

Metal Ion Activation in the Base Hydrolysis of Amides. Hydrolysis of the Dimethylformamidopentaamminecobalt(III) Ion

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Abstract: The rate of base hydrolysis of oxygen bonded $[\text{Co}(\text{NH}_3)_5\text{DMF}]^{3+}$ (DMF = *N,N*-dimethylformamide) has been determined in the temperature range 7–32°. Two reaction paths were detected. The major path corresponds to hydroxide ion attack at the carbonyl center, leading to $[\text{Co}(\text{NH}_3)_5\text{OOCH}]^{2+}$ and $\text{HN}(\text{CH}_3)_2$ ($\Delta H^\ddagger = 13.8 \text{ kcal mol}^{-1}$, $\Delta S^\ddagger = -12 \text{ cal deg}^{-1} \text{ mol}^{-1}$). The minor path leads to $[\text{Co}(\text{NH}_3)_5\text{OH}]^{2+}$ and DMF and is probably the dissociative conjugate base process ($\Delta H^\ddagger = 28 \text{ kcal mol}^{-1}$, $\Delta S^\ddagger = +35 \text{ cal deg}^{-1} \text{ mol}^{-1}$). Compared with hydrolysis of the uncoordinated species the amide cleavage is accelerated $\geq 10^4$ -fold, all contributed by the entropy term. It is concluded that only coordination of the carbonyl oxygen is required to activate such centers toward nucleophiles.

Very considerable accelerations (10^4 – 10^7 times) of the hydrolysis rates of amino acid derivatives have been observed when the derivative is incorporated as a chelate ligand in a transition metal complex.¹ This activation was attributed to coordination of the carbonyl oxygen, an assertion which has now been tested by examination of systems containing larger chelate rings² and of a carbonyl bound monodentate complex. While inert transition metal, carbonyl-O bonded complexes of carboxylic esters are not well characterized,³ those of simple amides, particularly dialkylamides, are familiar species. Such complexes therefore allow the determination of the extent to which amide reactivity is enhanced solely by coordination of the carbonyl oxygen. We wish to report here the results of an investigation of the base hydrolysis of the complex $[\text{Co}(\text{NH}_3)_5\text{DMF}](\text{ClO}_4)_3$ (DMF = *N,N*-dimethylformamide). In order that a detailed comparison might be made with a chelated amide, rate measurements^{1c} on the complex $[\text{Co}(\text{en})_2\text{glyN}(\text{CH}_3)_2]^{3+}$ have been extended to enable calculation of activation parameters.

Experimental Section

Instrumentation and Chemicals. Visible spectra and rate measurements were made on Cary 14 and 16K spectrophotometers, respectively. Infrared spectra were recorded using KBr disks on a Perkin-Elmer Model 457 instrument. Nmr spectra were obtained at 100 MHz on a JEOL Minimar spectrometer and mass spectra were measured on an Atlas M86 ratio recording instrument.

Dimethylformamide used for preparative work was Mallinckrodt LR grade. All chemicals used in kinetic studies were of analytical reagent standard, NaOH solutions being freshly prepared from May and Baker "Volucon" concentrate.

Synthesis. $[\text{Co}(\text{NH}_3)_5\text{DMF}](\text{ClO}_4)_3$. Solutions of $[\text{Co}(\text{NH}_3)_5\text{Cl}](\text{ClO}_4)_2$ (37 g) in DMF (100 ml) and AgClO_4 (25 g) in DMF (50 ml) were mixed and heated on a steam bath for 15 min. The coagulated AgCl was removed and the filtrate mixed with ether (500 ml) to precipitate a red oil. This was triturated with ethanol to give a pink powder (35 g). The complex was recrystallized from

water (600 ml, 25°) by adding excess NaClO_4 and cooling on ice: visible spectrum λ_{max} (nm) (ϵ_{max} , $M^{-1} \text{ cm}^{-1}$) 348 (69.2), 506 (79.4) (cf. 347, 62.5; 505, 76.0,⁴ 347, 66.7; 506, 77.3⁵); $\nu_{\text{C=O}}$ 1655 cm^{-1} ; pmr (δ in ppm from internal TMS in $\text{DMSO}-d_6$) -2.72 (NH_3 trans to O) -2.88, -3.03 ($\text{N}(\text{CH}_3)_2$ doublet); -3.83 (NH_3 cis to O); -7.43 (HC=O).

Anal. Calcd for $\text{CoC}_3\text{H}_{22}\text{Cl}_3\text{N}_6\text{O}_{13}$: Co, 11.43; C, 6.99; H, 4.30; N, 16.30; Cl, 20.63. Found: Co, 11.52; C, 7.10; H, 4.48; N, 16.51; Cl, 20.40.

