RSC Advances

COMMUNICATION

View Article Online
View Journal | View Issue

Cite this: *RSC Adv.*, 2015, **5**, 21396

Received 16th December 2014
Accepted 17th February 2015

DOI: 10.1039/c4ra16481d

www.rsc.org/advances

# A polymer supported ascorbate functionalized task specific ionic liquid: an efficient reusable catalyst for 1,3-dipolar cycloaddition†

Jayavant D. Patil,[a] Supriya A. Patil[b] and Dattaprasad M. Pore*[a]

A novel polymer supported ascorbate functionalized task specific ionic liquid was designed and synthesized. It has been demonstrated that the synthesized polymer supported ionic liquid acts as an efficient catalyst for regioselective Huisgen 1,3-dipolar cycloaddition of aryldiazonium tetrafluoroborate, sodium azide and terminal alkyne, which provide a series of 1,4-disubstituted-1,2,3-triazoles in high yields at room temperature as well as showing an aptitude for *in situ* incorporation of copper.

## Introduction

The increasing environmental consciousness of the chemical community has led to the search for more efficient methods for organic synthesis acquiring the principles of Green chemistry.[1] This goal was achieved by employing green catalysts/solvents (*e.g.*, water, ionic liquids) as well as efficient and cleanly reusable catalytic materials.[2] Ionic liquids have emerged as eco-friendly catalysts as well as multi-use reaction media and green solvent for a variety of applications due to the fact that they possess negligibly small vapor pressure, high thermal, chemical as well as electrochemical stability with widely tunable properties with regard to polarity, hydrophobicity, solvent miscibility, *etc.*[3] Despite these advantages, a series of drawbacks such as their high cost as compared to traditional catalysts and solvents, low biodegradability and (eco)toxicological properties still exists,[4] their recovery requires tedious process *viz.* distillation.[5] To circumvent the limitations raised with ILs, the use of supported ionic liquid phase (SILP) catalysts has been devised which possess advantages of ionic liquid media with solid support materials, enables the application of fixed-bed technology and the usage of significantly reduced amounts of the ionic liquid. It involve immobilization of ILs onto a surface of a porous high area support material.[6] A number of benefits arise from the use of SILP catalysts, some of which are the ease of separation of catalyst, simply by filtration, recycling and reproducibility as well as facilitating significant advances in selectivity. Due to these reasons, in last few years SILP catalysts have attracted attention of scientists and due to its influence several organic transformations have been successfully accomplished.[7]

1,2,3-Triazoles are an important class of heterocyclic compounds, the interest in their synthesis stems from their wide range of applications in pharmaceuticals, agro chemicals, dyes, photographic materials, corrosion inhibition,[8] *etc.* and biological activities such as antiviral, antiepileptic, antiallergic,[9] anticancer,[10] anti-HIV,[11] antimicrobial activities against gram positive bacteria and b3-adrenergic receptor agonist.[12] Due to such multifarious applications different methods have been exploited for their synthesis[13] and amongst them Huisgen 1,3-dipolar cycloaddition of azides with alkynes is the most popular method for the construction of 1,2,3-triazole framework.[14]

However, the early Huisgen 1,3-dipolar cycloaddition[15a–c] 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 1,5-disubstituted-1,2,3-triazoles.[15d,e]

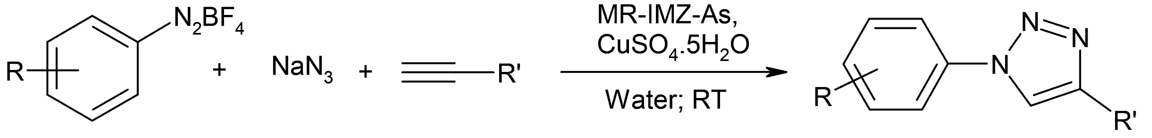
Sharpless *et al.* used Cu(I) salts to promote the reaction of azide with terminal alkynes to afford 1,4-disubstituted products.[16] Fokin and co-workers have developed the method employing microwave irradiations.[17] Moreover in recent years, several methods have been reported for the synthesis of triazoles[18] generally through the coupling reaction between alkynes and azides at high temperatures[19] and by using solid supported catalysts[20] or nanocatalysts.[21] Many of the literature methods are plagued by disadvantages such as use of organic solvent, no reusability of catalytic system, long reflux time, influence of microwave irradiation, organic azide as reagent

---

[a] *Department of Chemistry, Shivaji University, Kolhapur 416 004, India. E-mail: p_dattaprasad@rediffmail.com; Fax: +91 231 2692333; Tel: +91 231 2690571*

[b] *Department of Chemistry, Hanyang University, Sungdong-Ku, Haengdang-dong 17, Seoul, 133-791, Republic of Korea*

† Electronic supplementary information (ESI) available. See DOI: 10.1039/c4ra16481d



**Scheme 1** Polymer supported ascorbate functionalized task specific ionic liquid (MR-IMZ-As) catalyzed Huisgen 1,3-dipolar cycloaddition.

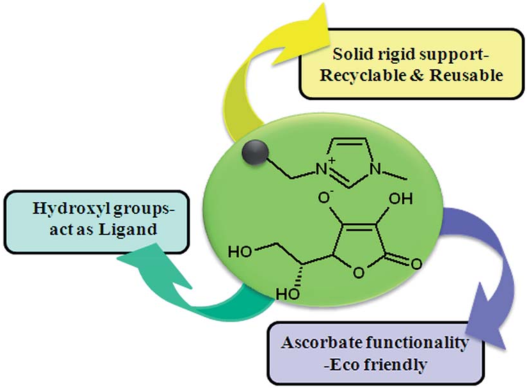


Fig. 1 Polymer supported ascorbate functionalized task specific ionic liquid (MR-IMZ-As).

and limited substrate scope. Thus, the development of an efficient, eco-friendly, regioselective protocol for Huisgen 1,3-dipolar cycloaddition having wide substrate scope operable at ambient temperature is highly warranted. To achieve this goal, we described synthesis of novel polymer supported ascorbate functionalized task specific ionic liquid [MR-IMZ-As] for synthesis of 1,4-disubstituted 1,2,3-triazoles employing click approach (Scheme 1).

