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A Green Synthesis of Benzimidazole Derivatives and Antibacterial Activity

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Abstract: *A simple catalyst free synthetic method has been developed by the synthesis of Benzimidazole derivatives from 2-chloro benzimidazole and different types of amine derivatives using BENZTONITE CLAY green solvent at room temperature. This method is simple, ecofriendly, rapid and generates 2-amino benzimidazole derivatives and good yield without use any catalysts. Newly synthesized compounds were screened for their antibacterial activity against E.Coli, Bacillus, Pseudomonas, and S.aureus. The structure of benzimidazole derivatives were confirmed by using IR, 1H NMR, Mass spectroscopy*

Keywords: 2-(chloromethyl)-1H-benzo[d]imidazole, catalyst free, green solvent

I. INTRODUCTION

Benzimidazole is an important heterocyclic organic compound. It is having important pharmacophore and a privileged structure in medicinal chemistry. Benzimidazole derivatives is used in different ways such as antifungal, antitubaricular, antioxidant, antiallergic, antiparasitic, herbicidal agent, human and veterinary medicine, anti-HIV, anti-histaminic, anti-ulcer, cardiotonic, antihypertensive, antiviral, anticancer[1-7] activities. We now designed and synthesized a series of novel benzimidazole derivatives from 2-(chloromethyl)-1H- benzo[d]imidazole by applying the principles of green chemistry using BENZTONITE CLAY[8] as an alternative reaction medium. PEG is non-toxic, Inexpensive, potentially recyclable and water soluble, which facilitates it is easily removal from the reaction product. [8-11]

II. EXPERIMENTAL

All the chemicals were used as purchased from S.D.Fine. Solvents and reagents were obtained from commercial sources. TLC analyses were done on plastic sheets coated with silica gel G and spotting was done using Iodine/UV lamp. IR spectra were recorded on a Perkin Elmer model 1000 instrument in KBr Pellet. ^{1}H NMR was recorded in $CDCl_3$/DMSO-d_6 using 400 MHz varian Gemini spectrometer and TMS as reference standard. Mass spectra were recorded on an Agilent-LCMS instrument.

General procedure for the preparation of 4a:

A mixture of 3(0.6gr,10mmol),6-Benzylaminopurine (0.9gr,10mmol), K_2CO_3(1gr,20mmol), KI(0.3gr,3mmol) and different solvent such as Acetonitrile/1,4Dioxane/THF/ETOH/MeOH/DMF was heated at 80-100°C for 2-4 hr. the progress of reaction was monitored by TLC, after completion of reaction, mixture was diluted with water and extracted with Ethyl Acetate (2x25ml). The combined organic layer was washed with water, brine and then dried with anhydrous Na_2SO_4. The organic layer was distilled under reduced pressure, gave respectively. [12-20]

General procedure for the preparation of 4(a-j) under BENZTONITE CLAY:

A mixture of powdered anhydrous K_2CO_3 (1 gr, 20mmol), KI (0.3gr, 3mmol) and 6-Benzyl amino purine/different amine derivatives (10 mmol) was taken in a mortar and ground with a pestle for few minutes. To this mixture, starting material 3(10 mmol) was added and the whole mixture was ground with pestle in the mortar at room temperature. After sometime monitored by TLC after then, mixture was treated with ice-cold water (50ml). Product separated by filtration,

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washed with water and dried to obtain products of room temperature. After sometime monitored by TLC after then, mixture was treated with ice-cold water (50 ml). Product separated by filtration, washed with water, and dried to obtain products of. In these products some compounds already reported. [21-23]

N-((1H-benzo[d]imidazol-2-yl)methyl)-N-benzyl-7H-purin-6-amine (4a):

^{1}H NMR (400 MHz, DMSO-d_6): 7.41ppm (d, 1H, Ar-H), 7.23(t, 1H, Ar-H), 7.23(t, 1H, Ar-H), 7.41(d, 1H, Ar-H), 5.4(s, 1H, NH), 4.9(s, 1H, CH_2), 5.8(s, 1H, CH_2), 12.5(d, 1H, NH), 8.5(d, 1H, CH), 7.9(s, 1H, CH), 7.25(d, 1H, Ar-H), 7.30(t, 1H, Ar-H), 7.28(t, 1H, Ar-H), 7.30(t, 1H, Ar-H), 7.26(d, 1H, Ar-H). ^{13}C NMR (400 MHz, DMSO-d_6): 139.2ppm, 118.6, 127.3, 127.3, 118.6, 139.2, 143.6, 60.1, 57.8, 140.1, 129.6, 130.4, 129.2, 130.4, 129.6, 169.7, 124.5, 150.2, 153.9, 155.3.

