# Proton Exchange and Base-catalysed Hydrolysis of the Cations *trans*-Dichloro[(*RSSR*)-1,4,8,11-tetra-azacyclotetradecane]cobalt(III) and *cis*-Dichloro[*RRRR*(*SSSS*)-1,4,8,11-tetra-azacyclotetradecane]-cobalt(III) †

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The ratio of the rate constants for the solvolysis ($k_2$) and the reprotonation ($k_{-1}$) of the amido-conjugate base of *trans*-[Co{*RSSR*-[*N,N',N'',N'''*-$^2H_4$]cyclam}Cl$_2$]$^+$ (cyclam = 1,4,8,11-tetra-azacyclotetradecane) has been determined from an analysis of the dependence of the amount of deuterium exchange in the recovered unreacted complex upon the extent of base hydrolysis in aqueous buffer solution: $k_2/k_{-1} = 0.79 \pm 0.15$ at 0 °C. Values for the deprotonation rate constants have been estimated. The rate constant ($k_{OH}$) for the base hydrolysis of the $^1H_4$ species has been measured over a range of temperatures and the curvature of the Eyring plot confirmed. The rate of proton exchange in *cis*-[Co{*RRRR*(*SSSS*)cyclam}Cl$_2$]$^+$ is considerably faster than base hydrolysis and the rate constant was determined directly using the $^2H_4$-labelled species in $^1H_2O$ buffer. The value of the ratio $k_2/k_{-1}$ was estimated to be 0.041 at 0 °C. The previously reported low enthalpy of activation for the base hydrolysis is not therefore a criterion for rate-limiting deprotonation.

In our studies of the details of the base-catalysed substitution reactions of amine(aniono)cobalt(III) complexes we have found a number of systems where the rate constants ($k_2$) for solvolysis of the amido-conjugate base forms are of a comparable magnitude to, or even significantly greater than, the rate constants ($k_{-1}$) for the reprotonation of these forms.[1-4] We observed that, in the case of reactions of the dichloro(1,9-diamino-3,7-diazanonane)cobalt(III) cations, the ratio $k_2/k_{-1}$ was greater than 20 for the *trans*-(*RS*)[2] and the *trans*-[*RR*(*SS*)] [3] isomers (*R* and *S* refer to the chiralities of the co-ordinated secondary nitrogens), whereas for the β-*cis*-[*RR*(*SS*)] isomer this ratio reduced to $5 \times 10^{-3}$.[5] In order to try to understand the factors that control this ratio we have studied the reactions of the corresponding [Co(cyclam)Cl$_2$]$^+$ complexes (cyclam = 1,4,8,11-tetra-azacyclotetradecane) which have so far been obtained in the *trans*-(*R*-3-*S*-2-*S*-3-*R*-2) and *cis*- and *trans*-[*RRRR*(*SSSS*)] forms [6] (2 and 3 signify the number of carbon atoms linking the nitrogens whose chirality is represented). All three species are very sensitive to base-catalysed solvolysis (especially the *cis* isomer) and it was suggested that this too generated an amido-conjugate base whose rate constants for dissociation and reprotonation were of a similar magnitude.[6] Although the *trans*-[Co(*RSSR*-cyclam)Cl$_2$]$^+$ isomer was the first example of a cobalt(III) complex for which it was shown that $k_{-1} < k_2$, the study was only semi-quantitative.[1]

The activation energies for the base hydrolysis of all three complexes were of a similar magnitude (9—11 kcal mol$^{-1}$, that for the *cis* isomer being the smallest) and it was suggested at the time that this was a reasonable criterion for assigning a similar rate-determining step. The relatively low values for $\Delta H_{OH}^{\ddagger}$ were consistent with the situation where $k_2 \gg k_{-1}$ and the general expression for base hydrolysis, $k_{OH} = nk_1k_2/(k_{-1} + k_2)$ (for a single set of $n$ equivalent amine protons), reduces to $k_{OH} = nk_1$. The activation energy would then be similar to that associated with proton exchange.[4] In this paper we report the proton-transfer reactions of the *trans*-[Co(*RSSR*-cyclam)-Cl$_2$]$^+$ and *cis*-[Co{*RRRR*(*SSSS*)-cyclam}Cl$_2$]$^+$ isomers and evaluate the ratios $k_2/k_{-1}$.

