A CARE STUDY ON SYNTHESIS OF 1,2,3-TRIAZOLE DERIVATIVES BY MEANS OF NANOPARTICLES AS A REUSABLE HETEROGENEOUS CATALYST

Abstract

In recent years, nanotechnology is an emerging trend for the synthesis of medicinally significant and biologically dynamic derivatives as a heterogeneous catalyst because it’s simple and effortless work-up procedure. On the other hand, 1,2,3-triazole derivatives belongs to N-heterocyclic compounds and exhibit enormous biological activities as medicinal important. In this current chapter, the examination on importance and role of nanotechnology in preparation of 1,2,3-triazole analogues has been discussed and it make helpful for synthetic chemists or research scholar’s for the advanced developments in nanotechnology.

Keywords: 1,2,3-Triazoles; Nanoparticles; Heterogeneous catalyst; Medicinal chemistry; N-Heterocyclic compounds.

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I. INTRODUCTION

Heterocyclic molecules and its derivatives are important class of organic compounds having one or more heteroatoms, such as nitrogen, oxygen, sulfur, or a combination of two or more heteroatoms, along with at least one carbon atom, within their cyclic structure.[1] Heterocyclic derivatives form the principal and mainly diverse group of organic derivatives, holding immense chemical, industrial[2] and biomedical[3] importance. Additionally, these compounds serve as crucial scaffolds for a extensive variety of biologically active natural and synthetic derivatives [4], pharmaceutical drugs [5] and agrochemicals.[6] Nowadays, academic and industrial chemists have revealed the curiosity in special types of nitrogen holding moieties, known as azahetrocyclic systems. Among the accessible *N*-heterocycles, azoles have become a considerable field of study owing to their exclusive structural properties.

Triazole is a heterocyclic compound containing five membered ring structure composed of 3 nitrogen and 2 carbon atoms. There are two isomers of triazole i.e., 1,2,3 triazole and 1,2,4 triazole as represented in Figure-1.

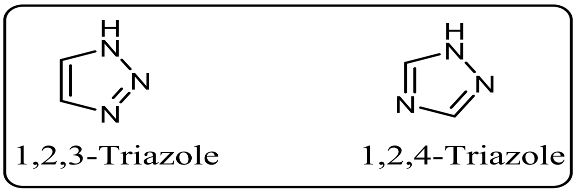


Figure 1: Isomeric forms of Triazoles

The remarkable stability of the triazole nucleus primarily arises from its structural properties, particularly emphasizing the role of aromaticity and resonance. This aromaticity is a result of the formation of an aromatic sextet, achieved by the donation of one π electron from each atom connected by double bonds, combined with the contribution of two electrons from a nitrogen atom [7]. The resonance stabilization further enhances the stability of the triazole nucleus, as evidenced by its ability to exist in various tautomeric forms. This unique combination of aromaticity and resonance plays a pivotal role in conferring the intriguing characteristics and fascinating properties of triazoles. (**Figure 2a & 2b**)

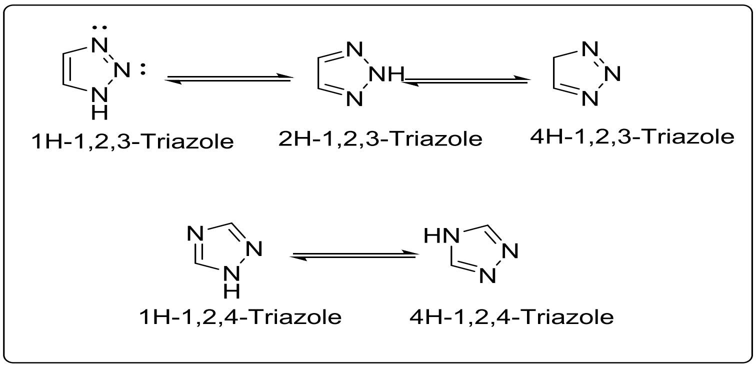


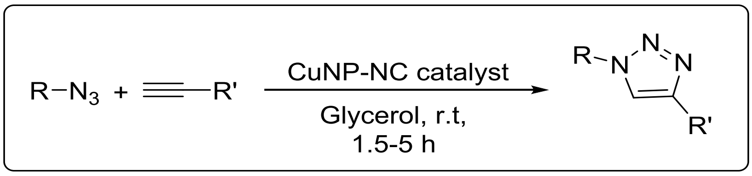
Figure 2: a) Tautomeric structures of 1,2,3-Triazole, b) Tautomeric structures of 1,2,4-Triazole.

