

1-(2-picoly)-substituted 1,2,3-triazole as novel chelating ligand for the preparation of ruthenium complexes with potential anticancer activity

Ioannis Bratsos,^{a} Damijana Urankar,^b Ennio Zangrando,^a Petia Genova-Kalou,^c Janez Košmrlj,^b Enzo Alessio,^a Iztok Turel^{b*}*

^a Dipartimento di Scienze Chimiche e Farmaceutiche, Università di Trieste, Via L. Giorgieri 1, 34127 Trieste, Italy.

^b Faculty of Chemistry and Chemical Technology, University of Ljubljana, Aškerčeva 5, Ljubljana, Slovenia.

^c Department of Virology, Laboratory of Herpesvirus Infections and Cell Cultures, National Centre of Infectious and Parasitic Diseases, 44A Stoletov Street, 1233 Sofia, Bulgaria.

SUPPORTING INFORMATION

Figure S1: Crystal packing of complex **1**.

Figure S2: ¹H NMR spectra of **1** and **2** in CDCl₃ at 25.0 °C.

Figure S3: The 2D homonuclear ¹H-¹H COSY and heteronuclear ¹H-¹³C HSQC NMR spectra of **1** in CDCl₃ at 25.0 °C.

Figure S4: ¹H NMR spectra of **3** and **4** in CD₃NO₂ at 25.0 °C.

Figure S5: The ¹H-¹H COSY NMR spectrum of **3** in CD₃NO₂ at 25.0 °C.

Figure S6: The 2D heteronuclear ¹H-¹³C HSQC and HMBC NMR spectra of **3** in CD₃NO₂ at 25.0 °C.

Figure S7: The 2D homonuclear ¹H-¹H COSY and heteronuclear ¹H-¹³C HSQC NMR spectrum of **4** in CD₃NO₂ at 25.0 °C.

Figure S8: ¹H NMR spectral changes during the aquation of **4** in D₂O at 25.0 °C.

Figure S9: ¹H NMR spectral changes upon addition of 100mM NaCl to equilibrated solution of **4** and **3a** in D₂O at 25.0 °C.

Figure S10: ¹H NMR spectral changes during the aquation of **5** in D₂O at 25.0 °C.

Figure S11: Time evolution of UV-Vis spectra of complexes **3**, **4** and **5** in H₂O at 25.0°C.

Figure S12: Time evolution of UV-Vis difference spectra during the aquation of complexes **4** and **5** in H₂O at 25.0°C.

Table 1 and 2: Tables with assignments of ¹H and ¹³C resonances (δ) for complexes **1** – **5** in various solvents and for hydrolysis products **3a** and **5a**.

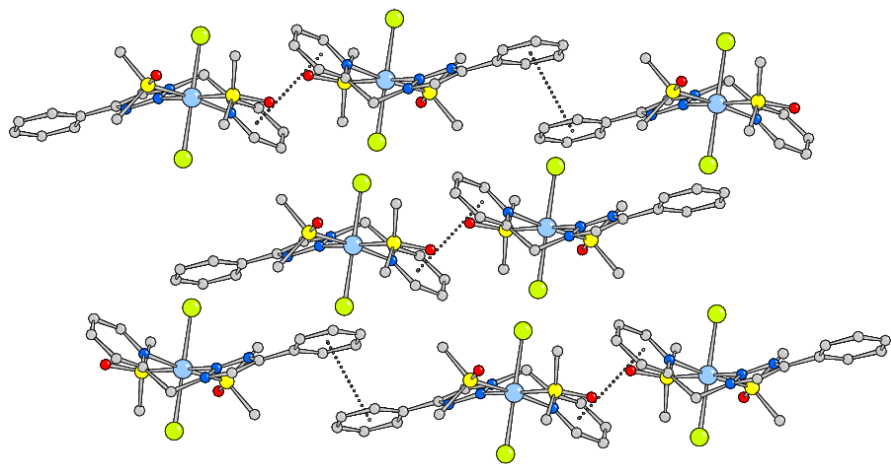


Figure S1. Crystal packing of complex **1** showing 1D arrays of complexes formed by stacking interactions between phenyl rings and between pyridyl rings of symmetry related complexes.

