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Copper-polymer nanocomposite: An efficient catalyst for green Huisgen click synthesis

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ABSTRACT

A new method for Huisgen [3+2] cycloaddition synthesis of 1,4- and 1,4,5-substituted-1*H*-1,2,3-triazoles was reported. The reaction was catalyzed by the product of thermolysis of copper (II) poly-5-vinyltetrazolate. Heterogeneous catalyst includes copper nanoparticles which supported on polymeric matrix. It presents recovered and recycled catalyst and the catalyzed reaction proceeds in aerobic conditions at room temperature in aqueous media.

1,2,3-Triazoles are basically five-membered nitrogen heterocyclic compounds. They have tremendous application in various research fields, including material chemistry,[1] polymer chemistry,[1] synthetic organic chemistry,[2] medicinal chemistry[3] and pharmaceutical synthesis.[4] In addition, 1,2,3-triazoles are important privileged scaffolds with a wide range of biological activities, such as anti-viral, hypoallergenic and anti-cancer.[4] The classical method for synthesis of 1,2,3-triazole derivatives is the Huisgen [3+2] cycloaddition reaction between the terminal alkynes and azides.[5–7] In 2002, the first copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) was discovered independently by the groups of Sharpless[8] and Meldal,[9] by whom 1,4-disubstituted-1*H*-1,2,3-triazoles were prepared regioselectively under mild conditions.[10] Until now, a number of CuAAC procedures have been developed including the use of Cu(II) complexes[8,11,12], Cu(I) complexes,[13] and Pd-containing complexes.[14] Above mentioned catalytic systems are highly efficient, but sometimes these reagents are far more expensive. However, the use of such catalyst entailes some drawbacks such as the need for high temperature, and in some cases the lack of recyclability of the catalyst. Therefore, although many effective catalysts for Huisgen [3+2] cycloaddition reaction are already known, the search for alternative, recyclable and less expensive catalysts remain relevant.

The present work is devoted to catalytic Huisgen [3+2] cycloaddition synthesis of 1,4- and 1,4,5-substituted-1*H*-1,2,3-triazoles. To date, many catalytic systems have been proposed for Huisgen [3+2] cycloaddition reaction, however most of them are not reusable and quite expensive. Taking into account these circumstances, herein we focused our attention on the catalytic synthesis of 1,4- and 1,4,5-substituted-1*H*-1,2,3-triazoles using our nanocopper-based heterogeneous catalyst.[16] The possibility to be reusable makes the heterogeneous catalyst even cheaper.

As the catalyst for 1,3-dipolar cycloaddition reaction between the terminal alkynes, sodium azide and benzyl chloride (Scheme 1a) (hereinafter referred to as Pathway 1) and for the reaction between alkynes and aryl azide (Scheme 1b) (hereinafter referred to as Pathway 2), we used the product of thermolysis of copper(II) poly-5-vinyltetrazolate (hereinafter referred to as Cu-Pol) (Scheme 1).

According to our previous work, the Cu-Pol catalyst was obtained by thermolysis of copper(II) poly-5-vinyltetrazolate with copper content equal to 53.57 wt%.[15,16]

Noteworthy, that copper nanoparticles (hereinafter referred to as Cu NPs), supported on polymer matrix, are resistant to oxidation on air and water action. Hence, polymer matrix increases the stability of the particles by altering their inherent sensitivity to oxygen and water.[15]

The obtained Cu-Pol nanocomposite was investigated as a catalyst in Huisgen cycloaddition reaction (Scheme 1). At the initial stage of our investigation, we effort to optimize the catalytic

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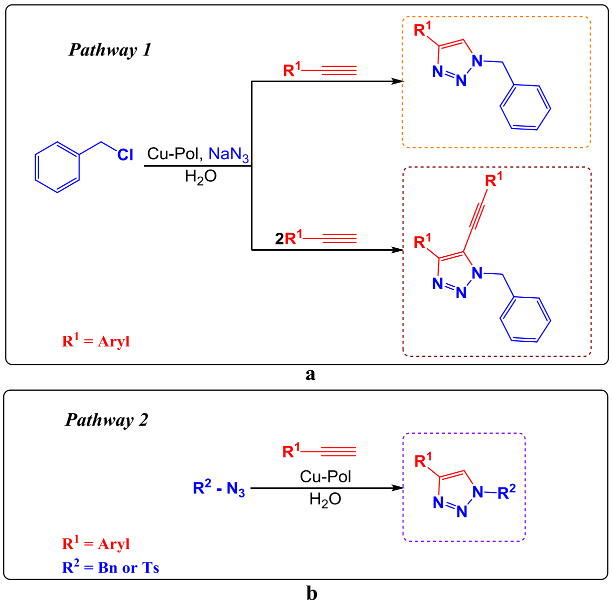


Scheme 1. a) Synthesis of 1-benzyl-4-aryl-1*H*-1,2,3-triazoles and 1-benzyl-4-aryl-5-(arylethynyl)-1*H*-1,2,3-triazoles (Pathway 1); b) Synthesis of 1,4-diaryl-1*H*-1,2,3-triazoles (Pathway 2).

