Electronic Supplementary Information

*Synthesis and characterization of **2a** and **2b***:

All manipulations were carried out under nitrogen using standard Schlenk techniques, and dried deoxygenated solvents.

2a: Ligand **1a** (0.67g, 1.90 mmol) and [$(C_6F_5)_2Zn$·toluene] (1.00g, 2.03 mmol) were refluxed in toluene (40 ml). After 12 hours the solution was cooled to room temperature and the volatiles were removed *in-vacuo*. The residue was extracted into warm dichloromethane (40 ml) and the solution was allowed to stand at ambient temperature to afford yellow prisms of **2a**. Yield: 0.74 g, 73 %; elemental analysis calcd (%) for $C_{132}H_{150}N_6O_{18}Zn_6$·7($CH_2Cl_2$)·2($C_2H_3N$): C 54.1, H 5.4, N 3.5; found: C 53.8, H 5.3, N 3.4; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.73 (s, 54H, C(C*H*$_3$)$_3$), 1.03 (s, 54H, C(C*H*$_3$)$_3$), 6.23 (d, 6H, J 7.94 Hz, aryl*H*), 6.56 (t, 6H, J 7.63 Hz, aryl*H*), 6.73 (s, 6H, J 2.15 Hz, aryl*H*), 7.03 (m, 6H, aryl*H*), 7.18 (m, 6H, aryl*H*), 7.49 (t, 6H, J 7.68 Hz, aryl*H*), 8.12 (s, 6H, C*H*=N). IR/cm^{-1}: 1584s, 1556s, 1528s, 1504m, 1456bs, 1297m, 1260s, 1194m, 1164s, 1096s, 1022s, 952m, 928w, 915w, 874m, 802s, 763m, 725m, 706m, 666w, 635w, 581w, 568w, 533w, 480w, 263w. ES-MS: 2149 (M^+ – **1a**), 2084 (M^+ – **1a** – Zn), 1730 (M^+ – 2**1a** – Zn), 1665 (M^+ – 2**1a** – 2Zn), 1247 (M^+ – 3**1a** – 3Zn).

2b: As for **2a**, but using **1b** (0.77g, 1.91 mmol) and [$(C_6F_5)_2Zn$·toluene] (1.00g, 2.03 mmol), affording **2b** as yellow solid. Recrystallization for dichloromethane at 0 ^{o}C afforded crystals suitable for X-ray diffraction. Yield, 0.66 g 68 %. elemental analysis calcd (%) for $C_{156}H_{162}N_6O_{18}Zn_6$·3($CH_2Cl_2$): C 62.5, H 5.5, N 2.8; found: C 62.2, H 5.4, N 2.6; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.81 (s, 54H, C(C*H*$_3$)$_3$), 1.17 (s, 54H, C(C*H*$_3$)$_3$), 5.54 (d, 5H, J 8.12 Hz, aryl*H*), 6.76 (t, 5H, J 7.59 Hz, aryl*H*), 6.87 (s, 5H, aryl*H*), 6.94 (d, 6H, J 2.47 Hz, aryl*H*), 7.14 (m, 7H, aryl*H*), 7.27 (m, 2H, aryl*H*), 7.59 (m, 6H, aryl*H*), 7.77 (s, 6H, aryl*H*), 8.00 (d, 6H, J 8.09 Hz aryl*H*), 8.46 (s, 6H, C*H*=N). IR/cm^{-1}: 1589s, 1570w, 1558m, 1530m, 1460bs, 1377s, 1326w, 1260s, 1165m, 1096m, 1022m, 882w, 800s, 746w, 723w, 604w, 508w, 482w. ES-MS: 1957 (M^+ – 2**1b** - Zn), 1891 (M^+ – 2**1b** - 2Zn), 1437 (M^+ – 3**1b** - 3Zn).

