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Facile synthesis of some novel 2-substituted-4,6-diarylpyrimidines using 4'-hydroxy-3',5'-dinitrochalcones and S-benzylthiouronium chloride

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Abstract: Various 4'-hydroxy-3',5'-dinitro substituted chalcones **1** and S-benzylthiouronium chloride (SBT) **2** in the presence of DMF-organic bases (morpholine/ pyrrolidine/ piperidine) gave 4,6-diaryl-2-(4-morpholinyl / 1-pyrrolidinyl /1-piperidinyl)- pyrimidines **4**, **5** and **6** in a facile one-pot conversion. In an another attempt reactants **1** and **2** yielded intermediate 2-benzylthiopyrimidines **3**, in presence of DMF, which on treatment with heterocyclic secondary amines gave products **4**, **5** and **6** in an alternate two-step process.

Keywords: Chalcone; S-benzylthiouronium chloride, heterocyclic secondary amines.

1. Introduction

Nitrogen containing heterocycles are significant synthetic target owing to their wide range of applications as medicinal compounds. Pyrimidines are the well known biologically important heterocycles and exhibited considerable pharmacological importance such as antibacterial[1], anti-inflammatory[2], cytotoxic[3,4], anticancer[5,6] and calcium channel blocker[7,8]. Chalcones are a chemical class that have been widely used as starting material for the synthesis of different sized bioactive aromatic systems of pharmacodynamic importance[9-15] due to the presence of α, β-unsaturated carbonyl functionality. Dicyandiamide (DDA) and S-benzylthiouronium chloride (SBT) have emerged from our laboratory[16,17] team as versatile reagents for the continued synthesis of 2, 4, 6- trisubstituted pyrimidines from α, β-

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unsaturated ketones and heterocyclic secondary amines. We herein report a facile conversion of 4'-hydroxy-3', 5'-dinitro substituted chalcones with SBT using DMF and heterocyclic secondary amine to afford 4, 6-diaryl-2-(4-morpholinyl / 1-pyrrolidinyl /1-piperidinyl)-pyrimidines **4a-h**, **5a-h** and **6a-h** respectively. **(Scheme- 1)**

