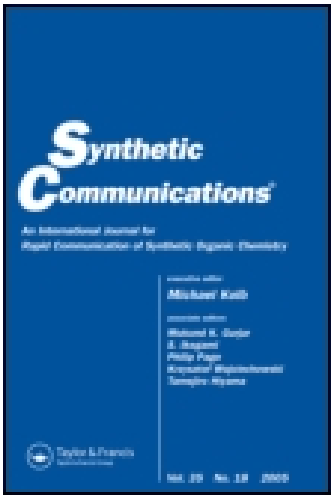

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Ultrasound Irradiated Synthesis of Bis-pyrimidine Derivative in Aqueous MediA

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ULTRASOUND IRRADIATED SYNTHESIS OF BIS-PYRIMIDINE DERIVATIVE IN AQUEOUS MEDIA

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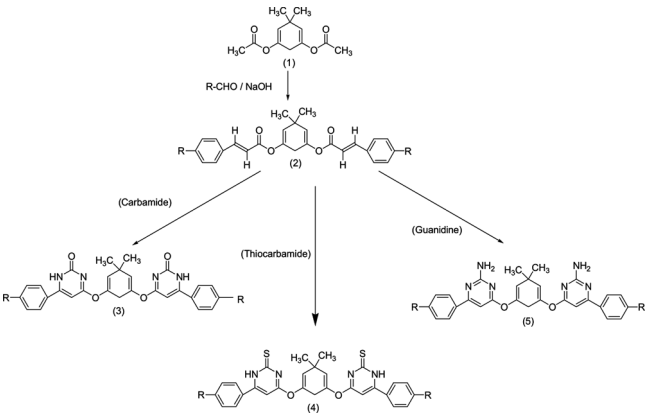
GRAPHICAL ABSTRACT



Abstract *Pyrimidine derivatives have been found to possess a broad spectrum of biological activities. Among various pyrimidine derivatives, bis-pyrimidine seems to be the rarely studied. A variety of methods have been reported for the preparation of this class of compound. However, in spite of their potential utility, some of the reported methods suffer from drawbacks such as long reaction times, cumbersome product-isolation procedures, and environmental concerns. Organic reactions in aqueous media have attracted increasing interest recently because of environmental issues and the understanding of biochemical processes. Ultrasound has increasingly been used in organic synthesis for greater yields, shorter reaction times or milder conditions.*

Keywords Aqueous media; bis-pyrimidine; conventional method; sonication method

INTRODUCTION

Highly functionalized pyrimidine derivatives are of great importance to the life-science industries, and many pyrimidine derivatives have been used for various medicinal applications (Fig. 1).[1–3] Pyrimidine derivatives and heterocyclic annelated

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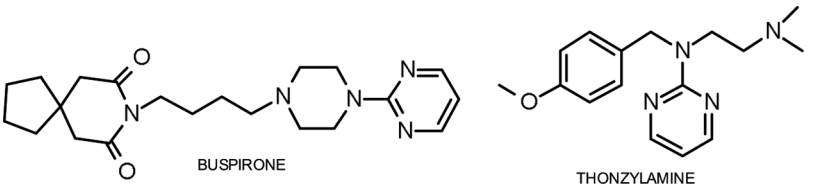


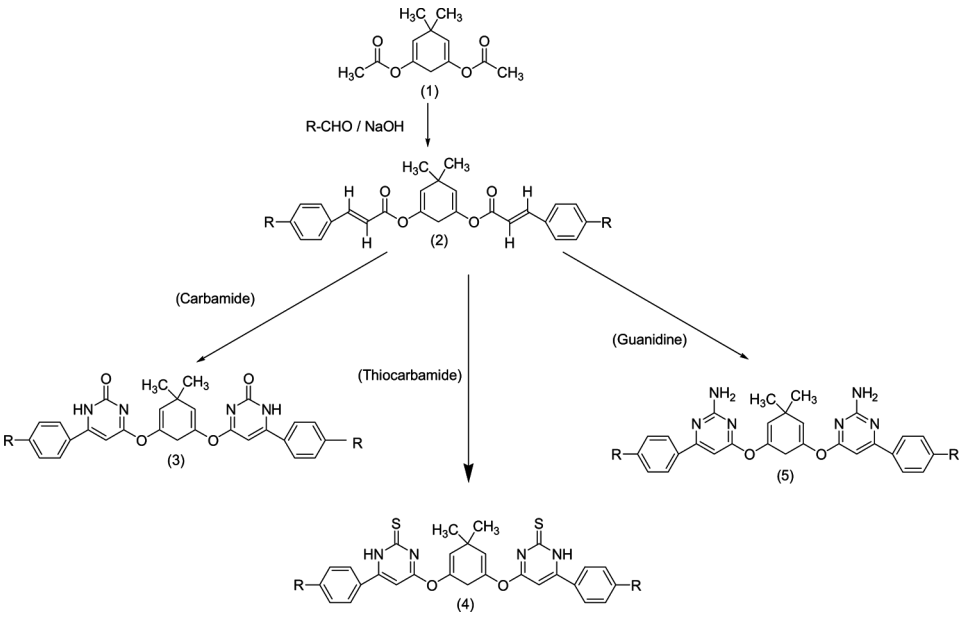
Figure 1. Pharmaceutical with subpyrimidine subunit.

