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Metal-free, effective and one-pot Synthesis of tetrahydro-pyrimidine-5-carbonitriles using boric acid as a green catalyst

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ABSTRACT:

A green, novel, Solvent-free, and efficient method has been developed for the tetra-hydro-pyrimidine derivatives one-pot three-component reaction ethyl cyanoacetate, aldehyde and Urea in the presence of Boric Acid. This method has cyclized various factionalized amines and aldehydes, including aliphatic, aromatics, and heteroaromatic compounds. The cyclisation of ethyl cyanoacetate, aldehyde and Urea these compounds occurred in a single step without any side reaction. The key benefits of this reaction are nontoxic, cheap, environment friendliness and biodegradable catalyst at normal green atmospheric conditions in the absence of solvent. This helps to make the procedure practical, affordable, and biodegradable.

Keywords. Ethyl cyanoacetate, Aldehyde, Urea, Boric Acid, Green reaction condition.

1. Introduction

Green synthesis has a large importance in current synthetic chemistry due to environmental, health and societal concerns [1]. It has many diverse scopes in different sectors like pharmaceutical, industry, and academia due to their facile, clean, efficient and non-polluting synthetic procedures that reduce the use of organic toxic catalysts, solvents and reagents. Except for a few solvents such as water, ethanol, glycerol, and ionic liquid, ethylene glycol (EG) is considered to be the most important green solvent which has a high boiling point, low viscosity, high specific energy and is easily miscible with many other organic solvents. These unique properties made it highly applicable in industry such as automobiles, fine chemicals, plastics, and textiles. It also plays important roles in nano chemistry such as reducing agent or ligand [2]. The need to reduce the amount of toxic waste and by-products arising from chemical processes requires increasing emphasis on the use of less toxic and environmentally compatible materials in the design of new synthetic methods. One of the most promising approaches is using green catalysts as the reaction media [3].

Pyrimidine compounds continue to attract great interest in the field of organic synthesis due to their various chemical and biological applications observed, especially in recent times. Heterocyclic compounds containing pyrimidine moiety are gaining the focus in recent research due to their wide range of biological activities such as anti-inflammatory, antioxidant, antimicrobial, antitumor, antiviral, antidepressant, antiplatelet, antihypertensive and herbicidal [4]. Additionally, pyrimidine-containing compounds are found in many pharmaceutical medications and as natural products. Pyrimidines are the most important member of all the diazines as this ring occurs in many compounds vital to living system. They are non-basic, stable, colourless and soluble in water [5]. The pKa value of pyrimidine is 1.3. The drop in the basicity is believed to be the consequence of destabilization of the N-1 protonated cations by the inductive electron withdrawal by the second nitrogen. The chemistry of pyrimidine is widely studied. The introduction of alkyl groups in pyrimidine enhances the basicity. The literature revealed that various synthetic methods and various reactions were reported for pyrimidines [6-8].

Pyrimidines are a class of aromatic heterocyclic organic compounds that play crucial roles in the structure and function of nucleic acids, which are the building blocks of genetic material in living organisms. There are three major pyrimidines: cytosine (C), thymine (T), and uracil (U). These molecules are essential components of DNA and RNA, the two types of nucleic acids [9-11]**.** Cytosine is one of the four nitrogenous bases found in DNA. It pairs with guanine (G) through specific hydrogen bonding interactions, forming a complementary base pair. The chemical structure of cytosine includes a pyrimidine ring composed of carbon and nitrogen atoms. Thymine is another pyrimidine found in DNA. It pairs with adenine (A) in DNA through hydrogen bonds, forming a complementary base pair. It is important to note that in RNA, thymine is replaced by uracil. Uracil is a pyrimidine base found in RNA. It pairs with adenine (A) in RNA through hydrogen bonds, forming a complementary base pair [12].

Unlike DNA, RNA does not contain thymine; instead, it contains uracil as the counterpart to adenine. The presence of pyrimidines in nucleic acids is fundamental to the storage and transmission of genetic information. The synthesis and regulation of pyrimidines are tightly controlled in living organisms, as they are essential for cellular processes such as DNA replication, transcription, and translation. Enzymes and metabolic pathways are involved in the biosynthesis of pyrimidines to maintain the necessary pool of these molecules within cells [13-16]. Understanding the structure and function of pyrimidines is crucial for various fields, including molecular biology, genetics, and medicinal chemistry. Researchers and scientists explore the roles of pyrimidines in health and disease, and this knowledge contributes to the development of therapeutic interventions and drugs targeting nucleic acid-related processes.

