IJPSR (2016), Vol. 7, Issue 11 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 11 June, 2016; received in revised form, 16 August, 2016; accepted, 28 September, 2016; published 01 November, 2016

# SYNTHESIS AND BIOLOGICAL EVALUATION OF SOME NEW PYRAZOLE DERIVATIVES

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**Keywords:**

Acetylfuran, Phenylhydrazine, Vilsmeier-Haack Reaction, Antimicrobial activity

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**ABSTRACT:** The synthesis of a novel of pyrazole derivatives was achieved by condensation of acetyl furan with phenyl hydrazine to give hydrazone (1) On the other hand, cyclization of α, β-unsaturated ketone. Using Vilsmeier reagent by DMF (dimethylformamid) and $POCl_3$ Phosphorusoxychloride) to give compound (2). The chemical structures of allnew compounds were established by IR, ¹HNMR, and mass spectra data. All the synthesized compounds were screened for in vitro antibacterial activity and most of them showed potency against both gram positive and gram negative bacteria. Compounds 4-(α-benzoyl aminoacrylic acid) – 3 - Furayl-1-phenylpyrazol, 4 - (α-benzoylaminomethylacrylate)-3-Furayl-1-phenylpyrazol, 4- (2-4-dinitrophenylhydrazone)-3-Furayl-1-phenylpyrazole showed the highest antibacterial activity against Bacillus subtilis strain with minium inhibition zone 19 mm.

**INTRODUCTION:** Pyrazole symbolizes a class of simple aromatic ring organic compounds of the heterocyclic series which is a 5-membered ring skeleton composed of three carbon and two nitrogen atoms. Ludwig Knorr was the first who coined the term pyrazole in 1883. In 1959, the first natural pyrazole, 1-pyrazolyl-alanine, was isolated from seeds of watermelons [1-2]. A bulk of literature is available to show the biological versatility such as anti-inflammatory [3], antibacterial [4-5], anti-convulsant [6], anticancer [7-8], anti-depressant [9], anti-hyperglycemic [10], antiviral [11], antipyretic [12], antioxidant [13], ant tubercular [14], fungicides [15], and analgesic activities [16].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.7(11).4414-21

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.7 (11).4414-21

These pyrazoles have also found applications in Transition-metal chemistry as an analytical reagent [17]. Pyrazoles are weak mono-acidic-bases, formatting with mineral acid salts which dissociate in a vacuum and hydrolyse in water.

The ring system is more stable and less reactive than that of pyrrole. N-Phenyl group being replaced by hydrogen, although C-phenyl groups (unless aminated or hydroxylated) There are number of attempts to accomplish their separation through ions formed by addition or loss a proton, or as a result of the association, which is indicated by cryoscopic measurements and by the higher boiling point of isomer sun substituted nitrogen[18].

## MATERIALS:

Determinations of melting points were performed in open glass capillaries using electro thermal BUCHI (B-540) hot storage melting-point apparatus and are uncorrected. Infra-red (IR) spectra were recorded on a Shimadzu 435 Spectrometer, using KBr discs and values were represented in $cm^{-1}$ at the Micro analytical Center, Cairo University. (MS) Mass spectra were run on Shimadzu QP-2010 spectrometer and Mass spectra were run on Hewlett Packard 5988 spectrometer at the Micro analytical Center, Cairo University, Egypt. $^1$HNMRspectrawas recorded on Bruker (300MHz) FT-NMR spectrometer using DMSO and the chemical shifts are given in δ (ppm) using tetramethylsilane (TMS) as an internal standard. Splitting patterns were designated as follows: s: singlet; d: doublet and m: multiplet.

The biological activity analysis was carried out at, Division of Pharmaceutical Industries, National Research Center, Cairo, Egypt. the compounds was made by thin layer chromatography (TLC) on silica gel-precoated aluminum sheets and the spots were detected by the aid of iodine vapour and by exposure to UV lamp at $\lambda_{254}$ nm for few seconds. Starting materials, MeOH, DMF, $POCl_3$, hexane and diethyl ether were either commercially available as reported in literature.

