Electronic Supplementary Material (ESI) for Photochemical & Photobiological Sciences.

Supporting Information

Title: Delayed release singlet oxygen sensitizers based on pyridone-appended porphyrins

Author(s): Susan Callaghan, Mikhail A. Filatov,* Elisabeth Sitte, Huguette Savoie, Ross W. Boyle, Keith J. Flanagan and Mathias O. Senge*

2. General Methods:

2.1 Synthetic and Characterization Protocol

Unless otherwise specified, all chemicals were purchased from Sigma-Aldrich and used without further purification. The synthetic procedures used to synthesize methyl 3,5-bis(bromomethyl)benzoate,[1] methyl 3-(bromomethyl)-5-formylbenzoate,[2] (3,5-bis(bromomethyl)phenyl)methanol[3] and 3,5-bis(bromomethyl)benzaldehyde[4] were adopted from literature. 5,10,15,20-tetrakis(3,5-bis(bromomethyl)phenyl)porphyrin (**TBMPP**) was synthesized in accordance with general procedure A.[5]

All air and/or water sensitive materials were handled using standard high vacuum techniques. Dry THF was obtained by passing through alumina under N_2 in a solvent purification systems and then further dried over activated molecular sieves. Dry DMF was purchased from Sigma-Aldrich. DCM was distilled from CaH_2. Unless otherwise specified all other solvents were used as commercially supplied. Where mixtures of solvents were used, ratios are reported by volume. Analytical thin layer chromatography was performed using silica gel 60 (fluorescence indicator F254, pre-coated sheets, 0.2 mm thick, 20 cm × 20 cm; Merck) plates and visualized by UV irradiation (l = 254 nm). Column chromatography was carried out using Fluka Silica Gel 60 (230–400 mesh; Merck) or aluminum oxide (neutral, activated with 6% H_2O, Brockman Grade III).

UV/Vis spectra were recorded in solutions using a Specord 250 spectrophotometer from Analytic Jena (1 cm path length quartz cell). Emission, excitation spectra and lifetimes were measured using a Cary Eclipse G9800A fluorescence spectrophotometer and Horiba Jobin Yvon Fluorolog 4.

Photo-irradiations were performed in quartz cuvettes (2 × 1 × 1 cm) using a polychromatic light source (Philips, 15V-150 W lamp), equipped with a 400 nm cut-off filter (Schott GG 400). The samples temperature controlled using a Peltier element (Cary Peltier 1×1 Cell Holder).

NMR spectra were recorded on a Bruker Advance III 400 MHz, a Bruker DPX400 400 MHz or an Agilent 400 spectrometer. Accurate mass measurements (HRMS) were carried out using a Bruker microTOF-Q™ ESI-TOF mass spectrometer. Mass spectrometry was performed with a Q-Tof Premier Waters MALDI quadrupole time-of-flight (Q-TOF) mass spectrometer equipped with Z-spray electrospray ionization (ESI) and matrix assisted laser desorption ionization (MALDI) sources in positive mode with trans-2-[3-(4-tert-butylphenyl)-2-methyl-2-propenylidene]malononitrile (DCTB) as the matrix. Melting points were measured using an automated melting point meter, SMP50 (Stuart).

2.2 Single Crystal X-ray Diffraction Protocol

Single crystal X-ray diffraction data for all compounds was collected on a Bruker APEX 2 DUO CCD diffractometer by using graphite-monochromated MoK_α (λ = 0.71073 Å) radiation and Incoatec IμS CuK_α (λ = 1.54178 Å) radiation. Crystals were grown by dissolving the compounds in CH_2Cl_2 and layering with MeOH. Crystals were mounted on a MiTeGen MicroMount and collected at 100(2) K by using an Oxford Cryosystems Cobra low-temperature device. Data was collected by using omega and phi scans and were corrected for Lorentz and polarization effects by using the APEX software suite.[6] Using Olex2, the structure was solved with the XT structure solution program, using the intrinsic phasing solution method and refined against $|F^2|$ with XL using least squares minimisation.[7]

Hydrogen atoms were generally placed in geometrically calculated positions and refined using a riding model. Details of data refinements can be found in Table S1. All images were prepared by using Olex2.

