Definitive Evidence Concerning the Mechanism of the N to N Rearrangement of a Pentaammine(nitrile amide-*N*)cobalt(III) Complex

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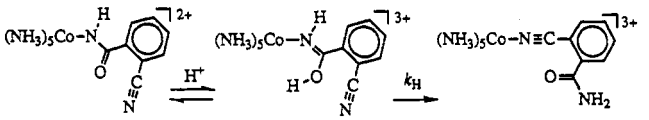
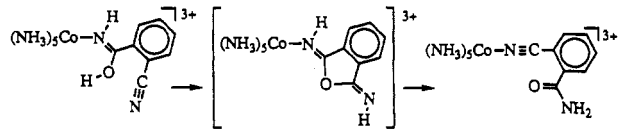
Introduction

A novel amide-*N* to nitrile-bonded linkage isomerization reaction was first identified for the amide-*N*-bonded pentaammine(2-cyanobenzamide)cobalt(III) ion by Balahura and Purcell.[1] In aqueous acid the complex is protonated at the amide group (pK_a = 0.4) and rearranges rapidly (k_H = 0.3 s^{-1}) to form the nitrile-bonded isomer:[1]

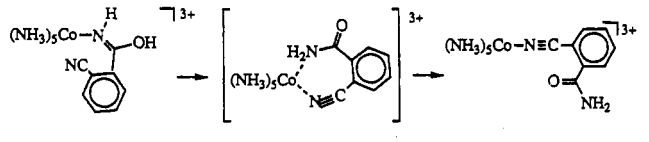


This rearrangement was unprecedented. The reactions of N-bonded amide complexes were first studied in peptide chelates, and it was found that in acid solution they rearranged to form the corresponding amide-*O* complexes.[2] Similar reactions, but with competitive solvolysis, have been observed in simple monodentate amide-*N* complexes.[3]

The mechanism suggested for the amide-*N* to nitrile-bonded linkage isomerization reaction involved neighboring group participation by the uncoordinated functional group through the formation of a cyclic intermediate:[1]

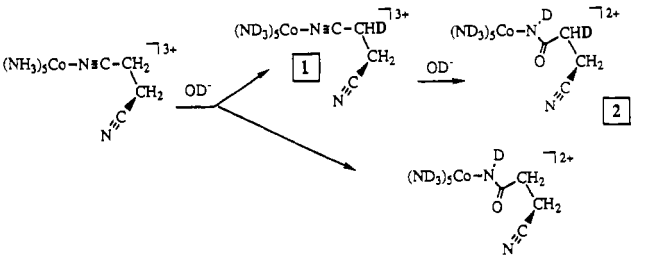


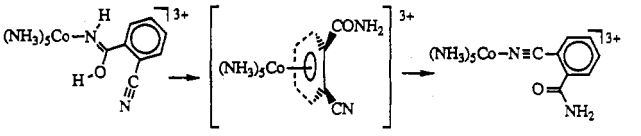
This proposal is unusual in that linkage isomerization is thought to occur without cleavage of the cobalt–nitrogen bond. While the conformation of the complex as shown and the rapidity of the reaction might favor this explanation, the possibility of a dissociative interchange mechanism, a more common pathway for cobalt(III) complexes,[4] cannot be ruled out. Shown as follows is an alternative conformation for the reactant, which would seem to inhibit formation of the cyclic organic intermediate while promoting normal linkage isomerization:



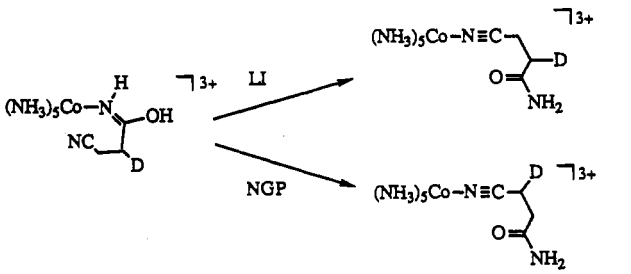
Another possibility is rearrangement through a π-bonded intermediate as suggested for the N to N rearrangements in the substituted tetrazole[5–8] and imidazole[9] complexes of pentaamminecobalt(III):

Scheme 1





We set out to distinguish between these mechanistic possibilities by preparing a complex whose structure was similar to that of the 2-cyanobenzamide ion but in which the carbon skeleton of the ligand was asymmetrically substituted. We chose succinic amide nitrile because (1) it could easily be substituted unsymmetrically in the $-CH_2-CH_2-$ backbone using D, (2) the position of substitution could be readily determined, and (3) the D substitution of itself did not introduce a bias toward a particular mode of rearrangement. Hence, if the mechanism involves neighboring group participation (NGP), then the substituent will swap its position relative to the two functional groups during the course of the reaction, but if the reaction takes place via Co–N rupture–dissociative interchange or the formation of a π-bonded intermediate (LI), then the substituent will not swap its position relative to the functional groups, and as a result, it will move from an adjacent to remote position relative to the metal ion:



Results

Synthesis of the asymmetrically substituted complex was achieved by selective deuteration of the pentaammine(succinonitrile)cobalt(III) complex **1**[10] and its subsequent base hydrolysis to a complex of succinic amide nitrile bonded through the amide nitrogen, **2**, Scheme 1. That complex is of similar structure to the cyanobenzamide complex but with an ethylenic rather than an aromatic backbone. Studies on the base hydrolysis of (acetonitrile)pentaamminecobalt(III) have shown that proton exchange at the methyl group occurred in parallel to hydrolysis of the coordinated nitrile. It was concluded that the exchange reaction was independent of base hydrolysis and its rate slightly

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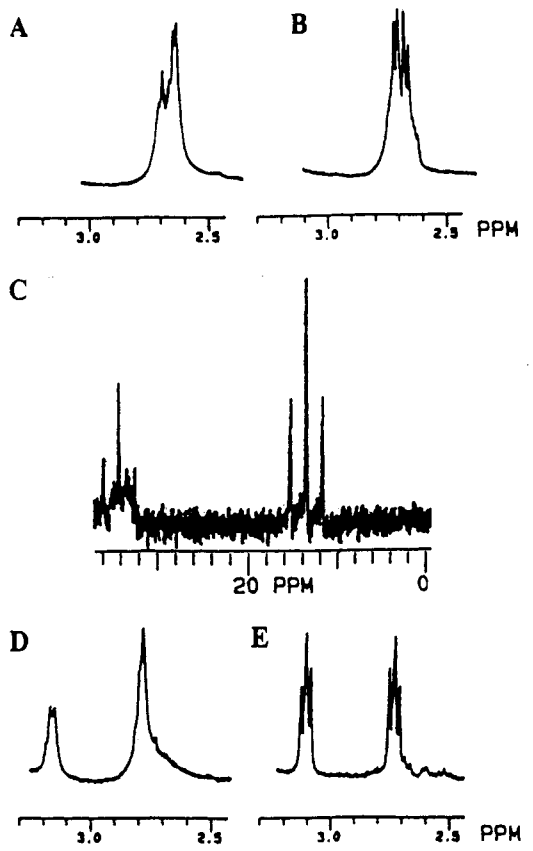

Figure 1. NMR spectra (D_2O) of partially deuterated (A, C, D) and undeuterated (B, E) linkage isomers of (succinic amide nitrile)-pentaamminecobalt(III).

faster.[11] In general, for nitrile complexes with the $[(NH_3)_5CoNCCH_2R]^{3+}$ structure, especially where R is an electron-withdrawing group, the methylene protons are quite acidic.[12] Thus, base hydrolysis of the succinonitrile complex in D_2O has produced an amide-*N*-bonded succinic amide nitrile complex, some of which is deuterated α to the coordinated functional group (Scheme 1). The α-methylene D is "locked-in" at the dinitrile stage since the amide product is inert to further exchange in basic D_2O. After hydrolysis the deuterated group is also inert to back-exchange in acidic H_2O, an important fact since we wanted to test the fate of the D in acidic H_2O.

^1H NMR spectra (solvent D_2O) of the amide-*N*-bonded succinic amide nitrile complex produced by reaction in D_2O, spectrum A, and its nondeuterated analogue, spectrum B (for comparison), are shown in Figure 1. From spectrum A it is clear that one of the methylene groups of the coordinated amide has been partially deuterated and this must be the α methylene group. The low-field methylene multiplet is less intense than the other at higher field which partly overlaps it, and the resolution in the AA'BB' coupling pattern has diminished; also D coupling leads to some broadening.

