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The Hydrolysis Products of *cis*-Diamminedichloroplatinum(II). I. The Kinetics of Formation and Anation of the *cis*-Diammine(aqua)chloroplatinum(II) Cation in Acidic Aqueous Solution

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Abstract

The rate of loss of the first chloro ligand (k_1) from *cis*-$PtCl_2(NH_3)_2$, to give an equilibrium *cis*-$PtCl_2(NH_3)_2$, *cis*-$PtCl(NH_3)_2(OH_2)^+$ and Cl^- mixture, has been measured spectrophotometrically in 0.1 M $HClO_4$, 1.0 M $HClO_4$ and 0.1 M $HClO_4$ plus 0.9 M $NaClO_4$ over a 22 °C temperature range. The absorbance versus time data were analysed in terms of first-order kinetics and the effect of $[H^+]$ and ionic strength (μ) in the above range, is small. At 25 °C ($\mu = 1.0$ M, $HClO_4$) kinetic parameters are $k_1 = 6.32 \times 10^{-5}$ s^{-1}, $E_a = 84.7 \pm 1.9$ kJ mol^{-1}, $\Delta S^{\#} = -49.4 \pm 3$ J K^{-1} mol^{-1}. Removal of the released Cl^- from the equilibrium solution (0.1 M $HClO_4$) by anion exchange chromatography with the resin in the ClO_4^- form gives a solution containing about 90% *cis*-$PtCl(NH_3)_2(OH_2)^+$. Addition of known amounts of Cl^- (as NaCl in $HClO_4$) to this solution allows a spectrophotometric measurement of the rate of the anation reaction (k_{-1}) to give a new equilibrium solution. At 25 °C ($\mu = 1.0$ M; NaCl, $HClO_4$), $k_{-1} = 6.26 \times 10^{-3}$ M^{-1} s^{-1}, $E_a = 77.2 \pm 1.5$ kJ mol^{-1} and $\Delta S^{\#} = -36.3 \pm 3$ J K^{-1} mol^{-1}. A knowledge of the forward and reverse rate constants allows calculation of the equilibrium constant (K_1) and from the variation of K_1 with temperature, ΔH° can be estimated. At 25 °C ($\mu = 1.0$ M) $K_1 = 1.01 \times 10^{-2}$ and ΔH° for the endothermic forward reaction is +7.5 kJ mol^{-1}.

Introduction

cis-$PtCl_2(NH_3)_2$ (Peyrone's Salt, *cis*-Platin or *cis*-DDP) is an important coordination compound, as it is used extensively in anti-tumor cancer therapy [1]. In water, the neutral complex releases chloride ion [reaction (1)] to give, eventually, an equilibrium system, and it is the hydrolysis products that are believed to be the active anti-tumor agents [2a]. The rate of the hydrolysis in water has been measured using conductivity [3–6], spectrophotometry [7–10], HPLC [11–12], Cl^- ion titration [13, 14], Cl^- ion specific electrode [15b], $^{36}Cl^-$ ion exchange [16, 17], or H^+ ion titration [16–18]. The latter technique can be used as, during the course of the reaction, the pH decreases [6] due to reaction (2).

$$\textit{cis}\text{-}PtCl_2(NH_3)_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \textit{cis}\text{-}PtCl(NH_3)_2(OH_2)^+ + Cl^- \qquad (1)$$

$$\textit{cis}\text{-}PtCl(NH_3)_2(OH_2)^+ \rightleftharpoons \textit{cis}\text{-}PtCl(OH)(NH_3)_2 + H^+ \qquad (2)$$

Use of acidic media would prevent the formation of any hydroxo species [by reverse of (2)] but these conditions have only been used when the reaction was followed by Cl^- ion release titration [13, 14] and, unfortunately, HNO_3 was the acid of choice. Nitrate ion is known to interfere in other hydrolysis reactions [19] and its innocence in the present system has yet to be proven. A survey of the literature shows that the rate constants obtained in the presence of HNO_3 [13, 14, 20] are significantly greater than those obtained in water alone or in water/$NaNO_3$ media [15–17] (Table 1).

