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THE APPLICATIONS OF NANOCATALYSTS IN THE SYNTHESIS OF HETEROCYCLIC COMPOUNDS

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ABSTRACT. Nanocatalysts in heterocyclic synthesis are a very important direction in producing eco-friendly compounds. These catalysts can be reused up to six times without losing their quantity and efficiency. Most of these nanocatalysts are cheap, available, economical and safe for the environment. In this review, I focused on the synthesis of furans, pyrans, chromenes and thiazoles from nanocatalysts. For example, pyranopyrazoles **8a-c** were synthesized by the multicomponent reactions between aldehydes **4a-c**, malononitrile (**5**), ethyl acetoacetate (**6**) and hydrazine hydrate (**7**) using titanium dioxide as a nanocatalyst.

KEY WORDS: Heterocyclic, Chromenes, Nanocatalysts, Eco-friendly compounds

INTRODUCTION

The synthesis of heterocyclic compounds using nanoparticle catalysts is one of the sustainable chemistry techniques and provides us with high yields of compounds, short reaction time, and recyclability of catalysts [1]. In the past, various classical methods were used to synthesize heterocyclic molecules [2]. These classical techniques depend on the use of expensive or toxic catalysts, thermal heating, longer reaction times, and high boiling solvents. Classic techniques are harmful to the environment and less safe, prompting researchers around the world to search for sustainable and environmentally friendly techniques to synthesize these heterocyclic compounds [3]. Sustainable chemistry aims to use safe techniques to synthesize bioactive compounds [4]. These sustainable technologies are still required to this day to synthesize safe and environmentally friendly compounds. Furthermore, the application of these techniques reduces the significant cost during the drug discovery process. Anastas, *et al.* also reported on the 12 basic principles of green synthesis [5, 6]. In addition to the use of nanocatalysts in heterocyclic synthesis, there are other environmentally friendly technologies such as solvent-free synthesis [7, 8], microwave-assisted organic synthesis [9, 10], sonochemical synthesis [11, 12], ionic liquid supported synthesis [13], and organic synthesis on water [14]. Various biological applications were shown by using nanoparticle catalysts in heterocyclic synthesis. The core and surface features of nanotechnology systems can be designed, for multimodal and individual usages. Such as therapeutic delivery, tissue engineering, bioimaging and biosensing. Nanoparticulate systems can transform badly absorbed, badly soluble, and bioactive substances into promising medicines. Using nanoparticle systems, researchers can demonstrate various drugs, genes and enzymes. The authors are waiting for promising pharmaceutics in the future using nanotechnology. Drugs manufactured in the future by nanotechnology are expected to include oral and parenteral drugs [15]. Recently, researchers have synthesized many nanocatalysts for the synthesis of heterocyclic compounds. For example, Javid *et al.* reported the synthesis of imidazoles catalyzed by silica supported $La_{0.5}Pb_{0.5}MnO_3$ nano particles as a novel and reusable perovskite oxide, also, they reported the synthesis of tetrahydrobenzo[*b*]pyrans in water using $Ni_{0.5}Zn_{0.5}Fe_2O_4$@HA-PRS nanoparticle [16, 17]. In this review, I overviewed the synthesis of furans, pyrans, chromenes, and thiazoles

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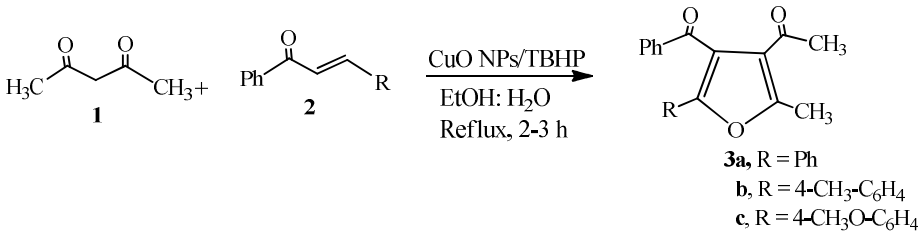
using nanocatalysts which are characterized by the high biological activities in the heterocyclic synthesis.

