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Research Article

Maghnite-H+ Clay as Acid Eco-Friendly Catalyst for the Synthesis of Pyrimidinone Derivatives

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ABSTRACT

A useful and efficient procedure was obtained for the synthesis of pyrimidinone derivatives 3a-f via reaction of 2-aminobenzimidazole 1a-b and β-cetoesters in the presence of proton exchanged algerian montmorillonite clay (MMT-H+) as green catalyst with high yields. The main advantages of using this protonated solid non-toxic catalyst in this synthesis are its availability and low cost, the simplicity of its use, the recycling possibilities without significant loss of its catalytic activity and its environmentally benign process.

Keywords: pyrimidine, 2-aminobenzimidazole, β-cetoesters, Maghnite-H+.

1. INTRODUCTION

Pyrimidine is a heterocyclic six-membered aromatic ring similar to benzene, and pyridine containing two nitrogen atoms is found in these compounds at positions 1 and 3 of the ring.1 The word pyrimidine was first introduced by Pinner in 1884, as the two chemicals, pyridine and amidine, possessed higher levels of structural similarity. Pyrimidines are a significant class of heterocyclic compounds found in bioactive molecules and in natural products. Recently, heterocyclic compounds with a pyrimidine moiety have been reported to have anti-oxidant,2 anti-inflammatory, 3 and anti-bacterial activities. 4 Some pyrimidine derivatives have been used as basic structures in several antiviral and antibiotic drugs, such as Iclaprim and Etravirine.5, 6

Numerous processes catalytic have been developed for the synthesis of pyrimidines and their derivatives by using solid polymer catalysts like Pyrazolyl-pyrimidine porous-organic-polymer, 7 PEG-OSO3H, 8 Amberlyst-15, 9 Researchers have also used various hazardous metal catalysts like iron,10 manganese,11 lead 12 and prepare pyrimidine derivatives. Furthermore, multi-component reactions have also been observed in the presence of nanoparticles such as copper,13 platinum,14 Cu@KF/clinoptilolite nanoparticles,15 Magnetic Fe3O4@TiO2@NH2@PMo12O40, 16 and heterogeneous catalysts like PTPSA @SiO2-Fe3O4,17 Mg-Al-LDH-immobilized-CuI,18 OMS-2, 19 γ-Fe2O3@Cu3Al-LDH/ HEPES, 20 guanidine hydrochloride,21 Fullerene-C60/NH2, 22 Cu/Cu2O@g-C3N4, 23 ZIF-8/ZnFe2O4/GO-OSO3H 24 have been broadly used.

Each of these methods has limitations such as low yield, long reaction times, the use of large quantities of volatile organic solvents, and the complexity of some work-up procedures. Therefore, the

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development of new strategies for the synthesis of Pyrimidinone derivatives, with advantages in terms of the use of less expensive and readily available catalysts or reagents, cleaner reactions, and simple product isolation, is of interest.

Green chemistry, in very simple terms, is just a different way of chemistry based mainly on the protection of our environment by preventing pollution and protecting our natural resources. Its basic principles include: avoiding the use of hazardous compounds, using renewable materials and catalysts, improving energy efficiency,... 25 Catalysts used in chemical reactions often have significant environmental problems associated with their chemical nature and reuse as well as the separation and purification of products formed in the reaction mixture. Accordingly, the search for new processes using heterogeneous catalysts more environmentally friendly represents a major challenge in organic synthesis. Natural and modified mineral clays which are low cost, easily available, as well as environmental friendly, have been used as heterogeneous catalysts for many applications and shown high efficiency in organic synthesis. 26

In this work, we are interested by using this type of catalyst for Pyrimidinone derivatives synthesis. So, we propose the use of a montmorillonite clay catalyst extracted from North West Algeria, also called Maghnite-H+,27 It has recently been used in the synthesis of bis-Schiff bases,28 and in the synthesis of macromonomers and polymers by cationic polymerization.29-32

Maghnite-H+ provides a new and potential route for the synthesis of Pyrimidinone derivatives 3a-f with good yields.

2. EXPERIMENTAL MATERIALS

All chemicals were obtained from sigma Aldrich and Biochem and were used withoutfurther purification. Raw-Maghnite, Algerian montmorillonite clay was procured from “BENTAL” (Algerian Society of Bentonite). Thin layer chromatography (TLC) was done on silica gel TLC aluminium plates (E. Merck Kieselgel 60 F-254) and were visualized by exposure to UV-light at 254 nm or iodine vapor for few seconds. Melting point in °C was determined in open capillaries using Electrothermal melting point apparatus Stuart MPS-10. 1H and 13C NMR spectra were acquired on a Bruker AQS-AVANCE spectrometer (400 MHz) at 25°C using DMSO-d6 as solvent.