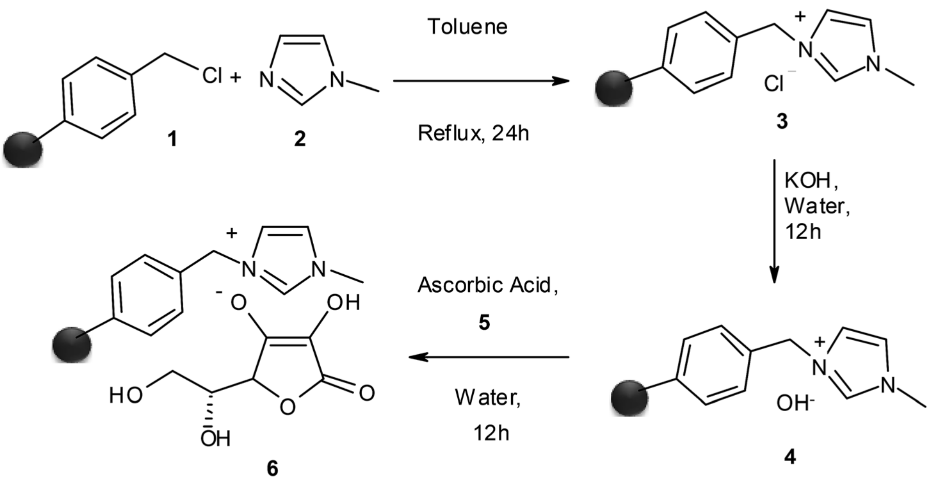
## Result and discussion

Initial attempts were focused on synthesis of novel polymer supported ionic liquid, which is ecofriendly, recyclable, having capacity to stabilize copper and cost effective for Huisgen 1,3-dipolar cycloaddition (Fig. 1).

In this context, we designed MR-IMZ-As Merrifield resin (polymer) supported ascorbate functionalized task specific ionic liquid. Initially, polymer supported ionic liquid **3** was prepared by treating Merrifield resin with 1-methyl imidazole in toluene employing reflux conditions for 24 h. This on anion exchange using potassium hydroxide in water for 12 h at room temperature furnished **4**. Formation of **3** and **4** was characterized by infrared spectroscopy. Finally, reacting suspension of **4** with a solution of ascorbic acid in water at room temperature for 12 h led polymer supported ascorbate functionalized task specific ionic liquid **6** (Scheme 2), which was characterized using IR, SEM and EDX analysis.

IR spectrum (Fig. 2) of MR-IMZ-As (C) shows, absorption band at 1720 $cm^{-1}$ corresponding to C═O stretching of lactone and at 1626, 1602, 1562 and 1158 $cm^{-1}$ corresponding to C═C, C═N, C–N and C–O stretching, respectively. The SEM images of MR-IMZ-As before and after use for present transformation exhibit the morphological differences (Fig. 3).

Next, we focused our attention to explore this novel polymer supported ascorbate functionalized task specific ionic liquid (MR-IMZ-As) in the 1,3-dipolar cycloaddition. Aromatic azides are generally used as one of the precursor in Huisgen 1,3-dipolar cycloaddition, they are also versatile intermediates in several organic reactions[22] *viz.* Ugi, Griess, Staudinger, Curtius and Schmidt, *etc.* Although, these organic azides are stable against most reaction conditions, low molecular weight azides are explosive, high temperatures lead to decomposition of the organic azides.[23] To overcome the drawbacks raised due to organic azides as direct precursors, scientific community



**Scheme 2** Preparation of polymer supported ascorbate functionalized task specific ionic liquid (MR-IMZ-As).

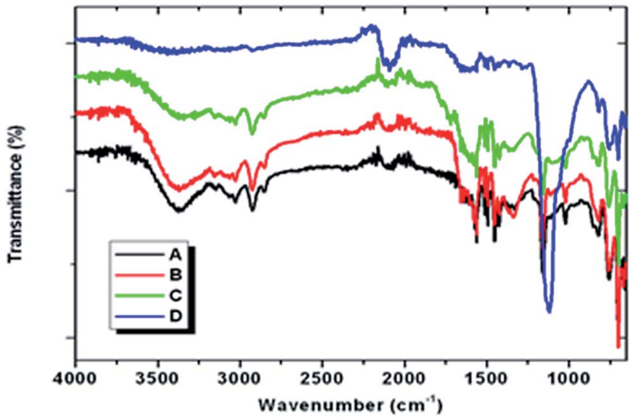


Fig. 2 IR spectra of MS-IM-Cl (A), MS-IM-OH (B), MS-IM-As (C) and MS-IM-As-Cu (D).

preferred *in situ* generation of organic azides to achieve a desired transformation.

Aryl diazonium salts are best ecofriendly alternative to organic azides as it easily generates aryl azide by reaction with sodium azide thus reduces the hazards derived from the isolation and handling of the azides. A scanty literature is available for Huisgen 1,3-dipolar cycloaddition involving *in situ* generation of aryl azides.[24] In these circumstances, initially a model reaction for Huisgen 1,3-dipolar cycloaddition of phenyldiazonium tetrafluoroborate, sodium azide and phenyl acetylene in water was carried out in presence of $CuSO_4 \cdot 5H_2O$ and catalytic amount of polymer supported ionic liquid (MR-IMZ-As) (Scheme 1). Pleasingly, corresponding 1,2,3-triazole was obtained in good yield within short time duration. By comparing the $^1H$ NMR data, with the literature reports, the product was confirmed as 1,4-disubstituted 1,2,3-triazole instead of 1,5-disubstituted 1,2,3-triazole.[25] Thus, the developed method act as a regioselective method.

For optimization of reaction conditions in terms of catalyst loading, model reaction was carried out with varied quantities of the catalyst. Best result was obtained using 25 mg (0.16 mmol) of catalyst in water at room temperature. We decided to employ these optimized conditions to probe the generality of the method. There was no difference in yield and reaction time when catalyst loading was increased to 30 mg (0.19 mmol). However, it took longer time for completion of the reaction when catalyst loading was reduced to 15 mg (0.09 mmol), 10 mg (0.064 mmol) or 5 mg (0.032 mmol). To check the effect of the catalyst and copper sulphate, a click reaction were performed without SILP and without copper sulphate, in both cases no product was obtained.

