

# SYNTHESIS AND CHARACTERIZATION OF NOVEL PYRIMIDINE DERIVATIVES FROM 2,3-FURANDIONES

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**Abstract:** Various novel pyrimidine-2(*1H*)-one and pyrimidine-2(*1H*)-thione derivatives **3a-m** have been synthesized efficiently in good yields by the treatment of 4-*p*-methylbenzoyl-5-*p*-methylphenyl-2,3-furandione (**1a**) and 4-(3,4-dimethoxybenzoyl)-5-(3,4-dimethoxyphenyl)-2,3-furandione (**1b**) with some ureas and thioureas **2**. Structures of these compounds **3** were established on the basis of elemental analysis, IR, <sup>1</sup>H- and <sup>13</sup>C-NMR spectral studies.

**Keywords:** 2,3-Furandione, pyrimidine-2(*1H*)-one, pyrimidine-2(*1H*)-thione, nucleophilic cycloaddition.

## Introduction

Pyrimidine bases are an integral part of nucleic acids and natural products. They serve as building blocks for numerous pharmaceuticals and occupy a unique place in heterocyclic and medicinal chemistry<sup>1</sup>. These compounds display anticonvulsant, anti-inflammatory, antibacterial, antimycotic, antifungal, antiviral, insecticidal and mitocidal activities<sup>2-8</sup>. In addition fused pyrimidines are selective inhibitors for multidrug resistance (MDR)<sup>9</sup>. Folate metabolism has long been recognized as an attractive target for cancer chemotherapy because of indispensable role of fused pyrimidine antifolates as antitumor agents<sup>10</sup>.

There are published reports about synthesis of some *1H*-pyrimidine derivatives from 2,3-furandiones<sup>11-13</sup>. Also conformational analysis and quantum chemical calculations were carried out by means of MMP2, CNDO, MNDO and AM1 approximation methods for the series of compounds being functionalised *1H*-pyrimidines<sup>14-16</sup>. In this study, the reactions of 4-*p*-methylbenzoyl-5-*p*-methylphenyl-2,3-furandione (**1a**) and 4-(3,4-dimethoxybenzoyl)-5-(3,4-dimethoxyphenyl)-2,3-furandione (**1b**) with some monosubstituted ureas and thioureas **2** were investigated. The reactions afforded the *1H*-pyrimidine derivatives **3a-m** which are potential drug compounds and all the compounds synthesized are original to this study.

## Scheme-1

## Experimental

Melting points were performed on an Electrothermal 9200 apparatus: They were uncorrected. The IR spectra measured on a Jasco Plus Model 460 FT-IR spectrometer, as KBr pellets. <sup>1</sup>H- and <sup>13</sup>C-NMR spectra were recorded on a Bruker instruments with CDCl<sub>3</sub> solvents at 300 and 75 MHz, respectively. Elemental analysis were carried out using LECO

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932 CHNS-O analyzer. All experiments followed by TLC using DC Alufolien 60 F254 Merck and Camag TLC lamp (254/366 nm). Solvents and other chemical reagents were purchased from Merck, Fluka, Sigma and Aldrich. The compounds **1** were prepared according to published method<sup>17</sup>.

#### Synthesis of 1*H*-Pyrimidines **3a-m**.

##### General Procedure.

Equimolar amounts of 2,3-furandiones and the corresponding urea or thiourea in benzene (30 mL) were heated, under reflux, for 1-6 h. The reaction mixture was concentrated under vacuum. The oily residue was treated with diethyl ether for 2-5 h at room temperature. The obtained solid product was filtered off and recrystallized from proper solvents.

