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## SYNTHESIS AND ANTIMICROBIAL EVALUATION OF NEW THIOPHENE AND 1,3,4-THIADIAZOLE DERIVATIVES

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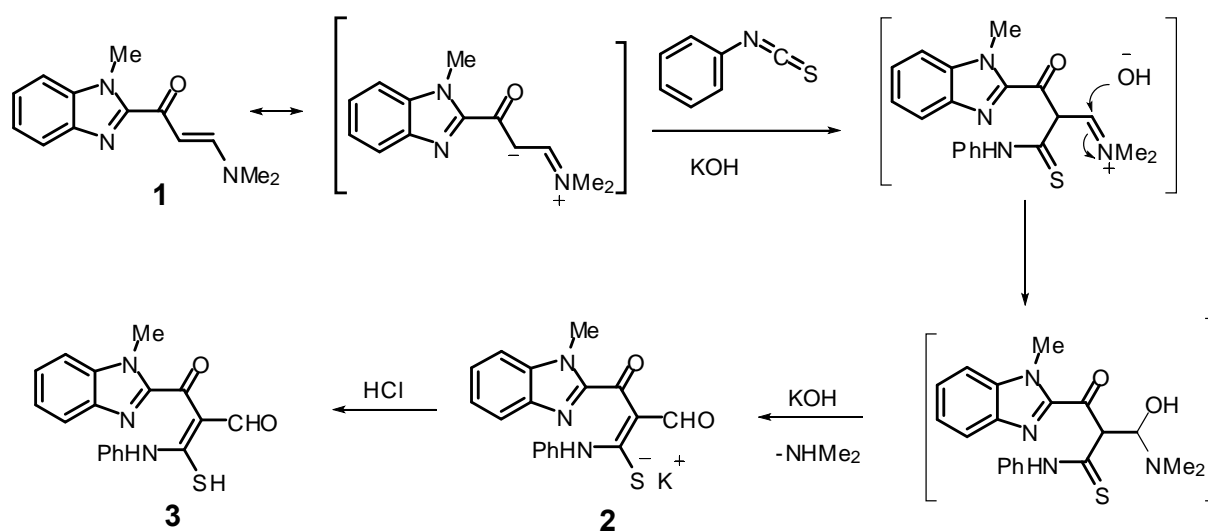
**Abstract** – A Facile route to some new thiophene derivatives *via* the reaction of 3-mercapto-2-(1-methylbenzimidazole-2-carbonyl)-3-phenylaminopropenal (**3**) with 1-aryl-2-bromoethanones, chloroacetonitrile and ethyl bromoacetate is reported. Reaction of **3** with hydrazonoyl halides afforded 1,3,4-thiadiazole derivatives incorporating a benzimidazole moiety. Antimicrobial and antifungal activities of selected examples of the new products were evaluated.

### INTRODUCTION

Enaminones are readily obtainable building blocks and their utility in heterocyclic synthesis has received a considerable interest.<sup>1,2,3,4,5,6,7</sup> Although the utility of the electron deficient C-1 and C-3 in enaminones towards nucleophiles has been extensively investigated, a little has been reported on reactivity of the electron rich C-2 in these compounds.<sup>8,9</sup> On the other hand, benzimidazole derivatives are among heterocyclic ring systems that have a wide range of unique pharmacological and biological potentialities. Some of benzimidazole derivatives are now included in many of commercialized drugs.<sup>10,11</sup> In continuation of our recent interest in the synthesis of heterocycles containing benzimidazole moiety,<sup>6,12</sup> we report here on the reaction of the versatile *E*-1-(1-methylbenzimidazol-2-yl)-3-*N,N*-dimethylaminoprop-2-enone (**1**) with phenyl isothiocyanate and the utility of the product 3-mercapto-2-(1-methylbenzimidazole-2-carbonyl)-3-phenylaminopropenal (**3**) in the synthesis of the titled compounds.

