



Synthesis, characterization and chelating properties of novel ligands

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ABSTRACT

Reaction between 4-bromo phenyl acid hydrazide with 4-[N'-(1-Ethoxycarbonyl-2-oxo-propylidene)-hydrazino]-2-hydroxy-benzoic acid in ethanol furnishes 1-[4-bromo-benzoyl]-3-methyl-4-(4-carboxy-3-hydroxy-phen-4-yl-hydrazono)-2-pyrazoline-5-ones (BrH-ASA). The transition metal complexes of Cu²⁺, Co²⁺, Ni²⁺, Mn²⁺ and Zn²⁺ of BrH-ASA have been prepared and characterized by elemental analyses, spectral studies, magnetic moment determination, molar conductivity measurement and microbicidal activity.

Keywords: 4-bromo phenyl acid hydrazide, 4-[N'-(1-Ethoxy carbonyl-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 other, antimicrobial, anticonvulsant, analgesic, antiinflammatory, antiplatelet, antitubercular and antitumoral activities. Hydrazones are associated with variety of pharmaceutical activities such as antitubercular¹⁻⁸, antibacterial, and antiactinomycotic. They also possess antidepressant, antiseptic, antimalarial⁹ Antimycobacteria¹⁹ effect, antibacterial¹, insecticidal², fungicidal³, antimicrobial⁴, asvitronectal receptes, antagonist⁵, anthelmintic⁶⁻⁸, anti-inflamontary⁹, etc activity. Such hydrazide can be derivatized in to azopyrazole compounds. These azopyrazole derivatives have received significant importance because of their biological activity.¹¹⁻⁹¹. 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 scheme-I.

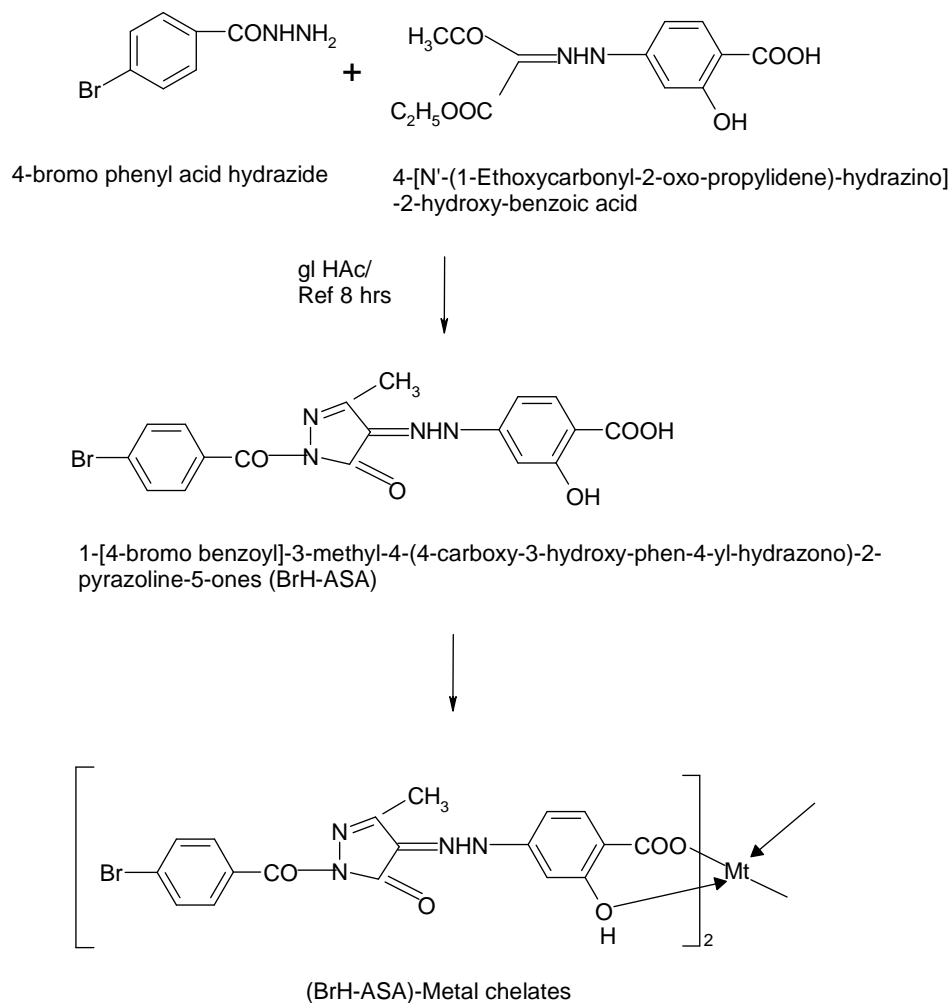
MATERIALS AND METHODS

Materials

4-bromo phenyl acid hydrazide was prepared by method reported in literature¹⁹. 4-[N'-(1-Ethoxycarbonyl-2-oxo-propylidene)-hydrazino]-2-hydroxy-benzoic acid was prepared by reported method²⁰. All other chemicals used were of analytical grade.

