Electronic Supporting Information

Materials and Methods Silicon(IV) phthalocyanine dichloride ($SiPcCl_2$), 4-hydroxypyridine, 3-hydroxypyridine, cisplatin, and $AgNO_3$ were commercially available and used as supplied. Dimethylformamide (DMF) used in this work was dried with anhydrous Na_2SO_4 for 3 days and distilled. Anhydrous toluene and pyridine was prepared following standard purification procedures.[1] Other solvents were obtained commercially and used as received. Complex **3** was synthesized following the similar procedure in literature.[2] ESIMS analyses were carried out using CH_3CN as solvent on a Finigan LCQ electrospray mass spectrometer. ^1H NMR spectra were acquired on a Bruker Avance DRX 500M spectrometer. Elemental analyses were performed with an Elementar Vario EL-III elemental analyzer.

Synthesis of bis(4-pyridinolato) silicon(IV) phthalocyanine (L_2) **L_2** was synthesized using a modified method reported in ref [3]. $SiPcCl_2$ (5.01 g, 8.19 mmol) was dispersed in 250 mL of anhydrous toluene, then 4-hydroxypyridine (1.61 g, 16.9 mmol) and 10 mL of pyridine were added. The mixture was stirred and refluxed for 24 h. After cooling to room temperature, the solid was filtered out and extracted with $CHCl_3$ (500 mL × 3). The $CHCl_3$ extracts were evaporated to dryness under reduced pressure. The residue was washed by 300 mL of CH_3CN for three times facilitated by ultrasound at room temperature and dried *in vacuo*. The product was obtained in the form of deep purple powder. Yield: 1.38 g, 1.89 mmol (23%). ^1H NMR ($CDCl_3$): δ= 9.71 (dd, J = 2.8, 5.4 Hz, 8H, Pc-H_α), 8.48 (dd, J = 2.8, 5.6 Hz, 8H, Pc-H_β), 6.83 (d, J= 6.2 Hz, 4H, Py-H_1), 2.56 ppm (d, J= 6.2 Hz, 4H, Py-H_2).

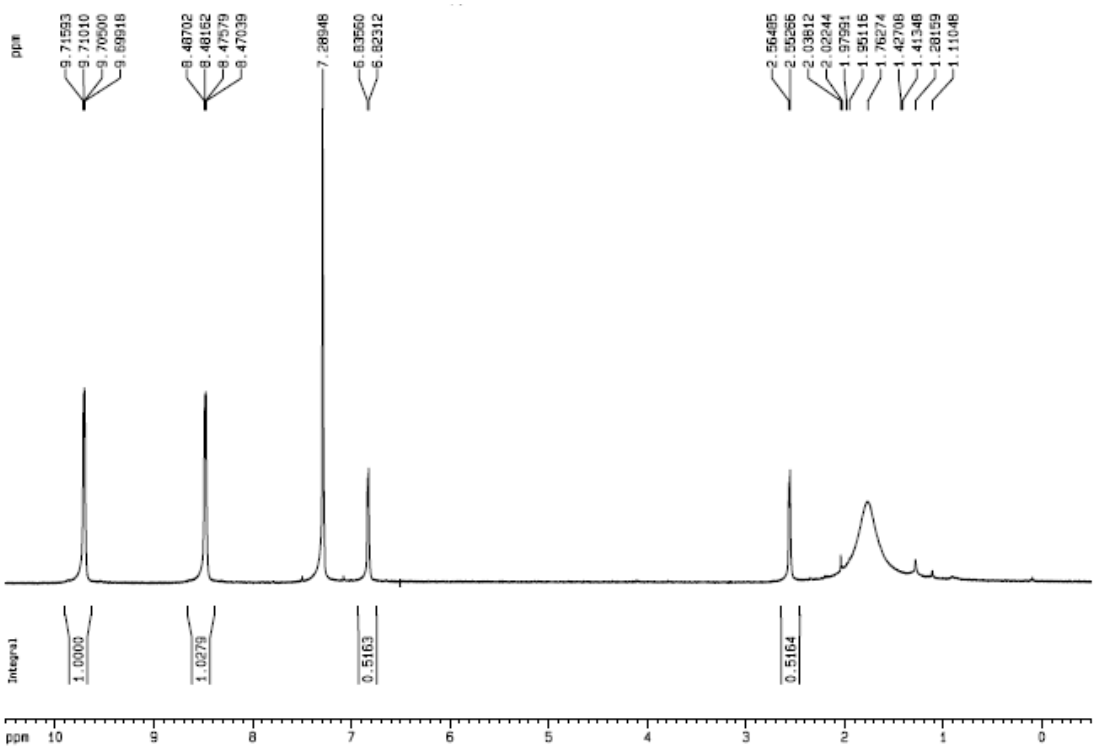

Figure S1. ^1H NMR spectrum of **L_2** in $CDCl_3$.

Synthesis of bis(3-pyridinolato)silicon(IV)phthalocyanine (L_1) **L_1** was synthesized using

3-hydroxypyridine as starting material following the same procedure of $\mathbf{L_2}$. Yield: 2.28 g, 3.13 mmol (38%). ^{1}H NMR ($CDCl_3$): δ = 9.70 (dd, J = 2.8, 5.6 Hz, 8H, Pc-H_α), 8.46 (dd, J = 2.8, 5.6 Hz, 8H, Pc-H_β), 7.04 (d, J = 4.6 Hz, 2H, Py-H_1), 5.76 (m, 2H, Py-H_2), 3.97 (s, 2H, Py-H_3), 2.97 ppm (d, J = 8.1 Hz, 2H, Py-H_4).

