

Studies on Dapsone in transition metal complexes

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Abstract: This article describes the preparation and characterization of three metal ion complexes of the sulpha drug, dapsone. Dapsone has three atoms that can potentially bind to the metal ion – nitrogen of the amino moiety, and oxygen and sulphur of the sulphone moiety. This study attempts to understand the nature of coordination between the dapsone and metal ion and elucidate the structure. All the metal complexes are characterized by quantitative chemical analysis and electrical conductivity measurements. Magnetic susceptibility is used to determine the number of unpaired electrons in the central metal atom. The structure of metal complexes, mode of attachment and strength of bonding are confirmed using IR spectral analysis. It is found that the complexes are non ionic in nature and are of tetrahedral morphology and the binding is through the sulphur of the sulphone group of dapsone.

Key words: dapsone, magnetic susceptibility, metal complexes, sulpha drug, tetrahedral morphology.

Introduction

4,4'-diaminodiphenylsulphone (DDS), popularly called Dapsone, is an antibiotic sulpha drug that is commonly used to treat leprosy, dermatitis, herpetiformis and Pneumocystis Carinii Pneumonia. It is a creamy white crystalline powder that is lightly soluble in water but freely soluble in alcohol and dilutes mineral acids. Dapsone finds application in various fields - it shows efficient pharmacological activity against mycobacterium leprea that occurs as cross activity in HIV infected patients who have switched from trimethoprim-sulphamethaxazole.¹ DDS has also been found to induce iron release in erythrocytes, which increases the free iron pool in spleen and liver.^{2,3} Apart from medicinal use, DDS has also been used to cure epoxy resins and the product has been found to have higher glass transition temperature, better thermal stability, lower co-efficient of thermal expansion and lower moisture absorption than other epoxy resins.⁴⁻⁶

The development of resistance of bacteria to many drugs including sulpha drugs has resulted in research to modify these molecules; one promising route to modify these drugs has been to complex them with metal ions.⁷⁻¹⁰ The ability of the active drug moiety to coordinate with a metal ion and to be subsequently released when required, makes them ideal for use in biological systems.¹¹⁻¹⁴

DDS can act as a weak ligand to coordinate with metal ions but there have been few studies on DDS metal ion complexes. DDS metal ion complexes are weak enough to be dissociated even by traces of moisture and water of hydration in salts.¹⁵⁻¹⁷ In 1963 Rao studied the infra red spectra of sulpha drugs and their solid complexes with transition metal chelation.¹⁸⁻²² Narang et.al, 1975, prepared various coloured metal complexes by treating hot alcoholic solutions of the sulpha drug with metal ions in 1:2 metal ion: sulpha drug molar ratios.²³

This work studies the preparation and characterization of DDS metal ion complexes. Complexation of cobalt, nickel and zinc salts with dapsone is investigated.

Experimental

4,4-Diaminodiphenylsulphone was purchased from Burroughs Wellcome (I) Ltd. Metal salts of cobalt, nickel and zinc were purchased from Qualigens Chemicals. Absolute alcohol and other reagents of analytical grade were procured from Ranbaxy and Merck Chemicals.

Chemical Analysis

Metal complexes with dapsone were prepared using dichlorides of cobalt, nickel and zinc. The chemical analysis of complexes involves quantitative estimation of the metal ion and the anion for arriving at the stoichiometric ratio.

The cobalt ions were estimated volumetrically by titration against standard EDTA solution, Eriochrome black-T being used as the indicator. The nickel ions were estimated volumetrically by titration against EDTA solution with murexide as indicator. Similarly zinc ions were estimated volumetrically by titration against standard EDTA solution with Eriochrome black -T as indicator.

Equipment and Spectral Analysis

Electrical conductivity and magnetic susceptibility measurements were used to determine the number of unpaired electrons present in the central atoms in the elucidation of their stereochemistry. Mercurytetrathio cyanatocobaltate^(II) was used as the magnetic standard for calibration the Guoy tube, the χ_g value for the magnetic standard being 16.44×10^{-6} . The effect of magnetic moment μ_{eff} per metal atom is $2.84 (\chi^1 M \times T_{\text{abs}})^{1/2}$. Infra red spectra were taken in potassium bromide pellets using a Perkin-Elmer 597 spectrometer to ascertain the mode attachment and strength of bonding between the ligand and metal ion.

Preparation of Dapsone -Metal Complexes

Dapsone was found to be freely soluble in alcohol. For the complex preparation, pure metal salts of cobalt, nickel and zinc were used. The metal salts were dehydrated by heating them below their melting points to about 110 °C and further keeping them in desiccators. The metals salts and dapsone were taken in molar ratios of 1:2.