Formation BrH-ASA

A mixture of 4-bromo phenyl acid hydrazide (BrH) (0.02 mole) and 4-[N'-(1-Ethoxycarbonyl-2-oxo-propylidene)-hydrazino]-2-hydroxy-benzoic acid (ASA) (0.02 mole) in glacial acetic acid (70 ml) was heated under reflux for 8hrs. Subsequently glacial acetic acid was distilled off and the lump mass was obtained. It was triturated with petroleum ether (40-60° C). The solid designated as BrH-ASA was isolated and dried in air. Yield was 67%. Its melting point was 205-7° C (uncorrected).



Where Mt: Cu⁺², Ni⁺², Zn⁺², Mn⁺², Co⁺²

Scheme-I

Elemental Analysis: C₁₈H₁₃N₄O₅Br (445):

	C%	H%	N%	Br%
Calculated:	48.55	2.92	12.58	17.95
Found :	48.40	2.80	12.50	17.40

Acid Value Theoretical : 125.8 mg KOH/1g. sample
 Found : 123.7 mg KOH/1g sample

IR Features	Wavenumber (cm ⁻¹)	Assignment
	1618 cm ⁻¹	C=N of pyrazolone
	3028, 1598, 1614 cm ⁻¹	Aromatic
	1695 cm ⁻¹	CO of COOH
	1725 cm ⁻¹	CO
	3548-2675 cm ⁻¹	OH
	2952, 1370 cm ⁻¹	CH ₃
	640 cm ⁻¹	Ar-Br

NMR (DMSO)	δ ppm	Multiplicity	Assignment
	7.1 – 7.52 (7H)	Multiplet	Aromatic
	4.73 (3H)	Singlet	CH ₃
	12.85 (1H)	Singlet	(COOH)
	5.1 (1H)	Singlet	(OH)
	2.8 (1H)	Singlet	(NH)

Synthesis of metal chelates of BrH-ASA

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

To a solution of BrH-ASA (44.5 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 BrH-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.

Measurements

The elemental analysis for C, H and N were carried out on elemental analyzer TF-EA 1101 (Italy). The halogen content was determined using Carius method. IR spectra of BrH-ASA and its metal complexes were scanned on a Nicolet 760 FTIR spectrophotometer in KBr. The NMR spectrum of BrH-ASA was scanned on Bruker NMR spectrophotometer using DMSO solvent. The metal content of the metal chelates were performed by decomposing a weighed amount of each metal complexes followed by EDTA titration as reported in literature²⁰. Magnetic susceptibility measurements 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.

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 method²¹. 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

RESULTS AND DISCUSSION

The parent ligand BrH-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 above.

Examination of IR spectrum (not shown) of BrH-ASA reveals that broad band of phenolic hydroxyl stretching is observed at 3548-2675 cm⁻¹ as well as additional absorption bands at 3028, 1598 and 1614 are characteristics of the salicylic acid^{18, 19}. Aromatic halogen is revealed at 640 cm⁻¹. The NMR data (shown in experimental part) also confirm the structure of BrH-ASA.

The Metal chelate of BrH-ASA with ions Cu²⁺, Co²⁺, Ni²⁺, Mn²⁺ and Zn²⁺, vary in colors. On the basis of the proposed structure as shown in the scheme, the molecular formula of the BrH-ASA ligand is C₁₈H₁₃N₄O₅Br. 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 [C₁₈H₁₂O₅N₄Br]₂M.2H₂O 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.

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

Compound	Empirical Formula	Mol. Cal. Gm/mol	Yield (%)	Elemental Analysis							
				C%		H%		N%		M%	
				Cal	Found	Cal	Found	Cal	Found	Cal	Found
HL (BrH-ASA)	C ₁₈ H ₁₃ N ₄ O ₅ Br	445	67	48.55	48.4	2.92	2.8	12.58	12.50	17.95 (%Br)	17.4 (%Br)
(L) ₂ Cu ²⁺	C ₃₆ H ₂₄ N ₈ O ₁₀ Br ₂ Cu ²⁺ ·2H ₂ O	987.5	68	43.72	43.60	2.41	2.30	11.32	11.20	6.42	6.4
(L) ₂ Co ²⁺	C ₃₆ H ₂₄ N ₈ O ₁₀ Br ₂ Co ²⁺ ·2H ₂ O	983	73	43.92	43.70	2.43	2.40	11.43	11.30	6.02	6.0
(L) ₂ Ni ²⁺	C ₃₆ H ₂₄ N ₈ O ₁₀ Br ₂ Ni ²⁺ ·2H ₂ O	983	67	43.93	43.80	2.42	2.40	11.41	11.30	6.03	6.0
(L) ₂ Mn ²⁺	C ₃₆ H ₂₄ N ₈ O ₁₀ Br ₂ Mn ²⁺ ·H ₂ O	979	74	44.11	44.00	2.41	2.40	11.42	11.30	5.64	5.50
(L) ₂ Zn ²⁺	C ₃₆ H ₂₄ N ₈ O ₁₀ Br ₂ Zn ²⁺ ·2H ₂ O	989	80	43.71	43.60	2.41	2.40	11.32	11.30	6.62	6.60

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 BrH-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 ions²²⁻²⁴. 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 BrH-ASA assigned to in-plane OH absorption²²⁻²⁴ is shifted towards higher frequency in the spectra is confirmed by a weak band at 1105 cm⁻¹ corresponding to C-O-M stretching²²⁻²⁴. 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 Zn²⁺ are paramagnetic while that of Zn²⁺ is diamagnetic.