In view of those uncertainties, we have felt it worthwhile to reinvestigate the kinetics of the first hydrolysis step of *cis*-$PtCl_2(NH_3)_2$ in $HClO_4$ media using the change (decrease) in absorbance at 304 nm (where *cis*-$PtCl_2(NH_3)_2$ has its maxima [16, 20–23]) to monitor the reaction. Our values for k_1 and K_1 ($=k_1/k_{-1}$) are sensibly different from those obtained in water (Tables 2 and 3) [5, 13, 16, 17] but the activation parameters associated with k_1 (Table 2) ($\Delta H^{\#}$ and $\Delta S^{\#}$) are quite similar to the aqueous data [5, 6, 9, 13, 14, 17].

We have also obtained *cis*-$PtCl(NH_3)_2(OH_2)^+$ in 0.1 M $HClO_4$ solution, essentially free from Cl^- ion using anion exchange techniques. Addition of controlled amounts of Cl^- ion allows the rate of

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TABLE 1. Summary of rate constants (k_1) previously obtained for the first hydrolysis step of *cis*-$PtCl_2(NH_3)_2$[a]

Temperature (℃) [K]	$10^5 \times k_1$ (s^{-1})
0.0 [273.2]	0.095^{b}
23.0 [275.5]	2.38^{c}
25.0 [298.2]	$2.5^{d}, 2.6^{e}, 2.3^{f}, 2.8^{b}, 2.35^{q}, 2.5^{h}, 2.47^{i}, 2.85^{j}$ (2.58 ± 0.2 mean) $3.67^{k,l}$ $\underline{3.8}^{m,n}, \underline{3.16}^{m,o}$
28.0 [301.2]	4.57^{j}
30.0 [303.2]	$6.63^{j}, 5.08^{b}, 3.5^{p}$
34.0 [307.2]	7.16^{j}
35.0 [308.2]	$7.58^{j}, 7.6^{d}$ $\underline{10.4}^{m,o}$
37.0 [310.2]	$11.7^{i}, 11.0^{e}, 11.6^{r}, 4.94^{q}, 11.0^{u}$
40.0 [313.2]	$16.5^{j}, 18.5^{s}, 21.2^{s}, 15.8^{s}$ $\underline{19.6}^{m,o}$
45.0 [318.2]	$\underline{33.0}^{m,o}$
45.3 [318.5]	$\underline{33.0}^{m,t}$
50.0 [323.2]	$36^{e}, 35^{h}$

[a] In H_2O (pH = 4–7) with and without added salts or buffers. [b] Ref. 5. [c] Ref. 15a. [d] Ref. 17. [e] Ref. 6. [f] Ref. 16. [g] Ref. 7. [h] Ref. 18. [i] Ref. 12a. [j] Ref. 9. [k] Ambient temperature. [l] Ref. 12b. [m] In 0.01 M HNO_3 (data are underlined). [n] Ref. 13. [o] Ref. 14. [p] Ref. 11. [q] Ref. 8. [r] Ref. 4b. [s] Ref. 10. [t] Ref. 20. [u] Ref. 15b.

anation (k_{-1}) to be measured spectrophotometrically, and a knowledge of k_1 and k_{-1} under the same ionic strength and acidity conditions (μ = 1.0 M) allows the equilibrium constant (K_1) associated with eqn. (1) to be calculated.

Experimental

cis-$PtCl_2(NH_3)_2$ was purchased from Aldrich or Sigma and used without further purification as the visible absorption spectral parameters in greater than 1 M HCl corresponded to those reported in the literature [16, 20–23].

Solutions of the appropriate electrolyte (0.1 M $HClO_4$, 1.0 M $HClO_4$ or 0.1 M $HClO_4$ plus 0.9 M $NaClO_4$) were allowed to reach thermal equilibrium in a 1.00 cm spectrophotometer cell and small samples of *cis*-$PtCl_2(NH_3)_2$ were added. Solubility was generally rapid and final concentrations of $(1-2) \times 10^{-3}$ M gave an initial absorbance reading of 0.2–0.4. Absorbance versus time data were recorded at 304.0, 260.0 and 236.0 nm at appropriately selected time intervals. Reactions were monitored for 6–8 half-lives and constant 'infinity' data, with the change in absorbance of about 0.15 units, were usually obtained.