##### 1-Methyl-5-(4-methylbenzoyl)-4-(4-methylphenyl)pyrimidine-2(*1H*)-one (**3a**).

From 0.50 g (1.63 mmol) **1a** and 0.12 g methylurea, 0.31 g (60%) **3a** was obtained after 5 h reaction time. Mp: 198 °C (1-butanol). IR (KBr, cm<sup>-1</sup>):  $\nu$  = 3064-2862 (aromatic and aliphatic C-H stretching), 1667, 1656 (C=O groups), 1604-1480 (C=C and C=N aromatic rings). <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  = 8.02 (s, 1H, C-6), 7.54-6.97 (four d, 8H, aromatic), 3.63 (s, 3H, N-CH<sub>3</sub>), 2.30 (s, 3H, Ar-CH<sub>3</sub>), 2.22 (s, 3H, Ar-CH<sub>3</sub>). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  = 192.02 (Ar-C=O), 172.75, 155.52, 151.42 (C-4, C-6 and C-2 atoms of pyrimidine ring, respectively), 144.39-128.94 (aromatic carbons), 116.95 (C-5), 39.03 (N-CH<sub>3</sub>), 21.66, 21.41 (2xAr-CH<sub>3</sub>). Elemental analysis: Calculated for C<sub>20</sub>H<sub>18</sub>N<sub>2</sub>O<sub>2</sub> (318.14): C, 75.45; H, 5.70; N, 8.80. Found: C, 75.56; H, 5.73; N, 8.76.

##### 1-Ethyl-5-(4-methylbenzoyl)-4-(4-methylphenyl)pyrimidine-2(*1H*)-one (**3b**).

From 0.50 g **1a** and 0.14 g ethylurea, 0.29 g (51%) **3b** was obtained after 6 h reaction time. Mp: 156 °C (ethanol). IR (KBr, cm<sup>-1</sup>):  $\nu$  = 3092-2878 (aromatic and aliphatic C-H stretching), 1661 (broad, C=O groups), 1605-1480 (C=C and C=N aromatic rings). <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  = 7.99 (s, 1H, C-6), 7.54-6.97 (four d, 8H, aromatic), 4.07-4.00 (q, 2H, N-CH<sub>2</sub>), 2.29 (s, 3H, Ar-CH<sub>3</sub>), 2.22 (s, 3H, Ar-CH<sub>3</sub>), 1.46-1.41 (t, 3H, aliphatic CH<sub>3</sub>-CH<sub>2</sub>). Elemental analysis: Calculated for C<sub>21</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub> (332.15): C, 75.88; H, 6.06; N, 8.43. Found: C, 76.16; H, 6.34; N, 8.63.

##### 1-Allyl-5-(4-methylbenzoyl)-4-(4-methylphenyl)pyrimidine-2(*1H*)-one (**3c**).

From 0.50 g **1a** and 0.17 g allylurea, 0.21 g (38%) **3c** was obtained after 4 h reaction time. Mp: 149 °C (2-propanol). IR (KBr, cm<sup>-1</sup>):  $\nu$  = 3087-2857 (aromatic and aliphatic C-H stretching), 1656 (broad, C=O groups), 1604-1481 (C=C and C=N aromatic rings). <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  = 7.96 (s, 1H, C-6), 7.54-6.97 (four d, 8H, aromatic), 6.06-5.92 (m, 1H, =CH-), 5.37-5.31 (t, 2H, =CH<sub>2</sub>), 4.60-4.58 (d, 2H, N-CH<sub>2</sub>), 2.29 (s, 3H, Ar-CH<sub>3</sub>), 2.22 (s, 3H, Ar-CH<sub>3</sub>). Elemental analysis: Calculated for C<sub>22</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub> (344.41): C, 76.72; H, 5.85; N, 8.13. Found: C, 76.91; H, 5.76; N, 8.14.

