Kinetic Studies of the Hydrolysis of Coordinated Nitriles
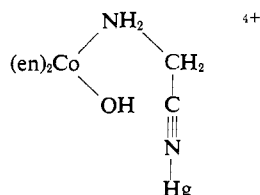
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Abstract: The kinetics of the reaction $(NH_3)_5CoN{\equiv}CR^{3+} + OH^- \rightarrow (NH_3)_5CoNHC({=}O)R^{2+}$ (R = 4-CNC_6H_4, 3-CNC_6H_4, 4-$COCH_3C_6H_4$, 4-$CHOC_6H_4$, 3-$CHOC_6H_4$) have been studied. For the 1,4-dicyanobenzene, 1,3-dicyanobenzene, and 4-acetylbenzonitrile complexes the hydrolysis follows the rate law $-d \ln [Co\ complex]/dt = k_h[OH^-]$. The values of k_h ($M^{-1} sec^{-1}$), at 25°, $\mu = 1.0\ M$ ($NaClO_4$), $\Delta H^{\pm}$ (kcal mol^{-1}), and $\Delta S^{\pm}$ (eu) are 369, 13.3, and -2 for the 1,4-dicyanobenzene complex, 322, 15.6, and $+5$ for the 1,3-dicyanobenzene complex, and 135, 12.3, and -7 for the 4-acetylbenzonitrile complex. The hydrolysis of the 3- and 4-formylbenzonitrile complexes is affected by hydration of the formyl substituent. The rate expression is $-d \ln [Co\ complex]/dt = \{(k_1 + k_2K^1 \cdot [OH^-])/(1 + K^1[OH^-])\}[OH]$ where K^1 is the equilibrium constant for the reaction $(NH_3)_5CoNCC_6H_4C({=}O)H^{3+} + OH^- \rightleftharpoons (NH_3)_5CoNCC_6H_4CH({-}O)OH^{2+}$ and k_1 and k_2 are the second-order rate constants for hydrolysis of the carbonyl and hydrate forms of the nitrile complex. For the 3-formylbenzonitrile complex $k_1 = 117\ M^{-1} sec^{-1}$ and $K^1 = 4.9\ M^{-1}$ at 25°, $\mu = 1.0\ M$ ($NaClO_4$) with $\Delta H^{\pm} = 15.4$ kcal mol^{-1}, and $\Delta S^{\pm} = +2$ eu. For the 4-formylbenzonitrile complex $k_1 = 142\ M^{-1} sec^{-1}$ and $K^1 = 10.4\ M^{-1}$ at 25°, $\mu = 1.0\ M$ ($NaClO_4$) with $\Delta H^{\pm} = 16.0$ kcal mol^{-1}, and $\Delta S^{\pm} = +5$ eu. The values of k_2 could not be established unambiguously. The results are discussed with respect to other nitrile hydrolysis reactions catalyzed by metal ions.

There have been a number of reports in the literature regarding the catalysis of the hydration of nitriles by metal ions.[1,2] In most cases catalysis has been effected by a labile metal ion such as Cu^{2+}, Co^{2+}, or Ni^{2+} and the implication is that the nitrile at some point becomes partially coordinated to the metal ion. In fact, no catalysis has been observed for the inert metal complex $[Co(en)_3]Cl_3$.[3] These reactions have been well studied by Breslow, Fairweather, and Keana[4] and they concluded that the mechanism of metal-catalyzed hydration of phenanthrolinenitrile involves external attack of hydroxide ion. The metal ion serves to stabilize the developing imino anion as external attack of hydroxide ion takes place. The same mechanism is favored in the observation of metal-catalyzed attack by a second organic ligand in a mixed complex of Cu^{2+} or Ni^{2+} with trishydroxymethylaminomethane and 2-cyanopyridine which produces 2-(2'-pyridyl)-4,4-dihydroxymethyl-Δ^2-isoxoazoline.[5]