### Synthesis of 1-phenyl-3-Furayl pyrazole-4-carbaldehyde (2):

Mixture of (0.01 mole) of acetyl furan , and (0.01 mole) of phenylhydrazine in 10ml Ethanol was refluxed in water bath for 4 h. the reaction mixture was cooled .the solid formed dried and crystallization from diethyl ether the formed of hydrazones (l) Show the following data; yellow color solid , Yield= 66.9%, MP. =75-73 $^{\circ}$C, and Mixture of 2.0gm (0.01 mole) of (I) Vilsmeier reagent, and 0.73 gm (0.01 mole) of DMF(di methyl form amid), 1.53gm (0.01 mole) of $POCl_3$ (Phosphorusoxychloride) was added drop wise with mechanical stirring for five hour. The reaction mixture was refluxed for six hours at 70-80$^{o}$C, then hydrolyzed on ice/water mixture, and neutralized by 5% NaOH Solution till pH4, the reaction mixture was cooled. The solid formed was filtered, washed with water, dried and crystallization from isopropanol. Show the following data Mp. 252-3 $^{\circ}$C; Yield: (90.2%), Infra-red spectra of compound (2) show: $\nu_{C=Oofald.}$1667.16,$\nu_{C=N}$1602.56, $\nu_{C=C}$ 1510.89, $\nu_{C\text{-}Hof\ 2\ adj.H}$820.02 and $\nu_{C\text{-}Hof\ 5\ adj.H}$ 731.10 $cm^{-1}$, $^1$HNMR (DMSO, 300 MHz) δppm=10.13 (s,1H,CHO), 9.31 (C-H Pyrazole), 6.54– 7.95 (m, 8H,Ar- H ), The mass spectra show the molecular ion peak at m/e = 238 $[M]^+$ ,78 %)The base ion peak at m/e=77 $[M]^+$ (-$C_8H_5N_2O$,100%),m/e= 209$[M]^+$ (- CHO,15.2 %), m/e=237$[M]^+$(-H,74%), m/e=210$[M]^+$(-CO ,20%).

### General method for preparation of compounds 3a, 3b:

Mixture of 0.24gm (0.001 mole) of compound (2), 0.18 gm, (0.001 mole) of benzoyl glycine ,0.12 gm. (0.001 mole) acetyl glycine and 0.04 gm.(0.001 mole) of sodium acetate in 5ml acetic anhydride. Was refluxed for two hours. The reaction mixture was cooled. hydrolyzed on ice/water. The solid formed was filtered, washed with water till pH7, then dried, crystallization from carbon tetrachloride.

### Synthesisof 4 - [2' - Phenyl-5'(4'H)-oxazolonyl methylidene]-3-Furayl-l-phenylpyrazole(3a):

Show the following data; MP. =206 -7 $^{\circ}$C Yield= 78.7%, Infra-red spectra of compound (3a) show: $\nu_{C=O}$1782.37, $\nu_{C=C}$1639, $\nu_{C=N}$ 1588.49 and $\nu_{C\text{-}O}$1227.4 $cm^{-1}$ , $^1$HNMR (DMSO-300 MHz): δ ppm = 8.1(m,2H,C-HPyrazole),7.94(m,2H,Ph-H),7.87 (m,3H,Ph-H),7.27– 7.64 (m, 5H, Ar-H),7.15 (CH=CH), The mass spectra show the molecular ion peak at m/e = 381 $[M]^+$ ,75 %)The base ion peak at m/e = 77$[M]^+$ (- $C_{17}H_{10}N_3O_3$ ,100 %),m/e=337 $[M]^+$(-$CO_2$,30.2%),m/e= 314 $[M]^+$(-$C_4H_3O$,15.5%), m/e=222$[M]^+$ (-$C_9H_5NO_2$ ,4.3%) .

### Synthesis of 4-[2' -methyl-5'(4'H)-oxazolony lmethylidene]-3-Furayl-l-phenylpyrazole(3b):

Show the following data; MP. =147-8 $^{\circ}$C Yield= 84.6%, Infra-red spectra of compound (3b) show: $\nu_{C=O}$ 1720.73, $\nu_{C=C}$ 1605, $\nu_{C=N}$ 1518.49 and $\nu_{C\text{-}O}$ 1237.3 $cm^{-1}$, The mass spectra show the molecular ion peak at m/e = 319 $[M]^+$, 2.1 %) The base ion peak at m/e = 237$[M]^+$ (- $C_3NO_2$ ,100 %), m/e=248M$]^+$(-$C_3H_3O_2$,4.5%), m/e = 222 $[M]^+$ (-$C_4H_3NO_2$,5.3%),m/e=77$[M]^+$ (-$C_{12}H_8N_3O_3$,55.3%, m/e=67$[M]^+$ (-$C_{14}H_{10}N_3O_2$ ,30.2%).

**General method for preparation of compounds 4a, 4b:**

Mixture of 0.23gm (0.00065 mole) of compounds (3a, 3b), and 0.026 gm. (0.00065 mole) sodium hydroxide in 25ml ethanol was refluxed for three hours. The solution was concentrated, diluted with 100 ml water and acidified with 2% solution HCL. The solid formed was filtered, washed with water, then dried and crystallization from ethanol.

