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Solvent-Free Microwave Assisted Fluorspar Mineral Reusable Catalyst for the Synthesis of Pyrimidines

Venkateshwarlu Jetti[1]*, Praveen Chidurala[1], Jyotsna S. Meshram[1]
1. Department of Chemistry, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur – 440 033, Maharashtra, India.

ABSTRACT

An easy solvent-free synthesis of pyrimidine derivatives from aldehydes, aceto acetanilide and urea/thiourea by using fluorspar mineral as catalyst has been described under microwave irradiation. The salient features of this one-pot protocol are short reaction times (4-5 min), excellent yields, cleaner reaction profiles and simple work-up. Also, the catalyst can be reused without any reduction in efficiency.

Keywords: Biginelli reaction, Pyrimidines, Fluorspar catalyst, Microwave irradiation.

*Corresponding Author Email: venkatesh.jetti@gmail.com
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INTRODUCTION

Green chemistry is a quickly developing field that provides us a proactive path for the sustainable progress of future science and technologies[1]. Green chemistry uses highly efficient and environmental benign synthetic procedures to deliver life saving medicines, accelerating guide optimization processes in drug discovery, with reduced needless environmental impact. Green chemistry also offers enhanced chemical process economics concomitant with a reduced environmental burden. From this point view, it is advantageous to use microwave as a safe, abundant and environmentally benign method instead of classical methods.

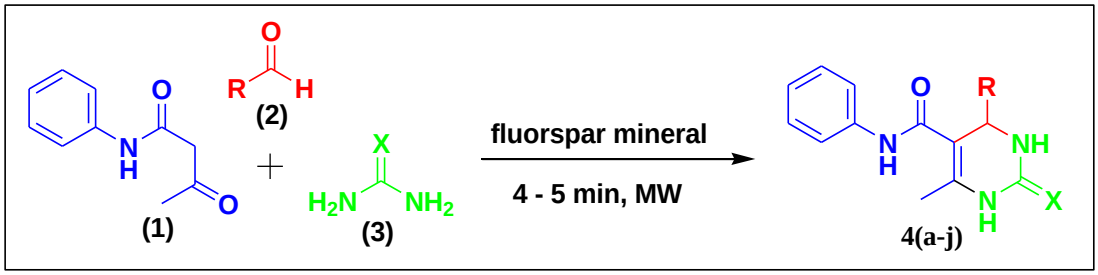
Microwave (MW) irradiation has gained popularity in the past decade as a powerful tool for rapid and efficient synthesis of a variety of organic compounds because of the selective absorption of microwave energy by polar molecules [2]. The application of MW irradiation to provide enhanced reaction rate and improved product yield in chemical synthesis has been extended to modern drug discovery [3] in complex multi-step synthesis [4], include solid-phase organic synthesis[5], the use of polymer supported reagents[6], synthesis on soluble polymer supports[7], parallel processing[8], the construction of libraries in automated format by use of microwave technology[9] and it is proving quite successful in the formation of a variety of carbon–heteroatom and carbon–carbon bonds [10].

In the past decade, pyrimidines and their derivatives have attracted considerable interest because they exhibit promising activities as calcium channel blockers, antihypertensive agents, as α-1a-antagonists and neuropeptide Y (NPY) antagonists[11]. Furthermore, several isolated bioactive marine alkaloids were also found to contain a 2-amino-1,4-dihydropyrimidinone-5-carboxylate core [12]. Most notable among them are batzalladine alkaloids, which have been found to be potent HIVgp-120-CD4 inhibitors[13]. Their derivatives exhibit a wide spectrum of biological effects including antifungal, antiviral, anticancer, antibacterial, anti-inflammatory, and antihypertensive effects [14].

Similarly, several therapeutically interesting biological activities of chromones have been reported including anticancer [15-19], anti-HIV [20-21] and anti oxidant properties [22-23]. The remarkable biological properties of these categories of heterocycles oriented our attention to the synthesis of the series of new heterocyclic derivatives combining urea/thiourea and ethyl/methyl acetoacetate moiety in one molecular frame as new possible biological active compounds. Herein, the synthesis of DHPMs of chromone, 7-hydroxy chromone as well as other aromatic aldehydes is reported in this paper under microwave irradiation. Thus, a synthesis of this heterocyclic nucleus has been of much importance in current years.

