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# Highly efficient and recyclable catalyst for the direct chlorination, bromination and iodination of terminal alkynes



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# ABSTRACT

Direct halogenation, including chlorination, bromination and iodination of terminal alkynes, are of great importance in organic synthesis. Here an efficient and recyclable nano-Ag/g-C<sub>3</sub>N<sub>4</sub> catalyst system was developed and proved to be remarkably active with 39 examples varied from chlorination, bromination to iodination, of which 14 runs have yielded more than 95% of the product. Recycling of the catalyst was also achieved without obvious activity loss after several runs: 99% yield was observed even after 5 runs in the bromination of phenylacetylene. The catalysts system is of low cost and easy to be prepared, making this procedure versatile, convenient and economic.

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## 1. Introduction

1-haloalkynes are a series of important and powerful building blocks in organic chemistry. They are not only the precursors of a variety of advanced structures such as conjugated diynes, enynes, substituted alkenes, heterocycles and functional polymers, but also conceived as a dual functionalized molecules due to their unique structures involving both controllable electrophilic and nucleophilic properties [1–4], as shown in Fig. 1.

Considering about the importance of haloalkynes, different methods of the preparation of them are developed during decades [1]. Among these protocols, the most commonly and widely used methods are the direct halogenations of C–H bonds in terminal alkynes [5,6]. However, satisfactory results can be observed only for bromination and iodination in a long period [7–9]. The chlorination of terminal alkynes under mild conditions, however, remains a challenge. Typical procedures often require the involvement of highly unstable alkyl lithium reagents under -78 °C [10,11]. Other improvements of chlorination of terminal alkynes including using hypochlorites [12] or PTC (phase transfer catalyst) [13–15]. For example, Szafert et al. have reported a Silver nitrate catalyzed chlorination of terminal alkynes, using TBAF (tetrabuty-lammonium fluoride) as the PTC [16]. It is noteworthy that PTC in this process was crucial, and no reaction occurred in the absence of

\* Corresponding author. E-mail address: hchenhao@mail.hzau.edu.cn (H. Chen). the PTC. Organic base, such as DBU (1,8-Diazabicyclo[5.4.0]undec-7-ene) was also reported as the catalyst for the preparation of chloroalkynes using NCP (N-chlorophthalimide) as the chlorination reagent [9], although only limited examples were achieved. Recently our group have developed a practical method for the chlorination of terminal alkynes using  $Ag_2CO_3$  as the catalyst and  $K_2CO_3$  as the base [17]. Although the recycled silver salts have lost the catalytical activity, good to high isolated yields were achieved for a variety of terminal alkynes, encouraging us to further explore the halogenation of terminal alkynes. Despite of all the methods mentioned above, there is still a lack of a general and convenient method suitable for the bromination, iodination as well as chlorination, as Fig. 2 showed. Here we would like to report our latest discoveries on the halogenation (including chlorination, bromination and iodination) of terminal alkynes using a universal catalyst.

## 2. Results and discussions

## 2.1. Bromination of alkynes

During our exploration, the recycling of catalyst stands as the first priority to fulfill the purpose of sustainable chemistry. The immobilization of metal catalyst is one of the choices. Since  $g-C_3N_4$  (graphitic carbon nitride) has shown a series of advantages such as low cost, easy to be prepared and functionalized, insoluble in most solvents and potential photocatalytic properties, and represents a series of heterogeneous catalyst in many fields [18–22],





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Fig. 1. Important organic structures from haloalkynes.



Fig. 2. Direct halogenation of terminal alkynes.

we have also applied it as the co-catalyst in our study. Ag was chosen as the metal catalyst due to the high activities in alkyne synthesis [6,17,23], and we have thus prepared the Ag/g-C<sub>3</sub>N<sub>4</sub> to initialize our research. The g-C<sub>3</sub>N<sub>4</sub> catalyst can be easily prepared by one-step polymerization of urea at 550 °C for 2 h in a muffle furnace with a heating rate of 5 °C/min. Ag (10.8 wt%) was introduced through a chemical deposition method, using NaBH<sub>4</sub> as the reductant, and the residue was dried at 60 °C for 12 h, resulting a light yellow powder as the final form. TEM image (Fig. 3) shows that the Ag particles are immobilized at the surface of C<sub>3</sub>N<sub>4</sub> as small nanoparticles with diameter of about 10–40 nm.

