

**SYNTHESIS AND SCREENING OF (E)-1-(4-(2-(((PHENYLAMINO)METHYL)AMINO)ACETYL)PHENYL)-4-(2-PHENYLHYDRAZONO)-3-(TRICHLOROMETHYL)-1H-PYRAZOL-5(4H)-ONE**

**L.K.Ravinrdanath, \*B.V.Chakravarthi S.Muralikrishna**

*Department of chemistry, S.K.University, Anantapuram  
Email ID; BV.CHAKRAVARTHI 115@gmail.com*

**ABSTRACT:**

Synthesis of (E)-1-(4-(2-(((phenylamino)methyl)amino)acetyl)phenyl)-4-(2phenylhydrazono)-3-(trichloromethyl)-1H-pyrazol-5(4H)-one achieved by reaction of E-2-(4-(5-oxo-4-(2-phenylhydrazono)-3-(trichloromethyl) acetic acid (2)) in presence of DMF, aq NaNO<sub>3</sub>, isobutyl formamide afforded corresponding compound (3) which was subjected to mannish reaction with cyclic secondary amines such as piperidine or morpholine or N-methyl piperazine in presence of formaldehyde in DMF to yield corresponding mannish base (E)-1-(4-(2-(((phenylamino)methyl)amino)acetyl)phenyl)-4-(2phenylhydrazono)-3-(trichloromethyl)-1H-pyrazol-5(4H)-one (4) in excellent yield. The structure of these newly synthesized compounds were characterised by <sup>1</sup>H-NMR, <sup>13</sup>C-NMR, Mass and IR elemental analysis

Keywords : - Pyrazolone , Mannich bases , β-lactam, urea .

**INTRODUCTION**

Heterocyclic chemistry is the most challenging and a handsomely rewarding field of study, since it always attracts the attention of scientists working not only in the area of natural products but also in synthetic chemistry. Moreover, in tune with the present trend “scientists to the door steps of common man”, there is always a challenging and rewarding task in search of more and more new scientific accomplishments. This is reflected by the voluminous data available in the literature on heterocyclic chemistry. Many useful drugs indeed have emerged from such investigations which strengthens the trend. Spectacular advanced has been made in this field to furtherance of the knowledge of relationship between chemical structure and biological activity. Thus, the successful application of this class of compounds in various fields ensures a limitless scope for the development of structurally novel compounds with a wide range of physico-chemical and biological properties.

Amongst different heterocyclic systems, the chemistry of five membered heterocycles with more than one heteroatom has gained importance as many of them exhibit pronounced bioactive nature. One such type of compounds includes pyrazoles and pyrazolines and pyrazolones. Hence, any attempt to study their detailed chemistry would add new dimensions to

the existing knowledge. Pyrazolones, pyrazoles and related heterocycles possess various types of biological activities. A good deal of importance is given to pyrazolone derivatives. It is due to their wide use in medical chemistry and some of them possess antituberculosis antineoplastic, antidiabetic, antifertility and antithyroid activity. In this perspective a study on synthesis, characterization, antimicrobial activity, and bioactive studies on some pyrazolone derivatives have been taken up.

#### Introduction

A brief account on 2-pyrazolines, their importance and various methods for their synthesis is discussed.

A five membered cyclic diene containing three carbons and two nitrogens is called a diazole. If two nitrogen atoms are adjacent, it is known as a pyrazole. If one double bond is present, it is a pyrazoline. The biological properties of pyrazoles are reviewed extensively. Several pyrazolines [1] and annulated pyrazoles [2-4] possess antimicrobial activity [15]

Pyrazole and its N-substituted derivatives are potential inhibitors and deactivators of liver alcohol dehydrogenase. Difenamizole [5] possesses analgesic activity greater than that of Aspirin

The trifluoro derivatives of pyrazoles [6 & 7] are about 0.5% as effective as an amebicide, comparable with Emetine and Metronidazole.

Several di and tri substituted pyrazole and pyrazoline derivatives<sup>6</sup> and 4-pyrazolyl pyridinium salts [8] possess hypoglycemic activity. Muzolimine [9,] 1-substituted 2-pyrazolin-5-one derivative is a highly active diuretic. It differs from other diuretics as it contains neither sulfonamide nor carboxyl group. Besides this, pyrazoline and indazole derivatives [10-12] are pharmacologically active and are useful as antiinflammatory drugs<sup>7,8</sup>.

As well as 3,5-pyrazolidinedione derivatives such as phenylbutazone [13] oxyphenbutazone [14] sulfinpyrazone [15] etc, are some of the important class of anti-inflammatory agents which are most widely used.

Acyl azides, in general, and *N*-protected  $\alpha$ -amino acid azides in particular, have occupied a place of their own importance in organic [16], and peptide as well as peptidomimetic [17], syntheses. They are extensively used in the preparation of amides and peptides, and a wide range of other compounds such as nitriles, and several classes of heterocycles. [16,18]. The Curtius rearrangement of acyl azides into isocyanates is of paramount value in synthetic chemistry. It is widely used in the preparation of amines, ureas and carbamates. A number of natural products and pharmacologically important compounds containing ureido linkages, [19], ureidopeptidomimetics, [20], partially modified retro-inverso (PMRI) peptides, formamides and unnatural amino acids have been prepared *via* this rearrangement. [17,22], Due to such vast utility of acid azides, the development of efficient routes for their synthesis is important. The two well known routes for the preparation of acid azides are the reaction of  $\text{NaN}_3$  with an acid chloride [23], or mixed anhydride. [24], The acid chloride method offers disadvantages at the preparation of acid chloride itself. These include prolonged reaction duration, incompatibility with acid cleavable groups, and storage and stability problems associated with moisture sensitive acid chlorides. Also the poor solubility of  $\text{NaN}_3$  inorganic reaction medium requires the usage of a phase transfer catalyst, [25], or catalysts such as  $\text{ZnI}_2$  [26], to improve the yield of acid azides. Alternately, protocols for the *in situ* generation of acid chlorides using  $\text{SOCl}_2/\text{DMF}-\text{NaN}_3$ , [26], cyanuric chloride/*N*-methylmorpholine, [27], triphosgene/triethylamine, [28],