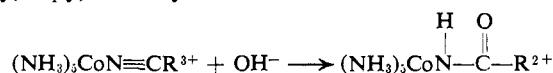It has also been shown that treatment of cis-[Co(en)_2(NH_2CH_2CN)Br]^{2+}$ with Hg^{2+} gives $[Co(en)_2glyNH_2]^{3+}$.[6] The reaction is envisaged to take place through the intermediate

$$(en)_2Co \overset{\displaystyle NH_2}{\underset{\displaystyle OH}{\diagup\diagdown}} \underset{\displaystyle \underset{N}{\overset{|||}{C}}}{\underset{\displaystyle \underset{Hg}{|}}{CH_2}} \quad {}^{4+}$$

where attack is by a coordinated hydroxide, and this is assisted by coordination of the nitrile to Hg^{2+}. Apparently Hg^{2+} can effectively stabilize the N^- formed in the cyano group as the coordinated nucleophile attacks it.

(1) K. Watanabe and K. Sakai, *Bull. Chem. Soc. Jap.*, **39**, 8 (1966).
(2) P. Barnard, *J. Chem. Soc. A*, 2140 (1969).
(3) S. Komiya, S. Suzuki, and K. Watanabe, *Bull. Chem. Soc. Jap.*, **44**, 1440 (1971).
(4) R. Breslow, R. Fairweather, and J. Keana, *J. Amer. Chem. Soc.*, **89**, 2135 (1967).
(5) R. Breslow and M. Schmir, *J. Amer. Chem. Soc.*, **93**, 4960 (1971).
(6) D. Buckingham, A. Sargeson, and A. Zanella, *J. Amer. Chem. Soc.*, **94**, 8246 (1972).

We have studied the kinetics of the reaction of a number of $(NH_3)_5CoN{\equiv}CR^{3+}$ complexes (R = 3-CNC_6H_4, 4-CNC_6H_4, 3-$CHOC_6H_4$, 4-$CHOC_6H_4$, 4-$COCH_3C_6H_4$, 2-py, 3-py) with hydroxide ion

$$(NH_3)_5CoN{\equiv}CR^{3+} + OH^- \longrightarrow (NH_3)_5CoN\overset{\displaystyle H}{\underset{}{-}}\overset{\displaystyle O}{\underset{}{\overset{\|}{C}}}{-}R^{2+}$$

In this case the nitrile nitrogen is already bonded to the metal atom in an inert complex; therefore, only external attack by hydroxide ion is possible. Thus it was of interest to compare our results to those mentioned previously in the systems where both external and internal nucleophilic attack can occur, as well as to the case of internal hydroxide ion attack in the Hg^{2+}-catalyzed reaction.

Experimental Section

Materials. All solutions were prepared from water triply distilled in an all-glass apparatus. Solutions of sodium perchlorate were prepared by dissolving G. F. Smith anhydrous $NaClO_4$ in water and filtering through 0.25 μ Millipore filters. The solutions were standardized by passing aliquots of the $NaClO_4$ solution through a cation-exchange resin in the hydrogen ion form ("Amberlite" resin IR-120(H), analytical grade) and titrating the liberated acid with standard sodium hydroxide. A series of standard NaOH solutions was prepared in 1.0 M $NaClO_4$ by dilution of a standard 1.0 M NaOH solution and the standard sodium perchlorate solution. These solutions were standardized by titrating with standard hydrochloric acid. The complexes were prepared and characterized as described previously.[7]

Kinetic Measurements. All kinetic measurements were made on a Durrum stopped-flow spectrophotometer. Kinetic data for the hydrolysis were obtained both in the ultraviolet and visible region. Both appearance of carboxamido complex and disappearance of nitrile were followed, and identical results were obtained. The nucleophile, OH^-, was kept in large excess over complex in order to ensure pseudo-first-order conditions. Rate constants were obtained from a plot of log $(A_t - A_\infty)$ *vs.* time where A_t and A_∞ are the absorbancies at time t and after the reaction was complete.

