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Monohydroxamic Acid Complexes of Iron(II and III), Cobalt(II and III), Copper(II) and Zinc(II)

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Iron(II) and Cobalt(III) complexes of monohydroxamic acids (aceto-, propiono- and steareo-) are reported for the first time. Spectral and magnetic properties indicate octahedral coordination via the oxygen atoms of the deprotonated hydroxamic acid ligand. Both series are relatively unstable, the former undergoing rapid oxidation to Fe(III) and the latter reduction to Co(II) with concomitant oxidation of the ligand to acetate. Complexes of Fe(III), Co(II), Cu(II) and Zn(II) are also reported.

Introduction

Interest in metal complexes of monohydroxamic acids, RCONR'OH (R,R' = alkyl, aryl) has increased greatly in the past decade primarily because of the biological importance of the naturally occurring hydroxamic acids which may function variously as growth factors, antibiotics, antibiotic antagonists, tumour inhibitors and cell division factors. The naturally occurring trihydroxamic acids are ideally designed for octahedral coordination to iron(III) and much of their biological activity is related to their highly specific chelation to iron(III) [1–3]. In view of the importance of naturally occurring hydroxamic acids, research continues on the design of related chelating agents, on the one hand in attempts to design iron(III) chelates as suitable oral sources of iron for mammals [4, 5] and, on the other hand, as suitable reagents for the treatment of metal-overload and related diseases such as Cooley's anaemia [6] and plutonium incorporation [7].

Monohydroxamic acids form typical octahedral complexes with metals via coordination through the oxygen atoms and formation of reasonably ionic metal–oxygen bonds [8]. Thus X-ray crystallographic studies of tris-(benzohydroxamato)iron(III) dihydrate [9], tris(benzohydroxamato)chromium(III) [10], tetrakis(N-isopropyl-3,3-dimethylbutanohydroxamato)thorium(IV) [11], and tetrakis(N-phenylbenzohydroxamato)hafnium(IV) [12] show coordination of the central metal atom by the oxygen atoms of the ligand. Analogous coordination through oxygen and sulphur atoms occurs in tris(N-methylthiobenzohydroxamato)cobalt(III), -chromium(III), -iron(III), and -manganese(III) [13]. However, the nickel(II) complex of the aminohydroxamic acid, glycinehydroxamic acid $NH_2CH_2–CO–NHOH$, provides the first example of a transition metal complex in which the *nitrogen atom* of the NHO^- group is coordinated rather than the oxygen atom [14]. In the case of Ni(II) and Co(II) complexes of phenyl (R = R' = Ph; R = Ph, R' = H) and methyl (R = R' = Me) substituted hydroxamic acids, polymeric and tetrameric structures are indicated and all attempts to cleave such polymers by prolonged reaction with nucleophiles such as pyridine were unsuccessful [8], whereas acetohydroxamic acid (AHA) and propionohydroxamic acid (PHA) form normal octahedral complexes, *e.g.* $Ni(AHA)_2 \cdot 2H_2O$ [15].

To date, complexes of iron(II) have not been reported and previous attempts to isolate complexes of Co(III) only resulted in formation of the Co(II) compounds. Very recently, Co(III) complexes of benzohydroxamic acid (BHA), *p*-nitrobenzohydroxamic acid, and N-methylhydroxamic acid (MAHA) have been isolated as low-spin complexes where R' = alkyl and high-spin where R' = H or when R contains an electron-withdrawing group such as *p*-nitro [16]. In this paper we report the first preparation of iron(II) and cobalt(III) complexes of the early members of the alkylhydroxamic acids, that is acetohydroxamic acid (AHA) and propionohydroxamic acid (PHA). Some additional complexes of Co(II), Fe(III), Cu(II) and Zn(II) with the ligands listed below are also reported.

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R	*R'*	*Name*	*Abbreviation*
CH_3	H	Acetohydroxamic Acid	AHA
C_2H_5	H	Propionohydroxamic Acid	PHA
$n\text{-}C_{17}H_{35}$	H	Steareohydroxamic Acid	SHA
C_6H_5	H	Benzohydroxamic Acid	BHA
BrC_6H_4	H	*p*-Bromobenzohydroxamic Acid	*p*-BrBHA
C_6H_5	C_6H_5	N-phenylbenzohydroxamic Acid	PBHA

TABLE I. Microanalyses, Melting Points, Magnetic Moments, Colours and Solubilities of Metal Hydroxamates.

