Supplementary Material (ESI) for Dalton Transactions

Supporting Information for:

The Preparation and Characterization of trans-Platinum(IV) Complexes with Unusually High Cytotoxicity

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X-ray crystallography:

Data collection for $\mathbf{2^{IV}}$ and $\mathbf{3^{IV}}$ was performed on an Enraf-Nonius Kappa CCD diffractometer equipped with Mo Kα radiation (λ = 0.71069 Å). Data reduction and cell refinement were carried out using DENZO and SCALE-PACK programs.[ESI-1] Both structures were solved by standard Patterson methods and refined by full-matrix least-squares methods based on F^2 using the SHELXL-97 [ESI-2] and WinGX [ESI-3] programs. All non-hydrogen atoms were refined anisotropically, and all hydrogen atoms were included in geometrically calculated positions and refined with isotropic displacement parameters according to the riding model.

The low value for theta(max) for $\mathbf{3^{IV}}$ (22.2°), is much lower than expected for Mo radiation (> 25°) because of the poor quality and small size of the crystal. Although the complex $\mathbf{3^{IV}}$ is chemically pure, its crystallization was not trivial, and only very small crystals of poor quality were obtained in several crystallization processes.

[ESI-1] Z. Otwinowsky, and W. Minor, *Methods Enzymol.* 1997, **276**, 307.

[ESI-2] G. M. Sheldrick, *SHELX97; University of Göttingen, Göttingen, Germany*, 1998

[ESI-3] L. J.Farrugia, *J. Appl. Crystallogr.* 1999, **32**, 837.

The crystal packing of $\mathbf{2}^{\mathbf{IV}}$ includes three water molecules of crystallization, which allows an unusual hydrogen bonding pattern. Neighboring $\mathbf{2}^{\mathbf{IV}}$ complexes form ribbons along the *a* axis connected by two-fold hydrogen bonds (Figure S1): N1(H)···O1, 2.750(3) Å; O1(H)···Cl1, 3.333(2) Å; and O2(H)···Cl2, 3.255(2) Å. In addition, the water molecules generate a 2D cluster extended on the *ab* plane, based on H-bonding interactions. This cluster can be classified as L4(6)6(7)8(8) (reference Infantes), merging tetragons (-O3-O5-O3-O5-), hexagons (-O2-O3-O3-O5-O4-O4-), and decagons (-O2-O3-O5-O4-O2-O3-O5-O4-): O3···O3, 2.755(5) Å; O3···O2, 2.700(3) Å; O3···O5, 2.780(4) Å; O4···O4, 2.754(5) Å; O4···O2, 2.761(3) Å; O4···O5, 2.732(4) Å; O5···O3, 2.732(3) Å. Thus, the polymeric ribbons are confined between clusters, leaning towards the hydroxido (O2···O3 and O2···O4) and amine (N11···O4, 2.874(3) Å; N11···O5, 2.892(3) Å) groups.

In complex $\mathbf{3}^{\mathbf{IV}}$, the methylamine ligand (C12) is placed over the planes defined by (Pt1,Cl1,Cl2,N1,N11) and (Pt1,O1,O2,N1,N11) with a dihedral angle (Pt1,N11,C12) of 65.5º and 25.2º, respectively, while the isopropylamine ligand is placed under these planes with a dihedral angle (Pt1,N11,C2) of 65,7º and 25.0º, respectively. Intermolecular interactions are observed in this structure just involving the oxygen of the hydroxide ligands and amino protons (Table S2)

Table S1. Hydrogen-bonding interactions (distances in Å) of complex **2**$^{\mathbf{IV}}$.

O3···O3$^{(i)}$	2.755(5)
O3···O2	2.700(3)
O3···O5$^{(ii)}$	2.780(4)
O4···O4$^{(iii)}$	2.754(5)
O4···O2	2.761(3)
O4···O5	2.732(4)
O5···O3$^{(iv)}$	2.732(3)
N11···O5	2.892(3)
N11···O4$^{(v)}$	2.874(3)
N11···O1$^{(vi)}$	2.750(3)

Symmetry operations: (i) –x+1, –y, –z+2; (ii) –x, –y+1, –z+2; (iii) –x+1, –y+1, –z+2; (iv) x, y+1, z; (v) –x, –y+1, –z+2; (vi) –x, –y+1, –z+1

Table S2. Hydrogen-bonding interactions (distances in Å) of complex **3**$^{\mathbf{IV}}$.

