RSC Advances

PAPER

View Article Online
View Journal | View Issue

Cite this: RSC Adv., 2014, 4, 42137

Cellulose supported cuprous iodide nanoparticles (Cell-CuI NPs): a new heterogeneous and recyclable catalyst for the one pot synthesis of 1,4-disubstituted – 1,2,3-triazoles in water†

Pramod V. Chavan,[a] Kapil S. Pandit,[a] Uday V. Desai,*[a] Makarand A. Kulkarni[a] and Prakash P. Wadgaonkar[b]

Received 29th May 2014
Accepted 22nd August 2014

DOI: 10.1039/c4ra05080k

www.rsc.org/advances

Cellulose supported cuprous iodide nanoparticles (Cell-CuI NPs) have been demonstrated for the first time as an efficient heterogeneous catalyst in the click synthesis of 1,4-disubstituted 1,2,3-triazoles by a one-pot three component reaction between aralkyl/alkyl bromides, alkynes and sodium azide in water. The catalyst has been characterized by XRD, HRTEM, SEM, ICP–AES, EDS as well as IR spectroscopy. It was found to be reusable for five consecutive runs without significant loss of activity.

Introduction

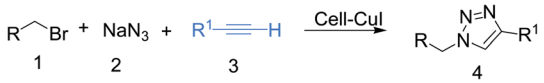
With the growing concern over environmental protection a great deal of attention has recently been focused on the development of green synthetic methodologies. In this context, the coupling of three or more components in a single step, the use of eco-benign solvents and the selection of a heterogeneous and reusable catalysts can be looked upon as three corners of an equilateral triangle representing green chemistry.[1] In particular, the last decade has witnessed tremendous developments in the field of heterogeneous catalysis.[2a] One important development in the field of heterogeneous catalysis is nano-catalysis.[2b] This is because nano catalysts, while retaining their intrinsic properties, are known to offer advantages as regards improvement in reactivity, selectivity as well as yields. Thus, design of a novel nano catalyst and exploration of it's catalytic potential in the synthesis of compounds having diverse applications is an attractive area of research.

1,2,3-Triazoles constitute an important class of heterocycles having diverse applications in the field of material science as well as pharmaceutical chemistry.[3–6] Many compounds containing 1,2,3-triazole structural motif are known to possess important biological activities such as anti-viral, anti-epileptic, anti-allergic, anti-cancer, anti-microbial as well as anti-HIV activities.[7–10] In addition, compounds belonging to this class are also useful as dyes, corrosion inhibitors, photographic materials, photo sensitizers, *etc.*[11] Owing to such a wide range of applications, synthesis of 1,2,3-triazoles is receiving increased attention.

For the synthesis of 1,2,3-triazoles several approaches are available.[12] However, thermally induced 1,3-dipolar cycloaddition between alkynes and azides is the most preferred pathway.[13] In overcoming few of the limitations associated with this cycloaddition protocol, Sharpless as well as Meldal introduced Cu(I) catalysed synthesis of 1,2,3-triazoles.[14a,b] Development of copper catalysed azide alkyne cycloaddition (CuAAC) proved to be an important milestone in the synthesis of 1,2,3-triazoles[15,16] and plethora of protocols were subsequently reported for their synthesis.[17–27] It is worthy to note that, most of these protocols, with variation in the nature of copper source, were two-component protocols involving the reaction between pre-synthesized azides and alkynes. In light of the well documented advantages of one-pot reactions and the difficulties associated with handling of low molecular weight azides, Appukkuttan *et al.* and Feldman *et al.* reported one-pot, three component synthesis of triazoles using copper (0)-copper(II) and copper(II) – sodium ascorbate combination as catalysts, respectively.[28a,b] These reports in fact opened a new door for copper catalysed one-pot synthesis of 1,2,3-triazoles. Thus, many modified protocols, mainly aimed at recovery and reuse of copper catalyst, were subsequently reported.[29a,b] With recent advances in the field of nano catalysis and after the discovery that, transition metal nano particles do serve as efficient catalysts,[30a,b] copper nanoparticles supported on alumina,[31a] CuI–Cu nanoparticles on activated carbon,[31b] copper-NPs on activated carbon,[31c] $CuFe_2O_4$ nanoparticles,[32a] graphene-γ-Fe_2O_3 magnetic nanoparticles,[32b] Cu–SiO_2 composites,[33a] Cu_2O nano crystals,[33b] CuBr supported on Oyster Shell Powder,[34a] CuBr supported on graphene oxide/Fe_3O_4,[34b] Cu(II) PBS bridged HPMOs,[34c] silica immobilised NHC-CuI,[35a] Cu^1-Zeolite,[35b] P_4VPy-

[a]Department of Chemistry, Shivaji University, Kolhapur, 416 004, India
[b]Polymer Science and Engineering Division, CSIR National Chemical Laboratory, Pune, 411 008, India. E-mail: uvdchem2011@gmail.com; Fax: +91-0231-2692333

† Electronic supplementary information (ESI) available. See DOI: 10.1039/c4ra05080k



Scheme 1 Cell-CuI-NPs catalysed synthesis of 1,2,3-triazoles.

CuI nanoparticles,[35c] Cu(II)-TD@nSiO$_2$,[36a] γ-Fe$_2$O$_3$/HAP nanoparticles,[36b] *etc.* have been reported in one-pot synthesis of 1,4-disubstituted −1,2,3-triazoles. Most of these protocols are although efficient, a few of them suffer from the drawbacks of tedious preparation of the catalyst, high reaction temperature, longer reaction time, *etc.* With these observations in mind and in tune with our continued interest in the development of green synthetic methodologies[37] we surmised that, there certainly exists scope for the development of a green and easily adaptable protocol for the synthesis of 1,2,3-triazoles. At the same time it was quite evident that, for the known synthesis of a target molecule, the main variant in practicing its green synthesis should essentially be aimed at the design of an easy to prepare, efficient, bio-compatible and reusable catalyst.

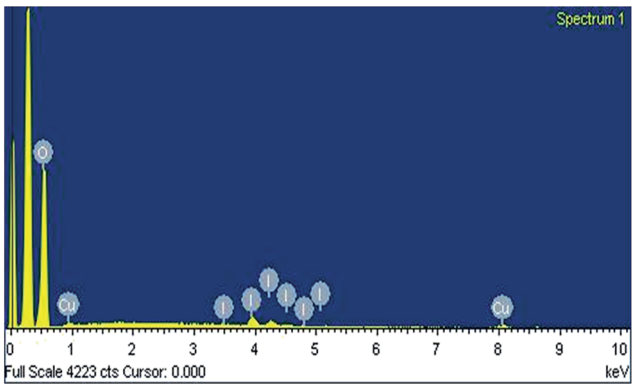


Fig. 1 EDS spectrum of Cell-CuI.

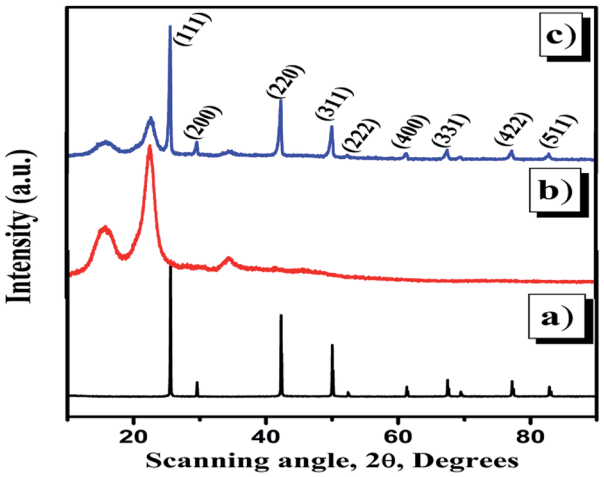


Fig. 2 XRD analysis of (a) CuI (b) cellulose and (c) cellulose supported CuI.

Cellulose is a naturally occurring biopolymer abundantly available in nature and serves as a bio-compatible support for the catalysts. Literature survey revealed that, Xu *et al.* have reported the use of cellulose supported Pd in Heck reaction[38] while Reddy *et al.* have reported the use of cellulose supported Cu (0) as catalyst in aza-Michel reaction.[39] In this article, we report the synthesis as well as use of cellulose supported CuI nanoparticles (Cell-CuI NPs) as a new catalyst in one-pot synthesis of 1,2,3-triazoles (Scheme 1).

