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Synthesis and Screening of (E)-1-(4-(2(((Phenylamino) Methyl) amino) acetyl) phenyl)-4-(2-phenylhydrazono)-3-(Trichloromethyl)-1H-pyrazol-5(4H)-one

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A B S T R A C T

Synthesis of (E)-1-(4-(2-(((phenylamino) methyl) amino) acetyl) phenyl)-4-(2phenyl hydrazono)-3-(trichloromethyl)-1H-pyrazol-5(4H)-onewasachievedbyreactionofE-2-(4-(5-o4(2phenylhydrazono)-3-(trichloromethyl acetic acid (2)) in presence of DMF, aq $NaNO_3$, isobutyl formamide afforded corresponding compound (3) which was subjected to mannich reaction with cyclic secondary amines such as piperidine or morphline or N-methyl piparazinein presence of formaldehyde in DMF to yield corresponding mannichbase (E)(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 characterized by H^1-NMR, C^{13}-NMR, Mass and IR elemental analysis

Keywords: Pyrozolone, Mannich bases, β-lactum, urea.

A R T I C L E I N F O

CONTENTS

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1. 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 physio-chemical and biological properties. Amongst different heterocyclic systems, the chemistry of five membered heterocycles with more than one hetero atom 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 medicinal 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 studied.

A brief review on 2-pyrazolines, their importance and various methods for their synthesis is discussed. 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] posses analgesic activity greater than that of Aspirin.

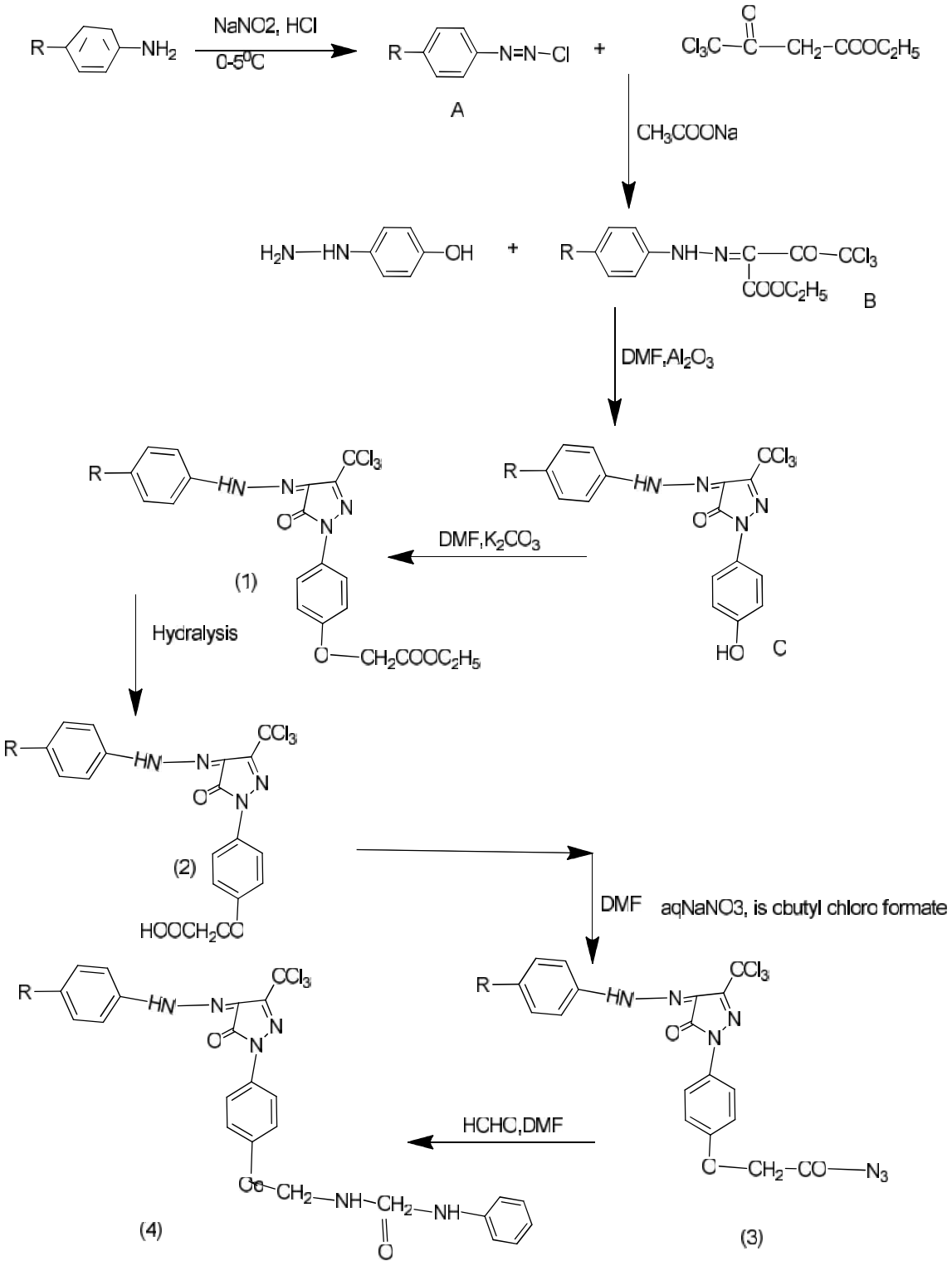
The trifluoro derivatives of pyrazoles [6&7] are about 0.5% as effective as an amebicide, comparable with Emetine and Metronidazole. Several di and tri substituted pyrazole and pyrazolines derivatives and 4-pyrazolyl pyridinium salt [8] possess hypoglycemic activity. Muzolimine [9] 1-substituted 2-pyrazolin-5-one derivative is a highly active diuretic. It differs from other diuretics as it contains neither sulfonamide nor carboxyl group. Besides this, pyrazolines and indazole derivatives [10-12] are pharmacologically active and are useful as antinflammatory drugs [7, 8]. As well as 3,5-pyrazolidinedionederivatives such as phenyl butazone [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 a-amino acid azidesin 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, 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 isocyanatesis 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 uriedo 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 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 NaN_3 inorganic reaction medium requires the usage of a phase transfer catalyst [25], or catalysts such as ZnI_2 [26], to improve the yield of acid azides. Alternately, protocols for the *in situ* generation of acid chlorides using $SOCl_2$/DMF–NaN_3 [26]

