

Structure of the Hydrated Platinum(II) Ion and the *cis*-Diammineplatinum(II) Complex in Acidic Aqueous Solution: An EXAFS Study

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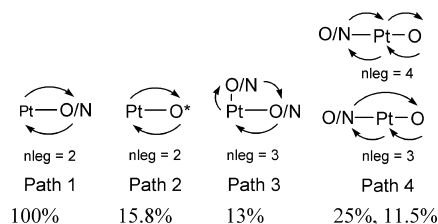
Careful analysis of Pt L₃-edge extended X-ray absorption fine structure (EXAFS) spectra shows that the hydrated platinum(II) ion in acidic (HClO₄) aqueous solution binds four water molecules with the Pt–O bond distance 2.01(2) Å and one (or two) in the axial position at 2.39(2) Å. The weak axial water coordination is in accordance with the unexpectedly small activation volume previously reported for water exchange in an interchange mechanism with associative character. The hydrated *cis*-diammineplatinum(II) complex has a similar coordination environment with two ammine and two aqua ligands strongly bound with Pt–O/N bond distances of 2.01(2) Å and, in addition, one (or two) axial water molecule at 2.37(2) Å. This result provides a new basis for theoretical computational studies aiming to connect the function of the anticancer drug *cis*-platin to its ligand exchange reactions, where usually four-coordinated square planar platinum(II) species are considered as the reactant and product. ¹⁹⁵Pt NMR spectroscopy has been used to characterize the Pt(II) complexes.

Introduction

Platinum(II) shows strong preference for square-planar coordination geometry,¹ rationalized by the crystal field stabilization energy for its d⁸ electronic configuration. The numerous substitution and oxidative-addition reactions studied for its complexes have played a major role in the development of organometallic chemistry.^{2,3} The antitumor activity of some of its complexes has also attracted great attention,^{4,5} following the discovery by Rosenberg and co-workers in 1969 that *cis*-platin, *cis*-diamminedichloroplatinum(II), inhibits cell division.⁶ Today, about 30 platinum-based drugs have entered clinical trials.⁷

When entering a cellular environment, the drug *cis*-platin is activated by substitution of one or both chloro-ligands with water molecules. This process is promoted by the lower

Scheme 1. Single- (SS) and Multiple-Scattering (MS) Pathways Considered in EXAFS Model Fittings of [Pt(H₂O)_n]²⁺ and [Pt(NH₃)₂(H₂O)_m]²⁺ Complexes (Models VI and VII in Tables 1 and 2), with Their Relative Amplitude Ratios Calculated in FEFF for Stationary Atoms ($\sigma^2 = 0.0 \text{ \AA}^2$)



chloride concentration in the cellular environment ($\sim 4\text{--}12 \text{ mmol}\cdot\text{dm}^{-3}$) than in the blood stream ($\sim 100 \text{ mmol}\cdot\text{dm}^{-3}$).^{7–10} However, structural information for hydrated platinum(II) species including the hydration products of *cis*-platin, which is essential for a better understanding of the reaction mechanism, is limited.¹¹

The hydration and hydrolysis of platinum(II) and *cis*-platin in aqueous solution, and the mechanism of water exchange,

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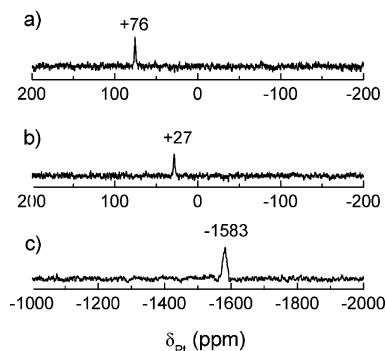


Figure 1. ^{195}Pt NMR spectra of (a and b) $[\text{Pt}(\text{H}_2\text{O})_n]^{2+}$ in ~ 5.0 and ~ 1.1 $\text{mol}\cdot\text{dm}^{-3}$ HClO_4 (aq), respectively (acid concentrations after dilution with D_2O) and (c) *cis*- $[\text{Pt}(\text{NH}_3)_2(\text{H}_2\text{O})_m]^{2+}$ in aqueous solution.

have previously been studied by extended X-ray absorption fine structure (EXAFS), ^{195}Pt and ^{17}O NMR spectroscopic methods, large-angle X-ray scattering (LAXS),^{12–16} kinetic measurements,¹⁷ as well as theoretical calculations.^{18–28} Two separate EXAFS studies, one combined with LAXS and the other with quantum-mechanical calculations, concluded that the hydrated platinum(II) ion in acidic aqueous solution coordinates four water molecules in square-planar geometry with the Pt–O distance 2.01–2.02 Å. No evidence was found for additional solvent molecules in the axial positions.^{12,13} However, a recent EXAFS study on the hydration of the chemically similar palladium(II) ion in concentrated HClO_4 reports two (or possibly one) axial water molecules weakly bound (Pd–O_{ax} 2.5 Å) to a square planar $[\text{Pd}(\text{H}_2\text{O})_4]^{2+}$ entity, which has four tightly bound water molecules at Pd–O 2.00(1) Å.²⁹ Similarly, in a LAXS study of $[\text{PtCl}_4]^{2-}$ in acidic aqueous solution, two loosely attached axial water molecules were proposed with Pt–O distances of 2.77 Å.³⁰