2.3 Cytotoxicity Protocol

Each compound was formulated in DMSO (anhydrous >99.9 %) and diluted in appropriate medium (Dulbecco's Modified Eagle's Medium with 4.5 g/L Glucose + 2 mM L-glutamine, no FCS) to give a range of concentrations (2×10^{-4} - 1×10^{-6} M). HT-29 cells (human colon adenocarcinoma) were adjusted to a concentration of 1×10^6 cells/mL. 800 µL was added to 200 µL of porphyrin at 5x concentration desired and incubated in the dark for 1 h at 37 °C in an atmosphere of 5% CO_2, after which they were centrifuged and washed in a 3× excess of medium to eliminate any unbound compound. Pellets of cells and compound were re-suspended in 1 mL medium and 4 x 100 µL of each cells (8×10^4) + dye concentration was transferred to two 96 wells plates. One plate was irradiated with broadband visible light (400 – 700 nm; 20 J/cm^2 provided by an Oriel quartz tungsten halogen lamp housing model 66188 powered by an Oriel 1100 W radiometric power supply model 69935), while the second plate served as a "dark toxicity" control. After irradiation, 5 µL of Fetal Bovine Serum was added to each well and the plates are returned to the incubator overnight. After 24 h, an MTT cell viability assay was performed and the results were expressed as % of cell viability versus compound concentration; an LD 90 (lethal dose where 90 % of the cells are killed) was determined from the resulting curves. Each experiment was repeated in triplicate (minimum).

2.4 Singlet Oxygen Sensor Green assay

Singlet Oxygen Sensor Green reagent was purchased from Thermo Fischer. Upon receipt, the reagent was stored -20 °C until required for use. The stock solutions were prepared in methanol: the content of one 100 µg vial was dissolved in 330 µL of methanol to make a stock solution of 5×10^{-4} M concentration. The working solutions of the reagent were prepared immediately before use, and any excess diluted reagent was discarded at the end of the work session.

A fluorescence cuvette containing 10^{-4} M solution of porphyrin **P1** or **P2** in THF was irradiated with broadband visible light for 1 h under stirring and cooling to 0 °C by a Peltier element. Subsequently, 31 µL of 1 mM NaOH solution in water (final NaOH concentration: 8.9×10^{-6} M) and 70 µL of 5×10^{-4} M SOSG solution in methanol (final SOSG concentration: 10^{-5} M) were added. After warming up to room temperature, the sample was placed into a fluorimeter and the fluorescence of SOSG in this solution was automatically recorded at variable periods of time (every 1-5 min) during 24 h. Fluorescence was excited 505 nm. In the case of **P2**, fluorescence measurements were performed at 40 °C using a Peltier element. In reference experiments SOSG solution fluorescence was monitored in the absence of the porphyrin under the same conditions. No increase of the sensor fluorescence was observed either at room temperature or at 40 °C.

3. X-ray Crystallography Data:

Table S1: Details of XRD data refinement.

Compound	***TBMPP***	***P1***
Empirical formula	$C_{48}H_{34}Br_4N_4$	$C_{68}H_{58}N_8O_8$
Formula weight	986.43	1115.22
Temperature/K	100.01	100.0
Crystal system	monoclinic	monoclinic
Space group	$P2_1/c$	$P2_1/c$
a/Å	15.8019(13)	17.1886(10)
b/Å	8.9658(7)	7.6152(4)
c/Å	14.5051(12)	20.9922(11)
α/°	90	90
β/°	107.3000(10)	100.509(4)
γ/°	90	90
Volume/Å³	1962.1(3)	2701.7(3)
Z	2	2
D_{calc} *g/cm³*	1.670	1.371
μ/mm⁻¹	4.144	0.738
F(000)	980.0	1172.0
Crystal size/mm³	0.17 × 0.13 × 0.07	0.4 × 0.2 × 0.05
Radiation	MoKα	CuKα
Wavelength/Å	λ = 0.71073	λ = 1.54178
2θ/°	5.286 to 58.336	5.228 to 130.492
Reflections collected	37651	32268
Independent reflections	5288	4549
R_{int}	0.0500	0.1757
R_{sigma}	0.0339	0.1264
Restraints	0	0
Parameters	253	385
GooF	1.019	1.039
R_1 *[I>=2σ (I)]*	0.0370	0.0767
wR_2 *[I>=2σ (I)]*	0.0885	0.1949
R_1 *[all data]*	0.0570	0.1181
wR_2 *[all data]*	0.0964	0.2307
Largest peak/e Å⁻³	1.35	0.53
Deepest hole/e Å⁻³	-1.11	-0.39

Crystal Data for TBMPP: $C_{48}H_{34}Br_4N_4$ (M = 986.43 g/mol): monoclinic, space group $P2_1/c$ (no. 14), a = 15.8019(13) Å, b = 8.9658(7) Å, c = 14.5051(12) Å, β = 107.3000(10)°, V = 1962.1(3) Å^3, Z = 2, T = 100.01 K, $\mu(MoK_\alpha)$ = 4.144 mm^{-1}, D_{calc} = 1.670 g/cm^3, 37651 reflections measured (5.286° ≤ 2θ ≤ 58.336°), 5288 unique (R_{int} = 0.0500, R_{sigma} = 0.0339) which were used in all calculations. The final R_1 was 0.0370 (I > 2σ(I)) and wR_2 was 0.0965 (all data).

