

from that typical of the tetrachlorodimethoxy complex to the spectrum whose parameters are given in Table II. The product also shows axial symmetry at 77°K. The addition of excess HCl to the solution causes the spectrum to revert to the original form. It seems that chloride is displaced by DMSO and that the process is reversible.

It appears likely that some ligand exchange may also have occurred in pyridine.

At present we are making an extensive study of the kinetics and equilibria in the ethoxide-methoxide exchange and the chloride-DMSO exchange.

The isotopic contact terms, K , may be calculated from the equations

$$A = -K - \frac{4}{7}\beta^2P + (g_{\parallel} - 2.0023)P + \frac{3}{7}(g_{\perp} - 2.0023)P$$

$$B = -K - \frac{2}{7}\beta^2P + \frac{11}{14}(g_{\perp} - 2.0023)P$$

for a d^1 ion and assuming the electron is in the $b_2(d_{xy})$ orbital.⁶ If P is taken for the "free ion" ($55.0 \times 10^{-4} \text{ cm}^{-1}$ for Mo^{3+} , *i.e.*, the average for the two isotopes and a net charge of $3+$ for the $\text{Mo}(\text{OCH}_3)_2^{3+}$ unit⁶), then we may also solve for β^2P and thus determine β^2 .

From the relationship

$$\chi = -\frac{3}{2} \left[\frac{hca_0^3}{2.0023g_n\beta_n\beta_e} \right] K$$

χ in atomic units may also be determined. To de-

termine g_n we employed an average value for the two isotopes

$$g_n = \frac{1/2(-0.9099 - 0.9290)}{5/2}$$

In Table IV are listed the values of K , χ , β^2 , and $P_{\text{complex}} (= \beta^2P_{\text{ion}})$. These values are comparable to those obtained for other Mo(V) complexes³⁻⁶ but the $-K$, and hence $-\chi$, are on the low side, which may indicate high ionic character. The β^2 are about 0.94 and suggest that the electron is essentially a b_2 electron.

TABLE IV

VALUES OF THE ISOTOPIC CONTACT TERM, K , AND χ AND β^2 FOR TETRACHLORODIALKOXOMOLYBDATES(V) IN METHANOL GLASSES AT 77°K

Compound	$-K$, $\text{cm}^{-1} \times 10^4$	$-\chi$, au	P , $\text{cm}^{-1} \times 10^4$	β^2
$\text{C}_5\text{H}_5\text{N}[\text{Mo}(\text{OCH}_3)_2\text{Cl}_4]$	44.7	5.72	51.9	0.945
$(\text{CH}_3)_4\text{N}[\text{Mo}(\text{OCH}_3)_2\text{Cl}_4]$	44.9	5.74	51.8	0.944
$\text{C}_9\text{H}_8\text{N}[\text{Mo}(\text{OCH}_3)_2\text{Cl}_4]$	44.7	5.72	51.6	0.940
$\text{C}_5\text{H}_6\text{N}[\text{Mo}(\text{OC}_2\text{H}_5)_2\text{Cl}_4]$	44.8	5.73	51.6	0.940

In the work with Nb(IV) we were able to employ an approximate molecular orbital treatment and make some estimates of the bonding parameters. However, in the present case there seems to be a large uncertainty in the spin-orbit coupling constant^{4,5} and since we are unable to locate the low-energy charge-transfer band and the $b_2 \rightarrow a_1$ transition, it seems wiser to postpone such a treatment.

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Cobalt(III)-Catalyzed Deuterium Exchanges on Ligands with Glycinate Rings¹

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The isotopic exchange in acidic heavy water of cobalt(III) polyaminocarboxylic acid chelates containing glycinate ring structures was followed by nuclear magnetic resonance spectroscopy by observing decreases in spectral intensities. The exchange process, occurring by pseudo-first-order decay, was studied in the acidity range 0.05 to 0.5 M acid at 85, 95, and 103°. Intermediate isotopic enantiomeric species were observed to be formed at the out-of-plane methylene carbon while the in-plane methylene protons did not undergo direct isotopic exchange. A major consideration in elucidating various features of the exchange process was the stereochemistry of the individual ligand. An enol intermediate has been proposed for the exchange mechanism.

Introduction

Acidic D_2O solutions of ethylenediaminetetraacetatocobalt(III), $[(\text{Co}(\text{EDTA}))^-]$, when heated, were observed by nuclear magnetic resonance (nmr) spectroscopy to undergo a decrease in intensity of the acetate

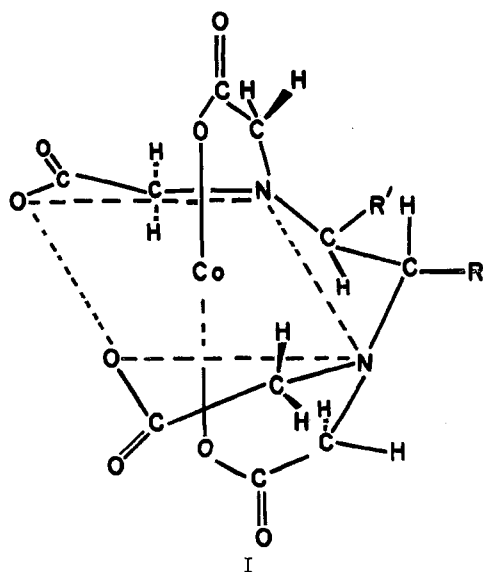
proton resonances, indicating that isotopic exchange was occurring. *trans*-1,2-Cyclohexanediamine- N,N' -tetraacetatocobaltate(III), $[\text{Co}(\text{CyDTA})^-]$, and *dl*-1,2-propylenediamine- N,N' -tetraacetatocobaltate(III), $[\text{Co}(\text{PDTA})^-]$, were also studied, providing additional insight into the isotopic exchange processes. Previous isotopic exchange studies of Co(III) chelates

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by Williams and Busch² indicated base-catalyzed deuterium exchange for $[\text{Co}(\text{EDTA})]^-$, $[\text{Co}(\text{en})_2(\text{glycine})]^{2+}$, and $[\text{Co}(\text{en})_2(\text{alanine})]^{2+}$.

