Electronic Supporting information

Effect of chirality in the anticancer activity of Pt(II) and Pt(IV) complexes containing the 1*R*,2*R* and 1*S*,2*S* enantiomers of *trans*-1,2-diamino-4-cyclohexene ligand (DACHEX), an analogue of the diaminocyclohexane used in oxaliplatin.

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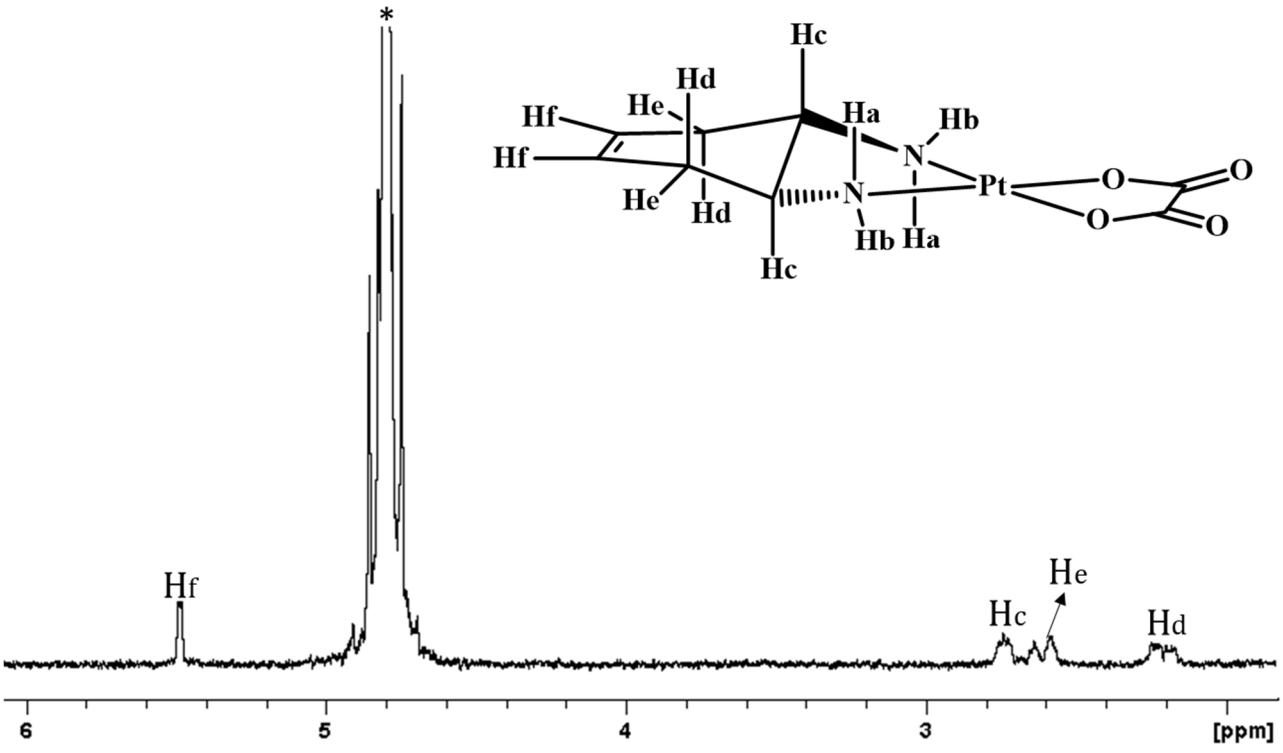

Figure S1. ^{1}H-NMR spectrum of **1** in D_2O (300 MHz). * marks residual solvent peak.

The ^{1}H-NMR spectrum shows a singlet at 5.48 ppm (integrating for 2 protons) attributed to the vinyl protons H_f. The signal at 2.73 ppm integrates for two protons and has been assigned to the methinic protons H_c. The methylene protons resonate at 2.61 ppm (H_e) and 2.24 ppm (H_d). The signals of the amino protons H_a and H_b are not detectable due to fast exchange with D_2O.

