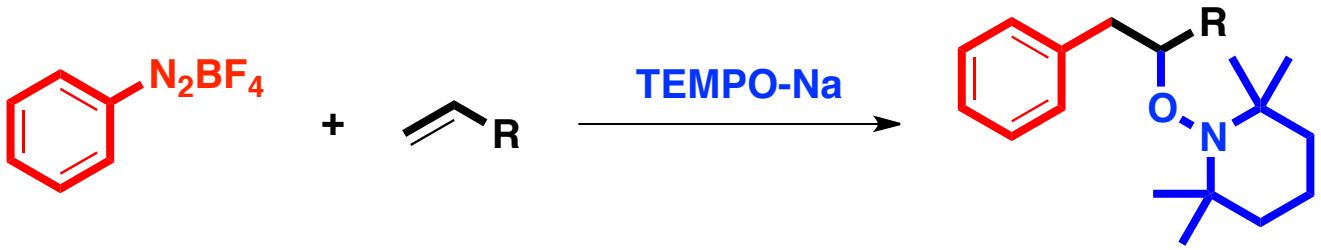
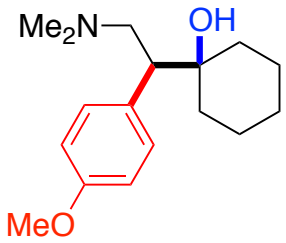
Transition-Metal-Free Oxyarylation of Alkenes with Aryl Diazonium Salts and TEMPONa

Marcel Hartmann, Yi Li, and Armido Studer
J. Am. Chem. Soc. ASAP
DOI: 10.1021/ja307638u

