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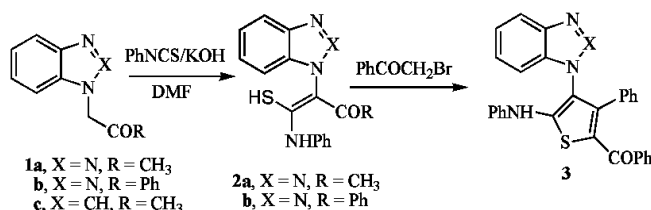
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Synthesis of new azolyl azoles and azinyl azoles from the reaction of compounds **1**, **4** and **7** with phenyl isothiocyanate is reported. Compound **10** reacts with benzene diazonium chloride to yield either phenylhydrazones **11** and **12** or the triazoloquinoline **13**.

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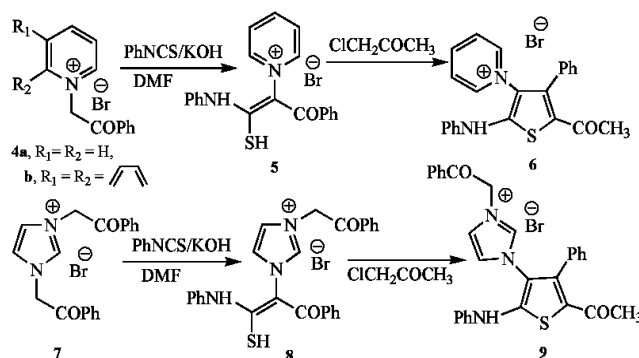
It is known that a methylene group attached to nitrogen atoms of azoles is activated toward electrophilic reagents and this feature has stimulated recent interest in the utility of azolylmethyl ketones as building block in heterocyclic chemistry [1-7]. In conjunction with previous work [7-9], we now report the synthesis of the title compounds **1**, **4**, **7** and **10**. As part of our ongoing program, we decided to synthesize new *N*-heteroarylazoles in order to explore the biological properties and the pyrolysis in the gas phase.

Scheme 1



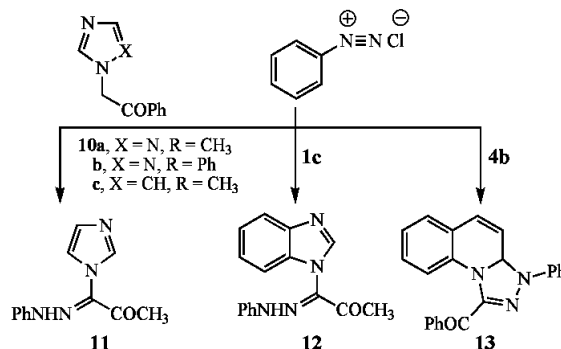
Compounds **1a** and **1b** react with phenyl isothiocyanate in dimethylformamide (DMF) in the presence of potassium hydroxide and after acidification of the reaction mixture compounds **2a** and **2b** are obtained. Analysis of <sup>13</sup>C-nmr data of compounds **2a** and **2b** shows a signal at *ca.* 190 ppm which is assigned to the presence of conjugated carbonyl carbon (CO) and the signal corresponding to the methylene group was not observed. NOE experiments show that the *Z* isomer of compound **2** was preferred over the *E* isomer indicating that the Ph and the R groups are close to each other (Figure 1). Similarly, compounds **4a** and **7** react with phenyl isothiocyanate to yield compounds **5** and **8** but these compounds could not be isolated. However, when compounds **2b**, **5a** and **8** were treated with chloroacetone or phenacyl bromide in the presence of potassium hydroxide thiophene derivatives **3**, **6**, and **9** were formed and isolated in good yields (see Schemes 1 and 2). Compounds **4b**, **10a** and **10b** failed to react with phenyl isothiocyanate under a variety of experimental conditions; diphenylthiourea was the only product isolated from these reactions.

