**Synthesis, some reactions of 3-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-5-(4-methoxyphenyl)furan-2(3H)-one Containing 1-phenyl-3-*p*-chlorophenyl pyrazole and investigation of their antibacterial, antifungal and anticancer activities**

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**Abstract:** New 3-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-5-(4-methoxyphenyl)furan-2(3H)-one **(3)** has been prepared by condensation carbaldehyde (1) with butyric acid (2). Reaction of 3 with hydrazine hydrate yielded the hydrazide derivative 4. Reaction of the hydrazide derivative 4 with benzoyl chloride yield N-benzoyl derivative 6. On the other hand, treatment of 6 with POCl3 afforded compound 5 not 8 and aminolysis of 3 with primary and/or secondary aliphatic amines gave the corresponding 9a-c. However, refluxing 3 with hydroxylamine hydrochloride in boiling pyridine gave oxazinone derivative 12. Reaction of 3 with ammonium acetate afforded the pyrrolone derivative 13. Friedel-Crafts reaction of 3 with toluidine gave compound 14. The structure of synthesized compound was elucidated on the basis of IR, H1NMR, 13CNMR, MS data and elemental analysis. The prepared compounds were tested for antibacterial, antifungal and anticancer activity.

[Adel M. El-Gendy, Hanadi Y. Medrasi, Mariam A. Al-Sheikh, Alaa A. Othman. **Synthesis, some reactions of 3-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-5-(4-methoxyphenyl)furan-2(3H)-one Containing 1-phenyl-3-*p*-chlorophenyl pyrazole and investigation of their antibacterial, antifungal and anticancer activities.** *N Y Sci J* 2020;13(5):77-90]. ISSN 1554-0200 (print); ISSN 2375-723X (online). <http://www.sciencepub.net/newyork>. 10. doi:[10.7537/marsnys130520.10](http://www.dx.doi.org/10.7537/marsnys130520.10).

**Keywords:** Furan-2(3H)-one, Pyrrolone, Pyridazinone and Oxazinone, Antimicrobial, Anticancer.

**Introduction**

The importance and diverse biological activities of furanone and pyrazole derivatives prompted us to report the synthesis of some new heterocyclebased chromophores based on furanone and pyrazole cores. Therefore, we will focus on the coupling of two excellent molecular moieties, furanone and pyrazole. This combination was suggested in an attempt to investigate the influence of this new structure on the anticipated biological activities, hoping to add some synergistic biological significance to the target molecule, pyrazole could be potentially improve the biological characteristics of furanone. Also, we will study the behavior of the new compound towards different nucleophile species in order to achieve heterocyclic transformations. Our purpose is that it may be possible to develop new organic functional materials through molecular design and synthesis. Moreover, furanone ring derivatives (α, β- unsaturated lactones) acquire a special place in natural chemistry and in heterocyclic chemistry, as the furanone system is a frequently encountered structural motif in many pharmacologically relevant compounds. They are active constituents of many natural and synthetic compounds exhibiting pronounced biological activities, such as anti-inflammatory [1], cardiotonic activity [2], analgesic [3], anticancer [4], anti-convulsant [5], anti-microbial [6] and antiviral activities [7].

Pyrazole and its derivatives constitutes an important class of heterocyclic compounds and has received widespread attention due to their diverse pharmacological activities such as anti-inflammatory–analgesic [8, 9, 10], antimicrobial [11, 12], anticancer [13, 14], antihypertensive [15, 16], antidiabetic [17, 18], antidepressant-anticonvulsant [19, 20] etc.

The products of ring opening of these compounds with nucleophiles are the precursors of a wide variety of biologically important heterocyclic systems viz. pyrrolones [21, 22], pyridazinones [23, 24], pyrazoles [25], triazoles [26], oxadiazoles [27, 28] and isothiazolones [29, 30]. The longstanding interest in these heterocyclic compounds is testified by the wide variety of methods reported in literature for their preparation. The conversion of 2(3H) furanone into other important heterocyclic systems of biological importance was described in a number of publications [3-9]. The furanone ring can be opened readily by a nucleophilic attack at the carbonyl of the ring system. The remainder of this study will focus on the use of this rich reactivity of furanones in the synthesis of

biologically interesting molecules. Pyridazinones, 1, 3, 4-oxadiazoles, 1, 2, 4-triazolesand pyrrolones are heterocyclic systems of diverse biological activities. Furanones have been proven to be excellent substrates for synthesizing such compounds. Thus, conversion of furanones these comounds should involve, in the first step, ring opening of the furanones into the corresponding acid hydrazides. This acid hydrazide is utilized as the key starting material for the synthesis of pyridazinones, 1, 3, 4-oxadiazoles, 1, 2, 4-triazole derivatives and pyrrolones.

**Results and Discussion**

In the present work, new 3-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-5-(4-methoxyphenyl)furan-2(3H)-one **(3)** has been prepared by condensation of 5-(4-chloro-phenyl)-2-phenyl-2H-pyrazole-3-carbaldehyde (**1**) with 4-(4-methoxy-phenyl)-4-oxo-butyric acid (2) in the presence of acetic anhydride and anhydrous sodium acetate under Perkin reaction condictions as showen in scheme 1. The structure of compound 3 was confirmed by correct analytical data. IR spectrum showed absorption band at 1743 cm-1 due to (C=O of γ lactone), 1599 cm-1 (C=C of α, β unsaturated ketone), 13CNMR revealed signal at 161.03 due to C=O of furanone and mass spectrum exhibited molecular ion peak at m/e 457.1 the correct mass of compound **3**.



**Scheme 1**

In this study, we intend to investigate the nucleophilic reaction of hydrazine hydrate with the furanone derivative **3** in refluxing benzene [**31**] to give the hydrazide derivative 2-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-4-(4-methoxyphenyl)-4-oxobutanehydrazide **(4).**

The structure of compound 4 was supported by correct analytical data, IR showed two absorption bands at 1665 cm-1, 1637 cm-1 due to –Ar-CO- and NHCO groups and 1HNMR spectrum exhibited signals at 3.19 (br.s, 2H, NH2), and at 6.56 (br.s, 1H, CONH), 13CNMR revealed two peaks at 158.63, 165.93 due to ArCO, NHCO. Also, mass spectrum showed the correct molecular ion peaks in addition to some of the abundant peaks (cf. experimental).

The present study aimed to use the hydrazide derivative 4 to prepare some useful biologically active heterocyclic compounds. Thus, heating the hydrazide derivative 4 with 6N hydrochloric acid gave compound absorption 4-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-6-(4-methoxyphenyl)-4,5-dihydropyridazin-3(2H)-one **(5)** as explain in scheme 2. The proposed structure was elucidated by IR spectrum which gave bands at 3210 cm-1(NH) and 1662 cm-1 (C=O lactam). 1HNMR spectrum exhibited signal at 13.1(s, 1H, HN-CO) and 13CNMR showed peak at 160.53 due to CO-NH.