Cyanuricchloride / *N*methylmorpholine [27], triphosgene /triethylamine, [28], *N*, *N*chloromethylene dimethyl ammonium 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-a-amino acids whose acid chlorides are unstable. Preparations of acid azides via mixed anhydrides have 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-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_2.

2. 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.1H NMR spectra were determined inDMSO-*d*6 solution on JOEL AL300Spectrometers. Proton chemical shifts (ð) are relative to tetramethylsilane as internalstadard and expressed in ppm.



3. Results and Discussion

A series of four novel mannich bases were obtained from substituted aniline by dissolving in suitable volume of water containing 2.5 - 3.5 equivalance of HCl by the application of heat to afford substituted phenyl diazonium chloride.(A). A is treated with a solution of sodium acetated in presence of ethyl trichloroacetoaceticester compound (B) is obtained. Compound (B) is condensedwith4– hydrazenyl phenol and DMF to obtain 3–trichloromethyl 4-substituted phenyl hydrazono) pyrazoline 5-one (C). Compound (C) is stirred at room temperature in presence of anhydrous K_2CO_3 to yield compound (1) which on amination with hydrazine hydrate in presence of ethanol afforded a ethyl 2-(4-(5 –oxo phenyl hydrazono)- 3-trichloro methyl)-4,5-di hydro –H pyrazol-1 –yl) phenoxy) 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-(tri chloro

methyl)-4,5-dihydro -1H –pyrazol-yl)-N^1-(2-oxo indoline -3-ylidene) aceto hydrazide (3). Compound (3) is reacted with mannich bases, formaldehyde and DMF (piperidine ,morpholine ,N-Methyl piparazine to obtain compound (4) N^1-(2- oxo-1-(4-substituted) hydrazono 3-(trichloro methyl)-4,5-dihydro-1H-pyrazol-1-yl)phenony) aceto hydrazide. 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^{0C} when the amine hydrochloride (or sulphate) usually crystallizes. The temperature is maintained at $0 – 5^{0C}$, 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 ethyltrichloro aceto aceticester(b)

