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Kinetics and Mechanism of the Zinc-Promoted Dissociation of Cyanide Ion from 1-Benzyl-4-cyano-1,4-dihydronicotinamide in Acetonitrile

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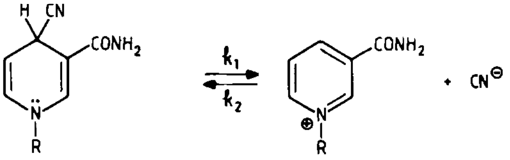
Rate and equilibrium constants for the dissociation of cyanide ion from 1-benzyl-4-cyano-1,4-dihydronicotinamide (BNA-CN) in acetonitrile at 25°C have been evaluated. Compared to water as the solvent, the dissociation constant in acetonitrile, $K_{diss} = 3.9(\pm 0.6) \times 10^{-7}$ M, is approximately a factor 10^6 lower. This reduction is brought about by a nearly 10^2 slower rate of dissociation ($k_1 = 2.6 \times 10^{-4}\ s^{-1}$) and a 10^4 faster rate of addition of cyanide ion in acetonitrile. Addition of zinc salts, like zinc perchlorate, zinc bromide, and zinc iodide, induce cyanide ion dissociation by both entrapment of cyanide ion and efficient promotion of the cyanide ion expulsion. Remarkably, the latter effect is dependent on the nature of the zinc counterion and increases in the order $ClO_4^- < Br^- < I^-$. It is concluded that the zinc-promoted cyanide expulsion is preceded by complex formation of zinc species with BNA-CN and that both Zn^{2+} and monoionized ZnX^+ species are active. A transition state model for the reaction is proposed. © 1988 Academic Press, Inc.

INTRODUCTION

The reversible dissociation of cyanide ion from 1-substituted-4-cyano-1,4-dihydronicotinamides in Eq. [1] has received much attention in view of its analogy with reactions of the NAD$^+$/NADH coenzyme couple (*1*),



[1]

BNA-CN: $R = CH_2\phi$ BNA$^+$: $R = CH_2\phi$

Study of this process as a model for NADH–NAD$^+$ transformations is particularly attractive because both forward and reverse reactions occur readily in water under nonenzymatic conditions. Rates and equilibria of cyanide ion addition to nicotinamide cations with various substituents R in aqueous solution have been investigated by several groups (*2–10*). It has been established that for $R = CH_2\phi$ in 1.0 M KCN (pH = 11.3) approximately 75% of the substrate exists as the

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1,4-adduct and that addition of cyanide ion to the pyridinium ring involves a product-like transition state (*2*). Moreover, studies of effects of surfactants and polyelectrolytes have revealed that the reaction is very sensitive to the reaction environment (*3, 4, 6, 8–10*). This observation is of particular interest in view of the important role that the reaction environment can have on the catalytic activity of enzymes. In alcohol dehydrogenase, for example, the nicotinamide moiety and the catalytically active zinc ion are located in a hydrophobic active site pocket (*11*) and it may be anticipated that the extent of charge development in the transition state of an NAD(H)–substrate reaction will be largely determined by the micropolarity and the catalytic groups at the active site of the enzyme. To obtain more insight into the effect of the reaction environment on NADH–NAD^+ transformations we have studied the cyanide ion dissociation of 1-benzyl-4-cyano-1,4-dihydronicotinamide (BNA-CN) in a solvent of polarity considerably lower than that of water, i.e., acetonitrile, and have compared the results with the previously determined data for the reaction in water.

In acetonitrile, the equilibrium of Eq. [1] lies far to the 1,4-adduct side. However, the equilibrium is completely shifted to the dissocation products upon addition of zinc salts. Magnesium salts have little effect. Zinc traps the cyanide ion liberated from the dissociation and, moreover, appears to be an efficient promoter of the cyanide ion expulsion. Remarkably, this activity is dependent on the nature of the zinc counterion.

