MICROWAVE ASSISTED SYNTHESIS OF SOME TETRAHYDROPYRIMIDINETHIONE, THIAZOLO[3,2-*a*]PYRIMIDINONE AND XANTHENEDIONE DERIVATIVES

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تم تحضير عدد من ١،٢،٣،٤-رباعي هيدروبيريميدين-٢-ثيون **2a-d** بكميات جيدة باستخدام التشعيع بالموجات متناهية الصغر. وقد أعطت حولقة المركبات **2a-c** بكواشف مختلفة مشتقات ثيازولوبيريميدينون **3-5**. وقد أعطى تفاعل دايمدون مع الألدهيدات العطرية والثيوريا –بالتشعيع بالموجات متناهية الصغر– مركبات زانثين داي أون **8a,b** كمركبات رئيسة. وقد تم التعرف على المركبات المحضرة بالطرق الطيفية.

A number of 1,2,3,4-tetrahydropyrimidine-2-thiones **2a-d**, have been synthesized using microwave irradiation in an appreciable yield. Cyclisation of **2a-c** with different reagents gave the thiazolopyrimidinone derivatives **3-5**. Reaction of dimedone with aromatic aldehydes and thiourea using microwave irradiation afforded the xanthenedione **8a,b** as a major product. The prepared compounds were fully identified by spectroscopic methods.

Keywords: 1,2,3,4-Tetrahydropyrimidinethiones, thiazolopyrimidinone, xanthenedione, microwave irradiation.

INTRODUCTION

Pyrimidines are very well known in medicinal chemistry for their therapeutic applications [1,2]. Many of 2-thioxopyrimidines were associated with broad spectrum of biological activity including antimicrobial [3-5], antifungal [6,7] and antitumor [8-10] properties. In the light of the above mentioned biological importance of the title compounds and due to our increased activity involved in the synthesis of a variety of nitrogen-containing heterocycles during the past few years [11-13], we report herein the synthesis of a series of novel pyrimidinethione, thiazolopyrimidinone and xanthenedione derivatives which have been structurally elucidated on the basis of spectroscopic means.

EXPERIMENTAL

Melting points are determined on an electrothermal's IA9000 series digital capillary melting point apparatus and are uncorrected. IR spectra were run (KBr discs) on Perkin Elmer FT spectrophotometer 1000. ^{1}H and ^{13}C-NMR spectra were recorded on a JEOL ECP 400 NMR spectrometer operating at 400 MHz in DMSO-d_6 unless otherwise stated with TMS as internal standard. DEPT and HETCOR experiments were recorded on 300 MHz instrument (Brucker, J.F.B. 288) at King Abdulaziz University, Jedda. Chemical shifts are given in δ ppm and coupling constants (*J*) are given in Hz. Electron impact (EI) MS spectra were carried on Shimadzu GCMSQP5050A spectrometer, DB-1 glass column 30 m, 0.25 mm, ionization energy 70 eV, at Chemistry Department, College of Science, King Saud University.

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General procedure for the synthesis of 4-Aryl-5-benzoyl-6-methyl-1,2,3,4-tetrahydro pyrimidine-2- thiones (2a-d):

Classical method: Compounds **2a-c** were synthesized following the reported method [15-17] for similar compounds. Yields obtained are shown in Table 1.

Microwave method: Equimolar amount of 0.02 mol of benzoylacetone, monosubstituted benzaldehyde and thiourea were mixed thoroughly, moistened with little amount of methanol and taken in an Erlenmeyer flask (100 mL), then it was subjected to microwave irradiation in a house oven at a power of 600 W for the time being depicted in Table 1. After completion of the reaction, the solid obtained was triturated with few drops of methanol, filtered, washed with hot methanol and dried to give the target compounds. The products (**2a-d**) were analyzed by spectroscopic means and were pure enough to be used in subsequent reactions without further purification. Compound **2a** was also prepared using neat (solvent free) microwave with 90% yield.

4-(3`-Methoxyphenyl)-5-benzoyl-6-methyl-1,2,3,4-tetrahydropyrimidine-2-thione (2a):
Bright yellow prisms, m.p. 215-216 °C; IR (cm^{-1}): 3179, 3278 (2NH), 1656 (C=O), 1195 (C=S); MS: *m/z* (%) 338 [M^+] (80) ($C_{19}H_{18}N_2O_2S$); ^{1}H-NMR (DMSO-d_6): Table 2; ^{13}C-NMR (DMSO-d_6): Figure 1.

4-(4`-Bromophenyl)-5-benzoyl-6-methyl-1,2,3,4-tetrahydropyrimidine-2-thione (2b):
Pale yellow powder, m.p. 140-142°C; IR (cm^{-1}): 3187, 3393 (2NH), 1663 (C=O), 1205 (C=S); MS: *m/z* (%) 386/388 [M^+] (47/41) ($C_{18}H_{15}BrN_2OS$); ^{1}H-NMR and ^{13}C-NMR (DMSO-d_6): Table 2.

4-(4`-Chlorophenyl)-5-benzoyl-6-methyl-1,2,3,4-tetrahydropyrimidine-2-thione (2c):
Beige prisms, m.p. 228-230°C; IR (cm^{-1}): 3283, 3406 (2NH), 1691 (C=O), 1201 (C=S); MS: *m/z* (%) 342/344 [M^+] (30/20) ($C_{18}H_{15}ClN_2OS$); ^{1}H-NMR and ^{13}C-NMR (DMSO-d_6): Table 2.