*N,N*-chloromethylenedimethylammonium chloride,[29], followed by coupling with an azide have also been reported. But these methods are not suitable for acids such as *N*-Boc/*Z*-α-amino acids whose acid chlorides are unstable. Preparation of acid azides *via* mixed anhydrides has been used to advantage. Yet, this method uses chloroformates which are inconvenient for handling. Katritzky *et al.*, recently prepared acid azides from acids in a two step route involving *N*-acyl benzotriazoles as stable and reactive intermediates. [30], Acid azides, such as Boc/*Z*-α-amino acidazides, have also been prepared through a multi-step route starting from acids by hydrazinolysis of the methyl/ethyl esters followed by reaction of the resultant hydrazide with nitrosyl donors like HNO<sub>2</sub>.

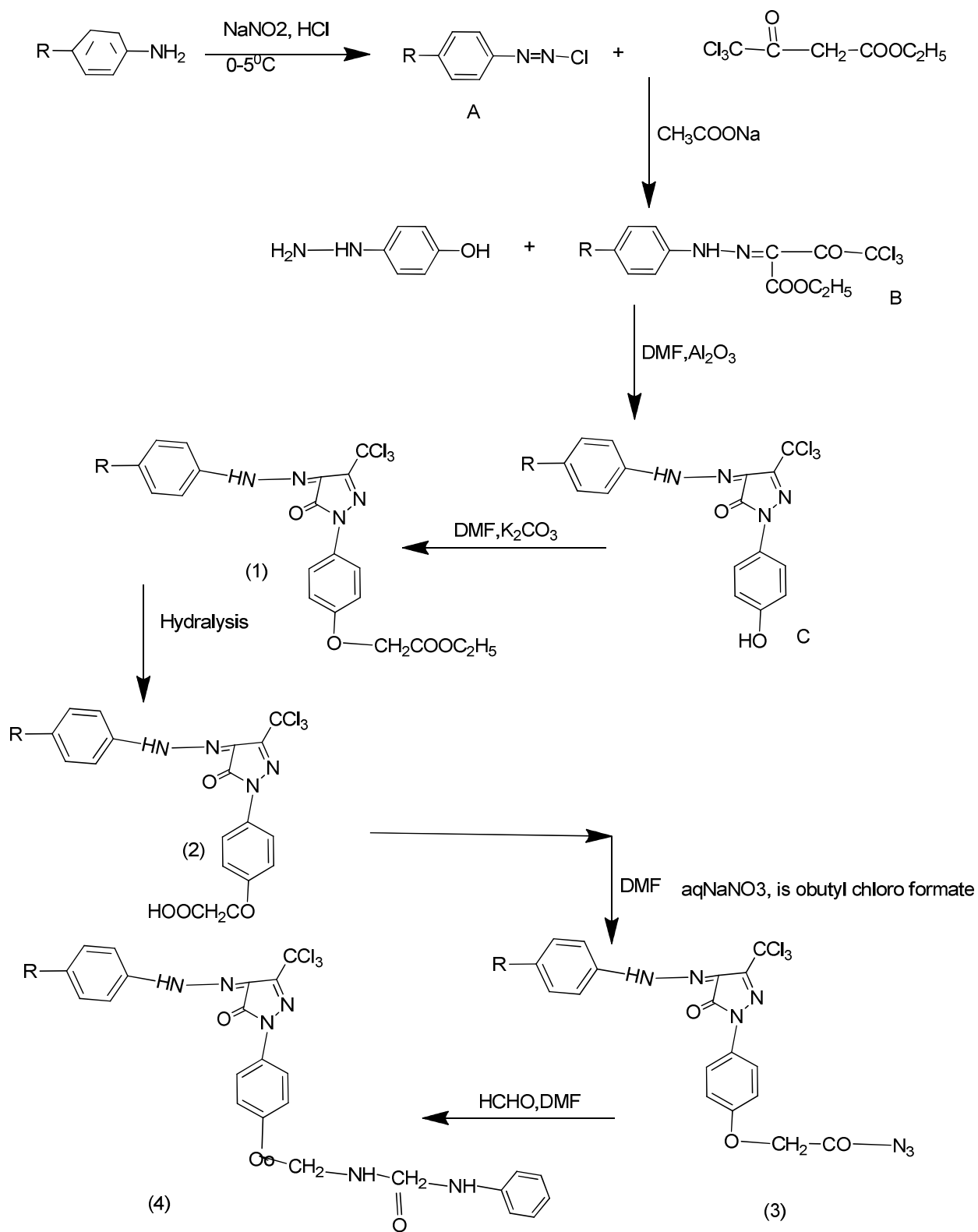
## MATERIALS AND METHODS

All the chemicals were used as received without further purification. Melting points were determined in open capillary tubes in Buchi530 circulating oil apparatus and are not corrected. Reactions were carried out using household micro oven (power consumption 1200 W, microwave frequency 2450 MHz) and monitored by thin layer chromatography (TLC) on silica gel plates (60 F254) visualizing with ultraviolet light or iodine spray. <sup>1</sup>H NMR spectra were determined in DMSO-*d*<sub>6</sub> solution on JOEL AL300 Spectrometers. Proton chemical shifts (δ) are relative to tetramethylsilane as internal standard and expressed in ppm.

