Electronic Supplementary Material (ESI) for Dalton Transactions.

Supporting information

to

Towards targeting anticancer drugs. Ruthenium(II)-arene complexes with biologically active naphthoquinone-derived ligand systems

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Table S1. Details of collected X-ray data for complexes **1a**, **3a**, **5a** and **6**.

	1a	**3a**	**5a**	**6**
Formula	$C_{22}H_{23}ClO_3Ru$	$C_{24}H_{27}ClO_3Ru \cdot 1.5H_2O$	$C_{22}H_{24}ClNO_3Ru$	$C_{13}H_{13}NO_3$
CCDC Nr.	1469089	1468156	1469090	1469091
Molecular weight (g mol^{-1})	471.92	527.09	486.94	231.25
Temperature (K)	100(2)	100(2)	100(2)	100(2)
Wavelength (Å)	0.71073	0.71073	0.71073	0.71073
Crystal system	monoclinic	triclinic	monoclinic	monoclinic
Space group	*P*2_1/*n*	*P*-1	*C2/c*	*P* 2_1/*n*
a (Å)	15.5644(8)	9.3210(15)	18.3763(6)	11.8478(4)
b (Å)	7.9491(4)	15.229(3)	9.2791(3)	6.9261(2)
c (Å)	15.7175(8)	17.358(3)	23.9785(8)	13.7030(4)
β (°)	100.110(2)	92.771(5)	98.607(2)	98.488(2)
Volume ($Å^3$)	1914.42(17)	2454.3(7)	4042.7(2)	1112.14(6)
Z	4	4	4	4
Calculated density (g cm^{-3})	1.627	1.353	1.600	1.381
Absorption coefficient (mm^{-1})	0.978	0.767	0.931	0.099
F(000)	948	1024.0	1984	488
Crystal size (mm × mm × mm)	0.36 × 0.32 × 0.30	0.15 × 0.12 × 0.03	0.32 × 0.28 × 0.16	0.38 × 0.1× 0.1
2θ (min, max) (°)	1.70, 27.88	2.189, 25.350	1.72, 27.84	3.00, 26.00
Limiting indices	-19 ≤ h ≤ 20 -10 ≤ k ≤ 10 -18 ≤ l ≤ 20	-12 ≤ h ≤ 13 -21 ≤ k ≤ 21, -19 ≤ l ≤ 22	-24 ≤ h ≤ 24 -12 ≤ k ≤ 11 -31 ≤ l ≤ 31	-12 ≤ h ≤ 14 -8 ≤ k ≤ 8 -16 ≤ l ≤ 16
Reflections collected / unique	22739 / 4558 [R(int) = 0.0547]	41883 / 8736 [R(int) = 0.0807]	22613 / 4780 [R(int) = 0.0397]	11807 / 2184 [R(int) = 0.0735]
Completeness to theta	99.7%	97.2%	99.3%	99.8%
Data / restraints / parameters	4558 / 0 / 248	8736 / 9 / 534	4778 / 0 / 261	2184 / 2 / 165
Goodness-of-fit on F^2)	1.047	1.052	1.043	1.044
Final R indices [I>2σ(I)]	R_1 = 0.0253, wR_2 = 0.0651	R_1 = 0.0398, wR_2 = 0.0841	R_1 = 0.0263, wR_2 = 0.0612	R_1 = 0.0531, wR_2 = 0.1083
R indices (all data)	R_1 = 0.0272, wR_2 = 0.0666	R_1 = 0.0549, wR_2 = 0.0892	R_1 = 0.0319, wR_2 = 0.0640	R_1 = 0.0893, wR_2 = 0.1243
Largest diff. peak and hole ($eÅ^{-3}$)	0.464 and -0.585	0.72 and -1.04	0.501 and -0.470	0.227 and -0.225

Table S2. Comparison between Pd(0)-catalyzed and peroxide-based synthesis of **2** and **3**.

	compound	Steps	Reaction time (h)	Yield (%)	Cost per gram (€)
Pd(0)	**2**	2	3.5	31	23.50
	3	2	3.5	28	26.39
peroxide	**2**	2	12	24	4.82
	3	2	14	16	12.37

