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Copper-alginates: a biopolymer supported Cu(II) catalyst for 1,3-dipolar cycloaddition of alkynes with azides and oxidative coupling of 2-naphthols and phenols in water

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Copper(II) ions immobilized onto a biopolymer (sodium alginate) is an effective heterogeneous catalyst for 1,3-dipolar cycloaddition of alkynes with azides and oxidative coupling of 2-naphthols and phenols in water to afford the 1,4-disubstituted 1,2,3-triazoles and biaryl compounds respectively in good yields. The catalyst was recovered quantitatively by simple filtration and reused for several times without significant loss of activity.

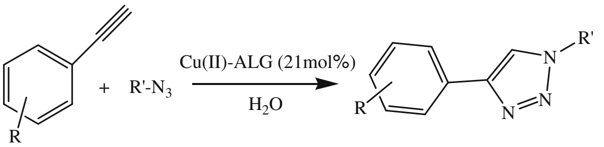
KEY WORDS: copper(II) catalyst; alginate; biopolymer; cycloaddition; alkynes; azides; oxidative coupling; phenols.

1. Introduction

The development of heterogeneous catalysts for the synthesis of fine chemicals is particularly attractive as it allows production and ready separation of large quantities of products with the use of a small amount of catalyst. Majority of the supports for catalytic applications are based on pure inorganic materials or functional polymers [1, 2]. Synthesis of these supports involves either high temperature calcinations or polymerization of petrochemical feed stocks. In recent years the emphasis of science and technology is shifting towards environmentally friendly and sustainable resources and processes. In this regard utilization biopolymers, which are cheap and widely abundant in nature, for any useful purposes are quite attractive to explore. From the catalysis point of view, these biopolymers have several interesting features, for example, they have high sorption capacity towards the metal ions, they can be molded in different forms viz., flakes, gel beads, membranes, fibers, hollow fibers or as sponges. These properties make them attractive to use as supports [3, 4]. In recent years, efforts have been devoted to use several biopolymers, for example cellulose [5], gelatin [6], starch [7], and chitosan [8] derivatives as supports for catalytic applications.

Alginates are an important naturally occurring biopolymers made up of mannuronic and guluronic residues, has shown in figure 1. They are the cell wall constituents of brown algae and quite abundant in nature. Alginates are used in a wide range of applications, particularly in food, industrial and pharmaceutical fields [9]. They are often used in immobilization of enzymes and proteins as well as for the controlled release of drugs [10, 11]. Apart from the above applications, alginates carrying carboxylate groups, capable of exchanging with metal cations are largely explored as biosorbents for heavy metal removal [12]. However, direct utilization of these metals exchanged alginates for catalytic applications are not known.

We have recently reported the cellulose biopolymer as a support for palladium and copper catalyzed C-C and C-N coupling reactions respectively [13–15]. In the present investigation, we have explored the copper (II)-alginate (Cu (II)-ALG) biopolymer supported catalyst for the regioselective synthesis of 1,4-disubstituted 1,2,3-triazoles in water, as represented in Scheme 1. We have further explored this catalyst for the oxidative coupling of 2-naphthols and phenols with air in water.



Scheme 1.

2. Experimental

2.1. Materials

Sodium alginate and $Cu(OAc)_2 \cdot H_2O$ was purchased from S. D. Fine chemicals Ltd, India and is used as

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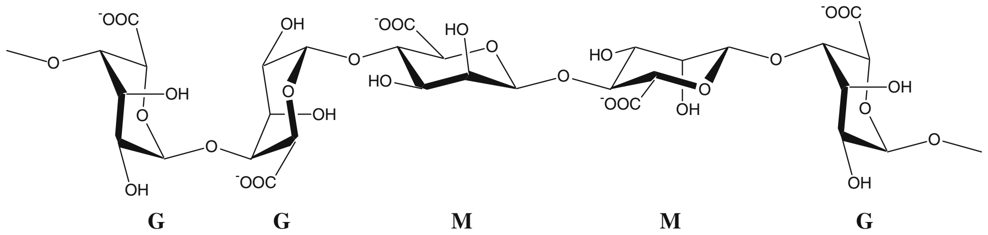


Figure 1. Alginate polymer conformation (G = α-L-Guluronate, M = β-D-mannuronate).

such. All the terminal alkynes, aryl azide, phenols and 2-naphthol derivatives are purchased from Aldrich.

