Linkage Isomerism in Cobalt(III) Pentaammine Complexes of 2-Pyridone

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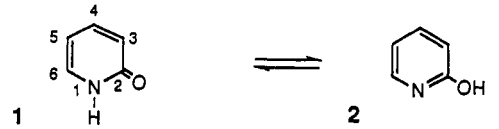
The reactions of the heterocyclic ligand 2-pyridone, coordinated to the cobalt(III)pentaammine moiety, have been investigated. The complex has been crystallized as the oxygen- and nitrogen-bonded linkage isomers in both protonated (neutral ligand) and deprotonated forms, a first for an ambidentate ligand–complex system, and these materials have been characterized by UV–visible, infrared, and ^1H and ^{13}C NMR spectroscopy. In aqueous solution (I = 1.0 M, NaCl, 25 °C) the pK_a of the O-bonded isomer is 6.83 ± 0.05, and that of the N-bonded form, 3.56 ± 0.05; these values are surprisingly close and are even closer in Me_2SO. In acid solution (water or Me_2SO) the (2-pyridone-*O*)pentaammine complex reacts slowly ($k_H = 1.3 \times 10^{-5}$ s^{-1}, 0.5 M $HClO_4$, 25 °C) and the products are the free ligand and the solvento complex; no N-bonded isomer is formed concurrently. In weakly basic solution the deprotonated O-bonded isomer rearranges slowly and completely to form the deprotonated N-bonded linkage isomer ($k_{ON(1)} = 1.2 \times 10^{-5}$ s^{-1}, 25 °C); the rate coincidentally is very much the same as in acid, but the reactions are different. The isomerization reaction has also been observed in Me_2SO, but it is both slower (ca. 4-fold) and detectably reversible (90% N- and 10% O-bonded forms, commencing with either isomer). The complex undergoes a very mild base-catalyzed reaction ($k_{OH} = 9 \times 10^{-5}$ M^{-1} s^{-1}; I = 1.0 M, $NaClO_4$, 25 °C), but up to 0.1 M OH^- (I = 1 M) no appreciable base-catalyzed hydrolysis was observed; decomposition is a problem above ca. 0.02 M OH^-. In acid solution (water or Me_2SO) the N-bonded isomer is protonated on oxygen, with essential retention of the imine-like bonded nitrogen. In aqueous acid the 2-pyridone-*N* complex rearranges with a small amount (18%) of parallel solvolysis to form the 2-pyridone-*O* complex, and the latter subsequently solvolyzes. The products of this reaction have been isolated by ion exchange chromatography and identified by visible spectrophotometry. The rates of rearrangement ($k_{NO(2)} = 3.8 \times 10^{-6}$ s^{-1}) and direct solvolysis ($k_s = 8.2 \times 10^{-7}$ s^{-1}) of the 2-pyridone-*N* complex have been determined. In Me_2SO, the protonated N-bonded form also rearranges and solvolyses concurrently; more than 90% is the O-bonded linkage isomer. The O-bonded form in Me_2SO initially gives significant amounts of protonated N-bonded isomer along with solvolysis. This apparent divergence from the aqueous chemistry is explained in terms of the position of the N/O equilibrium. The positions of the N/O equilibria for protonated and deprotonated isomers are related to the relative pK_as, and this matter and the observed solvent effects are discussed. The chemistry of these complexes is compared with that of the succinimide analogues, and the factors affecting O to N linkage isomerization reactions in coordinated amides are discussed.

Introduction

There have been many complexes of 2-pyridone (2H-pyridine-2-one) synthesized in which it occurs as a deprotonated bridging ligand.[1,2] The platinum(II) complexes of this type have been used to elucidate the structure of the platinum blues.[3] In contrast, only a few monodentate complexes have been prepared, an oxygen-bonded pentaamminecobalt(III) complex[4,5] and two platinum(II) complexes where the heterocycle is bonded through the nitrogen in the protonated and deprotoned forms.[6]

The heterocycle may exist as the keto **1** or the enol **2** tautomer and is potentially an ambidentate ligand. The position of the



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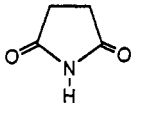
equilibrium is very solvent-dependent and in water the keto tautomer predominates.[7] In the solid state 2-pyridone has a planar unsymmetrical ring structure and takes the keto form, so an amide functional group forms part of the ring.[8] The amide proton is acidic in aqueous solution, pK_a 11.6 at 25 °C;[9] the uncharged ligand can also be protonated (pK_a 1.25).[10] This ligand in certain ways resembles succinimide **3**. We have studied its coordination chemistry to determine whether linkage isomerization and ligand hydrolysis occur as they do in the succinimide complexes.[11]

The oxygen-bonded pentaamminecobalt(III) complex of 2-pyridone **4** has been synthesized previously for electron-transfer studies[4,5] but its coordination chemistry has not been otherwise investigated.



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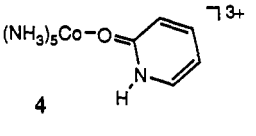

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Results

The ^1H and ^{13}C NMR spectra for the free pyridone ligand, its acid and base forms, and the protonated (neutral) and deprotonated (anionic) oxygen and nitrogen-bonded pentaamminecobalt(III) complexes are given in Tables 1 and 2; the atom numbering is shown in diagram **1** above. The spectra for the

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Table 1. ^{1}H NMR Spectral Data (δ, ppm) for 2-Pyridone and Its Pentaamminecobalt(III) Complexes, and (Pyridine)pentaamminecobalt(III), in Me_2SO-d_6 at 20 °C