1,2,3-Triazoles play a crucial role as pharmacophores, intermingle with biological receptors with elevated similarity owing to their unique characteristics. Their dipole nature, hydrogen bonding ability, stiffness, and solubility make them attractive in drug design. As a result, 1,2,3-triazole motifs are integral components of various drugs used in clinical therapy.[8]

Nano-chemistry is an emergent research field owing to their exclusive properties.[9,10] The progress in nanotechnology has led to an escalating the requirement for multifunctional materials. Extremely ordered nanomaterials function as outstanding catalysts due to their elevated surface area and surface functionalities. Therefore, synthesis of nanomaterials has paying attention immense deal of research awareness in the current years. The convention of nano-materials such as heterogeneous catalyst has expanded considerable responsibility in organic synthesis owing to straightforward work-up process, environmentally benevolent nature, recyclability, low expenditure and effortlessness of isolation.[11]. In essence, the pivotal role of heterocycles, notably 1,2,3-triazoles, spans from their structural attributes to diverse applications. They serve as vital pharmacophores in drug design, while also excelling as effective fungicides in agriculture. In the current chapter, we have highlighted the importance of 1,2,3-triazole chemistry synthesis using nano-particles as a heterogeneous catalyst and their enduring importance in advancing scientific and practical domains.

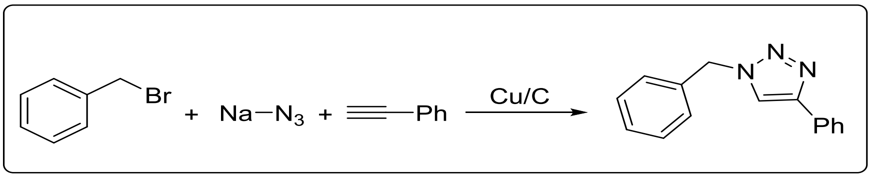
II. CHEMISTRY OF 1,2,3-TRIAZOLE SYNTNESIS USING NANOTECHNOLOGY

Mitali Chetia *et al.*[12] addressed the regioselective synthesis of 1,2,3-triazole derivatives by means of copper nanoparticles bearing heterogeneous nanocellulose as reusable catalyst. To synthesize the Cu NPs bearing nanocellulose, first the suspension of nanocellulose is treated with $CuSO_4.H_2O$ followed by the drop wise addition of hydrazine hydrate. The synthesized Cu NPs bearing nanocellulose are examined with FT-IR, XRD, TEM, SEM-EDX and it was found that the average size of the particle to be 6-7 nm. The scope of the synthesized Cu NPs bearing nanocellulose was studied for the synthesis of 1,4-disubstituted-1H-1,2,3-triazole as a recyclable heterogeneous catalyst using azide derivatives with acetylene analogues in glycerol as shown in Scheme-1 *via* 1,3-dipolar Huisgen cycloaddition reaction and found 68-99% yields. The reusability of synthesized catalyst was studied for the same reaction capable of five sets devoid of any significance loss of activity.



