Electronic Supplementary Material (ESI) for Dalton Transactions.

Electronic supplementary information

Bichromophoric ruthenium(II) bis-terpyridine-BODIPY based photosensitizers for cellular imaging and photodynamic therapy

Subhadeep Paul,[†] Sanmoy Pathak,[‡] Somarupa Sahoo,[†] Ram Chandra Maji,[†] Utso Bhattacharyya,[†] Dipankar Nandi[,‡] and Akhil R. Chakravarty*[,†]*

[†]Department of Inorganic and Physical Chemistry and [‡]Department of Biochemistry, Indian Institute of Science, Bangalore 560 012, India

Corresponding Authors

*D.N.: e-mail, nandi@iisc.ac.in

*A.R.C.: e-mail, arc@iisc.ac.in

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Materials:

All reagents and chemicals were purchased from commercial sources and used without further purification. $RuCl_3.xH_2O$ (39.0 % Ru content) was procured from Arora Matthey Ltd. (India) and subsequently converted to $Ru(DMSO)_4Cl_2$ following an established procedure.[S1] The solvent purification and drying for reactions were performed using established procedures and degassed with nitrogen using freeze pump thaw cycles or by purging with nitrogen (for alcohols) when necessary.[S2] Tetrabutylammonium perchlorate (TBAP) was obtained by adding perchloric acid into a saturated solution of tetrabutylammonium bromide in water in a dropwise fashion, following filtration and desiccation in a phosphorous pentoxide desiccator (*caution!* The compound to be used in small quantities). Cell culture media, buffer, staining dyes, and other chemicals used for biological assays were obtained from Sigma Aldrich or Invitrogen. Supercoiled (SC) pUC19 DNA (Plasmid from the University of California) used in DNA cleavage experiments was purchased from Bangalore Genie (India).

Instrumentation and methods:

The complexes used and other light-sensitive chemicals were handled under low light conditions or using amber colour glassware/ plasticware or wrapped in aluminium foil when necessary. Complexation and other air/moisture sensitive reactions were carried out in Schlenk vessels using a nitrogen atmosphere. All spectroscopic measurements were performed at 25 °C, unless otherwise mentioned. ^1H and ^{13}C NMR spectral acquisitions were made using Bruker Ultrashield 400 MHz and Bruker Ascend 500 MHz spectrometers; data analysis was performed using TopSpin 3.6.2 software. Chemical shifts (δ) in NMR are presented in parts per million (ppm) with reference to tetramethylsilane (δ 0.0). Mass spectral (ESI-MS) measurements were done using Agilent 6538 Ultra-High Definition (UHD) Accurate Mass Q-TOF spectrometer. Mass spectra simulation was performed using the Molecular Weight Calculator software. Elemental analysis was performed using Thermo Scientific Flash 2000 Organic Elemental Analyzer. IR spectroscopic characterization was done using the Perkin Elmer Spectrum BX spectrophotometer. A Control Dynamics (India) conductivity meter was used for Molar conductivity measurements. Electrochemical experiments were carried out using EG&G PAR model 253 VersaStat potentiostat/galvanostat with electrochemical analysis software 270 using a three-electrode setup having a glassy carbon working, platinum wire auxiliary, and a saturated calomel reference electrode (SCE) with 0.1 M TBAP as supporting electrolyte. Absorption and emission spectral measurements were carried out with SHIMADZU UV-2600 UV-Vis spectrophotometer and HORIBA JOBIN YVON FluroMax-4 and HORIBA Duetta Spectrometer, respectively. Luminescence lifetime measurements were performed with Horiba Jobin Yuvon Fluorocube-01-NL Fluorescence Lifetime System. Confocal microscopic images were captured using Olympus FV 3000 microscope and analysed using cellSens and ImageJ software. Flow cytometric analysis was done using FACS VERSE (BD Biosciences) and CytoFLEX (Beckman Coulter) instrument, and data analysis was done using FCS Express 5 and CytExpert software.

X-ray crystallographic details for L^1:

The compound was crystallized by slow evaporation of a saturated solution in a 1:1 chloroform-hexane mixture. A clear dark orange crystal having a block-shape with dimensions 0.5 × 0.4 × 0.4 mm^3 was mounted on a hair in perfluoroether oil. Data were collected using a Bruker D8 Quest diffractometer. Data were measured using ϕ and ω scans using MoK_α radiation. The highest resolution obtained was θ = 27.74° (0.76 Å). The indexing of diffraction pattern, and the unit cell refinement was executed using SAINT (Bruker, V8.38A, after 2013) on 9781 reflections, 11% of the total reflections. Data reduction, scaling, and absorption corrections were achieved using SAINT (Bruker, V8.38A, after 2013).[S3] The final completeness is 98.7% out to 27.74° in θ. Absorption correction was done by multi-scan method using SADABS-2016/2 (Bruker,2016/2). wR_2 (int) was 0.1364 before and 0.0700 after correction. The ratio between minimum to maximum transmission is 0.8354. The absorption coefficient μ of this material is 0.440 mm^{-1} at this wavelength (λ = 0.711Å), and the minimum and maximum transmissions are 0.623 and 0.746. The structure solution, and the space group *P*-1 (# 2) determination was done by Intrinsic Phasing included in ShelXT (Sheldrick, 2015) structure solution program and refinement was done by Least Squares using ShelXL (version 2017/1, Sheldrick, 2015) using Olex2 suite of programs.[S4] Anisotropic refinement was used for all non-hydrogen atoms. Hydrogen atoms were placed on geometrically calculated positions and riding model refinement was used for them. Positionally disordered chloroform molecule was treated by splitting chlorine atoms into two (part instruction). Crystal data and relevant details are given in Table S1.

The crystal structure of ligand L^1 gave one B-alerts in the cifcheck file. PLAT910_ALERT_3_B Missing # of FCF Reflection(s) Below Theta(Min). The missing reflections falls in the bim-stopper's shadow. This error is related to the diffractometer's limitation.

Emission quantum yield measurement:

The emission quantum yield of the complexes was measured in DMSO using fluorescein as a reference sample (Φ_f = 0.91 in 0.01 M NaOH solution). A series of solutions were prepared in DMSO (for complexes) or 0.01 M NaOH (for fluorescein), having an absorbance value less than 0.1. The samples were excited at 470 nm, and emission spectra were recorded between 480 nm to 700 nm. Linear fits were obtained from plots of integrated emission intensity vs. absorbance plot for each sample. The quantum yield value was calculated from the following equation.

$$\Phi_X = \Phi_{ST} \times (Grad_X/Grad_{ST}) \times (\eta_x^2/\eta_{ST}^2)$$

Grad represents gradient values obtained from linear plots, and ST and X represent standard and test samples, respectively. Grad stands for gradient values obtained from integrated emission intensity vs. absorbance plot, η represents the refractive index of the solvent used for the samples, Φ represents fluorescence quantum yield values.

Theoretical calculations:

All DFT (density functional theory) studies were done with the Gaussian 16 package. Geometry optimization and vibrational frequency calculations were done with lanl2dz (Los Alamos National Laboratory 2 Double-Zeta) basis set for all atoms using the M06 level of theory. The solvation effect of DMSO was included in the calculation using the integral equation formalism polarization continuum model (IEFPCM). TD-DFT (time-dependent density functional theory) calculations were carried out to obtain the electronic transition state energies and the intensities of the first 100 lowest energy states. Again, the calculation was performed using the lanl2dz basis set, M06 level of theory, and the solvation of DMSO utilizing the IEF- PCM model. The orbitals were analysed and plotted using the Chemcraft program.

DNA binding studies:

DNA binding experiments were performed in 5 mM Tris- HCl/NaCl buffer (pH 7.2) using DMF solution of the complexes (overall DMF concentration is 5% v/v). Calf thymus (ct) DNA solution was prepared by dissolving ct-DNA in 5 mM Tris-HCl/NaCl buffer, and the concentration of DNA was measured from absorbance at 260 nm with the known molar absorptivity 6600 M^{-1} cm^{-1}. The absorbance ratio value at 260 nm and 280 nm was approximately 1.9: 1, suggesting the DNA is free from protein. Absorption titrations were done by varying DNA concentration but keeping the complex concentration constant. Due corrections were made for changes in DNA concentration during titrations. A 5 min equilibration time was given after the addition of DNA and before UV data acquisition. The binding constant was obtained from the following equation.[S5]

$$[DNA] / (\varepsilon_a - \varepsilon_f) = [DNA] / (\varepsilon_b - \varepsilon_f) + 1 / K_b(\varepsilon_b - \varepsilon_f)$$

In the equation, ε_f represents the molar extinction coefficient of the metal complex, ε_a is the molar extinction coefficient of the complex at a particular DNA concentration, ε_b is the molar absorption coefficient of the complex fully bound to DNA, [DNA] is the concentration of ct-DNA.

Lipophilicity measurement:[S6]

Lipophilicity measurement of the complexes was done using a modified shake flask method. Saturated solutions of octanol with water and vice versa were prepared by shaking a mixture of water and octanol for 24 h at room temperature. The 20 μM solutions of the complexes were prepared in 2 ml water-saturated octanol, and an equal volume of octanol saturated water was added to it. The mixture was shaken at 250 rpm for 6 h, centrifuged, and then separated. Concentrations of the complexes in both octanol and aqueous layer were measured by absorption spectroscopy.

Solution phase stability and photostability studies:

Stability study of the complexes and rose Bengal was monitored by absorption spectroscopy in phenol red-free cell culture media (DMEM) containing 10% Fetal bovine serum (FBS). For checking the dark stability of the complexes, 10 μM solutions were kept at 37 °C, and

absorption spectra were recorded every 24 h interval up to 72 h. For the photostability study, 2 ml solution containing 10 μM photosensitizer was taken in a quartz cuvette and was irradiated from a 400-700 nm light source (2.4 mW/cm^2). Spectral measurements were carried out at specific intervals for 30 min light exposure with a UV-Vis spectrometer.

Singlet oxygen quantum yield measurement:

Photo-oxidation titration of 1,3-diphenylisobenzofuran (DPBF) was carried out to determine the singlet oxygen quantum yield in DMSO using rose Bengal as a standard. DMSO (3 ml) containing ~50 μM DPBF and respective sample was added in a quartz cuvette, followed by a photosensitizer. The solution was kept in the dark for 20 min for any possible reaction that can take place in dark. The cuvette was then irradiated with 400-700 nm visible light source (2.4 mW/cm^2) at 5 sec interval and the absorption spectra were recorded. The difference of initial absorbance and the absorbance value at 417 nm at a given irradiation time (ΔO.D.) is plotted as a function of irradiation time to obtain a linear fit. The singlet oxygen quantum yield value was calculated from the following equation.

$\Phi_{sample} = \Phi_{ST} \times (Slope_{sample}/Slope_{ST}) \times (F_{ST}/F_{sample})$

Where ST sands for standard, Φ denotes singlet oxygen quantum yield. $F = 1\text{-}10^{-OD}$.

DNA photocleavage studies:

The photoinduced DNA cleavage of supercoiled (SC) pUC19 DNA by complex **2** was studied by agarose gel (0.8 %) electrophoresis in 10% DMF-Tris HCl buffer (pH 7.2). Photoirradiation of the samples was done using 532 nm monochromatic laser source (power 100 mW, beam diameter 0.32 ± 0.02 mm, single-mode, model no. EXLSR-532-100-CDRH of Newport Corporation make, Spectra-Physics Laser Division, Santa Clara, C.A, U.S.A.) for 30 min. A total volume of 20 ml solution containing 1 μl DNA (33 μM), 50 mM sodium chloride, the complex solution with desired concentration, and quencher solution (if used) was incubated for 1 h at 37 °C followed by light irradiation or kept in the dark as per requirement. The loading dye (0.25% bromophenol blue, 0.25% xylene cyanol, 30% glycerol, 3 μL) was added to the samples and then loaded on 0.75 % agarose gel having 1.0 μg/ml ethidium bromide. Gel electrophoresis was carried out in a dark chamber for 2 h at 65 V in TAE (Tris-acetate- EDTA) buffer (pH ~ 8.5). The bands were visualized, and the band intensities were analysed using a UVITEC gel documentation system. Due corrections were made for the small amount of nicked circular (NC) DNA present in the original SC DNA sample and for the difference in binding affinity of EB towards different forms of DNA. For mechanistic studies to determine the nature of ROS, different quenchers and scavengers were added before photolysis. Sodium azide (10.0 mM) for singlet oxygen, potassium iodide (10.0 mM) for hydroxyl radical, catalase (4 unit) for hydrogen peroxide, tiron (10.0 mM) for superoxide was used as quenchers. A set of experiments was done by replacing Tris-HCl buffer with D_2O. Oxygen dependency on the photocleavage was monitored by applying three freeze pump thaw cycles using argon then subjected to photoirradiation. The error range observed for the determination of % NC from the experiments was 3 to 6 %.

Cellular assays

Cell culture conditions:

Adherent human cervical cancer (HeLa) and noncancerous human embryonic kidney (HEK-293) cells were cultured in Dulbecco's Modified Eagle Medium, and for human lung carcinoma (H1299) cell culture Roswell Park Memorial Institute (RPMI) 1640 were used. The cells were maintained at 37 °C under 5% CO_2 in the cell culture media supplemented with 10% Fetal bovine serum (FBS) and 1% Penicillin-Streptomycin and were passaged 2-3 times a week according to standard aseptic procedures. Cell cultures were started in 25 cm^2 flasks at 10^5 cells ml^{-1} and were sub-cultured when growth reached 80% confluency by discarding the old culture medium and washing the cells once with Dulbecco's phosphate-buffered saline (DPBS), followed by a detachment of the cell monolayer with trypsin-EDTA solution (0.25% w/v Trypsin/0.53 mM EDTA). The cell suspension was diluted with culture media and transferred into new culture vessels.

Cellular uptake experiments:

Exponentially growing HeLa cells were plated in a 12 well plate at a seeding density of 10^5 cells per well in DMEM and incubated at 37°C, 5% CO_2 24 h in an incubator for cell attachment. The cells were then treated with 5 μM of complex **1** and incubated for varying times (2 h, 4 h, 6 h, and 16 h). The cells were then rinsed, lifted with trypsin, and suspended in DPBS. Flow cytometric analysis was performed using a FACS VERSE (BD Biosciences) with 488 nm excitation, and emission was recorded using a FITC channel (500-550 nm).

For checking cellular uptake in different cell lines, HeLa and HEK293 cells were incubated with 10 mM complex **1** and incubated for 2 h followed by flow cytometric analysis.

Confocal microscopy:

Approximately 3×10^5 number of HeLa cells were plated in sterile glass-bottom Petri dishes and allowed to adhere for 24 h in an incubator under usual aseptic conditions. The 2 ml prewarmed metal complex solutions (2 μM for complex **1** and 15 μM for complex **2**) prepared in sterile DMEM were added to the sample dishes and incubated at 37°C for 4 h. Then the cells were thoroughly washed with DPBS and incubated with MitoTracker™ Deep Red FM (stains mitochondria) or LysoTracker™ Deep Red (stains lysosome) to stain the respective organelle following the supplier's instructions. The cells were then washed with PBS and incubated with Hoechst to stain the nucleus. Finally, the cells were imaged using a confocal microscope using a 60X oil objective lens. Images were collected and analysed using cellSens software.

