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## Part 1: SYNTHESIS AND REACTIONS OF SOME NEW PYRAZOLO[4,5-D]IMIDAZOLE DERIVATIVES AND SCREENING THEIR ANTIBACTERIAL AND ANTITUMOR ACTIVITIES

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**Part 1: SYNTHESIS AND REACTIONS OF SOME NEW PYRAZOLO[4,5-D]IMIDAZOLE DERIVATIVES AND SCREENING THEIR ANTIBACTERIAL AND ANTITUMOR ACTIVITIES**

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**Abstract**

Reaction of 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one with diazotized aromatic amines gave the corresponding diazenyl derivatives 1, which were condensed with carbonyl compounds to give the arylidene derivatives 2. Reaction of the parent pyrazolone with urea, thiourea and guanidine gave the pyrazoloimidazole derivatives 3. compound 3a reacted with thiourea in DMF to give the thiourea derivative 4. The reaction of 4 with malonic acid and acetyl chloride gave the pyrimidinedione derivative 5, which on reaction with thiourea in presence of sodium ethoxide gave the triazine derivative 6. S-alkylation of 6 with ethyl chloroacetate gave the ethyl acetate derivative 7, which on hydrolysis gave the corresponding acid, derivative 8 and on reaction with hydrazine hydrate gave the corresponding acetohydrazone 9. the reaction of compound 9 with salicylaldehyde gave the pynazolidinone 10, while with carbon disulphide in alkaline solution it gave the oxadiazole thione 11 respectively. Some of the new compounds showed antimicrobial and antitumor activities.

**Keywords:** Pyrazoloimidazole, pyrimidinedione, triazine, antimicrobial, antitumor.

**Introduction**

A large number of pyrazoles are reported to exhibit CNS depressant<sup>(1)</sup>, antibacterial<sup>(2)</sup>, antitumor<sup>(3)</sup> and antagonists<sup>(4)</sup> activities, while imidazoles exhibit antimicrobial<sup>(5)</sup>, antitumor<sup>(6)</sup>, antiproliferative<sup>(7)</sup> activities, and also act as inhibitors of copper corrosion<sup>(8)</sup> and as optoelectronic materials<sup>(9)</sup>. This prompted the authors to use 1-phenyl-3-methyl-1H-pyrazol-5(4H)-one as the key intermediate in the synthesis of new fused pyrazoloimidazole derivatives to screen their antimicrobial and antitumor activities.

**Experimental**

All melting points are uncorrected. IR spectra (KBr) were recorded with a Pye Unicam SP3-200 spectrophotometer. <sup>1</sup>H-NMR were measured with a Varian EM60

and Jeol-9 MHz instrument using TMS as internal standard and the mass spectra were measured with a FINNI-Gas 3300 mass spectrometer. The synthesis of various compounds are outlined in Schemes 1 and 2.

### **Synthesis of 3-methyl-1-phenyl-1H-pyrazole-4,5-dione 4-[N-(4-substituted phenyl)hydrazone] (1a-c).**

A cold solution of the appropriate diazotized aromatic amine (0.01 mol), namely p-tolyldiazenyl, p-anisyl diazenyl, p-diazenyl benzoic acid and/or was added gradually to a cold solution of 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (0.01) dissolved in pyridine (50 ml). The reaction mixture was kept in the ice chest for 2 h, with constant stirring. The solid obtained was filtered, washed with water and recrystallized from ethanol (1a m.p. 130°C, 1b m.p. 132°C, 1c m.p. 128°C ). Analysis for C<sub>17</sub>H<sub>16</sub>N<sub>4</sub>O (%) ; Calcd: C, 69.86, H 5.48, N 19.18; found: C, 69.84, H 5.46, N 19.16; for C<sub>17</sub>H<sub>16</sub>N<sub>4</sub>O<sub>2</sub> (%) ; Calcd: C, 66.23, H, 5.19, N, 18.19; found C, 66.20, H, 5.17, N, 18.17; for C<sub>17</sub>H<sub>14</sub>N<sub>4</sub>O<sub>3</sub> (%) ; Calcd: C, 63.35, H, 4.35, N, 17.39; found: C 63.33, H, 4.33, N, 17.37.