A solution of sodium acetate (1.0g) in 100 ml of aqueous alcohol (50%) is added to a solution of ethyl tri chloro acetoacetic ester (0.1 mole) in 50 ml of ethanol and the mixture is added to 0^0C. 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)-pyrozoline-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°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–ylidine) aceto hydrazide 1a (R=H) showed molecular ion (M^+) peaks at m/z 598.5

Synthesis of 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)-pyrozoline-5-one(C), anhydrous K_2CO_3, chloro ethylacetate 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–phenylhydrazone)–3–(trichloro methyl) –4,5–dihydro–1Hpyrazol–1–yl)phenoxy) acetate.

Synthesis of E-2-(4-(5-oxo-4-(2-phenylhydrazono)-3-(trichloromethylaceticacid)-4, 5 dihydro-1H-pyrazol-1-yl) phenoxy) acetic acid (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_2o (1:1:1)ratio, aq NaoH(2N) was added and refluxed for 6hrs . The progress of the reaction was monitored by cyclo hexane : ethyacetate (4:6) solvent mixture as an eluent. After completion of reaction solvent was evaporated under vaccum to give crude .The residue was washed with ethyl acetate to remove impurites. The residue was acidified with 1N HCl to give solid suspension which was filtered under vaccum 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 these newly synthesized compounds were characterised by ^{1}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^{-1}and the absorption signals were found at 3260(-NH), 2950 (OH), 3100(Ar-H), 2990 and 2960(aliphatic $CH_2$and CH_3) 1785 (CO of ester group), 1680 (C=N), and 1195(C-O-C of ester group)1195(C=S).

^{1}HNMR (300MHZ, $(CD)_2SO$, TMS); δ=4.89(S,2H,O-CH_2-CO), 4.23(s,2H,NH_2),10.97(S, 1H, Ar-NH-N=),6.85-7.85 (m,9H,C_6H_4 and C_6H_5), 9.23(s,1H,CO-NH) C^{13}Spectrum ($CDCl_3$); 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.O (CCl_3), 59.6(Cl_3C), (23.9,25.5,46.5,32.4,100.4,155.9), (Phenoxy), 166.3 (C=O-NH-NH_2),Yield 65%M.P.^{0}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 chloroform ate (1:1)was added and stirred for 20 min at 0^0C. 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_2SO_4 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).

^{1}H NMR(300MHZ,$(CD)_2SO$,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_2–CO), 6.87–7.83(m, 9H, Ar–H), C^{13}Spectrum ($CDCl_3$)δ=20.7,29.4,32.7,56.2,31.3,(Ar-c),65.6(-CH_2),153.8(-NH-N=C), 171.1(Pyrazol-C=O), 94.9 (CCl_3)155.6(CCl_3C)133.5(C=ONHNH_2),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.^{0}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 formaldehyde 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_2)

^{1}H NMR(300MHZ,$(CD)_2SO$,TMS);**δ=**1.49–1.53(m, 6H, $(CH_2)_3$ of piperidine ring), 2.25(t, 4H, CH_2–N–CH2 of piperidine ring), 4.05(s, 2H, N–CH2–N), 4.82(s, 2H, O–CH2–CO), 10.99(s, 1H, Ar–NH=N), 9.25(s, 1H, CO–NH), 6.85–7.82(m, 14H, Ar–H)

