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ARTICLE TYPE

Copper immobilized on ferromagnetic nanoparticles triazine dendrimer (FMNPs@TD-Cu(II))-catalyzed regioselective synthesis of 1,4disubstituted 1,2,3-triazoles

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Copper immobilized on ferromagnetic nanoparticles triazine dendrimer (FMNPs@TD-Cu(II)) has been demonstrated for the first time as a recoverable and reusable heterogeneous nanocatalyst in the click synthesis of 1,4-disubstituted 1,2,3triazoles by a one-pot three component reaction of halides, sodium azide and alkynes under mild conditions. The catalyst is very easy to handle and is environmentally safe and economical. FMNPs@TD-Cu(II) was characterized by transmission electron microscopy (TEM), scanning electron microscopy (SEM), X-ray diffraction (XRD), FT-IR and EDX methods.

1 Introduction

During the last few decades, a central focus of modern synthetic ²⁰ organic chemistry is the design of new reactions and synthesis strategies that make easy the synthesis of biologically active compounds with potential application in the pharmaceutical or agrochemical industries.

Dendrimers are considered as the fourth generation of ²⁵ macromolecule building which have potential applications in biology, chemistry, and material science.¹ Generally, dendrimer synthesis is performed in solution phase. Incomplete and side reactions are two distinctive problems associated with dendrimer preparation and magnitude of these problems increases when

³⁰ dendrimer synthesis is carried out on solid phase. It requires great efforts to optimize reaction conditions to remove these problems and because of this, there are only few reports on solid phase dendrimer synthesis.²

By immobilizing homogeneous catalysts on insoluble supports,

³⁵ the benefits of both homogeneous as well as heterogeneous catalysts are obtained. These catalysts can be separated simply from the products by a simple filtration. In the past years, some dendrimers covalently-bonded to the inorganic or polymeric supports have been competently prepared.³

⁴⁰ However, the active sites in heterogeneous catalysts are not as accessible as in a homogeneous catalysts, and so the activity of the catalyst is usually decreased. Consequently, we need a catalyst system that not only demonstrates high activity and selectivity (such as a homogeneous system) but also possesses the ⁴⁵ ease of catalyst separation and recovery (such as a heterogeneous system). These objectives can be obtained by nanocatalysis. Nanocatalysts bridge the gap between homogeneous and heterogeneous systems, keeping the desirable attributes of both systems.⁴

- ⁵⁰ Thus, nanocatalysts enjoy several advantages over conventional catalyst systems; however, separation and recovery of these tiny nanocatalysts from the reaction mixture is difficult. To overcome this problem, the use of magnetic nanoparticles has appeared as a viable solution; their insoluble and paramagnetic nature enables
- ss easy and effective separation of these catalysts from the reaction mixture with an external magnet.⁴

Ferromagnetic nanoparticles (FMNPs) have included an increasing attention in the fields of nanoscience and nanotechnology because of their incomparable and novel physicochemical properties that can be achieved in the light of their particle size and morphology. FMNPs improved with organic compounds have been widely employed for biomedical, biotechnological, and environmental applications, because their properties can be magnetically managed by applying an external magnetic field.⁵ In general, it makes accessible high potential applications, like DNA extraction, cell separation, gene directing, drug delivery, magnetic resonance imaging and heavy metal ion removal.⁶

Triazoles are an important class of heterocyclic organic ⁷⁰ compounds and have a large spectrum of biological activities like antiallergenic,⁷ anti-infective agents,⁸ anti-HIV,⁹ and antibacterial.¹⁰ In addition, compounds belonging to this class are also useful as dyes, corrosion inhibitors, photographic materials, and photosensitizers.¹¹

⁷⁵ For the synthesis of 1,2,3-triazoles several synthetic methods using various catalysts¹²⁻¹⁴ are accessible. Although, some of the reported methods are satisfactory, from the synthetic efficiency point of view, many of these methods suffer drawbacks such as

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tedious work-up procedures, long reaction times, low yields, drastic reaction conditions, co-occurrence of several side reactions, or the use of organic solvents remain problematic. Another drawbacks of some of the existing methods is that the s catalysts are destroyed during the work-up procedure and cannot be recovered and reused. Therefore, the introduction of efficient and green approaches using recoverable and reusable catalysts for the preparation of titled compounds is highly desirable.

