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Proceeding Paper

Efficient Synthesis of Multi-Component Spirooxindoles Using Fe3O4@SiO2@Pr-Tris(aminomethyl)amine: as Green Organocatalyst Reusable in Aqueous Environment †

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Abstract: Green chemistry as a powerful tool plays momentous role in various research fields such as synthetic organic, biomedical, industrial chemistry, In summary,an efficacious method is described for the synthesis of Spirooxindole derivatives using Fe_3O_4@SiO_2@Pr-Tris(aminomethyl)amine a green catalyst. This is a one-pot three-component condensation in water as a clean and environmentally favorable media. The present procedure proposes various remarkable privileges such as mild reaction conditions, simple work-up procedure and environment friendly. Moreover, the catalyst used is easily recovered by the external magnetic field and reused without significant deterioration in catalytic activity after at least five times.

Keywords: Spirooxindoles; magnetic nanocomposite; water; reusable catalyst; green chemistry

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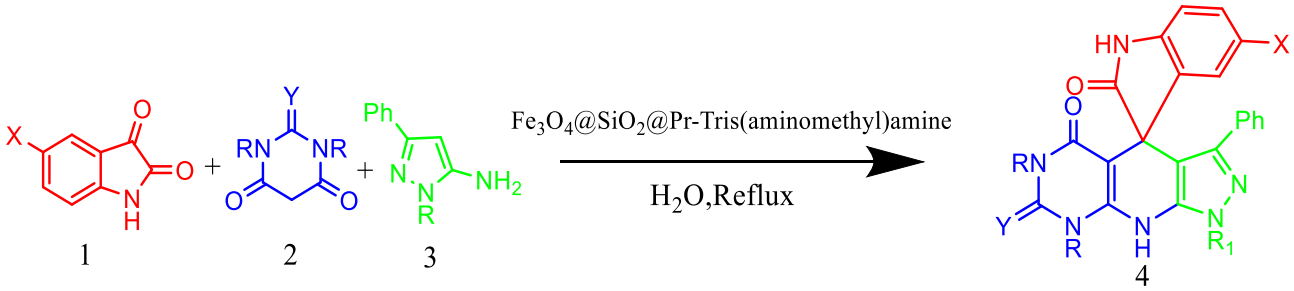
1. Introduction

Green chemistry is the design of chemical products and processes that minimize or eliminate the use of hazardous reagents or solvents and offers valuable synthesis of expected products in an economical manner. With the successful synthesis of green nanoparticles (NPs), recently numerous methodologies have been designed to synthesize metal NPs employing biological methods where enzymes, microorganisms, and plant extractsplay an important role in the formation of NPs. Among the biological methods, using plants for NP synthesis is safe, inexpensive, and the best eco-friendly alternative to more complex chemical and physical synthetic procedures, so can be used as an economic and suitable substitute for the large scale production of metal NPs [1].

Spirooxindoles, pyrimidines, and pyrazoles are very important classes of heterocyclic compounds. Spiroindoles are attractive targets in organic synthesis because of their highly evident pharmacological properties and biological activities, as well as wide-ranging utility as synthetic intermediates for alkaloids, drug candidates, and clinical pharmaceuticals. Pyrimidines represent a class of heterocyclic compounds of great importance in biological and pharmaceutical purposes such as antitumor, antibacterial, antifungal, antimalarial, and anti-inflammatory properties. The chemistry of pyrazole derivatives has been the subject of medical research because of their remarkable biological and pharmacological properties such as antitumor, antimicrobial, anti-inflammatory, antibacterial, antifungal, anticancer activities, and also as an analgesic agents. Thus, a hybrid of these three motifs could potentially lead to a series of structurally and biologically interesting compounds [2].

Herein, we report our results for a one-pot and green synthesis of spirooxindole derivatives derivatives using Fe_3O_4@SiO_2@Pr-Tris(aminomethyl)amine as a highly efficient magnetic nanocatalyst on water under reflux.



Scheme 1. Preparation of spirooxindole derivatives in the presence of Fe_3O_4@SiO_2@Pr-Tris(aminomethyl)amine.