$[\text{Co}(\text{en})_2\text{glyN}(\text{CH}_3)_2]_2\text{I}_2 \cdot \text{ClO}_4$. The complex was prepared as described previously.^{1c}

Anal. Calcd for $\text{CoC}_3\text{H}_{26}\text{N}_6\text{O}_3\text{ClI}_2$: C, 15.13; H, 4.13; N, 13.24. Found: C, 15.21; H, 4.38; N, 13.59.

Kinetics. Aqueous solutions of $[\text{Co}(\text{NH}_3)_5\text{DMF}](\text{ClO}_4)_3$ ($10^{-2} M$) and $\text{NaOH}-\text{NaClO}_4$ were rapidly mixed in a stopped-flow reactor. Rates of reaction were followed spectrophotometrically at 500 nm. Measurements were made for final OH^- concentrations between 0.050 and 0.50 M , an ionic strength of 1.0 M being maintained with NaClO_4 . The temperature was varied between 7 and 32°, and three–five runs were made for each condition.

Similar conditions applied to the rate measurements on $[\text{Co}(\text{en})_2\text{glyN}(\text{CH}_3)_2]^{3+}$, except that only a single $[\text{OH}^-]$ of 0.20 M was used and the wavelength was 300 nm.

Product Analysis. The reaction products from $[\text{Co}(\text{NH}_3)_5\text{DMF}]^{3+}$ were identified by pmr spectra for reactions conducted in $\text{D}_2\text{O}-\text{OD}^-$ and by separation of the cationic species on H^+ form Dowex 50Wx2 ion-exchange resin. Quantitative analysis was made by signal integration and visible spectrophotometry, respectively. Two product complexes, one 2+ and one 3+, were separated on the ion-exchange resin by elution with 1 M NaClO_4 (pH 3), then 3 M HCl . Solids were isolated from these eluates by reducing the volume of the NaClO_4 solution under vacuum until crystallization began and by adding ice-cold 60% HBr to the HCl solution (see ahead for details).

Anal. Perchlorate salt found: Co, 15.08; C, 3.35; H, 4.26; N, 17.59; Cl, 18.39; visible spectrum λ_{max} nm (ϵ_{max} $M^{-1} \text{ cm}^{-1}$) 350 (55.6) 500 (69.8) (1 M HClO_4). Cf. calcd for $[\text{Co}(\text{NH}_3)_5\text{OOCH}](\text{ClO}_4)_2$: Co, 15.19; C, 3.10; H, 4.16; N, 18.05; Cl, 18.27; visible spectrum 350 (55.8); 500 (69.4).⁶

Anal. Bromide salt found: Co, 15.1; H, 4.53; N, 17.90; Br, 61.2; visible spectrum 490 (48.6) (3 M HCl). Cf. calcd for $[\text{Co}(\text{NH}_3)_5\text{OH}_2]\text{Br}$: Co, 14.67; H, 4.26; N, 17.43; Br, 59.66; visible spectrum 492 (47.7).⁷

Oxygen Isotopic Tracer Experiments. (1) $[\text{Co}(\text{NH}_3)_5\text{DMF}](\text{ClO}_4)_3$ (5 g) was converted to its very soluble chloride salt by shaking for 5 min with an aqueous slurry of excess (10X) Cl^- form Dowex 1 X 8 anion-exchange resin. The resin was removed and acetone

(1) (a) D. A. Buckingham, L. G. Marzilli, and A. M. Sargeson, *J. Amer. Chem. Soc.*, **89**, 2772, 4539 (1967); (b) D. A. Buckingham, D. M. Foster, and A. M. Sargeson, *ibid.*, **90**, 6032 (1968); (c) D. A. Buckingham, C. E. Davis, D. M. Foster, and A. M. Sargeson, *ibid.*, **92**, 5571 (1970); (d) D. A. Buckingham, D. M. Foster, and A. M. Sargeson, *ibid.*, **92**, 5701 (1970).

(2) E. Baraniak, Ph.D. Thesis, Australian National University, 1973.

(3) J. K. Hurst and H. Taube, *J. Amer. Chem. Soc.*, **90**, 1174 (1968), for example, have described the relatively difficult preparation of the methyl acetate complex of pentaamminecobalt(III).

(4) E. S. Gould, *J. Amer. Chem. Soc.*, **87**, 4730 (1965).

(5) R. B. Jordan and R. J. Balahura, *J. Amer. Chem. Soc.*, **92**, 1533 (1970).

(6) R. B. Jordan, Ph.D. Thesis, University of Chicago, 1964.

(7) D. A. Buckingham, I. I. Olsen, and A. M. Sargeson, *J. Amer. Chem. Soc.*, **88**, 5443 (1966).

