Recent Developments in Copper-Catalyzed Aerobic Oxidative Coupling Reactions Using Oxygen as Oxidant

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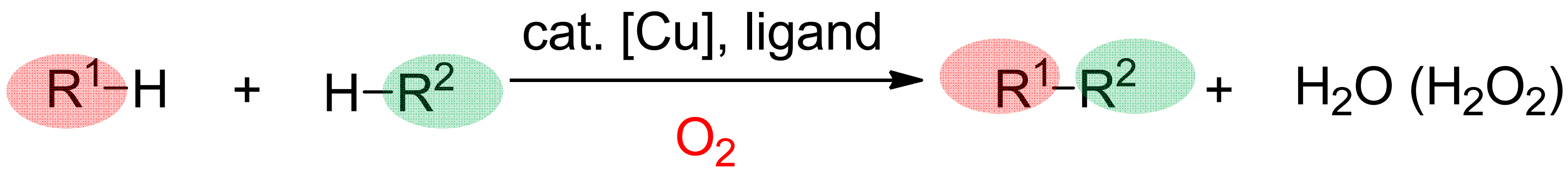
Transition Metal Catalyzed Aerobic Oxidative Coupling Reaction

$$R^1{-}H \quad + \quad H{-}R^2 \xrightarrow[O_2]{\text{catalyst, ligand}} R^1{-}R^2 \quad + \quad H_2O\ (H_2O_2)$$

- Activate two different C-H bonds or H-Heteroatom bonds
- Couple them via a transition metal catalyst
- Carry out the reaction in air or O_2, with O_2 as the oxidant

Stahl, S. S. *Angew. Chem. Int. Ed*. **2004**, *43*, 3400 – 3420.
Gligorich, K. M. Sigman, M. S. *Angew. Chem. Int. Ed*. **2006,** *45*, 6612-6615.
Gligorich, K. M. Sigman, M. S. *Chem. Commun*., **2009**, 3854-3867.

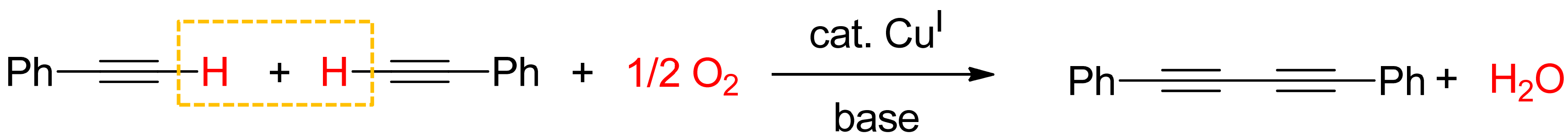
Copper Catalyzed Aerobic Oxidative Coupling Reaction



Why copper?

- Copper is relatively abundant in the earth's crust.
- Copper can bind and activate dioxygen well that perform a variety of critical biological functions.

Glaser Coupling (1869)



Gamez, P.; Aubel, P. G.; Driessen, W. L.; Reedijk, J. *Chem. Soc. Rev.*, **2001**, *30*, 376-385.
Lewis, E. A.; Tolman, W. B. *Chem. Rev.*, **2004**, *104*, 1047-1076.
Glaser, C. *Ber. Dtsch. Chem. Ges.* **1869,** *2,* 422.
Glaser, C. *Ann. Chem. Pharm.* **1870,** *154,* 137.

Pros and Cons of Oxidative Coupling Reaction

Attractions:

- Direct C-H functionalizaton
- High atom economy efficiency
- H_2O is generated as by-product environmentally friendly

Challenges:

- Homocoupling of the two nucleophiles
- Direct reaction of the nucleophiles with the oxidant

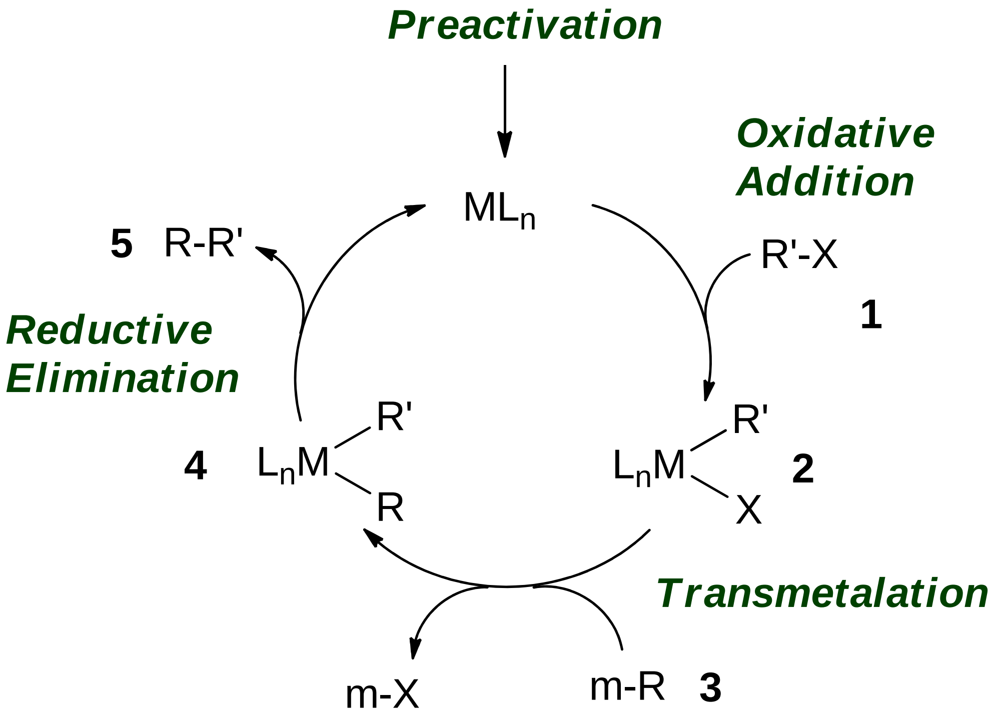
Stahl, S. S. *Angew. Chem. Int. Ed*. **2004**, *43*, 3400 – 3420.
Stahl, S. S. *Science,* **2005,** *309*, 1824-1826**.**
Gligorich, K. M.; Sigman, M. S. *Chem. Commun*., **2009**, 3854-3867.

Transition Metal Catalyzed Coupling Reaction Pattern

$$R\text{-}m \quad + \quad R'\text{-}X \xrightarrow{ML_n} R\text{-}R'$$

Nucleophile   Electrophile

M = Fe, Co, Ni, Cu, Pd, Ru, Rh ... ...



Armin de Meijere, François Diederich, *Metal-Catalyzed Cross-Coupling Reactions, 2nd, Completely Revised and Enlarged Edition,* Wieley-VCH, Weinheim, **2004**

Models for Coupling Reaction Bond Construction

- Classic Coupling Model

$$Nu^{\ominus} + E^{\oplus} \xrightarrow{\text{catalyst, ligand}} Nu{-}E$$

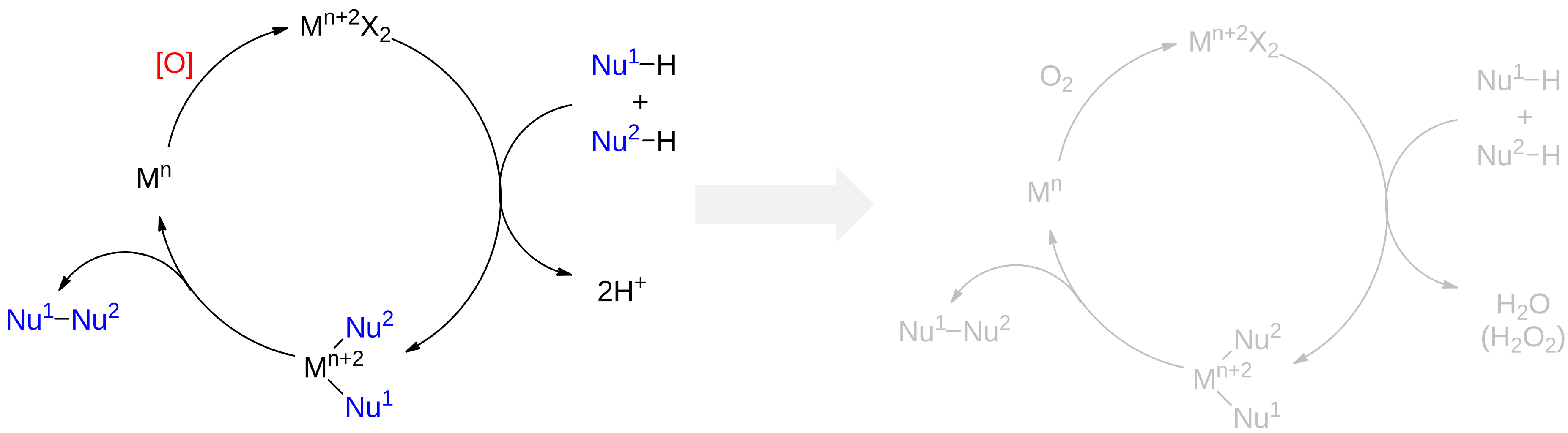
- Oxidative Coupling Model

$$Nu^{1\ominus} + Nu^{2\ominus} \xrightarrow[\text{[O]}]{\text{catalyst, ligand}} Nu^{1}{-}Nu^{2}$$

Liu, C.; Jin, L.; Lei, A. *Synlett.*, **2010**, *17,* 2527–2536.

To Combine Two Nucleophiles Together

$$Nu^1 + Nu^2 \xrightarrow[\text{Oxidant}]{\text{Catalyst}} Nu^1\text{-}Nu^2$$



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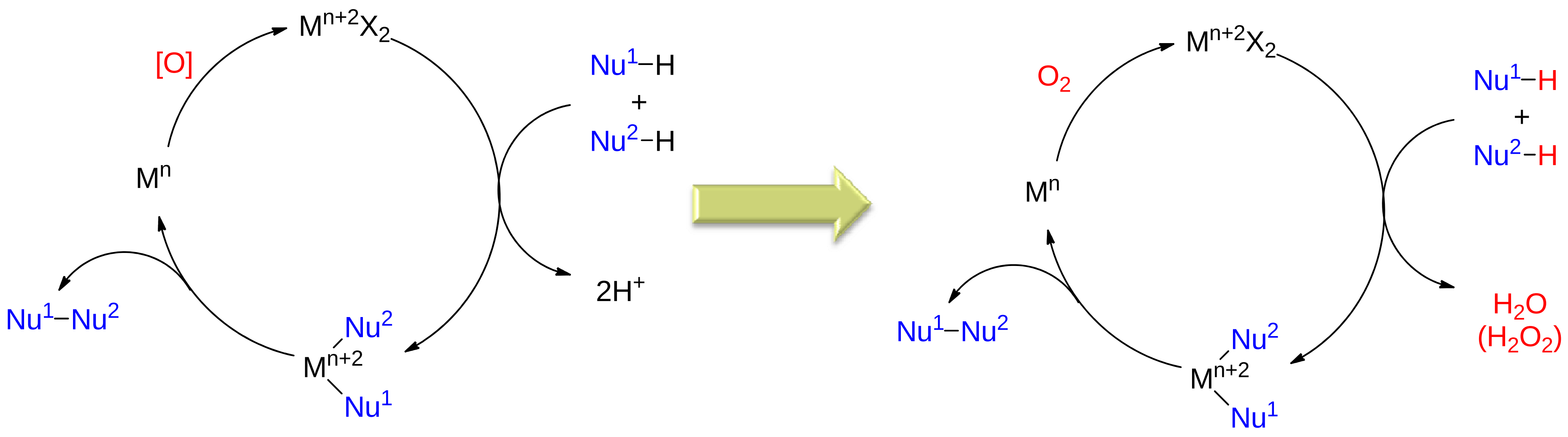
Gligorich, K. M.; Sigman, M. S. *Angew. Chem. Int. Ed*. **2006,** *45*, 6612-6615.

To Combine Two Nucleophiles Together

$$\mathrm{Nu^1} + \mathrm{Nu^2} \xrightarrow[\text{Oxidant}]{\text{Catalyst}} \mathrm{Nu^1\text{-}Nu^2}$$



Stahl, S. S. *Angew. Chem. Int. Ed*. **2004**, *43*, 3400 – 3420.
Gligorich, K. M.; Sigman, M. S. *Angew. Chem. Int. Ed*. **2006,** *45*, 6612-6615.

Why O_2 as Oxidant?

O_2 is the quintessential oxidant for chemical synthesis!

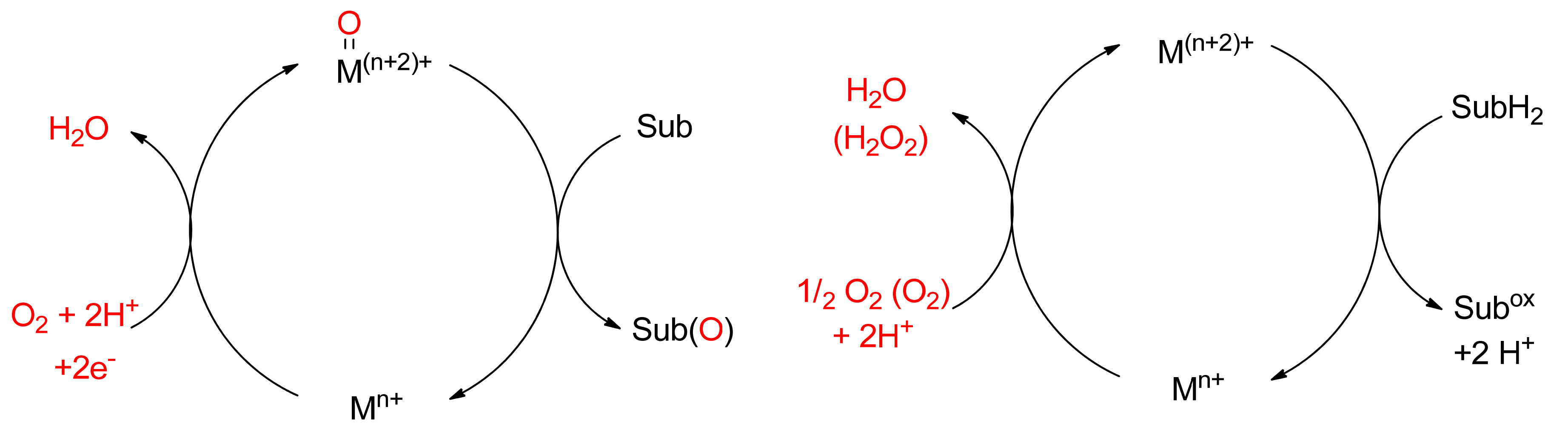
- Huge abundance in nature
- Available at virtually no cost
- Produces no environmentally hazardous by-products

Stahl, S. S. *Angew. Chem. Int. Ed*. **2004**, *43*, 3400 – 3420.
Stahl, S. S. *Science* **2005,** *309*, 1824-1826***.***

Metalloenzyme-catalyzed Aerobic Oxidation

a) Oxygenase Pathway

b) Oxidase Pathway



➢ In the **oxygenase pathway (a),** the substrate oxidation involves oxygen-atom transfer from molecular oxygen.

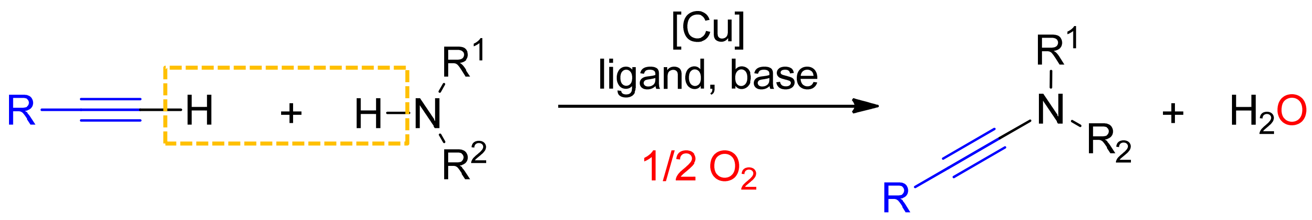
➢ The **oxidase pathway (b),** utilizes molecular oxygen as a electron/proton acceptor in the oxidation of the substrate.

Stahl, S. S. *Angew. Chem. Int. Ed*. **2004**, *43*, 3400 – 3420.
Stahl, S. S. *Science* **2005,** *309*, 1824-1826.