Crystal Data for P1: $C_{68}H_{58}N_8O_8$ (M =1115.22 g/mol): monoclinic, space group $P2_1/c$ (no. 14), a = 17.1886(10) Å, b = 7.6152(4) Å, c = 20.9922(11) Å, β = 100.509(4)°, V = 2701.7(3) Å^3, Z = 2, T = 100.0 K, $\mu(CuK_\alpha)$ = 0.738 mm^{-1}, D_{calc} = 1.371 g/cm^3, 32268 reflections

measured (5.228° ≤ 2θ ≤ 130.492°), 4549 unique (R_{int} = 0.1757, R_{sigma} = 0.1264) which were used in all calculations. The final R_1 was 0.0767 (I > 2σ(I)) and wR_2 was 0.2307 (all data).

The structure of **TBMPP** shows archetypical tetra-mesoarylsubstituted porphyrin with the macrocyclic ring being almost planar with a mean 24-atom deviation of 0.031 Å. The phenyl ring rotations (65.78 – 77.03(7)°) are larger than that for 5,10,15,20-tetraphenylporphyrin (*ca* 60°) but in-line with the expected angles from other *para*-substituted tetraphenylporphyrins such as 5,10,15,20-tetrakis(4-iodophenyl)porphyrin (61.42 – 72.27°).[8, 9] The C_a–C_{meso}–C_a angles do not display a large deviation, at 124.6(2)°, compared to that of the 5,10,15,20-tetraphenylporphyrin at 125.5°. The bromomethyl substituents are orientated at 110.2(2)° from the phenyl rings and can be seen to be pointing in the same direction around the periphery of the ring. In the moiety packing diagram, **Figure S2**, the porphyrin macrocycles show two alternating patterns. The first of these is the skewed overlap between the faces of the porphyrin rings at 40.69(4)° which results in a crossed pattern in the packing, **Figure S3**. Thus, no π-stacking is observed in the structure. The second is a step-wise packing pattern between porphyrins that are in line with each other with a distance of 4.083 (4) Å between the planes, **Figure S4**. This results from short contacts between the C57─H57···Br20 at 3.752(5) Å and C3─H3···Br20 at 3.265(3) Å linking the two porphyrin rings *via* a bromine atom.

The structure of **P1** show the slightly distorted macrocyclic ring with an average atom deviation from the 24-atom mean plane at 0.074 Å. Compared with its precursor compound **TBMPP** the phenyl rings rotations have decreased in size to 60.31 – 62.62(9)° which is similar to 5,10,15,20-tetraphenylporphyrin.[8] The C_a–C_{meso}–C_a angles are comparable to that of 5,10,15,20-tetraphenylporphyrin at 125.5(3)°. Additionally, the pyridone units are adjusted to an angle of 111.3(3)° to the phenyl rings typical of a sp^3 carbon. However, unlike its precursor, the direction of the pyridinone units consist of two substituents facing each other with respect to the oxygen atoms. This feature is aided by an extensive hydrogen bonded water bridge between the two pyridone oxygen atoms with a donor-acceptor distance of 2.739 – 2.771(6) Å, as seen in **Figure S5**. In the moiety packing, we can see that the water molecules form a channel between the porphyrin layers with a porphyrin-water-water-porphyrin style hydrogen bonded network. This results in an ordered layering system of porphyrin rings with a water channel between them, as seen in **Figure S5**.

