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SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITIES OF NEW 1-[(2, 3-DICHLOROANILINOMALONYL)-3-(N-2'-CYANOETHYL)-2-(N-BENZOYL) 2, 3-DICHLOROANILINO)]-5-PHENYL PYRAZOLINE DERIVATIVES

RAJ NARAYAN SHARMA[*], K. P. SHARMA[a] and S. N. DIXIT[a]

Department of Chemistry, NRI College of Engineering and Management,
GWALIOR - 474002 (M.P.) INDIA
[a]Department of Chemistry, SMS Govt. Model Science College, GWALIOR - 474002 (M.P.) INDIA

ABSTRACT

A series of new 1-[(2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline have been synthesized in 42 to 68 % yield, by the reaction of N-cinnamoyl-N-2'-cyanoethyl-2,3-dichloroaniline with ethyl-2-[(N-benzoyl) 2,3-dichloroanilido] aceto-hydrazide. Pyrazolines are yellow, cream and brown color solids, having high melting points. Identity of these products has been established by elemental analysis and spectral data. Newly synthesized compounds **(7a-t)** have been tested for their antibacterial activity against gram positive bacteria *S. albus*, *S. aureus* and gram negative bacteria *E. Coli* and *Pseudomonas poisonous*. The compound (**7a**, **7b**, **7c**, **7f**, **7g**, **7j**, **7m** and **7r**) show significant activity and the compound (**7i**, **7k**, **7l**, **7p** and **7t**) have shown moderate activity. The same compounds were tested for their antifungal activity against *Candida albicans*, *Aspergillus Niger* and *Alternaria alternata* at concentration of 30 mg/mL using sabouraud dextrose agar media. The compound (**7c**, **7j**, **7m** and **7r**) show significant activities and compound (**7a**, **7b**, **7f** and **7g**) were found to be moderately active against *Candida albicans* and *Aspergillus Niger*. All the other compounds did not show significant activity against the fungi at the concentration used. Some new compounds have been tested for antitubercular activity *in vitro* using *Mycobacterium tuberculosis*. The compounds were incorporated into Lowenstein Jensen egg medium having concentrations of 10 and 100 mg/mL and were inoculated with *Mycobacterium tuberculosis*, $H_{27,}$ Rv strains, incubated at 37^0C and observed, the compound (**7a**, **7b**, **7c**, **7f**, **7g**, **7j** and **7m**) inhibited the growth of *Mycobacterium tuberculosis* at 100mg/mL concentration while other compounds were found to be inactive.

Key words: 5-Phenyl pyrazoline, Synthesis, Characterization, Biological activities.

[*]Author for correspondence; E-mail: rajnarayan1974@gmail.com

INTRODUCTION

Considerable attention has been focused on pyrazolines and substituted pyrazolines due to their interesting biological activities. They have been found to possess anti-fungal[1], anti-depressant[2-7], anti-convulsant[8], anti-inflammatory[9-12], anti-bacterial[13,14], anti-cancer[15,16], anti-oxidant[17,18], anti-pyretic[19], anti-neoplastic activities[20,21], anti-viral[22], anti-amoebic[23-24], acaricidal agrochemical fungicides or insecticides[25], anti-cholinergic[26,27], anti-diabetic[28], anti-HIV[29-32], anti-malarial[33], anesthetic[34], anaxiolytic[35], anti-parasitic[36], anti-allergic[37], anti-microbial[38-40], anti-tuberculosis[41-44], tyrosinase inhibitor[45], blue photoluminescence and electroluminescence[46], food and chemical toxicology[47], herbicidal[48-50], hypoglycemic[51], hypotensive[52], immunosuppressive[53] and anti-tumor[54,55]. Moreover, many selectively chloro-substituted organic compounds show peculiar pharmacological and agrochemical properties. The work reported herein was aimed at the preparation of some new pyrazoline derivatives with anticipated biological activities.

EXPERIMENTAL

General

All chemicals were used of A. R. grade (either of B.D.H. or Excel-R or Extra pure E. Merck quality). The structures of the compounds were determined by elemental analysis, IR and NMR spectral data. All melting points were measured on an electrothermal melting point apparatus and are uncorrected. The infrared spectra were recorded in potassium bromide disks on a Pye Unicam SP 3-300 or a Shimadzu FT-IR 8101 PC infrared spectrophotometer. The ^{1}H NMR (200 MHz) and ^{13}C-NMR (50 MHz) spectra were recorded in DMSO-d_6 on a Varian Mercury VX 200 NMR using TMS as the internal reference. Mass spectra were measured on a GCMS-QP 1000 EX spectrophotometer at 70 eV. Purity of the compounds is checked on T.L.C. using silica Gel-G. Elemental analysis is performed on Carlo-Erba 1108 analyzer.

Synthesis of ethyl-2-[2, 3-dichloroanilido] ethanoate (1)

A mixture of 2, 3-dichloroaniline (10 mL) and diethylmalonate (20 mL) was refluxed for forty five minutes in a round bottomed flask fitted with an air condenser of such a length (14") that ethanol formed escaped and diethylmalonate flowed back into the flask. Contents were cooled, ethanol (30 mL) was added, when malon-2,3-dichlorodianilide separated out. It was filtered under suction. The filtrate was poured on to crushed ice (ca 160 g) and stirred when ethyl-2-(2, 3-dichloroanilido) ethanoate precipitated as green mass. On

recrystallization from aqueous ethanol (50%), ester was obtained as white crystals. Yield: 81 %, M. P.: 88^0C, M. W.: 276. Anal. calculation for $C_{11}H_{11}N_1O_3Cl_2$: Found: C 39.20, H: 03.24, O: 14.25, N: 4.14, Cl: 21.09, Calcd. C: 39.21, H: 03.26, O: 14.26, N: 04.15, Cl: 21.16. IR [KBr] ν_{max} cm^{-1} : 1665-1660 [C=O diketone], 1290 [-C-O- ester], 760-755 [2,3 disubstituted benzene], 1250 [C-Cl stretching], 1590, 1520, 1440 [C=C ring stretching], 3150 [N-H stretching], 3040[C-H aromatic], 1330-1322 [C-H stretching]. PMR (DMSO): δ 4.42 (2H, s, CO-CH_2-CO), 4.0 (2H, s, NH_2), 7.4-8.6 (3H, m, Ar-H), 9.2 (1H, s, CO-NH D_2O exchangeable), 10.6 [1H, s, Ar-NH D_2O exchangeable].

Synthesis of ethyl-2-[(N-benzoyl) 2, 3- dichloroanilido] ethanoate (2)

Benzoyl chloride (8.46 g; 0.06 mol), dioxane (6 mL), ethyl-2-(2,3-dichloroanilido) ethanoate (16.5 g; 0.06 mol) and triethylamine (6.06 g; 0.06 mol) were placed in a round bottomed flask carrying reflux condensor having calcium chloride guard tube. The contents were heated on a boiling water bath for two hours and kept over night when triethylamine hydrochloride separated. It was filtered under suction and the filtrate was poured on to crushed ice (ca 180 g) and stirred when ethyl-2-[(N-benzoyl) 2, 3-dichloroanilido]ethanoate separated as solid. It was filtered under suction, dried and purified by recrystallisation from aqueous methanol (1 : 1) in white crystals. Yield = 78.4 %, MP = 94°C Anal. calculation for $C_{18}H_{15}N_1O_4Cl_2$: [FW = 380], Calculated: N 02.95, C 45.64, H 03.38, O 13.50 , Cl 15.00, Found : N 02.94, C 45.62 , H 03.37, O 13.52, Cl 15.02. IR [KBr] ν_{max} cm^{-1}: 1720 [C=O diketone], 1300 [-C-O- ester], 762 [2,3-disubstituted benzene], 1090 [C-Cl stretching], 1590, 1520, 1440 [C=C ring stretching], 3160 [N-H stretching], 3040 [C-H aromatic], 1330-1322 [C-H stretching]. PMR (DMSO): δ 4.44 [2H, s, CO-CH_2-CO], 4.1 [2H, s, NH_2], 7.2-8.5 [3H, m, Ar-H], 9.4 [1H, s, CO-NH D_2O exchangeable], 10.8 [1H, s, Ar-NH D_2O exchangeable].