	NH_3				
	cis	*trans*	>NH	others[a,b]	assignt[c,d]
2-pyridone			11.76	6.14, t	H-5
				6.33, d	H-3
				7.39, m	H-4, H-6
2-pyridonium[e]				6.28, t	H-5
				6.43, d	H-3
				7.47, m	H-4, H-6
2-pyridone-*O*	3.96	2.65	12.94	6.72, d	H-3
				6.88, t	H-5
				7.93, m	H-4, H-6
2-pyridonato-*O*	3.89	2.62		6.40, t	H-3
				6.49, d	H-5
				7.24, t	H-4
				7.78, d	H-6
2-pyridone-*N*	3.71	3.26		6.85, d	H-3
				7.10, t	H-5
				7.75, d	H-6
				7.89, t	H-4
2-pyridonato-*N*	3.80	3.18		6.00, d	H-5
				6.30, t	H-3
				7.10, d	H-4
				7.30, t	H-6
(pyridine)pentaammine	3.68	3.46		7.75	H-3, H-5
				8.16	H-4
				8.38	H-2, H-6

[a] Centers of multiplets; shifts vs TMS. [b] d = doublet, t = triplet; often fine structure within these; m = multiplet. [c] See diagram **1** for numbering key. [d] Assignments based on well-known literature values for pyridine; refer to text for pyridone assignments. [e] Excess CF_3SO_3H added.

Table 2. ^{13}C NMR Spectral Data (δ, ppm) for 2-Pyridone, Its Pentaamminecobalt(III) Complexes and (Pyridine)pentaamminecobalt(III), in Me_2SO-d_6 at 20 °C

	C-2[a]	C-3	C-6	C-5	C-4
2-pyridone	163.0	120.1	135.7	105.4	141.3
2-pyridone-*O*	165.5	118.4	137.8	112.0	145.2
2-pyridonato-*O*	173.0	116.6	137.3	110.6	146.2
2-pyridone-*N*	168.1	118.7	142.9	113.2	150.2
2-pyridonato-*N*	174.0	116.9	138.2	109.8	148.1
(pyridine)pentaammine	153.1[b]	126.9	140.3	126.9	153.1

[a] See diagram **1** for numbering key; assignments follow from literature values for the free ligands. [b] –CH= not >C=O as in the 2-pyridone complexes.

related pyridinepentaamminecobalt(III) complex were recorded to assist in signal assignments. The spectral data for D_2O as solvent, required to interpret reactions in water followed by ^{1}H and ^{13}C NMR, are given in the supplementary material (Tables III and IV).

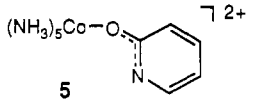
At 300 MHz, the free ligand proton coupling patterns are essentially first order, and this is also true of its complexes. Thus there are essentially two doublets and two triplets, with some fine structure; one doublet and its associated triplet has a greater gap. Only the absolute shifts and relative order of doublets and triplets change from one pyridone species to another. The couplets occur grouped, a doublet with the wider triplet at lower field, and the wider doublet with the narrow triplet at higher field. In some cases a doublet and its associated triplet are overlaid, but always the essential first-order coupling pattern remains, and a change in solvent (D_2O, $CDCl_3$, or Me_2SO-d_6) splits the overlay to confirm the doublet–triplet patterns. These observations and a 2D NMR experiment (DQCOSY) confirmed the proton couplings. Thus, the "inner" protons H_4 and H_5 comprise the triplets, and the outer protons H_3 and H_6, the doublets. The assignment of any one proton now leads automatically to the correct assignment of the others.

The proton-decoupled ^{13}C NMR spectrum for the free ligand had been previously assigned,[12] but a 2D NMR study (HETCOR) suggested that the assignments for C_6 and C_4 were reversed. Further, in a high resolution standard proton decoupled ^{13}C NMR, two of the five carbons had only one pair of ^{13}C satellites arising from ^{13}C–^{13}C coupling (the others each had two pairs); clearly these are C_2 and C_6. The magnitude of the ^{13}C–^{13}C coupling constants confirmed which carbon was directly connected to which. All carbons and their associated protons could therefore be assigned unambiguously; the highest field signal (doublet) in the ^{1}H NMR is H_5, in agreement with an earlier assignment.[13]

O-Bonded Pyridone Isomer. The 2-pyridone-*O* complex has been synthesized analytically pure by reacting the ligand with $[(NH_3)_5CoOSO_2CF_3](CF_3SO_3)_2$[14,15] in acetone. ^{1}H NMR spectra (Table 1) of the free ligand and the 2-pyridone-*O* complex suggest that the one tautomer, the keto form, is predominant; a broad >NH peak is observed at high frequency. The location of the cis and trans ammonia signals in this spectrum is characteristic of the Co–N_5O chromophore;[16] so too is the visible spectrum (ϵ_{524} 106 M^{-1} cm^{-1}).[17] The infrared spectrum of 2-pyridone has a large broad band for the NH stretching vibration at 3400 cm^{-1}; this is indicative of the intermolecular hydrogen bonding which occurs in the solid state[8] and also in liquid phases.[7] The complex however has a sharp NH stretch peak at 3680 cm^{-1}.

It reacts slowly in acid solution. After reaction for 1 week in aqueous acid, chromatography revealed that the only cobalt species present is the aquapentaammine ion. The rate constant for solvolysis in 0.1 M $HClO_4$ was $k_H = 1.3 \times 10^{-5}$ s^{-1} ($t_{1/2}$ = 15 h) and just a little slower in stronger acid and at higher ionic strength, $k_H = 8.7 \times 10^{-6}$ s^{-1}. The rate constant is of the same order of magnitude as that for the acid hydrolysis of oxygen-bonded N-substituted acetamide complexes.[15] No N-bonded isomer was observed at early and intermediate reaction times (vide infra; ^{1}H, ^{13}C NMR, ion-exchange chromatography).

