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COMMUNICATION

Copper Nanoparticles Generated by Aggregates of Hexarylbenzene derivative: A Reusable Catalyst for 'Click' Reaction

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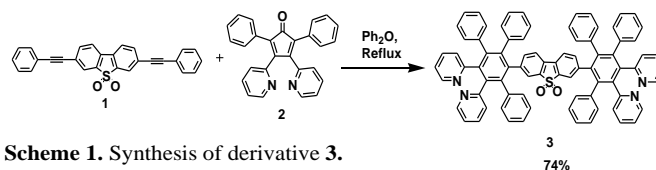
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Fluorescent aggregates of hexarylbenzene derivative 3 have been utilized as reactors for the preparation of copper nanoparticles in aqueous medium which serve as effective catalyst for alkyl-azide 'Click' reaction to synthesize 1,2,3-triazoles in excellent yields under solvent free condition. These nanocatalysts can be recycled and reused five times without significant loss of catalytic activity.

Copper catalyzed Huisgen-type-azide-alkyne 1,3-cycloaddition (CuAAC) reaction is the most efficient method for the synthesis of 1,2,3-triazole derivatives which have found widespread industrial applications as agro chemicals, dyes, corrosion inhibitors, optical brighteners, photographic materials etc.¹ This method for the synthesis of 1,2,3-triazole derivatives mimics the approach used by nature to generate important compounds. Since its discovery in 2002, a number of "CuAAC" procedures have been developed for making the synthesis of 1,2,3-triazoles more efficient and environment friendly and reaction mechanism of "click reaction" is getting matured.² In most of the "CuAAC" reactions, the Cu^I species is generated from CuSO₄ and sodium ascorbate, however, main problem is requirement of large quantity of metal catalyst which makes its removal difficult in the latter stage.³ Recently, much attention has also been paid to the use of copper nanoparticles (CuNPs) as catalyst in "CuAAC" reaction to synthesize 1,2,3-triazole, however, most of these reactions require reductants, organic solvents and high loadings of CuNPs.⁴ Very recently, amphiphilic dendrimer has been used as a catalytic nanoreactors which accelerate the "CuAAC" reactions of various substrates in water by utilizing relatively small loading of CuSO₄.⁵ However multisteps are required for the synthesis of amphiphilic dendrimer. Thus, development of reductant and solvent free more efficient catalytic method for "click reaction" requiring small amount of copper loading is still a challenge.

Our research work involves development of supramolecular assemblies and their utilization as reactors for the preparation of metal nanoparticles. Recently, we developed aggregates of hexaphenylbenzene derivative and utilized them as reactors for the preparation of ferromagnetic iron oxide (α -Fe₂O₃) nanoparticles.⁶ These nanocatalysts exhibited excellent catalytic activity in palladium, copper and amine free Sonogashira cross coupling reactions. In continuation of this work, we were then interested in the development of nanocatalysts for carrying out reducing agent



Scheme 1. Synthesis of derivative 3.

and solvent free "click reaction". It has been reported that for efficient click reaction, use of Cu^I species activated by nitrogen ligands is advantageous as such systems do not require any reductant and above all small amount of catalyst is generally needed.⁷ Keeping this in mind, we have designed and synthesized derivative 3 in which two hetero-oligophenylene units have been connected through a dibenzothiophene-S,S-dioxide moiety. We expected that presence of two oligophenylene groups could impart aggregation induced emission enhancement characteristics (AIEE) to the molecule. Further, pyridyl groups were incorporated in the molecule as these groups are well known for binding with copper ions.⁸ Based on this design strategy, we believed that these aggregates of derivative 3 could work as reactors for the generation of stable CuNPs which could be utilized for "CuAAC" reactions. As expected, derivative 3 exhibited AIEE characteristics and formed fluorescent aggregates in aqueous media which served as reactors for the preparation of stable CuNPs. To our pleasure, *in situ* generated CuNPs served as efficient, fast, reusable catalyst for carrying out "CuAAC" reaction under solvent free conditions. To the best of our knowledge, this is the first report where *in situ* generated CuNPs have been used for carrying out click reaction under solvent free condition. Further, the method being reported in the present manuscript for preparation of CuNPs is convenient over other methods reported in the literature.⁹

The hexarylbenzene derivative 3 was synthesized by the Diels-Alder reaction of 3,7-bis(phenylethynyl)dibenzo[b,d]thiophene 5,5-dioxide 1¹⁰ with 2,5-diphenyl-3,4-di(pyridin-2-yl)cyclopenta-2,4-dienone 2⁸ in diphenylether at 240°C in 74% yield (Scheme 1). The structure of derivative 3 was confirmed from its spectroscopic and analytical data (see ESI†, PS5-S7). The ¹H NMR spectrum of compound 3 showed two doublets at 8.14 and 7.05 ppm, one singlet at 7.11 ppm and four multiplets at 7.17-7.21, 6.94-6.96, 6.83-6.92 and 6.73-6.76 ppm corresponding to aromatic protons. A parent ion peak for M + H⁺ was observed at m/z 1133.38 in the electrospray ionization mass (ESI-MS) spectrum. These spectroscopic data corroborate the structure 3 for this compound.