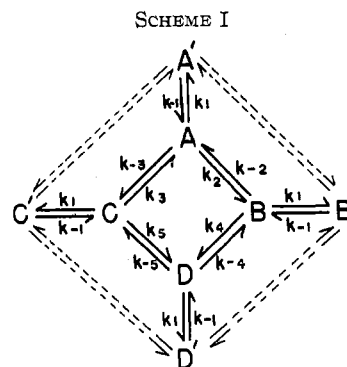
The rate of cobalt-acetate bond rupture³ in $[\text{Co}(\text{EDTA})]^-$ and the rate of cobalt-acetate bond formation^{4,5} in the hydrolysis⁶ of $[\text{Co}(\text{EDTA})\text{H}_2\text{O}]^-$, the chemistry of $[\text{Co}(\text{EDTA})\text{X}]^{2-}$ ($\text{X} = \text{halogen}$),⁷ the racemization of $(+)\text{-}[\text{Co}(\text{EDTA})]^-$,^{8,9} and the X-ray crystallography of $[\text{Co}(\text{EDTA})]^-$ ¹⁰ have provided the necessary background for an interpretation of various features of the acidic isotopic exchange mechanism. Considerable efforts have been made to elucidate the nature of Co(III)-ligand bonding which facilitates metal-catalyzed reactions. Examples of such Co(III) reactions have been observed in studies of the hydrolysis of Co(III) peptide complexes^{11,12} and the isotopic exchange of N-substituted protons of mixed ethylenediamine Co(III) complexes in near-neutral heavy water.^{2,13}

The Co(III) complexes of EDTA, CyDTA, and PDTA may be illustrated by the general form I, where $\text{R} = \text{R}' = \text{H}$ for $\text{Co}(\text{EDTA})^-$, R and R' are cyclohexane ring residues for $\text{Co}(\text{CyDTA})^-$, and $\text{R} = \text{CH}_3$, $\text{R}' = \text{H}$ for $\text{L-}[\text{Co}(\text{d-PDTA})]^-$.



Scheme I indicates the various routes by which different isotopic products may be formed.

A is the diprotonated out-of-plane methylene group, and A' is the diprotonated in-plane methylene group. B and C represent the different monodeuterated out-of-plane products of methylene configuration ($\text{C} < \begin{smallmatrix} \text{H} \\ \text{D} \end{smallmatrix}$).



$\text{C} < \begin{smallmatrix} \text{D} \\ \text{H} \end{smallmatrix}$. B' and C' represent the respective monodeuterated in-plane products. D is the fully deuterated out-of-plane methylene and D' is the fully deuterated in-plane methylene. In this work, evidence indicates that isotopic substitution occurs only on the out-of-plane methylene groups; hence, the paths shown by dotted lines are unimportant.

The interchange of out-of-plane glycinates with in-plane glycinates by a thermal racemization process^{14,15} is possible only in the case of $[\text{Co}(\text{EDTA})]^-$. The rate of racemization is assumed to be independent of isotopic influence and is, therefore, designated alike (k_1 and k_{-1}). In the case of $[\text{Co}(\text{CyDTA})]^-$ and $[\text{Co}(\text{PDTA})]^-$ complexes, racemization is prevented by steric effects (*vide supra*) and deuterated in-plane products (B', C', D') are not formed. In the case of $[\text{Co}(\text{EDTA})]^-$, formation of deuterated in-plane methylene products occurs *via* isotopic exchange of out-of-plane methylenes and subsequent thermal racemization.

The objective of this study was to elucidate the mechanism of the isotopic exchange, correlate various Co(III)-ligand stereochemistries with respective methylene AB splitting patterns, evaluate the synthetic utility for the preparation of various deuterium-labeled ligands, and extend insight into the nature of Co(III)-acetate bonding.

Experimental Section

The proton magnetic resonance spectra were recorded with a Varian A-60 high-resolution nmr spectrometer. An HA-100 Varian nmr spectrometer was used to ascertain conformation of the spectral parameters for the detailed $[\text{Co}(\text{PDTA})]^-$ spectra. The chemical-shift values of Co(III) chelates obtained in these laboratories were found to agree with the previously reported values for $[\text{Co}(\text{EDTA})]^-$ of Legg and Cooke¹⁶ and the later reported values for all three Co(III) chelates of Day and Reilley.¹⁷ The measurements of chemical shift were made using the side-band modulation technique. A Hewlett-Packard 241A oscillator and a Hewlett-Packard 5233L frequency counter were used, and the values were referenced to 3-(trimethylsilyl)propane sulfonate (TMS*). The precision in the listed values (Table I) was felt to be ± 0.005 ppm. The average deviations in the spectral parameters listed in Table I (with those of Day and Reilley) are $\Delta^*\delta$, ± 0.025 ppm; $\Delta\delta_{\text{AB}}$, ± 0.01 ppm; and ΔJ_{AB} , ± 0.47 cps. Values for the coupling constants and for changes in chemical shifts denoting protonation equilibria were measured on precalibrated

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TABLE I
 NMR SPECTRAL PARAMETERS FOR Co(III) COMPLEXES^a

Complex	δ, ppm	Acetate protons ^b			No. of protons	Figure designation	Methyl proton ^b	
		Av δ*	δ _{AB} , ppm	J _{AB} , cps			δ, ppm	J, cps
Co-EDTA	3.746	3.831	0.333	16.5	4	AB-one		
	3.916		0.147	18.5	4	AB-two		
Co-PDTA	3.760	3.734	0.691	18.5	2	AB-one	1.460	6.1
	3.898		0.213	18.5	2	AB-two		
	3.700		0.393	16.0	2	AB-three		
	3.671		0.264	16.0	2	AB-four		
Co-CyDTA	3.671	3.743	0.293	16.0	4	AB-one		
	3.816		0.888	18.75	4	AB-two		

^a δ* = chemical shift of pattern relative to TMS*; δ_{AB} = relative chemical shift of two AB protons. ^b Chemical shifts were measured to a precision of ±0.005 ppm.

chart paper, and the chemical-shift values reported here are relative to the values given in Table I. All nmr spectral measurements were made at ambient probe temperature (32.5 ± 0.1°).

EDTA, obtained from Fisher Scientific Co. as the tetraacid (H₄Y), and CyDTA, obtained from the Geigy Chemical Co. also as the tetraacid (H₄Y), were used without further purification. *dl*-H₄PDTA and all Co(III) chelates were synthesized and purified by the procedure of Dwyer and Garvin.¹⁸ Deuterium oxide was obtained from Columbia Organic Chemical Co. in 99% isotopic purity, which was sufficient for the present study. All other chemicals were of the highest available commercial purity and were used as received.

Solutions (to 2%) of the cobalt chelates were prepared by weighting out the dry, purified chelates and dissolving at room temperature. After dissolution, the desired amount of standardized concentrated nitric acid was added. The ionic strength of solution was not maintained constant by adding inert salt due to the high concentration of Co(III) chelates and added nitric acid.

