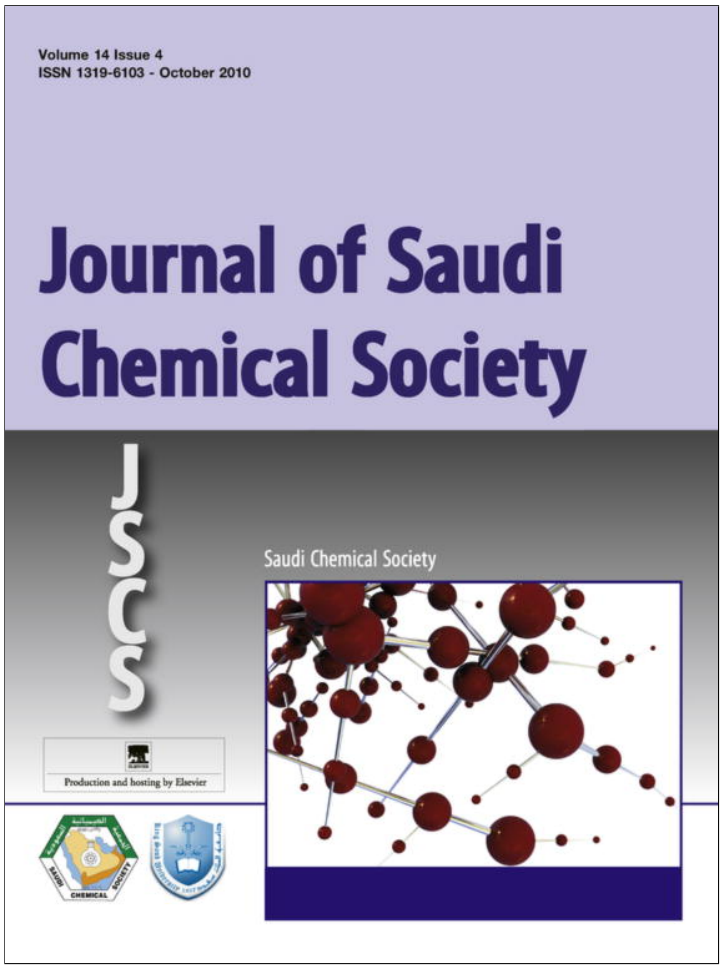

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ORIGINAL ARTICLE

Microwave assisted synthesis of substituted furan-2-carboxaldehydes and their reactions

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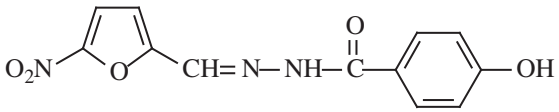
Abstract A series of 5-unsubstituted and 5-substituted furfurylidenes have been prepared, under thermal and non-thermal microwave irradiation methods, *via* condensation of furfural and its derivatives with some of active methylene compounds. Furthermore, various condensate products from these furfurylidenes,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

1. Introduction

Condensation products of some active methylene compounds with furan-2-carboxaldehydes or their 5-sustituted derivatives (Rabarova et al., 2004; Lacova et al. 2000) found to possess antimicrobial activity (Shigetaka et al. 1970; Shindhar et al., 1980). Nifuroxazide (NF) or Ambatrol is the active principle of Ercefuryl which is used for the treatment of acute bacterial diarrhea (Tabakovic and Tabakovic, 1999). NF is synthesized on laboratory and industrial scale by H_2SO_4 acid-catalysed condensation of *p*-hydroxybenzhydrazide with 5-nitrofuran-2-aldehyde (Carron et al., 1963; El-Obeid et al., 1985), or with 5-nitrofuran-2-aldehyde diacetate (Elsom and Hawkins, 1978).



NF

Ambatrol has known antibacterial properties (Leonard et al., 1985; Vanhoof et al., 1981; Thabaut and Durosoir, 1978) and is reported to be used as intestinal antiseptic in treatment of infectious diarrhea. The antimicrobial activity of its derivatives was evaluated against multi-resistent strains of *Staphylococcus* (Masunary and Tavares, 2007; Rando et al., 2002; Furlanetto et al., 2001). Pharmacological activity is mainly due to its configuration and is greatly diminished if

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the nitro group is shifted from position 5 to either the other two available positions (El-Obeid et al., 1985). However, 5-nitrothiophenes as well as 5-nitrofurans have been reported to be carcinogenic substances (Cohen et al., 1996).

Motivated by the aforementioned biological and pharmacological importance of the title compounds, we wish to report herein the synthesis of a series of some substituted furfurylidenes as well as various heterocyclic ring systems containing furyl moiety adopting microwave irradiation and thermal methods with the expectation that the synthesized products will be of significant biological activity.

2. Experimental

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}C NMR 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.

2.1. Typical procedure for the preparation of chalcones (3a–e)

They were prepared as reported for aromatic chalcones (El-Shehry et al., 2008).

To a stirred solution of the appropriate acetyl compound **2a–d** or compound **2e** (0.05 mol) in absolute ethanol (35 mL), KOH (25%, 10 mL) was added (temperature not raise above than 40 °C). Furfural (**1a**) or thiophene (**1b**) (0.05 mol) was added to the resulting solution with continuous stirring for 2 h. Then, the reaction mixture was allowed to stand overnight. The resulting solid product was collected by filtration, washed well with water and dried to give the corresponding chalcones **2a–e**, in high yields.

2.1.1. 3-(Furan-2-yl)-1-(naphthalen-1-yl)prop-2-en-1-one (3a)

Yield 91%, m.p. 53 °C; MS: m/z 248 [M^+]; H_δ: 6.51 (1H, m), 6.71 (1H, d, J = 3.6 Hz),), 7.51 (1H, m), 7.53–7.97 (8H, m), 8.1 (1H, dd, J = 1.3 and 8.5 Hz), 8.51 (1H, s); C_δ: 112.83, 116.41, 119.36, 124.49, 126.83, 127.89, 128.46, 128.62, 129.66, 129.99, 130.66, 132.66 (2C), 135.55, 145.04 (C-5 furan ring), 151.83 (C-2 furan ring), 189.58 (C═O).

2.1.2. 1-(4-bromophenyl)-3-(furan-2-yl)prop-2-en-1-one (3b)

Yield 87%, m.p. 58–60 °C; MS: m/z 276/278 [M^+]; H_δ: 6.51 (1H, dd, J = 1.5 and 5 Hz), 6.73 (1H, d J = 5 Hz), 7.39 (1H, d, J = 15.4 Hz), 7.52 (1H, d, J = 1.5 Hz), 7.59 (1H, d, J = 15.4 Hz), 7.62 (2H, d, J = 7.5 Hz), 7.89 (2H, d, J = 7.5 Hz); C_δ: 112.88, 116.83, 118.66, 127.97, 130.03 (2C), 131.18, 131.98 (2C), 136.92, 145.22, 151.59, 188.70 (C═O).

2.1.3. 3-(Furan-2-yl)-1-(4-methyl-2-phenylthiazol-5-yl)prop-2-en-1-one (3c)

Yield 86%, m.p. 120 °C; MS: m/z 295 [M^+]; H_δ: 2.75 (3H, CH_3), 6.56 (1H, m), 6.89 (1H, d, J = 4 Hz), 7.09 (1H, d, J = 15.4 Hz), 7.46 (3H, m), 7.52 (1H, d, J = 15.4 Hz), 7.70 (1H, brs), 7.96 (2H, dd); C_δ: 18.80, 113.34, 117.71, 121.81, 127.01 (2C), 129.49 (2C), 130.45, 131.56, 131.66, 132.83, 146.23, 151.19, 159.68, 168.76, 181.66 (C═O).