##### 1-Butyl-5-(4-methylbenzoyl)-4-(4-methylphenyl)pyrimidine-2(*1H*)-one (**3d**).

From 0.50 g **1a** and 0.19 g butylurea, 0.30 g (51%) **3d** was obtained after 4 h reaction time. Mp: 153 °C (ethanol). IR (KBr, cm<sup>-1</sup>):  $\nu$  = 3053-2872 (aromatic and aliphatic C-H stretching), 1653 (broad, C=O groups), 1615-1482 (C=C and C=N aromatic rings). <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  = 7.96 (s, 1H, C-6), 7.58-7.00 (four d, 8H, aromatic), 4.02-3.97 (t, 2H, N-CH<sub>2</sub>), 2.33 (s, 3H, Ar-CH<sub>3</sub>), 2.25 (s, 3H, Ar-CH<sub>3</sub>), 1.89-1.74 (m, 2H, CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>), 1.48-1.35 (m, 2H, CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>3</sub>), 1.00-0.95 (t, 3H, CH<sub>2</sub>-CH<sub>3</sub>). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  = 192.10 (Ar-C=O), 172.47, 154.97, 150.64 (C-4, C-6 and C-2 atoms of pyrimidine ring, respectively), 144.39-128.93 (aromatic carbons), 116.81 (C-5), 51.55 (N-CH<sub>2</sub>), 30.87 (CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>), 21.66 (Ar-CH<sub>3</sub>), 21.41 (Ar-CH<sub>3</sub>), 19.86 (CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>3</sub>), 13.65 (CH<sub>2</sub>-CH<sub>3</sub>). Elemental analysis: Calculated for C<sub>23</sub>H<sub>24</sub>N<sub>2</sub>O<sub>2</sub> (360.18): C, 76.64; H, 6.71; N, 7.77. Found: C, 76.61; H, 6.88; N, 7.86.

**1-Benzyl-5-(4-methylbenzoyl)-4-(4-methylphenyl)pyrimidine-2(*IH*)-one (3e).**

From 0.50 g **1a** and 0.25 g benzylurea, 0.37 g (58%) **3e** was obtained after 3 h reaction time. Mp: 174 °C (2-propanol). IR (KBr,  $\text{cm}^{-1}$ ):  $\nu = 3066\text{-}2857$  (aromatic and aliphatic C-H stretching), 1670, 1658 (C=O groups), 1618-1435 (C=C and C=N aromatic rings).  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ , ppm):  $\delta = 7.97$  (s, 1H, C-6), 7.49-6.95 (m, 13H, aromatic), 5.14 (s, 2H, N-CH<sub>2</sub>), 2.26 (s, 3H, Ar-CH<sub>3</sub>), 2.20 (s, 3H, Ar-CH<sub>3</sub>). Elemental analysis: Calculated for C<sub>26</sub>H<sub>22</sub>N<sub>2</sub>O<sub>2</sub> (394.17): C, 79.16; H, 5.62; N, 7.10. Found: C, 78.73; H, 5.69; N, 7.02.

**1-Methyl-5-(3,4-dimethoxybenzoyl)-4-(3,4-dimethoxyphenyl)pyrimidine-2(*IH*)-one (3f).**

From 0.50 g **1b** and 0.10 g methylurea, 0.38 g (74%) **3f** was obtained after 5.5 h reaction time. Mp: 236 °C (1-butanol). IR (KBr,  $\text{cm}^{-1}$ ):  $\nu = 3064\text{-}2842$  (aromatic and aliphatic C-H stretching), 1668, 1643 s (C=O groups), 1625-1493 (C=C and C=N aromatic rings), 1273 (broad, C-O-C).  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ , ppm):  $\delta = 8.48$  (s, 1H, C-6), 7.45-6.87 (m, 6H, aromatic), 3.88 (s, 3H, N-CH<sub>3</sub>), 3.74-3.51 (four s, 12H, Ar-OCH<sub>3</sub>). Elemental analysis: Calculated for C<sub>22</sub>H<sub>22</sub>N<sub>2</sub>O<sub>6</sub> (410.42): C, 64.38; H, 5.40; N, 6.83. Found: C, 64.15; H, 5.46; N, 6.86.