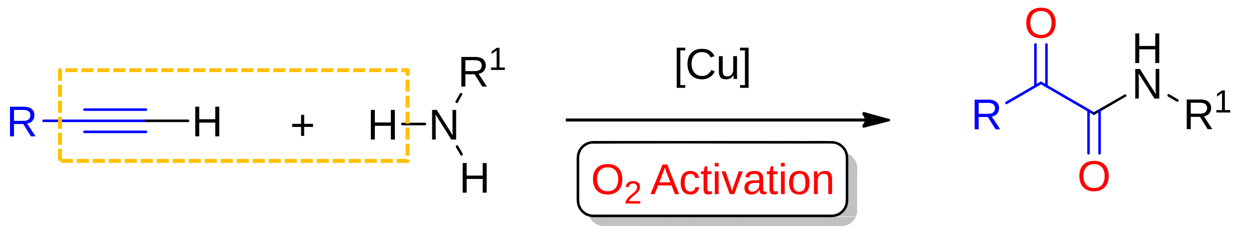
Examples of Oxygenase and Oxidase

C-N Functionalization of Terminal Alkynes

Stahl – Oxidase Pathway

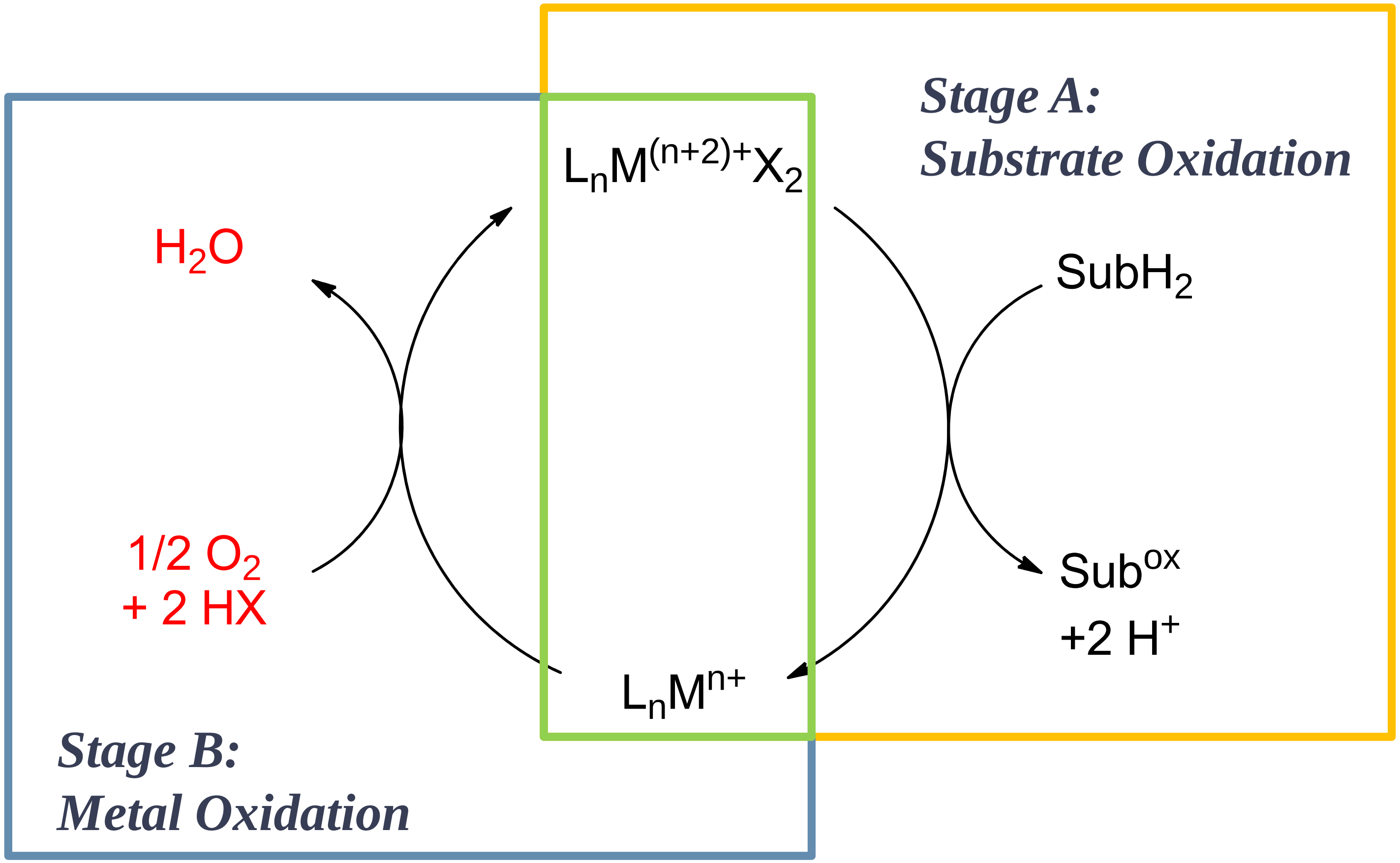


Jiao – Dioxygenase Pathway



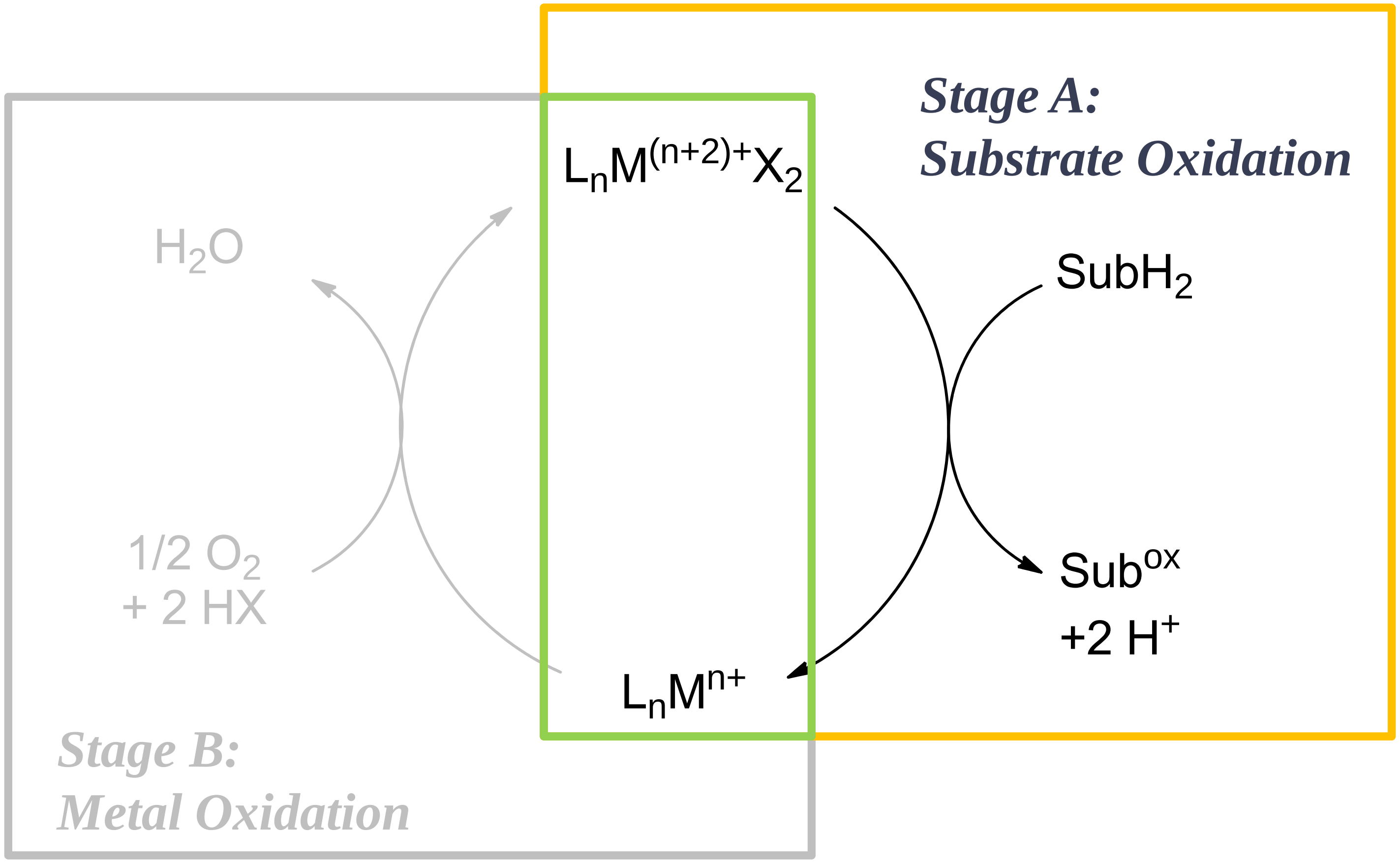
Hamada, T.; Ye, X.; Stahl, S. S. *J. Am. Chem. Soc.*, **2008**, *130*, 833–835.
Zhang, C.; Jiao, N. *J. Am. Chem. Soc.*, **2010**, *132*, 28–29.

Metal Catalyzed Oxidase Reactions



Stahl, S. S. *Angew. Chem. Int. Ed.* **2004**, *43*, 3400 – 3420.
http://www.chem.wisc.edu/content/investigation-fundamental-reactions-between-palladium-and-molecular-oxygen

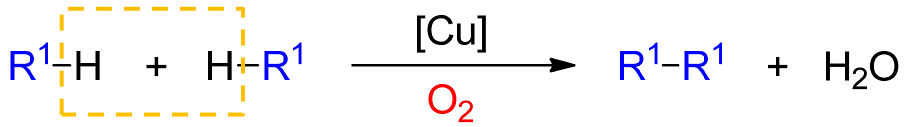
Metal Catalyzed Oxidase Reactions



Stahl, S. S. *Angew. Chem. Int. Ed.* **2004**, *43*, 3400 – 3420.
http://www.chem.wisc.edu/content/investigation-fundamental-reactions-between-palladium-and-molecular-oxygen

Outline

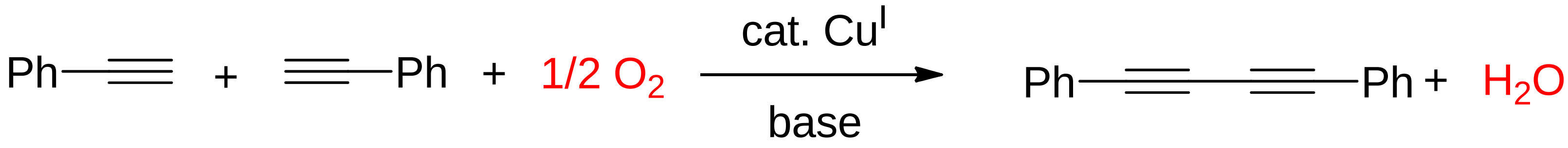
- Cu-Catalyzed Oxidative Homo-Coupling Reaction



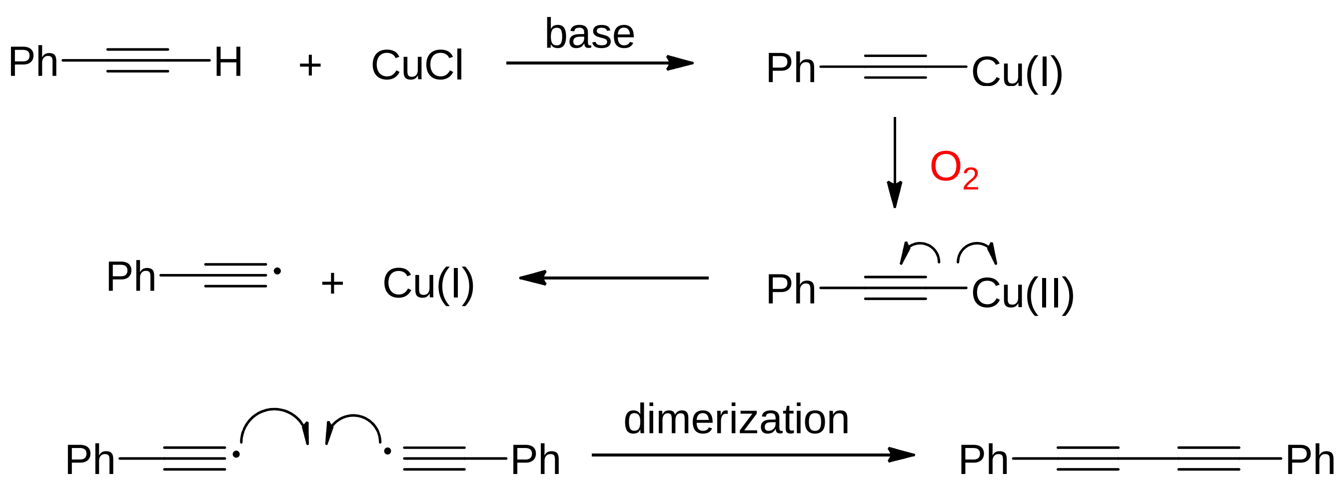
- Cu-Catalyzed Oxidative Hetero-Coupling Reaction
  - C-C Bond Formation
  - C-N Bond Formation
  - C-P Bond Formation

Cu Catalyzed Aerobic Oxidative C-C Bond Homocoupling Reaction

Glaser Coupling (1869)



One Possible Mechanism Pathway:



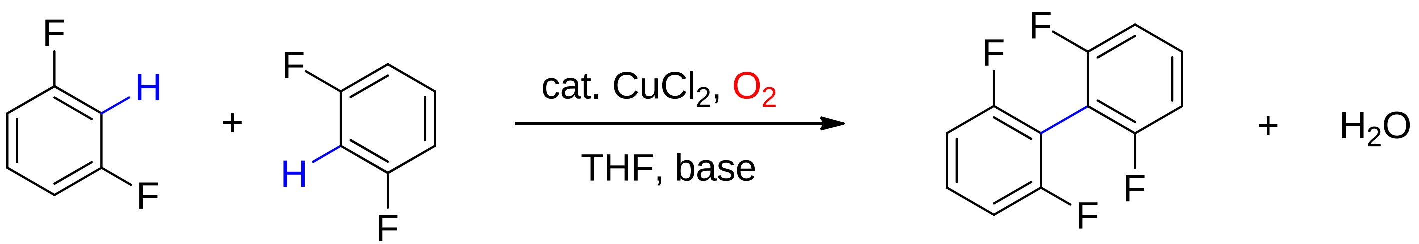
Glaser, C. *Ber. Dtsch. Chem. Ges.* **1869,** *2,* 422.
Glaser, C. *Ann. Chem. Pharm.* **1870,** *154,* 137.

Arene Dimerization

Aromatic Glaser-Hay Reaction

$$\mathrm{Ar{-}H} \xrightarrow[\text{THF, base}]{\text{cat. }CuCl_2,\ O_2} \mathrm{Ar{-}Ar}$$

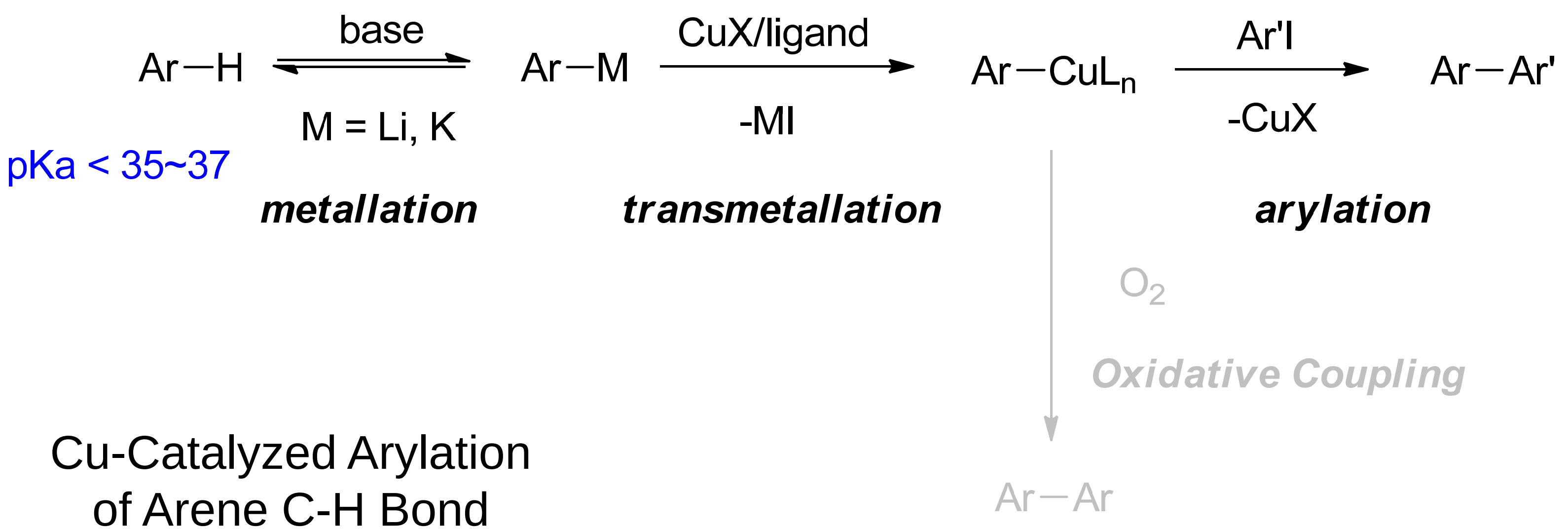
Copper-catalyzed, deprotonative dimerization of arenes by employing O_2 as the terminal oxidant.



Do, H.Q.; Daugulis, O. *J. Am. Chem. Soc.*, **2009**, *131*, 17052–17053.

Aromatic Glaser-Hay Reaction

Previous Work



Cu-Catalyzed Arylation
of Arene C-H Bond

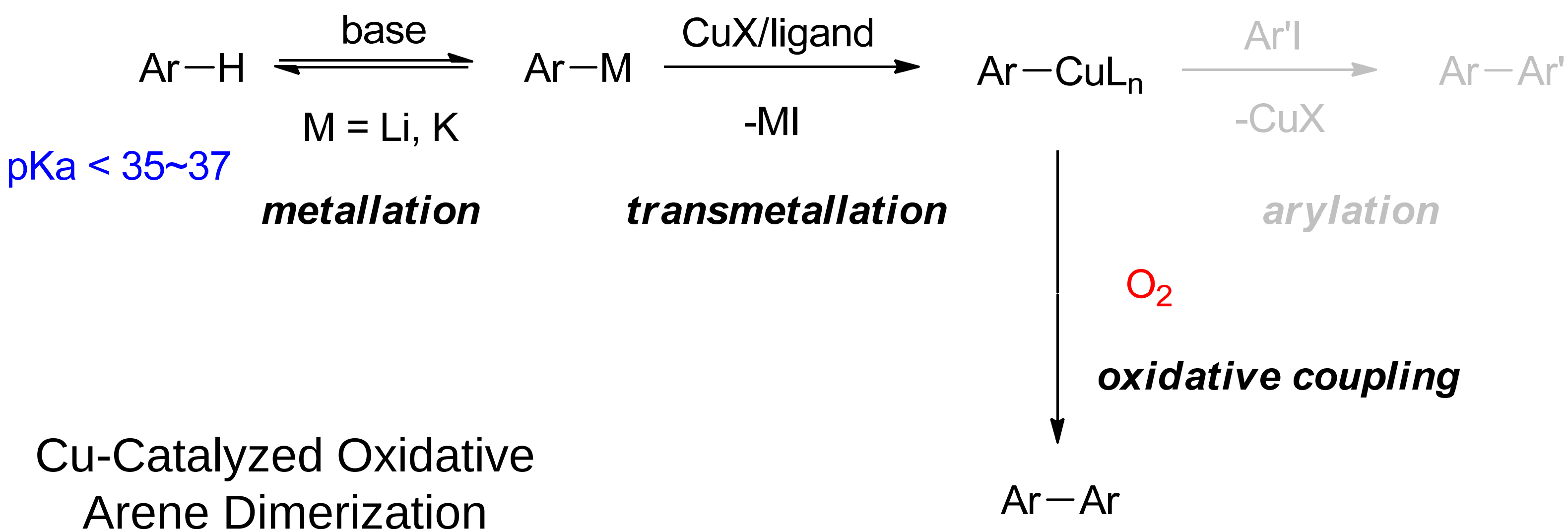
Do, H.-Q.; Daugulis, O. *J. Am. Chem. Soc.* **2007,** *129,* 12404-12405.

Do**,** H.-Q.; Daugulis, O. *J. Am. Chem. Soc.* ***2008,*** *130,* 1128.-1129

Do, H.-Q.; Khan, R. M. K.; Daugulis, O. *J. Am. Chem. Soc.* **2008**, *130,* 15185-15192.

