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Transition Metal Complexes of Monohydroxamic Acids

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Complexes of monohydroxamic acids and Fe(III), Co(II), Ni(II) and Cu(II) are shown to involve chelation via the oxygen atoms of the donor ligand. Spectral and magnetic properties of the complexes of Fe(III), Co(II), and Ni(II) indicate octahedral coordination with the latter two metal ions forming polymeric species. The monohydroxamic acid complexes show slightly larger 10Dq values than the corresponding aquo and acetylacetonato complexes. Cu(II) forms a square planar complex probably with a d_{xy} *ground state.*

Introduction

Monohydroxamic acids of the general formula RCON(R')OH are useful analytical reagents for a range of metal ions; in particular, the N-phenylbenzohydroxamic acid (R = R' = Ph) has been widely used [1, 2]. Despite their widespread analytical applications, or perhaps even because of them, there have been surprisingly few detailed structural or spectroscopic studies made of transition metal complexes of the mono-acids. The only X-ray diffraction study reported is that of iron(III) benzohydroxamate dihydrate in which normal octahedral co-ordination of the iron atom by the oxygen atoms of the ligand was observed [3]. To date, the majority of studies on complexes of hydroxamic acids have been solution studies with particular emphasis on determination of stability constants [4]. An example of this work is the determination of the stability constants of acetohydroxamic acid (R = CH_3, R' = H) for a large range of metal ions [5].

However, apart from isolated spectroscopic studies, *e.g.* the reported e.s.r. spectrum of the Cu(II) complex of N-methyldroxamic acid [6], to the best of our knowledge, there have been no comparative structural studies of these complexes reported so far.

In contrast, the past two decades have witnessed a marked increase in our knowledge of naturally occurring hydroxamic acids where they may function variously as growth factors, antibiotics, antibiotic antagonists, tumour inhibitors and cell division factors. Much of their biological activity seems to be related to their ability to chelate iron specifically [7–9], especially since the majority of naturally occurring hydroxamic acids are trihydroxamic acids which are ideally designed for octahedral co-ordination to iron(III). Examples of such Fe(III) complexes are provided by the Siderochromes which may be further subdivided into the sideromycins and sideramines which show antibiotic activity and growth factor activity, respectively.

The problem of iron-deficient anaemia is still serious, *e.g.* approximately 12% of non-pregnant and 20–58% of pregnant women in the United States show symptoms of this disease [10]. Consequently, we have attempted to design iron chelates as suitable oral iron sources, and have already reported the effectiveness of iron(III) acetohydroxamate in this regard [11]. At the same time, our attempts to relate biological activity to the bonding and structures of transition metal monohydroxamates revealed a dearth of knowledge in this area. In the present paper, we report comparative structural and spectroscopic studies of complexes of Cu(II), Ni(II), Co(II) and Fe(III) with the monohydraxamic acids listed below:

R	*R'*	*Name*	
CH_3	H	Acetohydroxamic	Acid(AHA)
C_2H_5	H	Propionohydramic	Acid(PHA)
C_6H_5	H	Benzohydroxamic	Acid(BHA)
CH_3	CH_3	N-Methylhydroxamic	Acid(MAHA)
C_6H_5	C_6H_5	N-Phenylbenzohydroxamic	Acid(PBHA).

The complexes prepared are listed in Table I, together with analytical data and magnetic moments.

Experimental

The primary monohydroxamic acids were prepared by acylation of hydroxylamine according to literature methods [12]; in some cases Blatt's synthesis was modified by using dry HCl to liberate

TABLE I. Elementary Analyses, Melting Points, Colours and Magnetic Moments of the Metal Hydroxamates.