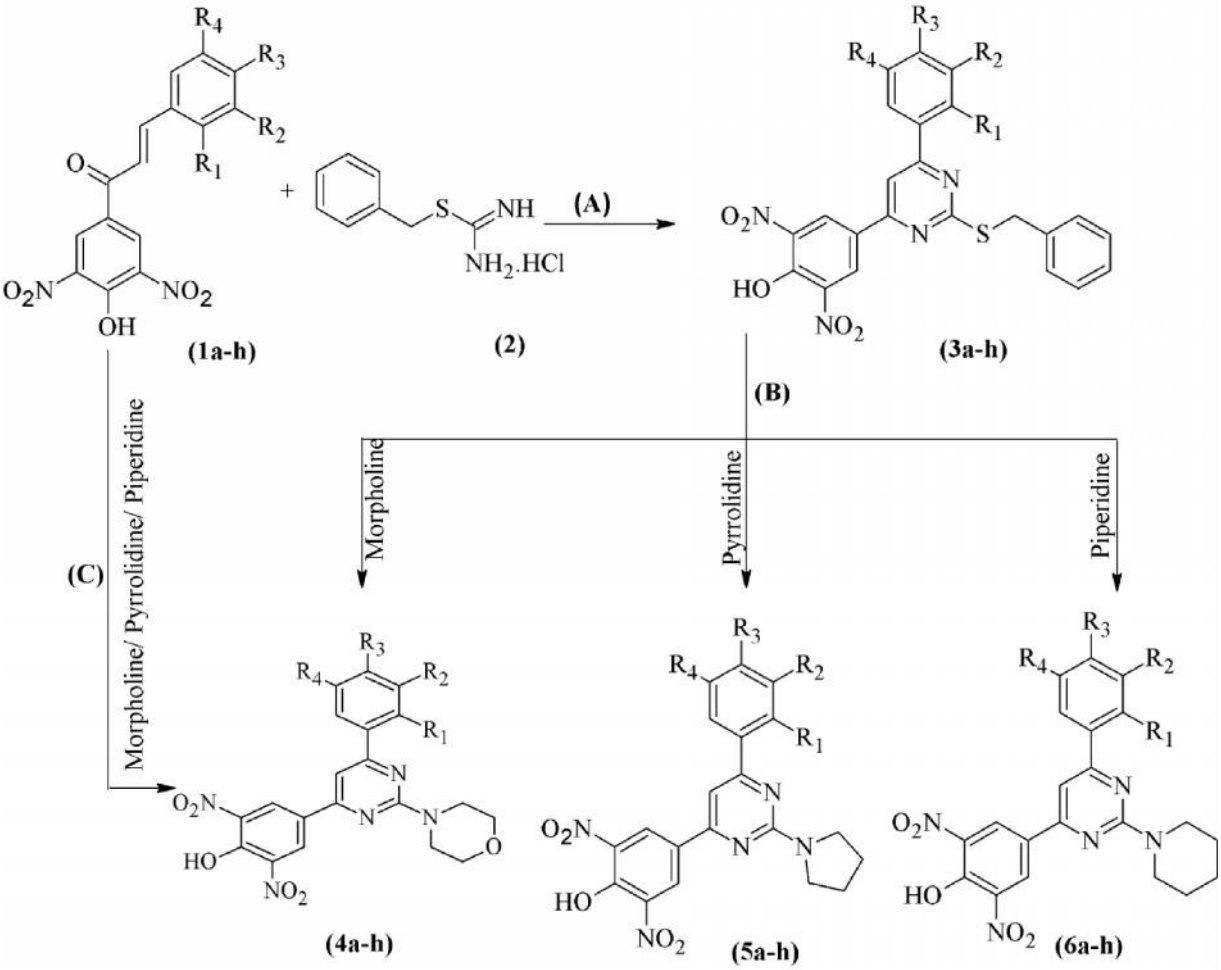
2. Results and discussion

In an effort to continuously develop novel pyrimidine molecules, the present study focused on the synthesis of some neoteric nitrochalcones and their facile conversion to substituted 4, 6-diaryl-2-(4-morpholinyl /1-pyrrolidinyl /1-piperidinyl)-pyrimidines. Nitroacetophenones were prepared by Bartlett *et al.* method[18]. All chemicals purchased from Sigma-Aldrich and Merck-Germany, used without further purification. Out of eight entries of nitrochalcones, synthesis of two nitrochalcones **1a-b** were reported by Ameta[14] *et al.* recently and the rest six new nitrochalcones **1c-h** are described in the present study. We have carried out the conversion of nitrochalcones to 4,6-diaryl-2-substituted pyrimidines in two attempts. Firstly, compound **1** on treatment with equimolar amount of SBT **2** and slight excess (1:1.2 mol) of morpholine / pyrrolidine / piperidine resulted 4,6-diaryl-2-substituted pyrimidines (**4a-h**, **5a-h** and **6a-h**) in one step. Secondly, equimolar quantity of **1** and **2** resulted 4,6-diaryl-2-benzylthiopyrimidines **3a-h** as intermediates which on treatment with slight excess (1:1.2 mol) of heterocyclic secondary amines resulted compounds **4a-h**, **5a-h** and **6a-h** in two step processes. The identity of synthesized compounds obtained by one and two-step methods were established by mix m.p, Co-TLC and super imposable IR spectra.

This transformation was also confirmed by the spectroscopic studies. In IR, the disappearance of band at 1665-1680 cm^{-1} due to the carbonyl group of chalcones and the appearance of band at 1595-1630 cm^{-1} due to cyclization, confirms the formation of intermediates **3a-h**. The ^{1}HNMR spectrum also confirms the synthesis of the compounds **3a-h** by a singlet at δ 4.30-4.56 (s, 2H, -S-CH_2-Ph). Further the compounds **4a-h, 5a-h** and **6a-h** showed the disappearance of ^{1}HNMR signal of the –S-CH_2-Ph group at δ 4.30-4.56 and appearance of multiplet at δ 3.50-4.55 for the –CH_2-N-CH_2- of morpholine / pyrrolidine / piperidine.

3. Conclusion

We have synthesized a novel series of 2- substituted-4, 6-diarylpyrimidines using nitrochalcones, SBT and various heterocyclic secondary amines using DMF as a solvent. The operational simplicity, rapid reaction and good yield of the resultant pyrimidines make this as a useful and alternate procedure.



Entry	a	b	c	d	e	f	g	h
R_1	H	H	H	H	OH	H	H	H
R_2	H	H	OCH_3	OCH_3	H	OH	OH	OCH_3
R_3	OCH_3	CH_3	OCH_3	OCH_3	H	OCH_3	H	OH
R_4	H	H	H	OCH_3	Br	H	H	Br

Scheme 1. *Reagents and conditions:* (A) DMF, reflux, 16-18 h. (B) and (C) Organic bases-DMF, reflux, 15-17 h

4. Experimental

General. All melting points were determined in open capillaries on Veego (VMP-MP) melting point apparatus and are uncorrected. IR spectra were recorded in KBr on a Perkin-Elmer spectrophotometer model RX I (υ_{max} in cm^{-1}). ^{1}HNMR ($CDCl_3$-solvent) on 500 MHz FT-NMR spectrometer Bruker AV III with TMS as an internal standard (chemical shift in δ ppm) and GC-MS (EI-MS fragment) performed on JEOL GC Mate spectrometer. The purity of compounds was routinely checked by TLC on Silica Gel-G plates using benzene: ethylacetate (9:1 v/v) as an eluent. The elemental analysis was carried out on a Carlo Erba 1108 analyzer and was within the ± 0.5 % of the theoretical values.

4.1. General procedure for the preparation of 1-(4-hydroxy-3, 5-dinitrophenyl)-3-phenyl propenones (1c-h):

A mixture of 4'-hydroxy-3',5'-dinitroacetophenone (0.01 mol) and substituted aromatic aldehydes (0.01 mol) was stirred in ethanol (30 mL) and then an aqueous solution of KOH (40%, 15 mL) was added to it. The mixture was kept overnight at room temperature and poured into crushed ice and acidified with dil HCl. The solid separated was filtered and recrystallized from ethanol.

*Physical data of compounds 1-(4-hydroxy-3, 5-dinitrophenyl)-3-phenyl propenones (**1c-h**):*

*(**1c**):* Yield (65%); mp. 91-93 °C; IR (KBr): 3445, 1666, 1630, 1522, 1378, 1115 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 3.40-3.65 (s, 6H, Ar-OCH_3), 6.85-7.20 (m, 3H, Ar-H), 7.55 (d, βH, J=16), 7.75 (d, αH, J=16), 8.20 (m, 2H, Ar-H), 11.91 (s, 1H, Ar-OH) ppm; MS *m/z* 374 (M^+). Anal. Calcd. for $C_{17}H_{14}N_2O_8$: C, 53.55, H, 3.90, N, 7.48 % Found: C, 53.20, H, 4.02, N, 7.28 %.

(**1d**): Yield (68%); mp. 70-72 °C; IR (KBr): 3435, 1660, 1628, 1521, 1370, 1119 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 3.45-3.72 (s, 9H, Ar-OCH_3), 6.80-7.25 (m, 2H, Ar-H), 7.58 (d, βH, J=16), 7.78 (d, αH, J=16), 8.30 (m, 2H, Ar-H), 11.99 (s, 1H, Ar-OH) ppm; MS *m/z* 404 (M^+). Anal. Calcd. for $C_{18}H_{16}N_2O_9$: C, 54.47, H, 3.99, N, 6.80 % Found: C, 54.84, H, 4.20, N, 6.68 %.

(**1e**): Yield (68%); mp. 78-80 °C; IR (KBr): 3568, 3441, 1668, 1638, 1525, 1372, 1115, 615 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 6.90-7.20 (m, 3H, Ar-H), 7.55 (d, βH, J=16), 7.75 (d, αH, J=16), 8.25 (m, 2H, Ar-H), 9.20 (s, 1H, Ar-OH), 11.91 (s, 1H, Ar-OH) ppm; MS *m/z* 409 (M^+). Anal. Calcd. for $C_{15}H_9BrN_2O_7$: C, 43.03, H, 2.58, N, 6.45 % Found: C, 43.36, H, 2.96, N, 6.12 %.