(400 ml) added with LiCl (20 g) to the filtrate. The pink crystals obtained (3 g) were thoroughly dried, then dissolved in ^{18}O enriched (nominally 1.6%) water (10 ml, 25°) and rapidly mixed with a solution of normal NaOH (0.8 g) in enriched water (5 ml, 25°). Reaction was allowed to proceed for 5 sec, during which time a small portion (~2 ml) was withdrawn for determination of the solvent oxygen composition. (Copious precipitation of $[\text{Co}(\text{NH}_3)_5(\text{OOCH})\text{Cl}_2]$ occurred within the 5 sec.) HClO_4 (12 M, 2 ml) was added to quench the reaction and the mixture diluted to ~500 ml with normal water and sorbed onto H^+ form Dowex 50Wx2 cation-exchange resin. Elution with 1 M NaClO_4 (pH 3) removed a major red band ($[(\text{NH}_3)_5\text{CoOOCH}]^{2+}$) and a minor orange band ($[(\text{NH}_3)_5\text{CoOH}_2]^{3+}$) was then eluted with 3 M HCl (column temperature 25°). The most concentrated central portion of this second eluate was mixed with an equal volume of ice-cold concentrated (60%) HBr and kept on ice to deposit small orange crystals of $[(\text{NH}_3)_5\text{CoOH}_2]\text{Br}_3$. Approximately 2 hr was required for this experiment. The crystals were washed thoroughly with methanol and ether and dried under high vacuum (at 25°) for 1 hr. The oxygen isotope composition was determined by two methods. (i) The bulk of the solid sample was heated at 80° under high vacuum in a closed system for 12 hr. The released water was distilled under high vacuum onto $\text{Hg}(\text{CN})_2\text{-HgI}_2$ contained in a breakseal tube which was then sealed and heated at 400° for 12 hr. The CO_2 formed⁸ was isolated, purified chromatographically on *sec*-butyl phthalate absorbed on Chromosorb P, and analyzed mass spectrometrically. (ii) A small portion of $[(\text{NH}_3)_5\text{Co}(\text{OH}_2)]\text{Br}_3$ was mixed with $\text{Hg}(\text{CN})_2\text{-HgI}_2$ and then treated as the water in (i).

To determine the solvent oxygen composition the reaction mixture sample was distilled under high vacuum to obtain solvent free of complexes. Because of the presence of $\text{HN}(\text{CH}_3)_2$ the distillate could not conveniently be equilibrated directly with CO_2 and consequently was analyzed by pyrolysis with $\text{Hg}(\text{CN})_2\text{-HgI}_2$ as in experiment i above.

(2) $[\text{Co}(\text{NH}_3)_5\text{DMF}]\text{Cl}_3$ (1 g), prepared from $[\text{Co}(\text{NH}_3)_5\text{DMF}](\text{ClO}_4)_3$ (2 g) as above, was dissolved in ^{18}O enriched water (3 ml, 25°) and mixed with a solution of normal NaOH (0.3 g) in enriched water (2 ml, 25°). The mixture was stirred vigorously for 15 sec to allow $[\text{Co}(\text{NH}_3)_5\text{OOCH}]\text{Cl}_2$ to precipitate; then this solid was filtered off. The oxygen composition of the solvent in the filtrate was determined as in experiment 1. The $[\text{Co}(\text{NH}_3)_5\text{OOCH}]\text{Cl}_2$ was washed thoroughly with methanol and ether and dried under high vacuum for 24 hr (25°). To determine its oxygen composition, a portion was pyrolyzed with $\text{Hg}(\text{CN})_2\text{-HgI}_2$. To establish that both oxygen atoms were sampled by this procedure, another portion was subsequently converted to the hexachlorothallate salt by addition of ice-cold H_3TiCl_6 (0.1 M in 6 M HCl) to its ice-cold solution in water. The precipitated solid was dried under high vacuum at 40° for 12 hr, then heated for 6 hr at 110° in an evacuated tube to release CO_2 . This method is known⁶ to result in sampling of both oxygen atoms. The chloride salt was also submitted for elemental analysis.

Anal. Calcd for $\text{CoCH}_6\text{N}_5\text{O}_2\text{Cl}_2$: Co, 22.67; C, 4.62; H, 6.20; N, 26.94. Found: Co, 23.2; C, 5.05; H, 6.09; N, 27.11.

