Bioinorganic Relevance of Some Cobalt(II) Complexes with Thiophene-2-glyoxal Derived Schiff Bases

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Abstract: Complexes of Co(II) with two new Schiff bases TEAB [2-hydroxy-4-[[2-oxo-2-(thiophen-2-yl)ethylidene]amino]benzoic acid] and TEPC [*N*-[2-oxo-2-(thiophen-2-yl)ethylidene]pyridine-3-carboxamide] have been synthesized and characterized with the help of elemental analysis, magnetic, mass, ¹H-NMR, ¹³C-NMR, IR and electronic spectral data. IR spectra manifest the coordination of the ligand to the metal ion through the carbonyl oxygen, azomethine nitrogen and thienyl sulphur atoms. With the help of electronic spectral data various ligand field parameters were also calculated. All these studies reveal the distorted octahedral Co(II) complexes. Synthesized compounds have also been screened against some micro organisms viz, *Escherichia coli*, *Proteus vulgaris*, *Aspergillus niger* and *Aspergillus flavus* with the help of 'filter paper disc' technique. It has been observed that the antimicrobial activities of metal complexes are higher than that of the free ligand.

Keywords: Schiff base, Magnetic, Electronic, Mass, NMR and Infrared studies, Octahedral Co(II) complexes, Antimicrobial studies.

Introduction

In the field of coordination complexes, Schiff base metal complexes¹ have a curious history. Considerable interest attached with the chemistry of Schiff bases² derived from heterocyclic aldehydes, glyoxals and primary amines. Various heterocyclic Schiff bases having oxygen, nitrogen and sulphur donor atoms, have been reported by several scientists³. In recent years, applications of Schiff bases and their metal complexes in pharmacological⁴ and non-pharmacological⁵ fields have been receiving increased attention.

In the course of present investigation, complex formation of TEAB [2-hydroxy-4-[[2-oxo-2-(thiophen-2-yl)ethylidene]amino]benzoic acid] and TEPC [*N*-[2-oxo-2-(thiophen-2-yl)ethylidene]pyridine-3-carboxamide] Schiff bases with Co(II) ion have been attempted.

Magnetic and electronic spectral data of these Co(II) complexes have been discussed on the basis of ligand field theory and the reacting sites in the ligands have been suggested on the basis of IR spectra. Mass and NMR spectral studies have been also discussed for the Schiff bases. In view of biological importance of these ligands and complexes, antibacterial and antifungal activities have also been screened.

Experimental

All the chemicals used were of AR grade and used without further purification. 2-acetyl thiophene⁶ and 2-thienyl glyoxal⁷ were prepared by slightly modified techniques of the literature methods.

Synthesis of TEAB

A mixture of 2-thienyl glyoxal (14 mL, 10 m mol) dissolved in 40 mL acetone and *p*-amino salicylic acid (15.3 g, 10 m mol) dissolved in 20 mL ethanol was refluxed on water bath for 6 h under stirring. On cooling to room temperature, dark purple brown crystals were obtained. The crystals were filtered and washed with ethanol, recrystallized from acetone and dried at ambient temperature and its purity was confirmed by TLC technique.

Figure 1. Synthesis of TEAB.

Synthesis of TEPC

A mixture of 2-thienyl glyoxal (14 mL, 10 m mol) dissolved in 40 mL acetone and nicotinamide (12 g, 10 m mol) dissolved in 20 mL ethanol was refluxed on water bath for 6 h under stirring. On cooling to room temperature, chocolate brown crystals were obtained. The crystals were filtered and washed with ethanol, recrystallized from acetone and dried at ambient temperature and its purity was confirmed by TLC technique.

Figure 2. Synthesis of TEPC.

Synthesis of complexes

A solution of Co(II) salt (chloride / nitrate 10 m mol) in 20 mL ethanol was directly mixed to the solution of the ligand TEAB / TEPC in the same solvent. The molar ratio of metal: ligand was 1:2 for both TEAB and TEPC Schiff bases. Reflux the above mixture for 3-4 h. On cooling, filter the product and the material was dried in air to get the crystals of metal chelates. The yield varied from 40-60%.

