Contribution from the Department of Chemistry,
Cleveland State University, Cleveland, Ohio 44115

Spectropolarimetric Kinetics of the Ligand-Exchange Reactions of the (Ethylenediaminetetraacetato)lead(II) Complex with (*R*)-(-)-1,2-Propylenediaminetetraacetic Acid

STEPHEN J. SIMON, JOHN A. BOSLETT, Jr., and KARL H. PEARSON*[1]

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Spectropolarimetry was used to study the kinetics of the ligand–ligand exchange reaction of (ethylenediaminetetraacetato)lead(II) with (*R*)-(-)-1,2-propylenediaminetetraacetic acid (*R*(-)PDTA) in basic solutions. Over the pH region of 10.0–12.3, the reaction was found to be second order overall, first order in the entering ligand, *R*(-)PDTA, and first order in the complex PbEDTA. The observed rate of the ligand-exchange reactions was found to increase rapidly with increasing pH. Analysis of this pH dependence of the ligand-exchange reaction showed three distinct areas of interest. In the pH region of 10.0–12.3, the predominant pathway involved the attack of the deprotonated species $R(-)PDTA^{4-}$. Any contributions from the attack of the monoprotonated species $R(-)HPDTA^{3-}$ was found to be negligible. In the pH region of 12.3–12.7, the attack by the $R(-)PDTA^{4-}$ and a monohydroxy-assisted reaction predominated in determining the overall rate of kinetics of this ligand exchange. At pH values greater than 12.7, a dihydroxy-assisted reaction significantly increased the overall rate of the ligand-exchange reaction. The calculated contribution to the total overall ligand-exchange reaction rate from the monohydroxy-assisted pathway increases from 0.06% at pH 10.04 to 24.2% at pH 12.89. Likewise, the percentage contribution to the total overall rate from the dihydroxy-assisted pathway increases from 3.0% at pH 12.40 to 19.0% at pH 12.89. The specific rate constant for the *R*(-)PDTA ligand-exchange reaction, $k^{PbEDTA}_{R(-)PDTA} = 8.57\ M^{-1}\ s^{-1}$, is compared to the previously obtained specific rate constants for ligand-exchange reactions in the lead–polyaminocarboxylate system.

In 1970, Reinbold and Pearson studied by polarimetric techniques the ligand-exchange reaction of (*R*,*R*)-(-)-*trans*-1,2-cyclohexanediaminetetraacetic acid, *R*,*R*(-)CDTA, with the (ethylenediaminetraacetato)lead(II) complex to give Δ-(+)-[Pb(*R*,*R*(-)CDTA)] over the pH range of 9–13.[2] They found that this ligand-exchange reaction was pH dependent and proposed three different mechanistic pathways which, based on molecular models and the steric influences of the entering ligand, gave the most favorable intermediates and accounted for the proper stereochemical product of these reactions.

Figure 1 shows the three possible rotamers of the tetranegative species of *R*(-)PDTA that can exist in aqueous solution. This figure is also applicable to the possible rotamers of EDTA in solution if the methyl group is replaced in each of the rotamer conformations with a proton. Rotamer I is the anti configuration which is geometrically unsuitable for octahedral chelation for either PDTA or EDTA. For EDTA, both rotamer II and rotamer III would form stable complexes since EDTA is symmetrical and a racemic mixture of gauche configurations corresponds to the Λ and Δ complexes of Figure 2, respectively. Likewise, rotamers II and III for *R*(-)PDTA are both in the gauche configuration with the methyl group axial in rotamer II and equatorial in rotamer III. Rotamer II corresponds to the Λ absolute configuration and rotamer III corresponds to the Δ absolute configuration of Figure 2. Molecular models show that the methyl group of the *R*(-)PDTA ligand is sterically hindered for one configuration of the metal complexes irrespective of whether the ligand is attached at four (nonplanar), five, or six positions to the metal atom. Rotamer II can be shown from molecular models to be the rotamer not favored in chelation due to the steric interactions of the axial methyl group. Thus, for the three possible rotamers of *R*(-)PDTA, the only configuration that is possible for octahedral coordination is rotamer III. Therefore, *R*(-)PDTA is completely stereospecific in its reaction with metal ions to form Δ metal complexes. The second major difference between PDTA and EDTA is that the stability constants of the PDTA–metal complexes are generally 1–2 log *K* units greater than EDTA–metal complexes. The methyl group of PDTA causes an inductive effect increasing the basicity of the PDTA nitrogens compared to those of EDTA, thus increasing the strength of the metal–nitrogen bonds and the stability of the complexes.

In this study spectropolarimetry was used to follow the ligand-exchange kinetics of optically active *R*-(-)-1,2-propylenediaminetetraacetic acid with the (ethylenediaminetetraacetato)lead(II) complex over the pH range of 10–13 as shown in eq 1.

$$(\pm)\text{-}[PbEDTA]^{2-} + R(-)PDTA^{4-} \rightleftharpoons \Delta\text{-}(+)\text{-}[Pb(R(-)PDTA)]^{2-} + EDTA^{4-} \quad (1)$$

Experimental Section

Reagents and Solutions. The standard solution of K_2H_2EDTA was prepared by dissolving a weighed amount of the recrystallized ethylenediaminetetraacetic acid into a solution containing 2 equiv of reagent grade KOH and standardized by titration with standard lead nitrate solution at pH 4.7 using 10% HMTA buffer and xylenol orange as the indicator. Standard lead nitrate solution was prepared from reagent grade lead nitrate and standardized against primary standard EDTA by the above procedure. (*R*)-(-)-1,2-propylenediaminetetraacetic acid was prepared by stereospecific condensation of the resolved propylenediamine with concentrated sodium chloroacetate in a strongly basic medium, followed by the use of a strong cation-exchange resin to obtain the free acid.[3] The standard solution of $K_3H(R(-)PDTA)$ was prepared by dissolving a weighed amount of the previously prepared *R*(-)PDTA acid, into a solution containing 3 equiv of KOH and standardized exactly as the EDTA solution.