## Results and discussions

A series of four novel mannish bases were obtained from substituted aniline by dissolving in suitable volume of water containing 2.5 - 3.5 equivalence of HCl by the application of heat to afford substituted phenyl diazonium chloride. (A). A is treated with a solution of sodium acetate in presence of ethyl trichloroacetate compound (B) is obtained. Compound (B) is condensed with 4-hydrazenyl phenol and DMF to obtain 3-trichloromethyl 4-substituted phenylhydrazono pyrazoline 5-one (C). Compound (C) is stirred at room temperature in presence of anhydrous K<sub>2</sub>CO<sub>3</sub> to yield compound (1) which amination with hydrazine hydrate in presence of ethanol afforded a ethyl 2-(4-(5-oxo phenyl hydrazono)-3-trichloromethyl)-4,5-dihydro-1H-pyrazol-1-yl)phenonyl) aceto hydrazide (2). Compound 2 is condensed with Isatin in presence of DMF to afford a 2-(4-(5-oxo-4-(2-(4-substituted)hydrazono)-3-(trichloromethyl)-4,5-dihydro-1H-pyrazol-1-yl)-N<sup>1</sup>-(2-oxo indoline-3-ylidene) aceto hydrazide (3). Compound (3) is reacted with mannish bases, formaldehyde and DMF (piperidine, morpholine, *N*-Methyl piperazine) to obtain compound (4) N<sup>1</sup>-(2-oxo-1-(4-substituted)hydrazono-3-(trichloromethyl)-4,5-dihydro-1H-pyrazol-1-yl)phenonyl) aceto hydrazide.

Comp	4a	4b	4c	4d	4e	4f
R	H	4-CH <sub>3</sub>	4-OCH <sub>3</sub>	4-Cl	4-NO <sub>2</sub>	4-CF <sub>3</sub>
X	CH <sub>2</sub>	CH <sub>2</sub>	CH <sub>2</sub>	CH <sub>2</sub>	CH <sub>2</sub>	CH <sub>2</sub>



The required primary amine is dissolved in a suitable volume of water containing 2.5 – 3.0 equivalents of hydrochloric acid (or sulphuric acid) by the application of heat if necessary. The solution thus obtained is cooled to 0<sup>o</sup>C when the amine hydrochloride (or sulphate) usually crystallizes. The temperature is maintained at 0 – 5<sup>o</sup>C, and the aqueous solution of sodium nitrite is added portion wise till there is free nitrous acid. The solution is tested for the later with an external indicator (moist potassium iodide starch paper). An excess of acid is always maintained to stabilize the diazonium salt, acid is harmful, the concentration of the acid is reduced to optimum value. The similar procedure is adopted for the preparation of other substituted phenyl diazonium chlorides.

### **Substituted phenyl diazonium ethyltrichloroacetoacetic ester(B)**

A solution of sodium acetate (1.0g) in 100 ml of aqueous alcohol (50%) is added to a solution of ethyltrichloroacetoacetic ester (0.1 mole) in 50 ml of ethanol and the mixture is added to 0<sup>o</sup>C. To this cold mixture, the corresponding diazonium chloride is added gradually till turbidity is observed. The addition is continued till yellow crystals separated out. These crystals are filtered, washed with water and dried.

### **3-Trichloromethyl-4-(substituted phenyl hydrazono)-pyrozone-5-one(C)**

Condensation of 4-substituted phenyl hydrazono acetoacetic ester **B** and 4- hydroxy phenyl hydrazine in the presence of catalytic amount of dimethyl formamide under microwave irradiation afforded **C**. In typical experimental procedure, a mixture of aryl hydrazono acetic ester **B**, 4-hydrazinyl phenol and dimethyl formamide (10 drops) was subjected to microwave irradiation at 150W intermittently at 30 sec intervals for 2 minutes. After complete conversion as indicated by TLC, the reaction mixture was cooled and heated with cold water. The precipitate **C** was filtered recrystallized from ethanol M.P. 159<sup>o</sup>C, yield 85%. The mass spectra of 2-(4-(5-oxo-4(2-phenyl hydrazono)-3-(trichloro methyl)-4,5-dihydro-1-H pyrazol-1-yl)phenoxy)N-(2-oxoindolin)-3-ylidene) aceto hydrazide **1a** (R=H) showed molecular ion (M<sup>+</sup>) peaks at m/z 598.5

### **ethyl 2-(4-(5-oxo phenyl hydrazono)-3-(trichloromethyl)-4,5-dihydro-1H -pyrazol-1-yl)phenoxy)acetohydrazide (1)**

A mixture of synthesized 3-trichloromethyl-4-(substituted phenyl hydrazono)-pyrozone-5-one(C), anhydrous K<sub>2</sub>CO<sub>3</sub>, chloroethylacetate and DMF was stirred at room temperature for 8 hours. The reaction mixture was diluted with ice cold water. The separated solid was identified as ethyl 2-(4-5-oxo-4-(2-phenylhydrazono)-3-(trichloromethyl)-4,5-dihydro-1Hpyrazol-1-yl)phenoxy) acetate.