The UV-vis absorption spectrum of derivative **3** in CH₃CN exhibits two absorption bands at 260 and 310 nm (Supporting Information, Fig. S4). However, in the presence of 50% H₂O in CH₃CN, the intensity of entire absorption spectra is gradually increased with the appearance of a level-off tail in the visible region (400–500 nm) that is attributed to the Mie scattering due to formation of aggregates (see ESI†, Fig. S4).¹¹ The formation of aggregates of derivative **3** was supported by a scanning electron microscopy (SEM) image of derivative **3** in H₂O/CH₃CN (1/1) which showed the presence of doughnut shaped aggregates (see ESI†, Fig. S5). The dynamic light scattering (DLS) studies also indicated the formation of aggregates having average diameter in the range of 400 nm (see ESI†, Fig. S6). The fluorescence spectrum of derivative **3** in CH₃CN exhibits an emission band at 390 nm ($\phi_0 = 0.11$)¹² when excited at 300 nm (see ESI†, Fig. S7). Upon addition of water fraction up to 50% (volume fraction) to the solution of **3** in CH₃CN, enhancement in emission intensity is observed and the emission band at 390 nm is red shifted to 405 nm ($\phi = 0.47$) (see Fig. S7 in ESI†). Further, an increase in fluorescence intensity of compound **3** is observed with increasing fraction of triethyleneglycol (TEG) (see ESI†, Fig. S8) and also with increasing concentration of compound **3** in CH₃CN (see ESI†, Fig. S9). These studies support the AIEE characteristics of the derivative **3**. The time-resolved fluorescence studies (Fig. S10, Supporting Information) showed that there is very small difference between fluorescence radiative rate constants¹³ (k_f) of derivative **3** in CH₃CN and in H₂O/CH₃CN (5:5, v/v) solvent mixture, however, large decrease in case of non-radiative decay constant (k_{nr}) was observed from $1.58 \times 10^9 \text{ S}^{-1}$ to $0.22 \times 10^9 \text{ S}^{-1}$ (see for PS11, in ESI†). From these results, we conclude that the deactivation of nonradiative decay due to restriction in the intramolecular rotational relaxation of the rotors linked to the core in case of derivative **3** is the principal reason of the AIEE phenomena.

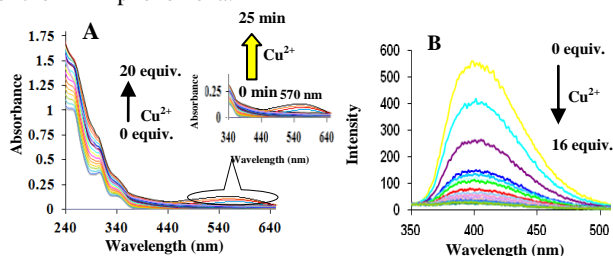


Figure 1. (A) UV-vis spectra of derivative **3** (1 μM) upon additions of 20 equiv. of Cu²⁺ ions in H₂O/CH₃CN (1/1). Inset showing appearance of a new band at 570 nm (B) Change in the fluorescence spectra of compound **3** (1 μM) upon additions of Cu²⁺ in H₂O/CH₃CN (1/1) buffered with HEPES, pH = 7.0; $\lambda_{\text{ex}} = 300 \text{ nm}$

