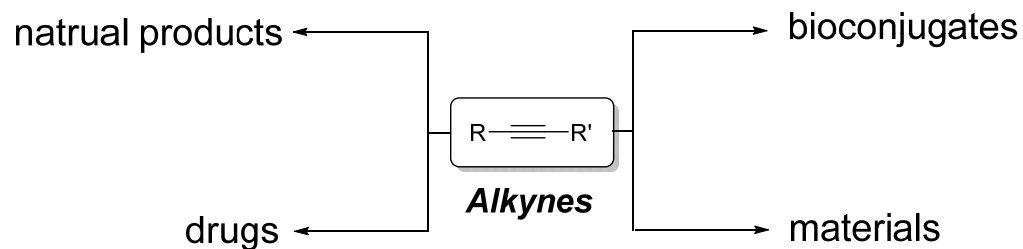


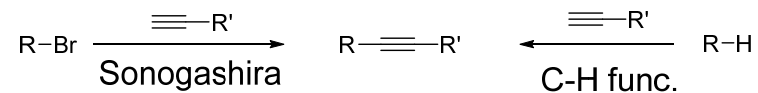
Application of EBX Reagents in Alkynylation Reactions

Reporter: Bo Xing

2017.01.03



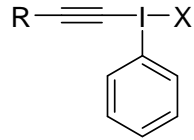
F. Diederich, P. J. Stang, R. R. Tykwinski, *Acetylene Chemistry: Chemistry, Biology and Material Science*, Wiley-VCH, **2005**.



R. Chinchilla, C. Najera, *Chem. Soc. Rev.* **2011**, *40*, 5084.

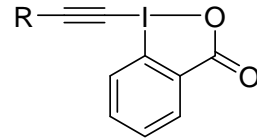
A. S. Dudink, V. Gevorgyan, *Angew. Chem. Int. Ed.* **2010**, *49*, 2096.

Hypervalent Iodine Reagents (HIR)



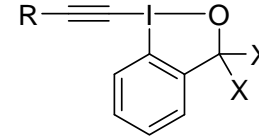
X = OTf, OTs, BF₄ ...

A



ethynylbenziodoxolone
(EBX-R)

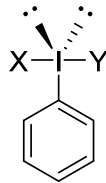
B



X = Me or CF₃

C

Umpolung of the reactivity and react as electrophilic alkynylated reagents



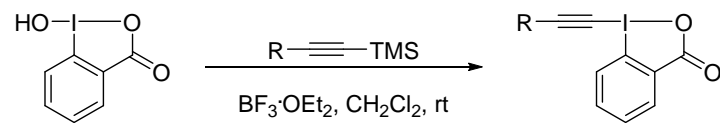
- X in a ring
- Better conjugation to arene

- Synthesis of EBX reagents
- Synthetic application of the reagent

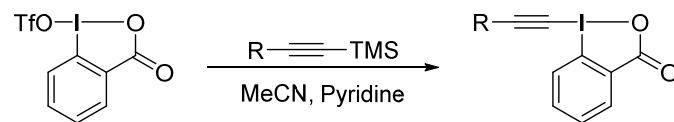
EBX reagents as electrophilic alkynylation synthons

EBX reagents as radical alkynylation synthons

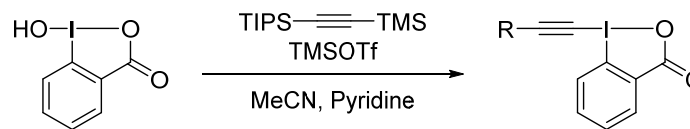
- Summary



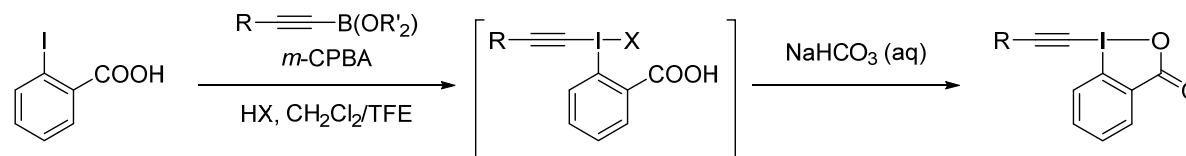
M. Ochiai, Y. Masaki, M. Shiro, *J. Org. Chem.* **1991**, *56*, 5511.



