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Multifunctional nanocatalytic system of 1,3,5-tris(2-hydroxyethyl) isocyanurate attached to chitosan by using EDTA for the synthesis of 4*H*-pyran derivatives †

Pooya Emami [1], Mohammad G. Dekamin [1,*], Mohammad Pazouki [2] and Mohammad Dohendou [1]

[1] Pharmaceutical and Heterocyclic Compounds Research Laboratory, Department of Chemistry, Iran University of Science and Technology, Tehran, Iran; pooya.emami76@gmail.com; mohammad.dohendou@gmail.com
[2] Energy Research Department of Materials and Energy Research Center; m.pazouki@merc.ac.ir
* Correspondence: mdekamin@iust.ac.ir; Iran University of Science and Technology, Tehran 16846-13114, Iran
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Abstract: The aim of this research was simple preparation of grafted 1,3,5-tris(2-hydroxyethyl isocyanurate) to the chitosan surface by using EDTA linker (CS-EDTA-THEIC) through a green and inexpensive procedure. The obtained nanomaterial was characterized via different spectroscopic, microscopic and analytical methods. Various techniques and methods namely Fourier transform infrared (FTIR), field emission scanning electron microscopy (FESEM), simultaneous thermogravimetric analysis (STA), and X-ray diffraction analysis (XRD) were utilized to identify the nanomaterial. This bio-based CS-EDTA-THEIC network contains appropriate basic and acidic active sites to act as a multifunctional catalyst. Finally, the CS-EDTA-THEIC nanomaterial was used in the multicomponent reaction for synthesis of *4H*-pyrans and showed excellent yields in short reaction times. Furthermore, the CS-EDTA-THEIC network, as a heterogeneous catalyst, illustrated magnificent reusability and can be used at least five times without significant loss of its activity.

Keywords: bio-derived materials; modified chitosan; MCRs; heterogeneous catalyst; green chemistry

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1. Introduction

Nowadays, multicomponent reactions (MCRs) are the main method for synthesizing complex molecules through simple and available substrates. These reactions have great advantages such as high efficiency, creating products with high purity, short reaction time and remarkable atomic economy [1-3]. Recently, there has been special attention given to the development of MCRs using catalysts that are metal-free and cost-effective to prevent environmental pollution [4]. Until now, the focus of catalyst research has been on increasing catalyst effectiveness and the ability for efficient recovery [5]. Chitosan is available in many forms depending on the amount of deacetylation, which can modify its properties, especially its immunological activity and its versatility, its low cost and its minimal toxicity make it attractive for use as medicine [6, 7].

In this study, the aim of the project is to prepare nanomaterial using chitosan, a non-toxic biopolymer, that can be decomposed by bacteria or other living organisms, thus avoiding environmental pollution. Chitosan is easily accessible and possesses antimicrobial properties, making it a subject of significant interest in the medicinal chemistry and biotechnology [8-10]. Since this popular biopolymer contains many amino and hydroxyl functional groups on its surface, it can be used alone or in its modified forms, as efficient bio-derived and biodegradable heterogeneous catalysts, in a variety of organic reactions

[6, 7, 11-16]. In continuation of our research on various biopolymeric- and other nanometric catalysts in different MCRs [10-12], we wish herein to report a new chitosan-based nanomaterial for one-pot synthesis of 2-amino-4*H*-pyran derivatives. The chitosan was grafted by using ethylenediaminetetraacetic acid (EDTA) and 1,3,5-tris(2-hydroxyethyl) isocyanurate (THEIC) to afford CS-EDTA-THEIC nanomaterial. The CS-EDTA-THEIC nanomaterial was characterized using common techniques such as Fourier infrared spectroscopy (FTIR) field emission scanning electron microscopy (FESEM), simultaneous thermogravimetric analysis (STA) and X-ray diffraction analysis (XRD). Subsequently, this multifunctional catalyst was utilized in the one-pot three-component reaction involving aromatic aldehydes, dimedone, and malononitrile for the synthesis of 4*H*-pyrans. Pyrans are six-membered heterocycles containing oxygen, and have shown promising applications in various fields, including pharmaceuticals, cosmetics, and agricultural chemicals [17, 18].

