Kinetics and mechanism of the substitution of aquapentacyanoferrate(III) by cytosine, cytidine and cytidine-5′-monophosphate

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Abstract

Kinetic, thermodynamic and spectral data are reported for the formation of low spin d^5 pentacyanoferrate(III) complexes of the type $Fe(CN)_5L$ starting from $Fe(CN)_5H_2O^{2-}$ for L = cytosine, cytidine and cytidine-5′-monophosphate. The complexes exhibit strong ligand-to-metal charge-transfer bands in the visible region. In the presence of excess L, the pseudo-first-order rate constant exhibits the behaviour $k_{obs} = k_f[L] + k_d$ for the overall reaction $Fe(CN)_5H_2O^{2-} + L \underset{k_d}{\overset{k_f}{\rightleftharpoons}} Fe(CN)_5L^{2-} + H_2O$. The temperature and pressure dependence of k_f and k_d, as well as of the overall equilibrium constant K ($= k_f/k_d$), were studied. The positive values of $\Delta S^{\ddagger}$ and $\Delta V^{\ddagger}$ for both reaction steps suggest the operation of a dissociatively activated mechanism. The results are discussed in comparison to other data for related substitution reactions reported in the literature.

Introduction

The structure and reactivity of pentacyanoferrate(II/III) complexes of the type $Fe(CN)_5L^{n-}$ are of theoretical and practical interest, and have received considerable attention over the last ten years [1–28]. Among others, these low spin iron complexes have been recognized as useful models for biological systems and have been used to investigate specific binding sites in amino acids and redox reactions of metalloproteins. Considerably less is known about the intimate nature of the interaction of pentacyanoferrate complexes with biologically important ligands.

We have recently studied [27] the interaction of nucleic bases, nucleosides and nucleotides with the hypotensive agent $Fe(CN)_5NO^{2-}$ and its decomposition products $Fe(CN)_5H_2O^{3-}$ and $Fe(CN)_5H_2O^{2-}$. Our preliminary observations have prompted us to perform a more detailed kinetic and thermodynamic study of the reaction given in (1), with L = cytosine, cytidine and cytidine-5′-monophosphate.

$$Fe^{III}(CN)_5H_2O^{2-} + L \underset{k_d}{\overset{k_f}{\rightleftharpoons}} Fe^{III}(CN)_5L^{2-} + H_2O \quad (1)$$

The reported activation parameters (especially $\Delta S^{\ddagger}$ and $\Delta V^{\ddagger}$) for both the forward and reverse reactions enable us to discuss the intimate nature of these reactions in more detail.

Experimental

Materials

$Fe^{III}(CN)_5H_2O^{2-}$ was prepared in solution from $Fe^{III}(CN)_5NO_3^{3-}$ according to the procedure described elsewhere [16]. In acidic and neutral solutions this procedure drastically reduces the possible formation of Fe(II) impurities that could exhibit catalytic properties [16]. The ligand solutions were prepared using the free base and nucleoside as pure compounds and the 5′-nucleotide as disodium salt (Sigma). The pH of the ligand and complex solutions was adjusted to 6 with NaOH or $HClO_4$. The ionic strength of the final reaction mixture was adjusted to 0.1 or 0.25 M using $NaClO_4$. All solutions were freshly

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prepared and protected from light. Chemicals of analytical reagent grade and doubly distilled water were used throughout this study.

Instrumentation and procedures

UV–Vis spectra were recorded on Perkin-Elmer Lambda 5 and Shimadzu UV-250 spectrophotometers. Kinetic measurements at ambient pressure were performed in the thermostated (±0.1 °C) cell compartment of the Lambda 5 instrument. Such measurements at elevated pressure (up to 150 MPa) were performed with the aid of a thermostated (±0.1 °C) high-pressure cell [29] placed inside a Zeiss DMR 10 spectrophotometer. The substitution reactions were followed kinetically at 510, 515 and 518 nm, which correspond to the absorbance maxima of $Fe^{III}(CN)_5L$ for L = cytosine, cytidine and cytidine-5′-monophosphate, respectively. In these measurements the concentration of Fe(III) was held constant at 1×10^{-3} M and that of L was varied between 5×10^{-3} and 0.25 M. The Swinbourne method [30] was employed to calculate the observed first-order rate constant for up to three half-lives of the reaction. pH measurements were performed on a Metrohm E 250 instrument equipped with a combined glass electrode of which the reference electrode was filled with a 3 M NaCl solution.

