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Oxidation of Dihydrazones of Diaryl α-Diketones to Diarylacetylenes Using Sodium Periodate

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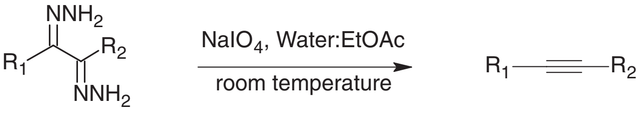
Oxidation of dihydrazones of α-diketones to acetylene was investigated by using sodium periodate. Further, the described method is also found to be suitable for deprotection of monohydrazones of aldehydes and ketones. The process is mild, efficient, and applicable to both electron-withdrawing and -donating substituents to give good to excellent yields.

Diarylacetylenes are an important class of organic compounds due to their incorporation in various organic reactions[1] as well as wide applications in bioactive molecules,[2] natural products[3] and organometallics.[4] The most common method for preparation of diarylacetylene is the Sonogashira coupling which includes coupling of phenylacetylene with aryl halide by using metal catalysts like Pd with various ligands,[5] Cu,[6] and $ZnCl_2$.[7] Numerous palladium complexes have been employed to catalyze this reaction in recent years, but the limited reusability of expensive Pd complexes has been a serious problem in industrial scale. Moreover, the reactions are generally air-sensitive and also require highly oxophilic phosphine ligands, while when copper catalysts are used, formation of the Glaser-type product[8] and the explosive nature of copper acetylide formed in the reaction are of great concern. In addition, amines such as piperidine, diethylamine, and triethylamine are required in most Sonogashira reactions and they add to the environmental burden. Recently, Abele and co-workers reported acetylene-free coupling of aryl halide with 1-bromo-2-chloroethane, however the reaction suffers from drawbacks such as formation of homocoupled product and low yield in the case of heterocyclic substrates.[9] Other methods for synthesis of diphenylacetylene includes reaction of dihydrazone of benzil with HgO,[10] nickel complexes,[11] copper catalysts,[12] aryl iodine(III) complexes,[13] and alkyl diarylbismuthinates.[14] In all these syntheses, there are detracting experimental limitations, including the use of toxic metal catalysts, high temperature, or long reaction time, or organic reagents like aryl iodine(III) salt where an equivalent amount of aryl iodide is formed as side product which is difficult to separate from desired product, and by considering all above facts there is still need to develop a mild, economical, and efficient method for synthesis of diarylacetylene.

As part of our ongoing research toward development of efficient methods using iodine reagents,[15] herein we report a mild and simple method for preparation of diarylacetylene using sodium periodate.

For our initial study benzil dihydrazone selected as our model substrate, which was prepared according to a standard procedure,[10] is treated with 2 equivalents of $NaIO_4$ in a biphasic system (water:EtOAc) at room temperature: rapid evolution of nitrogen was observed. After completion of the reaction diphenylacetylene was isolated (Scheme 1).



1a–13a **1b–13b**

Scheme 1. Benzil dihydrazone oxidation to diphenylacetylene using $NaIO_4$.

Table 1. Oxidation of dihydrazone to diphenylacetylene

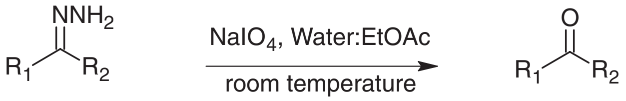
Compound	R_1	R_2	Yield of **b** /%[a]	Time /min
1	Ph	Ph	87	60
2	4-MeC_6H_4	4-MeC_6H_4	90	55
3	4-$OMeC_6H_4$	4-$OMeC_6H_4$	89	60
4	4-BrC_6H_4	4-BrC_6H_4	88	58
5	4-FC_6H_4	4-FC_6H_4	87	60
6	3-$NO_2C_6H_4$	3-$NO_2C_6H_4$	90	60
7	Ph	4-$NH_2C_6H_4$	91	50
8	Ph	4-$OMeC_6H_4$	90	57
9	Ph	4-ClC_6H_4	89	59
10	Furyl	Furyl	90	56
11	5-MeFuryl	5-MeFuryl	90	56
12	C_3H_7	CH_3	NR[b]	180
13	C_3H_7	C_3H_7	NR[b]	180

[a]Isolated yield by using column chromatography. [b]NR: No reaction.