N11(H) ···O1$^{(i)}$	2.802(12)
N1(H)···O2$^{(ii)}$	2.877(12)

Symmetry operations: (i) –x, y–1/2, –z+1/2; (ii) –x+1, y+1/2, –z+1/2

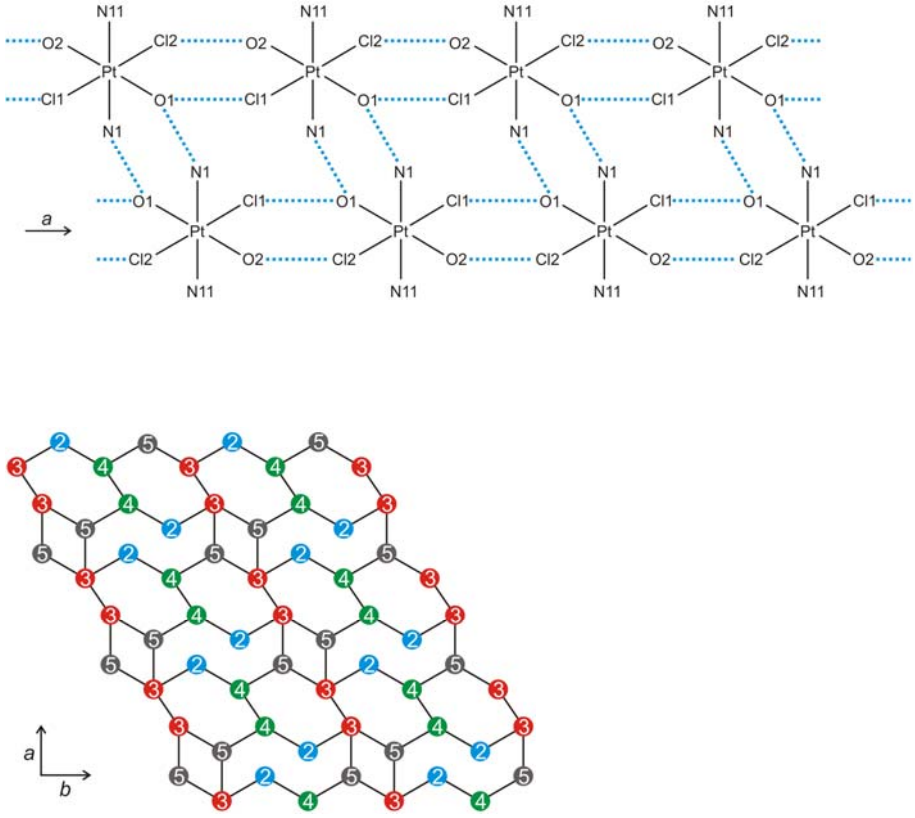
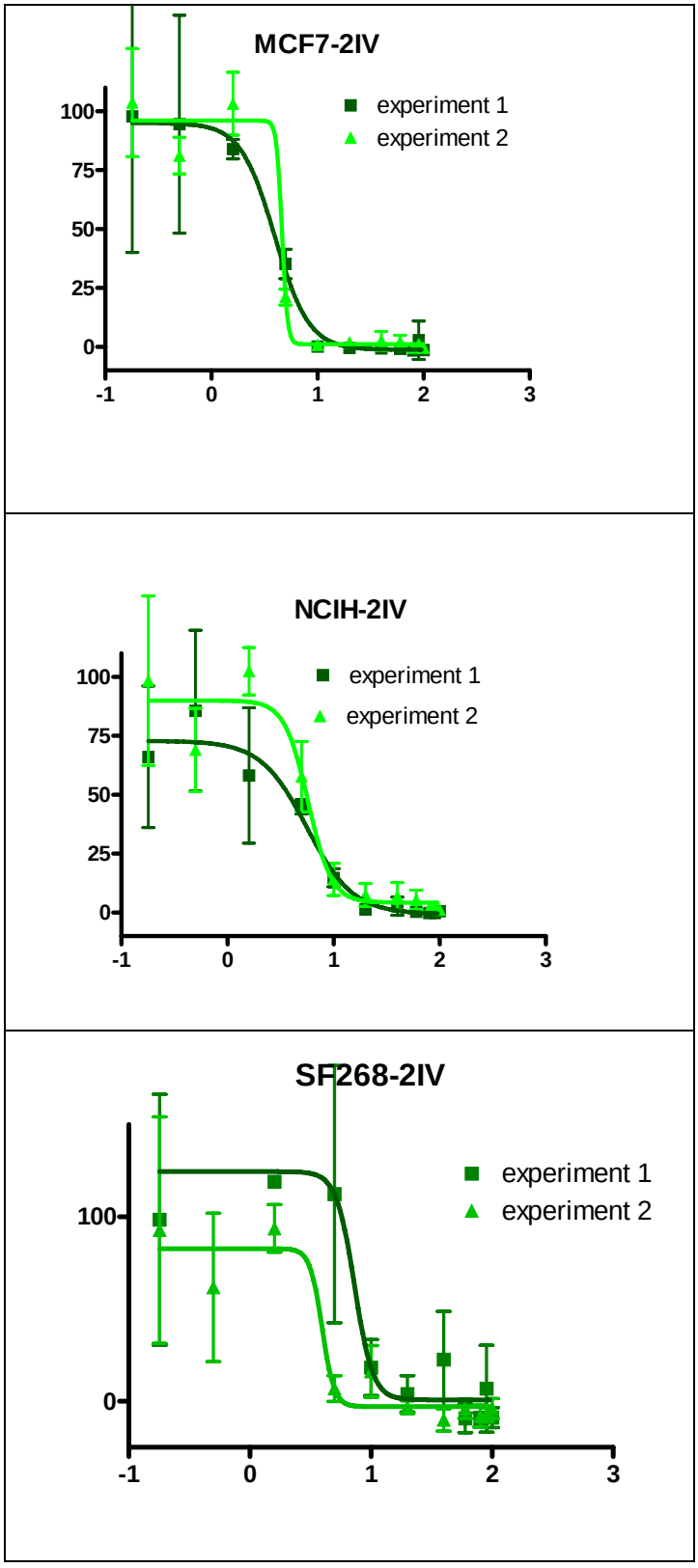
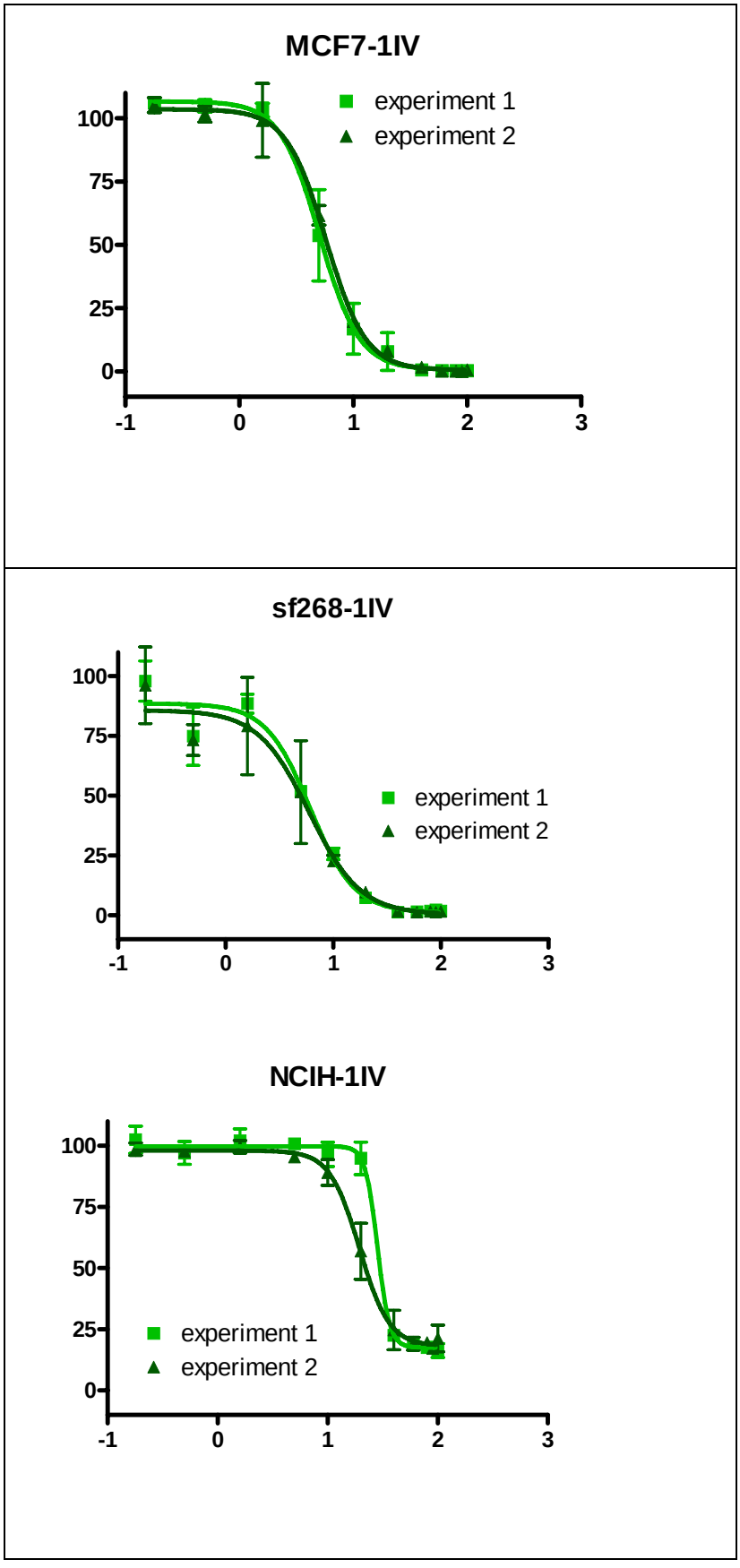