V. V. Zhdankin, C. J. Kuehl, A. P. Krasutsky, J. T. Bolz, A. J. Simonsen, *J. Org. Chem.* **1996**, *61*, 6547.

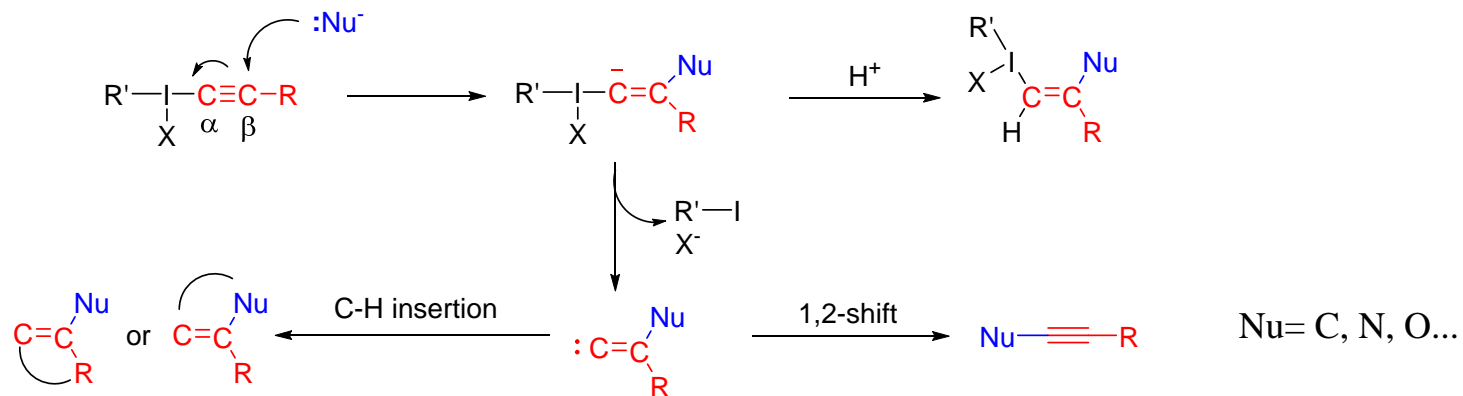


J. P. Brand, J. Waser, *Synthesis* **2012**, 44, 1155.

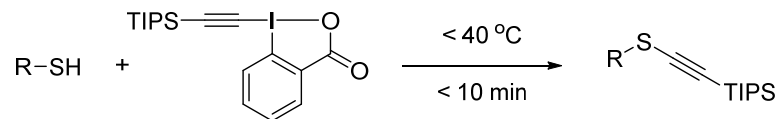


M. J. Bouma, B. Olofsson, *Chem. Eur. J.* **2012**, 18, 14242

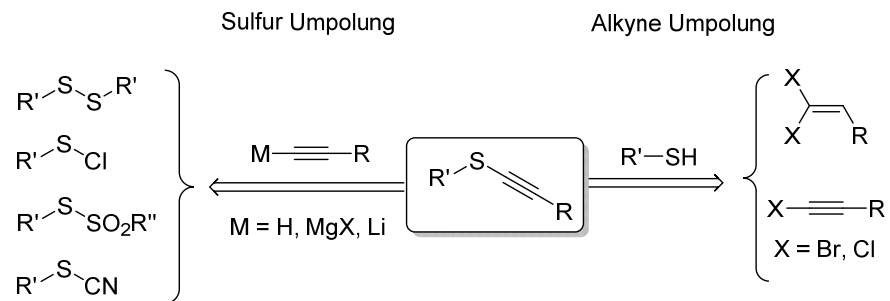
Mechanism for direct alkyynylation:



However, for $Nu = S$ or metal-mediated alkyynylation, hypervalent iodine(III) sometimes behave like a metal center.

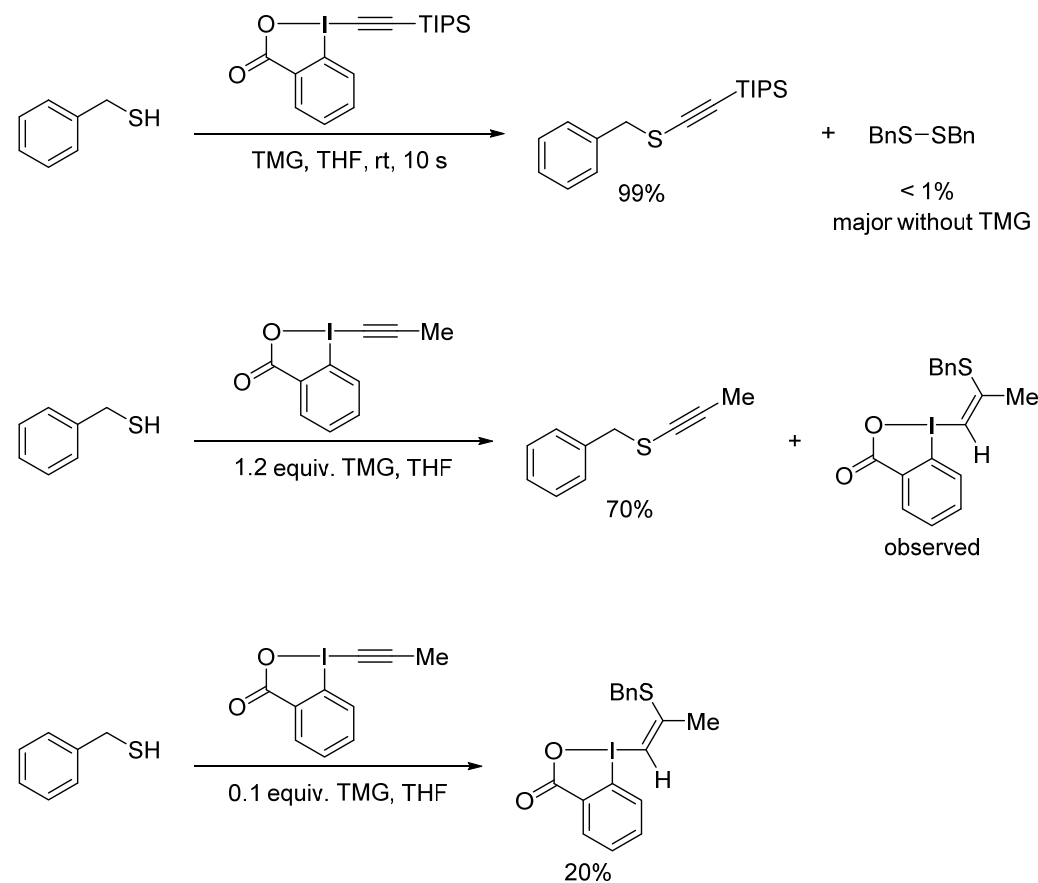
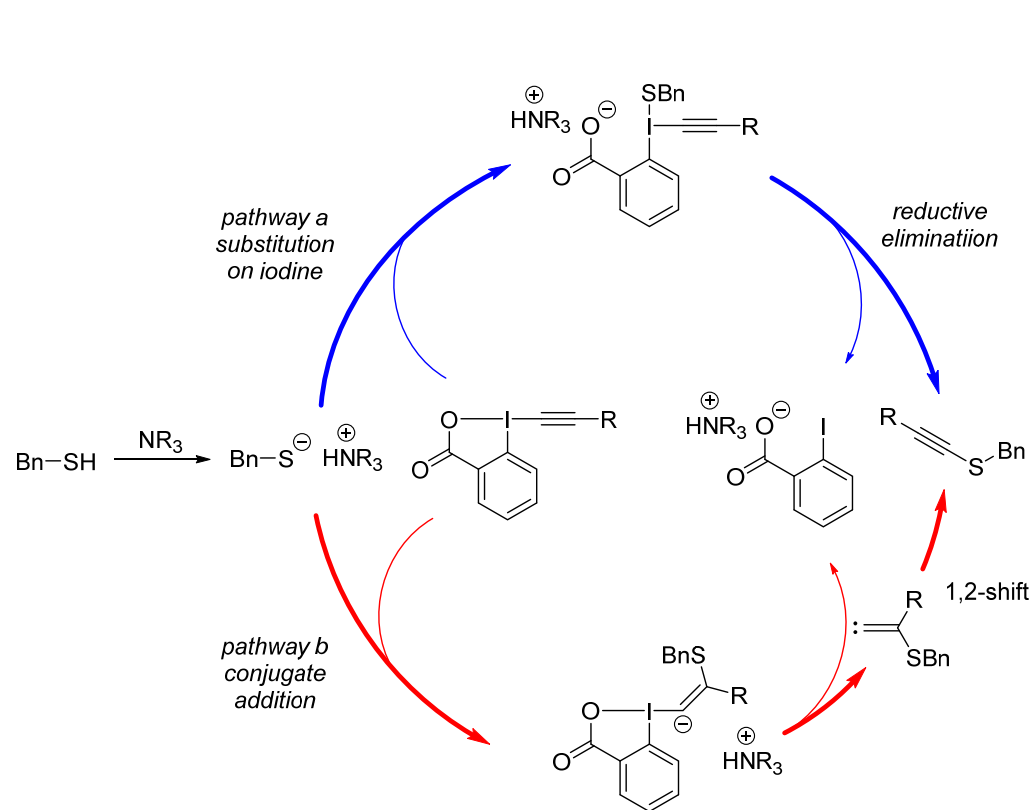


