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Supporting Information

for

Kinetics of Aquation and Anation of Ruthenium(II) Arene Anticancer Complexes, Acidity and X-ray Structures of Aqua Adducts

Fuyi Wang, Haimei Chen, Simon Parsons, Iain D. H. Oswald, James E. Davidson, Peter J. Sadler*[a]

Tables S1-S3

Figures S1-S10

[a] Professor Dr. P. J. Sadler, Dr F. Wang, H. Chen, Dr. S. Parsons, I. D. H. Oswald, J. E. Davidson
School of Chemistry, University of Edinburgh, West Main Road, Edinburgh EH9 3JJ (UK)
Fax: (+ 44)131-650-6452
Email: p.j.sadler@ed.ac.uk

Table S1. Selected bond lengths (Å) and angles (°) for [(η^6-THA)Ru(en)(H_2O)$_{0.5}$ (OH)$_{0.5}$][PF_6]$_{1.5}$ (**5A**) and [(η^6-DHA)Ru(en)(H_2O)][PF_6]$_2$·2(H_2O) (**6b**).

	5A	**6b (Ru2)**
Ru1-O1w	2.131(6)	2.155(5) (-O2)
Ru1-N1B	2.121(6)	2.135(6) (-N14)
Ru1-N2B	2.121(6) (N1B#)	2.118(6) (-N24)
Ru1-C1A	2.196(6)	2.264(7) (-C13)
Ru1-C2A	2.168(7)	2.184(7) (-C23)
Ru1-C3A	2.147(7)	2.164(7) (-C33)
Ru1-C4A	2.196(6) (C1A#)	2.180(8) (-C43)
Ru1-C5A	2.168(7) (C2A#)	2.201(8) (-C53)
Ru1-C6A	2.147(7) (C3A#)	2.213(7) (-C63)
N1B-Ru1-N2B	79.1(4) (N1B-Ru1-N1B#)	79.7(2) N14-Ru2-N24
N1B-Ru1-O1w	81.5(2)	82.9(2) (N14-Ru2-O2)
N2B-Ru1-O1w	81.5(2) (N1B#-Ru1-O1w)	80.6(2) (N24-Ru2-O2)

Table S2. Rate constants for the aquation or anation of ruthenium complexes.

Complex	k / s^{-1}	pK_a	Temp. / K	I / M	Ref.
Aquation					
$[Ru(H_2O)_5Cl]^+$	9.0×10^{-4}		296.8		1
Cis-$[Ru(H_2O)_4Cl_2]$	0.13		298.0		1
Trans-$[Ru(H_2O)_4Cl_2]$	0.14		298.0		1
$[(\eta^6\text{-Bip})Ru(en)Cl]^+$	1.23×10^{-3}		298.0	0.1	This work
$[(\eta^6\text{-THA})Ru(en)Cl]^+$	2.26×10^{-3}		298.0	0.1	This work
$[(\eta^6\text{-DHA})Ru(en)Cl]^+$	2.15×10^{-3}		298.0	0.1	This work
$[Ru(NH_3)_5Cl]Cl_2$	3.1×10^{-6}	4.2[a]	308	0.1	2
$[Ru(NH_3)_5Cl]Cl_2$	8.92×10^{-3} [b]		297.6	0.1	2
Cis-$[Ru(NH_3)_4Cl_2]Cl$	0.88×10^{-4}		298.0	0.1	3
Cis-$[Ru(en)_2Cl_2]Cl$	3.7×10^{-4}		298.0	0.1	3
Cis-α-$[Ru(trien)Cl_2]Cl$	42×10^{-4}		298.0	0.1	3
Cis-$[Ru(en)_2Cl(H_2O)]Cl$	2.7×10^{-5}	4[a]	298.0	0.01	4
$[Ru(NH_3)_5Cl]Cl_2$	10.8×10^{-6}		318.5	0.01	5
$[Ru(en)_2Cl_2]Cl$	3.23×10^{-5}		298.0	0.01	5
$[Ru(NH_3)_4Cl_2]Cl$	1.7×10^{-6}		298.0	0.1	6
$[Ru(en)_2Cl_2]^+$	4.2×10^{-6}		298.0	0.1	6
α-$[Ru(trien)Cl_2]^+$	4.8×10^{-7}		298.0	0.1	6
$[Ru(cyclam)Cl_2]^+$	3.0×10^{-7}		375	0.1	6
Anation or Water-exchange					
$[Ru(H_2O)_6]^{2+}$	1.8×10^{-2} [c]	6 - 8	298.0	0.5	7
$[Ru(H_2O)_6]^{3+}$	3.5×10^{-6} [c]	2.47	298.0	0.5	7
$[(\eta^6\text{-}C_6H_6)Ru(H_2O)_3]^{2+}$	11.5 [c]	3.5	298.0	0.5	8
$[(\eta^6\text{-}C_6H_6)Ru(en)(H_2O)]^{2+}$		7.9	293.0	0.1	9
$[(\eta^6\text{-}C_6H_6)Ru(bpy)(H_2O)]^{2+}$	6.8×10^{-2} [d]	6.9	293.0	0.3	10
$[(\eta^6\text{-cymene})Ru(bpy)(H_2O)]^{2+}$	8.5×10^{-2} [d]	7.2	293.0	0.3	10
$[(\eta^6\text{-}C_6Me_6)Ru(bpy)(H_2O)]^{2+}$	10.2×10^{-2} [d]	7.3	293.0	0.3	10
$[(\eta^6\text{-Bip})Ru(en)(H_2O)]^{2+}$	1.3×10^{-2} [e]	7.71	298.0	0.1	This work
$[(\eta^6\text{-THA})Ru(en)(H_2O)]^{2+}$	3.1×10^{-2} [e]	8.01	298.0	0.1	This work
$[(\eta^6\text{-DHA})Ru(en)(H_2O)]^{2+}$	2.9×10^{-2} [e]	7.89	298.0	0.1	This work

[a] pK_a values for the corresponding monoaqua complexes. [b] In 0.0018 M NaOH; [c] Rate constants for water exchange. [d] Average values of rate constants for the substitution of water by SCN^-, I^-, Br^-, N_3^- and thiourea. [e] Pseudo first-order rate constants for water substitution by chloride (0.1 M).