## Experimental

*Reagents and Preparations.*—*trans*-Dichloro[(*RSSR*)-1,4,8,11-tetra-azacyclotetradecane]cobalt(III) chloride was prepared by the method of Bosnich *et al.*[7] (Found: C, 32.8; H, 6.50; N, 15.3. $C_{10}H_{24}Cl_3CoN_4$ requires C, 32.8; H, 6.55; N, 15.3%). *trans*-Dichloro{[$^2H_4$]-(*RSSR*)-1,4,8,11-tetra-azacyclotetradecane}cobalt(III) chloride was prepared from the $^1H$ complex by recrystallising it from $D_2O$ (99.8%) until the i.r. spectrum of a hexachlorobutadiene mull showed no peak due to ν(N–H) at 3 156 cm$^{-1}$. Three times was sufficient. A small portion was dissolved in 0.1 mol dm$^{-3}$ hydrochloric acid and converted into the water-insoluble perchlorate by adding dilute $HClO_4$. The absence of any amine-bound protons was confirmed by the $^1H$ n.m.r. spectrum of this sample in [$^2H_6$]-dimethyl sulphoxide, in which it is very soluble (Found: C, 32.4; Cl, 28.0; N, 15.2. $C_{10}H_{20}Cl_3CoD_4N_4$ requires C, 32.5; Cl, 28.8; N, 15.2%).

cis-*Dichloro*{[$^2H_4$]-[RRRR(SSSS)]-1,4,8,11-*tetra-azacyclotetradecane*}*cobalt*(III) *chloride*. The salt *cis*-[Co(cyclam)-(CO$_3$)]Cl, prepared by the method of Poon and Tobe,[8] was dissolved in $D_2O$ (99.8%) containing a small amount (0.1 g in 50 cm$^3$) of $Li_2CO_3$. The solution was allowed to stand at room temperature overnight and the water was then removed by freeze drying. The extent of the amine proton exchange could not be monitored directly because the recovered material was deliquescent and could not be mulled. It was therefore necessary to convert small portions into *cis*-[Co(cyclam)-Cl$_2$]ClO$_4$ by the method described below so as to monitor the extent of exchange by i.r. or n.m.r. spectroscopy. The process was repeated until the $^1H$ n.m.r. spectrum indicated complete exchange of the amine protons (usually three cycles were sufficient). A saturated solution of dried hydrogen chloride in dried methanol (the presence of water seems to catalyse the reverse exchange even in very strong acid solution) was prepared at 0 °C and the deuteriated carbonato-complex dissolved in it. Reaction was fairly rapid and *cis*-[Co{[$^2H_4$]-*RRRR*(*SSSS*)-cyclam}Cl$_2$]Cl soon separated as violet crystals which were filtered off, washed with methanol and diethyl ether, and dried (Found: C, 31.3; N, 14.9. $C_{10}H_{20}Cl_3CoD_4N_4$ requires C, 32.5; N, 15.1%).

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† *Non-S.I. unit employed:* cal = 4.184 J.

The absence of exchange in the conversion of the carbonato- to the dichloro-complex was confirmed by $^1H$ n.m.r. and i.r. spectroscopy. It was necessary to convert the complex into its perchlorate because the $\nu(N-H)$ peaks in the i.r. spectrum of the chloride are broadened by hydrogen bonding, and the solubility of the chloride in dimethyl sulphoxide, while adequate for measuring the $^1H$ n.m.r. spectrum of the normal complex, is insufficient for this salt to be used for the detection of residual amounts of $^1H$. The two sharp N–H stretching peaks at 3 130 and 3 220 $cm^{-1}$ are absent in the spectrum of the $^2H_4$ complex. The *perchlorates* of the normal and the deuteriated *cis*- and *trans*-$[Co(cyclam)Cl_2]^+$ cations were prepared by dissolving the chlorides in 0.1 mol $dm^{-3}$ hydrochloric acid at 0 °C and adding excess of perchloric acid (3 mol $dm^{-3}$) to the cooled and stirred solution. The *trans* isomer is completely insoluble under these conditions and separates as a pale green powder. The *cis* isomer is more soluble and the recovery is not quantitative. Whereas the *trans* isomer is solvolytically inert under these conditions, the *cis* isomer must be treated as quickly as possible to reduce the loss in yield due to the uncatalysed aquation. The crystals were filtered off, washed with ethanol and diethyl ether, and air dried.

**CAUTION:** Although we have never encountered any problems, perchlorate salts of metal–amine complexes have been known to explode and special care should be taken, especially during grinding and mulling and when heating.

*Buffer solutions.* (*a*) pH > 7. Nitric acid (0.3 mol $dm^{-3}$) was added to a solution of 2,4,6-trimethylpyridine (0.3 mol $dm^{-3}$) until the pH was within the required region and after final dilution the ionic strength was adjusted to 0.10 mol $dm^{-3}$ by adding sodium nitrate solution.

(*b*) pH = 5. Standard acetic acid–sodium acetate buffers were used, with added sodium nitrate to maintain $I = 0.10$ mol $dm^{-3}$. In all cases the pH of the buffer solution was measured accurately at the reaction temperature using a glass electrode, calomel reference electrode, and a Radiometer PHM 26 pH meter calibrated against potassium hydrogenphthalate and borax buffers at the same ionic strength and temperature.