Cytotoxicity and photocytotoxicity:

Cell viability assays were performed in triplicates in flat bottom TC-treated polystyrene 96 well plates. An appropriate number of cells with at least 95% viability was transferred in 100

ml aliquots to the wells and placed in a 37°C, 5% CO_2 incubator and allowed to attach for 24 h to obtain approximately 10000 cells per well at the time of drug treatment. The media was refurbished with 100 μl fresh media, and Serial dilutions of metal complexes prepared in cell culture media were added in 100 μL volumes to the respective microplate wells having cells. Two sets of control wells without drug treatment were included in each microplate with either cells only or no cells. All microplates were incubated in the dark for 6 h in the incubator, and then cell culture media was replaced with DPBS. Microplates used for dark cytotoxicity determination were kept in the dark. The plates used for photocytotoxicity determination were exposed to visible light for 30 min (400-700 nm, 5 J cm^{-2}) using a Luzchem Photoreactor (Model LZC-1, Ontario, Canada). The buffer was then replaced with media, and all plates were returned to the incubator for a further 18 h. Cell viability was obtained using an MTT dye assay following an established procedure. Briefly, 25 μl of MTT solution (4 mg/ml) was added to each well and incubated for 3 h. The media was then discarded and 150 ml DMSO was added to each well, and absorbance was recorded with a TECAN microplate reader at 570 nm. The concentrations of the compounds where cell viability was reduced by 50% (IC_{50} values) for cytotoxicity were obtained from sigmoidal fits of the dose-response curves using GraphPad Prism. IC_{50} values of selected reported compounds are compared in a tabular form.[S7-S11]

Annexin V FITC/ propidium iodide assay:

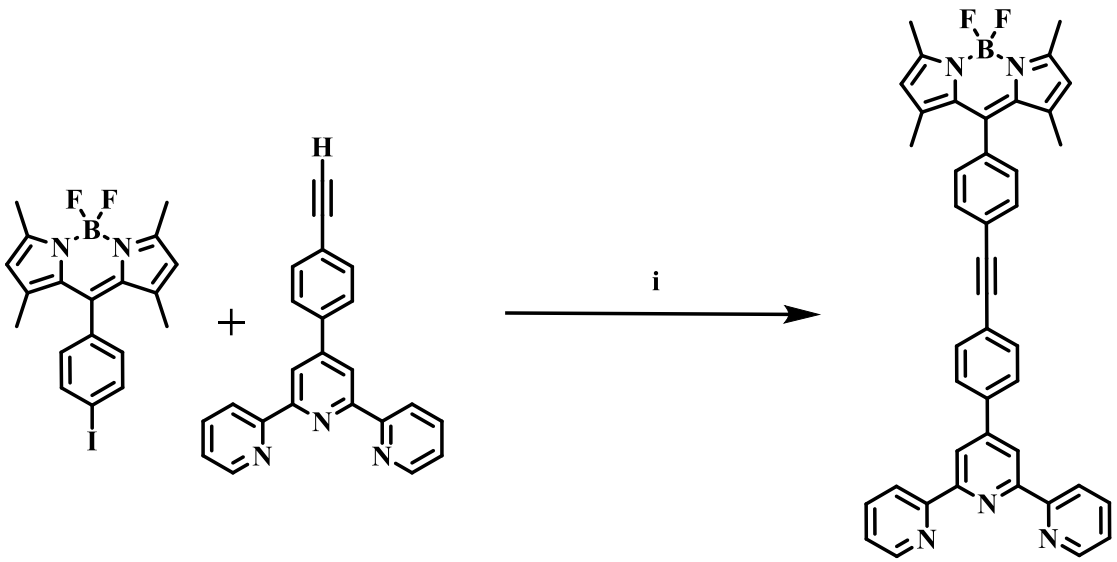
Approximately 10^5 cells were plated in 6 well plates and incubated for 24 h before complex treatment. Cells were then incubated with complex **2** with different concentrations (50 nM, 100 nM, 200 nm and 500 nM) for 4 h, and then a set of cells was exposed to light (400-700 nm, 2.4 mW/cm^2, 15 min) and another set was kept in the dark. The cells were then incubated further for another 1 h and processed for flow cytometric analysis. Annexin V- FITC/ propidium iodide staining was performed following supplier's guidelines (BioLegend) and analysed by flow cytometry.

DCFDA assay:

Human cervical cancer cells, HeLa (seeding density ~ 3×10^5 cells), were plated in 6-well plates and allowed to attach for 24 h. Cells were treated with 2 μM complexes (in 0.05% DMSO-DMEM) for 4 h in the dark. Cells were then trypsinized, processed, and stained with 5 μM DCFDA for 15 min at room temperature in the dark. Unstained and stained cells treated only with 0.05% DMSO were kept as control. A set of samples were exposed to light irradiation (400-700 nm, 2.4 mW/cm^2, 5 min). Flow cytometric analysis was performed using a 488 nm excitation, and fluorescence was collected between 500-550 nm.

SOSG (singlet oxygen sensor green) assay:

The experiment was performed following a similar protocol as DCFDA. SOSG staining was done following the supplier's guidelines (Invitrogen).



Scheme S1: Synthesis of ligand **L[1]**. (i) 0.18 equiv. $[Pd(PPh_3)_2Cl_2]$, 0.18 equiv. CuI, 0.18 equiv. PPh_3, THF-triethylamine mixture, 60° C for 48 h.

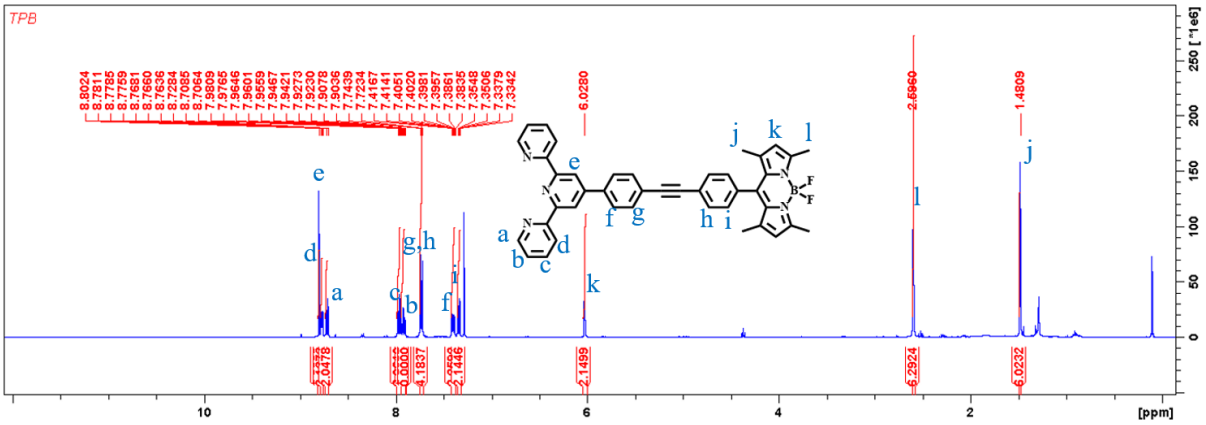


Fig. S1 ^{1}H NMR spectrum of ligand **L[1]** in $CDCl_3$. Inset shows ligand ISIS drawing

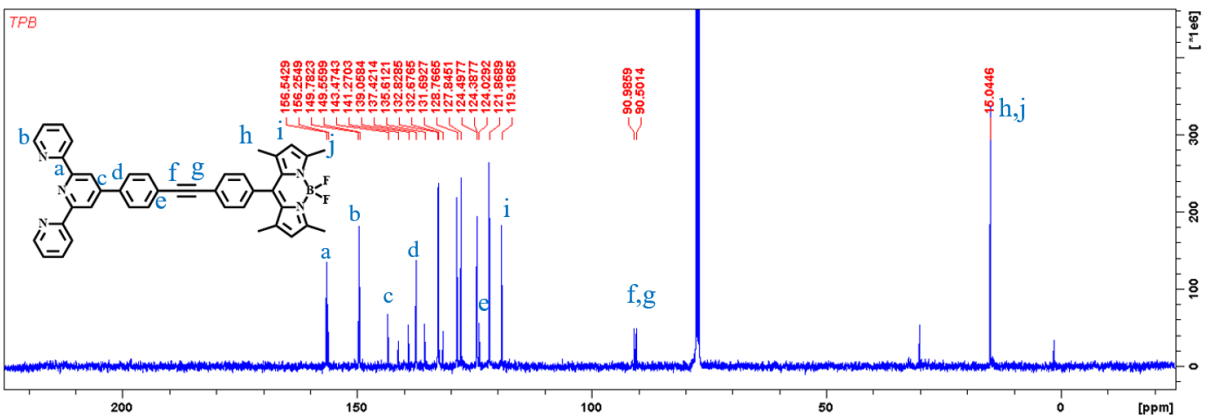


Fig. S2 ^{13}C NMR spectrum of ligand **L[1]** in $CDCl_3$. Inset displays ligand ISIS drawing

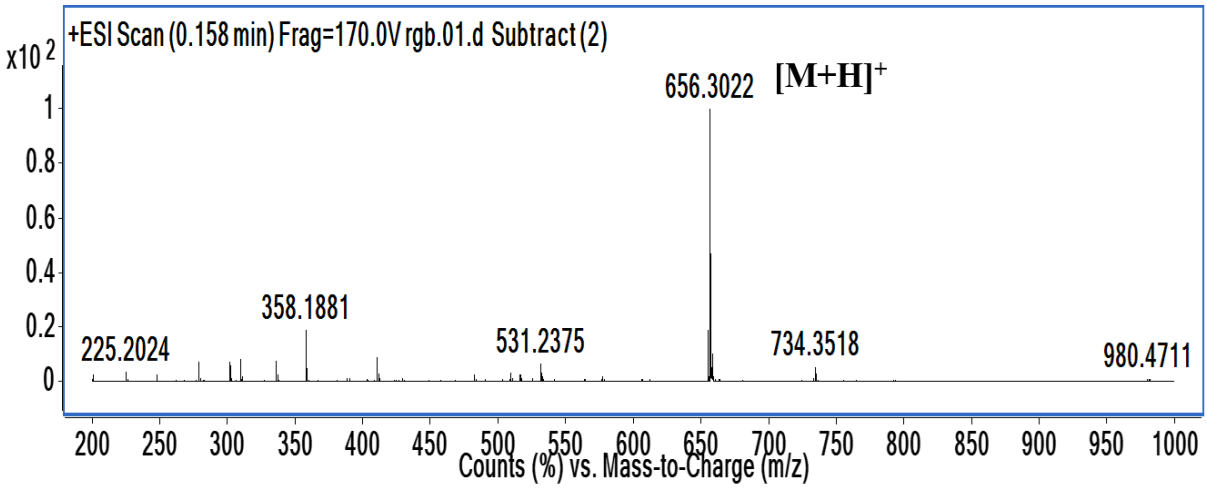


Fig. S3 Mass spectrum of **L¹** in acetonitrile with peak corresponding to $[M+H]^+$ (m/z) at 656.3022.

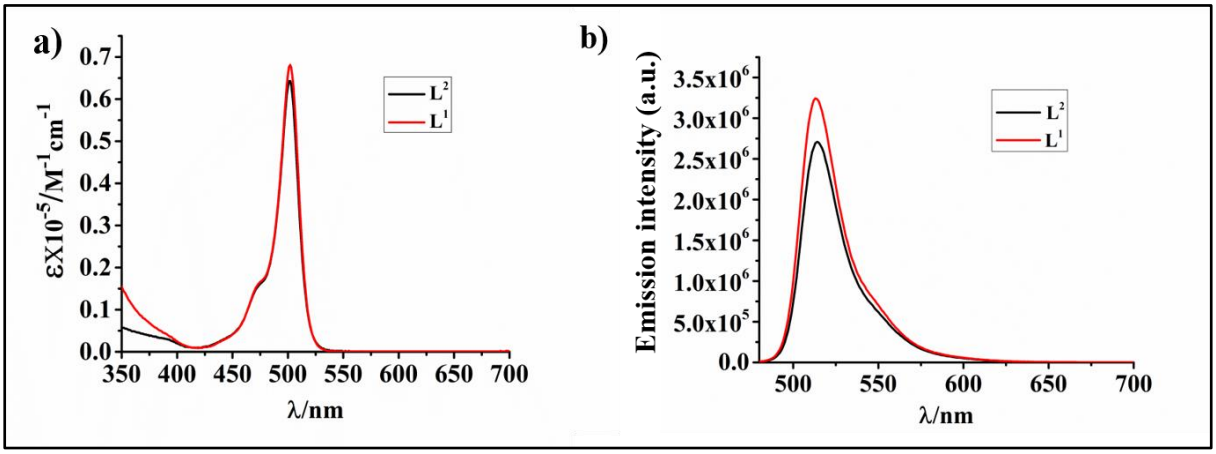


Fig. S4 a) absorption and b) emission spectra (λ_{ex} = 470 nm) of ligands **L¹** and **L²** in dichloromethane.

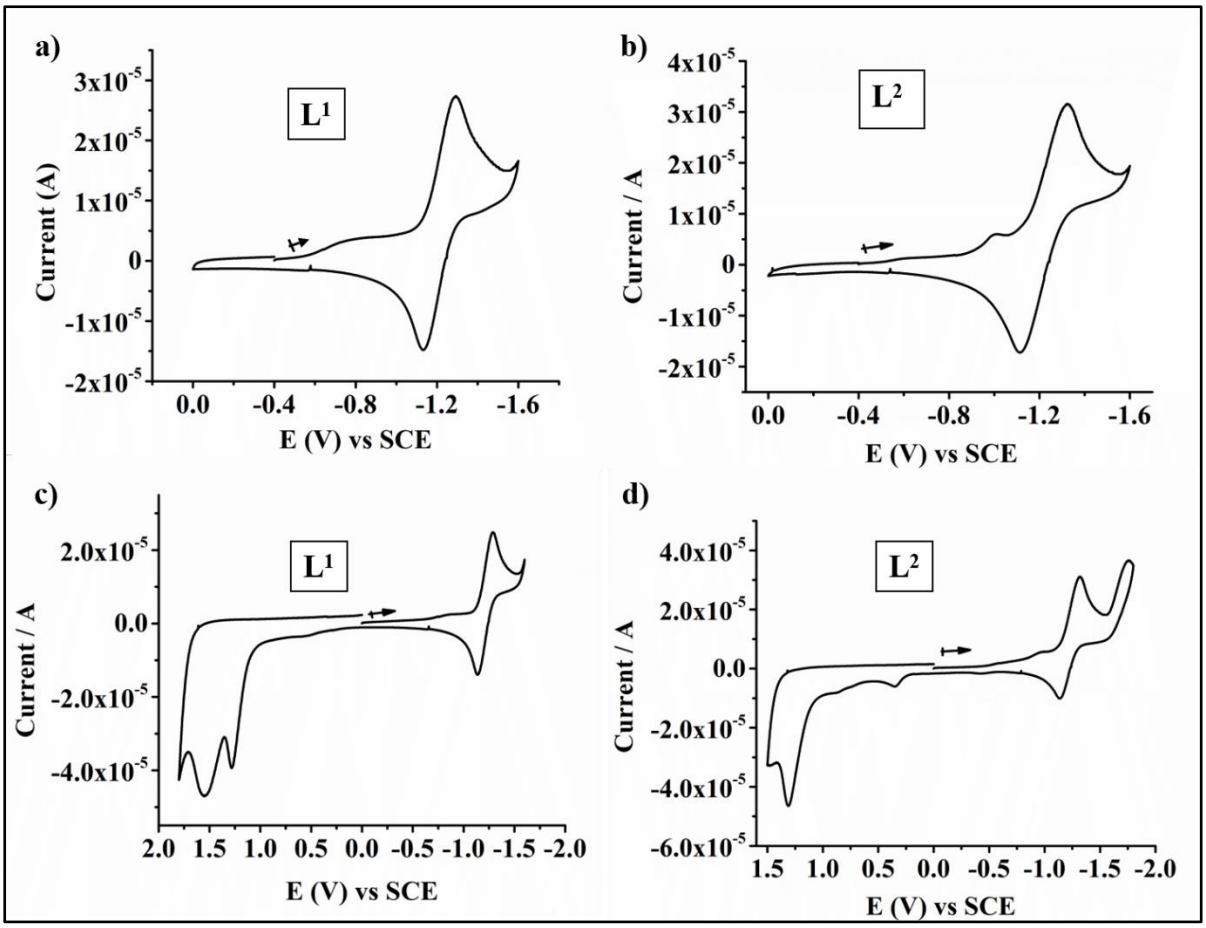


Fig. S5 Cyclic voltammograms of the ligands: a) and c) for Ligand L^1, b) and d) for Ligand L^2, in 0.1M TBAP-dichloromethane using 2.0 mmol ligand concentration at a scan rate of 100 mV sec^{-1}.

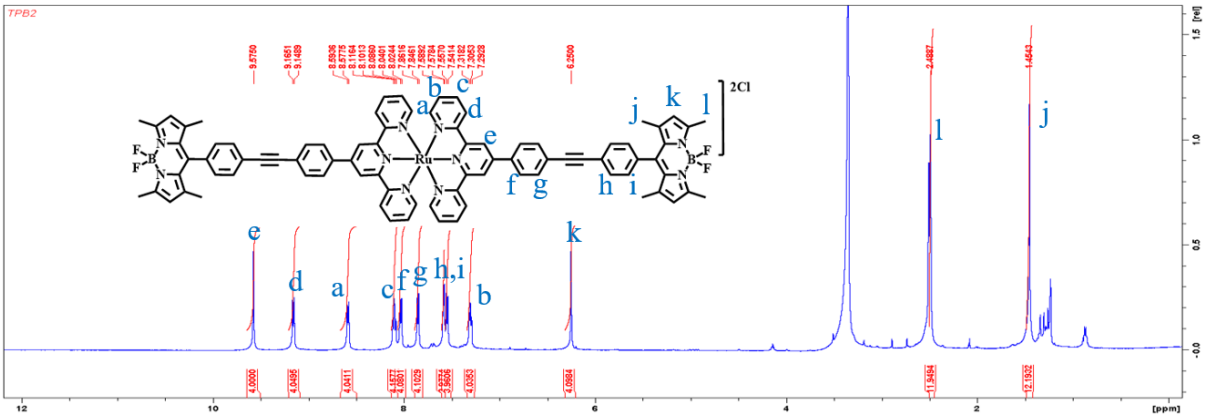


Fig. S6 ^1H NMR spectrum of complex **1** in DMSO-d_6. Inset shows the molecule with proton labeling scheme.

