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Copper iodide nanoparticles on poly(4-vinyl pyridine) as new and green catalyst for multicomponent click synthesis of 1,4-disubstituted-1,2,3-triazoles in water

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Abstract

Poly(4-vinyl pyridine) supported nanoparticle of copper(I) iodide is reported as a green and recyclable catalyst for the regioselective synthesis of 1,4-disubstituted-1*H*-1,2,3-triazoles from benzyl halides, sodium azide and terminal alkynes in water. This catalyst can be recovered by simple filtration and recycled up to 8 consecutive runs without any loss of its efficiency.

Keywords: Click chemistry; Poly(4-vinyl pyridine) supported; Nanoparticles; Copper(I) iodide; Triazoles

1,2,3-Triazoles are an important class of heterocyclic compounds that received significant attention from many pharmaceutical and organic chemists essentially because of the broad spectrum of their biological and pharmaceutical properties such as antibacterial, antiallergic, and anti-HIV activities. Furthermore, these compounds are used as dyes, corrosion inhibitors, photostabilizers, and photographic materials [1–4]. The main method for the synthesis of 1,2,3-triazoles is the Huisgen 1,3-dipolar cycloaddition reaction of azides with alkynes [5]. This cycloaddition reaction has become the model for click reactions. Polymer-supported reagents have more and more attracted attention as insoluble material in organic synthesis [6]. They recommend rewards such as reaction monitoring as well as improved safety, more than ever when the non-supported reagents are toxic or unsafe as they can be easily removed from reaction medium and recycled [7]. Additionally, employing an excess amount of reagent is permitted without the need for further purification. There are some reports on using polymer supported CuI as recoverable catalyst for synthesis of 1,2,3-triazoles between azides and alkynes via click reaction [8–13]. In recent years, nano-catalysis has emerged as a sustainable and competitive alternative to conventional catalysis since the nanoparticles possess a high surface-to-volume ratio, which enhances their activity and selectivity, while at the same time maintaining the intrinsic features of a heterogeneous catalyst [14]. In particular, the immobilization of copper(I) salt nanoparticles (CuNPs) on high-surface-area supports allows a higher stability and dispersity of the particles as well as a further exploitation of the special activity and recycling properties of the catalyst. For instance, CuNPs immobilized on aluminum oxyhydroxide nanofiber, copper nitride nanoparticles supported on a superparamagnetic mesoporous microsphere, $Cu_3N/Fe_3N/SiO_2$ and copper nanoparticles on activated

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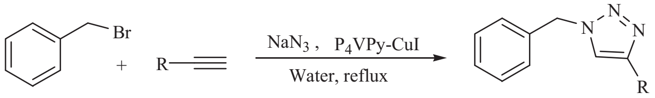


Scheme 1.

carbon were found to catalyze the click cycloaddition [15–18]. These catalysts possess increased advantages over their homogeneous counterparts. On the other hand, water has found widespread application in synthetic organic reactions as solvent because it is not only nontoxic and readily available at low cost, but also nonflammable and environmentally benign, providing opportunities for clean processing and pollution prevention [19]. Consequently, introduction of new catalysts which could be used under aqueous conditions that can promote the yields and reaction times is still in demand. Herein we wish to report the applicability of a new, green and reusable catalytic system based on Cu(I) nanoparticles supported by poly(4-vinyl pyridine) (P_4VPy-CuI) for one-pot multicomponent click synthesis of 1,4-disubstituted-1*H*-1,2,3-triazoles from benzyl halides, sodium azide and terminal alkynes in water (Scheme 1).

1. Results and discussion

The copper(I) iodide catalyst immobilized on poly(4-vinyl pyridine) was readily prepared in a one-step procedure. Poly(4-vinyl pyridine) was refluxed with a solution of CuI under N_2 atmosphere in EtOH for the synthesis of polymer-supported CuI nanoparticles. This method was developed for the effective synthesis of copper nanoparticles incorporated heterogeneously as catalyst in some organic reactions [18].