Table 1
Effects of solvents on the catalytic activity of Cu-Pol.[a]

No.	Solvent	Time/h	Isolated yield of 1a/%
1	PhMe	24	35
2	THF	15	47
3	EtOH	4.5	87
4	H_2O	3	96

[a] Under the conditions of Ref. 18.

Table 2
Different amounts of Cu–Pol nanocomposite catalyst in synthesis of (1a)[a] by pathway 1.

Entry	Catalyst loading/mol-%	Synthesis duration/h	Isolated yield of 1a/%
1	18	3	95
2	11	3	95
3	8	3	94
4	5	3	96
5	3	5	92
6	1	16	90
7	0.5	20	91
8	0.3	24	92
9	0.2	25	89

[a] Under the conditions of Ref. 18.

reaction on the one-pot three-component cycloaddition. We chose the reaction of synthesis of 1-benzyl-4-phenyl-1*H*-1,2,3-triazole as a model (Scheme 2).

Different solvents were scanned to find their effects on the catalytic activity of Cu-Pol in the model reaction (Table 1).

Product (1a) was obtained in excellent yields in all protonic solvents (Entries 3, 4) and the best result was obtained for water. It is important that, the water belongs to green solvents. It should been noted that by using homogeneous catalysts[8,11–13] in Huisgen click reactions the best results were obtained also for green solvents ($scCO_2$, ionic liquids, and water). Therefore, Cu-Pol nanocomposite is highly effective catalyst for cycloaddition reaction which proceed in preferred and suitable green solvent like water at room temperature.

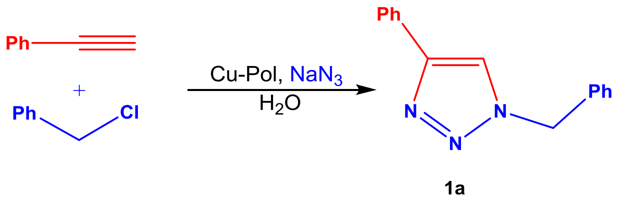
In case of pathways 1 and 2 (Scheme 1) high catalytic activity of Cu–Pol nanocomposite is explained by its high dispersity in water and interaction of organic reactants with Cu NPs attached to polymeric matrix. During the reaction, the hydrophobic nature of polymeric matrix surface allows the phenylacetylene and benzyl azide (it is formed at the interface) to interact on the surface of polymeric matrix thereby increasing the yields of **(1a)** (Scheme 2).[15]

Next, the model reaction was performed at room temperature catalyzed by different amounts of Cu-Pol nanocomposite. As shown in Table 2 (Entries 1–4), the model reaction could still finish in 3 h, when catalyzed by 5–11 mol-% Cu-Pol with almost the same yields as that when catalyzed by 18 mol-%. However, a further decrease of the loading of Cu-Pol nanocomposite (Entries 5–9) led to a long reaction time.

Our model experiments, concerned with the synthesis of (**1a**) by using Cu–Pol nanocomposite catalyst, show that it can be used as a reusable heterogeneous catalyst. Table 3 demonstrates changes in its catalyst efficiency for eight successive cycles of the use.

If to be limited to 90% yield of (1a) as acceptable for the practical use, the catalytic system can be reused seven times without considerable loss in the catalytic activity. After seven cycles, the catalytic activity of Cu–Pol nanocomposite begins to decrease more noticeably. We believe that the decrease in catalytic activity is caused by the loss of copper particles from the polymeric matrix surface, which can take place as a result of recovery procedure as well as during liquid phase cycloaddition synthesis. After seven cycles, copper content of nanocomposite is about 40 wt%.

Reusability of the catalyst is possibly due to stabilization of catalytically active copper particles by polymeric matrix. It should be noted that longer reaction time is practically not required when recycled catalyst is used. Thus, the optimized reaction conditions established, the scope of this reaction was then evaluated with respect to various substituted terminal alkynes. As shown in Table 4, these transformations displayed high functional group tolerance and proved to be a general method for the synthesis of 1,4- and 1,4,5-substituted-1*H*-1,2,3-triazoles using pathways 1 or 2 respectively (Scheme 1, Fig. 1). Terminal aryl or heteroaryl alkynes



Scheme 2. The model reaction for catalytic activities investigation.

Table 3
Reusability of Cu–Pol nanocomposite catalyst in synthesis of (1a)[a] by pathway 1.

Cycle number	Isolated yield (%)
1	96
2	94
3	95
4	92
5	91
6	93
7	90
8	86

[a] After completion of a previous cycle, the catalyst was recovered by a procedure, described in Experimental Section (Ref. 19), and then used again in the next cycle.