

SYNTHESIS AND ELECTROCHEMICAL PROPERTIES OF SOME PIROXICAM METAL COMPLEXES

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ABSTRACT

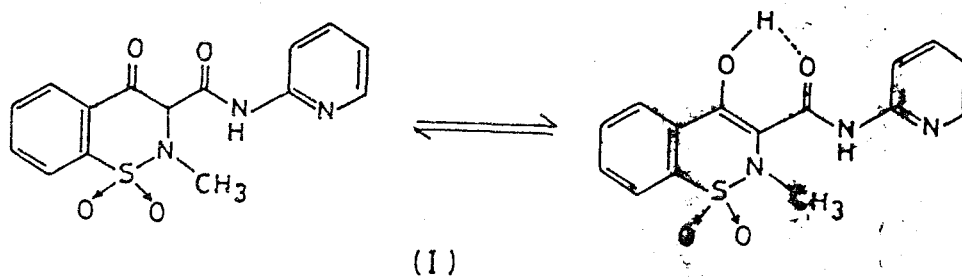
The metal complexes of piroxicam with Mn(III), Fe(III), Fe(II), Co(III), Ni(II), Cu(II) and Zn(II) were prepared and investigated by means of elemental analyses, i.r., electronic spectra, magnetism and molar conductance. The oxidation states of manganese, iron and cobalt complexes were confirmed by the cyclic voltammogram data. The values of magnetic moments (μ_{eff}) indicate that both Fe(II) and Cu(II) complexes are present in the dimeric form. The study also shows that, the number of ligand molecules around the central metal ion (except copper) coincides with the oxidation state.

INTRODUCTION

Piroxicam [4-hydroxy-2-methyl-N-(2-pyridyl)-2H-1,2-benzothiazine-3-carboxamide-1,1-dioxide] belongs to the class of acidic, non-

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steroid anti-inflammatory drugs. The compound is used as an effective analgesic and anti-inflammatory agent in rheumatoid arthritis and other inflammatory disorders in human.¹⁻³ Piroxicam comprises β -diketone moiety and other coordination sites, and has two possible tautomeric forms⁴ (I).



Spectrophotometric estimation of piroxicam through the reaction with different metal ions was carried out.⁵ However, no work has been done to clarify the mode of bonding of this drug with metal ions.

In the present work, the reactions between piroxicam and different metal ions (which commonly exist in biological fluids) have been carried out. The solid complexes obtained have been subjected to different analytical and spectral measurement to throw more light on the structure as well as the nature of bonding. The cyclic voltammograms of some of the complexes obtained have also been investigated.

EXPERIMENTAL

All chemicals were of reagent grade. The complexes were prepared by the dropwise addition of the stoichiometric amount of the metal chloride to the solution of the ligand (HL) in methanol, (1:2 molar ratio). The reaction mixture was stirred for 8 h. Water portions

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were added to the solution to accomplish the precipitation. The precipitates obtained were extracted by chloroform, which dissolved the complexes. After evaporation of chloroform, very pure bright precipitates were obtained, which were filtered off, washed several times with ether and dried over ($\text{CaCl}_2/\text{P}_4\text{O}_{10}$).

The analytical and physical measurements were carried out as previously described⁶.

Cyclic voltammetric measurements were carried out using an EG and G PAR computerized measuring system for electrochemical analysis model 250. Current-voltage curves were recorded on a Hewlett-Packard model 7440A X-Y recorder. Analytical cell model C-1H and a gold working electrode (Bioanalytical systems) were used together with a platinum counter electrode and an Ag/AgCl reference electrode. Dimethylformamide (DMF) was used as solvent and lithium chloride as supporting electrolyte for all measurements.