R = Aliphatic, Phenolic, Heterocyclic, Peptidic



- harsh conditions
- transition metals
- limited scope

R. Frei, J. Waser, *J. Am. Chem. Soc.* **2013**, *135*, 9620.



R. Frei, M. D. Wodrich, D. P. Hari, P.-A. Borin, C. Chauvier, J. Waser, *J. Am. Chem. Soc.* **2014**, *136*, 16563.

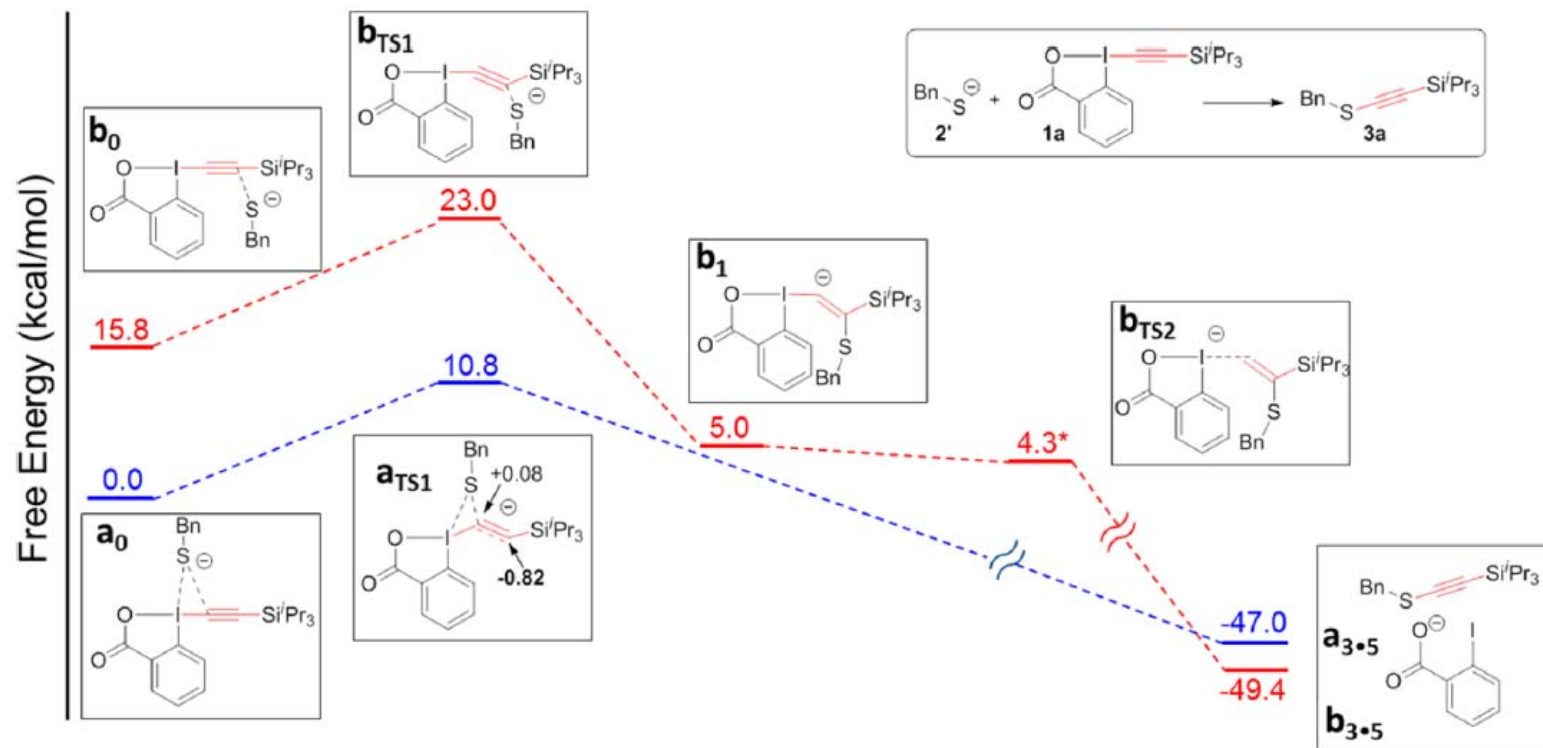


Figure 2. Reaction free energy profile [PBE0-dDsC/TZ2P//M06-2X/def2-SVP level in implicit THF solvent (COSMO-RS)] for the two possible mechanistic pathways **a** (blue) and **b** (red) for the reaction of TIPS-EBX (**1a**) with thiolate **2'**. *Positive ΔE at the M06-2X/def2-SVP level.

