

Supporting Information

Antitumoral effects of mitochondria-targeting neutral and cationic *cis*-[bis(1,3-dibenzylimidazol-2-ylidene)Cl(L)]Pt(II) complexes

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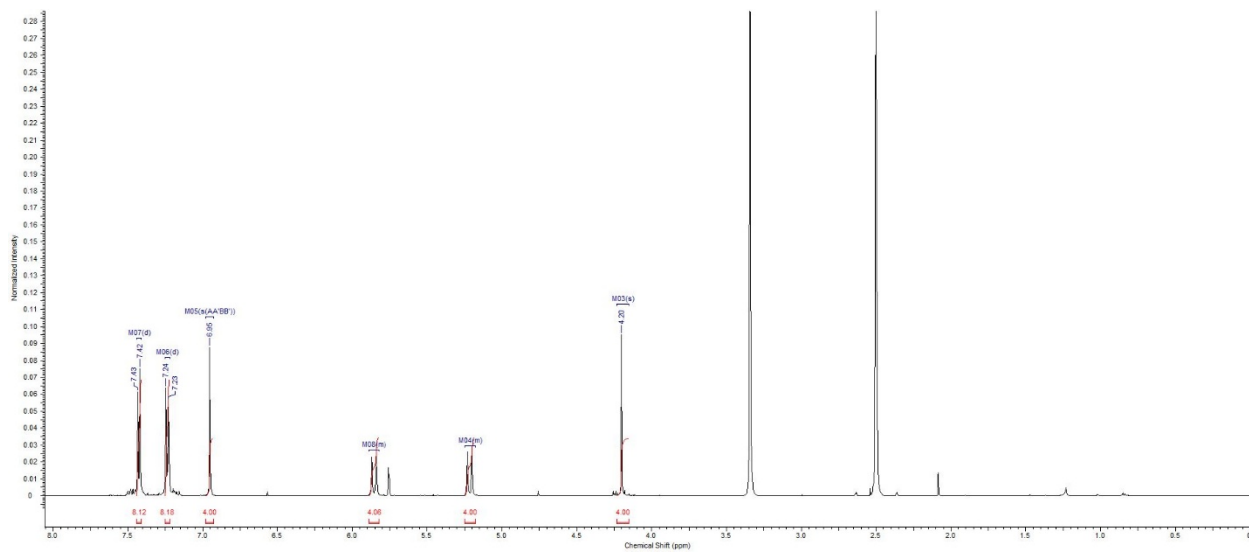


Figure S1. $^1\text{H-NMR}$ spectrum (500 MHz, $\text{DMSO-}d_6$) of complex 6.

