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Spectropolarimetric Kinetics of the Ligand-Exchange Reaction of the Ethylenediaminetetraacetatolead(II) Complex with D-(−)-*trans*-1,2-Cyclohexanediaminetetraacetic Acid

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Optically active D-(−)-*trans*-1,2-cyclohexanediaminetetraacetic acid (D(−)CDTA) was prepared from the resolved diamine by condensation with sodium chloroacetate, followed by strong cationic exchange techniques to obtain the acid form. The kinetics of the ligand-exchange reaction of ethylenediaminetetraacetatolead(II) with D-(−)-*trans*-1,2-cyclohexanediaminetetraacetic acid in basic solution was followed by spectropolarimetry. Over the pH region of 9.9–12.3, the reaction was found to be second order overall, first order in entering ligand D(−)CDTA and first order in the complex Pb–EDTA. An analysis of the pH dependence of the exchange reaction showed three distinct areas of interest. In the pH region 9.9–12.3, the predominant pathway involved the attack of the deprotonated species D(−)$CDTA^{4-}$. Any contribution from the attack of the species D(−)$HCDTA^{3-}$ was found to be negligible. In the pH region 12.3–12.7, a monohydroxy-assisted reaction predominated; at pH values greater than 12.7, a dihydroxy-assisted reaction was proposed. The rate expression was derived considering the proposed contributory species. Computer-assisted numerical analysis of the data showed excellent agreement with the proposed mechanisms. Because of the stereospecificity of the ligand D(−)CDTA and the great difference between the large molecular rotations of the optically active complex L*-(+)-[Pb-D(−)CDTA] and the ligand at 365 nm, highly sensitive kinetic measurements were made. The stereochemical mechanistic approach of the ligand exchange, based on molecular models and the steric influence of the entering ligand, shows that the proposed mechanisms give the most favorable intermediates and account for proper stereochemical products of these reactions.

trans-1,2-Cyclohexanediaminetetraacetic acid (CDTA) was first prepared by Schwarzenbach and Ackermann[2] in their study on the effect of the positions of the nitrogen atoms upon the thermodynamic stability of metal–ligand complexes for a series of cyclohexanediaminetetraacetic acids. CDTA forms more stable complexes with most of the metal ions than does ethylenediaminetetraacetic acid (EDTA) or 1,2-propylenediaminetetraacetic acid (PDTA).[3] This greater stability (generally 1–2 pK units for most of the metal complexes) can be attributed to the fact that during chelation, the carbon chain between the nitrogen atoms in both EDTA and PDTA has to be rotated to bring the nitrogen atoms into the same plane for chelation to occur between the nitrogen atoms and the metal ion. The thermodynamically preferred chair configuration of the *trans*-CDTA, with the nitrogen atoms in equatorial positions, demands that very little reorientation of the nitrogen atoms is necessary for chelation to occur.

Commercially available *trans*-CDTA is a racemic mixture of the two possible optical isomers, D(−) and L(+). Ferrone attempted the resolution of CDTA into its optical isomers using (+)-phenylethylamine, (+)-camphorsulfonate, and (−)-quinine, but none of these attempts gave a crystalline diastereoisomer.[4] He also tried to prepare the L(+) isomer of the acid by direct synthesis from L-(+)-*trans*-1,2-cyclohexanediamine and sodium chloroacetate following the general method used in the preparation of ethylenediaminetetraacetic acid but obtained only a viscous syrup which would not crystallize upon acidification.[4] Dwyer and Garvan failed in their attempt to resolve the racemic acid with (+)-cinchonine but were successful in the resolution by using the (−)-*cis*-dinitrobis(ethylenediamine)cobalt(III) ion.[5] This procedure is very long and tedious and the yield is extremely low.

The work by Dwyer and Garvan showed that only two of the four possible isomers of the metal chelate were obtained.[5] They were the $(+)_{546}$Co(−)$CDTA^-$ and $(-)_{546}$Co(+)$CDTA^-$ isomers, proving that either one of the two optical isomers of *trans*-CDTA is completely stereospecific in its reaction with the Co(III) ion. Models show that it is impossible to obtain the isomers $(+)_{546}$Co(+)$CDTA^-$ and $(-)_{546}$Co(−)$CDTA^-$ because of the fixed stereochemistry of the cyclohexane ring and its inability to accompany certain chirality due to steric hindrances of the methylene groups of the ring and the acetato groups (Figure 1). Failure to racemize solutions of these optically active complexes at 100° in the presence of activated charcoal confirmed this conclusion experimentally. This conforms with Jaeger's theory that one configuration of the complex is incompatible with one optical isomer of the ligand.[6]

D-(−)-*trans*-1,2-Cyclohexanediaminetetraacetic acid (D(−)CDTA) was prepared by stereospecific condensation of the resolved diamine with concentrated sodium chloroacetate in a strongly basic medium, followed by the use of a strong cationic exchange resin to obtain the free acid.

Polarimetry was first used by Bosnich and Dwyer to study the rate of ligand exchange of D-(−)-1,2-propylenediaminetetraacetic acid with several metal com-

(1) (a) Abstracted in part from the Ph.D. dissertation of P. E. R. (b) To whom all correspondence should be addressed.

(2) G. Schwarzenbach and H. Ackermann, *Helv. Chim. Acta*, **32**, 1682 (1949).

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(5) F. P. Dwyer and F. L. Garvan, *J. Amer. Chem. Soc.*, **83**, 2610 (1961).

(6) F. P. Dwyer and D. P. Mellor, "Chelating Agents and Metal Chelates," Academic Press, New York, N. Y., 1964, p 209.

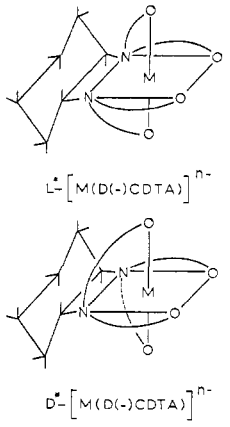


Figure 1.—Stereospecificity of D(−)CDTA in forming L*-[M-D(−)CDTA]$^{n-}$ complexes.

plexes of L-(+)-1,2-propylenediaminetetraacetate.[7] More recently Reilley and coworkers have obtained complementary information from polarimetry and nmr in their study of the kinetics of the exchange of metal complexes of ethylenediaminetetraacetate with optically active 1,2-propylenediaminetetraacetic acid.[8]

In this work spectropolarimetry was used to follow the ligand-exchange kinetics of optically active D-(−)-*trans*-1,2-cyclohexanediaminetetraacetic acid with the ethylenediaminetetraacetatolead(II) complex over the pH range of 10–13 as shown in

$$PbEDTA^{2-} + D\text{-}(-)CDTA^{4-} \rightleftharpoons L^*(+)\text{-}Pb\text{-}D(-)CDTA^{2-} + EDTA^{4-} \quad (1)$$