(**1f**): Yield (70%); mp. 160-162 °C; IR (KBr): 3555, 3442, 1670, 1630, 1530, 1375, 1118 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 3.45 (s, 3H, Ar-OCH_3), 6.95-7.30 (m, 3H, Ar-H), 7.35 (d, βH, J=16), 7.75 (d, αH, J=16), 8.30 (m, 2H, Ar-H), 9.10 (s, 1H, Ar-OH), 11.95 (s, 1H, Ar-OH) ppm; MS *m/z* 360 (M^+). Anal. Calcd. for $C_{16}H_{12}N_2O_8$: C, 53.90, H, 3.56, N, 7.60 % Found: C, 54.10, H, 3.75, N, 7.21%.

(**1g**): Yield (65%); mp. 85-87 °C; IR (KBr): 3560, 3451, 1671, 1633, 1528, 1380, 1123 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 6.85-7.30 (m, 4H, Ar-H), 7.35 (d, βH, J=16), 7.70 (d, αH, J=16), 8.35 (m, 2H, Ar-H), 9.35 (s, 1H, Ar-OH), 12.00 (s, 1H, Ar-OH) ppm; MS *m/z* 330 (M^+). Anal. Calcd. for $C_{15}H_{10}N_2O_7$: C, 55.25, H, 3.35, N, 8.98 % Found: C, 55.85, H, 3.85, N, 8.70 %.

(**1h**): Yield (69%); mp. 90-92 °C; IR (KBr): 3560, 3436, 1667, 1629, 1525, 1368, 1123, 625 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 3.40 (s, 3H, Ar-OCH_3), 6.85-7.30 (m, 3H, Ar-H), 7.38 (d, βH, J=16), 7.70 (d, αH, J=16), 8.25 (m, 2H, Ar-H), 9.15 (s, 1H, Ar-OH), 12.05 (s, 1H, Ar-OH) ppm; MS *m/z* 439 (M^+). Anal. Calcd. for $C_{16}H_{11}BrN_2O_8$: C, 43.76, H, 2.52, N, 6.38 % Found: C, 43.61, H, 2.70, N, 6.21 %.

4.2. General Procedure for the Synthesis of 4, 6-diaryl-2-(4-morpholinyl / 1-pyrrolidinyl /1-piperidinyl)-pyrimidines (4, 5, and 6)

4.2.1. Two step synthesis

*Step-I: Synthesis of Intermediate 4, 6-diaryl-2-benylthiopyrimidines **(3a-h)***

A mixture of substituted chalcones **1** (0.002 mol), SBT **2** (0.0022 mol) in DMF (50 mL) was refluxed on a water bath for 16-18 h. After completion of the reaction (monitored by TLC), the reaction mixture was cooled, diluted with water and kept under refrigeration. The resulting compounds were filtered and recrystallised from ethanol: benzene (2:1; v/v) to afforded analytical samples of **3a-h** in good yields.

*Physical data of compounds 4, 6-diaryl-2-benylthiopyrimidines **(3a-h)***

(**3a**): Yield (56%); mp. 148-150°C; IR (KBr): 3458, 3105, 3168, 1588, 1463, 1243, 1128, 1140 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 3.78 (s, 3H, Ar-OCH_3), 4.33 (s, 2H, -S-CH_2-), 7.10-7.60 (m, 9H, Ar-H), 7.80 (s, 1H), 7.9-8.10 (m, 2H), 12.18 (s, 1H, Ar-OH) ppm; MS: *m/z* (%) 490 (88, M^+), 468 (36), 244 (25), 123 (40), 90 (100). Anal. Calcd. for $C_{24}H_{18}N_4O_6S$: C, 58.77, H, 3.70, N, 11.42 %. Found: C, 58.70, H, 3.68, N, 11.38 %.

(**3b**): Yield (57%); mp. 180-182 °C; IR (KBr): 3477, 3144, 1605, 1494, 1237 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 2.34 (s, 3H, Ar-CH_3), 4.30 (s, 2H, -S-CH_2-), 7.30-7.73 (m, 9H, Ar-H), 7.85 (s, 1H), 7.85-8.05 (m, 2H), 12.11 (s, 1H, Ar-OH) ppm; MS: *m/z* (%) 474 (65, M^+), 239 (45), 161 (25), 90 (96). Anal. Calcd. for $C_{24}H_{18}N_4O_5S$: C, 60.72, H, 3.82, N, 11.8 %. Found: C, 60.66, H, 3.78, N, 11.78 %.

(**3c**): Yield (55%); mp. 210-212 °C; IR (KBr): 3469, 3115, 3160, 1595, 1465, 1244, 1115, 1140 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 3.82-3.90 (s, 6H, Ar-OCH_3), 4.32 (s, 2H, -S-CH_2-), 7.00-7.40 (m, 8H, Ar-H), 7.78 (s, 1H), 8.00-8.20 (m, 2H), 12.01 (s, 1H, Ar-OH) ppm; MS: *m/z* (%) 520 (58, M^+), 283 (28), 186 (45), 94 (100) 62 (12). Anal. Calcd. for $C_{25}H_{20}N_4O_7S$: C, 57.69, H, 3.87, N, 10.68 %. Found: C, 57.64, H, 3.81, N, 10.62 %.

(**3d**): Yield (56%); mp. 216-218 °C; IR (KBr): 3465, 3105, 3168, 1590, 1469, 1248, 1134 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 3.72-3.90 (s, 9H, Ar-OCH_3), 4.35 (s, 2H, -S-CH_2-), 7.2-7.40 (m, 7H, Ar-H), 7.73 (s, 1H), 7.95-8.20 (m, 2H), 12.10 (s, 1H, Ar-OH) ppm; MS: *m/z* (%) 550 (55, M^+), 281 (46), 143 (36), 90 (98), 63 (11). Anal. Calcd. for $C_{26}H_{22}N_4O_8S$: C, 56.72, H, 4.05, N, 10.18 %. Found: C, 56.68, H, 3.99, N, 10.10 %.