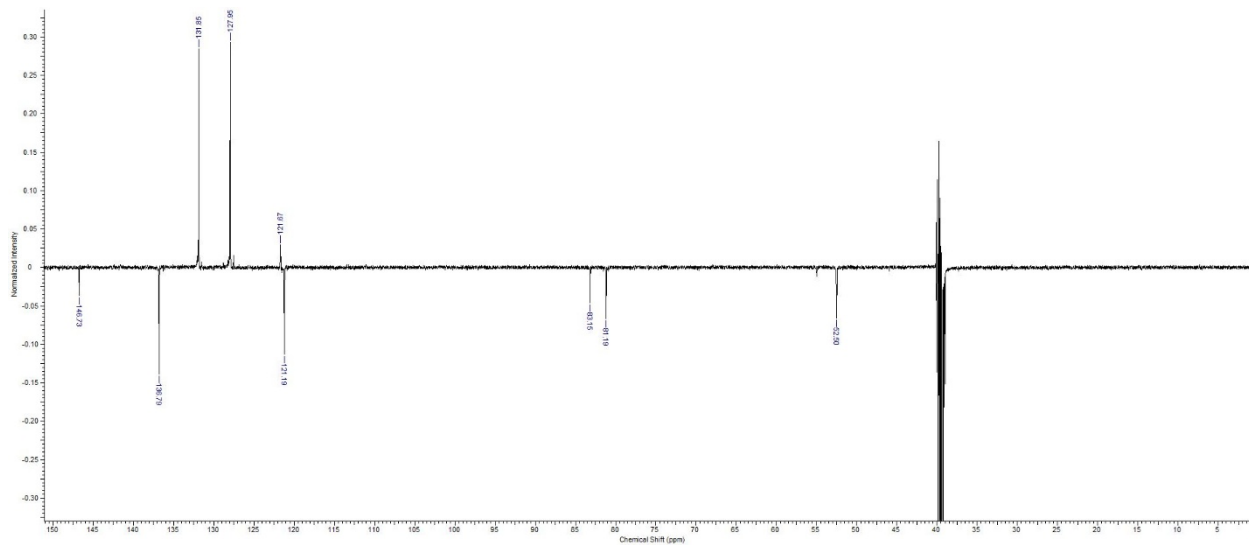


Figure S2. $^{13}\text{C-NMR}$ spectrum (125 MHz, $\text{DMSO-}d_6$) of complex 6.

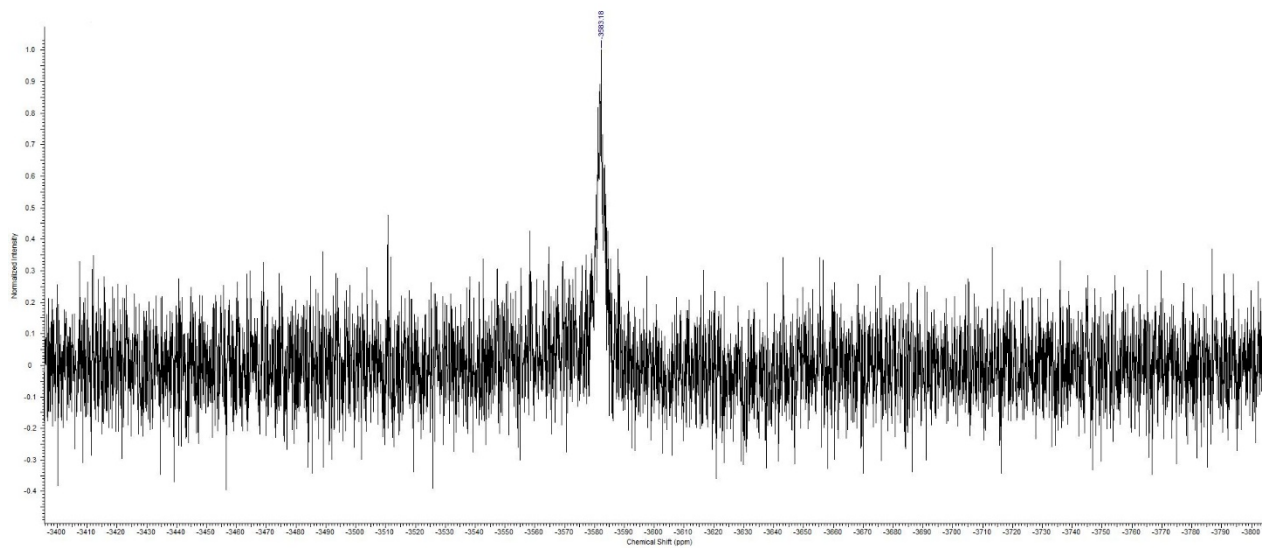


Figure S3. ^{195}Pt -NMR spectrum (DMSO- d_6) of complex 6.