EXPERIMENTAL

Materials. BNA-CN was prepared by addition of cyanide ion to 1-benzyl-3-aminocarbonylpyridinium bromide (BNA^+ Br^-) following the method described by Karrer and co-workers (*12*). 18-Crown-6 (99% purity) was obtained from Janssen Chimica (Belgium); $Zn(ClO_4)_2 \cdot 6H_2O$ (99% purity) was obtained from Ventron (W. Germany); $ZnBr_2$ (>99% purity), KCN (p.a.), $KClO_4$ (p.a.), KBr (p.a.), and KI (p.a.), were purchased from Merck. The acetonitrile used was of far-uv grade supplied by Fisons Scientific Equipment (England) and contained less than 0.05% water.

Sample solutions were made from stock solutions in acetonitrile. The appropriate amounts of BNA-CN (10^{-3} M), $Zn(ClO_4)_2 \cdot 6H_2O$ (10^{-1} M), and $ZnBr_2$ (10^{-1} M) were readily soluble in acetonitrile but for the preparation of the stock solutions of KCN (5.0×10^{-3} M), $KClO_4$ (5.0×10^{-2} M), KBr (7.56×10^{-2} M), and KI (7.56×10^{-2} M) 1.3 equivalents of 18-crown-6 was codissolved in order to achieve complete dissolution.

Spectroscopic measurements. Measurements were made with a Beckman DU-7 spectrophotometer equipped with a thermostated cell compartment maintained at 25.0 ± 0.1°C and supplied with a kinetic device. The dissociation constant of BNA-CN in acetonitrile was determined by measurement of the absorbance at 332 nm of a series of dilutions of a 10^{-3} M stock solution of BNA-CN in the concentration range 2.5×10^{-5}–10^{-4} M. In addition to BNA-CN, the sample solutions contained variable amounts of KCN, ranging in concentration from 0 to

TABLE 1

Determination of the Dissociation Constant of BNA-CN in Acetonitrile at 25.0°C

10^4 [BNA-CN]$_0$[a] M	10^6 [KCN][b] M	n[c]	E (332 nm)	$10^7 \cdot K_{diss}$ M
1.00	500	3	0.6206 (±0.0006)	
	250	3	0.6211 (±0.0005)	
	125	2	0.6195 (±0.0005)	
	5.00	2	0.5959 (±0.0008)	3.7 (±0.5)
	2.50	3	0.5898 (±0.0011)	3.8 (±0.5)
	1.25	2	0.5880 (±0.0007)	3.6 (±0.4)
	0.00	3	0.5817 (±0.0010)	4.1 (±0.5)
0.50	0.00	3	0.2828 (±0.0006)	4.3 (±0.4)
0.25	0.00	2	0.1364 (±0.0008)	4.2 (±0.5)

[a] From a 10^{-3} M stock solution of BNA-CN.

[b] From a 5×10^{-3} M stock solution of KCN containing 6.5×10^{-3} M 18-crown-6.

[c] Number of determinations.

5×10^{-4} M. In a 1.00 (±0.005) × 10^{-4} M BNA-CN solution containing (1.25–5.00) × 10^{-4} M KCN the cyanide concentration is high enough to suppress the dissociation of BNA-CN practically completely and an absorption of 0.6203 ± 0.0013 has been determined (Table 1). The dissociation of BNA-CN in the sample solutions could be directly determined from the absorption at 332 nm, since the dissociation products, BNA$^+$ and CN$^-$, have no absorption at this wavelength and Beers law is obeyed. The latter is confirmed by measurement of various dilutions of BNA-CN in 5×10^{-4} M KCN solution, which gave satisfactory reproducible values for the molar extinction. In sample solutions which contain no KCN, the dissociation equilibrium was reached very slowly and it took 7 or more h before the absorption of BNA-CN was measured.

Because of the small degree of dissociation of BNA-CN relatively small errors in the dissociation fraction give rise to much higher deviations in the dissociation constant. An averaged value for K_{diss} of 3.9(±0.7) × 10^{-7} M has been determined from 15 independent measurements with different concentrations of BNA-CN and KCN.

