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Neighboring-Group Participation in the Hydrolysis of Coordinated Nitriles

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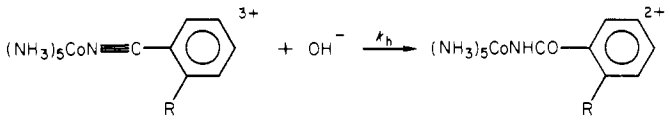
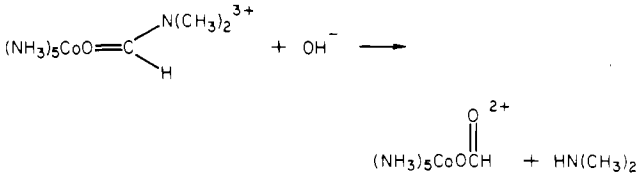
The hydrolysis reaction



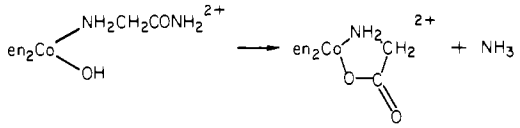
has been studied. For R = CN, k_h = 1050 ± 60 M^{-1} s^{-1}, $\Delta H^{\ddagger}$ = 13.6 ± 0.5 kcal mol^{-1}, $\Delta S^{\ddagger}$ = 1.0 ± 2 eu at 25 °C, and I = 1.0 M ($LiClO_4$). For R = $CONH_2$, k_h = (5.8 ± 0.5) × 10^6 M^{-1} s^{-1}, $\Delta H^{\ddagger}$ = 21.3 ± 0.5 kcal mol^{-1}, $\Delta S^{\ddagger}$ = 44 ± 2 eu at 25 °C, and I = 1.0 M ($LiClO_4$). The unusual kinetic parameters for the latter complex are attributed to neighboring-group participation by the amide group.

Introduction

Two modes of catalysis of organic hydrolysis reactions by metal ions have been established: (1) direct polarization of the substrate, as in the hydrolysis of the *N*,*N*-dimethylformamide complex[1]

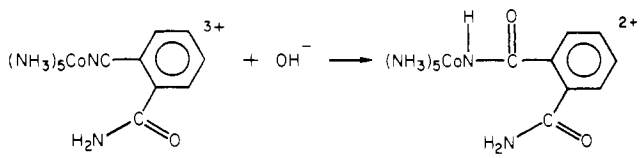


and (2) ionization to generate a coordinated nucleophile, as exemplified by the hydrolysis of coordinated glycine amide:[2]



Furthermore, a number of hydrolytic reactions in the absence of metal ions are accelerated by intramolecular nucleophilic participation of several functional groups.[3] For example, intramolecular participation of the amide group in the hydrolysis of β-benzyl esters of aspartyl peptides leads to a 10^6-fold increase in rate with respect to similar substrates without a neighboring amide group.[3a]

We wish to report an example of catalysis by a combination of direct polarization of a substrate by a metal ion and neighboring-group participation of an amide function on the substrate for the nitrile hydrolysis reaction

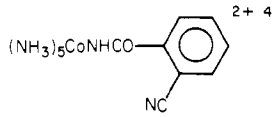


Experimental Section

All reagent solutions were prepared with water doubly distilled from an all-glass apparatus. both sodium bicarbonate and tris(hydroxymethyl)aminoethane (Tris) were Fisher Certified ACS and used without further purification. pH measurements were made with a Radiometer Type PHM 26 pH meter calibrated by two-buffer adjustment with pH 7.41 and pH 9.18 buffers from Fisher Scientific. The reference electrode was a glass electrode, and the other electrode was an Orion double-junction reference electrode, Model 90-02.00, with 10% ammonium nitrate salt bridge. All pH measurements were carried out on reactant solutions at I = 1.0 M, the ionic strength maintained with $LiClO_4$. The complexes were prepared and characterized as described in a previous study.[4]

Kinetics. Reactions were monitored with the use of a Durrum stopped-flow spectrophotometer. Rate constants were obtained under pseudo-first-order conditions from plots of log $(A_t - A_\infty)$ vs. time where A_t and A_∞ are the absorbance at time t and after the reaction is complete. Both complexes are very susceptible to hydrolysis when dissolved in water, and some special precautions were necessary. For the 1,2-dicyanobenzene complex, stock solutions were prepared which were 5 × 10^{-3} M in $HClO_4$ before mixing in the stopped flow.

