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REGULAR ARTICLE

Multicomponent click reactions catalysed by copper(I) oxide nanoparticles (Cu_2ONPs) derived using *Oryza sativa*

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Abstract. A procedure for the expedient synthesis of well-characterized Cu(I) oxide nanoparticles (Cu_2ONPs) from Cu(II) salts by employing Rice (*Oryza sativa*) as a cheap and ready source of reducing as well as stabilizing agent has been demonstrated. The judicious choice of rice as a catalyst has helped in the symbiotic combination of two events: *viz.,* acidic hydrolysis of starch to form glucose and the subsequent formal reduction of Cu^{2+} by the *in-situ* generated monosaccharide reducing sugar (glucose) under the alkaline condition to produce Cu_2O. Further, rice was also found to be effectively stabilizing the nanoparticles from agglomeration. Optical and microscopic techniques were suitably employed for the characterization of the nanoparticles of approximately 10 nm size. Furthermore, the specifically generated nanoparticles were found to be active catalysts in an aqueous medium for Azide-alkyne Huisgen cycloaddition (Click reaction) under base free condition *via* one-pot multi-component addition for the synthesis of mono-, bis- and tris-1,2,3-triazoles in good to excellent yields.

Keywords. Rice; cuprous oxide; mono-triazoles; bis-triazoles; tris-triazoles.

1. Introduction

In the last few decades, synthesis and application of cuprous oxide nanoparticles (Cu_2ONPs) have been a great point of interest from an economic perspective; Cu_2O, a p-type semiconductor having a bandgap of 1.9–2.2 eV absorbs light in the visible range of the electromagnetic spectrum and has been widely used in the solar energy conversion,[1] water splitting,[2] hydrogen evolution from ammonia-borane,[3] gas sensing,[4] catalysis,[5] templating,[6] lithium-ion batteries,[7] CO oxidation,[8] metal-insulator-metal resistive switching memory,[9] and several others applications. Due to its economical availability, functional diversity and low toxicity, synthesis of Cu_2ONPs as a functional nanomaterial have been pursued enthusiastically all over the world.

In recent years, the preparation of size and morphology specific Cu_2ONPs has been developed by employing various methods such as hydrothermal,[10] wet chemical,[11] solvothermal,[12] polyol,[13] microwave,[14] electrochemical depositions,[15] oxidative etching,[16] reverse micellar,[17] supersaturation[18] and microplasmic methods.[19] For more than a century, it is well known that at basic pH Cu(II) salts undergo reduction to form Cu_2O in the presence of a reducing sugar; a protocol widely in use for the analytical determination of glucose commonly known as Fehling reaction.[20] Adding to the list of methods described earlier, and as an off-spin of the same old basic chemistry, researchers have advantageously re-applied the same protocol for the generation of Cu_2O nanoparticles using glucose as the reducing agent.[21] Succeedingly, several other reducing agents such as ascorbic acid,[21e,22] hydrazine hydrate,[23] sodium borohydride,[24] and leaf extracts of *Tridax procumbens*,[25] lignin[26] have been introduced. Although most of these procedures involving reducing sugars were carried out at relatively milder reaction conditions while compared to other methods such as hydrothermal or electrochemical deposition, they still require the involvement of coordinating agents, surfactants and stabilizers either as stabilizing or as morphology directing agents. Therefore,

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a robust preparative method devoid of or with minimal use environmentally benign additives is highly desirable.

Within the boundary of click chemistry, the independent discovery of azide-alkyne cycloaddition (CuAAC) by Sharpless[27] and Meldal[28] has drawn immense attention towards utilization of various copper(I) salts as highly active catalysts for this vital organic transformation. CuAAC has been increasingly applied for the facile syntheses of agrochemicals,[29] pharmaceuticals,[30] polymers[31] and many other functional materials[32] due to its reliability, specificity and biocompatibility. Some of the prominent Cu(I) systems[28] for azide-alkyne cycloaddition (AAC) includes, $CuSO_4$-ascorbate system,[33] ligands supported Cu(I)/(II) and Cu-coordination complex,[34] polymer-supported Cu(I),[35] Cu(I)-zeolite,[36] copper nanoparticles,[37] metallic copper turning,[38] magnetic copper-iron nanoparticles,[39] magnetic nano-Fe_3O_4@-TiO_2/Cu_2O,[40] graphene supported Cu_2O nanoparticles,[41] charcoal supported Cu_2O nanoparticles,[42] and Cu_2O micro/nanoparticles.[43] All the above copper-based catalysts show good activity towards AAC reactions, however, they still require external addition of additives such as a surfactant, coordinating agent, polymers or solid support material.

In this study, we report the synthesis of a surfactant (or polymer) free Cu_2ONPs by making use of easily accessible home-available rice as a dual functioning agent, both as an *in-situ* generated source of reducing and stabilizing agents. Further, the synthesized Cu_2ONPs have been employed as an efficient catalyst in three-component click reactions for the synthesis of regio-selective 1,4-disubstituted 1,2,3-triazoles in water. The substrate scope includes synthesis of mono-,bis- and tris-1,4-disubstituted 1,2,3-triazoles with good to excellent yields.

