

## Synthesis and Characterization of the Novel Thiophene Derivatives

Adnan CETIN<sup>1\*</sup> Havva KURT<sup>2</sup> Sedat BOZARI<sup>2</sup>

**ABSTRACT:** The use of thiophene derivatives that have a stable structure in agriculture, food and pharmaceutical industries has revealed the necessity of synthesizing different derivatives. For this purpose, in the current study, some substituted thiophene derivatives have been designed and synthesized. The characterization of the synthesized compounds was determined by spectroscopic methods. The possible antimicrobial activities of these compounds (3-9, 10a-e, 11-13) were measured by disc diffusion method against gram positive (*Bacillus subtilis* ATCC 6633, *Staphylococcus aureus* 6538) and gram negative (*Enterobacter aerogenes* ATCC 13048, *Escherichia coli*) bacteria. The synthesized substituted thiophene compounds do not showed any antibacterial activities against test bacteria.

**Keywords:** Heterocyclic compounds, hydrazide, thiophene, oxadiazole, pyrazole

### Yeni Tiofen Türevlerin Sentezlenmesi ve Karakterizasyonu

**ÖZET:** Kararlı bir yapıya sahip tiyofen türevlerinin ziraat, gıda ve ilaç sanayilerinde kullanımı farklı türevlerinin sentezlenmesi gerekliliğini ortaya koymuştur. Bu amaçla, mevcut çalışmada bazı substitüe tiyofen türevleri tasarlanıp sentezlendi. Sentezlenen bileşiklerin karakterizasyonu, spektroskopik yöntemlerle belirlendi. Bu bileşiklerin (3-9, 10a-e, 11-13) olası antimikrobiyal aktiviteleri gram pozitif (*Bacillus subtilis* ATCC 6633, *Staphylococcus aureus* 6538) ve gram negatif (*Enterobacter aerogenes* ATCC 13048, *Escherichia coli*) bakterilere karşı disk difüzyon metodu ile ölçüldü. Sentezlenen substitüe tiyofen bileşiklerinin test bakterilerine karşı herhangi bir aktivite göstermediği belirlendi.

**Anahtar Kelimeler:** Heterosiklik bileşikler, hidrazid, tiyofen, okzadiazol, pirazol

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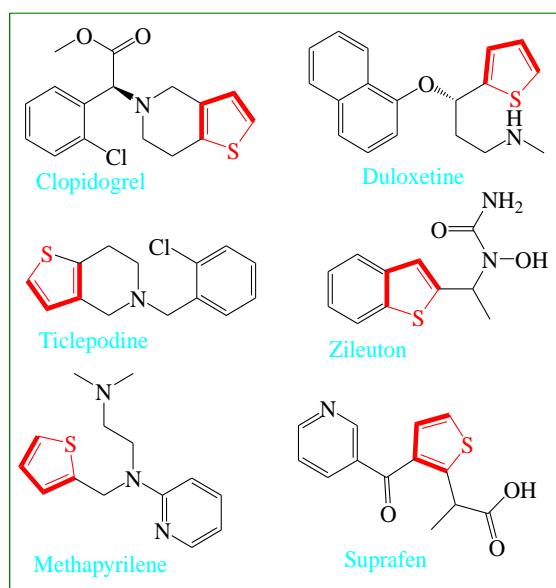
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## INTRODUCTION

Heterocyclic compounds are important compounds in the organic chemistry because of their significant properties in the various areas such as medicinal, food and agricultural industries (Fakhr et al., 2009; Gouda et al., 2010). Thiophene is a five-membered aromatic ring structure in the heterocyclic chemistry. It contains one sulfur atom as a heteroatom and four carbon atoms. Thiophene can extremely behave reactive like benzene in terms of having a pie electron cloud structure. The substituted thiophene derivatives are very well known for medicinal applications. Many substituted thiophene compounds have performed as chemotherapeutic and anticancer agents. For these reasons, substituted thiophene compounds

were also applied successfully in other fields such as pharmacology, agriculture and industrial applications. These compounds were used in the development of agricultural products and in drug research since they have diverse biological activities. Some known activities are antitubercular, analgesic, anti-inflammatory, anti-metabolite, anti-bacterial, antifungal, and antineoplastic (William, 1989; Moghaddam and Boinee, 2004; Parai et al., 2008; Pinto et al., 2008; Zarudnitskii et al., 2008; Isloor et al., 2010; Sagardoy et al., 2010; Andersson et al., 2012). Hence, they are popular targets for organic chemists. These compounds have been studied for a long time and still continue to attract considerable attention in literature. Some of the drugs that have substituted thiophene derives are showed in Figure 1.