Among the various procedures for the regioselective synthesis of ¹⁰ triazoles, development of copper catalysed azide alkyne cycloaddition (CuAAC) proved to be an important milestone in the synthesis of 1,2,3-triazoles.¹⁵⁻²⁰

Nanocatalysis has become an active area of research, because these materials exhibit better catalytic activity due to the 15 enhanced surface area towards organic transformations.²¹ Coppersupported magnetic nanoparticles have been investigated for the preparation of 1,4-disubstituted 1,2,3-triazoles.²²

In order to further improve the practicality of the CuAAC reaction and as a part of our ongoing research on the development ²⁰ of useful synthetic protocols,²³ herein, we describe a convenient and efficient one-pot method for the synthesis of 1,4-disubstituted 1,2,3-triazoles compounds using FMNPs@TD-Cu(II) as a recoverable and reusable nanocatalyst under mild conditions (Scheme 1).



⁴⁰ **Scheme 1** FMNPs@TD-Cu(II) catalyzed one-pot synthesis of 1,4-disubstituted 1,2,3-triazoles.

2 Results and discussion

2.1 Catalyst characterization

- ⁴⁵ The FMNPs@TD-Cu(II) was prepared by the route outlined in Scheme 2. Naked magnetic Fe₃O₄ nanoparticles were synthesized through chemical precipitation procedure, and subsequently were coated with 3-aminopropyltriethoxysilane (APTS). The reaction of cyanuric chloride (CC) with FMNPs-PA was performed at 25
- ⁵⁰ °C to substitute one chlorine atom of cyanuric chloride to produce FMNPs-CC1 which upon treatment with ethylenediamine gave FMNPs-TD (G1). The same procedure was applied to increase the dendrimer generation, FMNPs–CC2 and FMNPs-TD (G2). In the end, the reaction of G2 group with Cu(OAc)₂ was led to the

⁵⁵ corresponding Cu(II) supported on magnetic nanoparticles (FMNPs@TD-Cu(II)). The characterization of the catalyst was carried out by FT-IR, TGA, XRD, EDX, SEM, and TEM.



Scheme 2 Synthetic route of FMNPs@TD-Cu(II) catalyst.

The FT-IR spectrum for the FMNPs–PA (Fig. 1a) shows a stretching vibration at ~3464 cm⁻¹ which includes the ⁸⁰ contributions from both symmetrical and asymmetrical modes of the O-H bonds attached to the surface iron atoms. The presence of an adsorbed water layer is confirmed by a stretch for the vibrational mode of water found at 1653 cm⁻¹. The band formation between FMNPs and 3-aminopropyltriethoxysilane ⁸⁵ group is confirmed by Fe–O–Si absorption band that appears at ~985 cm⁻¹.²⁴ Also, the characteristic bands for C-H aliphatic bond appear at ~1460 and ~2921 cm.⁻¹ Moreover, the bands at ~1642 cm⁻¹ of the C=N is a good reason for the presence of triazine moiety on the Fe₃O₄ MNPs.

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Fig. 1 FT-IR spectrum of a: FMNPs-PA; b: G1; c: FMNPs-CC2; 10 d: G2.

