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Synthesis of some novel Mannich bases bearing pyrazolone moiety

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ABSTRACT

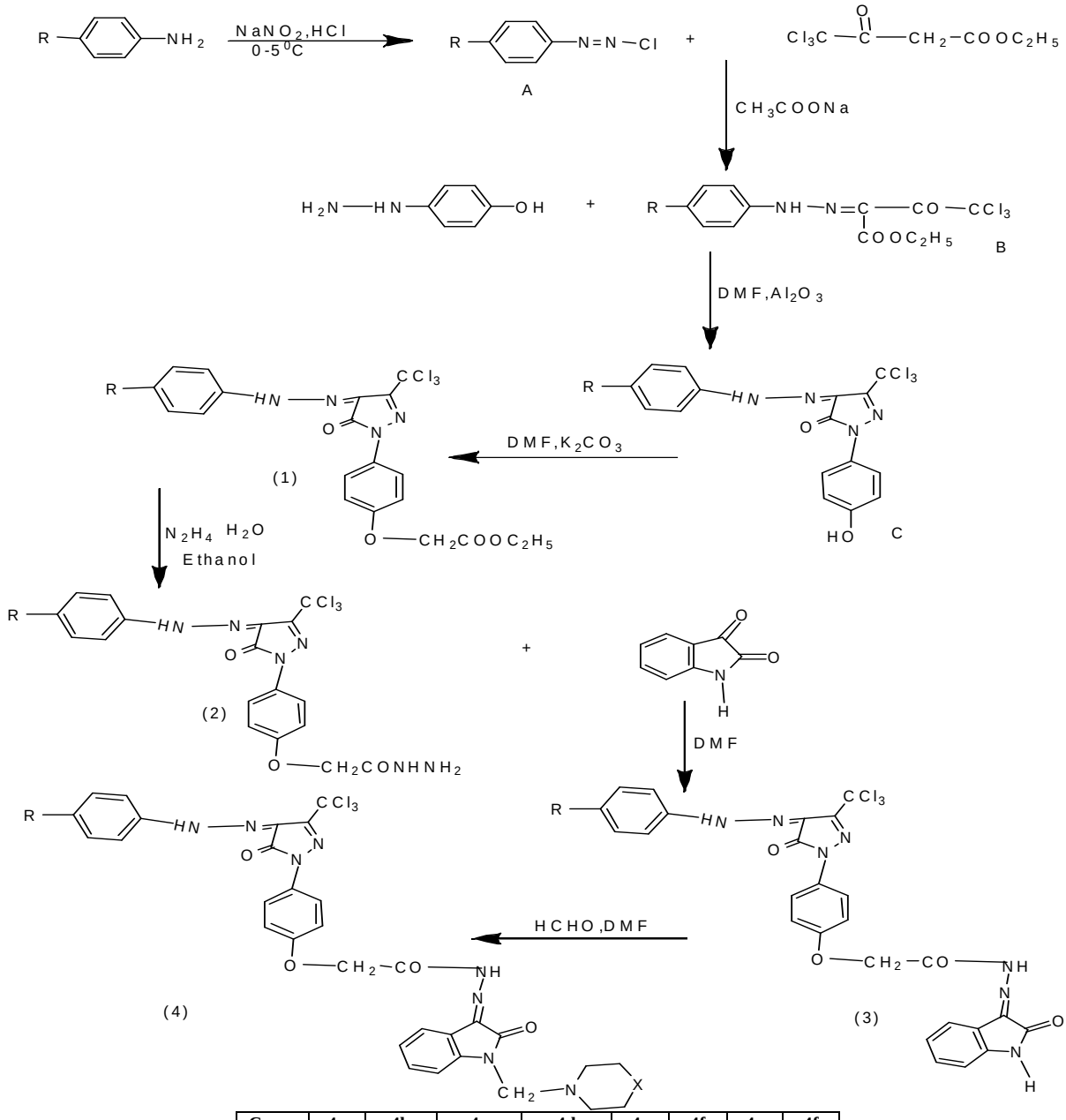
Synthesis of N^1(2-OXO-1-(piperidine-yl methyl) indoline 3-ylidine)-2-(4-(5-oxo-4(2-phenyl hydrazono)-3-trichloro methyl)-4,5-di hydro -1-H pyrazol-1-yl) phenoxy) aceto hydrazono) were synthesis by condensation of 2-(4-(5-oxo-4(2-phenyl hydrazono)-3-(trichloro methyl)-4,5,-di hydro-1-H pyrazol-1-yl) phenaxy)N-(2-oxoindoline)-3-ylidine) acetohydrazide with isatin offered corresponding ynthesis of N^1(2-OXO-1-(piperidine-yl methyl) indoline 3-ylidine)-2-(4-(5-oxo-4(2-phenyl hydrazono)-3-trichloro methyl)-4,5-di hydro -1-H pyrazol-1-yl) phenoxy) aceto hydrazide) this was subjected manich reaction with cyclic secondary amines such as piparardine or morpholine or N-methyl piparazine in presence of formaldehyde in DMF to give corresponding manich base sysnthsis of N^1-2oxo -1-(4-substituted hydrazono)3-(trichloromethyl)-4,5,-dihydro-1H-pyrazol-1yl)phenoxo)acetohydrazide in excelent yield. The structurer of these newly synthesis compound were charactrised by H^1-NMR,C^{13}-NMR,Mass and IR elemental analysis