**Scheme 2**

However, treatment of compound 4 with benzoyl chloride in boiling benzene led to the formation of *N*-(2-((3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl) methylene)-4-(4-methoxyphenyl)-4-oxobutanoyl) benzohydrazide **(6)** as shown in scheme 3. The structure of 6 was supported by IR spectrum which showed absorption bands at 3225, 3217 cm-1 due to two NH groups and at 1695, 1650, 1614 cm-1 due to three C=O groups. 1HNMR spectrum revealed a singlet signal for vinyl proton and three singlet due to three NH protons. In addition, mass spectrum showed the correct molecular ion peaks at m/e 593.2 in addition to the base peak at m/e 57.1.

Also, the authors investigated the reaction of compound 6 with 6N hydrochloric acid under reflux to yield 1-benzoyl-4-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-6-(4-methoxyphenyl)-1,4-dihydropyridazin-3(2H)-one **(**7**)** scheme 3. The structure of compound 7 was confirmed by IR spectrum which showed absorption bands at 1728, 1651 cm-1due to C=O (pyridazinone) and C=O amide respectively. The value for C=O absorption is a good support for the presence of triazinone structure. Also, mass spectrum showed the correct ion peak. 13CNMR showed peaks at 165.42, 169.3 due to CO-Ph and C3-pyridazinone respectively.

On the other hand, treatment of compound 6 with POCl3 gave compound 5 and did not yield 4-(3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)-1-(4-methoxyphenyl)-3-(5-phenyl-1,3,4-oxadiazol-2-yl)but-3-en-1-one **(8)** as we expected as shown in scheme 3. via debenzoylation followed by cyclizaion. The structure of 5 was elucidated by IR spectrum which revealed absorption bands at 3210 cm-1 and 1626 cm-1 due to NH and C=O respectively. 13CNMR showed peak at 160.41 (HN-CO). Also, mass spectrum and NMR confirmed the proposed structure 5. Aminolysis of furanone 3 with primary [31] and/or secondary amines namely, benzylamine [32], morpholine, and piperidine [26, 27, 30] afforded the corresponding 2-[3-chloro-phenyl)-1-phenyl-1*H*-pyrazol-4-yl-methelene]-4-(4-methoxyphenyl)-1-substituted-butane-1,4-dione **9a-c** as explained in scheme 4. The structure can be supported from correct analytical data and spectroscopic properties. IR spectrum showed bands due to C=O at lower frequency values and the presence of NH band which confirm the opening of the furanone ring by nucleophilic attack of amines. Also, 1HNMR spectrum showed one singlet signal in the downfield region due to the CO-NH protons.



**Scheme 3**

Treatment of 9a with HCl 6N under reflux [33] led the formation of 1-benzyl-3-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-5-(4-methoxyphenyl)-1,3-dihydro-2H-pyrrol-2-one **(10)** scheme 4. The structure was supported by IR spectrum which showed absence of any band due to NH group, 1HNMR showed no signal to (CO-CH2-C=C). In addition, mass spectrum showed the correct molecular ion peaks at m/e 546.1.



**Scheme 4**

However, refluxing furanone 3 with p-toluidine in the presence of freshly fused sodium acetate and acetic acid yielded 3-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-5-(4-methoxyphenyl)-1-(p-tolyl)-1,3-dihydro-2H-pyrrol-2-one **(11)** as describe in scheme 5. The structure was deduced from IR spectrum which revealed absence of NH group, 1HNMR which showed absence of CO-NH group and 13CNMR which exhibited peak at 169.08 due to C=O group.

Though, when furanone 3 was submitted to react with hydroxylamine hydrochloride in boiling pyridine the corresponding 5-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl) methylene)-3-(4-methoxyphenyl)-4,5-dihydro-6H-1,2-oxazin-6-one (**12**) was obtained scheme 5. IR spectrum showed absorption bands at 1727 cm-1 due to (C=O) respectively. The lower frequency value of C=O group confirmed the six membered oxazinone structure. 13CNMR exhibited peak at 164.07 due to C=O.

Refluxing furanone 3 with ammonium acetate [32] afforded 3-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl) methylene)-5-(4-methoxyphenyl)-1,3-dihydro-2H-pyrrol-2-one (**13**) scheme 5. IR spectrum showed absorption bands at 3145, 1700 cm-1 due to NH and C=O respectively, 1HNMR revealed signal at 10.46(s, 1H, NH-CO) and 13CNMR exhibited peak at 160.36 due to C=O.

Friedel-Crafts reaction [33] of furanone 3 with toluene in anhydrous aluminum chloride led to the formation of 3-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl) (p-tolyl)methyl)-5-(4-methoxyphenyl)furan-2(3H)-one **(14)** as shown in scheme 5. IR spectrum exhibited bands at 1751 cm-1(C=O γ-lactone) which confirm the nucleophilic attack to place at α, β-unsaturated ketone and not at O-C=O of furanone ring. 1HNMR revealed two signals at 7.11(s, 1H, furanone), 9.24(s, 1H, Ph-CH-pyrazolyl) which also support the attack at α, β-unsaturated ketone. Also, 13CNMR showed peak at 168.85 due to C=O.



**Scheme 5**

**Biological Study**

**a. Antimicrobial activity**

The results of antimicrobial activity of the prepared compounds were shown in (Table 1). Among the 14 prepared compounds studied, the compounds 9b and 14 showed a significant inhibition zones ranged between 21 and 26 mm against the gram-positive bacteria, *S. aureus* and *S. dermatitis*. Maximum zone of inhibition was observed with the compounds 9b and 14 (26 mm and 25 mm, respectively) against *S. aureus*, However, the prepared chemicals showed lower effects against gram negative bacteria and the inhibition zones were ranged between 8 mm and 14 mm. The greatest zone of inhibition against gram negative bacteria was noticed with compounds 3, 4, 9b, 9c, 13 against *E. coli* (13-14 mm) and 11 against *K.* sp. (13 mm). At the same time, the compound 14 showed the highest antifungal activity against *C. albicans*, *T. rubrum* with inhibition zones varied between 17 and 20 mm. The maximum zone of inhibition were 20 mm and 21 mm and recorded with the compounds 9b and 14, respectively against *T. rubrum*.