2. Experimental

2.1 *Materials and Physical measurements*

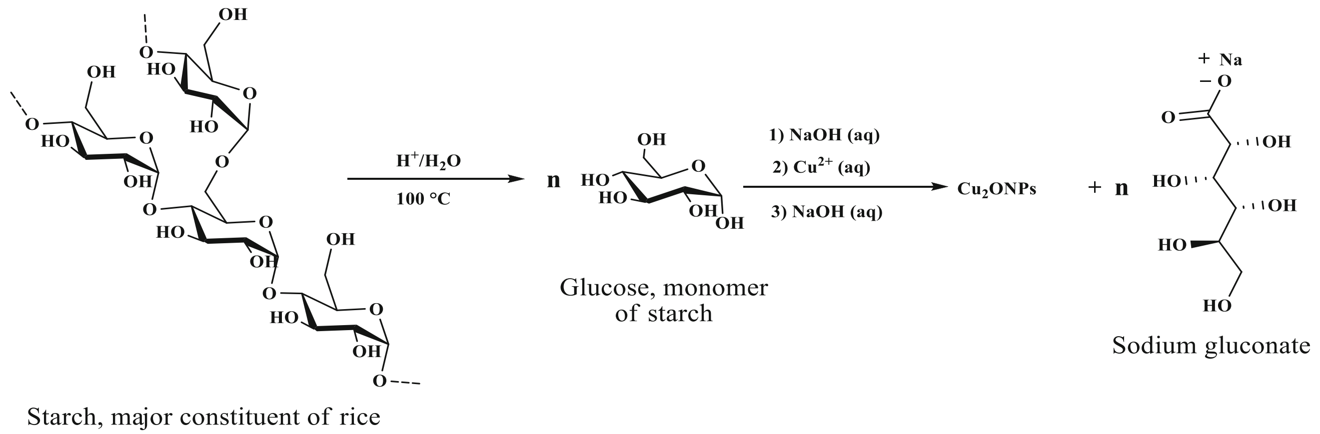
$CuSO_4.5H_2O$ was purchased from Finar Chemicals, India. NaOH from Merck, India, Conc. H_2SO_4 from Fischer Scientific, India. Organic precursors were purchased from Sigma Aldrich. Common solvents were obtained from SRL, India and used without further purification. Double distilled water was used as a solvent for the synthesis of Cu_2ONPs and for carrying out AAC reactions. UV-vis spectra of sample were recorded using JASCO V-650 Bio instrument. Powder XRD patterns were obtained using a Bruker D8 Avance instrument. Cu_2ONPs sample suitable for FE-SEM and TEM studies were prepared by the dip and lift-off methods. In a typical procedure, the sample was dispersed in distilled water by sonication and the silicon wafer/TEM grids were dipped into it with help of forceps and lifted it off, allowed it to air dry. FE-SEM images of Cu_2ONPs were recorded with a FEG-Quanta 400. XPS of Cu_2ONPs was recorded with a PHI Versa probe II with scanning XPS microprobe with a monochromatic Al Kα source (1486.6 eV). Thermal properties of synthesised Cu_2ONPs were studied on TGA7 (PerkinElmer) and DSC7 (PerkinElmer). ^{1}H NMR and ^{13}C NMR spectra of the products obtained from the click reactions were recorded on a Bruker Avance 400 MHz NMR or Bruker Avance 500 MHz NMR instruments. HR mass of unreported compounds was recorded using High-Resolution Q-Tof Mass.

2.2 *Synthesis of the Cu_2ONPs using rice*

In a typical procedure, 1.0 g of rice and 10 mL water (doubled distilled) was taken in a 100 mL round bottom flask followed by slow addition of 1.0 mL conc. H_2SO_4. The mixture was heated at 100 °C for one hour with continuous stirring. 10 mL of 5 N NaOH (aq) was added dropwise to neutralize (pH = 7, checked using pH paper) the acid. 1.25 g $CuSO_4.5H_2O$ dissolved in 20 mL water was added to the above reaction mixture followed by addition of 2.5 mL of 5 N NaOH. Stirring was continued at the same temperature for another one hour when the yellow coloured product (Cu_2ONPs) was observed to be formed. The reaction mixture was then cooled to room temperature and the product was collected by centrifugation, after being washed with water twice and dried under vacuum at room temperature.

2.3 *General procedure for the one-pot synthesis of mono-1,2,3-triazoles*

In a 50 mL round-bottomed flask benzyl bromide (1 mmol, 1 equiv.), NaN_3 (1.2 mmol, 1.2 equv.), a terminal alkyne (1.2 mmol, 1.2 equv.) and 5 mg Cu_2ONPs were placed in water (10 mL). The mixture was magnetically stirred under reflux (100 °C) for 30 min. The progress of the reaction was monitored by TLC or by visual inspection of the formation of solid products. After completion of the reaction, the mixture was cooled to room temperature and the solution was decanted. To the leftover residue, ethyl acetate (2 × 10 mL) was added, organic material dissolved in it and catalyst was recovered by centrifugation. The solution was evaporated to dryness using a rotary evaporator, and the crude product thus obtained was purified by short column chromatography with silica gel. The identities of the isolated compounds were confirmed by either matching the spectroscopic data of the compounds already reported in the literature and unreported compounds were further confirmed by recording HRMS.