Scheme 2



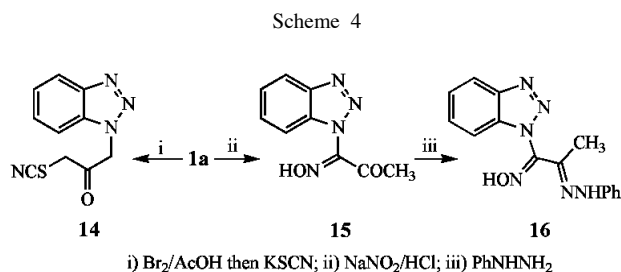
Like in previous reports [6] compounds **1c** and **10c** react with benzene diazonium chloride to yield the arylhydrazones **11** and **12**. However, these compounds did not condense with active methylene reagents, such as malononitrile derivatives, to yield pyridazinones as it was reported for benzotriazolyl derivatives [3]. Reaction of compound **4b** with benzenediazonium chloride did not afford the expected arylhydrazones, instead compound **13** was formed. This compound could be formed *via* further cyclization under these reaction conditions (see Scheme 3).

Scheme 3



Treatment of **1a** with bromine in acetic acid followed by reaction with potassium thiocyanate led to the thiocyanate

derivative **14**. Compound **1a** reacted with sodium nitrite in the presence of hydrochloric acid to yield oxime **15** which gave the phenylhydrazone **16** when reacted with phenylhydrazine. In a previous report [8] we assumed that oxime **15** underwent Beckman rearrangement. In fact, we verified that the Beckman rearrangement of oxime **15** did not take place under different experimental conditions (Scheme 4).



The presented results when combined with previous reports [3-9] clearly demonstrate that 2-azoly-1-substituted ethanones are valuable precursor for N-heteroaryl substituted azoles that are of interest for potential biological activity evaluation.

## EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded in KBr with a Pye Unicam SP 1100 spectrophotometer.  $^1\text{H}$  Nmr and  $^{13}\text{C}$  nmr were run in deuteriochloroform or dimethylsulfoxide- $d_6$  at 400 MHz with a Varian EM-390 spectrometer. Chemical shifts are reported in ppm values, using TMS as internal standard. Mass spectra were obtained under electron impact on MS 30 and MS 9 (AEI) at 70 eV. Microanalyses were performed on LECO CHNS-932. Compounds **1-3** were prepared following on published procedure [9].

### 1-Benzimidazol-1-yl-propan-2-one (**1c**).

To a solution of benzimidazole (1.18 g, 10 mmol) and triethylamine (1 ml) in acetone (20 ml) was added chloroacetone (0.91 g, 10 mmol) and the reaction mixture was refluxed for 4 hrs. After removal of the triethylamine hydrochloride by filtration, the filtrate was evaporated under vacuum and the resulting solid was collected and crystallized from toluene to give **1c** in 77 % yield, mp 136-137 °C, IR (KBr):  $\nu$  1720 (CO)  $\text{cm}^{-1}$ ;  $^1\text{H}$  nmr; (dimethylsulfoxide- $d_6$ ):  $\delta$  = 8.11 (s, 1H benzimidazole H-2), 7.79-7.19 (m, 4H benzimidazolyl H), 5.32 (s, 2H,  $\text{CH}_2$ ), 2.24 (s, 3H,  $\text{CH}_3$ );  $^{13}\text{C}$  nmr; (dimethylsulfoxide- $d_6$ ):  $\delta$  = 203.32 (CO), 145.6, 144.1, 142.9, 122.8, 122.5, 120.3, 116.3, 111.5, 54.3 ( $\text{COCH}_2$ ), 27.9 ( $\text{CH}_3$ ).

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_{10}\text{N}_2\text{O}$  (174.20): C, 68.94; H, 5.78; N, 16.08. Found: C, 68.97; H, 5.76; N, 16.08.