The resolved isotopic shifts in the ^{195}Pt NMR signals from the hydrated platinum(II) ion in ^{18}O -enriched aqueous

solution were interpreted as indicating four equivalent slow-exchanging aqua ligands in square-planar coordination geometry.¹⁵ Axial interactions with fast-exchanging water molecules could not be detected; if present their exchange frequency is too high to induce further splitting of the NMR signals. The slow water exchange of the hydrated platinum(II) ion was also followed by a high-pressure ^{17}O NMR study of platinum(II) perchlorate solutions mixed with ^{17}O -enriched water.¹⁶ Relatively small negative values were then obtained for the activation entropy ($\Delta S^\ddagger = -9 \pm 8$ $\text{J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$) and activation volume ($\Delta V^\ddagger = -4.6 \pm 0.2$ $\text{cm}^3\cdot\text{mol}^{-1}$), and an associative interchange (I_a) mechanism was proposed.^{31,32} According to Gröning and Elding, however, the mechanistic interpretation of such a small volume change still is an open question, in particular as they later obtained an even smaller value for the activation entropy ($\Delta S^\ddagger = 0 \pm 5$ $\text{J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$) using ^{195}Pt NMR.¹⁴

Two computational studies have been reported attempting to model water exchange reactions for the hydrated platinum(II) ion.^{18,19} In the first density functional theory (DFT) study a square planar $[\text{Pt}(\text{H}_2\text{O})_4]^{2+}$ complex with an optimized Pt–O distance of 2.04 Å was considered as the reactant. For the water exchange process an associative mechanism was suggested, assuming ideal trigonal bipyramidal coordination geometry in the transition state. A possible coordination of axial water molecules perpendicular to the equatorial plane was also considered in the ground state; however, the results were inconclusive and depended on the approximations used for the exchange and correlation functionals.¹⁸

In a more recent computational study, the water exchange reaction was again modeled for a H_2O molecule approaching $[\text{Pt}(\text{H}_2\text{O})_4]^{2+}$ in an associative mechanism. In the 5-coordinated, trigonal bipyramid-like transition state, three Pt–O distances varied in the range 2.0–2.1 Å, while two other Pt–O bonds, forming and breaking, were considerably longer (~ 2.4 Å).¹⁹ Neither of the two studies took the influence of explicit hydrogen-bonding to surrounding water molecules into account.

In a theoretical simulation of the hydration of square planar $[\text{Pt}(\text{NH}_3)_4]^{2+}$ and *trans*- $[\text{Pt}(\text{NH}_3)_2(\text{OH})_2]$ complexes, two different modes were considered for how a water molecule could approach the metal atom perpendicular to the equatorial plane: (i) with the water oxygen atom oriented toward Pt; (ii) with one hydrogen atom directed toward the Pt atom. For the $[\text{Pt}(\text{NH}_3)_4]^{2+}$ complex the most stable configuration was obtained via the first mode with Pt–O 3.25 Å for an electrostatic interaction between the positively charged Pt atom and the water oxygen. For the neutral *trans*- $[\text{Pt}(\text{NH}_3)_2(\text{OH})_2]$ complex, the most stable state was achieved for Pt(H)–O 3.5 Å in the second mode, where the Pt atom acts as a proton acceptor.²⁰

In recent years, several theoretical studies have addressed the hydrolysis of *cis*-platin and its analogues under various conditions, assuming associative mechanisms with four-

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Table 1. Model Curve-Fitting to the k^3 -Weighted EXAFS Oscillation for 0.16 mol·dm⁻³ *cis*-[Pt(NH₃)₂(H₂O)_{*m*}]²⁺ in Aqueous Solution^{a,b}

model	pathways	C.N.	<i>R</i> /Å	$\sigma^2 \times 10^3/\text{Å}^2$	<i>S</i> ₀ ²	$\Delta E_0/\text{eV}$	residue ^c
I (<i>m</i> = 2)	Pt–(O/N)	4	2.01 (2)	3.7	0.9 f	13.2	20.6
II (<i>m</i> = 2)	Pt–(O/N)	4	2.01 (2)	3.7	0.9 f	13.1	19.1
	Pt–O–Pt–N (<i>m</i> _{leg} = 4)	4	4.03 (2)	6.1			
	Pt–O–Pt–N (<i>m</i> _{leg} = 3)	4	4.03 c	6.1 c			
III (<i>m</i> = 2)	Pt–(O/N)	4	2.01 (2)	3.7	0.9 f	13.2	17.7
	(O/N)–Pt–(O/N) (<i>m</i> _{leg} = 3)	8	3.46 (2)	1.9			
	Pt–O–Pt–N (<i>m</i> _{leg} = 4)	4	4.00 (2)	8.8			
	Pt–O–Pt–N (<i>m</i> _{leg} = 3)	4	4.00 c	8.8 c			
IV (<i>m</i> = 3)	Pt–(O/N)	4	2.01 (2)	3.6	0.9 f	13.8	15.9
	Pt–O*	1	2.37 (2)	7.2			
V (<i>m</i> = 3)	Pt–(O/N)	4	2.01 (2)	3.6	0.9 f	13.5	13.9
	Pt–O*	1	2.37 (2)	7.7			
	Pt–O–Pt–N (<i>m</i> _{leg} = 4)	4	4.04 (2)	8.0			
	Pt–O–Pt–N (<i>m</i> _{leg} = 3)	4	4.04 c	8.0 c			
VI (<i>m</i> = 3)	Pt–(O/N)	4	2.01 (2)	3.6	0.9 f	13.8	12.3
	Pt–O*	1	2.37 (2)	7.8			
	(O/N)–Pt–(O/N) (<i>m</i> _{leg} = 3)	8	3.49 (2)	4.1			
	Pt–O–Pt–N (<i>m</i> _{leg} = 4)	4	4.01 (2)	9.1			
	Pt–O–Pt–N (<i>m</i> _{leg} = 3)	4	4.01 c	9.1 c			
VII (<i>m</i> = 4)	Pt–(O/N)	4	2.015 (2)	3.5	0.9 f	14.2	11.9
	Pt–O*	2	2.38 (2)	17.3			
	O/N)–Pt–(O/N) (<i>m</i> _{leg} = 3)	8	3.50 (2)	4.3			
	Pt–O–Pt–N (<i>m</i> _{leg} = 4)	4	4.01 (2)	9.0			
	Pt–O–Pt–N (<i>m</i> _{leg} = 3)	4	4.01 c	9.0 c			
VIII	Pt–(O/N)	4	2.015	3.5	0.9 f	14.0	13.2
	Pt–O*	2.7 r	2.395	22.0			
	Pt–O–Pt–N (<i>m</i> _{leg} = 4)	4	4.04 (2)	8.3			
	Pt–O–Pt–N (<i>m</i> _{leg} = 3)	4	4.04 c	8.3 c			

