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The Use of ^{13}C NMR Isotopomer Distributions for Following Proton Exchange and Unambiguously Assigning the Carbons and Coordinated Amine Protons in Multidentate Chelate Complexes of Cobalt(III)

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A method for unambiguously assigning amine proton and carbon backbone signals, in ^{1}H and ^{13}C NMR spectra respectively, is described. It is applied to multidentate amine complexes of cobalt(III), and the method relies upon different exchange rates for the inequivalent amine protons in the diamagnetic complex. Deuteration of the amines leads to both α and β isotopic shifts in the ^{13}C NMR spectrum, and it is the characteristic isotopomer patterns for an α-carbon which are mirrored in the β-carbon that permit the unequivocal assignments.

Introduction

Intrinsic isotope effects on NMR chemical shifts and their use in structural and mechanistic assignments are well-documented for organic, bioorganic, and organometallic systems but less so for traditional inorganic areas such as coordination chemistry.[1-3] In an era of high-resolution multinuclear NMR spectroscopy, the importance of isotopes is growing, one reason being the increasing ease of resolution of isotopomers arising from the secondary isotope effect. For example, the ^{31}P NMR spectrum of coordinated trimethyl phosphate hydrolyzed in ^{18}O-enriched H_2O shows two ^{31}P signals, one for ^{31}P–^{16}O and one at slightly higher field due to ^{31}P–^{18}O.[4] This upfield shift is characteristic and has been well exploited in the biochemical area.[5] Even larger isotope shifts are found for nuclei that display a wide chemical shift range in their compounds and where the isotope substitution involves the lighter atoms. Thus, for example, replacement of H by D on ^{59}Co can lead to a 5 ppm upfield shift.[6] Large isotope shifts can also be observed for protons in complexes such as [Fe^{II}sar]$^{2+}$ (undergoing deuteration at the amine sites), where a significant high-spin contribution in the ground state leads to a contact shift that effectively expands the chemical shift axis.[7]

Deuteration (or tritiation) is most readily achieved by exchange at acidic groups such as $-OH$, $-CO_2H$, or $-NH_2$; where these groups are attached to magnetic nuclei such as carbon-13 the isotopic shifts are observed in the ^{13}C signal. Often the value of the isotopic substitution strategy resides in an ability to separate the isotopomer signals, but the H and D isotopomers usually cannot be observed together because of exchange which is rapid on the NMR time scale. One way around the problem is to use a concentric-tube technique such as that employed successfully to identify C–OH groups in polysaccharides[8,9] by distinguishing C–OH (H_2O solvent) from C–OD (D_2O) in the ^{13}C NMR spectrum, but in general this method is compounded by the solvent isotope effect on chemical shift.

The rate of exchange of amine protons is greatly slowed by coordination to kinetically inert transition-metal ions such as Co(III), and the rate of exchange can be further controlled by pH variation.[10] If the amine is one of several in a multidentate

chelating ligand, and the amine protons exchange at different rates, the sites undergoing the exchange can be identified by observing the isotopic shifts of the carbons to which they are attached.[11] Of course, the exchange is also observed in the ^{1}H NMR spectrum as a loss of signal intensity for the appropriate amine.[10] However, the advantage of using ^{13}C and ^{1}H NMR spectroscopy to monitor the NH exchange process is in the ability to assign particular carbons, or pairs of carbons, to particular adjacent amine sites. Thus if the carbons can be assigned to particular sites in a molecule, so also can the amines.

The problem of correlating CH and NH protons is far less difficult than the one of assigning a particular amine proton (or carbon) to a particular resonance; the latter has been a long-standing one in coordination chemistry.[12,13] It should be emphasized that standard modern NMR techniques such as ^{1}H or ^{13}C detected proton–carbon or ^{1}H detected proton–nitrogen correlated 2D NMR spectroscopy are of limited usefulness in this regard. They can assist however with the identification of the CH$_2$ and adjacent NH or NH$_2$ protons, although they are only weakly coupled, but even so only associated pairs of CH$_2$ and NH (or NH$_2$) protons could be derived in this manner. In any event, the associated pairs of carbons and amine protons come out of the analysis we describe below for the assignment of resonances (^{1}H (NH only) and ^{13}C (all)) to particular structural sites.