The nature of the products was ascertained by submitting reaction mixtures (after reaction was complete) to cation-exchange chromatography and isolating the product. In all cases, the product of the hydrolysis reaction was identical with an authentic sample of the corresponding carboxamido complex as discussed in ref 7. For the hydrolysis of the 4-cyanobenzaldehyde complex, the reaction was also followed by recording the pmr spectrum in D_2O before and after the addition of NaOH.
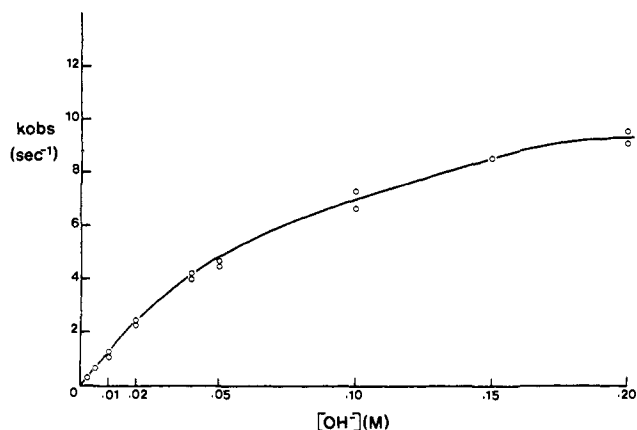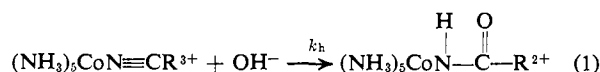
(7) R. J. Balahura, *Can. J. Chem.*, in press.

Figure 1. Plot of k_{obsd} vs. [OH$^-$] for hydrolysis of (NH$_3$)$_5$Co(4-cyanobenzaldehyde)$^{3+}$ at 25.1°, μ = 1.0 M (NaClO$_4$).

Results

Product analysis has established that the reaction studied is

$$(NH_3)_5CoN\equiv CR^{3+} + OH^- \xrightarrow{k_h} (NH_3)_5CoN-\overset{\overset{H}{|}}{C}-\overset{\overset{O}{\|}}{} R^{2+} \quad (1)$$

In all cases the carboxamido product was isolated and characterized. The reaction was shown to proceed quantitatively requiring one hydroxide ion per nitrile complex by observing the ultraviolet and visible spectrum and proton magnetic resonance spectrum before and after the addition of a stoichiometric amount of hydroxide and comparing the spectra to authentic samples of the product.

The hydrolysis of the 1,4-dicyanobenzene, 1,3-dicyanobenzene, and 4-acetylbenzonitrile complexes follows the rate law

$$\frac{-d \ln [\text{Co complex}]}{dt} = k_{obsd} = k_h[OH^-] \quad (2)$$

The rate constants and activation parameters are summarized in Table I. Tables of rate data for the hydrolysis of the complexes are available.[8]

Table I. Summary of Kinetic Results for Hydrolysis of (NH$_3$)$_5$CoN$\equiv$CR^{3+}

| N$\equiv$CR	$k_h{}^{25°}$, M^{-1} sec^{-1}	$\Delta H^{\ddagger}$, kcal mol^{-1}	$\Delta S^{\ddagger}$, eu
1,4-Dicyanobenzene	369	13.3 ± 1.5	−2 ± 4
1,3-Dicyanobenzene	322	15.6 ± 1.5	+5 ± 4
4-Acetylbenzonitrile	135	12.3 ± 1.5	−7 ± 4

The rate law for the hydrolysis of the 3- and 4-cyanobenzaldehyde complexes was not strictly first order with respect to hydroxide ion[8] and the disappearance of nitrile could be described by

$$\frac{-d \ln [\text{Co complex}]}{dt} = k_{obsd} = \frac{a + b[OH^-]}{1 + C[OH^-]}[OH^-] \quad (3)$$

A plot of k_{obsd} vs. [OH$^-$] is shown in Figure 1 for the 4-cyanobenzaldehyde complex and shows that as the hydroxide ion concentration is increased the rate