The lead complex of the EDTA was prepared by the addition of a stoichiometric quantity of the standard lead nitrate solution to the appropriate amounts of 2.0 M KNO_3 and standardized K_2H_2EDTA solution. This initial solution was 0.55 M in KNO_3. It was necessary to stir the solution vigorously during the addition of the standard lead solution to prevent the formation of insoluble Pb(PbEDTA).

The ionic strength of the reacting solution was maintained at 0.50 with KNO_3.

Apparatus. A modified Perkin-Elmer Model 141 photoelectric polarimeter, with a wavelength range of 650–240 nm, was used to monitor the change in the optical rotation of the reacting solutions during the course of the ligand-exchange reactions.[4,5] The wavelength used in this work was 365 nm, because of the large rotational differences between the Pb–*R*(-)PDTA complex and the ligand, *R*-(-)PDTA, at this wavelength and the high absorbance of the nitrate ion at lower wavelengths. This permitted high sensitivity of the kinetic measurements and provided direct comparison to the previously studied *R*,*R*(-)CDTA ligand-exchange reaction. A Haake Model KT 41 Kryokool constant-temperature circulator was used to control the temperature of the reaction at 20.00 ± 0.01 °C. The standard 1-dm flow-through polarimeter cell was attached to the reaction vessel by

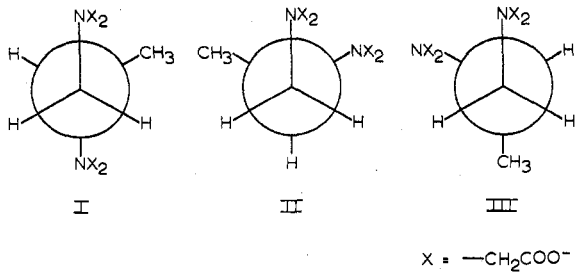

Figure 1. Rotamers of *R*(−)PDTA.

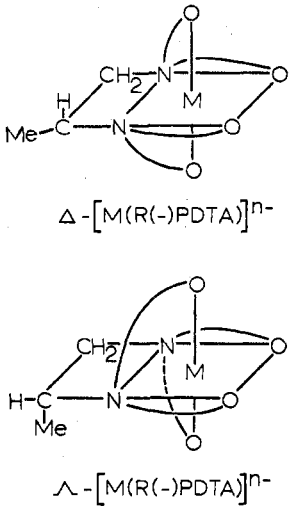

Figure 2. Stereospecificity of *R*(−)PDTA to form Δ-[M(*R*(−)-PDTA)]$^{n-}$ complexes.

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 s; thus, all measurements were made at times after the initial 5 s. The reaction vessel had a tight-fitting stopper which was fabricated to contain a thermometer, a pH combination electrode, fritted nitrogen gas inlet and outlet valves, and a small stopper for addition of the optically active ligand.

The pH of the reaction mixture was measured with an Orion Model 801 pH meter with a Sargent combination glass electrode. 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

As in the *R*,*R*(−)CDTA exchange with PbEDTA,[2] the ligand-exchange reaction with *R*(−)PDTA is first order in both entering ligand and the PbEDTA complex over the pH range of 10–13. In all cases, the reaction was made pseudo first order overall by using an approximate tenfold excess of the entering ligand. This large excess of entering ligand ensures that the exchange reaction proceeds essentially to completion due to the large value of $K_{stability}$ for PbPDTA.

For dilute solutions the observed optical rotation is directly proportional to the concentrations of the optically active species present; thus, polarimetry may be used to directly measure the extent of the reaction. The times for the exchange reactions to reach the equilibrium rotations range from about a minute for the highest pH solutions to about one hour for the lowest pH solutions. The actual equilibrium rotational values agreed closely with the rotational values calculated from the molecular rotations of *R*(−)PDTA and Δ-(+)-[Pb-*R*-(−)-PDTA] and their corresponding concentrations, assuming that the reaction has proceeded to completion. Values of k_{obsd} can be obtained from the slope of the plot of $-\ln|\alpha_t - \alpha_{eq}|$ vs. time.[2] The plots are linear for at least 2–3 half-life periods. The observed rate constants obtained for this ligand-exchange reaction are compiled in Table I.

The rate expression was found to be

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

where $(k_L^{MY})_T$ is the total specific rate constant for the exchange reaction of *R*(−)PDTA with PbEDTA, $[L]_T$ is the total analytical concentration of *R*(−)PDTA, [MY] is the PbEDTA complex concentration, and k_{obsd} is the observed pseudo-first-order rate constant. The observed rates were found to increase rapidly with pH. Consistent with the *R*,*R*(−)CDTA exchange with PbEDTA, four reactions (eq 3–6) are proposed

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

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

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

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

to contribute to the overall observed rate of the ligand-exchange reactions in the pH range studied. Abbreviations used are Y = ethylenediaminetetraacetate and L = (*R*)-(−)-1,2-propylenediaminetetraacetate. Charges on species are omitted. The rate expression may be 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_2PDTA^{2-}, H_3PDTA^-, and H_4PDTA 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 $HPDTA^{3-}$; 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 give eq 9.