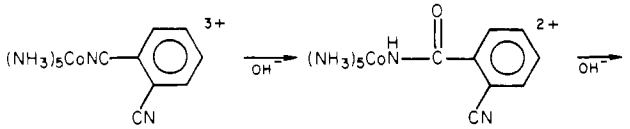
The 2-cyanobenzamide complex was generated in solution just prior to kinetic runs by adding $HClO_4$ to



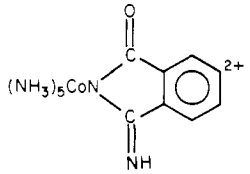
This solution was then adjusted to I = 1.0 M wth $LiClO_4$. The final [$HClO_4$] was 5 × 10^{-3} M before mixing. The complex concentration was generally 5 × 10^{-5} M after mixing. The pH range studied was between 7.2 and 9.3 with all measurements being made at the appropriate temperature in a thermostated vessel. The reaction was also monitored at pH 4 with the use of a Beckman Acta CIII spectrophotometer.

Results

The 1,2-Dicyanobenzene Complex. Previous work[4] has established that hydrolysis of the 1,2-dicyanobenzene complex was followed by cyclization as shown in the sequence



I II



III

(1) D. A. Buckingham, J. MacB. Harrowfield, and A. M. Sargeson, *J. Am. Chem. Soc.*, **96**, 1726 (1974).
(2) D. A. Buckingham, D. M. Foster, and A. M. Sargeson, *J. Am. Chem. Soc.*, **92**, 6151 (1970).
(3) (a) S. A. Bernhard, A. Berger, J. H. Carter, E. Katchalski, M. Sela, and Y. Shalitin, *J. Am. Chem. Soc.*, **84**, 2421 (1962); (b) J. A. Shafer and M. Morawetz, *J. Org. Chem.*, **28**, 1899 (1963); (c) M. T. Behme and E. H. Cordes, *ibid.*, **29**, 1255 (1964).
(4) Robert J. Balahura and W. L. Purcell, *Inorg. Chem.* **18**, 937 (1979).

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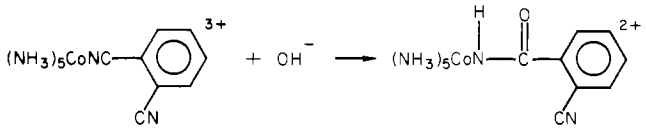
Table I. Kinetic Data[a] for the Reaction



T, °C	10^2[OH$^-$], M	k_{obsd}/[OH$^-$], M^{-1} s^{-1}
25.2	0.750	1030
	0.750	1110
	1.25	1050
	1.25	1060
	2.25	1040
	2.25	1000
	3.75	1140
	3.75	1110
	4.75	1110
	4.75	1110
	4.75	1090
34.4	0.750	2120
	0.750	2050
	1.25	2120
	1.25	2140
	2.25	2230
	2.25	2180
43.0	0.750	4160
	0.750	3930
	1.25	4230
	1.25	3980
	2.25	4240
	2.25	4260

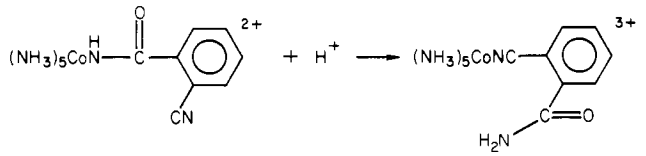
[a] λ = 267 nm; I = 1.0 M ($LiClO_4$).