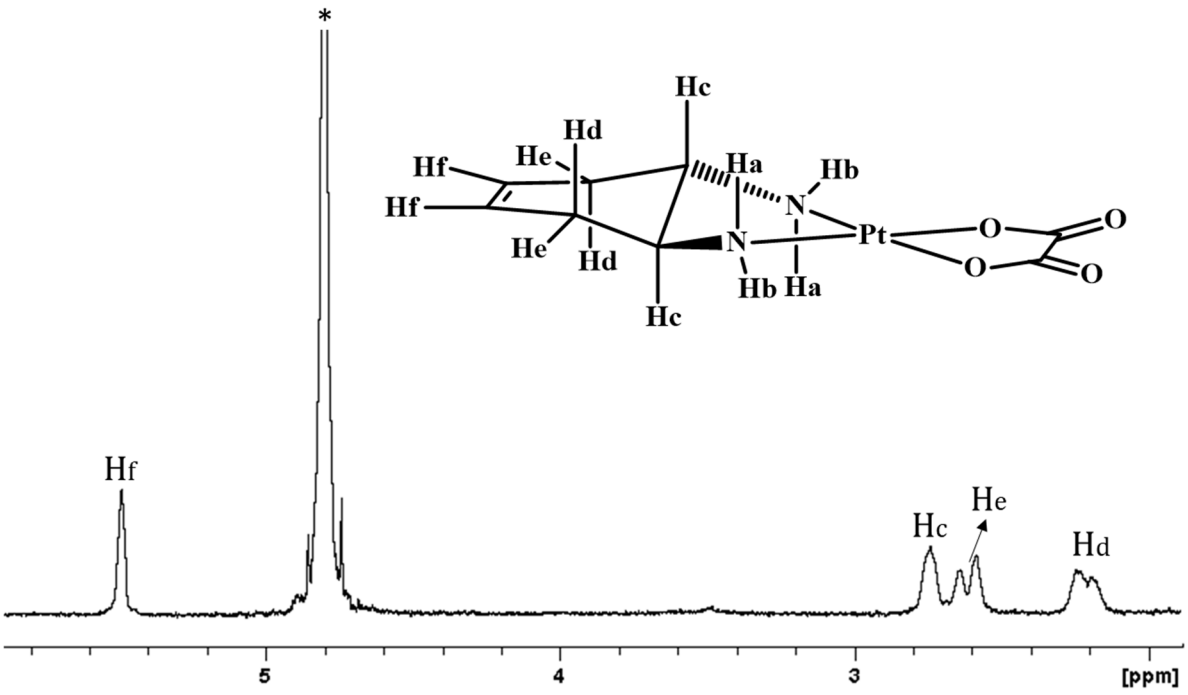

Figure S2. ^{1}H-NMR spectrum of **2** in D_2O (300 MHz). * marks residual solvent peak.