To obtain kinetic data, the nearly-saturated solutions (0.8 M) of the metal chelates were heated in a constant-temperature bath for the desired time. Subsequently, the samples were removed from the bath and the nmr spectra recorded at room temperature. The higher-temperature studies (103°) were carried out in much the same manner, using a standard micro reflux apparatus and about 15 ml of solution. Peak-area measurements (±2%) were made with a Keuffel and Esser 423G fixed-arm polar planimeter and the collected kinetic exchange data analyzed by conventional kinetic procedures.

Synthesis of certain deuterium labeled cobalt chelates was achieved by dissolving 7 g of the dried chelate in 25 ml of heavy water and adding the desired amount of 8 M nitric acid. The solutions were then heated for various periods either in a constant-temperature bath or at reflux. Nmr spectra were taken to determine the time for optimum isotopic yield. Subsequently, the chelates were precipitated from solution by Dwyer and Garvin's procedure.¹⁸

The conditions for the various isotopically labeled chelates synthesized are given in Table II.

TABLE II

Compd synthesized	Acid, M	Temp, °C	Time, hr	Isotopic yield of acetate	
				Out-of-plane	In-plane
4D-[Co(EDTA)] ⁻	0.33	95	10	80% D	15% D
8D-[Co(EDTA)] ⁻	0.33	103	25	90% D	80% D
4D-[Co(CyDTA)] ⁻	0.66	95	5	90% D	5% D
3D-[Co(PDTA)] ⁻	0.28	95	3	$\left\{ \begin{array}{l} 90\% \text{ C} < \text{H} \\ \text{D} \end{array} \right.$ (AB-one) $\left\{ \begin{array}{l} 60\% \text{ C} < \text{D} \\ \text{H} \end{array} \right.$ (AB-two)	5% D

Preparation of 3D-H₄PDTA.—The free ligand was displaced from 7 g of 3D-cobalt complex by the addition of 4 g of 98%

ethylenediamine, 1 g of activated charcoal, and 1 ml of 3% hydrogen peroxide to the solution. Air was drawn through the solution for 40 hr to ensure complete oxidation. During this time, the solution changes from purple to golden yellow, indicating the formation of *DL*-tris(ethylenediamine)cobalt (III). The charcoal was filtered off, and concentrated hydrochloric acid was added to adjust the solution pH to 2.0. The desired 3D-H₄PDTA precipitates on scratching and cooling. The yield was 40–50%.

Results

Co(EDTA)⁻.—The nmr spectra of [Co(EDTA)]⁻, shown in Figure 1, have been interpreted previously by Day and Reilley,¹⁷ Busch and Williams,² and Legg

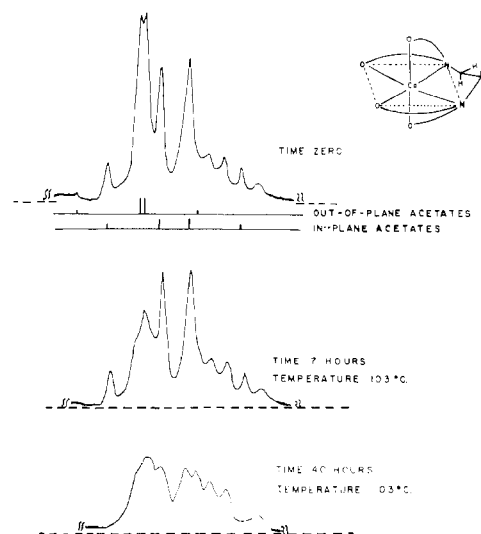


Figure 1.—The nmr spectra of [Co(EDTA)]⁻ heated in acidic D₂O for various periods.

and Cooke¹⁶ to be two AB patterns overlapping an A₂B₂ pattern. Each group of workers assigned the AB patterns to the two types of acetate geminal protons. The AB pattern with the greater chemical-shift difference is assigned to the in-plane (G)¹⁹ acetates while the more narrowly spaced, downfield AB pattern represents the out-of-plane (R)¹⁹ acetates (Figure 1). Legg and Cooke¹⁶ have discussed the [Co(EDTA)]⁻ nmr and, by analogy to similar Co(III) chelate ring structures, elucidated the dominant features which contribute to the greater chemical-shift difference observed in the in-plane acetate AB pattern. The A₂B₂ portion of the

(19) The letter designations for the various rings are those used by H. A. Weakleim and J. L. Hoard, *ibid.* **81**, 549 (1959).

nmr spectra was, consequently, assigned to the ethylenic portion of the chelate.

Acidic D₂O solutions of [Co(EDTA)]⁻ on heating exhibited a decrease in nmr spectral intensity of the downfield AB pattern while the other AB pattern remained relatively constant in intensity during this initial (7-hr) period of observation. This latter AB pattern could be diminished by exhaustive heating (40 hr).

To study the effect of acidity on the rate of decrease in nmr spectral intensity of both AB patterns, runs were carried out at various acidities. From these, it was learned that at higher acid strengths the decrease in both AB patterns was more rapid. The upper limit of the acidity studied was governed largely by the decomposition of the chelate *via* oxidation processes,^{3,15} incurring a loss of nmr spectral resolution to a degree such that an accurate analysis was no longer feasible. Furthermore, in the acidity range studied, [Co(EDTA)]⁻ is equilibrated with a protonated species [Co(H₂O)(HEDTA)] which is formed in excess acid in a matter of minutes at room temperature ($K_a = 1.3$ for 0.8 M chelate). Upon protonation of [Co(EDTA)]⁻ the only change in the nmr spectra is that the out-of-plane acetate AB pattern diminishes to half of its original area and a similarly shaped peak of corresponding area appears, presumably an AB pattern for which δ_{AB} is small.²⁰ The mean chemical shift of the protonated acetate is 0.083 ppm downfield from the center of the original AB pattern. No change was observed in the nmr spectra of the in-plane acetate resonances. Addition of base to [Co(H₂O)(HEDTA)] regenerated in a few seconds a spectrum identical with that of [Co(EDTA)]⁻. Hence, the water molecule is evidenced to be coordinated in the out-of-plane position while the EDTA is pentadentate. Higginson and co-workers^{3,5} have reported two isomeric species of the formula [Co(H₂O)(HEDTA)]. The isomer reported by Dyke and Higginson³ presumably has the water molecule in the out-of-plane position and the EDTA is pentadentate. The K_a reported is 1.28 (25°), $\mu = 1.0$.^{21a} In the other work of Shimi and Higginson⁵ the isomeric complex formed by addition of two protons to [Co(OH)(EDTA)]²⁻ has a K_a of 10⁻³,^{21a} and the loss of water from the complex giving [Co(EDTA)]⁻ is very slow, $t_{1/2} > 20$ min; presumably the isomer has the water coordinated in the in-plane position. Attempts to obtain a comparative nmr spectrum of this isomer of Shimi and Higginson⁵ were unsuccessful owing to broadened irregular-shaped resonances which suggested a mixture of isomers in the sample.