Isotope shifts can be detected for carbons two and three bonds remote from the point of isotope substitution, and in the present work we show that it is the isotopomer patterns for the remote carbons which allow an unambiguous assignment of *all* carbon resonances, and thus the associated amine proton signals.

Finally, we report attempts to observe by NMR spectroscopy diastereoisomers arising from chirality where two of the substituents on one chiral center are isotopes of the same element (stereoisotopomers).

Results and Discussion

The multidentate amine complex ion *exo-αβ*-[Co(tetraen)-OH$_2$]$^{3+}$ is one of several isomers,[13,14] and we will be referring to the exo- and endo-$\alpha\beta$ forms of several derivatives having different substituents (H_2O or Cl$^-$) and showing the topology in Figure 1 but differing in the configuration at one of the sec-NH centers, H-c; this proton may be exo (away) or endo (near) to the substituent, in the present case H_2O. These structures have been

(1) Jameson, C. J.; Mason, J. In *Multinuclear NMR*; Mason, J., Ed.; Plenum Press: New York, 1987; pp 80–82.
(2) Breitmaier, E.; Bauer, G. *^{13}C NMR Spectroscopy*; Harwood Academic: New York, 1984; p 31.
(3) Jameson, C. J. In *Nuclear Magnetic Resonance*; Webb, G. A., Ed.; Royal Society of Chemistry: London, 1980; Vol. 10, pp 22–24.
(4) Hendry, P.; Sargeson, A. M. *J. Chem. Soc., Chem. Commun.* **1984**, 164.
(5) Ratle, H. W. E. Reference 1, p 591.
(6) Bendall, M. R.; Doddrell, D. M. *Aust. J. Chem.* **1978**, *31*, 1141.
(7) Hagen, K. S.; Sargeson, A. M. *Abstracts*, 1st ICA Conference, Melbourne, 1986; RACI: Parkville, Australia, 1986; H2.
(8) Pfeiffer, P. E.; Valentine, K. M.; Parrish, F. W. *J. Am. Chem. Soc.* **1979**, *101*, 1265.
(9) Barrow, K. D.; Collins, J. G.; Rogers, P. L.; Smith, G. M. *Eur. J. Biochem.* **1984**, *145*, 173.

(10) Comba, P. C.; Jackson, W. G.; Marty, W.; Zipper, L. *Helv. Chim. Acta*, submitted for publication.
(11) Jackson, W. G.; Sargeson, A. M. Rearrangement in Coordination Complexes. In *Rearrangements in Ground and Excited States*; P. de Mayo, P., Ed.; Academic Press: New York, 1980, Vol. 2, pp 273–378. Jackson, W. G.; Sargeson, A. M. *Org. Chem. (N.Y.)* **1980**, *42*, 273–378.
(12) Buckingham, D. A.; Cresswell, P. J.; Sargeson, A. M. *Inorg. Chem.* **1975**, *14*, 1485.
(13) Marzilli, P. A. Ph.D. Dissertation, ANU, 1968.
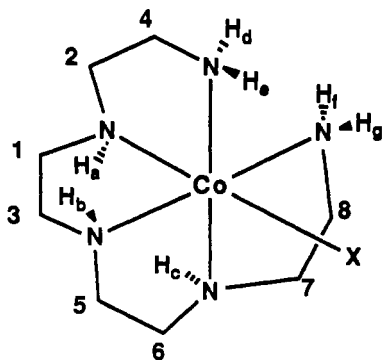(14) Buckingham, D. A.; Jackson, W. G.; Marzilli, P. A.; Sargeson, A. M. *Aust. J. Chem.*, submitted for publication.

Figure 1. Structure and atom-labeling scheme for the $\alpha\beta$-[Co(tetraen)X]$^{n+}$ ions (tetraen = $NH_2(CH_2)_2NH(CH_2)_2NH(CH_2)_2NH(CH_2)_2NH_2$). The NH proton at site c can be oriented toward (endo) or away (exo) from the X substituent.
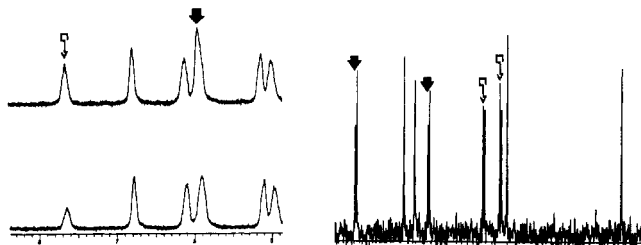

Figure 2. ^{1}H (left) and ^{13}C (right) NMR spectra for the *exo*-$\alpha\beta$-[Co(tetraen)OH$_2$]$^{3+}$ ion undergoing deuteration at the fastest and next fastest protons to exchange (in D$_2$O). Arrows indicate signals that are decreasing in intensity with time. In the ^{13}C NMR spectra, the signals immediately to the right are increasing in intensity.