The equilibrium constant for eqn. (1), $K=k_f/k_d=[Fe(CN)_5L]/[Fe(CN)_5H_2O^{2-}][L]$, was determined spectrophotometrically using the equation given in (2), where A_0, A and A_∞ represent the absorbance of $Fe(CN)_5H_2O^{2-}$, a mixture of $Fe(CN)_5H_2O^{2-}$ and $Fe(CN)_5L$, and of $Fe(CN)_5L$ at a particular wavelength, respectively. Plots of A versus $(A_0-A)/[L]$ were linear and K was calculated from the slope of such plots.

$$A=\frac{A_0-A}{K[L]}+A_\infty \qquad (2)$$

Results and discussion

A number of preliminary measurements were performed similar to those outlined before [27]. All reactions were performed at a pH of 6 to avoid possible deprotonation of $Fe(CN)_5H_2O^{2-}$ [28] and protonation of the nucleic base ligands (pK_a (N_3) = 4.6 and 4.3 for cytosine and cytidine, respectively [31]). Typical spectral changes observed during the reaction of $Fe(CN)_5H_2O^{2-}$ with L are illustrated in Fig. 1. This example clearly demonstrates the formation of new bands ascribed to ligand-to-metal charge-transfer transitions [17, 27]. A summary of the spectral data for a series of such complexes is given in Table 1.

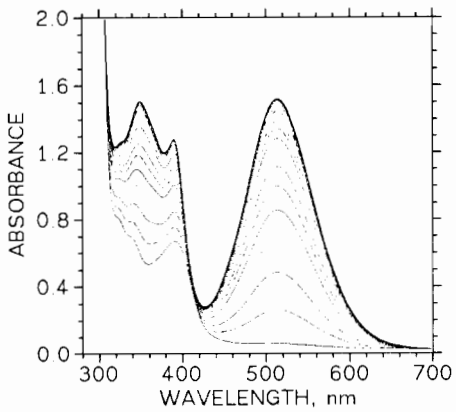

Fig. 1. Repetitive-scan spectra illustrating the formation of the $[Fe(CN)_5cytidine]^{2-}$ complex from $Fe(CN)_5H_2O^{2-}$ (1×10^{-3} M) and cytidine (0.25 M). T = 35.0 °C, pH = 6, μ = 0.25 M, Δt = 15 min.

In addition, it was observed that more $Fe(CN)_5L$ is produced at higher [L], indicating that we are dealing with an equilibrium situation as suggested in eqn. (1).

The formation kinetics of $Fe(CN)_5L$ exhibit good pseudo-first-order behaviour in the presence of an excess of L, and the observed kinetic data can be described by eqn. (3) as indicated in Fig. 2.

$$k_{obs}=k_f[L]+k_d \qquad (3)$$

The values of k_{obs} were measured as a function of [L], for various temperatures and pressures. The corresponding values of k_f and k_d are given along with the associated activation parameters in Tables 2 and 3. Plots of ln k_f and ln k_d versus pressure are linear in all cases and $\Delta V^{\ddagger}$ was calculated from the slope ($=-\Delta V^{\ddagger}/RT$) in the usual way [32]. In addition, the values of k_f and k_d were used to calculate K ($=k_f/k_d$) for reaction (1) and are compared with those determined spectrophotometrically and with other data reported in the literature, in Table 4.