$$\frac{k_{obsd}\left(1 + \frac{K_4}{[H^+]}\right)}{[L]_T} = \frac{k_1K_4}{[H^+]} + k_2 + \frac{k_3K_{OH_1}K_WK_4}{[H^+]^2} + \frac{k_4K_{OH_1}K_{OH_2}K_W{}^2K_4}{[H^+]^3} \quad (9)$$

Figure 3, a plot of the values in Table I, shows a curved line results which approximates that of a cubic equation and therefore confirms the assumption that the ligand exchange involves not only the reaction pathways of eq 3 and 4. Graphical and computer-assisted numerical regression analysis

Table I. Observed Pseudo-First-Order Rate Constants and Values of $1/[H^+]$ and $k_{obsd}(1 + K_4/[H^+])/[L]_T$ (20 °C; $\mu = 0.50$ (KNO_3))

pH	k_{obsd}, s^{-1}	$10^{-12}/[H^+]$, M^{-1}	$k_{obsd}(1 + K_4/[H^+])/[L]_T$[a]
10.041	1.24×10^{-2}	0.0109	1.681
10.569	3.03×10^{-2}	0.0371	5.440
10.894	4.24×10^{-2}	0.0783	10.57
11.001	4.98×10^{-2}	0.100	14.26
11.127	5.37×10^{-2}	0.134	18.44
11.449	6.23×10^{-2}	0.281	36.90
11.648	7.07×10^{-2}	0.445	61.41
11.756	6.82×10^{-2}	0.570	73.71
11.869	7.03×10^{-2}	0.740	96.12
11.998	7.21×10^{-2}	0.995	129.8
12.036	7.62×10^{-2}	1.09	148.8
12.102	7.36×10^{-2}	1.26	166.0
12.137	7.40×10^{-2}	1.37	180.2
12.145	7.26×10^{-2}	1.40	179.8
12.176	7.97×10^{-2}	1.50	211.4
12.290	7.42×10^{-2}	1.95	252.5
12.356	7.96×10^{-2}	2.27	314.8
12.384	7.92×10^{-2}	2.42	333.4
12.405	7.82×10^{-2}	2.54	345.1
12.421	8.02×10^{-2}	2.64	366.9
12.435	8.00×10^{-2}	2.72	377.6
12.437	8.55×10^{-2}	2.74	405.4
12.462	8.28×10^{-2}	2.90	415.3
12.497	8.74×10^{-2}	3.14	474.2
12.565	8.84×10^{-2}	3.67	559.2
12.601	9.01×10^{-2}	3.99	618.4
12.627	8.70×10^{-2}	4.24	633.3
12.655	8.91×10^{-2}	4.52	691.0
12.663	8.99×10^{-2}	4.60	710.0
12.705	9.57×10^{-2}	5.07	831.4
12.725	1.04×10^{-1}	5.31	945.6
12.745	1.03×10^{-1}	5.56	983.8
12.802	1.14×10^{-1}	6.34	1236
12.892	1.34×10^{-1}	7.80	1783

[a] The values of $k_{obsd}(1 + K_4/[H^+])/[L]_T$ were calculated using the value 10.84 for pK_4 of PDTA.[6]

of data in Table I shows that, over the pH region 10.0–12.3, the kinetic contribution of the dihydroxy-assisted pathway to the observed total rate is negligible and the cubic term may be neglected in eq 9. The value for the y intercept of approximately zero was obtained corresponding to the value of the specific rate constant for the attack of HL^{3-}, $k_{HL^{3-}}^{MY}$ or k_2. Thus, as in the *R,R*(−)CDTA exchange with PbEDTA[2] and the EDTA exchange with PbEDTA,[7] the attack by the HL^{3-} contributes very little to the overall rate of ligand exchange.

A multiple-regression analysis for the best quadratic curve fit of the data at pH <12.6 obtained parameter values of $b = 123.8 \times 10^{-12}$ and $c = 6.78 \times 10^{-24}$. Thus, the value of the specific rate constant k_L^{MY} or $k_1 = 8.57$ M^{-1} s^{-1} was obtained by dividing b by K_4 (1.44×10^{-11}). Likewise as in the *R,R*(−)CDTA ligand-exchange reaction, it was impossible to determine k_3, since K_{OH_1} is unknown. Table II shows the resolved rate constants and subsequent comparisons for the EDTA and PbEDTA exchange,[7] *R*(−)PDTA and PbEDTA exchange, *R,R*(−)CDTA and PbEDTA exchange,[2] and EDTA and PbPDTA exchange.[7]

The percentage contribution from the monohydroxy-assisted pathway (eq 5 and quadratic term in eq 9) is calculated for both the *R*(−)PDTA and the *R,R*(−)CDTA ligand-exchange

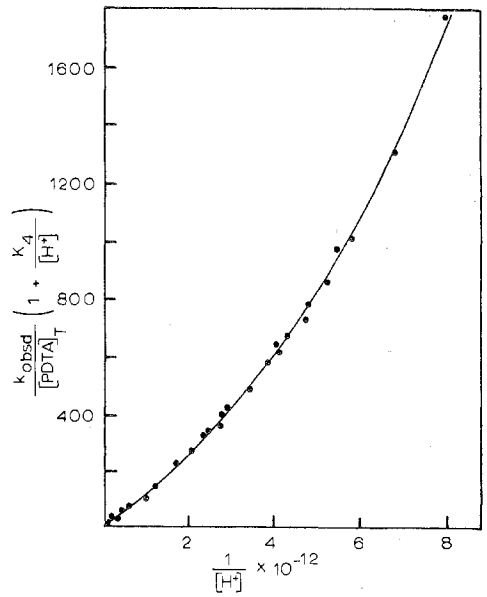

Figure 3. Plot of $k_{obsd}(1 + K_4/[H^+])/[PDTA]_T$ vs. $1/[H^+]$ showing the experimental points and calculated curve (20 °C, $\mu = 0.50$ (KNO_3)).

reaction with PbEDTA at specific pH values. This comparison is shown in Table III.

