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A Facile Solvent and Catalyst Free Synthesis of New Dihydro Pyrimidinones as Antimicrobial Agents

Hemant Hegde, Chuljin Ahn†, Santosh L. Gaonkar, and Nitinkumar S. Shetty*
Department of Chemistry, Manipal Institute of Technology, Manipal Academy of Higher Education, Manipal-576104, India.
**E-mail: nitin.shetty@manipal.edu*
†*Department of Biology and Chemistry, Changwon National University, Changwon 51140, Korea.*
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ABSTRACT. An efficient one pot multicomponent synthesis of pyrimidinone derivatives of Biginelli type is described. 4-amino-6-aryl-pyrimidine-5-carbonitrile molecules were synthesized efficiently via three-component Biginelli-type condensation of aldehyde, malononitrile, and semicarbazone as urea substituent in the presence of a catalytic amount of PEG-400 as green medium under microwave irradiation. The reactions proceeded efficiently in the presence of microwave radiation to afford the desired products in good to excellent yields. Products have been confirmed by IR, and NMR spectral analysis. All the molecules were tested for their antimicrobial activity against *E. coli, S. aureus, P. aeruginosa* and *C. tropicalis.* Some of the compounds have shown moderate to good inhibition efficiency against both gram-positive and gram-negative bacteria. The potent activity was observed against the fungal species with minimum inhibition concentration 12.5 μg/mL.

Key words: Dihydropyrimidinones, One-pot synthesis, PEG-400, Microwave synthesis

INTRODUCTION

Multifunctionalised pyrimidinones represent an important class of heterocyclic compounds due to their widespread therapeutic applications as anticancer, antiviral, and antimicrobial agents.[1] Owing to the biological significance, pyrimidinones have gained much attention of many researchers in the field of medicinal chemistry. Development of new and efficient methods in the synthesis of pyrimidinone always has been an important area of research, since it was first reported by Biginelli in 1891.[2]

The pyrimidinone derivatives are considered as key intermediates for the synthesis of biologically valuable compounds along with various medicinal properties of other derivatives.[3–5] Limited reports were found in the literature about the synthesis of *N*-substituted pyrimidinone, which prompted us to find a new efficient and eco-friendly procedure for the direct synthesis of novel *N*-substituted-pyrimidine-5-carbonitrile.

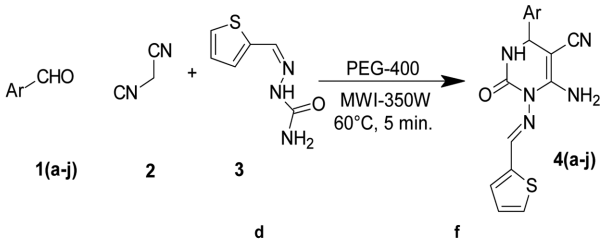
Recently, the use of other components in addition to β-ketoester and urea in the classical Biginelli reaction has emerged as one of the major research areas in terms of the preparation of various novel pyrimidinone derivatives.[6–9] Just as the Biginelli reaction operates in the presence of β-ketoester and urea, various other urea substituents and active methylene compounds are reported to develop new pyrimidinone derivatives. Also, a variety of synthetic approaches has been studied extensively for the conventional Biginelli reaction. Recently, PEG-400 assisted efficient synthesis of classical Biginelli reaction has been reported.[10]

Even though, extensive studies on the Biginelli type reactions have been reported in the literature, to best of our knowledge, there is no report on the Biginelli type reaction with semicarbazone as urea component as in the classical reaction. In present work, we are reporting Biginelli type condensation of an aldehyde, malononitrile and thiophene semicarbazone (as urea component in Biginelli reaction). Reaction proceeds with solvent and catalyst free condition in the presence of PEG-400 and microwave radiation.