Kinetic measurements. Measurements were made at 25.0°C by running repetitive scans in the range 220–400 nm, or by following the disappearance of the BNA-CN absorption maximum near 340 nm. The sample solutions were prepared from stock solutions and initially contained 1×10^{-4} M BNA-CN. The reaction was started by addition of zinc solution to the sample solution. The reaction follows strictly first-order kinetics with respect to BNA-CN and first-order rate constants were obtained from plots of $\ln(A_t - A_\infty)$ vs time. The spectrum after completion of the reaction was stable for many half-lives and was invariable both qualitatively and quantatively for that of equivalent concentrations of the pyridinium salt.

RESULTS

In acetonitrile, the equilibrium of the reversible cyanide addition is far to the side of the 1,4-adduct. At 25°C an averaged value for the dissociation constant, $K_{\text{diss}} = 3.9(\pm 0.6) \times 10^{-7}$ M, has been determined (see Experimental). Addition of 1.5×10^{-4} M of zinc perchlorate to a 10^{-4} M solution of BNA-CN induces a slow dissociation and after 2 h BNA-CN is completely dissociated into BNA^+ and zinc-bound cyanide ion. The reaction can be easily followed by monitoring the electron spectrum with time. The characteristic absorption of the 4-cyano-1,4-dihydronicotinamide group near 340 nm decreases during the reaction and the absorption of the 3-aminocarbonylpyridinium ion at 265 nm appears (Fig. 1). The reverse reaction, addition of cyanide ion to the pyridinium ring, is not observed, as is apparent from the complete disappearance of the absorption near 340 nm at the end of the reaction.

Increase of the zinc perchlorate concentration results in a rapid increase of the dissociation rate, indicating that the cyanide expulsion is promoted by the presence of zinc salt. As is illustrated in Fig. 2 the dissociation rate is most markedly increased in the low concentration range of zinc perchlorate. Increment of $[Zn(ClO_4)_2]$ from 1.0×10^{-4} to 5.0×10^{-3} M causes a 10-fold rate enhancement. Further increase of the zinc perchlorate concentration gives a much more moderate increase of the dissociation rate. Extrapolation of the reaction rate to zero zinc perchlorate concentration yields the rate constant for spontaneous cyanide ion expulsion k_1. From this value and the value for the dissociation constant K_{diss}, the rate constant for cyanide ion addition k_2 is calculated. In Table 2 these constants are collected together with the data in water obtained by Lindquist and Cordes (*2*).

The concentration rate profile in Fig. 2 has the characteristics of a saturation curve, although even at relatively high zinc perchlorate concentrations the expected plateau in reaction rate is not reached. Saturation curves are indicative

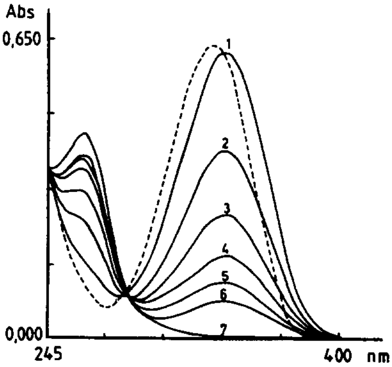

FIG. 1. Repetitive scan of a solution of BNA-CN (10^{-4} M) and $Zn(ClO_4)_2$ (10^{-2} M); 1–6, $\Delta t = 42$ s; 7, after 15 min. Dashed line is the absorbance spectrum of BNA-CN in acetonitrile without $Zn(ClO_4)_2$ added.