^a Fitting range $k = 3.2\text{--}14.3 \text{ \AA}^{-1}$; C.N. = coordination number (fixed); f = fixed, c = correlated, r = refined. Estimated error for bond distances is $\pm 0.02 \text{ \AA}$ and for disorder parameter (σ^2) is 0.0005 \AA^2 for Pt–O, 0.001 \AA^2 for 1 Pt–O*, and 0.002 \AA^2 for 2 Pt–O*. ^b Scattering pathways are shown in Scheme 1. ^c Residue (%) from the least-squares curve fitting is defined as $[\sum_{i=1}^N |y_{\text{exp}}(i) - y_{\text{theo}}(i)| / \sum_{i=1}^N |y_{\text{exp}}(i)|] \times 100$ where y_{exp} and y_{theo} are experimental and theoretical data points, respectively.

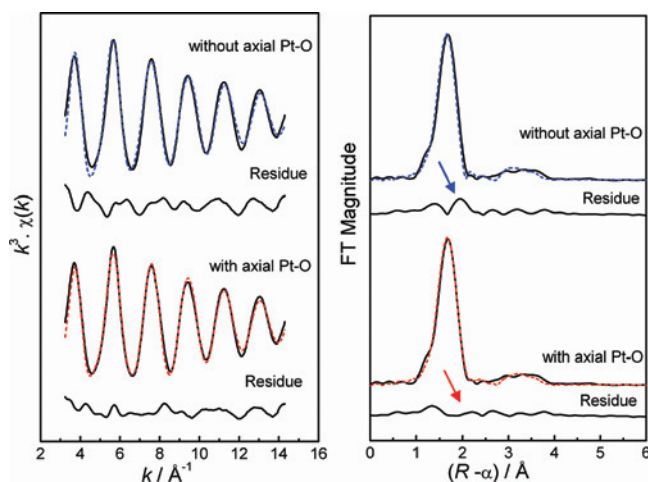


Figure 2. (left) Least squares curve fitting of the k^3 -weighted EXAFS functions (solid lines) for 0.16 mol·dm⁻³ *cis*-[Pt(NH₃)₂(H₂O)_{*m*}]²⁺ aqueous solution, without and with axial Pt–O* contribution (models **III** and **VI** in Table 1, respectively; dashes) and corresponding residues (= exp - fit). (right) Corresponding Fourier transforms.

coordinated square planar structures for both reactant and product.^{21–28} In one study, the most stable product was considered to be the neutral [Pt(NH₃)₂(OH)₂] complex,²¹ while another proposed that the active product of *cis*-platin reaching cellular DNA most likely is the monoqua, rather than the diaqua complex.²³ A recent DFT calculation, however, showed very similar activation barriers and reaction free energies for the different steps in the hydrolysis process of *cis*-platin.²⁷ Those results do not support computational studies that

rule out the involvement of *cis*-[Pt(NH₃)₂(OH)₂]²⁺ and *cis*-[Pt(NH₃)₂(OH)₂(OH)]⁺ species in the action of the drug and predict further hydrolysis to be thermodynamically unfavorable. However, a new situation arises for the reaction mechanism of the hydrated products of *cis*-platin, if their coordination geometry is not square planar. Axially coordinated water molecules could play a major role in the modeling of the reactivity and ligand substitution reactions of these complexes.^{9,18,32}

In the present study, we use high quality long-range EXAFS spectra to ascertain the presence of weakly coordinated solvent molecules in axial positions of the hydrated platinum(II) ion and its *cis*-diammine complex in acidic aqueous solutions.

Experimental Section

Starting Materials. *cis*-Platin, potassium tetrachloroplatinate(II), and silver perchlorate monohydrate were used as obtained from Sigma Aldrich.

