Dinuclear osmium(II) complexes for the visualisation of cellular DNA structure using electron microscopy†

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Supplementary Information

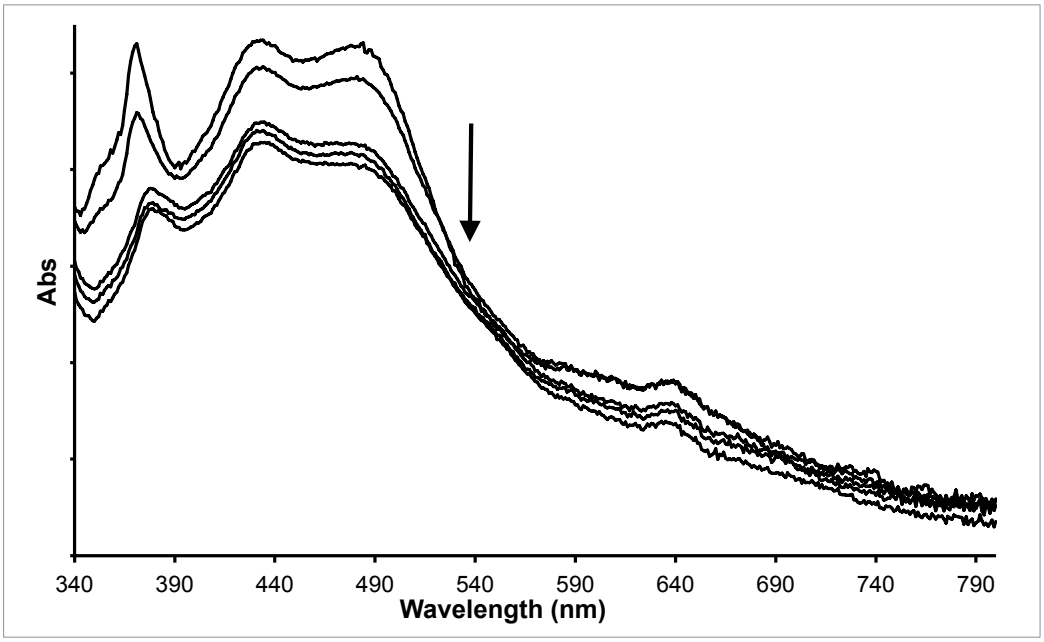
Synthesis

The hexafluorophophate salt of complex **1** was synthesized by a literature method.[1]

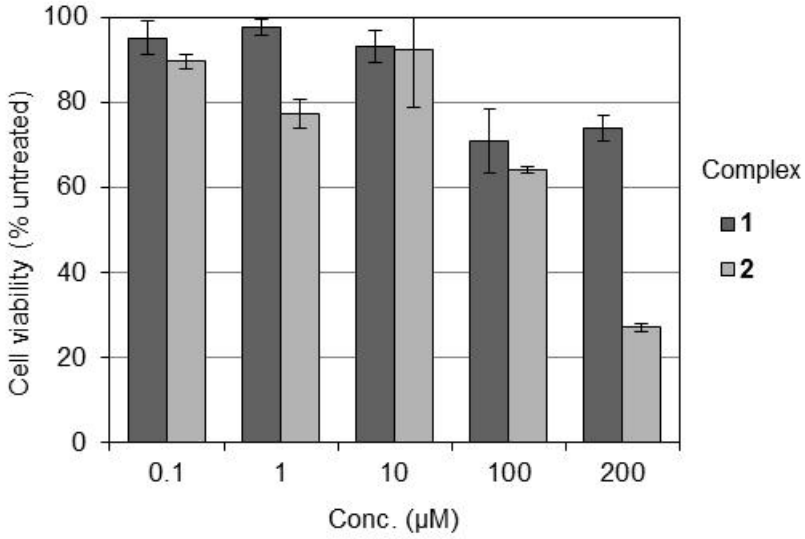
[**2**]$(PF_6)_2$ $Osphen_2Cl_2$ (300 mg,) and tpphz (200 mg) were refluxed in 20 mL of dry ethylene glycol under an argon atmosphere for 12 hours. After being left to cool, 100 mL of water was added and the complex precipitated out with addition of KPF_6. The black/brown solid was collected by centrifugation, and washed with 3x 20 mL water. The product was then purified using column chromatography on silica ($MeCN:H2O:KNO_3$:tBuOH, 60:40:10:5). The compound was collected pure as a nitrate salt from the main black band, and was converted to a PF_6 salt to give a dark black solid. To obtain analytically purity this crude product was converted to its chloride salt by anion metathesis and then passed through a LH20 sephadex size exclusion column eluted with methanol . Final yield = 10%. ^{1}H NMR (hexafluorophosphate salt; 400 MHz, CD_3CN) : δ 9.70 (d, 1H), 8.45 (dd, 2H), 8.29 (s, 2H), 8.16 (t, 2H), 7.97 (d, 1H), 7.79 (dd, 1H), 7.62 (dd, 2H). MS(ESI) - m/z (%): 544 (100) $[M+PF_6]^{3+}$, 888 (50) $[M+2PF_6]^{2+}$, 1920 (2) $[M+3PF_6]^+$ ^{1}H NMR (Chloride salt; 400 MHz, MeOD) : δ 9.86(d, 1H), 8.54 (m, 2H), 8.37 (d, 2H), 8.31 (m, 1H), 8.28 (dd, 1H), 8.07 (d, 1H), 7.92 (dd, 1H), 7.73 (m, 2H).