**Synthesis of 4-(α-benzoyl aminoacrylic acid)-3-Furayl-1-phenylpyrazol (4a):**

Show the following data; MP. =209-10 °C Yield= 62.4%, Infra-red spectra of compound (4a) show: $_{v\text{-}NH}$ 3324, $_{vC=OofPh}$1682$_{vC=Oof\ acid}$ 1628, $_{vC=N}$ 1576, and $_{vC=C}$1561.62cm$^{-1}$, $^{1}$HNMR (DMSO-300 MHz): δ ppm = 10.43(C-H acid),8.43 (m,3H,Ph-H),8.1(C-H Pyrazole),7.2– 7.96 (m,5H,Ar-H), The mass spectra show the molecular base ion peak at m/e = 399[M]$^{+}$ ,100 %), m/e = 382 [M]$^{+}$(- OH ,35 %),m/e=354 M]$^{+}$(-COOH,10.6%), m/e = 95 [M]$^{+}$ $C_{19}H_{14}NO_3$, 7.3%), m/e=77[M]$^{+}$ (-$C_{17}H_{12}N_3O_4$,86%).

**Synthesis of 4-(α-acetylaminoacrylic acid)-3-Furayl-1-phenylpyrazol (4b):**

Show the following data; MP. =152-3 °C Yield= 91.2%, Infra-red spectra of compound (4b) show: $_{v\text{-}NH}$ 3324, $_{vC=Oof\ CH3}$ 1688,$_{vC=Oof\ acid}$ 1632, $_{vC=N}$ 1580 and$_{vC=C}$ 1565cm$^{-1}$,The mass spectra show the molecular base ion peak at m/e = 337 [M]$^{+}$ ,100 %), m/e = 320[M]$^{+}$ (- OH ,40.5 %), m/e=292 [M]$^{+}$ (-COOH, 14.3%) , m/e= 279 [M]$^{+}$(-$C_2H_4NO$,7.2%), m/e=77[M]$^{+}$(- $C_{12}H_{10}N_3O_4$ ,73.8%).

**Synthesis of 4-(α-benzoylaminomethyl acrylate)-3-Furayl-1-phenylpyrazol (5):**

A suspension containing (0.0005 mole) of compound (3a), 0.19 gm. in 25 ml methanol and 0..04gm (0.0005mole) sodium acetate .was refluxed for 30 hours. The solution was concentrated and cooling, the solid formed was filtered, and crystallization from ethanol, Show the following data MP. = 222-3°C Yield = 82.2%, Infra-red spectra of compound (5) show: $_{v\text{-}NH}$ 3323,$_{vC=OofPh}$ 1761, $_{vC=Oof\ ester}$ 1720, $_{vC=N}$ 1674, and$_{vC=C}$ 1561cm$^{-1}$,$^{1}$HNMR (DMSO-300 MHz): δ ppm = 8.1(C-H Pyrazole) ,7.4– 8.2 (m,5H,Ar-H),6.64 (CH=C), 3.77(s,3H, CH3), The mass spectra show the molecular ion peak at m/e = 413 [M]$^{+}$ , 9.4 %) The base ion peak at m/e = 95[M]$^{+}$ (-$C_{20}H_{16}NO_3$ ,100 %), m/e=382 [M]$^{+}$ (-$OCH_3$, 8.5%), m/e= 308 [M]$^{+}$ ($C_7H_5O$,1.2%), m/e = 222[M]$^{+}$(-$C_{10}H_9NO_3$,4.1%), m/e=67[M]$^{+}$(-$C_{20}H_{16}N_3O_3$,48.2 %).

**Synthesis of 4-(α-benzoylaminoacrylic acid hydrazide)-3-Furayl-1-phenylpyrazol (6):**

A Mixture of 0.31 gm. (0.0008mole) of compound (3a). And 0.0008 ml (0.0008 moles) of 50% hydrazine hydrates in 20ml ethanol. Was refluxed for eight hours. The solution was concentrated and cooling, the solid formed was filtered, and crystallization from ethanol, Show the following data MP. = 204-5 °C, Yield = 75.6%, Infra-red spectra of compound (6) show: $_{vC\text{-}NH}$ 3431, $_{vNH2}$ 3280, $_{vC=O}$ 1668, $_{vC=N}$ 1622 and $_{vC=C}$ 1554 cm$^{-1}$,$^{1}$HNMR (DMSO-300 MHz): δ ppm = 8.4(C-H Pyrazole) ,7.2– 8.3 (m, 5H,Ar- H) ,6.54 (CH=C),1.9(-$NH_2$),The mass spectra show the molecular ion peak at m/e = 413 [M]$^{+}$ ,33 %) The base ion peak at m/e = 77[M]$^{+}$ (- $C_{17}H_{14}N_5O_3$ ,100 %), m/e=397 [M]$^{+}$ (-NH2, 3.5%) , m/e= 354 [M]$^{+}$(-$CH_3N_2O$ ,1.2%), m/e=293 [M]$^{+}$ (-$C_7H_6NO_3$, 20%) , m/e=67[M]$^{+}$(-$C_{19}H_{16}N_5O_2$,63%).