### **E-2-(4-(5-oxo-4-(2-phenylhydrazono)-3-(trichloromethylaceticacid)-4,5-dihydro-1H-pyrazol-1-yl) phenoxy) aceticacid(2)**

Synthesis of E-2-(4-(5-oxo-4-(2-phenylhydrazono)-3-(trichloromethylaceticacid)-4,5-DiHydro-1H-pyrazol-1-yl) Phenoxy) acetic acid was done by adding the solvent mixture tetrahydro Furan/ methyl alcohol /H<sub>2</sub>O (1:1:1)ratio, aq NaOH(2N) was added and refluxed for 6hrs . The progress of the reaction was monitored by cyclohexane : ethylacetate (4:6) solvent mixture as an eluent. After completion of reaction solvent was evaporated under vacuum to give crude .The residue was washed with ethyl acetate to remove impurities. The residue was acidified with 1N HCl to give solid suspension which was filtered under vacuum to give crude, purified by chromatography (60-120 Mesh silica gel eluent :70/ethylacetate –pet ether)to afford acid compound E-2-(4-(5-oxo-4-(2-phenylhydrazono)-3-(trichloromethyl aceticacid)-4,5-dihydro-1H-pyrazol-1-yl) phenoxy) aceticacid. The structures of this newly synthesized compounds were characterised by <sup>1</sup>H-NMR and IR spectral data.

**The IR(kBr)** spectrum of E-2-(4-(5-oxo-4-(2-phenylhydrazono)-3-(TrichloroMethyl aceticacid)-4,5-DiHydro-1H-pyrazol-1-yl) Phenoxy) aceticacid was recorded in the range 4000-667cm<sup>-1</sup> and the absorption signals were found at 3260(-NH), 2950 (OH), 3100( Ar-H), 2990 and 2960(aliphatic CH<sub>2</sub>and CH<sub>3</sub>) 1785 (CO of ester group), 1680 (C=N), and 1195(C-O-C of ester group)1195(C=S).

**<sup>1</sup>H NMR(300MHZ,(CD)<sub>2</sub>SO,TMS);** δ=4.89(s,2H,O-CH<sub>2</sub>-CO), 4.23(s,2H,NH<sub>2</sub>), 10.97(s,1H,Ar-NH-N=), 6.85-7.85(m,9H,C<sub>6</sub>H<sub>4</sub> and C<sub>6</sub>H<sub>5</sub>), 9.23(s,1H,CO-NH)

**C<sup>13</sup>Spectrum (CDCl<sub>3</sub>);** δ=30.5,27.7,24.6,152.7,102.0,32.7,20.8(Ar-C),155.6(NH-N=C), 147.0(Pyrazole-C=O), 96.0 (CCl<sub>3</sub>), 59.6(CCl<sub>3</sub>C), (23.9,25.5,46.5,32.4,100.4,155.9),- (Phenoxy), 166.3(C=O-NH-NH<sub>2</sub>), Yield 65% M.P.<sup>0</sup>C 150—152 Mol. C:58.25,H: 5.86,N: 22.65,O:12.85, found (%):C:58.37,H:5.94,N:22.70,O:12.97

**E-2-(4-(5-oxo-4(2-phenylhydrazono)-3-(trichloromethyl)-4,5-dihydro-1H-pyrazol-1-yl)phenoxy) acetyl azide(3)**

To solutions of acid in acetone triethyl amine (3eq) was added and stirred at 15 . To that isobutyl chloroformate (1:1)was added and stirred for 20 min at 0<sup>0</sup>C. After completion , reaction mixturer was poured in ice cold water (20ml) , extracted with diethylether (10 times). The organic layer was separated , washed with water , brine dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> Filtered and evaporated under vaccum to give crude oil. The curde oil was purified by column chromatography (60120 mesh silica gel eluent ;10/ EtOAc-pet ether) to give pure 2-(3-(4-chloro-3-oxo-1-((4-(4-triflomethyl)phenyl) E-2-(4-(5-oxo-4(2-Phenyl hydrazono)-3-(trichloromethyl)-4,5-dihydro-1H-pyrazol-1-yl)phenoxy)acetyl azide 3a

**IR(KBr):** 3205(-NH),3170(Indol -NH),1602(-C=N),1656(pyrazoline -C=O),1700(pyrazole- C=O), 1618(-CO-NH).

**<sup>1</sup>H NMR(300MHZ,(CD)<sub>2</sub>SO,TMS);**δ=9.28(s, 1H, CO-NH), 10.97(s, 1H, Ar-NH-N=), 10.54(s, 1H, Indole -NH), 4.85(s, 2H, O-CH<sub>2</sub>-CO), 6.87-7.83(m, 9H, Ar-H), C<sup>13</sup>Spectrum (CDCl<sub>3</sub>)δ=20.7,29.4,32.7,56.2,31.3,(Ar-c),65.6(-CH<sub>2</sub>),153.8(-NH-N=C),171.1(Pyrazol-C=O),94.9(CCl<sub>3</sub>)155.6(CCl<sub>3</sub>C)133.5(C=ONHNH<sub>2</sub>),21.6,28.5,27.7,119.1,133.9(Phenoxy), 25.2,25.7,126.0,131.3,119.0,139.115.6(Indoline-c) yield 70,M.P.<sup>0</sup>C 212-

