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TRANSITION METAL COMPLEXES OF ARYL AZOPYARAZOLE: SYNTHESIS, CHARACTERIZATION AND MICROBICIDAL ACTIVITIES

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

INTRODUCTION

Hydrazides have been demonstrated to possess, among others, antimicrobial, anticonvulsant, analgesic, anti-inflammatory, ant platelet, antitubercular and antitumor activities. Hydrazones are associated with diverse pharmaceutical activities such as antitubercular[1-8], antibacterial, and antiactinomycotic. Also possess antidepressant, antiseptic, antimalarial[9] Antimycobacteria[13] effect, antibacterial[1], insecticidal[2], fungicidal[3], antimicrobial[4], asvitronectial receptes, antagonist[5], anthelmintic [6-8], anti-inflamonatary[9], etc activity. Such hydrazide can be derivatized in to azopyrazole compounds. These azopyrazole derivatives have received significant importance because of their biological activity.[1-9] 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.

EXPERIMENTAL

Materials and methods

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

Formation NtH-ASA

A mixture of 4-nitro phenyl acid hydrazide (NtH) (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 NtH-ASA was isolated and dried in air. Yield was 57%. Its melting point was 207-210° C. (uncorrected).

Synthesis of metal chelates of NtH-ASA

The Cu^{2+},Co^{2+}, Ni^{2+}, Mn^{2+} and Zn^{2+} metal ion chelates of NtH-ASA have been prepared in a similar manner. The procedure is as follow-

To a solution of NtH-ASA (41.1 g 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 NtH-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 2h 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.

Elemental Analysis	C%	H%	N%
$C_{18}H_{13}N_5O_7$ (Mol. Wt. = 411)			
Calculated	52.55	3.26	17.03
Found	52.40	3.00	17.00
Acid Value			
Theoretical	136.3 mg KOH/1g. sample.		
Found	134.0 mg KOH/1g sample.		
IR Features	1630 cm^{-1}	C=N of pyrazolone	
	1597, 1498, 3028, 1612, 1030 cm^{-1}	Aromatic.	
	1694 cm^{-1}	CO of COOH	
	1720 cm^{-1}	CO	
	3200-3600 cm^{-1}	OH	
	2950, 1370, 2677 cm^{-1}	CH_3	
	1515-1560 cm^{-1}	Ar-NO_3	
NMR	7.1 – 7.64 (7H)	Multiplet	Aromatic
δ ppm (DMSO)	4.73 (3H)	Singlet	CH_3
	12.92 (1H)	Singlet	(COOH)
	5.1 (1H)	Singlet	(OH)
	2.8 (1H)	Singlet	(NH)

Measurements

The elemental analysis for C, H and N were carried out on elemental analyzer TF-EA.1101 (Italy). IR spectra of NtH-ASA and its metal complexes were scanned on a Nicolet 760 FTIR spectrophotometer in KBr. The NMR spectrum of NtH-ASA was scanned on Brucker 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 literature [14]. Magnetic susceptibility measurement of all the metal complexes was carried out at room temperature by the Gouy method. Mercury tetrathiocynatocobalate (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.

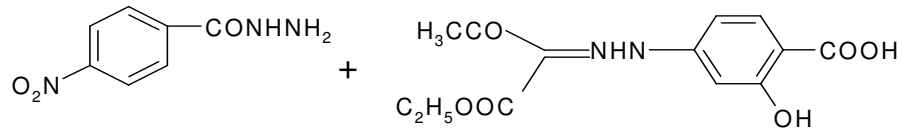
Antifungal activity

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 method [15]. 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:

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

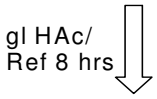
Where X= Area of colony in control plate, Y= Area of colony in test plate.

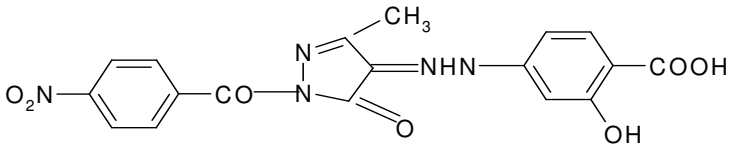
The fungicidal activity of all compounds is shown in Table-3.



