

Transition metal complexes of novel aryl azopyrazole: Synthesis, characterization and antifungal activities

Bhargav Trivedi, Niraj Shah, Sanjay Patel

Abstract-Reaction between 2,4-dichloro phenyl acid hydrazide with 4-[N'-(1-Ethoxycarbonyl-2-oxo-propylidene)-hydrazino]-2-hydroxy-benzoic acid in ethanol furnishes 1-[2,4-dichloro-benzoyl]-3-methyl-4-(4-carboxy-3-hydroxy-phen-4-yl-hydrazono)-2-pyrazoline-5-ones (dCIH-ASA). The transition metal complexes of Cu^{2+} , Co^{2+} , Ni^{2+} , Mn^{2+} and Zn^{2+} of dCIH-ASA have been prepared and characterized by elemental analyses, spectral studies, magnetic moment determination, molar conductivity measurement and microbicidal activity.

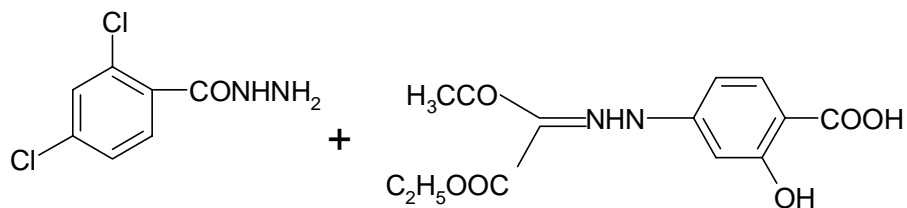
Keywords-2,4-dichloro phenyl acid hydrazide, 4-[N'-(1-Ethoxycarbonyl-2-oxo-propylidene)-hydrazino]-2-hydroxy-benzoic acid, metal chelates, spectral studies, magnetic moment and antifungal activity.

1 INTRODUCTION

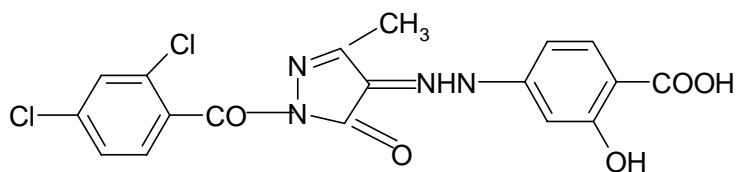
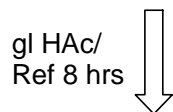
Hydrazides have been demonstrated to possess, among others, antimicrobial, anticonvulsant, analgesic, antiinflammatory, antiplatelet, antitubercular and antitumoral activities. Hydrazones are associated with diverse pharmaceutical activities such as antitubercular¹⁻⁸, antibacterial, and antiactinomycotic. Also possess antidepressant, antiseptic, antimalarial⁹ Antimycobacteria¹⁹ effect, antibacterial¹, insecticidal², fungicidal³,

antimicrobial⁴, asvitronectial receptes, antagonist⁵, anthelmintic⁶⁻⁸, anti-inflamatory⁹, etc activity. Such hydrazide can be derivatized in to azopyrazole compounds. These azopyrazole derivatives have received significant importance because of their biological activity¹⁻⁹. The area in which the azopyrazol salicylic acid molecule has not been developed, the present paper comprises the study of azopyrazol-salicylic acid combined molecule. The research work is shown in the following scheme.