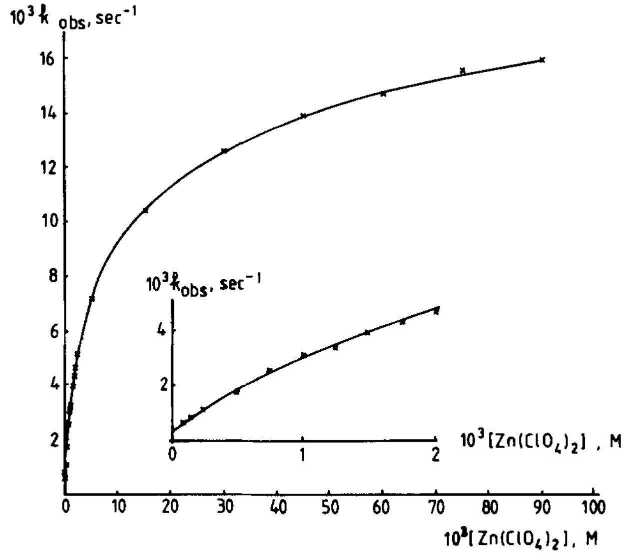

FIG. 2. Effect of zinc perchlorate concentration on the observed rate of cyanide ion dissociation from BNA-CN in acetonitrile ($[BNA\text{-}CN]_0 = 10^{-4}$ M, 25°C).

for complex formation of reactants preliminary to the rate-determining step. Another indication for the preliminary formation of a complex between BNA-CN and zinc (salt) is the gradual shift in the absorbance maximum from 332 to 343 nm which is observed upon addition of increasing amounts of zinc perchlorate in the 10^{-3}–10^{-2} mol range (Fig. 1). As it is known that most zinc salts are only partly dissociated in acetonitrile (*13, 14*), the effect of increasing concentration of perchlorate anion on the reaction rate was tested. Therefore extra amounts up to 3.25×10^{-2} M $KClO_4$ were added to a reactant solution containing 10^{-4} M BNA-CN and 10^{-2} M $Zn(ClO_4)_2$. As is illustrated in Fig. 3 only slight rate enhancements occur, indicating that the common ion effect for this salt is only very weak and that increase of the ionic strength and addition of 18-crown-6 (present in slight excess in the $KClO_4$ solution) does not have much effect on the reaction rate. However, substitution of zinc perchlorate by zinc bromide reveals

TABLE 2

Dissociation and Rate Constants for Reversible Cyanide Dissociation from BNA-CN (25°C)

	CH_3CN	H_2O[a]
K_{diss} (M)	3.9 (±0.6) × 10^{-7}	0.33
k_1 (s^{-1})	2.6 × 10^{-4}	2.15 × 10^{-2}
k_2 (M^{-1}, s^{-1})	667	6.50 × 10^{-2}

[a] Ref. (*2*), pH 11.3, ionic strength 1.0.

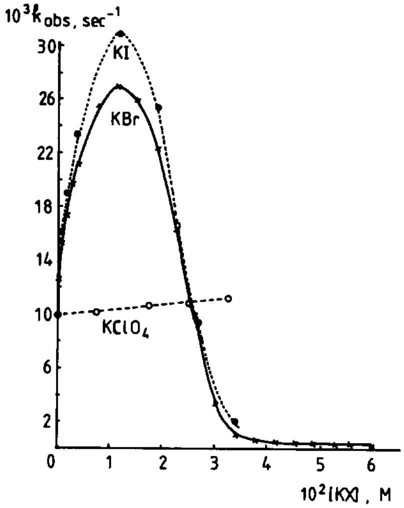

FIG. 3. Effect of addition of $KClO_4$, KBr, and KI on the rate of cyanide ion dissociation from BNA-CN in 10^{-2} M $Zn(ClO_4)_2$ solution in acetonitrile ($[BNA\text{-}CN]_0 = 10^{-4}$ M, 25°C).

that the nature of the counterion is of direct effect on the activity. Zinc bromide is a much weaker electrolyte in acetonitrile than is zinc perchlorate; nevertheless, it acts as a better promoter for the cyanide ion expulsion, as is apparent from the rate constants given in Table 3.

The higher activity of zinc bromide is not caused by differences in the water content of the two reactant solutions because equal reaction rates were obtained for zinc bromide solutions with and without amounts of water comparable to the zinc perchlorate solutions. Therefore, differences in reaction rate must arise from specific effects due to the counterion of zinc. For a further investigation of this effect, increasing amounts of KBr and KI were added to a reactant solution containing a 10^{-2} M solution of $Zn(ClO_4)_2$.

