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Complexation of Co(II) with 3,5-dinitrosalicylic acid: Synthesis, Spectral studies and Antibacterial activities

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Abstract
The metal complexes have been characterized by elemental analysis, electrical conductance and spectral studies. UV spectra of the complex shows intraligand and charge transfer transitions. Bonding of the metal ion through N- and O- donor atoms of the ligands is revealed by IR studies, and the chemical environment of the protons is confirmed by NMR studies. The agar cup method has been used to study the antibacterial activity of the complexes against the pathogenic bacteria E.Coli, S.aureus and Klebsiella pneumonia.

Keywords: Charge transfer transition, antibacterial activity, cobalt complex, spectral studies of metal complex

1. Introduction

Studies on their metal chelates could have much physiological and pharmacological relevance because the metal chelates of sulfa drugs have been found to be more bacteriostatic than the drugs themselves [1-2]. The role of metal ions in living systems has been well established in recent years. The use of transition metal complexes as medicinal compounds has become more and more prominent. These complexes offer a great diversity in their action; they do not only have anti-cancer properties but have also been used as anti-inflammatory [3], anti-infective [4] and anti-diabetic compounds [5]. Metal ions play pivotal roles in many biological processes, and the study of the roles of these metal ions in biological systems falls into the rapidly developing interdisciplinary field known as bioinorganic chemistry. When compared to other branches of natural sciences, bioinorganic chemistry seems to be an interesting discipline. However, there is a copious amount of information on the effects of metals on biological system. For instance, the toxicities of metal ions such as mercury, lead and chromium on the environment have been reported [6-7].

Metal chelation is a brilliant way to increase the lipophilic character of the organic moiety. Infact, on coordination, ligands would possibly improve their bioactivity profiles whereas some inactive ligands could acquire medicinal properties and consequently they have become a very important category of structure-selective binding agents for nucleic acids [8-9]. This research work discussed about the synthesis, characterization and antibacterial activity of Cobalt based complex of nitro derivative of salicylic acid. The effect of electron withdrawing nature in chelation is discussed by introducing nitro group in salicylic acid.

2. Experimental Section

2.1. Materials and Methods

Chemicals

All chemicals used in this work were reagent grade (BDH/ Aldrich), including the metal salts i.e. Co(NO3)2, Ethanol, Salicylic acid, conc.HNO3, conc.H2SO4, chloroform, DMSO, CaCl2, NH4OH. Double distilled water was used.

Instruments

The percentage compositions of C, H, and N of complexes were determined by using micro analytical methods on Perkin Elmer 240C (USA) elemental analyzer. Infrared spectra of the ligand and its complexes were carried out by using KBr pellets in the range (4000-400 cm^{-1}) on Bruker Infra red model 337. The electronic absorption was carried out by using a Shimadzu UV-1601 using DMSO as solvent. The Mass spectra were recorded by ESI technique on VG AUTOSPEC mass spectrometer instrument. The ^1H spectrum was recorded on Varian Gemini Unity Spectrometer by employing TMS as internal standard. Melting points of the ligand and decomposition temperature of complexes were determined on Polmon instrument (model No.MP-96). The Molar conductance measurements were carried out in DMSO (10^{-3} M) using Digisun Electronic Digital conductivity meter of model: DI-909 having a dip-type cell calibrated with KCl.

Biological activity

The antimicrobial tests were performed by the standard disc diffusion method. The antibacterial activity of the complexes was studied against E.Coli, S.aureus and S.Pneumoniae**.** Each of the metal complex compounds dissolved in DMSO at a concentration of 1 mg/ml was prepared. Paper discs of Whatman filter paper no. 1 were cut and sterilized in an autoclave. The paper discs were saturated with 10 µl of the metal complex compounds dissolved in DMSO solution or DMSO as negative control and were placed aseptically in the Petri dishes containing Nutrient agar media inoculated with the above mentioned two bacteria separately. The petridishes were incubated at 37 ^0C and the inhibition zones were recorded after 24 h of incubation.