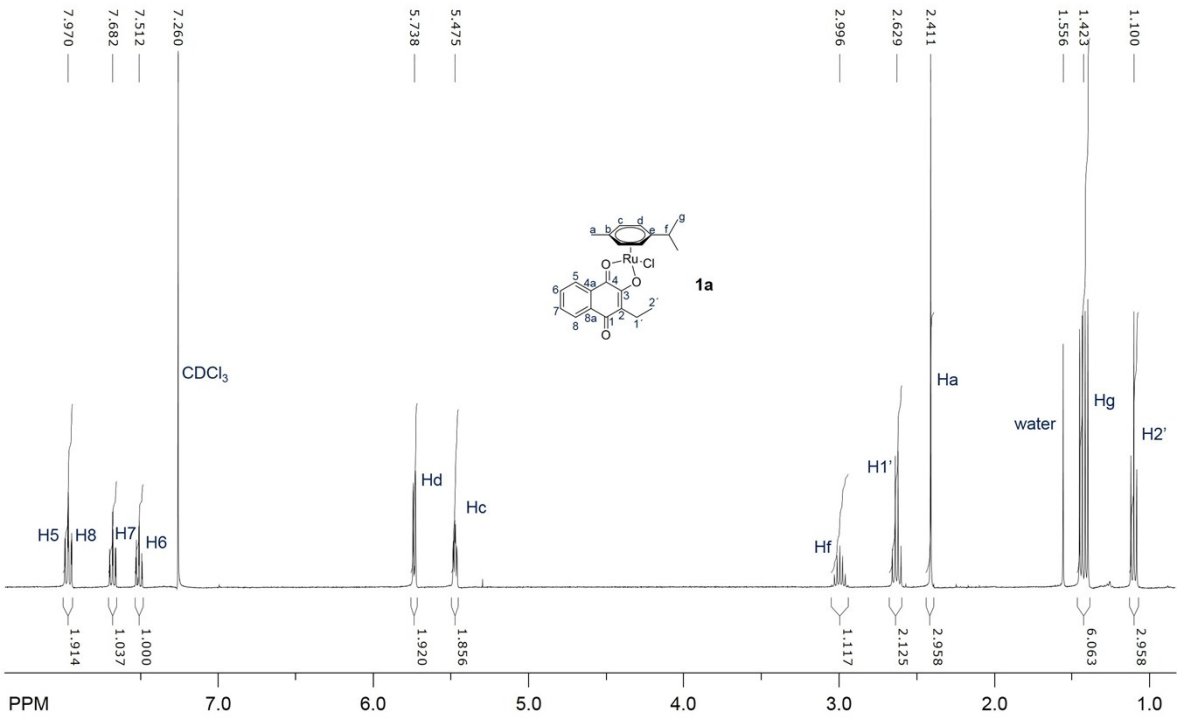

Figure S1. ^{1}H NMR spectrum of **1a** with assignment of the peaks and numbering scheme of the protons and carbon atoms.