### RESULTS AND DISCUSSION

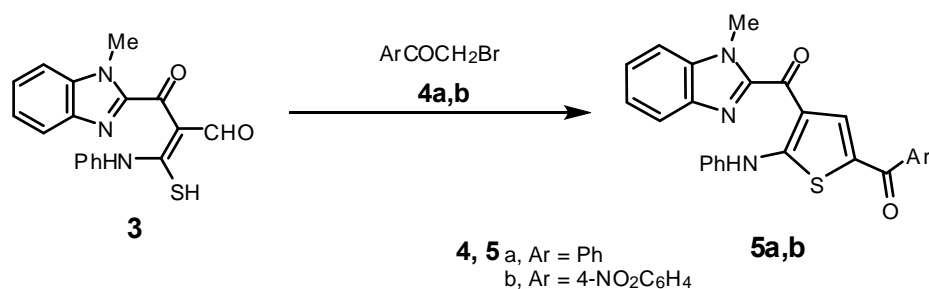
When *E*-1-(1-methylbenzimidazol-2-yl)-3-*N,N*-dimethylaminoprop-2-enone (**1**) was treated with phenyl isothiocyanate, in the presence of potassium hydroxide, it afforded the corresponding potassium salt **2**. The latter product was converted into 3-mercapto-2-(1-methylbenzimidazole-2-carbonyl)-3-phenylaminopropenal (**3**) upon treatment with hydrochloric acid (Scheme 1).



Scheme 1

The IR spectrum of compound **3** showed bands at 3346, 1670 and 1655  $\text{cm}^{-1}$  due to NH group and two carbonyl functions, respectively. A plausible mechanism for the formation of compound **3** is outlined in Scheme 1.

Compound **3** reacts with 1-aryl-2-bromoethanones **4a,b** in the presence of an equivalent amount of triethylamine to afford the corresponding thiophene derivatives **5a,b** (Scheme 2).

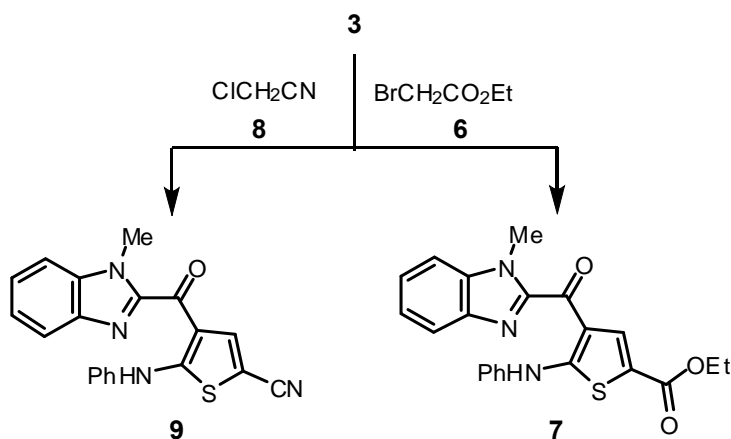


Scheme 2

The structures of the products **5a,b** were established by their elemental analysis and spectral data. For example, the IR spectrum of the compound **5a** showed an absorption band at 3323  $\text{cm}^{-1}$  due to NH group and two strong absorption bands at 1675, 1645  $\text{cm}^{-1}$  due to two carbonyl functions. The mass spectra of the isolated products showed, in each case, a peak corresponding to the molecular ion (see Experimental Part).

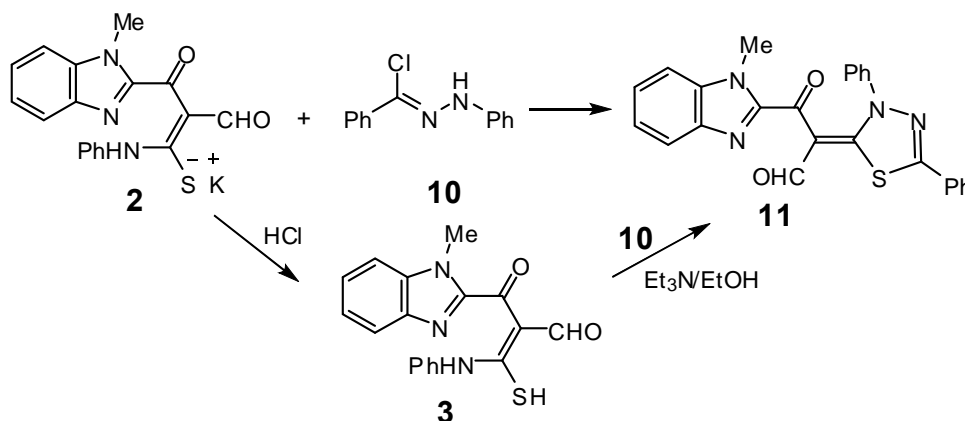
Similarly, compound **3** reacts with ethyl 2-bromoacetate (**6**) to afford 3-(1-methylbenzimidazol-2-yl)carbonyl-2-phenylaminothiophene-5-ethyl carboxylate (**7**) (Scheme 3). The structure of the latter product was assigned on the basis of its  $^1\text{H}$  NMR spectrum which revealed a triplet signal at  $\delta$  1.13 and a quartet signal at  $\delta$  4.12 ( $J = 6.9$  Hz) characteristic for  $\text{CH}_3\text{CH}_2$ -protons. Its IR spectrum showed band at 3319  $\text{cm}^{-1}$  due to NH group. The mass spectrum of the same product revealed a peak corresponding to its