Compound		Analysis (%)			Melting points (°C)	$\mu_{B.M.}$	Colour	Solubility
		C	H	N				
$Fe(AHA)_3 \cdot H_2O$	Calc.	25.30	4.60	14.93	178	5.47	Red	V.s. alc, ether, chloroform
	Found	25.80	4.30	15.10				
$Fe(PHA)_3 \cdot 2H_2O$	Calc.	30.88	5.35	11.77	169	5.58	Red/Brown	V.s. alc, ether, chloroform
	Found	30.35	5.16	11.77				
$Fe(SHA)_3 \cdot 3H_2O$	Calc.	62.31	11.35	4.04	155(d)	5.33	Orange/Red	V.s. alc.
	Found	60.84	10.98	3.70				
$Fe(PBBHA)_3 \cdot H_2O$	Calc.	35.42	2.36	5.84	158	5.81	Deep/Red	V.s. alc.
	Found	35.16	1.97	5.65				
$Fe(AHA)_2 \cdot H_2O$	Calc.	21.64	4.51	12.62	*	5.18	Yellow/Orange	Insoluble
	Found	21.52	4.46	12.42				
$Fe(PHA)_2 \cdot H_2O$	Calc.	28.82	5.60	11.21	*	5.18	Yellow/Orange	Insoluble
	Found	28.43	5.13	11.18				
$Fe(SHA)_2 \cdot H_2O$	Calc.	64.69	11.34	4.18	*	5.27	Yellow/Red	Insoluble
	Found	62.98	11.32	4.08				
$Fe(BHA)_2 \cdot H_2O$	Calc.	48.86	4.65	8.14	*	5.22	Yellow/Red	P.s. alc.
	Found	48.53	4.63	7.98				
$Fe(PBBHA)_2 \cdot H_2O$	Calc.	32.33	2.69	5.38	*	5.32	Yellow/Red	P.s. alc.
	Found	32.13	2.41	5.21				
$Co(AHA)_2 \cdot H_2O$	Calc.	21.33	4.14	12.40	188(d)	5.32	Brown	Insoluble
	Found	21.58	4.44	12.26				
$Co(PHA)_2 \cdot 2H_2O$	Calc.	28.46	5.53	11.07	192(d)	5.05	Brown	Insoluble
	Found	28.44	5.53	11.34				
$Co(SHA)_2 \cdot 2H_2O$	Calc.	62.51	10.71	4.06	182	5.33	Mauve	Insoluble
	Found	62.84	11.02	4.02				
$Co(PBBHA)_2 \cdot H_2O$	Calc.	33.13	2.36	5.52	203	5.80	Mauve	Insoluble
	Found	33.10	1.94	5.52				
$Co(AHA)_3 \cdot H_2O$	Calc.	24.09	4.68	14.04	*	$\chi_M \sim 75 \times 10^{-6}$ c.g.s.	Green	V.s. alc.
	Found	23.65	3.99	13.66				
$Co(PHA)_3 \cdot H_2O$	Calc.	31.67	5.86	12.31	*	$\chi_M \sim 80 \times 10^{-6}$ c.g.s.	Green	V.s. alc.
	Found	31.81	5.57	12.50				
$Cu(AHA)_2 \cdot 2H_2O$	Calc.	19.39	4.85	11.31	229(d)	2.09	Green	Insoluble
	Found	19.29	4.74	11.72				
$Cu(PHA)_2 \cdot H_2O$	Calc.	27.92	5.81	10.85	238(d)	2.01	Green	Insoluble
	Found	28.09	5.35	10.82				
$Cu(SHA)_2 \cdot 2H_2O$	Calc.	62.01	10.15	4.02	220	2.05	Light Green	Insoluble
	Found	61.48	9.82	3.95				
$Cu(PBBHA)_2 \cdot H_2O$	Calc.	32.98	2.32	5.49	205(d)	1.96	Green	Insoluble
	Found	32.44	1.86	5.56				
$Zn(SHA)_2 \cdot 2H_2O$	Calc.	62.11	10.33	3.92	161	Diamagnetic	White	Insoluble
	Found	62.76	10.33	4.23				
$Zn(PBBHA)_2$	Calc.	34.05	2.04	5.68	180	Diamagnetic	White	Insoluble
	Found	33.91	2.45	5.65				