### Preparation of Compounds **2a** and **2b**.

#### General Procedure.

To a stirred suspension of **1a** (or **1b**) (10 mmol) and phenyl isothiocyanate (1.35 g, 10 mmol) in dimethylformamide (20 ml)

and potassium hydroxide (0.06 g) was stirred overnight. The solvent was evaporated and the residue was ground with water and then neutralized with concentrated hydrochloric acid. The solid product so formed was collected and crystallized from ethanol.

### 3-Benzotriazol-1-yl-4-mercapto-4-phenylamino-but-3-en-2-one (**2a**).

This compound was obtained in 55 % yield, mp 172-173 °C, IR (KBr):  $\nu$  3010 (NH), 1654 (CO)  $\text{cm}^{-1}$ ;  $^1\text{H}$  nmr; (dimethylsulfoxide- $d_6$ ):  $\delta$  = 15.47 (s, 1H, SH), 8.21 (s, 1H, NH), 7.66-7.25 (m, 9H, Ar-H), 1.69 (s, 3H,  $\text{CH}_3$ );  $^{13}\text{C}$  nmr; (dimethylsulfoxide- $d_6$ ):  $\delta$  = 196.1 (CO), 146.2, 132.9, 130.2, 129.5, 128.5, 124.2, 118.9, 115.1, 113.5, 25.3 ( $\text{CH}_3$ ).

*Anal.* Calcd. for  $\text{C}_{16}\text{H}_{14}\text{N}_4\text{OS}$  (310.37): C, 61.91; H, 4.54; N, 18.05; S, 10.33. Found: C, 61.90; H, 4.61; N, 18.07; S, 10.34.

### 2-Benzotriazol-1-yl-3-mercapto-1-phenyl-3-phenylamino-propenone (**2b**).

This compound was obtained in 61 % yield, mp 174-176 °C, IR (KBr):  $\nu$  3163 (NH), 1607 (CO)  $\text{cm}^{-1}$ ;  $^1\text{H}$  nmr; (dimethylsulfoxide- $d_6$ ):  $\delta$  = 15.84 (s, 1H, SH), 8.38 (s, 1H, NH), 7.91-7.01 (m, 14H Ar-H);  $^{13}\text{C}$  nmr; (dimethylsulfoxide- $d_6$ ):  $\delta$  = 195.1 (CO), 190.3, 146.3, 139.9, 136.1, 134.3, 123.0, 129.5, 128.9, 128.5, 127.67, 125.4, 124.2, 123.9, 120.3, 113.2, 72.8.

*Anal.* Calcd. for  $\text{C}_{21}\text{H}_{16}\text{N}_4\text{OS}$  (372.44): C, 67.72; H, 4.32; N, 15.04; S, 8.6. Found: C, 67.70; H, 4.52; N, 15.16; S, 8.41.

### Preparation of Compounds **3**, **6** and **9**.

#### General Procedure.

To a stirred suspension of compound **1b** (or **4a** or **7**) (10 mmol), phenyl isothiocyanate (1.35 g, 10 mmol) and potassium hydroxide (0.06 g) in DMF (20 ml) the  $\alpha$ -haloketone (10 mmol) was added. The reaction mixture was stirred for 16 hours. Then, the reaction mixture was heated under reflux for an additional 4 hours. The solvent was evaporated under vacuum and the residue was ground with water and neutralized with concentrated hydrochloric acid. The solid product so formed was collected and crystallized from dioxane.

### (4-Benzotriazol-1-yl-3-phenyl-5-phenylamino-thiophen-2-yl)-phenyl-methanone (**3**).

This compound was obtained in 56 % yield, mp 282-283 °C, IR (KBr):  $\nu$  3049 (NH), 1622 (CO)  $\text{cm}^{-1}$ ;  $^1\text{H}$  nmr; (dimethylsulfoxide- $d_6$ ):  $\delta$  = 9.88 (s, 1H, NH), 9.36 (s, 1H imidazol H-2), 8.05-7.17 (m, 17H, 3phenyl and imidazole H-4, H-5), 5.98 (s, 2H  $\text{CH}_2$ ), 1.80 (s, 3H,  $\text{CH}_3$ ).