Calculated Values:C:52.16,H:3.00N:16.34,O:10.62,Cl:17.45

Found(%):C:52.26,H:3.01,N:16.58,O:10.72,Cl:17.58

**(E)-1-(4-(2-(((phenylamino)methyl)amino)acetyl)phenyl)-4-(2-phenylhydrazono)-3-(trichloromethyl)-1H-pyrazol-5(4H)-one 4(a)**

To a mixture of pure E-2-(4-(5-oxo-4(2- Phenyl hydrazono)-3-(trichloromethyl)-4,5-dihydro-1H-pyrazol-1-yl)phenoxy)acetyl azide.3(a)(1eq), in benzene (1eq) was added HCHO and refluxed for 16hrs. Progress of the reaction was monitored by TLC with acetone-ethyl acetate ( 6:4)as mobile phase. After completion of reaction solvent was evaporated under vaccum to give crude residue, purified by column chromatography 60-120 mesh silica gel to give 4a

**IR(KBr):** 3195(-NH),1610(-C=N),1676(Pyrazoline -c=o),1720(Indole-c=o),1654(-CONH),2933

**(CH<sub>2</sub>) <sup>1</sup>H NMR(300MHZ,(CD)<sub>2</sub>SO,TMS);**δ=1.49-1.53(m, 6H, (CH<sub>2</sub>)<sub>3</sub> of piperidine ring), 2.25(t, 4H, CH<sub>2</sub>-N-CH<sub>2</sub> of piperidine ring), 4.05(s, 2H, N-CH<sub>2</sub>-N), 4.82(s, 2H, O-CH<sub>2</sub>-CO), 10.99(s, 1H, Ar-NH=N), 9.25(s, 1H, CO-NH), 6.85-7.82(m, 14H, Ar-H)

**C<sup>13</sup>Spectrum of (CDCl<sub>3</sub>)**δ=20.8,27.7,29.2,102.01,152.7,32.68(Ar-c),59.8,(CH<sub>2</sub>)<sub>164</sub>(NHN=C), 117(Pyrazolc=o),90(CCl<sub>3</sub>),64(CCl<sub>3</sub>),158(C=ONHNH<sub>2</sub>),16.3,24.8,36.5,50.3(Phenoxy)25.2,33.6,117,147,155,(Indolinc)11.08,21.02,42.02,56.03(Piperidin C) yield 70,M.P.<sup>0</sup>C 155-158 Calculated Found(%):C:55.3,H:4.17,N:16.13,O:9.22,Cl:15.12

**(E)-1-(4-(2-(((phenylamino)methyl)amino)acetyl)phenyl)-4-(2-(p-tolyl)hydrazono)-3-(trichloromethyl)-1H-pyrazol-5(4H)-one 4(b):**

**IR(KBr):** 3170(-NH),1616(-CN),1674(PYRAZOLINE(-C=O)1715,1658(-CO-NH),2920(-CH<sub>2</sub>),

**<sup>1</sup>H NMR(300MHZ,(CD)<sub>2</sub>SO,TMS);**δ= 3.20(s, 3H, Ar-OCH<sub>3</sub>), 1.47-1.51(m, 6H, (CH<sub>2</sub>)<sub>6</sub> of piperidine ring), 2.28(t, 4H, CH<sub>2</sub>-N-CH<sub>2</sub> of piperidine ring), 4.10(s, 2H, N-CH<sub>2</sub>-N), 4.87(s, 2H, O-CH<sub>2</sub>-CO), 10.94(s, 1H, Ar-NH=N), 9.32(s, 1H, CO-NH), 6.89-7.79(m, 13H, Ar-H)

**C<sup>13</sup>Spectrum of (CDCl<sub>3</sub>)**δ=20.8,26.7,30.01,102.01,150.7,31.06(Ar-c),60.02(-CH<sub>2</sub>),164(-NH-N=C), 115(Pyrazolo-c=o),90(CCl<sub>3</sub>),65(CCl<sub>3</sub>),158(C=ONHNH<sub>2</sub>),16.03,24.8,36.05,

50.03(Phenoxy)25.02,21.08,26.03,25.03,33.06,117,148,152,(Indoline)10.02,20,41.02,55(piperidine) yield 70 M.P.<sup>o</sup>C 163-16 Found(%):C:55.93,H:4.37,N:15.81,O:9.03,Cl:14.83

**(E)-4-(2-(4-methoxyphenyl)hydrazono)-1-(4-(2-((phenylamino)methyl)amino)acetyl)phenyl)-3-(trichloromethyl)-1H-pyrazol-5(4H)-one 4(c)**

**IR(KBr):** 3120(-NH),1610(-C=N),1680(Pyrazoline-C=O),1712(Indole-C=O),1654(-CONH),2625(-CH<sub>2</sub>),  
**<sup>1</sup>H NMR(300MHZ,(CD)<sub>2</sub>SO,TMS);**δ=3.75(s, 3H, Ar-OCH<sub>3</sub>), 1.42-1.53(m, 6H, (CH<sub>2</sub>)<sub>6</sub> of piperidine ring), 2.31(t, 4H, CH<sub>2</sub>-N-CH<sub>2</sub> of piperidine ring), 4.13(s, 2H, N-CH<sub>2</sub>-N), 4.79(s, 2H, O-CH<sub>2</sub>-CO), 10.85 (s, 1H, Ar-NH=N), 9.28(s, 1H, CO-NH), 6.83-7.75(m, 12H, Ar-H