The simple and direct method originally reported by Biginelli[24] for the synthesis of dihydropyrimidinones often suffers from low yields of products in the case of substituted aromatic and aliphatic aldehydes [25]. This has led to the recent discovery of several one-pot methodologies for the synthesis of DHPM derivatives involving the use of a number of catalysts such as $ZrCl_4$ 26, $CuCl_2.2H_2O$–HCl [27], LiBr [28], $LaCl_3$-graphite[29], $InBr_3$[30], GaX_3[31], $ZnBr_2$[32], 1,1,3,3-tetramethylguanidinium trifluoroacetate[33], $Cu(OTf)_2$[34], [bmim] BF_4-immobilized Cu(II) acetylacetonate[35], [bmim] $[FeCl_4]$ [36]and CaF_2[37]. However, many of these methods also suffer from drawbacks, such as the involvement of expensive reagents. Though the reusability of the catalyst has been claimed in three cases [34-35], it has been demonstrated only for $Cu(OTf)_2$[34].

The use of solid acid catalysts has gained a vast importance in organic synthesis due to their several advantages such as no toxicity, reusability, low cost, operationally simplicity and ease of isolation after completion of the reaction. Here we reporting first time that fluorspar rock mineral (fluorite), which can be used as an effective reusable catalyst for the synthesis of pyrimidine derivatives (**Scheme 1**) under microwave irradiation. It is a cheap and non-toxic reagent.



Scheme 1: MW assisted synthesis of substituted pyrimidines using fluorspar mineral 4(a-j).

MATERIALS AND METHOD:

Materials:

All the chemicals and solvents were obtained from Merck (AR grade) and were used without further purification. Melting points were taken in an open capillary tube. The microwave assisted synthesis of 3,4-dihydropyrimidin-2(1*H*)-one compounds were carried out in a CEM – 908010, bench mate model, 300W laboratory microwave reactor. IR spectra were recorded on a Shimadzu Dr-8031 instrument. ^{1}H NMR and ^{13}C NMR spectra of the synthesized compounds were recorded on a Bruker-Avance (400 MHz), Varian-Gemini (200 MHz) spectrophotometer using $CDCl_3$ solvent and TMS as the internal standard. EI-MS spectra were determined on a LCQ ion trap mass spectrometer (Thermo Fisher, San Jose, CA, USA), equipped with an EI source. The

products were confirmed by comparisons with authentic samples, melting point, IR, ^{1}H, ^{13}C NMR and mass spectra.

Method:

Biological Screening:

The synthesized compounds were screened by agar diffusion method [38-39]. All human pathogenic bacteria *viz. Bacillus subtilis*, *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus vulgaris* and *Staphylococcus aureus* were obtained from the Kakatiyta University, Warangal, India. Stock solutions of compounds were diluted in dimethyl sulfoxide (DMSO) to give a final concentration for determining the Minimum inhibitory concentration (MIC) value. MIC was defined as the lowest concentration of compound is required for a complete inhibition of the bacterial growth after incubation time. For antibacterial activity Muller Hinton agar was used. The wells of 6 mm diameter were filled with 0.1 mL of each compound is diluted separately for each test of bacterial strain. The antibiotic Ampicillin used as reference antibacterial agent, for comparison. Inoculated plates were then incubated at 37 ^{0}C for 24 h. After incubation the antimicrobial (bacterial) activity was measured in terms of the zone of inhibition in mm as shown in Table 2.

Table 2. Antibacterial activity of pyrimidines 4(a-j) (zone of inhibition in mm).