Aromatic Glaser-Hay Reaction

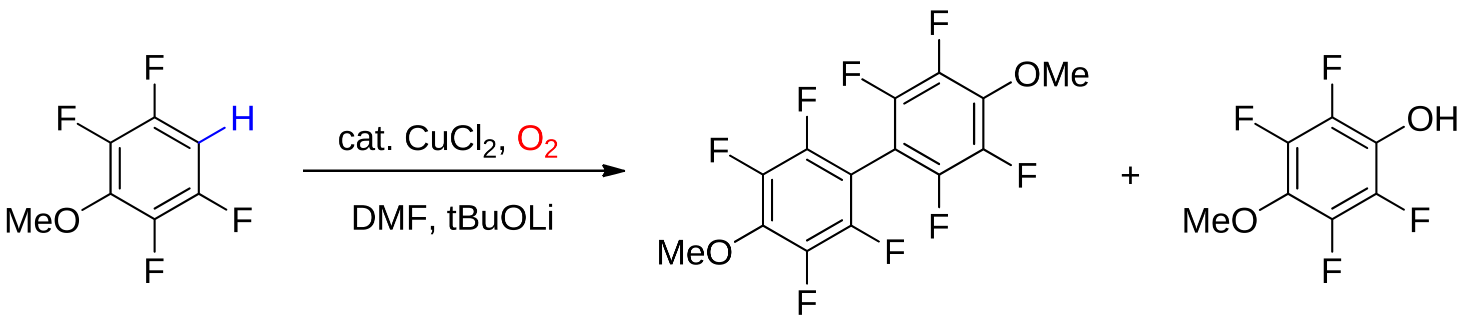
Inspiration from Previous Work



Cu-Catalyzed Oxidative
Arene Dimerization

Do, H.Q.; Daugulis, O. *J. Am. Chem. Soc.*, **2009**, *131*, 17052–17053.

Initial Study on Aromatic Glaser-Hay Reaction



Methoxytetrafluorobenzene **56%** **38%**

Solution

A less polarized C-metal bond in the intermediate is needed!

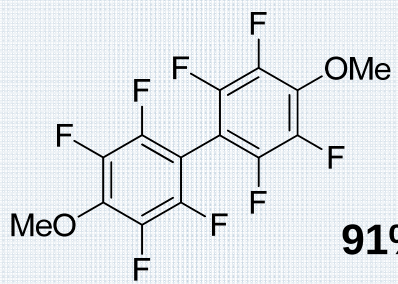
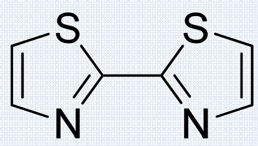
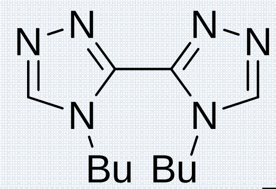
Formed by ArLi intermediate with O_2 or ArCu with hydroxide derived from water.

King, A. E.; Brunold, T. C.; Stahl, S. S. *J. Am. Chem. Soc.* **2009,** *131*, 5044-5045.
Do, H.Q.; Daugulis, O. *J. Am. Chem. Soc.*, **2009**, *131*, 17052–17053.

Substrate Scope of Aromatic Glaser-Hay Reaction

$$\mathrm{Ar{-}H} \xrightarrow[\text{THF, base, 0-50°C}]{\text{1-3 mol\% CuCl}_2\text{, O}_2} \mathrm{Ar{-}Ar}$$

- Hindered Zn and Mg amide bases were used
- Less acidic the arene H, the stronger base was needed

Base	Dicyclohexylamine : iPrMgCl•LiCl : $ZnCl_2$ (1.1 : 1 : 0.25)	iPrMgCl•LiCl : tetramethylpiperidine : $ZnCl_2$ (1 : 1.1 : 0.5)	iPrMgCl•LiCl : tetramethylpiperidine (1.1 : 1)
Product	 **91%**	 **71%**	 **73%**

Do, H.Q.; Daugulis, O. *J. Am. Chem. Soc.*, **2009**, *131*, 17052–17053.

Outline

- Cu-Catalyzed Oxidative Homo-Coupling Reaction

- Cu-Catalyzed Oxidative Hetero-Coupling Reaction

  - C-C Bond Formation

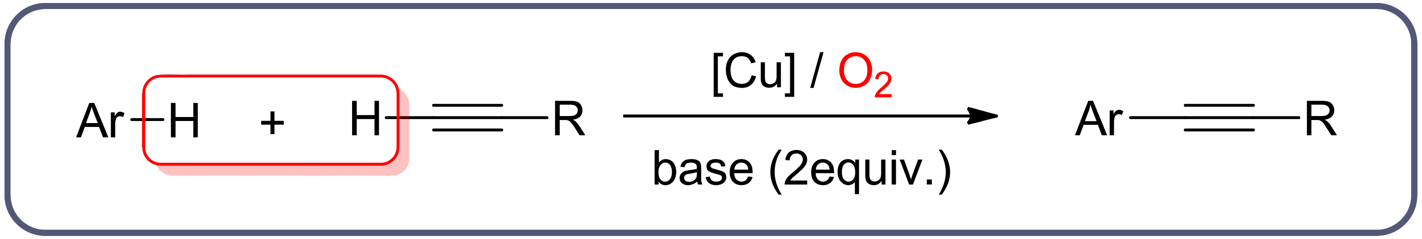
$$R^1{-}H \ + \ H{-}R^2 \xrightarrow[O_2]{[Cu]} R^1{-}R^2 \ + \ H_2O$$

  - C-N Bond Formation

  - C-P Bond Formation

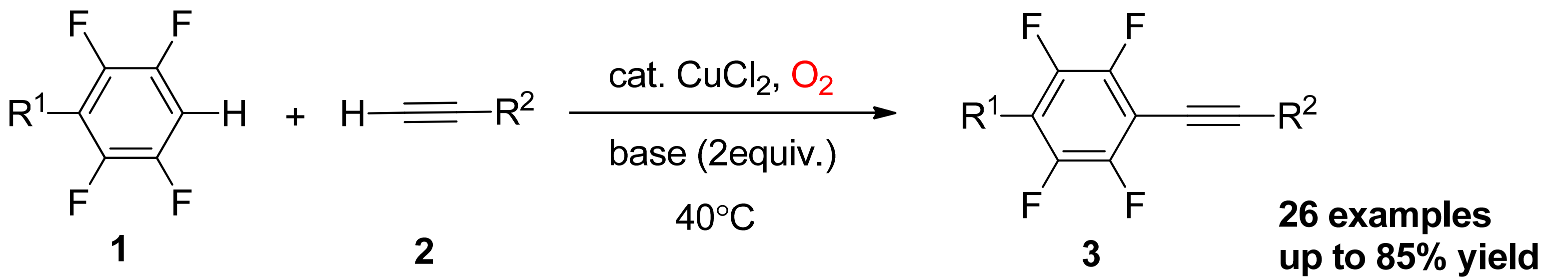
Cu-Catalyzed Direct Aerobic Alkynylation of Arenes with Terminal Alkynes

Direct Alkylation



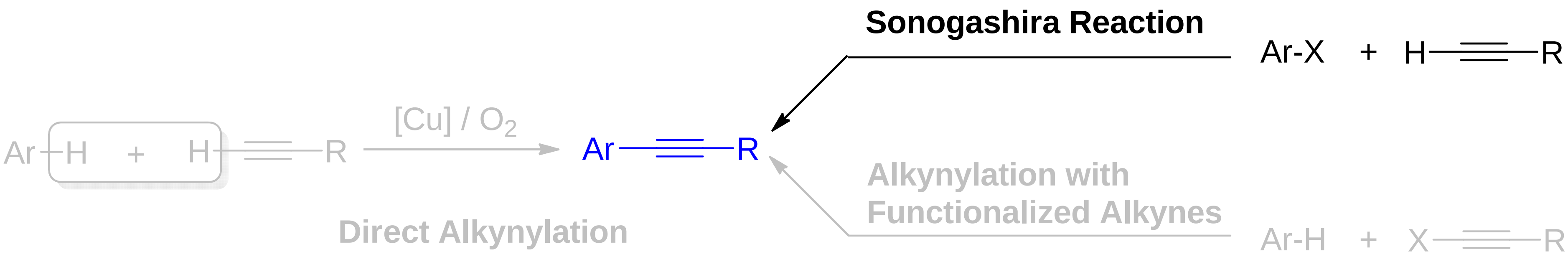
The first example of direct alkynylation of an aromatic C-H bond with terminal alkynes.

…but limited to polyfluroroarenes!

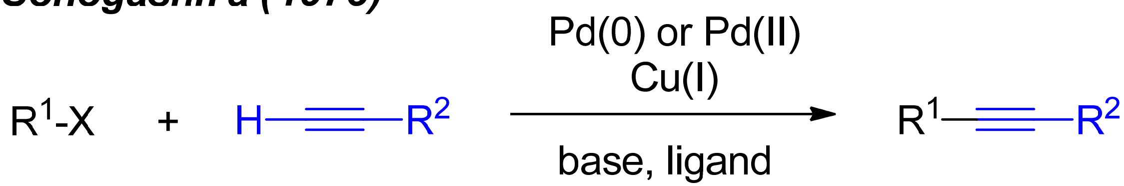


Wei, Y.; Zhao, H.; Kan, J.; Su, W. *J. Am. Chem. Soc.*, **2010**, *132*, 2522–2523.

Alkynylation of Arenes with Terminal Alkynes

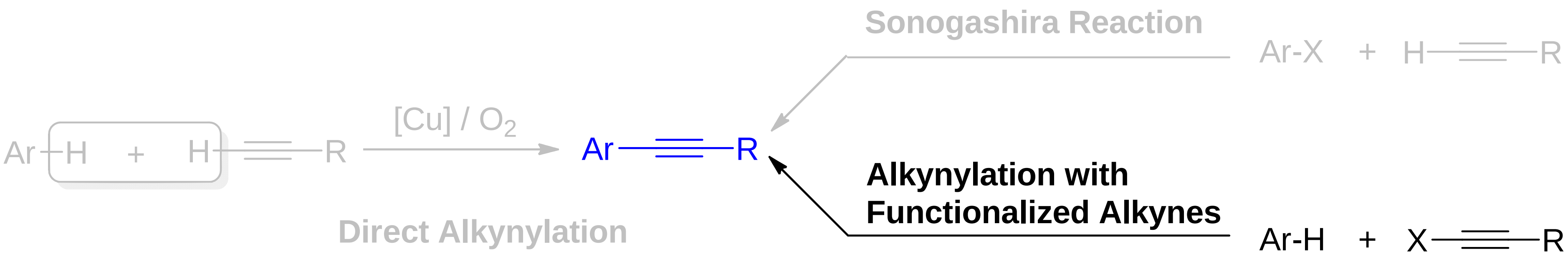


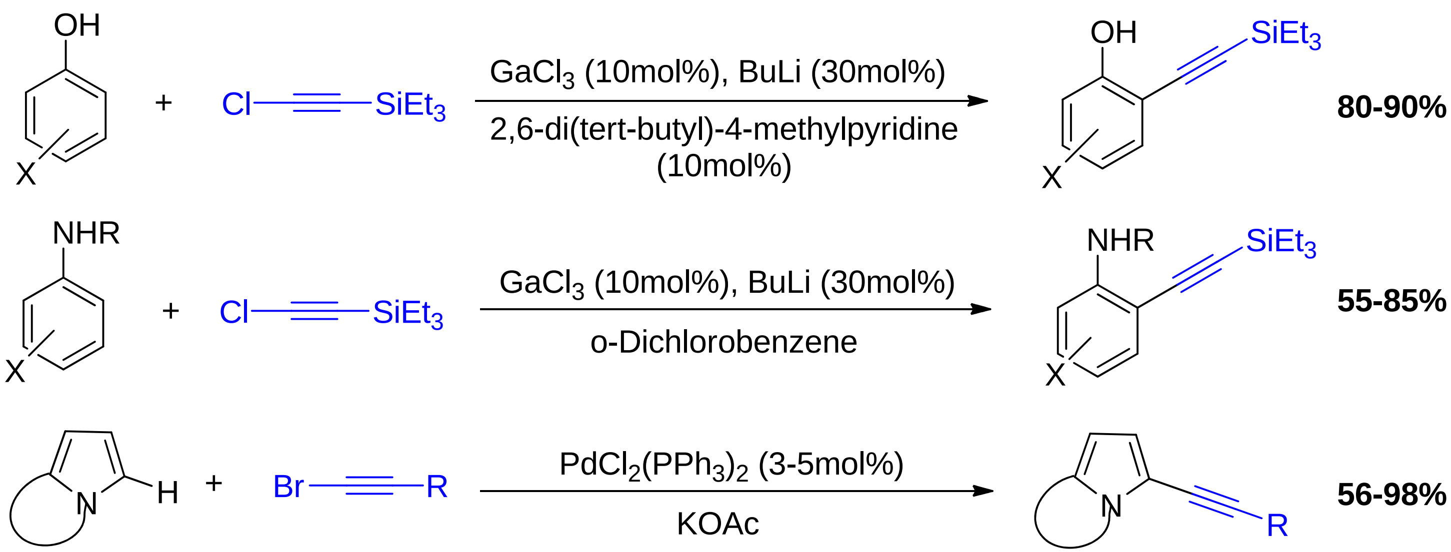
Sonogashira (1975)



Armin de Meijere, François Diederich, *Metal-Catalyzed Cross-Coupling Reactions, 2nd, Completely Revised and Enlarged Edition,* Wieley-VCH, Weinheim, **2004**
Wei, Y.; Zhao, H.; Kan, J.; Su, W. *J. Am. Chem. Soc.*, **2010**, *132*, 2522–2523.

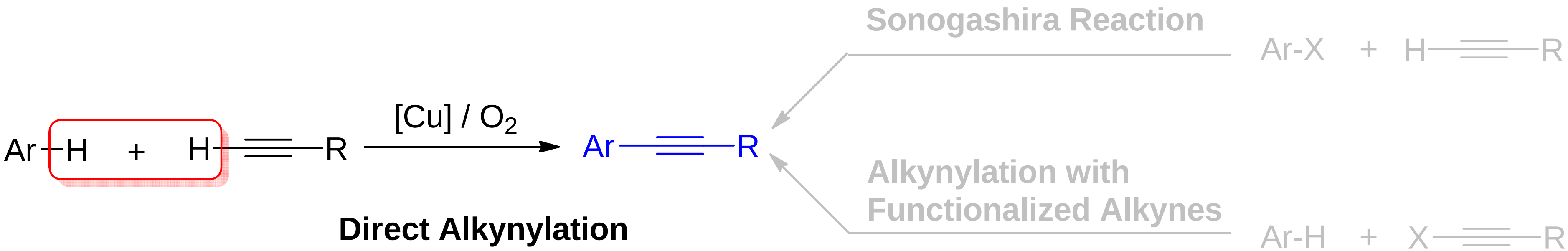
Alkynylation of Arenes with Terminal Alkynes

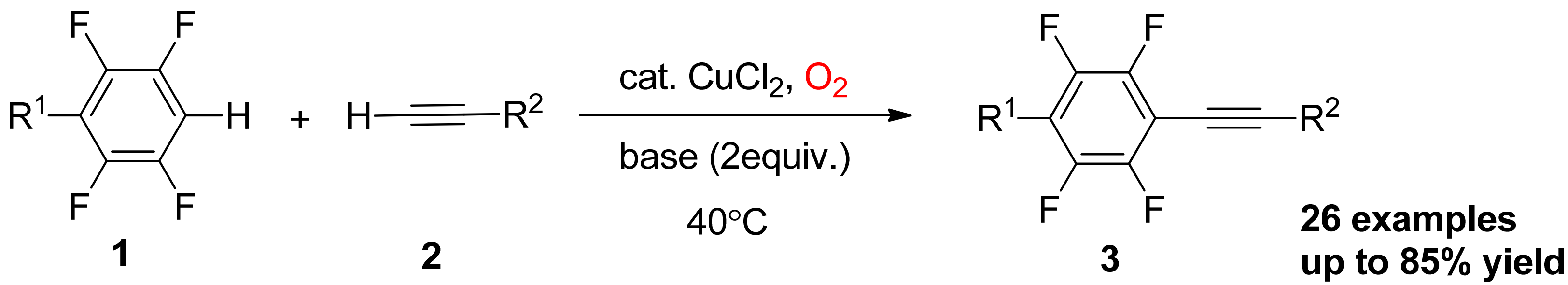




Kobayashi, K.; Arisawa, M.; Yamaguchi, M. *J. Am. Chem. Soc.* **2002,** *124,* 8528-8529.
Amemiya, R.; Fujii, A.; Yamaguchi, M. *Tetrahedron Lett.* **2004,** *45,* 4333-4335.
Seregin, I. V.; Ryabova, V.; Gevorgyan, V. *J. Am. Chem. Soc.* **2007,***129,* 7742-7744.

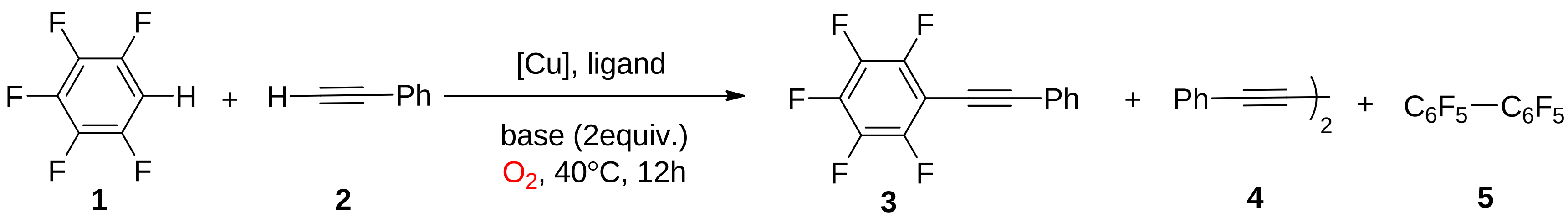
Cu-Catalyzed Direct Aerobic Alkynylation of Arenes with Terminal Alkynes





Wei, Y.; Zhao, H.; Kan, J.; Su, W. *J. Am. Chem. Soc.*, **2010**, *132*, 2522–2523.