Scheme 1. Proposed mechanism for the formation of Cu_2ONPs using hydrolysed rice.

2.4 *General procedure for the one-pot synthesis of mono-1,2,3-triazoles bearing one free acetylene*

In a 50 mL round-bottomed flask benzyl halide (1 mmol, 1 equiv), NaN_3 (1.2 mmol, 1.2 equiv.), diethynylbenzene (1 mmol, 1 equiv.) and 5 mg Cu_2ONPs were taken along with 10 mL water. The mixture was magnetically stirred under reflux condition (100 °C) for 30 min. Progress of the reaction was monitored by TLC and after completion of reaction products were purified *via* column chromatography.

2.5 *General procedure for the synthesis of bis-1,2,3-triazoles (Method-1)*

In round-bottomed flask α,α′-dibromo-p-xylene (0.5 mmol, 1 equiv.), NaN_3, (1.2 mmol, 1.2 equiv.), terminal alkyne (1.2 mmol, 1.2 equiv.) and 5 mg Cu_2ONPs were taken in water (10 mL). The mixture was magnetically stirred under reflux (100 °C) for 60 min. The progress of the reaction was monitored by the formation of solid on the wall of the reaction container. After completion of the reaction, the mixture was cooled to room temperature and the solution was decanted. The leftover residue was washed with dil. $NH_4Cl : NH_3$ solution (2 × 10 mL) whereupon copper got removed as blue colour copper-amine species followed by washing with ethyl acetate (2 × 10 mL) and the remaining solid product was dried under vacuum.

2.6 *General procedure for the synthesis of bis-1,2,3-triazoles (Method-2)*

The above-mentioned procedure was followed using 1,3-diethynylbenzene or 1,4-diethynylbenzene (0.5 mmol, 1 equiv.), benzyl bromide (1.2 mmol, 1.2 equiv.) sodium azide (1.2 mmol, 1.2 equiv.) and 5 mg Cu_2ONPs.

2.7 *General procedure for the synthesis of tris-1,2,3-triazoles*

In a round-bottomed flask 1,3,5-tris(bromomethyl)benzene (0.5 mmol. 1 equiv.), NaN_3, (1.8 mmol, 1.8 equv.), terminal alkyne (1.8 mmol, 1.8 equiv.) and 5 mg Cu_2ONPs were taken in water (10 mL). The mixture was magnetically stirred under reflux (100 °C) for 120 min. Monitoring the progress of the reaction and extraction of products was carried out by the above-mentioned procedure.

2.8 *Recyclability of catalyst*

In a 50 mL round-bottomed flask, benzyl bromide (3 mmol.), NaN_3 (3.6 mmol, 1.2 equiv.), terminal alkyne (3.6 mmol, 1.2 equiv.) and 15 mg Cu_2ONPs were placed in water (30 mL). The mixture was magnetically stirred under reflux (100 °C) for 30 min. After completion of the first reaction run, the product was extracted in ethyl acetate and purified by column chromatography to obtain the pure product. The aqueous layer which was collected by phase separation was centrifuged for 30 min at 2500 rpm and the catalyst was reused for next run. Following the same procedure, the subsequent experimental runs were performed and the catalyst was reused up to four cycles.

3. Results and Discussion

3.1 *Mechanism of Cu_2ONPs formation*

Major chemical constituent of rice is starch, a polymer of glucose, that is a reducing sugar. Reducing sugar content of rice was analysed by adopting dinitrosalicylic acid (DNS) protocol.[44] Scheme S1 (Supplementary Information) gives the summary of the reaction and condition for estimation of sugar content