*Anal.* Calcd. for  $\text{C}_{29}\text{H}_{20}\text{N}_4\text{OS}$  (472.56): C, 62.36; H, 4.33; N, 7.52; S, 5.74. Found: C, 62.57; H, 4.53; N, 7.94; S, 5.64.

### 1-(5-Acetyl-4-phenyl-2-phenylamino-thiophen-3-yl)-pyridinium Bromide (**6**).

This compound was obtained in 71 % yield, mp 218-219 °C, IR (KBr):  $\nu$  3057 (NH), 1608 (CO)  $\text{cm}^{-1}$ ;  $^1\text{H}$  nmr; (dimethylsulfoxide- $d_6$ ):  $\delta$  = 9.42 (s, 1H, NH), 8.01-6.74 (m, 19H Ar-H).

*Anal.* Calcd. for  $\text{C}_{23}\text{H}_{19}\text{BrN}_2\text{OS}$  (451.38): C, 73.70; H, 4.26; N, 11.85; S, 6.78. Found: C, 73.74; H, 4.28; N, 11.96; S, 6.82.

### 3-(5-Acetyl-4-phenyl-2-phenylamino-thiophen-3-yl)-1-(2-oxo-2-phenyl-ethyl)-3H-imidazol-1-ium Bromide (**9**).

This compound was obtained in 27 % yield, mp. 198-200 °C, IR (KBr):  $\nu$  3041 (NH), 1622 (CO)  $\text{cm}^{-1}$ ;  $^1\text{H}$  nmr; (dimethylsul-

foxide-d<sub>6</sub>):  $\delta$  = 10.05 (s, 1H, NH), 9.3 (1H pyridyl H-6;  $J$  = 4 Hz), 8.82 (1H pyridyl H-4), 8.3 (m, 2H, pyridyl H-3, H-5), 7.72-7.01 (m, 10H Ar-H), 1.95 (s, 3H, CH<sub>3</sub>).

*Anal.* Calcd. for C<sub>29</sub>H<sub>24</sub>BrN<sub>3</sub>O<sub>2</sub>S (558.49): C, 61.20; H, 4.24; N, 6.20; S, 7.10. Found: C, 61.22; H, 4.64; N, 6.14; S, 6.67.

#### 1,3-Bis-(2-oxo-2-phenylethyl)-3H-imidazol-1-ium Bromide (7).

To a solution of imidazole (0.68 g, 10 mmol) and triethylamine (1 ml) in acetone (20 ml) phenacylbromide (1.99 g, 10 mmol) was added. The reaction mixture was refluxed for 2 hrs. The solvent was evaporated under vacuum and the solid product was collected and crystallized from ethanol to give **7** in 74 % yield, mp 264-266 °C, IR (KBr):  $\nu$  3310 (OH), 1690 (CO) cm<sup>-1</sup>; <sup>1</sup>H nmr; (dimethylsulfoxide-d<sub>6</sub>):  $\delta$  = 9.16 (s, 1H imidazole H-2), 8.40-7.66 (m, 12H Ar-H and imidazole H-4 and H-5), 6.24, 6.22 (4H, 2CH<sub>2</sub>).

*Anal.* Calcd. for C<sub>19</sub>H<sub>17</sub>BrN<sub>2</sub>O<sub>2</sub> (385.25): C, 59.27; H, 4.44; N, 7.2. Found: C, 59.27; H, 4.42; N, 7.50.