Results and Discussion

The mode of bonding of DMF to Co in $[\text{Co}(\text{NH}_3)_5\text{DMF}]^{3+}$ must be established in order to interpret the kinetic behavior. It has been noted previously⁴ that the visible spectrum of the complex is indicative of a CoN_5O chromophore, and the position of the carbonyl stretching absorption in the infrared is not inconsistent with O bonding of DMF.^{5,9} However, the most definitive evidence is contained in the pmr spectrum. The appearance of a doublet for the N- CH_3 resonances in the pmr spectrum of free DMF has been interpreted as due to restricted rotation about the OC-N< bond as a result of partial double bonding involving the nitrogen lone pair of electrons.^{10,11} The retention of this doublet in the spectrum of $[\text{Co}(\text{NH}_3)_5\text{DMF}]^{3+}$ implies that such double bonding is retained, prohibiting

coordination of the nitrogen atom to the metal. The possibility that the nitrogen is coordinated and the methyl doublet results from coupling to the formyl proton may be excluded since the formyl proton resonance occurs as a single, sharp peak. Also such coupling is not detected in the free ligand spectrum. We therefore conclude that $[\text{Co}(\text{NH}_3)_5\text{DMF}](\text{ClO}_4)_3$ is the oxygen bonded linkage isomer.⁵

Coincidence of pmr resonances with those of added authentic compounds established that $[\text{Co}(\text{NH}_3)_5\text{OOCH}]^{2+}$, $\text{NH}(\text{CH}_3)_2$, and DMF were among the products of base hydrolysis of $[\text{Co}(\text{NH}_3)_5\text{DMF}]^{3+}$. Both product complexes, $[\text{Co}(\text{NH}_3)_5\text{OOCH}]^{2+}$ and $[\text{Co}(\text{NH}_3)_5\text{OH}_2]^{3+}$ (from $[\text{Co}(\text{NH}_3)_5\text{OH}]^{2+}$), were identified spectrally in ion-exchange eluates from separation of quenched reaction mixtures and characterized spectrally and analytically as the solids $[\text{Co}(\text{NH}_3)_5\text{OOCH}](\text{ClO}_4)_2$ and $[\text{Co}(\text{NH}_3)_5\text{OH}_2]\text{Br}_3$, subsequently isolated from these eluates. Under the conditions of the experiments neither DMF nor formate ion undergoes appreciable reaction with $[\text{Co}(\text{NH}_3)_5\text{OH}]^{2+}$ and base hydrolysis of $[\text{Co}(\text{NH}_3)_5\text{OOCH}]^{2+}$ is negligible.¹² Limited measurements of the product ratio $[\text{Co}(\text{NH}_3)_5\text{OH}]^{2+}/[\text{Co}(\text{NH}_3)_5\text{OOCH}]^{2+}$, determined spectrophotometrically following ion-exchange separation, were in good agreement with more extensive determinations of the ratio $[\text{DMF}]/[\text{HN}(\text{CH}_3)_2]$, measured by integration of pmr peaks (Table I). The latter method, though less

Table I. Temperature Dependence of Product Distribution $[\text{Co}(\text{NH}_3)_5\text{DMF}]^{3+}$ Base Hydrolysis

| Temp, °C | % DMF ^a | $[\text{DMF}]/[\text{HN}(\text{CH}_3)_2]$ | % $[\text{Co}(\text{NH}_3)_5\text{OH}]^{2+}$ b | $[\text{Co}(\text{NH}_3)_5\text{OH}]^{2+}/[\text{Co}(\text{NH}_3)_5\text{OOCH}]^{2+}$ |
|----------|--------------------|---|--|---|
| 0 | ~2 | ~0.02 | 2.7 | 0.028 |
| 11.0 | 5 ± 1 | 0.053 | | |
| 15.0 | 8.5 ± 0.6 | 0.093 | | |
| 25.0 | 12.0 ± 0.5 | 0.136 | | |
| 35.0 | 22 ± 1 | 0.282 | 24 | 0.316 |

^a Pmr data—results calculated as the average of between five and ten separate integrations. $[\text{OD}^-]$ was varied between 0.1 and 1.0 M without significant variation in relative peak heights being detected. (b) Spectrophotometric data—after ion-exchange separation. Reaction conducted in 0.5 M NaOH, $I = 1.0$ (NaClO_4).

accurate at the lower temperatures, was less susceptible to small errors due to product hydrolysis at the higher temperatures. Variation of the ratio $[\text{DMF}]/[\text{HN}(\text{CH}_3)_2]$ during the course of reaction was not detected. Thus, the hydrolysis involves competitive paths and two possible reaction schemes are shown in Schemes I and II.