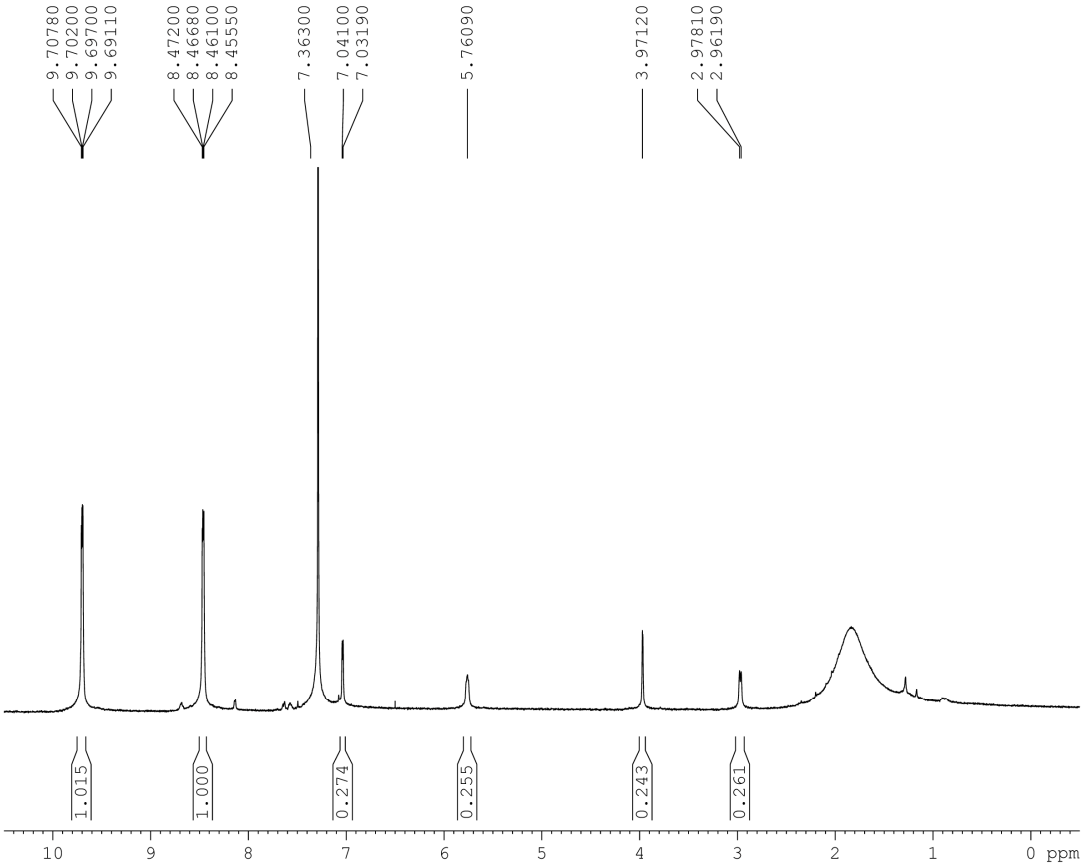

Figure S2. ^{1}H NMR spectrum of $\mathbf{L_1}$ in $CDCl_3$.

Synthesis of Complex 1 Cisplatin (213 mg, 0.710 mmol) and $AgNO_3$ (112 mg, 0.659 mmol) was dissolved in 10 mL of DMF and stirred at room temperature for 12 h. The turbid solution formed was centrifuged and the white solid was removed. The light yellow solution yielded was heated to 45 °C and 10 mL of DMF suspension of $\mathbf{L_1}$ (115 mg, 0.158 mmol) was added dropwise in 30 min. The mixture was further heated at 45 °C for 12 h. After that, the mixture was cooled to ambient temperature and then centrifuged at 10,000 rpm. The solid was discarded and the clear deep blue solution was mixed with 200 mL of Et_2O and stand for a few hours. The precipitated crude product was collected on a sinter glass filter and washed using water (7 mL × 3). The precipitate was further washed using acetone (10 mL × 3) and Et_2O (10 mL × 3) and then dried *in vacuo* and the product was obtained as a deep blue powder. Yield: 119 mg, 0.086 mmol (54%). ^{1}H NMR (d_6-DMSO): δ = 9.73 (dd, J = 2.9, 5.6 Hz, 8H, Pc-H_α), 8.59 (dd, J = 2.9, 5.6 Hz, 8H, Pc-H_β), 7.09 (d, J = 5.5 Hz, 2H, Py-H_1), 5.85 (dd, J = 5.5, 7.8 Hz, 2H, Py-H_2), 4.07 (d, J = 2.2 Hz, 2H, Py-H_3), 2.88 (d, J = 7.8 Hz, 2H, Py-H_4), 3.79 (s, NH_3), 3.51 ppm (s, NH_3). ESIMS (+): *m/z* calculated for $[C_{42}H_{36}Cl_2N_{14}O_2Pt_2Si]^{2+}$, 628.1; found, 628.5. Elemental analysis: calcd (%) for $C_{42}H_{36}Cl_2N_{16}O_8Pt_2Si$, C 36.50, H 2.63, N 16.22; found, C 35.68, H 2.77, N 15.42.