2.2. *Catalyst preparation and characterization*

The copper-alginate gel beads were prepared by adapting the calcium alginates procedure as reported in the literature [16]. The viscous sodium alginate solution (3% W/V) was taken in a separating funnel and the drops of it are allowed to fall into the aqueous solution of copper acetate monohydrate (20% W/V). The distance between separating funnel and cation solution must be adapted to the viscosity of the alginate solution to obtain uniform droplets. The beads were allowed to mature for 1 h without stirring and then collected in Buchner funnel, washed with distilled water to remove any unassociated metal ions and used as such for the reactions. These wet beads were analyzed for copper content by flame atomic absorption spectrometry (AAS), taking specific number (50 no's) of copper-alginate gel beads in triplicates. The average amount of copper in 50 beads was found to be 13.43 mg (0.21 mmol).

2.3. *Reaction procedures*

2.3.1. *General procedure for the synthesis of 1,2,3-triazoles*

To the stirred solution of phenylacetylene (1.1 mmol) and benzyl azide (1.0 mmol) in H_2O (3 mL) at room temperature was added copper alginate gel beads (50 no, 21 mol%). After 18 h of stirring, the reaction mixture was stirred with 10 ml ethyl acetate and filtered to remove catalyst, and the organic layer is separated and evaporated under vaccum to obtain the crude product. The crude product was purified by column chromatography on silica gel using ethyl acetate: hexane (20: 80) as eluant to give desired product. ^1H NMR ($CDCl_3$, 300 MHz) for 1-benzyl-4-phenyl-1H-[1,2,3]-triazole (isolated yield = 98%): δ = 5.55 (s, 2H), 7.25–7.37 (m, 8H), 7.58 (s, 1H), 7.75 (d, 2H, 8.3 Hz).

2.3.2. *General procedure for the oxidative coupling of 2-naphthol*

To the vigorously stirred suspension of 2-naphthol (1.0 mmol) in H_2O (5 mL) was added copper-alginate beads (about 50 No., 21 mol%) and refluxed with bubbling of air. After 18 h of stirring, the reaction mixture was treated with 10 ml of ethyl acetate and filtered to remove catalyst, and the organic layer was separated and evaporated under vaccum to obtain the crude product. The crude product is subjected to column chromatography on silica gel using ethyl acetate: hexane (20:80) as eluant to yield the desired product. The products are characterized by ^1H NMR spectral data. ^1H NMR ($CDCl_3$, 300 MHz) for1,1'-bi-2-naphthol: δ = 5.00 (s, 2H), 7.17 (d, 2H, J = 7.5 Hz), 7.29–7.40 (m, 6H), 7.89 (d, 2H, J = 9.06 Hz), 7.98 (d, 2H, J = 9.06 Hz).

3. Results and discussion

The preparation of Cu(II)-ALG gel beads is rather simple and was accomplished by adapting a similar protocol reported for the synthesis of calcium alginates [15]. An alginate solution was added drop wise into copper ion solution and Cu(II)-ALG gel beads are collected by simple filtration, which are shown in figure 2. Copper estimation was done in triplicates using specific number (50 no's) of Cu(II)-ALG beads, which corresponds to average of 13.4 mg (0.21 mmol) of copper in 50 beads.