After optimization of the reaction conditions, to delineate this approach, particularly in regards to library construction, this methodology was evaluated by using a diversely substituted aryldiazonium tetrafluoroborate reacted with sodium azide and terminal alkyne to provide corresponding 1,4-disubstituted 1,2,3-triazoles under optimized reaction conditions. The results are summarized in Table 1. Electron donating substituents like methyl, methoxy (entries 1, 2, 14; Table 1), and electron withdrawing substituents such as chloro, nitro groups and cyano at *para* position of aryldiazonium tetrafluoroborate (entries 3, 4, 5, 13; Table 1) are found to be equally effective towards the nucleophilic substitution of *in situ* generated aryl azide, followed by 1,3-dipolar cycloaddition. It is noteworthy that when alicyclic acetylene, 4-methyl and 4-chloro phenylacetylene are selected as representative of terminated alkyne also undergo clean reaction to produce the corresponding 1,4-disubstituted 1,2,3-triazoles employing optimized reaction conditions (entries 6–12, 15, 16; Table 1).

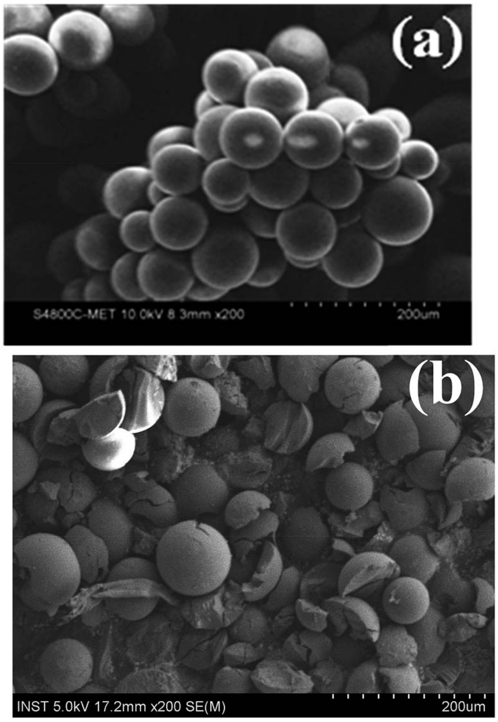


Fig. 3 SEM analysis of polymer supported ionic liquid (MR-IMZ-As) before use (a), after use (b).

The reusability of the catalyst is an important aspect from economical point of view. So recovery and reusability study of the catalyst was performed for the reaction of 2-methoxyphenyldiazonium tetrafluoroborate, sodium azide and phenylacetylene. After the completion of the first reaction, catalyst was recovered by simple filtration and washed with ethanol and acetone, dried at 80 °C for 1 h. TEM-EDS analysis (Fig. 4) of the catalyst after first cycle indicated the presence of copper. This clearly indicates *in situ* incorporation of copper with polymer supported ascorbate functionalized task specific ionic liquid during the progress of reaction. From the XPS spectrum of catalyst, the values of binding energy at 932.3 and 954.7 eV corresponding to the Cu $2p_{3/2}$ and Cu $2p_{1/2}$ and peak centered at 531.3, 284.5 eV represent O 1s and C 1s, respectively. This data of binding energy is in agreement with the literature and revealed presence of CuO[26a–c] while existence of copper as $Cu^{2+}$ is also confirmed by presence of the shake-up satellite peak[26d,e] with binding energy 940–950 eV (Fig. 5). Thus copper

**Table 1** Synthesis of 1,2,3-triazoles by click reaction of terminated alkynes, arenediazonium salts and sodium azide[a]

