Green Chemistry

Cite this: *Green Chem.*, 2012, **14**, 1298

www.rsc.org/greenchem

COMMUNICATION

Copper nanoparticulates in Guar-gum: a recyclable catalytic system for the Huisgen [3 + 2]-cycloaddition of azides and alkynes without additives under ambient conditions†

Ajeet Kumar,[a] Swati Aerry,[a] Amit Saxena,[a] Arnab de[b] and Subho Mozumdar*[a]

Received 15th January 2012, Accepted 6th March 2012
DOI: 10.1039/c2gc35070j

Cu-nanoparticulates in Guar-gum at room temperature were investigated for the first time as a recyclable catalytic system in organic synthesis. The catalytic potential of these materials were evaluated in the Huisgen [3 + 2]-cycloaddition of azides and alkynes without additives under ambient conditions which offers several advantages, *viz.* high yields, clean reactions, short reaction times, recyclability of the catalyst and a simple workup procedure.

Introduction

The chemistry of azides has come alive after the discovery of "Click" chemistry, discovered a few years back. "Click" chemistry is an alluring concept proposed by Sharpless *et al.* in 2001.[1] Since its discovery "Click" chemistry has generated interest to chemists in areas of catalysts, polymers, material science, synthesizing libraries of compounds and more importantly in drug discovery.[2,3] This approach, based on the joining of smaller units mimics the approach used by nature to generate substances. "Click" chemistry uses only the most practical and reliable chemical reactions to connect a diversity of structures bearing a wide variety of functional groups. However, the early Huisgen cycloaddition process required a strong electron-withdrawing substituent either on azide or on alkyne, and were often conducted at high temperature for a prolonged period of time, and usually led to the isolation of a mixture of 1,4-disubstituted and l,5-disubstituted-l,2,3-triazoles regioisomers and the electronic effect of the substituent groups on phenyl ring were not known clearly.[4–6] The increasing environmental consciousness of the chemical community has led to the search for more efficient and environmentally friendly methods for chemical syntheses.[7]