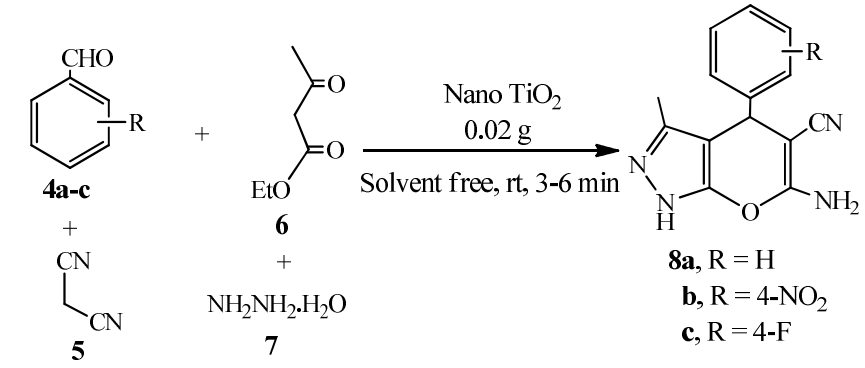
Synthesis of furans, pyrans, chromenes and thiazoles using nanocatalysts

Zaho *et al.* demonstrated the synthesis of 3,4-dicarbonyl furans by the reaction between 1,3-diketones and α, β unsaturated carbonyls in $MnO_2/ZnCl_2$ Catalyzed by CuO NPs in a corrosive acidic medium in the presence of 2-methylpropane-2-peroxol as an oxidizing agent (Scheme 1) [18, 19].



Scheme 1. Synthesis of 3,4-dicarbonylfuran derivatives **3a-c**.

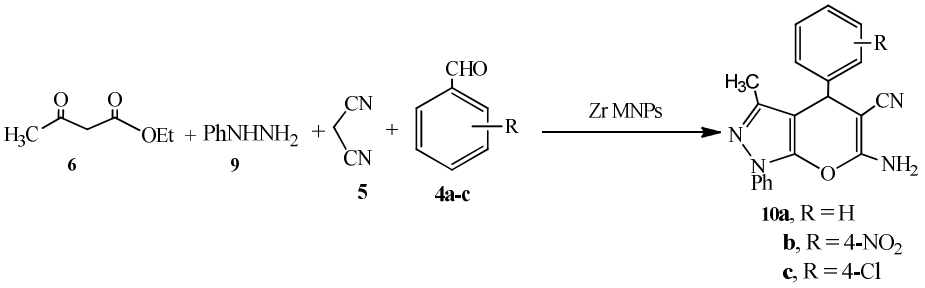
On the other hand, Reza *et al.* reported the synthesis of pyranopyrazoles **8a-c** by the reaction between aldehydes **4a-c**, malononitrile (**5**), ethyl acetoacetate (**6**) and hydrazine hydrate (**7**) using titanium dioxide as a nanocatalyst (Scheme 2) [20, 21].



Scheme 2. Synthesis of pyranopyrazoles **8a-c**.

Furthermore, Lorenzo *et al.* worked on the synthesis of 1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitriles by the reaction between ethyl acetoacetate (**6**), phenylhydrazine (**9**), malononitrile (**5**) and aromatic aldehydes **4a-c** using zirconium magnetic nanoparticles (Scheme 3). The suggested structure for zirconium magnetic nanocomposite is shown in (Figure 1) and its unique properties can be attributed to its microwave radiation and synthesis method [22].

Edjlali *et al.* published the synthesis of pyran's annulated heterocyclic systems **12a-c** by the reaction between cyclic CH-acids (**11**), malononitrile (**5**), benzaldehyde (**4a**) in water as a green solvent using titanium dioxide nanoparticles as a heterogeneous catalyst (Scheme 4) [23].



Scheme 3. Synthesis of 1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitriles **10a-c** using zirconium magnetic nanoparticles.