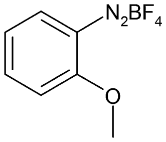
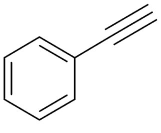
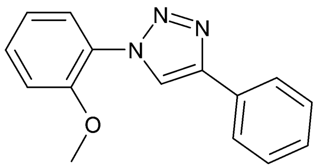
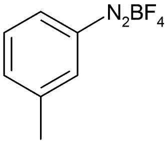
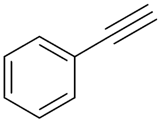
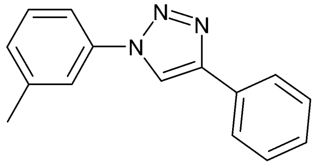
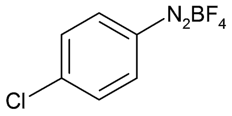
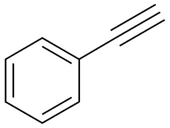
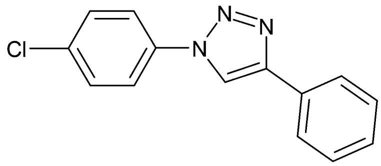
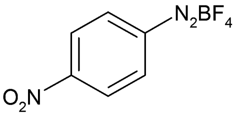
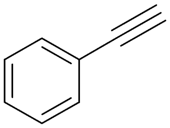
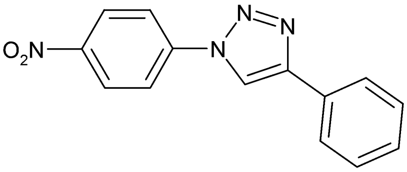
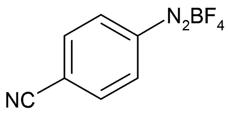
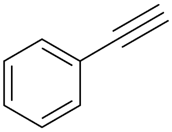
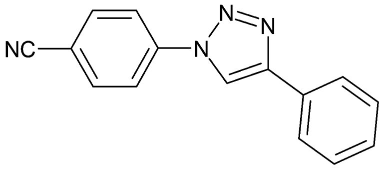
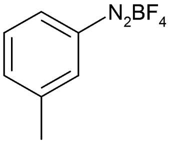
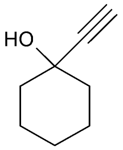
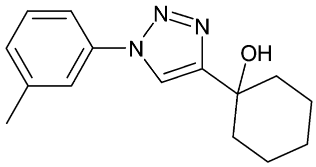
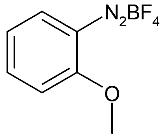
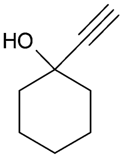
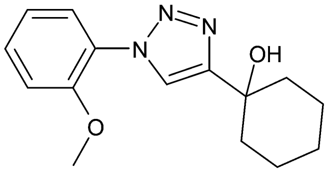
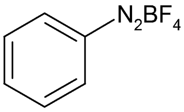
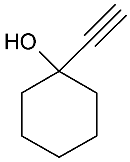
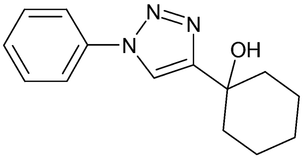
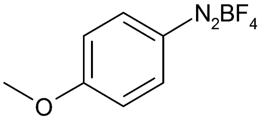
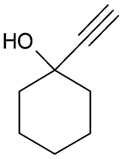
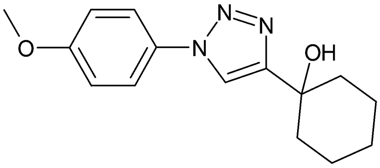
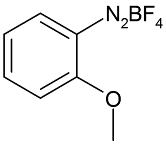
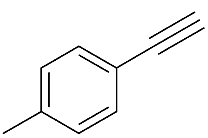
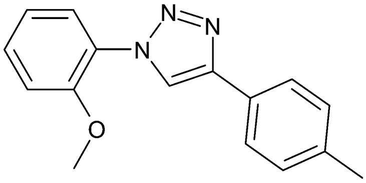
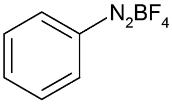
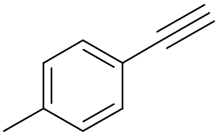
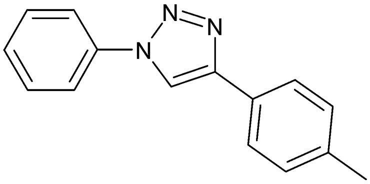
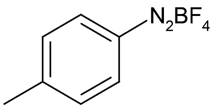
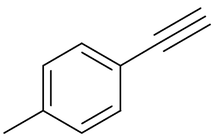
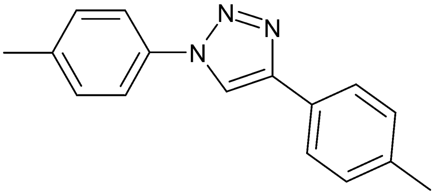
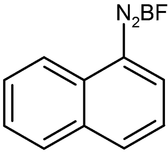
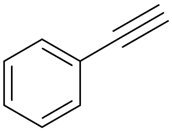
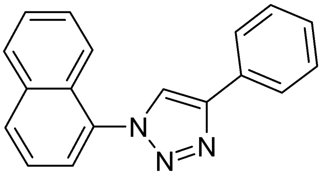
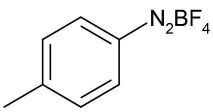
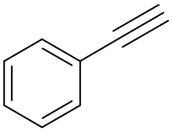
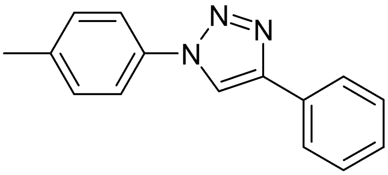
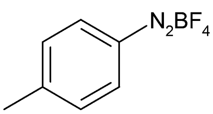
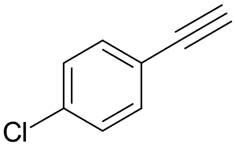
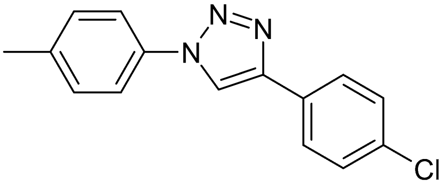
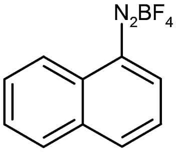
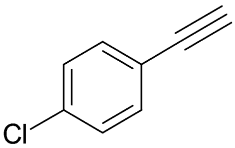
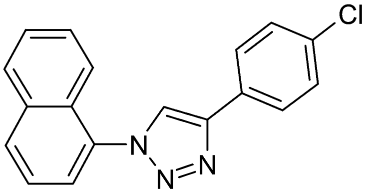
| Entry | Diazonium salt | Alkyne | Product | Time (h) | Yield[b] (%) |
|---|---|---|---|---|---|
| 1 |  |  |  | 2 | 94 |
| 2 |  |  |  | 2 | 92 |
| 3 |  |  |  | 2 | 82 |
| 4 |  |  |  | 2 | 79 |
| 5 |  |  |  | 2 | 80 |
| 6 |  |  |  | 2 | 90 |
| 7 |  |  |  | 2 | 92 |
| 8 |  |  |  | 2 | 90 |
| 9 |  |  |  | 2 | 96 |

Table 1 (*Contd.*)

| Entry | Diazonium salt | Alkyne | Product | Time (h) | Yield[b] (%) |
|---|---|---|---|---|---|
| 10 |  |  |  | 2 | 95 |
| 11 |  |  |  | 2 | 92 |
| 12 |  |  |  | 2 | 90 |
| 13 |  |  |  | 2 | 94 |
| 14 |  |  |  | 2 | 92 |
| 15 |  |  |  | 2 | 90 |
| 16 |  |  |  | 2 | 92 |

[a] Reaction conditions: aryldiazonium tetrafluoroborate (1 mmol), sodium azide (1 mmol), terminal alkyne (1 mmol), $CuSO_4 \cdot 5H_2O$ (10 mg, 0.04 mmol) and MR-IMZ-As (25 mg, 0.16 mmol) in water (5 mL). [b] Isolated yield.

incorporated in the catalyst in the form of CuO. Hence reusability study was carried out in absence of $CuSO_4 \cdot 5H_2O$. After 1st run copper content of the filtrate was determined using atomic absorption spectroscopy (AAS). No copper metal was detected in filtrate, which confirms the fact that polymer supported ascorbate functionalized task specific ionic liquid binds copper to minimize deterioration and metal leaching and facilitates efficient catalyst recycling. We observed that catalyst was reused at least for five times resulted 94, 94, 92, 90, 89 and 85% yield, respectively (Fig. 6). Metal leaching was also

