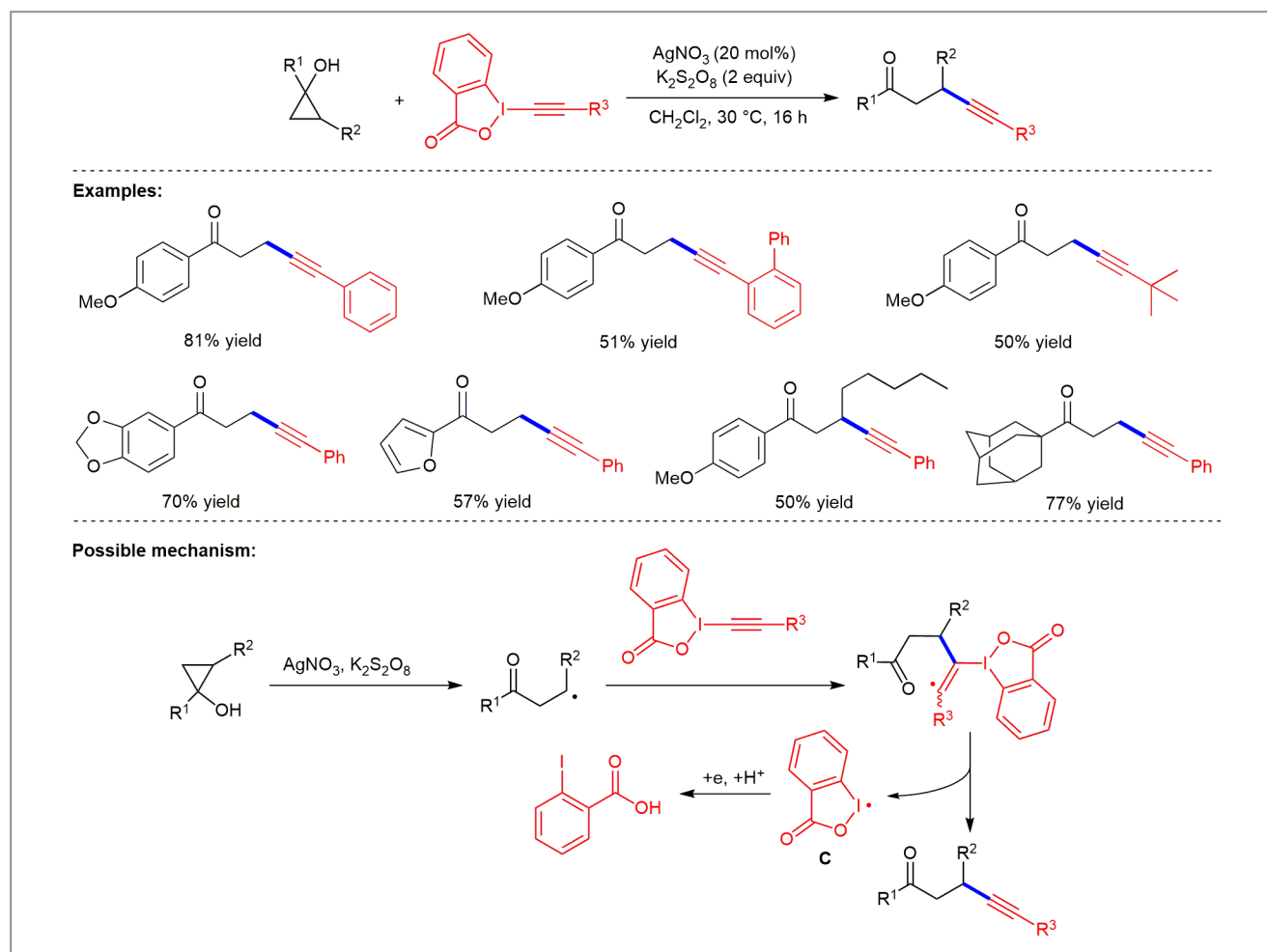


# Silver-Promoted Oxidative Ring-Opening/Alkynylation of Cyclopropanols: Facile Synthesis of 4-Yn-1-ones

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Alkynes are important structural motifs in natural products and functional materials as well as fundamental building blocks in synthetic chemistry and materials science. Among them, internal alkyl alkynes are readily prepared by the Sonogashira cross-coupling reaction of halides with terminal alkyl alkynes. However, the majority of these transformations are limited to aryl electrophiles which often require a copper co-catalyst, a base and a ligand to improve the yield, all of which complicate the procedure for organic synthesis and represent

a severe disadvantage for industrial applications. “To overcome these disadvantages, the development of new electrophilic alkynylating reagents, particularly with special reaction characteristics in the formation of C(sp)–C(sp<sup>3</sup>) bonds, have gained wide interest in the past decade,” said Professor Jin-Heng Li and Dr. Ye-Xiang Xie from Hunan University (P. R. of China). “Typically, attractive electrophilic alkynylating reagents include ethynyl benziodoxolones (EBXs), which were found to be appealing alkynylating reagents for building