Compound	Elemental Analysis				M.P. °C	Colour	$\mu_{B.M.}$
		C	H	N			
$Fe(BHA)_3 \cdot H_2O$	Calc.	52.32	3.88	9.47			
	Found.	52.64	3.99	8.41	178 (dec)	deep red	5.95
$Cu(BHA)_2$	Calc.	50.10	3.57	8.33			
	Found.	50.13	3.60	8.14	194 (dec)	blue green	1.99
$Ni(BHA)_2 \cdot H_2O$	Calc.	48.18	4.04	8.03			
	Found.	47.83	4.07	7.72	229 (dec)	green	3.51
$Co(BHA)_2 \cdot H_2O$	Calc.	48.15	4.04	8.02			
	Found.	48.00	4.07	7.70	193 (dec)	pink	5.17
$Fe(PBHA)_3 \cdot H_2O$	Calc.	65.93	4.54	5.91			
	Found	66.18	4.56	5.61	176 (dec)	red-brown	6.16
$Cu(PBHA)_2$	Calc.	63.99	4.14	5.74			1.98
	Found.	63.93	4.41	5.46	125 (dec)	light green	1.97
$Ni(PBHA)_2$	Calc.	64.63	4.18	5.80			
	Found.	64.57	4.16	5.71	111 (dec)	green	3.44
$Co(PBHA)_2$	Calc.	64.60	4.18	5.80			
	Found.	64.30	4.43	5.62	224 (dec)	pink	5.22
$Fe(MAHA)_3$	Calc.	33.77	5.63	13.13			
	Found.	34.01	5.45	13.15	230	red	5.32
$Cu(MAHA)_2$	Calc.	30.47	5.01	11.68			
	Found.	29.90	5.00	11.30	235	deep blue	1.78
$Ni(MAHA)_2$	Calc.	30.68	5.11	11.93			
	Found.	30.08	5.68	11.22	275 (dec)	green	3.07[a]
$Co(MAHA)_2$	Calc.	30.64	5.11	11.91			
	Found.	27.00	4.90	9.96		violet	

[a] Magnetic Moments measured by the N.M.R. method.

the free acid. Secondary monohydroxamic acids were prepared by O-acylation of N-substituted hydroxylamines. All complexes were prepared by direct reaction of a metal halide with the respective acid or its alkali metal salt in a suitable solvent (generally water or ethanol). Since chelation involves loss of protons, careful pH control is necessary. The iron(III) complexes precipitated as reddish solids when the reaction was carried out using anhydrous ferric chloride in dry ethanol. The Cu(II), Ni(II) and Co(II) complexes of BHA and PBHA precipitated quantitatively but $Cu(MAHA)_2$ required evaporation and recrystallization and $Ni(MAHA)_2$ and $Co(MAHA)_2$ formed as oils and proved difficult to purify, requiring several extractions and recrystallization, but even then the Co(II) product remained impure. Two sample preparations are given below.

Preparation of $Cu(BHA)_2$

2 g (0.014 mol) of BHA in 2.5 ml warm water was added to 1.75 g (0.007 mol) $CuSO_4 \cdot 5H_2O$. A blue-green precipitate resulted. After standing for six hours to ensure complete precipitation, the precipitate was filtered off, washed with warm water and dried *in vacuo* over P_2O_5 (yield 98.5%).

Preparation of $Fe(PBHA)_3 \cdot H_2O$

0.423 g (0.00156 mol) $FeCl_3 \cdot 6H_2O$ in warm water was added to 1 g (0.00469 mol) PBHA in ethanol. The pH of the resulting violet-coloured solution was raised by drop-wise addition of a 10% $NaHCO_3$ solution. The red product was filtered off, recrystallized from methanol or chloroform, and dried over silica gel (yield 69%).