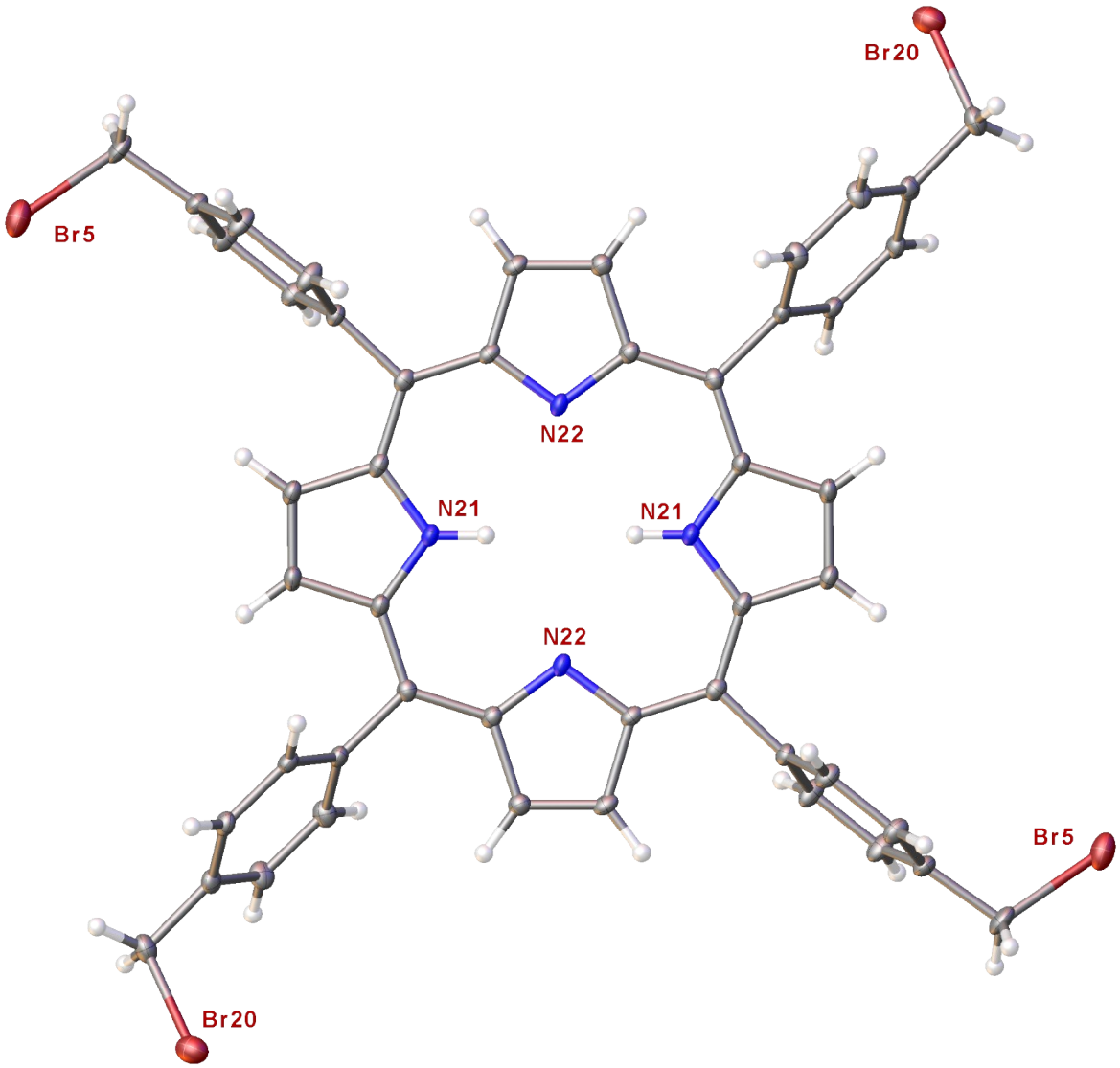


Figure S1: Molecular structure of **TBMPP** (thermal displacement 50%) showing all bromine atoms pointing in the one direction, orientated at 110.2(2)° from the phenyl rings.