Figure S1. Alternative view of **2a.**

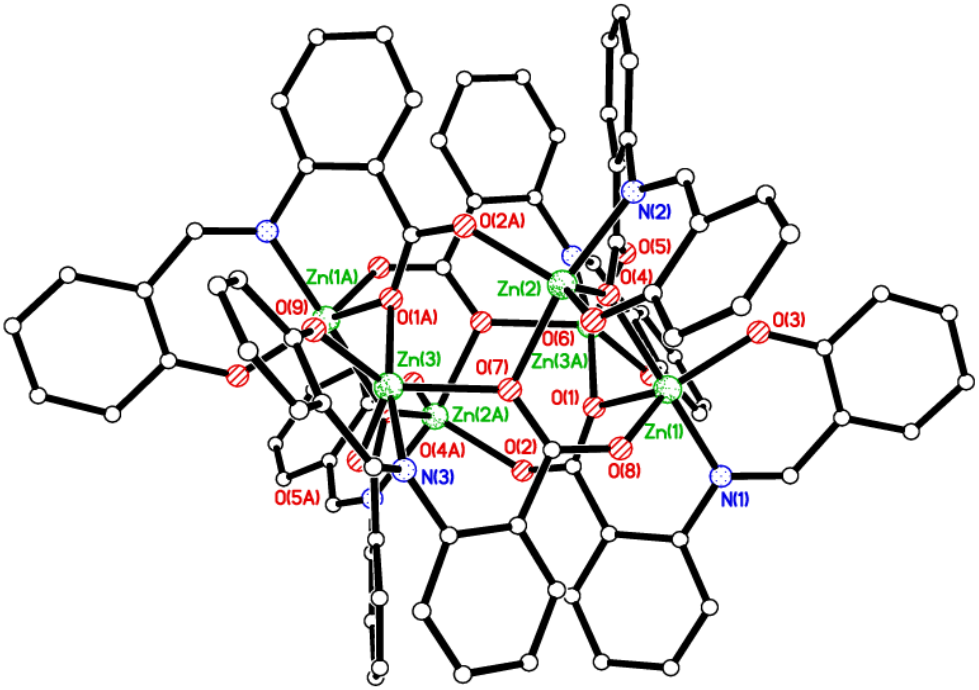
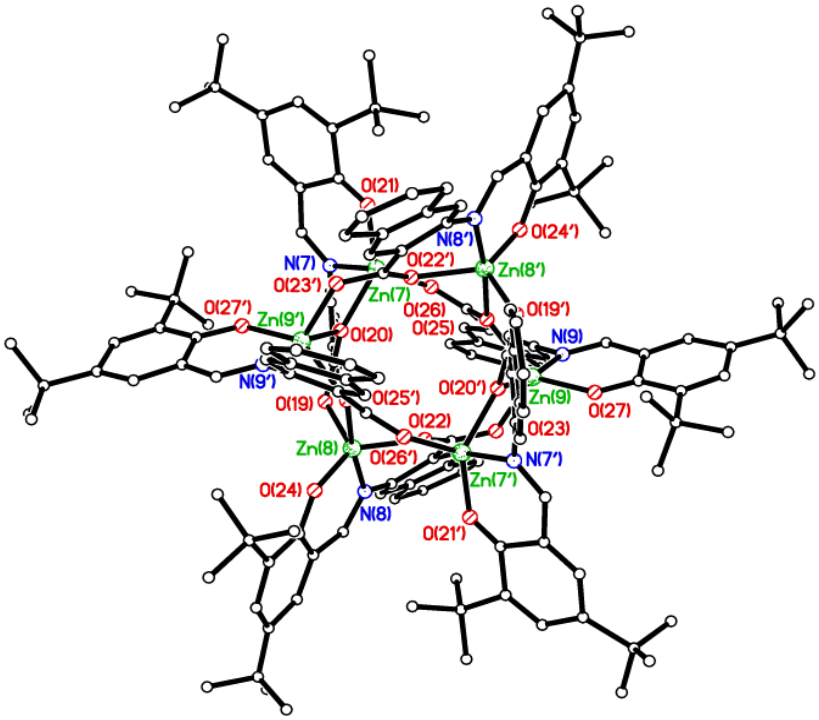


Figure S2. Alternative view of **2b**.



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Biological Methods.