Experimental Section

Resolution of Racemic *trans*-1,2-Cyclohexanediamine and Isolation of D-(−)-*trans*-1,2-Cyclohexanediamine.—Technical grade racemic *trans*-1,2-cyclohexanediamine was vacuum distilled at 12 mm with a boiling range of 75–80°. A 200-g sample of the racemic diamine was added dropwise with mechanical stirring to a solution of L-(+)-tartaric acid (350 g in 400 ml of water), maintaining the temperature below 55°. This mixture was allowed to cool to about 5° and was kept cold for 1 hr, after which it was filtered through a sintered-glass Büchner filter. The white crystals of the diastereoisomer, D-(−)-*trans*-cyclohexanediamine L-(+)-tartrate, were washed with 120 ml of ice water and allowed to dry. The crystals of the diastereoisomer were dissolved in the least amount of boiling water (~325 ml), by adding the crystals in small portions to a beaker of hot water with mechanical stirring to prevent burning of the product. Absolute ethanol (1000 ml) was added to the above solution and allowed to cool to about 5° with stirring for 1 hr before filtering. The specific rotation of a 1% solution of the diastereoisomer in water was determined at 589 nm to be +12.1° and this value compared favorably with the literature value of +12.0°.[9] This measurement served as the criterion of purity. The theoretical yield was 252 g; actual yield, 227 g (90.3%).

The diastereoisomer was suspended in water with stirring and solid sodium hydroxide was added. The color turned darker and the mixture separated into two layers. The upper layer was decanted off and distilled from solid potassium hydroxide under vacuum, with a boiling range of 75–80° at 12 mm. If sufficiently dry and of high purity, the D-(−)-*trans*-1,2-cyclohexanediamine crystallized to form a hygroscopic white solid with an approximate melting point of 45°.

Preparation of D-(−)-*trans*-1,2-Cyclohexanediaminetetraacetic Acid.—A 280-g (3-mol) amount of monochloroacetic acid in 150 ml of water was cooled to 10° and a cold solution of sodium hydroxide, 250 g (6 mol) in 500 ml of water, was added dropwise with mechanical stirring, maintaining the temperature below 16°. The previously resolved D-(−)-*trans*-1,2-cyclohexanediamine (58 g, 0.5 mol) was slowly added through a dropping funnel, keeping the temperature below 16°. This mechanically stirred reaction mixture was maintained at a temperature of 16° for 6 days and then raised to and kept at 19° for an additional 6 days. The pH of the solution was adjusted to 3.5 with concentrated HCl and the solution was evaporated on a steam bath in a current of air to a volume of 600 ml. The solid sodium chloride was removed by filtering the mixture through a sintered-glass Büchner funnel. The filtrate was poured into 2 l. of vigorously stirred absolute ethanol and stirred overnight to allow crystallization. The crystals were suspended in 600 ml of glacial acetic acid and heated with stirring to 40° in order to dissolve out the disodium salt of D(−)CDTA. The undissolved sodium chloride was removed by filtration and washed with an additional 30 ml of warm glacial acetic acid. This washing and the filtrate were combined and added slowly to 3 l. of benzene and allowed to stir overnight. The viscous syrup deposited was crystallized by decanting off the benzene and pouring the viscous syrup into 2 l. of rapidly stirred acetone. This mixture was stirred for 1 hr and the crystals formed were allowed to settle out. The acetone was decanted off and a fresh portion of 2 l. of acetone was added. The latter mixture was stirred overnight to dissolve out traces of acetic acid. It was then filtered and the white solid was allowed to air dry. The solid was dissolved in 1500 ml of deionized water and evaporated on a steam bath to approximately 1000 ml, thereby removing much of the acetic acid and acetone. The pale yellow solution was pumped onto a large heated ion-exchange column packed with Dowex 50W-X8, a strong cationic exchange resin which had been previously washed with 8 l. of hot 6 *N* HCl followed with 12 l. of deionized water to remove traces of ferric ion generally present in the material and to convert the resin to the acid form. The column was washed with 2 l. of cold deionized water and these first 2 l. of pale yellow eluate were discarded, as they contained traces of acetic acid and only negligible amounts of the optically active material as determined by checking the optical rotation. The column was then heated to 95–100° and the active acid eluted with boiling deionized water with an elution rate of approximately 10 l./hr. Elution was continued until the eluate no longer showed optical activity. Approximately 44 l. of hot water was required. This quantity of eluate was reduced to a volume of approximately 400 ml of vacuum stripping, and 600 ml of reagent grade acetone was added. After being allowed to cool overnight in an ice bath, white crystals formed. This mixture was filtered through a medium sintered-glass Büchner funnel and air dried. These crystals were dried overnight in a vacuum oven at 115° (3 mm). The theoretical yield, based on amount of D(−)chxn used, was 121 g; actual yield, 40.43 g (33.35%).

The specific rotation at 589 nm was determined to be −53.4° for a 0.5% aqueous solution. The literature value reported for the anhydrous acid was −53.0°.[5] The melting point was 236–238° with decomposition; lit.[5] mp 237°. *Anal.* Calcd for $C_{14}H_{22}N_2O_8$: C, 48.55; H, 6.40; N, 8.09; O, 36.96. Found: C, 48.78; H, 6.31; N, 8.20; O, 36.74. Microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn.

In addition to the above analyses, visual chelometric titrations with standard lead solution using xylenol orange as the indicator showed 100.0 ± 0.15% purity.

Reagents and Solutions.—A standard solution of EDTA was prepared by dissolving a weighed amount of the recrystallized material in a minimum amount of KOH and was standardized by titration with primary standard zinc at pH 10 with EBT as the visual indicator. A standard solution of optically active D(−)-CDTA was prepared by dissolving a weighed amount of the

(7) B. Bosnich, F. P. Dwyer, and A. M. Sargeson, *Nature (London)*, **186**, 966 (1960).

(8) J. D. Carr, K. Torrance, C. J. Cruz, and C. N. Reilley, *Anal. Chem.*, **39**, 1358 (1967).

(9) R. S. Treptow, *Inorg. Chem.*, **5**, 1593 (1966).

material prepared above in a minimum amount of KOH and was standardized by titration with standard lead solution at pH 4.7, using xylenol orange as the indicator.

The lead complex of EDTA was prepared by addition of the standard solution to a stoichiometric amount of a standard solution of lead nitrate. It was necessary to stir the solution vigorously during addition to prevent the formation of the insoluble Pb[PbEDTA].

The ionic strength of the solution was maintained at 0.50 in these studies with KNO_3, to avoid any changes that might be caused by changes in the ionic strength of the solution.