4-(4`-Nitrophenyl)-5-benzoyl-6-methyl-1,2,3,4-tetrahydropyrimidine-2-thione (2d):
Orange prisms, m.p. 215-216°C; IR (cm^{-1}): 3199, 3259 (2NH), 1679 (C=O), 1209 (C=S); MS: *m/z* (%) 353 [M^+] (9) ($C_{18}H_{15}N_3O_3S$), 307 [M-NO_2] (48), 231 [M-$C_6H_4NO_2$] (90); ^{1}H-NMR and ^{13}C-NMR (DMSO-d_6): Table 2.

General procedure for the synthesis of [5-Aryl-6-benzoyl-7-methyl-3-oxo-5*H*-thiazolo[3,2-*a*]pyrimidin-2-ylidene]-acetic acid ester (3a,b):
Molar amount of **2a,b** (0.002 mol) and dimethyl acetylenedicarboxylate (0.0025 mol) were mixed thoroughly and moistened with methanol (1 mL) in an Erlenmeyer flask (50 mL). After the evaporation of methanol, the mixture was subjected to microwave irradiation in a house oven at a power of 800 W for 20-23 minutes. The reaction mixture was then worked up as above to yield compounds **3a,b**.

[6-Benzoyl-5-(3`-methoxyphenyl)-7-methyl-3-oxo-5*H*-thiazolo[3,2-*a*]pyrimidin-2-ylidene]-acetic acid ester (3a): Bright yellow prisms, m.p. 142-144°C; IR (cm^{-1}): 1729, 1709, 1643 (3C=O); MS: *m/z* (%) 448 [M^+] (85) ($C_{24}H_{20}N_2O_5S$); ^{1}H-NMR (DMSO-d_6): δ 1.75 (3H, s,CH_3), 3.65, 3.78 (each 3H, s, 2OCH_3), 6.05 (1H, s, H-5), 6.67 (1H, s, 2`-H), 6.85 (1H, s, exocyclic vinyl proton), 6.81 (2H, m, H-4`and H-6`), 7.23 (1H, t, *J* = 7.7 Hz, H-5`), 7.46 (2H, t, phenyl protons), 7.61 (3H, m, phenyl protons); ^{13}C-NMR (DMSO-d_6): Figure 2.

[6-Benzoyl-5-(4`-bromophenyl)-7-methyl-3-oxo-5*H*-thiazolo[3,2-*a*]pyrimidin-2-ylidene]-acetic acid ester (3b): Orange prisms, 200-201°C; IR (cm^{-1}): 1732, 1705, (2C=O); MS: *m/z* (%) 496/498 [M^+] (15/17) ($C_{23}H_{17}BrN_2O_4S$); 341 [M-C_6H_4Br] (92) base peak; ^{1}H-NMR (DMSO-d_6): δ 1.76 (3H, s, CH_3), 3.79 (3H, s, OCH_3), 6.06 (1H, s, H-5), 6.84 (1H, s, exocyclic vinyl proton), 7.21 (2H, d, *J*=8.1 Hz, H-2`& H-6`), 7.62 (2H, d, *J* = 8.1 Hz, H-3`& H-5`), 7.44-7.51 (5H, m, phenyl protons).

General procedure for the synthesis of 5-Aryl-6-benzoyl-7-methyl-5*H*-thiazolo[3,2-*a*]pyrimidin-3-one (4a,b):
Equimolar amount of **2a,b** (0.005 mol) and chloro-acetic acid (0.005 mol) were mixed thoroughly in an Erlenmeyer flask (50 mL). The mixture was subjected to microwave irradiation in a house oven at a power of 800 W for the time shown in Table 3. The reaction mixture was then worked up as above to yield compounds **4a,b**.

6-Benzoyl-5-(3`-methoxyphenyl)-7-methyl-5*H*-thiazolo[3,2-*a*]pyrimidin-3-one (4a): Yellow prisms, m.p. 220-221°C; IR (cm^{-1}): 1779, 1670 (2C=O); MS: *m/z* (%) 378 [M^+] (80) ($C_{21}H_{18}N_2O_3S$); ^{1}H-NMR (DMSO-d_6): δ 1.74 (3H, s,CH_3), 3.67 (3H, s, OCH_3), 4.21 (2H, two d, *J*=17.6 Hz, AB system, CH_2), 5.95 (1H, s, H-5), 6.66 (1H, d. *J*=2.2 Hz, H-2`), 6.78 (1H, d, *J*=8.0 Hz, H-4`), 6.83 (1H, dd, *J*=8.0 and 2.2 Hz, H-6`), 7.24 (1H, t, *J*=8.0 Hz, H-5`), 7.44-7.58 (5H, m, phenyl protons); ^{13}C-NMR (DMSO-d_6): Figure 3.

6-Benzoyl-5-(4`bromophenyl)-7-methyl-5*H*-thiazolo[3,2-*a*]pyrimidin-3-one (4b): Bright yellow prisms, m.p. 198-199°C; IR (cm^{-1}): 1767, 1664 (2C=O); MS: *m/z* (%) 426/428 [M^+] (45/49) ($C_{20}H_{15}BrN_2O_2S$); ^{1}H-NMR (DMSO-d_6): δ 1.76 (3H, s,CH_3), 4.20 (2H, two d, *J*=16.3 Hz, AB system, CH_2), 5.97 (1H, s, H-5), 7.23 (2H, d, *J*=8.1 Hz, H-2`,H-6`), 7.61 (2H, d, *J*=8.1 Hz, H-3`& H-5`), 7.44-7.59 (5H, m, phenyl protons); ^{13}C-NMR (DMSO-d_6): δ 21.48 (CH_3), 33.10 (C-2), 56.69 (C-5), 115.64 (C-6), 122.49 (C-4`), 130.32 (C-2`& C-6`), 132.27 (C-3`& C-5`), 138.65 (C-1`), 142.42 (C-7), 151.60 (C-8a), 129.01, 129.49, 133.84 and 138.90 (ph-C), 171.46 (C=O), 195.14 (C=O).

