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Application of Ytterium Iron Garnet as a Powerful and Recyclable Nanocatalyst for the One-pot Synthesis of Octahydroquinazoline Derivatives under Solvent-free Conditions

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For the first time, we report the application of super paramagnetic nanoparticles of ytterium iron garnet (YIG) as a new recyclable and highly efficient heterogeneous magnetic catalyst for the one-pot synthesis of octahydroquinazoline derivatives *via* Bijinelly cyclcondensation reaction under solvent free conditions. Our method shows advantages such as lack of organic solvents, high yields of products, recyclability and operational simplicity.

Keywords: Nanoparticle, Vtterium iron garnet, Octahydroquinazoline, Bijinelly, Sol-gel

INTRODUCTION

Multi-component reactions (MCRs) are masterpieces of synthetic efficiency and reaction design and are of increasing importance in various research fields such as combinatorial chemistry, drug discovery programs, natural product synthesis, polymer chemistry and medicinal chemistry due to their high atom economy, bond forming efficiency low environmental impact, ease of execution and broad spectrum of applications [1-4]. Octahydroquinazoline derivatives are considered as an important class of azaheterocycles. The growing interest for their synthesis is mainly due to their broad spectrum of therapeutic and pharmacological properties such as anticancer, antidepressant, antiproliferative activity, anticonvulsant and anti-inflammatory [5-7]. Search for more potent and effective methodology has led to various reaction conditions in which numerous catalysts such as bronsted and lewis acids, heterogeneouscatalysts, biocatalysts and organo-catalysts have been used [8-10].

The traditional protocol for the preparation of octahydroquinazoline compounds was reported by bijinelly (1893), which involves the one-pot condensation of a ketoester, anaromatic aldehyde and urea under strong acidic conditions which often suffer from low yields. Interest in Bijinelly compounds due to their biological and pharmacological activities received much attention and as a result variation in the original three components and catalysts of the cyclocondensation reaction have been widely extended [11-13].

Recently significant attention has been paid to the use of nanocatalyst in the synthesis of organic compounds specially use of magnetic nano particles(MNPs) which has led to rapid removal, easy separation and facile reuse of the catalyst. Super paramagnetic nano particles of iron oxide are among the most promising MNPs due to their simple synthesis, ready availability, low cost and high surface activity.

Thus, we report here, for the first time, the application of ytterium iron garnet supermagnetic {$Y_3Fe_5O_{12}$ (YIG)} [14,15] as a novel, efficient and reusable catalyst for multicomponent synthesis of octahydroquinazolines *via* bijinelly cyclocondensation reaction under solvent-free conditions (Scheme 1).

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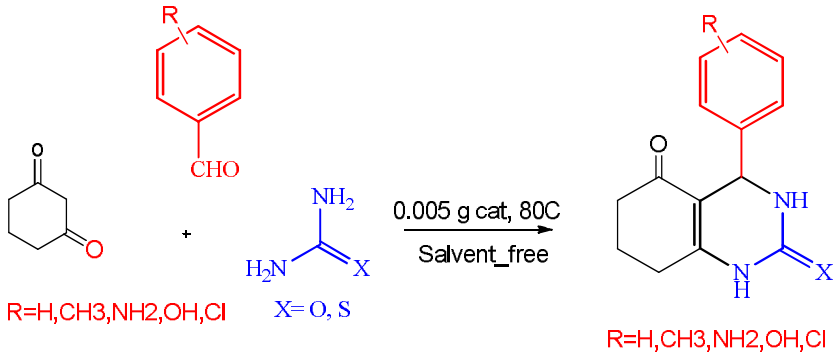


Scheme 1. One-pot preparation of Octahydroquinazoline derivatives

EXPERIMENTAL

General

All commercially available chemicals were purchased from Fluka and Merck companies and used without further purification. Ytterium iron garnet was prepared according to literature [14,15] with miner modification. IR spectra were recorded on a PEPKIN ELMER LXI85256 and Far-FTIR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded in DMSO-d6 on a Bruker Advanced DPX 400 MHz spectrometer using TMS as internal standard. Reaction monitoring was accomplished by TLC on silica gel polygram SILG/UV 254 plates. The prepared Garnet was identified with several analysis and compared with those reported. These SEM analyses were carried out using a LEO 1455VP Scanning Electron Microscope, operating at 1-30 KV, transmission electron microscopy (TEM) and thermogravimetric analysis (TGA).