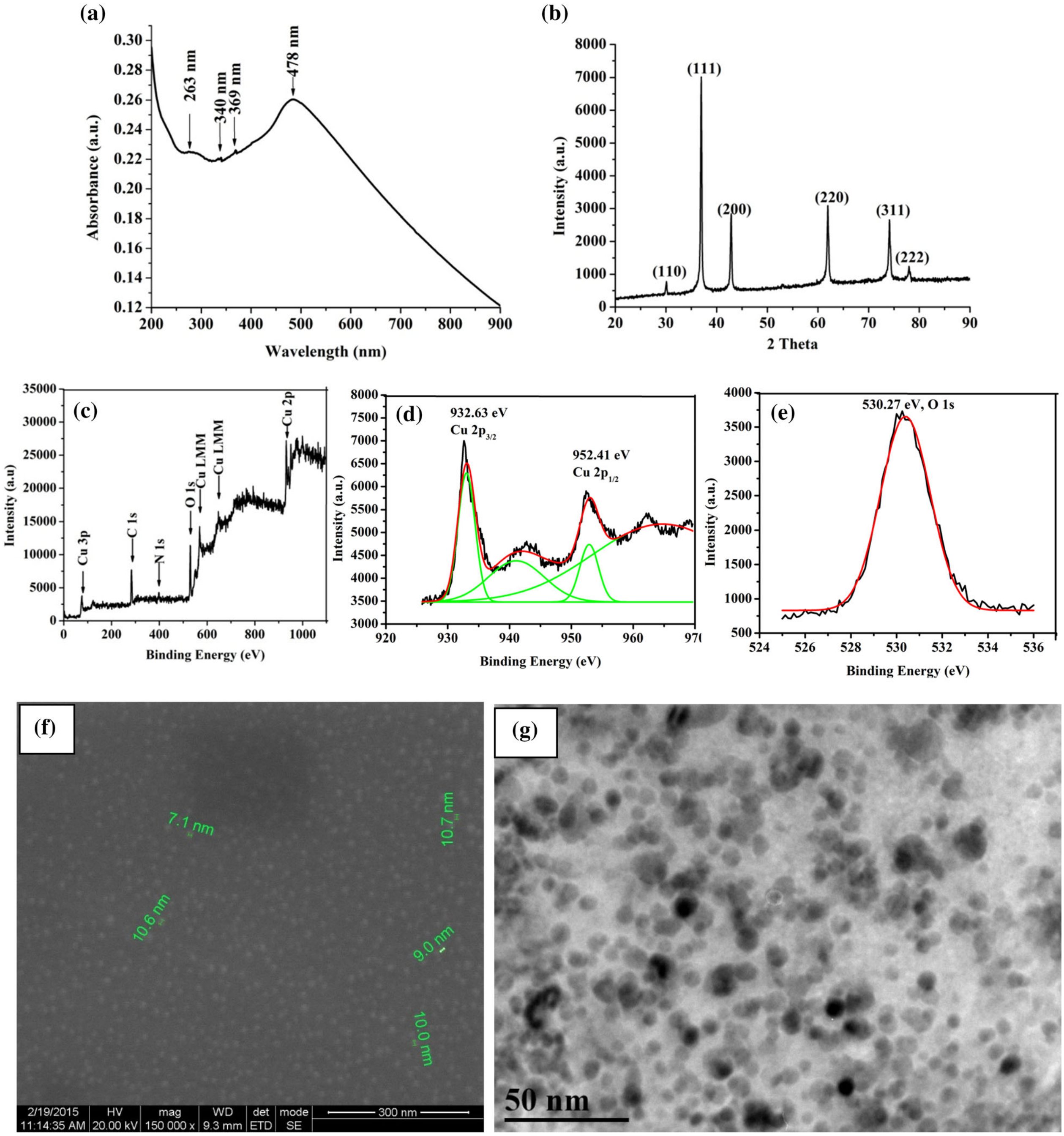


Figure 1. Characteristic feature of synthesized Cu_2ONPs (a) UV-Vis spectrum of Cu_2ONPs, (b) Powder XRD pattern of Cu_2ONPs, (c) XPS survey spectrum, (d) XPS high-resolution Cu 2p spectrum, (e) XPS high-resolution O 1s spectrum, (f) SEM image of Cu_2ONPs and (g) TEM image of Cu_2ONPs.

in rice. Cu_2ONPs was synthesised by cross-fertilizing the concepts of acidic hydrolysis of starch to give glucose and the property of alkaline Cu^{2+}(aq) to undergo reduction in the presence of glucose. On acidic agitation, (100 °C) glycosidic bonds of starch (rice) undergo cleavage to give its constituent monosaccharide (glucose). After one hour hydrolysis of rice, the reaction mixture was brought up to neutral pH by slow addition of NaOH (aq) followed by addition of Cu^{2+}(aq) with continuous stirring and then treatment with NaOH (aq) to increase the pH (8–9) to basic (Scheme 1).

Within 20 min, the colour of reaction mixture turned to yellow indicating the formation of Cu_2ONPs. Hydrolysed rice exhibited dual role, reduction of Cu^{2+} species at basic pH and stabilizations of formed Cu_2ONPs. Before adding Cu^{2+} (aq) to neutral hydrolysed rice mixture, 1 mL sample was collected and HR-MS was recorded which shows the existence of glucose in the reaction mixture (Figure S2a). After isolating Cu_2ONPs, the remaining aqueous phase was neutralized by slow addition of dilute H_2SO_4 and again HR-MS was recorded, which shows the existence of gluconic acid (Figure S2b) that is the oxidised product of glucose. These results clearly indicate that glucose from hydrolysed rice reduces Cu^{2+}(aq) to afford Cu_2O and it-self gets oxidised.

Various methods for synthesis of Cu_2ONPs were developed by many researchers which involved the use of commercial stabilizing agents (surfactants, polymers or ligands) or reducing agents ($NaBH_4$, Hydrazine hydrate, ascorbic acid, etc.) or both.[10–18] Du *et al.,* synthesized Cu_2ONPs with the size about 400–600 nm in water:ethylene glycol (1:1) solvent by microplasma method.[19] Li *et al*., synthesized Cu_2ONPs using lignin as both reducing and capping agents, with particle size in the range of 100–200 nm.[26] In our case, without making use of any commercial stabilizing agents and reducing agents, we got homogeneous particles size distribution in the range of 9–10 nm. Hence, the methods developed in the present case for the synthesis of Cu_2ONPs are economical and the size distribution is homogeneous.

