Supplemental Figures

Supplemental Figure 1. Related to Figure 4. Cytotoxicity of cisplatin analogues in H1975 cells

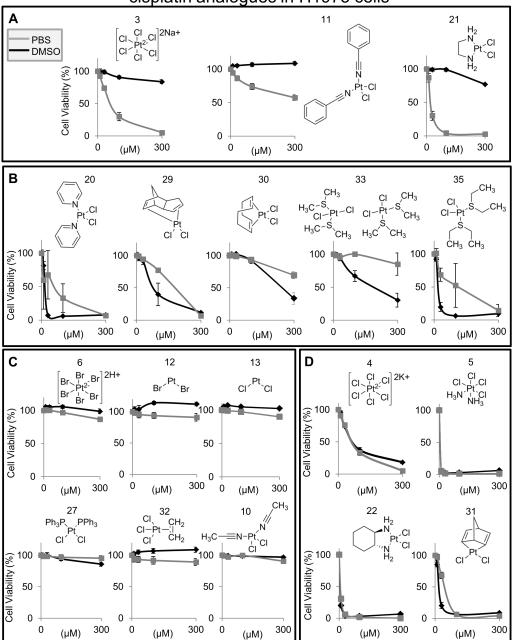
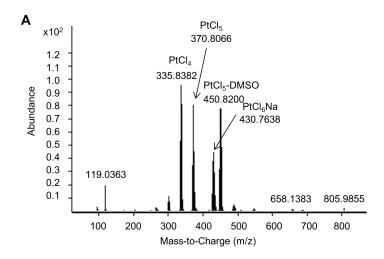


Figure S1 Related to Figure 4. Cytotoxicity of cisplatin analogs in H1975 Cells. Antidotes identified in the SAR study were solvated in DMSO or PBS and assessed for cytotoxicity in H1975 cells. A) DMSO inactivated the cytotoxic activity of complex 3, 11 and 21 while maintaining or improving their efficacy as cyanide antidotes. B) Complexes 20, 29, 30, 33 and 35 displayed increased ability to induce cell death when solvated in DMSO compared to PBS. C) Complexes 6, 10, 12, 13, 27 and 32 displayed minimal ability to induce cell death in both DMSO and PBS formulations at doses up to 300 μ M. D) Complexes 4, 5, 22 and 31, in both PBS and DMSO formulations were more cytotoxic than cisplatin. Data represented as the mean \pm SEM.

Supplemental Figure 2. Related to Figure 5 and 6. Identification of the products generated by the reaction of hexachloroplatinate(IV) with DMSO and their capacity to bind cyanide anions



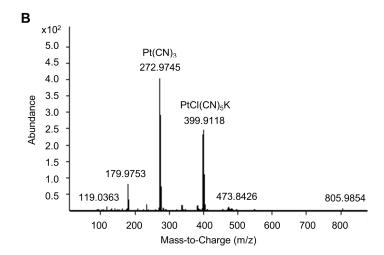


Figure S2 Related to Figure 5 and 6. Identification of the products generated by the reaction of hexachloroplatinate(IV) with DMSO and their capacity to bind cyanide anions. A) To decipher the chemical species created when hexachloroplatinate(IV) is dissolved in DMSO, we used ESI-MS. DMSO undergoes nucleophilic attack of the platinum atom, displacing one chloride ligand and generating PtCl₅-DMSO (m/z = 450). An ion signal detected at m/z = 430 corresponds to the starting material (PtCl₆Na). B) When cyanide is add to hexachloroplatinate(IV) that has been dissolved in DMSO the most abundant ion signals detected were at m/z = 272 and 399 corresponding to the platinum atom bound to 3 or 5 cyanide anions.

Supplemental Tables

Table S1. Related to Figure 1. Identification of the products generated from the reaction between cyanide and cisplatin (DMSO) using isotope distribution comparison of K12C14N versus K13C15N

Species	Peak in K ¹² C ¹⁴ N	Peak in K ¹³ C ¹⁵ N	Mass Difference
[Pt(CN) ₄]	337.9	345.9	8
$[Pt(CN)_3]$	272.9	278.9	6
$[Pt(CN)_3DMSO]$	350.9	356.9	6

Table S2. Related to Figure 3. Peaks observed for ESI+ mass spectra of cisplatin dissolved in DMSO

Species	Formula	Observed Mass	Calculated Mass
[Pt(NH3)2(Cl)(DMSO)]+	C2H12ClN2OPtS	342.9996	343.0085
[Pt(NH3)(Cl)(DMSO)2]+	C4H15ClNO2PtS2	403.9868	403.9959
$\mu NH2$ -[Pt(NH3)(Cl)(DMSO)]2+	C4H20Cl2N3O2Pt2S2	665.9661	665.9670