The cyclocondensation reaction of trifluoromethyl β-elimination diketone to produce the 6-trifluoromethyl-5-benzoyl-2-methylsulfanyl pyrimidines regio and chemo-selective method. Imines are formed by 2-aminopyridines and aldehyde use of Rh (III) catalyzed imidoyl C-H activation and coupling with diazo ester to give pyrido [1,2-a] pyrimidine-4-ones [17-20].
Some of the reported methods have their merit such as: Multi-step synthesis with the use of expensive harmful reagents and low yields. Thus, the development of an efficient method for the synthesis of biologically active compounds such as tetrahydro-pyrimidine-5-carbonitrile, in one step would be highly valuable and desirable.

Experimental

2.1 *Material and Methods*

The organic compounds, chemicals, and reagents (Spectrochem, Loba, Merck and Sigma-Aldrich) were used for the synthesis without any purification. The physical constant of synthesized molecules was determined in open-sealed capillary tubes. The organic compounds were characterized using ^{1}H-NMR and ^{13}C-NMR spectra. The reaction progress was monitored on an (Aluminium plate) TLC technique.

2.2 *General procedure for the cyclization of three component*

The reaction was performed between benzaldehyde (1 mmol), Urea (1 mmol) and Ethylcyano Acetate (1 mmol), in boric acid (5 mol %) under solvent-free conditions with the grindstone method at room temperature for the appropriate time. The reaction progress was monitored on TLC. After the completion of the reactions, the reaction mixture was added in water(15ml) and filtered, to obtain crude product. The catalyst is dissolved in water.

Spectral Data

2,4-dioxo-6-phenyl-1,2,3,4-tetrahydro-pyrimidine-5-carbonitrile (4a)

^{1}H NMR (400 MHz, DMSO, δ ppm): 6.0 (s, H, -NH), 10.0 (s, H, -NH), 7.30 (d, 1H, -CH), 7.21 (d, 1H, CH), 7.14 (d, 1H, CH), 7.21 (s, 1H, CH), 7.30(d, 1H, CH). ^{13}C NMR (400 MHz, DMSO, δ ppm): 168.9, 151.5, 164.4, 72.2, 134.9, 126.2, 128.4, 127.7, 128.4, 126.2, 117.2.

2,4-dioxo-6-p-tolyl-1,2,3,4-tetrahydro-pyrimidine-5-carbonitrile (4b)

^{1}H NMR (400 MHz, DMSO, δ ppm): 6.0 (s, H, -NH), 10.0 (s, H, -NH), 7.18 (d, 1H, -CH), 7.18 (d, 1H, CH), 7.01 (d, 1H, CH), 7.01 (d, 1H, CH), 2.35(q, 3H, CH_3). ^{13}C NMR (400 MHz, DMSO, δ ppm): 151.5, 164.4, 72.2, 168.9, 131.9, 136.9, 129.1, 126.1, 117.2. 20.9.

6-(4-Methoxy-phenyl)-2,4-dioxo-1,2,3,4-tetrahydro-pyrimidine-5-carbonitrile (4c)

^{1}H NMR (400 MHz, DMSO, δ ppm): 6.0 (s, H, -NH), 10.0 (s, H, -NH), 7.19 (d, 1H, -CH), 6.72 (d, 1H, CH), 6.72 (d, 1H, CH), 7.19 (d, 1H, CH), 3.73(q, 3H, CH_3). ^{13}C NMR (400 MHz, DMSO, δ ppm): 151.5, 164.4, 72.2, 161.2, 168.9, 131.9, 136.9, 129.1, 126.1, 127.2, 114.0, 117.2, 56.0.