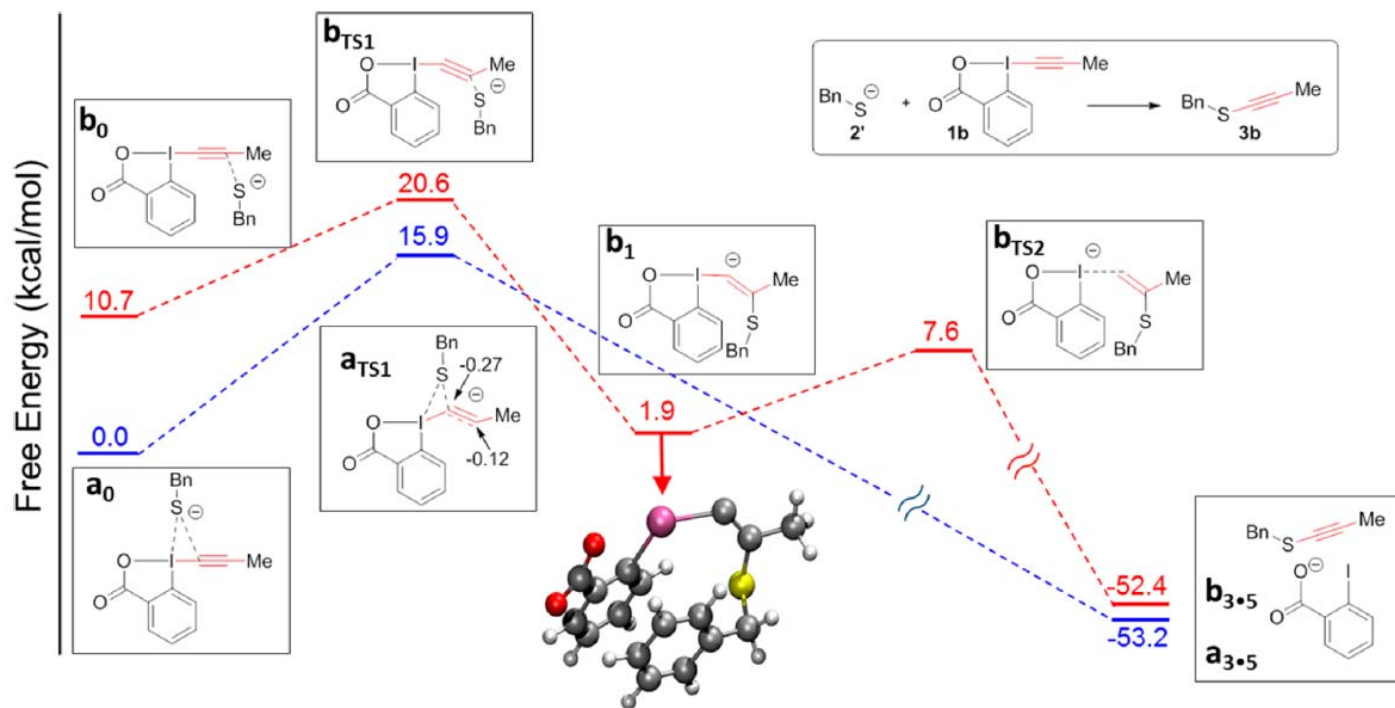
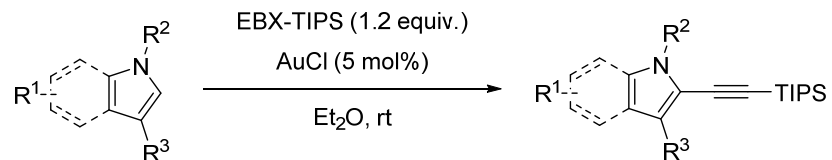
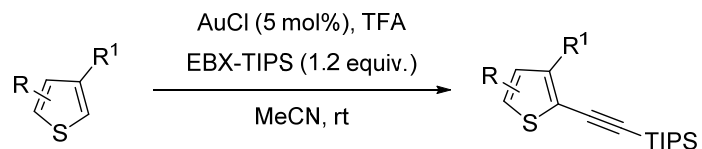


Figure 4. Reaction free energy profile [PBE0-dDsC/TZ2P//M06-2X/def2-SVP level in implicit THF solvent (COSMO-RS)] for the two possible mechanistic pathways **a** (blue) and **b** (red) for the reaction of Me-EBX (**1b**) with thiolate **2'**.

