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# Reactions of 5-(4-methoxy-3-methylphenyl)-2(3*H*)-furanone with some electrophilic and nucleophilic reagents

Mohamed Helmy Abd El-hamied Soliman and Sahar Said Ahmed El-Sakka *

*Chemistry Department, Faculty of Science, Suez University, Suez, 43527, Egypt*

* *Corresponding author at: Chemistry Department, Faculty of Science, Suez University, Suez, 43527, Egypt.*
*Tel.: +20.100.6054033. Fax: +20.62.3707040. E-mail address: sahar.alsakka@suezuniv.edu.eg (S.S.A. El-Sakka).*

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ABSTRACT

5-(4-Methoxy-3-methylphenyl)-2(3*H*)-furanone was prepared and reacted with some nucleophilic and electrophilic reagents. The condensation of furanone with aromatic aldehydes or phthalic anhydride yielded the corresponding 3-arylidenefuranone derivatives and phthalide, respectively. While the treatment of furanone with amines in refluxing ethanol led to the formation of amides. The reaction of the amides with thionyl chloride afforded the corresponding isothiazolones. The benzimidazole derivative was prepared via the reaction of the 2(3*H*)-furanone with *o*-phenylenediamine in boiling ethanol. However, hydrazine hydrate affected ring opening of furanone to give the corresponding acid hydrazide**,** which underwent in situ cyclization into the corresponding pyridazinone. The base catalyzed ethanolysis of furanone afforded the corresponding ethyl ester.

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## 1. Introduction

The furanone ring system has a wide range of interesting biological activities in addition of being recognized as a component of natural products. Compounds incorporating such heterocycles in their structure have been found to display broad spectrum of biological activities including anti-inflammatory [1-3], cardiotonic activity [4], analgesic [5], anticancer [6], anti-convulsant [7], anti-microbial [8] and antiviral activeties [9].

It is well known that the hydrogen atoms of the $CH_2$ group in 2(3*H*)-furanone are reactive and by virtue of this reactivity, the substance so readily undergoes condensation with aldehydes and ketones [10]. Besides their reactivity towards aldehydes and ketones, the ester moiety of these compounds is a favorable unit for nucleophilic attack that give acyclic products which on recyclization can afford other heterocyclic systems [9,11,12].

In continuation of our previous studies on the application of keto acids in the synthesis of different heterocyclic compounds [13,14], the present study describes the synthesis of 5-(4-methoxy-3-methylphenyl)-2(3*H*)-furanone (**2**) (via the lactonization of the 4-(4-methoxy-3-methylphenyl)-4-oxobutanoic acid [15] and its reactivity towards nucleophilic and electrophilic reagents. Elemental analysis, IR, $^1$H NMR, $^{13}$C NMR and MS spectral data were obtained to determine the structure of the new synthesized compounds.

## 2. Experimental

### 2.1. Instrumentation

All melting points reported are uncorrected and determined by the open capillary tube method on a Buchi 510 melting point apparatus. Elemental analyses were performed on a flash EA-1112 instrument. $^1$H NMR spectra were measured on Bruker (300 MHz) instrument and TMS was used as internal standard. IR spectra were recorded on a Perking Elmer 1430 ratio recording infrared spectrophotometer with CDS data station using KBr Wafer technique. Mass spectra were measured on a GC-MSQP 1000EX Shimadzu at Micro-Analytical Laboratory, Cairo University, Cairo, Egypt.

### 2.2. Synthesis

#### *2.2.1. Synthesis of 5-[4-methoxy-3-methylphenyl]-2(3H)-furanone (2)*

A mixture of 4-[4-methoxy-3-methylphenyl]-4-oxobutanoic acid (**1**) (0.01 mole) and acetic anhydride (3 mL) in