Figure S1. Hydrogen bonding patterns in **2**^{IV}

Figure S2: IC_{50} plots

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experiment 2
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50
25
0
-1
0
1
2
3
sf268-1IV
experiment 1
experiment 2
100
75
50
25
0
-1
0
1
2
3
NCIH-1IV
experiment 1
experiment 2
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75
50
25
0
-1
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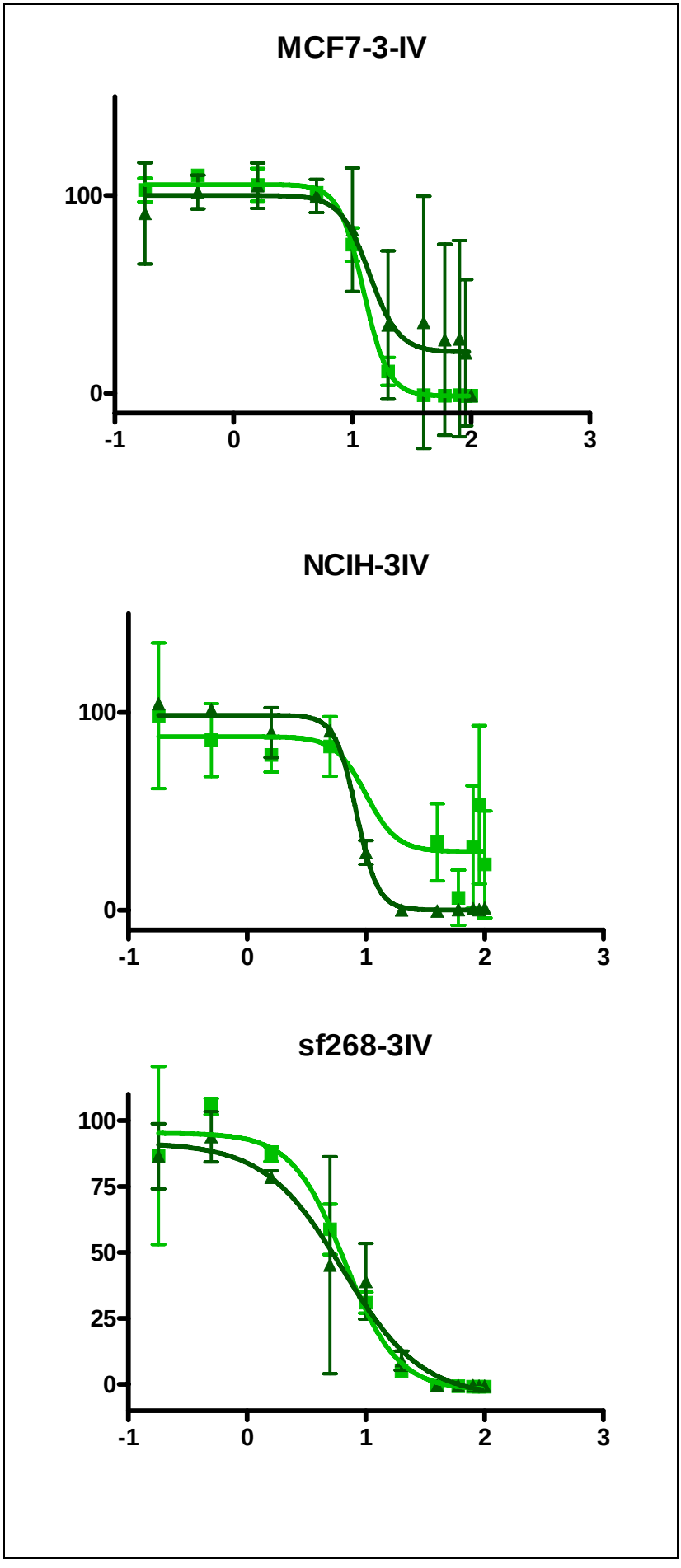
1
2
3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3
NCIH-3IV
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3
sf268-3IV
100
75
50
25
0
-1
0
1
2
3