Chemical shifts (δ) are reported in parts per million (ppm) relative to the internal standard tetramethylsilane (TMS, δ = 0.00 ppm).

2.1. General procedure for the preparation of Maghnite-H+ catalyst (MMT-H+)

The reaction was catalyzed by Maghnite-H+. It was prepared according to the following method 33, 34: An amount of 20g of raw-Maghnite in powder form was dried for two hours at a temperature of 105°C to remove any traces of water. After drying, the Maghnite was put in an Erlenmeyer containing 500ml distilled water, then 0.23M sulfuric acid solution was added at once to the mixture Maghnite / water and agitated by a mechanical stirrer for about two days at room temperature. After that, the mineral part of the whole mixture was washed by distilled water until it becomes a free from sulfate and finally dried at 105°C for about 2hours.

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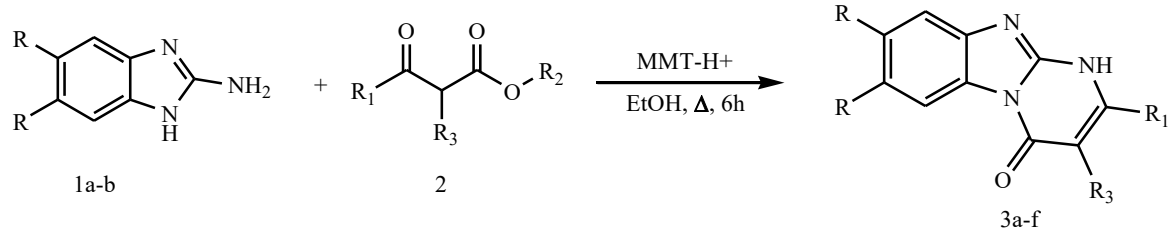
2.2. General method for synthesis of Pyrimidinone derivatives (3a-f)

2-aminobenzimidazole 1a-b (1mmol) is added to β-cetoesters 2 (1mmol) in 10ml ethanol with catalytic amount of montmorillonite-H+ (10%). The reaction mixture is refluxed for 6h. The progress of reaction is monitored by TLC. The crude product is dissolved with hot ethanol and then filtered to remove the solid catalyst. The filtrate is cooled to give the solid product. The resulting product is filtered, washed with ethanol and dried at 60-70°C to afford compound 3a-f (Scheme 1).



1a-b 2 3a-f

R= H, CH_3.

Scheme 1. Synthesis of Pyrimidinone derivatives 3a-f catalyzed by MMT-H+

7,8-Dimethyl-2,3-dihydrobenzo[4,5]imidazo[1,2-a]cyclopenta[d]pyrimidin-11(4H)-one(3a) Yellow powder (yield 87%), m.p. 249-251 °C; 1H NMR(400 MHz, DMSO-d6, δ in ppm): 1.98-2.09 (m, 2H), 2.30 (s, 6H, 2-CH3), 2.70- 2.85 (m, 4H), 7.50 (d, 2H, Harom), 10.85 (s, 1H, NH); 13C NMR(100MHz, DMSO-d6, δ in ppm):18.40, 21.69, 26.86, 34.26, 101.34, 114.69, 118.59, 122.48, 130,43, 145,82, 151.86, 159.87 (C=O).

7,8-Dimethyl-2-methylbenzo[4,5]imidazo[1,2-a]pyrimidin-4(1H)-one (3b) Yellow powder (yield 81%), m.p. 224-226 °C; 1H NMR(400 MHz, DMSO-d6, δ in ppm): 1.75 (s, 3H, CH3), 2.80 (s, 6H, 2-CH3), 5.82 (s, 1H, =CH), 7.81 (s, 2H, Harom), 11.20 (s, 1H, NH); 13C NMR(100MHz, DMSO-d6, δ in ppm):17.84, 18.12, 22.82, 98.28, 114.84, 119.46, 123.63, 131,28, 148,41, 155.46, 159.95 (C=O).

7,8-Dimethyl-2-methoxybenzo[4,5]imidazo[1,2-a]pyrimidin-4(1H)-one (3c) Yellow powder (yield 83%), m.p. 239-241 °C; 1H NMR(400 MHz, DMSO-d6, δ in ppm): 2.20 (s, 6H, CH3), 3.75 (s, 3H, O-CH3), 5.75 (s, 1H, =CH), 7.25 (s, 2H, Harom), 11.00 (s, 1H, NH); 13C NMR(100MHz, DMSO-d6, δ in ppm):17.76, 18.00, 52.14, 100.14, 114.76, 119.72, 123.77, 132,95, 146,21, 158.21(C=O), 179.28.