(8) See paragraph at end of paper regarding supplementary material.

gradually levels off. For the mechanism
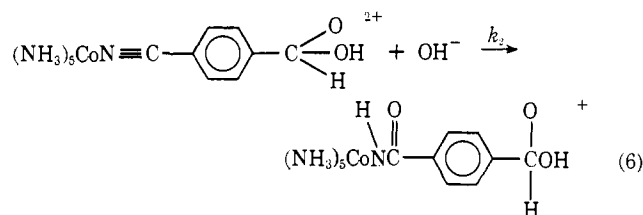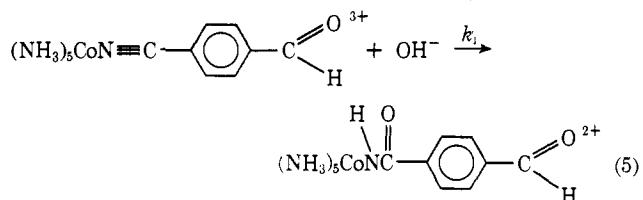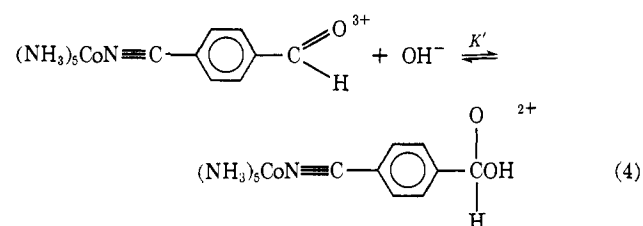
the rate expression is

$$\frac{-d \ln [\text{Co}^{3+}]}{dt} = \frac{k_1 + k_2 K'[OH^-]}{1 + K'[OH^-]}[OH^-] \quad (7)$$

By comparison of eq 3 and 7 one can readily see that $a = k_1$, $b = k_2 K'$, and $C = K'$. The full line in Figure 1 represents a nonlinear least-squares fit of the experimental points (circles) to the equation

$$\frac{k_{obsd}}{[OH^-]} = k' = \frac{k_1 + k_2 K'[OH^-]}{1 + K'[OH^-]} \quad (8)$$

The values obtained for k_1 and K' are summarized in Table II. Analogous behavior was observed for the

Table II. Summary of Kinetic Data for Hydrolysis of (NH$_3$)$_5$CoN$\equiv$CR^{3+}

N$\equiv$CR	T, °C	k_1, M^{-1} sec^{-1}	K', M^{-1}	$\Delta H^{\ddagger}$, kcal mol^{-1}	$\Delta S^{\ddagger}$, eu
3-Cyanobenzaldehyde	25.1	117	4.9	15.4 ± 2	2.4 ± 6
	30.3	174	2.9		
	35.3	285	3.9		
	40.3	416	2.1		
4-Cyanobenzaldehyde	25.1	142	10.4	16.0 ± 2	5.1 ± 6
	30.2	214	7.5		
	35.1	359	9.4		

3-cyanobenzaldehyde complex.[8] An nmr spectrum of the 4-cyanobenzaldehyde complex confirmed the presence of a hydrate form of the complex. Peaks at τ −0.06 and +3.88 were assigned to the formyl proton of the unhydrated and hydrated complexes, respectively. Integration of these peaks indicated that approximately 27% of the complex was in the hydrate form.

An attempt was also made to determine the equilibrium constant K' (eq 4) by studying the initial absorbancies at 285 nm recorded on the stopped flow with respect to hydroxide ion concentration. An analysis of these data in terms of eq 4 gave a K' of 7.3 ± 3 M^{-1}

in agreement with the value obtained from the kinetic data.

For the 3-cyanobenzaldehyde complex a similar analysis of the stopped-flow initial absorbancies gave $K' = 5.9 \pm 3$ M^{-1}, also in good agreement with the kinetic result.