Pure cobalt^(II) chloride was dissolved in a slight excess of anhydrous alcohol and heated in a flask fitted with a reflux condenser. To this boiling solution, a hot alcoholic solution of dapsone was added through the condenser such that the molar ratio of metal salt and dapsone was 1:2. The reaction mixture was refluxed for an hour. The alcohol in the reaction mixture was then evaporated and the concentrated solution was allowed to cool gradually. Pale pink coloured crystals of the complex were formed. The crystals were filtered, dried at 110°C in a hot air oven for an hour and kept in a desiccator. Similar methods were followed for nickel (II) chloride and zinc (II) chloride. Yellowish green crystals were obtained for nickel and white crystals for zinc. The volume of metals and chlorides were estimated by simple volumetric method.

Results and discussion

Molar conductance measurements were performed for all complexes to ascertain the ionic nature of the complexes. Table 1 indicates the physicochemical characteristics of dapsone metal complexes. Co^(II), Ni^(II), ions belong to d⁷ and d⁸ systems and hence are paramagnetic. Zinc^(II) ions, however, belong to the d¹⁰ system, with no unpaired electrons and hence the complex is diamagnetic.

Table 1. physicochemical characteristics of dapsone metal complexes.

S. No.	Complex	Mole ratio	Colour	Molar conductance (mhos)	No.of unpaired electron	Magnetic moment (μ_{eff})
1.	CoCl ₂ (DDS) ₂	1:2:2	Pale pink	17	3	4.62
2.	NiCl ₂ (DDS) ₂	1:2:2	Yellowish green	34	2	3.20
3.	ZnCl ₂ (DDS) ₂	1:2:2	White	16	-	-

IR spectrometry helps in determining the co-coordinating atom and the relative strength of bonding. Before considering the IR spectra of complexes, it is necessary to understand the various absorption peaks of the free dapsons (4,4'-diaminodiphenylsulphone).

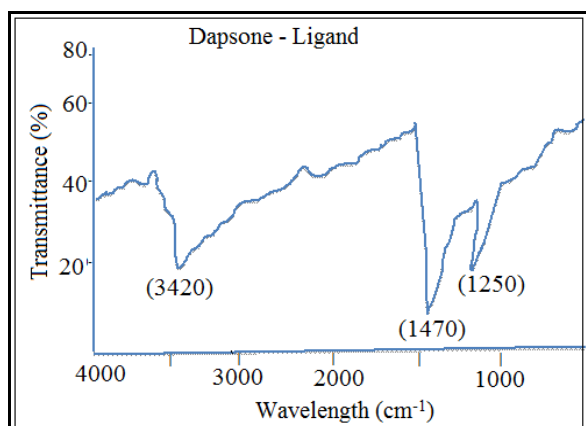


Figure.1. IR Spectrum of free dapsons ligand

The IR spectrum of dapsons is given in fig.1. Two prominent bands, one at 1250 cm^{-1} and other at 1470 cm^{-1} are observed for the ligands, which are due to the symmetric and asymmetric vibration of S-O bond of the sulphone group present in dapsons. Investigation for any shift of these frequencies after complexation will help understand the nature of coordination between the dapsons ligand and the central metal ion. The shift in IR absorption peaks with complexation will indicate which of the three potential electron donors (nitrogen, sulphur or oxygen) present in dapsons coordinates with the metal ion. Fig.2 shows that the proposed structure of free dapsons ligand.

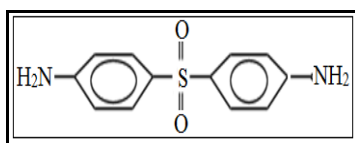


Figure 2. Proposed structure of dapsons ligand

Dichlorobis(diaminodiphenylsulphone)Cobalt^(II) complex

For this complex, the ratio of $\text{Co}^{(II)}$ ion and ligand is 1:2. The molar ratio of the complex shows two chlorine atoms and two ligand molecules attached to the central metal atom. The molar conductance value for a 10^{-3} molar solution of this complex is 17 mho, which indicates that the complex is non-ionic in nature, since for a 1:2 electrolyte, the conductance is expected to be in the range of 150 mho. The μ_{eff} value of $\text{Co}^{(II)}$ in this complex is 4.62 BM. This indicates that the $\text{Co}^{(II)}$ ion probably has a tetrahedral geometry.