Keywords: Pyrozolone, Manich bases, β-lactam, isatin

INTRODUCTION

Heterocyclic compounds are acquiring more importance in recent years because of their immense biological and pharmacological potency. Various biologically active synthetic compounds have five membered nitrogen containing heterocyclic ring in their structures. Many compounds bearing pyrazoles and their reduced forms pyrazolines constitute an interesting class of heterocycles due to their synthetic versatility and effective biological activities such as antimicrobial [1,2], antiviral [3], anti-inflammatory [4,5], antidepressant [6], antitubercular [7], antiamoebic [8],analgesic [9] activities. Literature survey reveals several synthetic protocols for the synthesis of these compoundsand the presence of this core in any molecule plays a key role in enhancing the activity. On the other hand, coumarinand its derivatives represent one of the important class of heterocyclic compounds possessing a wide range of biological activities. These include antibacterial [10], antifungal [11,12], antitumor [13,14], herbicidal, antiinflammatory[15] activities. Coumarins are oxygen containing heterocycles widely distributed in nature. They arealso used as additives in food, perfumes, agrochemicals, pharmaceuticals, and in the preparation of insecticides,optical brighteners, dispersed fluorescent and dye lasers.

Chalcones are 1,3-diaryl-2-propen-1-ones are natural or synthetic compounds prepared by claisen-schmidt condensation of aromatic aldehydes with acetophenones in presence of base and alcohol as solvent medium [16,17].These compounds found application in the synthesis of various heterocyclic compounds. Keeping in view of the above interesting pharmacological features, we hereby report the synthesis and antimicrobialactivity of a series of new pyrazoline derivatives.



Comp	4a	4b	4c	4d	4e	4f	4g	4f
R	H	4-CH_3	4-OCH_3	4-OC_2H_5	4-Cl	4-Br	4-H	4-H
X	CH_2	CH_2	CH_2	CH_2	CH_2	CH_2	CH_2	CH_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 usinghousehold micro oven (power consumption1200 W, microwave frequency 2450 MHz) andmonitored 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 (δ) arerelative to tetramethylsilane as internal standard and expressed in ppm.

RESULTS AND DISCUSSION

A series of four novel Maniche bases are afford substituted anilene is dissolved. In sutable volume of water. Containing 2.5 - 3.5 equivalence of Hcl by the application of heat afford to substituted phenyl dia zonium chloride.(a) .A is treated of a solutiton of sodium acetated in presence of ethyl trichloro aceto acetic ester (B)is obtained. B is condensed with 4 – hydrazenyl phenol and DMF was subjected to formed.3 –trichloromethyl 4-substituted phenylhydrazono) pyrazoline 5-one (c).compound (c) is stirred at room temperature in presence of anhydrous in $k_2 co_3$,chloro ethyl acetate and DMF (1) is formed. compound (1) an amination with hydrazine hydrate in presence of ethanol afford a ethyle 2-(4-(5 –oxo phenyl hydrazono)- 3-trichloro methyl)-4,5-di hydro –H pyrazol-1 –yl) pohenoxy) aceto hydrazide(2).compound 2 is condensed with Isatin in presence of DMF afford to a 2 –(4-(5-oxo -4-(2-4-substituted)hydrazono)-3-(tri chloro methyl)-4,5-di hydro -1H –pyrazol –yl)-N^1-(2-oxo indoline -3-ylidene) aceto hydrazide (3).compound (3) is reaction with Manich bases formaldehyde and DMF (piparadine ,morpholine ,N-Methyl piparazine to obtained compound (4) is formed.N^1-(2- oxo-1-(4-substitud) hydrazono 3-(trichloromethyl)-4,5-dihydro -1H-pyrazol-1-yl)phenony)acetohydrazide.