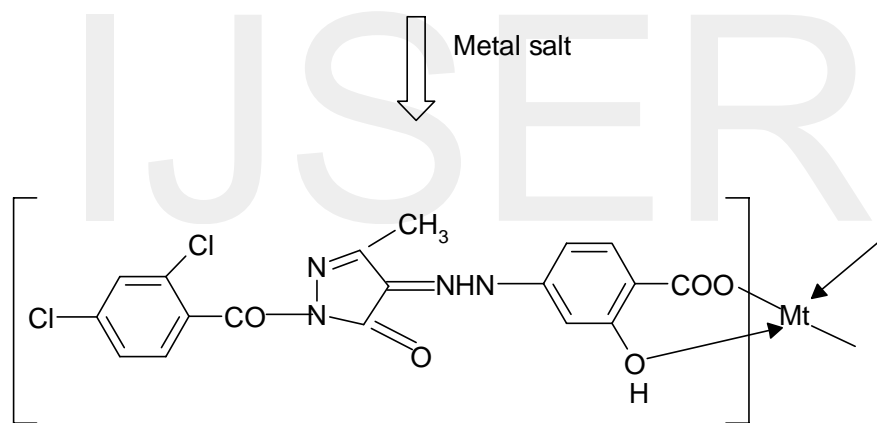
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2, 4-dichloro phenyl acid hydrazide 4-[N'-(1-Ethoxycarbonyl-2-oxo-propylidene)-hydrazino]-2-hydroxy-benzoic acid



1-[2,4-dichloro benzoyl]-3-methyl-4-(4-carboxy-3-hydroxy-phen-4-yl-hydrazono)-2-pyrazoline-5-ones (dCIH-ASA)



(dCIH-ASA)-Metal chelates

Where Mt: Cu^{+2} , Ni^{+2} , Zn^{+2} , Mn^{+2} , Co^{+2}

2 Materials and methods

2.1 Materials

2,4-dichloro phenyl acid hydrazide was prepared by method reported in literature^{10, 13}. 4-[N'-(1-Ethoxycarbonyl-2-oxo-propylidene)-hydrazino]-2-hydroxy-benzoic acid was prepared by reported method¹¹⁻¹⁴. All other chemicals used were of analytical grade.

2.2 Formation dCIH-ASA

A mixture of 2,4-dichloro phenyl acid hydrazide (dCIH) (0.002 mole) and 4-[N'-(1-Ethoxycarbonyl-2-oxo-propylidene)-hydrazino]-2-hydroxy-benzoic acid (ASA) (0.002 mole) in glacial acetic acid (25 ml) was heated under reflux for 8hrs. Subsequently glacial acetic acid was distilled off and the lump mass was crystallized from methanol. The solid designated as dCIH-ASA was isolated and dried in air. Yield was 64%. Its melting point was 220 - 222° C (uncorrected).

3 Elemental Analysis: C₁₈H₁₂N₄O₅Cl₂ (435)

	C%	H%	N%	Cl%
Calculated:	49.65	2.75	12.87	16.32
Found :	49.50	2.70	12.80	16.20

Acid Value:

Theoretical: 128.7 mg KOH/1g. sample.

Found: 126.5 mg KOH/1g sample.

IR Features

1630 cm ⁻¹	C=N of pyrazolone
3028, 1597, 1624 cm ⁻¹	Aromatic.
1498, 1028	
1693 cm ⁻¹	CO of COOH
1727 cm ⁻¹	CO
3548-2677 cm ⁻¹	OH
2951, 1373 cm ⁻¹	CH ₃
644 cm ⁻¹	Ar-Cl

NMR (DMSO)

δ ppm

7.1 – 7.6 (7H)	Multiplet	Aromatic
4.63 (3H)	Singlet	CH ₃
12.9 (1H)	Singlet	(COOH)
5.0 (1H)	Singlet	(OH)
2.8 (1H)	Singlet	(NH)

4 Synthesis of metal Chelates of dCIH-ASA :

The Cu²⁺, Co²⁺, Ni²⁺, Mn²⁺, and Zn²⁺ metal ion chelates of dCIH-ASA have been prepared in a similar manner. The procedure is as follow.

To a solution of dCIH-ASA (43.5g or 0.1 mole) in ethanol-acetone (1:1v/v) mixture (150 ml), 0.1N KOH solution was

added drop wise with stirring. The pasty precipitates were obtained at neutral pH. These were dissolved by addition of water to make a clear solution. It was diluted to 250 ml. by water and was known as stock solution. 25 ml of the stock solution (which contains 0.01 mole dCIH-ASA) was added drop wise to the solution of metal salt (0.005 mole metal ion) in water at room temperature. Sodium acetate or ammonia was added up to completion of the precipitation. The precipitates were digested on water bath at 80° C for 2hrs and were filtered, washed with water and finally air dried. It was amorphous powder. Yield was almost quantitative. The details are given in Table-1.