Encouraged by this result, we turned our attention toward various electron-donating and electron-withdrawing substituents on benzil dihydrazone, and it turned out that the process tolerates both electron-donating and electron-withdrawing substituents.[16] In all the cases desired acetylene was obtained in good yields (Table 1, compounds **2**–**9**). Under these reaction conditions heterocyclic dihydrazone also was found to give good yield of desired diarylacetylene (Table 1, compounds **10** and **11**). No reaction was observed in the case of dihydrazone of dialiphatic α-diketone (Table 1, compounds **12** and **13**).

Further, this method is applied to monohydrazone of benzil, however rather than the expected α-diazo ketone,[17] deprotection of monohydrazone back to benzil was observed (Scheme 2).

To evaluate further the scope of this method, these reaction conditions were applied to various hydrazones of aldehydes and ketones.[16] It was observed that electron-donating substituents give good yield of corresponding carbonyl compound in shorter reaction time (Table 2, compounds **17**, **18**, **20** and **21**), while electron-withdrawing substituents give less yield in longer time (Table 2, compound **22**). Hydrazone of aliphatic aldehyde and ketone also undergo deprotection in comparatively less yield



14a–24a **14b–24b**

Scheme 2. Deprotection of monohydrazone using $NaIO_4$.

Table 2. Deprotection of monohydrazone

Compound	R_1	R_2	Yield of **b** /%[a]	Time /min
14	Ph	OCPh	85	45
15	Ph	Me	87	35
16	Ph	Ph	87	30
17	$4\text{-}ClC_6H_4$	Me	90	35
18	$2\text{-}HOC_6H_4$	Me	86	40
19	Ph	H	89	30
20	$3,4\text{-}(OMe)_2C_6H_3$	H	90	25
21	$4\text{-}OMeC_6H_4$	H	87	25
22	$4\text{-}NO_2C_6H_4$	H	76	50
23	C_4H_9	CH_3	70	60
24	C_5H_{11}	H	72	60

[a]Isolated yield by column chromatography.

(Table 2, compounds **23** and **24**). Though this reaction is reported utilizing various reagents,[18] the above is still an efficient method due to the mild nature of sodium periodate.

In conclusion, we have shown that wide range of diarylacetylenes was prepared using mild conditions from dihydrazones of α-diketones using $NaIO_4$. The method is also suitable for deprotection of monohydrazones to corresponding carbonyl compound. Both these applications are general, practical, economical, and efficient.

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16 **Experimental procedures: Representative procedure for preparation of diarylacetylene.** *Synthesis of* ***1b*** *(Table 1)*: $NaIO_4$ (898 mg, 4 mmol) in biphasic system water:EtOAc (10 mL) was stirred at room temperature for 5 min, then **1a** (500 mg, 2 mmol) was added to the stirred solution. Finally the reaction mixture was stirred for 1 h and completion of reaction was confirmed by thin layer chromatography (5%, hexane:EtOAc). Reaction mixture was then diluted with water and extracted with $CHCl_3$ (3×10 mL), dried with Na_2SO_4, filtered, and concentrated in vacuo to isolate crude residue, which was further subjected to silica gel column chromatography using mixture of hexane:EtOAc (10:1) to get final pure product **1b**.

Representative procedure for deprotection of monohydrazone. *Synthesis of* ***14b*** *(Table 2)*: $NaIO_4$ (954 mg, 2.2 mmol) in water:EtOAc (10 mL) was stirred at room temperature for 5 min, then **14a** (500 mg, 2.2 mmol) was added to the stirred solution. Finally reaction mixture was stirred for 30 min, and after completion of reaction the product **14b** was isolated as described for **1b**. Detailed experimental procedure and spectral data of all compounds are given in Supporting Information which is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

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