Results and discussion

A simple method was developed for the preparation of cellulose supported CuI catalyst. In a typical procedure, to a stirred suspension of CuI (0.190 g, 1 mmol) in methanol (30 mL) was

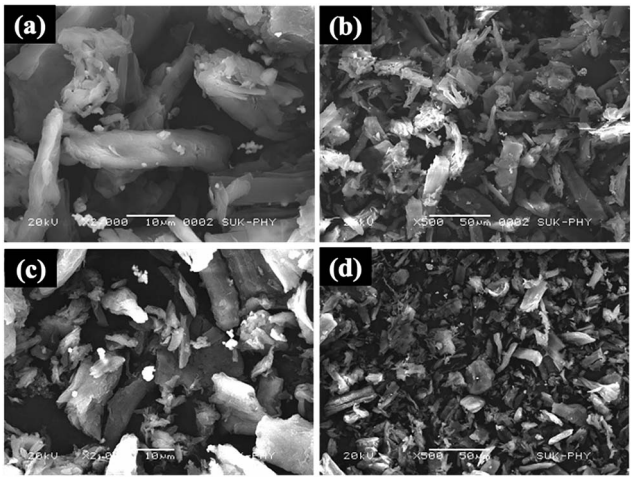


Fig. 3 SEM images of Cell – CuI. Before reaction: (a) 10 μm, (b) 20 μm; after reaction (c) 10 μm, (d) 20 μm.

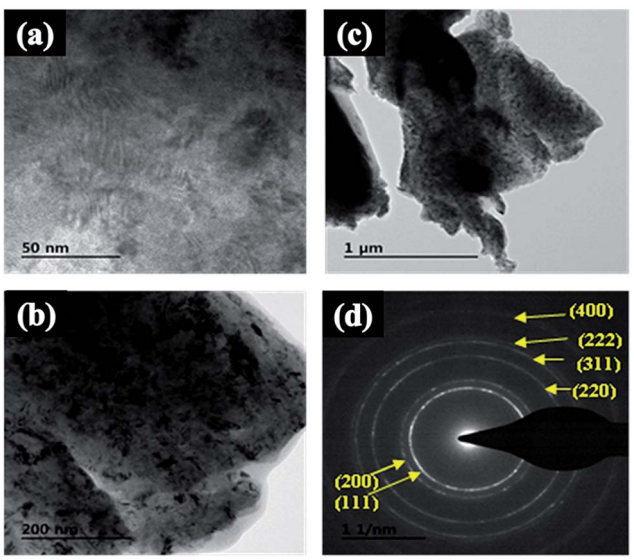


Fig. 4 HRTEM images of Cell-CuI on (a) 50 nm (b) 200 nm (c) 1 μm (d) SAED.

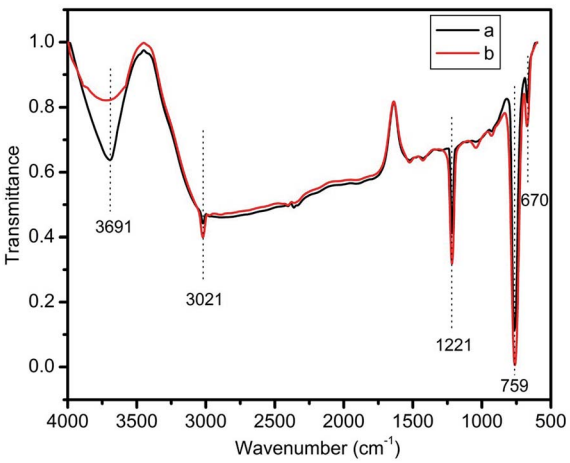
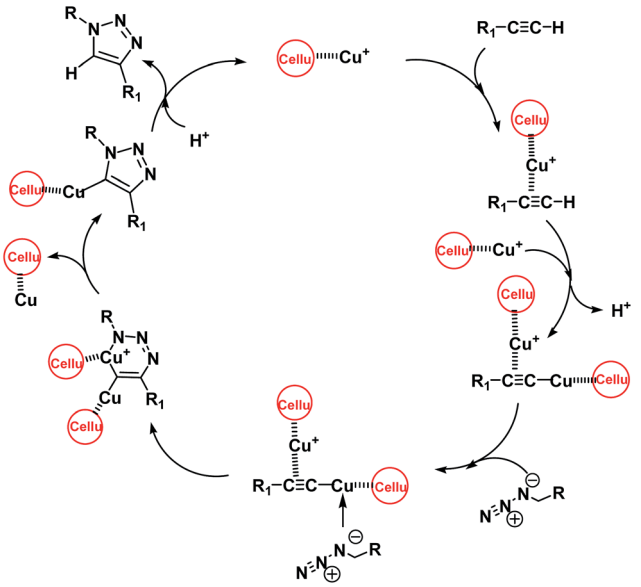


Fig. 5 FT-IR spectra of (a) cellulose and (b) cellulose supported CuI.

added microcrystalline cellulose (2 g) and stirring was continued overnight. The reaction mixture was filtered and the residue was washed repeatedly with methanol and finally with acetone. It was dried in air and then at 50 °C for six hours under vacuum. The resultant catalyst (Cell-CuI NPs) was characterised by XRD, HRTEM, SEM, ICP-AES, EDS, and FT-IR spectroscopy.

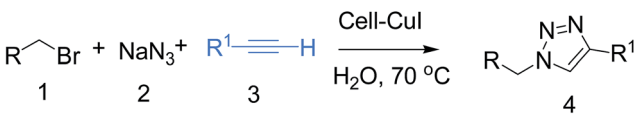
Copper content in the prepared catalyst was estimated by ICP-AES technique and it was found to be 2.4% (w/w). EDS image (Fig. 1) of the catalyst indicated the presence of CuI supported on cellulose. The analysis also confirmed the presence of CuI on support as its respective energy position at 0.92 keV (L line) and 8.04 keV (K line).

XRD pattern of CuI and cellulose supported CuI (Fig. 2a and c) showed eight peaks at $2\theta = 25.5°$, 29.5°, 42.2°, 50.0°, 61.2°, 67.45°, 77.20°, 82.8°. All the diffraction peaks and their positions for CuI, match well with JCPDS card (no. 01-076-0207) for cubic CuI. The crystallite size of CuI in Cell-CuI was determined using Scherer's formula. The peak of highest intensity [25.5° (1, 1, 1)] was selected to evaluate the particle diameter of CuI and it was found to be 33 nm. The average size of CuI particles on cellulose was estimated to be 28 nm. SEM image of the prepared catalyst indicated the deposition of nano-sized CuI crystals on cellulose (Fig. 3a and b). This reveals that, during preparation of the catalyst, possibly due to very low solubility of CuI in methanol, CuI gets converted to nano sized CuI and gets deposited over the surface of cellulose. HRTEM image of Cell-CuI (Fig. 4a–c) further confirms the presence of CuI on cellulose support with particle size 20–25 nm. SAED image (Fig. 4d) in HRTEM shows different lattice fringes which matches well with different planes of CuI according to XRD pattern.



Scheme 2 Plausible mechanism of formation of 1,2,3-triazoles.

Table 1 Optimization of the reaction conditions for one-pot synthesis of 1,2,3-triazole, **3a**, using Cell-CuI as catalyst[a]



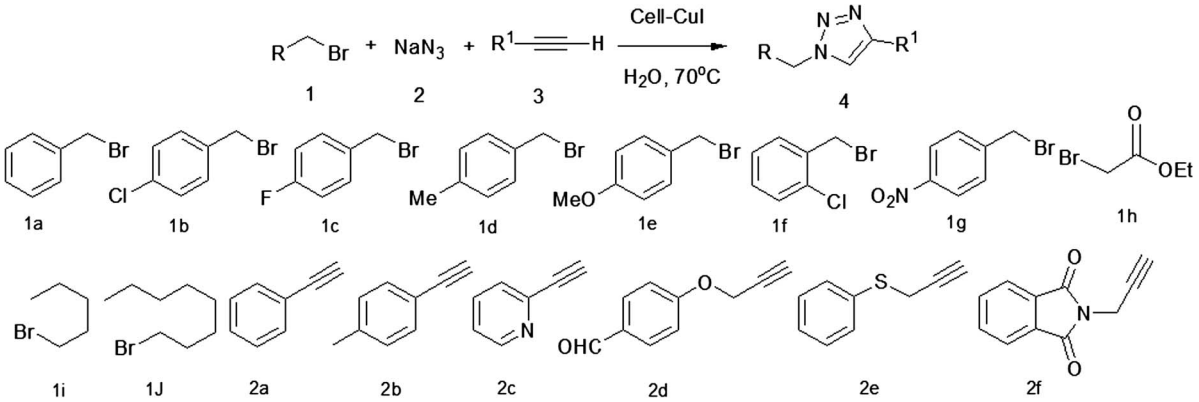
No.	Reaction medium	Catalyst (mg)	Temperature (°C)	Time (h)	Yield (%)[b]
1	Water	200, 150, 100, 75, 50	100, 90, 80, 70, 60	3, 3, 3, 3, 5	95, 94, 94, 84, 79
2	Ethanol	200, 150, 100	Reflux	4, 4, 4	86, 85, 82
3	Acetonitrile	200, 150, 100	Reflux	4, 4, 4	76, 73, 69
4	Tetrahydrofuran	200	Reflux	5	37
5	Toluene	200	100	5	67
6	Dichloromethane	200	Reflux	5	42
7	Dimethylformamide	200	100	5	61
8	Acetonitrile + water (1 : 1)	200	Reflux	5	78
9	Acetonitrile + water (1 : 3)	200	Reflux	5	83
10	*t*-Butanol + water (3 : 1)	200	Reflux	5	73