(a) Substituted phenyl diazonium chloride 1

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.

(b) Substituted phenyl diazonium ethyl trichloro aceto acetic ester

A solution of sodium acetate (1.0g) in 100 ml of aqueous alcohol (50%) is added to a solution of ethyl trichloro aceto acetic 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.

(c) 3-methyl-4-(substituted phenyl hydrazono)-pyrozoline-5-one

Condensation of 4-substituted phenyl hydrazono acetoacetic ester **(3)** and 4- hydraxy phenyl hydrazine (4) in the presence of catalytic amount of dimethyl formamide under microwave irradiation afforded **5**. In typical experimental procedure, a mixture of aryl hydrazono acetic ester **(3)**, 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 **5** was filtered recrystalized from ethanol M.P. 159°C, yield 85%. The 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 **10a** (R=H) showed molecular ion (M^+) peaks at m/z 598.5

1. Synthesis of ethyl 2–(4–(5–oxo phenyl hydrazono)–3–(trichloro methyl)–4,5–dihydro–H pyrazol–1yl) phenoxy) acetohydrazide

A mixture of synthesis of 1–(4–hydrophenyl)–4–2(phenyl hydrazono)–3–(trichloro methyl)–1H–pyrazol 5(4H)–one **5**, anhydrous K_2 CO_3, chloro ethyl acetate 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–phenyl hydrazone)–3–(trichloro methyl)–4,5–dihydro–1–H pyrazol–1–yl)phenoxy)acetate **6**

2. Synthesis of ethyl 2–(4–(5–oxo phenyl hydrazono)–3–(trichloro methyl)–4,5–dihydro–H pyrazol–1–yl)phenoxy)acetohydrazide 2(a)

The IR(KBr):- 3445, 3425, (2 bands) 3305, 1620, 1665, 1460 and 1455 cm^{-1} due to – NH_2, >NH and >C = N, cyclic carbonyl and five membered hetero cyclic ring respectivelyThe ^{1}H NMR (300MHz) spectra of signals 3.95(s, 2H, O–CH_2–CO),4.23(s, 2H, NH_2), 10.97(s, 1H, Ar–NH=N), 6.82–7.93(m, 9H, C_6H_5 and C_6H_4), 9.23(s, 1H, C=O–NH). C^{13}Spectrum of ($CDCl_3$)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.formula $C_{18}H_{15}Cl_3N_6O_3$ calculated values 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

2.Synthesis of ethyl 2–(4–(5–oxo phenyl hydrazono)–3–(trichloro methyl)–4,5–dihydro–Methyl pyrazol–1–yl)phenoxy)acetohydrazide 2(B)
IR(KBr):3420,3400(-NH_2) 3285(-NH) 1610(-C=N) 1650(-C=0) ^{1}H NMR(300MHZ,$(CD)_2SO$,TMS);δ=3.19(S,3H, Ar-CH_3),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,8H,C_6H_4 and C_6H_4) 9.23(s,1H,CO-NH) C^{13}Spectrum of ($CDCl_3$)δ=30.5,27.7,24.6,152.7,102.0,32.7,20.8,(Ar-c), 69.4 (CH_2) 155.6(NH-N=C),205(Pyrazole-C=O),92.5(CCl_3),56.3(CCl_3C),23.9,25.5,46.5,32.4,100.4,155.9 ,(Phenoxy,- 166.3 (C=O-$NHNH_2$), yield 60%M.P.^{0}C 150-153 Mol.formula $C_{19}H_{17}Cl_3N_6O_3$ Calculated values C:59.26,H: 6.17, N:21.76,O:12.14 Found(%) C:59.37, H: 6.25,N:21.87,O:12.23,

