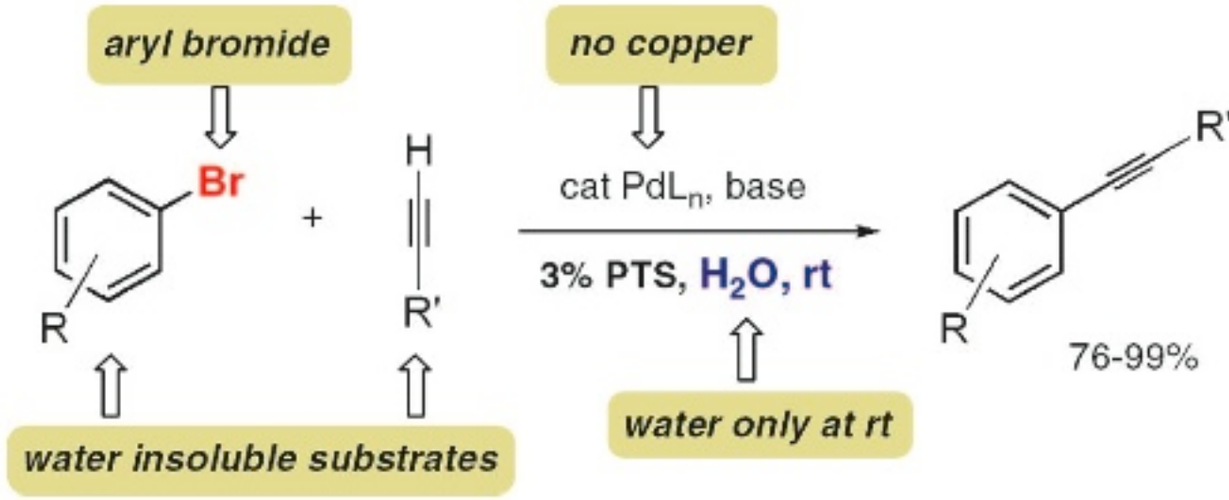
ORGANIC LETTERS

Sonogashira Couplings of Aryl Bromides: Room Temperature, Water Only, No Copper

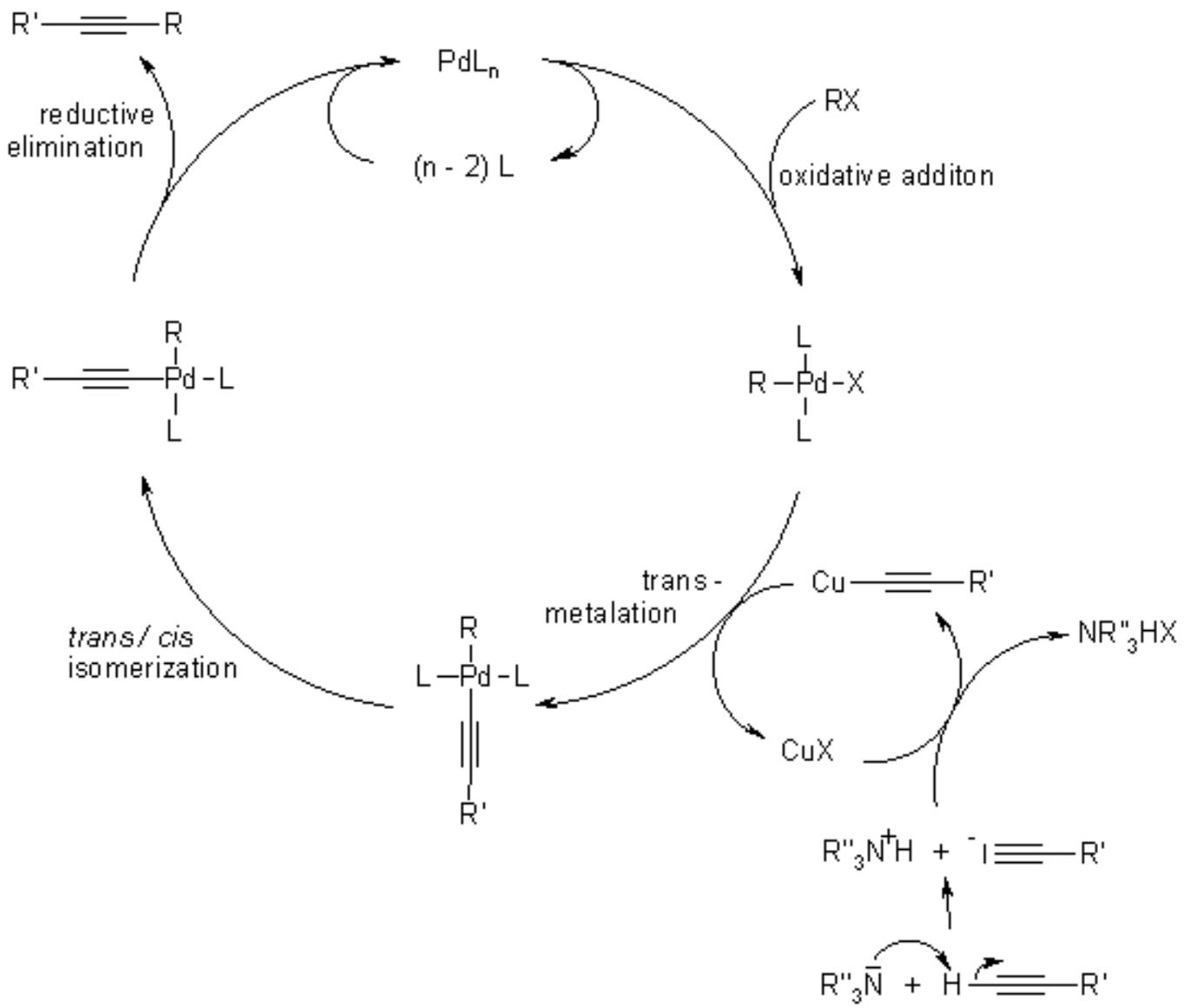


Bruce H. Lipshutz, David W. Chung, and Brian Rich

***Org.Lett.* ASAP Article**

Presentation By Nora Jameson