### **Synthesis of the arylidene derivatives (2a-g).**

To a solution of 1a and/or 1b (0.01 mol) in sodium ethoxide solution [from sodium (0.02 mol in absolute ethanol (20 ml)], aldehyde and/or ketone (0.01 mol) namely benzaldehyde, salicylaldehyde, furfural o-vaniline, acetylacetone and/or benzoyl acetone was added while stirring. The reaction mixture was then refluxed for 2 h. The solid that separated often cooling was filtered and recrystallized from ethanol (2a m.p. 165°C, 2b m.p. 172°C, 2c m.p. 170°C, 2e m.p. 170°C, 2f m.p. 120°C or propanol (2d m.p. 190°C, 2g m.p. 240°C). Analysis for C<sub>24</sub>H<sub>20</sub>N<sub>4</sub>O (%) : Calcd. C 75.79, H 5.26, N 14.74; found C 75.77, H 5.24, N 14.72; for C<sub>24</sub>H<sub>20</sub>N<sub>4</sub>O<sub>2</sub> (%) : Calcd. C 72.73, H 5.05, N 14.14; found C 72.71, H 5.03, N 14.12; for C<sub>24</sub>H<sub>20</sub>N<sub>4</sub>O<sub>3</sub> (%) : Calcd C 69.90, H 4.85, N 13.59 ; found C 69.78, H 4.83, N 13.57; for C<sub>22</sub>H<sub>18</sub>N<sub>4</sub>O<sub>2</sub> (%) : Calcd. C 71.35, H 4.86, N 15.14; found C 71.33, H 4.84, N 15.12; for C<sub>25</sub>H<sub>22</sub>N<sub>4</sub>O<sub>3</sub> (%) : Calcd. C 70.42, H 5.16, N 13.15; found C 70.40, H 5.14, N 13.13; for C<sub>22</sub>H<sub>22</sub>N<sub>4</sub>O<sub>2</sub> (%) : Calcd. C 70.59, H 5.88, N 14.97; found C 70.57, H 5.86, N 14.95; for C<sub>27</sub>H<sub>24</sub>N<sub>4</sub>O<sub>2</sub> (%) : Calcd. C 74.31, H 5.50, N 12.84; found C 74.30, H 5.49, N 12.82.

**Synthesis of 3-methyl-1-phenyl-4,6-dihydroimidazo[4,5-c]pyrazol-5-yl derivatives (3a-d).**

A mixture of 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one and/or 3-methyl-1H-pyrazol-5(4H)-one (0.01 mol), 10% sodium hydroxide (10 ml), absolute ethanol (20 ml), thiourea, urea and/or guanidine (0.01 mol) was refluxed for 6 h. The solid that separated was filtered off and recrystallized from ethanol (3a m.p. 130°C, 3b m.p. 122°C, 3c m.p. 133°C, 3d m.p. 140°C). Analysis for C<sub>11</sub>H<sub>10</sub>N<sub>4</sub>S (%): Calcd. C 57.39, H 4.35, N 24.35, S 13.91; found: C 57.37, H 4.33, N 24.33, S 13.90; for C<sub>5</sub>H<sub>6</sub>N<sub>4</sub>S (%): Calcd. C 38.96, H 3.90, N 36.36, S 20.78; found C 38.94, H 3.92, N 36.38, S 20.80, for C<sub>11</sub>H<sub>10</sub>N<sub>4</sub>O (%): Calcd. C 61.68, H 4.67, N 26.17; found C 61.66, H 4.65, N 26.15; for C<sub>11</sub>H<sub>11</sub>N<sub>5</sub> (%): Calcd C 61.97, H 5.16, N 34.86; found C 61.99, H 5.14, N 34.84.

