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Copper Powder–Mediated Homocoupling Reactions of Iodoacetylenes to Synthesize Symmetrical 1,3-Butadiynes

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Abstract: A new route to synthesize symmetrical 1,3-butadiynes from iodoacetylenes in the presence of copper powder and pyridine was developed. Moderate to excellent yields were obtained through an efficient and simple process involving the copper powder without any further activation.

Keywords: 1,3-Butadiynes; Copper powder; Homocoupling reaction; Iodoacetylenes

1,3-Butadiynes have been important intermediates in organic synthesis,[1] pharmaceuticals,[2] polymes,[3a,3b] and natural products.[3c] Numerous synthetic methods for their preparation have been developed. There are several Pd(0)-Cu(I)–catalyzed cross-coupling reactions, such as dimerization of terminal alkynes[4] or dimerization of alkynyl halides with terminal alkynes.[5] Alkynylstannanes,[6a] alkynylboronates,[6b] and alkynylsilanes[7] were also used to give 1,3-butadiynes. Damle and coworker's described an efficient synthetic method of 1,3-butadiynes from iodoacetylenes in the presence of $Pd(PPh_3)_4$ in N,N-dimethylformamide (DMF); however, $Pd(PPh_3)_4$ was expensive and sensitive to air.[8]

Another efficient and useful method for preparing 1,3-butadiynes was observed by Carl Glaser in 1869, who got 1,3-butadiynes from terminal

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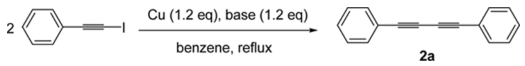
acetylenes with CuCl in the presence of NH_4OH.[9] Subsequently, many improved methods were developed to give 1,3-butadiynes.[10] Especially in the 1960s, Hay reported that terminal acetylenes could be transformed to 1,3-butadiynes at room temperature with oxygen or air by CuCl–pyridine or CuCl–tetramethylethylenediamine (TMEDA).[11] In short, a variety of cupric salts in the presence of organic bases have been employed in the past several decades.[12] However, moderate yields were obtained in most cases. Therefore, a simple and efficient methodology for synthesis of 1,3-butadiynes is of interest.

In 1901, Ullmann discovered that copper powder catalyzed the coupling of aromatic halides to produce biaryls,[13] which is an effective method for the construction of sp^2-sp^2 C-C bonds. The homocoupling of alkyl halides to construct sp^3-sp^3 C-C bonds utilizing a highly activated form of zero-valent copper has also been reported.[14] However, to the best of our knowledge, copper powder used to construct sp-sp C-C bonds has received relatively little attention.[15] Herein, we report a new route to synthesize 1,3-butadiynes from iodoacetylenes in the presence of copper powder and pyridine under mild reaction conditions.

EXPERIMENTAL

Our investigation began with an effort to optimize reaction conditions for the coupling of iodoacetylenes. 1-(2-Iodoethyny)benzene was chosen as

Table 1. Coupling of iodoacetylenes with copper powder



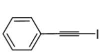
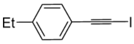
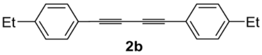
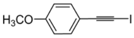
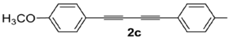
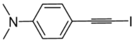
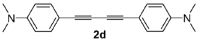
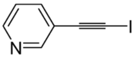
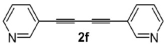
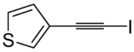
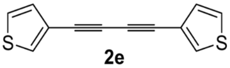
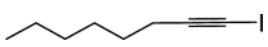
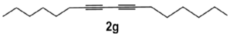
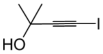
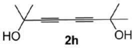
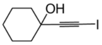
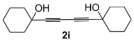
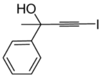
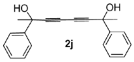
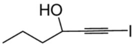
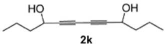
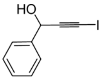
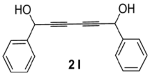
Entry	Base	Time (h)	**2a** yield (%)[a]
1	Pyridine	6	98
2	DMAP	6	98
3	PPh_3	8	30
4	Et_3N	3	Trace
5	K_2CO_3	6	Trace
6	None	6	—
7[b]	Pyridine	6	96
8[c]	Pyridine	12	49
9[d]	Pyridine	12	47

[a] Isolated yields.
[b] Reactions were performed under nitrogen.
[c] Copper powder (0.5 eq.) and pyridine (0.5 eq.) were used.
[d] Copper powder (0.5 eq.) and pyridine (1.2 eq.) were used.

a standard substrate for the optimization process. The results are shown in Table 1. Treatment of 1-(2-iodoethyny)benzene with 1.2 equiv of copper powder and 1.2 equiv of pyridine in benzene under reflux for 6 h afforded 1,4-diphenylbuta-1,3-diyne (**2a**) in 98% yield (entry 1, Table 1). When 4-dimethylaminopyridine (DMAP) was used as a base, the desired product (**2a**) was also obtained in an excellent yield. However, the choice of PPh_3 gave the desired product in 30% yield (entry 3, Table 1). Only a trace amount of desired product was observed when Et_3N or K_2CO_3 was used as a base. Thus, pyridine and DMAP were efficient bases for the course of this reaction. DMAP was more expensive than pyridine. Thus, pyridine was chosen as the most appropriate base for this reaction. The amount of copper powder was also crucial to this coupling reaction. Reactions of 0.5 equiv of copper powder with 0.5 and 1.2 equiv of pyridine afforded the desired product in 49% and 47% yields, respectively (entries 8, 9, Table 1). Almost 50% of starting material was recovered in these two cases. The use of CH_2Cl_2 and THF as solvent also led to the formation of the desired products (**2a**) in 95% and 94% yields; however, prolonging the reaction time to 12 h was needed. The desired product (**2a**) was obtained in 96% yield when the reaction was stirred under nitrogen. Thus, the reaction does not require the presence of air.