The binding behaviour of aggregates of derivative **3** was studied toward different metal ions (Cu²⁺, Fe²⁺, Fe³⁺, Hg²⁺, Co²⁺, Pb²⁺, Zn²⁺, Ni²⁺, Cd²⁺, Ag⁺, Ba²⁺, Mg²⁺, K⁺, Na⁺, and Li⁺) as their perchlorates/chloride salts, by UV-vis and fluorescence spectroscopy. In UV-vis studies, upon addition of Cu²⁺ ions (20 equiv.) to the solution of derivative **3** (1 μM) in mixed aqueous media (H₂O/CH₃CN, 1/1), an increase in the absorbance over entire spectral range from 250 to 500 nm is observed which suggest interaction between aggregates of derivative **3** and Cu²⁺ ions (Fig. 1A). A new broad absorption band at 570 nm is attributed to the Surface Plasmon excitation of Cu particles, which indicates the formation of CuNPs (Inset, Fig. 1A).¹⁴ In the fluorescence spectrum, on addition of Cu²⁺ ions to the solution of aggregates of derivative **3** in mixed aqueous media (H₂O/CH₃CN, 1/1), a significant quenching of the emission signal was observed (Fig. 2B). As for Cu²⁺, because of its paramagnetic property and unfilled d shell, Cu²⁺ could strongly quench the fluorescence of the derivative **3** through electron and/or energy transfer processes.¹⁵ The calculated Stern–Volmer constant of

aggregates of derivative **3** was $5 \times 10^5 \text{ M}^{-1}$ (see ESI†, Fig. S11) with lowest detection limit of 37 nM for Cu²⁺ ions (see ESI†, Fig. S12). Under the same conditions as used for Cu²⁺ ions, we also tested the fluorescence behavior of aggregates of **3** toward other metal ions but no significant change in fluorescence intensity was observed (see ESI†, Fig. S13).

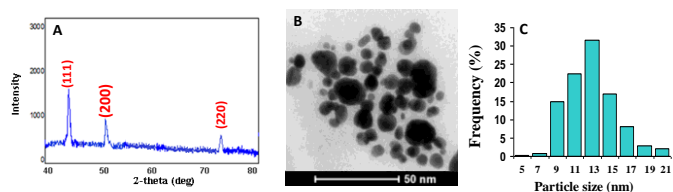


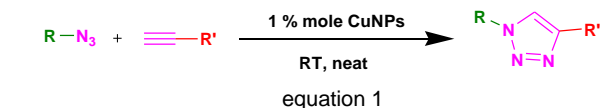
Figure 2. (A) The powder X-ray diffraction (XRD) analysis of the copper nanoparticles. (B) TEM (Tunneling electron microscopy) images of spherical copper nanoparticles. (C) On right side of these image their respective particle size distribution histogram.

To get insight into the mechanism of formation of CuNPs, we slowly evaporated the solution of aggregates of derivative **3** containing CuNPs. After several days, precipitates were observed. The precipitates were filtered and washed with CHCl₃ and THF. The ¹H NMR spectrum of the residue so obtained after evaporation of solvent showed the upfield shifting of aromatic signals (see ESI†, Fig. S14). On the basis of above results, we suggest that upon addition of Cu²⁺ ions to the solution of aggregates of derivative **3**, the copper ions enter the network of interconnected channels, interact with nitrogen atom of pyridyl moieties and get reduced to Cu(0). Thus, aggregates of derivative **3** functions as reactor and stabilizing agent for the preparation of nanoparticles at room temperature. The powder X-ray diffraction (XRD) studies of the precipitates showed the presence of diffraction peaks located at 2θ values of 43.4, 50.3 and 73.9 (Fig. 2A) which suggest the formation of crystal face-centered cubic (fcc) Cu(0).^{2e} Thus, XRD studies confirm the formation of CuNPs. The SEM-EDX spectrum (see ESI†, Fig. S15) of aggregates of **3** in presence of CuCl₂ show the presence of copper nanoparticles. The TEM image of aggregates of derivative **3** in the presence of copper ions showed the presence of nanospheres and the particle size of the formed nanoparticles was found to be 9 to 17 nm (Fig. 2B and 2C). On the basis of DLS measurement of the CuNPs an average diameter of 13.54 nm is suggested for CuNPs (see ESI†, Fig. S16), which is in agreement with the TEM studies. These results suggest that aggregates of derivative **3** have separated the copper ions and prevented the accumulation and air oxidation of CuNPs.

Having done all this, we were then interested to study the catalytic efficiency of *in situ* generated CuNPs in the ‘click’ reaction. We carried out 1,3-dipolar cycloaddition reaction between various acetylenes and azides to synthesize corresponding 1,2,3-triazole in solvent free conditions (Table 1). It was observed that, the reactions took place within very short time (25–35 min) and the products were obtained in excellent yield. The enhanced reactivity of the aggregates of derivative **3** stabilized CuNPs in the ‘CuAAC’ reactions could be attributed to following reasons (i) aggregates of derivative **3** provided enough binding sites to generate large number of CuNPs (ii) the small size and spherical shape of *in situ* generated CuNPs provided the large surface area for the catalytic reaction (iii) aggregates of derivative **3** assisted in bringing the reactant molecules closer to the catalytic sites. Further, the reusability of the CuNPs catalyst was examined under the conditions given in Table 1. In the first cycle, the product was obtained in quantitative yield with complete conversion of reactants. The resulting reaction mixture containing CuNPs catalyst was subjected to reaction for the next catalytic sequence by adding azide and alkyne and it was observed that the CuNPs can be re-used as a catalyst at least five times

without significant loss of catalytic activity (see PS15 in Supporting Information).

