The Pentacyanonitrosylferrate Ion. Part 3.[1] Reaction with the Carbanion of Ethyl Cyanoacetate

Anthony R. Butler*, Adrianne M. Calsy, and Christopher Glidewell
Department of Chemistry, The University, St. Andrews, Fife KY16 9ST, Scotland

The carbanion of ethyl cyanoacetate reacts with pentacyanonitrosylferrate(2−) (nitroprusside) to form a coloured adduct, which decomposes to an oxime and aquapentacyanoferrate(3−). Although the pK_a of ethyl cyanoacetate is similar to that of malononitrile, no second ionisation could be detected in the kinetic data. Reasons for this are discussed.

The reactions of nitroprusside $\{[Fe(CN)_5NO]^{2-}\}$ with carbon acids have been the subject of a number of studies;[1-4] most interest has been focused on the formation of an intensely coloured adduct which, from studies of the reactions of several other nucleophilic species with nitroprusside, is assumed to have structure (1). In previous work[1] we made a full study of the kinetics of adduct formation with several carbon acids, including malononitrile, and noted that a second ionisation of the carbon acid moiety may occur. Although we observed from the fading of the colour that the adduct underwent a subsequent reaction, we were unable to isolate and identify the organic product of this part of the reaction. Thus we were unable to substantiate the nitrosating action of nitroprusside.[5] Work by Swinehart and Schmidt[4] did show that reaction of nitroprusside and acetone under alkaline conditions results in nitrosation to give the 1-oxime of propane-1,2-dione ($CH_3COCH{=}NOH$) as the final product but, in this instance, extensive kinetic studies were not possible as the reaction conditions were necessarily highly alkaline and side reactions would have been extensive. In order to effect a full study, including kinetic data and product identification, for the reaction of a carbon acid with nitroprusside we turned to ethyl cyanoacetate, which is a fairly strong acid and for which the corresponding oxime $[HON{=}C(CN)CO_2Et]$ is a well characterised species.[6]

$$[Fe(CN)_5NO]^{2-} + X_2CH^- \rightleftharpoons \left[Fe(CN)_5N(O)CHX_2\right]^{3-}$$

(1)

$$(1) + H_2O \longrightarrow [Fe(CN)_5H_2O]^{3-} + X_2C{=}NOH$$

(2)

Scheme 1.

$$[Fe(CN)_5NO]^{2-} + 2HO^- \rightleftharpoons [Fe(CN)_5NO_2]^{4-} + H_2O$$

$$\rightleftharpoons [Fe(CN)_5H_2O]^{3-} + NO_2^-$$

Scheme 2.

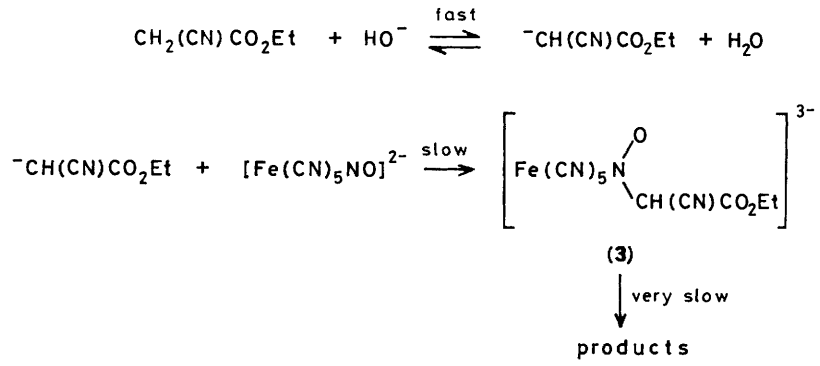
Results and Discussion

Product Isolation.—Addition of alkali to a solution containing ethyl cyanoacetate and sodium nitroprusside results in rapid formation of an intensely coloured red species which we assume has structure (3). We attempted to isolate this material as its sodium salt by cooling an alcoholic solution of the reactants. A hygroscopic reddish-brown solid was obtained which did not give consistent analyses. However, the arguments used previously[1] for the formation of such an adduct are relevant in this instance, and we shall assume that this is the first product of reaction. The colour fades within minutes and we turn now to the isolation of the final products of reaction.

