Heterocyclic Letters
Vol. 13| No.3|449-457|May-July|2023
ISSN : (print) 2231–3087 / (online) 2230-9632
CODEN: HLEEAI
http://heteroletters.org

AN ECO-FRIENDLY ULTRASOUND-ASSISTED ONE-POT THREE-COMPONENT SYNTHESIS OF 1,4-DIHYDROPYRIMIDO [1,2-*A*]BENZIMIDAZOLE DERIVATIVES CATALYZED BY MAGHNITE-H^+

Hadda Ben messaoud[1*], Boumadiene Benlahreche[1,2], Amar Djemoui[1], Lahcene Souli[1] and Mokhtar Boualem Lahrech[1*]

[1]*Laboratory of Organic Chemistry and Natural Substance, Faculty of Exact Sciences and informatics, Ziane Achour University-Djelfa, Algeria.*
[2]*Laboratory of Fine Chemistry, Department of Chemistry, Faculty of Exact and Applied Sciences, University of Oran1 Ahmed Ben Bella, PB 1524 El M'naouer, Algeria.*
**Corresponding Author. E-mail: lahrechmokhtarboualem@yahoo.fr; haddabenmessaoud2@gmail.com*

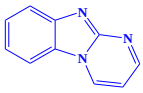
ABSTRACT
A simple and efficient procedure is developed for the synthesis of 1,4-dihydropyrimido[1,2-*a*]benzimidazole derivatives (DHPBz) *via* one-pot multi-component reaction of an aromatic aldehydes, ketones and 2-aminobenzimidazole, with use of a proton exchanged Algerian montmorillonite clay (Maghnite-H^+) as green catalyst under ultrasound irradiation. This approach has the major advantages of short reaction time, good yields, easy operation, low energy consumption, and environmental friendliness. In addition, the solid non-toxic catalyst could be removed from the reaction mixture by simple filtration and recyclable without a lack of catalytic activity. All of the products were characterized by IR and NMR spectroscopy, MS, and elemental analysis.

KEYWORDS: 1,4-dihydropyrimido[1,2-*a*]benzimidazole, One-pot multicomponent reactions, Benzaldehyde, ketone, 2-Aminobenzimidazole, Maghnite-H^+, Ultrasound irradiation.

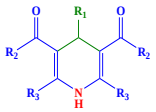
1. INTRODUCTION
Multi-component reactions (MCRs) have advanced tremendously in the last decade, and considerable efforts are still being made to develop these methodologie.[i] Multi-component reactions (MCRs) are a promising strategy in organic synthesis to produce bioactive molecules, because these molecules can be obtained rapidly and efficiently without the isolation of intermediates in only one reaction step.[ii]
The Pyrimido [1,2-a] benzimidazoles, 1,4-Dihydropyridines (1,4-DHPs) and the 1,8-dioxodecahydroacridines possess a broad variety of biological and pharmacological properties

such as antimicrobial,[iii] antimalarial,[iv] antiproliferative,[v] anticancer,[vi] antiviral,[vii] and anti-Alzheimer.[viii]

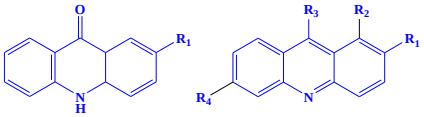
The Synthesis of these compounds are generally made by one-pot multicomponent reaction between an aldehyde, α-methylene such as ethyl acetoacetate or 1,3-cyclohexanedione or 1,3-diketone and ammonium acetate[ix] or amine.[x] Most of these synthesis are based mainly on traditional thermal methods in presence of organic solvents and a range of catalysts, such as: Brosted acid or Lewis acid, HCl , montmorillonite clay (Na^+–MMT) modified,[xi,xii] L-proline,[xiii] ρ-TsOH,[xiv] Amberlsyt-15,[xv] CAN,[xvi] Silica-supported sulfuric acid,[xvii] 2-Hydroxyethylammonium Acetate,[xviii] Alginic acid,[xix] Sodium 1-DodecaneSulfonic (SDS),[xx] 4-toluenesulfonic acid,[xxi] $[H\text{-}NMP]^+[HSO4]^-$,[xxii] $In(OTf)_3$,[xxiii] TPANPs/PAA[xxiv] and Cu-doped ZnO,[xxv] Therefore, there is a need to use a simple eco-friendly catalyst under moderate conditions to prepare 1,4-dihydropyrimido[1,2-*a*]benzimidazole.



