Metal Complexation Studies of 1-(4-Carboxy-3-hydroxy-*N*-methyl phenyl- amino methyl) 2-methyl perimidine

UMANG N. PATEL and ARUN SINGH*

Department of Chemistry,
Govt. Geetanjali P.G. Girls College, Bhopal, India.
dr.arunsingh@rediffmail.com

Received 16 February 2009; Accepted 22 April 2009

Abstract: Aminomethylation of 2-methyl perimidine was carried out by treating 2-methyl perimidine with formaldehyde and 4-aminosalicylic acid. The resultant compound was designed as 1-(4-carboxy-3-hydroxy-*N*-methyl phenylamino methyl)2-methyl perimidine. The transition metal complexes of Cu^{2+} , Co^{2+} , Ni^{2+} , Mn^{2+} and Zn^{2+} have been prepared and characterized by elemental analysis, spectral studies, magnetic moment determination, molar conductivity measurement and antimicrobial activity.

Keywords: 2-Methyl perimidine, 4-Aminosalicylic acid, Metal complexes, Magnetic moment, Antibacterial, Antifungal activity.

Introduction

Perimidine derivatives are of wide interest because of their diverse biological activities and chemical application. Several classical synthetic methods have been reported for synthesis of perimidine derivatives. The most widely used method for preparation of perimidine is the cyclocondensation reaction of 1,8-diaminonaphthalene with carboxylic acids under reflux condition microwave irradiation¹⁻¹⁴. Parity to this heterocyclic system say benzotriazole find wide use in medicine, agriculture and industry. The perimidine have active H atom at 1 position. If mannich reaction of perimidine with amino functionalized ligand say 4-aminosalicylic acid affect a novel ligand. Hence it was thought to undertake such mannich reaction of perimidine with PAS. Thus the present paper composes the synthesis, characterization and chelation property of a novel ligand having perimidine and PAS moiety. The research work is scanned in Scheme 1.

Experimental

2-Methyl perimidine was prepared by reported method¹⁵. All other chemicals used were of analytical grade.

Synthesis of 1-(4-carboxy-3-hydroxy-N-methyl phenylamino methyl)2-methyl perimidine

A mixture of 2-Methyl perimidine (0.02 mole), formaldehyde (0.02 mole) and 4-aminosalicylic acid was (0.02 mole) in ethanol (70 mL) was heated under refluxed for 4 h. Subsequently, ethanol was distilled off and the lump mass obtained. It was triturated with petroleum ether (40-60 °C). The solid designated as CMPP was isolated and dried in air. Yield was 78%. Its m.p was 173 °C. (Uncorrected).

Elemental analysis

C₂₀H₁₇N₃O₃ (347 g/mol)

	C%	H%	N%
Calculated:	69.16	4.89	12.10
Found:	69.10	4.80	12.00

IR Features: 1485-1522 cm⁻¹ Perimidine ring

3032,1502,1600 cm⁻¹ Aromatic
1683 cm⁻¹ CO of COOH
3200-3600 cm⁻¹ OH
2850, 2920 cm⁻¹ CH₂

NMR 7.1-7.7 ppm Multiplet aromatic

(DMSO) 2.57 ppm (2H) Singlet CH₂
10.0 ppm (1H) Singlet (COOH)
3.9 ppm (1H) Singlet (OH)
Not predicted (1H) NH

TGA Initial Weight loss: 13 %
Theoretical: 12.68 % (decarboxylation)

Synthesis of metal complexes of CMPP

Formation of CMPP metal complexes

The Cu²⁺, Co²⁺, Ni²⁺, Mn²⁺ and Zn²⁺ metal ion complexes of CMPP have been prepared in a similar manner. The procedure is as follow.

To a solution of CMPP (0.1 mole) in ethanol-acetone (1:1) mixture (150 mL), 0.1 N KOH solution was added drop wise with stirring. The pasty precipitates were obtained at neutral pH. These were dissolved by addition of water up to clear solution. It was diluted to 250 mL of the stock solution (which contains 0.01 mL CMPP) was added drop wise to the solution of metal salt (0.005 mole for divalent metal ions) in water at room temperature. Sodium acetate or ammonia was added up to complete precipitation. The precipitation was digested on water bath at 80 °C for 2 h. The digested precipitates of complex were filtered washed with water and air dried. It was amorphous powder. Yield was almost quantitative. The details are given in Table 1.

Table 1. Analytical data of the metal chelates of CMPP.