When the 2-pyridone-*O* complex was dissolved in aqueous Tris, an intensely red solution resulted and a pale red-brown complex was crystallized by the addition of $NaClO_4$ solution. The complex is stable in the solid state over many months. The ^{1}H and ^{13}C NMR spectra (Tables 1 and 2) show that the complex contains 2-pyridone while the visible and ^{1}H NMR spectra suggest that it is bonded through oxygen. The >NH signal is absent from the ^{1}H NMR and infrared spectra and the complex elutes from a cation exchange resin as a 2+ ion under basic conditions (pH ≥ 8). We conclude that this complex is the deprotonated species, (2-pyridonato-*O*)pentaamminecobalt(III) (**5**). If a solution of the complex is acidified (water or Me_2SO-d_6) the original protonated 2-pyridone-*O* complex is regenerated. The pK_a of the complex was determined by spectrophotometric titration to be 6.83 ± 0.05 (I = 1.00 M, NaCl, 25 °C), a substantial enhancement in acidity compared with that of the free ligand, 11.6.[9]



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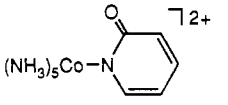

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The changes in the visible spectrum on deprotonation (first-band intensity increases) are not unlike those observed for the succinimide analogue,[11] and suggest some disruption of the chromophore through deprotonation at the remote nitrogen. This disruption is also evident in the ^{1}H NMR spectra; while deprotonation leads to a general shift to higher field of the ligand

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resonances for the free ligand and its O- and N-bonded complexes, the doublet–triplet–doublet–triplet pattern (high to low field) is broken for the deprotonated O-bonded isomer.

N-Bonded Pyridone Isomer. When the 2-pyridonato-*O* complex is dissolved in a buffer solution whose pH is just higher than the pK_a of the complex, it reacts slowly to produce an orange complex which also elutes as a 2+ ion from Sephadex resin. The very soluble complex was crystallized as the diperchlorate and less soluble nitrate perchlorate salts and was characterized by ^{1}H and ^{13}C NMR and UV–visible spectroscopy. The visible spectrum suggests a nitrogen-bonded species, and the ^{13}C NMR spectrum is consistent with the unique ligand being deprotonated 2-pyridone. In cobalt(III) pentaammine complexes the positions of the cis and trans ammine signals in the ^{1}H NMR spectrum are particularly sensitive to the nature of the ligating atom of the heteroligand.[16] In this complex the cis (δ, 3.80) and trans (δ, 3.18) signals point to that ligand being bonded to the cobalt through an sp^2 imine nitrogen. The (pyridine)pentaammine complex was synthesized and its NMR spectra recorded for comparison (Tables 1 and 2). From these data we conclude that the complex is the nitrogen-bonded linkage isomer, (2-pyridonato-*N*)pentaamminecobalt(III) (**6**).

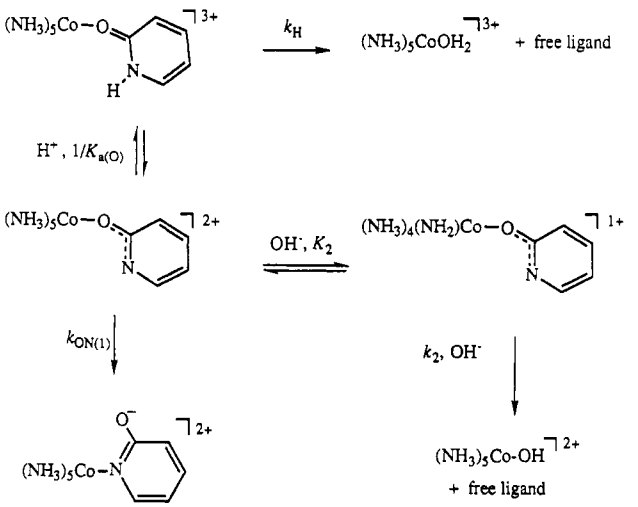
Acidification of a solution of the 2-pyridonato-*N* complex produces such a small change in the visible spectrum (λ or ϵ) that it suggests the protonated species is also an imine. In the ^{1}H NMR there is also little change in the cis and trans ammine signals and in the ligand proton signal pattern other than a general downfield shift which is usual for protonation. From this evidence and by analogy with amido-*N* and other ligand-*N* complexes we assume that the complex is protonated on the remote oxygen, retaining its imine nitrogen.[18] A crystal structure of a platinum(II) complex with 2-pyridone shows that it is N-bonded and O-protonated.[6]

The protonated form was crystallized and characterized, completing the isolation and characterization of all four species for the two linkage isomers, a first in the chemistry of such ambidentate ligand systems, which have attracted a lot of interest over the last 15 years. The pK_a for the N-bonded isomer was determined as 3.56 ± 0.05 (1 M NaCl, 25 °C), some 2 orders of magnitude greater than the O-bonded form. The reduction in pK_a relative to the free ligand and the N-bonded form being more acidic than its O-bonded isomer are usual,[11] but the pK_a difference of just 2.3 units between the isomers is the smallest thus far observed (cf. $[Co(NH_3)_5(CH_3CONH_2)]^{3+}$, $\Delta(pK_a)$ = 8.6[15,19]).

Oxygen to Nitrogen Rearrangement. In water the spontaneous O to N linkage isomerization reaction is observed only when the complex is deprotonated on the ligand. The reaction is slow but eventually goes to completion. In Me_2SO the reaction of the deprotonated complex is even slower (ca. 4-fold), and is reversible. The final composition was determined as 90% N- and 10% O-bonded isomer by both ^{1}H and ^{13}C NMR, a common result starting with either isomer and hence a true equilibrium position. Solvolysis of the deprotonated isomers in either water or Me_2SO was never observed.

The reaction of the O-bonded form in water is mildly base-catalyzed. However above ca. 0.02 M [OH$^-$] the kinetics of the reaction could not be monitored much beyond a half-life because of decomposition, which limited the accuracy of the data. Data were obtained by the usual D_∞ (var) method, but at higher [OH$^-$] for limited D, t data, a fixed (calculated) D_∞ value was used; the isosbestic point (519 nm, ϵ 55.0) between the deprotonated N-bonded isomer and the hydroxopentaamminecobalt(III) species was employed under these conditions because it did not presuppose

Scheme 1



the product distribution. The kinetic data (for pH ≥ 9) fitted the relation $k_{obsd} = k_{ON(1)} + k_{OH}[OH^-]$ where $k_{ON(1)} = (1.2 \pm 0.1) \times 10^{-5}$ s^{-1} and $k_{OH} = (9 \pm 1) \times 10^{-5}$ M^{-1} s^{-1}. The variation of the observed and calculated rate constants with [OH$^-$] is shown in Figure 1 (supplementary material).