6-(4-Dimethylamino-phenyl)-2,4-dioxo-1,2,3,4-tetrahydro-pyrimidine-5-carbonitrile (4d)

^{1}H NMR (400 MHz, DMSO, δ ppm): 6.0 (s, H, -NH), 10.0 (s, H, -NH), 7.12 (d, 1H, -CH), 6.54 (d, 1H, CH), 6.54 (d, 1H, CH), 7.12 (d, 1H, CH), 2.85(q, 3H, CH_3), 2.85(q, 3H, CH_3).
^{13}C NMR (400 MHz, DMSO, δ ppm): 151.5, 164.4, 72.2, 168.9, 117.2,124.4, 127.1, 113.0, 143.7, 43.6

6-(4-Chloro-phenyl)-2,4-dioxo-1,2,3,4-tetrahydro-pyrimidine-5-carbonitrile (4e)

^{1}H NMR (400 MHz, DMSO, δ ppm): 6.0 (s, H, -NH), 10.0 (s, H, -NH), 7.24 (d, 1H, -CH), 7.22 (d, 1H, CH), 7.22 (d, 1H, CH), 7.24 (d, 1H, -CH). ^{13}C NMR (400 MHz, DMSO, δ ppm): 151.5, 164.4, 72.2, 168.9, 117.2, 133.0, 127.6, 128.8,
133.0, 127.6, 128.8,

6-(4-Hydroxy-phenyl)-2,4-dioxo-1,2,3,4-tetrahydro-pyrimidine-5-carbonitrile (4f)

^{1}H NMR (400 MHz, DMSO, δ ppm): 6.0 (s, H, -NH), 10.0 (s, H, -NH), 7.13 (d, 1H, -CH), 6.68 (d, 1H, CH), 6.68 (d, 1H, CH), 7.13 (d, 1H, -CH). 5.00 (s, 1H, OH). ^{13}C NMR (400 MHz, DMSO, δ ppm): 151.5, 164.4, 72.2, 168.9, 117.2, 127.5, 127.6, 115.6,
156.5, 127.6.

6-(2-Nitro-phenyl)-2,4-dioxo-1,2,3,4-tetrahydro-pyrimidine-5-carbonitrile (4g)

^{1}H NMR (400 MHz, DMSO, δ ppm): 10.0 (s, H, -NH), 6.0 (s, H, -NH), 8.14 (d, 1H, -CH), 7.40 (d, 1H, CH), 7.60 (d, 1H, CH), 7.56 (d, 1H, -CH). ^{13}C NMR (400 MHz, DMSO, δ ppm): 151.5, 164.4, 72.2, 168.9, 117.2, 130.0, 146.1, 123.5, 128.6, 134.5, 127.1.

6-(2-Hydroxy-phenyl)-2,4-dioxo-1,2,3,4-tetrahydro-pyrimidine-5-carbonitrile (4h)

^{1}H NMR (400 MHz, DMSO, δ ppm): 10.0 (s, H, -NH), 6.0 (s, H, -NH), 6.68 (d, 1H, -CH), 6.97 (d, 1H, CH), 6.77 (d, 1H, CH), 7.13 (d, 1H, -CH), 5.00 (s, 1H, OH). ^{13}C NMR (400 MHz, DMSO, δ ppm): 151.5, 164.4, 72.2, 168.9, 117.2, 122.1, 155.0, 115.6,
129.1, 121.0, 127.6.

2,4-dioxo-6-styryl-1,2,3,4-tetrahydro-pyrimidine-5-carbonitrile (4i)

^{1}H NMR (400 MHz, DMSO, δ ppm): 10.0 (s, H, -NH), 6.0 (s, H, -NH), 7.30 (d, 1H, -CH), 7.21 (d, 1H, CH), 7.14 (d, 1H, CH), 7.21 (d, 1H, -CH), 7.30 (d, 1H, -CH), 6.85 (d, 1H, -CH), 6.65 (d, 1H, CH). ^{13}C NMR (400 MHz, DMSO, δ ppm): 151.5, 164.4, 76.2, 170.0, 117.2, 125.9, 128.8, 134.9, 126.2, 128.4, 127.7.

6-(4-Nitro-phenyl)-2,4-dioxo-1,2,3,4-tetrahydro-pyrimidine-5-carbonitrile (4j)

^{1}H NMR (400 MHz, DMSO, δ ppm): 10.0 (s, H, -NH), 6.0 (s, H, -NH), 7.56 (d, 1H, -CH), 8.14 (d, 1H, CH), 8.14 (d, 1H, CH), 7.56 (d, 1H, -CH). ^{13}C NMR (400 MHz, DMSO, δ ppm): 151.5, 164.4, 72.2, 168.9, 117.2, 141.0, 127.1, 123.5, 147.6.