Molecular weights in solution were measured by the isopiestic method, using a Perkin-Elmer Model 115 instrument calibrated with solutions of benzil in chloroform, acetone or ethanol as appropriate. Infrared spectra were recorded on a P.E. 457 grating instrument as 2% CsBr discs. Far i.r. spectra were recorded on a Grubb Parsons Cube Interferometer. Electronic spectra of solutions were measured on a P.E. 402 Spectrophotometer and reflectance spectra of solids on a Unicam SP500 instrument with a reflectance attachment and MgO as standard. E.S.R. spectra were recorded on a Decca X Band Spectrometer on bulk powder measurements. Magnetic moments were measured on a Newport Variable Temperature Gouy Balance. Solution moments were determined in $CDCl_3$ on a Varian HR 60A NMR Spectrometer by the Evans method [13].

TABLE II. Molecular weights.

Compound	M.W. Theor. (Monomer)	M.W. Found^a	Solvent
$Cu(PBHA)_2$	487.53	449.87	Chloroform^b
$Cu(MAHA)_2$	239.53	245.01	Chloroform^b
$Fe(MAHA)_3$	319.81	309.76	Acetone^c
$Ni(MAHA)_2$	234.88	442.30	Acetone^c
		458.38	Ethanol^d
		939.41	Chloroform^b

^{a}Molecular weight values accurate to ±5%. ^{b}Concentration range for chloroform: 6×10^{-4} to $5 \times 10^{-3}M$. ^{c}Concentration range for acetone: 2×10^{-3} to $9 \times 10^{-3}M$. ^{d}Concentration range for ethanol: 3×10^{-3} to $2 \times 10^{-2}M$.

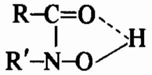
Results and Discussions

The complexes vary in colour from red to blue and are generally air-stable. The stability increases with increasing size of substituent R and R′ such that it is not possible to isolate any stable complexes of AHA whereas both BHA and PBHA form the complete range. Increasing substitution also leads to decreasing solubility. The series of Fe(III) complexes of MAHA, BHA, and PBHA are stable and soluble in a range of solvents. Molecular weight studies showed that $Fe(MAHA)_3$ is monomeric in acetone (Table II). The Cu(II) complexes of MAHA and PBHA are both monomeric in chloroform (Table II), although $Cu(BHA)_2$ is insoluble. In contrast, the Ni(II) and Co(II) complexes of both BHA and PBHA are insoluble in all common solvents; however, $Ni(MAHA)_2$ was found to be tetrameric in chloroform, and, for limited concentration ranges, dimeric in acetone and ethanol (Table II). Both the spectral and magnetic properties of the Ni(II) and Co(II) complexes (in the solid state) indicate octahedral symmetry about the metal ion, and we suggest, therefore, that the MAHA complexes of Ni(II) and Co(II) are both tetrameric in the solid state with structures similar to that reported for the known tetramer of the closely related $Co(acac)_2$ [14]. The completely insoluble Ni and Co complexes of BHA and PBHA are then probably highly polymeric in structure. All attempts to cleave this structure by prolonged reaction with strong electron donors such as pyridine failed, arguing for high stability of the polymer.

Infrared Spectra

The infrared spectra of the hydroxamic acids and their metal complexes were measured in the range 4000–250 cm^{-1} and far infrared spectra in the range 400–10 cm^{-1} obtained for $Cu(PBMA)_2$, $Cu(MAHA)_2$ and $Co(PBHA)_2$. In general the spectra are very complex and reliable assignments can only be made on the basis of a full *Normal Coordinate Analysis* which was carried out for a number of complexes as described in the following paper, where extensive coupling is shown to occur for a number of vibrations making qualitative deductions unreliable.

However, one point is clear from purely qualitative reasoning, namely, the broad band in the 1610–1585 cm^{-1} region present in all the free ligands which is attributed to the ketonic carbonyl and its broadening to intramolecular H bonding:



undergoes a shift of about 40–60 wavenumbers on complexation which is consistent with chelation by the ketonic oxygen atom. In the region below 950 cm^{-1} most bands are sensitive to the nature of the metal ion and/or the substituent, but further discussion of these bands is given in the subsequent paper.