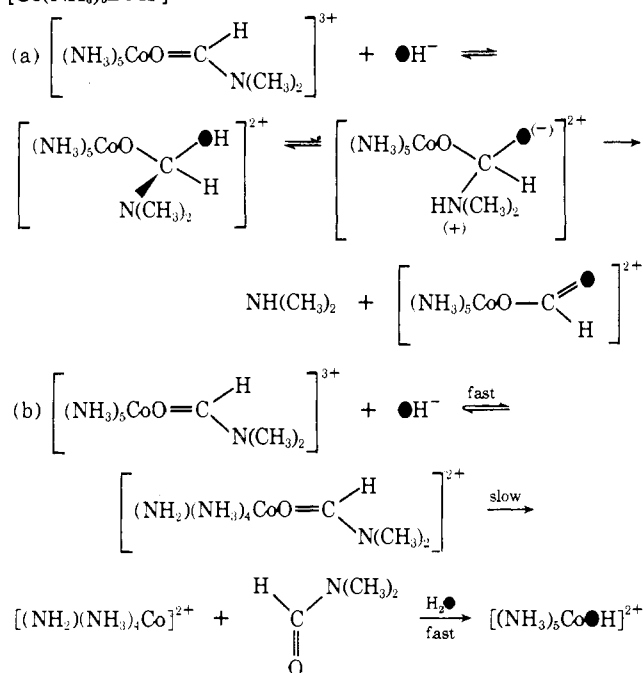
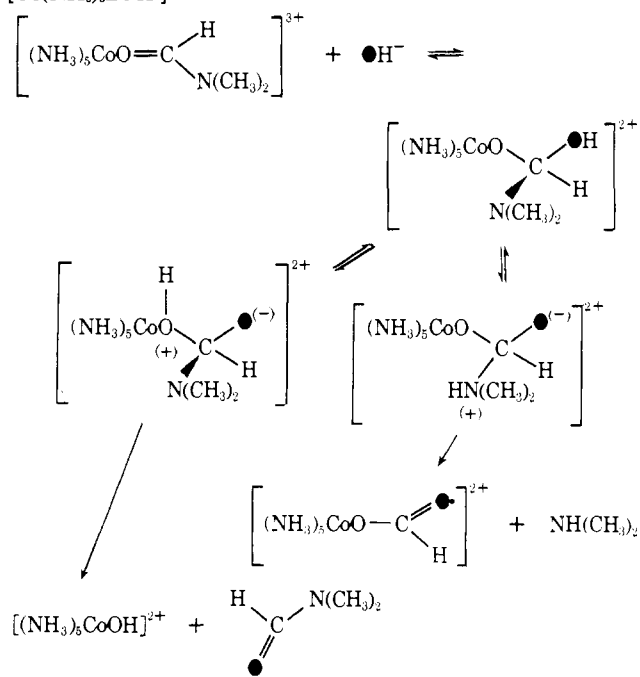
The schemes differ in the paths leading to $[\text{Co}(\text{NH}_3)_5\text{OH}]^{2+}$ and are readily distinguished by oxygen tracer experiments. Only the conjugate base reaction (Scheme 1b) leads to incorporation of solvent oxygen, provided that the reactant $[\text{Co}(\text{NH}_3)_5\text{DMF}]^{3+}$ complex does not undergo oxygen exchange prior to hydrolysis. Such exchange would, of course, lead to >50% incorporation of label in the $[\text{Co}(\text{NH}_3)_5\text{OOCH}]^{2+}$ product and this was not observed in the oxygen isotope

(12) A value of $5.8 \times 10^{-4} \text{ M}^{-1} \text{ sec}^{-1}$ has been determined⁶ for the second-order rate constant for the reaction (involving Co-O bond cleavage) at 25°.

(8) M. Anbar and S. Guttman, *J. Appl. Rad. Isotopes*, **5**, 233 (1959).
 (9) E. W. Randall, C. M. Silcox-Yolder, and J. J. Zuckerman, *Inorg. Chem.*, **5**, 2240 (1966).

(10) W. D. Phillips, *J. Chem. Phys.*, **23**, 1363 (1955).

(11) H. Gutowsky and C. H. Holm, *J. Chem. Phys.*, **25**, 1228 (1956).

Scheme I. Possible Reaction Scheme for the Base Hydrolysis of $[\text{Co}(\text{NH}_3)_5\text{DMF}]^{3+}$ **Scheme II.** Possible Reaction Scheme for the Base Hydrolysis of $[\text{Co}(\text{NH}_3)_5\text{DMF}]^{3+}$ 

composition of the products of the base hydrolysis of $[\text{Co}(\text{NH}_3)_5\text{DMF}]^{3+}$ in ^{18}O enriched solvent, Table II. Considering that some oxygen exchange in $[\text{Co}(\text{NH}_3)_5\text{OH}_2]^{3+}$ would have occurred in the 2 hr required to isolate the bromide salt,¹³ it is apparent that the oxygen of the $[\text{Co}(\text{NH}_3)_5\text{OH}]^{2+}$ was derived largely from the solvent. The extent of incorporation of solvent oxygen in the $[\text{Co}(\text{NH}_3)_5\text{OOCH}]^{2+}$ ion shows only one of the oxygen atoms of the complex was derived from this source. Since oxygen exchange in $[\text{Co}(\text{NH}_3)_5\text{OH}]^{2+}$ is very slow under the conditions,¹⁴ this ion must derive from a path involving Co-O fission and not including $[\text{Co}(\text{NH}_3)_5\text{OOCH}]^{2+}$ as an intermediate. Provided