At pH >12.6, the dihydroxy-assisted pathway (the cubic term in eq 9) increases in importance to the overall rate of exchange. The values from the quadratic fit for parameters b and c ($a = 0$) were inserted into the cubic expression with the corresponding values of x and x^2. The difference between

$$Y_{obsd} = \frac{k_{obsd}}{[L]_T}\left(1 + \frac{k_4}{[H^+]}\right)$$

and $(bx + cx^2)$ was attributed to the contributions of the dihydroxy-assisted mechanism, the cubic term, dx^3 of eq 9. The average numerical value obtained for d was 6.81×10^{-37}, within this pH range. Values calculated for d were essentially constant. Similar to the above case of the monohydroxy mechanism it was impossible to obtain a value for the specific rate constant k_4, since K_{OH_1} and K_{OH_2} are unknown.

The contribution of the cubic term, dx^3, was found to increase from 3% at pH 12.405 to 19% at pH 12.892. The same analysis for the *R,R*(−)CDTA exchange showed a dihydroxy contribution of 6% at pH 12.429 to 22.3% at pH 12.945. Table III shows the comparison of the dihydroxy-assisted mechanism contribution for the *R,R*(−)CDTA and *R*(−)PDTA exchanges with PbEDTA at specific pH values. Reinbold and Pearson presented optical rotatory data showing that the formation of a mixed OH–CDTA–Pb complex as a possible equilibrium product does not occur to any large extent.[2] The optical rotatory data showed the absence of polymeric species such as Pb–CDTA–Pb. Thus, a mono or dihydroxy PbEDTA species is of an intermediatory nature in the mechanism of these exchanges.

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

Table II. Specific Rate Constants and Rate Comparisons

Ligand-exchange reaction	k_L^{MY}, M^{-1} s^{-1}	$k_{EDTA}^{PbEDTA}/k_L^{MY}$	$k_{R(-)PDTA}^{PbEDTA}/k_L^{MY}$
EDTA + PbEDTA[7]	65.0		0.13
R(−)PDTA + PbEDTA	8.57	7.6	
EDTA + PbPDTA[7]	1.23	53	7.0
R,R(−)CDTA + PbEDTA[2]	0.408	160	21

Table III. Calculated Percentage Contribution from the Monohydroxy- and Dihydroxy-Assisted Mechanisms with Increasing pH for *R*(−)PDTA and *R*,*R*(−)CDTA Ligand-Exchange Reactions

	R(−)PDTA		*R*,*R*(−)CDTA	
pH	Mono-hydroxy[a]	Dihy-droxy[b]	Mono-hydroxy[a]	Dihy-droxy[b]
9.928			0.55	
10.041	0.06			
11.001	0.54			
11.257			10.5	
11.449	1.52			
11.577			19.6	
11.864			32.3	
11.869	3.90			
12.080			43.7	
12.102	6.48			
12.131			46.6	
12.145	7.12			
12.290	9.66			
12.296			56.5	
12.405	11.8	3.0		
12.421	12.2	3.2		
12.429			59.6	6.0
12.435	12.5	3.4		
12.437	12.6	3.5		
12.462	13.2	3.8		
12.477			61.3	7.0
12.492			61.9	7.4
12.497	14.0	4.4		
12.525			63.0	8.1
12.555			63.8	8.7
12.565	15.8	5.8		
12.601	16.7	6.7		
12.624			65.4	10.6
12.627	17.4	7.4		
12.630			65.5	10.7
12.655	18.2	8.3		
12.663	18.4	8.5		
12.705	19.6	10.0		
12.721			67.1	13.8
12.725	20.1	10.7		
12.745	20.7	11.5		
12.762			67.2	14.9
12.799			67.2	16.3
12.802	22.1	14.1		
12.848			67.1	18.3
12.892	24.2	19.0		
12.945			66.0	22.3

[a] Calculated from the ratio of the monohydroxy contribution factor, cx^2, of eq 9 to the total contribution from all three pathways ($Y = bx + cx^2 + dx^3$). [b] Calculated from the ratio of the dihydroxy contribution factor, dx^3, of eq 9 to the total contribution from all three pathways ($y = bx + cx^2 + dx^3$).

those observed experimentally as is shown in Figure 3.

Discussion

CDTA forms more stable complexes with most of the metal ions than does PDTA or EDTA.[8] The stability difference is generally 1–2 log K units for most metal complexes in going from CDTA to PDTA to EDTA as the chelating ligand. This can be attributed to the fact that for chelation to occur between the nitrogen atoms of PDTA and EDTA and the metal ion, the carbon chain between nitrogen atoms has to be rotated to bring the nitrogen atoms into the same plane. The thermodynamically preferred chain 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. The alkyl substituents of PDTA and CDTA produce an inductive effect and increase the basicities of the ligand nitrogens as compared to those of EDTA.

However, the rate data shown in Table II suggest that steric considerations in going from EDTA to PDTA to CDTA as the attacking ligand are much more important in determining the rate of ligand–ligand exchange for metal complexes. The specific rate constant $k^{PbEDTA}_{R,R(-)CDTA}$ is approximately 160 times slower than the specific rate constant k^{PbEDTA}_{EDTA}. Likewise, the specific rate constant $k^{PbEDTA}_{R(-)PDTA}$ is approximately 7.6 times slower than the specific rate constant k^{PbEDTA}_{EDTA}. The necessity of steric alignment during chelation increases in going from a two-carbon chain between the nitrogens of the EDTA ligand to a methyl-substituted two-carbon chain in which the orientation of the methyl group of necessity is equatorial in the octahedral complex of *R*(−)PDTA (see Figure 2).