**Table 1. Antimicrobial activity of different prepared compounds (20 mg/ml) against gram positive bacteria (*Staphylococcus aureous* PC1219, *Staphylococcus epdermatitis*), gram negative bacteria (*Escherichia coli* NCIM2065, *Klebseilla* sp.), and fungi (*Candida albicans*, *Trycophyton rubrum*).**

|  |  |
| --- | --- |
| **Chemical No.** | **Zone of inhibition (mm)** |
| **Gram positive** | **Gram negative** | **Fungi** |
| ***S. aureus*** | ***S. dermatitis*** | ***E. coli*** | ***K.* sp.** | ***C. albicans*** | ***T. rubrum*** |
| 3 | 17±1.3 | N | 13±0.2 | 09±0.2 | 06±0.1 | 06±0.2 |
| 4 | 12±0.6 | 10±0.4 | 13±0.4 | 11±0.4 | N | N |
| 5 | N | N | N | N | N | N |
| 6 | N | N | N | N | N | N |
| 7 | N | N | 10±0.5 | 08±0.5 | 9±0.8 | 17±0.7 |
| 8 | N | N | N | N | N | N |
| 9a | N | N | 09±0.2 | 10±0.1 | N | N |
| 9b | 26±1.7 | 21±1.6 | 13±0.7 | 11±0.6 | 09±0.5 | 17±0.3 |
| 9c | N | N | 13±0.4 | 11±0.3 | 07±0.2 | 08±0.4 |
| 10 | 18±0.9 | 15±0.7 | 12±0.7 | 11±0.3 | 09±0.7 | 18±0.9 |
| 11 | 08±0.4 | 09±0.6 | N | N | 11±0.1 | 07±0.6 |
| 12 | N | N | N | N | 08±0.6 | 06±0.3 |
| 13 | 18±0.7 | 10±0.3 | 14±0.6 | 13±0.5 | 08±0.5 | 08±0.7 |
| 14 | 25±1.5 | 22±1.3 | N | N | 11±0.5 | 20±1.1 |
| Positive control | 25±2.1 | 26±2.0 | 28±2.4 | 26±2.7 | 25±2.4 | 27±2.5 |

N: Negative effect, Positive control: Streptomycin (30 µg) for bacteria and Amphotericin B (100 μg) for fungi

**b. Antitumor activity**

***In vitro* anticancer activity of the prepared compounds**

The cytotoxicity of the prepared compounds was evaluated in vitro against the human hepatocellular (HepG2) cancer cell lines. For comparison, the cytotoxicity of cisplatin, which is the most widely used anticancer drug for the treatment and prevention of cancer cells was evaluated under the same conditions. The results of inhibition concentration that killed 50% of cells (IC50) of cisplatin and the tested compounds are shown in (Table 2). It was evident that the tested compounds displayed some cancer-cell-growth inhibition after 24 hours of in vitro treatments in the following order 12 > 5 > 9b > 9c. 12 and 5 showed moderate inhibitory effect, with an IC50 value of 79.62 μg/ml.

**Table 2*. In vitro* cytotoxicity of the compounds against HepG2 cancer cell lines that showed IC50 values of cisplatin and the tested compounds.**

|  |  |
| --- | --- |
| **Compound** | **IC50 (μg/ml)** |
| Cisplatin | 31.14 |
| 12 | 79.62 |
| 5 | 98.34 |
| 9b | 168.53 |
| 9c | 186.89 |

**Tumor profiling in the different group of mice upon prepared compounds treatments**

As compared to the EAC–bearing mice (control group), the results showed that the treatment with cisplatin (2 mg/kg/6 consecutive days) daily after one day of tumor inoculation led to a significant decrease in total volume and total number of tumor cells. The treatment 5 and 12 showed the highest antitumor effects when compared with the EAC–bearing group of mice that was evidenced by low tumor volumes and tumor cells count (Table 3).

**Table 3. Total Ehrlich Ascetic Carcinoma (EAC) volume, count and viability of the different groups of tumor-bearing mice (AH).**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Compounds** | **Total volume (ml)** | **Total count (×106/mouse)** | **Viable cells (×106/mouse)** | **Dead cells (×106/mouse)** |
| EAC-control | 13 ± 1.3 | 610 ± 7.8 | 603 ± 7.17 | 7 ± 0.9 |
| Cisplatin (Reference drug) | 0.8 ± 0.23 | 52 ± 1.02 | 9 ± 0.98 | 43 ± 3.9 |
| 5 | 3 ± 0.83 | 110 ± 1.41 | 45 ± 2.02 | 65 ± 2.8 |
| 9b | 9.5 ± 1.56 | 398 ± 1.29 | 330 ± 1.15 | 68 ± 1.52 |
| 9c | 10 ± 1.84 | 455 ± 1.43 | 415 ± 1.56 | 40 ± 1.31 |
| 12 | 2.5 ± 0.63 | 100 ± 1.25 | 30 ± 2.02 | 70 ± 2.8 |

**Conclusion**

In summary, we have reported an effective and simple reaction for the synthesis of novel heterocyclic compounds such as pyrrolone, pyridazinone and oxazinone derivatives utilizing furanone ring. It is proved, that some of the synthesized compounds exhibited significant inhibition zones against gram positive bacteria and a lower effects against gram negative bacteria. At the same revealed highest antifungal activety. Compounds10 and 6 showed moderate cancer cell growth inhibition. Also, showed the highest antitumor effects against Ascetic Carcinoma

**Experimental**

**General**

All purchased solvents and chemicals were of analytical grade and used without further purification. All melting points were determined using open capillaries on a Büchi melting point B-540 apparatus and are uncorrected. Infrared spectra were recorded on a Nicollet Magna 520 FT-IR spectrophotometer using potassium bromide disks and signals are reported in cm-1. 1H and 13C NMR spectra were recorded on (JNM-ECA 500 MHz) made by Joel Japan at Mansoura University using DMSO-d6 as a solvent, and TMS as an internal standard; the chemical shifts are given in δ units (ppm). Abbreviations used for NMR signals: *s* = singlet, *d* = doublet, *t* = triplet, and *m* = multiple. Mass spectra were performed on a Shimadzu mass spectrometer at 70 eV. The mass spectra were recorded on a Shimadzu GC-MS QP-2010 plus mass spectrometer operating at 70eV at the Micro-analytical Center of Cairo University.

**Synthesis of 3-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-5-(4-methoxyphenyl)furan-2(3H)-one (3).**

A mixture of 5-(4-chloro-phenyl)-2-phenyl-2H-pyrazole-3-carbaldehyde (1) (2.807 gm, 0.01 mol) and 4-(4-methoxyphenyl)-4-oxo-butyric acid (2) in (8 mL) acetic anhydride and freshly fused sodium acetate (0.8 gm, 0.01 mol) was refluxed for 4 hours. The reaction mixture was allowed to cool down to room temperature. Then, it was poured in small portions while stirring into ice cold water (50 mL). The solid product obtained was filtered off, washed several times with water and crystallized from acetic acid to afford compound 3.

Yield= 60%, yellow crystals; m.p.: 228°C.

**IR** (νmax, cm-1): (1743(C=O of γ-lactone), 1624 (C=N), 1599(C=C), 749,705 (monosubstituted benzene), 828(p-substituted benzene).

**1H-NMR** (DMSO-d6): δH (ppm): 3.83(s, 3H, CH3-O), 7.08 (m, 2H, Ar-H), 7.1(s, 1H, furanone), 7.42(t, 1H, *J* =7.5 *Hz*, Ar-H), 7.5(s, 1H, CH=C), 7.58 (t, 2H, *J* = 7.5 *Hz*, Ar-H), 7.63-7.7(m, 4H, Ar-H), 7.8(m, 2H, Ar-H), 8.04(d, 2H, *J* = 7.5, Ar-H), 9.22 (s, 1H, pyrazolyl).

