prefers to distort tetragonally, while the Co(III) center in the reaction[25]

$$Cr^{2+} + \textit{trans}\text{-}Co(en)_2NH_3Cl^{2+} + 5H^+ = CrCl^{2+} + Co^{2+} + NH_4^+ + 2enH_2^{2+}$$

prefers to distort toward a square-based pyramid.[25]

The data in Table VI concerning the two Cr(II)-catalyzed aquations of chlorochromium(III) complexes illustrate the decreased sensitivity to nonbridging ligands that is observed in this system. A further example of this phenomenon is illustrated in Figure 1 where a plot of the logarithm of the rate of Fe(II) reduction of chlorocobalt(III) complexes against the logarithm of the Cr(II)-catalyzed aquation of chlorochromium(III) complexes is to be found.[5,9,26] The observed slope, 0.45, shows that the Cr(II)-catalyzed aquation, the mechanism of which is electron transfer in nature,[26] is less than half as sensitive to a change in nonbridging ligands than is the Fe(II) reduction of the chlorocobalt(III) complexes.

Acknowledgments.—This research was supported by the National Institutes of Health (Grant GM-14830). The author thanks Professor John Endicott for helpful discussions and a preprint of the results of reductions with $Ru(NH_3)_6^{2+}$.

(26) A. E. Ogard and H. Taube, *J. Am. Chem. Soc.*, **80**, 1084 (1958).

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Mechanism and Steric Course of Octahedral Aquation. XI.[1] The Mechanism of Isomerization of *cis*-Hydroxoaquo(1,4,8,11-tetraazacyclotetradecane)cobalt(III) Cations

By C. K. Poon and M. L. Tobe

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The *cis* to *trans* isomerization of *cis*-$Co(cyclam)Cl_2^+$ (cyclam = 1,4,8,11-tetraazacyclotetradecane) has been shown to go by way of the labile *cis*-$Co(cyclam)(OH)H_2O^{2+}$ cation. The isomerization of this species is accompanied by exchange of two of the four amine protons and it is assumed that this exchange leads to the inversion of the configurations of the nitrogen atoms concerned. The kinetics of the exchange of the amine protons of *trans*-$Co(cyclam)(H_2O)_2^{3+}$ and *trans*-$Co(cyclam)(OH)H_2O^{2+}$ have been examined as a function of pH. It is proposed that the facile hydrogen exchange and isomerization of these hydroxoaquo complexes is a consequence of an intramolecular proton transfer from nitrogen to oxygen and that this process allows the otherwise unfavored exchange with inversion of configuration to take place.

Introduction

The substitution reactions of the cobalt(III) complexes of 1,4,8,11-tetraazacyclotetradecane (cyclam) have been shown to proceed with complete retention of configuration.[1-3] In part X[1] we reported that a solution, originally containing *cis*-[Co(cyclam)Cl_2]Cl in 0.01 *M* hydrochloric acid, underwent three spectrophotometrically distinct changes, the first two of which could be identified as successive stereoretentive solvolytic displacements of the coordinated chlorine, *i.e.*

$$\textit{cis}\text{-}Co(cyclam)Cl_2^+ + H_2O \longrightarrow \textit{cis}\text{-}Co(cyclam)(Cl)H_2O^{2+} + Cl^- \quad (1)$$

$$\textit{cis}\text{-}Co(cyclam)(Cl)H_2O^{2+} + H_2O \rightleftarrows \textit{cis}\text{-}Co(cyclam)(H_2O)_2^{3+} + Cl^- \quad (2)$$

The third process, which was very slow under these conditions, was a *cis* to *trans* change since the final spectrum was identical with that of a mixture of *trans*-$Co(cyclam)Cl_2^+$ and *trans*-$Co(cyclam)(H_2O)Cl^{2+}$ at equilibrium under identical conditions.[3]

It was thought that the main cause of the stereoretentive behavior of these complexes was the restriction placed upon the configuration that could be adopted by the secondary nitrogen atoms[2] and that stereochemical change would require concomitant inversion of the configuration of certain of the nitrogen atoms. Since the most likely path for such an inversion is through the exchange of the amine protons, this paper sets out to examine the isomerization, to identify the reaction path, or paths, and to study the relationship between proton exchange and inversion.

Experimental Section

The preparation, properties, and analyses of the complexes used in this work have been reported elsewhere.[1] All other reagents were of AnalaR grade when available or else of reagent grade. D_2O (99.7%) was obtained from Norsk Hydro, and DCl was obtained as a 20% solution in D_2O (99% D) from E. Merck, A.G., and was diluted as necessary with D_2O. Small quantities of $DClO_4$ in D_2O were prepared by adding AR perchloric acid (72%) to D_2O and then evaporating this solution to small bulk *in vacuo* over P_2O_5. A fresh sample of D_2O was then added and the process was repeated. Noninterfering buffers have been described elsewhere.[3]

The isomerization reactions were followed spectrophotometrically by techniques depending upon the rate of the reaction. For the very slow reactions ($t_{1/2} > 6$ hr) the reaction solution was

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(1) C. K. Poon and M. L. Tobe, *J. Chem. Soc., A*, 1549 (1968).

(2) B. Bosnich, C. K. Poon, and M. L. Tobe, *Inorg. Chem.*, **4**, 1102 (1965).