**Figure 1.** Some of the important examples of substituted thiophenes

The cyclocondensation reactions of  $\alpha$ ,  $\beta$ -unsaturated carbonyl compounds have used widely to preparation of substituted thiophenes. Moreover, the various methods for the synthesis of substituted triazole and oxadiazole compounds were reported in literature (Zhang et al., 2002; Ramazani and Rezaei, 2010). They have also brought out significant pharmacological and biological activities

(Naresh et al., 2013; Patel et al., 2013). The structures having substitute 1,2,4-triazoles and 1,3,4-oxadiazoles were performed in many different studies (Christophe et al., 2011; Maddila et al., 2013). Previous studies have reported that these compounds are important goals of the molecules in the field of synthetic and medicinal chemistry. Aim of the present study was to synthesise substituted thiophene

compounds, their characterization and investigating their possible antibacterial activities.

## MATERIAL AND METHODS

### General

All chemical materials were available commercially from Sigma and Merck companies. Melting points of synthesized compounds were performed on an Electrothermal Scientific Flash 2000. Shimadzu IR-470 spectrophotometer is used to measure the infrared spectra of synthesized compounds.  $^1\text{H}$  (400 MHz) and  $^{13}\text{C}$  (100 MHz) NMR spectra were recorded on a Bruker DRX-400 high performance digital FT-NMR spectrometer. Elemental analyses were carried out on Thermo Scientific Flash 2000. The mass spectrum was measured on Agilent 5973 Mass Spectrometer.

### Synthesis of *N*-(4-phenyl-2-thioxothiazol-3(2*H*)-yl)-2-(thiophen-2yl)acetamide (3)

Potassium thiocarbazine 2 (0.5 mmol, 0.143 g) was added to ethanol (10 ml). The phenyl bromide (0.5 mmol, 0.199 g) was added to prepared solution. The mixture was refluxed for 3 h. Then, reaction process was allowed to room temperature. The precipitated solid was filtered. It was washed with ethanol. The product was dried. It was crystallized from ethanol. Yield (0.23 g, 67%); M.p: 206-208 °C; IR ( $\nu$ ,  $\text{cm}^{-1}$ ): 3142, 3065, 1680, 1498-1442.  $^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 9.05 (s, 1H), 7.28-6.52 (m, 10H, aromatic), 3.45 (s, 2H).  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 189.47, 167.26, 154.63, 132.09, 130.71, 130.12, 129.65, 129.0, 128.46, 128.12, 125.15, 124.35, 123.18, 110.68, 36.25. ESI MS (M+H)<sup>+</sup>: 333.1.

### Synthesis of ethyl 2-(5-(thiophen-2ylmethyl)-1,3,4-oxadiazol-2-ylthio)acetate (4)

2 (0.5 mmol, 0.143 g) was dissolved to ethanol (10 ml). The ethyl-2-bromoacetate (0.5 mmol, 0.167 g) was added to prepared solution.

The mixture was refluxed for 3 hours. The reaction was allowed to room temperature. The precipitated solid was filtered. It was washed with ethanol. The product was dried. It was crystallized from ethanol. Yield (0.12 g, 39%); M.p: 248 °C; IR ( $\nu$ ,  $\text{cm}^{-1}$ ): 3080, 2925, 1721, 1497-1444.  $^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 6.95-6.55 (m, 3H, aromatic), 4.01 (m, 2H), 3.76 (m, 2H), 3.32 (m, 2H), 1.24 (m, 3H).  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 166.36, 151.15, 139.09, 131.35, 126.55, 123.33, 120.42, 57.53, 38.25, 26.17, 14.20. ESI MS (M+H)<sup>+</sup>: 285.0.

### Synthesis of 4-phenyl-1-(2-(thiophen-2yl)acetyl) thiosemicarbazide (5)

2-(thiophen-2yl)acetohydrazide 1 (0.5 mmol, 0.156 g) and phenyl isothiocyanate (1 mmol, 0.135 g) were refluxed in dry benzene (15 ml) for 5 h. The process was allowed to room temperature. The precipitated solid was filtered. It was washed with ethanol. The product was dried. It was crystallized from ethanol. Yield (0.15 g, 52%); M.p: 211 °C; IR ( $\nu$ ,  $\text{cm}^{-1}$ ): 3235, 3210, 3065, 2890, 1682, 1671, 1502-1432.  $^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 9.37 (d,  $J$ = 9.6, 1H), 7.20-6.54 (m, 8H, aromatic), 4.15 (s, 1H), 3.36 (s, 2H), 1.96 (d,  $J$ = 5.8, 1H).  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 178.39, 167.57, 135.47, 133.22, 131.56, 130.23, 129.74, 129.12, 128.43, 127.67, 126.05, 119.26, 30.25. ESI MS (M+H)<sup>+</sup>: 292.3.

### Synthesis of 4-phenyl-5-(thiophen-2ylmethyl)-4*H*-1,2,4-triazole-3-thiol (6)

5 (1 mmol, 0.291 g) was refluxed in potassium hydroxide solution (5 ml) for 4 h. After the reaction mixture was filtered hot. It was kept overnight at room temperature. Precipitated solid was washed with water, filtered and the obtained product was dried. It was crystallized with ethanol. Yield (0.16 g, 55%); M.p: 244-246 °C; IR ( $\nu$ ,  $\text{cm}^{-1}$ ): 3065, 2885, 2668, 1620, 1498-1442.  $^1\text{H}$ -NMR (400

MHz, CDCl<sub>3</sub>)  $\delta$  (ppm): 12.10 (s, 1H). 7.15-6.60 (m, 8H, aromatic), 3.35 (s, 2H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm): 170.55, 165.37, 140.69, 132.15, 131.16, 130.72, 129.54, 128.40, 127.97, 127.85, 126.94, 123.10, 26.49. ESI MS (M+H)<sup>+</sup>: 274.0.