Figure 3. ^{1}H (left) and ^{13}C (right) NMR spectra for the *exo*-$\alpha\beta$-[Co(tetraen)OH$_2$]$^{3+}$ ion showing completed exchange for the first two NH protons and partial exchange for the third, fourth, and fifth protons (in D$_2$O). Arrows indicate signals that are decreasing in intensity with time (at pH 5, on a time scale of minutes to hours). In the ^{13}C NMR spectra, the signals immediately to the right are increasing in intensity.

established by X-ray crystallography.[15] This sec-NH is referred to as a "planar" or "flat" sec-NH where it is the central part of two chelate arms arranged meridionally (which is "flat" on a time average); the other sec-NH centers are referred to as "angular" where they are central to facially arranged chelate arms. The chirality at nitrogen is fixed in the facial arrangement but can adopt either configuration in the meridional arrangement.

The [Co(tetraen)X]$^{n+}$ complexes exchange their NH protons by a base-catalyzed process that is slow (minutes to hours) in neutral to mildly acidic D$_2$O solution.[11] Epimerization can occur at the planar NH center in the $\alpha\beta$ isomer as a result of the deprotonation–reprotonation process, which also leads to exchange. However, it is known that reprotonation with retention (i.e. H–D exchange) is at least 1000-fold faster than N-inversion in these complexes,[11] and there is no epimerization at the planar NH for any of the molecules reported herein in the time scale of the reactions investigated (for even the protons slowest to exchange).

The problem is to unambiguously assign specific NH signals in the ^{1}H NMR spectrum to specific sites in the [Co(tetraen)OH$_2$]$^{3+}$ molecule. All NH protons are inequivalent, including the NH$_2$ protons H-d and H-e and likewise H-f, H-g; the protons in the latter pairs are intrinsically diastereotopic due to the overall asymmetry of the complex ion. We had not hoped to individually assign, for example, H-d and H-e, but it was useful to discover which of the four NH$_2$ protons belonged to the set H-d, H-e and which to H-f, H-g.

The 300-MHz proton NMR spectrum (Figure 2) shows six NH resonances, one corresponding to two protons, and thus accounting for all seven protons. The two-proton signal is an accidental degeneracy; it is resolved, for example, in the closely related chloro derivative considered below, and the degeneracy was confirmed by the proton-exchange studies now described. The proton-decoupled ^{13}C NMR spectrum shows the tetraen carbon backbone as eight well-spaced singlets.
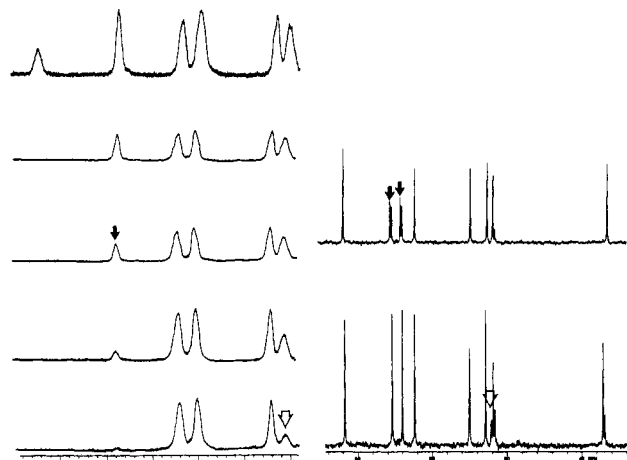
(15) Snow, M. R.; Buckingham, D. A.; Marzilli, P. A.; Sargeson, A. M. *Chem. Commun.* **1969**, 891.
(16) Balahura, R. J.; Jordan, R. B. *J. Am. Chem. Soc.* **1970**, *92*, 1533.

