Microwave versus Ultrasound assisted Synthesis of Substituted Furan-2-Carboxaldehydes and their Reactions

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Abstract

A series of 5- unsubstituted and 5- substituted furfurylidenes have been prepared under thermal as well as non-thermal microwave and ultrasound irradiation methods from condensation of furfural and its derivatives with some methylene active compounds. Further, other condensate products from these arylidenes, which contain halogen or sulpher atoms, were also prepared. Structural elucidation of the synthesized compounds was determined on the basis of various spectroscopic methods.

Keywords: Furfurylidenes, 5- substituted furfurylidenes, 2-thioxopyrimidines, ultrasound and microwave irradiation.

Introduction

Condensation products of some active methylene compounds with furan-2-carboxaldehydes or their 5-sustituted derivatives[1-3] were found to possess antimicrobial activit [4,5]. Many of 2-thioxopyrimidines were associated with broad spectrum of biological activity including antimicrobial[6-8], antifungal[9,10] and antitumor. [11-13] Some furfurylidenes and 2- thioxopyrimidines derived from these arylidenes are observed to have moderate antimicrobial activity[1]. The latter compounds were synthesized by microwave irradiation and conventional methods. Recently, we have reported the synthesis of some furan condensate products utilizing the conventional and microwave irradiation methodologies. The yields of the majority of the prepared condensate were low with advantage of the purity of compounds obtained by microwave irradiation method. Due to the aforementioned biological importance of the title compounds[1,14-16] ,we report herein the synthesis of a series of some substituted furfurylidenes as well as some novel 2-thioxopyrimidines furyl moiety adopting simple and efficient ultrasound method. Microwave irradiation method was also used for comparison purposes.

Material and Methods

Melting points are determined on an electrothermal's IA9000 series digital capillary melting point apparatus. IR spectra (KBr disks) were recorded on a Perkin Elmer FT spectrophotometer 1000. ^{1}H and ^{13}CNMR spectra were recorded on a JEOL ECP 400 NMR spectrometer operating at 400 MHz using $CDCl_3$ and DMSO-d_6 as solvents with TMS as internal standard, at Chemistry Department, College of Science, King Saud University. Electron impact (EI) MS spectra were measured on a Shimadzu GCMSQP5050A mass spectrometer, DB-1 glass column 30 m, 0.25 mm, ionization energy 70 eV, at Chemistry Department, College of Science, King Saud University.

Ultrasound and Microwave experiments were carried in a J.P. Selecta Cod: 3001732 and in a Parasonic oven(Japan) Model no. NN-CD987w espectively. Methods A, B, C refer to ultrasound(US), microwave(MW) and classical heating respectively.

Synthesis of chalcones (5a-c & 6a-c)
Classical method: Compounds 5 & 6 were synthesized as reported in literature [14,17].
Microwave method: Compounds 5a-c were synthesized following the reported method[1].

Synthesis of (7a-c and 8a-c)
Method A: A mixture of the 5a-c and 6a-c (0.01 mol) and thiourea (0.02 mol) in ethanol (30 ml) was placed in a 100 mL conical flask, and was then irradiated in the water bath of an ultrasonic cleaner for 30 min at 80^{o}C. The solid product formed was filtered off, washed with ethanol, dried and recrystallized from ethanol to give 7 and 8.
Microwave and Classical Methods: Compounds 7a,c and 8a,c were synthesized as reported in the literature[1].

6-(Furan-2-yl)-4-(4-methoxyphenyl) pyrimidine-2(1*H*)-thione(7b): Yields 83^A, 56^B %, m.p. 112^{o}C; IR (KBr, cm^{-1}): 3390(br, NH), 3064, 2942, 1618,1614, 1590, 1500, 1431, 1229(C=S); ^{1}HNMR ($CDCl_3$)□ : 3.81 (s, 3H,OCH_3), 6.70, 7.72, 8.16 (each 1H, m, furan), 7.08 (2H, d, *J*=8.0 Hz), 7.68 (2H, d, *J*=8.0 Hz), 6.84(1H, s), 12.74 (1H, s, NH); ^{13}C NMR ($CDCl_3$) □: 55.58, 11.08, 112.20, 143.62, 155.10, , 114.22(2C), 125.42, 130.18(2C), 162.81, 108.62, 156.45, 164.88, 180.96(C=S).

4-(Furan-2-yl)-6-(4-methoxyphenyl) pyrimidine-2(1*H*)-thione(8b):Yields 78^A, 52^B %, m.p. 232-234.^{o}C; IR (cm^{-1}): 3342(NH), 3042, 2978, 1631, 1602, 1500, 1423, 1253 (C=S); ^{1}HNMR ($CDCl_3$)□□ 3.83 (s, 3H, OCH_3), 6.59 (1H, d, *J*= 2.5 Hz), 6.65 (1H, d, *J*= 3.8 Hz), 7.74(1H, m), 6.95 (2H, d, *J*=8.0 Hz), 7.51 (2H, d, *J*=8.0 Hz), 6.91(1H, s), 12.60 (1H, s, NH); ^{13}C NMR ($CDCl_3$)□: 55.8, 108.20,

110.32, 142.10, 144.50, 121.24(2C), 123.80, 129.72(2C), 160.12, 104.86, 162.88, 170.15, 181.18(C=S).