Apparatus.—A Perkin-Elmer Model 141 photoelectric polarimeter was used to monitor the change in the optical rotation of the solution during the course of the reaction. This instrument had potentiometric readout of the observed optical rotation; thus, the change in the optical rotation as a function of time was readily available in analog form using a Sargent Model SRL recorder. The polarimeter had the following five wavelengths available: 589, 578, 546, 436, and 365 nm. However, in this work 365 nm was used extensively because of the greater molecular rotation of the Pb-D(−)CDTA complex at this wavelength, thereby increasing the sensitivity of the kinetic measurements. The reaction vessel was constructed from large glass tubing with two 8-mm glass tubes attached, one at the bottom center and the other one-fifth of the way up the side. This vessel had an approximate capacity of 125 ml and was jacketed to achieve thermostatic control. A Haake Model KT 41 Kryokool constant-temperature circulator was used to control the temperature of the reaction vessel to an accuracy of 20.00 ± 0.01°. The standard 1-dm flow-through polarimeter cell was attached to the reaction vessel by Tygon tubing. The reaction vessel was positioned over a magnetic stirrer and a magnetic stir bar, placed in the vessel, functioned both to stir the solution and to pump it through the flow-through polarimeter cell. The mixing and response time of the stirrer and polarimeter to additions of optically active materials was approximately 5 sec; thus, all measurements were made at times after the first initial 5 sec.

The pH of the reaction mixture was measured at the start of the reaction with an Orion Model 801 pH meter equipped with a Sargent combination glass electrode. No buffers could be used to control the pH, as they would interfere with the reaction being studied. The solution for each kinetic run was degassed by bubbling previously saturated N_2 gas through the reaction solution for 15 min before adding the exchange ligand. The nitrogen atmosphere was maintained throughout the kinetic run and the pH remained constant within experimental error.

Results

Differing initial concentrations of both reactants were used, and the results indicated that over the pH range of 10–13, the reactions were first order in D(−)-CDTA and first order in PbEDTA. In all cases, the reaction was made pseudo first order overall by using a large excess of the entering ligand. An approximate tenfold excess of the entering ligand was found to be sufficient to make the overall reaction pseudo first order and to go to completion because of the large value of $K_{\text{stability}}$ for PbCDTA. Thus the rate expression was found to be

$$\text{rate} = (k_L^{MY})_T[L]_T[MY] = k_{obsd}[MY] \qquad (2)$$

where $(k_L^{MY})_T$ is the total specific rate constant for the exchange reaction of D(−)CDTA with PbEDTA, $[L]_T$ is the total concentration of D(−)CDTA in all of its possible ionic forms, [MY] is the concentration of the lead–EDTA complex, and k_{obsd} is the observed pseudo-first-order rate constant. For dilute solutions, the observed optical rotation is directly proportional to the concentrations of the optically active species present in solution. Thus, the value of k_{obsd} may be obtained from the slope of the plot of $-\ln(\alpha_t - \alpha_{eq})$ *vs.* time as shown in a typical plot, Figure 2. The values of the

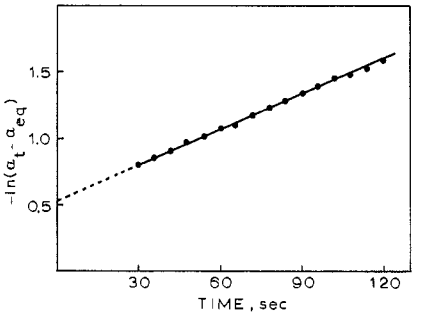


Figure 2.—Plot of $-\ln(\alpha_t - \alpha_{eq})$ *vs.* time for the exchange reaction at pH 12.525.

observed pseudo-first-order rate constants, k_{obsd}, are shown in Table I, along with the values of the total

TABLE I
OBSERVED PSEUDO-FIRST-ORDER AND SECOND-ORDER RATE CONSTANTS AT 20° AND μ = 0.5 (KNO_3)

pH	10^3[D(−)-CDTA], *M*	10^4[Pb-EDTA], *M*	k_{obsd}, sec^{-1}	$(k_L^{MY})_T$, sec^{-1} M^{-1}
9.928	6.735	9.091	3.36×10^{-5}	4.99×10^{-3}
10.920	6.735	9.091	5.71×10^{-4}	8.48×10^{-2}
11.257	6.735	9.091	5.88×10^{-4}	8.73×10^{-2}
11.340	6.735	9.091	6.63×10^{-4}	9.85×10^{-2}
11.577	6.735	8.935	1.37×10^{-3}	2.03×10^{-1}
11.691	6.735	8.935	1.35×10^{-3}	2.00×10^{-1}
11.864	6.735	8.935	2.12×10^{-3}	3.15×10^{-1}
12.080	6.735	8.935	3.44×10^{-3}	5.11×10^{-1}
12.121	6.735	8.935	3.14×10^{-3}	4.66×10^{-1}
12.131	6.735	8.935	3.62×10^{-3}	5.38×10^{-1}
12.296	6.735	8.935	5.08×10^{-3}	7.54×10^{-1}
12.328	6.735	8.935	4.71×10^{-3}	6.99×10^{-1}
12.429	10.95	8.545	1.03×10^{-2}	9.41×10^{-1}
12.477	10.08	8.935	8.06×10^{-3}	8.00×10^{-1}
12.492	6.735	8.935	7.30×10^{-3}	1.08
12.525	7.632	8.935	9.32×10^{-3}	1.22
12.555	7.632	8.935	9.54×10^{-3}	1.25
12.624	10.08	8.935	1.33×10^{-2}	1.32
12.630	10.08	9.091	1.31×10^{-2}	1.30
12.721	10.08	9.091	1.72×10^{-2}	1.71
12.762	10.08	9.091	1.55×10^{-2}	1.54
12.799	10.08	9.091	1.56×10^{-2}	1.55
12.848	10.08	8.935	2.50×10^{-2}	2.48
12.945	7.632	8.935	2.52×10^{-2}	3.30

specific rate constants, $(k_L^{MY})_T$, for the various pH values. The latter were obtained by dividing the observed pseudo-first-order rate constants by the total concentration of the entering ligand. In all cases these plots, Figure 2, were linear for at least 2–3 half-life periods. Times for the exchange reactions to reach equilibrium rotations ranged from a few minutes for the highest pH solutions to about 30 hr for the lowest pH solutions. The equilibrium rotations agreed within experimental error with the rotational values calculated from the molecular rotations of D(−)CDTA and L*-(+)-[Pb-D(−)CDTA] and their concentrations assuming that the reaction had proceeded to completion.

