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Methyl Methacrylate Grafted to Chitosan as a Biopolymeric Nanocatalyst for the One-Pot Three-Component Synthesis of Imidazole derivatives

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Abstract: In recent years, various research has been accomplished on the catalytic applications of chitosan and its derivatives. In this research, methyl methacrylate grafted to chitosan (Cs-PMMA) was employed, as a new biopolymeric nanocatalyst, for the synthesis of imidazole derivatives through multi-component reaction (MCR) strategy. Characterization of the obtained nanomaterial has been done via different spectroscopic, microscopic, and analytical methods such as Fourier transform infrared (FTIR), X-ray diffraction analysis (XRD) and field emission scanning electron microscopy (FESEM). This nanocatalyst showed high yields of the products and short reaction times. The Cs-PMMA heterogeneous catalyst illustrated magnificent reusability and can be used at least six times without significant loss of its activity.

Keywords: Green Chemistry; Heterogeneous catalyst; Nanocatalyst; MCRs; Chitosan; Imidazole derivatives.

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1. Introduction

Multicomponent reactions (MCRs) are efficient chemical processes that involve combining three or more reactants in a single step, resulting in complex and functional end products. MCRs are advantageous due to their ability to create diverse and complicated structures, produce high yields, demonstrate efficient atom economy, and minimize reaction time [1]. In recent years, one-pot MCRs, which are categorized in the first branch of green chemistry principles (*viz.,* preventing waste), have been recognized as a superior synthetic procedure for the construction of various and numerous complex molecules [2]. Typically, a MCR employs a minimum of three reactants (or three reaction centers), and most of the contents from the starting materials are incorporated into product structures demonstrating simplicity, efficiency, selectivity, convergence, atom economy, and also cost- and time-effectiveness [3]. After Strecker's reaction in 1850 [4], which is the first authoritative article in the field of synthesis of organic compounds by a one-pot multi-component method, and up to now, numerous MCRs have been described for the synthesis of heterocyclic compounds. It is worthy of note that in recent decades, some heterocyclic-containing drugs, natural products, and other attractive and useful materials have been prepared using MCRs. To date, catalyst research has been primarily focused on enhancing catalyst activity and efficient recovery [5-7]. The aim of this study is to develop a nanomaterial using chitosan, a non-toxic biopolymer that can be degraded by bacteria or other organisms, thus preventing environmental pollution. Chitosan (CS) is readily available and has antimicrobial properties, so it is of significant interest in medicinal chemistry and biotechnology [7-10]. Given the numerous amino and hydroxyl functional groups on its surface, this widely used biopolymer can serve on its own or modified forms, as heterogeneous catalytic systems, in a variety of organic reactions [11,12]. As part of our ongoing research on various biopolymeric and other nanoscale catalysts in different MCRs [10-15]. We wish herein to report on a new chitosan-based nanomaterial for one-pot synthesis of imidazole derivatives. Chitosan was grafted using methyl metaacrylic acid (MMA) to produce the CS-PMMA nanomaterial. The CS-PMMA nanomaterial was characterized using traditional methods such as Fourier transform infrared (FTIR) spectroscopy, field emission scanning electron microscopy (FESEM), simultaneous thermogravimetric analysis (STA), and X-ray diffraction analysis (XRD).

2. Experimental

2.1 Materials

Chitosan (MW = 100000-300000 Da) was purchased from Across Organics. Methyl Methacrylate (MW = 100.12 g.mol-1, d = 0.943 g.cm^{-3}), benzil, ammonium acetate, different aromatic aldehydes were purchased from prominent international chemical companies including SIGMA-Aldrich & Merck.

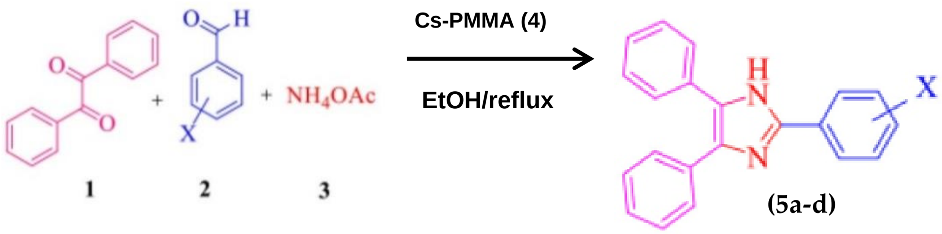
2.1.1 General Procedure for the Preparation of Methyl Methacrylate Grafted to Chitosan (Cs-PMMA, **4**)

The Cs-PMMA was prepared according to our previous work with slight modifications by using chitosan instead of Arabic gum [12].

2-(4-Chlorophenyl)-4,5-diphenyl-4,5-dihydro-1*H*-imidazole (**5b**). M.P = 264 -266 ^{o}C; ^{1}H NMR (500 MHz, DMSO-d_6): 12.73 (s, 1H), 8.11 (d, *J* = 8.4 Hz, 2H), 7.52 (d, *J* = 8.4 Hz, 2H), 7.50 (t, *J* = 6.7 Hz, 4H), 7.42 (d of d, *J* = 7.3 Hz, 4H), 7.36 (t, *J* = 7.8 Hz, 2H); FTIR (KBr, cm^{-1}): 3423.37, 3061.45, 1605.32, 1444.81 [10, 12, 13].

