

## Synthesis, characterisation and biological applications of mixed ligand cobalt (II) complexes containing Dithiocarbamates and Diamines

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### ABSTRACT

Dithiocarbamates are highly versatile, mono-ionic chelates that form stable complexes with many transition metals and main group elements. Complexes of cobalt(II) piperidine dithiocarbamate and diamines such as Ethylene diamine, Diethylene triamine and Triethylene tetramine have been synthesised. The complexes have been characterized by IR, UV-Vis and EPR spectral studies, Thermal and magnetic studies. The biological studies on the complexes (Bactericidal, fungicidal and cytotoxicity) indicated promising activities of the complexes.

**Keywords:** Cobalt(II)Pentamethylenedithiocarbamate-En/dien/trien, mixed ligand dithiocarbamate complexes, anti-bacterial, antifungal and anticancer activities.

### 1. INTRODUCTION

Dithiocarbamates ( $R_2CNS_2$  – or  $RHCNS_2$ ) are just one example of the general class of monoionic 1,1-dithiolate ligands which also includes other commonly utilised ligands such as xanthates, carbamates, dithiophosphates and many others [1]. Among the ligands coordinating through sulphur atoms, dithiocarbamates are deserving much attention in recent years, and a large number of dithiocarbamate complexes have been synthesised so far. These compounds are being investigated in order to gain insight into the nature of the sulphur-/metal bond in many biomolecules [2]. Their metal complexes present striking features and have diversified applications, such as high pressure lubricant synthetic intermediates [3], fungicides [4], pesticides and accelerators used in vulcanisation [5]. Dithiocarbamates have invited much research due to their interesting biological, structural, magnetic, electrochemical and thermal properties [2,6-15]. The vast number of dithiocarbamate complexes reported for d-block elements confirms the versatility of the ligand, allowing it to accommodate the varied requirements of the metal involved [16]. In particular, the extensive metal centered electrochemistry of dithiocarbamate complexes and their ability to stabilise a range of oxidation states are important features in their applications, which encompasses material science, medicine and agriculture [2]. Very recently dithiocarbamates have been reported to

act as good ligands for gold surfaces, either in the coating of the nanoparticles or to form monolayers on Au(1 1 1) surfaces [17]. They have been used as anchoring agents (to stabilise) for nanoparticles in recent times [18]. Herein we report the synthesis, characterisation and application of mixed ligand complexes of Co(II) prepared from piperidine based dithiocarbamate and ethylene diamine(en)/ diethylene triamine(dien)/ triethylene tetramine(trien).

### 2. Experimental Section

The chemicals employed for the preparation are of Analar grade and hence used without further purification. The Cobalt chloride hexa hydrate used for the synthesis is of analytical grade. Piperidine, carbon disulphide, Ethylene diamine, diethylenetriamine, triethylenetetraamine are pure grade chemicals from Merck. The chloroform used as solvent in all our studies is distilled by standard procedures.

#### 2.1. Preparation of the complexes $[Co(amine)(Pmdtc)_2]$

The complexes  $[Co(amine)(pmdtc)_2]$  Where amine stands for en/dien/trien were prepared by a two step process as reported in the literature [15].

**Step 1:** Preparation of Pentamethylene dithiocarbamate (pmdtc):

The dithiocarbamate was prepared by adding equimolar volumes of Carbon disulphide to

Piperidine and chloroform with constant stirring under ice cold conditions [2 – 4 °C]. To this was added an equimolar solution of NaOH in water, a white precipitate was obtained. The precipitate was washed with ether and filtered over vacuum and dried.

**Step 2:** Preparation of the complexes [Co(amine)(pmdtc)<sub>2</sub>].

To one equivalent of the metal, added one equivalent of amine (en/dien/trien) and stirred for 5 min. To this added two equivalent of pmdtc and stirred for 20 min. A green precipitate was obtained. This was filtered over vacuum and dried in an oven at 60 °C. The complexes were purified by repeated washings with water, alcohol and recrystallized from chloroform.

