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METAL COMPLEXES OF HYDROXAMIC ACID ANALOGS

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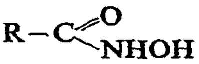
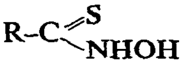
Hydroxamic acids,  $R-C\begin{smallmatrix}\nearrow O\\ \searrow NHOH\end{smallmatrix}$ (I), and some of their derivatives form characteristic colored chelate compounds with metal ions such as Fe^{3+}, Ti^{4+}, UO_2^{2+}, V^{5+}, etc., and thesereactions have been applied to the colorimetric determination of these ions. Of these, the formation of a red to violet ferric complex is available for the qualitative or quantitative assay of a variety of organic compounds which can be easily converted into I, such as carboxylic acids, alcohols or phenols, esters, acid chlorides, acid anhydrides and amides[1]. In addition, a number of hydroxamic acids have been found in microorganism products[2]. From such analytical and pharmacological interest, a great deal of work has been carried out on hydroxamic acids, but this paper deals only with problems concerning the comparative studies of the chemical properties and metal complexes of the following hydroxamic acid analogs.



$R-C\begin{smallmatrix}\nearrow S\\ \searrow NHOH\end{smallmatrix}$ (II) Thiohydroxamic acids

$R-X-C\begin{smallmatrix}\nearrow Y\\ \searrow NHOH\end{smallmatrix}$

$X = NH, Y = O$ (III) 3-Hydroxyureas
$X = NH, Y = S$ (IV) 3-Hydroxy-2-thioureas
$X = O, \quad Y = O$ (V) *N*-Hydroxycarbamates

1. *Tautomerism in and dissociation constants of the ligands*

These compounds like the hydroxamic acids can exist in two tautomeric forms ($a \rightleftharpoons b$) and their monoanions can exist in three forms (c–e) in equilibrium. Such tautomeric equilibria are more complicated in the case of III and IV, and forms f–i may be taken into consideration.

Although some discrepancies have remained[3], it has been shown that hydroxamic acids (I) exist in the ketoform (Ia, Y = O) both in the solid state and in solution[4–7], and that the hydrogen atom of the imino group NH of I dissociates predominantly to form the mesomeric monoanion $Ie_1 \leftrightarrow Ie_2$[8–12], that is, I is essentially an N-acid[9].

Although thiohydroxamic acids (II) are generally written in the thiol form (IIb, Y = S) on the basis of their chemical reactivity[1,3–16] recent work has indicated[17] that II exists in the thione-form (IIa, Y = S) in the solid state but in both

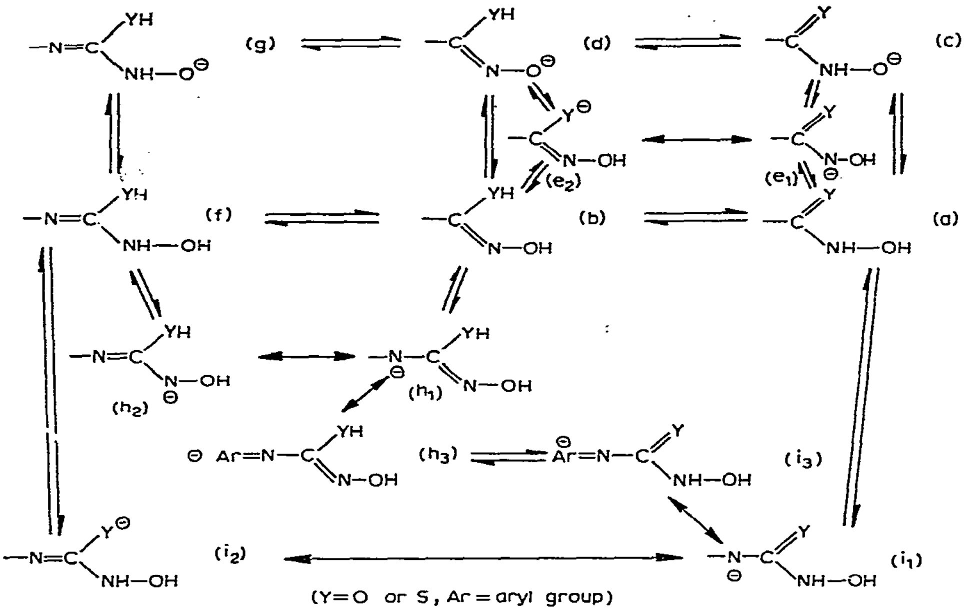
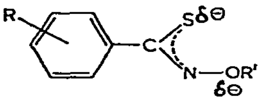
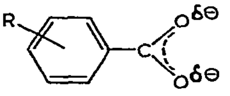
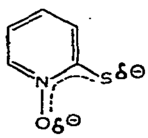