Preparation of Nano Garnet

Compounds of composition $Y_3Fe_5O_{12}$ were prepared according to literature [14,15] by a sol-gel method. Weighed amounts of $Y(NO_3)_3.6H_2O$ (1.557 g) and $Fe(NO_3)_3.9H_2O$ (2.737 g) were first dissolved in Deionized water and the mixture was stirred at room temperature. To this solution, Citric acid (6.833 g) was added and the mixture was refluxed at 80 °C for 60 min to allow gel formation and then dried at 115 °C for 24 h. The dried powder was ground and annealed at temperature 1000 °C for 4 h. The composition of sample was identified by X-Ray diffraction with CuK radiation (Fig. 1).

Typical Procedure for the Preparation of 4-Sihydropyrimidin-2(1H)-ones

A mixture of dimedon (2 mmol), urea/thiourea (3 mmol), aromatic aldehyde (1 mmol), and $Y_3Fe_5O_{12}$ (0.005 g) was heated at 80 °C. Completion of the reaction was indicated by TLC [TLC acetone/n-hexane (1:3)]. After completion of the reaction the catalyst was easily removed from the product by use of an external magnet. The removed catalyst was washed with ethanol to remove residual product and dried under vacuum. Product was isolated from reaction medium by decantation without using organic solvents (Fig. 2). The crude product was purified by recrystallization in ethanol to afford the pure product.

RESULTS AND DISCUSSION

$Y_3Fe_5O_{12}$ (YIG) is an example of ferrimagnetic ceramic which is used in passive microwave devices. It belongs to a group of magnetic oxides characterized by specific magnetic and magneto-optical properties. It contains Fe^{3+} and Y^{3+} ions which are distributed between different sites of the compound [16]. The nano (YIG) was prepared according to the reported procedure [17] with minor modification. The surface-to-volume ratios of nanoparticles are very large and crucial in their catalytic effect in organic synthesis, therefore increasing proportion of this ratio with decreasing particle size makes the nanoparticles highly reactive catalyst. Because of small size of the prepared nano YIG (about 40-50 nm, see the supporting materials) and therefore its high surface area and expectation for the exposed active sites and contact areas with reactants and also regular distribution of Fe^{3+} and Y^{3+} on its surface, we