(continued on facing page)

TABLE I. *(continued)*

Compound		Analysis (%)			Melting points (°C)	$\mu_{B.M.}$	Colour	Solubility
		C	H	N				
$Zn(BHA)_2 \cdot H_2O$	Calc.	46.62	3.63	7.71	172	Diamagnetic	White	Insoluble
	Found	47.27	3.37	7.87				
$Zn(PBHA)_2$	Calc.	63.80	4.49	5.72	170	Diamagnetic	White	Insoluble
	Found	63.63	4.26	5.76				

*Not observed, as decomposition occurred too quickly.

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

Experimental

Primary monohydroxamic acids were prepared by acylation of hydroxylamine in the presence of a base followed by addition of a calculated amount of hydrochloric or acetic acids at ice temperature [17]. For the aceto-, propiono- and steareohydroxamic acids, it is essential to modify the above procedure by using very dry ethanol and substituting sodium ethoxide for potassium hydroxide.

In the preparation of the complexes, careful pH control is essential when the appropriate metal salt is reacted with the hydroxamic acid (or its alkali metal salt) in a suitable solvent (ethanol, methanol or water). Some sample preparations are given below:

Preparation of $Fe(AHA)_2 \cdot H_2O$

0.01 mol of $FeCl_2$ (anhydrous) was dissolved in the minimum quantity of dry alcohol at room temperature and added to 0.03 mol of the potassium salt of AHA in dry ethanol. The mixture was stirred for six hours under dry nitrogen, potassium chloride filtered off, and the filtrate evaporated down to one-third volume. The yellow-red precipitate was filtered immediately under nitrogen and dried at room temperature under nitrogen (yield: 15%).

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

0.01 mol of $FeCl_3$ (anhydrous) in 100 ml dry ethanol was added to 0.03 mol AHA in 25 mls dry ethanol. The addition of sodium ethoxide (0.48 mol) increased the initial pH of 0.8 to 8.0. The solution was filtered (to remove NaCl), concentrated to 20 ml volume and left at 0 °C for 48 hours. Red-brown crystals were filtered off and recrystallized from isopropyl alcohol. The product was dried at 110 °C for 2 hours (yield: 67%).

Preparation of $Co(AHA)_2 \cdot H_2O$

0.01 mol of $CoCl_2 \cdot 6H_2O$ was dissolved in the minimum amount of ethanol and added to a saturated solution of 0.02 mol AHA in ethanol. The pH was raised to 6.9 by the addition of sodium ethoxide. The mixture was filtered, and concentrated to one-third volume, and left at 0 °C for 72 hours. A brown powder was filtered off, and dried over calcium chloride.

Preparation of $Co(AHA)_3 \cdot H_2O$

Cobalt(III) hydroxide was prepared by a modified procedure of Ley and Winkler [18]. $Co(NO_3)_2 \cdot 6H_2O$ (0.01 mol) was treated with an excess of a solution of $NaBO_3 \cdot 4H_2O$ dissolved in 0.1 *M* NaOH. The resulting black precipitate was treated with ethanol several times in a centrifuge, dried under nitrogen and refluxed gently for 10 hours with 0.03 mol of KAHA in 50 ml dry ethanol under nitrogen. The hot dark-green solution was filtered under nitrogen, concentrated to 5 ml and allowed to cool. A green precipitate separated and was filtered off under nitrogen (yield: 21%). The product was stable for only five minutes.

Preparation of $Cu(AHA)_2 \cdot 2H_2O$

The preparation is similar to that of $Co(AHA)_2$ but the pH was adjusted to 5.1 rather than 6.9. The resulting green insoluble product was purified by several extractions with ethyl acetate.