*Kinetics.*—The reactions were followed spectrophotometrically using either a Pye-Unicam SP 1750 or a Perkin-Elmer 554 spectrophotometer. The cell housing was thermostatted by circulating water in the first instance and electrically (making use of the Peltier effect) in the second. The temperatures were measured by a platinum resistance thermometer placed in the cell housing. Solutions of dilute nitric acid or the appropriate buffer were brought to the required temperature and the reaction was started by adding a small quantity (0.10 $cm^3$) of a solution of the perchlorate of the complex in dimethyl sulphoxide or by adding a small amount of the solid chloride salt. The absorbance change at a suitable wavelength (chosen after preliminary multiple-scanning experiments) was followed as a function of time and the first-order rate constants were determined in the usual ways, *e.g.* from the slopes of plots of $\ln(A_t - A_\infty)$ against time when the subsequent stages were either too fast or too slow to interfere, or by Guggenheim's method when the changes overlapped.

*Proton-exchange Studies.*—The *trans*-$[Co(cyclam)Cl_2]^+$ isomer was studied by the method of Marangoni *et al.*[2] A weighed amount of the N-deuteriated chloride (0.1096 g) was dissolved in water (3 $cm^3$) and brought to the reaction temperature in a 10.00-$cm^3$ volumetric flask. The appropriate buffer solution, also thermostatted at the reaction temperature, was added to bring the volume up to 10.00 $cm^3$ and to start the reaction. The reaction mixture was kept in the thermostat for the appropriate time and the reaction was then stopped by pouring this solution into ice-cold perchloric acid (25 $cm^3$, 3 mol $dm^{-3}$). This mixture was set aside at 0 °C for 3 h in order to ensure complete precipitation of the perchlorate salt of the unreacted *trans*-dichloro-cation which was then filtered off through a previously weighed sintered-glass crucible, washed with a small amount of ice-cold 0.1 mol $dm^{-3}$ perchloric acid, then ethanol and finally diethyl ether, and dried gently to constant weight. The filtrate was treated with hydrochloric acid (4 $cm^3$, 12 mol $dm^{-3}$) and warmed on a steam-bath for 3 h. The solution was cooled and the precipitate filtered off from the colourless filtrate through a weighed sintered-glass filter and washed and dried to constant weight as above.

A weighed amount of the deuteriated *cis* chloride (0.10 g) was added to cold water (30 $cm^3$) at 0 °C and the mixture stirred vigorously until all the complex had dissolved. The buffer solution (50 $cm^3$), previously brought to 0 °C, was added and, after the appropriate reaction time at this temperature, perchloric acid (50 $cm^3$, 3 mol $dm^{-3}$) was added. After 2—3 min the unreacted dichloro-cation started to crystallise out as its perchlorate and the mixture was frozen in an acetone–solid $CO_2$ freezing mixture for 2—7 min. The frozen mixture was then allowed to thaw at room temperature and the perchlorate was filtered off, washed with ice-cold 0.3 mol $dm^{-3}$ perchloric acid then ice-cold water, and finally air dried.

Proton n.m.r. spectra were measured with a Varian HA200 F.T. NMR spectrometer. The complex perchlorate (0.015 g) was dissolved in $[^2H_6]$dimethyl sulphoxide (0.5 $cm^3$) and the spectrum recorded with $SiMe_4$ as reference. Infrared spectra of Nujol or hexachlorobutadiene mulls between NaCl windows were measured with a Perkin-Elmer 177 i.r. spectrometer.

## Results

*Proton Exchange in trans*-$[Co(cyclam)Cl_2]^+$.—The $^1H$ n.m.r. spectrum of a normal sample of *trans*-[Co(*RSSR*-cyclam)-$Cl_2]ClO_4$ in $[^2H_6]$dimethyl sulphoxide is characterised by a multiplet δ (1.6—2.2, 4 H) assigned to the middle methylene protons in the six-membered rings, a multiplet between δ 2.30 and 2.90 (16 H plus the dimethyl sulphoxide protons), and a broad singlet (δ 6.40, 4 H) assigned to the amine protons. The absence of the last peak in the spectrum of the N-deuteriated complex confirms this assignment. The extent of exchange was determined by comparing the area under this peak with the area under the peaks at δ 1.6—2.2.

The separation of the unreacted material from the reaction product takes advantage of the insolubility of *trans*-$[Co(cyclam)Cl_2]ClO_4$ in dilute perchloric acid. The reaction product, *trans*-$[Co(cyclam)(OH)Cl]^+$, solvolyses rapidly and with further exchange to *trans*-$[Co(cyclam)(OH)(H_2O)]^{2+}$ and the two species are instantly converted into the soluble chloroaquo- and diaquo-complexes on acidification. This also serves to stop any further proton exchange or base-catalysed hydrolysis and the uncatalysed aquation of the species is slow. On warming the filtrate with hydrochloric acid the aquo-complexes are reconverted into *trans*-$[Co(cyclam)Cl_2]^+$ which separates as its insoluble perchlorate on cooling. The recovery is quantitative and the fraction of reaction, $F_r$, was determined from the relationship $F_r = m_r/(m_r + m_u)$, where $m_u$ and $m_r$ are the masses of the recovered unreacted dichloro-perchlorate and the reconverted product. In the case of the study at 25 °C where subsequent exchange made valueless an analysis of the exchange in the product, no attempt was made to recover the product and $F_r$ was calculated from the mass of the recovered unreacted material and the value of $m_u + m_r$ estimated from the known mass of chloride salt used.