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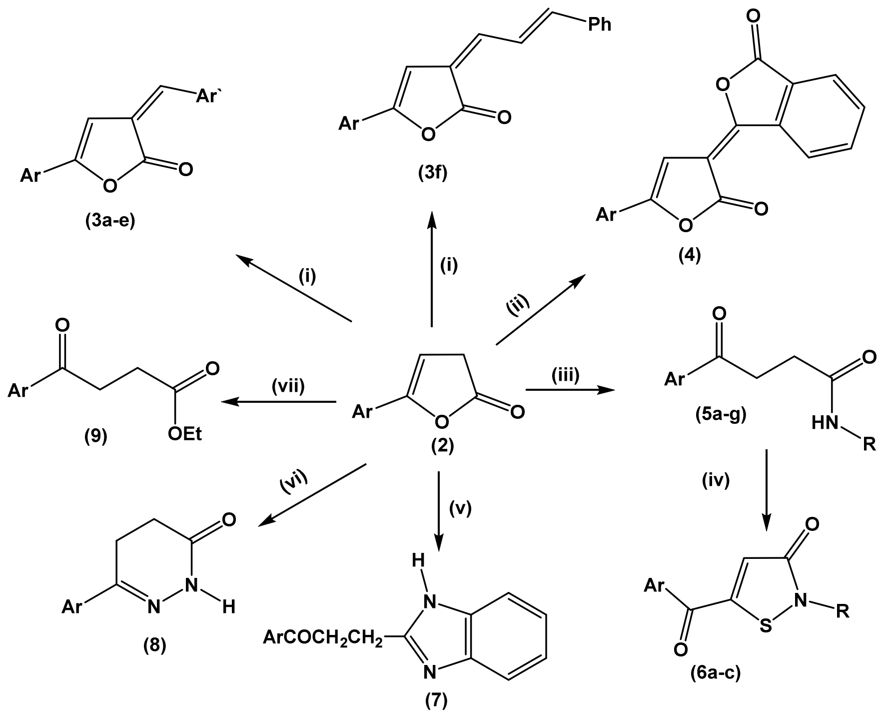


| Ar | Comp. | Ar' | Comp. | Ar' | Comp. | Ar' |
|---|---|---|---|---|---|---|
| 4-Meo-3-Me-$C_6H_3$ | 3a | Ph | 5a | Benzyl | 6a | Benzyl |
| | 3b | 4-$MeOC_6H_4$ | 5b | Phenyl | 6b | Phenyl |
| | 3c | 4-$ClC_6H_4$ | 5c | 4-Tolyl | 6c | 4-Tolyl |
| | 3d | 4-$CHOC_6H_4$ | 5d | Pentyl | | |
| | 3e | Furyl-2 | 5e | Cyclohexyl | | |
| | | | 5f | 2-$OHC_6H_4$ | | |
| | | | 5g | 2-$OHCH_2CH_2$- | | |

*Conditions*: (i) aromatic aldehydes, sodium acetate, acetic anhydride; (ii) phthalic anhydride, sodium acetate, acetic anhydride; (iii) amines, ethanol; (iv) thionyl chloride, stirring; (v) *o*-phenylenediamine, ethanol; (vi) hydrazine hydrate, ethanol; (vii) sodium ethoxide, ethanol.

**Scheme 1**

20 mL toluene was heated under reflux for 1 h, the reaction was then cooled, the solid product obtained after cooling was collected by filtration and recrystallized from ethanol to give compound **2** [15].

### *2.2.2. Synthesis of 3-arylidene-5-[4-methoxy-3-methyl phenyl]-2(3H)-furanone (3a-f) and phthalal (4)*

To a solution of 5-[4-methoxy-3-methylphenyl]-2(3H)-furanone (**2**) (0.01 mole) in acetic anhydride (10 mL), we added the respective aromatic aldehyde, or phthalic anhydride (0.01 mole) and anhydrous sodium acetate (0.01 mole). The reaction mixture was heated under reflux for 2 h, the solid product that separated after cooling was filtered off and crystallized from the proper solvent to give the title products (Scheme 1).

*3-Benzylidene-5-[4-methoxy-3-methylphenyl]-2(3H)-furanone* (**3a**): Color: Yellow. Yield: 68%. M.p.: 171-173 °C. FT-IR (KBr, ν, $cm^{-1}$): 1754 ν(C=O), 1610 ν(C=C). $^1H$ NMR (300 MHz, DMSO-$d_6$, δ, ppm): 2.26 (s, 3H, $CH_3Ar$), 3.89 (s, 3H, $OCH_3$), 6.79-7.64 (m, 10H, Ar-H and CH olefinic). Anal. calcd. for $C_{19}H_{16}O_3$: C, 78.06; H, 5.52. Found: C, 78.31; H: 5.27 %.

*3-(4-Methoxybenzylidene)-5-[4-methoxy-3-methylphenyl]-2(3H)-furanone* (**3b**): Color: Yellow. Yield: 64%. M.p.: 182-183 °C. FT-IR (KBr, ν, $cm^{-1}$): 1769 ν(C=O), 1603 ν(C=C). $^1H$ NMR (300 MHz, DMSO-$d_6$, δ, ppm): 2.27 (s, 3H, $CH_3Ar$), 3.88 (s, 3H, $OCH_3$), 3.89 (s, 3H, $OCH_3$), 6.77-7.63 (m, 9H, Ar-H and CH olefinic). Anal. calcd. for $C_{20}H_{18}O_4$: C, 74.52; H, 5.63. Found: C, 74.67; H, 5.39%.