Current Lit 08/30/2008

Sonogashira Coupling: Possible Catalytic Cycle

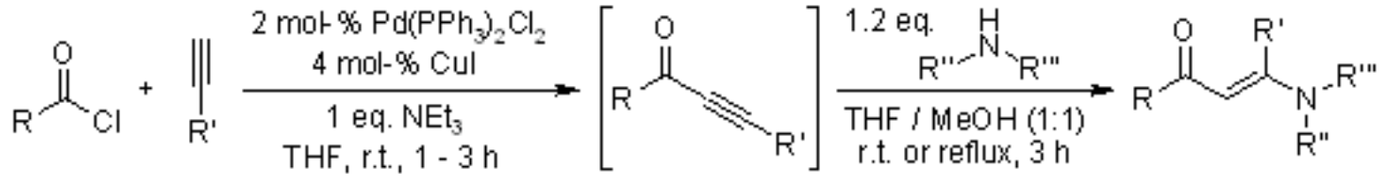


Seminal Publications:

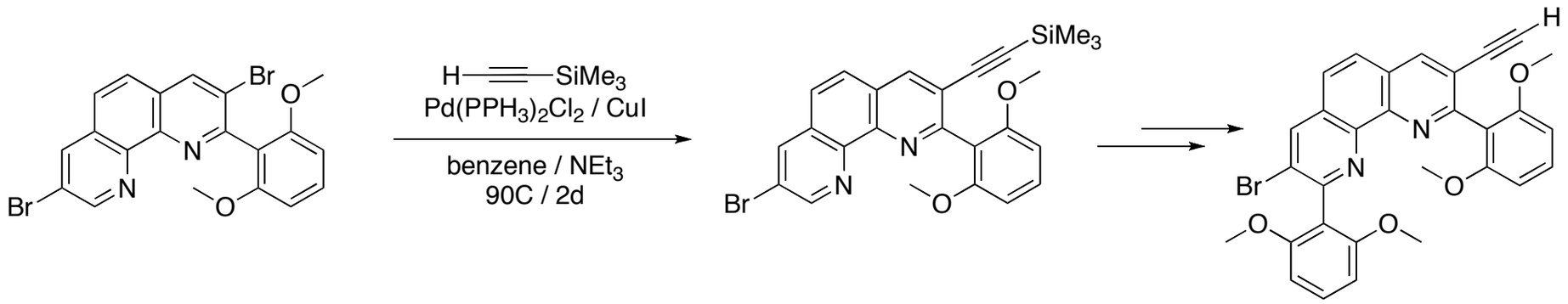
K. Sonogashira, Y. Tohda, N. Hagihara. *Tetrahedron Letters* **1975** 16 (50): 4467–4470