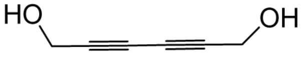
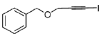
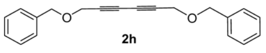
Under these optimized conditions, various iodoacetylenes were submitted to the reaction, and the representative results are shown in Table 2. Clearly, the substituents on the phenyl ring have an effect on the yields of the reaction. The presence of 4-ethyl and 4-methoxy groups on the aromatic ring did not diminish the efficiency, and reactions stirred for 12 h afforded the corresponding coupling products **2b** and **2c** in 96% and 97% yields, respectively. However, when a bromo or chloro group was on the aromatic ring, the reaction was complex, and the corresponding 1,3-butadiyne was not obtained under the same conditions. Substrates containing a nitrogen atom gave low yields, which might be due to its basic feature. For example, when 4-(2-iodoethynyl)-N, N-dimethylbenzenamine and 3-(2-iodoethynyl)pyridine were submitted to the reaction under the standard conditions, the corresponding products **2d** and **2e** were obtained in 23% and 24% yields, respectively. It is notable that when 4-dimethylaminopyridine (DMAP) was used instead of pyridine, the yields of desired products were improved to 43% and 87%, respectively (entries 4, 5, Table 2). Treatment of 3-(2-iodoethynyl)thiophene with copper powder and pyridine for 12 h afforded product **2f** in 94% yield. Homocoupling reaction of aliphatic iodoacetylene proceeded smoothly and gave a good yield. The reaction system was also effective for substrates containing a hydroxyl group (entries 8–13, Table 2). High yields were achieved when substrates have secondary or tertiary hydroxyl

Table 2. Dimerization of various iodoacetylenes using optimized conditions

Entry	Substrate	Time (h)	Product	Yield[a] (%)
1		6	 2a	98
2		12	 2b	96
3		12	 2c	97
4		20	 2d	23 (43[b])
5		12	 2f	24 (87[b])
6		12	 2e	94
7		12	 2g	80
8		12	 2h	96
9		12	 2i	81
10		12	 2j	79
11		12	 2k	72
12		12	 2l	42

(*Continued*)

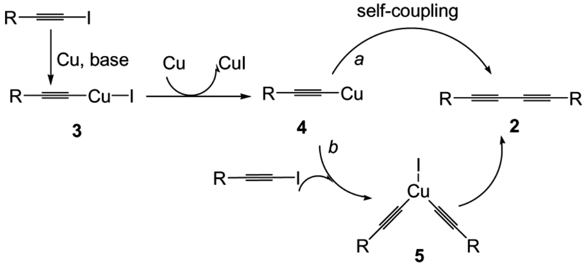
Table 2. Continued

Entry	Substrate	Time (h)	Product	Yield[a] (%)
13		12	 **2m**	45
14		10	 **2h**	80

[a]Isolated yields.
[b]Copper powder (1.2 eq.) and DMAP (2 eq.) were used.

groups. But, the substrate derived from propargyl alcohol gave the product **2m** in 45% yield. These results imply that the acidity of the hydroxyl group might have an effect on the reaction. The greater acidity of alcohols afforded lower yields of the desired products. The yield of corresponding product was improved to 80% when propargyl alcohol was protected by a benzyl group (entry 14, Table 2).

The current understanding of the mechanism of copper-mediated oxidative iodoacetylentic coupling reaction remains unsatisfactory. On the basis of these observations and previous investigations,[12] two plausible pathways are illustrated for this sp-sp homocoupling of iodoacetylenes (Scheme 1). Initially, DMAP acts as a Lewis base to polarize the C–I bond of iodoacetylenes[16] and mediates the reaction of iodoacetylenes and copper powder to generate intermediates **3**. The intermediates **3** give alkynylcoppers **4** in the presence of copper powder. Then, alkynlcoppers **4** are self-coupled to provide their respective homocoupled products (pathway *a*). Alternatively, alkynylcopppers **4** can undergo oxidative addition with the second equivalent of iodoacetylenes to generate an intermediate copper (III) species **5**,[12f] followed by reductive



Scheme 1. Plausible mechanism for the homocoupling of iodoacetylenes.

elimination and formation of the desired homocoupling products (pathway *b*).[14] At present, we cannot definitively determine which pathway the homocoupling of iodoacetylenes might use. The mechanistic details of this reaction need further investigation.

CONCLUSION

In summary, we have developed a new route to synthesize 1,3-butadiynes from iodoacetylenes in the presence of inexpensive copper powder and pyridine under mild reaction conditions. This method is an efficient and simple process for the synthesis of 1,3-butadiynes involving the copper powder without any further activation. Although terminal alkynes need first to be transformed into the iodo derivatives, the presence of copper powder and base has received relatively little attention in constructing sp-sp C-C bond formation, which makes the present procedure interesting and valuable compared to the traditional methods.

EXPERIMENTAL

General Procedure for the Preparation of 1,3-Butadiynes (Table 2)

To a solution of copper powder (0.36 mmol) and pyridine (0.36 mmol) in benzene (3 mL) in a round flask, iodoacetylene (0.3 mmol) was added. The resulting mixture was refluxed for the required length of time. The reaction was cooled at room temperature and extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine and then dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to give the crude products, which were purified by silica-gel chromatography to afford the corresponding product.

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