The following four equations may be considered as possible reactions contributing to the overall observed rate of the ligand exchange reaction

$$PbY + L \xrightarrow{k_1} PbL + Y \quad (3)$$

$$PbY + HL \xrightarrow{k_2} PbL + Y \quad (4)$$

$$PbY + L \xrightarrow{OH^-\text{-catalyzed } k_3} PbL + Y \quad (5)$$

$$PbY + L \xrightarrow{di\text{-}OH^-\text{-catalyzed } k_4} PbL + Y \quad (6)$$

Abbreviations used are: Y, ethylenediaminetetraacetate; L, D-(−)-*trans*-1,2-cyclohexanediaminetetraacetate. Charges on species are omitted. The rate expression may be then written for this series of reactions as

$$k_{obsd} = k_1[L^{4-}] + k_2[HL^{3-}] + k_3K_{OH_1}[OH^-][L^{4-}] + k_4K_{OH_1}K_{OH_2}[OH^-]^2[L^{4-}] \quad (7)$$

Terms involving any contribution from ionic species H_2CDTA^{2-}, H_3CDTA^-, and H_4CDTA were neglected, since the fraction of the total concentration of L in any of these three forms is negligible in the pH range 10–13. The value for the total specific rate constant, $(k_L^{MY})_T$, is obtained by dividing the observed pseudo-first-order rate constant, k_{obsd}, by the total analytical concentration of L. Thus eq 7 becomes

$$\frac{k_{obsd}}{[L]_T} = \frac{k_1[L^{4-}]}{[L]_T} + \frac{k_2[HL^{3-}]}{[L]_T} + \frac{k_3K_{OH_1}[OH^-][L^{4-}]}{[L]_T} + \frac{k_4K_{OH_1}K_{OH_2}[OH^-]^2[L^{4-}]}{[L]_T} \quad (8)$$

The fractions $[HL^{3-}]/[L]_T$ and $[L^{4-}]/[L]_T$ are equal to $[H^+]/([H^+] + K_4)$ and $K_4/([H^+] + K_4)$, respectively, neglecting in the denominator those terms which contribute less than 0.1%. K_4 is the dissociation constant for $HCDTA^{3-}$; K_{OH_1} and K_{OH_2} are equilibrium constants for the formation of the mono- and dihydroxy PbEDTA intermediates, respectively; K_w has its usual meaning. Substitution of these values into eq 8 and rearrangement gives eq 9. Equation 9 may be simplified by dividing through by $[H^+]$ and substituting for $[OH^-]$ its value from the ion product of water. This result is given in

$$\frac{k_{obsd}([H^+] + K_4)}{[L]_T} = k_1K_4 + k_2[H^+] + k_3K_{OH_1}[OH^-]K_4 + k_4K_{OH_1}K_{OH_2}[OH^-]^2K_4 \quad (9)$$

$$\frac{k_{obsd}\left(1 + \frac{K_4}{[H^+]}\right)}{[L]_T} = \frac{k_1K_4}{[H^+]} + k_2 + \frac{k_3K_{OH_1}K_wK_4}{[H^+]^2} + \frac{k_4K_{OH_1}K_{OH_2}K_w^2K_4}{[H^+]^3} \quad (10)$$

The total specific rate constants, $(k_L^{MY})_T$, were resolved into the individual contributing rate constants by graphical and computer-assisted numerical regression techniques of eq 10. This result is presented in Figure 3. In the pH region 9.9–12.3, the kinetic contribution of the dihydroxy-assisted pathway to the total rate is negligible and the cubic term may be neglected in eq 10. A value for the y intercept of 0.005 M^{-1} sec^{-1} for k_2, the specific rate constant for the attack of HL^{3-}, indicates that the attack by the HL^{3-} species contributes very little to the overall observed rate of exchange.

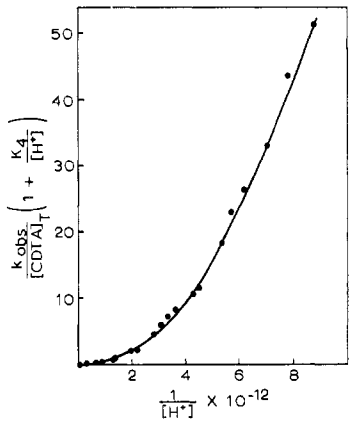


Figure 3.—Plot of $(k_{obsd}/[CDTA]_T)(1 + K_4/[H^+])$ *vs.* $1/[H^+]$ showing the experimental points and the calculated curve (20°, μ = 0.50 (KNO_3)).

At the pH values lower than 12.6, the contribution due to the dihydroxy-assisted mechanism is small compared to the total overall rate; thus, the attack by the ionic species L^{4-} and the monohydroxy-assisted pathway predominate in this region. A multiple-regression analysis was solved for the best quadratic curve using a computer for the data points at pH <12.6 in order to obtain the values for the parameters b and c. The numerical values obtained for the parameters b and c were 0.678 × 10^{-12} and 0.440 × 10^{-24}, respectively. The value for k_L^{MY} or k_1 = 0.408 M^{-1} sec^{-1} was obtained by dividing the value of b (0.678 × 10^{-12} sec^{-1}) by K_4 (1.66 × 10^{-12} M). This value of k_{CDTA}^{PbEDTA} is *ca.* 160 times slower than that previously found for k_{EDTA}^{PbEDTA}.[8] The large difference in the rates of exchange is attributed to the steric influences of the entering ligand, D(−)CDTA. It was impossible to obtain a value for the specific rate constant k_3, since the value of the equilibrium constant K_{OH_1} is unknown.

At pH >12.6, the dihydroxy-assisted pathway (the cubic term of eq 10) increases in importance to the overall rate of exchange. The values obtained from the above quadratic fit for the parameters a, b, and c were inserted into the cubic expression with the corresponding values of x and x^2. The difference between y and $(a + bx + cx^2)$ was attributed to the contribution of the cubic term, dx^3. An average numerical value was obtained for the parameter d of 1.69 × 10^{-38}. Similar to the above case with the monohydroxy species, it was impossible to obtain the value for the specific rate constant k_4, since K_{OH_1} and K_{OH_2} are unknown. Within this pH region, the values calculated for the parameter d were essentially constant. The contribution of the cubic term dx^3 was found to increase from 6% at pH 12.429 to 22% at pH 12.945.

Values of y_{calcd} were then calculated from the evaluated parameters a, b, c, and d and their corresponding terms x, x^2, and x^3. Although there is some scatter of the data points, the calculated values of y agreed within experimental error with those observed experimentally as is shown in Figure 3.

Reilley, *et al.*,[8] have reported that no evidence could be obtained either by spectrophotometry or by nmr for an appreciable formation of mixed hydroxy–EDTA–lead complexes, even up to pH 13.0. The optical rotatory data presented in Figure 4 confirm that the

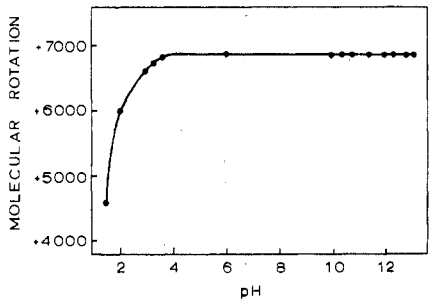


Figure 4.—Molecular rotation of L*-(+)-[Pb-D(−)CDTA] *vs.* pH at 365 nm, μ = 0.50 (KNO_3).

formation of a mixed hydroxy–CDTA–lead complex as a possible equilibrium product does not occur to any large extent. The data suggest the absence of polymeric species such as Pb–CDTA–Pb in this system. The optical rotatory data would be expected to be very sensitive to small changes in the structure and/or type of coordination of the complex because of accompanying changes in the overall symmetry of the complex.