pyrimidines continue to attract great interest because of the wide variety of interesting biological activities observed for these compounds, such as anticancer,[4] antiviral,[5] antitumor,[6] anti-inflammatory,[7] and antimicrobial activities [8]. Among various pyrimidine derivatives, bis- pyrimidines derivatives seem to be rarely studied. A variety of methods have been reported for the preparation of this class of compounds. In 2007, Nagaraj and Reddy [9] reported that the reaction of α, β unsaturated carbonyl with carbamide, thiocarbamide, and guanidine hydrochloride in the presence of potassium hydroxide was carried out in the absolute ethanol, but it suffered disadvantages such as longer reaction time (5–8 h) and economic and environmental concerns.

The recent interest in green chemistry has posed a new challenge for organic synthesis in that new reaction conditions need to be found that reduce the emission of volatile organic solvents and the use of hazardous toxic chemicals. Organic reactions in aqueous media have attracted interest because of environmental issues and the understanding of biochemical processes. As a reaction solvent, water offers many practical and economic advantages including low cost, safe handling, and environmental compatibility. Considering these facts many reactions using aqueous media have been reported.[10–12]

Ultrasound increasingly has been used in organic synthesis in the past three decades compared with traditional methods. When an ultrasonic wave propagates through a liquid, the local pressure varies with time and space. If a bubble is present in the liquid, its radius will expand and contract in response to these pressure changes. For low-amplitude pressure excursions, these oscillations are sinusoidal and may last for many acoustic cycles, a phenomenon called stable cavitation. Under certain conditions, however, these oscillations may become unstable, leading to the rapid collapse of a bubble during a single acoustic half-cycle. This phenomenon is called transient cavitation. High temperatures and pressures are generated within the bubble during its final stage of collapse that are thought to produce hydrogen atoms and hydroxyl radicals in aqueous solutions. Some investigators feel that the temperature is sufficient to generate free radicals, which are sometimes produced for stable cavitation as well. The ultrasound irradiation technique is more convenient, gives better yields, and reduces reaction time.[13–25]

Continuing our investigations[26–29] of the application of ultrasound in organic synthesis, we report a swift and practical green procedure for the synthesis of bis-pyrimidine from bis-cinamate with carbamide/thiocarbamides/guanidine in sodium acetate–acetic acid aqueous solution under ultrasounic irradiation Scheme 1.



Scheme 1. Bis-pyrimidine derivative.

RESULTS AND DISCUSSION

The reaction of 3,3-dimethyl-1,5-dihydroxy-1,4-cyclohexadiene **1** with acetic anhydride yielded bis-1,5-[acetoxy]-3,3-dimethyl-1,4-cyclohexadiene, which was converted into bis-1,5-[substituted cinnamate]-3,3-dimethyl-1,4-cyclohexadiene **2** when stirred with substituted aromatic aldehydes in presence of 2 N sodium hydroxide for 1 h. Formation of compound **2** was evidenced by the appearance of a signal at 7.8 ppm (α,β-unsaturated carbonyl) in the ^{1}H NMR spectra and in the infrared (IR) spectral band due to carbonyl at 1634 cm^{-1}. In the ^{13}C NMR spectra, the signal 188.24 ppm was observed due to O=C< in compound **2**. The reaction of carbamide with α,β-unsaturated compounds in conjugation with carbonyl afforded bis-1,5[1′H,5′H-dihydro-6′-(4 substitutedpheny)-2′-oxo-pyrimidin-4′-oxy]-3,3-dimethyl-1,4-cyclohexadiene **3**. In ^{1}H NMR spectra of compound **3**, the signal at 8.30 was observed due to –NH-, and in the IR spectra the bands at 3100 (-N-H-) and 1620 cm^{-1} (-C=O-) were also confirmed. In ^{13}C NMR spectra, the signals at 144.04 ppm and 162.33 ppm were observed due to –C=N- and C=O respectively.