The amount of organic moieties attached to FMNPs was measured by using TGA and elemental analysis. The TGA plots of FMNPs-PA, FMNPs-CC1, G1, FMNPs-CC2 and G2 show that thermal decomposition occurred in two steps (Fig. 2). Weight 15 loss first occurred in the temperature range of 150 to 250 °C; and next above 250 °C. The first step weight loss corresponds to elimination of physically adsorbed water. The second-step weight loss is due to removal of organic moieties on the surface. The TGA results are summarized in Table 1. The observed total 20 weight loss for FMNPs-PA, FMNPs-CC1, G1, FMNPs-CC2, and G2 are 7%, 10.4%, 11.2%, 13.1% and 15.3%, respectively. The weight loss of G1 and G2 appears about 11.2% and 15.3% at 250-550 °C is contributed to the thermal decomposition of 3-

aminopropyltrimethoxysilane, triazine, and diamines groups and ²⁵ shows an irreversible process (Fig. 2c,e). On the basis of these values, the theoretical conversion at each stage is 41% (FMNPs-PA \rightarrow FMNPs-CC1), 88% (FMNPs-CC1 \rightarrow G1), 54% (G1 \rightarrow FMNPs-CC2) and 95% (FMNPs-CC2 \rightarrow G2).



Fig. 2 TGA curve of: (a) MNPs-PA, (b) MNPs-CC1, (c) G1, (d) MNPs-CC2, (e) G2.

Table 1 Thermogravimetric analysis (TGA) results

	<u> </u>			
Entry	Sample	Organic (wt%)	Organic (mmol/g MNPs)	Yield (%)
		(111/0)	(minol/g min (1.5)	(/0)
1	FMNPs-PA	7.02	1.20	-
2	FMNPs-CC1	10.43	0.50	41
3	G1	11.21	0.44	88
4	FMNPs-CC2	13.10	0.24	54
5	G2	15.32	0.23	95

60 A summary of the elemental analysisand TGA data is presented in Table 2, indicating a good agreement between the two methods.

Fable 2 Elementa	ana	lysis	resu	lts
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Entry	Sample		С	Н	Ν	Total
		TGA(Wt%)	4.35	0.97	1.69	7.02
1	FMNP-PA	EA(wt%)	4.68	1.04	1.69	7.54
_		TGA(Wt%)	3.64	0.35	2.83	10.43
2	FMNPs-CC1	EA(wt%)	3.66	0.36	2.84	10.48
_		TGA(Wt%)	5.31	0.94	4.95	11.21
3	Gl	EA(wt%)	5.52	0.97	5.15	11.66
		TGA(Wt%)	6.37	0.60	2.70	13.10
4	FMNPs-CC2	EA(wt%)	6.46	0.61	2.74	13.29
_		TGA(Wt%)	8.65	1.28	5.38	15.32
5	G2	EA(wt%)	8.83	1.31	5.49	15.64

⁷⁰ The XRD patterns of magnetite and FMNPs@TD-Cu(II) are depicted in Figure 3. The magnetite XRD peaks clearly seen in XRD profile such as 220, 311, 400, 422, 511 and 440 (JCPDS file, no. 901-3024).

The crystallite size of the catalysts was determined by 75 Debye–Scherrer equation was found to be 23.5 nm, which is an agreement with the result obtained from the TEM which shows a size distribution between 20 and 35 nm (Fig.5b).

The copper content of FMNPs@TD-Cu(II), measured by ICP analysis, was obtained to be 0.41 mmol per gram of ⁸⁰ FMNPs@TD-Cu(II) catalyst. The EDX results in Fig. 4 shows that Cu exists in the nanoparticles.



Fig. 3 The XRD pattern of (a) FMNPs and (b) FMNPs@TD-⁸⁰ Cu(II).

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The FMNPs (Fig. 5a) and FMNPs@TD-Cu(II) (Figure 5b) was also characterized by TEM. The dark colored regions or black spots in the photograph correspond to the Fe₃O₄ species while the ⁵ colorless parts being that of silica.

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20 Fig. 5 TEM images of a:FMNPs-SiO2; b: FMNPs@TD-Cu(II).