The direct nitrosating agent, sodium nitrite in acid solution, reacts readily with ethyl cyanoacetate to give the oxime, which is extracted from solution by means of methylene dichloride. We used a similar extraction procedure for the nitrosation of ethyl cyanoacetate by nitroprusside in alkaline solution. The oxime was obtained in an isolated yield of only 23%. It was not clear if this low yield was a consequence of multiple products or an inefficient extraction procedure. We decided, therefore, to determine the yield more accurately by an isotopic dilution technique.

We prepared [^{14}C]ethyl cyanoacetate and subjected it to reaction with nitroprusside under alkaline conditions. A substantial excess of inactive ethyl cyanoacetate oxime was added and the oxime was extracted. The molar activity of the oxime thus isolated indicated 49—54% yield of the oxime based on the amount of nitroprusside present. Clearly the oxime is a major product of reaction; reasons for the less than quantitative yield will be discussed later.

In order to establish the inorganic product of reaction, shown as the aquapentacyanoferrate ion (2) in Scheme 1, we used ^{13}C n.m.r. spectroscopy. The spectrum of 90% ^{13}C-labelled nitroprusside has been recorded[7] and consists of a doublet centred at 134.4 (equatorial cyano groups) and a quintet centred at 132.4 p.p.m. (axial cyano group). A 0.025M-solution of this material in the presence of 0.202M-ethyl cyanoacetate and an accumulation time of 3 h showed only an unresolved peak at 134.3 p.p.m. due to the isotopic label. The quintet was lost in the noise. Immediately after addition of NaOH (0.088M) the spectrum of the reaction mixture was recorded over 3 h. A much reduced signal at 134.3 p.p.m. was observed and a new peak at 175.4 p.p.m. was recorded. This latter peak, which is probably the pentacyano complex resulting from the nitrosation of ethyl cyanoacetate by nitroprusside but could be the result of reaction between nitroprusside and hydroxide, proved difficult ot identify with certainty. In our previous study of the ^{13}C n.m.r. spectra of pentacyanoferrate complexes[7] we assigned a signal at 172.8 p.p.m. to the equatorial cyano groups of $[Fe(CN)_5H_2O]^{3-}$ and a signal at 176.7 p.p.m. to the equatorial groups of $[Fe(CN)_5NO_2]^{2-}$. Both complexes are formed by the action of hydroxide on nitroprusside (Scheme 2) and the proximity of the signals makes distinction difficult. Also, chemical shifts do depend upon the



Scheme 3.

Table 1. Kinetic data for the reaction of nitroprusside[a] with the carbanion of ethyl cyanoacetate[b] at 25 °C

$10^2[HO^-]_t$/M[c]	$10^2[^-CH(CN)CO_2Et]_e$/M[d]	$10^4[HO^-][^-CH(CN)CO_2Et]_e$/M^2	$k_{obs.}$/s^{-1}
2.00	1.80	0.36	14
2.50	2.22	0.62	20
4.00	3.40	2.04	29
5.00	4.26	3.15	33
6.25	4.71	7.25	36
7.50	5.15	12.1	33
9.00	5.45	19.4	44

[a] Initial concentration 1.88×10^{-3}M. [b] Stoicheiometric concentration 6.25×10^{-2}M. [c] Stoicheiometric concentration of hydroxide. [d] Equilibrium concentration of carbanion.

conditions under which they are recorded. Had there been conversion into an Fe^{III} complex this would have been paramagnetic and have no detectable ^{13}C n.m.r. spectrum.

We think that the signal at 17.4 p.p.m. is not due to $[Fe(CN)_5NO_2]^{4-}$ for the following reasons:

(i) Replacement of NO_2^- by H_2O in $[Fe(CN)_5NO_2]^{4-}$ is a fairly slow process.[8] In an experiment using a high-field n.m.r. spectrometer, where a spectrum could be obtained in 5 min, we noted that the spectrum obtained after 50 min was the same as that obtained within 10 min of mixing.

(ii) Formation of $[Fe(CN)_5NO_2]^{4-}$ is inconsistent with the isolation of the oxime as the organic product of reaction.