**Synthesis of N-(3-methyl-1-phenyl-1,6-dihydroimidazo[4,5-c]pyrazol-5-yl) thiourea (4)**

A mixture of 3a (0.01 mol) and thiourea (0.01 mol) in DMF (30 ml), was refluxed for 16 h., cooled then poured onto ice. The solid obtained was filtered off and recrystallized from ethanol to give (4) (m.p. 190°C). Analysis for C<sub>12</sub>H<sub>12</sub>N<sub>6</sub>S (%): Calcd. C 52.90, H 4.40, N 30.90, S 11.80; found C 52.50, H 4.20, N 30.60, S 11.50.

**Synthesis of 1-acetyl-3-(3-methyl-1-phenyl-1,6-dihydroimidazo[4,5-c] pyrazol-5-yl)-2-thioxodihydro-4,6-(1H,5H) pyrimidinedione (5)**

A mixture of 4 (0.01 mol), malonic acid (0.01 mol) and acetyl chloride (1 ml) was heated on a water-bath for 2 h, cooled then poured onto ice. The solid obtained was filtered off and recrystallized from ethanol to give (5) (m.p. 210°C). Analysis for C<sub>17</sub>H<sub>14</sub>N<sub>6</sub>O<sub>3</sub>S (%): Calcd. C, 53.40, H 3.70, N 22.00, S 8.40; found C 53.20, H 3.50, N 22.2, S 8.30.

**Synthesis of 4-methyl-7-(3-methyl-1-phenyl-1,6-dihydroimidazo[4,5-c] pyrazol-5-yl)-2,6-dithioxo-1,2,6,7-tetrahydro-8H-pyrimido[1,6-a]-1,3,5-triazin-8-one (6)**

A mixture of 5 (0.01 mol), thiourea (0.01 mol) and sodium ethoxide solution [from sodium (0.01 mol) in absolute ethanol (30 ml)] was refluxed for 8 h., cooled

then poured onto ice. The solid obtained was filtered off and recrystallized from ethanol to give (6) (m.p. 188°C). Analysis for  $C_{18}H_{14}N_8OS_2$  (%): Calcd. C, 51.18, H 3.31, N 26.54, S 15.17; found C 51.20, H 3.30, N 26.52, S 15.15.

#### **Synthesis of ethyl-2- [ ( 3-methyl-1-phenyl -1, 6-dihydroimidazo [4,5-c] pyrazol-5-yl ) sulfanyl ] acetate (7)**

A mixture of 3a (0.01 mol) and ethyl chloroacetate (0.015 mol) in dry acetone (50 ml) containing anhydrous potassium carbonate (0.03 mol) was heated on a water bath for 24 h. The reaction mixture was filtered while hot then the excess solvent was evaporated under reduced pressure. The solid obtained was recrystallized from ethanol to give (7) (m.p. 205°C). Analysis for  $C_{15}H_{16}N_4O_2S$  (%): Calcd. C, 57.0, H 5.1, N 17.7, S 10.1; found C 57.2, H 5.00, N 17.5, S 10.0.

#### **Synthesis of 2-[(3-methyl-1-phenyl-1,6-dihydroimidazo[4,5-c] pyrazol-5-yl) sulfanyl] acetic acid (8)**

A mixture of 7 (0.01 mol) and sodium hydroxide (0.032 mol dissolved in 4 ml of water) in ethanol (50 ml) was refluxed for 3 h. After cooling the reaction mixture was acidified with dilute HCl. The solid that separated was filtered, washed with water and recrystallized from ethanol to give (8) (m.p. 196°C). Analysis for  $C_{13}H_{12}N_4O_2S$  (%): Calcd. C 54.17, H 4.17, N 19.44, S 11.11; found C 54.15, H 4.14, N, 19.40, S 11.10.

