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Research Article

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Multicomponent Click Synthesis of β-Hydroxy/Benzyl 1,2,3-Triazoles Catalyzed by Magnetically Recyclable Nano Iron Oxide in Water

M. S. R. Murty*, Mohana Rao Katiki and Dilip Kommula

Medicinal Chemistry & Pharmacology Division, Discovery Laboratory, CSIR-Indian Institute of Chemical Technology, Uppal Road, Hyderabad-500007, India.

**Corresponding author: E-mail: msrmurty@ymail.com; Tel.: +91-40-27191658*

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Abstract: Iron oxide nanoparticles have been found to effectively catalyze the multicomponent synthesis of 1,2,3-triazoles from azide precursors, such as epoxides and organic halides in water. The formation of the product proceeds in one pot through a mechanism that involves *in situ* generated organic azide intermediate, followed by rapid ring closure of this intermediate with terminal alkynes. In the presence of nano-Fe_2O_3, click reaction proceeds in short reaction times and the resulting products are obtained in good yields. Aqueous reaction medium, easy recovery of catalyst, efficient recycling and high stability of the catalyst render the protocol sustainable and economic.

Keywords: Triazoles, Epoxides, Nano Iron Oxide, Magnetic Separation, Water, Click Chemistry

1. INTRODUCTION

Nanochemistry is an exponentially growing research field in modern science. The nanoscale catalysts can provide higher surface areas and lower coordinating sites, which are responsible for the higher catalytic activity [1]. Among the various nano materials, magnetic nano particles (MNPs) have received a great deal of attention because of their unique properties and potential applications in various fields including magnetic fluids [2], catalysis [3-4], data storage [5], environmental remediation [6], hyperthermia [7], magnetically assisted drug delivery [8], magnetic separation of biomolecules [9], magnetic resonance imaging (MRI) contrast agents [10], magnetic sensors [11] and magnetic refrigeration [12]. MNPs have great potential in view of the their recovery, since the magnetic separation provides a convenient method for the separation of magnetized species from the reaction mixture with an external magnet and is simpler and more efficient than conventional separation with filtration or centrifugation [13-14].

Triazoles are an important class of compounds, as they form important components in pharmacologically active compounds and are associated with a wide spectrum of activities. 1,2,3-Triazoles have found widespread use in pharmaceuticals and agrochemicals [15-17]. In particular, 1,4-

disubstituted 1,2,3-triazoles found to exhibit significant biological activities such as anticancer [18], antitubercular [19], antifungal [20], antibacterial [21], anti HIV [22], anti-inflammatory [23], antimalarial activity [24] and antioxidant [25]. Several drugs like carboxyamidotriazole, cefatrizine, rufinamide and tazobactam bear 1,2,3-triazole in their structure (Figure **1**) [26-27]. The synthesis of substituted 1,2,3-triazoles strongly relies on Huisgen's 1,3-dipolar cycloaddition between organic azides and substituted alkynes [28]. Since β-hydroxytriazoles have become increasingly useful and important in drugs and pharmaceuticals [29], the development of a simple and efficient method for their synthesis in a single-step operation is desirable.