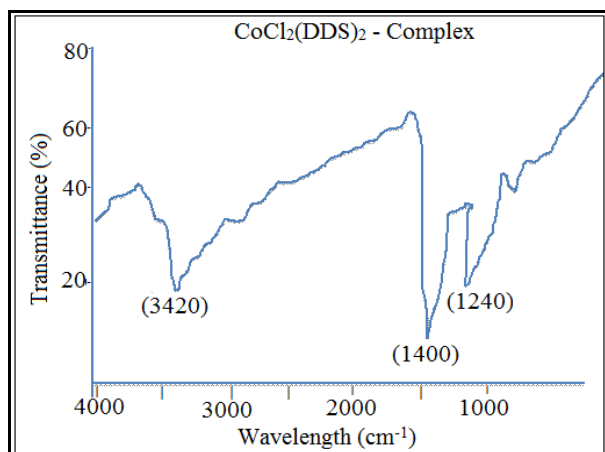


Figure 3. IR Spectrum of dichlorobis(diaminodiphenylsulphone)Cobalt^(II) complex

Fig.3 and fig.4. shows the IR spectrum and proposed structure of this complex. There is no significant shift in N-H stretching frequencies in this complex. Hence, the nitrogen of the NH₂ group is not coordinated to the metal atom. There is a significant shift noticed in ν_{s-o} (str) frequencies.

Table 2. IR spectra of ligand and metal complexes and important band with assignment (cm⁻¹)

S.No.	Ligand/Complex	ν_{s-o} (Symmetry)	ν_{s-o} (Asymmetry)	ν_{s-H}
1.	Dapsone	1250	1470	3420
2.	CoCl ₂ (DDS) ₂	1240	1400	3420
3.	NiCl ₂ (DDS) ₂	1130	1410	3420
4.	ZnCl ₂ (DDS) ₂	1200	1460	3420

Table 2 shows that the absorption band due to S-O symmetric stretching observed at 1250 cm⁻¹ in the uncoordinated molecule has been shifted to a lower frequency of 1240 cm⁻¹ in the complex. Similarly, the absorption band due to S-O asymmetric stretching observed at 1470 cm⁻¹ in the free dapsone molecule has been shifted to a lower frequency of 1400 cm⁻¹ in complex. This indicates that the bonding occurs between the sulphur and the metal atom in the complex.

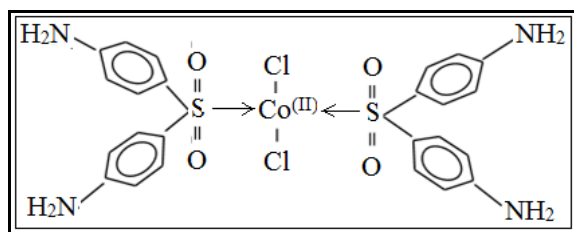


Figure 4. Proposed structure of Dichlorobis(diaminodiphenylsulphone)Cobalt^(II) complex

Dichlorobis(diaminodiphenylsulphone)Nickel^(II) complex

For this complex Ni^(II) ion and ligand ratio is 1:2, as before. Thus, there are two chlorine atoms and two ligand molecule attached to the central metal atom. The molar conductance value for a 10⁻³ molar solution of this complex is 34 mho, which indicates that the complex is non-ionic in nature, since for a 1:2 electrolyte, the conductance is expected to be in the range of 150 mho. The μ_{eff} value of Ni^(II) in this complex is 3.20 BM. This indicates that the Ni^(II) ion complex is probably of tetrahedral geometry.

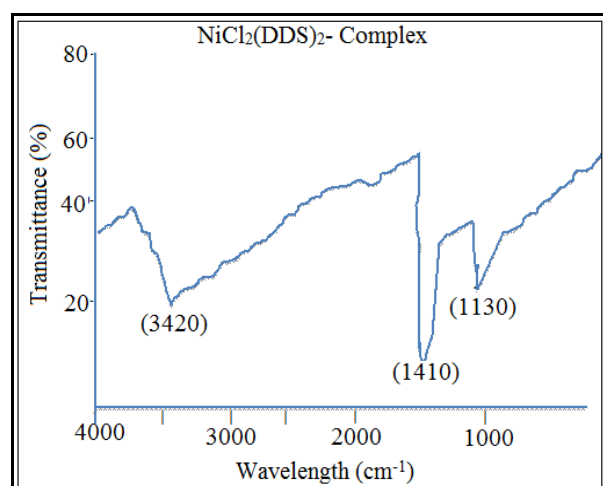


Figure 5. IR Spectrum of dichlorobis(diaminodiphenylsulphone)Nickel^(II) complex

Fig.5 and fig.6.indicates that IR spectrum proposed structure of this complex. There is no significant shift in N-H stretching frequencies noted in this complex, as before. Hence, the nitrogen of the NH₂ group is not coordinated to the metal atom. There is a significant shift noticed in ν_{s-o} (str) frequencies. The absorption band due to S-O symmetric stretching observed at 1250 cm⁻¹ in the uncoordinated molecule is shifted to lower frequency (1130 cm⁻¹) in the complex and the absorption band due to S-O asymmetric stretching decreases from

1470 cm^{-1} for the free molecule to 1410 cm^{-1} in the complex. This indicates that the bonding occurs between the sulphur and the metal atom in the complex.