3. Synthesis of ethyl 2–(4–(5–oxo phenyl hydrazono)–3–(trichloro methyl)–4,5–dihydro–Methoxy pyrazol–1–yl)phenoxy)acetohydrazide 2(c)
IR(KBr):3425,3405(NH_2),3200(NH),1615(C=N),1655(C=O)^{1}HNMR300MHZ,$(CD)_2SO$,TMS);δ=3.7(s,3H,-o-CH_3) 4.92(s, 2H O-CH_2-CO) 4.23(S,2H,NH_2) 10.95 (S,1H,Ar-NH-N=), 6.83-7.90 (m,8H,C_6H_4andC_6H_4) 9.22(S,1H,CONH))C^{13}Spectrumof($CDCl_3$)δ=30.5,27.7,24.6,152.7,102.0,32.7,20.8,(Arc),68.7(CH_2),144.9(-NH-N=C)197.9(PyrazoloneC=O),90(CCl_3),143(CCl_3),166.3(-c=o-$NHNH_2$) 23.9,25.5,46.5,32.4,100.4,155.9 ,(Phenoxy) yield 75%M.P.^{0}C154-156 Mol.formula $C_{19}H_{17}Cl_3N_6O_3$ Calculated values:C:55.85,H:5.68,N:19.85,O:15.85 Found(%) C:57.00 H:6.00 N:21.00,O:16.00

4. Synthesis of ethyl 2–(4–(5–oxo phenyl hydrazono)–3–(trichloro methyl)–4,5–dihydro–ethoxy pyrazol–1–yl)phenoxy)acetohydrazide 2(d)
IR(KBr):3435,3415(-NH2),3300(-NH),1615(-C=N),1660(-C=O)^{1}H NMR(300MHZ,$(CD)_2SO$,TMS);δ=1.78(t, 3H, CH_3), 3.20 (q, 2H, O–CH_2), 4.93(s, 2H, O–CH_2–CO), 4.18(s, 2H, NH_2), 10.96(s, 1H, Ar–NH–N=), 6.89–7.92(m, 8H, C_6H_4 and C_6H_4), 9.20(s, 1H, CO–NH) C^{13}Spectrum of ($CDCl_3$)δ=31.05,26.14,151.02101.03,31.02,21.8(Ar-c)65.03(-CH2),155. 03(-NH-N=C),197.9(Pyrazolon 90(CCl_3),72(CCl_3C)165.03(-C=ONHNH$_2$),22.8,25.5, 45.5, 31.4, 98.5,154.9(Phenoxy) yield 80 M.P.^{0}C 165-168 Mol.formula $C_{20}H_{19}Cl_3N_6O_4$ Calculated values: C:57.85,H:6.18,N:20.20,O:15.35 Found(%) C:57.97,H:6.28,N:20.28,O:15.45

5. Synthesis of ethyl 2–(4–(5–oxo phenyl hydrazono)–3–(trichloro methyl)–4,5–dihydro–choloro pyrazol–1–yl)phenoxy)acetohydrazide 2(e)
IR(KBr):3420,3400(NH_2),3275(NH),1610(C=N),1660(C=O)^{1}HNMR(300MHZ,$(CD)_2SO$,TMS);δ=4.89(s, 2H, O–CH_2–CO), 4.20(s, 2H, NH_2), 10.93(s, 1H, Ar–NH–N=), 6.82–7.96(m, 8H, C_6H_4 and C_6H_4), 9.15(s, 1H, CO–NH) C^{13}Spectrum of ($CDCl_3$)δ=32.01,27.14,153.05,102.02,32.32,22.02(Ar-c),46.07(-CH_2)136.8(-NH-N==C),205.3(Pyrazolc=o),89.0(CCl_3),158.3(CCl_3C),168.03(C=0NHNH$_2$),20.0,2707,35.3,46.5,68.4,119.1,139.9(Phenoxy) yield 75 M.P.^{0}C173-174 Mol.formula $C_{18}H_{14}Cl_4N_6O_3$ Calculated values:C:53.29, H:5.10,N:20.66, O:11.76,Cl:8.66 Found(%):C:53.39,H:5.19,N:20.76,O:11.86,Cl:8.77