Andrew G. Myers and Peter S. Dragovich *Org. Synth* **1998** Coll. Vol. 9: 117

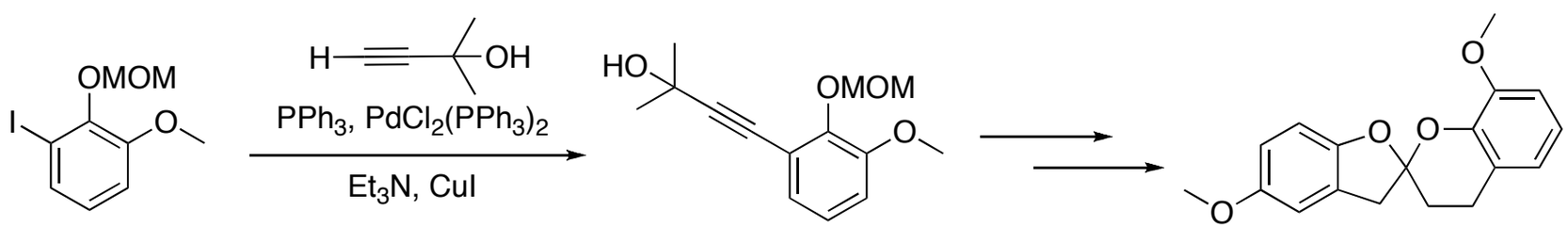
Sonogashira Coupling as a Tool in Organic Synthesis



A. S. Karpov, T. J. J. Müller, *Synthesis*, **2003**, 2815-2826.

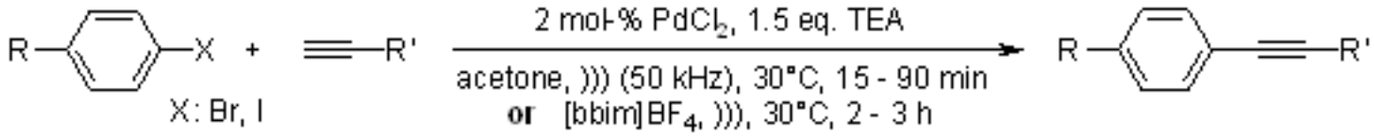


S. Liu, C. Michel, M. Schmittel, *Org. Lett.*, **2000,** 2(25); 3959-3962.

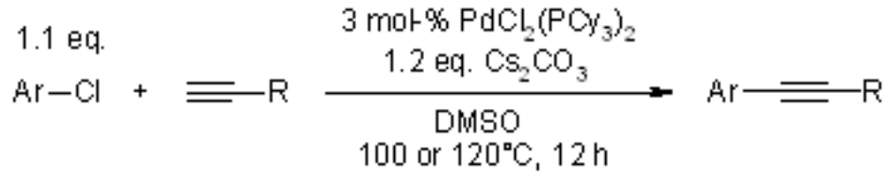


K.Y. Tsang, M. A. Brimble, J. B. Bremmer, *Org. Lett.*, **2003**, 5(23); 4425-4427.

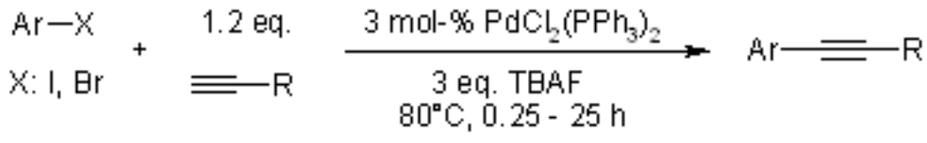
No Copper Sonogashira Couplings



A. R. Gholap, K. Venkatesan, R. Pasricha, T. Daniel, R. J. Lahoti, K. V. Srinivasan, *J. Org. Chem.*, **2005**, 70, 4869-4872.