2.1.4. 1-(4-Methoxyphenyl)-3-(thiophen-2-yl)prop-2-en-1-one (3d)

Yield 97%, m.p. 99–101 °C; MS: m/z 244 [M^+]; H_δ: 3.84 (3H, OCH_3), 6.95 (2H, d, J = 8.8 Hz), 7.05 (1H, m), 7.31(1H, d, J = 5.2 Hz), 7.32 (1H, d, J = 15.4 Hz), 7.36 (1H, d, J = 5.2 Hz), 7.90 (1H, d, J = 15.4 Hz), 7.99 (2H, d, J = 8.8 Hz); C_δ: 55.54, 113.92 (2C), 120.69, 128.37, 128.54, 130.78 (2C), 131.05, 131.80, 136.43, 140.64, 163.49, 188.07 (C═O).

2.1.5. 2-(Furan-2-ylmethylene)-6-methoxy-3,4-dihydronaphthalen-1(2H)-one (3e)

Yield 88%, m.p. 74 °C; MS: m/z 254 [M^+]; H_δ: 2.93 (2H, t, J = 6.65 Hz), 3.26 (2H, t, J = 6.65 Hz), 3.82 (3H, OCH_3), 6.48 (1H, m), 6.64 (1H, d, J = 3.4 Hz), 6.68 (1H, d, J = 2.7 Hz), 6.83 (1H, s), 7.46 (1H, s), 7.5 (1H, d, J = 8.0 Hz), 8.05 (1H, d, J = 8.0 Hz), one proton lost; C_δ: 112.83, 116.41, 119.36, 124.49, 126.83, 127.89, 128.46, 128.62, 129.66, 129.99, 130.66, 132.66, 135.55, 145.04, 151.83, 189.58 (C═O).

2.2. General procedure for the synthesis of compounds 4a,b,e

2.2.1. Microwave method

To an equimolar amount of **3a**,**b**,**e** and thiourea (0.02 mole), a few drops of methanol was added. Then, the reaction mixture was irradiated in a domestic microwave oven operating at a power of 600 W for the time being depicted in Table 1. After trituration of the reaction product with a few drops of methanol, the precipitated solid was collected by filtration, washed with hot methanol and dried to give the target compounds **4a**,**b**,**e**. Compound **4e** was also prepared using neat (solvent free) microwave with 82% yield.

2.2.2. Classical method

Compounds **4a**,**b**,**e** were synthesized following the reported method (Al-AlShaikh et al., 2006) for similar compounds.

Table 1 Yields and reaction conditions used for the synthesis of **4** and **6**.

Compd. No.	MW method (*A*) (600 W)	Classical method (*B*)	Reaction time (min)	
	Yields (%)	Yields (%)	A	B
4a	53	69	3	2 h
4b	66	78	2	3 h
4c	48	61	2	3 h
6a	24	–	5	–
6b	36	–	5	–
6c	41	–	5	–
6d	56	–	5	–
6e	37	–	5	–
11a	31	–	2	–
11b	36	–	1	–

*2.2.3. 4-(Furan-2-yl)-6-(naphthalen-1-yl)-3,4-dihydropyrimidine-2(1H)-thione (**4a**)*
Yield 69%, m.p. 267–269 °C; IR (cm^{-1}): 3373, 3168 (NH), 1601, 1500, 1432, 1223 (C═S); ^{1}H NMR (DMSO-d_6) δ: 6.48–7.56 (3H, m, furan ring protons), 7.48 (1H, d, J = 8.4 Hz), 7.72 (1H, d, J = 8.4 Hz), 7.56 (3H, m), 7.52 (1H, s), 8.06 (2H, m), 12.90 (1H, s, NH); ^{13}C NMR (DMSO-d_6) δ: 103.50 (C-5), 109.38, 110.07, 123.40, 125.24, 126.08, 126.20, 127.73, 128.02, 128.32, 133.14, 133.56, 134.70, 141.70, 144.10, 164.51 (C-4), 175.22 (C-6), 180.82 (C═S).

*2.2.4. 6-(4-Bromophenyl)-4-(furan-2-yl)-3,4-dihydropyrimidine-2(1H)-thione (**4b**)*
Yield 61%, m.p. 267–269 °C; IR (cm^{-1}): 3367, 3189 (NH), 2987, 2932, 11598, 1500, 1443, 1258 (C═S); ^{1}H NMR ($CDCl_3$) δ: 6.52 (1H, m), 6.56 (1H, d, J = 2.5 Hz), 6.71 (1H, d, J = 3.8 Hz), 7.23 (2H, d, J = 8.5 Hz), 7.37 (1H, s), 7.51 (2H, d, J = 8.5 Hz), 12.82 (1H, s, NH); ^{13}C NMR ($CDCl_3$) δ: 102.22, 109.52, 110.20, 122.85, 128.38 (2C), 129.74, 130.94 (2C), 141.35, 143.82, 163.68 (C–O), 167.54, 182.71 (C═S).

*2.2.5. 4-(Furan-2-yl)-8-methoxy-5,6-dihydrobenzo[h]quinazoline-2(1H)-thione (**4e**)*
Yield 78%, m.p. 267–269 °C; IR (cm^{-1}): 3373, 3168 (NH), 1601, 1500, 1432, 1236 (C═S); ^{1}H NMR ($CDCl_3$) δ: 2.96 (2H, t, J = 6.6, CH_2), 3.29 (2H, t, J = 5.7, CH_2), 3.86 (3H, s, OCH_3), 6.50 (1H, m), 6.66 (1H, d, J = 2.5 Hz), 6.71 (1H, d, J = 3.6 Hz), 6.86 (1H, dd, J = 2.2 & 8.8 Hz), 7.54 (1H, s, Ar-H), 8.08 (1H, d, J = 8.8 Hz); ^{13}C NMR ($CDCl_3$) δ: 26.87, 28.89, 55.54, 112.23, 112.36, 113.33, 116.28, 122.33, 127.19, 130.74, 132.19, 144.21, 146.12, 152.59, 163.52 (C–O), 186.39 (C═S).

*2.3. Synthesis of (**6a–e**)*

A mixture of 5-substituted furfural **1a**,**b**,**d** (0.01 mol), 1,3-dicarbonyl compounds **5a**,**b** (0.01 mol), thiourea (0.02 mol) and a few drops of acetic acid (1 ml) was mixed and irradiated in domestic microwave oven for 3–4 min at a power of 400 W. The resulting solid product was filtered off, washed with ethanol, dried and recrystallized from ethanol.

*2.3.1. Ethyl 4-(5-bromofuran-2-yl)-6-phenyl-2-thioxo-1,2-dihydropyrimidine-5-carboxylate (**6a**)*
Yield 24%, m.p. > 320 °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%) ($C_{17}H_{13}N_2O_3SBr$).

*2.2.2. Ethyl 6-(2-chlorophenyl)-4-(furan-2-yl)-2-thioxo-1,2-dihydropyrimidine-5-carboxylate (**6b**)*
Yield 36%, m.p. 106-108 °C; IR (cm^{-1}): 3447 (NH), 3038 (aromatic CH), 2985 (aliph. CH), 1719 (ester CO), 1221 (C═S); ^{1}H NMR ($CDCl_3$) δ: 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}C NMR ($CDCl_3$) δ: 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.

*2.3.3. Ethyl 4-(furan-2-yl)-6-methyl-2-thioxo-1,2-dihydropyrimidine-5-carboxylate (**6c**)*
Yield 41%, m.p. > 320 °C; IR (cm^{-1}): 3317, 3186 (NH), 2965 (aliph. CH), 1731 (ester CO), 1247 (C═S); ^{1}H NMR (DMSO-d_6) δ: 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) δ: 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).