The stereochemical hindrances with *R*,*R*(−)CDTA are even more severe. Due to the fixed stereochemistry of the trans-1,2-substituted cyclohexane ring, *R*,*R*(−)CDTA has a subsequent inability to accommodate certain chirality due to the steric hindrances encountered between the methylene groups of the ring and the acetato groups upon chelation in octehedral complexes. Thus, both *R*(−)PDTA and *R*,*R*(−)-CDTA are optically active and completely stereospecific in their reactions with octahedral metal ions to form Δ metal complexes.

Kinetic rate data in Table II provide insight into the steric effects for leaving ligands vs. those for entering ligands. The addition of the methyl group to the leaving ligand decreases the specific rate constant by approximately 50 times for the ligand-exchange reaction EDTA + PbPDTA compared to the ligand-exchange reaction EDTA + PbEDTA. The specific rate constant, $k^{PbEDTA}_{R(-)PDTA}$, is approximately 7 times greater than the specific rate constant, k^{PbPDTA}_{EDTA}. This demonstrates that the steric hindrances encountered by the leaving ligand are more effective at slowing the ligand-exchange reaction than are similar steric hindrances encountered when the same ligand is the entering ligand. Considering the ligand exchange of EDTA with the complex PbPDTA, the methyl group of the coordinated PDTA tends to keep the dentate groups in a position favorable for bonding by hindering the rotation of the iminodiacetato groups away from the central metal ion. This results in an additional energy barrier that would have to be overcome in order to achieve ligand–ligand exchange and gives rise to a decreased reaction rate. Also, the electron-donating properties of the methyl group increase the basicities of the PDTA nitrogen atoms as compared to those of EDTA, thus increasing the strength of the metal to nitrogen bonds. Further, the direct ligand substitution of CDTA with PbCDTA would be inhibited due to the acute steric hindrances of the entering and leaving ligands. The stereochemistry of the cyclohexane ring limits the freedom of any breaking acetato group and CDTA tends to form sexadentate complexes more readily than either PDTA or EDTA. Many PDTA and EDTA complexes can be isolated where the PDTA or EDTA is quinquedentately coordinated whereas due to the rigid stereochemistry of the CDTA, quinquedentate chelation is not favored. Halogen–EDTA and –PDTA complexes in which the halogen is in the inner coordination sphere can be isolated from solution from the respective Co(III)–EDTA and –PDTA complexes with a hydrohalic acid. However, the isolation of the corresponding halo–CDTA complex is impossible, since it immediately dissociates in the absence of a large excess of hydrohalic acids.

Rorabacher and Margerum have shown that ligand substitution reactions involving multidentate ligands 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.[9] 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 Λ and Δ isomers of PbEDTA, the series of