The degree of deuteration was assessed from the proton-coupled ^{13}C spectrum C shown in the same figure. It is consistent with a mixture of $[(ND_3)_5CoNDCOCD_2CH_2CN]^{2+}$, $[(ND_3)_5CoNDCOCHDCH_2CN]^{2+}$, and $[(ND_3)_5CoNDCOCH_2CH_2CN]^{2+}$. Exchange at $-CH_2-$ should yield both $-CHD-$ and $-CD_2-$, depending upon the extent of reaction, since the relative rate constants for the sequence are similar; indeed, neglecting kinetic isotope effects, they are statistically related (2:1). For a $-CH_2-$ group the C is split simply into a 1:2:1 triplet ($^1J_{CH}$ = 125 Hz). In a $-CHD-$ group the signal splitting pattern is more complex: a doublet ($^1J_{CH}$ = 125 Hz), each line of which is split further into a 1:1:1 triplet ($^1J_{CD}$ = 20 Hz), is expected. The net result is a doublet of triplets spanning 165 Hz. For $-CD_2-$, a 1:2:3:2:1 quintet spanning 80 Hz is expected. D-substitution also leads to upfield isotopic C shifts.[13] Notwithstanding these complexities, the fraction of the amide complex remaining undeuterated could be easily estimated from the ratio of the heights of the central peak in each branch of the spectrum. From spectrum C it was determined that 51 ± 5% of the α site remained $-CH_2-$, with the balance comprising $-CHD-$ and $-CD_2-$; it was not necessary to know the relative amounts of the individual deuterated species.

The regioselectively deuterated complex was reacted in aqueous acid, and the partially deuterated product $[(NH_3)_5CoNCCH_2CH_2CONH_2]^{3+}$ crystallized. Its ^1H NMR spectrum was recorded in D_2O and is shown as spectrum D in Figure 1, while spectrum E is that of the undeuterated analogue. The methylene group adjacent to the coordinated nitrile group gives rise to the signal at lower field; it is deshielded by the nitrile group and the metal ion. It is this group which is partially deuterated to the same extent, at least qualitatively, as the $-CH_2-$ group which was adjacent to the amide group in the starting material.

The results were quantified by the proton-coupled ^{13}C NMR spectra in Me_2SO-d_6. For $[(NH_3)_5CoNHCO(CH_2)_2CN]^{2+}$, the partially deuterated $-CH_2-$ next to the bound amide resonates at δ 34.2, while the signal for $-CH_2-$ adjacent to the remote nitrile is centered at δ 13.6 ppm. For the acid rearrangement product $[(NH_3)_5CoNC(CH_2)_2CONH_2]^{3+}$, the methylene carbon at δ 14.4 ppm is the deuterated one and it is now adjacent to the bound nitrile group; the other $-CH_2-$ signals are at lower field, centered at δ 28.9 ppm. [Note the "reversal" in $-CH_2-$ shifts between reactant and product in the ^{13}C NMR spectra, yet the signal for the deuterated $-CH_2-$ is at lower field in each case; in the ^1H NMR spectra, the shift "reversal" is less obvious.] The fraction $-CH_2-$ α to the $-CN$ relative to that α to the $-CONH_2$ functionality was 0.51 ± 0.05 in the reactant and 1.79 ± 0.15 in the rearrangement product, clearly indicating an essentially complete transfer of D [for a ligand cyclization mechanism the product fraction is predicted to be 1.96, as against 0.51 for conventional linkage isomerization]. These findings are consistent with a ligand cyclization mechanism since the labeled group has appeared to migrate with respect to the functional groups while remaining adjacent to the metal ion. Of course, what has happened is the amide group has been dehydrated to a nitrile, and at the other end of the bifunctional ligand a nitrile has been hydrated to an amide. The same water molecule appears to be involved, since the rearrangement also occurs in nonaqueous solution.[14]

On repetition of these experiments, base hydrolysis of the dinitrile complex in D_2O/OD^- at a lower temperature yielded an amide-*N* complex which was more highly deuterated in the α methylene group. But more significantly, the high-resolution proton-*decoupled* ^{13}C NMR spectrum clearly revealed, for the $-CH_2-$ group which was *not* deuterated, a useful isotopomer pattern (Figure 2). Three signals spaced by 5.5 Hz were observed, attributable to $-CH_2-CH_2-$, $-CHD-CH_2-$, and $-CD_2-CH_2-$, from lowest to highest field, respectively, and their intensities yield directly the relative amounts of these species (30% undeuterated complex, and 35% mono- and 35% dideuterated).[15] The same isotopomer patterns were observed in each of the signals

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(14) Detailed synthesis, characterization, and reactions of these and other amide–nitrile complexes are to be described in a forthcoming publication.
(15) The $-CH_2-CH_2-$ singlet is seen at lower field (Figure 2), of the same intensity as the $-CH_2-CH_2-$ component of the upper field isotopomer triplet, and superimposed on the 1:1:1 triplet for $-CHD-CH_2-$, $^1J_{HD}$ = 20 Hz, which shows an upfield isotopic shift which also happens to be 20 Hz at the instrument's 75-MHz field strength; the $-CD_2-CH_2-$ multiplet signals are lost in the noise.