Hydrated *cis*-Diammineplatinum(II) Ion. An $\sim 0.16 \text{ mol} \cdot \text{dm}^{-3}$ perchlorate solution of [Pt(NH₃)₂(H₂O)_{*m*}]²⁺ was prepared using a modification of the procedure by Appleton.³³ Silver perchlorate monohydrate (3.33 mmol) dissolved in 5 mL boiled, oxygen-free water was added to a solution of *cis*-platin (1.66 mmol) in 35 mL water under argon atmosphere. The mixture was stirred in darkness for 4 h at 60 °C, and 18 h at room temperature. The precipitated silver chloride (reaction 1) was filtered off and the volume of the

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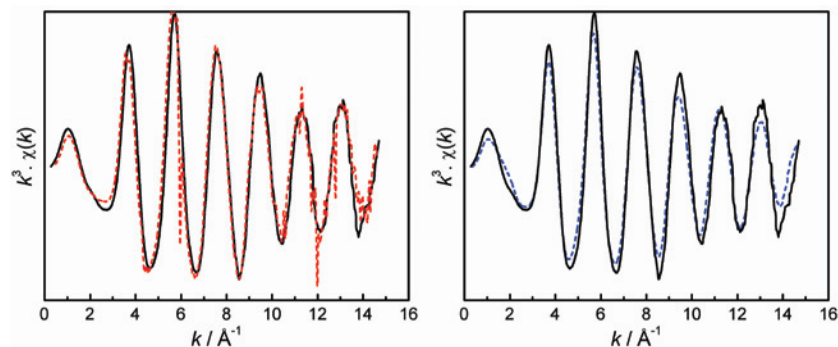


Figure 3. EXAFS spectra of $0.16 \text{ mol} \cdot \text{dm}^{-3} [\text{Pt}(\text{H}_2\text{O})_n]^{2+}$ in $\sim 7.5 \text{ mol} \cdot \text{dm}^{-3} \text{ HClO}_4$ (black solid line, PF) compared with those of (left) $0.1 \text{ mol} \cdot \text{dm}^{-3} [\text{Pt}(\text{H}_2\text{O})_n]^{2+}$ in $\sim 1.7 \text{ mol} \cdot \text{dm}^{-3} \text{ HClO}_4$ (red dashed line, SSRL) and (right) $0.16 \text{ mol} \cdot \text{dm}^{-3} [\text{Pt}(\text{NH}_3)_2(\text{H}_2\text{O})_m]^{2+}$ (pH = 2.1; blue dashed line, PF).

Table 2. Model Curve-Fitting to the k^3 -Weighted EXAFS Oscillation for $0.16 \text{ mol} \cdot \text{dm}^{-3} [\text{Pt}(\text{H}_2\text{O})_n]^{2+}$ in 7.5 M HClO_4 Aqueous Solution^{a,b}

model	paths	C.N.	$R/\text{Å}$	$\sigma^2 \times 10^3/\text{Å}^2$	S_0^2	$\Delta E_0/\text{eV}$	residue ^c
I ($n = 4$)	Pt–O	4	2.01	2.7	0.9 f	14.0	22.6
II ($n = 4$)	Pt–O	4	2.01	2.7	0.9 f	13.9	20.5
	Pt–O–Pt–O ($m_{\text{leg}} = 4$)	4	4.03	2.6			
	Pt–O–Pt–O ($m_{\text{leg}} = 3$)	4	4.03 c	2.6 c			
III ($n = 4$)	Pt–O	4	2.01	2.7	0.9 f	14.0	19.4
	O–Pt–O ($m_{\text{leg}} = 3$)	8	3.45	1.3			
	Pt–O–Pt–O ($m_{\text{leg}} = 4$)	4	4.01	4.6			
	Pt–O–Pt–O ($m_{\text{leg}} = 3$)	4	4.01 c	4.6 c			
IV ($n = 5$)	Pt–O	4	2.01	2.6	0.9 f	14.3	20.2
	Pt–O*	1	2.38	7.8			
V ($n = 5$)	Pt–O	4	2.01	2.7	0.9 f	14.0	17.5
	Pt–O*	1	2.39	8.4			
	Pt–O–Pt–O ($m_{\text{leg}} = 4$)	4	4.03	3.5			
	Pt–O–Pt–O ($m_{\text{leg}} = 3$)	4	4.03 c	3.5 c			
VI ($n = 5$)	Pt–O	4	2.01	2.6	0.9 f	14.2	16.6
	Pt–O*	1	2.39	8.8			
	O–Pt–O ($m_{\text{leg}} = 3$)	8	3.48	3.6			
	Pt–O–Pt–O ($m_{\text{leg}} = 4$)	4	4.01	4.8			
	Pt–O–Pt–O ($m_{\text{leg}} = 3$)	4	4.01 c	4.8 c			
VII ($n = 6$)	Pt–O	4	2.01	2.6	0.9 f	14.4	16.5
	Pt–O*	2	2.40	17.5			
	O–Pt–O ($m_{\text{leg}} = 3$)	8	3.48	4.5			
	Pt–O–Pt–O ($m_{\text{leg}} = 4$)	4	4.01	4.8			
	Pt–O–Pt–O ($m_{\text{leg}} = 3$)	4	4.01 c	4.8 c			
VIII	Pt–(O/N)	4	2.01	2.6	0.9 f	14.2	17.4
	Pt–O*	2.0 r	2.41	16.2			
	Pt–O–Pt–N ($m_{\text{leg}} = 4$)	4	4.03	3.6			
	Pt–O–Pt–N ($m_{\text{leg}} = 3$)	4	4.03 c	3.6 c			

^a Fitting range $k = 3.3\text{--}14.5 \text{ Å}^{-1}$; C.N. = coordination number (fixed); f = fixed, c = correlated, r = refined. Estimated error for bond distances is $\pm 0.02 \text{ Å}$ and for disorder parameter (σ^2) is 0.0005 Å^2 for Pt–O, 0.001 Å^2 for 1 Pt–O*, and 0.002 Å^2 for 2 Pt–O*. ^b Scattering pathways are shown in Scheme 1. ^c Residue (%) from the least-squares curve fitting is defined as $[\sum_{i=1}^N |y_{\text{exp}}(i) - y_{\text{theo}}(i)| / \sum_{i=1}^N |y_{\text{exp}}(i)|] \times 100$ where y_{exp} and y_{theo} are experimental and theoretical data points, respectively.

filtrate reduced to 10 mL (pH = 2.1). The resulting $[\text{Pt}(\text{NH}_3)_2(\text{H}_2\text{O})_m]^{2+}$ complex was characterized by means of ^{195}Pt NMR, resulting in a chemical shift at -1583 ppm relative to K_2PtCl_6 (0 ppm).