**Table 1.** Amine proton–deuterium exchange accompanying base hydrolysis of *trans*-[Co{[$^2H_4$]-*RSSR*-cyclam}$Cl_2$]$^+$ [a]

| Temp./°C | Time/s | $m_u$/g | $m_r$/g | ($m_u$ + $m_r$)/g | $F_r$ | $N_u$ |
|---|---|---|---|---|---|---|
| 0.0 [b] | 300 | 0.1168 | 0.0133 | 0.1301 | 0.091 | 0.096 |
| | 650 | 0.0924 | 0.0386 | 0.1310 | 0.280 | 0.466 |
| | 1 080 | 0.0897 | 0.0427 | 0.1314 | 0.300 | 0.422 |
| | 1 667 | 0.0802 | 0.0492 | 0.1296 | 0.376 | 0.500 |
| | 2 514 | 0.0698 | 0.0592 | 0.1290 | 0.457 | 0.518 |
| 25.0 [c] | 120 | 0.1171 | | | 0.089 | 0.000 |
| | 260 | 0.1061 | | | 0.175 | 0.055 |
| | 340 | 0.0981 | | | 0.238 | 0.093 |
| | 540 | 0.0883 | | | 0.313 | 0.180 |
| | 960 | 0.0709 | | | 0.540 | 0.590 |
| | 1 500 | 0.0575 | | | 0.550 | 0.860 |

[a] In water at $I$ = 0.10 mol dm$^{-3}$ and [complex] = 0.030 mol dm$^{-3}$. [b] 2,4,6-Trimethylpyridine–$HNO_3$ buffer (0.15 mol dm$^{-3}$), pH 7.800. [c] 2,6-Dimethylpyridine–$HNO_3$ buffer (0.15 mol dm$^{-3}$), pH 6.540.

In addition to the appearance of the peak at δ 6.40 as the reaction proceeded, small peaks developed at δ 6.15 and 6.85. These had the breadth of amine-proton signals but only constituted a few per cent of the total amine-proton signal. They did not correspond to traces of aquo-species left by inadequate washing and, while the peak at δ 6.15 is similar to that found for labile *trans*-[Co{*RRRR*(*SSSS*)-cyclam}$Cl_2$]$^+$, we have been unable to identify the other peak. The $^2$H n.m.r. spectrum of the fully N-deuteriated material has two N–D peaks, the minor one being only some 6% of the size of the main one and corresponding closely to the peak of the labile *trans*-dichloro-species. We believe that one of the developing signals in the recovered unreacted material is due to an impurity that is present in the N-deuteriated starting material, while the other may be forming in the act of base hydrolysis. By confining our attention to data within the first half-life of the reaction we have been able to ignore these side effects in the subsequent calculation. However, we eventually intend to carry out a detailed study of this observation. The data for the experiments at 0 and 25 °C are collected in Table 1.

*Proton Exchange in cis*-[Co{RRRR(SSSS)-cyclam}$Cl_2$]$^+$.—In contrast to the *trans*-*RSSR*-dichloro-species, the *cis* complex is solvolytically labile and cannot be recovered from solution once it has reacted; the aquo-species readily isomerise to the stable *trans* form, especially in basic solution.[9] It was therefore necessary to adopt the technique that proved successful in the previous study of the β-*cis*-dichloro(1,9-diamino-3,7-diazanonane)cobalt(III) isomer,[5] namely to exchange the protons in the stable carbonato-species and to convert this into the dichloro-complex under conditions where there was no proton exchange or isomerisation.

The $^1$H n.m.r. spectrum of *cis*-[Co{*RRRR*(*SSSS*)-cyclam}-$Cl_2$]$ClO_4$ in [$^2H_6$]dimethyl sulphoxide is characterised by multiplets at δ 1.55—2.20 (8 H), 2.25—2.96 (8 H), and 3.15—3.45 (4 H) assigned to the methylene protons, plus two broad peaks at δ 5.74 (2 H) and 7.10 (2 H) assigned to the amine protons. The last two peaks are absent in the spectrum of the N-deuterio-complex. Addition of small amounts of LiCl to the solution of the perchlorate causes the peak at δ 5.74 to shift downfield until it passes the other peak, which remains unaffected. This phenomenon has been shown to be due to ion association [10] and it is assumed that the shifted peak can be assigned to the protons on nitrogens *trans* to co-ordinated chlorine, since the associating chloride anion would be expected to go as far from the anionic ligands as possible.