Our results for k_2 could not be reliably established since $k_1 >>> k_2$ and they are not included in the discussion. However, for $k_1 >>> k_2 K'[OH^-]$, eq 8 can be rearranged to give

$$\frac{1}{k'} = \frac{K'}{k_1}[OH^-] + \frac{1}{k_1} \qquad (9)$$

Thus, a plot of $1/k'$ vs. $[OH^-]$ should yield a straight line, with intercept $1/k_1$ and slope K'/k_1. Such a plot for the 4-cyanobenzaldehyde complex is shown in Figure 2. The values of k_1 and K' obtained from this plot are in excellent agreement with those summarized in Table II. The 3-cyanobenzaldehyde complex also gave straight line plots according to eq 9.

Equation 4 can be written more completely as
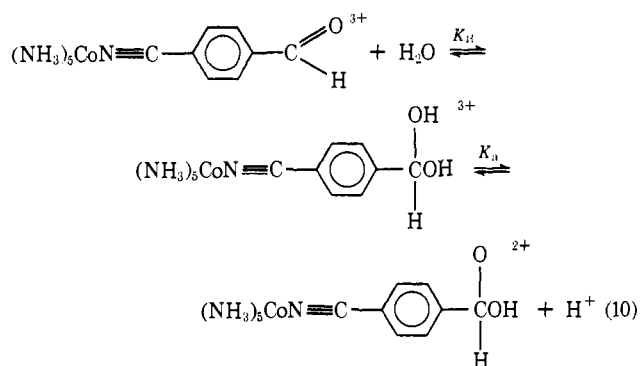
However, since the equilibrium constants K_H and K_a are not independent, we could obtain only $K' = K_H K_a/K_w$ from analysis of our data. In order for $K_H K_a/K_w \sim 10$ as required by the kinetic analysis K_a would have to be $\sim 2 \times 10^{-13}$ M (assuming $K_H \sim 0.4$ as indicated by the nmr results). It is difficult to find related systems to check the validity of this value.

A recent study[9] of aromatic aldehydes in sodium hydroxide solutions provides some support for the values obtained for K' from the kinetic results. Bover and Zuman have observed changes in the uv spectrum of 3- and 4-cyanobenzaldehyde in sodium hydroxide solutions which indicate reversible addition of hydroxyl ions as shown in eq 11. The values of K_2 (our K')

$$ArCHO + OH^- \underset{K_2}{\rightleftharpoons} ArCH(OH)O^- \qquad (11)$$

obtained for 3- and 4-cyanobenzaldehyde are 5.5 and 8.7 M^{-1}, respectively. These values are very close to those obtained for the complexes (i.e., 4.9 $\pm$ 3 and 10.4 $\pm$ 3 M^{-1}, respectively) and support the given mechanism.

Discussion

Catalysis of the hydration of nitriles by labile metal ions in aqueous solution can involve either external or internal attack of hydroxide on the coordinated nitrile. These two modes of reaction are kinetically indistinguishable for the labile metal ion systems. For the complexes described in this study only external hydrox-

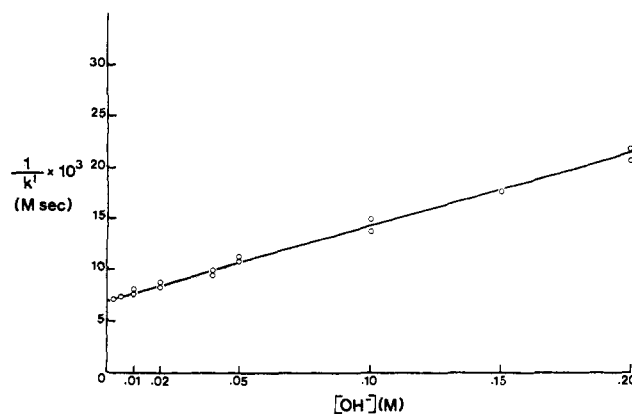(9) W. Bover and P. Zuman, J. Amer. Chem. Soc., 95, 2531 (1973).