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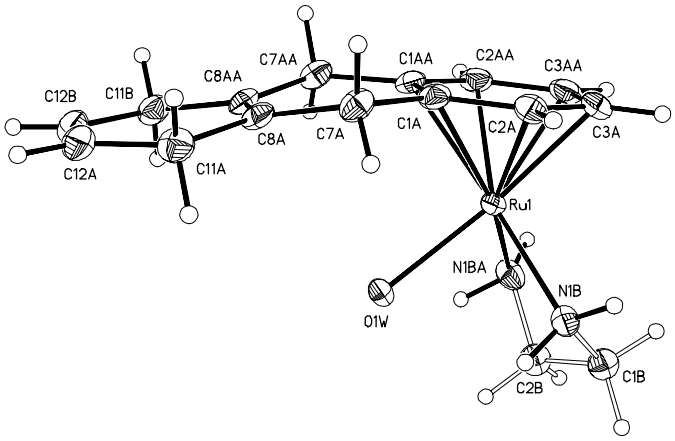
Table S3. Activation parameters for the aquation or anation of ruthenium arene complexes $[(\eta^6\text{-arene})Ru(en)X]^{n+}$ (X = Cl, H_2O)

Complex	E_a / kJ mol^{-1}	$\Delta H^{\ddagger}$ / kJ mol^{-1}	$\Delta S^{\ddagger}$ / J K^{-1} mol^{-1}
$[(\eta^6\text{-Bip})Ru(en)Cl]^+$ **1**	75.6 ± 0.6	73.1 ± 0.6	-55.7 ± 2.0
$[(\eta^6\text{-THA})Ru(en)Cl]^+$ **2**	81.9 ± 6.8	79.4 ± 6.8	-30.7 ± 22.9
$[(\eta^6\text{-DHA})Ru(en)Cl]^+$ **3**	93.6 ± 14.2	91.2 ± 14.2	7.48 ± 30.8
$[(\eta^6\text{-Bip})Ru(en)(H_2O)]^{2+}$ **4**	76.7 ± 1.3	74.1 ± 1.3	-13.6 ± 4.5
$[(\eta^6\text{-THA})Ru(en)(H_2O)]^{2+}$ **5**	62.3 ± 13.0	59.8 ± 13.0	-56.4 ± 43.7
$[(\eta^6\text{-DHA})Ru(en)(H_2O)]^{2+}$ **6**	77.4 ± 12.2	74.9 ± 12.2	-5.82 ± 41.0
$[(\eta^6\text{-Benzene})Ru(en)Cl]^+$ **7**[a]	82.1 ± 2.1	79.5 ± 3.4	-30.8 ± 11.5

[a] In 100 mM $NaClO_4$ solution, the aquation rate constants for **7** were determined to be (0.55 ± 0.01), (1.02 ± 0.01), (1.98 ± 0.02), (3.21 ± 0.02), (5.41 ± 0.05) and (8.39 ± 0.09) × 10^{-3} s^{-1} at 288, 293, 298, 303, 308 and 313 K, respectively.

a) cation 5A



b) cation 5B

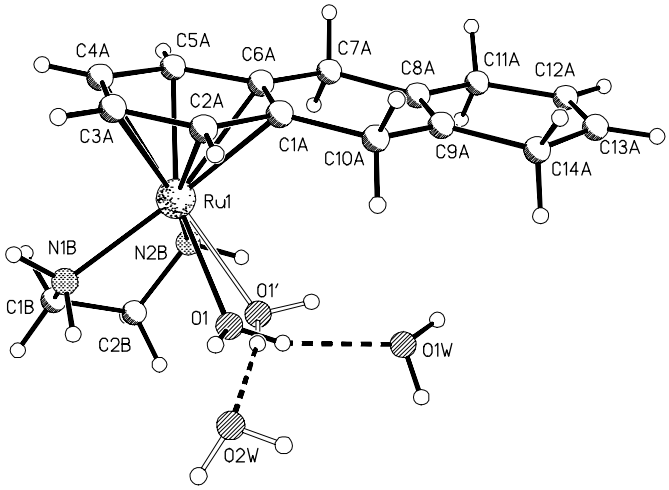
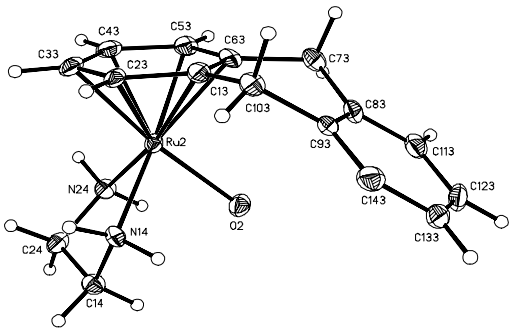
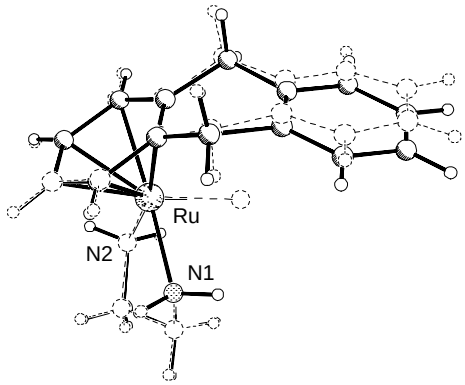


Figure S1. X-ray structures for a) cation **5A**, and b) cation **5B.** For **5B**, the coordinated OH_2 was disordered and placed at two positions O1 and O1' with occupancy factors of 0.7 and 0.3, respectively, and the H-bonded OH_2 was placed correspondingly at two positions O1w (0.7) and O2w (0.3).