Because of the high solvolytic lability of the *cis*-dichloro-complex it was not possible to study the reaction under conditions where the rate of exchange is large compared to that of the background solvolysis. Fortunately, the rate of exchange proved to be much faster than that of base hydrolysis and the analysis used for the *trans* isomer was unnecessary. The rate constant for proton exchange was determined from the way in which the fraction of exchange in the recovered unreacted complex changed with time. The fact that this complex was being consumed in a parallel reaction that did not involve deprotonation did not interfere and $k_1$ was obtained from the relationship $\ln(1 - F_{ex}) = k_1t +$ constant. It was, however, necessary to have an accurate knowledge of the reaction time, $t$, and the pH of the reaction mixture and to work in a buffer of sufficient capacity in order to ensure that the pH remained constant.

**Table 2.** Amine proton–deuterium exchange * in *cis*-[Co{[$^2H_4$]-*RRRR*(*SSSS*)-cyclam}$Cl_2$]$^+$

| Reaction time/s | $N_u$ | |
|---|---|---|
| | N–H *trans* to N | N–H *trans* to Cl |
| 360 | 0.117 | 0.677 |
| 540 | 0.130 | 0.849 |
| 720 | 0.094 | 1.021 |
| 900 | 0.105 | 1.160 |
| 1 200 | 0.130 | 1.380 |

$k_{ex} = (9.05 \pm 0.49) \times 10^{-4}$ s$^{-1}$

* At 0 °C, pH = 5.18 ($CH_3CO_2H$ + $CH_3CO_2Na$, 0.10 mol dm$^{-3}$), [complex] = 0.0034 mol dm$^{-3}$, and $I$ = 0.10 mol dm$^{-3}$.

The $^1$H n.m.r. spectrum of the recovered unreacted complex showed that exchange takes place exclusively at the nitrogens *trans* to Cl (δ 5.74). There is a small signal at δ 7.10 corresponding to 0.1 proton which remains constant throughout the run and is probably due to incomplete exchange in the starting complex. There is no further exchange in these protons even at a higher pH when the base hydrolysis is the major solvolytic pathway for consumption of the dichloro-species. The data are collected in Table 2.

*Temperature and Isotope Effects on the Rates of Acid and Base Hydrolysis*.—We have shown previously [6] that there was an indication of a departure from linearity of the plot of $\ln(k_{OH}/T)$ against $T^{-1}$ for the base hydrolysis of *trans*-[Co(*RSSR*-cyclam)$Cl_2$]$^+$ but we were unable, because of the lack of suitable equipment, to follow the reaction at low enough temperatures to confirm this. This has now been remedied and the data for the reaction, over the temperature range 0—25.4 °C, are given in Table 3 and plotted in Figure 1.

The isotope effects for the base hydrolysis of the *trans*-[Co(*RSSR*-cyclam)$Cl_2$]$^+$ cation were readily determined by

**Table 3.** First-order and derived second-order [a] rate constants for the base-catalysed hydrolysis of *trans*-[Co(*RSSR*-cyclam)Cl$_2$]Cl [b]

| Temp./°C | pH | $10^{14}K_w$/dm$^6$ mol$^{-2}$ | $10^7$[OH$^-$]/mol dm$^{-3}$ | $10^3k_{obs.}$/s$^{-1}$ | $10^{-3}k_{OH}$/dm$^3$ mol$^{-1}$ s$^{-1}$ |
|---|---|---|---|---|---|
| 0.4 | 8.58 | 0.185 | 7.06 | 2.9 | 4.1 |
| 5.4 | 8.50 | 0.302 | 9.56 | 6.2 | 6.5 |
| 10.4 | 8.32 | 0.478 | 9.99 | 12.2 | 12.2 |
| 15.4 | 8.21 | 0.740 | 12.0 | 25.0 | 20.8 |
| 20.4 | 8.13 | 1.114 | 15.0 | 45 | 30 |
| 25.4 | 8.01 | 1.649 | 16.9 | 70 | 41 |

[a] $k_{OH} = k_{obs.}/[OH^-]$ (correction for background solvolysis is negligible). [b] In aqueous 2,4,6-trimethylpyridine–HNO$_3$ buffers; $I = 0.1$ mol dm$^{-3}$.