Pyrimido [1,2-a] benzimidazoles



1,4-Dihydropyridines (1,4-DHPs)



1,8-dioxodecahydroacridines

Figure 1

Green chemistry has become a big and regular headline in the twenty-first century as a means of reducing chemical waste on the environment. Its main ideas are to reduce the amount of solvents used, to use renewable efficient heterogeneous catalysts, and to increase energy efficiency.[xxvi]

As a result, the use of a montmorillonite clay catalyst, also known as Maghnite, which has already shown interesting catalytic properties, was recommended. [xxvii] When exchanged with high charge density cations, such as protons, montmorillonites possessing both Brönsted and Lewis acid sites produce active acid catalysts. [xxvii] When compared to other clays, Algerian montmorillonite has a higher proportion of SiO_2 and a lower concentration of Al_2O_3. Table 1 shows percentage changes in chemical composition, between raw and proton exchanged algerian MMT. These differences, in particular, must have a major impact on the physico-chemical properties of this exchanged montmorillonite.[xxviii]

Table 1. Algerian montmorillonite (raw and H^+ exchanged) chemical composition. [xxviii]

Échantillon	SiO_2	Al_2O_3	Fe_2O_3	MgO	CaO	Na_2O	K_2O	TiO_2	SO_3	As	Perte d'eau à 110° C
Alg-MMT brute (%)	69.39	14.67	1.16	1.07	0.3	0.5	0.79	0.16	0.91	0.05	11
Alg-MMT-H^+ (%)	71.7	14.03	0.71	0.8	0.28	0.21	0.77	0.15	0.34	0.01	11

Sonochemistry is one axis of green chemistry research in which the molecules interact significantly due to the powerful application of ultrasound irradiation. These technique has been used more frequently as a clean and simply protocol to synthesize Schiff bases under milder conditions in shorter reaction times providing higher yields without generation of pollution comparing with traditional methods requiring solvents and longer reaction time.[xxix]

As part of our continuing efforts on the development of new routes for the synthesis of heterocyclic compounds.[xxx] Herein, we wish to the synthesis of some new 1,4-dihydropyrimido [1,2-a] benzimidazoles (DHPBz) derivatives **4a-f** (figure 1) via one-pot multi-component reaction of aldehyde **1**, ketones **2** and 2-aminobenzimidazole **3**, in the presence of catalytic amounts of maghnite-H^+ under ultrasound irradiation.

2. EXPERIMENTAL

2.1. Materials

All research chemical reagents: 2-aminobenzimidazole, Aldehydes (Benzaldehyde, 3-hydroxy-5-methoxybenzaldehyde, 4-methoxybenzaldehyde) and ketones (Sigma aldrich) were purchased from (Sigma-Aldrich) and they are used as received. Raw-Maghnite, Algerian montmorillonite clay was procured from "BENTAL" (Algerian Society of Bentonite). The progress of the reactions was monitored by thin layer chromatography (TLC) on silica gel plates (TLC Silica gel 60 F254) using éluants (hexan/AcOEt). Melting points of all synthesized compounds were measured by Kofler bench method (HEIZBANK System Kofler Type WME N° 6973), and visualizing by iodine as agent. FT-IR spectra were recorded on FT-IR spectrophotometer (Atlas Manual Hydraulic Press 15T, GS15011) using KBr pellets technique. 1H NMR and 13C NMR spectra were recorded at 400 MHz (BRUKER Avance spectrometers) in DMSO-d6 using as internal standards the residual DMSO signal for 1H NMR (δ = 2.50 ppm), and the following multiplicity abbreviations were used: s, singlet; d, doublet; t, triplet; q, quadruplet; m, multiplet. Ultrasonication was performed in a KQ-250E ultrasound with a frequency of 40 kHz and an output power of 150 W.

2.2.Preparation of Maghnite-H^+

All the reactions were catalyst by Maghnite-H^+. It was prepared according to the following method: 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 500 ml 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 become a free from sulfate and finally dried at 105°C for about 2hours.[xxx]

2.3.General procedure for the synthesis of 1,4-dihydropyrimido [1,2-a] benzimidazoles (DHPBz) derivatives 4a-f.

A mixture of aldehyde **1** (1mmol), ketone compounds **2** (1mmol) and 2-amino benzimidazole **3** (1 mmol) in 5ml methanol with catalytic amount of maghnite-H^+ (10%wt). The amount of 10% of catalyst was selected after preliminary reaction tests. The mixture was exposured to the ultrasound at 45-60°C with reaction times of 1h (Scheme 1). After the completion of the reaction (monitored by TLC), and isolate the solid catalyst, cooling and filtration the crystalline powder were collected, then washed and dried at 60-70°C to afford compounds **4a-f**.