**13CNMR** (DMSO-d6): 55.45 (CH3-O), 99.66 (C4-furanone), 114.58 (C4-pyrazolyl), 116.7, 119.4, 120.39, 122.7, 123.31, 126.98, 127.52, 129.03, 129.6, 130.38, 130.45, 168.81 (Ar-H), 128.97 (C5-pyrazolyl), 139 (C3-furanone), 133.8 (HC=C), 152.59 (C5-furanone), 154.75 (C3-pyrazolyl), 161.03 (C2-furanone).

**MS,** m/z (%): 457.1 (M+ +3) (10.20), 456.1(M++2) (35.2), 455.1(M++1) (30.68), 454.1(M+) (100), 453.15(4.13), 426(2.2), 425 (2.11), 291(3.10), 135.1(8.82), 107.1(1.54), 92(2.11), 77(10.42).

**Anal. Calcd for C27H19ClN2O3 (454.11):** C, 71.29; H, 4.21; N, 6.16.

**Found:** C, 71.35; H, 4.31; N, 6.12

**Synthesis 2-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-4-(4-methoxyphenyl)-4-oxobutanehydrazide (4).**

A mixture of compound 3 (4.55 gm, 0.01 mol) in benzene (50 mL) and hydrazine hydrate (0.6408 gm, 0.02 mol) was heated under reflux for 4 hours. The solid separated upon concentrating the reaction mixture and cooling was filtered off, dried and recrystallized from EtOH to give white crystals 4.

Yield=96%, white crystals; m.p.: 210°C.

**IR** (νmax, cm-1): 3310-3290 (NH2), 3194 (NH), 2821 (CH-alphatic), 1665, 1637 (C=O), 1595 (C=N), 1533 (C=C), 743,691 (monosubstituted benzene), 831 (p-disubstituted benzene).

**1H-NMR** (DMSO-d6): δH (ppm): 3.19(br.s, 2H, NH2 exchangeable), 3.74(s, 3H, O-CH3), 4.33 (s, 2H, -CH2-CO), 6.56 (br.s, 1H, CONHNH2 exchangeable), 6.91(m, 2H, Ar-H), 7.1(t, 1H, *J* =6 *Hz*, Ar-H), 7.2-7.33(m, 3H, Ar-H), 7.35(s, 1H, CH=C), 7.4(t, 2H, *J* =7.5 *Hz*, Ar-H), 7.61-7.66(m, 3H, Ar-H), 7.94(d, 2H, *J* =9 *Hz*, Ar-H), 8.69(s, 1H, pyrazolyl).

**13CNMR** (DMSO-d6): 42.97 (CH2-CO), 55.14 (CH3-O), 89.19 (CH-CO), 113.43 (C4-pyrazolyl), 116.62, 117.82, 118.95, 126.90, 126.94, 128.33, 128.93, 129.44, 130.20, 131.05, 135.68, 139.04 (Ar-H), 128.1 (C5-pyrazolyl), 133.38 (CH=C), 151.24 (C3-pyrazolyl), 158.63 (CO-NHNH2), 165.93 (CO-CH2).

**MS,** *m/z* (%): 489.25 (M++3) (0.03), 488.1 (M++2) (0.06), 487.1(M++1) (0.06), 486.1(M+) (0.27), 471.1(10.52), 470.1(37,56), 469.1(33.97), 468.1(100), 467.15(10.48), 455.1(5.3), 454.1(7.91), 453.1(7.9), 452.1(8.69), 410.1(3.14), 409.1(3.98), 365.1(4.72), 325(4.3), 292(2.09), 291(2.23), 77(9.61).

**Anal.Calcd for C27H23ClN4O3 (486.15):** C, 66.60; H, 4.76; N, 11.51.

**Found:** C, 66.50; H, 4.71; N, 11.56.

**Synthesis of 4-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-6-(4-methoxyphenyl)-4,5-dihydropyridazin-3(2H)-one (5).**

**Method A:** A mixture of compound 4 (4.87 gm, 0.01 mol) and (10 mL) 6N HCl was heated under reflux for 2 hours. The solid that separated out after cooling was crystallized from EtOH to give compound 5.

**Method B:** phosphorus oxychloride (10 mL) was added drop wise to compound 6 (11.82 gm, 0.02 mol). The reaction mixture was refluxed for 1 hours at 100℃, then left to cool, poured onto into ice-cold water (20 ml), neutralized with 1.0 N NaHCO3. The precipitate obtained was filtered off, washed with water and recrystallized from EtOH to obtain compound 5.

Yield A= 98%, B=25%, orange crystals; m.p.: 204°C.

**IR** (νmax, cm-1): 3210 (NH), 2840 (CH2-pyridazinone ring), 1662 (C=O), 1605 (C=N), 1579 (C=C), 685,756 (monosubstituted benzene), 843 (p-disubstituted benzene).

**1H-NMR** (DMSO-d6): δH (ppm): 3.77 (s, 3H, CH3-O), 3.92(s, 2H, CH2 of pyridazine), 6.98(d, 2H, J = 6.5 *Hz*, Ar-H), 7.29(t, 1H, *J* = 6 *Hz*, Ar-H), 7.35(s, 1H, CH=C), 7.4(t, 1H, *J* = 7.5 *Hz*, Ar-H), 7.5(d, 3H, *J* = 6.5 *Hz*, Ar-H) 7.6(m, 2H, Ar-H), 7.7(m, 2H, Ar-H), 7.8(d, 2H, *J* = 9 *Hz*, Ar-H), 8.43 (s, 1H, pyrazolyl), 13.1(s, 1H, NH-CO).

**13CNMR** (DMSO-d6): 24.74 (C5-pyridazinone), 55.25 (CH3-O), 114.27 (C4-pyazolyl), 116.83, 118.13, 126.26, 127.03, 127.37, 128.35, 128.74, 128.99, 129.18, 129.53, 131.98, 141.23, 127.03 (C5-pyrazolyl), 132.67 (CH=C), 139.38 (C4-pyridazinone), 149.39 (C6- pyridazinone), 160.02 (C3-pyrazolyl), 160.53(C3- pyridazinone).

**MS,** m/z (%): 471 (M++3) (10.69), 470 (M++2) (38.37 ), 469 (M++1) (38.84), 468 (M+) (100), 467.1(22.71), 453 (2.79), 367(3.85), 365 (9.17), 330 (6.56), 292 (3.57), 291(2.93), 78 (3.17),77 (27.77), 76.1 (3.31), 51(4.43).