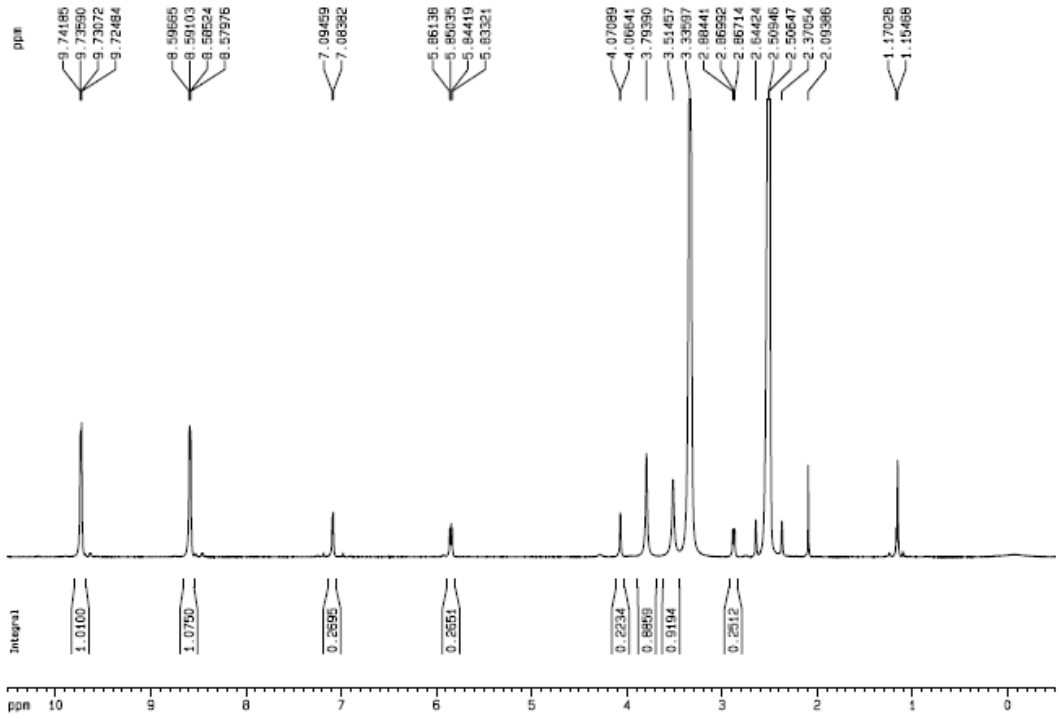

Figure S3. ^{1}H NMR spectrum of **1** in d_6-DMSO.

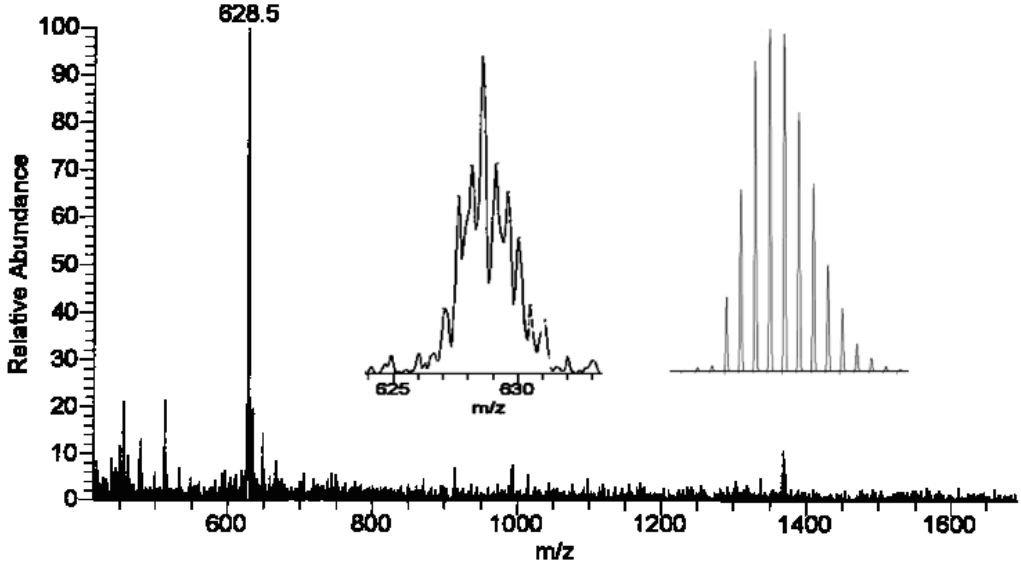

Figure S4. ESIMS spectrum of **1**.

Synthesis of Complex 2 This complex was synthesized using $\mathbf{L_2}$ following the same procedure of **1** except the reaction temperature was 80 °C. Yield: 113 mg, 0.082 mmol (52%). ^{1}H NMR (d_6-DMSO): δ= 9.73 (m, 8H, Pc-H_α), 8.61 (m, 8H, Pc-H_β), 6.90 (d, J = 6.6 Hz, 4H, Py-H_1), 2.57 (d, J = 6.6 Hz, 4H, Py-H_1), 3.82 (s, NH_3), 3.79 (s, NH_3). ESIMS (+): *m/z* calculated for $[C_{42}H_{36}Cl_2N_{14}O_2Pt_2Si]^{2+}$, 628.1; found, 629.3. Elemental analysis: calcd (%) for $C_{47}H_{48}Cl_2N_{16}O_8Pt_2Si$, C 36.50, H 2.63, N 16.22; found, C 36.00, H 2.90, N 14.80.

