Synthesis and Base Hydrolysis of Pentaammine *N,N*-Dimethylformamide and Acetonitrile Complexes of Rh(III) and Ir(III)

Neville J. Curtis and Alan M. Sargeson*

Contribution from the Research School of Chemistry, Australian National University, GPO Box 4, Canberra, ACT 2601, Australia. *Received February 25, 1983*

Abstract: The synthesis and base hydrolysis of pentaamminerhodium(III) and -iridium(III) complexes of acetonitrile and dimethylformamide (DMF) are discussed and compared to the analogous cobalt(III) and free ligand chemistry. Coordination to metal ion results in a large increase in the rate of base hydrolysis of the coordinated ligands (ca. 10^6-fold). In all four cases, the kinetics fit the rate equation $k_{obsd} = k_1[OH^-] + k_2[OH^-]^2$. For the path k_1 the rate enhancement is manifest in a large increase in the ΔS^* term, while the values of ΔH^* are essentially the same as for the free ligand. Values of k_1 of 0.85 M^{-1} s^{-1} (Rh), 0.23 M^{-1} s^{-1} (Ir) and 0.44 M^{-1} s^{-1} (Rh), 0.38 M^{-1} s^{-1} (Ir) are found for complexes of CH_3CN and DMF, respectively, at 25.1 °C. In D_2O solution, k_1 is 0.48 M^{-1} s^{-1} (CH_3CN) and 0.60 M^{-1} s^{-1} (DMF) for the Ir(III) compounds at 25.1 °C. Activation parameters for the bimolecular reaction (k_1) are ΔH^* = 77 kJ mol^{-1} (CH_3CN) and 58 kJ mol^{-1} (DMF) and for ΔS^* (CH_3CN) = 9 J mol^{-1} K^{-1} (Rh) and 2 J mol^{-1} K^{-1} (Ir) and (DMF) = -58 J mol^{-1} K^{-1} (Rh) and -62 J mol^{-1} K^{-1} (Ir). Mechanistic aspects of the two-term rate laws are discussed and compared to the chemistry of the free ligands.

Hydrolysis of nitriles and amides by OH^- to the amide and carboxylate ion, respectively, is known to be enhanced by coordination of the substrate, at least with some metal ions. However, the origin of the enhancement still has obscure aspects. In particular, the base hydrolyses of σ-bound complexes of acetonitrile or benzonitrile coordinated to such metals as Co(III),[1,2] Rh(III),[3,4,5] Ir(III),[4] Ru(III),[3,5] and Ru(II)[5] have been well studied. In some cases enormous rate enhancements are found; for instance, $[(NH_3)_5RuNCCH_3]^{3+}$ hydrolyses 10^8-fold faster[5] than the free ligand. In related work, activations of 10^4-10^5 were seen for Co(III) complexes of dimethylformamide[6] (DMF) and glycinamide.[6] Some temperature dependence studies of first-row transition-metal complexes have been made,[2,7,8] but no detailed studies were carried out. Strict comparisons may be made between the reactions of acetonitrile and DMF in the free and pentaamminecobalt(III) forms, since both studies were carried out in aqueous solution. For both these systems it was found that the enhancement was due to a considerable increase in the entropy of activation while the enthalpies were essentially the same in the free and complexed molecules. Similar relatively high values of ΔS^* were seen for the pentaamminecobalt(III) complexes of benzonitrile[7] and other aromatic nitriles.[8]

In order to investigate whether the activation parameters obtained for the base hydrolyses of free and coordinated acetonitrile and DMF complexes of pentaamminecobalt(III) do represent a real effect rather than just fortuitous coincidence, we have prepared and studied the analogous Rh and Ir compounds. In addition we wished to examine the effect of varying the metal ion on the hydrolysis and especially the effect of the radial extension of the d-orbitals that may interact with these unsaturated organic molecules through π-bonding. Since ligand loss from Rh(III) and Ir(III) ammines is generally slower than for Co(III), the hydrolyses are more amenable to study at high base concentrations, a factor that may prove useful in the elucidation of the ligand reaction mechanisms of these compounds. Herein we report the synthesis of acetonitrile and dimethylformamide complexes, the kinetics of their base hydrolyses, and the characterization of the reaction products.

Results

The syntheses of pentaamminerhodium(III) and -iridium(III) acetonitrile and *N,N*-dimethylformamide complexes were readily achieved by heating the pentaammine trifluoromethanesulfonate[9] complex with the relevant solvent. For both the acetonitrile compounds, the base hydrolyses proceeded to give single products, which, on the basis of their ^1H NMR spectra, isolation, and analysis, were shown to be the deprotonated acetamido complexes (pK_a = ca. 3),[1] analogous[1] to that formed from $[(NH_3)_5CoNCCH_3]^{3+}$ (eq 1). Similarly, for the base hydrolyses

$$[(NH_3)_5M\ NCCH_3]^{3+} + OH^- \rightarrow [(NH_3)_5MNHCOCH_3]^{2+} \quad (1)$$

of the DMF compounds, the sole products observed were the metal-coordinated formato species and dimethylamine (eq 2).

$$[(NH_3)_5M\ OCHN(CH_3)_2]^{3+} + OH^- \rightarrow [(NH_3)_5M\ OOCH]^{2+} + HN(CH_3)_2 \quad (2)$$

Unlike the pentaamminecobalt(III) analogue,[6] there was no evidence for any ligand loss via a conjugate base mechanism to give free DMF and the pentaamminehydroxo species. For the acetonitrile complexes of Co, Rh, and Ir, integration of the methyl peak in the NMR, with reference to an internal standard, showed that the methyl groups exhibited similar proton exchange properties in 0.5 M NaOD solutions. In all cases approximately 35% of the protium label was lost to solvent during the hydrolysis. This is consistent with previous work[1] where it was shown that the rate of proton exchange was 40% faster than the rate of hydrolysis.