#### Synthesis of *N*-phenyl-5-(thiophen-2-ylmethyl)-1,3,4-oxadiazol-2-amine (7)

3 (1 mmol, 0.291 g) was added in ethanol (2.5 ml). The sodium hydroxide solution (1ml) was added prepared solution. Solutions of iodine and potassium iodide were added drop wise with stirring till color of iodine persisted. The obtained mixture was heated in the water bath for 5 hours. The mixture was allowed to room temperature. The obtained product was filtered. After it was dried, it was crystallized with ethanol. Yield (0.098 g, 34%); M.p: 231 °C; IR (v, cm<sup>-1</sup>): 3235, 3080, 2875, 1610, 1498-1443. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm): 7.10-6.38 (m, 8H, aromatic), 3.89 (s, 1H), 3.36 (s, 2H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm): 164.72, 157.24, 142.63, 139.57, 131.52, 130.24, 129.62, 129.10, 128.63, 127.16, 124.07, 119.63, 28.57. ESI MS (M+H)<sup>+</sup>: 258.3.

#### Synthesis of 1-(5-amino-3-hydroxy-1*H*-pyrazol-1-yl)-3-(thiophen-2-yl)propan-2-one (8)

1 (1 mmol, 0.156 g) was dissolved in potassium hydroxide (10% 5 ml). The dissolved ethylcyano acetate (1 mmol, 0.099 g) in ethanol (10 ml) was added prepared solution. The mixture was refluxed for 10 h. The process was allowed to room temperature. The mixture was diluted with water. It was acidified by concentrate hydrochloric acid. The precipitated solid was filtered. It was washed with water. After it was dried, It was crystallized by *N,N*-dimethylformamide: ethanol (1:1). Yield (0.07 g, 28%); M.p: 284-286 °C; IR (v, cm<sup>-1</sup>): 3415, 3158, 3080, 2865, 1665, 1498-1444. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm): 7.26-6.70 (m, 4H,

aromatic), 5.36 (s, 1H), 3.86 (s, 2H), 3.34 (s, 2H), 2.48 (s, 2H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm): 193.07, 147.12, 144.10, 130.26, 129.50, 128.18, 126.27, 122.47, 46.74, 25.49. ESI MS (M+H)<sup>+</sup>: 238.1.

#### Synthesis of 2-phenyl-5-(thiophen-2-ylmethyl)-1,3,4-oxadiazole (9)

1 (1 mmol, 0.156 g) and benzoic acid (1 mmol, 0.122 g) were added in trifluoroacetic acid (5 ml). The mixture was heated for 6 h. The process was allowed to room temperature. The crushed ice was added and kept overnight. The precipitated solid was neutralized with sodium bicarbonate. It was washed with water and filtered. It was crystallized from ethanol. Yield (0.1 g, 36%); M.p: >300 °C; IR (v, cm<sup>-1</sup>): 3080, 2865, 1670, 1498-1442. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm): 7.37- 6.39 (m, 8H, aromatic), 3.35 (s, 2H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm): 162.14, 158.69, 135.06, 132.45, 130.10, 129.56, 129.12, 128.94, 128.16, 127.62, 126.38, 121.31, 28.41. ESI MS (M+H)<sup>+</sup>: 243.1.

#### Synthesis of *N*-(substituted benzylidene)-2-(thiophen-2-yl)acetohydrazide (10a-e)

1 (0.5 mmol, 0.078 g) and various aromatic aldehydes (benzaldehyde, 2-hydroxy benzaldehyde, 2-hydroxy, 5-nitro benzaldehyde, thiophene-2-carbaldehyde, 4-trimethyl amino benzaldehyde, respectively) (0.5 mmol) were refluxed with a few drops glacial acid in ethanol (10 ml) for 4 hours. The mixture was allowed to room temperature. Then cold water was added. The obtained precipitate solid filtered and it was crystallized from ethanol.

#### Synthesis of *N*-benzylidene-2-(thiophen-2-yl)acetohydrazide (10a)

10a was prepared according to general procedure. Yield (0.08 g, 61%); M.p: 214-216 °C; IR (v, cm<sup>-1</sup>): 3210 (-NH), 3080, 2870, 1680, 1668, 1562, 1498-1442. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm): 8.30 (s, 1H), 8.05 (s, 1H), 7.85-

6.95 (m, 8H, aromatic), 2.98 (s, 2H).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 169.87, 145.34, 135.66, 131.24, 130.28, 129.36, 129.04, 128.65, 127.23, 124.60, 122.83, 116.72, 35.68. Anal. Calcd. For  $\text{C}_{13}\text{H}_{12}\text{N}_2\text{OS}$ : C, 63.91; H, 4.96; N, 11.46. Found: C, 63.96; H, 5.00; N, 11.42.