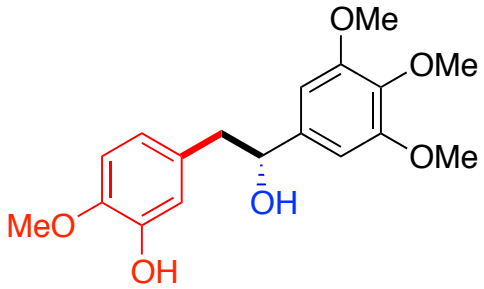


Joshua Sacher
Wipf Group Current Literature
October 6, 2012

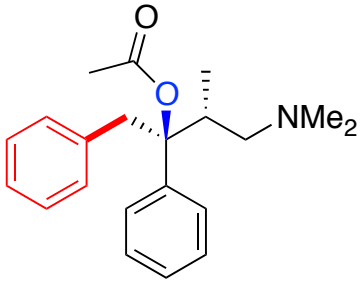
Pharmaceuticals and Natural Products



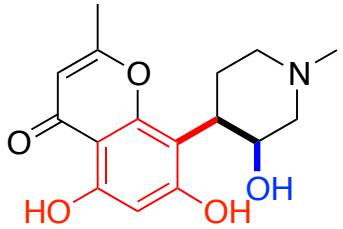
Effexor



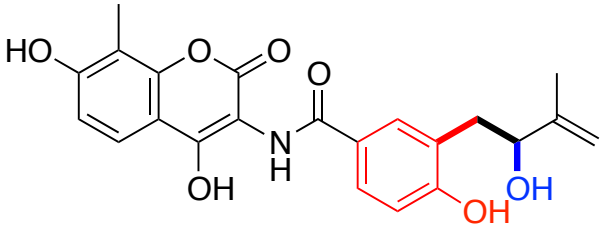
Combrestatin



Darvon



Rohitukine

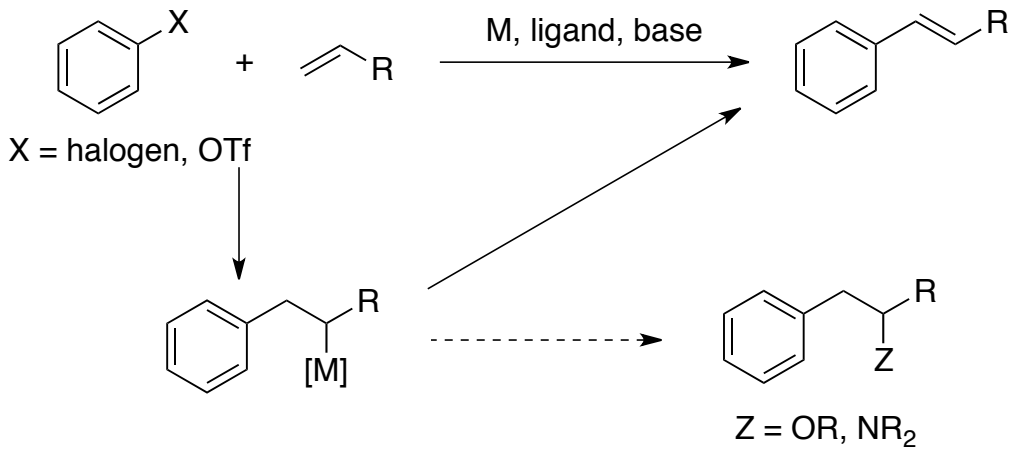


Coumabiocin F

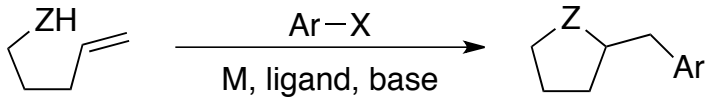
de Souza, N. J. *In Human Medicinal Agents from Plants*. ACS, **1993**, 331
Cheenpracha, S.; Vidor, N. B.; Yoshida, W. Y.; Davies, J.; Chang, L. C. *J. Nat. Prod.* **2010**, *73*, 880.

Alkene Arylation

- Heck Reaction



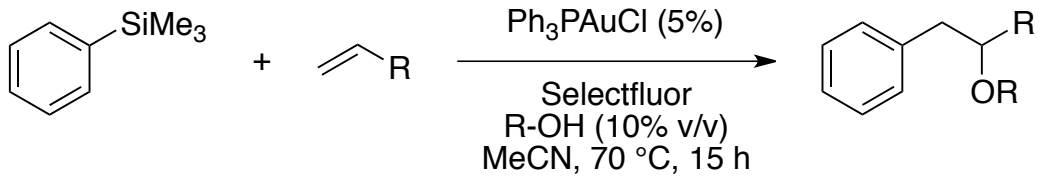
- TM Catalyzed Carboetherification/amination



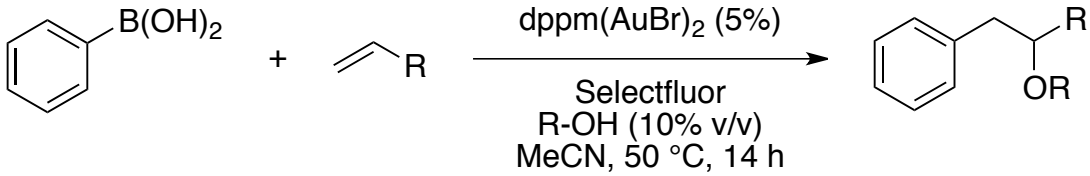
Wolfe, J. P. *Synlett*, **2008**, 2913.
Schultz, D. M.; Wolfe, J. P. *Synthesis*, **2012**, *44*, 351

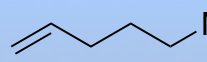
β-Aryl-α-Heteroalkanes

- Au-Catalyzed oxyarylations
  - Russell:



  - Toste:



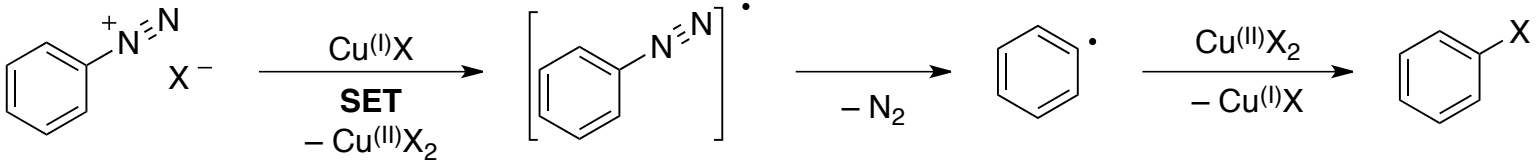
Alkene:  N(Phth)

