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Short communication

Cu_2O/nano-$CuFe_2O_4$: A novel and recyclable magnetic catalyst for three-component coupling of carbonyl compounds–alkynes–amines under solvent-free condition

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ABSTRACT

Cu_2O/nano-$CuFe_2O_4$ magnetic composite with different loadings of Cu_2O has been synthesized by feasible and low-cost method. The as-prepared composite was fully characterized by FT-IR, XRD, FEG-SEM, EDS and VSM analyzer. The catalytic activity of magnetic composite for synthesis of propargylamines was evaluated. The catalyst has many obvious advantages and easily separated via an external magnet. It can be reused for five successive runs.

1. Introduction

The catalysts with magnetic nanoparticle-based materials have attracted significant attention in organic transformations, because they posses specific futures including reduce temperature, increase reaction yield, great selectivity, high stability, efficient recovery and good reusability [1]. Among them, the iron oxides are usually applied as simplest magnetically recoverable catalysts, as they are nontoxic, cheap in preparation, amenable to functionalization and easy to handle [2]. They have been extensively used in some organic reactions such as, C–C and C–X couplings [3,4], reduction [5], oxidation [6] and multi-component reactions [7]. While iron oxide NPs could catalyze several reactions, the catalytic scope of magnetic NPs could be expanded by incorporation of a second metal (for example Cu) in the spinal structure of Fe_3O_4. The second metal opens up new catalytic avenues, while the residual iron component continues to provide an effective way in order to do magnetic recovery [8].

Multi-component coupling reactions (MCRs) are a very powerful tool to synthesize various organic compounds from simple starting material via a one-pot methodology. An attractive example of such a process that has been widely studied in recent years is (A^3-coupling) via C–H activation of terminal alkynes [9,10]. The propargylamines that result from A^3 coupling reactions are high valuable building blocks in organic synthesis. They are considered as an important synthetic intermediates for the preparation of various nitrogen-containing biologically active compounds and pharmaceutical important compounds [11,12].

The most conventional methods for the synthesis of propargylamines involve three-component coupling of aldehydes, amines and terminal alkynes in the presence of appropriate catalyst. In recent years, some heterogeneous catalysts are developed for A^3-coupling reactions [13–16]. Although all these methods are effective, these have some drawbacks such as, use of expensive or toxic solvents, tedious work-up procedures, low yields, long reaction times and complex catalyst preparation process. Hence, development of a facile, environmentally friendly and low cost protocol for one-pot synthesis of propargylamine derivatives is an attractive goal for researchers.

We reported herein, synthesis of inexpensive, reusable and magnetically separable Cu_2O/nano-$CuFe_2O_4$ magnetic composite and application of it in synthesis of various propargylamine derivatives under solvent-free reaction conditions (Scheme 1).

2. Experimental

2.1. Preparation of composite

2.1.1. Preparation of nano-$CuFe_2O_4$

The $CuFe_2O_4$ nano-particles were prepared according to literature report [17].

2.1.2. Preparation of $CuFe_2O_4$/Cu_2O composite

Four types of composite with different molar ratios of $CuFe_2O_4$:Cu_2O were synthesized. Nano-$CuFe_2O_4$ (0.036–0.324 g) was dispersed in