Physical measurements

Percentage of C, N and H were determined micro analytically at RSIC, Punjab Univ. Chandigarh and the percentage of Co(II) in the complexes was determined by the standard method using pyridine and ammonium thiocyanate as precipitants. Melting points of the synthesized compounds were determined in open glass capillaries using melting point apparatus. Magnetic susceptibility measurements were determined at room temperature on 'EG&G model-155' by VSM (vibrating sample magnetometer) method at RSIC, IIT- Madras.

The NMR spectra were recorded on Bruker-300 Ultrashield-300 MHz NMR spectrometer. The mass spectra were recorded at Torrent Pharmaceuticals Ltd., Ahmedabad. Electronic spectra of complexes were carried out on 'Elico SL-171' spectrometer at 25°C using ethanol/acetone as solvent at Department of Chemistry, R.B.S. College, Agra. IR spectra were recorded using KBr pellets on 'Perkin Elmer-137 and 577' spectrometer in the region ~4000-200cm⁻¹ at Alembic Ltd. Vadodara and RSIC, Punjab Univ., Chandigarh .

Results and Discussion

Mass spectral studies

On the basis of the "bar graph" presentation of the Schiff bases, we can observed that the peaks at m/z 154 and m/z 126 are the parent ion peaks of the Schiff bases TEAB and TEPC respectively and the peak at m/z 274 and m/z 244 is corresponding to the molecular weight (M^+) of the TEAB and TEPC respectively.

In the case of TEAB other peaks at m/z 230, 257, 137 and 190 supports the fragmentation of carboxylic group, hydroxyl group, salicylic acid and thiophene ring respectively. Peaks at m/z 150 and m/z 124 are due to the fragmentation at the azomethine linkage.

In the case of TEPC other peaks at m/z 166 and m/z 160 supports the loss of pyridine ring and thiophene ring respectively. Peaks at m/z 121 and m/z 124 are due to the fragmentation at the azomethine linkage. Therefore, the observed fragmented ion peaks for both the Schiff bases are also in confirmation with their structures.

NMR spectral studies

¹H NMR

¹H NMR spectrum of Schiff bases TEAB & TEPC were recorded in CDCl₃. In the spectra of TEAB, a sharp singlet at δ 8.21 assigned as azomethine proton and a broad singlet found due to hydroxylic proton and carboxylic OH having in the chemical shift range of δ 10.31- δ 11.33. Peaks due to thienyl protons present at position 3, 4 & 5 found at (s, δ 8.00), (m, δ 6.92) and (t, δ 7.37) respectively. Peaks due to protons present in benzene ring at position 3,5 & 6 found at (d, δ 6.85), (d, δ 6.77) and (d, δ 7.90) respectively.

In the spectra of TEPC, a sharp singlet peak at δ 8.43 is present due to azomethine proton. Peaks due to thienyl protons present at position 3, 4 & 5 found at (s, δ 8.04), (m, δ 7.50) and (t, δ 7.05) respectively. Peaks due to protons present in pyridine ring at position 2, 4, 5 & 6 found at (d, δ 9.25), (m, δ 8.30), (m, δ 7.58) and (m, δ 8.58) respectively.

¹³C NMR

¹³C NMR spectrum of both the Schiff bases was also recorded in CDCl₃. In the spectra of TEAB, peaks due to azomethine carbon, carbonyl carbon and carboxylic carbon found at δ 160.11, δ 186.52 and δ 172.44 respectively. Chemical shift due to the carbon atoms present in the thiophene ring, at position 2, 3, 4 & 5 has been found at δ 145.59, δ 133.78, δ 124.97 and δ 128.03 respectively and Chemical shifts due to the benzene ring, for the position 1 to 6 has been found at δ 100.26, δ 164.15, δ 108.37, δ 150.86, δ 116.50 and δ 130.72 respectively.