DFT Calculations

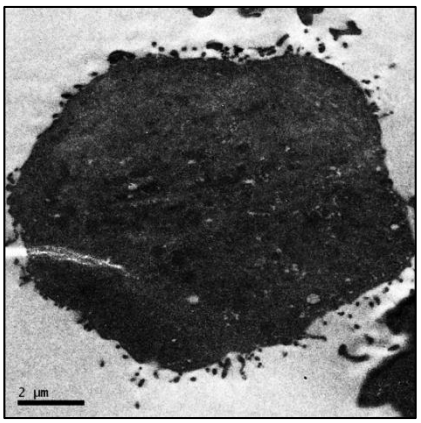
Density functional theory (DFT) calculations were performed using Gaussian09, version D.01.[2] The B3LYP functional[3] was used throughout with the 6-311G** basis set[4] on all C, N, H, and O. A Stuttgart-Dresden pseudopotential[5] was used on Ru or Os throughout. This computational procedure was found to give good correlation with experiment in previous work.[6] The starting atomic coordinates of complex 1 are based on previous calculations on a similar system.[7] All the calculations performed on these systems were done using water as the solvent via a polarizable continuum model (PCM)[8] using the standard parameters as supplied by Gaussian. The following procedure was used. First, the complexes were optimized in their singlet ground state. Harmonic frequencies were calculated upon convergence to obtain the IR spectrum. No imaginary frequencies were found, confirming the structures as minima. The overlay was created using vROCS v. 3.1.2.[9]



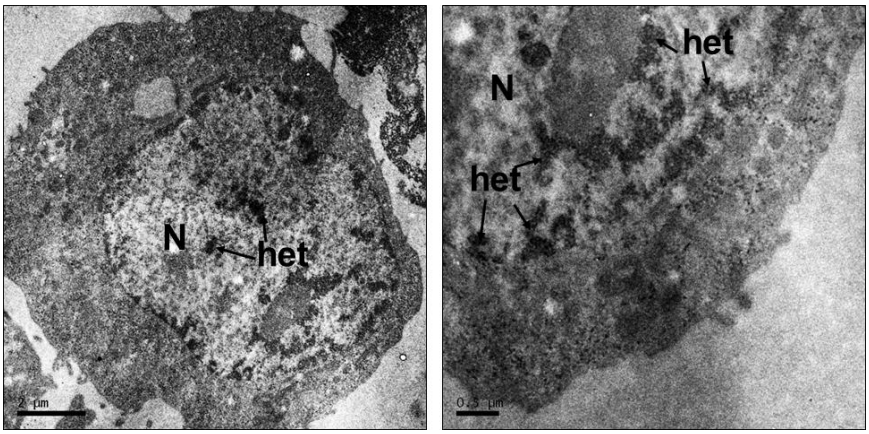
Supplementary Figure 1. Changes in the UV-Visible spectrum of [**2**]Cl4 on progressive addition of calf-thymus DNA.



Supplementary Figure 2. Cytotoxicity of **1** and **2** towards MCF7 human breast cancer cells (24 h exposure time).



Supplementary Figure 3. TEM of MCF7 cell incubated with **1** (500 µM, 1 h) showing minimal intracellular definition.



Supplementary Figure 4. TEM of MCF7 cell incubated with **2** (500 µM, 1 h) showing intracellular definition, particularly heterochromatin (het) staining within the cell nucleus (N).

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