General procedure for the synthesis of 5-Aryl-6-benzoyl-2-(4`bromobenzylidene)-7-methyl-5*H*-thiazolo[3,2-*a*]pyrimidin-3-one (5a-c):
Equimolar amount of **2a,b** (0.002 mol), chloro-acetic acid (0.002 mol) and *p*-bromobenzaldehyde (0.002 mol) were mixed thoroughly in an Erlenmeyer flask (25 mL) and subjected to microwave irradiation in a house oven at a power of 800 W for the time shown in Table 3. The reaction was then worked up as above to yield compounds **5a,b**.

6-Benzoyl-2-(4`bromobenzylidene)-5-(3``methoxyphenyl)-7-methyl-5*H*-thiazolo[3,2-*a*]pyrimidin-3-one(5a): Brown powder, m.p. 130-132°C; IR (cm^{-1}): 1745, 1678 (2C=O), 1658, (C=C); MS: *m/z* (%) 544/546 [M^+] (41/47) ($C_{28}H_{21}BrN_2O_3S$); ^{1}H-NMR ($CDCl_3$): δ 1.89 (3H, s, CH_3), 3.70 (3H, s, OCH_3), 6.31(1H, s, H-5), 6.76 (1H, dd, *J*= 2.2 and 8.0 Hz, H-4``), 6.82 (1H, d, *J*=2.2 Hz, H-2``), 6.90 (1H, d, *J*=8.0 Hz, H-6``), 7.21 (1H, t, *J*=8.0 Hz, H-5``), 7.35(2H, d, *J*=8.8Hz, H-2`& H-6`), 7.36-7.38 (2H, m, benzoyl *m*- proton), 7.50 (1H t, *J*=8.1Hz, benzoyl *p*-proton) 7.53-7.60 (2H, m, benzoyl *o*- proton), 7.73 (1H, s, exocyclic vinyl proton), 7.7.59(2H, d, *J*=8.8Hz, H-3`& H-5`) ^{13}C-NMR ($CDCl_3$): δ 21.17 (CH_3), 57.51 (OCH_3), 55.36 (C-5), 113.27, 114.51, 117.89, 119.27, 126.02, 128.79, 128.91, 130.75, 131.10, 131.40, 131.50, 132.83, 133.41, 134.20, 138.32, 139.84, 158.01 and 160.05 (olefinic and aromatic sp^2 carbons) 164.63 (C=O), 195.21(C=O).

6-Benzoyl-2-(4`-bromo-benzylidene)-5-(4``bromophenyl)-7-methyl-5*H*-thiazolo[3,2-a]pyrimidin-3-one (5b): Orange powder, m.p. 181-183°C; IR (cm^{-1}): 1748, 1679 (C=O), 1639, (C=C); MS : *m/z* (%) 592/594 [M^+] (41/47) ($C_{27}H_{18}Br_2N_2O_2S$); ^{1}H-NMR (DMSO): δ 1.76 (3H, s,CH_3), 6.12(1H, s, H-5), 7.23 (2H, d, *J*=8.1 Hz, H-2″& H-6″), 7.47 (2H, t, *J*=7.7 Hz, benzoyl *m*-proton), 7.51 (2H, d, *J*=8.1 Hz, H-3″ & H-5″), 7.57 (2H, d, *J*=8.1 Hz, H-2′ & H-6′), 7.62 (2H, d, *J*=8.0 Hz, H-3′ & H-5′), 7.76 (3H, m, benzoyl *o* & *p*-protons), 7.84 (1H, s, exocyclic vinyl proton).

6-Benzoyl-2-(4`-bromo-benzylidene)-5-(4``chlorophenyl)-7-methyl-5*H*-thiazolo[3,2-a]pyrimidin-3-one (5c): Beige prisms m.p. 174-176°C; IR (cm^{-1}): 1753, 1684 (C=O), 1651, (C=C); MS: *m/z* (%) 548/550 [M^+] (23/29) ($C_{27}H_{18}BrClN_2O_2S$); ^{1}H-NMR (DMSO): δ 1.75 (3H, s, CH_3), 6.13 (1H, s, H-5), 7.29 (2H, d, *J*=8.8 Hz, H-2″ & H-6″), 7.37 (2H, d, *J*=8.8 Hz, H-3″ & H-5″), 7.46 (2H, t, *J*=8.0 Hz, benzoyl *m*- proton), 7.55 (3H, m, H-2′, H-6′ & benzoyl *p*-proton), 7.61 (2H, d, *J*=8.1 Hz, H-3′ & H-5′), 7.74 (2H, m, benzoyl *o*- proton & exocyclic vinyl proton).
Compounds **5a,b** were also obtained using microvave method through the reaction of **4a,b** with 4-bromobenzaldehyde.