It was also shown that the cyclization reaction was about 1000 times slower than the hydrolysis of the coordinated nitrile. The UV spectra of the starting dinitrile and complexes II and III are shown in Figure 1. The spectra indicated that the reaction of interest, the hydrolysis of the coordinated nitrile, could be monitored at 267 nm, an isosbestic point for II and III. Data obtained at 267 nm are collected in Table I. The hydrolysis reaction follows the rate law

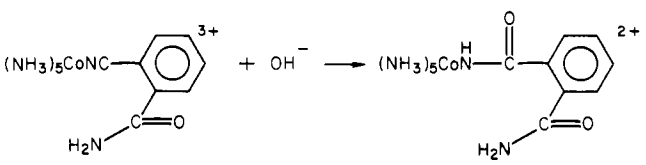
$$-\text{d ln [Co complex]}/dt = k_{obsd} = k_h[OH^-]$$

The data in Table I give k_h(25 °C) = 1050 ± 60 M^{-1} s^{-1} with $\Delta H^\ddagger$ = 13.6 ± 0.5 kcal mol^{-1} and $\Delta S^\ddagger$ = 1.0 ± 2 eu.

The 2-Cyanobenzamide Complex. This complex was extremely susceptible to hydrolysis of the coordinated nitrile and was generated in solution by the rapid linkage isomerization reaction below just prior to kinetic studies.



The base hydrolysis reaction was studied



in Tris and carbonate buffers at concentrations from 0.025 to 0.25 M. Formation of the 2-carboxamidobenzamide complex was followed at 307 nm. Plots of k_{obsd} vs. [OH$^-$] are given in Figure 2 for the four temperatures studied. All the data are collected in Table II. It is clear that the reaction does not depend on buffer concentration over the range studied, and the simple rate law obtained for the 1,2-dicyanobenzene complex applies. The data give k_h(25 °C) = (5.8 ± 0.5) × 10^6 M^{-1} s^{-1} with $\Delta H^\ddagger$ = 21.3 ± 0.5 kcal mol^{-1} and $\Delta S^\ddagger$ = 44 ± 2 eu.

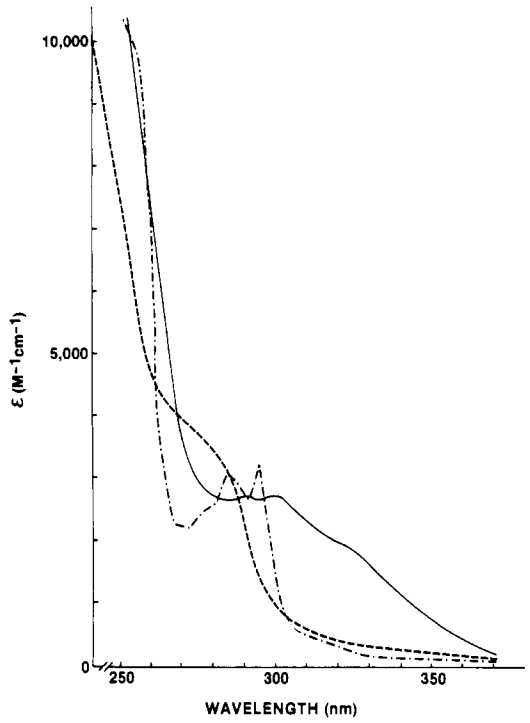
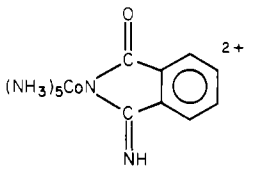
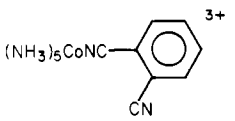


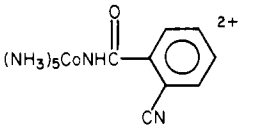
Figure 1. Ultraviolet spectra:



in 0.1 M NaOH, —;



in 0.1 M $HClO_4$, -·-;

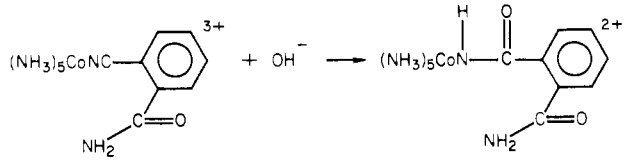


in neutral solution, ---.