Similarly, the bis-1,5-[substituted cinnamate]-3,3-dimethyl-1,4-cyclohexadiene **2** on treatment with thiocarbamide underwent cyclization to afford bis-1,5[1′H, 5′H-dihydro-6′-(4-substitutedpheny)-2′-thioxo-pyrimidin-4′-oxy]-3,3-dimethyl-1,4-cyclohexadiene **4** (Scheme 1).

Compound **4** showed the result as compound **3** except for the thioxo group, which was at 196.34 ppm in the ^{13}C NMR spectra. Guanidine hydrochloride treated with **2** yielded bis-1,5[1′H,5′H-dihydro-6′-(4-substitutedpheny)-2′-thioxo-pyrimidin-4′-oxy]-3,3-dimethyl-1,4-cyclohexadiene **5**. The IR spectrum of **5** showed NH_2 stretching bands at 3243–3300 cm^{-1}. In its ^{1}H NMR spectrum, the chemical

Table 1. Physical and analytical data of compounds **2**, **3**, **4**, and **5**

Entry	R	Mp (°C)	Yield (%) method A	Yield (%) method B	Molecular weight
2a	H	200–2	82.10	72.23	400.21
2b	OCH_3	215–17	84.23	73.46	460.23
2c	OH	198–99	83.84	72.39	432.89
3a	H	242–45	82.71	74.32	480.51
3b	OCH_3	261–63	83.49	73.09	540.56
3c	OH	231–33	85.75	73.21	512.51
4a	H	187–89	82.43	76.89	512.64
4b	OCH_3	197–99	84.10	72.98	572.6
4c	OH	176–78	83.86	73.32	544.64
5a	H	168–71	84.23	74.56	478.54
5b	OCH_3	177–79	82.32	73.23	538.59
5c	OH	157–59	82.98	75.78	510.54

shifts due to NH_2 were observed at 2.69 ppm. Appearance of two peaks due to C=N at 143.71 and 147.37 ppm in ^{13}C NMR confirmed the formation of **5**. It was observed that in the presence of sodium acetate in aqueous acetic acid the yield of pyrimidines was increased. To verify the effect of ultrasound irradiation, in the absence of ultrasound, we performed the reaction of bis-substituted cinnamate with carbamide/thiocarbamides/guanidine by refluxing for 3–4 h. The yield of pyrimidine was 73–79% (Table 1). While under ultrasound irradiation, the reaction completed within 45 min at room temperature with 82–86% yield. It was clear that the ultrasound could accelerate the reaction to obtain bis-pyrimidines. The compounds obtained by both the routes were identical, as they showed the same melting points and similar spectral data.

EXPERIMENTAL

Melting points of all synthesized compounds were determined in open capillary tubes on an electrothermal apparatus and are uncorrected. The purity of the compounds was monitored by thin-layer chromatography (TLC) on silica-gel-coated aluminium plates (Merck) as adsorbent and ultraviolet light as visualizing agent. IR spectra (potassium bromide in cm^{-1}) were recorded on a Perkin-Elmer spectrophotometer in the range of 4000–400 cm^{-1}. ^1H NMR spectra were recorded on a Varian 500-MHz NMR spectrophotometer using deuteriochloroform as solvent and trimethylsilane as an internal standard (chemical shifts in δ ppm), and mass (ms) spectra were taken on a Jeol sx-102/PA-6000 (EI) spectrometer. CHN estimations were recorded on a Carlo Erba 1108 (CHN) elemental analyzer. The experiment under ultrasound irradiation was carried out in a probe sonicator manufactured by Dakshin.