General procedure for the synthesis of 4-Aryl-7,7-dimethyl-2-thioxo-1,3,4,6,7,8-hexahydro-1*H*-quinazolin-5-one (7a,b) and **9-Aryl-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-2*H*-xanthene-1,8-dione (8a,b):** Equimolar amount of 0.02 mol of dimedone, aromatic aldehyde, namely 4-chlorobenzaldehyde and 4-bromobenzaldehyde, and thiourea were mixed thoroughly, moist with little amount of methanol and taken in an Erlenmeyer flask (100 mL) and was subjected to microwave irradiation in a house oven at a power of 600 W for 2-3 minutes. After completion of the reaction (monitored by TLC), the solid obtained was boiled with methanol, filtered, washed with hot methanol and dried to give **7a,b**. The filtrate was cooled to furnish **8a,b**.

4-(4`Chlorophenyl)-7,7-dimethyl-2-thioxo-1,3,4,6,7,8-hexahydro-1*H*-quinazolin-5-one (7a): Yellow powder, m.p.235-234°C; IR (cm^{-1}): 3377 (2NH), 1721 (C=O), 1180 (C=S), MS: *m/z* (%) 320/322 [M^+] (17/25) ($C_{16}H_{17}ClN_2OS$); ^{1}H-NMR ($CDCl_3$, drops of DMSO-d_6): δ 0.88 (3H, s, CH_3), 1.01 (3H, s, CH_3), 2.15 (2H, two d, AB system, *J*=16.2 Hz, CH_2 at 8 position), 2.39 (2H, two d, AB system, *J*=16.2 Hz, CH_2 at 6 position), 5.17 (1H, d, *J*=2.9 Hz, H-4), 7.21 (2H, d, *J*=8.0Hz, H-2`& H-6`) and 7.41(2H, d, *J*=8.0Hz, H-3`& H-5`), 9.71 (1H, br.s, N_3-H), 10.65(1H,s,N_1-H); ^{13}C-NMR ($CDCl_3$,drops of DMSO-d_6): δ 27.5, 28.90, 31.85 (2C), 50.30 (sp^3 dimedone moiety carbons), 52.17(C-4), 108.30, 128.83, 129.07, 132.63, 142.83 and 149.38 (olefinic and aromatic sp^2 carbons), 175.18 (C=S), 194.21 (C=O).

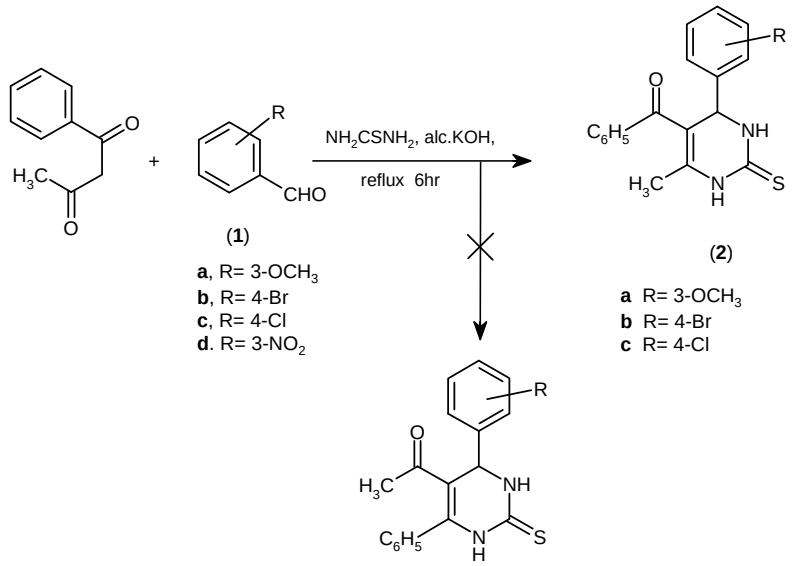
4-(4`Bromophenyl)-7,7-dimethyl-2-thioxo-2,3,4,6,7,8-hexahydro-1*H*-quinazolin-5-one (7b): Yellow powder, m.p. 178-180°C; IR (cm^{-1}): 3393, 3187 (2NH), 1663(C=O), 1205(C=S), MS: *m/z* (%) 364/366 [M^+] (15/18) ($C_{16}H_{17}BrN_2OS$); ^{1}H-NMR ($CDCl_3$, drops of DMSO-d_6): δ 0.86 (3H, s, CH_3), 1.02 (3H, s, CH_3), 2.09-2.45 (4H, m, $2CH_2$), 5.15 (1H, d, *J*=3.0 Hz, H-4), 7.41 (2H, d, *J*=8.1Hz, H-2`& H-6`) and 7.54 (2H, d, *J*=8.1Hz, H-3`& H-5`) 9.68 (1H, br.s, N_3-H), 10.62 (1H, br.s, N_1-H).

9-(4`Chlorophenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-2*H*-xanthene-1,8-dione (8a): Pale yellow hairy crystals, m.p. 220-222°C; IR (cm^{-1}): 1679 (C=O), 1625 (C=C); MS: *m/z* (%) 384/386[M^+] (15/13) ($C_{23}H_{25}ClO_3$), 273[M-C_6H_4Cl] (87); ^{1}H-NMR ($CDCl_3$): δ 0.92 (6H, s, $2CH_3$), 1.05 (6H, s, $2CH_3$), 2.2 (4H, m, $2CH_2$), 2.48 (4H, s, $2CH_2$), 4.70 (1H, s, H-9), 7.18 (2H, d, *J*=8.0Hz, H-2`& H-6`) and 7.29 (2H, d, *J*=8.0Hz, H-3`& H-5`); ^{13}C-NMR ($CDCl_3$): Figure 4.