*2.3.4. Ethyl 4-(furan-2-yl)-6-phenyl-2-thioxo-1,2-dihydropyrimidine-5-carboxylate (**6d**)*
Yield 56%, m.p. 118 °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) δ: 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) δ: 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.

*2.3.5. Ethyl 4-(5-(2-nitrophenyl)furan-2-yl)-6-phenyl-2-thioxo-1,2-dihydropyrimidine-5-carbo-xylate (**6e**)*
Yield 36%, m.p. 132 °C; IR (cm^{-1}): 3397 (NH), 3043 (aromatic CH), 2981 (aliph. CH), 1728 (ester CO), 1228 (C═S); ^{1}H NMR (DMSO-d_6) δ: 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) δ: 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.

*2.4. Synthesis of 3-(4-substituted phenyl)-1-(furan-2-yl)prop-2-en-1-ones (**9a–c**)*

They were prepared as reported for aromatic chalcones (El-Baih et al., 2006).

A mixture of KOH (0.055 mol), water (20 ml), ethanol (15 ml), 2-acetyl furan **7** (0.043 mol) and the appropriate aldehyde **8a**–**c** (0.043 mol) was stirred at 30–40 °C for 2 h and kept overnight. It was then filtered, washed with water and with ethanol, dried and refluxed with glacial acetic acid (10 ml) for 2 h. The crystals separated after cooling were filtered and washed with water, dried and used with any further purification.

*2.4.1. 3-(4-Bromophenyl)-1-(furan-2-yl)prop-2-en-1-one (**9a**)*
Yield 62%, m.p. 95 °C; IR (KBr, cm^{-1}): 3125, 3090, 1675, 1662, 1601, 1567, 1423, 1397, 1362; ^{1}H NMR ($CDCl_3$) δ: 6.77 (1H, m), 7.61 (1H), 7.63 (1H), 7.71 (2H), 7.77 (1H), 7.79–7.84 (2H, m); ^{13}C NMR ($CDCl_3$) δ:112.66, 119.73, 122.58, 123.91, 130.56 (2C), 131.78 (2C), 133.61, 141.31, 148.43, 152.77, 176.36.

*2.4.2. 3-(4-Chlorophenyl)-1-(furan-2-yl)prop-2-en-1-one (**9b**)*
Yield 86%, m.p.131 °C; IR (KBr, cm^{-1}): 3124, 1656, 1604, 1407, 1394, 1334; ^{1}H NMR ($CDCl_3$) δ: 6.76 (1H, m), 7.47(2H, d, J = 8.5 Hz), 7.69 (2H, m), 7.78–7.86 (3H, m), 8.05 (1H); ^{13}C NMR ($CDCl_3$) δ: 112.51, 119.53, 122.39, 128.72 (2C), 130.19, 133.14 (2C), 134.91, 141.07, 148.24, 152.67, 176.23.

*2.4.3. 1-(Furan-2-yl)-3-(4-methoxyphenyl)prop-2-en-1-one (**9c**)*
Yield 79%, m.p. 80 °C; IR (KBr, cm^{-1}): 3129 2999, 2839, 1656, 1600, 1515, 1425, 1398, 1341; ^1H NMR ($CDCl_3$) δ: 3.76 (s, 3H), 6.73 (1H, m), 6.69 (2H, d, J = 8.5 Hz), 7.52 (1H, d, J = 15.8 Hz), 7.71 (1H, d, J = 15.8 Hz), 7.36 (2H, d, J = 8.5 Hz), 7.74 (2H, d, J = 8.5 Hz); ^{13}C NMR ($CDCl_3$) δ: 55.12, 112.49, 114.24 (2C), 114.64, 118.77, 119.15, 126.85 (2C), 142.65, 147.85, 152.93, 161.23, 176.63.

*2.5. Synthesis of **11a**,**b***

Compound **11a**,**b** were prepared as reported in the literature (Al-AlShaikh et al., 2006). A mixture of **9a**,**b** (2 mole), thiourea (2 mole), AcOH (1 ml) was placed in Erlenmeyer flask (100 ml) and the reaction mixture was irradiated in a domestic microwave oven operating at a power of 600 W for the time being depicted in Table 1. The cold reaction mixture was triturated with ethanol, and the solid product was filtered off and recrystallized from ethanol.

*2.5.1. 4-(4-Bromophenyl)-6-(furan-2-yl)pyrimidine-2(1H)-thione (**11a**)*
Yield 31%, m.p. 102 °C; IR (KBr, cm^{-1}): 3386, 3157(br, NH), 3051, 1647, 1598, 1502, 1437, 1358, 1231 (C═S).

*2.5.2. 4-(4-Chlorophenyl)-6-(furan-2-yl)pyrimidine-2(1H)-thione (**11b**)*
Yield 35%, m.p. 96–98 °C; IR (KBr, cm^{-1}): 3400 (br, NH), 3040, 1654, 1590, 1500, 1466, 1424, 1363, 1212 (C═S).

*2.6. Synthesis of (**13a–f**)*

2.6.1. Classical method
Compounds **13a–f** were synthesized following the reported method (El-Shehry et al., 2008) for similar compounds and in good yields, which are shown in Table 1.

*2.6.2. 3-(4-Bromophenyl)-5-(furan-2-yl)-1H-pyrazole (**13a**)*
Brown crystals, Yield 23%, m.p. 90 °C (Reflux 5 h); ^1H NMR ($CDCl_3$) δ: 6.53 (1H, brs), 6.82 (1H, m), 7.21 (1H, d, J = 2.4 Hz), 7.47 (1H, d, J = 3.1 Hz), 7.52–7.59 (4H, m); ^{13}C NMR ($CDCl_3$) δ: 106.82, 111.75, 142.09, 156.94 (furan carbons), 98.80, 134.77, 146.60 (pyrazole carbons), 132.20, 128.31 (2C), 131.15 (2C), 122.80.

*2.6.3. 3-(4-Clorophenyl)-5-(furan-2-yl)-1H-pyrazole (**13b**)*
Brown solid, Yield 24%, 21% (700 W, 4 min), m.p. 122–124 °C (Reflux 6 h); ^1H NMR ($CDCl_3$) δ: 6.55(1H, s), 6.88 (1H, m), 7.13 (1H, d, J = 2.1 Hz), 7.49 (1H, d, J = 3.6 Hz), 7.52, 7.92 (each 2H, d, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$) δ:107.28, 112.50, 142.88, 157.22 (furan carbons), 99.20, 134.23, 146.85 (pyrazole carbons), 131.31, 128.8 (2C), 131.15 (2C), 122.80.

*2.6.4. 3-(4-Methoxyphenyl)-5-(furan-2-yl)-1H-pyrazole (**13C**)*
Yellowish solid, Yield 22%, m.p. 130–132 °C (Reflux 7 h); ^1H NMR ($CDCl_3$) δ: 3.82 (3H, s), 6.53 (1H, s), 6.68 (1H, m), 6.99 (1H, d, J = 2.4 Hz), 7.56 (1H, d, J = 2.4 Hz), 7.04, 7.49 (each 2H, d, J = 8.6 Hz); ^{13}C NMR ($CDCl_3$) δ: 55.70, 106.91, 111.42, 142.90, 157.70 (furan carbons), 100.18, 134.70, 146.58 (pyrazole carbons), 125.87, 114.65 (2C), 128.22 (2C), 161.13.