**Anal.Calcd for C27H21ClN4O2 (468.14):** C, 69.15; H, 4.51; N, 11.95.

**Found:** C, 69.20; H, 4.48; N, 11.93.

**Synthesis of N-(2-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl) methylene)-4-(4-methoxyphenyl)-4-oxobutanoyl) benzohydrazide(6).**

Benzoyl chloride (1.41 gm, 0.01 mol) was added to solution of 4 (4.87 gm, 0.01 mol) in 20 mL dry benzene. The reaction mixture was heated under reflux at 70℃ for 3 hours. The solid separated after concentration of solvent under reduced pressure was filtered off, washed with water and recrystallized from chloroform to yield compound 6.

Yield = 96%, yellow powder; m.p.: 345°C.

**IR** (νmax, cm-1): 3225, 3217 (NH, NH), 2831 (CH-aliphatic), 1695, 1650, 1614 (C=O), 1613 (C=N), 1599(C=C), 754,709 (monosubstituted benzene), 831(p-disubstituted benzene).

**1H-NMR** (DMSO-d6): δH (ppm): 3.74(s, 3H, CH3-O), 4.31(s, 2H, CH2-CO), 7.13(s, 1H, CH=C), 7.31(t, 1H, *J* = 7.5 *Hz*, Ar-H), 7.46 - 7.53(m, 5H, Ar-H), 7.65 (t, 3H, Ar-H), 7.71(d, 2H, *J* = 7.5 *Hz*, Ar-H), 7.8-7.9(m, 4H, Ar-H), 8.24 (t, 3H, *J* = 8.5 *Hz*, Ar-H), 8.65(s, 1H, pyrazolyl), 9.60 (br. s, 1H, NH-CO, exchangeable), 10.12(br.s, 1H, NH-CO-Ph, exchangeable).

**13CNMR** (DMSO-d6): 55.4 (CH2-CO), 55.62 (CH3-O), 114.34 (C4-pyrazolyl), 99.9, 116.7, 118.8, 119.2, 120.4, 122.8, 123.3, 127.01, 127.5, 129.0, 129.5, 129.6, 130.0, 130.5, 130.6, 138.8 (Ar-H), 128.8 (C5-pyrozolyl), 133.8 (CH=C), 135.5 (CH-CO), 151.1 (C3-pyrazolyl), 154.7 (C-CO-NH), 161.08 (NHNH-CO-ph), 168.8 (CO-CH2).

**MS**, m/z (%): 592.9 (M++2) (2.24), 591.6(M++1) (2.57), 590.2(M+) (7.14), 579.6(8.13), 578.6(6.69), 577.6(16.28), 576.6(6.92), 551.55(20.30), 550.5(5.39), 537.45(5.56), 453(7.95), 368.4(6.01), 367.25(6.86), 341.2(5.39), 339.25(6.13), 313.3(18.06), 239.25(7.04), 98.1(11.29), 97.1(12.18), 95.1(10.57), 93.1(5.14), 85.05(17.44), 84.1(17.02), 83.1(27.43), 82.1(10.58), 81.1(19.69), 79.1(9.59), 77.1(13.74), 73.0(20.77), 71.1(38.4), 70.1(22.08), 69.1(45.5), 67.0(21.89), 60(23.03), 59.1(11.82), 57.1(100), 56.1(30.56), 55.1(93.02), 54.1(14.73), 53.1(10.70), 51(8.13).

**Anal.Calcd for C34H27ClN4O4 (590.17):** C, 69.09; H, 4.60; N, 9.48.

**Found:** C, 69.20; H, 4.71; N, 9.56.

**Synthesis of 1-benzoyl-4-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-6-(4-methoxyphenyl)-1,4-dihydropyridazin-3(2H)-one (7).**

A mixture of (5.91 gm, 0.01 mol) of compound 6 and (10 mL) 6N HCl was heated under reflux for 1 hours. The solid that separated out after cooling was washed with water and crystallized from EtOH to give compound 7.

Yield = 60%, yellow powder; m.p.: 274°C.

**IR** (νmax, cm-1): 3316(NH), 1728, 1651(C=O), 1622(C=N), 1598(C=C), 755,709 (monosubstituted benzene), 836 (p-disubstituted benzene).

**1H-NMR** (DMSO-d6): δH (ppm): 3.77(s, 3H, CH3-O), 6.87(s, 1H, pyridazino), 6.9(d, 1H, *J* = 9 *Hz*, Ar-H), 7.04(d, 2H, *J* = 8.5 *Hz*, Ar-H), 7.12(s, 1H, CH=C), 7.3-7.7(m, 11H, Ar-H), 7.84(d, 2H, *J* = 9 *Hz*, Ar-H), 8.07(d, 2H, *J* = 9 *Hz*, Ar-H), 9.24(s, 1H, pyrazolyl), 11.2(s, 1H, NH-CO).

**13CNMR** (DMSO-d6): 55.24 (CH3-O), 98.65 (C5- pyridazinone), 114.12 (C4-pyrazolyl), 102.59, 114.21, 116.8, 119.36, 120.39, 121.79, 126.22, 127.38, 127.47, 128.97, 129.05, 129.89, 130.06, 130.09, 131.40, 146.52 (Ar-H), 128.76 (C5-pyrazolyl), 132.47 (C6- pyridazinone), 133.74 (CH=C), 138.95 (C4-pyridazinone), 152.68 (C3-pyrazolyl), 165.42 (CO-Ph), 169.03 (C3- pyridazinone).

**MS**, m/z (%): 575.2 (M++3) (13.59), 574.2 (M++2) (40.20), 573.2(M++1) (40.0), 572.2(M+) (100),469.1(3.14), 468.15(3.45), 467.1(7.71), 454.1 (5.00), 453.1 (7.81), 452.1 (10.55), 105.1(20.74), 77.1(22.09), 51(3.23).

**Anal.Calcd for C34H25ClN4O3 (572.16):** C, 71.26; H, 4.40; N, 9.78.

**Found:** C, 71.20; H, 4.38; N, 9.73.

**General procedure for synthesis of 2-[3-chloro-phenyl)-1-phenyl-1*H*-pyrazol-4-yl-methelene]-4-(4-methoxyphenyl)-1-substituted-butane-1,4-dione (9a-c)**

A mixture of furanone 3 (4.55 gm, 0.01 mol) in dry benzene (30 mL) was reacted with primary and/or secondary amines namely, benzylamine, morpholine, and/or piperidine (0.01 mol) was refluxed for 4 h. The solid products that separated after cooling and evaporation of excess solvent under reduced pressure were filtered off and recrystallized from a suitable solvent to yield (9a-c) respectively.

**N-benzyl-2-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-4-(4-methoxyphenyl)-4-oxobutanamide (9a).**

Yield = 85%, white crystals; m.p.: 190°C.

**IR** (νmax, cm-1): 3242 (NH), 2930, 2842 (CH-alphatic), 1672, 1635 (C=O), 1598 (C=N), 1533 (C=C), 758,692 (monosubstituted benzene), 832 (p-disubstituted benzene).

