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Part 2: SYNTHESIS AND REACTIONS OF SOME NEW IMIDAZO[4,5-C]PYRAZOLE AND PYRAZOLO[3,4-D]PYRIMIDINE DERIVATIVES

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Part 2: SYNTHESIS AND REACTIONS OF SOME NEW IMIDAZO[4,5-C]PYRAZOLE AND PYRAZOLO[3,4-D]PYRIMIDINE DERIVATIVES

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Abstract

Reactions of 3-methyl-1-phenyl-4,6-dihydroimidazo[4,5-c]pyrazole-5(1H)-thione with carbonyl compounds gave the arylidene derivatives 2 and 3, with ricinoleic acid, phosphorus oxychloride/phosphorus pentachloride mixture and copper bronze gave the adduct 4, the chloro derivative 5 and the dimer with desulfurization 7. The behaviour of the chloroderivative towards hydrazine and primary amines have also been studied. On the other, reaction of 5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one with aromatic aldehydes gave the arylidene derivatives 8a-d, which on reaction with thiourea gave the pyrazolopyrimidinethione derivatives 9. The behaviour of compounds 9 towards copper bronze, sodium nitrite/acetic acid mixture, acrylonitrile and formaldehyde/ morpholine and its reaction with compound 1 in presence of copper bronze have also been taken into consideration.

Keywords: Pyrazoloimidazole, pyrazolopyrimidine, pyrazolone

A large number of pyrazoles are reported to exhibit CNS depressant¹, antibacterial², antitumor³ and antagonists⁴ activities, while imidazoles exhibit antimicrobial⁵, antitumor⁶ and antiproliferative⁷ activities. On the other hand, pyrazolopyrimidine derivatives exhibit anti-inflammatory, antitumor, antimycobacterial, antifungal and antiviral activities⁸⁻¹⁰.

In view of these reports and in continuation of our recent works¹¹⁻¹³ we synthesized new imidazopyrazole and pyrazolopyrimidine derivatives.

Experimental

All melting points are uncorrected. IR spectra (KBr) were recorded with a Pye Unicam SP3-200 spectrophotometer. ¹H-NMR were measured with a Varian EM60 and Jeol-9 MHz instrument using TMS as internal standard and 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-[2-(4-chlorophenyl) ethenyl] -1-phenyl -3a ,4-dihydroimidazo [4,5-c]pyrazole-5(1H)thione (2) and 4-methyl-5-(1-phenyl-5-thioxo-1,3a,4,5-tetrahydroimidazo[4,5-c]pyrazol-3-yl)-4-penten-2-one (3)

A mixture of **1** (0.01 mol), p-chlorobenzaldehyde and/or acetyl-acetone (0.01 mol) was added in a course of 30 minutes to a well stirred solution of sodium ethoxide [prepared from sodium metal (0.11 gm in absolute ethanol (30 ml))]. Stirring was continued for further 3 h, then the reaction mixture was left overnight. The excess alcohol was removed under reduced pressure and the residue was treated with water, acidified with dil. HCl and extracted with ether. The ethereal layer was washed with aqueous sodium carbonate, water and dried. The ether was removed under reduced pressure and the pale yellow solid obtained was crystallized from ethanol (**2** m.p. 176°C, **3** m.p. 198°C). Analysis for C₁₈H₁₃N₄SCl (%): Calcd. C 61.30, H 3.70, N 15.90, S 9.10, Cl 10.10; found C 61.00, H 3.50, N 15.70, S 9.00, Cl 10.00; for C₁₆H₁₆N₄OS (%): Calcd. C 61.50, H 5.10, N 17.90, S 10.30; found C 61.30, H 5.00, N 17.70, S 10.00.