The values of k_f and k_d for all investigated L are very similar and demonstrate that we are dealing with a relatively slow equilibration process. Furthermore, the values of K are small and significantly smaller than for many other nucleophiles recorded in Table 4. The agreement between the kinetically and spectrophotometrically determined values of K is rather good and indicates that the selected experimental procedures give reliable and consistent data. The stability constants of the $Fe^{III}(CN)_5L$ complexes cover 6 orders of magnitude, whereas those of the corresponding Fe(II) complexes cover only a range of 2 orders of magnitude [6]. Our values for the cytosine, cytidine and cytidine-5′-monophosphate complexes, namely 4.3, 2.8 and 5.2 M^{-1}, respectively, are close to that reported for quinoxoline (1.3 M^{-1})

TABLE 1. LMCT spectra of some pentacyanoferrates(III)

Ligand L	R_{max} (nm) [E_{max} (M^{-1} cm^{-1})]	Reference
Imidazole	475[376], 403[1180], 356[981]	17
Pyrazole	450, 439	17
Benzimidazole	505[1605], 382[700], 352[950]	17
4-Aminopyridine	560[2750], 320[2910]	17, 33
Cytosine	510	27
Cytidine	515[>2000], 393, 350	27
CMP	518	27

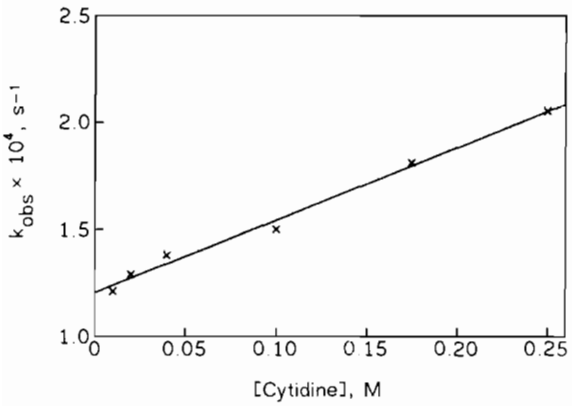

Fig. 2. Ligand concentration dependence of the substitution of $Fe(CN)_5H_2O^{2-}$ by cytidine. $T = 35.0$ °C, pH = 6.0, μ = 0.25 M [cytidine] = 1×10^{-2} to 0.25 M, $[Fe(CN)_5H_2O^{2-}] = 1 \times 10^{-3}$ M.

[11] but significantly larger than the value for *N*-methylpyrasinium (0.47 M^{-1}) [33]. The latter one is cationic and a very poor Brönsted base. Toma and Creutz [6] pointed out that for unsaturated N donor ligands there is a good correlation between the value of K and the pK_a value of the ligand, indicating that the basicity of the ligand controls the value of K. The pK_a values are also included in Table 4 to allow such a correlation. It follows that although this correlation can account for some of the data in Table 4, the results of the present study indicate that other factors must also play an important role in determining the magnitude of K. We assume that steric hindrance and the introduction of certain substituents must account for the generally much smaller values found in this study and the fact that the cytosine complex has a value almost 370 times smaller than that calculated for the pyrimidine complex [11].

We now turn to a discussion of the activation parameters. The significantly positive values of $\Delta S^{\ddagger}$ and $\Delta V^{\ddagger}$ emphasize the dissociative nature of the ligand substitution mechanism on the $Fe^{III}(CN)_5$ moiety [34]. This would be in general agreement with the *trans*-labilization property of coordinated cyanide. Noteworthy is the observation that both $\Delta V^{\ddagger}(k_f)$ and $\Delta V^{\ddagger}(k_d)$ vary significantly with the nature of L, the variation in the case of $\Delta V^{\ddagger}(k_d)$, i.e. involving

TABLE 2. Rate and activation parameters for the reaction $Fe(CN)_5H_2O^{2-} + L \underset{k_d}{\overset{k_f}{\rightleftharpoons}} [Fe(CN)_5L]^{2-} + H_2O$ at ambient pressure and pH = 6.0

