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Der Pharma Chemica, 2015, 7(4):261-265
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X
CODEN (USA): PCHHAX

Solvent-free synthesis, characterization and antimicrobial activity of complexes of 2-hydroxybenzoic acid hydrazide with some M(II) chlorides (M= Co and Ni)

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ABSTRACT

This work describes the synthesis and in vitro studies on complexes of 2-Hydroxybenzoic hydrazide (HBH with Nickel(II)Chloride and Cobalt(II)Chloride. The 2-Hydroxybenzoic hydrazide (HBH) ligand was prepared by a solvent-free method. The chelates were characterized by elemental analysis, molar conductance and spectral studies. The antimicrobial activities of the ligand and their metal chelates have also been screened.

Key words: 2-Hydroxybenzoic hydrazide derivatives, chelates, characterization, antimicrobial activity.

INTRODUCTION

In recent years, solvent-free reactions has been one of the major interesting research areas due to depleting energy resources and the problem of environmental pollution associated with solvent disposal [1]. There is a need for development of synthetic reactions which are simple and which exhibit high atom economy. As a society, we are increasingly aware of the environmental impact of human activity and consequently of the need to develop cleaner and more energy–efficient technology. Environmental concern on the other hand provides a compelling incentive to develop chemical reactions that minimize waste production [2]. The main basis for this interest is the potential reduction in environmental contamination as well as the increased convenience associated with the elimination of solvent from synthesis reaction [3]

In the last decade, much interest has been focused on compound containing hydrazide and hydrazone moieties and their complexes with first row transition metals ions [4]. Such interest has been growing due to their use in medicine [for treatment of tuberculosis] biological systems and analytic chemistry [5]. The coordination chemistry of acyl hydrazide is an intensive area of study and numerous transition metal complexes have synthesized a number of new acyl hydrazides and hydrazones because of their ease of synthesis.The reason for the biological importance of 2-Hydroxybenzoic hydrazides is the presence of salicylic acid which is a colourless, crystalline organic substance, widely used in organic synthesis. Most of these complexes have been synthesized by the traditional method using volatile organic compounds as solvents [6].

In continuation of our studies of the synthesis of metal complexes of biologically active molecules, we report the synthesis of complexes of the title transition metals with 2-hydroxybenzoic acid hydrazide without the use of solvent. The complexes will be characterized by some physicochemical properties while the ligand and complexes will be subjected to antimicrobial screening.

MATERIALS AND METHODS

Materials and Instruments: 2-Hydroxybenzoate and hydrazine hydrate were obtained from Sigma-Aldrich Chemical Ltd while the metal chlorides and other reagents and solvents used where from BDH Limited. They were all used without further purification.

Melting point were recorded with staunt melting point apparatus SMP30 and uncorrected for both ligand and metal complexes. Infrared spectra of both ligand and metal complexes were recorded on SHIMADZU FTIR-8400 spectrometer in the frequency range 4000-400cm^{-1}, the measurement were carried out with samples in KBr disc. UV-visible spectra were recorded using Jenway 6405 UV/Vis spectrometer in range 1200-200nm in ethanol. Conductivity measurement were made in 10^{-3}M solution of the complexes and ligand in absolute ethanol at ambient temperature using conductivity meter Jenway PMC3.Elemental analysis were performed on a Perkin Elmer 2400 instrument and antimicrorobial activity of the ligand and metal complexes were evaluated by the agar-well diffusion method using two gram positive and two gram negative bacteria.

Synthesis of Ligand (2-Hydroxybenzoic hydrazide (HBH): The Hydrazide was prepared using standard method [7]. 5.0ml of hydrazine hydrate was added to 14ml of 2-Hydroxybenzoate in 100ml of absolute ethanol. Antibumping granules were added to prevent bumping. The mixture was then refluxed for 6 hours in a 250ml round bottom flask.

The crystal formed was white in colour and it was filtered and weighed. (Yield = 8g; 50%).

Synthesis of$[N_1(HBH)_2]CL_2$ Complex: 4mmol (0.608g) of 2-Hydroxybenzoic hydrazide and 2mmol (0.475g) of nickel (II) chloride ($NiCl_2$. $6H_20$) were weighed into an agate motar which has been washed and dried before use. The reactants were grinded together for 15minutes. The reaction was monitored by TCL using Chloroform/ methanol (9:1) till no trace of reactants were found. The compound was purified by recrystallization from ethanol. The equation for the reaction is shown below in eq. 1The $[Co(HBH)_2]CL_2$ Complex was similarly prepared.

$$NiCl_2.6H_2O + SAH \xrightarrow{\text{15 min. grinding}} [Co(SAH)_{2]}Cl_{2.}6H_2O \text{ ....eq.1}$$

Antimicrobial Activity: The antimicrobial activity of the ligand and its complexes were tested against the bacterial species, *Staphylococcus aureus, Escherichia coli and Salmonella typhi and* the fungal species *Rhizepus stolonifer and candida albicans* by agar disc diffusion method. Streptomycin and Nystatin were used as standards for antibacterial and antifungal agents. The standard samples of antimicrobial activity were done at 100uglml concentration in DMSO. The test organism were grown on nutrient agar medium in petri plates. The antibacterial and antifungal activities of the ligand and it's metal complexes were done at 50, 100 and 200uglml concentration in DMSO solvent by the minimum incubatory concentration (MIC) method. The disc were placed on the previously seeded plates incubated at 37^{0}C. The diameter of inhibition zone around each disc was measured after 24hrs for bacterial and 72hrs for fungal species. Activity was determined by measuring the diameter of the zone showing complete inhibition (mm).