Fig. 1.

the thiol- and thione-forms in the liquid or in solution. Marked differences are found between the spectra of II in solution and in the solid. The SH band is absent in the solid state, whereas not only a SH band but also two other bands, assumed to be non-associated NH or OH stretching bands, appear in solution. Moreover, spectral changes associated with deuteration closely resemble those of thioureas or thioamides which include the thioureid group $\overset{|}{-\mathrm{N}}-\overset{|}{\mathrm{C}}=\mathrm{S}$. Table I shows that the dissociation constants (pKa values) of II are nearly the same as those of O-methyl derivatives of II, $\mathrm{R{-}C}\begin{smallmatrix}\mathrm{SH}\\ \mathrm{NOCH_3}\end{smallmatrix}$ (VI), which exist in the thiol-form in all states. Furthermore, in the correlation of pKa values with Hammett's constants as shown in Fig. 2, the reaction constants of both the II and VI series are about 1.0, much the same value as for the benzoic acid series (k), so that there is no doubt that the monoanions of II exist in the tautomeric forms IIe_1 ↔ IIe_2 and the analogous mesomeric structure (j) may be proposed.


(j)


(k)


(l)

Similar structures (l) have been found for 2-mercaptopyridine N-oxide[18].

Little or no work has been done on the structures or tautomeric equilibria of

3-hydroxy ureas (III), 3-hydroxy-2-thioureas (IV) and *N*-hydroxycarbamates (V), except for some studies on hydroxyurea,[19–21] and *N*,*N*-bis(phenylcarbamoyl)-hydroxylamine.[22,23] Hurd has proposed[24] structure IIf (Y = O) for III on the basis of his finding that III fails to undergo the rearrangements which are so customary in compounds containing the hydroxamic acid group. There is no doubt, however, that III, IV and V all exist predominantly as the keto (IIIa, Va, Y = O) or thione (IVa, Y = S) (Fig. 1) form in the solid and in solution from our examination of their infrared spectra. The spectra of III and V show close analogies with those of ureas or amides and hydroxamic acids respectively, and the spectra of IV not only resemble those of thioureas or the thioneform of II but also give no SH band even in solution. Hammett's law is also valid[51] in the III series and their derivatives as shown in Fig.2. In these cases, however, Hammett's σ_p^- value (1.270)[25] and Bekkum's value (−0.266)[26] are applied for *p*-nitro and *p*-dimethylamino derivatives, indicating that mesomeric para interactions (m) have considerable contributions for III and their derivatives in the same manner as for the aniline[26] and sulfonamide series[27]. Since the reaction constant of III and their derivatives are

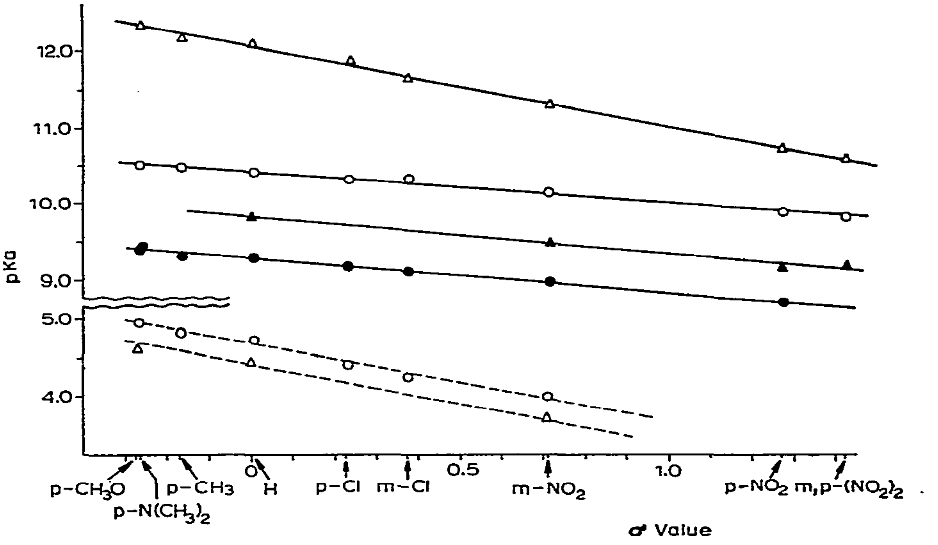
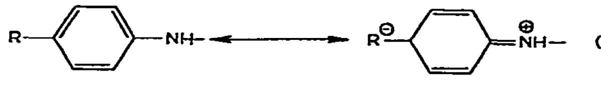