The rate profile in Fig. 3 shows a striking bell-shaped curve with increasing halide ion concentration, with a rate optimum near 1.2×10^{-2} M, thus slightly above the concentration where equimolar amounts of zinc ion and halide ion are

TABLE 3

Effect of Zinc Counterion on the Rate of Cyanide Ion Dissociation from BNA-CN

10^3 [salt] M	$Zn(ClO_4)_2 \cdot 6H_2O$	$ZnBr_2$
	($10^3 \cdot k_{obs}$, s^{-1})	
1.0	2.40	4.30
5.0	6.60	21.6
10.0	9.40	34.9

TABLE 4

Shift of the Absorbance Maximum of BNA-CN at Increasing KBr Concentration (CH_3CN, 25°C, 10^{-2} M $Zn(ClO_4)_2$, 10^{-4} M BNA-CN)

10^2 [KBr]	λ_{max} (nm)
0.00	340
1.13	340
2.26	338
2.64	338
2.74	336
2.84	335
3.02	334
3.40	334
6.00	333

present. Further increase of the halide ion concentration results in a fast reduction in reaction rate; in the presence of 6 equivalents of KBr the rate constant is 2.50×10^{-4} s^{-1}, only 2.5% of that in the absence of KBr and equal to the rate constant for the spontaneous cyanide ion dissociation. The reduction in reaction rate coincides with a decreased complexation of zinc species with BNA-CN, as is apparent from the concomitant decrease of the shift of the absorbance maximum of BNA-CN (Table 4).

DISCUSSION

The dissociation constants in Table 2 indicate that BNA-CN in acetonitrile is only very slightly dissociated into BNA^+ and CN^-, and that the dissocation constant in acetonitrile is approximately 10^6 times lower than that in water. This shows that a decrease of the dielectric constant of the medium from $\varepsilon = 78$ (H_2O) to 39 (CH_3CN) has a dramatic effect on the position of the equilibrium. The large shift to the 1,4-adduct in acetonitrile can be reconciled with a reduced solvation of the nicotinamide cation and the cyanide anion and an enhanced solvation of the neutral adduct form. In terms of reaction rates, the major contribution to the shift in equilibrium originates from a ca. 10^4 times increase of the rate of cyanide ion addition (k_2). The reverse reaction, the cyanide ion expulsion from BNA-CN (k_1), proceeds ca. 100 times slower in acetonitrile than in water. The larger sensitivity for decrease of the solvent polarity which is exhibited by the cyanide addition reaction supports the idea of a late, product-like transition state for this reaction in water (*2*). In this case the transition state has relatively little charge separation and a decrease of the solvent polarity will cause a larger destabilization of the ionic reactant state than of the transition state, resulting in a reduction of the free energy of activation for the addition process. The cyanide ion dissociation will be less affected by decrease of the solvent polarity because of the smaller difference in effect in the transition state and neutral product state.

Addition of zinc salts to BNA-CN in acetonitrile results in complete dissociation. The action of zinc is twofold. First, it induces the slow, complete shift of the equilibrium to the ionic species by entrapment of the cyanide ion. Second, zinc acts as an efficient promoter for the cyanide expulsion. The concentration rate profile of Fig. 2 strongly suggests that complex formation between zinc and BNA-CN precedes the zinc-promoted cyanide ion dissociation. Evidence for rapid complex formation is found in the observation that addition of zinc perchlorate to a solution of BNA-CN causes an immediate shift of the absorption maximum toward longer wavelength. Ultraviolet and NMR measurements have revealed that zinc salts in acetonitrile undergo a fast and reversible interaction with the carbonamide group of 1-benzyl-1,4-dihydronicotinamide (BNAH) (*13b*). Complexation of metal ions to the carbonamide oxygen has also been suggested for other 1,4-dihydronicotinamides and related compounds (*15*). The longer wavelength shift can be ascribed to a larger polarization of the dihydronicotinamide group toward the dipolar resonance form b, which has the largest contribution to the electronic transition of the dihydronicotinamide group (*16*) (see Chart 1).