Compd	**Concentration of compounds 100 µg/ml Zone of inhibition (mm)**				
	Gram +Ve			**Gram -Ve**	
	Bacillus subtilis	***Proteus vulgaris***	***Staphylococcus aureus***	***Escherichia coli***	***Klebsiella pneumonia***
4a	35	32	25	32	33
4b	15	17	-	22	19
4c	18	24	15	-	25
4d	28	32	>40	34	33
4e	34	25	22	28	14
4f	23	20	24	29	22
4g	-	25	19	16	-
4h	15	-	13	-	12
4i	27	33	32	29	35
4j	35	36	>40	35	28
Ampicillin	>40	>40	>40	>40	>40

Key to symbols: Inactive = (inhibition zone - mm); slightly active = (inhibition zone (1 to 20 mm); moderately active = (inhibition zone 21 to 30 mm); highly active = (inhibition zone >31 mm).

Preparation of pyrimidine derivatives using fluorspar as a catalyst under MW irradiation:

A mixture of substituted aldehyde (10 mmol), aceto acetanilide (10 mmol), urea/thiourea (15 mmol) and fluorspar (10 mol %) was placed in a glass tube which was loosely closed. The reaction mixture was irradiated for 4-5 min (Table 1) with 100W microwaves at 110 ^{0}C in MW oven in the temperature control mode. The completion of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was poured into crushed ice. The resulting suspension was filtered. The collected solid was recrystallized from ethanol to get the pure product.

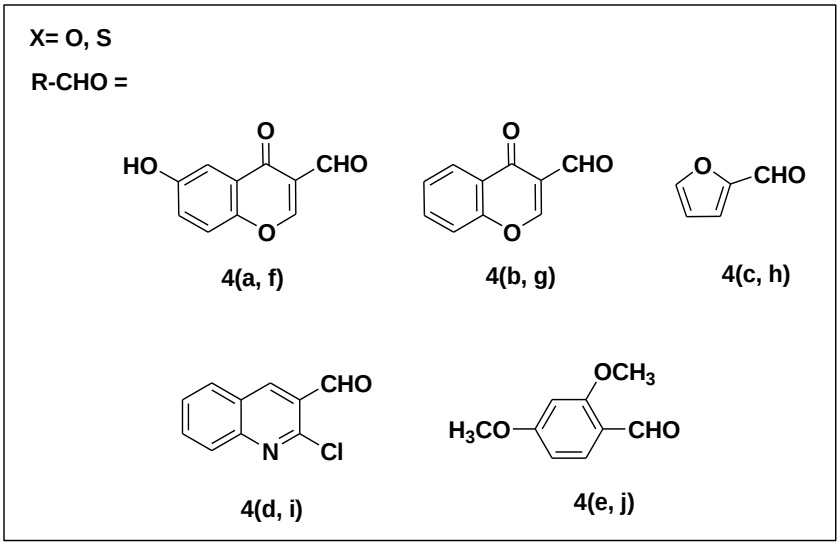
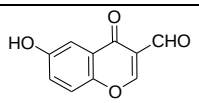
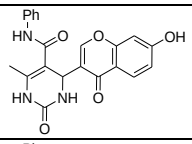
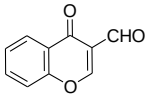
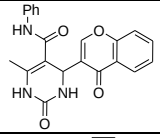
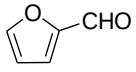
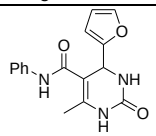
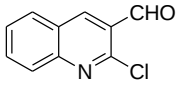
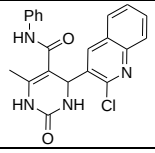
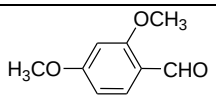
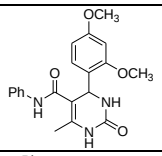
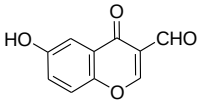
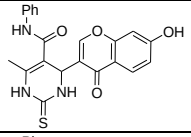
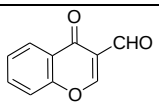
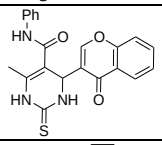
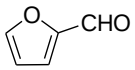
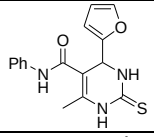
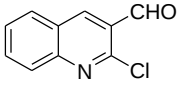
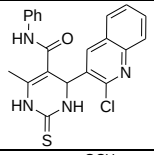
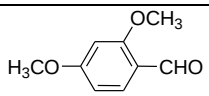
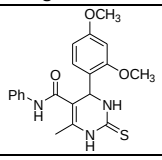


Table 1. Fluorspar catalyzed solvent-free synthesis of substituted pyrimidines 4(a-j) under MW irradiation.