Synthesis of ethyl-2-[(N-benzoyl) 2, 3-dichloroanilido] acetohydrazide (3)

Ethyl-2-[(N-benzoyl) 2, 3-dichloroanilido]ethanoate (10.98 g; 0.03 mol), ethanol (8 mL) and hydrazine hydrate (15 mL; 70%) were mixed together and stirred for thirty five minutes. Ethyl-2-[(N-benzoyl) 2, 3-dichloroanilido] acetohydrazide was filtered under suction and recrystallised from ethanol in white crystals. Yield; 76 %, MP = 172°C, MW 366 Anal. calculation for $C_{16}H_{13}N_3O_3Cl_2$: Calculated: N 09.04, C 41.32 ,H 03.01 ,O 10.33, Cl 15.28, Found: N 09.01, C 41.30, H 03.00, O 10.31, Cl 15.27. *IR [KBr]* ν_{max} cm^{-1}*:* 3160 [N-H stretching], 3048 [C-H aromatic], 1660 [C=O diketone], 1432 [C-Cl aromatic], 1595, 1520, 1445 [C=C ring stretching]. *PMR (DMSO):* δ 4.44 (2H, s, CO-CH_2-CO), 4.1 (2H, s, NH_2), 7.2-8.5 (3H, m, Ar-H), 9.4 (1H, s, CO-NH D_2O exchangeable), 10.9 (1H, s, Ar-NH D_2O exchangeable).

Monocyanoethylation of 2, 3-dichloroaniline (4)

A 250 mL three necked flask equipped with a stirrer, reflux condenser and thermometer was charged with 2, 3-dichloroaniline (0.1 mol, 16.2 g), acrylonitrile (0.1 mol, 10.6 g) and cupric acetate monohydrate (1.02 g, 4 % by weight of the amine). The mixture was stirred and refluxed on boiling water bath for three hours. The dark mixture was then transferred to a 250 mL distilling flask fitted with a 15.2 cm modified vigorous column and the unchanged acrylonitrile was first collected at 100 mm (water pump). The distillation was continued and the unchanged 2, 3-dichloro aniline B.P. 252^0C/0.5 mm was recovered. The N-cyanoethyl-2, 3-dichloroaniline was obtained as light yellow colored viscous liquid at 175-176^0C/mm, which solidified after keeping overnight. Yield: 15.7 g (97 %)., M.P. 82^0C

Preparation of cinnamoyl chloride (5)

Cinnamic acid (10 g, 0.067 mol) and thionyl chloride (12.0 mL) were taken in a round bottomed flask fitted with a reflux condenser carrying a calcium chloride guard tube. The contents were refluxed on a water bath for two and half hours in a fume cupboard until the evolution of HCl gas ceased from the guard tube. After cooling, liquid was carefully transferred to a Claisen flask and distilled under reduced pressure, when unreacted thionyl chloride distilled over first. Cinnamoyl chloride was collected at 165-166^0C/ 18-20 mm pressure.

Synthesis of N-cinnamoyl –N-2'-cyanoethyl -2, 3-dichloroaniline (6)

Solution of cinnamoyl chloride (3.5 g, 0.02 moL), dioxane (2 mL), N-2'-cyanoethyl -2, 3-dichloro aniline (7.90 g, 0.02 mol) and triethylamine (2.1 g) were placed in a round bottomed flask having a Liebig condenser carrying calcium chloride guard tube. The contents were heated for two hours on a boiling water bath. On keeping overnight, triethylamine hydrochloride separated as solid. It was filtered and contents were concentrated, when crystals separated out. Two crystallization from ethanol gave shining white needles. Yield: 55 %, M.P.: 156^0C, Anal. Calculated for $C_{18}H_{14}Cl_2N_2O$; M.W. 345; N: 4.5, Cl: 11.3 ; found N: 4.3, Cl : 11.2 %, IR [KBr] ν_{max} cm^{-1} : 3280-3050 (C-H stretching, aromatic), 2955 and 2890 (C-H stretching, aliphatic (asymmetric) and C-H stretching, aliphatic (symmetric), 2215 (C-N stretching), 1655 (C=C stretching, benzene ring), 1645 C=O (stretching, tertiary amide), 1615, 1575, 1455, (C=C ring stretching), 1050, 750, (2, 3-disubstituted benzene).

Synthesis of 1-[(2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline (7)

A mixture of N-cinnamoyl-N-2'-cyanoethyl -2, 3-dichloroaniline (0.345 g; 0.001

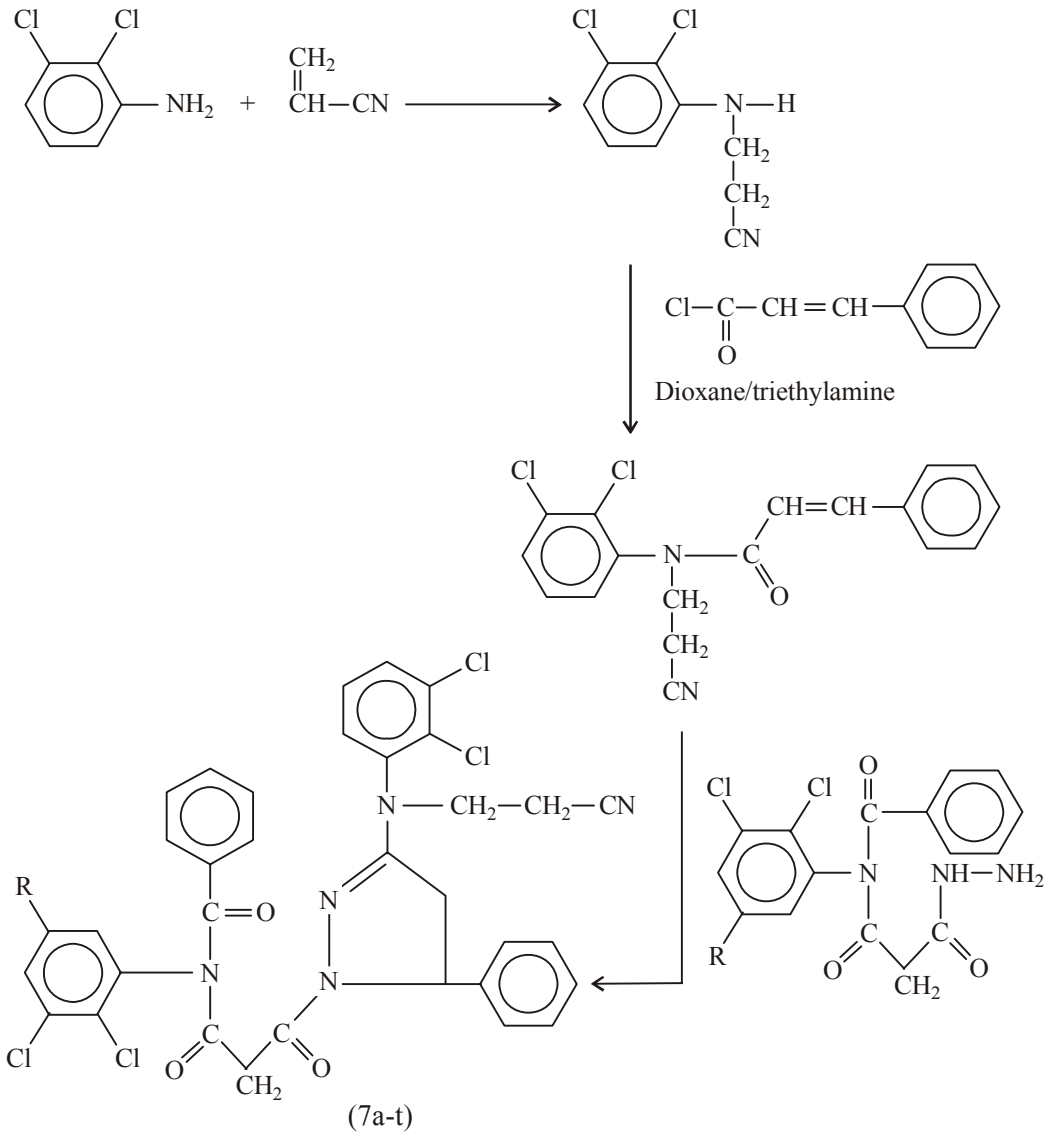
mol), ethyl-2-(2, 3-dichloroanilido) acetohydrazide (0.262 g; 0.001 mol), dioxane (3 mL), and glacial acetic acid (2 drops) was refluxed for five hours. The solid, which separated during the course of heating, was filtered under suction and purified by washing thrice with hot ethanol, when the pyrazoline was obtained as yellow needles. Yield: 61 %, M.P.: 254^0C, M.W.: 693, Anal. Calculated for $C_{34}H_{25}Cl_4N_5O_3$: Cl: 12.5; N: 6.8, found Cl: 12.7, N: 6.6%. U.V. [($\lambda^{Et\ OH}_{Max}$ nm), log ε]: 214.3 (4.94), 318.9 (4.78). IR [KBr] ν_{max} cm^{-1} : 3300-2860 [broad band due to (i) N-H stretching, secondary amide (Intra-molecular hydrogen bond), (ii) C-H stretching , aromatic, (iii) C-H stretching, aliphatic], 2240 (C N stretching), 1660 [C=O and N-H (amide)], 1590 (C=N stretching), 1580, 1470, 1420 (C=C ring stretching, aromatic), 1040, 820, (C-Cl stretching, 2, 3-disubstituted aromatic ring). ^{1}H NMR (250 MHz, δ ppm, DMSO-d_6,): 2.22-2.46 (2H, s, CH_2), 3.4-3.9 (3H, s, CH_3), 4.12-4.40(1H, s, NH), 6.95-7.40 (13H, m, ArH). 3.17 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.65 H_Z, C_4- H_A of pyrazoline ring). 3.92 (1H, dd J_{MA} = 17.80 Hz, J_{MX} = 13.60 Hz, C_4-H_M of pyrazoline ring), 4.70 (1H, d, J = 16.13 Hz COCH -geminal proton), 5.58 (1H, dd J_{MX} 12.80 H_Z, J_{AX} = 4.60 Hz, C_5-H_X of pyrazoline ring). ^{13}C NMR: ∂/ppm 179.58 (C=O), 159.78 (C=N), 141.05, 137.65, 134.45, 131.85 (4C, ArC's), 132.48, 130.55, 128.66, 125.77, 112.28 (5C, Ar CH's), 62.67 (CH_2, ester), 61.83 (C-5, pyrazoline), 46.95 (C-4, pyrazoline), 18.86 (CH_3); MS-FAB$^+$: m/z: 589 [M]. Synthetic sequence for new pyrazolines has been outlined in **Scheme 1**.