A similar absorbance shift is observed when water is replaced by acetonitrile as the solvent. The increase of the solvent polarity permits a larger polarization in the dihydronicotinamide moiety and consequently the absorption maximum shifts from 332 to 340 nm. Besides complexation with the carbonamide oxygen, the metal ion in principle can also interact with the cyanogroup. In the transition state, interaction is a prerequisite for activity in the cyanide ion expulsion, but interaction is not obligatory in the reactant state. However, the smaller shift that is observed for BNA-CN (from 332 to 343 nm) compared to that for BNAH (from 346 to 366 nm) upon addition of zinc salts may serve as an indication that the cyanogroup is also involved in the complexation in the reactant state, since interaction of the cyanogroup with metal ion enhances the electron-withdrawing character of this group and thwarts the red shift of the absorbance maximum induced by ligation to the carbonamide oxygen.

Since there is a distinct effect of the zinc counterion on the observed rate enhancements, the promotional activity of zinc salts cannot be attributed to Zn^{2+} species only. Conductivity experiments indicate that zinc perchlorate in acetonitrile shows some association and that other zinc salts like zinc bromide behave as only weak electrolytes (*13a*). It must be recognized, therefore, that especially

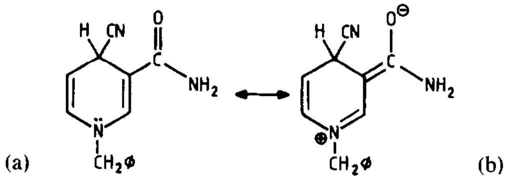

CHART 1

at higher concentrations of zinc perchlorate, not only free Zn^{2+} ion, but also monoionized $Zn(ClO_4)^+$ and undissociated $Zn(ClO_4)_2$ species, each with their specific solvation, can be present. However, in order to avoid needless complexity in the kinetic equations, all these zinc species are lumped together as $\mathrm{Zn}X$, in which $[\mathrm{Zn}X]$ is equal to the total concentration of zinc perchlorate added.

The reaction scheme which leads to the complete cyanide ion dissociation from BNA-CN may then be represented as

$$\mathrm{BNA\text{-}CN} \xrightarrow[\text{slow}]{k_1} \mathrm{BNA}^+ + \begin{array}{c} \mathrm{CN}^- \\ {\scriptstyle \mathrm{Zn}X}\big\downarrow{\scriptstyle \ \text{fast}} \\ \mathrm{Zn}X\mathrm{CN}^- \end{array} \qquad [2]$$

$$\mathrm{BNA\text{-}CN} + \mathrm{Zn}X \overset{K_c}{\rightleftarrows} \mathrm{BNA\text{-}CN} \cdot \mathrm{Zn}X \qquad [3]$$

$$\mathrm{BNA\text{-}CN} \cdot \mathrm{Zn}X \overset{k_c}{\rightarrow} \mathrm{BNA}^+ + \mathrm{Zn}X \cdot \mathrm{CN}^-. \qquad [4]$$

Kinetic evaluation of this scheme gives the expression for the observed rate constant,

$$k_{\mathrm{obs}} = k_1 + \frac{k_c K_c[\mathrm{Zn}X]}{1 + K_c[\mathrm{Zn}X]}. \qquad [5]$$

At very low concentrations of zinc perchlorate the term $K_c[\mathrm{Zn}X]$ can be neglected and the observed rate becomes approximately proportional to $[\mathrm{Zn}X]$ (Fig. 2, inset). The intercept obtained by extrapolation to zero zinc perchlorate concentration gives the rate constant for spontaneous cyanide ion dissociation, $k_1 = 2.5 \times 10^{-4}\ \mathrm{s}^{-1}$. The slope of the tangent to the rate profile gives a value for $k_c K_c = 3.67$.