Compound	Empirical Formula	Mol. Cal g/mole	Yield %	Elemental Analysis, %							
				C		H		N		M	
				Calcd	Found	Calcd	Found	Calcd	Found	Calcd	Found
CMPP	C ₂₀ H ₁₇ N ₃ O ₃	347	78	69.16	69.10	4.89	4.80	12.10	12.00	-----	-----
[CuCMPP (H ₂ O) ₂]	C ₄₀ H ₃₂ N ₆ O ₆ Cu ²⁺ 2(H ₂ O)	791.54	55	60.64	60.61	4.04	4.00	10.64	10.00	8.02	8.00
[CoCMPP (H ₂ O) ₂]	C ₄₀ H ₃₂ N ₆ O ₆ Co ²⁺ 2(H ₂ O)	786.93	51	60.99	60.00	4.06	3.99	10.67	10.55	7.48	7.40
[NiCMPP (H ₂ O) ₂]	C ₄₀ H ₃₂ N ₆ O ₆ Ni ²⁺ 2(H ₂ O)	786.69	53	61.01	61.00	4.06	3.55	10.67	10.00	7.46	7.39
[MnCMPP (H ₂ O) ₂]	C ₄₀ H ₃₂ N ₆ O ₆ Mn ²⁺ 2(H ₂ O)	782.93	56	61.30	61.28	4.08	3.98	10.72	10.00	7.01	6.99
[ZnCMPP (H ₂ O) ₂]	C ₄₀ H ₃₂ N ₆ O ₆ Zn ²⁺ 2(H ₂ O)	793.39	59	60.49	60.35	4.03	3.85	10.58	10.50	8.24	8.20

Measurements

The elemental analysis for C, H and N were carried out on elemental analyzer. IR spectra of CMPP and its metal complexes were scanned on a Nicolet 760 FTIR spectrophotometer in KBr. The metal content of the metal chelate were performed by decomposing a weighed amount of each metal complexes followed by EDTA titration as reported in literature¹⁶. Magnetic susceptibility measurement of all the metal complex was carried out at room temperature by the Gouy method. Mercury tetrathiocyanatocobaltate(II) Hg [Co (NCS)₄] was used as a calibrant. The diffused reflectance spectra of solid metal complex were recorded on a Backman DK Spectrophotometer with a solid reflectance attachment, MgO was employed as the reflectance compound.

Antifungal activity

The fungicidal activities of all the compounds were studied at 1000 ppm concentration *in vitro*. Plant pathogenic organisms listed in Table 3 were used. The antifungal activity of all the samples was measured by cup plate method¹⁷. Each of the plant pathogenic strains on a potato dextrose agar (PDA) medium contained potato 200 g, dextrose 20 g, agar 20 g and water 1 litre, 5 days old culture were employed. The compounds to be tested were suspended (1000 ppm) in a PDA medium and autoclaved for 15 min. at 15 atm pressure. These medium were poured into sterile Petri plate and the organisms were incubated after cooling the Petri plated. The percentage inhabitation for fungi was calculated after 5 days using the formula give below.

$$\text{Percentage of Inhibition} = \frac{100 (X-Y)}{X}$$

Where X: Area of colony in control plate

Y: Area of colony in test plate

The fungicidal activity all compounds are shown in Table 3.

Results and Discussion

The parent ligand CMPP was an amorphous yellow powder, soluble in various solvents like dioxane, DMSO and DMF. The results of elemental analysis of the ligand are reported in Table 1. They are consistent with the predicted structure as shown in Scheme 1.

Examination of IR spectrum (not shown) of CMPP reveals that a broad band of phenolic hydroxyl stretching is observed at 3200-3600 cm⁻¹ as well as additional absorption bands at 3030 cm⁻¹, 1500 and 1600 are characteristics of the salicylic acid^{18,19}. The strong bands at 1680 cm⁻¹ for C=O. The NMR data (shown in experimental part) also confirm the structure of CMPP. The metal complex of CMPP with the metal ions Cu²⁺, Co²⁺, Ni²⁺, Mn²⁺, and Zn²⁺ vary in colours. On the basics of the proposed structure as shown in Scheme 1, the molecular formula of the CMPP ligand is C₁₅H₁₄N₄O₃ which upon complexion coordinates with one central metal atom at four coordination sites and with two water molecules. Therefore the general molecule formula of the resulting metal complex is [C₃₀H₂₆N₈O₆] M 2(H₂O) for divalent metal ions. This has been confirmed by results of elemental analysis of all the five metal chelate and their parent ligand. The data of elemental analysis reported in Table 1 are in arrangement with the calculated values of C, H and N based on the above mentioned molecular formula of parent ligand as well as metal complex.