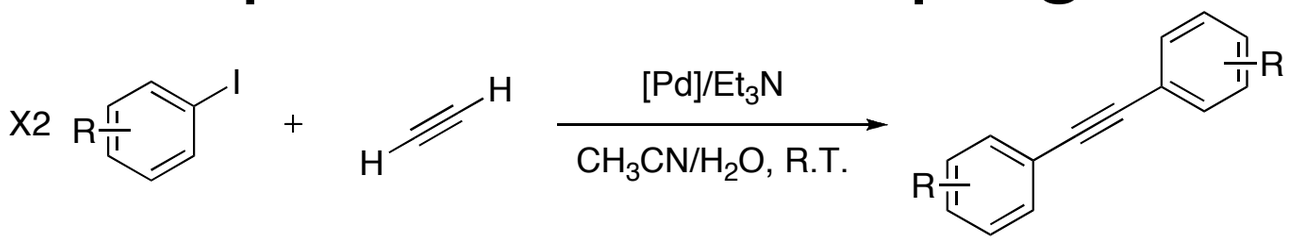


C. Yi, R. Hua, *J. Org. Chem.*, **2006**, 71, 2535-2537.

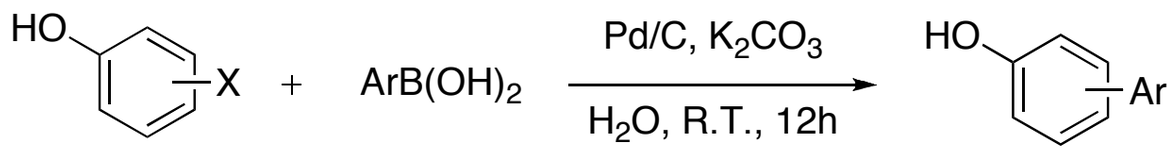


Y. Liang, Y.-X. Xie, J.-H. Li, *J. Org. Chem.*, **2006**, 71, 379-381.

Aqueous Cross-Coupling

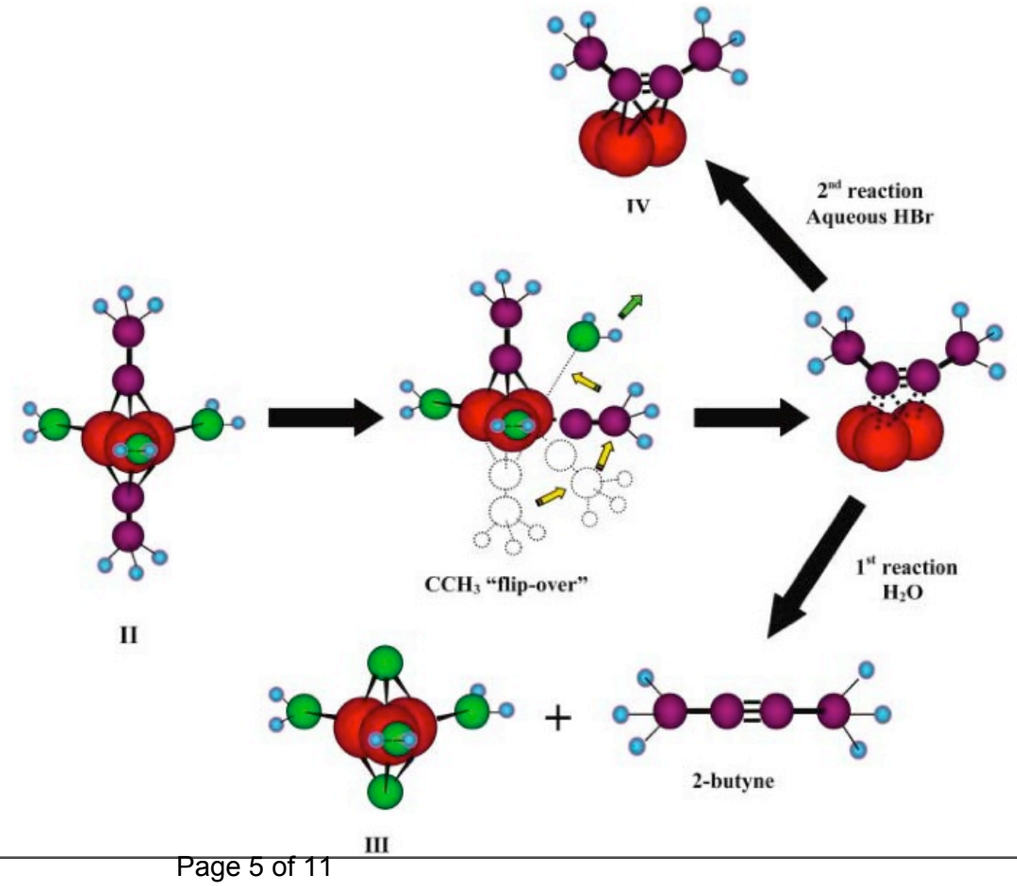


C. Li, D. Chen, C.W. Costello, *Org. Proc. Res. Dev.*, **1997**, 1 (4), 325 -327.

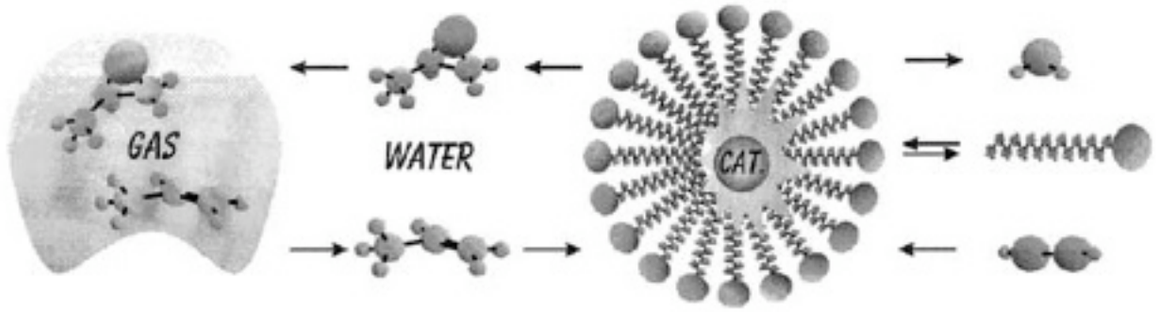


