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Synthesis and Characterization of Some New Pyrazole Compounds

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***Abstract* - In this paper the synthesis of some pyrazole derivatives are reported. The reaction of phenyl hydrazine with ethyl acetoacetate gave 3-methyl-1-phenyl-5-pyrazolone(1), which then treated with malonitrile and benzaldehyde to give 6-amino-3-methyl-1,4-dihydropyrano [2,3-b]pyrazole-5-carbonitrile(2) which considered assynthone for prepare some new pyrazole derivatives (3a-j).The structure of the prepared compounds was suggested in the IR ,^{1}H-NMR,^{13}C-NMR and UV Spectroscopy.**

***Keywords* - Pyrazoline, pyrazolederivatives, biological activity**

I. INTRODUCTION

Pyrazoles are the important members of heterocyclic compounds with two adjacent nitrogen in a five-membered ring system. Among the two nitrogen atoms; one is basic and the other is neutral in nature. These are aromatic molecules due to their planar conjugated ring structures with six delocalized π-electrons [1].Pyrazoles have been the recent target of numerous methodologies, mostly due to their biological activitysuch as antibacterial [2], antitumor [3], anticancer and as anti-flammatory [4]. Some pyrazoles also act as Painting and Photography Industry [5] .other of them showed cytotoxic and pro-oxidant potentials on cultured human whole blood cells [6].Some of them areDegradable agricultural materials[7] and with pharmaceutical applications [8].

II. EXPERIMENTAL SETUP

Melting points were measured on Electrothermal 9300 (uncorrected). FTIR spectra were recovered using KBr disk Fourier-Transform, Tensor Co. Brucker, 2003, Germany. UV spectra were performed on Shimadzu UV-VIS Recording UN-160 Spectrophotometer using chloroform as a solvent. 1HNMR spectra were obtained from Brucker (400 MHz) Swiss, using $CDCl_3$, as solvent, TMS as internal standard.

A. Preparation of 3-methyl-1-phenyl-5-pyrazolone (1)A:

method (A) [9]:

A (0.05 mol) of ethyl acetoacetate, (0.05 mol) of phenyl hydrazine and (1 ml) of acetic acid were heated at (100oC) for (1hrs.) with stirring, then mixture was cooled,(30ml) of ethers was added with stirring until The solid product was formed, then filtered and wash with excess of ethers, and recrystallized from ethanol to give the product as white crystal(m.p. 118-120o C. Yield 80%)

method (B):

A (0.05 mol) of ethyl acetoacetate, (0.05 mol) of phenyl hydrazine and (5ml) of absolute ethanol were heated at (50°C) for (15min.)was sonicated in ultrasound , then mixture was cooled, stirring until The solid product was formed, and recrystallized from ethanol to give the product as white crystal(m.p. 118-120° C. Yield 84%)

B. Preparation of 6-amino-3-methyl-1,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile(2):

method (A)[10] :

In a beaker 100ml, a (0.005mol) of compound(1), (0.005mol) of benzaldehyde,(0.005mol)of malonitrile and (5 ml.) of sodium hydroxide in (5ml.) of water ,the mixture was stirring at 100°C for (1hr.), cooled and the solid was washed with cold and recrystallized from

ethanol to give the product as white crystal(m.p. 168-170°C. Yield 80%)

method (B)[10]:

A mixture of (0.005 mol) of compound(1), (0.005 mol) of benzaldehyde,(0.005mol)of malonitrileand (5ml) of absolute ethanol were heated at (50°C) for (15min.)was sonicated in ultrasound , then the mixture was cooled, stirring until The solid product was formed, and recrystallized from ethanol to give the product as white crystal(m.p. 168-127° C. Yield 90%).

C. *Preparation of 5-amino-4,8,9-trihydro-3-methyl-1,4-diphenyl-pyrazyolo[3´,4´,2,3]pyrano[5.6-d] pyrimidine-7-thione*(3a) *[12]*

A mixture of (0.005mol) thiourea, (0.005 mol) of compound (2) were dissolve in (20ml.)of absolute ethanol and mixture of (0.023 gm in 20 ml. of absolute ethanol) was added then the mixture was refluxed for (6hrs.)then the mixture was cooled and poured into crushed ice with several drops of hydrochloric acid were added , the solid product was filtered and recrystallized from ethanol to give compound (3a)

D. *Preparation of 5-amino-4 ,9-dihydro-3-methyl-1,4-diphenyl-pyrazyolo[3´,4´,2,3]pyrano[5.6-d] pyrimidine-7-thione(3b)[13]*

By using mixture of (0.005 mol) from compound(2) and (5 ml.) from formamide and the mixture was refluxed for (6hrs.)half hour ,then the mixture was cooled and poured into crushed ice with several drops of hydrochloric acid were added , the solid product was filtered and recrystallized from ethanol to give compound (3b).

