Kinetics of Reaction of Imidazole, Glycine, and L-Histidine with the Aquapentacyanoferrate(II) Ion

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The properties and reactivity of the pentacyanoferrate(II) complexes of imidazole (imH), glycinate (glyO), and L-histidine (his) are reported. The rates of formation, starting from $[Fe(CN)_5(OH_2)]^{3-}$ {generated by aquation of $[Fe(CN)_5(NH_3)]^{3-}$}, are typically of first order with respect to the concentration of the ligands, with k_f = 240, 28.0, and 320 $dm^3\ mol^{-1}\ s^{-1}$, respectively. The kinetics of dissociation of the complexes, measured in the presence of an excess of dimethyl sulphoxide, show saturation behaviour with respect to this reactant. The limiting rates of dissociation are 1.33×10^{-3} (imH), 2.67×10^{-3} (glyO$^-$), and $5.3 \times 10^{-4}\ s^{-1}$ (his) at 25 °C and I = 0.100 mol dm^{-3} ($Li[ClO_4]$). L-Histidine, in zwitterionic form, reacts with $[Fe(CN)_5(OH_2)]^{3-}$ to yield two isomers in solution. The predominant form contains iron co-ordinated to the hindered N^3 nitrogen of imidazole in the L-histidine ligand. This isomer is labile and dissociates rapidly, k = 0.109 s^{-1} to form the inert and stable N^1 isomer. Similar behaviour, but involving the three N-co-ordinating sites of histidine, is observed in alkaline solutions. The strain energy associated with substitution adjacent to the iron centre is estimated as 3.4 kcal mol^{-1}. A correlation of the limiting rates of dissociation with the ligand-field energies in the complexes is presented.

MOST amino-acids and peptides possess a number of functional groups which can participate in metal-binding processes.[1,2] The success of a particular functional group competing against others in the vicinity becomes important for the understanding of metal protein reactions, and also of biological systems in which the properties of proteins are modified by specific interactions with metal ions.[3] The interest in reactions of amino-acids with the pentacyanoferrate(II) ion is mainly associated with the fact that this ion typically co-ordinates only one additional ligand and can be used as a probe for the binding properties of the several functional groups. Also important is the ease of water substitution [4] in $[Fe(CN)_5(OH_2)]^{3-}$ to form stable complexes with biologically important bases such as imidazole [5] and purine [6] and with a number of saturated and unsaturated bases with nitrogen [7,8] and sulphur [9,10] donor atoms.

In this paper we report the kinetics and spectral properties of pentacyanoferrate(II) complexes of imidazole, glycine, and L-histidine in aqueous solution. Related to this study is the excellent work of Shepherd [11] on the association of imidazoles with the pentacyanoferrate-(II) and -(III) ions, which appeared when this work was being completed. We have extended the preceding study to examine the kinetic properties of the imidazole and amino-acid complexes of pentacyanoferrate(II) and to explore the competition between the various functional groups in these ligands.

EXPERIMENTAL

The salt $Na_3[Fe(CN)_5(NH_3)]\cdot 3H_2O$ was prepared from $Na_2[Fe(CN)_5(NO)]\cdot 2H_2O$ (Carlo Erba) following the conventional procedure [12] and recrystallized several times from concentrated ammonia. Imidazole (imH) (Aldrich) was recrystallized from benzene. Glycine (gly) (Carlo Erba) and L-histidine (his) (Aldrich) were used as supplied. The complexes of pentacyanoferrate(II) with imH, gly, and his were prepared in solution by direct substitution into the aquated $[Fe(CN)_5(NH_3)]^{3-}$ ion.[4,7] They were also isolated as solids using the following procedure. Sodium amminepentacyanoferrate(II) (1 g, 3 mmol) was dissolved in water (*ca.* 50 cm^3) in the presence of at least a five-fold excess of the ligand. After 15 min potassium iodide (10 g) was added to allow the precipitation of the potassium salts with ethanol. In some cases, instead of a precipitate, a viscous oil was formed during the addition of ethanol. The products were separated by filtration or decantation and redissolved in water (*ca.* 50 cm^3), in the presence of the ligand (2 mmol) and KI (10 g). The complex was reprecipitated with ethanol and the procedure was repeated once more. The glycine complex was isolated as a crystalline material, but in anionic form, of composition $K_4[Fe(CN)_5(NH_2CH_2CO_2)]\cdot 4H_2O$ (Found: C, 17.2; H, 2.4. Calc. for $C_7H_{12}FeK_4N_6O_6$: C, 17.2; H, 2.45%). The imidazole complex was isolated as a yellow powder of probable composition $K_3[Fe(CN)_5(imH)]\cdot 3H_2O$ (Found: C, 22.6; H, 1.6. Calc. for $C_8H_{10}FeK_3N_7O_3$: C, 23.1; H, 2.15%). The histidine complex was isolated as a yellow solid of probable composition $K_3[Fe(CN)_5(his)]\cdot 3H_2O$ (Found: C, 25.5; H, 2.5. Calc. for $C_{11}H_{15}FeK_3N_8O_5$: C, 25.9; H, 2.6%). This complex seems to be air sensitive and shows evidence of decomposition after some weeks in the desiccator.

Visible and u.v. spectra were obtained on a Cary model 14 spectrophotometer fitted with thermostatted cell compartments. This instrument was also employed for the kinetics of dissociation of the substituted pentacyanoferrates. Rapid kinetics measurements were made using a Durrum model D-110 stopped-flow apparatus equipped with a Kel-F flow system. Infrared spectra of the complexes as