#### Synthesis of *N*-(2-hydroxybenzylidene)-2-(thiophen-2-yl) acetohydrazide (10b)

10b was prepared according to general procedure. Yield (0.08 g, 57%); M.p: 230-232 °C; IR (v,  $\text{cm}^{-1}$ ): 3345, 3237, 3086, 2875, 1675, 1664, 1576, 1496-1442.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 8.26 (s, 1H), 7.93 (s, 1H), 7.82-6.83 (m, 7H), 5.49 (s, 1H), 4.18 (s, 2H).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 170.15, 159.65, 142.37, 135.28, 131.02, 130.62, 129.54, 128.14, 127.35, 125.72, 123.68, 121.93, 43.37. Anal. Calcd. For  $\text{C}_{13}\text{H}_{12}\text{N}_2\text{O}_2\text{S}$ : C, 59.98; H, 4.65; N, 10.76. Found: C, 60.01; H, 4.69; N, 10.79.

#### Synthesis of *N'*-(2-hydroxy-5-nitrobenzylidene)-2-(thiophen-2-yl)acetohydrazide (10c)

Compound 10c was prepared according to general procedure. Yield (0.07 g, 44%); M.p: 260-263 °C; IR (v,  $\text{cm}^{-1}$ ): 3245, 3084, 2870, 1676, 1662, 1570, 1498-1442.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 8.30 (s, 1H), 7.96 (s, 1H), 7.74-6.75 (m, 6H, aromatic), 5.75 (s, 1H), 4.32 (s, 2H).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 177.42, 169.20, 149.20, 146.38, 138.08, 135.24, 133.49, 130.52, 129.42, 128.73, 124.28, 118.06, 34.64. Anal. Calcd. For  $\text{C}_{13}\text{H}_{11}\text{N}_3\text{O}_4\text{S}$ : C, 51.14; H, 3.63; N, 13.76. Found: C, 51.23; H, 3.58; N, 13.79.

#### Synthesis of 2-(thiophene-2-yl)-*N'*-(thiophen-2-ylmethylene)acetohydrazide (10d)

Compound 10d was prepared according to general procedure. Yield (0.05 g, 37%); m.p 242-245 °C; IR (v,  $\text{cm}^{-1}$ ): 3218, 3086, 2874, 1682, 1656, 1579, 1498-1444.  $^1\text{H-NMR}$  (400

MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 8.20 (s, 1H), 8.02, (s, 1H), 7.58-6.62 (m, 6H, aromatic), 3.91 (s, 2H).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 169.02, 145.67, 139.58, 136.62, 134.13, 130.36, 129.61, 126.34, 122.87, 119.03, 36.43. Anal. Calcd. For  $\text{C}_{11}\text{H}_{10}\text{N}_2\text{OS}_2$ : C, 52.78; H, 4.03; N, 11.19. Found: C, 52.79; H, 4.04; N, 11.15.

#### Synthesis of *N'*-(4-(dimethylamino)benzylidene)-2-(thiophen-2-yl) acetohydrazide (10e)

Compound 10e was prepared according to general procedure. Yield (0.08 g, 52%); M.p: 219-221 °C; IR (v,  $\text{cm}^{-1}$ ): 3241, 3084, 2869, 1678, 1667, 1552, 1498-1442.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 8.34 (s, 1H), 7.96 (s, 1H), 7.17- 6.61 (m, 7H, aromatic), 3.56 (s, 2H), 2.69 (s, 6H).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 170.17, 147.23, 140.16, 137.28, 134.63, 132.58, 130.13, 129.51, 128.25, 127.57, 125.06, 123.63, 39.18, 32.70. Anal. Calcd. For  $\text{C}_{15}\text{H}_{17}\text{N}_3\text{OS}$ : C, 62.69; H, 5.96; N, 14.62. Found: C, 62.73; H, 5.95; N, 14.56.

#### Synthesis of 3-oxo-3-phenyl-*N*-(2-(thiophen-2-yl)acetyl) propanehydrazide (11)

Compound 1 (1 mmol, 0.156 g) was added in ethyl acetoacetate (5 ml). The solution was refluxed for 5 h. The mixture was allowed to room temperature. The mixture was diluted with petrol ether. The precipitated solid was filtered. It was washed by water. The obtained product was crystallized from ethanol. Yield (0.15 g, 44%); M.p: 291-293 °C; IR (v,  $\text{cm}^{-1}$ ): 3296, 3257, 3086, 2874, 1723, 1665, 1654, 1496-1442.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 9.91, 8.70 (m, 2H), 7.90-6.67 (m, 8H, aromatic), 3.51 (s, 2H), 3.15 (s, 2H).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 191.38, 164.24, 158.08, 136.71, 132.88, 130.42, 130.04, 129.56, 128.86, 128.77, 127.41, 126.06, 124.56, 38.54, 33.09. ESI MS (M+H)<sup>+</sup>: 303.2.