Fig. 2. Correlation of pKa with Hammett's Constant

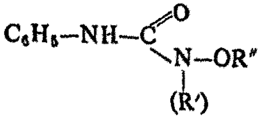
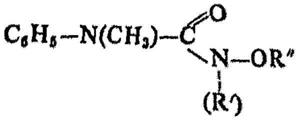
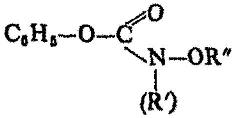
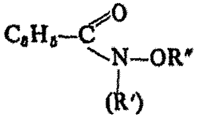
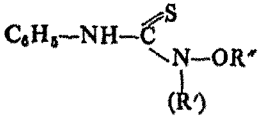
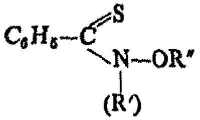
○———○	$C_6H_5NHCONHOH$ Series	pKa = $-0.41\sigma+10.44$
△———△	$C_6H_5NHCONHOCH_3$ Series	pKa = $-1.02\sigma+12.08$
▲———▲	$C_6H_5NHCON(CH_3)OH$ Series	pKa = $-0.48\sigma+9.84$
●———●	$C_6H_5NHCON(C_6H_5)OH$ Series	pKa = $-0.41\sigma+9.28$
○---------○	$C_6H_5CSNHOH$ Series	pKa = $-0.98\sigma+4.67$
△---------△	$C_6H_5CSNHOCH_3$ Series	pKa = $-1.00\sigma+4.41$



(m)

TABLE 1

DISSOCIATION CONSTANTS OF HYDROXAMIC ACID ANALOGS AND THEIR DERIVATIVES

Substituent / Compound	$R'=H$				$R'=CH_3$	$R''=H$			
	$R''=H$	$R''=CH_3$	$R''=$ $-COC_6H_5$	$R''=$ $-CONHC_6H_5$	$R''=CH_3$	$R'=CH_3$	$R'=C_6H_5$	$R'=$ C_6H_5CO-	$R'=$ C_6H_5NHCO-
 $C_6H_5{-}NH{-}C(=O){-}N(R'){-}OR''$	10.4_4	12.1_2	8.9_3 $(8.40)^{*,10)}$	(decomp.)	>13	9.8_4	9.4_1	6.7_0	8.1_3
 $C_6H_5{-}N(CH_3){-}C(=O){-}N(R'){-}OR''$	(decomp.)					10.3_5	10.4_8		
 $C_6H_5{-}O{-}C(=O){-}N(R'){-}OR''$	9.6_3	9.4_9				9.0_6	8.8_1		
 $C_6H_5{-}C(=O){-}N(R'){-}OR''$	$8.78^{55,56)}$ 8.93	$8.89^{10)}$ $8.88^{12)}$	$(8.08)^{*,10)}$			$8.5_9^{12)}$	$8.15^{29)}$ $8.27^{55)}$		
 $C_6H_5{-}NH{-}C(=S){-}N(R'){-}OR''$	7.9_0	8.9_3				7.5_4	7.2_1		
 $C_6H_5{-}C(=S){-}N(R'){-}OR''$	4.7_3	4.4_5							

*Values in 80% methylcellosolve.

All compounds were determined in 3% ethanol ($\mu = 0.20$) by a potentiometric or spectrophotometric method, except those cited from the literature.

(decomp.) means that the pKa value of this compound cannot be determined because of decomposition in alkaline solution.

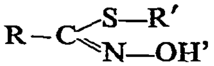
no more than 1.0 whereas those of the aniline or phenol series are more than 2.0[28], such dissociations as formulated in h_1 or i_1 (fig. 1) are less likely. Consequently, the reaction constants (about 1.0) of 1-aryl-3-methoxyurea series and those (about 0.4) of the 1-aryl-3-methyl (or phenyl)-3-hydroxyurea series may be explained satisfactorily by assuming that their monoanions exist in the forms IIIe and IIIc ($Y = O$), respectively (fig. 1). Hence we assume that III dissociates in the form IIIc because the reaction constant of III is the same as that of 1-aryl-3-methyl-3-hydroxyurea. The amount of form c in the equilibria can be calculated to be about 95% for III and IV and about 75% for V. This may be devised from the pKa values of the corresponding derivatives described in Table I according to Exner's procedure[10].