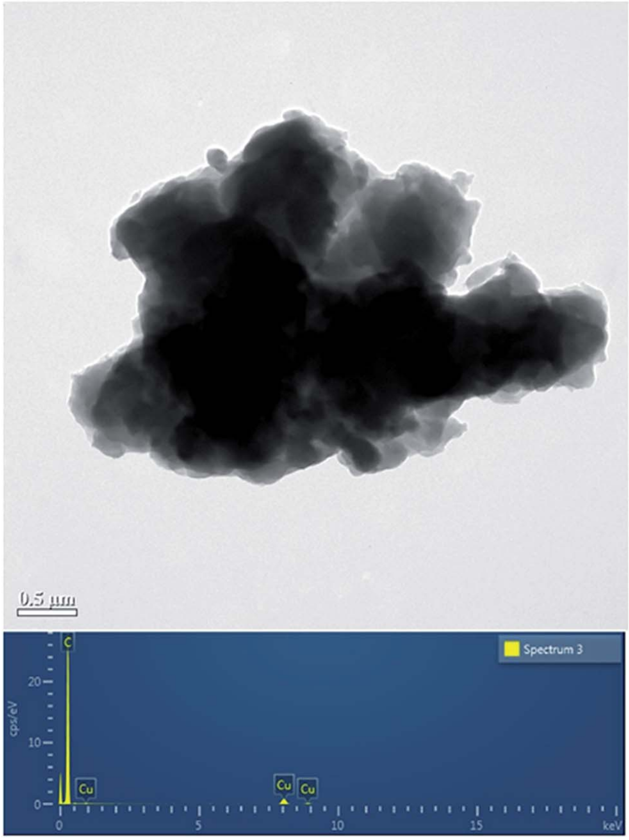


Fig. 4 TEM-EDS analysis of used polymer supported ionic liquid (MR-IMZ-As).

studied by TEM-EDS analysis of the catalyst before and after the 5th cycle. After 1st and 5th cycle the concentration of *in situ* incorporated Cu was found to be 3.33 wt% and 3.09 wt%, respectively.

## Conclusion

We have described an efficient, regioselective and green procedure for the one-pot synthesis of 1,4-disubstituted 1,2,3-triazoles catalyzed by *in situ* incorporated copper with polymer supported ascorbate functionalized task specific ionic liquid in water at room temperature. This protocol provides advantages such as operational simplicity, general applicability, one-pot synthesis of triazoles from diazonium salts, high yields, involving room temperature and recyclability of the catalyst up to the fifth run without any appreciable loss of activity. High purity and yields of the product, excellent regioselectivity and circumventing the problems encountered with the isolation of organic azides, enable one to adhere to greener and cost effective approach for Huisgen cycloaddition.

## Experimental

### General information

Alkynes (Aldrich/Alfa Aesar), sodium azide (Spectrochem, Mumbai) and copper sulphate pentahydrate (Spectrochem, Mumbai) were used as received. All reactions were carried out in air atmosphere in predried glassware. Infrared spectra were measured with an Agilent Cary (IR-630) spectrophotometer. $^1$H NMR and $^{13}$C NMR spectra were recorded on a Brucker AC

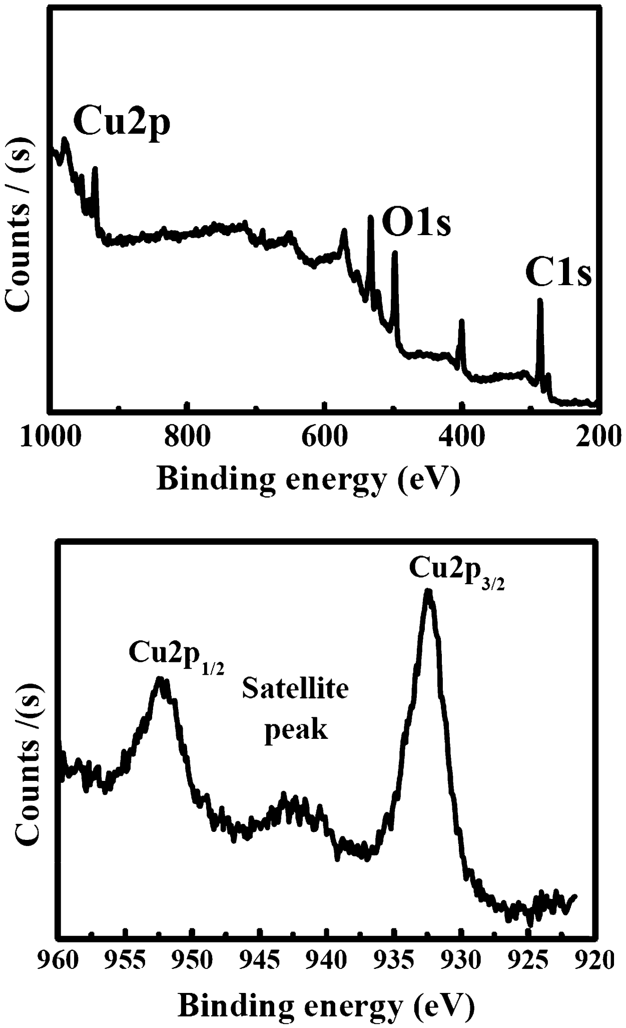


Fig. 5 XPS data of used polymer supported ionic liquid (MR-IMZ-As).

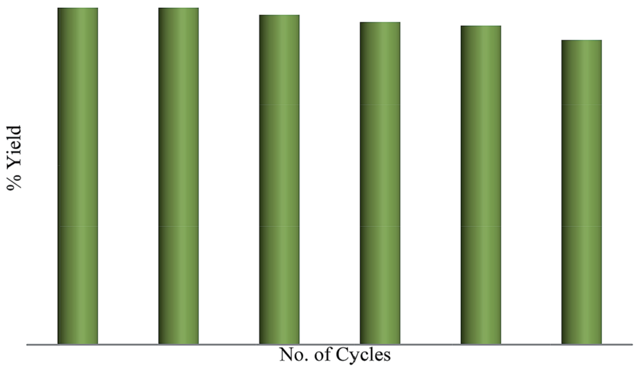


Fig. 6 Reusability of used polymer supported ionic liquid (MR-IMZ-As).

spectrometer (300 MHz for $^1$H NMR and 75 MHz for $^{13}$C NMR), using $CDCl_3$ as solvent and tetramethylsilane (TMS) as an internal standard. Chemical shifts ($\delta$) are expressed in parts per million (ppm) and coupling constants are expressed in hertz (Hz). Mass spectra were recorded on a Shimadzu QP2010 GCMS. FESEM was performed using a HITACHI S-4800. TEM-EDS were determined using energy dispersive X-ray analyser EM912 coupled to transmission electron microscopy (TEM) JEOL-2100F transmission electron microscope. X-ray photoelectron (XPS) was recorded on VG Multilab ESCA 2000 system.