Base hydrolysis rates for all four compounds were measured in the range of $[OH^-]$ of 0.05-M 0.5 M NaOH at various temperatures between 12.2 and 43.6 °C and at a constant ionic strength of 1.0 M, maintained by sodium perchlorate. In all cases the observed reactions were greater than first order in hydroxide concentration. The effect is not great, but it is significant. It resulted in an increase for the ratio $k_{obsd}/[OH^-]$ of 20-40% in going from 0.1 to 0.4 M base. Figure 1 shows selected examples of this effect. The effect is reproducible under a range of electrolyte conditions.[30] For instance, in 1.0 M $NaClO_4$ solutions the ratio of the observed rates (k_{obsd}) for 0.4-0.1 M NaOH for the base hydrolysis of $[(NH_3)_5IrNCCH_3]^{3+}$ is 4.77 ± 0.11 while in 3.0 M $NaClO_4$ the ratio is 4.48 ± 0.06 and for 1.0 M $NaClO_4$ solutions containing 6 M urea it is 5.03 ± 0.12. Similarly, for

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Table I. Calculated Values[a] for Second- (k_1) and Third-Order (k_2) Rate Constants for the Base Hydrolyses Reactions

	$(NH_3)_5Rh(DMF)$		$(NH_3)_5Ir(DMF)$	
temp, °C	k_1	k_2	k_1	k_2
12.2	0.164 ± 0.003	0.102 ± 0.010[b]	0.137 ± 0.004	0.149 ± 0.015[b]
18.6	0.267 ± 0.009	0.248 ± 0.031[b]	0.260 ± 0.002	0.213 ± 0.007[b]
25.1	0.444 ± 0.017	0.581 ± 0.053[b]	0.381 ± 0.008	0.645 ± 0.026[b]
31.8	0.847 ± 0.006	0.639 ± 0.023[b]	0.724 ± 0.029	1.039 ± 0.106[c]
	$(NH_3)_5Rh(CH_3CN)$		$(NH_3)_5Ir(CH_3CN)$	
temp, °C	k_1	k_2	k_1	k_2
12.2	-[d]		0.0557 ± 0.0015	0.0569 ± 0.0044[c]
18.6	-[d]		0.108 ± 0.001	0.126 ± 0.003[c]
25.1	0.846 ± 0.006	0.850 ± 0.019[b]	0.228 ± 0.008	0.220 ± 0.028[c]
31.8	1.63 ± 0.030	1.45 ± 0.14[e]	0.477 ± 0.001[f]	
36.7	2.83 ± 0.060[f]			
43.6	5.33 ± 0.07[g]			
	$(ND_3)_5Ir(CH_3CN)$		$(ND_3)_5Ir(DMF)$	
temp, °C	k_1	k_2	k_1	k_2
25.1	0.481 ± 0.011	0.372 ± 0.041[b]	0.600 ± 0.018	1.07 ± 0.05[c]

[a] As calculated from eq 3. Units: k_1, M^{-1} s^{-1}, k_2, M^{-2} s^{-1}. I = 1.0 M ($NaClO_4$). [b] $[OH^-]$ = 0.1–0.4 M. [c] $[OH^-]$ = 0.1–0.5 M. [d] Product insoluble in this medium at this temperature. [e] $[OH^-]$ = 0.1–0.3 M. [f] $[OH^-]$ = 0.05–0.2 M. [g] $[OH^-]$ = 0.1–0.2 M.

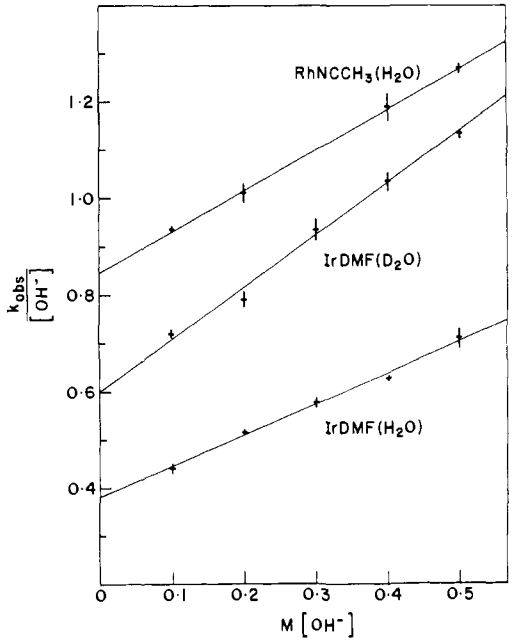

Figure 1. Plot of $k_{obsd}/[OH^-]$ vs. $[OH^-]$ for representative substrates, in H_2O and D_2O, at 25.1 °C, illustrating the two-term rate law, as in eq 3.

the Rh(III) acetonitrile complex, the ratio is 5.09 ± 0.15 in 1.0 M $NaClO_4$/NaOH, while in $LiClO_4$/LiOH, it is 5.22 ± 0.15. Control experiments for the base hydrolysis of $[(NH_3)_5CoCl]^{2+}$ under similar conditions showed no change in the ratio of $k_{obsd}/[OH^-]$ for a comparable range in $[OH^-]$. The kinetic behavior of $[(NH_3)_5CoNCCH_3]^{3+}$ was also reexamined at high base concentration, by necessity at a low temperature (12.2 °C), and it was found that a slight, but barely significant rise in the value of $k_{obsd}/[OH^-]$ occurred. The change, an increase of 9 ± 5% over a range of $[OH^-]$ of 0.1–0.4 M, was considerably smaller than that seen for the Ir(III) complex at that temperature (30 ± 3%) and for the Rh(III) compound at 25.1 °C (27 ± 4%). These results indicate that an activity coefficient effect is not the cause of this behavior since all three ions should have very similar thermodynamic properties in this context. The observed data were found to fit a rate law of the form

