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A facile copper(I)-catalyzed homocoupling of terminal alkynes to 1,3-diynes with diaziridinone under mild conditions

Yingguang Zhu and Yian Shi

Department of Chemistry, Colorado State University, Fort Collins, Colorado 80523, United States

Abstract

A novel and efficient Cu(I)-catalyzed oxidative homocoupling of terminal alkynes with diaziridinone as oxidant is described. Various terminal alkynes can be transformed into the corresponding 1,3-diynes in good yields. The reaction process is base-free, operationally simple, and amenable to gram scale.

1,3-Diynes are present in natural products¹ and biologically active molecules.² They are also important structural motifs found in various oligomers, polymers, and materials.³ A variety of processes have been developed for the preparation of 1,3-diynes.^{4–11} The oxidative coupling of terminal alkynes represents one of the most straightforward and widely used approaches to these types of compounds. Various effective methods have been developed, including Cu-mediated¹² or catalyzed,¹³ Co-catalyzed,¹⁴ Pd-catalyzed,¹⁵ and bimetallic Pd/Cu,¹⁶ Ni/Cu¹⁷ catalyzed systems. Although significant progress has been made in this area, the development of new, mild, and efficient procedure is still desirable and valuable.

In our earlier studies, we have shown that di-*tert*-butyldiaziridinone (**1**)^{18,19} is a highly effective nitrogen source for the Pd(0)-²⁰ and Cu(I)-²¹ catalyzed diamination of olefins. Recently, we have shown that di-*tert*-butyldiaziridinone (**1**) can also be used for the oxidation of alcohols²² and oxidative coupling of anilines²³ using Cu(I) as catalyst. During our studies on the oxidation of alcohols, 1,6-diphenylhexa-2,4-diyne-1,6-dione (**4a**) instead of 1-phenylpropynone (**3a**) was obtained in 31% yield under the reaction conditions when propargyl alcohol **2** was used as substrate (Scheme 1). This observation prompted us to further investigate this homocoupling process of terminal alkynes. Herein we wish to report our preliminary studies on this subject.

The alkyne coupling was investigated with phenylacetylene (**3b**) as test substrate. Treating **3b** with 0.51 equiv. of diaziridinone **1** and 5 mol% CuBr in CH₃CN at rt for 2 h gave 1,3-diyne **4b** in 54% yield (Table 1, entry 1). A complete conversion was achieved with 0.90 equiv. of **1**, giving **4b** in 80% yield (Table 1, entry 3). No coupling products were observed without CuBr catalyst or diaziridinone **1** (Table 1, entries 6 and 7).

The generality of this oxidative homocoupling was subsequently investigated. As shown in Table 2, various aromatic terminal alkynes with either electron-donating or electron-withdrawing substituents were smoothly coupled to give the corresponding 1,3-diynes in 64–83% yields (Table 2, entries 1–8). 3-Ethynylthiophene was effectively converted to 1,3-diyne **4j** in 79% yield (Table 2, entry 9). Various nonaromatic terminal alkynes were also effective substrates for this oxidative homocoupling, giving the corresponding 1,3-diynes in 64–81% yields (Table 2, entries 10–15). As illustrated in the case of 1-ethynyl-4-(trifluoromethyl)benzene (**3e**), the coupling method is amenable to gram scale (Table 2, entry 4).

While a precise understanding of the reaction mechanism awaits further study, a plausible catalytic cycle is proposed in Scheme 2. The CuBr first reductively cleaves the N–N bond of di-*tert*-butyldiaziridinone (**1**) to form four-membered Cu(III) species **A** and/or Cu(II) nitrogen radical **B**,^{21e,f} which reacts with terminal alkyne **3** to form dialkynyl Cu(III) species **C**,^{4a,b} which undergoes the reductive elimination to afford 1,3-diyne **4** and regenerate the CuBr catalyst.

In summary, we have developed a mild and efficient method for the oxidative homocoupling of terminal alkynes with CuBr as catalyst and di-*tert*-butyldiaziridinone (**1**) as oxidant. Various terminal alkynes can be effectively coupled to give the corresponding 1,3-diynes in good yields. The reaction is base-free, operationally simple, and also amenable to gram scale. The results further demonstrate the synthetic utility of diaziridinones. Further efforts to develop other coupling processes with this class of compounds are currently underway.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Scheme 1.
Cu(I)-catalyzed oxidative homocoupling of **2**.

Scheme 2.

Proposed catalytic cycle for the oxidative homocoupling.

Table 1

Optimization of reaction conditions^a

Entry	1 (X equiv.)	Time (h)	Conv. ^b (%)	Yield ^c (%)
1	0.51	2	67	54
2	0.75	2	89	74
3	0.90	2	100	80
4	1.0	2	100	78
5 ^d	0.90	2	100	80
6 ^e	0.90	24	0	—
7	0	24	0	—

^a All reactions were carried out with phenylacetylene (**3b**) (0.60 mmol), di-*tert*-butyl diaziridinone (**1**), and CuBr (0.030 mmol) in CH₃CN (0.9 mL) at rt unless otherwise stated.

^b The conversion was based on phenylacetylene (**3b**) and determined by the ¹H NMR analysis of the crude reaction mixture.

^c Isolated yield based on **3b**.

^d The reaction was carried out under a rigorous argon atmosphere.

^e The reaction was carried out in the absence of CuBr.

Table 2

Oxidative homocoupling of terminal alkynes^a

Entry	Substrate 3	Product 4	Yield ^b (%)
1	3b , X = H	4b	80
2	3c , X = <i>p</i> -Me	4c	77
3	3d , X = <i>p</i> - ^t Bu	4d	79
4 ^c	3e , X = <i>p</i> -CF ₃	4e	83
5	3f , X = <i>p</i> -F	4f	81
6	3g , X = <i>m</i> -Cl	4g	80
7	3h , X = <i>o</i> -Cl	4h	64
8	3i , X = <i>o</i> -CF ₃	4i	74
9			79
10			64
11			81
12	3l , ⁿ C ₆ H ₁₃ -C≡CH	4l , ⁿ C ₆ H ₁₃ -C≡C-C≡C-C ₆ H ₁₃ ⁿ	76
13			71
14			79
15			75

^a All reactions were carried out with alkyne **3** (0.60 mmol), di-*tert*-butyldiaziridinone (**1**) (0.54 mmol), and CuBr (0.030 mmol) in CH₃CN (0.9 mL) at rt for 2 h unless otherwise stated. For entry 6, the reaction time was 6 h. For entry 7, 1.0 equiv. of **1** was used, and the reaction time was 7 h. For entries 12, 13, and 15, the reactions were carried out with alkynes **3** (0.60 mmol), di-*tert*-butyldiaziridinone (**1**) (0.66 mmol), and CuBr (0.060 mmol) in CDCl₃ (0.9 mL) at rt for 5 h.

^b Isolated yield based on alkyne **3**.

^c The reaction was carried out on 10 mmol scale of **3e**.