#### **Synthesis of 2- [(3-methyl-1-phenyl-1,6- dihydroimidazo [4,5-c]pyrazol-5-yl)sulfanyl ] acetohydrazide (9)**

To a solution of 7 (0.01 mol) in absolute ethanol (25 ml), hydrazine hydrate (0.01 mol) was added and the reaction mixture was refluxed for 6 h. The solid that separated after concentration and cooling was recrystallized from propanol to give (9) (m.p. 215°C). Analysis for  $C_{13}H_{14}N_6OS$  (%): Calcd. C 51.70, H 4.60, N 27.80, S 10.60; found C 51.68, H 4.40, N 27.50, S 10.40.

#### **Synthesis of 5-(2-hydroxyphenyl)-4-[(3-methyl-1-phenyl-1,3a-dihydroimidazo [4,5-c] pyrazol-5-yl)sulfanyl]-3-pyrazolidinone (10)**

A mixture of (9) (0.01 mol), salicylaldehyde (0.01 mol) and absolute ethanol (25 ml) was refluxed for 6 h. After cooling and removing the excess solvent under reduced pressure, the solid obtained was recrystallized from ethanol to give (10) (m.p 220°C).

Analysis for  $C_{20}H_{18}N_6O_2S$  (%): Calcd. C 59.10, H 4.40, N 20.70, S 18.82; found C 59.00, H 4.20, N 20.50, S 18.80.

**Synthesis of 5- [(3-methyl-1-phenyl-1,6-dihydroimidazo[4,5-c] pyrazol-5-yl ) sulfanyl ] methyl -1,3,4-oxadiazole-2(3H)-thione (11)**

To a suspension of (9) (0.01 mol) in ethanol (15 ml) was added carbon disulfide (5 ml) and powered KOH (0.005 mol) and the reaction mixture was refluxed on a water bath for 6 h., cooled then poured onto ice and acidified with few drops of dilute HCl. The solid obtained was recrystallized from ethanol to give (11) (m.p.  $198^{\circ}C$ ). Analysis for  $C_{14}H_{12}N_6OS_2$  (%): Calcd. C 48.8, H 3.5, N 24.4, S 18.6; found C 48.6, H 3.3, N 24.2, S 18.4.

**Antimicrobial activity**

Antimicrobial activity of compounds 1a, 3a, 4, 5, 9, 10 and 11 was tested by the disk diffusion method. Whatman No.1 filter paper disks were sterilized by autoclaving for one hour at  $140^{\circ}C$ . Sterile disks were impregnated with tested compounds. Agar plates were uniformly surface inoculated by fresh broth cultures of *Staphylococcus aureus* and *Escherichia coli* (as Gram positive strains), *Bacillus subtilis* (as Gram negative strains), *Candida albicans* (as yeast), *Aspergillus funigatus* (as fungi). Impregnated disks were placed on the medium, suitably spaced apart, and the plates were incubated at  $5^{\circ}C$  for 1h to permit good diffusion and then transferred to an incubator at  $28^{\circ}C$  for 24 h. The zones of inhibition were measured. DMF was used as a solvent and chloramphenicol was used as a standard antibacterial agent and terbinafin was used as standard antifungal agent<sup>(10)</sup>.

**Antitumor activity**

The method used is that trypan blue exclusion<sup>(11)</sup>

**Procedure**

1 ml of tumor cells which is drawn from mice bearing (E.A.C)

- 1) In sterile test tubes, where  $2.5 \times 10^5$  tumor cells/ml were suspended in phosphate buffer saline.
- 2) 3 Different concentrations for each compound (25, 50, 100 mg/ml).
- 3) Added  $2.5 \times 10^5$  tumor cells for each tube.
- 4) Incubate at  $37^{\circ}C$  for 2 hours.
- 5) From sample cells + trypan blue volume by volume on slide.
- 6) Examine under microscope.

- 7) Dead cells stained blue and live cells not stained.
- 8) Then carried out to calculate the percentage of non viable cells.