Hydrated Platinum(II) Ion, $[\text{Pt}(\text{H}_2\text{O})_n]^{2+}$. An acidic Pt(II) perchlorate solution was prepared in a similar way as described previously.^{15,33–36} Potassium tetrachloroplatinate(II) (4.25 mmol) was dissolved in 200 mL 1.0 M perchloric acid. The solution was

flushed with argon to prevent oxidation, heated to 70 °C and kept in darkness while stirring until all solid had dissolved. Silver perchlorate monohydrate (36.9 mmol) in 200 mL aqueous solution was added slowly in portions of 13–15 mL/h for 3 h, followed by ca. 50 mL/h for another 3 h, to avoid precipitation of sparingly soluble $\text{Ag}_2[\text{PtCl}_4]$. The mixture was stirred in darkness during continued heating at 70 °C for 12 days and, then, cooled to 0 °C . The precipitated silver chloride was filtered off and the filtrate, now containing $\sim 10 \text{ mmol} \cdot \text{dm}^{-3}$ platinum(II), was placed in a 500 mL three-neck flask and electrolyzed (137 V) over a period of 5 days (115 h) to deposit the excess silver ions on the cathode (Pt foil). The volume of the resulting bright yellow solution was reduced using a rotary evaporator (at 82 °C) to 26.5 mL, until $[\text{Pt}^{2+}] =$

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0.16 mol·dm⁻³ and [H⁺] ~ 7.5 mol·dm⁻³. The solution was flushed with argon and stored at approximately 2 °C. After dilution of the NMR sample with D₂O ([H⁺] ~ 5.0 mol·dm⁻³), its ¹⁹⁵Pt NMR chemical shift was observed at +76 ppm [relative to K₂PtCl₆ (0 ppm) at 300 K]. To reduce the acidity and the perchlorate concentration, solid KOH was added to a portion of the above acidic stock platinum(II) solution in an ice bath. The KClO₄ precipitate (solubility <0.1 mol·dm⁻³ KClO₄ in cold water) was filtered off resulting in a solution with [Pt²⁺] ~ 0.1 mol·dm⁻³ and [H⁺] ~ 1.7 mol·dm⁻³ for which the ¹⁹⁵Pt NMR chemical shift after dilution with D₂O was observed at +27 ppm ([H⁺] ~ 1.1 mol·dm⁻³).

NMR Measurements. ¹⁹⁵Pt NMR spectra were obtained at 300 K (27 °C) by means of a Bruker AMX2–300 spectrometer at 64.5 MHz, using a 10 mm broadband (BBO) probe, 30° pulse and zg30 pulse program. D₂O (~20–30%) was added for shimming and the spectra were externally calibrated relative to an aqueous (10% D₂O) solution of K₂[PtCl₆] (0 ppm).³⁷ With this calibration the chemical shift for K₂[PtCl₆] was –1624 ppm. In total, 10 000 scans were recorded for the acidic [Pt(H₂O)_n]²⁺ solutions in ~7.5 and ~1.7 mol·dm⁻³ HClO₄ (~5.0 and ~1.1 mol·dm⁻³ HClO₄, after dilution with D₂O) with repetition time of 0.136 s. The spectral line width at half-height was 97 and 132 Hz, respectively. For the *cis*-diammineplatinum(II) aqueous solution, 600 scans were collected with 0.20 s repetition time giving a spectral line width at half-height of 790 Hz.

EXAFS Spectroscopy. Pt L₃-edge EXAFS spectra of the three aqueous solutions, 0.16 mol·dm⁻³ Pt²⁺(aq) in ~7.5 mol·dm⁻³ HClO₄, 0.1 mol·dm⁻³ Pt²⁺(aq) in ~1.7 mol·dm⁻³ HClO₄, and 0.16 mol·dm⁻³ [Pt(NH₃)₂(H₂O)_n]²⁺ (pH = 2.1), were collected at beamline 12-C at the Photon Factory (PF) of the High Energy Accelerator Research Organization, Tsukuba, Japan, and at beamline 2-3 of the Stanford Synchrotron Radiation Laboratory (SSRL). Both facilities operated under dedicated conditions: PF at 2.5 GeV and 350–450 mA, and SSRL at 3.0 GeV and 70–100 mA. Harmonics from the double crystal monochromators, Si[111] at PF and Si[220] at SSRL, were rejected by detuning the focused beam to 50% of maximum intensity at the end of the scan range. The solutions were enclosed in 5 mm Teflon spacers between 5 μm X-ray polypropylene film windows. For each sample, 6–8 scans were collected at room temperature in transmission mode using nitrogen in the first ion chamber (I₀), and argon in the second one (I₁). Before averaging, the energy scale was calibrated externally by assigning the first inflection point of the Pt L₃-edge of a Pt foil to 11564 eV.