**C<sup>13</sup>Spectrum of(CDCl<sub>3</sub>)**δ=20.08,27.7,29.02,102.02,152.07,32.68(Arc),62.03(CH<sub>2</sub>),163(N=C)115(C=ONH<sub>2</sub>)16.3,24.8,36.05,5.03(Phenoxy)25.4,21.03,26.03,24.03,32.03,116.02,145.03,153(Indoline)11.02,20.21,41.12,55.51(piperidine) yield 70 M.P.<sup>o</sup>C 165-167

Found(%):C:55.93,H:4.37,N:15.81,O:9.03,Cl:14.83

**(E)-4-(2-(4-chlorophenyl)hydrazono)-1-(4-(2-((phenylamino)methyl)amino)acetyl)phenyl)-3-(trichloromethyl)-1H-pyrazol-5(4H)-one 4(d)**

**IR(KBr):** 3175(-NH),1614(-C=N),1674(Pyrazoline-C=O),1656(-CONH),2915(-CH<sub>2</sub>)

,**<sup>1</sup>H NMR(300MHZ,(CD)<sub>2</sub>SO,TMS);**δ= 1.75(t, 3H, -CH<sub>3</sub>), 3.32(q, 2H, O-CH<sub>2</sub>), 1.42-1.53(m, 6H, (CH<sub>2</sub>)<sub>6</sub> of piperidine ring), 2.31(t, 4H, CH<sub>2</sub>-N-CH<sub>2</sub> of piperidine ring), 4.21(s, 2H, N-CH<sub>2</sub>-N), 4.80(s, 2H, O-CH<sub>2</sub>-CO), 10.91 (s, 1H, Ar-NH=N), 9.33(s, 1H, CO-NH), 6.93-7.87(m, 13H,Ar-H)

**C<sup>13</sup>Spectrum of (CDCl<sub>3</sub>)**δ=20.08,26.02,28.32,101.32,153.102.3,32.65(Ar-c),61.03(-CH<sub>2</sub>),162(-NH-N=C)115(C=ONH<sub>2</sub>)16.3,21.02,35.03,45.03(Phenoxy)25.4,21.03,25.03,21.03,31.03,116.02,145.03,153(Indoline) 11.02,20.21,41.12,55.51(piperidine) yield 75 M.P.<sup>o</sup>C 158-159

Found(%):C:55.28,H:4.47,N:15.17,O:10.84,Cl:14.2

**(E)-4-(2-(4-nitrophenyl)hydrazono)-1-(4-(2-((phenylamino)methyl)amino)acetyl)phenyl)-3-(trichloromethyl)-1H-pyrazol-5(4H)-one 4(e)**

**IR(KBr):** - 3155(-NH),1616(-C=N),1674(Pyrazoline),1714(Indole-C=O),1658(-CONH),2920(-CH<sub>2</sub>),

**<sup>1</sup>H NMR(300MHZ,(CD)<sub>2</sub>SO,TMS);**δ=1.45-1.57(m, 6H, (CH<sub>2</sub>)<sub>3</sub> of piperidine ring), 2.34(t, 4H, CH<sub>2</sub>-N-CH<sub>2</sub> of piperidine ring), 4.23(s, 2H, N-CH<sub>2</sub>-N), 4.75(s, 2H, O-CH<sub>2</sub>-CO), 10.96 (s, 1H, Ar-NH=N), 9.41(s, 1H, CO-NH), 6.89-7.95(m, 12H,Ar-H)

**C<sup>13</sup>Spectrum of(CDCl<sub>3</sub>)**δ=20.08,25.02,29.101.32,155,102.3,31.65(Arc),60.13(CH<sub>2</sub>),165N=C)114(C=ONH<sub>2</sub>)16.13,21.02,35.03,41.03(Phenoxy)25.4,22.03,25.03,20.03,31.03,115.02,145.03,153(Indoline) 11.02,20.21,41.12,55.51(piperidine) yield 75 M.P.<sup>o</sup>C 160-161

Found(%):C:52.28,H:3.84,N:15.36,O:8.79,Cl:13.

**(E)-1-(4-(2-((phenylamino)methyl)amino)acetyl)phenyl)-3-(trichloromethyl)-4-(2-(4-(trifluoromethyl)phenyl)hydrazono)-1H-pyrazol-5(4H)-one 4(f)**

**IR(KBr):** 3170(-NH),1614(-C=N),1674(Pyrazoline-C=O),1716(Indole-C=O),1626(-CONH),2625(-CH<sub>2</sub>),

**<sup>1</sup>H NMR(300MHZ,(CD)<sub>2</sub>SO,TMS);**δ= 1.42-1.53(m, 6H, (CH<sub>2</sub>)<sub>3</sub> of piperidine ring), 2.52(t, 4H, CH<sub>2</sub>-N-CH<sub>2</sub> of piperidine ring), 4.18(s, 2H, N-CH<sub>2</sub>-N), 4.79(s, 2H, O-CH<sub>2</sub>-CO), 10.91(s, 1H, Ar-NH=N), 6.92-7.85(m, 12H,Ar-H), 8.97(s, 1H, CO-NH)

**C<sup>13</sup>Spectrum of (CDCl<sub>3</sub>)**δ=20.08,23.23,29.100.32,154,102.3,30.65(Arc), 59.13(CH<sub>2</sub>),168(NHN=C)112(C=ONH<sub>2</sub>)15.13,20.02,35.03,41.03(Phenoxy)25.4,21.03,25.03,19.03,29.03,.02, 115145.03,153(Indoline) 11.02,19.23,40.12,50.12(piperidine) yield 80 M.P.<sup>o</sup>C 160