Magnetic Moments

The magnetic moments of the solid complexes are given in Table I, and, where possible, compared with solution moments. The iron(III) complexes all show moments consistent with octahedral coordination and a high-spin configuration. The cobalt(II) complexes have moments of about 5.2 B.M. which are consistent with a high-spin octahedral configuration and a $^4T_{1g}$ ground state [15].

The Ni(II) series have moments in the 3.1–3.5 B.M. range and are clearly inconsistent with a square

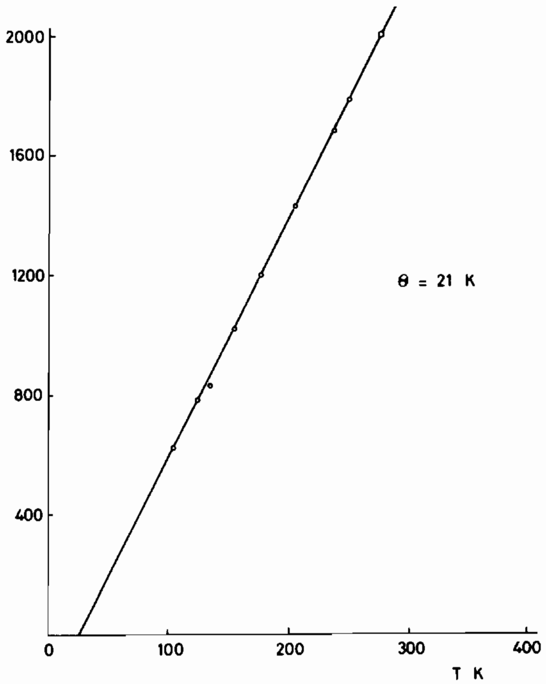


Figure. Plot of reciprocal magnetic susceptibility *versus* temperature for $Ni(PBHA)_2$.

planar diamagnetic structure. A paramagnetic tetrahedral complex with a $^3T_1$ ground state would give the observed room temperature moment which should decrease with decreasing temperature. In contrast, the experimental moment increases slightly with decreasing temperatures (see Figure), and clearly the observed moment is more consistent with an octahedral structure, allowing for mixing of states *viz.* spin–orbit coupling by the expression

$$2.83 \quad 1-\frac{4\lambda}{10Dq}$$

using a free-ion value of λ and a value of 10Dq of approximately 9kK (see Table IV).

The Cu(II) complexes show moments of nearly 2 B.M. which are greater than that expected (1.73 B.M.) for completely separated Cu(II) ions, but no stereochemical information can be obtained in this case.

Electronic Spectra

The observed transitions and assignments based on the Tanabe Sugano diagrams [16] for an octahedral field are given in Tables IIIa–IIId.

In the case of the Fe(III) complexes, intraligand bands may obscure some of the very weak spin-forbidden d–d bands; however, the fairly sharp band at about 20,000 cm^{-1} is assigned to the $^6A_{1g} \rightarrow {}^4A_{1g}$, ^4E_g transition and may then be used to calculate the nephelauxetic parameter β_{35} by comparison with the analogous free ion transition $^6S \rightarrow {}^4G$. The value of β_{35} so obtained (~0.70) is quite low and indicates some covalency in the Fe–O bonds in these complexes; however, the decrease in β_{35} is more pronounced for the phenyl substituted ligands than for Fe(MAHA)$_3$, suggesting that the former have a greater tendency towards covalency than the latter.

Ligand-field theory predicts three spin-allowed transitions for octahedral Co(II) but the first ($^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$) is not always observed above 10,000 cm^{-1}. Assignment of the other transitions to $^4T_{1g}(F) \rightarrow {}^4A_{2g}$ and $^4T_{1g}(F) \rightarrow {}^4T_{2g}(P)$ respectively, as in Table III, enables calculations to be made both of 10Dq and the Racah parameter B from standard equations [17]. β_{35} can also then be calculated, taking B (free ion) as 971 cm^{-1}. The values so obtained are given in Table III, and the β_{35} value indicates a lower degree of covalency than in the iron case.