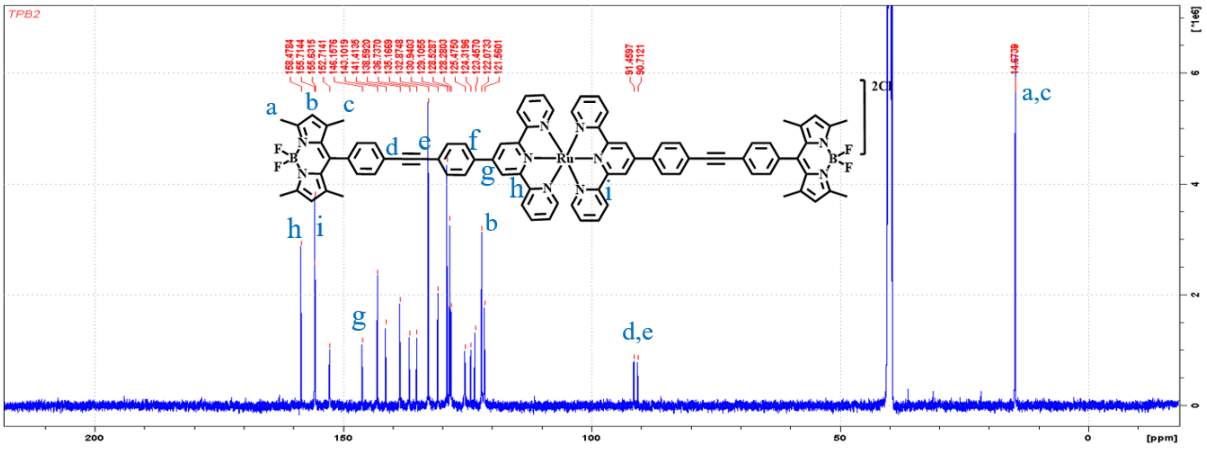


Fig. S7 ^{13}C NMR spectrum of complex **1** in DMSO-d_6 with labeling scheme.

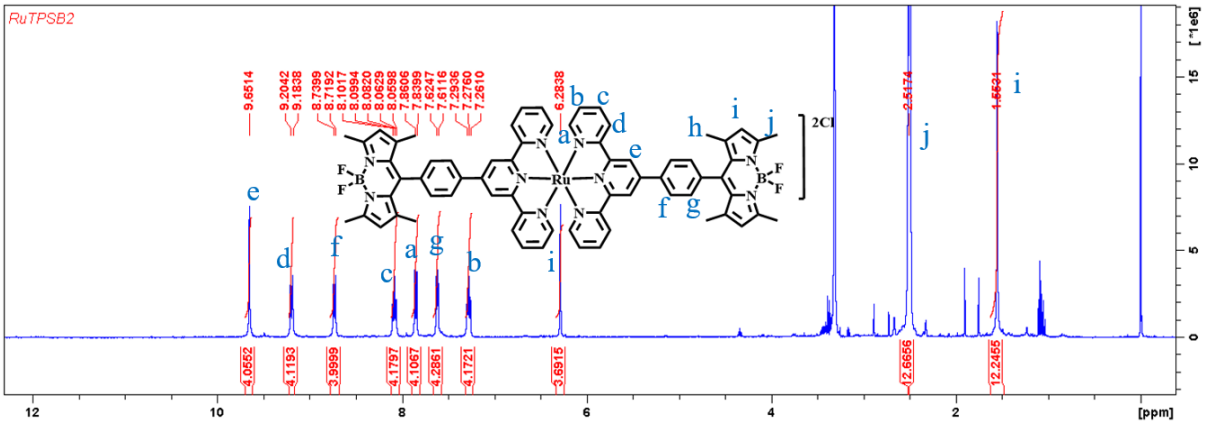


Fig. S8 ^{1}H NMR spectrum of complex **2** in DMSO-d_6 with proton labeling scheme.

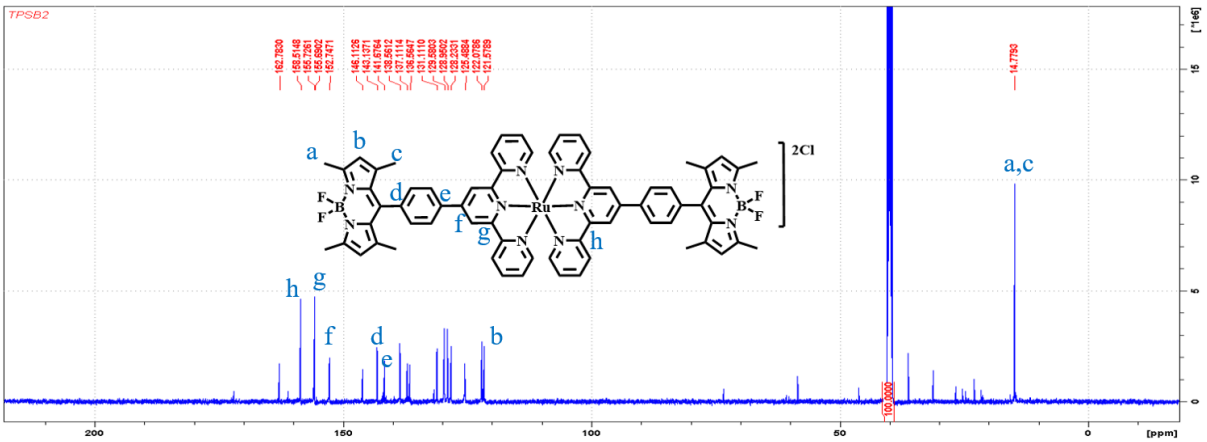


Fig. S9 ^{13}C NMR spectrum of complex **2** in DMSO-d_6 with labeling scheme.

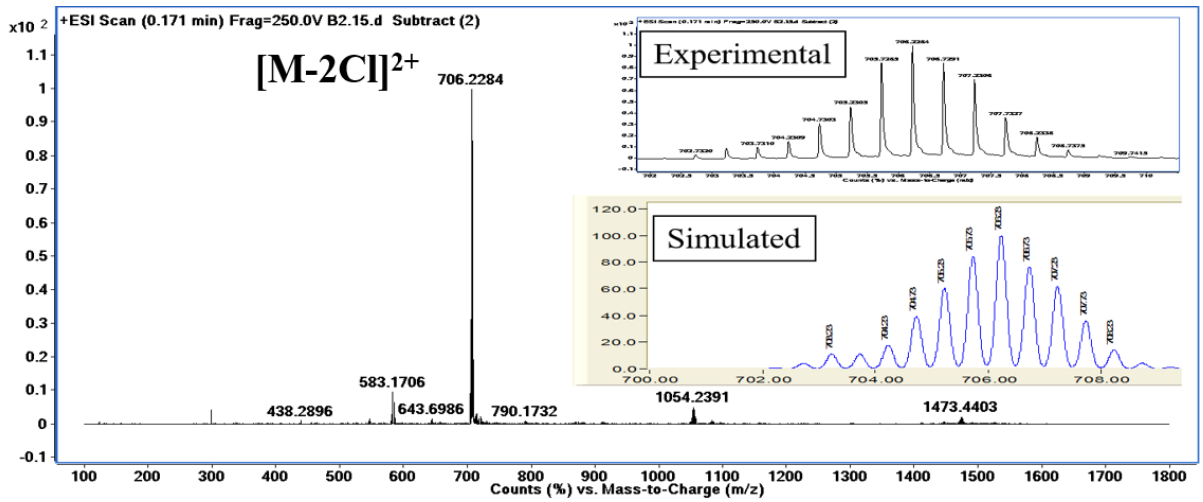


Fig. S10 Mass spectrum of complex **1** recorded in methanol with peak corresponding to $[M-2Cl]^{2+}$ (m/z) at 706.2284. The insets show simulated and experimental isotopic distribution.

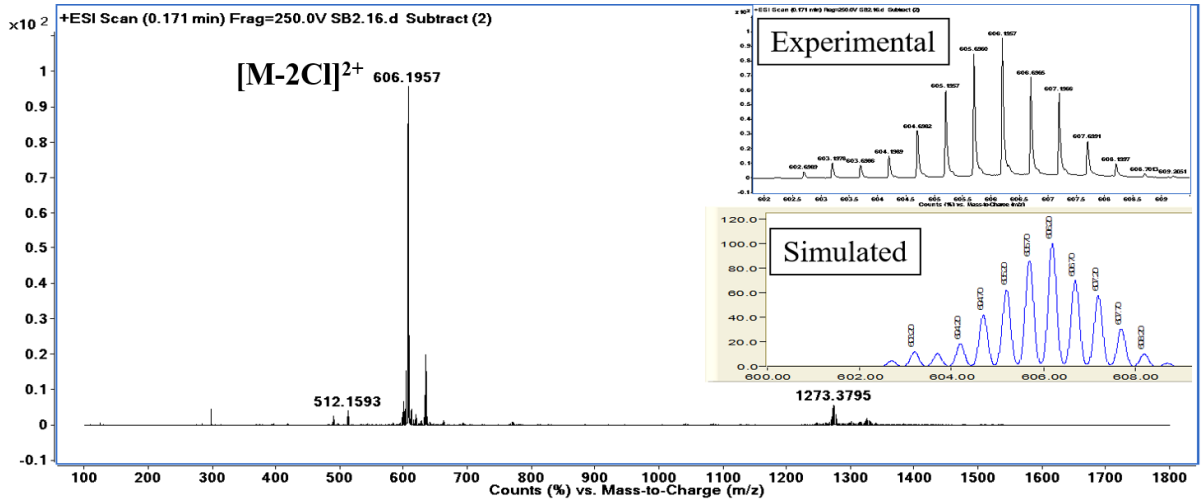


Fig. S11 Mass spectrum of complex **2** recorded in methanol with peak corresponding to $[M-2Cl]^{2+}$ (m/z) at 606.1957. The insets show simulated and experimental isotopic distribution.

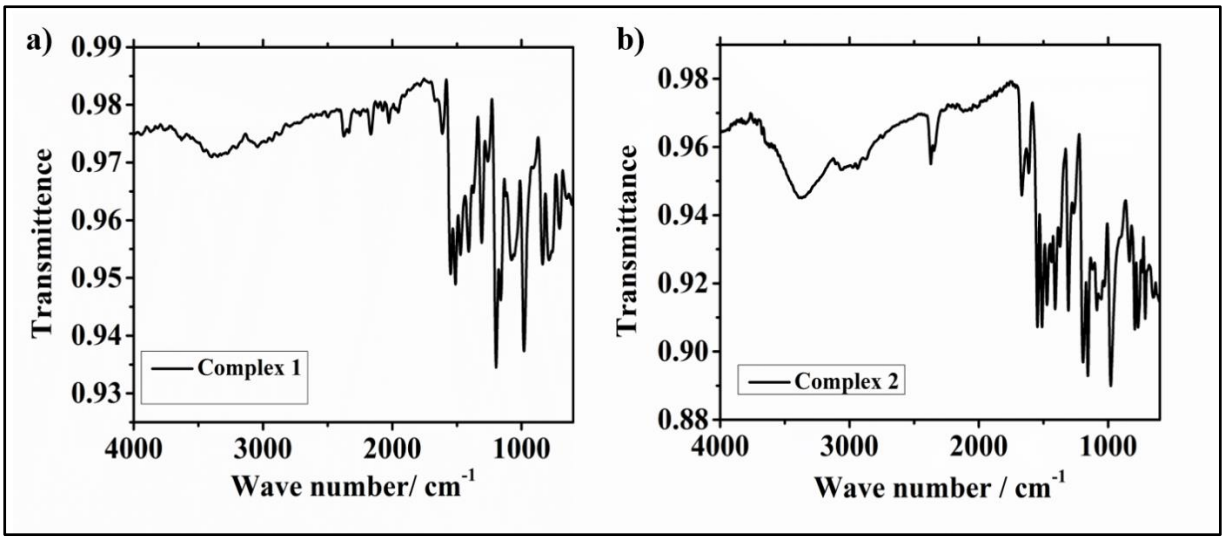


Fig. S12 Solid state IR spectra of the complexes: a) complex **1** and b) complex **2**.

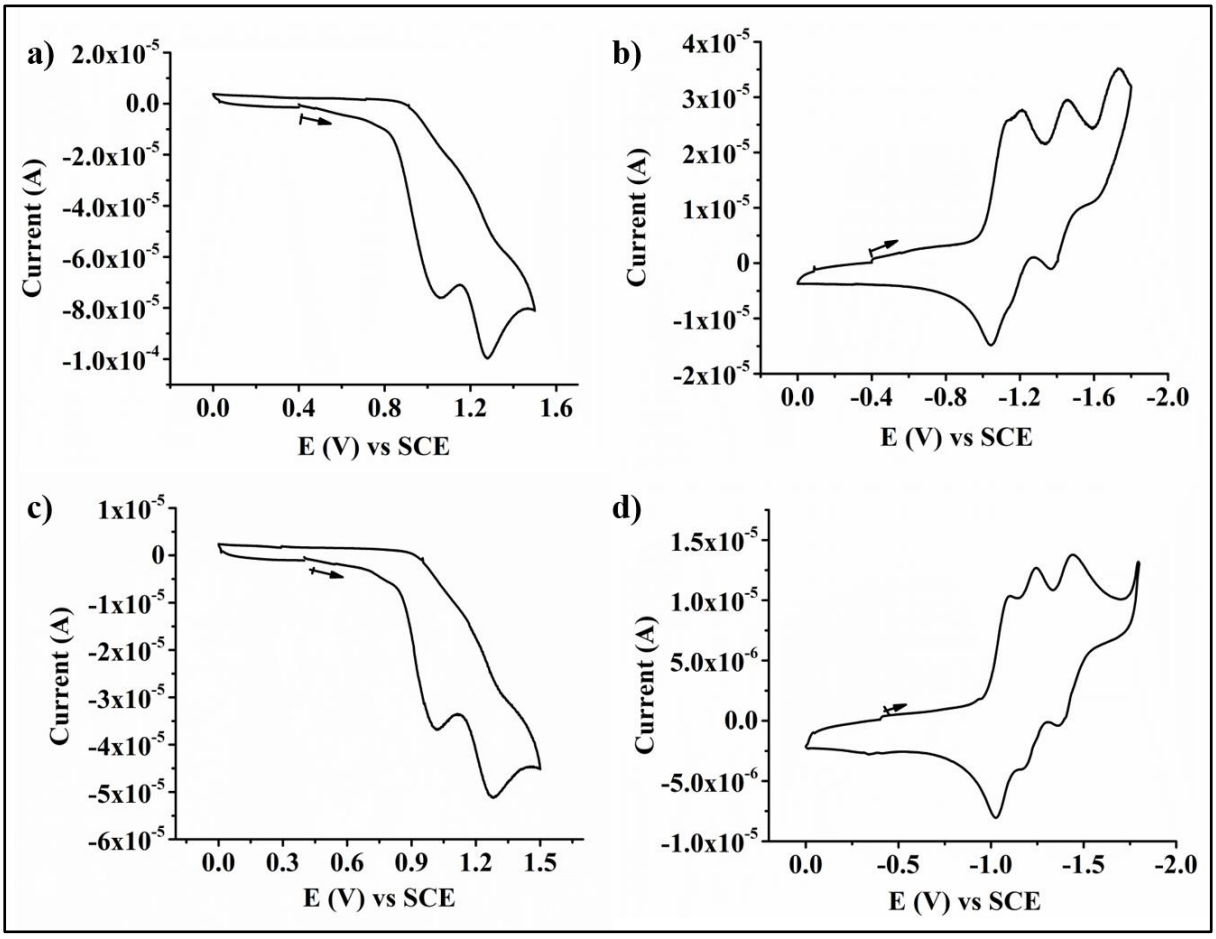


Fig. S13 Cyclic voltammograms of the complexes: a) and b) for complex **1**, c) and d) for complex **2**, in 0.1M TBAP-DMF using 2.0 mmol complex concentration at a scan rate of 100 mV sec^{-1}.

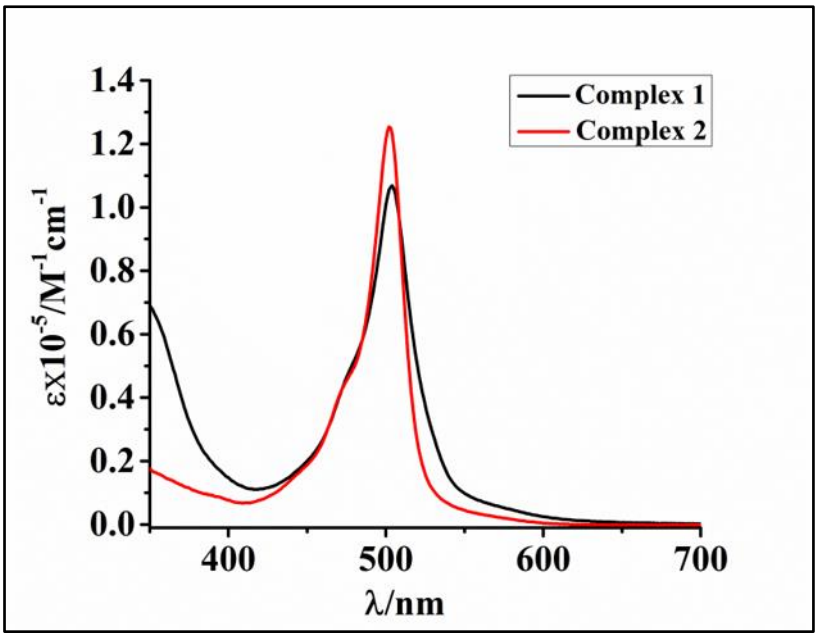


Fig. S14 Absorption spectra of the complexes in 10% DMSO-DPBS.