EXPERIMENTAL

Synthesis and Analysis

Chemicals were procured from commercial sources like Merck, LobaChemie, Spectrochem, Sigma Aldrich and are used as such without further purification. The reactions were carried out with Raga's microwave systems in RB flask with condenser. The purity of synthesized compounds and the progress of reactions were determined by thin layer chromatography (TLC) on Merck pre-coated silica gel 60 F_{254} aluminum sheets, by using UV light and Iodine vapors as visualizing agent. Melting points were determined by using Buchi-510 melting point apparatus



Ar = **a**: Ph, **b**: 4-Cl-Ph, **c**: 4-Me-Ph, **d**: 4-NO_2-Ph, **e**: 4-OMe-Ph, **f**: 2,4-di-Cl-Ph, **g**: 3,4-di-OMe-Ph, **h**: 3-NO_2-Ph, **i**: thiophene 2-yl, **j**: 2-OMe-napthyl

***Scheme* 1.** Synthesis of 6-amino-pyrimidne-5-carbonitrile derivative.

and are uncorrected. IR spectra were taken on a Shimadzu FT-IR 8400s spectrophotometer using the KBr pellet technique. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance Drx- 400 MHz spectrophotometer using DMSO-d_6 as the solvent and TMS as an internal standard. Elemental analysis was performed by using Perkin Elmer 2400 CHN elemental analyzer.

Thiophene semicarbazones was synthesized by using reported procedure, where semicarbazide hydrochloride and sodium acetate were dissolved in water. Thiophene-2-carboxaldehyde was dissolved separately in a minimum amount of ethanol and added to the above solution with stirring. Reaction mixture was heated gently under a water bath for 10 min and allowed to cool. Precipitate thus formed was filtered and dried.[11–15]

General Procedure for the Synthesis of 6-Amino-pyrimidne-5-carbonitrile derivative (*Scheme* 1): Mixture of aldehyde **1** (1 mmol), malononitrile **2** (1 mmol) and thiophene semicarbazone **3** (1 mmol) in polyethylene glycol (PEG-400) (5 mL) were taken and the mixture was irradiated with microwave radiation with 350 W power at 60 °C for 5 minutes. On completion of the reaction (as confirmed by TLC), the reaction mixture was quenched into crushed ice and stirred at room temperature. Solid thus formed was collected by filtration, washed with water, and recrystallized from ethanol to give pure product.

CHARACTERIZATION DATA

6-Amino-2-oxo-4-phenyl-1-{(*E*)-[(thiophen-2-yl)-methylidene]amino}-1,2,3,4-tetrahydropyrimidine-5-carbonitrile (4a)

Yield, 92%; m.p. 179–181 °C; IR (KBr, cm^{-1}): 3454, 3282, 2227, 1691, 1645, 1600, 1585, 1093, 827; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.50 (s, 1H, C-H), 6.28 (s, 2H, NH_2), 7.48 (t, J = 7.6 Hz, 1H, Ar–H), 7.52–7.63 (m, 3H, Ar–H), 7.66–7.77 (m, 5H, Ar–H), 7.80 (d, J = 7.6 Hz, 1H, Ar–H), 8.14 (d, J = 7.6 Hz, 1H, Ar–H), 10.25 (s, 1H, N–H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ: 82.5, 114.7, 113.1, 128.2, 128.3, 129.5, 130.1, 129.7, 130.8, 131.5, 134.3, 135.1, 135.9, 137.8, 138.7, 139.3, 156.4, 161.2 ppm; Anal. Calcd. for $C_{16}H_{13}N_5OS$: C, 59.43; H, 4.05; N, 21.66; O, 4.95, S, 9.92%. Found: C, 59.42; H, 4.03; N, 21.65; O, 4.94; S, 9.91%.

6-Amino-4-(4-chlorophenyl)-2-oxo-1-{(*E*)-[(thiophen-2-yl)methylidene]amino}-1,2,3,4-tetrahydropyrimidine-5-carbonitrile (4b)

Yield, 89%; m.p. 183–185 °C; IR (KBr, cm^{-1}): 3486, 3279, 2221, 1687, 1635, 15980, 1583, 1084, 819; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.52 (s, 1H, C-H), 6.19 (s, 2H, NH_2), 7.52 (t, J = 7.6 Hz, 1H, Ar–H), 7.56–7.68 (m, 3H, Ar–H), 7.7–7.79 (m, 5H, Ar–H), 7.90 (d, J = 7.6 Hz, 1H, Ar–H), 8.17 (d, J = 7.6 Hz, 1H, Ar–H), 10.19 (s, 1H, N–H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ: ^{13}C NMR (125 MHz, DMSO-d_6) δ: 82.3, 113.3, 114.7, 128.5, 128.9, 129.5, 130.9, 129.7, 130.7, 131.8, 134.4, 135.1, 135.8, 136.8, 138.7, 139.3, 157.5, 161.6 ppm; Anal. Calcd. for $C_{16}H_{12}ClN_5OS$: C, 53.71; H, 3.38; Cl, 9.91; N, 19.57; O, 4.47; S, 8.96%. Found: C, 53.71; H, 3.38; Cl, 9.91; N, 19.57; O, 4.47; S, 8.96%.