In separate experiments acid-quenched product mixtures for reaction in 0.1 M NaOH (I = 1 M, $NaClO_4$, 25.0 °C) were chromatographed after about 25% reaction (at accurately known times), before decomposition had set in. Different eluents were used in different experiments, one which better separates N-bonded isomer from the hydroxopentaammine ion, and another which better separates unreacted O-bonded isomer from its linkage isomer. In no case did we observe any hydroxopentaammine complex. We conclude that base-catalyzed hydrolysis is not competitive with base-catalyzed O- to N- linkage isomerization; although, note that, even in 0.1 M [OH$^-$], the reaction proceeds ca. 50% via the spontaneous pathway. An interesting observation was that for solutions reacted too long in basic solution, hydroxopentaamminecobalt(III) did appear among the products, and this must arise from some subsequent reaction associated with the decomposition products (most likely Co(II)).

Rate constants for reaction in base were also derived from these experiments ($k_{obsd} = (2.1 \pm 0.2) \times 10^{-6}$ s^{-1}), and this value is adjudged better than that directly determined spectrophotometrically for 0.1 M OH$^-$.

The reactions of 2-pyridone-*O* complex are summarized in Scheme 1. From this a rate law with three terms is predicted:

$$k_{obsd} = \frac{1}{(1 + [H^+]/K_{a(O)} + [OH^-]K_2)} \left\{k_{ON(1)} + k_2K_2[OH^-] + \frac{k_H[H^+]}{K_{a(O)}}\right\}$$

To a very good approximation this simplifies to

$$k_{obsd} = \left\{\frac{k_H[H^+]/K_{a(O)}}{(1 + [H^+]/K_{a(O)})} + k_{ON(1)} + \frac{k_{OH}[OH^-]}{(1 + K_2[OH^-])}\right\}$$

where $k_{OH} = k_2K_2$. The first term corresponds to reaction in acid, the middle term to reaction in neutral solution, and the last term to reaction in base; k_H, $k_{ON(1)}$, and k_{OH} are the constants determined experimentally from the kinetics. Note that $K_{a(O)}$, while determined independently, was not obtained from kinetic data because $k_H \sim k_{ON(1)}$, and hence there was very little change in rate on going from acid to weakly basic solution.

Nitrogen to Oxygen Rearrangements. In acid solution the nitrogen-bonded complex isomerizes to the 2-pyridone-*O* species.

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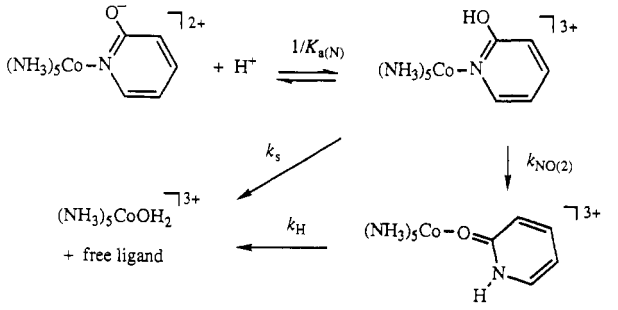
Scheme 2



The latter solvolyzes with a specific rate larger than the specific rate of isomerization, but not greatly so; thus, it was possible to isolate it from the reaction mixture by chromatography, and it was identified by its characteristic visible spectrum. Scheme 2 shows the reactions of the 2-pyridonato-*N* complex. In acid sufficient to protonate all the N-bonded isomer, the simple consecutive first-order reaction scheme:

$$\mathbf{A} \xrightarrow{k_1} \mathbf{B} \xrightarrow{k_2} \mathbf{C}$$

can be applied, where $k_1 = k_{NO(2)} + k_s$ and $k_2 = k_H$; species **B** is the first-formed mixture of the O-bonded isomer and the aquapentaamminecobalt(III) complex, in the ratio $k_{NO(2)}/k_s$ respectively (Scheme 2).[18]

The reaction in aqueous acid was monitored spectrophotometrically and absorbance–time data were fitted by weighted, non-linear least-squares analysis to the following equation which follows[18] from the above reaction scheme:

$$D = \left[(D_0 - D_\infty) + \frac{(k_{NO(2)} + k_s)(D_B - D_\infty)}{k_H - (k_{NO(2)} + k_s)}\right] e^{-(k_{NO(2)} + k_s)t} + \left[\frac{(k_{NO(2)} + k_s)(D_B - D_\infty)}{k_H - (k_{NO(2)} + k_s)}\right] e^{-k_H t} + D_\infty$$

D_0 and D_∞ are the measured absorbances of the solution at the beginning and the end of the reaction. The rate of solvolysis of the protonated O-bonded isomer, k_H, has been measured independently. D_B is a theoretical quantity, the final absorbance of the solution if there had been no consecutive solvolysis of the O-bonded isomer, and is a measure of the relative contributions from the two parallel reaction pathways.

$$D_B = [Co]\{f\epsilon_p + (1-f)\epsilon_q\}$$

where f is the mole fraction of the 2-pyridone-*O* complex at the end of the reaction if there had been no consecutive solvolysis, ϵ_p and ϵ_q are the molar extinction coefficients of the 2-pyridone and aquapentaammine complexes respectively at the wavelength used, and [Co] is the concentration of all the cobalt species present.[18] The data fit led to values for $\{k_{NO(2)} + k_s\}$ and f $\{=k_{NO(2)}/(k_{NO(2)} + k_s)\}$. The other rate terms are defined in Scheme 2. The individual rate constants were thus evaluated from their sum and ratio: $k_{NO(2)} = 3.8 \times 10^{-6}$ s^{-1}, $k_s = 8.2 \times 10^{-7}$ s^{-1}, corresponding to 83% direct linkage isomerization.