[1] H. C. Freeman, in 'Inorganic Biochemistry,' ed. G. L. Eichhorn, Elsevier, Amsterdam, 1973, vol. 1, ch. 4.
[2] R. J. Sundberg and R. B. Martin, *Chem. Rev.*, 1974, **74**, 471.
[3] E. Breslow, in ref. 1, ch. 7.
[4] H. E. Toma and J. M. Malin, *Inorg. Chem.*, 1973, **12**, 2080.
[5] H. E. Toma, J. M. Martins, and E. Giesbrecht, *Ciencia*, 1975, **27**, 105.
[6] J. M. Malin, unpublished work.
[7] H. E. Toma and J. M. Malin, *Inorg. Chem.*, 1973, **12**, 1039; 1974, **13**, 1772.
[8] A. D. James, R. S. Murray, and W. C. E. Higginson, *J.C.S. Dalton*, 1974, 1273; P. J. Aymonino and J. A. Olabe, *J. Inorg. Nuclear Chem.*, 1976, **38**, 225.
[9] H. E. Toma, J. M. Malin, and E. Giesbrecht, *Inorg. Chem.*, 1973, **12**, 2084.
[10] Z. Bradic, D. Pavlovic, I. Murati, and S. Ašperger, *J.C.S. Dalton*, 1974, 344; J. Legros, *J. Chim. phys.*, 1964, **61**, 923.
[11] R. E. Shepherd, *J. Amer. Chem. Soc.*, 1976, **98**, 3329.
[12] G. Brauer, 'Handbook of Preparative Inorganic Chemistry,' vol. 2, 2nd edn., Academic Press, 1965, p. 1511.

mulls in Nujol of Fluorolube were recorded on Perkin-Elmer model 337 or 180 spectrophotometers. N.m.r. spectra in D_2O, with Bu^tOH as internal reference, were obtained using a Varian T-60 spectrometer.

RESULTS AND DISCUSSION

Spectra.—The electronic spectra of the pentacyanoferrate(II) complexes of imidazole, glycinate, and L-histidine are shown in Figure 1. The visible-absorption band in these complexes can be assigned to the *d–d* transition from the $^1A_1$ ground state to the $^1E(1)$ excited states, based on a comparison with the absorption spectra of many other pentacyano-ferrates [13] and -cobaltates.[14]

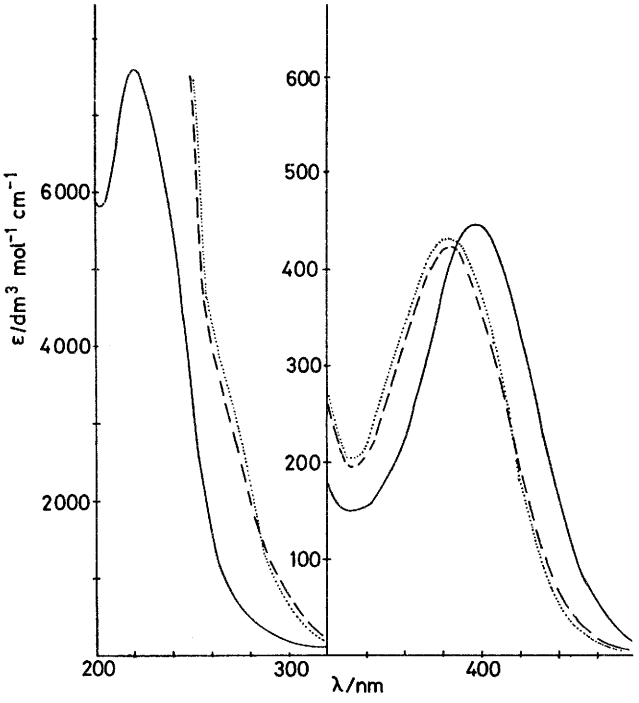


FIGURE 1 Visible–u.v. spectra of pentacyanoferrate(II) complexes of glycinate ion (——), imidazole (· · · ·), and L-histidine (— — — —) in aqueous solution

In crystal-field theory the energy of the $^1A_1$–$^1E(1)$ transition can be expressed [15] by (1), where $Dt = \frac{2}{7}(Dq_{CN} - Dq_L)$ and C is a Racah parameter. To a first approximation, if one assumes that the Dq and C values for the cyanides are nearly constant in $[Fe(CN)_5L]$ complexes, the energy of the *d–d* band is directly correlated with the Dq values of the ligand L. The Dq parameter is very sensitive to the nature of the metal–ligand bond, increasing systematically with the σ-donor and π-acceptor strengths of the ligands.

$$E[^1A_1\text{–}^1E(1)] = 10Dq - (35/4)Dt - C \quad (1)$$

The difference $Dq_{CN} - Dq_L$, expressed by the Dt parameter, can be used to evaluate the extent of tetragonal distortion in the complexes, which is zero for L = $[CN]^-$. As the tetragonal distortion increases in passing from O_h to C_{4v} symmetry the inversion centre disappears, and the Laporte restriction becomes less effective. Therefore, an increase in intensity should parallel the shift of the energies of the *d–d* transition, a view which seems to be verified in the following $[Fe(CN)_5L]$ complexes, with L = H_2O ($\nu_{max.}$ 22 700, ε 650), NH_3 ($\nu_{max.}$ 25 200, ε 450), glycinate ($\nu_{max.}$ 25 300, ε 450), imidazole ($\nu_{max.}$ 26 100, ε 430), and dimethyl sulphoxide (dmso) ($\nu_{max.}$ 28 400 cm^{-1}, ε 210 dm^3 mol^{-1} cm^{-1}).

The visible-absorption spectrum of the glycinato-complex is very similar to those of the corresponding complexes of ammonia and methylamine, indicating co-ordination through the amine group. Imidazole, although less basic than ammonia and glycinate by two orders of magnitude, produces a higher field strength as a consequence of its probable involvement in π-back-bonding interactions with the pentacyanoferrate(II) ion. Histidine is probably co-ordinated through the imidazole group because of the similarity of the *d–d* spectra of the imidazole and histidine complexes.

The u.v. spectra of the pentacyanoferrate(II) complexes are dominated by strong charge-transfer (c.t.) transitions from the metal to the cyanides, superimposed on the internal transitions in the heterocyclic ligand. For the imidazole and histidine complexes a shoulder is observed at *ca.* 270 nm, suggesting a metal-to-ligand c.t. transition, analogous to those characteristic of pentacyanoferrate(II) complexes of *N*-heterocycles.[7]

Another piece of evidence for co-ordination through the imidazole group in the histidine complex is given by the spectra of the oxidized derivatives. As reported by Shepherd,[11] a low-energy transition is observed in the visible spectra of the pentacyanoferrate(III) complexes of the imidazoles. This band was assigned to the imidazole-to-iron c.t. transition by comparison with the spectra of the penta-ammineruthenium(III) analogue.[11] The bands are observed at 470 and 480 nm for the pentacyano(imidazole)ferrate(III) and pentacyano(L-histidine)-ferrate(III) complexes, respectively, and do not appear in the spectra of the pentacyano(glycinato)ferrate(III) and amminepentacyanoferrate(III) complexes.