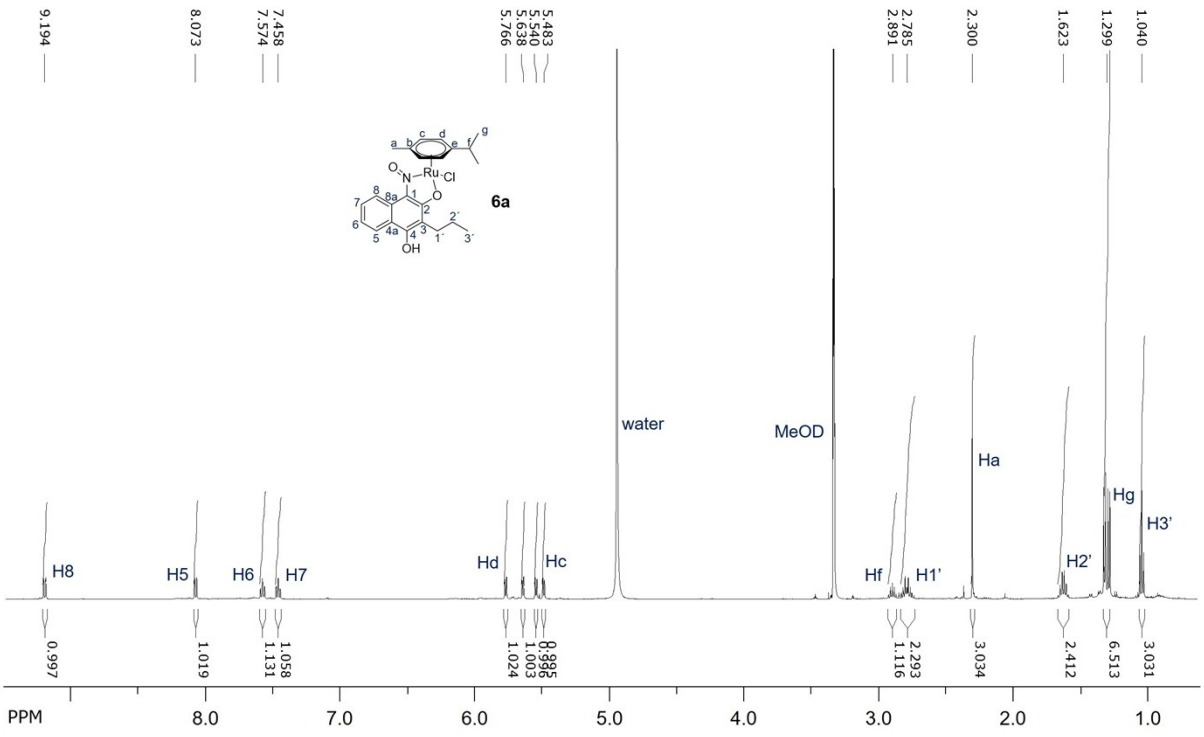

Figure S2. [1]H NMR spectrum of **6a** in MeOD with assignment of the peaks and numbering scheme of the protons and carbon atoms.

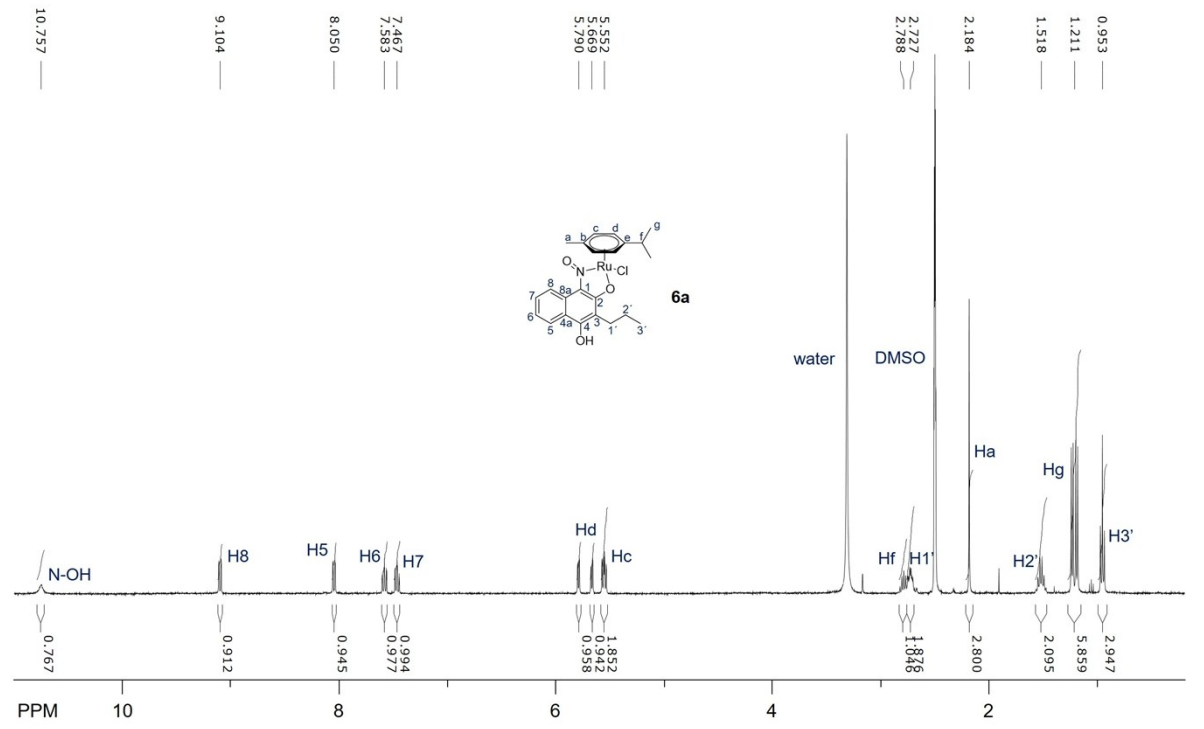

Figure S3. [1]H NMR spectrum of **6a** in DMSO with assignment of the peaks and numbering scheme of the protons and carbon atoms.