The kinetic parameters of the complex can be separated by rewriting Eq. [5] to the reciprocal expression

$$\frac{1}{k_{\mathrm{obs}} - k_1} = \frac{1}{k_c K_c[\mathrm{Zn}X]} + \frac{1}{k_c}. \qquad [6]$$

A plot of $(k_{\mathrm{obs}} - k_1)^{-1}$ vs $[\mathrm{Zn}X]^{-1}$ should give a straight line with slope $(k_c K_c)^{-1}$ and intercept k_c^{-1}.

A good linear relation is observed for the concentration range $[Zn(ClO_4)_2] = 1.0 \times 10^{-4}$–$75 \times 10^{-4}$ M (Fig. 4) and a complexation constant, $K_c = 316(\pm 15)\ \mathrm{M}^{-1}$, and a rate constant for cyanide expulsion from the complex, $k_c = 1.16(\pm 0.06) \times 10^{-2}\ \mathrm{s}^{-1}$, is calculated. These values are in agreement with the determined value for $k_c K_c$ of 3.67 for $Zn(ClO_4)_2$ concentrations below 10^{-4} M (*vide supra*). At concentrations larger than 75×10^{-4} M deviations from the linear relationship are observed, in the sense that the observed rate constants become increasingly higher than those calculated. From the curvature in Fig. 4 it can be concluded that this deviation is due to a continuous decrease of K_c and an increase of k_c, respectively. As an illustration, for the range 75×10^{-4}–900×10^{-4} M $Zn(ClO_4)_2$, mean values for K_c of 122 M^{-1} and for k_c of $1.67 \times 10^{-2}\ \mathrm{s}^{-1}$ can be calculated, but it should be

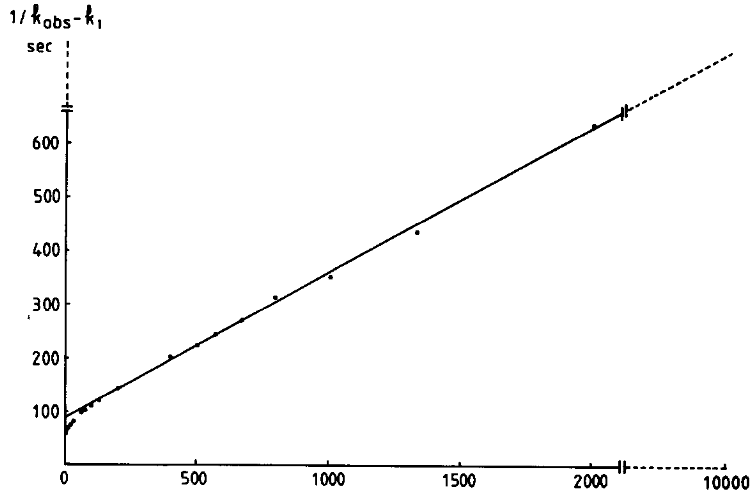

FIG. 4. Plot of $(k_{obs} - k_1)^{-1}$ vs $[Zn(ClO_4)_2]^{-1}$ for the concentration range (50–900) × 10^{-4} M. The linear relationship is equally maintained in the concentration range (1–50) × 10^{-4} M $Zn(ClO_4)_2$.

kept in mind that these values are only the result of averaging smoothly decreasing values of K_c and increasing values of k_c, respectively.

The observed decrease in complexation constant most probably originates from a reduction of the ionization of zinc perchlorate at higher concentrations (*13a*). It is reasonable to expect that due to increased ligation the affinity of zinc species for the substrate decreases in the order $Zn^{2+} > Zn(ClO_4)^+ > Zn(ClO_4)_2$. The effect will be that the apparent complexation constant becomes smaller when the fraction of partly ionized or unionized zinc perchlorate increases. The increase of k_c, then, seems to be the direct consequence of the higher fraction of the zinc–substrate complex in which the perchlorate anion is ligated to zinc. The effect of this ligation can be that in the complex the zinc counterion is in the proximity of the nicotinamide ring and is able to stabilize the developing positive charge in the transition state during cyanide expulsion. It has been shown before that negative groups in the neighborhood of a nicotinamide ring have a catalytic effect on the charge development in the nicotinamide ring. Dihydronicotinamides containing neighboring carboxylate groups reduce *N*-acridinium ion in nonaqueous solution much more rapidly than homologous derivatives lacking this group (*17*).