The ^1H n.m.r. spectra of the pentacyanoferrates gave little information on the co-ordination sites since the changes in the chemical shifts were very small for the complexes when compared to those for the free ligands. Our results were consistent with those reported by Shepherd [11] for the imidazole and L-histidine complexes. For the glycinato-complex, which has not been reported before, the chemical shifts of the methylene group were observed at 1.95 and 1.82 p.p.m., for the free ligand and the complex, respectively, with respect to the Bu^tOH internal standard in D_2O.

The cyanide-stretching frequencies for the pentacyanoferrate(II) complexes of glyO (glycinate), imH, and his were observed at 2 080w, 2 045s, and 2 028s, 2 085w,

[13] H. E. Toma, E. Giesbrecht, J. M. Malin, and E. Fluck, *Inorg. Chim. Acta*, 1975, **14**, 11.

[14] V. M. Miskowsky and H. B. Gray, *Inorg. Chem.*, 1975, **14**, 401.

[15] L. Tosi and J. Danon, *Inorg. Chem.*, 1964, **3**, 150.

2 045s, and 2 014s, and 2 095w, 2 045s, and 2 025s cm^{-1}, respectively. These bands are sensitive to the oxidation state of the central ion, being shifted to the 2 100—2 200 cm^{-1} region in the case of cyanoferrate(III) complexes. Four i.r.-active modes of vibration, belonging to the A_1 and E representations, can be responsible for the observed absorption bands. However, it has been suggested [15] that the assignment is complicated by vibrational effects in the solids, and will not be attempted in this work. Two groups of absorption bands at 570—580 and 400—430 cm^{-1} have been associated [15] in a number of pentacyanoferrates with FeCN bending and Fe–C stretching, respectively. They are observed at 570s and 400—450w cm^{-1} in the case of the present complexes.

The asymmetric and symmetric vibrational modes of the carboxylate group were observed at 1 580—1 590 and 1 400—1 420 cm^{-1}, respectively, being practically the same for gly, his, and their complexes with the pentacyanoferrate(II) ion. Co-ordination has been reported [16] to increase the separation of the vibrational frequencies of the carboxylate group, especially when the equivalence of the CO bonds is removed. Therefore, since the vibrations of the carboxylate groups remained unchanged their co-ordination in the complexes can be excluded.

Kinetics of Formation.—The kinetics of the reaction between $[Fe(CN)_5(OH_2)]^{3-}$ and the several ligands were investigated by the stopped-flow technique, following the decay of the reactant at 440 nm or the formation of the products at 398 (glyO) or 383 nm (imH and his). Typical first-order behaviour was observed during at least two half-lives, with the ligands always present in large excess. The observed rate constants increased linearly with the concentration of the ligands (Figure 2). From Figure 2, by using the relative gradients indicated, a comparison can be made of the observed second-order rate constants with those previously reported for many other pentacyanoferrates. The rates of formation for the imidazole and histidine complexes fall in the range expected for neutral ligands, even though his is present in zwitterionic form. For the glycinato-complex the rates are comparable to those of typically anionic ligands such as $[CN]^-$ and $[NO_2]^-$, and approximately ten times slower than the rates of the imidazole and histidine reactions.

The mechanisms of substitution in $[Fe(CN)_5(OH_2)]^{3-}$ can be described in terms of a dissociative S_N1 process or an S_N1–ion-pair process, depending on the charges associated with the attacking ligands. In both cases the dissociation of the co-ordinated water constitutes the rate-determining step. For a typical S_N1 mechanism,

$$[Fe(CN)_5(OH_2)]^{3-} \underset{k_a}{\overset{k_{-a}}{\rightleftharpoons}} [Fe(CN)_5]^{3-} + H_2O \quad (2)$$

$$[Fe(CN)_5]^{3-} + L \xrightarrow{k_L} [Fe(CN)_5L]^{3-} \quad (3)$$

if one assumes a steady-state approximation for $[Fe(CN)_5]^{3-}$, the theoretical rate constant is expressed by [4] $k_f = k_L k_{-a}[L]/(k_a + k_L[L])$. Considering that the term k_a in this mechanism incorporates the concentration of the solvent (55.5 mol dm^{-3}) and assuming that water and the ligand L are approximately equal in their efficiency as attacking ligands, we note that, for $k_L[L]$ to be comparable with k_a, [L] must be extremely large. Therefore, under the conditions of this study, $k_a \gg k_L[L]$ and $k_f = k_L(k_{-a}/k_a)[L]$. According to this mechanism the differences between the rates of reaction of neutral

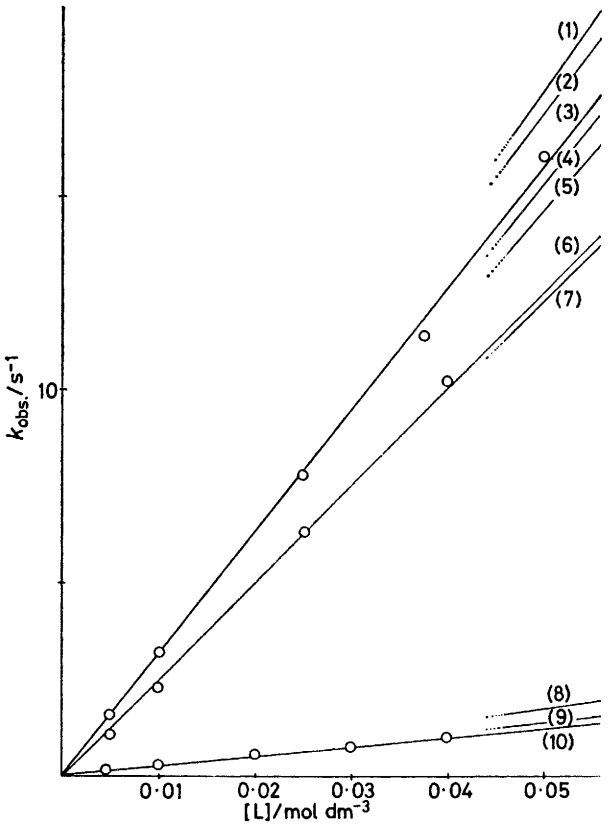


FIGURE 2 Rates of formation of pentacyanoferrate(II) complexes of (1) pyridine,[5] (2) methylpyridine,[5] (3) L-histidine, (4) CO (N. Moroi and H, Toma, unpublished work), (5) isonicotinamide,[5] (6) imidazole, (7) dimethyl sulphoxide,[9] (8) $[NO_2]^-$ (G. Davies and A. R. Garafalo, *Inorg. Chem.*, 1976, **15**, 1101), (9) $[CN]^-$, and (10) glycinate

and anionic ligands are associated with the k_L term. This rate constant involves the diffusion-controlled approach of the ligand L to form an encounter complex, followed by metal–ligand bond formation in the inner sphere of the reactant. Both steps are expected to depend to some extent on the nature and charge of the attacking ligand.