Discussion

Ligand substitution reactions involving multidentate ligands have been shown by Rorabacher and Margerum[10] to proceed by a series of intermediates in equilibrium with one another in which a successively greater number of coordination sites are occupied by the entering ligand and fewer by the leaving ligand. In the case where the entering ligand is a stereospecific optically active ligand, this sequence of reaction steps must predict the correct stereochemistry of the reaction product. Because the initial solution is racemic, *i.e.*, an equal distribution of D* and L* isomers of PbEDTA, the series of mechanistic steps must also account for the stereospecifically obtained reaction product from this racemic solution.

It is evident that the increase in the rate of the exchange is greater than could be accounted for only by the increase in the concentration of the attacking species, L^{4-}, upon deprotonation of HL^{3-} at the higher pH values. From the reaction order it is inferred that the intermediates in this system involve a stepwise aquation of PbEDTA and the attack of D(−)CDTA upon the aquated species. Thus, one bond at a time breaks from the EDTA molecule in the lead complex with its place being taken by a solvent water molecule and the D(−)CDTA forming one bond at a time as the solvent water molecules are lost in turn until the ligand substitution is complete. Such a sequence has been suggested in numerous other ligand-exchange reactions. Three criteria are preserved in the proposed mechanisms: (I) an acetato group will be the first dentate to form a bond from the D(−)CDTA to lead because of the steric hindrances encountered by a nitrogen approaching the lead ion without prior acetato bond formation; (II) subsequent bond formation will be only to dentates which will complete a five-member ring; (III) each bond rupture will destroy only one chelate ring. Intermediates with both EDTA and D(−)CDTA molecules bonded through one nitrogen atom each such that the nitrogens are *cis* to each other have been proved by molecular models to be sterically impossible.

Mechanism I. Exchange of D(−)CDTA with Pb-EDTA.—In dealing with the aquo-assisted ligand exchange of D(−)CDTA with the PbEDTA complex, the mechanistic pathways proposed for this exchange reaction must consider both optical isomers of the PbEDTA complex, as the racemate is an equal distribution of the two optically active complexes D*-[PbEDTA] and L*-[PbEDTA] and must give the correct optically active product L*-(+)-[Pb-D(−)CDTA]. Thus, the attack of the ligand upon the PbEDTA complex will be considered as two separate series of reactions, although, for this case, both reactions are operative and occur simultaneously. These series of reactions are shown in Figure 5. The proposed sequences are not the only possible sequences giving the correct stereochemical product; however, they are the sequences that were shown by models to involve the least amount of steric hindrances and the most stable intermediates. Work by Eigen[11] has shown that rapid association and dissociation of water occur within the inner coordination sphere. Thus, aquation of the complex could easily occur in positions (1), (2), (3), and (6). Because of the planes of symmetry involved in the PbEDTA complex, positions (1) and (6) are exactly alike sterically; similarly, positions (2) and (3) are identical. Less steric hindrance is incurred if the acetato group of the attacking ligand attacks in axial positions. Thus, the first step of all pathways proposed involve attack of an acetato group of the entering ligand upon position (6) after aquation has occurred.

In Figure 5, the assignments of steps Va to VIa and Vb to VIb as the rate-determining steps are in agreement with data for the ligand-exchange reactions of the EDTA complexes of calcium, cadmium, and strontium with EDTA. From intermediate VIa, for ligand exchange, aquation can occur in positions (1) and (3). Intermediate VIIa shows aquation in position (3) and then chelation by the second nitrogen atom of D(−)-CDTA yielding intermediate VIIIa. Thus, step VIIa to VIIIa is assigned the stereochemical determining step (sds). From VIIIa stepwise displacement occurs to form L*[Pb-D(−)CDTA]. From intermediate VIa, if aquation occurs in position (1), the attack by the second nitrogen atom of D(−)CDTA is sterically impossible due to the steric limitations of the cyclohexane ring. Likewise from VIb, aquation can occur in position (1) or (2). Aquation in position (1) to form VIIb and then displacement to form VIIIb, with VIIb

(10) D. B. Rorabacher and D. W. Margerum, *Inorg. Chem.*, **3**, 382 (1964).

(11) M. Eigen in "Advances in the Chemistry of the Coordination Compounds," S. Kirschner, Ed., Macmillan, New York, N. Y., 1961.

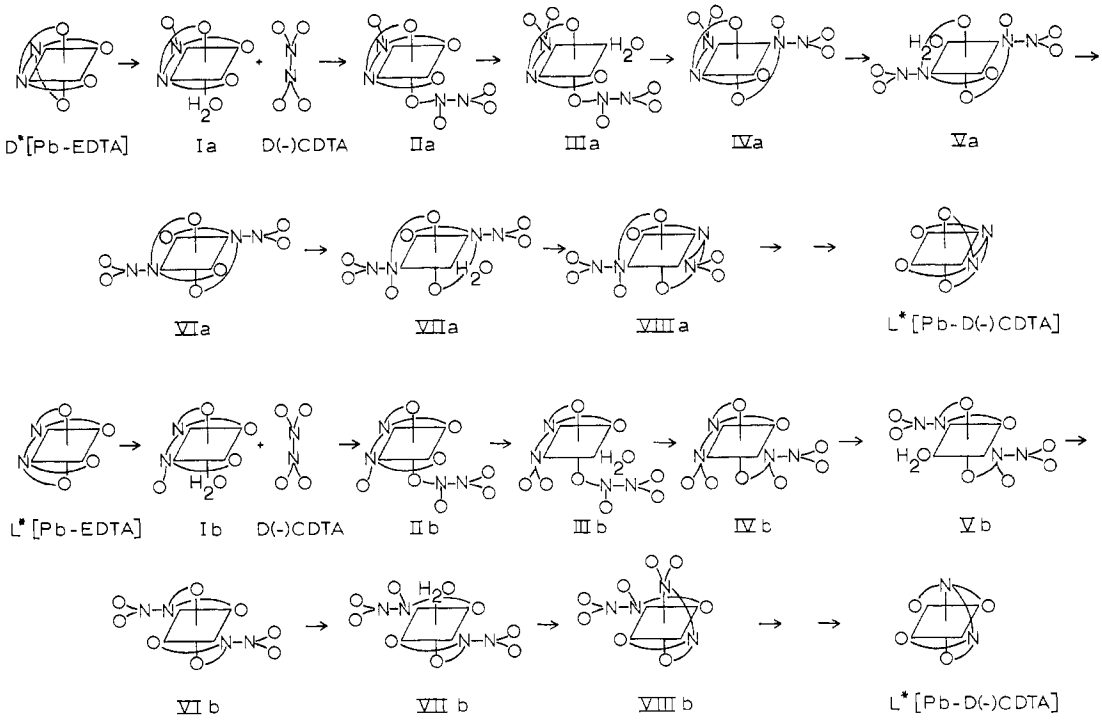


Figure 5.—Proposed mechanism for the exchange of D(−)CDTA with lead–EDTA, considering both stereoisomers of lead–EDTA.

to VIIIb being the stereochemical determining step, and subsequent displacements yield the observed stereochemical product L*[Pb-D(−)CDTA]. If aquation occurs in intermediate VIb at position (2), the attack by the second nitrogen atom of D(−)CDTA is sterically impossible as above.