molecular ion at  $m/z$  405. In a similar manner, compound **3** reacts with chloroacetonitrile (**8**) to give the corresponding 5-cyano-3-(1-methylbenzimidazol-2-yl)carbonyl-2-phenylaminothiophene (**9**) (Scheme 3). The IR spectrum of the latter product revealed an absorption band at  $3332\text{ cm}^{-1}$  due to NH group and a strong absorption band at  $2192\text{ cm}^{-1}$  due to nitrile function.



Scheme 3

Treatment of the potassium salt intermediate **3** with *N*-phenylbenzohydrazonoyl chloride (**10**) afforded a single product (as examined by TLC) which was identified as 3,5-diphenyl-2-(1-methylbenzimidazol-2-oyl-2-formylmethylidene)-2,3-dihydro-1,3,4-thiadiazole (**11**) (Scheme 4).

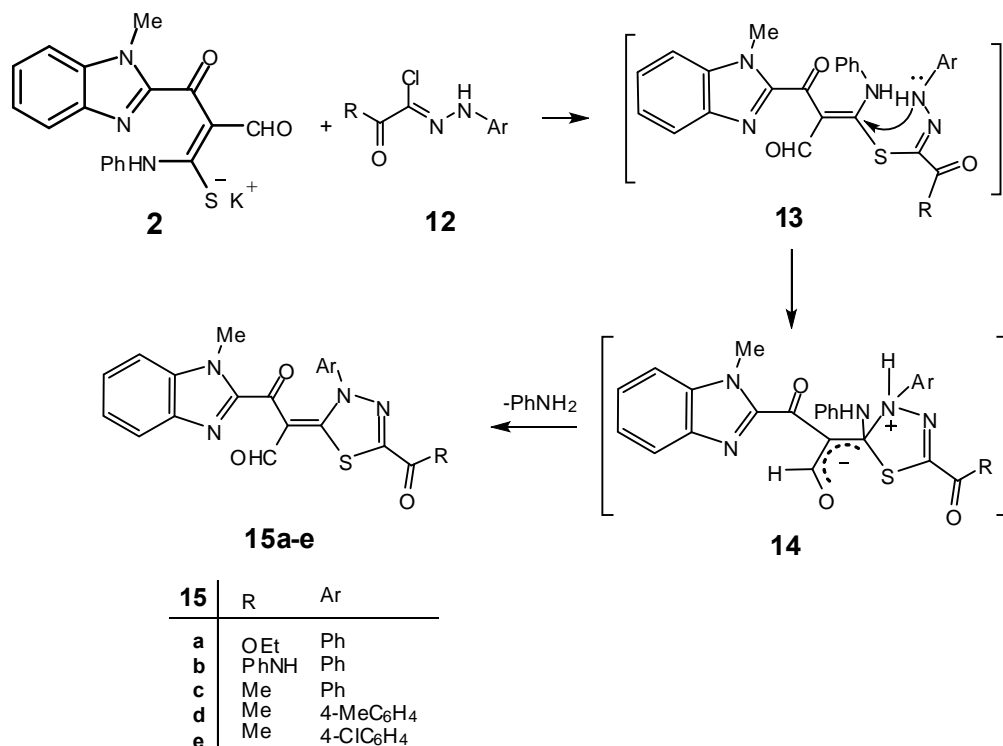


Scheme 4

The structure of compound **11** was supported by its alternate synthesis from the reaction of 3-mercapto-2-(1-methylbenzimidazole-2-carbonyl)-3-phenylaminopropenal (**3**) with the hydrazonoyl chloride **10** in the presence of triethylamine (Scheme 4).