(3) C. K. Poon and M. L. Tobe, *J. Chem. Soc., A*, 2069 (1967).

made up at room temperature and aliquots of approximately 12 ml were sealed into Pyrex tubes which were then placed simultaneously into the thermostat. Tubes were withdrawn and cooled at known times and the contents were transferred to 4-cm silica spectrophotometric cells. Unicam SP 700 or SP 800 or Cary 14 spectrophotometers were used, as convenient, when a range of wavelength had to be scanned. Single wavelength measurements were made with a Unicam SP 500 spectrophotometer. Reactions having half-lives between 30 min and 6 hr were studied by dissolving a known weight of complex in a known weight of reaction solution previously brought to the reaction temperature. Samples were withdrawn at known times by pipet and frozen to stop the reaction. Measurements were made as above. For half-lives between 5 and 30 min the reaction mixture, prepared as above, was transferred to a thermostated spectrophotometric cell and the reaction was followed *in situ,* either at a fixed wavelength or by a periodic scanning of the appropriate part of the spectrum. For the reactions whose half-lives were between 10 sec and 5 min the reaction was started in the spectrophotometric cell and followed with the spectrophotometer locked at one wavelength and the chart moving at a constant, known rate. Reactions of half-life less than 1 sec were followed with a stopped-flow, fast-mixing apparatus in which the reagents, separately brought to the reaction temperature, were simultaneously injected into a Teflon mixing chamber from which they entered the silica observation cell. The flow was stopped when the driving block attached to the syringe pistons hit a "stop," and the subsequent change in the transmission of the solution in the observation chamber was measured by a photon multiplier, displayed on an oscilloscope and recorded on high-speed Polaroid film.

Infrared spectra of Nujol or hexachlorobutadiene mulls between KBr disks were measured with a Perkin-Elmer 337 IR spectrometer. The aqueous solution spectra in the region 1.4–1.8 μ were measured with a Cary 14 spectrophotometer, the solutions being in thermostated silica cells.

The pH of the buffer solutions was measured with a Cambridge pH meter and a glass electrode. The titrimetric pH determination of the acid dissociation constants of the aquo complexes was carried out with an automatic-recording ABU 16 Radiometer.

Results

(1) **Kinetics of Isomerization in the Presence of Chloride Ions.**—In this set of experiments the associated aquation and anation processes were fast compared to the slow isomerization and so the rate of change of optical density was a direct measure of the rate of *cis* to *trans* isomerization. The change followed a first-order rate law and the rate constant, k_{obsd}, was obtained from the slope of the plot of log $(D_t - D_\infty)$ against time, where D_t and D_∞ are the optical densities at 530 mμ at time t and at the end of the reaction, respectively. The complex was provided as *cis*-[Co(cyclam)Cl$_2$]Cl and dissolved in the appropriate amount of solvent previously brought to the reaction temperature. Any additional chloride was provided as sodium chloride solution and added after all the complex had dissolved. Sufficient time was allowed for the first two stages to finish before any measurements were made. The rate of isomerization was studied as a function of chloride concentration and the results are collected in Table I.

TABLE I

OBSERVED FIRST-ORDER RATE CONSTANTS FOR THE *cis* TO *trans* ISOMERIZATION IN THE PRESENCE OF EXCESS CHLORIDE AT 60.5° AND 0.01 *M* ACID

[Complex], m*M*	Ionic strength, *M*	[Cl$^-$], *M*	$10^4 k_{\text{obsd}}$, sec^{-1}
1.6	0.51	0.021	5.3
1.1	0.09	0.081	3.2[a]
1.2	0.51	0.111	2.7
0.82	0.21	0.210	1.9
1.2	0.31	0.301	1.5[a]
0.80	0.51	0.411	1.2
1.5	0.51	0.511	0.98
0.65	0.51	0.511	0.96
1.2	1.01	1.01	0.52

[a] Acid provided as HNO$_3$; otherwise HCl was used.

(2) **Kinetics of Isomerization in the Absence of Coordinating Anions.**—Although it is possible to prepare crystalline *cis*-[Co(cyclam)(H$_2$O)$_2$](ClO$_4$)$_3$,[1] it was more convenient to generate the material in solution whenever it was required. By taking advantage of the fact that both steps of the base hydrolysis of the *cis*-dichloro cation take place with complete retention of configuration,[1] it was possible to make an aqueous solution of *cis*-[Co(cyclam)(OH)$_2$]OH by passing a solution of a known amount of *cis*-[Co(cyclam)Cl$_2$]Cl down a column of a strong anion-exchange resin in the hydroxide form. The effluent was then added to the appropriate buffer solution and the isomerization followed spectrophotometrically at 520 mμ at 25°. The change in optical density followed a first-order rate law and the first-order rate constant, k_{obsd}, was determined in the usual way. The dependence of rate constant upon pH is shown in Figure 1 where it will be seen that the rate is at a maximum at pH 6.8.

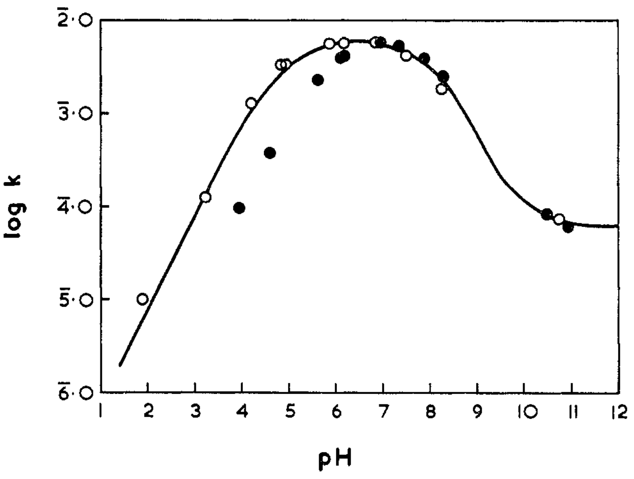

Figure 1.—Log k_{obsd} for the isomerization of *cis*-Co(cyclam)(H$_2$O)$_2{}^{3+}$ and its conjugate bases: ○, in the absence of chloride ions (μ = 0.05 *M*); ●, in the presence of chloride ions (μ = [Cl$^-$] = 0.202 *M*), at 25.0°. The drawn curve is calculated from constants given in the text.