Cell Viability Studies. MTS assays were performed using a CellTiter 96® AQ_{ueous} Non-Radioactive Cell Proliferation Assay (Promega). All cell lines used have been described earlier [1]. All cells were incubated at 37 ˚C. Freshly harvested CHO or HeLa cells were suspended in DMEM (Invitrogen) with 10% Foetal Calf serum and 2mM glutamine, THP-1 and HL-60 cells in RPMI (Invitrogen) with 10% Foetal Calf serum and 2mM glutamine, at a concentration of $1x10^5$ cells /mL. The cells were incubated in experimental media consisting of DMEM or RPMI supplemented with the test compounds dissolved in DMSO at different concentrations for 72 hrs at 37 °C in a humidified atmosphere and 5% CO_2. After incubation, cell viability was assessed using the CellTiter 96 Aqueous One Solution Cell Proliferation Assay (Promega). The 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium (MTS) tetrazolium compound is bioreduced by cells into a colored formazan product that is soluble in tissue culture medium [2]. This conversion is presumably accomplished by NADPH or NADH produced by dehydrogenase enzymes in metabolically active cells [3]. Aliquots of 20 µl of the CellTiter 96 Aqueous One Solution Reagent were added directly to the wells and the plates were incubated for 4 h at 37 °C in a humidified atmosphere, 5% CO_2 and then absorbance at 490 nm was read with a plate reader. The quantity of formazan product as measured by the absorbance at 490 nm is directly proportional to the number of living cells in culture [3].

Colocalisation studies. Visualisation of mitochondria with pdsred-mito. To visualize mitochondria, cells were grown on coverslips overnight and then transfected with pdsred-mito using Fugene™ (Roche, Burgess Hill, UK) according to the manufacturer's instruction. 24 hours after transfection cells were loaded with **2a**. After a further 18-24 hours cells were washed three times with PBS and analysed under the microscope.

Visualisation of acidic vesicles. Cells were grown on coverslips overnight and were loaded with **2a** 12 hours before the LysoTracker® Red stain. Cells were then exposed for 15min at 37 °C to LysoTracker® Red (50 nM) These conditions are optimal for labelling and for minimizing interference with intravesicular pH (5). Cells were then washed three times with ice-cold PBS before they were prepared for microscopy. NBDCalAm localizes into acidic vesicles and was used to as a control for imaging [6].

Nuclear stain: Dapi (4',6-diamidino-2-phenylindole) (Sigma is a fluorescent stain that binds strongly to A-T rich regions in DNA. Cells were incubated for 2-4 hours with 2a before Dapi was added at a final concentration of 5 ng/µL.

Image acquisition. CHO cells were grown on coverslips overnight, incubated with compounds for different time points at 37°C. Cells were washed three times in ice-cold PBS and either mounted on glass-slides or used imaged as live cells. Inhibition of cellular endocytosis was achieved by incubating the cells for at least 60 minutes before addition of calixarene ligands with 0.4M sucrose, (25 µg/mL), filipin (5 µg/mL), monensin (50 µM), nystatin (50 µg/mL) or methyl-ß-cyclodextrin (10mM) as described earlier [1,4]. Pictures were acquired using a Leica DMII inverted fluorescence microscope.