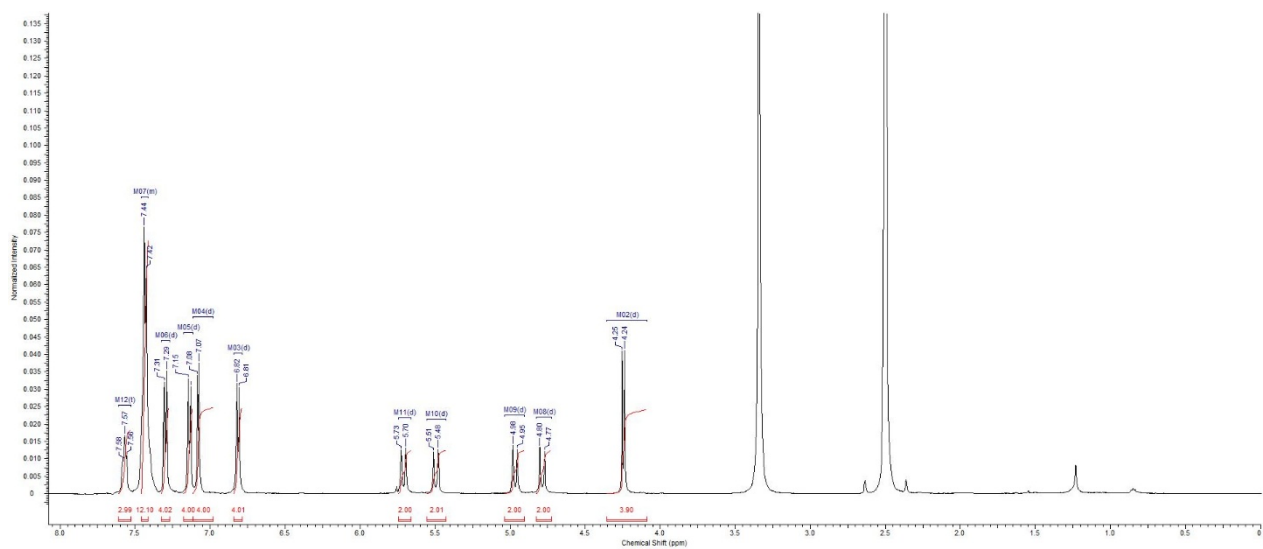


Figure S4. ^1H -NMR spectrum (500 MHz, DMSO- d_6) of complex 7.

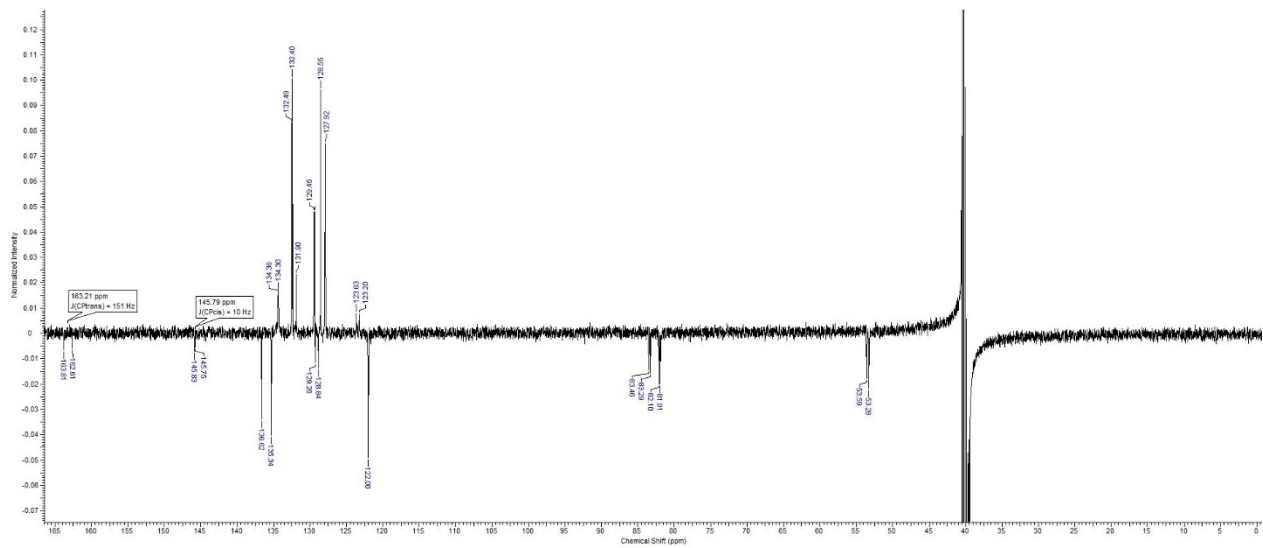


Figure S5. ^{13}C -NMR spectrum (125 MHz, $\text{DMSO-}d_6$) of complex 7.