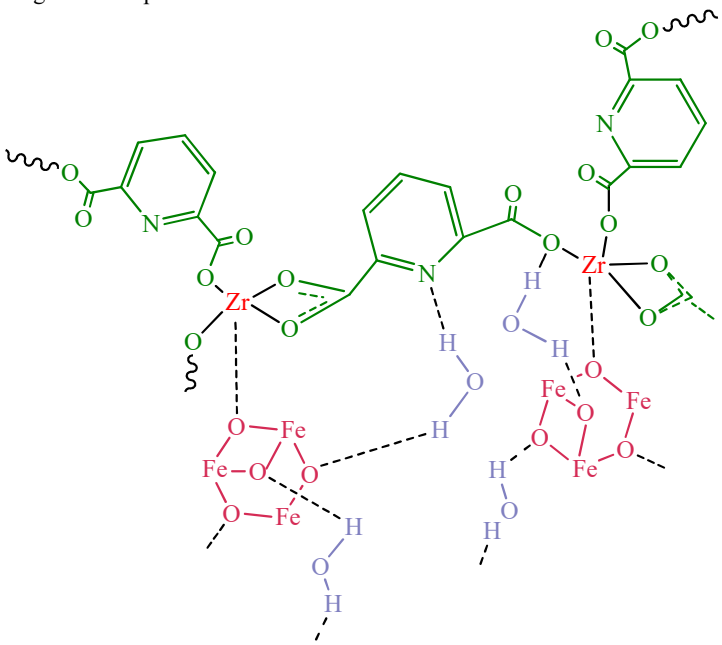
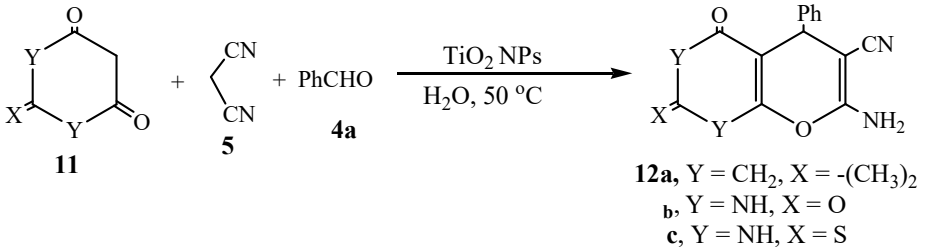
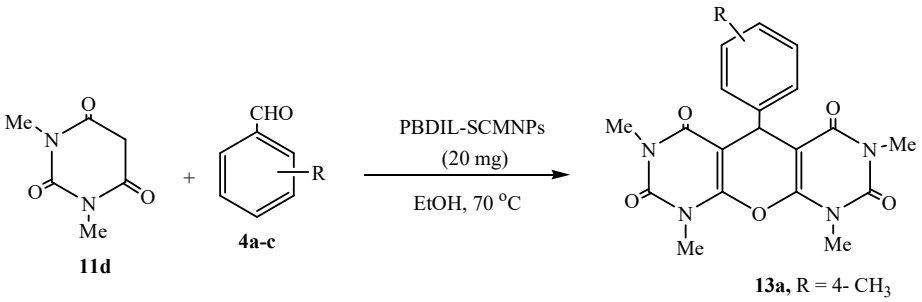


Figure 1. Suggested structure for zirconium magnetic nanocomposite.



Scheme 4. Synthesis of pyran's annulated heterocyclic systems **12a-c** using TiO_2 nanoparticles.

Similarly, Ramin *et al.* published the synthesis of pyrans using silica-coated magnetic nanoparticles functionalized with piperidinium benzene-1,3-disulfonate as a new efficient reusable catalyst by the condensation reaction between *N,N*-dimethylbarbituric acid and aldehydes **4a-c** (Scheme 5). The suggested structure for PBDIL-SCMNPs is shown in (Figure 2) [24].



Scheme 5. Synthesis of pyrans **13a-c** using PBDIL-SCM nanoparticles.