$$\frac{k_{obsd}}{[OH^-]} = k_1 + k_2[OH^-] \qquad (3)$$

from which values (Table I) of k_1 and k_2 were obtained. There

Table II. Observed Rate Constants (×10^3) in Buffered Solutions for Base Hydrolysis of Pentaammine Complexes of Acetonitrile and DMF (25.0 °C, 0.1 M I)

		buffer concentration			10^3-
buffer	pH	0.1 M	0.2 M	0.3 M	k_B[a]
	$(NH_3)_5RhNCCH_3^{3+}$				
1-butylamine[b]	10.57[c]	0.640	0.829	1.17	2.7
	10.88[d]	1.48	2.07	2.49	5.2
	11.24[d]	2.99	3.73	4.44	7.2
	11.69[d]	7.41	8.58	9.75	11.7
NH_3[e]	10.33[c]	0.282	0.316	0.364	0.39
diisopropylamine	11.27[d,f]	3.17		3.26	
	$(NH_3)_5Ir(DMF)^{3+}$				
1-butylamine[b]	10.57[c]	0.266	0.275	0.301	
	10.81[c]	0.575	0.622	0.643	
	11.24[c]	1.23	1.30	1.30	
	11.69[d]	3.13	3.37	3.66	
pyrrolidine	11.55[d,f]	3.21	3.17	2.97	

[a] As defined in eq 4. [b] pK_a = 10.75, ref 11. [c] Single determinations. [d] Triplicate determinations. [e] pK_a = 9.47, ref 29. [f] Equimolar RNH_3^+ and RNH_2.

was no evidence for any significant contribution from a spontaneous, water-catalyzed reaction for any of the compounds studied. For the acetonitrile compounds, only a small range of base concentrations were amenable to study at higher temperatures because of the relatively fast kinetics. In these cases, it was found that there were no significant changes in the ratio $k_{obsd}/[OH^-]$ and so a single rate constant is quoted (Table I). The second-order rate constant determined for $[(NH_3)_5RhNCCH_3]^{3+}$ at 25.1 °C is in reasonable agreement with the previously[3] found value (1.0 ± 0.1 M^{-1} s^{-1}), measured at a lower pH. Data at a variety of temperatures gave good Arrhenius plots from which values for ΔH^* and ΔS^* were determined. These are shown in Table III along with the previously determined values for the cobalt(III) analogues and the free ligands.

The kinetics of base hydrolysis of the pentaammine acetonitrile and DMF complexes of iridium were also studied, at 25.1 °C in D_2O solution,[10] and the results are shown in Table I. As for the reactions in H_2O, both these compounds exhibited a two-term kinetic law, with terms for $[OD^-]$ and $[OD^-]^2$. For the DMF complex, both rate constants were increased in D_2O, the ratio of $k(D_2O)/k(H_2O)$ being 1.57 for k_1 and 1.66 for k_2. Slightly higher

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Table III. Activation Parameters[a] (25 °C) for Second-Order Base Hydrolyses

compd	ΔH^*, kJ mol^{-1}	ΔS^*, J mol^{-1} K^{-1}	ref
$(NH_3)_5Co(CH_3CN)$	76 ± 2	20 ± 7	2
$(NH_3)_5Rh(CH_3CN)$	76 ± 2	9 ± 6	
$(NH_3)_5Ir(CH_3CN)$	77 ± 2	2 ± 7	
CH_3CN	77	−96	2
$(NH_3)_5Co(DMF)$	57 ± 2	−56 ± 7	6
$(NH_3)_5Rh(DMF)$	58 ± 3	−58 ± 11	
$(NH_3)_5Ir(DMF)$	57 ± 4	−62 ± 13	
DMF	59	−118	25
DMF (acid)	72	−107	25

[a] Errors indicate one standard deviation from data in Table I and literature data.

ratios were seen for the acetonitrile compound, with the k_1 ratio being 2.11, and 1.69 for k_2.

The base hydrolysis of $[(NH_3)_5RhNCCH_3]^{3+}$ was also examined at lower pH (Table II) in buffer solutions of between 0.1 and 0.3 M ammonia, 1-butylamine, and diisopropylamine. For the first two buffers, when the pH was kept constant, but the buffer concentration was increased while the ionic strength was maintained at 1.0 M, there was a marked increase in the rate of reaction implying some form of buffer catalysis. For 1-butylamine (pK_a = 10.75[11]) this effect was greater at higher pH; that is k_B, as defined in eq 4, increased with concentration of free base. There

$$k_{obsd} = k_B[\text{total buffer}] + k_1[OH^-] \quad (4)$$

was no evidence for significant catalysis by the acid form of the buffer. In contrast, with diisopropylamine, which has a similar pK_a to that for 1-butylamine, there appeared to be no significant increase in the rate of hydrolysis with increasing buffer strengths for analogous concentrations of free base. The isolated product derived from the base hydrolysis in ammonia solution had an identical ^1H NMR spectrum with that for the product from the hydroxide-mediated reaction.

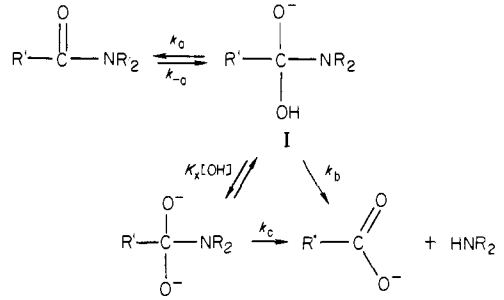
The base hydrolysis of $[(NH_3)_5IrOCHN(CH_3)_2]^{3+}$ was also studied (Table II) in 1-butylamine and pyrrolidine buffers. In butylamine-containing solutions, only a small buffer effect was observed, the variation with buffer concentration being much smaller than for the corresponding results from the nitrile experiments. While there appeared to be a small effect from the basic form of the buffer (Table II, pH 11.69), the results at lower pH indicate that there is not a significant contribution from the acid form. Similarly, there was no evidence for large buffer effects in pyrrolidine-containing solutions.