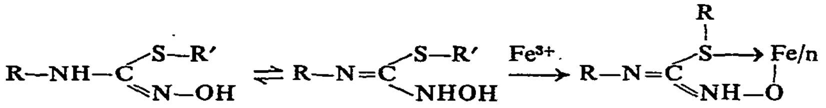
To summarize, it can be concluded that the II series are mostly N-acidic, while the III series are mostly O-acidic, and the pKa values decrease in the order III > V > I > IV > II. The value calculated above for Vc, however, indicates that other tautomeric forms can exist, and further more, as described later, the existence of tautomer f is indicated for 1-phenyl-3-hydroxy-2-methylisothiourea. Therefore, more complete studies are necessary to draw definitive conclusions about the tautomeric equilibria of these hydroxamic acid analogs in solution.

2. *Reactivities with metal ions and the structures of the metal complexes*

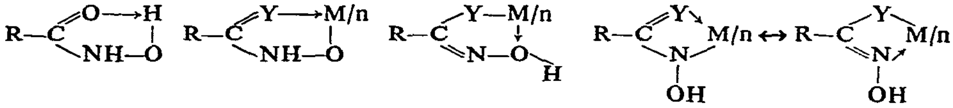
It is characteristic of hydroxamic acids (I) to show color reactions with Fe^{3+}, Ti^{4+}, $UO_2{}^{2+}$, and V^{5+}, and to give water-insoluble precipitates with Cu^{2+}.[29–31] 3-Hydroxyureas (III) and *N*-hydroxycarbamates (V) also show a sensitive blue to bluish violet color formation with Fe^{3+} and will precipitate with Cu^{2+}, but they show no reaction with Ti^{4+}, $UO_2{}^{2+}$ and V^{5+}. 3-Hydroxy-2-thiourea (IV) also reacts with Fe^{3+} and Cu^{2+}, but not with Ti^{4+}, V^{5+}, and further will react with a few heavy metals such as Ag^{1+}, Co^{2+}, Ni^{2+}, Pd^{2+}, Hg^{2+}, Pb^{2+} and Pt^{4+}, because of the presence of sulfur as a ligand atom. As reported already,[32–34] the reactivities of thiohydroxamic acids (II) with metal ions are considerably different from those of III, IV and V. They are not only apt to give precipitates with various transition metal ions, but also give characteristic color reactions with Fe^{3+}, $UO_2{}^{2+}$, Ti^{4+}, V^{5+} and Cu^{2+}. Whereas *O*-methylthiohydroxamic acids (VI) or various compounds[35] with mercapto and oxime groups in positions favorable for coordination, such as 2-mercaptoacetophenone oxime, 3-mercaptopropiophenone oxime and 5-nitro-2-mercaptobenzaldoxime, form precipitates with some transition metals, they give no reaction with UO_2^{2+}, Ti^{4+} and V^{5+}, and moreover reduce Fe^{3+} to Fe^{2+} and yield Cu^{1+} salts with Cu^{2+}. Thus it appears that II has both the properties of I and those of reagents which contain the mercapto group.

Compounds which are able to react with metal ions appear to contain the following functional groups, $-\mathrm{C}{\scriptstyle\genfrac{}{}{0pt}{}{\nearrow \mathrm{SH}}{\searrow \mathrm{NOR'}}}$, or $-\mathrm{C}{\scriptstyle\genfrac{}{}{0pt}{}{\nearrow\!\!\!\nearrow \mathrm{Y}}{\searrow \mathrm{N(R')}\text{—}\mathrm{OH}}}$ ($Y = O$ or S, $R' =$

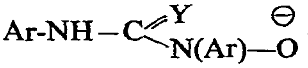
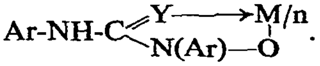
H or alkyl etc.). The only exception[51] among the compounds tested is 3-hydroxy-2-alkyl-isothiourea (VII, R′ = alkyl), which gives a blue color with Fe^{3+}. Since S-alkylthiohydroxamic acid,  $\mathrm{R-C}\begin{matrix}\diagup\mathrm{S-R'}\\ \diagdown\mathrm{N-OH}\end{matrix}$, does not show any color reaction with Fe^{3+}, it is considered probable that VII is isomerized to a hydroximino type (VIIf) in solution and thus forms the iron-chelate (VIIn).