RESULTS AND DISCUSSION

The Co(II) and Ni(II) complexes of HBH were synthesized by reaction of metal salts with HBH by grinding. The method produced a yield in the range of 74-77% within a shorter time of 15minutes as compared to 50-60% by classical solution phase method which usually takes 3 hours for reaction to complete. The complexes were characterized by conductivity measurements, TLC, Infrared and UV-Vis spectroscopy. The complexes where found to be sparingly soluble in water and methanol. The physical properties of the various complexes are collected in table 1. The molar conductance values measured in 10^{-3}M absolute ethanol at ambient temperature was 66.4 NS/Cm for the Ni complexes and 28.4NS/Cm for the Co complexes. The results showed that the complexes are electrolytes because of the high conductivity values. The high melting point range (148-205^{0}C) of the complexes is also an indication of their non-hygroscopic nature. Elemental analysis of the complexes for C,H,N are consistent with the proposed formulae as shown in Table 1. In all, the physical properties and stoichiometric ratio data for the two complexes were in good agreement with those obtained in literature [8-11].

Table 1: Some Physical Constant For Both Ligand And Complexes

Ligand/Complex Molecular Formular	Mol. Weight gmol^{-1}	MP(^{o}C)	E. analysis % Found (calcd)				Molar conc. (NS/cm)	TDS (Mg/L)
			C	H	N	M		
SAH ($C_2H_8O_2$)	152.09	148-150	54.61 (55.31)	5.04 (5.26)	17.96 (18.41)		3.4	1.5
[Ni(SAH)$_2$] ($C_{14}H_{16}N_4O_4Ni$)	362.88	178-181	45.61 (46.29)	4.16 (4.41)	15.04 (15.43)	16.10 (16.4)	66.4	32.7
[Co(SAH)$_2$] ($C_{14}H_{1\,6}N_4O_4Co$)	363.08	198-205	45.60 (46.27)	4.05 (4.43)	15.26 (15.89	16.52 (16.6)	28.4	0.03

UV-Visible spectra: The UV-visible spectra of the Co(II) complexes exhibits 3 bands at 372, 550 and 867 nm. These bands are assigned to $^4T_{1g}{}^{\rightarrow}{}^4T_{1g}(p)$, $^4T_{1g}{}^{\rightarrow}{}^4A_{2g}$ and $^4T_{1g}{}^{\rightarrow}{}^4T_{2g}$ transitions respectively. These bands confirm an octahedral configuration [12]. The Ni(II) complex exhibits 2 bands centred at 427 and 578nm which may be tentatively assigned to $^3T_1$ (F) $^{\rightarrow}$ $^3T_2$ (F) and $^3T_1$ (F) $^{\rightarrow}$ $^3A_2$ (F) transitions respectively. These bands confirm a tetrahedral configuration [12]. These modes are also in agreement with data obtained for Ni(II)HBD and Co(II)HBD synthesized in a solvent medium.

Infrared spectra: The relevant IR spectra bands of the ligand and the complexes are given in table 2. Hydroxybenzoic hydrazide as a ligand, provides two potential donor sites, viz O and N. Owing to the presence of lone pair electrons on the nitrogen atom of the azomethine group, schiff bases form several complexes with metal ions. The infrared spectra of the HBD ligand and its complexes, as shown in table 2, have been assigned mainly for those specific frequencies directly involved in complex formation. The vibrational band at the range of 3143-3153cm^{-1} assigned to vN-H in the ligand shifted to a lower wavelength (3123-3141cm-1) in the both complexes. This is probably due to coordination of the metal via nitrogen atom of the N-H group in the ligand. The band observed at the 1103cm^{-1} and 1370cm^{-1} corresponds to the V(N-N) and V(C-N) stretching [13]. The band corresponding to V(C=O) at 1592cm^{-1} is shifted by about 30cm^{-1} to a lower frequency, supporting the coordination of the carbonyl oxygen. However the vibrational frequencies of the ring V(N-H) and V(C-N) remains almost unaffected, indicative of non participation of these groups in coordination. The presence of water of crystallization in the complexes is revealed by a broad band at between 3475 and 3496 cm^{-1} and the results of elemental analysis also supported the presence of water of crystallization [14].