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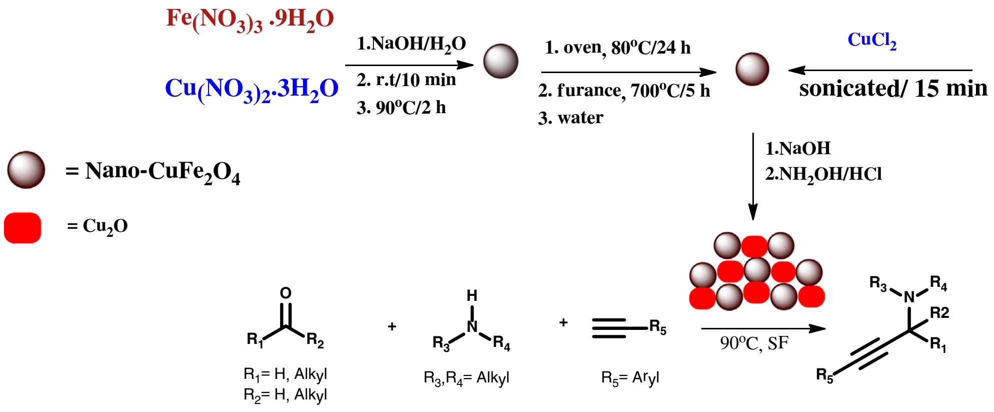


Scheme 1. Synthesis of propargylamines using Cu_2O/nano-$CuFe_2O_4$ magnetic composite.

80 mL of deionized water. 5 mL of (0.1 mol/L) $CuCl_2$ solution was added into the aqueous $CuFe_2O_4$ and sonicated for 15 min. Then, 1.8 mL of (1.0 mol/L) NaOH solution was added drop-by-drop under sonication. The resulting solution turned light blue immediately, indicating the formation of $Cu(OH)_2$ precipitate. Eventually, 12 mL of (0.1 mol/L) $NH_2OH \cdot HCl$ was rapidly injected over 5 s into the solution. The solutions were kept in the water bath for 1 h and centrifuged for 3 min. After the top solution was decanted, the precipitate was washed with 6 mL of a 1:1 volume ratio of water and ethanol three times. The Cu_2O/nano-$CuFe_2O_4$ was collected as a brown solid and can be stored in a tight vessel for several months without any change in color or reactivity.

2.2. General procedure for synthesis of 1-(1,3-diphenylprop-2-ynyl)piperidine (**4a**)

A mixture of benzaldehyde (0.106 g, 1.0 mmol), piperidine (0.102 g, 1.2 mmol), phenylacetylene (0.153, 1.5 mmol) and Cu_2O/nano-$CuFe_2O_4$ magnetic composite (0.010 g) (the Cu_2O content in the catalyst was 0.002 g or 0.015 mmol, so for 1 mmol of reactant, 0.015 mmol of Cu_2O is needed, which is equal to 0.01 g magnetic composite) were mixed and heated at 90 °C for 1 h under solvent free condition. After completion of the reaction, the reaction mixture was cooled to room temperature and diluted with hot ethanol (10 mL). Then, the catalyst was separated by an external magnet from the cooled mixture, washed with acetone, dried in oven and re-used for a consecutive run under the same reaction conditions. The filtrate was concentrated and the resulting residue was purified by short column chromatography on silica gel to afford the desired product in excellent yield (96%).

3. Results and discussion

3.1. Characterization of Cu_2O/nano-$CuFe_2O_4$ composite

The FT-IR spectra of the $CuFe_2O_4$ in the region of 400–4000 cm^{-1} clearly indicated the bands centered at 3400 and 563 cm^{-1}, which justify the OH and metal-O stretching mode, respectively. Compared to $CuFe_2O_4$, the composite had same absorption peaks, with more intensity at metal-O region (see ESI).

The morphology, chemical purity and their stoichiometry of $CuFe_2O_4$ and Cu_2O/nano-$CuFe_2O_4$ composite (optimized amount) were visualized by SEM and EDX analyses (Figs. 1 and 2). It can be observed that the as-prepared nano-$CuFe_2O_4$ particles are uniform and nearly spherical in shape and possess a smooth and clean surface. Fig. 1B shows the SEM image of Cu_2O/nano-$CuFe_2O_4$ composite. Numerous Cu_2O particles can be clearly seen in composite. Compared to the $CuFe_2O_4$, the composite