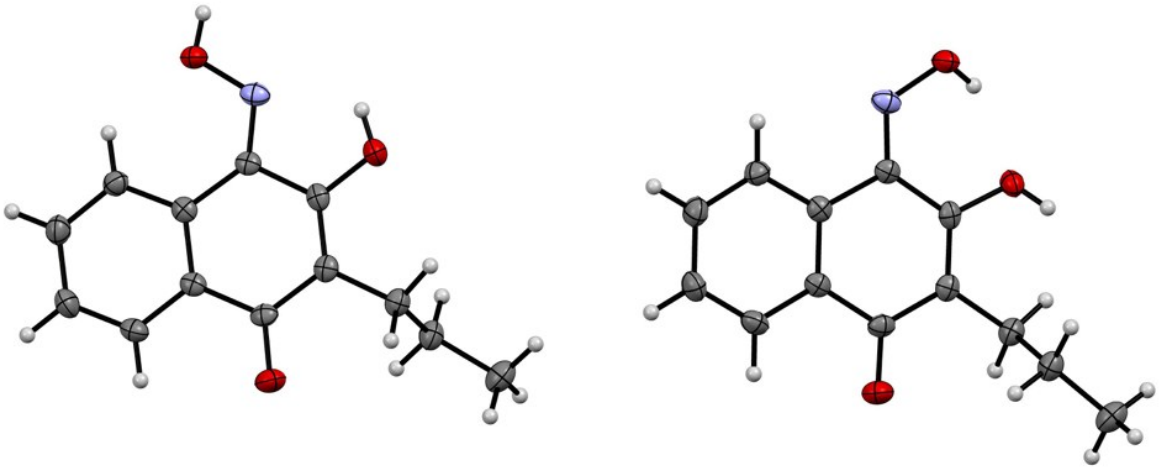

Figure S4. Molecular structures of the *E* (right) and *Z* isomers of **6** drawn at 50% probability level.

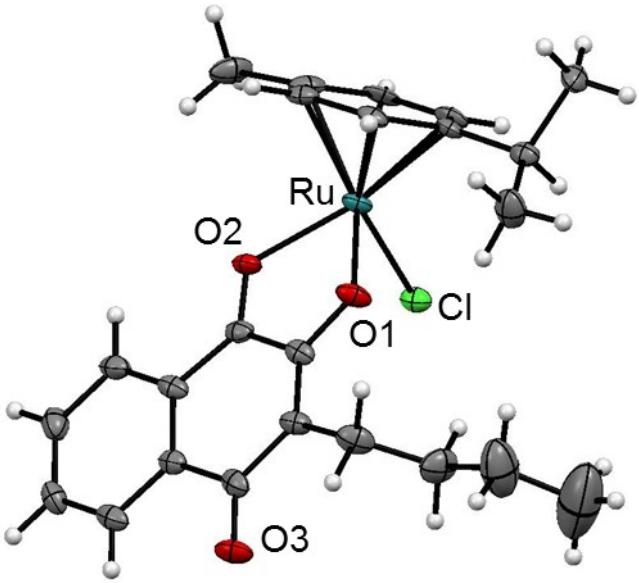

Figure S5. Molecular structure of **3a** drawn at 50% probability level. Solvent molecules were omitted for clarity.

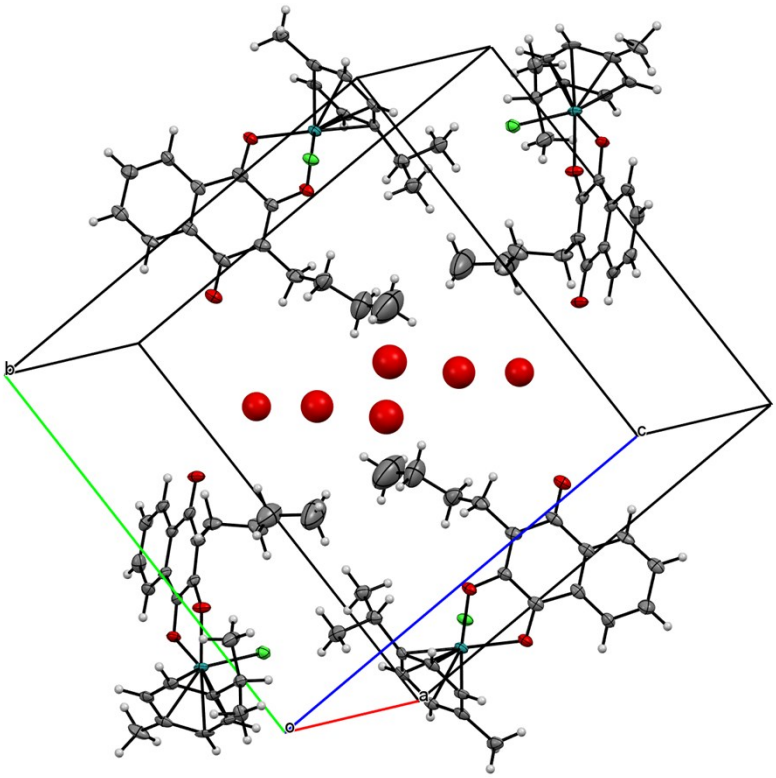

Figure S6. Unit cell of **3a** including the electron density for the embedded solvent molecules.