The rates of formation of the glycinato-complex increase with ionic strength (Table 1). This behaviour, which is typical of reactions between ions of the same charge, contrasts with the slight decrease observed in the rates of complexation with the neutral dmso, imH, and his ligands. In this case, specific electrolyte

[16] K. Nakamoto, 'Infrared Spectra of Inorganic and Co-ordination Compounds,' 2nd edn., Wiley–Interscience, New York, 1970, p. 233.

effects may be involved,[17] specifically those related to ion-pair formation between the cyanoferrates and lithium ions in aqueous solution. Evidence for this kind of association has been reported [18] for the pentacyanoferrate(II) complex, based on potentiometric measurements with specific ion electrodes.

Kinetics of Dissociation.—Dissociation of the substituted pentacyanoferrates takes place to a very small extent at room temperature. The kinetics are more conveniently studied in the presence of a ligand, such as dmso, which has a strong affinity for the pentacyanoferrate(II) ion,[9] and thus can drive to completion the dissociation of the complex. The rates of substitution can be studied as a function of the dimethyl sulphoxide concentration, at a fixed [L], to yield the dependence illustrated in Figure 3.

TABLE 1

Rates of formation of pentacyanoferrate(II) complexes of glycinate, imidazole, and L-histidine

Ligand	θ_c/°C	I [a]/mol dm^{-3}	k_2/ dm^3 mol^{-1} s^{-1}
Glycinate [b]	12.0	0.100	8.7
	16.7	0.100	14.1
	25.0	0.050	20.5
	25.0	0.100	28.0
	25.0	0.500	41.0
	25.0	1.00	46.5
	27.3	0.100	34.4
	30.3	0.100	43.1
Imidazole [c]	11.6	0.100	80
	19.0	0.100	141
	22.0	0.100	169
	25.0	0.100	240
	25.0	1.00	212
	32.5	0.100	490
Histidine [d]	11.5	0.100	104
	19.0	0.100	186
	25.0	0.050	342
	25.0	0.100	320
	25.0	0.500	233
	25.0	1.00	184
	27.3	0.100	400
	30.1	0.100	510

[a] Ionic strength adjusted with lithium perchlorate; [Fe(CN)$_5$(OH$_2$)$^{3-}$] = 5 × 10^{-5}—9 × 10^{-5} mol dm^{-3}. [b] Glycine–lithium glycinate (1 : 1) buffer, 0.5 × 10^{-2}—5.0 × 10^{-2} mol dm^{-3}. [c] [imidazole] = 0.5 × 10^{-2}—10.0 × 10^{-2} mol dm^{-3}. [d] [histidine] = 0.5 × 10^{-2}—5.0 × 10^{-2} mol dm^{-3}, zwitterionic form.

According to the previously proposed scheme [7] for the

$$[Fe(CN)_5L]^{3-} \underset{k_L}{\overset{k_{-L}}{\rightleftharpoons}} [Fe(CN)_5]^{3-} + L \quad (-3)$$

$$[Fe(CN)_5]^{3-} + H_2O \overset{k_a}{\rightleftharpoons} [Fe(CN)_5(OH_2)]^{3-} \quad (-2)$$

$$[Fe(CN)_5]^{3-} + \text{dmso} \underset{k_{-dmso}}{\overset{k_{dmso}}{\rightleftharpoons}} [Fe(CN)_5(\text{dmso})]^{3-} \quad (4)$$

dissociation reactions of the pentacyanoferrates, the observed rate constant is given by (5) where L = glyO,

$$k_{obs.} = \frac{k_{-L}k_{dmso}[\text{dmso}] + k_L k_{-dmso}[L]}{k_L[L] + k_{dmso}[\text{dmso}]} \quad (5)$$

imH, or his. The rate constants k_{dmso} and k_{-dmso} were reported to be 240 dm^3 mol^{-1} s^{-1} and 7.5 × 10^{-5} s^{-1} at 25 °C and I = 1.00 mol dm^{-3} in lithium perchlorate. At I = 0.100 mol dm^{-3} k_{dmso} was measured in this work as 345 dm^3 mol^{-1} s^{-1}. When the product k_{dmso}[dmso] exceeds k_L[L] it is possible to show that the observed rate constant, $k_{obs.}$, gradually approaches k_{-L}, the rate constant for the dissociation of the ligand L in the complex. Similarly, at low concentrations of dmso, $k_{obs.}$ approaches k_{-dmso}.

For the glycinato-complex the concentration of the ligand ion was maintained at 1 × 10^{-3} mol dm^{-3}; therefore, the product k_{glyO}[glyO] = 2.5 × 10^{-2} s^{-1} is much smaller than the product k_{dmso}[dmso], even for the lowest concentration reported here for dmso. In this case, as predicted by equation (5), the observed rate constants should become independent of the concentration of dmso,

