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Propargylamines formed from three-component coupling reactions catalyzed by silver oxide nanoparticles†

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Xin Zhou, Yi Lu, Ling-Ling Zhai, Yue Zhao, Qing Liu and Wei-Yin Sun*

An economic, efficient and green silver oxide nanoparticle catalyzed three-component coupling reaction of aldehydes, amines and alkynes was developed. This method provided various propargylamines in moderate to high yield at room temperature in air. The silver oxide nanoparticles could be separated simply and reused without significant decrease of activity.

Environmentally benign, efficient, economical and green synthesis in organic chemistry has become more and more important in chemical research.[1] Over the past decade, one-pot three-component coupling reactions of aldehydes, amines and alkynes (A^3-coupling) for the synthesis of propargylamines have obtained tremendous development.[2] Since Li's group reported gold catalyzed three-component coupling reaction for the first time in 2003,[3] numerous efficient three-component coupling reactions in different solvents catalyzed by various metal catalysts such as Ag(I) salt,[4] Cu(I) salt,[5] Au(III) salen complexes,[6] In(III) salt,[7] Fe(III) salt[8] were developed, respectively.

In recent years, with the progress of nanoscience, the catalytic properties of nanoparticles have attracted particular attention.[9] For instance, Mozumdar *et al.* have reported gold[10] and copper[11] nanoparticle catalyzed three-component coupling of aldehydes, amines and alkynes for the synthesis of propargylamines. Wang *et al.* have represented an efficient three-component coupling reaction catalyzed by silver oxide nanoparticles immobilized on different templates.[12] Very recently, Reddy[13] and Li[1b] developed reusable Fe_3O_4 nanoparticles to catalyze three-component coupling reactions effectively several times without significant loss of catalytic activity.

However, high reaction temperature and long reaction time are the major obstructions in the three-component coupling reactions catalyzed by these reported metal nanoparticles. Herein, we report an efficient recyclable silver oxide nanoparticle catalyzed A^3-coupling reaction at room temperature in air without additional co-catalyst or ligand. Our group has reported silver(I) complex catalyzed three-component coupling reactions recently.[14] Because of the complicated and time-consuming procedure to prepare the complex, we attempted to use the silver oxide nanoparticle catalyst by adopting a much simpler and more direct approach. The silver oxide nanoparticles were readily prepared according to the reported procedure,[15] and the SEM image of the nanoparticles is shown in Fig. 1. The size of the silver oxide nanoparticles was among 1.0 to 2.0 μm with the size distribution as previously reported.[15]

Initially, phenylacetylene, cyclohexanecarboxaldehyde and pyrrolidine were chosen for the reaction based on the previous reports. In the presence of 5 mol% of silver oxide nanoparticles, the A^3-coupling reaction was carried out in various solvents at room temperature in air (Table 1). Among the solvents tested, chloroform was the most effective reaction medium for the three-component coupling reaction with a yield of 79% (Table 1, entry 12). When we employed dichloromethane, acetonitrile, DMF, DMSO or 1,2-dichloroethane (DCE) as the solvents, product **1a** was

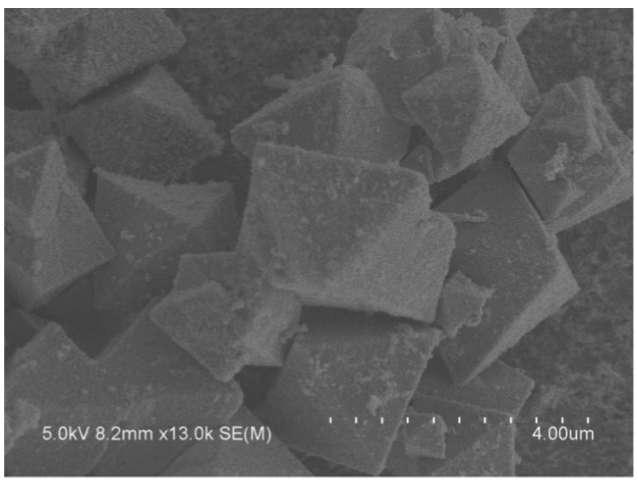

Fig. 1 The SEM image of the silver oxide nanoparticles.