[a] Reaction conditions: benzyl bromide (1 mmol), phenyl acetylene (1 mmol), sodium azide (1. 1 mmol), solvent, catalyst, temperature. [b] Yields refer to isolated product.

Comparison of the FT-IR spectra of cellulose and cellulose supported CuI indicated that, when CuI gets supported on cellulose intensity of broad band due to hydroxyl group in cellulose decreases appreciably (Fig. 5a). Furthermore, IR spectrum of cellulose supported CuI (Fig. 5b) exhibits a characteristic band at 670 cm^{-1} indicating the presence of copper.

After the preparation followed by adequate characterisation of the prepared catalyst, we planned to initially explore it's catalytic potential in click synthesis of 1,2,3-triazoles using

Table 2 Cell-CuI catalyzed click synthesis of 1,4-disubstituted-1,2,3-triazoles[a]



Entry	Halide (1)	Alkyne (2)	Product (4)	Time (h)	Yield[b] (%)	TON	TOF	M.P. °C Obs./(Lit)[Ref]
1	**1a**	**2a**	**4aa**	2	96	2487	1243	127–130/(128–130)[31b]
2	**1b**	**2a**	**4ba**	4	89	2355	588	142–145/(143–144)[41d]
3	**1c**	**2a**	**4ca**	4	91	2408	602	128–130/(129–131)[41a]
4	**1d**	**2a**	**4da**	3	89	2355	785	104–107/(105–106)[41b]
5	**1e**	**2a**	**4ea**	4	87	2302	575	133–135/(136–137)[41e]
6	**1f**	**2a**	**4fa**	5	88	2328	465	79–81/(79–81)[41c]
7	**1g**	**2a**	**4ga**	5	94	2487	497	150–155/(156–157)[31b]
8	**1h**	**2a**	**4ha**	5	85	2249	450	99–102/(99)[41a]
9	**1i**	**2a**	**4ia**	6	82	2170	361	66–68/(68–70)[36b]
10	**1j**	**2a**	**4ja**	6	81	2143	357	75–77/(74–75)[41a]
11	**1a**	**2b**	**4ab**	3	89	2355	785	142–146/(150)[41f]
12	**1b**	**2b**	**4bb**	4	88	2328	582	140–143
13	**1c**	**2b**	**4cb**	4	92	2434	608	140–144/(150–151)[41g]
14	**1d**	**2b**	**4db**	4	89	2355	588	118–120/(—)[41g]
15	**1e**	**2b**	**4eb**	4	93	2461	615	132–135/(—)[35a]
16	**1f**	**2b**	**4fb**	4	87	2302	575	115–118
17	**1a**	**2c**	**4ac**	4	86	2276	568	110–113/(114–115)[41h]
18	**1b**	**2c**	**4bc**	4	85	2249	562	115–117
19	**1c**	**2c**	**4cc**	4	90	2381	595	102–104/(104–106)[41i]
20	**1d**	**2c**	**4dc**	4	87	2302	575	105–108/(—)[32a]
21	**1f**	**2c**	**4fc**	4	84	2223	555	107–110
22	**1g**	**2c**	**4gc**	5	87	2302	460	156–159/(177–178)[41j]
23	**1h**	**2c**	**4hc**	5	83	2196	439	117–120
24	**1a**	**2d**	**4ad**	3	85	2249	749	105–108/(99–100)[41k]
25	**1b**	**2d**	**4bd**	4	90	2381	595	108–111
26	**1c**	**2d**	**4cd**	4	89	2355	585	101–104
27	**1d**	**2d**	**4dd**	4	85	2249	562	118–122
28	**1g**	**2d**	**4gd**	4	96	2545	635	128–132
29	**1a**	**2e**	**4ae**	4	80	2116	529	63–66/(65)[41l]
30	**1a**	**2f**	**4af**	3	85	2249	749	177–179/(176–177)[41e]
31	**1b**	**2f**	**4bf**	4	85	2249	562	175–176
32	**1c**	**2f**	**4cf**	3	95	2513	837	143–146
33	**1d**	**2f**	**4df**	3	87	2302	767	164–166
34	**1e**	**2f**	**4ef**	4	84	2222	555	145–148/(149–150)[41e]
35	**1f**	**2f**	**4ff**	4	85	2249	562	145–148

[a] Reaction conditions: benzyl bromide(1 mmol), alkyne(1 mmol) and sodium azide (1.1 mmol), Cell-CuI (3.5 mol%), water (3 mL), 70 °C. [b] Yields refer to pure isolated compounds.

benzyl bromide, phenyl acetylene and sodium azide as model substrates (Scheme 1).

To begin with, to a well stirred mixture of benzyl bromide (1 mmol), phenyl acetylene (1 mmol) and sodium azide (1.1 mmol) was added Cell-CuI (200 mg; ~0.07 mmol of CuI) as catalyst. Stirring was continued at room temperature under solvent-free condition. Timely analysis of the reaction mixture (TLC) did not indicate any appreciable progress of the reaction. So as to examine the effect of solvent, the model reaction was then carried out in different reaction media. However, the results were not encouraging. Hence the model reactions were then carried out at the reflux temperature of the selected reaction medium and it was truly gratifying to notice that, the formation of desired 1-benzyl-4-phenyl-1*H*-1,2,3-triazole, **4aa**, proceeds to completion with the choice of water as an eco-benign reaction medium. Further optimisation of the reaction conditions with respect to reaction temperature as well as catalyst loading revealed that, in aqueous medium desired triazole **4aa** is obtained in excellent yield at 70 °C using 100 mg of Cell-CuI (~0.035 mmol of CuI, 3.7 mol%) as the catalyst (Table 1). Compared to benzyl bromide, benzyl chloride being less toxic, less expensive and easier to handle, the model reaction was then carried out using benzyl chloride as the substrate. However, the reaction required longer time and furnished a mixture of products (TLC).

Mechanism of copper catalysed synthesis of 1,2,3-triazoles has been the subject of exhaustive study and those have recently been reviewed by Berg *et al.*[40] They have emphasised on dinuclear mechanism of CuAAC. Based upon their studies we propose following mechanism for the formation of 1,2,3-triazoles (Scheme 2).

The nano sized catalysts are claimed to offer the advantages of better yields, more reactivity as well as selectivity. In support of this claim, we planned to compare the catalytic efficiency of Cell-CuI NPs with commercially available CuI. Accordingly, two model reactions were carried out under the established reaction conditions using Cell-CuI NPs (100 mg, 3.7 mol% CuI) and commercially available CuI (7 mg, 3.7 mol%) as catalysts. Upon completion of the reactions followed by routine work-up, the expected triazole, **4aa**, was obtained in 94% and 72% yield, respectively. The results clearly justify the choice of Cell-CuI NPs as the catalyst in one-pot synthesis of 1,2,3-triazoles (Table 1).