(**3e**): Yield (56%); mp. 195-197 °C; IR (KBr): 3460, 3485, 3110, 3155, 1590, 1472, 1255, 848 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 4.35 (s, 2H, -S-CH_2-), 7.15-7.50 (m, 8H, Ar-H), 7.70 (s, 1H), 8.02-8.25 (m, 2H), 9.78 (s, 1H, Ar-OH), 12.12 (s, 1H, Ar-OH) ppm; MS: *m/z* (%) 555 (40, M^+), 281 (46), 147 (38), 91 (100), 65 (15). Anal. Calcd. for $C_{23}H_{15}BrN_4O_6S$: C, 49.74, H, 2.72, N, 10.09 %. Found: C, 49.68, H, 2.68, N, 10.01 %.

(**3f**): Yield (55%); mp. 188-190 °C; IR (KBr): 3445, 3465, 3115, 3160, 1593, 1465, 1244, 843 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 3.80 (s, 3H, Ar-OCH_3), 4.32 (s, 2H, -S-CH_2-), 6.89-7.40 (m, 8H, Ar-H), 7.75 (s, 1H), 8.15-8.35 (m, 2H), 9.70 (s, 1H, Ar-OH), 12.11 (s, 1H, Ar-OH) ppm; MS: *m/z* (%) 506 (55, M^+), 278 (40), 171 (28), 90 (100). Anal. Calcd. for $C_{24}H_{18}N_4O_7S$: C, 56.91, H, 3.58, N, 11.06 %. Found: C, 56.88, H, 3.48, N, 11.00 %.

(**3g**): Yield (54%); mp. 148-150 °C; IR (KBr): 3445, 3467, 3112 3158 , 1596 , 1465, 1246 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 4.30 (s, 2H, -S-CH_2-), 6.88-7.40 (m, 9H, Ar-H), 7.70 (s, 1H), 8.00-8.15 (m, 2H), 9.50 (s, 1H, Ar-OH), 12.08 (s, 1H, Ar-OH) ppm; MS: *m/z* (%) 476 (75, M^+), 278 (48), 135 (35), 90 (85). Anal. Calcd. for $C_{23}H_{16}N_4O_6S$: C, 57.97, H, 3.38, N, 11.76 %. Found: C, 57.89, H, 3.32, N, 11.71 %.

(**3h**): Yield (56%); mp. 135-137 °C; IR (KBr): 3443, 3461, 3115, 3155, 1597, 1136, 1465, 1243, 843 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 3.80 (s, 3H, Ar-OCH_3), 4.32 (s, 2H, -S-CH_2), 7.15-7.40 (m, 8H, Ar-H), 7.78 (s, 1H), 8.05-8.20 (m, 2H), 9.35 (s, 1H, Ar-OH), 11.95 (s, 1H, Ar-OH) ppm; MS: *m/z* (%) 585 (62, M^+), 285 (56), 223 (33), 145 (14), 92 (88). Anal. Calcd. for $C_{24}H_{17}BrN_4O_7S$: C, 49.24, H, 2.93, N, 9.13 %. Found: C, 49.19, H, 2.89 N, 9.09 %.

*Step-II: Synthesis of **4a**-h from **3a-h***

To a solution of **3** (0.002 mol) and organic bases (0.0024 mol) in DMF (50 mL) was refluxed on a water bath for 15-17 h. After completion of the reaction (monitored by TLC), the reaction mixture was cooled, diluted with water and kept under refrigeration. The resulting compounds were filtered and recrystallised from ethanol-benzene (2:1 v/v) to afforded analytical samples of **4a-h** in good yields.

4.2.2. One step synthesis.

The compound **4a** was prepared in one step. A mixture of substituted chalcones **1** (0.002 mol), **2** SBT (0.0022 mol) and morpholine (0.0024) in DMF (50 mL) was refluxed on a water bath for 15-17 h. The reaction mixture was cooled, diluted with water and kept under refrigeration. The separated compounds were filtered which on recrystalization from ethanol-benzene (2:1 v/v) afforded analytical samples of **4a.** Compounds **4b-h**, **5a-h** and **6a-h** were similarly prepared by the above methods.

*Physical data of compounds 4,6-diaryl-2-(4-morpholinyl)- pyrimidines (**4a-h**):*

(**4a**): Yield (55%); mp. 201-203 °C; IR (KBr): 3462, 3112, 1601, 1479, 1260, 1135 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 3.00-3.15 (m, 4H, -CH_2-N-CH_2-), 3.75 (s, 3H, Ar-OCH_3), 3.70-3.90 (m, 4H, -CH_2-O-CH_2-), 6.80-7.30 (m, 4H, Ar-H), 7.70 (s, 1H), 8.48-8.62 (m, 2H), 12.00 (s, 1H, Ar-OH). MS *m/z* (%) 453 (56, M^+), 338 (36), 253 (100), 186 (23), 96 (80). Anal. Calcd. For $C_{21}H_{19}N_5O_7$: C, 55.63 H, 4.22, N, 15.45 %. Found: C, 55.61 H, 4.18, N, 15.41 %.

(**4b**): Yield (54%); mp. 148-150 °C; IR (KBr): 3462, 2927, 3112, 1592, 1477, 1248 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ=2.35 (s, Ar-CH_3), 3.50-3.70 (m, 4H, -CH_2-N-CH_2-), 3.75-3.90 (m, 4H, -CH_2-O-CH_2-), 6.80-7.15(m, 4H, Ar-H), 7.80 (s, 1H), 8.25-8.55 (m, 2H), 12.0 (s, 1H, Ar-OH) ppm; MS *m/z* (%) 437 (53, M^+), 356 (42), 268 (23), 173 (98), 94 (47). Anal. Calcd. For $C_{21}H_{19}N_5O_6$: C, 57.66, H, 4.38, N, 16.01 %. Found: C, 57.61, H, 4.31, N, 15.98 %.