(13) A. C. Rutenberg and H. Taube, *J. Chem. Phys.*, **20**, 825 (1952).(14) H. R. Hunt and H. Taube, *J. Amer. Chem. Soc.*, **80**, 2642 (1958).**Table II.** Oxygen Isotope Analysis of Products of Base Hydrolysis of $[\text{Co}(\text{NH}_3)_5\text{DMF}]^{3+}$ in ^{18}O Enriched Aqueous Sodium Hydroxide

| Species | R | % incorporation of solvent O ^a |
|---|---------------------|---|
| 1. Solvent | 0.0285 | |
| $[\text{Co}(\text{NH}_3)_5\text{OH}_2]\text{Br}_3$ | 0.0226 ^b | 77 |
| | 0.0233 ^c | 80 |
| 2. Solvent | 0.0306 | |
| $[\text{Co}(\text{NH}_3)_5\text{OOCH}]\text{Cl}_3$ | 0.0169 | 50 |
| $[\text{Co}(\text{NH}_3)_5\text{OOCH}]\text{Cl}_3(\text{TiCl}_4)_2$ | 0.0161 | 47 |
| 3. Standard CO ₂ | 0.00346 | |

^a Calculated as $100\{[R_{\text{comp}}/(2 + R_{\text{comp}})] - [R_{\text{CO}_2}/(2 + R_{\text{CO}_2})]/[R_{\text{sol}}/(2 + R_{\text{sol}})] - [R_{\text{CO}_2}/(2 + R_{\text{CO}_2})]\}$, $R = m/e$ 46/44. ^b CO₂ obtained from H₂O generated by thermal dehydration of $[\text{Co}(\text{NH}_3)_5\text{OH}_2]\text{Br}_3$. ^c CO₂ obtained by direct pyrolysis of $[\text{Co}(\text{NH}_3)_5\text{OH}_2]\text{Br}_3$ with $\text{Hg}(\text{CN})_2\text{-HgI}_2$.

Co-O cleavage (aquation) in the tetrahedral intermediate does not occur, a separate base catalyzed path is required for this product, and we ascribe this to the S_NICB process proposed for other pentaamminecobalt(III) acido complexes.

The activation enthalpies found in the (S_NICB) base hydrolysis of pentaamminecobalt(III) complexes are typically ~ 30 kcal mol⁻¹,¹⁵ whereas those found in the base hydrolysis of simple amides are considerably smaller, typically ~ 15 kcal mol⁻¹.¹⁶ Thus, if Scheme I represents the base hydrolysis of $[\text{Co}(\text{NH}_3)_5\text{DMF}]^{3+}$, a marked temperature dependence of the product ratio would be expected. As is shown in Table I, this was found. From a linear plot of log (product ratio) vs. $1/T$ these data were used to interpolate values of the product ratio appropriate to the temperatures at which rates of disappearance of $[\text{Co}(\text{NH}_3)_5\text{DMF}]^{3+}$ were measured.

Rate constants for the disappearance of $[\text{Co}(\text{NH}_3)_5\text{DMF}]^{3+}$ were obtained from linear plots of log ($A_t - A_\infty$) against time ($> 3t_{1/2}$). Values of A_∞ were taken at $\sim 20t_{1/2}$ since interference from hydrolysis of both formate and ammine ligands was detected over longer periods particularly at the higher temperatures. No deviation from a first-order dependence on $[\text{OH}^-]$ was observed although the variation in $[\text{OH}^-]$ was limited to maintain the conditions for pseudo-first-order kinetics. Values for the second-order rate constants for $[\text{Co}(\text{NH}_3)_5\text{DMF}]^{3+}$ disappearance in base and their division into contributions from the separate reaction paths are given in Table III. Activation parameters thereby calculated for the reaction path forming the formate complex are $\Delta H^\ddagger = 13.8 \pm 0.5$ kcal mol⁻¹ and $\Delta S^\ddagger = -12 \pm 1$ cal deg⁻¹ mol⁻¹ and for the conjugate base path to $[(\text{NH}_3)_5\text{CoOH}]^{2+}$ are $\Delta H^\ddagger = 28 \pm 1$ kcal mol⁻¹ and $\Delta S^\ddagger = +35 \pm 5$ cal deg⁻¹ mol⁻¹.