E. *Preparation of ethyl- 5-amino-3-methyl-1,4-diphenyl-4,7-dihydro-1H-pyrrolo[3´,2´,5,6]pyrano[2.3-c]pyrazyolo-6-carboxylate(3c)[14]*

A mixture of (0.005mol) ethyl chloro acetate ,(0.005 mol) of compound (2) were dissolve in (20ml.)of dry acetone and 1 gm of potassium carbonate, the mixture was refluxed for (12hrs) then the mixture was cooled and poured into crushed , the solid product was filtered and recrystallized from ethanol to give compound (3c)

F. *Preparation of ethyl- 5-amino-3-methyl-1,4-diphenyl-4,7-dihydro-1H-pyrrolo[3´,2´,5,6] pyrano [2.3-c] pyrazyolo -6-carboxylic acid (3d)[14]*

A mixture of(0.005mol) ethyl chloro acetic acid ,(0.005 mol) of compound (2) were dissolve in (20ml.)of absolute ethanol then the mixture was refluxed for (12hrs.),cooled and poured into crushed ice, the solid product was filtered and recrystallized from ethanol to give compound (3d).

G. *Preparation of 5,7-diamino-6-cyano-4 ,9-dihydro-3-methyl-1,4-diphenyl-pyrazyolo[3´,4´,2,3]pyrano[5.6-d]pyridine (3e)[12]*

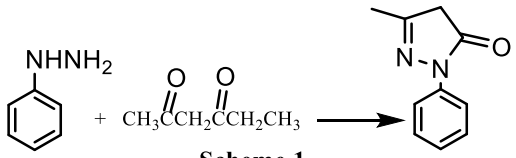
A mixture of(0.005mol) malonitrile ,(0.005 mol) of compound (2) were dissolve in (20ml.)of dimethyl amine and 0,5 gm of triethyl amine were added, then the mixture was refluxed for (6hrs.), cooled and poured into crushed , the solid product was filtered and recrystallized from ethanol to give compound (3e)

Table I
Physical data for compounds (3a-e)

Comp. No.	Molecular Formula	**m.p.** (°C)	Yield **(%)**	Color
3a	$C_{21}H_{17}N_5OS$	138-140	80	Light brown
3b	$C_{21}H_{17}N_5O$	100-98	85	brown
3c	$C_{24}H_{22}N_4O_3$	160-162	60	brown
3d	$C_{22}H_{18}N_4O_3$	200	65	white
3e	$C_{23}H_{18}N_6O$	118-120	90	Green yellowish

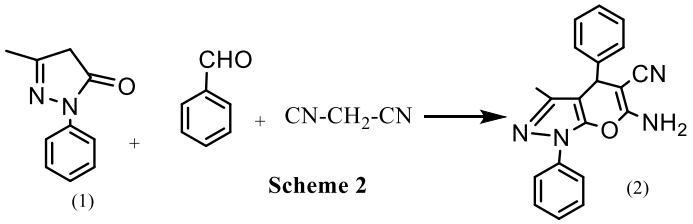
III.RESULTS AND DISSCUSION

In view of the potential medical and biological activity of a number pyrazole derivatives. Many pyrazole compounds have interesting pharmacological properties and some well-known pyrazole compound used as pharmaceutical inhibitors of Cyclooxygenase-2. In the present work the synthesis of some substituted pyrazoles are achieved .Thus the3-methyl-1-phenyl-5-pyrazolone(1)was synthesized from ethyl acetoacetate which was reacted with phenyl hydrazine in acetic acid to give pyrazolone (1) as scheme1 .