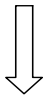
4-nitro phenyl acid hydrazide

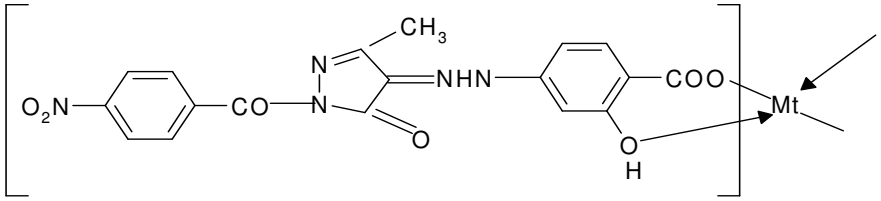
4-[N'-(1-Ethoxycarbonyl-2-oxo-propylidene)-hydrazino] -2-hydroxy-benzoic acid





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





(NtH-ASA)-Metal chelates

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

Scheme-1

RESULTS AND DISCUSSION

The parent ligand NtH-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 NtH-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 1612

are characteristics of the salicylic acid [12, 13]. The NMR data (shown in experimental part) also confirm the structure of NtH-ASA.

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

Metal Chelates	Molecular formula	M.Wt Gm/ mole	Yield %	% Metal analysis		Elemental Analysis					
						%C		%H		%N	
				Cald.	Found	Cald.	Found	Cald.	Found	Cald.	Found
HL (NtH-ASA)	$C_{18}H_{13}N_5O_7$	411	57	-	-	52.55	52.54	3.26	3.0	17.03	17.0
$(L)_2\ Cu^{+2}$	$C_{36}H_{24}N_{10}O_{14}Cu^{+2}.2H_2O$	919.5	67	6.91	6.8	47.03	47.0	2.62	2.5	15.21	15.2
$(L)_2\ Ni^{+2}$	$C_{36}H_{24}N_{10}O_{14}Ni^{+2}.2H_2O$	915	67	6.42	6.4	47.22	47.0	2.61	2.5	15.33	15.2
$(L)_2\ Mn^{+2}$	$C_{36}H_{24}N_{10}O_{14}Mn^{+2}.2H_2O$	911	65	6.05	6.0	47.44	47.3	2.64	2.6	15.43	15.4
$(L)_2\ Co^{+2}$	$C_{36}H_{24}N_{10}O_{14}Co^{+2}.2H_2O$	915	71	6.43	6.4	47.25	47.2	2.61	2.6	15.31	15.2
$(L)_2\ Zn^{+2}$	$C_{36}H_{24}N_{10}O_{14}Zn^{+2}.2H_2O$	921	72	7.03	7.0	46.92	46.7	2.60	2.5	15.20	15.2

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

Metal chelate	Magnetic Moment μ_{eff} (B.M.)	Molar Conductivity $\Omega m\ ohm^{-1}\ cm^2\ mol^{-1}$	Absorption band (cm^{-1})	Transitions
$(L)_2\ Mn^{+2}$	5.2-6.0	6.72	23787 18411 16723	6 A1g→ $^4A_{1g}$ ($4E_g$) 6 A1g→ ^4T2g(4G) 6 A1g→ ^4T_1g(4G)
$(L)_2\ Co^{+2}$	4.4-5.2	28.10	24932 19883 2423	^{4} T1g(F)→ $^4T_{2g}$ (P) ^{4} T1g(F) → $^4A_{2g}$ ^{4} T1g(F) →$^4T_{2g}$ (F)
$(L)_2\ Ni^{+2}$	2.9-3.4	9.10	22317 15712	$^3A_{2g} \rightarrow {}^3T_{1g}$ (P) $^3A_{2g} \rightarrow {}^3T_{1g}$ (F)
$(L)_2\ Cu^{+2}$	1.7-2.2	4.12	24615 14972	CT $^2B_{1g} \rightarrow {}^2A_{1g}$
$(L)_2\ Zn^{+2}$	D(*)	9.12	--	--

D(*) (Zn^{2+} Diamagnetic in Nature.)