**1-Allyl-5-(3,4-dimethoxybenzoyl)-4-(3,4-dimethoxyphenyl)pyrimidine-2(*IH*)-one (3g).**

From 0.50 g **1b** and 0.13 g allylurea, 0.43 g (79%) **3g** was obtained after 6 h reaction time. Mp: 229 °C (1-butanol). IR (KBr,  $\text{cm}^{-1}$ ):  $\nu = 3063\text{-}2840$  (aromatic and aliphatic C-H stretching), 1672, 1644 (C=O groups), 1623-1486 (C=C and C=N aromatic rings), 1279, 1267 (C-O-C).  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ , ppm):  $\delta = 7.95$  (s, 1H, C-6), 7.31-6.66 (m, 6H, aromatic), 6.07-6.00 (m, 1H, =CH-), 5.42-5.37 (t, 2H, =CH<sub>2</sub>), 4.65-4.63 (d, 2H, N-CH<sub>2</sub>), 3.98-3.80 (four s, 12H, Ar-OCH<sub>3</sub>).  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ , ppm):  $\delta = 191.18$  (Ar-C=O), 171.33, 154.95, 153.70 (C-4, C-6 and C-2 atoms of pyrimidine ring, respectively), 149.37-110.00 (aromatic and olefinic carbons), 121.02 (C-5), 56.06-55.86 (4xAr-OCH<sub>3</sub>), 52.78 (N-CH<sub>2</sub>). Elemental analysis: Calculated for C<sub>24</sub>H<sub>24</sub>N<sub>2</sub>O<sub>6</sub> (436.46): C, 66.04; H, 5.54; N, 6.42. Found: C, 65.81; H, 5.86; N, 6.25.

**1-Butyl-5-(3,4-dimethoxybenzoyl)-4-(3,4-dimethoxyphenyl)pyrimidine-2(*IH*)-one (3h).**

From 0.50 g **1b** and 0.15 g butylurea, 0.33 g (58%) **3h** was obtained after 5 h reaction time. Mp: 201 °C (ethanol). IR (KBr,  $\text{cm}^{-1}$ ):  $\nu = 3076\text{-}2837$  (aromatic and aliphatic C-H stretching), 1671, 1643 (broad, C=O groups), 1623-1487 (C=C and C=N aromatic rings), 1266 (broad, C-O-C).  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ , ppm):  $\delta = 8.47$  (s, 1H, C-6), 7.45-6.87 (m, 6H, aromatic), 3.98-3.91 (t, 2H, N-CH<sub>2</sub>), 3.81-3.64 (s, 12H, Ar-OCH<sub>3</sub>), 1.72-1.65 (m, 2H, CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>), 1.36-1.27 (m, 2H, CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>3</sub>), 0.92-0.88 (t, 3H, CH<sub>2</sub>-CH<sub>3</sub>). Elemental analysis: Calculated for C<sub>25</sub>H<sub>28</sub>N<sub>2</sub>O<sub>6</sub> (452.50): C, 66.36; H, 6.24; N, 6.19. Found: C, 66.24; H, 6.32; N, 6.45.

**1-Benzyl-5-(3,4-dimethoxybenzoyl)-4-(3,4-dimethoxyphenyl)pyrimidine-2(*IH*)-one (3i).**

From 0.50 g **1b** and 0.12 g benzylurea, 0.28 g (76%) **3i** was obtained after 3.5 h reaction time. Mp: 233 °C (1-propanol). IR (KBr,  $\text{cm}^{-1}$ ):  $\nu = 3061\text{-}2837$  (aromatic and aliphatic C-H stretching), 1677, 1644 (C=O groups), 1622-1437 (C=C and C=N aromatic rings), 1274, 1264 (C-O-C).  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ , ppm):  $\delta = 7.92$  (s, 1H, C-6), 7.40-6.60 (m, 11H, aromatic), 5.20 (s, 2H, N-CH<sub>2</sub>), 3.93-3.81 (four s, 12H, Ar-OCH<sub>3</sub>).  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ , ppm):  $\delta = 191.05$  (Ar-C=O), 171.29, 155.23, 153.68 (C-4, C-6 and C-2 atoms of pyrimidine ring, respectively), 151.86-109.98 (aromatic carbons), 117.13 (C-5), 56.06-55.85 (4xAr-OCH<sub>3</sub>), 53.79 (N-CH<sub>2</sub>). Elemental analysis: Calculated for C<sub>28</sub>H<sub>26</sub>N<sub>2</sub>O<sub>6</sub> (486.50): C, 69.12; H, 5.39; N, 5.76. Found: C, 68.78; H, 5.57; N, 6.04.