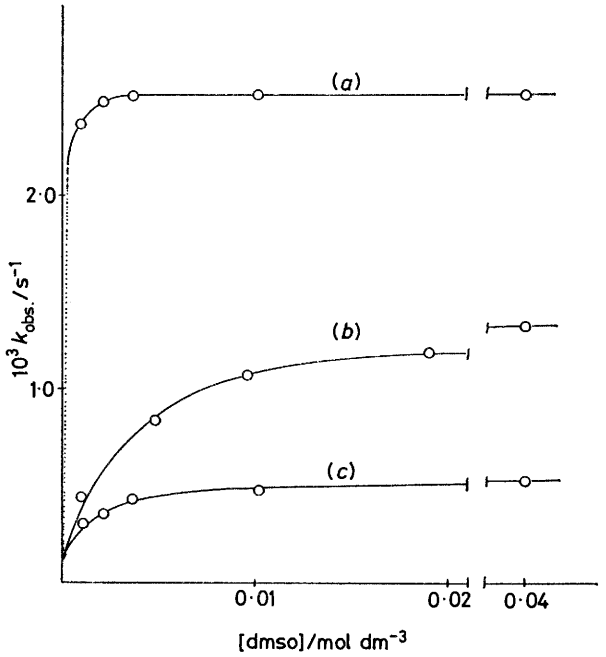


FIGURE 3 Observed rate constants of dissociation of pentacyanoferrate(II) complexes of (*a*) glycinate, (*b*) imidazole, and (*c*) L-histidine, at several dimethyl sulphoxide concentrations

and practically identical to the rates of dissociation of the glycinate ligand in the complex. This kind of behaviour can be better seen from Figure 3. Using a higher concentration of the free ligand, as in the imidazole and L-histidine systems illustrated in Figure 3, the saturation point shifts in the direction of higher concentrations of dmso.

The limiting rates of dissociation of the pentacyanoferrate(II) complexes of glyO, imH, and his are collected in Table 2. Analogously to the behaviour observed in the formation kinetics, the rates of dissociation show a slight decrease with ionic strength, probably caused by medium effects. The histidine and imidazole complexes dissociate more slowly than the glycinato-complex, despite the strong basicity of the amine group, which exceeds that of imidazole by *ca.* two pK_a units. The

[17] A. D. Pethybridge and J. E. Prue, *Progr. Inorg. Chem.*, 1972, **17**, 327.

[18] R. W. Chlebek and M. W. Lister, *Canad. J. Chem.*, 1966, **44**, 437.

simplest explanation for this apparent inversion is that d_π–p_π-back-bonding interactions can promote a strong

TABLE 2

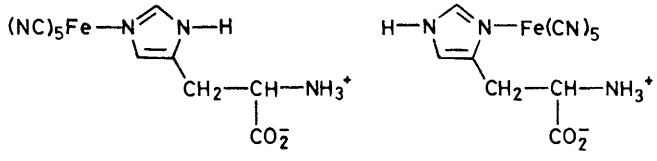
Limiting rates of dissociation of pentacyanoferrate(II) complexes of glycinate, imidazole, and L-histidine

Ligand	θ_c/°C	I [a]/mol dm^{-3}	$10^3 k_{-L}$/s^{-1}
Glycinate [b]	14.0	0.100	0.53
	19.1	0.100	1.14
	25.0	0.050	2.65
	25.0	0.100	2.67
	25.0	0.500	2.33
	25.0	1.00	1.99
	30.3	0.100	5.1
	36.0	0.100	10.1
Imidazole [c]	13.9	0.100	0.262
	19.4	0.100	0.50
	25.0	0.100	1.33
	25.0	1.00	1.01
	29.8	0.100	2.72
	35.1	0.100	6.0
Histidine [d]	10.0	0.100	0.066
	19.1	0.100	0.236
	25.0	0.050	0.51
	25.0	0.100	0.53
	25.0	0.500	0.48
	30.3	0.100	1.19
	32.0	0.100	1.40
	34.9	0.100	2.38

[a] Ionic strength adjusted with lithium perchlorate; [Fe(CN)$_5$L] = 2×10^{-4} mol dm^{-3}. [b] Glycine–glycinate buffer, 10^{-3} mol dm^{-3}. [c] [imidazole] = 5×10^{-3} mol dm^{-3}. [d] [histidine] = 9×10^{-3} mol dm^{-3}.

stabilization of the imidazole complexes, more than compensating for the decrease in basicity of the ligands.

Steric Effects: Kinetics of Isomerization.—Molecular models of histidine show that if both the N^1 and N^3 nitrogens of the imidazole ring are available for co-ordination the N^3 atom would be expected to form less-stable unidentate complexes due to steric effects of the substituent at C^4. Tautomerism in imidazoles is a well



N^1 isomer N^3 isomer

established fact [19] which can also occur in the histidine ligand, although, to our knowledge, its quantitative evaluation has not been attempted. The existence of tautomerism suggests that two isomers of the complex [Fe(CN)$_5$(his)]$^{3-}$ could be independently formed, through rapid attack of the [Fe(CN)$_5$]$^{3-}$ ion on the N^1 and N^3 sites of histidine.

Some evidence of isomers was obtained by scanning the spectra of rapidly mixed solutions of [Fe(CN)$_5$(OH$_2$)]$^{3-}$ (acetate buffer, with trace amounts of ascorbic acid) and his, under argon. As can be seen from Figure 4, the spectral changes are very small, but consistent with an isomerization process between two sites of similar ligand-field strength. Since the direct evaluation of the relative amounts of each isomer in the mixture is not possible, competitive kinetics experiments with dmso were employed as a tentative approach to the problem. In the presence of dmso the labile N^3 isomer was expected to be rapidly converted into the [Fe(CN)$_5$(dmso)]$^{3-}$ complex, without interference from the inert N^1 isomer. Thus, by following the decay of the N^3 isomer it should be possible to evaluate its limiting rates of dissociation,

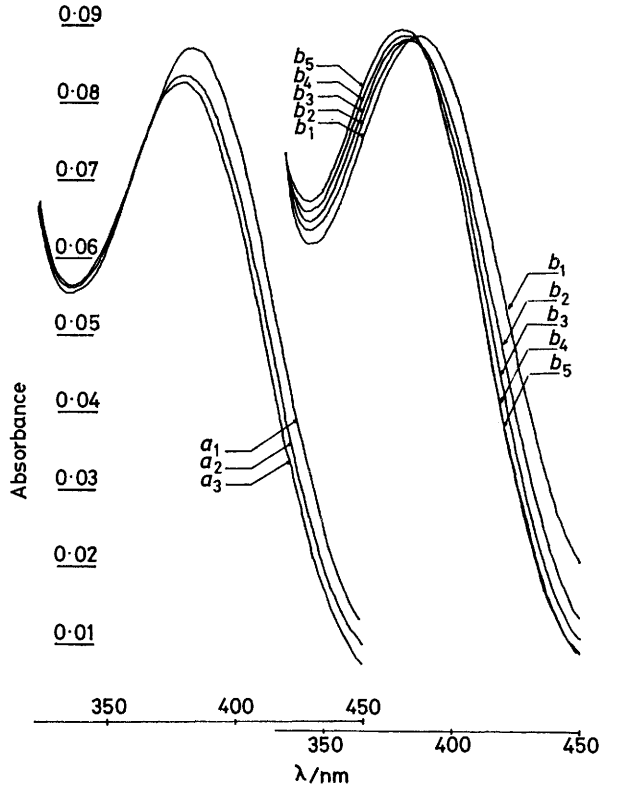


FIGURE 4 Spectral changes associated with the isomerization of [Fe(CN)$_5$(his)]$^{3-}$: (*a*) in neutral solutions [after (a_1) 40 s, (a_2) 130 s, (a_3) 300 s]; and (*b*) in basic solutions [after (b_1) 25 s, (b_2) 100 s, (b_3) 180 s, (b_4) 300 s, and (b_5) 600 s]