6. Synthesis of ethyl 2–(4–(5–oxo phenyl hydrazono)–3–(trichloro methyl)–4,5–dihydro–bromo pyrazol–1–yl)phenoxy)acetohydrazide 2(f)
IR(KBr):3444.3424(NH_2)3290(NH),1605(C=N)1658(C=O)^{1}HNMR(300MHZ,$(CD)_2SO$,TMS);δ=4.85(s, 2H, O–CH_2–CO), 4.20(s, 2H, NH_2), 10.95(s, 1H, Ar–NH–N=), 6.85–7.93(m, 8H, C_6H_4 and C_6H_4), 9.18(s, 1H, CO–NH)) C^{13}Spectrum of ($CDCl_3$)δ=20.6,32.7,29.4,58.6(Ar-c) 68.07(-CH_2)137.7(-NH-N=C119.0(Pyrazolone-c=o),87.1(CCl_3)158.3(CCl_3)166.3(-C=ONHNH$_2$),23.9,25.5,46.5,32.4100.4,155.9 yield 65M.P.^{0}C167-169 Mol. formula $C_{18}H_{15}Cl_3BrN_6O_3$ Calculated Values:C:47.98,H:4.60,N:18.07, O:10.78 Found(%):C:48.11, H:4.71, N:18.17O:10.89

7. Synthesis 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 3(a)
IR(KBr) 3205(-NH),3170(Indol -NH),1602(-c=N),1656(pyrazoline –C=O),1700(indole- 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, 13H, Ar–H), C^{13}Spectrum of ($CDCl_3$)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 212-214 Mol.formula $C_{26}H_{18}Cl_3N_7O_4$ 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

8. Synthesis 2–(4–(5–oxo–4(2–phenyl hydrazono)–3–(trichloro methyl)–4,5–dihydro–1–Methyl pyrazol–1–yl)phenoxy)N–(2–oxoindolin)–3–ylidine) aceto hydrazide 3(b)
IR(KBr):3180(-NH),3140(Indol-NH),1600(-C=N),δ1654(Pyrazoline-C=O),1700(IndoleC=O),1622(CO-NH),^{1}H NMR(300MHZ,$(CD)_2SO$,TMS);δ=3.18(s, 3H, Ar–CH_3), 10.95(s, 1H, Ar–NH–N=), 9.24(s, 1H, CO–NH), 4.83(s, 2H, O–CH_2–CO), 6.85–7.79(m, 12H, Ar–H), 10.57(s, 1H, Indole –NH) C^{13}Spectrum of($CDCl_3$) δ=26.9, 29.4,32.7,31.3,56.2,(Ar-c),59.8(-CH_2),155.6(-NH-N=C),118(Pyrazol =O), 90.2(CCl_3), 150(CCl_3) 155.6 (C=ONHNH$_2$), 22.0,27.7,35.3,46.5,32.6,119.1(Phenoxy)25.2,26.3,21.8,25.4,39.4,47.9,117,147.09(Indoline-c))yield70,M.P.^{0}C240-241Mol.formula$C_{27}H_{20}Cl_3N_7O_4$Calculated Values:C:53.10,H:3.17,N:16.10,O:10.31,Cl:17.21 Found(%):C:53.02,H:3.27,N:16.03,O:10.47,Cl:17.18

9. Synthesis 2–(4–(5–oxo–4(2–phenyl hydrazono)–3–(trichloro methyl)–4,5–dihydro–1–Methoxy pyrazol–1–yl)phenoxy)N–(2–oxoindolin)–3–ylidine) aceto hydrazide 3(c)
IR(KBr):3100(-NH),3150(indole-NH),1505(-C=N),1654(Pyrazoline-C=O),1701(Indole-C=O),1625(-CO-NH),^{1}H NMR(300MHZ,$(CD)_2SO$,TMS);δ=3.72(s, 3H, O–CH_3), 10.96(s, 1H, Ar–NH–N=), 9.26(s, 1H, CO–NH), 4.79(s, 2H, O–CH_2–CO), 6.83–7.75(m, 12H, Ar–H), 10.55(s, 1H, Indole –NH C^{13}Spectrum of ($CDCl_3$) δ=25.9,29.431.06,31.3,56.2,(Ar-c),59.8(-CH_2),156.6(-NH-N=C),115(Pyrazol-C=O),91.02(CCl_3), 152(CCl_3c) 155.6(C=ONHNH$_2$),21.02,26.07,36.03,47.02,32.6,119.1(Phenoxy),25.2,25.03,21.8,25.4,40.04,47.9,117,147.09(Indoline -c)) yield 70,M.P.^{0}C 230-234 Mol.formula $C_{27}H_{20}Cl_3N_7O_5$ Calculate Values:C:51.67, H:3.06N:15.04, O:12.05, Cl:16.23 Found(%):C:51.67,H:3.18,N:15.62,O:12.75,Cl:16.74