Pathways could be proposed that would lead to the D*-(−)-[Pb-D(−)CDTA]; however, considerations with models confirmed that D(−)CDTA reacts stereospecifically to form exclusively L*-(+)-[Pb-D(−)-CDTA]. Reactions 1 and 2 in Table II show the other possible sequences that result in the correct stereochemical product, but each involved sterically unfavorable steps.

Mechanism II. Monohydroxy-Assisted Exchange of D(−)CDTA with PbEDTA.—Reference to Figure 3 clearly shows that the rate of ligand exchange increases rapidly as the hydroxide concentration is increased. This increase in the rate of reaction is significantly greater than can be accounted for by the increasing concentration of the attacking species L^{4-}; if this was the only effect, the rate would increase in some linear fashion and all points would fall on an extension of the linear portion of Figure 3.

Thus, over the pH region of 12.3–12.7, the predominant reaction proposed involves a monohydroxy assisted pathway. Such a mixed hydroxy–lead–EDTA species is of an intermediatory nature. The effect of OH is to reduce the stability of PbEDTA complex and thereby allow more rapid aquation and dissociation of the leaving ligand from the original complex.

Upon considering monohydroxy intermediate species, the question of the position of the OH is important. Possible positions for the OH are (1), (2), and (3). The models indicate that both positions (2) and (3) are less effective in weakening the complex and assisting ligand exchange, due to a great amount of steric hindrances between the acetato groups of the leaving ligand and the cyclohexane ring of the entering ligand. Less steric interferences are involved if the OH is in position (1). Maximum overall weakening of the coordinate covalent bonding is achieved by the OH in the (1) position.

The stereochemical considerations of the two optical isomers of PbEDTA, L*–[PbEDTA] and D*–[PbEDTA], are simplified by considering the OH to be in position (1), since both isomers result in identical intermediates when the two acetato groups of EDTA are displaced from the axial positions (1) and (6). In Figure 6, intermediates Ia and Ib are identical with intermediates Ia and Ib of Figure 5. Intermediate II is obtained by OH attack on the (1) position of both Ia and Ib. From intermediates II to VII the three criteria above were obeyed. The reaction of intermediate V to VI has been assigned the rate-determining step. Step VII to VIII is the stereochemical determining step with subsequent very rapid aquation and displacement to form L*[Pb-D(−)CDTA].

Table II, reactions 4–8, shows possible pathways in which the OH group is not in the (1) position. In such cases, the stereochemistries of the intermediates are not identical; thus, consideration of the possible isomers is necessary. In all of these cases where the OH group is in the plane of the nitrogens, the entering ligand encountered large amounts of steric interferences between the acetato groups of the leaving ligand and the cyclohexane ring of the entering ligand.

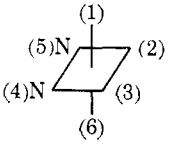
Mechanism III. Dihydroxy-Assisted Exchange of D(−)CDTA with PbEDTA.—At pH values greater

TABLE II

MECHANISMS THAT GIVE THE CORRECT STEREOCHEMICAL PRODUCT BUT ARE ELIMINATED ON THE BASES OF STERIC HINDRANCES OR UNFAVORABLE INTERMEDIATES

Type of exchange	Reaction sequence[a]	Comments
1. Ligand exchange with D*–[PbEDTA]	1. $Ac_I(6)$; 2. $N_I(2)$; 3. $N_{II}(3)$; 4. $Ac_I(5)$; 5, 6. $Ac_{II}(1, 4)$	1. There is considerable steric hindrance for the attack of N_{II}
2. Ligand exchange with L*–[PbEDTA]	1. $Ac_I(6)$; 2. $N_I(3)$; 3. $N_{II}(1)$; 4. $Ac_I(2)$; 5, 6. $Ac_{II}(4, 5)$	2. Same as 1
3. Mono-OH-assisted reaction, OH in (1)	1. $Ac_I(6)$; 2. $N_I(2)$; 3. $Ac_I(5)$; 4. $N_{II}(3)$; 5, 6. $Ac_{II}(1, 4)$	3. There is considerable steric hindrance for the attack of N_I between Ac's on the nearest N and the cyclohexane ring
4. Mono-OH-assisted reaction, OH in (2), considering L*–[PbEDTA]	1. $Ac_I(6)$; 2. $N_I(3)$; 3. $Ac_I(4)$; 4. $N_{II}(1)$; 5, 6. $Ac_{II}(2, 5)$	4. Same as 3
5. Mono-OH-assisted reaction, OH in (3), considering L*–[PbEDTA]	1. $Ac_I(6)$; 2. $N_I(2)$; 3. $Ac_I(3)$; 4. $N_{II}(1)$; 5, 6. $Ac_{II}(4, 5)$	5. Same as 3
6. Mono-OH-assisted reaction, OH in (2), considering D*–[PbEDTA]	1. $Ac_I(6)$; 2. $N_I(3)$; 3. $Ac_I(2)$; 4. $N_{II}(1)$; 5, 6. $Ac_{II}(4, 5)$	6. Same as 3
7. Mono-OH-assisted reaction, OH in (3), considering D*–[PbEDTA]	1. $Ac_I(6)$; 2. $N_I(2)$; 3. $Ac_I(5)$; 4. $N_{II}(3)$; 5, 6. $Ac_{II}(1, 4)$	7. Same as 3
8. Mono-OH-assisted reaction, OH in (3), considering D*–[PbEDTA]	1. $Ac_I(6)$; 2. $N_I(2)$; 3. $Ac_I(3)$; 4. $N_{II}(1)$; 5, 6. $Ac_{II}(4, 5)$	8. Same as 3
9. Di-OH-assisted reaction, OH's in (1) and (2)	1. $Ac_I(6)$; 2. $N_I(2)$; 3. $Ac_I(3)$; 4. $N_{II}(1)$; 5, 6. $Ac_{II}(4, 5)$	9. Unfavorable intermediate, the  ring; steric hindrance between Ac's on N(5) interferes with Ac's of N_{II}
10. Di-OH-assisted reaction, OH's in (1) and (2)	1. $Ac_I(6)$; 2. $N_I(3)$; 3. $Ac_I(2)$; 4. $N_{II}(4)$; 5, 6. $Ac_{II}(1, 5)$	10. Same as 9
11. Di-OH-assisted reaction, OH's in (1) and (2)	1. $Ac_I(6)$; 2. $N_I(3)$; 3. $Ac_I(4)$; 4. $N_{II}(1)$; 5, 6. $Ac_{II}(2, 5)$	11. Same as 9
12. Di-OH-assisted reaction, OH's in (1) and (3)	1. $Ac_I(6)$; 2. $N_I(2)$; 3. $Ac_I(3)$; 4. $N_{II}(1)$; 5, 6. $Ac_{II}(4, 5)$	12. Same as 9
13. Di-OH-assisted reaction, OH's in (1) and (3)	1. $Ac_I(6)$; 2. $N_I(3)$; 3. $Ac_I(2)$; 4. $N_{II}(4)$; 5, 6. $Ac_{II}(1, 5)$	13. Same as 9
14. Di-OH-assisted reaction, OH's in (1) and (3)	1. $Ac_I(6)$; 2. $N_I(2)$; 3. $Ac_I(5)$; 4. $N_{II}(3)$; 5, 6. $Ac_{II}(1, 4)$	14. Same as 9
15. Di-OH-assisted reaction, OH's in (2) and (3), considering D*–[PbEDTA]	1. $Ac_I(6)$; 2. $N_I(2)$; 3. $Ac_I(3)$; 4. $N_{II}(1)$; 5, 6. $Ac_{II}(4, 5)$	15. Steric hindrance dictated by the stereochemistry of the cyclohexane ring; OH's eliminated too rapidly
16. Di-OH-assisted reaction, OH's in (2) and (3), considering D*–[PbEDTA]	1. $Ac_I(6)$; 2. $N_I(2)$; 3. $Ac_I(5)$; 4. $N_{II}(3)$; 5, 6. $Ac_{II}(1, 4)$	16. Same as 15
17. Di-OH-assisted reaction, OH's in (2) and (3), considering L*–[PbEDTA]	1. $Ac_I(6)$; 2. $N_I(2)$; 3. $Ac_I(3)$; 4. $N_{II}(1)$; 5, 6. $Ac_{II}(4, 5)$	17. Same as 15
18. Di-OH-assisted reaction, OH's in (2) and (3), considering L*–[PbEDTA]	1. $Ac_I(6)$; 2. $N_I(3)$; 3. $Ac_I(2)$; 4. $N_{II}(4)$; 5, 6. $Ac_{II}(1, 5)$	18. Same unfavorable intermediate as in 9; OH's eliminated too rapidly.
19. Di-OH-assisted reaction, OH's in (2) and (3), considering L*–[PbEDTA]	1. $Ac_I(6)$; 2. $N_I(3)$; 3. $Ac_I(4)$; 4. $N_{II}(1)$; 5, 6. $Ac_{II}(2, 5)$	19. Same as 18.