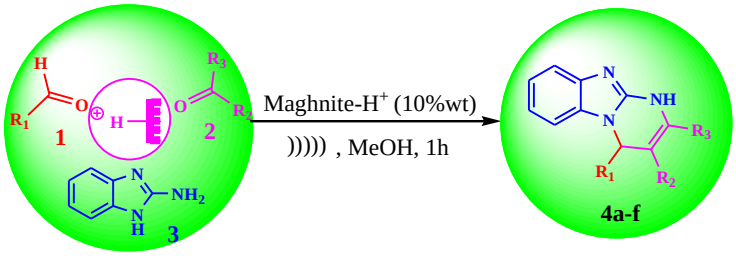
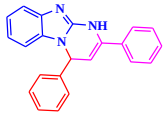
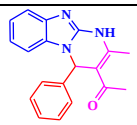
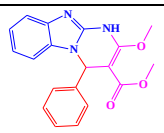
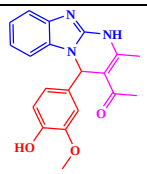
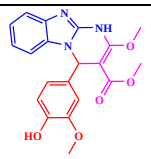
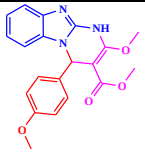


Figure 2. One-pot three compounds reaction for synthesis of 1,4-dihydropyrimido[1,2- a] benzimidazole derivatives using Maghnite-H^+.

2.4. Characterization and spectroscopic data

Data for 2,4-diphenyl-1,4-dihydropyrimido[1,2-a]benzimidazole (**4a**) : white powder, (lit. mp. 249°C), FT-IR (ν_{max} in cm^{-1}): 3419 (NH), 3034 (aromatic C-H), 1627 (C=N), 1573 (aromatic C-C). ^{1}H NMR (400 MHz, DMSO-d_6, δ in ppm): 10.02 (s, -NH-), 8.12 (2H,dd, H_6,H_3, J = 15.8,7.8 Hz, Ar-H), 7.64 (1H,d, H_2, J = 6.6 Hz, Ar-H), 7.41 (2H,d, H_{14},H_{18}, J = 7.0 Hz, Ar-H), 7.35 (2H,d, $H2_1$, H_{25}, J = 6.1 Hz, Ar-H), 7.25 (2H, t, H_{14}, H_{16}, J = 7.4 Hz, Ar-H), 7.15 (2H, H_{22}, H_{24}, t, J = 6.9 Hz, Ar-H), 7.01 (2H, d, H_{16}, H_{23}, J = 8.4 Hz, Ar-H), 6.87 (1H, H_{26}, d, J = 3.9 Hz, -C=C-H), 6.33 (1H, H_{10}, d, J = 3.9 Hz, =C-C-H), 5.28 (1H, d, H_1, J = 7.7 Hz, -C=C-H). ^{13}C NMR (100MHz, DMSO-d_6, δ in ppm): 148.62, 143.00, 142.32, 134.89, 132.19, 129.30, 128.98, 128.37, 126.91 , 126.32 , 121.86 , 116.41, 98.03, 57.19.

Table 2. Physical data of the synthesized compounds **4a-f** using maghnite-H^+

Entry	Product	Ultrasound irradiation		Conventional heating[xxx]		M.P °C
		Time (h)	Yield* %	Time (h)	Yield* %	
1	 **4a**	1	89	2	81.53	260<
2	 **4b**	1	88	4	80	260<
3	 **4c**	1	87	4	75	245-246
4	 **4d**	1	85	4	75	248-250
5	 **4e**	1	86	3	72	260<
6	 **4f**	1	86	4	79	242-244

(*) Isolated yield of product using maghnite-H^+

Data for 1-**(**2-methyl-4-phenyl-1,4-dihydropyrimido[1,2-*a*]benzimidazol-3-yl)ethanone (**4b**) : yellow powder, FT-IR (ν_{max} in cm^{-1}): 3471 (NH), 3037 (aromatic C-H), 1653 (C=O), 1610 (C=N), 1562 (aromatic C-C), 1521 (-CH_3). ^{1}H NMR (400 MHz, DMSO-d_6, δ in ppm): 10.79 (s, 1H,-NH-), 7.42 (3H, d, H_{10}, H_{13}, *J*= 7.4Hz, Ar-H), 7.33 (1H, t, H_8,H_9, *J*= 7.8Hz , Ar-H), 7.27 (2H, t, H_6, H_4, *J*= 7.6Hz, Ar-H), 7.17 (1H, d, H_7, H_3, *J* = 7.2 Hz, Ar-H), 7.04 (1H, s, H_5, Ar-CH), 6.98 (1H, s, H_5, Ar-CH), 6.59 (1H, s, H_6, Ar-CH), 2.50 (1H, s,-CH_3) 2.23 (3H, s,-CH_3). ^{13}C NMR (100MHz, DMSO-d_6, δ in ppm): 129.07, 128.31, 127.65, 122.23,120.63, 117.32, 110.47, 56.17, 31.14, 20.18.