Some characteristics of the synthesized compounds are shown in Table 1. Analytical and spectral data (U.V., I.R., ^{1}H NMR, FAB$^+$-MS) confirmed the structures of the new compounds.

1-[(2, 3-Dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloro-anilino)]-5- phenyl pyrazoline (7a)

Yield: 61 %, M.P.: 254^0C, M.W.: 693, Anal. Calculated for $C_{34}H_{25}Cl_4N_5O_3$; Cl: 12.5; N: 6.8, found Cl: 12.7, N: 6.6%. U.V. [($\lambda^{Et\ OH}_{M\ ax}$ nm), log ε]: 214.3 (4.94), 318.9 (4.78). IR [KBr] ν_{max} cm^{-1} : 3300-2860 [broad band due to (i) N-H stretching, secondary amide (Intra-molecular hydrogen bond), (ii) C-H stretching, aromatic, (iii) C-H stretching, aliphatic], 2240 (C N stretching), 1660 [C=O and N-H (amide)], 1590 (C=N stretching), 1580, 1470, 1420 (C=C ring stretching, aromatic), 1040, 820, (C-Cl stretching, 2, 3-disubstituted aromatic ring). ^{1}H NMR (250 MHz, δ ppm, DMSO-d_6,): 2.22-2.46 (2H, s, CH_2), 3.4-3.9 (3H, s, CH_3), 4.12-4.40 (1H, s, NH), 6.95-7.40 (13H, m, ArH). 3.17 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.65 H_Z, C_4- H_A of pyrazoline ring). 3.92 (1H, dd J_{MA} = 17.80 Hz, J_{MX} = 13.60 Hz, C_4-H_M of pyrazoline ring), 4.70 (1H, d, J = 16.13 Hz COCH geminal proton), 5.58 (1H, dd J_{MX} 12.80 H_Z, J_{AX} = 4.60 Hz, C_5-H_X of pyrazoline ring). ^{13}C NMR: ∂/ppm 179.58 (C=O), 159.78 (C=N), 141.05, 137.65, 134.45, 131.85 (4C, ArC's), 132.48, 130.55, 128.66, 125.77, 112.28 (5C, Ar CH's), 62.67 (CH_2, ester), 61.83 (C-5, pyrazoline), 46.95 (C-4, pyrazoline), 18.86 (CH_3);

MS-FAB$^+$: m/z: 589 [M].



Scheme 1: The reaction scheme for the complete synthesis of compounds

1- [(o-Methyl) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline (7b)

Yield: 42 %, M.P.: 273^{0}C, M.W.: 707, Anal. Calculated for $C_{35}H_{27}Cl_4N_5O_3$, N: 4.2; found N: 4.1, Cl: 8.4; found Cl: 8.3 %. U.V. [(λ^{EtOH}_{max} nm), log ε]: 214.6(4.90), 319.4 (4.82).

IR [KBr] ν_{max} cm^{-1} : 3300-2890 [broad band due to (i) N-H stretching, secondary amide (Intra-molecular hydrogen bond) (ii) C-H stretching, aromatic, (iii) C-H stretching, aliphatic], 2242 (C≡N stretching), 1650 [C=O and N-H (amide)], 1580 (C=N stretching), 1585, 1478, 1430 (C=C ring stretching, aromatic), 1045, 822, (C-Cl stretching, 2,3-disubstituted aromatic ring). ^{1}H NMR (250 MHz, δ ppm, DMSO-d_6,): 2.23-2.48 (2H, s, CH_2), 4.16-4.30(1H, s, NH), 6.90-7.45 (13H, m, ArH). 3.10 (1H, dd, J_{AM} = 16 H_Z, J_{AX} = 4.60H_Z, C_4- H_A of pyrazoline ring). 3.98 (1H, dd J_{MA} = 17.90 Hz, J_{MX} = 13.80 Hz, C_4-H_M of pyrazoline ring), 4.60 (1H, d, J = 16.43 Hz COCH geminal proton), 5.70 (1H, dd J_{MX} 12.40 H_Z, J_{AX} = 4.50 Hz, C_5-H_X of pyrazoline ring). ^{13}C NMR: ∂/ppm 181.58 (C=O), 158.74 (C=N), 143.07, 136.54, 133.40, 130.74 (4C, ArC's), 131.47, 130.36, 126.62, 124.70, 114.31 (5C, Ar CH's), 63.66 (CH_2, ester), 60.81 (C-5, pyrazoline), 46.91 (C-4, pyrazoline), 18.82 (CH_3); MS-FAB$^+$: m/z: 604 [M].