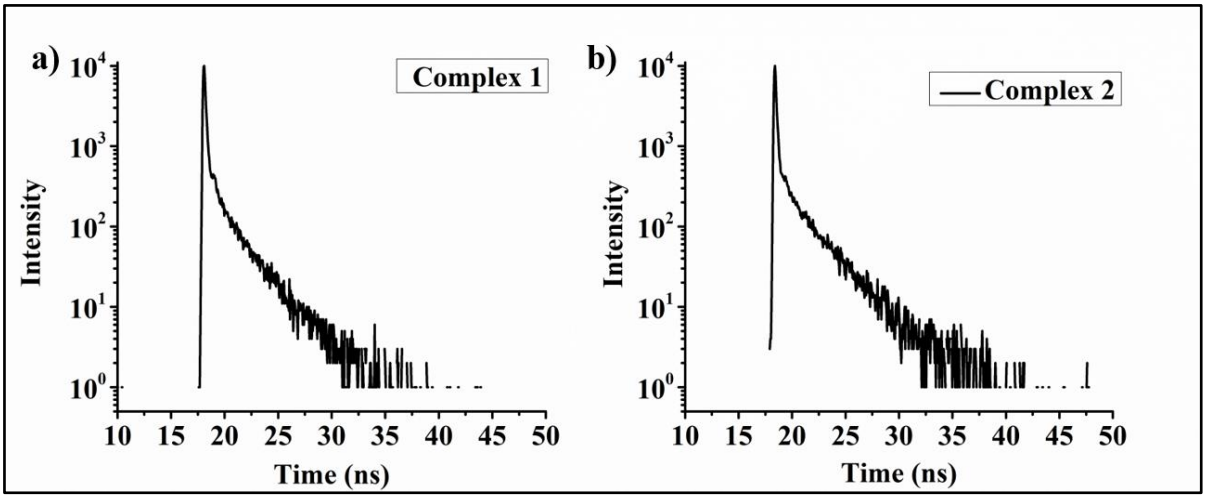


Fig. S15 Fluorescence decay curves of (a) complex **1** and (b) complex **2** in acetonitrile.

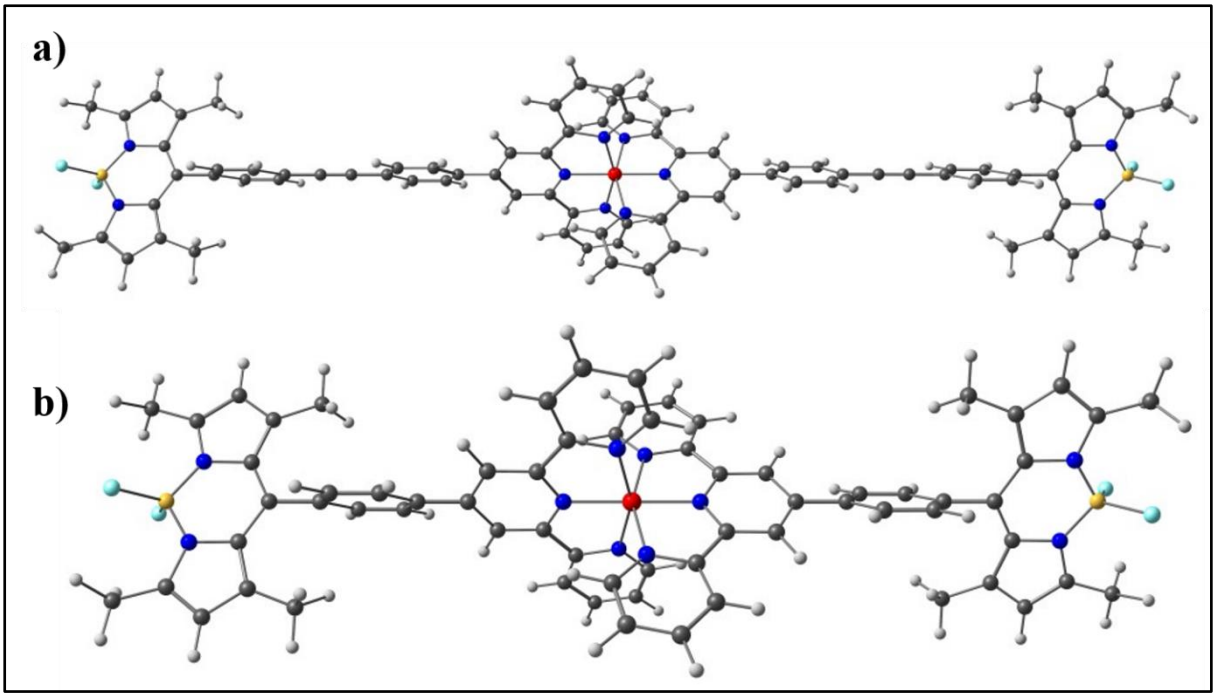


Fig. S16 Energy minimized structures of the complexes: a) complex **1** and b) complex **2**. Colour codes: Red – Ruthenium; Blue – Nitrogen; Dark grey – Carbon; Pale grey – Hydrogen; Dark yellow – Boron; Sky blue – Fluorine.

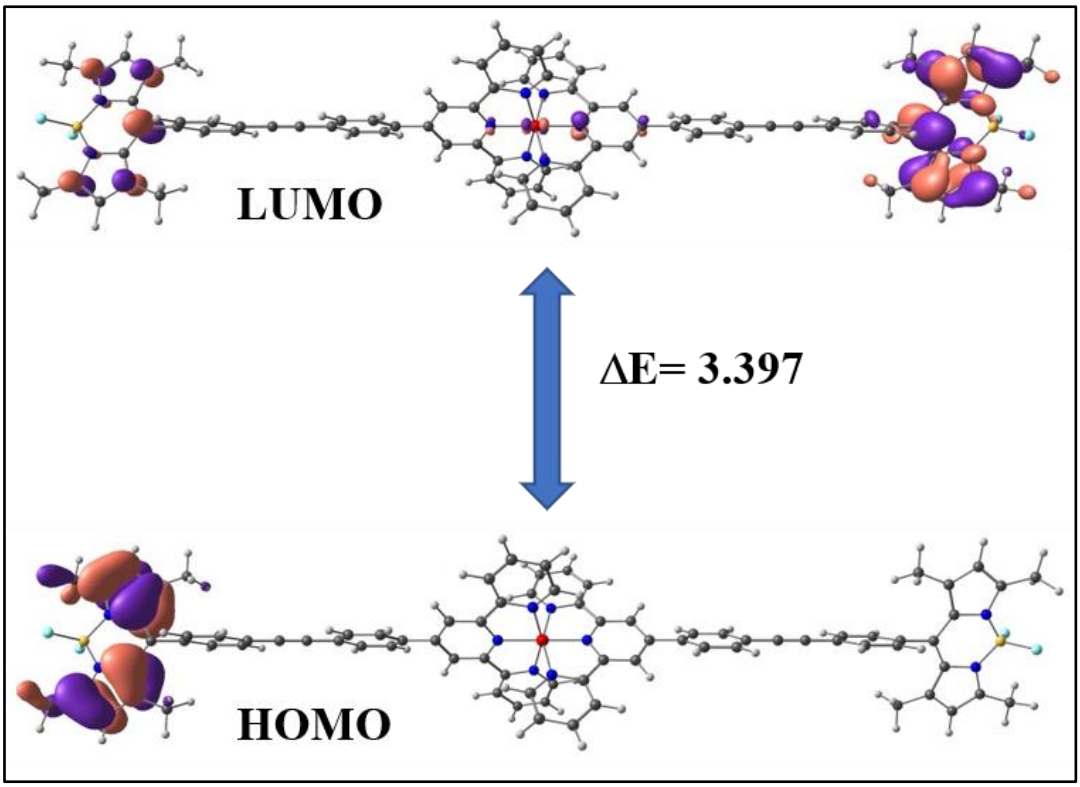


Fig. S17 Frontier molecular orbitals of complex **1**. Contour value 0.03. Colour codes: Red – Ruthenium; Blue – Nitrogen; Dark grey – Carbon; Pale grey – Hydrogen; Dark yellow – Boron; Sky blue – Fluorine.

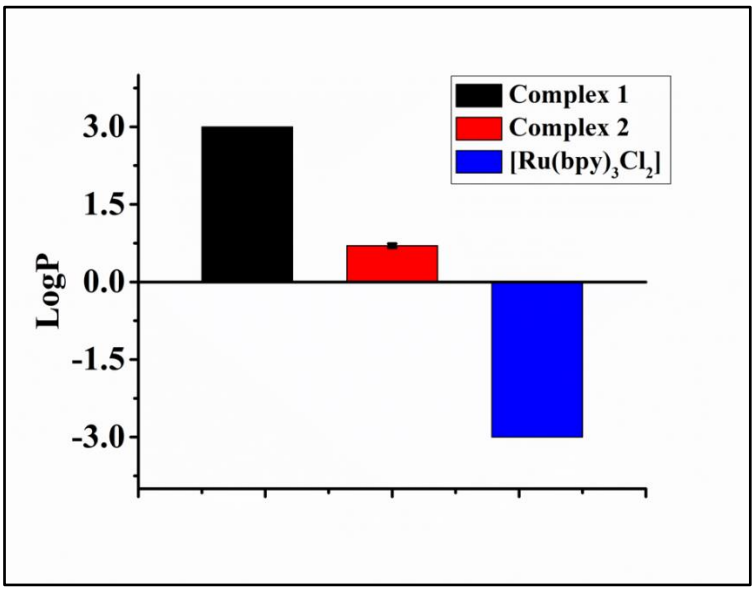


Fig. S18 Octanol−water partition coefficients of complexes **1**, **2** and $[Ru(bpy)_3]Cl_2$. The data for the bpy complex are taken from reference 6.

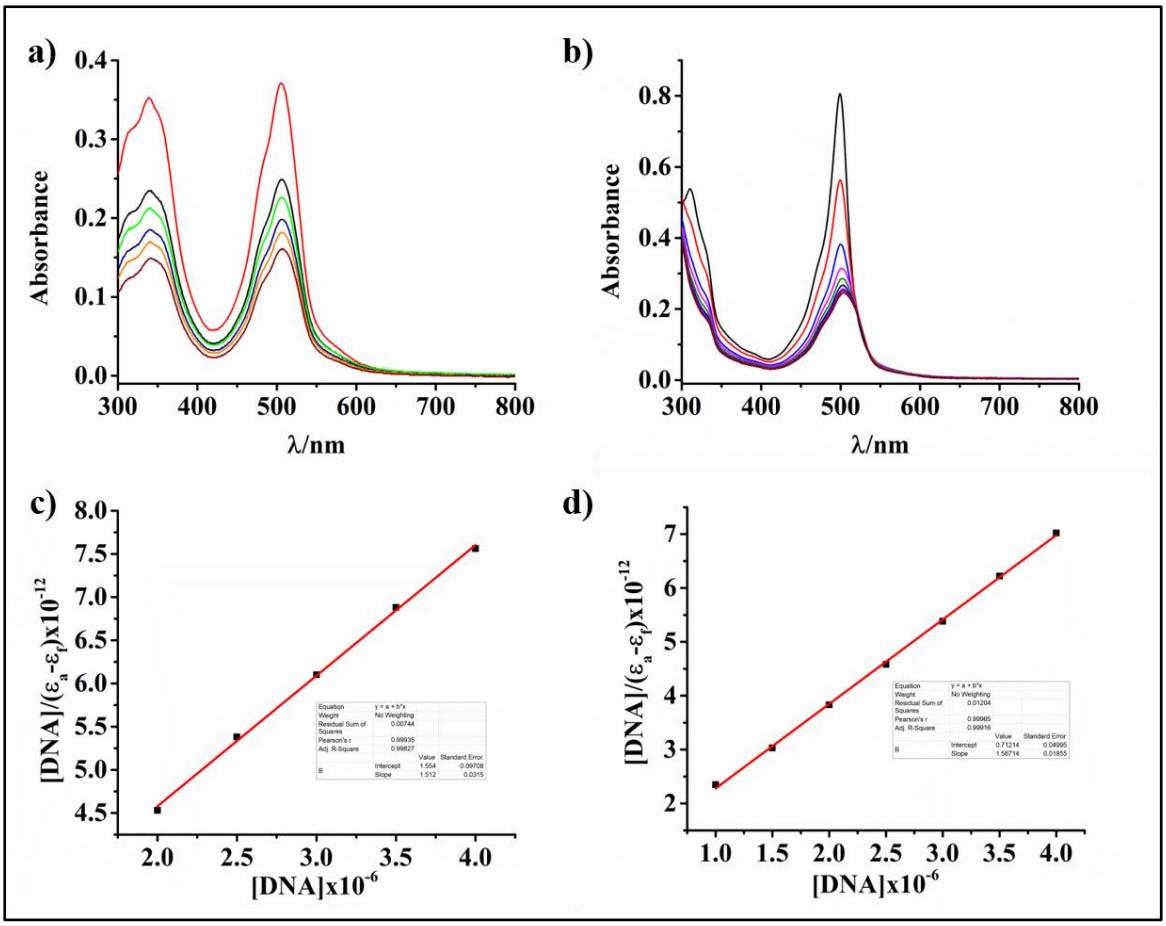


Fig. S19 DNA binding constant (K_b) measurement for the complexes using UV- visible spectroscopy and the corresponding [DNA]/(ε_a–ε_f) vs. [DNA] plots. Panels a) and c) are for complex **1**, and panels b) and d) are for complex **2**.

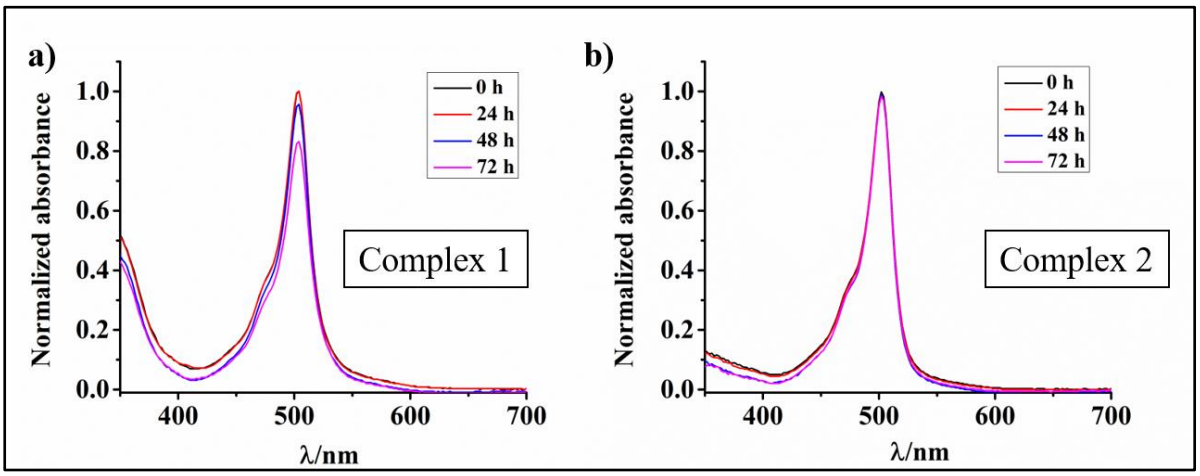


Fig. S20 Change in the absorption spectral traces with time for the complexes: a) complex **1** and b) complex **2** in 1:9 (V/V) DMSO-DMEM (phenol red-free with 10% FBS). The experiments were carried out at 37 °C over a period of 72 h and the spectra were recorded at certain intervals as mentioned in the figure insets.

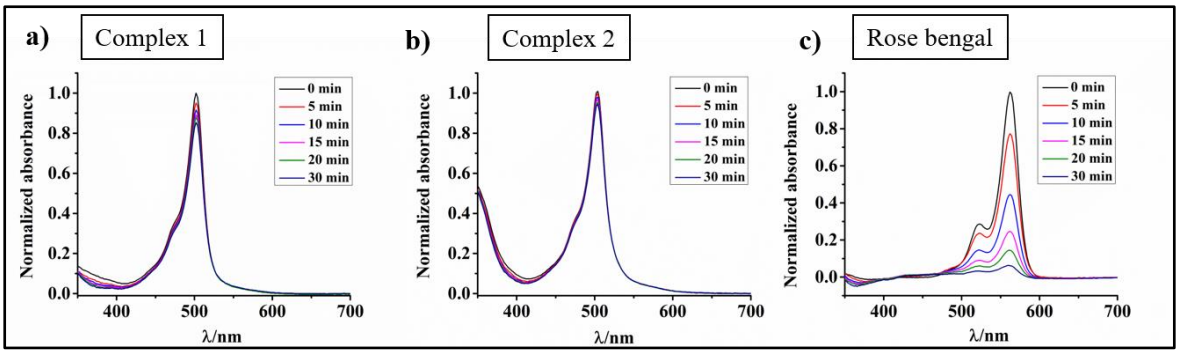


Fig. S21 Photostability studies: a) complex **1**, b) complex **2** and c) rose Bengal in 1:9 (V/V) DMSO-DMEM (phenol red-free with 10% FBS) (400-700 nm, 2.4 mW/cm^2 light source was used for irradiation).