In order to determine the contribution made to the pH dependence by the acid–base equilibria of the diaquo and hydroxoaquo complexes, the appropriate pK_a values were determined. A titrimetric method was used, but, since the isomerization is rapid in the intermediate pH region, it was necessary to obtain the first pK_a by titrating a freshly prepared solution of *cis*-Co(cyclam)(H$_2$O)$_2{}^{3+}$ with standard alkali and the second pK_a by titrating a solution of *cis*-Co(cyclam)-

$(OH)_2^+$ with standard acid. The determination of the pK_a values for the corresponding *trans* isomer was made in the same way and, since the interference from isomerization is no longer present, a slower spectrophotometric method was also used. The results are collected in Table II.

Table II

pK_a Values for *cis*- and *trans*-Co(cyclam)$(H_2O)_2^{3+}$ in Aqueous Solution at 25° and Ionic Strength 0.5 *M* ($NaClO_4$)

	pK_a(1)	pK_a(2)
trans-Co(cyclam)$(H_2O)_2^{3+}$	2.9 ± 0.1	7.2 ± 0.1
	2.82[a]	7.22[a]
cis-Co(cyclam)$(H_2O)_2^{3+}$	4.9 ± 0.2	8.0 ± 0.2

[a] Spectrophotometric determination.

(3) Anation of *cis*-Co(cyclam)(OH)H_2O^{2+} by Thiocyanate.—The process

$$cis\text{-Co(cyclam)}(H_2O)OH^{2+} + SCN^- \longrightarrow cis\text{-Co(cyclam)(OH)}NCS^+ + H_2O$$

was fast and could only be followed by a stopped-flow technique. Equal volumes of a solution containing the buffer 2,6-dimethylpyridine–perchloric acid and the sodium thiocyanate and one containing *cis*-[Co(cyclam)$(OH)_2$]OH were independently brought to the reaction temperature and then injected into the mixing chamber of the apparatus. The anation was followed spectrophotometrically at 400 mμ. The pH of the reaction mixture (6.90) was determined independently. At this pH 92% of the complex is present in the form of the hydroxoaquo cation. The rate constants are reported in Table III.

Table III

Pseudo-First-Order Rate Constants for the Anation of *cis*-Co(cyclam)(OH)H_2O^{2+} by Thiocyanate in 2,6-Dimethylpyridine–Perchloric Acid Buffer (pH 6.90) at 25.0°, Ionic Strength 1.0 *M*, and [Complex] = 0.01 *M*

	[NCS⁻], *M*		
	0.50	0.70	0.92
k_{obsd}, sec^{-1}	0.63	0.78	1.0

(4) The Relationship between Proton Exchange and Isomerization.—Preliminary studies by infrared and nmr analyses of the solutions of *cis*-Co(cyclam)$(H_2O)_2^{3+}$ in moderate or weakly acidic D_2O showed that isomerization and exchange took place at similar rates and that the *trans* product exchanged its protons readily. In order to fix and examine the *trans* product at early stages of the reaction, the following procedure was adopted. Samples of *cis*- and *trans*-[Co(cyclam)$(H_2O)_2$]$(ClO_4)_3$ were separately dissolved in two identical solutions of DCl and NaCl in D_2O such that the final pH[4] was 2.65 and the chloride concentration was 0.5 *M*. The two solutions were placed in thin-walled test tubes which were then immersed in a water bath (96°) for 1 min and then cooled rapidly in ice. A separate experiment showed that, under these conditions, the temperature of the solutions rose to 60° and that approximately 10% of the *cis* complex had isomerized to the *trans* form. It was also shown that all of the *trans* complex was rapidly converted to the dichloro form and most of the *cis* complex to the chloroaquo form. Solid sodium perchlorate was added to the cooled reaction mixture and the *trans*-Co(cyclam)Cl_2^+ cation separated quantitatively as its insoluble perchlorate. The *cis*-Co(cyclam)(Cl)H_2O^{2+} which remained in solution when the *trans* complex was filtered off was then precipitated as its insoluble tetraphenylborate. Each complex was carefully dried and the infrared spectrum of its Nujol mull was measured. The absorption spectra in the region 3400–2000 cm^{-1}, where the N–H and N–D stretching bands are found, are shown in Figure 2, together with a control in which HCl and H_2O were used. Inspection of these spectra show that, whereas there is very little exchange in the recovered, unreacted *cis* complex, the *trans* material obtained by isomerization of the *cis* substrate is extensively but not completely deuterated. Thus it must be concluded that the proton exchange occurred either during or else after the act of isomerization. It will be shown below that the data in section 1 demonstrate that essentially all of the isomerization involves a *cis* species that does not contain any coordinated chloride. Thus, the *trans* product is initially formed without any coordinated chloride even though, under the experimental conditions, it is rapidly anated to the *trans*-Co(cyclam)Cl_2^+. An independent experiment demonstrated that