In Me_2SO, the protonated N-bonded form also rearranges and solvolyses concurrently (rate constant k_1), and then the O-bonded isomer solvolyses (k_2) completely, as in water. In Me_2SO however, the ratio k_1/k_2 is substantially greater than in water. Indeed, the primary and secondary reactions in Me_2SO coincidentally have almost identical specific rates, and thus the first-formed product distribution was easily determined from the early-time NMR spectra. More than 90% is the O-bonded linkage isomer; a steady state N/O isomer equilibrium (favoring O) is approached before the eventual complete solvolysis of both isomers.

In a separate study the O-bonded form in Me_2SO initially gives significant amounts of protonated N-bonded isomer along with solvolyzed product. The kinetic product distribution was not determined precisely because the N-bonded isomer solvolyzes with about the same rate constant for its production and because the parallel isomerization equilibrium is reversible, favoring the reactant. However it was clear that solvolysis predominated initially.

The equilibrium isomer ratio in Me_2SO could not be directly measured because of competing solvolysis, and we did not carry out detailed kinetic studies which would have allowed its determination. The rates of reaction for both the protonated O- and N-bonded isomers were determined semiquantitatively from the amount of residual isomer at given times in the ^{1}H NMR. These data, coupled with the product distribution results, led to an estimate for the equilibrium N/O ratio (K'_{ON}) of ca. 0.2 for Me_2SO as solvent.

The reaction rate for the O-bonded isomer is only about 3-fold larger than for the N-bonded form in water, and therefore the fact that one does not see any N-bonded isomer as an initial product when commencing with the O-bonded form cannot be kinetic in origin. The contrast to the aqueous chemistry is therefore attributed to the different position of the N/O equilibrium which is more toward the oxygen form for the protonated isomers in water and thus prevents O to N rearrangement being detected. Curiously this is the reverse of the solvent effect for the deprotonated linkage isomers.

Discussion

The oxygen-bonded complex for uncharged 2-pyridone is the more stable form, and in acidic aqueous solution its rate of solvolysis is comparable with that of tertiary amide complexes.[15] In the protonated complexes the N to O rearrangement is essentially complete in water; in common with other amide complexes the protonated N-bonded species is thermodynamically unstable with respect to the oxygen-bonded form so no O to N isomerization reaction is observed. In the synthesis, the kinetic preference for oxygen coordination to cobalt(III) is compatible with the preexisting tautomeric equilibrium of the free ligand in water, i.e., the cyclic amide form as distinct from a hydroxopyridine. The acidity of the ligand is increased by coordination, 6.8 *cf.* 11.6.[9] The change in acidity ($\Delta pK = 4.8$) is comparable with that observed in several amide-*O* complexes[15] but is not as great as that (6.8) found in oxygen-bonded succinimide.[11]

The shift in equilibrium in Me_2SO to the point where there are comparable amounts of both oxygen and nitrogen-bonded isomers has not been seen previously for pentaamminecobalt(III)-ligand systems of this kind. The observation suggests that the equilibrium in water, while clearly well to the side of the O-bonded form (say, >20:1), is not overwhelmingly so, and this is a clear difference from the acyclic amide chemistry. The N- and O-bonded isomer equilibrium for the deprotonated pyridone species is the reverse situation in two senses. First, the N-bonded form is preferred for the acyclic amide, completely in water (say, ≥60:1), while in Me_2SO the O-bonded form assumes increased relative stability (90% N, 10% O). Second, the direction of the solvent effect is opposite to that observed for the protonated isomers. We see no clear explanation since a few kilojoules difference in solvation energies is sufficient to account for such variations.

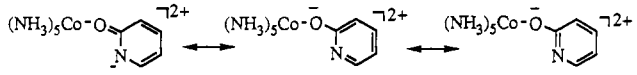
The deprotonated monodentate oxygen-bonded isomer is the second such structure isolated, and it is stable indefinitely in the solid state. The spontaneous isomerization in aqueous solution to the N-bonded form is an intramolecular reaction and is quite slow, $k_{ON(1)} = 1.2 \times 10^{-5}$ s^{-1} at 25 °C, $^1/_{10}$th of the rate of the comparable reaction in the succinimido-*O* complex.[11] The electron-withdrawing substituent in the imide complex enhances the rate and this phenomenon has been observed in N to O isomerization reactions of acyclic monodentate amides.[20] At

(20) Fairlie, D. P.; Angus, P. M.; Fenn, M. D.; Jackson, W. G. *Inorg. Chem.* **1991**, *30*, 1564–1569.

neutral pH the spontaneous linkage isomerization of the 2-pyridonato-*O* complex is the only reaction detected, as was the case with the succinimide system. The lack of concurrent solvolysis in these spontaneous isomerization reactions has been taken as evidence of some associative character in what is principally a dissociative interchange mechanism.[21] Also like the succinimide system, base-catalyzed linkage isomerization was observed, albeit much less pronounced here. This reaction no doubt occurs by the usual S_N1 CB process.

The rate of reaction of the protonated O-bonded isomer is very nearly the same as that for its deprotonated form. This is unusual; in the succinimide system for example, the protonated form is substantially more reactive. However the reactions in acid and neutral conditions are different in the present work. Thus the aquation reaction is faster in acid, which is usual, while the rearrangement is faster for the deprotonated species, which also is usual. Although in acid the O- to N- rearrangement is not observable because the equilibrium is unfavorable, k_{aquation} must be less than $^1/_{20}$th $k_{\text{isomerization}}$.

In most acyclic C-substituted amide complexes lack of ligand hydrolysis has been attributed simply to the dominance of the ligand substitution reaction.[15] This is unlikely to be the case with the 2-pyridonato-*O* ion as the rate of base-catalyzed solvolysis is rather small. A more likely cause is the delocalized electronic structure of the aromatic ligand. The amide group, protonated or deprotonated, is in conjugation with the heterocyclic ring and is not sufficiently polarized by coordination to the metal ion to be susceptible to nucleophilic attack by hydroxide ion (or water):

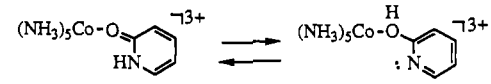


Not surprisingly the 2-pyridonato-*N* complex does not undergo ligand hydrolysis either; in this it resembles acyclic amido-*N* complexes which are not activated by coordination through nitrogen.[22] But this complex is unique among the amido-*N*[20] and imido-*N* complexes[11,23] in that it can be observed to isomerize to the O-bonded form in aqueous solution.