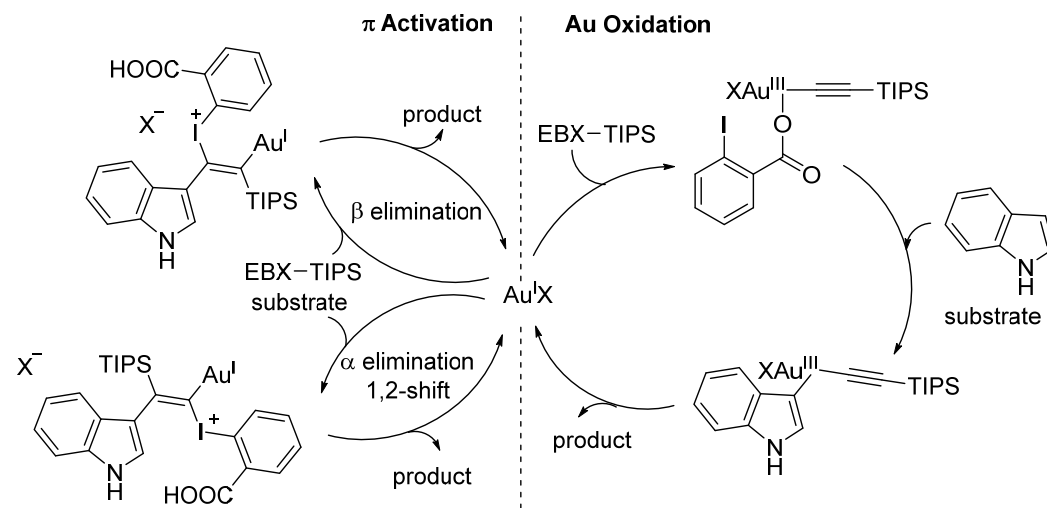


J. P. Brand, J. Charpentier, J. Waser, *Angew. Chem. Int. Ed.* **2009**, *48*, 9346

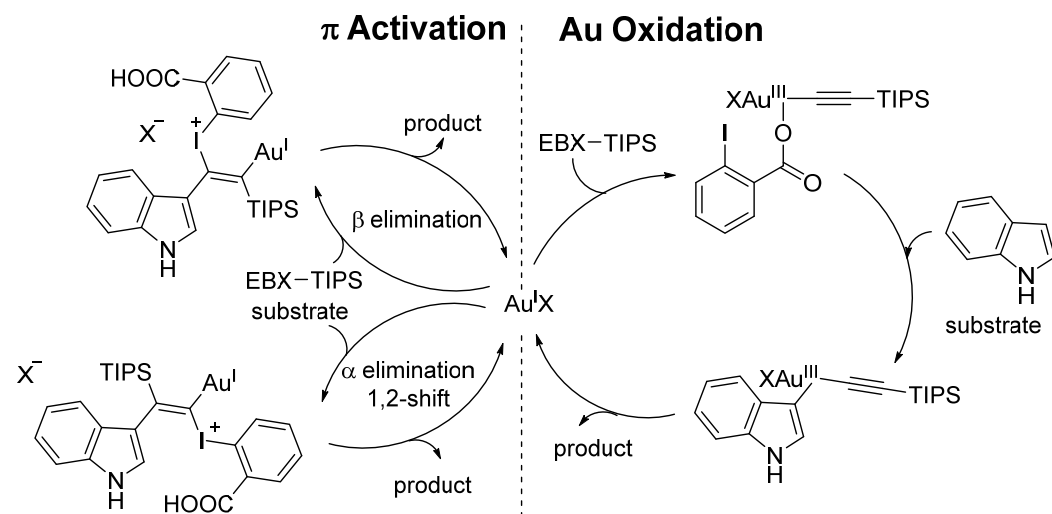


J. P. Brand, J. Waser, *Angew. Chem. Int. Ed.* **2010**, *49*, 7304

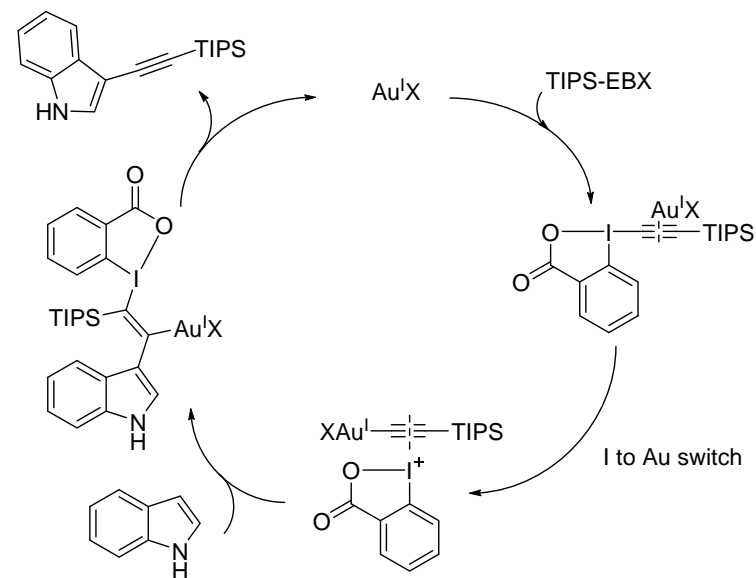
Mechanism proposed:

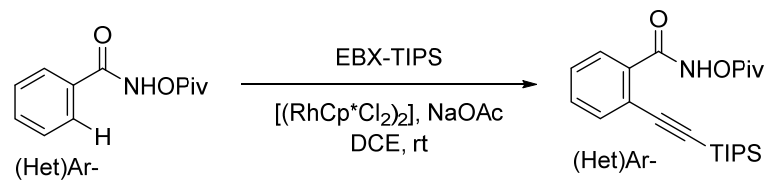


Mechanism proposed:

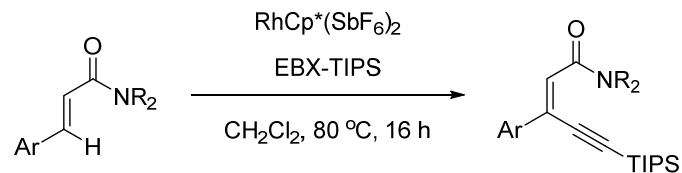


Mechanism computed:

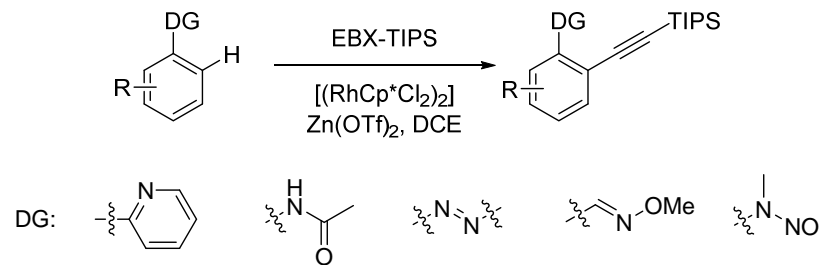




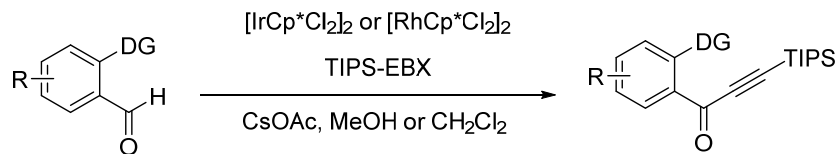
C. Feng, T.-P. Loh, *Angew. Chem. Int. Ed.* **2014**, *53*, 2722.