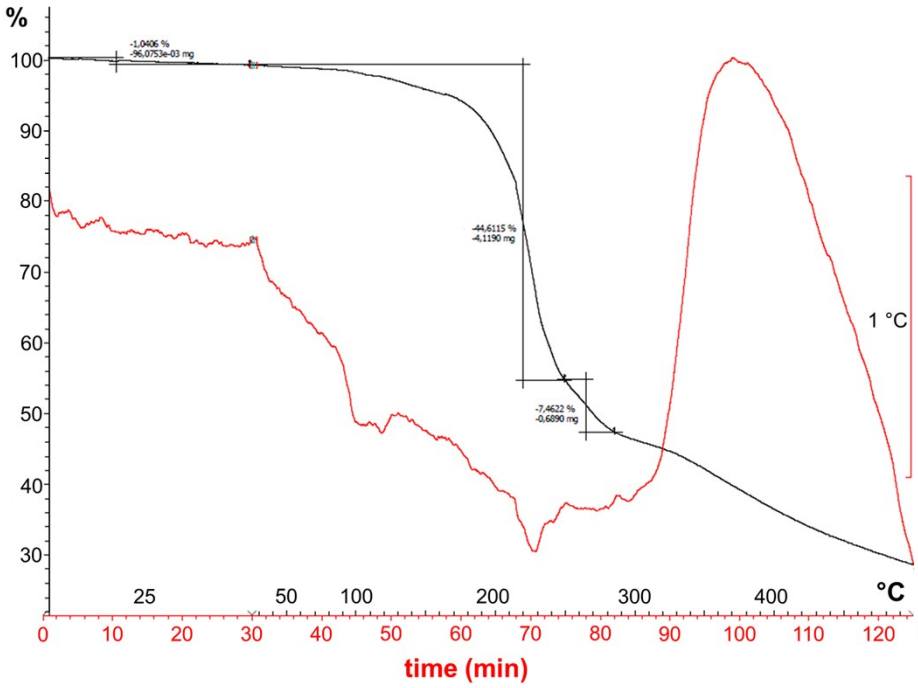

Figure S7. Thermogravimetric analysis of complex **3a**.

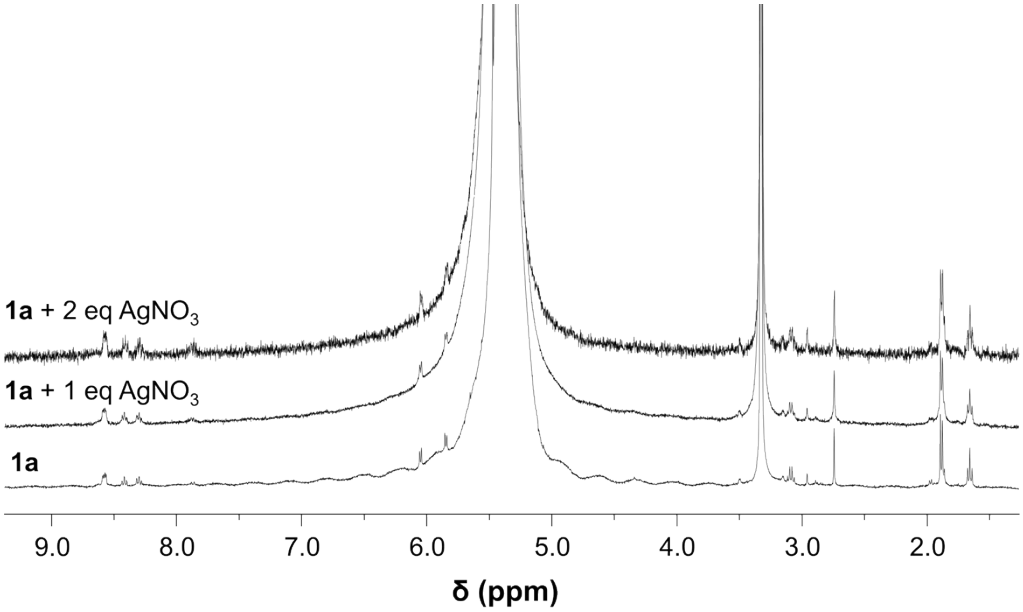

Figure S8. The reaction between **1a** and $AgNO_3$ in 20 mM phosphate buffer (pH 7.4) followed by ^1H NMR spectroscopy.