**Synthesis of α, α¯bis ((3-Furayl-1-Phenyl pyrazolyl) -4-methylidene) cyclohexanone: (7)**

A mixture of 0.2gm (0.00085 mole) of compound (2),and 0.17 ml. (0.0017 mole) cyclohexanone in 50% aqueous (DMSO) dimethylsulphoxide and 10 ml sodium hydroxide was stirred at 100°C for five hours. After cooling and neutralization with diluted HCL. The solid formed was filtered, washed with water, then dried and crystallization from ethanol, Show the following data MP. = 273-4°C, Yield = 83 %, Infra-red spectra of compound (7) show: $_{vC=C}$ 3055, $_{vC=O}$ 1659and $_{vC=N}$ 1628cm$^{-1}$, $^{1}$HNMR (DMSO-300 MHz): δ ppm = 8.43(s,C-H Pyrazole) ,8.41(D,CH=CH),7.1– 7.42 (m, 5H,Ar-H),1.55 (t,2H,$CH_2$), The mass spectra show the molecular ion peak at m/e = 538 [M]$^{+}$ ,15.6 %)The base ion peakatm/e=67[M]$^{+}$(-$C_{30}H_{23}N_4O_2$,100%),m/e=510 [M]$^{+}$(-CO, 23%), m/e=444 [M]$^{+}$(-$C_6H_6O$ ,20.6%), m/e=222 [M]$^{+}$ (-$C_{20}H_{16}N_2O_2$, 4%), m/e=95[M]$^{+}$(-$C_{30}H_{23}N_2O_2$,4.3%).

**Synthesis of 4-(2¯4¯-dinitrophenylhydrazone)-3-Furayl-1-phenylpyrazole (8):**

A mixture of 0.083 gm (0.00085 mole). of concentrated sulphuric acid $H_2SO4$ was added

coutiosouly to a suspension of 0.17 gm (0.00085mole) 2.4dinitrophenyl hydrazine(DNP) in 10 ml methanol. The solution was wormed and filtered. And 0.2 gm (0.000085 mole) of compound (2) was added to the filtrate with stirring. The solid formed was filtered, and crystallization from ethanol, Show the following data MP = 281-2 °C, Yield = 87.2%, Infra-red Spectra of compound (8) show: $_{v\text{-NH}}$3230 ,$_{vC=N}$ 1612, $_{vC=C}$ 1524, $_{vC\text{-H of 2 adj.H}}$ 815and $_{vC\text{-H of 5 adj.H}}$ 724 $cm^{-1}$, $^{1}$HNMR (DMSO-300 MHz):δ ppm = 7.2-8.4 (m,5H, Ar- H), 8.6(CH=N), 7.1 (-NH)The mass spectra show the molecular ion peak at m/e=418$[M]^{+}$,32.6 %)The base ion peak at m/e = 67 $[M]^{+}$(- $C_{16}H_{11}N_6O_4$ ,100 %), m/e=372 $[M]^{+}$(-$NO_2$, 76.1%),m/e=326 $[M]^{+}$(-$N_2O_4$,65.3%), m/e=222 $[M]^{+}$ (-$C_6H_4N_4O_4$,3.2%), m/e=95$[M]^{+}$(-$C_{16}H_{11}N_4O_4$,3.4%).