In the case of Ni(II) in an octahedral environment, ligand field theory predicts three spin-allowed d–d transitions, but again the lowest energy one is frequently not observed. As in the above case of the cobalt complexes, assignments of the $^3A_{2g} \rightarrow {}^3T_{1g}(F)$ and $^3A_{2g} \rightarrow {}^3T_{1g}(P)$ are given in Table III, and application of the standard equations [17] to these transition energies enables calculation of 10Dq and

TABLE IIIa. Electronic Spectra.

Compound	Solvent	Transitions				β_{35}
		π–π^*, d–π	$^6A_{1g} \rightarrow {}^4A_{1g}, {}^4E_g$	$^6A_{1g} \rightarrow {}^4T_{1g}$	$^6A_{1g} \rightarrow {}^4T_{2g}$	
Fe(BHA)$_2$·H$_2$O	Refl.	37.0	20.8	(17.4)	(16.3)	0.634
	EtOH	40.0	22.7			0.692
	H$_2$O	40.4	22.2			0.677
Fe(PBHA)$_3$·H$_2$O	Refl.		22.2		(16.0)	0.677
	EtOH	28.5	22.7			0.692
	H$_2$O		23.8			0.726
Fe(MAHA)$_3$	EtOH	45.0	23.8			0.726
	H$_2$O	51.3	23.2			0.707
Fe(H$_2$O)$_6^{3+}$[a]			24.6	18.5	12.6	0.75

[a] Ref. 20.

TABLE IIIb.

	Solvent	$^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$	$^4T_{1g}(F) \rightarrow {}^4A_{2g}$	$^4T_{1g}(F) \rightarrow {}^4T_{2g}(P)$	β_{35}	10Dq, kK
Co(BHA)$_2$·H$_2$O	Refl.	10.00	(16.12)	19.23	0.878	8.60
Co(PBHA)$_2$	Refl.	10.00	(14.81)	18.52	0.869	7.92
Co(MAHA)$_2$	H$_2$O			18.87	0.900	8.54

[b] Ref. 21.

TABLE IIIc.

	Solvent	$^3A_{2g} \rightarrow {}^3T_{2g}$	$^3A_{2g} \rightarrow E_g(D)$	$^3A_{2g} \rightarrow {}^3T_{1g}(F)$	$^3A_{2g} \rightarrow {}^1T_{2g}(D)$	$^3A_{2g} \rightarrow {}^3T_{1g}(P)$	π_3–π_4	β_{35}	10Dq, kK
Ni(BHA)$_2$·H$_2$O	Refl.	10.00	(13.31)	15.04		26.67		0.897	9.06
Ni(PBHA)$_2$	Refl.	10.00	(12.50)	14.61	(22.9)	29.41		0.92	9.71
Ni(MAHA)	CHCl$_3$			15.55		23.98	34.23	0.85	9.23
	H$_2$O			15.24		26.32		0.56	10.07
	Acetone			15.82		24.39	40.82	0.59	10.20
Ni(H$_2$O)$_6^{2+}$ [b]		8.5	15.2	13.8	(22.0)	25.3		0.75	8.5

[b] Ref. 21.

TABLE IIId.

		Observed Absorption Bands* (kK)								
Cu(BHA)$_2$	Reflectance		25.0					15.9	12.7	
Cu(PBHA)$_2$	Reflectance		25.67			(17.9)	(16.12)	15.27	(11.90)	(11.10)
	Chloroform	33.5	29.07			(17.9)		16.3	12.7	
	Pyridine						16.67	14.07		
Cu(MAHA)$_2$	Reflectance		25.97	(23.2)	(19.23)	(17.2)		16.07	(14.92)	
	Chloroform		28.57		19.23			16.53		12.7
	Water	44.44	28.57					16.13		
	Ethanol	40.82	28.99					15.90		
	Pyridine						(16.53)	15.12		

* In all the above Tables (IIIa–IIId), shoulders are shown in parenthesis.