Synthesis of 11-hydroxy-9-[(3-methyl-1-phenyl-1,3a-dihydroimidazo [4,5-c]pyrazol-5-yl)sulfonyl]hexadecanoic acid (4)

A mixture of **1** (0.01 mole) and ricinoleic acid (0.01 mol) in dry benzene (50 ml) containing few drops of piperidine was shaken vigorously, then left overnight. After removal of solvent under reduced pressure, the residue was triturated with light petrol (b.p. 40-60°C) and crystallized from benzene to give (**4**) (m.p. 70°C). Analysis of C₂₇H₄₀N₄O₃S (%): Calcd. C 64.80, H 8.00, N 11.20, S 6.40; found C 64.78, H 8.20, N 11.00, S 6.20.

Synthesis of 5-chloro-3-methyl-1-phenyl-1,3a-dihydroimidazo[4,5-c] pyrazole (5)

A mixture of **1** (0.01 mol), phosphorus oxychloride (3 ml) and phosphorus pentachloride (0.5 g) was heated on a water bath for 2 h., cooled then poured onto ice. The solid obtained was filtered off and crystallized from ethanol to give (**5**) (m.p. 232°C). Analysis for C₁₁H₉N₄Cl (%): Calcd. C 56.80, H 3.90, N 24.10, Cl 15.30; found C 56.60, H 3.70, N 24.00, S 15.00.

Synthesis of 5-substituted-3-methyl-1-phenyl-1,3a-dihydroimidazo [4,5-c] pyrazole (6a-d)

A mixture of **5** (0.01 mol), hydrazine hydrate and/or primary amine namely ethylamine, 2-aminopyridine, aniline (0.01 mol) in ethanol (30 ml) was refluxed for 3 h. The solid obtained after concentration and cooling was crystallized from petroleum ether (b.p. 60-80°C) (**6a** m.p. 120°C, **6b** m.p. 135°C), propanol (**6c** m.p. 183°C) or ethanol (**6d** m.p. 160°C). Analysis for $C_{11}H_{12}N_6$ (%): Calcd C 57.90, H 5.30, N 36.80; found C 57.70, H 5.00, N 36.60; for $C_{13}H_{15}N_5$ (%): Calcd. C 64.70, H 6.20, N 29.00; found C 64.50, H 6.00, N 29.20; for $C_{16}H_{14}N_6$ (%): Calcd. C 66.20, H 4.80, N 29.00; found C 66.00, H 4.60, N 29.20; for $C_{17}H_{15}N_5$ (%): Calcd. C 70.60, H 5.20, N 24.20; found C 70.40, H 5.00, N 24.00.

Synthesis of 5,5'-bis [3-methyl-1-phenyl-4,6-dihydroimidazo[4,5-c] pyrazole (7) and bis 4-(2-hydroxy phenyl)-3-methyl-1-phenyl-1,5-dihydro-6H-pyrazolo[3,4-d]pyrimidine-6-thione (10)

To a solution of **1** and/or **9** (0.01 mol) in dry xylene (50 ml), copper bronze (3 g) was added and the reaction mixture was refluxed for 10 h. The solid obtained after filtration the reaction mixture while hot, concentration and cooling was crystallized from benzene (7 m.p. 137°C) or butanol (10 m.p. 272°C). Analysis for $C_{22}H_{22}N_6$ (%): Calcd. C 66.30, H 5.50, N 28.10; found: C 66.60, H 5.30, N 28.00; for $C_{36}H_{26}N_8O_2$ (%): Calcd. C 71.80, H 4.30, N 18.60; found: C 71.60, H 4.00, N 18.40.