In a similar manner, the hydrazonoyl halides **12a-e** react with the potassium salt intermediate **3**, to afford, the corresponding thiadiazole derivatives **15a,b** (Scheme 5). The structure of thiadiazole derivatives **15a-e** was assigned on the basis of their elemental analysis and spectral data. For example, the  $^1\text{H}$  NMR

spectrum of compound **15a**, revealed a triplet signal at  $\delta$  1.25 and a quartet signal at  $\delta$  4.06 ( $J = 6.9$  Hz) characteristic for  $\text{CH}_3\text{CH}_2$ -protons. The mass spectrum of the same compound revealed a peak corresponding to its molecular ion at  $m/z$  434. Also, its IR spectrum showed three strong absorption bands at 1680, 1665, 1650  $\text{cm}^{-1}$  and 2759  $\text{cm}^{-1}$ , due to three carbonyl functions and CH of formyl group, respectively.



Scheme 5

## EXPERIMENTAL

All melting points were measured on a Gallenkamp melting point apparatus. The infrared spectra were recorded in potassium bromide disks on a Pye Unicam SP 3300 and Shimadzu FT IR 8101 PC infrared spectrophotometers. The NMR spectra were recorded on a Varian Mercury VX-300 NMR spectrometer.  $^1\text{H}$  spectra were run at 300 MHz and  $^{13}\text{C}$  spectra were run at 75.46 MHz in deuterated chloroform ( $\text{CDCl}_3$ ) or dimethyl sulfoxide ( $\text{DMSO}-d_6$ ). Chemical shifts were related to that of the solvent. Mass spectra were recorded on a Shimadzu GCMS-QP 1000 EX mass spectrometer at 70 e.V. Elemental analyses (C, H, N, S) were carried out at the Microanalytical Center of Cairo University, Giza, Egypt. The enaminone **1**,<sup>6</sup> 1-aryl-2-bromoethanones **4a,b**,<sup>13</sup> and hydrazoneyl halids **10**, **12a-e**<sup>14,15,16,17</sup> were prepared according to the reported literature.

### 3-Mercapto-2-(1-methyl benzimidazol-2-yl)-3-phenylaminopropenal (**3**)

To a stirred solution of KOH (0.56 g, 10 mmol) in DMF (20 mL), *E*-1-(1-methylbenzimidazol-2-yl)-3-

*N,N*-dimethylaminoprop-2-enone **1** (2.29 g, 10 mmol) was added. After stirring for 30 min., phenyl isothiocyanate (1.35 g, 10 mmol) was added to the resulting mixture. Stirring was continued for 6 h, and then poured over crushed ice containing HCl. The solid product so formed was filtered off, washed with water, dried and finally crystallized from EtOH/DMF to afford 3-mercapto-2-(1-methylbenzimidazol-2-oyl)-3-phenylaminopropenal (**3**); Yield: 60%, mp 115-116 °C; IR (KBr)  $\nu_{\max}$  /cm<sup>-1</sup>: 3346 (NH), 2760 (CH formyl) 2590 (SH), 1670, 1655 (2CO); <sup>1</sup>H NMR, (CDCl<sub>3</sub>)  $\delta$  3.21 (s, 3H, CH<sub>3</sub>), 6.93-7.56 (m, 9H, Ar H's), 9.56 (s, 1H, CHO), 9.89 (1s, 1H, SH, D<sub>2</sub>O-exchangable), 11.25 (1s, 1H, NH, D<sub>2</sub>O-exchangable). MS (*m/z*) 337 (M<sup>+</sup>, 44%). Anal. Calcd for C<sub>18</sub>H<sub>15</sub>N<sub>3</sub>O<sub>2</sub>S: C, 64.08; H, 4.48; N, 12.45; S, 9.50. Found: C, 64.23; H, 4.39; N, 12.43; S, 9.46.

**Reaction of 3-mercapto-2-(1-methylbenzimidazol-2-oyl)-3-phenylaminopropenal (3), with 1-aryl-2-bromoethanone 4a,b ethyl bromoacetate 6 and with chloroacetonitril 8**

**General Procedure.** To a solution of compound **3** (0.33 g, 1 mmol) and an appropriate 1-aryl-2-bromoethanone **4**, ethyl bromoacetate (**6**) or chloroacetonitrile (**8**) (1 mmol), in EtOH (20 mL), and triethylamine (0.5 mL) was added. The reaction mixture was refluxed for 4-6 h, and then allowed to cool. The formed solid product was filtered off, washed with EtOH and recrystallized from DMF/H<sub>2</sub>O to afford the corresponding thiophene derivatives **5a,b**, **7** and **9**, respectively.