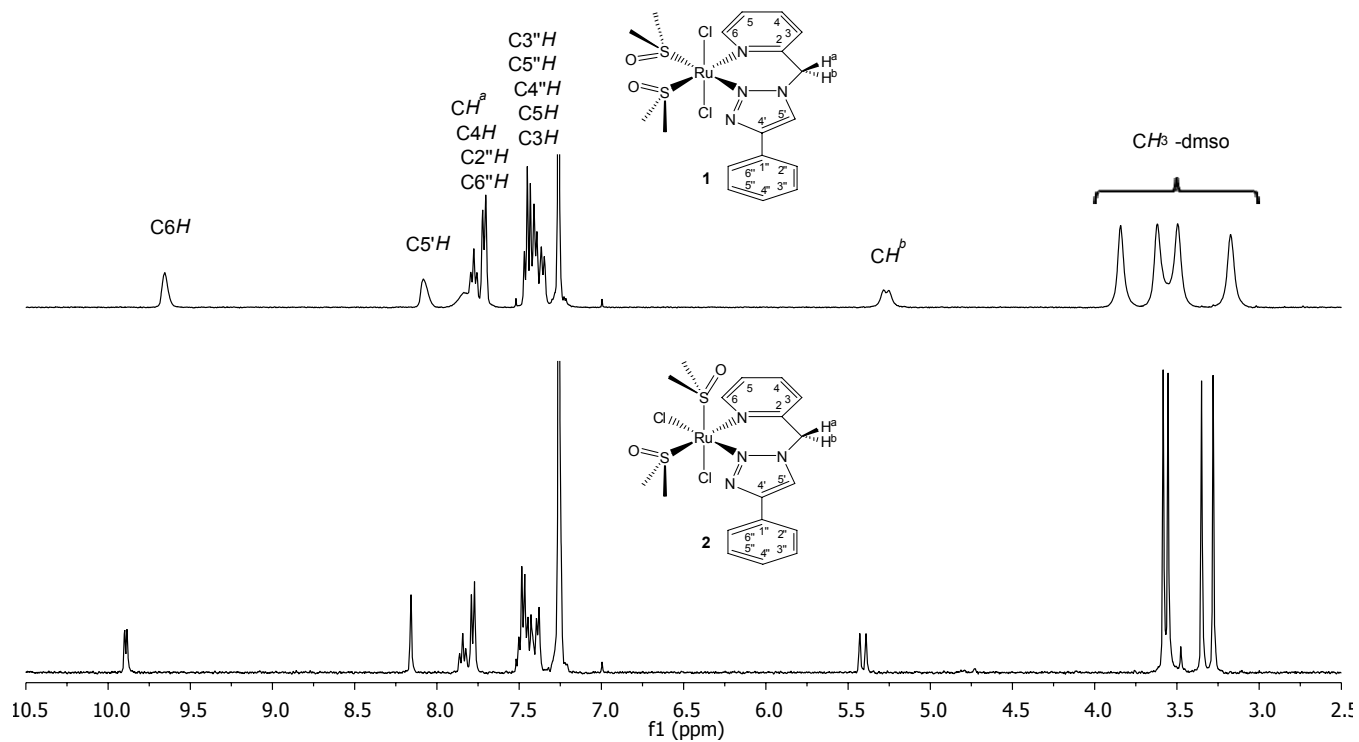


Figure S2. ¹H NMR spectra of **1** (top) and **2** (bottom) in CDCl₃ at 25.0 °C.

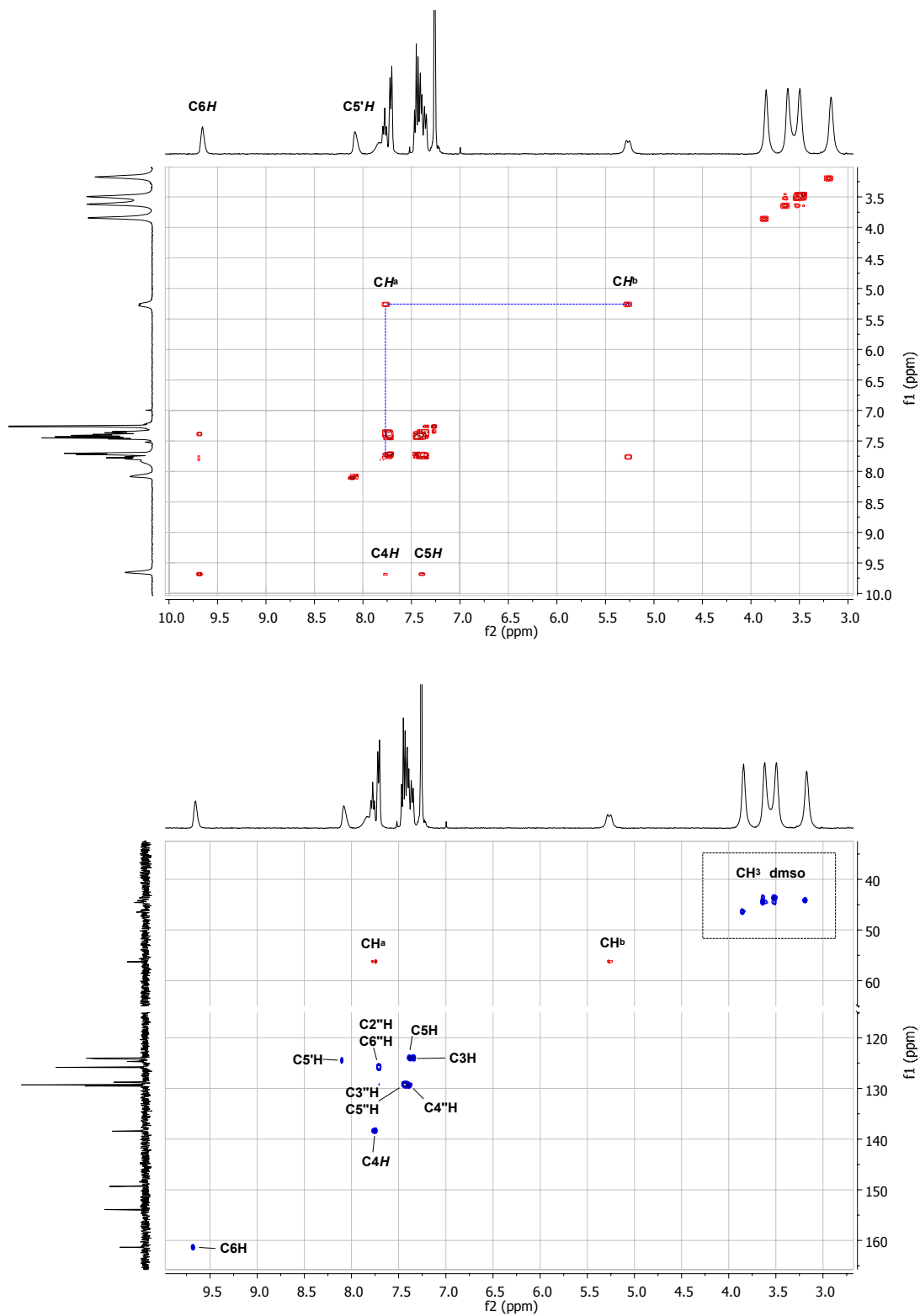


Figure S3. The 2D homonuclear ^1H - ^1H COSY (top) and heteronuclear phase-sensitive ^1H - ^{13}C HSQC (bottom, red cross-peaks = CH_2 ; blue cross-peaks = CH or CH_3) NMR spectra of **1** in CDCl_3 at 25.0°C .