3.2 *Characterization of synthesised Cu_2ONPs*

The UV-Vis spectrum of Cu_2ONPs (Figure 1a) shows a characteristic absorption feature at 478 nm, blue shift compared to bulk Cu_2O.[45] This blue shift in the UV-visible absorption spectrum is the confirmation for nano-sized particles with an increase in the bandgap to 2.59 eV compared to the theoretical direct bandgap, 2.137 eV (bulk Cu_2O). The bandgap measurement was done by using the formula $E_g = hc/\lambda$ where h is the Planck's constant, c is the speed of light and λ is the wavelength at which the synthesised Cu_2ONPs show a characteristic absorption pick. The absorption peak at 369 nm corresponds to particle size of dimension 2–3 nm and the peaks at 263 nm and 340 nm correspond to O-Cu-O and Cu-O-Cu charge transfer bands.[46,47] Powder X-Ray diffraction (Figure 1b) shows the entire characteristic Bragg's reflection at appropriate 2θ, (110), (111), (200), (220), (311) and (222). The obtained XRD results are consistent with the values in the standard Joint Committee on Powder Diffraction Standards (JCPDS No. 05-0667).[21d] Valance state of synthesised Cu_2ONPs was further conformed by XPS, X-ray photoelectron spectroscopy (Figure 1c–e). In the full scan spectrum, binding energy peak appears around 282, 401, 531 and 933 eV corresponding to Carbon (C 1s), Nitrogen (N 1s), oxygen (O 1s) and copper (Cu 2p), respectively. Detection of $Cu2p_{3/2}$ and $Cu2p_{1/2}$ peaks position at 932.63 and 952.41 eV respectively, indicate the existence of cuprous ion (Cu^+) and O 1s core level peak at 530.27 eV combined together confirm, the sample was Cu_2O and the results are in good agreement with the data in the literature.[23b,26,48] SEM image (Figure 1f) and TEM image (Figure 1g) show homogeneous particle size distribution of average particle size of 9–10 nm. Thermogravimetric analysis (TGA) curve and derivative of weight as a function of temperature show a small weight loss 2.5% at 147 °C and total weight loss till 228 °C appear to be around 4.2%, which may be due to the presence of low molecular weight biochemical content of rice. Major carbohydrate content loss was observed in the range of 250–450 °C, a total of 14.4% (Figure 2).

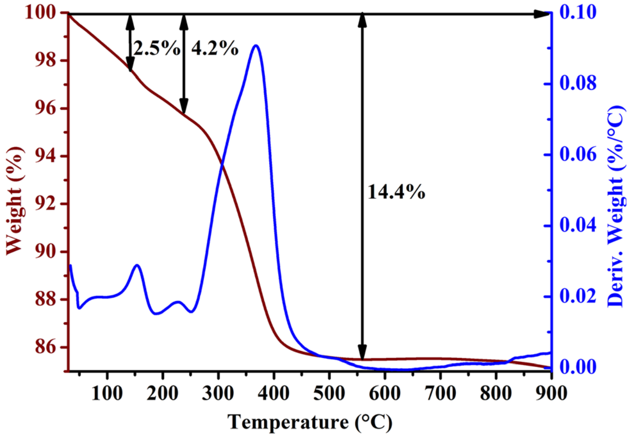
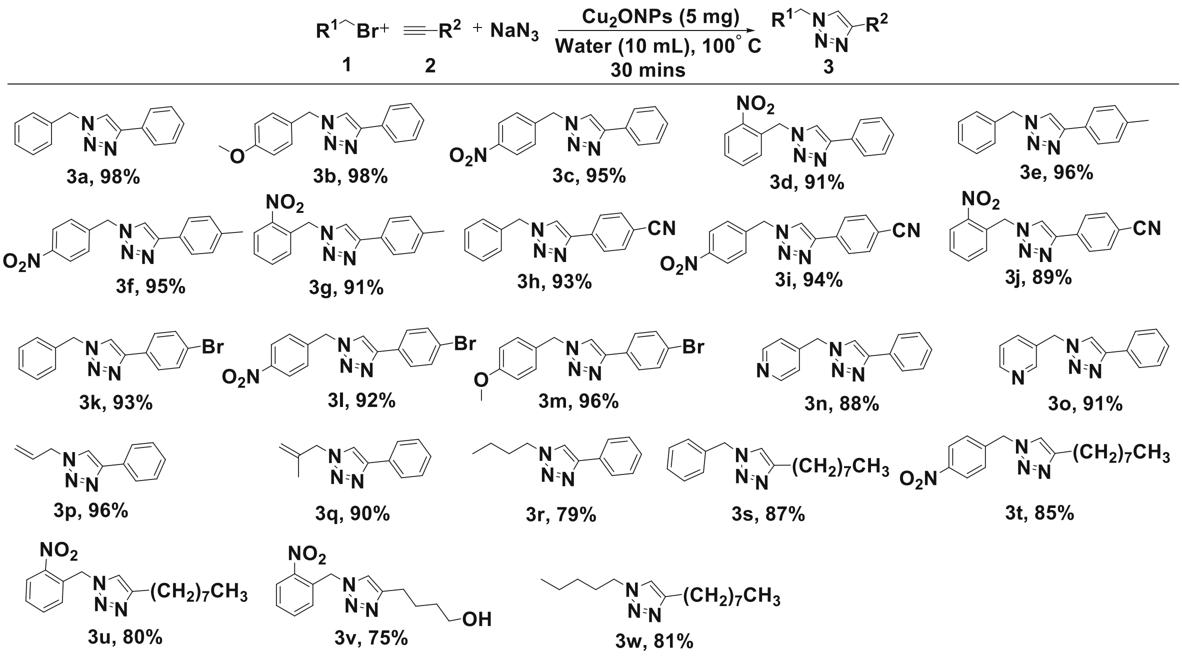


Figure 2. TGA and Derivative weight loss curve of Cu_2ONPs.