To test the catalytic activity of the prepared catalyst, we initiate the investigation with the bromination of terminal alkynes with NBS (N-bromosuccinimide), which yields 1-bromoalkynes, a kind of important and widely used precursors in organic synthesis [24–28]. Phenylacetylene (**1a**) was used as the substrate to optimize the reaction conditions, and the results are shown in Scheme 1. The catalyst has shown excellent activities even under room temperature, with 4 mol% of the catalyst loading (catalyst loading is calculated according to Ag) to generate 99% of the product **2a** in less than 3 h.

Different substrates were then used under the optimized conditions, and we are pleased to observe that all the substrates we tested have achieved excellent results, and the yields are listed in Scheme 2. The substituents on the aryl moieties, either electron-



Fig. 3. TEM image of Ag@C<sub>3</sub>N<sub>4</sub>-10.8 wt%.

	NBS, Ag/C <sub>3</sub> N <sub>4</sub>	_	
<u> </u>	a acetone, r.t.		2a
entry	cat. loading (mol%)	time (h)	yield (%)
1	2	3	22
2	4	3	99
3	6	3	91
4	8	3	99
5	10	3	95
6	4	0.5	38
7	4	1	56
8	4	1.5	76
9	4	2	93
10	4	2.5	99
11	4	10	93

conditions: 0.5 mmol phenylacetylene, 0.5 mmol NBS, 2 mL acetone, GC yield.

Scheme 1. Bromination of phenylacetylene under different conditions.

withdrawing or electron-donating ones, do not have obvious influences on the yields. Heteroaryl substituted alkynes, such as **2m** and **2n**, also gave excellent isolated yields. Terminal diynes, which are less stable than ordinary terminal alkynes, also gave excellent yields (**2o** and **2p**).

#### 2.2. Iodination of alkynes

We have then further applied the catalyst in the iodination experiments, and found that the catalyst performed excellently again. Using NIS (N-iodosuccinimide) as the iodination reagent, high yields of 1-iodoalkynes were observed in all runs, ranging from 88% to 99% with 12 different examples, and details are listed in Scheme 3. Aryl substituents on the alkynes with either electron withdrawing or donating groups all gave satisfactory yields (**3b**-**3e**). The positions of the substitution group on the aryl ring of



All yields are isolated yields. a: 8 mol% catalyst loading.

Scheme 2. Bromination of different substrates.

the substrate have no obvious effect to this reaction (3**f**-3**h**). Heteroaryl groups were tolerated in this reaction too (3**i** and 3**j**).

#### 2.3. Chlorination of alkynes

Compared with bromination and iodination, the chlorination of terminal alkynes is of more challenging, and has attracted much more attentions in recent years [9,29,30]. We have recently reported an efficient method of the direct chlorination of terminal alkynes using  $Ag_2CO_3$  as the catalyst and NCS (N-chlorosuccinimide) as the chlorine source [17]. Although high yields and broad substrate scope were achieved, considerable loss in catalytic activity was observed for the recycled catalyst. Here we have also explored the activity of this new catalyst for the chlorination of terminal alkynes, and results are listed below.

Considering that the reactivity of NCS is relatively lower compared with NIS or NBS, we have set the reaction temperature at 50 °C comparing to the previous room temperature. However, only moderate yield was observed (entry 5, 67%). Further optimizations were then conducted, and the results were shown in Scheme 4. It is found that MeCN performs the best among various solvents, and base is crucial to this process, which  $K_2CO_3$  was proved to be a suitable one. Best result was obtained when 2.0 eq of NCS was employed under 50 °C, with almost quantitative transformation of terminal alkynes (entry 16, 99%). Lower temperature led to the decline of the reaction rate (entries 16–19). With these results in hand, we have applied the optimized conditions to the chlorination of a variety of terminal alkynes, and satisfying yields were observed again, as shown in Scheme 5. Both EWG and EDG substituted aryl group are tolerable in these transformations, and the heterocyclic substituted acetylenes have also performed well (entries 7, 8), indicating the universality of the catalyst. Alkynes with formyl group could also be good substrates (entry 9).

# 2.4. Recycling and discussion of the catalyst

The recycling tests of the catalyst activity for the bromination of terminal alkynes have also been explored. At first, we have simply isolated the catalyst from the reaction system by centrifugation and applied it in the next bromination process, but unfortunately no reactivity was observed at all. Following XRD analysis of the catalyst showed that after the first bromination, the valence of Ag have changed from 0 to 1, indicating that the immobilized Ag (0) have been transformed into AgBr during the bromination, as shown in Fig. 4. Similar results were also observed in the process of chlorination and iodination, showing a valence change in the reaction. Thus we suppose that the reduction of the recycled Ag (I) may reactivate the catalyst, and NaBH<sub>4</sub> aqueous solution was used in this process as the reductant.