[a] Number in the parentheses indicates the coordination site using the numbering system shown in the diagram below.



than 12.7, the agreement between values of y_{obsd} and y_{calcd}, assuming only the monohydroxy-assisted pathway, is no longer sufficient to explain the great increase in the rate of the ligand exchange. Deviations from the quadratic-curve fit are great in this region. It appears plausible to consider the contribution of a dihydroxy-assisted reaction in this pH region. At this point the stereochemistry becomes quite involved. Maintaining the initial aquo attack at position (6), it is necessary to consider dihydroxy intermediates formed at positions (1) and (2), (1) and (3), and (2) and (3). In Figure 7, the initial attack of OH is in position (1) to give intermediate I, which is identical with intermediate II in Figure 6. The second attack by OH on intermediate I, Figure 7, can be at position (2) giving IIa or at (3) giving IIb. In intermediates IIa and IIb the rapid loss of water and attack of D(−)CDTA on position (6) yield the intermediates IIIa and IIIb, respectively. In intermediate IIIa with the OH's in the (1) and (2) positions, the speed of breaking the nitrogen–nitrogen chelate ring is increased and the attack of water in position (5) yields intermediate IVa. Thus, the whole back side of intermediate IVa is sterically unhindered and open for very rapid attack by the entering

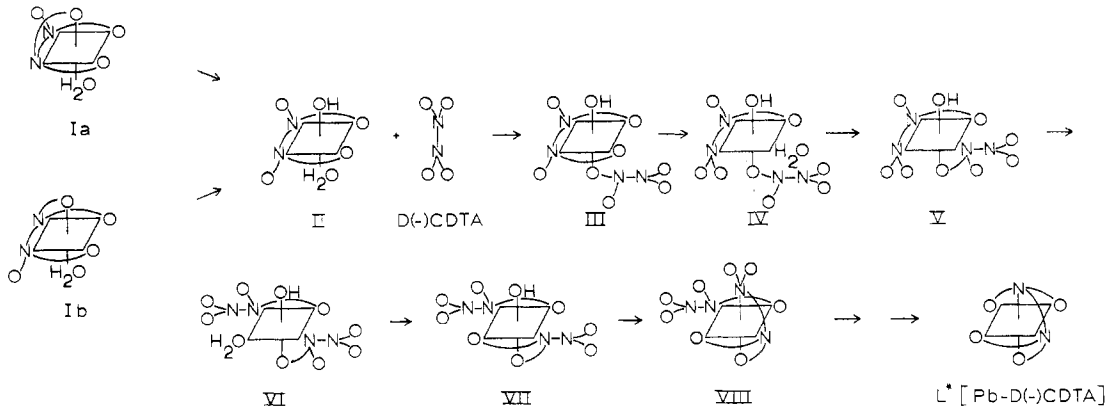


Figure 6.—Proposed mechanism for the monohydroxy-assisted exchange of D(−)CDTA with lead–EDTA.