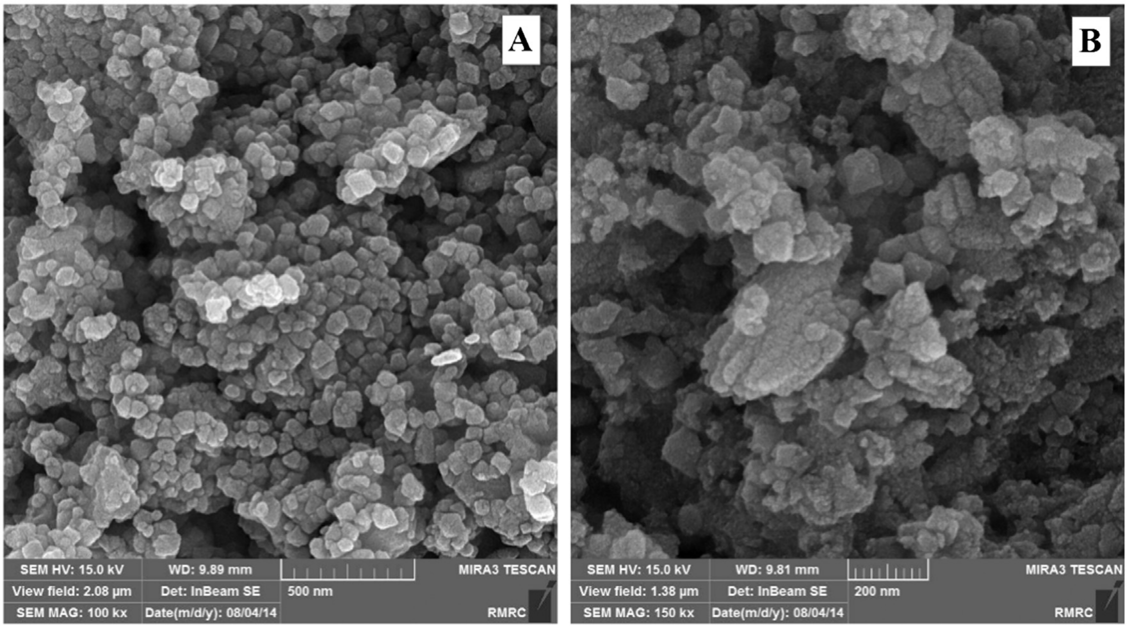
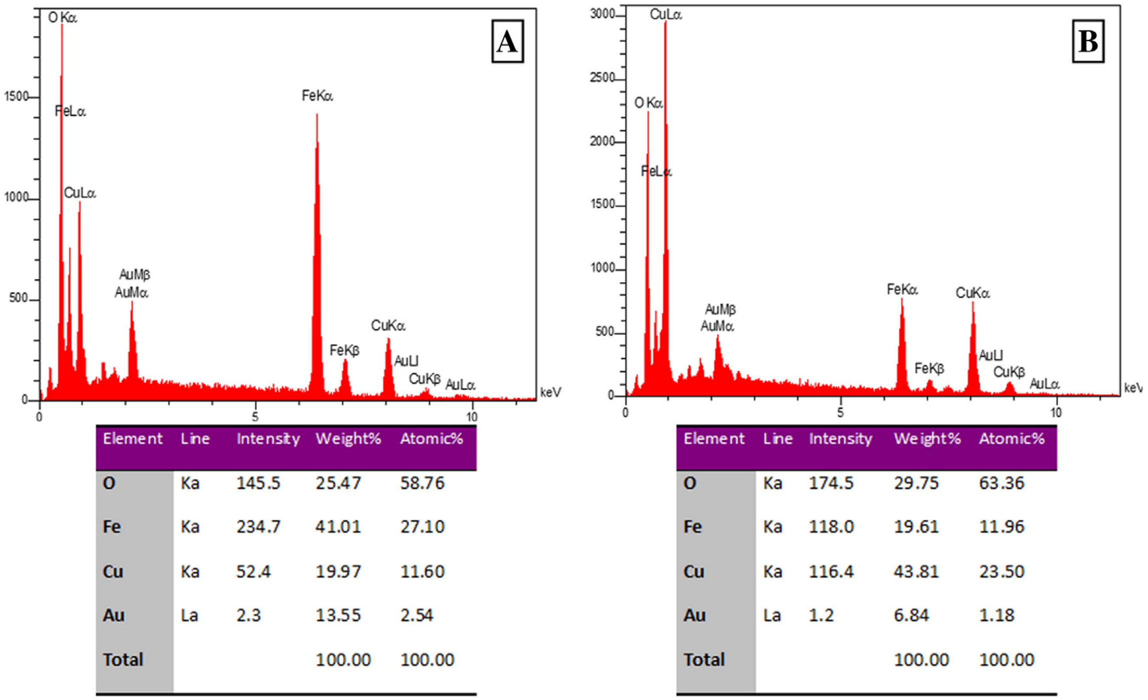