Coordination Chemistry Institute, State Key Laboratory of Coordination Chemistry, School of Chemistry and Chemical Engineering, Nanjing National Laboratory of Microstructures, Nanjing University, Nanjing 210093, China.
E-mail: sunwy@nju.edu.cn; Fax: +86 25 8331 450

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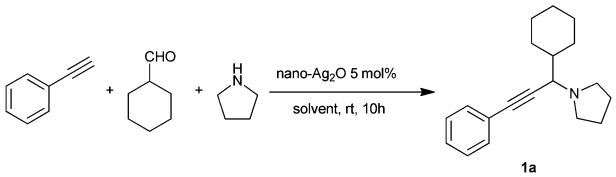
Table 1 Optimization of the reaction conditions[a]



Entry	Solvent	Yield (%)[b]
1	CH_2Cl_2	65
2	CH_3CN	60
3	DMF	65
4	DMSO	70
5	DCE	67
6	THF	50
7	CH_3OH	27
8	CH_2CH_2OH	32
9	*n*-Hexane	31
10	Toluene	44
11	H_2O	44
12	$CHCl_3$	79
13[c]	$CHCl_3$	43
14[d]	$CHCl_3$	80

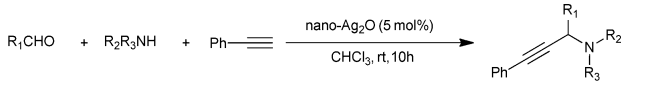
[a] All reactions were carried out with cyclohexanecarboxaldehyde (1.0 mmol), pyrrolidine (1.1 mmol), phenylacetylene (1.2 mmol) and silver oxide nanoparticles (0.05 mmol) in different solvents (2 mL) at room temperature for 10 h. [b] Isolated yield based on cyclohexanecarboxaldehyde. [c] 0.02 mmol silver oxide nanoparticles were used as catalyst. [d] 0.10 mmol silver oxide nanoparticles were used as catalyst.

generated in slightly low yields (Table 1, entries 1–5). Meanwhile, THF, methanol, ethanol, *n*-hexane, toluene and water only afforded **1a** in moderate or low yields (Table 1, entries 6–11). Compared to using 5 mol% catalyst, a much lower yield was observed by using 2 mol% (Table 1, entry 13), however, no significant increase was found when increasing the catalyst amount to 10 mol% (Table 1, entry 14). In addition, we found that 10 h was most suitable for the reaction (Table S1†).

Finally, the optimized reaction condition was obtained: 1.0 equivalent of aldehyde, 1.1 equivalents of amine, 1.2 equivalents of alkyne and 5 mol% of silver oxide nanoparticles in chloroform at room temperature in the air for 10 h. Only 8% product was obtained when silver oxide powder (5 mol%) was applied as catalyst under the same reaction conditions. The low yield indicated that Ag_2O nanoparticles, owing to the larger surface area than their powder form, presented far superior catalytic activities in the A^3-coupling reaction.

With the optimized reaction conditions in hand, various aldehydes and secondary amines were chosen as substrates to expand the scope of this coupling reaction to prepare a variety of propargylamines (Table 2). In general, aliphatic aldehydes and secondary amines underwent the A^3-coupling reaction smoothly to provide good yields (Table 2, entries 1–7). Then, we chose diphenylamine, as well as primary amines, such as *n*-pentylamine and 4-toluenesulfonamide, as substrates, and no desirable products were obtained even when we prolonged the reaction time to 24 h (Table 2, entries 8–10). It is possible that primary amines are not suitable for this reaction. It was found that

Table 2 Silver oxide nanoparticles catalyzed three-component coupling of aldehyde, amine and phenylacetylene[a]