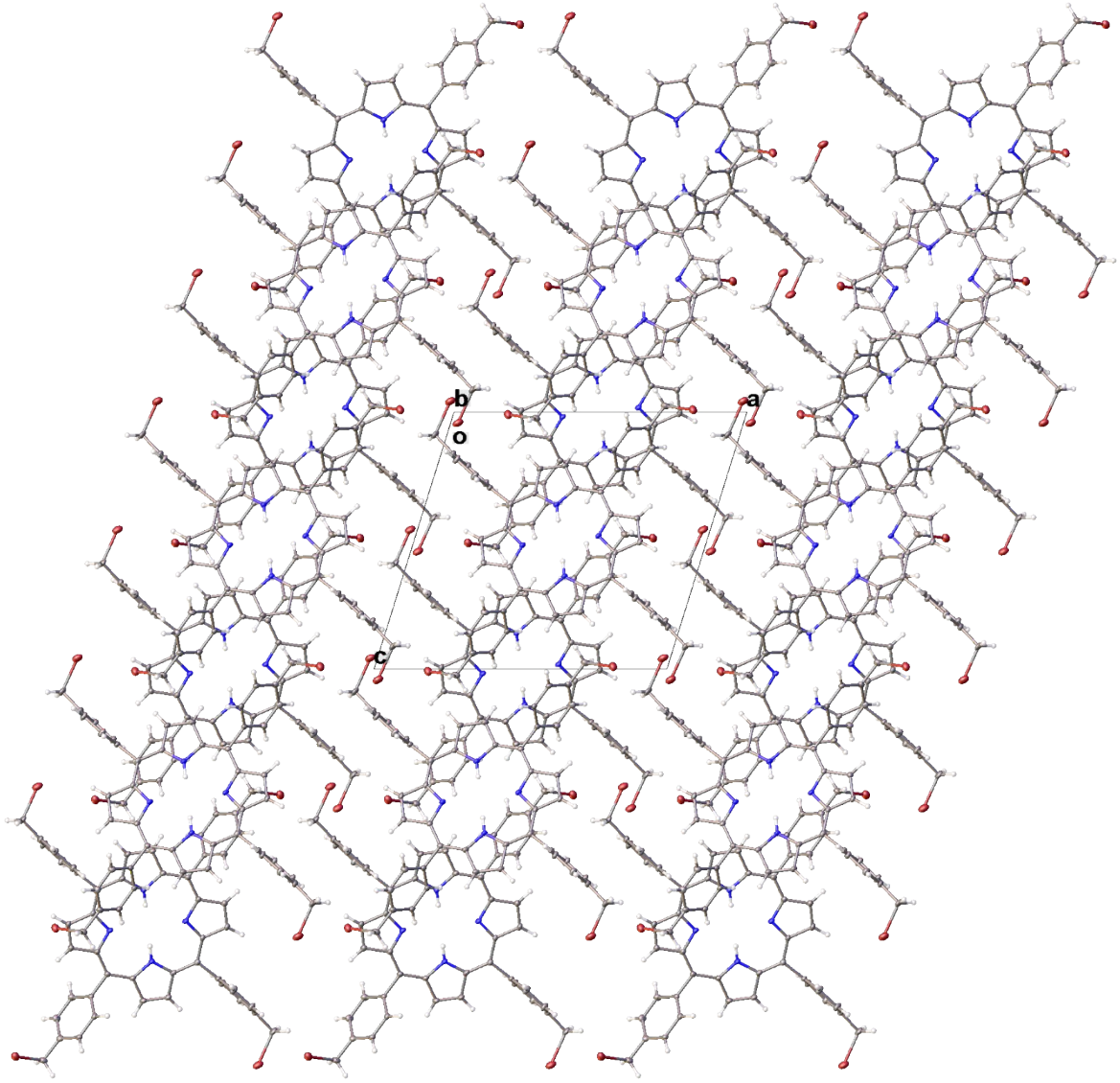


Figure S2: Moiety packing of **TBMPP**, looking down the b-axis showing overall packing arrangement of the macrocycles. Atom labels have been omitted for clarity.

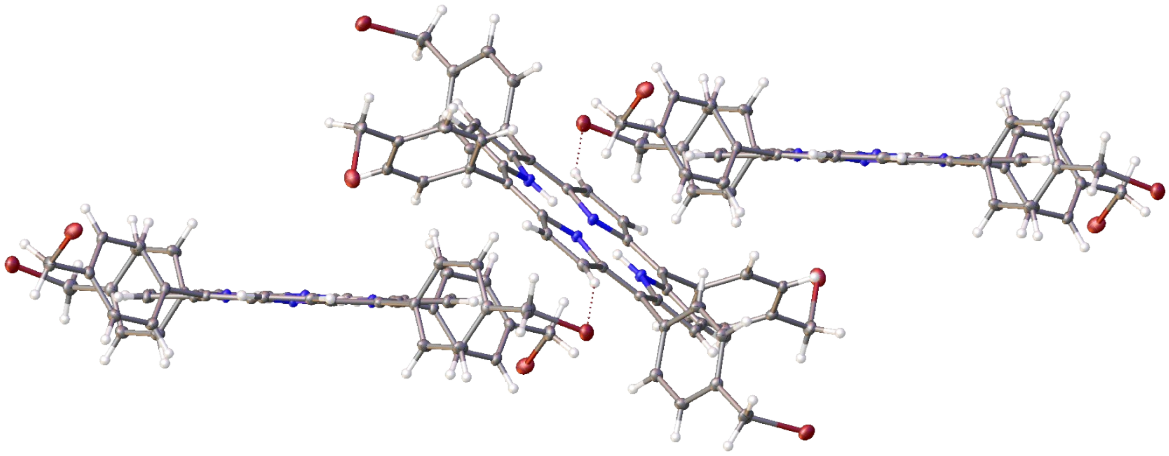


Figure S3: Partial moiety packing of **TBMPP**, looking down the a-axis showing the skewed packing pattern. The angle between the porphyrin planes is 40.69(4)°. Bromine···hydrogen interactions indicated by dotted lines. Atom labels have been omitted for clarity.

