

Synthesis and physicochemical studies of copper complex of lansoprazole

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ABSTRACT

Copper (II) complex has been synthesized with Lansoprazole 2 [[[methyl -4 (2,2,2 trifluoroethoxy) 2-pyridinyl] methyl] sulfinyl] -1H-benzimidazole] (L) which is an antiulcerative drug. Complex has been characterized by elemental analysis, conductivity measurement, IR and NMR spectral studies. The molar conductance measurement of the complex in DMSO indicates that the complex is non ionic in nature. Spectral measurements showed that the ligand co-ordinates to metal ion through benzimidazole ring. The results show that ligand acts as bidentate and indicate square planar geometry of the metal complex.

Key words: Copper complex, Lansoprazole, synthesis.

INTRODUCTION

Investigations are going on the formation of metal complexes with benzimidazole ligand. Benzimidazole and its derivatives play an important role in analysis and in several biological reactions. Benzimidazole derivatives exhibit antibacterial, antihelmintic and insecticidal activities¹⁻³. Transition metal complexes containing benzimidazole are widely used as catalysts for hydrogenation, hydroformylation, oxidation and others reactions⁴⁻⁶. The present paper discusses the synthesis and characterization of Cu(II) with 2 [[[methyl – 4 (2,2,2 trifluoroethoxy) 2 – pyridinyl] methyl] sulfonyl] – 1H – benzimidazole] [L].

EXPERIMENTAL

Pure sample of lansoprazole molecular formula $C_{16}H_{14}F_3N_3O_2S$ and molecular weight 369.36 was obtained from Cipla Pharmaceuticals Ltd.

Mumbai. Metal salt $CuCl_2 \cdot 2H_2O$ was of Merck chemicals. Melting point of Lansoprazole is 166°C. The solvents used were distilled water and acetone. All chemicals were of Analytical Grade. The elemental microanalyses of C, H, and N for ligand were carried out with Thomas and Coleman Analyzer Carlo Erba 7106. The percentage of elements in ligand are calculated to be C = 52.02, N = 11.3 and H = 3.82 while the experimentally determined values are found to be C = 52.71, N = 11.05 and H = 3.51.

Ligand-metal Ratio

20ml of the ligand (0.01 M) was diluted to 200 ml using 60% acetone and titrated against $CuCl_2 \cdot 2H_2O$ (0.02 M) solution prepared in 60% acetone. Conductance was recorded after each addition of metal salt. Graph is plotted between corrected conductance and volume of metal salt added. From the equivalence point in the graph, It has been concluded that the complex formation of

the ligand with Copper takes place in the ratio 2:1 (L:M) Stability constant and free energy change were also calculated by using Job's method of continuous variation⁷ modified by Turner and Anderson⁸.

Synthesis of complex

For the synthesis of complex of Lansoprazole-copper, 2 mol of the ligand was dissolved in 100ml of acetone – water mixture (60:40) and added slowly to a solution 1mol of copper chloride solution(solvent acetone–water (60:40) mixture). The mixture was refluxed for 3 hours, cooled and filtered . A brown colored crystalline complex was separated. The complex was washed with acetone – water mixture ,dried and weighted (yield 32%) and melting point was recorded.

RESULTS AND DISCUSSION

The synthesized complex is colored and stable. It is soluble in DMF and DMSO and insoluble

in all other organic solvents. Analytical data and conductometric studies suggest 2:1 [L:M] ratio for Lansoprazole-Cu complex. The low value of molar conductance ($9.20 \text{ ohm}^{-1} \text{ cm}^2 \text{ mol}^{-2}$) suggests non-electrolytic nature of complex. Analytical data of this complex is in agreement with the composition $(\text{C}_{16}\text{H}_{18}\text{F}_3\text{N}_3\text{O}_2\text{S})_2\text{Cu}$.