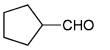
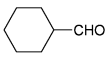
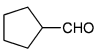
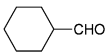
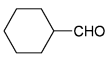
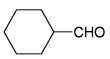
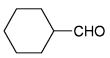
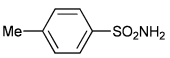
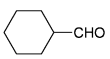
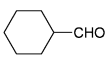
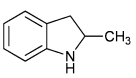
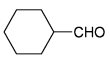
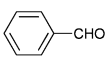
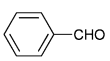
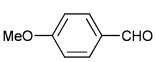
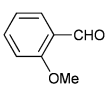
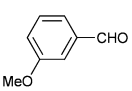
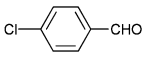
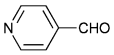
Entry	Aldehyde	Amine	Yield (%)[b]
1			94
2			67
3			80
4	$CH_3(CH_2)_5CHO$		99
5	$CH_3(CH_2)_5CHO$		92
6	paraformaldehyde		48
7			77
8		Ph_2NH	NR[c]
9		$CH_3(CH_2)_4NH_2$	NR[c]
10			NR[c]
11			48
12			trace
13			9.4
14			79
15			80
16			75
17			55
18			42

Table 2 (*Continued*)

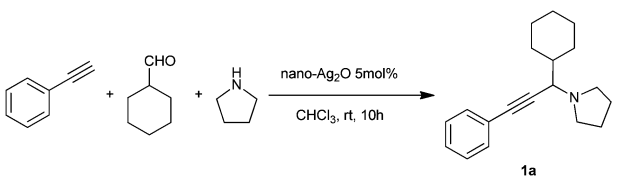
Entry	Aldehyde	Amine	Yield (%)[b]
19			64
20			25

[a] All reactions were carried out with aldehyde (1.0 mmol), amine (1.1 mmol), phenylacetylene (1.2 mmol) and silver oxide nanoparticles (0.05 mmol) in chloroform (2 mL) at room temperature for 10 h. [b] Isolated yield based on aldehyde. [c] The reaction was carried out for 24 h.

aromatic amines, such as indoline, 2-methylindoline, and 1,2,3,4-tetrahydroquinoline, gave low yields (Table 2, entries 11–13). Next, we examined the effect of aromatic aldehydes (Table 2, entries 14–19). Both electron-donating and electron-withdrawing substituted aromatic aldehydes gave moderate to good yields. The *para*- and *ortho*-methoxyl-substituted aromatic aldehydes displayed higher reactivity than the *meta*-substituted one due to the electronic effect. Furthermore, heterocyclic aldehydes such as 4-pyridinecarboxyaldehyde showed low yield (Table 2, entry 20). In addition, 1-pentyne was tested, however no product was obtained.

To check the activity of the residual catalyst, the nanoparticles were isolated and washed with ethanol, air-dried and reused directly for the next cycle of the reaction without further purification. As can be seen in Table 3, the silver oxide nanoparticles could be cycled at least 6 times without significant decrease of yields.

Table 3 Silver oxide nanoparticles catalyzed three-component coupling of phenylacetylene, cyclohexanecarboxaldehyde and pyrrolidine[a]



1a

Cycle	Yield (%)[b]	Cycle	Yield (%)[b]
1	79	4	78
2	79	5	77
3	79	6	77

[a] All reactions were carried out with aldehyde (1.0 mmol), amine (1.1 mmol), phenylacetylene (1.2 mmol) and silver oxide nanoparticles (0.05 mmol, for cycle 1) or recovered silver oxide nanoparticles (0.05 mmol, for other cycles) in chloroform (2 mL) at room temperature for 10 h. [b] NMR yield using dibromomethane as an internal standard.

In summary, we have developed an efficient, economic and environmentally benign silver oxide nanoparticle catalyzed three-component coupling of aldehyde, amine and alkyne (A^3-coupling). The method allows us to prepare a variety of progargylamines in moderate to high yield with water as the only theoretical by-product under mild conditions in air, and no additional co-catalyst or ligand is required. Furthermore, the catalyst can be recovered readily and reused directly without significant loss of activity. The simple preparation and reusability of the catalyst which shows significant advantages make this reaction more economical and environmentally acceptable.

Acknowledgements

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