In the spectra of TEPC, peaks due to azomethine carbon found at δ 160.33. Chemical shift due to carbonyl carbon attached to thiophene ring found at δ 184.14 and carbonyl carbon attached to pyridine ring found at δ 173.59. Chemical shift due to the carbon atoms present in the thiophene ring, at position 2, 3, 4 & 5 has been found at δ 150.48, δ 133.12, δ 123.46 and δ 129.22

respectively. Chemical shifts found at δ 152.00, δ 135.26, δ 138.70, δ 125.79 and δ 156.50 are due to the 2, 3, 4, 5 & 6 carbon position of the pyridine ring respectively. By the help of above ^1H and ^{13}C NMR spectra features, we can propose the structures of both the Schiff bases.

Magnetic susceptibility measurements

The effective magnetic moment values of all the Co(II) complexes lie in the range of 4.5–5.2 BM, which suggested a distorted octahedral geometry⁸ (Table 1). These values are much higher than the spin only value of 3.87BM. These μ_{eff} values in all the complexes may arise due to electron pairing in the formation of strong covalent bond involving the use of 3d electron of Co(II) ion or spin-spin interaction.

Table 1. Analytical, magnetic and physical properties of ligands and their Co(II) complexes.

S.No	Compounds	m.p. °C	Color	Elemental analysis (% found / Calculated)						μ_{eff} (B.M.)
				C	H	N	S	Cl	M	
1.	TEAB	98-100	Purple- Brown	56.33/ 56.72	3.26/ 3.29	5.36/ 5.08	11.02/ 11.64	-	-	-
2.	Co(TEAB) ₂ Cl ₂	110-115	Dark- brown	45.33/ 45.89	2.50/ 2.66	4.02/ 4.22	9.92/ 9.32	10.83/ 10.42	8.5/8.6	4.7
3.	Co(TEAB) ₂ (NO ₃) ₂	85-90	Reddish brown	42.01/ 42.57	2.55/ 2.47	7.63/ 7.29	8.30/ 8.74	-	7.97/ 8.03	5.00
4.	TEPC	95-98	Chocolate brown	58.8/ 59.9	3.34/ 3.30	12.2/ 11.4	13.47/ 13.12	-	-	-
5.	Co(TEPC) ₂ Cl ₂	112-124	Pale- brown	38.12/ 38.52	2.26/ 2.15	7.02/ 7.48	8.93/ 8.57	18.17/ 18.95	16.01/ 15.75	4.5
6.	Co(TEPC) ₂ (NO ₃) ₂	80-85	Dark- brown	33.29/ 33.73	2.01/ 1.88	13.6/ 13.11	7.60/ 7.40	-	13.3/ 13.79	5.2

Electronic spectral studies

The distorted octahedral geometry of the complexes was also supported by electronic spectra⁹ of these complexes. The electronic spectra of the Co(II) complexes gave three bands. König's method¹⁰ was used to ascertain the correct positions of the bands. In the complex [Co(TEAB)₂Cl₂] (a), the assignments of the spectral bands are as follows: $^4\text{T}_{2g}(\text{F}) \leftarrow ^4\text{T}_{1g}(\text{v}_1) \approx 8225 \text{ cm}^{-1}$, $^4\text{A}_{2g} \leftarrow ^4\text{T}_{1g}(\text{F})(\text{v}_2) \approx 17551 \text{ cm}^{-1}$, and $^4\text{T}_{1g}(\text{P}) \leftarrow ^4\text{T}_{1g}(\text{F})(\text{v}_3) \approx 20980 \text{ cm}^{-1}$. The ligand field parameters v_3/v_1 , v_3/v_2 , Dq/B , B and β values have been found to be 2.55, 1.99, 0.67, 931 and 0.95 respectively, which agree with the values of distorted octahedral Co(II) complexes.

The spectrum of [Co(TEAB)₂(NO₃)₂] (b), showed three absorption bands around $v_1 \sim 10120$, $v_2 \sim 19600$ and $v_3 \sim 22090 \text{ cm}^{-1}$, which may be attributed to the three spin-allowed transitions. Same as mentioned above and the values of parameters v_3/v_1 , v_3/v_2 , Dq/B , B and β are 2.18, 1.12, 1.10, 946 and 0.97 and 0.97 respectively, expected for a distorted octahedral¹² structure. In the electronic spectrum of [Co(TEPC)₂Cl₂] (c), the three absorption bands are at $v_1 = 8285$, $v_2 = 17680$ and $v_3 = 20075 \text{ cm}^{-1}$ and for complex [Co(TEPC)₂(NO₃)₂] (d), these values are at 11655, 20080 and 22970 cm^{-1} respectively. The ligand field parameters for these complexes are also in the range (Table 2), suggesting distorted octahedral geometry of these Co(II) complexes.