Data for Methyl-2-methoxy-4-phenyl-1,4-dihydropyrimido[1,2-*a*]benzimidazole-3-carboxylate (**4c**): white powder, FT-IR (ν_{max} in cm^{-1}): 3417 (NH), 3061 (aromatic C-H), 1749 (C=O), 1604 (C=N), 1583 (aromatic C-C), 1456 (-CH_3). ^{1}H NMR (400 MHz, DMSO-d_6, δ in ppm): 12.08 (s, 1H,-NH-), 7.45 (d, 1H, H_3, H_6, *J*=7.9Hz, Ar-H), 7.38 (d, 3H, H_1, H_2, H_4, *J* = 6.4 Hz, Ar-H), 7.19 (t, 3H, H_4, H_5, H_7, *J* = 7.3 Hz, Ar-H), 7.11 (t, 1H, H_{22}, *J* = 7.5 Hz, Ar-H), 6.99 (d, 1H, H_{23}, *J* = 7.9 Hz, Ar-H), 6.88 (d, 1H, H_{10}, *J* = 4.4 Hz, -C=C-H), 6.14 (d, 1H, H_8, *J* = 4.3 Hz, -C=C-H), 3.65 (s, 3H,-CO-CH_3), 3.46(s, 3H,-CH_3. ^{13}C NMR (100MHz, DMSO-d_6, δ in ppm): 167.69, 166.59, 164.27, 148.00, 137.21, 132.81, 129.63, 129.30, 126.84 , 122.43, 121.73 , 117.83, 110.20, 55.69 , 55.31 , 53.41.

Data for 1-[4-(4-hydroxy-3-methoxyphenyl)-2-methyl-1,4-dihydropyrimido[1,2-*a*]benzimidazole-3-yl]ethanone (**4d**) : yellow powder, FT-IR (ν_{max} in cm^{-1}): 3527 (NH), 3101 (aromatic C-H) ,1652(C=O), 1598 (C=N), 1556 (aromatic C-C), 1516 (-CH_3). ^{1}H NMR (400 MHz, DMSO-d_6, δ in ppm): 10.66 (s, 1H,-NH-), 8.97 (s, 1H,-OH), .750 (d, *J*=7.5Hz, 1H, H_7 , Ar-H), 7.34 (d, 1H, H_6 , Ar-H), 7.06 (d, *J*=7.5Hz, 1H, H_5 ,Ar-H), 6.77 (d, *J*=7.9Hz, 1H, H_4 ,Ar-H), 6.65 (d, 1H,Ar-H), 6.51 (s, 1H, Ar-CH), 3.72 (s, 3H,-CH_3), 2.47 (s, 3H,-CH_3), 2.21 (s, 3H,-CH_3). ^{13}C NMR (100MHz, DMSO-d_6, δ in ppm): 196.00, 147.72, 146.77, 145.99, 142.83, 133.07, 132.18, 122.11, 120.47, 120.18, 117.23 , 115.99 , 112.48 , 110.69 , 109.05, 56.20, 31.13, 20.05.

Data for methyl-4-(4-hydroxy-3-methoxyphenyl)-2-methoxy-1,4-dihydropyrimido [1,2-*a*] benzimidazole-3-carboxylate (**4e**) : yellow powder, FT-IR (ν_{max} in cm^{-1}): 3552 (NH), 3057 (aromatic C-H), 1701 (C=O), 1635 (C=N), 1570 (aromatic C-C). ^{1}H NMR (400 MHz, DMSO-d_6, δ in ppm): 9.22 (s, H,-NH-), 7.44(d, 2H, H_{10}, H_{13} , *J* = 7.8 Hz, Ar-H), 7.09 (t, 2H, H_8, H_9, *J* = 7.3 Hz, 2H), 7.02 (s, 1H, H_{24}, -OH), 6.97 (d,2H, *J* = 7.6 Hz, Ar-H), 6.77 (d, 2H, *J* = 8.0 Hz, Ar-H), 6.73 (d, 2H, Ar-H), 6.41 (d, 2H, H1, -C=C-H), 5.93 (d, 3H, -(CO)-O-CH_3), 3.71 (s, 3H, -O-CH_3), 3.64 (s, 3H, -CH_3). ^{13}C NMR (100MHz, DMSO-d_6, δ in ppm): 167.78, 148.54, 147.54, 132.90, 127.62, 122.24, 121.56, 119.30, 117.73, 116.03, 111.69, 110.41, 56.20, 55.51, 53.25.