10. Synthesis 2–(4–(5–oxo–4(2–phenyl hydrazono)–3–(trichloro methyl)–4,5–dihydro–1–ethoxy pyrazol–1–yl)phenoxy)N–(2–oxoindolin)–3–ylidine) aceto hydrazide 3(d)
IR(KBr):3195(-NH),3155(indole-NH),1604(-C=N),1654(Pyrazoline-C=O),1701(Indole-C=O),1624(-CO-NH),^{1}H NMR(300MHZ,$(CD)_2SO$,TMS);δ=1.73(t, 3H, CH_3), 3.24(q, 2H, O–CH_2), 10.93(s, 1H, Ar–NH–N=), 4.81(s, 2H, O–CH_2–CO), 6.9–7.98(m, 12H, Ar–H), 10.61(s, 1H, Indole –NH) C^{13}Spectrum of ($CDCl_3$) δ=20.7, 31.3, 32.7, 29.4, 56.5, 29.4(Ar-C),73.2(-CH_2),156(-NHN=C),197(Pyrazol-c=o) 87.3(CCl_3), 70(CCl_3C), 156(C=ONHNH$_2$), 21.0,25.7, 78.6,29.9,102.0, 152.07(Phenoxy), 21.8,25.2,26.3,39.6,47.9,45.8,117.5,147.0(indolinec) yield 75,M.P.^{0}C 223-224 Mol.formula $C_{28}H_{22}Cl_3N_7O_5$Calculate Values: C:52.41, H:3.436 N:15.23, O:12.42,Cl:16.35 Found(%): C:52.41, H:3.43, N:15.28,O:12.48,Cl:16.38

11. Synthesis 2–(4–(5–oxo–4(2–phenyl hydrazono)–3–(trichloro methyl)–4,5–dihydro–1–Chloro pyrazol–1–yl)phenoxy)N–(2–oxoindolin)–3–ylidine) aceto hydrazide 3(e)
IR(KBr):3175(-NH),3140(Indole-NH),1605(-C=N),1654(Pyrozoline-C=O),1701(Indole-C=O),1624(-CONH),^{1}H NMR(300MHZ,$(CD)_2SO$,TMS);δ=9.28(s, 1H, CO–NH), 10.89(s, 1H, Ar–NH–N=), 4.84(s, 2H, O–CH_2–CO), 6.85–7.92(m, 12H, Ar–H), 10.59(s, 1H, Indole –NH) C^{13}Spectrum of ($CDCl_3$)δ=20.7,29.4,32.7,(Ar-C)60.8(-CH_2)137(-NH-N=C),120(Pyrazole)77.08(CCl_3), 69(CCl_3), 137(C=ONHNH$_2$),32.9, 50.4,129.8,127.7132.0,122.0 (Phenoxy), 24.9,25.7,126.0, 131.3,43.3,48.9,117,147,155.01(Indoline c) yield 75,M.P.^{0}C 223-225 Mol.formula $C_{26}H_{17}Cl_4N_7O_4$ Calculate Values: C:49.24,H:3.43N:15.12,O:10.12Cl:22.13Found(%):C:49.44H:2.96,N:15.53,O:10.14Cl:22.18

12. Synthesis 2–(4–(5–oxo–4(2–phenyl hydrazono)–3–(trichloro methyl)–4,5–dihydro–1–Bromine pyrazol–1–yl)phenoxy)N–(2–oxoindolin)–3–ylidine) aceto hydrazide 3(F)
IR(KBr): 3190(-NH),3150(Indole-NH),1604(-C=N),1654(Pyrazine-C=O),1701(Indole-C=O),1624(-CO-NH),^{1}H NMR(300MHZ,$(CD)_2SO$,TMS);δ=9.79(s, 1H, CO–NH), 10.95(s, 1H, Ar–NH–N=), 4.91(s, 2H, O–CH_2–CO), 6.93–8.02(m, 12H, Ar–H), 10.63(s, 1H, Indole –NH) C^{13}Spectrum of ($CDCl_3$) δ=20.7, 29.4,31.6, (Arc)60.8(CH_2), 137(C=ONHNH$_2$),32.9,50.4,129.8,127.7,132.0,122(Phenoxy),24.9,25.7,126.0,131.2,43.3,48.9,117,147,155.0(Indolenec) yield 80,M.P.^{0}C 241-243 Mol. formula $C_{26}H_{17}Cl_3BrN_7O_4$ Calculate Values: C:46.10, H:2.45 N:14.13, O:9.23Cl:15.03Found(%):C:46.15,H:2.15,N:14.49,O:9.46,Cl:15.53