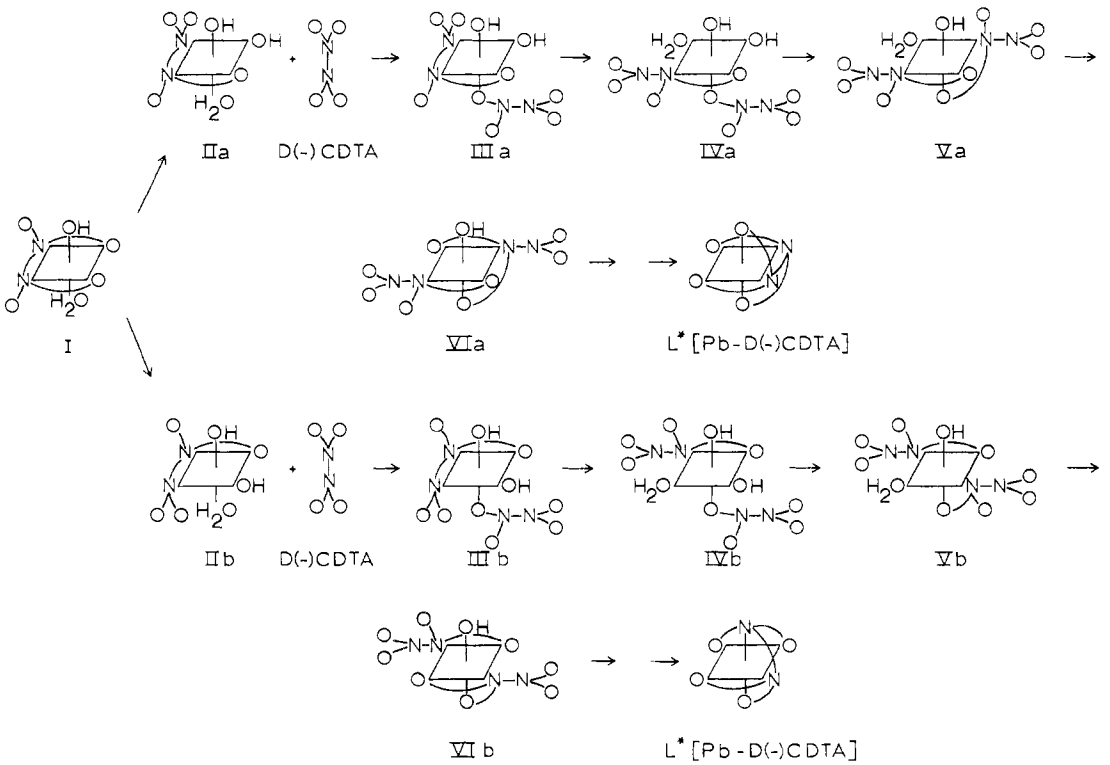


Figure 7.—Proposed mechanism for the dihydroxy-assisted exchange of D(−)CDTA with lead–EDTA.

D(−)CDTA. In intermediate IVa, the nitrogen attacks in position (2) to yield Va. It is sterically impossible for the nitrogen of the D(−)CDTA molecule to attack in position (5) as has been stated above. Intermediate Va then undergoes stepwise reactions through intermediate VIa to the final product L*[Pb-D(−)CDTA]. Likewise, from intermediate IIIb, the dissociation of the nitrogen on position (4) gives intermediate IVb, with the front side of the intermediate open for attack as above. Thus, in the b series of the dihydroxy-assisted reactions, the attack on the intermediate IVb by the nitrogen of the D(−)CDTA is again in the cis position to the coordinated acetato group containing the OH, yielding intermediate Vb. As stated above, it is sterically impossible for the nitrogen of the entering D(−)CDTA to attack and coordinate in position (4). Intermediate Vb then undergoes successive stepwise reactions through intermediate VIb to the final product L*[Pb-D(−)CDTA]. Thus, the proposed mechanisms with the two possible favorable pathways for ligand exchange in the dihydroxy-assisted reaction lead to the large increase in the rate of the ligand exchange.

Table II, reactions 9–14, considers other possible pathways where the dihydroxy intermediates are in the (1) and (2) or (1) and (3) positions. The major criticism of these sequences is that they involve a less favorable intermediate, the five-member N,N chelate ring, compared to the five-member N,O chelate ring. The thermodynamic stability of this type of intermediate would be expected to be low, as lead coordinated much more strongly with oxygen than with nitrogen. With this type of intermediate involved in the second step of the reaction pathway, the exchange reaction would be expected to be more rapid than was observed.

Table II, reactions 15–19, considers the possibilities of the dihydroxy intermediates formed with OH groups occupying positions (2) and (3) and water in the (6) position. In all these reaction pathways, the major criticisms are as follows: (I) the attack of the initial OH, whether it be in position (2) or (3), is not consistent with the above-proposed mechanisms; (II) the hydroxy groups are eliminated too soon in the reaction sequence to account properly for the observed increase in the rate; (III) the entering ligand experiences great steric hindrances between its cyclohexane ring and the acetato groups of the leaving ligand.

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The Influence of Sulfite Ion upon the Rate of Aquation of Various Complexes of Chromium(III) Ion. The Stability of Sulfitochromium(III) Ion[1]

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Chromium(III) forms a sulfite complex $CrOSO_2^+$ rapidly and reversibly, suggesting strongly that it forms without breaking the chromium(III)–oxygen bond in hexaaquochromium(III) ion. The equilibrium quotient for formation of this species at 25°, $I = 0.25\ M$, is $Q_1 = [CrOSO_2^+][H^+]/[Cr^{3+}][HOSO_2^-] = 0.061$. Dimeric hydroxychromium(III) ion, $Cr_2(OH)_2^{4+}$, also forms a relatively stable sulfite complex. Coordinated sulfite labilizes chromium(III), and the rates of several ligand-substitution reactions of chromium(III) in the presence of sulfite have been studied; these are the aquation of chlorochromium(III) ion, the aquation of isothiocyanatochromium(III) ion, the aquation of isomeric bis(isothiocyanato)chromium(III) ions, and the decomposition of dimeric hydroxychromium(III) ion. These reactions of chromium(III) complexes of charge $\leq 2+$ are first order in sulfite ion, with no evidence for measurable association of sulfite ion at the highest concentrations studied.

Introduction

Sulfite ion as a ligand has been shown to labilize other ligands bonded to the same metal ion.[2] In these earlier investigations, the complexes studied were $Co(NH_3)_5SO_3^+$ and $Co(CN)_5SO_3^{4-}$, in each of which the sulfite ligand is assumed to be sulfur bonded. The present study deals with the stability of aquosulfitochromium(III) ion, which is oxygen bonded, and the influence of sulfite ion on the rates of aquation of chloro- and isothiocyanatochromium(III) species and upon the rate of decomposition of dimeric hydroxychromium(III) ion.[3] The labilizing effect of sulfite ion upon chromium(III) appears to be qualitatively similar to that reported recently for nitrite ion.[4]

Experimental Procedures

Reagents.—Except where noted, reagent grade chemicals were used without further purification. Solutions were prepared with doubly distilled water; between distillations, the water was passed through an ion-exchange deionizer.

Chromium(III) perchlorate was prepared by reduction of reagent grade chromium trioxide with reagent grade hydrogen peroxide in perchloric acid solution. The hydrated salt was then crystallized from the solution. Previously described methods were used to prepare aqueous perchloric acid solutions of chromium(III) complexes with thiocyanate ion[5,6] and chloride ion.[7] Solutions of the individual chromium(III) complexes were stored at 0° in the dark for periods up to several weeks.

A solution containing dimeric hydroxychromium(III) ion ($Cr_2(OH)_2^{4+}$), calcium ion, and perchlorate ion was prepared by the method of Thompson.[3b] Oxygen gas was passed through a chromium(II) perchlorate solution (containing zinc(II) ion) for 20 min; the chromium(III) dimer formed was separated from other cationic species by ion exchange using a 15 in. × 0.5 in. column of Dowex 50W-X8, 200–400 mesh resin and using 1.2 *M* calcium perchlorate solution as the eluting agent.

Solutions of chromium(III) species were analyzed for total chromium by a spectrophotometric method.[8] Before determination of total chromium in solutions of dimeric hydroxychromium(III), the calcium(II) ion (used as eluting agent) was removed by ion exchange.

The concentration of calcium(II) ion in the stock solution of dimeric hydroxychromium(III) ion was measured by an ion-exchange method. The aliquot was loaded on a column of Dowex 50W resin in the hydrogen ion form, and the amount of acid liberated was determined by titration with standard base;

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