

Synthesis, characterisation and electrochemical behaviour of Cu(II), Co(II), Ni(II) and Zn(II) complexes derived from acetylacetone and *p*-anisidine and their antimicrobial activity

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Abstract. Neutral tetradentate N_2O_2 type complexes of Cu(II), Ni(II), Co(II) and Zn(II) have been synthesised using the Schiff base formed by the condensation of acetylacetone and *p*-anisidine. Microanalysis, molar conductance, magnetic susceptibility, IR, UV-Vis, 1H NMR, CV and EPR studies have been carried out to determine the structure of the complexes. From the data, it is found that all the complexes possess square-planar geometry. The EPR spectrum of the copper complex in DMSO at 300 K and 77 K was recorded and its salient features are reported. All the title complexes were screened for antimicrobial activity by the well diffusion technique using DMSO as solvent. The minimum inhibitory concentration (MIC) values were calculated at 37°C for a period of 24 h. It has been found that all the complexes are antimicrobially active and show higher activity than the free ligand.

Keywords. Metal(II) tetradentate complexes, Schiff base complexes, EPR, CV, 1H -NMR spectra.

1. Introduction

Schiff bases of *p*-substituted aniline and its complexes have a variety of applications in biological,¹ clinical² and analytical³ fields. Earlier work has shown that some drugs show increased activity when administered as metal chelates rather than as organic compounds.^{1,2} A few metal(III) complexes containing *b*-diketones, *b*-ketamines and other related ligands have been reported.^{4–10} It is well-known from the literature that much work has been done on the synthesis, characterisation and electrochemical studies of first row transition metal complexes of Schiff bases. In continuation of our work,¹¹ we report herein the synthesis of a new type of bidentate ligand formed by the condensation of acetylacetone and *p*-anisidine. In the present study, we have used a group of alicyclic *b*-ketamines which are abbreviated in general as AcPA. It coordinates with the metal(II) ion in a bidentate manner through the enolisable carbonyl group of acetylacetone and the azomethine nitrogen atoms of the *p*-substituted aniline of the Schiff base. The structure of the Schiff base is shown in chart 1.

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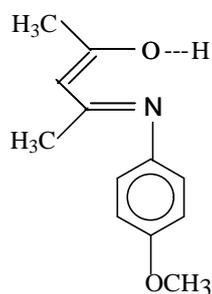


Chart 1.

2. Experimental

All chemicals were used of AnalaR grade. IR spectra were recorded in KBr medium on a Perkin–Elmer 783 spectrophotometer. $^1\text{H-NMR}$ spectra were recorded in CDCl_3 on a Bruker instrument using tetramethyl silane (TMS) as internal standard. UV-Vis spectra of all the complexes were recorded in DMSO on a Shimadzu UV-1601 spectrophotometer. Microanalytical data were determined using an Elementar vario EL at the Regional Sophisticated Instrumentation Centre, Central Drug Research Institute, Lucknow. Magnetic susceptibility measurements of the complexes in the solid state were determined by a Gouy balance at room temperature using mercury(II) tetrathiocyanatocobaltate(II) as the calibrant. Molar conductances of the complexes were measured in ethanol at room temperature using a Systronic conductivity bridge type 305. Electrochemical measurements were carried out on an Electrochemical analyser model BAS-27 voltammograph. ESR spectra of the copper complex were recorded on a Varian E112 X-band spectrometer at the Regional Sophisticated Instrumentation Centre, Indian Institute of Technology, Mumbai using TCNE as the g -marker.

2.1 Synthesis of Schiff base

An ethanolic (20 ml) solution of recrystallised *p*-anisidine (12.3 g, 0.1 M) and acetylacetone (10.2 ml, 0.1 M) was taken in equimolar ratio in an ethanolic medium and the mixture was refluxed for about 4 h on a water bath in presence of few drops of piperidine as condensing agent.¹² The reaction mixture on ice-cooling gave orange-yellow semisolid which was preserved in a desiccator. Yield: 60% (m.p. 86°C).

2.2 Synthesis of complexes

An ethanolic (20 ml) solution of Schiff base (2.05 g, 0.01 M) was mixed with metal(II) chloride (0.005 M) in ethanol (20 ml) solution and the mixture was then refluxed for 2 h on a water bath. The refluxed material was concentrated and cooled at 0°C. The solid product obtained was filtered, washed with ethanol and dried *in vacuo*.