Various other crystal and ligand field parameters¹³ for all the Co(II) complexes have been also calculated. The values of these parameters are also in confirmation with distorted octahedral complexes (Table 2).

Table 2. Electronic spectral data and compound values of some ligand field parameters for Co (II) complexes

Parameters	Complexes			
	Co(TEAB) ₂ Cl ₂	Co(TEAB) ₂ (NO ₃) ₂	Co(TEPC) ₂ Cl ₂	Co(TEPC) ₂ (NO ₃) ₂
ν_1	8225	10120	8285	11655
ν_2	17551	19600	17680	20080
ν_3	20980	22090	20075	22970
B	931	946	863	1044
C	4189.5	4257	38863.5	4698
F^2	1529.5	1554	1417.7	1715
F^4	119.7	121.6	110.9	134.2
10Dq	6259	10433	9414	10950
Dq/B	0.67	1.10	1.09	1.04
f	695.4	1159.2	1046	1216.6
h	0.208	0.208	0.916	-0.29
β	0.95	0.97	0.88	1.07
β %	5	3.2	12	-7
ν_3/ν_1	2.55	2.18	2.42	1.97
ν_3/ν_2	1.19	1.12	1.13	1.14
π	14960.2	16963.8	15679.3	18769.6
Π	1973.7	2005.5	1829.5	2213.2
Π/B	2.12	2.12	2.12	2.12

[Here ν_1 , ν_2 & ν_3 = Observed spin allowed transition, B & C = Racah parameters, F^2 & F^4 = Slater-Condon parameters, 10Dq = Crystal field parameter from numerical fitting, f & h = Crystal field and Nephelauxetic parameters for the ligands used in the complexes, β & β % = Nephelauxetic ratio and (%) covalence character, π = Mean pairing energy, Π = Exact spin pairing energy]

Infrared spectral studies

In order study the binding mode of the Schiff bases to metal in the complexes, IR spectra¹⁴ of the free ligands are compared to metal complexes. In the IR spectra of TEAB, three sharp bands found at ~ 1626 , ~ 1289 and ~ 1982 cm^{-1} are due to $\nu\text{C}=\text{N}$, $\nu\text{C}-\text{S}-\text{C}$ and $\nu\text{C}=\text{O}$ bending vibrations respectively. In both the metal complexes of this Schiff base viz. (a) and (b), $\nu\text{C}=\text{N}$ band shifts to ~ 1611 and ~ 1612 cm^{-1} respectively, confirms the coordination through azomethine nitrogen¹⁵. The $\nu\text{C}-\text{S}-\text{C}$ bands at ~ 1275 and ~ 1277 cm^{-1} respectively indicates the coordination of thienyl sulphur and $\nu\text{C}=\text{O}$ bands at ~ 1701 and ~ 1708 cm^{-1} respectively confirms the involvement of carbonyl oxygen in coordination¹⁶. The values and the position of the νOH band are almost retained $+3$ cm^{-1} in these complexes indicates that phenolic oxygen atom do not take part in coordination¹⁷.