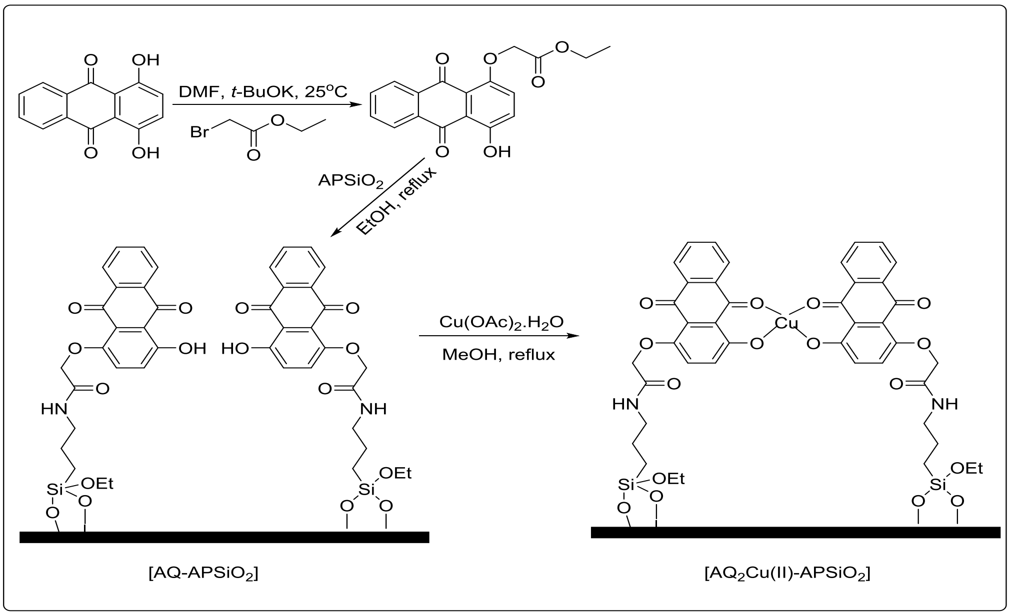
Scheme 1: CuNP-NC catalysed cycloaddition reaction of azides and alkynes.

Hashem Sharghi *et al*.[13] discussed the three component coupling reaction of sodium azide, terminal alkynes and alkyl/benzyl halides for the green synthesis of 1,2,3-triazole analogues employing with copper NPs on charcoal as heterogeneous catalyst in water as a environmental friendly solvent. The catalyst was synthesized by using CuI and active carbon in ethanol and it was observed that the 9.97% copper content in it. The synthesized catalyst was experienced by using XRD, SEM, AFM, FR-IR, ICP and the size of the Cu-NPs on activated carbon was observed to be 283.3 nm. The application of the Cu-NPs on activated carbon was studied in the preparation of 1,2,3-triazole derivatives using catalytalic amount of Cu/C for the coupling reaction between sodium azide, terminal alkynes and alkyl/benzyl halides and found 91-69% yield as described in Scheme-2. The reusability of Cu/C was experiential for the same coupling reaction equal to ten cycles without any importance failure of activity.



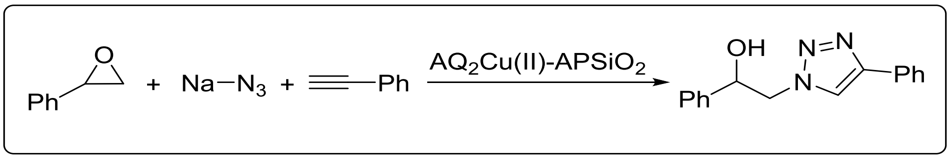
Scheme 2: Synthesis of substituted 1,2,3-triazole using Cu/C as heterogeneous catalyst.

Sharghi, H. *et al.*[14] reported the region-selective synthesis of three constituent coupling reaction of sodium azide, terminal alkynes and wide range of epoxides for the synthesis of β-hydroxy 1,4-disubstituted 1,2,3-triazole derivatives using recyclable heterogeneous catalyst of 1,4-dihydroxyanthraquinone-copper(II) aminopropyl silica gel nanoparticles [$Aq_2Cu(II)-APSiO_2$]. The synthesis of novel 1,4-dihydroxyanthraquinone-copper(II) nanoparticle catalyst was addressed in three steps. In first step (4-hydroxy-9,10-dioxo-9,10-dihydroanthracen-1-yloxy)-acetic acid ethyl ester was synthesized using 1,4-dihydroxyanthraquinone, ethyl 2-bromoacetate and *t*-BuOK. In second step (4-hydroxy-9,10-dioxo-9,10-dihydroanthracen-1-yloxy)-acetic acid ethyl ester was treated with aminopropyl silica gel ($APSiO_2$) to obtained the $AQ-APSiO_2$ heterogeneous ligand followed by the reaction with $Cu(OAc)_2.H_2O$ in methanol to achieved the target nanoparticles as described in Scheme-3. On the other hand it was totally characterized by ICP, XRD, AFM, SEM, FT-IR and TG analysis for nitrogen adsorption.