2.3 Biological activity

The *in vitro* biological screening effects of the investigated compounds were tested against the bacteria *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, and the

Table 1. Physical characteristics and analytical and magnetic susceptibility data of the complexes.

Compound	Colour	Found (Calcd.) (%)				m_{eff} (BM)
		M	C	H	N	
AcPA	Orange-yellow	–	60.0 (60.1)	6.2 (6.3)	5.5 (5.9)	–
Cu(AcPA) ₂	Red	12.4 (12.7)	59.8 (60.2)	6.0 (6.3)	5.4 (5.9)	1.51
Ni(AcPA) ₂	Red	11.3 (11.9)	60.4 (60.8)	6.1 (6.3)	5.6 (5.9)	–
Co(AcPA) ₂	Green	11.4 (11.6)	60.9 (61.4)	6.1 (6.3)	5.3 (5.9)	3.58
Zn(AcPA) ₂	Colourless	12.3 (12.5)	60.6 (60.9)	5.9 (6.3)	5.6 (5.9)	–

fungus, *Aspergillus niger* by the well diffusion method using agar nutrient as the medium. Stock solutions (10^{-3} M) were prepared by dissolving the compounds in DMSO solution. In a typical procedure, a well was made on the agar medium inoculated with microorganisms. The well was filled with the test solution using a micropipette and the plate was incubated at 35°C for 24 h. During this period, the test solution diffused and the growth of the inoculated microorganisms was affected.

3. Results and discussion

Physical characteristics, microanalytical and magnetic susceptibility data of the complexes are given in table 1. The analytical data of all the complexes correspond to the general formula $M(\text{AcPA})_2$. Magnetic susceptibility values of the complexes at room temperature are consistent with square-planar geometry around the central metal ions. The chelates show no appreciable conductance, and this supports the hypothesis of their neutral nature.

3.1 ¹H NMR spectra

The ¹H NMR spectrum of the ligand in CDCl₃ shows signals at 13.2, 6.4–7.3, 5.8, 3.7, 1.6 and 1.2 δ downfield from TMS, assigned to the enolic OH, phenyl, methine, methoxy and two methyl groups protons respectively. In the ¹H-NMR spectrum of the zinc complex, the enolic OH proton signal is found to be absent, confirming deprotonation and its subsequent involvement in coordination.

3.2 IR spectra

The IR spectrum of the Schiff base has a broad absorption band at 3190 cm^{-1} which is assigned to the enolisable OH group of the acetylacetone moiety. The breadth of this band indicates the presence of hydrogen bonds. The assignments are strengthened by the disappearance of the band in the metal chelates in which enolic protons are completely displaced by metal(II) ions. The ligand has no absorption at 1700 cm^{-1} which indicates that free carbonyl groups are absent and so the ketimine structure is ruled out. The strong absorption in the 1620 cm^{-1} region is assigned as the azomethine group present in the Schiff base. In all the metal complexes, the azomethine group is shifted to lower frequency in the region 1600–1580 cm^{-1} which indicates that chelation takes place through the azomethine group. The metal complexes show new bands in the regions 480–

450 cm⁻¹ and 400–350 cm⁻¹ which are due to the formation of M–N and M–O bonds respectively.

3.3 Electronic absorption spectra

The electronic absorption spectra of the Schiff base and its Cu(II), Co(II) and Ni(II) complexes were recorded at room temperature using DMSO as the solvent. The electronic spectrum of the free ligand shows a band at 25,706 cm⁻¹ which is assigned as intra-ligand charge transfer band (INCT). The Cu(II) complex shows a *d–d* band in the region 21,881 cm⁻¹ due to ²B_{1g} → ²A_{1g} transition which supports square-planar geometry. The Co(II) complex shows absorption in the region 16,366 cm⁻¹ corresponding to ¹A_{1g} → ¹B_{1g} transition which also supports square-planar geometry. The Ni(II) complex shows absorption in the region 20,000 cm⁻¹ assigned to ¹A_{1g} → ¹B_{1g} transition which again suggests square-planar geometry.