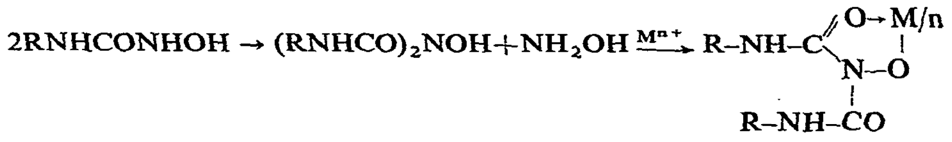

(VII) (VIIf) (VIIn)

Although isolated metal complexes of I have the constitution ML_n (M = metal ion, L = monoanion of ligand, n = valency of the metal ion)[36], no studies of their structures have been done up to now. Nevertheless, metal complexes of I have customarily been written in the chelate form Ip (Y = O) apart from one exception[3] which was presented in the form Ir. Since there is no doubt that the series I have structures as indicated in Io and which includes intramolecular hydrogen bonding[4–7], form Ip is very reasonable for their metal complexes. If, however, I dissociates into Ie as found by Exner[10], then two other possible structures, described in Iq and Ir (Y = O) should be taken into consideration. The structures of the metal complexes


(Io) (p) (q) (r_1) (r_2)
(y = O or S)

of the I series should be further re-examined from the point of view of the dissociation of I in solution.

It has been revealed[38] that the metal complexes of 3-hydroxy-1,3-diarylureas and 3-hydroxy-1,3-diaryl-2-thioureas have the constitution ML_n [M = Cu^{2+}, Ni^{2+}, Co^{2+}, L =  $\mathrm{Ar\text{-}NH-C}\begin{matrix}\diagup\!\!\diagup\mathrm{Y}\\ \diagdown\mathrm{N(Ar)-\overset{\ominus}{O}}\end{matrix}$ (Y = O or S)], and their structures are presumed to be of the form  $\mathrm{Ar\text{-}NH\text{-}C}\begin{matrix}\diagup\!\!\diagup\mathrm{Y\longrightarrow M/n}\\ \diagdown\mathrm{N(Ar)-O}\end{matrix}$. According to our observations,[51] however, compounds which have no substituents at the 3-position, namely III and IV, fail to form metal complexes because of the instabilities of the ligands. By warming or long standing, the V series are decomposed gradually while the II series give metal complexes of the *N,N*-dicarbamoylhydroxylamines (VIII), the structures of which are presumed to be of the form IX. If metal ions are absent, solutions of III are very stable, so that the strong chelate-forming abilities of VIII are likely to facilitate the following reactions.

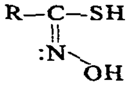


$$2RNHCONHOH \rightarrow (RNHCO)_2NOH + NH_2OH \xrightarrow{M^{n+}} R\text{-}NH\text{-}C\begin{smallmatrix}O\rightarrow M/n\\ N-O\end{smallmatrix}\ (N\text{-}CO\text{-}NH\text{-}R)$$

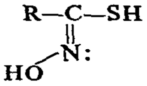
(III) (VIII) (IX)

$(M = Fe^{3+}, Co^{2+}, Cu^{2+})$

Cambi and his co-workers[39] have determined the magnetic moments of metal complexes of II, and they proposed the structures IIr which include four-membered chelate rings with oxime oxygen. The present authors have indicated[40] that the spectral changes of these metal complexes upon deuteration are quite different from those of the thione-form thiohydroxamic acids which include the $-\overset{|}{N}-\overset{|}{C}=S$ group, but are closely analogous to those of some derivatives which include the oxime group, such as $\left(R-C\begin{smallmatrix}S-CH_3\\N-OH\end{smallmatrix}\right)$ (X) and $\left[(R-C\begin{smallmatrix}S-\\N-OH\end{smallmatrix})_2\right]$ (XI). Furthermore, the authors have found[35] that derivatives, such as X and XI, and the sodium or zinc salts of benzothiohydroxamic acid yield various rearranged products, such as phenylisothiocyanate, *N,N'*-diphenylthiourea and *S*-methylphenylthiocarbamate, under almost the same conditions as those in which the Beckmann or Lossen rearrangements are carried out. These facts clearly indicate that the oxime group of II has a syn configuration (IIs) to the sulfur atom, so that the R group can migrate from carbon to nitrogen.