SEM image is shown in Figure 6. The SEM image shows that FMNPs (Figure 6a) and FMNPs@TD-Cu(II) (Figure 6b) have a mean diameter of about 35 nm and a nearly spherical shape, which is consistent with XRD, SEM and TEM image shows the

³⁰ nanoparticles are well dispersed and uniform in shape and size.





Fig. 6 SEM images of a: FMNPs-SiO₂; b: FMNPs@TD-Cu(II).

Figure 7 shows the magnetization curves of Fe_3O_4 and FMNPs@TD-Cu(II). As can be observed from the figure, the saturation magnetization was decreased. The lower saturation ⁷⁵ magnetization of the FMNPs@TD-Cu(II) relative to that of bare Fe_3O_4 nanoparticles, can be attributed to the formation of a silica shell around the Fe_3O_4 core.



60 Fig. 7 Magnetization curves of Fe₃O₄ and FMNPs@TD-Cu(II).

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2.2 Catalytic studies

Initially, for screening experiments, three-component reaction between phenylacetylene (1 mmol), benzyl choloride (1 mmol), and sodium azide (1.1 mmol) was selected as a model reaction 5 (Table 3). The model reaction was first carried out in the absence of FMNPs@TD-Cu(II). Stirring was continued in H2O-EtOH (1:1) as solvent at 25 °C. Timely analysis of the reaction mixture (TLC) did not indicate any appreciable progress of the reaction. (Table 3, entry 1). In the presence of FMNPs@TD-Cu(II) (8 mg), 10 the corresponding product was obtained in 99% yield (Table 3, entry 2). Then, the same reaction was carried out in the presence of FMNPs@TD-Cu(II) (8 mg) in different single and mixed solvents at room temperature (Table 3, entries 3-8). As shown, the maximum yields were obtained in both H₂O-EtOH (1:1) and 15 H₂O-MeOH (1:1) mixed solvent systems (Table 3, entries 2 and 8). However, H₂O-EtOH (Table 3, entry 12) was preferred because of safety problems. Next, we examined the catalyst loading (5-10 mg), and 8 mg was found to be the optimum catalyst loading for completion of this reaction. However, upon ²⁰ decreasing the loading of catalyst to 5 mg and 6 mg reduced the yields to 55 and 68 respectively (Table 3, entries 9 and 10). When a catalyst loading of 10 mg was used, the yield of the product was 98%, but the reaction rate increased, so that the reaction was complete within 10 min (Table 3, entry 11).

25 Table 3 Optimization of the reaction conditions^a

Ph-==			N=N	
+	NaN ₃		PhN_/	≻−Ph
Ph-Cl	H ₂ CI		~ ·	
Entry	FMNPs-TD@Cu(II)	Solvent	Time	Yield ^b
	(ma)		(min)	(0/.)

(mg) (min) 1 - H ₂ O/EtOH (1:1) 15	(%) - 99
1 - $H_2O/EtOH(1:1)$ 15	- 99
	99
2 8 $H_2O/EtOH(1:1)$ 15	
3 8 EtOH 15	80
4 8 CH ₃ CN 15	50
5 8 DMF 15	68
6 8 EtOAc 15	37
7 8 H ₂ O 15	73
8 8 $H_2O/MeOH(1:1)$ 15	95
9 5 $H_2O/EtOH(1:1)$ 15	55
10 6 $H_2O/EtOH(1:1)$ 15	68
11 10 H ₂ O/EtOH (1:1) 10	98

^aReaction conditions: Phenylacetylene (1 mmol), benzyl choloride (1 mmol), sodium azide (1.1 mmol), sodium carbonate (1 mmol) FMNPs@TD-Cu(II), 25 °C.

^bIsolated yields.