6-Amino-4-(4-methylphenyl)-2-oxo-1-{(*E*)-[(thiophen-2-yl)methylidene]amino}-1,2,3,4-tetrahydropyrimidine-5-carbonitrile (4c)

Yield, 82%; m.p. 188–190 °C; IR (KBr, cm^{-1}): 3458, 3281, 2223, 1695, 1629, 1599, 1585, 1093, 827; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.57 (s, 1H, C-H), 6.35 (s, 2H, NH_2), 7.51 (t, J = 7.6 Hz, 1H, Ar–H), 7.55–7.71 (m, 3H, Ar–H), 7.67–7.77 (m, 5H, Ar–H), 7.89 (d, J = 7.6 Hz, 1H, Ar–H), 8.17 (d, J = 7.6 Hz, 1H, Ar–H), 10.27 (s, 1H, N–H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ: 83.1, 114.4, 113.7, 128.9, 128.5, 129.3, 130.1, 129.2, 130.7, 131.1, 134.2, 135.1, 136.1, 137.8, 138.8, 139.3, 156.4, 161.1 ppm; Anal. Calcd. for $C_{17}H_{15}N_5OS$: C, 60.52; H, 4.48; N, 20.76; O, 4.74, S, 9.50%. Found: C, 60.51; H, 4.50; N, 20.75; O, 4.75, S, 9.53%.

6-Amino-4-(4-methoxyphenyl)-2-oxo-1-{(*E*)-[(thiophen-2-yl)methylidene]amino}-1,2,3,4 tetrahydro pyrimidine-5-carbonitrile (4d)

Yield, 79%; m.p. 169–171 °C; IR (KBr, cm^{-1}): 3460, 3282, 2226, 1693, 1649, 1600, 1585, 1093, 827; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.58 (s, 1H, C-H), 6.32 (s, 2H, NH_2), 7.49 (t, J = 7.6 Hz, 1H, Ar–H), 7.51–7.67 (m, 3H, Ar–H), 7.65–7.76 (m, 5H, Ar–H), 7.82 (d, J = 7.6 Hz, 1H,

Ar–H), 8.17 (d, J = 7.6 Hz, 1H, Ar–H), 10.28 (s, 1H, N–H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ: 81.9, 113.8, 113.7, 128.9, 128.4, 128.7, 130.2, 129.6, 130.1, 131.4, 133.8, 135.1, 136.2, 137.6, 138.6, 139.3, 156.2, 161.1 ppm; Anal. Calcd. for $C_{17}H_{15}N_5O_2S$: C, 57.78; H, 4.28; N, 19.82; O, 9.05, S, 9.07%. Found: C, 57.79; H, 4.25; N, 19.83; O, 9.03, S, 9.04%.

6-Amino-4-(4-nitrophenyl)-2-oxo-1-{(*E*)-[(thiophen-2-yl)methylidene]amino}-1,2,3,4-tetrahydropyrimidine-5-carbonitrile (4e)

Yield, 78%; m.p. 192–194 °C; IR (KBr, cm^{-1}): 3454, 3282, 2227, 1691, 1645, 1600, 1585, 1093, 827; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.52(s, 1H, C-H), 6.26 (s, 2H, NH_2), 7.47 (t, J = 7.6 Hz, 1H, Ar–H), 7.51–7.62 (m, 3H, Ar–H), 7.64–7.75 (m, 5H, Ar–H), 7.84 (d, J = 7.6 Hz, 1H, Ar–H), 8.13 (d, J = 7.6 Hz, 1H, Ar–H), 10.26 (s, 1H, N–H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ: 81.9, 113.4, 113.9, 128.5, 128.7, 129.1, 130.4, 129.7, 130.4, 131.7, 134.1, 135.2, 136.5, 138.0, 138.9, 139.4, 156.8, 161.3 ppm; Anal. Calcd. for $C_{16}H_{12}N_6O_3S$: C, 52.17; H, 3.28; N, 22.81; O, 13.03, S, 8.70%. Found: C, 52.18; H, 3.26; N, 22.78; O, 13.04, S, 8.71%.