Entry	Product	Aldehyde	X	Product	Time (min)	Yield[a] (%)	M.P (^{0}C)
1	4a		O		5	85	211-215
2	4b		O		4	87	207-210
3	4c		O		5	78	201-204
4	4d		O		4	85	235-238

5	4e		O		4.5	81	195-198
6	4f		S		4	80	218-223
7	4g		S		5	86	211-214
8	4h		S		5	75	205-209
9	4i		S		4.5	77	228-232
10	4j		S		4	90	202-206

[a] Isolated yields

(4a)1,2,3,4-tetrahydro-6-methyl-2-oxo-4-(4-oxo-4H-chromen-3-yl)-N-phenylpyrimidine-5-carboxamide: IR (KBr, cm^{-1}): 3115, 3251 and 3300 (N–H), 1685, 1698 and 1726 (C=O str.), 1646 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 2.39 (s, 3H, CH_3), 5.05 (d, 1H, CH), 6.9-8.1 (m, 9H, Ar-H), 7.13 (s, 1H, CH-O-C), 9.25 (s, 1H, NH), 7.6 (s, 1H, NH); 8.32 (br s, 1H, NH); ^{13}C NMR: δ 17.7 (-CH_3), 37.2 (-CH), 109.3, 115.5, 117.6, 118.4,123.2, 126.4, 129.3, 135.6, 146.5, 150.5, 158.1 for aromatic carbons; 148.4, 163.4, 183.3 for C=O; ms: m/z 375 ($M^{\pm}$), elemental analysis: Anal. Calcd. for $C_{21}H_{17}N_3O_4$: C, 67.19; H, 4.56; N, 11.19. Found: C, 67.08; H, 4.45; N, 11.12.

(4b)1,2,3,4-tetrahydro-4-(7-hydroxy-4-oxo-4H-chromen-3-yl)-6-methyl-2-oxo-N-phenylpyrimidine-5-carboxamide: IR (KBr, cm^{-1}): 3550 (O-H), 3257, 3165 and 3290, (N-H), 1720, 1780 and 1651 (C=O), 1630 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 2.34 (s, 3H, CH_3), 5.02 (d, 1H, CH), 6.6-8.2 (m, 8H, Ar-H), 7.2 (s, 1H, CH-O-C), 9.17 (s, 1H, NH), 7.5 (s, 1H, NH), 8.34 (br s,1H, -NH), 10.54 (br s, 1H, OH); ^{13}C NMR δ 18.4 (-CH_3), 39.1 (-CH), 108.2, 116.7, 117.2, 119.6, 123.5, 126.1, 128.2, 133.2, 145.2, 151.3, 158.7 for aromatic carbons; 150.2, 162.1, 184.1 for C=O; ms: m/z 391 ($M^{\pm}$), elemental analysis: Anal. Calcd. for $C_{21}H_{17}N_3O_5$: C, 64.45; H, 4.38; N, 10.74. Found: C, 64.32; H, 4.47; N, 10.62.

(4c)4-(furan-2-yl)-1,2,3,4-tetrahydro-6-methyl-2-oxo-N-phenylpyrimidine-5-carboxamide: IR (KBr, cm^{-1}): 3280, 3210 and 3130 (N-H), 1710, 1790 and 1690 (C=O), 1642 (C=C); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 2.25 (s, 3H, CH_3), 4.67 (s, 1H), 6.5-7.8 (m, 11H, Ar-H), 8.24 (br s, 1H, -NH), 7.68 (s, 1H, NH), 9.21 (s, 1H, NH); ^{13}C NMR δ 19.1 (-CH_3), 43.2 (-CH), 107.5, 109.5, 112.2, 120.6, 123.8, 128.7, 134.2, 144.6, 148.5 for aromatic carbons, 152.9 (C), 150.5 and 161.3 for C=O; ms: m/z 297 ($M^{\pm}$), elemental analysis: Anal. Calcd. for $C_{16}H_{15}N_3O_3$: C, 64.64; H, 5.09; N, 14.13. Found: C, 64.72; H, 5.01; N, 14.21.