Discussion

The hydrolysis of the complexes described in this study occurs by external hydroxide ion attack at the nitrile carbon atom. Coordination of the nitrile group to the $(NH_3)_5Co^{3+}$ moiety causes the nitrile carbon to become more electrophilic, thus making it more susceptible to attack by OH$^-$. In addition, the metal is able to stabilize the resulting imino anion formed upon addition of OH$^-$. For 3- and 4-substituted benzonitriles, electronic effects are expected to play a dominant role in the hydrolysis reaction, and it is found that strongly electron-withdrawing substituents accelerate the reaction as expected. For 2-substituted benzonitriles, steric and neighboring group effects are also possible. However, for the 2-cyano derivative

Table II. Kinetic Data[a] for the Reaction



T, °C	buffer[b]	[buffer], M	$10^7 \times$ [OH⁻],[c] M	$10^{-6}k_{obsd}/[OH^-]$, $M^{-1}\ s^{-1}$
25.5	T	0.0250	6.20	6.29, 6.32
	T	0.0750	7.70	6.94, 6.97, 6.57, 6.38
	T	0.0500	8.30	5.72, 5.60
	T	0.125	8.50	5.95, 5.78
	T	0.175	8.60	6.55, 6.60
	T	0.100	8.90	5.73, 5.90
	T	0.250	9.10	6.19, 6.00, 6.24
	T	0.150	10.0	5.50, 5.59
	C	0.0500	40.0	5.92, 5.70
	C	0.114	41.0	6.88, 6.61, 6.68, 6.98
	C	0.125	45.0	6.47, 6.42
	C	0.100	48.0	5.75, 5.69
	C	0.227	52.0	6.29, 6.29, 6.54, 6.46
	C	0.0500	52.0	6.00, 5.94, 6.35, 6.38
	C	0.250	54.0	7.09, 6.57
	C	0.150	55.0	5.58, 6.14
	C	0.217	98.0	6.26, 6.04, 5.80, 6.37
	T	0.250	102	6.29, 6.47, 6.60, 6.41
	C	0.0500	112	5.43
	C	0.100	135	6.00, 5.85
	C	0.150	135	6.04, 6.26
	C	0.200	148	6.16, 6.32
	C	0.250	158	6.52, 6.52, 6.33, 6.27
	C	0.206	182	6.10, 6.04
33.0	T	0.125	1.55	17.7, 18.3
	T	0.125	5.40	16.7, 17.1
	T	0.125	9.10	16.4, 15.8
	T	0.125	18.6	15.9, 16.4
	T	0.125	55.0	15.4, 15.9
38.0	T	0.125	4.30	28.4, 28.4
	T	0.125	7.80	26.9, 25.8
	T	0.125	15.5	26.8, 28.1
	T	0.125	48.0	29.4, 26.7
43.2	T	0.125	3.55	46.5, 48.7
	T	0.125	6.30	46.8, 45.9
	T	0.125	12.3	50.7, 50.3
	T	0.125	37.0	43.5, 44.4

[a] Each entry represents a separate determination and is the average of at least three traces. $\lambda = 307$ nm; $I = 1.0$ M ($LiClO_4$). [b] T = Tris/Tris-H⁺ buffer; C = HCO_3^-/CO_3^{2-} buffer. [c] The pH was measured on reactant solutions at each temperature and [OH⁻] calculated.

models show that no particular steric impediments to attack of hydroxide exist and the linear C≡N linkages are far enough apart to preclude a neighboring group effect. In fact, the rate of hydrolysis of the 1,2-dicyanobenzene complex is approximately three times faster than that for the 1,3- and 1,4-dicyanobenzene complexes. This is reasonable in light of the increased electron-withdrawing character of the cyano group in the 2-position compared to that in the 3- and 4-positions. The activation parameters for the hydrolysis of the 1,2-dicyanobenzene compound also fall in the range expected from a study of other $(NH_3)_5CoNCR^{3+}$ complexes—$\Delta H^\ddagger$ = 12.3–16.5 kcal mol⁻¹, and $\Delta S^\ddagger$ = −7 to +5 eu (Table III).