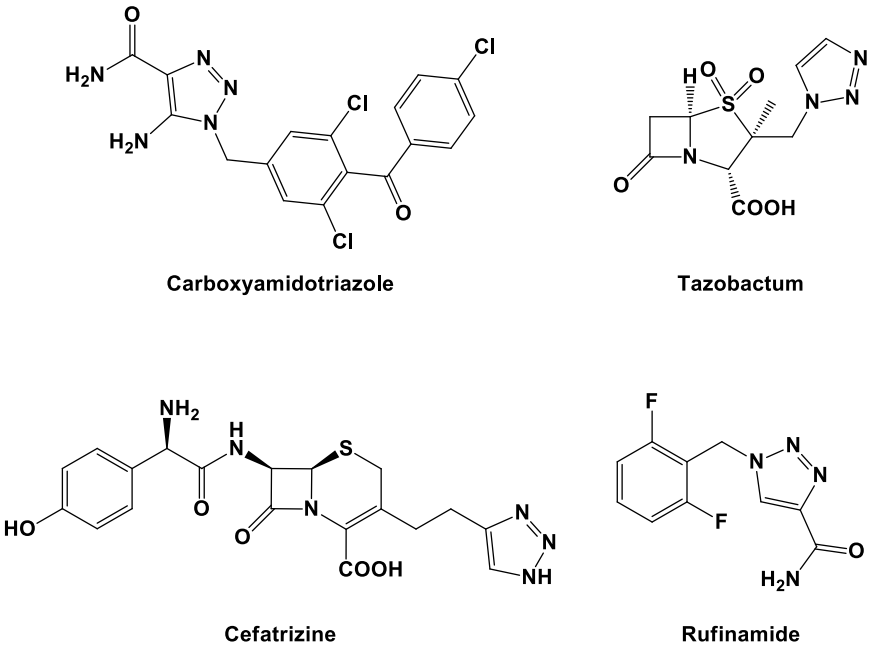
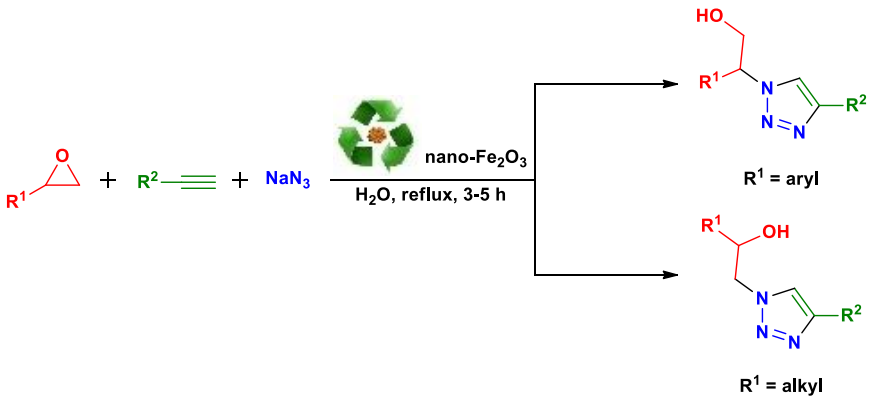
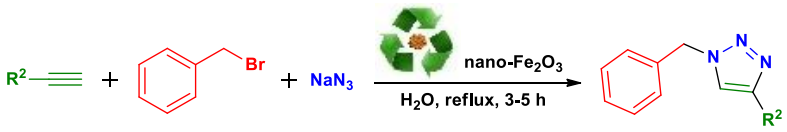


Figure 1. Drugs containing 1,2,3-triazole group

Recently, a few procedures have been reported for the multicomponent synthesis of β-hydroxy triazoles by the opening of epoxides in presence of heterogeneous catalysts like copper nanoparticles on activated carbon, copper ferrite nano particles and copper supported on the SiO_2 nanoparticles in water [30-32]. The nanoparticles have been employed as novel catalysts for various organic transformations [33-35], which inspired us to focus our attention on the aspect of an iron oxide nanoparticle-catalyzed click reaction. In continuation of our research program in this field of development of efficient methods using the magnetically recyclable iron oxide nanoparticles [36], herein, we report a one-pot, three-component reaction for the synthesis of 1,4-disubstituted β-hydroxy/benzyl triazoles by the reaction of epoxides/benzyl bromide with sodium azide and terminal alkynes in water (Scheme **1** and **2**).



Scheme 1. Multicomponent synthesis of triazoles from epoxides



Scheme 2. Multicomponent synthesis of triazoles from benzyl bromide

2. EXPERIMENTAL SECTION

2.1 Instruments and reagents

All chemicals, reagents and the catalyst were obtained from Aldrich (Sigma–Aldrich, Saint Louis, MO, USA) or Spectrochem Pvt. Ltd. (Mumbai, India) and were used without further purification. The reactions were monitored by thin-layer chromatography (TLC) using Merck silica gel glass plate (60 F254, 0.25 mm), and TLC plates were visualized by UV light or I_2 stain. Column chromatography was carried out with Merck 60–120 sized mesh silica gel using ethyl acetate and hexane as eluent. All products were characterized by their NMR, IR and HRMS spectra. The ^{1}H NMR (500 MHz) spectra and ^{13}C NMR (100 MHz) spectra were recorded on Bruker Avance 500 Nuclear Magnetic Resonance spectrometer taking the compounds in $CDCl_3$ using TMS as an internal standard. The chemical shifts (δ) were reported in parts per million (ppm) downfield from TMS and coupling constants ^{n}J values were expressed in Hz. IR spectra (KBr) were recorded on Thermo Nicolet Nexus 670 FTIR Spectrometer (ν in cm^{-1}). HRMS were recorded on Thermo Scientific Exactive Orbitrap Mass Spectrometer under Electron Spray Ionization conditions preparing sample solution in Methanol. Melting point was measured on Electrothermal 9100 Melting point apparatus. Surface morphology was recorded on Hitachi S-3000N

Scanning Electron Microscope. X-Ray diffraction (XRD) pattern was obtained on a Bruker D8 Advance X-Ray Powder Diffractometer.