Cu-Catalyzed Aerobic Alkynylation of Pentafluorobenzene with Phenylacetylene

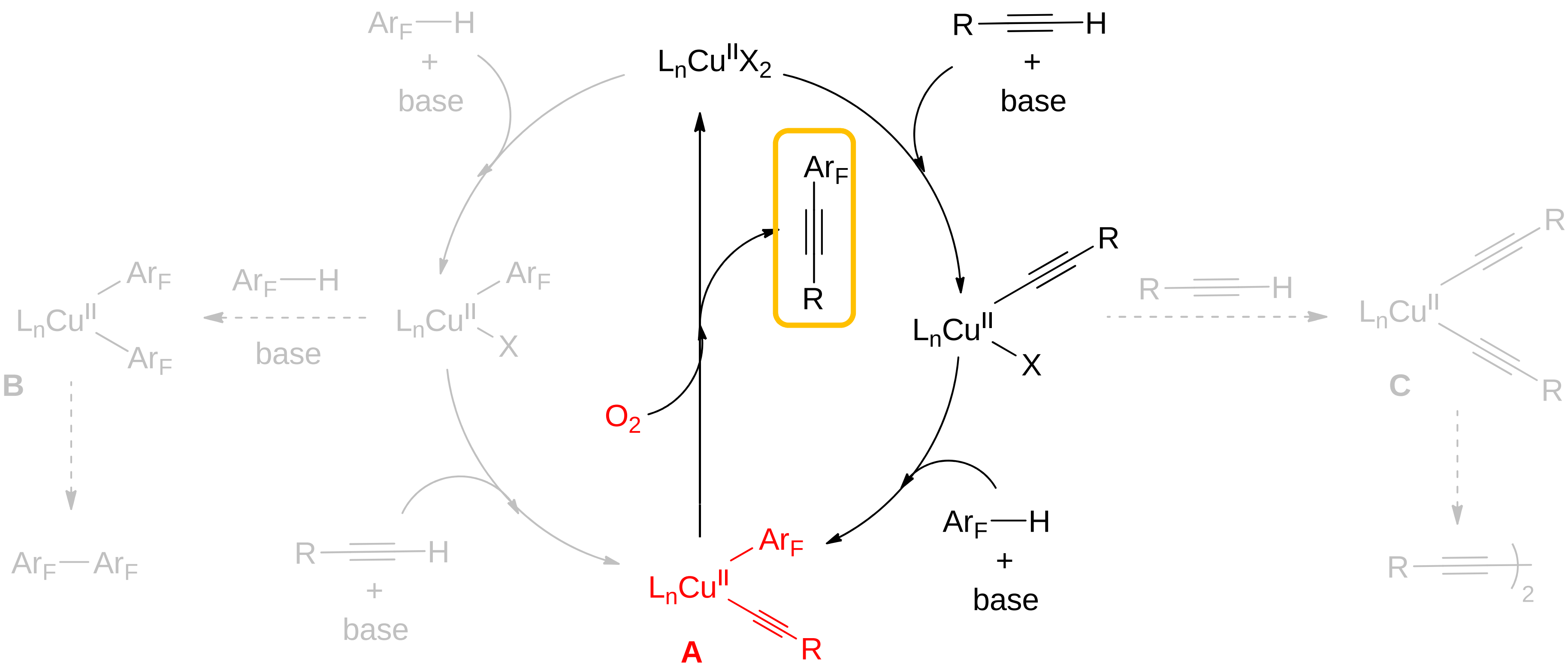


Entry	Reaction Condition (equiv. of reagents)	Solvent	% Yield 3 (4/5)
1	$CuCl_2$ (20 mol%.), O_2 (1atm), $NaHCO_3/K_3PO_4$ (2equiv.)	DMSO, 70°C	**undetectable** (>90/-)
2	$CuCl_2$ (20 mol%), O_2 (1atm), tBuOLi (2equiv.)	DMSO, 40°C	**11** (57/5)
3	$CuCl_2$ (20 mol%), O_2 (1atm), tBuOLi (2equiv.), 1,10-phenanthroline (0.2equiv.)	DMSO, 40°C	**49** (38/4)
4	$CuCl_2$ (20 mol%), O_2 (1atm), tBuOLi (2equiv.), 1,10-phenanthroline (0.2equiv.) DDQ (0.15equiv.)	DMSO, 40°C	**72** (24/7)
5	$CuCl_2$ (30 mol%), O_2 (1atm), tBuOLi (3equiv.), 1,10-phenanthroline (0.3 equiv.) DDQ (0.15equiv.)	DMSO, 40°C	**85** (14/13)

Wei, Y.; Zhao, H.; Kan, J.; Su, W.; *J. Am. Chem. Soc.*, **2010**, *132*, 2522–2523.

Proposed Mechanism of Cu-Catalyzed Direct Aerobic Alkynylation

Cross-Coupling Pathway



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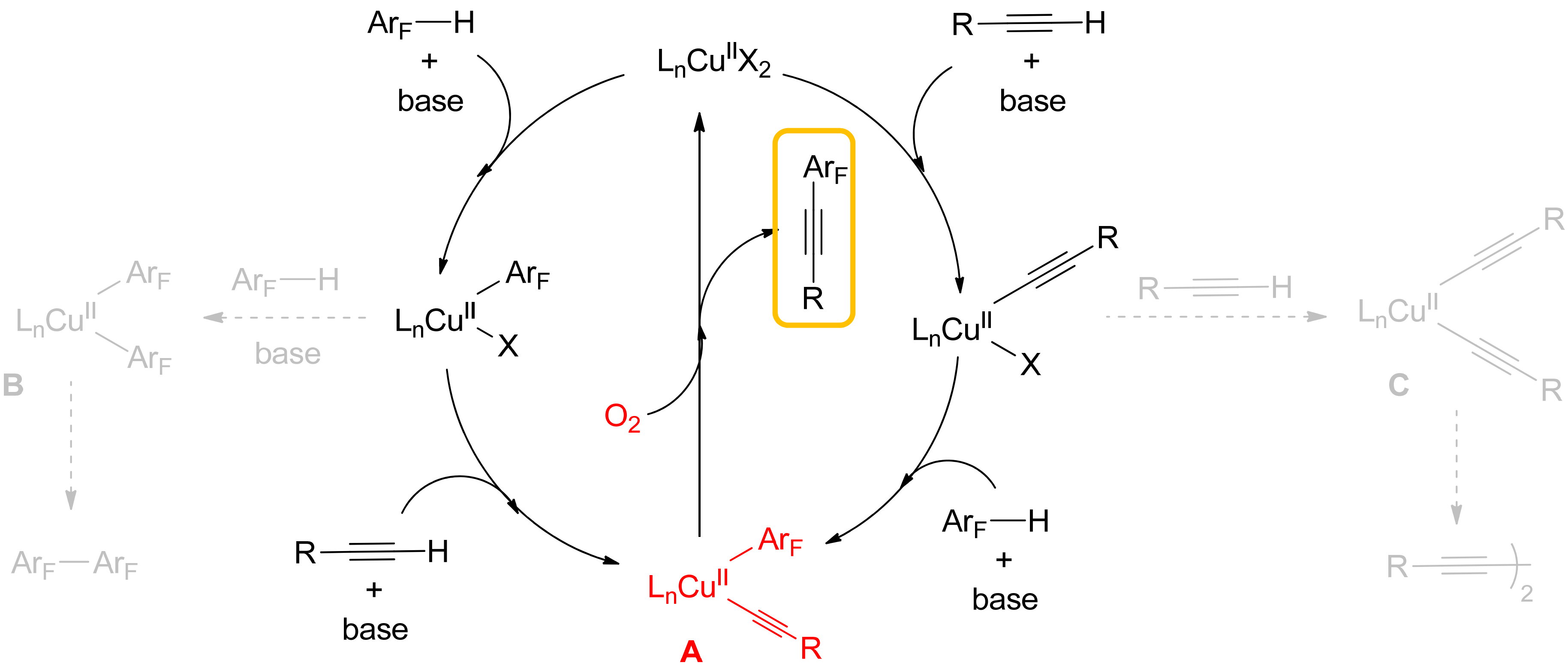
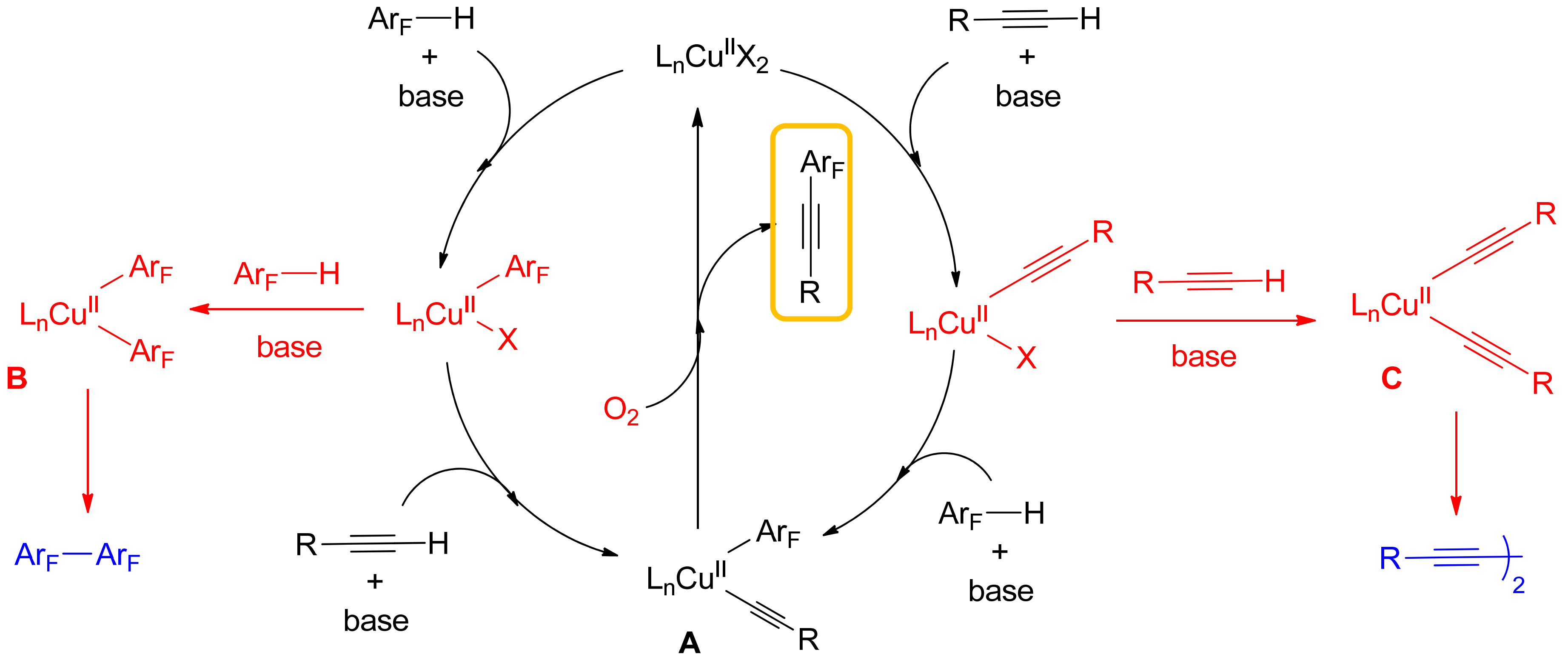


Wei, Y.; Zhao, H.; Kan, J.; Su, W. *J. Am. Chem. Soc.*, **2010**, *132*, 2522–2523.

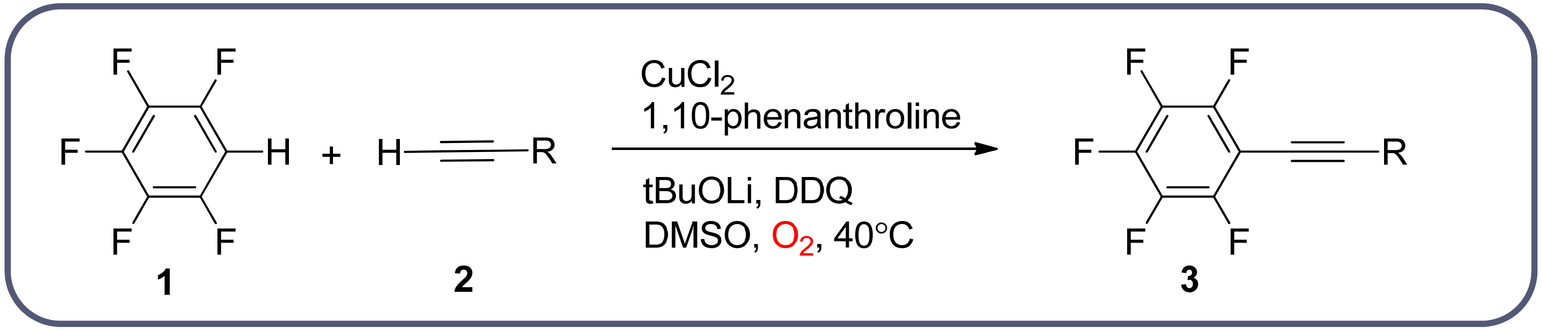
Proposed Mechanism of Cu-Catalyzed Direct Aerobic Alkynylation

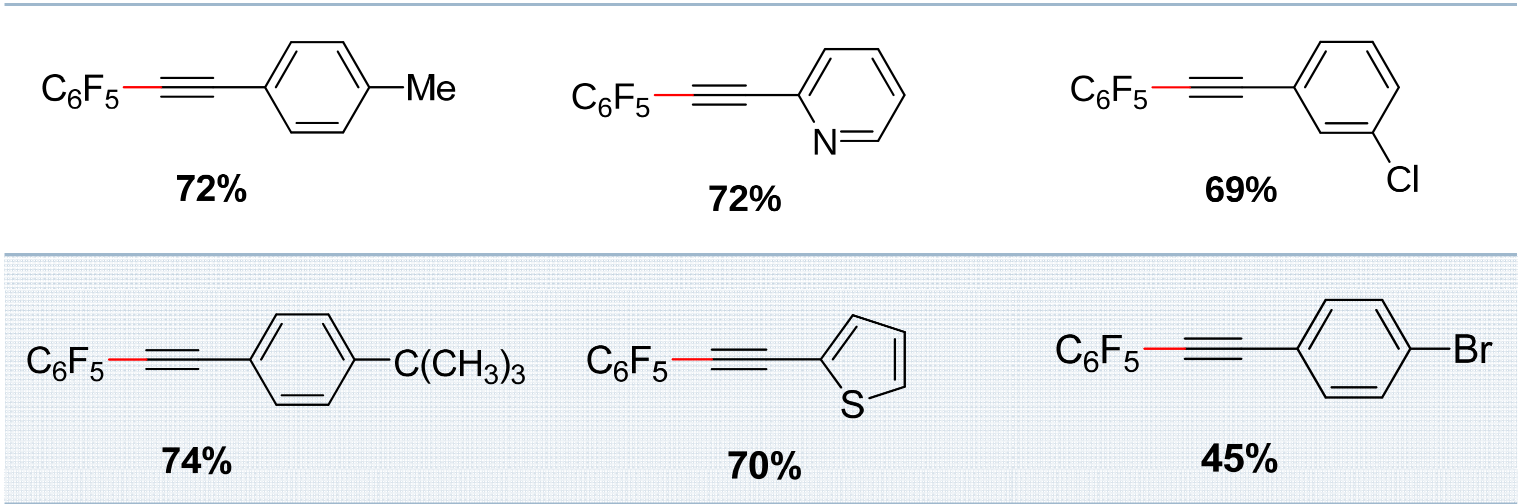
Homo-Coupling and Cross-Coupling Pathway



Wei, Y.; Zhao, H.; Kan, J.; Su, W. *J. Am. Chem. Soc.*, **2010**, *132*, 2522–2523.

Substrate Scope of Cu-Catalyzed Direct Aerobic Alkynylation





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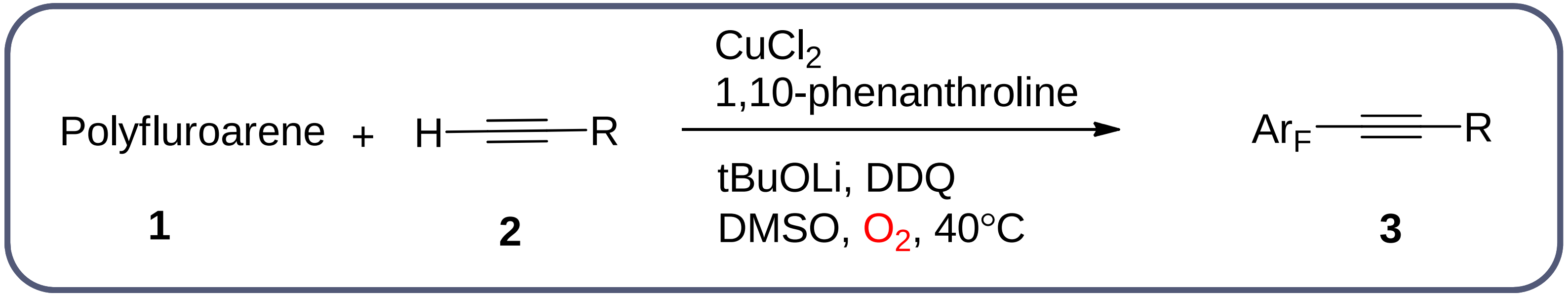
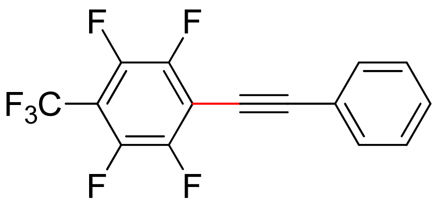
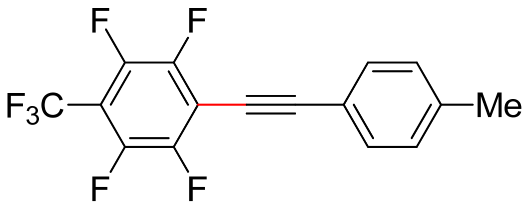
Substrate Scope of Cu-Catalyzed Direct Aerobic Alkynylation

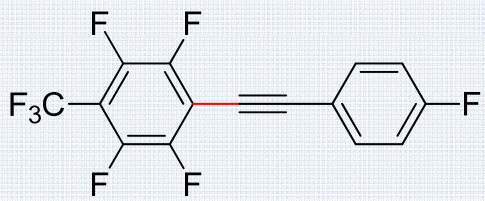




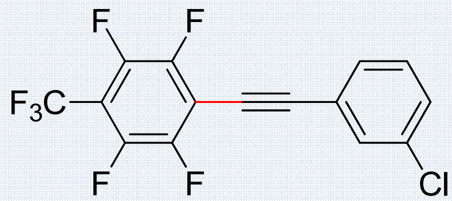
84%



76%



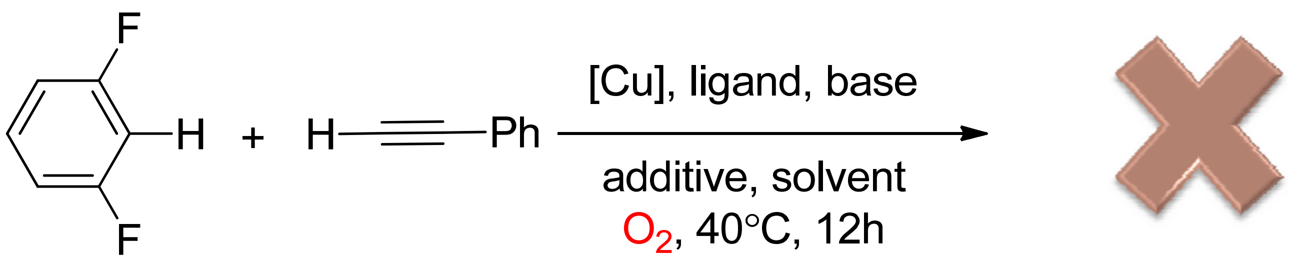
85%

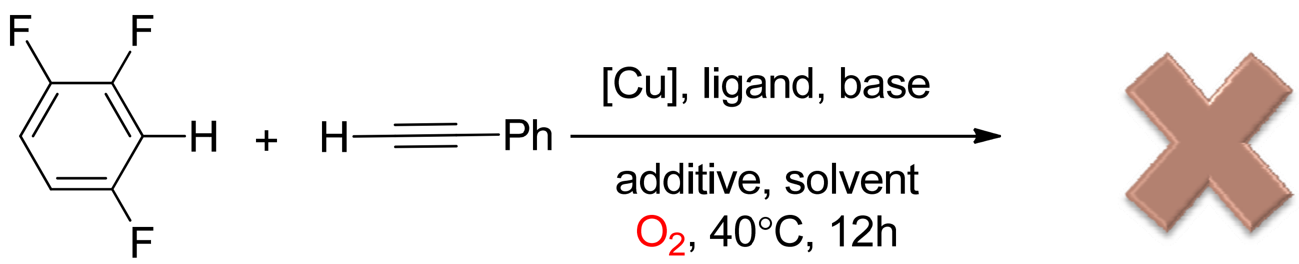


70%

Wei, Y.; Zhao, H.; Kan, J.; Su, W.; *J. Am. Chem. Soc.*, **2010**, *132*, 2522–2523.