After these reduction steps, the recycled catalysts did have shown excellent activities in the halogenation process. Fig. 5 listed

$R = \frac{NIS, 4 \text{ mol}\% \text{ Ag/C}_3 \text{N}_4}{2}$						
	1 a	cetone, 3 h	i, r.t. 3			
product	yield (	%) pro	duct	yield (%)		
3a 🖉 💻	—I 90	3g	Br	99		
3b EtO	— <u>—</u>	3h		94		
3c	<b>≕</b> —I 94	3i		88 <sup>a</sup>		
3d Br	<u> </u>	3j		95 <sup>a</sup>		
3e CI	<u> </u>	3k		98		
3f	98 —I	31		—I 93 <sup>a</sup>		

All yields are isolated yields; a: 8 mol% catalyst loading.

Scheme 3. Iodination of terminal alkynes.

	Dh	NCS, Ag/C <sub>3</sub> N <sub>4</sub> 0.5 eq. base, 3 h		PhCl 4	
	1				
entry	solvent	base	NCS (eq.)	T/ºC	yield (%)
1	MeOH	K <sub>2</sub> CO <sub>3</sub>	1.0	50	26
2	n-PrOH	$K_2CO_3$	1.0	50	44
3	i-PrOH	K <sub>2</sub> CO <sub>3</sub>	1.0	50	46
4	i-BuOH	K <sub>2</sub> CO <sub>3</sub>	1.0	50	58
5	Acetone	$K_2CO_3$	1.0	50	67
6	MeCN	K <sub>2</sub> CO <sub>3</sub>	1.0	50	73
7	$CH_2CI_2$	K <sub>2</sub> CO <sub>3</sub>	1.0	50	37
8	DMF	K <sub>2</sub> CO <sub>3</sub>	1.0	50	30
9	THF	K <sub>2</sub> CO <sub>3</sub>	1.0	50	0
10	MeCN	NaOH	1.0	50	0
11	MeCN	NEt <sub>3</sub>	1.0	50	11
12	MeCN	Na <sub>2</sub> S	1.0	50	5
13	MeCN	none	1.0	50	0
14	MeCN	$Cs_2CO_3$	1.0	50	47
15	MeCN	K <sub>2</sub> CO <sub>3</sub>	1.5	50	87
16	MeCN	K <sub>2</sub> CO <sub>3</sub>	2.0	50	99
17	MeCN	K <sub>2</sub> CO <sub>3</sub>	2.0	40	87
18	MeCN	K <sub>2</sub> CO <sub>3</sub>	2.0	30	81
19	MeCN	K <sub>2</sub> CO <sub>3</sub>	2.0	20	56

Scheme 4. Optimization of chlorination.



All yields are isolated yields; a: 8 mol% catalyst loading.

Scheme 5. Chlorination of terminal alkynes.



Fig. 4. XRD analysis of the catalyst before and after the bromination XRD patterns of  $Ag@C_3N_4$  catalysts. (a) After the reaction. (b) Before the reaction.

the activities of the catalyst after several runs in the bromination of terminal alkynes, from which we can find out that even after 5 runs the recycled catalyst had still performed excellently, without any obvious loss in catalytical activity. According to these procedures, we proposed that the catalytic process was initiated from nano silver particles, which was then oxidized to active Ag(I), the active catalytic center for the formation of halo-alkynes. At the end of the process, the active Ag(I) was transformed to unactive immobi-



Fig. 5. Recycle test for the catalyst in the bromination of phenylacetylene.

lized AgBr, and the reduction of AgBr to nano silver particles would reactive the catalyst.

The leaching of the Ag was also discussed. After the bromination of phenylacetylene using our catalyst, the mixture was centrifuged, and hydrochloric acid (0.1 mol/L) was added dropwise to the supernatant. However, the supernatant remained clear. ICP-MS analysis showed that the Ag lost was 0.0128% after one catalytic circle. There are also reported examples that confirmed the absence of metal leaching including Ag deposit on g-C<sub>3</sub>N<sub>4</sub> [31,32], indicating the excellent stability and recyclability of the catalyst.

# 3. Conclusion

In summary, we have developed a general, versatile and highly efficient  $Ag/C_3N_4$  catalyst for the chlorination, bromination and iodination of the terminal alkynes. The yields of the halogenated products are above 90% in most cases, proved by nearly 40 examples, including the relatively challenging chlorination process. Moreover, the catalyst could be reused after reduction for more than 5 times without any obvious loss in activity.

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## Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jcat.2017.07.019.

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