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

Sample	Zone of inhibition at 1000 ppm (%)				
	PE	*BT*	*N*	*T*	*A*
NtH-ASA	55	52	61	49	50
$(L)_2\ Cu^{+2}$	75	75	71	80	77
$(L)_2\ Mn^{+2}$	55	45	46	46	49
$(L)_2\ Co^{+2}$	63	58	63	81	61
$(L)_2\ Zn^{+2}$	72	73	58	75	71
$(L)_2\ Ni^{+2}$	61	49	50	63	56

PE= *Penicillium expansum*; BT= *Botrydepladia thiobromine*;
N=*Nigras Pora sp.*; T= *Trichothesium sp.*; *A=A. Niger*

The Metal chelate of NtH-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 the scheme, the molecular formula of the NtH-ASA ligand is $C_{18}H_{13}N_5O_7$. 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 $C_{36}H_{24}N_{10}O_{14}$. $M.2H_2O$ 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.

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 NtH-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 ions[16-18]. 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 NtH-ASA assigned to in-plane OH absorption[16-18] is shifted towards higher frequency in the spectra is confirmed by a week band at 1105 cm^{-1} corresponding to C-O-M stretching[16-18]. Thus all of these characteristics features of the IR studies supported the structure of the metal chelates as shown in scheme-1.

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.

The diffuse electronic spectrum of the $[Cu(NtH\text{-}ASA)_2(H_2O)_2]$ metal complex shows broad bands at 14972 and 24615 cm^{-1} due to the $^2B_{1g} \rightarrow {}^2A_{1g}$transition and charge transfer respectively, suggesting a distorted octahedral structure [19-21] for the $[Cu(NtH\text{-}ASA)_2(H_2O)_2]$ complex. Which is further confirmed by the higher value of μ_{eff} of the $[Cu\ (NtH\text{-}ASA)_2(H_2O)_2]$ complex. The $[Ni\ (NtH\text{-}ASA)_2(H_2O)_2]$ complex gave two absorption bands respectively at 22317 and 15712 corresponding to $^3A_{2g} \rightarrow {}^3T_{1g}$ (P) and $^3A_{2g} \rightarrow {}^3T_{1g}$ (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 $[Ni(NtH\text{-}ASA)_2(H_2O)_2]$ complex. The spectra of $[Mn(NtH\text{-}ASA)_2(H_2O)_2]$ shows weak bands at 23787, 18411, and 16723 cm^{-1} which are assigned to the transitions $^6A1g \rightarrow {}^4A_{1g}$ ($4E_g$),
$^6A1g \rightarrow {}^4T2g(4G)$ and $^6A1g \rightarrow {}^4T_1g(4G)$, respectively. They also suggest an octahedral structure for the $[Mn\ (NtH\text{-}ASA)_2(H_2O)_2]$ chelate. The spectrum comprised the band ground at 19053cm^{-1} and other weak band ground at 23001 cm^{-1}. The latter has not very long tail. These may have the transition $^6A_{1g} \rightarrow {}^4T_{2g}$ (4G) and $^6A_1 \rightarrow {}^4T_1$ (4G). The high intensities of the bands suggest that there might be a charge transfer in origin. μ_{eff} is found to be lower than normal range. As the spectrum of the $[Zn(NtH\text{-}ASA)_2(H_2O)_2]$ 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 electrolytic [22] in nature of 1:2 type and molar conductivity values are in the range of 4.12-28.10 $Ohm^{-1}\ Cm^{-1}$.

The antifungal activities of all the compounds measured for various plant pathogens. Inspection of the result shown in Table-3 indicates that all compounds exhibits good toxicity for fungi. Out of all the compounds, copper chelates are more toxic than other. These compounds almost inhibit the fungi about 80%.

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