Synthesis of the arylidene derivatives (8a-d)

To a solution of 1-phenyl-3-methyl pyrazolone (0.01 mol) in sodium ethoxide solution [from sodium 0.02 mol in absolute ethanol (20 ml)], aromatic aldehydes namely salicylaldehyde, p-chlorobenzaldehyde, furfural and/or vanillin (0.01 mol) was added with stirring. Stirring was continued for further 3 h, then left overnight. The excess alcohol was removed under reduced pressure and the residue was treated with water, then acidified with dil HCl and extracted with ether. The solid obtained after removing ether under reduced pressure was crystallized from ethanol (**8a** m.p. 187°C, **8b** m.p. 205°C, **8c** m.p. 197°C, **8d** m.p. 170°C). Analysis for $C_{17}H_{14}N_2O_2$ (%): Calcd. C 73.40, H 5.00, N 10.10; found C 73.20, H 5.20, N 10.00; for $C_{17}H_{13}N_2OCl$ (%): Calcd. C 68.80, H 4.40, N 9.40, Cl 12.00; found C 68.60, H 4.80, N 9.20, Cl 12.20; for $C_{15}H_{12}N_2O_2$ (%): Calcd. C 71.40, H 4.80, N 11.10; found C 71.20, H 4.60, N 11.00; for $C_{18}H_{16}N_2O_3$ (%): Calcd. C 70.13, H 5.20, N 9.10; found C 70.10, H 5.19, N 9.09.

Synthesis of 4-(arylidene-3-methyl-1-phenyl-1,5-dihydro-6H-pyrazolo [3,4-d]pyrimidine-6-thione (9a-d)

To a solution of 8a-d, 10% sodium hydroxide (10 ml), absolute ethanol (30 ml), thiourea (0.01 mol) was added and the reaction mixture was refluxed for 6 h. The solid obtained after removal of solvent was washed with water and crystallized from ethanol (**9a** m.p. 133°C, **9b** m.p. 150°C, **9c** m.p. 140°C, **9d** m.p. 128°C). Analysis for C₁₈H₁₄N₄SO (%) Calcd: C 64.70, H 4.20, N 16.80, S 9.60; found: C 64.50, H 4.00, N 16.60, S 9.40; for C₁₈H₁₃N₄SCl (%): Calcd C 61.28, H 3.69, N 15.89, S 9.10, Cl 10.7; found C 61.30, H 3.70, N 15.90, S 9.07, Cl 10.10; for C₁₆H₁₂N₄SO (%) Calcd C 62.30, H 3.90, N 18.20, S 10.40; found C 62.50, H 3.70, N 18.00, S 10.20; for C₁₉H₁₆N₄SO₂ (%): Calcd C 62.60, H 4.40, N 15.40, S 8.80; found: C 62.40, H 4.20, N 15.20, S 8.60.

Synthesis of 5-(6-{[4-(3-hydroxy-4-methoxyphenyl)-3-methyl-1-phenyl-5,6-dihydro-1H-pyrazolo[3,4-d]pyrimidine-6-yl]disulfonyl}-3-methyl-1-phenyl-5,6-dihydro-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-2-methoxyphenol (11).

To a cooled well stirred suspension of **9** (0.01 mol) in ethanol (25 ml) was added portionwise a cooled aqueous solution of sodium nitrite (0.04 mol in 25 ml of water) and acetic acid (2 ml). Stirring was continued for 3 h while keeping the temperature of the reaction mixture below 5°C. The obtained product was filtered off, washed with water and crystallized from ethanol to give (**11**) (m.p. 230°C). Analysis for C₃₈H₃₀N₈O₄S₂ (%): Calcd C 62.80, H 4.10, N 15.40, S 8.80; found C 62.60, H 4.00, N 15.20, S 8.60.

Synthesis of 3-{[4-(2-hydroxyphenyl)-3-methyl-1-phenyl-5,6-dihydro-1H-pyrazolo[3,4-d]pyrimidin-6-yl]sulfonyl}propanenitrile (12)

To a solution of **9a** (0.01 mol) in pyridine (20 ml), acrylonitrile (0.02 mol) was added and the reaction mixture was refluxed for 6 h. After cooling, the reaction mixture was poured into cold 10% HCl. The separated product was filtered off, washed with water and crystallized from ethanol to give (**12**) (m.p. 122°C). Analysis for C₂₁H₁₇N₅OS (%) Calcd C 65.12, H 4.40, N 18.10, S 8.30; found C 65.10, H 4.42, N 18.12, S 8.32.