L	T (°C)	k_f (M^{-1} s^{-1})	k_d (s^{-1})	$\Delta H^{\ddagger}(k_f)$ (kJ/mol)	$\Delta H^{\ddagger}(k_d)$ (kJ/mol)	$(\Delta S^{\ddagger}(k_f)$ (J/mol K)	$\Delta S^{\ddagger}(k_d)$ (J/mol K)
Cytosine	35.0	2.89E-4	6.68E-5	134 ± 6	121 ± 4	120 ± 20	66 ± 11
	40.0	7.16E-4	1.57E-4				
	45.0	1.41E-3	3.17E-4				
	50.0	3.6E-3	6.3E-4				
Cytidine	30.0	1.18E-4	5.19E-5	116 ± 10	116 ± 5	63 ± 34	57 ± 17
	35.0	3.32E-4	1.20E-4				
	40.0	6.14E-4	2.19E-4				
	45.0	1.13E-3	5.03E-4				
CMP	30.0	1.81E-4	2.59E-5	97 ± 10	122 ± 3	5 ± 32	69 ± 8
	35.0	3.05E-4	5.87E-5				
	40.0	7.34E-4	1.19E-4				
	45.0	1.08E-3	2.71E-4				

TABLE 3. Rate data for the reaction $Fe(CN)_5H_2O^{2-} + L \underset{k_d}{\overset{k_f}{\rightleftharpoons}} Fe(CN)_5L^{2-} + H_2O$ as a function of pressure[a]

L	P (MPa)	k_f (M^{-1} s^{-1})	k_d (s^{-1})	$\Delta V^{\ddagger}(k_f)$ (cm^3 mol^{-1})	$\Delta V^{\ddagger}(k_d)$ (cm^3 mol^{-1})
Cytosine	5	1.13E-3	1.36E-4	3.1 ± 0.6	2.5 ± 0.5
	50	1.09E-3	1.27E-4		
	100	1.05E-3	1.22E-4		
	150	9.36E-4	1.18E-4		
Cytidine	5	4.27E-4	2.18E-4	4.5 ± 0.2	9.5 ± 1.2
	50	3.88E-4	1.73E-4		
	100	3.59E-4	1.43E-4		
	150	3.31E-4	1.29E-4		
CMP	5	1.13E-3	1.11E-4	6.3 ± 1.0	12.8 ± 1.1
	50	9.30E-4	8.41E-5		
	100	8.53E-4	6.68E-5		
	150	7.75E-5	4.75E-5		

[a]Temperature = 40.0 °C; pH = 6.0.

TABLE 4. Formation constants for some pentacyanoferrate(III) complexes

L	K^a (M^{-1})	pK_a	Remarks
4-Aminopyridine	6.8×10^5	9.17	refs. 17, 33
Imidazole	3.4×10^5	7.1	ref. 18
Pyridine	9.4×10^3	5.3	ref. 33
Isonicotinamide	5.2×10^3	3.65	ref. 33
Pyrazine	1.7×10^3	0.65	ref. 33
Pyrimidine	1.6×10^3	1.3	ref. 11
$2\text{-}CO_2imH^-$	35	7.2	ref. 22
Cytosine	4.3(k); 7.0(s)	4.6	$T = 35$ °C, pH = 6.0[b]
Cytidine	2.8(k); 3.5(s)	4.3	$T = 35$ °C, pH = 6.0[b]
CMP	5.2(k)		$T = 35$ °C, pH = 6.0[b]
Quinoxaline	1.3		ref. 11
N-Methylpyrasinium	4.7×10^{-1}	−5.8	ref. 33

[a]k = kinetic method; s = spectrophotometric method. [b]This work.

the breakage of the Fe–L bond, is significantly larger than for $\Delta V^{\ddagger}(k_f)$. This trend can be partially accounted for by the fact that the breakage of the Fe–H_2O bond will be a common process for the forward reaction in all three cases. It must however be kept in mind that in terms of the limiting dissociative (D) mechanism outlined in (4), for which the rate expression is given in (5)* k_f is a composite function such that $\Delta V^{\ddagger}(k_f)$ will also be a composite, viz. $\Delta V^{\ddagger}(k_f) = \Delta V^{\ddagger}(k_1) - \Delta V^{\ddagger}(k_{-1}) + \Delta V^{\ddagger}(k_2)$.