*2.6.5. 3-(4-Bromophenyl)-5-(furan-2-yl)-1-phenyl-1H-pyrazole (**13d**)*
Greenish solid, Yield 51%, 41% (700 W, 4 min), m.p. 85–86 °C (Reflux 6 h); ^1H NMR ($CDCl_3$) δ: 6.68 (1H, s), 6.92 (1H, m), 7.58 (1H, d, J = 1.8 Hz), 7.86 (1H, d, J = 2.9 Hz), 7.62–7.68 (4H, m), 7.42 (1H, t), 7.57–7.65 (4H, m); ^{13}C NMR ($CDCl_3$) δ: 107.11, 111.85, 142.72, 156.97 (furan carbons), 106.50, 127.12, 149.74 (pyrazole carbons), 123.20, 124.45 (2C), 126.32, 128.08 (2C), 129.45 (2C), 132.20 (2C), 132.44, 138.80.

*2.6.6. 3-(4-Chlorophenyl)-5-(furan-2-yl)-1-phenyl-1H-pyrazole (**13e**)*
Yellow powder, Yield 49%, m.p. 109–111 °C (Reflux 9 h); ^1H NMR ($CDCl_3$) δ: 6.70 (1H, s), 6.92 (1H, m), 7.58 (1H, d, J = 2.2 Hz), 7.76 (1H, d, J = 3.4 Hz), 7.55, 7.96 (each 2H, dd), 7.41 (1H, t, J = 7.9), 7.58–7.62 (4H, m); ^{13}C NMR ($CDCl_3$) δ: 107.21, 112.30, 142.80, 157.72 (furan carbons), 107.21, 127.10, 149.94 (pyrazole carbons), 124.32 (2C), 126.30, 128.74 (2C), 129.25 (2C), 129.42 (2C), 131.40, 134.20, 139.72.

*2.6.7. 3-(4-Methoxyphenyl)-5-(furan-2-yl)-1-phenyl-1H-pyrazole (**13f**)*
Yellow solid, Yield 35%, m.p. 118–120 °C (Reflux 7 h); δ: 3.80 (3H, s), 6.68 (1H, s), 6.92 (1H, m), 7.47 (1H, d, J = 2.2 Hz), 7.69 (1H, d, J = 3.1 Hz), 7.05, 7.54 (each 2H, d, J = 8.5 Hz), 7.45 (1H, t, J = 8.5), 7.58–7.63(4H, m); ^{13}C NMR ($CDCl_3$) δ: 55.80, 106.99, 112.10, 142.87, 157.40 (furan carbons), 108.30, 128.50, 149.10 (pyrazole carbons), 125.22, 114.80 (2C), 128.52 (2C), 160.90, 124.55 (2C), 126.20, 128.88 (2C), 138.76.

*2.7. General procedure for the synthesis of (**14a–f** and **15a–f**)*

2.7.1. 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), appropriate aromatic aldehyde **1a–f** (0.01 mol) and piperidine (3 drops) was heated under reflux for 15 min. The solid product formed was then cooled, filtered, washed with ethanol and recrystallised from ethanol.

2.7.2. 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 **1a–f** (0.01 mol) were mixed and irradiated by microwave (300 W). The solid product was triturated with methanol, filtered, washed with ethanol (96%), dried and recrystallized from ethanol.

*2.7.3. 5-(furan-2-ylmethylene)thiazolidine-2,4-dione (**14a**)*
Yield 55^A, 16^B%, m.p. 225 °C; IR (KBr, cm^{-1}): 1339, 1610, 1684, 1719, 3034, 3227; EIMS: m/z 195[M^+] ($C_8H_5NO_3S$) 20.8%; ^1H NMR ($CDCl_3$) δ: 6.72 (1H, m), 7.06 (1H, d J = 4 Hz), 7.55 (1H, brs), 7.59 (1H, br s); C_δ:113.73, 118.69, 118.79, 120.63, 147.69, 149.48, 167.30, 168.89 (2C═O).

*2.7.4. 5-((5-(2-chlorophenyl)furan-2-yl)methylene)thiazolidine-2,4-dione (**14b**)*
Yield 46^A, 13^B%, m.p. 240 °C; 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 ($CDCl_3$) δ: 6.76 (1H, d, J = 3.7 Hz), 7.19 (1H, d, J = 3.7 Hz), 7.41 (–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 ($CDCl_3$) δ: 114.08, 117.95, 119.63, 121.60, 130.51, 127.68, 129.32, 130.94, 127.29, 128.09, 148.81, 153.78, 167.41, 169.16 (2C═O).

*2.7.5. 5-((5-(2-nitrophenyl)furan-2-yl)methylene)thiazolidine-2,4-dione (**14c**)*

Yield 18^{A}, m.p. 274 °C; IR (KBr, cm^{-1}): 1346, 1459, 1500, 1603, 1669, 3031, 3161; ^{1}H NMR ($CDCl_3$) δ: 7.21, 7.25 (each 1H, furan), 7.62 (1H, –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 ($CDCl_3$) δ: 113.59, 117.67, 124.87 (–CH═), 122.08, 133.24, 147.17, 122.00, 130.55, 129.80, 120.74, 150.69, 152.07, 167.24, 168.80 (2C═O).

*2.7.6. 5-((5-bromofuran-2-yl)methylene)thiazolidine-2,4-dione (**14d**)*

Yield 39^{A}, 20^{B}%, m.p 240 °C; 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%); ^{1}H NMR ($CDCl_3$) δ: 6.84 (1H, d, J = 3.66 Hz), 7.07 (1H, d, J = 4 Hz), 7.52 (1H, –C═CH), 12.32 (NH); ^{13}C NMR ($CDCl_3$) δ: 115.40, 117.00, 120.33 (–CH═), 120.94, 126.80, 151.05, 166.69, 168.07 (C═O).

*2.7.7. 5-((5-ethylfuran-2-yl)methylene)thiazolidine-2,4-dione (**14e**)*

Yield 19^{A}, 12^{B}%, m.p. 174 °C; IR (KBr, cm^{-1}): 1342, 1384, 1462, 1563, 1618, 1678, 1740, 1837, 2986, 3038, 3171, 3382; ^{1}H NMR ($CDCl_3$) δ: 1.11 (3H, t), 2.62 (2H, q), 6.29 (1H, d, J = 3.5 Hz), 6.90 (1H, d, J = 4 Hz), 7.43 (1H, –C═CH), 12.34 (NH); ^{13}C NMR ($CDCl_3$) δ: 20.79, 10.98, 108.49, 113.23, 118.22, 119.78, 147.47, 166.77, 168.55 (C═O).

*2.7.8. 5-((4,5-dimethylfuran-2-yl)methylene)thiazolidine-2,4-dione (**14f**)*

Yield 45^{A}, 15^{B}%, m.p.230 °C; 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%; ^{1}H NMR ($CDCl_3$) δ: 1.91, 2.24 (each s, 3H), 6.82, 7.39 (each s, 1H), 11.50 (brs, NH); ^{13}C NMR ($CDCl_3$) δ: 9.07, 11.41, 117.78, 118.07, 118.29, 121.89, 146.40, 153.00, 166.88, 168.65 (C═O).

*2.7.9. 4-(Furan-2-ylmethylene)-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (**15a**)*

Yield 70^{A}, 24^{B}%, m.p. 133 °C; IR (KBr, cm^{-1}): 1365, 1594, 1621, 1685, 3117; EIMS: m/z 252[M^+] 7.5%; ^{1}H NMR ($CDCl_3$) δ: 2.29 (3H, CH_3), 6.68 (1H, m, J = 1.5 Hz), 7.72 (1H, d), 8.72 (1H, d J = 5.7 Hz), 7.28 (1H, –C═CH), 7.16 (1H, t, 7.5 Hz), 7.41 (2H, m), 7.95 (2H, d, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ: 13.11, 114.87, 114.92, 148.53 (–CH═), 129.30, 148.63, 150.01, 150.75, 162.16 (C═O), 119.05 (2C), 125.03 (2C), 128.97, 138.60.

