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SYNTHESIS OF P-METHOXY ISONITROSO ACETOPHENONE (P-MINAP) WITH TRANSITION METAL ION CU(II), CO(II), NI(II), FE (II) AND FE (III) FOR COMFORT STRAINS OF RESISTANCE MICRO-ORGANISMS

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ABSTRACT

The metal complexes of transition metal Cu(II), Co(II), Ni(II), Fe (II) and Fe (III) where synthesized by using p-methoxy isonitroso acetophenone (P-MINAP). The newly synthesized complexes where characterized by element analysis, Infrared Spectra (IR), Nuclear Magnetic Resonance Spectra (NMR) and Magnetic properties. On the basis of these studies complexes have octahedral geometry. Antibacterial and antifungal activity of these ligand and complexes where determine against E. coil, S. aureus, P. aeruginosa, B. subtilis, B. cereus, K. pneumonae, C. albicans, A. niger, Fusarium oxysporium. Invitro antibacterial and antifungal screening of these compounds relived that most of the compounds exhibited potted inhibited potential activity.

KEYWORDS: -p-MINAP, Cu(II), Co(II), Ni(II), Fe (II), Fe (III), IR, NMR, Magnetic Susceptibility, Octahedral geometry.

INTRODUCTION

Transition metal complexes of bidentate oxime have been the most widely studied co-ordination compound in the past few years due to their unusual magnetic properties, novel structural feature and relevance to biological system.[1-3] With significant development in the field of biological activity of metal chelates plays vital role in the causes and treatment of Cancer.[4-5] The ligand p-bromoisonitrosoacetophenone (p-BrINAP) and p-chloroisonitrosoacetophenone (P-ClINAP) have also been studied for few transition metals.[6-7]

However, structural studies of the complexes of Transition metals with p-methoxy isonitroso acetophenone have not been reported so far. The present paper describes the synthesis and characterization of complexes of Transition metals Cu(II), Co(II), Ni(II), Fe (II) and Fe(III) with p-methoxy isonitroso acetophenone on the basis of elemental analysis, IR Spectra, NMR Spectra, Magnetic properties and Antimicrobial activity.

Experimental Section

All the chemicals used were of A.R. grade. The basic principle underlying this preparation is that of Claisen rearrangement.[5] The ligand p-Methoxy isonitroso acetophenone (P-MINAP) is commercially available in the market. It was synthesized by dissolving 11.5 g of sodium in 230 ml of absolute alcohol and to these solution small portions of 58 ml amyl nitrate and 65 ml of p-Methoxy acetophenone was added with constant stirring and cooling in the freezing mixture containing ice and sodium chloride at about 0^oC. The mixture was kept for three days in a well Stoppard bottle in a refrigerator. At the end of this time, the yellowish green color mixture of sodium salt was obtained. It was filtered and dried in air. The dried sodium salt was dissolved in minimum quantity of ice cooled water and treated with equal volume of water-ethanol mixture. Precipitated p-methoxy isonitroso acetophenone was then filtered through suction and dried in vacuum .The crude product was recrystallized from benzene. Its melting point was found to be 299 ^{0}C.

Preparation of Cu (p-MINAP)$_2$ complex

1:2 stoichiometric ratios of Copper Nitrate and (p-MINAP) were dissolved in minimum quantity of absolute alcohol and equal volume of distilled water. The copper nitrate solution was added to the reagent solution drop wise with constant stirring. The pH of the resultant solution was adjusted to 6 –7 with HCl / NH_4OH. A pinkish colored complex thus formed was digested on water bath for several hours; it was filtered, washed with distilled water& dried. It was recrystallized from chloroform and finally analyzed for copper, carbon, hydrogen and nitrogen.

Preparation of Co (p-MINAP)$_2$ complex

1:2 stoichiometric ratios of Cobalt Nitrate and (p-MINAP) were dissolved in minimum quantity of absolute alcohol and equal volume of distilled water. The cobalt nitrate solution was added to the reagent solution drop wise with constant stirring. The pH of the resultant solution was adjusted to 5 –5.5 with HCl / NH_4OH. A pinkish colored complex thus formed was digested on water bath for several hours; it was filtered, washed with distilled water& dried. It was recrystallized from chloroform and finally analyzed for cobalt, carbon, hydrogen and nitrogen.

Preparation of Ni (p-MINAP)$_2$ Complex

1:2 stoichiometric ratios of nickel acetate hydrated and (p-MINAP) were dissolved in minimum quantity of absolute alcohol and equal volume of distilled water. The nickel acetate solution was added to the reagent solution drop wise with constant stirring. The pH of the resultant solution was adjusted to 2.8 to 3.1. Then the solution was kept in a boiling water bath for 30 minutes, a yellowish colored complex was separated. It was filtered, washed with distilled water, dried at 100^0C for 4 hours. It was recrystallized from chloroform and finally analyzed for nickel, carbon, hydrogen and nitrogen.