6-Amino-4-(2,4-dichlorophenyl)-2-oxo-1-{(*E*)-[(thiophen-2-yl)methylidene]amino}-1,2,3,4-tetrahydropyrimidine-5-carbonitrile (4f)

Yield, 86%; m.p. 186–188 °C; IR (KBr, cm^{-1}): 3452, 3282, 2223, 1691, 1645, 1600, 1585, 1093, 827; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.53 (s, 1H, C-H), 6.29 (s, 2H, NH_2), 7.53 (t, J = 7.6 Hz, 1H, Ar–H), 7.56–7.68 (m, 3H, Ar–H), 7.61–7.72 (m, 5H, Ar–H), 7.84 (d, J = 7.6 Hz, 1H, Ar–H), 8.19 (d, J = 7.6 Hz, 1H, Ar–H), 10.28 (s, 1H, N–H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ: 82.3, 113.4, 114.1, 128.5, 128.6, 129.3, 130.2, 129.2, 130.8, 131.6, 134.1, 135.6, 136.1, 138.0, 139.0, 139.6, 156.9, 161.3 ppm; Anal. Calcd. for $C_{16}H_{13}N_5O_2S$: C, 48.99; H, 2.83; N, 17.85; Cl, 18.08; O, 4.08; S, 8.17%. Found: C, 49.02; H, 2.82; N, 17.87; Cl, 18.05; O, 4.07; S, 8.19%.

6-Amino-4-(3,4-dimethoxyphenyl)-2-oxo-1-{(*E*)-[(thiophen-2-yl)methylidene]amino}-1,2,3,4-tetrahydropyrimidine-5-carbonitrile (4g)

Yield, 83%; m.p. 178–180 °C; IR (KBr, cm^{-1}): 3454, 3282, 2227, 1691, 1645, 1600, 1585, 1093, 827; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.53 (s, 1H, C-H), 6.31 (s, 2H, NH_2), 7.55 (t, J = 7.6 Hz, 1H, Ar–H), 7.57–7.68 (m, 3H, Ar–H), 7.70–7.81 (m, 5H, Ar–H), 7.83 (d, J = 7.6 Hz, 1H, Ar–H), 8.15 (d, J = 7.6 Hz, 1H, Ar–H), 10.27 (s, 1H, N–H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ: 82.5, 114.4, 113.4, 128.7, 128.7, 129.0, 129.5,130.4, 130.3, 131.3, 134.0, 134.9, 136.3, 137.8, 139.0, 139.6, 156.9, 161.5 ppm; Anal. Calcd. for $C_{18}H_{17}N_5O_3S$: C, 56.38; H, 4.47; N, 18.27; O, 12.52, S, 8.36%. Found: C, 56.40; H, 4.46; N, 18.25; O, 12.55, S, 8.34%.

6-Amino-4-(2-methoxynaphthalen-1-yl)-2-oxo-1-{(*E*)-[(thiophen-2-yl)methylidene]amino}-1,2,3,4-tetrahydropyrimidine-5-carbonitrile (4h)

Yield, 85%; m.p. 196–198 °C; IR (KBr, cm^{-1}): 3072, 2190, 1700, 1602, 1591, 1574, 1556, 1488, 1083, 842, 815, 750, 741; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.46 (s, 1H, C-H), 6.31 (s, 2H, NH_2), 7.54 (t, J = 7.6 Hz, 1H, Ar–H), 7.56–7.66 (m, 3H, Ar–H), 7.69–7.80 (m, 5H, Ar–H), 7.83 (d, J = 7.6 Hz, 1H, Ar–H), 8.17 (d, J = 7.6 Hz, 1H, Ar–H), 10.26 (s, 1H, N–H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ: 82.2, 113.8, 114.4, 121.9, 122.8, 123.7, 124.3, 125.6, 126.3, 127.0, 127.5, 128.2, 129.0, 129.5, 130.5, 131.3, 134.0, 135.4, 136.3, 138.0, 139.0, 139.6, 143.0, 146.7, 147.0, 149.5, 161.5, 192.4 ppm; Anal. Calcd. for $C_{21}H_{17}N_5O_2S$: C, 62.52; H, 4.25; N, 17.36; O, 7.93, S, 7.95%. Found: C, 62.52; H, 4.25; N, 17.36; O, 7.93, S, 7.95%.

