On the Effect of Cyanide Ion on the Reaction of Pentacyanonitrosylferrate(2 −) with Cysteine

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The effect of cyanide ion on the reaction of $[Fe(CN)_5(NO)]^{2-}$ with cysteine was considered and it was found that the reaction between cystine and cyanide ion must be taken into account in the mechanism, especially at higher concentrations of cyanide ion. This reaction regenerates cysteine. In contrast to earlier reports, two coloured intermediates were detected during the reaction of $[Fe(CN)_5(NO)]^{2-}$ with cysteine.

Studies of reactions between pentacyanonitrosylferrate(2 −) and a wide variety of nucleophilic species have led to a number of interesting kinetic[1,2] and preparative[3,4] results. The interaction of this complex with compounds containing an SH group has physiological importance, and its hypotensive effect is attributed to this type of reaction.[5] The reaction with cysteine was described first by Scagliarini[6] and more recently Morando *et al.*[7] studied the kinetics of this reaction. They detected the rapid formation of a coloured intermediate C, probably $[Fe(CN)_5(NOSR)]^{3-}$ [8,9] (where RS^- is the cysteinate anion). For the disappearance of C the parallel reaction paths (1)—(4) were suggested.[7] Paths (1)—(3) were proposed on the basis of the effect of cyanide ion on the reaction, which was kinetically described by equation (5) where k_{exp} is the pseudo-first-order rate constant for disappearance of C. The inhibitory effect of cyanide ions represented by the first term of equation (5) is in accordance with the fact that a small amount of cyanide ion can stabilize the colour.[10]

$$\begin{array}{l} C \overset{K}{\rightleftharpoons} [Fe(CN)_4(NOSR)]^{2-} + CN^- \\ \qquad\qquad \xrightarrow{k_1'} [Fe(CN)_5(NO)]^{3-} + \tfrac{1}{2}RSSR \end{array} \tag{1}$$

$$C \xrightarrow{k_2} [Fe(CN)_5(NO)]^{3-} + RSSR \tag{2}$$

$$C + CN^- \xrightarrow{k_3} [Fe(CN)_6]^{4-} + \text{products} \tag{3}$$

$$C + RS^- \xrightarrow{k_4} [Fe(CN)_5(NO)]^{3-} + \text{products} \tag{4}$$

$$k_{exp.} = k_1[CN^-]^{-1} + k_2 + k_3[CN^-] \tag{5}$$

It is well known that cyanide ion reacts with cystine according to equations (6) and (7).[11] Since cystine is formed in reactions (1) and (2) it seems to be reasonable to take reaction (6) into consideration when interpreting the reaction mechanism in the presence of cyanide ion. The regeneration of cysteine in reaction (6) can also be considered as an inhibitory effect of cyanide ion. A kinetic study of reactions (6) and (7) was carried out by Gawron *et al.*[12] The kinetic parameters were determined at 28 °C and 0.05 mol dm^{-3} ($NaNO_3$) ionic strength. These conditions differ from those applied by Morando *et al.* [25 °C and I = 1.5 mol dm^{-3} (NaCl)].

$$RSSR + CN^- \longrightarrow RS^- + RSCN \tag{6}$$

$$RSCN \xrightarrow{\text{fast}} \text{cyclic product} \tag{7}$$

In the present paper we report kinetic data for the reaction between cyanide ion and cystine under appropriate conditions and discuss the role of reaction (6) in the reaction of pentacyanonitrosylferrate(2 −) with cysteine.

Experimental

All reagents were analytical grade. Water was doubly distilled before use. Oxygen was removed from the solutions by bubbling argon through them.

The visible and u.v. spectra were obtained on a Beckman Acta III spectrophotometer. The pH was measured with a Radelkis OP 205/1 pH meter.

The kinetic experiments were monitored spectrophotometrically at 235 nm by following the changes in absorbance with formation of cysteine. The temperature was maintained at 25 ± 0.2 °C, the ionic strength at 1.5 mol dm^{-3} (NaCl), and the pH between 8.5 and 9.2 (using borate buffer). Freshly deaerated solutions of cystine were used in each run. For each experiment the NaCN was freshly dissolved in deaerated buffer. The initial concentration of cystine was 5×10^{-4} mol dm^{-3} and cyanide ion was in 20—200 fold excess. In each case, pseudo-first-order behaviour was found up to 90% conversion. The pseudo-first-order rate constants reported are the average from at least two (usually more) measurements, which did not differ by more than 10%.

Results

No change in absorption spectrum was found when pentacyanonitrosylferrate(2 −) and cystine were mixed, but a change was found upon addition of cyanide ions (Figure 1, spectra 1 and 2). The observed spectrum is nearly identical to that of the coloured intermediate published by Morando *et al.*[7] The probable explanation for the slight difference is given later. This result indicates the indirect formation of cysteine in reaction (6).