#### Preparation of Compounds 11, 12 and 13.

##### General Procedure.

A solution of compound **1c** (or **4b** or **10c**) (10 mmol) in ethanol (10 ml) was treated with sodium acetate (2 g) and a solution of aryldiazonium chloride (prepared from the corresponding aromatic amine (10 mmol) and the appropriate quantities of both hydrochloric acid and sodium nitrite) was added dropwise under stirring at room temperature for 1 hour. The solid product was collected by filtration and crystallized from dioxane.

#### 1-Imidazol-1-yl-1-(phenyl-hydrazono)-propan-2-one (11).

This compound was obtained in 61 % yield, mp 248-250 °C, IR (KBr):  $\nu$  3165 (NH), 1678 (CO) cm<sup>-1</sup>; <sup>1</sup>H nmr; (dimethylsulfoxide-d<sub>6</sub>):  $\delta$  = 10.61 (s, 1H, NH), 7.68 (s, 1H imidazol H-2), 7.40 (d, 1H,  $J$  = 8Hz imidazol H-5), 7.36-7.00 (m, 6H, Ar-H and imidazole H-4), 2.51 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C nmr; (dimethylsulfoxide-d<sub>6</sub>):  $\delta$  = 191.8 (CO), 144.0, 138.6, 136.1, 130.6, 129.9, 129.7, 121.2, 115.9, 25.8 (CH<sub>3</sub>).

*Anal.* Calcd. for C<sub>12</sub>H<sub>12</sub>N<sub>4</sub>O (228.25): C, 63.14; H, 5.29; N, 24.54. Found: C, 63.15; H, 5.42; N, 24.59.

#### 1-Benzoimidazol-1-yl-1-(phenyl-hydrazono)-propan-2-one (12).

This compound was obtained in 72 % yield, mp 263-264 °C, IR (KBr):  $\nu$  3165 (NH), 1678 (CO) cm<sup>-1</sup>; <sup>1</sup>H nmr; (dimethylsulfoxide-d<sub>6</sub>):  $\delta$  = 10.82 (s, 1H, NH), 8.22 (s, 1H benzimidazol H-2), 7.77-7.03 (m, 9H, Ar-H), 2.59 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C nmr; (dimethylsulfoxide-d<sub>6</sub>):  $\delta$  = 192.0 (CO), 145.3, 144.1, 143.9, 134.1, 130.3, 128.9, 124.3, 123.9, 121.5, 120.8, 115.9, 110.0, 107.5, 25.8 (CH<sub>3</sub>).

*Anal.* Calcd. for C<sub>16</sub>H<sub>14</sub>N<sub>4</sub>O (278.31): C, 69.05; H, 5.07; N, 20.13. Found: C, 69.00; H, 5.08; N, 20.08.

#### Phenyl-(3-phenyl-3,3a-dihydro-[1,2,4]triazolo[4,3-d]quinolin-1-yl)-methanone (13).

This compound was obtained in 51 % yield, mp 106-108 °C, IR (KBr):  $\nu$  1641 (CO) cm<sup>-1</sup>; <sup>1</sup>H NMR (dimethylsulfoxide-d<sub>6</sub>):  $\delta$  = 8.02 (d, 1H,  $J$  = 8Hz, H5), 7.95 (d, 1H,  $J$  = 8Hz, H6), 7.2-7.92 (m, 13H, Ar-H), 7.01 (d, 1H,  $J$  = 6Hz, H3a), 4.4 (d, 1H,  $J$  = 6Hz, H4); <sup>13</sup>C NMR (dimethylsulfoxide-d<sub>6</sub>):  $\delta$  = 192.00 (CO), 156.2, 144.6, 143.2, 142.7, 135.3, 130.1, 129.5, 128.9m 128.5, 127.5, 127.1, 122.5, 120.5, 118.9, 113.3, 112.5, 111.2, 68.9.