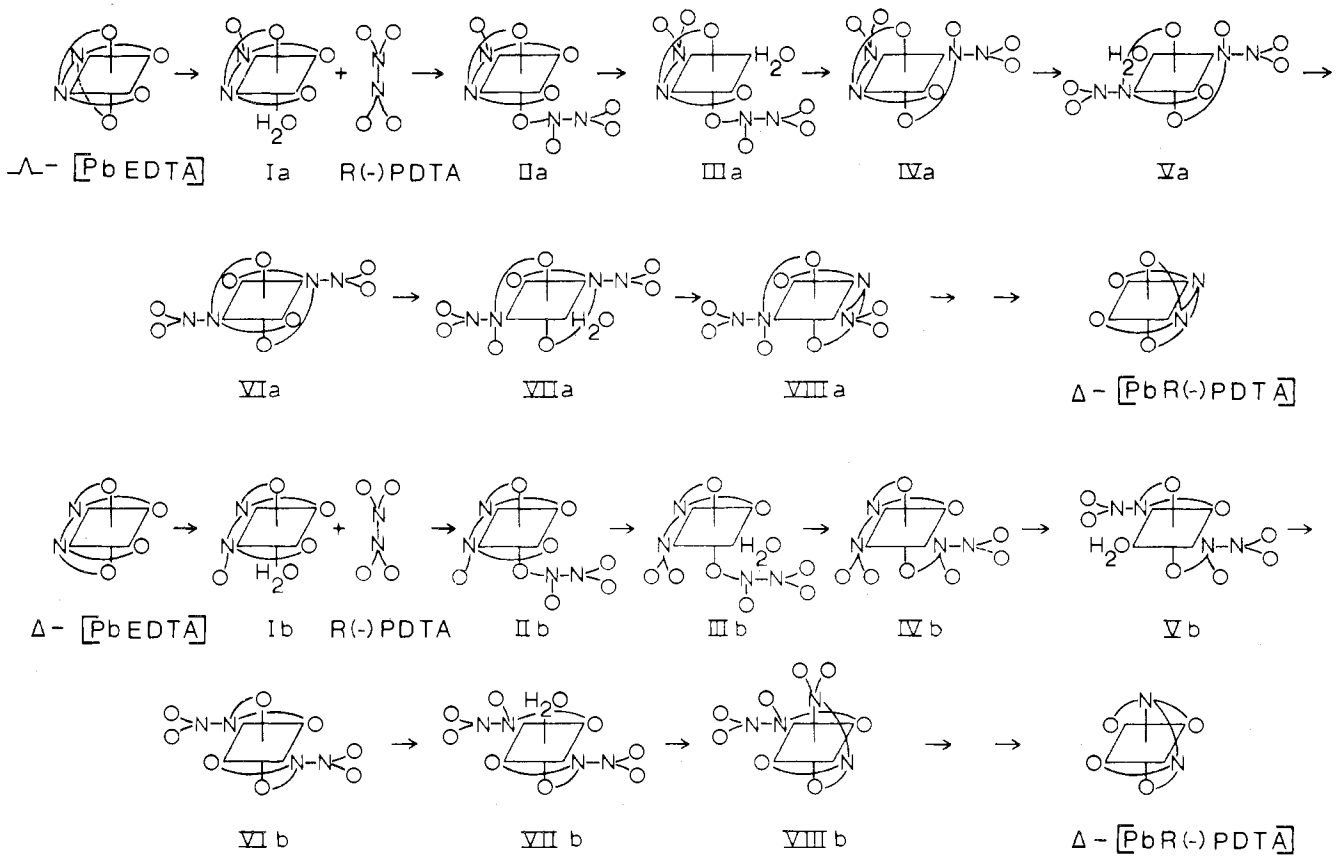

Figure 4. Proposed mechanism for the aquo-assisted exchange of *R*(−)PDTA with PbEDTA, considering both stereoisomers of PbEDTA.

mechanistic steps must also account for the stereospecifically obtained reaction product. From the reaction order it is inferred that the intermediates in this system involve a stepwise aquation of PbEDTA and the attack of *R*(−)PDTA 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 *R*(−)PDTA forming one bond at a time as the solvent water molecules are lost in turn until the ligand substitution is complete. Three criteria are preserved in the proposed mechanisms: (I) an acetato group will be the first dentate to form a bond from the *R*(−)PDTA 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-membered ring; (III) each bond rupture will destroy only one chelate ring. Intermediates with both EDTA and *R*(−)PDTA 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 *R*(−)PDTA with PbEDTA. The mechanistic pathways proposed for the aquo-assisted ligand-exchange reaction must consider both optical isomers of the PbEDTA complex, Λ- and Δ-[PbEDTA], and must give the correct optically active product Δ-(+)-[Pb(*R*(−)PDTA)]. Thus, the attack of the ligand upon the PbEDTA complex is considered as two separate and simultaneous series of reactions. These series of reactions are shown in Figure 4. The proposed sequences are those that are shown by models to involve the least amount of steric hindrance and the most stable intermediates. Eigen has shown that rapid association and dissociation of water occur within the inner coordination sphere.[10] Thus, aquation of the complex could easily occur in positions 1–3 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 proposed pathways involves attack of an acetato group of the entering ligand upon position 6 after aquation has occurred.

In Figure 4, 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.

Based on molecular models and the steric influences of the entering ligand, the proposed sequences for the aquo-assisted mechanism occur with slight differences in steric hindrances for EDTA, *R*(−)PDTA, and *R,R*(−)CDTA attack up to step Va and Vb. However, the steps Va → VIa and Vb → VIb occur with the necessity of steric alignment for the attacking ligand. In intermediate Va the displacement of the water at position 5 and the subsequent attachment of the second ligand acetato group to form intermediate VIa requires very little orientation of the entering ligand in the EDTA + PbEDTA exchange. Thus, very rapid ligand–ligand exchange occurs in this reaction. However, in the case of the *R*(−)PDTA as the attacking ligand, due to the stereochemistry of this ligand, the steric requirements in forming the stereospecific complex slow down the rate of exchange due to steric interactions. With *R,R*(−)CDTA these steric interactions are much greater due to the fixed sterochemistry of the cyclohexane ring and its large bulkiness. The same type of interactions occur at intermediate Vb when the second acetato group attaches to position 4. From intermediate VIa, aquation can occur at positions 1 and 3. If aquation occurred at position 1, the attack of the second nitrogen of either *R*(−)PDTA or *R,R*(−)CDTA and subsequent displacements would lead to complexes of absolute configuration of Λ which are sterically impossible for these stereospecific ligands. Thus, aquation and subsequent attack is shown to occur at position 3 and the step VIIa → VIIIa is

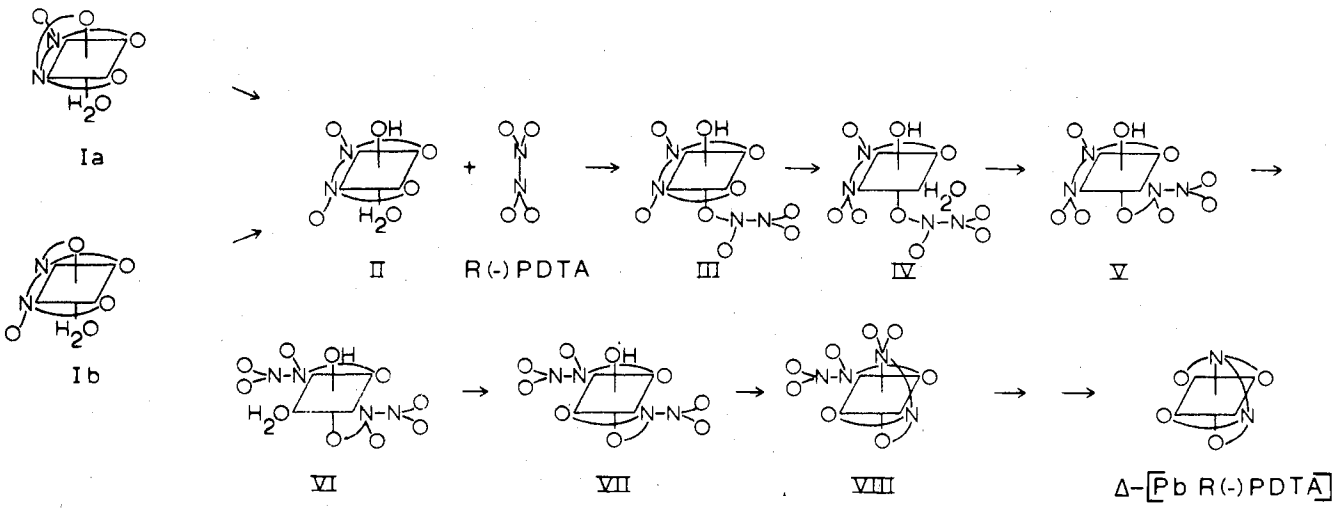

Figure 5. Proposed mechanism for the monohydroxy-assisted exchange of *R*(−)PDTA with PbEDTA.