**1H-NMR** (DMSO-d6): δH (ppm): 3.4(s, 2H, CH2-CO), 3.73(s, 3H, CH3-O), 4.06(d, 1H, CH2-N), 4.28(d, 1H, NH-CO), 6.71(s, 1H, CH=C), 6.8(d, 2H, *J* = 7 *Hz*, Ar-H), 7.12–7.20(m, 5H, Ar-H), 7.28(d, 2H, *J* = 9 *Hz*, Ar-H), 7.3(t, 1H, *J* = 7.5 *Hz*, Ar-H), 7.4(t, 2H, *J* = 7.5 *Hz*, Ar-H), 7.6(m, 4H, Ar-H), 8.0 (d, 2H, J=7.5 Hz, Ar-H), 8.72(s, 1H, pyrazolyl).

**13CNMR** (DMSO-d6): 43.40 (CH2-CO), 44.34 (CH2-NH), 55.14 (CH3-O), 113.46 (C4-pyrazolyl), 89.33, 116.84, 118.98, 118.93, 126.41, 126.43, 126.99, 128.06, 128.61, 129.74, 129.55, 130.29, 130.99, 131.05, 138.35, 139.04 (Ar-H), 127.76 (C5-pyrazolyl), 133.45 (CH=C), 135.56 (CH-CO), 151.42 (C3-Pyrazolyl), 158.73 (CO-NH), 167.62(CO-CH2).

**MS**, m/z (%): 564.1 (M++3) (3.13), 563.1 (M++2) (8.99 ), 562.1(M++1) (8.88), 561.1 (M+) (21.97), 546.1 (12.51), 545.1 (36.72), 544.1 (35.87), 543.1 (89.15), 456(13.98), 455(14.18), 454(43.83), 453.1(8.85), 452(22.15), 426(12.58), 409(7.59), 374(8.49), 208(7.20), 136.1(8.74), 135.1(100), 143.15 (6.62), 90.1(5.18), 77(39.30), 51(3.57).

**Anal.Calcd for C34H28ClN3O3 (561.18):** C, 72.66; H, 5.02; N, 7.48.

**Found:** C, 72.64; H, 5.10; N, 7.53.

**2-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-4-(4-methoxyphenyl)-1-morpholinobutane-1,4-dione (9b).**

Yield=70%, yellow crystals; m.p.: 175°C.

**IR** (νmax, cm-1): 2954, 2854 (CH- alphatic), 1674, 1601 (C=O), 1575 (C=N), 1550 (C=C), 754, 686 (monosubstituted benzene), 830 (p-disubstituted benzene).

**1H-NMR** (DMSO-d6): δH (ppm): 3.59(br.s, 8H, morpholine), 3.83(s, 3H, CH3-O), 4.32 (s, 2H, CH2-CO), 6.52(s, 1H, CH=C), 7.01(d, 2H, *J* = 9.5 *Hz*, Ar-H), 7.34(t, 1H, *J* = 7 *Hz,* Ar-H), 7.50-7.62(m, 6H, Ar-H), 7.8(d, 2H, *J* = 9 *Hz*, Ar-H), 7.9(d, 2H, *J* = 8.5 *Hz*, Ar-H), 8.77(s, 1H, pyrazolyl).

**13CNMR** (DMSO-d6): 43.1 (CH2-CO), 55.59 (CH3-O), 66.07 (CH2-N-morpholine), 71.3(CH2-N-morpholine), 113.87 (C4-pyrazolyl), 115.56, 118.74, 122.03, 126.84, 128.83, 129, 129.21, 129.60, 130.64, 131.02, 139.16, 170.50 (Ar-H), 128.26 (C5-pyrazolyl), 131.18 (C=CH), 133.2(CH=C), 150.35 (C3-pyrazolyl), 163.36 (CO-N), 195.85 (CO-CH2).

**MS**, m/z (%): 544.2 (M++3) (1.12), 543.15 (M++2) (3.61), 542.15(M++1) (3.27), 541.2 (M+) (9.12), 457.1 (4.13), 456.1 (13.1), 455.1 (11.81), 454.1 (32.46), 319.1(4.13), 208(3.32),136(8.81), 135.1(100), 134.1(4.2), 107.1 (7.54), 92(6.69), 77(22.22), 70(5.53).

**Anal.Calcd for C31H28ClN3O4 (541.18):** C, 68.69; H, 5.21; N, 7.75.

**Found:** C, 68.64; H, 5.23; N, 7.80.

**2-((3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl)methylene)-4-(4-methoxyphenyl)-1-(piperidin-1-yl)butane-1,4-dione (9c).**

Yield = 60%, white crystals; m.p.: 168°C.

**IR** (νmax, cm-1): 2933, 2853 (CH- alphatic), 1678, 1599 (C=O), 1575 (C=N), 1544 (C=C), 762,694 (monosubstituted benzene), 827 (p-disubstituted benzene).

**1H-NMR** (DMSO-d6): δH (ppm): 1.4-1.5(m, 6H, 3CH2), 3.54 (br.m, 4H, 2N-CH2), 3.83(s, 3H, CH3-O), 4.32 (s, 2H, CH2-CO), 6.4 (s, 1H, CH=C), 7.02(m, 2H, Ar-H), 7.34(t, 1H, *J* = 7.5 *Hz*, Ar-H), 7.50-7.65 (m, 6H, Ar-H), 7.8(d, 2H, *J* = 8 *Hz*, Ar-H),7.9(m, 2H, Ar-H), 8.77(s, 1H, pyrazolyl).

**13CNMR** (DMSO-d6): 24.23 (C4-pipridine), 25.1(C3,5-pipredine), 45.1(CH2-CO), 46.5(C3,5-pipredine), 55.58 ( CH3-O), 113.85 (C4-pyrazolyl), 115.97, 118.72, 121.09, 126.81, 128.81, 129.31, 129.58, 129.59, 130.61, 131.25, 131.81, 163.30 (Ar-H), 128.23 (C5-pyrazolyl), 133.14 (HC=C), 139.18 (C=CH), 150.23 (C3-pyrazolyl), 170.17 (CO-N), 195.76 (CO-CH2).

**MS,** m/z (%): 542.2 (M++3) (1.45), 541.2 (M++2) (4.75 ), 540.2(M++1) (4.58), 539.2 (M+) (12.5), 457.1 (10.97), 456.1 (37.09), 455.1 (32.13), 454.1 (100), 406.1( 9.41), 405.1(7.97), 404.1(25.84), 321.1(8.53), 293.1(4.38), 291.1(7.62), 136.1(5.27), 135.1(60.61), 92(10.51), 84.1(6.70), 77(44.61), 69.1(8.64), 64(4.69), 56(4.35), 51(6.05).

**Anal.Calcd for C32H30ClN*3*O3 (539.20):** C, 71.17; H, 5.60; N, 7.78.

**Found:** C, 71.12; H, 5.63; N, 7.80.

**Synthesis of 1-benzyl-3-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-5-(4-methoxyphenyl)-1,3-dihydro-2H-pyrrol-2-one (10).**

A mixture of (5.3 gm, 0.01 mol) of compound 9a and (10 mL) 6N HCl was heated under reflux for 1 hours. The solid that separated out after cooling was washed with water and crystallized from EtOH to give compound 10.