Genaral procedure for the synthesis of synthesis of (10a-g)

Method A : A mixture of the 2a-e (0.01 mol), 1,3-dicarbonyl compounds 9a,b (0.01 mol) and thiourea (0.02 mol) in ethanol (30 ml) was placed in a 100 mL conical flask, and was then irradiated in the water bath of an ultrasonic cleaner(a J.P. Selecta) for 15-25 min at 80^{o}C. The solid product formed was filtered off, washed with ethanol, dried and recrystallized from ethanol.

Method B : A mixture of 5-substituted furfural 2a-e (0.01 mol), 1,3-dicarbonyl compounds 9a,b (0.01 mol),thiourea (0.02 mol) and a few drops of acetic acid (1ml) was mixed and irradiated in domestic microwave oven for 5-8 min at a power of 550 W. The resulting solid product was filtered off, washed with ethanol and dried.

Method C : A mixture of the aldehyde 2b, d (0.01 mol), 1,3-dicarbonyl 9a (0.01 mol), thiourea (0.02 mol) and piperidine(3 drops) was heated under reflux in ethanol, for 60 miniutes. The solid product formed was then cooled, filtered, washed with ethanol and recrystallised from ethanol.

Ethyl4-(5-bromofuran-2-yl)-6-phenyl-2-thioxo-1,2-dihydropyrimidine-5-carboxylate (10a): Yield 59^{A},24^{B}, 32^{C}%, m.p. > 320^{o}C; IR (cm^{-1}): 3312 (NH), 3024 (aromatic CH), 2967 (aliph. CH), 1722 (ester CO),1234 (C=S); MS *m/z*: 404/406[M^{+}] (22%, 21.8%) ($C_{17}H_{13}N_2O_3SBr$).

Ethyl4-[5-(4-chloro-phenyl)-furan-2-yl]-6-phenyl-2-thioxo -1, 2-dihydro-pyrimidine-5- carboxylate (10b): Yield 67^{A},36^{B}, 42^{C}%, m.p. 106- 108^{o}C; IR (cm^{-1}): 3447 (NH), 3038 (aromatic CH), 2985 (aliph. CH), 1719 (ester CO),1221 (C=S); ^{1}H NMR ($CDCl_3$) □:1.19 (3H, t, *J*= 6.7 Hz , CH_3), 4.22 (2H, q, *J*= 6.7 Hz, CH_2), 6.56 (1H, m),6.59 (1H, m), 6.93 (1H, d, *J*= 3.3 Hz), 7.33 (2H, d, *J*=8 Hz), 7.68 (2H, d, *J*=8 Hz), 12.18 (1H, s, NH); ^{13}CNMR ($CDCl_3$) □:14.18, 61.60, 113.56, 120.05, 126.92, 127.76, 128.35, 129.40(2C), 130.50, 130.68 (2C),133.82, 148.37, 153.85, 165.08, 184.45(C=S).

Ethyl4-(furan-2-yl)-6-methyl-2-thioxo-1, 2-dihydropyrimidine-5-carboxylate (10c): Yield 75^{A},41^{B} %, m.p. > 320^{o}C; IR (cm^{-1}): 3317, 3186 (NH), 2965 (aliph. CH), 1731 (ester CO), 1247 (C=S); ^{1}HNMR (DMSO-d_6) □: 1.22 (3H, t, *J*= 6.5 Hz, CH_3), 4.19 (2H, q, *J*= 6.5 Hz,CH_2), 2.39 (3H, s,CH_3), 6.57 (1H,m), 6.63 (1H, d, *J*= 2 Hz), 7.48 (1H, d, *J*= 3.4 Hz), 11.10 (1H, brs, NH); ^{13}C NMR (DMSO-d_6) □: 14.08,18.24, 62.3, 109.32, 109.95, 141.62, 143.40, 162.15, 165.21 (C=O), 167.32, 182.46 (C=S).

Ethyl4-(furan-2-yl)-6-phenyl-2-thioxo-1,2-dihydropyrimidine-5-carboxylate (10d): Yield 66^{A},56^{B}%, m.p. 118^{o}C; IR (cm^{-1}): 3418 (NH), 3077 (aromatic CH), 2970, 2918 (aliph. CH), 1725 (ester CO),1237 (C=S); ^{1}H NMR (DMSO-d_6) □: 1.11 (3H, t, *J*= 6.65 Hz,CH_3), 4.12 (2H, q, *J*= 6.54 Hz, CH_2), 6.06 (1H,s, H-4), 6.70-7.62 (8H, m, 5 Ph-H + 3 furan-H), 12.43, 12.48 (1H each, s, 2NH); ^{13}C NMR (DMSO-d_6) □: 13.73, 45.10, 60.44, 102.82, 127.21 (2C), 127.49, 127.87, 128.11(2C), 128.44, 130.56, 131.05, 133.61,152.83, 160.87, 176.25, 183.44(C=S).