*2.7.10. 4-((5-(2-Chlorophenyl)furan-2-yl)methylene)-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (**15b**)*

Yield 31^{A}, m.p.166 °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%); ^{1}H NMR ($CDCl_3$) δ: 2.34 (3H, CH_3), 7.20–7.61 (9H, m), 7.97 (3H, m) 11.70 (NH); ^{13}C NMR ($CDCl_3$) δ: 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, 156.08, 162.25, 162.19 (C═O).

*2.7.11. 3-Methyl-4-((5-(2-nitrophenyl)furan-2-yl)methylene)-1-phenyl-1H-pyrazol-5(4H)-one (**15c**)*

Yield 24^{A}, m.p. 162 °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%; ^{1}H NMR ($CDCl_3$) δ: 2.27 (3H, CH_3), 7.19–7.32 (2H, m, H-furan), 7.17 (1H, –C═CH), 8.67, 7.60, 7.92, 7.95 (each 1H, nitrated phenyl), 6.89–7.62 (5H); ^{13}C NMR ($CDCl_3$) δ: 12.70, 113.88, 124.05, 132.03 (–CH═), 122.50, 147.41, 125.95, 129.72, 129.33, 124.43, 151.04, 153.46, 161.54 (C═O), 123.17, 149.46, 118.54 (2C), 128.49 (2C), 127.79, 138.10.

*2.7.12. 4-((5-Bromofuran-2-yl)methylene)-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (**15d**)*

Yield 74^{A}, 75^{B}%, m.p. 160 °C; IR (KBr, cm^{-1}): 1357, 1411, 1500, 1598, 1634, 1671, 2938, 3075; ^{1}H NMR ($CDCl_3$) δ: 2.28 (3H, CH_3), 6.63, 7.14 (each 1H, furan), 7.17 (1H, –C═CH), 7.42 (3H), 7.91 (2H, dd); ^{13}C NMR ($CDCl_3$) δ: 12.26, 116.10, 118.27 (2C), 121.96, 124.19, 126.15, 126.86, 128.17 (2C), 129.58, 137.69, 148.99, 152.01, 161.22 (C═O).

*2.7.13. 4-((5-Ethylfuran-2-yl)methylene)-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (**15e**)*

Yield 18^{A}, 64^{B}%, 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 ($CDCl_3$) δ: 1.30 (3H, t), 2.78 (2H, q), 2.30 (3H, CH_3), 7.39, 7.96 (each 1H, furan), 7.37 (1H, –C═CH); ^{13}C NMR ($CDCl_3$) δ: 10.92, 12.30, 21.37, 110.02, 117.94, 118.28 (2C), 123.89, 126.56, 128.41 (2C), 128.78, 137.95, 149.21, 161.49 (C═O), 165.50.

*2.7.14. 4-((4,5-Dimethylfuran-2-yl)methylene)-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (**15f**)*

Yield 61^{A}, 75^{B}%, 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 ($CDCl_3$) δ: 1.90, 2.33, 2.38 (each 3H, s, CH_3), 6.82 (1H, s, H-furan), 7.19 (1H, –C═CH), 7.22 (1H, t), 7.42 (2H, J = 8.8 Hz), 7.87 (2H, J = 8.8 Hz); ^{13}C NMR ($CDCl_3$) δ: 10.04, 11.80, 14.42, 110.80, 113.11, 117.78, 148.25, 149.98, 118.62 (2C), 128.90 (2C), 128.04, 140.30, 142.10, 132.07, 147.82, 164.80 (C═O).

*2.8. Synthesis of 2-furylidenemalononitrile (**16a**,**b**) and ethyl 2-cyano-3-(furan-2-yl)propenoate (**16c**,**d**)*

A mixture of furan-2-carboxaldehyde (3 mmol) and malononitrile or Ethyl cyanoacetate (3 mmol) was placed in a 2 mL beaker covered with a watch glass and was then irradiated with microwave (350 W) for 2–3 min. The cold reaction mixture was treated with ethanol; the solid product was filtered, dried and recrystallized. Compound **12a** was also prepared in a large scale with good yield (88%) following the procedure in the literature (Al-Mutairi et al., 2009).

*2.8.1. 2-((Furan-2-yl)methylene malononitrile (**16a**)*

Yield 82%, m.p. 73–75 °C; MS: m/z 144[M^+]; ^{1}H NMR (CD_3OD) δ:7.32 (1H, d, J = 3.7 Hz), 6.69 (1H, dd), 7.78

(1H, d, J = 1.5 Hz), 7.51 (1H, =CH); ^{13}C NMR (CD_3OD) δ: 148.07, 123.87, 114.54, 143.20, 149.74 (–C=CH), 77.22, 112.72 (CN), 113.94 (CN).

*2.8.2. 2-((5-(2-Chlorophenyl)furan-2-yl)methylene)malononitrile (**16b**)*

Yield 59%, m.p. 155 °C; ^{1}H NMR (CD_3OD) δ:7.23–7.34 (2H, m), 7.30–7.48 (3H, m), 7.42 (–C=CH), 8.10 (1H, d, J = 8 Hz); ^{13}C NMR (CD_3OD) δ: 150.94, 106.89, 109.95, 156.20, 143.94 (–C=CH), 74.12, 113.71 (CN), 113.65 (CN), 136.88, 132.24, 128.71, 130.21, 128.11, 128.67.

*2.8.3. Ethyl 2-cyano-3-(furan-2-yl)acrylate (**16c**)*

Yield 79%, m.p. 72 °C; ^{1}H NMR (CD_3OD) δ: 1.35 (3H, t), 4.32 (2H, q), 6.63 (1H, dd), 7.36 (1H, d, J = 3.8 Hz), 7.72 (1H, d), 7.99 (1H, =CH); ^{13}C NMR (CD_3OD) δ: 14.11, 61.80, 152.10, 110.22, 112.69, 143.81, 156.98 (–C=CH), 94.21, 117.68 (CN), 163.24 (C=O).

*2.8.4. Ethyl 3-(5-(2-chlorophenyl)furan-2-yl)-2-cyanoacrylate (**16d**)*

Yield 63%, m.p.115 °C; ^{1}H NMR (CD_3OD) δ: 1.36 (3H, t), 4.35 (2H, q), 7.23–7.29 (2H, m), 7.35–7.43 (3H, m), 7.92 (–C=CH), 8.11 (1H, d, J = 8 Hz); ^{13}C NMR (CD_3OD) δ: 14.17, 61.26, 150.82, 107.30, 110.37, 156.08, 156.48 (–C=CH), 93.82, 117.73 (CN), 163.61 (C=O), 137.20, 132.11, 128.94, 130.31, 127.80, 128.74.

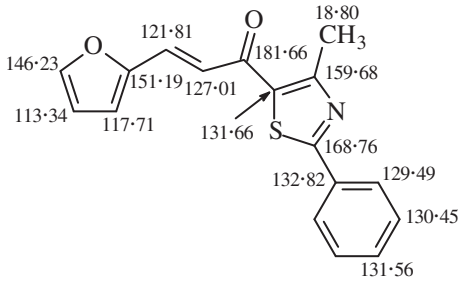


Figure. 1 C_δ data of **3c**.

*2.9. Synthesis of **17** and **19a–c***

To a solution of the arylidenemalononitrile (**16a**) (0.01 mol) and the active methylene 1,3-thiazolin-2,5-dione or **18a–c** (0.01 mol) in methanol (50 ml) was added 0.1 ml of morpholin. The mixture was heated to boiling and left at room temperature overnight. The solid product formed was filtered off, washed with ethanol, dried and recrystallized from ethanol.