Next, we turned our attention to examine generality of the reaction conditions. Accordingly benzyl bromide component in the model reaction was replaced with 4-chloro, 4-fluoro, 4-methyl, 4-methoxy, 4-nitro as well as 2-chloro benzyl bromide (**1a–g**). In each case, corresponding 1,2,3-triazole was obtained in excellent yield (Table 2, entries 1–7) and most gratifyingly, the resultant product did not require any further purification by conventional methods. During the extension of the protocol towards aliphatic bromides it was observed that, with the choice of ethyl bromoacetate as an activated aliphatic bromide, the reaction furnished desired triazole, **4ha**, in acceptable yield (Table 2, entry 8). However, in case of non-activated alkyl halides like *n*-pentyl bromide as well as *n*-octyl bromide, the reaction required longer reaction time and furnished corresponding triazoles in lower yields (Table 2, entry 9, 10). During evaluation of the scope of the protocol, it was further observed that the protocol developed was also effective with structurally diverse alkynes *viz.* *p*-tolyl ethyne, 2-pyridyl ethyne, phenyl propargyl thioether, 4-(prop-2-ynyloxy) benzaldehyde, and *N*-propargyl phthalimide (**2b–f**). The reactions once again furnished expected 1,2,3-triazoles in excellent yields as well as purity (Table 2). Since the protocol developed proved to be of wide generality to furnish range of 1,2,3-triazoles in excellent yields as well as purity, we believed that, the protocol would be of general use if scaled up. Accordingly, the model reaction between benzyl bromide, phenyl acetylene and sodium azide was carried out on 20 mmol scale when the reaction proceeded smoothly and furnished corresponding 1,2,3-triazole, **4aa**, in 96% yield.

In heterogeneously catalysed reactions reusability as well as stability of the catalyst is of importance both from economical and environmental point of view. Hence, after completion of gram scale model reaction, the catalyst was separated by filtration, washed with ethyl acetate, acetone, dried in air and was used in next run. It was noticed that the recovered catalyst could be used for five consecutive cycles without appreciable change in the yield of desired triazole (Fig. 6). From the stability view point, we initially checked the leaching behaviour of the catalyst. Thus, after separation of the catalyst, the resultant filtrate was analysed using AAS. The results were negative. In substantiation of this observation, we also performed ICP-AES analysis of the recovered catalyst. During the analysis of the catalyst recovered after fifth cycle, only 0.6% leaching of the catalyst was noticed. SEM images (Fig. 4c and d) of the reused catalyst did not exhibit any morphological changes during recycling of the catalyst.

In recent years there being many reports on the development of new catalysts for one-pot synthesis of 1,2,3-triazoles, lately we planned to compare the protocol developed by us with the protocols reported recently for the same purpose. From the results summarized in Table 3, we concluded that, each protocol has its own merits as well as demerits. However, from view point of cost, operational simplicity, ease of preparation of the catalyst, its easier separation from the reaction mixture and avoidance of conventional purification, the protocol developed by us is superior and easily adaptable.

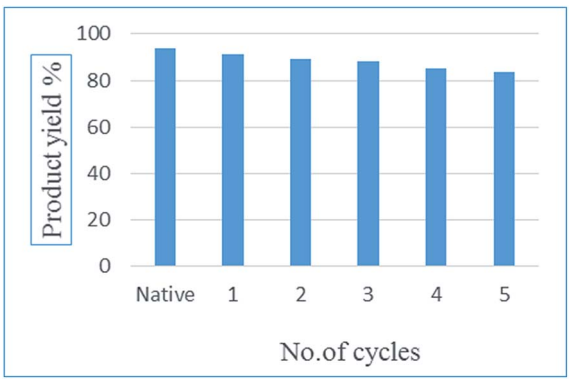


Fig. 6 Reusability of the Cell-CuI catalyst.

Table 3 Comparison of catalytic efficiency of Cell-CuI with other reported catalysts in synthesis of **4aa**

No.	Catalyst (mol% mg^{-1})	Conditions	Time (h)	Yield (%)	Ref.
1	Cell-CuI NPs 100 mg	70 °C, H_2O	2	96	This work
2	Cu–Al_2O_3 NPs, 10 mg	RT, H_2O	3	92	31*a*
3	Cu NPs on charcoal (1 mol%)	100 °C, H_2O	0.6	91	31*b*
4	Cu NPs on activated carbon (0.5 mol%)	70 °C, H_2O	3	98	31*c*
5	Zn/C, (10 mol%)	50 °C, DMF	15	81	41*c*
6	Cu^I–Zeolite (Cu^I-USY),10 mol%	90 °C, H_2O	15	90	35*b*
7	$CuFe_2O_4$ NPs, 5 mol%	70 °C, H_2O	3	93	32*a*
8	Cu/SiO_2 composite (10 mol%)	70 °C, H_2O	12	93	33*a*
9	Silica immobilised NHC-Cu(I), 0.5 mol% Cu	80 °C, H_2O	6	98	35*a*
10	P_4VPy-CuI NPs (100 mg)	100 °C, H_2O	15[a]	90	35*c*
11	Cu_2O nanocrystals (cube)	55 °C, EtOH	7	88	33*b*
12	OSPs – CuBr, 2.5 mol%	70 °C, H_2O	4	91	34*a*
13	γ-Fe_2O_3/HAP NPs, 5 mol%	100 °C, H_2O	5	87	36*b*
14	CuBr on graphene oxide/Fe_3O_4 (benzyl chloride), 5 mol%	80 °C, H_2O microwave	8 h, 10[a]	98, 98	34*b*
15	Cu(II)/PBS/HMPO, 10 mg	100 °C, H_2O	3.5	96	34*c*
16	Graphene-γ-Fe_2O_3 magnetic nano–composite, 50 mg	60 °C, H_2O, inert atmosphere	NR	92	36*c*

[a] Time in minutes; NA: not reported.

Conclusion

In summary, we have reported the preparation, characterisation as well as use of cellulose supported CuI nanoparticles (Cell-CuI NPs) as a new heterogeneous catalyst in click synthesis of 1,2,3-triazoles. Use of water as an eco-benign reaction medium, excellent yields, avoidance of conventional purification techniques and reusability of the catalyst for five consecutive runs without appreciable change in composition as well as activity of the catalyst make this green protocol a viable alternative for one-pot synthesis of 1,4-disubstituted-1,2,3-triazoles.

Experimental

General methods

Benzyl halides (Aldrich), alkynes (Aldrich/Alfa Aesar), sodium azide (Sd Fine Chemicals, Mumbai), copper(I) iodide (Spectrochem, Mumbai) and microcrystalline cellulose (SRL, Mumbai) were used as received. All the melting points were recorded using Kumar melting point apparatus. IR spectra were recorded as neat using Thermo Scientific Nicolet iS10 FT-IR Spectrometer. ^{1}H NMR (300 MHz) and ^{13}C NMR (75.4 MHz) spectra were recorded using Bruker Avance-II spectrometer. High resolution mass spectra (HRMS) were recorded using Thermo Scientific Q-Exactive, Accela 1250 pump, instrument. X-Ray Powder Diffraction (XRD) data were collected on X-Ray Powder Diffractometer D2 PHASER, Bruker. Copper content in the supported catalyst was determined by inductively coupled plasma atomic emission spectroscopy (ICP-AES) using ARCOS ICP-AES. Scanning electron micrographs were obtained using JSM-7600 F instrument. HRTEM were obtained using Transmission Electron Microscopy (TEM) micrographs, TECNAI F20 Philips operated at 200 kV.

Preparation of cellulose supported cuprous iodide (Cell-CuI) catalyst

To a stirred well suspension of CuI (0.190 g, 1 mmol) in methanol (30 mL) was added microcrystalline cellulose (2 g) and stirring was continued overnight. The reaction mixture was filtered and residue was washed repeatedly with methanol and finally with acetone. It was dried in air and then at 50 °C for six hours under vacuum. The resultant catalyst (Cell-CuI) was characterised by XRD, HRTEM, SEM, ICP-AES, EDS, and FT-IR techniques.

Representative procedure: synthesis of 1-benzyl-4-phenyl-1*H*-1,2,3-triazole, 4aa

Benzyl bromide (1 mmol), sodium azide (1.1 mmol) and phenyl acetylene (1 mmol) were placed in a round bottom flask. Water (2 mL) and cellulose-CuI (0.1 gm) were added and the reaction mixture was heated at 70 °C. After completion of the reaction (TLC), the reaction mixture was filtered and the filter was washed with ethyl acetate (4 × 10 mL). The organic extract was washed with water, brine and dried over Na_2SO_4. The removal of solvent under vacuum furnished corresponding 1,2,3-triazole, which did not require further purification. The recovered catalyst was washed with acetone, dried in air and reused.