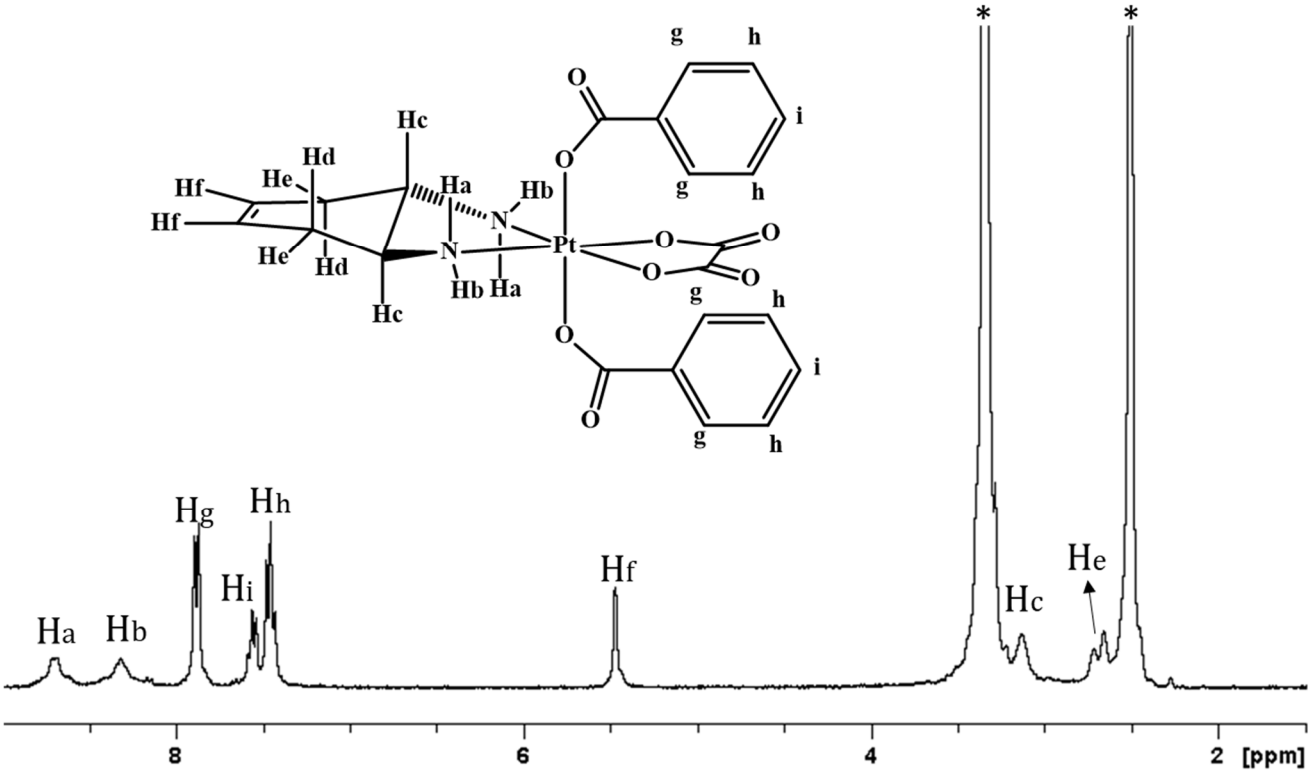

Figure S3. ^{1}H-NMR spectrum (300 MHz) of **4** in DMSO-d_6. * marks residual solvent peaks.