**Scheme 1** Silver-promoted oxidative ring-opening/alkynylation of cyclopropanols and possible mechanism

diverse ynone molecules by the C-alkynylation with aldehydes,” they continued. “Therefore, it would be welcome to develop new strategies involving the use of new electrophilic alkynylating reagents for producing diverse alkyl alkynes.” Professor Li’s laboratory has been particularly interested in the oxidative radical coupling methodology for the construction of carbon–carbon or carbon–heteroatom bonds. In light of these, Professor Li and co-workers reasoned that the stable alkyl carbon-centered radicals would be trapped by the electrophilic alkynyl hypervalent iodide reagents through an oxidative radical process. Recently, Professor Li’s group found a way to prove their hypothesis: a new silver-promoted oxidative radical alkynylation strategy was documented for the synthesis of alkyl alkynes under mild conditions, in which ethynyl benziodoxolones were used as the electrophilic alkynylating reagents to react with various cyclopropanols in the presence of  $\text{AgNO}_3$  and  $\text{K}_2\text{S}_2\text{O}_8$  (Scheme 1).

“This method allows selective radical cleavage of the C–C bond in a wide range of cyclopropanols to form the stable alkyl carbon-centered radicals followed by coupling with various alkynes, including aryl- and alkyl-substituted alkynes, and represents a mild and practical route to assemble alkyl alkynes,” said Professor Li and Dr. Xie, who added: “Although the Sonogashira cross-coupling reaction, which starts from aryl or alkenyl halides and terminal alkynes, has been well established for incorporating alkyne moieties into organic molecules, the synthesis of aliphatic alkynes from alkyl electrophiles still remains a formidable challenge.” Now, Professor Li and co-workers have established a new oxidative radical coupling strategy for the synthesis of aliphatic alkynes from the reaction of electrophilic EBXs with the alkyl carbon-centered radicals, which avoid the use of alkyl electrophiles with lower reactivity.

At the beginning of this research, a series of experiments examining the catalytic systems were performed, and the ring opening/alkynylation reaction was found to occur in the presence of either silver salts or potassium persulfate. “Surprisingly, the reaction could take place without silver salts, albeit with a lower yield,” said Professor Li and Dr. Xie. “A similar yield (49%) was obtained when three equivalents of  $\text{K}_2\text{S}_2\text{O}_8$  were used in the absence of  $\text{AgNO}_3$ . The results suggest that  $\text{AgNO}_3$  may play two roles, as an accelerator and an oxidant.”

The control experiments support a radical process for the ring-opening/alkynylation reaction (Scheme 1). Professor Li and Dr. Xie explained: “The reaction of cyclopropanol with EBX was completely suppressed when using a stoichiometric amount of radical inhibitor (3 equiv), including TEMPO and BHT. According to the results and the proposed mechanism,

while  $\text{K}_2\text{S}_2\text{O}_8$  served as the oxidant to generate the alkyl carbon-centered radical intermediate, silver salts might play at least two roles: as the catalyst to initiate the formation of the alkyl carbon-centered radical intermediate and as Lewis acid to stabilize the radical intermediates.”

Professor Li and Dr. Xie emphasized that compared to the traditional cross-coupling reaction, there are two features worthy of note in this strategy: (1) simple operation, as the reaction does not require additives, such as copper co-catalysts, bases and ligands, and proceeds at 30 °C under neutral reaction conditions, thus providing no complicated purification steps, and (2) generality, as the broad substrate scope results in the construction of diverse aliphatic alkynes, including dialkyl alkynes and alkyl aryl alkynes.

Professor Li and Dr. Xie concluded: “In this report, a great challenge was how to stabilize the alkyl carbon-centered radicals from oxidative opening of cyclopropanols, and we were lucky to find that silver salts can fill this role: they serve not only as an oxidant but also as a catalyst to improve the reaction. Inspired by these, if one discovers a catalyst which has enough activity to directly stabilize a wide range of active radical intermediates from the common chemical bonds, especially different C–H bonds in unactivated alkanes and arenes, the oxidative radical coupling between a radical and an electrophile will inarguably become the most versatile method in chemical research in the future.”

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