2.1.2 General Procedure for the Synthesis of Imidazole Derivatives **5a-d**

In a 50-ml round-bottom flask, aromatic aldehydes (**1**, 1.0 mmol), benzil (**2**, 1.0 mmol), ammonium acetate (**3**, 2.5 mmol), and 10 mg of CS-PMMA (**4**) were added to 3 ml of EtOH, and then the mixture was refluxed. The reaction progress was monitored *via* thin-layer chromatography, and after completion of the reaction, the crude product was purified by crystallization in EtOH. Also, the separated CS-PMMA catalyst was dried and used for the next runs. The general scheme of the multicomponent reaction for the synthesis of imidazole derivatives is shown in **Scheme 1**.



Scheme 1. Synthesis of imidazole derivatives via one-pot three component condensation of benzil (**1**) aromatic aldehydes (**2**), ammonium acetate (**3**) in the presence of CS-PMMA catalyst (**4**).

3. Results and Discussion

3. 1 *Characterization*

In this part of our investigation, various spectrometric and microscopic analyzes including FTIR and FESEM were carried out to characterize the catalyst. First, a band appeared at 1732 cm^{-1}, 1650 cm^{-1} and 1082 cm^{-1} in the FTIR analysis, indicating the ester, amide, and alcohol groups, respectively. The broad band at 3450 cm^{-1} represent the primary amine and alcoholic functional groups participating in hydrogen bonding (**Figure 1**).

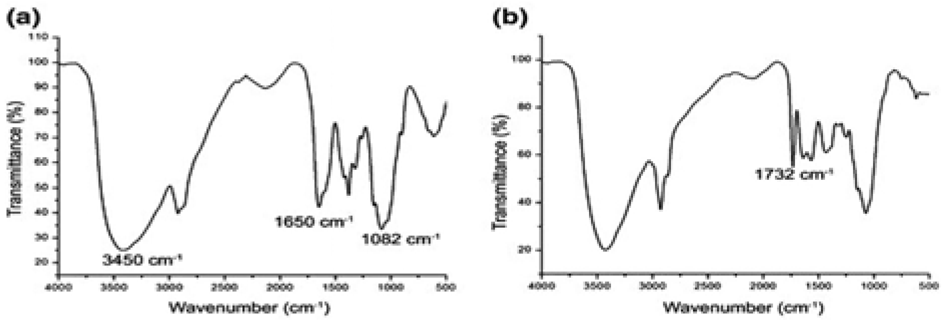


Figure 1. FTIR spectra of chitosan (a) and chitosan-g-PMMA (b).

FESEM analysis is one of the most commonly utilized techniques for determination of morphology, composition, and structure of surfaces of nanomaterials. Spherical nanoparticles having almost same diameter were observed (**Figure 2**).

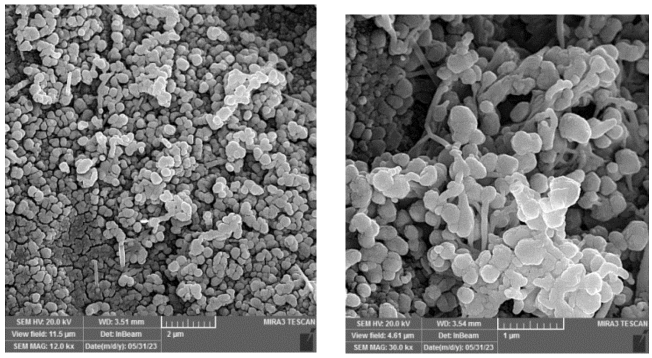
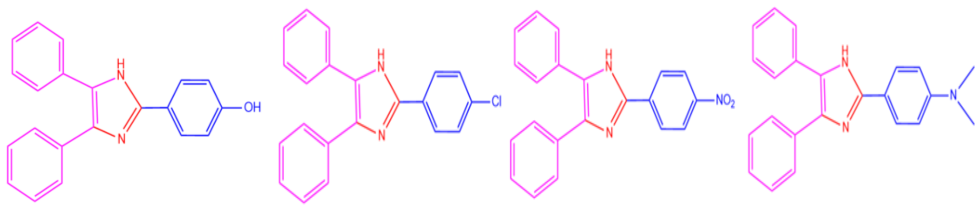


Figure 2. FESEM images of the CS-PMMA catalyst.

As data provided in Scheme 2 show, by using a small quantity of the CS-PMMA (4, 10 mg), the desired products were synthesized with high efficiency and in a short time period. Another advantage of this organocatalyst is the possibility of easy separation and recycling from the reaction mixture with minimal effort. This catalyst was reused in at least five experiments without a significant loss in its catalytic activity.



5a	5b	5c	5d
Yield : 91%	Yield : 97%	Yield : 93%	Yield : 90%

Scheme 2. Scope of imidazole derivatives (5a-d) synthesis catalyzed by CS-PMMA (4).

4. Conclusion

In summary, the low-cost, environmentally friendly catalyst, which is easily prepared, has advantages such as easy separation, good recycling, and remaining of the catalytic activity for up to five cycles. The new CS-PMMA catalyst was utilized in the multicomponent reaction for the synthesis of imidazole derivatives. Also, it was found that EtOH is the best solvent for synthesizing of imidazole derivatives under reflux conditions.

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