Data for methyl-2-methoxy-4-(4-methoxyphenyl)-1,4-dihydropyrimido[1,2-*a*]benzimidazole-3-carboxylate(**4f**) : yellow powder, FT-IR (ν_{max} in cm^{-1}): 3446 (NH), 3055 (aromatic C-H), 1747 (C=O), 1701 (C=N), 1612 (aromatic C-C), 1456 (-CH_3). ^{1}H NMR (400 MHz, DMSO-d_6, δ in ppm): 12.07 (s, 1H,-NH-), 7.43 (d, 1H, *J* = 7.9 Hz , H_{10}, Ar-H), 7.15 (t, 1H, *J* = 8.3 Hz, H_8, Ar-H), 7.10 (d,1H , *J* = 7.6 Hz, H_3, Ar-H), 6.96 (d, 1H , *J* = 7.9 Hz ,H_4, Ar-H), 6.79 (d, 1H, -C=C-H), 6.03 (d, 1H, Ar-H), 3.74 (s, 3H,-CH_3), 3.64 (s, 3H,-CH_3), 2.50 (s, 3H,-CH_3). ^{13}C NMR (100MHz, DMSO-d_6, δ in ppm): 167.72, 164.55, 159.99, 148.00, 132.83, 128.89, 128.48, 122.32, 121.63, 117.77, 114.98, 110.32 , 55.65, 53.30, 14.29.

3. RESULTS AND DISCUSSION

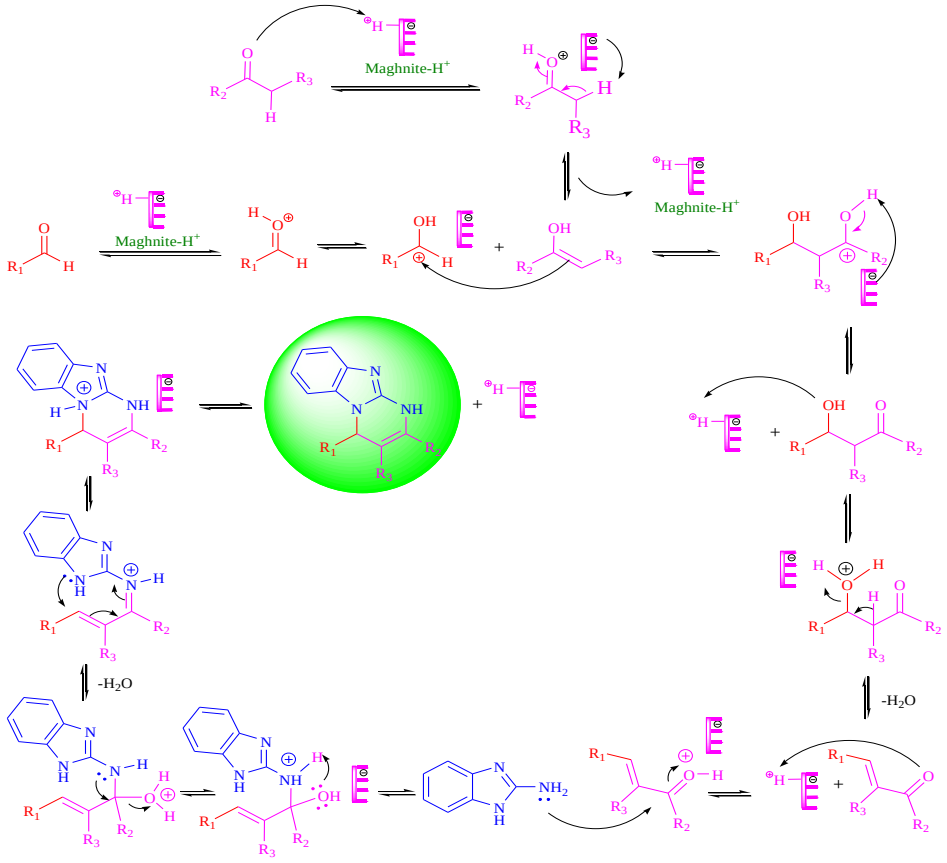
The production of 1, 4-dihydropyrimido[1,2-a]benzimidazole derivatives (DHPBz) **4a-f** was obtained by combining aldehydes **1** with ketones compounds **2** and 2-aminobenzimidazole **3**, catalyzed by maghnite-H^+ under ultrasound irradiation (Scheme 2).