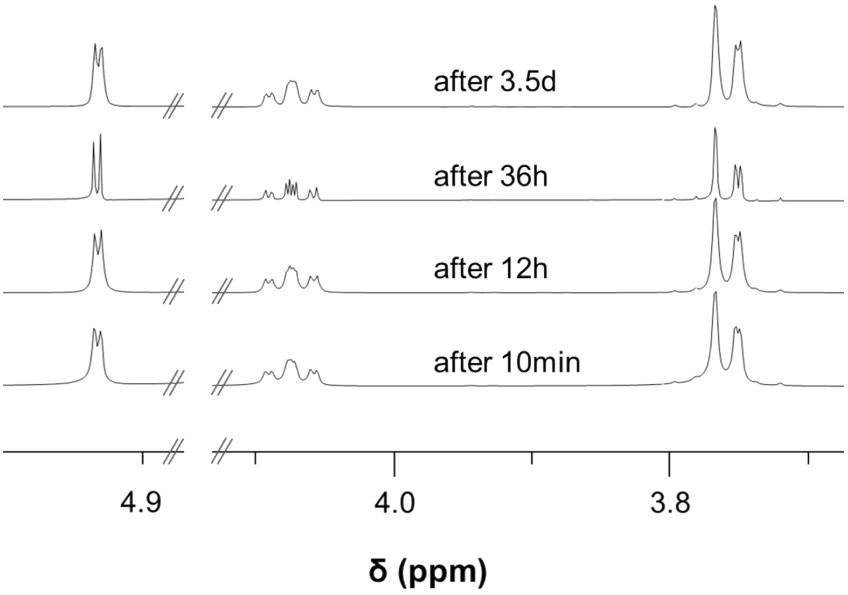

Figure S9. Stability of AsH in 20 mM phosphate buffer (pH 7.4) followed by ^1H NMR spectroscopy over 3.5 days.

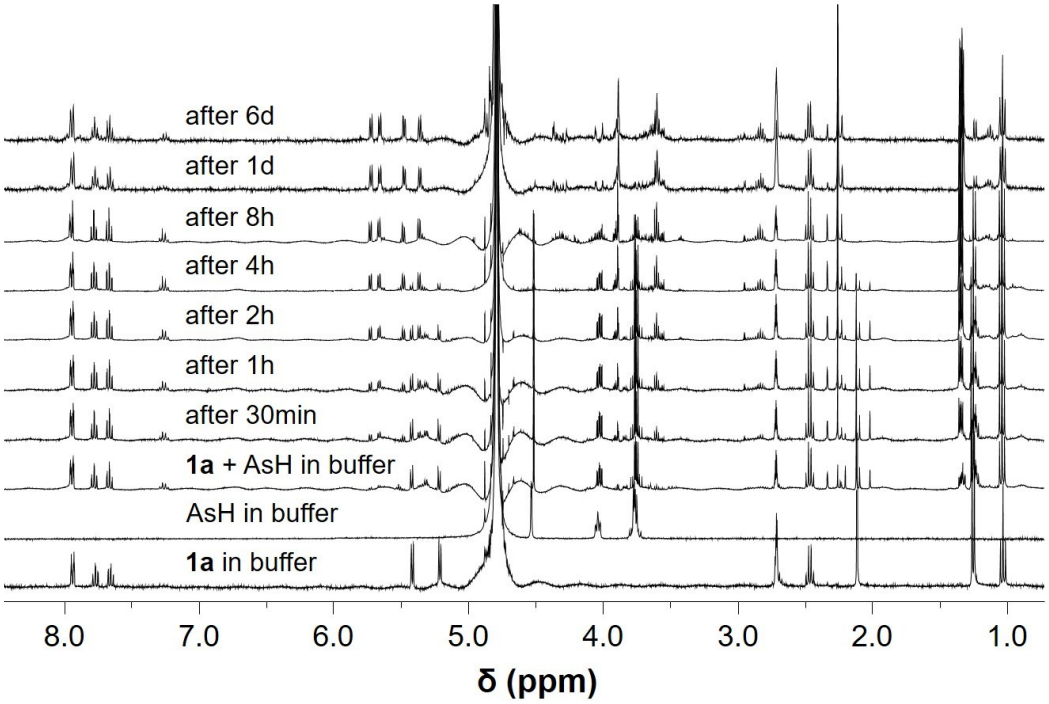

Figure S10. Time course of the reaction between **1a** and AsH in 20 mM phosphate buffer (pH 7.4) followed by ^{1}H NMR spectroscopy.