1- [(m-Methyl) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline (7c)

Yield: 53 %, M.P.: 264^{0}C, M.W.: 707, Anal. Calculated for $C_{35}H_{27}Cl_4N_5O_3$, Cl: 10.6; N: 5.2, found Cl: 10.5, N: 5.0%. U.V. [(λ^{EtOH}_{max} nm), log ε]: 212.2 (4.92), 318.6 (4.78). IR [KBr] ν_{max} cm^1 : 3300-2950 [broad band due to (i) N-H stretching, secondary amide (Intra-molecular hydrogen bond), (ii) C-H stretching, aromatic, (iii) C-H stretching, aliphatic], 2240 (C≡N stretching), 1670 [C=O and N-H (amide)], 1575 (C=N stretching), 1560, 1430, 1410 (C=C ring stretching, aromatic), 1050, 815, (C-Cl stretching, 2, 3-disubstituted aromatic ring). ^{1}H NMR (250 MHz, δ ppm, DMSO-d_6,): 2.32-2.56 (2H, s, CH_2), 4.35-4.55 (1H, s, NH), 6.40-7.20 (13H, m, ArH). 3.10 (1H, dd, J_{AM} = 17 H_Z, J_{AX} = 4.55 H_Z, C_4- H_A of pyrazoline ring). 3.88 (1H, dd J_{MA} = 17.70 Hz, J_{MX} = 13.55 Hz, C_4-H_M of pyrazoline ring), 4.68 (1H, d, J = 16.16 Hz COCH geminal proton), 5.66 (1H, dd J_{MX} 12.60 H_Z, J_{AX} = 4.40 Hz, C_5-H_X of pyrazoline ring). ^{13}C NMR: ∂/ppm 167.56 (C=O), 154.61 (C=N), 143.01, 136.62, 133.43, 130.85 (4C, ArC's), 132.48, 130.55, 128.66, 125.77, 112.28 (5C, Ar CH's), 62.67 (CH_2, ester), 61.83 (C-5, pyrazoline), 45.92 (C-4, pyrazoline), 18.84 (CH_3); MS-FAB$^+$: m/z: 604 [M].

1-[(p-Methyl) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline (7d)

Yield: 58 %, M.P.: 244^{0}C, M.W.: 707, Anal. Calculated for $C_{35}H_{27}Cl_4N_5O_3$; Cl: 11.6; N: 5.7, found Cl: 11.4, N: 5.6%. U.V. [(λ^{EtOH}_{max} nm), log ε]: 227.3 (4.96), 319.6 (4.70). IR [KBr] ν_{max} cm^{-1} : 3300-3040 [broad band due to (i) N-H stretching, secondary amide (Intra-molecular hydrogen bond), (ii) C-H stretching , aromatic, (iii) C-H stretching, aliphatic], 2250 (C≡N stretching), 1620 [C=O and N-H (amide)], 1570 (C=N stretching), 1550, 1460,

1430 (C=C ring stretching, aromatic), 1040, 825, (C-Cl stretching, 2, 3-disubstituted aromatic ring). ^{1}H NMR (250 MHz, δ ppm, DMSO-d_6): 2.14-2.41 (2H, s, CH_2), 4.28-4.35(1H, s, NH), 6.80-7.60(13H, m, ArH). 3.28 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.61 H_Z, C_4- H_A of pyrazoline ring). 3.87 (1H, dd J_{MA} = 17.79 Hz, J_{MX} = 13.58Hz, C_4-H_M of pyrazoline ring), 4.68 (1H, d, J = 16.45 Hz COCH geminal proton), 6.11 (1H, dd J_{MX} 13.30 H_Z, J_{AX} = 4.65 Hz, C_5-H_X of pyrazoline ring). ^{13}C NMR: ∂/ppm 174.55 (C=O), 157.77 (C=N), 139.15, 135.65, 133.44, 131.80 (4C, ArC's), 131.42, 129.85, 126.62, 124.64, 111.17(5C, Ar CH's), 64.61 (CH_2, ester), 62.81 (C-5, pyrazoline), 45.92 (C-4, pyrazoline), 17.93 (CH_3); MS-FAB$^+$: m/z: 604 [M].

1-[(o-Chloro) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline (7e)

Yield: 49 %, M.P.: 268^{0}C, M.W.: 727.5, Anal. Calculated for $C_{34}H_{24}Cl_5N_5O_3$; Cl: 12.0; N: 4.7, found Cl: 12.1, N: 4.5%. U.V. [(λ^{EtOH}_{max} nm), log ε]: 215.5 (5.10), 319.2 (5.16). IR [KBr] ν_{max} cm^{-1} : 3300-3110 [broad band due to (i) N-H stretching, secondary amide (Intra-molecular hydrogen bond), (ii) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2290 (C≡N stretching), 1680 [C=O and N-H (amide)], 1540 (C=N stretching), 1530, 1490, 1440 (C=C ring stretching, aromatic), 1080, 890, (C-Cl stretching, 2, 3-disubstituted aromatic ring). ^{1}H NMR (250 MHz, δ ppm, DMSO-d_6,): 3.10-3.18 (2H, s, CH_2), 4.19-4.55(1H, s, NH), 6.87-7.20 (13H, m, ArH). 3.10 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.62 H_Z, C_4- H_A of pyrazoline ring). 4.05 (1H, dd J_{MA} = 18.10 Hz, J_{MX} = 13.90 Hz, C_4-H_M of pyrazoline ring), 4.60 (1H, d, J = 16.19 Hz COCH geminal proton), 5.45 (1H, dd J_{MX} 13.15 H_Z, J_{AX} = 5.10 Hz, C_5-H_X of pyrazoline ring). ^{13}C NMR: ∂/ppm 164.79 (C=O), 154.72 (C=N), 147.22, 143.60, 138.44, 132.83 (4C, ArC's), 130.79, 128.85, 123.63, 121.72, 115.26 (5C, Ar CH's), 64.60 (CH_2, ester), 60.92 (C-5, pyrazoline), 47.15 (C-4, pyrazoline), 19.10 (CH_3); MS-FAB$^+$: m/z: 623 [M], 624 [M+1].

1-[(m-Chloro) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline (7f)

Yield: 60 %, M.P.: 262^{0}C, M.W.: 727.5, Anal. Calculated for $C_{34}H_{24}Cl_5N_5O_3$; Cl: 14.6; N: 5.8, found Cl: 14.2, N: 5.6%. U.V. [(λ^{EtOH}_{max} nm), log ε]: 214.6 (4.97), 322.4 (4.81). IR [KBr] ν_{max} cm^{-1} : 3300-3120 [broad band due to (i) N-H stretching, secondary amide (Intra-molecular hydrogen bond), (ii) C-H stretching, aromatic, (iii) C-H stretching , aliphatic], 2240 (C≡N stretching), 1658 [C=O and N-H (amide)], 1605 (C=N stretching), 1570, 1460, 1430 (C=C ring stretching, aromatic), 1070, 830, (C-Cl stretching, 2, 3-disubstituted aromatic ring). ^{1}H NMR (250 MHz, δ ppm, DMSO-d_6,): 2.58-2.87 (2H, s, CH_2), 4.35-4.62 (1H, s, NH), 7.10-7.55 (13H, m, ArH). 3.34 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.70 H_Z,

C_4- H_A of pyrazoline ring). 4.15 (1H, dd J_{MA} = 17.90Hz, J_{MX} = 13.20 Hz, C_4-H_M of pyrazoline ring), 4.60 (1H, d, J = 16.44 Hz COCH geminal proton), 5.55 (1H, dd J_{MX} 13.30 H_Z, J_{AX} = 4.70 Hz, C_5-H_X of pyrazoline ring). ^{13}C NMR: ∂/ppm 178.57 (C=O), 155.65 (C=N), 144.11, 138.64, 135.44, 132.82 (4C, ArC's), 131.88, 130.15, 126.60, 123.80, 116.26 (5C, Ar CH's), 61.66 (CH_2, ester), 59.95 (C-5, pyrazoline), 47.93 (C-4, pyrazoline), 18.95(CH_3); MS-FAB$^+$: m/z: 623 [M], 624 [M+1].