### Synthesis of 3-phenyl-1-(2-(thiophen-2yl)acetyl)-1,2-dihydropyrazol-5-one (12)

Compound 11 (0.43 mmol, 0.13 g) was added in the potassium hydroxide solution (2 M, 10 ml). The solution was refluxed for 5 hours. The mixture was allowed to room temperature. The mixture was acidified by concentrate hydrochloric acid. The precipitated solid was filtered and washed with water. The obtained product was crystallized by ethanol. Yield (0.05 g, 39%); M.p: >300 °C; IR (v, cm<sup>-1</sup>): 3254, 3080, 2865, 1678, 1497-1442. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm): 8.10-6.75 (m, 8H), 5.35 (s, 1H), 3.37 (s, 2H), 2.25 (s, 1H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm): 171.35, 164.39, 158.52, 139.46, 136.90, 135.70, 133.20, 130.42, 129.64, 128.93, 127.81, 126.12, 123.55, 112.56, 34.45. ESI MS (M+H)<sup>+</sup>: 285.0.

### Synthesis of 1-(3,5-diphenyl-1H-pyrazol-1-yl)-3-(thiophen-2yl)propan-2-one (13)

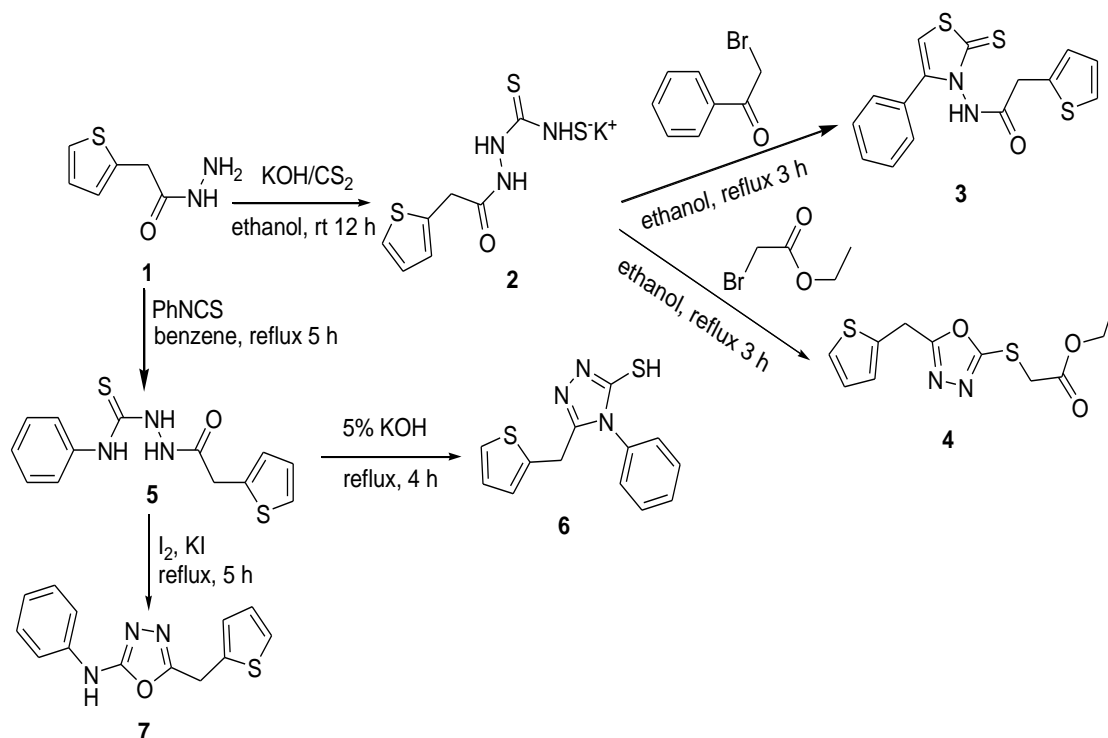
Compound 1 (1 mmol, 0.156 g) and 1,3-diphenylpropane-1,3-dione (1 mmol, 0.224 g) were added in a few drops *N,N*-dimethylformamide and glacial acid (5 ml). The reaction was mixed at room temperature for 12 h. The mixture was diluted by water. The precipitated solid was filtered and dried. It was crystallized from *N,N*-dimethylformamide: ethanol (1:10). Yield (0.29 g, 78%); M.p: 225-227 °C; IR (v, cm<sup>-1</sup>): 3080, 2857, 1648, 1598, 1497-1442. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm): 7.96-6.50 (m, 14H), 5.57 (s, 2H), 4.26 (s, 2H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm): 183.41, 145.74, 142.42, 134.03, 131.26, 130.90, 130.15, 129.84, 129.12, 129.02, 128.42, 128.13, 127.58, 127.16, 126.08, 126.63, 125.85, 124.77,

121.76, 117.95, 62.10, 46.35. ESI MS (M+H)<sup>+</sup>: 359.2.

