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Click synthesis of 1,4-disubstituted-1,2,3-triazoles catalysed by $CuO–CeO_2$ nanocomposite in the presence of amberlite-supported azide

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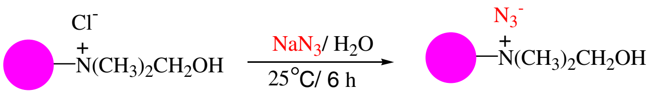
Abstract. A $CuO–CeO_2$ nanocomposite in the presence of amberlite-supported azide has been used for the click synthesis of 1,4-disubstituted-1,2,3-triazoles in good yields. This catalyst can be reused several times without any significant decrease in the catalytic activity.

Keywords. Click chemistry; $CuO–CeO_2$ nanocomposite; amberlite-supported azide; 1,4-disubstituted-1,2,3-triazoles.

1. Introduction

Nanocrystalline oxides have proved to be useful to chemists in the laboratory and in industry due to the good activation of adsorbed compounds and reaction rate enhancement, selectivity, easier work-up, recyclability of the supports and eco-friendly reaction conditions.[1–5] Also, practical applications of nanocomposite metal oxides as catalysts in organic synthesis have increased due to their high catalytic activity resulting from their large surface area.[6,7] Recently, we have reported the preparation of $CuO–CeO_2$ nanocomposite and its catalytic activity for the synthesis of aryl-14*H*-dibenzo[a-j]xanthenes.[8] This catalyst is safe, easy to handle, environmentally benign and has shown very good catalytic activity. Therefore, we decided to study of click synthesis of 1,4-disubstituted-1,2,3-triazoles in the presence of this catalyst. Owing to the diversity in pharmacological activities, the synthesis of 1,2,3-triazoles has received significant attention.[9,10] The main method for the synthesis of these compounds is the Huisgen 1,3-dipolar cycloaddition reaction of azides with alkynes, which has become the model for click reactions.[11] 1,3-dipolar cycloadditions have been used in drug discovery, chemical biology and medicinal chemistry as well as in materials science and solid phase organic synthesis.[12] Sodium azide is a potent toxin and can be absorbed through the mucous membranes. The use of excess sodium azide during nucleophilic substitution reactions in organic processes pollutes the environment since it is not usually recovered from reaction medium. Such drawbacks could be obviated using the supported azide anion. Recently, we have reported multicomponent synthesis of triazole derivatives with amberlite-supported azide as the source of azide ion.[13] amberlite-supported azide was easily prepared from its corresponding chloride form via ion exchange using 10% NaN_3 aqueous solution (scheme 1).

In general, as a catalyst, a Cu(I) salt is directly used, or Cu(II) after reduction.[14–17] The Cu(II)-catalysed azide-alkyne cycloaddition (CuAAC) reactions[18,19] have also been reported. In previous studies, we reported the preparation of copper iodide nanoparticles supported on poly(4-vinylpyridine) (P_4VPy-CuI) and their application in click synthesis of triazoles.[20,21] In continuation of these studies, herein we report a green recyclable catalyst for regioselective click synthesis of 1,4-disubstituted-1,2,3-triazoles from α-halo ketones or benzyl halides and terminal alkynes in the presence of amberlite-supported azide (scheme 2).



Scheme 1. Preparation of amberlite-supported azide.

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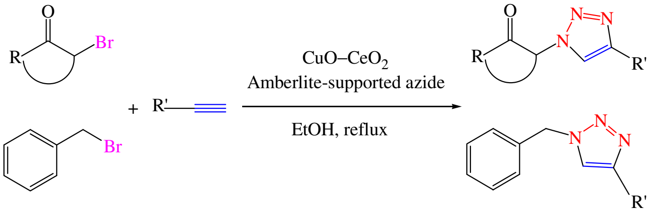
[*] For correspondence



Scheme 2. CuO–CeO$_2$ nanocomposite-catalysed click synthesis of 1,4-disubstituted-1,2,3-triazoles.

2. Experimental

Chemicals were purchased from Fluka and Merck chemical companies. Products were characterized by comparison of their spectroscopic data (NMR, IR) and physical properties with those reported in the literature. Yields refer to isolated pure products.

Table 1. CuO–CeO$_2$ nanocomposite-catalysed synthesis of triazole derivatives.