*3-(4-Chlorobenzylidene)-5-[4-methoxy-3-methylphenyl]-2(3H)-furanone* (**3c**): Color: Yellow. Yield: 80%. M.p.: 203-205 °C. FT-IR (KBr, ν, $cm^{-1}$): 1782 ν(C=O), 1594 ν(C=C). $^1H$ NMR (300 MHz, DMSO-$d_6$, δ, ppm): 2.27 (s, 3H, $CH_3Ar$), 3.90 (s, 3H, $OCH_3$), 6.74-7.60 (m, 9H, Ar-H and CH olefinic). Anal. calcd. for $C_{19}H_{15}ClO_3$: C, 69.84; H, 4.63. Found: C, 69.53; H, 4.76%.

*3-(4-Formylbenzylidene)-5-[4-methoxy-3-methylphenyl]-2(3H)-furanone* (**3d**): Color: Orange. Yield: 83%. M.p.: 283-285 °C. FT-IR (KBr, ν, $cm^{-1}$): 1768 ν(C=O), 1694 ν(C=O). $^1H$ NMR (300 MHz, DMSO-$d_6$, δ, ppm): 2.33 (s, 3H, $CH_3Ar$), 3.91 (s, 3H, $OCH_3$), 6.80-7.97(m, 9H, Ar-H and CH olefinic), 10.06 (s, 1H, CHO). Anal. calcd. for $C_{20}H_{16}O_4$: C, 74.99; H, 5.03. Found: C, 74.73; H, 5.31%.

*3-Furfurylidene-5-[4-methoxy-3-methylphenyl]-2(3H)-furanone* (**3e**): Color: Yellow. Yield: 71%. M.p.: 199-200 °C. FT-IR (KBr, ν, $cm^{-1}$): 1774 ν(C=O), 1626 ν(C=C). $^1H$ NMR (300 MHz, DMSO-$d_6$, δ, ppm): 2.27 (s, 3H, $CH_3Ar$), 3.89 (s, 3H, $OCH_3$), 6.57-7.67 (m, 8H, Ar-H and CH olefinic). MS (EI, *m/z* (%)): 282 (58.5%) ($M^+$). Anal. calcd. for $C_{17}H_{14}O_4$ (282.29): C, 72.33; H, 5.00. Found: C, 72.51; H, 4.85 %.

*3-Cinnamylidene-5-[4-methoxy-3-methylphenyl]-2(3H)-furanone* (**3f**): Color: Orange. Yield: 69%. M.p.: 184-186 °C. FT-IR (KBr, ν, $cm^{-1}$): 1767 ν(C=O), 1612 ν(C=C). $^1H$ NMR (300 MHz, DMSO-$d_6$, δ, ppm): 2.26 (s, 3H, $CH_3Ar$), 3.89 (s, 3H, $OCH_3$), 6.61-7.59 (m, 12H, Ar-H and CH olefinic). MS (EI, *m/z* (%)): 318

(42.9%, M+). Anal. calcd. for $C_{21}H_{18}O_3$: C, 79.23; H, 5.70. Found: C, 79.57; H, 5.49%.

*3-[5-(4-Methoxy-3-methylphenyl)-2-oxo-furylidene]phthalal* (**4**): Color: Red. Yield: 71%. M.p.: 270-272 °C. FT-IR (KBr, ν, cm-1): 1772 ν(C=O), 1639 ν(C=C). 1H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 2.27 (s, 3H, $CH_3$Ar), 3.90 (s, 3H, $OCH_3$), 6.76-7.86 (m, 8H, Ar-H). MS (EI, *m/z* (%)): 334 (30.6%, M+). Anal. calcd. for $C_{20}H_{14}O_5$: C, 71.85; H, 4.22. Found: C, 71.63; H, 4.04%.

### *2.2.3. Alternative preparation of compound 3a-f*

To a mixture of 4-[4-methoxy-3-methylphenyl]-4-oxo-butanoic acid (**1**) (0.01 mole) and freshly fused sodium acetate (0.01 mole), aromatic aldehyde (0.01 mole) and 3.0 mL acetic anhydride were added. The reaction mixture was heated on a hot plate whereby a clear solution was obtained. Heating was continued, on a steam-bath till a solid separated out. The solid obtained was filtered off, washed with hot-water and then recrystallized from the suitable solvent.