(4d)4-(2-chloroquinolin-3-yl)-1,2,3,4-tetrahydro-6-methyl-2-oxo-N-phenylpyrimidine-5-carboxamide : IR (KBr, cm^{-1}): 3110, 3230 and 3295 (N-H), 1730, 1770 and 1665 (C=O), 1610 (C=C); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 2.31 (s, 3H, CH_3), 4.75 (s, 1H), 6.7-7.5 (m, 10H, Ar-H), 8.2 (br s, 1H, -NH), 7.72 (s, 1H, NH), 9.12 (s, 1H, NH); ^{13}C NMR δ 17.8 (-CH_3), 41.5 (-CH), 108.7, 121.3, 123.4, 126.2, 127, 127.9, 129, 130.6, 132.4, 135.1, 136.6, 145.7, for aromatic carbons, 152 (C), 150.8 and 163.3 for C=O; ms: m/z 392 ($M^{\pm}$), elemental analysis: Anal. Calcd. for $C_{21}H_{17}ClN_4O_2$: C, 64.21; H, 4.36; N, 14.26. Found: C, 64.29; H, 4.47; N, 14.16.

(4e)1,2,3,4-tetrahydro-4-(2,4-dimethoxyphenyl)-6-methyl-2-oxo-N-phenylpyrimidine-5-carboxamide: IR (KBr, cm^{-1}): 3128, 3226 and 3286 (N-H), 1710, 1775 and 1660 (C=O), 1624 (C=C); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 2.25 (s, 3H, CH_3), 3.85 (s, 6H, OCH_3), 4.8 (s, 1H), 6.5-7.5 (m, 8H, Ar-H), 8.12 (br s, 1H, -NH), 7.75 (s, 1H, NH), 9.25 (s, 1H, NH); ^{13}C NMR δ 17.4 (-CH_3), 41 (-CH), 56.5 (-OCH_3), 101.7, 107.4, 113.6, 121.9, 123.1, 129.5, 134.4, 146.2 157.9, 158.5, for aromatic carbons, 151.3 and 162.4 for C=O; ms: m/z 367 ($M^{\pm}$), elemental analysis: Anal. Calcd. for $C_{20}H_{21}N_3O_4$: C, 65.38; H, 5.76; N, 11.44. Found: C, 65.47; H, 5.68; N, 11.56.

(4f) 1,2,3,4-tetrahydro-6-methyl-4-(4-oxo-4H-chromen-3-yl)-N-phenyl-2-thioxopyrimidine-5-carboxamide: IR (KBr, cm^{-1}): 3155, 3224 and 3345 (N–H), 1660, 1690 and 1735 (C=O str.), 1624 (C=C); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 2.25 (s, 3H, CH_3), 5.26 (d, 1H, CH), 6.9-7.5 (m, 9H, Ar-H), 7.17 (s, 1H, CH-O-C), 9.32 (s, 1H, NH), 7.51 (s, 1H, NH); 8.30 (br s, 1H, NH); ^{13}C NMR: δ 17.9 (-CH_3), 37.0 (-CH), 109.6, 115.1, 117.3, 118.8,123.1, 126.6, 129.1, 135.9, 146, 150.8, 157.7 for aromatic carbons; 148.6, 163.1, 183.8 for C=O; ms: m/z 391 ($M^{\pm}$), elemental analysis: Anal. Calcd. for $C_{21}H_{17}N_3O_3S$: C, 64.43; H, 4.38; N, 10.73. Found: C, 64.34; H, 4.32; N, 10.82.