(**4c**): Yield (56%); mp. 113-115 °C; IR (KBr): 3465, 3120, 1599, 1480, 1251, 1115 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 3.55-3.70 (m, 4H, -CH_2-N-CH_2-), 3.60-3.88 (m, 4H, -CH_2-O-CH_2-), 3.80-4.00 (two s, 6H, Ar-OCH_3), 6.88-7.45 (m, 3H, Ar-H), 7.78 (s, 1H), 8.45-8.63 (m, 2H), 12.01 (s, 1H, Ar-OH) ppm. MS *m/z* (%) 483 (52, M^+), 372 (35), 263 (100), 189 (12), 91 (12). Anal. Calcd. For $C_{22}H_{21}N_5O_8$: C, 54.66, H, 4.38, N, 14.49 %. Found: C, 54.64 H, 4.32 N, 14.47 %.

(**4d**): Yield (57%); mp. 89-91 °C; IR (KBr): 3467, 3118, 1600, 1478, 1256, 1108 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 3.50-3.75 (m, 4H, -CH_2-N-CH_2-), 3.65-3.90 (m, 4H, -CH_2-O-CH_2-), 3.70-3.90 (three s, 9H, Ar-OCH_3), 6.80-7.20 (s, 2H, Ar-H), 7.75 (s, 1H), 8.40-8.60 (m, 2H), 11.90 (s, 1H, Ar-OH) ppm; MS *m/z* (%) 513 (45, M^+), 384 (25), 281 (36), 217 (100), 162 (32), 104 (47). Anal. Calcd. For $C_{23}H_{23}N_5O_9$: C, 53.80, H, 4.52, N, 13.64 %. Found: C, 53.78, H, 4.48, N, 13.60 %.

(**4e**): Yield (56%); mp. 150-152 °C; IR (KBr): 3462, 3500, 3119, 1591, 1471, 1257, 835 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 3.50-3.75 (m, 4H, -CH_2-N-CH_2-), 3.70-3.92 (m, 4H, -CH_2-O-CH_2-), 6.85-7.25 (m, 3H, Ar-H), 7.70 (s, 1H), 8.45-8.62 (m, 2H), 9.10 (s, 1H, Ar-OH), 12.00 (s, 1H, Ar-OH) ppm. MS *m/z* (%) 518 (56, M^+), 315 (32), 253 (25), 135 (100), 93 (28). Anal. Calcd. For $C_{20}H_{16}BrN_5O_7$: C, 46.35, H, 3.11, N, 13.51 %. Found: C, 46.31, H, 3.05, N, 13.49 %.

(**4f**): Yield (55%); mp. 180-182 °C; IR (KBr): 3462, 3518, 3115, 1594, 1468, 1258 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 3.50-3.80 (m, 4H, -CH_2-N-CH_2-), 3.80 (s, 3H, Ar-OCH_3), 3.70-3.95 (m, 4H, -CH_2-O-CH_2-), 6.50-7.00 (m, 3H, Ar-H), 7.55 (s, 1H), 8.42-8.61 (m, 2H), 9.22 (s, 1H, Ar-OH), 12.20 (s, 1H, Ar-OH) ppm; MS *m/z* (%) 469 (85, M^+), 368 (32), 261 (100), 178 (14), 103 (45). Anal. Calcd. For $C_{21}H_{19}N_5O_8$: C, 53.70, H, 4.91, N, 14.91 %. Found: C, 53.65, H, 4.88, N, 14.86 %.

(**4g**):Yield (53%); mp. 97-99 °C; IR (KBr): 3462, 3480, 3118, 1598, 1485, 1249 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 3.40-3.60 (m, 4H, -CH_2-N-CH_2-), 3.70-3.96 (m, 4H, -CH_2-O-CH_2-), 6.85-7.25 (m, 4H, Ar-H), 7.45 (s, 1H), 8.40-8.65 (m, 2H), 9.54 (s, 1H, Ar-OH), 12.00 (s, 1H, Ar-OH) ppm; MS *m/z* (%) 439 (52, M^+), 343 (42), 221 (100), 169 (21), 98 (32). Anal. Calcd. For $C_{20}H_{17}N_5O_7$: C, 54.67, H, 3.90, N, 15.94 %. Found: C, 54.65, H, 3.88, N, 15.91 %.

(**4h**):Yield (56%); mp. 78-80 °C; IR (KBr): 3462, 3505, 3119, 1597, 1487, 1251, 1145, 834 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 3.50-3.72 (m, 4H, -CH_2-N-CH_2-), 3.80 (s, 3H, Ar-OCH_3), 3.65-3.90 (m, 4H, -CH_2-O-CH_2-), 6.90-7.20 (m, 3H, Ar-H), 7.65 (s, 1H), 8.45-8.62 (m, 2H), 9.10 (s, 1H, Ar-OH), 12.10 (s, 1H, Ar-OH) ppm; MS *m/z* (%) 548 (54, M^+), 348 (45), 243 (23), 180 (100), 97 (23). Anal. Calcd. For $C_{21}H_{18}BrN_5O_8$: C, 46.00, H, 3.31, N, 12.77 %. Found: C, 46.02, H, 3.30, N, 12.75 %.

*Physical data of compounds 4,6-diaryl-2-(1-pyrrolidinyl)-pyrimidines (**5a-h**):*

(**5a**):Yield (57%); mp. 230-232 °C; IR (KBr): 3458, 3108, 1603, 1477, 1261, 1138 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ=1.70-1.90 (m, 4H, -CH_2-CH_2-), 3.78 (s, 3H, Ar-OCH_3), 3.72-3.90 (m, 4H, -CH_2-N-CH_2-), 6.80-7.20 (m, 4H, Ar-H), 7.35 (s, 1H), 8.41-8.63 (m, 2H), 12.00 (s, 1H, Ar-OH) ppm; MS *m/z* (%) 437 (45, M^+) 321 (25), 278 (100), 159 (28), 91 (44). Anal. Calcd. For $C_{21}H_{19}N_5O_6$: C, 57.66, H, 4.38, N, 16.01 %. Found: C, 57.63, H, 4.37, N, 16.00 %.