By comparison, the results obtained for the 2-cyanobenzamide complex are unusual. The rate of hydrolysis is approximately 10^4 times faster than that expected on the basis of the electron-withdrawing ability of the amide group. In fact, on this basis, the rate of hydrolysis of the 2-cyanobenzamide complex would be predicted to be less than half the rate found for the 1,2-dicyanobenzene complex. Furthermore, this enhanced rate resides solely in the more favorable entropy of activation, $\Delta S^\ddagger$ = +44 eu, which dominates the unfavorable

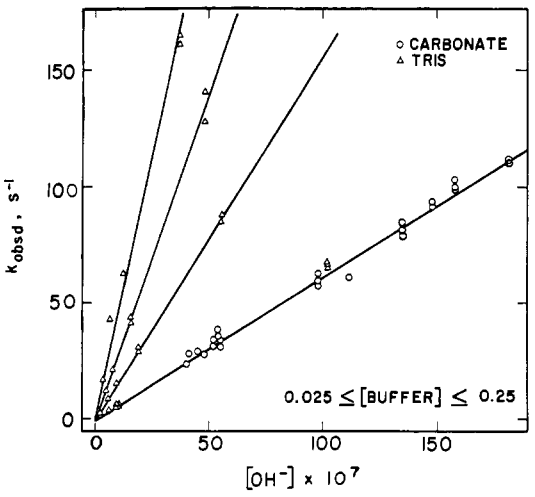
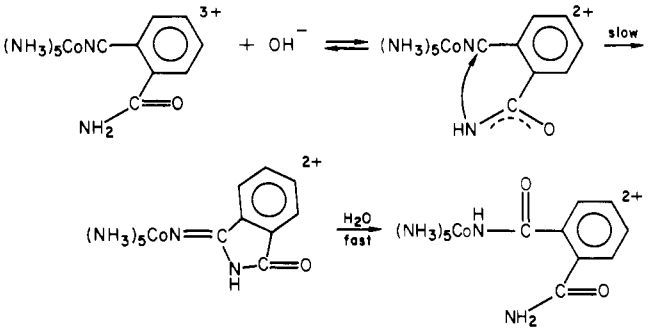
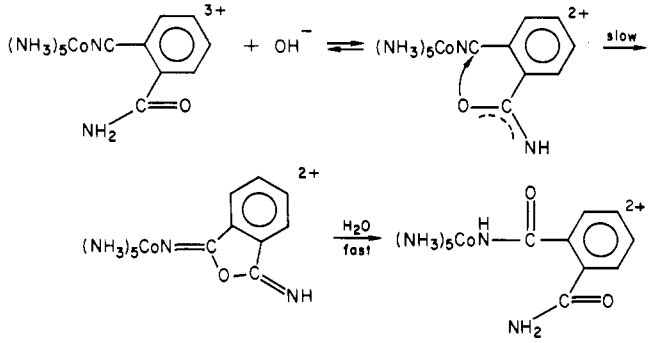


Figure 2. Kinetic data for the hydrolysis of the 2-cyanobenzamide complex at 25.5, 33.0, 38.0, and 43.2 °C.

Scheme I



Scheme II



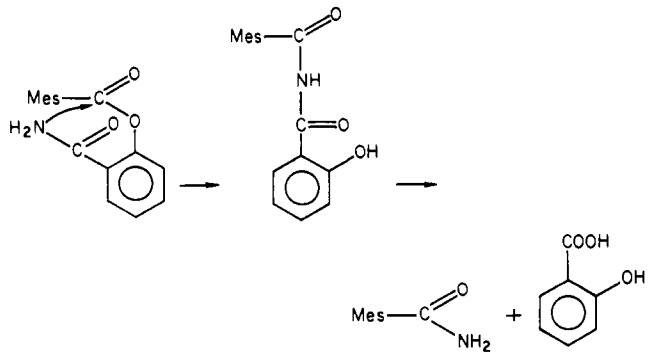
enthalpy, $\Delta H^\ddagger$ = 21.3 kcal mol⁻¹. The data also indicate that the reaction is specific hydroxide catalyzed (vide infra). Since ortho amide groups are known to participate in a wide variety of nucleophilic reactions,[5] it seems reasonable that the "extra" rate enhancement observed here is due to ortho-group participation. The observed large positive entropy appears to indicate a mechanism where there is some charge neutralization in going to the transition state as well as desolvation of OH⁻. Two mechanisms consistent with the observations are given in Schemes I and II. Kinetically it is not possible to distinguish between the formation of the isoindole (Scheme I) and the isoimide (Scheme II) intermediates. Of the many examples in the literature of the participation of an ortho amide group in nucleophilic reactions, only in a few cases has it been possible to differentiate between N and O attack. Topping and Tutt[6] have clearly shown that N attack occurs

