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Copper Grafted on Silica-Coated Magnetic Nanoparticles A Highly Efficient and Synergistic Organocatalyst:A sustainable and Eco-friendly Reusable Catalyst for Click Reaction.

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Abstract: In this research Cu(II) complex supported on Fe_3O_4@SiO_2@Pr-AIPA core–shell magnetic nanoparticles core–shell magnetic nanoparticles (MNPs) was prepared and applied for synthesis of 1,2,3-Triazole by click reaction. This compounds are one of the most important classes of N-heterocyclic compounds, have applications in pharmaceutical chemistry. Fe_3O_4@SiO_2@Pr-AIPA-Cu MNPs efficiently catalyzed a click reaction between alkyl halides, Sodium Azide, and Alkynes to synthesize corresponding products in high to excellent yields. Among heterogeneous catalysts, MNPs have seen much attention due to high surface-to-volume ratio and their easy separation. The catalyst was recovered using an external magnetic field, and recycled for subsequent reactions without substantial loss of efficiency. The catalyst was recovered using an external magnetic field, and recycled for subsequent reactions without substantial loss of efficiency.

Keywords: 1,2,3-Triazole, Heterogeneous catalyst, Cycloaddition, Click reaction

1. Introduction

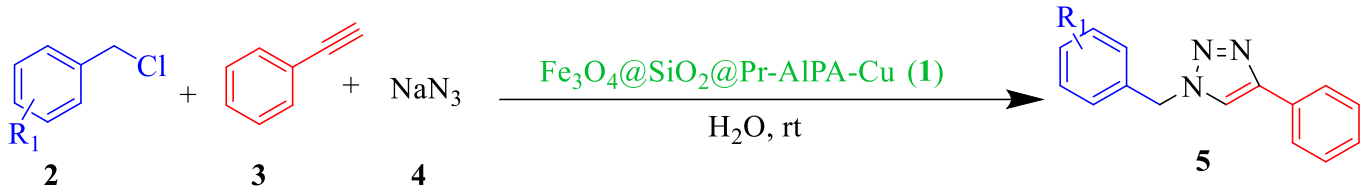
Multi-component reactions (MCRs) are considered to be an important arsenal in synthetic and medicinal chemistry. These reactions have been strategically employed in various synthetic transformations where classical methods usually involve many steps with tedious procedures. The MCR approach provides high yields, atom-/step economy, reduced reaction time, is eco-friendly, and acts as an amenable tool for the generation of a library of new chemical entities (NCEs), especially in the drug discovery process. Extensive research has led to copious developments in the field of MCRs. The developments have emerged with different synthetic approaches. [1-3].

Nowadays, magnetic nanoparticles (MNPs) as efficient supports for catalysts are a class of nanoparticles that can be administered using magnetic fields [4]. MNPs are easily dispersed in the reaction vessel in the absence of a magnetic field and providing a large surface area. After completing the reactions, the MNPs catalysts can be isolated efficiently from the product by magnetic separation, without catalyst filtration and centrifugation.

There are many heterocyclic ring structures, which have been designed in such a way that their binding efficiency with the receptor increases after structural modifications. This medicinal chemistry is a boon to the researchers and provides long-term advancement in the medical field. One of the motif is triazoles, which have been explored widely and still its scope is inevitable. Triazoles are heterocyclic organic compounds containing five-membered ring with three nitrogen and two carbon atoms. Two isomeric forms of triazoles are existed namely 1,2,3-triazole and 1,2,4-triazole.These motifs are effective amide surrogates in bioactive molecules because of their strong dipole moments. Triazoles can also be used as a linker and show bioisosteric effects on peptide linkage, aromatic ring, double bonds and an

imidazole ring. Some unique features like hydrogen bond formation, dipole-dipole and π stacking interactions of triazole compounds have increased their importance in the field of medicinal chemistry as they bind with the biological target with high affinity due to their improved solubility. In general, the molecular specifications of the 1,4-disubstituted 1,2,3-triazoles are somewhat similar to amide bonds in terms of distance and planarity clearly shown in[5].1,2,3-Triazoles have received considerable interest because of their useful applications as pharmaceutical agents, agrochemicals, dyes, corrosion inhibitors, photostabilizers and photographic materials[6, 7].

Herein, we report our results for a one-pot and green synthesis of 1,4-Disubstituted 1,2,3-Triazoles derivatives using Fe_3O_4@SiO_2@Pr-AIPA-Cu as a highly efficient magnetic nanocatalyst on water under room temperature.