The absorbance versus time data were analysed in terms of a first-order rate law using more than 15 point-by-point calculations for each wavelength and the data were then averaged to give the mean k_1 ± the standard deviation reported in Table 4. Values of k_1 were constant within experimental error over more than four half-lives and wavelength independent.

Solutions of *cis*-$PtCl(NH_3)_2(OH_2)^+$ in 0.1 M $HClO_4$, essentially free from ionic Cl^-, were prepared by allowing solutions of *cis*-$PtCl_2(NH_3)_2$ (50 mg in 50 ml of 0.1 M $HClO_4$) to aquate for six half-lives (either overnight at room temperature or 2 h at 40 ℃ and then several hours at room temperature). Samples of this equilibrium solution (10 ml) were allowed to flow slowly (0.5 ml/min) through a short (~4.0 × 0.5 cm) column of ion exchange resin in the ClO_4^- form, that had been prewashed with 0.1 M $HClO_4$, at room temperature. The first 4 ml of effluent were discarded and a total of about 8 ml was collected, the last portions by addition of a small volume of 0.1 M $HClO_4$ to the column once the original sample had passed through. Preliminary experiments using ~0.002 M HCl in 0.1 M $HClO_4$ showed that this technique removed more than 95% of the ionic chloride ion present.

TABLE 2. Summary of kinetic parameters obtained for the first hydrolysis step of *cis*-$PtCl_2(NH_3)_2$ at 25.0 ℃

Solvent	$10^5 \times k_1$ (s^{-1})	$\Delta H^{\#}$ (kJ mol^{-1})	$\Delta S^{\#}$ (J K^{-1} mol^{-1})	$\Delta V^{\#}$ (cm^3 mol^{-1})	Reference
H_2O	2.8	83	−58		9
H_2O	2.8	90	−25		5
H_2O	2.6	81.5	−58		6
H_2O	2.5	82.3	−59		17
0.001 M HNO_3				−9.5 ± 1.2[a]	20
0.01 M HNO_3	3.2	91	−25		14
0.1 M $HClO_4$	7.56	73.7 ± 3	−76.5 ± 5		this work
0.1 M $HClO_4$ + 0.9 M $NaClO_4$	8.51	76.2 ± 3	−67.3 ± 6		this work
1.0 M $HClO_4$	6.32	82.3 ± 1.9	−49.4 ± 4		this work

[a] At 45.3 ℃.

TABLE 3. Summary of data for the equilibrium constants (K_1) associated with the first hydrolysis step of *cis*-$PtCl_2(NH_3)_2$ (eqn. (1)) in water

Added electrolyte	T (°C)	$10^5 \times k_1$ (s^{-1})	$10^3 \times k_{-1}$ (M^{-1} s^{-1})	$10^3 \times K_1$	Reference
None	0	0.095	0.23	4.1	5
	25	2.8	7.3	3.7	5
	30	5.08	13.5	3.8	5
0.2 M KNO_3	25	2.58	6.4	4.05	13
0.318 M KNO_3	25	2.58	7.1	3.63	16
	35	7.59	17.3	4.37	16
0.318 M Na_2SO_4	25	2.5	7.6	3.3	17
	35	7.6	19.5	3.9	17
μ = 0.3 M	50	39	120	3.3	7

TABLE 4. Spectrophotometrically determined first-order rate constants (k_1) for the first step in the acid hydrolysis of *cis*-$PtCl_2(NH_3)_2$[a]