Found(%):C:49.67,H:3.62,N:14.48,O:8.27,Cl:13.58

Antibacterial activity by disc diffusion method for Synthesis (E)-1-(4-(2-(((phenylamino)methyl)amino)acetyl)phenyl)-4-(2-phenylhydrazono)-3-(trichloromethyl)-1H-pyrazol-5(4H)-one **4(a-f)**

S.No.	Compd	R	X	Zone of inhibition (mm)			
				Staphylococcus aureus NCCS 2079	Bacillus Cereus NCCS 2106	Escherichia coli NCCS 2065	Pseudomonas aeruginos NCCS 2200
1	4a	H	CH <sub>2</sub>	6	5	5	7
2	4b	CH <sub>3</sub>	CH <sub>2</sub>	6	5	4	6
3	4c	OCH <sub>3</sub>	CH <sub>3</sub>	4	5	4	5
4	4d	Cl	CH <sub>2</sub>	8	6	4	7
5	4e	NO <sub>2</sub>	CH <sub>2</sub>	12	14	11	12
6	4f	CF <sub>3</sub>	CH <sub>2</sub>	12	13	11	12
cefaclor				19	22	19	20

#### CONCLUSION:

- 1) Further more the substitution with phenyl group having a chloro group at p-position showed better activities.
- 2) Pyrazolone and its derivaties were found to play an important role in medicinal chemistry as herbicidal, fungicidal bacterial, anti-inflammatory.

#### ACKNOWLEDGEMENT:

- 1) My sincer thanks to UGC authorities for providing financial assistance to continue research inbetter manner.
- 2) Iam very thankful to s.k.university authorities for providing such an environment for doing better research very much.
- 3) It's my pleasure to express my thans to department of chemistry for giving an opportunity to research.
- 4) I express my sincere thanks to my research supervisor Prof L.K. Ravindranath Garu

#### References:

- [1] M. Tramontini and L. Angioloni, *Mannich-Bases, Chemistry and Uses*, CRC, Boca Raton, F.L. (1994).
- [2] M. Arend, B. Westermann and N. Risch, *Angew. Chem Int Ed*, **37**, 1044 (1998).
- [3] S.K. Sridhar, S.N. Pandeya, J.P. Stables and A.Ramesh, *Eur. J. Pharm. Scien.*, **16 (3)**, 129 (2002).
- [4] J.R. Dimmock and P. Kumar, *Curr. Med. Chem.*, **4(1)**, 1 - 22 (1977).
- [5] I.A. Poplevskaya, G.N. Kondaurou, K.A. Abdullin, L.K. Shipunova, G.B. Chermanova ad O.K. Kabiev, *Tr. Inst. Khim. Nauk. Akad. Nauk. Kaz., SSR*, **52**, 52 (1980); *Chem. Abstr.*, **94**, 120781 (1981).
- [6] P. C agniant, G. Krisch, M. Wierzbicki, F. Lepage, D. Cagniant, D. Loebenber, R. Parmegianin Scherlock, *Eur. J. Med. Chem.*, **15**, 439 (1980).