2.2 General Procedure for the synthesis of β-hydroxy 1,2,3-triazoles 3a–3g

The epoxide (1.0 mmol), sodium azide (1.2 mmol) and the alkyne (1.0 mmol) were added to a suspension of nano-Fe_2O_3 (10 mol %) in water (3 mL). The reaction mixture was heated to reflux and monitored by TLC until total conversion of the starting materials. After completion of the reaction, the catalyst was separated with the aid of a magnet. The separated catalyst was washed several times with methanol, dried under vacuum. Water (10 mL) was added to the resulting mixture, followed by extraction with EtOAc (3×10 mL). The collected organic phases were dried with anhydrous Na_2SO_4. The solvent was removed under vacuum to give the corresponding triazole, which was purified by silica gel column chromatography using ethyl acetate/hexane as eluent.

***2-phenyl-2-(4-phenyl-1H-1,2,3-triazol-1-yl)ethanol* (3a)**[37]

White solid, mp 126–127 °C; IR (KBr) ν/cm^{-1} 3381, 3120, 3091, 2925, 1606, 1487, 1457, 1424, 1220, 1075, 1049, 759, 692; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, J = 7.0 Hz, 2H), 7.69 (s, 1H), 7.43 – 7.30 (m, 6H), 7.28 – 7.24 (m, 2H), 5.67 (dd, J = 8.2, 3.8 Hz, 1H), 4.67 – 4.60 (m, 1H), 4.27 – 4.19 (m, 1H), 3.32 (t, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.7, 135.9, 130.1, 129.1, 129.0, 128.8, 128.2, 127.0, 125.6, 120.5, 67.2, 65.2; HRMS (ESI) calcd. for $C_{16}H_{16}ON_3$, 266.1287 $[M + H]^+$; found, 266.1285.

***2-(4-(4-methoxyphenyl)-1H-1,2,3-triazol-1-yl)-2-phenylethanol* (3b)**

Yellow oil; IR (KBr) ν/cm^{-1} 3405, 2924, 1616, 1496, 1457, 1250, 1070, 756, 701; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 – 7.66 (m, 2H), 7.62 (s, 1H), 7.40 – 7.35 (m, 2H), 7.33 – 7.25 (m, 2H), 7.07 (d, J = 8.8 Hz, 1H), 6.95 – 6.87 (m, 2H), 5.66 (dd, J = 8.2, 4.5 Hz, 1H), 4.68 – 4.59 (m, 1H), 4.26 – 4.18 (m, 1H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 139.0, 136.7, 133.0, 130.4, 129.1, 128.8, 128.4, 127.1, 126.9, 126.8, 119.7, 114.2, 67.2, 65.6, 55.3; HRMS (ESI) calcd. for $C_{17}H_{18}O_2N_3$, 296.1393 $[M + H]^+$; found, 296.1393.

***2-(4-(4-fluorophenyl)-1H-1,2,3-triazol-1-yl)-2-phenylethanol* (3c)**

Yellow oil; IR (KBr) ν/cm^{-1} 3422, 2923, 1494, 1458, 1229, 1072, 757, 700; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 – 7.71 (m, 2H), 7.67 (s, 1H), 7.43 – 7.35 (m, 2H), 7.33 – 7.25 (m, 2H), 7.15 – 7.05 (m, 2H), 5.68 (dd, J = 8.3, 3.7 Hz, 1H), 4.68 – 4.59 (m, 1H), 4.27 – 4.19 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.7, 139.2, 129.1, 129.0, 128.9, 128.7, 128.5, 127.4, 127.3, 127.1, 126.7, 115.8, 67.2, 65.4; HRMS (ESI) calcd. for $C_{16}H_{15}ON_3F$, 284.1193 $[M + H]^+$; found, 284.1191.

***2-phenyl-2-(4-(pyridin-2-yl)-1H-1,2,3-triazol-1-yl)ethanol* (3d)**[37]

Yellow oil; IR (KBr) ν/cm^{-1} 3387, 2924, 1601, 1454, 1421, 1247, 1073, 746, 701; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 – 8.48 (m, 1H), 8.20 – 8.13 (m, 2H), 7.78 (t, J = 7.6 Hz, 1H), 7.42 – 7.33 (m, 3H), 7.31 – 7.27 (m, 2H), 7.25 – 7.20 (m, 1H), 5.73 (dd, J = 8.2, 3.8 Hz, 1H), 4.63 (dd, J = 8.2, 4.1 Hz, 1H), 4.25 (dd, J = 8.3, 3.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.7, 149.0, 147.7, 137.1, 135.8, 129.0, 128.9, 128.4, 127.4, 127.1, 122.9, 122.8, 120.3, 67.2, 64.8; HRMS (ESI) calcd. for $C_{15}H_{15}ON_4$, 267.1240 [M + H]$^+$; found, 267.1240.