### *2.2.4. General procedure for the synthesis of N-substituted-4-[4-methoxy-3-methylphenyl]-4-oxo-butanamide (5a-g)*

To a solution of the furanone (**2**) (0.01 mole) in 30 mL ethanol, amine (0.02 mole) was added dropwise with occasional shaking whereby the color of the furanone gradually disappeared with the formation of a colorless solid. The reaction mixture was heated under reflux for 2 h, during which the color of the furanone disappeared completely. On cooling, a colorless solid separated out which was filtered off and recrystallized from the suitable solvent (Scheme 1).

*N-Benzyl-4-[4-methoxy-3-methylphenyl]-4-oxo-butanamide* (**5a**): Color: White. Yield: 78%. M.p.: 134-135 °C. FT-IR (KBr, ν, cm-1): 3239 ν(NH), 1677 ν(C=O), 1601 ν(C=C). 1H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 6.84-7.88 (m, 8H, Ar-H), 6.15 (b, 1H, N-H), 4.44-4.46 (d, 2H, *J* = 5.9, NH-C$H_2$), 3.90 (s, 3H, $OCH_3$), 3.34-3.38 (t, 2H, $J_1$ = 6.7, ArCOC$H_2$$CH_2$CO), 2.63-2.68 (t, 2H, $J_1$ = 6.6, ArCOC$H_2$C$H_2$CO), 2.24 (s, 3H, $CH_3$Ar). 13C NMR (75 MHz, DMSO-$d_6$, δ, ppm): 197.35, 171.29, 161.17, 139.61, 130.14, 129.08, 128.15, 127.11, 126.62, 125.67, 109.85, 55.63, 42.02, 32.94, 29.30, 15.97. MS (EI, *m/z* (%)): 311 (4.2%, M+). Anal. calcd. for $C_{19}H_{21}NO_3$: C, 73.29; H, 6.80; N, 4.50. Found: C, 73.48; H, 6.57; N, 4.69%.

*N-Phenyl-4-[4-methoxy-3-methylphenyl]-4-oxo-butanamide* (**5b**): Color: White. Yield: 73%. M.p.: 152-154 °C. FT-IR (KBr, ν, cm-1): 3284 ν(NH), 1659 ν(C=O), 1601 ν(C=C). 1H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 8.4 (b, 1H, N-H), 6.83-7.89 (m, 8H, Ar-H), 3.89 (s, 3H, $OCH_3$), 3.39-3.43 (t, 2H, *J* = 6.5 Hz, ArCOC$H_2$$CH_2$CO), 2.79-2.83 (t, 2H, *J* = 6.6 Hz, ArCOC$H_2$C$H_2$CO), 2.24 (s, 3H, $CH_3$Ar). 13C NMR (75 MHz, DMSO-$d_6$, δ, ppm): 197.28, 170.42, 161.23, 139.36, 130.16, 129.01, 128.61, 128.15, 125.70, 122.80, 118.82, 109.88, 55.64, 32.71, 30.38, 15.97. Anal. calcd. for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71. Found: C, 72.49; H, 6.27; N, 4.56%.

*N-(4-Tolyl)-4-[4-methoxy-3-methylphenyl]-4-oxo-butanamide* (**5c**): Color: White. Yield: 75%. M.p.: 155-156 °C. FT-IR (KBr, ν, cm-1): 3347 ν(NH), 1669 ν(C=O), 1601 ν(C=C). 1H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 8.40 (b, 1H, N-H), 6.84-7.89 (m, 7H, Ar-H), 3.90 (s, 3H, $OCH_3$), 3.38-3.42 (t, 2H, *J* = 6.6 Hz, ArCOC$H_2$$CH_2$CO), 2.77-2.81 (t, 2H, *J* = 6.6 Hz, ArCOC$H_2$C$H_2$CO), 2.24 (s, 3H, $CH_3$Ar), 2.30 (s, 3H, $CH_3$Ar). 13C NMR (75 MHz, DMSO-$d_6$, δ, ppm): 197.31, 170.14, 161.22, 136.87, 131.62, 130.16, 129.00, 128.14, 125.70, 118.84, 109.88, 55.63, 32.73, 30.32, 20.38, 15.97. MS (EI, *m/z* (%)): 311 (5.2%, M+). Anal. calcd. for $C_{19}H_{21}NO_3$: C, 73.29; H, 6.80; N, 4.50. Found: C, 73.63; H, 6.42; N, 4.21%.