^{15}N-labeled $(NH_3)_5Ir^{15}NCCH_3^{3+}$ ion was treated with OH^- and the sole product was $(NH_3)_5Ir^{15}NHCOCH_3^{2+}$ with all the label contained in the amide N atom. This experiment excludes the possibility of an intramolecular attack by coordinated aminato ion at the nitrile C atom to generate a four-membered cyclic amidine complex, which could have then hydrolyzed to the pentaammine acetamido complex. Under these circumstances, 50% of the label would have appeared in the coordinated cis ammonias.

Discussion

The observation that the rate laws show a second-order dependence on $[OH^-]$ is a new finding for the base hydrolyses of acetonitrile and DMF complexes of this type. There are a number of possibilities for this behavior, and some of these will examined. One interpretation of the second-order path is that OH^- removes an initial proton from a coordinated ammonia ligand and that this complex ion is inherently more reactive to attack by OH^-, at the ligand, than the initial species. Such a proposition is not attractive on electrostatic grounds, since the positive charge is lessened. Similar arguments apply to the reactivity of ion pairs like $[(NH_3)_5ML,OH]^{2+}$. It is also unattractive for low-spin d^6 systems of this type in which all the t_{2g} levels are filled. Inductively, the coordinated aminato ligand would only serve to promote electron density into the ligand bonding orbital and so weaken the bond between the metal and the acetonitrile or DMF ligands. We assume therefore that the two-term rate law is a consequence of the chemistry of the coordinated ligands themselves and the two ligand systems will be treated separately.

Scheme I



Base hydrolysis of uncoordinated amides[12] has been extensively studied and, in general, the mechanism may be described as in Scheme I. Initial attack (k_a) of hydroxide ion gives the monodeprotonated tetrahedral intermediate, which can decompose via water (k_b) or general acid catalysis to the corresponding acid and amine. Alternatively, at higher pH, a second tetrahedral intermediate may be formed by deprotonation of the initial adduct. Decomposition of this species (k_c) gives the acid and amine, as before. Kinetic laws containing a second order term in $[OH^-]$ have been identified, though only for amides with electron-withdrawing substituents, such as anilides.[13] These are accommodated in terms of the second ionization as shown in Scheme I. The general rate constant, using steady-state kinetics, for the reaction can be written[12] as (in the absence of buffer catalysis) in eq 5.

$$k_{obsd} = \frac{k_a[OH^-](k_b + k_cK_x[OH^-])}{k_{-a} + k_cK_x[OH^-] + k_b} \quad (5)$$

It is further apparent from the observed rate law in the present study (eq 3) that $k_{-a} + k_b \gg k_cK_x[OH^-]$ and that k_b must be of the order of $k_cK_x[OH^-]$, which therefore implies that $k_{-a} \gg k_b$. The observed rate constants may therefore be approximated as $k_1 = k_ak_b/k_{-a}$ and $k_2 = k_ak_cK_x/k_{-a}$. The rate constant k_1 derives from the decomposition of the tetrahedral intermediate I while k_2 is linked with the decay of intermediate II.

As the course of the hydrolysis in phosphate buffer was monitored at a pH ca. 12, only two species, reactant and product, are apparent in the ^1H NMR spectra. Two signals were seen for the nonequivalent methyl groups in the coordinated DMF along with a singlet for the product methylamine. Neither of the two intermediates was observed, nor was there any evidence for coalescence of the *gem*-dimethyl groups as would be expected if k_{-a} were smaller than the rate constant for rotation about the C–NMe_2 bond in I, assuming both k_a and k_b are less than k_{-a}. The rate constant k_{-a} should be greater than 10^2 s^{-1}, but it is difficult to assess the rotational lifetime and thence to estimate k_{-a}.

In 1.0 M hydroxide the contributions to the overall rate of hydrolysis from the paths via I ($k_1[OH^-]$) and II ($k_2[OH^-]^2$) are approximately equal. Since a term second order in base is observed in the high base region and given that analysis above is correct it must be concluded that the rate-determining step in this path is the decomposition of I via II and not the addition of hydroxide ion ($k_a[OH^-]$). The latter situation would effect only a first-order dependence on $[OH^-]$. Given that $k_cK_x[OH^-]$ is rate determining, it follows that k_b must be the rate-determining step for the path first order in $[OH^-]$. Thus both the $k_a[OH^-]$ and k_{-a} paths must be rapid relative to k_b and $k_cK_x[OH^-]$. However we are not able

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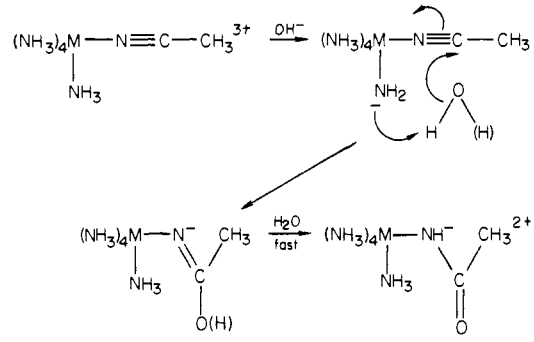
Scheme II



to assign an absolute value for the equilibrium constant $k_a[OH^-]/k_b$ since we are unable to separate the terms k_a and k_b (or k_a and k_cK_x) in the rate constant k_1 (or k_2).