1-phenoxy-3-(4-phenyl-1H-1,2,3-triazol-1-yl)propan-2-ol **(3e)**[38]

White crystalline solid, mp 134–135 °C; IR (KBr) ν/cm^{-1} 3423, 2923, 1597, 1493, 1462, 1245, 1076, 1044, 754, 693; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.73 (d, J = 7.0 Hz, 2H), 7.38 (t, J = 7.3 Hz, 2H), 7.34 – 7.27 (m, 3H), 6.99 (t, J = 7.3 Hz, 1H), 6.92 (d, J = 8.6 Hz, 2H), 4.76 – 4.69 (m, 1H), 4.60 – 4.51 (m, 2H), 4.10 – 3.99 (m, 2H), 1.82 – 1.55 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0, 147.5, 130.1, 129.6, 128.8, 128.1, 125.6, 121.5, 121.3, 114.5, 68.9, 68.7, 53.0; HRMS (ESI) calcd. for $C_{17}H_{18}O_2N_3$, 296.1393 [M + H]$^+$; found, 296.1389.

1-isopropoxy-3-(4-phenyl-1H-1,2,3-triazol-1-yl)propan-2-ol **(3f)**[38]

Yellow oil; IR (KBr) ν/cm^{-1} 3414, 2921, 2852, 1462, 1373, 1282, 1126, 1076, 973, 917, 764, 696; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.81 (d, J = 8.0 Hz, 2H), 7.42 (t, J = 7.9 Hz, 2H), 7.36 – 7.30 (m, 1H), 4.59 (dd, J = 10.3, 3.6 Hz, 1H), 4.49 – 4.42 (m, 1H), 4.24 – 4.17 (m, 1H), 3.61 (quint, J = 12.2, 6.1 Hz, 1H), 3.51 (dd, J = 9.6, 4.5 Hz, 1H), 3.39 – 3.34 (m, 1H), 1.25 (s, 1H), 1.17 (dd, J = 6.1, 2.5 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.5, 132.7, 129.4, 129.0, 128.7, 128.0, 125.6, 121.1, 72.4, 69.3, 68.8, 53.0, 50.6, 21.9; HRMS (ESI) calcd. for $C_{14}H_{20}O_2N_3$, 262.1550 [M + H]$^+$; found, 262.1549.

2-(4-phenyl-1H-1,2,3-triazol-1-yl)cyclopentanol **(3g)**

Yellow oil; IR (KBr) ν/cm^{-1} 3422, 2923, 2852, 1456, 1264, 1084, 764, 695; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 – 7.72 (m, 2H), 7.49 – 7.45 (m, 1H), 7.44 – 7.37 (m, 2H), 7.35 – 7.30 (m, 1H), 4.60 (t, J = 6.1 Hz, 1H), 4.06 – 3.76 (m, 1H), 2.47 – 2.37 (m, 1H), 2.31 – 2.09 (m, 2H), 2.01 – 1.89 (m, 3H), 1.25 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.1, 130.8, 130.2, 128.7, 128.0, 125.5, 77.7, 68.3, 22.6, 20.1; HRMS (ESI) calcd. for $C_{13}H_{16}ON_3$, 230.1287 [M + H]$^+$; found, 230.1284.

2.3 General Procedure for the synthesis of benzyl 1,2,3-triazoles 5a, 5b

The benzyl bromide (1.0 mmol), alkyne (1.0 mmol) and sodium azide (1.2 mmol) were added to a to a suspension of nano-Fe_2O_3 (10 mol %) in H_2O (3 mL). The reaction mixture was stirred at reflux and monitored by TLC until total conversion of the starting materials. After completion of the reaction, the catalyst was separated with the aid of a magnet. Water (10 mL) was added to the reaction mixture, followed by extraction with ethyl acetate (3 × 10 mL). The resulting organic phase was dried with anhydrous Na_2SO_4 and the solvent was evaporated under vacuum. The residue was purified by column chromatography (silica gel, hexane– ethyl acetate) to give the desired benzyl 1,2,3-triazoles.