$$\begin{array}{ccc} Fe(CN)_5H_2O^{2-} & \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} & Fe(CN)_5^{2-} + H_2O \\ & & +L,\ k_2 \downarrow \uparrow -L,\ k_{-2} \\ & & Fe(CN)_5L^{2-} \end{array} \qquad (4)$$

$$k_{obs} = \frac{k_1k_2[L] + k_{-1}k_{-2}}{k_{-1} + k_2[L]}$$

$$\approx k_1k_2[L]/k_{-1} + k_{-2} = k_f[L] + k_d \qquad (5)$$

Of these three terms, the first two will be independent of L, whereas the last one will depend on the nature (especially the partial molar volume) of L. It is this contribution that could account for the trend in

*Equation (5) can be simplified as indicated since plots of k_{obs} versus [L] are linear over the whole range of [L], from which it follows that $k_2[L] \ll k_{-1}$ under the selected experimental conditions (see Fig. 2).

$\Delta V^{\ddagger}(k_f)$, although the overall effect is not very large (see Table 3).

The values of $\Delta V^{\ddagger}(k_f)$ reported in this study are considerably smaller than those reported recently for the solvolysis of $Fe(CN)_5NO_2^{3-}$, viz. +27(DMF), +26(DMSO) and +20(MeOH) $cm^3\ mol^{-1}$ [35]. This difference and the fact that $\Delta V^{\ddagger}(k_f)$ depends on the nature of L (see Table 3) suggest that the substitution reactions of $Fe(CN)_5H_2O^{2-}$ most probably follow a dissociative interchange (I_d) instead of the limiting D mechanism as outlined in (6).

$$Fe(CN)_5H_2O^{2-} + L \overset{K_3}{\rightleftharpoons} \{Fe(CN)_5H_2O^{2-} \cdot L\} \underset{k_{-4}}{\overset{k_4}{\rightleftharpoons}} Fe(CN)_5L^{2-} + H_2O \quad (6)$$

Under the selected experimental conditions the rate expression for this mechanism is given in (7), from which it follows that $\Delta V^{\ddagger}(k_f) = \Delta \bar{V}(K_3) + \Delta V^{\ddagger}(k_4)$.

$$k_{obs} = k_4 K_3[L] + k_{-4} = k_f[L] + k_d \quad (7)$$

It may be reasonable, to expect that $\Delta \bar{V}(K_3)$ will be small and similar for the different L, such that the variation in $\Delta V^{\ddagger}(k_f)$ may be related to the nature of L. A similar argument can account for the strong variation of $\Delta V^{\ddagger}(k_d)$, i.e. $\Delta V^{\ddagger}(k_{-4})$, with the leaving group L. The overall $\Delta \bar{V}$ ($= \Delta V^{\ddagger}(k_f) - \Delta V^{\ddagger}(k_d)$) for reaction (1) decreases from approx. zero to -5 and -6 $cm^3\ mol^{-1}$ for the binding of cytosine, cytidine and CMP, respectively. These $\Delta \bar{V}$ values roughly correlate with the expected partial molar volume of the entering ligand.

We conclude that the available rate and activation parameters support the operation of a dissociatively activated substitution process in all investigated reactions of $Fe^{III}(CN)_5H_2O^{2-}$ and $Fe^{III}(CN)_5L$. The absolute magnitude of the reported $\Delta V^{\ddagger}$ for the system studied in this paper is significantly smaller than that reported for substitution reactions of $Fe^{II}(CN)_5L$, which are generally accepted to follow a D mechanism [16, 34, 36] and therefore favours the overall operation of an I_d mechanism.