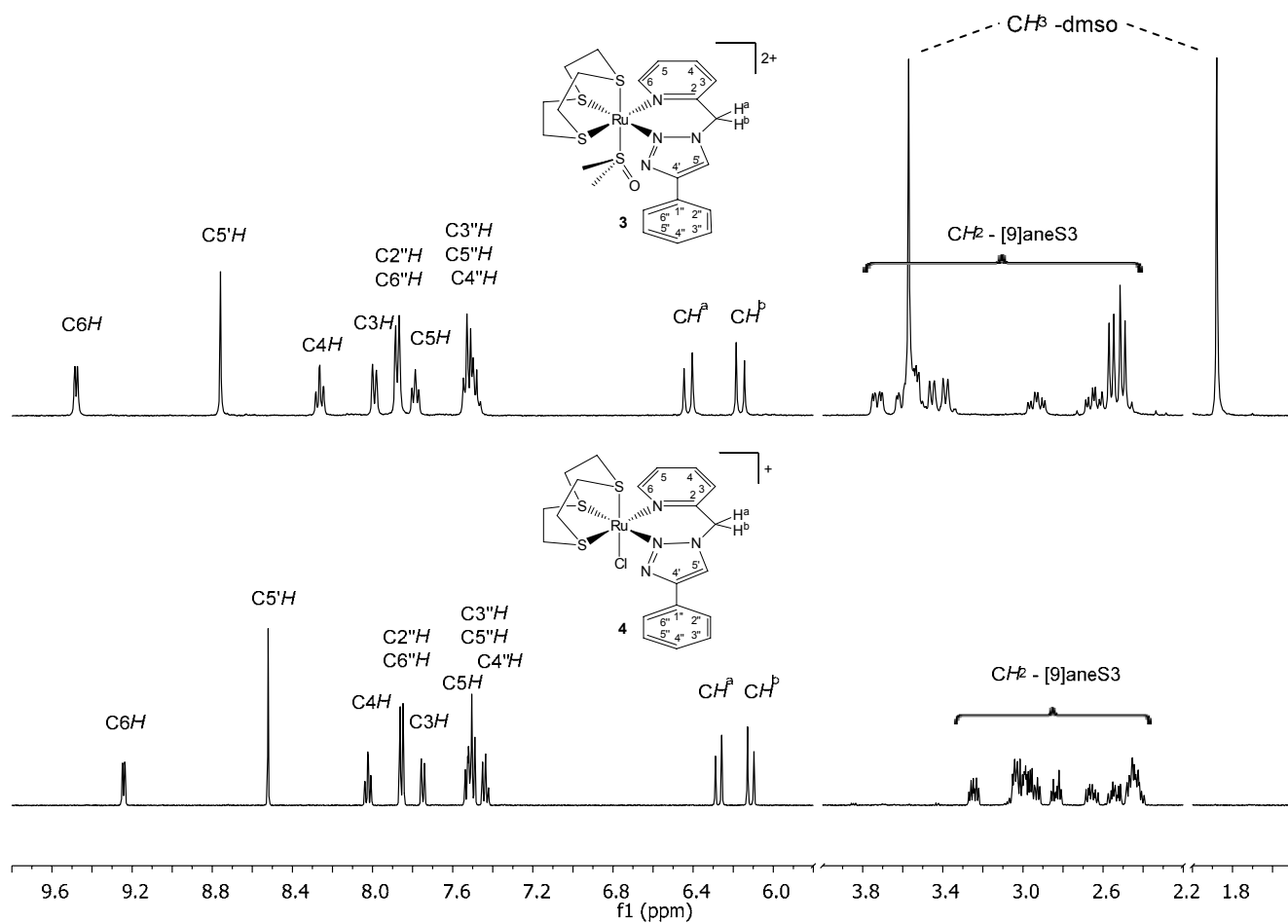


Figure S4. ¹H NMR spectra of **3** (top) and **4** (bottom) in CD₃NO₂ at 25.0 °C.

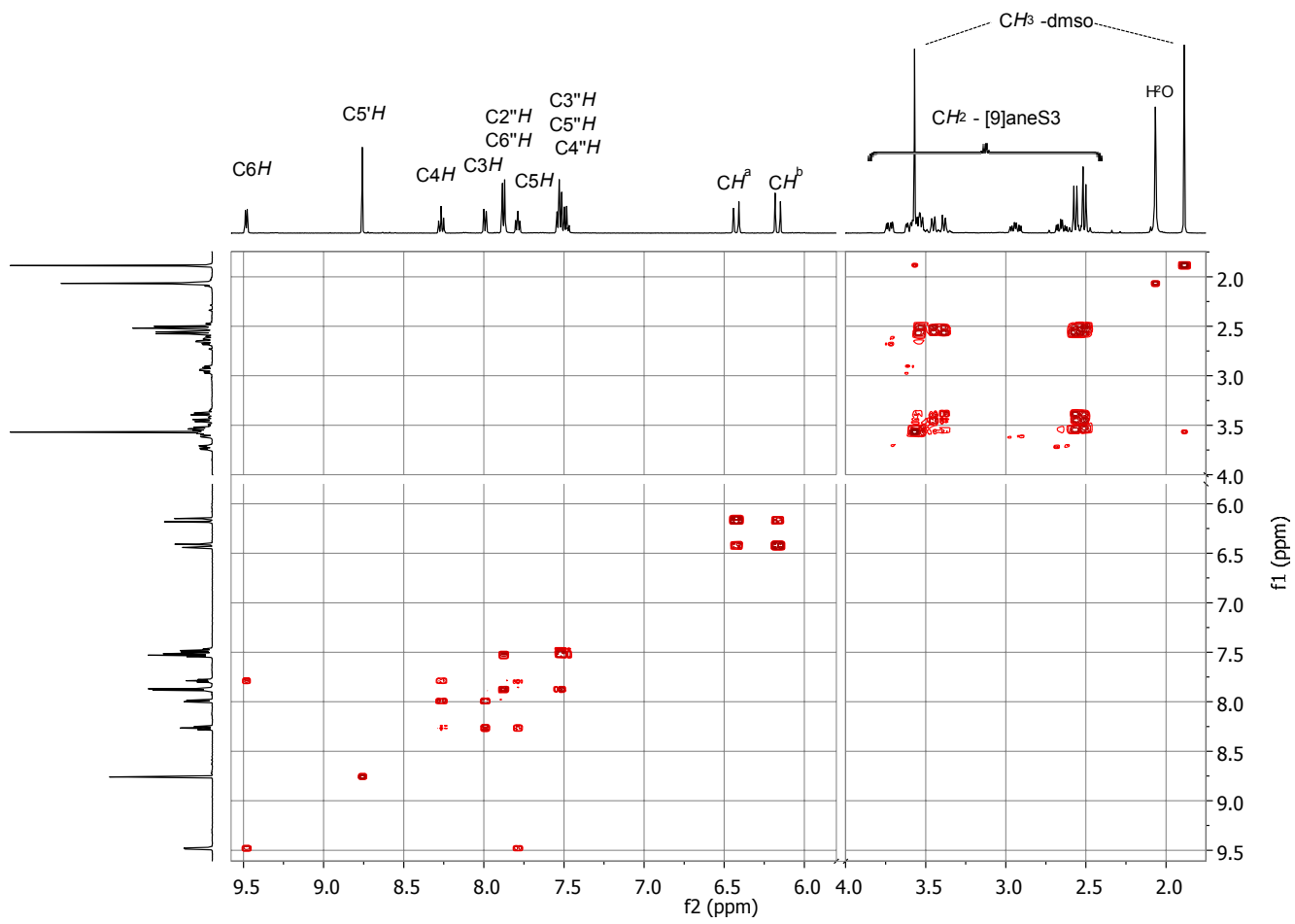


Figure S5. The ^1H - ^1H COSY NMR spectrum of **3** in CD_3NO_2 at 25.0 °C.