1-benzyl-4-phenyl-1H-1,2,3-triazole **(5a)**[30]

White crystalline solid, mp 129–130 °C; IR (KBr) ν/cm^{-1} 3140, 2923, 1607, 1456, 1282, 1069, 766, 693; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 – 7.78 (m, 2H), 7.66 (s, 1H), 7.44 – 7.36 (m, 5H), 7.34 – 7.27 (m, 3H), 5.58 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.1, 134.6, 130.5, 129.1, 128.9, 128.8, 128.7, 128.1, 128.0, 125.6, 119.4, 54.2; HRMS (ESI) calcd. for $C_{15}H_{14}N_3$, 236.1182 $[M + H]^+$; found, 236.1182.

1,4-bis(1-benzyl-1H-1,2,3-triazol-4-yl)benzene **(5b)**

Yellow oil; IR (KBr) ν/cm^{-1} 3066, 2924, 1603, 1456, 1229, 1068, 798, 710; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, J = 8.5 Hz, 2H), 7.76 (s, 1H), 7.71 (s, 1H), 7.44 – 7.37 (m, 3H), 7.35 – 7.24 (m, 7H), 7.12 – 7.06 (m, 2H), 5.60 (s, 2H), 5.56 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.0, 137.6, 135.3, 134.3, 133.2, 131.6, 129.2, 129.1, 128.8, 128.1, 127.0, 126.3, 126.0, 119.8, 54.3, 51.8; HRMS (ESI) calcd. for $C_{24}H_{21}N_6$, 393.1822 $[M + H]^+$; found, 393.1829.

3. RESULTS AND DISCUSSION

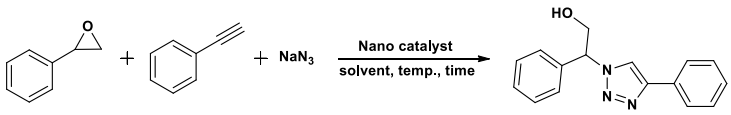
3.1 Chemistry

A preliminary survey of reaction conditions was conducted with styrene oxide **1a**, phenyl acetylene **2a** and sodium azide as a model reaction. In the first instance, the impact of catalyst was tested. As shown in Table **1**, in the absence of catalyst, no cyclization product was obtained after stirring for 24 h (entry 1). Then, we focused our attention on using various nano catalysts, which might help to reduce the reaction time and afford the desired product in good yields (Table **1**, entries 2–5). Among the nano catalysts tested, nano-Fe_2O_3 was catalyzed the reaction most efficiently (Table **1**, entry 5). The effect of solvents was also studied and it was observed that the reaction was effective in polar solvents, such as H_2O, CH_3OH, CH_3CN, DMF and DMSO whereas no product was observed in toluene and THF (Table **1**, entries 5–11). As indicated in Table **1**, the reaction could be progressed very efficiently in H_2O (entry 5). This solvent was chosen as a green solvent for the synthesis of triazoles.

To further improve the yield, the same reaction was carried out in the presence of 2, 5, 10 and 20 mol% of nano-Fe_2O_3 (Table **1**, entries 5, 12–14). From the results shown in Table **1**, it is clear that the yields depend on the amount of catalyst and the optimum amount of catalyst was 10 mol% (entry 5). To our surprise, the reaction in water did not proceed even after prolonged stirring at room temperature (Table **1**, entry 15). But by performing the reaction at 50 °C (Table **1**, entry 16) encouragingly the reaction afforded the corresponding product in 55% yield. With further increase in temperature to 100 °C the yield increased to 81% (Table **1**, entry 5). Thus, the optimized reaction conditions turned out to be using 10 mol% nano-Fe_2O_3 in water at the reflux temperature for 5 h.

With the optimized conditions defined, the scope of the iron oxide catalyzed click reaction was further expanded with a variety of epoxides and alkynes. The results are summarized in Table **2**. The alkynes bearing either electron-withdrawing or electron-donating groups reacted satisfactorily to furnish the corresponding 1,4-disubstituted β-hydroxy 1,2,3-triazoles in near quantitative yields (Table **2**, entries 2 and 3). The presence of heterocyclic moiety such as pyridyl group in the alkyne was equally effective towards the epoxide opening, followed by 1, 3-dipolar cycloaddition (Table **2**, entry 4). The reactivity of glycidyl phenyl ether and isopropyl glycidyl ether (Table **2**, entries 5 and 6) was further explored and examined (Scheme **3**). These epoxides gave a single regioisomer with preferential attack at the less hindered terminal carbon atom which was confirmed by the reported literature [39]. In the case of cyclopentene oxide, the stereochemistry of the ring-opened product was found to be *trans* selectivity, suggesting the occurrence of an S_N2 pathway for the epoxide ring-opening step, as expected (Table **2**, entry 7) [39].