3.3 *Catalytic study using synthesised Cu_2ONPs towards 1,2,3-triazole formation*

Many researchers have synthesized mono-, bis- and tris-1,2,3-triazoles using Cu_2ONPs and Cu_2O based catalysts. Zhang *et al.*,[35d] López-Ruiz *et al.*,[42] Zhang *et al.*,[43a] and Jiang *et al.*,[43c] have synthesized mono-1,4-disubstituted 1,2,3-triazoles *via* cycloaddition of chosen organic azides and acetylenes. Nemati *et al.*,[40] Roy *et al.*,[41c] Tsai *et al.*,[43b] and Chanda *et al.*,[43d] have synthesized mono-1,4-disubstituted 1,2,3-triazoles *via* one-pot multicomponent reactions. Synthesis of bis- and tris-1,2,3-triazole have been reported via click reaction between organic azides and acetylenes.[41a,43b] Here, rice-mediated synthesised Cu_2ONPs was used as an efficient catalyst for the synthesis of all the three mono-, bis- and tris-1,2,3-triazoles in water *via* one-

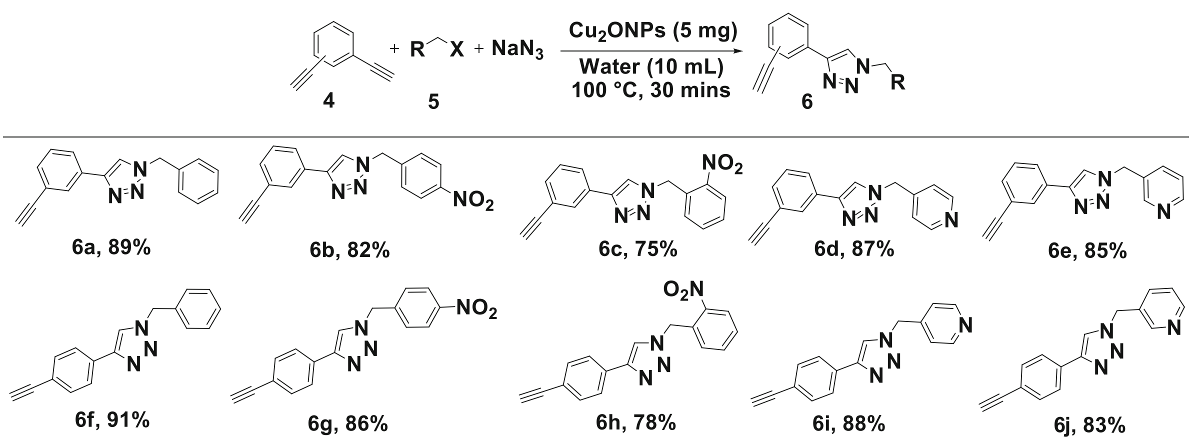
Table 1. Cu_2ONPs catalysed azide-alkyne cycloaddition to prepare mono-triazoles using in-situ generated benzyl azide and terminal alkyne[a]



3a, 98%; 3b, 98%; 3c, 95%; 3d, 91%; 3e, 96%; 3f, 95%; 3g, 91%; 3h, 93%; 3i, 94%; 3j, 89%; 3k, 93%; 3l, 92%; 3m, 96%; 3n, 88%; 3o, 91%; 3p, 96%; 3q, 90%; 3r, 79%; 3s, 87%; 3t, 85%; 3u, 80%; 3v, 75%; 3w, 81%

Reaction condition: Alkyl hallide (1 mmol), acetylene (1.2 mmol), Sodium azide (1.2 mmol); [a]Isolated yield

Table 2. Synthesis of mono-triazoles bearing one free acetylene group on substrate via one-pot multi component reaction catalysed by Cu_2ONPs.[a]