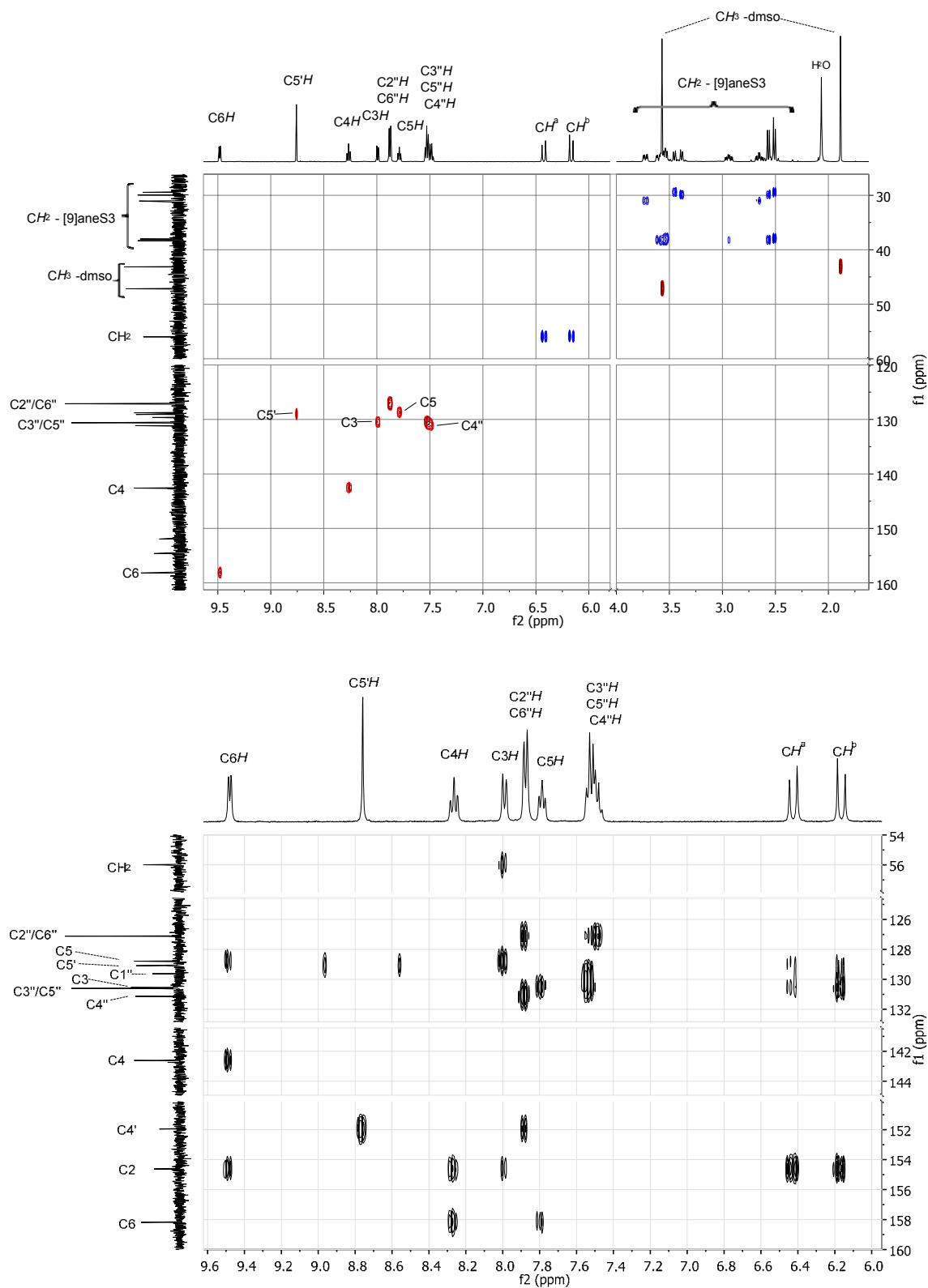


Figure S6. The 2D heteronuclear phase-sensitive ^1H - ^{13}C HSQC (top, blue cross-peaks = CH_2 ; red cross-peaks = CH or CH_3) and HMBC (downfield region, bottom) NMR spectra of **3** in CD_3NO_2 at $25.0\text{ }^\circ\text{C}$.