Under the optimized reaction conditions, the scope of the methodology was investigated for the synthesis of various 1,4-³⁰ disubstituted 1,2,3-triazoles and the results are described in Table 4. Various benzylic, allylic and aliphatic halides afforded excellent yields of the products under these reaction conditions (Table 4). Aliphatic halides are usually known to be less reactive than aromatic ones, but with this catalytic system, the reaction of ³⁵ phenylacetylene with hexyl bromide (Table 4, entry 9) proceeded

efficiently to provide the desired 1,4-disubstituted 1,2,3-triazole in 93% yields. In addition, α -bromoacetophenone reacted

Table 4	FMNPs@TD-Cu(II)	Catalyzed	click	synthesis	of	1,4-
disubstitu	uted 1,2,3-triazoles ^a					

R ¹	H ₂ X	FMNPs@TD-Cu(II) DH-H₂O/Na₂CO₃, 25 °C	N=N R ² N	∕−R¹
Entry	R ¹ —==	R^2 -CH ₂ X	Yield % ^b /t (min)	Ref.
1		CH2CI	99 (15)	25
2	<hr/>	Me-CH ₂ CI	99 (22)	25
3	СНО		95 (20)	-
4	СНО	E Me- ← CH ₂ CI	98 (16)	-
5		MeO-CH ₂ Br	95 (25)	12b
6		O ₂ N-CH ₂ Cl	95 (40)	26
7		Ph-CH ₂ Br	97 (35)	-
8		Br	94 (40)	27
9		$C_6H_{13}Br$	93 (30)	28
10		O U U C -CH ₂ Br	95 (27)	28
11		© O C−CH₂Br	90 (37)	2b

^aThe purified products were characterized by mp, ¹H and ¹³C NMR spectroscopy.

CH₂Br

^b Yields refer to pure isolated products

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smoothly with phenylacetylene to produce the corresponding β-keto-1,2,3-triazole in 95% yield within 27 min (Table 4, entry 10).
2-Bromo-1-(furan-2-yl)ethanone, as a heteroaromatic
⁴⁵ substrate, also worked well in this reaction under similar reaction conditions to afford the desired product in 90% yield after 37 min (Table 4, entry 11). Aryl acetylenes such as phenylacetylene and 2-(prop-2-ynyloxy)benzaldehyde as well as alkyl acetylenes such as 1-hexyne reacted rapidly and smoothly to produce the

98 (20)

2b

corresponding 1,4-disubstituted 1,2,3-triazoles in excellent yields (Table 4). Interestingly, the presence of aldehyde group did not interfere with this reaction, and desired products were obtained in excellent yields (Table 4, entries 3 and 4). It is noteworthy that ⁵ the reactions were completed within 15-40 minutes at 25 °C, and the products were produced in excellent yields with high purity and excellent regioselectivity, in which only 1,4-regioisomeric products were formed.

A comparison of the efficiency of this method with selected ¹⁰ previously methods²⁹⁻³¹ is collected in Table 5. As can be seen, the present protocol is indeed superior to several of the other protocols.

Table 5 Comparison of click synthesis of 1,4-disubstituted 1,2,3triazoles by the FMNPs@TD-Cu(II) catalytic system with some 15 of those reported in the literature

Product	Conditions ^{Ref.}	Yield% ^b /Time
Ph_N_Ph	this work C/Cu NPs/H ₂ O/70 °C ²⁹ 5 mol%/Cu/H ₂ O/55 °C ³⁰	99 (15 min) 98 (6 h) 94 (25 h)
Ph	this work C/Cu NPs/H ₂ O/70 °C ²⁹ 0.5 mol% Cu NPs/C/H ₂ O- EtOH/70 °C ³¹	97 (30 min) 80 (7 h) 82 (7 h)

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The reusability of the catalyst for the cycloaddition reaction of phenyl acetylene, sodium azide and benzyl chloride, was subsequently investigated. When the reaction was completed, the mixture was separated catalyst by an external magnet then diluted ²⁰ with water and EtOAc. The catalyst was separated by simple filtration, dried, and used for subsequent runs. Thus, after recovery the catalyst was subjected to a second reaction from which it gave the desired product in 97% yield; the average chemical yield for six consecutive runs was 96%, which clearly

²⁵ demonstrates the practical recyclability of this catalyst (Fig. 8). The slight decrease of catalytic activity should be due to the normal loss of the catalyst during the work-up stage.



