Copper-Catalyzed Electrophilic Alkyne Transfer: Accessing Important Building Blocks for Synthetic and Medicinal Chemistry by Reversing the Logic of Bond Disconnection

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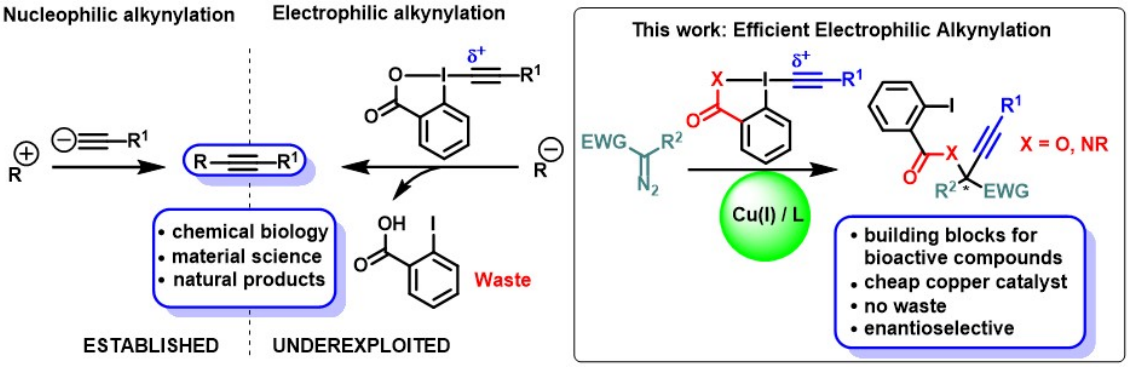
Alkynes are widely represented in biologically active natural products, materials, and medicines. Their use in cycloaddition reactions with azides ("Click Chemistry") has found widespread applications in the synthesis of nanomaterials, chemical biology, and drug delivery.[1a] Consequently, the efficient synthesis of structurally diverse alkynes is a prominent objective in chemical research. One of the most often used methods for the synthesis of alkynes consists in the addition of acetylenes anions on electrophilic positions of molecules. In contrast, the reversed polarity approach, -the addition of alkynes onto nucleophiles- has been less investigated, limiting the structural diversity and potential applications of this important class of compounds. In this context, hypervalent iodine reagents, a fascinating class of reagents based on iodine, have been used extensively for *electrophilic* alkynylations due to their exceptional reactivity.[1b,1c] However, alkynylations using hypervalent reagents generates one equivalent of a side-product, leading to waste generation. In 2016, our group developed an unprecedented copper-catalyzed reaction for the introduction of alkynes onto organic molecules, in which all the parts of the reagents are incorporated into the product.[2a] Key for success was the use of cyclic hypervalent iodine reagents –EthynylBenziodoXolones (EBX), now also commercially available- and diazo compounds as reactive small organic molecules. This reaction is highly practical and proceeds under mild conditions for a broad range of substrates. It uses a cheap base metal catalyst (copper), whereas other methods in the field are based on the use of expensive precious transition metals, such as rhodium or palladium. Herein, we will describe further important extensions of our work of high significance for synthetic and medicinal chemistry: 1) The development of an asymmetric reaction giving access to enantioenriched products.[2b] This is an important breakthrough, as the enantiomers of organic compounds have different bioactivities. 2) The introduction of a new hypervalent iodine reagent (EBZ) allowing us to synthesize alkyne-containing amino acids,[2c] which are key building blocks for the synthesis of bioactive compounds.



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