### Results and Discussion

The reaction of 1-phenyl-3-methyl-1H-pyrazolo-5(4H)-one with aromatic diazonium chloride derivatives gave the corresponding diazenyl compounds (1a-c), through elimination of HCl and rearrangement. The structure of the diazenyl derivatives was derived from the IR spectrum of 1a which showed bands for C=O at 1650, C=N at 1600 and NH at 3372  $\text{cm}^{-1}$ . The  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ ) spectrum of 1a exhibited signals at  $\delta$  (ppm): 8.87-7.18 (9H, m, Ar-H), 2.49 (3H, s,  $\text{CH}_3$  of pyrazolone) and 2.12 (3H, s, Ar- $\text{CH}_3$ ). The mass spectrum of (1a) showed the parent ion peak at  $m/z$  292 (73.5%).

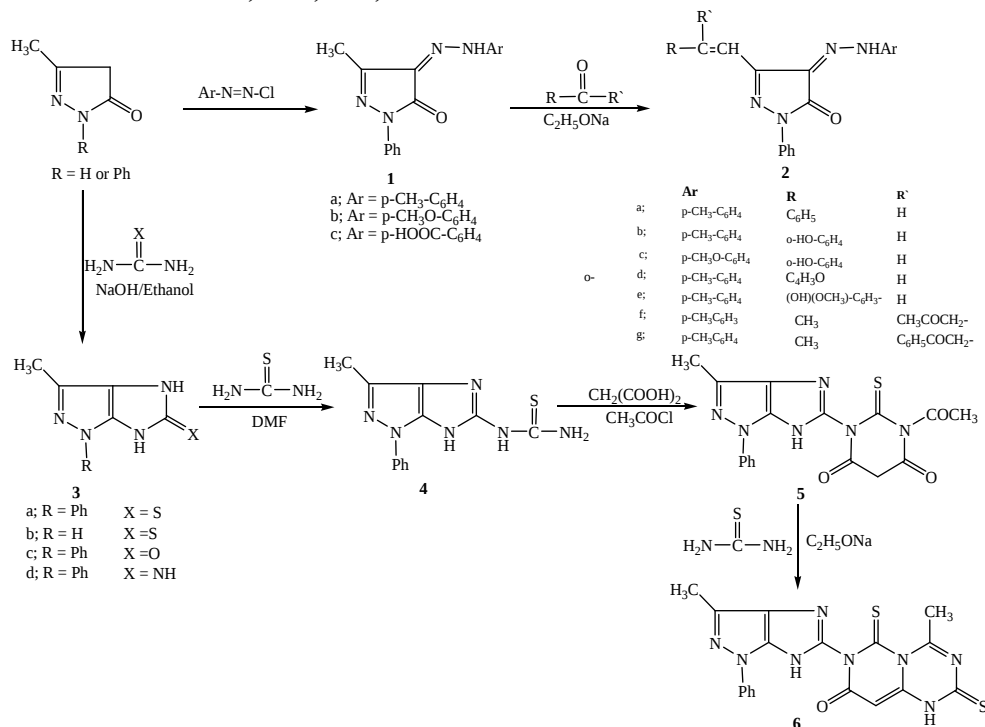
The condensation of the diazenyl derivatives (1a and 1b) with carbonyl compounds namely benzaldehyde, salicylaldehyde, furfural, o-vanilin, acetyl acetone and/or benzoyl acetone in presence of sodium ethoxide gave the arylidene derivatives 2a-g. Their IR spectra showed bands at 1656-1644, 1605-1581, 3281-3264  $\text{cm}^{-1}$  for C=O, C=N and NH. The  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ ) spectrum of 2b exhibited signals at  $\delta$  (ppm): 6.53-6.48 (13H, m, Ar-H), 2.28 (3H, s,  $\text{CH}_3$ ), 2.48 and 2.5 (2H, 2 x d, -CH=CH-), 10.25 (s, 2H, NH and OH). The mass spectrum of 2b showed the parent ion peak at  $m/z$  396 (12.1%).