C^{13} Spectrum of($CDCl_3$)δ=20.8, 27.7, 29.2, 102.01, 152.7, 32.68(Arc),59.8,(CH_2)164(NHN=C), 117(Pyrazolc=o), 90(CCl_3), 64(CCl_3), 158(C=ONHNH$_2$), 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.^{0}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_2),

^{1}H NMR (300MHZ,$(CD)_2SO$,TMS);δ= 3.20(s, 3H, Ar–OCH_3), 1.47–1.51(m, 6H, $(CH_2)_6$ of piperidine ring), 2.28(t, 4H, CH_2–N–CH_2 of piperidine ring), 4.10(s, 2H, N–CH_2–N), 4.87(s, 2H, O–CH_2–CO), 10.94(s, 1H, Ar–NH=N), 9.32(s, 1H, CO–NH), 6.89–7.79(m, 13H, Ar–H)

C^{13} Spectrum of ($CDCl_3$)δ=20.8,26.7,30.01, 102.01, 150.7,31.06(Ar-c), 60.02(-CH_2), 164(-NH-N=C), 115 (Pyrazolo-c=o), 90 (CCl_3), 65(CCl_3),158 (C=ONHNH$_2$), 16.03, 24.8,36.05,50.03 (Penoxy)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.^{0}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-(((phenyl amino)methyl)amino)acetyl)phenyl)-3-(trichloro methyl)-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_2),

^{1}H NMR (300MHZ,$(CD)_2SO$,TMS);δ=3.75(s, 3H, Ar–OCH_3), 1.42–1.53(m, 6H, $(CH_2)_6$ of piperidine ring), 2.31(t, 4H, CH_2–N–CH_2 of piperidine ring), 4.13(s, 2H, N–CH_2–N), 4.79(s, 2H, O–CH_2–CO), 10.85 (s, 1H, Ar–NH=N), 9.28(s, 1H, CO–NH), 6.83–7.75(m, 12H, Ar–H.

C^{13}Spectrum of ($CDCl_3$)δ=20.08,27.7,29.02,102.02,152.07, 32.68(Arc),62.03(CH_2),163(N=C)115C=ONHNH$_2$)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.^{0}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_2)

^{1}H NMR(300MHZ,$(CD)_2SO$,TMS);δ= 1.75(t, 3H, –CH_3), 3.32(q, 2H, O–CH_2), 1.42–1.53(m, 6H, $(CH_2)_6$ of piperidine ring), 2.31(t, 4H, CH_2–N–CH_2 of piperidine ring), 4.21(s, 2H, N–CH_2–N), 4.80(s, 2H, O–CH_2–CO), 10.91 (s, 1H, Ar–NH=N), 9.33(s, 1H, CO–NH), 6.93–7.87(m, 13H,Ar–H)

C^{13} Spectrum of ($CDCl_3$)δ=20.08,26.02,28.32,101.32, 153.102.3, 32.65(Ar-c),61.03(-CH_2),162(-NH-N=C) 115 (C=ONHNH$_2$)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.^{0}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-(((phenyl amino)methyl)amino)acetyl)phenyl)-3-(trichloromethyl) -1H pyrazol-5(4H)-one4(e)

IR (KBr): 3155(-NH),1616(-C=N), 1674(Pyrazoline), 1714 (Indole-C=O),1658(-CONH), 2920(-CH_2),

^{1}H NMR (300MHZ,$(CD)_2SO$,TMS);δ=1.45–1.57(m, 6H, $(CH_2)_3$ of piperidine ring), 2.34(t, 4H, CH_2–N–CH_2 of piperidine ring), 4.23(s, 2H, N–CH_2–N), 4.75(s, 2H, O–CH_2–CO), 10.96 (s, 1H, Ar–NH=N), 9.41(s, 1H, CO–NH), 6.89–7.95(m, 12H, Ar–H)

C^{13}Spectrum of ($CDCl_3$)δ=20.08,25.02,29.101.32,155, 102.3, 31.65(Arc), 60.13(CH_2), 165N=C) 114 (C=ONH NH$_2$)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.^{0}C 160-161

