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Short Communication

Copper nanoparticles supported on CeO_2 as an efficient catalyst for click reactions of azides with alkynes

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ABSTRACT

Readily prepared copper nanoparticles supported on CeO_2 have been found to effectively catalyse the 1,3-dipolar cycloaddition (CuAAC) of a variety terminal alkynes and organic azides generated in situ from sodium azide and different organic halides furnishing the corresponding 1,2,3-triazoles in excellent yields. Cu nanoparticles supported on CeO_2 have been characterized by X-ray diffraction analysis, energy dispersive X-ray analysis, scanning electron microscope and transmission electron microscope. The salient features of the present protocol are shorter reaction time, mild reaction conditions, reusability of the catalyst, and applicability to a wide range of substrates.

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1. Introduction

The 1,3-dipolar cycloaddition of organic azides and terminal alkynes is one of the most attractive synthetic tools for convenient and reliable construction of 1,2,3-triazole derivatives, whose subunits are often found in a rich source of various biologically and pharmacologically active molecules [1–5]. The most catalytically active metal for these reactions is copper. Different copper sources have been described for the 1,3-dipolar azide-alkyne cycloaddition, including simple salts and transition metal complexes in homogeneous or heterogeneous form [6–13]. Many of these homogeneous catalysis processes, which often are the first choice of chemists because of their high activity and selectivity, however are not easy to handle, difficult to separate, and have limited reuse potential often due to contamination with final products or formation of metal-complexes [14–20]. Catalyst separation and reusability of the catalyst is a critically important issue for the sustainable development of any catalytic process [21–23].

To overcome this drawback, in recent years, due to higher stability and dispersibility of nanoparticles as well as the demand for higher activity and recyclability of catalysts, copper nanoparticles are supported over a variety of organic and inorganic supports. Due to high reaction rate and high turnover numbers (TON) of this type of catalysts, heterogeneous copper nano-catalysis has emerged as a sustainable and competitive alternative to conventional catalysis [24–29].

With the aim to expand and improve catalytic applications of CuNPs-based catalysts, we want to present herein preparation of copper nanoparticles supported on CeO_2, and the study of its catalytic performance in the 1,3-dipolar cycloaddition of organic azides and alkynes (CuAAC).

2. Experimental

2.1. Materials

Chemicals and solvents were purchased from Merck and Fluka and were used without further purification.

2.2. Synthesis of CeO_2 nanoparticles

An aqueous solution (10 cm^3) of $Ce(NO_3)_3.6H_2O$ (1.0 g) was basified with a NaOH solution (1.0 M; 10 mL), and a white precipitate of $Ce(OH)_4$ was obtained. The solid of $Ce(OH)_4$ was washed with *water* for several times and dried at 50 °C. 1.0 g of urea (as a fuel) was mixed and pulverized with $Ce(OH)_4$. Then the residual solid was ground and calcinated at 400 °C for 5 h.

2.3. Synthesis of copper nanoparticles supported on CeO_2 (Cu/CeO_2)

Copper nanoparticles supported on CeO_2 was prepared by an impregnation method using $Cu(NO_3)_2$ as a source for Cu. The required amount of $Cu(NO_3)_2$, to give 10 wt% Cu loading, was mixed and was

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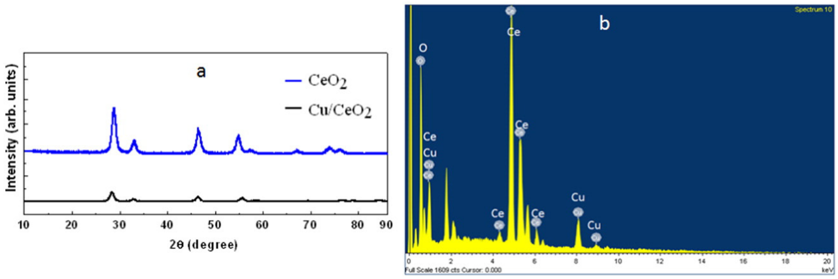


Fig. 1. a) XRD pattern of CeO_2 and Cu/CeO_2 nanoparticles; b) EDXS analysis of the final catalyst.

pulverized with CeO_2. Methanol (20 mL) was added to the mixture of $Cu(NO_3)_2$ and CeO_2. This mixture was mechanically stirred to ensure the homogeneous distribution of Cu(II) over the CeO_2. Then, CH_3OH was evaporated using a rotary evaporator. After impregnation, Cu(0) nanoparticles were obtained by reduction of the Cu(II)/CeO_2 with hydrazine hydrate.