a) Cation **6b**



b) Cation **6a** (dotted)/**6b**(solid)



c) H-bonding

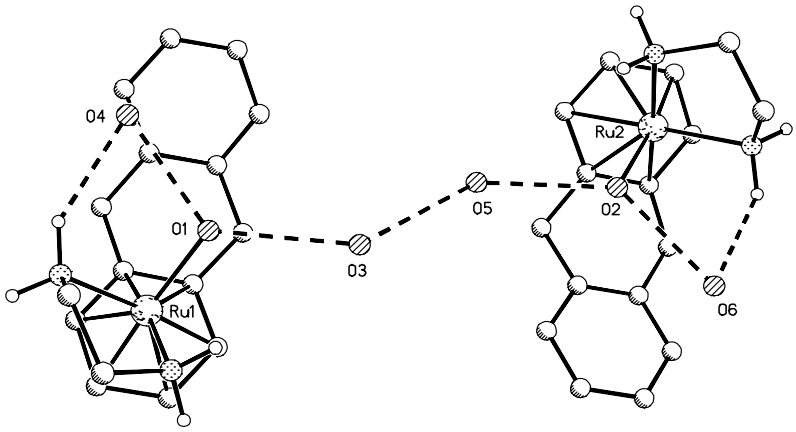


Figure S2. a) X-ray structure and atom numbering scheme for $[(\eta^6$-DHA)Ru(en)$(H_2O)]^{2+}$ (**6b**) in complex **6**. b) Comparison of the conformations of the two cations **6a** and **6b** in the asymmetric unit, alignments are based on a superposition of the labelled atoms (Ru, N1 and N2 of en). c) Intermolecular hydrogen bonding involving en NH and O(w) in the crystal structure of complex **6**.

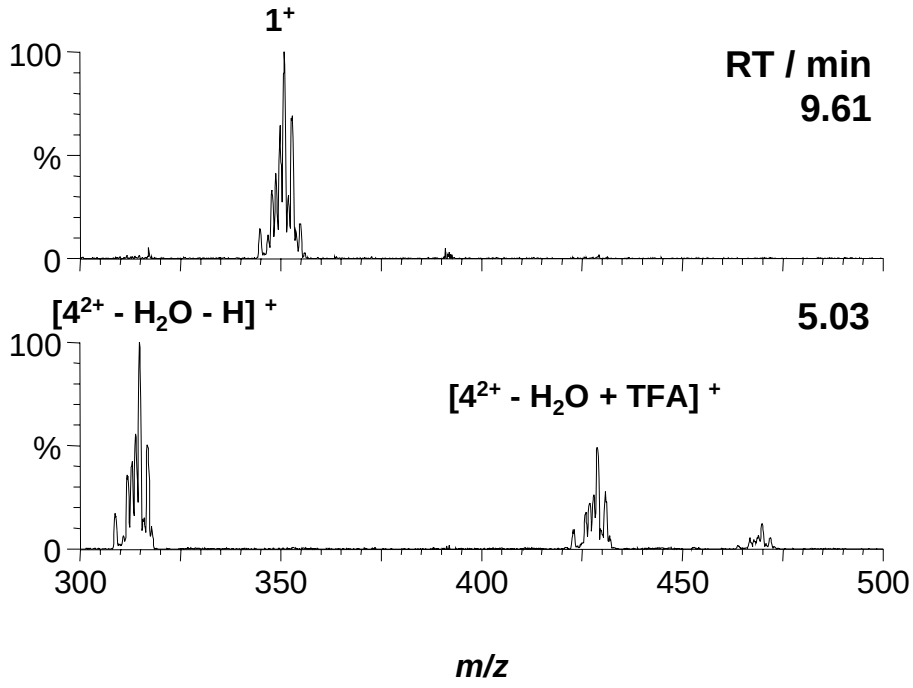


Figure S3a. Online ESI mass spectra of HPLC fractions from a 2 mM aqueous solution of $[(\eta^6\text{-Bip})Ru(en)Cl][PF_6]$ (**1**). Two singly-charged ion peaks were observed for the fraction eluting at 5.03 min (Figure 2). The ion peak at *m/z* 314.8 is assignable to the hydrolysis product $[(\eta^6\text{-Bip})Ru(en)(H_2O)]^{2+}$ ($\mathbf{4}^{2+}$) after loss of the aqua ligand and a proton (calc. *m/z* 315.0 for $[\mathbf{4}^{2+} - H_2O - H]^+$), and the ion peak at *m/z* 428.9 corresponds to a TFA adduct of the aqua product $[(\eta^6\text{-Bip})Ru(en)(CF_3COO)]^+$ (calc. *m/z* 429.0 for $[\mathbf{4}^{2+} - H_2O + TFA]^+$). TFA is the ion-pairing reagent used for the HPLC separation. For the second fraction at 9.61 min, one singly-charged ion peak at *m/z* 350.9 was detected, assignable to the intact cation $[(\eta^6\text{-Bip})Ru(en)Cl]^+$ (calc. *m/z* 351.0 for $\mathbf{1}^+$).