H. Sakurai, T. Tsukuda, T. Hirao, *J. Org. Chem.*, **2002**, 67(8); 2721-2722.

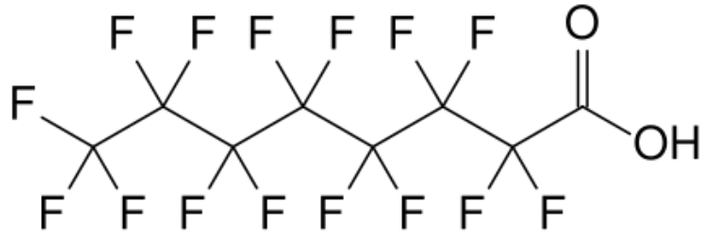
A. Bino, M. Ardon, and E. Shirman, *Science,* 8 April **2005** 308: 234-235



Micellar Catalysis

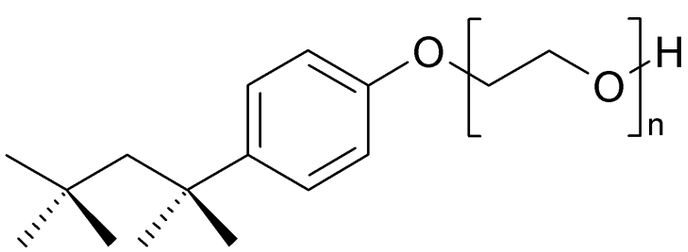


J. H. M. Heijnen, V. G. de Bruijn, L. J. P. van den Broeke and J. T. F. Keurentjes *Chem. Engineering and Processing* Vol. 42, 3, **2003**, Pages 223-230

