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Synthesis, Characterization and Biological Evaluation of Histamine Dithiocarbamate Metal Complexes

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ABSTRACT

A series of novel bidentate dithiocarbamate ligand 2-(-1H-imidazole-4-yl)ethanamine (IEADTC) was prepared by new synthetic method. The synthetic sodium salt of 2-(-1H-imidazole-4-yl) ethanamine (IEADTC) dithiocarbamate ligand is followed by the reaction of Copper and Nickel Chlorides to get corresponding complexes. There forming complexes were characterized by Elemental Analysis, IR, ^{1}H NMR, ESR TGA-DTA and antimicrobial analysis.

INTRODUCTION

There has been intense interest in the coordination compounds of unsaturated sulphur donor chelating ligands, dithiocarbamates, and their related molecules from chemists, physicists, biologists and theoreticians alike owing to their interesting chemical properties and possible wide applications[1-4]. Interest in molecular structural investigations and chemical studies of these metal chelates covers a full gamut of areas ranging from general considerations of metal-sulphur bonding and the formation of four-membered chelate rings to the employment of these ligands in inorganic qualitative analysis[5], their practical application in organic syntheis[6], medicine[7], biology[8], and their uses as vulcanisation accelerators[9], floatation agents, fungicides[10], pesticides[11], radiation protectors[12], antioxidants[13] and photostabilisers of polymers[14]. Their role in material science has also been quite significant. The interesting low spin, high spin crossover phenomenon was first reported in an iron (III) dithiocarbamate complex[15]. There are several metal dithiocarbamate complexes with bridging sulphur centres which are known to participate actively in super exchange phenomenon imparting novel magnetic properties to these systems[16]. In this article, the interesting ligation characteristics of dithiocarbamates and structural features of their various transition metal complexes in general and the coordination chemistry and stereochemistry of complexes in particular, along with the scope of this article covers the relatively unattended aspect of the primary amine derived dithiocarbamates, synthesis, characterization and antimicrobial activity of Copper (II) and Ni (II) complexes of dithiocarbamates.

MATERIALS AND METHODS

Experimental

Copper chloride anhydrous was obtained from Fluka, 2-(-1H-imidazole)ethaneamine and carbon disulfide were purchased from Aldrich. Other chemicals used were of analytical reagent or higher purity grade. Solvents used were of reagent grade and purified before use by the standard methods. Conductivity measurement was carried out by a Systronics Conductivity Bridge 305, using a conductivity cell of cell constant 1.0 double distilled water was used as solvent. Electronic absorption spectra were measured on JASCO UV/VIS-7850 recording spectrophotometer. Infrared spectra were recorded on a JASCO-460 plus FT-IR

spectrophotometer in the range of 4000-400 cm^{-1} in KBr pellets. Micro chemical analysis of carbon, hydrogen and nitrogen for the complexes were carried out on a Herause CHNO-Rapid elemental analyzer. ^{1}H NMR spectra were recorded on a Brucker DRX-500 Advance Spectrometer at 500 MHz in DMSO-discussing tetramethylsillane as internal reference standard. Melting points were measured on a Unimelt Capillary Melting Point Apparatus and reported uncorrected.

Preparation of Sodium salt of dithiocarbamate ligands

0.05 mol of amine was dissolved in 30 ml of absolute alcohol in a clean beaker which was placed in ice bath. To this cold solution add 5 ml of sodium hydroxide (10N) solution, and then add pure carbon disulphide (0.05 ml) drop-wise with constant stirring .The contents were stirred mechanically for about 30 min, sodium salt of dithiocarbamate precipitated out. It was dried over and recrystallized from ethanol.

Preparation of Cu (II) and Ni (II) Complexes,

Synthesis of [Cu ($(IEADTC)_2$)Cl_2]

The aqueous solution of 0.05 mol of Copper Chloride was added with constant stirring to an aqueous solution of 0.01 mol of Sodium salt of 2-(-1H-imidazole-4-yl)ethanamine dithiocarbamate ligand. The reaction mixture was stirred at room temperature for 2 hours. The colored (yellow) precipitates were obtained. The precipitates were filtered and washed with water and then with methanol and dried over calcium chloride in desiccator's Yield: 78% and decomposes at $110^{0}C$.