The preparations of the other complexes are similar to the above, differing usually in the pH employed. Table I lists analytical data, melting points, colour, solubility and magnetic moments.

Infrared spectra were recorded in the region 4000–200 cm^{-1} on Perkin Elmer 457 and 283B instruments as KBr and CsBr discs. Electronic spectra (190–850 nm) of solutions were measured on PE402 and PE552 spectrophotometers. Reflectance spectra (350–1000 nm) were obtained on a Pye-Unicam SP500. Magnetic moments were determined on a Newport Variable Temperature Gouy Balance. Solution moments were evaluated on a P.E. R12 NMR instrument using the Evans method [19]. A Hilger and Watts H1170 Atomic Absorption Spectrometer was used for the metal analyses. Molecular weights were taken on chloroform solutions using a Perkin Elmer Model 115 (isopiestic) instrument, calibrated with benzil solution.

Results and Discussion

The complexes vary in colour from red to blue-green. Stability increases with increasing size of substituent. Thus, the complexes of BHA, *p*-BrBHA, PBHA and SHA are stable indefinitely, in marked contrast to those of AHA and PHA. Cobalt(II) and copper(II) complexes of AHA, PHA and SHA are insoluble, those of Fe(II) and Co(III) slightly soluble and those of Fe(III) soluble in a range of polar solvents. The insoluble Co(II), Ni(II), Cu(II) and Zn(II) complexes are probably polymeric in structure. Attempts to cleave them by prolonged reaction with electron donors such as pyridine failed. However, acetylacetone, acetophenone and tetraalkylthiuram disulphides displace the monohydroxamate group, except for Co(II) and Zn(II). Molecular weight studies show that $Co(AHA)_2$ is a tetramer (MW_{obs} 850; MW_{cal} 896) as observed previously for $Ni(MAHA)_2$ and again presumably with a structure analogous to that of $[Co(acac)_2]_4$ [20].

The iron(II) and cobalt(III) compounds are the first examples of complexation of these valence states by AHA and PHA. Both series are very unstable and all analytical and spectral determinations must be made rapidly to minimise decomposition. It is suggested that $Fe^{II}(AHA)_2\cdot H_2O$ decomposes according to the following scheme:

$$\begin{array}{l} 3Fe^{II}(AA)_2\cdot H_2O \rightarrow 2Fe^{III}(AA)_3\cdot H_2O + Fe^{o} + H_2O \\ \qquad\qquad\qquad \big\downarrow O_2 \\ \qquad\qquad\qquad 2Fe^{III}(AA)_3\cdot H_2O + Fe(OH)_3 \end{array}$$

The reaction was followed by monitoring the I.R. spectrum in the 600–200 cm^{-1} region. The characteristic $\nu_{as}(Fe{-}O)$ and $\nu_s(Fe{-}O)$ stretching modes of $Fe(AA)_2\cdot H_2O$ at 530 cm^{-1} and 315 cm^{-1} respectively shift to the corresponding bands of $Fe(AA)_3\cdot H_2O$ at 470 cm^{-1} and 280 cm^{-1} respectively; the change is complete in 30 minutes under nitrogen. An additional band appears at 560 cm^{-1} and is attributed to the $\nu_{as}(Fe{-}O)$ of $Fe(OH)_3$. Extraction of the decomposition product with isopropanol gave an analytically pure sample of $Fe(AA)_3\cdot H_2O$ and the residue after extraction analysed as pure $Fe(OH)_3$. The rate of decomposition was followed by the rate of disappearance of the $^5T_{2g} \rightarrow {}^5E_g$ transition of $Fe(AA)_2\cdot H_2O$ at 950 nm in the solid state by diffuse reflectance measurements to yield a first-order rate constant of 3.17×10^{-4} sec^{-1}.