Substrate Scope of Cu-Catalyzed Direct Aerobic Alkynylation



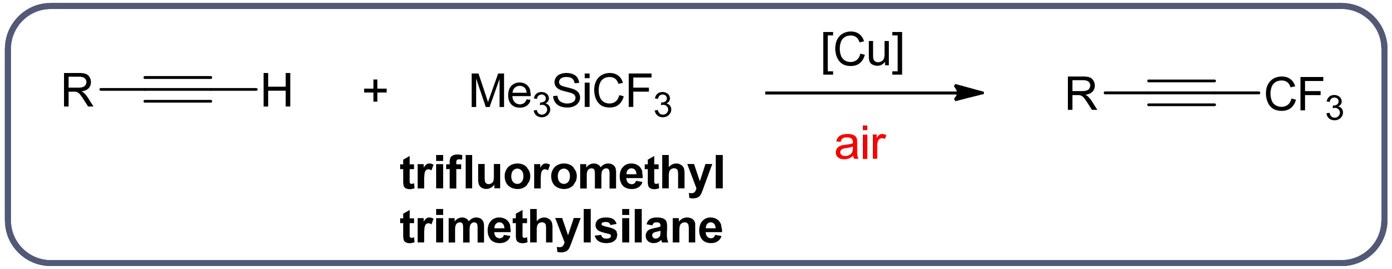


Both tri- and difluoroarenes are unreactive.

Wei, Y.; Zhao, H.; Kan, J.; Su, W. *J. Am. Chem. Soc.*, **2010**, *132*, 2522–2523.

Cu Mediated Aerobic Oxidative Trifluoromethylation of Terminal Alkynes

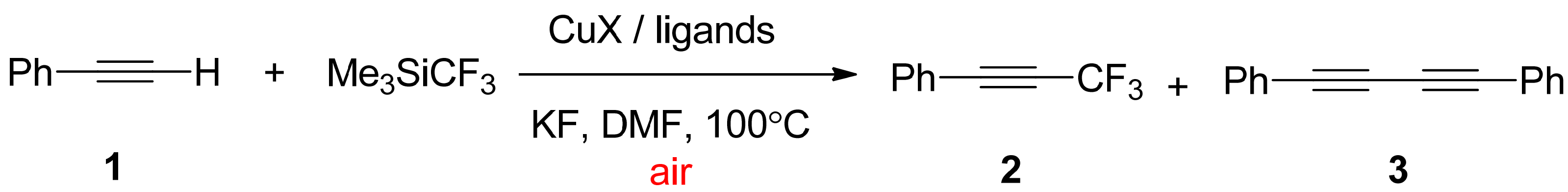
The first example of a copper-mediated oxidative trifluoromethylation.

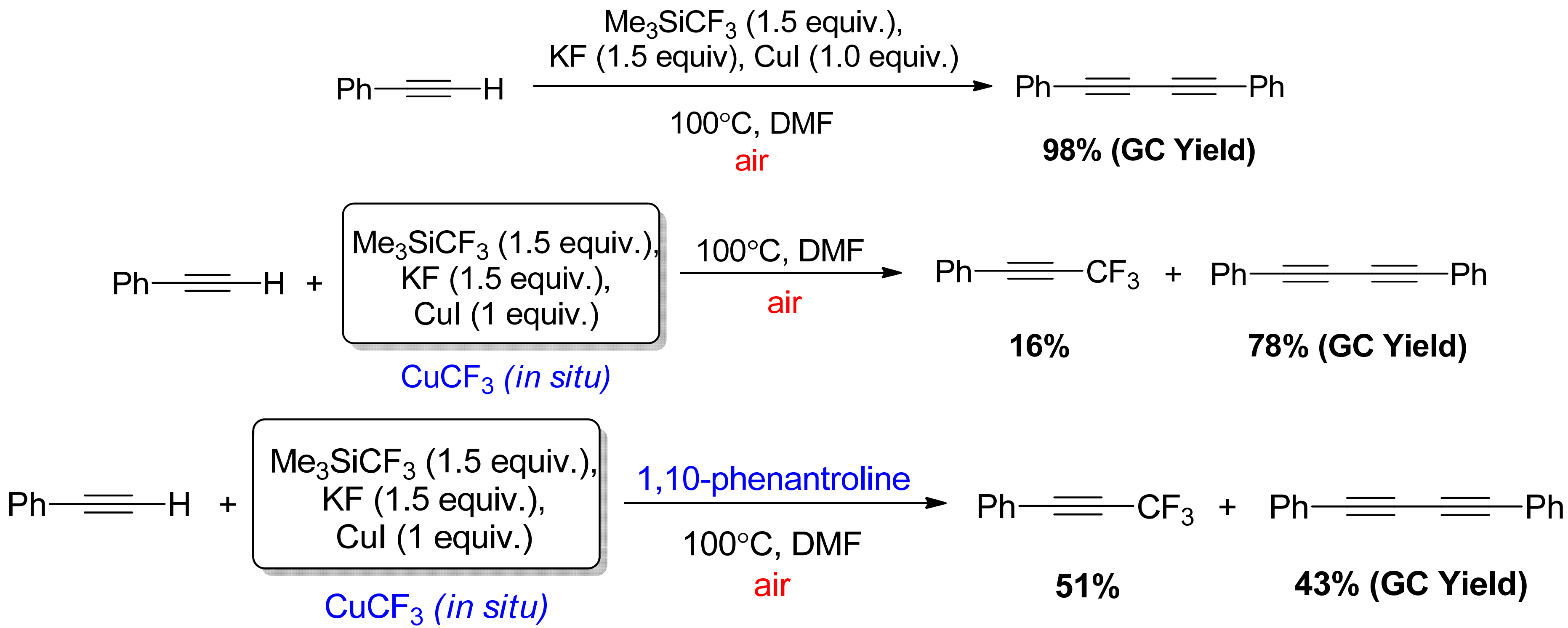


- In situ generated $CuCF_3$
- Direct oxidative coupling of terminal alkynes

Chu, L.; Qing, F. *J. Am. Chem. Soc.*, **2010**, *132*, 7262–7263.

Initial Study on Aerobic Oxidative Trifluoromethylation

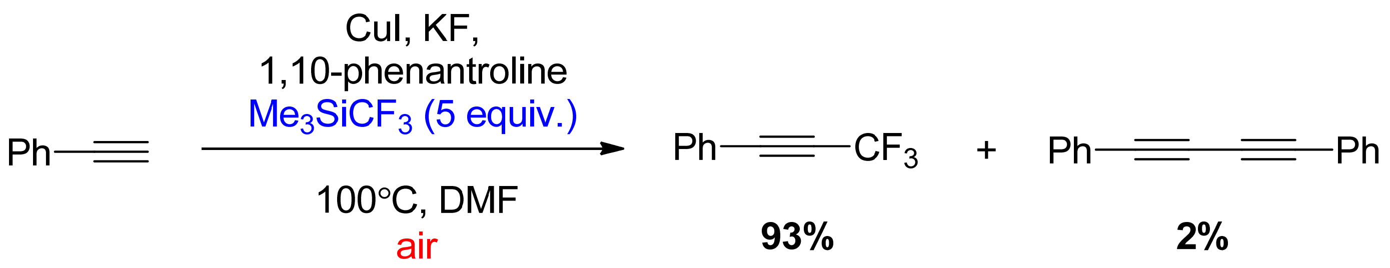




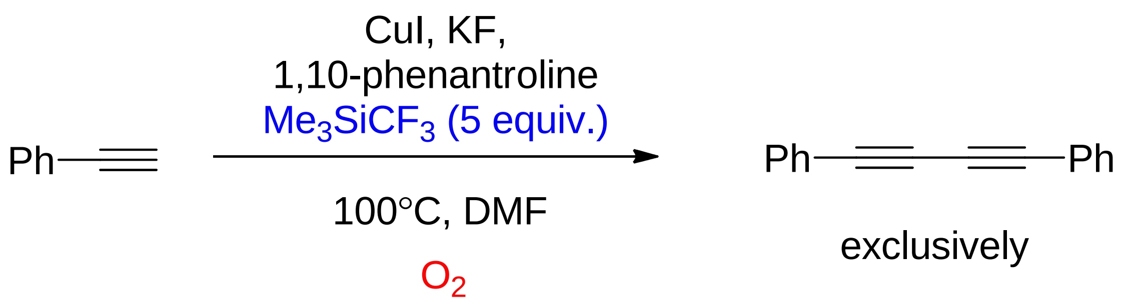
Chu, L.; Qing, F. *J. Am. Chem. Soc.*, **2010**, *132*, 7262–7263.

Initial Study on Aerobic Oxidative Trifluoromethylation

Under dry air



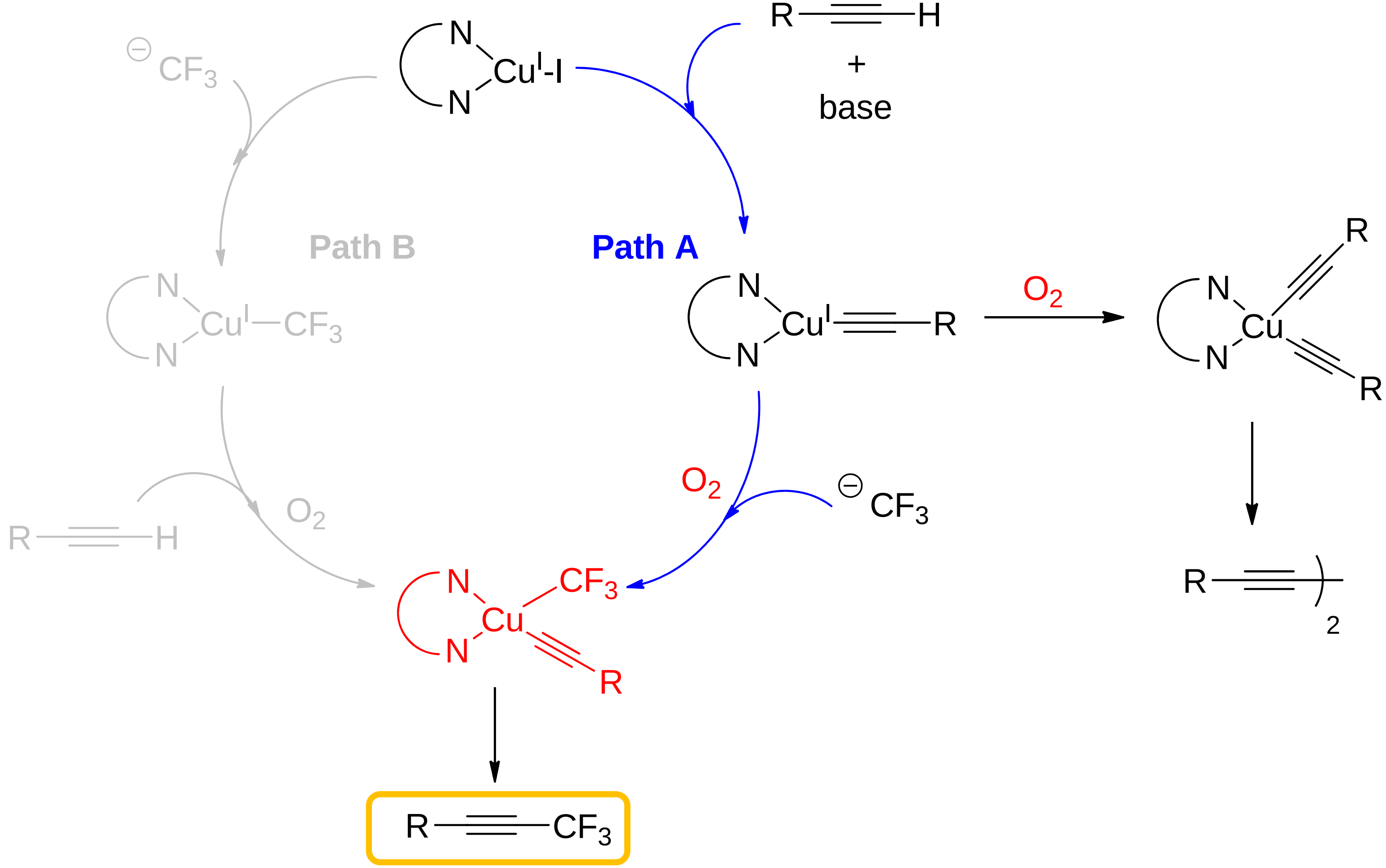
Under O_2



Reactive $CuCF_3$ was quenched by high concentration of O_2

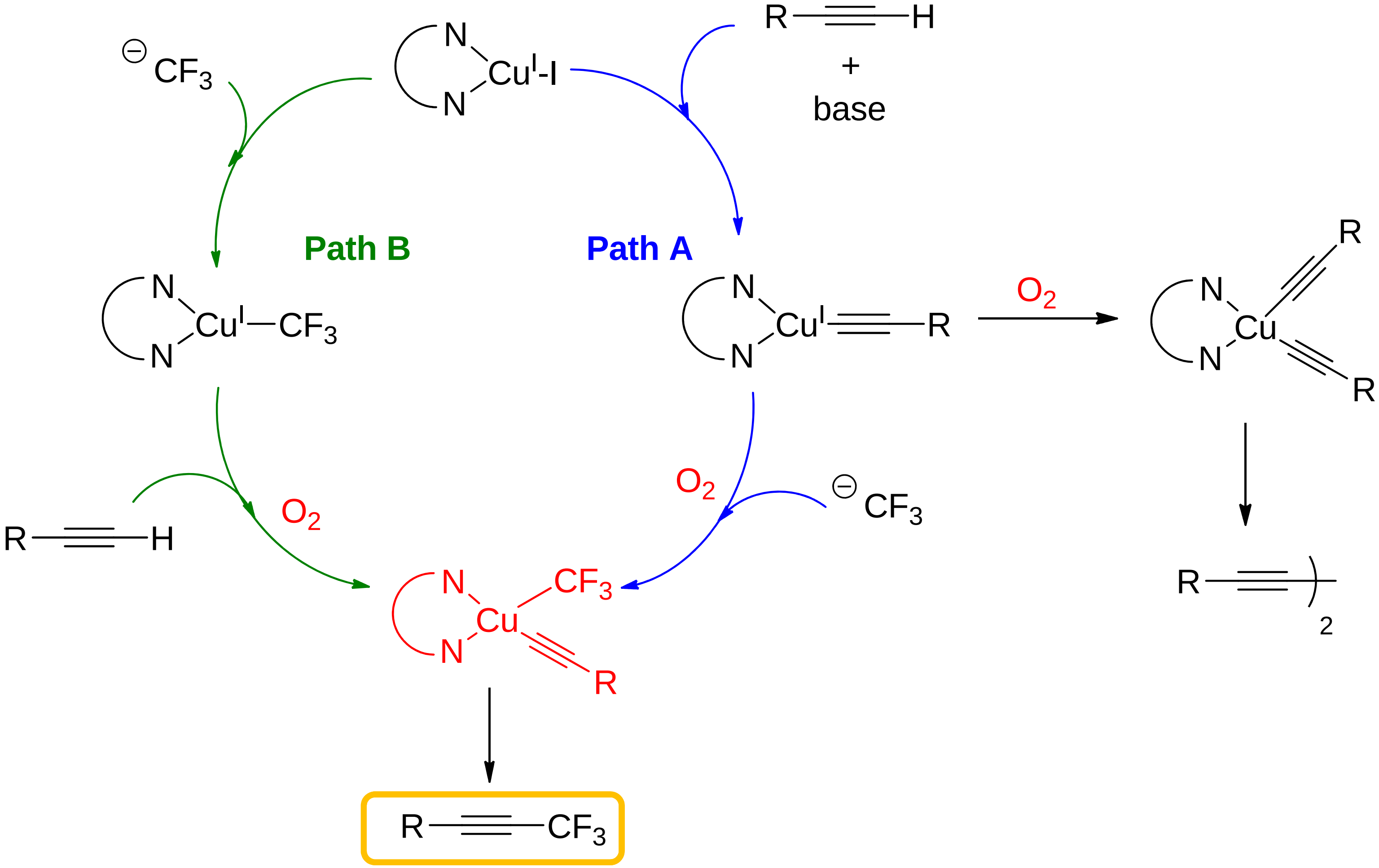
Chu, L.; Qing, F. *J. Am. Chem. Soc.*, **2010**, *132*, 7262–7263.
Wiemers, D. M. Burton, D. J. *J. Am. Chem. Soc.*, **1986**, *108*, 832–834.

Plausible Reaction Pathways for Aerobic Oxidative Trifluoromethylation



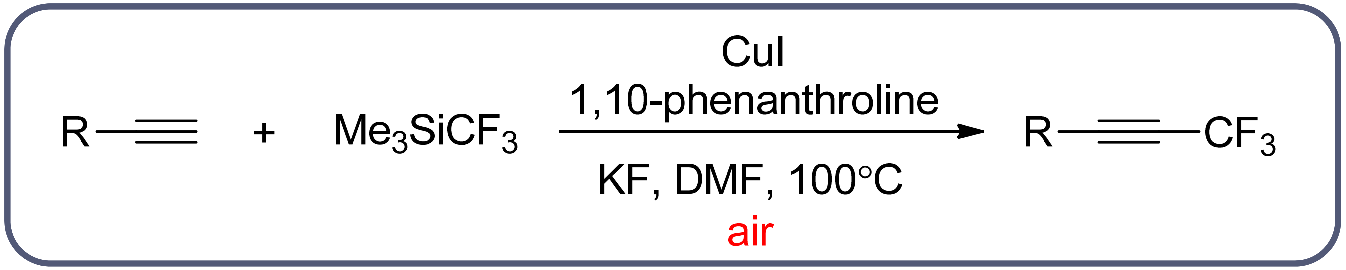
Chu, L.; Qing, F. *J. Am. Chem. Soc.*, **2010**, *132*, 7262–7263.