Table 2: Infrared Data for Ligand and complex

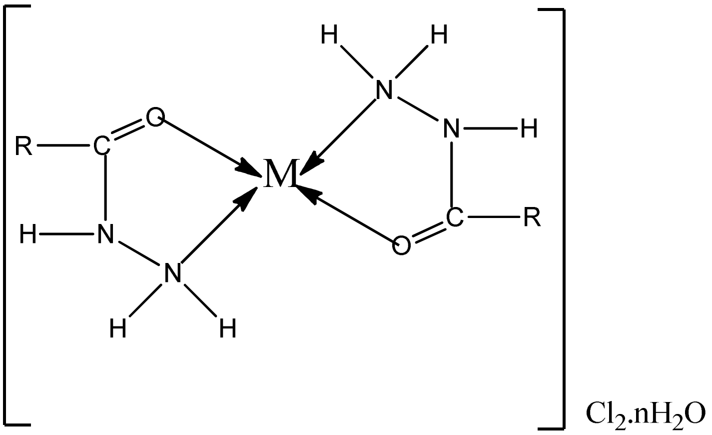
Complex	vOH (cm-1)	∇vOH (cm-1)	vC=O (cm-1)	∇vC=O (cm-1)	vNH (cm-1)	∇V(NH) (cm-1)
SAH	3320.31		1592.29		3143.77	
Co(SAH)$_2$	3299.35	20.96	1546.96	45.33	3199.32	55.55
Ni(SAH)$_2$	3294.21	26.10	1545.03	47.26	3195.42	51.65

Antimicrobial activity: Results of the antimicrobial activity of the complexes and ligand against the growth of micro-organism is summarized in table 3. From the results, inhibition is found to increase with increase in concentration of metal complexes. The result also show that metal complexes have a high activity against each class of organism [15]. The activity is related to the nature and structure of the complex. However, all the complexes show higher activity against *E. coli* as compared to *S. typhi* and *S. aureus*. Antibacterial activity can be ordered as Ni(HBH)$_2$> Co(HBH)$_2$> HBH. These complexes do not show strong concentration dependence of antibacterial activity, as compared to antifungal activities of the same complexes. The relation between chelation and toxicity is very complex and expected to be a function of steric, electronic and pharma-kinetic factor along with mechanistic pathway [15]. The activity of these complexes and liquid follows the order; N$_I$(II) > Co(II) > HBH. A comparative study of the ligand and its complexes indicates that metal complexes exhibits higher antimicrobial activity than the free ligand. Such increased activity of the complexes can be explained on the basis of the overtone concept and Tweedy chelation theory [16]. According to the overtone concept of cell permeability, the lipid membrane surrounding the cell favours the passage of only lipid soluble materials; due to which liposolubility is an important factor controlling the microbial activity. On chelation, the polarity of the metal ion will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with donor groups. Furthermore, the mode of action of the compound may involve formation of a hydrogen bond through the azomethine group with the active centre of the cell constituents resulting in interference with normal cell processes.

Table 3: Antibacterial and Antifungal results of the compounds

Compound	Concentration (Ng/ml)	Diameter of zones showing complete inhibition				
		E. coli	*S.Typhi*	*S. aureus*	*R.stolonifer*	*C.albicans*
SAH	50	5	4	4	3	2
	100	7	6	6	3	3
	200	9	7	5	5	4
$Co(SAH)_2$	50	11	9	8	7	6
	100	13	11	9	9	8
	200	16	14	13	10	9
$Ni(SAH)_2$	50	16	12	11	8	7
	100	20	17	16	10	9
	200	23	22	21	12	10
Streptomycin	100	30	31	32	-	-
Nystatin	100	-	-	-	35	33

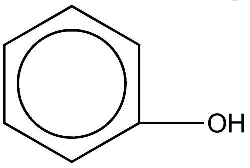
Proposed structure of complexes: The coordination chemistry of some hydrazide (including HBH) with transition metal ion (Ni and Co) has been reported. [12]. In this case, the 2-Hydroxybenzoic hydrazide has several donor site but because of steric hindrances, the ligand can provide a maximum of two donor atoms to one metal centre. The spectroscopic studies suggested that the 2-Hydroxybenzoic hydrazide acts as a bidendate ligand and it's coordination to the metal centre occur via one of the hydrazide nitrogen atom and also the carbonyl oxygen atom and forms slightly distorted octahedral geometry. The proposed geometry of the complex is shown in fig 3.1.



Where M=Ni or Co and n= 4,6 or 10

Figure 3.1: Suggested structure of the complexes

and R =



CONCLUSION

The synthesis procedure for the ligand and metal complexes were carried out carefully and effectively. The Co(II) and Ni(II) complexes of 2-Hydroxybenzoic hydrazide were prepared by the mechanochemical reaction of metal salt and 2-Hydroxybenzoic hydrazide. The formation of the reaction product was indicated by a change in colour, in which $[Co(HBH)_2]$ and $[Ni(HBH)_2]$ gave pink and green colourations respectively. A yield of 70-78% yield was achieved after 15minutes, unlike the classical methodwhich gives a lesser yield of 50-60% at about 3-4hours. Results from the characterization of the ligand and complexes suggests that the hydrazide acts as a bidentate donor ligand coordinating through the azomethine nitrogen and carbonyl group, while the chloride ions are in the outer coordination sphere. The inhibitory activity of the complexes and ligand against the growth of the test micro-organism was seen to have increased with increase in concentration of metal complexes.

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