*Anal.* Calcd. for C<sub>23</sub>H<sub>17</sub>N<sub>3</sub>O (351.40): C, 78.61; H, 4.87; N,

11.95. Found: C, 78.68; H, 5.04; N, 11.19.

#### 1-Benzotriazol-1-yl-3-thiocyanato-propan-2-one (14).

A mixture of compound **1a** (1.75 g, 10 mmol) and bromine (0.8 g, 10 mmol) in acetic acid was stirred for 2 hours. After stirring, potassium thiocyanate (0.97 g) was added and the reaction mixture was stirred for additional 4 hours. The reaction mixture was poured onto water and neutralized with a dilute hydrochloric acid solution (0.1 N) resulting in a solid precipitate. The solid residue was collected by filtration and crystallized from dimethylformamide to give **14** in 53 % yield, mp 178-180 °C, IR (KBr):  $\nu$  2156 (CN), 1743 (CO) cm<sup>-1</sup>; <sup>1</sup>H nmr; (dimethylsulfoxide-d<sub>6</sub>):  $\delta$  = 8.09-7.41 (m, 4H, benzotriazole H), 6.00 (2H, CH<sub>2</sub>SCN), 4.56 (CH<sub>2</sub>); <sup>13</sup>C nmr; (dimethylsulfoxide-d<sub>6</sub>):  $\delta$  = 202.2 (CO), 146.0, 134.7, 128.3, 124.9, 120.1, 118.8 (CN), 57.5, 28.2.

*Anal.* Calcd. for C<sub>10</sub>H<sub>8</sub>N<sub>4</sub>OS (232.26): C, 51.71; H, 3.47; N, 24.12; S, 13.80. Found: C, 51.75; H, 3.50; N, 24.24; S, 13.96.

#### 1-Benzotriazol-1-yl-propan-1,2-dione-1-oxime (15).

A suspension of compound **1a** (1.75 g, 10 mmol) and hydrochloric acid (20 ml) in the presence of sodium nitrite (0.69 g) was stirred overnight at room temperature and then poured onto ice water. The solid was collected and crystallized from ethanol to give **15** in 79 % yield, mp 152-154 °C, IR (KBr):  $\nu$  3310 (OH), 1705 (CO) cm<sup>-1</sup>; <sup>1</sup>H nmr; (dimethylsulfoxide-d<sub>6</sub>):  $\delta$  = 13.88 (s, 1H, N-OH), 8.17-7.46 (m, 4H, benzotriazole H), 2.65 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C nmr; (dimethylsulfoxide-d<sub>6</sub>):  $\delta$  = 191.8 (CO), 145.0, 142.9, 133.8, 129.6, 127.6, 125.6, 118.9, 112.5, 25.8 (CH<sub>3</sub>).

*Anal.* Calcd. for C<sub>9</sub>H<sub>8</sub>N<sub>4</sub>O<sub>2</sub> (204.19): C, 52.94; H, 3.94; N, 27.43. Found: C, 52.92; H, 3.41; N, 27.49.

#### 1-Benzotriazol-1-yl-2-(phenylhydrazono)-propan-1-one Oxime (16).

A mixture of compound **15** (2.04 g, 10 mmol) and phenylhydrazine (1.08 g, 10 mmol) in ethanol (10 ml) was refluxed for 1 h. The solvent was evaporated under vacuum, and the solid residue was collected and crystallized from ethanol to give **16** in 54 % yield, mp 198-200 °C, IR (KBr):  $\nu$  3294 (OH), 3012(NH) cm<sup>-1</sup>; <sup>1</sup>H nmr; (dimethylsulfoxide-d<sub>6</sub>):  $\delta$  = 12.55 (s, 1H, N-OH), 9.72 (s, 1H, NH), 8.21-6.52 (m, 9H, benzotriazole H, Ar-H), 2.36 (s, 3H, CH<sub>3</sub>).

*Anal.* Calcd. for C<sub>15</sub>H<sub>14</sub>N<sub>6</sub>O (294.31): C, 61.16; H, 4.79; N, 28.55. Found: C, 61.40; H, 4.83; N, 28.26.

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