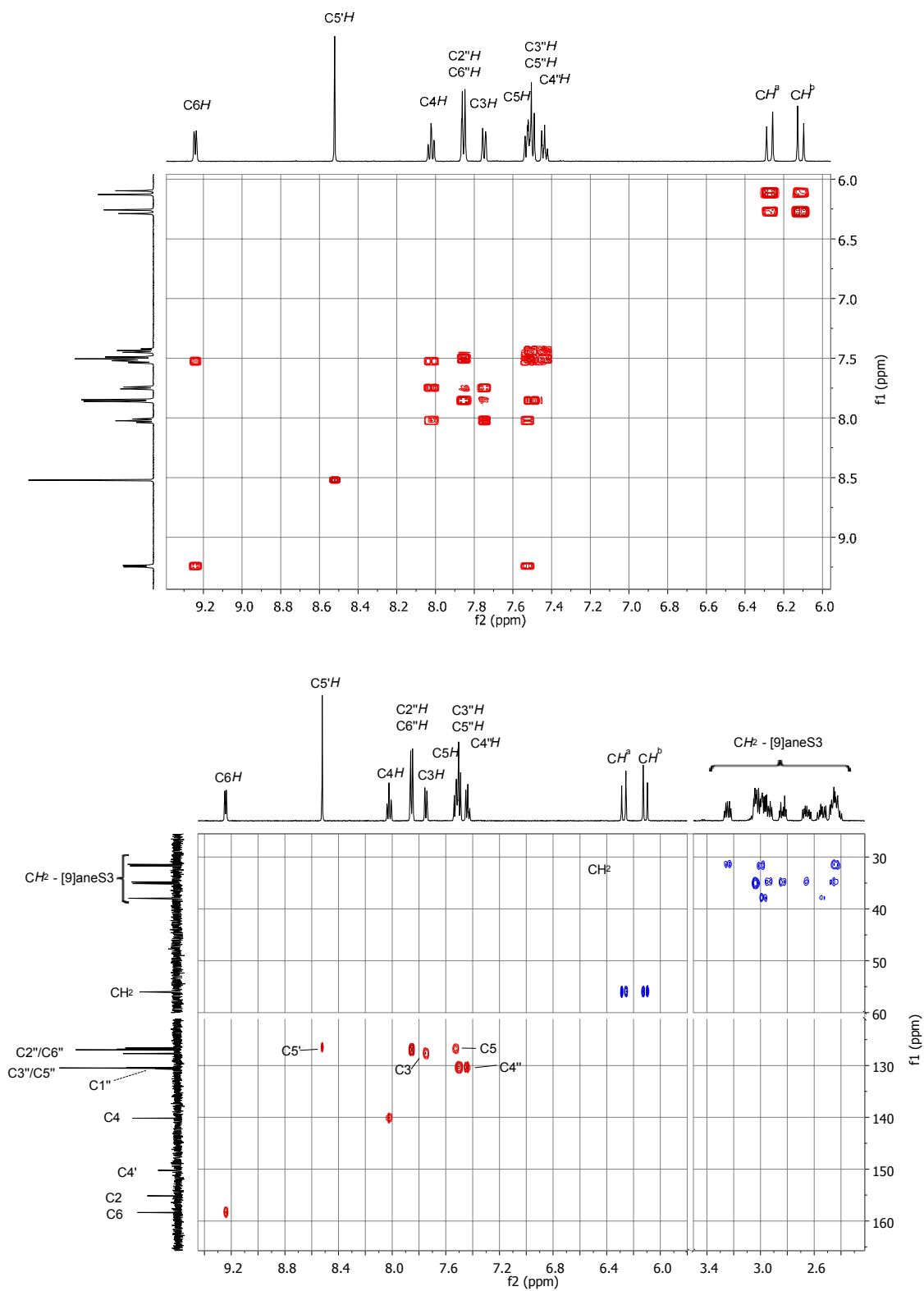


Figure S7. The 2D homonuclear ^1H - ^1H COSY (downfield region, top) and heteronuclear phase-sensitive ^1H - ^{13}C HSQC (bottom, blue cross-peaks = CH_2 ; red cross-peaks = CH or CH_3) NMR spectrum of **4** in CD_3NO_2 at $25.0\text{ }^\circ\text{C}$.

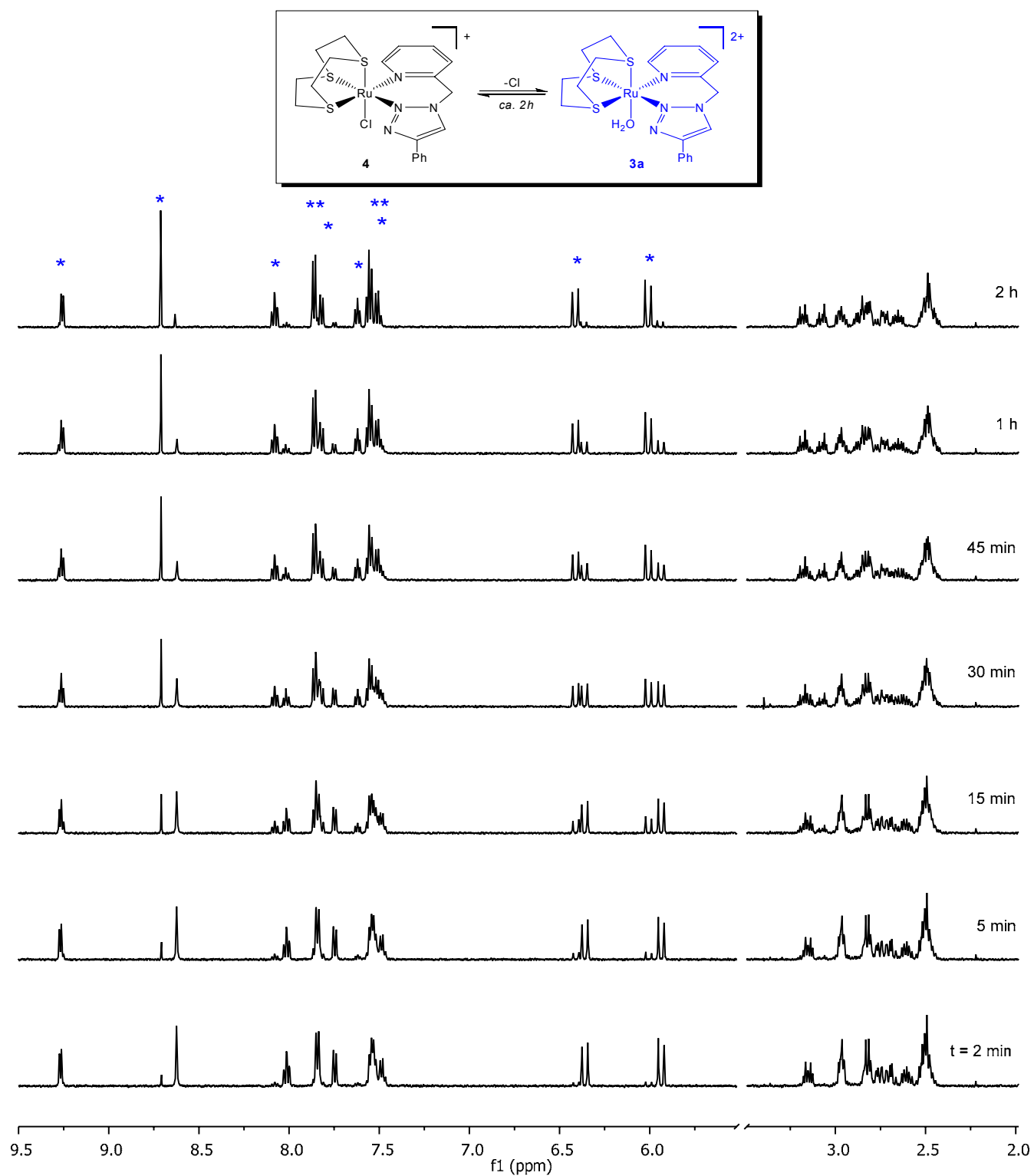


Figure S8. ^1H NMR spectral changes during the hydrolysis of **4** (2.0 mM) in D_2O at 25.0 °C. With (*) are indicated the resonances of the **ptp** ligand of the aqua species **3a**.