Inspection of IR spectra (not shown) of metal complexes reveals that all the spectra are identical in all respects. The comparison of IR spectrum of the parent ligand CMPP with that of its each metal complex has revealed certain characteristics differences.

One of the significant differences to be expected between the IR spectrum of the parent ligand and its metal complex is the presence of more broadened bands in the region of 3200-3600 cm^{-1} for the metal complex as the oxygen of the O-H group of the ligands forms a coordination bond with the metal ions¹⁸⁻²⁰. This is explained by the fact that water molecules might have strongly absorbed to the metal chelate sample during their formation.

Another noticeable difference is that the bands due to the COO^- anion at 1600 cm^{-1} in the IR spectrum of the each metal complex. The band at 1400 cm^{-1} in the IR spectrum of CMPP assigned to in plane OH determination¹⁸⁻²⁰ is shifted towards higher frequency in the spectra of the metal complex due to the formation of metal oxygen bonds. This has been further confirmed by a weak bands at 1105 cm^{-1} corresponding to C-O-M stretching¹⁸⁻²⁰. Thus all of these characteristics features of the IR studies suggested the structure of the metal complex as shown in Scheme 1.

Scheme 1

Examination of data of the metal content in each compound revealed a 1:2 metal:ligand (M:L) stoichiometry in all of the complex of divalent metal ions. Magnetic moment (μ_{eff}) of each of the metal complex is given in Table 2. Examination of these data reveals that all complexes other than that of Zn^{2+} are paramagnetic while those of Zn^{2+} are diamagnetic.

Table 2. Magnetic moment & reflectance data of the metal complexes.

Complex	Magnetic moment μ_{eff} (B.M)	Absorption band, cm^{-1}	Transitions
Cu-CMPP	1.95	22279	C.T
		15430	${}^2\text{B}_{1g} \rightarrow {}^2\text{A}_{1g}$
Ni- CMPP	3.82	20333	${}^3\text{A}_{2g} \rightarrow {}^3\text{T}_{1g}$ (P)
		14471	${}^3\text{A}_{1g} \rightarrow {}^3\text{T}_{1g}$ (F)
Co- CMPP	4.42	26811	${}^4\text{T}_{1g}$ (F) $\rightarrow$ ${}^4\text{T}_{2g}$ (F)
		15786	${}^4\text{T}_{1g}$ (F) $\rightarrow$ ${}^4\text{A}_{2g}$
		8975	${}^4\text{T}_{1g}$ (F) $\rightarrow$ ${}^4\text{T}_{2g}$ (P)
Mn- CMPP	4.86	24240	${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{1g}$ (4Eg)
		18320	${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{2g}$ (4G)
		16730	${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{1g}$ (4G)
Zn- CMPP	Diamagnetic	-----	-----

The diffuse electronic spectrum of the $[\text{CuCMPP}(\text{H}_2\text{O})_2]$ metal complex shows broad bands at 15430 and 22279 cm^{-1} due to the ${}^2\text{B}_{1g} \rightarrow {}^2\text{A}_{1g}$ transition and charge transfer, respectively suggesting a distorted octahedral structure²³⁻²⁵ for the $[\text{CuCMPP}(\text{H}_2\text{O})_2]$ complex. Which is further confirmed by the higher value of μ_{eff} of the $[\text{CuCMPP}(\text{H}_2\text{O})_2]$ complex. The $[\text{NiCMPP}(\text{H}_2\text{O})_2]$ complex gave two absorption bands at 14471, 20333 corresponding to ${}^3\text{A}_{2g} \rightarrow {}^3\text{T}_{1g}$ (P) and ${}^3\text{A}_{1g} \rightarrow {}^3\text{T}_{1g}$ (F) transitions. $[\text{CoCMPP}(\text{H}_2\text{O})_2]$ complex gave three absorption bands at 15786, 26811 cm^{-1} . Thus absorption bands at 26811, 15688 and 8975 cm^{-1} corresponding to ${}^4\text{T}_{1g}$ (F) $\rightarrow$ ${}^4\text{T}_{2g}$ (F), ${}^4\text{T}_{1g}$ (F) $\rightarrow$ ${}^4\text{A}_{2g}$, ${}^4\text{T}_{1g}$ (F) $\rightarrow$ ${}^4\text{T}_{2g}$ (P) the diffuse, reflectance spectra and the value of the magnetic moments (μ_{eff}) indicate an octahedral configuration for the $[\text{NiCMPP}(\text{H}_2\text{O})_2]$ and $[\text{CoCMPP}(\text{H}_2\text{O})_2]$ complex. The spectra of $[\text{MnCMPP}(\text{H}_2\text{O})_2]$ shows weak bands at 16730, 18320 and 24240 cm^{-1} assigned to the transitions ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{1g}$ (4G), ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{2g}$ (4G) and ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{1g}$ (4Eg) respectively suggesting an octahedral structure for the $[\text{MnCMPP}(\text{H}_2\text{O})_2]$ chelate. As the spectrum of the $[\text{ZnCMPP}(\text{H}_2\text{O})_2]$ is not well resolved, it is not interpreted but its μ_{eff} value shows that it is diamagnetic as expected.