Yield = 96%, yellow crystals; m.p.: 186°C.

**IR** (νmax, cm-1): 3025 (CH- alkene), 1690 (C=O), 1626 (C=N), 1599 (C=C), 749,699 (monosubstituted benzene), 847 (p-disubstituted benzene).

**1H-NMR** (DMSO-d6): δH (ppm): 3.77 (s, 3H, CH3-O), 4.83(s, 2H, CH2-N), 6.69(s, 1H, CH=C), 6.9–7.02 (m, 4H, Ar-H), 7.13(s, 1H, pyrrolone), 7.18 (t, 1H, *J* = 7.5 *Hz*, Ar-H), 7.27 (t, 2H, *J* = 7 *Hz,* Ar-H), 7.3 (t, 1H, *J* = 7.5 *Hz,* Ar-H), 7.42-7.44(m, 2H, Ar-H), 7.5 (t, 2H, *J* = 7.5 *Hz*, Ar-H), 7.63-7.70 (m, 4H, Ar-H), 8.06 (d, 2H, *J* = 7.5 *Hz*, Ar-H), 9.71 (s, 1H, pyrazolyl).

**13CNMR** (DMSO-d6): 43.79 (CH2-N), 55.32 (CH3-O), 100.44 (C4-pyrrolon), 113.52 (C4-pyrazolyl), 114.17, 117.03, 118.13, 119.25, 120.19, 123.16, 126.35, 127, 127.29, 128.76, 129.02, 129.84, 130.48, 130.96, 147.6, 169.96 (Ar-H), 128.18 (C5-pyrazolyl), 134.1 (HC=C), 139.1 (C3-pyrrolon), 138.1 (C5-pyrrolon), 152.60 (C3-pyrazolyl), 160.13 (C2-pyrrolon).

**MS,** m/z (%): 546.1(M++3) (13.65), 545.1 (M++2) (41.70), 544.1(M++1) (40.56), 543.1 (M+) (100), 454.1 (9.50), 453.1 (8.49), 452.1 (25.14), 417.1 (4.20), 411( 3.54), 409.1(9.66), 325(11.23), 359(4.86), 91.1(39.78), 77(10.78), 65(7.44)

**Anal.Calcd for C34H26ClN3O2 (543.17):** C, 75.06; H, 4.82; N, 7.72.

**Found:** C, 75.10; H, 4.83; N, 7.85.

**Synthesis of 3-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-5-(4-methoxyphenyl)-1-(p-tolyl)-1,3-dihydro-2H-pyrrol-2-one (11).**

A mixture of furanone 3 (4.55 gm, 0.01 mol), p-toluidine (1.6 gm, 0.01 mol) and (1.64 gm, 0.01 mol) of freshly fused sodium acetate in (50 mL) acetic acid was refluxed for 12 h. and left overnight, then the reaction mixture was poured into water to give yellow precipitate which filtered off, washed several times with water and recrystallized from EtOH to yield compound 11.

Yield = 60%, yellow crystals; m.p.: 230°C.

**IR** (νmax, cm-1): 2920 (CH), 1683(C=O), 1623(C=N), 1599(C=C), 754,688 (monosubstituted benzene), 830(p-disubstituted benzene).

**1H-NMR** (DMSO-d6): δH (ppm): 2.29(s, 3H, CH3-Ph), 3.74(s, 3H, CH3-O), 6.8(s, 1H, CH=C), 6.88(d, 2H, *J* = 7 *Hz* Ar-H), 6.9(d, 2H, *J* = 2.5 *Hz,* Ar-H), 7.11(s, 1H, pyrrolone), 7.18(d, 2H, *J* = 8.5 *Hz*, Ar-H), 7.25(d, 2H, *J* = 8.5 *Hz*, Ar-H), 7.43(t, 1H, *J* = 7.5 *Hz*, Ar-H), 7.5-7.70 (m, 7H, Ar-H), 8.08(d, 2H, *J* = 9 *Hz*, Ar-H), 9.22(s, 1H, pyrazolyl).

**13CNMR** (DMSO-d6): 20.69 (CH3-Ph), 55.28 (CH3-O), 113.84 (C4-pyrazolyl), 101.07(C4-pyrrolone), 117.07, 119.01, 119.55, 120.27, 122.88, 127.25, 128.65, 128.96, 129.04, 129.27, 129.32, 129.61, 130.48, 130.9, 138.2, 150.13 (Ar-H), 128.83 (C5-pyrazolyl), 133.2 (HC=C), 140.5 (C3-pyrrolone), 146.42 (C5-pyrrolone), 152.2 (C3-pyrazolyl), 169.08 (C2-pyrrolone).

**MS,** m/z (%): 546.1 (M++3) (14.3), 545.15 (M++2) (41.43), 544.15(M++1) (42.22), 543.15 (M+) (100), 542.15 (6.89), 514.1(3.61), 244.1(7.71), 91.1 (11.8), 89.1 (1.36), 77 (13.02), 65( 8.1).

**Anal.Calcd for C34H26ClN3O2 (543.17):** C, 75.06; H, 4.82; N, 7.72.

**Found**: C, 75.12; H, 4.84; N, 7.86.

**Synthesis of** **5-[3-(4-chloro-phenyl)-1-phenyl-1*H*-pyrazol-4-yl-methylene]-3-(4-methoxyphenyl)-4,5-dihydro-[1,2]oxazin-6-one (12).**

A mixture of furanone 3 (4.55 gm, 0.01 mol) and hydroxylamine hydrochloride (1.04 gm, 0.015 mol) in pyridine (20 mL) was heated under reflux for 5h. The reaction mixture was left to cool, then it was poured into crushed ice and neutralized with concentrated HCl. The precipitate was filtered off, washed with water and recrystallized from EtOH to yield 12.

Yield = 90%, white crystals; m.p.: 160°C.

**IR** (νmax, cm-1): 2850 (CH2- alphatic) 1727 (C=O), 1637 (C=N), 1597 (C=C), 751,695 (monosubstituted benzene), 831 (p-disubstituted benzene).

**1H-NMR** (DMSO-d6): δH (ppm): 3.81(s, 3H, CH3-O), 3.91 (s, 2H, oxazinone), 7.06(m, 2H, Ar-H), 7.31 (t, 1H, *J* = 8 *Hz*, Ar-H), 7.4 (t, 2H, *J* = 8 *Hz*, Ar-H), 7.5(m, 2H, *J* = 2.5 *Hz,* Ar-H), 7.68(s, 1H, CH=C), 7.72-7.7(m, 4H, Ar-H), 7.8(d, 2H, *J* = 7.5 *Hz,* Ar-H), 8.50(s, 1H, pyrazolyl ).