The Cobalt present in the complex was estimated using ICP-OES. The nitrogen and sulphur were estimated by Kjeldhal's method and barium sulphate method respectively. TG/DTA were recorded in NETZSCH STA 449F3 thermal analyser with a heating rate of 10°/min in static air atmosphere. Magnetic susceptibility studies were carried out using Vibrating sample magnetometer Lakeshore VSM 7410. UV-Visible absorption spectra were recorded using a Shimadzu UV 1600 model spectrometer. The IR spectrum of the complexes were recorded as KBr disc using Shimadzu Spectrometer. The EPR spectra of the complexes were recorded using JES-FA200 EPR spectrometer in the region from 1000-8000 gauss. The bactericidal and fungicidal activities of the complexes were studied by agar disc diffusion method [19]. The anti-cancer activities were studied using the MTT assay method [20].

### 3. RESULTS AND DISCUSSION

The elemental analysis data on the complexes Table-I confirm the proposed composition [Co(en)(pmdtc)<sub>2</sub>], [Co(dien)(pmdtc)<sub>2</sub>], [Co(trien)(pmdtc)<sub>2</sub>]. All the complexes were found to be completely soluble in chloroform, completely soluble in DMSO on heating and partially soluble in alcohol and practically insoluble in water. The electrical molar conductance of the complexes at a concentration of about 10<sup>-3</sup> M in chloroformic solution was found to be 5-10 Ohm<sup>-1</sup> cm<sup>2</sup> mol<sup>-1</sup> indicating the non-electrolytic nature of the complexes [23]. The thermal analysis data from TGA/DTA on the three complexes are furnished in table 1. The thermograms were run up to 1000°C. The decomposition of the complexes starts around 300°C. The amine complexes decompose to CoS around 720°C and on further decomposition forms CoO around 820°C. The trend is similar in all three complexes. The final residual mass %

obtained around 1000°C in the TG plot corresponds to that of the metal % in the complex. IR spectral data on the complexes are given in table 2. The bands around 3400cm<sup>-1</sup> is assigned to νN-H. The bands around 2930cm<sup>-1</sup> corresponds to νC-H of the piperidine ring while the aliphatic C-H of the amine part appear between 2800cm<sup>-1</sup> and 2900cm<sup>-1</sup>. The bands in the region 1239cm<sup>-1</sup> corresponds to C=S symmetric stretching. The bands in the region 1360cm<sup>-1</sup> corresponds to N-C stretching. The two bands around 890-1010 cm<sup>-1</sup> indicated the coordination of the dithiocarbamate moiety occurred in bidentate fashion and that the dithiocarbamate was monoionic [24]. The electronic spectral data are presented in table 1. The spectra of the complexes show three peaks in the regions 639nm, 425-480nm and 333-393nm. These peaks indicate the presence of an octahedral environment of ligands around the Co(II) ion [22-24]. EPR studies showed a single peak at, g=2.009(en), 1.844(dien), 2.115(trien) confirming the presence of high spin d<sup>7</sup> system of cobalt. The value of g=2.115 in the trien complex gives a clear indication of covalent character of the metal to ligand bond and delocalisation of the unpaired electron into the ligand. The magnetic susceptibility studies of these complexes show an increase in mass in the presence of the magnetic field and the VSM plot of magnetic moment Vs field shows hysteresis loop indicating Ferro magnetism. Observation of loop with a negligible height and the coercivity suggest that these complexes have particles of significantly small size and are magnetically significant.

#### 3.1. Anti- microbial and Anti-Cancer activities

The anti bacterial and anti fungal studies were performed by the disc diffusion method. The data is furnished in table 3 and 4. These compounds are found to possess reasonable antibacterial against Staphylococcus aureus, E. coli, Aeromonas hydrophila and Vibrio spp. The complexes were found to be inactive against Pseudomonas aeruginosa even at a concentration of 1000µg. The complexes are found to show increased activity with increasing concentrations as shown in the table 3. The complexes were found to show an increasing activity when moved from en to dien to trien indicating that the activity is proportional to the ring size. However in the Staphylococcus aureus, the trien analogue is found to show lesser activity than en and dien. The antifungal activity data are furnished in table 4. The en and trien analogues possess considerable fungicidal activity against Candida albicans and Rhizopus spp. The Dien analog was found to be active against Candida albicans at a high concentration and was inactive at lower

concentrations. Except the trien complex, all others were found to be inactive against *Aspergillus niger*.