We observed through the experimental results (Table 2), that these synthesis show good yields

(85-89%) in shortless time compared to other classical methods. Furthermore, the catalyst from the reactionnal mixture can be removed and recycled up to three times without loss of catalytic activity.

The structures of compounds obtained **4a-f** are well confirmed by the melting points and on basis of analysis of their spectral data (FT-IR, ^{1}H NMR and ^{13}C NMR), compared to the values of the literature.[xxx]

A mechanism, presented in Scheme 3, is proposed to explain the role of the Maghnite-H^{+} for the synthesis of 1, 4-dihydropyrimido[1,2-*a*]benzimidazole derivatives (DHPBz) **4a-f**.



Scheme 3. Proposed mechanism of the synthesis of 1,4-dihydropyrimido[1,2-a]benzimidazole derivatives using Maghnite-H^{+}.

3.1. Infrared Spectroscopy (FT-IR)

The FT-IR spectrum of all synthesized compounds exhibit characteristic bands in the ranges of 3500-3400, 1652-1701cm^{-1} and weak band at 1701-1598cm^{-1} which assignable to N-H, C=O and C=N stretching vibrations respectively. This indicators, evidence of the react of aldehydes **1** with ketones compounds **2** and 2-aminobenzimidazole **3** and confirms the formation of the desired product. In all the 1,4-dihydropyrimido[1,2-a]benzimidazole derivatives **4a-f**, was shown absorption strong bands at 3055-3037 and 1612-1562 cm^{-1} due to aromatic (C-H) and (C-C) stretching vibrations respectively. IR spectrum of compounds **4a-f** show absorption band at 1456-1516 cm^{-1} which can be assigned to -CH_3 stretching.

3.2. Nuclear Magnetic Resonance (NMR)

In ^{1}H-NMR spectra of all synthesized compounds show singlet at 12.08-9.22 ppm indicating the presence of secondary amino group (-NH-). The aromatic protons resonate as multiplet in

the region of δ 8.12-6.03ppm. The spectrum of compounds **4a, 4c, 4e** and **4f** shows the -C=C-H signal around 6.88-6.41ppm. The spectrum of the compound **4c** shows the group (-CO-CH_3), signal around 3.65 ppm. In addition, the absence of -CH_3 signal clearly indicates the formation of compound derivatives **4b-f** signal around 3.74-2.47ppm. Moreover, the ^{1}H-NMR spectrum of **4d** reveal the presence of a singlet at 8.97 ppm corresponding to hydroxyl group O-H. All ^{1}H and ^{13}C-NMR spectral data are in good agreement with those of literature. [xxx]

4.CONCLUSION

In conclusion, we have described a simple and efficient alternative methodologies by ultrasound irradiation for the synthesis of 1,4-dihydropyrimido[1,2-a]benzimidazole (DHPBz) derivatives using maghnite-H^+ as a green catalyst by one-pot three-component reaction of aldehydes, ketones derivatives compounds and 2-aminobenzimidazole. Compared with conventional methods, the procedure offers several advantages, including high yields (85-89%) in shorter reaction times and possible reuse of the catalyst by heating up to a temperature above without significant loss of activity.

ACKNOWLEDGEMENTS

The authors acknowledge the laboratory of organic chemistry and natural substance, faculty of exact sciences and informatics, Ziane Achour university of Djelfa, Algeria and the Ministry of Higher Education and Scientific Research in Algeria for their financial support.

REFERENCES

i. Cao, C. P., Lin, W., Hu, M. H., Huang, Z. B., Shi, D. Q. (2013). Highly efficient construction of pentacyclic benzo [b] indeno-[1, 2, 3-de][1, 8] naphthyridine derivatives via four-component domino reaction. *Chemical Communications*, *49*(62), 6983-6985.

ii. Yang, J., Li, Q., Zhang, J., Lin, W., Wang, J., Wang, Y., Shi, D. (2013). Ultrasound-promoted one-pot, four-component synthesis of pyridin-2 (1H)-one derivatives. *Molecules*, *18*(12), 14519-14528.

iii. Djemoui, A., Ouahrani, M. R., Naouri, A., Souli, L., Rahmani, S. E., Boualem, L. M. (2018). Eco-friendly and highly efficient one-pot synthesis of symmetrical and unsymmetrical 1, 4-dihydropyridine derivatives using triethylamine as catalyst in ethanol medium. *Heterocyclic Letters*, *8*(2), 455-467.