^{1}H and Waltz-proton-decoupled ^{13}C NMR spectra were run at each stage of the series of seven distinct deuteration processes. In D$_2$O the lowest field NH signal was the first to disappear, followed closely by one (and only one) of the signals comprising the accidental degeneracy. (The remaining proton here proved one of the two slowest to exchange.) The exchange rates were such that these two protons were essentially fully deuterated before any others even commenced to exchange (Figure 3). From the ^{13}C NMR spectra obtained during (Figure 2) and at the end of this stage of exchange (Figure 3), the corresponding α-carbon signals could be easily assigned because the isotopomers –C–ND– and –C–NH– arising from the deuteration processes are easily resolved. New C signals appear in pairs, each component of a new pair being ca. 0.1 ppm to higher field of the corresponding signal of the original pair. The magnitude and direction of the shift are consistent with the expected[1-3] secondary isotope effect for $-C_\alpha-ND-C_\alpha-$ vs $-C_\alpha-NH-C_\alpha-$, and the observation of only one set of new signals establishes that the exchanging NH centers are secondary; i.e. that they bear only one exchangeable proton. Furthermore, each pair of new signals grew at different rates, and so the amine signal associated with each pair could be clearly identified.

It is important to note that remote C–D coupling (in –C–ND–) is not observed, even when the line widths are as narrow as 0.5 Hz, and presumably this is because of the intervening quadrupolar nitrogen.

The third NH proton to exchange, much more slowly than the other two, was identified as the remaining sec-NH, also giving rise to a new pair of carbon signals on deuteration (Figure 3). It remained to assign these three pairs of carbons, and hence the corresponding α-NH protons, unambiguously to the specific pairs (C-1, C-2), (C-3, C-5), and (C-6, C-7).

The four other NH signals exchanged even more slowly. Since all sec-NH signals have been identified, these must be the terminal NH$_2$ protons. In the ^{13}C NMR spectrum the signal of a carbon which is α to a particular NH$_2$ was replaced first by a new signal 0.1 ppm upfield, which in turn was replaced by another 0.2 ppm upfield from the original. This (transient) tripling of just the one carbon signal (at a time) is characteristic of C attached to NH$_2$ and distinguishes it from a C attached to a sec-NH (Figure 3). This stepwise exchange at NH$_2$ was observed for just two carbons, the two at highest field, and of these, the one at lower field was affected earlier. Also, it was apparent that the individual protons on each NH$_2$ were exchanging at different (but not greatly different) rates. The ^{1}H NMR spectra run in conjunction with the ^{13}C spectra revealed that the two NH signals at highest field in the ^{1}H spectrum were associated with the carbon at second highest field in the ^{13}C spectrum (Figure 3). The remaining NH signals

Table I. ^{1}H NMR Data for *exo*- and *endo*-αβ-[Co(tetraen)X]$^{n+}$ in Acidified D$_2$O (ppm Downfield from NaTPS)

| | X = OH$_2$ | | | X = Cl$^-$ | | |
| | δ, ppm | | | δ, ppm | | |
assgnt[a]	exo	endo	Δ(δ),[b] ppm	exo	endo	Δ(δ),[b] ppm
flat sec-NH: H-c	7.65	7.10	0.55	7.10	6.90	0.20
cis-angular-sec-NH: H-b	6.77	6.67	0.10	6.53	6.30	0.23
term-NH$_2$: H-d, H-e	6.10	6.16	−0.06	5.76	5.76	0
	5.90	5.96	−0.06	5.40	5.52	−0.12
trans-angular-sec-NH: H-a	5.90	5.70	0.20	5.90	5.76	0.14
term-NH$_2$: H-f, H-g	5.10	5.30	−0.20	4.72	4.70	0.02
	4.95	4.96	−0.01	4.60	4.70	−0.10

[a] Refer to Figure 1 for amine proton labeling scheme. [b] δ(exo) − δ(endo).