	R-OH	Ph-$SiMe_3$	Ph-$B(OH)_2$
1	MeOH	71%	79%
2	EtOH	69%	85%
3	*t*-BuOH	[27%]	33%
4	AcOH	79%	62%

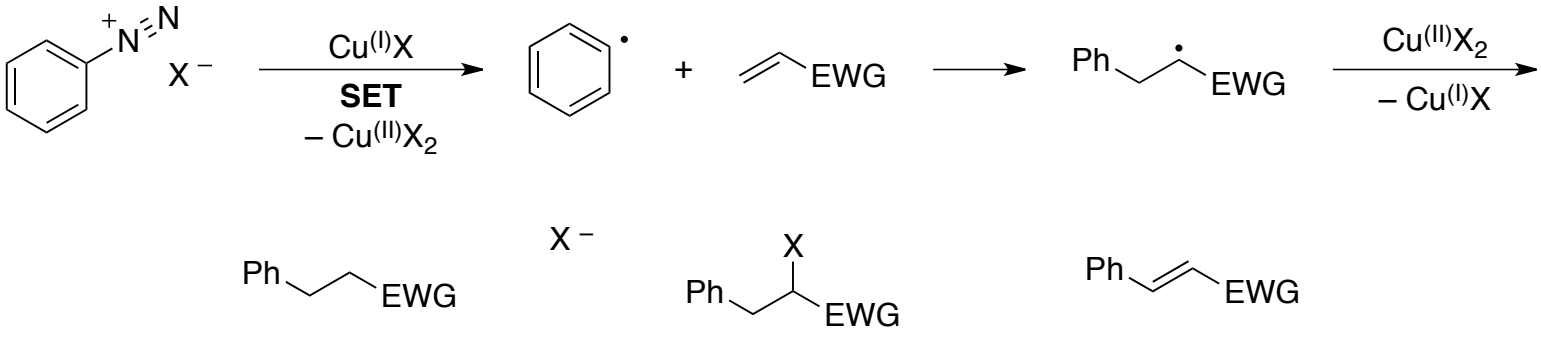
Ball, L. T.; Green, M.; Lloyd-Jones, G. C.; Russell, C. A. *Org. Lett.* **2010**, *12*, 4724
Melhado, A. D.; Brezovich, W. E., Jr.; Lackner, A. D.; Toste, F. D. *J. Am. Chem. Soc.* **2010**, *132*, 8885