2. Experimental Section

2.1. General

Reagents and Apparatus

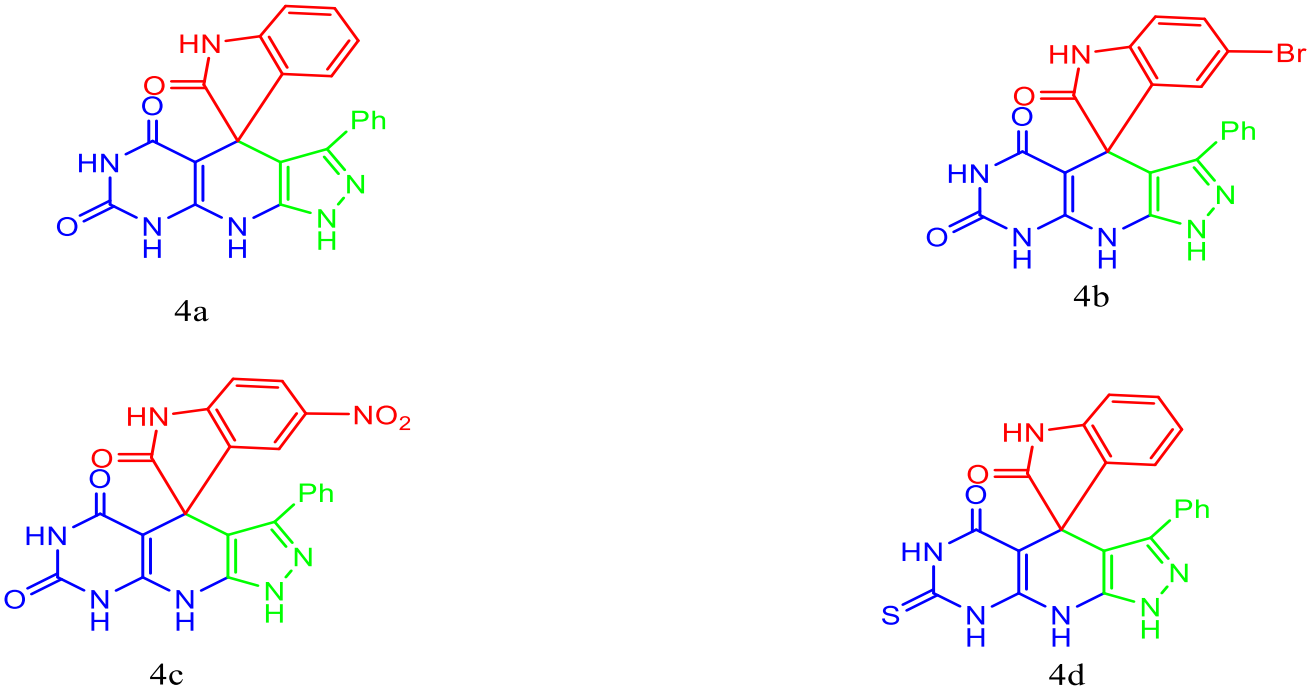
All chemical reagents were purchased from international chemical companies including Merck and Sigma-Aldrich. To determine the completion of the reaction, analytical thin-layer chromatography (TLC) was performed on pre-coated silica-gel plates (Merck Silica Gel F254). Product stains were detected either 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. Typical Procedure for the Preparation of 3′-phenyl-spiro[indoline-3,4′-pyrazolo [4′,3′:5,6]pyrido[2,3-d]pyrimidine]-2,5′,7′(6′H,8′H,9′H)-trione Catalyzed by Fe_3O_4@SiO_2@Pr-Tris(aminomethyl)amine NPs (4a-d)

A mixture of 1,3-diphenyl-1*H*-pyrazol-5-amine (0.24 g, 1 mmol), barbituric acid (0.13 g, 1 mmol), isatine (0.15 g, 1 mmol), and Fe_3O_4@SiO_2@Pr-Tris(aminomethyl)amine as a catalyst (10 mg) under refluxing water (5 mL) was stirred (the progress of the reaction was monitored by TLC). After the completion of the reaction (TLC), the solution was cooled to room temperature, the precipitated product was filtered and washed with water (10 mL) and ethanol (5 mL), and finally dried to afford the crude product. The crude precipitate was dissolved in DMF and again filtered for catalyst separation. Finally, water was added into the solution and the product was extracted and recrystallized by EtOH to afford the pure product as white powder.

3. Results and Discussion

Finally, to further explore the potential of this novel catalyst for spiroheterocyclic synthesis, this methodology was evaluated using different isatins, barbituric acids, and 1*H*-pyrazol-5-amines under these appropriate reaction conditions (5 mL of water, reflux, 10 mg catalyst). The results are summarized in Scheme 2. As can be seen, the corresponding spirooxindole derivatives were synthesized by the one-pot, three-component condensation in high to excellent yields in the presence of Fe_3O_4@SiO_2@Pr-Tris(aminomethyl)amine as a powerful and reusable catalyst.



Scheme 2. Synthesis of spiro[indoline-pyrazolo[4′,3′:5,6]pyrido[2,3-d]pyrimidine]trione derivatives.

4. Conclusions

Green chemistry as a powerful tool plays momentous role in various research fields such as synthetic organic, biomedical, industrial chemistry, In summary,an efficacious method is described for the synthesis of Spirooxindole derivatives using Fe_3O_4@SiO_2@Pr-Tris(aminomethyl)amine a green catalyst. This is a one-pot three-component condensation in water as a clean and environmentally favorable media. The present procedure proposes various remarkable privileges such as mild reaction conditions, simple work-up procedure and environment friendly. Moreover, the catalyst used is easily recovered by the external magnetic field and reused without significant deterioration in catalytic activity after at least five times.

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