From an analysis of the nmr spectra for the heated

acidic D₂O solution of [Co(EDTA)]⁻, it was found that the initial decrease in the lower field AB pattern followed the kinetic expression

$$\frac{d}{dt} [\text{CoY}_H] = -k[\text{D}_2\text{O}^+]^n[\text{CoY}_H]$$

where [CoY_H] represents the concentration of the species containing out-of-plane methylenes present as the light hydrogen isotope. n was found to be 1.3 at 95° and 1.0 at 103°.^{21b}

An initial hypothesis was that the decrease in nmr spectral intensities was due to an isotopic exchange and that no other change in the structure of the chelate molecule had occurred. Acidic light water solutions of perdeuterio [Co(EDTA)]⁻ (prepared as described in the Experimental Section) were heated, whereupon nmr spectra identical with that of the original starting material were obtained. Analysis from the nmr spectra of the isotopic effect showed that $k_D/k_H = 6$ (where k_D is the rate of deuteration of the out-of-plane acetates in acidic heavy water and k_H is the rate of protonation of the out-of-plane acetates in light water). Further studies showed that the in-plane acetates became deuterated almost exclusively *via* a racemization mechanism. The out-of-plane acetates of the chelates were deuterated while the in-plane acetates had remained virtually all H¹ (giving 4D-[Co(EDTA)]⁻). This was achieved through the proper choice of kinetic conditions (see Experimental Section). The 4D-[Co(EDTA)]⁻ was isolated and placed in an acidic solution of light water. Nmr spectra for the heated 4D-[Co(EDTA)]⁻ solution showed that the out-of-plane acetates increased in area due to the exchange of D for H; however, the in-plane acetates at the same time decreased in intensity until such time as the out-of-plane acetates were about 60% H¹, and only then did the in-plane acetates begin to return to their original nmr spectral intensity. It was postulated from the foregoing study that the in-plane acetates do not undergo direct isotopic exchange under acidic conditions but can only become deuterated *via* a racemization mechanism. The racemization mechanism could occur through a trigonal twist mechanism⁹ or *via* an electron-exchange process¹⁴ between [Co(EDTA)]⁻ and [Co(EDTA)]²⁻. Either process would lead to an interchange of the positions of the two types of ligand acetates. The rate of racemization of [Co(EDTA)]⁻ has been reported to be pH independent at pH 2-4 (*vide supra*). Moreover, the mechanism proposed for the thermal racemization, which involves no ligand-cobalt bond ruptures, suggests a pH independence in the acidity range studied for the isotopic exchange.^{9,22}

It was found using nmr techniques that the rate of isotopic racemization for 4D-[Co(EDTA)]⁻ was comparable to the rate of optical thermal racemization for (+)-[Co(EDTA)]⁻ in the acidity range at which isotopic exchange of the out-of-plane acetate protons occurs. Hence, it was concluded that the thermal

(20) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," McGraw-Hill Book Co., New York, N. Y., 1964, p 89.

(21) (a) The K_a of 1.28 corresponds to a composite process, composed of severing the out-of-plane ligand-metal bond, protonation of the ligand, and the addition of H₂O to the vacated metal site. The K_a of 10⁻³ corresponds to the simple process of ionization of the dangling, "potentially in-plane" carboxylic group. (b) The oxidation processes which incur loss of spectral resolution become significant in the studies at 95°.

(22) J. C. Bailar, *J. Inorg. Nucl. Chem.*, **8**, 172 (1958).

racemization mechanism is a major factor in the deuteration of the in-plane acetate protons.

The contribution toward isotopic racemization from an electron-exchange mechanism, which would occur if $[\text{Co}(\text{EDTA})]^{2-}$ were present, can only be qualitatively evaluated. It is estimated from nmr spectra that the concentration of $[\text{Co}(\text{EDTA})]^{2-}$ is below 0.005 *M* in the heated acidic D_2O chelate solutions. On the basis of the known rates of electron exchange,¹⁴ it was concluded that the contribution of any electron-exchange process to the deuteration of the in-plane acetates is negligibly small. The effect of molecular asymmetry on the isotopic exchange, as found in the cases of $[\text{Co}(\text{CyDTA})]^-$ and $[\text{Co}(\text{PDTA})]^-$, was not observed to produce a detectable amount of an asymmetric $\text{C} < \begin{smallmatrix} \text{H} \\ \text{D} \end{smallmatrix}$ geminal acetate in the $[\text{Co}(\text{EDTA})]^-$ chelate.

$[\text{Co}(\text{CyDTA})]^-$.—The acetate portion of the nmr spectra of the $[\text{Co}(\text{CyDTA})]^-$ complex has been interpreted by Day and Reilley¹⁷ to consist of two types of AB patterns which overlap a portion of the cyclohexane methine resonances. The nmr spectrum of this complex, which is identical with that reported by the previous workers, is shown in Figure 2 (spectrum A). Previously, no specific assignment of the two AB patterns to the two types of acetates was made.

Acidic D_2O solutions of $[\text{Co}(\text{CyDTA})]^-$, when heated, were observed to undergo changes as shown in Figure 2, spectra B, C. One observes that AB-two collapses to a single peak which at its maximum area corresponds to 80% of the area of two protons. The chemical shift of this single peak was found to be identical with that of the lower-field member of the AB pattern.²³ In no instance did the AB-one resonance diminish in area, even upon heating in 1 *M* acid for 40 hr at 103° (spectrum C).

On the basis of the difference in the rate of isotopic exchange of AB-one and AB-two, the latter is assigned, by analogy from similar studies reported here for $[\text{Co}(\text{EDTA})]^-$, to the out-of-plane acetate and the former to the in-plane acetate. The lower-field singlet in spectrum B, Figure 2, corresponds to a single product, either C or B in the general scheme. Subsequent heating (35 hr, 95°) serves to convert the complex into its final tetradeuterio form, spectrum C. However, when 4D- $[\text{Co}(\text{CyDTA})]^-$ was heated (25 hr, 95°) in an acidic light water solution, an nmr spectrum shown as "regenerated" was obtained, which shows a singlet whose chemical shift corresponded to the up-field member of AB-two. The "regenerated" spectrum indicates that an isotopic enantiomer on the out-of-plane acetate has been formed.²⁴ Further heating (80 hr, 95°) results in an nmr spectrum identical with spectrum A being obtained. The initial rate of formation of the enantiomeric out-of-plane acetate was