*2.9.1. 5-Amino-7-(furan-2-yl)-2-oxo-3,7-dihydro-2H-pyrano[2,3-d]thiazole-6-carbonitrile (**17**)*

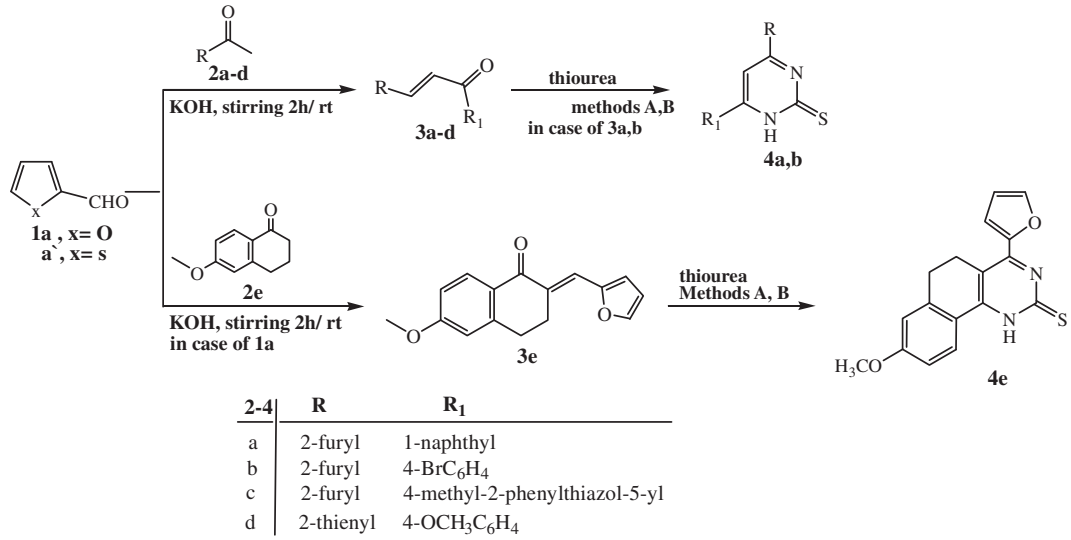
Yield 26%, could not be induced to crystallize; IR (KBr, cm^{-1}): 3436, 3034, 2265, 1656, 1611, 1339; EIMS: m/z 261[M^+] ($C_{11}H_7N_3O_3S$) (11.2%); ^{1}H NMR (DMSO-d_6) δ: 4.29 (1H, s), 6.25, 6.37, 7.61 (furan ring protons), 6.98 (2H, brs, NH_2), 10.82 (1H, s, NH); ^{13}C NMR (DMSO-d_6) δ: 28.75 (C-4), 58.11 (C-3), 97.23, 107.62, 111.45, 119.60, 141.85, 149.11, 153.20, 158.42 (C-2), 163.52 (C=O).

*2.9.2. 6-Amino-4-(furan-2-yl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (**19a**)*

Yield 47%, could not be induced to crystallize; 3084, 3017, 2947, 2265, 1646, 1598, 1501, 1443, 1356; EIMS: m/z 318[M^+] ($C_{18}H_{14}N_4O_2$) (11.2%); ^{1}H NMR (DMSO-d_6) δ: 1.95 (3H, s, CH_3), 4.91 (1H, s), 6.16, 6.41, 7.56 (furan ring protons), 6.81 (2H, brs, NH_2), 7.61 (2H, d, J = 8 Hz), 7.48–7.57 (3H, m); ^{13}C NMR (DMSO-d_6) δ: 12.80 (CH_3), 27.60, 59.12, 106.66, 110.43, 141.95, 152.51, 117.34, 119.40, 128.63, 147.15, 122.60 (2C), 129.45 (2C), 126.26, 160.88 (C-2).

*2.9.3. 6-Amino-4-(furan-2-yl)-3-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (**19b**)*

Yield 57%, m.p. 205 °C; IR (KBr, cm^{-1}): 3416, 3068, 2274, 1646, 1601, 1504, 1452; ^{1}H NMR (DMSO-d_6) δ: 5.20 (1H, s), 6.09 (1H, d, J = 3 Hz), 6.22 (1H, m), 7.52 (1H, d,



2-4	R	R_1
a	2-furyl	1-naphthyl
b	2-furyl	4-BrC_6H_4
c	2-furyl	4-methyl-2-phenylthiazol-5-yl
d	2-thienyl	4-$OCH_3C_6H_4$

Method A: KOH, EtOH reflux 2h; **Method B:** MW

Scheme 1

J = 1.7 Hz), 7.32–7.49 (5H, m, aromatic), 7.07 (2H, brs, NH_2), 12.95 (1H, s, NH); ^{13}C NMR (DMSO-d_6) δ: 30.05, 55.06, 94.86, 105.93, 110.15, 120.43, 126.14 (2C), 127.77, 128.59 (3C), 138.09, 142.06, 155.16, 155.83, 160.88.

*2.9.4. 6-Amino-4-(furan-2-yl)-3-methyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (**19c**)*

Yield 59%, m.p. 207 °C; IR (KBr, cm^{-1}): 3436, 3061, 2970, 2937, 2312, 1643, 1504, 1364; EIMS: m/z 242[M$^+$] ($C_{12}H_{10}N_4O_2$) (23%); ^{1}H NMR (DMSO-d_6) δ: 1.96 (3H, s, 3-CH_3), 4.76 (1H, s), 6.16 (1H, d, J = 2.95 Hz), 6.33 (1H, m), 7.50 (1H, d, J = 1.5 Hz) (furan ring protons), 6.95 (2H, brs, NH_2), 12.15 (1H, s, NH); ^{13}C NMR (DMSO-d_6) δ: 9.27 (CH_3), 29.55 (C-4), 53.78 (C-3), 94.83, 105.38, 109.95, 120.33, 135.62, 141.95, 154.53, 155.40, 161.20 (C-2).

3. Results and discussion

3.1. Chemistry

Many condensation products of furfural or its 5-substituted derivatives with active methylene compounds showed various biological activities, such as antimicrobial. Accordingly, in this project we decide to prepare some new organic compounds based on furan ring which contain halogen or sulpher which might have biological effects. These compounds were prepared mainly following the non-thermal microwave irradiation method. However, the conventional method has been used in some cases. In general, the microwave irradiation synthesis of the target compounds in comparison to the conventional method offers more advantages such as reduced reaction time, simplicity, reduced pollution and high purity, although the yields are remarkably better in conventional method.

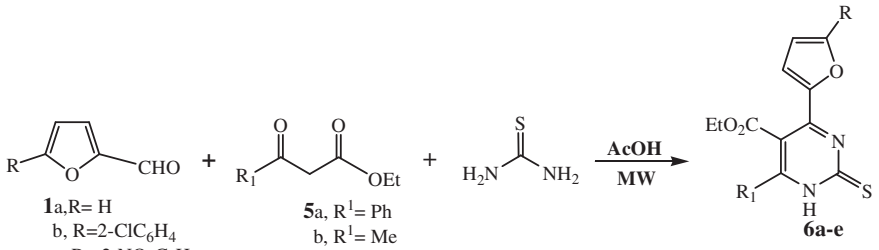
The chalcones (**1a–h**) derived from furfural (furan-2-carboxaldehyde **1a**) and thiophene-2-carboxaldehyde (**1a′**) were prepared following the procedure in the literature (El-Shehry et al., 2008; Abid and Azam, 2006), from reaction of furfural with the appropriate methylene active compounds. Similarly, compounds **9a–c** were also synthesized starting by 2-acetyl furan (**7**). The ^{1}H and ^{13}C NMR spectral data of all prepared chalcones were in complete consistent with their structures (see Section 2). The ^{13}C data of **1c** are depicted in Fig. 1.