*N-Pentyl-4-[4-methoxy-3-methylphenyl]-4-oxo-butanamide* (**5d**): Color: White. Yield: 77%. M.p.: 84-85 °C. FT-IR (KBr, ν, cm-1): 3317 ν(NH), 1678 ν(C=O), 1650 ν(C=O), 1601 ν(C=C). 1H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 7.84-7.87 (d, 1H, *J* = 8.7 Hz, Ar-H), 7.81 (s, 1H, Ar-H), 7.87 (s, 1H, NH), 6.84-6.86 (d, 1H, *J* = 8.1 Hz, Ar-H), 3.90 (s, 3H, $OCH_3$), 3.69-3.74 (t, 2H, *J* = 6.9 Hz, NC$H_2$$CH_2$), 3.33-3.37 (t, 2H, *J* = 6.8 Hz, ArCOC$H_2$$CH_2$), 2.65-2.69 (t, 2H, *J* = 6.8 Hz, ArCOC$H_2$C$H_2$), 2.24 (s, 3H, $CH_3$Ar), 0.86-1.53 (m, 9H, $CH_3CH_2CH_2CH_2$). 13C NMR (75 MHz, DMSO-$d_6$, δ, ppm): 197.37, 170.97, 161.15, 130.13, 129.08, 128.10, 125.65, 109.84, 55.62, 33.00, 29.35, 28.69, 21.81, 15.96, 13.88. Anal. calcd. for $C_{17}H_{25}NO_3$: C, 70.07; H, 8.65; N, 4.81. Found: C, 70.34; H, 8.49; N, 4.99%.

*N-Cyclohexyl-4-[4-methoxy-3-methylphenyl]-4-oxo-butanamide* (**5e**): Color: White. Yield: 75%. M.p.: 164-165 °C. FT-IR (KBr, ν, cm-1): 3331 ν(NH), 1676 ν(C=O), 1602 ν(C=C). 1H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 7.83-7.86 (d, 1H, *J* = 9.0 Hz, Ar-H), 7.78 (s, 1H, Ar-H), 7.37 (s, 1H, NH), 6.81-6.84 (d, 1H, *J* = 8.4 Hz, Ar-H), 3.88 (s, 3H, $OCH_3$), 3.19-3.24 (t, 2H, *J* = 6.6 Hz, ArCOC$H_2$$CH_2$CO), 2.90-2.94 (m, 1H, N-C*H* of cyclohexyl group), 2.60-2.64 (t, 2H, *J* = 6.3 Hz, ArCOC$H_2$C$H_2$CO), 2.23 (s, 3H, $CH_3$Ar), 1.12-2.00 (m, 10H, cyclohexyl group). 13C NMR (75 MHz, DMSO-$d_6$, δ, ppm): 197.88, 174.58, 161.01, 130.11, 129.33, 128.04, 125.57, 109.80, 55.60, 49.37, 33.75, 33.34, 30.20, 25.03, 24.21, 15.97. MS (EI, *m/z* (%)): 303 (0.34%, M+). Anal. calcd. for $C_{18}H_{25}NO_3$: C, 71.26; H, 8.31; N, 4.62. Found: C, 71.54; H, 8.67; N, 4.79%.

*N-(2-Hydroxyphenyl)-4-[4-methoxy-3-methylphenyl]-4-oxo-butanamide* (**5f**): Color: White. Yield: 66%. M.p.: 170-172 °C. FT-IR (KBr, ν, cm-1): 3420 ν(OH), 3305 ν(NH), 1673 ν(C=O), 1645 ν(C=O), 1599 ν (C=C). 1H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 8.94 (b, 1H, O-H), 8.47 (b, 1H, N-H), 6.82-7.88 (m, 7H, Ar-H), 3.90 (s, 3H, $OCH_3$), 3.42-3.46 (t, 2H, *J* = 6.5 Hz, ArCOC$H_2$$CH_2$CO), 2.87-2.91 (t, 2H, *J* = 6.4 Hz, ArCOC$H_2$C$H_2$CO), 2.24 (s, 3H, $CH_3$Ar). 13C NMR (75 MHz, DMSO-$d_6$, δ, ppm): 197.27, 171.06, 161.23, 147.60, 130.17, 129.01, 128.16, 126.44, 125.70, 124.40, 121.99, 118.92, 115.80, 109.88, 85.22, 55.64, 32.90, 30.14, 15.97. Anal. calcd. for $C_{18}H_{19}NO_4$: C, 69.00; H, 6.11; N, 4.47. Found: C, 69.24; H, 5.97; N, 4.73%.