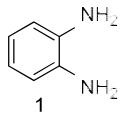
N-((1H-benzo[d]imidazol-2-yl) methyl) butan-2-amine (4j):

^{1}H NMR (400 MHz, DMSO-d_6): 7.41ppm (d, 1H, Ar-H), 7.23(t, 1H, Ar-H), 7.23(t, 1H, Ar-H), 7.41(d, 1H, Ar-H), 5.4(s, 1H, NH), 4.9 (d, 2H, CH2), 3.2(m, 1H, NH), 2.91(m, 1H, CH), 1.57(m, 1H, CH_2), 1.23(d, 3H, CH_3), 0.97(t, 3H, CH_3). ^{13}C NMR (400MHz, DMSO-d_6):139.2ppm, 118.6, 127.3, 127.3, 118.6, 139.2, 143.6, 49.3, 58.7, 33.2, 23.8, 11.9.

III. RESULTS AND DISCUSSION

Scheme-1:

O-phenylene di amine (1) was treated with glycolic acid in presence of 4N HCL at reflux condition for 4hr obtained previously reported 1H-benzo[d]imidizole-2-yl)methanol[17](2).Latter on treatment with $SOCl_2$ at room temperature for 2hr, obtained already reported 2-(chloromethyl)-1H-benzo[d]imidazole[18](3). The reaction of (3) with 6-Benzyl amino purine, K_2CO_3, and KI under refluxing different solvents such as Acetonitrile, DMF, 1,4-Dioxane, MeOH, ETOH, THF, BENZTONITE CLAY, after then resulted in the formation of N-((1H-benzo[d]imidazol- 2-yl)-N-benzyl-7H-purin-6-amine.



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Reagents & conditions: a: glycolic acid, 4N HCl, reflux for 4hr b: $SOCl_2$, room temperature for 2hr c: K_2CO_3, KI, Acetonitrile, DMF, 1, 4-Dioxane, THF, MeOH, ETOH, BENZTONITE CLAY, 6-benzyl amino purine.

The reaction of (3) with 6-benzyl amino purine in presence of different solvents and different reaction conditions, reaction is monitored by TLC and subsequent workup yielded product identical with one to each one, in all respects characterized by comparison with IR, M.P Data. BENZTONITE CLAY use as a solvent, obtained good yield compared to remaining all solvent systems.

Entry	Solvent	Time/min.	Yield (%)
1	Solvent-free	600	-
2	Acetonitrile	160	74
3	DMF	175	68
4	THF	200	80
5	1,4-Dioxane	190	82
6	MeOH	225	60
7	ETOH	210	65
8	BENZTONITE CLAY	40	96

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Scheme-2:

Reaction between 3 and 6-Benzyl amino purine in the presence of BENZTONITE CLAY we obtained good yield and less time. BENZTONITE CLAY has been found to be a general one and has been extended to different nitrogen nucleophilic substrates such as 6-Benzyl amino purine, Isobutyl amine, Piperidine, Morpholine, pyrrolidine, Benzyl amine, Diethylamine, Piperazine, Methyl piperazine, n-Butyl amine.

Biological Activity:

Newly synthesized compounds were screened for antibacterial activity study purpose micro-organisms employed were Gram positive (Bacillus, S.aureus), Gram negative (E.Coli, Pseudomonas).

Table-3: Antibacterial activity (Diameters in mm of zone of inhibition)

Sr.No	product	E.Coli(mm)	Bacillus(mm)	S.aureus(mm)	Pseudomonas
1	4a	24	28	20	21
2	4b	25	22	18	16
3	4c	22	19	13	12
4	4d	16	17	14	18
5	4e	13	11	10	10
6	4f	11	11	<10	<10
7	4g	12	10	13	10
8	4h	13	10	11	11
9	4i	15	13	13	12
10	4j	16	18	19	14

IV. CONCLUSION

In summary, we have developed a simple and efficient method for preparation of new Benzimidazole derivatives in solution phase and also under catalyst-free conditions using BENZTONITE CLAY at room temperature. Present protocol has several advantages, particularly catalyst-free condition, during workup, water was used which is free from organic solvent, readily available catalyst.

REFERENCES

[1] Ayhan-Kilcigil, G.; Altanlar, N. Synthesis Anti-fungal properties of some benzimidazole derivatives. Turk. J. Chem., 2006, 30, 223-228.

[2] Mohamed, B.G.; Hussein, M.A.; Abdel-Alim, A.M.; Hashem, M. Synthesis and antimicrobial activity of some new 1-alkyl-2-alkyl thio-1, 2, 4-triazolobenzimidazole derivatives. Arch. Pharm. Res., 2006, 29, 26-33.

[3] Nakano, H.; Inoue, T.; Kawasaki, N.; Miyataka, H.; Matsumoto, H.; Taguchi, T.; Inagaki, N.; Nagai, H.; Satoh, T. Synthesis of benzimidazole derivatives as antiallergic agent with 5-lipoxygenase inhibiting action. Chem.Pharm. Bull., 1999, 47, 1573-1578.