3.4 Magnetic susceptibility measurements

Magnetic moment of the Cu(II) complex is 1.51 BM which shows the presence of one unpaired electron. This value is lower than the spin-only value and is due to mixing of orbital angular momentum from excited state via spin-orbit coupling. The magnetic moment of Ni(II) complex is zero which indicates that the complex has square-planar structure. The magnetic moment of the Co(II) complex is 3.58 BM and is also indicative of square-planar configuration.¹³

3.5 EPR spectra

EPR spectra of Cu(AcPA)₂ recorded in DMSO at 300 and 77 K are given in figure 1. The spin Hamiltonian parameters of the complexes were calculated and are summarised in table 2. The spectrum of Cu(AcPA)₂ at 300 K shows one intense absorption band in the high field region and is isotropic due to the tumbling motion of the molecules. However, this complex in the frozen state at 77 K shows four well-resolved peaks of low intensities in the low-field region and one intense peak in the high-field region. No band corresponding to *M_s = ± 2* transition was observed in the spectrum ruling out any Cu–Cu interaction. The *g*-tensor values of Cu(II) complex can be used to derive the ground state. In square-planar complexes the unpaired electrons lie in the *d_{x²-y²}* orbital giving ²B_{1g} as the ground state with *g_∥* > *g_⊥* while the unpaired electron lies in the *d_{z²}* orbital giving ²A_{1g} as the ground state with *g_⊥* > *g_∥*. From the observed values, it is clear that *g_∥* > *g_⊥*, which indicates that the structure of the complex is square-planar and that the unpaired electron is predominantly in the *d_{x²-y²}* orbital.^{14,15} The molecular orbital coefficients, **a**² (covalent in-plane *s*-bonding) and **b**² (covalent in-plane *p*-bonding) were calculated using the following equations:

$$\mathbf{a}_{\text{Cu}}^2 = -(A_{\parallel}/0.036) + (g_{\parallel} - 2.0023) + 3/7(g_{\perp} - 2.0023) + 0.04,$$

$$\mathbf{b}^2 = (g_{\parallel} - 2.0023)E/-8I\mathbf{a}^2,$$

where *I* = 828 cm⁻¹ for the free ion and *E* is the electronic transition energy of ²B_{1g} → ²A_{1g}. From table 2, it is clear that in-plane *s*-bonding (0.81) is more covalent than in-plane *p*-bonding (1.4).

3.6 Cyclic voltammetric study

The cyclic voltammogram of the Cu(II) complex obtained in DMSO (figure 2) solution at room temperature shows a redox process corresponding to the copper(II)/copper(III) couple at $E_{p_a} = +1.18$ V and the associated cathodic peak at $E_{p_c} = 0.45$ V. This couple is found to be quasi-reversible as the peak separation between the anodic and cathodic potential is very high. But the ratio between the anodic and cathodic currents suggests that the process is simple one-electron transfer, quasi-reversible process.^{16,17}