Synthesis of 4-(2-furyl)-3-methyl-5-(4-morpholinyl methyl)-1-phenyl-1,5-dihydro-6H-pyrazolo[3,4-d]pyrimidine-6-thione (13).

A mixture of **9a** (0.01 mol), formaldehyde (40%, 0.7 ml), morpholine (0.02 mol) in a mixture of methanol-acetone (2:1) (50 ml), was refluxed for 18 h. The residue obtained after removing of the solvent under reduced pressure, was triturated with

petroleum ether (b.p. 40-60°C), then crystallized from ethanol to give **13** (m.p. 240°C). Analysis for C₂₁H₂₁N₅O₂S (%): Calcd. C 61.90, H 5.20, N 17.20, S 7.90; found C 61.70, H 5.00, N 17.00, S 7.70.

Synthesis of 4-(2-furyl)-3-methyl-6-(3-methyl-1-phenyl)-1,3a,4,5-tetrahydroimidazo[4,5-c]pyrazolo-5-yl)-1-phenyl-1H-pyrazolo[3,4-d]pyrimidine (14).

To a solution of **9c** (0.01 mol) and **1** (0.01 mol) in dry xylene (50 ml), copper bronze (3 g) was added and the reaction mixture was refluxed for 10 h. The solid obtained after filtration the reaction mixture while hot, concentration and cooling was crystallized from butanol to give **14** (m.p. 260°C). Analysis for C₂₇H₂₁N₈O (%): Calcd. C 68.50, H 4.43, N 23.70; found C 68.50, H 4.40, N 23.72.

Results and Discussion

3-Methyl-1-phenyl-4,6-dihydroimidazo[4,5-c]pyrazole-5(1H)-thione (**1**)¹³ was used as key intermediate for the preparation of several imidazo[4,5-c]pyrazole derivatives.

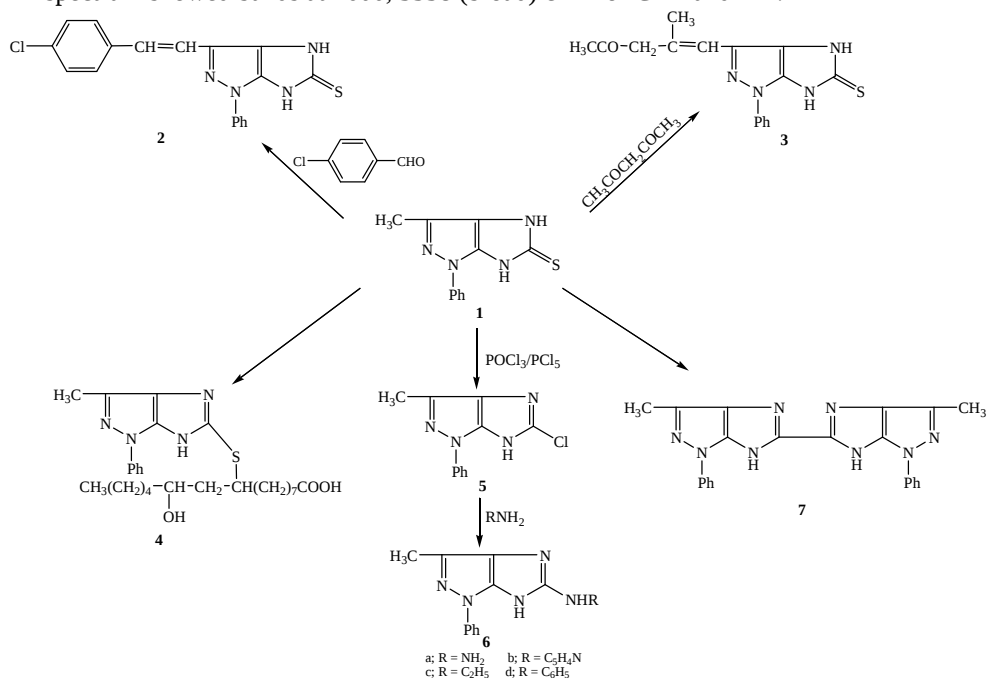
Thus, reaction of **1** with carbonyl compounds namely p-chloro-benzaldehyde and/or acetyl acetone in the presence of sodium ethoxide (under Claisen reaction conditions) gave the condensed products **2** and **3**, respectively. The structure of compound **2** was derived from correct analytical data and from the mass spectrum which showed the parent ion peak at m/z 352 (78.95%) (calculated for the isotope ³⁵Cl), while the structure of compound **3** was derived from correct analytical data and from the IR spectrum which showed bands at 1693, 1597, 1257, 3423 cm⁻¹ for C=O, C=N, C=S and NH.