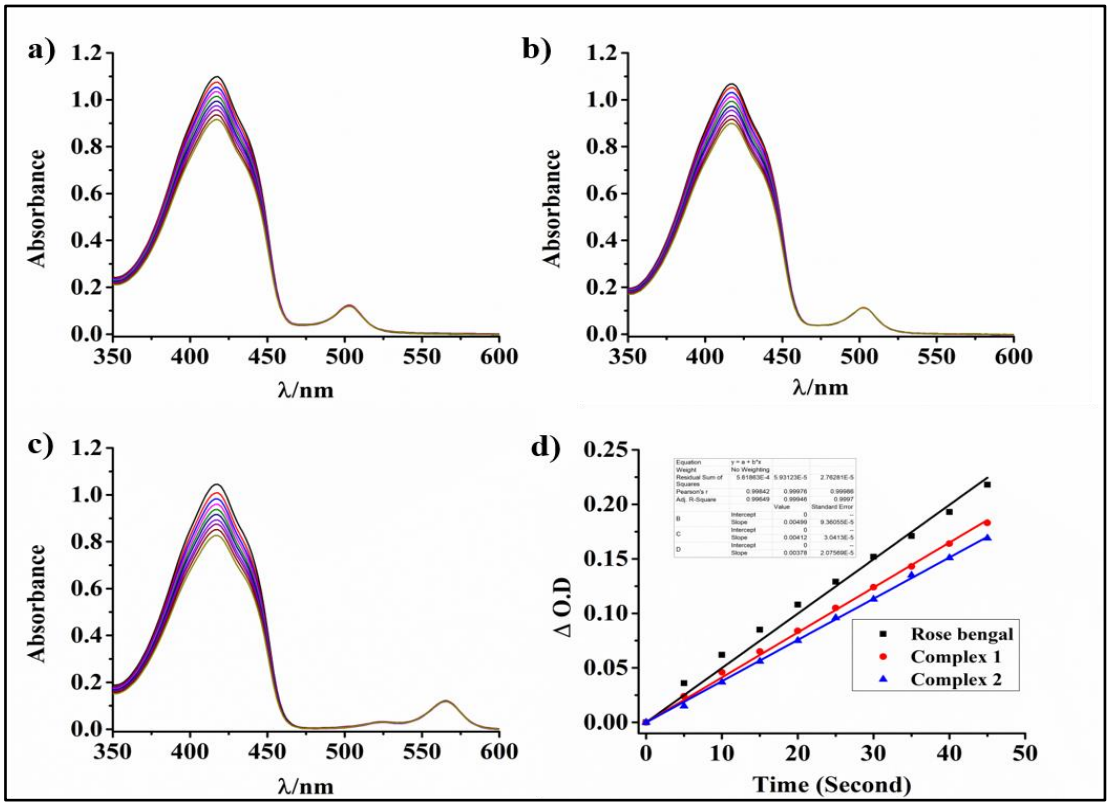


Fig. S22 Changes in the absorption spectra of DPBF containing complexes on light irradiation: a) complex **1**, b) complex **2** and c) rose Bengal. A 400-700 nm light source (2.4 mW/cm^2) was used for irradiation. d) Linear fits of ΔO.D. vs. irradiation time for determination of singlet oxygen quantum yield.

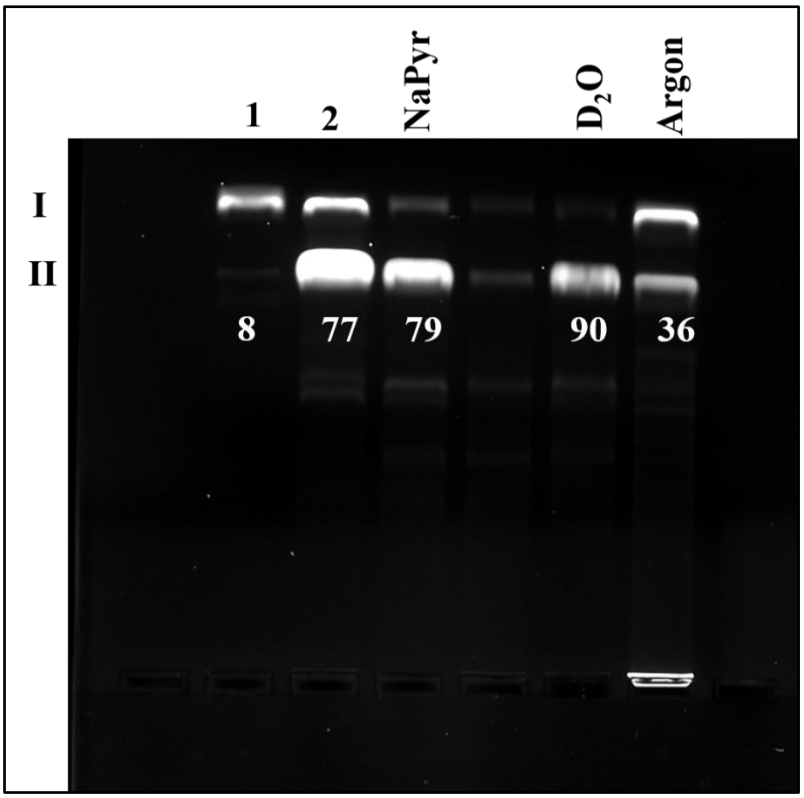


Fig. S23 Photoinduced cleavage of pUC19 DNA by complex **2** in presence and absence of quenchers or special conditions applied. Lane 1, DNA; Lane 2, DNA treated with complex **2** and exposed to light irradiation. Other lanes contain DNA with complex **2** exposed to irradiation with additives or special conditions as mentioned (form-I is supercoiled DNA and form-II is nicked circular DNA, the percent of nicked circular DNA is mentioned on the lanes, NaPyr = sodium pyruvate).

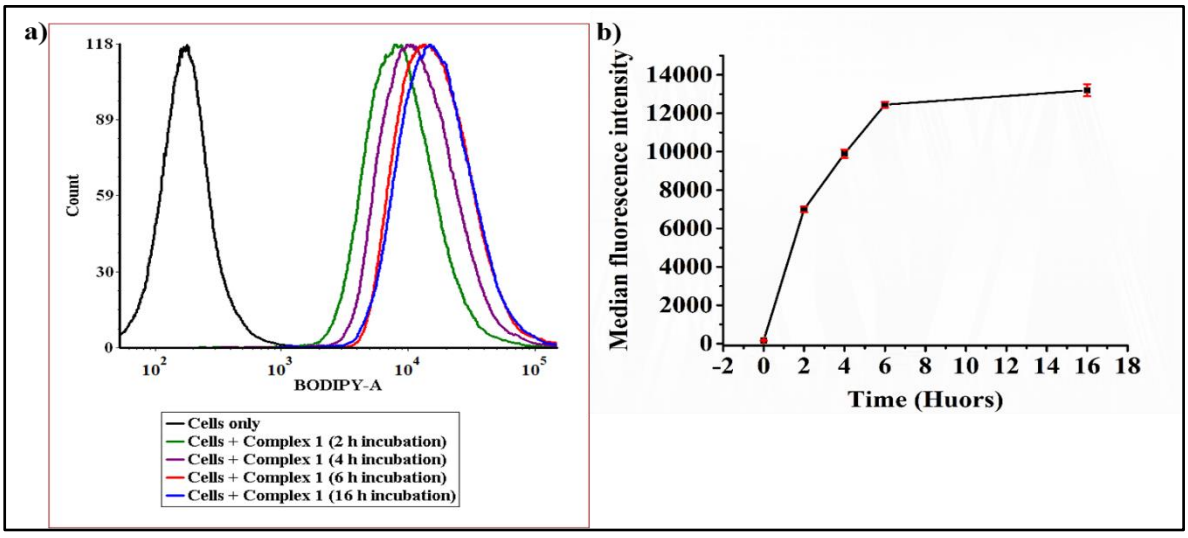


Fig. S24 Time-dependent cellular uptake studies in HeLa cells monitored by flow cytometric analysis of complex **1**. (a) Histogram plots (normalized to peak height) and (b) median fluorescence intensity plots.

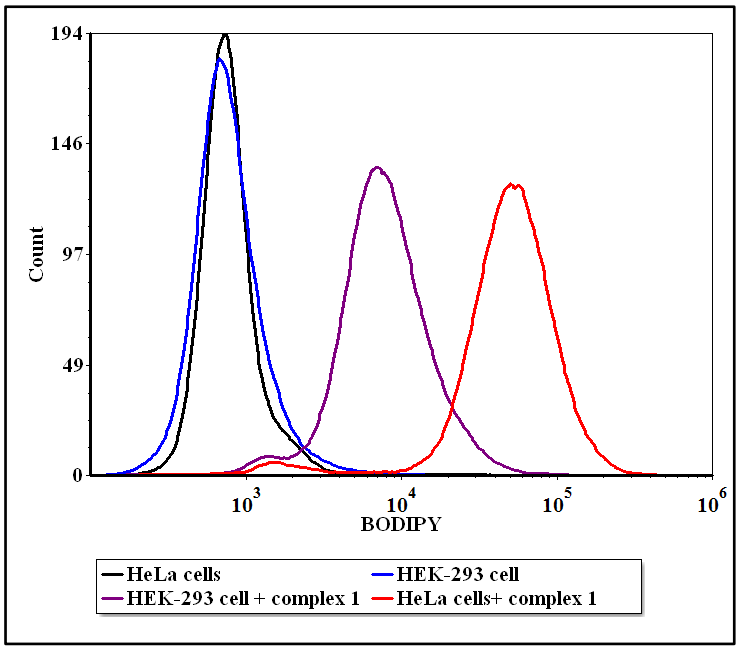


Fig. S25 Cellular incorporation of complex **1** in different cell lines monitored by flow cytometry. Median fluorescence intensity values: Hela cells, 646; HEK-293 cells, 632; HeLa cells+ complex **1**, 42071; HEK-293 cells+ complex **1**, 6192.

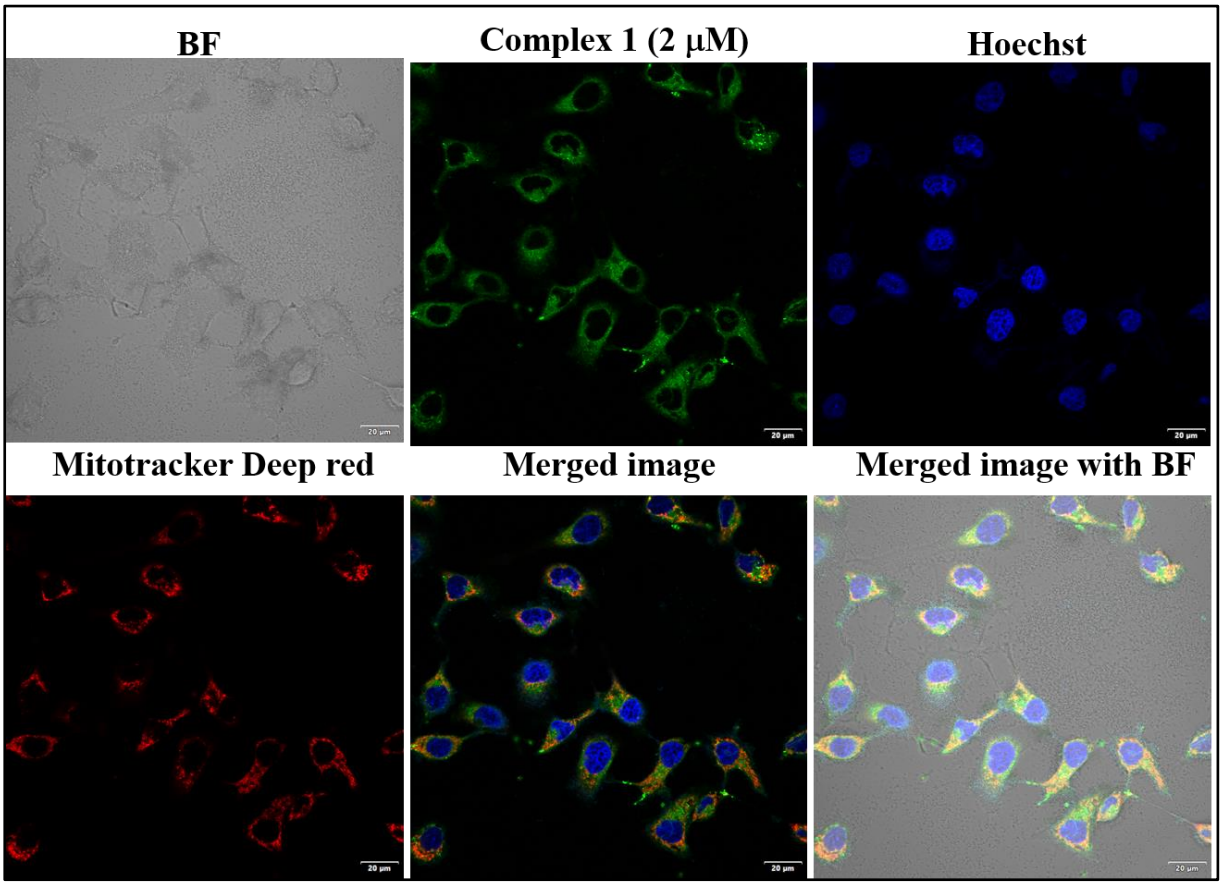


Fig. S26 Co-localization analysis of complex **1** in HeLa cells with nuclear (Hoechst) and mitochondria (Mitotracker Deep red) staining dyes using confocal laser scanning microscopy. Scale bar = 20 μm. BF represents brightfield image.

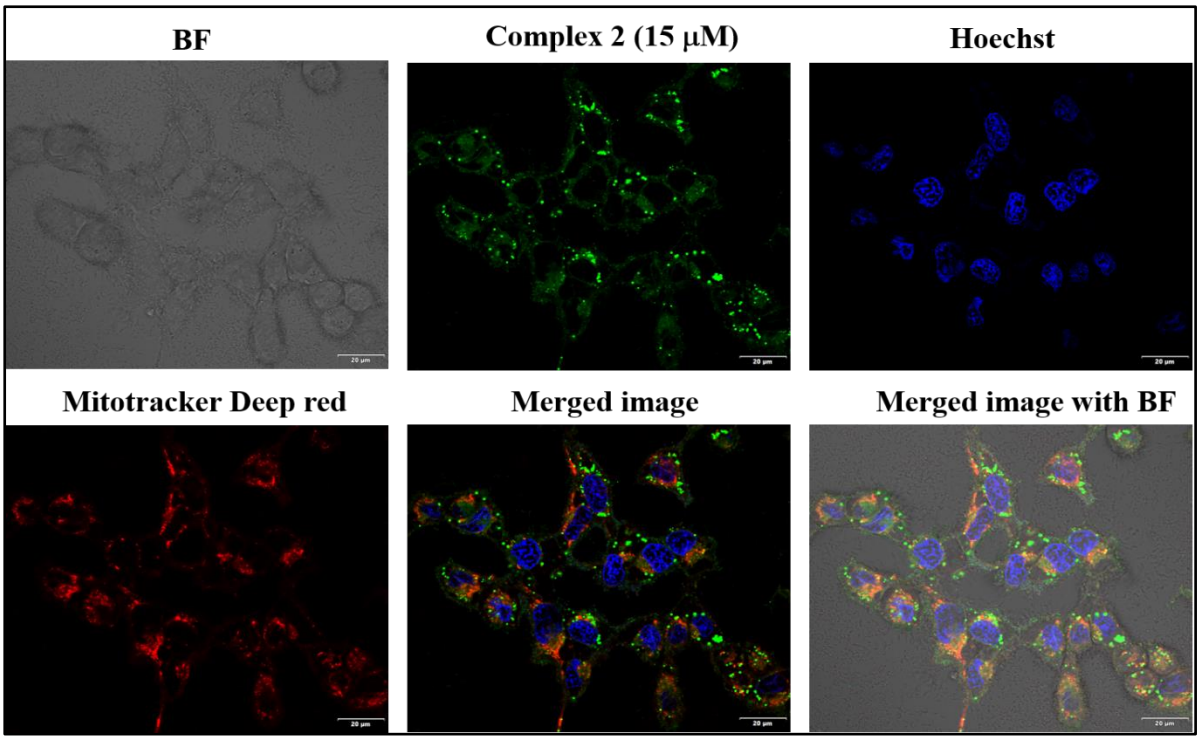


Fig. S27 Co-localization analysis of complex **2** in HeLa cells with nuclear (Hoechst) and mitochondria (Mitotracker Deep red) staining dyes using confocal laser scanning microscopy. Scale bar = 20 μm. BF is brightfield image.