2,3-dihydrobenzo[4,5]imidazo[1,2-a]cyclopenta[d]pyrimidin-11(4H)-one (3d) Yellow powder (yield 86%), m.p. 245-247 °C; 1H NMR(400 MHz, DMSO-d6, δ in ppm): 1.98-2.09 (m, 2H), 2.73 (t, 2H), 2.85(t, 2H), 7.28 (t, 1H, Harom), 7.38-7.63 (m, 2H, Harom), 8.42 (d, 1H, Harom), 10.79 (s, 1H, NH); 13C NMR(100MHz, DMSO-d6, δ in ppm):21.69, 26.86, 34.26, 110.34, 111.69, 119.48, 122.85, 126,83, 149,98, 150.13, 157.78 (C=O).

2-methylbenzo[4,5]imidazo[1,2-a]pyrimidin-4(1H)-one (3e) Yellow powder (yield 80%), m.p. 219-221 °C; 1H NMR(400 MHz, DMSO-d6, δ in ppm): 2.30 (s, 3H, CH3), 5.82 (s, 1H, =CH), 7.27 (dd, 1H,

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Harom), 7.41 (dd, 1H, Harom), 7.61 (d, 1H, Harom), 8.38 (d, 1H, Harom), 11.13 (s, 1H, NH); 13C NMR(100MHz, DMSO-d6, δ in ppm): 22.28, 98.29, 114.84, 119.63, 127.28, 138,25, 149,60, 155.46, 159.95 (C=O).

2-methoxybenzo[4,5]imidazo[1,2-a]pyrimidin-4(1H)-one (3f) Yellow powder (yield 82%), m.p. 235-237 °C; 1H NMR(400 MHz, DMSO-d6, δ in ppm): 3.72 (s, 3H, O-CH3), 5.69 (s, 1H, =CH), 7.28 (s, 2H, Harom), 7.52 (d, 2H, Harom), 10.90 (s, 1H, NH); 13C NMR(100MHz, DMSO-d6, δ in ppm): 44.89, 71.56, 111.69, 120.05,130.15, 138,96, 145,97, 159.47(C=O), 171.77.

3. RESULTS AND DISCUSSION

In this work, a green, non-toxic and recyclable catalyst (proton-exchanged Algerian montmorillonite MMT-H^+) was used for the synthesis of pyrimidinone derivatives (Scheme 1).

To investigate the catalytic effect on the reaction yield, tests are carried out with different amounts of catalyst for the compound (3a). The results shown (Table 1) show that the use of 10% of catalyst at 79°C. Is the most effective and the yield obtained was 87% for 6 hours in ethanol (scheme 1).

Table 1. Catalytic effect on synthesis of Pyrimidinone derivatives (3a-f) catalyst by Maghnite-H+.

Entry	Cat (%)	Time(h)	T(°C)	Yield (%)
	10	6	Reflux	87.2
	20			79.3
	30			72.82

Cat: Maghnite-H+

In general, pyrimidinone derivatives 3a-f were obtained in good yields when mixtures of 2-aminobenzimidazole (1a-b) with β-ketoesters and 10% Maghnite-H+ were refluxed in ethanol for 6 hours (Table 2). The desired products precipitate upon cooling of the reaction mixture and filtration yields analytically pure material. The experimental results (Table 2) obtained by this reaction show good yields compared to those in the literature.

The results obtained from this study allowed us to propose the mechanism for the formation of pyrimidinone derivatives 3a-f (scheme 2). The formation of these compounds can be explained by a nucleophilic attack of the lone pair of the amino nitrogen atom on the carbonyl of the ketone function. The resulting intermediate, formed by the elimination of a water molecule, followed by an esterification reaction, leads to the backbone of the pyrimidinone derivatives. Cyclization involves the attack of the intracyclic nitrogen to produce the pyrimidinone derivatives 3a-f.

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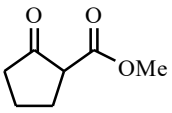
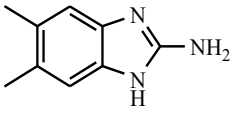
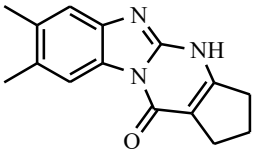
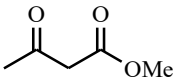
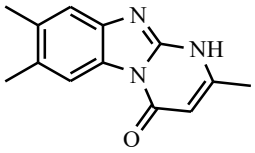
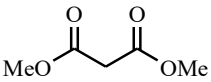
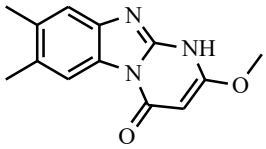
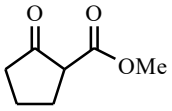
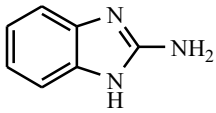
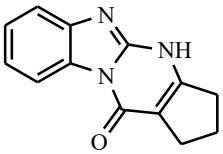
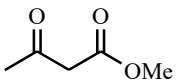
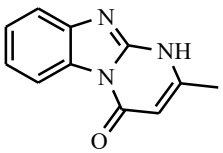
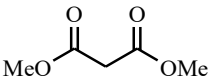
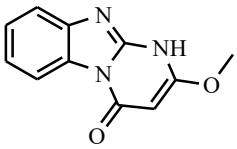
Table 2. Physical data of the synthesized compounds (3a-f) using Maghnite-H+