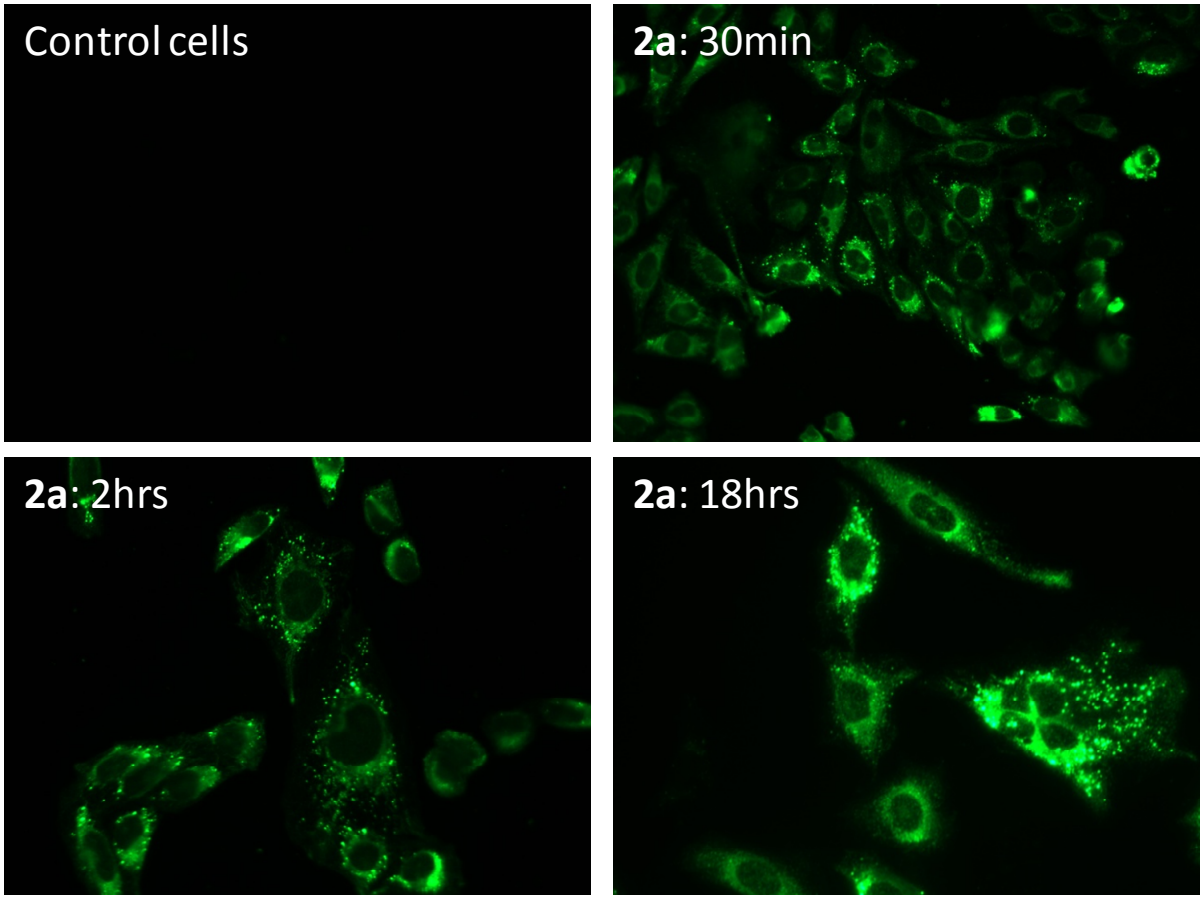

Figure S3. Uptake kinetics in CHO cells: **2a** is visible in cells 30 mins after incubation.

Pictures were taken on live cells using a Leica fluorescence microscope.

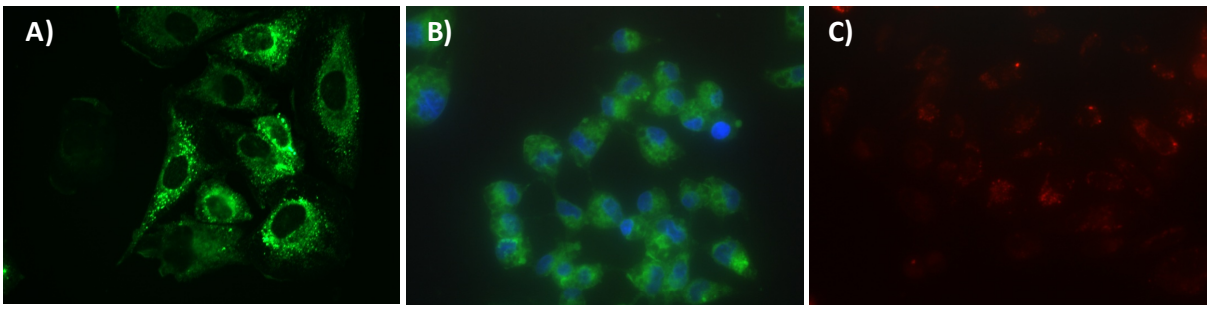

Figure S4: Cho cells were grown on coverslips over night, stained with a) **2a**, b) NBDCalAm and DAPI, c) LysoTracker® Red for 2 hours. Cells were then incubated with monensin,for 1 hour and mounted on a glasslide. Pictures were taken on live cells using a Leica fluorescence microscope.