6-Methyl-2,4-dioxo-1,2,3,4-tetrahydro-pyrimidine-5-carbonitrile (4k)

^{1}H NMR (400 MHz, DMSO, δ ppm): 10.0 (s, H, -NH), 6.0 (s, H, -NH), 1.71 (q, 3H, CH_3).
^{13}C NMR (400 MHz, DMSO, δ ppm): 151.5, 164.4, 75.8, 165.8, 117.2, 16.2.

6-Ethyl-2,4-dioxo-1,2,3,4-tetrahydro-pyrimidine-5-carbonitrile (4l)

^{1}H NMR (400 MHz, DMSO, δ ppm): 10.0 (s, H, -NH), 6.0 (s, H, -NH), 2.00 (t, 2H, CH_2), 1.06 (q, 3H, CH_3). ^{13}C NMR (400 MHz, DMSO, δ ppm): 151.5, 164.4, 75.0, 170.4, 117.2, 23.9, 7.7.

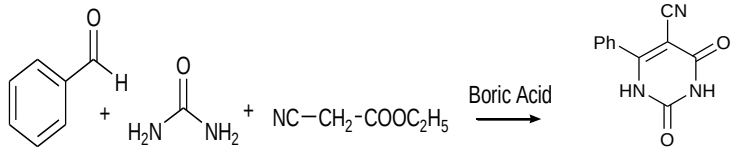
2. Result and Discussion

In this context, we introduce an efficient one-pot three-component reaction of aldehydes **A** Urea **B** and Ethylcyano Acetate **C** and the green method for synthesis of tetrahydro-pyrimidine using grinding and also in the presence of catalytic amounts of Boric Acid (5 mol %).

To develop a more efficient process, reduce the number of separate reaction steps, and minimize by-products for the synthesis of tetrahydro-pyrimidines and in continuous of our previous work on the development of new and efficient methods for the preparation of heterocyclic compound a convenient, practical, inexpensive, rapid procedure for the preparation of tetrahydro-pyrimidine derivatives was reported.

To explore the scope and versatility of this method, various catalysts and solvents were investigated. We used the reaction of Aromatic Aldehyde (**A**, 1 mmol), and Urea (**B**, 1 mmol) Ethylcyano Acetate (**C**, 1 mmol), for the preparation of compound **D** as a model and various catalysts and solvents such as Diammonium hydrogen phosphate [(NH4)2HPO4] (DAHP), Potassium Carbonate, glacial acetic acid (HOAc), ethanol, glycol, water and N, N-dimethylformamide (DMF) as Catalyst and solvent were used, also reaction was checked in solvent-free condition at room tamp respectively. All the reactions were carried out at the room tamp. The results are summarized in **Table 1**. The temperature characteristics of a catalyst under grinding conditions are dependent on the dielectric properties of the catalyst. This fact is shown in **Table 1**, where the best result was achieved using Boric acid as a catalyst. So Boric acid was chosen as the reaction catalyst. To optimize the other reaction conditions the different

temperatures for the same reaction were examined, so the green method at grinding condition gave the highest yield and the minimum temperature reached during the reaction was 40˚C. **Table 2** shows the results obtained in the reaction of a series of representatives with aldehydes **A** Urea **B** and Ethylcyano Acetate **C** under the green method. We have used catalyzed by Boric Acid at grinding conditions for the preparation of the corresponding product. In this manner and to optimize the reaction conditions the catalytic amount of Boric Acid was varied finding that 5 mol% of Boric Acid afforded the best yields. It is important to note that in the absence of Boric Acid, the reaction times increased, meanwhile the yield is decreased mainly. The result is summarized in **Table 2.** To optimize the reaction conditions the catalytic amount of Boric Acid was varied finding that 5 mol% of Boric Acid afforded the best yields.



A **B** **C** **D**

Scheme 1. Synthesis of 2,4-Dioxo-6-phenyl-1,2,3,4-tetrahydro-pyrimidine-5-carbonitrile

Table 1. Optimization of reaction condition for the synthesis of compound.