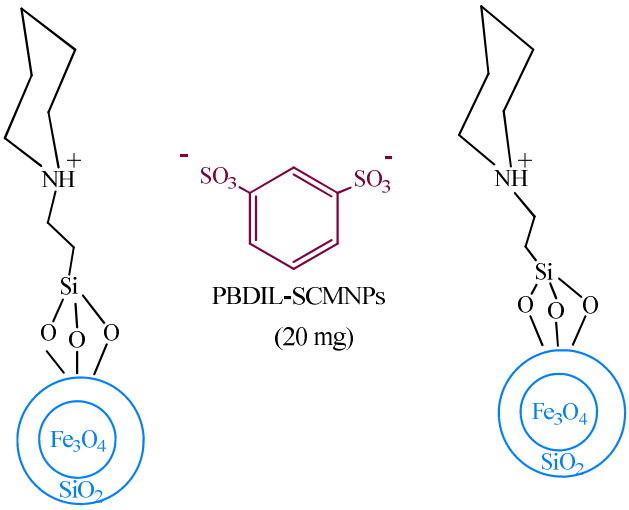
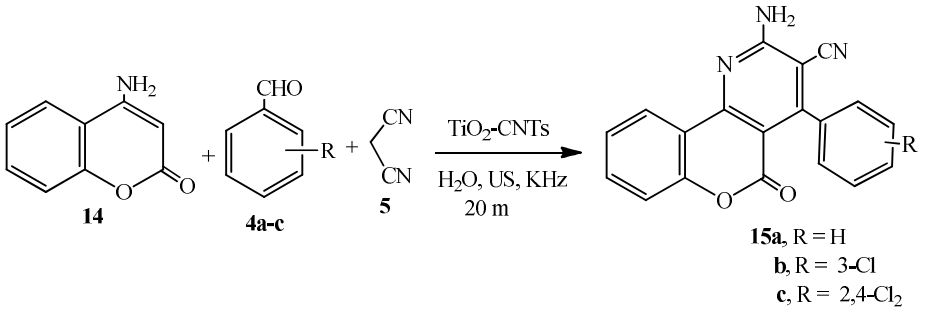


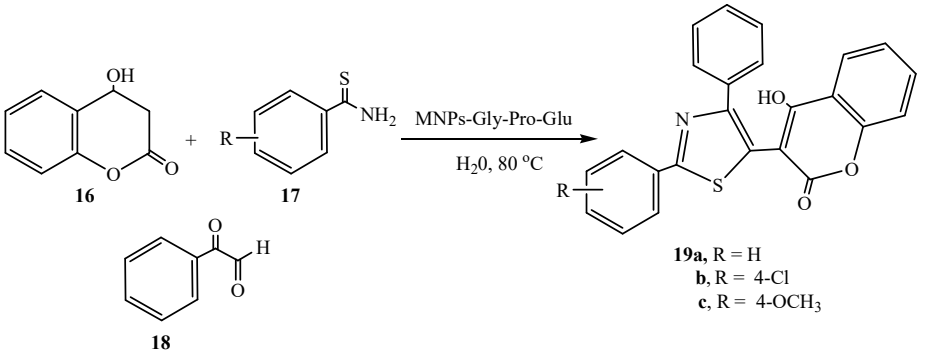
Figure 2. Suggested structure for PBDIL-SCMNPs.

In another instance, Abdolmohammadi *et al.* published the synthesis of chromeno[*b*]pyridines **15a-c** by the reaction between 4-aminocoumarin (1**4**), aromatic aldehydes **4a-c** and malononitrile (**5**) using TiO_2-CNTs as a catalyst under ultrasonic irradiation in a short time and high yield, due to the nanocatalysts have a large surface area compared to their volume, which increases the chances of interaction between molecules (Scheme 6) [25, 26].



Scheme 6. Synthesis of chromeno[*b*]pyridines **15a-c**.

Arabpoor *et al.* demonstrated the synthesis of thiazoles **19a-c** by the condensation reaction between 4-hydroxy coumarin (**16**), thiobenzamide (**17**) and phenylglyoxal monohydrate (**18**) using MNPs-Gly-Pro-Glu (Scheme 7) [27, 28].



Scheme 7. Synthesis of trisubstituted 1,3-thiazole derivatives **19a-c** in presence of MNPs-Gly-Pro-Glua–c.

CONCLUSION

In this review, the synthesis of furans, pyrans, chromenes and thiazoles using nanocatalysts was overviewed. Utilization of nanocatalysts in organic synthesis plays a very important role because it is reusable, cheap, economically and safe on the environmental. Also, the nanocatalysts have a large surface area compared to their volume, which increases the chances of interaction between molecules and leads to increasing yield and shortening the reaction time.

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