1-[(p-Chloro) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline (7g)

Yield: 64 %, M.P.: 267^{0}C, M.W.: 727.5, Anal. Calculated for $C_{34}H_{24}Cl_5N_5O_3$; Cl: 15.6; N: 6.2, found Cl: 15.4, N: 6.0%. U.V. [(λ^{EtOH}_{max} nm), log ε]: 216.3 (5.20), 340.6 (4.88). IR [KBr] ν_{max} cm^{-1} : 3300-2960 [broad band due to (i) N-H stretching, secondary amide (Intra-molecular hydrogen bond), (ii) C-H stretching, aromatic, (iii) C-H stretching, aliphatic], 2290 (C≡N stretching), 1680 [C=O and N-H (amide)], 1620 (C=N stretching), 1575, 1465, 1415 (C=C ring stretching , aromatic), 1035, 825, (C-Cl stretching, 2, 3-disubstituted aromatic ring). ^{1}H NMR (250 MHz, δ ppm, DMSO-d_6,): 2.86-3.10 (2H, s, CH_2), 4.19-4.45 (1H, s, NH), 6.90-7.42 (13H, m, ArH). 3.28 (1H, dd, J_{AM} = 17H_Z, J_{AX} = 4.68 H_Z, C_4- H_A of pyrazoline ring). 3.70 (1H, dd J_{MA} = 17.81 Hz, J_{MX} = 13.30 Hz, C_4-H_M of pyrazoline ring), 4.20 (1H, d, J = 16.48 Hz COCH geminal proton), 5.22(1H, dd J_{MX} 12.89 H_Z, J_{AX} = 4.57 Hz, C_5-H_X of pyrazoline ring). ^{13}C NMR: ∂/ppm 169.52 (C=O), 157.78 (C=N), 152.20, 148.65, 142.44, 138.85 (4C, ArC's), 134.48, 132.53, 129.68, 123.77, 126.27 (5C, Ar CH's), 64.67 (CH_2, ester), 62.60 (C-5, pyrazoline), 47.25 (C-4, pyrazoline), 18.35 (CH_3); MS-FAB$^+$: m/z: 623 [M], 624 [M+1].

1-[(o-Methoxy) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline (7h)

Yield: 67 %, M.P.: 247^{0}C, M.W.: 723, Anal. Calculated for $C_{35}H_{27}Cl_4N_5O_4$; Cl: 13.2; N: 6.5, found Cl: 13.0, N: 6.6%. U.V. [(λ^{EtOH}_{max} nm), log ε]: 215.3 (5.04), 318.4(4.79). IR [KBr] ν_{max} cm^{-1} : 3300-2880 [broad band due to (i) N-H stretching, secondary amide (Intra-molecular hydrogen bond), (ii) C-H stretching, aromatic, (iii) C-H stretching, aliphatic], 2270 (C≡N stretching), 1640 [C=O and N-H (amide)], 1575 (C=N stretching), 1570, 1455, 1440 (C=C ring stretching, aromatic), 1050, 810, (C-Cl stretching, 2, 3-disubstituted aromatic ring). ^{1}H NMR (250 MHz, δ ppm, DMSO-d_6,): 2.38-2.51 (2H, s, CH_2), 4.29-4.50(1H, s, NH), 6.90-7.20 (13H, m, ArH). 3.27 (1H, dd, J_{AM} = 17 H_Z, J_{AX} = 4.55 H_Z, C_4- H_A of pyrazoline ring). 3.98 (1H, dd J_{MA} = 17.90 Hz, J_{MX} = 13.80 Hz, C_4-H_M of pyrazoline ring), 4.82 (1H, d, J = 16.23 Hz COCH geminal proton), 5.51 (1H, dd J_{MX} 11.90 H_Z, J_{AX} = 4.40 Hz, C_5-H_X of pyrazoline ring). ^{13}C NMR: ∂/ppm 173.52 (C=O), 158.70 (C=N), 144.10,

138.62, 135.65, 130.85 (4C, ArC's), 133.38, 131.40, 129.46, 123.80, 116.18 (5C, Ar CH's), 63.66 (CH_2, ester), 63.68(C-5, pyrazoline), 45.92(C-4, pyrazoline), 19.15 (CH_3); MS-FAB$^+$: m/z: 620 [M].

1-[(m-Methoxy) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline (7i)

Yield: 71 %, M.P.: 256^{0}C, M.W.: 723, Anal. Calculated for $C_{35}H_{27}Cl_4N_5O_4$; Cl: 13.9; N: 6.9, found Cl: 13.6, N: 6.8%. U.V. [(λ^{EtOH}_{max} nm), log ε]: 218.1 (4.95), 317.9 (4.68). IR [KBr] ν_{max} cm^{-1} : 3300-2910 [broad band due to (i) N-H stretching, secondary amide (Intra-molecular hydrogen bond), (ii) C-H stretching, aromatic, (iii) C-H stretching, aliphatic], 2240 (C≡N stretching), 1660 [C=O and N-H (amide)], 1590 (C=N stretching), 1585, 1480, 1410 (C=C ring stretching, aromatic), 1060, 825, (C-Cl stretching, 2, 3-disubstituted aromatic ring). ^{1}H NMR (250 MHz, δ ppm, DMSO-d_6,): 2.12-2.49 (2H, s, CH_2), 4.14-4.45 (1H, s, NH), 7.10 -7.40 (13H, m, ArH). 3.22 (1H, dd, J_{AM} = 19H_Z, J_{AX} = 4.59 H_Z, C_4- H_A of pyrazoline ring). 4.10(1H, dd J_{MA} = 17.80 Hz, J_{MX} = 13.65 Hz, C_4-H_M of pyrazoline ring), 4.74 (1H, d, J = 16.10 Hz COCH geminal proton), 5.70 (1H, dd J_{MX} 12.40 H_Z, J_{AX} = 4.70 Hz, C_5-H_X of pyrazoline ring). ^{13}C NMR: ∂/ppm 178.56 (C=O), 153.77 (C=N), 142.05, 139.40, 132.45, 130.80 (4C, ArC's), 131.45, 129.80, 127.84, 125.70, 113.18 (5C, Ar CH's), 61.67 (CH_2, ester), 62.82 (C-5, pyrazoline), 46.65 (C-4, pyrazoline), 18.42 (CH_3); MS-FAB$^+$: m/z: 620[M].

1-[(p-Methoxy) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline (7j)

Yield: 74 %, M.P.: 260^{0}C, M.W.: 723, Anal. Calculated for $C_{35}H_{27}Cl_4N_5O_4$; Cl: 14.5; N: 7.2, found Cl: 14.3, N: 6.9%. U.V. [(λ^{EtOH}_{max} nm), log ε]: 216.4 (4.93), 318.7 (4.76). IR [KBr] ν_{max} cm^{-1} : 3300-2890 [broad band due to (i) N-H stretching, secondary amide (Intra-molecular hydrogen bond), (ii) C-H stretching, aromatic, (iii) C-H stretching, aliphatic], 2230 (C≡N stretching), 1680 [C=O and N-H (amide)], 1610 (C=N stretching), 1590, 1520, 1460 (C=C ring stretching, aromatic), 1030, 840, (C-Cl stretching, 2, 3-disubstituted aromatic ring). ^{1}H NMR (250 MHz, δ ppm, DMSO-d_6,): 2.20-2.56 (2H, s, CH_2), 4.10-4.80(1H, s, NH), 6.85-7.10 (13H, m, ArH). 3.18 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.62 H_Z, C_4- H_A of pyrazoline ring). 3.97 (1H, dd J_{MA} = 18.20 Hz, J_{MX} = 13.50Hz, C_4-H_M of pyrazoline ring), 4.80 (1H, d, J = 16.18 Hz COCH geminal proton), 5.60 (1H, dd J_{MX} 12.70 H_Z, J_{AX} = 4.65 Hz, C_5-H_X of pyrazoline ring). ^{13}C NMR: ∂/ppm 174.55 (C=O), 158.71 (C=N), 143.10, 138.60, 137.45, 133.85 (4C, ArC's), 132.48, 130.55, 128.66, 125.75, 114.68 (5C, Ar CH's), 62.80 (CH_2, ester), 63.20 (C-5, pyrazoline), 46.80 (C-4, pyrazoline), 18.86 (CH_3); MS-FAB$^+$: m/z: 620 [M].