Figure 2. Plot of $1/k'$ vs. $[OH^-]$ for hydrolysis of $(NH_3)_5Co(4$-cyanobenzaldehyde$)^{3+}$ at 25.1°, $\mu = 1.0 M$ (NaClO$_4$).

Table III. Summary of Kinetic Data for Hydrolysis of Nitriles

Complex	$k^{25°}$, M^{-1} sec^{-1}	$\Delta H^{\ddagger}$, kcal mol^{-1}	$\Delta S^{\ddagger}$, eu
$(NH_3)_5Co(1,4$-dicyanobenzene$)^{3+}$	369	13.3	−2
$(NH_3)_5Co(1,3$-dicyanobenzene$)^{3+}$	322	15.6	+5
$(NH_3)_5Co(4$-acetylbenzonitrile$)^{3+}$	135	12.3	−7
$(NH_3)_5Co(4$-cyanobenzaldehyde$)^{3+}$	142	16.0	+5
$(NH_3)_5Co(3$-cyanobenzaldehyde$)^{3+}$	117	15.4	+2
$(NH_3)_5Co(3$-cyanophenoxide$)^{2+\ a}$	3.57	15.1	−5.5
$(NH_3)_5Co(4$-cyanophenoxide$)^{2+\ a}$	0.18	16.3	−7.4
$(NH_3)_5Co(benzonitrile$)^{3+\ a}$	18.8	16.5	+3
$(NH_3)_5Co(2$-cyanopyridine$)^{3+}$	1570		
$(NH_3)_5Co(3$-cyanopyridine$)^{3+}$	365		
Ni(2-cyano-1,10-phen$)^{2+\ b}$	2.4×10^4	15.1	14
Ni(2-cyanopyridine$)^{2+\ b}$	6.3×10^7	13.7	23

[a] Reference 10. [b] Reference 4.

ide ion attack can take place since the cobalt complexes are inert to substitution. Thus, in principle, the kinetic parameters obtained for the cobalt complexes may allow us to distinguish between the two possible mechanisms. Table III summarizes the kinetic data for the systems of interest. The rates of hydrolysis are sensitive to substitution in the 3- and 4-positions on the aromatic ring. Since substitution at these positions should not present any steric impediments to attack by the nucleophile, electronic effects must play a dominant role. The stereochemical change at the reaction site is from a linear $-N\equiv C-R$ linkage to the trigonal carboxamido linkage $-(NH)C(=O)R$. Apparently the electron-withdrawing influence of the $(NH_3)_5Co^{3+}$ group polarizes the nitrile bond making the carbon much more electrophilic and thus more susceptible to nucleophilic attack. The metal is also able to stabilize the imino anion formed $(-\overline{N}=C(R)OH)$ upon addition of hydroxide to the carbon. Thus one would expect strongly electron-withdrawing groups to accelerate the reaction. The data in Table III are in qualitative agreement with these ideas.

On this basis one might expect to obtain a linear free-energy relationship for the rate constants. A Hammett plot shows the general trends expected but is certainly not quantitative. It should also be pointed out that the σ value for the meta O$^-$ reported by Pinnell, Wright, and Jordan[10] should be −0.71 rather than

(10) D. Pinnell, G. B. Wright, and R. B. Jordan, J. Amer. Chem. Soc., 94, 6104 (1972).

−0.19. This change negates the quantitative relationship between log k and σ, but the results are in general agreement with expected trends.