Table II. Upfield Isotopic Shifts (Hz) in the 75.48-MHz High-Resolution ^{13}C NMR Spectra of *exo*-αβ-[Co(tetraen)X]$^{n+}$ in Acidified D$_2$O at 25 °C

| deuter- | X = OH$_2$ | | X = Cl$^-$ | |
ation site[a]	α shift	β shift	α shift	β shift
f, g	C-8: 9.2, 9.2[b]	C-7: 1.5,[c] 2.4[b]	C-8: 9.3, 9.3[b]	C-7: 1.7,[c] 2.1[b]
d, e	C-4: 8.6, 8.5[b]	C-2: 0.6,[c] 0.7[b]	C-4: 9.2, 9.2[b]	C-2: 1.0,[c] 1.3[b]
c	C-6: 9.0	C-8: 1.2	C-6: 9.1	C-8: 1.3
	C-7: 8.9	C-5: 1.3	C-7: 9.1	C-5: 1.8
b	C-3: 8.4	C-1: 0.6	C-3: 8.5	C-1: 0.7
	C-5: 8.9	C-6: 0.6	C-5: 8.4	C-6: 0.7
a	C-2: 8.5	C-3: 1.7	C-2: 8.6	C-3: 1.5
	C-1: 8.2	C-4: 1.7	C-1: 8.6	C-4: 1.5

[a] For amine site lettering and atom numbering refer to Figure 1. [b] Shifts due to first and then second D substitution. [c] Strong suggestion of an extra signal between these.


PPM relative to SIMe$_4$
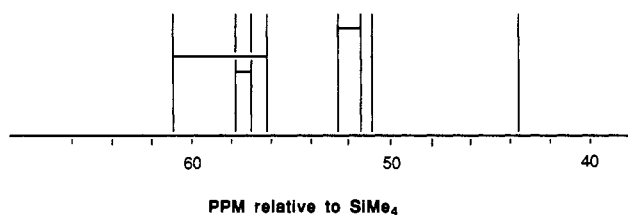
Figure 4. ^{13}C NMR spectral associations: carbons α to a particular NH are joined, and those α to an NH$_2$ are unjoined.

are obviously associated with the remaining carbon signal, and this was confirmed by the spectra for the advanced stages of deuteration.

Figure 4 summarizes the identification of carbons α to a particular NH (joined) and those α to an NH$_2$ (unjoined).

The assignments for two of the three sec-NH protons hinges on the correct identification of the two terminal carbons, C-8 and C-4. The ^{1}H chemical shifts for NH trans to the substituent X are predictable but the cis less so,[12] and the term-NH$_2$ groups in the present complex are both cis to X (Figure 1). However, the ^{13}C NMR spectra for a number of *exo*- and *endo*-αβ-[Co(tetraen)X]$^{n+}$ derivatives reveal that the chemical shifts for all but one carbon (that at −26 ppm, relative to dioxane) are especially sensitive to the configuration at the planar sec-NH (NH exo or endo to X); they are less sensitive to the X group.[14] Because the configuration at the planar sec-NH affects the adjacent ring conformations, for the carbons in question it will affect C-8 most and C-4 least, and we therefore confidently assign the −26 ppm carbon as C-4. The basis for this assignment is further supported by observations[17] on the ^{13}C NMR spectra for numerous *exo*- and *endo*-[Co(dien)(diamine)X]$^{n+}$ ions where the NH$_2$ assignments are unambiguous.

Attempted assignments based on the ^{1}H NMR spectra alone are at best tenuous.[12,13] To illustrate the point, the chemical shifts for *exo*- and *endo*-[Co(tetraen)X]$^{n+}$ (X = OH$_2$, Cl$^-$) in acidic D$_2$O are given in Table I. It would seem that the lowest field NH is the planar sec-NH because this shows the greatest shift when this center is inverted. This assignment for the aqua isomers would be correct (vide infra). However, for the corresponding isomeric chloro pair, this same proton signal is *not* the most sensitive to