**5-Benzoyl-3-(1-methylbenzimidazol-2-oyl)-2-phenylaminothiophene (5a)**

Yield: 84%; mp 197-198 °C; IR (KBr)  $\nu_{\max}$  /cm<sup>-1</sup>: 3323 (NH), 1675, 1645 (2 CO); <sup>1</sup>H NMR, (DMSO-*d*<sub>6</sub>)  $\delta$  3.96 (s, 3H, N-CH<sub>3</sub>), 6.35 (s, 1H, Thiophene-4-CH), 7.11-7.72 (m, 14H, ArH's), 10.86 (s, 1H, NH, D<sub>2</sub>O-exchangeable). <sup>13</sup>C NMR,  $\delta$  31.95, 110.25, 111.80, 114.89, 116.58, 121.28, 123.08, 126.85, 134.58, 134.95, 138.26, 140.25, 141.58, 142.00, 144.87, 159.46, 166.25, 179.85, 186.03. MS (*m/z*) 437 (M<sup>+</sup>, 41%). Anal. Calcd for C<sub>26</sub>H<sub>19</sub>N<sub>3</sub>O<sub>2</sub>S: C, 71.38; H, 4.38; N, 9.60; S, 7.33. Found: C, 71.49; H, 4.33; N, 9.58; S, 7.29.

**3-(1-Methylbenzimidazol-2-oyl)-5-(4-nitrobenzoyl)-2-phenylaminothiophene (5b)**

Yield: 82%; mp 220-222 °C; IR (KBr)  $\nu_{\max}$  /cm<sup>-1</sup>: 3390 (NH), 1670, 1650 (2 CO); <sup>1</sup>H NMR, (DMSO-*d*<sub>6</sub>)  $\delta$  3.90 (s, 3H, N-CH<sub>3</sub>), 6.52 (s, 1H, Thiophene-4-CH), 7.01-7.56 (m, 13H, ArH's), 10.99 (s, 1H, NH, D<sub>2</sub>O-exchangeable). <sup>13</sup>C NMR,  $\delta$  31.92, 110.85, 112.58, 114.80, 117.09, 121.28, 122.98, 127.55, 134.56, 137.76, 140.88, 142.00, 142.58, 144.87, 150.20, 157.92, 166.25, 179.55, 185.01. MS (*m/z*) 482 (M<sup>+</sup>, 54%). Anal. Calcd for C<sub>26</sub>H<sub>18</sub>N<sub>4</sub>O<sub>4</sub>S: C, 64.72; H, 3.76; N, 11.61; S, 6.65. Found: C, 64.85; H, 3.73; N, 11.56; S, 6.60.

**3-(1-Methylbenzimidazol-2-oyl)-2-phenylaminothiophene-5-ethylcarboxylate (7)**

Yield: 85%; mp 214-215 °C; IR (KBr)  $\nu_{\max}$  /cm<sup>-1</sup>: 3319 (NH), 1720, 1650 (2 CO); <sup>1</sup>H NMR, (DMSO-*d*<sub>6</sub>)  $\delta$  1.13 (t, 3H, CH<sub>3</sub>, *J* = 6.9 Hz), 3.96 (s, 3H, N-CH<sub>3</sub>), 4.12(q, 2H, CH<sub>2</sub>, *J* = 6.9 Hz), 6.46 (s, 1H, thiophene-4-CH), 7.27-7.75 (m, 9H, ArH's), 10.25 (s, 1H, NH, D<sub>2</sub>O-exchangable). <sup>13</sup>C NMR,  $\delta$  18.25, 31.92, 58.72, 110.22, 111.95, 114.21, 114.39, 121.28, 127.55, 129.55, 132.98, 134.56, 136.89, 140.05,

143.90, 159.92, 175.15, 181.21. MS ( $m/z$ ) 405 ( $M^+$ , 29%). Anal. Calcd for  $C_{22}H_{19}N_3O_3S$ : C, 65.17; H, 4.72; N, 10.36; S, 7.91. Found: C, 65.22; H, 4.81; N, 10.25; S, 7.88.