2.4. General procedure for azide–alkyne cycloaddition

Alkyne (0.5 mmol), the organic halide (0.55 mmol), NaN_3 (0.55 mmol) were added to a suspension of Cu/CeO_2 in H_2O (2 mL). The reaction mixture was warmed to 70 °C and stirred for 4 h. The reaction is monitored by TLC. After total conversion of the starting materials, water (5 mL) was added to the resulting mixture and catalyst was recovered by filtration. Then the product was extracted with EtOAc (2 × 10 mL). The collected organic phases were dried with anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to give the corresponding triazoles, which did not require any further purification. The catalyst must be washed with ethanol, and then dried in vacuum in order to use the next run without addition of any fresh catalyst.

3. Results and discussion

3.1. Catalyst characterization

The XRD technique was used in order to identify the phases present in the samples. In Fig. 1 XRD profiles of the CeO_2 and Cu supported on CeO_2 samples are shown. XRD features allow to detect only the CeO_2 Fm3m cubic fluorite phase while peaks related to Cu were not detected (JCPDS file no. 34–0394) [30,31]. It can be known that the copper species are well dispersed on the surface of CeO_2. Also for CeO_2 and Cu/CeO_2 no characteristic peaks from other impurities are detected in the patterns demonstrating that the samples have high phase purity. Energy dispersive X-ray spectroscopy (EDXS) confirms the presence of 9.3% Cu in Cu/CeO_2 sample.

The Cu L-edge XANES spectra for Cu/CeO_2 nanoparticles were shown in Fig. S1. The peaks at 936 and 956 eV indicate L3 2p3/2–4 s and L2 2p1/2–4 s transition, respectively. There is no experimental evidence of $2p_{3/2} \rightarrow 3d$ transition, clearly indicates that copper is mainly 0 oxidation state on the CeO_2 with an $[Ar]3d^{10}4s^1$ like electronic configuration for the Cu atoms the ground state.