TABLE IV. ESR Spectra of Magnetically Concentrated Powders.

Compound	$g_x = g_y$ [a]	g_z [a]	Uncorrected		G [b]	λ
			H_1 (gauss)	$g_x = g_y$		
$Cu(PBHA)_2$	2.068 ± 0.001	2.25 ± 0.001	130	2.055	3.7	–521
$Cu(MAHA)_2$	2.066 ± 0.001	2.25 ± 0.001	77	2.055	3.8	–512
$Cu(BHA)_2$	2.090 ± 0.005	2.14 ± 0.005	96	2.077	1.56	

[a] g_x, g_y and g_z values are calculated using Gaussian line shapes. g_z is not affected by correction. [b] $G = (g_z - 2)/(g_x - 2)$.

β_{35} to be made (see Table III). The shoulder on the low frequency side of the $^3A_{2g} \rightarrow {}^3T_{1g}(F)$ band was assigned to an intra-subshell transition $^3A_{2g} \rightarrow E_g$ and the weak shoulder at 22.9 kK in the reflectance spectrum of $Ni(PBHA)_2$ to the spin-forbidden $^3A_{2g} \rightarrow {}^1T_{2g}(D)$. The calculated values of 10Dq again indicate a fairly weak ligand field with quite small π-bonding between t_{2g} metal orbitals and ligand π-orbitals. The β_{35} value is similar to that calculated for other octahedral Ni(II) complexes of O-donor ligands (Table III). On replacement of methyl by phenyl, the value of 10Dq increases, indicating decreased π-interaction. This could be due to withdrawal of electron density from the ligand π-orbitals by conjugation of the phenyl groups.

With the exception of $Cu(MAHA)_2$, the spectra of the Cu(II) complexes were obtained as reflectance spectra, and consequently stereochemical deductions are questionable. Nevertheless, the spectra are similar to those of the Cu(II) β-diketonates [18] (see Table III), and so, by analogy with the reported single-crystal polarised spectra of bis(3-methylpentane-2,4-dionate)Cu(II) [19], we suggest a d_{xy} ground state for the Cu(II) hydroxamate with square-planar geometry. Interestingly, square-planar complexes of Cu(II) are sensitive to axial perturbation, and similarly the Cu(II) hydroxamate spectra show a marked red shift in pyridine solution indicative of co-ordination by pyridine in axial positions.

Shoulders at ~600 and ~610 nm for $Cu(PBHA)_2$ and $Cu(MAHA)_2$ respectively, which do not shift in pyridine solution are tentatively assigned to the d_{xy}–$d_{x^2-y^2}$ transition. The 10Dq value is slightly higher than that for the corresponding aquo and acetylacetonate complexes, but smaller than that for ammines and ethylenediammine.

E.S.R. Spectra

In the absence of a suitable diamagnetic host lattice, the e.s.r. spectra of the Cu(II) hydroxamates were measured as non-dilute powder samples, and the resulting g values are listed in Table V.

Using values of 16.67 kK and 16.39 kK for the electronic transition $d_{xy} \rightarrow d_{x^2-y^2}$ for $Cu(PBHA)_2$ and $Cu(MAHA)_2$ respectively, values of $\lambda_{\parallel}$ occur at –521 and –512 cm^{-1}, about 62% of the free ion value of –828 cm^{-1}, which may be attributable to a considerable amount of in-plane and out-of-plane π-bonding, and a significant degree of covalency.

Unfortunately, powder spectra cannot be used unambiguously to assign the ground state since the essentially axial spectra for both $Cu(PBHA)_2$ and $Cu(MAHA)_2$ are consistent with either a $d_{x^2-y^2}$ or d_{xy} ground state; nevertheless, the comparison with the crystal spectrum of $Cu(acac)_2$ supports our previous suggestion of a d_{xy} ground state based on magnetic moment data.

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