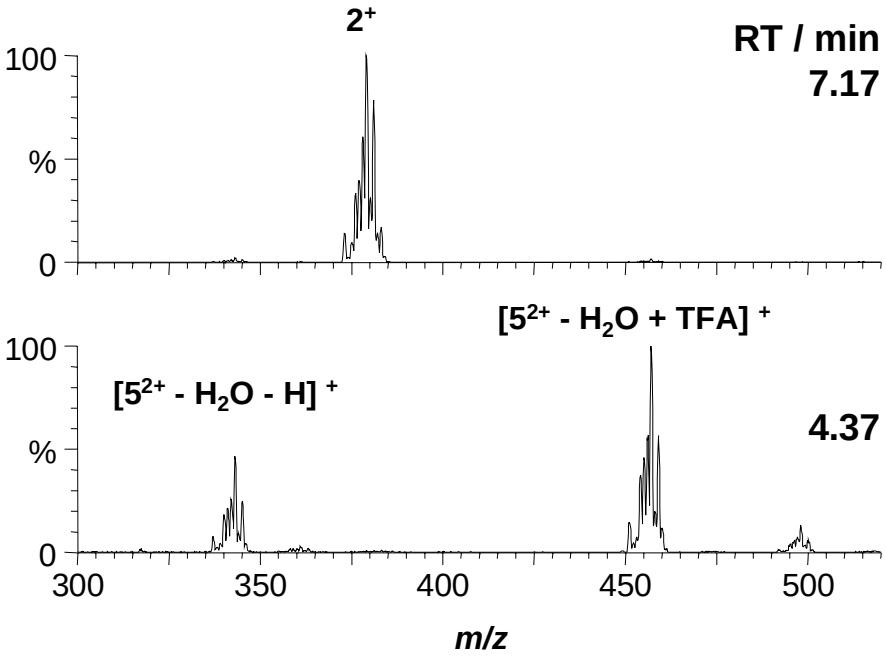


Figure S3b. Online ESI mass spectra of HPLC fractions from a 2 mM aqueous solution of $[(\eta^6\text{-THA})Ru(en)Cl][PF_6]$ (**2**). Two singly-charged ion peaks were observed for the fraction eluting at 4.37 min (Figure 2). The ion peak at *m/z* 343.1 is assignable to the hydrolysis product $[(\eta^6\text{-THA})Ru(en)(H_2O)]^{2+}$ ($\mathbf{5}^{2+}$) after loss of the aqua ligand and a proton (calc. *m/z* 343.1 for $[\mathbf{5}^{2+} - H_2O - H]^+$), and the ion peak at *m/z* 457.1 corresponds to a TFA adduct of the aqua product $[(\eta^6\text{-THA})Ru(en)(CF_3COO)]^+$ (calc. *m/z* 457.1 for $[\mathbf{5}^{2+} - H_2O + TFA]^+$). For the second fraction at 7.17 min, one singly-charged ion peak at *m/z* 379.1 was detected, assignable to the intact cation $[(\eta^6\text{-THA})Ru(en)Cl]^+$ (calc. *m/z* 379.1 for $\mathbf{2}^+$).

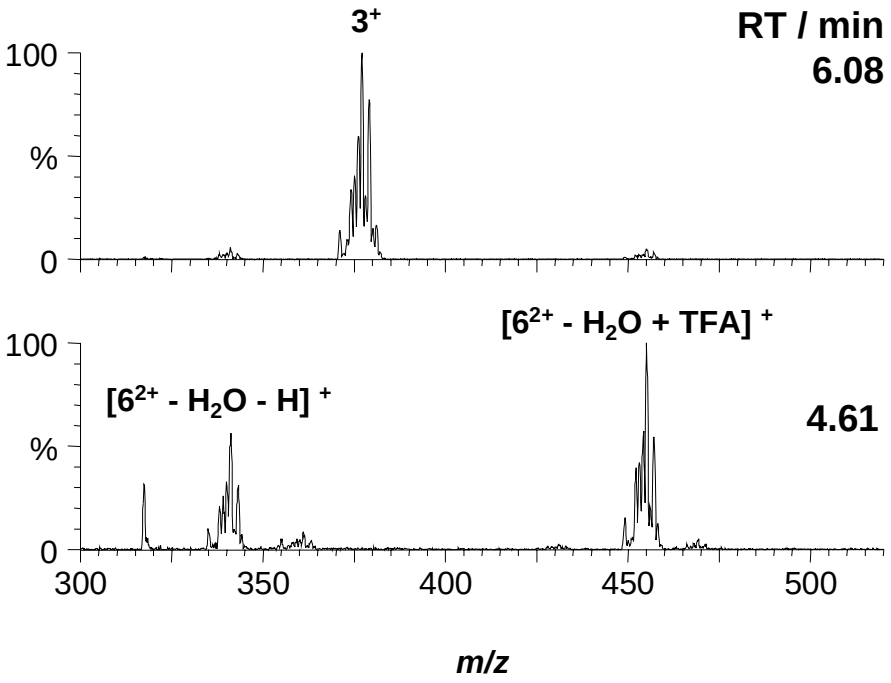


Figure S3c. Online ESI mass spectra of HPLC fractions from a 2 mM aqueous solution of $[(\eta^6\text{-DHA})Ru(en)Cl][PF_6]$ (**3**). Two singly-charged ion peaks were observed for the fraction eluting at 4.61 min (Figure 2). The ion peak at *m/z* 341.1 is assignable to the hydrolysis product $[(\eta^6\text{-DHA})Ru(en)(H_2O)]^{2+}$ ($\mathbf{6}^{2+}$) after loss of the aqua ligand and a proton (calc. *m/z* 341.1 for $[\mathbf{6}^{2+} - H_2O - H]^+$), and the ion peak at *m/z* 455.1 corresponds to a TFA adduct of the aqua product $[(\eta^6\text{-DHA})Ru(en)(CF_3COO)]^+$ (calc. *m/z* 455.1 for $[\mathbf{6}^{2+} - H_2O + TFA]^+$). For the second fraction at 6.08 min, one singly-charged ion peak at *m/z* 377.1 was detected, assignable to the intact cation $[(\eta^6\text{-DHA})Ru(en)Cl]^+$ (calc. *m/z* 377.0 for $\mathbf{3}^+$).