9-(4`Bromophenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-2*H*-xanthene-1,8-dione (8b): Yellowish hairy crystals, m.p. 238-240°C; IR (KBr cm^{-1}): 1683 (C=O), MS: *m/z* (%) 428/430 [M^+] (21/29) ($C_{23}H_{25}BrO_3$), 373 [M-C_6H_4Br] (90); ^{1}H-NMR ($CDCl_3$): δ 0.96 (6H, s, $2CH_3$), 1.08 (6H, s, $2CH_3$), 2.19 (4H, m, $2CH_2$), 2.44 (4H, s, $2CH_2$), 4.66 (1H, s, H-9), 7.14 (2H, d, *J*=8.1Hz, H-2`& H-6`) and 7.31 (2H, d, *J*=8.1Hz, H-3`& H-5`); ^{13}C-NMR ($CDCl_3$): δ 27.35, 29.34, 31.63, 32.28, 40.90 (sp^3 dimedone moiety carbons), 50.74 (C-9), 115.23, 130.22, 131.05, 132.63, 143.23 and 162.69 (olefinic and aromatic sp^2 carbons), 196.65 (C=O).

RESULTS AND DISCUSSION

Chalcones are reacted with thiourea in ethanol/potassium hydroxide affording the corresponding pyrimidine-2-thione derivatives. This is the most common procedure for the synthesis of the latter compounds [15]. On the other hand, Pyrimidine-2-thiones were also prepared in one pot three components reaction by refluxing the aromatic aldehyde (**1**), proper ketone containing active methylene group and thiourea in basic ethanol solution for 4 hr [15,16]. We followed the two procedures to obtain compounds (**2a-d**) (scheme 1a). Unfortunately, the yields in both cases were not satisfied. The latter reaction was then carried out under microwave irradiation in the presence of solvent in order to ensure the reactant miscibility. Thus, benzoylacetone, aromatic aldehyde (**1**) and thiourea were mixed together and moistened with methanol and then subjected to microwave irradiation (scheme 1b). This reaction gave higher product yields of **2a-d** and in a very short time. However, as it can be seen from Table 1, the yield is relatively low for **2d** and this may be attributed to the strong electron withdrawing effect of nitro group in the aldehyde **1d**, and the yield was much lower at irradiation by a power of 800 W. In fact, we were not able to obtain **2d** following the classical method [16] even at much longer time than that for obtaining **2a-c** by the same procedure. The time was extended to 24 hours but the starting material was still present as indicated by TLC.



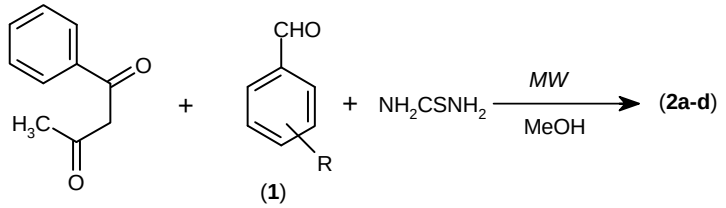
Scheme 1a

Table 1: Yields and reaction conditions used for the synthesis of 2a-d

Compd. No.	MW method (600 W)		Classical method	
	Reaction time (sec)	Yields (%)	Reaction time (h)	Yields (%)
2a	42	95	4	48
2b	60	88	4	45
2c	180	79	4	25
2d	140	52	4	-
2d	140*	33	24	-

* at 800 W

The IR spectrum of **2a-d** showed an absorption band in the range of 3179-3406 cm^{-1} corresponding to the NH stretching (see experimental) and another band at 1195-1209 cm^{-1} due to C=S stretching. Further, these spectra revealed an intense band at 1656-1691 cm^{-1} due to conjugated C=O stretching. The mass spectrum of **2a** displayed a molecular ion peak [M^+] at *m/z* 338 which is consistent with its molecular formula $C_{19}H_{18}N_2O_2S$. The ^{1}H-NMR spectrum of compound **2a** exhibited two singlets, each integrated for three protons at δ 1.76 and δ 3.73 corresponding to the resonances of an olefinic methyl and methoxyl groups respectively. The spectrum also showed two singlets at δ 10.01 and δ 9.36 (broad) due to the resonances of the two NH protons, in addition to a doublet at δ 5.43 (J = 3.0 Hz) due to the methine proton at position 4 as clearly explored by HETCOR experiment. Thus, the broad signal at δ 9.36 is attributed to the latter NH group. The ^{1}H-NMR spectrum revealed signals of the nine aromatic protons in **2a**, all of them are multiplets except the one at δ 6.77 which in turn is attributed to the proton at position 2 of the methoxylated ring. Table 2 contains the ^{1}H-NMR data of substituted pyrimidine-2-thiones **2a-d**.



(**1**)

a, R= 3-OCH_3
b, R= 4-Br
c, R= 4-Cl
d. R= 3-NO_2

Scheme 1b

The reaction of benzoylacetone with an aromatic aldehyde and thiourea is expected to give either **2** or **2A**. However, the latter is excluded on the basis of NMR data of the reaction product. In the ^{1}H-NMR spectrum, the methyl signal appeared at δ 1.76 indicating undoubtedly that it is an olefinic methyl and not of acetyl methyl nature as in **2A**. Further, due to the electronegative effect of the carbonyl group in **2**, a downfield shift of the phenyl protons of the latter group was observed. ^{13}C-NMR of **2a** (Fig. 1) revealed 17 signals, and this is as expected for the proposed structure. Three of these signals in the aliphatic sp^3 region belong to the methine carbon at δ 55.06 and two methyl carbons at δ 56.37 (OCH_3) and δ 18.15 (olefinic CH_3). The C=O and C=S gave signals at δ 195.18 and δ 174.93 respectively. The assignments of all carbons in **2a-d** (Fig. 1, Table 2) are basically made by the aid of the off resonance, DEPT and HETCOR NMR experiments, and in part, by comparison to ^{13}C-NMR spectra of structurally related compounds [17].