### Typical procedure for the preparation of polymer supported ascorbate functionalized ionic liquid catalyst (MR-IMZ-As)

**Preparation of imidazolium-loaded polymeric support (MR-IMZ-Cl).** In 100 mL round bottom flask were added Merrifield peptide resin (2% cross linked, 2–4 mmol Cl per g) 5 g, *N*-methyl imidazole (0.0609 mmol) in toluene (25 mL) and refluxed for 24 hours. On completion, the reaction mixture was cooled to room temperature. It was then filtered and the residue obtained was washed with toluene, 0.1 M HCl, water and methanol sequentially followed by drying under reduced pressure to afford imidazolium-loaded polymeric support.

**Preparation of imidazolium-loaded polymeric support (MR-IMZ-OH).** (MR-IMZ-Cl) (1.0 g) was suspended in 10 mL aqueous solution of KOH (0.448 g). The resulting mixture was stirred for 24 h at room temperature, Afterward the polymer was filtered and washed with water, methanol and dried under vacuum to afford (MR-IMZ-OH).

**Preparation of polymer supported ascorbate anionic ionic liquid catalyst (MR-IMZ-As).** A mixture of the imidazolium loaded polymeric support (MR-IMZ-OH) (1.0 g) and ascorbic acid (1.408 g, 8 mmol) was suspended in water (20 mL). The mixture was then stirred at room temperature for 24 h. On completion, the reaction mixture was filtered and the polymeric support was washed vigorously with distilled water (10 mL × 5), MeOH (10 mL × 5) and dried under reduced pressure to give (MR-IMZ-As).

**General procedure for synthesis of 1,4-disubstituted 1,2,3-triazole.** In a 50 mL round bottom flask aryldiazonium tetrafluoroborate (1 mmol), sodium azide (1.2 mmol), alkyne (1.0 mmol), $CuSO_4\cdot 5H_2O$ (10 mg, 0.04 mmol) and MR-IMZ-As (25 mg, 0.16 mmol) were mixed and stirred in 5 mL water. The reaction was allowed to proceed for 2 h at room temperature. Reactions were monitored by Thin Layer Chromatography (TLC) using aluminium backed silica gel 60 ($F_{254}$) plates. After completion of the reaction, the reaction mixture was filtered and quenched with water (10 mL) the organic products were separated from the reaction mixture by extraction with ethyl acetate (15 mL × 2). The organic layer was dried over $Na_2SO_4$ and the solvent was removed under reduced pressure then the product was purified by silica gel column chromatography.

## Acknowledgements

We gratefully acknowledge the DST New Delhi for financial assistance under Fast Track Scheme [no. SB/FT/CS-154/2012].

## References

1 (*a*) P. T. Anastas and J. C. Warner, *Green Chemistry Theory and Practice*, Oxford University Press, Oxford, 1998; (*b*) A. S. Matlack, *Introduction to Green Chemistry*, Marcel Dekker, New York, 2001; (*c*) M. Poliakoff, J. M. Fitzpatrick, T. R. Farren and P. T. Anastas, *Science*, 2002, **297**, 807; (*d*) M. Lancaster, *Green Chemistry: An Introductory Text*, RSC Publishing, Cambridge, 2002; (*e*) R. A. Sheldon, I. W. C. E. Arends and U. Henefeld, *Green Chemistry and Catalysis*, Wiley-VCH, Weinheim, 2007.

2 (*a*) S. E. García-Garrido, J. Francos, V. Cadierno, J.-M. Basset and V. Polshettiwar, *ChemSusChem*, 2011, **4**, 104; (*b*) A. Fihri, D. Cha, M. Bouhrara, N. Almana and V. Polshettiwar, *ChemSusChem*, 2012, **5**, 85; (*c*) N. Madhavan, C. W. Jones and M. Weck, *Acc. Chem. Res.*, 2008, **41**, 1153; (*d*) A. Schätz, R. N. Grass, W. J. Stark and O. Reiser, *Chem.–Eur. J.*, 2008, **14**, 8262; (*e*) S. Bhadra, B. Sreedhar and B. C. Ranu, *Adv. Synth. Catal.*, 2009, **351**, 2369.

3 (*a*) J. D. Holbrey and K. R. Seddon, *J. Chem. Soc., Dalton Trans.*, 1999, 2133; (*b*) T. Welton, *Chem. Rev.*, 1999, **99**, 2071; (*c*) M. J. Earle, P. B. Mc Cormac and K. R. Seddon, *Green Chem.*, 1999, **1**, 23; (*d*) H. Olivier-Bourbigou, L. Magna and D. Morvan, *Appl. Catal., A*, 2010, **373**, 1; (*e*) J. P. Hallett and T. Welton, *Chem. Rev.*, 2011, **111**, 3508.

4 (*a*) M. T. Garcia, N. Gathergood and P. J. Scammells, *Green Chem.*, 2005, **7**, 9; (*b*) K. M. Docherty and C. F. Kulpa, *Green Chem.*, 2005, **7**, 185; (*c*) C. Pretti, C. Chiappe, D. Pieraccini, M. Gregori, F. Abramo, G. Monni and L. Intorre, *Green Chem.*, 2006, **8**, 238.

5 (*a*) M. J. Earle, J. M. S. S. Esperanca, M. A. Gilea, J. N. C. Lopes, L. P. N. Rebelo, J. W. Magee, K. R. Seddon and J. A. Widegren, *Nature*, 2006, **72**, 1391; (*b*) A. W. Taylor, K. R. J. Lovelock, A. Deyko, P. Licence and R. G. Jones, *Phys. Chem. Chem. Phys.*, 2010, **12**, 1772.

6 (*a*) A. Riisager, R. Fehrmann, M. Haumann and P. Wasserscheid, *Top. Catal.*, 2006, **40**, 91; (*b*) C. Van Doorslaer, J. Wahlen, P. Mertens, K. Binnemans and D. D. Vos, *Dalton Trans.*, 2010, **39**, 8377; (*c*) C. P. Mehnert, *Chem.–Eur. J.*, 2005, **11**, 50.