As stated above pyrazole and imidazole derivatives displayed a wide spectrum of pharmacological activities. In the present work, the reaction of 1-phenyl-3-methyl-1H-pyrazol-5(4H)-one and/or 1H-pyrazolo-3-methyl-5(4H)-one with thiourea, urea and/or guanidine in alkaline medium gave the corresponding pyrazolo imidazole derivatives 3a-d. The IR spectrum of 3a showed bands at 1615, 1258 for C=N and C=S. The  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ ) spectrum of 3a exhibited signals at  $\delta$  (ppm): 7.83-7.03 (5H, m, Ar-H), 2.13 (3H, s,  $\text{CH}_3$ ), while its mass spectrum showed the parent ion peak at  $m/z$  230 (61.9%).

Compound (3) exists in a thione-thiol tautomerism. The existence of the thiol form was proved by its reaction with thiourea in boiling DMF to give the thiourea derivative (4), through the nucleophilic attack by nitrogen of thiourea to the carbon of the thione moiety followed by elimination of one mole of  $\text{H}_2\text{S}$ . Its IR spectrum showed bands at 1598, 1223, 3421  $\text{cm}^{-1}$  (broad) for C=N, C=S and  $\text{NH}_2 + \text{NH}$ , its  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ ) spectrum exhibited signals at  $\delta$  (ppm): 7.77-7.20 (5H, m, Ar-H), 2.15 (3H, s,  $\text{CH}_3$ ), while its mass spectrum showed the parent ion peak at  $m/z$  272 (65.22%).

The structure of (4) was further confirmed by its reaction with malonic acid and acetyl chloride to give the pyrimidinedione derivative (5), which is in accordance with a previous publication<sup>(12)</sup>. Its IR spectrum showed bands at 1715, 1704, 1598,, 1234, 3397  $\text{cm}^{-1}$  for  $\text{COCH}_3$ ,  $\text{CO}$ ,  $\text{C}=\text{N}$ ,  $\text{C}=\text{S}$  and  $\text{NH}$ . Its  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ ) spectrum exhibited signals at  $\delta$  (ppm): 7.78-7.23 (5H, m, ArH), 2.28 (3H, s,  $\text{CH}_3$ ), 2.48 (3H, s,  $\text{COCH}_3$ ), 3.61 (2H, s,  $\text{CH}_2$ ), while its mass spectrum showed the parent ion peak at  $m/z$  382 (75%).

Compound (5) was used as a starting material for the preparation of the triazine derivative (6). Thus the reaction of 5 with thiourea in presence of sodium ethoxide gave the triazine derivative (6). The IR spectrum showed bands at 1730, 1625, 1250, 3451  $\text{cm}^{-1}$  for  $\text{C}=\text{O}$ ,  $\text{C}=\text{N}$ ,  $\text{C}=\text{S}$ ,  $\text{NH}$ .



Scheme 1

The thiol form of 3 was also confirmed by its reaction with ethyl chloroacetate in boiling dry acetone containing anhydrous potassium carbonate to give the S-alkylated product 7. Its infrared spectrum was devoid of  $\nu\text{C}=\text{S}$  and showed the characteristic  $\text{C}=\text{O}$  (ester) at 1739.  $\text{cm}^{-1}$  the  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ ) spectrum exhibited signals at  $\delta$  (ppm): 7.84-7.37 (5H, m, Ar-H), 3.94 (2H, s,  $\text{SCH}_2\text{CO}$ ), 2.44 (2H, q,