Ethyl 4-(5-(2-nitrophenyl)furan-2-yl)-6-phenyl-2-thioxo-1,2-dihydropyrimidine-5-carbo-xylate (10e): Yield 61^{A}, 36^{B}%, m.p. 132^{o}C; IR (cm^{-1}): 3397 (NH), 3043 (aromatic CH), 2981 (aliph. CH), 1728 (ester CO), 1228(C=S); ^{1}H NMR (DMSO-d_6) □: 1.26 (3H, t, *J*=6.5 Hz, CH_3), 4.23 (2H, q, *J*= 6.5 Hz, CH_2), 6.72 (2H, m), 7.27-7.87 (9H, Ar-H), 12.43, (1H, s, NH); ^{13}C NMR (DMSO-d_6) □: 14.40, 61.90, 112.26, 112.72, 117.98, 123.46,123.76, 128.76, 129.27, 129.35, 130.54, 130.49, 132.23, 132.63, 136.55, 147.86, 150.53, 152.61, 165.01,180.93.

Ethyl4-[5-(4-bromo-phenyl)-furan-2-yl]-6-methyl-2-thioxo-1,2-dihydro-pyrimidine-5- carboxylate (10f): Yield 57^{A}, 53^{B}%, m.p. 167^{o}C; IR (cm^{-1}): 3198 (NH), 2945 (aliph. CH), 1730 (ester CO), 1242 (C=S); ^{1}HNMR (DMSO-d_6) □: 1.29 (3H, t, *J*= 6.5 Hz, CH_3), 4.19 (2H, q, *J*= 6.5 Hz,CH_2), 2.21 (3H, s,CH_3), 6.59 (1H, d, *J*= 3.1 Hz), 7.11 (1H, d, *J*= 3.1 Hz), 7.37 (2H, d, *J*=8 Hz), 7.53 (2H, d, *J*=8 Hz), 11.30 (1H, brs, NH); ^{13}C NMR (DMSO-d_6)□: 13.72, 60.97, 16.20, 105.67, 108.42, 112.50, 123.22, 129.20(2C), 130.68 (2C), 135.52, 141.44, 150.32, 154.80, 160.34, 165.08, 184.45(C=S).

Ethyl4-[5-(4-bromo-phenyl)-furan-2-yl]-6-phenyl-2-thioxo-1,2-dihydro-pyrimidine-5- carboxylate (10g): Yield 60^{A}, 51^{B}%, m.p. 201^{o}C; IR (cm^{-1}): 3214 (NH), 2943 (aliph. CH), 1734 (ester CO), 1238 (C=S); ^{1}HNMR (DMSO-d_6) □: 1.29 (3H, t, *J*= 6.5 Hz, CH_3), 4.19 (2H, q, *J*= 6.5 Hz,CH_2), 6.48 (1H, d, *J*= 3.1 Hz), 6.92 (1H, d, *J*= 3.1 Hz), 7.22 (2H, d, *J*=7.6 Hz), 7.31 (2H, d, *J*=7.6 Hz), 7.39 (2H, d, *J*=8 Hz), 7.49 (2H, d, *J*=8 Hz), 11.30 (1H, brs, NH); ^{13}C NMR (DMSO-d_6) □: 13.72, 60.97, 106.98, 108.14, 113.60, 123.11, 126.28(2C), 127.88, 128.54 (2C), 134.83, 129.25(2C), 130.68 (2C), 135.90, 142.24, 151.33, 153.98, 159.28, 165.15, 183.85(C=S).

Genaral procedure for the synthesis of (11a-h and 12a-h)

Method A : A mixture of 1,3-thiazolin-2,5-dione or 3-Methyl-1-phenyl-1*H*-pyrazol-5(4*H*)one (0.01 mol) and aromatic aldehyde 2a-h (0.01 mol) in ethanol (25 ml) was placed in a 100 mL conical flask, and was then irradiated in the water bath of an ultrasonic cleaner(a J.P. Selecta) for 15-20 min at 80^{o}C. The solid product formed was filtered off, washed with ethanol, dried and recrystallized from ethanol.

Method B. A mixture of 1,3-thiazolin-2,5-dione or 3-Methyl – 1 – phenyl – 1 *H* – pyrazol – 5 (4*H*)one (0.01 mol), aromatic aldehyde 2a-h(0.01 mol) were mixed and

irradiated by microwave for 3-12 min at a power of 350 W. The solid product was triturated with methanol, filtered, washed with ethanol (96%) and dried.

Method C: A mixture of 1,3-thiazolin-2,5-dione or 3-Methyl-1-phenyl-1*H*-pyrazol-5(4*H*)one (0.01 mol), appropriate aromatic aldehyde 2a-f (0.01 mol) and piperidine (3 drops) was heated under reflux in ethanol(25 ml) for 1 hr. The solid product formed was then cooled, filtered, washed with ethanol and recrystallised from ethanol.