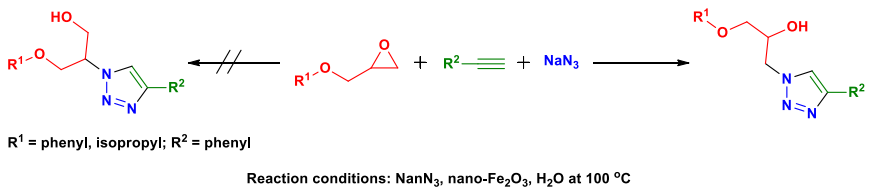
Table 1. Optimization of the reaction conditions[a]



1a 2a 3a

Entry	Nano catalyst	Catalyst loading (mol%)	Solvent	Time (h)	Temparature (°C)	Yield[b] (%)
1	No Catalyst	-	H_2O	24	100	0
2	CoO	10	H_2O	24	100	trace
3	NiO	10	H_2O	24	100	trace
4	ZnO	10	H_2O	24	100	0
5	**Fe_2O_3**	**10**	**H_2O**	**5**	**100**	**81**
6	Fe_2O_3	10	CH_3OH	5	65	52
7	Fe_2O_3	10	CH_3CN	5	82	37
8	Fe_2O_3	10	DMF	5	100	41
9	Fe_2O_3	10	DMSO	5	100	49
10	Fe_2O_3	10	$C_6H_5CH_3$	24	110	0
11	Fe_2O_3	10	THF	24	60	0
12	Fe_2O_3	2	H_2O	5	100	74
13	Fe_2O_3	5	H_2O	5	100	77
14	Fe_2O_3	20	H_2O	5	100	81
15	Fe_2O_3	10	H_2O	24	rt	0
16	Fe_2O_3	10	H_2O	5	50	55

[a]Reaction conditions: styrene oxide **1a** (1 mmol), phenyl acetylene **2a** (1 mmol), sodium azide (1.2 mmol) and catalyst (10 mol%) in solvent (3 mL) were stirred at reflux. [b]Isolated yield.

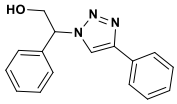
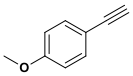
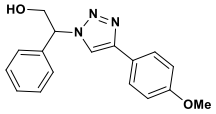
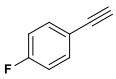
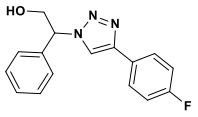
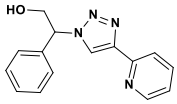
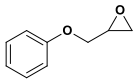
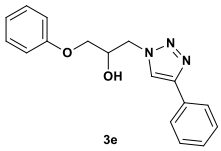
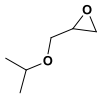
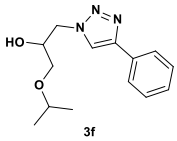
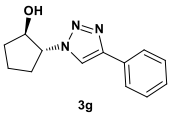


R^1 = phenyl, isopropyl; R^2 = phenyl

Reaction conditions: $NanN_3$, nano-Fe_2O_3, H_2O at 100 °C

Scheme 3

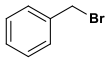
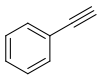
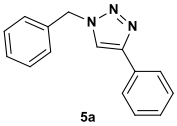
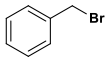
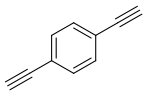
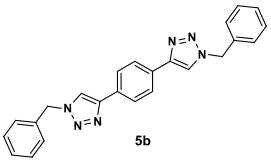
Table 2. Synthesis of 1,4-disubstituted β-hydroxy 1,2,3-triazoles

Entry	Epoxide	Alkyne	Time (h)	Product	Yield[b] (%)
1	 1a	 2a	5	 3a	81
2	 1a	 2b	5	 3b	76
3	 1a	 2c	5	 3c	73
4	 1a	 2d	4	 3d	78
5	 1b	 1a	5	 3e	80
6	 1c	 1a	3	 3f	83
7	 1d	 1a	4	 3g	80

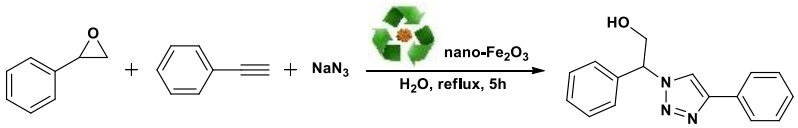
[a]Reaction conditions: epoxide (1 mmol), alkyne (1 mmol), sodium azide (1.2 mmol) and nano-Fe_2O_3 (10 mol%) in water (3 mL) were stirred at reflux. [b]Isolated yield after column chromatography.