Compound **1** exists on a thione-thiol tautomerism. The existence of the thiol form was proved by the study of its behaviour towards unsaturated fatty acid namely ricinoleic acid in dry benzene and in the presence of few drops of piperidine to give the adduct **4**. Its IR spectrum was devoid of C=S band and showed bands at 1729, 1616, 3324 cm⁻¹ (broad) for C=O (acid), C=N, NH and OH. Its mass spectrum showed the parent ion peak at m/z 500 (63.36%).

The reaction of the nucleophilic reagent phosphorus oxychloride with compound **1**, also supports the presence of the thiol form. Thus, compound **1** reacts with POCl₃/PCl₅ to give the corresponding chloro derivative **5**. Its IR spectrum showed the characteristic bands for C=N and C-Cl at 1600 and 492 cm⁻¹, respectively. Its mass spectrum showed M - 2]⁺ at m/z 230 (61.9%).

The chloro compound **5** was used to prepare the hydrazine and substituted amino derivatives, by its reaction with hydrazine hydrate and primary amines namely ethylamine, 2-aminopyridine and/or aniline in boiling ethanol to give compounds **6a-d**. The reaction proceeds through the nucleophilic attack at the carbon atom bearing the more electronegative chlorine atom, with one molecule of the NH_2 component with the elimination of one molecule of HCl . The IR spectrum of **6c** showed bands for $\text{C}=\text{N}$ and NH at 1594 and 3423 cm^{-1} .

Dimerization of compound **1** has also been taken into consideration. Thus, reaction of **1** with copper bronze in boiling xylene gave compound **7**. Its IR spectrum showed bands at $1600, 3338$ (broad) cm^{-1} for $\text{C}=\text{N}$ and NH .



Scheme 1

Interestingly, reaction of 5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one with aromatic aldehydes, namely salicylaldehyde, p-chloro benzaldehyde, furfural and/or vaniline in the presence of sodium ethoxide (Claisen conditions) affords the corresponding arylidene derivatives **8a-d**. The IR spectra of **8a-c** showed bands at $1701\text{-}1680, 1601\text{-}1598\text{ cm}^{-1}$ for $\text{C}=\text{O}$ and $\text{C}=\text{N}$, in addition a band at 3404 cm^{-1} for

OH for compound 8a. The $^1\text{H-NMR}$ (DMSO-d_6) spectrum of 8b exhibited signals at δ (ppm): 7.84-7.10 (10H, m, ArH + =CH) and 2.20 (3H, s, CH_3). The mass spectrum of 8a showed peak at m/z 261 $[\text{M} - \text{OH}]^+$ (78.33%), while the mass spectrum of 8b showed the parent ion peak at m/z 296 (44.40%).

As stated above pyrimidine derivatives displayed a wide spectrum of pharmacological activities. In the present work, reaction of compounds **8a-d** with thiourea gave the pyrazolopyrimidine derivatives **9a-d**, which is in accordance with previous result¹⁴. The IR spectrum of **9c** showed bands at 1620, 1227, 3417 cm^{-1} for C=N, C=S and NH.