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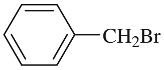
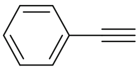
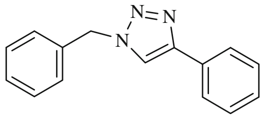
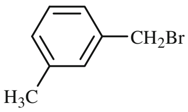
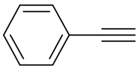
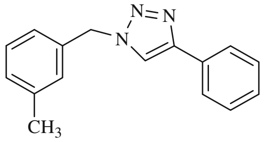
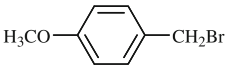
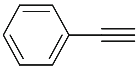
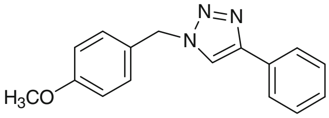
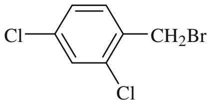
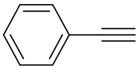
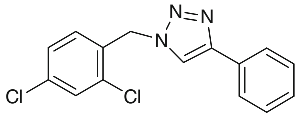
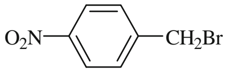
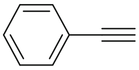
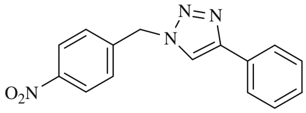
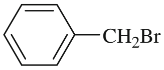
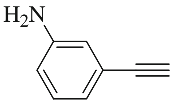
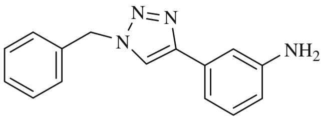
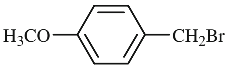
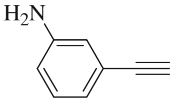
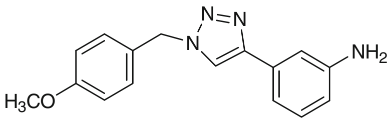
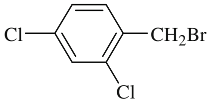
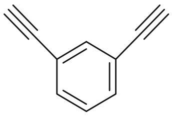
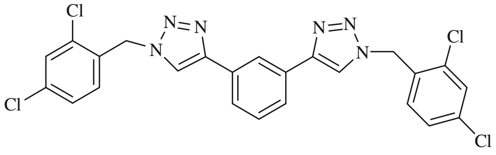
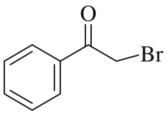
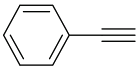
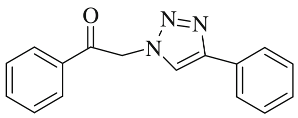
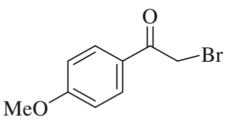
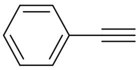
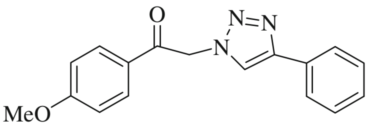
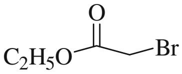
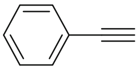
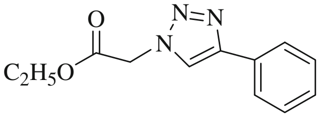
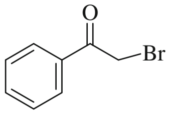
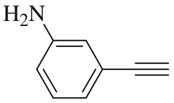
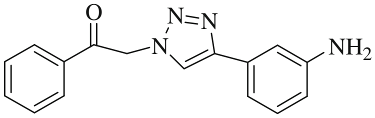
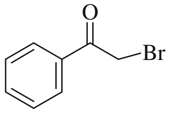
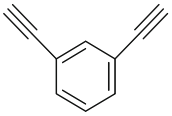
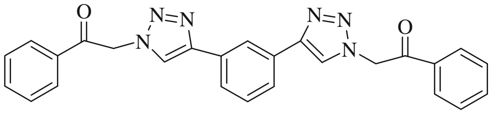
1				65	91	128–130
2				60	90	108–110
3				45	90	117–118
4				60	89	148–150
5				75	91	139–140
6				70	89	136–138
7				60	92	139–141
8				120	91	188–189
9				60	92	145–147
10				45	92	141–143

Table 1. (Continued).

Entry	Substrate	Alkyne	Product	Time (min)	Yield (%)[a]	M.P. (°C)[b]
11				90	88	110–112
12				90	89	144–146
13				120	89	299–300

[a] Isolated yield.

[b] Products were characterized by comparison of their spectroscopic data (NMR and IR) and melting points with those reported in the literature.[23–25]

2.1 *Catalyst preparation*

CuO–CeO$_2$ nanocomposite was prepared by co-precipitation method using aqueous solution of cerium and copper nitrates and drop-wise KOH as precipitant agent under vigorous mixing while temperature and pH was fixed at unique values. Then, acquired sample was filtered, washed and calcined to obtain final catalyst for using in the synthesis of 1,4-disubstituted-1,2,3-triazoles.