2.2. Synthesis of 3,5-dinitrosalicylic acid

The preparation of 3,5-DNSA is shown in figure.1. This preparation must be carried out in the fume cupboard since nitrous fumes are evolved.2.5g of pure 8-hydroxyquinoline was dissolved in 10ml of concentrated sulphuric acid in a litre flask equipped with a reflux condenser. 10ml of fuming nitric acid was added at a time. The flask was shacked well and cool in ice-water during the addition much heat is evolved and a clear yellow solution was obtained. A few fragments of porous porcelain was added and heat the mixture gradually on a water bath to 100^0C during 45 minutes. At 70-80^0C the reaction became vigorous. The flask was cooled in cold water. The mixtures was maintained at 100^0C for 15 minutes with occasional shaking, and then transfers it to an oil bath at 100^0C raise the temperature to 180^0C over 30 minutes and keep it at 130 – 140^0C for 1 hour. The flask was allowed to cool; crystals commence to separate at about 90^0C. The reaction mixture was poured into 3-4 litres of ice-water. The separated crystal was filtered, wash with water and dry. The yield 3,5-dinitrosalicylic acid (m.p.178^0C) is 1.7g.

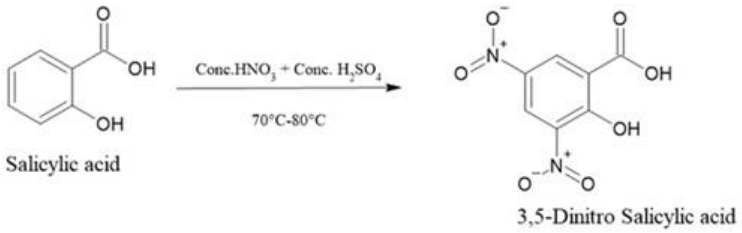


Figure 1: Reaction equation of synthesis of the 3,5-dinitrosalicylic acid (3,5-DNSA)

2.3. Synthesis of cobalt complex of 3,5-dinitrosalicylic acid [$Co(3,5\text{-}DNSA)_2$]

Co(II) ion salt solution was prepared by dissolving 3.87g (0.02 mol) $CoCl_2.6H_2O$ in 25ml of distilled water. The solution of the metal salt was added slowly with stirring in a separate 20ml of distilled water containing 2.32 g of 3,5-dinitrosalicylic acid (0.02) at room temperature maintaining the pH between 6.0-6.5 by adding dilute solution of

KOH. The synthesis was carried out with stirring at room temperature. After 1 hour, the complex separated out. The complex was washed well with distilled water, recrystallized, filtered, dried in vacuum and weighed. (Yield: 73%).

3. Results and Discussion

3.1. Physical properties

Table 1: Analysis and physical characteristics of 3,5-DNSA and [Co(3,5-DNSA)$_2$]

Compound	Color	Yield (%)	Melting point (^{0}C)	Molar mass (gmol^{-1})	% found (calculated) C	H	N	Λ_m (ohm^{-1}cm^2 mol^{-1})
3,5-DNSA	Yellow	73%	178^{0}C	283.1	69.00 (69.09)	5.43 (5.69)	5.90 (5.01)	0.6
[Co(3,5-DNSA)$_2$]	Dark blue	71%	>360	342.03	64.34 (64.90)	4.03 (4.25)	3.07 (3.11)	2.2

The physical parameters for 3,5-DNSA and [Co(3,5-DNSA)$_2$] are shown in table 1. The colour of 3,5-DNSA and [Co(3,5-DNSA)$_2$] are yellow and dark blue respectively. The melting point of the complex is increased because of increasing molecular mass. The elemental analysis of carbon, hydrogen and nitrogen are similar to calculated values. The molar conductance value clearly shows that enhancement of conducting electric current in metal complex.