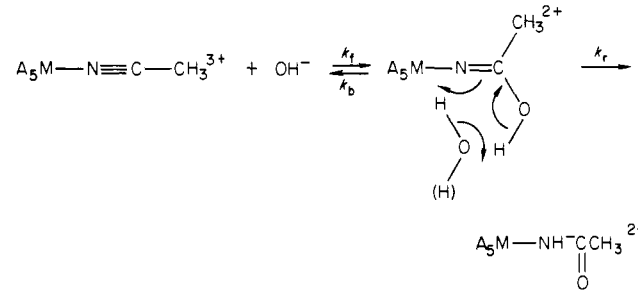
The effect of the metal ion on the relative stabilities and pK_a's of the intermediate species relative to those for free DMF may be rationalized as follows. The metal ion is similar to a proton in terms of neutralizing negative charge, though in general it is not as effective.[14] For instance, the pK_a of $(NH_3)_5CoOH_2$ is considerably (ca. 8–9 pK_a units) lower than that of $H\text{-}OH_2^+$, and $(NH_3)_6Co^{3+}$ is less acidic than $H\text{-}NH_3^+$ (>6 units). This effect leads to an increased acidity for intermediate I arising from the coordinated amide in Scheme I, and under the basic conditions of these experiments leads to an increased access to the intermediate II (Scheme I). It probably accounts for the observation of the second-order term in the rate law which is not seen for the free ligand.[12] For the path first order in hydroxide, the metal ion would be expected to enhance k_a and inhibit k_{-a} and k_b, relative to the free amide. The implication of this analysis is that the rate increase on coordination is coming solely from the enhanced rate of addition of hydroxide at the carbonyl center, reflected in the equilibrium constant $k_a[OH^-]/k_{-a}$. Although it could also arise from a change in the ratio k_b/k_{-a}, it is difficult to envisage that relatively hard acids like $(NH_3)_5M^{3+}$ would affect such a ratio dramatically, especially when the metal is not bound to either leaving group.

The isotope effects[10,15] do not help greatly in the assignment of mechanism, but some characteristics emerge. For the term first order in hydroxide, protonation of the leaving group cannot be important in the rate-determining step since $k_b(H_2O)$ would be expected to be greater than $k_b(D_2O)$. However $k_a(OD^-) > k_a(OH^-)$ would be anticipated, and this factor could dominate the preequilibrium and account for the observed effect $(k_1(D_2O)/k_1(H_2O) \sim 1.5)$. For the term second order in hydroxide, a similar argument applies except that the analysis of the isotope effect is complicated by the coupling of two equilibria.

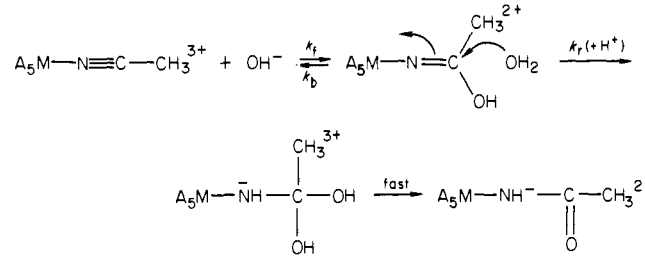
It is inconceivable that NMe_2^- leaves as the anion from either I or II especially since it is coordinated to a positive ion. Presumably protonation by the solvent is either very early or late in the activation process for the loss of the leaving group since the isotope effects are small and inverted. A complementary fact is the absence of significant general acid catalysis which has been seen, at least for uncoordinated trifluoroacetanilide.[16] Coordination of intermediate II would make it more difficult to protonate the leaving group, and it follows, therefore, that protonation should occur late in the activation process.

In contrast to the chemistry of uncoordinated amides, the base hydrolysis of nitriles[17] has received far less attention, and as far as we are aware no work has been reported in which a two-term rate law, as in eq 3, has been observed. In addition, the base hydrolysis in D_2O has not been examined.

Scheme III



Scheme IV



We now consider two plausible mechanisms (Schemes II and III) that are consistent with the rate law and the tracer experiment for the hydrolysis of the nitrile complexes. Each involves addition of OH^- at the nitrile carbon to generate the imidolato complex, and we assume that this is rearranged to the acetamido product. There is no good reason to suspect the imidolato complex is a stable form. A crystallographic analysis[18] of $[(NH_3)_5CoNHCOCH_3](ClO_4)_2$ gives bond lenghts of 1.339 Å (N–C) and 1.267 Å (C–O) more characteristic of a delocalized amide than a localized imidol, which would be expected to correlate more with coordinated imines. For example, the imine bond length in a N-coordinated 2-carboxy-Δ^1-pyrroline[19] is 1.292 and 1.252 Å for a nonconjugated case[20] as compared to 1.486 Å for a single bond.[19] Similarly, the C–O bond length in alcohols,[21] 1.43 Å, is considerably longer than that in amides,[21] is 1.23 Å. We assert therefore that the final product is the deprotonated acetamido complex.[1] Similarly, this appears to be the case for the Rh(III) and Ir(III) compounds.

Since the kinetic expression contains terms for both a first- and second-order path in $[OH^-]$ for both Rh(III) and Ir(III), and possibly also Co(III), over a range of temperatures, it is reasonable to assume that the two routes are chemically similar. For this reason, only those mechanisms where OH^- may be effectively substituted for H_2O will be considered.

Deprotonation (Scheme II) of a coordinated ammonia could occur as a rapid preequilibrium followed by rate-determining addition of H_2O (k_1) or OH^- (k_2) at the nitrile carbon. This addition is assisted by the intramolecular conjugate base ($L_5CoNH_2^-$) removing a proton from the nucleophilic H_2O or OH^- in a concerted manner. Subsequent protonation of the acetamido nitrogen could be fast (pK_a > 14). Such paths accommodate the rate law and avoid the need to generate O^{2-} (pK_a = ~25).[22]

The second mechanism involves a preequilibrium attack of hydroxide on the coordinated ligand, with subsequent proton rearrangement being the rate-determining step (Scheme III).