The protonated N-bonded isomer rearranges to the corresponding O-bonded form in water and Me_2SO; the isomerization is measurably reversible in Me_2SO. The N- to O- rearrangement is common to amides,[18,20] peptides,[24] and ureas,[21] but was not observed in the succinimide or phthalimide systems. For the latter, the N-bonded complexes are unusually inert while their O-bonded complexes are unusually reactive, and this fact coupled with arguments based on relative acidities of the O- and N-bonded forms and the (known) position of equilibrium for the deprotonated isomers suggests that the N-bonded isomers of the neutral ligands may be the more stable.[11,23] The observation of *direct* N to O isomerization for the 2-pyridone system in water is the first for an amide. Previous studies of amide N to O isomerization reactions involved primary amides whose rates of solvolysis are much faster than their rates of rearrangement in water; their reactions were observed directly only in sulfolane and Me_2SO.[18,20] In water the 2-pyridone-*O* complex solvolyzes like a tertiary amide complex, sufficiently slowly so that it does not escape detection when formed from the protonated N-bonded isomer.

The N to O rearrangement in acid solution occurs at a rate comparable to that of the formamide-*N* complex, and this is further evidence that the complex is protonated on oxygen. Nitrogen-protonated species rearrange much more rapidly.[18]

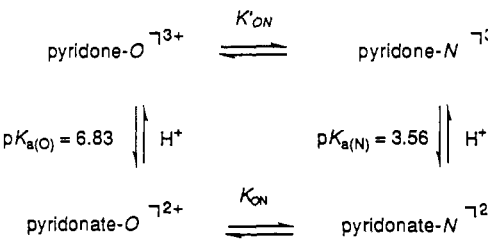
The observation of the reverse process, O to N rearrangement, for the protonated species raises the interesting question of mechanism. In the related succinimide system we argued that protonation of the nitrogen stopped rearrangement to the N-bonded form. Clearly in the present case therefore rearrangement must proceed via its O-protonated tautomer which has an available lone pair on nitrogen:



An alternative mechanism, involving ligand dissociation and reentry, can be eliminated on the grounds that once the ligand is dissociated it remains uncoordinated (in acid conditions the free pyridone is protonated). The rearrangement in this sense is intramolecular, as indeed are most if not all linkage isomerization reactions of this kind.

The pyridone system is the first where we have been able to actually measure linkage isomerization rates for both the 2+ and 3+ complex ions (as distinct from estimating limits). For Me_2SO both forward and reverse reactions were observed for the 2+ and 3+ complex ions. The O to N rate constant was estimated as 5.8×10^{-6} s^{-1} (25 °C), to be compared with 2.8×10^{-6} s^{-1} for the same reaction of the deprotonated species. Surprisingly these are very similar, perhaps reflecting the compensation of having a better (neutral) leaving group but unfavorable tautomeric equilibrium position for the 3+ ion. In contrast, in water the O to N rate constants for the 2+ and 3+ complex ions must differ appreciably, the deprotonated ion being faster by at least a factor of 100; the effect of solvent on the position of the tautomeric equilibrium could account for this. For the N to O rearrangement in Me_2SO, the 3+ ion is about 100-fold more reactive, perhaps simply reflecting the improved leaving group (neutral), a factor not compensated by proton addition to the incoming oxygen (anionic), which might have been expected to have reduced its nucleophilicity.

Finally, it is of interest to see the connectivity between the N- and O-bonded isomer equilibria for the 2+ and 3+ complex ions in relation to the acidity constants:



The analysis for these sorts of cyclic equilibria has been carried out previously, most recently for the analogous succinimide system.[11] We do not have precise equilibrium constant data for water since both the 2+ and 3+ equilibria are all to one side, albeit opposite sides. A relationship exists between the constants, namely:

$$\frac{K'_{ON}}{K_{ON}} = \frac{K_{a(O)}}{K_{a(N)}}$$

Now, given the known relative values of the pK_as, $K_{aO}/K_{aN} = 10^{-3.27}$, it follows that if the 2+ equilibrium lies very substantially to the side of the N-bonded form, e.g. $K_{ON} = 10^3$, then K'_{ON} must be $10^3 \times 10^{-3.27} = 0.5$. But K'_{ON} appears to be less than this ($\leq^1/_{20}$ at least), which implies $K_{ON} = 10^2$ or smaller. The point is that neither the 2+ nor 3+ equilibrium can be substantially to one side, but nevertheless each is sufficiently displaced so that the residual isomer escapes detection.

(21) Fairlie, D. P.; Jackson, W. G. *Inorg. Chim. Acta*, **1988**, *150*, 81–100.
(22) Sigel, H.; Martin, R. B. *Chem. Rev.* **1982**, *82*, 385–426.
(23) Angus, P. M.; Jackson, W. G. Manuscript in preparation.
(24) Margerum, D. W.; Dukes, G. R. Kinetics and Mechanisms of Metal-ion and Proton-transfer Reactions of Oligopeptide Complexes; In *Metal Ions in Biological Systems*; Sigel, H., Ed.; Marcel Dekker, New York; 1974; Vol. 1, pp 157–212.