(4g)1,2,3,4-tetrahydro-4-(7-hydroxy-4-oxo-4H-chromen-3-yl)-6-methyl-N-phenyl-2-thioxopyrimidine-5-carboxamide: IR (KBr, cm^{-1}): 3555 (O-H), 3245, 3175 and 3281, (N-H), 1712, 1785 and 1638 (C=O), 1623 (C=C); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 2.29 (s, 3H,

CH_3), 5.27 (d, 1H, CH), 6.7-8.1 (m, 8H, Ar-H), 7.0 (s, 1H, CH-O-C), 9.14 (s, 1H, NH), 7.7 (s, 1H, NH), 8.29 (br s,1H, -NH), 10.61 (br s, 1H, OH); ^{13}C NMR δ 18.1 (-CH_3), 39.5 (-CH), 108.6, 116.2, 117.7, 119.1, 123.2, 125.7, 128.8, 132.8 145.5, 151.8, 158.4 for aromatic carbons; 151.2, 162.8, 184.5 for C=O; ms: m/z 407 ($M^{\pm}$), elemental analysis: Anal. Calcd. for $C_{21}H_{17}N_3O_4S$: C, 61.90; H, 4.21; N, 10.31. Found: C, 61.79; H, 4.27; N, 10.23.

(4h)4-(furan-2-yl)-1,2,3,4-tetrahydro-6-methyl-N-phenyl-2-thioxopyrimidine-5-carboxamide: IR (KBr, cm^{-1}): 3295, 3260 and 3145 (N-H), 1726, 1779 and 1667 (C=O), 1646 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 2.2 (s, 3H, CH_3), 4.92 (s, 1H), 6.5-7.6 (m, 11H, Ar-H), 8.15 (br s, 1H, -NH), 7.61 (s, 1H, NH), 9.32 (s, 1H, NH); ^{13}C NMR δ 18.5 (-CH_3), 43.7 (-CH), 106.9, 109.1, 112.6, 120.4, 124.4, 128.5, 134.4, 144.2, 148.9 for aromatic carbons, 153.2 (C), 150.7 and 162.1 for C=O; ms: m/z 313 ($M^{\pm}$), elemental analysis: Anal. Calcd. for $C_{16}H_{15}N_3O_2S$: C, 61.32; H, 4.82; N, 13.41. Found: C, 61.42; H, 4.71; N, 13.54.

(4i)4-(2-chloroquinolin-3-yl)-1,2,3,4-tetrahydro-6-methyl-N-phenyl-2-thioxopyrimidine-5-carboxamide: IR (KBr, cm^{-1}): 3115, 3246 and 3264 (N-H), 1742, 1758 and 1669 (C=O), 1624 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 2.37 (s, 3H, CH_3), 4.82 (s, 1H), 6.6-7.6 (m, 10H, Ar-H), 8.51 (br s, 1H, -NH), 7.65 (s, 1H, NH), 9.23 (s, 1H, NH); ^{13}C NMR δ 17.9 (-CH_3), 41.2 (-CH), 108.4, 121.7, 123.8, 126.5, 127.7, 127.4, 129.5, 130.1, 132, 135.6, 136.1, 145.3, for aromatic carbons, 152.5 (C), 150.4 and 163.5 for C=O; ms: m/z 408 ($M^{\pm}$), elemental analysis: Anal. Calcd. for $C_{21}H_{17}ClN_4OS$: C, 61.68; H, 4.19; N, 13.70. Found: C, 61.53; H, 4.25; N, 13.67.

(4j)1,2,3,4-tetrahydro-4-(2,4-dimethoxyphenyl)-6-methyl-N-phenyl-2-thioxopyrimidine-5-carboxamide: IR (KBr, cm^{-1}): 3125, 3234 and 3281 (N-H), 1730, 1763 and 1675 (C=O), 1627 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 2.3 (s, 3H, CH_3), 3.75 (s, 6H, OCH_3), 4.84 (s, 1H), 6.5-7.4 (m, 8H, Ar-H), 8.1 (br s, 1H, -NH), 7.78 (s, 1H, NH), 9.22 (s, 1H, NH); ^{13}C NMR δ 17.1 (-CH_3), 41.5 (-CH), 56.2 (-OCH_3), 101.4, 107.1, 113.8, 121.5, 123.6, 129.2, 134.8, 145.1 157.3, 158.1, for aromatic carbons, 151.1 and 162.5 for C=O; ms: m/z 383 ($M^{\pm}$), elemental analysis: Anal. Calcd. for $C_{20}H_{21}N_3O_3S$: C, 62.64; H, 5.52; N, 10.96. Found: C, 62.73; H, 5.45; N, 10.88.