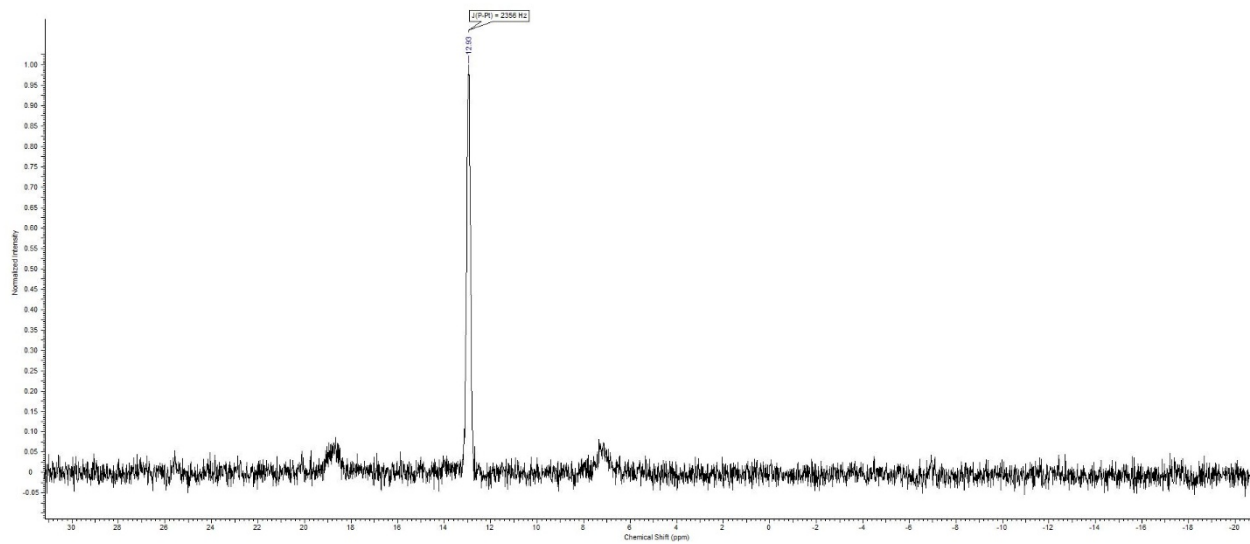


Figure S6. ^{31}P -NMR spectrum ($\text{DMSO-}d_6$) of complex 7.

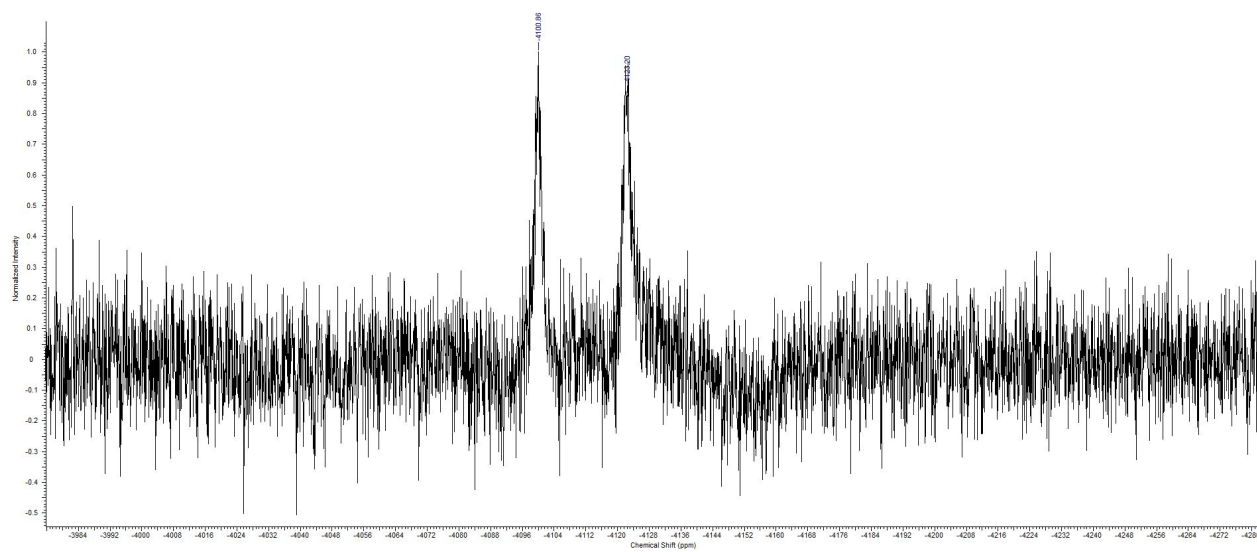


Figure S7. ^{195}Pt -NMR spectrum ($\text{DMSO-}d_6$) of complex **7**.