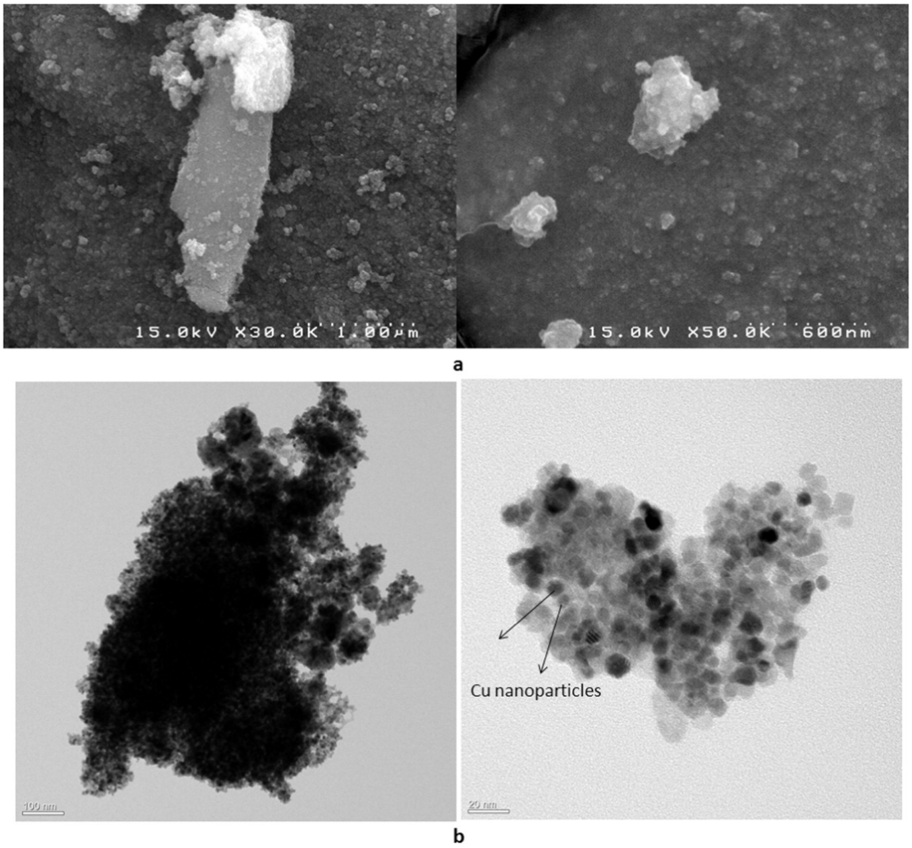
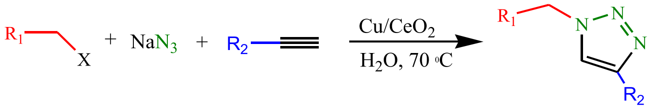
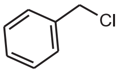
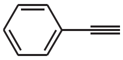
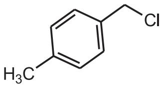
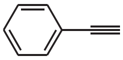
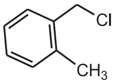
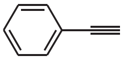
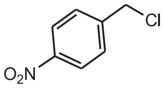
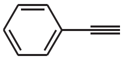
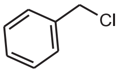
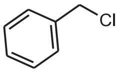
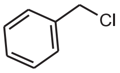
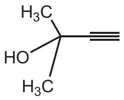
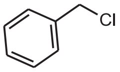
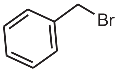
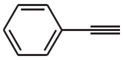
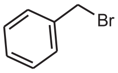
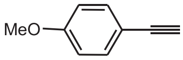
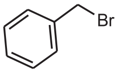
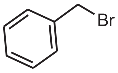
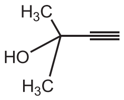
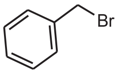


Fig. 2. a) SEM images; b) TEM images of CeO_2 and Cu/CeO_2 nanoparticles.

Table 1
Cycloaddition of alkyl halides with terminal alkynes in the presence of Cu/CeO_2.



Entry	Aliphatic halide	Alkyne	Yield (%)[a]
1			96
2			91
3			80
4			96
5			94
6			95
7			62
8			66
9			96
10			95
11			95
12			71
13			85

[a] Isolated yield.

Due to the smaller size of copper nanoparticles, the specific surface area of the as-obtained Cu/CeO_2 sample calculated from the BET curve reaches about 8.13 $m^2\ g^{-1}$, which is bigger than that of CeO_2nanoparticles (6.40 $m^2\ g^{-1}$).

SEM and TEM observations of Cu/CeO_2 were carried out and shown in Fig. 2. From the TEM image it can be seen that the particles are nearly spherical with relatively uniform diameters and the particle size is found to be 8–15 nm.

3.2. Catalytic effects

The Cu/CeO_2 catalyst demonstrated to be very efficient in the multicomponent 1,3-dipolar cycloaddition of terminal alkynes and organic azides yielded in situ from sodium azide and different organic halides. As shown in Table S1, phenylactelylene and benzyl chloride were chosen as model starting compounds for the optimization of the reaction conditions. Without catalyst, no product was obtained after 12 h (entry 1). When the amount of the Cu was increased from 0.3 mmol% to 1.8 mmol%, the yield of product increased dramatically from 68 to 95% (entries 2–7). With a further increase of the catalyst amount to 2.1 mmol%, no significant change in yield was observed (entry 8). Interestingly, from the different solvents tested, water was found to be the most effective for this reaction (entries 6 and 9–14). As indicated in Table S1, a significant improvement in the product yield was observed at higher temperatures than room temperature (entries 15–17). The reaction is completed at 4 h and thus, using 6 mg of Cu/CeO_2 catalyst (1.8 mmol% Cu) and heating at 70 °C in water, the reaction of phenylacetylene with benzyl chloride and sodium azide, gave 1-benzyl-4-phenyl-1H-1,2,3-triazole almost quantitatively in 4 h of reaction time (entry 19).