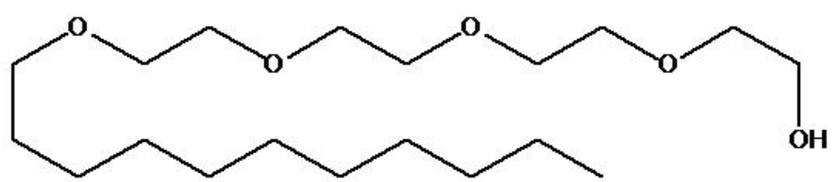


perfluorooctanoic acid

D. C. Berndt, M. E. Ayoub, M. H. Akhavan-Tafti, *Int. J. of Chem. Kinetics,* Vol 19, 6, **1987**, 513-518

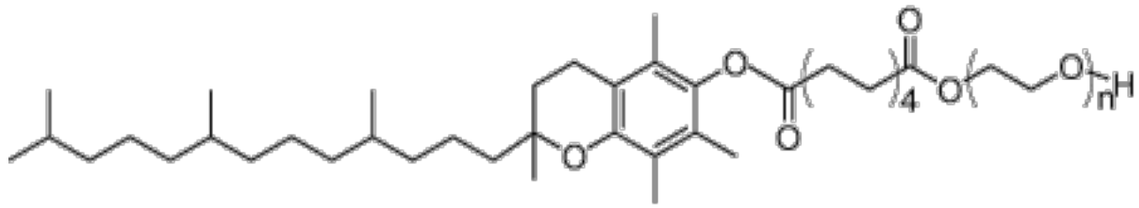


Triton®-X100

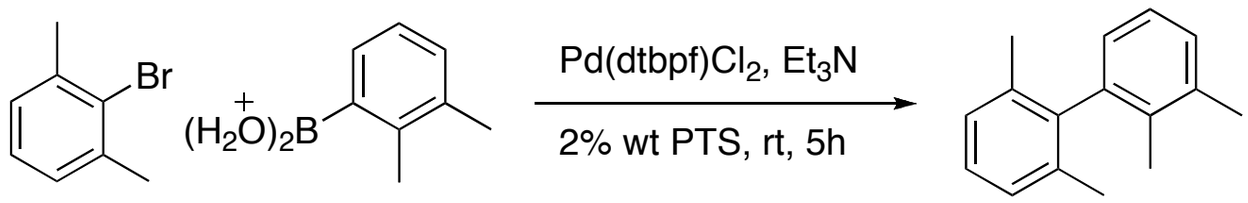


Brij® 30

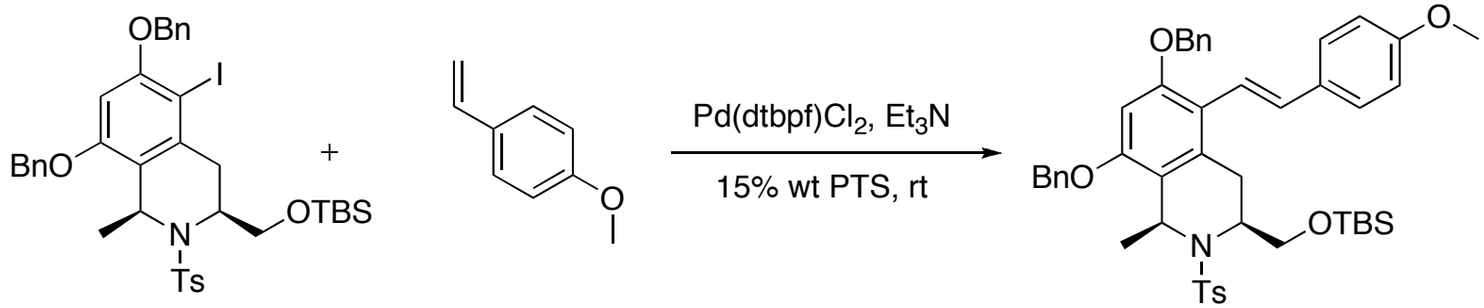
Aqueous Mediated Coupling
The use of *PTS*: micellar catalyst



PTS (n = ca. 13)

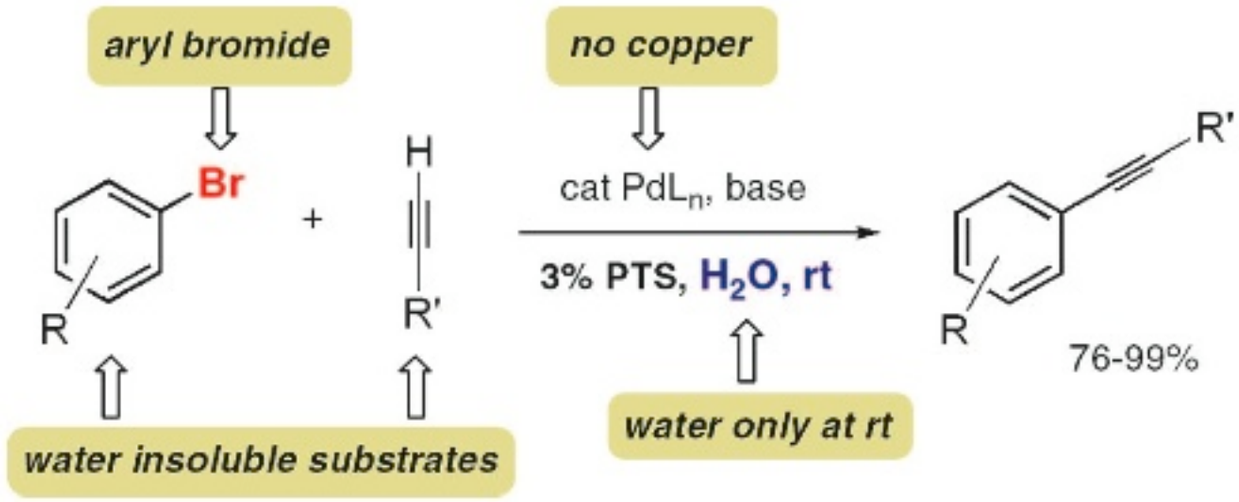


Lipshutz, B. H. et al. *Org. Lett.* **2008**, 10, 1333.