Anal. Calcd. For C, 25.94; H 4.35; N, 6.05; Cl, 15.35; Cu, 13.73; Found: C, 24.92; H, 3.96; N, 5.9; Cl, 14.35; Cu, 12.98

Synthesis of [Ni (IEADTC)Cl_2]

The aqueous solution of 0.05 mol of Nickel Chloride was added with constant stirring to an aqueous solution of 0.01 mol of Sodium salt of 2-(-1H-imidazole-4-yl)ethanamine dithiocarbamate ligand in the presence of small quantity of triethylamine. The reaction mixture was stirred at room temperature for 2 hours. The colored (light green) precipitates were obtained.

The precipitates were filtered and washed with water and then with methanol and dried over calcium chloride in a desiccators. Yield: 80% and decomposes at 110^0 C.

Anal. Calcd. For C, 26.43; H, 4.44; N, 6.17; Cl, 15.60; Mn, 12.09 Found: C, 25.53; H, 4.4; Cl, 15.2; Ni, 11.99; N, 5.99.

RESULTS AND DISCUSSION

The solid reflectance spectra data for the Cu and Mn of 2- amino 2- methyl 1-propanol metal complexes. The **[Cu ((IEADTC)$_2$)Cl$_2$]** and **[Ni (IEADTC)Cl$_2$]** complexes exhibit magnetic property and has an electronic spectrum which can be assigned to low spin Cu (II) and Ni (II) in an Octahedral Environment. Intra ligand electronic transition is then…C…S…S and S…C…S chronophers of the dithiocarbamate moiety .Thus the peak at 646 nm and the shoulder at 499 nm arise from 1A1g_1T1g and 1A1g_ 1T2g transitions, respectively. The other lower peaks are probably charge-transfer in origin.

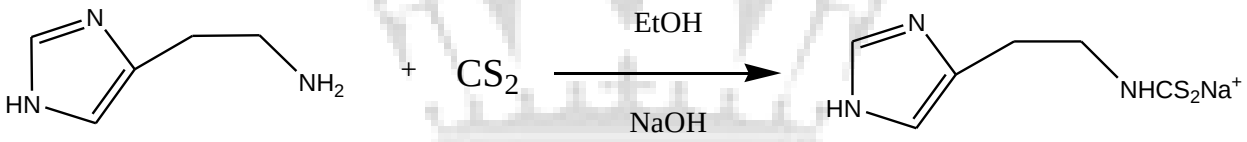
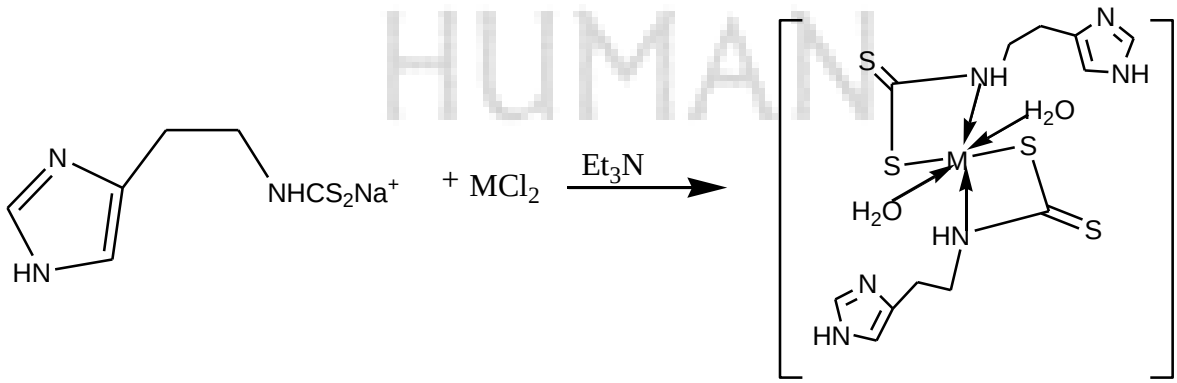