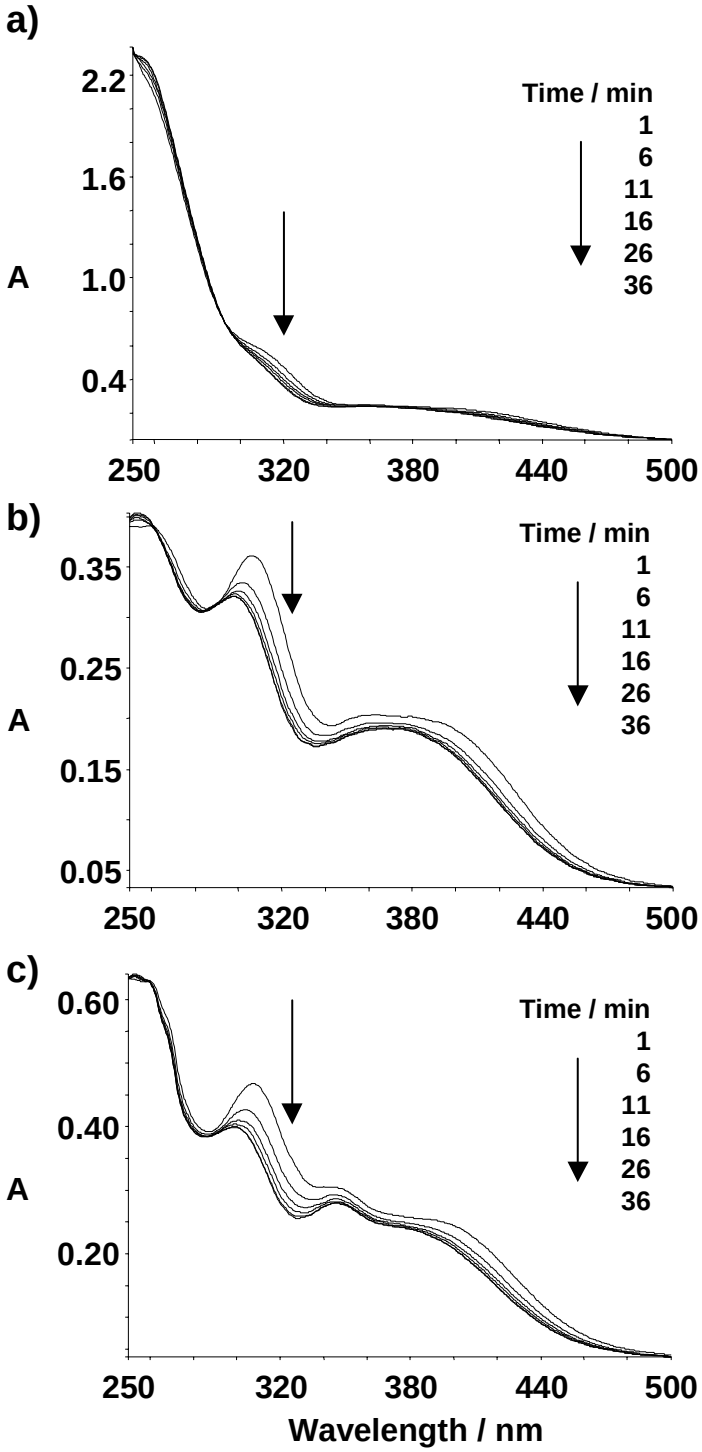


Figure S4. Time evolution of UV-Vis spectra of a) complex **1** (0.3 mM, pH 6.29), b) complex **2** (0.5 mM, pH 6.37), and c) complex **3** (0.5 mM, pH 6.41) in 100 mM $NaClO_4$ solution at 298 K.