### 5-Cyano-3-(1-methylbenzimidazol-2-oyl)-2-phenylaminothiophene (9)

Yield: 80%; mp 179-180 °C; IR (KBr)  $\nu_{\max}$  / $cm^{-1}$ : 3332 (NH), 2192 (CN), 1670 (CO);  $^1H$  NMR, (DMSO- $d_6$ )  $\delta$  3.62 (s, 3H, N-CH<sub>3</sub>), 6.59 (s, 1H, thiophene-4-CH), 7.11-7.65 (m, 9H, ArH's), 9.28 (s, 1H, NH, D<sub>2</sub>O-exchangable).  $^{13}C$  NMR,  $\delta$  31.92, 110.22, 111.95, 112.85, 114.21, 114.39, 121.28, 123.55, 132.98, 134.56, 136.89, 142.58, 144.90, 159.92, 178.15. MS ( $m/z$ ) 358 ( $M^+$ , 38%). Anal. Calcd for  $C_{20}H_{14}N_4OS$ : C, 67.02; H, 3.94; N, 15.63; S, 8.95. Found: C, 67.13; H, 3.86; N, 15.57; S, 8.98.

### Reaction of 3-mercapto-2-(1-methylbenzimidazol-2-oyl)-3-phenylaminopropenal (3) or its potassium salt intermediate 2, with hydrazonoyl halid 10 or 12a-e

**General procedure: Method A.** To a solution of compound **3** (0.33 g, 1 mmol) in EtOH (20 mL), and an appropriate hydrazonoyl halide **10** or **12** (1 mmol), triethylamine (0.5 mL) was added. The reaction mixture was heated under reflux, where a colored precipitate started to take place within 5-20 min., heating was continued for further 2 h, then the reaction mixture allowed to cool. The formed solid was filtered off, washed with EtOH and recrystallized from EtOH/DMF to afford the corresponding thiadiazole derivatives **11** and **15a-e** respectively in 80-85% yields.

**Method B.** The appropriate hydrazonoyl halide **10** or **12** (10 mmol) was added portionwise over a period of 30 min. to a solution of potassium salt intermediate **2**, and the reaction mixture was stirred for 12 h, during which hydrazonoyl halide dissolved and a yellowish-red colored product precipitated. The solid product was filtered off, washed with water, dried and recrystallized from EtOH/DMF to afford products identical in all respect (mp, mixed mp and spectra) with those obtained by method A above.

### 3,5-Diphenyl-2-(1-methylbenzimidazol-2-oyl-2-formylmethylidene)-2,3-dihydro-1,3,4-thiadiazole (11)

Yield: 81%; mp 231-233 °C; IR (KBr)  $\nu_{\max}$  / $cm^{-1}$ : 2753 (CH formyl), 1665, 1652 (2 CO), 1590 (C=N);  $^1H$  NMR, (DMSO- $d_6$ )  $\delta$  3.81 (s, 3H, N-CH<sub>3</sub>), 7.17-7.88 (m, 14H, ArH's), 9.79 (s, 1H, CHO).  $^{13}C$  NMR,  $\delta$  31.92, 102.56, 110.98, 114.78, 119.68, 121.87, 123.09, 127.50, 130.02, 132.55, 134.56, 136.89, 142.58, 144.90, 146.80, 166.05, 185.01, 186.00. MS ( $m/z$ ) 438 ( $M^+$ , 40%). Anal. Calcd for  $C_{25}H_{18}N_4O_2S$ : C, 68.48; H, 4.14; N, 12.78; S, 7.31. Found: C, 68.33; H, 4.22; N, 12.83; S, 7.33.

### 2-(1-Methylbenzimidazol-2-oyl-2-formylmethylidene)-3-phenyl-2,3-dihydro-1,3,4-thiadiazole-5-ethyl carboxylate (15a)

Yield: 78%; mp 245-247 °C; IR (KBr)  $\nu_{\max}$  / $cm^{-1}$ : 2759 (CH formyl), 1680, 1665, 1650 (3 CO), 1601 (C=N);  $^1H$  NMR, (DMSO- $d_6$ )  $\delta$  1.25 (t, 3H, CH<sub>3</sub>,  $J = 6.9$  Hz), 3.66 (s, 3H, N-CH<sub>3</sub>), 4.06 (q, 2H, CH<sub>2</sub>,  $J = 6.9$  Hz), 6.97-7.55 (m, 9H, ArH's), 9.99 (s, 1H, CHO).  $^{13}C$  NMR,  $\delta$  17.09, 31.91, 59.98, 110.98, 114.78, 119.68, 121.87, 123.01, 123.09, 127.50, 132.85, 134.64, 136.89, 141.20, 146.45, 156.78, 166.89, 185.01, 186.00. MS ( $m/z$ ) 434 ( $M^+$ , 24%). Anal. Calcd for  $C_{22}H_{18}N_4O_4S$ : C, 60.82; H, 4.18; N, 12.90; S, 7.38.