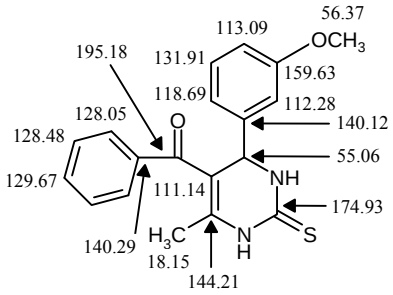
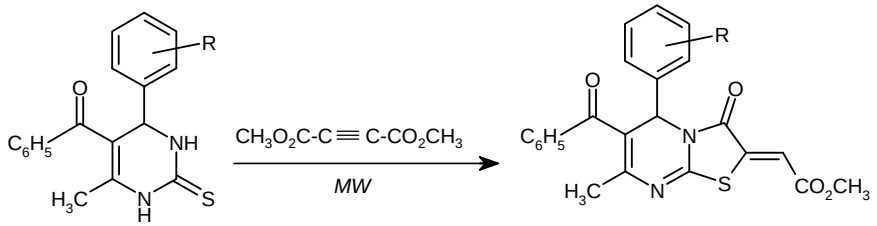


Figure 1: ^{13}C-NMR assignments of 2a.

We were also intended to study the reactions of the prepared pyrimidine-2-thiones under microwave irradiation to optimize the product yields of these reactions. Therefore, reaction of **2a,b** with dimethyl acetylenedicarboxylate gave the corresponding condensation products **3a,b** with good yield (scheme 2).



2a,b

a R= 3-OCH_3
b R= 4-Br

3a,b

Scheme 2

Table 2: ^{1}H- and ^{13}C-NMR spectral data of compounds (2a-d) (in DMSO-d_6), (δ in ppm, *J* in Hz)

Compd. No.	^{1}H-NMR	^{13}C-NMR
2a	1.76 (3H, s, CH_3), 3.73 (3H, s, OCH_3), 5.43 (1H, d, *J*=3.0, H-4), 6.77 (1H, s, H-2`), 6.76 (1H, d, *J*=7.6, H-4`), 6.84 (1H, d, *J*=7.5, H-6`), 7.20 (1H, t, *J*=8.0, H-5`), 7.39 (2H, t, *J*=7.6, phenyl *m*-protons), 7.49 (3H, m, phenyl *o*& *p*-protons), 9.36 (1H, br. s, N_3-H), 10.01 (1H, s, N_1-H).	see Figure 1
2b	1.70 (3H, s, CH_3), 5.27 (1H, d, *J*=2.90, H-4), 7.15 (2H, d, *J*=8.0, H-2`& H-6`), 7.54 (2H, d, *J*=8.0, H-3`& H-5`),7.42-7.55 (5H, m, phenyl protons), 9.72 (1H, br. s, N_3-H), 10.42 (1H, s, N_1-H).	18.61 (CH_3), 55.28 (C-4), 110.28 (C-5), 142.85 (C-6), 128.46 (C-2`& C-6`), 132.11 (C-3`& C-5`), 121.38 (C-4`), 140.69 (C-1`), 129.16, 129.25, 132.50 and 142.82 (phenyl carbons), 174.86 (C=S), 194.92 (C=O).
2c	1.71 (3H, s,CH_3), 5.29 (1H, d, *J*=3.6, H-4), 7.21 (2H, d, *J*=8.1, H-2`& H-6`), 7.39 (2H, d, *J*=8.1, H-3`& H-5`),7.41-7.56 (5H, m, phenyl protons), 9.72 (1H, br.s, N_3-H), 10.42 (1H,.s, N_1-H).	18.63 (CH_3), 55.22 (C-4), 110.33 (C-5), 142.41 (C-6), 128.47 (C-2`& C-6`), 132.50 (C-3`& C-5`), 132.82 (C-4`), 140.69 (C-1`), 128.83, 129.25, 132.50 and 142.84 (phenyl carbons), 174.85 (C=S), 194.94 (C=O).
2d	1.70 (3H, s,CH_3), 5.59 (1H, d, *J*=2.8, H-4), 7.30 (2H, d, *J*=7.5, H-2`& H-6`), 8.05 (2H, d, *J*=7, H-3`& H-5`), 7.45 (2H, t, *J*=8.0, phenyl *m*- protons), 7.54(1H, t, *J*=8.0, phenyl *p*-proton), 7.81(2H, d, *J*=8.0, phenyl *o*-protons), 8.71 (1H, br. s, N_3-H), 9.74 (1H,.s, N_1-H).	18.02 (CH_3), 53.60 (C-4), 109.9 (C-5), 152.12 (C-6), 123.10 (C2`& C6`), 128.05 (C3`& C5`), 146.40 (C-1`), 148.5 (C-4`), 129.0, 129.72, 134.32 and 136.70 (phenyl carbons), 178.18 (C=S), 187.80 (C=O).