Fig. 1. The SEM image of the (A) nano-$CuFe_2O_4$, (B) Cu_2O/nano-$CuFe_2O_4$ (2:8 mol ratio) magnetic composite.



Element	Line	Intensity	Weight%	Atomic%
O	Ka	145.5	25.47	58.76
Fe	Ka	234.7	41.01	27.10
Cu	Ka	52.4	19.97	11.60
Au	La	2.3	13.55	2.54
Total			100.00	100.00

Element	Line	Intensity	Weight%	Atomic%
O	Ka	174.5	29.75	63.36
Fe	Ka	118.0	19.61	11.96
Cu	Ka	116.4	43.81	23.50
Au	La	1.2	6.84	1.18
Total			100.00	100.00

Fig. 2. The EDX curves of the (A) nano-$CuFe_2O_4$, (B) Cu_2O/nano-$CuFe_2O_4$ (2:8) magnetic composite.

has a rougher surface because the Cu_2O particles are randomly diffused in $CuFe_2O_4$ nano-particles. The elemental composition of the $CuFe_2O_4$ from EDX analysis was also exhibited in Fig. 2A and shows the presence of Cu, Fe and O elements. The EDX spectrum of Cu_2O/nano-$CuFe_2O_4$ was shown in Fig. 2B and it implies that the composite mainly consists of $CuFe_2O_4$:Cu_2O.

Room-temperature magnetization study shows that the composites have super-paramagnetic properties (Fig. 3). There was no hysteresis in the magnetization for the two types of materials. The saturation magnetization of $CuFe_2O_4$ and Cu_2O/nano-$CuFe_2O_4$ was 33.86 and 18.39 emu/g, respectively. Obviously, after the preparation of Cu_2O/nano-$CuFe_2O_4$, its magnetic response was affected due to mixing with non-magnetic material. Nonetheless, this magnetic property is enough and the Cu_2O/nano-$CuFe_2O_4$ could be completely and quickly separated from the reaction mixture.

Fig. 4 shows the X-ray diffraction patterns of $CuFe_2O_4$ and as-made samples with different Cu_2O molar ratios (from 9:1 to 6:4 mole ratio of $CuFe_2O_4$ to Cu_2O). The typical diffraction peaks can be well assigned to the diffraction of $CuFe_2O_4$ nanoparticles with spinal phase from the (101), (200), (211), (221), (303) and (224) planes, respectively. Compared to $CuFe_2O_4$, new diffraction peaks located at 29.5 (110), 36.7 (111), 42.5 (200), 52.7 (211), 61.6 (220), and 73.7 (311) can be indexed to the diffraction of Cu_2O rhombic dodecahedral crystals in the cubic phase, which suggest the presence of Cu_2O in as-made composites. No additional diffraction peaks were observed, which could be attributed to complete reduction of copper(II) to copper(I). Because of the different