RESULTS AND DISCUSSION

Vibrational spectra

The comparison between the i.r. spectrum of the ligand and those of its complexes (**Table 1**) leads to the following considerable points:

- 1- $\nu(\text{NH})$ of the ligand at 3340 cm^{-1} shows no shift in its frequency, indicating that (-NH) doesn't participate in the coordination.
- 2- $\nu(\text{CC}) + \nu(\text{CN})$ of the pyridine ring at $(1595\text{-}1580)\text{ cm}^{-1}$ has no significant shift in the complexes, also the $\nu(\text{-SO}_2\text{N})$ at 1155 cm^{-1} displays no considerable shift. This indicates that the two nitrogen

Table 1. Elemental analyses, magnetic moment, conductance, i.r. and electronic spectra of the complexes.

compound	colour	Found (calcd.) C H	μ_{eff} (B.M.)	Λ_m in DMF ($\text{cm}^2 \Omega^{-1} \text{mole}^{-1}$)	i.r. (cm^{-1}) ν_{NH}	$\nu(\beta\text{-diketone}$ chelate ring)	$\nu\text{C}=\text{C}+\nu\text{C}-\text{N}$ of pyridine ring	ν amide II	$\nu(\text{SO}_2-\text{N})$	Electronic spectra in mulls (nm)	melting point ($^{\circ}\text{C}$).
HL					3340 ^b (s)	1630 ^c (vs/sharp)	1595 (w) 1580 (s)	1530 (vs)	1155 (vs)	325, 250	200
(1) $[\text{MnL}_3]_2\text{EtOH}$	canary yellow	51.7 (51.7) 4.0 (4.2)	diomag.	6.1	3360 (sh)	1640 (vs)	1600-1570 (split.)	1520 (sh)	1158 (vs)	423, 251	160
(2) $[\text{FeL}_3]$	brick-red	51.5 (51.6) 3.4 (3.4)	4.09	5.7	3380 (m)	1600 (vs)	1565 (m)	1520 (s)	1157 (s)	530, 397, 281, 220	150
(3) $[\text{Fe}_2\text{L}_4(\text{H}_2\text{O})_2]$	orange	49.2 (49.0) 3.5 (3.5)	2.1	7.7	3340 (sh)	1630-1600 (vs/broad)	1570 (s)	1520 (s)	1160 (s)	516, 393, 275	115
(4) $[\text{CoL}_3]_3\text{EtOH}$	canary yellow	51.7 (51.5) 4.7 (4.6)	diomag.	5.6	b	1640-1605 (vs/broad)	1570 (s)	1520 (s)	1160 (s)	423, 251	140
(5) $[\text{NiL}_2(\text{H}_2\text{O})_2]$	light green	48.0 (47.7) 3.6 (3.7)	2.82	6.3	b	1640-1605 (vs/broad)	1570 (s)	1520 (s)	1160 (s)	655(sh), 600, 438	d
(6) $[\text{Cu}_2\text{L}_2\text{Cl}_2]_2\text{EtOH}$	dirty green	42.4 (42.5) 3.4 (3.3)	1.16	4.8	3340 (m)	1630-1600 (vs/broad)	1570(m)	1530-1500 (split.)	1160 (s)	628 (br), 429, 318, 255	d
(7) $[\text{ZnL}_2(\text{EtOH})_2]_2\text{EtOH}$	yellow	50.0 (49.5) 4.9 (5.0)	diomag.	10.2	3360 (sh)	1640 (vs)	1600-1570 (split.)	1520 (s)	1158 (s)		175

a. : or vOH, b. : covered by broad vOH of water or EtOH, c. : amide I, d. : thermally stable above 250 $^{\circ}\text{C}$

Synthesis and electrochemical properties

atoms of the pyridine ring and (-SO₂N) group do not participate in the coordination.⁶

3- The band observed at (1640-1600) cm⁻¹ are assigned to $\nu(\text{CO})$ (amide I) and $\nu(\beta\text{-diketone chelate ring})$, respectively.⁷

The above arguments indicate that the ligand coordinates through the β -diketone moiety. The molar conductance values (**Table 1**) indicate non-electrolytic of the complexes.⁶