At first, for the optimization of the reaction conditions, the reaction between benzyl bromide, phenyl acetylene and sodium azide was chosen as a model and its behavior was studied under a variety of conditions. The best result was achieved by carrying out the reaction of benzyl bromide, phenyl acetylene, sodium azide (with 1:1:1.1 mol ratio) in the presence of 0.1 g of P_4VPy-CuI under reflux condition in water (Table 1, entry 1). Using these optimized conditions, the reaction of various terminal alkynes and benzyl halides was explored. All the products were cleanly isolated with simple filtration and evaporation of solvent. The solid products were easily recrystallized from a

Table 1
Click synthesis of 1,4-disubstituted 1,2,3-triazoles catalyzed by P_4VPy-CuI.

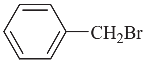
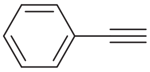
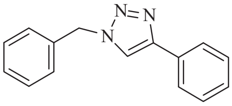
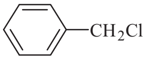
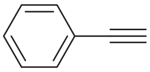
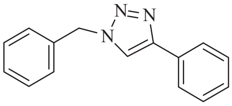
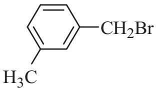
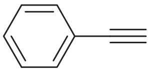
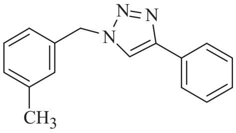
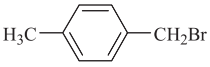
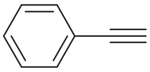
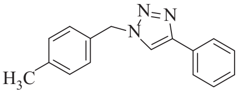
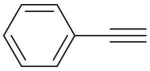
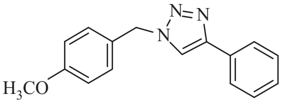
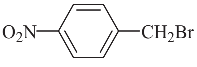
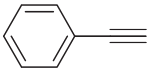
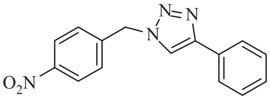
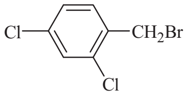
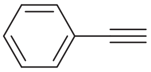
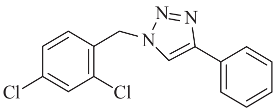
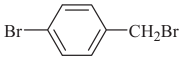
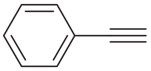
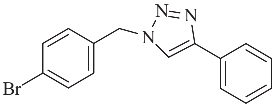
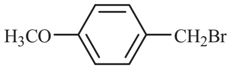
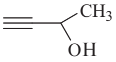
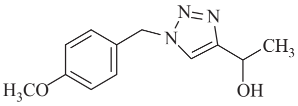
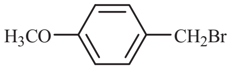
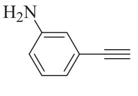
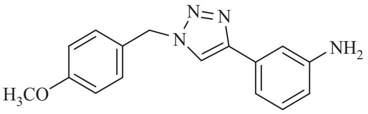
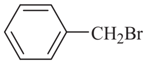
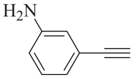
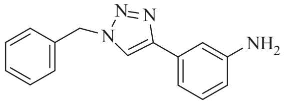
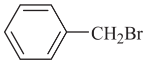
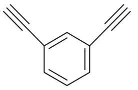
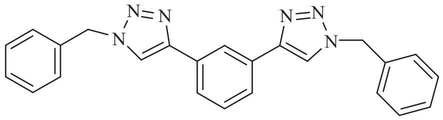
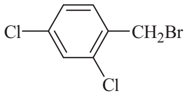
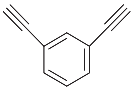
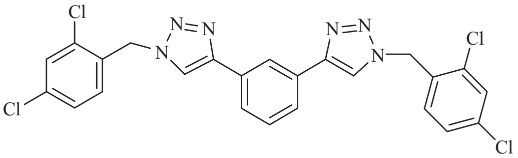
Entry	Benzyl halide	Alkyne	Product	Time (min)	Yield (%)[a]
1				15	90
2				15	89
3				25	88
4				20	88
5				30	87
6				35	86

Table 1 (*Continued*)

Entry	Benzyl halide	Alkyne	Product	Time (min)	Yield (%)[a]
7				25	88
8				20	89
9				30	75
10				35	86
11				25	88
12				40	82
13[b]				45	83

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[a] Isolated yield.