5- (furan – 2 - ylmethylene) thiazolidine -2, 4-dione (11a): Yield, 69^A, 16^B, 55^C%, m.p. 225 ^oC; IR (KBr, cm^{-1}): 1339, 1610, 1684, 1719, 3034, 3227; EIMS: *m/z* 195$[M^+](C_8H_5NO_3S)$20.8%; ^1H NMR($CDCl_3$) □: 6.72(1H,m), 7.06(1H,d *J*=4 Hz), 7.55 (1H), 7.59(1H,brs,-CH=), 11.70(NH); ^{13}C NMR($CDCl_3$) □: 113.73, 118.69, 118.79, 120.63, 147.69(-CH=), 149.48, 167.30 & 168.89(2C=O).

5-((5-(2-Chlorophenyl)furan-2-yl)methylene) thiazolidine-2,4-dione (11b): Yield 53^A, 13^B, 46^C %, m.p. 240 ^oC; IR (KBr, cm^{-1}): 1342, 1467, 1501, 1608, 1691, 3031,3173; EIMS: *m/z*305/307$[M^+](C_{14}H_8NO_3SCl)$(13.4%,3.85%); ^1H NMR($CDCl_3$) □: 6.76(1H, d, *J*=3.7 Hz), 7.19(1H, d, *J*=3.7Hz), 7.41(1H,brs, -CH=), 7.15(1H,t, *J*=8 Hz), 7.27(1H,t, *J*=8 Hz), 7.33(1H, d, *J*=8 Hz), 7.80(1H, dd, *J*=1.5 & 8 Hz),11.71(NH); ^{13}C NMR($CDCl_3$) □: 114.08, 117.95, 119.63, 121.60, 130.51, 127.68, 129.32, 130.94, 127.29,128.09, 148.81(-CH=), 153.78, 167.41 & 169.16(2C=O).

5-((5-(2-nitrophenyl)furan-2-yl)methylene)thiazolidine-2,4-dione (11c): Yield 45^A, 18^C, m.p. 274 ^oC; IR (KBr, cm^{-1}): 1346, 1459, 1500, 1603, 1669, 3031, 3161; ^{1}HNMR($CDCl_3$) □: 7.21& 7.25(each 1H, furan), 7.62(1H, s,-C=CH), 7.67(1H,t, *J*=8 Hz), 7.82(1H,t, *J*=8 Hz), 7.90(1H, d, *J*=8 Hz),8.15(1H, d, *J*=8 Hz), 12.22(NH); ^{13}C NMR($CDCl_3$) □: 113.59, 117.67, 122.08, 124.87, 133.24, 122.00, 130.55, 129.80, 120.74, 147.17, 150.69(-CH=), 152.07, 167.24 & 168.80(2C=O).

5-((5-bromofuran-2-yl)methylene)thiazolidine-2,4-dione (**11d**): Yield 60^A, 20^B, 39^C, m.p 240 ^oC; IR (KBr, cm^{-1}): 1329, 1355, 1458, 1541, 1603, 1686, 1716, 3031, 3162; EIMS:*m/z* 273/275$[M^+](C_8H_4NO_3SBr)$ (8.9%, 8.2%); ^1H NMR($CDCl_3$) □: 6.84(1H, d, *J*=3.66 Hz), 7.07(1H, d, *J*=4Hz), 7.52(1H,s, -C=CH), 12.32(NH); ^{13}C NMR($CDCl_3$) □: 115.40, 117.00, 120.94, 126.80, 149.33(-CH=), 151.05, 166.69 & 168.07(2C=O)..

5-((5-(4-Bromo-phenyl)furan-2-yl)methylene) thiazolidine-2,4-dione (11e): Yield 74^A, 41^B%, m.p. 249 ^oC; IR (KBr, cm^{-1}): 1510, 1600, 1613, 1660,3161; ^{1}HNMR ($CDCl_3$) □: 7.11& 7.38(each 1H, furan), 7.62(1H,s, -C=CH), 7.57(1H,t, *J*=7.9 Hz), 7.69(1H, d, *J*=7.9 Hz), 12.40(NH); ^{13}C NMR($CDCl_3$) □: 106.83, 110.20, 122.50, 123.13, 127.23(2C), 129.35, 132.28(2C), 142.22, 150.10(-CH=), 155.85, 166.31& 167.20(2C=O).

5-((4,5-dimethylfuran-2-yl)methylene)thiazolidine-2,4-dione (**11f**): Yield 61^A, 15^B, 45^C %, m.p.230oC; IR (KBr, cm–1): 1339, 1389, 1457, 1517, 1589, 1621, 1670, 1826, 2945, 3008,3142, 3335; EIMS: *m/z* 223$[M^+](C_{10}H_9NO_3S)$9.44%; ^1H NMR($CDCl_3$)□: 1.91 & 2.24, (each 3H, s, CH_3), 6.82,7.39(each s, 1H,furan), 11.50(brs, NH); ^{13}C NMR($CDCl_3$)□: 9.07, 11.41, 117.78, 118.07, 118.29, 121.89, 146.40(-CH=),153.00, 166.88 & 168.65 (2C=O).