Bis-1,5-[substituted cinnamate]-3,3-dimethyl-1,4-cyclohexadiene (2a–c)

Method A (ultrasound). A mixture of substituted aromatic aldehyde (0.02 mol), **1** (2.45 ml, 0.01 mol), and NaOH (10 ml, 20% w/v) in 5 ml of ethanol was stirred and exposed to ultrasound irradiation for 35 min. The reaction mixture

was monitored by TLC. After completion of the reaction, the product was separated out, washed with solvent ether, and recrystallized from ethanol.

Method B (conventional). A solution of substituted aromatic aldehydes (0.02 mol), **1** (2.45 ml, 0.01 mol), and NaOH (10 ml, 20% w/v) in 5 ml of ethanol was stirred for 2.5 h. The reaction was monitored by TLC. After completion of the reaction, the contents were poured on crushed ice. The solid obtained was filtered off, washed with water, and recrystallized from ethanol to get compounds **2a–c**.

Bis-1,5-[cinnamate]-3,3-dimethyl-1,4-cyclohexadiene (2a). This compound was obtained as white crystals, mp 200–202 °C; IR (potassium bromide) ν max/cm^{-1}: 2912 (CH), 1745 C=O), 1625 (C=C); ^{1}H NMR (deuteriochloroform): δ 0.96 (s, 6-H, $2 \times CH_3$), 2.44 (s, 2-H, CH_2), 4.69 (s, 2-H, CH), 7.82 (s, 4H, α, β-unsaturated carbonyl), 6.98–8.02 (m, 10-H, aromatic protons); ^{13}C NMR: 27.28 $(CH_3)_2$, 37.33 (CH_2), 74.23 (tetrahedral carbon), 108.21-131.56 (C=C & Ar-C), 188.42 (C=O), MS: m/z 402 (m^{+2}). Anal. calcd. for $C_{26}H_{24}O_4$: C, 78.21; H, 6.01. Found: C, 77.87; H, 6.21.

Bis-1,5-[4′′-methoxy cinnamate]-3,3-dimethyl-1,4-cyclohexadiene (2b). This compound was obtained as light green crystals, mp 215–217 °C; IR (potassium bromide) ν max/cm^{-1}: 2980 (CH), 1752 (C=O), 1620 (C=C); ^{1}H NMR (deuteriochloroform): δ 1.07 (s, 6-H, $2 \times CH_3$), 2.25 (s, 2-H, CH_2), 3.73 (s, 6-H, OCH_3), 4.75 (s, 2-H, CH), 7.89 (s, 4-H, α,β-unsaturated carbonyl), 6.88–7.89 (m, 8-H, aromatic proton); ^{13}C NMR: 26.32 $(CH_3)_2$, 37.89 (CH_2), 41.21 (OCH_3), 74.45 (tetrahedral carbon), 111.32–132.43 (C=C & Ar-C), 189.09 (C=O); MS: m/z 462 (m^{+2}). Anal. calcd. for $C_{28}H_{28}O_6$: C, 73.04; H, 6.08. Found: C, 72.84; H, 6.24.

Bis-1,5-[4′′-hydroxy cinnamate]-3,3-dimethyl-1,4-cyclohexadiene (2c). This compound was obtained as yellow crystals, mp 198–199 °C; IR (potassium bromide) ν max/cm^{-1}: 3421 (OH), 3012 (CH), 1631 (C=O), 1610 (C=C); ^{1}H NMR (deuteriochloroform): δ 0.98 (s, 6-H, $2 \times CH_3$), 2.34 (s, 2-H, CH_2), 4.56 (s, H, OH), 4.67 (s, 2-H, CH), 7.76 (s, 4-H, α,β-unsaturated carbonyl), 6.95–7.79 (m, 8-H, aromatic proton). ^{13}C NMR: 26.86 $(CH_3)_2$, 37.64 (CH_2), 40.76 (OCH_3), 74.32 (tetrahedral carbon), 113.41–131.83 (C=C & Ar-C), 189.98 (C=O); MS: m/z 432 (m^{+2}). Anal. calcd. for $C_{28}H_{26}O_6$: C, 72.22; H, 5.67. Found: C, 72.14; H, 5.63.