Catalyst/Solvent	Time (min)	T(^{0}C)	Yield(%)
K_2CO_3	5h	80^0	42
DAHP	10	120^0	91
Toluensulfonic Acid (p-TSA)	3-4 h	80^0	91
Rhodium (III)	1h	140^0	94
$ZrCl_4$	24 h	r.t	83
$CHCl_3$	1	Reflux	90
MeCN	8	Reflux	95
HOAc	10	120	42
EtOH	7	120	61
Glycol	8	120	72
H_2O	12	120	71
DMF	5	120	93
Solvent-free	7	120	70

Table 2. Preparation of 2,4-Dioxo-6-phenyl-1,2,3,4-tetrahydro-pyrimidine-5-carbonitrile

Product	Ar	Yield [%]	Time(min)	M.P/ B.P	Molecular Formula
4a	C_6H_5 -	60	15	288	$C_{11}H_7N_3O_2$
4b	4-H_3C-C_6H_4	**58**	**17**	**205**	$C_{12}H_9N_3O_2$
4c	4-H_3CO-C_6H_4	**50**	**16**	**205**	$C_{13}H_9N_3O_3$
4d	4-$(H_3C)_2N$-C_6H_4	58	**18**	**205**	$C_{13}H_{12}N_4O_2$
4e	4-CI-C_6H_4	**55**	**15**	**390**	$C_{11}H_6ClN_3O_2$
4f	4-HO-C_6H_4	**55**	**18**	**205**	$C_{11}H_7N_3O_3$ (280)
4g	2-NO_2 – C_6H_4	**60**	**19**	**205**	$C_{11}H_6N_4O_4$ (272)
4h	2-HO- C_6H_4	**65**	**18**	**612**	$C_{11}H_7N_3O_3$
4i	C6H5CH=CHCHO	**70**	**17**	**305**	$C_{11}H_9N_3O_2$

4j	4-NO_2-C_6H_4	**65**	**18**	**220**	$C_{11}H_6N_4O_4$
4k	CH_3 -	**70**	**18**	**205**	$C_6H_5N_4O_2$
4l	CH_3-CH_2 -	**72**	**19**	**210**	$C_7H_7N_3O_2$

* All product gave satisfactory green method

3. Conclusions

The newly developed, green, metal-free, and efficient methodology has been developed for the synthesis of tetrahydro-pyrimidine-5-carbonitrile derivatives via three-component condensation of aromatic aldehyde, urea and ethylcyanoacetate grinding conditions and in the presence of the catalytic amount of a cheap catalyst boric acid. This protocol is a highly effective, eco-friendly reaction with moderate conditions, excellent yields, high selectivity, ease of separation, and solvent-free reaction, showing the criterion for a green chemistry practice. The prepared organic compound was characterized by using ^{1}H-NMR and ^{13}C-NMR techniques.

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4. References

1. Atapour-Mashhad, H., Soukhtanloo, M., Massoudi, A., Shiri, A., & Bakavoli, M. (2016). Synthesis and evaluation of cytotoxicity of 6-amino-4-aryl-2-thioxo-1, 2, 3, 4-tetrahydropyrimidine-5-carbonitriles. Russian Journal of Bioorganic Chemistry, 42, 316-322.
2. Eweas, A. F., Abdallah, Q. M., & Hassan, E. S. (2014). Design, synthesis, molecular docking of new thiopyrimidine-5-carbonitrile derivatives and their cytotoxic activity against HepG2 cell line. Journal of Applied Pharmaceutical Science, 4(12), 102-111.
3. Mohamed, M. S., Awad, S. M., & Ahmed, N. M. (2011). Synthesis and antimicrobial activities of new indolyl-pyrimidine derivatives. Journal of Applied Pharmaceutical Science, (Issue), 76-80.
4. Mohamed, M. S., Awad, S. M., & Ahmed, N. M. (2011). Synthesis and antimicrobial activities of new indolyl-pyrimidine derivatives. Journal of Applied Pharmaceutical Science, (Issue), 76-80.
5. Ould M'hamed, M., & Alduaij, O. K. (2014). An efficient one-pot synthesis of new 2-thioxo and 2-oxo-pyrimidine-5-carbonitriles in ball-milling under solvent-free and catalyst-free conditions. Phosphorus, Sulfur, and Silicon and the Related Elements, 189(2), 235-241.
6. Abdel-Latif, E., Fahad, M. M., & Ismail, M. A. (2020). Synthesis of N-aryl 2-chloroacetamides and their chemical reactivity towards various types of nucleophiles. Synthetic Communications, 50(3), 289-314.
7. Balasubramaniyan, S., Irfan, N., Umamaheswari, A., & Puratchikody, A. (2018). Design and virtual screening of novel fluoroquinolone analogs as effective mutant DNA GyrA inhibitors against urinary tract infection-causing fluoroquinolone resistant Escherichia coli. RSC advances, 8(42), 23629-23647.
8. Navabshan, I., Sakthivel, B., Pandiyan, R., Antoniraj, M. G., Dharmaraj, S., Ashokkumar, V., ... & Show, P. L. (2021). Computational lock and key and dynamic trajectory analysis

of natural biophors against COVID-19 spike protein to identify effective lead molecules. Molecular biotechnology, 63(10), 898-908.