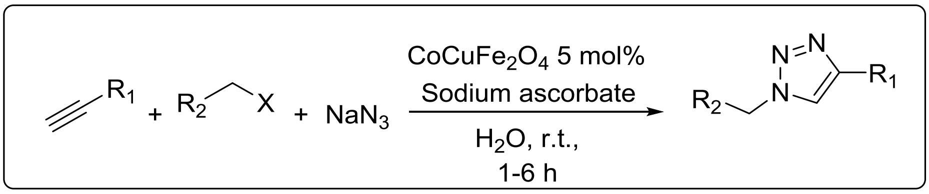
Scheme 3: Synthesis of title nanoparticles $AQ_2Cu(II)-APSiO_2$.

The scope of the novel catalyst was employed in the synthesis of β-hydroxy 1,4-disubstituted 1,2,3-triazole derivatives in 81-97% yield as shown in Scheme-4. The reusability of the novel heterogeneous catalyst was tested for ten times and found without loss of any catalytic activity.



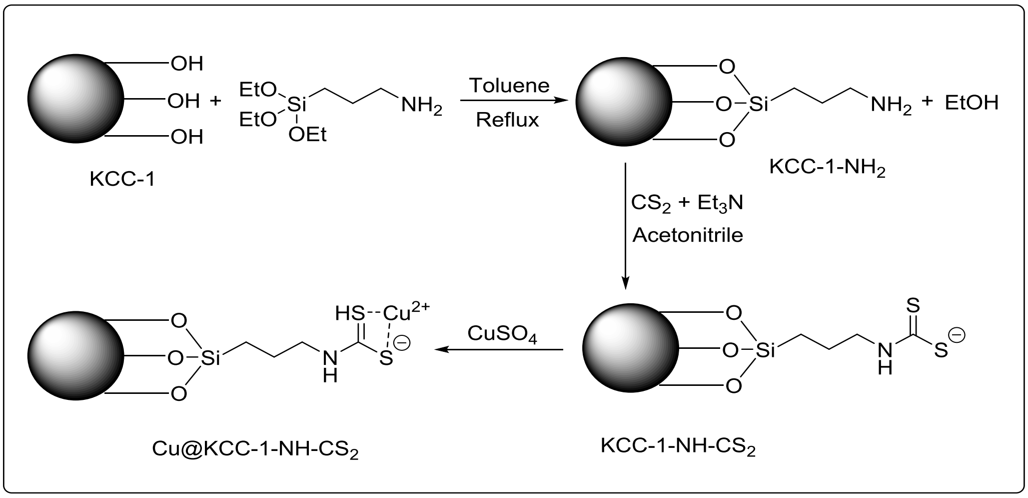
Scheme 4: Synthesis of 1,4-disubstituted β-hydroxy 1,2,3-triazoles.

Moghaddam F. M. *et al.*[15] addressed the production of 1,5-disubstituted 1,2,3-trizole derivatives by means of cobalt-copper ferrite nanoparticles ($CoCuFe_2O_4$) at room temperature *via* [3+2] Huisgen cycloaddition reaction. The $CoCuFe_2O_4$ nanoparticles were synthesized by using co-precipitation procedure.[16] On the other hand the synthesized $CoCuFe_2O_4$ nanoparticles were examined by FT-IR, TEM, EDS, AAS, VSM, SEM and XPS. The metal of Co and Cu present in synthesized $CoCuFe_2O_4$ nanoparticles was found to be 5.2 wt% and 10 wt% respectively using AAS technique and moreover the size of the $CoCuFe_2O_4$ nanoparticles was observed as 30 nm by applying Scherrer equation using XRD physical technique. To observe the extent of the $CoCuFe_2O_4$ nanoparticles, the catalytic amount of the synthesized NPs were employed in Huisgen [3+2] cycloaddition reaction with reactants of terminal alkyene derivatives, alkyl/aryl halides and sodium azide as made known in Scheme-5 with excellent quantitative yields of 76-99%.