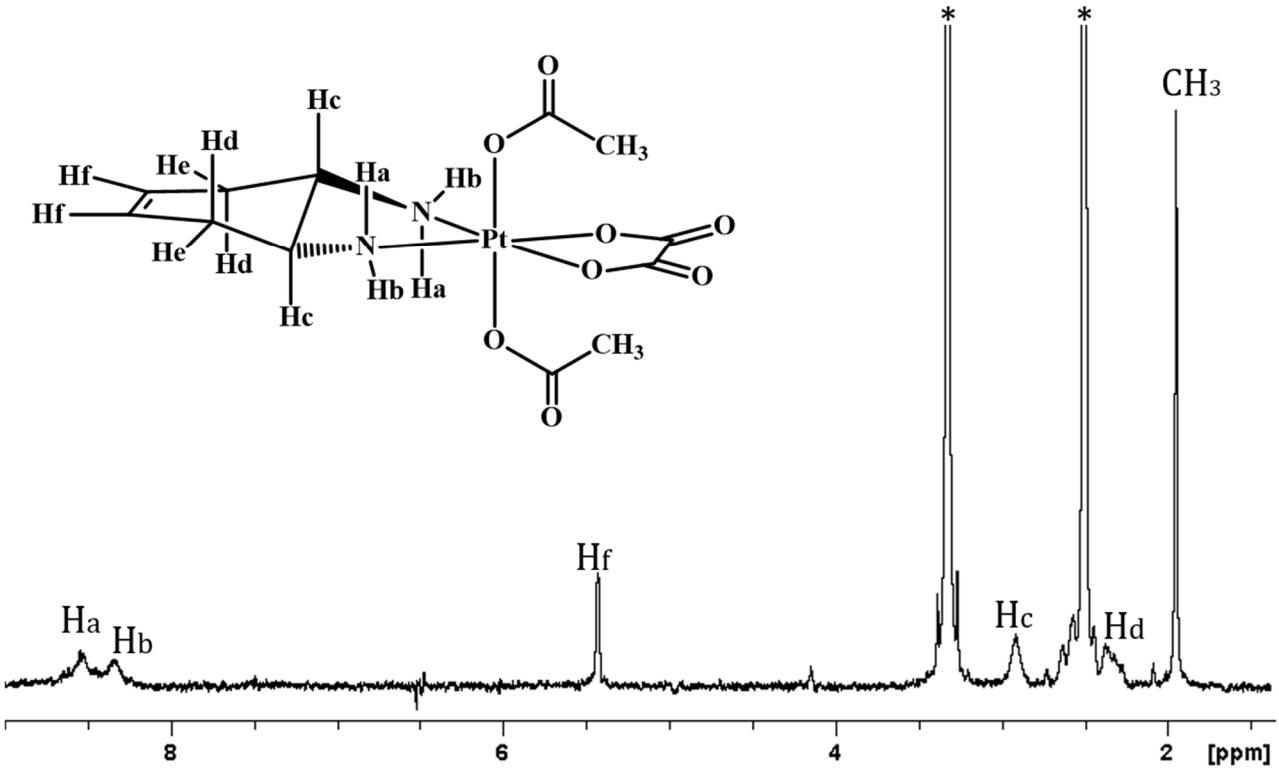

Figure S4. ^{1}H-NMR spectrum (300 MHz) of **5** in DMSO-d_6. * marks residual solvent peaks.

The ^{1}H-NMR spectrum shows two singlets at 8.55 and 8.39 ppm assigned, respectively, to the amino proton H_a in the pseudo-axial position and to the amino proton H_b in the pseudo-equatorial position. The singlet at 5.42 ppm (2H) is attributed to the H_f vinyl protons. The signal at 2.90 ppm (2H) has been assigned to the methine protons H_c. From the NMR spectrum it was not possible to detect the methylene protons H_e, since their signal overlaps with the solvent signal. The methylene protons H_d resonate at 2.32 ppm, while the signal at 1.94 ppm (6H) is attributed to the methyl groups of the acetate axial ligands.