Figure 1



M= $CuCl_2$, $MnCl_2$

Figure 2

Infrared Spectrum

Two regions in the IR spectrum of the **[Cu ((IEADTC)$_2$)Cl$_2$]** and **[Ni (IEADTC)Cl$_2$]** complexes have proven valuable in arguments concerning the electronic and structural characteristics of this compound. The presence of the thiourid band between 1545-1430 cm^{-1} suggests a considerable double bond character in the C…N bond vibration of the S_2C-NR_2 group. The band present in the 967 cm^{-1} range is attributed to the prevailing contribution of (C…S) vibrations. These ranges have been used defectively in differentiating between monodentate, bidentate dithiocarbomate ligands. The presence of only one strong band supports bidentate coordination of the dithioligands, where as a doublet is expected in the case of monodentate coordination. The (C…S) and (C...N) stretching frequencies fall in the 1035 cm^{-1} (1001 cm^{-1} for the free ligand) and 1478 cm^{-1} respectively. The methyl group in the complex, as medium strong bands in the 2960 cm^{-1} range can be related to the asymmetric CH_3 stretching vibration.

^{1}H-NMR Spectra

The NMR spectrum of the **[Cu ((IEADTC)$_2$)Cl$_2$]** and **[Ni (IEADTC)Cl$_2$]** complexes showed at 2.3-2.4 ppm, which may be assigned to the hydroxyl protons. The peak at 7.9-7.98 attributed to NH protons of thiourid nitrogens in both complexes. Other signals are also appeared in the region 0.98, 1.5, 3.8 ppm.

Antimicrobial Activity

Antimicrobial test was performed on four bacterias (*Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa*) and two fungus (*Candida albicans* and *Candida tropicalis*). The media used were prepared by dissolving separately 2 g of the nutrient broth powder and 38 g of the Mueller Hinton agar powder in 250 ml and 1 L of deionized water, respectively. The two media were sterilized in an autoclave at 121^{0}C for 15 minutes and then stored overnight in a refrigerator after cooling. Cultures of the microorganisms were prepared in sterile nutrient broth and incubated for 24 hours at 37^{0}C for the bacteria and at 27^{0}C for the fungi. 0.1 ml of each of the overnight cultures in sterile test tubes with caps was made up to 10 ml with 9.9 ml of sterile deionized water to give 1:100 or 10-2 dilution of the microorganisms. The technique used for the study was agar-well diffusion. Solutions of concentration 10 mg/ml of the compounds were made in dimethylsulphoxide (DMSO). DMSO was also used as the

negative control. The positive controls for bacteria and fungi were discs of commercial antibiotics manufactured by Abtek Biological Limited and Fluconazole dissolved in DMSO. The discs were carefully placed on the inoculated media with the aid of sterile forceps. The plates inoculated with bacteria were incubated at 37^0C for 24 hours, and those inoculated with fungi were incubated at 27^0C for 72 hours. Afterwards, the zones of inhibition of microbial growth that appeared around the wells of the compounds were examined and the diameters measured and recorded in millimeters (mm). Antimicrobial activity of the Cu (II) and Ni (II) complexes was evaluated *in vitro* against Gram positive bacteria- *Staphylococcus aureus and Bacillus subtilis*, Gram negative bacteria- *Escherichia coli*, *Pseudomonas aeruginosa*, and fungi, *Candida albicans, Candida tropicalis*. The results for the complexes and commercial antibiotics used as positive controls are listed in (Table 1).

Table No. 1

Growth inhibition zone in millimeters (mm)						
	Bacteria				**Fungi**	
	Gram +Ve		**Gram -Ve**			
	S.aur	***B. subt***	***E. coli***	***P. aerug***	***C. alb***	***C. trop***
[Cu((IEADTC)$_2$)Cl$_2$]	14	14	15	14	14	15
[Ni ((IEADTC)$_2$)Cl$_2$]	13	15	14	114.5	16	14
FLU			-----	----	15	15
DMSO	12	14	15	16	----	---

CONCLUSION

Cu (II) and Ni (II) complexes of 2-(-1H-imidazole-4-yl)ethanamine (IEADTC)dithiocarbamate have been synthesized and characterized. The ligand moiety exhibits a bidentate coordination mode in the Cu (II) and Ni (II) complexes. Solid reflectance spectra and magnetic data indicate that the complexes are Paramagnetic and Octahedral. The complexes show selective activity towards some of the test microorganisms.

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