It is possible that the signal at 175.4 p.p.m. is due to a complex other than $[Fe(CN)_5NO_2]^{4-}$ and $[Fe(CN)_5H_2O]^{3-}$. For example, it is known[9] that, under some circumstances, oximes react with nitroprusside to give an oximato complex. However, we observed that at concentrations similar to those already mentioned, the ^{13}C n.m.r. spectrum of nitroprusside was unchanged by addition of the oxime of ethyl cyanoacetate. Thus, although observation of a signal at 175.4 p.p.m. is right for formation of a pentacyanoferrate complex, we have not established this complex unambiguously as $[Fe(CN)_5H_2O]^{3-}$. The situation is complicated by the facts that this complex can exist[10] as the dimer $[Fe_2(CN)_{10}]^{6-}$ and that it may ionise[11] to give $[Fe(CN)_5OH]^{4-}$. These may explain the difference in chemical shift for this complex in the reaction mixture from that in water. What is certain is that during nitrosation there is no breakdown of nitroprusside to free cyanide as has been suggested for its physiological action.[12]

Kinetic Studies.—Formation of the colour due to the adduct (3) was found to occur on the stopped-flow time scale. The formation as a function of hydroxide concentration under pseudo-first-order conditions with hydroxide and ethyl cyanoacetate both in substantial excess over nitroprusside was examined and the results are displayed in Table 1.

Table 2. Kinetic data for the decomposition of the adduct (3) obtained from sodium nitroprusside[a] and ethyl cyanoacetate[b] at 25 °C

$[HO^-]_t$/M[c]	0.010	0.020	0.040	0.063	0.088	0.150	0.188	0.250
$10^2k_{obs.}$/s^{-1}	3.11	2.66	2.76	3.11	3.11	3.18	3.16	2.84

[a] Initial concentration 1.88×10^{-3}M. [b] Initial concentration 6.25×10^{-2}M. [c] Stoicheiometric concentration of hydroxide.

In our previous study[1] we established that the rate-determining step in the reaction of a malononitrile with nitroprusside is not proton removal; cyanocarbons appear to be almost 'normal acids' in the Eigen sense.[13] The rate-determining step in the present reaction is, therefore, likely to be reaction of the ethyl cyanoacetate carbanion with nitroprusside, and to substantiate this from the kinetic data we need to know the pK_a of ethyl cyanoacetate. Lienhard and Jencks[14] report a value of 11.7, which is surprisingly low when compared with malononitrile (11.4)[13] and diethyl malonate (13.3).[15] The value quoted by Leinhard and Jencks[14] is for an ionic strength of 1M. All our kinetic studies were made at 0.1M and so it seemed worthwhile to determine the pK_a at that value. The alkaline hydrolysis of ethyl cyanoacetate is too rapid[16] to permit measurement of the pK_a by potentiometric means. We used, therefore, the kinetics of alkaline hydrolysis,[14] assuming that only the un-ionised form reacts with hydroxide. The pK_a value obtained at $I = 0.1$M was 11.74, hardly different from the previously reported value at $I = 1$M.

With this information we calculated the concentration of carbanion at each stoicheiometric hydroxide concentration shown in Table 1; there is a rectilinear relationship between $k_{obs.}$ and the carbanion concentration (Figure). This suggests that the rate-determining step is the reaction between carbanion and nitroprusside (Scheme 3). In the case of malononitrile, an acid of similar pK_a, the situation is rather different.[1] There is no rectilinear relationship between $k_{obs.}$ and carbanion concentration as a second ionisation occurs leading to a rectilinear relationship between $k_{obs.}$ and the product $[^-CH(CN)_2][HO^-]$. We calculated the equivalent product for the data in Table 1; it does not yield a convincing rectilinear curve and there is a large intercept on the ordinate which is difficult to understand in chemical terms and was not obtained with the data for malononitrile. It is thus clear that, in spite of the similarity of the pK_a values, malononitrile and ethyl cyanoacetate have substantially different behaviour. There are two possible explanations. First, the former could the more readily undergo a second ionisation. Secondly, malononitrile is a true cyanocarbon