Fig. 8 Recyclability of FMNPs@TD-Cu(II) for the preparation of ³⁵ 1-benzyl-4-phenyl-1H-1,2,3-triazole.

To test for leaching we filtered the catalyst after 8 min and the reaction continued uninterrupted in the absence of catalyst. We found that the reaction was not completed, even at long reaction times. These observations showed FMNPs@TD-Cu(II) is stable

⁴⁰ under the reactions, and can be recycled multiple times.

3 Conclusions

In conclusion, the synthesis and characterization of a new stable and heterogeneous catalyst, Cu(II) containing Fe₃O₄ triazine dendrimer (FMNPs@TD-Cu(II)), is reported. FMNPs@TD-45 Cu(II) catalyzes three-component reaction for the construction of 1,4-disubstituted1,2,3-triazole from phenylacetylenes, sodium azide and aromatic, heteroaromatic, allylic and aliphatic halides. The reaction has good substrate scope and furnishes the products in excellent yields and regioselectivity. Furthermore, the catalyst 50 is stable under the reaction conditions and can be recycled and reused several times without a significant loss in activity. Importantly, recovery of the catalyst can be accomplished easily using a simple external magnet. Therefore, this synthetic methodology can be considered as a useful practical achievement 55 in the preparation of these important heterocyclic compounds. Further studies are on going in our laboratory to understand other applications of the catalyst in various organic reactions.

4 Experimental

4.1 Material and physical measurements

60 The materials were purchased from Merck and Fluka and were used without any additional purification. All reactions were monitored by thin layer chromatography (TLC). Melting points were determined using a Stuart Scientific SMP2 apparatus. FT-IR spectra were determined on a Perkin-Elmer 683 instrument. ¹H 65 and ¹³C NMR spectra were recorded on a Bruker (200, 500 MHz) spectrometer in CDCl₃ as solvent. X-ray powder diffraction obtained on SE1FERT-3003TT. patterns were Thermogravimetric analysis (TGA) was carried out on a PL-STA-1640 form heating rate of the range of 30-600 °C. Scanning 70 electron microscopy measurements were performed on a VEGA TESCAN microscope (FE-SEM). Transmission electron microscopy (TEM) measurements were carried out on a Zeiss-EM10C Germany operating at 80 Kv and formvar carbon coated grid Cu Mesh 300.

75 **4.2** Preparation and modification of large-scale the ferromagnetic nanoparticles (FMNPs)

FMNPs modified with citrate groups were prepared according to reported literature procedure.³² Iron (III) chloride hexahydrate (5.40 g, 20 mmol) and iron (II) chloride tetrahydrate (2 g, 10 ⁸⁰ mmol) were dissolved in deionized H₂O (120 mL) under N₂ atmosphere. Then, 10 mL of ammonium hydroxide 25% was quickly added into the solution under rapid mechanical stirring (500 rpm), and the mixture was heated up to 60 °C, while stirred vigorously by a mechanical stirrer for 1 hour under N₂ atmosphere. After cooling to room temperature, the resultant nanoparticles were gathered using a external magnet and the collected magnetic solid were dispersed in a 200 mL of trisodium citrate solution (0.3 M) and heated at 80 °C for 1 hour. Finally, the precipitates were collected using an external magnet and ⁹⁰ washed with acetone to eliminate remainder trisodium citrate.

4.3 Preparation of silica-coated FMNPs

The surface modified FMNPs (1 g) were redispersed in deionized H₂O (50 mL) by the ultrasonic treatment for 25 min. Subsequently, the resulting dispersion was centrifuged for 30 min ⁵ and adjusted to 2.0 wt %. Then, 2 mL of the ferro fluid was first diluted with H₂O (40 mL), the resultant suspension and NH₃.H₂O (5 mL) were poured into ethanol (140 mL) with stirring at 40 °C. A solution of TEOS (1 mL) in EtOH (10 mL) was added to the dispersion in a dropwise manner under continuous mechanical ¹⁰ stirring. Then, the resultant dispersion was stirred mechanically for 14 hours at 25 °C. Finally, the silica-coated ferromagnetic nanoparticles were composed by magnetic separation and washed with EtOH and deionized H₂O.