Pyrimidine-2-thiones **4a**,**b**,**e** were obtained on treatment of the corresponding chalcones **3a–e** with thiourea (Scheme 1) under microwave irradiation, but yields were low although, the product obtained are of high purity (TLC). Alternatively, treatment of **3a–d** with thiourea in ethanol/potassium hydroxide afforded **4a**,**b**,**e** in moderate yields. On the other hand, **4a** was prepared in one pot three components reaction of furfural (**1a**), chalcone **3a** and thiourea under microwave irradiation the yield was also low (see Section 2).

The effort was then directed to Bignelli reaction aiming to improve yields of pyrimidine-2-thiones under assisted microwave irradiation technique, starting by some representatives of **1** (Scheme 2). Therefore, compounds **6a–e** were prepared in on pot reaction of **1a–d**, ethyl acetoacetate or ethyl 2,4-dioxo-4-phenylbutanoate and thiourea; still no enhanced improvements in the yield. Even though, when the latter reaction carried out under basic conditions, the yield was almost the same. Yields and reaction conditions used for the synthesis of **4** and **6** are given in Table 1.

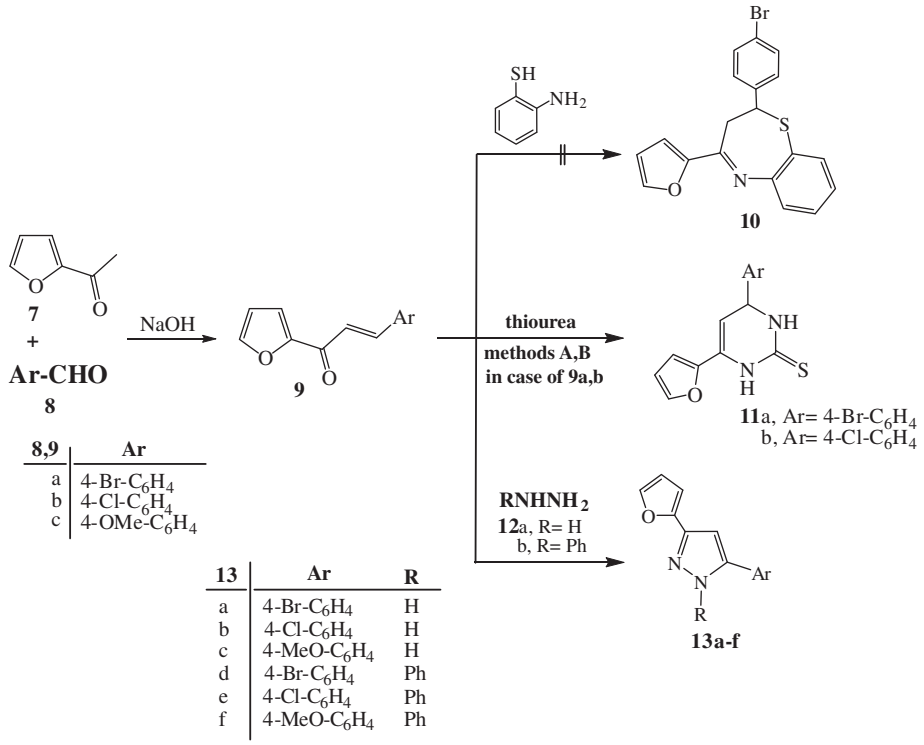
Based furan ring chalcones **9a–c** were easily obtained and in good yields according to the procedure in the literature (El-Shehry et al., 2008). These chalcones reacted with hydrazine and phenyl hydrazine to give the corresponding pyrazoles **13a–f**. Further condensation of **9a**,**b** with thiourea led to the formation of the corresponding thienopyrimidine products (**11a**,**b**). The structures of **9**, **11** and **13** were unambiguously identified by combination of their various spectroscopic data. Reaction of **9a–c** with thiophenol either by conventional heating method or under *MW* irradiation, under the same experimental conditions as for **11** and **13**, did not give the expected thiazepine **10**. However, the latter compound is formed in the mixture after refluxing even up to 15 h, as inferred from the corresponding NMR spectra (see Scheme 3).

The 2-furancarboxaldehydes (**1a–f**) condense with the containing active methylene group, 1,3-thiazolin-2,5-dione, following thermal classical method and *MW* irradiation, to give the corresponding condensates **14a–f**. Both methods gave moderate yields with the advantage of *MW* method of being cleaner reaction. The structures of **14a–f** are determined on the basis of their spectroscopic data and in particular NMR. Thus, ^{1}H NMR spectra of **14a–f** exhibited a singlet, integrated for one proton at δ 7.39–7.62 range due to the resonance of a methane proton in the structure. In the ^{13}C NMR, the carbon of this group appears at around δ 149 as verified from HETCOR experiment with the exception of **14e** and **14f** which appears at δ 137.95 and δ 132.07, respectively. The latter spectrum also revealed a signal at δ_C 161.22–164.80 attributed



6	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

Scheme 2



8,9	Ar
a	4-Br-C_6H_4
b	4-Cl-C_6H_4
c	4-OMe-C_6H_4

13	Ar	R
a	4-Br-C_6H_4	H
b	4-Cl-C_6H_4	H
c	4-MeO-C_6H_4	H
d	4-Br-C_6H_4	Ph
e	4-Cl-C_6H_4	Ph
f	4-MeO-C_6H_4	Ph

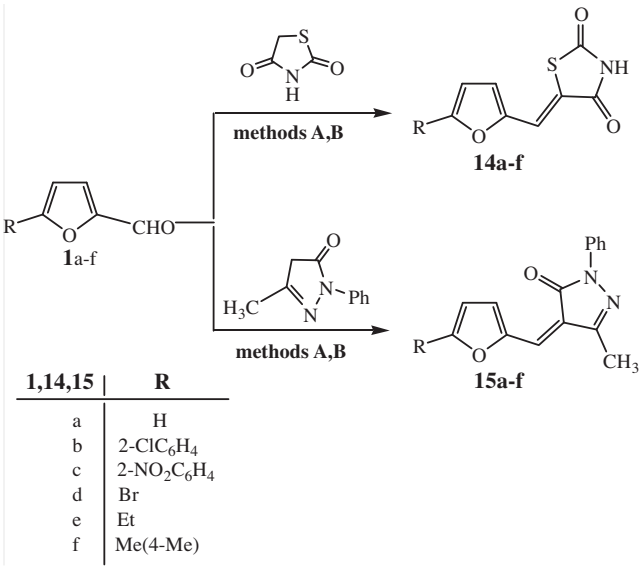
Scheme 3

Table 2 Yields and reaction conditions used for the synthesis of **14** and **15**.