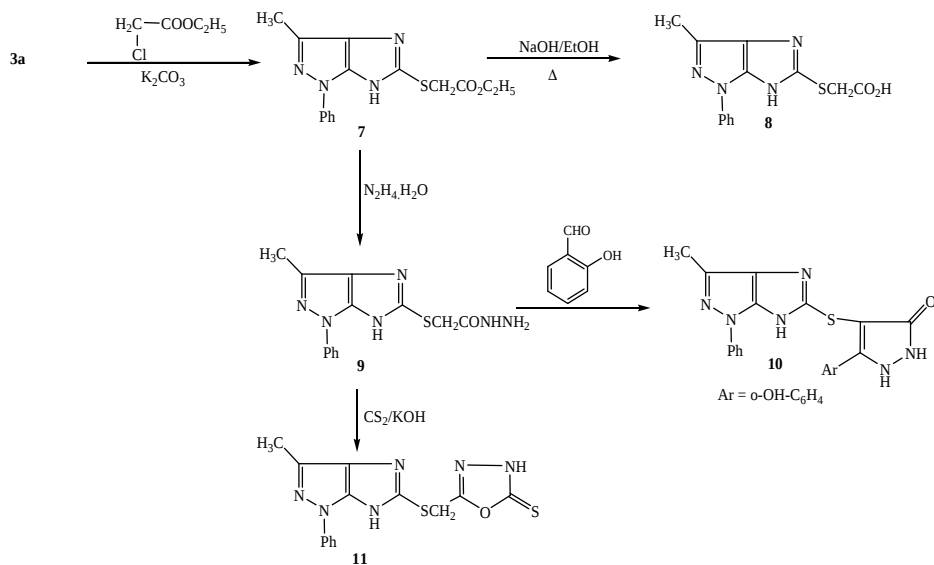
$\text{CH}_3\text{CH}_2$ ), 1.82 (3H, t,  $\text{CH}_3\text{CH}_2$ ), 2.13 (3H, s,  $\text{CH}_3$ ), 11.9 (1H, s, NH), while its mass spectrum showed  $\text{M} - \text{CH}_3]^+$  at  $m/z$  301 (59%).

The structure of 7 was chemically confirmed by alkaline hydrolysis to give the corresponding acid (8). Its IR spectrum was devoid of C=O (ester) and showed bands at 1706, 1597, 3415  $\text{cm}^{-1}$  (broad) for C=O (acid), C=N, NH + OH.

Further confirmation for compound 7 was its reaction with hydrazine hydrate to give the hydrazide derivative (9). Its IR spectrum showed bands at 1701, 1598, 3064  $\text{cm}^{-1}$  (broad) for C=O (amide), C=N,  $\text{NH}_2 + \text{NH}$ , while its mass spectrum showed  $\text{M} - 2]^+$  at  $m/z$  300 (22.05%).

Compound 9 was used as key intermediate for the introduction of new heterocyclic rings. Thus, the reaction of 9 with salicylaldehyde gave the pyrazolidinone derivative (10). The IR spectrum showed bands at 1741, 1597, 3394  $\text{cm}^{-1}$  (broad) for C=O, C=N, NH + OH.

Furthermore, compound (9) underwent ring closure reaction with carbon disulfide to give the oxadiazole thione derivative (11). Its IR spectrum showed bands at 1597, 1180, 3395  $\text{cm}^{-1}$  (broad) for C=N, C=S, NH.



**Scheme 2**

The results of antimicrobial activity tests are listed in Table 1.

From the table the pyrazolone derivatives were slightly effectives among the tested. while compounds 3a, 9, 10 and 11 against Bacillus sbutilis gave moderate results.

The results of screening antitumor activity tests are listed in Table 2. From the table compounds 3a, 7, and 11 showed good antitumor activity.

**Table (1) Antimicrobial activity of some compounds**

Sample	1a			3a			4			5			9			10			11		
	1	5	2.	1	5	2.	1	5	2.	1	5	2.	1	5	2.	1	5	2.	1	5	2.
	.Conc			5			5			5			5			5			5		
	mg/ml			mg/ml			mg/ml			mg/ml			mg/ml			mg/ml			mg/ml		
Staphylococcus aureus	0	0	0	+	+	0	+	0	0	0	0	0	+	+	0	+	+	+	+	+	+
Escherichia coli	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Bacillus sbutilis	+	+	0	+	+	+	+	0	0	0	0	0	+	+	+	+	+	+	+	+	+
Candida albicans	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Aspergillus funigatus	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

beyond

**Table 2: Antitumor activity of the compounds using (E.A.C)**

Sample	Inhibition of cell viability %		
	µg/ml		
	100	50	25
3a	96%	80%	60%
5	0	0	0
7	97%	80%	69%
9	70%	30%	10%
11	97%	79%	63%