Compound **9** was used for the preparation of several new pyrazolo-pyrimidine derivatives. Thus, treatment of **9a** with copper bronze in boiling xylene gave the bis-compound **10**, the reaction is accompanied by desulfurization with dimerization of the thione **9a**. The structure of compound 10 was derived from correct analytical data, from its IR spectrum which showed bands at 1594, 3122 cm^{-1} for C=N and OH. Its $^1\text{H-NMR}$ (DMSO-d_6) spectrum exhibited signals at δ (ppm) 7.82-7.17 (18H, m, Ar-H), 2.14 (6H, s, 2 x CH_3) and 11.52 (2H, s, 2 x OH).

Interestingly, dimerization of compound **9** can also occur but without desulfurization, when **9d** was treated with sodium nitrite/acetic acid mixture to give **11**, which is in accordance with a previous result.¹⁴

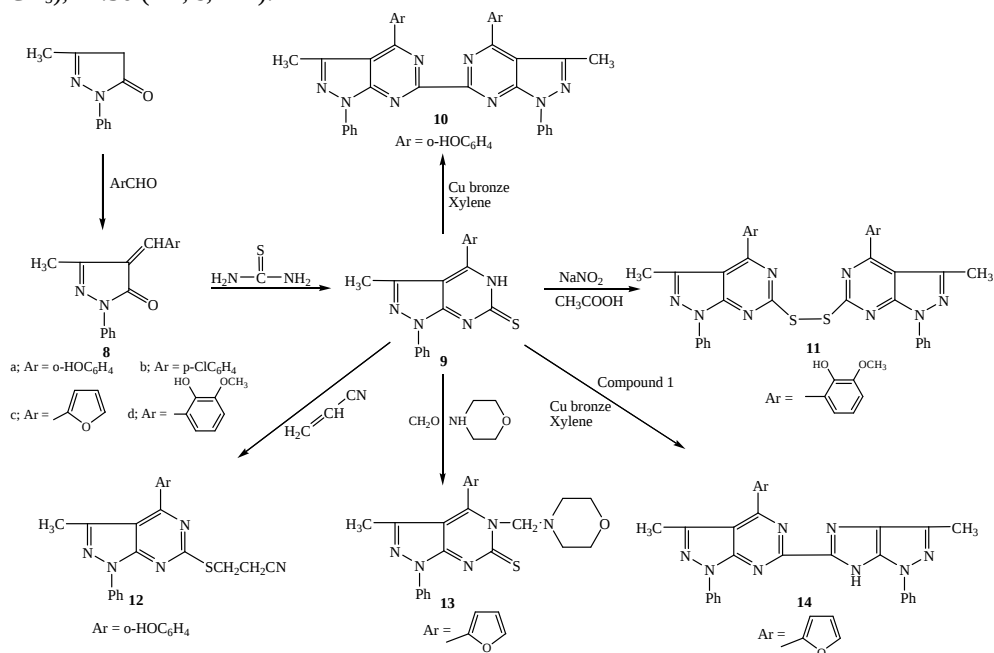
Structure of compound **11** was derived from correct analytical data, its IR spectrum showed bands at 1640, 1340 and 3446 for C=N, -S-S-, OH. Its mass spectrum showed the parent ion peak at m/z 726 (40%).

Reaction of **9a** with acrylonitrile in boiling pyridine afforded the corresponding S-cyanoethylated product **12**. Its mass spectrum showed ion peak at m/z 372 $[\text{M} - \text{CH}_3]^+$ (74%).

Reaction of **9c** with formaldehyde and morpholine (Mannich reaction) gave the Mannich base **13**. Its IR spectrum showed bands at 1594 and 1240 cm^{-1} for C=N and C=S, while its mass spectrum showed the parent ion peak at m/z 407 (50%).