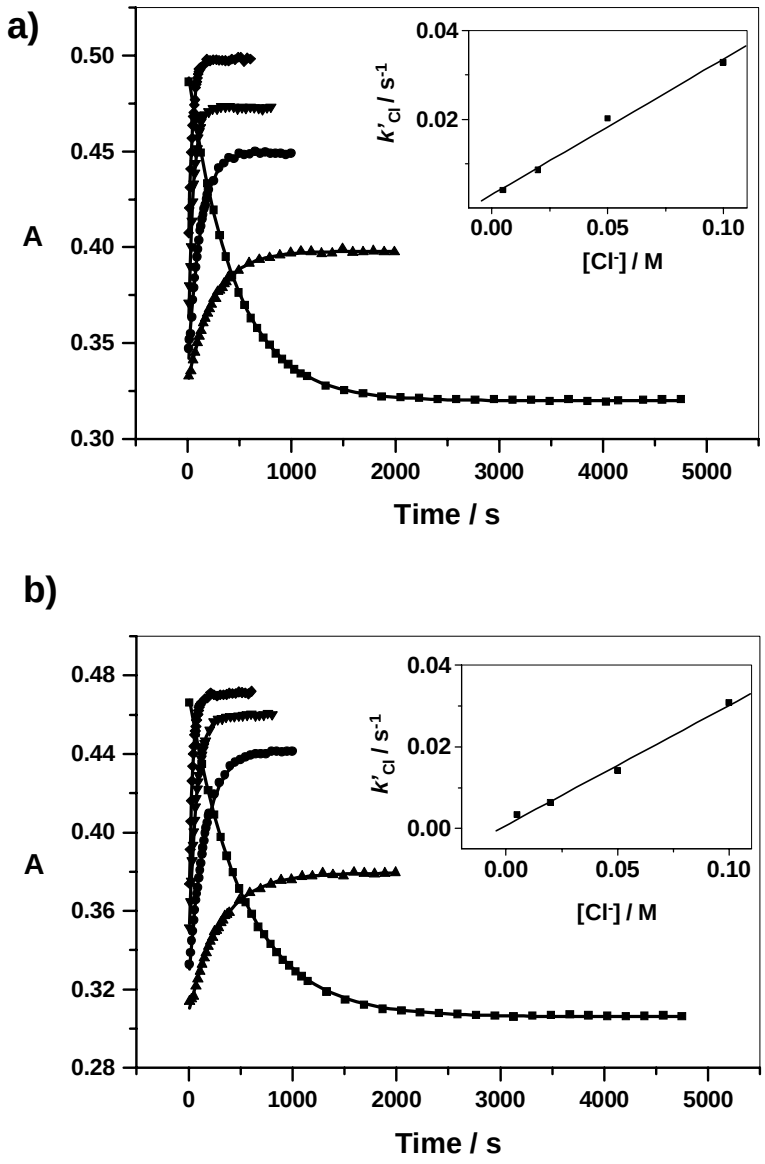


Figure S5. Time-dependence of the absorbance at 315 nm (**2**) and 316 nm (**3**) for the hydrolysis of a) complex **2** (0.5 mM, pH 6.37) and b) complex **3** (0.5 mM, pH 6.41) in 100 mM $NaClO_4$ solution at 298 K. The full lines represent computer fits giving the first order rate constants listed in Table 6 for the aquation, and pseudo-first order rate constants for anations. Labels: aquation (■), anation with addition of 5 (▲), 20 (●), 50 (▼) or 100 (♦) mM NaCl to the hydrolysis equilibrium solution.

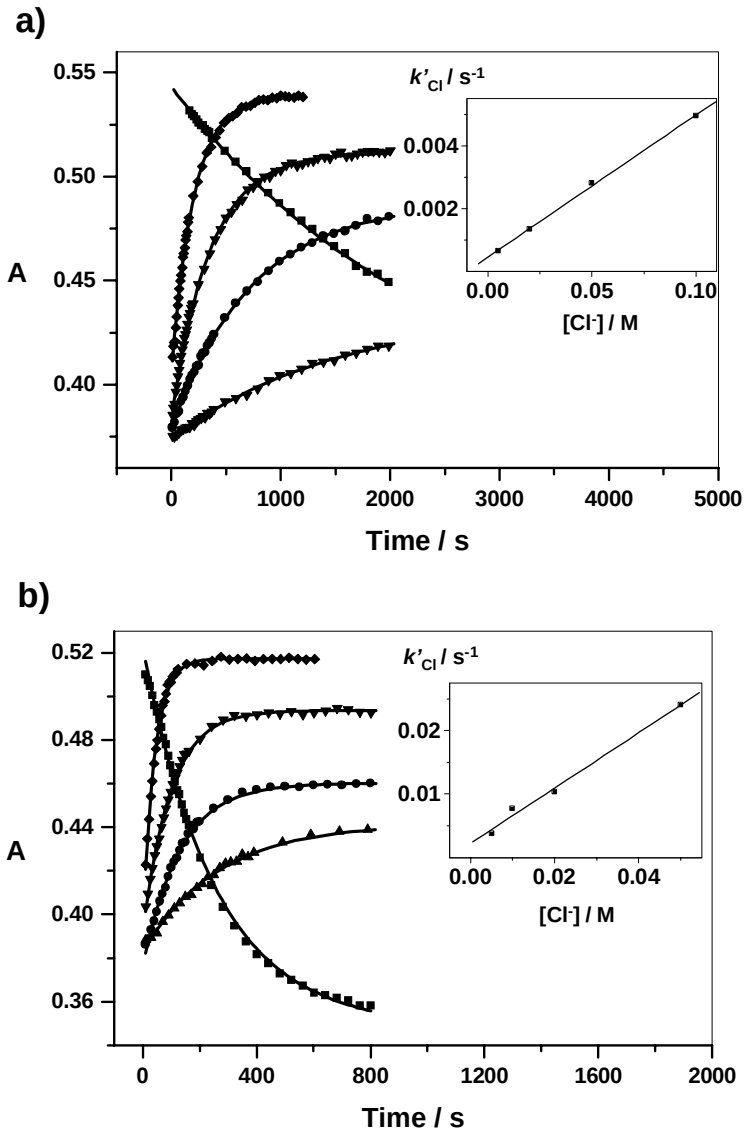


Figure S6. Time-dependence of the absorbance at 319 nm for the hydrolysis of 0.3 mM complex **1** in 100 mM $NaClO_4$ solution at a) 288 and b) 310 K. The full lines represent computer fits giving the first order rate constants listed in Table 6 for the aquation, and pseudo-first order rate constants for anations. Labels: aquation (■), anation with addition of 5 (▲), 20 (●), 50 (▼) or 100 (♦) mM NaCl to the hydrolysis equilibrium solution.

