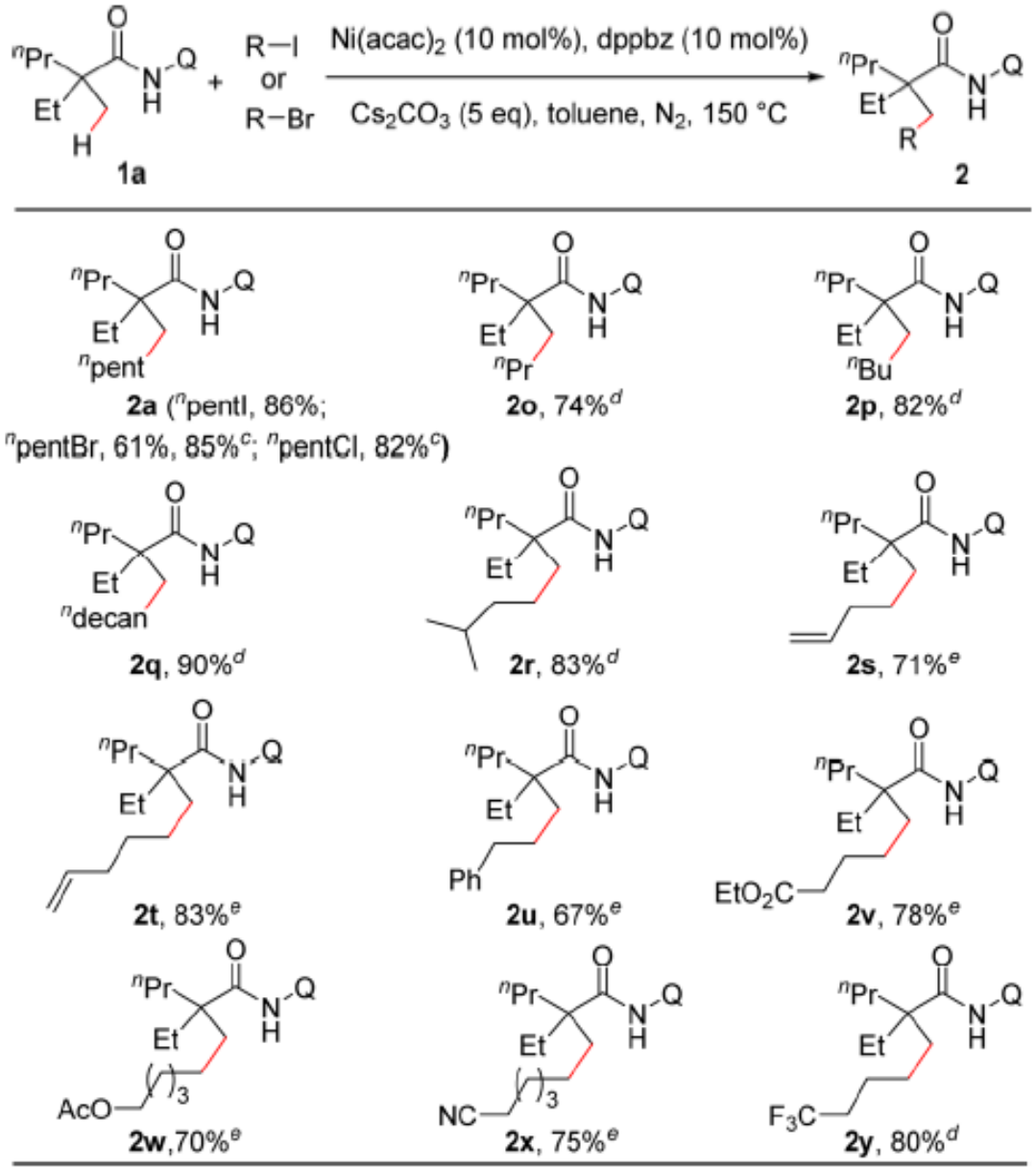








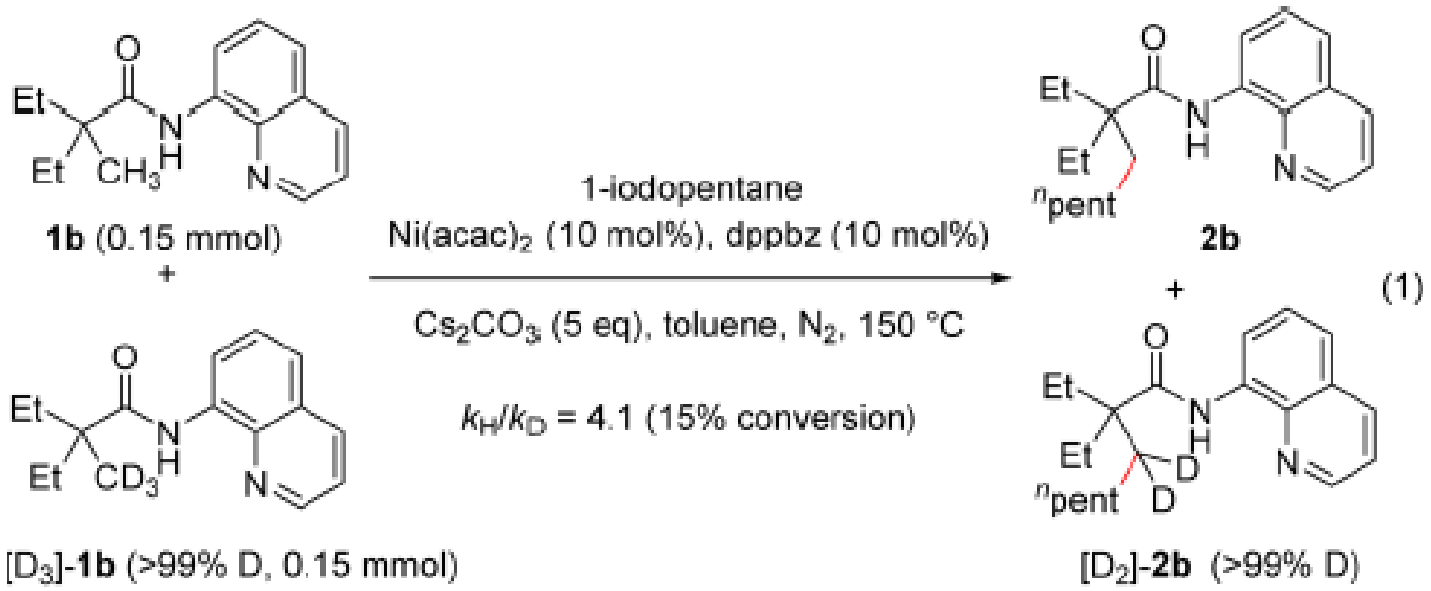
Scope of Alkyl Halides

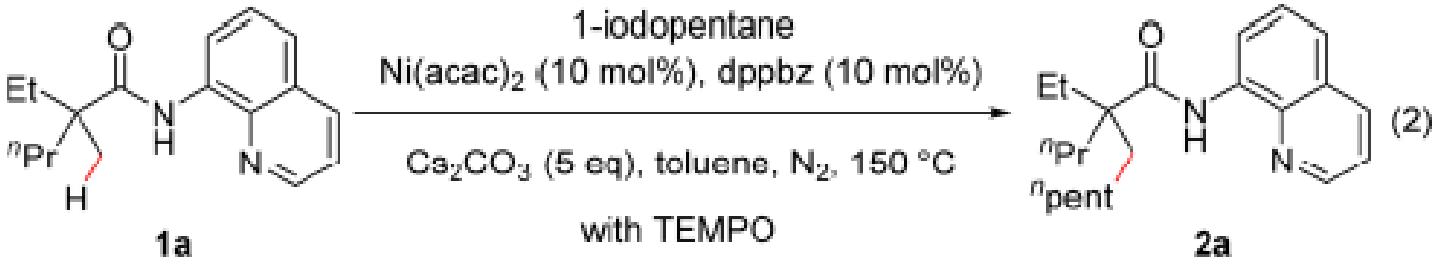


Secondary alkyl halides and benzyl bromide failed to provide the desired products

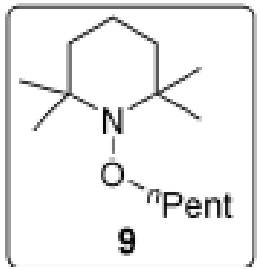
This reaction tolerated a variety of functional groups

Deuterium Labeling and Radical Trapping Experiments





TEMPO (eq)	Yield of **2a** (%)
3.0	48
5.0	18
8.0	trace



The cyclometalation of amide 1 with a nickel species is *the rate determining step* in the process.

Proposed Reaction Mechanism