Para-Aminobenzoic acid-functionalized silica-coated Fe_3O_4 nanoparticles: a highly efficient supported organocatalyst for on-water synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones

Hamidreza FaniMoghadam, Mohammad G. Dekamin*

Pharmaceutical and Heterocyclic Compounds Research Laboratory, Department of Chemistry, Iran University of Science and Technology, Tehran, 16846-13114, Iran.

** Corresponding author E-mail: mdekamin@iust.ac.ir ;Tel: +98-21-77240640-50; fax: +98-21-73021584*

Abstract

New *para*-aminobenzoic acid (PABA) grafted on silica-coated Fe_3O_4 nanoparticles (Fe_3O_4@SiO_2@Pr-PABA) were prepared. The efficiency of the new Fe_3O_4@SiO_2@Pr-PABA nanoparticles, as a heterogenous nanocatalyst, was examined in the synthesis of biologically-active 2,3-disubstituted-2,3-dihydroquinazolin-4(1*H*)-one derivatives *via* one-pot three-component condensation of isatoic anhydride, aromatic aldehydes and aromatic amine on water under reflux conditions. The advantages of this green protocol are low catalyst loading, high to quantitative yields of the favorable products, short reaction times and easy separation and recycle of catalyst.

Keywords: Para-Aminobenzoic acid-functionalized silica-coated Fe_3O_4 nanoparticles; Supported organocatalyst; On-Water synthesis; 2,3-Dihydroquinazolin-4(1H)-ones.

1. Introduction

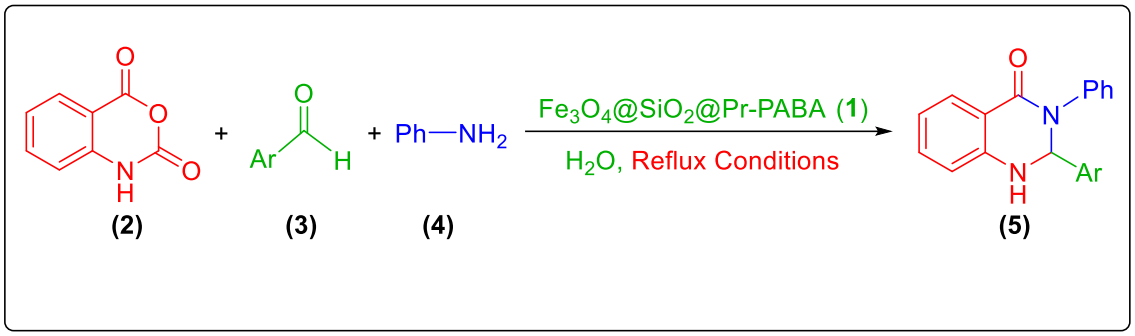
Multicomponent reactions are well-established as a powerful tool for the rapid construction of complex and structurally diverse compounds from relatively simple building blocks [1]. High atom-economy, chemical efficiency and convergence are typical features of such one-pot condensations of at least three different starting materials [2].

Heterocyclic compounds are worldwide in all facets of modern chemistry such as synthetic materials, organic, bioorganic, bioinorganic, catalysis, medicinal and

pharmaceutical sciences [3]. Derivatives of 2,3-dihydroquinazolin-4(1*H*)-one as an important category of heterocyclic compounds, have stimulated interest in medicinal chemistry [4]. Due to important properties of 2,3-dihydroquinazolin-4(1*H*)-ones and their diverse biological activities, different methods and catalysts have been developed for the synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones in recent years [5].

Nowadays, magnetic nanoparticles (MNPs) as efficient supports for catalysts are a class of nanoparticles that can be administered using magnetic fields [6]. MNPs are easily dispersed in the reaction vessel in the absence of a magnetic field and providing a large surface area [7]. After completing the reactions, the MNPs catalysts can be isolated efficiently from the product by magnetic separation, without catalyst filtration and centrifugation [8-10].

Herein, we report our results for a one-pot and green synthesis of 2,3-dihydroquinazolin-4(1*H*)-one derivatives using Fe_3O_4@SiO_2@Pr-PABA (**1**) as a highly efficient magnetic nanocatalyst on water under reflux conditions.



Scheme 1. Synthesis of 2,3-dihydroquinazolin-4(1*H*)-one derivatives catalyzed by Fe_3O_4@SiO_2@Pr-PABA (**1**).