The antifungal activity of all the compounds measured for various plant pathogens. Inspection of the result shown in Table 3 indicates that all compounds are good toxic for fungi. Out of all the compounds copper chelate is more toxic than other. These compounds almost inhibit the fungi about 70%. Hence produced metal chelate can be employed as garden fungicides.

Table 3. Antifungal Activity of Ligand CMPP and its metal complexes.

Sample	Zone of inhibition of fungus at 1000 ppm, %				
	PE	BT	N	T	RN
(CMPP)- Mn^{2+}	61	72	68	72	70
(CMPP)- Co^{2+}	63	62	78	70	71
(CMPP)- Ni^{2+}	68	73	70	73	74
(CMPP)- Cu^{2+}	82	79	81	86	78
(CMPP)- Zn^{2+}	62	65	70	74	71
CMPP	63	66	60	60	65

PE= *Penicillium expansum*, BT= *Botrydepladia thiobromine*, N=*Nigrospra sp.*, T= *Trichothesium sp.*
RN= *Rhizopus nigricans*

References

1. Caliendo G, Carlo R, Meli R, Perissutti, Santagada V, Silipo C and Vittoria A, *Eur J Med Chem.*, 1993, **28**, 969.
2. Bu X, Deady LW, Finaly G J, Baguley B C and Denny W A, *J Med Chem.*, 2001, **44**, 2004.
3. Di-martino J L, Jacquault P, Bazureau J P and Hamelin J, *Bull Soc Chimique*, 1996, **133**, 587.
4. Hendrickson J B and Hussoin M S, *J Org Chem.*, 1987, **52**, 4137.
5. Morita N, Dickstein J I and Miller S I, *J Chem Soc Perkin Trans.*, 1979, **1**, 2103.
6. Deady L W and Rodemann T, *J Heterocycl Chem.*, 1998, **35**, 1417.
7. Caddick S, *Tetrahedron*, 1993, **51**, 1403.
8. Foroughifar N, Mobinikhaledi A and Fathinejad Jirandehi H, *Phosphorus, Sulfur and Silicon and the Related Elements*, 2003, **178**, 1241.
9. Langa F de La Cruz P, de La Hoz A, Diaz-Ortiz A and Diez-Barra E, *Contemp Org Synth.*, 1997, **4**, 373.
10. Varma R S, *Green Chem.*, 1999, **1**, 43.
11. Foroughifar N, Mobinikhaledi A and Fathinejad Jirandehi H and Memar S, *Phosphorus, Sulfur and Silicon and Silicon and the Related Elements*, 2003, **178**, 1269.
12. Bose A K, Banik B K, Lavlinskaia N, Jayaraman M and Manhas M S, *Chemtech.*, 1997, **27**, 18.
13. Foroughifar N and Mobinnikhaledi A, *Asian J Chem.*, 2002, **14**, 614.
14. Mobinikhaledi A and Foroughifar N, *Phosphorus, Sulfur and Silicon and Silicon and the Related Elements*, 2004, **179**, 1175.
15. Mobinikhaledi A, Amrollahi M A, Foroughifar N and Fathinejad jirandehi H, *Asian J Chem.*, 2005, **17**(4), 2411.
16. Radjohn N, *Org Synthesis*, Coll. Vol. IV Willey & Sons N.Y, 1963.
17. Baily W R and Scott E G, *Diagnostic Microbiology*, The C.V. Moshy Co. St. Lovis 1966, 257.
18. Silverstein R M, *Spectrometric Identification of Organic Compounds*, 5th Edn. John Wiley, 1991.
19. Kemp W, *Orgnatic Spectroscopy*, ELBS. Macmillan' UK, 1998.
20. Nakamoto K, *Infrared Spectra of Inorganic and Coordiantion Compound*, Wiley NY 1970.
21. Lever ABP, *Inorganic Electronic Spectroscopy*, Elsevir NY, 1968.
22. Figgis B N, *Introduction to Ligands Field*, Wiley Estern Ltd. NY 1976.
23. Carlin R N and Van Dryneveldt A, J, *Magnetic properties of Transition Metal Compound*, Springe- Verlag, NY, 1997.