### 3.2. Anticancer studies

The anticancer activities of these complexes (Figure 1-3) were studied using MTT

assay method on MCF-7 cell line (Breast Cancer). In parallel the activity was tested on VERO cell line(normal cell line). The selectivity index of all the complexes were found to be 4 [Selectivity index =IC<sub>50</sub> for norml cell line /IC<sub>50</sub> for cancerous cell line], indicating considerable activity of the complexes as anticancer agents.

**Table - 1: Elemental composition and Electronic spectral data**

Molecular Weight	Residue % TGA (theo) exp	λmax(nm)	%Co (theo) exp	%s (theo) exp	%N (theo) exp	Complexes
440.93	(16.08) 13.7	639,440, 390	(13.36) 14.18	(29.03) 30.12	(12.70) 12.32	[Co <sub>ii</sub> (en)(pmdtc)2]
483.93	(15.48) 14.1	639,480, 393	(12.17) 12.93	(26.45) 27.02	(14.46) 15.51	[Co <sub>ii</sub> (dien)(pmdtc)2]
526.93	(14.21) 10.7	632,424, 333	(11.18) 11.38	(24.29) 24.93	(15.85) 15.32	[Co <sub>ii</sub> (trien)(pmdtc)2]

**Table - 2: IR spectral data cm<sup>-1</sup>**

vC-S (sym)	vN-C (str)	vC=S (asy)	vC-H (amine)	vC-H (pip)	vN-H (str)	Complexes
1003,871	1358	1238.5	2856	2930.	3421	[Co <sub>ii</sub> (en)(pmdtc)2]
1003,949	1359	1239.5	2856	2930	3433	[Co <sub>ii</sub> (dien)(pmdtc)2]
1003,952	1357	1239.5	2854.	2937	3432	[Co <sub>ii</sub> (trien)(pmdtc)2]

**Table - 3: Anti-Bacterial Studies**

Antibiotic (1mg/ml)	Zone of Inhibition(mm)			Bacteria	Complex
	Concentration(µg/ml)				
	500	750	1000		
7	5	6	8	<i>Staphylococcus aureus</i>	
7	4	5	6	<i>E.coli</i>	
-	-	-	-	<i>Pseudomonas aeruginosa</i>	[Co <sub>ii</sub> (en)(pmdtc)2]
6	5	6	7	<i>Aeromonas hydrophila</i>	
8	4	5	7	<i>Vibrio spp.</i>	
8	6	8	9	<i>Staphylococcus aureus</i>	
8	4	6	7	<i>E.coli</i>	
-	-	-	-	<i>Pseudomonas aeruginosa</i>	[Co <sub>ii</sub> (dien)(pmdtc)2]
8	4	6	8	<i>Aeromonas hydrophila</i>	
7	5	6	8	<i>Vibrio spp.</i>	
7	4	5	6	<i>Staphylococcus aureus</i>	
8	8	9	10	<i>E.coli</i>	
-	-	-	-	<i>Pseudomonas aeruginosa</i>	[Co <sub>ii</sub> (trien)(pmdtc)2]
7	7	8	9	<i>Aeromonas hydrophila</i>	
7	8	9	10	<i>Vibrio spp.</i>	

Table - 4: Anti-Fungal Studies					
Antibiotic (1mg/ml)	Zone of Inhibition(mm)			Fungi	Complexes
	Concentration( $\mu\text{g/ml}$ )				
	500	750	1000		
9	6	7	9	<i>Candida albicans</i>	
5	-	-	-	<i>Aspergillus niger</i>	[Co <sub>ii</sub> (en)(pmdtc)2]
8	5	6	7	<i>Rhizopus spp.</i>	
8	-	-	7	<i>Candida albicans</i>	
7	-	-	-	<i>Aspergillus niger</i>	[Co <sub>ii</sub> (dien)(pmdtc)2]
9	-	-	-	<i>Rhizopus spp.</i>	
7	4	5	6	<i>Candida albicans</i>	
8	-	-	7	<i>Aspergillus niger</i>	[Co <sub>ii</sub> (trien)(pmdtc)2]
8	5	6	7	<i>Rhizopus spp.</i>	