This rationale can accommodate the *measurable* solvent effect on the equilibria. Ordinarily, linkage isomer equilibria in pentaamminecobalt(III) systems are so much to one side in water that a change in solvent to Me_2SO has no measurable effect. However, for the 2-pyridone system, in Me_2SO the 3+ equilibrium constant K'_{ON} is ca. 0.2, different but not dramatically so, to a value ca. 0.03 in water. Most of this difference arises from the increased $k_{ON(2)}$ value (ca. 40-fold) (although $k_{NO(2)}$ is also increased (ca. 6-fold)), and mechanistically we have argued that there is a solvent shift in the tautomeric equilibrium governing the O to N rearrangement. Conversely, for the 2+ equilibrium, a shift to Me_2SO stabilizes the O-bonded form; K_{ON} changes from ca. 60 in water to ca. 9 in Me_2SO; the 5-fold reduction in the value of k_{ON} mostly accommodates this. The cyclic equilibrium requirement that a change in the ratio K'_{ON}/K_{ON} ca. (1/30)/60 = 1/1800 in water to now only (1/5)/9 = 1/45 in Me_2SO requires a significant reduction in the relative acidity constants, ca. 1.6 pK units. Thus, for Me_2SO, the acidity of the O-bonded isomer must be enhanced relative to the N-bonded form, although trends in absolute values are unknown. Our only previous experience has been with the $[(NH_3)_5Co–NHC(OH)CH_3]^{3+}$ ion where the acidity in water and Me_2SO were fortuitously very similar.[15]

Experimental Section

UV–visible spectra were obtained with a Cary 210 spectrophotometer using quartz cells. IR spectra were measured with a JASCO A-100 spectrophotometer in Nujol mulls with NaCl windows. ^1H and ^{13}C NMR spectra were obtained with a Varian XL 300 spectrometer with a probe temperature of 20 °C using Me_2SO-d_6 or D_2O (Aldrich) as solvent; shifts are given as ppm downfield from TMS (Me_2SO) or DSS (D_2O); the triflate ion was observed at δ 122.3 (q, J = 318 Hz) in D_2O and at δ 121.1 (q, J = 322 Hz) in Me_2SO. All complexes analyzed satisfactorily for at least H, C, N. Ion exchange media were SP Sephadex C-25 and Dowex 50W-X2 (200–400 mesh) resins. $[(NH_3)_5Co(pyridine)](ClO_4)_3\cdot H_2O$[17,25,26] was prepared from $[(NH_3)_5CoOSO_2CF_3](CF_3SO_3)_2$ (3.0 g).[14,15] Visible spectrum (0.1 M Tris, M^{-1} cm^{-1}): ϵ_{474} 63.0; ϵ_{338} 54.5; *cf.* ϵ_{475} 64.0, ϵ_{338} 52;[17] ϵ_{480} 46, ϵ_{340} 39;[25] ϵ_{474} 63.8, ϵ_{340} 54.4.[26]

***Caution!* Perchlorate salts are potentially explosive.**

$[(NH_3)_5CoOC(CH)_4NH](CF_3SO_3)_3\cdot H_2O$. 2-Hydroxypyridine (Aldrich, 3.0 g) and $[(NH_3)_5CoOSO_2CF_3](CF_3SO_3)_2$ (3.0 g)[14,15] were stirred in AR acetone (30 mL) for 1 h. The products were oiled out in ether, taken up in acetone, and crystallized by the addition of ether. The dark pink crystals were recrystallized from water as the triflate salt by the addition of concentrated sodium triflate solution, and the final product was washed with ether, and air-dried (yield 0.75 g, 35%). Visible spectrum (0.10 M $HClO_4$, M^{-1} cm^{-1}): ϵ_{524} 106; *cf.* ϵ_{523} 105.[5] A less soluble triperchlorate salt was obtained from the purified triflate salt by recrystallization from water using $HClO_4$ (70%) as precipitant.

$[(NH_3)_5CoOC(CH)_4N](ClO_4)_2\cdot H_2O$. The deprotonated oxygen-bonded species was prepared by dissolving $[(NH_3)_5CoOC(CH)_4NH](CF_3SO_3)_3\cdot H_2O$ in 0.1 M Tris. The pale red-brown complex was crystallized quantitatively by the addition of cold concentrated $NaClO_4$ solution, washed with ethanol and ether, and air-dried. Visible spectrum (0.1 M Tris, M^{-1} cm^{-1}): ϵ_{523} 145.

$[(NH_3)_5CoN(CH)_4CO](ClO_4)_2\cdot H_2O$. The 2-pyridone-*O* complex (0.75 g) was dissolved in water, and sufficient Tris was added to deprotonate it (the solution turned deep red). The solution was left for 4 days in a sealed flask and then diluted with water and chromatographed on Sephadex. The resin was first eluted with 0.5 M NaCl (pH 8, Tris) to remove the soluble reduction products. The bright orange complex was then eluted with 0.5 M $NaClO_4$ (pH 7, phosphate buffer); the residual oxygen-bonded isomer and some aquapentaammine complex eluted directly after it. The volume of eluate was immediately reduced by rotary evaporation, and the complex crystallized after addition of $NaClO_4$ and ethanol and chilling. The crystals were washed with ethanol and ether and air-dried (0.20 g, 31%). Visible spectrum (0.1 M Tris, M^{-1} cm^{-1}): ϵ_{490} 75. The less soluble double salt $[(NH_3)_5CoN(CH)_4CO]NO_3\cdot ClO_4$ was obtained as golden plates by using $LiNO_3$ and $NaClO_4$ as precipitants instead of just $NaClO_4$.

$[(NH_3)_5CoN(CH)_4C(OH)](ClO_4)_3\cdot H_2O$. To a saturated solution of the deprotonated N-bonded isomer in water was added a quarter volume of $HClO_4$ (70%) and the solution cooled in ice. Orange-yellow needles separated in good yield. These were collected, washed with 2-propanol and ether, and air-dried.

Kinetic Studies. The reactions of the 2-pyridonato-*N* complex in 0.5 M $HClO_4$ (I = 1.00 M, $LiClO_4$) and of the 2-pyridone-*O* complex in 0.1 M $HClO_4$ were monitored at 520 nm using a Varian 2300 spectrophotometer (25.00 ± 0.05 °C). The cobalt (III) concentration of the initial solution and the ratio of direct solvolysis to linkage isomerization were determined[18] using the following visible spectral data at 520 nm: 2-pyridone-*N*, ϵ 37; 2-pyridone-*O*, ϵ 105; aquapentaammine, ϵ 41 M^{-1} cm^{-1}. These two reactions were followed to completion.