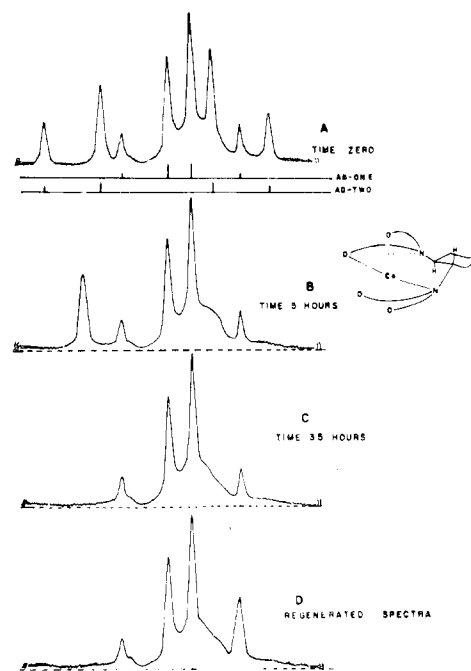
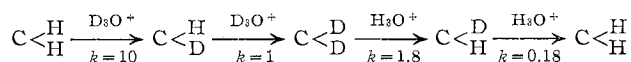


Figure 2.—The acetate portion of the nmr spectrum (A) of $[\text{Co}(\text{CyDTA})]^-$. AB-one is assigned to the in-plane acetate while AB-two is assigned to the out-of-plane acetate. Spectra B and C show the result of heating acidic heavy water solutions for various periods. Spectrum D denotes the formation of an enantiomeric (to spectrum B) $\text{C} < \begin{smallmatrix} \text{H} \\ \text{D} \end{smallmatrix}$ species on the out-of-plane acetate methylene.

six times slower than the converse reaction in heavy water.

The effect of increasing acidity on these reactions was much the same as observed for similar experiments with $[\text{Co}(\text{EDTA})]^-$, except there was no nmr evidence to suggest the protonation equilibria $\text{CoY}^- + \text{H}^+ \rightarrow \text{CoHY}$ for $[\text{Co}(\text{CyDTA})]^-$. From a kinetic analysis of the nmr spectra, it was found that at higher acid strengths the rate of decrease in intensity of the out-of-plane AB pattern was more rapid. Values for the rate of exchange at each acidity are given in Table III. A rate expression of the same form as was given for $[\text{Co}(\text{EDTA})]^-$ was applicable in these cases, and *n* was found to be 1.0 at 95°. The relative rate of the isotopic exchange reaction from the starting material to form the intermediate $\text{C} < \begin{smallmatrix} \text{H} \\ \text{D} \end{smallmatrix}$ species compared to the rate of the formation of the tetradeuterio product is about 10:1 as shown in the schematic



$[\text{Co}(\text{PDTA})]^-$. The nmr spectrum of $[\text{Co}(\text{PDTA})]^-$ consists of four overlapping AB patterns which have been attributed to the four types of nonequivalent acetate protons (upper pattern of Figure 3). No assignment of these AB patterns to corresponding methylene groups of the complex was made previously.¹⁷ The spectral patterns of the methine and the methylenic hydrogens of the propylene fragment are not of concern in this work.

(23) J. A. Pople, W. G. Schneider, and J. H. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., New York, N. Y., 1959, p 161.

(24) A. Rauk, E. Buncel, R. Y. Moir, and S. Wolfe, *J. Am. Chem. Soc.*, **87**, 5498 (1965).

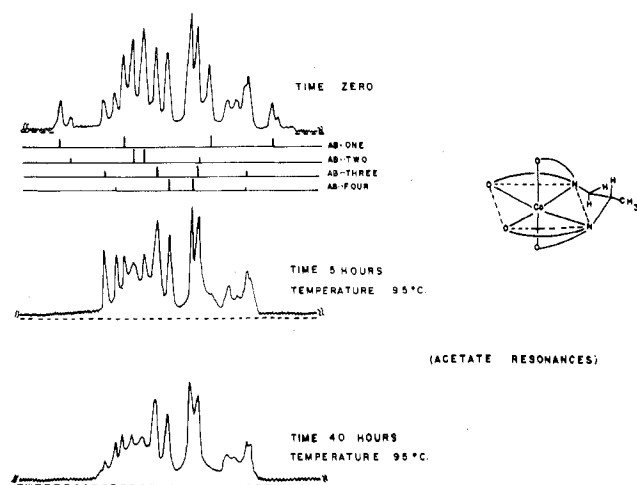


Figure 3.—The nmr spectra of $[\text{Co}(\text{PDTPA})]^-$ heated in acidic D_2O for various periods. AB-one represents the out-of-plane acetate nearest the methyl group while AB-two represents the other out-of-plane acetate. AB-three represents the in-plane acetate nearest the methyl group while AB-four represents the other in-plane acetate.

Acidic D_2O solutions of $[\text{Co}(\text{PDTPA})]^-$, when heated, exhibited changes in their nmr spectra similar to those observed in the previously mentioned chelates (Figure 3). The AB-one pattern disappears with the formation of a singlet whose mean chemical shift is calculated to be that of the lower-field member of this AB-one pair. Further heating results in complete isotopic exchange for this AB pattern (bottom spectrum).

The AB-two pattern, which is more closely spaced than the first AB pattern, lies in the most complex portion of the resonance pattern and the determination of the relative amounts of $\text{C} \begin{smallmatrix} \text{H} \\ \text{D} \end{smallmatrix}$ vs. $\text{C} \begin{smallmatrix} \text{D} \\ \text{H} \end{smallmatrix}$ intermediates was not possible. However, the net exchange rate of AB-two appeared to be more rapid than the rate of disappearance of the singlet associated with AB-one.

The AB-three and AB-four patterns were not observed to undergo exchange even at the highest acidity (0.8 M acid) and longest heating periods (40 hr at 95°). $[\text{Co}(\text{PDTPA})]^-$ was observed by nmr to form the protonated species $[\text{Co}(\text{H}_2\text{O})(\text{HPDTPA})]$. The methyl doublet was observed to shift 0.081 ppm upfield upon protonation of the chelate, enabling a calculation of K_a (equal to 1.0) to be made. The acetate portion of the spectrum of $[\text{Co}(\text{H}_2\text{O})(\text{HPDTPA})]$, due to insufficient spectral resolution (either at 60 or 100 Mc), was not evaluated.

The kinetic analysis of the initial isotopic exchange data for $[\text{Co}(\text{PDTPA})]^-$ showed the same rate expression to be followed that was found in the two previous studies. n was found to be 1.1 at 95° , and the rates of exchange are given in Table III.