Diazonium Salts as Aryl Radical Precursors

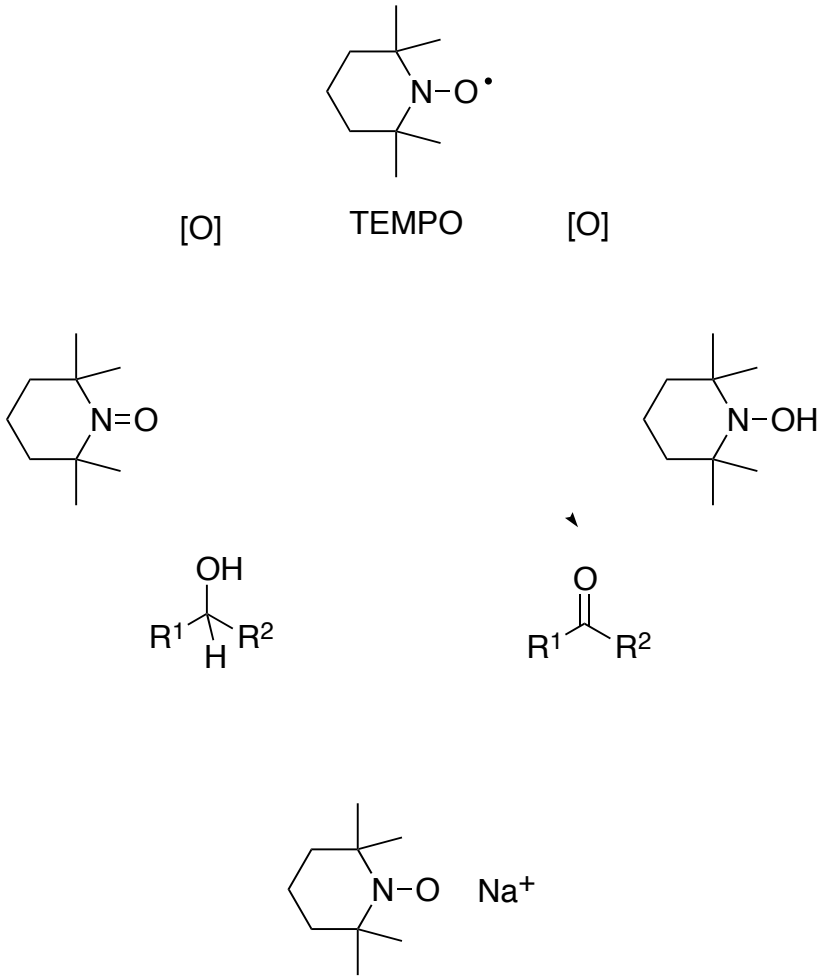
- Sandmeyer Reaction



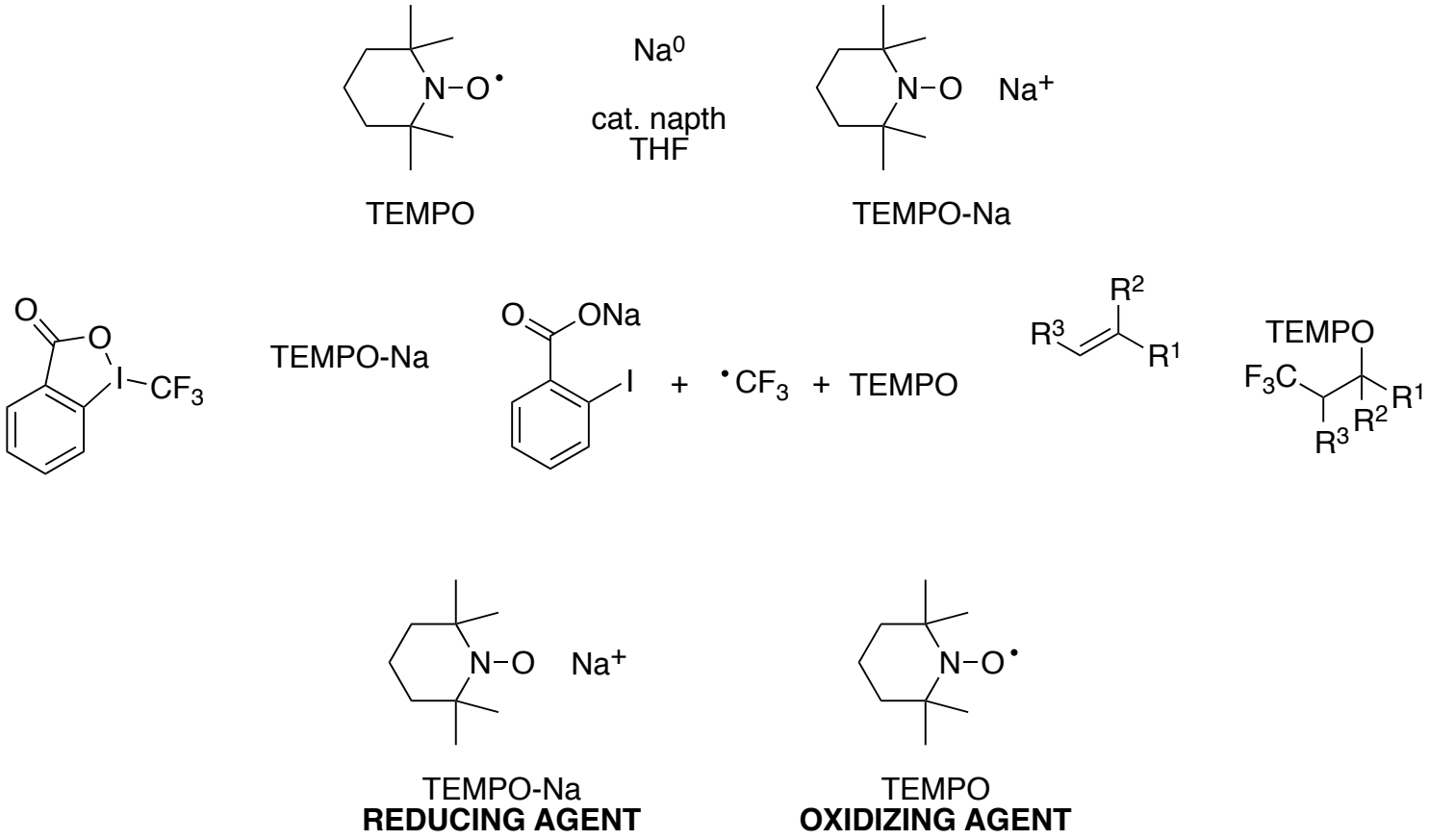
- Meerwein Arylation



Normal Reactions with TEMPO