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

Metal chelate	Magnetic Moment μ_{eff} (B.M.)	Molar Conductivity $\text{ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$	Absorption band (cm ⁻¹)	Transitions
(L) ₂ Cu ²⁺	2.16	7.10	23365 15650	CT ² B _{1g} → ² A _{1g}
(L) ₂ Ni ²⁺	3.38	9.20	22491 13117	³ A _{2g} → ³ T _{1g} (P) ³ A _{2g} → ³ T _{1g} (F)
(L) ₂ Co ²⁺	5.10	23.68	22984 17194 8876	⁴ T _{1g} (F) → ⁴ T _{2g} (P) ⁴ T _{1g} (F) → ⁴ A _{2g} ⁴ T _{1g} (F) → ⁴ T _{2g} (F)
(L) ₂ Mn ²⁺	5.94	5.97	23408 18576 16122	6 A _{1g} → ⁴ A _{1g} (4E _g) 6 A _{1g} → ⁴ T _{2g} (4G) 6 A _{1g} → ⁴ T _{1g} (4G)

Zn²⁺ diamagnetic in Nature.

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

Sample	Zone of inhibition of fungus at 1000ppm (%)				
	PE	BT	N	T	A
BrH-ASA	53	52	46	52	49
(L) ₂ -Cu ²⁺	85	86	75	73	81
(L) ₂ -Co ²⁺	69	61	71	59	56
(L) ₂ -Ni ²⁺	63	53	69	50	50
(L) ₂ -Mn ²⁺	46	49	63	49	47
(L) ₂ -Zn ²⁺	71	75	73	60	71

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

The diffuse electronic spectrum of the [Cu(BrH-ASA)₂(H₂O)₂] metal complex shows broad bands at 15764 and 24504 cm⁻¹ due to the ²B_{1g} → ²A_{1g} transition and charge transfer respectively, suggesting a distorted octahedral structure²⁵⁻²⁷ for the [Cu(BrH-ASA)₂(H₂O)₂] complex. Which is further confirmed by the higher value of μ_{eff} of the [Cu(BrH-ASA)₂(H₂O)₂] complex. The [Ni(BrH-ASA)₂(H₂O)₂] complex gave two absorption bands respectively at 22491 and 13117 corresponding to ³A_{2g} → ³T_{1g} (P) and ³A_{2g} → ³T_{1g} (F) transitions. Thus diffused absorption bands

in the reflectance spectra and the values of the magnetic moments μ_{eff} indicate an octahedral configuration for the $[\text{Ni}(\text{BrH-ASA})_2(\text{H}_2\text{O})_2]$ complex. The spectra of $[\text{Mn}(\text{BrH-ASA})_2(\text{H}_2\text{O})_2]$ shows weak bands at 23408, 18576, and 16122 cm^{-1} which are assigned to the transitions ${}^6\text{A}_{1\text{g}} \rightarrow {}^4\text{A}_{1\text{g}} (4\text{E}_{\text{g}})$,

${}^6\text{A}_{1\text{g}} \rightarrow {}^4\text{T}_{2\text{g}}(4\text{G})$ and ${}^6\text{A}_{1\text{g}} \rightarrow {}^4\text{T}_{1\text{g}}(4\text{G})$, respectively. They also suggest an octahedral structure for the $[\text{Mn}(\text{BrH-ASA})_2(\text{H}_2\text{O})_2]$ chelate. The spectrum comprised the band ground at 19012 cm^{-1} and other weak band ground at 23001 cm^{-1} . The latter has not very long tail. These may have the transition ${}^6\text{A}_{1\text{g}} \rightarrow {}^4\text{T}_{2\text{g}}(4\text{G})$ and ${}^6\text{A}_{1\text{g}} \rightarrow {}^4\text{T}_{1\text{g}}(4\text{G})$. 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 $[\text{Zn}(\text{BrH-ASA})_2(\text{H}_2\text{O})_2]$ 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 electrolytic²⁸ in nature of 1:2 type and molar conductivity values are in the range of $5.97\text{-}23.68\text{ Ohm}^{-1}\text{ Cm}^2\text{ mol}^{-1}$.

The antifungal activities of all the compounds were measured for various plant pathogens. Inspection of the result shown in Table-3 indicates that all compounds are good toxic for fungi. Out of all the compounds, copper chelate is more toxic than other. These compounds almost inhibit the fungi about 85%.

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