0.1 M $HClO_4$ $10^4 \times k_1$ (s^{-1})		1.0 M $HClO_4$ $10^4 \times k_1$ (s^{-1})		0.1 M $HClO_4$ + 0.9 M $NaClO_4$ $10^4 \times k_1$ (s^{-1})	
obs. (T (°C))	calc.[b]	obs. (T (°C))	calc.[b]	obs. (T (°C))	calc.[b]
1.19 ± 0.15 (29.9)	1.24	1.25 ± 0.08 (30.1)	1.12	1.74 ± 0.29 (30.5)	1.51
1.82 ± 0.09 (34.1)	1.88	1.64 ± 0.06 (33.9)	1.70	2.03 ± 0.19 (34.8)	2.34
2.20 ± 0.67 (34.9)	2.03	1.74 ± 0.15 (35.0)	1.91		
2.47 ± 0.04 (36.7)	2.41	2.29 ± 0.21 (37.2)	2.41	2.74 ± 0.12 (36.9)	2.87
3.21 ± 0.20 (39.9)	3.27	3.33 ± 0.90 (40.1)	3.28	3.38 ± 0.27 (40.1)	3.93
4.43 ± 0.04 (43.0)	4.35	4.48 ± 0.75 (42.9)	4.37	4.60 ± 0.11 (42.9)	5.14
5.21 ± 0.30 (44.9)	5.17	5.47 ± 0.26 (44.7)	5.25	6.45 ± 0.17 (45.0)	6.26
9.54 ± 0.63 (50.1)	8.22	8.81 ± 0.09 (49.8)	8.71	11.2 ± 0.37 (50.2)	10.1
11.2 ± 0.79 (52.5)	10.5	12.0 ± 0.34 (53.2)	12.1	13.8 ± 0.11 (53.1)	13.1

[a] Data are the mean ± the standard deviation from greater than 15 values at three wavelengths (304, 260 and 236 nm). [b] Calculated from the activation parameters cited in Table 2.

Equal volumes (1.0 ml) of *cis*-$PtCl(NH_3)_2(OH_2)^+$ [~1.6 mM (λ_{max} = 269 ± 2 nm, λ_{min} = 241 ± 2 nm) in 0.1 M $HClO_4$] and Cl^- ion (NaCl) in $HClO_4$ of sufficient concentration to give a final ionic strength of 1.0 M, were thermally equilibrated and mixed. In all cases the initial [Cl^-] was greater than 10 times [Pt]. Absorption spectral changes were monitored at 305.0, 260.0 and 235.0 nm and the absorbance versus time data were analysed using first-order kinetics to give k_{obs} (s^{-1}) (Table 5). Values of k_{-1} (M^{-1} s^{-1}) were obtained using the expression $k_{-1} = k_{obs}$ $[Cl^-]^{-1}$. Activation parameters associated with k_1 and k_{-1} (Tables 2 and 5) were computer calculated from the variation of the rate constant with temperature [24].

Results and Discussion

The rate of hydrolysis of *cis*-$PtCl_2(NH_3)_2$ is a well studied reaction [3–18]. There are, however, certain fundamental issues to be decided before studies on this and other biologically active molecules can be regarded as definitive. Not the least of these is: should the reaction be investigated under physiological conditions [2b] (biologically relevant) where the nature of the hydrolysis products is ill defined, or should the reaction conditions be chosen so that product control can be maintained? Under the latter regime the data will be specific and definitive but could well be quite unrelated to the biological situation [2b]. Nevertheless, it is likely that such specifically controlled data can be extrapolated to the biological situation more easily than attempting to interpret the unspecific data with a variety of unknown parameters. We have adopted the position of using abiological conditions in the hope that the relevant extrapolations can be made.

The present example provides an excellent illustration of the problem as many of the hydrolysis studies have been made in water. Unless stringent controls are adopted, water will have a natural pH of less than 7 due to dissolved CO_2. This means that the concentrations of H^+ and OH^- are ill defined and the

TABLE 5. Spectrophotometrically measured chloride ion anation rate constants (k_{-1}) for reaction (1) at μ = 1.0 M ($HClO_4$)[a, b]