Electronic spectra and magnetism

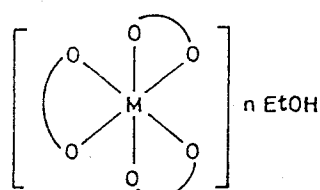
The Fe(III)-complex shows an intense band 397 nm, which is due to charge transfer (C.T). The shoulder located at 530 nm is assigned to ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{2g}$ transition in a six coordination.⁸ The observed value of magnetic moment (4.09 B.M.) is lower than the value expected for five unpaired electrons (5.9 B.M.). This subnormal magnetic moment can be explained by suggesting a structure with super-exchange interaction between two iron atoms.⁸

The spectrum of Fe(II)-complex displays two bands in the visible and u.v. regions above the wavelength at which the ligand began to absorb. The low intensity band (516 nm) may be due to d-d transition in hexa coordination. The other band at 393 nm is assigned to metal→ligand charge transfer (which is responsible for the orange colour). The anomalous value of magnetic moment (2.1 B.M.) from that of high spin Fe(II) can be attributed to the higher metal-metal interaction.^{9,10}

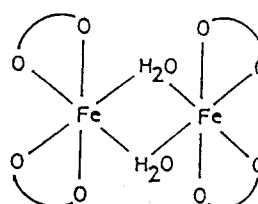
The observed band at 600 nm in the spectrum of the Ni(II) complex is assigned to $\nu_3({}^3\text{A}_{2g} \rightarrow {}^3\text{T}_{1g})$ transition in an octahedral geometry.¹¹ This geometry was confirmed by the observed value of magnetic moment (2.82 B.M.). The copper complex possess a square planar

geometry as evidenced by the appearance of one broad band centered at 630 nm. The lower value of its magnetic moment (1.16) is attributed to the metal-metal interaction.^{12,13}

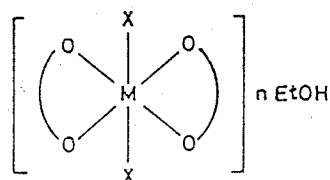
For the Mn(III) and Co(III) complexes, the charge transfer band (C.T) is only observed at 433-423 nm above the absorption of the ligand. This (C.T) band is being responsible for the canary yellow colour of the complexes. The values of the magnetic moment suggest a low spin diamagnetic complexes.¹¹ On the basis of the above discussion and the data given in **Table (1)**, the following structures can be suggested:



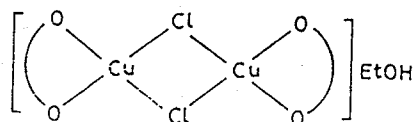
- M = Mn , n = 2 Complex (1)
 M = Fe , n = 0 Complex (2)
 M = Co , n = 3 Complex (4)



Complex (3)



- M = Ni , X = H₂O , n = 0 Complex (5)
 M = Zn , X = EtOH , n = 1 Complex (7)



Complex (6)

Synthesis and electrochemical properties

Electrochemical behaviour of the complexes

Cyclic voltammograms of $2 \times 10^{-3} \text{M}$ solutions of complexes 1-4 in DMF containing 0.1M LiCl as supporting electrolyte at gold electrode, were recorded and the data obtained are compiled in **Table 2**. The first reduction peak corresponds to a reversible diffusion-controlled process as revealed from the linear relationship between the peak currents and the square root of the scan rate¹⁴. This redox peak could be attributed to $\text{M}^{\text{III}}/\text{M}^{\text{II}}$ redox process as has been observed in a closely related systems.^{15,16} The second reduction peak corresponds to reduction of some centers in the ligand. The cyclic voltammogram (CV) of Fe^{II} -complex (**Table 2**) is quite different from that of Fe^{III} complex. In that there were two consecutive cathodic peaks at -402 and -668 mV and one anodic peak at -462 mV. This can be taken as a further supporting evidence for the dimeric nature of this complex. These cathodic peaks could be attributed to the reduction process of the dimeric complex to give the mixed valence. ($\text{Fe}^{\text{II}} \text{Fe}^{\text{II}} / \text{Fe}^{\text{II}} \text{Fe}^{\text{I}}$). The latter could be reduced to give Fe^{I} . This may indicate that the mixed valence complex is less stable than the Fe^{I} complex. The obtained cathodic peak values were close to Fe^{II} complexes of par-naphthaloquinones.¹⁷

Table (2): Cyclic voltammetric data of the complexes (1-4).