**13CNMR** (DMSO-d6): 25.25 (C5-oxazinone), 55.42 (CH3-O), 114.58 (C4-pyrazolyl), 115.99, 118.12, 123.49, 126.31, 127.4, 128.26, 128,94, 129.28, 129.50, 136.59, 139.3, 153.43 (Ar-H), 128.77 (C5-pyrazolyl), 131.2 (C4-oxazinone), 132.79 (HC=C), 149.32 (C3-pyrazolyl), 161.49 (C6-oxazinone), 164.07 (C3-oxazinone).

**MS**, m/z (%): 472 (M++3) (8.63), 471 (M++2) (31.16), 470(M++1) (34.98), 469 (M+) (81.2), 468 (33), 456 (11.47), 455 (12.11), 454 (30.90), 453( 8.58), 428(10.24), 427(35.49), 426(44.11), 425 (100), 424.1 (41.19), 423(18.48), 412(16.45), 411(14.74), 410(42.18), 409.1(6.18), 389.1(5.73), 318(5.74), 316(6.83), 292(7.17), 291(13.57), 257(7.44), 256(6.37), 255(7.29), 104(7.99), 92(4.58), 90(4.50), 78 (6.35), 77(56.53), 76.1(7.03), 75(5.72), 64(4.81), 63(4.98), 51(11.77).

**Anal.Calcd for C27H20ClN3O3 (469.12):** C, 69.01; H, 4.29; N, 8.94.

**Found:** C, 69.12; H, 4.34; N, 8.96.

**Synthesis of 3-((3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl)methylene)-5-(4-methoxyphenyl)-1,3-dihydro-2*H*-pyrrol-2-one (13).**

A mixture of (4.55 gm, 0.01 mol) of furanone 3 and (1.92 gm) ammonium acetate was heated under reflux for 4 hours. The solid that separated out after cooling was washed was filtered off and washed several times with water and crystallized from CHCl3 to form compound 13.

Yield = 97%, white crystals; m.p.: 204°C.

**IR** (νmax, cm1): 3145 (NH), 1700 (C=O), 1623 (C=N), 1599 (C=C), 756,684 (monosubstituted benzene), 834 (p-disubstituted benzene).

1H-NMR (DMSO-d6): δH (ppm): 3.82(s, 3H, CH3-O), 6,85(s, 1H, CH=C), 6.94(s,1H, pyrrolone), 7.05(d, 2H, *J* = 8.5 *Hz*, Ar-H), 7.47(t, 1H, *J* = 7.5 *Hz,* Ar-H), 7.63(t, 2H, *J* = 7.5 *Hz*, Ar-H), 7.63-7.69(m, 4H, Ar-H), 7.8(d, 2H, *J* = 9 *Hz*, Ar-H), 8.07(d, 2H, *J* = 9.5 *Hz,* Ar-H), 9.13(s, 1H, pyrazolyl), 10.46(s, 1H, NH-CO).

**13CNMR** (DMSO-d6): 55.39 (CH3-O), 96.18 (C4-pyrrolone), 114.28 (C4-pyrazolyl), 117.3, 117.57, 119.31, 122.30, 127.21, 128.99, 129.61, 130.21, 130.43, 130.85, 153.2, 170.84 (Ar-H), 128.13 (C5-pyrazolyl), 133.59 (HC=C), 139.03 (C3-pyrrolone) 144.28 (C5-pyrrolone), 152.1(C3-pyrazolyl), 160.36 (C2-pyrrolone).

**MS**, m/z (%): 456 (M++3) (10.40), 455.1 (M++2) (38.13 ), 454.1(M++1) (34.29), 453.1 (M+) (100), 452.1 (14.29), 438.1 (6.47), 203 (3.30), 134.1 (4.22), 91.1( 6.19), 78.1(3.87),77.1(36.74), 76.1 (3.43), 69.1 (4.31), 64(2.66), 63(2.81), 57.1 (7.87), 51(10.30)

**Anal.Calcd for C27H20ClN3O2 (453.12):** C, 71.44; H, 4.44; N, 9.26.

**Found:** C, 71.48; H, 4.38; N, 9.33.

**Synthesis of 3-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl) (p-tolyl)methyl)-5-(4-methoxyphenyl)furan-2(3H)-one (14).**

To a mixture of anhydrous aluminum chloride (2.67 gm, 0.025 mol) in dry toluene (50 mL), (4.55 gm, 0.01 mol) of furanone 3 was added gradually. Then, the reaction mixture was stirred for 2 days at room temperature. The complex formed was poured onto ice dil. HCl (50 mL) and then steam distilled to remove excess toluene. The precipitate formed was extracted, washed with water and crystallized from EtOH to produce compound 14.

Yield = 65%, red powder; m.p.: 200°C.

**IR** (νmax, cm-1): 2929 (CH- alphatic), 1751 (C=O, γ-lactone), 1667 (C=N), 1625 (C=C), 755,686 (monosubstituted benzene), 830 (p-disubstituted benzene).

**1H-NMR** (DMSO-d6): δH (ppm): 3.7(s, 3H, CH3-ph), 3.84 (s, 3H, CH3-O), 4.2(s, 1H, CH-Ph), 7.04-7.09(m, 4H, Ar-H), 7.11(s, 1H, furanone), 7.32(t, 1H, *J* = 7.5 *Hz*, Ar-H), 7.4(t, 1H, *J* = 7.5 *Hz*, Ar-H), 7.5-7.83(m, 9H, Ar-H), 7.89(d, 1H, *J* = 7.5 *Hz*, Ar-H), 8-807(m, 2H, Ar-H), 9.24(s, 1H, pyrazolyl).

**13CNMR** (DMSO-d6): 30 (CH3-Ph), 55.4 (CH-Ph), 55.49 (CH3-O), 55.9(C3-furanone), 99.71 (C4-furanone), 113.8 (C4-pyrazolyl), 114.6, 116.79, 118.6, 119.04, 119.48, 120.4, 122.8, 123.36, 126.2, 127.02, 129.09, 129.69, 130.97, 133.43, 161.90 (Ar-H), 128.93 (C5-pyrazolyl), 138.86 (C5-furanone), 152.67 (C3-pyrazolyl), 168.85 (C2-furanone).

**MS**, m/z (%): 549.1 (M++3) (0.40), 548.1 (M++2) (0.93 ), 547.1(M++1) (0.93), 546.1(M+) (2.35), 457.1(9.8), 456.1(34.89), 455.1(31.46), 454.1(100), 242(7.96), 243(5.93), 244(3.59), 178(3.80), 136.1(7.06), 135(76.54), 134.15(3.32), 107.1(11.07), 104.1(5.08), 92(16.03), 78(6.11), 77(71.68), 76(6.92), 75(4.43), 64(7.25), 63(4.63).

**Anal.Calcd for C34H27ClN2O3 (546.17):** C, 74.65; H, 4.98; N, 5.17.

**Found:** C, 74.60; H, 4.88; N, 5.13.

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7/25/2020