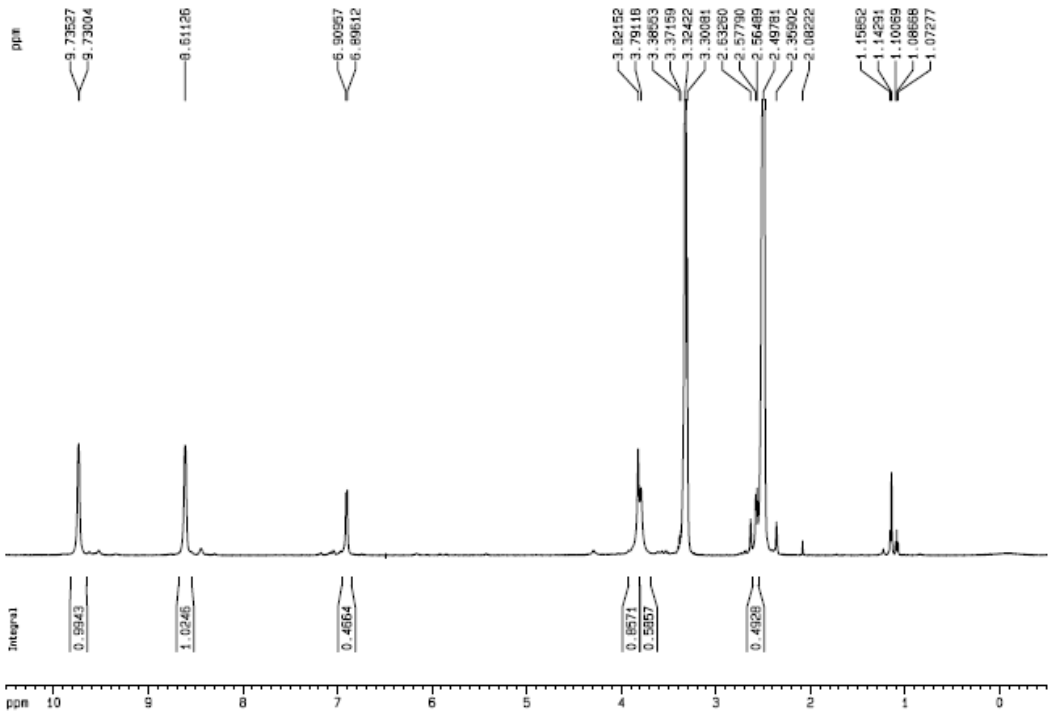

Figure S5. ^{1}H NMR spectrum of **2** in d_6-DMSO.

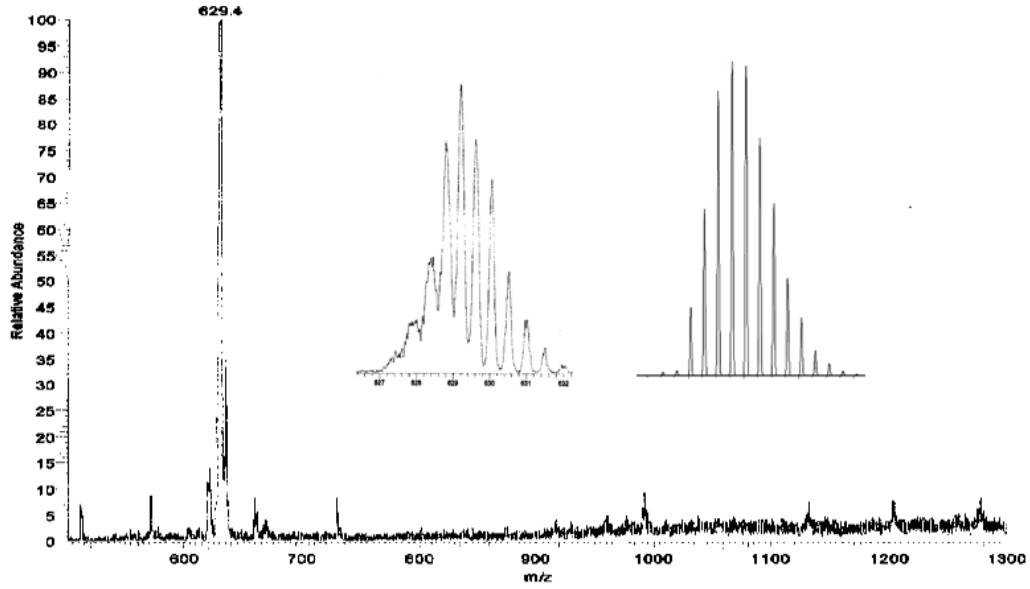

Figure S6. ESIMS spectrum of **2**.

Photophysical studies The UV-Vis spectra were measured on a Perkin-Elmer LAMBDA-35 spectrometer. The absorption peaks at 659 nm in the UV-Vis spectra of the complexes can be distinguished in their second derivative spectra. Fluorescence spectra were recorded on an AMINCO Bowman Series 2 luminescence spectrometer.

Fluorescence quantum yields (Φ_F) were measured according to the relationship: $\Phi_{F(sample)} = (F_{sample} / F_{reference}) (A_{reference} / A_{sample}) (n_{sample}^2 / n_{reference}^2) \Phi_{F(reference)}$, where F, A, n are the integrated fluorescence intensity (Ex = 610 nm), the absorbance at the excitation wavelength ($A_{610\ nm}$), and

the refractive index of the solvent, respectively. Zinc phthalocyanine (ZnPc) in 1-chloronaphthalene was used as a standard with a literature value for Φ_F = 0.30.[4] The Φ_F measurements were performed using very dilute solutions to minimize the self-absorbance.

Table S1. Photophysical data for **1** and **2** in DMF.