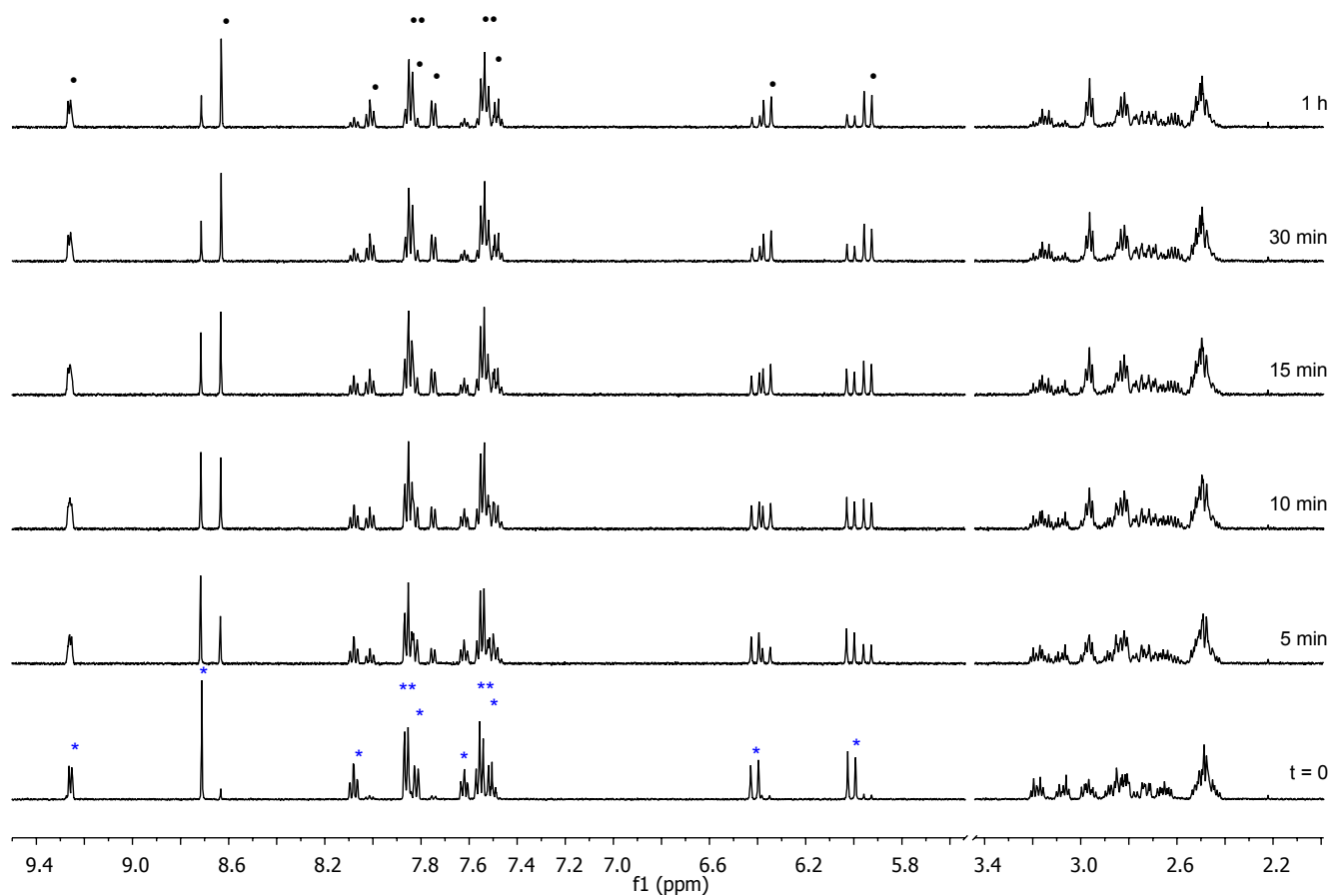


Figure S9. ^1H NMR spectral changes upon addition of 100mM NaCl to equilibrated solution (after 1d) of **4** and **3a** in D_2O at 25.0 $^\circ\text{C}$. With (*) and (•) are indicated the resonances of the **ppt** ligand of the aqua species **3a** and of the **4**, respectively.