EXAFS Data Analysis. The procedures for extracting the EXAFS spectra using the WinXAS 3.1 program,³⁸ and for simulating the EXAFS oscillation for a model by means of the FEFF 8.1 program,³⁹ have been described elsewhere.⁴⁰ For the experimental spectra, energy conversion into *k*-space was performed using a threshold energy of E₀ = 11564.5 – 11565.0 eV for the solutions. In the least-squares refinements, when fitting theoretical model functions χ(*k*) to the *k*³-weighted experimental EXAFS oscillation, the coordination numbers (C.N.) and amplitude reduction factor (S₀² = 0.9) were fixed, allowing the structural parameters, i.e. the interatomic distance (*R*) and Debye–Waller parameter (*σ*), as well as ΔE₀ to float. The accuracy of the bond distances *R* is estimated to be within ±0.02 Å, including systematic errors. The influence

of systematic errors in the refined parameters was estimated by varying the fitting ranges, models, methods of splining and using different EXAFS data analysis programs.

For simulating the EXAFS oscillations for all possible single-scattering (SS) and multiple-scattering (MS) pathways involving the O/N atoms in the hydrated platinum(II) species, a structural model was used to generate an input file for the FEFF 8.1 program. In the model used for the Pt²⁺(aq) and [Pt(NH₃)₂(H₂O)_m]²⁺ ions, the platinum ion was placed 0.1 Å above the equatorial plane of four O/N atoms with Pt–(O/N)_{eq} 2.0 Å and one water oxygen atom in axial position with Pt–O_{ax} 2.4 Å. Reliable scattering parameters (amplitude and phase shift) for hydrogen atoms involved in bonding are still difficult to obtain by the FEFF 8.1 program,⁴¹ and the minor scattering contributions from the hydrogen atoms of the NH₃ and H₂O ligands were ignored. The scattering pathways with amplitude ratios (calculated for stationary atoms) higher than 10% relative to the single scattering path 1 are shown in Scheme 1.

Results and Discussion

Structure of the Hydrated *cis*-Diammineplatinum(II) Ion. The ¹⁹⁵Pt NMR spectrum of the [Pt(NH₃)₂(H₂O)_m]²⁺ solution shows one peak with chemical shift of –1583 ppm. The similarity to previously reported values of –1583.7 and –1587 ppm for [Pt(NH₃)₂(H₂O)₂]²⁺ (see Figure 1c),^{42,43} indicates a single Pt(II) complex in the sample.

EXAFS model curves were fitted to the *k*³-weighted EXAFS spectrum of this solution by least-squares methods varying structural parameters for different combinations of the SS and MS pathways in Scheme 1 (see Table 1). The Pt–(O/N) bond distance for the four strongly coordinated ammine/aqua ligands in the equatorial plane consistently emerged as 2.01(2) Å (SS path 1). Addition of MS pathways (3 and 4 in Scheme 1) slightly improved the fit (models II and III in Table 1). The MS path 4 is about 4.01 Å, i.e. twice the SS path 1, while the refined value of MS path 3, ~3.49 Å, is slightly longer than that expected within the equatorial plane, ~3.42 Å. Also, its disorder parameter is smaller than expected, and the refined parameters for this path evidently include contributions also from the somewhat longer (~3.8 Å) *n*_{leg} = 3 pathways involving the axial water oxygen. However, a comparison of the results from models V and VI in Table 1 shows that the inclusion of this representation of the *n*_{leg} = 3 MS-pathways does not affect the main structural parameters. The best fits were obtained when including one (or two) axial water molecules in the models, i.e. path 2 (Pt–O*) with a refined distance of 2.37(2) Å (models VI–VII in Table 1).

Figure 2 compares the EXAFS curve-fitting for the *cis*-[Pt(NH₃)₂(H₂O)_m]²⁺ complex in aqueous solution, using models with and without axial water contribution (Table 1) and shows that the residues clearly improve when including the axial Pt–O* distance in model VI. In the Fourier-transform of the curve-fitted EXAFS function, the small peak

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remaining in the residue for model **III** disappears by adding the Pt–O* path in model **VI**.

We also considered a model with two axial water molecules, coordinated on both sides of the equatorial plane (model **VII**, Table 1). Refinement of the structural parameters of path 2 for axial water molecules (model **VIII**) resulted in the Pt–O* distance 2.39(2) Å and a very high disorder parameter ($\sigma^2 = 0.022 \text{ \AA}^2$) for the coordination number C.N. = 2.7. Note that the C.N. is strongly correlated to the disorder parameter. Constraining the Pt–O* coordination number to 2.0 (model **VII**) gave $\sigma^2 = 0.017(2) \text{ \AA}^2$, which still is quite high for a mean distance of 2.38 Å for two Pt–O* bonds. For model **VI** with a single Pt–O* path the disorder parameter is reasonably large, $\sigma^2 = 0.008(1) \text{ \AA}^2$.

Structure of the Hydrated Platinum(II) Ion. Two aqueous solutions of platinum(II) were prepared in ~ 7.5 and $\sim 1.7 \text{ mol} \cdot \text{dm}^{-3}$ HClO₄. The ¹⁹⁵Pt NMR spectra, after dilution with D₂O to $[\text{H}^+] \sim 5.0$ and $\sim 1.1 \text{ mol} \cdot \text{dm}^{-3}$ HClO₄, respectively, showed chemical shifts at +76 and +27 ppm relative to K₂[PtCl₆] at 300 K; see Figure 1a and b. The ¹⁹⁵Pt chemical shift previously reported for 40 mmol·dm⁻³ Pt(II) in 1.0 mol·dm⁻³ HClO₄ at 296 K was +31 ppm.^{14,15} Note that the ¹⁹⁵Pt NMR chemical shifts are temperature dependent (ca. 1 ppm K⁻¹),¹⁵ and are very sensitive to the environment of the platinum atom.^{15,37} The perchloric acid concentration has been recommended to be 0.5 mol·dm⁻³ or higher to avoid any risk of hydrolysis.^{14,33} For hydrated platinum(II), large chemical shifts corresponding to lower shielding have previously been observed with increasing HClO₄ concentration (about 200 ppm from 1 to 10 mol·dm⁻³ HClO₄).³⁶ However, no inner-sphere perchlorato complexes were observed in the NMR study, even though the structural changes in the highly acidic solvent is likely to increase ion pairing.