**1-Ethyl-5-(4-methylbenzoyl)-4-(4-methylphenyl)pyrimidine-2(*IH*)-thione (3j).**

From 0.50 g **1a** and 0.17 g ethylthiourea, 0.34 g (60%) **3j** was obtained after 4 h reaction time. Mp: 195 °C (ethanol). IR (KBr,  $\text{cm}^{-1}$ ):  $\nu = 3060\text{-}2857$  (aromatic and aliphatic C-H stretching), 1654 (C=O), 1607-1480 (C=C and C=N aromatic

rings), 1183 (C=S). <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, ppm): δ = 8.12 (s, 1H, C-6), 7.53-6.96 (four d, 8H, aromatic), 4.55-4.48 (q, 2H, N-CH<sub>2</sub>), 2.29 (s, 3H, Ar-CH<sub>3</sub>), 2.21 (s, 3H, Ar-CH<sub>3</sub>), 1.54-1.50 (t, 3H, aliphatic CH<sub>2</sub>-CH<sub>2</sub>). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>, ppm): δ = 191.82 (Ar-C=O), 181.20 (C=S), 164.58, 149.24 (C-4 and C-6 atoms of pyrimidine ring, respectively), 144.85-129.09 (aromatic carbons), 121.01 (C-5), 52.76 (N-CH<sub>2</sub>), 21.72, 21.47 (2xAr-CH<sub>3</sub>), 13.65 (CH<sub>2</sub>-CH<sub>2</sub>). Elemental analysis: Calculated for C<sub>21</sub>H<sub>20</sub>N<sub>2</sub>OS (348.13): C, 72.38; H, 5.79; N, 8.04; S, 9.20. Found: C, 72.22; H, 5.69; N, 7.89; S, 9.10.

#### 1-Phenyl-5-(4-methylbenzoyl)-4-(4-methylphenyl)pyrimidine-2(1H)-one (3k).

From 0.50 g **1a** and 0.25g phenylthiourea, 0.21 g (33%) **3k** was obtained after 1 h reaction time. Mp: 249 °C (methanol). IR (KBr, cm<sup>-1</sup>): ν = 3031-2857 (aromatic and aliphatic C-H stretching), 1657 (C=O), 1604-1463 (C=C and C=N aromatic rings), 1178 (C=S). <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, ppm): δ = 8.09 (s, 1H, C-6), 7.66-7.06 (m, 13H, aromatic), 2.34, 2.24 (two s, 6H, Ar-CH<sub>3</sub>). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>, ppm): δ = 191.61 (Ar-C=O), 182.50 (C=S), 165.63, 149.99 (C-4 and C-6 atoms of pyrimidine ring, respectively), 145.02-126.48 (aromatic carbons), 120.33 (C-5), 21.76, 21.58 (2xAr-CH<sub>3</sub>). Elemental analysis: Calculated for C<sub>25</sub>H<sub>20</sub>N<sub>2</sub>OS (396.13): C, 75.73; H, 5.08; N, 7.07; S, 8.09. Found: C, 75.97; H, 5.37; N, 6.94; S, 8.30.

#### 1-Ethyl-5-(3,4-dimethoxybenzoyl)-4-(3,4-dimethoxyphenyl)pyrimidine-2(1H)-thione (3l).

From 0.50 g **1b** and 0.13 g ethylthiourea, 0.40 g (72%) **3l** was obtained after 6 h reaction time. Mp: 138 °C, (ethanol). IR (KBr, cm<sup>-1</sup>): ν = 3067-2836 (aromatic and aliphatic C-H stretching), 1648 (C=O), 1610-1483 (C=C and C=N aromatic rings), 1264 (C-O-C), 1179 (C=S). <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, ppm): δ = 8.06 (s, 1H, C-6), 7.36-6.65 (m, 6H, aromatic), 4.59-4.50 (q, 2H, N-CH<sub>2</sub>), 3.89-3.78 (four s, 12H, Ar-OCH<sub>3</sub>), 1.63-1.56 (t, 3H, aliphatic CH<sub>2</sub>-CH<sub>2</sub>). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>, ppm): δ = 190.90 (Ar-C=O), 180.96 (C=S), 163.53, 153.99 (C-4 and C-6 atoms of pyrimidine ring, respectively), 152.17-110.04 (aromatic carbons), 56.10-55.89 (Ar-OCH<sub>3</sub>), 52.71 (N-CH<sub>2</sub>), 13.64 (CH<sub>2</sub>-CH<sub>2</sub>). Elemental analysis: Calculated for C<sub>23</sub>H<sub>24</sub>N<sub>2</sub>O<sub>5</sub>S (440.51): C, 62.71; H, 5.49; N, 6.36; S, 7.28. Found: C, 63.03; H, 5.71; N, 6.61; S, 7.06.