The IR spectra⁹⁻¹³ of ligand and complex have been recorded and the probable assignments are given in Table 2. In the IR spectra of ligand band appearing at 3456 cm^{-1} due to NH stretching remains unaffected in the complex indicate non involvement of imino nitrogen . The shift of the $\nu\text{C} = \text{N}$ and $\nu\text{S} = \text{O}$ by $10\text{-}15\text{ cm}^{-1}$ in the complex indicates that these groups are involved in the complexation The band at 1038 cm^{-1} in the ligand is due to aromatic sulfoxide stretching shifted to 1056 cm^{-1} in the complex which indicates the involvement of oxygen of sulfoxide in complex formation. The next IR band of structural significance of the ligand appears at 1587 cm^{-1} which may be assigned to $\nu\text{C} = \text{N}$ is shifted downward at 1579

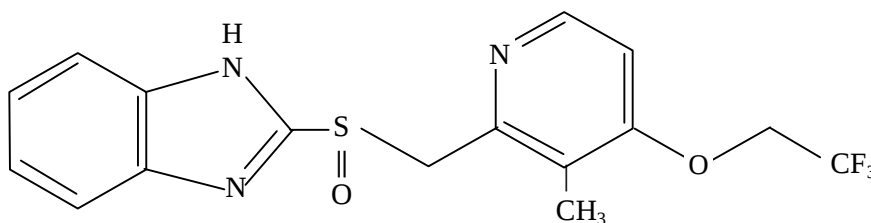


Fig. 1: Structure of lansaprazole

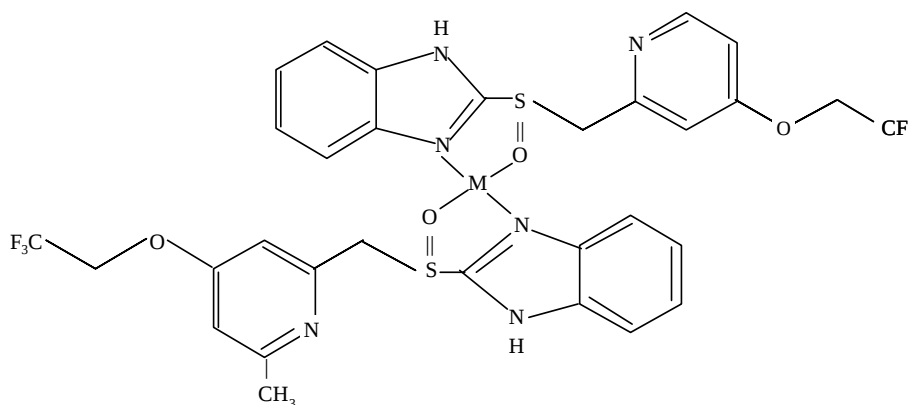


Fig. 2: Structure of Lansoprazole-copper Complex

Table 1: Analytical data of Lansoprazole-Cu Complex

S. No.	Composition of Complex (m-wt.)	Colour	Yield %	m.p.	Elemental Analyses (%) : Found (Cal)			
					C	H	N	M
1	C ₁₆ H ₁₄ F ₃ N ₃ O ₂ S (369.36)	White		177°C	52.71	3.05	11.05	-
2	(C ₁₆ H ₁₄ F ₃ N ₃ O ₂ S ₂) ₂ Cu (802.22)	Brown	32	210°C	47.52 (47.91)	3.10 (3.51)	10.20 (10.47)	7.21 (7.91)

Table 2 : IR Absorption data of the complex in cm⁻¹

Ligand and complex	$\nu(\text{NH})\text{cm}^{-1}$	$\nu(\text{C} = \text{N}) \text{cm}^{-1}$	$\nu(\text{S} = \text{O})\text{cm}^{-1}$	$\nu(\text{M-N})\text{cm}^{-1}$	$\nu(\text{M-O})\text{cm}^{-1}$
Ligand (C ₁₆ H ₁₄ F ₃ N ₃ O ₂ S)	3456	1587	1038	-	-
Complex (C ₁₆ H ₁₄ F ₃ N ₃ O ₂ S ₂) ₂ Cu	3452	1579	1056	465	797

cm⁻¹ in the complex. The linkage through azomethine nitrogen atom was further supported by the appearance of a band in the far IR region at 465 cm⁻¹ in the complex that may be assignable to M-N frequency. Additional bands in the complex in the region 797 cm⁻¹ compared with IR spectra of free ligand has tentatively been assigned to (M-O) and new band appeared at 1380 cm⁻¹ in the complexes might be due to chelate ring formation in complex.

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