5 Measurements

The elemental analysis for C, H and N were carried out on elemental analyzer TF-EA.1101 (Italy). IR spectra of dCIH-ASA and its metal complexes were scanned on a Nicolet 760 FTIR spectrophotometer in KBr. The NMR spectrum of dCIH-ASA was scanned on Bruker NMR spectrophotometer using DMSO solvent. The metal content of the metal chelate were performed by decomposing a weighed amount of each metal complexes followed by EDTA titration as reported in literature¹⁴. Magnetic susceptibility measurement of all the metal complexes were carried out at room temperature by the Gouy method. Mercury tetrathiocyanatocobalate (II), Hg[Co(NCS)₄], was used as a calibrant. The diffused reflectance spectra of solid metal complex were recorded on a Backman DK Spectrophotometer with a solid reflectance attachment, MgO was employed as the reflectance compound. The electrical conductivity of all the complexes was measure in acetonitrile at 10⁻³ M concentration. All these analysis are given in Table-2.

6 Antifungal activity

The fungicidal activity of all the compounds was studied at 1000 ppm concentration in vitro plant pathogenic organisms listed in Table-3. The antifungal activities of all the samples were measured by cup plate method¹⁵. Each of the plant pathogenic strains on potato dextrose agar (PDA) medium. Such a PDA medium contained potato 200 gms, dextrose 20gms, agar 20gms and water 1 liter. 5 days old cultures were employed. The compounds to be tested were suspended (1000ppm) in a PDA medium and autoclaved at 120° C for 15 min. at 15 atmospheric pressure. These medium were poured into sterile Petri plate and the organisms were inoculated after cooling the Petri plate. The percentage inhabitation for fungi was calculated after 5 days using the formula given below:

$$\text{Percentage of inhibition} = \frac{100(x - y)}{x}$$

Where X= Area of colony in control plate, Y= Area of colony in test plate. The fungicidal activity of all compounds are shown in Table-3

7 Results and Discussion

The parent ligand dCIH-ASA was an amorphous brown powder, soluble in various solvents like dioxane, DMSO and DMF. The results of elemental analysis of the ligand are reported in experimental part. They are consistent with the predicted structure as shown in Scheme earlier.

Examination of IR spectrum (not shown) of dCIH-ASA reveals that broad band of phenolic hydroxyl stretching is observed at 3200-3600 cm^{-1} as well as additional absorption bands at 3028, 1597 and 1624 cm^{-1} are characteristics of the salicylic acid^{18, 19}. The NMR data (shown in experimental part) also confirm the structure of dCIH-ASA.

The Metal chelate of dCIH-ASA with ions Cu^{2+} , Co^{2+} , Ni^{2+} , Mn^{2+} , Zn^{2+} , vary in colors. On the basis of the proposed structure as shown in Scheme, the molecular formula of the dCIH-ASA ligand is $\text{C}_{18}\text{H}_{12}\text{N}_4\text{O}_5\text{Cl}_2$. This upon complexation, coordinates with one central metal atom at four coordination sites and with two water molecules. Therefore the general molecular formula of the resulting metal chelate is $[\text{C}_{18}\text{H}_{11}\text{O}_5\text{N}_4\text{Cl}_2]2\text{M}.2\text{H}_2\text{O}$ for divalent metal ions. This has been confirmed by results of elemental analysis reported in Table-1. The data are in agreement with the calculated values.