**Synthesis of 4-[(2'-Phenyl-2'-imidazolin-5'-onyl)methylidene]-3-Furayl-l- phenylpyrazole(9)**

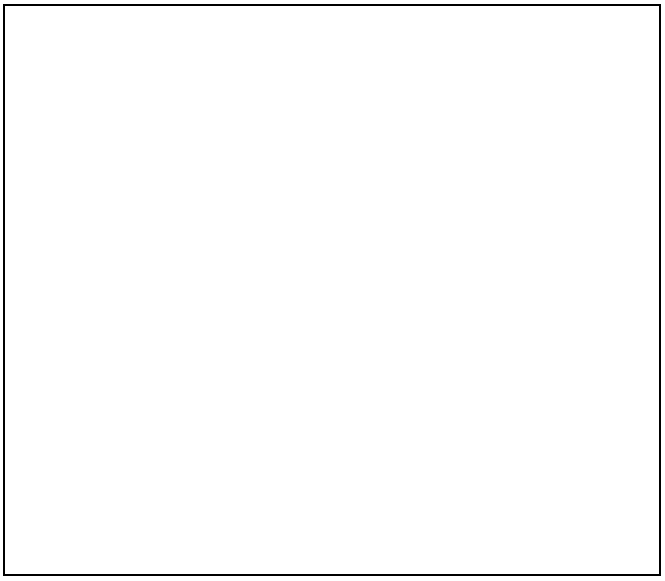
A Mixture of 0.2gm (0.00085 mole) of compound (2), and 0.27 gm. (0.0017 mole) of benzamidine hydrochloride dehydrate and 0.2 gm. (0.0017 mole) of Ethylchloroacetate in 20ml n- propanol . Was refluxed with strring for one hours. The solid formed was filtered, washed with methanol, water, and finally with methanol, then dried and crystallization from n-butanol, Show the following data MP. = 324-5°C, Yield = 92.8 %, Infra-red spectra of compound (9)$_{vc\text{-NH}}$ 3105, $_{vC=O}$1705,$_{vC=C}$ 1640and $_{vC=C}$ 1640$cm^{-1}$,1HNMR ( DMSO-300 MHz): δ ppm = 8.43 (s,C-H Pyrazole) ,8.01(-NH),6.98– 7.86 (m, 13H, H aroma), The mass spectra show the molecular ion peak at m/e = 380 $[M]^{+}$ ,39.2 %)The base ion peak at m/e = 67$[M]^{+}$ (-$C_{19}H_{13}N_4O$, 100%),m/e=352$[M]^{+}$(-CO, 5.9%), m/e=248 $[M]^{+}$(-$C_8H_6NO$,13.6%),m/e=222$[M]^{+}$ (-$C_9H_6N_2O$, (20.3%), m/e = 95$[M]^{+}$ (- $C_{19}H_{13}N_2O$, 45.2%).

**Synthesis of 4, 3-[(6-Amino-5-cyano-4- -phenyl] -3-Furayl-1-phenylpyrazole (10):**

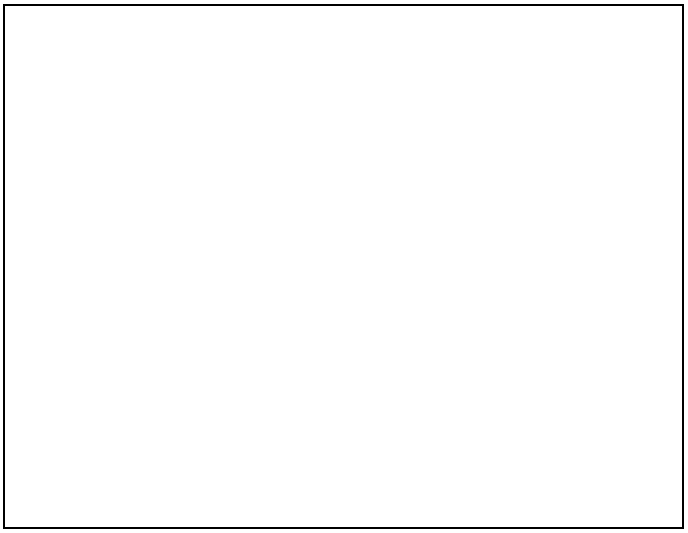
A Mixture of 0.03gm (0.000125 moles) of compound (2), and 0.008 gm. (0.000125 mole) of malononitrile and in 20ml absolute ethanol and few drops of piperidine were refluxed for four hours. After cooling the separated solid was filtered, dried, and crystallization from ethanol, Show the following data MP. = 204-5°C. Yield = 89.4 %, The spectra of compound (10) show $^{1}$HNMR (DMSO-300 MHz): δ ppm = 8.43(s, C-H Pyrazole), 7.86–7.45 (m, 8H, H aroma), 6.98 (D, CH=CH), The mass spectra show the molecular ion peak at m/e = 286 $[M]^{+}$ ,16.2 %) The base ion peak at m/e = 67$[M]^{+}$ (-$C_{13}H_7N_4$, 100%), m/e=285$[M]^{+}$(-H, 33.2%),m/e=260 $[M]^{+}$(-CN,52.1%),m/e=259$[M]^{+}$ (-HCN, (13.2%), m/e = 95$[M]^{+}$ (- $C_{13}H_7N_2$,6.2%).

**RESULTS AND DISCUSSION:**

Substituted phenyl hydrazines were prepared by heating substituted a acetyl furan with different hydrazines in methanol under reflux for 4-5 h. Vilsmeier-Haack reaction of phenyl hydrazines using DMF and $POCl_3$ afforded 1-phenyl-3-Furayl pyrazole-4-carbaldehyde in good yields and in high purity. The structures were confirmed on the basis of IR, $^{1}$HNMR and mass spectral data according to scheme(1).

