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Copper-catalyzed synthesis of 1,2-diketones via oxidation of alkynes

Ning Xu [a], Da-Wei Gu [b], Yan-Sheng Dong [c], Feng-Ping Yi [c], Liangzhen Cai [a], Xin-Yan Wu [a,*], Xun-Xiang Guo [b,*]

[a] *Key Laboratory for Advanced Materials and Institute of Fine Chemicals, East China University of Science and Technology, Shanghai 200237, China.*
[b] *Shanghai Center for Systems Biomedicine, Ministry of Education Key Laboratory of Systems Biomedicine, Shanghai Jiao Tong University, Shanghai 200240, China*
[c] *School of Perfume and Aroma Technology, Shanghai Institute of Technology, Shanghai 201418, China*

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ABSTRACT

The direct oxidation of internal alkynes proceeds efficiently in the presence of CuI as a catalyst to afford the corresponding 1,2-diketones in good yields. This strategy offers a simple and efficient route for the synthesis of 1,2-diketones from an inexpensive copper catalyst and easily available internal alkynes. The advantage of present protocol is further demonstrated by the synthesis of quinoxaline derivatives from alkynes and 1,2-diaminobenzene *via* one-pot procedure.

1,2-Diketones are one of important structural motifs in a variety of molecules with interesting physiological and biological activities.[1] It is found that 1,2-diketones have been used as useful building blocks in organic synthesis,[2] particularly for the construction of important heterocycles, such as quinoxalines, and imidazoles.[3]

A lot of synthetic protocols have been developed for the synthesis of 1,2-diketones.[4] As one of the most straightforward process for the synthesis of 1,2-diketones, the oxidation of internal alkynes, which are easily accessible by the Sonogashira coupling,[5] has received much attention in the past few years.[6-11] Among them, the transition-metal-catalyzed direct oxidation of internal alkynes is particularly attractive and efficient. However, most reported examples are use of expensive transition-metal complexes, such as palladium,[7] gold,[8] and ruthenium,[9] as the catalyst. Recently, although the use of a combination of copper powder and selectfluor as a catalyst has been reported for the synthesis of 1,2-diketones,[11] the reaction suffers from a limitation of the use of toxic selectfluor. Therefore, the development of efficient inexpensive transition-metal-catalyzed protocols to access of 1,2-diketones is still highly desirable because of their important biological and pharmacological properties.

We recently have developed Cu-catalyzed methods to construct heterocycles.[12] As our interests to focus on inexpensive copper complexes as catalysts, we report here a novel method for the synthesis of 1,2-diketones through Cu-catalyzed oxidation of internal alkynes. Using this reaction protocol, the 1,2-diketones were obtained in good yields in the presence of inexpensive copper catalyst from easily available internal alkynes.

Initially, we choose 1,2-diphenylethyne **1a** as a model substrate to test the reaction. The reaction of **1a** in the presence of 20 mol% $Cu(OAc)_2$ as a catalyst with 1.5 equiv of $K_2S_2O_8$ as an oxidant in DMSO at 120 °C for 24 hours afforded the desired product **2a** in 3% yield (Table 1, entry 1). The catalyst CuO gave 4% yield of **2a** (Table 1, entry 2). The yield was increased to 35% when $CuCl_2$ was used in the reaction (Table 1, entry 3). Interestingly, the copper (I) complex of CuCl also afforded product **2a** in 31% yield (Table 1, entry 4). To our delight, the employment of CuI as a catalyst provided product **2a** in 57% yield (Table 1, entry 5). We applied CuI to examine other reaction conditions. The use of benzoquinone (BQ) and TBHP afforded trace amount of product **2a** (Table 1, entries 6-7). Although $PhI(OAc)_2$ gave product **2a** in 34% yield (Table 1, entry 8), the yield was increased to 68% when $Na_2S_2O_8$ was used as an oxidant (Table 1, entry 9). We investigated several solvents. The use of DMF, toluene, and 1,4-dioxane provided product **2a** in trace amount of yields (Table 1, entries 10-12). In the examination of reaction temperature, 140 °C was found to be the optimal one (Table 1, entries 13-14). The reaction also proceeds well under N_2 to give **2a** in 74% yield (Table 1, entry 15). In addition, we found that the desired product **2a** was obtained in 82%

* Corresponding author. Tel.: +86-21-3420-4190
E-mail: xinyanwu@ecust.edu.cn (X.-Y. Wu)
xunxiang_guo@sjtu.edu.cn (X.-X. Guo)