5-((5-ethylfuran-2-yl)methylene)thiazolidine-2,4-dione (**11g**):Yield 68^A , 12^B,19^C %, m.p. 174^{o}C; IR (KBr, cm^{-1}): 1342, 1384, 1462, 1563, 1618, 1678, 1740, 1837, 2986, 3038,3171, 3382; ^1H NMR($CDCl_3$) □: 1.11(3H, t, CH_3), 2.62(2H, q, CH_2), 6.29(1H, d, *J*=3.5 Hz), 6.90(1H, d, *J*=4 Hz),7.43(1H, s,-C=CH), 12.34(NH); ^{13}C NMR($CDCl_3$) □: 10.98, 20.79, 108.49, 113.23, 118.22, 119.78, 147.47(-CH=), 153.09, 166.77 & 168.55(2C=O).

5-((5-Nitrofuran-2-yl)methylene) thiazolidine-2,4-dione (11h): Yield 56^A, 30^B, m.p. 279 ^oC; IR (KBr, cm^{-1}): 1346, 1459, 1609, 1622, 1663, 3180; ^{1}HNMR($CDCl_3$) □: 7.51& 7.68(each 1H, furan), 7.58(1H, s,-C=CH), 10.85(NH); ^{13}C NMR($CDCl_3$) □: 113.95, 117.30, 126.25, 142.40, 154.91(-CH=), 158.50, 166.32 & 167.14(2C=O).

4-(Furan-2-ylmethylene)-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (12a): Yield 79^A 24^B, 70^C %, m.p. 133 ^oC; IR (KBr, cm^{-1}): 1365,1594, 1621, 1685, 3117; EIMS: *m/z* 252$[M^+]$ 7.5%; ^{1}HNMR($CDCl_3$) □: 2.29(3H, CH_3), 6.68(1H,m, *J*=1.5 Hz), 7.72(1H,d), 8.22(1H, d *J*=3.7 Hz), 7.20(1H,s ,-CH=), 7.16(1H, t, 7.5 Hz), 7.41(2H,m), 7.95 (2H,d, *J*= 8Hz); ^{13}C NMR($CDCl_3$) □: 13.11, 114.87, 114.92, 129.30, 148.53, 148.63(-CH=), 150.01, 150.75, 162.16(C=O), 119.05(2C), 125.03(2C), 128.97, 138.60.

4-((5-(2-Chlorophenyl)furan-2-yl)methylene)-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (12b): Yield 62^A, 31^C %, m.p.166^{o}C; IR (KBr, cm^{-1}): 1383, 1442, 1499, 1600, 1611, 1684, 2914; EIMS: *m/z* 362/364$[M^+](C_{21}H_{15}N_2O_2Cl)$(21.2%, 6.15%); ^1H NMR($CDCl_3$) □: 2.34 (3H, CH_3), 7.20-7.61(9H,m),7.97(3H,m); ^{13}C NMR($CDCl_3$) □: 13.24, 115.99, 118.85, 119.19(2C), 124.93, 127.18, 127.37,128.46, 129.00 (2C), 130.21, 131.37, 131.72, 138.69, 149.93, 150.08(-CH=), 156.08, 162.25, 162.19 (C=O).

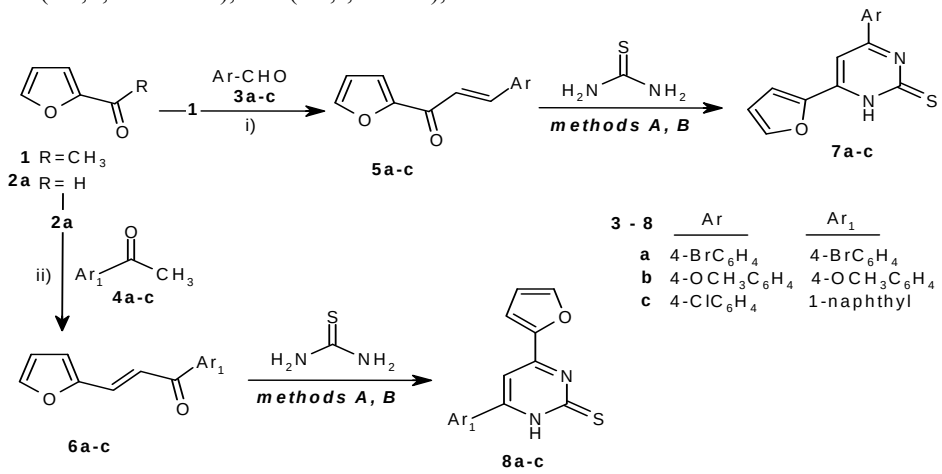
3-Methyl-4-((5-(2-nitrophenyl)furan-2-yl)methylene)-1-phenyl-1*H*-pyrazol-5(4*H*)-one (**12c**): Yield 53^A, 24^C%, m.p. 162^{o}C; IR (KBr, cm^{-1}): 1332, 1446, 1501, 1591, 1623, 1677, 2923, 3165; MS: *m/z* 373$[M^+](C_{21}H_{15}N_3O_4)$25.8%; ^1H NMR($CDCl_3$) □: 2.27 (3H,CH_3), 7.19-7.32(2H,m, H-furan),7.17(1H,s,-C=CH), 8.67, 7.60, 7.92 & 7.95(each 1H, nitrated phenyl), 6.89-7.62(5H); ^{13}C NMR($CDCl_3$) □:

12.70,113.88, 124.05, 132.03, 122.50(2C), 147.41, 125.95, 129.72, 129.33, 124.43, 151.04, 153.46, 161.54(C=O), 123.17, 149.46(-CH=), 118.54 (2C), 128.49(2C), 127.79, 138.10.