Gram-scale synthesis of 1-benzyl-4-phenyl-1*H*-1,2,3-triazole, 4aa

Benzyl bromide (20 mmol), phenyl acetylene (20 mmol) and sodium azide (22 mmol) were placed in 100 mL of round bottom flask. Water (30 mL) and cellulose-CuI (2 gm) were added and the reaction mixture was heated at 70 °C. After completion of the reaction (TLC), the reaction mixture was filtered and washed with ethyl acetate (4 × 20 mL). The collected organic extract was washed with water, brine and dried over Na_2SO_4. The solvent

was removed under vacuum to give corresponding 1-benzyl-4-phenyl-1*H*-1,2,3-triazole, in excellent yield (96%) as well as purity.

All the compounds were adequately characterised by physical as well as chemical methods. Spectral data of unknown compounds is summarised below. For original spectra of unknown compounds please see ESI.†

1-(4-Chlorobenzyl)-4-*p*-tolyl-1*H*-1,2,3-triazole, 4bb. Off-white solid; M.P.: 140–143 °C; IR (neat): 2917, 2359, 1716, 1559, 1489, 1340, 1219, 1089, 1048, 848, 754, 723 cm^{-1}; ^1H NMR (300 MHZ, $CDCl_3$): δ 2.38 (s, 3H), 5.55 (s, 2H), 7.23 (d, 2H, $J = 7.8$ Hz), 7.27 (d, 2H, $J = 2.4$ Hz), 7.35–7.38 (m, 2H), 7.38 (d, 2H, $J = 1.8$ Hz), 7.64 (s, 1H), 7.70 (d, 2H, $J = 8.4$ Hz);^{13}C NMR (75.4 MHz, $CDCl_3$): δ 21.27 (CH_3), 53.47 (CH_2), 119.09 (ArCH), 125.64 (ArCH), 127.48 (ArC), 129.36 (ArCH), 129.37(ArCH), 129.52 (ArCH), 133.22 (ArC), 134.84 (ArC), 138.19 (ArC), 148.36 (ArC); HRMS: mass calculated for $[C_{16}H_{14}ClN_3]$: 284.0955 $[M + H]^+$ and 306.0774 $[M + Na]^+$; obs. mass: 284.0949 $[M + H]^+$ and 306.0768 $[M + Na]^+$.

1-(4-Methoxybenzyl)-4-*p*-tolyl-1*H*-1,2,3-triazole, 4eb. Yellow-brown solid; M.P. 132–135 °C; IR (neat): 3091, 2917, 1716, 1599, 1513, 1456, 1108, 1078, cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.37 (s, 3H), 3.82 (s, 3H), 5.51 (s, 2H), 6.93 (d, 2H, $J = 8.7$ Hz), 7.21–7.29 (m, 4H), 7.60 (s, 1H),7.69 (d, 2H, $J = 8.1$ Hz); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 21.27 (CH_3), 53.79 (CH_2), 55.35 (OCH_3), 114.51 (ArCH), 118.97 (ArCH), 125.61 (ArCH), 126.65 (ArC), 127.69 (ArC), 129.50 (ArCH), 129.68 (ArCH), 137.99 (ArC), 148.16(ArC), 159.95(ArC); HRMS: mass calculated for $[C_{17}H_{17}N_3O]$: 280.1450 $[M + H]^+$ and 302.1269 $[M + Na]^+$; obs. mass: 280.1444 $[M + H]^+$ and 302.1264 $[M + Na]^+$.

1-(2-Chlorobenzyl)-4-*p*-tolyl-1*H*-1,2,3-triazole, 4fb. White solid; M.P.: 115–118 °C; IR (neat): 2359, 1498, 1475, 1447, 1353, 1221, 1116, 1080, 1048, 836, 774, 752, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.38 (S, 3H), 5.72 (s, 2H), 7.22 (s, 1H), 7.248 (s, 2H), 7.30–7,36 (m, 2H), 7.47 (m, 1H), 7.72 (d, 2H, $J = 8$ Hz), 7.74 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 21.28(CH_3), 51.41(CH_2), 119.46 (ArCH), 125.64 (ArCH), 127.63(ArCH), 129.50 (ArCH), 129.91 (ArCH), 130.20(ArCH), 130.25 (ArCH), 132.61 (ArC), 133.42 (ArC), 138.08 (ArC), 148.23 (ArC); HRMS: mass calculated for $[C_{16}H_{14}ClN_3]$: 284.0955 $[M + H]^+$ and 306.0774 $[M + Na]^+$; obs. mass: 284.0949 $[M + H]^+$ and 306.0768 $[M + Na]^+$.

2-(1-(4-Chlorobenzyl)-1*H*-1,2,3-triazol-4-yl) pyridine, 4bc. Pale yellow solid; M.P.: 115–117 °C; IR (neat): 2917, 2848, 2342, 1716, 1683, 1594, 1540, 1430, 1344, 1228, 1079, 995, 783, 765, 740 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.58 (s, 2H), 7.25–7.39 (m, 5H), 7.80–7.86 (m, 1H), 8.17 (s, 1H), 8.22 (d, 1H, $J = 8.1$ Hz), 8.56 (d, 1H, $J = 3.6$ Hz); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 3.67 (CH_2), 120.61 (ArCH), 122.51 (ArCH), 123.12 (ArCH), 129.40 (ArCH), 129.60 (ArCH), 132.81 (ArC), 134.98 (ArC), 137.83 (ArCH), 147.89 (ArC), 148.85 (ArCH), 149.49 (ArC); HRMS: mass calculated for $[C_{14}H_{11}ClN_4]$: 271.0750 $[M + H]^+$ and 293.0570 $[M + Na]^+$; obs. mass: 271.0745 $[M + H]^+$ and 293.0564 $[M + Na]^+$.

2-(1-(2-Chlorobenzyl)-1*H*-1,2,3-triazol-4-yl) pyridine, 4fc. Pale yellow solid; M.P.: 107–110 °C; IR (neat): 3160, 3050, 1716, 1680, 1604, 1434, 1355, 1226, 1193, 1088, 1072, 994 cm^{-1}; ^1H NMR (300 MHz, CDCl3): δ 5.73 (s, 2H), 7.21–7.35 (m, 4H), 7.44 (d, 1H, $J = 7.5$ Hz), 7.76–7.82 (m, 1H), 8.19 (s, 1H), 8.21 (m, 1H), 8.56 (m, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 51.65 (CH_2), 120.43 (ArCH), 122.42 (ArCH), 122.96 (ArCH), 127.61 (ArCH), 130.02 (ArCH), 130.38 (ArCH), 130.58 (ArCH), 132.15 (ArC), 133.77 (ArC), 137.29 (ArCH), 148.22 (ArC), 148.98 (ArCH), 149.95 (ArC); HRMS: mass calculated for $[C_{14}H_{11}ClN_4]$: 271.0750 $[M + H]^+$ and 293.0570 $[M + Na]^+$; obs. mass: 271.0745 $[M + H]^+$ and 293.0564 $[M + Na]^+$.

2-(1-(4-Nitrobenzyl)-1*H*-1,2,3-triazol-4-yl) pyridine, 4gc. Yellow solid; M.P.: 156–159 °C; IR (neat): 2918, 2848, 2342, 1594, 1568, 1543, 1515, 1430, 1418, 1352, 1228, 1121, 1079, 995, 783 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.73 (s, 2H), 7.25–7.29 (m, 1H), 7.48 (d, 2H, $J = 8.4$ Hz), 7.79–7.84 (m, 1H), 8.17 (s, 1H), 8.20–8.27 (m, 3H), 8.57 (d,1H $J = 4.8$ Hz); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 53.35 (CH_2), 120.62 (ArCH), 122.71 (ArCH), 123.29 (ArCH), 124.38 (ArCH), 128.78 (ArCH), 137.73 (ArCH), 141.35 (ArC), 148.18 (ArC), 148.73 (ArCH), 149.37 (ArC), 156.28(ArC); HRMS: mass calculated for $[C_{14}H_{11}N_5O_2]$: 282.0991 $[M + H]^+$ and 304.0810 $[M + Na]^+$; obs. mass: 282.0986 $[M + H]^+$ and 304.0805 $[M + Na]^+$.