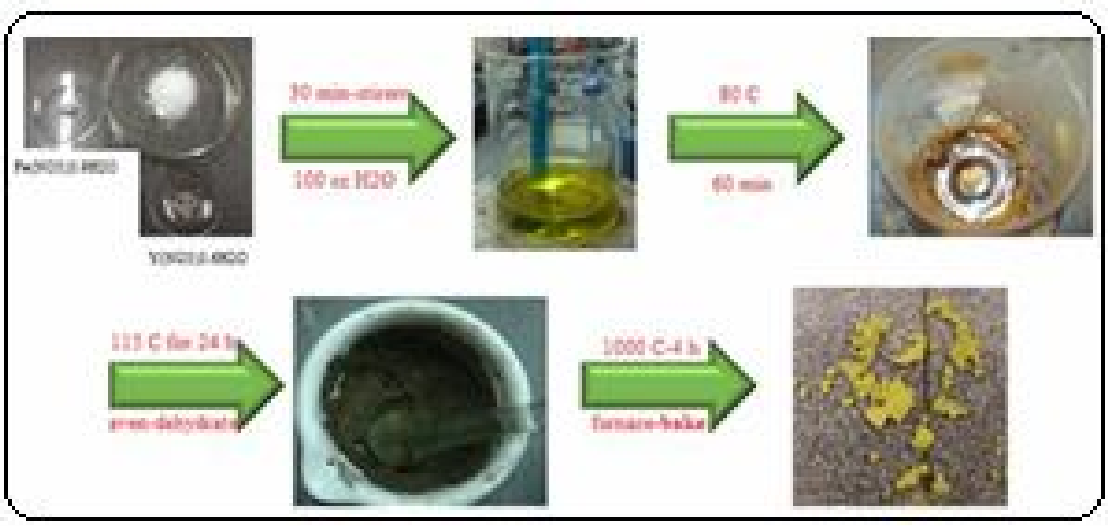


Fig. 1. Yttrium iron garnets $Y_3Fe_5O_{12}$.

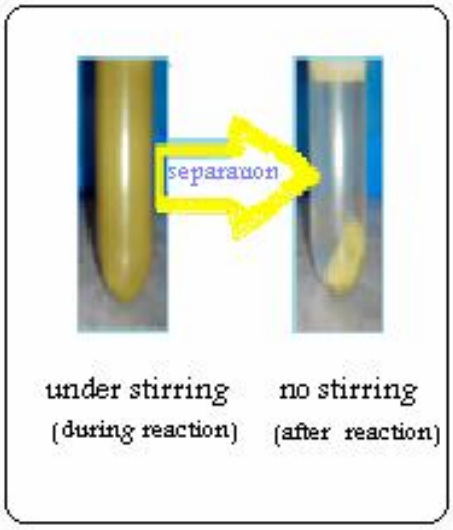
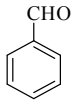
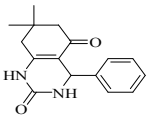
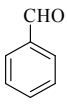
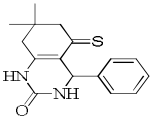
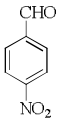
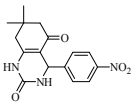
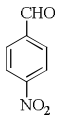
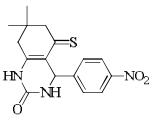
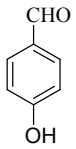
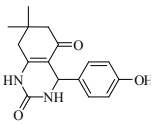
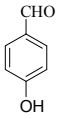
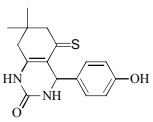
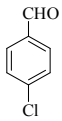
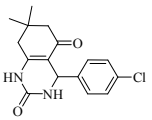
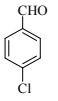
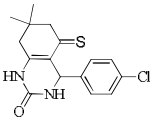
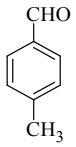
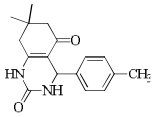
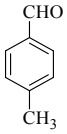
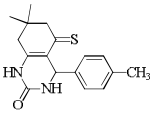
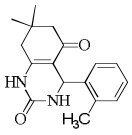
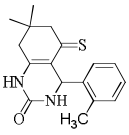
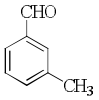
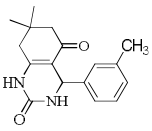
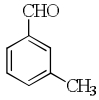
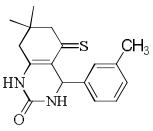


Fig. 2. Product isolation without using organic solvents.

decided to examine its catalytic activity in a few multicomponent reactions.

We investigated the use of YIG as a catalyst for the synthesis of polyhydroquinolines, pyranopyrazoles, 2-amino-4H-chromenes and octahydroquinazoline derivatives under different reaction conditions with and without a solvent and found out that YIG is the most promising and potent catalyst for the one-pot synthesis of octahydroquinazolines in good to high yields in solid state or solvent-free conditions. Thus, the three-component cyclocondensation reaction was conducted via reaction of different aromatic aldehydes bearing electron releasing or electron withdrawing substituents, a diketone and urea in the presence of catalytic amount of YIG under solvent-free conditions (Scheme 1).