4-((5-Bromofuran-2-yl)methylene)-3-methyl-1-phenyl-1*H*-pyrazol-5(4H)-one (12d): Yield 72[A], 75[B], 74[C] %, m.p. 160°C; IR (KBr, cm^{-1}): 1357, 1411, 1500, 1598, 1634, 1671, 2938, 3075; ^{1}HNMR($CDCl_3$) □: 2.28(3H,CH_3), 6.63 & 7.14(each 1H, furan), 7.17 (1H,s,-C=CH), 7.42(3H), 7.91(2H, dd); ^{13}CNMR($CDCl_3$) □: 12.26, 116.10, 118.27(2C), 121.96, 124.19, 126.15, 128.17(2C), 129.58, 137.69,148.99(-CH=), 155.75, 152.01, 161.22 (C=O).

4-((5-(4-Bromophenyl)furan-2-yl)methylene)-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (12e): Yield 69[A], 62[B]%, m.p.152°C; IR (KBr, cm^{-1}): 1383, 1512, 1601, 1611, 1680, 2914; ^{1}H NMR($CDCl_3$) □: 2.11 (3H, CH_3), 7.6.73& 7.04(each 1H, furan), 7.13(1H, t, *J* =7.5 Hz), 7.25(1H,s,-C=CH), 7.30-7.49(6H,m), 7.39 (2H, d, *J*=7.5 Hz) ; ^{13}C NMR($CDCl_3$) □: 15.28, 107.22, 114.42, 120.38(2C), 123.15, 124.20, 128.72(2C), 129.20(2C), 131.98(2C), 133.43, 135.64, 138.20, 142.83, 151.88(-CH=), 155.11, 156.72, 164.33(C=O).

4-((4,5-Dimethylfuran-2-yl)methylene)-3-methyl-1-phenyl-1*H*-pyrazol-5(4H)-one (12f):Yield 79[A], 75[B], 61[C]%, m.p. 164 °C; IR (KBr, cm^{-1}): 1350, 1408, 1482, 1577, 1630, 1664, 2939, 3020; EIMS: *m/z* 280[M^+]($C_{17}H_{16}N_2O_2$); ^{1}H NMR($CDCl_3$) □: 1.90, 2.33, 2.38(each 3H, s, CH_3), 6.82(1H,s, H-furan), 7.19(1H,s,-C=CH), 7.22(1H,t), 7.42(2H, *J*=8.8 Hz), 7.87(2H, *J*=8.8 Hz); ^{13}C NMR($CDCl_3$) □: 10.04, 11.80, 14.42, 110.80, 113.11, 117.78, 142.10, 118.62(2C), 128.90(2C), 128.04, 140.30, 147.82(-CH=), 149.98, 152.07, 164.80(C=O).



Scheme 1

Table 1
Yields and reaction conditions used for the synthesis of 7, 8, 10

Compd. No.	US(80°C)		MW[a](350 W)		Reflux[a]	
	t(min)	Yield (%)[b]	t(min)	Yield (%)[c]	t(min)	Yield(%)[b]
7a	**30**	**75**	**2**	**31**	**-**	**-**
7b	**30**	**83**	**2**	**56**	**-**	**-**
7c	**30**	**68**	**2**	**36**	**-**	**-**
8a	**30**	**81**	**2**	**66**	**120**	**78**
8b	**30**	**78**	**2**	**52**	**-**	**-**
8c	**30**	**72**	**3**	**53**	**180**	**69**
10a	**15**	**59**	**5**	**24**	**60**	**32**
10b	**25**	**67**	**5**	**36**	**60**	**42**
10c	**15**	**75**	**5**	**41**	**-**	**-**
10d	**15**	**66**	**5**	**56**	**-**	**-**
10e	**25**	**61**	**5**	**37**	**-**	**-**
10f	**25**	**57**	**6**	**53**	**-**	**-**
10g	**25**	**60**	**8**	**51**	**-**	**-**

[a] for comparison
[b] yields of isolated and recrystallized products
[c] yields of isolated products