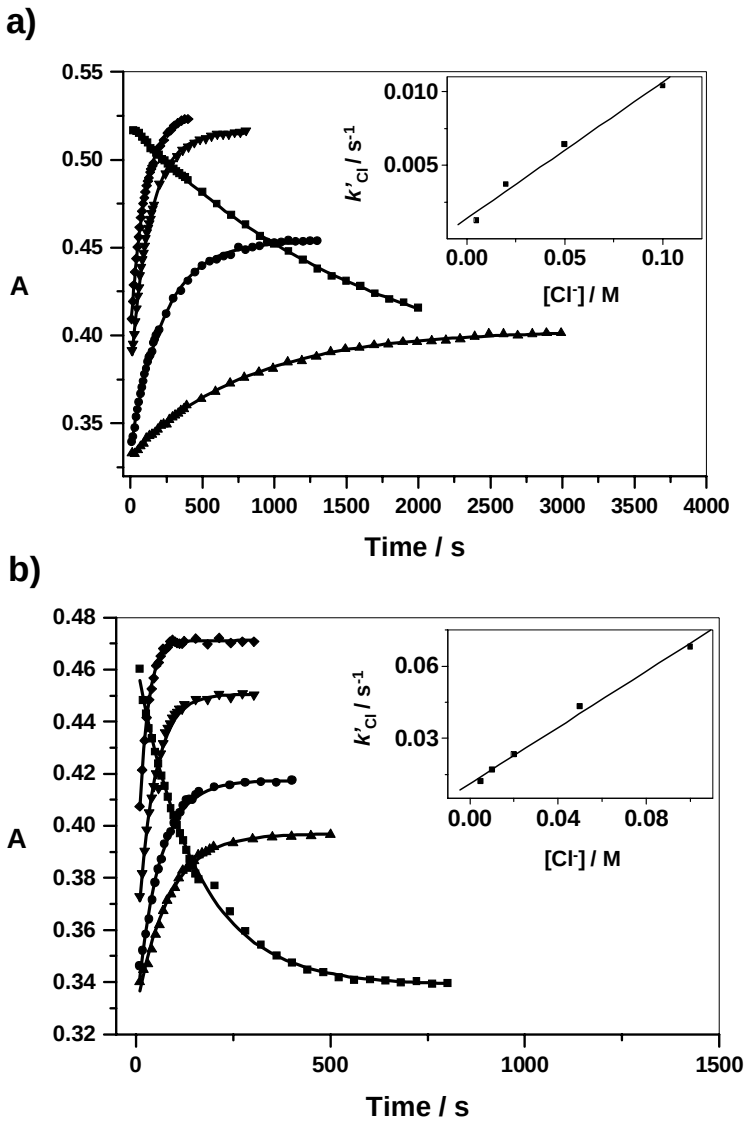


Figure S7. Time-dependence of the absorbance at 315 nm for the hydrolysis of 0.5 mM complex **2** in 100 mM $NaClO_4$ solution at a) 288 and b) 310 K. The full lines represent computer fits giving the first order rate constants listed in Table 6 for the aquation, and pseudo-first order rate constants for anations. Labels: aquation (■), anation with addition of 5 (▲), 20 (●), 50 (▼) or 100 (♦) mM NaCl to the hydrolysis equilibrium solution.

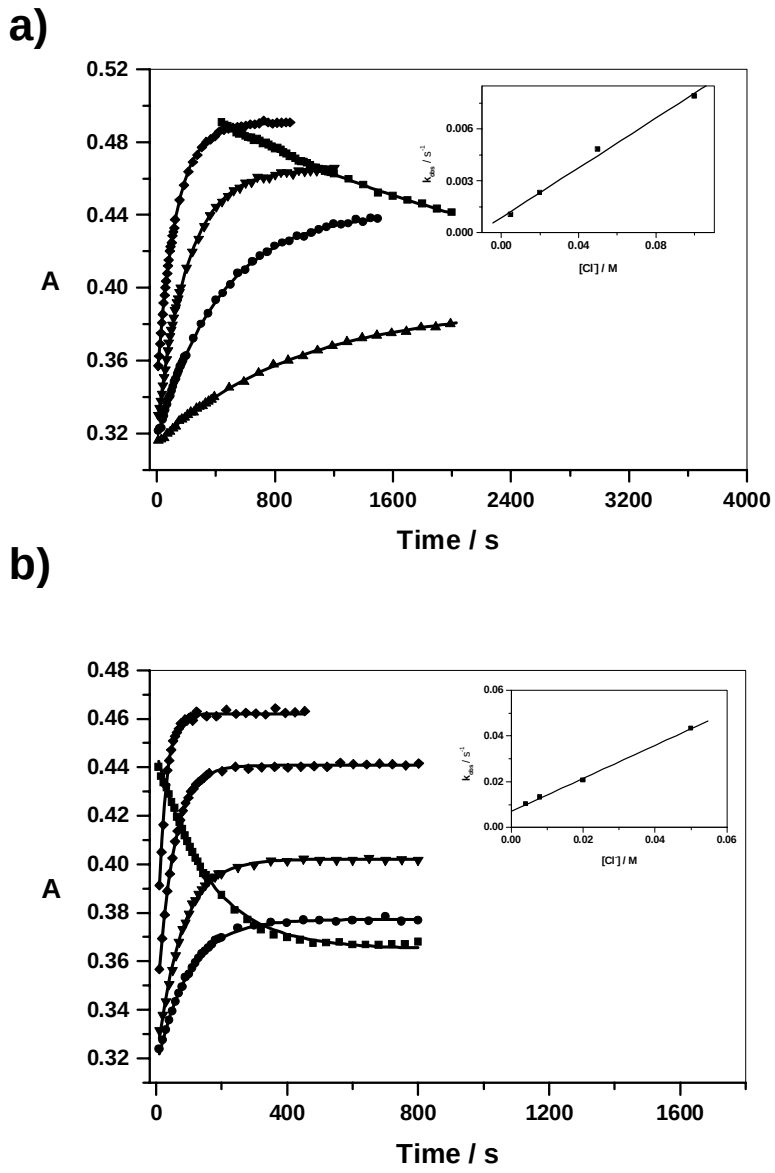


Figure S8. Time-dependence of the absorbance at 316 nm for the hydrolysis of 0.5 mM complex **3** in 100 mM $NaClO_4$ solution at a) 288 and b) 310 K. The full lines represent computer fits giving the first order rate constants listed in Table 6 for the aquation, and pseudo-first order rate constants for anations. Labels: aquation (■), anation with addition of 5 (▲), 20 (●), 50 (▼) or 100 (♦) mM NaCl to the hydrolysis equilibrium solution.