4.4 Preparation of FMNPs coated by 3-15 aminopropyltriethoxysilane (FMNPs-PA)

The obtained silica-coated FMNPs powder (1.5 g) was dispersed in 250 mL H₂O-EtOH (1:1) solution by sonication for 30 min, and then APTS (2.5 mL) was added to the mixture. The reaction resulting mixture was mechanically stirred under N₂ atmosphere ²⁰ for 8 h at room temperature. The suspension was centrifuged to separate the precipitated material, which was then re-dispersed in ethanol by sonication. The final product was separated by an external magnet and washed five times with ethanol and stored in a fridge for future use.

25 4.5 Preparation of triazine-based dendrimer supported on FMNPs-PA (G2 or FMNPs-TD)

A mixture of FMNPs-PA (2 g), cyanuric chloride (1.85 g, 10 mmol) and triethylamine (1.4 mL, 10 mmol) in THF (10 mL) was shaken for 10 hours at 25 °C. The solid material (MNPs-CC1) ³⁰ was separated by an external magnet and washed five times with hot THF and then dried in a vacuum oven at 50 °C. Then, to a slurry of FMNPs-CC1 (1 g) in DMF (12 mL), ethylenediamine (0.53 mL, 8 mmol) and triethylamine (1.1 mL, 8 mmol) were added. The resulting mixture was mechanically stirred at 60 °C ³⁵ for 12 hours. The resulting first generation (FMNPs-TD or G1) was separated by an external magnet, washed five times with hot ethanol and dried in a vacuum oven at 50 °C. The second generation FMNPs-TD (G2) was prepared according to the above procedure for the preparation of G1. A mixture of G1 (1 g),

- ⁴⁰ cyanuric chloride (CC) (1.66 g, 9 mmol) and triethylamine (1.2 mL, 9 mmol) in THF (20 mL) was shaken for 14 hours at 25 °C. The final sample was separated by an external magnet (FMNPs-CC2) washed with hot THF in five times and dried in a vacuum oven at 50 °C. Then, to a slurryof FMNPs-CC2 (1 g) in DMF (20
- ⁴⁵ mL) were added ethylenediamine (0.63 mL, 9.5 mmol) and triethylamine (1.3 mL, 9.5 mmol). The resulting mixture was stirred at 60 °C for 14 hours and then separated by an external magnet. The resulting second generation of ferromagnetic nanoparticles supported dendrimer (G2 or FMNPs-TD) was ⁵⁰ washed with hot ethanol five times and dried in a vacuum oven at
- 50 °C.

4.6 Preparation of Cu(II) containing ferromagnetic nanoparticles triazinedendrimer (FMNPs@TD-Cu(II))

To a mixture of ferromagnetic nanoparticles supported dendrimer ⁵⁵ (G2) (0.5 g) in DMF (10 mL) was added Cu(OAc)₂ (0.09 g, 0.5 mmol). The mixture was stirred for 6 hours at 25 °C. The resulting mixture was separated by an external magnet, the solid material was washed sequentially with 25 mL of acetone and then dried in a vacuum oven at 40°C. Finally, FMNPs@TD-Cu(II) ⁶⁰ catalyst was obtained as a dark green solid.