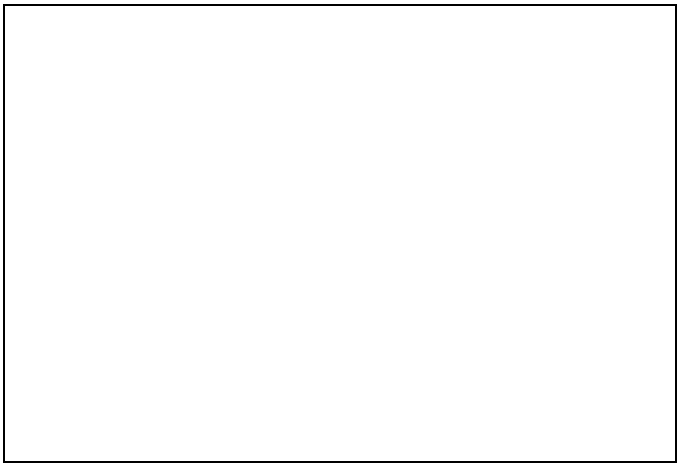


The aldehyde (2) were converted into 4-[2' -Phenyl-5'(4'H)-oxazolonylmethylidene]-3-Furayl-l-phenylpyrazole(3a) and 4-[2' -methyl-5'(4'H)-oxazolonyl methylidene] - 3- Furayl - l-phenyl pyrazole (3b) to react with benzoyl glycine ,acetyl glycine in presence of sodium acetate in 5ml acetic anhydride The structures were confirmed on the basis of IR, $^{1}$H NMR and mass spectral data according to scheme (2) and the end product (3a, 3b) to hydrolysis with sodium hydroxide to yield4-(α-benzoyl aminoacrylic acid)-3-Furayl-1-phenyl pyrazol(4a)4-(α-acetylaminoacrylicacid)- 3-Furayl-1-phenylpyrazol(4b)The structures were confirmed on the basis of IR, $^{1}$H NMR and M.S. data according to scheme (2).

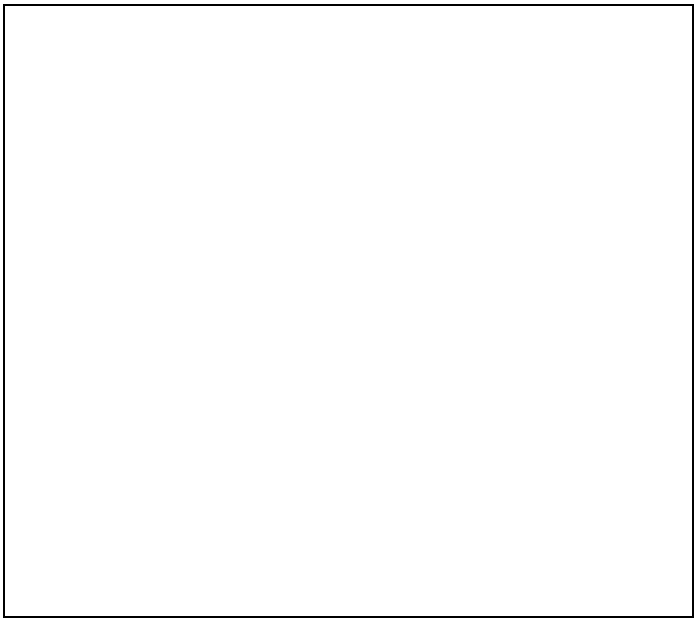


And the hydrolysis of compound (3a) with sodium acetatetoformed4-(α-benzoylaminomethylacrylate)-3-Furayl-1-phenylpyrazol(5) and react with hydrazine hydrate to formed the 4-(α-benzoylaminoacrylic acid hydrazide) – 3 - Furayl-1-phenylpyrazol(6)The structures were confirmed on the basis of IR, $^1$HNMR and M.S. data according to scheme (3)

and The aldehyde (2) were converted into α, α$^-$-bis((3-Furayl-1-Phenylpyrazolyl) – 4 -methylidene) cyclohexanone(7), 4-(2-4—dinitrophenyl hydra zone) -3-Furayl-1-phenylpyrazole (8) to react with cyclohexano n in 50% aqueous (DMSO) dimethyl sulphoxide , concentratedsulphuricacid$H_2SO4$and .4dinitrophenyl hydrazine(DNP) The structures were confirmed on the basis of IR, $^1$H NMR and mass spectral data according to scheme (4)