1-[(p-Fluoro) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline (7k)

Yield: 52 %, M.P.: 244^0C, M.W.: 711, Anal. Calculated for $C_{34}H_{24}Cl_4F_1N_5O_3$; Cl: 10.4; N: 5.2, found Cl: 10.5, N: 4.9%. U.V. [(λ^{EtOH}_{max} nm), log ε]: 222.5 (4.98), 317.9 (4.73). IR [KBr] ν_{max} cm^{-1} : 3300-2860 [broad band due to (i) N-H stretching, secondary amide (Intra-molecular hydrogen bond), (ii) C-H stretching, aromatic, (iii) C-H stretching, aliphatic], 2250 (C≡N stretching), 1660 [C=O and N-H (amide)], 1575 (C=N stretching), 1570, 1460, 1430 (C=C ring stretching, aromatic), 1070, 860, (C-Cl stretching, 2, 3-disubstituted aromatic ring). ^{1}H NMR (250 MHz, δ ppm, DMSO-$d_{6,}$): 2.18-2.34 (2H, s, CH_2), 4.16-4.70(1H, s, NH), 6.70-7.10 (13H, m, ArH). 3.16 (1H, dd, J_{AM} = 17 $H_{Z,}$ J_{AX} = 4.60 H_Z, C_4- H_A of pyrazoline ring). 3.93 (1H, dd J_{MA} = 17.90 Hz, J_{MX} = 13.70 Hz, C_4-H_M of pyrazoline ring), 4.90 (1H, d, J = 16.40 Hz COCH geminal proton), 5.55 (1H, dd J_{MX} 12.90 H_Z, J_{AX} = 4.55 Hz, C_5-H_X of pyrazoline ring). ^{13}C NMR: ∂/ppm 176.47 (C=O), 156.78 (C=N), 142.05, 137.62, 135.45, 132.84 (4C, ArC's), 130.28, 129.50, 126.60, 122.70, 111.88 (5C, Ar CH's), 63.10 ($CH_{2,}$ ester), 62.40 (C-5, pyrazoline), 47.10 (C-4, pyrazoline), 18.95 (CH_3), MS-FAB$^+$: m/z: 608[M].

1-[(o-Bromo) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline (7l)

Yield: 59 %, M.P.: 258^0C, M.W.: 772, Anal. Calculated for $C_{34}H_{24}Cl_4N_5O_3Br$; Cl: 10.9; N: 5.3, found Cl: 10.5, N: 5.2%. U.V. [(λ^{EtOH}_{max} nm), log ε]: 210.2 (4.93), 318.7 (4.85). IR [KBr] ν_{max} cm^{-1} : 3300-2880 [broad band due to (i) N-H stretching, secondary amide (Intra-molecular hydrogen bond), (ii) C-H stretching, aromatic, (iii) C-H stretching, aliphatic], 2230 (C≡N stretching), 1620 [C=O and N-H (amide)], 1555 (C=N stretching), 1605, 1510, 1490 (C=C ring stretching , aromatic), 1060, 840, (C-Cl stretching, 2, 3-disubstituted aromatic ring). ^{1}H NMR (250 MHz, δ ppm, DMSO-$d_{6,}$): 2.20-2.54 (2H, s, CH_2), 4.25-4.45 (1H, s, NH), 6.80-7.30 (13H, m, ArH). 3.25 (1H, dd, J_{AM} = 18 $H_{Z,}$ J_{AX} = 4.55 H_Z, C_4- H_A of pyrazoline ring). 4.04 (1H, dd J_{MA} = 17.70 Hz, J_{MX} = 13.50 Hz, C_4-H_M of pyrazoline ring), 4.80 (1H, d, J = 16.66 Hz COCH geminal proton), 5.68 (1H, dd J_{MX} 13.10 H_Z, J_{AX} = 4.70 Hz, C_5-H_X of pyrazoline ring). ^{13}C NMR: ∂/ppm 178.70 (C=O), 158.72 (C=N), 141.10, 138.40, 136.49, 130.85 (4C, ArC's), 131.48, 130.32, 127.66, 124.77, 113.38 (5C, Ar CH's), 62.60 ($CH_{2,}$ ester), 61.84 (C-5, pyrazoline), 45.92 (C-4, pyrazoline), 19.06 (CH_3); MS-FAB$^+$: m/z: 669 [M].

1-[(o-Ethoxy) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline (7m)

Yield: 63 %, M.P.: 267^0C, M.W.: 738, Anal. Calculated for $C_{36}H_{29}Cl_4N_5O_4$; Cl: 12.1;

N: 6.0, found Cl: 12.2, N: 5.8%. U.V. [(λ^{EtOH}_{max} nm), log ε]: 212.5 (4.98), 318.4 (4.88). IR [KBr] ν_{max} cm^{-1} : 3300-2920 [broad band due to (i) N-H stretching, secondary amide (Intra-molecular hydrogen bond), (ii) C-H stretching, aromatic, (iii) C-H stretching, aliphatic], 2260 (C≡N stretching), 1640 [C=O and N-H (amide)], 1580 (C=N stretching), 1590, 1480, 1460 (C=C ring stretching, aromatic), 1050, 860, (C-Cl stretching, 2, 3-disubstituted aromatic ring). ^{1}H NMR (250 MHz, δ ppm, DMSO-d_6,): 2.30-2.44 (2H, s, CH_2), 4.14-4.40(1H, s, NH), 6.80-7.20 (13H, m, ArH). 3.17 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.60 H_Z, C_4- H_A of pyrazoline ring). 3.95 (1H, dd J_{MA} = 17.80 Hz, J_{MX} = 13.65 Hz, C_4-H_M of pyrazoline ring), 4.55 (1H, d, J = 16.35 Hz COCH geminal proton), 5.50(1H, dd J_{MX} 12.90 H_Z, J_{AX} = 4.65 Hz, C_5-H_X of pyrazoline ring). ^{13}C NMR: ∂/ppm 176.58 (C=O), 156.74 (C=N), 140.05, 136.65, 135.45, 132.90 (4C, ArC's), 131.46, 130.52, 129.66, 126.72, 112.44 (5C, Ar CH's), 62.90 (CH_2, ester), 61.88 (C-5, pyrazoline), 46.35 (C-4, pyrazoline), 18.80 (CH_3); MS-FAB$^+$: m/z: 634 [M].

1-[(m-Ethoxy) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline [7n]

Yield: 65 %, M.P.: 251^{0}C (d), M.W.: 738, Anal. Calculated for $C_{36}H_{29}Cl_4N_5O_4$; Cl: 12.5; N: 6.2, found Cl: 12.3, N: 6.0%. U.V. [(λ^{EtOH}_{max} nm), log ε]: 210.2 (4.89), 318.5 (4.72). IR [KBr] ν_{max} cm^{-1} : 3300-2890 [broad band due to (i) N-H stretching, secondary amide (Intra-molecular hydrogen bond), (ii) C-H stretching, aromatic, (iii) C-H stretching, aliphatic], 2240 (C≡N stretching), 1670 [C=O and N-H (amide)], 1570 (C=N stretching), 1580, 1460, 1430 (C=C ring stretching, aromatic), 1055, 830, (C-Cl stretching, 2, 3-disubstituted aromatic ring). ^{1}H NMR (250 MHz, δ ppm, DMSO-d_6): 2.14-2.26 (2H, s, CH_2), 4.18-4.30 (1H, s, NH), 7.0-7.30 (13H, m, ArH). 3.15 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.60 H_Z, C_4-H_A of pyrazoline ring). 3.90 (1H, dd J_{MA} = 17.90 Hz, J_{MX} = 13.55 Hz, C_4-H_M of pyrazoline ring), 4.75(1H, d, J = 16.12 Hz COCH geminal proton), 5.55(1H, dd J_{MX} 12.70 H_Z, J_{AX} = 4.50 Hz, C_5-H_X of pyrazoline ring). ^{13}C NMR: ∂/ppm 174.54 (C=O), 153.78 (C=N), 143.10, 140.64, 137.45, 136.85 (4C, ArC's), 133.48, 131.55, 127.66, 124.57, 112.28 (5C, Ar CH's), 64.65 (CH_2, ester), 62.85 (C-5, pyrazoline), 46.45 (C-4, pyrazoline), 18.95 (CH_3); MS-FAB$^+$: m/z: 634 [M].