*N-(2-Hydroxyethyl)-4-[4-methoxy-3-methylphenyl]-4-oxo-butanamide* (**5g**): Color: White. Yield: 64%. M.p.: 107-108 °C. FT-IR (KBr, ν, cm-1): 3449 ν(OH), 3351 ν(NH), 1674 ν(C=O), 1631 ν(C=O), 1601 ν(C=C). 1H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 6.82-7.86 (m, 4H, Ar-H+ NH), 6.53 (b, 1H, OH), 3.88 (s, 3H, $OCH_3$), 3.69-3.72 (t, 2H, $J_1$ = 5.1, $J_2$ = 4.5 Hz, NC$H_2$$CH_2$OH), 3.40-3.43 (m, 2H, N$CH_2$C$H_2$OH), 3.30-3.35 (t, 2H, $J_1$ = 6.9, $J_2$ = 6.3 Hz, ArCOC$H_2$$CH_2$CO), 2.59-2.63 (t, 2H, $J_1$ = 6.6, $J_2$ = 6.6 Hz, ArCOC$H_2$C$H_2$CO), 2.22 (s, 3H, $CH_3$Ar). 13C NMR (75 MHz, DMSO-$d_6$, δ, ppm): 197.35, 171.37, 161.16, 130.14, 129.06, 128.10, 125.66, 109.85, 59.89, 55.62, 41.49, 32.98, 29.30, 15.96. Anal. calcd. for $C_{14}H_{19}NO_4$: C, 63.38; H, 7.22; N, 5.28. Found: C, 63.71; H, 6.98; N, 5.52%.

### *2.2.5. Synthesis of 5-[4-methoxy-3-methylbenzoyl]-2-(substituted)isothiazol-3(2H)-one (6a-c)*

Thionyl chloride (20 mL, 0.17 mole) was added to (0.001 mole) of N-substituted butanamide derivatives (**5a-c**), the initially insoluble material gradually dissolved, the mixture was stirred at room temperature for 4 h. The excess thionyl chloride was then evaporated under vacuum. The solid obtainned was collected by filtration and recrystallized from a suitable solvent to give 3(2*H*)-isothiazolones (**6a-c**) (Scheme 1).

*2-Benzyl-5-[4-methoxy-3-methylbenzoyl]-isothiazol-3(2H)-one* (**6a**): Color: Yellow. Yield: 77%. M.p.: 124-125 °C. FT-IR (KBr, ν, cm-1): 1654 ν(C=O), 1622 ν(C=C). 1H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 6.89-7.83 (m, 8H, Ar-H), 6.80 (s, 1H, vinylic proton), 5.01 (s, 2H, $NCH_2$), 3.93 (s, 3H, $OCH_3$), 2.26 (s, 3H, $CH_3$Ar). Anal. calcd. for $C_{19}H_{17}NO_3S$: C, 67.24; H, 5.05; N, 4.13. Found: C, 67.51; H, 5.37; N, 4.34%.

*2-Phenyl-5-[4-methoxy-3-methylbenzoyl]-isothiazol-3(2H)-one* (**6b**): Color: Yellow. Yield: 73%. M.p.: 211-213 °C. FT-IR (KBr, ν, cm-1): 1647 ν(C=O), 1613 ν(C=C). 1H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 6.93-7.91 (m, 8H, Ar-H), 6.83 (s, 1H, vinylic proton), 3.96 (s, 3H, $OCH_3$), 2.29 (s, 3H, $CH_3$Ar).

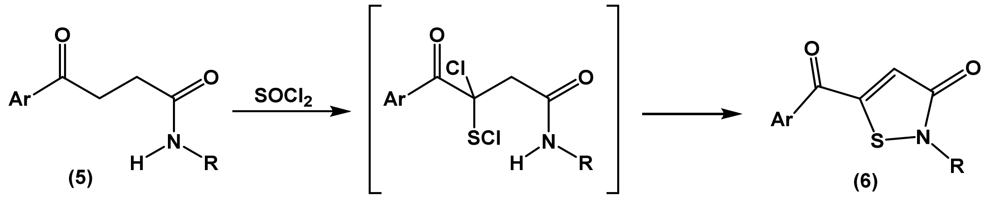


**Figure 1.** The cyclization reaction of amides with thionyl chloride.

$^{13}$C NMR (75 MHz, DMSO-$d_6$, δ, ppm): 185.03, 166.10, 162.68, 153.82, 136.23, 131.69, 130.49, 129.49, 127.65, 126.84, 124.43, 119.67, 110.51, 55.96, 15.85. Anal. calcd. for $C_{18}H_{15}NO_3S$: C, 66.44; H, 4.65; N, 4.30. Found: C, 66.50; H, 429; N, 4.59%.