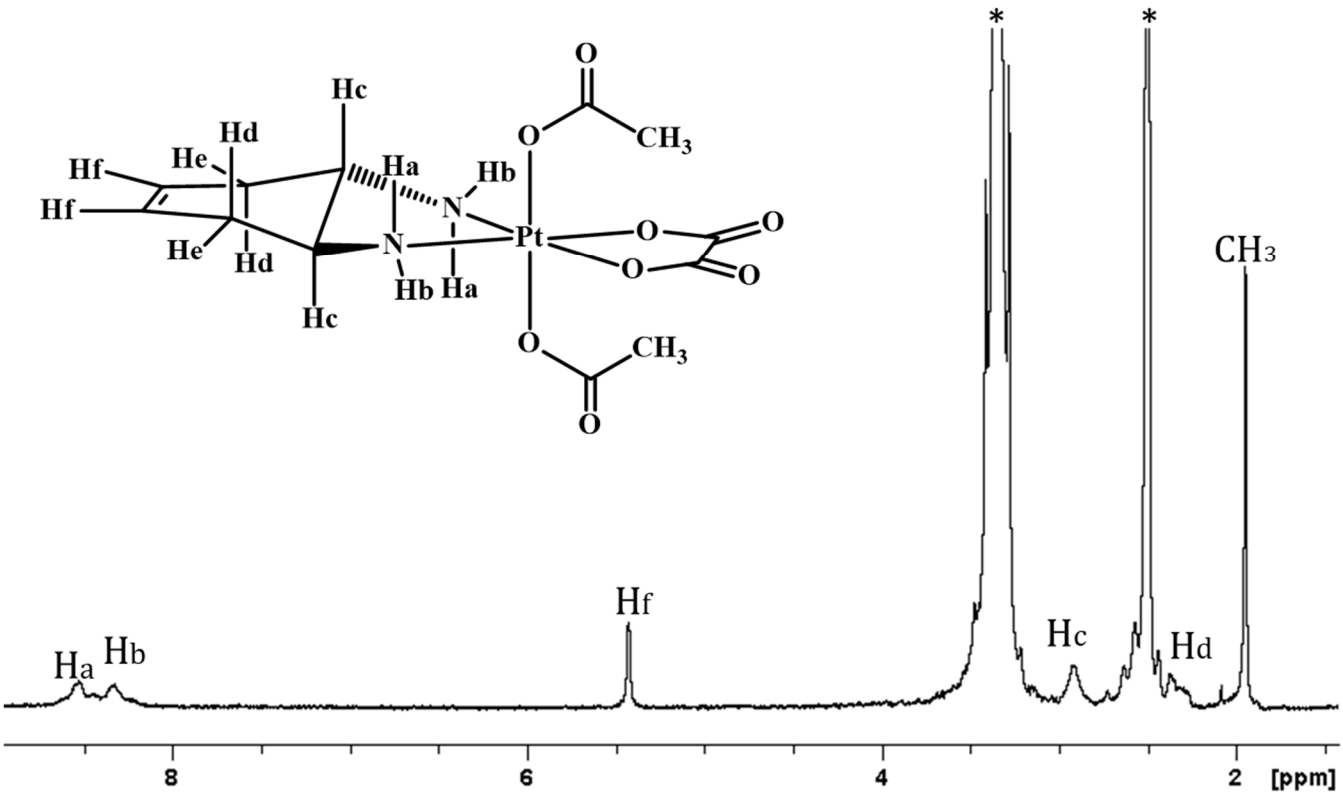

Figure S5. ^{1}H-NMR spectrum (300 MHz) of **6** in DMSO-d_6. * marks residual solvent peaks.