Scheme 1. One-Pot Synthesis of 1,4-Disubstituted 1,2,3-Triazoles from benzyl halide, Sodium Azide, and Alkynes catalyzed by Fe_3O_4@SiO_2@Pr-AIPA-Cu**.**

2. Experimental Section

2.1. General

Reagents and Apparatus

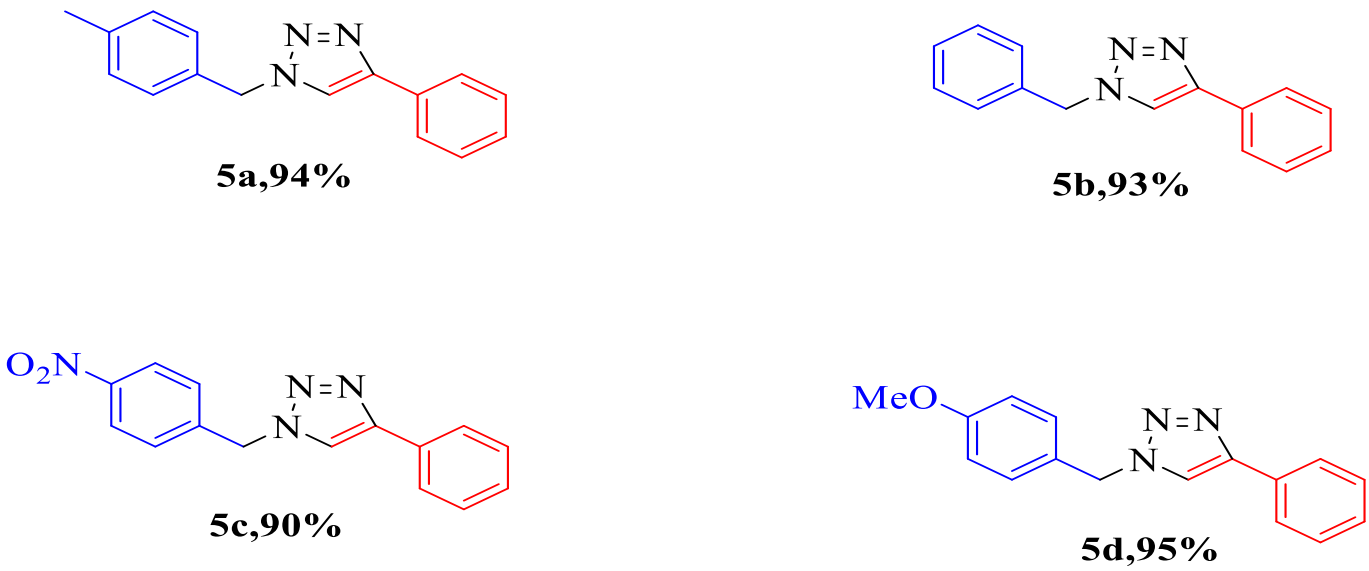
All chemical reagents were purchased from international chemical companies including Merck and Sigma-Aldrich. To determine the completion of the reaction, analytical thin-layer chromatography (TLC) was performed on pre-coated silica-gel plates (Merck Silica Gel F254). Product stains were detected either under UV light or by placing in an iodine chamber. Also, melting points were determined in open capillaries using an Electrothermal 9100 apparatus.

2.2. General procedure for the synthesis of 1,4-Disubstituted 1,2,3-Triazoles **(5a–d)** catalyzed by Fe_3O_4@SiO_2@Pr-AIPA-Cu**.**

A mixture of the alkyne (0.5 mmol), benzyl halide (0.52 mmol) and sodium azide (0.55 mmol) was successively added to Fe_3O_4@SiO_2@Pr-AIPA-Cu (0.01 mmol) in 2 mL water and heated at room temperature**.** Reaction completion was monitored by TLC. After the extraction of the organic layer with ethyl acetate (2 × 10 mL), the residue water was removed by CaCl2. The ethyl acetate was eliminated under vacuum to obtain the corresponding product. The recovered catalyst washed with ether and ethyl acetate, dried and then utilized for the next run.

3. Results and Discussion

The catalytic activity of by Fe_3O_4@SiO_2@Pr-AIPA-Cu was evaluated in the green synthesis of 1,4-Disubstituted 1,2,3-Triazolesfrom derivatives by condensing is benzyl halide, Sodium Azide, and Alkynes derivatives in water under room temperature. According to **Scheme 2**, using 10 mg of by Fe_3O_4@SiO_2@Pr-AIPA-Cu as nanocatalyst, the desired products were synthesized with high yield and in short times. Another advantage of this nanocatalyst is the ability to magnetically separate and recycle the nanocatalyst for at least five runs from the product mixture with minimal effort.



Scheme 2. Scheme 1. One-Pot Synthesis of 1,4-Disubstituted 1,2,3-Triazoles**(5a–d)** from benzyl halide, Sodium Azide, and Alkynes catalyzed by Fe_3O_4@SiO_2@Pr-AIPA-Cu**.**

4.Conclusion

In this research Cu(II) complex supported on Fe_3O_4@SiO_2@Pr-AIPA core–shell magnetic nanoparticles core–shell magnetic nanoparticles (MNPs) was prepared and applied for synthesis of 1,2,3-Triazole by click reaction. This compounds are one of the most important classes of N-heterocyclic compounds, have applications in pharmaceutical chemistry. Fe_3O_4@SiO_2@Pr-AIPA-Cu MNPs efficiently catalyzed a click reaction between alkyl halides, alkynes, and sodium azide to synthesize corresponding products in high to excellent yields. Among heterogeneous catalysts, MNPs have seen much attention due to high surface-to-volume ratio and their easy separation. The catalyst was recovered using an external magnetic field, and recycled for subsequent reactions without substantial loss of efficiency. The catalyst was recovered using an external magnetic field, and recycled for subsequent reactions without substantial loss of efficiency.

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