assigned the stereochemical determining step (sds). Likewise, from intermediate VIb, aquation can occur in positions 1 and 2. Aquation at position 2 and subsequent nitrogen attack are impossible for both *R*(−)PDTA and *R,R*(−)CDTA, since again the wrong stereochemical product would be formed. Thus, aquation in position 1 to form VIIb and then displacement to form VIIIb are proposed with VIIb → VIIIb being the stereochemical determining step. From mechanistic steps VIIIa and VIIIb subsequent displacements yield the correct stereochemical products, Δ-(+)-[Pb(*R*(−)PDTA)] or Δ-(+)-[Pb(*R,R*(−)CDTA)].

Mechanism II. Monohydroxy-Assisted Exchange of *R*(−)PDTA with PbEDTA. Figure 3 clearly shows that over the pH range of 12.3–12.7 the increase in the rate of the *R*(−)PDTA + PbEDTA reaction is significantly greater than can be accounted for by the increasing concentration of the attacking species $R(-)PDTA^{4-}$, due to increasing pH. The reaction mechanism proposed for the *R*(−)PDTA ligand-exchange reactions in this pH region involves a monohydroxy-assisted pathway. The effect of OH is to reduce the stability of the PbEDTA and to allow more rapid aquation and dissociation of the leaving ligand from the original complex.

Figure 5 shows the proposed sequence for the monohydroxy-assisted exchange of *R*(−)PDTA with PbEDTA. Starting with the aquation in position 6, the possible coordination sites for the hydroxy group are at positions 1–3. However, in positions 2 and 3 the OH is in the plane of the EDTA nitrogens and the entering ligand encounters steric interferences with the acetato groups of the leaving ligand. Position 1 offers less steric interferences and allows maximum overall weakening of the PbEDTA complex.[2]

The stereochemical considerations of the two optical isomers of PbEDTA, Δ-[PbEDTA] and Λ-[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 5, intermediates Ia and Ib are identical with intermediates Ia and Ib of Figure 4. Intermediate II is obtained by OH attack on the 1 position of both Ia and Ib. 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 Δ-[Pb(*R*(−)PDTA)]. In the rate-determining step V to VI, the OH assists in breaking the bond between the EDTA nitrogen and the lead ion which allows the second acetato group of the entering *R*(−)PDTA ligand to attack at position 4 with a reduction of steric hindrances. Thus, the steric hindrances in this rate-determining step are less than those involved when the second acetato group of the entering *R*-(−)PDTA ligand attacks in the aquo-assisted mechanism.

Mechanism III. Dihydroxy-Assisted Exchange of *R*(−)-PDTA with PbEDTA. At pH values greater than 12.7, the agreement between values of y_{obsd} and y_{calcd}, assuming only the monohydroxy-assisted pathway, is insufficient to explain the great increase in the rate of the *R*(−)PDTA exchange. Deviations from the quadratic curve fit are greater than 10% in this region. Thus, a dihydroxy-assisted mechanism is proposed for this pH region and the stereochemistry of the reacting species 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 6, the initial attack of OH is in position 1 to give intermediate I, which is identical with intermediate II, in Figure 5. The second attack by OH on intermediate I, Figure 6, can be at position 2 giving IIa or at position 3 giving IIb. In intermediates IIa and IIb the rapid loss of water and attack of *R*(−)PDTA 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 *R*(−)PDTA. In intermediate IVa, the nitrogen attacks in position 2 to yield Va. It is sterically impossible for the nitrogen of the *R*(−)PDTA molecule to attack in position 5. Intermediate Va then undergoes stepwise reactions through intermediate VIa to the final product Δ-[Pb(*R*(−)PDTA)]. Likewise, from intermediate IIIb, the dissociation of the nitrogen on position 4 gives intermedidate IVb, with the front side of the intermediate open for attack. Thus, in the b series of the dihydroxy-assisted reactions, the attack on the intermediate IVb by the nitrogen of the *R*(−)PDTA is again in the cis position to the coordinated acetato group containing the OH, yielding intermediate Vb. It is sterically impossible for the nitrogen of the entering *R*(−)PDTA to attack and coordinate in position 4. Intermediate Vb then undergoes successive stepwise reactions through intermediate VIb to the final product Δ-[Pb(*R*(−)-PDTA)]. 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. Other possible pathways for the dihydroxy-assisted mechanisms with the hydroxides in the 1 and 2, 1 and 3, and 2 and 3 positions and water in the 6 position were considered and ruled out as the major pathways