*2-(4-Tolyl)-5-[4-methoxy-3-methylbenzoyl]-isothiazol-3 (2H)-one* (**6c**): Color: Yellow. Yield: 78%. M.p.: 187-189 °C. FT-IR (KBr, ν, cm$^{-1}$): 1652 ν(C=O), 1592 ν(C=C). $^1$H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 6.93-7.90 (m, 7H, Ar-H), 6.83 (s, 1H, vinylic proton), 3.96 (s, 3H, $OCH_3$), 2.29 (s, 3H, $CH_3$Ar), 2.40 (s, 3H, $CH_3$Ar). $^{13}$C NMR (75 MHz, DMSO-$d_6$, δ, ppm): 166.07, 162.66, 137.33, 133.65, 131.67, 130.47, 129.87, 126.79, 124.42, 119.67, 110.51, 55.95, 20.59, 15.85. Anal. calcd. for $C_{19}H_{17}NO_3S$: C, 67.24; H, 5.05; N, 4.13. Found: C, 67.34; H, 5.29; N, 3.91%.

### *2.2.6. Reaction of 5-[4-methoxy-3-methylphenyl]-2(3H)-furanone (2) with o-phenylenediamine*

To a solution of the furanone (0.01 mole) in 30 mL ethanol, amine (0.01 mole) was added with occasional shaking. The reaction mixture was heated under reflux for 4 h. On cooling, a colorless solid separated out which was filtered off and recrystallized from ethanol to give 2-[2-(4-methoxy-3-methyl benzoyl)ethyl]benzimidazol (**7**) (Scheme 1). Color: White. Yield: 71%. M.p.: 192-194 °C. FT-IR (KBr, ν, cm$^{-1}$): 3303 ν(NH), 1674 ν(C=O), 1624 ν(C=C). $^1$H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 6.73-7.87 (m, 8H, Ar-H and NH), 3.89 (s, 3H, $OCH_3$), 3.40-3.44 (t, 2H, $J$ = 6.6 Hz, $COCH_2CH_2CO$), 2.76-2.80 (t, 2H, $J$ = 6.9 Hz, $COCH_2CH_2CO$), 2.24 (s, 3H, $CH_3$Ar). $^{13}$C NMR (75 MHz, DMSO-$d_6$, δ, ppm): 197.56, 170.43, 161.23, 142.17, 130.16, 129.03, 128.17, 126.28, 125.33, 123.31, 115.93, 115.55, 109.88, 55.64, 33.08, 29.81, 15.97. Anal. calcd. for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.68; H, 6.35; N, 9.34%.

### *2.2.7. Hydrazinolysis of 5-[4-methoxy-3-methylphenyl]-2 (3H)-furanone*

To a solution of furanone (**2**) (0.01 mole) in ethanol (20 mL), hydrazine hydrate (0.012 mole) was added and the reaction mixture was heated under reflux for 4 h. The precipitate that formed after cooling was filtered off, washed with cooled ethanol and crystallized from ethanol to give 6-[4-methoxy-3-methylphenyl]-4, 5-dihydro-3(2*H*)-pyridazinone (**8**) (Scheme 1). Color: White. Yield: 67%. M.p.: 152-153 °C. FT-IR (KBr, ν, cm$^{-1}$): 3200 ν(NH), 2923 ν(CH, aliphatic), 1659 ν(C=O). $^1$H NMR (300 MHz, $CDCl_3$, δ, ppm): 6.78-7.59 (m, 4H, Ar-H and NH), 3.89 (s, 3H, $CH_3O$), 2.86-2.88 (t, 2H, $J$ = 6.6 Hz, H-4 pyridazine), 2.47-2.54 (t, 2H, $J$ = 6.6 Hz, H-5 pyridazine), 2.15 (s, 3H, $CH_3$). Anal. calcd. for $C_{12}H_{14}N_2O_2$: C, 66.04; H, 6.47; N, 12.84. Found: C, 66.15; H, 6.41; N, 12.79%.

### *2.2.8. Base catalyzed ethanolysis of 5-[4-methoxy-3-methyl phenyl]-2(3H)-furanone*

A mixture of 2.0 g of the furanone (**2**) and 20 mL sodium ethoxide (prepared from 0.3 g sodium and 20 mL absolute ethanol) was heated under reflux for 3 h. After cooling, the reaction mixture was neutralized with 10% HCl to give a white precipitate. The product obtained was crystallized from ethanol to give ethyl 4-[4-methoxy-3-methylphenyl]-4-oxo-butanoate (**9**) (Scheme 1). Color: White. Yield: 63%. M.p.: 110-111 °C. FT-IR (KBr, ν, cm$^{-1}$): 1723 ν(C=O), 1669 ν(C=O), 1600 ν(C=C). $^1$H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 6.84-7.87 (m, 3H, Ar-H), 4.13-4.20 (q, 2H, $J$ = 7.2 Hz, $CH_2CH_3$), 3.89 (s, 3H, $OCH_3$), 3.24-3.29 (t, 2H, $J$ = 6.9 Hz, $COCH_2CH_2CO$), 2.71-2.76 (t, 2H, $J$ = 6.9 Hz, $COCH_2CH_2CO$), 2.25 (s, 3H, $CH_3$Ar), 1.24-1.29 (t, 3H, $J$ = 7.2 Hz, $CH_2CH_3$). Anal. calcd. for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 66.94; H, 7.45 %.