RESULTS AND DISCUSSION:

Alkaline earth fluorite is found as fluorspar (fluorite) in nature. It occurs in huge quantities and serves as sources for fluorine-based products. Herein, we wish to report that these mineral can work as a catalyst for the Biginelli condensation of aldehydes and urea/thiourea with 1,3-dicarbonyl compound under microwave irradiation. In this decade, solvent free organic synthesis has received considerable attention due to growing worldwide concerns over chemical wastes and

future resources. From these points of view, the present methodology offers advantage over classical ones that have been performed in organic solvents (Scheme 1).

Naturally occurring green fluorspar were purchased in the form of crystalline block and hammered into pieces of 1–3 mm in size before use. The model reaction of aceto acetanilide 1 (10 mmol), aldehyde 2 (10 mmol), urea/thiourea 3 (15 mmol), and fluorspar (10 mol %) gave the pure product in 70-90% yield (Table 1). It was seen that the efficiency of the catalyst is not reduced on reuse. The catalyst was used for 10 reactions and the results were summarized in Table 1. Thiourea has been used with similar success to provide the corresponding pyrimidines (5-10) which is also of much interest with respect to its biological activity.

In the current study, the naturally available rock mineral fluorspar is used as a catalyst for Biginelli reaction. The use of fluorspar mineral catalyst under microwave irradiation plays an important role in the synthesis of pyrimidine derivatives, the reaction times are reduced and the yields of the products are higher under microwave irradiation. Based on the results of this study, it seems that the microwave irradiation improves the reaction times and yields. However, in the absence of catalyst fluorspar, the reaction did not proceed even after extending reaction time. We have not tried the methods for aliphatic aldehydes.

Antibacterial studies:

The antibacterial activity of the synthesized ten pyrimidines **4(a-j)** compounds against human bacterial (Gram +ve and Gram -ve) pathogens as determined by agar diffusion method with Ampicillin as reference control was investigated the maximum antimicrobial activity and inhibition zone were observed for compounds **4a, 4e** and **4j** against *B. subtilis* while compounds **4d, 4f** and **4i** showed moderate activity and all other compounds showed low activity against this pathogen. For *P. vulgaris* the compounds **4a, 4d, 4i** and **4j** showed good antibacterial activity as that of the reference compound Ampicillin while **4c, 4e** and **4g** showed moderate activity the other compounds showed low activity against this pathogen. The compounds **4d, 4i** and **4j** showed very good activity against the bacteria *S. aures* while compounds **4a, 4e** and **4f** showed moderate activity. For the pathogen *E. coli* the compounds **4a, 4d** and **4j** showed good inhibitory activity, while **4b, 4e, 4f** and **4i** showed moderate activity and all other compounds showed low activity against this pathogen. For the pathogen *K. pneumonia* the compounds **4a, 4d** and **4i** showed good inhibitory activity, while **4c, 4f** and **4i** showed moderate activity and all other compounds showed low activity against this pathogen.

The derived compounds **4a, 4d, 4i** and **4j** were found to be effective in controlling all the test pathogens and particularly the compounds **4d** and **4j** found to be effective in ***S. aureus*** . The activity is very much comparable to the reference control. Further biological studies are required to validate the effective compounds of the present study as an antimicrobial agent. The results are summarized in **Table 2** antibacterial activity against five human bacterial pathogens. The overall antibacterial activity of the synthesized compounds attributed in the presence of pyrimidine substituted compounds.

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CONCLUSION:

In the conclusion, we have observed that the use of fluorspar mineral catalyst under microwave irradiation plays an important role in the synthesis of pyrimidine derivatives, thereby reducing reaction times and improving yields of the products from good to excellent. However, in the absence of catalyst fluorspar, the reaction did not proceed even after extending reaction time. Several compounds could be identified as the most biologically active member in comparison with the Ampicilline drug. By this study the titled 3,4-dihydropyrimidin-2(1*H*)-ones derivatives represent a class that needs further investigation with the hope of finding new antimicrobial agents.

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