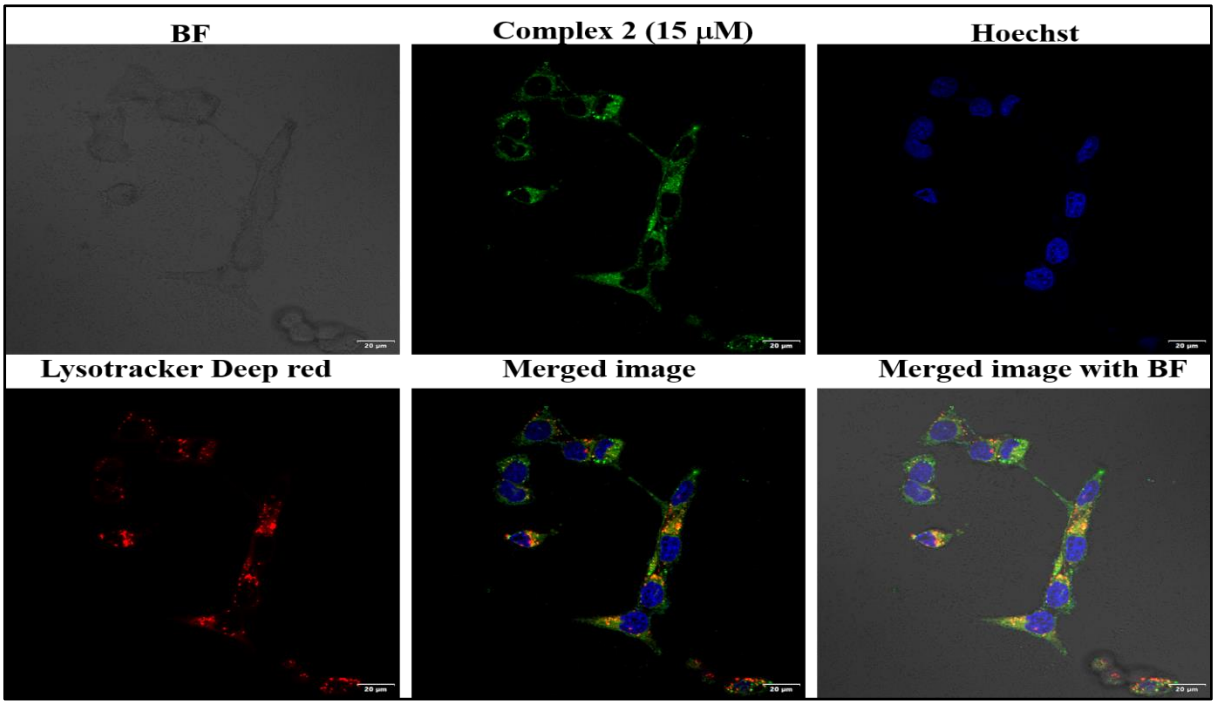


Fig. S28 Co-localization analysis of complex **2** in HeLa cells with nuclear (Hoechst) and lysosome staining (Lysotracker Deep red) dyes using confocal laser scanning microscopy. Scale bar = 20 μm. BF means brightfield image.

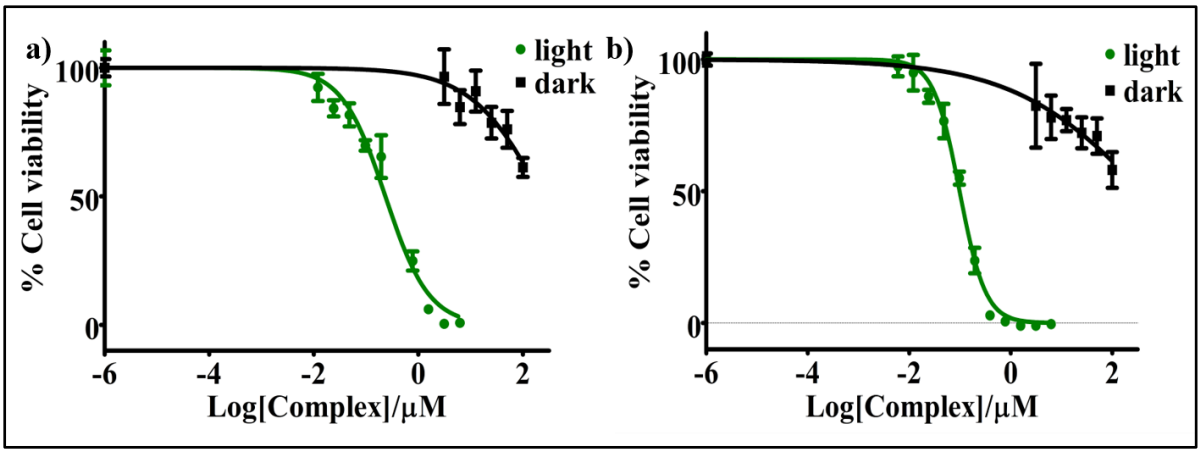


Figure S29: Cell viability assay plots obtained from MTT assay in HeLa cell line: a) complex **1** and b) complex **2**. Light dose: 400-700 nm (5 J/cm^2, 30 min exposure).

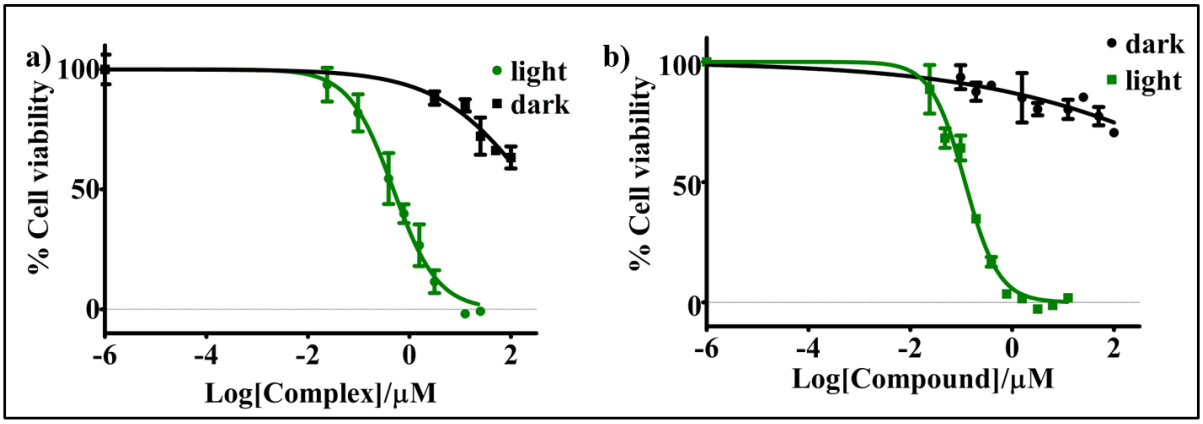


Fig. S30 Cell viability assay plots obtained from MTT assay in H1299 cell line: a) complex **1** and b) complex **2**. Light dose: 400-700 nm (5 J/cm^2, 30 min exposure).

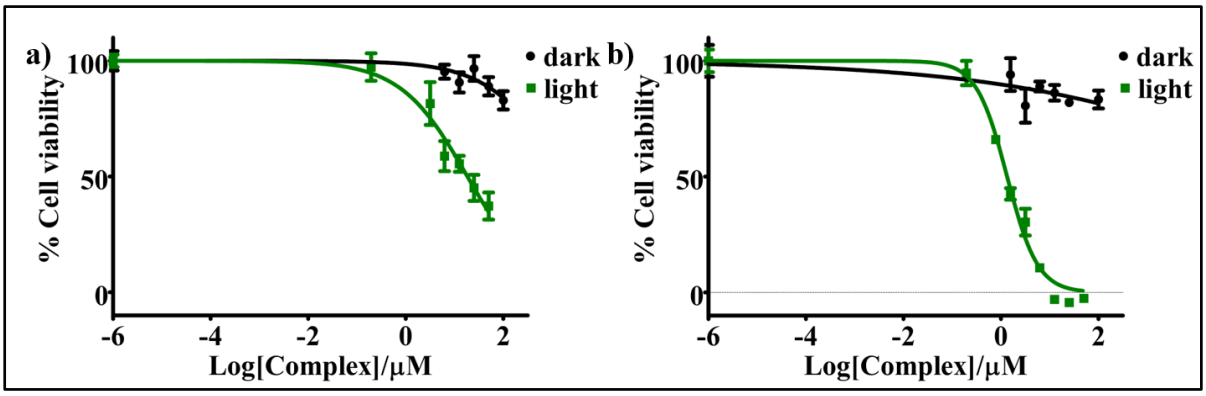


Fig. S31 Cell viability assay plots obtained from MTT assay in HEK-293 cell line: a) complex **1** and b) complex **2**. Light dose: 400-700 nm (5 J/cm^2, 30 min exposure).

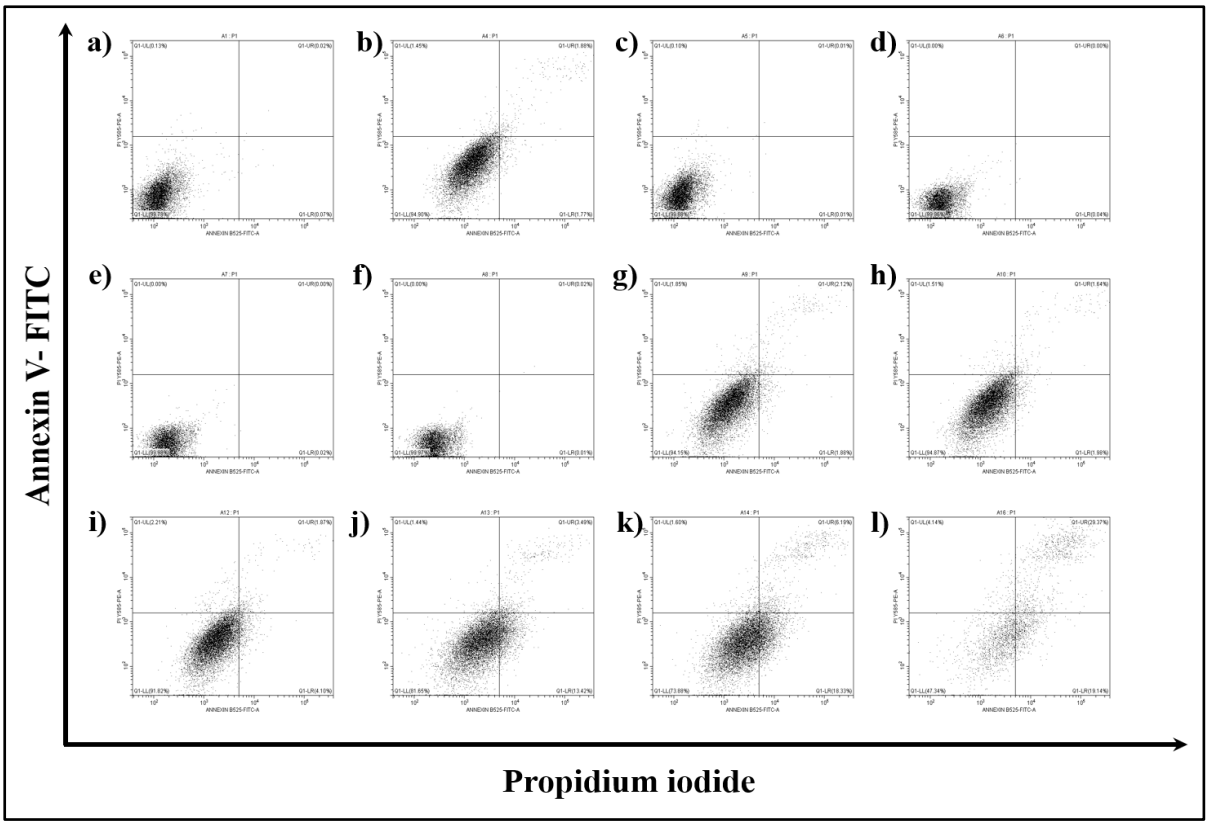


Fig. S32 Annexin V- FITC/propidium iodide dual staining assay in HeLa cells using complex **2**. a) Cells only, b) cells with Annexin V- FITC and propidium iodide, c) cells with 0.05 µM complex **2**, d) cells with 0.10 µM complex **2**, e) cells with 0.20 µM complex **2**, f) cells with 0.50 µM complex **2**, g) cells with 0.05 µM complex **2** and Annexin V- FITC and propidium iodide in Dark, h) cells with 0.10 µM complex **2** and Annexin V- FITC and propidium iodide in dark, i) cells with 0.50 µM complex **2** and Annexin V- FITC and propidium iodide in dark, j) cells with 0.05 µM complex **2** and Annexin V- FITC and propidium iodide with light irradiation, k) cells with 0.10 µM complex **2** and Annexin V- FITC and propidium iodide with light irradiation, l) cells with 0.50 µM complex **2** and Annexin V- FITC and propidium iodide with light irradiation. Light irradiation was done using 400-700 nm (2.4 mW/cm^2, 15 min) photo-reactor.

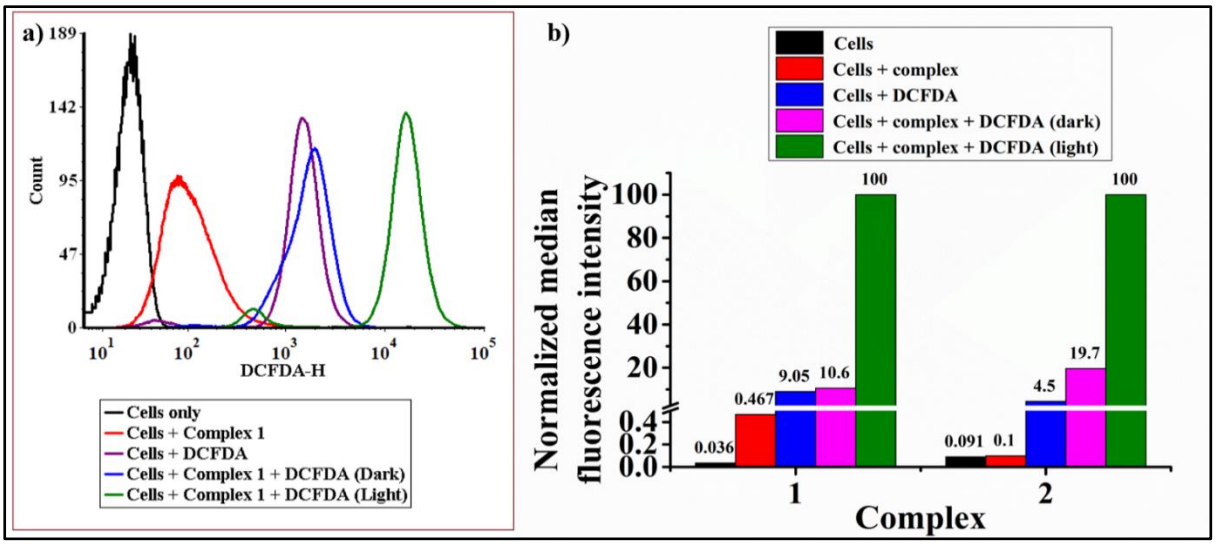


Fig. S33 DCFDA assay in HeLa cells using 2 µM complex **1**: a) histograms and b) bar diagrams.

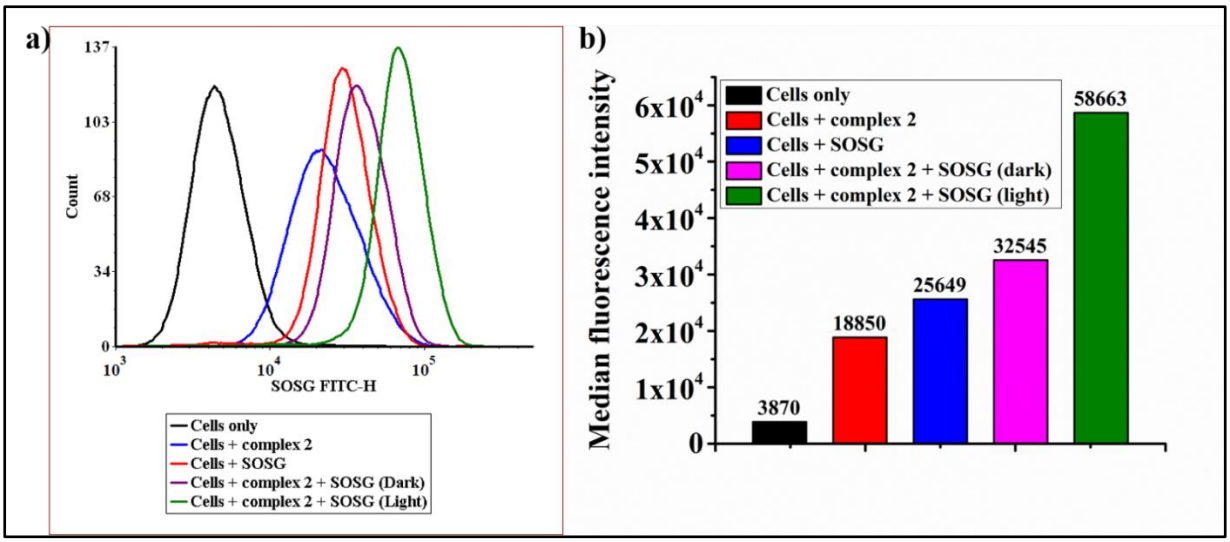


Fig. S34 SOSG assay in HeLa cells using 2 μM complex **2**: a) histograms and b) bar diagrams.