## RESULTS AND DISCUSSION

2-(thiophen-2yl)acetohydrazide (1) was purchased commercially. It was used as starting material. Firstly, the potassium thiocarbazine (2) was prepared according the literature (Meltzer et al., 1953). The potassium thiocarbazine (2) was obtained from reaction 2-(thiophen-2yl)acetohydrazide (1), carbon disulfide and potassium hydroxide in ethanol. *N*-(4-phenyl-2-thioxothiazol-3(2H)-yl)-2-(thiophen-2yl)acetamide (3) and ethyl 2-(5-(thiophen-2ylmethyl)-1,3,4-oxadiazol-2-ylthio)acetate (4) were synthesized from potassium thiocarbazine (2) and 2-bromoacetophenone or ethyl 2-bromoacetate in boiling ethanol in Scheme 1.

The IR spectrum of compound 3 showed 3142 cm<sup>-1</sup> corresponding -NH amide and 1680 cm<sup>-1</sup> carbonyl group absorption bands. The <sup>1</sup>H NMR spectrum revealed δ 9.0 ppm signal (-NH) proton of amide in the region. The <sup>13</sup>C NMR spectrum revealed 189.4 ppm signal of the thiocarbonyl (C=S) and δ 36.2 ppm signal of methylene carbon in the region. The IR spectrum of 1,3,4-oxadiazol 4 showed 1721 cm<sup>-1</sup> ester carbonyl group absorption band. The <sup>1</sup>H-NMR spectrums revealed δ 3.9, 3.5 and 3.3 ppm signals protons of methylene in the region and δ 1.2 ppm signals protons of methyl in the region. The <sup>13</sup>C NMR spectrum revealed δ 166.3 ppm signal of ester carbonyl and δ 151.1 ppm signal carbon of (C5) in the region.



Scheme 1. Synthesis of 3, 4, 5, 6 and 7

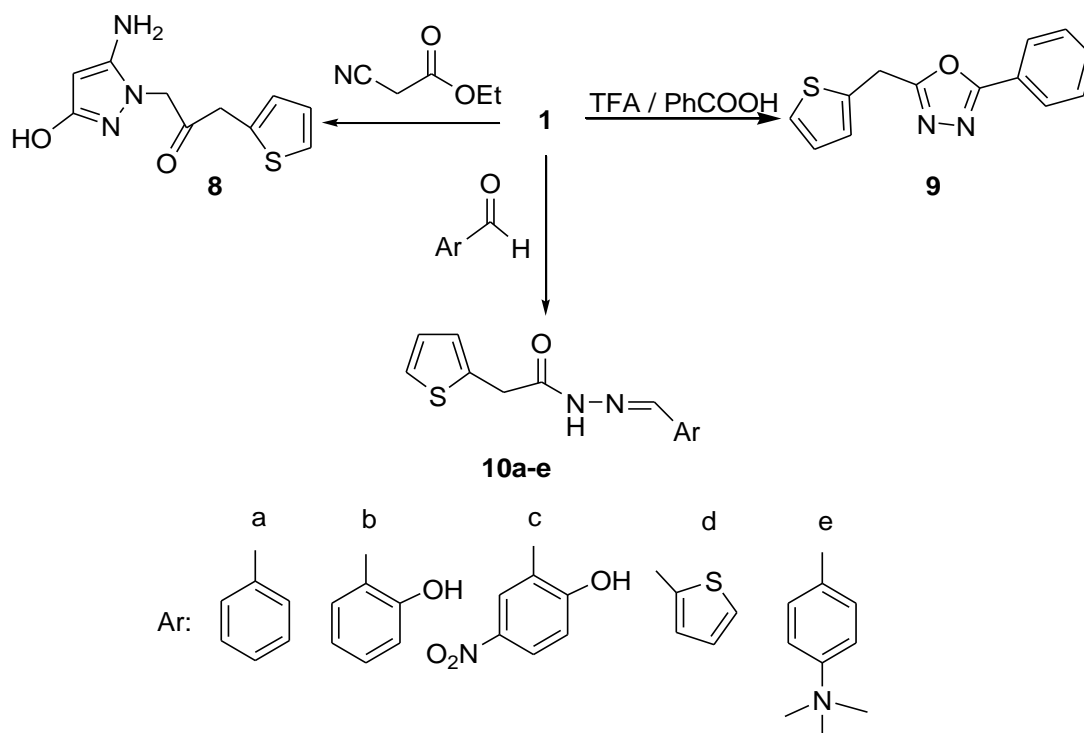
4-phenyl-1-(2-(thiophen-2-yl)acetyl)thiosemicarbazide (5) was prepared via reaction of 1 and phenyl isothiocyanate in boiling dry benzene. The IR spectrum of thiosemicarbazide 5 showed 3235 and 3210  $\text{cm}^{-1}$  1682, 1671  $\text{cm}^{-1}$  corresponding -NH hydrazide and thioamide carbonyl groups absorption bands, respectively. The  $^1\text{H}$  NMR spectrum revealed  $\delta$  9.3 ppm signal (-NH) proton of hydrazide, 3.3 ppm signals (- $\text{CH}_2$ ) protons of methylene and 1.9 ppm the signals (-NH) proton of amine in the region. The  $^{13}\text{C}$  NMR spectrum revealed  $\delta$  178.3 and 167.5 ppm signals (thiocarbonyl and carbonyl of carbohydrazide) in the region and 30.2 ppm signal of methylene carbon in the region. 4-phenyl-5-(thiophen-2-ylmethyl)-4H-1,2,4-triazole-3-thiol (6) was conducted to intramolecular cyclization of compound 5 in boiling potassium hydroxide solution. The IR spectrum of 1,2,4-triazole derivative 6 showed 2668  $\text{cm}^{-1}$  corresponding -SH absorption band. The  $^1\text{H}$  NMR spectrum revealed  $\delta$  12.1 ppm signal -SH proton in the region and  $\delta$  7.1-6.6 ppm multiplied signals (-CH) protons of