The structure of **3a,b** was assigned on the basis of spectroscopic methods. IR spectrum of **3a** lacks the absorption band of NH stretching and this clearly indicated that –NH protons were involved in the cyclization. Further, this spectrum is characterized by three intense peaks at 1729 cm^{-1}, 1709 cm^{-1} and 1643 cm^{-1} (three conjugated C=O) while its mass spectrum displayed the molecular ion peak [M^+] at *m/z* 448. The ^{1}H-NMR spectrum of **3a** exhibited three sharp singlets, each integrated for three protons, readily recognized as arising from the two methoxyl protons (δ 3.65 and δ 3.78) and the olefinic methyl (δ 1.75) protons. Another three singlets, but each integrated for one proton, appeared in this spectrum at δ 6.05, δ 6.76 and δ 6.85 due to the resonances of the methine proton at position 5, the proton at position 2 of the methoxylated ring and the exocyclic vinyl proton respectively. Aromatic protons in **3a** appeared at the expected chemical shifts and integral values (experimental). The ^{13}C-NMR spectral data of **3a** (Fig. 2) were in consistent with the proposed structure.

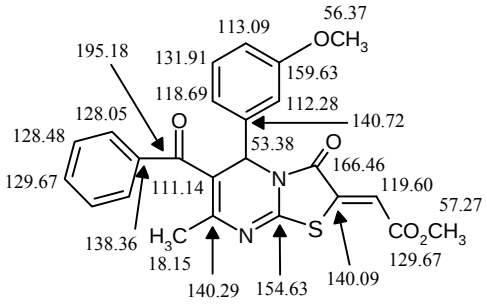


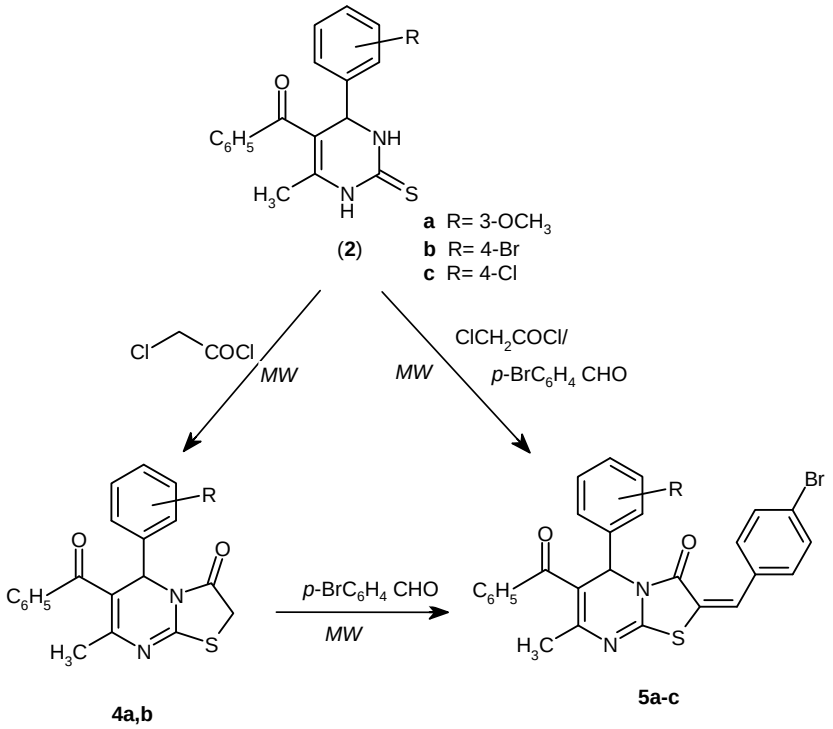
Figure 2: ^{13}C-NMR assignments of 3a.

Compound **2** was condensed with chloro-acetic acid under microwave irradiation to give the corresponding 5-Aryl-6-benzoyl-7-methyl-5*H*-thiazolo[3,2-*a*]pyrimidin-3-one (**4**). The latter is condensed with *p*-bromobenzaldehyde, following the same method to yield **5** in good yield. Compound **5** was also obtained in one pot three components synthesis using microwave irradiation from the action of chloroacetic acid and thiourea on the pyrimidine-2-thione **2**. These reactions are outlined in scheme 3.

Table 3:Yields and reaction conditions used for the MW synthesis of 4,5

Compd. No.	Reaction time (min.)	Yield (%)	M.p. (^{o}C)
4a	25	91	220-221
4b	16	82	198-199
5a	4	76	130-132
5b	18	73	181-183
5c	23	65	174-176

Characterization of **4, 5** was based mainly on the spectroscopic means. Thus, IR spectra of **4a** showed two carbonyl absorption bands at 1779 $cm^{-1}$and 1670 cm^{-1}, with the disappearance of absorption bands due to the NH amidic groups. Further, resonances of these NH protons disappeared in the ^{1}H-NMR spectra of compounds **4** and **5**. The latter spectrum of **4a** was characterized by resonances of two non-equivalent protons of the methylene group of thiazole ring centered at δ 4.21 and forming AB system. The ^{1}H-NMR spectrum of **4a** also revealed two singlets at δ 1.74 (CH_3) and at δ 3.67 (OCH_3) along with the characteristic multiplets with the appropriate chemical shifts and coupling constants for the nine aromatic protons (see experimental). The ^{13}C-NMR data of **4a** which are depicted in figure 3 (see experimental for **4b**), are in full agreement with its structure.