By analogy with $[\text{Co}(\text{CyDTA})]^-$ and $[\text{Co}(\text{EDTA})]^-$, the AB-one and AB-two patterns are assigned on the basis of isotopic exchange to the out-of-plane acetates. The methylene group which yields the AB-one pattern, having a high degree of asymmetry in isotopic substitution, was assigned to the out-of-plane acetate

TABLE III
RATE OF DEUTERIUM EXCHANGE OF Co^{III} CHELATES
(0.8 M CHELATE IN D_2O)

Species	k (sec^{-1}) $\times 10^5$	$[\text{D}_3\text{O}^+]$, M^a	$(k/[\text{D}_3\text{O}^+])$ $\times 10^4$
$[\text{Co}(\text{EDTA})]^-$, 95°	0.6	0.080 ^d	7.6
	1.05	0.145	7.2
	1.9	0.215	9.0
	3.0	0.456	6.6
$[\text{Co}(\text{EDTA})]^-$, 103°	0.8	0.058 ^d	14.3
	1.4	0.088	16
	1.8	0.11	16
	3.3	0.18	18
	5.5	0.33	16
$[\text{Co}(\text{CyDTA})]^-$, 85°	2.3	0.165	14
	3.4	0.240	14
	4.1	0.33	12
	5.8	0.455	13
	7.7	0.587	13
	9.8	0.790	12
$[\text{Co}(\text{CyDTA})]^-$, 95°	7.7	0.31	25
	15	0.52	29
	18	0.62	29
	25	0.79	31
$[\text{Co}(\text{CyDTA})]^-$, 103°	13	0.33	39
	30	0.52	57
	32	0.65	49
$[\text{Co}(\text{PDTPA})]^-$, 85°	2.90	0.115 ^d	25
	7.7	0.281	27
	10.4	0.372	28
	15.8	0.586	27
$[\text{Co}(\text{PDTPA})]^-$, 95°	2.8	0.048 ^d	58
	4.2	0.055	76

^a Acidity of solution; no attempt made to hold ionic strength constant. Rates refer to formation of intermediates illustrated in the general scheme (see text). ^b For the process $\text{A} \xrightarrow[k = k_2]{\text{D}_3\text{O}^+} \text{B} + \text{C}$, neglecting racemization process and secondary isotopic effects. ^c For the process $\text{A} \xrightarrow[k = k_2]{\text{D}_3\text{O}^+} \text{B}$ (in the general scheme).

^d Corrected acidity for chelate buffer.

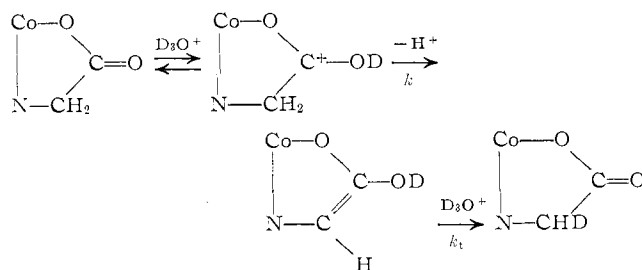
nearest the methyl group (see Discussion). In order to assign the AB-three and AB-four patterns to the respective positions on the asymmetric ligand, a 3D- $[\text{Co}(\text{PDTPA})]^-$ complex was prepared (see Experimental Section). This chelate exhibits a spectrum identical with the middle one in Figure 3. The 3D chelate was converted with ethylenediamine into tris(ethylenediamine)cobalt(III) trichloride and free $\text{H}_4(3\text{D-PDTPA})$.

A cobalt(III) chelate of the liberated $\text{H}_4(3\text{D-PDTPA})$ was then prepared, and its spectrum was used to elucidate which one of the in-plane acetate resonances, AB-three or AB-four, corresponded to the acetate on the end of the molecule closest to the methyl group. Since one-half of the asymmetric $\text{C} \begin{smallmatrix} \text{H} \\ \text{D} \end{smallmatrix}$ acetate will be found as an in-plane methylene in the recombination sequence, one could expect to observe some of the asymmetric methylene in either AB-three or AB-four. The spectra showed the recombined species to have a chemical shift identical with that of the lower field member of AB-three. Hence, AB-three represents the resonances of the in-plane ring nearest the methyl group.

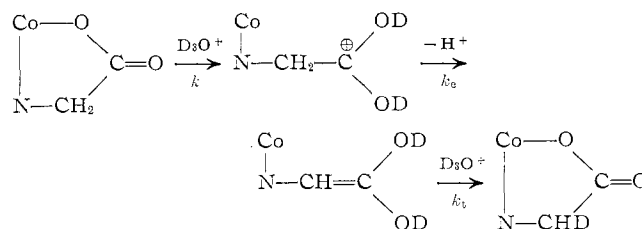
Furthermore, spectra were taken of the free $H_4(3D\text{-PDTA})$ at various acidities to resolve a previously reported ambiguity²⁵ in change of the relative chemical-shift positions for the two types of acetates of PDTA⁴⁻ at high pH. The $H_4(3D\text{-PDTA})$, having one type of acetate asymmetrically deuterated, confirmed the spectral interpretation previously reported.

Discussion

Several mechanisms for the isotopic exchange in acidic solution of the Co(III) chelates suggest themselves. First, the rapid protonation of an out-of-plane acetate may be followed by breakage of one of the geminal proton-carbon bonds, yielding an enol. The enol would subsequently be attacked by a deuterium (in heavy water) and tautomerize to give the starting form of the acetate but with a net result of deuteration.



k_e is the rate constant for enolization and k_t is the rate constant for tautomerization. A second mechanism would be the rapid protonation of the out-of-plane acetate, followed by the rupture of the metal-carboxylate bond, and the generation of a free carbonium ion intermediate as shown (below). Enolization and tautomerization of this free carbonium ion would result in a net deuteration.



The isotopic exchange could be expressed as

$$\frac{-d[\text{CoY}_H]}{dt} = k_1[\text{D}_3\text{O}^+][\text{CoY}_H] + k_2[\text{D}_3\text{O}^+][\text{CoDY}_H]$$

where the second term represents the monoprotonated complex. Since $[\text{CoDY}_H] = [\text{D}_3\text{O}^+][\text{CoY}_H]/K_a$

$$\frac{-d[\text{CoY}_H]}{dt} = [\text{D}_3\text{O}^+][\text{CoY}_H] \left\{ k_1 + k_2 \frac{[\text{D}_3\text{O}^+]}{K_a} \right\}$$

Plots of the logarithm of the observed pseudo-first-order isotopic exchange rate constant *vs.* the logarithm of the acidity are linear with a slope of near unity (see Results) for all three cobalt complexes; hence, k_2 is estimated to be less than k_1 by a factor of ten or greater. Quantitative studies of acidities greater than those

reported for each chelate were not feasible due to insufficient spectral resolution.