The Co(III) complexes decompose more rapidly than the corresponding Fe(II) series according to the overall stoichiometric scheme:

$$Co^{III}(AA)_3\cdot H_2O \rightarrow Co^{II}(OOCCH_3)_2\cdot H_2O + \\ + CH_3COOH + NH_2OH$$

The reaction is complete in ethanol solution under nitrogen within 6 minutes. The pink cobalt(II) acetate was filtered off in quantitative yield and shown to be analytically pure. Quantitative formation of acetic acid and hydroxylamine in the above scheme was confirmed by standard methods [21]. However, monitoring the above reaction from the I.R. spectrum in the region700–200 cm^{-1} showed a shift in $\nu_{as}(Co{-}O)$ from 460 cm^{-1} in $Co^{III}(AA)_2\cdot H_2O$ to 520 cm^{-1} characteristic of $\nu_{as}(Co{-}O)$ in $Co^{II}(AA)_2\cdot H_2O$. A similar change occurred in ν_s-(Co–O). The presence of $Co^{II}(AA)_2\cdot H_2O$ was also indicated by formation of the 555 nm (λ_{max}) band in the electronic spectrum (see Table II). It thus appears that the reduction of Co(III) to Co(II) and oxidation of the coordinated AA^- ligand to CH_3COO^- proceeds via formation of $Co^{II}(AA)_2$ as intermediate. Tentatively, it is suggested that the water molecule of $Co^{III}(AA)_2\cdot H_2O$ may, during the initial reduction to Co^{II}, form a hydroxide ion which then attacks the coordinated AA^- ligand in $Co^{II}(AA)_2$ to give the observed products, CH_3COOH and NH_2OH.

The infrared spectra of these complexes are similar to those previously reported [8]. Electron withdrawal from the carbonyl group increases electron density in the C–N bond, resulting in a lowering of 50 cm^{-1} in the carbonyl frequency compared to the free ligands, and an increase of *ca.* 15 cm^{-1} in the C–N frequency. It must be emphasized that extensive mixing of these normal modes occurs, necessitating a normal coordinate analysis which will be discussed in a separate paper.

The magnetic moments (solid state and solution) of these complexes are given in Table I. The Fe(III) and Fe(II) complexes are consistent with high-spin octahedral coordination. Magnetic moments of *ca.* 5.1 BM are observed for the Co(II) complexes, indicating a high-spin octahedral configuration and a $^4T_{1g}$ ground state. Diamagnetic behaviour is expected for the Co(III) complexes ($\chi_m = -75 \times 10^{-6}$ c.g.s.) and is indeed observed. Only the room temperature moment could be obtained, and the development of paramagnetism with time, confirming the formation of the Co(II) rearrangement products discussed above, was clearly evident. These results contrast somewhat with those reported by Raymond *et al.* [16] where it is suggested that complexes with

TABLE IIa. Electronic Spectra.

Compound	Solvent	Transitions				β_{35}
		$\pi-\pi^*$, d$-\pi$	$^6A_{1g} \rightarrow {}^4A_{1g}, {}^4E_g$	$^6A_{1g} \rightarrow {}^4T_{1g}$	$^6A_{1g} \rightarrow {}^4T_{2g}$	
$Fe(SHA)_3$	Ethanol	(39.2)	(23.1)	(19.8)		0.73
	Benzene	(33.9)	(22.2)	(19.4)		0.68
$Fe(AHA)_3$	Ethanol	(40.3)	(22.5)			0.69
	Isopropanol	(41.6) (38.5) (31.3)	(22.7)			0.69
$Fe(PHA)_3$	Ethanol	(42.5) (35.7) (29.4)	(23.0)			0.70
	Isopropanol	(41.6) (34.0)	(22.5)			0.69
$Fe(BrBHA)_3$	Refl.	(36.4)	(20.8)	(17.4)	(16.1)	0.63
	Ethanol	(35.7) (29.9)	(21.1)			0.64

TABLE IIb.

	Solvent	Charge Transfer	$^5T_{2g} \rightarrow {}^5E_g$
$Fe(AHA)_2$	Refl.	(17.4)	(10.50)
$Fe(PHA)_2$	Refl.	(17.4)	(10.66)
$Fe(BHA)_2$	Refl.	(16.7)	(10.39)
$Fe(SHA)_2$	Refl.	(17.2)	(10.32)
$Fe(PBHA)_2$	Refl.	(16.5)	(10.30)

Table IIc.