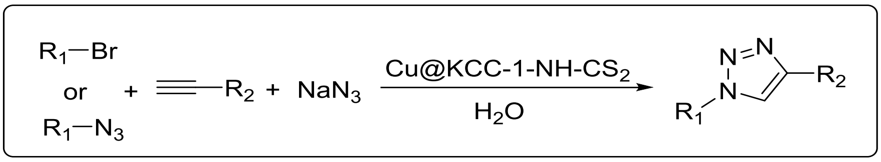
Scheme 5: $CoCuFe_2O_4$ nanoparticles catalysed [3+2] cycloaddotion reaction.

Anvari, M. *et al.*[17] illustrated the extremely one-pot synthesis of well-organized 1,2,3-triazole analogues in water as a environmentally benign solvent using novel copper nanoparticles doped in wrinkled fibrous nanosilica (Cu@KCC-1-NH-CS_2) as a reusable heterogeneous catalyst. The novel Cu@KCC-1-NH-CS_2 was prepared in two step procedure. The primary step expresses the process of KCC-1-NH-CS_2 and the second step explains the synthesis of Cu@KCC-1-NH-CS_2 by the reaction between the copper(II) sulfate solution and KCC-1-NH-CS_2 as depicted in Scheme-6. On the other hand, the novel catalyst was fully characterized by physicochemical techniques like FT-IR, SEM, TEM, EDX and it exhibit the 133 m^2g^{-1} as high surface area was calculated by BET equation might be cause the outstanding catalytic performance.



Scheme 6: Preparation of Cu@KCC-1-NH-CS_2 heterogeneous catalyst

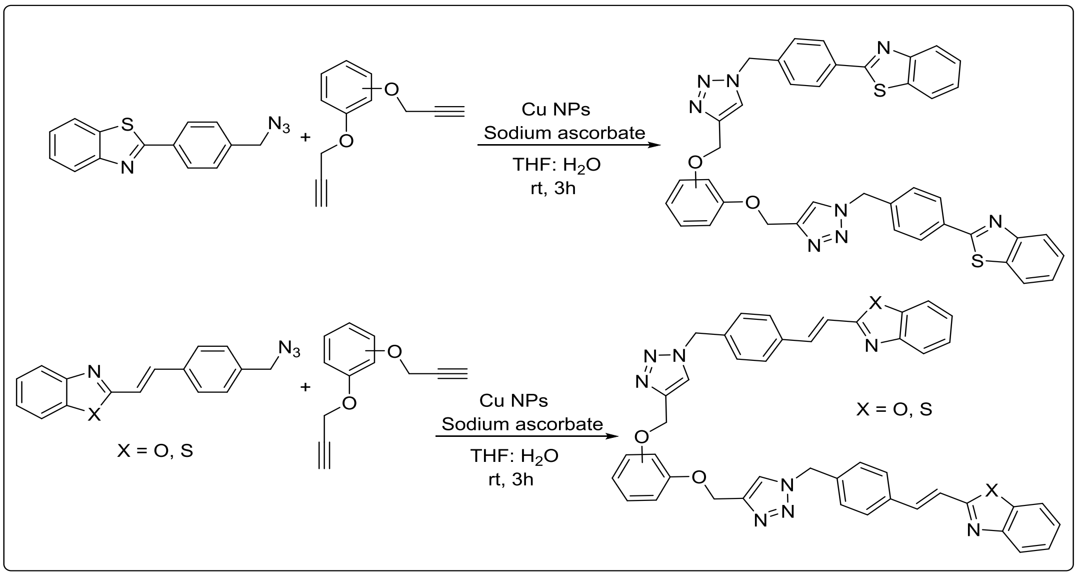
The scope of the Cu@KCC-1-NH-CS_2 was employed in the synthesis of 1,4-disubstituted 1,2,3-triazole derivatives using various aryl halides or several aryl azides, terminal alkyene analogues along with sodium azide produces the tremendous yields 92-100% as expressed in Scheme-7. Moreover, the authors studies the reusability of Cu@KCC-1-NH-CS_2 nanocatalyst up to five cycles with low lose in its catalytic activity.