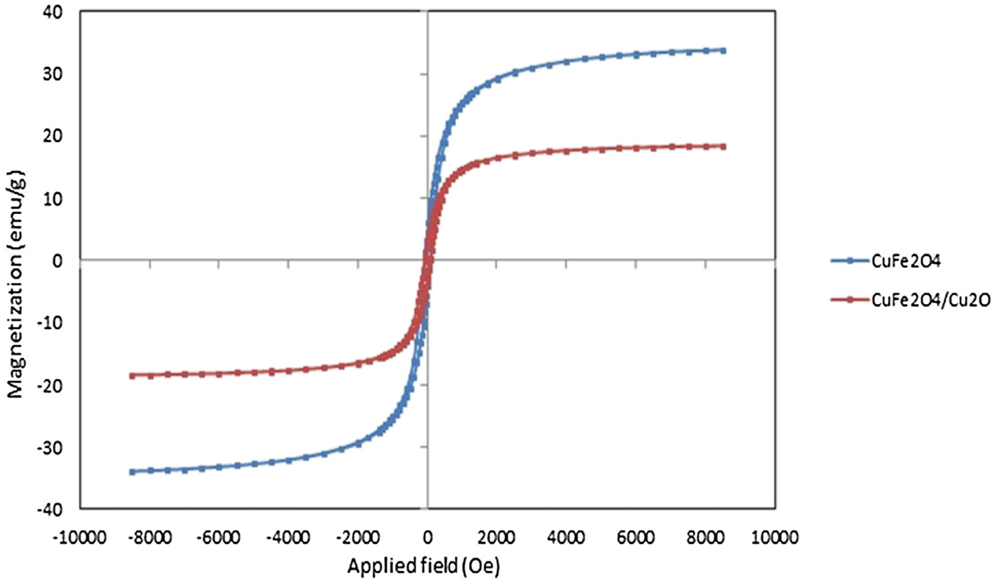


Fig. 3. The magnetization curves of $CuFe_2O_4$ and Cu_2O/nano-$CuFe_2O_4$ (2:8) magnetic composite.

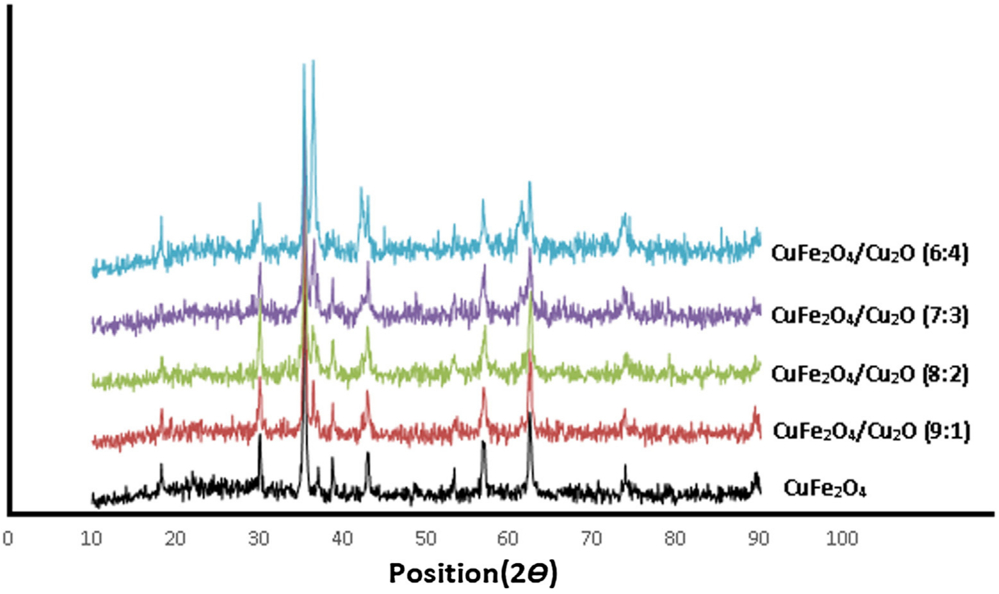


Fig. 4. The X-ray diffraction patterns of $CuFe_2O_4$and Cu_2O/nano-$CuFe_2O_4$ with different weight ratios.

content of Cu_2O in samples the intensity of all the peaks in the XRD patterns becomes gradually stronger with the increase of the Cu_2O/$CuFe_2O_4$ weight ratio, but the intensity of peak (111) increased obviously.