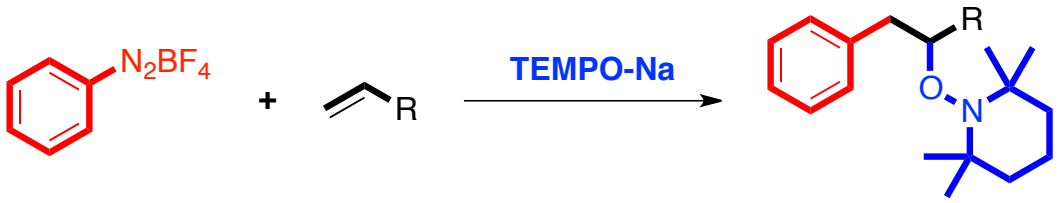


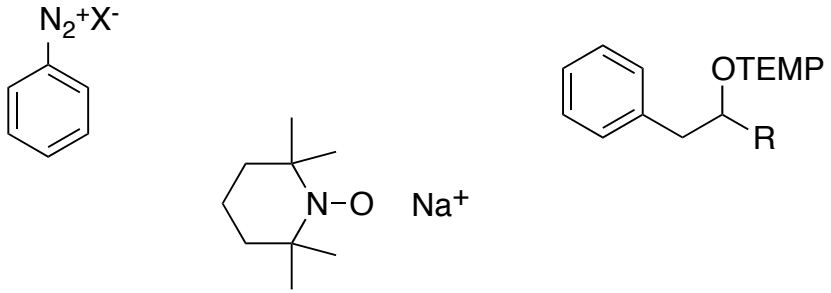
TEMPO-Na



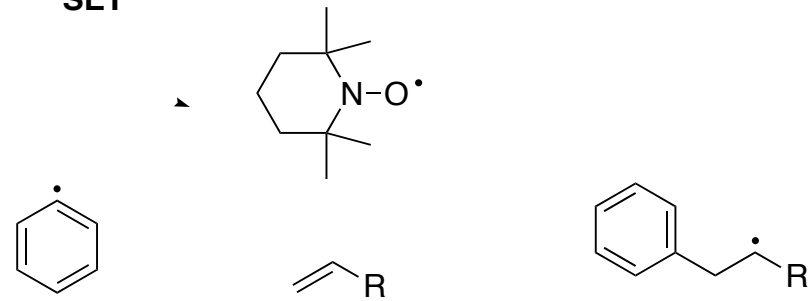
Li, Y.; Studer, A. *Angew. Chem. Int. Ed.*, **2012**, *51*, 8221