Scheme 7: Synthesis of 1,2,3-triazole derivatives using Cu@KCC-1-NH-CS_2.

Tamilselvan Abiraman *et al.*[18] addressed the straight forward preparation of substituted 1,2,3-triazole analogues by means of Sub 1 nm Poly(acrylic acid)-Capped Copper Nanoparticles [PAACC NPs] as a catalyst via Click chemistry under ultrasound irradiation using alkyl azide analogues and terminal alkyene substrates as depicted in Scheme-8.

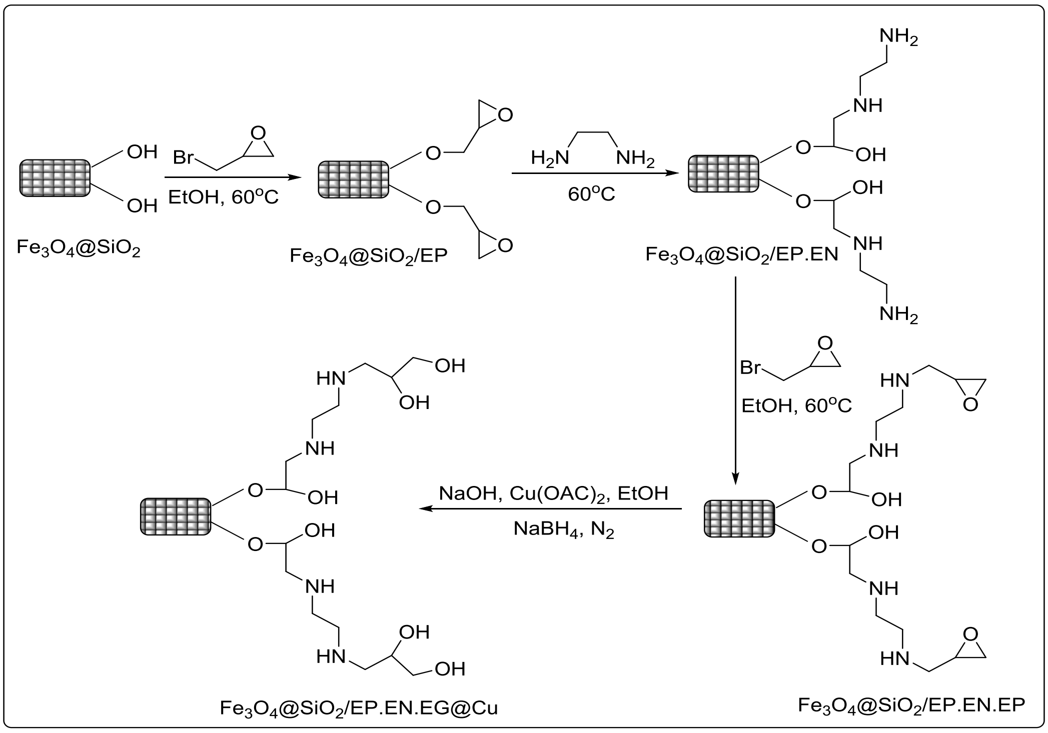
The synthesis of novel PAACC NPs was carried out as follows, initially the mixture of copper nitrate trihydrate and poly(acrylic acid) was irradiate under ultrasound followed by the drop wise addition of NaOH to maintain the pH at 9 added and the colour of resulting solution is dark blue. To the above solution add L-ascorbic acid solution and subsequent ultrasound irradiation then the color of the solution turns from blue to yellow consequentially by the production of Cu NPs. The reaction was sustained for an additional 30 min, cooled and dried at room temperature to obtain the Cu NPs. It was observed that the Cu% present on poly(acrylic acid) was 33 as expressed in Scheme-9. The synthesized NPs be fully experienced by XPS, DRS UV-visible, FESEM, PL and HRTEM analytical spectroscopic methods. Furthermore, PAACC NPs exhibit the orange fluorescence at 560 nm peak range.