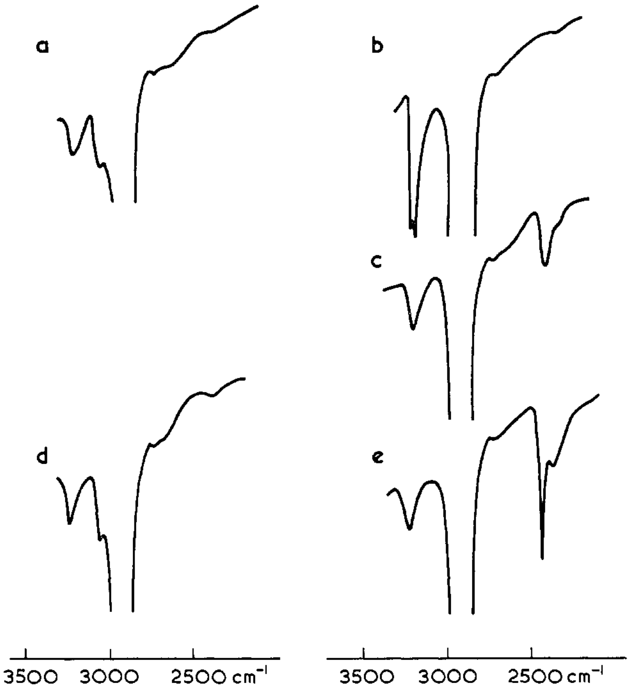

Figure 2.—Infrared spectra of Nujol mulls of *cis*-[Co(cyclam)(H_2O)Cl][$B(C_6H_5)_4$]$_2$ and *trans*-[Co(cyclam)Cl_2]ClO_4: (a) undeuterated *cis* isolated from the reaction *cis*-[Co(cyclam)$(H_2O)_2$]$(ClO_4)_3$ + Cl^- in H_2O; (b) undeuterated *trans* isolated from the reaction *trans*-[Co(cyclam)$(H_2O)_2$]$(ClO_4)_3$ + Cl^- in H_2O; (c) *trans* from the reaction *trans*-Co(cyclam)$(H_2O)_2^{3+}$ + Cl^- in D_2O at pH[4] 2.65 (isolated after 1 min at 60°, [Cl^-] = 0.5 *M*); (d) *cis* from the reaction *cis*-Co(cyclam)$(H_2O)_2^{3+}$ + Cl^- in D_2O at pH 2.65 (isolated after 1 min at 60°, [Cl^-] = 0.5 *M*); (e) *trans* formed from the *cis* diaquo complex in (d).

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[4] No attempt was made to measure pD. The figure given is the direct reading from a pH meter used in conjunction with a glass electrode.

this complex does not exchange its amine protons within the time of the experiment. The experiment, using *trans*-[Co(cyclam)$(H_2O)_2$]$(ClO_4)_3$, shows clearly that, between the time the *trans* species is generated and the time that it is converted to the dichloro complex, a considerable amount of proton exchange has occurred. However, this is nowhere nearly sufficient to account for all of the exchange observed in the isomerization.

A semiquantitative attempt was made to estimate the extent of exchange by comparing the relative intensities of the bands assigned to the N–H and the N–D stretches in the mull spectrum. A calibration curve was constructed using known mixtures of undeuterated and fully deuterated *trans*-[Co(cyclam)Cl_2]ClO_4 and the isotopic composition of the unknown sample read off from this. It has been pointed out by Block and Gold[5] that this treatment is not exact when there is more than one exchangeable proton; nevertheless, the quality of the data obtained by this approximation is sufficient for the arguments that follow. For the typical experiment shown in Figure 2, it is found that the *trans* product obtained from the *cis* substrate is some 80% exchanged whereas that obtained by the anation of the *trans* diaquo complex is only 50% exchanged, these values being reliable to ±5%. An analogous method of calibration could not be used for the *cis*-[Co(cyclam)$(H_2O)Cl$][$B(C_6H_5)_4$]$_2$ complex, but inspection shows that the amount of exchange cannot be large, probably in the region of 10%. While bearing in mind the approximate nature of these data, one can reason that, since the *trans* complex would exchange to the extent of 50% from the time it was formed to the time it was fixed as the dichloro cation, if x (%) exchange had occurred by the time it was formed, $0.5(100 - x)\%$ would take place afterward. Thus $x + 0.5(100 - x) = 80\%$, so that $x = 60\%$.[6] Of this exchange some 10% took place before isomerization and so one can conclude that approximately half the protons in the complex are exchanged in the course of the isomerization.