(IIs) (syn-form),



(IIt) (anti-form)

From these results it is clear that the metal complexes of II include an oxime group and that the oxime group of the ligand has a syn configuration. It is evident that the metal complexes of II should have the structure IIq (Y = S) in which a five-membered chelate ring is formed with the oxime oxygen.

This structure (IIq) has been confirmed by X-ray crystallographic studies as shown in Fig. 3[41,42]. It is the first time that *cis*- and *trans*-isomers, of a nickel complex with bidentate ligands, have been isolated even though such isomers are well-known in platinum or palladium complexes. The two sulfur atoms in the nickel complexes of β-mercaptoamines and related ligands have a *cis* orientation. A reason why the mercapto group favors *cis* orientation has been put forward by Busch[43] in terms of the pi-bonding tendencies of sulfur atoms and the symmetry of the appropriate central atom d-orbitals. One more interesting point in Fig. 3 is that intermolecular hydrogen bonds are formed between the nitrogen and oxygen atoms of two adjacent molecules; thus the complexes are likely to have intermediate structures between the oxime form IIq and the oximino one IIp. The bond lengths clearly indicate that the C—N bonds have a considerable double bond character.

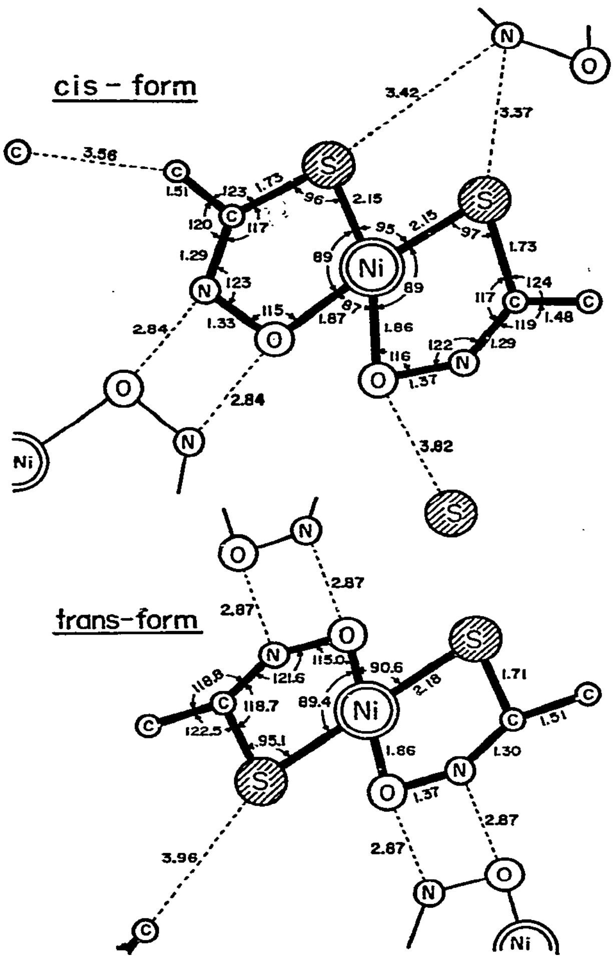


Fig. 3. Crystal Structures of cis- and trans-(acetothiohydroxamato)Ni (II)

It has been found that the metal complexes of II are monomeric in solution[32]. If the monomeric complexes in solution have the oxime group as in the solid state, the oxime group is expected to be alkylated or acylated in the same manner as found[44] for bis (dimethylglyoxime) nickel or palladium or platinum complexes of 2-pyridinealdoxime. Although the alkylations are not successful, benzoylation of the nickel salts (XII) of II in chilled alkaline solution yields[35] the benzoylated nickel complexes, XIVu or XIVv, which apparently have the properties of metal chelate compounds. As already reported[45], the benzoylation of II in alkaline solution gives unstable S-benzoylated compounds or S,O-dibenzoyl derivatives which have no ability to form metal complexes. Therefore, the formation of XIV seems to proceed by the direct benzoylation of the anionic nickel chelates (XIII) which are stable in alkaline solution. The C = O stretching bands of XIV occur at