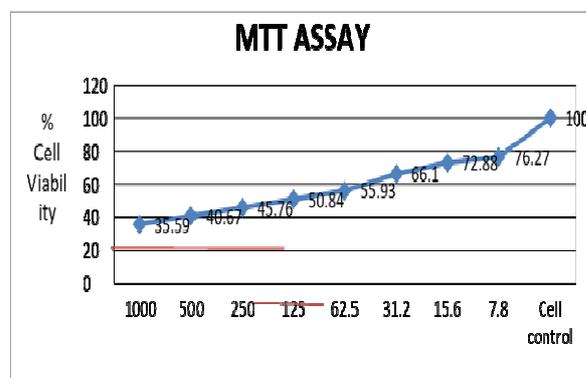


Figure - 1: Anticancer activity of en complex.

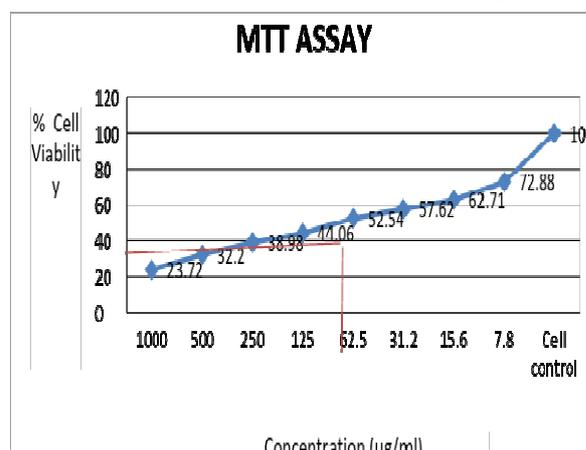


Figure 2: Anticancer activity of dien complex.

#### 4. CONCLUSION

The complexes, from the above elemental and spectral analysis, are proposed to have an octahedral geometry with two dithiocarbamate ligands coordinating in a bidentate fashion through the sulphur atoms and one diamine coordinating through the nitrogen atoms. The antimicrobial studies and the anticancer studies show promising applications in the field of medicines.

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#### 5. REFERENCES

- Coucouvanis D. The chemistry of the dithioacid and 1,1-dithiolate complexes, 1968-1977. **Prog. Inorg. Chem.** 1979; 26: 301-469.
- Bond AM and Martin RL. Electrochemistry and redox behaviour of transition metal dithiocarbamates. **Coord. Chem. Rev.** 1984; 54: 23.
- Joris SJ. On the mechanism of decomposition of dithiocarbamates. **J. Phys. Chem.** 1970; 74: 860.
- Onwudiwe DC and Ajibade PA. Synthesis, Characterization and Thermal Studies of Zn(II), Cd(II) and Hg(II) Complexes of N-Methyl-N-Phenyldithiocarbamate: The Single Crystal Structure of [(C<sub>6</sub>H<sub>5</sub>)(CH<sub>3</sub>)NCS<sub>2</sub>]<sub>4</sub>Hg<sub>2</sub>. **Int.J.Mol.Sci.** 2011; 12: 1964-1978.
- Beer PD. Self assembled dithiocarbamate-copper (ii) macrocycles for electrochemical anion recognition. **Chem. Commun.** 2001; 4: 199-200.
- Elgemeie GH and Sayed SH. Synthesis and Chemistry of Dithiols. **Synthesis**, 2001; 1747.
- Mukerjee AK and Ashare R. Isothiocyanates in the chemistry of heterocycles. **Chem. Rev.** 1991; 91: 1.
- Thermochim and Acta Boas UG. Facile synthesis of aliphatic isothiocyanates and thioureas on solid phase using peptide