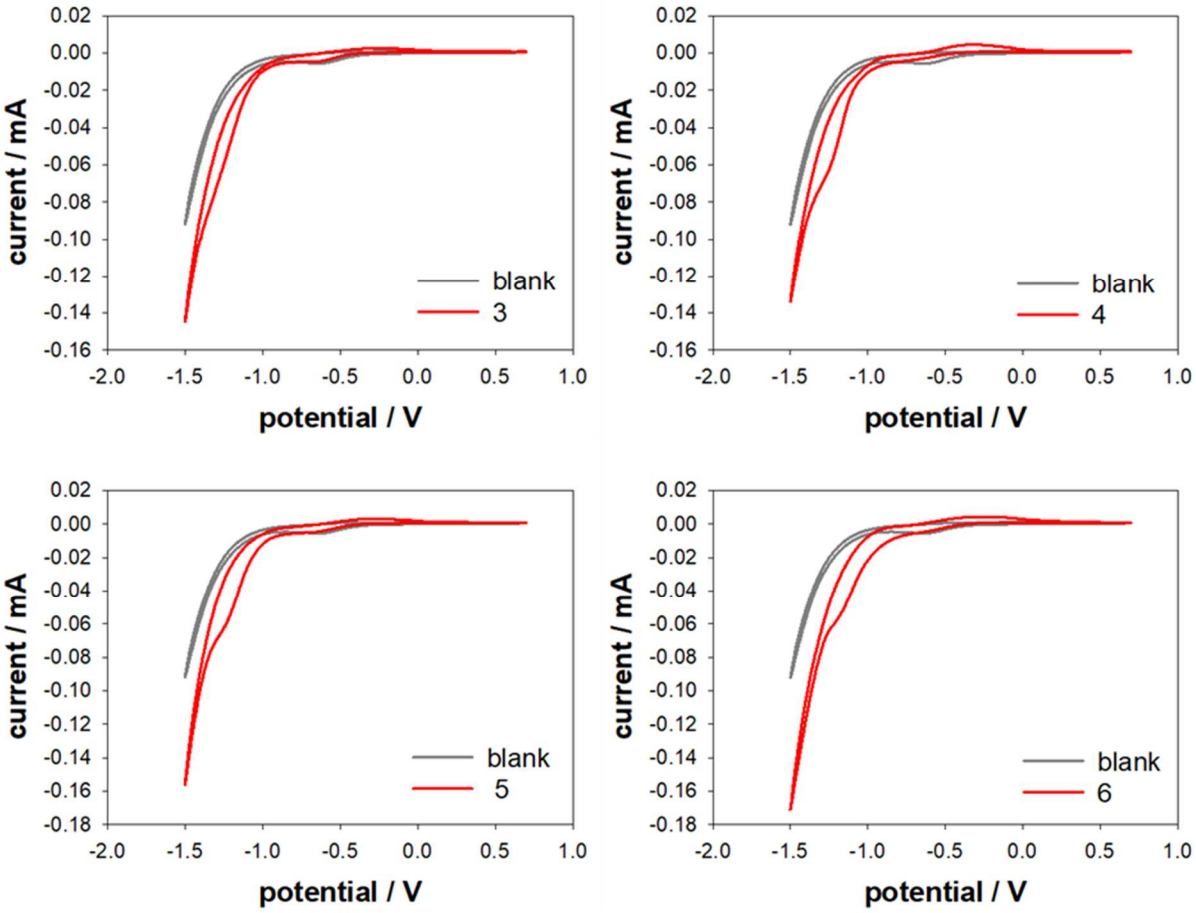

Figure S6. Cyclic voltammograms of Pt(IV) complexes **3**–**6** (red) recorded at a glassy carbon electrode in buffered aqueous solution (PBS, pH = 7.4, I = 0.1) containing 5 mM NaCl as supporting electrolyte and $5 \cdot 10^{-4}$ M Pt(IV) complex. Scan rate 20 mV/s. The CV plot of the blank solution is overlaid in grey.

Sulforhodamine B (SRB) assay

The HCT-15 cells were seeded at $5x10^3$ cells per well in 96-well plates. After 24 hours, the medium was replaced with fresh medium containing dissolved tested compounds at increasing concentrations. After 72 hours, cells were fixed in cold trichloroacetic acid solution (final concentration 10% in medium) and left at 4 °C for 2 hours. The fixative solution was removed and wells were washed five times with distilled water. 50 μL Sulforhodamine B (0.4% m/v) solution was added to each well for 15 minutes. Wells were then washed with glacial acetic acid five times and air dried. 150 μL Tris (10 mM) solution was added to each well and plates were gently shaken for 10 minutes on a mechanical shaker, or until the remaining dye was completely resuspened. The inhibition of cell growth was determined by measuring the absorbance of each well at 540 nm using a Bio-Rad 680 microplate reader. Dose–response curves were fitted and IC_{50} values were calculated using the four parameter logistic model (4PL).

Table S1. *In vitro* cytotoxic activity of the Pt(II, IV) complexes measured by the SRB test.

	HCT-15 IC_{50} **(μM) ± S.D.**
Racemate (1 & 2)	6.5±1.1
1 (*R,R*)	3.3±0.6
2 (*S,S*)	8.5±2.0
Racemate (OBz)	0.2±0.1
3 (*R,R*)	4.3±0.8
4 (*S,S*)	0.5±0.2
Racemate (OAc)	1.9±0.4
5 (*R,R*)	5.5±0.7
6 (*S,S*)	1.1±0.6
cisplatin	18.5±3.1
oxaliplatin	3.1±0.9

Cell cultures were treated for 72 h with increasing concentrations of tested compounds. Cytotoxicity was evaluated with the SRB test. IC_{50} values were calculated by 4-parameters logistic model ($p < 0.05$).