Uptake of **1** and **2** into 518A2 cells via ICP-MS

Table S1. Uptake of **1** or **2** in 518A2 melanoma cells, after 8 h of incubation with 1 or 5 μM of the complexes.

	ng Pt/ 10^6 cells	
	1 μM	5 μM
1	17.4 ± 3.9	362 ± 33
2	124 ± 21	774 ± 83

Experimental procedure of electrophoretic mobility shift assays (EMSA) with complexes 1, 2, 6, 7 and cisplatin

The effects of 1, 2, 6, and 7 on the topology of circular pBR322 plasmid DNA were investigated via EMSA. Changes in the running behaviour of the DNA bands during agarose gel electrophoresis indicate an interaction between the platinum complexes and the plasmid DNA, forcing it from the compact covalently closed circular (ccc) form into the bulkier open circular form. 1.5 µg of pBR322 plasmid DNA (> 90% in the ccc form, ThermoFisher) in TE-buffer (*cf.* EtdBr Assay) were treated with 0, 5, 10, 25 or 50 µM of the platinum complexes (final sample volume 20 µL) for 24 h at 37 °C. After addition of 5×DNA sample buffer (Tris/HCl 10 mM, 25% glycerine, bromphenol blue, pH 8.0, sterile filtered) agarose gelelectrophoresis (1% in Tris/HCl 4.5 mM, boracic acid 4.5 mM, EDTA 1.25 mM, pH 8.3) was run at 66 V for 4 h. DNA bands were stained for 30 min with EtdBr and documented with a UV transilluminator.