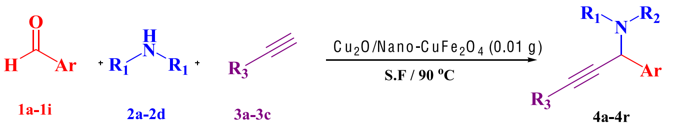
3.2. Catalytic application of Cu_2O/nano-$CuFe_2O_4$ magnetic composite

The catalytic activity of the magnetic composite with different weight ratios was tested by the model reaction of benzaldehyde, phenyl acetylene and piperidine using 0.01 g magnetic composite in solvent free condition at 90 °C. The catalytic performance of Cu_2O/nano-$CuFe_2O_4$ magnetic composite with a weight ratio of 8:2 was the best. It was found that no change in yield was obtained with increase of Cu_2O loading in magnetic composite. Therefore, the optimal weight ratio of $CuFe_2O_4$:Cu_2O 8:2 was selected for optimization of the reaction (see ESI).

The reaction of benzaldehyde, phenylacetylene and piperidine was selected as a template reaction in various solvents, temperatures and loadings of magnetic composite (see ESI). Interestingly, the reaction was performed under the solvent-free condition at 90 °C in high yield of product. We carried out the model reaction in the presence of $CuFe_2O_4$ as a catalyst under solvent-free condition at 90 °C and the poor yield of product was formed even after 2 h. Moreover, the reaction did not occur in the absence of the catalyst after prolonged reaction time. A higher reaction temperature or the catalyst amount does not make an obvious difference in the yield of product. Accordingly, the best condition was found when the reaction was performed under solvent-free condition in the presence of 0.01 g Cu_2O/nano-$CuFe_2O_4$ at 90 °C, confirming that the Cu_2O was essential in the composite for this transformation.

So, with the optimized reaction condition in hand, the generality of reaction was studied with arylacetylenes including electron-donating

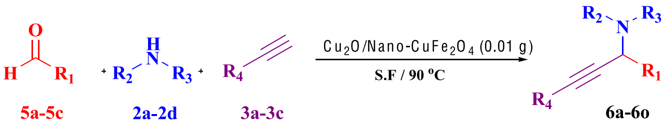
Table 1
Three-component coupling of aromatic aldehydes, secondary-amines and terminal alkynes.[a]



Product	Ar	R_1	R_2	R_3	Time (min)	Yield[b] (%)
4a	**1a:** C_6H_5	**2a:** $-(CH_2)_5-$		**3a:** C_6H_5	60	96
4b	**1b:** p-Cl-C_6H_4	**2a**		**3a**	60	93
4c	**1c:** o-Cl-C_6H_4	**2a**		**3a**	60	86
4d	**1d:** p-Br-C_6H_4	**2a**		**3a**	55	94
4e	**1e:** p-Me-C_6H_4	**2a**		**3a**	65	92
4f	**1f:** p-MeO-C_6H_4	**2a**		**3a**	70	89
4g	**1g:** o-Thiophene	**2a**		**3a**	60	95
4h	**1h:** p-$CHOC_6H_4$	**2a**		**3a**	65	92
4i	**1i:** 2-Naphthyl	**2a**		**3a**	50	95
4j	**1a**	**2a**		**3b:** p-$CH_3C_6H_4$	80	84
4k	**1a**	**2a**		**3c:** p-F-C_6H_4	95	82
4l	**1a**	**2b:** $-(CH_2)_2-O-(CH_2)_2-$		**3a**	60	95
4m	**1b**	**2b**		**3a**	75	90
4n	**1e**	**2b**		**3a**	80	88
4o	**1d**	**2b**		**3a**	65	86
4p	**1a**	**2b**		**3b**	75	85
4q	**1a**	**2c:** $-(CH_2)_4-$		**3a**	65	80
4r	**1a**	**2d:** C_2H_5	C_2H_5	**3a**	60	60