- coupling reagents. **Tetrahedron Lett.** 2004; 45: 269.
9. Scarcia V. Palladium and platinum dithiocarbamate complexes containing mono- and diamines. **Polyhedron.** 1999; 18: 2827-2837.
  10. Cavalheiro ETG. Correlation between ionic radius and thermal decomposition of Fe(II), Co(II), Ni(II), Cu(II) and Zn(II)dithiocarbamates. **Thermochim Acta**, 2000; 356: 79 – 84.
  11. Cavalheiro ETG. Correlation between i. r. spectra and thermal decomposition of cobalt(II), nickel(II), copper(II) and mercury(II) complexes with piperidinedithiocarbamate and pyrrolidinedithiocarbamate. **Transition Met.chem.** 2000; 25: 69-72.
  12. Siddiqi KS and Nishat N. Synthesis and Characterization of Succinimide and Phthalevhde Dithiocarbamates and their Complexes with Some Transition Metal Ions., **Synth.React.Inorg.Met.-Org.Chem.** 2000; 30: 1505-1518.
  13. Cesur H. Synthesis, characterization, and spectral and thermal studies of some divalent transition metal complexes of benzylpiperazine dithiocarbamate., **Synth.React.Inorg.Met.-Org.Nano-Met.Chem.** 2001; 31(7): 1271-1283.
  14. Faraglia G. Mixed Pt(ii) and palladium (ii) dithiocarbamate complexes and amines: synthesis , characterisation and cell assay., **J.Inorg.Biochem.** 2001; 83: 31-40.
  15. Nabipour H. Synthesis of a new dithiocarbamate cobalt complex and its nanoparticles with the study of their biological properties. **Intl.J.Nano.dimn.** 2011; 1(3): 225-232.
  16. Hogarth G. Transition Metal Dithiocarbamates: 1978-2003. **Progress in Inorganic Chemistry**; 2005; 53: 71-561.
  17. Morf P and Raimondi. Dithiocarbamates: functional and versatile linkers for the formation of self-assembled monolayers. **Langmuir.** 2006; 22: 658-663.
  18. Edward R. Knight and Multimetallic Arrays. Bi-, Tri-, Tetra-, and Hexametallic Complexes Based on Gold(I) and Gold(III) and the Surface Functionalization of Gold Nanoparticles with Transition MetalsThe use of conductivity measurements in organic solvents for the characterisation of coordination compound. **Inorg. Chem.**, 2009; 48(8): 3866-3874.
  19. Alina A Dobre. Preliminary studies on the antimicrobial activity of essential oils against food borne bacteria and toxigenic fungi; **The Annals of the University Dunarea de Jos of Galati Fascicle VI – Food Technology**, 2011; 35(2): 16-26.
  20. Nasrin yazdanpanahi. Effect of Boswellia Thurifera Gum Methanol Extract on Cytotoxicity and P53 Gene Expression in Human Breast Cancer Cell Line. **Iranian journal of Pharmaceutical Research**; 2014; 13(2): 719-724.
  21. Geary WJ. The use of conductivity measurements in organic solvents for the characterisation of coordination compounds. , **Coord.Chem. Rev.** 1971; (7): 81.
  22. Serrano J. New dithiocarbamate and xanthate complexes of nickel(II) with iminophosphines. **Inorg.Chem.Acta.** 2003; 355: 33-40.
  23. Vuckovic G. Preparation, characterization and redox properties of o,o'-geometrical isomers of  $\mu$ - $\alpha$  and  $\mu$ - $\beta$ -aminoisobuty-rato co(ii) complexes with n,n',n',n'''-tetrakis(2-pyridylmethyl)-1,4,8,11-tetraazacyclotetradecane. **J.Coordination .Chem**, 1997; 42: 241.
  24. Sovili SP and BabicSamardzi. Cobalt(III) Complexes with a Tetraaza Macrocyclic Ligand and Some Heterocyclic Dithiocarbamates. **Syn.React.Inorganic Met.Org.Chem.** 1999; 29: 1655.