(5) A. J. Kirby and A. R. Fersht, *Prog. Bioorg. Chem.* **1**, 50 (1971).
(6) R. M. Topping and D. E. Tutt, *Chem. Commun.*, 699 (1966).

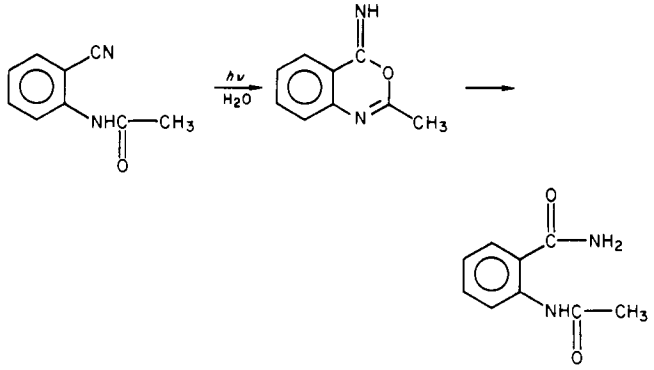
Table III. Kinetic Parameters for Hydration of Nitriles

species	$k_h^{25°}$, M^{-1} s^{-1}	$\Delta H^{\ddagger}$, kcal mol^{-1}	$\Delta S^{\ddagger}$, eu	ref
C_6H_5CN	8.2×10^{-6}	19.9	−15	15
$(NH_3)_5Co(NCC_6H_5)^{3+}$	18.8	16.5	+3	15
2-cyano-1,10-phen	2.6×10^{-3}	15.7	−20	16
Ni(2-cyano-1,10-phen)$^{2+}$	2.4×10^{4}	15.1	+14	16
$(NH_3)_5Co$(1,4-dicyanobenzene)$^{3+}$	369	13.3	−2	17
$(NH_3)_5Co$(1,3-dicyanobenzene)$^{3+}$	322	15.6	+5	17
$(NH_3)_5Co$(4-cyanobenzaldehyde)$^{3+}$	142	16.0	+5	17
$(NH_3)_5Co$(2-cyanopyridine)$^{3+}$	1570			17
$(NH_3)_5Co$(3-cyanopyridine)$^{3+}$	365			17
cis-$(en)_2Co(OH)(NH_2CH_2CN)^{2+}$	1.15×10^{-2}	10.7	−31	18
$(NH_3)_5Co$(1,2-dicyanobenzene)$^{3+}$	1050	13.6	+1	this work
$(NH_3)_5Co$(2-cyanobenzamide)$^{3+}$	5.8×10^{6}	21.3	+44	this work
$(NH_3)_5Ru(NCC_6H_5)^{3+}$	2.0×10^{3}			10
$(NH_3)_5Ru(NCCH_3)^{3+}$	2.2×10^{2}			10
$(NH_3)_5Ru(NCCH_3)^{2+}$	$<6 \times 10^{-5}$			10

in the hydrolysis of a sterically hindered ester (Mes = 2,4,6-trimethylphenyl):

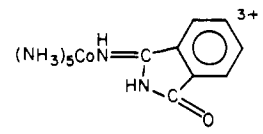


An isoimide intermediate[7] is required in the photochemically catalyzed hydration of the nitrile shown:



In the present case only indirect arguments can be made favoring N attack and Scheme I.

If the hydrolysis reaction is carried out in the pH range 2–5, a second-order rate constant identical with that found at alkaline pH's is obtained by dividing the observed rate constant by the hydroxide ion concentration. However, the product at these pH's is not the diamide complex obtained under basic conditions, and the structure IV has been suggested.[8] However, IV is rapidly converted to the diamide by addition of base.