(17) Jackson, W. G. Unpublished results.
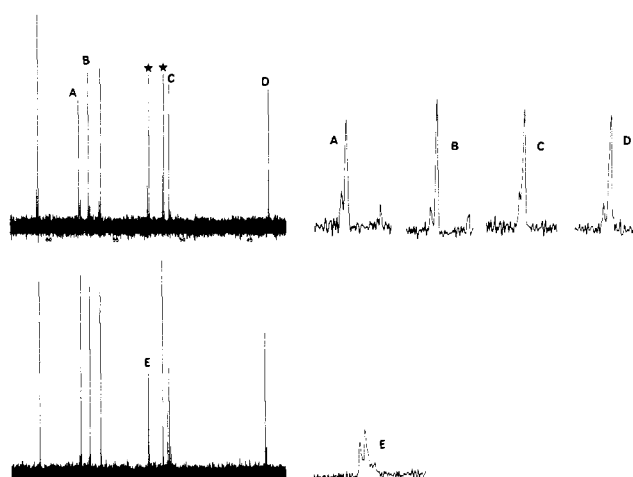
Figure 5. Resolution-enhanced ^{13}C NMR spectra (25 °C, D$_2$O) for the *exo*-αβ-[Co(tetraen)OH$_2$]$^{3+}$ ion at the stage of partial exchange of the first two protons, having C$_β$–C$_α$–NH:C$_β$–C$_α$–ND isotopomer ratios of 1:3 (A, C) and 1:4 (B, D). The α isotopomer patterns are apparent in the left spectra, and the β as well in the expanded spectral regions on the right.

inversion of the nitrogen. The cis-angular-sec-NH in particular, and three other protons show comparable shift differences between the two isomers.

It follows from the assignment of C-8 (and hence C-4) for the exo aqua ion that the highest field pair of NH$_2$ protons in the ^{1}H NMR spectrum (Figure 2) are H-f and H-g, and the next two to lower field are H-d and H-e.

At 75.48 MHz, the upfield isotopic shift on the carbons is about 8.5–9.5 Hz. High-resolution spectra ($w_{1/2}$ = ca. 0.5 Hz) for the exo aqua ion as well as several other exo and endo derivatives reveal no obvious correlation between the magnitude of the shift and structural environment—the variations are very small (<1 Hz) for carbon α to the flat or angular sec-NH or terminal NH$_2$ groups (Table II).

With higher resolution the isotopic shifts for the carbons β to the exchanging NH or NH$_2$ groups are observed; the upfield shifts are small, in the range 0.6–2.4 Hz (Table II). Although the range is <2 Hz, the shifts show a proportionately larger variation with chemical environment than the α shifts, but there is no obvious

Figure 6. ^{1}H and ^{13}C NMR assignments for the *exo*-$\alpha\beta$-[Co(tetraen)-OH$_2$]$^{3+}$ ion. For the lettering and numbering scheme refer to Figure 1.

Figure 7. Resolution-enhanced ^{13}C NMR spectra (25 °C, D$_2$O) for the *exo*-$\alpha\beta$-[Co(tetraen)OH$_2$]$^{3+}$ ion at the stage of complete exchange of the three secondary amine protons and partial exchange at the terminal NH$_2$ groups. The α isotopomer patterns are apparent in the left spectra, and the β in the expanded spectral regions on the right.

correlation with gross structural features. We return to this point again later.

The observation of these β isotopic shifts allows the unambiguous assignments of individual carbon resonances. By matching isotopomer patterns for the carbons α and β to an exchanging NH, we can establish the carbon–carbon connectivity, provided the exchange rates are not perchance identical. This point is illustrated by reference to Figure 5, which shows the resolution-enhanced Waltz-proton-decoupled ^{13}C NMR spectrum for the system at the time when one sec-NH is 75% exchanged (each of two α-C signals is a 1:3 pattern; 9.0-Hz separation between corresponding signals in each pair), one sec-NH is 80% exchanged (α-C, 1:4 patterns, 8.5-Hz separations), and the other NH protons have not significantly exchanged yet. The expanded spectral regions show four sets of β-carbon signals with isotopic shifts of around 2 Hz, two (A, C) having the 1:3 isotopomer ratio and two (B, D) the 1:4 ratio. To clarify, C-8 (C, Fig 5) has the β 1:3 pattern, and since C-7 is joined to it, this must be one of the two carbons comprising the α 1:3 carbon pair (*, Fig 5), and the other carbon in this α pair is thus C-6 (refer to Figure 4). At this stage we do not know which is C-6 and which is C-7. This pair of carbons is associated with the NH between them, i.e. H-c (Figure 1), and H-c can therefore be assigned in the ^{1}H NMR spectrum as the second fastest exchanging proton.