(**5b**):Yield (56%); mp. 88-90 °C; IR (KBr): 3467, 2923, 3114, 1595, 1481, 1258 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 1.70-1.93 (m, 4H, -CH_2-CH_2-), 2.24 (s, 3H, Ar-CH_3), 3.61-3.79 (m, 4H, -CH_2-N-CH_2-), 6.90-7.25 (m, 4H, Ar-H), 7.61 (s,1H), 8.41-8.62 (m, 2H), 12.10 (s, 1H, Ar-OH) ppm; MS *m/z* (%) 421 (58, M^+) 305 (36), 261 (100), 115 (25), 82 (54). Anal. Calcd. For $C_{21}H_{19}N_5O_5$: C, 59.85, H, 4.54, N, 16.62 %. Found: C, 59.83, H, 4.51, N, 16.60 %.

(**5c**):Yield (56%); mp. 125-127 °C; IR (KBr): 3465, 3123, 1598, 1478, 1259, 1120 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 1.71-1.98 (m, 4H, $-CH_2-CH_2-$), 3.52-3.75 (m, 4H, $-CH_2-N-CH_2-$), 3.70-3.99 (two s, 6H, Ar-OCH_3), 6.90-7.35 (m, 3H, Ar-H), 7.70 (s,1H), 8.40-8.60 (m, 2H), 12.10 (s, 1H, Ar-OH) ppm; MS *m/z* (%) 467 (85, M^+), 358 (22), 252 (54), 123 (22), 96 (41). Anal. Calcd. For $C_{22}H_{21}N_5O_7$: C, 56.53, H, 4.53, N, 14.98 %. Found: C, 56.48, H, 4.48, N, 14.96 %.

(**5d**):Yield (53%); mp. 71-73 °C; IR (KBr): 3460, 3132, 1589, 1476, 1253, 1110 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 1.70-1.90 (m, 4H, $-CH_2-CH_2-$), 3.52-3.70 (m, 4H, $-CH_2-N-CH_2-$), 3.71-3.78 (three s, 9H, Ar-OCH_3), 7.00-7.35 (m, 2H, Ar-H), 7.70 (s, 1H), 8.35-8.55 (m, 2H), 12.05 (s, 1H, Ar-OH) ppm; MS *m/z* (%) 497 (62, M^+), 318 (32), 261 (74), 159 (100), 102 (40). Anal. Calcd. For $C_{23}H_{23}N_5O_8$: C, 55.53, H, 4.66, N, 14.08 %. Found: C, 55.50, H, 4.63, N, 14.02 %.

(**5e**):Yield (56%); mp. 160-162 °C; IR (KBr): 3503, 3118, 1588, 1487, 1266, 828 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ=1.70-1.92 (m, 4H, $-CH_2-CH_2-$), 3.55-3.73 (m, 4H, $-CH_2-N-CH_2-$), 6.85-7.25 (m, 3H, Ar-H), 7.75 (s, 1H), 8.41-8.60 (m, 2H), 9.50 (s, 1H, Ar-OH), 12.12 (s, 1H, Ar-OH) ppm; MS *m/z* (%) 502 (52, M^+), 352 (80), 223 (100), 154 (45), 91 (11). Anal. Calcd. For $C_{20}H_{16}BrN_6O_5$: C, 47.83, H, 3.21, N, 13.94 %. Found: C, 47.79, H, 3.19, N, 13.11 %.

(**5f**):Yield (55%); mp. 125-127 °C; IR (KBr): 3462, 3516, 3112, 1595, 1477, 1256 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 1.70-1.90 (m, 4H, $-CH_2-CH_2-$), 3.58-3.78 (m, 4H, $-CH_2-N-CH_2-$), 3.86 (s, 3H, $-OCH_3$), 6.85-7.20 (m, 2H, Ar-H), 7.65 (s, 1H), 8.35-8.55 (m, 2H), 9.40 (s, 1H, Ar-OH), 12.00 (s, 1H, Ar-OH) ppm; MS *m/z* (%) 453 (45, M^+), 334 (87), 278 (100), 146 (52), 104 (55). Anal. Calcd. For $C_{21}H_{19}N_5O_7$: C, 55.63, H, 4.22, N, 15.45 %. Found: C, 55.58, H, 4.18, N, 14.41 %.

(**5g**): Yield (54%); mp. 92-94 °C; IR (KBr): 3462, 3490, 3121, 1601, 1465, 1266 cm^1; ^1H NMR (500 MHz, $CDCl_3$): δ= 1.70-1.95 (m, 4H, $-CH_2-CH_2-$), 3.52-3.70 (m, 4H, $-CH_2-N-CH_2-$), 6.80-7.20 (m, 4H, Ar-H), 7.70 (s, 1H), 8.42-8.60 (m, 2H), 8.80 (s, 1H,Ar -OH), 12.10 (s, 1H, Ar-OH) ppm; MS *m/z* (%) 423 (45, M^+), 323 (12), 252 (100), 143 (38), 98 (54). Anal. Calcd. For $C_{20}H_{17}N_5O_6$: C, 56.74, H, 4.05, N, 16.54 %. Found: C, 56.72, H, 4.01, N, 16.51 %.

(**5h**):Yield (56%); mp. 89-91 °C; IR (KBr): 3462, 3512, 3118, 1595, 1475, 1253, 1134, 830 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 1.83-1.98 (m, 4H, $-CH_2-CH_2-$), 3.52-3.78 (m, 4H, $-CH_2-N-CH_2-$), 3.85 (s, 1H, Ar-OCH_3), 7.00-7.30 (m, 3H, Ar-H), 7.75 (s, 1H), 8.35-8.58 (m, 2H), 9.10 (s, 1H, Ar-OH), 12.1 (s, 1H, Ar-OH) ppm; MS *m/z* (%) 532 (52, M^+), 324 (100), 230 (45), 154 (54), 99 (22). Anal. Calcd. For $C_{21}H_{18}BrN_5O_7$: C, 47.38, H, 3.41, N, 13.16 %. Found: C, 47.35, H, 3.38, N, 13.12 %.