The kinetics of the reaction of the 2-pyridonato-*O* complex in aqueous base were measured at 519 nm (isosbestic point for the two potential products, N-bonded isomer and hydroxopentamminecobalt(III); ϵ 55) in buffers made from partly neutralized ethanolamine and triethylamine; p[H^+] was determined as previously described,[15] and in NaOH solutions (ConvoL), [OH^-] = 0.020–1.00 M. At lower [OH^-] deprotonated O-bonded isomer was used as reactant so as not to consume the initial OH^-. The reaction itself did not consume OH^-. The ionic strength was maintained at 1.00 M ($NaClO_4$). Because of progressive product decomposition above ca. 0.02 M NaOH these reactions could be followed only for about one to two half-lives. In the data analysis, D_∞(calc) values were used for data not exceeding $2t_{1/2}$. The complex was generated *in situ* by adding solid samples of the 2-pyridonato-*O* complex directly to solutions preequilibrated at 25.0 °C.

Product Distribution Data. The concentrations of 2-pyridonato-*O* and -*N* at equilibrium in aqueous Tris were determined by allowing separate solutions of 2-pyridonato-*N* and 2-pyridonato-*O* to equilibrate for $5t_{1/2}$ and then chromatographing the products on Sephadex. The column was eluted rapidly with 0.5 M NaCl (pH 5) to remove the orange N-bonded isomer. The aquapentaammine and 2-pyridone-*O* complexes were eluted together with 1.0 M NaCl (pH 3). The concentrations of the 2-pyridone-*O* and 2-pyridonato-*N* complexes were determined spectrophotometrically using the following spectroscopic data recorded for the appropriate medium: 2-pyridonato-*N*, ϵ_{490} 75; 2-pyridone-*O*, ϵ_{520} 105, ϵ_{490} 66; aquapentaammine, ϵ_{490} 48, ϵ_{520} 40 M^{-1} cm^{-1}.

The base hydrolysis reaction for 2-pyridonato-*O* complex was studied chromatographically also. Samples of ca. 0.4 mmol dissoved in 0.100 M NaOH (I = 1.00 M, $NaClO_4$) at 25.0 °C were allowed to react at this temperature for ca. $1t_{1/2}$ (accurately timed, ca. 240 min) and then quenched with 1 M $HClO_4$ (10 mL). Sorption on Sephadex ion-exchange resin, washing, and elution led to the separation of unreacted O-bonded isomer and products. In the first pair of experiments, two different eluants were used, 0.45 M $NaClO_4$ buffered with acetate (0.05 M; pH 5), and then 0.125 M NaH_2PO_4. This effected the separation of N-bonded isomer (ϵ_{487} 75) from residual O-bonded isomer (ϵ_{521} 160) and any $[(NH_3)_5CoOH]^{2+}$ which elutes close to but behind the 2+ deprotonated O-bonded linkage isomer. In the second set of experiments, Na^+ phosphate buffer alone was used as the eluant (0.5 M, pH 7). This also nicely separates the N- (ϵ_{488} 75) and O-bonded isomers (ϵ_{524} 143), but here the hydroxo ion (ϵ_{492} 51) elutes just behind the first band. In none of these experiments was the $[(NH_3)_5CoOH]^{2+}$ product observed. After normalization, the average amount of recovered O-bonded isomer was 74% at 240 min, corresponding to $k_{obsd} = 2.1 \times 10^{-5}$ s^{-1}.

Identification of Reaction Products of the 2-Pyridonato-*N* Complex in Aqueous Acid. A sample of the 2-pyridonato-*N* complex was dissolved in 0.5 M $HClO_4$ and allowed to react for 15 h. The solution was diluted with water and chromatographed on Sephadex. The column was eluted with 0.5 M NaCl (pH 5) to remove unreacted N-bonded isomer as a 2+ ion and then with 0.5 M NaCl (pH 3) which almost completely separates the aquapentaammine complex and a dark pink 3+ ion. The central section of the dark pink band had a spectrum corresponding to the 2-pyridone-*O* complex.

Product and Equilibrium Distributions by ^1H and ^{13}C NMR. The slow reactions of the deprotonated isomers were conveniently followed by both ^1H and ^{13}C NMR for both D_2O and Me_2SO-d_6 as solvents. The N- and O-bonded isomer reactions were studied in parallel. Under such circumstances, at any time the ratio of peak heights for N-bonded isomer growing from the O-bonded isomer to corresponding peak heights for the O-bonded isomer growing from the N-bonded isomer is always the

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(26) Nordmeyer, F. R.; Taube, H. *J. Am. Chem. Soc.* **1966**, *88*, 4295–4297.

equilibrium ratio (K_{ON}). Provided the peak intensities can be measured sufficiently accurately at earlier times, this method obviates the need to follow very slow reactions through to completion. The reactions of the corresponding O- and N-bonded protonated complexes were also followed by NMR in both solvents. We observed the growth and subsequent decay of N-bonded isomer formed from its O-bonded species in Me_2SO. No N-bonded isomer was observed in acidic D_2O.

Determination of the Acidity Constants of the 2-Pyridone-*O* and 2-Pyridone-*N* Complexes. The procedure used was automated spectrophotometric titration at 25.0 °C as previously described; 1.00 M NaCl was the common medium.[11]

Acknowledgment. Financial support from the Australian Research Council is gratefully acknowledged. We also acknowledge the advice of Dr. A. P. Arnold and assistance of Mrs. M. Prág in measuring the acidity constants, Dr. J. Grant Collins for advice on NMR, and the ANU Microanalytical Service for the analyses.

Supplementary Material Available: Spectral data (Tables III and IV) and rate data (Figure 1) (3 pages). Ordering information is given on any current masthead page.