Lipshutz, B. H.; Taft, B. R. *Org. Lett.* **2008**, 10, 1329.

Title Paper Sonogashira Couplings of Aryl Bromides: Room Temperature, Water Only, No Copper

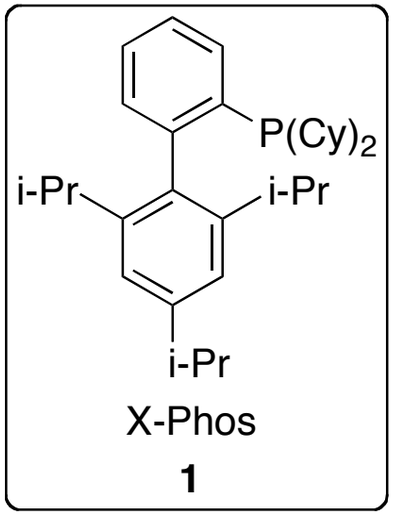


Unprecedented Sonogashira cross-coupling in water at ambient temperatures

Absence of both copper and organic solvent

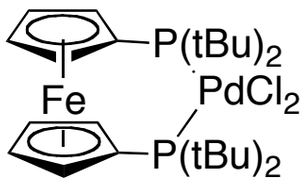
Use of commercially available reagents

Ligand Studies



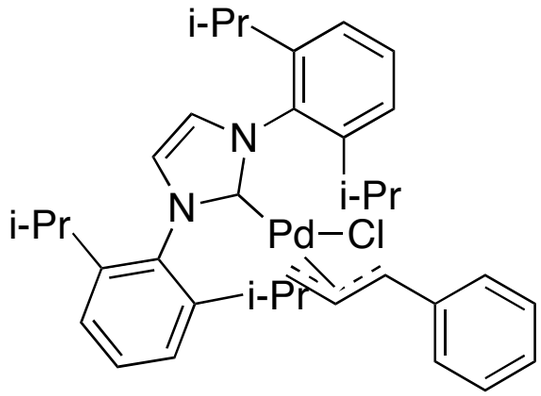
X-Phos

1



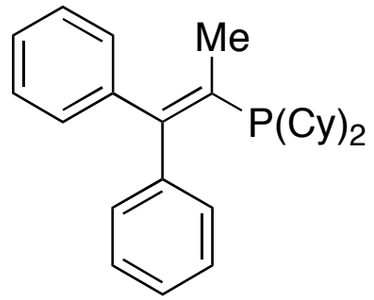
$Pd(dtbpf)Cl_2$

2



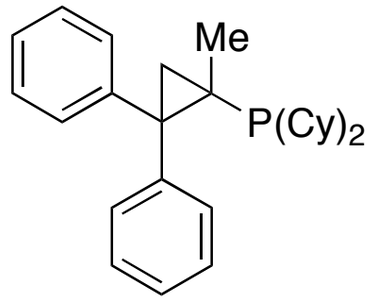
Neolyst^{TM}CX31

3



(Cy-vBRIDP)