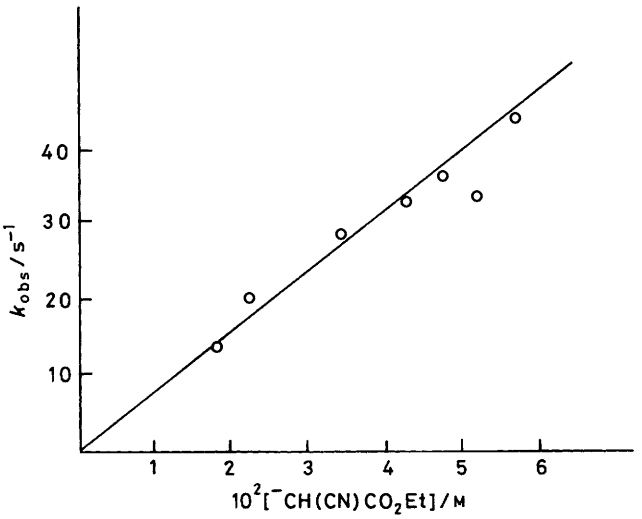


Figure. Kinetic data for the reaction of nitroprusside with the carbanion of ethyl cyanoacetate

and so its acid behaviour is more normal, in the Eigen sense, than that of ethyl cyanoacetate; this may not be so in the case of its nucleophilicity which is what governs its behaviour in reaction with nitroprusside. At the moment we favour the latter explanation. The matter has recently been discussed in some detail by Kresge and co-workers.[13]

The colour due to (3) fades rapidly and we examined the kinetics of this process as a function of acid concentration (Table 2). It is clear that $k_{obs.}$ is independent of hydroxide concentration and this is consistent with complete conversion of nitroprusside into (3) and slower decomposition of (3) into $[Fe(CN)_5]^{3-}$ and the oxime from ethyl cyanoacetate. The pentaco-ordinated species is rapidly solvated to give $[Fe(CN)_5H_2O]^{3-}$.

One of the complications in this study was that both ethyl cyanoacetate and nitroprusside react with hydroxide. The rate of reaction of ethyl cyanoacetate carbanion is much greater than that of hydroxide and so it is possible to obtain kinetic data on a stopped-flow spectrophotometer for formation of (3) without difficulty. However hydrolysis, particularly of ethyl cyanoacetate, was found to be a problem in the preparative studies. The ^{13}C n.m.r. spectra all showed substantial formation of cyanoacetic acid and ethanol. This can be explained if we assume that formation of (3) is an equilibrium process. The absence of a non-zero intercept in the Figure indicates that the reverse rate coefficient must be small (although the scatter in points makes assessment of the intercept difficult) but this is sufficient to allow formation of some cyanoacetic acid and ethanol during the slow decomposition of (3). Thus, the low yield of oxime can be explained. However, the yield is not very low and we can confirm the conclusion of McGarvey and Kimura[17] that, in alkaline conditions, nitroprusside is an effective nitrosating agent on a preparative scale.

Experimental

Reagents where AnalaR where available. Sodium nitroprusside solutions were carefully protected from light by the use of aluminium foil. Ethyl cyanoacetate oxime was prepared by the action of acid sodium nitrite upon ethyl cyanoacetate.[6] [^{14}C]Ethyl cyanoacetate was prepared by the esterification[18] of cyanoacetic acid (3.90 g; 0.047 mol) with [^{14}C]ethanol (10 ml; 5 mCi l^{-1}). The activity of the product was 161 μCi mol^{-1}. Sodium [$^{13}C_5$]nitroprusside was prepared by a literature method.[7]

Reaction of Ethyl Cyanoacetate with Nitroprusside.—Sodium hydroxide (0.02 mol) was added to a solution of sodium nitroprusside (6 g; 0.02 mol) and ethyl cyanoacetate (2.28 g; 0.02 mol) in water (50 ml) and ethanol (10 ml) with stirring. The solution went bright red but the colour quickly faded to yellow. After 10 min the solution was neutralised (HCl) and extracted with methylene dichloride. The extract was dried ($MgSO_4$) and the solvent removed by evaporation to give white crystals of ethyl cyanoacetate oxime (yield 23%), m.p. 128 °C (lit.,[19] 129 °C); $\delta_H(CDCl_3)$ 1.40 (3 H, t) and 4.45 (2 H, q); $\delta_C[(CD_3)_2CO]$ 13.6, 64.0, 126.2, and 159.5 p.p.m.