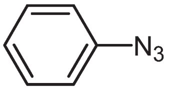
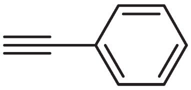
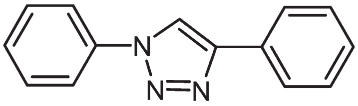
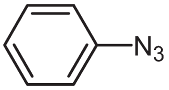
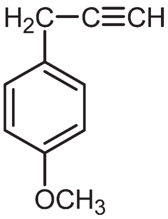
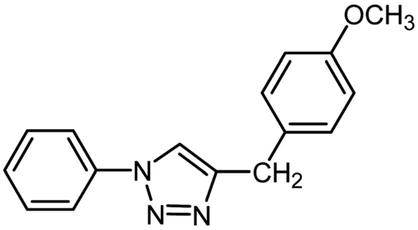
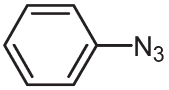
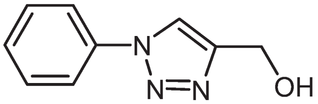
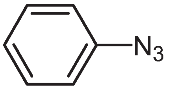
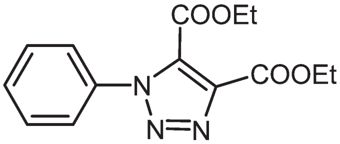
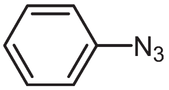
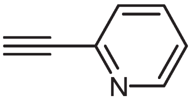
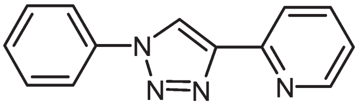
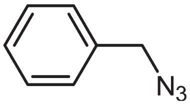
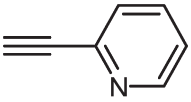
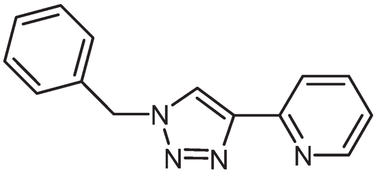
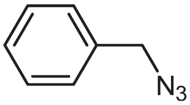
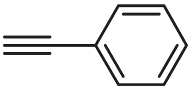
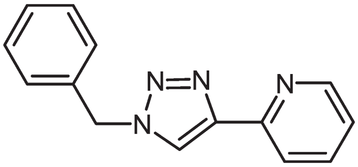
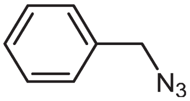
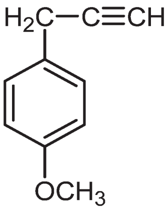
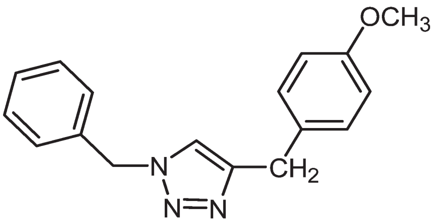
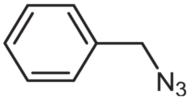
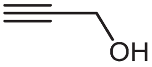
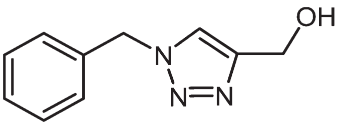
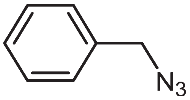
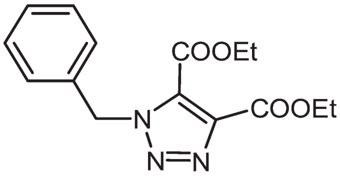
Therefore, it is desirable to develop a new, convenient and regio-controlled synthetic approach for the formation of triazoles. Recently, some important concepts and transition-metal catalysts to overcome the above drawbacks have been proposed.[8–11] Herein, we describe the virtues of copper nanoparticulates in Guar-gum polymer (Cu/GG) as a simple, inexpensive, and especially general and efficient heterogeneous catalyst for use in this emerging area. It is now well established that polymers are excellent host materials for the preparation of metal nanoparticles. Polymers act as a surface-capping agent when the nanoparticles are embedded or encapsulated in a polymer. Various synthetic polymers, such as poly(vinyl alcohol),[12,13] poly(vinyl pyrrolidone),[14] polystyrene,[15] and poly(methyl methacrylate),[16] have been used in the synthesis of metal nanoparticles. However, very little work has been carried out in which a natural polysaccharide has been used as a capping agent for the stabilization of metal nanoparticles. Recently, the synthesis of natural-polymer-stabilized selenium nanoparticles by the reduction of selenious acid by ascorbic acid was reported.[17] Natural polymers, because of their large abundance, biodegradability, and reactivity (due to the presence reactive functional groups), may show a better ability to stabilize nanoparticles. Guar-gum (GG) is a naturally occurring edible carbohydrate polymer found in the seeds of *Cyamopsis tetragonolobus*. It is a non-ionic, branched-chain polymer, consisting of straight-chain mannose units joined by β-D-(1–4) linkages having a-D-galactopyranose units attached to this linear chain by (1–6) linkages. The structure of Guar-gum is very complex and it has several hydroxyl groups, which can effectively bind metal clusters. So this property of Guar-gum can be exploited for the stabilization of copper nanoparticles generated *in situ*. Guar-gum has a very strong tendency to form gel in aqueous solution. This gel is highly viscous in nature and hence, can entrap, protect and stabilize the synthesized nanoparticles in its strong gelly mesh for a longer period of time and in the process act as an excellent surface capping agent. Guar-gum is not soluble in organic solvents and so this is an added advantage as the catalyst can be recovered from the organic reaction media by mild centrifugation and can be reused again and again, retaining the catalytic efficiency of the entrapped Cu-nanoparticles. As it is not soluble in organic solvents, so it does not interfere with the reaction pathway thus helps in maintaining the purity of the reaction. As both copper and copper oxide nanoparticles are expected as the species present within the Guar mesh, a reducing agent may not be needed to carry out the proposed cycloaddition reaction. In this communication, we wish to draw attention towards an efficient and environmentally benign protocol for an alternative

---

[a] *Department of Chemistry, University of Delhi, Delhi 110007, India. E-mail: subhoscom@yahoo.co.in; Tel: +919810728438*
[b] *Department of Microbiology and Immunology, Columbia University Medical Centre, USA*