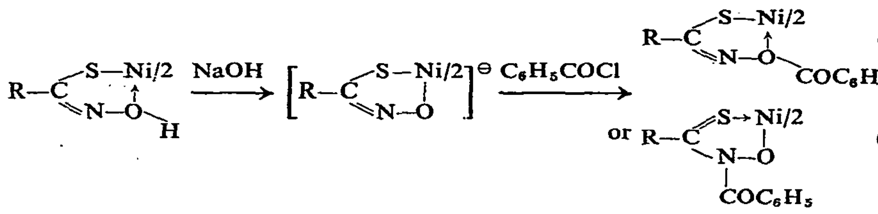
TABLE 2

COMPARATIVE DATA OF FERRIC COMPLEXES OF HYDROXAMIC ACID ANALOGS

($R' = H, CH_3, C_6H_5$; $R'' = C_6H_5NH\text{-}, C_6H_5\text{-}$)

Ligand	*3 : 1 Complex*		*2 : 1 Complex*		*1 : 1 Complex*	
	*pH for formation**		*pH for formation*		*pH for formation*	
	λ_{max}, mμ (ν *cm*$^{-1}$)	(ε)	λ_{max}, mμ (ν *cm*$^{-1}$)	(ε)	λ_{max}, mμ (ν *cm*$^{-1}$)	(ε)
	Weak alkali		pH 6–5		pH 4–2	
$C_6H_5\text{-NHCO}\underset{\overset{\mid}{R'}}{\text{N}}\text{-OH}$	500	(2200–3000)	555	(1800–2500)	620	(1100)
	(20.00×10^3)		(16.02×10^3)		(16.13×10^3)	
	Weak alkali		pH 6–5		pH 4–2	
$C_6H_5\text{-}\underset{\overset{\mid}{CH_3}}{\text{N}}\text{-CO}\underset{\overset{\mid}{CH_3}}{\text{N}}\text{-OH}$	460	(5000)	545	(3000)	600	(1800)
	(21.74×10^3)		(18.35×10^3)		(16.67×10^3)	
	Weak alkali		pH 6–5		pH 4–2	
$C_6H_5\text{-O-CO}\underset{\overset{\mid}{R'}}{\text{N}}\text{-OH}$	450	(3000)	510	(1800)	580	(700–1000)
	(22.22×10^3)		(19.61×10^3)		(17.24×10^3)	
	Weak alkali—pH 5		pH 4–2		pH 2–1	
$C_6H_5\text{-CO}\underset{\overset{\mid}{R'}}{\text{N}}\text{-OH}$	420–450	(5000)	500	(3200)	540	(1900)
	($23.81\text{–}22.22\times10^3$)		(20.00×10^3)		(18.52×10^3)	
	pH 6–4		pH 4–2		pH 2–1	
$C_6H_5\text{-NHCO}\underset{\overset{\mid}{R''CO}}{\text{N}}\text{-OH}$	450	(5000)	500	(2800)	540	(1900)
	(22.22×10^3)		(20.00×10^3)		(18.52×10^3)	
	Neutral-weak acid		Weak acid			
$C_6H_5\text{-NHCS}\underset{\overset{\mid}{R'}}{\text{N}}\text{-OH}$	480(2500–3300)	620sh	500sh	600(unstable)		?
	(20.83×10^3)		(16.67×10^3)			
	pH 6.5–5		pH 2–0.2			
$C_6H_5\text{-CSNHOH}$	480(2100)	580(1900)	580	(2000)		?
	(20.83×10^3)	(17.24×10^3)	(17.24×10^3)			

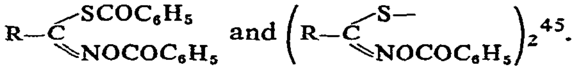
*Except $C_6H_5CON(R')OH$, $C_6H_5NHCON(R''CO)OH$ and $C_6H_5CSNHOH$, the spectra were determined in ethanol. In these cases, pH means pH values determined for an aqueous solution prepared under the same conditions as those of the ethanol solution used for spectral examination.



(XIVu)

(XIVv)

1720–1730 cm^{-1} for aliphatic compounds and at 1740 cm^{-1} for aromatic compounds in carbon tetrachloride solution. These frequencies may be compared with those of the $-\overset{|}{N}-\overset{|}{C}=O$ band of tribenzoylhydroxylamine at 1715 cm^{-1},[46] or by looking at the shifts to lower frequencies of $-N-OC=O$ bands with coordination as illustrated in XIVu, with absorption at 1771 ± 2 cm^{-1} for tribenzoylhydroxylamine[46] or for O-benzoyl derivatives such as


$R-C\begin{smallmatrix}\nearrow SCOC_6H_5\\ \searrow NOCOC_6H_5\end{smallmatrix}$ and $\left(R-C\begin{smallmatrix}\nearrow S-\\ \searrow NOCOC_6H_5\end{smallmatrix}\right)_2$[45].