Scheme 3

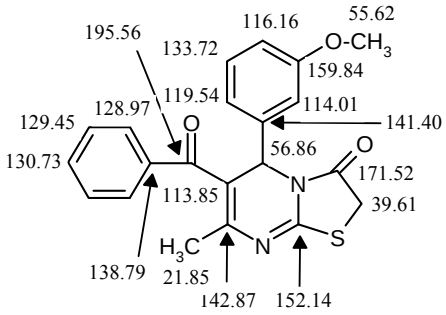
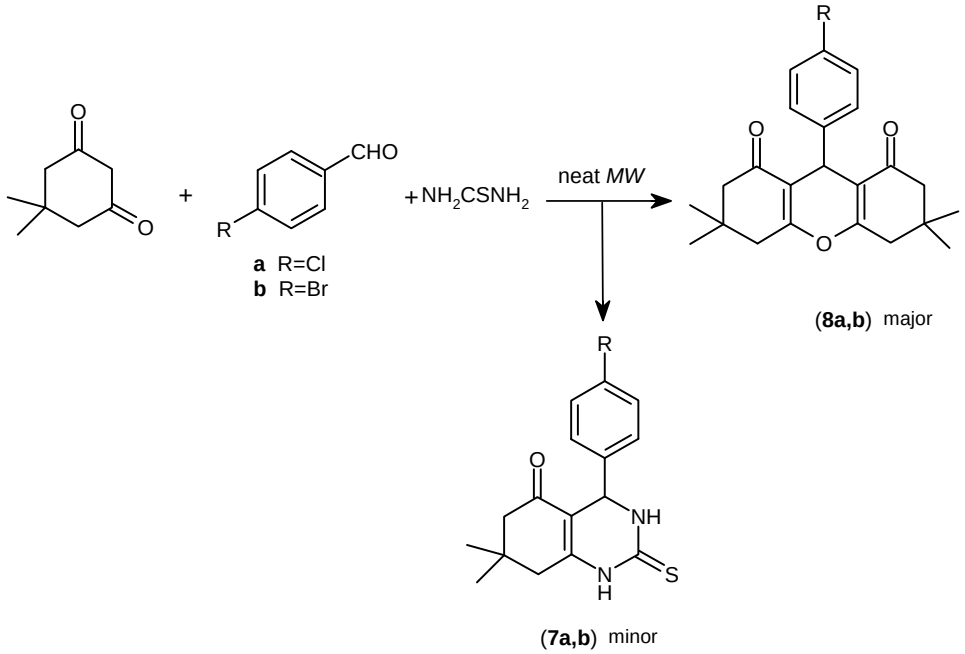


Figure 3: ^{13}C-NMR assignments of 4a.

The structures of **5a-c** were unambiguously characterized by their spectral data. Their IR spectra were similar to the corresponding spectra of **4a,b**. The respective changes in the ^{1}H-NMR spectra of **5a-c** compared to the same spectra of **4a,b** are that the disappearance of AB pattern of CH_2 in the spectra of the latter compound, and instead a signal due to exocyclic vinyl proton [18] and two doublet signals for 4-bromophenyl appeared in the ^{1}H-NMR spectra of **5a-c**. The ^{13}C-NMR data of **5a,b** were in good agreement with their structures. These spectral data are shown in the experimental section.

The reaction of dimedone (**6**) with aromatic aldehydes and thiourea has been recently reported [5]. This resulted in the formation of the corresponding tetrahydropyrimidine-2-thiones (**7**) in appreciable yields. The reaction has been carried out by heating equimolar amounts of the three components under microwave irradiation in the absence of solvent and catalyst. We have decided to repeat the reaction following the procedure has been adopted in this work for the preparation of **2a-d**, in order to compare the results of the procedures. Accordingly, heating of dimedone, aromatic aldehyde and thiourea using microwave irradiation in the presence of solvent gave the corresponding pyrimidine-2-thione (**7a,b**) as a minor component, while compound **8** was the major one in this reaction (scheme 4).



Scheme 4

Identity of **7a,b** was based on spectroscopic methods (IR, MS, NMR). The IR spectrum of **8a** exhibited an intensive and sharp peak at around 1679 cm^{-1} which is attributed to a conjugated carbonyl function. This spectrum showed no peak above 3100 cm^{-1} indicating the absence of –NH and –OH groups. The mass spectrum of **8a** showed a molecular ion peak at m/z 384, while the base peak was at m/z 273 due to the fragment [M-ClC_6H_4). The ^{1}H-NMR spectrum of **8a** showed a singlet signal at δ 4.70 which is assigned to the methine proton. This spectrum revealed in the aliphatic region, two singlets, each integrated for 4 protons in addition to other two singlets, each integrating for six protons. These spectral data confirm undoubtedly the presence of two dimedone units placed symmetrically in the molecule. The aromatic protons resonated as two doublets at the expected chemical shifts due to 4-chlorophenyl protons in **8a** and 4-bromophenyl protons in **8b**. The ^{13}C-NMR data of 8a,b are in good agreement of the proposed structures as it could be seen from Figure 4 and experimental respectively. The assignments of all carbons in 8a,b were made by the aid of DEPT experiment.

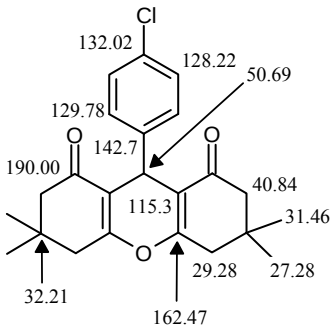


Figure 4: ^{13}C-NMR assignments of 8a.

Conclusion:

In the present work, we reported an efficient and comfortable synthesis of novel 4-Aryl-1,2,3,4-tetrahydropyrimidine-2-thiones under microwave irradiation using methanol as a solvent. Further, some reactions of the target compounds have been carried out under microwave irradiation also leading to an appreciable yield of condensed products. Also we have demonstrated the use of microwave irradiation compared to the classical refluxing method.

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