Bis-1,5[1′H,5′H-dihydro-6′-(substitutedpheny)-2′-oxo-pyrimidin-4′-oxy]-3,3-dimethyl-1,4-cyclohexadiene (3a–c), Bis-1,5[1′H,5′H-dihydro-6′-(substitutedpheny)-2′-thioxo-pyrimidin-4′-oxy]-3,3-dimethyl-1,4-cyclohexadiene (4a–c), and Bis-1,5[5′H-6′-(substitutedpheny)-2′-amino-pyrimidin-4′-oxy]-3,3-dimethyl-1,4-cyclohexadiene (5a–c)

Method A (ultrasound). A mixture of carbamide/thiocarbamide/guanidine (1.2 g, 0.02 mol), **2** (2.45 ml, 0.01 mol), and (2.46 g, 0.03 mol) sodium acetate was dissolved in an aqueous acetic acid solution (6 mL, $HAc/H_2O = 2/1$,v/v) in a 50-mL conical flask. The mixture was exposed to ultrasound for 45 min. Upon completion of the reaction (monitored on TLC), the mixture was poured on crushed ice. The

product precipitated out was filtered, washed with water, and recrystallized from ethanol.

Method B (conventional). A solution of carbamide (1.2 g, 0.02 mol), **2** (2.45 ml, 0.01 mol), and sodium acetate (2.46 g, 0.03 mol) was dissolved in aqueous acetic acid solution (6 mL, $HAc/H_2O = 2/1$,v/v) and refluxed on a water bath for 4 h. The reaction was monitored by TLC. After completion of the reaction, the contents were poured on crushed ice. The solid obtained was filtered off, washed with water, and recrystallized from ethanol.

Bis-1,5[1′H,5′H-dihydro-6′-(pheny)-2′-oxo-pyrimidin-4′-oxy]-3,3-dimethyl-1,4-cyclohexadiene (3a). This compound was obtained as brown crystals, mp 242–245 °C; IR (potassium bromide) ν max/cm^{-1}: 3100 (NH), 2930 (CH), 1620 (C=O), 1589 (C=N), 1322 (C-N), ^{1}H NMR (deuteriochloroform): δ 0.97 (s, 6-H, $2 \times CH_3$), 2.44 (s, 2-H, CH_2), 4.72 (s, 2-H, CH), 7.12–7.45 (m, 12-H, C-H & Ar-H), 8.30 (s, 2-H, NH); ^{13}C NMR: 27.28 ($2 \times CH_3$), 32.18 (CH_2), 73.54 (tetrahedral carbon), 115-128.33 (C=C & Ar-C), 144.01 (C=N), 162.32 (C=O). MS: m/z 482 (m^{+2}). Anal. calcd. for $C_{28}H_{24}N_4O_4$: C, 69.99; H, 5.03; N, 11.66. Found: C, 69.95; H, 5.02, N, 11.61.

Bis-1,5[1′H,5′H-dihydro-6′-(4′-methoxypheny)-2′-oxo-pyrimidin-4′-oxy]-3,3-dimethyl-1,4-cyclohexadiene (3b). This compound was obtained as yellow crystals, mp 261–263 °C; IR (potassium bromide) ν max/cm^{-1}: 3023 (NH), 2923 (CH), 1626 (C=O), 1582 (C=N), 1332 (C-N), ^{1}H NMR (deuteriochloroform): δ 0.96 (s, 6-H, $2 \times CH_3$), 2.43 (s, 2-H, CH_2), 3.91 (s, 6-H, OCH_3), 4.56 (s, 2-H, CH), 7.03–7.56 (m, 10-H, C-H & Ar-H), 8.32 (s, 2-H, NH); ^{13}C NMR: 27.23 ($2 \times CH_3$), 32.12 (CH_2), 42.12 (OCH_3), 73.21 (tetrahedral carbon), 112.23-128.33 (C=C & Ar-C), 144.23 (C=N), 164.10 (C=O). MS: m/z 542 (m^{+2}). Anal. calcd. for $C_{30}H_{28}N_4O_6$: C, 69.66; H, 5.22; N, 10.36. Found: C, 69.62; H, 5.18, N, 11.32.