Ethyl 2-(4-(pyridin-2-yl)-1*H*-1 2 3-triazol-1-yl) acetate, 4hc. Grey solid; M.P.: 117–120 °C; IR (neat): 3165, 3042, 2969, 2345, 1742, 1712, 1684, 1610, 1545, 1440, 1215 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.32 (t, 3H, $J = 7.2$ Hz), 4.30 (q, 2H, $J = 7.2$ Hz), 5.24 (s, 2H), 7.28–7.30 (d,1H, $J = 9$ Hz), 7.81–7.87 (t, 1H, $J = 7.8$ Hz), 8.23 (d, 1H, $J = 7.8$ Hz), 8.37 (s, 1H), 8.61 (d, 1H, $J = 4.5$ Hz); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 14.07 (CH_3), 51.08 (CH_2), 62.57 (CH_2), 120.42 (ArCH), 122.99 (ArCH), 123.51 (ArCH), 137.05 (ArCH), 148.69 (ArCH), 149.97 (ArC), 149.31 (ArC), 166 (C═O); HRMS: mass calculated for $[C_{11}H_{12}N_4O_2]$: 233.1039 $[M + H]^+$ and 255.0858 $[M + Na]^+$; obs. mass: 233.1033 $[M + H]^+$ and 255.0852 $[M + Na]^+$.

4-((1-(4-Chlorobenzyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy) benzaldehyde, 4bd. Off white solid; M.P.: 108–110 °C; IR (neat): 3100, 2918, 1675, 1601, 1572, 1507, 1457, 1160, 1112, 772, 756 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.28 (s, 2H), 5.53 (s, 2H), 7.09 (d, 2H, $J = 8.4$ Hz), 7.24 (d, 2H, $J = 8.4$ Hz), 7.36 (d, 2H, $J = 8.4$ Hz), 7.59 (s, 1H), 7.83 (d, 2H, $J = 8.7$ Hz), 9.89 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 53.58 (CH_2), 62.14 (CH_2), 115.07 (ArCH), 122.77 (ArCH), 129.41 (ArCH), 129.46 (ArCH), 130.40 (ArC), 131.99 (ArCH), 132.80 (ArC), 135.01 (ArC) 143.84 (ArC), 163.08 (ArC), 190.75 (CHO); HRMS: mass calculated for $[C_{17}H_{14}ClN_3O_2]$: 328.0853 $[M + H]^+$; obs. mass: 328.0847 $[M + H]^+$.

4-((1-(4-Fluorobenzyl)-1*H*-1 2 3-triazol-4-yl)methyl) benzaldehyde, 4cd. White solid; M.P.: 101–104 °C; IR (neat): 3129, 2844, 1683, 1603, 1540, 1457, 1231, 1222, 1131, 1110, 744 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.27 (s, 2H), 5.52 (s, 2H), 7.09 (d, 4H, $J = 7.8$), 7.29 (s, 2H), 7.57 (s, 1H), 7.83 (d, 2H, $J = 8.1$ Hz), 9.89 (s, 1H, CHO); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 53.57 (CH_2), 62.16 (CH_2), 115.07 (ArCH), 116.07 (ArCH), 116.36 (ArCH), 122.70 (ArCH),129.99 (ArC), 130.10 (ArCH), 130.40 (ArC), 131.97 (ArC), 143.76 (ArC), 163.09 (ArC), 190.72 (CHO); HRMS: mass calculated for $[C_{17}H_{14}FN_3O_2]$: 312.1148 $[M + H]^+$ and 334.0968 $[M + Na]^+$; obs. mass: 312.1143 $[M + H]^+$ and 334.0962 $[M + Na]^+$.

4-((1-(4-Methylbenzyl)-1*H*-1,2,3-triazol-4-yl)methyl) benzaldehyde, 4dd. Off white solid; M.P.: 118–122 °C; IR (neat): 3145, 3095, 2890, 1693, 1643, 1623, 1555, 1465, 1248, 1200, 745 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.36 (s, 3H), 5.26 (s, 2H), 5.50 (s, 2H), 7.09 (d, 2H, $J = 8.7$ Hz), 7.20 (s, 4H), 7.55 (s, 1H), 7.83 (d,

2H, $J = 8.7$ Hz), 9.88 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 21.16 (CH_3) 54.15 (CH_2), 62.18 (CH_2), 115.08 (ArCH), 122.73 (ArCH), 128.22 (ArCH), 129.85 (ArCH), 130.33 (ArC), 131.25 (ArC), 131.98 (ArCH), 138.90 (ArC), 143.51 (ArC), 163.15 (ArC), 190.78 (CHO); HRMS: mass calculated for $[C_{18}H_{17}N_3O_2]$: 308.1399 $[M + H]^+$ and 330.1218 $[M + Na]^+$; obs. mass: 308.1394 $[M + H]^+$ and 330.1213 $[M + Na]^+$.

4-((1-(4-Nitrobenzyl)-1*H*-1,2,3-triazol-4-yl) methoxy) benzaldehyde, 4gd. Yellow solid; M.P.: 128–132 °C; IR (neat): 2917, 2849, 1703, 1684, 1653, 1600, 1540, 1472, 1457, 1345, 1128, 1108, 755 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.30 (s, 2H), 5.69 (s, 2H), 7.10 (d, 2H, $J = 8.7$ Hz), 7.43 (d, 2H, $J = 8.4$ Hz), 7.68 (S, 1H), 7.84 (d, 2H, $J = 8.7$ Hz), 8.23 (d, 2H, $J = 8.7$ Hz), 9.89 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 53.26 (CH_2), 62.08 (CH_2), 115.04 (ArCH), 123.09 (ArCH), 124.37 (ArCH), 128.68 (ArCH), 130.46 (ArC), 132.01 (ArCH), 141.33 (ArC), 144.23 (ArC), 148.16 (ArC), 162. 99 (ArC), 190.74 (CHO); HRMS: mass calculated for $[C_{17}H_{14}N_4O_4]$: 339.1093 $[M + H]^+$ and 361.0913 $[M + Na]^+$; obs. mass: 339.1088 $[M + H]^+$ and 361.0907 $[M + Na]^+$.

2-((1-(4-Chlorobenzyl)-1*H*-1,2,3-triazol-4-yl) methyl)isoindoline-1,3-dione, 4bf. White solid; M. P.: 174–176 °C; IR (neat): 2918, 2849, 1771, 1709, 1653, 1466, 1436, 1104, 777, 755, 711 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.99 (s, 2H), 5.46 (s, 2H), 7.21 (d, 2H, $J =$ 8.4 Hz), 7.35 (d, 2H, $J = 8.4$ Hz), 7.53 (s, 1H), 7.73 (m, 2H), 7.86 (m, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 33.04 (CH_2), 53.44 (CH_2), 122.66 (ArCH), 123.47 (ArCH), 129.34 (ArCH), 129.44 (ArCH), 132.02 (ArC), 132.93 (ArC), 134.11 (ArCH), 134.85 (ArC), 143.35 (ArC), 167.64 (C═O); HRMS: mass calculated for $[C_{18}H_{13}ClN_4O_2]$: 353.0805 $[M + H]^+$ and 375.0625 $[M + Na]^+$; obs. mass: 353.0800 $[M + H]^+$ and 375.0619 $[M + Na]^+$.

2-((1-(4-Fluorobenzyl)-1*H*-1,2,3-triazol-4-yl) methyl)isoindoline-1,3-dione, 4cf. Off white solid; M.P.: 143–146 °C; IR (neat): 3140, 2850, 1765, 1643, 1593, 1550, 1448, 1235, 1200, 1140, 750, 708 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.97 (s, 2H), 5.46 (s, 2H), 7.05 (t, 2H, $J = 8.7$ Hz), 7.26 (dd, 2H, $J = 4.5$ & 5.1 Hz), 7.52 (S, 1H), 7.72 (m, 2H), 7.85 (m, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 33.04 (CH_2), 53.43 (CH_2), 115.97 (ArCH), 116.26 (ArCH), 122.61 (ArC), 123.44 (ArCH), 129.94 (ArCH), 130.05 (ArC), 130.29 (ArC),132.03 (ArC), 134.09 (ArCH), 167.63 (C═O); HRMS: mass calculated for $[C_{18}H_{13}FN_4O_2]$: 337.1101 $[M + H]^+$ and 359.0920 $[M + Na]^+$; obs. mass: 337.1095 $[M + H]^+$ and 359.0915 $[M + Na]^+$.

