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Nuclear Magnetic Resonance Studies of Diamagnetic Metal–Diethylenetriaminepentaacetate Complexes

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The ^{1}H NMR and ^{13}C NMR spectra of the alkaline earth and diamagnetic rare earth metal complexes of DTPA are discussed in terms of the labilities of the metal–oxygen and metal–nitrogen bonds. The various resonance splitting patterns observed in the alkaline earth spectra are correlated with the patterns predicted for possible hexadentate structures involving all three nitrogen donors and averaging for the other three coordination sites by four of the ligand carboxylate groups. A heptadentate structure is proposed for the complexes of DTPA with the lanthanides in which the unbound ligand group is the lone acetate group of the middle nitrogen.

Introduction

An earlier paper[1] reported ^{1}H NMR studies of the complexes in an aqueous solution of alkaline earth and diamagnetic lanthanide (La, Lu, Y) cations with ethylenediaminetetraacetate (EDTA), *N*-(hydroxyethyl)ethylenediaminetriacetate (HEDTA), and *N*-methylethylenediaminetriacetate (MEDTA). The pattern of the ^{1}H NMR spectra indicated coordination via the nitrogen and carboxylate donors in all three ligands. Moreover, the patterns were consistent with short-lived M–N and M–O bonds (on the NMR time scale) in the alkaline earth complexes. For the lanthanides, the M–O bond was found to be labile in all systems but the M–N bond lifetime was long for Lu and Y complexes and even for La in the HEDTA complex.

We have extended the NMR studies to complexes of the more complicated diethylenetriaminepentaacetate anion, DTPA, using both ^{1}H and ^{13}C NMR. DTPA possesses five carboxylate and three potential nitrogen donor atoms (Figure 1). However, molecular models of the La–DTPA complex indicate that DTPA cannot act as an octadentate ligand. If both terminal nitrogens and the four terminal carboxylate groups are coordinated, either the middle nitrogen or the middle carboxylate group can be coordinated but not both (i.e., CN = 7). For Hg(II)[2a] and Ni(II)[2b] complexes, ^{1}H and ^{13}C NMR spectra have been interpreted by DTPA coordination involving the three nitrogen atoms with labile M–O bonding such that the four terminal carboxylate groups average to three M–O interactions giving the metal ion a CN of 6. We can expect the alkaline earths (CN = 6) to have similar coordination while the lanthanide–DTPA complexes can have higher coordination (e.g., CN = 7).

Experimental Section

A stock solution of DTPA was prepared to be 0.05 M in H_2O (for ^{13}C spectra) or D_2O (for ^{1}H NMR). The DTPA used for these studies was obtained as the neutral acid from Aldrich Chemical Co., Inc. The complexes for ^{1}H NMR studies were prepared as described previously by mixing an aliquot of the ligand solution with an amount of the appropriate metal solution, also in D_2O, to have a 1:1 mole ratio at pD of 7–8 (using NaOD) for lanthanide complexes and 8–10 for the alkaline earth complexes. The final concentration of the metal–DTPA complexes was approximately 0.05 M. The solutions for ^{13}C spectroscopy were prepared similarly in H_2O solution with enough D_2O for field frequency lock purposes.

^{1}H NMR spectra were obtained with either the Bruker 90-MHz or Bruker 270-MHz spectrometers of the FSU NMR laboratory by using the pulsed Fourier transform mode with a deuterium lock. The spectra were measured at 30 °C relative to an internal standard, sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS). Then proton-decoupled Fourier-transform ^{13}C spectra (deuterium lock) were obtained at 67.9 MHz on the Bruker HX-270 spectrometer. Measurements were made with 13-mm sample tubes with 5 to 6 mL of solution. The temperature was 29 °C and an internal standard of dioxane (the shifts are reported relative to Me_4Si) was used.

Results

^{1}H NMR spectra of the DTPA ligand are shown in Figures 1 and 2 and ^{13}C spectra are shown in Figure 3. The ^{1}H and ^{13}C spectra of the $DTPA^{5-}$ anion were measured at pH 11.