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References

1 A. G. Sharpe, *The Chemistry of Cyano Complexes of the Transition Metals,* Academic Press, London, 1976.
2 J. A. McCleverty, *Chem. Rev., 79* (1979) 53.
3 K. K. Pandey, *Coord. Chem. Rev., 51* (1983) 69.
4 A. R. Butler and Ch. Glidewell, *Chem. Soc. Rev., 16* (1987) 361.
5 R. Bendix and H. Hennig, *J. Prakt. Chem., 326* (1984) 962.
6 H. E. Toma and C. Creutz, *Inorg. Chem., 16* (1977) 545.
7 H. E. Toma, E. Giesbrecht, J. M. Malin and E. Fluck, *Inorg. Chim. Acta, 14* (1975) 11.
8 J. L. Brisset and M. Biquard, *Inorg. Chim. Acta, 53* (1981) L125.
9 A. D. James and R. S. Murray, *J. Chem. Soc., Dalton Trans.,* (1975) 1530.
10 H. E. Toma, F. G. Filho, A. A. Batista and E. Giesbrecht, *An. Acad. Bras. Cienc., 56* (1984) 57.
11 A. L. Coelho, H. E. Toma and J. M. Malin, *Inorg. Chem., 22* (1983) 2703.
12 H. E. Toma and J. M. Malin, *Inorg. Chem., 12* (1973) 2080.
13 A. D. James, R. S. Murray and W. C. E. Higginson, *J. Chem. Soc., Dalton Trans.,* (1974) 1273.
14 G. Stochel, R. van Eldik, H. Kunkely and A. Vogler, *Inorg. Chem., 28* (1989) 4314.
15 G. Stochel and Z. Stasicka, *Polyhedron, 4* (1985) 491.
16 G. Stochel, R. van Eldik, E. Hejmo and Z. Stasicka, *Inorg. Chem., 27* (1988) 2767.
17 C. R. Johnson, W. W. Henderson and R. E. Shepherd, *Inorg. Chem., 23* (1984) 2754.
18 C. R. Johnson, R. E. Shepherd, B. Man, S. O'Donell and W. Dressick, *J. Am. Chem. Soc., 102* (1980) 6227.
19 H. E. Toma, J. M. Martins and E. Giesbrecht, *J. Chem. Soc., Dalton Trans.,* (1978) 1610.
20 C. R. Johnson and R. E. Shepherd, *Inorg. Chem., 22* (1983) 3506.
21 R. E. Shepherd, *J. Am. Chem. Soc., 98* (1976) 3329.
22 E. M. Sabo, R. E. Shepherd, M. S. Rau and M. G. Elliott, *Inorg. Chem., 26* (1987) 2897.
23 D. R. Eaton and J. M. Watkins, *Inorg. Chem., 24* (1985) 1424.
24 H. E. Toma, A. A. Batista and H. A. Gray, *J. Am. Chem. Soc., 104* (1984) 7509.
25 A. Kathó, Z. S. Bódi, L. Dózsa and M. T. Beck, *Inorg. Chim. Acta, 83* (1984) 145.
26 M. T. Beck and L. Dozsa, *Bioinorg. Chem., 7* (1977) 1.
27 G. Stochel and R. van Eldik, *Inorg. Chim. Acta, 174* (1990) 217.
28 J. H. Espenson and S. G. Wolenuk, *Inorg. Chem., 11* (1972) 2034.
29 F. K. Fleischmann, E. G. Conze, D. R. Stranks and H. Kelm, *Rev. Sci. Instrum., 45* (1974) 1427.
30 E. S. Swinbourne, *J. Chem. Soc.,* (1960) 2371.
31 E. L. J. Breet and R. van Eldik, *Inorg. Chem., 26* (1987) 2517.
32 R. van Eldik (ed.), *Inorganic High Pressure Chemistry: Kinetics and Mechanism,* Elsevier, Amsterdam, 1986.
33 N. V. Hrepic and J. M. Malin, *Inorg. Chem., 18* (1979) 409.
34 R. van Eldik, T. Asano and W. J. le Noble, *Chem. Rev., 89* (1989) 549.
35 G. Stochel and R. van Eldik, *Inorg. Chim. Acta, 155* (1989) 95.
36 K. Bal Reddy and R. van Eldik, *Inorg. Chem., 30* (1991) 596.