Entrée	β-étoesters	2-aminobenzimidazole	Conditions opératoires	Yield* (%) Exp ** (Lit.)	M.P. (°C) Exp** (Lit.)
1		 **1b**	 **3a**	87 (80)	249-251 (250) [35]
2			 **3b**	81 (74)	224-226 (225) [35]
3			 **3c**	83 (75)	239-241 (240) [35]
4		 **1a**	 **3d**	86 -	245-247 -
5			 **3e**	80 -	219-221 -
6			 **3f**	82 -	235-237 -

(*) Isolated yield of product using montmorillonite-H+. The structure of products are determined by NMR and all spectral data are in good agreement with those of literature.
(**) Exp.: Experimental value (Lit.: literature value).

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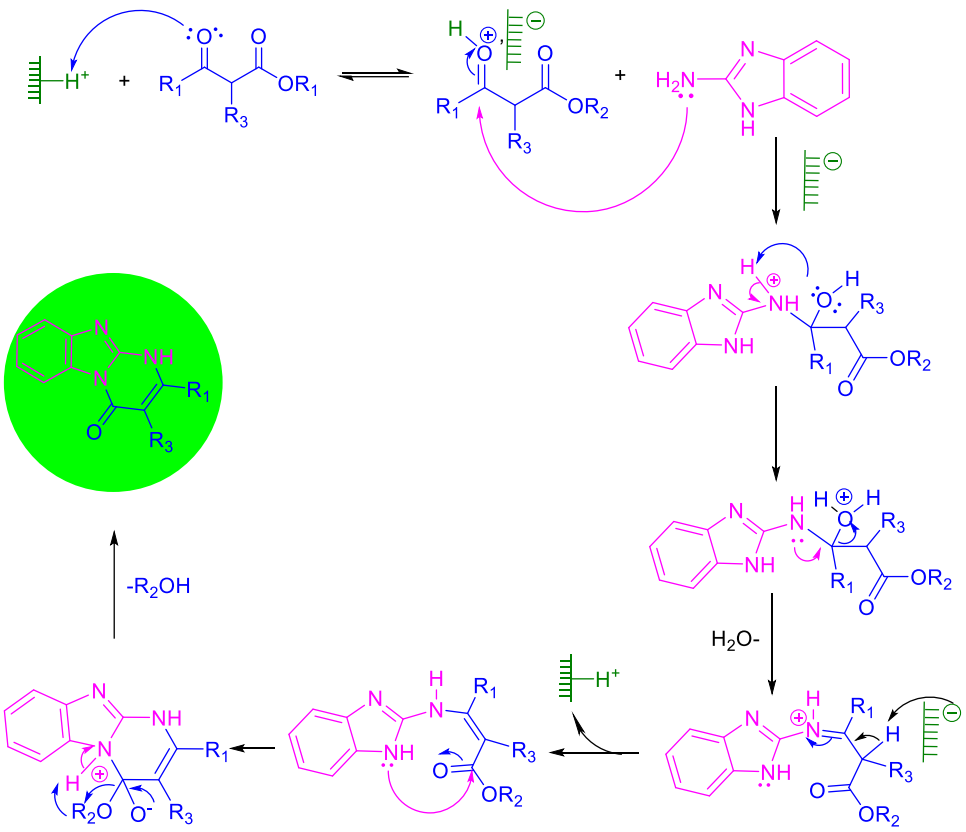

Scheme2. Proposed mechanism of the synthesis of Pyrimidinone derivatives (3a-f) derivatives using Maghnite-H+

4. CONCLUSION

The montmorillonite-H+ (MMT-H+) was found to be an efficient green heterogeneous acidic catalyst for the synthesis of pyrimidinone derivatives. This catalyst was easy to prepare, environmentally friendly, highly stable and can be recycled without significant loss of activity. The distinguished advantageous of present synthetic method are use of inexpensive catalyst, simple reaction workup, good yields and reusability of catalyst.

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