Coordination to $(NH_3)_5Co^{3+}$ results in a large increase in the hydrolysis rate. The usual conditions for hydrolysis of nitriles to amides involve concentrated acids or bases at elevated temperatures whereas the reactions described here are virtually instantaneous in dilute base at room temperature. The rate enhancement with respect to hydrolysis of the free ligands ranges from 10^6 M^{-1} sec^{-1} for the case of benzonitrile[11] to 10^{11} M^{-1} sec^{-1} for 2-cyanopyridine.[12] For intramolecular attack of hydroxide assisted by Hg^{2+} as demonstrated for the reaction cis-$[Co(en)_2(NH_2CH_2CN)Br]^{2+}$ → $[Co(en)_2glyNH_2]^{3+}$, the rate of enhancement is estimated as $>10^{18}$.[6] In principle this difference in rate enhancement may allow one to differentiate between external and internal attack of hydroxide ion for the labile metal ion systems where both paths are possible. For example, the rate enhancement of 10^7 M^{-1} sec^{-1} for the hydration of 2-cyano-1,10-phenanthroline is similar to that obtained for the $(NH_3)_5Co^{3+}$ complexes where only external attack of hydroxide is possible. This suggests that external attack also takes place for the Ni^{2+}-catalyzed hydration of 2-cyano-1,10-phenanthroline. However, for 2-cyanopyridine, the Ni^{2+}-catalyzed reaction is some 10^4 times greater than that found for the analogous Co^{3+} system and the same comparison is not valid. Due to a lack of data on the free ligands no other comparisons are possible.

The 3- and 4-cyanobenzaldehyde complexes are of interest because they provide kinetic evidence for the ionized form of the gem-diol. The equilibrium constant K' for eq 4 can be shown to be a composite of K_H, K_a, and K_w where K_H is the equilibrium constant for addition of water to the formyl substituent to form the gem-diol, K_a is the dissociation constant for the gem-diol, and K_w is the ion product of water. Values of K' obtained by Bover and Zuman and by Greenzaid[13] are nearly the same as those obtained for the complexes. This indicates that the polarizing effect of the metal ion is concentrated in the metal–nitrile bond and that the remote groups are little affected. It is known that the

pK_a's of the $(NH_3)_5Co^{3+}$ complexes of 3- and 4-cyanophenol are 1 to 1.5 pK_a units more acidic than for the uncomplexed ligands.[14] This is a relatively small effect when compared to the pK_a's of protons that are located on atoms bonded directly to Co(III) where the pK_a's are enhanced by >14 pK_a units.[15] Thus it is reasonable that the hydrolysis is greatly affected by binding to the metal but that addition of OH^- to the formyl group is little affected. Thus the K_H and K_a values for the complexes may be qualitatively applicable to the free ligands. Since the complexes are soluble in D_2O, direct observation of the gem-diol can sometimes be made. The value of $K_a = 2 \times 10^{-13}$ M for the 4-cyanobenzaldehyde complex seems reasonable in light of the analysis due to Greenzaid.[13]

The enzyme ricinine nitrilase[16] is capable of hydrolyzing a number of organic nitriles, but the mechanistic details of its role in this reaction are uncertain. However, inhibition of hydrolysis is caused by reagents that react with thiol groups on the enzyme. Zervos and Cordes[17] have studied the hydrolysis of N-benzyl-3-cyanopyridinium ion catalyzed by mercaptoethanol and find that this reaction exhibits similar behavior to the enzyme-promoted reaction. Their results suggest that thiol groups can act as nucleophilic reagents and exert a catalytic effect in this manner. It should be noted however that the presence of metal ions in the enzyme has not been ruled out[16b] and catalysis could also occur via the same general path outlined previously.

We are presently investigating the reaction of various sulfur nucleophiles with the pentaamminecobalt(III) complexes.

(11) K. B. Wiberg, *J. Amer. Chem. Soc.*, **77**, 2519 (1955).
(12) E. Laviron, *C. R. Acad. Sci.*, **250**, 3671 (1960).
(13) P. Greenzaid, *J. Org. Chem.*, **38**, 3164 (1973).

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(15) R. J. Balahura and R. B. Jordan, *J. Amer. Chem. Soc.*, **92**, 1533 (1970).
(16) (a) W. G. Robinson and R. H. Hook, *J. Biol. Chem.*, **239**, 4527 (1964); (b) R. H. Hook and W. G. Robinson, *ibid.*, **239**, 4263 (1964).
(17) C. Zervos and E. Cordes, *J. Amer. Chem. Soc.*, **90**, 6892 (1968).