9. Sugumaran, A., Pandiyan, R., Kandasamy, P., Antoniraj, M. G., Navabshan, I., Sakthivel, B., ... & Ngamcharussrivichai, C. (2022). Marine biome-derived secondary metabolites, a class of promising antineoplastic agents: A systematic review on their classification, mechanism of action and future perspectives. Science of the Total Environment, 836, 155445.
10. Balasubramaniyan, S., Irfan, N., Senthilkumar, C., Umamaheswari, A., & Puratchikody, A. (2020). The synthesis and biological evaluation of virtually designed fluoroquinolone analogs against fluoroquinolone-resistant Escherichia coli intended for UTI treatment. New Journal of Chemistry, 44(31), 13308-13318.
11. Puratchikody, A., Irfan, N., & Balasubramaniyan, S. (2019). Conceptual design of hybrid PCSK9 lead inhibitors against coronary artery disease. Biocatalysis and Agricultural Biotechnology, 17, 427-440.
12. Santhaseelan, H., Dinakaran, V. T., Sakthivel, B., Somasundaram, M., Thanamegam, K., Devendiran, V., ... & Rathinam, A. J. (2022). Bioactive efficacy of novel carboxylic acid from halophilic Pseudomonas aeruginosa against methicillin-resistant Staphylococcus aureus. Metabolites, 12(11), 1094.
13. Irfan, N., Balasubramaniyan, S., Ali, D. M., & Puratchikody, A. (2023). Bioisosteric replacements of tyrosine kinases inhibitors to make potent and safe chemotherapy against malignant cells. Journal of Biomolecular Structure and Dynamics, 41(19), 9437-9447.
14. Nagendran, S., Balasubramaniyan, S., & Irfan, N. (2023). Virtually screened novel sulfathiazole derivatives as a potential drug candidate for methicillin-resistant Staphylococcus aureus and multidrug-resistant tuberculosis. Journal of Biomolecular Structure and Dynamics, 41(11), 5086-5095.
15. Venkatesh, G., Vennila, P., & Balasubramaniyan, S. (2024). Solvent effects, chemical reactivity, docking and antimicrobial activity of silver and gold nanocages glimepiride: Experimental and theoretical calculations. Chemical Physics Impact, 8, 100498.
16. Kotakonda, M., Marappan, M., Dharmar, P., Sakthivel, B., & Sunnapu, P. (2023). Isolation and Identification of Bioactive Compounds with Antimicrobial Activity from Marine Facultative Anaerobe, Bacillus subtilis. Current Pharmaceutical Biotechnology, 24(5), 698-707.
17. Kenwade S, Khot S, Kapase V, Desai S (2016). Environmentally, Benign Protocol For The Synthesis of Some Novel Oxadiazinane-4-Thione Derivatives as Promising Agent in Biliary Tract Disorders Treatment. Word Journal of Pharmaceutical Research, 5(8), 930-937.
18. Bhosale V, Sasane K, Sasane D, Kapase V and Patil L(2018). Oxone and Iodobenzene are useful reaction system for synthesis of 2-aminothiazole derivatives from easily available thiourea and alkyl / aryl ketones. IJPSR, 9(8), 3469-3473.
19. Bhosale Vikas R., Sasane Nitin A., Sasane Kulbhushan A., and Patil Limbaraj R. (2019), Intrinsic catalytic activity of an acidic ionic liquid as a solvent for synthesis of 2-amino thiazole derivatives. JETIR, , 6 (1), 642-647.
20. Bhosale Vikas R., Kapase Valmik, Sasane Kulbhushan A., and Patil Limbaraj R., (2022), Microwave irradiated green and efficient synthesis of substituted 1H1,2,4-triazol-3-substituted carboxylic acid and their Schiff bases and comparative study of their microbial activities, Bull. Env. Pharmacol. Life Sci, (1), 1611-1618.