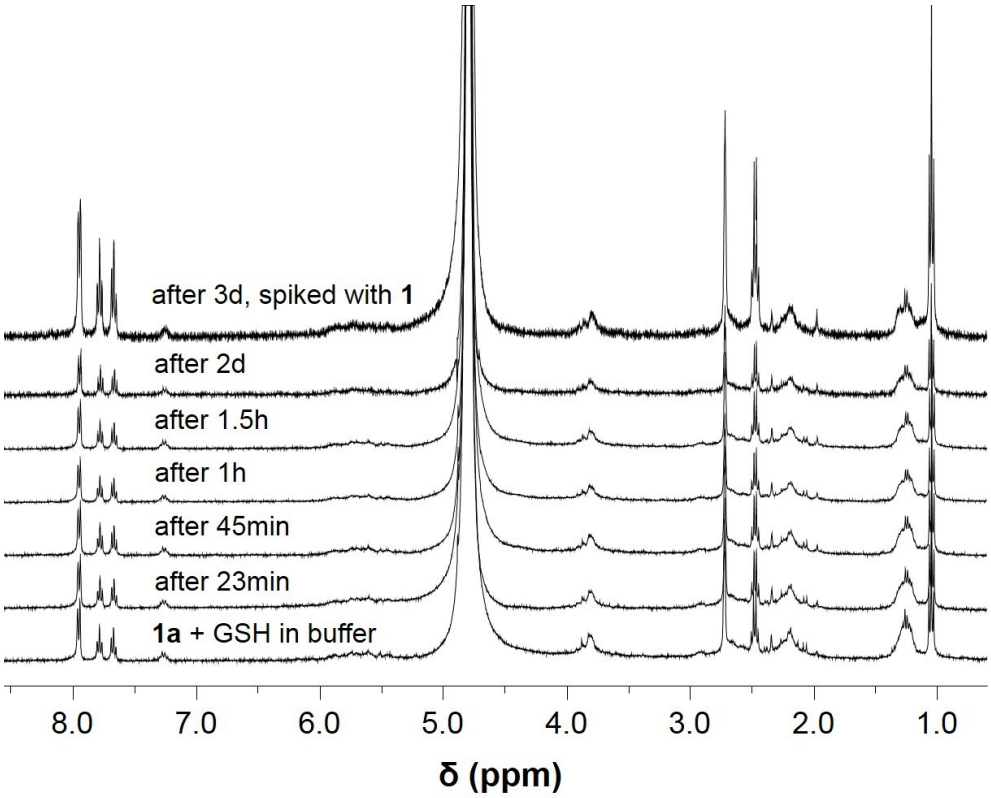

Figure S11. Time course of the reaction between **1a** and GSH in 20 mM phosphate buffer (pH 7.4) followed by ^{1}H NMR spectroscopy.

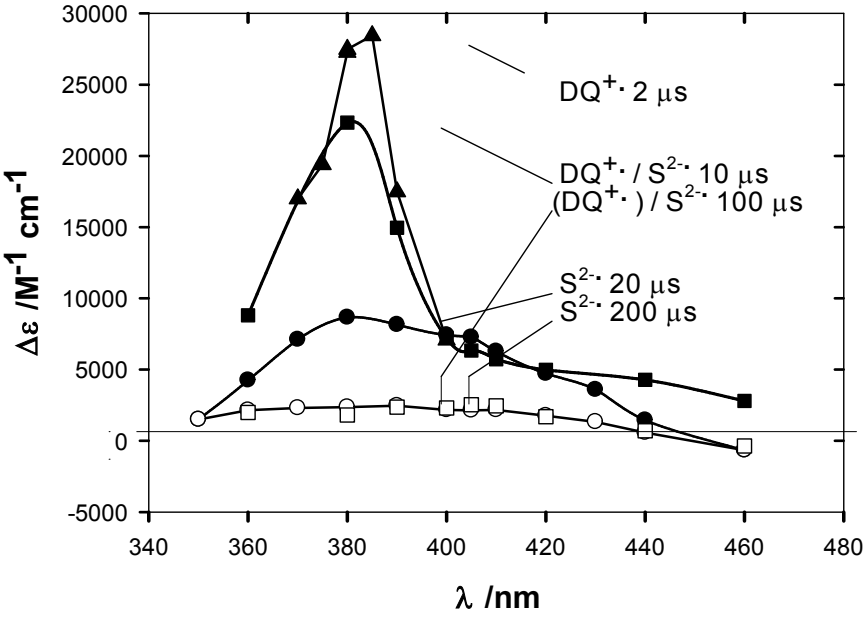

Figure S12. 1-Electron reduction spectra recorded after pulse radiolysis of a mixture of **1a** (S^{-}) and Diquat (DQ^{2+}).

Table S3. clog*P* values for ligands **1**–**5** calculated with ChemDraw 12.0, Molinspiration (www.molinspiration.com) and the average log*P* from the ALOGPS 2.1 program.[1]

Compound	clog*P*		
	ChemDraw	*Molinspiration*	*ALOGPS 2.1*
	naphthoquinones		
1	2.73	2.22	1.86
2	3.26	2.61	2.30
3	3.79	3.17	2.76
4	4.32	3.67	3.20
L	3.70	3.16	2.76
	oximes		
5^{ox}	3.33	2.61	1.99
6^{ox}	3.86	3.00	2.43
7^{ox}	4.39	3.56	2.89
8^{ox}	4.92	4.07	3.44
	nitroso		
5^{nit}	2.80	3.28	2.93
6^{nit}	3.32	3.67	3.38
7^{nit}	3.85	4.23	3.84
8^{nit}	4.38	4.73	4.30