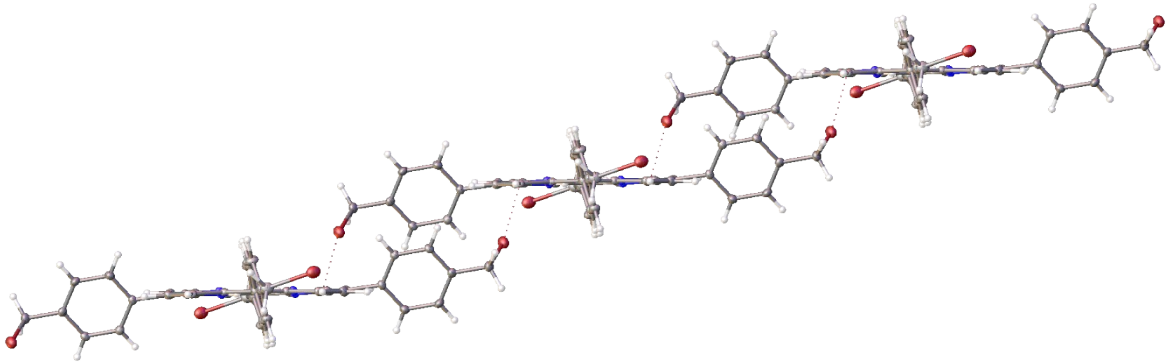


Figure S4: Partial moiety packing of **TBMPP**, looking down the a-axis showing the step-wise packing pattern. The distance between the 24-atom mean planes is 4.083(4) Å. Bromine···hydrogen interactions indicated by dotted lines. Atom labels have been omitted for clarity.

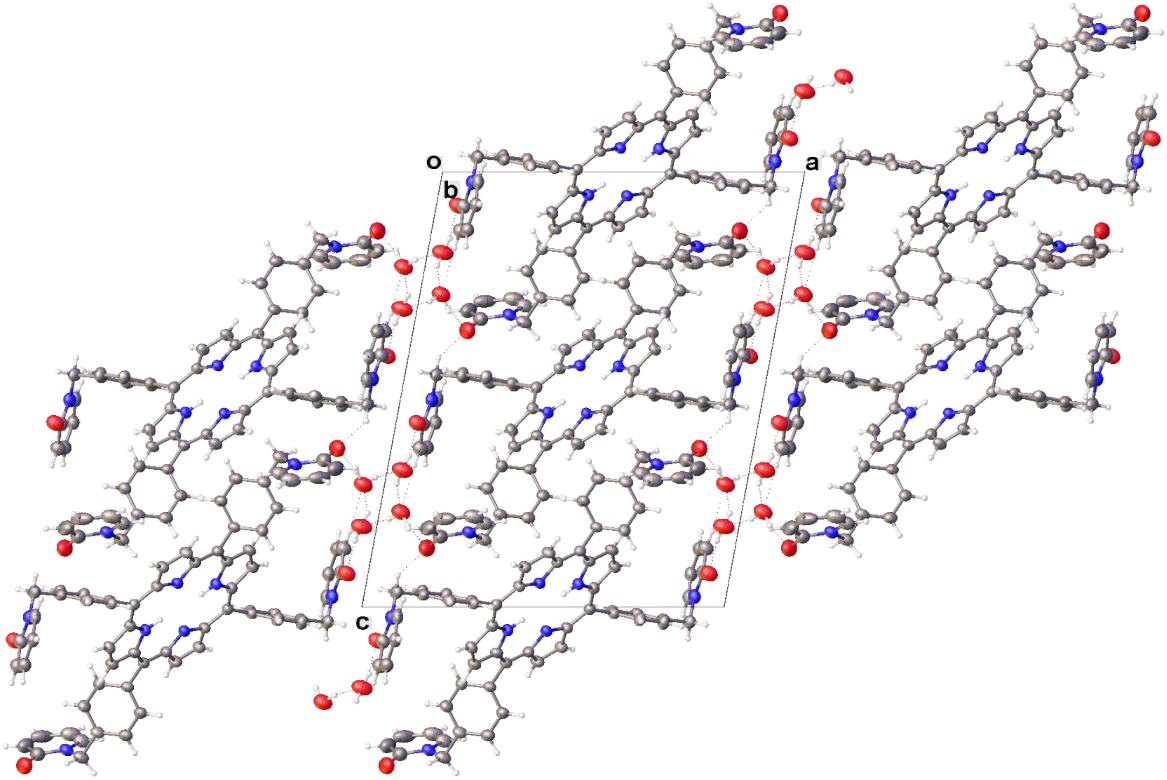


Figure S5: Moiety packing of **P1**, looking down the b-axis showing channels of water molecules between the porphyrin layers. Hydrogen bonds are indicated by dotted lines. Atom labels have been omitted for clarity.

4. Experimental Data:

4.1 General Procedures

General Procedure A: Lindsey porphyrin synthesis

Pyrrole (1 eq.) and the appropriate aldehyde (1 eq.) were dissolved in DCM under anhydrous conditions. Following the addition of boron trifluoride diethyl etherate (0.1 eq.), the reaction was stirred at rt for 2 h. DDQ (0.75 eq.) was added and the reaction was stirred at rt for 30 min. TEA (10 μL) was added to convert the product into free-base form. The crude product was purified by filtration through a plug of silica (DCM).