(5) **The Kinetics of Proton Exchange in the *trans*-Co(cyclam)$(H_2O)_2^{3+}$ Cation and Related Species.**—The complexity of the exchange processes of the *cis*-Co(cyclam)$(H_2O)_2^{3+}$ system, especially the complications arising from the isomerization, have prevented us, so far, from carrying out a successful detailed quantitative study of the exchange kinetics. The *trans* isomer presents a much simpler system for study and many of the effects that are pertinent in the discussion of the *cis* complex can be examined more conveniently here. The *trans*-Co(cyclam)$(H_2O)_2^{3+}$ cation is thermodynamically stable in perchlorate media and all four amine hydrogens are equivalent.[1] In addition, the two pK_a values are so widely different (Table II) that more than 90% of the complex is in the form of the aquohydroxo complex over a wide range (4–6) of pH. The kinetics of proton exchange were followed by the method of Basolo, *et al.*,[7] whereby the complex, provided as *trans*-[Co(cyclam)$(H_2O)_2$]$(ClO_4)_3$, was dissolved in $DClO_4$–D_2O or else was dissolved in D_2O and partially neutralized with NaOD solution,[8] and the infrared spectrum in the region 1.3–1.8 μ was recorded from time to time during the reaction. Peaks at 1.42 and 1.69 μ increased in absorbance (and thus were assigned to overtones of the O–H stretch of the solvent) whereas the peak at 1.58 μ slowly disappeared and could therefore be assigned to an N–H stretch overtone. The change in optical density followed a first-order rate law and the rate constant, determined in the usual way, was independent of the peak chosen. Those reactions in the higher pH region that were too fast to allow a full scan at each point of time were followed at a single wavelength. Owing to the weakness of the absorption bands and the lack of suitable scale expansion facilities, it was not possible to obtain data of high precision. The values recorded in Table IV nevertheless indicate that the rate is not greatly dependent on pH over the range 3.2–6.7.

TABLE IV

FIRST-ORDER RATE CONSTANTS FOR THE N–H EXCHANGE WITH D_2O OF *trans*-Co(cyclam)$(D_2O)_2^{3+}$ AND RELATED DEPROTONATED SPECIES AS A FUNCTION OF pH[4] AT 21° AND IONIC STRENGTH 0.50 *M* ($NaClO_4$)

[Complex], m*M*	pH	10^2k_{obsd}, sec^{-1} [a]
0.087	1.12	0.046[b]
0.064	2.16	0.22
0.084	3.20	1.4 ± 0.4
0.080	3.90	1.5 ± 0.5
0.080	4.68	2.0 ± 1.0
0.080	5.36	2.0 ± 1.0
0.064	6.70	3.0 ± 1.5

[a] The rate constants refer to exchange of all four equivalent protons. [b] Measured at 25°.

Discussion

The *cis* to *trans* isomerization of the substrate, originally provided as *cis*-[Co(cyclam)Cl_2]Cl is retarded by chloride ions in less basic solution and follows a complex pH dependence. The retardation can be shown to obey a relationship of the form $k_{obsd} = 1/(a[Cl^-] + b)$, and, by plotting $1/k_{obsd}$ against $[Cl^-]$, a straight line of slope 1.73×10^4 sec M^{-1} and intercept 1.65×10^3 sec is obtained. This is consistent with a mechanism in which a species A^{n+} isomerizes by a slow first-order process but is also in equilibrium with an unreactive chloro adduct

$$A^{n+} \xrightarrow{k} B^{n+} \quad \text{(isomerization)} \qquad (3)$$

$$A^{n+} + Cl^- \overset{K}{\rightleftharpoons} ACl^{(n-1)+} \qquad (4)$$

which leads to the relationship

$$k_{obsd} = \frac{k}{1 + K[Cl^-]} \qquad (5)$$

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(5) H. Block and V. Gold, *J. Chem. Soc.*, 966 (1959).

(6) We thank a referee for correcting our algebra here.

(7) F. Basolo, J. W. Palmer, and R. G. Pearson, *J. Am. Chem. Soc.*, **82**, 1073 (1960).

(8) It was necessary to use a self-buffering system here since all of the kinetically noninterfering buffers absorbed in the region where measurements were made.

Since, under the experimental conditions used, no *cis*-dichloro complex is present, A must be identified with the pH-controlled equilibrium mixture of *cis*-Co(cyclam)$(H_2O)_2{}^{3+}$, *cis*-Co(cyclam)(OH)H_2O^{2+}, and *cis*-Co(cyclam)$(OH)_2{}^+$, and $ACl^{(n-1)+}$ is the *cis*-Co(cyclam)$(H_2O)Cl^{2+}$ cation. The absence of chloride retardation in neutral and basic solution indicates that there is no significant amount of the hydroxochloro complex at equilibrium. At 60.5° and $[H^+] = 0.01$ M: $k = 1/\text{intercept} = 6.1 \times 10^{-4}$ sec^{-1} and $K = \text{slope/intercept} = 10.5\ M^{-1}$.

In the absence of chloride, the dependence of k_{obsd} upon hydrogen ion concentration takes the form

$$k_{obsd} = \frac{c[H^+] + d}{[H^+]^2 + K_1(cis)[H^+] + K_1(cis)K_2(cis)} \tag{6}$$

and the curve drawn to the data in Figure 2 is the best fit, in which $c = 7.5 \times 10^{-8}\ M$ sec^{-1} and $d = 7.5 \times 10^{-18}\ M^2$ sec^{-1}. The pH dependence of the rate in the presence of chloride is also shown in Figure 2. At low pH the two curves are parallel but the retarding effect of chloride diminishes at pH >5 and disappears at pH $\geqslant 6.8$. In this region, the fraction of the complex containing coordinated chlorine is negligible.