*Physical data of compounds 4,6-diaryl-2-(1-piperidinyl)-pyrimidines (**6a-h**):*

(**6a**): Yield (54%); mp. 190-192 °C; IR (KBr): 3468, 3123, 1597, 1483, 1257, 1128 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 1.40-1.62 (m, 6H, $-(CH_2)_2-$), 3.40-3.71 (m, 4H, $-CH_2-N-CH_2-$), 3.79 (s, 3H, Ar-OCH_3), 6.90-7.20 (m, 4H, Ar-H), 7.65 (s, 1H), 8.35-8.60 (m, 2H), 12.00 (s, 1H, Ar-OH) ppm; MS *m/z* (%) 451 (78, M^+), 387 (25), 235 (100), 153 (14), 93 (26). Anal. Calcd. For $C_{22}H_{21}N_5O_6$: C, 58.53, H, 4.69, N, 15.51 %. Found: C, 58.51 H, 4.65, N, 15.48 %.

(**6b**): Yield (56%); mp. 95-97 °C; IR (KBr): 3453, 2928, 3117, 1602, 1475, 1260 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 1.30-1.58 (m, 6H, -$(CH_2)_3$-), 2.35 (s, 3H, Ar-CH_3), 3.40-3.72 (m, 4H, -CH_2-N-CH_2-), 6.60-7.00 (m, 4H, Ar-H), 7.65 (s, 1H), 8.30-8.55 (m, 2H), 12.01 (s, 1H, Ar-OH) ppm; MS *m/z* (%) 435 (40, M^+) 356 (100), 281 (26), 148 (23), 97 (45). Anal. Calcd. For $C_{22}H_{21}N_5O_5$: C, 60.68, H, 4.86, N, 16.08 %. Found: C, 60.63, H, 4.81, N, 15.99 %.

(**6c**): Yield (56%); mp. 143-145 °C; IR (KBr): 3473, 3109, 1595, 1474, 1263, 1123 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 1.30-1.50 (m, 6H, -$(CH_2)_2$-), 4.40-4.71 (m, 4H, -CH_2-N-CH_2-), 3.80-4.95 (two s, 6H, Ar-OCH_3), 6.90-7.35 (m, 3H, Ar-H), 7.70 (s, 1H), 8.45-8.62 (m, 2H), 12.09 (s, 1H, Ar-OH) ppm; MS *m/z* (%) 481 (78, M^+), 332 (58), 261 (100), 131 (25), 105 (58). Anal. Calcd. For $C_{23}H_{23}N_5O_7$: C, 57.38, H, 4.82, N, 14.55 %. Found: C, 57.36, H, 4.78, N, 14.51 %.

(**6d**): Yield (55%); mp. 98-100 °C; IR (KBr): 3466, 3118, 1599, 1478, 1258, 1109 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 1.40-1.65 (m, 6H, -$(CH_2)_2$-), 3.42-3.65 (m, 4H, -CH_2-N-CH_2-), 3.71-3.86 (three s, 9H, Ar-OCH_3), 6.95-7.35 (m, 2H, Ar-H), 7.66 (s, 1H), 8.42-8.65 (m, 2H), 12.00 (s, 1H, Ar-OH) ppm; MS *m/z* (%) 511 (56, M^+), 321 (52), 235 (36), 153 (100), 108 (52). Anal. Calcd. For $C_{24}H_{25}N_5O_8$: C, 56.36, H, 4.93, N, 13.69 %. Found: C, 56.33, H, 4.92, N, 13.71 %.

(**6e**): Yield (54%); mp. 120-123 °C; IR (KBr): 3462, 3498, 3135, 1598, 1471, 1253, 818 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 1.48-1.68 (m, 6H, -$(CH_2)_3$-), 3.48-3.71 (m, 4H, -CH_2-N-CH_2-), 6.92-7.25 (m, 3H, Ar-H), 7.65 (s, 1H), 8.42-8.60 (m, 2H), 9.10 (s, 1H, Ar-OH), 12.18 (s, 1H, Ar-OH) ppm; MS *m/z* (%) 516 (54, M^+), 454 (41), 378 (100), 236 (24), 162 (21), 98 (23). Anal. Calcd. For $C_{21}H_{18}BrN_5O_6$: C, 48.85, H, 3.51, N, 13.56 %. Found: C, 48.83, H, 3.50, N, 13.52 %.

(**6f**): Yield (57%); mp. 112-114 °C; IR (KBr): 3462, 3509, 3124, 1588, 1473, 1252 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 1.42-1.65 (m, 6H, -$(CH_2)_3$-), 3.42-3.75 (m, 4H, -CH_2-N-CH_2-), 3.84 (s, 3H, Ar-OCH_3), 6.80-7.10 (m, 3H, Ar-H), 7.55 (s, 1H), 8.21-8.55 (m, 2H), 9.54 (s, 1H, Ar-OH), 12.12 (s, 1H, Ar-OH) ppm; MS *m/z* (%) 467 (74, M^+), 328 (32), 225 (80), 153 (100), 96 (52). Anal. Calcd. For $C_{22}H_{21}N_5O_7$: C, 56.13, H, 4.54, N, 14.89 %. Found: C, 56.07, H, 4.51, N, 14.85 %.

(**6g**): Yield (56%); mp. 125-127 °C; IR (KBr): 3452, 3491, 3122, 1598, 1479, 1254 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 1.35-1.53 (m, 6H, -$(CH_2)_3$-), 3.48-3.70 (m, 4H, -CH_2-N-CH_2-), 6.80-7.30 (m, 4H, Ar-H), 7.60 (s, 1H), 8.35-8.58 (m, 2H), 8.90 (s, 1H, Ar-OH), 12.10 (s, 1H, Ar-OH) ppm; MS *m/z* (%) 437 (51, M^+), 312 (36), 221 (100), 142 (45), 103 (12). Anal. Calcd. For $C_{21}H_{19}N_5O_6$: C, 57.66, H, 4.38, N, 16.01%. Found: C, 57.64, H, 4.35, N, 15.98 %.