Temperature (°C) [K]	$[Cl^-]_i$[c] (M)	$10^4 \times k_{obs}$[d] (s^{-1})	$10^3 \times k_{-1}$[e] ($M^{-1} s^{-1}$)	$10^3 \times k_{-1}$ (mean) ($M^{-1} s^{-1}$)	$10^3 \times k_{-1}$ (calc.)[f] ($M^{-1} s^{-1}$)
10.0 [283.2]	0.25	3.48 ± 0.52	1.39 ± 0.21	1.22 ± 0.11	1.20
	0.35	4.07 ± 0.39	1.17 ± 0.11		
	0.40	5.36 ± 0.93	1.34 ± 0.23		
	0.50	5.96 ± 0.81	1.19 ± 0.16		
	0.60	7.39 ± 0.86	1.23 ± 0.14		
	0.75	8.04 ± 1.49	1.07 ± 0.20		
	0.90	10.33 ± 1.26	1.15 ± 0.14		
15.0 [288.2]	0.25	4.57 ± 0.52	1.83 ± 0.21	2.11 ± 0.22	2.12
	0.35	6.91 ± 0.77	1.97 ± 0.22		
	0.45	9.51 ± 0.83	2.11 ± 0.81		
	0.60	13.47 ± 1.93	2.24 ± 0.32		
	0.75	15.5 ± 0.94	2.07 ± 0.12		
	0.90	22.3 ± 1.5	2.47 ± 0.16		
20.0 [293.2]	0.1	3.63 ± 0.44	3.63 ± 0.44	3.54 ± 0.34	3.68
	0.9	31.2 ± 2.3	3.46 ± 0.25		
25.0 [293.2]	0.05	3.88 ± 0.27	6.76 ± 0.54	6.31 ± 0.32	6.26
	0.125	7.63 ± 0.40	6.34 ± 0.33		
	0.15	9.36 ± 0.50	6.24 ± 0.33		
	0.20	12.6 ± 0.8	6.30 ± 0.40		
	0.25	14.7 ± 1.2	5.88 ± 0.48		
30.0 [303.2]	0.05	5.44 ± 0.34	10.9 ± 0.7	10.5 ± 0.4	10.5
	0.10	10.6 ± 0.20	10.6 ± 0.2		
	0.125	12.6 ± 0.70	10.1 ± 0.6		

[a] $[PtCl(NH_3)_2(OH_2)^+] \sim 1.6 \times 10^{-3}$ M. [b] Ionic strength adjusted to 1.0 M using NaCl and $HClO_4$. [c] Initial Cl^- concentration ($\geq 10 \times$ [Pt]). [d] Spectrophotometrically determined pseudo-first-order rate constant. Mean of data calculated at λ = 260 and 305 nm. [e] $k_{-1} = k_{obs}[Cl^-]^{-1}$. [f] Calculated from the activation parameters E_a = 77.2 kJ mol^{-1}, $\Delta S^{\#} = -36.3$ J K^{-1} mol^{-1}.

buffering capacity is unknown. Dissolution of *cis*-$PtCl_2(NH_3)_2$ in water does not change the pH. Coordinated NH_3 groups have the potential to act as proton donors, but the extent of this in most coordination complexes is small and strong proton acceptors are required. Nevertheless, there are some complexes where hydrolysis proceeds via the $[OH^-]$ present at pH = 3 [25]. As the hydrolysis of *cis*-$PtCl_2(NH_3)_2$ proceeds [eqn. (1)] the pH will drop [eqn. (2)]. In this situation the products are the chloroaqua and the chlorohydroxo in an ill defined ratio, as the pK_a for reaction (2) is unknown. Hydroxo ligands coordinated to Pt(II) are known to be rather inert [26] and the production of the chlorohydroxo will reduce the chloroaqua concentration and thus reduce the reversibility inherent in (1). Hydroxo ligands coordinated to Pt(II) also influence *cis* labilisation more than coordinated water molecules, so loss of the second chloro ligand may be a possibility [18]. We have shown that the rate of loss of the chloro ligand from *cis*-$PtCl(NH_3)_2(OH_2)^+$ is slower than the loss of the first chloro ligand from *cis*-$PtCl_2(NH_3)_2$, whereas the rate from *cis*-$PtCl(OH)(NH_3)_2$ is comparable or greater [5, 18]. Consequently, while *cis*-$PtCl_2(NH_3)_2$ certainly solvolyses in water, the nature of the products cannot be predicted and the rate of reaction can only be securely monitored by measuring the rate of loss of the starting material [12]. We (and others [27]) have been unable to obtain reliable rate constants for this reaction in water using spectrophotometry as the absorbance versus time data are wavelength dependent due to the changing ratio of secondary products as the reaction proceeds.