Found(%):C52.28,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)-one4 (f)

IR(KBr): 3170(-NH),1614(-C=N),1674(Pyrazoline-C=O),1716(Indole-C=O),1626(-CONH),2625(-CH_2)**,**

^{1}H NMR(300MHZ,$(CD)_2SO$,TMS);δ= 1.42–1.53(m, 6H, $(CH_2)_3$ of piperidine ring), 2.52(t, 4H, CH_2–N–CH_2 of piperidine ring), 4.18(s, 2H, N–CH_2–N), 4.79(s, 2H, O–CH_2–CO), 10.91(s, 1H, Ar–NH=N), 6.92–7.85(m, 12H,Ar–H), 8.97(s, 1H, CO–NH)

C^{13}Spectrum of **($CDCl_3$)δ=**20.08,23.23,29.100.32,154, 102.3,30.65(Arc), 59.13(CH_2),168(NHN=C) 112 (C=ONH NH_2) 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.^{0}C 160

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

Table 1

Comp	4a	4b	4c	4d	4e	4f
R	H	4-CH_3	4-OCH_3	4-Cl	4-NO_2	4-CF_3
X	CH_2	CH_2	CH_2	CH_2	CH_2	CH_2

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

S. No	Compound	R	X	Zone of inhibition (mm)			
				Staphylococcus aureus NCCS 2079	**Bacillus Cereus NCCS 2106**	**Escherichia coli NCCS 2065**	**Pseudomanas aeruginos NCCS 2200**
1	4a	H	CH_2	6	5	5	7
2	4b	CH_3	CH_2	6	5	4	6
3	4c	OCH_3	CH_3	4	5	4	5
4	4d	Cl	CH_2	8	6	4	7
5	4e	NO_2	CH_2	12	14	11	12
6	4f	CF_3	CH_2	12	13	11	12
cofactor				19	22	19	20

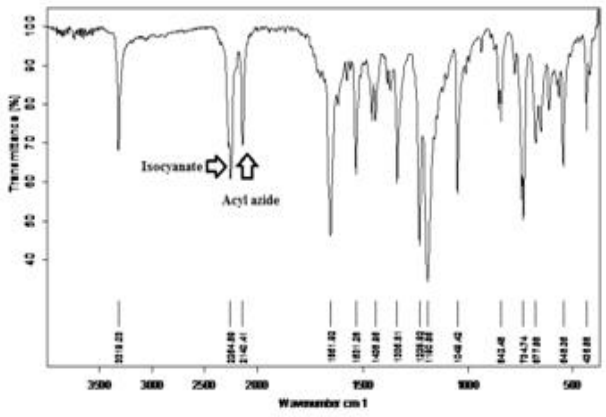


Figure 1

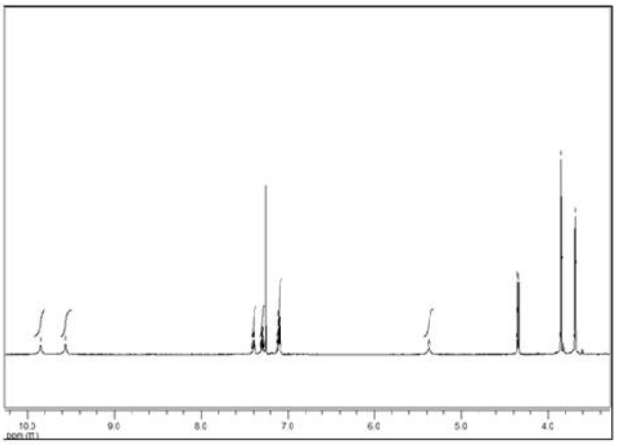


Figure 2

4. Conclusion

Furthermore the substitution with phenyl group having a chloro group at p-position showed better activities. Pyrazolone and its derivatives were found to play an important role in medicinal chemistry as herbicidal, fungicidal bacterial activity.

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