For the isotopic dilution experiment, equal volumes of [^{14}C]ethyl cyanoacetate, sodium nitroprusside, and sodium hydroxide (all 0.18M) were mixed and the reaction was allowed to go to completion. A ten-fold amount of inactive oxime was added after neutralisation and the whole was extracted with methylene dichloride. Counting proved difficult as ethyl cyanoacetate oxime is an exceptionally strong quenching agent. Quenching curves were set up by measuring the decrease in count upon addition of known amounts of inactive oxime to a solution of [^{14}C]ethanol of known activity. From these data the amount of active oxime in a quenched solution containing inactive oxime could be ascertained. In several determinations the yield ranged from 49 to 54%.

Most of the n.m.r. spectra were recorded with a 1.9 T instrument. Those with an accumulation time of 5 min were obtained with a 8.5 T instrument at the S.E.R.C. Regional N.m.r. Service, University of Edinburgh.

Rate constants were measured by use of a HiTech stopped-flow spectrophotometer set at 480 nm connected to an Apple microcomputer *via* a transient recorder. Sodium hydroxide solution was placed in one syringe and a mixture of ethyl cyanoacetate and sodium nitroprusside in the other. The concentrations were arranged so that there was always a large excess of carbanion over nitroprusside. Correlation coefficients were always better than 0.99. The ionic strength was maintained at 0.1M by addition of KCl. All rate constants were measured at 25 °C. Decomposition of (3) to oxime was studied by the use of a Unicam SP8-100 spectrophotometer.

References

1 Part 2, A. R. Butler, C. Glidewell, V. Chaipanich, and J. McGinnis, *J. Chem. Soc., Perkin Trans. 2*, 1986, 7.
2 K. W. Loach and T. A. Turney, *J. Inorg. Nucl. Chem.*, 1961, **18**, 179.
3 T. Weyl, *Ber. Dtsch. Chem. Ges.*, 1875, **11**, 2175.
4 J. H. Swinehart and W. G. Schmidt, *Inorg. Chem.*, 1967, **6**, 232.
5 D. L. H. Williams, *Adv. Phys. Org. Chem.*, 1983, **18**, 381.
6 L. Wolff, *Justus Liebig's Ann. Chem.*, 1902, **325**, 129.
7 A. R. Butler, C. Glidewell, A. R. Hyde, and J. McGinnis, *Inorg. Chem.*, 1985, **24**, 2931.
8 J. H. Swinehart and P. A. Rock, *Inorg. Chem.*, 1966, **5**, 573.
9 V. Hankonyi, N. Burger, and V. Karas-Gasparec, *Z. Phys. Chem. (Leipzig)*, 1975, **256**, 87.
10 A. D. James and R. S. Murray, *J. Chem. Soc., Dalton Trans.*, 1976, 1182.
11 D. H. Macartney and A. McAuley, *Inorg. Chem.*, 1979, **18**, 2891; G. Davies and A. R. Garafalo, *ibid.*, 1980, **19**, 3543; H. E. Toma, A. A. Batista, and H. B. Gray, *J. Am. Chem. Soc.*, 1982, **104**, 7509.
12 A. R. Butler, C. Glidewell, J. McGinnis, and W. I. K. Bisset, *Clin. Chem.*, 1987, **33**, 490, and references therein.
13 M. Hojatti, A. J. Kresge, and W.-H. Wang, *J. Am. Chem. Soc.*, 1987, **109**, 4023.
14 G. E. Lienhard and W. P. Jencks, *J. Am. Chem. Soc.*, 1965, **87**, 3863.
15 R. G. Pearson and J. M. Mills, *J. Am. Chem. Soc.*, 1950, **72**, 1692.
16 W. A. Drushel, *Am. J. Sci.*, 1912, **33**, 27.
17 G. J. McGarvey and M. Kimura, *J. Org. Chem.*, 1986, **51**, 3915.
18 J. K. H. Inglis, *Org. Synth.*, 1928, **8**, 74.
19 O. Diels and E. Borgwardt, *Ber. Dtsch. Chem. Ges.*, 1921, **54**, 1334.

Received 6th August 1987; *Paper* 7/1455