Complex	λ_{max} / nm (ε / 10^4 M^{-1} cm^{-1})	λ_{em} / nm	Φ_F	Φ_Δ
1	355 (6.01), 618 (3.23), 659 (3.23), 688 (18.9)	696	0.21	0.24
2	355 (5.89), 618 (3.09), 659 (3.10), 688 (18.2)	695	0.19	0.22

Singlet oxygen quantum yields (Δ) were measured using the DPBF method.5 Red light laser (650 nm) was used as the light source and DMF solution of ZnPc was chosen as the reference (Δ = 0.56).5

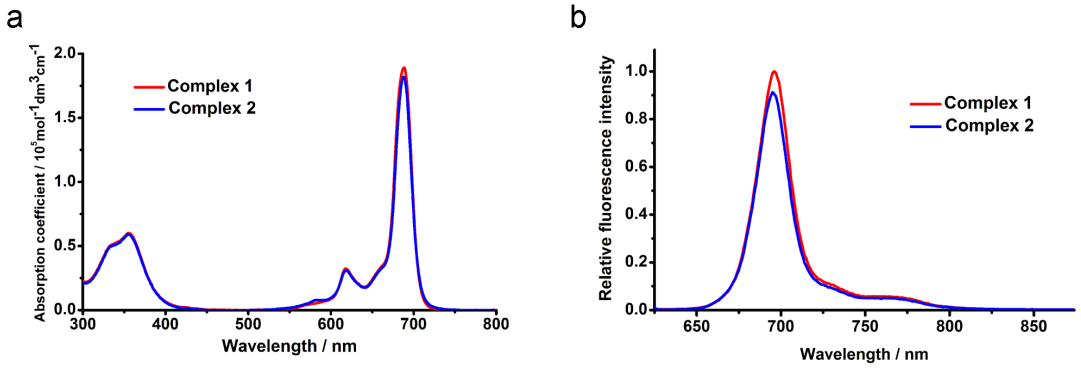

Figure S7. UV-Vis spectra (a) and fluorescence spectra (b) of complex **1** and **2** in DMF.

Cell culture The HeLa human cervical cancer cells (ATCC) were thawed from a frozen stock and were passed every 2 to 3 days. HeLa cells were incubated in Dulbecco's Modified Eagle's Medium (DMEM) containing 10% fetal bovine serum (FBS) at 37 °C under 5% CO_2.

Cytotoxicity and photocytotoxicity MTT assay was employed to test the cytotoxicity and photocytotoxicity. HeLa cells were seeded onto 96-well plates and incubated in DMEM containing 10% FBS over night at 37 °C under 5% CO_2. The medium was exchanged for a fresh one and stock solution of **3** or cDDP or fresh prepared DMSO solution of **1** or **2** (containing 10% (v/v) Cremophor EL) was added to achieve different concentrations. Then the cells were dark-incubated for 24 h followed by 60 min exposure to the red light (600 - 710 nm, 20 $mW \cdot cm^{-2}$) from a projector coupled with a red light band-pass filter. After irradiation, the cells were further incubated in dark for 24 h. For testing the cytotoxicity in dark, the cells were dark-incubated for 48 h after administration of the complexes. After co-incubation with the complexes, 10 µL / well 3-(4,5-dimethylthiazol-2-yl)-2,5 -diphenyltetrazolium bromide (MTT) stock solution (4 mg / mL) was added and the cells were further incubated for 2 h. Then 100 µL DMF/H_2O (v:v = 1:1) solution of SDS (m:v = 10%) was added. After 20 h incubation, the absorption of the solution at 570 nm was measured by a Tecan Sunrise platereader.

Table S1. The cytotoxicity data shown in Figure 1 with the SD values. The experiments were carried out in triplicate. The experiments in dark were carried out with three wells per condition, and experiments under irradiation were carried out with one well per condition.

compound	Inhibition ratio in dark (%)				Inhibition ratio under red light irradiation (%)			
	10^{-4} M	10^{-5} M	10^{-6} M	10^{-7} M	10^{-4} M	10^{-5} M	10^{-6} M	10^{-7} M
cDDP	100.0 ± 2.1	52.3 ± 17.6	9.7 ± 9.6	0.1 ± 8.7	100.0 ± 0.3	67.9 ± 0.0	17.2 ± 3.1	2.3 ± 0.6
3	97.2 ± 0.4	46.7 ± 2.3	25.9 ± 1.5	10.5 ± 6.0	98.6 ± 0.2	43.7 ± 0.7	4.6 ± 4.5	1.4 ± 2.9
1	47.3 ± 16.3	16.7 ± 12.3	4.0 ± 6.9	0.9 ± 2.7	100.0 ± 0.6	100.0 ± 0.4	99.4 ± 0.2	24.8 ± 2.4
2	54.5 ± 5.4	20.0 ± 11.5	12.9 ± 18.3	4.1 ± 5.4	100.0 ± 1.2	101.2 ± 0.4	95.4 ± 0.1	8.3 ± 2.6

Hoechst 33342 staining HeLa cells were seeded at 2 × 10^5 cells per well on a 24-well plate with 1 mL growth medium per well and incubated over night. The medium was exchanged for a fresh one and the DMSO solution of **1** or **2** prepared as above was administrated into the medium to reach the concentration of 10 μM. The cells were incubated with or without red light irradiation as described in the cytotoxcity experiment. After incubation, the medium was exchanged for a fresh medium containing Hoechst 33342 at a concentration of 5 μg/mL. After 10 - 15 min staining, the stained HeLa cells were observed directly in the well using an Olympus IX 71 microscope (Ex = 330 - 385 nm, Em = 420 nm). For control experiment, HeLa cells incubated for 48 h neither in the presence of the complexes nor under red light irradiation were stained and imaged as above.

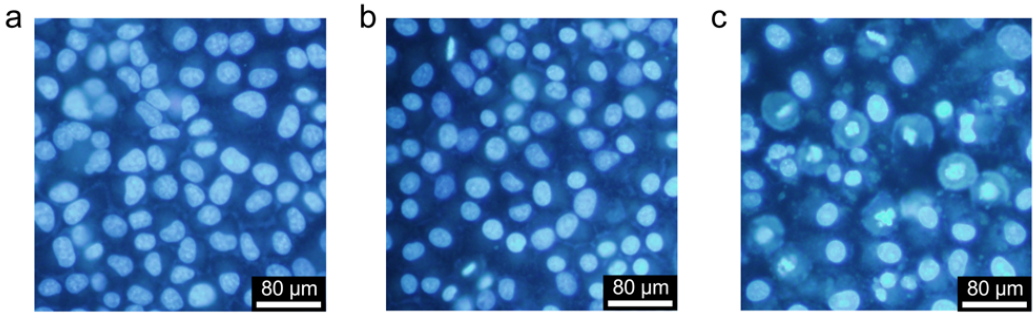

Figure S8. Hoechst 33342 staining of HeLa cells incubated with **1** (10 μM) for 48 h in the dark (b) or with red light irradiation (600 – 710 nm, 20 mW cm^{-2}, 1 h) (c). (a) shows the result of the control experiment without addition of **1**/**2** or red light irradiation.