13. Synthesis N'(2–oxo–1–(piperidine–yl methyl) Indoline–3–ylidine)–2–(4–(5–oxo–4–(2–phenyl hydrazono)–3–(trichloro methyl)–4,5–dihydro–1–H pyrazol–1–yl)phenoxy) aceto hydrazide4(a)
IR (KBr):CH_2 (x) 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, 13H, Ar–H) C^{13}Spectrum of ($CDCl_3$)δ=20.8,27.7,29.2,102.01,152.7,32.68(Ar-c)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(PiparadinC) yield 70,M.P.^{0}C 155-158 Mol.formula $C_{32}H_{29}Cl_3BrN_8O_4$ Calculate Found(%):C:55.3,H:4.17,N:16.13,O:9.22,Cl:15.12

14. Synthesis N'(2–oxo–1–(piperidine–yl methyl) Indoline–3–ylidine)–2–(4–(5–oxo–4–(2–phenyl hydrazono)–3–(trichloro methyl)–4,5–dihydro–1–Methyl pyrazol–1–yl)phenoxy) aceto hydrazide4(B)
IR(KBr):CH_2(X),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, 12H, 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 Mol.formula$C_{33}H_{31}Cl_3N_8O_4$ Found(%):C:55.93,H:4.37,N:15.81,O:9.03,Cl:14.83

15. Synthesis N'(2–oxo–1–(piperidine–yl methyl) Indoline–3–ylidine)–2–(4–(5–oxo–4–(2–phenyl hydrazono)–3–(trichloro methyl)–4,5–dihydro–1–Methoxy pyrazol–1–yl)phenoxy) aceto hydrazide4(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)yield70M.P.^{0}C165-167Mol.formula$C_{33}H_{31}Cl_3N_8O_5$ Found(%):C:55.93,H:4.37,N:15.81,O:9.03,Cl:14.83

16. Synthesis N'(2–oxo–1–(piperidine–yl methyl) Indoline–3–ylidine)–2–(4–(5–oxo–4–(2–phenyl hydrazono)–3–(trichloro methyl)–4,5–dihydro–1–ethoxy pyrazol–1–yl)phenoxy) aceto hydrazide4(d)
IR(KBr):CH_2(X),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, 12H,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 Mol.formula $C_{34}H_{33}Cl_3N_8O_5$ Found(%):C:55.28,H:4.47,N:15.17,O:10.84,Cl:14.2

17. Synthesis N'(2–oxo–1–(piperidine–yl methyl) Indoline–3–ylidine)–2–(4–(5–oxo–4–(2–phenyl hydrazono)–3–(trichloro methyl)–4,5–dihydro–1–Chloro pyrazol–1–yl)phenoxy) aceto hydrazide4(e)
IR(KBr): -CH_2(-X),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,CONH),6.897.95(m,12H,ArH)C^{13}Spectrumof($CDCl_3$)δ=20.08,25.02,29.101.32,155,102.3,31.65(Arc),60. 13(CH_2),165N=C)114(C=ONHNH_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}C160-161 Mol.formula $C_{34}H_{28}Cl_4N_8O_4$ Found(%):C52.28, H:3.84,N:15.36,O:8.79,Cl:13.58

18. Synthesis N'(2–oxo–1–(piperidine–yl methyl) Indoline–3–ylidine)–2–(4–(5–oxo–4–(2–phenyl hydrazono)–3–(trichloro methyl)–4,5–dihydro–1–Bromo pyrazol–1–yl)phenoxy) aceto hydrazide4(f)
IR(KBr):CH_2(X),3170(NH),1614(C=N),1674(PyrazolineC=O),1716(IndoleC=O),1626(CONH),2625(CH_2),^{1}HNMR (300MHZ,$(CD)_2SO$,TMS);δ= 1.42–1.53(m, 6H, $(CH_2)_3$ of piperidine ring), 2.52(t, 4H, CH_2NCH_2 of piperidinering) 4.18(s,2H,NCH_2N),4.79(s,2H,OCH_2CO),10.91(s,1H,ArNH=N),6.927.85(m,12H,ArH),8.97(s,1H,CONH)C^{13}Spectrumof($CDCl_3$)δ=20.08,23.23,29.100.32,154,102.3,30.65(Arc),59.13(CH_2),168(NHN=C)112(C=ONHNH_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)yield80M.P.^{0}C160Mol.formula$C_{32}H_{28}BrCl_3N_8O_4$Found(%):C:49.67,H:3.62,N:14.48,O:8.27,Cl:13.58