Table 1. The One-pot Three-component Condensation Reaction of Aromatic Aldehydes (1 mmol), Dimedon (2 mmol) and Urea /Thiourea (3 mmol) Promoted by Nano Garnet (0.005 g) under Solvent-free Conditions at 80 °C

Entry	Aldehyds	Urea/ thiourea	Product	Time (min)	R%	Entry	Aldehyds	Urea/ thiourea	Product	Time (min)	R%
1		Urea		15	94	11		thiourea		15	94
2		Urea		15	90	12		thiourea		15	90
3		Urea		15	89	31		thiourea		15	89
4		urea		15	91	14		thiourea		15	91
5		urea		15	88	15		thiourea		15	88
6		urea		20	80	61		thiourea		20	84
7		urea		15	88	17		thiourea		15	90

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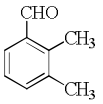
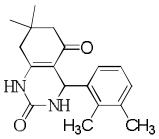
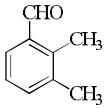
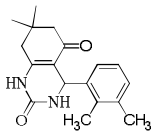
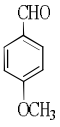
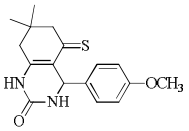
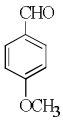
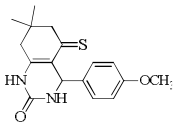
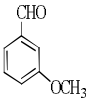
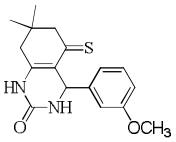
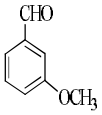
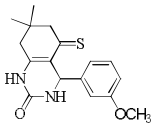
8		urea		20	78	18		thiourea		20	75
9		urea		15	91	19		thiourea		15	90
10		urea		15	88	20		thiourea		15	91

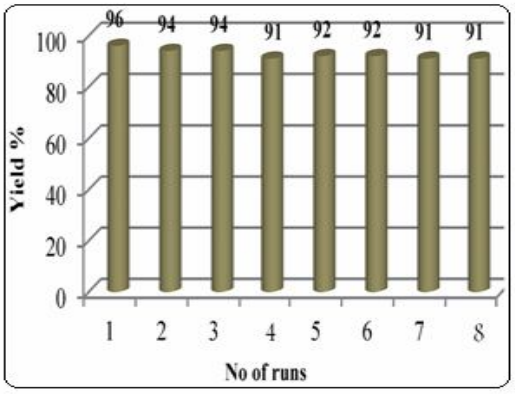


Fig. 3. Reusability of YIG in synthesis of octahydroquinazoline derivatives under solvent free conditions.

The results are summarized in Table 1.

All products were identified by comparison of their melting points, FT-IR, ^{1}H NMR and ^{13}C NMR with the data reported for the same compounds in literature. The solid catalyst could be recovered and reused conveniently for several times with satisfactory yields. Thus, to investigate the retention of the activity of the catalyst, the catalyst was reused seven times in the one-pot multi-component synthesis of octahydroquinazoline derivatives after the completion of each reaction (Fig. 3). The catalyst could be easily recovered by magnetic separation and washed with ethanol, dried and reused. Reusability Of YIG in synthesis of octahydroquinazoline derivatives under solvent free conditions.

CONCLUSIONS

We have developed a simple, clean, efficient and environmentally friendly approach for the one-pot synthesis of octahydroquinazolin derivatives using super-paramagnetic nanoparticle of yttrium iron garnet as a recyclable catalyst under solvent-free conditions. This

procedure offers several advantages, including high yield, short reaction time, simple work-up procedure, and ease of separation of catalyst by an external magnet. The time taken for complete conversion (monitored by TLC) and the isolated yields are recorded in Table 1.

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