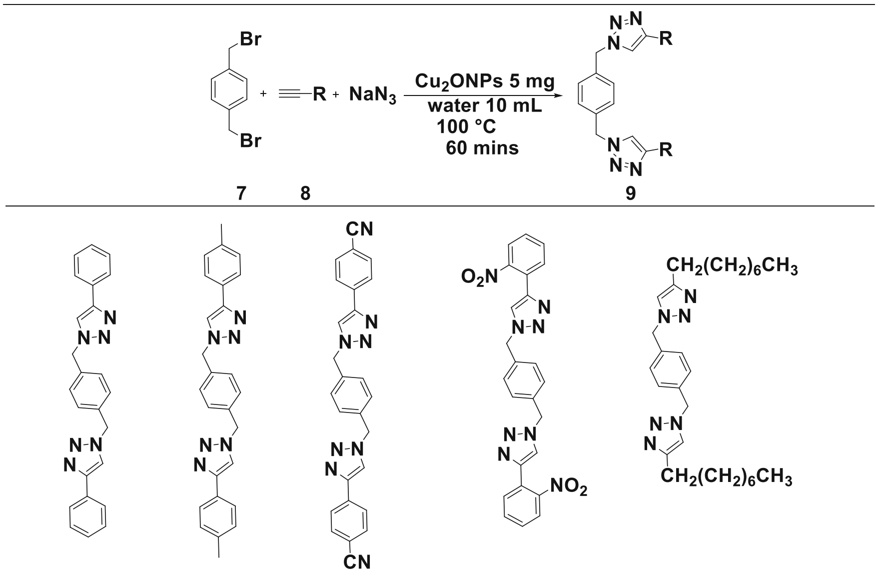


6a, 89%; 6b, 82%; 6c, 75%; 6d, 87%; 6e, 85%; 6f, 91%; 6g, 86%; 6h, 78%; 6i, 88%; 6j, 83%

Reaction condition: Alkyl hallide (1 mmol), acetylene (1.2 mmol), Sodium azide (1.2 mmol); [a]Isolated yield.

pot multicomponent reactions. The synthesized bis- and tris-1,2,3-triazole can be used as polydentate ligands for research in supramolecular coordination chemistry. 5 mg of Cu_2ONPs was used in each transformation. Good to the excellent yields of desired products were obtained. In the case of mono triazole synthesised product, the catalyst recovery was very much feasible, as the product were soluble in ethyl acetate. After completion of the reaction, the product was extracted in ethyl acetate, dried by adding

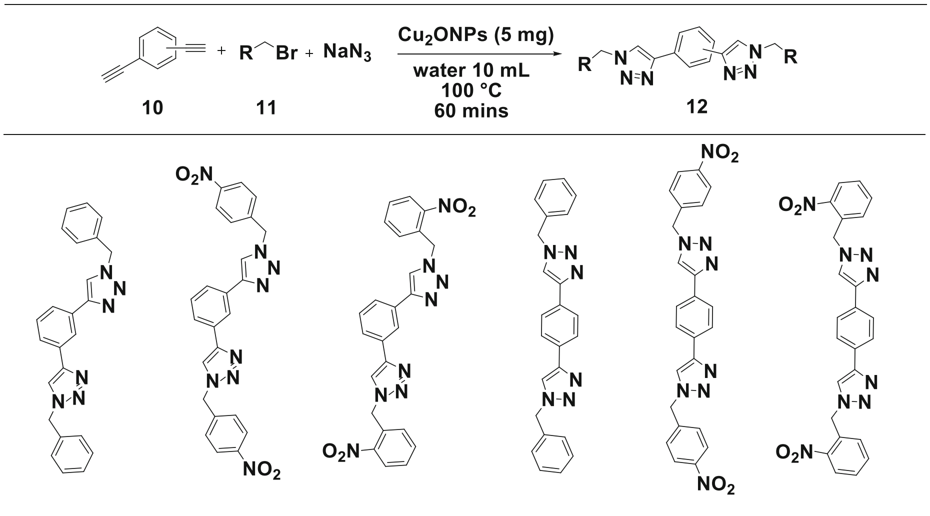
Table 3. Synthesis of bis-triazoles (method-1) *via* one-pot multi component reaction catalysed by Cu_2ONPs^a



9a, 84% 9b, 85% 9c, 81% 9d, 72% 9d, 80%

Reaction condition: α-α' dibromo-p-xylene (0.5 mmol), acetylene (1.2 mmol) and NaN_3 (1.2 mmol);
[a]Isolated yield

Table 4. Synthesis of bis-triazoles (method-2) *via* one-pot multicomponent reaction catalysed by Cu_2ONPs^a

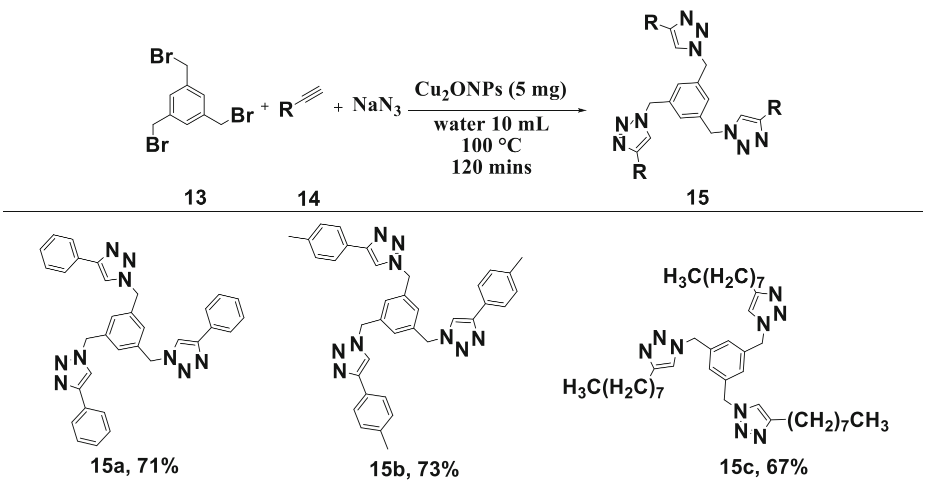


12a, 82% 12b, 80% 12c, 75% 12d, 84% 12e, 80% 12f, 77%

Reaction condition: diacetylene (0.5 mmol), alkyl bromide (1.2 mmol) and NaN_3 (1.2 mmol);
[a]Isolated yield