The observed ratio $k_D/k_H = 6$ denotes the breakage of a C-H (or C-D) bond as the rate-controlling step.²⁶⁻²⁸ If the first step (k) were dominant, the ratio of k_D/k_H would be near unity.²⁷ Previous studies of acid-catalyzed halogenation of ketones show k is large compared to either k_e or k_t .²⁸ An activation energy (E^*) of 28.0 kcal for $[\text{Co}(\text{EDTA})]^-$, 25.6 kcal for $[\text{Co}(\text{PDTA})]^-$, and 23.4 kcal for $[\text{Co}(\text{CyDTA})]^-$ (all at 95°) has been calculated for the acid-catalyzed isotopic exchange, which compares with an activation energy of 20.7 kcal ($\sim 25^\circ$) for hydrogen ion catalyzed iodination of ketones.²⁸ A direct analogy is not permitted, as E^* may be a function of temperature.

Furthermore, $[\text{Co}(\text{CyDTA})]^-$ was not observed to form a protonated complex, unlike the other two Co(III) chelates; nevertheless, a similar isotopic exchange occurs. One notes that the structure of the protonated complexes is reported to have the protonated acetate uncoordinated while a water molecule occupies the sixth ligand site.^{4,29} Model compounds were chosen to see if isotopic exchange occurred in acidic solution in the absence of metal ions. Acetic acid and glycine in 2 *M* acid refluxing for 72 hr did not undergo changes in their nmr spectra; thus, isotopic exchange does not occur to any measurable extent. Hence, it was concluded that the first mechanism proposed explains best all the observations made in this study.

The relationship between the chelate stereochemistry and the isotopic exchange processes is important. Hoard and co-workers¹⁰ have determined the conformation of $[\text{Co}(\text{EDTA})]^-$ by X-ray crystallography. Briefly, the stereochemistry of this complex is such that the in-plane acetate (G) rings are strained and bent, while the out-of-plane acetate rings (R) are planar and strain-free. The metal-carboxylate bond is longer in the R ring (1.915 Å) than in the G ring (1.885 Å). Hence, it is postulated from the stereochemistry of this complex and the nmr observations reported here that the difference in ability of the two nonequivalent acetate protons to undergo isotopic exchange is a function of ring strain. The strain-free ring readily undergoes enolization, while the bent, strained ring requires a larger energy to enolize. The order of metal-carboxylate bond distances predicts the out-of-plane methylene carbon to have the least electron density. While an X-ray analysis has not been reported for $[\text{Co}(\text{CyDTA})]^-$ and $[\text{Co}(\text{PDTA})]^-$, some conclusion might be drawn from the comparison of $[\text{Fe}(\text{OH}_2)\text{CyDTA}]_2^-$ and $[\text{Fe}(\text{OH}_2)\text{EDTA}]^-$, for which X-ray data show the metal-ligand conformation to be virtually identical.³⁰ From nmr spectra, one can de-

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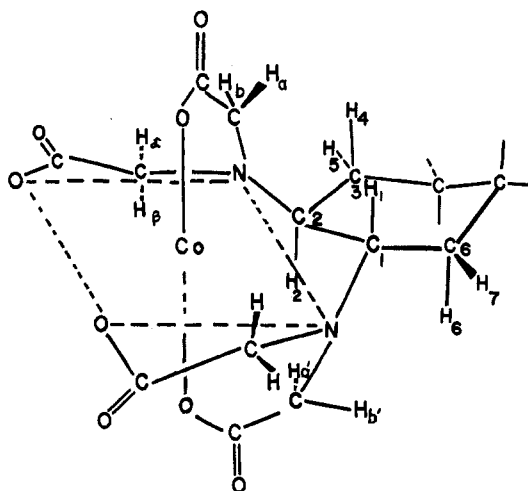
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duce the following regarding the relative ligand-cobalt conformation: ν_{AB} , which is comparable in all three Co(III) chelate in-plane acetate rings, has been interpreted by Legg and Cooke¹⁶ to arise from the non-symmetrical environment of the geminal acetate protons with respect to the carbonyl group (due to the bent ring). Thus, the in-plane acetate methylene protons in all three chelates are expected to have relatively the same stereochemistry. However, the AB patterns assigned to the out-of-plane acetate protons do not have the same ν_{AB} . The respective values are [Co(EDTA)]⁻, 0.147 ppm; [Co(CyDТА)]⁻, 0.888 ppm; and [Co(PDTA)]⁻, 0.213 and 0.691 ppm (J_{AB} is nearly the same (18.5 cps) in all the chelates). Features which might contribute to the ν_{AB} differences are bending of the R ring with respect to the carbonyl, which can probably be ruled out by the isotopic exchange observations, the anisotropic magnetic shielding by carbon-carbon single bonds,^{31,32} and any interaction of H_a with axial cyclohexane ring protons or the equatorial methyl group, in [Co(CyDТА)]⁻ and [Co(PDTA)]⁻, respectively.

Calculations for the anisotropic shielding have assumed the contribution of C-C bonds greater than three bonds removed from the given proton to be negligible as R (the radial distance) becomes large. However, in the model constructed for [Co(CyDТА)]⁻ (where H_a and H_b —identical to H_a' and H_b' —are the out-of-plane methylene hydrogens). R is sufficiently small (2.5 Å) so that some contribution of the C_2 - C_3 bond can be anticipated. As proton H_a lies directly above C_2 - C_3 , it should be shielded relative to H_b . However, if a maximum value for θ is used, the anisotropic shielding can account for only 30% of ν_{AB} . The failure of C-C bond anisotropies to account for a substantial portion of the $\Delta\nu_{AB}$ and the observations that the upfield member of the methylene pair exchanges more easily ($k_{H_a} = 10k_{H_b}$) suggest that the primary feature producing ν_{AB} is some interaction of H_a with H_1 and H_4 .