The use of buffers is not without criticism. These will control the product ratio, but if the hydroxo/aqua equilibrium constant [eqn. (2)] is unknown, the now constant product ratio still cannot be calculated. More serious, is the introduction of spurious or catalytic counter ions in the buffer medium. Pt(II) systems are known to be very susceptible to nucleophilic attack and phosphate [9, 10, 27], acetate, citrate, tris or other buffer counter ions could easily influence the solvolysis reaction. Nor are these reagents particularly close to the biological regime.

We have thus decided to systematically study the rate of solvolysis of *cis*-$PtCl_2(NH_3)_2$ in media where the products can be predicted with some certainty. By investigating the hydrolysis in acidic conditions we are confident that the influence of *cis*-$PtCl(OH)(NH_3)_2$ on the reaction rate can be reduced to zero, and only *cis*-$PtCl(NH_3)_2(OH_2)^+$ and Cl^- ions will be produced. We have chosen $HClO_4/NaClO_4$ as the background electrolyte as these are UV transparent and the ClO_4^- ion has only weak nucleophilic properties. The UV absorption spectra of solutions of *cis*-$PtCl_2(NH_3)_2$ in $HClO_4$ (0.1–1.0 M) slowly change with time at 25 °C. The absorbance at 305 nm (a maximum for the dichloro) decreases and the absorbance at 246 nm (a minimum for the dichloro) increases. Isosbestic points at 282 ± 2 and 242 ± 2 are maintained (Fig. 1). Contrary to certain statements in the literature, the maintenance of an isosbestic point in the absorption spectral profile of a reacting compound provides no information on the number of species being produced. A single compound producing a single compound will maintain an isosbestic point, but so will a single compound producing two compounds in a constant ratio. The presence of a well maintained isosbestic point certainly indicates that a reaction sequence such as A → B → C is unlikely.

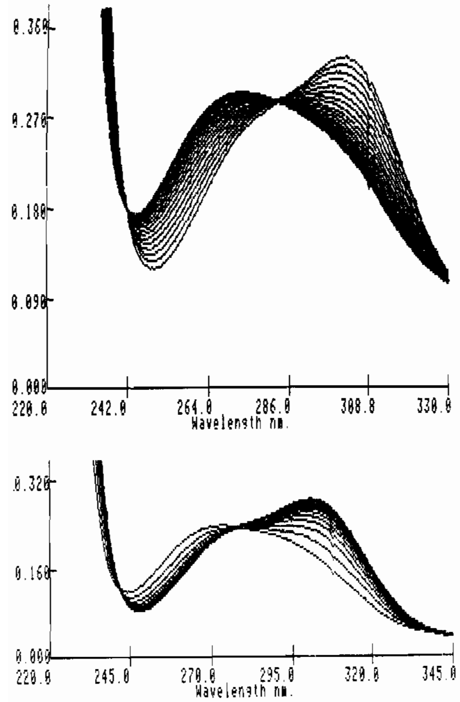

Fig. 1. Spectrophotometric scans for the aquation (upper) of *cis*-$PtCl_2(NH_3)_2$ (0.1 M $HClO_4$: 43 °C: 5 min intervals) and anation (lower) of *cis*-$PtCl(NH_3)_2(OH_2)^+$ (0.03 M Cl^-: $\mu = 1.0$ M; $HClO_4$, NaCl: 30 °C: 3 min intervals). For the forward reaction (aquation) the absorbance at 300 nm decreases and for the reverse (anation) the absorbance increases. Both reactions maintain the same isosbestic points (282 ± 2 and 242 ± 2 nm).

The same isosbestic points are developed in the reverse reaction when Cl^- ion is added to *cis*-$PtCl(NH_3)_2(OH_2)^+$ (Fig. 1).