IV

At a pH 7.5, this reaction is too fast to observe on the stopped flow. Thus we suggest that IV is the conjugate acid of the intermediate postulated in Scheme I. It would be reasonable to expect IV to be converted to the diamide in base in a diffusion-controlled step.

The identity of the intermediate as an imide in Scheme I is also implied by the fact that the reaction is base catalyzed but becomes nearly independent of acidity in the range pH 2–5. This suggests the imide structure since an isoimide would be expected to exhibit both acid and base catalysis.[9]

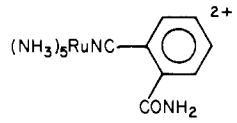
The apparent lack of a buffer term in the rate law deserves comment. In a study[10] of the hydrolysis of the pentaammineruthenium(III) complexes of acetonitrile and benzonitrile, it was found that the formation of the carboxamido complexes was affected by the buffer. For bicarbonate–carbonate buffer, it was suggested that this was due to general-base catalysis of water attack on the nitrile carbon atom or rate-determining direct attack of carbonate on the nitrile carbon atom to give an adduct such as $(NH_3)_5Ru^{III}N{=}C(OCO_2^-)R$. Furthermore, Creaser, Dyke, Sargeson, and Tucker[11] have shown that CN^- attacks the nitrile carbon atom of $(NH_3)_5CoNCCH_3^{3+}$ in the first step of a novel amino acid synthesis. In the present case, it appears reasonable to assume that the ortho amide group functions to directly attack the nitrile carbon atom to form an intermediate which rapidly decomposes to the carboxamido product. The ortho amide group is ideally positioned to provide a localized high concentration of nucleophile at the active site. It has been established from other studies that the amide ion is 10^2–10^3 times more reactive than coordinated hydroxide.[12] Furthermore, coordinated hydroxide is more reactive than external hydroxide which is approximately 100 times more reactive than CO_3^{2-}.[10] Thus it is not surprising that in this work attack of buffer at the nitrile function is not observed.

The rather large increase in entropy was unexpected. For reactions where the nitrile is coordinated to the metal center and where there is no possibility of neighboring-group participation, the rate acceleration of 10^6–10^7 results from an increase in $\Delta S^{\ddagger}$ (see Table III). This increase has been attributed to charge neutralization in the addition complex and desolvation of the OH^- ion. On the other hand, a decrease in $\Delta S^{\ddagger}$ results from attack on nitriles by coordinated OH^- ion where charge neutralization has already been accomplished (Table III). In the present case the increase in entropy apparently results from charge neutralization and desolvation of the ortho amide anion during formation of the cyclic in-

(7) T. D. Roberts, L. Munchausen, and H. Shechter, *J. Am. Chem. Soc.*, **97**, 3112 (1975).
(8) Reference 4. Several attempts at obtaining an X-ray crystal structure have failed due to decomposition of the crystal.
(9) M. L. Ernst and G. L. Schmir, *J. Am. Chem. Soc.*, **88**, 3001 (1966).
(10) A. W. Zanella and P. C. Ford, *Inorg. Chem.*, **14**, 42 (1975).
(11) I. I. Creaser, S. F. Dyke, A. M. Sargeson, and P. A. Tucker, *J. Chem. Soc., Chem. Commun.*, 289 (1978).
(12) D. A. Buckingham, C. E. Davis, and A. M. Sargeson, *J. Am. Chem. Soc.*, **92**, 6159 (1970).

termediates in Schemes I and II as well as desolvation of the OH^- ion.