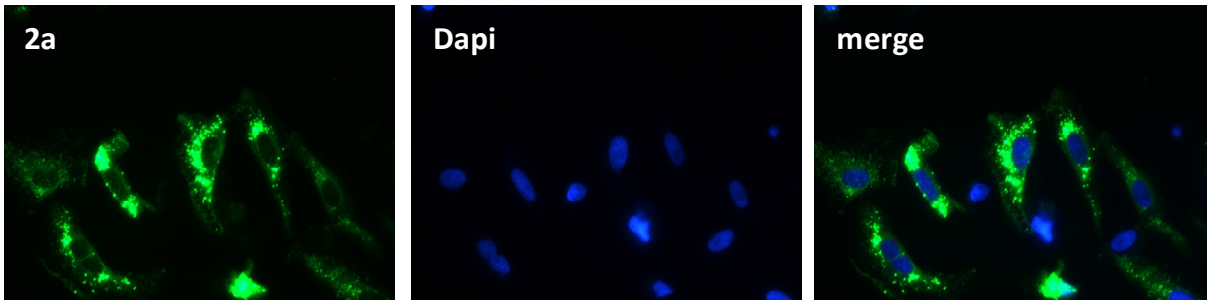

Figure S5: Cho cells were grown on coverslips over night, stained with **2a** and DAPI. Pictures were taken on live cells using a Leica fluorescence microscope.

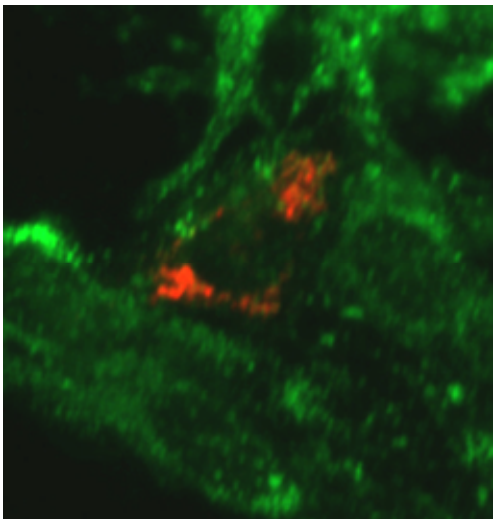

Figure S6: Cho cells were grown on coverslips over night, transfected with pdsred-mito and after 36 hours stained with **2a** for 12 hours. Pictures were taken on live cells using a Leica fluorescence microscope

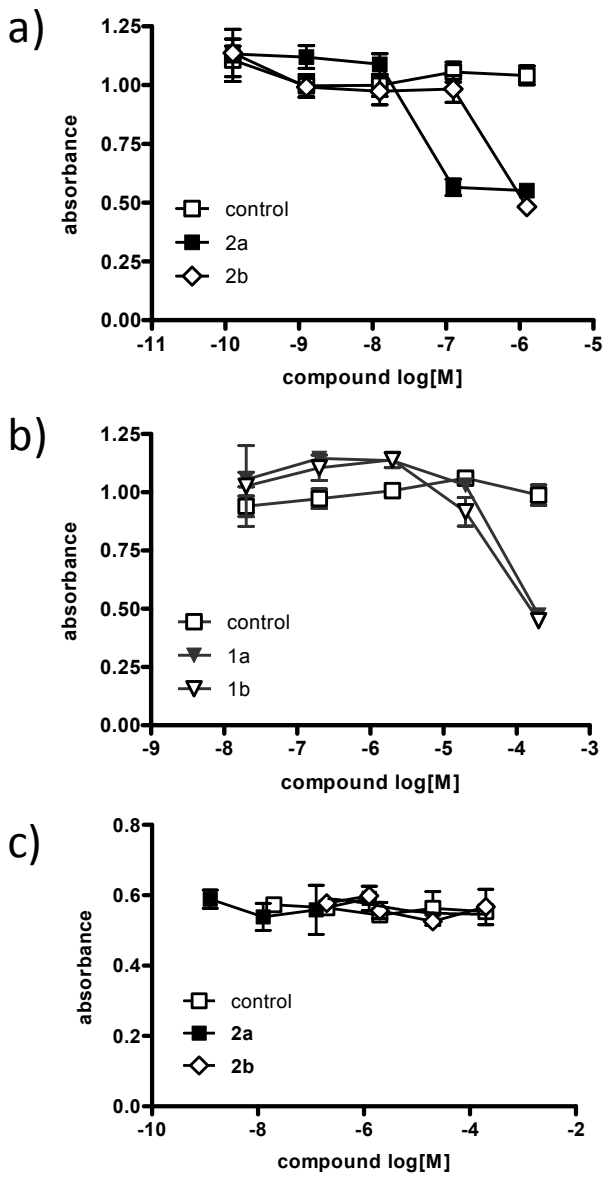

Figure S7. Cell viability assay in CHO cells (a, b) and HL-60 cells (c), tested for proliferation after 72 hours using an MTS kit. DMSO used as a control in all studies, data represent mean ± SEM of at least three independent experiments done in duplicate. Absorbance shown is directly proportional to the number of living cells in culture