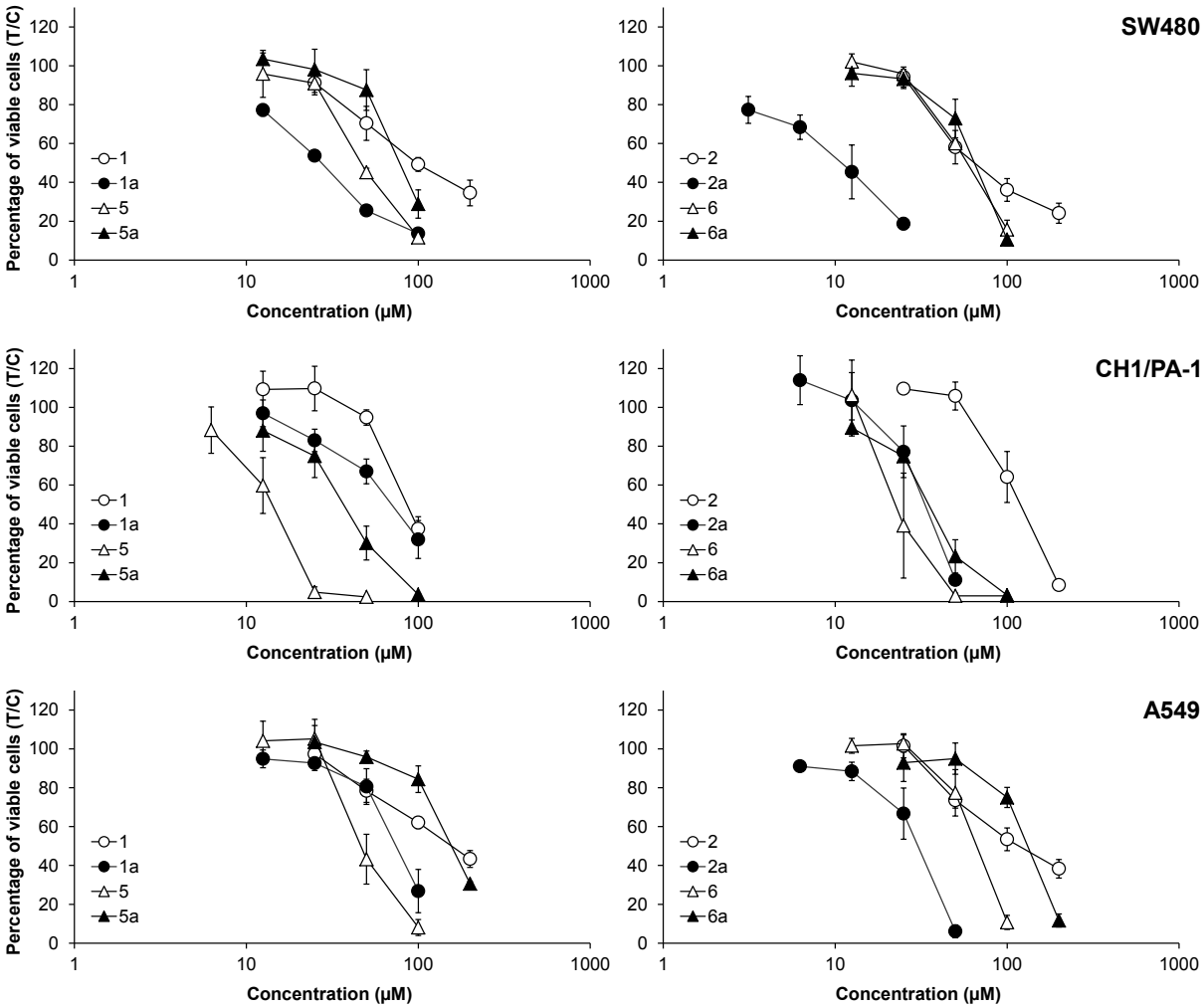

Figure S13. Concentration–effect curves of ligands **1**, **2**, **5** and **6** and the respective Ru(cym)Cl complexes in human colon carcinoma (SW480), ovarian teratocarcinoma (CH1/PA-1) and non-small cell lung carcinoma cells (MTT assay, exposure time 96 h).

References

1. I. V. Tetko, J. Gasteiger, R. Todeschini, A. Mauri, D. Livingstone, P. Ertl, V. A. Palyulin, E. V. Radchenko, N. S. Zefirov, A. S. Makarenko, V. Y. Tanchuk and V. V. Prokopenko, *J. Comput.-Aided Mol. Des.*, 2005, **19**, 453.