In the IR spectra of TEPC, $\nu\text{C}=\text{N}$, $\nu\text{C}-\text{S}-\text{C}$, $\nu\text{C}=\text{O}$ and $\nu\text{C}-\text{N}-\text{C}$ stretching vibrations are at the expected values of ~ 1618 , ~ 1272 , ~ 1681 and ~ 1690 cm^{-1} respectively. In the complexes (c) and (d), the ligand band of $\nu\text{C}=\text{N}$ shifted to ~ 1603 and ~ 1610 cm^{-1} respectively, indicating the coordination of azomethine nitrogen. The $\nu\text{C}-\text{S}-\text{C}$ vibrations of these complexes are at ~ 1275 and ~ 1273 cm^{-1} respectively, indicates the non involvement of thienyl sulphur with metal. Appearance of the broad peaks at ~ 1672 and ~ 1688 cm^{-1} respectively, which are due to shifting in $\nu\text{C}=\text{O}$ bands, also indicates the coordination through carbonyl oxygen. The position and other characteristics of the band $\nu\text{C}-\text{N}-\text{C}$ are retained ± 1 cm^{-1} in both the above complexes¹⁸. This indicates that the pyridine nitrogen do not take part in coordination.

In the complexes additional bands are also appear in the region $\sim 287\text{--}294\text{ cm}^{-1}$ and $\sim 1120\text{--}1157\text{ cm}^{-1}$. These vibrations have been ascribed to $\nu\text{M-Cl}$ and ν_2 band of NO_3^- group respectively indicating coordination. All the above coordination sites are further confirmed by the $\nu\text{M-O}$, $\nu\text{M-N}$ and $\nu\text{M-S}$ stretching bands at the expected values $\sim 520\text{--}545$ and $\sim 441\text{--}445\text{ cm}^{-1}$ and $\sim 331\text{--}340\text{ cm}^{-1}$ respectively¹⁹ in all the complexes as we have discussed here.

Microbiocidal assay

Synthesized Schiff bases and their corresponding metal complexes were tested for the growth inhibitory activity against phytopathogenic bacteria *viz.* *Escherichia coli* and *Proteus vulgaris*, and fungi *viz.* *Aspergillus niger* and *Aspergillus flavus* using 'Filter paper disc' method²⁰ at 250, 500 and 1000 ppm level in acetone/ethanol. For screening antibacterial activity 'Nutrient Agar' and for antifungal activity 'Potato Dextrose Agar'²¹ was used as a growth medium. Sterilized filter paper discs of 5 mm diameter were soaked in the solutions of different concentrations of synthesized compounds and introduced on sterilized culture media. The plates were incubated for 24-30 h at $35\pm 2^\circ\text{C}$ for bacteria and 72-96 h at 28°C for fungi. The zones of inhibition based upon zone size around the discs were measured. The measured zone of inhibition against the growth of various microorganisms is listed in Table 3. It is clear from the microbiocidal screening data that the metal complexes are more toxic in comparison to their parent ligand itself. Hence complexation increases the antimicrobial activity²² such increased activity of the metal complexes can also be explained on the basis of 'Chelation theory'²³.

Table 3. Antimicrobial data of synthesized compounds

S.No	Compounds	Conc. ppm	Inhibition Zone, in mm			
			<i>E. coli</i>	<i>P. vulgaris</i>	<i>A. niger</i>	<i>A. flavus</i>
1.	TEAB	1000		6		10
		500	*	7	*	9
		250		8		8
		1000		8		9
2.	$\text{Co(TEAB)}_2\text{Cl}_2$	500	*	7	*	10
		250		9		12
		1000		7		12
3.	$\text{Co(TEAB)}_2(\text{NO}_3)_2$	500	*	9	*	10
		250		11		8
		1000	6		8	
4.	TEPC	500	-	*	6	*
		250	-		8	
		1000	6		9	
5.	$\text{Co(TEPC)}_2\text{Cl}_2$	500	6	*	6	*
		250	-		8	
		1000	8		10	
6.	$\text{Co(TEPC)}_2(\text{NO}_3)_2$	500	8	*	6	*
		250	7		8	

Note : ('-' = not measurable, * = not tested)

Conclusion

All the spectral studies suggest that the Schiff bases are tridentate in nature having O, N and S donor atoms. The complexes having six coordinate system with octahedral geometry. All the compounds are bioactive showing good antimicrobial property. The proposed structures of the complexes are

Figure 3. Structure of Complex.
Co(TEAB)₂Cl₂ / Co(TEAB)₂(NO₃)₂

Figure 4. Structure of Complex.
Co(TEPC)₂Cl₂ / Co(TEPC)₂(NO₃)₂

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