#### 1-Allyl-5-(3,4-dimethoxybenzoyl)-4-(3,4-dimethoxyphenyl)pyrimidine-2(1H)-thione (3m).

From 0.50 g **1b** and 0.15 g allylthiourea, 0.46 g (81%) **3m** was obtained after 4.5 h reaction time. Mp: 190 °C (2-propanol). IR (KBr, cm<sup>-1</sup>): ν = 3063-2834 (aromatic and aliphatic C-H stretching), 1655 (C=O), 1610-1479 (C=C and C=N aromatic rings and allyl group), 1267, 1248 (C-O-C), 1176 (C=S). <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, ppm): δ = 8.60 (s, 1H, C-6), 7.71-6.82 (m, 6H, aromatic), 6.14-6.04 (m, 1H, =CH-), 5.51-5.29 (t, 2H, =CH<sub>2</sub>), 5.16-5.10 (d, 2H, N-CH<sub>2</sub>), 3.82-3.63 (four s, 12H, Ar-OCH<sub>3</sub>). Elemental analysis: Calculated for C<sub>24</sub>H<sub>24</sub>N<sub>2</sub>O<sub>5</sub>S (452.52): C, 63.70; H, 5.35; N, 6.19; S, 7.09. Found: C, 63.38; H, 5.51; N, 5.90; S, 6.77.

## Results and Discussion

The reactions of 2,3-furandiones (**1a,b**) with the corresponding ureas or thioureas proceed smoothly in benzene under reflux for 1-6 h to produce 1H-pyrimidine derivatives **3a-m** in 33-81% yields (see Scheme-1).

The structure of new compounds **3a-m** were deduced from their elemental analysis, <sup>1</sup>H- and <sup>13</sup>C-NMR spectra. The <sup>1</sup>H-NMR spectrum of **3a** exhibited one singlet readily recognized as arising from C-H proton of C<sub>6</sub> atom (δ 8.02 ppm) at pyrimidine ring and four doublets for the other aromatic protons (δ 7.54-6.97 ppm). The signals of the methyl groups observed as a singlet at δ 3.63, 2.30 and 2.22 ppm. The proton decoupled <sup>13</sup>C-NMR spectrum of **3a** showed 16 distinct resonances. The <sup>13</sup>C-NMR spectrum of **3a** exhibited aroyl carbonyl resonance at δ = 192.02 ppm. The chemical shift for C<sub>4</sub>, C<sub>6</sub>, C<sub>2</sub> at pyrimidine ring appeared at δ 172.75, 155.52 and 151.42 ppm, respectively. Also, methyl groups observed

at  $\delta$  39.03 ppm for N-CH<sub>3</sub> and 21.66, 21.41 ppm for Ar-CH<sub>3</sub>. In the IR spectrum of compound 3a, the (C=O) absorption bands observed at 1667 and 1656 cm<sup>-1</sup>. The spectral data of other synthesized compounds are in good agreement with the proposed structure.

Previously, the mechanism of formation of 1*H*-pyrimidine derivatives from the 2,3-furandione with the ureas or semicarbazones was reported<sup>12-15</sup>. The reaction mechanism is similar to published methods. It is outlined in Scheme-2. The structure of those previously studied compounds had already been determined by X-ray examination<sup>11,18-21</sup>.

#### Scheme-2

The formation of compounds 3 may be initiated by Micheal-type addition, via nucleophilic attack at C-5 of the furan ring in 1 by the -NH<sub>2</sub> group of urea or thiourea as the nucleophile and during this interaction ring opened to give 2-oxo-3-butenic acid derivated intermediate forms. The following steps progressed closing ring and subsequent elimination of CO<sub>2</sub> and H<sub>2</sub>O to give 1*H*-pyrimidine derivatives 3.