Agarose gels of EMSA with 1, 2, 6, 7 or cisplatin

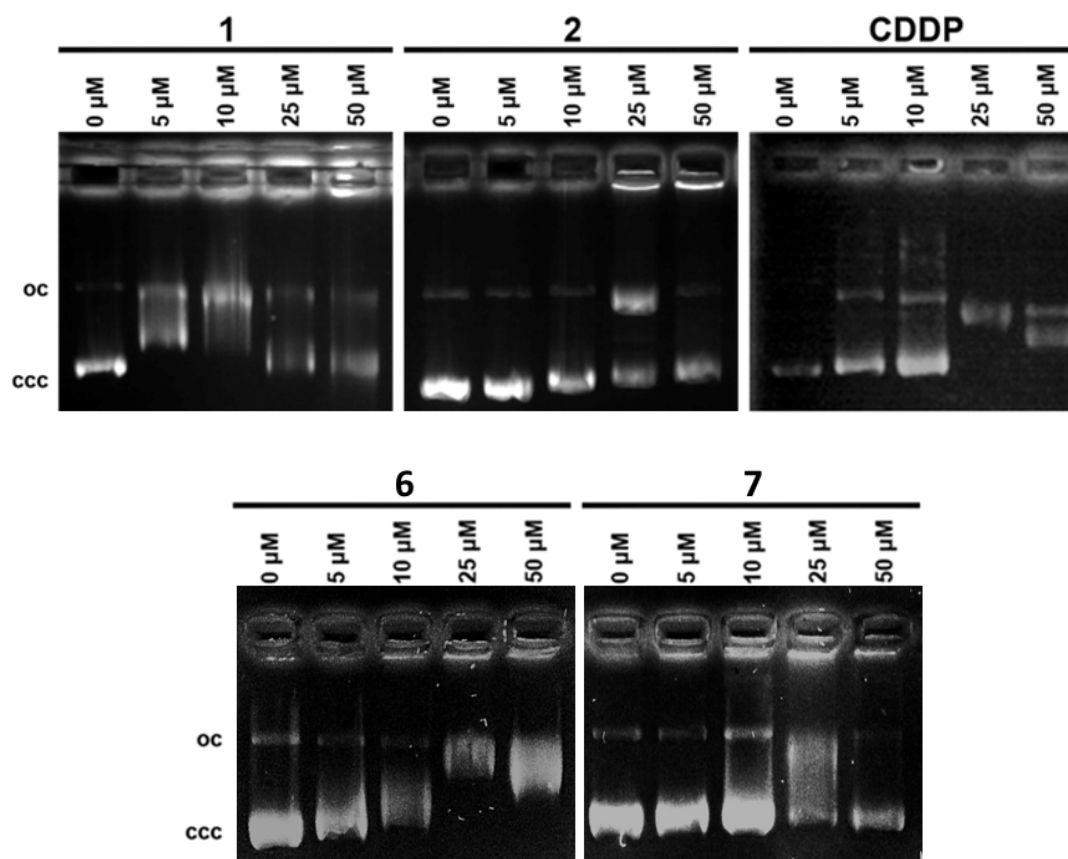


Figure S8. Agarose gel of EMSA with pBR322 plasmid DNA after 24 h of incubation with 1, 2, 6, 7 or cisplatin at 0, 5, 10, 25 or 50 µM.

Experimental procedure for tubulin polymerisation assays of 6, 7 and CA-4

The tubulin binding capacity of complexes 6, 7 as well as of the known tubulin polymerisation inhibitor CA-4, which served as a control, was investigated using the tubulin polymerisation assay which was conducted in clear black 96-well plates (Brand). A 2-fold polymerisation buffer was freshly prepared by adding 20% glycerol and GTP (end concentration 3 mM) to BRB80-Buffer. To 50 μL /well 2-fold polymerisation buffer were added 11.1 μL of 10-fold substance solution and gently mixed. The corresponding solvent and combretastatin A4 served as controls. The microplate reader was pre-heated to 37 $^{\circ}\text{C}$ and 50 μL /well of purified pig brain solution was added. The progression of the optical density at 340 nm was observed in 20 sec intervals for at least 120 min, using a Tecan Microplate reader. The assay was conducted twice per compound and concentration, and mean values of each double determination were calculated. The values of the optical density were plotted against time in 5 min intervals.

Tubulin polymerisation assays with 6, 7 and CA-4

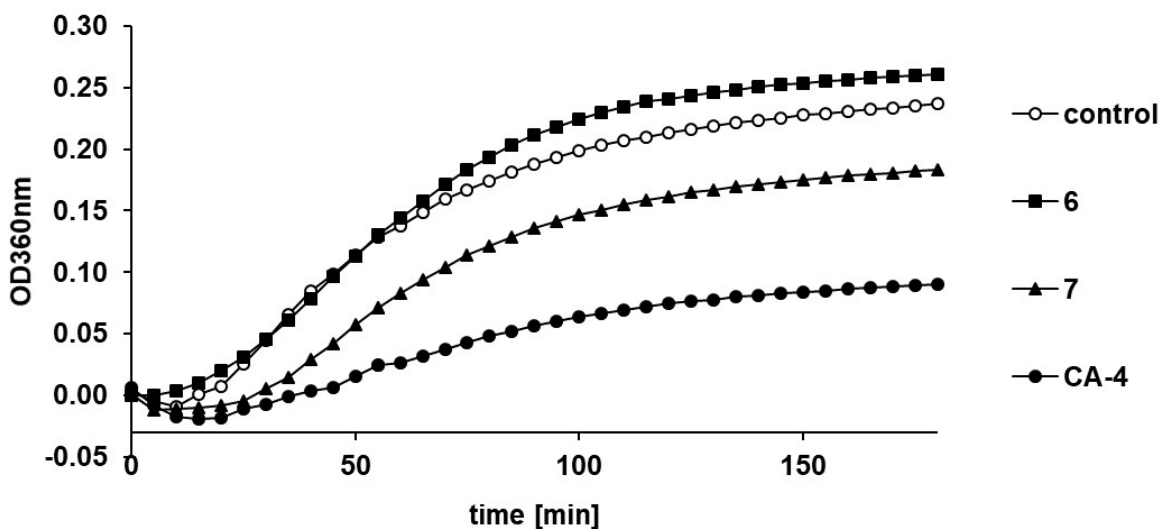


Figure S9. Progression of polymerisation of purified tubulin monomers in response to treatment with 10 μM each of complexes 6 and 7 and combretastatin A4 for 3 h; mean values of double determinations