General Procedure B: Nucleophilic substitution of bromine by pyridone

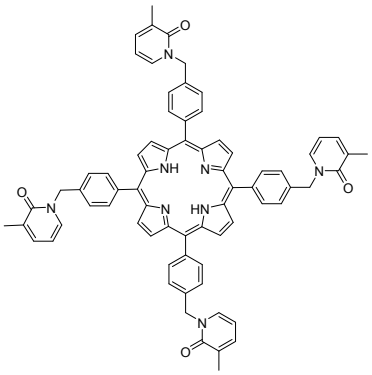
Bromoporphyrin (1 eq.) and the appropriate pyridone (10, 15 or 30 eq.) were dissolved in THF under anhydrous conditions. NaH (10, 15 or 30 eq.) was washed with hexane to remove the oil, dispensed in dry THF and added to the reaction vessel. The reaction was refluxed for 6 h and allowed to cool to rt. The resulting precipitate was filtered and washed with DCM. Combined filtrates were evaporated *in vacuo* and the residue was recrystallized from DCM-MeOH mixture to give analytically pure products.

General Procedure C: De-esterification

To a solution of porphyrin (1 eq.) dissolved in THF was added KOH (200 eq.) dissolved in MeOH. The reaction was heated to reflux for 24 h. The reaction was allowed to cool, the precipitate was removed and the solvent was evaporated *in vacuo*. Water was added and the precipitated product was filtered. The product was recrystallized from a mixture of DCM, MeOH and acetone.

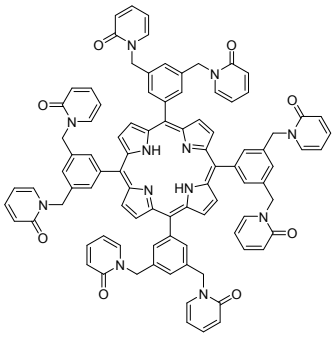
4.2 Experimental Details

5,10,15,20-Tetra(4-((3-methyl-2-oxopyridin-1(2H)-yl)methyl)phenyl)porphyrin, **P2**



Compound **P2** was synthesized in accordance with general procedure B using **TBMPP** (300 mg, 0.030 mmol) pyridone (337 mg, 3.55 mmol), NaH (73 mg, 3.04 mmol) and THF (150 mL) to yield a purple solid (0.80 g, 63 %). M.p. > 300 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 8H), 8.53 (d, J = 8.0 Hz, 8H), 7.92 (d, J = 8.0 Hz, 8H), 7.66 (d, J = 6.8 Hz, 4H), 7.56 (d, J = 6.9 Hz, 4H), 6.59 (t, J = 6.9 Hz, 4H), 5.67 (s, 8H), 2.35 (s, 12H), -0.70 (s, 4H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.48, 145.79, 139.44, 138.97, 138.79, 137.73, 135.15, 130.78, 128.40, 127.91, 122.34, 115.28, 112.39, 107.08, 52.77, 17.63 ppm; UV/Vis (DMSO): λ_{max} (log ε) = 420 (5.69), 516 (4.29), 550 (4.02), 591 (3.77), 648 nm (3.76); HRMS (ESI): *m/z* found 1098.4586, calcd for $[M+H]^+$ $C_{72}H_{58}N_8O_4$ 1098.4581.

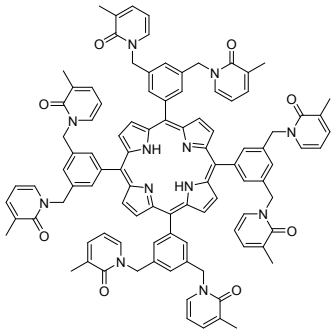
5,10,15,20-Tetrakis(3,5-bis((pyridin-2(1H)-one)methyl)phenyl)porphyrin, P3



Compound **P3** was synthesized in accordance with general procedure B using compound **5** (200 mg, 0.15 mmol), 2-hydroxypyridine (419 mg, 4.41 mmol), THF (100 mL) and NaH

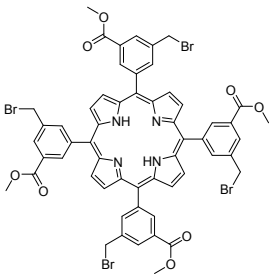
(176 mg, 60%, 4.41 mmol) to yield a purple crystals (126 mg, 58 %). M.p.= > 300 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 8H), 8.01 (s, 8H), 7.66 (s, 4H), 7.51 (d, J = 4.8 Hz, 8H), 7.38 – 7.32 (m, 8H), 6.64 (d, J = 9.1 Hz, 8H), 6.24 (t, J = 6.0 Hz, 8H), 5.48 (s, 16H) -2.96 (s, br, 2H) ppm; UV/Vis (DMSO): λ_{max} (log ε) = 422 (5.54), 518 (4.27), 553 (4.08), 592 (3.95), 647 nm (3.93); HRMS (MALDI) *m/z* calcd. for $C_{92}H_{70}N_{12}O_8$ $[M]^+$: 1470.5440, 1470.5432 found.