2. Materials and Methods

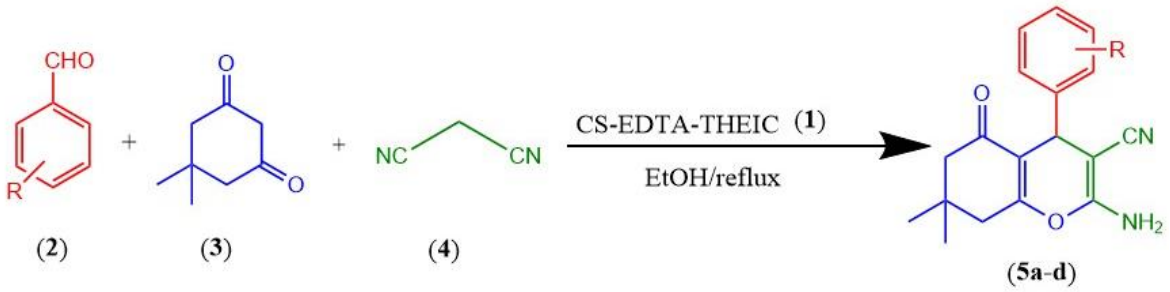
2.1. Materials

Chitosan (MW = 100000-300000 Da) was purchased from Acros Organics. Ethylenediaminetetraacetic acid (EDTA, MW = 292.24 g.mol^{-1}), dimedone, malononitrile and different aromatic aldehydes were purchased from prominent international chemical companies include SIGMA-Aldrich & Merck.

2.2. Methods

2.2.1. General procedure for the synthesis of 4H-pyran derivatives (5a-d)

In a 10 mL round-bottom flask, aromatic aldehydes (**2**, 1 mmol), dimedone (**3**, 1 mmol), malononitrile (**4**, 1.1 mmol) and 10 mg of CS-EDTA-THEIC (**1**) were added into 2.5 mL 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-EDTA-THEIC catalyst was dried and used for next runs. The general scheme of the multicomponent reaction for synthesis of 4*H*-pyran derivatives were shown in **Scheme 1**.



Scheme 1. Synthesis of 4*H*-pyran via one-pot three component condensation of aromatic aldehydes (**2**), dimedone (**3**), malononitrile (**4**) in the presence of CS-EDTA-THEIC catalyst.

3. Results and Discussion

In this part, various spectrometric and microscopic analyzes including FTIR, FESEM were carried out to characterize the catalyst. First, in FTIR analysis, a band appeared at 1735 cm^{-1}, 1689 cm^{-1} and 1636.7 cm^{-1} in the FTIR analysis, indicating the ester, carboxylic acid and amid functional groups, respectively. The following bands at 2960.2 cm^{-1} was showing saturated C–H groups (**Figure 1**).

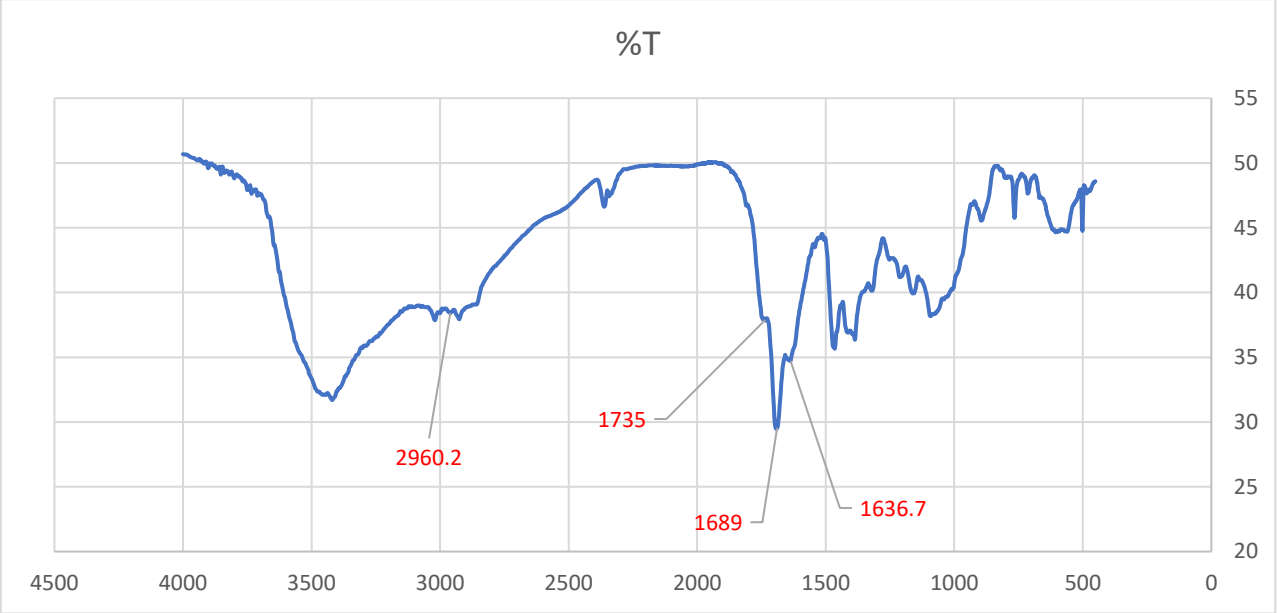


Figure 1. FT-IR spectrum of CS-EDTA-THEIC catalyst.

FESEM analysis is a high-magnification microscopic method that can be used to study the morphology, composition and structure of surfaces at the nanoscale. In Figure 2, the FESEM image of the prepared nanomaterials in which was observed a layered state on it's surface.