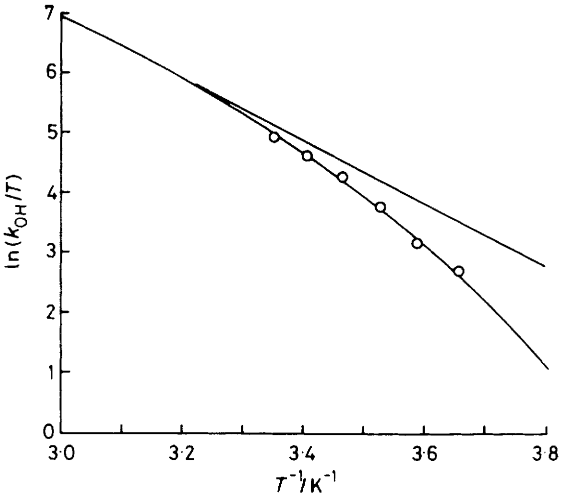

**Figure 1.** Plot of ln($k_{OH}/T$) against $T^{-1}$ for the base hydrolysis of *trans*-[Co(*RSSR*-cyclam)Cl$_2$]$^+$. The curve is calculated for $T_\alpha$ = 2.5 °C, $\Delta\Delta H^\ddagger$ = 15.0 kcal mol$^{-1}$, $\Delta H_1^\ddagger$ = 10.7 kcal mol$^{-1}$, and $k_1^\alpha$ = 2.5 × 10$^{-3}$ dm$^3$ mol$^{-1}$ s$^{-1}$ (see text for definitions)

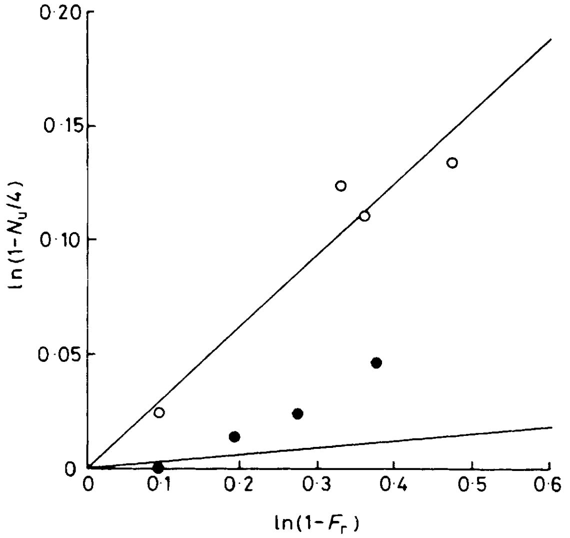

**Figure 2.** Plot of ln(1 − $N_u$/4) against ln(1 − $F_r$) at 0 (○) and 25 °C (●). The line for the 25 °C data is calculated for a ratio of $k_2/k_{-1}$ = 7.9 (see text)

comparing the first-order rate constants for the solvolysis of the normal (undeuteriated) and $^2H_4$ complexes at a temperature where $k_2$ is sufficiently large compared to $k_{-1}$ for the results to be meaningful and not complicated by parallel proton exchange. Both complexes were examined under the same conditions (temperature and pH) in aqueous solution of high enough pH for the reaction to go exclusively by way of the base-catalysed pathway. The good linearity of the plot of ln($A_t - A_\infty$) against time for the $^2H_4$ isomer and the observation of a significant isotope effect was added proof that there was no serious back exchange in the unreacted complex. A similar study was made of the *cis*-[Co{*RRRR*(*SSSS*)-cyclam}-Cl$_2$]$^+$ cation but because of the fact that $k_{-1} \gg k_2$ it was not possible to determine the isotope effect associated with base hydrolysis. However, a significant isotope effect was observed in the uncatalysed reaction.

## Discussion

It has been shown that, if a complex with $n$ equivalent exchanging protons forms a conjugate base that can either regain a proton from water (rate constant $k_{-1}$) or undergo further reaction (rate constant $k_2$), the number of protons that have exchanged in the recovered unreacted complex, $N_u$, is related to the fraction of reaction that has occurred, $F_r$, by the expression $N_u = n[1 - (1 - F_r)^{k_{-1}/nk_2}]$.[2] This expression, which neglects to take account of the primary isotope effect in the system, is most useful when $k_{-1}$ and $k_2$ are of similar magnitudes. When $k_{-1} \gg k_2$, $N_u$ will approach $n$ while $F_r$ is still very small and it is more convenient to determine $k_1$ (the rate constant for proton exchange) independently from the classical first-order treatment of the proton-exchange data, $k_1 = k_{obs.}/[OH^-]$, where $k_{obs.}$ is the negative slope of the plot of ln($n - N_u$) against time, assuming no isotopic dilution. The ratio $k_2/k_{-1}$ is then given by $k_{OH}/(nk_1 - k_{OH})$.[5]