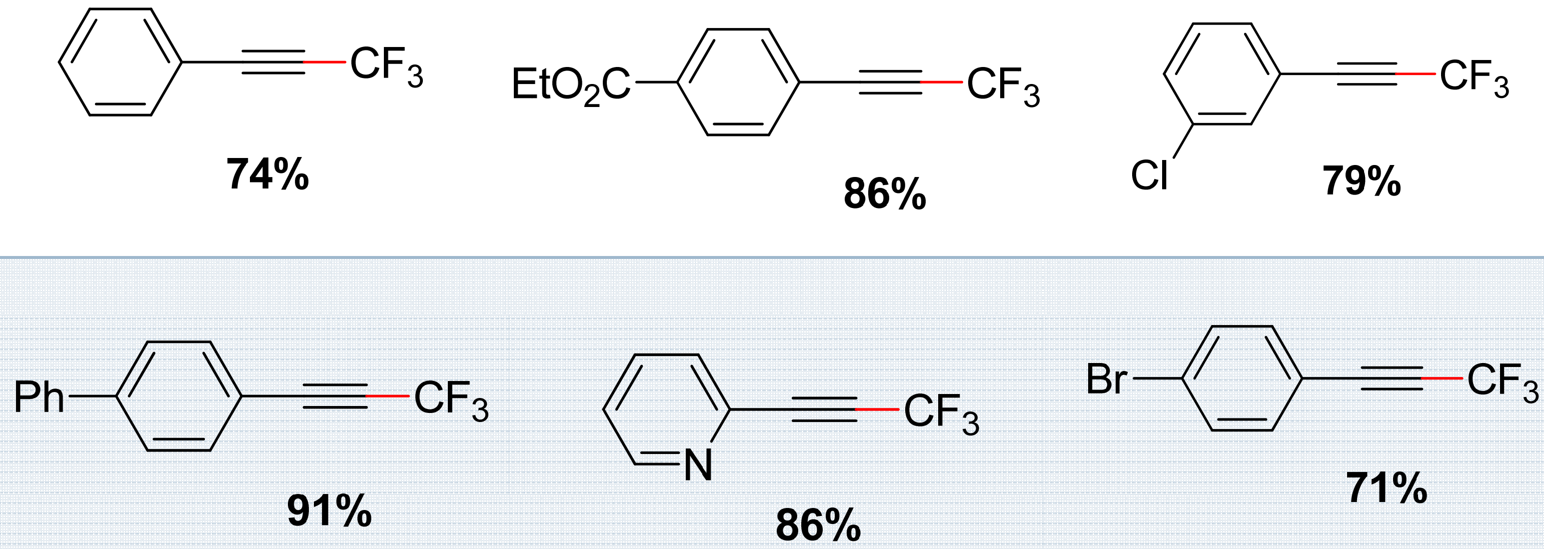
Plausible Reaction Pathways for Aerobic Oxidative Trifluoromethylation



Chu, L.; Qing, F. *J. Am. Chem. Soc.*, **2010**, *132*, 7262–7263.

Substrate Scope of Aerobic Oxidative Trifluoromethylation





Chu, L.; Qing, F. *J. Am. Chem. Soc.*, **2010**, *132*, 7262–7263.

Outline

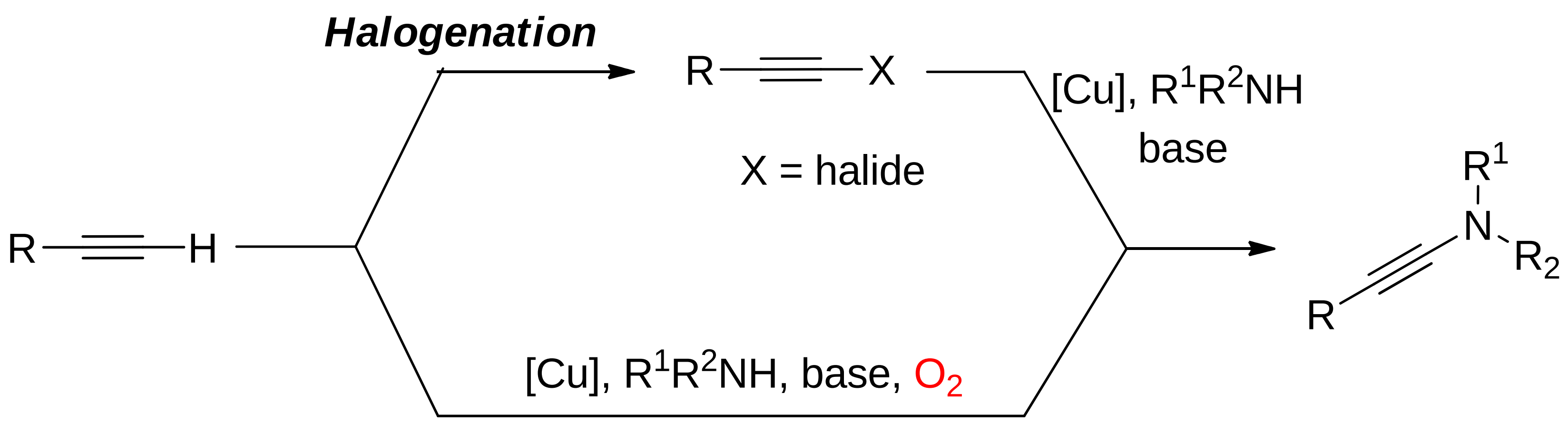
- Cu-Catalyzed Oxidative Homo-Coupling Reaction
- Cu-Catalyzed Oxidative Hetero-Coupling Reaction
  - C-C Bond Formation
  - C-N Bond Formation

$$R^1\text{–H} + \text{H–NRR'} \xrightarrow[O_2]{[Cu]} R^1\text{–NRR'} + H_2O$$

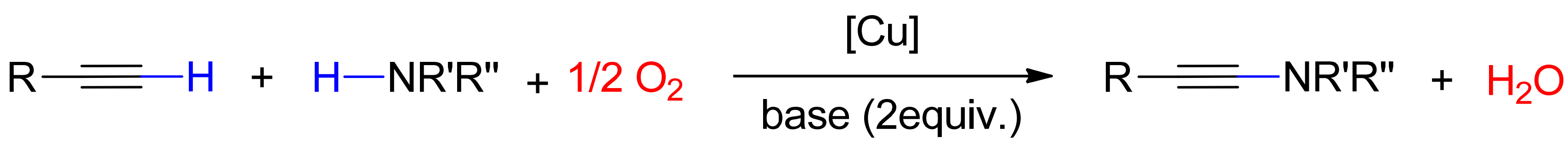
  - C-P Bond Formation

Amidation of Terminal Alkynes

Coupling via Alkynyl Halide

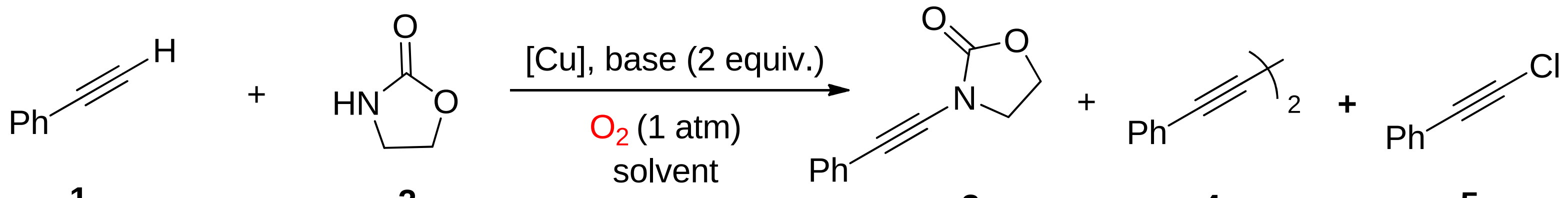


Direct Coupling of Terminal Alkynes



Hamada, T.; Ye, X.; Stahl, S. *J. Am. Chem. Soc.*, **2008**, *130*, 833–835.
DeKorver, K. A.; Li, H.; Lohse, A. G.; Hayashi, R.; Lu, Z.; Zhang, Y.; Hsung, R. P. *Chem. Rev*. **2010**, *110*, 5064–5106.

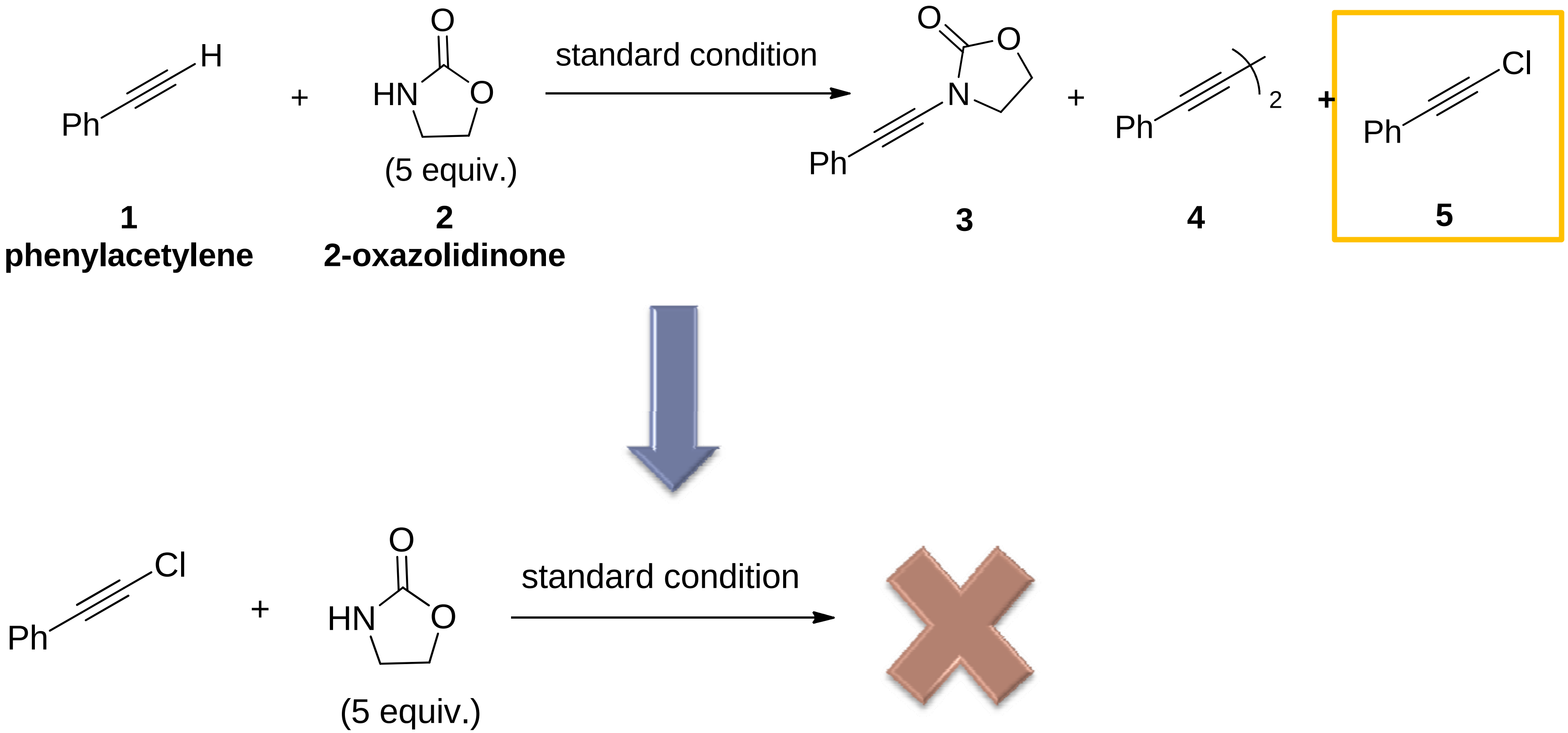
Cu Catalyzed Aerobic Oxidative Amidation of Terminal Alkynes



Entry	Reaction Condition (equiv. of reagents)	Solvent	% Yield 3 (4/5)
1	$CuCl_2$ (2), Cs_2CO_3 (2), 1 equiv. of **2**	DMSO 70°C	**26** (42/17)
2	$CuCl_2$ (2), Cs_2CO_3 (2), 5 equiv. of **2**	DMSO 70°C	**89** (4/-)
3	$CuCl_2$ (0.2), Cs_2CO_3 (2), , 5 equiv. of **2**	DMSO 70°C	**Trace** (19/-)
4	$CuCl_2$ (0.2), Na_2CO_3 (2), Pyridine (2), 5 equiv. of **2**	DMSO 70°C	**90** (4/-)
5	$CuCl_2$ (0.2), Na_2CO_3 (2), Pyridine (2), 1 equiv. of **2**	Toluene 70°C	**69** (16/4)

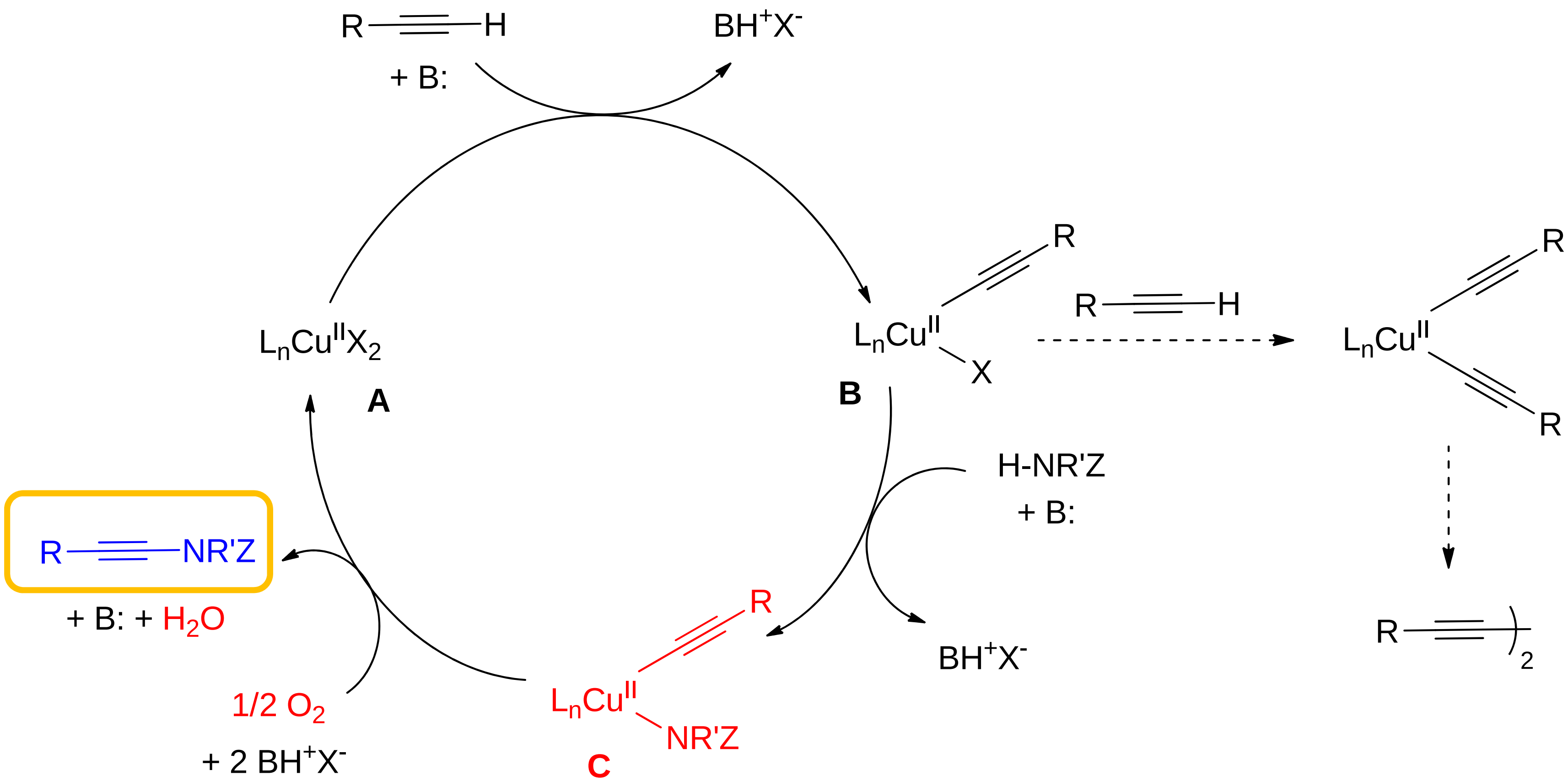
Hamada, T.; Ye, X.; Stahl, S. *J. Am. Chem. Soc.*, **2008**, *130*, 833–835.

Mechanistic Study of Cu Catalyzed Aerobic Oxidative Amidation of Terminal Alkynes



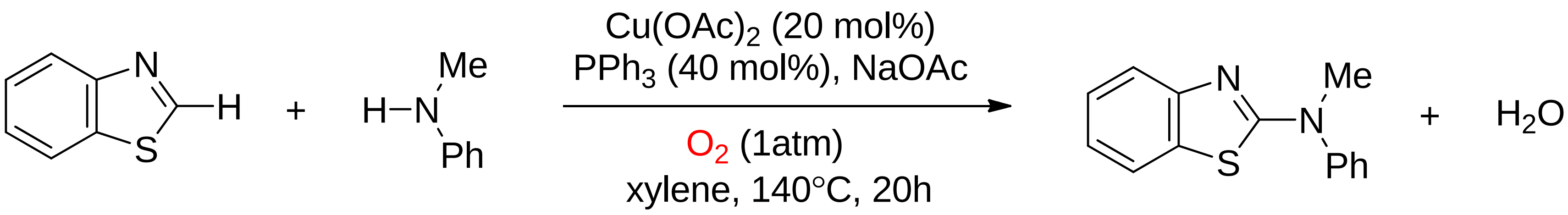
Hamada, T.; Ye, X.; Stahl, S. *J. Am. Chem. Soc.*, **2008**, *130*, 833–835.