1-[(p-Ethoxy) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline [7o]

Yield: 61 %, M.P.: 243^{0}C, M.W.: 738, Anal. Calculated for $C_{36}H_{29}Cl_4N_5O_4$; Cl: 11.7; N: 5.8, found Cl: 11.4, N: 5.5%. U.V. [(λ^{EtOH}_{max} nm), log ε]: 218.2 (4.88), 318.6 (4.72). *IR [KBr]* ν_{max} cm^{-1} : 3300-2930 [broad band due to (i) N-H stretching, secondary amide (Intra-molecular hydrogen bond), (ii) C-H stretching, aromatic, (iii) C-H stretching, aliphatic],

2250 (C≡N stretching), 1640 [C=O and N-H (amide)], 1555 (C=N stretching), 1590, 1450, 1430 (C=C ring stretching, aromatic), 1045, 840, (C-Cl stretching, 2, 3-disubstituted aromatic ring). ^{1}H NMR (250 MHz, δ ppm, DMSO-d_6): 2.20-2.46 (2H, s, CH_2), 4.10-4.45 (1H, s, NH), 6.90-7.30 (13H, m, ArH). 3.20 (1H, dd, J_{AM} = 19 H_Z, J_{AX} = 4.80 H_Z, C_4- H_A of pyrazoline ring). 3.90 (1H, dd J_{MA} = 17.60 Hz, J_{MX} = 13.65Hz, C_4-H_M of pyrazoline ring), 4.70 (1H, d, J = 16.20 Hz COCH geminal proton), 5.65(1H, dd J_{MX} 12.60 H_Z, J_{AX} = 4.70 Hz, C_5-H_X of pyrazoline ring). ^{13}C NMR: ∂/ppm 181.52 (C=O), 162.78 (C=N), 142.20, 138.65, 137.42, 133.84(4C, ArC's), 129.88, 128.50, 127.60, 126.75, 110.38 (5C, Ar CH's), 63.67 (CH_2, ester), 61.83 (C-5, pyrazoline), 46.65 (C-4, pyrazoline), 18.99 (CH_3); MS-FAB$^+$: m/z: 634 [M].

1-[(m-Bromo) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline (7s)

Yield: 57 %, M.P.: 249^{0}C, M.W.: 772, Anal. Calculated for $C_{34}H_{24}Cl_4N_5O_3Br$; Cl: 10.5; N: 5.2, found Cl: 10.2, N: 4.9%. U.V. [(λ^{EtOH}_{max} nm), log ε]: 214.3 (4.90), 318.4 (4.70). IR [KBr] ν_{max} cm^{-1} : 3300-2890 [broad band due to (i) N-H stretching, secondary amide (Intra-molecular hydrogen bond), (ii) C-H stretching, aromatic, (iii) C-H stretching, aliphatic], 2240 (C≡N stretching), 1660 [C=O and N-H (amide)], 1570 (C=N stretching), 1570, 1490, 1470 (C=C ring stretching, aromatic), 1050, 830, (C-Cl stretching, 2, 3-disubstituted aromatic ring). ^{1}H NMR (250 MHz, δ ppm, DMSO-d_6): 2.28-2.52 (2H, s, CH_2), 4.13-4.30 (1H, s, NH), 6.90-7.55 (13H, m, ArH). 3.15 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.70 H_Z, C_4-H_A of pyrazoline ring). 3.95 (1H, dd J_{MA} = 17.70 Hz, J_{MX} = 13.50 Hz, C_4-H_M of pyrazoline ring), 4.60 (1H, d, J = 16.10 Hz COCH geminal proton), 5.80 (1H, dd J_{MX} 12.90 H_Z, J_{AX} = 4.70 Hz, C_5-H_X of pyrazoline ring). ^{13}C NMR: ∂/ppm 178.57 (C=O), 157.77 (C=N), 140.15, 136.64, 134.40, 130.80 (4C, ArC's), 130.18, 128.75, 127.66, 125.78, 113.19(5C, Ar CH's), 61.62(CH_2, ester), 61.70 (C-5, pyrazoline), 46.90 (C-4, pyrazoline), 18.75 (CH_3); MS-FAB$^+$: m/z: 669 [M].

1-[(p-Bromo) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline (7t)

Yield: 49 %, M.P.: 253^{0}C, M.W.: 772, Anal. Calculated for $C_{34}H_{24}Cl_4N_5O_3Br$; Cl: 9.0; N: 4.4, found Cl: 8.9, N: 4.3%. U.V. [(λ^{EtOH}_{max} nm), log ε]: 210.2 (4.94), 318.7 (4.76). IR [KBr] ν_{max} cm^{-1} : 3300-2850 [broad band due to (i) N-H stretching, secondary amide (Intra-molecular hydrogen bond), (ii) C-H stretching, aromatic, (iii) C-H stretching, aliphatic], 2250 (C≡N stretching), 1650 [C=O and N-H (amide)], 1580 (C=N stretching), 1560, 1480, 1440 (C=C ring stretching, aromatic), 1040, 840, (C-Cl stretching, 2, 3-disubstituted aromatic ring). ^{1}H NMR (250 MHz, δ ppm, DMSO-d_6): 2.20-2.44 (2H, s, CH_2),

4.15-4.45 (1H, s, NH), 6.90-7.45 (13H, m, ArH). 3.20 (1H, dd, J_{AM} = 17 H_Z, J_{AX} = 4.60 H_Z, C_4-H_A of pyrazoline ring). 3.90 (1H, dd J_{MA} = 17.85 Hz, J_{MX} = 13.65Hz, C_4-H_M of pyrazoline ring), 4.75 (1H, d, J = 16.15 Hz COCH geminal proton), 5.55 (1H, dd J_{MX} 12.85H_Z, J_{AX} = 4.64 Hz, C_5-H_X of pyrazoline ring). ^{13}C NMR: ∂/ppm 180.55 (C=O), 161.78 (C=N), 142.15, 138.65, 136.45, 133.80 (4C, ArC's), 131.46, 128.50, 127.65, 125.70, 114.27 (5C, Ar CH's), 62.68 (CH_2, ester), 60.88 (C-5, pyrazoline), 47.20 (C-4, pyrazoline), 18.95 (CH_3); MS-FAB$^+$: m/z: 669 [M].

Most of the pyrazolines are high melting and light yellow or cream colored solids. The data of new products are furnished in Table 1.

Table 1: (Unsubstituted/substituted)1-[(2,3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl) - 2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline

CS. No.	R	Color	M.P. (˚C)	Yield (%)	M.W.	Molecular formula
7a.	H	Yellow	254	61	693	$C_{34}H_{25}Cl_4N_5O_3$
7b.	CH_3 (o)	Cream	273	42	707	$C_{35}H_{27}Cl_4N_5O_3$
7c.	CH_3 (m)	Light yellow	264	53	707	$C_{35}H_{27}Cl_4N_5O_3$
7d.	CH_3 (p)	Light yellow	245	58	707	$C_{35}H_{27}Cl_4N_5O_3$
7e.	Cl (o)	white	268	49	727.5	$C_{34}H_{24}Cl_5N_5O_3$
7f.	Cl (m)	Light yellow	262	60	727.5	$C_{34}H_{24}Cl_5N_5O_3$
7g.	Cl (p)	Cream	267	64	727.5	$C_{34}H_{24}Cl_5N_5O_3$
7h.	O-CH_3 (o)	Yellow	247	67	723	$C_{35}H_{27}Cl_4N_5O_4$
7i.	O-CH_3 (m)	White	256	71	723	$C_{35}H_{27}Cl_4N_5O_4$
7j.	O-CH_3 (p)	Cream	260	74	723	$C_{35}H_{27}Cl_4N_5O_4$
7k.	F (p)	Yellow	244	52	711	$C_{34}H_{24}Cl_4N_5O_3F_1$
7l.	Br (o)	Dark brown	258	59	772	$C_{34}H_{24}Cl_4N_5O_3Br$
7m.	O-C_2H_5 (o)	L. Brown	267	63	738	$C_{36}H_{29}Cl_4N_5O_4$
7n.	O-C_2H_5 (m)	Brown	251	65	738	$C_{36}H_{29}Cl_4N_5O_4$
7o.	O-C_2H_5 (p)	Brown	243	61	738	$C_{36}H_{29}Cl_4N_5O_4$
7p.	CO_2H (o)	Brown	253	69	738	$C_{35}H_{25}Cl_4N_5O_5$