In the *trans*-[Co(*RSSR*-cyclam)Cl$_2$]$^+$ complex there are four equivalent amine protons, *i.e.* $n = 4$, but the fact that there is an isotope effect ($k_1^H/k_1^D = 1.8$, see below) means that the above treatment overestimates the amount of exchange in the unreacted material for a particular $k_2/k_{-1}$ ratio and that this error becomes more serious as $F_r$ increases. However, this error is small compared to that introduced by re-entry of chloride into the aquo-complexes during the time required for the unreacted perchlorate to precipitate, the position of solvolytic equilibrium lying well towards the dichloro-species under the experimental conditions.[7] This serves to underestimate $F_r$ and overestimate $N_u$ (since extensive exchange occurs in the hydroxoaquo-complex formed after the act of base hydrolysis). An attempt was made to determine the ratio $k_2/k_{-1}$ by plotting ln($1 - N_u/n$) against ln($1 - F_r$) which should give a straight line of slope = $k_{-1}/nk_2$ that passes through the origin. The data obtained at 0 °C obey this relationship reasonably well, giving $k_2/k_{-1} = 0.79 \pm 0.15$, but the data obtained at 25 °C give a curved plot, the value of $k_2/k_{-1}$ apparently decreasing as the reaction progresses (Figure 2). The absence of any detectable exchange in the product recovered after 10% reaction suggests a considerable increase in the ratio $k_2/k_{-1}$ on increasing the temperature to 25 °C. (Indeed, all the data points are consistent with an increase in this ratio.) It must be concluded then that $\Delta H_2^{\ddagger}$ is greater than $\Delta H_{-1}^{\ddagger}$ and, as the temperature is raised above 25 °C, the system approaches the limit where $k_2 \gg k_{-1}$ and $k_{OH}$ tends to $4k_1$ (*i.e.* deprotonation becomes rate limiting). As $T^{-1}$ decreases the observed enthalpy of activation ($-R \times$ slope of the Eyring plot) approaches a limit that corresponds to $\Delta H_1^{\ddagger}$. At the lowest temperatures the ratio $k_2/k_{-1}$ decreases and, were it possible to cover a wide enough range of temperature, the other limit $k_{OH} = nk_1k_2/k_{-1}$ would be approached as $k_{-1} \gg k_2$. The plot of $\ln(k_{OH}/T)$ against $T^{-1}$ would again become linear, but now with slope $= -R(\Delta H_1^{\ddagger} + \Delta H_2^{\ddagger} - \Delta H_{-1}^{\ddagger})$ which must be steeper than that at smaller $T^{-1}$. It should be pointed out that, in this type of change in the rate-limiting step, the negative slope of the Eyring plot must always change from the small to the larger limiting value. If $\Delta H_2^{\ddagger} > \Delta H_{-1}^{\ddagger}$ then the $\Delta H_1^{\ddagger}$ slope will be approached as $1/T$ decreases but if $\Delta H_{-1}^{\ddagger}$ were the greater the $\Delta H_1^{\ddagger}$ limit would be reached at larger values of $T^{-1}$. It is for this reason that we need to know whether the ratio $k_2/k_{-1}$ increases or decreases on raising the temperature. Using the value of $\Delta H_1^{\ddagger}$ obtained from measurements at higher temperatures (10.7 kcal mol$^{-1}$),[6] the best fit to the experimental curve for $\ln(k_{OH}/T)$ against $T^{-1}$ was obtained using the expression $k_{OH} = 4k_1k_2/(k_{-1} + k_2)$ with variable parameters $T_\alpha$, the temperature at which $k_2 = k_{-1}$, $\Delta H_2^{\ddagger} - \Delta H_{-1}^{\ddagger}$ ($= \Delta\Delta H^{\ddagger}$), and $k_1$ at $T_\alpha$ ($= k_1^\alpha$). {It can readily be shown that $k_2/k_{-1} = X = \exp[-\Delta\Delta H^{\ddagger}(T^{-1} - T_\alpha^{-1})/R]$; $k_1 = k_1^\alpha(T/T_\alpha)\cdot\exp[-\Delta H_1^{\ddagger}(T^{-1} - T_\alpha^{-1})/R]$; and $k_{OH} = 4k_1X/(1 + X)$.} The best fit, that also agrees well with the experimentally determined value for $k_2/k_{-1}$ at 0 °C, requires that $T_\alpha = 2.5$ °C, $k_1^\alpha = 2.5 \times 10^3$ dm$^3$ mol$^{-1}$, and $\Delta\Delta H^{\ddagger} = 15$ kcal mol$^{-1}$. The curve is plotted in Figure 1. The value for $k_2/k_{-1}$ at 25 °C, calculated from these data, is 7.9; the line corresponding to this value is plotted in Figure 2.