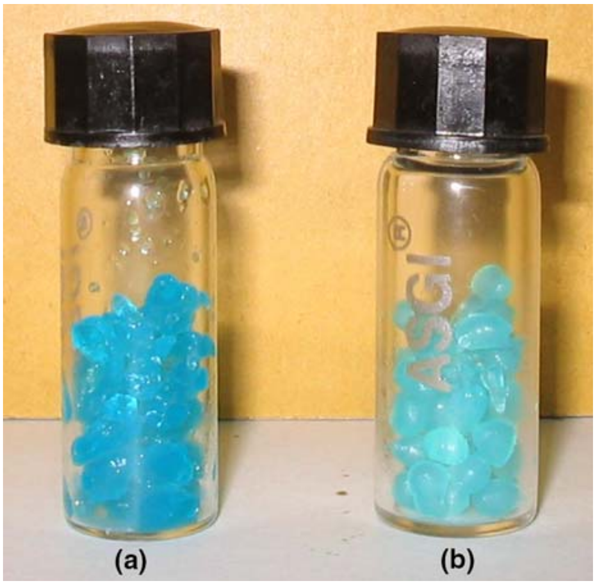


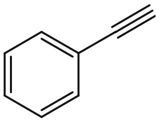
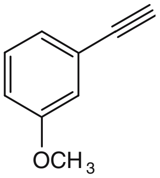
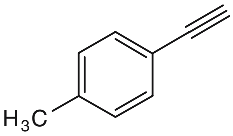
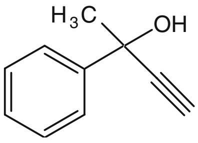
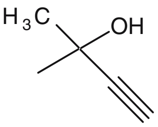
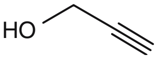
Figure 2. Copper alginate gel beads (a) before and (b) after cycloaddition reaction.

Copper catalyzed 1,3-dipolar cycloaddition of azides with alkynes discovered by Sharpless and co-workers is widely studied in recent years [17]. It is postulated that this particular reaction proceeds *via* a copper-acetylide intermediate, generated from Cu(I) and the terminal alkyne, which then participates in a cycloaddition process with the coordinated azide. The active Cu(I) catalysts are introduced directly in the form of different copper(I) salts, generated *in situ* from Cu(II) salts with reducing agents or by the *in situ* oxidation of copper metal turnings. We have recently reported that simple $Cu(OAc)_2 \cdot H_2O$ is also highly active for the cycloaddition of azides with alkynes [18]. Making use of high affinity of alginates towards divalent metal ions, we have initially tested Cu(II)-ALG catalyst for 1,3-dipolar cycloaddition reactions between terminal alkynes and alkyl azides in water as represented in Scheme 1 and the results are summarized in Table 1.

A variety of alkynes were subjected to the cycloaddition reaction with benzyl azide using specific number (50 no's) of Cu(II)-ALG gel beads, which corresponds to an average of 21 mol% of the copper. The reaction of phenylacetylene and benzyl azide in water with 21 mol% of the catalyst resulted in 100% of product, with an exclusive 1,4-regioselectivity. While under similar conditions a blank experiment in water provided only 20% of the product. Similar results are obtained even with sodium alginate in water. These results suggests that the catalytic activity is associated with the immobilized copper(II) ions. Both 3-ethynylanisole and 4-ethynyltoluene having an electron-donating group underwent quantitative conversion with benzyl azide (see Table 1). In the case of aliphatic alkynes, propargyl alcohol gave lower conversion, whereas substituted derivatives resulted in higher yields. Irrespective of the nature of alkynes, complete 1,4-regioselectivity is observed in all the experiments with the present catalyst.

In order to confirm that this process is truly heterogeneous, the catalyst and the product were separated by simple filtration, and the solid mixture

Table 1
Cu(II)-ALG (50 no, 21 mol%) catalyzed 1,3-cycloaddition reactions between terminal alkynes (1.1 mmol) and benzyl azide (1 mmol) in water (3 mL)

Alkyne	%Yield (1, 4-isomer)[a]		
	Cycle 1	Cycle 2	Cycle 3
	> 98,20[b]	> 98	> 98
	> 98	> 98	> 98
	> 98	> 98	> 98
	> 98	> 98	> 98
	> 98	> 98	> 98
	86	83	77

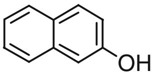
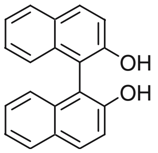
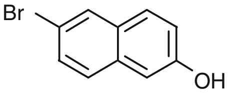
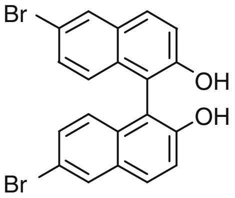
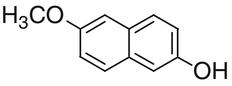
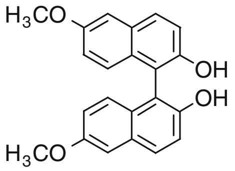
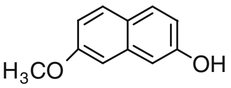
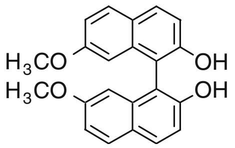
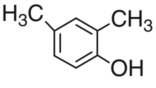
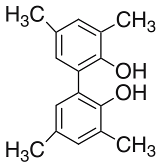
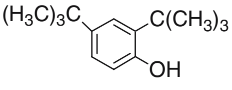
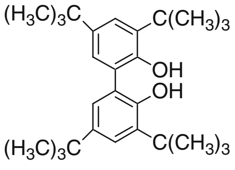
[a]NMR yield based on benzyl azide starting material; [b]With the blank experiment; reaction time = 18 h.