Preparation of Fe (p-MINAP)$_2$ complex

1:2 stoichiometric ratios of Ferrous Sulphate and (p-MINAP) were dissolved in minimum quantity of absolute alcohol and equal volume of distilled water. The Ferrous Sulphate solution was added to the reagent solution drop wise with constant stirring. The pH of the resultant solution was adjusted to 3.5 - 4 with HCl / NH_4OH. A yellowish green colored complex thus formed was digested on water bath for 20 minutes; it was filtered, washed with distilled water, dried at 90℃ for several hours. It was recrystallized from chloroform and finally analyzed for copper, carbon, hydrogen and nitrogen.

Preparation of Fe (p-MINAP)$_3$ complex

1:3 stoichiometric ratios of Ferric Chloride and (p-MINAP) were dissolved in minimum quantity of absolute alcohol and equal volume of distilled water. The Ferric chloride solution was added to the reagent solution drop wise with constant stirring. The pH of the resultant solution was adjusted to 5 - 6 with HCl / NH_4OH. A Brown colored complex thus formed was digested on water bath for 3 hours; it was filtered, washed with distilled water. It was recrystallized from chloroform and finally analyzed for copper, carbon, hydrogen and nitrogen.

RESULTS AND DISCUSSION

Analysis data and some properties of the complexes are reported in Table 1. On the basis of analytical data Cu(II), Co(II), Ni(II), Fe (II) and Fe (III) complexe can be represented as Cu(p-MINAP)$_2$, Co(p-MINAP)$_2$, Ni(p-MINAP)$_2$, Fe(p-MINAP)$_2$ & Fe(p-MINAP)$_3$. The complexe are colored and have good thermal stability. They are insoluble in water and dilute alkali solution suggesting absence of a free oxime group due to removal of oximino proton during complexation. This is supported the infrared spectral studies. The molar conductance values in nitrobenzene indicate their non-electrolytic nature.[8]

Table 1: Analytical Data, Color At room temperature.

COMPLEX	COLOUR	% C	% H	% N	% M
Cu (p-MINAP)$_2$	Yellowish green	57.47 (57.64)	5.26 (5.29)	6.70 (6.67)	15.14 (15.22)
Co (p-MINAP)$_2$	Pinkish	57.47 (57.64)	5.26 (5.29)	6.70 (6.67)	15.14 (15.22)
Ni (p-MINAP)$_2$	Greenish	41.64 (41.32)	2.18 (2.36)	6.72 (6.60)	14.15 (14.25)
Fe (p-MINAP)$_2$	Yellowish green	57.57 (57.64)	5.27 (5.29)	6.60 (6.67)	15.19 (15.22)
Fe(p-MINAP)$_3$	Brown	59.01 (59.79)	4.55 (4.45)	7.37 (7.74)	10.28 (10.30)

Infrared Spectra

I.R. spectra (4000-400 cm^{-1}) of the complexes are practically identical. The frequencies of some significant band of the free ligand and those of the metal complexes are reported in Table 3. The observed frequencies of different groups in the metal complexes have been assigned on the basis of literature data.

The v_{O-H} of the oxime group observed at 3289 cm^{-1} in (p-MINAP) is absent in the spectra of the complexes suggesting replacement of the oxime proton by the metal ion during complexation.[11] The peak observed near 1628, 1622, 1602 cm^{-1} in spectrum of M (p-MINAP)$_2$ and Fe(p-MINAP)$_3$ may be assigned to the perturbed $v_{C=0}$ and /or $v_{C=N}$ stretching vibration involving bonding through oxygen, and nitrogen donor atoms. A band appears in the range 1300-1200 cm^{-1} is reported that N-oxide (N→O) stretching mode in aromatic ring compounds.[12] The bands at 1062, 1089, in M(p-

MINAP)$_2$ and Fe(p-MINAP)$_3$ are attributed to the N-O stretching in the ligand.[13]

It is significant to note that for metal complexes reported to have coordination only through the oxime oxygen or nitrogen atoms only. One medium to strong band at around 1050 or 1200-1250 cm^{-1} is found leading to a symmetrical six member ring structure[14] or asymmetrical five member ring structure.