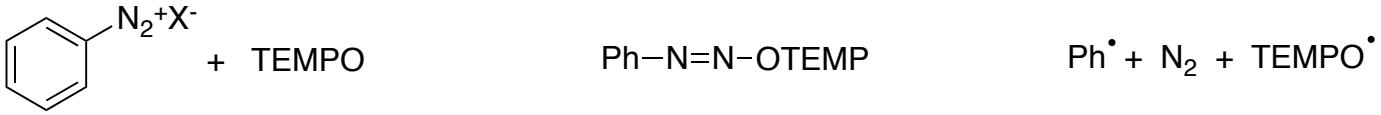
TEMPO-Na Oxyarylation Mechanism



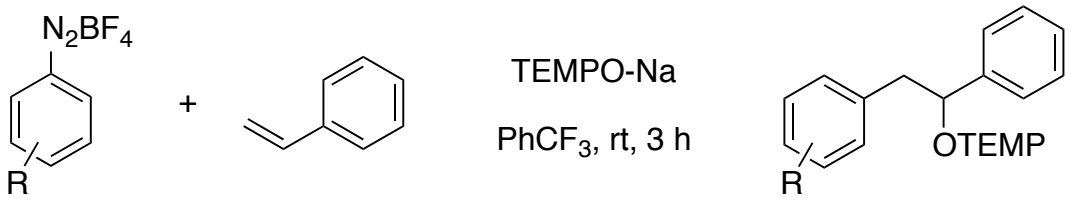


SET



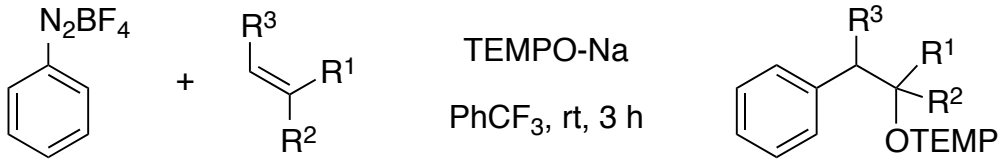


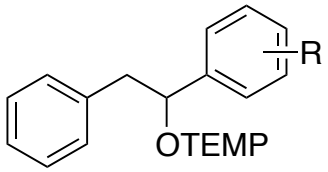
Scope of the Reaction: Aryl Diazoniums



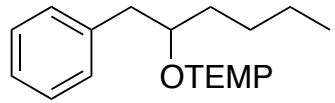
	R	Yield
1	H	89%
2	4-Ph	75%
3	**4-MeO**	**81%**
4	**4-CO_2Me**	**83%**
5	4-I	63%
6	**4-Br**	**82%**
7	**3-Br**	**84%**
8	**2-Br**	**81%**
9	2,4-Me_2	80%

Scope of the Reaction: Alkenes

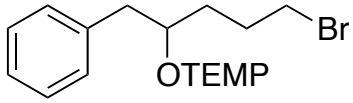




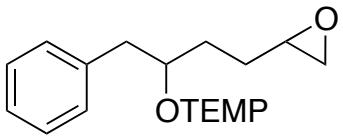
	R	Yield
1	4-Me	74%
2	4-OMe	80%
3	4-Cl	70%
4	4-CN	72%
5	4-CF_3	84%
6	4-Br	82%
7	3-F	65%
8	3-Br	83%
9	3-OMe	76%
10	3-CF_3	77%
11	2-Br	81%
12	2-OMe	79%
13	2-F	75%