(**6h**): Yield (56%); mp. 100-102 °C; IR (KBr): 3464, 3518, 3120, 1593, 1480, 1253, 1138, 816 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ= 1.35-1.52 (m, 6H, -$(CH_2)_3$-), 3.40-3.65 (m, 4H, -CH_2-N-CH_2-), 3.74 (s, 1H, Ar-OCH_3), 7.00-7.30 (m, 3H, Ar-H), 7.70 (s, 1H), 8.25-8.64 (m, 2H), 8.80 (s, 1H, Ar-OH), 12.05 (s, 1H, Ar-OH) ppm; MS *m/z* (%) 564 (56, M^+), 354 (36), 256 (41), 154 (25), 105 (102). Anal. Calcd. For $C_{22}H_{20}BrN_5O_7$: C, 48.37, H, 3.69, N, 12.82 %. Found: C, 48.33, H, 3.68, N, 12.80 %.

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References

[1] Gahlot, U. S.; Rao, S. S.; Dulawat, S. S.; Ameta, K. L.; Verma, B. L. A facile one-pot microwave assisted conversion of 3'-5'-dibromo/ diiodo-4'-hydroxy substitutes chalcones to 2-substituted -4,6-diaryl pyrimidines using S-benzylisothiouronium chloride (SBT) and their antibacterial activities, *Afinidad*. 2003, *60*, 558-562.

[2] Nofal, Z. M.; Fahmy, H. H.; Zarea, E.S.; El-Eraky, W. Synthesis of new pyrimidine derivatives with evaluationof their anti-inflammatory and analgesic activities, *Acta pol. pharm*. 2011, *68*, 507-517.

[3] Yit, C. C.; Das, N. P. **Cytotoxic effect of butein on human colon adenocarcinoma cell proliferation,** *Cancer Lett*. 1994, ***82*,** 65-72.

[4] Jiang, B.; Yang, C. G.; Xiong, W. N.; Wang, J. Synthesis and cytotoxicity of evaluation of novel indolylpyrimidines and indolylpyrazines as potential antitumor agents, *Bioorg. Med. Chem.* 2001, *9*, 1149-1154.

[5] Rostom, S. A.; Ashour, H. M.; Abd El Razik, H. A. Synthesis and biological evaluation of some novel polysubstituted pyrimidine derivatives as potential antimicrobial and anticancer agents, *Arch. Pharm(Weinheim)*. 2009, *342*, 299-310.

[6] El-Deeb, I. M.; Lee, S. H. Design and synthesis of new anticancer pyrimidines with multiple-kinase inhibitory effect, *Bioorg. Med. Chem.* 2010, *18*, 3860-3874.

[7] Zorkun, I. S.; Sarac, S.; Celebi, S.; Erol, K. Synthesis of 4-aryl-3,4-dihydropyrimidin-2(1H)-thione derivatives as potential calcium channel blockers, *Bioorg. Med. Chem*. 2006, *14*, 8582-8589.

[8] Grover, G. J.; Dzwonczyk, S.; McMullen, D. M.; Nomandin, D.E.; Parham, C.S.; Sleph, P.G.; Moreland, S. Pharmacologic profile of the dihydropyrimidine calcium channel blockers SQ 32,547 and SQ 32,946[correction of SQ 32,946], *J. Cardio. Pharma.* 1995, *26(2)*, 289–294.

[9] Bhat, B. A.; Dhar, K. L.; Puri, S.C.; Saxena, A. K.; Shanmugavel, M.; Qazi, G. N. Synthesis and biological evaluation of Chalcones and their derived Pyrazoles as potential cytotoxic agents, *Bio org. Med. Chem. Lett.* 2005, *15,* 3177-3180.

[10] Ameta, K. L.; Rathore, N. S.; Kumar, B. Synthesis and *in vitro* Anti breast Cancer Activity of some novel 1, 5-benzothiazepine derivatives, *J. Serbian Chemical Society.* 2011, doi: 10.2298/JSC110715219A.

[11] Blotny, G. Recent applications of 2,4,6-trichloro-1,3,5-triazine and its derivatives in organic synthesis, *Tetrahedron*. 2006, *62*, 9507-9522.

[12] Zhou, Y.; Sun, Z.; Froelich, J. M.; Hermann, T.; Wall, D. Structure-activity relationships of novel antibacterial translation inhibitors; 3,5-Diaminopiperidinyl triazines, *Bioorg. Med. Chem. Lett*. 2006, *16*, 5451-5456.

[13] Rao, S. S.; Gahlot, U. S.; Dulavat, S. S.; Vyas, R.; Ameta, K. L.; Verma, B. L. Microwave-induced improved synthesis and antibacterial activities of some chalcones and their 1-acyl-3,5-diaryl-2-pyrazolines, *Afinidad.* 2003, *60*, 271-276.

[14] Ameta, K. L.; Kumar, B.; Rathore, N. S. Microwave induced improved synthesis of some novel substituted 1, 3-diarylpropenones and their antimicrobial activity, *E- J. Chem*. 2011, *8*, 665-670.

[15] Ameta, K. L.; Rathore, N. S.; Kumar, B. Synthesis of some novel chalcones and their facile one-pot conversion to 2-aminobenzene-1, 3-dicarbonitriles using malononitrile, *An. Univ. Bucuresti. Chimie.* 2011, *20(1)*, 15-24.

[16] Sharma, P.; Hussain, K. F.; Sukhwal, S.; Kothari, S.; Singhal, M.; Verma, B. L. A convenient one-pot synthesis of 2-substituted-4,6-diryl pyrimidines, *Indian J. Chem*. 1999, *38B*, 966-968.

[17] Kothari, S.; Vyas, R.; Verma, B. L. A facile one pot conversion of 3',5'-dibromo-4-hydroxy substituted chalcone to pyrimidine derivatives and their antibacterial and herbicidal activity, *Indian J. Heterocyclic Chem*. 1999, *8*, 285-288.

[18] Bartlett, P. D.; Trachtenberg, E. N. 5,7-dinitro-7-coumaranone and the mechanism of biomolecular nucleophilic displacement reaction in phenacyl compounds, *J. Am. Chem. Soc*. 1958, *80*, 5808-5812.