The proton rearrangement could be accomplished by a solvent (k_1) or OH^--catalyzed path, as shown, to give the stable acetamido complex. The imidolato nitrogen need not be especially basic,[23]

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and it is harder to gauge the pK_a of the hydroxyl group, but the acetamido nitrogen center has a $pK_a > 14$ and the coordinated amide is a very weak base indeed ($pK_a \ll 0$). Given this understanding the rearrangement will be favorable.

We have also considered and rejected a mechanism based on covalent catalysis of the rearrangement of the imidolato complex, as in Scheme IV. Hydrolysis of imidates[24] has been shown to proceed via initial attack of water followed by decomposition of the resulting tetrahedral intermediate. This step must involve the protonated iminium ion since the imine itself is inert to attack by nucleophiles. Clearly, the coordinated imidolato species should also be unreactive since it is imine like.

A value for $k(D_2O)/k(H_2O)$ of greater than 1 is consistent[10] with a transition state in which hydroxide ion is added to a substrate. This could be a consequence of the superior nucleophilic character of the OD^- ion in D_2O over that of OH^- in H_2O, and the effect is relatively small, consistent with a secondary isotope effect. The isotope effects are not inconsistent with either mechanism (Schemes II or III) provided hydrogen abstraction occurs early or late in the transition state. However, the mechanism in Scheme II should not be general base catalyzed, unlike that of Scheme III. The only problem in the general base pattern is the failure of the diisopropylamine to effect catalysis. This may be a deviation arising from hindrance to the approach of such a sterically crowded system.

The activation parameters (Table III) for both series of compounds show the same trend. For the pentaammine acetonitrile complexes of Co(III), Rh(III), Ir(III), and free ligand, the values of ΔH^* are the same, while there is a slight decrease (less positive) in the values of ΔS^* in going from Co(III) to Ir(III). However, for all complexes, the activation entropies are considerably more positive than for the free ligand. The values for the DMF series indicate a similar trend. The values for ΔH^* for the metal-coordinated DMF compounds are significantly different from that for the acid-catalyzed reaction.[25] Thus there does not appear to be any gross effect of substituting Ir(III) for Co(III) which would be expected if the degree of orbital overlap between the π^*-orbitals of the ligand and the d-orbitals of the metal ion is important.

The effects seen here are reminiscent of those in the Radziszewski reaction. Comparing the activation parameters for attack by hydroxide and hydroperoxide (HOO^-) on benzonitrile,[26] it is found that the ΔH^* terms are identical while for the latter nucleophile there is a large increase in the value of ΔS^*. It has been proposed that the relatively high hydroperoxide reactivity is due to the availability of the proton,[27] via a cyclic transition state, although an α effect has also been claimed.[28]

The implication in these studies is that the addition of the nucleophile is not rate determining and that the effect of polarization of the ligand by the metal ion is therefore obscured. Either entropy effects governing proton transfers from one atom to another dominate the kinetics and the activation enthalpies for these processes in the free ligand and complex systems are very similar or the entropy differences for the systems arise largely from charge neutralization effects reflected in the preequilibira.

Experimental Section

Kinetics. All kinetics were run under pseudo-first-order conditions using at least a 10-fold excess of base over substrate. A hand-operated stopped-flow apparatus was used, with substrate in one drive syringe and base in the other; ionic strength in both solutions was adjusted to 1 M with $NaClO_4$. The hydrolyses were monitored at 235 nm ($RhCH_3CN$) or 250 nm (others) on a Cary 118C spectrophotometer. Good first-order plots were obtained which were linear for at least 5 half-lives and were analyzed by computer by best fit to an exponential ($RhCH_3CN$, RhDMF, IrDMF) or Guggenheim plot ($IrCH_3CN$). Triplicate reproducibility was enforced. At least four different base concentrations were used in the range 0.05–0.5 M NaOH, depending on substrate and temperature. Values of k_1 and k_2 were obtained from a least-squares analysis using eq 3. Errors quoted represent one standard deviation. NaOH solutions were diluted from standard stocks while NaOD solutions were prepared from the calculated amount of NaOH (Analar) dissolved in 99.7% D_2O and verified by titration. Buffer kinetics were run on a Hewlett-Packard 8450A spectrophotometer equipped with a 89100A temperature controller. Ionic strength was maintained at 1.0 M by the addition of $NaClO_4$, and all runs were performed at 25.0 ± 0.1 °C. Buffer solutions were prepared by dilution of a standard stock of 25% (v/v) ammonia or freshly distilled amine which was partially neutralized by the addition of HCl. Minor changes in the observed pH's for each set of buffers, at the same pH, were corrected by the addition of HCl or NaOH solution. Measurements of pH were made under nitrogen with a Radiometer PHM 26 pH meter equipped with a G202B glass and K 4112 calomel electrodes, calibrated by using standard buffers.

Spectroscopy. Electronic spectra of the new Rh complexes (distinct peaks were not seen for most of the Ir compounds) were recorded on a HP8450 instrument in aqueous solution. Maxima and corresponding extinction coeffients are given. Infrared spectra were recorded in KBr disks on a Perkin-Elmer 683 or 225 spectrophotometer. NMR spectra were measured on Jeol PMX 60 or Varian HA-100 instruments, with Me_4Si or DSS as internal references. Total proton counts are not given where water peaks interfered with the integration procedure.