The rate enhancement for nitrile hydrolysis due to catalysis by the ortho carboxamide function has been quantified via rate comparisons with utilization of metal-coordinated nitrile groups. It is impossible to measure the rate of nitrile hydrolysis in uncoordinated *o*-cyanobenzamide since this molecule reacts with base to give the cyclic product 3-iminoisoindol-1-one.[13,14] However, Zanella and Ford have demonstrated that nitriles coordinated to the pentaammineruthenium(II) moiety exhibit little if any rate enhancement for the nitrile to amide hydrolysis reaction vis-â-vis the uncoordinated nitrile molecule[10] (Table III). This latter observation suggests a means of evaluating the effectiveness of the ortho-group participation in our system. When the complex



is reacted with base, the coordianted nitrile group is hydrolyzed to the carboxamido function as evidenced by the identification of Ru(II) and Ru(III) carboxamido complexes by analogy with the data of Zanella and Ford. Although side reactions are a complicating factor here, preliminary kinetic studies of this reaction yield second-order rate constants in the range 0.2–0.5 M^{-1} s^{-1} at 25 °C. This corresponds to a rate enhancement of 5–6 orders of magnitude over the rate of hydrolysis of free and pentaammineruthenium(II)-coordinated benzonitrile where, of course, no ortho-group catalysis operates. Hence, for the pentaamminecobalt(III) complex of *o*-cyanobenzamide, the (2×10^6)-fold rate enhancement due to cobalt(III) coordination combined with the $(10^5$–$10^6)$-fold enhancement due to the neighboring amide function leads to an enormous rate enhancement of 11–12 orders of magnitude. It remains to be demonstrated in subsequent studies whether metal ion catalysis and neighboring-group assistance will operate cooperatively in other nitrile hydrolysis reactions.

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Registry No. Pentaammine(1,2-benzenedicarbonitrile-*N*)cobalt(3+), 53739-00-7; pentaammine(2-cyanobenzamide-N^2)cobalt(3+), 69120-40-7; pentaammine(2,3-dihydro-3-imino-1*H*-isoindol-1-onato-N^2)cobalt(2+), 69120-38-3; pentaammine(2-cyanobenzamidato-N^1)cobalt(2+), 68893-64-1.

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Electrochemical Behavior of Metal Tricarbonyl Complexes of Several Tridentate Macrocycles Containing Soft (P, S) Ligating Sites[1]

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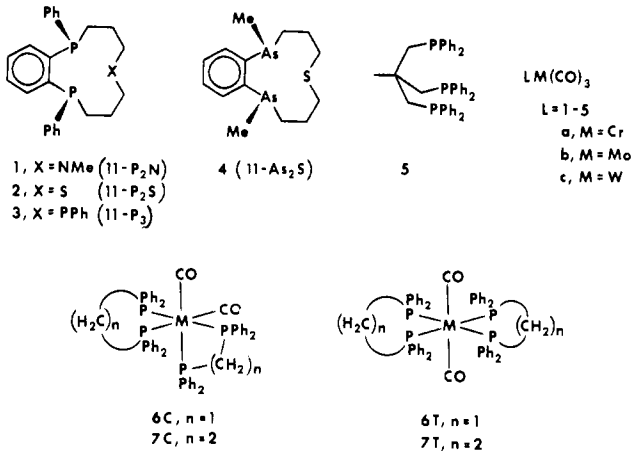
A series of *fac* group 6 metal tricarbonyl complexes of 11-membered tridentate macrocycles (ligating sites P_2N, P_2S, P_3, and As_2S) have been studied by cyclic voltammetry. These complexes undergo quasi-reversible single-electron oxidations with redox potentials dependent on the nature of X in the 11-P_2X series. The range of oxidation potentials is 0.42–0.47 V for a series X = N, S, P with a particular metal, with ease of oxidation decreasing as X is varied from N to S to P.

Introduction

The importance of macrocyclic coordinating ligands in controlling the electronic properties of a coordinated metal ion has long been recognized.[2] Because of their similarity with the biologically important heme proteins, tetraaza macrocyclic complexes have been investigated extensively.[3] It is also clear that metal–macrocycle coordination and aggregation profoundly influence the facility of photoinduced redox reactions in the primary photoprocesses of both green-plant and bacterial photosynthesis.[4]

In order to more clearly delineate the effect of other strongly coordinating macrocyclic ligands on the electronic and redox properties of complexed metals, we have undertaken an electrochemical study of a series of *fac*-$(CO)_3$M(macrocycle)

Chart I



complexes, where M is a group 6 metal (Chart I). We describe herein the effect of *fac*-tridentate metal coordination by the macrocycles **1**–**4** on the redox properties (specifically, oxidation potential and stability of the complex) and the

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