In order to take account of the effect of pH on the distribution of the isomerizing substrate among the various aquo and hydroxo complexes, the general scheme

$$\begin{tikzcd}
\mathit{cis}\text{-Co(cyclam)(H}_2\text{O)}_2{}^{3+} \arrow[r, "R_1"] \arrow[d, shift right, "-H^+"'] & \mathit{trans}\text{-Co(cyclam)(H}_2\text{O)}_2{}^{3+} \arrow[d, shift right, "-H^+"'] \\
\mathit{cis}\text{-Co(cyclam)(OH)H}_2\text{O}^{2+} \arrow[r, "R_2"] \arrow[u, shift right, "+H^+\ K_1(cis)"'] \arrow[d, shift right, "-H^+"'] & \mathit{trans}\text{-Co(cyclam)(OH)H}_2\text{O}^{2+} \arrow[u, shift right, "+H^+\ K_1(trans)"'] \arrow[d, shift right, "-H^+"'] \\
\mathit{cis}\text{-Co(cyclam)(OH)}_2{}^{+} \arrow[r, "R_3"] \arrow[u, shift right, "+H^+\ K_2(cis)"'] & \mathit{trans}\text{-Co(cyclam)(OH)}_2{}^{+} \arrow[u, shift right, "+H^+\ K_2(trans)"']
\end{tikzcd}$$

can be written, where R represents the rate of reaction along the designated path. Two consequences of this scheme need to be considered depending upon the pH dependence of the actual conversion rates. In scheme I, the individual rates are of the form $R = k'[\text{complex}]$; *i.e.*, all of the pH dependence arises from the distribution of the substrate in the preequilibrium. Since the acid–base processes are fast compared with the *cis* to *trans* changes, the over-all conversion follows a first-order rate law at constant pH and the observed rate constant can be shown to obey the pH dependence

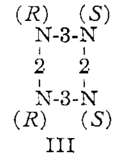
$$k_{obsd} = \frac{k_a[H^+] + k_bK_1(cis)[H^+] + k_cK_1(cis)K_2(cis)}{[H^+]^2 + K_1(cis)[H^+] + K_1(cis)K_2(cis)} \tag{7}$$

where k_a, k_b, and k_c are the first-order rate constants associated with the diaquo, hydroxoaquo, and dihydroxo species, respectively. In scheme II, the individual rates take the form $R = k''[\text{complex}][OH^-]$ and the hydrogen ion dependence of the observed first-order rate constant becomes

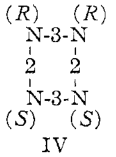
$$k_{obsd} = \frac{k_1K_w[H^+] + k_2K_wK_1(cis) + k_3K_wK_1(cis)K_2(cis)[H^+]^{-1}}{[H^+]^2 + K_1(cis)[H^+] + K_1(cis)K_2(cis)} \tag{8}$$

where k_1, k_2, and k_3 are the second-order rate constants for the base-catalyzed isomerization, and K_w is the ionic product of water. Equation 7 reduces to the observed expression (eq 6) if k_a (the rate constant for the isomerization of the diaquo complex) is negligibly small, and (8) reduces to (6) if the k_3-containing term is negligible compared to the other two terms in the numerator. Under these circumstances it is not possible to distinguish between schemes I and II from the kinetics alone and it is necessary to use extrakinetic information to identify the isomerizing species.

In order to elucidate this problem it is necessary to understand why these cyclic tetramine complexes are generally reluctant to undergo stereochemical change. In substitution reactions of octahedral complexes containing only unidentate, or unhindered bidentate ligands, the constraints imposed by these ligands on the steric course are either negligible or else confined to the need of the bidentate to occupy *cis* positions. With more complicated ligand systems it is necessary to take account of the constraints placed upon the chelate system by the configurational requirements of the donor atoms. This has been discussed in greatest detail in connection with the secondary nitrogen donors of garland[9-11] and cyclic[2] tetramine ligands. With the cyclic amine complexes the situation is simplified by the possibility of only one *cis* isomer but this is countered by the five possible nonenantiomeric forms of the ligand that have to be considered, as against two for the garland tetradentate. Until now we have only been able to detect one form of the *trans* (unfolded) and one form of the *cis* (folded) macrocycle, and, on the basis of the proton magnetic resonance of the diaquo complexes,[1] arguments based on ring strain,[2] and analogy with the known structure of the Ni(cyclam)Cl_2 analog,[12] the *trans* isomer has been assigned the *meso* form, either III or IV, and the *cis* isomer is thought to be the *RRRR* (*SSSS*) racemate, V. We



III



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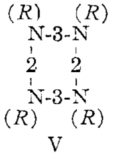

V

have, as yet, been unable to assign these configurations of the secondary nitrogens with the same certainty as has been done in the case of the open-chain quadridentates,[10,13] but the structures of the *cis*- and *trans*-dichloro chlorides are currently being studied by X-ray diffraction. The *R,S* designation is based on the sequence rules of Cahn, Ingold, and Prelog[14] and replaces the (+),(−) designation of the direction of the axial amino protons.[2] The Roman numerals representing the configurations have been retained. If this assignment of configuration is correct, then the ob-

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(9) B. Bosnich, R. D. Gillard, E. D. McKenzie, and G. A. Webb, *J. Chem. Soc., A*, 1331 (1966).

(10) A. M. Sargeson and G. H. Searle, *Inorg. Chem.*, **6**, 787 (1967).

(11) A. M. Sargeson and G. H. Searle, *ibid.*, **6**, 1032 (1967).

(12) B. Bosnich, R. Mason, P. J. Pauling, G. B. Robertson, and M. L. Tobe, *Chem. Commun.*, 97 (1965).

(13) H. C. Hamilton, Jr., and M. D. Alexander, *J. Am. Chem. Soc.*, **89**, 5065 (1967).

(14) R. S. Cahn, C. K. Ingold, and V. Prelog, *Angew. Chem. Intern. Ed. Engl.*, **5**, 385 (1966).