Generally, the synthesis of 1,2,3-triazoles through click chemistry involves *in situ* generated azides from organic halides. In this regard, we explored some alternative substrates to the epoxides as azide precursors which, being compatible with the standard reaction conditions, could expand the versatility of the catalyst (Scheme **2**). As an example, benzyl bromide was regioselectively transformed into the corresponding 1,4-substituted benzyl 1,2,3-triazole in high yield and short reaction time (Table **3**, entry 8). The bistriazole **5b** was obtained in good yield from diyne **2e** and two equivalents of benzyl bromide and sodium azide (Table **3**, entry 9).

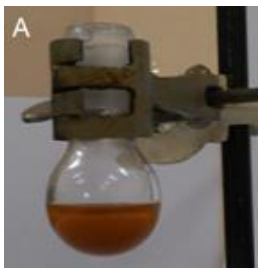
Table 3. Synthesis of 1,4-disubstituted benzyl 1,2,3-triazoles

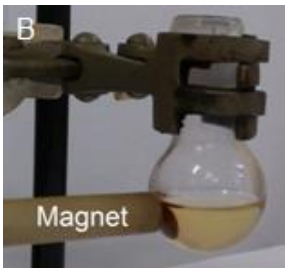
Entry	Epoxide	Alkyne	Time (h)	Product	Yield[b] (%)
8	 4a	 2a	3	 5a	85
9	 4a	 2e	5	 5b	82[c]

[a]Reaction conditions: benzyl bromide (1 mmol), alkyne (1 mmol), sodium azide (1.2 mmol) and nano-Fe_2O_3 (10 mol%) in water (3 mL) were stirred at reflux. [b]Isolated yield after column chromatography. [c] benzyl bromide (2 mmol), sodium azide (2.4 mmol) and nano-Fe_2O_3 (20 mol%) in water (6 mL).



1a 2a 3a





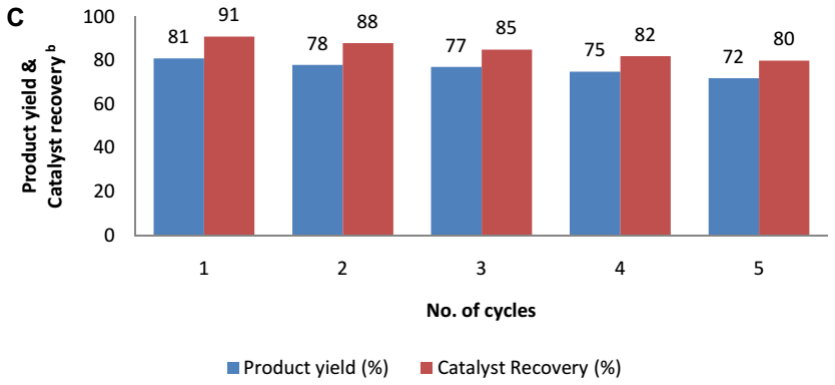


Figure 2. Magnetic separation (A) the dispersion of catalyst in reaction mixture (B) the separation of catalyst with an external magnet and (C) recyclability of nano-Fe_2O_3[a]

[a]Reaction conditions: styrene oxide **1a** (1 mmol), phenyl acetylene **2a** (1 mmol), sodium azide (1.2 mmol) and nano-Fe_2O_3 (10 mol%) in water (3 mL) were refluxed for 5 h. [b]Isolated yield.