Proposed Mechanism of Cu Catalyzed Aerobic Oxidative Amidation of Terminal Alkynes

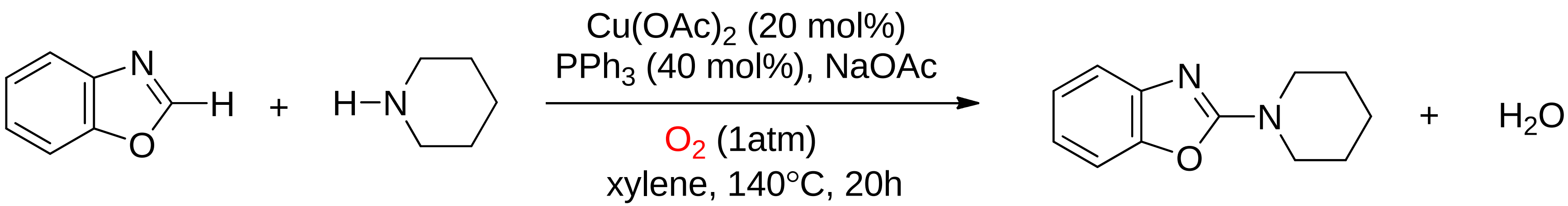


Hamada, T.; Ye, X.; Stahl, S. *J. Am. Chem. Soc.*, **2008**, *130*, 833–835.

Cu Catalyzed Direct Amination of Benzothiazoles and Benzoxazoles



Benzothiazole **N-Methylaniline** **81%**



Benzoxazole **Piperidine** **72%**

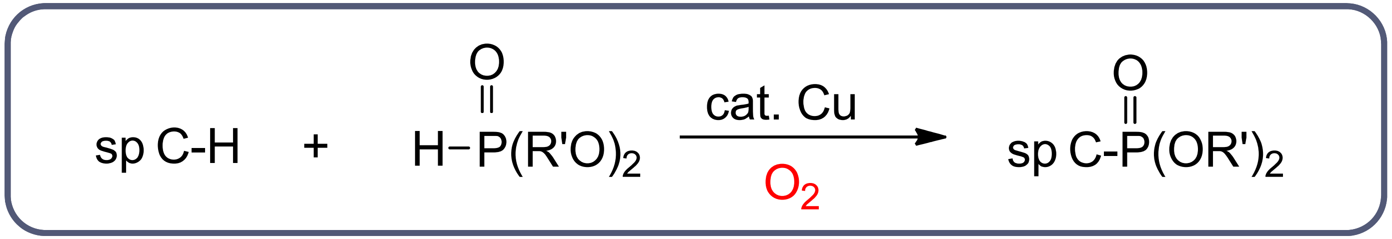
Monguchi, D.; Fujiwara, T.; Furukawa, H.; Mori, A. *Org. Lett.,* **2009**, *11*, 1607-1610.

Outline

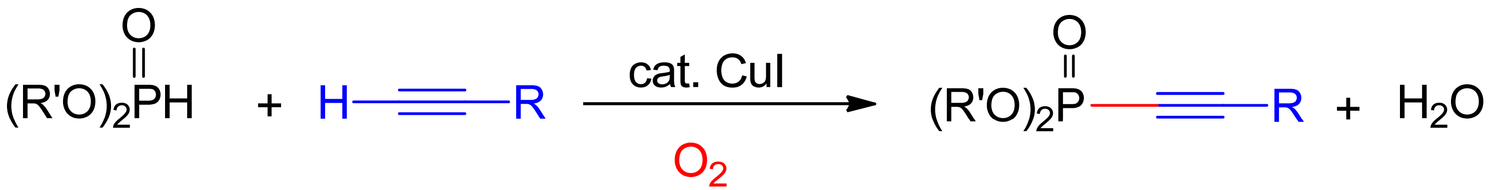
- Cu-Catalyzed Oxidative Homo-Coupling Reaction
- Cu-Catalyzed Oxidative Hetero-Coupling Reaction
  - C-C Bond Formation
  - C-N Bond Formation
  - C-P Bond Formation

$$R^1\boxed{-H \quad + \quad H-}P(O)(OR')_2 \xrightarrow[O_2]{[Cu]} R^1-P(O)(OR')_2 \quad + \quad H_2O$$

Cu Catalyzed Aerobic Phosphonation of sp C



A new methodology for catalytically constructing C-P bonds:



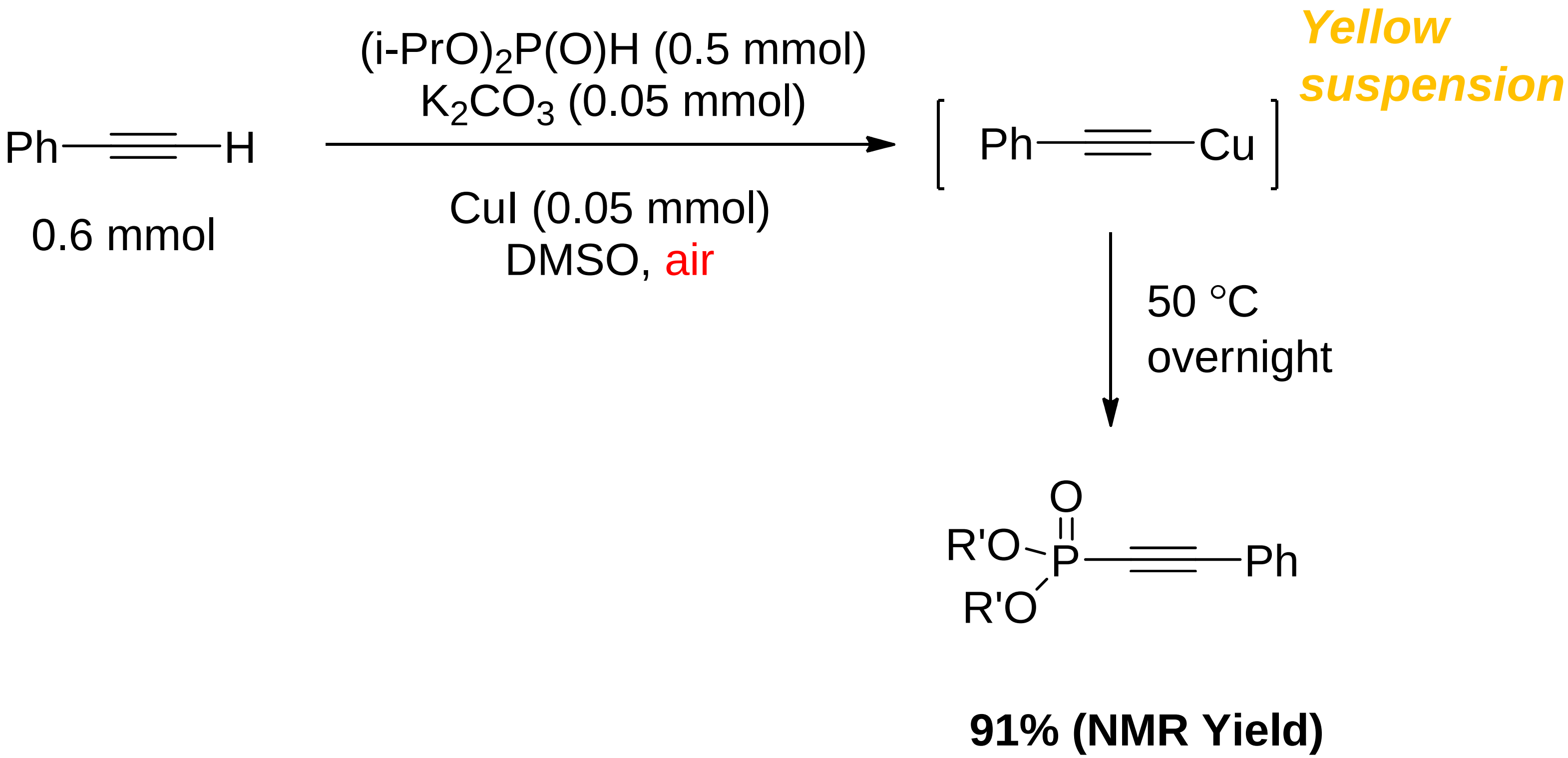
H-phosphonate

Alkynylphosphonate

Gao, Y.; Zhao, Y.; Zhou, Y.; Han, L. *J. Am. Chem. Soc.*, **2009**, *131*, 7956–7957.

Cu Catalyzed Aerobic Phosphonation of sp C

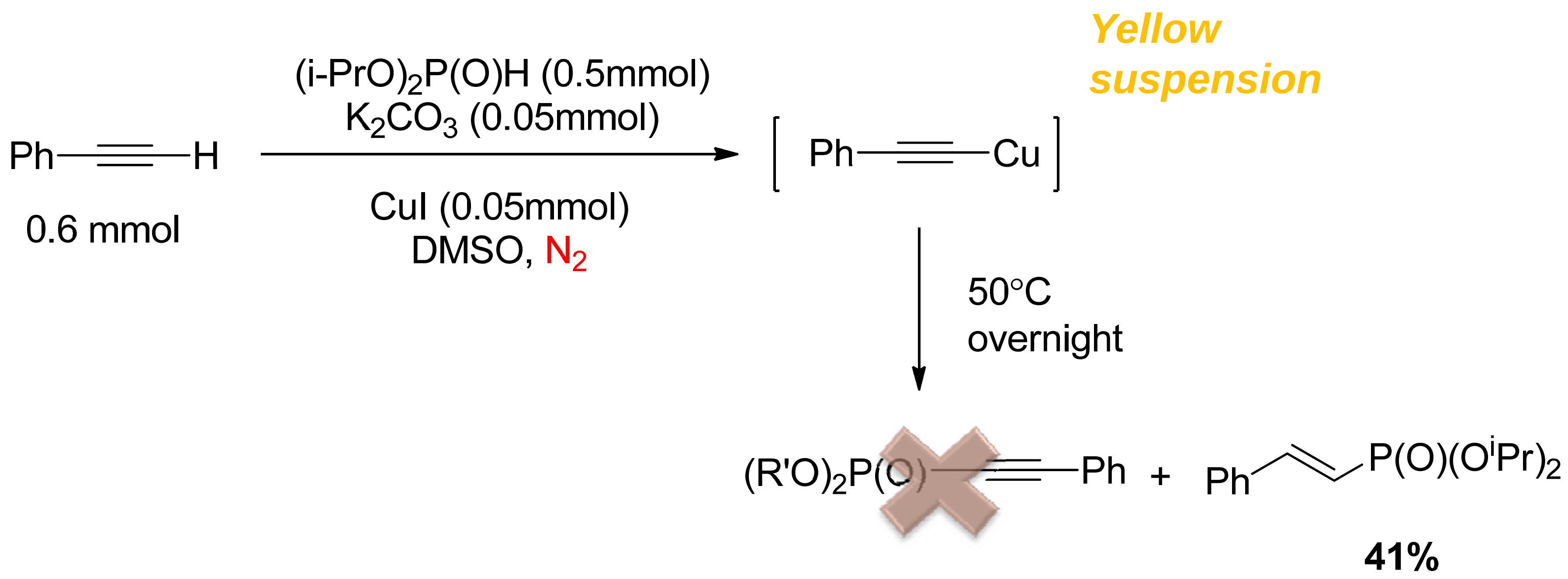
Under dry air



Gao, Y.; Zhao, Y.; Zhou, Y.; Han, L. *J. Am. Chem. Soc.*, **2009**, *131*, 7956–7957.
\Nakamura, E.; Mori, S. *Angew. Chem. Int. Ed*. **2000**, 39,3750-3771.

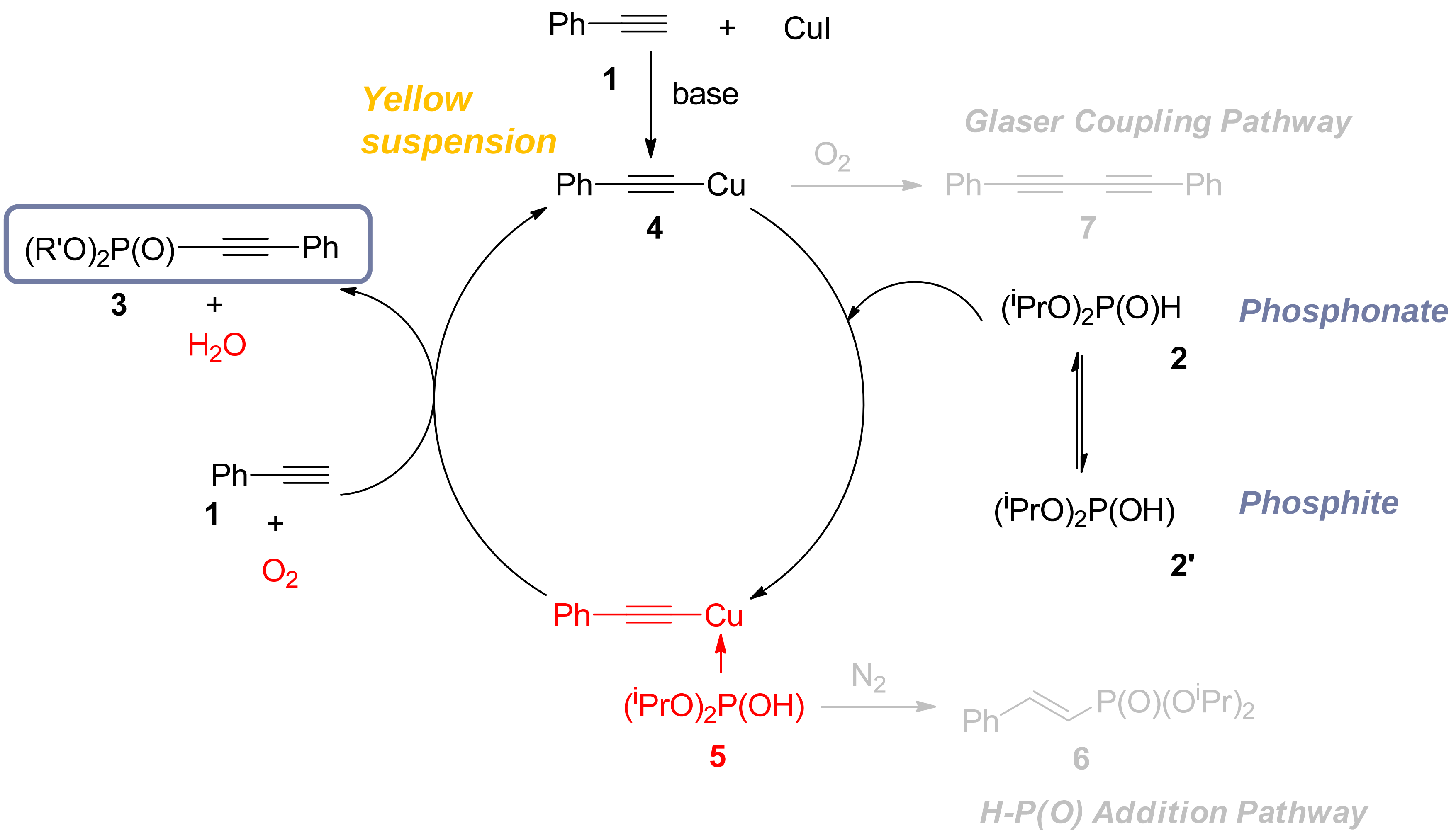
Cu Catalyzed Aerobic Phosphonation of sp C

Under N_2



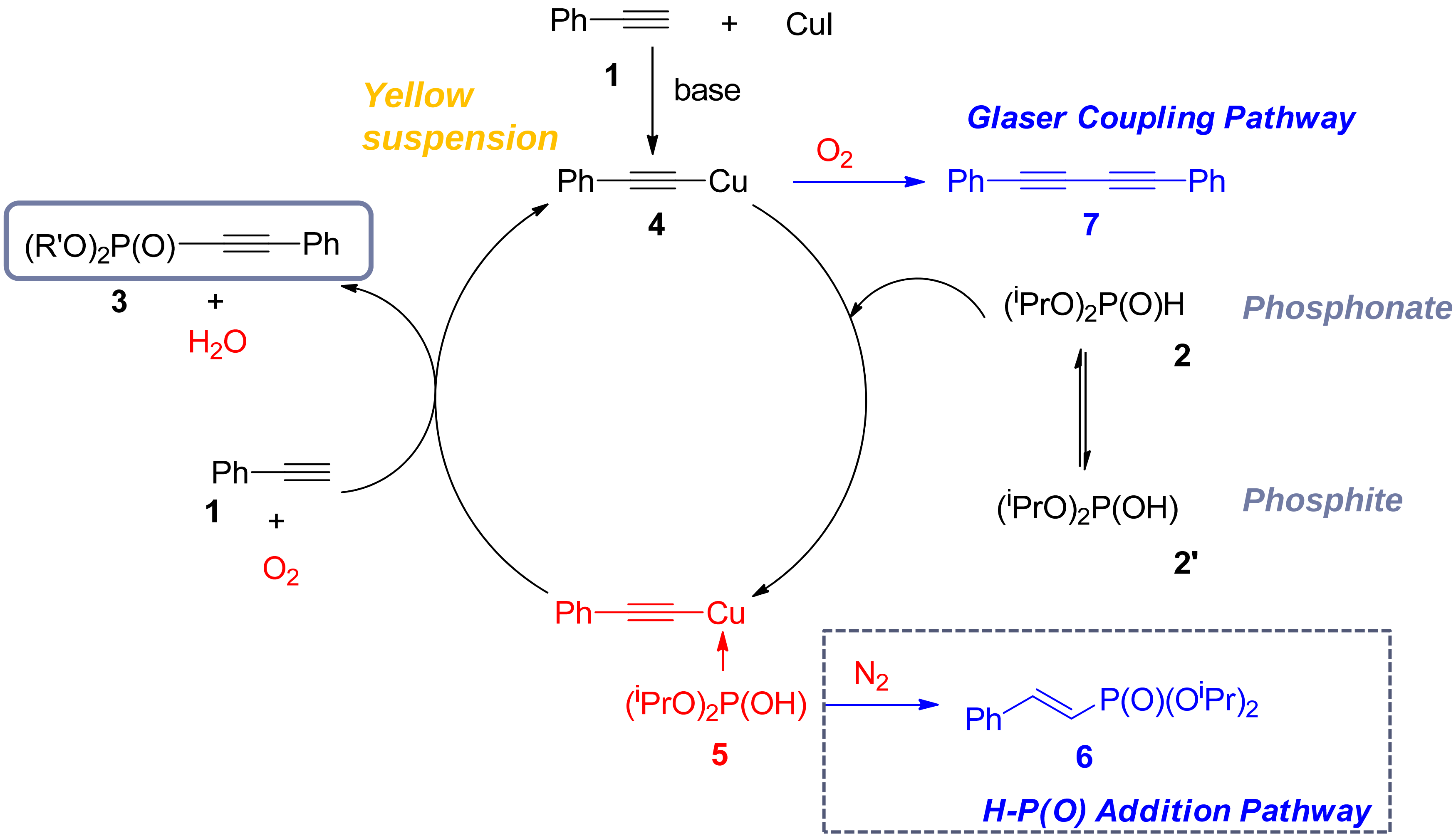
Gao, Y.; Zhao, Y.; Zhou, Y.; Han, L. *J. Am. Chem. Soc.*, **2009**, *131*, 7956–7957.
Nakamura, E.; Mori, S. *Angew. Chem. Int. Ed*. **2000**, 39, 3750-3771.
Niu, M.; Fu, H.; Jiang, Y.; Zhao, Y. *Chem. Commun.* **2007,** 272-274*.*

Proposed Reaction Path Cu Catalyzed Aerobic Phosphonation of sp C



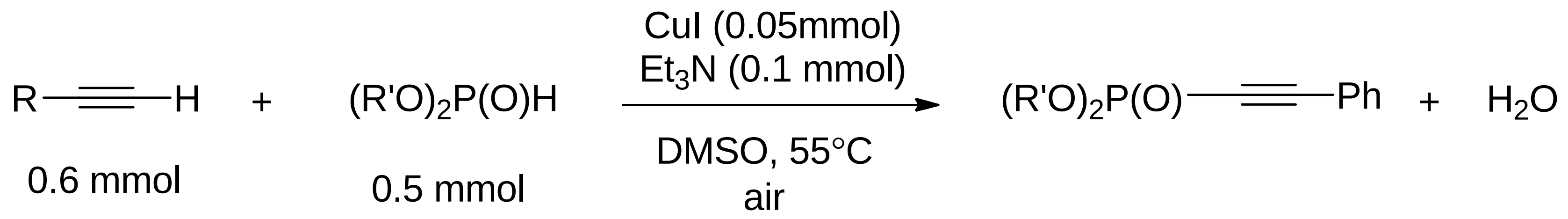
Gao, Y.; Zhao, Y.; Zhou, Y.; Han, L. *J. Am. Chem. Soc.*, **2009**, *131*, 7956–7957.