The pseudo-first-order rate constant for the reaction of cyanide with cystine increases linearly with increasing initial concentration of cyanide ions (Figure 2). In the range pH 8.5—9.2 there is no noticeable change in $k_{obs.}$ according to Gawron *et al.*[12] From these observations the rate equation (8) can be written for the formation of cysteine, where k is 3.2×10^{-2} dm^3 mol^{-1} s^{-1}, in good agreement with the value determined by Gawron *et al.*[12]

$$\text{rate} = k[CN^-][RSSR] \tag{8}$$

Discussion

The role of reaction (6) in the effect of cyanide ions on the reaction of $[Fe(CN)_5(NO)]^{2-}$ with cysteine can be considered in

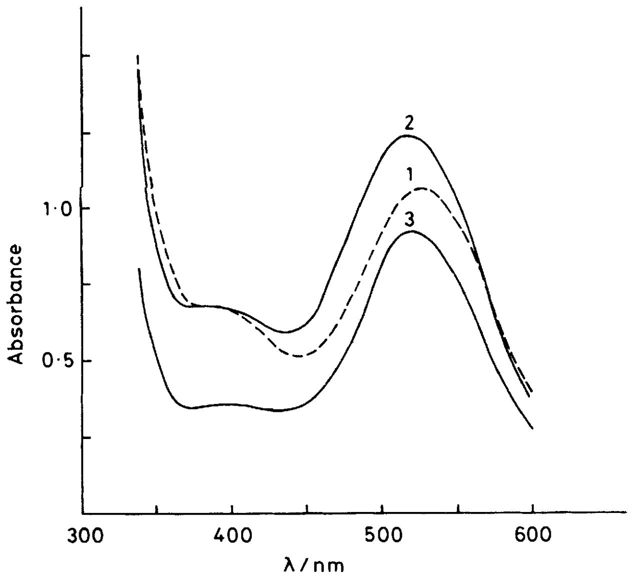


Figure 1. Visible absorption spectra of the intermediate in the reaction of $[Fe(CN)_5(NO)]^{2-}$ with cysteine (1), with cystine and cyanide ions (2), and with cysteine and cyanide ions present initially (3). $[Fe(CN)_5(NO)^{2-}] = 2.5 \times 10^{-2}$, $[RS^-] = 5 \times 10^{-4}$, $[RSSR] = 5 \times 10^{-4}$, and $[CN^-] = 2.5 \times 10^{-2}$ mol dm^{-3}, pH = 8.9

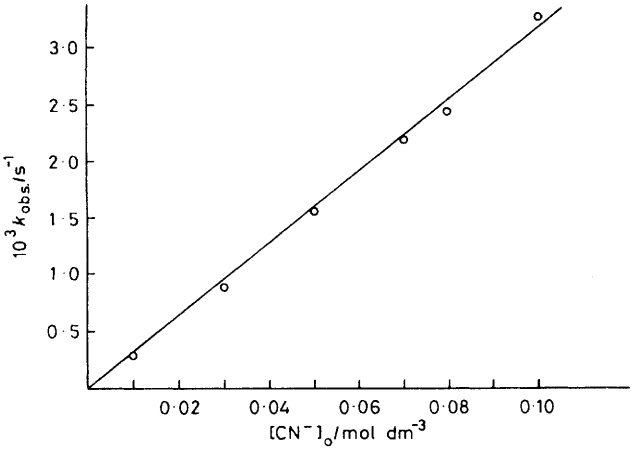


Figure 2. Dependence of the pseudo-first-order rate constants ($k_{obs.}$) with the concentration of cyanide ions. $[RSSR] = 5 \times 10^{-4}$ mol dm^{-3}

terms of equations (9) and (10). Bearing in mind the very fast formation of C from the complex and cysteine, this model is only valid for a large excess of complex and cyanide ions. Reaction (9) summarizes all the possible parallel reaction paths for disappearance of the coloured intermediate, and reaction (10) represents the regeneration of C in reaction (6); k_I and k_{II} are functions of the concentration of cyanide ions. The differential equations (11) and (12) may be derived from equations (9) and (10). Solving these equations by the matrix method for the concentration of C as a function of time we obtain equation (13) where C_0 is the initial concentration of C and λ_1 and λ_2 are the roots of quadratic equation (14).

$$C \xrightarrow{k_I} \tfrac{1}{2}RSSR \qquad (9)$$

$$RSSR \xrightarrow{k_{II}} C \qquad (10)$$

$$d[C]/dt = -\,k_I[C] + k_{II}[RSSR] \qquad (11)$$

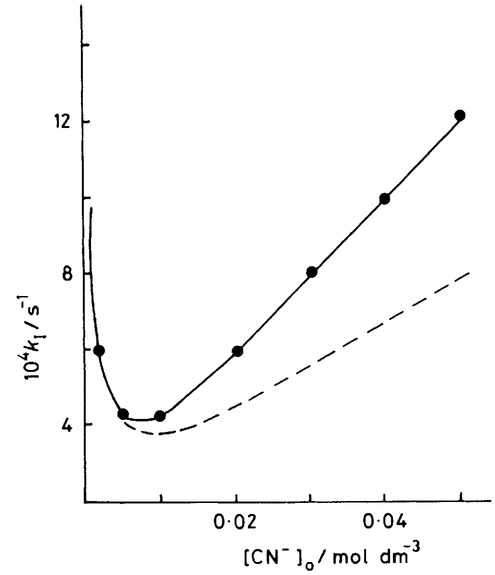


Figure 3. Dependence of k_I on the concentration of cyanide ion (●). The solid curve was calculated as described in the text, the broken curve from the change in $k_{exp.}$ from equation (5)

$$d[RSSR]/dt = \tfrac{1}{2}k_I[C] - k_{II}[RSSR] \qquad (12)$$

$$C(t) = C_0/(\lambda_1 - \lambda_2)[(k_1 + \lambda_1)\exp(\lambda_2 t) - (k_1 + \lambda_2)\exp(\lambda_1 t)] \qquad (13)$$