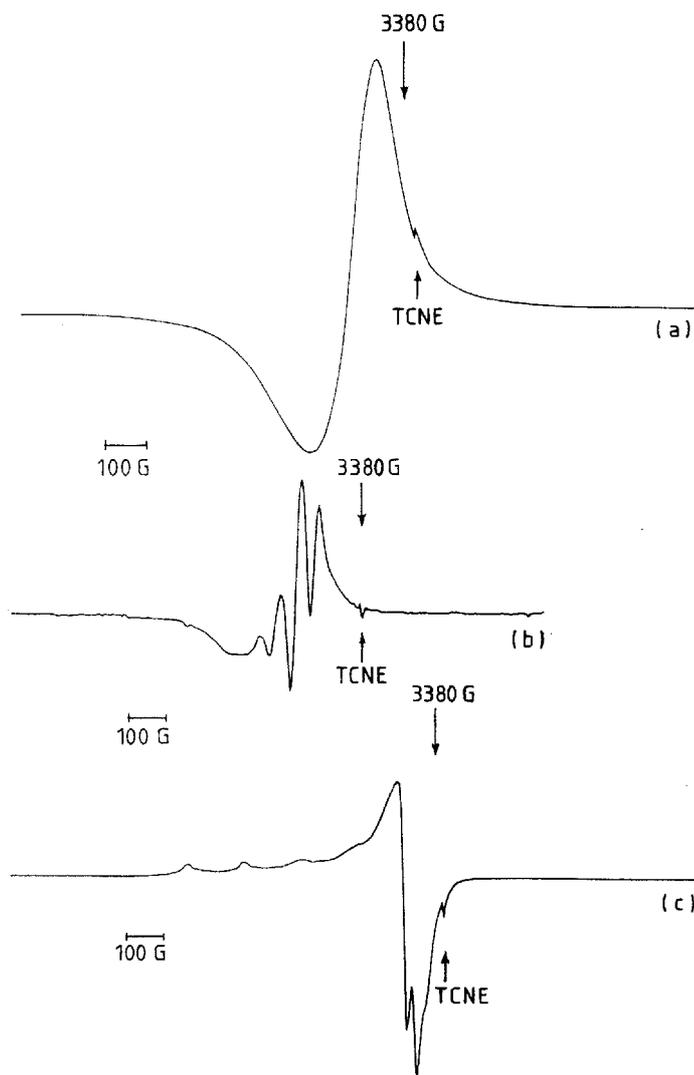
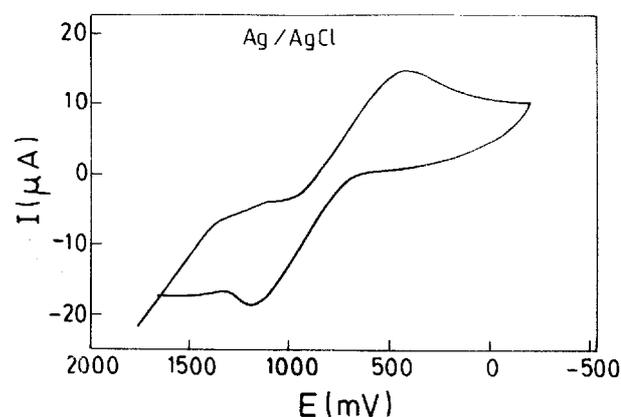


Figure 1. EPR spectra of $\text{Cu}(\text{AcPA})_2$ complex in solid at (a) 300 K, DMSO (b) 300 K and (c) 77 K.

Table 2. Spin-Hamiltonian parameters of Cu(II) complex in DMSO at 300 and 77 K.

Complex	Temp.	$A_{\parallel} \times 10^{-4}$ (cm^{-1})	$A_{\perp} \times 10^{-4}$ (cm^{-1})	$A_{\text{iso}} \times 10^{-4}$ (cm^{-1})	g_{\parallel}	g_{\perp}	g_{iso}	a^2	b^2
Cu(AcPA) ₂	77 K	140	47	78	2.328	2.067	2.15	0.81	1.4
Cu(AcPA) ₂	300 K	–	–	50	–	–	2.11	–	–
Cu(AcPA) ₂ in solid	300 K	–	–	53	–	–	2.10	–	–

**Figure 2.** Cyclic voltammogram of Cu(AcPA)₂ at 300 K in DMSO solution; Scan rate 100 mVs⁻¹.

3.7 Biological activity

Antibacterial activity of the ligand and its complexes have been carried out against bacteria like *S. aureus*, *E. coli*, *B. subtilis* and the fungus, *A. niger*, using nutrient agar medium by the well diffusion method.¹⁸ It is observed from these studies that metal chelates have a higher activity than the free ligand. Such increased activity of the metal chelates can be explained on the basis of Overtone's concept and chelation theory.¹⁹ According to Overtone's concept of cell permeability the lipid membrane that surrounds the cell favours the passage of only lipid soluble materials due to which liposolubility is an important factor that controls antimicrobial activity. On chelation, the polarity of the metal ion is reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with donor groups. Further, it increases the delocalisation of *p*-electrons over the whole chelate ring and enhances the lipophilicity of the complex. This increased lipophilicity enhances the penetration of the complexes into lipid membranes and blocking of metal binding sites on the enzymes of the micro-organism.

4. Conclusions

We have synthesised Cu(II), Ni(II), Co(II) and Zn(II) complexes using the Schiff base formed by the condensation of acetylacetone and *p*-anisidine. The complexes were

characterised by spectral and magnetic studies to establish the proposed four-coordinated square-planar geometry.

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