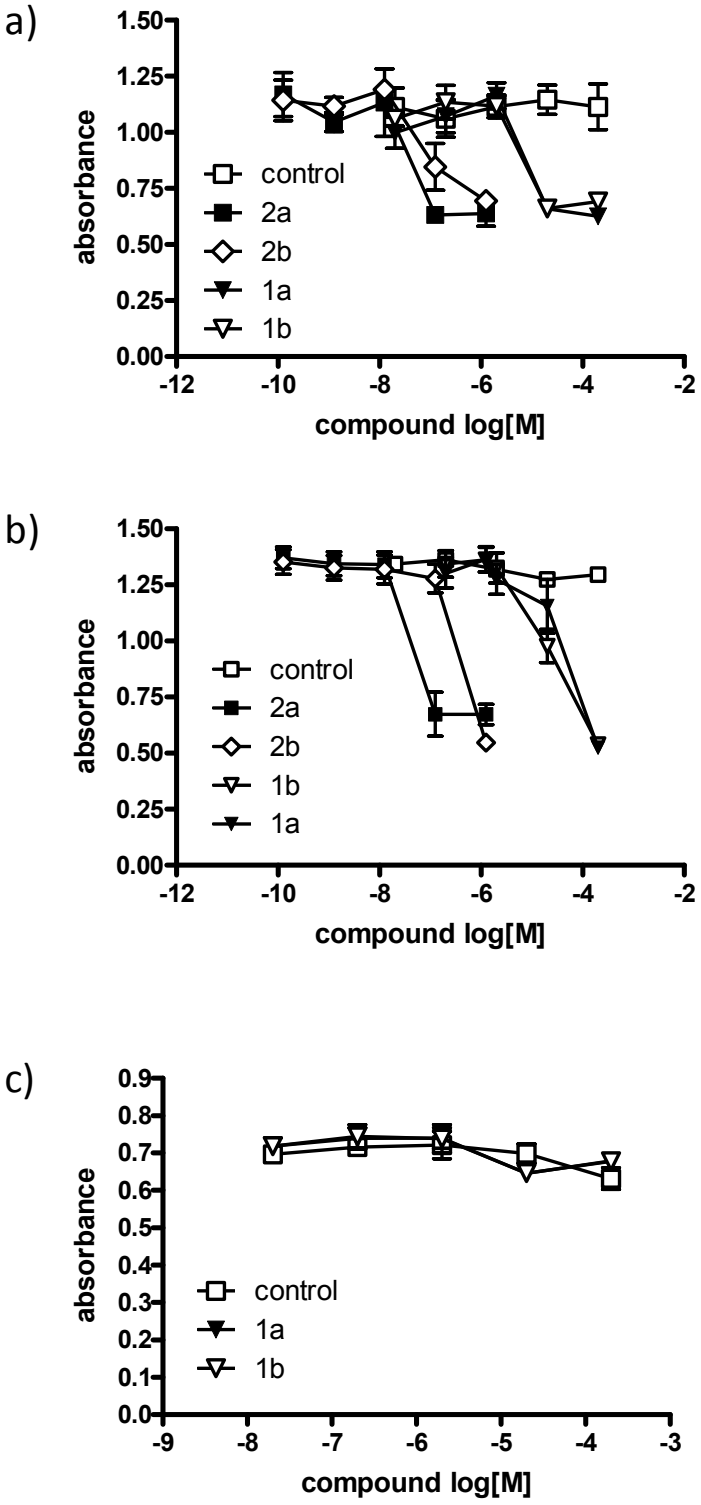

Figure S8: Representative cell viability assays a) THP-1, b) HeLa, c) HL60 cells tested for proliferation after 72 hours using an MTS assay. DMSO was used as a vehicle control in all studies, data represent at least mean ±SEM of at least three independent experiments done in duplicate.