as well as the relative rates of formation of the two isomers in solution. The proposed scheme is as follows:

$$\text{N}^1\text{-his} \underset{}{\overset{K}{\rightleftharpoons}} \text{N}^3\text{-his} \quad (6)$$

$$[\text{Fe(CN)}_5(\text{OH}_2)]^{3-} + \text{N}^3\text{-his} \underset{k_{-\text{N}(3)}}{\overset{k_{\text{N}(3)}}{\rightleftharpoons}} [\text{Fe(CN)}_5(\text{N}^3\text{-his})]^{3-} \quad (7)$$

$$[\text{Fe(CN)}_5(\text{OH}_2)]^{3-} + \text{N}^1\text{-his} \xrightarrow{k_{\text{N}(1)}} [\text{Fe(CN)}_5(\text{N}^1\text{-his})]^{3-} \quad (8)$$

$$[\text{Fe(CN)}_5(\text{OH}_2)]^{3-} + \text{dmso} \xrightarrow{k_{\text{dmso}}} [\text{Fe(CN)}_5(\text{dmso})]^{3-} \quad (9)$$

The [Fe(CN)$_5$]$^{3-}$ intermediate, generated from the dissociation of the N^3 isomer, is expected to be readily converted into the [Fe(CN)$_5$(OH$_2$)]$^{3-}$ ion rather than to the N^1 isomer or to the dmso complex, since water, as the solvent, is present in a much higher excess than the

[19] J. Elgero, C. Marzin, P. Linda, and A. R. Katritzky, *Adv. Heterocyclic Chem.*, 1976, Suppl. 1, p. 278.

ligands.[4] The rates of reaction, starting from $[Fe(CN)_5(OH_2)]^{3-}$, in the presence of an excess of dmso and his, can be expressed by (10).

$$-d[Fe(CN)_5(OH_2)^{3-}]/dt = k_I[Fe(CN)_5(OH_2)^{3-}] \quad (10)$$

where

$$k_I = \frac{[k_{N(1)} + k_{N(3)}K][his]}{1 + K} + k_{dmso}[dmso]$$

$$[his] = [N^1\text{-his}] + [N^3\text{-his}]$$

The decay of the N^3 isomer is expected to be governed by $k_{-N(3)}$. Since $k_{-N(1)}$ and k_{-dmso} are much smaller than $k_{-N(3)}$, one can assume that they do not contribute to the steady-state concentration of the $[Fe(CN)_5(OH_2)]^{3-}$ ion,

$$[Fe(CN)_5(OH_2)^{3-}] = \frac{k_{-N(3)}[Fe(CN)_5(N^3\text{-his})]}{\{[k_{N(1)} + k_{N(3)}K][his]/(1 + K)\} + k_{dmso}[dmso]} \quad (11)$$

expressed by (11). Based on the steady-state approximation above, the derived rate law for the dissociation of

$$-d[Fe(CN)_5(N^3\text{-his})]/dt = k_{II}[Fe(CN)_5(N^3\text{-his})] \quad (12)$$

where

$$k_{II} = \frac{(\{k_{N(1)}[his]/(1 + K)\} + k_{dmso}[dmso]k_{-N(3)}}{\{[k_{N(1)} + k_{N(3)}K][his]/(1 + K)\} + k_{dmso}[dmso]}$$

the N^3 isomer is (12). The denominator of k_{II} is identical to the expression for k_I, which gives the observed rate constant for the formation of the substituted pentacyanoferrates.

Values of k_I and k_{II} were obtained independently from the kinetics of formation and dissociation of the N^3 isomer, with the L-histidine concentration constant at 2.5×10^{-2} mol dm^{-3}, and dimethyl sulphoxide varying from 0.5×10^{-2} to 2.5×10^{-2} mol dm^{-3}. The formation reaction takes place very rapidly, being complete within a few milliseconds. The dissociation of the N^3 isomer requires many seconds for completion, and is accompanied by large absorbance changes at 390 nm. Since one of the products, $[Fe(CN)_5(dmso)]^{3-}$, has only a slight absorption at this wavelength, it seems that a considerable amount of the histidine complex should be originally present as the N^3 isomer.

The influence of the concentration of dmso and of the temperature on the observed rate constants, k_I and k_{II}, can be seen in Table 3. Considering equation (13), a

$$k_Ik_{II} = \frac{k_{N(1)}k_{-N(3)}[his]}{1 + K} + k_{-N(3)}k_{dmso}[dmso] \quad (13)$$

plot of k_Ik_{II} against the dimethyl sulphoxide concentration should be linear at a constant histidine concentration. This kind of behaviour is illustrated in Figure 5, at three different temperatures. The rates of formation of the dimethyl sulphoxide complex, k_{dmso}, were measured independently in this work (Table 3) to allow the calculation of $k_{-N(3)}$ by using the gradients of the plots in Figure 5. The quotients $k_{N(1)}/(1 + K)$ and $k_{N(3)}K/(1 + K)$ were evaluated from the intercept, and from the values of k_I in equation (10).