Cellular uptake HeLa cells were seeded at 2 × 10^5 cells per well on 12-well plates and incubated over night. The medium was exchanged for a fresh medium (2 mL / well) and HeLa cells were dark-incubated with 10 μM **1** or **2** as above for 24 h. Then the medium was removed, cells were incubated with trypsin solution for 1 min. After digestion, the cells were rinsed with PBS (1 mL × 3). Cell numbers were counted using trypan blue staining and then cells were dispersed in 50 μL of ultrapure water. Then 70 μL of HNO_3 (ca. 16 M, G.R.) was added into the solution and heated to 95 °C for 2 h. After that, the solution was treated with 20 μL of H_2O_2 (30%) at 95 °C for 2 h followed by treatment with 35 μL of HCl (ca. 12 M, G.R.) at 37 °C for 0.5 h. Finally, the solution was diluted to 1.00 mL and the platinum content was determined in triplet using a Perkin-Elmer ELAN 9000 ICP-mass spectrometer.

For the fluorescence quantification, HeLa cells were incubated and treated with **1** or **2** as above for 24 h. Then the medium was removed, and the cells were lysed by treatment with 25 μL of lysis buffer (50 mM Tris-HCl, 150 mM NaCl, 0.1% NT-40, 0.1% Triton, 4 mM EDTA, 1 mM

DTT) for 0.5 h on ice. Then DMSO was added to keep the volume of the solution to be 100 μL. The fluorescence of the samples were measured on a Tecan Safire platereader (Ex = 620 nm, Em = 690 nm). The concentrations were accounted according to a series of standard samples prepared by adding quantified DMSO stock solution of **1** or **2** to the cell lysate.

Intracellular localization investigations: About 10^4 HeLa cells were seeded on a coverslip (18 mm × 18 mm) in a culture dish (6 cm diameter) and incubated in 3mL DMEM growth medium supplemented with 10% for 24 h FBS at 37 °C under 5% CO_2 atmosphere. Then the medium was exchanged for a fresh batch. DMSO solution of **1** or **2** (0.5 mM) was added into the culture system to acquire a final concentration of ca. 10 μM and the cells were further incubated for 24 h under the same condition. Then coverslip was mounted onto a microscope slide using 50% glycerin in PBS for taking photographs. Fluorescence images were taken using a Leica TCS SL confocal microscope. The 633 nm laser was chosen as the excitation source and the fluorescence images were imaged after passing a band-pass filter (650 nm -750 nm).

Circular dichroism (CD) studies The stock solution of calf thymus (CT) DNA was prepared by dissolving CT DNA in Tris-HCl buffer saline (5 mM Tris-HCl, 50 mM NaCl, pH = 7.4) at 4 °C. The concentration of the CT DNA stock solution was determined by the absorption intensity at 260 nm (ε = 6600 $M^{-1}\cdot cm^{-1}$). Complex **1** or **2** was dissolved in DMSO and used as a fresh solution. The final solution for CD measurements contained 100 μM CT DNA, 10% DMSO (v/v) for preventing precipitation of the complexes in Tris-HCl buffer saline. **1** or **2** is of different concentrations reaching various complex / DNA ratios. After 12 h incubation at 298 K, the CD spectra were recorded at the scan speed of 10 $nm\cdot min^{-1}$ on a Jasco J-810 automatic recording spectropolarimeter with a 1 cm pathway cell.

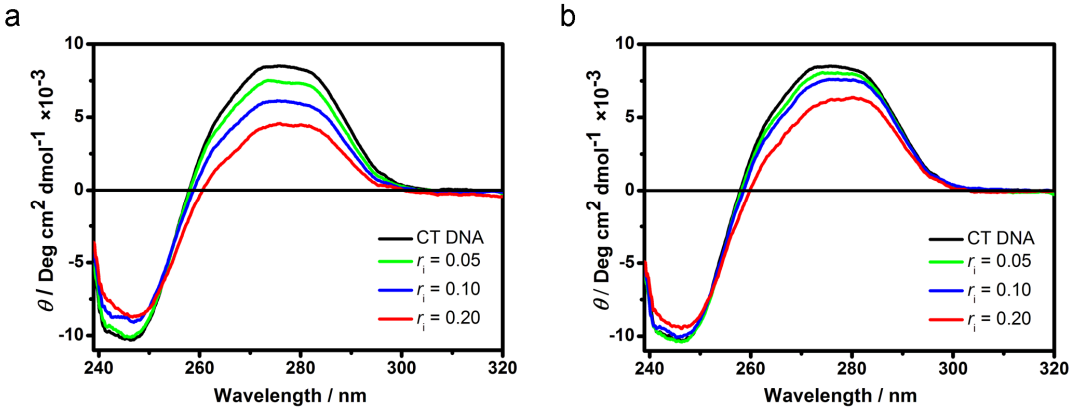

Figure S10. CD spectra of CT DNA (100 μM) in the absence (black line) and prescence (colored line) of complexes **1** and **2** at different r_i value.