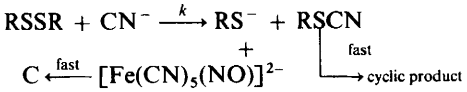
$$\lambda^2 + k_I k_{II} + \tfrac{1}{2}k_I k_{II} = 0 \qquad (14)$$

First we consider the two extreme cases. When $k_I \gg k_{II}$ it follows from equations (11) and (12) that $d[C]/dt = -k_I[C]$. In this situation k_I can be calculated by the pseudo-first-order treatment of *C vs. t* curves. Consequently there is no effect of reaction (10). When $k_{II} \gg k_I$ then RSSR is in a steady state with $d[RSSR]/dt = 0$ and $[RSSR]t = \tfrac{1}{2}k_I/k_{II}[C]$. Substituting the steady-state concentration of RSSR into equation (11) we obtain $d[C]/dt = \tfrac{1}{2}k_I[C]$. Therefore in this situation the pseudo-first-order rate constant is $\tfrac{1}{2}k_I$. Consequently reaction (10) results in a 50% decrease in the pseudo-first-order rate constant. Since the actual decrease was more than an order of magnitude,[7] reaction (6) is not solely responsible for the effect of cyanide ions.

When the values of k_I and k_{II} are comparable the pseudo-first-order rate constants for reaction (6) have been substituted into equation (13) as k_{II} at different concentrations of cyanide ions. Then sets of *C vs. t* curves have been calculated by varying k_I, until the pseudo-first-order rate constant of one of them agreed with $k_{exp.}$ calculated from equation (5), that is with the experimental values of Morando *et al.*[7] (Evidently the curves are not perfectly first order but did show linearity up to 60—70% conversion according to the usual logarithmic transformation.) The dependence of the k_I values thus obtained on the concentration of cyanide ions is shown in Figure 3, and can be approximated by the equation used by Morando *et al.*[7] [equation (5)]. The parameters are in reasonable agreement: $k_1 = 8 \times 10^{-7}$ (8×10^{-7}) mol dm^{-3} s^{-1}, $k_2 = 1.4 \times 10^{-4}$ (1.8×10^{-4}) s^{-1}, and $k_3 = 2.2 \times 10^{-2}$(1.2×10^{-2}) dm^3 mol^{-1} s^{-1}.

All these results mean that it is necessary to extend the scheme suggested by Morando *et al.* Thus when the concentration of cyanide ions is more than 0.02 mol dm^{-3} the regeneration of cysteine influences the kinetic behaviour according to equations (15) and (16). Direct evidence for the above reactions is that when the concentrations of the reactants are high enough (*ca.* 0.1 mol dm^{-3}) cystine is precipitated from the solution, but no precipitate is observed in the presence of an appropriate concentration of cyanide ions (*ca.* 0.2 mol dm^{-3}).

$$\mathrm{C} \xrightarrow{k_{1-4}} [\mathrm{Fe(CN)_5(NO)}]^{3-} + \mathrm{RSSR} \qquad (15)$$



(16)

Furthermore, in the absence of cyanide ions, initially the proportions of each different path for the disappearance of C can be estimated from equation (5). The term $k_3[\mathrm{CN}^-]$ is negligible therefore equation (5) can be rewritten as in (17)

$$k_{\mathrm{exp}} = k_1[\mathrm{CN}^-]_e^{-1} + k_2 \qquad (17)$$

where $[\mathrm{CN}^-]_e$ is the equilibrium concentration at time *t*. Using $k_{\mathrm{exp}} = 3.15 \times 10^{-3}$ s^{-1} (ref. 7) and $k_2 = 1.4 \times 10^{-4}$ s^{-1} (this work), the proportion of the reaction path occurring through the prior loss of cyanide ion is more than 90%. The equilibrium concentration of cyanide ions is *ca.* 2×10^{-4} mol dm^{-3} when the initial concentration of cysteine is 5×10^{-4} mol dm^{-3} and $t = 0$. Consequently the concentration of the tetracyanoiron species is also 2×10^{-4} mol dm^{-3}. Therefore, it seems more appropriate to consider the formation of two coloured intermediates in this reaction. This conclusion is supported by spectrum 3 in Figure 1. The absorption spectra of the intermediates differ, although only slightly, in the presence and in the absence of cyanide ions. This is the explanation for the difference in the spectra found for the intermediates mentioned earlier.

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