In order to gain more insight into the role of the counterion in the zinc-promoted reaction the effect of zinc bromide was also studied. Remarkably, this salt shows a larger activity, notwithstanding that it is a much weaker electrolyte in acetonitrile than is zinc perchlorate. The limited ionization of zinc bromide is supposed to be largely restricted to its monoionized species, $ZnBr^+$ and Br^- (*13*), and it is most probable that the larger activity of zinc bromide originates from a better promotion of the cyanide expulsion by $ZnBr^+$ species than by Zn^{2+} and

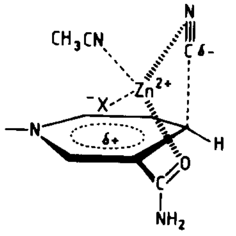

FIG. 5. Possible transition state structure accounting for counterion effect in the zinc-promoted cyanide expulsion from BNA-CN.

$Zn(ClO_4)^+$. This effect can be ascribed to a more favorable interaction of the bromide ion in the BNA-CN · $ZnBr^+$ complex with the incipient positive charge in the transition state compared to the more diffuse perchlorate anion.

The effect of bromide as zinc counterion is clearly demonstrated in Fig. 3, where an optimum in rate profile is observed upon addition of KBr to the solution. Addition of bromide ion to the zinc perchlorate solution results initially in the formation of $ZnBr^+$ and finally in the formation of $ZnBr_2$. The increase in rate observed with increasing KBr concentrations up to 1.2×10^{-2} M can be explained as the result of the increase of $ZnBr^+$ species in solution. Higher concentrations of bromide ion convert the active $ZnBr^+$ species to the inactive $ZnBr_2$ species and consequently the reaction rate decreases.

The inactivity of $ZnBr_2$ species finds its primary origin in the inability of $ZnBr_2$ to form complexes with BNA-CN of the same type as do Zn^{2+} and $ZnBr^+$ or, more likely, to form complexes with BNA-CN at all. Table 4 shows that upon increment of the KBr concentration the long wavelength shift due to BNA-CN · ZnX^+ complexation is rapidly vanishing, providing strong support for the absence of $ZnBr_2$ complexation. At 6.00 M KBr addition, the rate constant of 2.50×10^{-4} s^{-1} is essentially the same as that found for the spontaneous cyanide dissociation, which means that $ZnBr_2$, although unable to activate the cyanide expulsion, is still able to trap the cyanide ion liberated from spontaneous dissociation. Addition of KI to the zinc perchlorate solution gives effects similar to those produced by addition of KBr. Because the iodide ion has a larger polarizability than the bromide ion, the larger maximum in rate that is observed likely originates from stronger interaction of iodide with the pyridinium ring in the transition state (*18*).

A possible model for the transition state structure which rationalizes the observed effects is visualized in Fig. 5.

For geometrical reasons interaction of zinc with both the carbonamide oxygen and the cyano group can only be achieved by *side* coordination of zinc with the π-system of the cyano group.[2] If an anionic species is one of the ligands of zinc it can be located either in a syn-position just above the nicotinamide ring as is shown in Fig. 5 or in an anti-position oriented away from the ring (not shown).

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[2] Side coordination of metal ions to cyano groups has previously been suggested, mainly based on ir, and has been proven very recently by X-ray for molybdenum complexes (*19*). The present reaction provides kinetic support that this type of coordination is possible for the zinc ion.

Orientation above the ring, then, allows a favorable interaction with the incipient positive charge in the nicotinamide ring during cyanide expulsion, accounting for the observed counterion effect on the reaction rate.

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