Compound	First wave (mV)			Second wave (mV)
	E _p c	E _p a	ΔE	
[MnL ₃].2EtOH	- 338	- 170	168	- 1100
[FeL ₃]	- 312	- 240	72	- 996
[Fe ₂ L ₄ (H ₂ O) ₂]	- 402	- 462	-	1040
	- 668			
[CoL ₃].3EtOH	- 318	- 225	93	- 1020

REFERENCES

1. N.E. Pitts and R.R. Proctor "Piroxicam" Academic press, London (1978).
2. C.M. Williamson, Curr. Med. Res. Opin., **8**, 622, (1983).
3. R.N. Brogden, R.C. Heel, T.M. Speight and G.S. Avery, Drugs, **22**, 165, (1981).
4. M. Mihalic', H. Hofman, F. Kajfez, J. Kufinec, N. Blazevic and Zinic', Acta Pharm. Jugoslav., **32**, 13, (1982).
5. S. El-Khateeb, S. Abdel Fattah, S. Abdel Razeq and M. Tawakel, Anal. Lett., **22**, 101, (1989).
6. A.M. Donia and H.A. El-Boraey, Transition Met. Chem., **18**, 315, (1993).

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7. J.B. Lambert, H.F. Shurvell, L. Verbit, R.G. Cooks and G.H. Stout
"Organic Structural Analysis" Macmillan Publishing Co.,
Inc., New York, 1976.
8. A.N. Sunder Ram and C.P. Prabhakaran, Indian J. of Chem., **15**,
980, (1977).
9. S.K. Sharma, R.K. Mahajan, B. Kapila and V.P. Kapila,
Polyhedron, **2**, 973, (1983).
10. R.K. Boggess, J.W. Hughes, C.W. Chew and J.J. Kemper, J. Inorg.
Nucl. Chem. **43**, 939, (1981).
11. A.B.P. Lever, Inorganic Electronic Spectroscopy, Elsevier,
Amsterdam (1968).
12. R.K. Parashar, R.C. Sharma, A. Kumar and G. Mohan, Inorg.
Chim. Acta, **151**, 201, (1988).
13. J.J. Grzybowski, P.H. Merrell and F.L. Urbach, J. Inorg. Chem. **17**,
3078, (1978).
14. R.S. Nicholson and I. Shain, Anal. Chem., **36**, 706, (1964).
15. J.A. Bonadies, M.J. Maroney and V.L. Pecoraro, Inorg. Chem.,
28, 2044, (1989).
16. P. Cofré, S.A. Richert, A. Sobkowiak and D.T. Sawyer, Inorg.
Chem., **29**, 2645, (1990).
17. R. Garge, S. Padhye and T.P. Tuchagues, Inorg. Chim. Acta., **157**,
239, (1989).

تحضير ودراسة الخواص الكهروكيميائية لبعض متراكبات البيروكسكام مع أيونات الفلزات

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قسم الكيمياء - كلية العلوم - جامعة المنوفية

فى هذا البحث تم تحضير متراكبات البيروكسكام مع أيونات المنجنيز
الثلاثى ، الحديد الثنائى والثلاثى ، الكوبالت الثلاثى والنيكل والنحاس والزنك
الثنائىة . وقد تم التعرف على نظام الترابط من خلال دراسات طيف الأشعة تحت
الحمراء والمرئية والتحليل العنصرى والتوصيل الكهربى فى المحاليل ، وقياس
العزم المغناطيسى عند درجة حرارة الغرفة .

تم تأكيد حالات الأكسدة لأيونات الفلزات فى المتراكبات من خلال قياس جيد
الأكسدة والإختزال لها .

كما أوضحت قياسات العزم المغناطيسى أن متراكبات الحديد الثنائى والنحاس
الثنائى توجد فى الصورة المزدوجة (الديره) بينما باقى المتراكبات توجد فى
الصورة المنفردة .