TABLE V

DERIVED RATE CONSTANTS FOR THE ISOMERIZATION, MUTAROTATION, OR PROTON EXCHANGE OF SOME TETRAMINE COBALT(III) COMPLEXES

	Scheme I		Scheme II		
	k_b, sec^{-1}	k_c, sec^{-1}	k_1, M^{-1} sec^{-1}	k_2 M^{-1} sec^{-1}	Temp, °C
cyclam (*cis* → *trans*)	6.0×10^{-3}	6.0×10^{-5}	7.8×10^{5}	60	25
trien [*trans*-(*SS*) → *cis*-(*SR*)]	10^{-1}–10^{a}	...	1.5×10^{10}	...	15
cyclam (*trans* proton exchange)	2×10^{-2}	$<2 \times 10^{-1}$	4×10^{9}	$<10^{5}$	21

[a] Calculated using an estimated pK_a of *trans*-(*SS*)-Co(trien)$(H_2O)_2^{3+}$ of 3–5.

served *cis* to *trans* isomerization ought to involve simultaneous inversion of the configuration of two of the nitrogens. The most likely way of inverting such a coordinated nitrogen is by way of proton exchange and the experiments reported in section 4 indicate quite clearly that the isomerization is accompanied by the exchange of two protons. It is also reasonable to believe that the kinetics of isomerization closely parallel those of proton exchange and the exchange kinetics of the protons of the *trans* complex which have been directly measured do indeed follow the same type of pH dependence as the isomerization of the *cis* complex.

Sargeson, *et al.*, have recently reported[15] a detailed study of the kinetics of the pH-dependent isomerization of *trans*-(*SS*)-Co(trien)$(H_2O)_2^{3+}$ (trien = 1,4,7,10-tetraazadecane) to the D-β-*cis*-(*SR*)-Co(trien)$(H_2O)_2^{3+}$ cation and the pH-independent isomerization of the *trans* complex to the D-β-*cis*-(*SS*)-Co(trien)$(H_2O)_2^{3+}$ isomer. The former reaction parallels very closely the isomerization reaction of the cyclam complexes whereas the latter is an isomerization of the type that is common in the nonstereorestrictive bis-ethylenediamine analogs. Over the narrow range of acid concentration examined ($0 < \text{pH} < 1.3$) the acid dependence was of the form $k_{\text{obsd}} = k + (k'/[H^+])$ and only the second term was relevant to the (*SS*) to (*SR*) change. The more complicated expressions, eq 7 and 8, will reduce to this simple inverse dependence if (a) the $[H^+]^2$ term dominates the denominator (*i.e.*, virtually all of the complex is in the form of the diaquo species) and (b) the second and third terms in the numerator are small compared to the first term (this is not unlikely at pH <2). In interpreting these kinetics, Sargeson has chosen the base-catalyzed mechanism for proton exchange, *i.e.*, scheme II. This is fully consistent with the known mechanisms of amine proton exchange in complexes where aquohydroxo equilibria do not interfere with the kinetics and where the rate-determining step is thought to be attack by free or ion-associated hydroxide[5,7,16,17] or any other suitable base[18] upon the amine proton. We would like to suggest that, in the isomerization processes of the cyclam and also of the trien complexes, that part of the proton exchange that leads to inversion of the secondary nitrogen and hence to isomerization is best represented by scheme I and involves the hydroxoaquo and dihydroxo complexes rather than a direct attack of hydroxide on the diaquo complex. This can be looked upon as an intramolecular proton transfer from the nitrogen to the "internal base" coordinated hydroxide. This conclusion is based on the following reasoning.

(1) The absolute magnitudes of the rate constants are more consistent with scheme I than with scheme II. The observed rate constants have been analyzed according to expressions 7 and 8 and the derived values for k_b, k_c, k_1, and k_2 are collected in Table V. First to be noted is the absence of a k_a term in the treatment according to scheme I. This is required by the mechanism since the diaquo complex does not contain coordinated hydroxide. Whereas k_1, calculated for *cis*-Co(cyclam)$(H_2O)_2^{3+}$, is of the right order of magnitude for a base-catalyzed proton exchange in a tripositive cation of this type,[7] k_2 is exceptionally small since the usual decrease in rate as a result of the reduction of charge is only a factor of 10–100.[7,19] The value of k_1, calculated from the data for the mutarotation of the *trans*-Co(trien)$(H_2O)_2^{3+}$ cation, 1.5×10^{-10} M^{-1} sec^{-1}, is some 10^2 times larger than any previously reported rate constant for a proton exchange in a cobalt(III)–amine complex and that for *trans*-Co(cyclam)$(H_2O)_2^{3+}$ is not much smaller. In addition, the reduction of rate constant by a factor $>10^4$ on going from k_1 to k_2 is far greater than would be expected from the reduction of charge. These difficulties do not arise if scheme I is adopted.

(2) Although only in the third case in Table V are we dealing with a direct measurement of proton-exchange rates, the other entries set a lower limit to their value. Where it has been possible to make a comparison, it appears that the rates of proton exchange and rates of inversion of these secondary nitrogen atoms in the aquo and hydroxoaquo complexes are of similar magnitude. This is quite different to the observations of Sargeson, *et al.*, on the behavior of complexes containing asymmetric secondary nitrogen atoms, where the rate of hydrogen exchange is faster by factors from 4000[16] to 100,000,[17,20] depending upon the nature of the substrate. None of the complexes thus examined contained an internal base which would allow the internal proton-transfer mechanism. We therefore suggest that the intramolecular mechanism presents the means whereby the otherwise stereochemically unfavored proton transfer with inversion of the secondary nitrogen can be facilitated.