As a point of interest this investigation deals with the reaction of the pyrazolopyrimidine thione **9c** and the pyrazoloimidazole thione **1** in boiling xylene

in presence of copper bronze. The reaction proceeds through desulfurization and formation of compound **14**. Its infrared spectrum was devoid of $\nu\text{C}=\text{S}$ and showed bands at 1616 and 3452 cm^{-1} for $\text{C}=\text{N}$ and NH , while its $^1\text{H-NMR}$ (DMSO- d_6) spectrum exhibited signals at δ (ppm): $7.81\text{--}7.13$ (13H, m, Ar-H), 2.13 (6H, s, 2 x CH_3), 11.50 (1H, s, NH).

**Scheme 1**

References

1. IBRAHIM, A.M., SALEH, A.M. AND ZOHD, 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 SCOCCITI, 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 GAZIBDZHANGAN, 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. RASHAD, A.E., HEGAB, M.I., ABDEL-MEGEID, R.E., MICKY, J.A. AND ABDEL-MEGEID, F.M.E. *BIOORG. Med. Chem.* 16, 7102-7106 (2008).
9. SHAHEEN, F., BADASHAH, A., GIELEN, M., GIECK, C., JAMIL, M., AND DE VOS, D. *J. Organomet. Chem.* 693, 1117-1126 (2008).
10. SON, J., ZHAO, L., BASNET, A., THAPA, P., KARKI, R., NA, Y., JAHNG, Y., JEONG, T. CH., JEONG, B., LEE, C. AND LEE, E., *Eur. J. Med. Chem.* 43, 675-682 (2008).
11. ABD EL-GHAFFAR, N.F., KASSAB, R.R.S. AND SOLIMAN, F.M.A. *Al-Azhar Bull. Sci.* 11(1) 161-170 (2000).
12. ABD EL-GHAFFAR, N.F., DAWOOD, N.T. AND SOLIMAN, F.M.A. *Al-Azhar Bull. Sci.* 11(2) 147-154 (2000).
13. ABD EL-GHAFFAR, N.F., KADAH, M.S., RADWAN, A.M., ABD EL-AL, S.N. AND SALMAN, A.S. *Al-Azhar Bull. Sci.* (under press).
14. SAMMOUR, A., SELIM, M.I.B., NOUR EL-DEEN, M.M., ABD EL-HALIM, M., *J. Egypt. Chem.* 13(1), 7-24 (1970).

الملخص العربي

الجزء الثاني : تشييد وتفاعلات بعض مركبات الاميدازو [C-5,4] بيرازول الجديدة ومشتقات البيرازولو [d-4,3] بيريميدين

تفاعل 3-ميثيل-1-فينيل-4، 1 - داي هيدرواميدازو [C-5.4] بيرازول - 5 (H1) - ثيون مع مركبات الكبرونيل تعطي مشتقات الأريلدين، 2، 3 .
ومع حمض الريسينوليك ، ومخلوط ثالث كلوريد الفسفور / وخامس كلوريد الفسفور خراطة النحاس يعطي مركب 4 ، ومشتق الكلور 5 ، والدايمر مع الديسلفريزاشن 7 .
سلوك مشتق الكلور تجاه الهيدرازين، والأمينات الأولية تم دراستها أيضا .
وتفاعل 5-ميثيل-2-فينيل-4،2- داي هيدرو-3H بيرازول-3- أون مع الالدهيدات الأروماتية تعطي مشتقات الأريلدين 8- د . الذي يتفاعل مع الثيوپوريا ويعطي مشتق البيرازولو بيريميدين ثيون 9 .
سلوك المركب 9 مع مخلوط خراطة النحاس ونيتريت الصوديوم وحمض الاستك ، والاكريلونيتربل ، والفومالدهيد والمورفين ، وتفاعله مع مركب 1 في وجود خراطة النحاس أخذ أيضا في الاعتبار .