The k^3 -weighted EXAFS spectra of the hydrated platinum(II) ion in ~ 7.5 and $\sim 1.7 \text{ mol} \cdot \text{dm}^{-3}$ aqueous HClO₄ solutions are very similar, Figure 3 (left), even though they were measured at different synchrotron facilities (SSRL and PF), and the two solutions show 48 ppm difference in their ¹⁹⁵Pt NMR chemical shifts (Figure 1a and b). Figure 3 (right) shows that the EXAFS spectrum of the hydrated platinum(II) ion also resembles that of the *cis*-diammineplatinum(II) complex in aqueous solution, because the EXAFS back-scattering parameters are very similar for water oxygen and ammine nitrogen atoms, which cannot be differentiated.

To evaluate the structural models for the hydrated platinum(II) ion by least-squares curve-fitting to the k^3 -weighted EXAFS oscillation, the less noisy EXAFS spectrum of the platinum(II) ion in $\sim 7.5 \text{ M HClO}_4$ aqueous solution was used. Different combinations of the SS and MS paths shown in Scheme 1 were used (Table 2) as for the hydrated *cis*-diammineplatinum(II) ion. Quite similar results emerged, consistently showing that the Pt(II) ion is surrounded by four tightly bound water molecules at 2.01(2) Å. This is close to the Pt–O distance (2.01–2.02 Å) obtained in the previous EXAFS and LAXS studies^{12,13} and also to the Pt–(O/N) bond length obtained for the hydrated *cis*-diammineplatinum(II) ion (Table 1). The best fits with minimum residues were obtained when axial water (path 2, Pt–O*) was included (Table 2, models **VI** and **VII**). However, the introduction of two axial water molecules in model **VII** or refining the

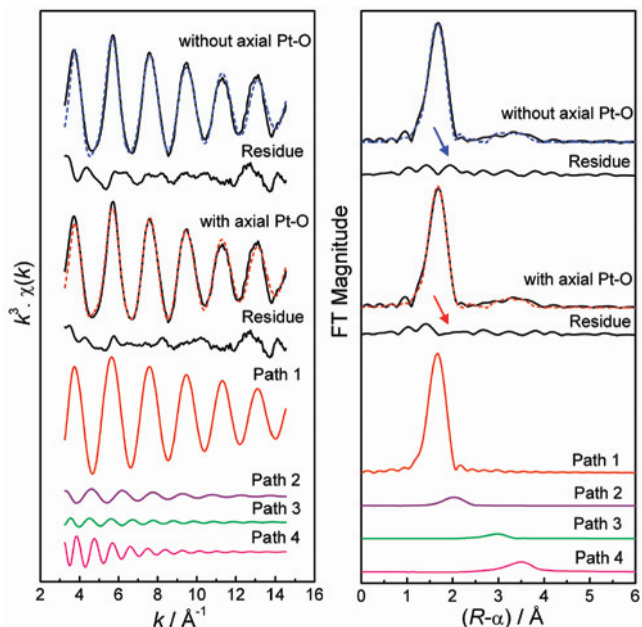


Figure 4. k^3 -Weighted EXAFS functions (black solid lines) for 0.16 M Pt²⁺(aq) in 7.5 M HClO₄. (left, top) Comparison between two models (dashes) without and with axial Pt–O (models **III** and **VI** in Table 2) and corresponding residues (= exp - fit). (left, below) Individual contributions for model **VI**, based on the scattering paths shown in Scheme 1. (right) Corresponding Fourier transforms.

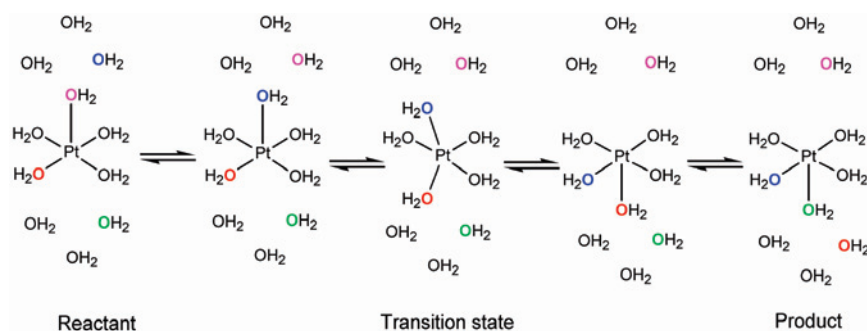
coordination number in model **VIII** (Table 2) again resulted in high values of the disorder parameter (σ^2), 0.016–0.017(2) Å². The refined distance for the Pt–O* path with one axial water molecule in model **VI**, 2.39(2) Å, and the disorder parameter $\sigma^2 = 0.009(1) \text{ \AA}^2$, are not significantly different from the corresponding values for the hydrated *cis*-diammineplatinum(II) complex (cf. Table 1).