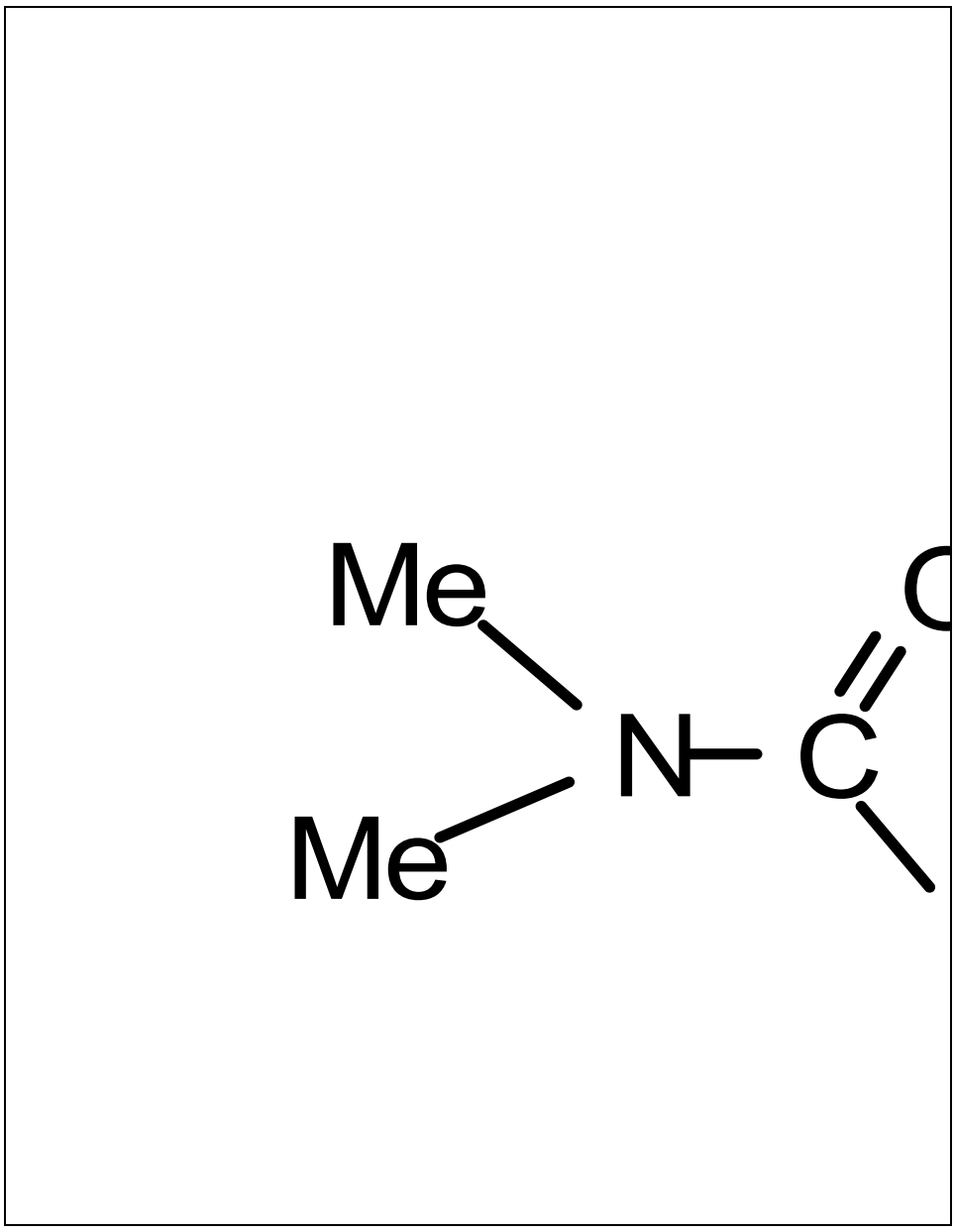


and The aldehyde (2) react with benzamidine hydrochloride dehydrate and Ethylchloroacetate , malononitrile to formed the compounds 4-[(2'-Phenyl-2'-imidazolin-5'-onyl) methylidene]-3-Furayl-l- phenylpyrazole(9) 4, 3-[(6-Amino-5--cyano-4- -phenyl]-3-Furayl-1-phenylpyrazole (10) The structures were confirmed on the basis of IR, $^1$HNMR and mass spectral data according to scheme (5)



A possible mechanism for cyclization along with formylation of pyrazole is outlined in scheme (6). The proposed mechanism is initial electrophilic attack of Vilsmeier-Haack reagent (A) on hydrazone(1) yielded the intermediate (B)which subsequently losses amolecule of HCl to provide intermediate (C). The nucleophilic attack by N-H group initiates the cyclisation and the resulting pyrazole intermediate losses $Me_2NH$ to give the

more stable pyrazole derivative (D). The pyrazole (D) react with another molecule of V.H. reagent (A) in an electrophilic substitution process giving an minimum salt (E), which is hydrolysed to corresponding 4-formyl pyrazole (2) as depicted in scheme (6), In summary the electrophilic attack of first Vilsmeier –Haack (VH) complex at the probable attacking site of hydrazones results into cyclisation. While electrophilic attack of second (VH) complex forms formyl product after hydrolysis. Finally intra molecular (1,5) hydrogen shift, cyclisation and elimination of $NHMe_2$ to give pyrazole derivative with this series of pyrazole aldehydes in hand.