The rate data for $[\text{Co}(\text{en})_2\text{glyN}(\text{CH}_3)_2]^{3+}$ were analyzed as before¹⁰ and the rate constants given in Table III lead to the activation parameters $\Delta H^\ddagger = 13.5 \pm 0.5$ kcal mol⁻¹ and $\Delta S^\ddagger = -14 \pm 1$ cal deg⁻¹ mol⁻¹.

The values of the parameter k_C indicate the extent to which base hydrolysis of the O-bound amide is promoted by coordination to Co(III). From published

(15) F. Basolo and R. G. Pearson "Mechanisms of Inorganic Reactions," 2nd ed, Wiley, 1967, p 180.

(16) R. J. E. Talbot in "Comprehensive Chemical Kinetics," C. H. Bamford and C. F. H. Tipper, Ed., Vol. 10, Elsevier, Amsterdam, 1972, p 275.

Table III. Rate Constants for the Reactions between $[\text{Co}(\text{NH}_3)_5\text{DMF}]^{3+}$ and $[\text{Co}(\text{en})_2\text{glyN}(\text{CH}_3)_2]^{3+}$ and Hydroxide Ion as a Function of Temperature^d

| Temp, °C | [NaOH], M | $10^3 k_{\text{obsd}}$, sec ⁻¹ | k_{OH} , M ⁻¹ sec ⁻¹ ^a | k_{C} , M ⁻¹ sec ⁻¹ ^b | k_{CB} , M ⁻¹ sec ⁻¹ ^c |
|--|-----------|--|--|---|--|
| (i) $[\text{Co}(\text{NH}_3)_5\text{DMF}]^{3+}$ | | | | | |
| 32.1 | 0.10 | 25, 23, 24, 25, 23, 23 | 2.4 | 1.9 | 0.47 |
| 25.0 | 0.05 | 6.0, 6.0, 6.0 | | | |
| | 0.25 | 33, 32, 33 | 1.3 | 1.1 | 0.17 |
| | 0.50 | 63, 68, 68, 68 | | | |
| 19.8 | 0.10 | 7.2, 7.2, 7.3 | | | |
| | 0.50 | 36, 35 | 0.72 | 0.65 | 0.068 |
| 16.0 | 0.10 | 5.6, 5.2 | | | |
| | 0.50 | 30, 28, 26, 26, 27 | 0.55 | 0.51 | 0.040 |
| 7.8 | 0.50 | 13, 14, 13, 14 | 0.27 | 0.26 | 0.011 |
| (ii) $[\text{Co}(\text{en})_2(\text{glyN}(\text{CH}_3)_2)]^{3+}$ | | | | | |
| 34.6 | 0.200 | 33.4, 35.4 | 1.74 | | |
| | | 34.8, 35.4 | | | |
| 25.0 | 0.200 | 17.2, 17.6, 17.2 | 0.87 | | |
| 14.5 | 0.200 | 7.11, 7.28, 7.28 | | | |
| | | 7.44, 7.11 | 0.36 | | |
| 4.5 | 0.200 | 2.81, 2.67 | 0.13 | | |
| | | 2.59, 2.64 | | | |

^a Mean rate constant for the disappearance of complex: $k_{\text{OH}} = k_{\text{obsd}}/[\text{OH}^-]$. For $[(\text{NH}_3)_5\text{CoDMF}]^{3+}$ $k_{\text{OH}} = k_{\text{C}} + k_{\text{CB}}$. ^b Rate constant for the formation of $[\text{Co}(\text{NH}_3)_5\text{OOCH}]^{2+}$ and $\text{HN}(\text{CH}_3)_2$. ^c Rate constant for the formation of $[\text{Co}(\text{NH}_3)_5\text{OH}]^{2+}$ and DMF by the $\text{S}_{\text{N}}1\text{CB}$ process. The expression $k_{\text{C}}/k_{\text{CB}} = [\text{Co}(\text{NH}_3)_5\text{OOCH}]^{2+}/[\text{Co}(\text{NH}_3)_5\text{OH}]^{2+} = [\text{HN}(\text{CH}_3)_2]/[\text{DMF}]$ was used to calculate these values. ^d $I = 1.0(\text{NaClO}_4)$; $[\text{complex}] = 5 \times 10^{-3} \text{ M}$ ($[\text{Co}(\text{NH}_3)_5\text{DMF}]^{3+}$), 10^{-3} M ($[\text{Co}(\text{en})_2\text{glyN}(\text{CH}_3)_2]^{3+}$).