The scheme whereby proton exchange, coupled with

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[15] D. A. Buckingham, D. A. Marzilli, and A. W. Sargeson, *Inorg. Chem.*, **6**, 1032 (1967).

[16] B. Halpern, A. M. Sargeson, and K. R. Turnbull, *J. Am. Chem. Soc.*, **88**, 4630 (1966).

[17] D. A. Buckingham, L. G. Marzilli, and A. M. Sargeson, *ibid.*, **89**, 825 (1967).

[18] C. K. Poon and M. L. Tobe, *Chem. Commun.*, 156 (1968).

[19] J. W. Palmer and F. Basolo, *J. Phys. Chem.*, **64**, 778 (1960).

[20] D. A. Buckingham, L. G. Marzilli, and A. M. Sargeson, *J. Am. Chem. Soc.*, **89**, 3428 (1967).

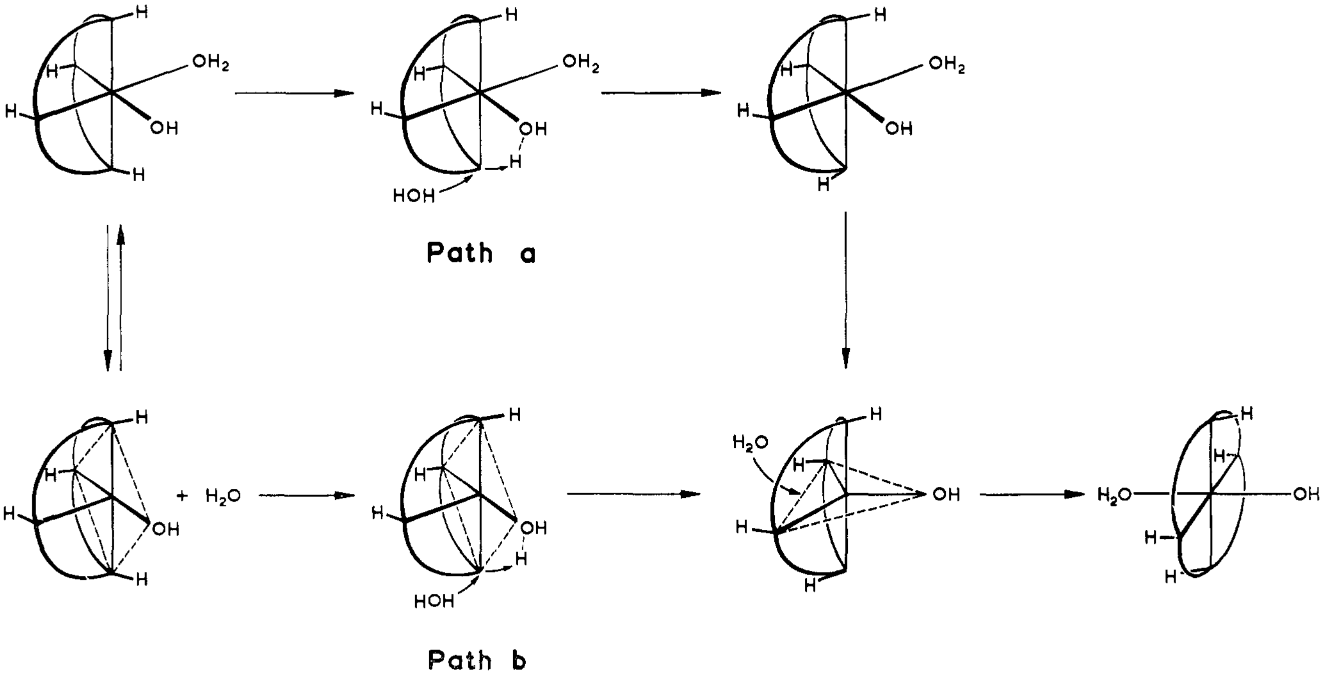

Figure 3.—Diagrammatic representation of the alternative modes of internal proton exchange resulting in *cis* to *trans* isomerization. It is presumed that the exchange and inversion at the second nitrogen follows rapidly without further stereochemical change.

water exchange, leads to a *cis* to *trans* change is shown in Figure 3. Although we do not know the rate of water exchange of *cis*-Co(cyclam)(OH)H_2O^{2+}, we can say that, if the mechanism of anation is the same as in other aquo complexes,[21] *i.e.*, essentially dissociative, then the rate of water exchange must be greater than the highest observed anation rate. The data for thiocyanate anation indicates that water exchange is very much faster than isomerization. Two alternative paths are presented, but the experimental evidence does not allow a choice between nitrogen inversion in the octahedral complex prior to dissociation and nitrogen inversion in the presumably tetragonal-pyramidal five-coordinate intermediate, which then has time to change to the trigonal-bipyramidal form before it picks up a water molecule. Sargeson[15] favors exchange in the five-coordinate intermediate, a process which would overcome the objection that inversion of a nitrogen in the octahedral substrate would lead to the formation of a more strained species; however, it is suggested that this exchange takes place as a result of interaction with an external hydroxide ion. In view of the vanishingly small concentrations of both of the species involved in this bimolecular process such a mechanism would require a rate constant far in excess even of that expected for an encounter process. The intramolecular transfer of a proton from nitrogen to oxygen within the five-coordinate intermediate would not suffer from this restriction.

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[21] F. Basolo and R. G. Pearson, "Mechanisms of Inorganic Reactions," 2nd ed, John Wiley & Sons, Inc., New York, N. Y., 1967, pp 193–207.