Only two distinct ^{1}H NMR resonances are observed for the DTPA anion. Since the areas of the two peaks at 2.6 and 3.1 ppm are 4:5, the peak at 3.0 ppm is assigned to the protons of the acetate groups and that at 2.6 ppm to those of the ethylenic groups. An unresolved shoulder of the 3.1-ppm peak is of the approximate relative intensity to indicate that one acetate, presumably the group attached to the middle nitrogen, has a slightly different resonance than the four terminal acetate groups. These resonances correspond well[1] to the values of the acetate and ethylenic protons of $EDTA^{4-}$, $MEDTA^{3-}$, and $HEDTA^{3-}$. In Figure 3 we assign the single ^{13}C resonance at 179 ppm to the five carboxylate carbons, the resolved doublet at 60 ppm to the methylenic carbons (a and d, respectively), and the resonances at 58.4 and 57.5 ppm to the ethylenic carbons. These assignments agree with previous reports of ^{13}C spectra of $DTPA^{5-}$[2a,3] and $EDTA^{4-}$.[4]

For the ^{1}H NMR spectrum of SrDTPA in Figure 1, on the basis of our experience with the spectra of the other aminopolycarboxylate complexes, we suggest that an AB quartet centered at 3.3 ppm is present for the four terminal acetate groups and a singlet at 3.2 ppm for the middle acetate group. Integration over the lower field half of the AB quartet (~3.4 ppm) accounts for four of the ten protons giving a total of eight in the AB pattern and two in the singlet. The AB pattern indicates that all four terminal carboxylate groups are equivalent and the Sr–N bond of the terminal nitrogens is long-lived.[5] The singlet for the middle carboxylate could be due to a short-lived Sr–N bond for the middle nitrogen or to no interaction between the Sr and the middle carboxylate group. CaDTPA has a similar spectrum with an AB quartet baricenter of 3.4 ppm and a singlet at 3.3 ppm. The AB quartet of MgDTPA is centered at 3.5 ppm, a singlet is observed at 3.40 and another at 3.45 ppm. The extra singlet can be assigned to MgHDTPA which forms at these pH values.[6] The BaDTPA spectrum exhibits two singlets indicating a shorter lifetime for the Ba–N(terminal) bonds. A similar change from AB quartet to singlet is observed for EDTA complexes of Lu and Y (AB pattern) vs. La (singlet) and seems due to the relationship between cation charge density and the bond lifetime.

The ^{13}C spectrum of DTPA in the calcium complex is generally similar to the LaDTPA spectrum of Figure 3. However, the x,y resonances are a doublet of 4:1 relative intensities indicating equivalence for the four x carbons but a different resonance for the y carbon. Both ^{1}H NMR and

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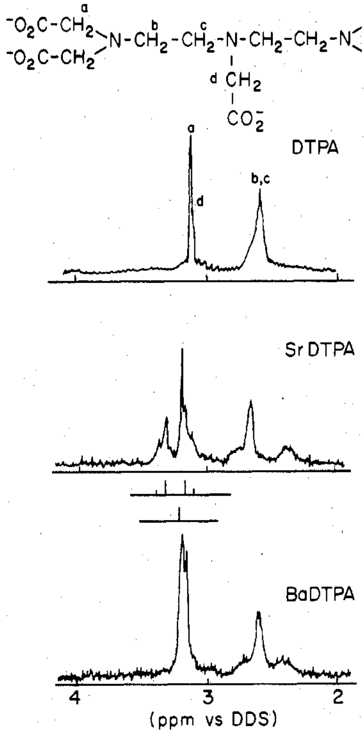

Figure 1. ^{1}H NMR spectra of solutions of NaDTPA, SrDTPA, and BaDTPA.

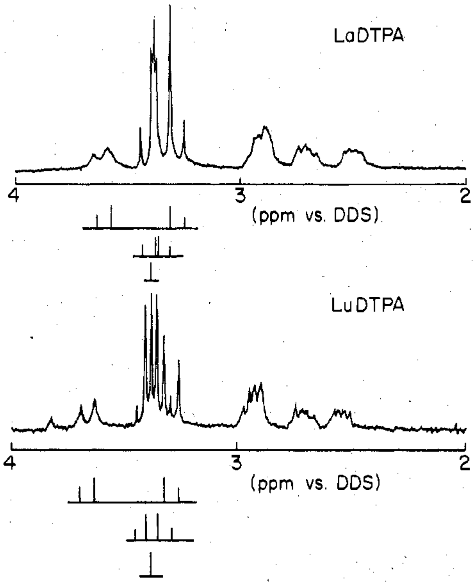

Figure 2. ^{1}H NMR spectra of LaDTPA and LuDTPA.

the ^{13}C spectra of DTPA in the alkaline earth complexes are consistent with the hexadentate structure proposed for the HgDTPA and NiDTPA complexes with all three nitrogens bonded and averaging of the four terminal carboxylate groups in short-lived interactions at the remaining three coordination sites. The fifth (middle) carboxylate is noninteracting or interacts much less often to produce a nonequivalent, singlet behavior.