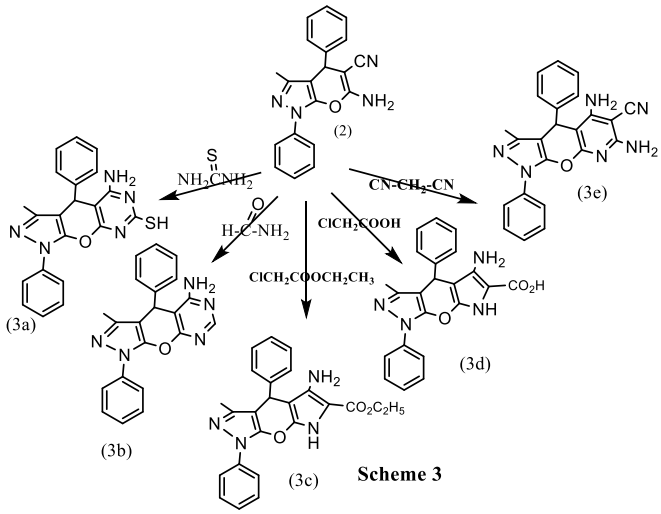
Scheme 1 (1)

The FT-IR spectrum for compound(1) manifests a strong absorption band at (1596cm^{-1})due to stretching vibration of C=N group, at(3190.3387cm^{-1}) and at (784cm^{-1}) forC-S-C group. While the U.V. spectrum shows a maximum absorption at wavelength at (312nm) which indicated a blue shift .The ^{1}H-NMR spectrum shows singlet band at δ (1.97ppm)(3H)for CH_3 group, doublet at(3.05 ppm) (2H) for CH_2 group. Also, the aromatic part for (5H) showed multiplet in the range (7.28-7.85ppm) ,while ^{13}C-NMR Spectrum Showed The carbon signal of C=O group appeared at δ values 174.7 and other carbons signal are appeared at δ values(16.8,42.9,124.1,127.9,138.3,163.1). The 6-amino-3-methyl-1,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile(2) was prepared via treatment of 3-methyl-1-phenyl-5-pyrazolone(1)with malonitrile and benzaldehyde as shown in scheme 2.



(1) **Scheme 2** (2)

The FT-IR spectrum for compound(3) showedabsorption band at (1659cm^{-1})due to stretching vibration of C=C group, at(1592cm^{-1}) for C=N group and at (3322,3420cm^{-1}) for NH_2group. While the U.V. spectrum shows a maximum absorption at wavelength at (276nm) which indicated a blue shift. The ^{1}H-NMR spectrum shows singlet band at δ (1.95ppm)(3H)for CH_3 group, broad band at(4.69 ppm)(1H)for CH group ,at (6.85ppm) due to NH_2group.Also the aromatic part for multiplet in the range(7.22-7.38ppm) and at the range(7.53-7.81ppm) while ^{13}C-NMR Spectrum Showed The carbon signal of CH_3 group at (13.6ppm), at (25.9ppm) due to carbon which attached wit phenyl group,also other signals at (59.9ppm)for C=C ,(117.8ppm) for C≡N,at (147.1ppm)for C=N while other carbons signal are appeared at δ values(119.2,154.3,122.3,125.2,124.9,126.8,129.1,126.3, 135.2ppm) due to aromatic carbon and other carbon in compound(2). Pyrazole derivative compounds (3a-j) are synthesized via reactions of compound (2) with other reagents according scheme 3.



Scheme 3

The IR spectra for compounds (3a-e) showed characteristic absorption peak in the regionat (1598-1625 cm^{-1}) stretching for (C=N) group, and at (3026-3354 cm-^{1}) due to (NH_2) group. While the U.V. spectrum shows a maximum absorption at wavelength at the region (287-340 nm). The ^{1}H-NMR spectra for compounds (3a-e) in (DMSO-d_6) in ppm showed significant peaks as the following. .singlet in the range (1.89- 1.94ppm) due to CH_3group,broadpeak at the range(5.33-5.84)for CH group in these compounds,also the two protons of

(NH_2)group were appeared in the range (5.84-6.48ppm).in addition the aromatic part showed multiplet in the range(7.11-7.81ppm) due to aromatic protons. Finally^{13}C-NMR Spectra showed peaks for the carbon signal appeared at δ values as shown in table II.

IV. REFERENCES

[1] Ahasan N. B. and Md, R.Islam (2007). Bangladesh J.Pharmacol.;2,81-87.

[2] Srivastava R. and Abdul-Wahab(2012). Ultra-Chemistry;8(2), 265-268.

[3] KuoS.C.,L.J.Huang,H.Nakamura(1984).J.Med.Chem.27,539-544.

[4] Wang S.L.,D.Liu,Z.J.Zheng,S.Shan,C.M.Croce,S.M. M.Srinivasula.E.S.Alnermi,Z.Huang(2000)Proc.Natl.Acad.Sci.,97,7124-7129.