2-((1-(4-Methylphenyl methyl)-1*H*-1,2,3-triazol-4-yl) methyl)-isoindoline-1,3-dione, 4df. Yellow solid; M. P.: 164–166 °C; IR (neat): 3123, 1771, 1713, 1613, 1462, 1425, 1131, 1115, 771, 708 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.35 (s, 3H), 4.97 (s, 2H), 5.44 (s, 2H), 7.17 (s, 4H), 7.49 (s, 1H), 7.72 (m, 2H), 7.85 (m, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 21.15 (CH_3), 33.08 (CH_2), 54.01 (CH_2), 122.53 (ArCH), 123.44 (ArCH), 128.16 (ArCH), 129.77 (ArCH), 131.39 (ArC), 132.05 (ArC), 134.06 (ArCH), 138.71 (ArC), 143.08 (Ar–C), 167.65 (C═O); HRMS: mass calculated for $[C_{19}H_{16}N_4O_2]$: 333.1352 $[M + H]^+$ and 355.1171 $[M + Na]^+$; obs. mass: 333.1346 $[M + H]^+$ and 355.1165 $[M + Na]^+$.

2-((1-(2-Chlorobenzyl)-1*H*-1 2 3-triazol-4-yl)methyl)isoindoline-1,3-dione, 4ff. Pale yellow solid; M.P.: 145–148 °C; IR (neat): 3035, 2948, 1769, 1690, 1600, 1450, 1435, 1145, 1115, 765, 740 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.99 (s, 2H), 5.63 (s, 2H), 7.15–7.44 (m, 4H), 7.62 (s, 1H), 7.72 (m, 2H), 7.85 (m, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 33.43 (CH_2), 51.37 (CH_2), 122.99 (ArCH), 123.42 (ArCH) 127.57 (ArCH), 129.88 (ArCH), 130.18 (ArCH) 130.29 (ArCH), 131.98 (ArC), 132.48 (ArC), 133.48 (ArC), 134.04 (ArCH) 143.53 (ArC), 164.52 (C═O); HRMS: mass calculated for $[C_{18}H_{13}ClN_4O_2]$: 353.0805 $[M + H]^+$ and 375.0625 $[M + Na]^+$; obs. mass: 353.0800 $[M + H]^+$ and 375.0619 $[M + Na]^+$.

Acknowledgements

Authors (UVD and PVC) thank University Grants Commission (UGC), New Delhi, India for financial assistance and for the award of teacher fellowship, respectively. We gratefully acknowledge Dr A. S. Burungale, Principal, Yashavantrao Chavan Institute of Science, Satara, for encouragement.

References

1 For recent reviews and monographs, see (*a*) R. A. Sheldon, I. Arends and U. Hanefeld, *Green Chemistry and Catalysis*, Wiely-VCH, Weinheim, 2007; (*b*) A. J. Wangelin, H. Neumann, D. Gördes, S. Klaus, D. Strübing and M. Beller, *Chem.–Eur. J.*, 2003, **9**, 4286–4294; (*c*) P. Anastas and N. Eghboli, *Chem. Soc. Rev.*, 2010, **93**, 301–312; (*d*) M. B. Gawande, V. D. B. Bonifácio, R. Luque, P. S. Branco and R. S. Varma, *Chem. Soc. Rev.*, 2013, **42**, 5522–5551.

2 (*a*) L. Yin and J. Liebscher, *Chem. Rev.*, 2007, **107**, 133–173; (*b*) L. L. Chng, N. Erathodiyil and J. Y. Ying, *Acc. Chem. Res.*, 2013, **46**, 1825–1837.

3 (*a*) J. F. Billing and U. J. Nilsson, *J. Org. Chem.*, 2005, **70**, 4847–4850; (*b*) K. D. Bodine, D. Y. Gin and M. S. Gin, *Org. Lett.*, 2005, **7**, 4479–4482; (*c*) F. Fazio, M. C. Bryan, O. Blixt, J. C. Paulson and C. Wong, *J. Am. Chem. Soc.*, 2002, **124**, 14397–14402.

4 S. Löber, P. Raodriguez-Loaiza and P. Geminer, *Org. Lett.*, 2003, **5**, 1753–1755.

5 (*a*) J. K. Lee, Y. S. Chi and L. S. Choi, *Langmuir*, 2004, **20**, 3844–3847; (*b*) J. P. Collman, N. K. Devaraj and C. E. D. Chidsey, *Langmuir*, 2004, **20**, 1051–1053; (*c*) H. R. Rengifo, L. Chen, C. Grigoras, J. Ju and J. T. Koberstein, *Langmuir*, 2008, **24**, 7450–7456.

6 (*a*) M. J. Genin, D. A. Allwine, D. J. Anderson, M. R. Barbachyn, D. E. Emmert, S. A. Garmon, D. R. Graber, K. C. Grega, J. B. Hester, D. K. Hutchinson, J. Morris, R. J. Reischer, C. W. Ford, G. E. Zurenko, J. C. Hamel, R. D. Schaadt, D. Stapert and B. H. Yagi, *J. Med. Chem.*, 2000, **43**, 953–970; (*b*) D. R. Buckel, C. J. M. Rockell, H. Smith and B. A. Spicer, *J. Med. Chem.*, 1986, **29**, 2262–2267.

7 T. Lee, M. Cho, S. Y. Ko, H. J. Youn, D. J. Baek, W. J. Cho, C. Y. Kang and S. Kim, *J. Med. Chem.*, 2007, **50**, 585–589.

8 (*a*) Y. Xia, Z. Fan, J. Yao, Q. Liao, W. Li, F. Qu and L. Peng, *Bioorg. Med. Chem. Lett.*, 2006, **16**, 2693–2698; (*b*) Y.-C. Duan, Y.-C. Ma, E. Zhang, X.-J. Shi, M.-M. Wang, X.-W. Ye and H.-M. Liu, *Eur. J. Med. Chem.*, 2013, **62**, 11–19.

9 (*a*) S. Palhagen, R. Canger, O. Henriksen, J. A. Van Parys, M. E. Riviere and M. A. Karolchyk, *Epilepsy Res.*, 2001, **43**, 115–124; (*b*) R. Alvarez, S. Velazquez, A. San-Felix,

S. Aquaro, E. D. Clercq, C.-F. Perno, A. Karlsson, J. Balzarini and M. J. Camarasa, *J. Med. Chem.*, 1994, **37**, 4185–4194.

10 (*a*) B. R. Buckle, D. J. Outred, C. J. M. Rockell, H. Smith and B. A. Spicer, *J. Med. Chem.*, 1983, **26**, 251–254; (*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**, 254–272.

11 (*a*) H. Dehne, in *Methoden der Organischen Chemie (Houben-Weyl)*, ed. E. Schumann, Thieme, Stuttgart, 1994, vol. E8d, pp. 305–405; (*b*) W.-Q. Fan 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, pp. 1–126.

12 (*a*) G. L'abbe, *Chem. Rev.*, 1969, **69**, 345–363; (*b*) R. Huisgen, in *1,3-Dipolar Cycloaddition Chemistry*, ed. A. Padwa, Wiley, New York, 1984, ch. 1, pp. 1–176; (*c*) A. Padwa, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon, Oxford, 1991, vol. 4, pp. 1069–1109; (*d*) K. V. Gothelf and K. A. Jørgensen, *Chem. Rev.*, 1998, **98**, 863–909.

13 For reviews on 1,3-dipolar cycloadditions please see: (*a*) C. K. Sha and A. K. Mohanakrishan, in *Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products*, ed. A. Padwa and W. H. Pearson, Wiley, New York, 2003, pp. 623–680; (*b*) S. Karlsson and H. E. Hogberg, *Org. Prep. Proced. Int.*, 2001, **33**, 103–172.

14 (*a*) H. C. Kolb, M. G. Finn and K. B. Sharpless, *Angew. Chem., Int. Ed.*, 2001, **40**, 2004–2021; (*b*) C. W. Tornoe, C. Christensen and M. Meldal, *J. Org. Chem.*, 2002, **67**, 3057–3062.

15 V. V. Rostovtsev, L. G. Green, V. V. Fokin and K. B. Sharpless, *Angew. Chem., Int. Ed.*, 2002, **41**, 2596–2599.

16 F. Himo, T. Lovell, R. Hilgraf, V. V. Rosrovtsev, L. Noodleman, K. B. Sharpless and V. V. Fokin, *J. Am. Chem. Soc.*, 2005, **127**, 210–216.

17 (*a*) B. H. Lipshutz and B. R. Taft, *Angew. Chem., Int. Ed.*, 2006, **45**, 8235–8238; (*b*) C. T. Lee, S. Huang and B. H. Lipshutz, *Adv. Synth. Catal.*, 2009, **351**, 3139–3142.