2.2 *General procedure*

Benzyl bromide (1 mmol) and phenyl acetylene (1 mmol) were added to round-bottom flask containing 10 mL of EtOH, CuO–CeO$_2$ nanocomposite (0.1 g) and amberlite-supported azide (1 g) were added at once to the mixture. The suspension was stirred under reflux conditions for appropriate number of times (table 1). After completion of the reaction as followed by TLC, the catalyst and resin were filtered and washed with hot acetone (2 × 5 mL). The filtrate was evaporated to dryness, and the solid residue recrystallized from EtOH/H$_2$O (1:3 v/v) to gave crystalline pure product.

2.3 *Reusing of the catalyst and reagent*

The filtered mixture of resin and catalyst were washed with 25 mL of distilled water and stirred for 6 h in 50 mL of 10% NaN$_3$ aqueous solution and dried under vacuum at 50°C before the next run. The exchange capacity of the amberlite-supported azide was determined by passing sodium chloride solution (1M) through the amberlite-supported azide packed in a column. The amount of sodium salt of the nucleophile in the eluent was then titrated with 0.01 M hydrochloric acid using methyl orange as an indicator. The exchange capacity of the amberlite-supported nucleophile was calculated to be 3.5 mmol/g of N_3^-.

3. Results and discussion

The catalyst was synthesized by co-precipitation method and characterized by XRD, BET specific surface area, ESEM and EDS analysis.[8] To optimize the reaction conditions, the reaction of benzyl bromide, phenylacetylene and amberlite-supported azide was chosen as a model and its behaviour was studied under a variety of conditions (table 2).

The best result was achieved by carrying out the reaction of benzyl bromide and phenylacetylene (1:1 mol/ratio) in the presence of 0.1 g of CuO–CeO$_2$ nanocomposite and 1 g of amberlite-supported azide under reflux conditions in ethanol as the solvent

Table 2. Optimization of the reaction conditions.

Entry	Conditions[a]	Time (min)	Yield (%)[b]
1	CH_3CN	120	75
2	CH_2Cl_2	120	45
3	H_2O	90	72
4	CH_3OH	60	88
5	CH_3CH_2OH	65	91

[a] The reaction was performed in the presence of 0.1 g of CuO–CeO$_2$ and 1 g of amberlite-supported azide under reflux conditions.

[b] Isolated yield

Table 3. Recyclability study of CuO–CeO$_2$.

Run	1	2	3	4	5
Time (min)	65	65	70	75	75
Yield (%)[a]	91	90	90	88	88

[a]Isolated yield

(table 1, entry 1). Using these optimized conditions, the reaction of various terminal alkynes, benzyl halides and α-halo ketones were explored. All the products were easily isolated by straightforward filtration and evaporation of the solvent. A simple purification technique is one of the key characteristics of click reactions. The solid products were recrystallized from a mixture of ethanol/water (1:3 v/v), or in some cases, from hot ethanol. It is very important to note that the corresponding triazoles were obtained in high yields and good regioselectivities.

Click cyclizations were confirmed by the appearance of a singlet in the region of 8–8.5 ppm for the triazole derivate from α-halo ketones and 7.8–8.5 ppm for the trizole derivate from benzyl halides in ^{1}H-NMR spectra which corresponds to the hydrogen on 5-position of triazole ring and confirms the regioselective synthesis of 1,4-disubstituted triazole regioisomers.[22] Moreover, the recyclability of the catalyst is also important. To investigate these properties, the reaction of benzyl bromide with phenyl acetylene was selected again as a model (table 3). After the completion of reaction, the catalyst and resin were filtered and washed with distilled water, then treated with aqueous NaN$_3$ solution to reload the amberlite-supported azide. Then, the catalyst and resin were dried and stored for another consecutive run. This process was repeated for four runs and no appreciable decrease in the yield was observed.

4. Conclusion

In conclusion, we have described the CuO–CeO$_2$ nanocomposite as a green and efficient catalyst in the presence of amberlite-supported azide catalysed click synthesis of 1,4-disubstituted-1,2,3-triazoles under reflux conditions in ethanol as the solvent. This catalyst and reagent can be reused at least four times without significant decrease of catalytic activity. Moreover, high yields of products, short reaction times, ease of work-up and clean procedures, should make the present method a useful and important addition for the synthesis of triazole derivatives. Studies on other applications of this catalyst for carbon–carbon and carbon–heteroatom bond forming reactions are underway in our laboratory.

Supplementary information

The spectra of compounds that synthesized in the presence of CuO–CeO$_2$ nanocomposite can be seen at www.ias.ac.in/chemsci.

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