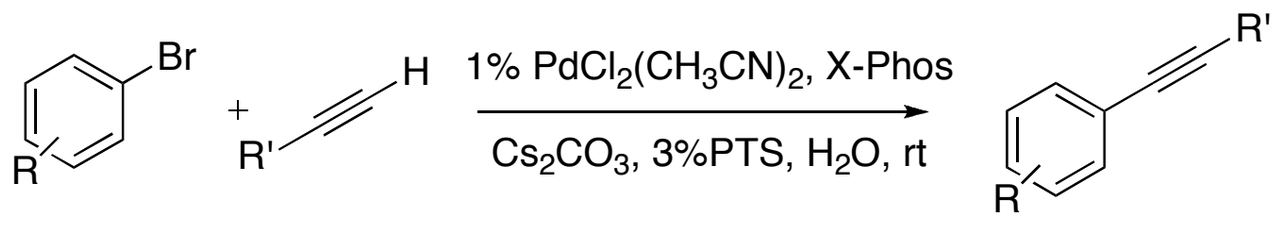
4



5 R = Cy (Cy-cBRIDP)
6 R - tBu (cBRIDP)

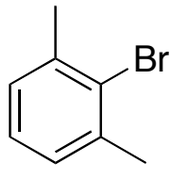
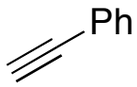
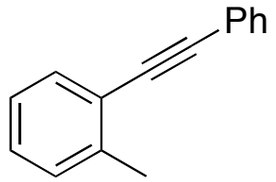
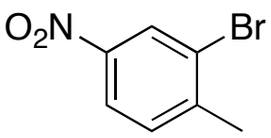
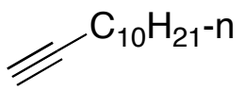
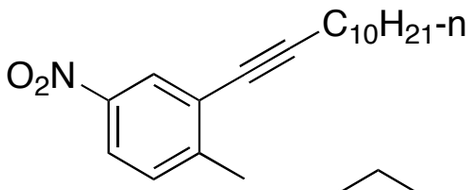
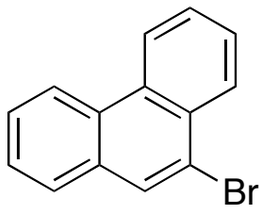
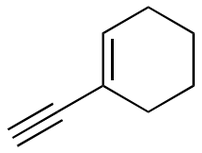
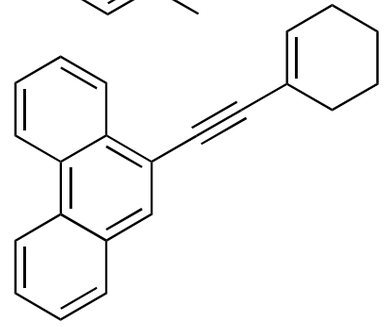
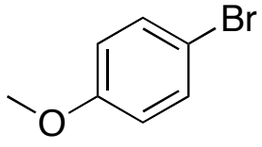
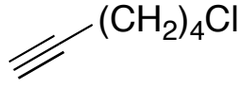
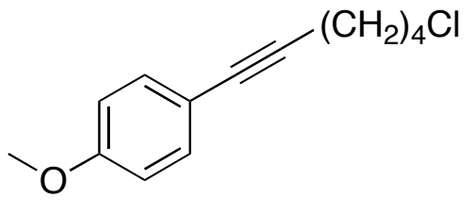
degassed solvents used for X-Phos, obtained best results with commercially available ligand and catalyst

using catalyst **6** obtained similar results using degassed or nondegassed solvent



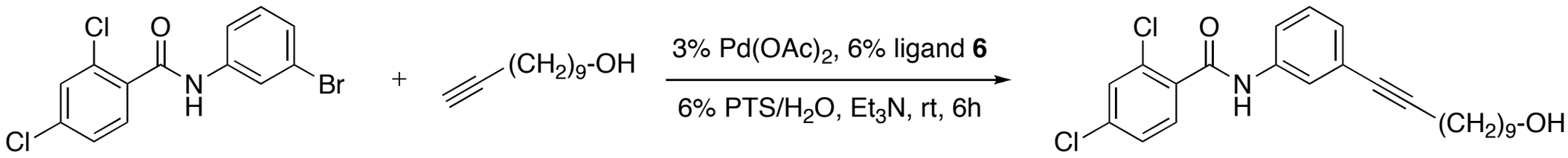
Suzuki, K.; Fontaine, A.; Hori, Y.; Kobayashi, T. *Synlett* **2007**, 3206–3208.

Reaction Scope

Ar-Br	alkyne	base	time	product	yield
		Cs_2CO_3	20h		99%
		Et_3N	18h		99%
		Et_3N	21h		98%
		$(n\text{-}Bu)_3N^c$	23h		0%
		$(n\text{-}Oct)_3N^c$	23h		0%

Using PdCl2(CH3CN)2 + Ligand **I** in 3% PTS/H2O at rt

Conclusions



Aryl bromide Sonogashira Coupling in aqueous solvent

Absence of copper and organic solvents

Reactions at ambient temperatures

Use of PTS as micellar catalyst

Possible applications in industrial chemistry