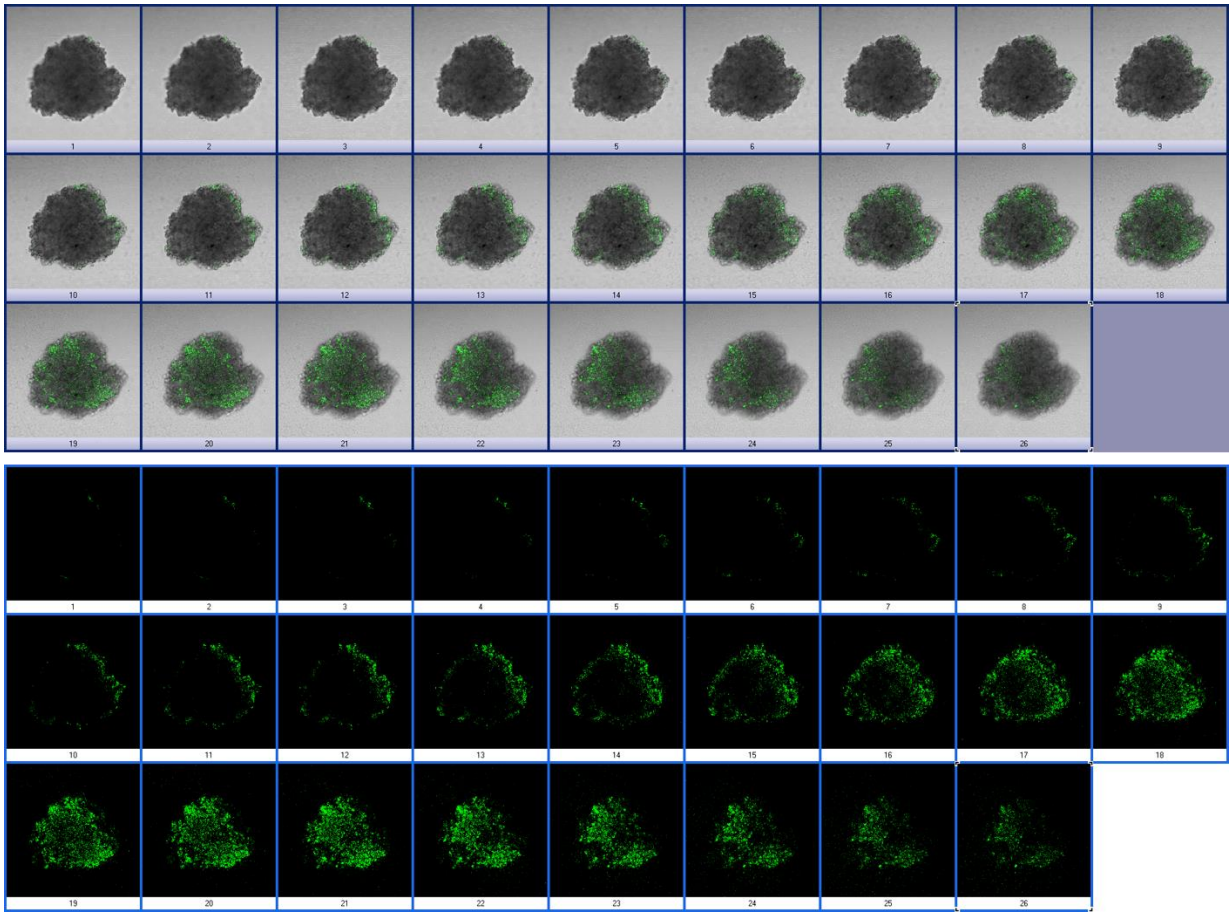
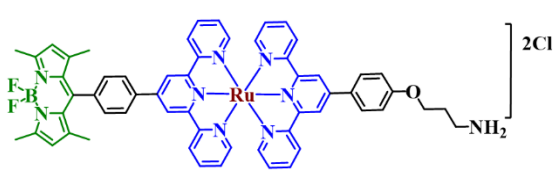


Fig. S35 Z-stack confocal images of HeLa MCTs stained with 2 μM complex **1**. Slice width 5 μm.

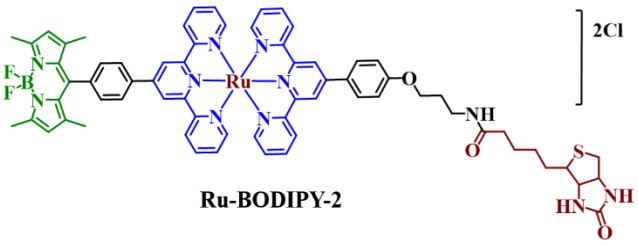
Table S1. A comparison of the photophysical properties of the complexes with previously reported molecules

Complex	λ_{max}/nm (ε/ $M^{-1}cm^{-1}$)[a]	λ_{em}/nm[a]	Φ_f	Φ_Δ[b]	$K_b \times 10^{-6}$ (M^{-1})[c]
Complex 1	500 (1.55×10^5)	516	<0.01	0.62	1.22
Complex 2	501 (1.38×10^5)	516	0.02	0.61	2.46
Ru-BODIPY-1	502 (3.69×10^4)	512	<0.01	0.57	3.38
Ru-BODIPY-2	502 (5.33×10^4)	513	<0.01	0.67	3.16

[a] In DMSO. Complexes **1** and **2** have significantly higher molar extinction coefficient (ε) values than their reported analogues. [b] Measured in DMSO using 1,3-diphenyl-isobenzofuran (DPBF) as a chemical trap of $^1O_2$. A 400-700 nm light source for photo-irradiation was used for exposure. Rose Bengal was used as a standard [Φ_Δ (singlet oxygen quantum yield) = 0.74 in DMSO]. [c] Intrinsic ct-DNA binding constant (K_b) obtained from UV-Vis spectral studies (ct, calf thymus).



Ru-BODIPY-1



Ru-BODIPY-2

Table S2. Selected crystallographic parameters of Ligand **L[1]**

Formula	$C_{44}H_{34}BCl_6F_2N_5$
$D_{calc.}$/ g cm^{-3}	1.360
μ/mm^{-1}	0.440
Formula Weight	894.27
Colour	clear dark orange
Shape	block
Size/mm^3	0.50×0.40×0.40
T/K	296.15
Crystal System	triclinic
Space Group	*P*-1
a/Å	11.218(7)
b/Å	14.339(8)
c/Å	15.150(9)
α/°	67.92(3)
β/°	75.53(2)
γ/°	82.16(3)
V/Å^3	2184(2)
Z	2
Z'	1
Wavelength/Å	0.710760
Radiation type	MoKα
Θ_{min}/°	2.895
Θ_{max}/°	27.740
Measured Refl.	87538
Independent Refl.	10058
Reflections with I > 2(I)	5092
R_{int}	0.0746
GooF	1.017
wR_2 (all data)	0.3057
wR_2	0.2454
R_1 (all data)	0.1819
R_1	0.0973

$W = 1/[s^2 (F_o^2) + (0.1397P)^2 + 2.0037P]$, where $P = (F_o^2 + 2F_c^2)/3$

Table S3. Selected bond length and bond angles obtained from crystal structure of **L[1]**

Atom	Atom	Length/Å
F1	B1	1.391(5)
F2	B1	1.380(5)
N4	C31	1.405(4)
N4	C35	1.340(5)
N4	B1	1.543(5)
N5	C38	1.338(5)
N5	B1	1.518(5)

Atom	Atom	Atom	Angle/°
C31	N4	B1	124.6(3)
C35	N4	C31	108.2(3)
F1	B1	N4	109.7(3)
F1	B1	N5	110.6(3)
F2	B1	F1	109.3(3)
F2	B1	N4	108.9(3)
F2	B1	N5	110.7(3)
N5	B1	N4	107.6(3)

Table S4. Coordinates for energy minimized structure of complex **1**

CARBON	6.0	-18.154572000	-1.175768000	0.386320000
NITROGEN	7.0	-19.568424000	-1.200575000	0.394534000
BORON	5.0	-20.460604000	-0.027764000	0.014374000
NITROGEN	7.0	-19.581578000	1.151931000	-0.373815000
CARBON	6.0	-18.167862000	1.143117000	-0.368640000
CARBON	6.0	-17.466402000	-0.012553000	0.008388000
CARBON	6.0	-20.006028000	2.392661000	-0.752055000
CARBON	6.0	-18.876305000	3.205063000	-0.994061000
CARBON	6.0	-17.720391000	2.447108000	-0.759202000

CARBON	6.0	-17.691670000	-2.474669000	0.776512000
CARBON	6.0	-18.838178000	-3.245271000	1.014493000
CARBON	6.0	-19.977711000	-2.446044000	0.773510000
CARBON	6.0	-15.276714000	0.196475000	1.204683000
CARBON	6.0	-15.981590000	-0.004728000	0.006478000
CARBON	6.0	-15.278186000	-0.199142000	-1.193719000
CARBON	6.0	-13.880016000	0.207854000	1.204826000
CARBON	6.0	-13.164978000	0.007475000	0.002723000
CARBON	6.0	-13.881465000	-0.198417000	-1.197594000
CARBON	6.0	-16.321523000	2.956926000	-0.906777000
CARBON	6.0	-21.442875000	2.763334000	-0.863719000
CARBON	6.0	-21.409367000	-2.838662000	0.878379000
CARBON	6.0	-16.286887000	-2.968669000	0.921826000
FLUORINE	9.0	-21.330717000	0.330275000	1.118949000
FLUORINE	9.0	-21.339482000	-0.391002000	-1.080458000
CARBON	6.0	-2.180780000	-2.651823000	-2.544215000
CARBON	6.0	-1.235786000	-3.404464000	-3.249511000
CARBON	6.0	0.128036000	-3.176404000	-3.023469000
CARBON	6.0	0.506713000	-2.201195000	-2.098821000
NITROGEN	7.0	-0.404489000	-1.471126000	-1.414669000
CARBON	6.0	-1.751189000	-1.687984000	-1.628101000
CARBON	6.0	-2.656698000	-0.843760000	-0.833385000
NITROGEN	7.0	-1.995085000	0.018233000	-0.009827000
CARBON	6.0	-2.654612000	0.881197000	0.814373000
CARBON	6.0	-1.747096000	1.723719000	1.608594000
CARBON	6.0	-2.174489000	2.689149000	2.524056000
CARBON	6.0	-1.227781000	3.440034000	3.228921000
CARBON	6.0	0.135507000	3.208618000	3.003082000
CARBON	6.0	0.511956000	2.231920000	2.079089000

NITROGEN	7.0	-0.400900000	1.503541000	1.395337000
CARBON	6.0	-4.051415000	-0.859228000	-0.845322000
CARBON	6.0	-4.771078000	0.019927000	-0.008057000
CARBON	6.0	-4.049303000	0.898413000	0.828069000
CARBON	6.0	-6.248036000	0.019965000	-0.006480000
CARBON	6.0	-6.970149000	-0.281466000	-1.179747000
CARBON	6.0	-8.364433000	-0.281076000	-1.182073000
CARBON	6.0	-9.082387000	0.017701000	-0.002762000
CARBON	6.0	-8.361833000	0.318137000	1.174531000
CARBON	6.0	-6.967547000	0.320726000	1.168555000
CARBON	6.0	-10.510565000	0.015348000	-0.000728000
CARBON	6.0	-11.735607000	0.012284000	0.000911000
CARBON	6.0	18.160521000	-1.175406000	-0.364364000
NITROGEN	7.0	19.574413000	-1.194229000	-0.369200000
BORON	5.0	20.460942000	-0.017267000	0.011388000
NITROGEN	7.0	19.576384000	1.161556000	0.390806000
CARBON	6.0	18.162463000	1.146327000	0.382070000
CARBON	6.0	17.466774000	-0.013637000	0.007828000
CARBON	6.0	19.993919000	2.405752000	0.765263000
CARBON	6.0	18.859714000	3.213425000	1.002834000
CARBON	6.0	17.708099000	2.449685000	0.767062000
CARBON	6.0	17.703916000	-2.477766000	-0.750113000
CARBON	6.0	18.854225000	-3.244533000	-0.982343000
CARBON	6.0	19.989824000	-2.439624000	-0.741981000
CARBON	6.0	15.279871000	0.178990000	-1.195935000
CARBON	6.0	15.981958000	-0.011687000	0.005637000
CARBON	6.0	15.275707000	-0.200443000	1.205067000
CARBON	6.0	13.883168000	0.186097000	-1.200140000
CARBON	6.0	13.165309000	-0.007697000	0.001370000

CARBON	6.0	13.878994000	-0.203596000	1.205027000
CARBON	6.0	16.306653000	2.953969000	0.909343000
CARBON	6.0	21.428093000	2.789447000	0.868815000
CARBON	6.0	21.423321000	-2.826948000	-0.841302000
CARBON	6.0	16.301563000	-2.978479000	-0.896034000
FLUORINE	9.0	21.336654000	0.339139000	-1.088937000
FLUORINE	9.0	21.334562000	-0.375522000	1.112707000
CARBON	6.0	2.171478000	-2.516811000	2.667533000
CARBON	6.0	1.224114000	-3.223518000	3.415854000
CARBON	6.0	-0.138985000	-2.999537000	3.181454000
CARBON	6.0	-0.514604000	-2.075372000	2.204591000
NITROGEN	7.0	0.398894000	-1.390180000	1.478374000
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CARBON	6.0	2.653177000	-0.805942000	0.861326000
NITROGEN	7.0	1.994537000	0.011787000	-0.008347000
CARBON	6.0	2.657322000	0.826962000	-0.877298000
CARBON	6.0	1.752870000	1.626262000	-1.718247000
CARBON	6.0	2.183743000	2.539456000	-2.684255000
CARBON	6.0	1.239678000	3.249511000	-3.433579000
CARBON	6.0	-0.124469000	3.030487000	-3.200576000
CARBON	6.0	-0.504400000	2.107772000	-2.224014000
NITROGEN	7.0	0.405895000	1.419406000	-1.496784000
CARBON	6.0	4.047760000	-0.823806000	0.876300000
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CARBON	6.0	6.247988000	0.003846000	-0.005549000
CARBON	6.0	6.967766000	-0.247175000	1.181037000
CARBON	6.0	8.361992000	-0.248391000	1.186205000
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CARBON	6.0	8.364788000	0.248646000	-1.193899000
CARBON	6.0	6.970550000	0.252317000	-1.190982000
CARBON	6.0	10.510907000	-0.003515000	-0.001980000
CARBON	6.0	11.735959000	-0.005497000	-0.000610000
HYDROGEN	1.0	-18.911292000	4.240191000	-1.304550000
HYDROGEN	1.0	-18.860784000	-4.280175000	1.326835000
HYDROGEN	1.0	-15.825198000	0.345751000	2.130984000
HYDROGEN	1.0	-15.827840000	-0.353244000	-2.118537000
HYDROGEN	1.0	-13.333816000	0.368242000	2.129163000
HYDROGEN	1.0	-13.336354000	-0.354172000	-2.123367000
HYDROGEN	1.0	-15.824133000	2.516667000	-1.779272000
HYDROGEN	1.0	-16.331175000	4.042691000	-1.040511000
HYDROGEN	1.0	-15.700544000	2.722065000	-0.034722000
HYDROGEN	1.0	-21.540861000	3.792885000	-1.214128000
HYDROGEN	1.0	-21.966347000	2.100161000	-1.561140000
HYDROGEN	1.0	-21.947243000	2.670869000	0.104710000
HYDROGEN	1.0	-21.984134000	-2.093805000	1.438402000
HYDROGEN	1.0	-21.865488000	-2.915720000	-0.115547000
HYDROGEN	1.0	-21.499238000	-3.807427000	1.374545000
HYDROGEN	1.0	-15.792671000	-2.522497000	1.793132000
HYDROGEN	1.0	-16.284202000	-4.054421000	1.056027000
HYDROGEN	1.0	-15.670282000	-2.727334000	0.048431000
HYDROGEN	1.0	-3.239332000	-2.815880000	-2.707879000
HYDROGEN	1.0	-1.558579000	-4.154447000	-3.961596000
HYDROGEN	1.0	0.888551000	-3.739062000	-3.549876000
HYDROGEN	1.0	1.551534000	-1.991966000	-1.894131000
HYDROGEN	1.0	-3.232677000	2.855819000	2.687461000
HYDROGEN	1.0	-1.548849000	4.191258000	3.940478000
HYDROGEN	1.0	0.897328000	3.769816000	3.529159000