anhydrous sodium sulphate and purified by column chromatography. For mono triazole products, in almost all cases the reactions proceeded smoothly to completion within 30 min. The presence of hetero ring and functional group ($-CH_3$, $-OCH_3$, $-NO_2$, -CN, etc.) on either of the substrate did not affect the product formation. The triazoles **3n** and **3o** of Table 1 and the triazoles **6d**, **6e**, **6i** and **6j** of Table 2, were prepared using the free bases 4-(chloromethyl)pyridine and 3-(chloromethyl)pyridine that were extracted from

Table 5. Synthesis of tris-triazoles *via* one-pot multicomponent reaction catalysed by Cu_2ONPs^a



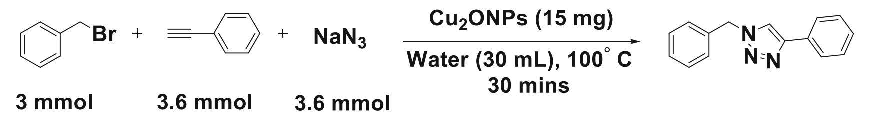
15a, 71%

15b, 73%

15c, 67%

Reaction condition: 1,3,5-tris(bromomethyl)benzene (0.5 mmol), acetylene (2 mmol), NaN_3 (2 mmol); ^{a}Isolated yield

Table 6. Recycling of catalyst



No. of cycles	Yields (%)^a
1	98
2	95
3	91
4	83

^{a}Isolated yield

their hydrochloride salts. Hex-5-yne-1-ol (Table 1, entry 3v) gave lesser yield, maybe free hydroxyl group reacts with benzyl bromide as a competitive substrate against sodium azide. In case of bis-triazoles (Tables 3 and 4) and tris-triazoles (Table 5), as the desired product were insoluble in light and volatile solvent the product isolation were at the cost of catalyst recovery but it was free from purification technique. For the synthesis of mono-1,2,3-triazoles, the catalyst was reused up to four cycles (Table 6). With an increase in the number of recycling of catalyst, a decrease in the yield of product was observed. For practical application, reusability of catalyst is a vital parameter. To study this parameter, a new set of the reaction was performed by increasing the reaction constituents (benzyl bromide, sodium azide, phenylacetylene, Cu_2ONPs and water) by three-fold. By increasing the reaction constituents, it's become easier to isolate the catalyst after each cycle with minimal loss. We successfully reused the catalyst up to four cycles without significant loss of product yield (Table 6). The decrease of yield in successive cycles may be attributed to the agglomeration of nanoparticles as observed in TEM image (Figure 3) after the first cycle.

4. Conclusions

We have synthesized Cu_2ONPs with homogeneous particle size distribution (9–10 nm) using rice as a source of reducing and stabilizing agents by cross-fertilizing the concept of acidic hydrolysis of starch (polysaccharides) to give corresponding monosaccharide (glucose) and Fehling reactions. The catalytic

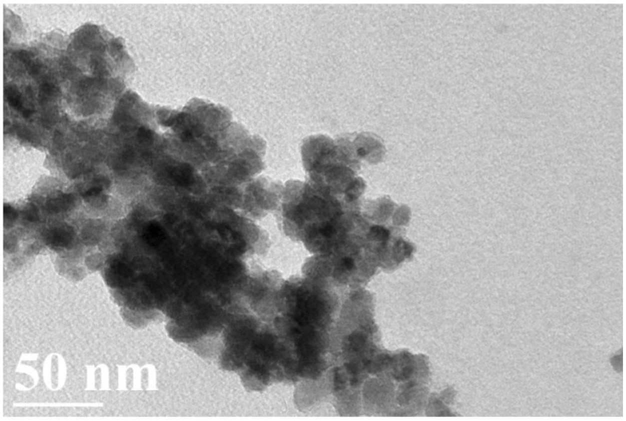


Figure 3. TEM image of Cu_2ONPs after first recycling.

activity of synthesised Cu_2ONPs was explored towards the synthesis of mono-1,4-disubstituted 1,2,3-triazoles, bis-1,4-disubstituted 1,2,3-trizoles and tris-1,4-disubstituted 1,2,3-triazoles *via* one-pot multi-component click reactions, in good to excellent yields. The catalyst was recycled up to four cycles without significant loss in yields. The synthesized bis-1,4-disubstituted 1,2,3-trizoles and tris-1,4-disubstituted 1,2,3-triazoles can be used as polydentate ligands for research in supramolecular chemistry.

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