aromatic ring. The  $^{13}\text{C}$  NMR spectrum revealed  $\delta$  170.5 and 165.3 ppm signals carbons of (C3) and (C5) of 1,2,4-triazole ring in the region. 1,3,4-oxadiazol-2-amine derivative (7) was conducted to compound 5, potassium iodide and iodine in the presence of sodium hydroxide solution. The IR spectrum of 1,3,4-oxadiazol (7) showed 3235  $\text{cm}^{-1}$  corresponding -NH group and 1610  $\text{cm}^{-1}$  (C=N) group absorption bands. The  $^1\text{H}$ -NMR spectrum revealed  $\delta$  3.8 ppm signal (-NH) proton of amine, between  $\delta$  7.1 and 6.3 ppm the (-CH) protons of aromatic ring. The  $^{13}\text{C}$  NMR spectrum revealed  $\delta$  164.7 and 157.2 ppm signals carbons of (C5) and (C2) of 1,2,4-triazole ring in the region, respectively.

1-(5-amino-3-hydroxy-1H-pyrazol-1-yl)-2-(thiophen-2-yl)ethanone (8) was obtained resulting intramolecular cyclization ethyl cyanoacetate and compound 1 in boiling ethanol. The IR spectrum of compound 8 showed 3415  $\text{cm}^{-1}$  corresponding (-OH) hydroxyl, 3158  $\text{cm}^{-1}$  (- $\text{NH}_2$ ) amine and 1665  $\text{cm}^{-1}$  (C=O) carbonyl groups, respectively. The  $^1\text{H}$ -NMR spectrum revealed  $\delta$  5.3 and 3.3 ppm signal (-OH) proton

and (-NH<sub>2</sub>) protons in the region, respectively. The <sup>13</sup>C NMR spectrum revealed δ 147.1, 144.1 ppm signals carbons of (C3) and (C5) of aromatic ring in the region and 193.0 ppm signal carbonyl group in the region. 1,3,4-oxadiazole derivative (9) was synthesized from heating 1 and benzoic acid in the presence of trifluoro acetic acid. The <sup>1</sup>H NMR spectrum revealed δ 3.3 ppm signals (-CH<sub>2</sub>) protons of methylene and δ 7.3-6.3 ppm the (-CH) protons of aromatic

ring. The <sup>13</sup>C NMR spectrum revealed δ 162.1, 158.6 ppm signals carbons of (C2) and (C5) in the region and δ 28.4 ppm signals of methylene carbons, respectively. A series hydrazones 10a-e were synthesized from condensation of compound 1 and aromatic aldehydes (benzaldehyde, 2-hydroxybenzaldehyde, 2-hydroxy-5-nitrobenzaldehyde, thiophene-2-carbaldehyde, 4-dimethyl amino benzaldehyde) in ethanol in Scheme 2.