Table 1. CuNPs Catalyzed Cycloaddition reactions between various azides and alkynes using 1 mole% CuNPs^a.



Entry	Azide	Alkyne	solvent	Time	Yield(%) ^b
1.			Neat	25 min	96
2.			Neat	30 min	92
3.			Neat	30 min	91
4.			Neat	25 min	95
5.			Neat	35 min	92
6.			Neat	25 min	96

^a See equation 1. All the reactions were carried out using 1 mmol azide and 1.05 mmol alkyne in the presence of CuNPs catalyst (1 mol%) neat at room temperature. ^b Isolated yield by crystallization.

The efficiency of the *in situ* generated CuNPs has been tested for the reaction between hexyl azide and phenyl acetylene with various amounts of catalyst, down to 5 ppm of copper. The reaction is quantitative up to 5 ppm of CuNPs at room temperature during 15 h (entry 11) and 82% of yield is achieved (Table 2). Such an extremely low quantity of copper has never been successfully used under solvent free condition at room temperature for “CuAAC” reactions before the present study. Thus, results in the present manuscript are better than those reported in literature.¹⁶

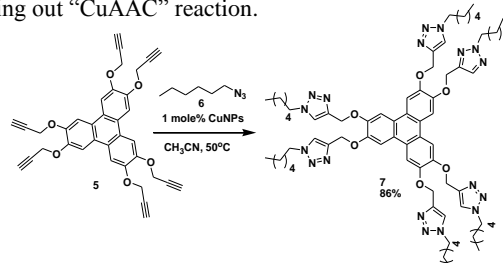
Table 2. CuNPs catalyzed azide-alkyne cycladdition reaction between hexyl azide and phenyl acetylene using various amounts of CuNPs^a.

Entry	CuNPs(ppm)	Time(h)	Yield(%)	TON	TOF (h ⁻¹)
7.	10000(1mol%)	0.4	95	95	228
8.	1000	2	95	940	470
9.	100	3.5	95	9500	2714.2
10.	10	10	94	93000	9300
11.	5	15	82	164000	10933
12.	0	15	0	0	0

^aAll the reactions were carried out with 1 mmol of azide, 1.05 mmol of alkyne using various amounts of CuNPs under solvent free condition at room temperature.

To evaluate the practical applicability of the *in situ* generated CuNPs, the “CuAAC” reaction was used for synthesis of triphenylene-based liquid crystalline derivative **7**. We have chosen derivative **7**¹⁷ as a candidate due to its potential applications in supramolecular chemistry and material chemistry. Further, its synthesis involves formation of six triazole rings in one step (Scheme 2). Previously, derivative **7** was obtained by ‘click reaction’ of precursor **5** with hexyl-azide in the presence of CuI in DMF in 58%. It took 24 hrs for completion of this reaction. Interestingly, as shown in Scheme 2, in presence of 1 mol% of *in situ* generated CuNPs in CH₃CN, the reaction was completed in 15 h and product

was obtained in 86% yield. Acetonitrile (2 ml) was used in this reaction as solvent for the dissolution the reactants. This study demonstrates the practical utility of *in situ* generated CuNPs for carrying out “CuAAC” reaction.



Scheme 2. Synthesis of Triphenylene-based discotic liquid crystal **7** bearing 1,2,3-triazole groups using “click” chemistry in presence of 1 mole% CuNPs.

In conclusion, we designed and synthesized AIEE active hexarylbenzene derivative **3** which forms fluorescent aggregates in aqueous media. Interestingly, these aggregates served as reactors and stabilizer for the preparation of CuNPs. The *in situ* generated CuNPs served as effective catalyst for ‘Click’ reaction to synthesize 1,2,3-triazole and can be recycled and reused five times without significant loss of their catalytic activity. Apart from this, the *in situ* generated CuNPs also served as very active catalyst for the synthesis of triphenylene-based discotic material **7**.

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Notes and references

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† Electronic Supplementary Information (ESI) available: General data, characterization data of derivative **3**, UV-vis and fluorescence studies. ¹H NMR spectra and data of the “click” reaction products. See DOI: 10.1039/b000000x/

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