iv. Werbel, L. M., Curry, A., Elslager, E. F., Hess, C. A., Hutt, M. P., Youngstrom, C. (1969). article empty pyrimido 1, 2-a benzimidazoles, 2, 3-dihydro-1H-cyclopenta 4, 5 pyrimido 1, 2-a benzimidazoles, and s-triazolo 1, 5-a pyrimidines as potential antimalarial agents. *Journal of Heterocyclic chemistry*, *6*(6), 787-796. doi.org/10.1002/jhet. 5570060603.

v. Nawrocka, W., Sztuba, B., Dryś, A., Wietrzyk, J., Kosendiak, J., Opolski, A. (2006). Synthesis and antiproliferative activity in vitro of new 2-aminobenzimidazole derivatives. Part 3 [1]. Reactions of 2-arylideneaminobenzimidazole with selected 1, 3-diketones. *Polish Journal of Chemistry*, *80*(2), 279-287.

vi. Abdel-hafez, A. A. M. (2007). Benzimidazole condensed ring systems: New synthesis and antineoplastic activity of substituted 3, 4-dihydro-and 1, 2, 3, 4-tetrahydro-benzo [4, 5] imidazo [1, 2-a] pyrinnidine derivatives. *Archives of pharmacal research*, *30*(6), 678-684.

vii. Mazzucco, M. B., Talarico, L. B., Vatansever, S., Carro, A. C., Fascio, M. L., D'Accorso, N. B., Damonte, E. B. (2015). Antiviral activity of an N-allyl acridone against dengue virus. *Journal of biomedical science*, *22*(1), 1-12.

viii. Saeedi, M., Safavi, M., Karimpour-Razkenari, E., Mahdavi, M., Edraki, N., Moghadam, F. H., Akbarzadeh, T. (2017). Synthesis of novel chromenones linked to 1, 2, 3-triazole ring system: Investigation of biological activities against Alzheimer's disease. *Bioorganic chemistry*, *70*, 86-93.

ix. Hantzsch, A. (1881). Condensationsprodukte aus Aldehydammoniak und ketonartigen Verbindungen. *Berichte der deutschen chemischen Gesellschaft*, *14*(2), 1637-1638.

x. Amar Djemoui; Mohammed Ridha Ouahrani; Abdelkader Naouri; Lahcen Souli; Salah-Eddin Rahmani, Lahrech Mokhtar Boualem, (2018). Eco-friendly and highly efficient one-pot synthesis of symmetrical and unsymmetrical 1,4-dihydropyridine derivatives using triethylamine as catalyst in ethanol medium. *Heterocyclic Letters*, 8(2), 455-467.

xi. Pada, R.S., Nandaniya, R.N., Ram, H.K., Shah,V. H. **(**2012). Synthesis of some new 1,4-dihydropyrimido[1,2-a]benzimidazoles and evaluation of their biological activity. *J. Chem. Phar. Res*., 4(7): 3557-3561.

xii. Makhsous, M., Shirini, F., Seddighi, M., Mazloumi, M. (2020). Efficient synthesis of pyrimido [1, 2-a] benzimidazoles and ethyl pyrimido [1, 2-a] benzimidazole-3-carboxylates using brönsted acidic ionic liquid supported on nanoporous Na+-montmorillonite. *Polycyclic Aromatic Compounds*, *40*(2), 494-501. doi: 10.1080/10406638.2018.1454967.

xiii. K. Venkatesan, Suresh S. Pujari, and Kumar V. Srinivasan.(2009). Proline-Catalyzed Simple and Efficient Synthesis of 1,8-Dioxo-decahydroacridines in Aqueous Ethanol Medium *Synthetic Communications1*, 39, 228.doi: 10.1080/00397910802044306.

xiv. Jamalian, A., Miri, R., Firuzi, O., Amini, M., Moosavi-Movahedi, A. A., Shafieea, A. (2011). Synthesis, cytotoxicity and calcium antagonist activity of novel imidazolyl derivatives of 1, 8-acridinediones. *Journal of the Iranian Chemical Society*, *8*(4), 983-991.

xv. Kaya, M., Yıldırır, Y., Çelik, G. Y. (2011). Synthesis and antimicrobial activities of novel bisacridine-1, 8-dione derivatives. *Medicinal chemistry research*, *20*(3), 293-299.