Found: C, 60.76; H, 4.22; N, 12.83; S, 7.47.

**5-(Carboxamido-*N*-phenyl)-2-(1-Methylbenzimidazol-2-oyl-2-formylmethylidene)-3-phenyl-2,3-dihydro-1,3,4-thiadiazole (15b)**

Yield: 80%; mp 295-297 °C; IR (KBr)  $\nu_{\max}$  /cm<sup>-1</sup>: 3395 (NH), 2759 (CH formyl), 1680, 1669, 1650 (3 CO), 1601 (C=N); <sup>1</sup>H NMR, (DMSO-*d*<sub>6</sub>)  $\delta$  3.79 (s, 3H, N-CH<sub>3</sub>), 7.07-7.88 (m, 14H, ArH's), 9.89 (s, 1H, CHO), 10.96 (s, 1H, NH, D<sub>2</sub>O-exchangable). <sup>13</sup>C NMR,  $\delta$  31.91, 110.05, 114.50, 118.98, 120.85, 121.89, 122.52, 123.45, 129.50, 129.78, 132.02, 134.89, 136.05, 141.00, 146.65, 158.01, 159.99, 165.00, 186.81, 188.00. MS (*m/z*) 481 (M<sup>+</sup>, 34%). Anal. Calcd for C<sub>26</sub>H<sub>19</sub>N<sub>5</sub>O<sub>3</sub>S: C, 64.85; H, 3.98; N, 14.54; S, 6.66. Found: C, 64.76; H, 3.92; N, 14.60; S, 6.75.

**5-Acetyl-2-(1-methylbenzimidazol-2-oyl-2-formylmethylidene)-3-phenyl-2,3-dihydro-1,3,4-thiadiazole (15c)**

Yield: 85%; mp 278-280 °C; IR (KBr)  $\nu_{\max}$  /cm<sup>-1</sup>: 2759 (CH formyl), 1675, 1650, 1645 (3 CO), 1598 (C=N); <sup>1</sup>H NMR, (DMSO-*d*<sub>6</sub>)  $\delta$  2.55 (s, 3H, CH<sub>3</sub>), 3.67 (s, 3H, N-CH<sub>3</sub>), 7.27-7.78 (m, 9H, ArH's), 10.02 (s, 1H, CHO). <sup>13</sup>C NMR,  $\delta$  24.06, 31.92, 110.15, 114.00, 118.18, 120.85, 121.19, 129.78, 134.58, 136.95, 141.10, 146.55, 157.91, 159.19, 186.81, 188.00, 193.85. MS (*m/z*) 404 (M<sup>+</sup>, 43%). Anal. Calcd for C<sub>21</sub>H<sub>16</sub>N<sub>4</sub>O<sub>3</sub>S: C, 62.36; H, 3.99; N, 13.85; S, 7.93. Found: C, 62.33; H, 3.92; N, 13.90; S, 7.98.

**5-Acetyl-2-(1-methylbenzimidazol-2-oyl-2-formylmethylidene)-3-(4-methylphenyl)-2,3-dihydro-1,3,4-thiadiazole (15d)**

Yield: 76%; mp 258-260 °C; IR (KBr)  $\nu_{\max}$  /cm<sup>-1</sup>: 2760 (CH formyl), 1680, 1655, 1645 (3 CO), 1606 (C=N); <sup>1</sup>H NMR, (DMSO-*d*<sub>6</sub>)  $\delta$  2.25 (s, 1H, CH<sub>3</sub>), 2.79 (s, 3H, COCH<sub>3</sub>), 3.65 (s, 3H, N-CH<sub>3</sub>), 7.17-7.48 (m, 8H, ArH's), 10.25 (s, 1H, CHO). <sup>13</sup>C NMR,  $\delta$  20.35, 24.06, 31.92, 110.58, 114.60, 120.85, 121.65, 129.05, 129.78, 134.88, 136.95, 141.10, 145.85, 157.01, 159.51, 186.90, 188.00, 193.79. MS (*m/z*) 418 (M<sup>+</sup>, 34%). Anal. Calcd for C<sub>22</sub>H<sub>18</sub>N<sub>4</sub>O<sub>3</sub>S: C, 63.14; H, 4.34; N, 13.39; S, 7.66. Found: C, 63.05; H, 4.29; N, 13.46; S, 7.73.