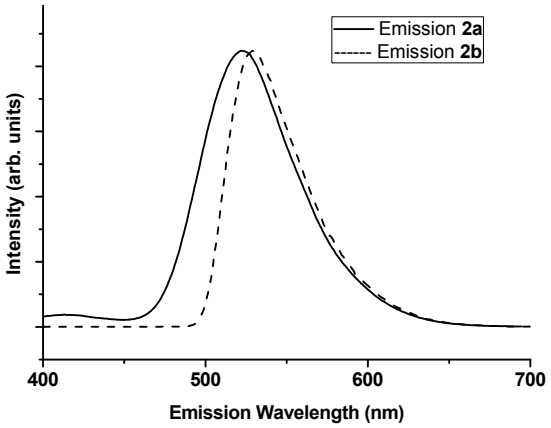

Figure S10. Normalized photoluminescence emission under excitation wavelength 350 nm, showing both **2a** and **2b** emit green light at peak 522.3 and 529.3 nm, respectively

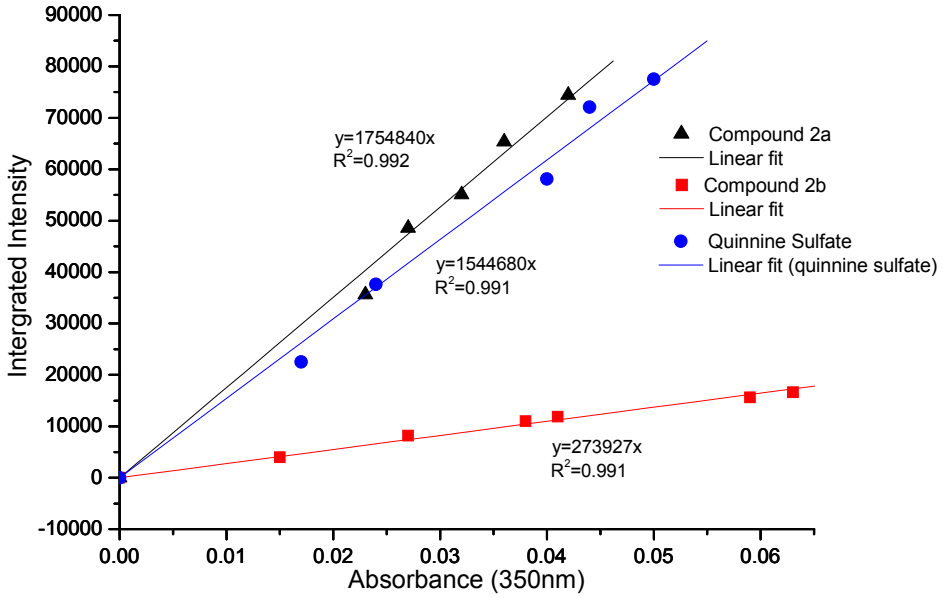

Figure S11. Quantum yield calculation for compound **2a** and **2b**.

The photoluminescence (PL) emission spectra were taken for samples dissolved in toluene in a quartz cuvette (10 mm × 10 mm), using a Perkin-Elmer LS55 spectrophotometer with emission slit width of 5 nm. The excitation wavelength was set at 350 nm.

The quantum yield (QY) was calculated by preparing solutions of the sample at varying concentrations in toluene, and measuring the absorbance at 350 nm and the area under the

emission peak at each different concentration. The absorbance was plotted against the area and compared to a standard of known quantum yield (quinine sulphate). [7] This data was used to obtain a value for the quantum yield.

The quantum yield of compounds in toluene was calculated using the following equation:

$$Q = Q_R\left(\frac{Grad}{Grad_R}\right)\left(\frac{\eta^2}{\eta_R^2}\right)$$

Q=Quantum yield

Q_R=Quantum yield of reference

η = refractive index of sample

η_R = refractive index of Reference

Here Quinine Sulphate was used as reference, which has a quantum yield of 54.6% when dissolved in 1N H_2SO_4. 1N (0.5M) H_2SO_4 had a refractive index of 1.346, while the refractive index of Chloroform **is** 1.49.

$$Q_{2a} = 54.6\,(1754840/1544680) \times (1.49^2/1.346^2) = 76.0\ \%$$

$$Q_{2b} = 54.6\,(273927/1544680) \times (1.49^2/1.346^2) = 11.9\ \%$$

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