Similarly, C-6 is joined to C-5, and these show the 1:3 α and β patterns, respectively, thus C-5 is identified as A. From Figure 4 it follows that the partner to C-5 (A) is C-3 (B). These carbons span the cis-angular-sec-NH, H-b, which is thus identified in the ^{1}H NMR spectrum as the third fastest proton to exchange. The remaining carbons must be C-1 and C-2, which span the remaining sec-NH, that trans to the aqua group and the fastest to exchange (H-a). C-1 and C-2 cannot at this stage be individually assigned. These carbons have the α 1:4 isotopomer pattern, and C-4 and C-3, which are joined to these and one atom more remote from the exchanged NH center, must therefore show the β 1:4 pattern, which they do. All amine protons, the terminal NH$_2$ and the three sec-NH, have now been unambiguously assigned as summarized in Figure 6.

Carbons C-8, C-4, C-5, and C-3 have been identified, and it remained to distinguish C-7 from C-6 and distinguish C-2 from C-1. The β shifts resulting from the deuteration at the next fastest (third) exchanging proton (H-b, Figure 1) allowed this. The α exchange, stopped at the stage corresponding to an α 4:6 C-N-H:C-ND pattern (not shown), revealed the 4:6 β isotopomer patterns in two carbons, thus identified as C-6 and C-1. These particular β isotopic shifts were each ca. 0.6 Hz and were difficult to detect. The assignments resulting from their detection are
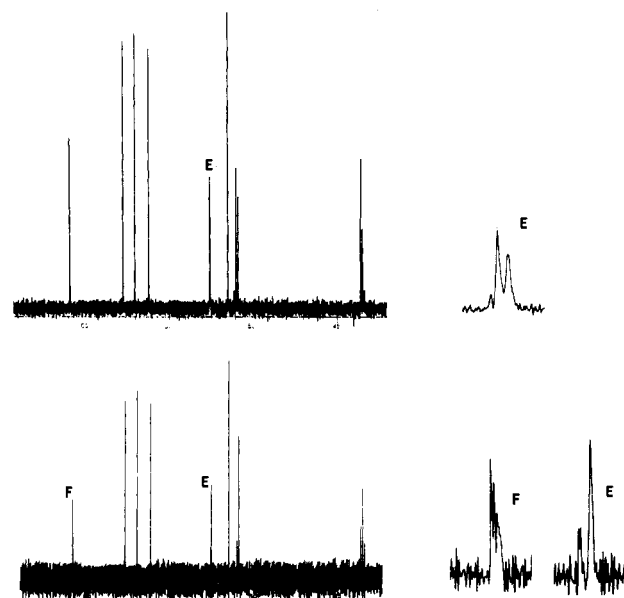
however confirmed, as detailed below. Figure 6 gives the complete assignments for the ^{13}C NMR spectrum of the *exo*-$\alpha\beta$-[Co(tetraen)OH$_2$]$^{3+}$ ion recorded in acidic D$_2$O.

The identification of the sec-NH proton H-b spanned by the carbon pair C-5 and C-3 is independent of the preliminary assignment as to which of the carbons α to the terminal NH$_2$ groups is C-8 and which is C-4. This can be shown by reversing the assignments and following through the logic, although it leads to a reversal in the C-5 and C-3 assignments. Intuitively this is reasonable, since this NH site is unique in being the only site to have two -CH$_2$-CH$_2$-NH- substituents.

The last protons to exchange were the primary NH$_2$. ^{13}C NMR spectra recorded late in the HD-exchange sequence and at the stage of significant D incorporation into both sites (Figure 7) show clearly that the signal assigned as C-4 is associated with the lowest field carbon signal, assigned as C-2, because the isotopomer patterns are identical. It is also clear that the peaks assigned as C-8 and C-7 show the expected α and β isotopomer patterns due to partial exchange at H-f and H-g, confirming the assignments shown in Figure 6.

The ^{1}H (NH region; Table I) and ^{13}C NMR spectra for the chloro complex *exo*-$\alpha\beta$-[Co(tetraen)Cl]$^{2+}$ were assigned by using the same strategies (Table II). The exo complexes have similar spectra, distinctly different from those for endo-$\alpha\beta$ isomers.[14] However this fact cannot be used as a reliable basis for assignments of individual carbons in the ^{13}C spectra; for example, the positions for C-5 and C-3 in aqua complex were reversed compared to those in the chloro derivative. Further, the NH trans to Cl, H-a, is located unambiguously. This is an important result because there has always been a need to relate proton-exchange rates to specific NH sites in such molecules; deprotonation at a coordinated amine is an important component of the mechanisms for epimerization and base hydrolysis.[10,18,19] In particular, it has been generally assumed that amine protons trans to Cl⁻ tend to be the most acidic (i.e., the fastest to exchange), and often this was the basis for the assignment.[10,12] Clearly, sites can now be identified without prior knowledge of relative acidities.