- [7] Korea Inst. of Science and Technology; *Jpn. Kokai Tokkyo Koho, JP*, 5,867,693 (1983). *Chem. Abstr.*, **99**, 7047A (1983).
- [8] J.R. Dimmock, S.K. Raghavan, B.M. Logan and G.E. Bigam, *Eur. J. Med. Chem.*, **18**, 249 (1983).
- [9] H. Bundgaard, *Methods in Enzymology.*, **112**, 347 (1985).
- [10] K. Masuda, T. Toga and N. Hayashi, *J. Labelled Compd.*, **11**, 301 (1975); *Chem. Abstr.*, **84**, 121730f (1976).
- [11] J.S. Fowler, *J. Org. Chem.*, **42**, 2637 (1977).
- [12] E. Schreier, *Helv. Chim. Acta.*, **59**, 585 (1977).
- [13] Gadre J.N. and Dubhashi V.B., *Indian J. Heterocycl. Chem.*, **3**, 1994, 181.
- [14] Pandeya S.N, Usha L, Pandey A & Bajpal S.K, *Indian J. Heterocycl. Chem.*, **6**, 1977, 313.
- [15] Pandeya S.N, Sriram D, DeClercq E, annecouque C & Witvrouw M, *Indian J. Pharm. Sci.*, **60**, 1998, 207 16. Lingaiah N, Narender R & Dattatreya M.A, *Indian J. Chem.*, **378**, 1998, 1254.
- [16] (a) S. Brase, C. Gil, K. Knepper and V. Zimmermann, *Angew. Chem., Int. Ed.*, **2005**, **44**, 5188–5240 and references cited therein; (b) E. F. V. Scriven and K. Turnbull, *Chem. Rev.*, **1988**, **88**, 297–368 and references therein
- [17] For peptide synthesis using acid azides see: (a) J. Lutz, H.-J. Musiol, and L. Moroder, Vol. E22a, pp 427 in *Houben-Weyl: Synthesis of Peptides & Peptidomimetics*, M. Goodman, A. Felix, L. Moroder and C. Toniolo, ed.; Georg Thieme Verlag: Stuttgart, New York; For the utility of Boc/Z-amino acid azides in total synthesis of ribonuclease in solution, see: (b) N. Fujii and H. J. Yajima, *J. Chem. Soc., Perkin Trans. 1*, **1981**, 831–841 and references cited therein; For Fmoc-acid azides as peptide coupling agents see: (c) V. V. Suresh Babu, K. Ananda and G. R. Vasanthakumar, *J. Chem. Soc., Perkin Trans. 1*, **2000**, 4328–4331; For applications of acid azides in peptidomimetics synthesis see: (d) M. Chorev, *Biopolymers Peptide Sci*, **2005**, **80**, 67–84; (e) M. D. Fletcher and M.M. Campbell, *Chem. Rev.*, **1998**, **98**, 763–795.
- [18] C. O. Kangani, B. W. Day and D. E. Kelley, *Tetrahedron Lett.*, **2008**, **49**, 914–918.
- [19] (a) A. Palani, S. Shapiro, M. D. McBriar, J. W. Clader, W. J. Greenlee, B. Spar, T. J. Kowalski, C. Farley, J. Cook, M. VanHeek, B. Weig, K. O'Neill, M. Graziano and B. Hawes, *J. Med. Chem.*, **2005**, **48**, 4746–4749; (b) J. R. Merritt, J. Liu, E. Quadros, M. L. Morris, R. Liu, R. Zhang, B. Jacob, J. Postelnek, C. M. Hicks, W. Chen, E. F. Kimble, W. L. Rogers, L. O'Brien, N. White, H. Desai, S. Bansal, G. King, M. J. Ohlmeyer, K. C. Appell and M. L. Webb, *J. Med. Chem.*, **2009**, **52**, 1295–1301.
- [20] (a) B. S. Patil, G. R. Vasanthakumar and V. V. Suresh Babu, *J. Org. Chem.*, **2003**, **68**, 7274–7280; (b) V. V. Sureshbabu, B. S. Patil and R. Venkataramanarao, *J. Org. Chem.*, **2006**, **71**, 7697–7705; (c) L. Fischer, V. Semetey, J.-M. Lozano, A.-P. Schaffner, J.-P. Briand, C. Didierjean and G. Guichard, *Eur. J. Org. Chem.*, **2007**, 2511–2525; (d) G. Guichard, V. Semetey, C. Didierjean, A. Aubry, J.-P. Briand and M. Rodriguez, *J. Org. Chem.*, **1999**, **64**, 8702–8705; (e) G. Guichard, V. Semetey, M. Rodriguez and J.-P. Briand, *Tetrahedron Lett.*, **2000**, **41**, 1553–1557.
- [21] (a) J.M. Bermann and M. Goodman, *Int. J. Pept. Prot. Res.*, **1984**, **23**, 610–620; (b) M. Chorev and M. Goodman, *Int. J. Pept. Prot. Res.*, **1983**, **21**, 268–265; For the synthesis of aminoalkyl formamides see: (c) N. S. Sudarshan, N. Narendra, H. P. Hemantha and V. V. Sureshbabu, *J. Org. Chem.*, **2007**, **72**, 9804–9807; (d) V. V. Sureshbabu, N. Narendra and G. Nagendra, *J. Org. Chem.*, **2009**, **74**, 153–157; For unnatural amino acids see: (e) E. A. Englund, H. N. Gopi and D. H. Appella, *Org. Lett.*, **2004**, **6**, 213–215.
- [22] For selected reports see: (a) P.W. Erhardt, *J. Org. Chem.*, **1979**, **44**, 883–884; (b) G. W. Rewcastle and W. A. Denny, *Synthesis*, **1985**, 220–222; (c) A. E. Luedtke and J.

- W. Timberlake, *J. Org. Chem.*, 1985, **50**, 268–270; (d) A. Padwa, M. A. Brodney, B. Liu, K. Satake and T. Wu, *J. Org. Chem.*, 1999, **64**, 3595–3607; (e) C. K. Govindan, *Org. Process Res. Dev.*, 2002, **6**, 74–77; For the use of HN3/pyridine: (f) J. M. Lemmens, W. W. J. M. Blommerde, L. Thijs and B. Zwanenburg, *J. Org. Chem.*, 1984, **49**, 2231–2235.
- [23] For selected reports see: (a) M. Chorev, S. A. MacDonald and M. Goodman, *J. Org. Chem.*, 1984, **49**, 821–827; (b) C. Bolm, C. L. Dinter, I. Schiffers and L. Defrere, *Synlett*, 2001, 1875–1877; (c) E. A. Englund, H. N. Gopi and D. H. Appella, *Org. Lett.*, 2004, **6**, 213–215; (d) R. K. Boekman and L. M. Reeder, *Synlett*, 2004, 1399–1405; (e) P. H. Dussault and Chunping Xu, *Tetrahedron Lett.*, 2004, **45**, 7455–7457.
- [24] J. R. Pfister and W. E. Wymann, *Synthesis*, 1983, 38–39.
- [25] G. K. Surya Prakash, P. S. Iyer, M. Arvanaghi and G. A. Olah, *J. Org. Chem.*, 1983, **48**, 3358–3359.
- [26] A. Padwa, K. R. Crawford, P. Rashatasakhon and M. Rose, *J. Org. Chem.*, 2003, **68**, 2609–2617.
- [27] A. P. Bandgar and S. S. Pandit, *Tetrahedron Lett.*, 2002, **43**, 3413–3414.
- [28] V. K. Gumaste, B. M. Bhawal and A. R. A. S. Deshmukh, *Tetrahedron Lett.*, 2002, **43**, 1345–1346.
- [29] H. Eilingsfeld, M. Seefelder and H. Weidinger, *Angew. Chem.*, 1960, **72**, 836–845.
- [30] A. R. Katritzky, K. Widyan and K. Kirichnko, *J. Org. Chem.*, 2007, **72**, 5802–5804. in.

Received on September 15, 2014.