K. D. Collins, F. Lied, F. Glorius, *Chem. Commun.* **2014**, *50*, 4459.

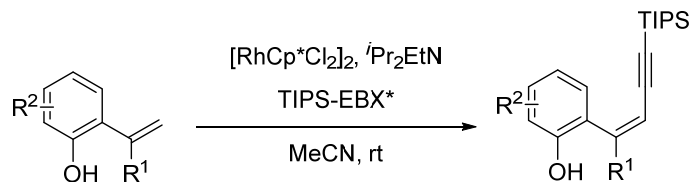


F. Xie, Z. Qi, S. Yu, X. Li, *J. Am. Chem. Soc.* **2014**, *136*, 4780.



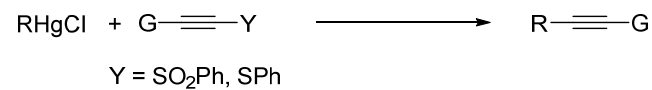
H. Wang, F. Xie, Z. Qi, X. Li, *Org. Lett.* **2015**, *17*, 920.

W. Ai, Y. Wu, H. Tang, X. Yang, Y. Yang, Y. Li, B. Zhou, *Chem. Commun.* **2015**, *51*, 7871.

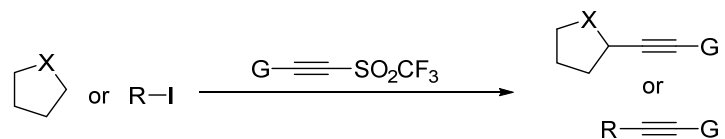


P. Finkbeiner, U. Kloeckner, B. J. Nachtsheim, *Angew. Chem. Int. Ed.* **2015**, *54*, 4949.

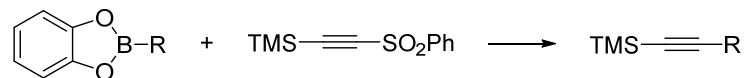
Radical reagents reported before:



G. A. Russell, P. Ngoviwatchai, H. I. Tashtoush, A. Pla-Dalmau, R. K. Khanna, *J. Am. Chem. Soc.* **1988**, *110*, 3530.

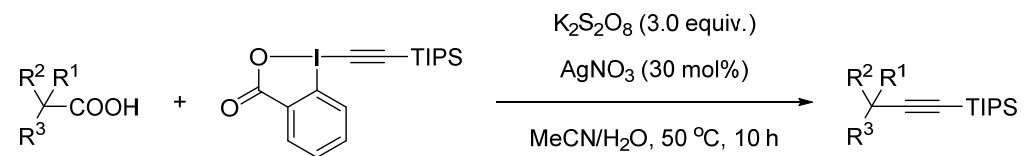


J. Gong, P. L. Fuchs, *J. Am. Chem. Soc.* **1996**, *118*, 4486.

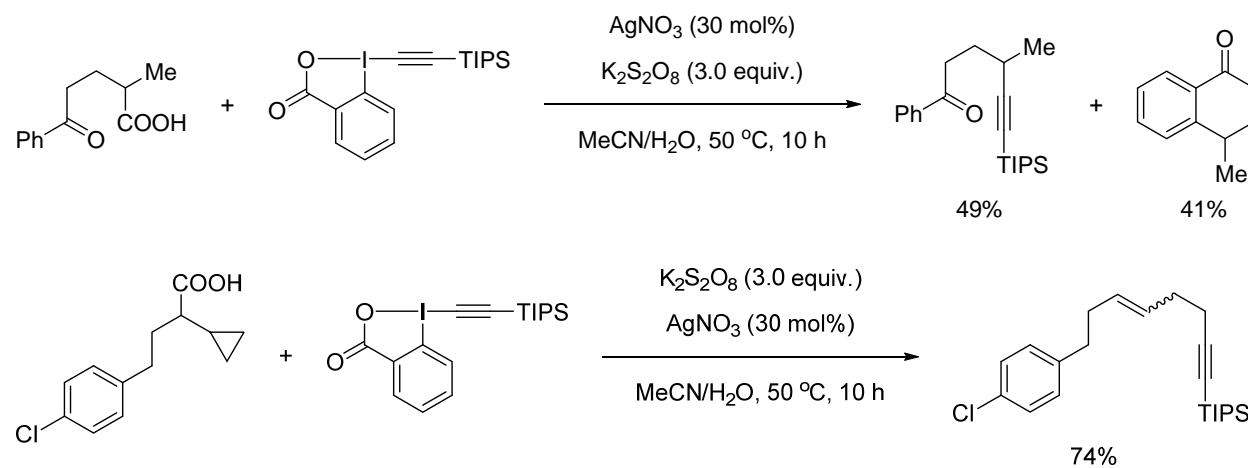


A.-P. Schaffner, V. Darmency, P. Renaud, *Angew. Chem. Int. Ed.* **2006**, *45*, 5847.

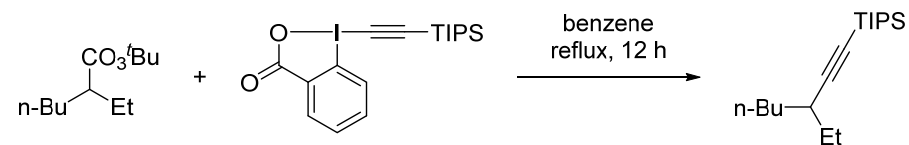
First report:



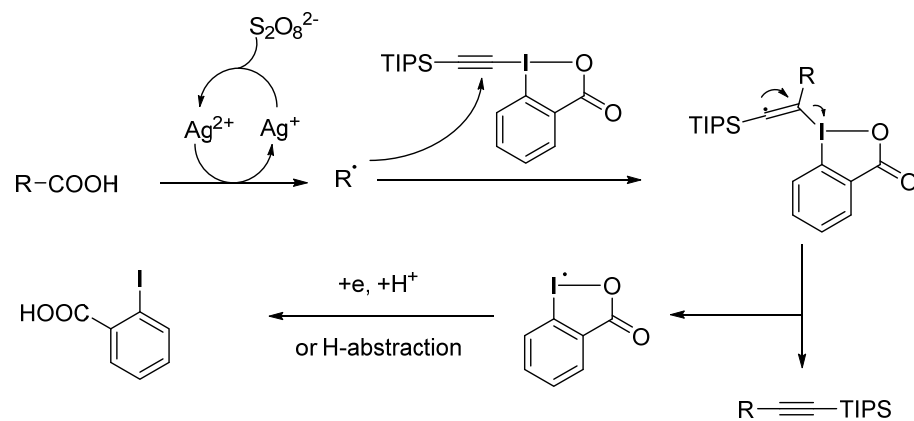
Mechanism studies:

X. Liu, Z. Wang, X. Cheng, C. Li, *J. Am. Chem. Soc.* **2012**, *134*, 14330.

Radical confirmed experiment:

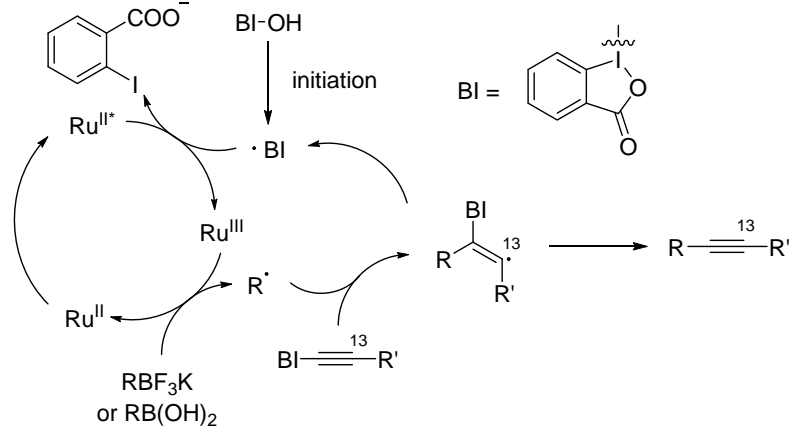
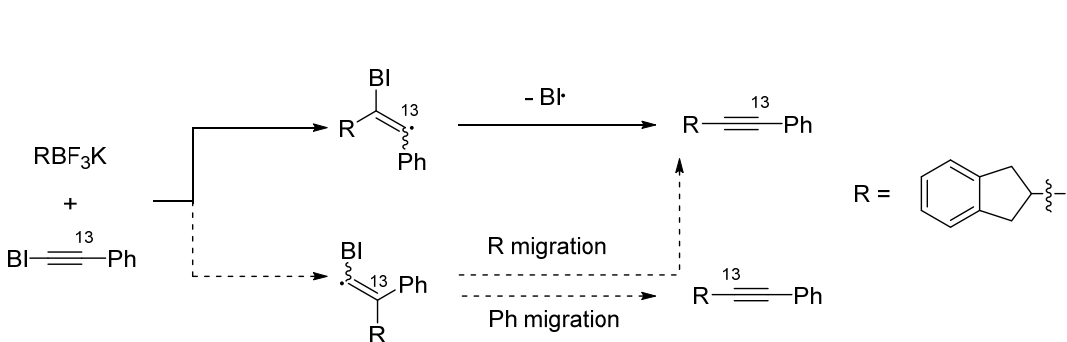
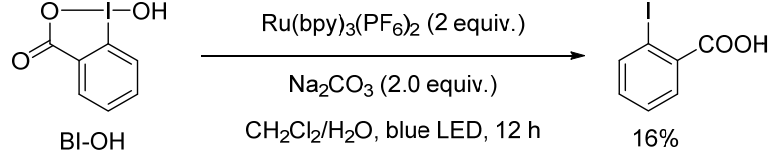
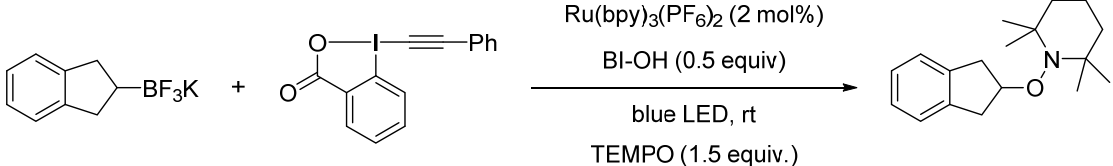
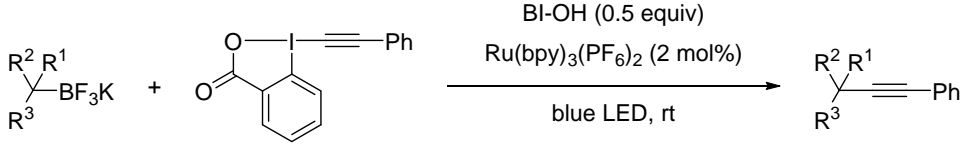


Mechanism proposed:

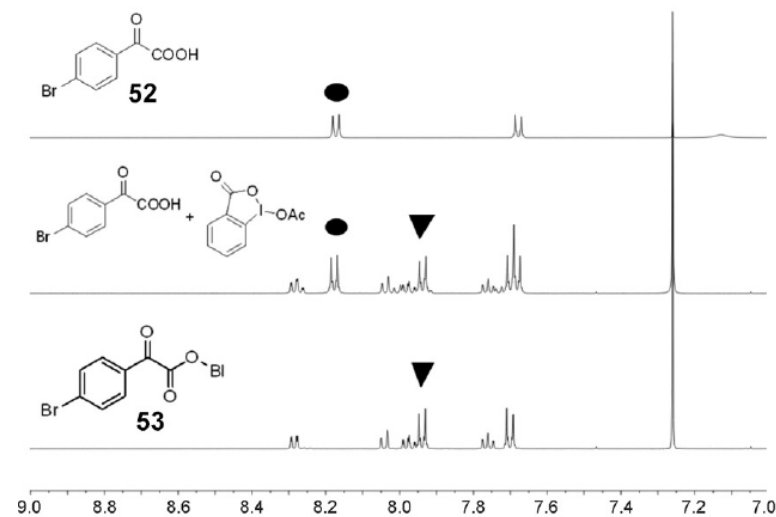
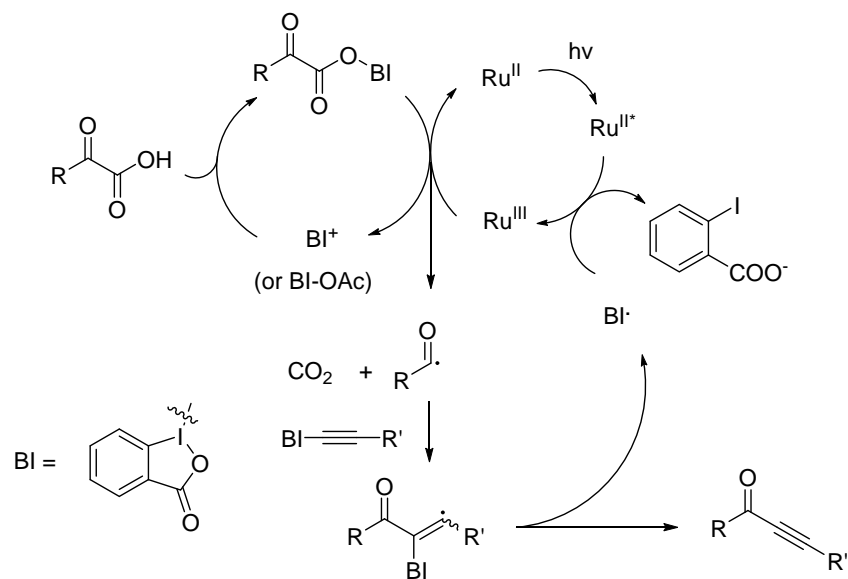
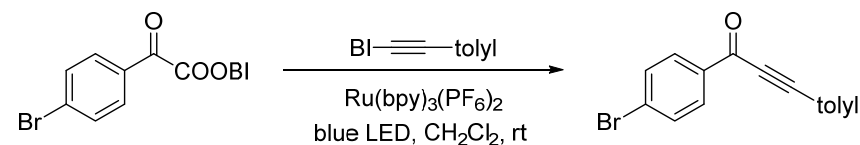
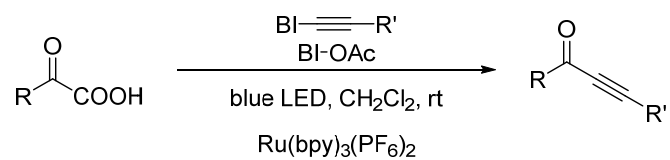


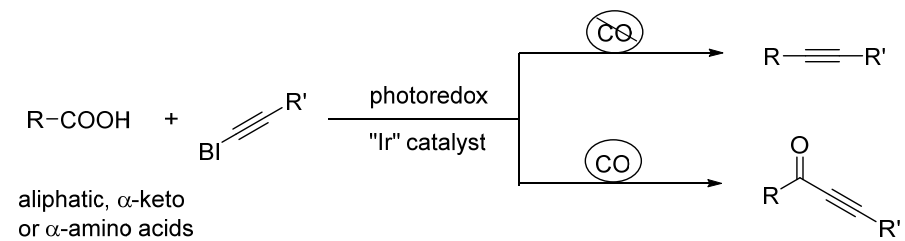
X. Liu, Z. Wang, X. Cheng, C. Li, *J. Am. Chem. Soc.* **2012**, *134*, 14330.

Combination with photoredox catalysis:

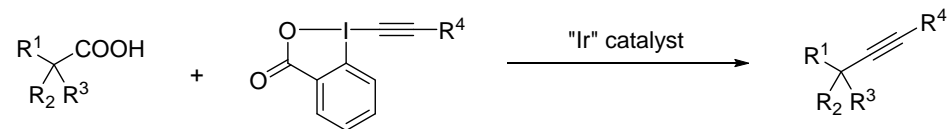


Application in ynone synthesis:



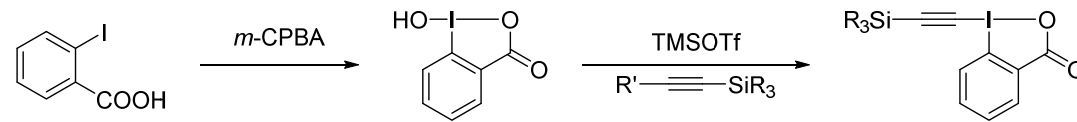


Q.-Q. Zhou, W. Guo, W. Ding, X. Wu, X. Chen, L.-Q. Lu, W.-J. Xiao, *Angew. Chem. Int. Ed.* **2015**, *54*, 11196.



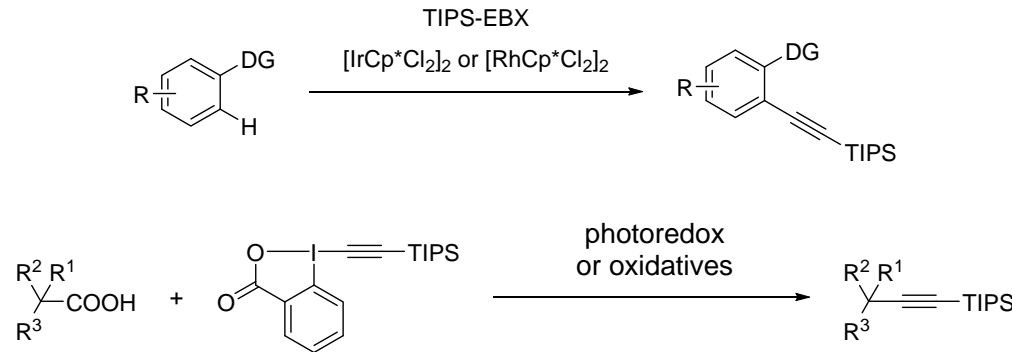
F. L. Vaillant, T. Courant, J. Waser, *Angew. Chem. Int. Ed.* **2015**, *54*, 11200.

Preparation



- easy to access
- multigram scalable

Application



- mild condition
- functional tolerance
- high efficiency

Thank you for your attention