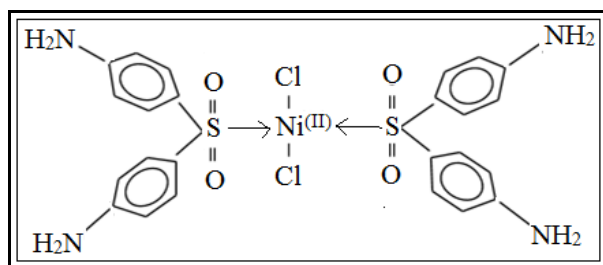


Figure 6. Proposed structure of Dichlorobis(diaminodiphenylsulphone)Nickel^(II) complex

Dichlorobis(diaminodiphenylsulphone)Zinc^(II) complex

Here too, the ratio of $\text{Zn}^{(II)}$ ion and ligand is 1:2, with two chlorine atoms and two ligand molecules attached to the central metal atom. This complex is non ionic as well, as shown by the molar conductance value of 16 mho for a 10^{-3} molar solution instead of the 150 mho expected for an ionic complex. $\text{Zn}^{(II)}$ ion belongs to the d^{10} diamagnetic system and hence magnetic susceptibility measurements are of no use to ascertaining the geometry of this complex.

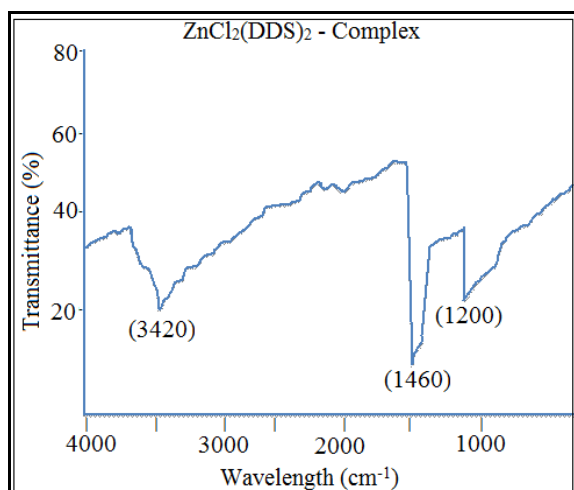


Figure 7. IR Spectrum of dichlorobis(diaminodiphenylsulphone)Zinc^(II) complex

Fig.7 and fig.8. shows that the IR spectrum and proposed structure of this complex. As with the earlier complexes, there are no significant shifts in N-H stretching frequencies in this complex indicating that the complexation is not between the nitrogen and the metal ion. However, as before, there is significant shift noticed in ν_{s-o} (str) frequencies. The absorption band due to S-O symmetric stretching reduces from 1250 cm^{-1} in the uncoordinated molecule to 1200 cm^{-1} in complex and the absorption band due to S-O asymmetric stretching reduces from 1470 cm^{-1} to 1460 cm^{-1} in complex, indicating bonding between the S and the metal ion.

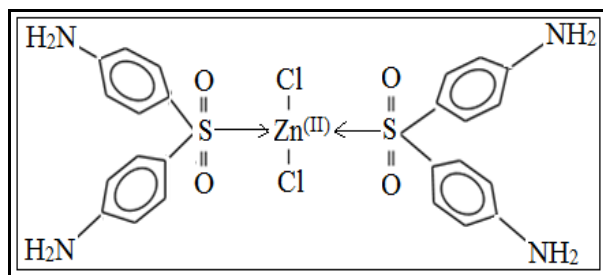


Figure 8. Proposed structure of Dichlorobis(diaminodiphenylsulphone)Zinc^(II) complex

Conclusions

The experimental techniques, general characteristics and methods of preparing dapsone complexes with CoCl_2 , NiCl_2 and ZnCl_2 have been studied. The structural aspects of these complexes have also been investigated. The metal ligand ratio has been found to be 1:2 for all complexes. For the CoCl_2 , and NiCl_2 complexes, the μ_{eff} per metal atom is 4.62 and 3.2 BM respectively. Magnetic susceptibility measurements are irrelevant for the diamagnetic zinc complex. All metals tend to form tetrahedral complexes with dapsone. The low molar conductance values of the complexes indicate their non-ionic nature. From the IR spectra of these complexes, it has been found that the sulphur atom in the S-O group of dapsone co-ordinates with the metal ion.

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