Compound	Solvent	$^1T_{2g} \rightarrow {}^1A_{1g}$	$^1T_{1g} \rightarrow {}^1A_{1g}$	$^3T_{1g} \rightarrow {}^1A_{1g}$
$Co(AHA)_3$	Ethanol	(27.4)	(17.1)	
$Co(PHA)_3$	Ethanol	(27.4)	(16.9)	

Table IId.

	Solvent	Transition				
		$^4T_{1g}(F)-{}^4T_{2g}(F)$	$^4T_{1g}(F)-{}^4T_{2g}(F)$	$^4T_{1g}(F)-{}^4T_{2g}(F)$	β	10Dq, kK
$Co(AHA)_2$	Refl.	(18.0)	(15.6)	(>10.0)	0.83	8.30
$Co(PHA)_2$	Refl.	(18.2)	(15.3)	(>10.0)	0.86	8.30
$Co(SHA)_2$	Refl.	(18.3)	(15.2)	(>10.0)	0.84	8.11
$Co(Br\text{-}BHA)_2$	Refl.	(18.9)	(16.0)	(>10.0)	0.86	8.53

TABLE IIe.

Compound	Solvent	Transition Observed Absorption bands				
$Cu(AHA)_2$	Refl.	(23.5)	(19.24)	(15.4)		
$Cu(PHA)_2$	Refl.	(23.8)	(19.24)	(15.4)		
$Cu(SHA)_2$	Refl.	(24.1)	(18.0)	(15.4)	(12.0)	(11.10)
$Cu(Br\text{-}BHA)_2$	Refl.	(24.4)	(17.9)	(15.7)	(12.6)	
$Cu(BHA)_2$	Refl.	(25.0)	(18.2)	(15.9)	(12.7)	

R′ = H should be paramagnetic. The Cu(II) complexes have moments of 2 BM and show no evidence for metal–metal bridging. For the paramagnetic complexes, the Curie–Weiss Law is followed, and θ values are uniformly small. The Zn(II) complexes are diamagnetic as expected.

Electronic Spectra

The observed transitions and assignments based on the Tanabe Sugano diagrams [22] for an octahedral field are given in Tables IIa–IIe. 10Dq and β_{35} values were calculated for the complexes of Fe(III) and Co(II) as described in our previous paper [8]. The spectra of the Fe(II) complexes show a broad band at *ca.* 585 nm (*ca.* 17 kK) assigned to a charge transfer transition and a weaker band at *ca.* 955 nm (*ca.* 10 kK) assigned to the $^5T_{2g} \rightarrow {}^5E_g$ transition. For the isoelectronic Co(III) complexes, the $^1A_{1g}$ ground state crosses the $^5T_{2g}$ state at low 10Dq values and, interestingly, Raymond *et al.* observe that such crossing is proton dependent for certain paramagnetic Co(III) complexes of some hydroxamate acids since deprotonation forms the corresponding hydroximate complex anion which is low-spin [16]. In the present work, the Co(III) complexes of AHA and PHA are low-spin and their electronic spectra show only the spin-allowed bands.

Because of the insolubility of the Cu(II) complexes, the visible spectra were obtained as reflectance spectra, and are similar to those of Cu(acac)$_2$ and Cu(salim)$_2$ implying coplanar stereochemistry [23]. In the Cu(II) hydroxamates the most common form of π-bonding is out-of-plane using the d_{xz} and d_{yz} orbitals, which as they are filled, enable negative charge to be back donated to the ligand. Square coplanar complexes of Cu(II) are sensitive to axial perturbation so the d_{xz}, d_{z^2} and d_{yz} levels should be raised in energy, while the $d_{x^2-y^2}$ and d_{xy} levels remain unchanged. The spectra consist mainly of one broad band centred at 15.5 kK and another absorption with a shoulder at 19.2 kK.

In view of the fact that both the electronic spectra and magnetic moments of the Fe(II) complexes are consistent with octahedral coordination, it seems reasonable to suggest an oligomeric structure for these complexes similar to that suggested for Fe(acac)$_2$ [24] although the relative instability of these complexes precluded molecular weight determinations.

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