xvi. Kidwai, M., Bhatnagar, D. (2010). Ceric ammonium nitrate (CAN) catalyzed synthesis of N-substituted decahydroacridine-1, 8-diones in PEG. *Tetrahedron Letters*, *51*(20), 2700-2703.

xvii. Mansoor, S. S., Aswin, K., Logaiya, K., Sudhan, S. P. N. (2014). Aqua-mediated synthesis of acridinediones with reusable silica-supported sulfuric acid as an efficient catalyst. *Journal of Taibah University for Science*, *8*(3), 265-275.

xviii. Wang, Y., Liu, X., Du, C. (2017). Dihydroquinolines via the Hantsch Reaction using Hydroxylammonium Carboxylates as Efficient and Recyclable Catalysts under Solvent-free Conditions. *Organic Preparations and Procedures International*, *49*(1), 28-34.

xix. Marjani, A. P., Khalafy, J., Mahmoodi, S. (2016). A simple one-pot synthesis of new 9-aroyl-3, 4, 6, 7, 9, 10-hexahydro-1, 8 (2H, 5H)-acridinediones. *Arkivoc*, *3*, 262-270.

xx. Shi, D. Q., Shi, J. W.,Yao, H. (2009). Three-component one-pot synthesis of polyhydroacrodine derivatives in aqueous media. *Synthetic Communications*, *39*(4), 664-675.

xxi. Putic, A., Stecher, L., Prinz, H., Müller, K. (2010). Structure–activity relationship studies of acridones as potential antipsoriatic agents. 1. Synthesis and antiproliferative activity of simple N-unsubstituted 10H-acridin-9-ones against human keratinocyte growth. *European journal of medicinal chemistry*, *45*(8), 3299-3310.

xxii. Naeimi, H., Nazifi, Z. S. (2014). A facile one-pot ultrasound assisted synthesis of 1, 8-dioxo-octahydroxanthene derivatives catalyzed by Brønsted acidic ionic liquid (BAIL)

under green conditions. *Journal of Industrial and Engineering Chemistry*, *20*(3), 1043-1049.

xxiii. Kim, M. S., Yim, K. G., Son, J. S., Leem, J. Y. (2012). Effects of Al concentration on structural and optical properties of Al-doped ZnO thin films. *Bulletin of the Korean Chemical Society*, *33*(4), 1235-1241.

xxiv. Nasr-Esfahani, M., Rafiee, Z., Kashi, H. (2016). Nanoparticles tungstophosphoric acid supported on polyamic acid: catalytic synthesis of 1, 8-dioxo-decahydroacridines and bulky bis (1, 8-dioxo-decahydroacridine) s. *Journal of the Iranian Chemical Society*, *13*(8), 1449-1461.

xxv. Alinezhad, H., & Mohseni Tavakkoli, S. (2013). Efficient and convenient synthesis of 1, 8-dioxodecahydroacridine derivatives using Cu-doped ZnO nanocrystalline powder as a catalyst under solvent-free conditions. *The Scientific World Journal*, *2013*.

xxvi. (a) *Anastas, P. T.; Warner, J. C.*(1998). *Green Chemistry: Theory and Practice. Oxford University Press, p30,* ISBN. 9780198502340. (b) Clark, J. H. (2002). Solid Acids for Green Chemistry. *Acc. Chem. Res*, **2002**, 35 , 791-797, doi: 10.1021/ar01 0072a.

xxvii. Belbachir, M., Bensaoula, A. (2006). Composition and method for catalysis using bentonites. *U. S. Pat.*, US 7,094,823 B2.

xxviii. Benlahreche, B., Taleb, A., Lahrech, M. B., & Hacini, S. (2019). Isatin Aldazines Synthesis using A Proton Exchanged Algerian Montmorillonite Clay as Acid Eco-friendly Catalyst. *Bulletin of Chemical Reaction Engineering & Catalysis*, *14*(3), 551-557.

xxix. Venkatesan, K.; Satyanarayana, V. S. V.; Sivakumar, A.(2011). Ultrasonic Assisted Synthesis of Naphthalene Substituted Schiff Base Derivatives and Their Antioxidant Activity Studies *Journal of the Chinese Chemical Society*, 2011, *58*, 583-589.

xxx. Ben messaoud, H., Djemoui, A., Souli, L., Benlahrech, B., Naouri, A., Lahrech. M. B.(2020). Maghnite-H^+ clay as a green catalyst was used for the synthesis of new 1,4-dihydropyrimido[1,2-A]benzimidazole derivatives. *Heterocyclic Letters,*10 (4), 551-558.

Received on March 27, 2023.