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

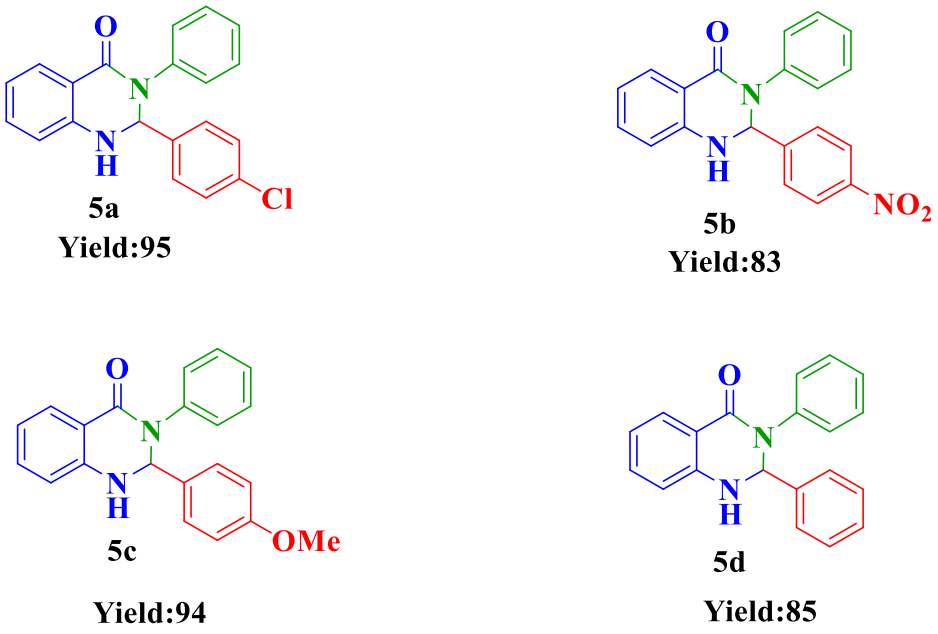
light or by placing in an iodine chamber. Also, melting points were determined in open capillaries using an Electrothermal 9100 apparatus.

*2.2. General procedure for the synthesis of 2,3-disubstituted-2,3-dihydroquinazolin-4(1H)-ones (**5a-d**) catalyzed by Fe_3O_4@SiO_2@Pr-PABA (**1**)*

A mixture of isatoic anhydride (**2,** 1.0 mmol), amine (**4**, 1.0 mmol), aromatic aldehyde (**3**, 1.0 mmol) and Fe_3O_4@SiO_2@Pr-PABA (**1**, 10 mg) was heated in 3 ml of water at 100 °C for an appropriate time as mentioned in Table 2. After completion of the reaction, as monitored by TLC [eluent: *n*-hexane: EtOAc: 3:1], the catalyst was separated using an external magnet and the residue was concentrated to result in the crude product. Finally, the crude product was recrystallized from EtOH to obtain the pure product.

3. Results and Discussion

The catalytic activity of Fe_3O_4@SiO_2@Pr-PABA (**1**) was evaluated in the green synthesis of 2,3-dihydroquinazolin-4(1*H*)-one derivatives by condensing isatoic anhydride, amine and aryl aldehyde derivatives in water under reflux conditions. According to Scheme 2, using 10 mg of Fe_3O_4@SiO_2@Pr-PABA (**1**) 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. Scope of 2,3-dihydroquinazolin-4(1*H*)-one derivatives (**5a**–**d**) synthesis catalyzed by Fe_3O_4@SiO_2@Pr-PABA (**1**).

Conclusion

In summary, *p*ara-aminobenzoic acid supported on silica-coated Fe_3O_4 nanoparticles (Fe_3O_4@SiO_2@Pr-PABA) was found to be an efficient magnetic heterogeneous nanocatalyst for the synthesis of medicinally important 2,3-dihydroquinazolin-4(1*H*)-one derivatives. The one-pot three-component condensation of isatoic anhydride, aromatic aldehydes and aromatic amine in aqueous media under refluxing conditions. Furthermore, this protocol benefits from avoiding the use of green nature of the solvent, mild conditions, operational simplicity, low catalyst loading and high yield of products with short reaction time.

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