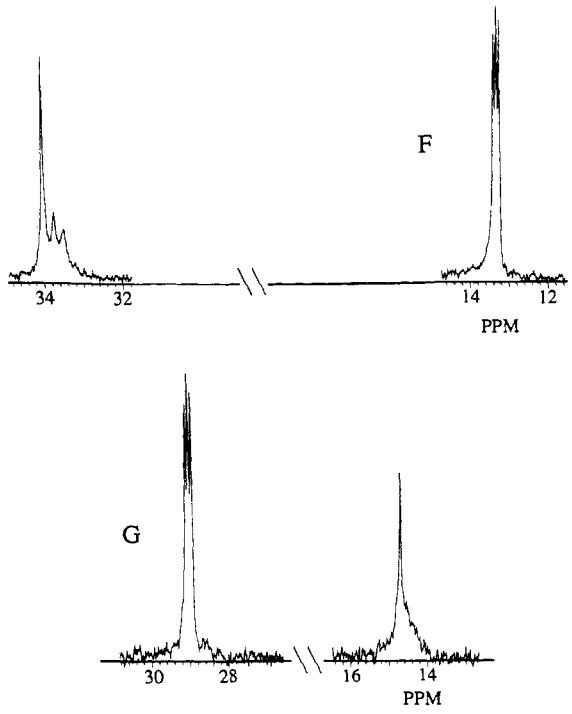

Figure 2. High-resolution proton-decoupled ^{13}C NMR spectra for methylene-deuterated $[(NH_3)_5CoNHCO(CH_2)_2CN]^{2+}$ (F) and its acid rearrangement product $[(NH_3)_5CoNC(CH_2)_2CONH_2]^{3+}$ (G) in Me_2SO-d_6. The ppm scales are aligned vertically.

for the 1:2:1 triplet in the proton-*coupled* ^{13}C NMR spectrum. On rearrangement in acid, the isolated nitrile amide complex again revealed an isotopomer pattern for the undeuterated $-CH_2-$ signal (spacings 6 Hz), and this isotopomer pattern retained the precise relative intensities seen in the reactant (Figure 2). Any contribution from a rearrangement via the usual linkage isomerization route would have enhanced this $-CH_2-CH_2-$ signal relative to the $-CHD-CH_2-$ and $-CD_2-CH_2-$ components, and clearly the contribution is insignificant (Figure 2).

Discussion

Neighboring group participation has been reported in 1,2-disubstituted benzene complexes and was usually identified by the isolation of cyclized reaction products.[1,16] In the present case that was not possible as the ligand structure is not altered by the reaction; a cyclized species, if involved, is only a transient intermediate and never observed. However the labeling experiment, demonstrating the absence of Co–N bond cleavage during rearrangement, is strong evidence for the neighboring group participation mechanism. The driving force for the reaction is the formation of the nitrile-bonded complex which is the thermodynamically more stable linkage isomer.[17] The reaction is a novel example of linkage isomerization.

Experimental Section

The 300-MHz ^1H and 75.48 MHz ^{13}C NMR spectra were recorded on a Varian XL-300 spectrometer with a probe temperature of 20 °C. In D_2O solutions the internal reference was sodium dimethylsilapentanesulfonate (δ 0.00 ppm); for ^{13}C spectra in Me_2SO-d_6 the central peak of the solvent resonances was used (δ 39.37 ppm, vs $SiMe_4$).

Partially Deuterated $[(NH_3)_5CoNHCOCH_2CH_2CN](ClO_4)_2\cdot H_2O$. $[(NH_3)_5CoNCCH_2CH_2CN](ClO_4)_3.H_2O$[10] (0.50 g) was dissolved in 0.1 M NaOD (50 mL), and the solution was stirred in a sealed flask for 1 h. The solution was filtered to remove byproducts and the desired complex crystallized by the addition of $NaClO_4$. The complex was recrystallized from water with concentrated $NaClO_4$ solution, washed with ethanol and ether, and air-dried. The ^1H NMR spectrum was recorded in D_2O and the proton-coupled ^{13}C nmr spectrum in Me_2SO-d_6 as the complex is much more soluble in the latter solvent. A sample of the title complex was dissolved in basic D_2O and its ^1H NMR spectrum recorded immediately and again after 2 h. These two spectra were identical.

Rearrangement of the Partially Deuterated Complex in Aqueous Acid. The partially deuterated amide-bonded complex described above was dissolved in 0.1 M $HClO_4$ and left to react for 12 h. The yellow nitrile-bonded product was crystallized by addition of 6 M $HClO_4$, washed with ethanol and ether, and air-dried. ^1H and ^{13}C NMR spectra were recorded in acidified D_2O and Me_2SO-d_6. The ^1H NMR spectrum of the undeuterated, nitrile-bonded complex was recorded in acidified D_2O 1 h after dissolution; no D incorporation was observed.

Acknowledgment. This work was supported by the Australian Research Council.

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