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Table-1. Analytical Data of the Metal Chelates of HL (i.e. dClH-ASA)

Metal Chelates	Molecular formula	M.Wt Gm/mole	Yield %	% Metal analysis		Elemental analysis							
						%C		%H		%N		%Cl	
				Cald.	Found	Cald.	Found	Cald.	Found	Cald.	Found	Cald.	Found
HL(dCl-ASA)	$C_{18}H_{12}N_4O_5Cl_2$	435	64	--	--	49.65	49.50	2.75	2.70	12.87	12.80	16.32	16.2
(L) ₂ Cu ⁺²	$C_{36}H_{22}N_8O_{10}Cl_4Cu^{+2}.2H_2O$	967.5	77	6.6	6.6	44.6	44.5	2.3	2.2	11.6	11.6	14.6	14.6
(L) ₂ Ni ⁺²	$C_{36}H_{22}N_8O_{10}Cl_4Ni^{+2}.2H_2O$	963	80	6.1	6.0	44.9	44.8	2.3	2.3	11.6	11.5	14.7	14.6
(L) ₂ Mn ⁺²	$C_{36}H_{22}N_8O_{10}Cl_4Mn^{+2}.2H_2O$	959	77	5.7	5.7	45.0	45.0	2.3	2.2	11.6	11.5	14.8	14.7
(L) ₂ Co ⁺²	$C_{36}H_{22}N_8O_{10}Cl_4Co^{+2}.2H_2O$	963	78	6.1	6.0	44.9	44.8	2.3	2.2	11.6	11.5	14.7	14.7
(L) ₂ Zn ⁺²	$C_{36}H_{22}N_8O_{10}Cl_4Zn^{+2}.2H_2O$	969	83	6.7	6.6	44.6	44.5	2.2	2.2	11.5	11.4	14.6	14.6

Inspection of the IR Spectra (not shown) of metal chelates reveals that all the spectra are identical in all respects. The comparison of IR spectrum of the parent ligand dCIH-ASA with that of its each metal chelates has revealed certain characteristics differences.

One of the significant differences to be expected between the IR spectrum of the parent ligand and its metal chelates is the presence of more broadened bands in the region of 3200-3600 cm^{-1} for the metal chelates as the oxygen of the O-H group of the ligands forms a coordination bond with the metal ions¹⁶⁻¹⁸. Another noticeable difference is the band due to the COO⁻ anion at 1600 cm^{-1} in the IR spectrum of the each metal chelates. The band at 1400 cm^{-1} in the IR

Spectrum of dCIH-ASA assigned to in-plane OH absorption¹⁶⁻¹⁸ is shifted towards higher frequency in the spectra is confirmed by a weak band at 1105 cm^{-1} corresponding to C-O-M stretching¹⁶⁻¹⁸. Thus all of these characteristics features of the IR studies supported the structure of the metal chelates as shown in the scheme.

Examination of data of the metal content in each compound revealed a 1:2 metal: ligand (M: L) stoichiometry in all of the chelate of divalent metal ions.

Magnetic moment (μ_{eff}) of each of the metal chelates is given in Table-2. Examination of these data reveals that all chelates other than that of Zn^{2+} are para magnetic while those of Zn^{2+} are diamagnetic.

Table -2 Magnetic Moment and Reflectance Spectral data of Metal Chelates of dCIH –ASA ligand

Metal chelate	Magnetic Moment μ_{eff} (B.M.)	Molar Conductivity $\Omega\text{m ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$	Absorption band (cm^{-1})	Transitions
$(\text{L})_2 \text{Cu}^{2+}$	1.98	7.98	24387 15620	CT ${}^2\text{B}_{1g} \rightarrow {}^2\text{A}_{1g}$
$(\text{L})_2 \text{Ni}^{2+}$	3.37	8.20	22196 14114	${}^3\text{A}_{2g} \rightarrow {}^3\text{T}_{1g}(\text{P})$ ${}^3\text{A}_{2g} \rightarrow {}^3\text{T}_{1g}(\text{F})$
$(\text{L})_2 \text{Co}^{2+}$	5.14	29.10	24126 19712 8661	${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{2g}(\text{P})$ ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{A}_{2g}$ ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{2g}(\text{F})$
$(\text{L})_2 \text{Mn}^{2+}$	5.93	9.10	23816 17794 15894	$6\text{A}_{1g} \rightarrow {}^4\text{A}_{1g}(4\text{E}_g)$ $6\text{A}_{1g} \rightarrow {}^4\text{T}_{2g}(4\text{G})$ $6\text{A}_{1g} \rightarrow {}^4\text{T}_{1g}(4\text{G})$
$(\text{L})_2 \text{Zn}^{2+}$	D(*)	10.02	--	--

Zn^{2+} Diamagnetic in Nature.