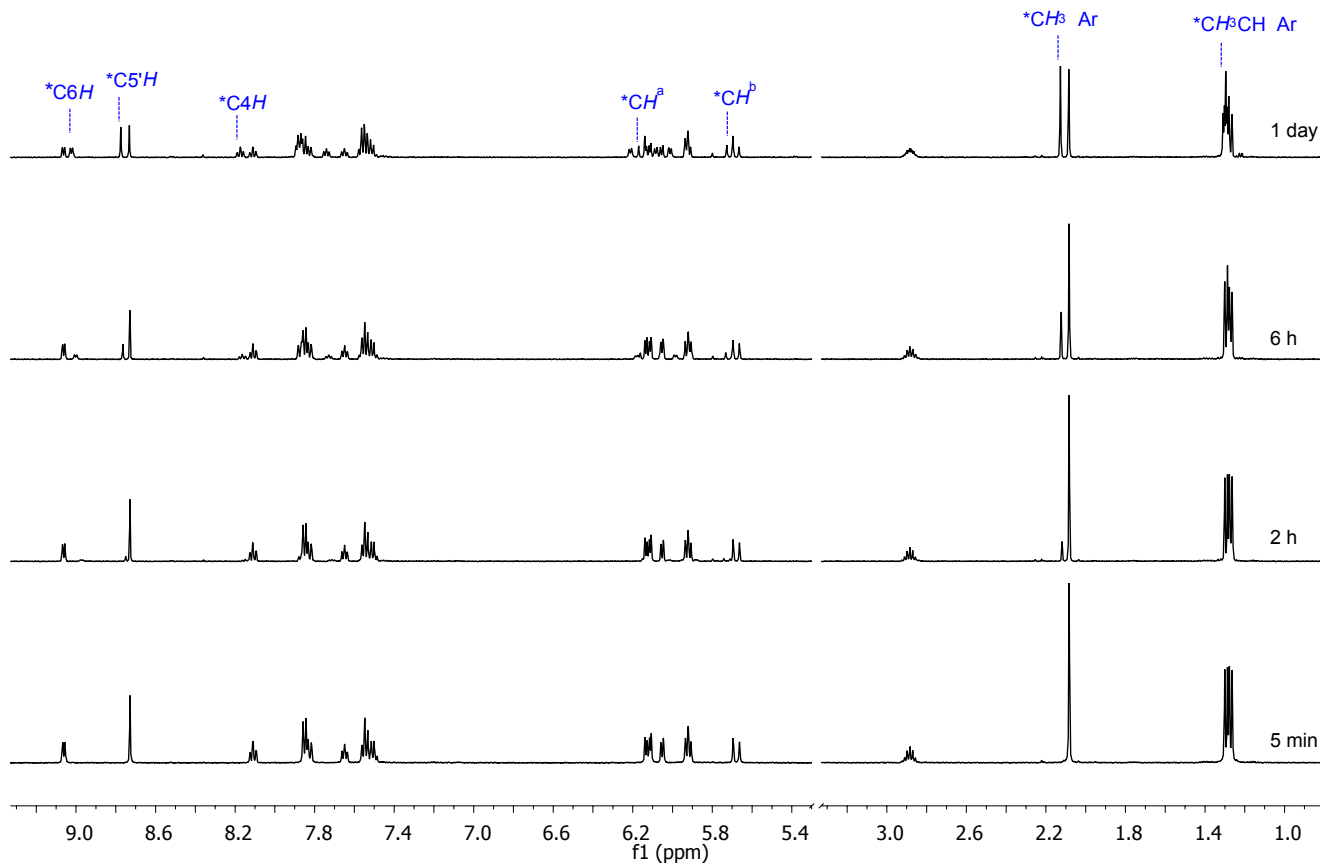
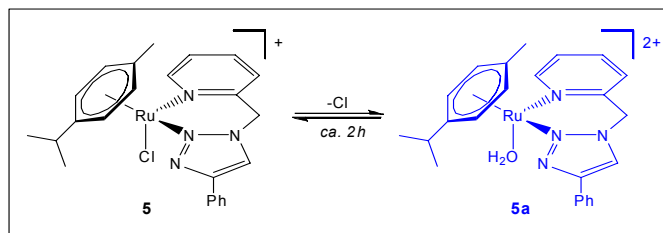


Figure S10. ^1H NMR spectral changes during the hydrolysis of **5** (2.0 mM) in D_2O at 25.0 $^\circ\text{C}$. With (*) are indicated selected resonances of the aqua species **5a**.

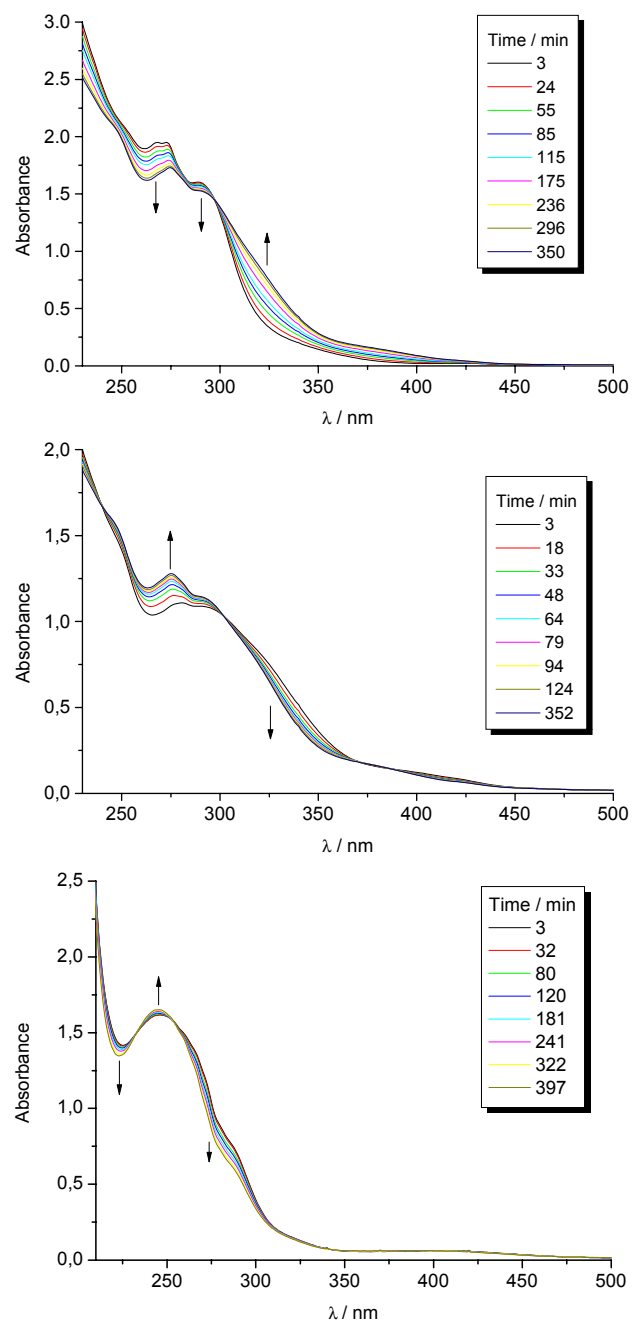


Figure S11. Time evolution of UV-Vis spectra of complexes **3** (top), **4** (middle) and **5** (bottom) in H₂O at 25.0 °C.