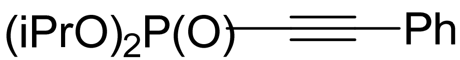
Proposed Reaction Path Cu Catalyzed Aerobic Phosphonation of sp C



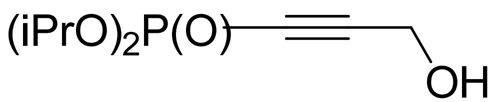
Gao, Y.; Zhao, Y.; Zhou, Y.; Han, L. *J. Am. Chem. Soc.*, **2009**, *131*, 7956–7957.

Substrate Scope for Cu Catalyzed Aerobic Phosphonation of sp C

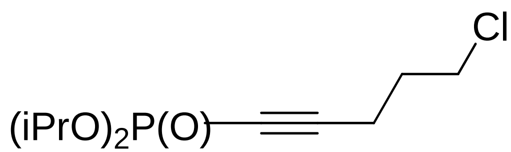




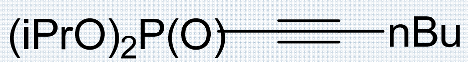
93% (83%)



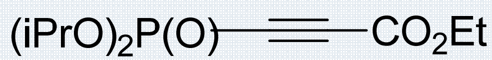
95% (83%)



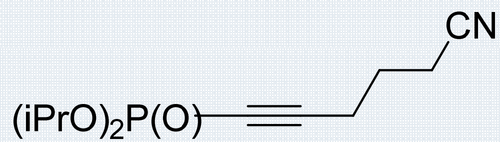
94% (82%)



85% (72%)



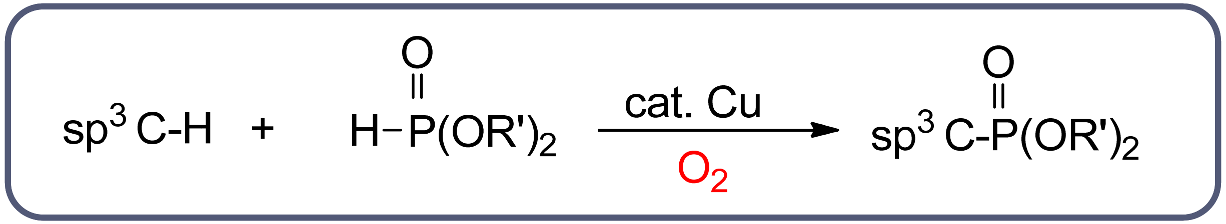
98% (82%)

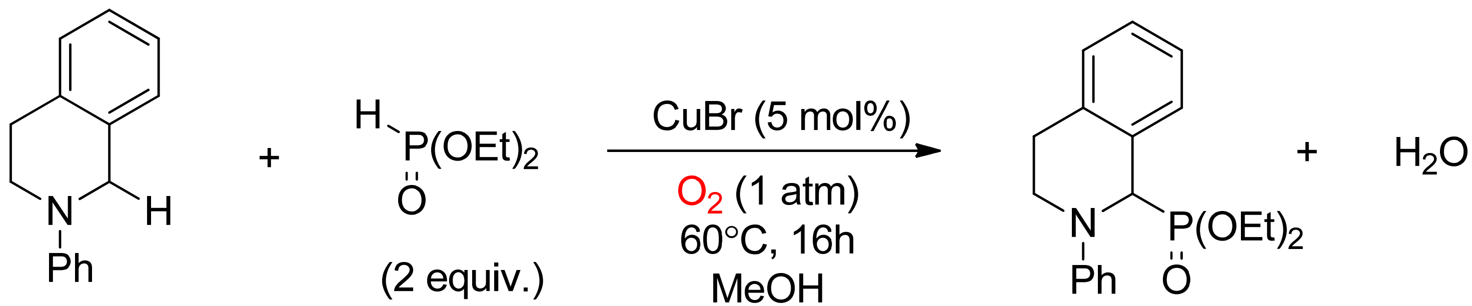


99% (88%)

Gao, Y.; Zhao, Y.; Zhou, Y.; Han, L. *J. Am. Chem. Soc.*, **2009**, *131*, 7956–7957.

Cu Catalyzed Aerobic Phosphonation of sp^3 C





Diethyl phosphonate

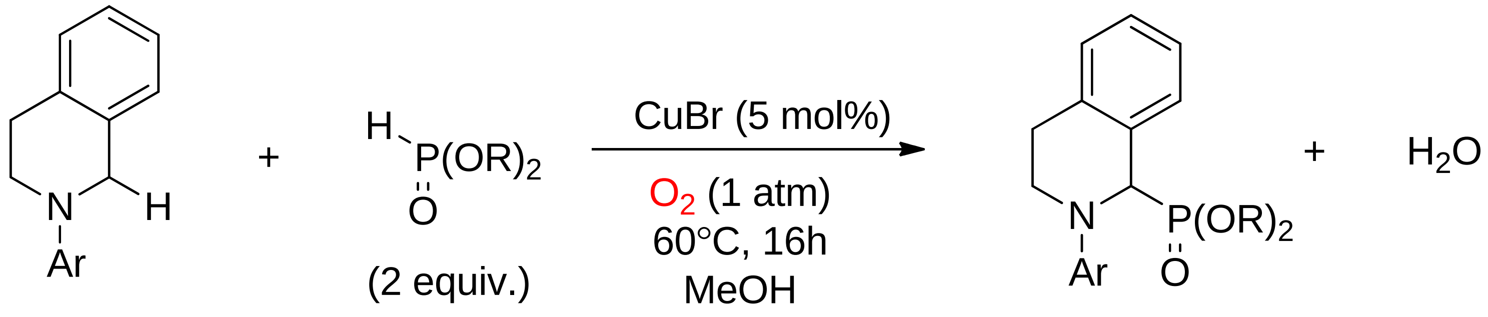
N-phenyltetrahydroisoquinoline

α-Aminophosphonate

79% (95%)

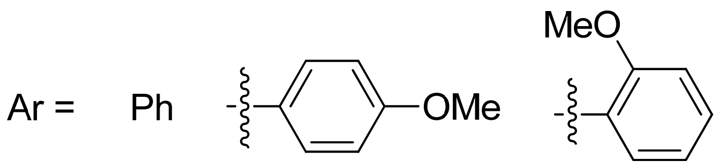
Basle, O.; Li, C-J. *Chem. Comm.*, **2009**, 4124-4126.

Mechanistic Study of Cu Catalyzed Aerobic Phosphonation of sp^3 C

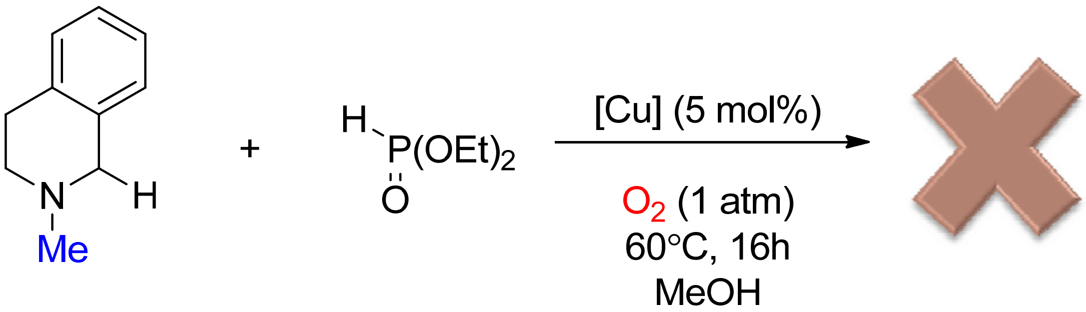


1 **2** **3**

Aryl-protected amines is an important feature.



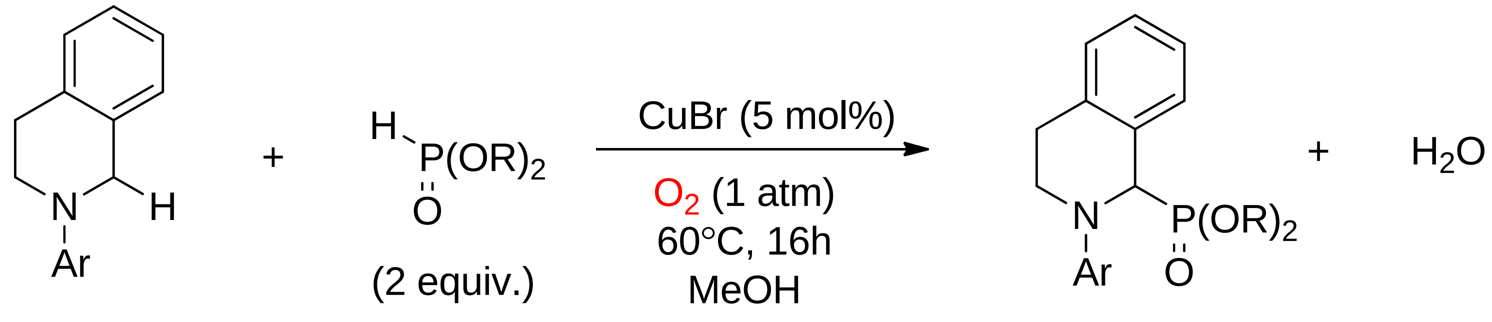
PMP **OMP**



Aryl group can stabilize the oxidized form of the tertiary amine.

Basle, O.; Li, C-J. *Chem. Comm.*, **2009**, 4124-4126.

Mechanistic Study of Cu Catalyzed Aerobic Phosphonation of sp^3 C



1 **2** **3**

A molecular oxygen uptake experiment shows

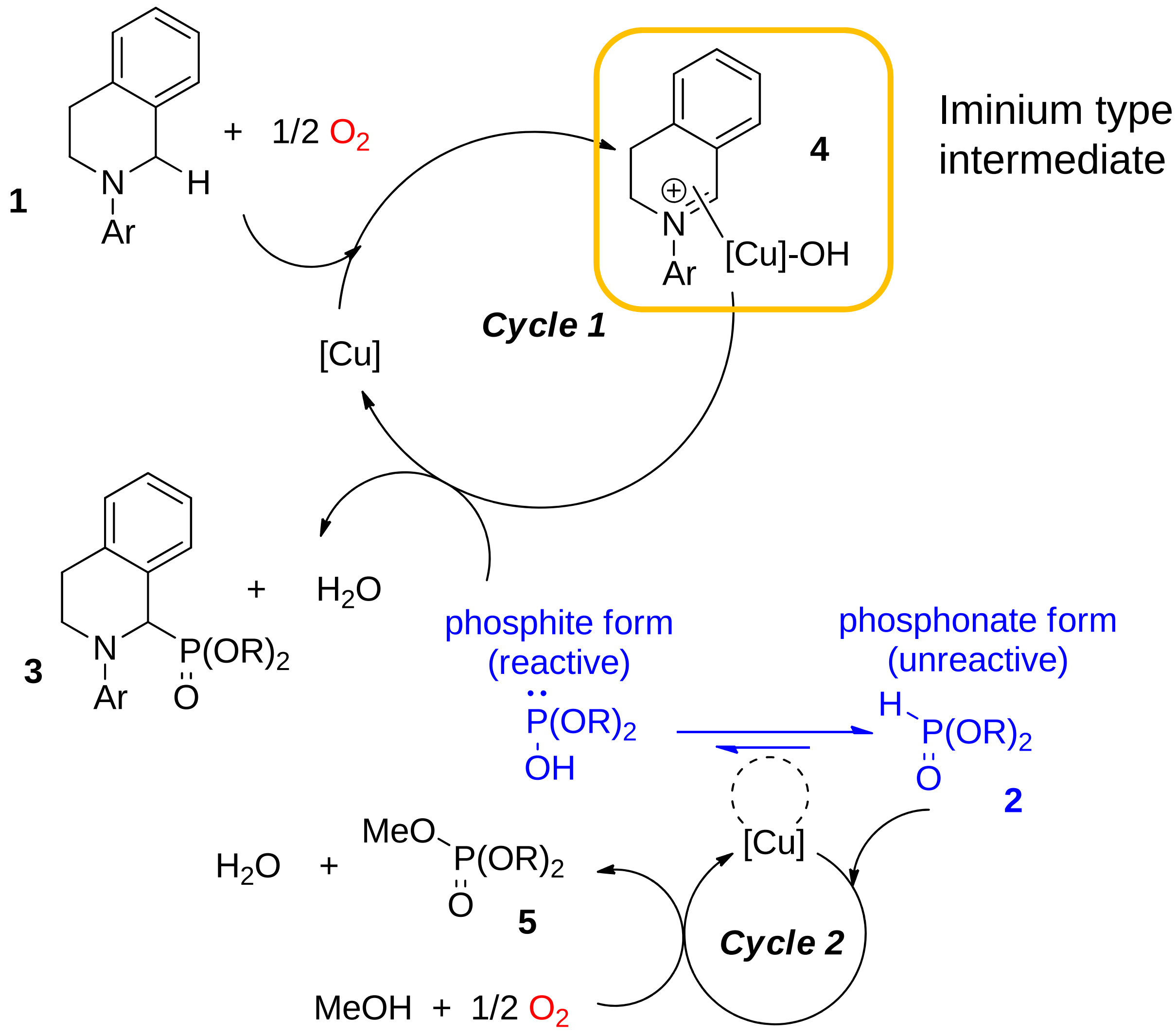
i. a total consumption of 1 equiv. of O_2 for the generation of 1 equiv. of desired product **3**;

ii. 1 equiv. of **1** and 1 equiv. of **2** consumes 0.5 equiv. of O_2.

O_2 is involved in the oxidation of excess **2** to methyl phosphate

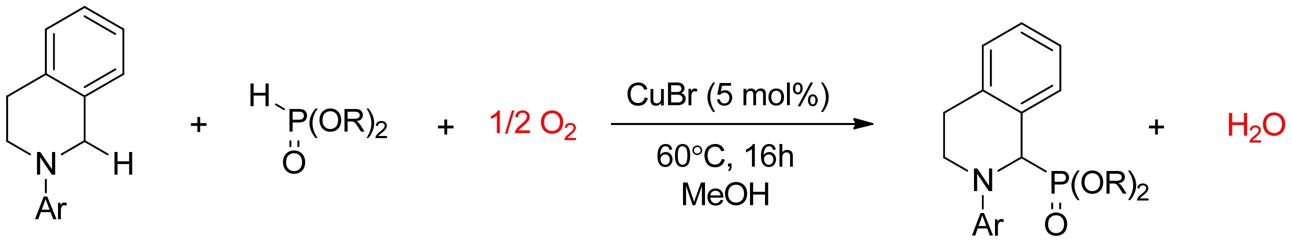
Basle, O.; Li, C-J. *Chem. Comm.*, **2009**, 4124-4126.

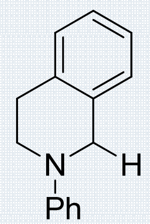
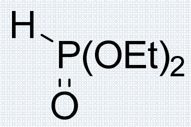
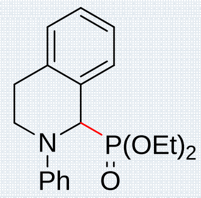
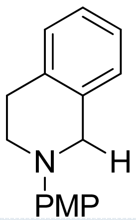
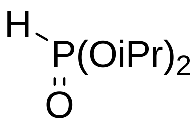
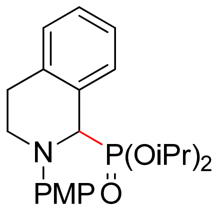
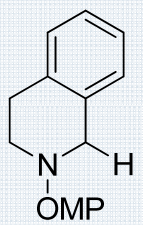
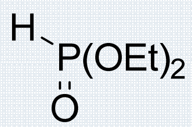
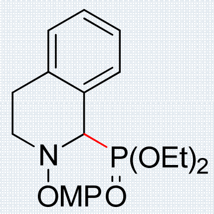
Possible Mechanism Pathway for Cu Catalyzed Aerobic Phosphonation of sp^3 C



Basle, O.; Li, C-J. *Chem. Comm.*, **2009**, 4124-4126.

Substrate Scope of Cu Catalyzed Aerobic Phosphonation of sp^3 C



Entry	Amine		Phosphite	Product	% Yield
1					79 (95)
2		PMP = p-methoxyphenyl			73 (75)
3		OMP = o-methoxyphenyl			69 (85)

Basle, O.; Li, C-J. *Chem. Comm.*, **2009**, 4124-4126.

Summary

- Copper-catalyzed aerobic oxidative coupling reactions enable direct C-H functionalization, and can be a powerful tool for constructing C-C bonds and C-heteroatom bonds.

- Reactions are conducted in air or an O_2 atmosphere, with O_2 as a stoichiometric oxidant. H_2O or H_2O_2 is generated as a by-product.

- However, this chemistry is still in its infancy. The substrate scope is very limited for some reactions.

Acknowledgement

- Dr. Baker
- Dr. Maleczka
- Dr. Smith, Dr. Wulff
- Baker’s Group: Gina, Hui, Heyi, Quanxuan, Wen, Yiding, Greg, Salinda, Cat and Kayla
- Li, Hong, Yong, Chunjuan and Hao
- Xin, Ipek, Herbert, Wenjun and Jason

THANK YOU!