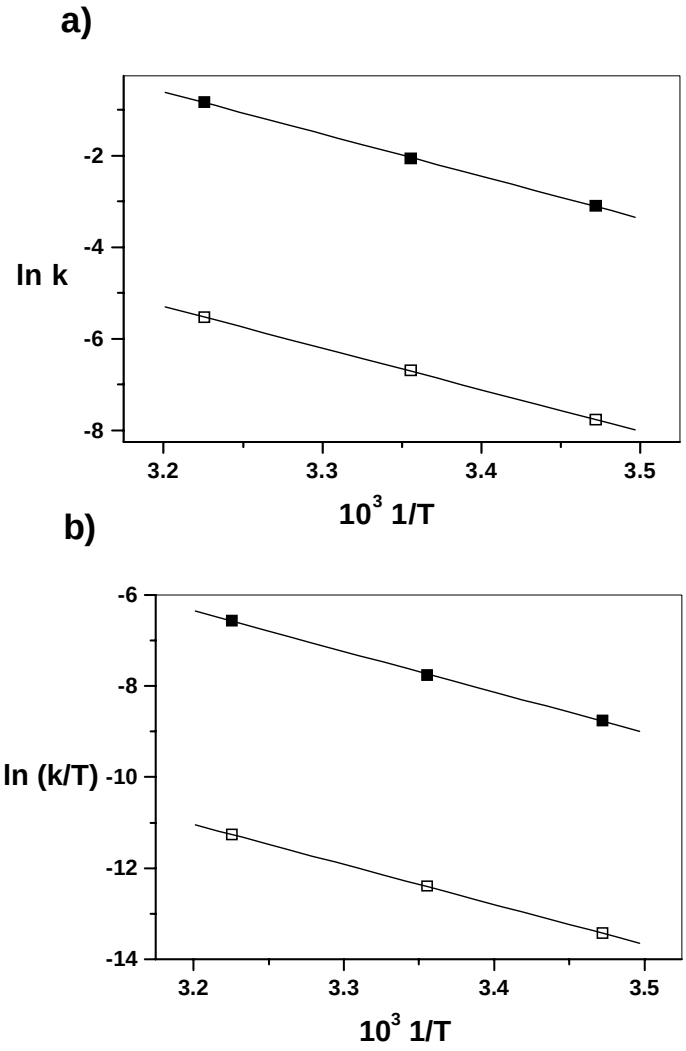


Figure S9. a) Arrhenius plots for the aquation (□) of complex **1** and the anation (■) of complex **4** in 100 mM $NaClO_4$. The solid lines are computer best fits with slopes ($-E_a$ / R) of -9.09×10^3 and -9.21×10^3, giving values of E_a = 75.6 (aquation) and 76.6 (anation) kJ mol^{-1}, respectively. b) Eyring plots for the aquation (□) of complex **1** and the anation (■) of complex **4** in 100 mM $NaClO_4$. The slopes ($-\Delta H^{\ddagger}$ / R) are -8.79×10^3 and -8.91×10^3, leading to $\Delta H^{\ddagger}$ = 73.1 (aquation) and 74.1 (anation) kJ mol^{-1}, respectively. The intercepts ($\ln(\mathbf{k}/\boldsymbol{h}) + \Delta S^{\ddagger}/R$) are 17.1, 22.2 leading to $\Delta S^{\ddagger}$ = -55.6 (aquation) and -13.6 (anation) J K^{-1} mol^{-1}, respectively.

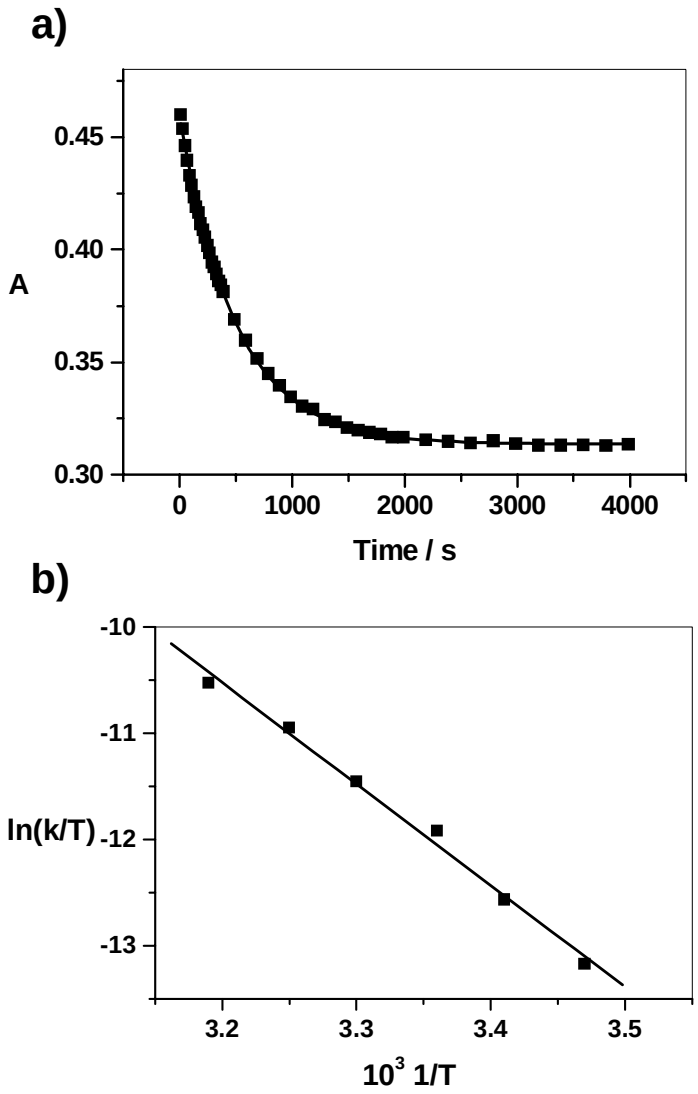


Figure S10. a) Time-dependence of the absorbance at 315 nm for the aquation of 0.5 mM complex **7** in 100 mM $NaClO_4$ solution at 298 K. The full lines represent computer fits giving the first order rate constants to be $(1.98 \pm 0.02) \times 10^{-3}$ s^{-1}. b) Eyring plot. The slope ($-\Delta H^{\ddagger} / R$) is -9.56×10^3, leading to $\Delta H^{\ddagger} = 79.5$ kJ mol^{-1}, and the intercept ($\ln(\mathbf{k}/\boldsymbol{h}) + \Delta S^{\ddagger}/R$) is 20.1, leading to $\Delta S^{\ddagger} = -30.8$ J K^{-1} mol^{-1}.