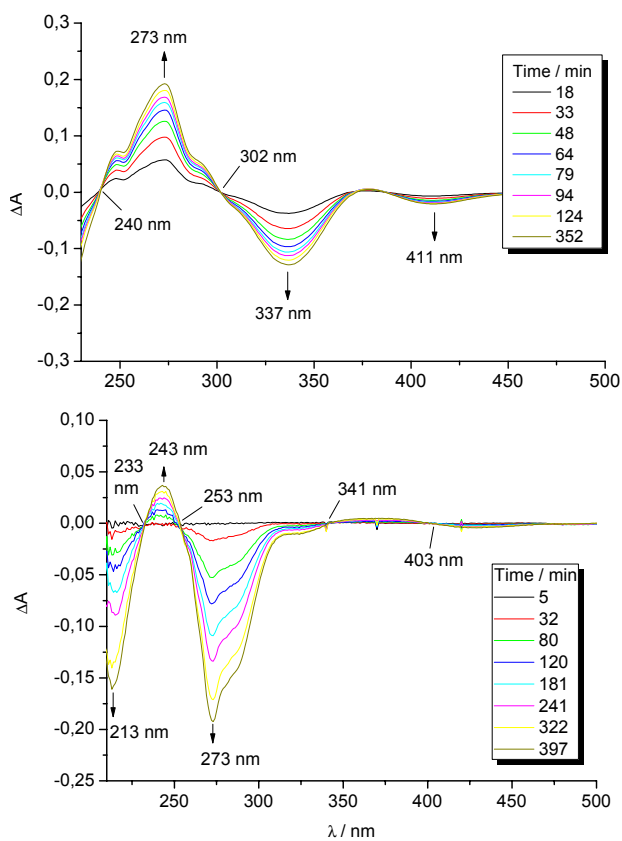


Figure S12. Time evolution of UV-Vis difference spectra during the aquation of complexes **4** (top) and **5** (bottom) in H₂O at 25.0 °C. $\Delta A = A_t - A_0$, where A_t = absorbance at time t and A_0 = absorbance at $t = 2$ min (i.e. the time at which the first spectrum was recorded).

Table S1. Assignments of ^1H resonances (δ) for complexes **1** – **5** in various solvents and for hydrolysis products **3a** and **5a**.

	Free ppt			1		2		3		3a	4		5		5a
	D ₂ O	CDCl ₃	DMF*	CDCl ₃	CD ₃ NO ₂	CDCl ₃	CD ₃ NO ₂	D ₂ O	CD ₃ NO ₂	D ₂ O	D ₂ O	CD ₃ NO ₂	D ₂ O	DMF*	D ₂ O
3	7.41-7.49	7.20-7.35	7.31-7.43	7.48-7.31	7.65	7.52-7.36	7.67	7.95	7.99	7.82	7.74	7.74	7.94-7.72	8.00	n.a.
4	7.92	7.69	7.87	7.92-7.64	7.97	7.83	8.02	8.23	8.26	8.08	8.01	8.02	8.11	8.25	8.17
5	7.41-7.49	7.20-7.35	7.31-7.43	7.48-7.31	7.53-7.40	7.52-7.36	7.56-7.48	7.74	7.79	7.62	7.49	7.60-7.38	7.65	7.76	7.74
6	8.52	8.61	8.59	9.67	9.56	9.90	9.74	9.34	9.48	9.26	9.27	9.24	9.06	9.24	9.02
CH^a	5.82	5.70	5.84	7.92-7.64	7.59	7.52-7.36	7.01	6.32	6.42	6.41	6.36	6.28	6.17-6.08	6.48	n.a.
CH^b				5.26	5.69	5.41	5.87	6.11	6.16	6.01	5.94	6.10	5.68	5.96	5.71
5'	8.37	7.94	8.70	8.11	8.56	8.16	8.58	8.83	8.76	8.71	8.62	8.52	8.72	9.15	8.77
2''/6''	7.83	7.82	7.92-7.98	7.92-7.64	7.87	7.78	7.92	7.89	7.88	7.86	7.84	7.85	7.94-7.72	7.96-7.90	n.a.
3''/5''	7.53	7.41	7.43-7.50	7.48-7.31	7.53-7.40	7.52-7.36	7.56-7.48	7.54	7.59-7.42	7.59-7.53	7.53	7.60-7.38	7.58-7.45	7.58-7.50	n.a.
4''	7.41-7.49	7.20-7.35	7.31-7.43	7.48-7.31	7.53-7.40	7.52-7.36	7.45	7.54	7.59-7.42	7.53-7.48	7.53	7.60-7.38	7.58-7.45	7.49-7.42	n.a.
CH₃ - dmsO				3.86/ 3.64/ 3.52/ 3.19	3.78/ 3.52/ 3.37/ 3.17	3.59/ 3.56/ 3.35/ 3.28	3.41/ 3.41/ 3.40/ 3.19	3.54/ 1.99	3.57/ 1.88						

*from the ref.: D. Urankar, B. Pinter, A. Pevec, F. De Proft, I. Turel and J. Košmrlj, *Inorg. Chem.*, 2010, **49**, 4820-4829.

n.a.: not assigned. These resonances are not well resolved since they are overlapped with resonances of **5**.

Table S2. Assignments of ^{13}C resonances (δ) for complexes **1** – **5** in various solvents.

	Free ppt	1		2	3	4	5
	DMF*	CDCl_3	CD_3NO_2	CDCl_3	CD_3NO_2	CD_3NO_2	DMF*
2	156.1	153.9	156.3	151.8	154.6	155.1	154.2
3	122.9	124.0	125.9	124.1	130.5	127.7	127.1
4	138.0	138.4	140.1	138.6	142.6	140.2	141.2
5	123.9	124.2	124.5	124.3	128.8	126.8	126.7
6	150.3	161.4	161.8	159.9	158.2	158.4	159.1
CH₂	55.7	56.3	56.7	56.1	56.0	56.0	55.2
4'	147.7	149.3	149.9	148.8	152.0	150.2	150.1
5'	122.7	124.7	126.9	125.1	129.1	126.6	127.5
1''	132.0	128.8	126.7	128.4	129.6	130.7	129.8
2''/6''	126.0	125.8	126.8	125.6	127.1	127.0	126.1
3''/5''	129.5	129.3	130.4	129.5	130.6	130.5	129.8
4''	128.5	129.5	130.3	129.8	131.1	130.4	129.8
CH₃ - dmsO		46.5/44.6/ 44.2/43.7	46.4/44.6/ 44.5/43.8	45.9/45.8 45.3/44.5	47.2/43.1		
CH₂ [9]aneS₃					38.4/38.3/ 38.1/31.1/ 30.0/29.5	37.9/35.1/ 34.9/34.8/ 31.7/31.4	

*from the ref.: D. Urankar, B. Pinter, A. Pevec, F. De Proft, I. Turel and J. Košmrlj, *Inorg. Chem.*, 2010, **49**, 4820-4829.