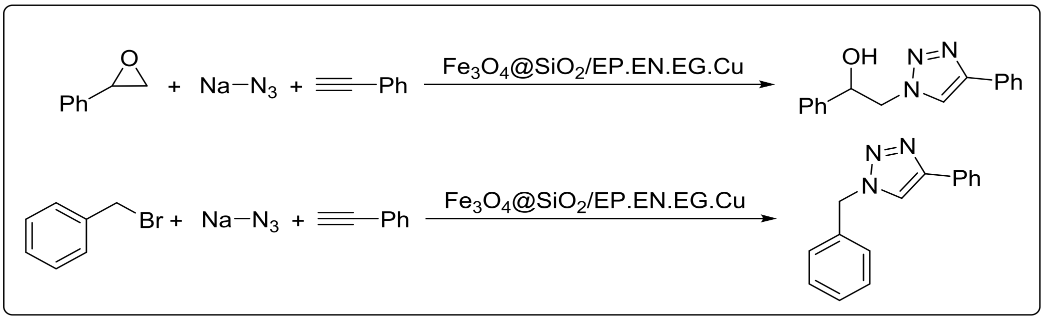
Scheme 8: PAACC employed synthesis of Triazole derivatives.

$$Cu(NO_3)_2 + PAA \xrightarrow[15\ min]{NaOH} PAA\text{-}Cu(OH)_2 \xrightarrow[5\ min.]{L\text{-}AA} PAA\text{-}Cu_2O \xrightarrow{30\ min.} PAA\text{-}Cu$$

Scheme 9: Synthesis of PAACC NPs under ultrasound irradiation



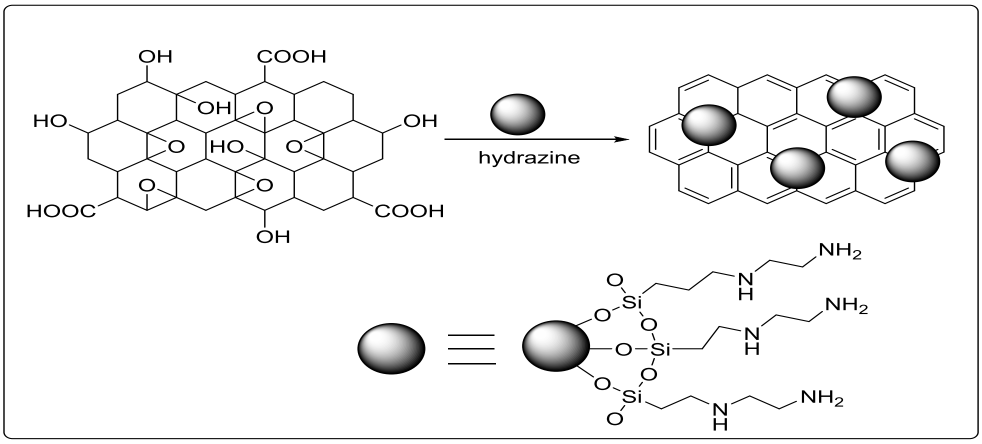
Scheme 10: Preparation of Fe_3O_4@SiO_2/EP.EN.EG.Cu nanocatalyst



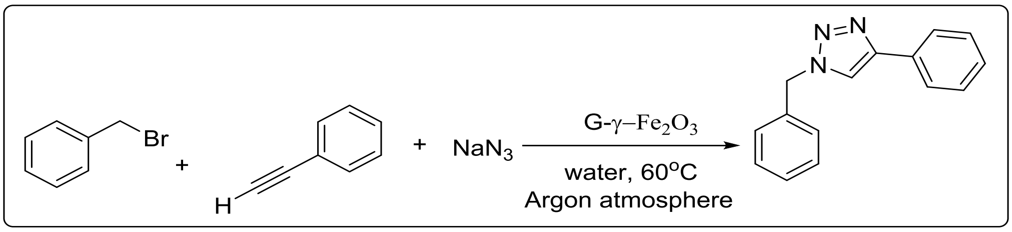
Scheme 11: Synthesis of 1,2,3-triazole analogues using magnetic $Fe_3O_4@SiO_2$/EP.EN.EG.Cu nanocatalyst