Bis-1,5[1′H,5′H-dihydro-6′-(4′-hydroxypheny)-2′-oxo-pyrimidin-4′-oxy]-3,3-dimethyl-1,4-cyclohexadiene (3c). This compound was obtained as colorless crystals, mp 231–233 °C; IR (potassium bromide) ν max/cm^{-1}: 3320 (OH), 3009 (NH), 2910 (CH), 1614 (C=O), 1576 (C=N), 1339 (C-N); ^{1}H NMR (deuteriochloroform): δ 0.99 (s, 6-H, $2 \times CH_3$), 2.47 (s, 2-H, CH_2), 4.60 (s, 2-H, CH), 5.09 (s, 2-H, OH), 6.98–7.43 (m, 10-H, C-H & Ar-H), 8.28 (s, 2-H, NH). ^{13}C NMR: 28.01 ($2 \times CH_3$), 32.32 (CH_2), 73.45 (tetrahedral carbon), 110.56–128.33 (C=C & Ar-C), 145.10 (C=N), 165.04 (C=O); MS: m/z 514 (m^{+2}). Anal. calcd. for $C_{28}H_{24}N_4O_6$: C, 65.62; H, 4.72; N, 10.93. Found: C, 65.59; H, 4.69, N, 10.89.

Bis-1,5[1′H,5′H-dihydro-6′-(pheny)-2′-thioxo-pyrimidin-4′-oxy]-3,3-dimethyl-1,4-cyclohexadiene (4a). This compound was obtained as brown crystals, mp 187–189 °C; IR (potassium bromide) ν max/cm^{-1}: 3043 (NH), 2924 (C-H), 1220 (C=S), 1579 (C=N), 1345 (C-N); ^{1}H NMR (deuteriochloroform): δ 0.96 (s, 6-H, $2 \times CH_3$), 2.43 (s, 4-H, CH_2), 4.74 (s, 2-H, CH), 7.11-7.63 (m, 12-H, C-H & Ar-H), 8.27 (s, 2-H, NH). ^{13}C NMR: 27.12 ($2 \times CH_3$), 31.79 (CH_2), 73.89 (tetrahedral carbon), 115.23-131.47 (C=C & Ar-C), 144.65 (C=N), 196.34 (C=S); MS: m/z 514 (m^{+2}). Anal. calcd. for $C_{28}H_{24}N_4O_2S_2$: C, 65.60; H, 4.72; N, 10.93; S, 12.51. Found: C, 65.58; H, 4.68, N, 10.89; S, 12.48.

Bis-1,5[1′H,5′H-dihydro-6′-(4-methoxypheny)-2′-thioxo-pyrimidin-4′-oxy]-3,3-dimethyl-1,4-cyclohexadiene (4b). This compound was obtained as white crystals, mp 197–199 °C; IR (potassium bromide) ν max/cm^{-1}: 3020 (NH), 2901 (C-H), 1224 (C=S), 1556 (C=N), 1331 (C-N), ^{1}H NMR (deuteriochloroform): δ 0.95 (s, 6-H, 2 × CH_3), 2.44 (s, 4-H, CH_2), 3.89 (s, 6-H, OCH_3), 4.71 (s, 2-H, CH), 7.00–7.87 (m, 10-H, C-H & Ar-H), 8.10 (s, H, NH). ^{13}C NMR: 27.29 (2 × CH_3), 32.41 (CH_2), 42.23 (OCH_3), 73.74 (tetrahedral carbon), 113.03–136.31 (C=C & Ar-C), 145.00 (C=N), 195.67 (C=S); MS: m/z 574 (m^{+2}). Anal. calcd. for $C_{30}H_{28}N_4O_4S_2$: C, 62.92; H, 4.93; N, 9.78; S, 11.20. Found: C, 62.89; H, 4.89, N, 9.76; S, 11.15.

Bis-1,5[1′H,5′H-dihydro-6′-(4-hydroxypheny)-2′-thioxo-pyrimidin-4′-oxy]-3,3-dimethyl-1,4-cyclohexadiene (4c). This compound was obtained as light yellow crystals, mp 176–178 °C; IR (potassium bromide) ν max/cm^{-1}: 3412 (OH), 2990 (NH), 2982 (C-H), 1228 (C=S), 1551 (C=N); 1339 (C-N); ^{1}H NMR (deuteriochloroform): δ 0.98 (s, 6-H, 2 × CH_3), 2.43 (s, 4-H, CH_2), 4.72 (s, 2-H, CH), 5.65 (s, 2-H, OH), 7.17-7.67 (m, 10-H, C-H & Ar-H), 8.29 (s, 2-H, NH); ^{13}C NMR: 28.21 (2 × CH_3), 31.28 (CH_2), 73.79 (tetrahedral carbon), 112.18–135.56 (C=C & Ar-C), 144.23 (C=N), 196.29 (C=S). MS: m/z 546 (m^{+2}). Anal. calcd. for $C_{28}H_{24}N_4O_4S_2$: C, 61.75; H, 4.44; N, 10.29; S, 11.77. Found: C, 61.71; H, 4.40, N, 10.25; S, 11.72.