**References**

1. Ibrahim, A.M., Saleh, A.M. and Zohdi, H.F., *Molecules* 9, 109-116 (2004).
2. Liu, X., Wang, S. and Song, B., *Chinese J. Appl. Chem.* 23(12), 1355-1358 (2006).
3. Park, H., Lee, K., Park, S., Ahn, B., Lee, J., Cho, H. and Lee, K., *Bioorg. Med. Chem. Lett.* 15(13), 3307-3312 (2005).
4. Hall, A., Bit, R.A., Brown, S.H., Chowdhury, A., Gilbin, G.M.P., Hurst, D.N., Kilford, I.R., Lewell, X., Maylor, A. and Scociti, T., *Bioorg. Med. Chem. Lett.* 18(5), 1592-1597 (2008).
5. Luca, L., *Cur. Med. Chem.* 13(1), 1-23 (2006).
6. Iradyan, M.A., Iradyan, N.S., Stepanyan, G.M., Arsenyan, F.G. and Garibdzhanyan, B.T., *Pharm. Chem. J.* 35(4), 183-185 (2001).
7. Chung, H., Hong, S., You, H., Park, R. and Ryu, C., *Bioorg. Med. Chem.* 14(17), 5795-5801 (2006).
8. Zhang, D., Gao, L., Zhou, G. and Lee, K., *J. Appl. Electrochem.* 38(11), 71-76 (2008).
9. Fang, Z., Wang, S., Zhao, L., Xu, Z., Ren, J., Wang, X. and Yang, Q. *Materials Lett.*, 61(26), 4803-4806 (2007).
10. Gould, J.C. and Bowie, J.M., Determination of bacterial sensitivity to antibiotics, *Edinburgh Med. J.* 59, 178-199 (1952).
11. Mclimans, et al., *J. Immunol.*, 79, 428 (1957).
12. Abd El-Ghaffar, N.F., Kassab, R.R.S. and Soliman, F.M.A., *Al-Azhar Bull. Sci.*, 11(1), 161-170 (2000).

## الملخص العربي

**الجزء الأول: تشييد وتفاعلات بعض مشتقات البيرازولو [4,5 - د] إמידازول الجديدة ومسح النشاط البكتيري والسرطاني لها.**

1. تفاعل 3 - ميثيل -1- فنيل - H 1 - بيرازول - 5 - (4H) - أون مع الأمينات الأرومانية تعطى مشتقات الدياتزونيل 1. بينما تفاعلها مع مركبات الكربونيل تعطى مشتقات الأريلدين 2.
2. تفاعل خماسي البيرازولون مع اليوريا، الثيوبوريا، والجوانيديين يعطى مشتقات البيرازولو إמידازول 3. مركب 3 يتفاعل مع الثيوبوريا في وجود DMF ليعطى مشتق الثيوبوريا 4.
3. تفاعل مركب 4 مع حمض المالونيك والأستيل كلوريد يعطى مشتق البيريميدين ديون 5. الذي يكون تفاعله مع الثيوبوريا في وجود إيثوأكسيد الصوديوم يعطى مشتق الترايزين 6.
4. S-ألكيليشن للمركب 6 مع إيثيل كلورواستات يعطى مشتق الإيثيل أستات 7. الذي يعطى بالهيدروليسيس مشتق الحمض المقابل 8. والذي يعطى بتفاعله مع الهيدرازين هيدرات الأسيثوهيدرازيد 9.
5. تفاعل المركب 9 مع سالسيلاً لدهيد يعطي بيراز وليدينون 0.10 بينما مع الكربون داي سلفات في محلول قلوي يعطي أكسادايا زول ثيون 11 . بعد المركبات الجديدة لها نشاط بكتيري ونشاط سرطاني .