**5-Acetyl-3-(4-chlorophenyl)-2-(1-methylbenzimidazol-2-oyl-2-formylmethylidene)-2,3-dihydro-1,3,4-thiadiazole (15e)**

Yield: 84%; mp 297-298 °C; IR (KBr)  $\nu_{\max}$  /cm<sup>-1</sup>: 2760 (CH formyl), 1680, 1655, 1649 (3 CO), 1596 (C=N); <sup>1</sup>H NMR, (DMSO-*d*<sub>6</sub>)  $\delta$  2.75 (s, 3H, COCH<sub>3</sub>), 3.65 (s, 3H, N-CH<sub>3</sub>), 7.03-7.58 (m, 8H, ArH's), 10.35 (s, 1H, CHO). <sup>13</sup>C NMR,  $\delta$  24.16, 31.92, 110.18, 114.62, 120.55, 121.55, 129.15, 129.88, 134.89, 136.95, 141.10, 145.86, 157.10, 159.51, 186.91, 188.00, 193.70. MS (*m/z*) 438 (M<sup>+</sup>, 54%). Anal. Calcd for C<sub>21</sub>H<sub>15</sub>ClN<sub>4</sub>O<sub>3</sub>S: C, 57.47; H, 3.44; N, 12.77; S, 7.31. Found: C, 57.56; H, 3.50; N, 12.67; S, 7.26.

## BIOLOGICAL EVALUATION

The antibacterial and antifungal activity were carried out at the Microbiology Division of Microanalytical Center of Cairo university, using the diffusion plate method.<sup>18,19,20</sup> A bottomless cylinder

containing a measured quantity (1mL, mg/mL) of the sample was placed on a plate (9 cm diameter) containing a solid bacterial medium (nutrient agar broth) or fungal medium (Dox's medium) which has been heavily seeded with the spore suspension of the test organism. After incubation (24 h for bacteria and 5 days for fungi), the diameter of the clear zone of inhibition surrounding the sample is taken as measure of the inhibitory power of the sample against the particular test organism. The test results are depicted in Table 1.

**Table 1. Antibacterial and Antifungal Activities of the Synthesized Compounds**

COMPOUNDS NO.	INHIBITION ZONE DIAMETER (IZD) (MM/MG OF COMPOUND TESTED)		
	Gram (-)	Gram (+)	Fungus
	(EC)	(SA)	(CA)
<b>Control</b>	0.0	0.0	0.0
<b>5a</b>	16 ++	16 ++	14 ++
<b>5b</b>	14 ++	13 +	12 ++
<b>7</b>	11 ++	12 ++	11 ++
<b>9</b>	11 ++	11 ++	11 ++
<b>11</b>	16 ++	16 ++	13 ++
<b>15a</b>	11 ++	12 ++	12 ++
<b>15b</b>	12 ++	13 ++	11 ++
<b>15c</b>	16 ++	17 ++	12 ++
<b>15d</b>	13 ++	14 ++	12 ++
<b>Amphotericin B</b>	--	--	18 ++
<b>Tetracycline</b>	26 +++	22 ++	--

The test results are on the following basis:

The solvent used: ethanol.

Concentration of the sample in 100 µg/mL.

IZD = 2-10 mm beyond control = + (low activity).

IZD = 11-24 mm beyond control = ++ (moderate activity).

IZD = 25-35 mm beyond control = +++ (high activity).

The selected compounds were tested *in vitro* against gram negative bacteria, Escherichia coli anaerobic (EC), gram positive bacteria, Staphylococcus aureus (SA), and antifungal activity against Candida albicans (CA). Tetracycline and Amphotricine were used as references antibiotics to evaluate the potency of the tested compounds under the same condition.

The test results revealed that all compounds exhibited moderate activity against two bacterial species and Candida albicans (CA).

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