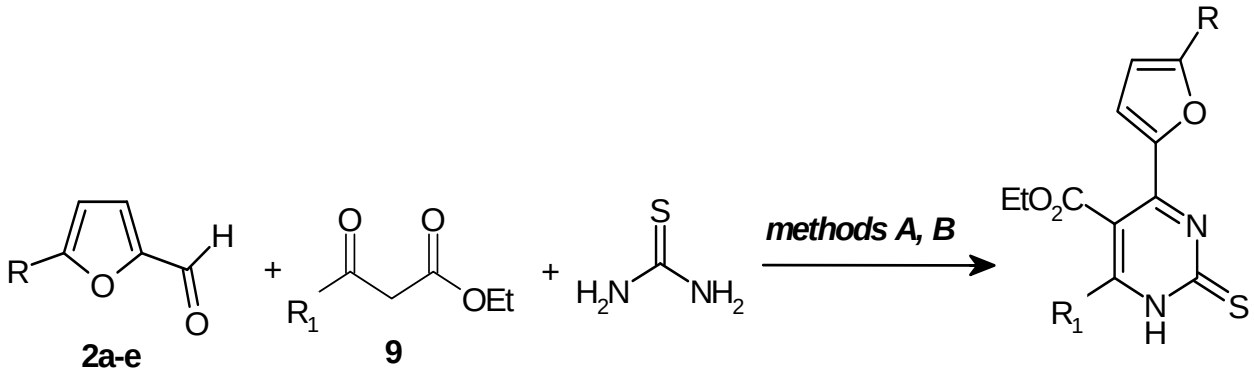
4-((5-Ethylfuran-2-yl)methylene)-3-methyl-1-phenyl-1-*H*-pyrazol-5(4H)-one (**12g**): Yield 70[A], 64[B],18[C] %, m.p. 83°C; IR (KBr, cm^{-1}): 1346, 1404, 1502, 1598, 1635, 1656, 2948, 2992, 3032; EIMS:*m/z* 280[M^+]($C_{17}H_{16}N_2O_2$); ^{1}H NMR($CDCl_3$) □: 1.30(3H, t), 2.78(2H, q), 2.30(3H,CH_3), 7.39 & 7.96(each 1H, furan), 7.27(1H,s, -C=CH); ^{13}C NMR($CDCl_3$) □: 10.92, 12.30, 21.37, 110.02, 117.94, 118.28 (2C), 123.89, 126.56, 128.41(2C), 128.78, 137.95, 147.85(-CH=), 149.21, 161.49, 165.50.

3-Methyl-4-((5-nitrofuran-2-yl)methylene)-1-phenyl-1-*H*-pyrazol-5(4*H*)-one (**12h**): Yield 63[A], 70[B]%, m.p. 146 °C; IR (KBr, cm^{-1}): 1341, 1468, 1603, 1623, 1683, 2932; ^{1}HNMR($CDCl_3$) □: 2.06 (3H, CH_3), 7.24(1H, t, *J* =7.5 Hz), 7.12(1H, t), 7.48 & 7.74(each 1H, furan), 7.48(1H, s,-C=CH), 7.58 (2H, d, *J*=7.5 Hz); ^{13}C NMR($CDCl_3$) □: 16.09, 114.20, 116.38, 120.40(2C), 123.92, 128.68(2C), 132.35, 139.12 142.85, 150.60(-CH=), 155.64, 159.44, 164.10(C=O).

Results and Discussion

Many condensation products of furfural or its 5-substituted derivatives with active methylene compounds showed various biological activities, such as antimicrobial. Accordingly, various condensate products including 2-thioxopyrimidines, based on furfural and its 5-substituted derivatives with some methylene active compounds have been prepared, under the eco-friendly ultrasound and microwave irradiation techniques. The conventional method has also been demonstrated in the preparation of some target compounds for comparison purposes. In general, ultrasound method was found to be an efficient one for the the preparation of the target compounds either through a single reaction or three component synthesis of these compounds(Tables 1 and 2). The chalcones (5a-c, 6a-c) derived from 2-acetylfuran(1) and furfural (furan-2-carboxaldehyde 2a) were prepared following the procedure in the literature[17,18], from reaction of 1 and 2a with aromatic aldehydes (3a-c) and acetophenones (4a-c) respectively. The structures of these prepared chalcones were confirmed from their ^{1}H and ^{13}C NMR spectral data. Pyrimidine-2-thiones 7a-c were obtained on treatment of the corresponding chalcones 5a-c with thiourea (scheme 1) under ultrsound irradiation, in 68-83% yields. Compounds 8a-c were also obtained in good yields(Table 1) on reaction of 6a-c with thiourea. On the other hand, synthesis of 7a-c and 8a-c under microwave irradiation gave also pure compounds, but yields were slightly low.