6-Amino-4-(furan-2-yl)-2-oxo-1-{(*E*)-[(thiophen-2-yl)methylidene]amino}-1,2,3,4-tetrahydropyrimidine-5-carbonitrile (4i)

Yield, 86%; m.p. 192–194 °C; IR (KBr, cm^{-1}): 3454, 3282, 2227, 1691, 1645, 1600, 1585, 1093, 827; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.50 (s, 1H, C-H), 6.28 (s, 2H, NH_2), 7.48 (t, J = 7.6 Hz, 1H, Ar–H), 7.52–7.63 (m, 3H, Ar–H), 7.66–7.77 (m, 5H, Ar–H), 7.80 (d, J = 7.6 Hz, 1H, Ar–H), 8.14 (d, J = 7.6 Hz, 1H, Ar–H), 10.25 (s, 1H, N–H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ: 82.8, 114.4, 113.4, 128.7, 128.7, 129.0, 130.4, 129.5, 130.5, 131.3, 134.0, 135.4, 136.3, 138.0, 139.0, 139.6, 156.9, 161.5 ppm; Anal. Calcd. for $C_{14}H_{11}N_5O_2S$: C, 53.66; H, 3.54; N, 22.35; O, 10.21, S, 10.23%. Found: C, 53.68; H, 3.51; N, 22.36; O, 10.19, S, 10.22%.

6-Amino-2-oxo-4-(thiophen-2-yl)-1-{(*E*)-[(thiophen-2-yl)methylidene]amino}-1,2,3,4-tetrahydropyrimidine-5-carbonitrile (4j)

Yield, 88%; m. p. 190–192 °C; IR (KBr, cm^{-1}): 3462, 3276, 2221, 1684, 1639, 1605, 1575, 1079, 809; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.50 (s, 1H, C-H), 6.28 (s, 2H, NH_2), 7.48 (t, J = 7.6 Hz, 1H, Ar–H), 7.52–7.63 (m, 3H, Ar–H), 7.66–7.77 (m, 5H, Ar–H), 7.80 (d, J = 7.6 Hz, 1H, Ar–H), 8.14 (d, J = 7.6 Hz, 1H, Ar–H), 10.25 (s, 1H, N–H) ppm;

^{13}C NMR (100 MHz, DMSO-d_6) δ: 81.9, 113.8, 113.7, 128.9, 128.0, 128.5, 130.1, 129.2, 130.3, 131.1, 134.2, 135.7, 136.5, 138.2, 139.3, 139.7, 157.6, 162.1 ppm; Anal. Calcd. for $C_{14}H_{11}N_5OS_2$: C, 51.05; H, 3.37; N, 21.26; O, 4.86, S, 19.47%. Found: C, 51.03; H, 3.38; N, 21.23; O, 4.88: S, 19.43%.

RESULTS AND DISCUSSION

Initially, chlorobenzaldehyde (**1b**), malononitrile and thiophene semicarbazone are considered as the model substrate for the one pot multicomponent synthesis of pyrimidinone derivative (**4b**). Under refluxing condition (i.e. at 100 °C) the reaction furnished the pyrimidinone (**4b**) in 4 h with 76% yield. The same reaction components were subjected to microwave irradiation at 60 °C with 350 W power and resulted in the 92% yield in 5 minutes. With the optimized reaction conditions, the scope of the reaction was verified with different aldehydes. Reaction gave good yields even with heterocyclic aldehydes (furfural and thiophene-2 aldehyde) and polycyclic aldehydes like 2-methoxy naphthaldehyde.

All the synthesized molecules were characterized by FTIR analysis followed by ^{1}H and ^{13}C NMR spectroscopy. FTIR spectra of **4a** showed the characteristic peaks at 1580, 2227 and 3452 cm^{-1} corresponding to imine group, nitrile group and amine group, respectively. On the other hand, ^{1}H NMR spectrum showed signals corresponding to C_4-H and N-H protons at δ 3.50 and δ 6.28, respectively, which clearly confirmed the cyclisation. Also, ^{13}C NMR confirmed the presence of -CN group having the signal at δ 82.5. All the molecules showed these characteristic peaks at its corresponding range. This confirmed the formation of the titled product. Mechanism of Biginelli type reactions have been well explored. But the exact role of PEG-400 in this type of reaction is still not understood and needs to be further explored.