[5] Sunitha S.,K.K.Aravindakshan(2011),Int.J.Pharm Biomed Sci.2(4),108-113.

[6] Esvet Akbas1, FatihCaglarCelikezen , Hasan Turkez , OzlemOzdemir, AdemRuzgar , ErdemErgan and ErtanSahin(2017), Cogent Chemistry ; 3, 1344115

[7] ZakiM.E.A., SolimanH.A.,O.AHiekal,A.E.Z.Rashad (2006), Naturforsch;61,1-5.

[8] H.S.Sohal,A.Goyal,R.Sharma,R.K.hareand S. Kumar (2013),Eur. J.of Chemistry;4(4),450-453.

[9] Verma R.,P.Chwla and ShailendraK.Saraf(2012),Der Pharmacia Scince;3(5),546-555.

[10] Xiang W. and W.Wei (2006),E-Journal of Chemistry ;2(2),121-125.

[11] A.A.Fadda A.A.H-Abdel-Rhman,E.H.Khlil(2012), American J.of Org.Chem.;2(2),7-13.

[12] E.C.Taylor,JR and W.Norman (1956);78(16),5108.

[13] A.K.Elziaty ,O.E.A.Mostafa,E.A.EL-Bordany,M. Nabil and H.M.F.Madkour(2014),Inter.J.ofScien. &Eng.Res.;5(1),727-735.

Table II
Spectral data for compounds (3a-e)

Comp.		^{13}CNMR	**U.V.**	**FTIR (KBr) γcm^{-1}**

No.	^{1}HNMR **δ (ppm) DMSO-d_6**	**δ (ppm) DMSO-d_6**	**$CHCl_3$ ʎ max nm**	**C=N**	**NH_2**	**others**
3a	δ 1.89 (S, 3H, CH_3), δ 5.41 (b, 1H, CH), δ 6,45 (d, 2H,NH_2), δ 7.17-7.378 (m, 5H, ArH), δ 7.54-7.81(m, 5H, ArH), δ 12.21 (s, 1H, SH),	14.1,41.4,102.4,119.5,122.4,125.4,126,7,128.4,129,4 ,136.7,137.4,147.7,165.9.173.2,175.7	340	1625	3220 3225	1188 (C=S)
3b	δ 1.92 (S, 3H, CH_3), δ 5.38 (b, 1H, CH), δ 6,48 (d, 2H,NH_2), δ 7.11-7.32 (m, 5H, ArH), δ 7.48-7.78(m, 5H, ArH), δ 8.52 (s, 1H, CH=N),	13.9,40.7,101.8,119.2,120.3,122.1,125.3,126.3,128.5,129.4,130.2 ,136.6,137.5,147.5,165.7.173.7,175.4	300	1598	3032 3059	`1173 C-O-C
3c	δ 1.94 (S, 3H, CH_3), δ 1.32(S, 3H, $CH_2\underline{CH_3}$), δ 5.33 (b, 1H, CH),), δ 4.32(S, 1H, $\underline{CH_2}CH_3$) , δ 7.15-7.31 (m, 5H, ArH), δ 7.43-7.77(m, 5H, ArH), δ 11.86 (d, 2H,NH_2)	13.94,40.6,101.55,119.7,120.35,122.1,125.4, 126.2,128.55,129.5,130.2 ,136.6,137.6,147.2,165.4.173.6,175.6	287	1599	3197 3327	1719 C=O 3100 NH
3d	δ 1.91 (S, 3H, CH_3), δ 5.34 (b, 1H, CH),5.84(d, 2H,NH_2) , δ 7.16-7.32 (m, 5H, ArH), δ 7.44-7.75(m, 5H, ArH), δ 11.86 (s, H,NH), δ 12.18 (s, H,OH).	9.94,42.4,101.6,114.3,119.3,120.2,122.1,125.2,126.4,128.52,129.8,130.5 ,136.8,137.6,147.8,165.9.172.9,175.8	322	1599	3284 3354	3480 OH
3e	δ 1.94 (S, 3H, CH_3), δ 5.41 (b, 1H, CH),6.34(d, 2H,NH_2) , 6.88(d, 2H,NH_2) ,δ 7.19-7.33 (m, 5H, ArH), δ 7.41-7.79(m, 5H, ArH).	13.34,43.6,101.2,119.2,120.6,122.45,125.2,126.6,128.5,129.9,130.7 ,136.4,137.7,147.5,165.7.173.2,175.2.	340	1601	3026 3128	1185 C-O