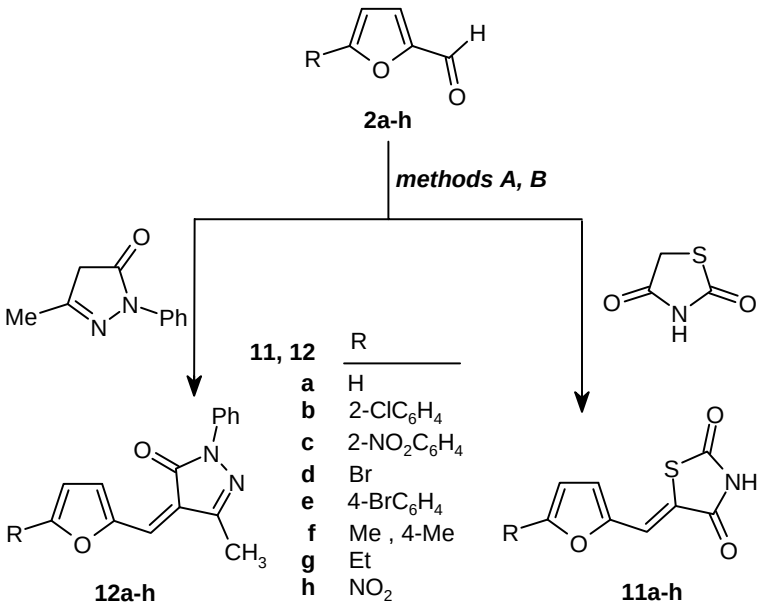
Trial to prepare the pyrimidine-2-thiones 7a and 8b adopting the above mentioned green chemistry methods following the three components reaction failed to give the desired products. The effort was then directed to Bignelli reaction in order to synthesize pyrimidine-2-thiones[10] through three components reaction, under ultrasound and microwave irradiation techniques (scheme 2). Therefore, compounds 10a-e were prepared in on pot reaction of 2a-e, ethyl acetoacetate or ethyl 2,4-dioxo-4-phenylbutanoate and thiourea, but in lower yields than those of 7 and 8. Yields and reaction conditions used for the synthesis of 7, 8 and 10 are given in table 1.



	R
a	H
b	2-ClC_6H_4
c	2-NO_2C6H_4
d	Br
e	4-BrC_6H_4

10	R	R_1
a	Br	Ph
b	2-ClC_6H_4	Ph
c	H	Me
d	H	Ph
e	2-$NO_2C_6H_4$	Ph
f	4-BrC_6H_4	Me
g	4-BrC_6H_4	Ph

Scheme 2



Scheme 3

Table 2

Yields and reaction conditions used for the synthesis of 11 a-h, 12 a-h

Compd. No.	US(80 °C)		MW[a](350 W)		Reflux[a]	
	t(min)	Yield (%)[b]	t(min)	Yield (%)[c]	t(min)	Yield(%)[b]
11a	**15**	**69**	**4**	**16**	**60**	**55**
11b	**15**	**53**	**2**	**13**	**60**	**46**
11c	**20**	**45**	**-**	**-**	**60**	**18**
11d	**15**	**60**	**7**	**20**	**60**	**39**
11e	**20**	**74**	**10**	**41**	**-**	**-**
11f	**15**	**61**	**12**	**15**	**60**	**45**
11g	**15**	**68**	**9**	**12**	**60**	**19**
11h	**20**	**56**	**10**	**30**	**-**	**-**
12a	**15**	**79**	**2**	**24**	**60**	**70**
12b	**15**	**62**	**-**	**-**	**60**	**31**
12c	**20**	**53**	**-**	**-**	**60**	**24**
12d	**15**	**72**	**5**	**75**	**60**	**74**
12e	**20**	**69**	**5**	**62**	**-**	**-**
12f	**15**	**76**	**5**	**75**	**60**	**61**
12g	**15**	**70**	**5**	**64**	**60**	**18**
12h	**20**	**63**	**5**	**70**	**-**	**-**

a: for comparison
b: yields of isolated and recrystallized products
c: yields of isolated products

2-furancarboxaldehydes (2a-h) condense with the containing active methylene goup, 1,3-thiazolin-2,5-dione, following ultrasound and MW irradiation methods, to give the corresponding condensates 11a-h. Both methods gave moderate yields (Table 2) with the advantage of ultrasound method, which gave high yields of 11a-h than those yields of the same compounds obtained under microwave irradiation[1]. The structures of 11a-h are determined on the basis of their spectroscopic data and in particular NMR. Thus, ^{1}H NMR spectra of 11a-h exhibited a singlet, integrated for one proton at 7.39-7.62 range due to the resonance of the proton of the methylene group in the structure. In the ^{13}C NMR, the carbon of this group appears at range 145.40-150.69 as verified from HETCOR experiment with the exception of 11h which appears at 154.91. The latter spectrum also revealed a signal at 167.14-169.16 attributed to the amidic carbonyl carbon in 11a-h. Similarly, the proton methylene group signal

appears at 7.17-7.28 in the 1H NMR spectra of 12 with the exception of the proton signal of 12h which desheilded to 7.48. The carbon signal of the methylene group resonates at 161.22-164.80 ppm in the ^{13}C NMR spectra of 12a-h. The yields and reaction conditions used for the synthesis of 11a-h and 12a-h are given in table 2.

Conclusion

Synthesis of some 5-unsubstituted and 5-substituted furfurylidenes and some other structurally related heterocycles has been described using microwave and ultrasound irradiation methods. Microwave and ultrasound irradiation as a green synthetic approach have gradually been used in organic synthesis over the last three decades. Structural elucidation of the target compounds was fully demonstrated by various spectral data.

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