Table 2: Infrared Spectral Frequencies (4000 to 400 cm $^{-1}$) of ligand and metal complexes.

p-MINAP	Cu (II)	Ni (II)	Co (II)	Fe (II)	Fe(III)	Assignment of group
3290	---	---	---	---	----	OH, Ar-H
---	3430	3405	3450	3430	3432	Ar-H
1640	---	---	---	---	---	C=O
---	1630	1612	1625	1630	1635	C=N, C=O
---	1260	1184	1260	1260	1255	N O
1080	1060	1081	1055	1060	1065	N-Oxide
---	840	795	839	840	842	N-O
763	757	756	759	757	755	Para Sub.
693	695	601	698	695	695	

NMR Spectra

NMR Spectra of Cu(p-MINAP)$_2$, Co(p-MINAP)$_2$, Ni(p-MINAP)$_2$, Fe(p-MINAP)$_2$ and Fe (p-MINAP)$_3$ in DMSO solution exhibit peaks due to –CH group, CH$_2$ group & aromatic ring protons & does not show any proton signal due to =NOH group. This suggest that their complexes have been formed by the replacement of the proton of the =NOH group by the metal ion. It is interesting to note that the peaks due to –CH$_2$ protons in Fe (p-MINAP)$_2$ appear at lower value compared to that of –CH$_2$ proton in the reagent p-MINAP. Further signals of aromatic ring protons in these complexes occur at lower and very lower field side with respect to that of aromatic ring signal in P-MINAP. The donar atom is closest to the metal ion which involved in the formation of metal ligand bond.

Nuclear magnetic resonance signals observed in P-methoxy isonitroso acetophenone (p-MINAP) and its metal complexes are shown in Table 3

Table 3: Assignments of Nuclear Magnetic Resonance Signals in p-MINAP & Metal Complexes All Values in δ scale.

Complex	=NOH	Aromatic Ring	-CH Group	-CH2 Group	-OCH$_3$ Group
p-MINAP	8.29	7.17	6.72	3.36	3.79
Cu(p-MINAP)$_2$	---	7.19	6.35	3.33	3.76
Co (p-MINAP)$_2$	---	7.20	6.25	3.34	3.75
Ni (p-MINAP)$_2$	---	7.18	6.24	3.32	3.80
Fe(p-MINAP)$_2$	---	7.15	6.70	3.25	3.78
Fe(p-MINAP)$_3$	---	7.21	6.28	3.31	3.80

Antimicrobial activity

Antibacterial activity of the synthetic metal complexes of p-methoxy isonitroso Acetophenone was examined against *E. coli, S. aureus, P. aeruginosa, B. subtilis, B. cereus and K. pneumonae*. Antifungal activity of the same compounds was evaluated against *C. albicans, A. niger and F. oxysporium*. Assays were performed in agar media with final concentration of 500µg/mL. All the synthesized compounds are effective at this concentration of 500µg/mL. The results showed that the ligand (p-MINAP) and synthesized complexes of p-MINAP exhibited poor to good antibacterial and antifungal activities against all the tested strains. Complexes of Cu (p-MINAP)$_2$, Co(p-MINAP)$_2$, Ni(p-MINAP)$_2$, Fe (p-MINAP)$_2$ and Fe(p-MINAP)$_3$ were shown maximum zone of inhibition and hence were found to inhibit the growth of all tested strains of bacteria and fungi. It may be due to the more penetrating power of iron complexes to the cell wall of bacteria, which prevents the biosynthesis of peptidoglycan or may find better fit at the receptor site as compared to other compounds. Though the ligand exhibited antibacterial and antifungal activity against all the tested strains, its activity is less when compared with its metal complexes and hence suggested its unsuitability against all the strains. None of the synthesized complex showed more activity as compared to the standard drug.

Table 4: Antibacterial Activity Data of p-MINAP & Synthesized Complex.

Compound	**Bacteria along with zone of inhibition(mm)**					
	E. Coil	***S. aureus***	***P. aeruginosa***	***B. Subtilis***	***B. cereus***	***K.penumonae***
P-MINAP	10	12	11	10	13	12
Cu(p-MINAP)$_2$	14	16	15	14	17	16
Co (p-MINAP)$_2$	13	16	14	14	16	17
Ni (p-MINAP)$_2$	14	15	16	13	17	16
Fe(P-MINAP)$_2$	14	16	15	16	14	17
Fe(P-MINAP)$_3$	12	15	13	16	15	16
Gentamycin	17	20	18	18	20	19

Table 5: Antifungal Activity Data of P-MINAP & Synthesized complex.

Compound	**Fungi along with zone of inhibition(mm)**		
	C. albicans	***A. niger***	***Fusarium oxysporium***
P-MINAP	13	12	11
Cu(p-MINAP)$_2$	18	16	19
Co (p-MINAP)$_2$	19	17	18
Ni (p-MINAP)$_2$	19	18	19
Fe(P-MINAP)$_2$	15	14	16
Fe(P-MINAP)$_3$	15	12	14
Miconazole	22	21	22

CONCLUSION

On the basis of analytical, IR, NMR spectral data and magnetic properties, the metal ligand composition was found to be 1: 2 and 1:3. The geometry of complex octahedral geometry has been assigned to Cu (II), Co(II), Ni(II), Fe (II) and Fe (III) Complex. *Invitro*, Antibacterial and Antifungal screening of these relived that most of the compounds exhibited potted inhibited potential activity.

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