A remarkable fact shown in Table 3 is that at least 90% of the $[Fe(CN)_5]^{3-}$ moiety binds to the N^3 site of the histidine ligand. Surprisingly, the N^1 site, which is not hindered sterically, seems less available for co-ordination. Considering that the rates of substitution in $[Fe(CN)_5(OH_2)]^{3-}$ are practically insensitive to the nature of the attacking ligand, one can deduce that the protonated N^1 form predominates in the tautomeric equilibrium of his. Assuming that $k_{N(1)} = k_{N(3)}$, the equilibrium constant K for the tautomerization process equals 9. This means that 90% of the N^1 sites in his are occurring as the protonated form; therefore, only 10% are available for co-ordination.*

TABLE 3

Rates of formation and dissociation of the N^3-isomer of $[Fe(CN)_5(his)]^{3-}$

θ_c / °C	10^2[dmso] / mol dm^{-3} [a]	k_I	$10k_{II}$ / s^{-1}	$k_{-N(3)}$	$k_{N(3)}K/(1 + K)$ / dm^3 mol^{-1} s^{-1}	$k_{N(1)}/(1 + K)$ / dm^3 mol^{-1} s^{-1}
15.0	0.50	4.4	0.065			
	1.00	5.3	0.087			
	1.50	6.1	0.108	0.026 5	135	15
	2.00	6.7	0.129			
	2.50	7.2	0.140			
	2.00 [b]	2.9				
25.0	0.50	10.1	0.278			
	1.00	12.5	0.390			
	1.50	13.5	0.467	0.109	300	35
	2.00	15.5	0.510			
	2.50	17.5	0.564			
	2.00 [b]	6.9				
33.0	0.50	20.0	0.78			
	1.00	25.6	1.07			
	1.50	29.5	1.37	0.270	560	60
	2.00	33.5	1.58			
	2.50	36.5	1.75			
	2.00 [b]	17.5				

[a] $I = 0.100$ mol dm^{-3} (Li[ClO$_4$]), $\lambda_{max.} = 390$ nm, [histidine] $= 2.50 \times 10^{-2}$ mol dm^{-3}, [Fe(CN)$_5$L] $= 1.5 \times 10^{-4}$ mol dm^{-3}. [b] Conditions identical to *a*, but [histidine] = 0.

* A similar conclusion has been made for the reaction between *trans*-[Ru(NH$_3$)$_4$(SO$_3$)(OH$_2$)] and his in aqueous solution, although the sterically hindered isomer has not been detected (H. Taube, personal communication).

Kinetic and Equilibrium Parameters.—A summary of the rates and activation parameters, as well as the stability constants evaluated from the kinetic data, is shown in Table 4. The activation enthalpies, which

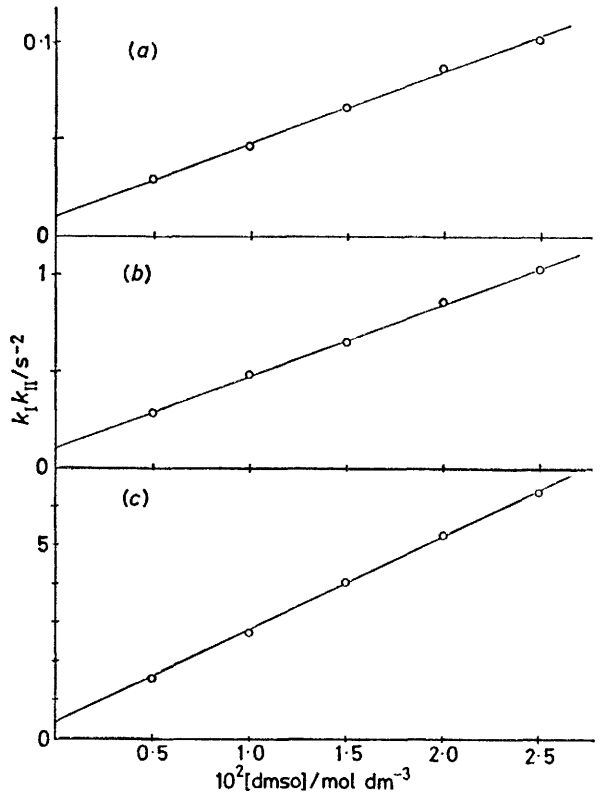


FIGURE 5 Plots of $k_I k_{II}$ *versus* the dmso concentration at (*a*) 15 °C, (*b*) 25 °C, and (*c*) 33 °C

parallel the rates of dissociation of the several pentacyanoferrates, also determine the trends in the equilibrium parameters.

TABLE 4

Kinetic and equilibrium parameters * of pentacyanoferrate(II) complexes of glycinate, imidazole, and L-histidine

	glyO	imH	N^1-his	N^3-his
(*a*) Formation				
k_f/dm^3 mol^{-1} s^{-1}	28.0	240	320	320
$\Delta H^‡$/kcal mol^{-1}	14.7	15.2	15.4	15.4
$\Delta S^‡$/cal K^{-1} mol^{-1}	−3	3	5	5
(*b*) Dissociation				
k_d/s^{-1}	2.67×10^{-3}	1.33×10^{-3}	5.3×10^{-4}	0.109
$\Delta H^‡$/kcal mol^{-1}	23.2	24.3	25.2	21.8
$\Delta S^‡$/cal K^{-1} mol^{-1}	7	10	11	10
(*c*) Equilibrium				
K/dm^3 mol^{-1}	1.05×10^4	1.80×10^5	5.9×10^5	2.9×10^3
ΔH/kcal mol^{-1}	−8.5	−9.1	−9.8	−6.4
ΔS/cal K^{-1} mol^{-1}	−10	−7	−6	−5

* 25 °C, I = 0.100 mol dm^{-3} (Li[ClO_4]).

Comparison between the two isomers of the L-histidine complex shows that steric effects in the neighbourhood of the N^3 atom destabilize the isomer by *ca.* 3.4 kcal mol^{-1}.* This value is comparable to the 3.1 kcal mol^{-1} reported by Shepherd [11] for the strain energy associated with methylation adjacent to the iron centre in the pentacyano(4,5-dimethylimidazole)ferrate(II) complex, as compared to the imidazole analogue.

* Throughout this paper: 1 cal = 4.184 J.

Isomerization Kinetics in Alkaline Solutions.—In alkaline solutions histidine offers three non-equivalent sites for co-ordination to the pentacyanoferrate(II) ion: the N^1 and N^3 atoms and the NH_2 group. Evidence for a complex isomerization behaviour was obtained from the spectra of freshly prepared solutions of $[Fe(CN)_5(OH_2)]^{3-}$ (acetate buffer, 10^{-3} mol dm^{-3}, with trace amounts of ascorbic acid) and lithium L-histidinate, under argon (see Figure 3).