Cont…

CS. No.	R	Color	M.P. (˚C)	Yield (%)	M.W.	Molecular formula
7q.	CO_2H (m)	Brown	249	64	738	$C_{35}H_{25}Cl_4N_5O_5$
7r.	CO_2H (p)	L. brown	258	52	738	$C_{35}H_{25}Cl_4N_5O_5$
7s.	Br (m)	Brown	249	57	772	$C_{34}H_{24}Cl_4N_5O_3Br$
7t.	Br (p)	Brown	253	49	772	$C_{34}H_{24}Cl_4N_5O_3Br$

All compounds gave satisfactory elemental analysis.

Biological evaluation

Antibacterial activity

Newly synthesized compounds ***(7a-t)*** have been tested for their antibacterial activity against gram positive bacteria *S. albus, S. aureus* and gram negative bacteria *E. coli* and *Pseudomonas poisonous* by agar plate disc diffusion method at 30 µg/mL concentration. Ampicillin and tetracycline were used as reference compound. The compound (***7a***, ***7b***, ***7c***, ***7f***, ***7g***, ***7j***, ***7m*** and ***7r***) show significant activity and the compound (***7i***, ***7k***, ***7l***, ***7p*** and ***7t***) *have* show moderate activity.

Antifungal activity

The same compounds were tested for their antifungal activity against *Candida albicans, Aspergillus Niger and Alternaria alternata* at concentration of 30 mg/mL using sabouraud dextrose agar media. The compound (***7c***, ***7j***, ***7m*** and ***6r***) show significant activities and compound (***7a, 7b***, ***7f*** and ***7g***) were found to be moderately active against *Candida albicans and Aspergillus Niger.* All the other compounds did not show significant activity against the fungi at the concentration used.

Tuberculostatic activity

Some new compounds have been tested for antitubercular activity *in vitro* using *Mycobacterium tuberculosis***.** The compounds were incorporated into Lowenstein Jensen egg medium having concentrations of 10 and 100 mg/mL and were inoculated with *Mycobacterium tuberculosis***,** $H_{27,}R_V$ strains, incubated at 37^0C and observed, weekly for the growth of organism for eight weeks. The compound (***7a***, ***7b***, ***7c***, ***7f***, ***7g***, ***7j***, and ***7m***) inhibited the growth of *Mycobacterium tuberculosis* at 100 mg/mL concentration. Other compounds were found to be inactive. Results are assembled in Table 2.

Table 2: Tuberculostatic activity of new pyrazolines

S. No.	Compounds	Growth at conc. [mg/mL]	
		10	**100**
7a.	1-[(2, 3-Dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline	+	0
7b.	1- [(o-Methyl) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline	+	0
7c.	1- [(m-Methyl) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl) -2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline	+	0
7d.	1- [(p-Methyl) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline	+	+
7e.	1- [(o-Chloro) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline	+	+
7f.	1- [(m-Chloro) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline	+	0
7g.	1- [(p-Chloro) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline	+	0
7h.	1- [(o-Methoxy) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline	+	+
7i.	1- [(m-Methoxy) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline	+	0
7j.	1- [(p-Methoxy) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline	+	+
7k.	1- [(p-Fluoro) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline	+	+
7l.	1- [(o-Bromo) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline	+	+
7m.	1- [(o-Ethoxy) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline	+	0

Cont…

S. No.	Compounds	Growth at conc. [mg/mL]	
		10	100
7n.	1- [(m-Ethoxy) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline	+	+
7o.	1- [(p-Ethoxy) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline	+	+
7s.	1- [(m-Bromo) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline	+	+
7t.	1- [(p-Bromo) 2, 3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazoline	+	+

'+' and '0' indicate presence and inhibition of growth, respectively

RESULTS AND DISCUSSION

Newly synthesized 1-[(2,3-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-benzoyl) 2, 3-dichloroanilino)]-5- phenyl pyrazolines have been synthesized by the reaction of N-cinnamoyl-N-2'-cyanoethyl-2,3-dichloroaniline with ethyl-2-[(N-benzoyl) 2,3-dichloroanilido] acetohydrazide. Pyrazolines are yellow, cream and brown color solids, having high melting points. Identity of these products has been established by elemental analysis and spectral data. Newly synthesized compounds (***7a-t***) have been tested for their antibacterial activity against gram positive bacteria *S. albus , S. aureus* and gram negative bacteria *E. coli* and *Pseudomonas poisonous* .The compound (***7a***, ***7b***, ***7c***, ***7f***, ***7g***, ***7j***, ***7m*** and ***7r***) show significant activity and the compound (***7i***, ***7k***, ***7l***, ***7p*** and ***7t***) *have* show moderate activity. These compounds were tested for their antifungal activity against *Candida albicans, Aspergillus niger and Alternaria alternata* at concentration of 30 mg/mL using sabouraud dextrose agar media. The compound (***7c***, ***7j 7m*** and ***7r***) show significant activities and compound (***7a***, ***7b***, ***7f*** and ***7g***) were found to be moderately active against *Candida albicans and Aspergillus Niger.* All the other compounds did not show significant activity against the fungi at the concentration used. These new compounds have been tested for antitubercular activity *in vitro* using *Mycobacterium tuberculosis***.** The compounds were incorporated into Lowenstein Jensen egg medium having concentrations of 10 and 100 mg/mL and were inoculated with *Mycobacterium tuberculosis***,** $H_{27,}$ Rv strains, incubated at 37^0C and observed, the compound (***7a***, ***7b***, ***7c***, ***7f***, ***7g***, ***7j*** and ***7m****)* inhibited the growth of *Mycobacterium tuberculosis* at 100 mg/mL concentration, while other compounds were found to be inactive.

CONCLUSION

Newly synthesized compounds (***7a-t***) have been tested for their antibacterial activity against gram positive bacteria *S. albus, S. aureus* and gram negative bacteria *E. coli* and *Pseudomonas poisonous*. The compound (***7a***, ***7b***, ***7c***, ***7f***, ***7g***, ***7j***, ***7m*** and ***7r***) show significant activity and the compound (***7i, 7k, 7l, 7p*** and ***7t***) have show moderate activity. These compounds were tested for their antifungal activity against *Candida albicans, Aspergillus niger and Alternaria alternata* at concentration of 30 mg/mL using sabouraud dextrose agar media. The compound (***7c***, ***7j***, ***7m*** and ***7r***) show significant activities and compound (***7a, 7b, 7f, and 7g***) were found to be moderately active against *Candida albicans and Aspergillus niger.* All the other compounds did not show significant activity against the fungi at the concentration used. Some new compounds have been tested for antitubercular activity *in vitro* using *Mycobacterium tuberculosis***.** The compounds were incorporated into Lowenstein Jensen egg medium having concentrations of 10 and 100 mg/mL and were inoculated with *Mycobacterium tuberculosis***,** $H_{27,}$ Rv strains, incubated at 37^0C and observed, the compound (**7a**, **7b**, **7c**, **7f**, **7g**, **7j** and **7m**) inhibited the growth of *Mycobacterium tuberculosis* at 100mg/mL concentration, while other compounds were found to be inactive.

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