[a] Reaction condition: aldehydes (1 mmol), amines (1.2 mmol), alkynes (1.5 mmol), and Cu_2O/nano-$CuFe_2O_4$ (0.010 g) under solvent-free conditions at 90 °C.
[b] Isolated yield.

Table 2
Three-component coupling of aliphatic aldehydes, secondary-amines and terminal alkynes.[a]



Product	R_1	R_2, R_3	R_4	Time (min)	Yield[b] (%)
6a	**5a:** H	**2a**: $-(CH_2)_5-$	**3a:** C_6H_5	40	94
6b	**5a**	**2a**	**3b:** p-$CH_3C_6H_4$	40	85
6c	**5a**	**2b:** $-(CH_2)_2-O-(CH_2)_2-$	**3a**	40	93
6d	**5a**	**2c:** $-(CH_2)_4-$	**3a**	40	85
6e	**5a**	**2d:** C_2H_5 C_2H_5	**3a**	45	75
6f	**5b:** C_6H_{11}	**2a**	**3a**	45	90
6g	**5b**	**2b**	**3b**	45	80
6h	**5b**	**2b**	**3a**	45	89
6i	**5b**	**2c**	**3a**	45	82
6j	**5b**	**2d**	**3a**	45	65
6k	**5b**	**2a**	**3c:** p-F-C_6H_4	45	85
6l	**5c:** $-(CH_2)_2-Me$	**2a**	**3a**	45	92
6m	**5c**	**2b**	**3a**	45	90
6n	**5c**	**2c**	**3a**	45	81
6o	**5c**	**2d**	**3a**	45	70

[a] Reaction condition: aliphatic aldehydes (1 mmol), amines (1.1 mmol), alkynes (1.1 mmol), and Cu$_2$O/nano-CuFe$_2$O$_4$ (0.010 g) under solvent-free conditions at 90 °C.
[b] Isolated yield.

Table 4
Comparison of catalytic activity of Cu$_2$O/nano-CuFe$_2$O$_4$ with reported magnetically separable catalysts for synthesis of propargyl amines **4a** and **6a**.

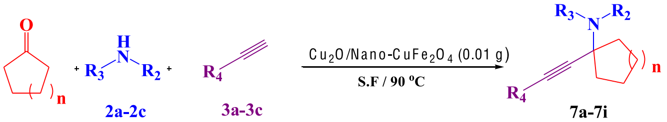
Product	Catalyst	Time	Condition	Yield (%)	Ref.
4a	Graphene-Fe_3O_4	24 h	CH_3CN/80 °C	Trace	[21]
4a	$CuFe_2O_4$	4 h	Toluene/80 °C	86	[22]
4a	Fe_3O_4	24 h	THF/80 °C	45	[23]
4a	Fe_3O_4	16 h	Toluene/110 °C	75	[24]
4a	$Cu(OH)_X.Fe_3O_4$	3 h	S.F/120 °C	99	[25]
4a	$Cu_2O/CuFe_2O_4$	60 min	S.F/90 °C	96	This work
6a	Graphene-Fe_3O_4	24 h	CH_3CN/80 °C	92	[21]
6a	Fe_3O_4	24 h	THF/80 °C	80	[23]
6a	$Cu_2O/CuFe_2O_4$	40 min	S.F/90 °C	94	This work

and electron-withdrawing groups, secondary aliphatic amines and aromatic aldehydes (Table 1). We further investigated the reaction of some aliphatic aldehydes in the reaction and results were listed in Table 2.