In the forward reaction, the intensity difference between *cis*-$PtCl_2(NH_3)_2$ and *cis*-$PtCl(NH_3)_2(OH_2)^+$ at 304, 260 and 236 nm is sufficient to enable reasonably accurate rate constants k_1 to be calculated according to the first-order rate law $k_1t = \ln[(A_\infty - A_0)(A_\infty - A_t)^{-1}]$ where A_0 and A_∞ are the absorbance at $t = 0$ and $t =$ 'infinity' and A_t is the absorbance at time = t. Table 4 lists the values for k_1 obtained in this way in 0.1 M $HClO_4$, 1.0 M $HClO_4$ and 0.1 M $HClO_4$ plus 0.9 M $NaClO_4$ over a 22 K temperature range. It should be noted that reaction (1) is proceeding to equilibrium and simple first-order kinetics are not strictly applicable to the $A \rightleftharpoons B + C$ system [5, 15, 28]. Nevertheless, most investigators have ignored the contribution from the reverse reaction [14], and our data shows that the equilibrium (1) is substantially (>90%) to the chloroaqua form at the *cis*-$PtCl_2(NH_3)_2$ concentrations used (see Table 7). Inspection of the data shows that the rate constant associated with the first step in the acid hydrolysis of *cis*-$PtCl_2(NH_3)_2$ is independent of $[H^+]$ and ionic strength in the measured range (0.1–1.0 M).

The hydrogen ion independence is normal for complexes of this type with strongly acidic leaving groups [29] and the ionic strength independence is also in agreement with the Debye–Huckle theory for a reactant with zero charge [30].

Comparison of the data in Table 4 with that in Table 1, however, shows that the k_1 data obtained in acid conditions are about 2–3 times greater than those previously obtained in water (pH = 4–7), indicating complete elimination of the chlorohydroxo complex from the system. There were indications in the literature that H^+ and/or NO_3^- may be having an acceleratory influence on the reaction rate (underlined values in Table 1 are those determined in 0.01 M HNO_3). We have measured k_1 in 0.1 M HNO_3 and find the rate ($10^4k_1 = 3.3 \pm 0.4$ s^{-1} at 37.6 °C) is reasonably close to that determined in $HClO_4$ ($10^4k_1 = 2.47 \pm 0.04$) at 36.7 °C. Indeed, rate data at ~37.5 °C in 0.1 M *p*-toluenesulfonic acid, 0.1 M trifluoroacetic acid, 0.1 M acetic acid and 0.05 M H_2SO_4 are quite comparable with the data in 0.1 M $HClO_4$. This is not the situation for 0.05 M oxalic, malonic or tartaric acids and *cis*-$PtCl(NH_3)_2(OH_2)^+$ is not the final product.

The variation of k_1 with temperature allows an estimation of the activation parameters associated with the forward reaction in eqn. (1) (Table 2). It is difficult to make comparisons with earlier data

TABLE 6. Forward (k_1) and reverse (k_{-1}) rate constants and equilibrium constants (K_1) for the first step in the acid hydrolysis of *cis*-$PtCl_2(NH_3)_2$ in $HClO_4$ (μ = 1.0 M)

T (°C) [K]	$10^5 \times k_1$ [a] (s^{-1})	$10^3 \times k_{-1}$ [b] ($M^{-1}\ s^{-1}$)	$10^3 \times K_1$ [c,d]
10.0 [283.2]	1.03	1.20	8.58
15.0 [288.2]	1.94	2.12	9.15
20.0 [293.2]	3.54	3.68	9.62
25.0 [298.2]	6.32	6.26	10.1
30.0 [303.2]	11.1	10.5	10.6
35.0 [308.2]	19.2	17.4	11.3
40.0 [313.2]	32.6	28.1	11.6
45.0 [318.2]	54.3	44.8	12.1
50.0 [323.2]	89.2	70.3	12.7

[a] Calculated from the expression (1.0 M $HClO_4$) $k_1 = 4.413 \times 10^{10}\ e^{-84.73/RT}$ (Tables 4 and 2). [b] Calculated from the expression $k_{-1} = 2.104 \times 10^{11}\ e^{-77.21/RT}$ (Table 5). [c] Calculated from the expression $K_1 = k_1/k_{-1}$ which is equivalent to $-\ln K_1 = 7.52(RT)^{-1} + 1.562$. [d] The variation of K_1 with temperature indicates that the forward reaction is endothermic and from c, $\Delta H° = 7.52$ kJ mol^{-1} (cf. $\Delta H° = 14.2$ kJ mol^{-1} [16] in water). Other thermodynamic parameters associated with the forward reaction are $\Delta G°_{(298.2)} = -11.4$ kJ mol^{-1} and $\Delta S°_{(298.2)} = 63$ J K^{-1} mol^{-1}.