4.7 General procedure for synthesis of 1,2,3-triazoles in the presence of FMNPs@TD-Cu(II) nanocatalyst

A mixture of sodium carbonate (0.1 g, 1mmol) and FMNPs@TD-Cu(II) (0.008 g, containing 0.41 mmol Cu(II))/g in 3 mL of H₂O-65 EtOH (1:1) in a round bottom flask (25 mL) was stirred for 1 min. NaN₃ (0.04 g, 0.6 mmol) was added and vigorously stirred for few seconds. Then a halide derivative (0.5 mmol) and a acetylene derivative (0.5 mmol) were added to the reaction medium, and the mixture was stirred at 25 °C for the indicated 70 reaction time (Table 4). The reaction progress was monitored by TLC (eluent: n-hexane/EtOAc, 5:1). After completion of the reaction, the mixture was diluted with water and ethyl acetate and the catalyst was recovered using an external magnet. The organic layer was separated, and the aqueous layer was extracted with 75 ethyl acetate (3 \times 5 mL). The organic phases were combined, dried with magnesium sulfate, filtered, and concentrated under reduced pressure to afford the pure triazole in most cases. The recovered catalyst was reused for further runs without removing the catalyst from the flask. Spectral and analytical data for new 80 compounds follow.

4.7.1 2-((1-Benzyl-1*H*-1,2,3-triazol-4-yl)methoxy)benzaldehyde (Table 4, entry 4)

Light yellow solid; M.p.: 115 °C: ¹H NMR (500 MHz, CDCl₃): δ 5.31 (s, 2H), 5.55 (s, 2H),7.05-7.58 (m, 9H), 7.82 (s, 1H), 10.41 ⁸⁵ (s, 1H); ¹³C NMR (125 MHz, CDCl₃): δ 53.85, 62.09, 112.51, 120.82, 122.27, 124.54, 127.61, 128.18, 128.43, 128.71, 133.78, 135.50, 143.31, 159.92, 189.07; Anal. Calcd for C₁₇H₁₅N₃O₂: C, 69.61; H, 5.15; N, 14.33. Found: C, 69.47; H, 5.34; N, 14.40.

4.7.2 2-((1-(4-Methylbenzyl)-1*H*-1,2,3-triazol-4-yl)methoxy)b-90 enzaldehyde (Table 4, entry 5)

Light yellow solid; M.p.: 119 °C; ¹H NMR (500 MHz, CDCl₃): δ 2.32 (s, 3H), 5.39 (s, 2H), 5.77 (s, 2H), 7.06-7.27 (m, 6H), 7.56-7.81 (m, 2H), 7.83-8.09 (m, 1H), 10.42 (s, 1H); ¹³C NMR (125 MHz, CDCl₃): δ 22.89, 53.08, 62.07, 112.48, 115.66, 115.83, 95 120.87, 121.01, 122.11, 128.27, 129.48, 129.54, 135.51, 143.42, 159.87, 167.39, 189.07; Anal. Calcd for C₁₈H₁₇N₃O₂:C, 70.34; H, 5.58; N, 13.67. Found: C, 70.18; H, 5.51; N, 13.55.

4.7.3 1-([1,1'-Biphenyl]-4-ylmethyl)-4-phenyl-1*H*-1,2,3-triazole (Table 4, entry 8)

¹⁰⁰ White solid; M.p.:185 °C; ¹H NMR (200 MHz, CDCl₃): δ 5.11 (s, 2H), 7.25-7.63 (m, 12H), 7.55-7.63 (m, 1H), 7.71 (s, 1H), 7.79-7.83(m, 1H); ¹³C NMR (50 MHz, CDCl₃): δ 52.54, 122.02, 122.32, 128.20, 128.28, 128.49, 128.62, 129.51, 129.58, 129.69,

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130.02, 131.94, 134.72, 136.58, 137.07; Anal. Calcd for C₂₁H₁₇N₃: C, 80.00; H, 5.50; N, 13.49. Found: C, 80.21; H, 5.43; N, 13.61.

Acknowledgements

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Graphical Abstract

The synthesis, characterisation and catalytic activity of FMNPs@TD-Cu(II) for the synthesis of 1,4-disubstituted 1,2,3-5 triazoles is reported.



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