ANTIMICROBIAL ACTIVITY

The antibacterial activity of the newly synthesized compounds was evaluated using well diffusion method in nutrient agar media. Antibacterial activity of compounds against 12 hour old bacterial culture of a *Escherichia coli* NCIM 2574, *Pseudomonas aeruginosa* NCIM 2036, *Staphylococcus aureus* NCIM 2079, and a fungal culture of *Candida tropicalis* NCIM 3471, was performed *in vitro* by measuring the zone of inhibition.[16,17] Nutrient agar media (about 12–15 mL) was poured into each petri plate and allowed to solidify by placing inside the laminar air flow for 20 min. 100 μL of 0.5 McFarland standard of bacterial/fungal suspension was inoculated on the agar media and spread on the whole surface with a sterile cotton bud. Using a sterile cork borer, 8-mm wells were made on the seeded agar plates. Working solutions of the test compounds in DMSO were made at 10 mg/mL and 50 μL of each 3% stock solution of the compound was dispensed in the wells. The plates were incubated at 37 °C for 12 h and observed for the zone of inhibition in millimeter. DMSO was used as a negative control. Ciprofloxacin was used as an antibacterial standard and fluconazole as an antifungal standard. All the molecules were tested for antimicrobial activity zone of inhibition method as a preliminary screening, out of which **4a** and **4g** were selected for the determination of MIC.

***Table* 1.** Inhibitory zone (diameter) mm of synthesized compounds against tested bacterial and fungal strains by well diffusion method

Compound	*E. coli*	*S. aureus*	*P. aeruginosa*	*C. tropicalis*
4a	*40*	*41*	24	*32*
4b	38	38	29	19
4c	22	19	32	15
4d	29	12	35	23
4e	33	37	20	19
4f	36	39	17	28
4g	*40*	36	32	27
4h	26	24	25	16
4i	31	34	23	17
4j	28	21	37	19
Ciprofloxacin	*43*	*47*	*44*	-
Fluconazole	--	--	--	36

DETERMINATION OF MINIMUM INHIBITORY CONCENTRATION (MIC)

The minimum inhibitory concentration was determined using serial dilution method. The stock solution was prepared by taking 10 mg/mL concentration in DMSO. The stock solution was serially diluted to five times by taking 50 μL of it. Further, 50 μL of each serially diluted compound was added to microplate wells. The microbial cultures were grown on nutrient agar and turbidity was adjusted to 0.5 McFarland concentrations and 50 μL of this culture was also added to each well. After proper mixing, the microplate contents were kept for incubation at room temperature (30 °C) for 12 h. After 12 h of incubation, 0.5 μL of mixture from each well was dispensed on the agar plate

and checked for the growth of bacterial/fungal colony.

Among the two tested molecules (**4a** and **4g**), **4a** showed the inhibition of *E. coli* and *S. aureus* up to 25 μg/mL concentration against both species of bacteria, which was little higher than the standard ciprofloxacin, that showed the inhibition at 3.12 μg/mL concentration. But, the compound **4g** did not show any considerable inhibition (with conc. >100 μg/mL). Also, **4a** showed a significant activity against fungal species under study with minimum inhibitory concentration up to 12.5 μg/mL. Whereas fluconazole showed inhibition at 3.12 μg/mL.

CONCLUSION

We reported the catalyst and solvent free synthesis and antimicrobial activity of highly substituted pyrimidinone derivatives. The synthetic method involved microwave irradiation along with PEG-400 as a reaction medium. Reaction proceeded efficiently at low temperature than the conventional method and time was reduced drastically to 5 min. The reaction exhibited the advantage of catalyst and solvent free synthesis of pyrimidinones in short time with very good yield. All the molecules were tested for their antimicrobial growth inhibition efficiency. Few of them showed moderate activity. The compound **4a** with no substitution on aromatic aldehyde group found to be efficient (with MIC: 25 μg/mL) in inhibiting the growth of gram-positive and gram-negative bacteria. Best antifungal activity was observed with MIC 12.5 μg/mL, which was nearest to that of the standard drug fluconazole.

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