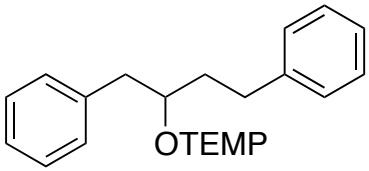
52%



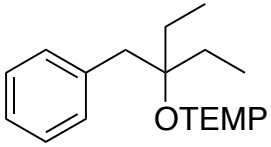
55%



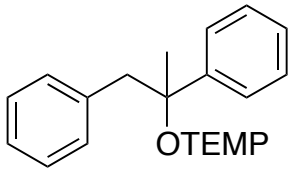
52%



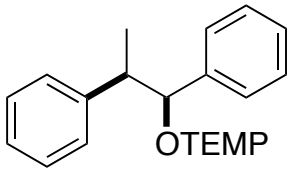
66%



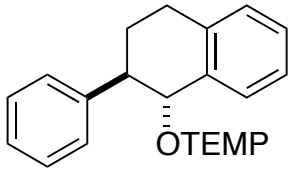
60%



67%

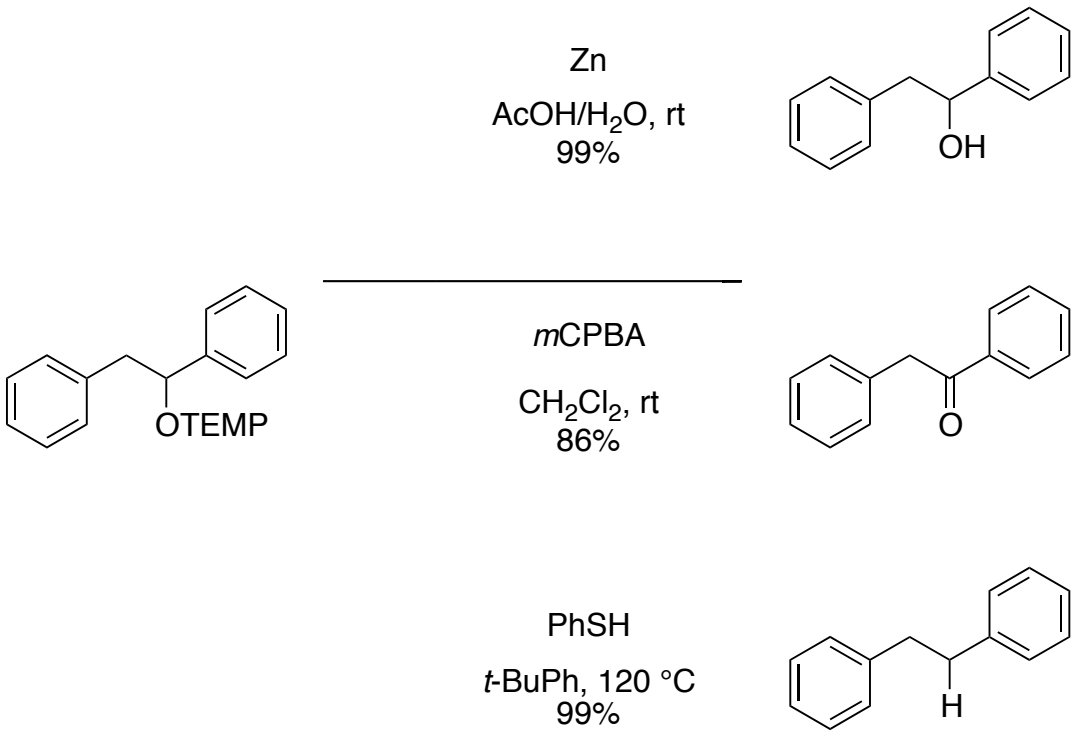


53%, 88:12 dr



49% >98:2 dr

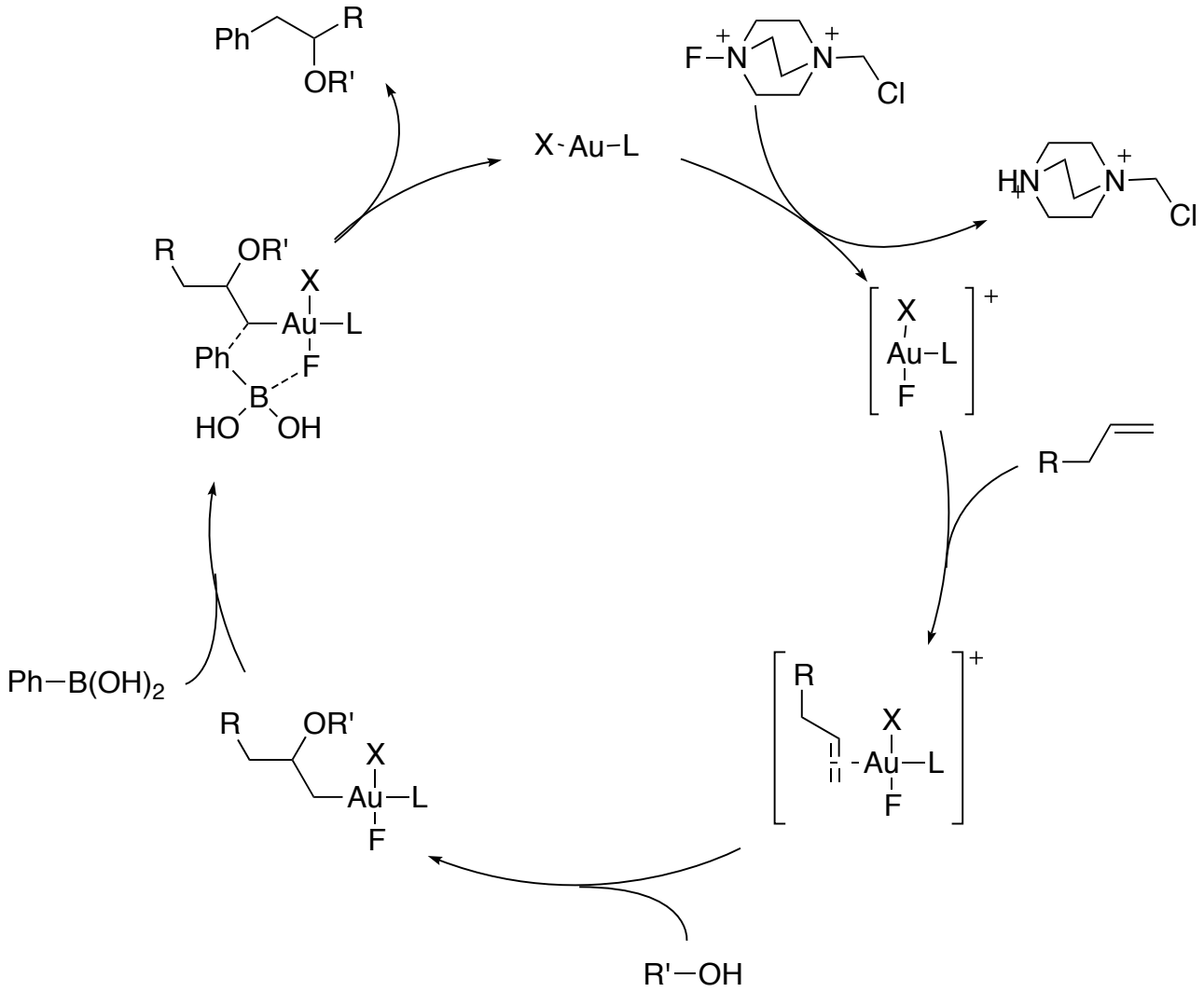
…So Now What?


Zn
AcOH/H2O, rt
99%
OH
OTEMP
mCPBA
CH2Cl2, rt
86%
O
PhSH
t-BuPh, 120 °C
99%
H

Summary

- New method for oxyarylation of alkenes
  - Potentially useful alternative to TM cat reactions
  - Mild conditions, fast reactions
  - Good functional group compatibility
  - Unaffected by sterics/electronics
  - Easy to do further transformations
- Drawbacks
  - Low yields for aliphatic alkenes
  - Excess alkene needed
  - TEMPO-Na freshly prepared
  - More substrates? Selectivity with dienes?

Au-catalyzed Mechanism



Melhado, A. D.; Brezovich, W. E., Jr.; Lackner, A. D.; Toste, F. D. *J. Am. Chem. Soc.* **2010**, *132*, 8885
Tkatchouk, E.; Mankad, N. P.; Benitez, D.; Goddard, W. A., III; Toste, F. D. *J. Am. Chem. Soc.* **2011**, *133*, 14293