† Electronic supplementary information (ESI) available: Procedural details for the synthesis and characterization of copper nanoparticulates in Guar-gum associated with this article can be found, in the online version. See DOI: 10.1039/c2gc35070j

Table 1 Huisgen [3 + 2]-cycloaddition of azides and alkynes using copper nanoparticulates in Guar-gum

Entry	Azide	Alkyne	Product	Time (h)	Yield (%)
1				5	98
2				5	94
3				5	95
4				5	92
5				5	98
6				5	97
7				5	98
8				5	95
9				5	92
10				5	94

Reaction conditions: The reaction has been performed using the azide (1 mmol), alkyne (1.2 mmol), catalyst (10 mg) in ethanol (5 mL) at room temperature.

Table 2 Comparison at various conventional protocols used for Huisgen [3 + 2]-cycloaddition of azides and alkynes

Sr. No.	Protocol	Reaction time	References
1	Copper-in-charcoal at room temperature	10 h	Ref. 18
2	PVP-stabilized copper-np at room temperature	15–45 min	Ref. 19
3	Copper-in-zeolite at room temperature	15 h	Ref. 20
4	Copper catalyst (Cu/AlO(OH) in pluronics P123	12 h	Ref. 21
5	CuI with *N*,*N*′-dimethylethylenediamine (DMEDA) as stabilizing ligand	20 h	Ref. 22
6	Cu-np with Et_3N at 65 °C at room temperature	30 min	Ref. 23
7	$CuSO_4 \cdot 5H_2O$/sodiumascorbate at room temperature	8 h	Ref. 11
8	125 °C heating using 100 W microwave irradiation	10–15 min	Ref. 24
9	Cu-particulates in Guar-gum at room temperature	5 h	Our method

recyclable catalytic system for the Huisgen [3 + 2]-cycloaddition of azides and alkynes without additives under ambient conditions.

Results and discussion

The findings on the cycloaddition of different azides compounds with different terminal alkynes at room temperature catalyzed by Cu-nanoparticulates stabilized in Guar-gum have been presented. The reaction takes place in a neutral medium like ethanol without the use of any bases. It may be postulated that the proposed catalyst nanoparticles play a redox role in accelerating the cycloaddition reaction and thus may promote the formation of triazole products. The classical cycloaddition of phenyl acetylene with benzyl azide has been used to explore the catalytic efficiency of these Guar-gum stabilized Cu-nanoparticles without any catalyst, this reaction did not take place in ethanol at room temperature even after 72 hours of stirring and the starting materials could be recovered. In order to further evaluate the efficiency of this methodology, a number of azides and terminal alkynes were further subjected to cycloaddition reaction using Guar-gum stabilized Cu-nanoparticles at room temperature and the products obtained have been tabulated in Table 1. It is important to note that there is a lack of functional group interference. Various substituted azides readily participated in this transformation and tolerance for variations in the acetylene component was also excellent. A comparison of some selected protocols in literature and our methods is listed in Table 2. In case of nanoparticles, the surface of particles is considered to be more reactive because of unfilled valencies of the surface atom. Also, the surface area of the catalyst increases tremendously when size approaches to nano level. To prove the efficacy of the catalytic system and its potential experiment in industries recyclability of the catalyst was checked. The catalyst could be recycled efficiently by separating them from the reaction mixture by mild centrifugation. They could be employed as a catalyst for the successive reactions. The relation between the number of cycles of the reaction and the catalytic activity in terms of yield is presented in Fig. 1. The catalytic system worked extremely well even up to five subsequent cycles with almost 95% yield. It has been observed that with the increasing number of cycles of the reaction, the catalytic activity of the nanoparticles decreases insignificantly while the reaction time was delayed. The difference between delayed time in the second and fourth cycle is much higher than that corresponding to fifth cycle. These observations suggest that after few cycles the catalytic efficiency could be preserved although, at higher reaction times when compared with the first cycle. It has been reported that some polymer-encapsulated nanoparticulates do aggregate after the catalytic reaction.[25] Thus the above result may be supposed to be induced by the agglomeration of the Guar-gum containing copper nanoparticles as catalyst. However, this point requires stricter experimental confirmation. The difference in QELS data before and after reaction (see ESI†) clearly shows the agglomeration of the catalyst. However, agglomeration of the catalyst does not affect the catalytic efficiency to a large extent. In order to check the leaching and stability of the catalyst the reaction mixture was further characterised after recovery of the catalyst (Fig. 6 in ESI†) and no trace of leaching was observed which was further confirmed by allowing the recovered reaction solvent to react further without adding catalyst and even after 24 hours the reactants remain unreacted. Thus, the proposed methodology is very clean and ‘green’.