Electrophoretic mobility shift assay pUC19 DNA (200 ng / 10 μL) was incubated with **1** or **2** at various complex / nucleotide ratios for 12 h at 37 °C in dark. The mixtures were loaded onto a 1.0% agarose gel. Following the electrophoresis at 50 mV for 2 h in TAE buffer (40 mM Tris acetate, 1 mM EDTA), the gel was stained with 0.5 $\mu g\cdot mL^{-1}$ ethidium bromide (EB) for 0.5 h and the bands were visualized and photographed using UVP BioImaging Systems.

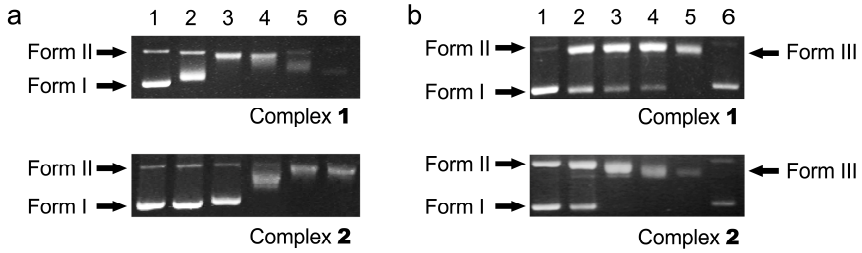

Figure S11. a) Agarose gel electrophoresis of pUC19 DNA incubated with **1** or **2** for 24 h at 310 K. Lane 1: DNA control, lane 2 – 6: the r_i values of 0.015, 0.045, 0.060, 0.150, 0.225, respectively. b) Agarose gel electrophoresis of pUC19 DNA (33 μM in bp) incubated with **1** or **2** for 2h at 298 K. Lane 1, DNA control; lane 2-5, the concentration of **1**/**2** of 1, 3, 5, 10 μM, respectively, under red light (650 nm, 70 mW, 2 h); lane 6, 10 μM **1**/**2**, in the dark.

Photocleavage studies pUC19 DNA (200 ng / 10 μL) was incubated with **1** or **2** at various concentrations at room temperature for 12 h in the dark. Then the solutions were illuminated with 650 nm red light laser (70 mW, 2 h) or remained in the dark at 25 °C. The reactions were then quenched by adding 2 μL of 6× loading buffer (30 mM EDTA, 36% glycerol, 0.05% xylene cyanol FF, 0.05% bromophenol blue) after which the resulting samples were loaded onto a 1.0% agarose gel containing EB. Following the electrophoresis at 50 mV for 2 h in TAE buffer (40 mM Tris acetate, 1 mM EDTA), the bands were visualized and photographed using UVP BioImaging Systems.

The reactive oxygen species were probed by the addition of radical scavengers or reaction inhibitors. pUC19 DNA (200 ng / 10 μL) was incubated with **1** (5 μM) or **2** (3 μM) at room temperature for 12 h in dark. Then 1 mM DMSO (as a diffusible hydroxyl radical scavenger), 100 μM NaN_3 (as a singlet oxygen scavenger), or 100 μM KI (as a hydrogen peroxide scavenger) was added into the solutions followed by the same procedures of irradiation, quenching, electrophoresis, and photographing. Densitometric analysis of EB fluorescence was conducted for quantification of each form of DNA. Because the intercalation of EB to supercoiled (SC) DNA is weaker than those to nicked and linear DNA, a correction factor of 1.47 was adopted for the estimation of concentration of SC DNA.[6]

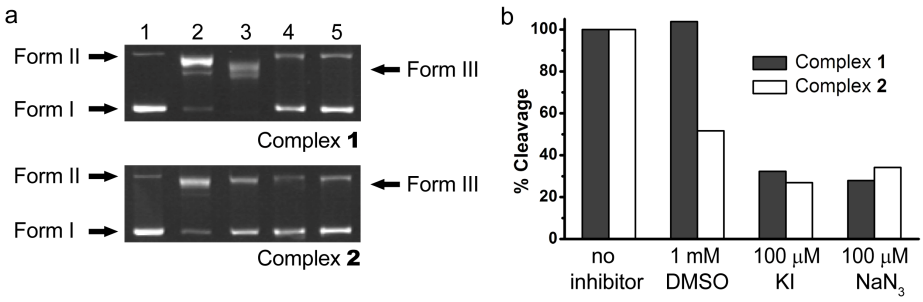

Figure S12. a) Agarose gel electrophoresis of pUC19 DNA (33 μM in bp) incubated with 1 (5 μM) or 2 (3 μM) with radical scavengers for 2 h at 298 K under red light irradiation (650 nm, 70 mW, 2 h). Lane 1, DNA control; lane 2, DNA + 1/2, + red light; lane 3 -5, DNA + 1/2 + 1 mM DMSO (a diffusible hydroxyl radical scavenger), 100 μM KI (a hydrogen peroxide scavenger), 100 μM

NaN_3 (a singlet oxygen scavenger), respectively, under red light as above. b) Histogram representation of the DNA red light DNA cleavage (nicked + linear) in Figure S11a.