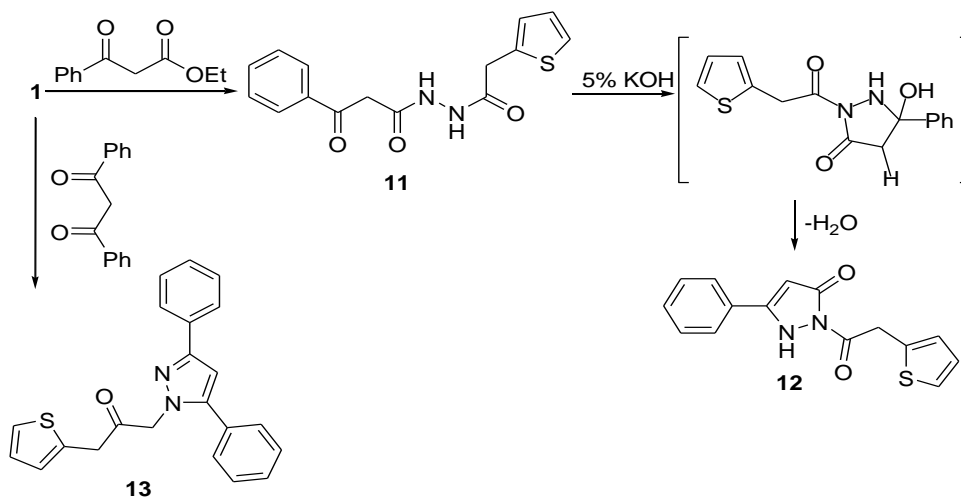


Scheme 2. Synthesis of 8, 9 and 10a-e

The IR spectrum of compounds 10a-e showed corresponding absorption bands between 3345 and 3210 cm<sup>-1</sup> (-NH) of hydrazones, besides between 1682 and 1675 cm<sup>-1</sup> imine peaks (C=N). IR spectrum showed 1668, 1664, 1662, 1656 and 1667 cm<sup>-1</sup> (C=O) carbonyl peaks of hydrazones, respectively. The <sup>1</sup>H NMR spectrum revealed between δ 4.3 and 2.9 ppm signals

(-CH<sub>2</sub>) protons of methylene, δ 7.9-6.5 ppm the (-CH) protons of aromatic ring, around δ 8.2 ppm proton of imine signals (-N=CH) in the region. 3-oxo-3-phenyl-N-(2-(thiophen-2-yl)acetyl)propane hydrazone (11) was synthesized by refluxing reaction of compound 1 and ethyl benzoylacetate in Scheme 3.





Scheme 3. Synthesis of 11, 12 and 13

IR spectrum of compound 11 showed 3296, 3257  $\text{cm}^{-1}$  absorption bands corresponding (-NH) groups and 1668, 1664  $\text{cm}^{-1}$  (C=O) carbonyls groups, respectively. The  $^1\text{H-NMR}$  spectrum revealed  $\delta$  9.9 ppm signals (-NH) protons of molecule  $\delta$  11, 3.1 ppm the signals (-CH<sub>2</sub>) protons of methylene and  $\delta$  8.7-6.6 ppm the (-CH) protons of aromatic ring. The  $^{13}\text{C}$  NMR spectrum revealed  $\delta$  191.3, 164.2 ppm signals carbonyl of groups in the region and  $\delta$  33.09 ppm the signals of methylene carbons, respectively.

3-phenyl-1-(2-(thiophen-2-yl) acetyl)-1,2-dihydro pyrazol-5-one (12) was synthesized from cyclization followed its dehydration and intermediate product which occurred by refluxing compound 11 dissolved potassium hydroxide solution. The IR spectrum of compound 12 showed 3254  $\text{cm}^{-1}$  corresponding (-NH) of pyrazole ring absorption bands and 1678  $\text{cm}^{-1}$  (C=O) carbonyl of pyrazole ring, respectively. The  $^1\text{H-NMR}$  spectrum revealed  $\delta$  2.2 ppm signal (-NH) proton of pyrazole, 3.3 ppm signals (-CH<sub>2</sub>) protons of methylene and  $\delta$  8.1-6.3 ppm the (-CH) protons of aromatic ring. The  $^{13}\text{C}$  NMR spectrum revealed  $\delta$  171.3, 164.3 ppm signals carbons of (C3) and (C5) of aromatic ring and  $\delta$  34.4 ppm the signals of methylene carbons in the region. 2-(3,5-diphenyl-1H-pyrazol-1-yl)-1-(thiophen-2-

yl)ethanone (13) was synthesized from 1 and 1,3-diphenylpropane-1,3-dione with a catalytic amount of DMF in glacial acid. The IR spectrum of compound 13 showed 1648  $\text{cm}^{-1}$  corresponding (C=O) absorption band. The  $^1\text{H}$  NMR spectrum revealed  $\delta$  7.9-6.5 ppm signal (-CH) protons of aromatic ring. The  $^{13}\text{C}$  NMR spectrum revealed  $\delta$  183.4 ppm signal carbonyl group in the region.

## CONCLUSION

The application areas of thiophene-derived polymers are now considerably increased. The areas of their use vary considerably. As we mentioned above, the mostly using area is medicine, agriculture and food industry. Besides, it is known that these compounds have a potential to be used in dye, electronic and opto-electrochromic devices, biodiagnostics and conductivity-based sensor devices too (Roncali, 1992; Kuila and Nandy, 2006; Mortaheb et al., 2012). As it is seen these derives should have different features. All of the synthesized compounds were structurally characterized. Furthermore, new synthesized compounds were carried out against important pathogenic microorganisms. The samples (3-9, 10a-e, 11-13) were separately tested against *Bacillus subtilis* ATCC 6633 and *Staphylococcus aureus* 6538 as examples of Gram-positive bacteria,

*Enterobacter aerogenes* ATCC 13048 and *Escherichia coli* as examples of Gram-negative bacteria (Ren et al., 2002). The present results indicated that these compounds were not showed antibacterial activity. The further studies must be done for the electronic, opto-electrochromic or bio diagnostics features.

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