[b] 2 mmol of the benzyl halide was used.

mixture of ethanol/water (1:3, v/v) or in some cases from ethanol (Table 1, entries 12 and 13). It is very important to note that the corresponding triazole was obtained in high yield and regioselectivity. Click cyclizations were confirmed by the appearance of a singlet in the region of 7.8–8.5 ppm 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. It is also noteworthy that resin does not suffer from extensive mechanical degradation after running. For a true heterogeneous catalyst, supported catalyst should not leach to the reaction mixture. Moreover the recyclability of the supported catalyst is also important and should not suffer from mechanical degradation. To investigate these properties for our introduced catalyst and reagent, the reaction of benzyl bromide with phenyl acetylene was selected again as model. Polymer supported CuI can be reused up to 8 runs without any significant yield decreases. The copper content of the catalyst was measured with atomic emission spectroscopy after 8 runs. Almost consistent activity was observed over 8 runs. Next we checked the leaching of CuI into the reaction mixture from the poly(4-vinyl pyridine) support using ICP-AES. The difference between the copper content of the fresh and reused catalysts (8th run) is only 3% which indicates the low leaching amount of copper iodide catalyst into the reaction mixture. Finally, in order to evaluate the efficiency and superiority of our introduced catalyst, we began to run the reaction between benzyl halide and phenyl acetylene in the presence of pure CuI at the same conditions. The obtained results showed that pure CuI could not be reused, need much more reaction time and give the product in low yield.

In conclusion, we have developed a mild, simple and green procedure for the one-pot regiospecific synthesis of biologically important 1,4-disubstituted-1*H*-1,2,3-triazoles via Huisgen 1,3-dipolar cycloaddition reaction between terminal alkynes, benzyl halides and NaN_3 using recyclable P_4VPy-CuI in water as reaction medium at reflux conditions. The introduced catalyst can promote the yields and reaction times over 8 runs with very low leaching amounts of supported catalyst into the reaction mixture. Moreover, ease of work-up and clean procedure, will make the present method an useful and important addition to the present methodologies for the synthesis of 1,4-disubstituted-1,2,3-triazoles.

2. Experimental

2.1. General

All products were characterized by comparison of their spectroscopic data (^{1}H NMR, IR) and physical, properties with those reported in the literature. Poly(4-vinyl pyridine), 2% cross-linked DVB (mesh 50–60) which is a white water insoluble polymer and of interest due to its high electrical conductivity was purchased from Aldrich company.

2.2. Preparation of the polymer supported catalyst

CuI (0.381 mg) was put in 30 mL ethanol, and magnetically stirred at reflux temperature for 4 h under nitrogen atmosphere in the presence of dry poly(4-vinyl pyridine) (1.0 g, mesh 50–60). The solvent was filtered, the resin washed with CH_3CN (2×20 mL) and dried under vacuum at 60 °C overnight. The weight increase was 0.31 g (1.63 mmol CuI), which gave a polymer loading of 1.24 mmol CuI g^{-1}. The exact copper content of poly(4-vinyl pyridine)-CuI was measured using ICP-AES. The loading of supported catalyst was calculated to be 1.32 mmol CuI g^{-1} of resin. Scanning electron microscopy (SEM), X-ray diffraction (XRD) analysis, atomic absorption and IR experimental techniques were used to characterize the catalyst.

2.3. General procedure for synthesis of 1,4-disubstituted triazoles

Benzyl halide (1 mmol), alkyne (1 mmol) and sodium azide (1.1 mmol) were placed together in a round-bottom flask containing 10 mL of water. Poly(4-vinyl pyridine)-CuI (0.1 g) was added to the mixture. The suspension was magnetically stirred under reflux conditions for appropriate time according to Table 1. After completion of the reaction as followed by TLC (*n*-hexane:ethyl acetate, 4:1), the resin was filtered and washed with hot ethanol (2×5 mL). The recovered catalyst was washed with acetone, dried and stored for another consecutive reaction run. The filtrates were evaporated to dryness, and then the solid residue was recrystallized in ethanol/water (1:3, v/v) to give pure product crystals.

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