data for the hydrolysis of uncoordinated DMF,¹⁷ the activation parameters $\Delta H^\ddagger = 14.2 \text{ kcal mol}^{-1}$, $\Delta S^\ddagger = -28 \text{ cal deg}^{-1} \text{ mol}^{-1}$ may be calculated. Clearly, as in other metal-activated reactions^{1d, 18-20} the activation is evidenced largely in ΔS^\ddagger , corresponding to a temperature independent acceleration which amounts to a factor of nearly 10^4 . While it is tempting to rationalize this effect on ΔS^\ddagger in terms of desolvation arising from charge neutralization in the metal ion complex-hydroxide ion transition state,¹⁸ such an argument cannot account for the fact that attack by neutral nucleophiles is apparently enhanced through an increase in ΔS^\ddagger .^{1c, 21} A more general rationalization can, however, be offered on the basis of the assumption that addition of any nucleophile to the free substrate results in generation of a transition state of considerable polarity or H-bonding ability. Formation of this transition state would then require markedly increased solvent structuring in its vicinity, corresponding to a negative contribution to ΔS^\ddagger . In a highly positively charged metal ion-substrate complex, solvent structuring about the ground-state molecule would be extensive and approach of a nucleophile to form the transition state would lead to only a slight change in solvation requirements (possibly in either direction).²² Thus,

(17) S. Langlois and A. Broche, *Bull. Soc. Chim. Fr.*, 812 (1964).

(18) G. L. Johnson and R. J. Angelici, *J. Amer. Chem. Soc.*, **93**, 1106 (1971).

(19) (a) R. Breslow, R. Fairweather, and J. Keana, *J. Amer. Chem. Soc.*, **89**, 2135 (1967); (b) R. Breslow and M. Schmir, *ibid.*, **93**, 4960 (1971).

(20) Note, however, that exceptions are known where the effect on ΔH^\ddagger is also significant; see ref 18 and D. Pinnell, G. B. Wright and R. B. Jordan, *J. Amer. Chem. Soc.*, **94**, 6104 (1972).

(21) The activation parameters measured by D. A. Buckingham, J. Dekkers, A. M. Sargeson, and M. Wein, *J. Amer. Chem. Soc.*, **94**, 4032 (1972), for water attack on $[\text{Co}(\text{en})_2\text{glyOEt}]^{3+}$ cannot be compared with those specifically for water attack on free glyOEt, since these are unknown. However, the activation entropies for water attack on a wide variety of esters are typically -40 to $-50 \text{ cal deg}^{-1} \text{ mol}^{-1}$; see A. J. Kirby in "Comprehensive Chemical Kinetics," Vol. 10, C. H. Bamford and C. F. H. Tipper, Ed., Elsevier, 1972, pp 156-157.

(22) This argument is also consistent with the fact (see references quoted in ref 18) that the effect on ΔS^\ddagger diminishes as the charge on the metal ion-substrate complex decreases.

the "activating" effect of the metal ion could be viewed as arising from its elimination of an inhibitory solvation requirement in the uncoordinated substrate reaction. Alternatively, it is possible that facilitation of addition to the carbonyl center and stabilization of the tetrahedral intermediate by the metal ion²³ has rendered elimination, rather than addition, the rate-determining step of the hydrolysis. Activation parameters for the spontaneous and metal ion promoted processes are then no longer strictly comparable, though entropic factors (as above and others²³) would still be expected to be important.

The data for the amide cleavage in $[\text{Co}(\text{NH}_3)_5\text{DMF}]^{3+}$ are remarkably similar to those for the analogous hydrolysis of $[\text{Co}(\text{en})_2\text{glyN}(\text{CH}_3)_2]^{3+}$ which yields chelated glycine and dimethylamine. It would appear, therefore, that the involvement of the (coordinated) carbonyl group in a five-membered chelate ring is not an important factor in determining the reactivity, though it may lead to repression of a path involving base catalyzed dissociation of the carbonyl oxygen from the metal.²⁴ This conclusion is supported by studies of similar reactions in six-membered chelate ring systems.² Thus, it is apparent that if carbonyl coordination is the mode of activation utilized by hydrolytic metalloenzymes²⁵ such as carboxypeptidase A only a single coordination site need be available for substrate attachment, although considerable catalysis over and above that demonstrated here is required.

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(23) D. A. Buckingham, J. Dekkers, and A. M. Sargeson, *J. Amer. Chem. Soc.*, **95**, 4173 (1973).

(24) For the base hydrolysis of chelated glycinamide in $[\text{Co}(\text{en})_2\text{glyNH}_2]^{3+}$ it has been shown (D. A. Buckingham, D. M. Foster, and A. M. Sargeson, *J. Amer. Chem. Soc.*, **92**, 6151 (1970)) that a possible reaction path involving base catalyzed ring opening followed by rapid intramolecular hydrolysis is not involved to an appreciable extent. It is assumed the same is true for glycinedimethylamide.

(25) See ref 1c and references therein.