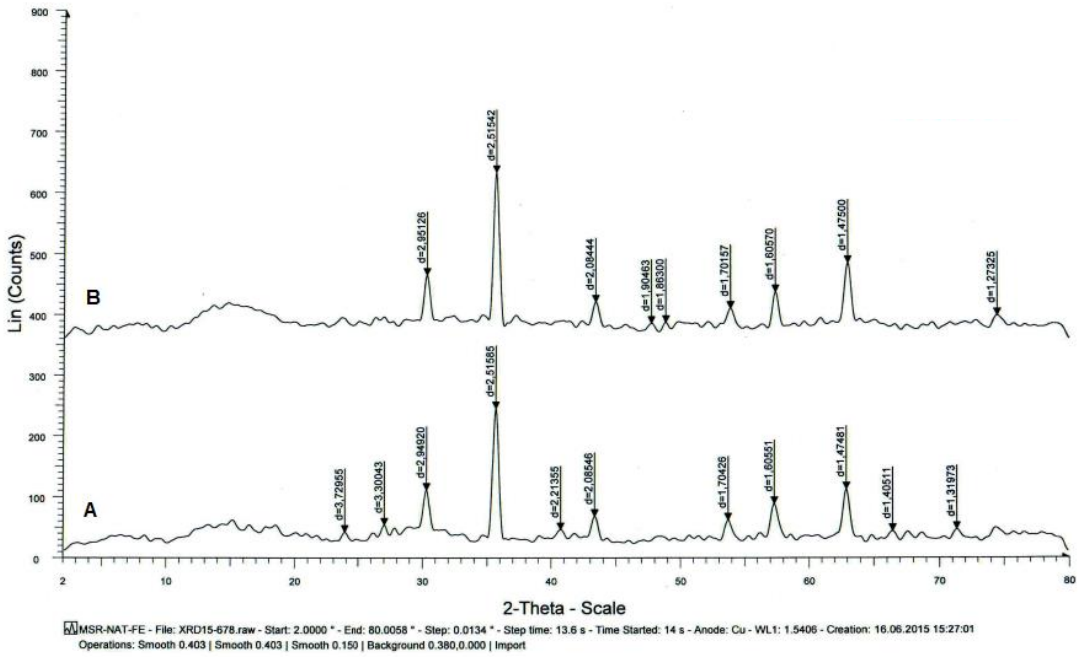


Figure 3. X-Ray Diffraction Patterns of (a) native nano-Fe_2O_3 (b) nano-Fe_2O_3 after fifth cycle

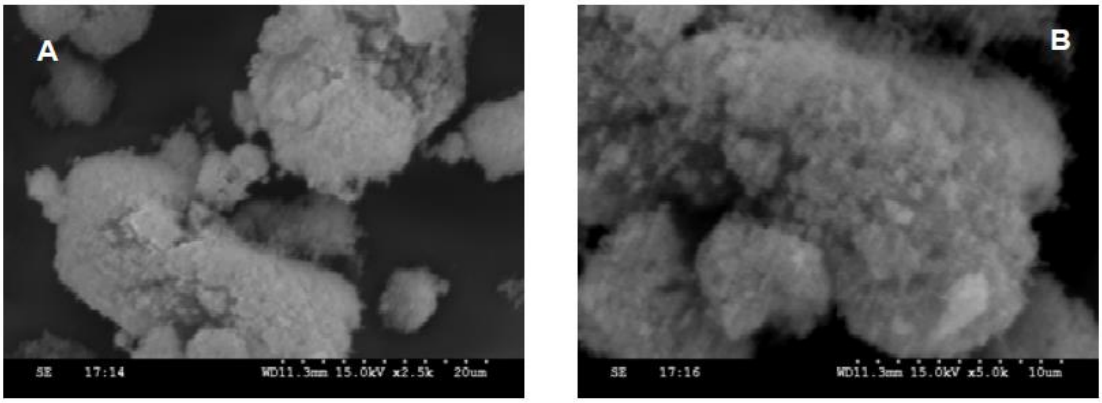


Figure 4. SEM images of (A) nano-Fe_2O_3 before use (B) same nano-Fe_2O_3 after fifth cycle.

3.2 Recyclability of nano-Fe_2O_3 catalyst

The recyclability of nano-Fe_2O_3 was examined using styrene oxide **1a**, phenyl acetylene **2a** and sodium azide as model reaction. After completion of the reaction, the reaction mixture was cooled to room temperature and the catalyst was recovered magnetically, washed several times with methanol and dried at 60 °C for 30 min. The recovered catalyst was reused directly in the next cycle with fresh reactants, under the same conditions. The nano-Fe_2O_3 catalyst was reused for five times without any change in activity (Figure **2**). The powder XRD patterns of nano-Fe_2O_3 catalyst before and after the reaction are displayed in Figure **3**. No substantial variation was observed in the powder XRD patterns of fresh and used catalyst, revealing the retention of the original structure of nano-Fe_2O_3 in the used catalyst. The SEM image of the catalyst taken after the fifth cycle of the reaction does not show a significant change in the morphology and the size of the catalyst, which indicates the retention of the catalytic activity after recycling (Figure **4**).

4. CONCLUSION

In summary, we have developed a simple and efficient protocol for the synthesis of 1,4-disubstituted β-hydroxy/benzyl 1,2,3-triazoles *via* a three component reaction of epoxide/benzyl bromide, sodium azide and an alkyne catalyzed by nano-Fe_2O_3 in water without using any toxic solvent or co-catalyst. The formation of the product involves *in situ* generation of organic azide intermediate, followed by rapid ring closure with terminal alkynes to form 1,2,3-triazole derivatives. This protocol is a clean and safe process and can be used to generate a diverse range of products in good yields. Moreover, this nanocatalyst can be recycled and reused for five times without loss of catalytic activity.

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The authors declare no conflict of interest