2D [^{1}H, ^{15}N] HSQC NMR investigations The 4 mM stock solution of 5'-GMP was prepared by dissolving 5'-GMP disodium salt (Aldrich-Sigma) into mixed D_2O/H_2O (v:v = 1:4) and adjusting the pH value of the solution to 2.6 - 3.2 with aqueous $HClO_4$. The freshly prepared 2 mM DMF solution of **1** or **2** (250 μL) was mixed with 250 μL of stock solution of 5'-GMP. For studying the reactions in dark, the pH* value of the mixed solution was quickly readjusted to 6.32 for **1** or 5.61 for **2** by adding NaOH solution. The solution was then transferred to a NMR tube followed by NMR monitoring. For studying the reactions under red light irradiation, the pH* value of the mixed solution was quickly readjusted to 6.40 for **1** or 6.41 for **2** by adding NaOH solution. The solution was transferred into a NMR tube and bubbled with argon stream for about 2 min. After that the NMR tube were sealed immediately using a plastic plug with an optical fiber piercing through it. The optical fiber is coupled with a red light solid laser generator to conduct 650 nm multi-mode red light laser into the solution at 298 K. The output power at the end of the optical fiber was measured to be 52 mW by an LPE-1B power meter. After irradiation, the NMR tube was quickly mounted into the NMR spectrometer for acquisition.

2D [^{1}H, ^{15}N] HSQC spectra were recorded in a phase-sensitive mode using the TPPI quadrature detection scheme on a Bruker Avance DRX 500M spectrometer at room temperature. The ^{15}N chemical shifts were referenced externally to $^{15}NH_4Cl$ (1.0 M) in 1 M HCl at 0 ppm.

Since guanine residue of DNA is the primary target of platinum-based drugs, the interaction between ^{15}N-labelled **1** and **2** (^{15}N-**1** and ^{15}N-**2**) and guanine 5'-monophosphate (5'-GMP) has been monitored using 2D [^{1}H, ^{15}N] HSQC NMR technique (Figure S12). In the spectrum of ^{15}N-**1**, two cross-peaks with ^{15}N chemical shifts of -61.9 and -70.0 ppm were observed which can be assigned to the NH_3 groups *trans* to the Cl and the pyridyl group, respectively (Figure S12). When reacting ^{15}N-**1** or ^{15}N-**2** with 5'-GMP for 12 h in the dark, two new ^{1}H/^{15}N cross-peaks with equal intensity appeared at -67.05/4.15, -64.81/3.74 or -67.38/4.16, -62.33/3.70 ppm which can be assigned to mono-GMP adducts of the two complexes. As judged by the intensities of the new peaks, the adduct formation appears significantly slower than that of cisplatin. Due to the complicated nature of the reaction products, full assignment of each individual peaks require further intensive work. However, it is evident from the current data that the guanine binding ability of complexes **1** and **2** can be modulated using red light. To the best of our knowledge, this appears to be one of the rare examples in which the reactivity of platinum-based complex toward guanine can be manipulated by a red light irradiation.

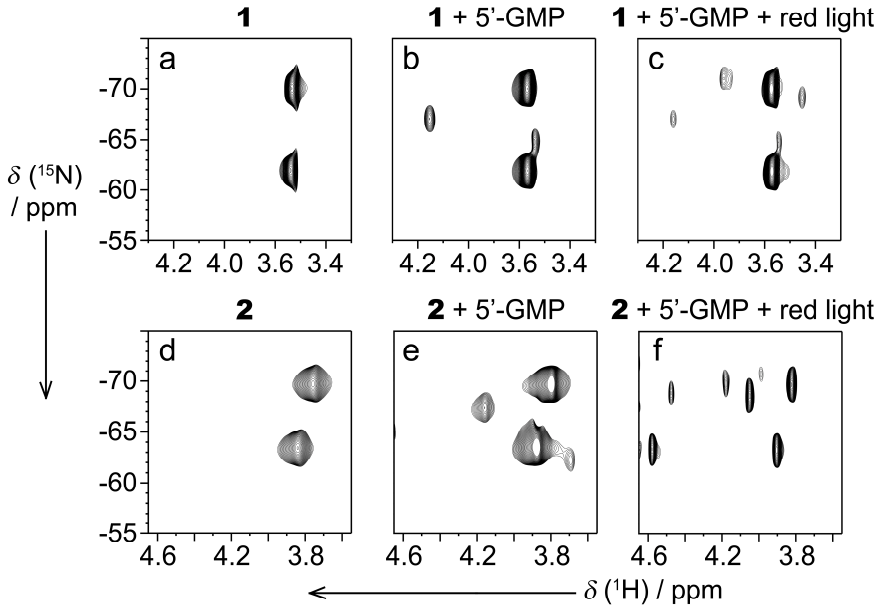

Figure S13. 2D [1H, 15N] HSQC NMR spectra of ^{15}N-**1** and ^{15}N-**2** in DMF-H2O-D2O mixed solvent (v : v : v = 5 : 4 : 1) (a, d) in the presence of 5'-GMP (molar ratio 1:2) in the dark (b, e) or under red light laser irradiation (650 nm, 52 mW, 6h) (c, f) at pH* 6.2 - 6.4, 298 K.

References

[1] *Purification of Laboratory Chemicals, 5th Ed*. (Eds.: W. L. F. Armarego, C. L. L. Chai) Elsevier, Burlington, **2003**, pp. 343, 370.

[2] L. S. Hollis, A. R. Amundsen, E. W. Stern, *J. Med. Chem*. **1989**, *32*, 128-136.

[3] J.-D. Huang, W.-P. Fong, E. Y. M. Chan, M. T. M. Choi, W.-K. Chan, M.-C. Chan, D. K. P. Ng, *Tetrahedron Lett*. **2003**, *44*, 8029-8032.

[4] G. Ferraudi in *Phthalocyanines - Properties and Applications, Vol. 1* (Eds.: C. C. Leznoff, A. B. P. Lever) VCH, New York, **1989**, pp. 301.

[5] W. Spiller, H. Kliesch, D. Wöhrle, S. Hackbarth, B. Röder, G. Schnurpfeil, *J. Porphyrins Phthalocyanines* **1998**, *2*, 145-158.

[6] Y. Jin, J. A. Cowan, *J. Am. Chem. Soc*. **2005**, *127*, 8408-8415.