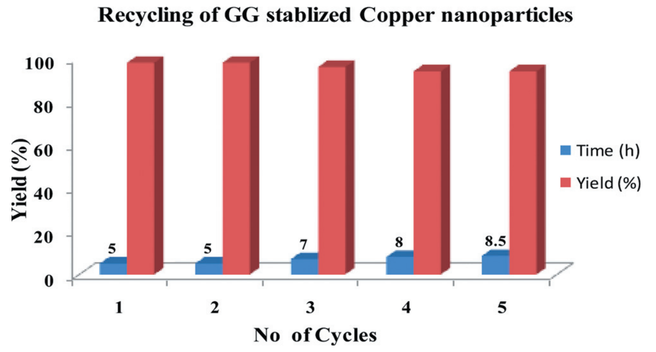


Fig. 1 Recycling of Guar-gum stabilized copper nanoparticles for the cycloaddition of benzyl azide and phenyl acetylene in ethanol (Table 1, entry 1).

As in all other metal nanoparticles catalyzed organic reactions, the solvent used have a strong effect in deciding the reaction path, time of completion of the reaction and the yield of the product. Usually, the increase in polarity leads to increase in reaction rate. This behaviour can be attributed to the influence of the solvent on the transition state and to a change in the capacity of the catalyst for proton transfer. When polar reagents are used, the transition-state complex is better solvated by polar solvents and the partition of the reactants at the solid–liquid interface is higher, decreasing the activation free enthalpy and enhancing the reaction rate.

The cycloaddition between benzyl azide and phenyl acetylene has been investigated in various solvents with all the other parameters kept constant and the results have been tabulated in Table 3. Best results were obtained with ethanol and *t*-butanol : water (3 : 1). In the presence of acetonitrile several products were

Table 3 Effect of polarity of the solvent on Huisgen [3 + 2]-cycloaddition of azides and alkynes using copper nanoparticulates in Guar-gum

		Yield (%)	Time (h)
Solvent	Ratio	Table 1 entry 1	
t-Butanol	Neat	91	6
Water	Neat	64	12 (catalyst degraded)
Ethanol	Neat	98	5
Acetonitrile	Neat	Several spots	—
THF	Neat	Incomplete	>72
t-Butanol : water	3 : 1	99	10
t-Butanol : water	1 : 1	98	5
Ethanol : water	3 : 1	98	8

Reaction conditions: The reaction has been performed using the azide (1 mmol), alkyne (1.2 mmol) and catalyst (10 mg).

formed while the reaction in THF was not complete even after 72 hours of vigorous stirring.

Conclusions

In conclusion, it can be said that highly efficient Click chemistry between organic azides and terminal alkynes can be heterogeneously catalyzed by Cu-nanoparticulates embedded or entrapped within the highly viscous mesh of Guar-gum in ethanol at room temperature. Solubility issues, copper contamination and modest yields usually associated with the choice of copper salt are completely averted. External ligands and addition of base known to accelerate Click reactions were not required. The encouraging results of recyclability which appears to be unaffected by exposure to air, makes this method facile, clean, cost effective and 'green'.

Experimental

Lyophilized powder of Guar-gum stabilized Cu-nanoparticulates (10 mg) is added to a clean oven dried 25-mL round-bottom flask fitted with a stir bar and septum. Absolute ethanol (5 mL) is added slowly to the sidewalls of the flask to rinse the powdered catalyst down. While the heterogeneous solution is stirred, azide (1.0 mmol) and alkyne (1.2 mmol) are added. The round-bottom flask is stirred at room temperature and the progress of the reaction is monitored by TLC until complete consumption of azide takes place. After the completion of the reaction, the reaction mixture is centrifuged (5000 rpm, 10 min) to pellet out the catalyst. The catalyst can then be washed with absolute ethanol to remove all the organic impurities. These particles can be dried and reused for the next reaction. The filtrate is further treated with ethyl acetate to ensure complete transfer. The volatile compounds are removed in vacuum to give pure triazole. The structures of all the products were unambiguously established on the basis of their spectral analysis (IR, ^{1}H NMR and MS mass spectral data) (see ESI†).