Bis-1,5[5′H-6′-(pheny)-2′-amino-pyrimidin-4′-oxy]-3,3-dimethyl-1,4-cyclohexadiene (5a). This compound was obtained as green crystals, mp 168–171 °C; IR (potassium bromide) ν max/cm^{-1}: 3243 (NH_2), 2910 (C-H), 1567 (C=N), 1378 (C-N); ^{1}H NMR (deuteriochloroform): δ 0.97 (s, 6-H, 2 × CH_3), 2.44 (s, 2-H, CH_2), 2.69 (s, 4-H, NH_2), 4.75 (s, 2-H, CH), 7.03–7.73 (m, 12-H, C-H & Ar-H); ^{13}C NMR: 27.32 (2 × CH_3), 32.43 (CH_2), 74.09 (tetrahedral carbon), 112.58–135.23 (C=C & Ar-C), 143.71 (C=N), 147.37 (C=N); MS: m/z 480 (m^{+2}). Anal. calcd. for $C_{28}H_{26}N_6O_2$: C, 70.28; H, 5.48; N, 17.56. Found: C, 70.24; H, 5.42, N, 11.53.

Bis-1,5[5′H-6′-(4′-methoxypheny)-2′-amino-pyrimidin-4′-oxy]-3,3-dimethyl-1,4-cyclohexadiene (5b). This compound was obtained as yellow crystals, mp 177–179 °C; IR (potassium bromide) ν max/cm^{-1}: 3221 (NH_2), 2978 (C-H), 1532 (C=N), 1345 (C-N); ^{1}H NMR (deuteriochloroform): δ 0.99 (s, 6-H, 2 × CH_3), 2.43 (s, 2-H, CH_2), 2.64 (s, 4-H, NH_2), 3.90 (s, 6-H, OCH_3), 4.74 (s, 2-H, CH), 7.08–7.75 (m, 10-H, C-H & Ar-H); ^{13}C NMR: 26.68 (2 × CH_3), 31.23 (CH_2), 74.89 (tetrahedral carbon), 112.12–134.156 (C=C & Ar-C), 144.32 (C=N), 146.56 (C=N); MS: m/z 540 (m^{+2}). Anal. calcd. for $C_{30}H_{30}N_6O_4$: C, 66.90; H, 5.61; N, 15.60. Found: C, 66.87; H, 5.58, N, 15.58.

Bis-1,5[5′H-6′-(4′-hydroxypheny)-2′-amino-pyrimidin-4′-oxy]-3,3-dimethyl-1,4-cyclohexadiene (5c). This compound was obtained as colorless crystals, mp 157–159 °C; IR (potassium bromide) ν max/cm^{-1}: 3412 (OH), 3235 (NH_2), 2923 (C-H), 1543 (C=N), 1339 (C-N); ^{1}H NMR (deuteriochloroform): δ 0.97 (s, 6-H, 2 × CH_3), 2.44 (s, 2-H, CH_2), 2.66 (s, 4-H, NH_2), 4.76 (s, 2-H, CH), 5.03 (s, 2-H, OH), 7.02–7.68 (m, 10-H, C-H & Ar-H); ^{13}C NMR: 27.54 (2 × CH_3), 32.87 (CH_2), 73.34 (tetrahedral carbon), 112.45–133.23 (C=C & Ar-C), 144.45 (C=N), 146.5

(C=N); MS: m/z 512 (m^{+2}). Anal. calcd. for $C_{28}H_{26}N_6O_4$: C, 65.87; H, 5.13; N, 16.46. Found: C, 65.85; H, 5.10, N, 16.42.

CONCLUSION

We have described a practical and convenient procedure for the synthesis of bis-pyrimidine in sodium acetate–acetic acid aqueous solution at room temperature under ultrasounic irradiation as well as conventional method.

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