Figure 4 shows the EXAFS curve-fitting for the hydrated platinum(II) ion, using the models **III** and **VI** (Table 2), without and with the Pt–O* scattering path included, respectively. As for the hydrated *cis*-diammineplatinum(II) ion (cf. Figure 2), the corresponding Fourier transform for model **III** shows a small peak in the residue, which disappears when the axial Pt–O* path is included in model **VI**. Also when analyzing the EXAFS spectrum of the hydrated platinum(II) ion by means of the EXAFSPAK software,⁴⁴ similar improvements in the fits (decreasing residues) were obtained by including axial water in the fitted model. The resulting parameters were not significantly different: 4 Pt–O 2.01(2) Å ($\sigma^2 = 0.0026(5) \text{ \AA}^2$) and 1 Pt–O* 2.39(2) Å ($\sigma^2 = 0.009(1) \text{ \AA}^2$), or 2 Pt–O* 2.41(2) Å ($\sigma^2 = 0.015(2) \text{ \AA}^2$); see Figures S1 and S2 in the Supporting Information.

The σ^2 values obtained when constraining the Pt–O* coordination number to 2.0 (model **VII**) are quite high and similar for the two different platinum(II) complexes studied. Therefore, the model **VI** with one axial water molecule, which corresponds to a structurally reasonable disorder, is preferred, while the possibility of two coordinated axial water molecules with additional disorder from a dynamical exchange cannot be ruled out.

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Scheme 2. Proposed Water Exchange Mechanism in a 5-Coordinated Hydrated Pt(II) Ion, $[\text{Pt}(\text{H}_2\text{O})_5]^{2+}$, through an Interchange (I_a) Mechanism, with $\text{Pt}-\text{O}_{\text{eq}}$ 2.01(2) Å and $\text{Pt}-\text{O}_{\text{ax}}$ 2.39(2) Å in Reactant and Product (See Text)



These results are comparable to those obtained from an EXAFS study on palladium(II) hydration, also with four water molecules tightly bound to the Pd^{2+} ion in the equatorial plane with $\text{Pd}-\text{O}$ 2.00(1) Å, $\sigma^2 = 0.0030(3)$ Å². Two (or possibly one) loosely coordinated axial water molecules were proposed with the $\text{Pd}-\text{O}$ distance 2.5 Å and a disorder parameter of $\sigma^2 = 0.015(5)$ Å².²⁹ Recent theoretical calculations on the structure of a hydrated $[\text{Pd}(\text{H}_2\text{O})_4]^{2+}$ ion also proposed two axial water molecules at $\text{Pd}-\text{O}_{\text{ax}} \sim 2.68$ Å.⁴⁵

It is likely that a five-coordinated hydrated platinum(II) ion attains a tetragonal pyramidal configuration, although the magnitude of the displacement of the Pt-atom toward the axial oxygen atom cannot be deduced from the EXAFS modeling. Optimized tetragonal pyramidal geometries show displacements between 0.1 and 0.2 Å for a number of penta-hydrated divalent first row transition metal ions.⁴⁶

Ion-pairing could occur between the hydrated platinum(II) ion and perchlorate ions in the highly concentrated HClO_4 acid (~ 7.5 mol. dm^{-3}). However, as shown in Figure 3(left), the EXAFS oscillations of the hydrated platinum(II) ion in ~ 7.5 and in ~ 1.7 mol. dm^{-3} HClO_4 are quite alike. Moreover, the $\text{Pt}-\text{O}^*$ distances obtained are very similar to that of hydrated *cis*-diammineplatinum(II) (pH = 2.1) where the perchloric acid concentration is quite low. These observations do not support any significant inner-sphere ion pairing, i.e. direct $\text{Pt}^{2+}-\text{OClO}_3^-$ coordination in ~ 7.5 mol. dm^{-3} HClO_4 .

Conclusions

High quality Pt L_3 -edge EXAFS spectra of the hydrated platinum (II) and *cis*-diammineplatinum(II) ions in acidic aqueous solutions have been obtained and analyzed. Model curve fittings to the EXAFS oscillations of the hydrated platinum(II) ion are consistent with four tightly bound equivalent water molecules at the $\text{Pt}-\text{O}$ distance 2.01(2) Å and one (or possibly two) axial water molecule(s) at 2.39(2) Å. The axial water coordination would explain the previously reported small activation volume for the slow water exchange in the $[\text{Pt}(\text{H}_2\text{O})_4]^{2+}$ entity ($\Delta V^\ddagger = -4.6 \pm 0.2$ cm³ mol⁻¹),¹⁶ as corresponding to an interchange mechanism, e.g., relocating an axial water molecule in a 5-coordinated tetragonal

pyramidal reactant over a trigonal bipyramid-like transition state to an equatorial position (Scheme 2).

Also for the hydrated *cis*-diammineplatinum(II) complex a similar coordination environment is found. A *cis*- $[\text{Pt}(\text{NH}_3)_2(\text{H}_2\text{O})_m]^{2+}$ ($m = 3-4$) complex is formed by four strongly bonded ammine/water molecules with $\text{Pt}-\text{O}/\text{N}$ bond distances 2.01(2) Å and one (or possibly two) axial water molecule(s) at $\text{Pt}-\text{O}$ 2.37(2) Å. The similarity of the EXAFS disorder parameters for the two different complexes favors models VI (Tables 1 and 2); i.e., a tetragonal pyramidal structure with one axial water molecule, even though an elongated octahedral configuration with two coordinated axial water molecules cannot be excluded.

The coordination of axial water already in the ground-state structures provides a new basis for theoretical computational studies, in particular when connecting the function of the anticancer drug *cis*-platin to its ligand exchange reactions, where usually four-coordinated species are considered as the ground-state and product.

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Supporting Information Available: Curve fittings of the k^3 -weighted EXAFS spectrum of hydrated Pt(II) ion using the EXAFSPAK program. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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