The rates of formation of the three isomers followed a typically first-order law with respect to the concentration of the $[Fe(CN)_5(OH_2)]^{3-}$ ion and the total concentration of lithium L-histidinate. The second-order rate constant was measured as $k_I' = 91 \pm 4$ dm^3 mol^{-1} s^{-1} at 25 °C and I = 0.100 mol dm^{-3} (Li[ClO_4]). This value is approximately three times the rate constant for the glycinate ligand, being consistent with the polyfunctional character of the L-histidinate ion.

The rates of isomerization were practically independent of the concentration of the free L-histidinate ion (1.0×10^{-2}—5.0×10^{-2} mol dm^{-3}), with typical first-order behaviour during at least two half-lives. The isomerization constant, $k_{iso.} = (8.4 \pm 0.5) \times 10^{-3}$ s^{-1}, probably refers to the conversion of the labile N^3- and NH_2-co-ordinated histidinate ion into the stable and inert N^1 isomer. The isomerization is complete within a few minutes of the mixing of the reactants. To determine the rates of dissociation of the N^1 isomer an excess of dmso (0.100—0.200 mol dm^{-3}) over the L-histidinate ligand (5×10^{-3} mol dm^{-3}) was introduced after the isomerization reaction. Under these conditions, as demonstrated earlier, the slow dissociation of the N^1 isomer should proceed according to a limiting rate law. The observed rate constant in this case is $k'_{-N(1)} = 5.2 \times 10^{-4}$ s^{-1} at 25 °C, λ 390 nm, and I = 0.100 mol dm^{-3} (Li[ClO_4]). This value is practically identical to those obtained for the corresponding reactions in neutral solutions, where histidine was present as a zwitterionic ligand.

If dmso is introduced before the isomerization, *i.e.* within 15—20 s after mixing the $[Fe(CN)_5(OH_2)]^{3-}$ and lithium histidinate solutions, a rapid first-order decay of the N^3 and NH_2 isomers can be observed. The observed rate constant, under saturation conditions for the dimethyl sulphoxide ligand, was $k'_{-N(3)} + k'_{-NH_2} = 7.0 \times 10^{-2}$ s^{-1}.

The rate constants $k'_{-N(3)}$ and k'_{-NH_2} should be quite similar, otherwise a first-order rate law would not be

$$[Fe(CN)_5(N^3\text{-hisO})]^{4-} \xrightarrow[+\ \text{dmso}]{k'_{-N(3)}} [Fe(CN)_5(\text{dmso})]^{3-} + \text{hisO}^- \quad (14)$$

obtained for the parallel dissociative processes (14) and (15). As for the $k_{-N(1)}$ and $k'_{-N(1)}$ constants, the rates of dissociation of the N^3 isomers are of comparable magni-

tude, with his in anionic or zwitterionic form. This seems to indicate that the rates of dissociation of the

$$[Fe(CN)_5(NH_2\text{-hisO})]^{4-} \xrightarrow[+\ dmso]{k'_{-NH_2}} [Fe(CN)_5(dmso)]^{3-} + hisO^- \quad (15)$$

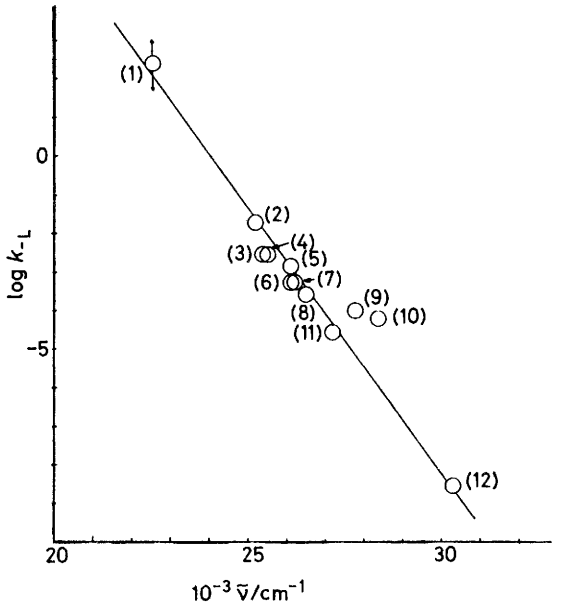


FIGURE 6 Correlation of the rate constants of dissociation of pentacyanoferrate(II) complexes $[Fe(CN)_5L]^{n-}$ with the energy of the lowest *d–d* transition in the visible. L = OH_2 (1), NH_3 (2), $glyO^-$ (3), $NMeH_2$ (4), imH (5), his (6), $hisO^-$ (7), methylpyrazinium (8), $[SO_3]^{2-}$ (9), dmso (10), $[AsO_3]^{2-}$ (11), and $[CN]^-$ (12)

co-ordinated amino-acids are not substantially influenced by their charges.

Ligand-field Effects on the Rates of Dissociation.—A comparison of the rates of dissociation of the imidazole, glycinato, and histidine complexes with those previously reported for several other pentacyanoferrates can be seen in Figure 6. The energies of the $^1A_1$–$^1E(1)$ transition in the visible were chosen to rationalize the comparison, since they are related to the ligand-field stabilization in the complexes.

Over several orders of magnitude, the rate constants [7,9,10] of dissociation of $[Fe(CN)_5L]$ complexes parallel the energies of the $^1A_1$–$^1E(1)$ transition.[13] The glycinato-complex is located near the typical N-saturated bases, ammonia and methylamine. The imidazole and N^1-histidine complexes seem more related to those of N-unsaturated bases (*e.g.* pyrazine), where back-bonding interactions have been shown [7] to be of great importance.

The correlation in Figure 6 also explains why the carboxylate group fails to compete with the amine and imidazole groups for co-ordination with the pentacyanoferrate(II) ion. Most typical oxygen bases, carbonates, sulphates, carboxylates, nitrates, and phosphates, as well as the halides, are located near to water in the spectrochemical series. Consequently, they are not good candidates for complexation with the pentacyanoferrate(II) ion. Sulphur ligands constitute an important class to be investigated. A stable complex has been observed in the case of methionine, with some evidence of co-ordination through the sulphur atom. A number of S-containing amino-acids are under investigation in this laboratory.

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