## 3. Results and discussion

The starting compound 2(3*H*)-furanone (**2**) has been synthesized via the lactonization of the 4-(4-methoxy-3-methylphenyl)-4-oxobutanoic acid (**1**) with acetic anhydride. The reactivity of the methylene unit of 2(3*H*)-furanone (**2**) has been studied for various condensation reactions (Scheme 1). Thus, the condensation of furanone (**2**) with aromatic alde-hydes in acetic anhydride in the presence of sodium acetate, using different procedures, afforded the corresponding 3-aryli dene-5-(4-methoxy-3-methylphenyl)-2(3*H*)-furanones (**3**) in good yields. The proposed structures of these compounds were supported by the identity of their melting points with that of authentic samples prepared from the reaction of the corresponding 4-(4-methoxy-3-methylphenyl)-4-oxo-butanoic acid (**1**) with aromatic aldehydes and acetic anhydride in the presence of anhydrous sodium acetate. The structures of compounds **3a-f** were confirmed from their spectral analyses, where IR spectra revealed strong absorption bands in the region 1754-1782 cm$^{-1}$ corresponding to the carbonyl groups of the 2(3*H*)-furanone rings (e.g. νC=O of α,β-unsaturated lactones). It was found that there is no difference in the yield and the purity of the 3-arylidene derivatives prepared by the different methods used. Attempts to synthesize *bis*-ylidene compound from the reaction of two or more moles of 2(3*H*)-furanone (**2**) with terphthaladehyde were not successful.

The condensation of 2(3*H*)-furanone (**2**) with phthalic anhydride in acetic anhydride in the presence of fused sodium acetate under similar conditions afforded the corresponding phthalide (**4**). The aminolysis of 2(3*H*)-furanone (**2**) with primary amines (aliphatic or aromatic) was proceeded readily and stopped at the stage of the formation of the N-substituted butanamides (**5a-g**), which were isolated with quantitative yields. The $^1$H NMR spectroscopy has been used in order to establish the open chain structure of propionamides which were characterized by the [-$CH_2CH_2$-] methylene proton signals, which appear as two distinct triplets at approximately δ 2.59-2.91 and 3.19-3.46 ppm.

The treatment of butanamide (**5a-c**) with an excess of thionyl chloride at room temperature has been found to give the corresponding isothiazolones (**6a-c**) [16,17]. The cycliza-tion reaction of amides with thionyl chloride has been suggested to precede through intermediate sulfinyl chlorides, resulting from the oxidation of the methylene group adjacent to the aroylcarbonyl (Figure 1).

The furanone (**2**) was converted to the corresponding benzimidazole (**5**) by the reaction with *o*-phenylenediamine in refluxing ethanol. Apparently, the reaction of furanone (**2**) with *o*-phenylenediamine causes the opening of the furan ring with the formation of the corresponding amide, which undergoes in situ cyclization into the corresponding benzimidazole (**7**).

The hydrazinolysis of 2(3*H*)-furanone (**2**) with hydrazine hydrate in ethanol caused ring opening with the formation of the corresponding acid hydrazide which also undergoes in situ cyclization into the corresponding pyridazinone (**8**). The base catalyzed ethanolysis of the furanone (**2**) with sodium ethoxide was conducted in refluxing ethanol and afforded the corresponding ethyl ester (**9**). The IR spectrum showed two strong carbonyl absorption bands in the region 1723 and 1669 $cm^{-1}$ corresponding to the ester and keto groups, respectively. In the $^1H$ NMR spectrum, the signal characteristic for the ethyl group ($CH_3CH_2O$) appeared as triplet at $\delta$ 1.24-1.29 and quartet at $\delta$ 4.13-4.20, respectively.

## 4. Conclusion

The present work describes the synthesize 5-(4-methoxy-3-methylphenyl)-2(3*H*)-furanone and to study its reactivity towards nucleophilic and electrophilic reagents for further investigations. 3-Arylidene-2(3*H*)-furanones were prepared from the reaction of 2(3*H*)-furanone with the corresponding aromatic aldehydes. The treatment of furanone with amines gave the corresponding butanamides which afforded the corresponding isothiazolones on reaction with thionyl chloride. The chemical structures of these compounds were confirmed by IR, $^1H$ NMR, $^{13}C$ NMR, mass spectroscopy and elemental analysis.

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