The analysis described in this article can be extended to other diamagnetic and kinetically inert metal ion complexes of multi-

(18) Buckingham, D. A.; Foxman, B. M.; Herlt, A. J.; Jackson, W. G.; Marzilli, P. A.; Sargeson, A. M. *Inorg. Chem.*, to be submitted for publication.

(19) Tobe, M. L. In *Advances in Inorganic and Bioinorganic Mechanisms*; Sykes, A. G., Ed.; Academic Press: New York, 1983; Vol. 2, p 1.
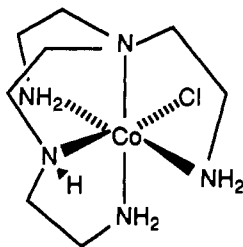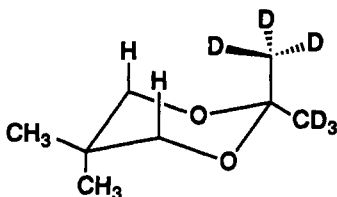
Figure 8. The s-[Co(trenen)Cl]$^{n+}$ ion.

Figure 9.

dentate amines. In the s-[Co(trenen)Cl]$^{2+}$ ion,[14] for example (Figure 8), the assignment of the sec-NH is clear from the doubling in the α-C on deuteration, while the two kinds of NH_2 cis to Cl can be individually assigned on the basis of the β isotopomer distributions.[17]

Finally, we mention efforts to resolve stereoisotopomers by ^{13}C NMR spectroscopy, where the diastereoisomerism arises from the presence of an asymmetric center R–NHD–R′. Deuteration at a terminal amine in the exo-$\alpha\beta$-[Co(tetraen)X]$^{n+}$ ions (H-f, H-g, Figure 1) results in the C-8 signal moving upfield by 9 Hz. This signal is actually due to two species, diastereomers which differ in the configuration at nitrogen for the –CH_2–NHD– portion of the molecule; that these two NH sites are chemically distinct is clear from the ^{1}H NMR spectrum (Figure 2). The same is true of C-4 when H-d or H-e (but not both) on the same N is deuterated (Figure 1). However, at high resolution ($w_{1/2}$ = 0.5 Hz)

these ^{13}C peaks remained singlets, and the effect on the chemical shift due to the change in stereochemistry with the interchange of H and D is obviously smaller than 0.5 Hz. Curiously, the more remote C signals, β to these chiral –NHD– centers, showed distinct evidence of doubling (Table II), consistent with resolution of stereoisotopomers, but higher resolution than presently achieved will be needed to make this convincing. It has been noted that the β isotopic shifts seem more sensitive to stereochemical modifications, and presently this is not understood.

Secondary isotopic shifts appear to be largely a through-bond effect arising from the different vibrational frequencies of (in this case) N–H and N–D.[1-3] We are pursuing the problem with related molecules, noting that in at least one case (Figure 9)[20] a through-space effect of five-bond-remote isotopic substitution has been observed.

Experimental Section

The complexes were fully characterized samples from batches used previously.[14,18] ^{1}H and ^{13}C NMR spectra were obtained for degassed D_2O solutions (internal dioxane reference) with use of a Varian XL300 spectrometer, a broad-band probe thermostated at 25 °C, high-precision 5-mm tubes, and Waltz-proton-decoupling to maintain temperature control (^{13}C). With good temperature control and with a digital resolution of 0.1 Hz/point, standard pulsing, an acquisition time of 0.9 s, zero time delays, and resolution enhancement in the FID processing, line widths of 0.2 Hz were obtained for dioxane and about 0.5 Hz for complex ion carbons, all of which are adjacent to quadrupolar [14]N. Complex concentrations were typically 0.1 M.

(20) Anet, F. A. L.; Dekmezian, A. H. *J. Am. Chem. Soc.* **1979**, *101*, 5449.