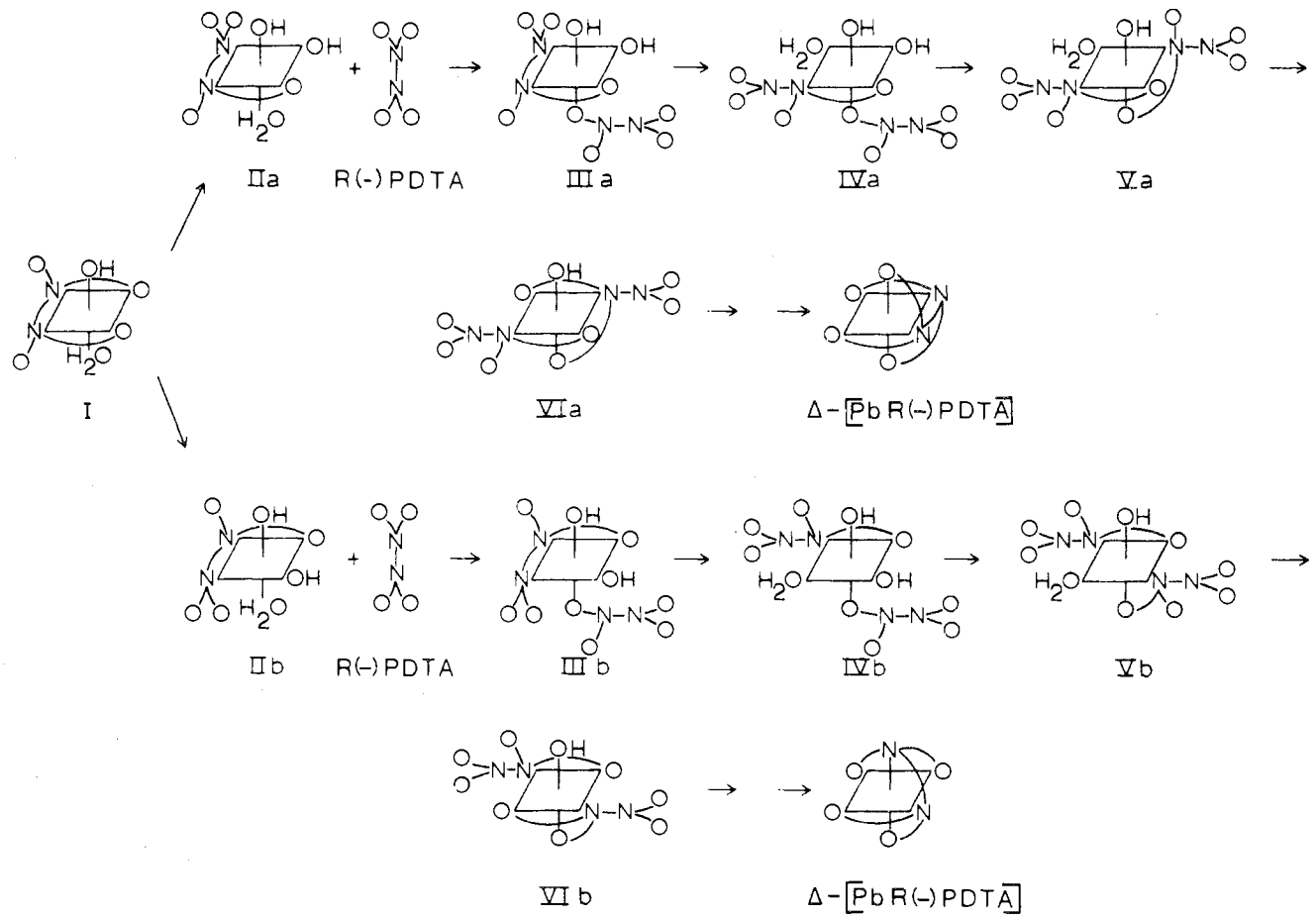

Figure 6. Proposed mechanism for the dihydroxy-assisted exchange of *R*(−)PDTA with PbEDTA.

similar to the *R*,*R*(−)CDTA ligand-exchange reaction with PbEDTA.[2]

Consideration of the proposed mechanisms, Figures 4–6, and the stereochemical mechanistic approach leads to the conclusion that much greater steric hindrance would be expected for the attack of *R*,*R*(−)CDTA on the PbEDTA complex than for the attack of *R*(−)PDTA. In support of this, Table II shows that the specific rate constant for the *R*,*R*(−)CDTA attack on the PbEDTA complex is 21 times less than the specific rate constant for attack of *R*(−)PDTA. In addition, it would be expected that monohydroxy- and dihydroxy-assisted pathways would contribute more significantly to the overall rate of reaction for the very sterically hindered *R*,*R*(−)CDTA for the *R*(−)PDTA exchange. This is verified by comparing the resolved, pH-dependent percentage contributions of each mechanism from the kinetic data of *R*(−)-PDTA ligand exchange with those of *R*,*R*(−)CDTA ligand exchange. From Table III it may be seen that at pH 12.2 the monohydroxy-assisted contribution is approximately 50% of the total reaction rate of *R*,*R*(−)CDTA; the monohydroxy-assisted contribution for *R*(−)PDTA is merely 8% at this pH. At pH greater than 12.2, the predominant pathways are hydroxy assisted for the *R*,*R*(−)CDTA exchange and at pH 12.9 the summation of the monohydroxy- and dihydroxy-assisted contribution to the total reaction rate for the *R*,*R*-(−)CDTA exchange is approximately 88%. However, for the *R*(−)PDTA ligand exchange in the pH region studied, the hydroxy-assisted pathways are never the predominant pathways, since at pH 12.9 the summation of the monohydroxy- and dihydroxy-assisted contribution is only 43%. Due to the comparatively lessened steric hindrance encountered for the EDTA reaction with PbEDTA, the monohydroxy- and dihydroxy-assisted mechanisms' contribution to the overall rate of exchange would be much less significant.

Registry No. PbEDTA, 11112-42-8; *R*(−)PDTA, 15456-17-4; *R*,*R*(−)CDTA, 28684-63-1.

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(1) To whom correspondence should be addressed.
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