Since neither O-benzoyl nor N-benzoyl thiohydroxamic acid can be synthesized, direct comparison of the infrared spectra of XIV with those of their ligands is impossible; and the evidence is insufficient to drawn a final conclusion about the alternative XIVu or XIVv structures.

3. *Comparative studies of ferric complexes of hydroxamic acid analogs*

As described in the preceeding sections, the formation of ferric complexes is a general reaction of hydroxamic acid (I) and its analogs (II–V). The literature[47–50] dealing with ferric complexes of I has suggested the existence of three types of complexes which have ligand-metal ratios of 3 : 1, 2 : 1 and 1 : 1 dependant on the pH and the ratio of ligand to Fe^{3+}. Although there are some discrepancies in the literature, the properties of the ferric complexes of the benzohydroxamic acid series are shown in Table II.

Although studies of the properties and constitution of the ferric complexes of III, IV and V in solution are still in progress by the present authors and many uncertainties remain, the following conclusions may be drawn from the preliminary results obtained up to now. Compounds which have pKa values higher than those of I, such as III and V, produce more bathochromic ferric complexes in the higher pH ranges compared with I, whereas the reactions of *N*,*N*-dicarbamoylhydroxylamines (VIII) are almost the same as those of I. Thus the reactions of the hydroxamic acid group with Fe^{3+} seem likely to be affected not by the structures of the ligand anions in solution, but rather by the pKa values of the ligands. The ferric complexes of III and V are very unstable in water, but remarkably stabilized in methanol, ethanol and butanol. Furthermore, it has been found that the constitution of the complexes changes also as a function of the ferric salt used; ferric perchlorate gives both the 2 : 1 and 1 : 1 complexes of III and V in weakly acidic ethanol, while ferric chloride forms only 1 : 1 complexes irrespective of the ratio of ligand to Fe^{3+}. These results may indicate that the coordinative abilities of the hydroxamic acid analogs towards Fe^{3+} decrease with increase of the pKa values of the ligands; ligands such as III and V can compete with water but not with chloride.

The compounds which include a sulfur atom, the thiohydroxamic acids (II) and *N*-hydroxy-2-thioureas (IV), show somewhat different behavior towards Fe^{3+}. The absorption band of the 3 : 1 complexes splits in the visible region, and the 1 : 1 complexes are not observed spectrophotometrically, Table II[51]. The spectra of the ferric complexes of the thioacetohydroxamic acids show two absorption maxima at 480 mμ and 580 mμ in a solution of pH 5 to 6.5 being independent of the ratio of ligand to Fe^{3+}; furthermore these spectra are the same as those of the pure synthesized 3:1 complexes in various organic solvents. At pH 6 the continuous variation method, the slope ratio method and the molar ratio method indicate the formation of a 3 : 1 complex at all wave lengths used, while the analogous experiments at pH 2 indicate the formation of the 2 : 1 complex, the spectra of which show absorption maxima at 580 mμ. This 2 : 1 complexis is remarkably stabilized in the presence of a large excess of Fe^{3+}. Furthermore, paper-electrophoresis at pH 6 gives only one spot which does not exhibit any migration, whereas the blue spot migrates cathodeward at pH 1.5. From these results it is concluded that the two absorption maxima at pH 6 are not due to a mixture of the 3 : 1 and 2 : 1 complexes, but are due to the 3 : 1 complex alone. The reasons, however, why the visible spectra are split are not known although closely analogous spectra have been found for S,O-coordinated 3 : 1 ferric complexes of 2-mercaptopyridine-1-oxide[52] and L-cysteine.[53] As mentioned above, 2 : 1 ferric complex of thioacetohydroxamic acid is very stable even in strong acid at less than pH 1 so long as a large excess of Fe^{3+} is present. Lastly, it is interesting that 2-mercaptopyridine-1-oxide oxidizes Fe^{2+} to Fe^{3+} and forms 3 : 1 ferric complexes in the pH range 2 to 6.[51,54] Similar results are found for thioacetohydroxamic acid, and therefore this reaction is available for the colorimetric determination of total iron irrespective of its valence state.

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