The same methodology was successfully applied to a wide range of diversely substituted phenylacetylenes with a mixture of benzyl bromides/chlorides and sodium azide to produce the corresponding 1,4-disubstituted-1,2,3-triazoles. The results are summarized in Table 1. The substitution of electron withdrawing and electrondonating groups on the phenyl ring of the benzylhalides and the phenyl acetylenes did not have any appreciable influence on the outcome of the reaction. Furthermore, minor steric hindrance was observed for ortho substituents on the benzyl chloride as compared to the para derivative (entries 2 and 3). Aliphatic alkynes required longer reaction times to give high yields compared with aromatic alkynes, but the reactions also gave good yields when the reaction time was extended to 12 h (entries 7 and 8). Replacement of benzyl chloride with benzyl bromide seem not to have a decisive effect on the catalytic activity, as benzyl bromide reacted to give the corresponding 1,2,3-triazole products in essentially quantitative yields (entries 7–9), except for aliphatic alkynes (entries 12 and 13).

It is noteworthy that the degree of copper leaching during these experiments was below the atomic absorption spectrometry detection limit, since no presence of copper was detected in the aqueous phase of the residue mixture.

The reusability of Cu/CeO_2 nanoparticles was also examined. After the reaction, the catalyst was separated by centrifugation, washed three times with water and methanol, dried at 50 °C, and subjected to the subsequent run. The catalyst can be used for three times without dramatic yield loss. The comparison of efficiency of catalyst on repeated use is reported in Fig. S2. Small losses of catalyst mass during washing procedure may be caused in the low diminution in the activity from the first to the third cycle. It is important to note that the total mass of catalyst employed is very low (6 mg), thus the loss of only 1 mg of catalyst when handling the sample, means loss of 17% of the total mass of catalyst.

In order to show the merit and efficiency of the present catalytic system, the catalytic behavior of Cu/CeO_2 catalyst was compared with previously reported copper nanoparticles catalysts. As shown in Table 2, the catalytic reactivity of Cu/CeO_2 is superior to some of the previously reported catalysts in terms of reaction conditions. In contrast to previously reported systems, the present catalytic system does not suffer from the harsh reaction conditions, such as much amount of catalyst (entries 2–5), addition of an additive agent (entries 3, 5) and using of hazardous solvents (entries 3–5). Also other advantages of our catalytic system are simple catalyst preparation and in situ generation of organic azides from sodium azide and different organic halides.

4. Conclusions

In conclusion, we have developed a simple and efficient protocol for the synthesis of the corresponding 1,2,3-triazoles through 1,3-dipolar cycloaddition of terminal alkynes with organic azides generated in situ from sodium azide and different organic halides using copper nanoparticles supported on CeO_2 as an efficient and recyclable catalyst. The above protocol has been performed efficiently to provide the desired products in excellent yields. Simple operation, easy separation, wide in scope, short reaction times, readily available starting materials and

Table 2
Recently reported catalytic systems for azide-alkyne cycloaddition by copper nanoparticles catalysts.

Entry	Catalyst	Conditions	Yield (%)	Ref.
1	Cu/CeO_2	6 mg catalyst/H_2O/4 h/70 °C	96	Present work
2	Cu NPs/silica coated maghemite	40 mg catalyst/H_2O/2 h/70 °C	83	[32]
3	Cu NPs/aminopropyl-silica	40 mg catalyst/$PhNHNH_2$/THF/2 h/25 °C	38	[33]
4	Cu NPs	60 mg catalyst/EtOH/5 h/25 °C	95	[34]
5	Cu NPs	60 mg catalyst/Et_3N/THF/30 min/65 °C	95	[35]

reagents and inexpensive and recyclable catalyst are the salient features of this method.

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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.2016.07.006.

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