(several studies only used a very narrow temperature range) but our data for $\Delta H^{\#}$ and $\Delta S^{\#}$ in acid are certainly not grossly disparate with the data obtained in water. If all our data are combined, we obtain $10^5 k_{-1}$ (25.0 °C) = 7.1×10^{-5} s^{-1}, $\Delta H^{\#} = 78.7 \pm 1.6$ kJ mol^{-1} and $\Delta S^{\#} = -60.3 \pm 3$ J K^{-1} mol^{-1} at 25 °C in acid solution (0.1–1.0 M $HClO_4$) at μ = 0.1–1.0 M ($NaClO_4$).

We have now been able to isolate *cis*-$PtCl(NH_3)_2(OH_2)^+$ in chloride ion free 0.1 M $HClO_4$ solution using anion exchange chromatography. Addition of excess Cl^- to solutions of this cation produce varying amounts of *cis*-$PtCl_2(NH_3)_2$, the extent of the reaction depending on the $[Cl^-]$. Only restricted $[Cl^-]$ ranged could be used to determine the rate of reaction and in all cases $[Cl^-]_i$ was greater than 10 times $[Pt]_i$ so that pseudo-first-order kinetics could be obtained for the reverse of eqn. (1). Rate constants (k_{obs}, s^{-1}) are listed in Table 5 for a range of $[Cl^-]$. These pseudo-first-order constants were used to obtain values of k_{-1} ($M^{-1}\ s^{-1}$) using the expression $k_{-1} = k_{obs}[Cl^-]^{-1}$. The validity of this procedure is justified on four points: (a) the constancy of k_{-1} values so obtained, over a range of $[Cl^-]$; (b) plots of k_{obs} versus $[Cl^-]$ are linear and pass through the origin at $[Cl^-] = 0$; (c) plots of ln k_{-1} (where k_{-1} is obtained over a $[Cl^-]$ range of 0.025–0.9 M) versus $1/T$(K) are linear and give sensible values for the activation parameters (Table 5); the data for k_{-1} are in excellent agreement with those previously obtained (indirectly) in water (Tables 3 and 6).

Combining the temperature dependence expression for $k_{-1} = 2.104 \times 10^{11}\ e^{-77.21/RT}$ and $k_1 = 4.413 \times 10^{10}\ e^{-84.73/RT}$ (both at μ = 1.0 M, $HClO_4$) gives the temperature dependence for the equilibrium constant $K_1 = k_1/k_{-1}$ in the form $-\ln K_1 = 7.52(RT)^{-1} + 1.562$. Thus $\Delta H°$ for the endothermic forward reaction is calculated to be 7.52 kJ mol^{-1}. The variation of K_1 with temperature (Table 6) is small, and rather more precisely established than has been possible from previous studies (Table 3).

Data in Table 7 give the equilibrium hydrolysis product concentrations (μ = 1.0 M, $HClO_4$) for various initial *cis*-$PtCl_2(NH_3)_2$ concentrations, in the absence of added chloride ion.

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TABLE 7. Equilibrium concentrations (mmol l^{-1}) for the reaction *cis*-$PtCl_2(NH_3) \rightleftharpoons$ *cis*-$PtCl(NH_3)_2(OH_2)^+ + Cl^-$ (K_1) in aqueous $HClO_4$ (μ = 1.0 M) at 25.0 °C using $K_1 = 1.0 \times 10^{-2}$

Initial concentration (mM) *cis*-$PtCl_2(NH_3)_2$	Equilibrium concentrations (mM)	
	cis-$PtCl_2(NH_3)_2$	*cis*-$PtCl(NH_3)_2(OH_2)^+ = Cl^-$
100	73	27
10	4	6
1.6	0.2	1.4
1.0	0.1	0.9

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