3.2. UV spectral characterization of 3,5-DNSA and [Co(3,5-DNSA)$_2$]

Table 2: UV spectral datas for 3,5-DNSA and [Co(3,5-DNSA)$_2$]

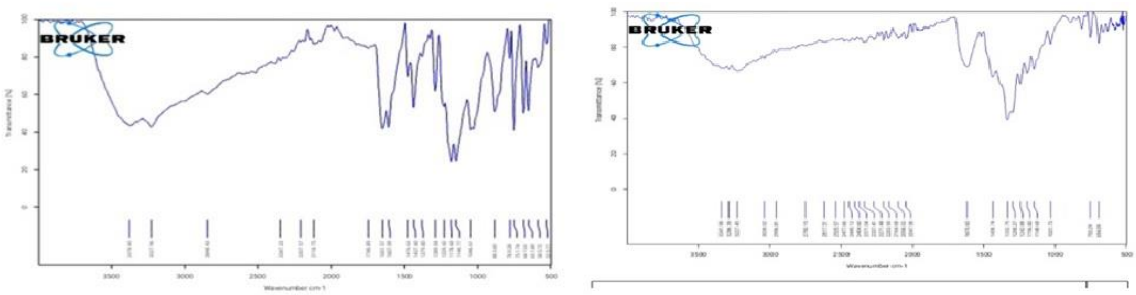
Compound	Wave Number nm	Wave Number cm^{-1}	ε_{max} molar^1 cm^1	Assignment	Suggested structure
3,5-DNSA	279	35842.2	2213	$\pi \rightarrow \pi^*$	
	324	30864.1	1232	$n \rightarrow \pi^*$	
[Co(II)(3,5-DNSA)$_2$]	270	37037	1557	L.F	Square planar
	302	33222.5	1554	L.F	
	348	28735.6	1120	C.T	
	711	14064.9	22	$^1A_{1g} \rightarrow {}^1E_{1g}(P)$	
	797	12547	22	$^1A_{1g}(F) \rightarrow {}^1B_{1g}(F)$	

The UV/Visible datas are shown in table.2. The UV-Vis spectrum of 3,5-dinitrosalicylic acid showed a band centered at 279 nm. It was assigned π-π* due to intra-ligand charge transfer (ILCT). The UV-Vis spectrum of [Co(3,5-DNSA)$_2$] showed a band at 270nm which was assigned to be π-π* due to intra-ligand charge transfer(ILCT). The sharp band centered at 348nm was assigned to be ligand to metal charge transfer (LMCT). The broad band at 711 nm and 797 nm was due to $^1A_{1g} \rightarrow {}^1E_{1g}(P)$ and $^1A_{1g}(F) \rightarrow {}^1B_{1g}(F)$ d-d transitions respectively which suggested that complexation occurred.

3.3. IR spectra analysis

FT-IR spectra of 3,5-DNSA and [Co(II)(3,5-DNSA)$_2$]

The FT-IR spectrum of 3,5-DNSA and [Co(II)(3,5-DNSA)$_2$] are shown in figure 2. On the basis of the reported infra red spectra of amino acids, salicylic acid and its metal complexes [10-12], some of the important bands have been assigned.



(a) **(b)**

Figure 2: *IR spectrum of 3,5-DNSA (a) and [Co(3,5-DNSA)$_2$] (b) in the region of 500 to 4000 cm^{-1}*