The contributions of normal C-H bonds to the gross magnetic shielding have been evaluated by Musher³¹

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and surmised to be small. Thus, there may be some electron orbital interaction of the axial cyclohexane protons (H_1 and H_4 , or H_2 and H_5) and the nearest acetate proton (H_a or H_a'). This electron interaction would probably produce a local paramagnetic effect to the electronic nuclear shielding.³³ To calculate the amount of the paramagnetic effect, the proper expression for ψ (interaction) must be chosen, which in this instance is not feasible. The geometric model (assuming that the cyclohexane ring does not significantly alter the metal-ligand conformation from that found in [Co(EDTA)]⁻³⁰) for [Co(CyDТА)] indicates that H_4 is actually much closer to H_a than is H_1 . Hence, the interaction between H_4 and H_a , which contributes to ν_{AB} , apparently plays a dominant role in the stereochemistry of the enol transition states. Studies of the rate of products formed from asymmetric enol intermediates of classical organic molecules conclude³⁴ that the initial (kinetic) product results from the reagent attacking the lobes of the transition intermediate sp^2 carbon from the least-hindered direction. This kinetic product is, in most instances, not the more stable product (thermodynamic product). In the enol intermediate proposed for the acid-catalyzed isotope exchange of [Co(CyDТА)]⁻, the incoming deuterium from the solvent shell finds the sp^2 methylene carbon least hindered on the remote side of H_4 ; hence, the kinetic product expected would have the deuterium in the position formerly occupied by H_b . This product is probably of higher energy than its enantiomorph (the thermodynamic product), but the rate of formation of the thermodynamic product is such that a further kinetic analysis of the reconversion of the kinetic product to the thermodynamic product, as would occur in D_2O - H_2O mixtures, is not feasible owing to the tendency of the chelate solutions to decompose at long heating periods (several days). The following experiment supports the above assignment: the 2D-[Co(CyDТА)]⁻ product was isolated (spectrum like spectrum B in Figure 2) and the ligand (2D-EDTA) was recovered from the chelate by a cyanide procedure identical with that described by Dwyer¹⁸ for PDTA. Then a cobalt chelate of 2D-CyDТА was prepared. The nmr spectrum of this species showed the deuterium to be in the position of the lower field member of AB-one. As the acetate in-plane ring is bent (by analogy to [Co(EDTA)]⁻), the proton closer to the plane of the carbonyl oxygen will appear at lower field, namely H_a . Molecular models show that when the CyDТА nitrogen is inverted, as in the free ligand, H_a and H_a' are effectively interchanged.

In the case of [Co(PDTA)]⁻, the metal-ligand conformation of the complex has been found to be similar to that in [Co(EDTA)]⁻ with the methyl group equatorial.³⁵⁻³⁷ Thus, the conformation for [Co(PDTA)]⁻

(33) Reference 23, pp 166-183.

(34) For a fuller discussion of this subject, see H. E. Zimmerman in "Molecular Rearrangements," P. DeMayo, Ed., Interscience Publishers, New York, N. Y., 1963, Chapter 6.

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would be similar to the drawing shown for $[\text{Co}(\text{CyDTA})]^-$, but where C_4 and C_8 are hydrogens.

By analogy to $[\text{Co}(\text{EDTA})]^-$, the interaction of H_1 and H_8 in $[\text{Co}(\text{PDTA})]^-$ is felt to be small. However, as the methyl group so strongly prefers the equatorial conformation that only two complexes of *dl*-PDTA are formed,³⁵⁻³⁷ it is felt that there exists a significant steric interaction of H_8 with the equatorial methyl protons. This steric interaction contributes to ν_{AB} of AB-one and to the observed difference in the isotopic exchange rate of H_8 and H_1 in a manner as previously pointed out in the case of $[\text{Co}(\text{CyDTA})]^-$. Moreover, it has been pointed out (Results) that H_8 was interchanged with H_1 in the liberation of the 3D-PDPA ligand and re-formation of the cobalt complex. Thus, H_8 is assigned to the lower-field members of AB-one of the $[\text{Co}(\text{PDTA})]^-$ nmr spectra. As the equatorial methyl is relatively removed from H_8' and H_1' and no steric interaction can be anticipated, no attempt is made to assign H_8' and H_1' to the respective nmr resonances.

Previous workers²⁵ in determining the protonation scheme of free PDPA⁴⁻ hypothesized that the chemical-shift difference between the protons nearest to the asymmetric atom which causes the difference is likely

to persist over the greater pH range. Although using a different basis in the present work to interpret the same protonation scheme, a concurring conclusion was reached.

The method of obtaining selectively deuterated chelates in fairly high yields reported here could be useful to obtain isotopically-labeled chelons to study various intermolecular rates of exchange, racemization rates, and electron-transfer processes. Furthermore, the postulate set forth here which relates isotopic reactivity and nmr spectra can be extended to elucidate other analogous chelate hyperfine splitting patterns. Mixed Co(III) chelates of racemic amino acids and selected asymmetric ligands are being evaluated as possible routes for obtaining optically pure amino acids.

Thus, it is anticipated that the chelate models chosen to study the scope of the acid-catalyzed isotopic exchange in heavy water will provide additional insight into the nature of the metal-Co(III) carboxylate bonding.

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Metal Complexes of the Amino Acid DL-Methionine

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The donor properties of the amino acid methionine, $\text{CH}_3\text{SCH}_2\text{CH}_2\text{CH}(\text{NH}_2)\text{COOH}$ (HMT), were investigated for a number of transition and nontransition metal ions, Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II), Al(III), Ag(I), Cd(II), Hg(II), Pb(II), Bi(III), Rh(III). Methionine behaves as an anionic ligand (Mt) and generally forms neutral complexes, $\text{M}^{\text{II}}\text{Mt}_2$ and $\text{M}^{\text{III}}\text{Mt}_3$, in which the metal attains its usual higher coordination number by linking with the N atom of the $-\text{NH}_2$ group and with one or both of the O atoms of the $-\text{COO}^-$ group. In these complexes the S atom of the $-\text{SCH}_3$ group is still available for coordination, as shown by the formation of mixed-metal complexes with Ag(I), for example, $\{\text{Cr}_2\text{Ag}_3\text{Mt}_6\}(\text{ClO}_4)_3$. Conversely, methionine forms with Ag(I) an anionic complex, $[\text{AgMt}_2]^-$, in which only the S atom coordinates, and mixed-metal complexes may then be formed by subsequent coordination of the $-\text{NH}_2$ and $-\text{COO}^-$ groups to metal ions such as Ni(II) and Cu(II). To help in the structural study of methionine complexes, a number of the corresponding complexes of the amino acid norleucine, $\text{CH}_3(\text{CH}_2)_5\text{CH}(\text{NH}_2)\text{COOH}$, were prepared and investigated.

Introduction

It is well known¹⁻⁷ that aminocarboxylic acids act as negatively charged chelating ligands toward metal ions, coordinating both through the $-\text{NH}_2$ and the

$-\text{COO}^-$ groups. In contrast only sparse information is available on the donor ability of sulfur-containing amino acids, in which the sulfur atom is also a possible ligating site. For the anion of cysteine, $-\text{SCH}_2\text{CH}(\text{NH}_2)\text{COO}^-$, both sulfur-to-metal and oxygen-to-metal bonds have been shown⁸ to exist in solid complexes of Zn(II), Cd(II), and Hg(II), whereas sulfur and nitrogen appear to be the ligating atoms toward Ni(II) in aqueous solution.⁹ With methionine, $\text{CH}_3\text{SCH}_2\text{CH}_2\text{CH}(\text{NH}_2)\text{COOH}$ (HMT), formation constants

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