Table 3. Antifungal Activity of Ligand dCIH-ASA and its metal chelates.

Sample	Zone of inhibition at 1000 ppm (%)				
	PE	BT	N	T	A
dCI-ASA	65	52	48	45	55
$(\text{L})_2 \text{Cu}^{2+}$	70	67	75	79	73
$(\text{L})_2 \text{Mn}^{2+}$	48	45	59	57	45
$(\text{L})_2 \text{Co}^{2+}$	60	61	68	65	68
$(\text{L})_2 \text{Zn}^{2+}$	65	62	70	75	72

(L) ₂ Ni ⁺²	59	54	61	58	65
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PE= Penicillium expansum; BT= Botrydepladia thiobromine;
N=Nigras Pora sp.; T= Trichothesium sp.; A=A. Niger

The diffused electronic spectrum of the [Cu(dCIH-ASA)₂(H₂O)₂] metal complex shows broad band at 15620 and 24387 cm⁻¹ due to the ²B_{1g} → ²A_{1g} transition and charge transfer respectively, suggesting a distorted octahedral structure^{19,21} for the [Cu(dCIH-ASA)₂(H₂O)₂] complex. Which is further confirmed by the higher value of μ_{eff} of the [Cu(dCIH-ASA)₂(H₂O)₂] complex. The [Ni(dCIH-ASA)₂(H₂O)₂] complex gave two absorption bands respectively at 22196 and 14114 corresponding to ³A_{2g} → ³T_{1g} (P) and ³A_{2g} → ³T_{1g} (F) transitions. Thus diffused absorption bands in the reflectance spectra and the value of the magnetic moments μ_{eff} indicate an octahedral configuration for the [Ni(dCIH-ASA)₂(H₂O)₂] complex. The spectra of [Mn(dCIH-ASA)₂(H₂O)₂] shows weak bands at 23816, 17794, and 15894 cm⁻¹ which are assigned to the transitions ⁶A_{1g} → ⁴A_{1g} (4E_g), ⁶A_{1g} → ⁴T_{2g} (4G) and ⁶A_{1g} → ⁴T_{1g} (4G), respectively. They also suggest an octahedral structure for the [Mn(dCIH-ASA)₂(H₂O)₂] chelate. The spectrum comprised the band ground at 19043cm⁻¹ and other weak band ground at 23096 cm⁻¹. The latter has not very long tail. These may have the transition ⁶A_{1g} → ⁴T_{2g} (4G) and ⁶A_{1g} → ⁴T_{1g} (4G). The high intensities of the bands suggests that there might be a charge transfer in origin. μ_{eff} is found to be lower than normal range. As the spectrum of the [Zn(dCIH-ASA)₂(H₂O)₂] is not well resolved, it is not interpreted but its μ_{eff} value shows that it is diamagnetic as expected.

Conductivities of all the complexes were measured in acetonitrile solvent and all the complexes were found to be electrolytic²² in nature of 1:2 type and molar conductivity values are in the range of 8.2-29.10 Ohm⁻¹ Cm⁻¹.

The antifungal activity of all the compounds measured for various plant pathogens. Inspection of the result shown in Table-3 indicates that all compounds exhibit good toxicity for fungi. Out of all the compounds, copper chelates are more toxic than others. These compounds almost inhibit the fungi about 75%. Hence produced metal chelates can be employed as garden fungicides. Further work in this direction is in progress.

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