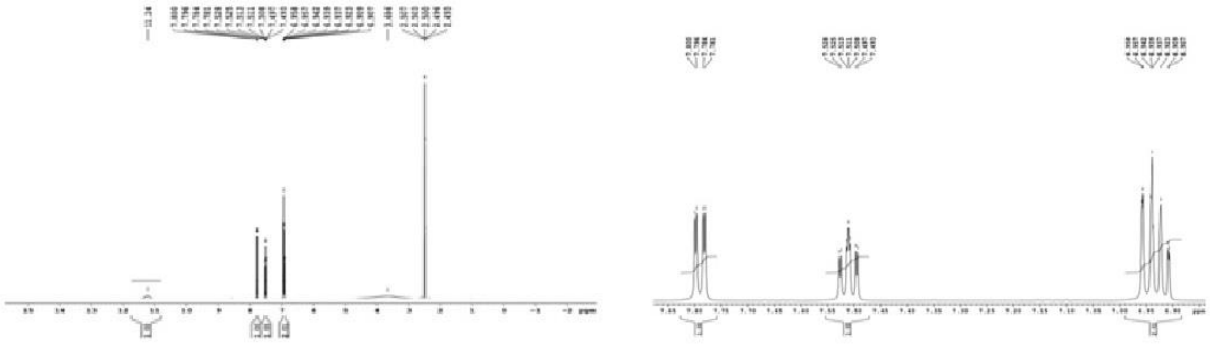
IR Spectral data for 3,5-DNSA (KBr, cm^{-1}): 1614 (C-N), 1236(C-O), 3260 (O-H), 2104 (NO_2), 1367 (C=C), 1057 (C-H).

IR Spectral data for [Co(3,5-DNSA)$_2$] (KBr, cm^{-1}): 1603 (C-N), 1348 (C-O), 2047 (NO_2), 1332 (C=C), 1106 (C-H), 694 (M-N), 752 (M-O).

A broad band was observed in the region between 3260 cm^{-1} due to asymmetric and symmetric O-H stretching modes. The ν(CO) band is observed at 1236 cm^{-1}. The position of this band undergoes variation depending on metal complex under study [13, 14]. The ν(C-N) mode observed at 1614cm^{-1} in the spectra of free 3,5-DNSA ligand is found to be shifted to lower wave number, in the range of 1603cm^{-1} in the spectra of complexes. The stretching vibrations 2104cm^{-1} and 2047cm^{-1} indicates the presence of N-O bond in 3,5-DNSA and [Co(3,5-DNSA)$_2$] respectively.

An important feature of infrared spectra of the metal complexes with 3,5-DNSA is the absence of band 3260cm^{-1} due to the O-H stretching vibration of the free O-H group of 3,5-DNSA. This observation leads to the conclusion that complex formation takes place by deprotonation of the hydroxyl group of 3,5-DNSA moiety. Some new bands of weak intensity observed in the regions around 694cm^{-1} and 752cm^{-1} may be ascribed to the M-O and M-N vibrations respectively.

3.4. Nuclear magnetic resonance spectra of the 3,5-DNSA



(a) (b)

Figure 3: *^{1}H NMR spectrum of 3,5-DNSA in the region of -2 to 15ppm (a) and 6.8 to 7.85 ppm (b)* ^{1}H NMR (300 MHz, DMSO-d_6, δ / ppm): 11.24 (OH), 7 to 8 (Ar-H).

Figure 3. represents the ^{1}H-NMR spectrum of 3,5-DNSA.The spectrum shows the singlet signal at (δ = 11.24 ppm) is assigned to the (O-H) proton of carboxylic acid group. The multiplet signal in the range of 7 to 8ppm is assigned to the aromatic protons.

3.5. Mass spectrum of the 3,5-DNSA

The ESI mass spectra of the ligand recorded at room temperature is shown in figure 4. The ligand [L] shows a molecular ion peak at m/z 284.2, which corresponds to [L+H] peak as the calculated m/z being 283.1.

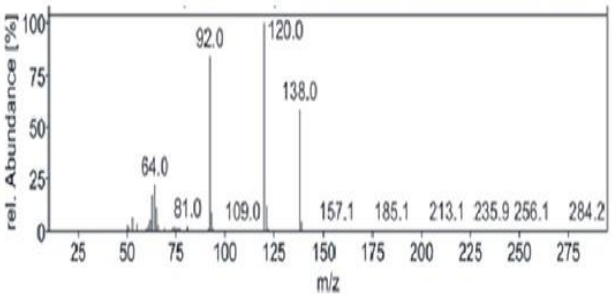


Figure 4: *Mass spectrum of 3,5-DNSA*

From the above results, the structure of the complex is shown in figure.5. But the stability of the complex is affected by the presence of nitro group. Because of the nitro group is a electron withdrawing group, the tendency of donating electron from -OH and –COOH group to the cobalt metal ion is decreased.