[4] Valdez, J.; Cedillo, R.; Hernandez-Campos, A.; Yepez, L.; Hernandez-Luis, F.; Navarrete-Vazquez, G.; Tapia, A.; Cortes, R.; Hernandez, M.; Castillo, R. Synthesis and antiparasitic activity of 1H- Benzimidazole derivatives. Bioorg. Med. Chem. Lett., 2002, 12, 2221-2224.

[5] A Chemirri; S Grasso; AM Monforte; PMonforte; M Zappala. I Farmaco, 1991, 46, 925- 933.

[6] Klshihara; T lchikawa; Y Komuro; S Ohara; K Hotta; F Arzneim. Drug Res., 1994, 44, 827-830.

[7] T.Sriinivas Reddy, Hitesh Kalahari, V. Ganga Reddy, Vipul Bansal, Ahmed Kamal, Ravi Shukla, Design, synthesis and Biological evaluation of 1,3-di phenyl-1H pyrazole derivatives containing benzimidazole Skeleton as potential anticancer and apoptosis inducing agents, European Journal of Medicinal Chemistry 101 (2015) 790-805.

[8] Dindianan Patil ,Gurumeet Wadhawa sodium sulphate as mild and versatile catalyst for the rapid synthesis of β-acetamido ketones and ketoesters via a three component reaction, Unique journal of pharmaceutical and biological sciences 01 (03): 2013, Page 45-47 ISSN 2347-3614

[9] Indianan D. Patil Dnyandeo K. Mhaske Gurumeet C. Wadhawa anhydrous nickel chloride as efficient catalyst UTCS 2013 1(1) 58-61 978-81-905776-99-9

[10] Indianan D. Patil Dnyandeo K. Mhaske Gurumeet C. Wadhawa Ultrasonic promoted synthesis of N-benzylidenethiophene 2 carbohydrazide UTCS 2013 1(1) 75-77 978-81-905776-99-9

[11] Gurumeet C. Wadhawa, Indianan D. Patil ,Dnyandeo K. Mhaske Bentonite clay in green synthesis of betaacetaamido ketones and their microbial activity EISD Envoi mental Issue for sustainable development 2014 1(1), 89-95 ISBN 978-81-930-154-0-7

[12] Gurumeet C Wadhawa, Indianan D. Patil Dnyandeo K. Mhaske. Bentonite clay in green synthesis of betaacetaamido ketones bio nano frontiess Vol 8 issue 3 ,2015 ,140-142, ISSN 0974-0678

[13] Indianan D. Patil Dnyandeo K. Mhaske Gurumeet C. Wadhawa synthesis of biological potent chromones derivatives IRTCPS 2015 1(1) 56-60 978-81-92394-0-3

[14] Gurumeet Wadhawa Green protocol for synthesis of 7 (1Hbenzimidazol-2-Yl)-5-(Substituted Phenyl). Pyrido [2, 3-D] Pyrimidin-4-Amine. international journal of chemical and physical sciences 7(7) 158-161 2319-6602

[15] Gurumeet Wadhawa Yashwant Gaikwad Vitthal S Shivankar Synthesis of the coumarine under green approach using ferrous sulphates JOURNAL OF PHARMA RESEARCH 2019 8(4),132-135

[16] Gurumeet Wadhawa Yashwant Gaikwad one pot four component dakin west synthesis of betaacetamido ketone research journey 1(1)117-120 168 A

[17] Gurumeet Wadhawa Yashwant Gaikwad Vitthal S Shivankar Haldighati soil an efficient recyclable and inexpensive catalyst innovation for sustainable development 2019 1(1) 38-42 980-32-145-7188

[18] Gurumeet Wadhawa Yashwant Gaikwad Vitthal S Shivankar one pot four component dakin west synthesis of betaacetamido ketone by green route innovation for sustainable development 2019 1(1) 61-65 980-32-145-7188

[19] Gurumeet Wadhawa Yashwant Gaikwad Vitthal S Shivankar synthesis of 4 aryl 3-4 dihydropyrimidine innovation for sustainable development 2019 1(1) 31-38 980-32-145-7188

[20] Gurumeet Wadhawa Yashwant Gaikwad Vitthal S Shivankar ferrous sulphate catalysed synthesis by microwave innovation for sustainable development 2019 1(1) 108-110 980-32-145-7188

[21] Gurumeet Wadhawa Yashwant Gaikwad Vitthal S Shivankar PINEAPPLE JUICE AS EFFIE CENT CATALYST FOR 2 NAPTHOLNRIC 2019 1(1) 83-87 980-32-145-7188

[22] Gurumeet Wadhawa Yashwant Gaikwad Vitthal S Shivankar one pot conversion of heterocyclic compounds NRIC 2019 1(1) 79-83 980-32-145-7188

[23] Gurumeet Wadhawa Yashwant Gaikwad Vitthal S Shivankar CE Complex an efficient, recyclable and inexpensive catalyst for the one-pot synthesis of 5-alkoxycarbonyl-4-aryl-3, 4-dihydropyrimidin-2 (1H)-ones derivatives.2020 tathapi Journal 9 (19) 503-508