The LaDTPA and the LuDTPA (the YDTPA spectrum is very similar to that of LuDTPA the ^{1}H NMR spectra) have two different AB patterns for the four terminal acetate groups and a singlet for the middle acetate. If the scale of the ^{13}C spectrum of LaDTPA (Figure 3) is expanded, the x,y resonance is found to be a triplet of 2:1:2 intensities indicating a doublet for the x carbons. Again the spectra are consistent with a model of coordination to the three nitrogen atoms with the Ln–N bond being long-lived for the terminal nitrogens and, perhaps, for all three bonds. Nonequivalence of the terminal carboxylates has been observed for the Ln complexes with HEDTA and MEDTA and attributed to slightly different average Ln–O bond distances. The lack of an AB pattern indicates the fifth (middle) carboxylate to be unbonded in the lanthanide complexes.

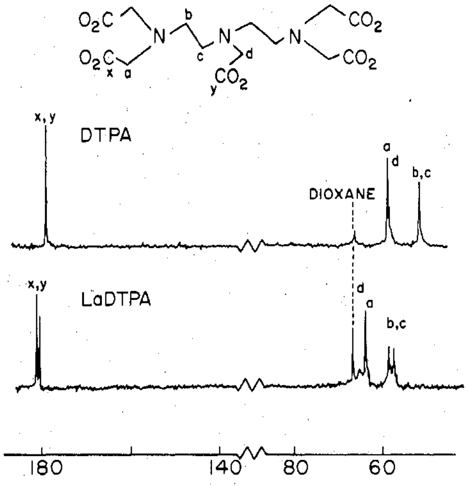

Figure 3. Carbon-13 spectra of solutions of NaDTPA and LaDTPA.

An uncertainty in our assignments and their interpretation of the spectra in Figure 2 is associated with the fact that the two outer lines of one of the AB patterns (~3.6 ppm) are broader than the lines of the other half (~3.3 ppm). We can offer no definitive interpretation. A possible explanation is that some exchange is occurring between the two types of acetates represented by the two AB quartets. The broadening of the multiplet lines would be proportional to their distances from the average of the baricenter which is about 3.4 ppm. This would result in more broadening of the lines near 3.6 than of those near 3.3 ppm. The resolution is not sufficient to ascertain if the ratio of the widths exceeds the ratio of the distances from the center of gravity which is a necessary condition of this explanation. No alternative assignment other than as part of an AB quartet seems reasonable, particularly in view of the fact that similar broadening is observed for LaDTPA, YDTPA, and LuDTPA in all three of which the broadened lines are able to be associated with a similar AB quartet. Moreover, the lack of other broad lines in these acetate spectra restricts any exchange broadening to rather narrow time limits.

For the alkaline earth complexes, the broad ethylenic resonances between 2.3 and 2.8 ppm can be explained by a conformation with equivalence of the four b protons and nonequivalence of the four c protons with two protons pointing to the metal and two directed away from the metal. Wagging of the ethylenic backbone does not destroy the nonequivalence of these two pairs. In the ethylenic region of the ^{1}H NMR spectra of the lanthanide–DTPA complexes a similar pattern of three resonance lines of relative areas 2:1:1 is observed. The similarity in this region for both the lanthanide and alkaline earth spectra suggests that the conformation of the two ethylenediamine backbones is probably similar in all the metal–DTPA complexes.

In summary, we conclude that DTPA complexes with lanthanides only as a heptadentate ligand with an unbound carboxylate. This is consistent with analysis of the thermodynamics of complexation.[7] Comparison of the entropies of complexation with those of other aminopolycarboxylate systems indicated interaction of lanthanide cations with only four carboxylate groups while comparison of the enthalpies indicated coordination with the three nitrogens.

Registry No. DTPA^{5-}, 14047-41-7; SrDTPA^{3-}, 69351-96-8; BaDTPA^{3-}, 69351-97-9; LaDTPA^{2-}, 69351-98-0; LuDTPA^{2-}, 69351-99-1.

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Nuclear Magnetic Resonance Relaxation in Symmetrical Cobalt(III) Complexes

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Cobalt-59 and nitrogen-14 longitudinal and transverse relaxation times have been measured in the symmetrical cobalt complex ions hexacyanocobaltate(III), tris(ethylenediamine)cobalt(III), and hexaamminecobalt(III). The ^{59}Co line width in hexacyanocobaltate(III) is narrow, 2–3 Hz, characteristic of symmetrically complexed quadrupole nuclei. The cobalt relaxation in the two N-bonded complexes, however, is complicated by a scalar interaction of the second kind from cobalt coupled to first coordination sphere nitrogen-14. Analysis of the nitrogen scalar contribution from the cobalt and nitrogen relaxation data gives the scalar coupling constants $J(^{59}\mathrm{Co}–^{14}\mathrm{N}) = 40.8 \pm 2.1$ and 50 ± 2.5 Hz for hexaammine and tris(ethylenediamine) complexes, respectively. In the ethylenediamine complex, cobalt coupling to the methylene and ammine protons is also observed by ^{1}H-decoupled cobalt relaxation data in H_2O and D_2O solutions. The pH dependence of the cobalt relaxation times for the N-bonded complexes clearly demonstrates the formation of the complex ion conjugate base.