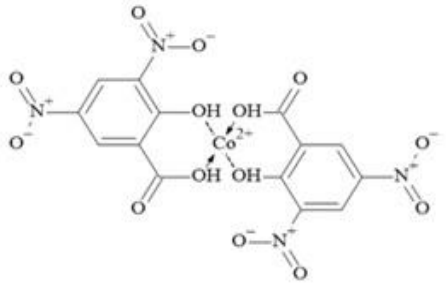


Figure.5: *Structure of Co(II)bis(3,5-dinitro salicylic acid)*

3.6. Antimicrobial Activity

Table 4: Inhibition zone diameter in (mm) for the 3,5 DNSA and $[Co(II)(3,5\text{-}DNSA)_2]$

Compounds	E.Coli (mm)			S.aureus (mm)			Klebsiella pneumonia (mm)		
	10µl	20µl	30µl	10µl	20µl	30µl	10µl	20µl	30µl
SAHY	9	10	12	12	11	9	14	11	10
$[Ni(SAHY)_2]$	11	13	14	14	17	14	16	19	20

The invitro anti bacterial activity of the ligand and its complex has been carried out against the E.Coli, S.aureus and Klebsiella pneumonia using disc diffusion method by taking DMSO as solvent.

A comparative study of the growth inhibition zone values of 3,5 DNSA and $[Co(II)(3,5\text{-}DNSA)_2]$ indicate that metal complexes exhibit higher anti bacterial activity than the free ligand and the same is indicated from the results given in the table.4. This is probably due to the greater lipophilic nature of the complex. Such increased activity of the metal chelates can be explained on the basis of overtone's concept and Tweedy's chelation theory [15]. According to Overtone's concept of cell permeability, the lipid membrane that surrounds the cell favors the passage of only lipid soluble materials due to which lipo solubility is considered to be an important factor that controls the anti 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 positive charge of metal ion with donor groups. Further, it increases the delocalization of the π electrons over the whole chelate ring and enhances the lipophilicity of the

complex. This increased lipophilicity enhances the penetration of the complex into lipid membrane and thus blocks the metal binding sites on enzymes of microorganisms [16]. These metal complexes also disturb the respiration process of the cell and thus block the synthesis of proteins, which restricts further growth of the organism. The variation in the activity of complex against different organisms depend either on the impermeability of the cells of the microbes or difference in ribosomes of microbial cells. The inhibition zones of antibacterial activity are presented in the Table.4.

The antibacterial activity of 3,5 DNSA and [Co(II)(3,5-DNSA)$_2$] were tested in vitro against bacteria such as E.Coli, S.aureus and Klebsiella pneumonia by agar disc method. The compounds were tested at the concentration 0.5 mg/mL in DMSO. From table.4, it is clear that the inhibition by metal chelates is higher than that of a ligand and results are in good agreement with previous findings with respect to comparative activity of 3,5 DNSA and [Co(II)(3,5-DNSA)$_2$]. Such enhanced activity of metal chelates is due to lipophilic nature of the metal ions in complexes. The increase in activity with concentration is due to the effect of metal ions on the normal process. The action of compounds may involve the formation of hydrogen bond with the active center of cell constituents, resulting in interference with the normal cell process.

4. Conclusion

The 3,5 DNSA and [Co(II)(3,5-DNSA)$_2$] metal complex have been structurally characterized. The spectral data show that the ligand act as neutral and bidentate coordinating through nitrogen atom of the nitro group and oxygen atom of the hydroxyl group of salicylic acid. Based on analytical and spectral data, the complex is assigned to be in square planar geometry. Biological studies of the complex reveal that they show better activity when compared to that of the 3,5 DNSA.

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