Syntheses. $[(NH_3)_5IrCH_3CN](ClO_4)_2CF_3SO_3 \cdot H_2O$. $[(NH_3)_5IrOSO_2CF_3](CF_3SO_3)_2$ (2.0 g) was refluxed in 50 mL of dry acetonitrile for 6 h, cooled, and evaporated in vacuo. The resultant white powder was dissolved in water (15 mL) and the product crystallized overnight at 4 °C, after the addition of a solution of 2.5 g of $NaClO_4 \cdot H_2O$ and 0.5 g $NaCF_3SO_3 \cdot H_2O$ in 5 mL of water: yield 1.62 g after washing with 25% diethyl ether in ethanol; NMR Me_2SO δ 2.39 (s, 3 H), 4.4 (br, 15 H); IR (KBr disk) 2334 cm^{-1}; UV λ 245 nm (ε 205). Anal. Calcd for $C_3H_{17}N_6Cl_2F_3IrO_{12}S$: C, 5.29; H, 2.51; N, 12.33; S, 4.71. Found: C, 5.3; H, 2.7; N, 12.3; S, 4.5.

$[(NH_3)_5IrOCHNMe_2](ClO_4)_3$. $[(NH_3)_5IrOSO_2CF_3](CF_3SO_3)_2$ (2.0 g) was heated in dry DMF for 4 h at 80 °C and subsequently cooled. Addition of the reaction solution to 200 mL of diethyl ether, with vigorous stirring, yielded a white solid, which was dissolved up in 15 mL of warm water and recrystallized by the addition of a solution of 10 g of $NaClO_4 \cdot H_2O$ in 5 mL of water: yield 1.44g after washing with 1:1 diethyl ether/ethanol. NMR (Me_2SO) δ 2.95 (s, 3 H), 3.10 (s, 3 H), 4.5 (br, 15 H), 7.91 (s, 1 H); IR 1670 cm^{-1}.

Anal. Calcd for $C_3H_{22}N_6Cl_3\ IrO_{13}$: C, 5.55; H, 3.42; N, 12.95. Found: C, 5.8; H, 3.3; N, 12.5.

$[(NH_3)_5RhCH_3CN](ClO_4)_2CF_3SO_3$. $[(NH_3)_5RhOSO_2CF_3](CF_3SO_3)_2$ (3.18 g) was refluxed in 20 mL of dry acetonitrile for 2 h, cooled, and solvent removed in vacuo. The white powder was recrystallized by dissolving it in 15 mL of water and addition of a solution of 2.5 g of $NaClO_4 \cdot H_2O$ and 0.5 g $NaCF_3SO_3 \cdot H_2O$ in 5 mL of water. After washing with 25% diethyl ether in ethanol, 2.52 g of the mixed salt was obtained. NMR (Me_2SO) δ 2.59 (s) 3.9 (br s); IR 2339 cm^{-1}; UV λ 253 (121), 302 (161) nm. Anal. Calcd for $C_3H_{18}N_6Cl_2F_3O_{11}Rh$: C, 6.24; H, 3.14; N, 14.56; S, 5.56. Found: C, 6.2; H, 3.0; N, 14.2; S, 5.3.

$[(NH_3)_5RhOCHNMe_2](ClO_4)_3$. $[(NH_3)_5RhOSO_2CF_3](CF_3SO_3)_2$ (2.54 g) was dissolved in 5 mL of dry DMF and the solution left at 60 °C for 2 h. Addition of 20 mL of ethanol followed by 200 mL of diethyl ether gave a white powder, which was recrystallized by dissolution in 10 mL of warm water and addition of 5 g of $NaClO_4 \cdot H_2O$ in 2 mL of water. After washing with ethanol and diethyl ether, 1.88 g of the product was obtained. NMR (Me_2SO) δ 2.94 (s, 3 H), 3.08 (s, 3 H), 3.7–4.1 (br, s 15 H), 7.85 (s, 1 H); IR 1670 cm^{-1}; UV, λ 260 (sh 150), 324 (173) nm. Anal. Calcd for $C_3H_{22}N_6Cl_3O_{13}Rh$: C, 6.44; H, 3.96; N, 15.02. Found: C, 6.2; H, 4.0; N, 14.8.

$[(NH_3)_5RhNHCOCH_3](ClO_4)_2$. To $[(NH_3)_5RhCH_3CN](ClO_4)_2CF_3SO_3$ (0.50 g) dissolved in 5 mL of warm water was added in 1 mL of 1 M NaOH, the mixture left for 10 min, and the acetamido complex precipitated by the addition of 2 g of $NaClO_4 \cdot H_2O$ in mL of H_2O. After filtration and washing with 50% diethyl ether in ethanol 0.31 g of the complex was obtained as pale yellow needles:[3] NMR (Me_2SO) δ 1.88 (s, 3 H), 3.3 (br, 3 H), 3.6 (br, 12 H), 4.6 (br, 1 H); IR 1585 cm^{-1}.

$[(NH_3)_5IrNHCOCH_3](ClO_4)_2$. To a solution of 400 mg of the acetonitrile complex, dissolved in 5 mL of warm water was added 0.6 mL of 1 M NaOH, the mixture left for 30 min, and the acetamido compound

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(30) **Note Added in Proof**: The two-term rate law is also observed in NaCl-containing solutions (I = 1.0 M), for the base hydrolyses of the iridium compounds.

precipitated by the addition of 2 g of $NaClO_4 \cdot H_2O$. Yield 230 mg, a further crop of 42 mg was obtained by the addition of ethanol. NMR (Me_2SO), δ 1.87 (s, 3 H), 3.95 (br, 3 H), 4.3 (br, 12 H), 5.2 (br, 1 H); (D_2O, in basic solution) δ 2.05 (s); (0.5 M DCl) δ 2.36 (s); IR 1585 cm^{-1}. Anal. Calcd for $C_2H_{19}N_6Cl_2IrO_9$: C, 4.50; H, 3.58; N, 15.73. Found: C, 4.7; H, 3.4; N, 14.9.