7 (*a*) H. Hagiwara, Y. Sugawara, K. Isobe, T. Hoshi and T. Suzuki, *Org. Lett.*, 2004, **6**, 2325; (*b*) M. Gruttadauria, S. Riela, P. L. Meo, F. D'Anna and R. Noto, *Tetrahedron Lett.*, 2004, **45**, 6113; (*c*) S. S. Shinde, B. S. Lee and D. Y. Chi, *Tetrahedron Lett.*, 2008, **49**, 4245; (*d*) J. Joni, M. Haumann and P. Wasserscheid, *Adv. Synth. Catal.*, 2009, **351**, 423; (*e*) H. Hagiwara, *Synlett*, 2012, **23**, 837.

8 (*a*) M. Whiting, J. Muldoon, Y.-C. Lin, S. M. Silverman, W. Lindstrom, A. J. Olson, H. C. Kolb, M. G. Finn, K. B. Sharpless, J. H. Elder and V. V. Fokin, *Angew. Chem., Int. Ed.*, 2006, **45**, 1435; (*b*) H. C. Kolb and K. B. Sharpless, *Drug Discovery Today*, 2003, **8**, 1128; (*c*) M. J. Giffin,

H. Heaslet, A. Brik, Y. C. Lin, G. Cauvi, C.-H. Wong, D. E. McRee, J. H. Elder, C. D. Stout and B. E. Torbett, *J. Med. Chem.*, 2008, **51**, 6263; (*d*) W.-Q. Fann and A. R. Katritzky, in *Comprehensive Heterocyclic Chemistry II*, ed. A. R. Katritzky, C. W. Rees and E. F. V. Scriven, Elsevier Science, Oxford, 1996, vol. 4, p. 1.

9 D. R. Buckle, C. J. M. Rockell, H. Smith and B. A. Spicer, *J. Med. Chem.*, 1986, **29**, 2262.

10 (*a*) F. Pagliai, T. Pirali, E. D. Grosso, R. D. Brisco, G. C. Tron, G. Sorba and A. A. Genazzani, *J. Med. Chem.*, 2006, **49**, 467; (*b*) S. A. Bakunov, S. M. Bakunova, T. Wenzler, M. Ghebru, K. A. Werbovetz, R. Brun and R. R. Tidwell, *J. Med. Chem.*, 2010, **53**, 254; (*c*) A. H. Banday, S. A. Shameem, B. D. Gupta and H. M. Sampath Kumar, *Steroids*, 2010, **75**, 801.

11 R. Alvarez, S. Velazquez, A. San-Felix, S. Aquaro, E. De Clercq, C.-F. Perno, A. Karlsson, J. Balzarini and M. J. Camarasa, *J. Med. Chem.*, 1994, **37**, 4194.

12 L. L. Brockunier, E. R. Parmee, H. O. Ok, M. R. Candelore, M. A. Cascieri, L. F. Colwell, L. Deng, W. P. Feeney, M. J. Forrest, G. J. Hom, D. E. MacIntyre, L. Tota, M. J. Wyvratt, M. H. Fisher and A. E. Weber, *Bioorg. Med. Chem. Lett.*, 2000, **10**, 2111.

13 (*a*) E. Haldón, E. Álvarez, M. C. Nicasio and P. J. Pérez, *Chem. Commun.*, 2014, **50**, 8978; (*b*) X. Liu, J. Li and B. Chen, *New J. Chem.*, 2013, **37**, 965; (*c*) J. D. Patil and D. M. Pore, *RSC Adv.*, 2014, **4**, 14314; (*d*) D. M. Pore, P. G. Hegade, M. M. Mane and J. D. Patil, *RSC Adv.*, 2013, **3**, 25723; (*e*) S. Ueda and H. Nagasawa, *J. Am. Chem. Soc.*, 2009, **131**, 15080; (*f*) D. V. Batchelor, D. M. Beal, T. B. Brown, D. Ellis, D. W. Gordon, P. S. Johnson, H. J. Mason, M. J. Ralph, T. J. Underwood and S. Wheeler, *Synlett*, 2008, 2421; (*g*) P. Yin, W.-B. Ma, Y. Chen, W.-C. Huang, Y. Deng and L. He, *Org. Lett.*, 2009, **11**, 5482.

14 (*a*) V. Sai Sudhir, R. B. Nasir Baig and S. Chandrasekaran, *Eur. J. Org. Chem.*, 2008, 2423; (*b*) V. Sai Sudhir, N. Y. Phani Kumar, R. B. Nasir Baig and S. Chandrasekaran, *J. Org. Chem.*, 2009, **74**, 7588; (*c*) F. Amblard, J. H. Cho and R. F. Schinazi, *Chem. Rev.*, 2009, **109**, 4207; (*d*) S. Dedola, S. A. Nepogodiev and R. A. Field, *Org. Biomol. Chem.*, 2007, **5**, 1006; (*e*) E. M. Sletten and C. R. Bertozzi, *Acc. Chem. Res.*, 2011, **44**, 666; (*f*) D. Kumar and V. B. Reddy, *Synthesis*, 2010, 1687; (*g*) R. B. N. Baig and R. S. Varma, *Chem. Commun.*, 2012, **48**, 5853; (*h*) V. Ganesh, V. S. Sudhir, T. Kundu and S. Chandrasekaran, *Chem.–Asian J.*, 2011, **6**, 2670; (*i*) D. Kumar, G. Patel and V. B. Reddy, *Synlett*, 2009, 399; (*j*) D. Kumar, V. B. Reddy, A. Kumar, D. Mandal, R. Tiwari and K. Parang, *Bioorg. Med. Chem. Lett.*, 2011, **21**, 449.

15 (*a*) R. Huisgen, *Proc. Chem. Soc., London*, 1961, 357; (*b*) *1,3-Dipolar Cycloaddition Chemistry*, ed. R. Huisgen and A. Pawda, Wiley, New York, 1984, p. 1; (*c*) R. Huisgen, *Pure Appl. Chem.*, 1989, **61**, 613; (*d*) V. V. Rostovtsev, L. G. Green, V. V. Fokin and K. B. Sharpless, *Angew. Chem., Int. Ed.*, 2002, **41**, 2596; (*e*) C. Chiappe, B. Mennucci, C. S. Pomelli, A. Sanzone and A. Marra, *Phys. Chem. Chem. Phys.*, 2010, **12**, 1958.