19. Synthesis N'(2–oxo–1–(piperidine–yl methyl) Indoline–3–ylidine)–2–(4–(5–oxo–4–(2–phenyl hydrazono)–3–(trichloro methyl)–4,5–dihydro–1–H pyrazol–1–yl)phenoxy) aceto hydrazide4(g)
IR(KBr):O(-x),3193(-NH),1620(-C=N),1681(Pyrazoline-C=O),1710(Indole-C=O),1660(CONH),2920(-CH_2),^{1}H NMR(300MHZ,$(CD)_2SO$,TMS);δ=3.41(t, 4H, –CH_2–O–CH_2– of morpholine ring), 2.57(t, 4H, CH_2–N–CH_2 of

morpholine ring), 4.15(s, 2H, N–CH_2–N), 4.78(s, 2H, O–CH_2–CO), 10.95(s, 1H, Ar–NH=N), 8.92(s,1H,CONH), 6.837.76(m,13H,ArH)C^{13}Spectrumof($CDCl_3$)δ=20.08,23.02,02101.32,154,101.2330.65(Arc),59.13(CH_2),162(NHN =C)113(C=ONHNH_2)15.12,20.02,32.0340.03(Phenoxy)21.04,21.02,21.03,19.03,30.03,115.02,143.03,153(Indoline) 11.02,20.21,41.12,55.51(piperidine) yield 85 M.P.^{0}C 159 Mol.formula $C_{31}H_{27}C3N_8O_5$ Found(%): C:53.44,H:3.87, N:16.09,O:11.49, Cl:1508

20. Synthesis N'(2–oxo–1–(piperidine–yl methyl) Indoline–3–ylidine)–2–(4–(5–oxo–4–(2–phenyl hydrazono)–3–(trichloro methyl)–4,5–dihydro–1–H pyrazol–1–yl)phenoxy) aceto hydrazide4(h)
IR(KBr):-NCH_3(X),3180(-NH),1617(-C=N),1666(Pyrazoline-C=O),1710(Indole-C=O),1657(-CONH),2920(-CH_2),), ^{1}H NMR(300MHZ,$(CD)_2$SO,TMS);δ= 2.34(s, 3H, N–CH_3), 2.45(t, 4H, –CH_2–N–CH_2– of piperazine ring), 2.53(t, 4H, CH_2–N–CH_2 of piperazine ring), 4.17(s, 2H, N–CH_2–N), 4.81(s, 2H, O–CH_2–CO), 10.93(s, 1H, Ar–NH=N), 8.89(s, 1H, CO–NH), 6.76–7.81(m, 13H,Ar–H) C^{13}Spectrum of ($CDCl_3$) δ=20.08, 23.02,02101.32, 154,101.23, 30.65(Arc), 59.13(CH_2),162(NHN=C)113(C=ONHNH_2)15.12,20.02,32.0340.03(Phenoxy) 21.04, 21.02,21.03,19.03,30.03,115.02,143.03,153(Indoline)11.02,20.21,41.12,55.51(piperidine)yield80M.P.^{0}C157Mol.for mula$C_{32}H_{30}C_3N_9O_4$ Found(%):C:54.16,H:4.23,N:17.23,O:9.06,Cl:14.80

Antibacterial activity by disc diffusion method.

Table 1. Antibacterial activity of synthesized compounds (4a-f)

Compound	Compound Zone of inhibition (mm) at 100 µg/ml concentration		
4(a)	**B.subtilis**	**E.coli**	**P.aeruginosa**
4(b)	11	10	08
4(c)	14	13	13
4(d)	16	14	14
4(e)	17	16	15
4(f)	10	09	-
Streptomycin	24	22	22

Comp	4a	4b	4c	4d	4e	4f	4g	4f
R	H	4-CH_3	4-OCH_3	4-OC_2H_5	4-Cl	4-Br	4-H	4-H
X	CH_2	CH_2	CH_2	CH_2	CH_2	CH_2	CH_2	CH_2

CONCLUSION

1) Further more the substitution with phenyl group hahing 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, antiflammatory.

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