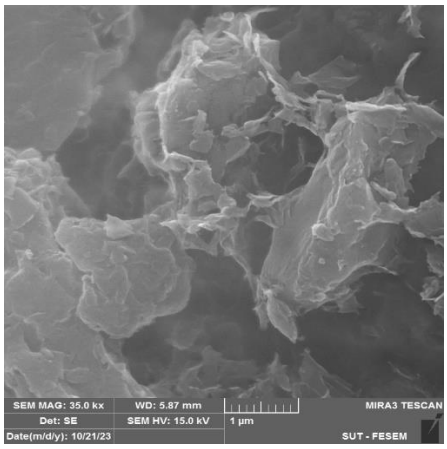
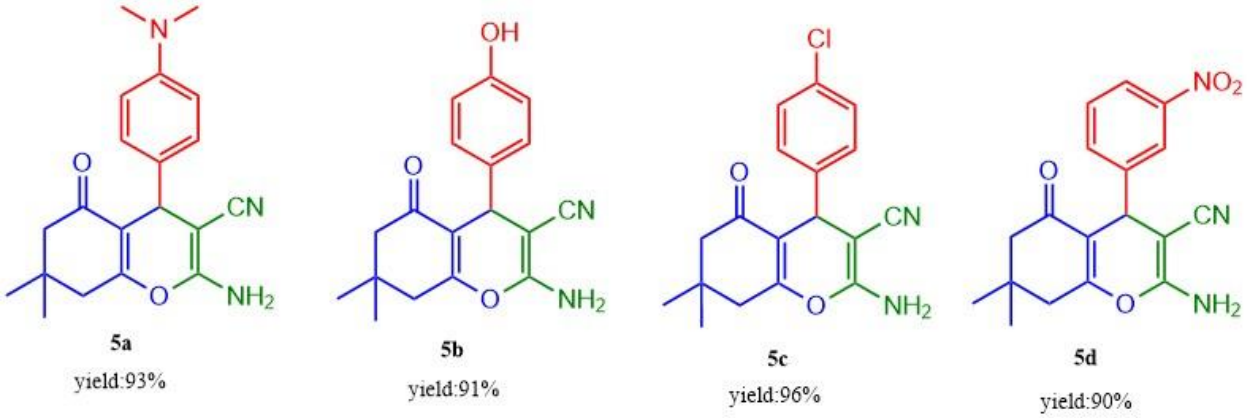


Figure 2. FESEM image of the CS-EDTA-THEIC catalyst.

In this multicomponent reaction, the synthesis of 2-amino-4-(4-chlorophenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile was chosen as a model reaction. Various conditions were tested for it, including the reaction in different solvents and in each of these solvents it was carried out once at room temperature and under reflux conditions. Also, various amounts of CS-EDTA-THEIC catalyst were also included in the optimization processes. At the end of these experiments, the best result was obtained by using 10 mg of catalyst in ethanol as solvent under reflux conditions and reacting for 15 min.

According to **Scheme 2**, the yields of the desired derivatives were obtained in the presence of 10 mg of catalyst within 15 - 35 minutes. It should be noted that the mentioned derivatives showed much lower yields (31-39 %) and longer reaction time (>1.5 h) when no catalyst was used. Also, according to **Scheme 2,** with a small amount of CS-EDTA-THEIC (**1**), as a heterogeneous catalyst (10 mg), desired products were synthesized with

high efficiency and short reaction time. Possibility of easy separation and recycling of the catalyst from mixture with minimal effort is another advantage of this organocatalyst. This catalyst was reused in at least five experiments without significant loss of the catalytic activity



Scheme 2. Scope of 4*H*-pyran derivatives (**5a-d**) synthesis catalyzed by CS-EDTA-THEIC.

The measured melting points of the derivatives discussed in this paper are summarized in **Table 1**.

Table 1. Comparison of the melting point of mentioned derivatives with relevant references.

Derivatives	m.p (obs) (°C)	m.p (ref) (°C)
5a	211-213	210-212 [1]
5b	223-225	224-226 [1]
5c	209-211	208-210 [4]
5d	207-209	209-211 [4]

In general, the proposed mechanism for the synthesis of 2-amino-3-cyano-4*H*-pyran derivatives by the one-pot three-component reaction of aromatic aldehydes, dimedone, and malononitrile is similar to proposed mechanism by other catalysts having both carboxylic and hydroxyl groups simultaneously [4, 19].

4. Conclusion

Briefly, the inexpensive and eco-friendly catalyst, which is easily prepared, has advantages such as easy separation, good recovery, and maintenance of the catalytic activity up to five cycles. The novel catalyst of CS-EDTA-THEIC was used in the multi-component reaction for the synthesis of 4*H*-pyran derivatives. In addition, it was found that EtOH is the best solvent for the synthesis of 4*H*-pyran derivatives under reflux conditions.

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