Ebadi Amin *et al*.[19] illustrated the straight forward preparation of substituted 1,2,3-triazole analogues using $Fe_3O_4@SiO_2$/EP.EN.EG.Cu magnetic nanostructured core-shell as heterogeneous catalyst under mild circumstances *via* cycloaddition of 1,3-dipolar procedure. The preparation of the novel $Fe_3O_4@SiO_2$/EP.EN.EG.Cu magnetic nanostructured core-shell as depicted in Scheme-10. On the other hand the synthesized catalyst was characterized by using physiochemical techniques and it was observed that the 100 nm is the average size of the nanospheres. To observe the scope of the result, the synthesis of 1,2,3-triazoles compounds was assessed through the reaction of various epoxides, alkyl or benzyl halides with phenylacetylene, azide of sodium and found outstanding 85-98% yields as addressed in Scheme-11. Moreover, the authors played a more concentration on reusability of catalyst up to seven times with small reduce of catalytic activity.

Noor Salam *et al.* described the straight forward one-pot synthesis of 1,2,3-triazole derivatives using recyclable graphene-γ-Fe_2O_3 magnetic nano-composite materials via [3+2] cycloaddition reaction as prescribed in Scheme-12.[20] Graphene-γ-Fe_2O_3 magnetic nano-composite materials was prepared by the reaction of graphene oxide in KOH solution with silica coated γ-Fe_2O_3 followed by the addition of hydrazine solution as depicted in Scheme-13. The extent of the novel synthesized graphene nano-composite catalyst was observed in the synthesis of substitiuted 1,2,3-triazole derivatives using benzyl bromide, phenyl acetylene and azide of sodium in water as a environment friendly solvent and found 70-93% yields.



Scheme 12: Preparation of graphene-γ-Fe_2O_3 nano-composite



Scheme 13: Synthesis of 1,2,3-triazole derivatives using graphene-γ-Fe_2O_3 nano-composite

Fe_3O_4 NPs were synthesized by using $FeCl_3.6H_2O$ and $FeCl_4.4H_2O$ via co-precipitation method followed by the Stober process for coating on Fe_3O_4 NPs with silica shell to obtain the Fe_3O_4@SiO_2. The reaction of 3-chloropropyltrimethoxysilane with synthesized Fe_3O_4@SiO_2 followed by the reaction with hydrazine hydrate to obtained the intermediate. Isatoic anhydride is added to the above intermediate to replace the hydrazine. Finally the Cu(II) was loaded by the reaction of copper (II) acetate to obtained the Cu(II)MNPs.

III. CONCLUSION

In summary, 1,2,3-triazole derivatives have employing a extraordinary manifestation for the motivation that of their adjustable understanding in the medicinal chemistry. During this chapter, we have communicated a preparation of 1,2,3-triazole analogues using variety of nanoparticles as reusable heterogeneous catalyst. This chapter can substantiate to be extremely helpful for synthetic chemists or research scholar's in the progression of new procedures for the enormous synthesis of medicinally energetic new 1,2,3-triazole analogues and large-scale production of biologically active novel 1,2,3-triazole analogues using novel nanoparticles.

IV. CONFLICT OF INTEREST

The authors have officially approved to incorporate their work as a chapter within the book entitled "Futuristic Trends in Chemical, Material Sciences & Nanotechnology".

V. LIST OF ABBREVIATIONS

- ICP: Inductively Coupled Plasma
- XRD: X-Ray Diffraction
- AFM: Atomic Force Microscopy
- SEM: Scanning Electron Microscopy
- FT-IR: Fourier transform infrared
- TG: Thermo gravimetry
- TEM: Transmission electron microscopy
- EDS: Energy-dispersive X-ray spectroscopy
- AAS: Atomic absorption spectroscopy
- VSM: Value stream mapping
- XPS: X-ray photoelectron spectroscopy
- N2-BET: Nitrogen Brunauer-Emmett-Teller

- DRS UV-Visible: Diffuse reflectance spectroscopy Ultraviolet-Visible
- FE-SEM: Field emission scanning electron microscopy
- HR-TEM: High-resolution transmission electron microscopy

VI. ACKNOWLEGDEMENT

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