HYDROGEN	1.0	1.556309000	2.020075000	1.874703000
HYDROGEN	1.0	-4.583671000	-1.562690000	-1.476236000
HYDROGEN	1.0	-4.579881000	1.602312000	1.459913000
HYDROGEN	1.0	-6.441558000	-0.487959000	-2.106245000
HYDROGEN	1.0	-8.908625000	-0.504352000	-2.094321000
HYDROGEN	1.0	-8.903980000	0.540428000	2.088235000
HYDROGEN	1.0	-6.436870000	0.527987000	2.093689000
HYDROGEN	1.0	18.889112000	4.249318000	1.311326000
HYDROGEN	1.0	18.881846000	-4.280634000	-1.290294000
HYDROGEN	1.0	15.830565000	0.323655000	-2.121664000
HYDROGEN	1.0	15.823155000	-0.346663000	2.132476000
HYDROGEN	1.0	13.339132000	0.338608000	-2.127086000
HYDROGEN	1.0	13.331708000	-0.354532000	2.130316000
HYDROGEN	1.0	15.809198000	2.515746000	1.782805000
HYDROGEN	1.0	16.311355000	4.040400000	1.037876000
HYDROGEN	1.0	15.688654000	2.712304000	0.037020000
HYDROGEN	1.0	21.524283000	3.758414000	1.363421000
HYDROGEN	1.0	21.998449000	2.041815000	1.429620000
HYDROGEN	1.0	21.884141000	2.862327000	-0.125460000
HYDROGEN	1.0	21.997554000	-2.080011000	-1.399056000
HYDROGEN	1.0	21.875759000	-2.902422000	0.154434000
HYDROGEN	1.0	21.518655000	-3.795471000	-1.336943000
HYDROGEN	1.0	15.807396000	-2.538841000	-1.770658000
HYDROGEN	1.0	16.303819000	-4.064900000	-1.024718000
HYDROGEN	1.0	15.682000000	-2.735360000	-0.025222000
HYDROGEN	1.0	3.229594000	-2.678027000	2.836953000
HYDROGEN	1.0	1.544498000	-3.934986000	4.167455000
HYDROGEN	1.0	-0.901300000	-3.526989000	3.740689000
HYDROGEN	1.0	-1.558780000	-1.872121000	1.990719000

HYDROGEN	1.0	3.242582000	2.696849000	-2.852710000
HYDROGEN	1.0	1.563392000	3.959746000	-4.184918000
HYDROGEN	1.0	-0.884280000	3.560640000	-3.760664000
HYDROGEN	1.0	-1.549466000	1.908194000	-2.011120000
HYDROGEN	1.0	4.576656000	-1.492653000	1.546415000
HYDROGEN	1.0	4.584330000	1.506317000	-1.559968000
HYDROGEN	1.0	6.437694000	-0.412864000	2.114785000
HYDROGEN	1.0	8.903962000	-0.432718000	2.108412000
HYDROGEN	1.0	8.908888000	0.431103000	-2.115224000
HYDROGEN	1.0	6.442566000	0.419921000	-2.125572000
RUTHENIUM	44.0	-0.000226000	0.015416000	-0.009402000

Table S5. Coordinates for energy minimized structure of complex **2**

CARBON	6.0	-11.244673000	1.158944000	-0.390497000
NITROGEN	7.0	-12.658402000	1.180476000	-0.393464000
BORON	5.0	-13.546625000	0.009059000	0.000841000
NITROGEN	7.0	-12.663172000	-1.162331000	0.404781000
CARBON	6.0	-11.249643000	-1.149376000	0.396524000
CARBON	6.0	-10.552926000	0.002810000	0.001393000
CARBON	6.0	-13.083017000	-2.397681000	0.804905000
CARBON	6.0	-11.950169000	-3.202553000	1.058159000
CARBON	6.0	-10.797219000	-2.445054000	0.808777000
CARBON	6.0	-10.786081000	2.452701000	-0.802645000
CARBON	6.0	-11.935110000	3.217344000	-1.046588000
CARBON	6.0	-13.072025000	2.419267000	-0.788936000
CARBON	6.0	-8.363573000	-0.233420000	-1.191385000
CARBON	6.0	-9.068029000	-0.000665000	0.000139000
CARBON	6.0	-8.361575000	0.229506000	1.191018000
CARBON	6.0	-6.966120000	-0.240944000	-1.190360000

CARBON	6.0	-6.247224000	-0.004628000	-0.001390000
CARBON	6.0	-6.964167000	0.233098000	1.188481000
CARBON	6.0	-9.396370000	-2.946974000	0.965014000
CARBON	6.0	-14.518296000	-2.770058000	0.929397000
CARBON	6.0	-14.504914000	2.806956000	-0.894310000
CARBON	6.0	-9.382857000	2.946247000	-0.964187000
FLUORINE	9.0	-14.413596000	-0.365719000	-1.100543000
FLUORINE	9.0	-14.427770000	0.382134000	1.089921000
CARBON	6.0	-2.174704000	2.601053000	2.595672000
CARBON	6.0	-1.228097000	3.334303000	3.319028000
CARBON	6.0	0.135234000	3.109117000	3.087280000
CARBON	6.0	0.511908000	2.156382000	2.138673000
NITROGEN	7.0	-0.400841000	1.445217000	1.436974000
CARBON	6.0	-1.747052000	1.658983000	1.656335000
CARBON	6.0	-2.654180000	0.835686000	0.841963000
NITROGEN	7.0	-1.994859000	-0.006452000	-0.003612000
CARBON	6.0	-2.655600000	-0.848185000	-0.848494000
CARBON	6.0	-1.749649000	-1.671939000	-1.663741000
CARBON	6.0	-2.178612000	-2.613913000	-2.602576000
CARBON	6.0	-1.233009000	-3.347616000	-3.326790000
CARBON	6.0	0.130646000	-3.123002000	-3.096386000
CARBON	6.0	0.508656000	-2.170344000	-2.148227000
NITROGEN	7.0	-0.403114000	-1.458722000	-1.445722000
CARBON	6.0	-4.049148000	0.851406000	0.856364000
CARBON	6.0	-4.768837000	-0.005547000	-0.002208000
CARBON	6.0	-4.050636000	-0.862995000	-0.861521000
CARBON	6.0	11.245515000	1.159604000	0.398143000
NITROGEN	7.0	12.659225000	1.178946000	0.404584000
BORON	5.0	13.546748000	0.008522000	0.005934000

NITROGEN	7.0	12.662847000	-1.164178000	-0.394092000
CARBON	6.0	11.249098000	-1.148318000	-0.390362000
CARBON	6.0	10.553166000	0.004797000	0.003220000
CARBON	6.0	13.081227000	-2.401010000	-0.790972000
CARBON	6.0	11.947386000	-3.203187000	-1.049036000
CARBON	6.0	10.795400000	-2.443379000	-0.803562000
CARBON	6.0	10.787845000	2.453536000	0.810488000
CARBON	6.0	11.937480000	3.216161000	1.058228000
CARBON	6.0	13.073789000	2.416793000	0.802304000
CARBON	6.0	8.361881000	-0.226340000	1.192835000
CARBON	6.0	9.068280000	0.002910000	0.001765000
CARBON	6.0	8.363646000	0.230266000	-1.190712000
CARBON	6.0	6.964483000	-0.233674000	1.189681000
CARBON	6.0	6.247294000	-0.001031000	-0.001082000
CARBON	6.0	6.966230000	0.233705000	-1.190377000
CARBON	6.0	9.394160000	-2.942700000	-0.964730000
CARBON	6.0	14.515539000	-2.783296000	-0.896893000
CARBON	6.0	14.506953000	2.802591000	0.911005000
CARBON	6.0	9.385050000	2.949367000	0.968892000
FLUORINE	9.0	14.420609000	-0.365184000	1.101561000
FLUORINE	9.0	14.421270000	0.384439000	-1.088424000
CARBON	6.0	2.175801000	2.581137000	-2.623860000
CARBON	6.0	1.229491000	3.307172000	-3.354843000
CARBON	6.0	-0.133948000	3.082110000	-3.123589000
CARBON	6.0	-0.511032000	2.137006000	-2.167535000
NITROGEN	7.0	0.401426000	1.432990000	-1.458291000
CARBON	6.0	1.747738000	1.646289000	-1.677528000
CARBON	6.0	2.654523000	0.830116000	-0.855635000
NITROGEN	7.0	1.994733000	-0.006151000	-0.004641000

CARBON	6.0	2.655094000	-0.841018000	0.847292000
CARBON	6.0	1.748856000	-1.658642000	1.668355000
CARBON	6.0	2.177487000	-2.593502000	2.614421000
CARBON	6.0	1.231625000	-3.321094000	3.344438000
CARBON	6.0	-0.131953000	-3.097579000	3.112501000
CARBON	6.0	-0.509618000	-2.152340000	2.156813000
NITROGEN	7.0	0.402407000	-1.446782000	1.448550000
CARBON	6.0	4.049495000	0.846883000	-0.868364000
CARBON	6.0	4.768879000	-0.003045000	-0.002536000
CARBON	6.0	4.050083000	-0.854721000	0.862070000
HYDROGEN	1.0	-11.981448000	-4.232351000	1.386209000
HYDROGEN	1.0	-11.961379000	4.247365000	-1.374330000
HYDROGEN	1.0	-8.910250000	-0.402931000	-2.115043000
HYDROGEN	1.0	-8.906781000	0.400585000	2.115261000
HYDROGEN	1.0	-6.436829000	-0.400577000	-2.125735000
HYDROGEN	1.0	-6.433427000	0.391186000	2.123294000
HYDROGEN	1.0	-8.898930000	-2.486258000	1.826928000
HYDROGEN	1.0	-9.402413000	-4.029493000	1.122839000
HYDROGEN	1.0	-8.777664000	-2.730084000	0.086732000
HYDROGEN	1.0	-14.611816000	-3.803655000	1.268877000
HYDROGEN	1.0	-15.032346000	-2.116011000	1.642411000
HYDROGEN	1.0	-15.035599000	-2.665062000	-0.030763000
HYDROGEN	1.0	-15.078887000	2.055185000	-1.445921000
HYDROGEN	1.0	-14.959062000	2.892127000	0.099832000
HYDROGEN	1.0	-14.598579000	3.770556000	-1.399698000
HYDROGEN	1.0	-8.890077000	2.480234000	-1.825901000
HYDROGEN	1.0	-9.383255000	4.028341000	-1.124985000
HYDROGEN	1.0	-8.763195000	2.728417000	-0.086763000
HYDROGEN	1.0	-3.232896000	2.763169000	2.763536000

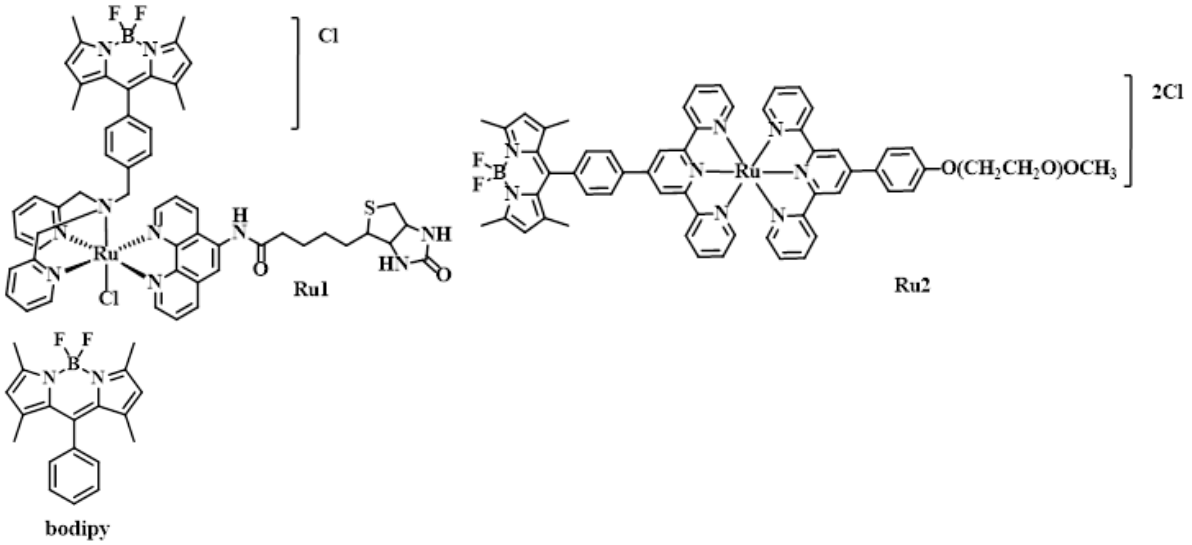
HYDROGEN	1.0	-1.549320000	4.067188000	4.049382000
HYDROGEN	1.0	0.896898000	3.657060000	3.627370000
HYDROGEN	1.0	1.556278000	1.950434000	1.928296000
HYDROGEN	1.0	-3.237035000	-2.775613000	-2.769383000
HYDROGEN	1.0	-1.555249000	-4.080428000	-4.056769000
HYDROGEN	1.0	0.891536000	-3.671333000	-3.637174000
HYDROGEN	1.0	1.553299000	-1.964793000	-1.938839000
HYDROGEN	1.0	-4.581316000	1.537749000	1.506052000
HYDROGEN	1.0	-4.583948000	-1.548883000	-1.510764000
HYDROGEN	1.0	11.977548000	-4.232757000	-1.377879000
HYDROGEN	1.0	11.964481000	4.245784000	1.387178000
HYDROGEN	1.0	8.907079000	-0.393430000	2.117811000
HYDROGEN	1.0	8.910248000	0.398871000	-2.114583000
HYDROGEN	1.0	6.433992000	-0.390555000	2.124818000
HYDROGEN	1.0	6.437167000	0.389189000	-2.126558000
HYDROGEN	1.0	8.900694000	-2.481621000	-1.828706000
HYDROGEN	1.0	9.398817000	-4.025332000	-1.121842000
HYDROGEN	1.0	8.772664000	-2.724180000	-0.088803000
HYDROGEN	1.0	14.612570000	-3.746437000	-1.402532000
HYDROGEN	1.0	15.086538000	-2.029257000	-1.448474000
HYDROGEN	1.0	14.970334000	-2.867127000	0.097073000
HYDROGEN	1.0	15.078449000	2.050633000	1.464917000
HYDROGEN	1.0	14.963860000	2.886130000	-0.082016000
HYDROGEN	1.0	14.600561000	3.766611000	1.415603000
HYDROGEN	1.0	8.890905000	2.486911000	1.831748000
HYDROGEN	1.0	9.386714000	4.031982000	1.126197000
HYDROGEN	1.0	8.765917000	2.729482000	0.091633000
HYDROGEN	1.0	3.234084000	2.743084000	-2.791355000
HYDROGEN	1.0	1.551013000	4.034343000	-4.090756000

HYDROGEN	1.0	-0.895383000	3.624413000	-3.669662000
HYDROGEN	1.0	-1.555485000	1.931538000	-1.957102000
HYDROGEN	1.0	3.235858000	-2.754351000	2.782397000
HYDROGEN	1.0	1.553602000	-4.048312000	4.080105000
HYDROGEN	1.0	-0.893043000	-3.641166000	3.657779000
HYDROGEN	1.0	-1.554186000	-1.947974000	1.945880000
HYDROGEN	1.0	4.581689000	1.528908000	-1.522543000
HYDROGEN	1.0	4.582832000	-1.535439000	1.517157000
RUTHENIUM	44.0	-0.000047000	-0.006794000	-0.004607000

Table S6. IC_{50} values (μM) of some previously reported compounds[S7-S11]

Compound	Cell line	IC_{50} in dark	IC_{50} in light	PI
Photofrin[a]	Hela	25	2.57 ± 0.12	10
Cisplatin[b]	HeLa	10.8 ± 0.8	n.d	n.d
$[Ru(tpy)_2]^{2+}$[b]	HeLa	>100	>100	n.d
Ru1[c]	A549	>100	0.98 ± 0.04	>100
Ru2[d]	A549	>53	1.50	>35
bodipy[e]	A549	>100	1.2 ± 0.09	> 83
PPIX[f]	A2780	>100	4.53 ± 0.61	> 22

[a] 24 h drug exposure, IC_{50} represented in μg/ml, 5 J/cm^2 light dose, 72 h post incubation (data taken from ref 7). [b] 4 h compound treatment and 44 h post incubation, Light dose 3.1 J/cm^2, 480 nm, (data taken from ref 8) [c] 4 h compound treatment and 20 h post incubation, 10 J/cm^2 light dose from 400-700 nm light source, (data taken from ref 9). [d] 24 h compound treatment and 24 h post incubation, 0.48 J/cm^2 light dose from 500 nm light source, (data taken from ref 10). [e] 2 h compound treatment, 20 h post incubation, 2.2 J/cm^2 light dose from 400- 700 nm light source. [f] 4 h compound treatment, 44 h post incubation, 3.1 J/cm^2 light dose from 480 nm light source (data taken from ref 11).



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