The direct study of proton exchange in the *cis* complex indicates that exchange is considerably faster than base hydrolysis. The rate constant for the exchange of D by H is $3.2 \times 10^6$ dm$^3$ mol$^{-1}$ s$^{-1}$ at 0 °C, and, assuming that the isotope effect is the same as in the *trans* isomer ($k_H/k_D = 1.8$), this would suggest that $k_1$ for the $^1H_4$ system is $5.8 \times 10^6$ dm$^3$ mol$^{-1}$ s$^{-1}$. Combining this with $k_{OH} = 4.54 \times 10^5$ dm$^3$ mol$^{-1}$ s$^{-1}$, the expression $k_2/k_{-1} = k_{OH}/(2k_1 - k_{OH})$ (in this case there are two equivalent protons) gives $k_2/k_{-1} = 0.041$. While this is not as small as the value ($5 \times 10^{-3}$) found[5] for β-*cis*-dichloro[*RR*(*SS*)-1,9-diamino-3,7-diazanonane]cobalt(III), it is small enough for the proton-transfer process to be treated as a pre-equilibrium, *i.e.* $k_{OH} \approx 2k_1k_2/k_{-1}$. The low enthalpy of activation for the base hydrolysis ($\Delta H_{OH}^{\ddagger} = 9.3$ kcal mol$^{-1}$)[6] is therefore not a good criterion for rate-limiting deprotonation. Unfortunately, because of the high overall lability of the complex, it was not possible to determine the ratio $k_2/k_{-1}$ at a high enough temperature to ascertain, even semi-quantitatively, the magnitude (or even sign) of $\Delta H_2^{\ddagger} - \Delta H_{-1}^{\ddagger}$, and so it is not possible to say whether $\Delta H_1^{\ddagger}$ is greater or less than $\Delta H_{OH}^{\ddagger}$. A study of the way in which these enthalpies of activation, especially $\Delta H_1^{\ddagger}$ and $\Delta H_{-1}^{\ddagger}$, vary from substrate to substrate is called for but it must await a considerable improvement in the precision of the proton-exchange experiments.

The primary isotope effects of base hydrolysis, which can be measured directly when $k_2$ is sufficiently greater than $k_{-1}$, indicate that $k_{OH}^{H}/k_{OH}^{D} = 1.8$, where these rate constants are values for $k_{OH}$ determined for the $^1H_4$ and $^2H_4$ (amine hydrogen) forms of *trans*-[Co(*RSSR*-cyclam)Cl$_2$]$^+$ in buffered aqueous solutions at pH = 7.40 and $I = 0.1$ mol dm$^{-3}$ at 25 °C ($10^2k_{obs.} = 1.73$ and 0.94 s$^{-1}$ for the $^1H_4$ and $^2H_4$ complexes respectively. No corrections are needed for the uncatalysed solvolysis). This value does not differ greatly from that found for the *RS* and *RR*(*SS*) isomers of the corresponding 1,9-diamino-3,7-diazanonane cation[4] and the same explanation as to why it is so low must apply here also. It is worth noting that it has been suggested that proton transfer from co-ordinated nitrogen to hydroxide takes place within pre-formed ion pairs.[11,12]

A comparison of the overall first-order rate constants, $k_{obs.}$, for solvolysis of the corresponding $^1H_4$ and $^2H_4$ forms of the *cis*-[Co{*RRRR*(*SSSS*)-cyclam}Cl$_2$]$^+$ cation indicates no significant isotope effect at pH 5.98, 20.4 °C where 67% of the reaction goes by the base-catalysed pathway ($10^2k_{obs.} = 2.36$ and 2.26 s$^{-1}$ for the $^1H_4$ and $^2H_4$ complexes respectively). This is expected since the $^2H_4$ complex will have exchanged the $^2H$ on the nitrogens *trans* to Cl long before there has been any significant base hydrolysis. It is these nitrogens that provide the labilising amido-group. A primary isotope effect is observed, however, in the uncatalysed aquation at pH = 2.0 (where 99.98% of the solvolysis is uncatalysed) at 20 °C, the ratio of $k_{aq}$ values for the $^1H_4$ and $^2H_4$ dichloro-species being 1.26 ($10^3k_{obs.} = 7.96$ and 6.32 s$^{-1}$ for the $^1H_4$ and $^2H_4$ complexes respectively). Primary isotope effects of this magnitude have been observed before[13,14] and ascribed to the assistance to solvolysis provided by solvent water which can be hydrogen bonded both to the leaving chloride and a proton on an amine group *cis* to it. The *RRRR*(*SSSS*) form of the *cis*-[Co(cyclam)Cl$_2$]$^+$ complex provides, in principle, an ideal system to test this hypothesis. Only the two hydrogens on the mutually *trans* nitrogens point in the direction of the chlorides; the other two point towards each other on the other side of the complex. Furthermore, it should be possible to make use of the big differences in the exchange rates of the two types of hydrogen and study their isotope effects separately. Preliminary experiments with some of the partially exchanged perchlorates obtained as part of the proton-exchange studies suggest that the isotope effect on replacing the protons on the nitrogens *trans* to chlorine (*i.e.* those remote from the leaving group) is much more marked than that found when the protons *cis* to the leaving group are replaced by deuterons.

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