Nucleophilicity of -NH<sub>2</sub> group at thiourea is higher than corresponding urea. So, The yields of pyrimidine-2(1*H*)-thiones are higher except for 3k, because of steric hindrance and resonance effect of phenyl group at phenylthiourea.

In conclusion, the compounds synthesized are significant preliminary compounds due to the fact that original 1*H*-pyrimidine derivatives include 4-methylphenyl or 3,4-dimethoxyphenyl groups in their structures. We think about that these compounds may be important from a medicinal point of view as well as their widespread biological significance.

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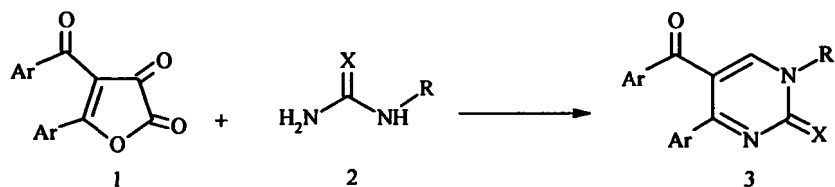
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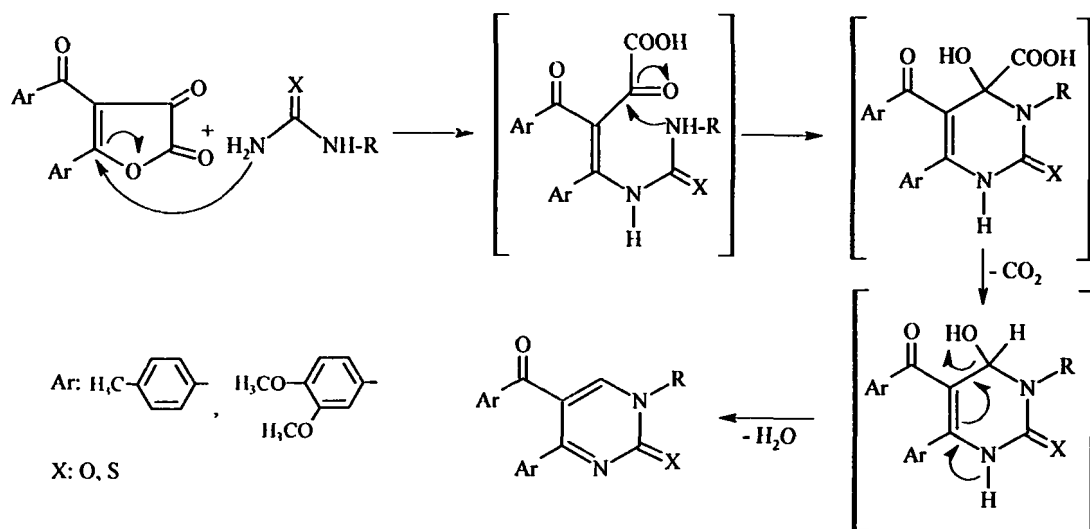
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## Schemes and Captions



3	Ar	R	X	m.p. (°C)	Yield (%)
a		-CH <sub>3</sub>	O	198	60
b		-C <sub>2</sub> H <sub>5</sub>	O	156	51
c		-CH <sub>2</sub> -CH=CH <sub>2</sub>	O	149	38
d		-C <sub>4</sub> H <sub>9</sub>	O	153	51
e		-CH <sub>2</sub> -Ph	O	174	58
f		-CH <sub>3</sub>	O	236	74
g		-CH <sub>2</sub> -CH=CH <sub>2</sub>	O	229	79
h		-C <sub>4</sub> H <sub>9</sub>	O	201	58
i		-CH <sub>2</sub> -Ph	O	233	76
j		-C <sub>2</sub> H <sub>5</sub>	S	195	60
k		-Ph	S	249	33
l		-C <sub>2</sub> H <sub>5</sub>	S	138	72
m		-CH <sub>2</sub> -CH=CH <sub>2</sub>	S	190	81

Scheme-1



Scheme-2