18 (*a*) S. Chassaing, A. S. S. Sido, A. Alix, M. Kumarraja, P. Pale and J. Sommer, *Chem.–Eur. J.*, 2008, **14**, 6713–6721; (*b*) S. Chasseing, A. Alix, T. Boningari, K. S. S. Sido, M. Keller, P. Kuhn, B. Louis, J. Sommer and P. Pale, *Synthesis*, 2010, 1557–1567.

19 I. Jlalia, H. Elamar, F. Meganem, J. Herscovici and C. Girard, *Tetrahedron Lett.*, 2008, **49**, 6756–6758.

20 P. Li, L. Wang and Y. Zhang, *Tetrahedron*, 2008, **64**, 10825–10830.

21 U. Sirion, Y. J. Bae, B. S. Lee and D. Y. Chi, *Synlett*, 2008, 2326–2330.

22 J. Albadi, M. Keshavarz, F. Shirini and M. Vafaie-nezhad, *Catal. Commun.*, 2012, **27**, 17–20.

23 P. K. Khanna, R. Gokhale and V. V. V. S. Subbarao, *J. Mater. Sci.*, 2004, **39**, 3773–3776.

24 B. Kaboudin, R. Mostafalu and T. Yokomatsu, *Green Chem.*, 2013, **15**, 2266–2274.

25 A. Kumar, S. Aerry, A. Saxena, A. De and S. Mozumdar, *Green Chem.*, 2012, **14**, 1298–1301.

26 M. Chtchigrovisky, A. Primo, P. Gonzalez, K. Molviger, M. Robitzer, F. Quignard and F. Taran, *Angew. Chem., Int. Ed.*, 2009, **48**, 5916–5920.

27 R. B. Nasir Baig and R. S. Varma, *Green Chem.*, 2013, **15**, 1839–1843.

28 (*a*) P. Appukkuttan, W. Dehaen, V. Fokin and E. V. D. Eycken, *Org. Lett.*, 2004, **6**, 4223–4225; (*b*) A. Feldman, B. Colasson and V. V. Fokin, *Org. Lett.*, 2004, **6**, 3897–3899.

29 (*a*) C. O. Kappe and E. V. D. Eycken, *Chem. Soc. Rev.*, 2010, **39**, 1280–1290; (*b*) X. Xiong and L. Cai, *Catal. Sci. Technol.*, 2013, **3**, 1301–1307.

30 For recent Review see: (*a*) B. Bervaux and F. E. Du Parez, *Chem. Sci.*, 2012, **3**, 959–966; (*b*) T. Jin, M. Yan and Y. Yamamoto, *ChemCatChem*, 2012, **4**, 1217–1229.

31 (*a*) M. L. Kantam, V. S. Jaya, B. Sreedhar, M. M. Rao and B. M. Choudary, *J. Mol. Catal. A: Chem.*, 2006, **256**, 273–277; (*b*) H. Sharghi, R. Khalifeh and M. M. Doroodmand, *Adv. Synth. Catal.*, 2009, **351**, 207–218; (*c*) F. Alonso, Y. Moglie, G. Radivoy and M. Yus, *Adv. Synth. Catal.*, 2010, **352**, 3208–3214; (*d*) F. Alonso, Y. Moglie, G. Radivoy and M. Yus, *Org. Biomol. Chem.*, 2011, **9**, 6385–6395.

32 (*a*) B. S. P. Anilkumar, K. H. V. Reddy, B. Madhav, K. Ramesh and Y. V. D. Nageswar, *Tetrahedron Lett.*, 2012, **53**, 4595–4599; (*b*) N. Salam, A. Sinha, P. Mondal, A. S. Roy, N. R. Jana and S. M. Islam, *RSC Adv.*, 2013, **3**, 18087–18098.

33 (*a*) C. S. Radatz, L. D. A. Soares, E. R. Vieira, D. Alves, D. Russowsky and P. H. Schneider, *New J. Chem.*, 2014, **38**, 1410–1417; (*b*) K. Chanda, S. Rej and M. H. Huang, *Chem.–Eur. J.*, 2013, **19**, 16036–16043.

34 (*a*) X. Xiong, L. Cai, Y. Jiang and Q. Han, *ACS Sustainable Chem. Eng.*, 2014, **2**, 765–771; (*b*) X. Xiong, H. Chen, Z. Tang and Y. Jiang, *RSC Adv.*, 2014, **4**, 9830–9837; (*c*) A. N. Prasad, B. M. Reddy, E.-Y. Jeong and S.-E. Park, *RSC. Adv.*, 2014, **4**, 29772–29781.

35 (*a*) L. Wan and C. Cai, *Catal. Lett.*, 2012, **142**, 1134–1140; (*b*) V. Bénéteau, A. Olmos, T. Boningari, J. Sommer and P. Pale, *Tetrahedron Lett.*, 2010, **51**, 3673–3677; (*c*) J. Albadi, M. Keshavarz, M. Abedini and M. Vafaie-nezhad, *Chin. Chem. Lett.*, 2012, **23**, 797–800.

36 (*a*) M. Nasr-Esfahani, I. Mohammadpoor-Baltork, A. R. Khosropour, M. Moghadam, V. Mirkhani, S. Tangestaninejad and H. A. Rudbari, *J. Org. Chem.*, 2014, **79**, 1437–1443; (*b*) S. R. Kale, S. S. Kahandal, M. B. Gawandeb and R. V. Jayaram, *RSC Adv.*, 2013, **3**, 8184–8192.

37 (*a*) S. D. Mitragotri, D. M. Pore, U. V. Desai and P. P. Wadgaonkar, *Catal. Commun.*, 2008, **9**, 1822–1826 and references therein; (*b*) M. A. Kulkarni, V. R. Pandurangi, U. V. Desai and P. P. Wadgaonkar, *C. R. Chim.*, 2012, **15**, 745–752; (*c*) M. A. Kulkarni, U. P. Lad, U. V. Desai, S. D. Mitragotri and P. P. Wadgaonkar, *C. R. Chim.*, 2013, **16**, 148–152; (*d*) M. A. Kulkarni, K. S. Pandit, U. P. Lad, U. V. Desai and P. P. Wadgaonkar, *C. R. Chim.*, 2013, **16**, 689–695.

38 Y. Xu, L. Zhang and Y. Cui, *J. Appl. Polym. Sci.*, 2008, **110**, 2996–3000.
39 K. Rajender Reddy and N. S. Kumar, *Synlett*, 2006, **14**, 2246–2250.
40 R. Berg and B. F. Straub, *Beilstein J. Org. Chem.*, 2013, **9**, 2715–2750.
41 (*a*) L. S. Campbell-Verduyn, L. Mirfeizi, R. A. Dierckx, P. H. Elsinga and B. L. Feringa, *Chem. Commun.*, 2009, **16**, 2139–2141; (*b*) J. González, V. M. Pérez, D. O. Jiménez, G. Lopez-Valdez, D. Corona and E. Cuevas-Yañez, *Tetrahedron Lett.*, 2011, **52**, 3514–3517; (*c*) X. Meng, X. Xu, T. Gao and B. Chen, *Eur. J. Org. Chem.*, 2010, 5409–5414; (*d*) Z.-X. Wang and Z.-G. Zhao, *J. Heterocycl. Chem.*, 2007, **44**, 89–92; (*e*) U. Sirion, Y. J. Bae, B. S. Lee and D. Y. Chi, *Synlett*, 2008, **15**, 2326–2330; (*f*) Z. Gonda and Z. Novak, *Dalton Trans.*, 2010, **39**, 726–729; (*g*) B. R. Buckley, S. E. Dann, D. P. Harris, H. Heaney and E. C. Stubbs, *Chem. Commun.*, 2010, **46**, 2274–2276; (*h*) D. Wang, N. Li, M. Zhao, W. Shi, C. Ma and B. Chen, *Green Chem.*, 2010, **12**, 2120–2123; (*i*) Y. Kitamura, K. Taniguchi, T. Maegawa, Y. Monguchi, Y. Kitade and H. Sajiki, *Heterocycles*, 2009, **77**, 521–532; (*j*) T. Y. Kim, A. B. S. Elliott, K. J. Shaffer, C. J. McAdam, K. C. Gordon and J. D. Crowley, *Polyhedron*, 2013, **52**, 1391–1398; (*k*) R. Kumar, J. Arora, A. K. Prasad, N. Islam and A. K. Verma, *Med. Chem. Res.*, 2013, **22**, 5624–5631; (*l*) F. Saleem, G. K. Rao, A. Kumar, G. Mukherjee and A. K. Singh, *Organometallics*, 2013, **32**, 3595–3603.