16 V. V. Rostovtsev, L. G. Green, V. V. Fokin and K. B. Sharpless, *Angew. Chem., Int. Ed.*, 2002, **41**, 2596.

17 P. Appukkuttan, W. Dehaen, E. Van der Eycken and V. V. Fokin, *Org. Lett.*, 2004, **6**, 4223.

18 (*a*) N. Mukherjee, S. Ahmmed, S. Bhadra and B. C. Ranu, *Green Chem.*, 2013, **15**, 389; (*b*) R. B. N. Baig and R. S. Varma, *Green Chem.*, 2012, **14**, 625; (*c*) B. S. P. A. Kumar, K. H. V. Reddy, B. Madhav, K. Ramesh and Y. V. D. Nageswar, *Tetrahedron Lett.*, 2012, **53**, 4595; (*d*) R. Hudson, C. J. Li and A. Moores, *Green Chem.*, 2012, **14**, 622; (*e*) J.-A. Shin, Y.-G. Lim and K.-H. Lee, *J. Org. Chem.*, 2012, **77**, 4117; (*f*) J. Andersen, S. Bolvig and X. Liang, *Synlett*, 2005, 2941; (*g*) J. Yan and L. Wang, *Synthesis*, 2010, 447; (*h*) Y.-B. Zhao, Z.-Y. Yan and Y.-M. Liang, *Tetrahedron Lett.*, 2006, **47**, 1545; (*i*) B. J. Borah, D. Dutta, P. P. Saikia, N. C. Barua and D. K. Dutta, *Green Chem.*, 2011, **13**, 3453.

19 (*a*) K. Kamata, Y. Nakagawa, K. Yamaguchi and N. Mizuno, *J. Am. Chem. Soc.*, 2008, **130**, 15304; (*b*) A. Kolarovič, M. Schnürch and M. D. Mihovilovic, *J. Org. Chem.*, 2011, **76**, 2613; (*c*) S. Karlsson and H. E. Hogberg, *Org. Prep. Proced. Int.*, 2001, **33**, 103.

20 (*a*) C. Girard, E. Onen, M. Aufort, S. Beauviere, E. Samson and J. Herscovici, *Org. Lett.*, 2006, **8**, 1689; (*b*) S. Chassaing, M. Kumarraja, A. S. S. Sido, P. Pale and J. Sommer, *Org. Lett.*, 2007, **9**, 883; (*c*) T. Miao and L. Wang, *Synthesis*, 2008, 363; (*d*) S. Chassaing, A. S. Sido, A. Alix, M. Kumarraja, P. Pale and J. Sommer, *Chem.–Eur. J.*, 2008, **14**, 6713; (*e*) B. H. Lipshutz and B. R. Taft, *Angew. Chem., Int. Ed.*, 2006, **45**, 8235; (*f*) B. Movassagh and N. Rezaei, *Tetrahedron*, 2014, **70**, 8885; (*g*) I. Jlalia, F. Gallier, N. Brodie-Linder, J. Uziel, J. Augé and N. Lubin-Germain, *J. Mol. Catal. A: Chem.*, 2014, **393**, 56.

21 (*a*) H. Sharghi, R. Khalifeh and M. M. Doroodmand, *Adv. Synth. Catal.*, 2009, **351**, 207; (*b*) F. Alonso, Y. Moglie, G. Radivoy and M. Yus, *Adv. Synth. Catal.*, 2010, **352**, 3208; (*c*) D. Raut, K. Wankhede, V. Vaidya, S. Bhilare, N. Darwatkar, A. Deorukhkar, G. Trivedi and M. Salunkhe, *Catal. Commun.*, 2009, **10**, 1240.

22 S. Brase, C. Gil, K. Knepper and V. Zimmermann, *Angew. Chem., Int. Ed.*, 2005, **44**, 5188.

23 (*a*) J. T. Fletcher and J. E. Reilly, *Tetrahedron Lett.*, 2011, **52**, 5512; (*b*) K. Barral, A. D. Moorhouse and J. E. Moses, *Org. Lett.*, 2007, **9**, 1809; (*c*) K. Odlo, E. A. Hoydahl and T. V. Hansen, *Tetrahedron Lett.*, 2007, **48**, 2097; (*d*) A. K. Feldman, B. Colasson and V. V. Fokin, *Org. Lett.*, 2004, **6**, 3897; (*e*) N. M. Smith, M. J. Greaves, R. Jewell, M. V. D. Perry, M. J. Stocks and J. P. Stonehouse, *Synthesis*, 2009, 1391.

24 (*a*) S. Roy, T. Chatterjee and S. M. Islam, *Green Chem.*, 2013, **15**, 2532; (*b*) F. Alonso, Y. Moglie, G. Radivoy and M. Yus, *Org. Biomol. Chem.*, 2011, **9**, 6385; (*c*) A. Zarei, *Tetrahedron Lett.*, 2012, **53**, 5176.

25 L. Zhang, X. Chen, P. Xue, H. H. Y. Sun, I. D. Williams, K. B. Sharpless, V. V. Fokin and G. Jia, *J. Am. Chem. Soc.*, 2005, **127**, 15998.

26 (*a*) J. Morales, J. P. Espinos, A. Caballero, A. R. Gonzalez-Elipe and J. A. Mejias, *J. Phys. Chem. B*, 2005, **109**, 7758; (*b*) J. P. Espinos, J. Morales, A. Barranco, A. Caballero, J. P. Holgado and A. R. Gonzalez-Elipe, *J. Phys. Chem. B*, 2002, **106**, 6921; (*c*) N. Toshima and Y. Wang, *Langmuir*, 1994, **10**, 4574; (*d*) S. Roy, T. Chatterjee, B. Banerjee, N. Salam, A. Bhaumik and Sk M. Islam, *RSC Adv.*, 2014, **4**, 46075; (*e*) G. Zhang, J. Long, X. Wang, W. Dai, Z. Li, L. Wu and X. Su, *New J. Chem.*, 2009, **33**, 2044; (*f*) Y. Wan, J. Ma, Z. Wang, W. Zhou and S. Kaliaguine, *Appl. Catal., B*, 2005, **59**, 235.