Introduction

Cobalt-59 nuclear magnetic resonance has provided useful information about the structure and dynamics of cobalt(III) metal environments.[1] The ^{59}Co NMR chemical shifts are known to be very large so that even subtle differences in the second coordination sphere of complexes may be detected.[2] Although the cobalt(III) NMR spectrum is readily detected, a major difficulty arises if the symmetry at the cobalt nucleus is low because the lines become prohibitively broad through very efficient relaxation by the nuclear electric quadrupole interaction. On the other hand, symmetrical cobalt complexes are readily investigated in solution by standard techniques.[3]

When the cobalt nucleus experiences a symmetrical environment such as in a tetrahedral or octahedral ion, NMR relaxation due to the nuclear electric quadrupole interaction is expected to be inefficient. The nuclei of the central atom of symmetrical ions such as the perchlorate or permanganate ions yield readily observed NMR spectra although they possess significant quadrupole moments. In both cases the NMR quadrupole relaxation mechanism for the central nucleus is inefficient, and line widths on the order of a few hertz are reported.[4,5] In the case of cobalt(III) complexes the hexacyanocobaltate(III) ion has such a narrow spectral line, but other symmetrical complexes such as hexaamminecobalt(III) ion and nitrogen-substituted analogues have line widths on the order of 100 hertz. The present study was undertaken to examine the NMR relaxation of these symmetrical cobalt(III) complexes to determine the source of this apparent anomaly in the cobalt(III) systems. A detailed understanding of relaxation in these chemically inert cobalt(III) complexes is important because they provide very useful models for investigating the nature of nuclear electric quadrupole contributions to the NMR relaxation of ions in solution.[6]

We have found that in N-bonded cobalt(III) complexes several mechanisms contribute to the ^{59}Co NMR relaxation. In particular measurements of both longitudinal and transverse relaxation rates for ^{59}Co and ^{14}N coupled with a series of isotopic substitution experiments have permitted resolution of the several relaxation contributions. Most notable is a large contribution from a scalar interaction between ^{59}Co and ^{14}N.

Experimental Section

Potassium hexacyanocobaltate(III), tris(ethylenediamine)cobalt(III) chloride, and hexaamminecobalt(III) chloride were synthesized and purified by standard procedures by using reagent grade chemicals.[7] Deuterium oxide (99.87 mol % D_2O) was purchased from Bio-Rad Laboratories. Complete deuteration of complex ammine protons, verified by the cobalt-59 resonance,[8] was accomplished by recrystallizing the cobalt complexes at least three times from D_2O.

The NMR relaxation measurements on cobalt-59 and nitrogen-14 were performed in a 1.4-T field by using a spectrometer assembled in this laboratory.[9] Cobalt-59 longitudinal relaxation times, T_1, were measured by inversion recovery with phase alternation. Transverse relaxation times, T_2, for $K_3Co(CN)_6$ were measured by the Carr–Purcell–Meiboom–Gill sequence[10] since in this complex the measured line width is controlled by magnetic field inhomogeneity. A representative Carr–Purcell–Meiboom–Gill spin echo experiment on cobalt-59 in 1.25 M $K_3Co(CN)_6$ is shown in Figure 1. Line widths from the Fourier transform spectra were used as a measure of T_2 for all other samples. Estimated error for these measurements is 5%. Nitrogen-14 T_1 measurements were made at 4.3 MHz without phase alternation of the 90° pulses in order to minimize the pulse widths. Estimated error for the nitrogen measurements is 10%. The phase-modulated broad-band proton decoupling used in these experiments was calibrated by observing the proton-decoupled oxygen-17 resonance in enriched water at neutral pH. Probe temperature was 32 ± 1 °C.

Results and Discussion

The ^{59}Co NMR spectra for hexacyanocobaltate(III) ion, hexaamminecobalt(III) ion, and tris(ethylenediamine)cobalt(III) ion are shown in Figure 2. The chemical shift differences are characteristically large, and satellite lines are clear in the hexacyanocobaltate(III) spectrum. The satellite lines account for 6% of the cobalt signal which is consistent

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