$[(NH_3)_5IrOOCH](ClO_4)_2$. A suspension of 200 mg of the DMF complex in 2 mL of 2M NaOH was swirled for 10 min at ambient temperature. A solution of 1g of $NaClO_4 \cdot H_2O$ in 1 mL of water was added, the mixture cooled, and white crystals of the product were filtered: yield of 0.16 g (100%); NMR (Me_2SO) δ 4.2-4.7 (br, 15 H), 7.70 (s, 1 H); IR 1645 cm^{-1}. Anal. Calcd for $CH_{16}N_5Cl_2IrO_{10}$: C, 2.30; H, 3.09; N, 13.44. Found: C, 2.7; H, 3.2; N, 13.4.

$[(NH_3[_5RhOOCH](ClO_4)_2$. This was prepared in the same manner as the above compound in quantitative yield. NMR Me_2SO δ 3.6 (br), 3.8 (br), 7.91 (d, 2.5 Hz); IR 1630 cm^{-1}; UV λ 266 (106), 321 (142) nm. Anal. Calcd for $CH_{16}N_5Cl_2O_{10}Rh$: C, 2.78; H, 3.73; N, 16.21. Found: C, 3.2; H, 3.8; N, 16.3.

^{15}N Experiment. Acetonitrile (1 mL, 100% label) was condensed onto 100 mg of the iridium triflate complex and the solution heated for 4 h at 80 °C for 4 h. After cooling, the acetonitrile was removed in vacuo and 1 mL of 1 M NaOH added. This was then quenced by the addition of concentrated HCl to give a pH of ca. 2 and the resultant mixture evaporated and left on the vacuum line for 24 h. The 100-MHz ^1H NMR spectrum of the white powder in 0.1 M DCl in D_2O showed only a doublet at δ 2.48 (J = 2 Hz) and a broad band at δ 4.4 corresponding to the coordinated ammonias. There were no obvious satellite peaks for this signal, resulting from ^{15}N-^1H coupling which are typically of the order of 60 Hz and therefore would be clearly visible in this spectrum. In a control experiment, using acetonitrile-^{14}N, the same spectrum was observed except that the acetamide peak at δ 2.45 was a singlet.

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Registry No. $[(NH_3)_5IrCH_3CN](ClO_4)_2CF_3SO_3$, 88035-84-1; $[(NH_3)_5Ir(DMF)](ClO_4)_3$, 88035-85-2; $[(NH_3)_5RhCH_3CN](ClO_4)_2CF_3SO_3$, 88035-86-3; $[(NH_3)_5Rh(DMF)](ClO_4)_3$, 68851-29-6; $[(NH_3)_5RhNHCOCH_3](ClO_4)_2$, 52843-08-0; $[(NH_3)_5IrNHCOCH_3](ClO_4)_2$, 88035-87-4; $[(NH_3)_5IrOOCH](ClO_4)_2$, 15646-83-0; $[(NH_3)_5RhOOCH](ClO_4)_2$, 15612-60-9; $[(NH_3)_5IrOSO_2CF_3](CF_3SO_3)_2$, 84254-59-1; $[(NH_3)_5RhOSO_2CF_3](CF_3SO_3)_2$, 84254-57-9; CH_3CN, 75-05-8; DMF, 68-12-2.

Supplementary Material Available: Tables of the observed rate constants for base hydrolysis of the title compounds, as a function of $[OH^-]$ and $[OD^-]$ (2 pages). Ordering information is given on any current masthead page.

Geometrical and Stereochemical Factors in Metal-Promoted Amide Hydrolysis

John T. Groves* and R. Rife Chambers, Jr.

Contribution from the Department of Chemistry, The University of Michigan, Ann Arbor, Michigan 48109. *Received April 22, 1983*

Abstract: The importance of the precise geometric orientation of a metal in metal-promoted amide hydrolysis has been demonstrated. Large rate enhancements (10^3-10^6) at neutral pH were found in zinc and copper complexes in which the metal is forced to lie above the plane of an amide. For this study, lactams 1-[(6-(dimethylamino)methyl)-2-pyridyl)methyl]hexahydro-1,4-diazepin-5-one (**1**) and 1-[(6-((bis(carboxymethyl)amino)methyl)-2-pyridyl)methyl]hexahydro-1,4-diazepin-5-one (**2**) were synthesized. Titrimetrically determined formation constants indicated that both **1** and **2** readily bind divalent metals (Cu^{2+}, Ni^{2+}, Zn^{2+}, Co^{2+}). Detailed investigations of the various metal complexes were possible over a wide range of pH. At 50 °C, the Cu^{2+}-promoted hydrolysis of **1** exhibited a sigmoidal pH-rate profile. The rates increased commensurate with the ionization of a metal-bound water molecule. A similar behavior was observed with the **2**-Zn^{2+} complex at 70 °C. Both Cu^{2+} and Zn^{2+} greatly facilitate amide hydrolysis at pH 7. Compared to base hydrolysis of the lactams with no metal, a rate enhancement of 9×10^5 and 1.0×10^3 was observed with the **1**-Cu-OH_2 and **2**-Zn-OH_2 complexes, respectively. Activation parameters for the metal-promoted hydrolyses indicated that catalysis results from a substantial increase in $\Delta S^{\ddagger}$. These observations are interpreted in terms of nucleophilic catalysis by a metal-hydroxo species in basic media. Concurrent carbonyl oxygen exchange accompanied base hydrolysis of **1**. By contrast, significant oxygen-18 exchange was not observed during the Cu^{2+}-promoted hydrolysis of **1**. These results are considered in the context of the known stereoelectronic control in the cleavage of tetrahedral intermediates.

The acceleration of enzymic reactions can be attributed to specific chemical effects such as entropic advantage, transition-state binding, and chemical catalysis by neighboring groups.[1] The study of simple model systems has served to probe the relative importance of such effects and as a test of perceived insight into a particular mechanism.[2] Carboxypeptidase A (CPA), a C-terminal peptidase, has become a paradigm case of a substantiated enzymic mechanism.[3] Surprisingly, in the 16 years since the first, high-resolution X-ray structural data for CPA have been avail-

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