Compd. No.	Classical method (*A*)	MW method (*B*) (300 W)	Reaction time (min)	
	Yields (%)	Yields (%)	A	B
14a	70	24	15	2
14b	31	–	15	–
14c	24	–	15	–
14d	74	75	15	1
14e	18	64	15	1
14f	61	75	15	7
15a	55	16	15	4
15b	46	13	15	2
15c	18	–	15	–
15d	39	20	15	7
15e	19	12	15	9
15f	45	15	15	12

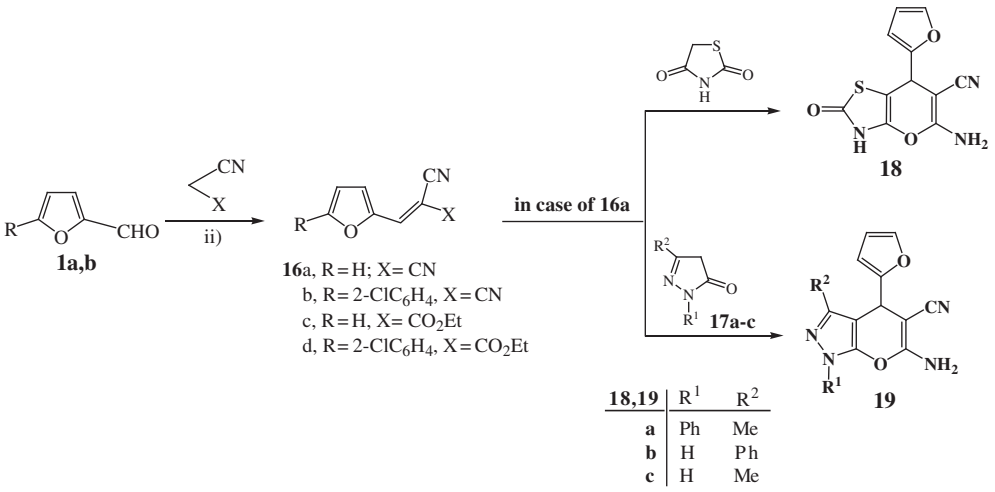
to the amidic carbonyl carbon in **14a**–**f**. Similarly, compound 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)one reacted with **1a**–**f** under the same experimental conditions above utilizing the classical method to give **15a**–**f**. The yields and reaction conditions used for the synthesis of **14a**–**f** and **15a**–**f** are depicted in Table 2 (see Scheme 4).

Compounds **1a**,**b** react with ethyl cyanoacetate and malononitrile utilizing conventional method to give the corresponding furilydenes **16a**–**d** in excellent yields. The structures of these products were confirmed on the basis of their spectroscopic data. Furilydenes **16a**–**d** are found to react smoothly under microwave irradiation as exemplified by **16a**, with the active methylene compounds, 1,3-thiazolidin-2,5-dione and **17a**–**c** to give the corresponding amino-thiazole and pyrazole derivatives **18** and **19a**–**c**, in moderate to good yields and in a very pure cases. IR, NMR and Mass spectral data of **16**, **18** and **19** were in complete consistent with their structures. Thus, the IR spectra of **18** and **19** showed the presence of amino and cyano groups absorption bands. The EIMS spectrum of **18** showed a peak at *m*/*z* 261 corresponding to the molecular ion. The singlet at δ 4–5 in the ^{1}H NMR spectrum is due to the resonance of the proton at position 4 in pyran



1,14,15	R
a	H
b	2-ClC_6H_4
c	2-$NO_2C_6H_4$
d	Br
e	Et
f	Me(4-Me)

Scheme 4



Scheme 5

Table 3 Antimicrobial activity test compounds.

Test organisms compound	Zone of inhibition in diameter (mm)			
	Pseudomonas aeruginosa	*Escherichia coli*	*Staphylococcus aureus*	*Bacillus subtilis*
4b	0.0	0.0	0.0	0.0
4c	0.0	0.0	0.0	0.0
9d	0.0	0.0	5	2
9e	0.0	0.0	2	3
10d	20	0.0	20	10
10e	0.0	0.0	16	10
16a	0.0	0.0	0.0	2
16b	0.0	0.0	0.0	5
16c	0.0	0.0	0.0	0.0
DMSO	0.0	0.0	0.0	0.0
Netilmicin	20	17	17	15

ring. Complete NMR data of these amino-thiazole and pyrazole derivatives are depicted in the experimental section (see Scheme 5).

3.2. Antibacterial studies

Compounds **4b**, **4c**, **9d**, **9e**, **10d**, **10e**, **16a**, **16b**, and **16c** were tested in vitro against *Pseudomonas aeruginosa, Escherichia coli*, as Gram-negative bacteria and *Staphylococcus aureus*, *Bacillus* subtilis, as Gram-positive bacteria.

The disc agar diffusion method (Mdrray and Baran, 2003) was applied in this study. The test compounds were dissolved in DMSO at concentration of 5 mg/ml, 5000 μg were aseptically transferred onto sterile discs of Whatman filter paper (5 mm diameter). The discs were then placed onto the surface of the inoculated plates previously prepared and then incubated at 37 °C for 22 h. The results of the study have been used antibiotic disk Netilmicin 10 μg to compare the vital influence of vehicles on each of the bacteria.

The inhibition zones were recorded in mm (Table 3). The diameters less than 5 mm indicated no effect. (A disc impregnate with 5000 μg of DMSO was used as control for each microorganism).

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References

Abid, M., Azam, M.A., 2006. Bioorg. Med. Chem. Lett. 16, 2812–2816.
Al-AlShaikh, M.A., Al.-Hazimi, Al-Marhoon, Hassan, M.A., 2006. J. Saudi Chem. Soc. 10 (3), 527–538.
Al-Mutairi, T.M., Al-Hazimi, Hassan M.A., El-Baih, F.E.M., 2009. J. Saudi Chem. Soc. 13 (2), 199–207.
Carron, M., Jullien, A., Julia, Th., Garczynska, C., 1963. Ann. Pharm. Fr. 21, 287.
Cohen, S.M., Erturk, E., Bryan, G.T., 1996. J. Natl. Cancer Inst. 57 (2), 277.

El-Baih, F.E.M., Al-Rasheed, H.H., Al-Hazimi, Hassan M.A., 2006. J. Saudi Chem. Soc. 9 (3), 575–596.
El-Obeid, H.A., Elnima, E.L., Al-Badr, A.A., 1985. Pharm. Res. 42.
El-Shehry, H., Al-Hazimi, Hassan M.A., Korraa, M.M.S., 2008. J. Saudi Chem. Soc. 12 (3), 353–366.
Elsom, I.S., Hawkins, D.R., 1978. J. Labelled Comp. 14, 799.
Furlanetto, M., Santosand, M., Tavares, L.C., 2001. Braz. J. Pharm. Sci. 37, 62.
Lacova, M., Gasparova, R., Loos, D., Liptay, T., Pronayova, N., 2000. Molecules 5, 167.
Leonard, F., Andremont, A., Tancrede, C., 1985. J. Appl. Bacteriol. 58 (6), 545.
Mdrray, P.R., Baran, E.Jo., 2003. Clin. Microbiol.
Masunary, A., Tavares, L.C., 2007. Bioorg. Med. Chem. 15, 4229.
Rabarova, E., Kois, P., Lacova, M., Krutosikova, A., 2004. ARKIVOK (i), 110–122.
Rando, D.C., Sato, D.N., Siqueira, L., Malvezzi, A., Leite, C., do_Amaral, A., Ferreira, E.L., Tavares, L.C., 2002. Bioorg. Med. Chem. 10, 557.
Shigetaka, Y., Akira, T., G.-Nan, Y., H-Chein, H., 1970. Yakugaku Zasshi 90, 1150 (CA, 73: 120433x (1970)).
Shindhar, D.R., Sastry, C.V.R., Vaidya, N.K., 1980. J. Indian Chem. Soc. 57, 1118 (CA, 94: 174765j (1981)).
Tabakovic, R., Tabakovic, I., 1999. Reactive Funct. Polym. 39, 263–268.
Thabaut, A., Durosoir, J. L., 1978. Gazette Med., France 85, 4516.
Vanhoof, R., Coignau, H., Stas, G., Butzler, J.P., 1981. Acta Clin. Belg. 36 (3), 126.