**Antimicrobial screening:**

The antibacterial activities of the synthesized compounds were tested against *Escherichia coli* NRRL B-210 and Pseudomonas NRRL B-23 (Gram -ve bacteria), *Bacillus subtilis* NRRL B-543 and *Staphylococcus aureus* NRRL B-313 (Gram +ve bacteria) using nutrient agar medium. The antifungal activity of these compounds was also tested against *Candida albicans* NRRL Y-477 using Sabouraud dextrose agar medium.

**Agar Diffusion Medium:**

The synthesized compounds were screened *in vitro* for their antimicrobial activity against, by agar diffusion method (Cruickshank *et al*.1975). 0.5 ml suspension of each of the aforementioned

microorganisms was added to sterile nutrient agar media at 45°C and the mixture was transferred to sterile Petri dishes and allowed to solidify. Holes of 0.9cm in diameter were made using a cork borer. Amounts of 0.1ml of the synthesized compounds were poured inside the holes. A hole filled with DMSO was also used as control. The plates were left for 1 hour at room temperature as a period of pre-incubation diffusion to minimize the effects to variation in time between the applications of the different solutions. The diameters of the inhibition zone of were measured and compared with that of the standard and the values were tabulated. The same method was carried out using Sabouraud dextrose agar medium on using *Candida albicans* NRRL Y-477. The plates were then incubated at 30°C for 24 hours and observed for antibacterial activity. The diameters of inhibition zone were measured and compared with that of the standard, the values were tabulated. Ciprofloxacin (50µg/ml) and Fusidic acid (50µg/ml) were used as standard for antibacterial and antifungal activity respectively [19-21]. The observed zone of inhibition is presented in **Table 1.**

**TABLE 1: *IN VITRO* ANTIMICROBIAL ACTIVITY BY AGAR DIFFUSION METHOD OF TESTED COMPOUNDS**

| Compds. | Microorganism inhibition zone diameter mm (Relative inhibition %) | | | | |
|---|---|---|---|---|---|
| | Gram +ve bacteria | | Gram –ve bacteria | | Fungi |
| | ***BacillusSubtilis*** | ***Staphylococcus aureus*** | ***Escherichiacoli*** | ***Pseudomonas aeuroginosa*** | ***Candida albicans*** |
| 2 | 13(65) | 13(68.4) | 18(94.7) | 12(66.7) | 13(65) |
| 3a | 12(60) | 18(94.7) | 17(89.5) | -ve(0) | 12(60) |
| 3b | 17(85) | 17(89.5) | 18(94.7) | 12(66.7) | 14(70) |
| 4a | 19(95) | 16(84.2) | 12(63.2) | 13(72.2) | 12(60) |
| 4b | 14(70) | 14(73.7) | 13(68.4) | 17(94.4) | 13(65) |
| 5 | 19(95) | 13(68.4) | 12(63.2) | -ve(0) | 18(90) |
| 6 | 13(65) | 12(63.2) | 12(63.2) | 16(88.9) | 12(60) |
| 7 | 13(65) | 14(73.7) | 16(84.2) | 14(77.8) | 14(70) |
| 8 | 19(95) | 18(94.7) | 12(63.2) | 13(72.2) | 17(85) |
| 9 | 15(75) | 14(73.7) | 13(68.4) | 16(88.9) | 14(70) |
| Ciprofloxacin | 20(100) | 19(100) | 19(100) | 18(100) | - |
| Fusidic acid | - | - | - | - | 20(100) |

Highly active (+++)= (inhibition zone > 17 mm)
Moderately active (++)=(inhibition zone 12 - 16 mm)
Slightly active (+)= (inhibition zone 8 - 11 mm)
Inactive (-ve) = (inhibition zone < 8 mm)

**CONCLUSION**: In the present study, our attention was focused on the synthesis and antimicrobial, antifungi evaluation of pyrazol derivatives compound. The antimicrobial activity of compounds 3b,4a, 5,8 indicated Highly activity against *Bacillus subtilis* (Gram +ve bacteria) and moderate activity to compounds 2,3a,4b, 6,7,9 and the compound 2,3a,3b,7 the Highly activity against against *E coli* (Gram -ve bacteria) while the compounds 4a,4b,5,6,8,9 moderate activity. And the antifungal activity the compounds 5,8 is highly activity against *Candida albicans* while the compunds 2,3a,3b,4a,4b,6,7,9 is moderate activity.

**ACKNOWLEDGEMENT:** The authors are thankful to the Department of organic chemistry of Menoufia University, Egypt for providing literature survey facility to carry out the work.

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**How to cite this article:**
Md. Hamed A, El Gokha AA, Abdelwahed RER, Mohamed AA, EL-Torgoman AM and El-Tantawy El Sayed I: Synthesis and biological evaluation of some new pyrazole derivatives. Int J Pharm Sci Res 2016; 7(11): 4414-21.doi: 10.13040/IJPSR.0975-8232.7(11).4414-21.