was washed with excess of ethyl acetate to remove product from the catalyst. Though there is a slight decrease in intensity of the color, the gel bead structure of the Cu(II)-ALG catalyst is intact as seen in figure 1b. The change in color of the beads could be because of small amount of copper loss mainly from the surface of the gel beads. These gel beads are directly used for further recycle experiments. From the Table 1, it is very clear that the catalytic activity of the present system is intact even after three cycles. Moreover all the substrates gave an excellent conversion and good regio-selectivity with recovered catalyst. Whereas, with recovered aqueous solution only 23% conversion was observed, which is comparable with blank experiment.

The present Cu(II)-ALG catalyst is further explored for oxidative coupling of 2-naphthols and phenols with air in water. The oxidative coupling of 2-naphthols and phenols has widespread interest, because the resulting products are used as building blocks of many natural products and as ligands for a wide range of organic transformations [19]. Most of the reported catalysts for this reaction are homogeneous in nature. There are only few heterogeneous catalysts using metal ion exchanged zeolites, clays and metal oxides reported in halogenated organic solvents or water [20–23]. The present catalyst shows a very good activity for oxidative coupling of phenols and 2-naphthol derivatives with air in an environmentally benign solvent, water and results are summarized in Table 2. Reaction of 2-naphthol upon

Table 2

Cu(II)-ALG (50 no, 21 mol%) catalyzed oxidative coupling of 2-naphthols/phenols (1 mmol) in water (5 mL)

Substrate	Product	Yield (%)[a]
		83, 82[b]
		79
		86
		76
		64
		61

[a] Isolated yield; [b] Yield after 3rd cycle; reaction time = 18 h; reaction temperature = 100 °C.

treatment with 21 mol% of Cu(II)-ALG catalyst under constant flow of air at 100 °C gave 83% of the BINOL product (see Table 2). All other substituted 2-naphthols derivatives also efficiently proceeded to afford the corresponding BINOL derivatives in 68–76% yields. The present procedure was further applied to the oxidative coupling of substituted phenols, which afforded the coupled products in good yields. The bead structure of the Cu(II)-ALG gels was collapsed under the present conditions, which is in contrary to the cycloaddition reactions performed at room temperature. However, the catalyst recovered after the first cycle shows good activity during the recycle experiments and no reaction was observed with the recovered aqueous solution.

To check the copper leaching in cycloaddition and oxidative coupling reaction, the catalyst and the aqueous solution extracted with ethyl acetate were separately subjected to AAS. For example in cycloaddition reaction between phenylacetylene and benzyl azide it is observed that the amount of copper in the recovered catalyst is 13.22 mg (as against 13.4 mg in the original catalyst), whereas in recovered aqueous solutions it is 0.15 mg which corresponds to the copper leaching of 1.33% and 1.11% respectively. In general the copper leaching in cycloaddition reactions with different substrates was in the range between 0.98 and 1.33%.

Similarly in oxidative coupling reaction with 2-naphthol it is observed that the amount of copper in the recovered catalyst is 13.15 mg (as against 13.4 mg in the original catalyst), whereas in recovered aqueous solutions it is 0.21 mg, which corresponds to the copper leaching of 1.86% and 1.56% respectively. In general the copper leaching in cycloaddition reactions with different substrates was in the range between 1.43 and 1.82%.

4. Conclusion

In conclusion, we have successfully utilized the alginate as a biopolymer support for the synthesis of copper(II) catalyst, which is further applied for 1,3-dipolar cycloaddition of alkynes with azides and oxidative coupling of 2-naphthols and phenols in an environmentally benign solvent, water. The catalyst was recovered quantitatively by simple filtration and reused for several times without significant loss of activity.

Acknowledgments

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