In general, both aromatic aldehydes and arylacetylenes bearing electron-donating substituents as well as electron-withdrawing groups and aliphatic aldehydes provided the desired products in good to moderate yields within short reaction time. The cyclic amines such as morpholine and pyrrolidine gave similar results to those obtained with piperidine, whereas diethylamine rendered the corresponding product in modest yield. Unfortunately, the amines with aromatic substituted were examined and gave poor results.

The excellent catalytic activity of Cu$_2$O/nano-CuFe$_2$O$_4$ magnetic composite toward the synthesis of propargylamines (A^3 coupling) prompted us to explore its further application for the three-component coupling of ketones, secondary amines and arylacetylenes (KA^2 coupling) (Table 3). To date, only few methods have been developed in this field and therefore, this restriction necessitates the development of new catalyst for KA^2 coupling reaction [18–20].

Table 3
Three-component coupling of cyclic aliphatic ketones, secondary-amines and terminal alkynes.[a]



Product	Cyclic ketone	R_2, R_3	R_4	Time (min)	Yield[b] (%)
7a	c-Pentanone	**2a:** $-(CH_2)_5-$	**3a:** C_6H_5	140	83
7b	c-Pentanone	**2b:** $-(CH_2)_2-O-(CH_2)_2-$	**3a**	140	80
7c	c-Pentanone	**2c:** $-(CH_2)_4-$	**3a**	140	83
7d	c-Hexanone	**2a**	**3a**	150	87
7e	c-Hexanone	**2a**	**3b:** p-$CH_3C_6H_4$	180	80
7f	c-Hexanone	**2b**	**3a**	150	84
7g	c-Hexanone	**2b**	**3b**	180	79
7h	c-Hexanone	**2c**	**3a**	150	88
7i	c-Hexanone	**2b**	**3c:** p-F-C_6H_4	160	81

[a] Reaction condition: ketones (1.5 mmol), amines (1 mmol), alkynes (1.5 mmol), and Cu$_2$O/nano-CuFe$_2$O$_4$ (0.010 g) under solvent-free conditions at 90 °C.
[b] Isolated yield.

The reaction condition for KA^2 coupling reaction was optimized and the desired quaternary carbon-containing propargylamine **7d** could be isolated in 87% yield. The scope of the KA^2 coupling reaction was evaluated using cyclic ketones, secondary amines and alkynes, applying the optimal condition, and exhibited good reactivity (Table 3). It is worth nothing that, aromatic ketones gave none of the desired product, which is in accordance with earlier studies [18–20].

The comparison of the catalytic activity of Cu$_2$O/nano-CuFe$_2$O$_4$ magnetic composite with the reported magnetically recoverable catalyst for the synthesis of propargyl amines of **4a** and **6a** is depicted in Table 4. The results clearly indicate that Cu$_2$O/nano-CuFe$_2$O$_4$ has many merits over the reported methods in terms of catalytic activity, reaction time, yields and diversity of products.

3.2.1. Recycling of the catalyst

The recyclability of Cu$_2$O/nano-CuFe$_2$O$_4$ magnetic composite was studied in synthesis of diphenylprop-2-ynyl piperidine **4a** under the optimized condition. No significant loss in catalytic activity was observed after five runs, suggesting that Cu$_2$O leaching is not meaningful for Cu$_2$O/nano-CuFe$_2$O$_4$ magnetic composite.

4. Conclusion

In conclusion, we have developed an efficient method for the synthesis of tertiary and quaternary carbon-containing propargylic amines catalyzed by Cu$_2$O/nano-CuFe$_2$O$_4$ magnetic composite under solvent-free condition. Ready availability of starting materials, mild reaction condition, simple experimental procedure and easy recovery and reusability of catalyst are some conspicuous features of this methodology.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.catcom.2015.03.009.

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