Acknowledgements

This work is dedicated to Professor Sneh Kumar Dogra on his 70th birthday.

S. M., S. A and A. K. acknowledge the financial support from the Department of Science & Technology (DST) and University Grant Commission (UGC), Government of India, respectively.

Notes and references

1 H. C. Kolb, M. G. Finn and K. B. Sharpless, *Angew. Chem., Int. Ed.*, 2001, **40**, 2004.
2 P. Wu and V. V. Fokin, *Aldrichimica Acta*, 2007, **40**, 7.
3 H. C. Kolb and K. B. Sharpless, *Drug Discovery Today*, 2003, **8**(24), 1128.
4 S. Kamijo, T. Jin, Z. Huo and Y. Yamamoto, *J. Org. Chem.*, 2004, **69**, 2386.
5 G. L'abbe, *Chem. Rev.*, 1969, **69**, 345.
6 K. V. Gothelf and K. A. Jorgensen, *Chem. Rev.*, 1998, **98**, 863.
7 P. T. Anastas and J. C. Warner, *Green Chemistry: Theory and Practice*, Oxford University Press, Oxford, 1998.
8 Z. X. Wang and H. L. Lin, *Chem. Commun.*, 2003, 2450–2451.
9 A. Krasinski, V. V. Fokin and K. B. Sharpless, *Org. Lett.*, 2004, **6**, 1237.
10 W. G. Lewis, L. G. Green, F. Grynszpan, Z. Radic, P. R. Carlier, P. Taylor, M. G. Finn and K. B. Sharpless, *Angew. Chem., Int. Ed.*, 2002, **41**, 1053.
11 V. V. Rostovtsev, L. G. Green, V. V. Fokin and K. B. Sharpless, *Angew. Chem., Int. Ed.*, 2002, **41**, 2596.
12 P. K. Khanna, N. Singh, S. Charan, V. V. V. Subbarao, R. Gokhale and U. P. Mulik, *Mater. Chem. Phys.*, 2005, **93**, 117.
13 K. S. Chou and C. Y. Ren, *Mater. Chem. Phys.*, 2000, **64**, 241.
14 P. K. Khanna, R. Gokhale and V. V. V. Subbarao, *J. Mater. Sci.*, 2004, **39**, 3773.
15 D. Wu, X. Ge, Y. Huang, Z. Zhang and Q. Ye, *Mater. Lett.*, 2003, **57**, 3549.
16 O. L. A. Monti, J. T. Fourkas and D. J. Nesbitt, *J. Phys. Chem. B*, 2004, **108**, 1604.
17 H. Y. Zhang, J. Zhang, H. Y. Wang and H. Y. Chen, *Mater. Lett.*, 2004, **58**, 2590.
18 B. H. Lipshutz and B. R. Taft, *Angew. Chem., Int. Ed.*, 2006, **45**, 8235.
19 A. Sarkar, T. Mukherjee and S. Kapoor, *J. Phys. Chem. C*, 2008, **112**, 3334.
20 S. Chassaing, M. Kumarraja, A. S. S. Sido, P. Pale and J. Sommer, *Org. Lett.*, 2007, **9**, 883.
21 I. S. Park, M. S. Kwon, Y. Kim, J. S. Lee and J. Park, *Org. Lett.*, 2008, **10**, 497.
22 L. Ackermann, H. K. Potukuchi, D. Landsberg and R. Vicente, *Org. Lett.*, 2008, **10**, 3081.
23 F. Alonso, Y. Moglie, G. Radivoy and M. Yus, *Tetrahedron Lett.*, 2009, **50**, 2358.
24 P. Appukkuttan, W. Dehaen, V. V. Fokin and E. V. Eycken, *Org. Lett.*, 2004, **6**, 4223.
25 R. Narayanan and M. A. El-Sayed, *J. Phys. Chem. B*, 2005, **109**, 12663.