5,10,15,20-Tetrakis(3,5-bis((3-methylpyridin-2(1H)-one)methyl)phenyl)porphyrin, P4



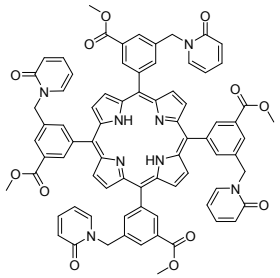
Compound **P4** was synthesized in accordance with general procedure B using compound **5** (200 mg, 0.15 mmol), 3-methyl-1,2-dihydropyridin-2-one (482 mg, 4.41 mmol), THF (100 mL) and NaH (176 mg, 60 % in mineral oil, 4.41 mmol) to yield purple crystal (152 mg, 65 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 8.73 (s, 8H), 7.97 (s, 8H), 7.62 (s, 4H), 7.36 (d, J = 4.2 Hz, 8H), 7.18 (d, J = 5.9 Hz, 8H), 6.12 (t, J = 6.7 Hz, 8H), 5.42 (s, 16H), 2.16 (d, J = 10.6 Hz, 24H), -2.96 (s, 2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.21, 143.13, 138.83, 137.07, 136.15, 134.95, 133.36, 133.33, 130.41, 126.85, 119.33, 106.35, 52.39, 17.55 ppm; UV/Vis (DMSO): λ_{max} (log ε) = 423 (5.79), 518 (4.37), 553 (4.12), 592 (3.87), 647 nm (3.83); HRMS (MALDI): *m/z* calcd. for $C_{100}H_{86}N_{12}O_8$ [M]: 1582.6692, 1582.6741 found.

5,10,15,20-((3-Methoxycarbonyl-5-(bromomethyl)phenyl)porphyrin, 7



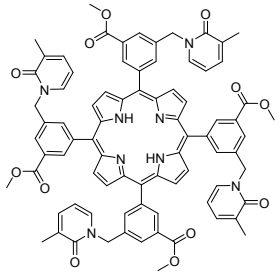
Compound **7** was synthesized in accordance with general procedure A using pyrrole (50 mg, 0.747 mmol), methyl 3-(bromomethyl)-5-formylbenzoate (193 mg, 0.747 mmol), DCM (75 mL), boron trifluoride diethyl etherate (9 µl, 10.5 mg, 7.47 × 10^{-5} mol) and DDQ (121 mg, 0.56 mmol) to yield a purple solid (96 mg, 42 %). M.p.= >300 °C; R_f = 0.4 (DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 8.81 (s, 12H), 8.51 (s, 4H), 8.43 (s, 4H), 4.80 (s, 8H), 3.99 (s, 12H), -2.83 (s, 2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.66, 142.81, 138.89, 137.14, 134.84, 129.70, 129.57 118.70, 32.44 ppm; UV/Vis (DCM): λ_{max} (log ε) = 421 (5.12), 516 (2.71), 550 (2.27), 590 (2.18), 645 nm (1.87); HRMS (MALDI): *m/z* calcd. for $C_{56}H_{42}Br_4N_4O_8$ [M]: 1213.9736, 1213.9762 found.

5,10,15,20-((3-Methoxycarbonyl-5-(pyridin-2(1H)-one)phenyl)porphyrin, 8



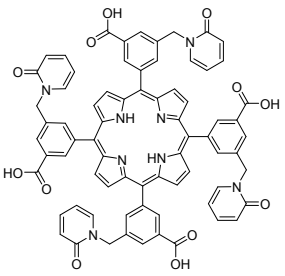
Compound **8** was synthesized in accordance with general procedure B using compound **7** (250 mg, 0.21 mmol), 2-hydroxypyridine (294 mg, 3.09 mmol), THF (100 mL) and NaH (123 mg, 60% in mineral oil, 3.09 mmol). The product was purified by recrystallization from MeOH and DCM to yield purple crystals (200 mg, 77 %). M.p. = >300 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 4H), 8.74 (d, *J* = 3.8 Hz, 8H), 8.39 (s, 4H), 8.30 (s, 4H), 7.51 (d, *J* = 5.7 Hz, 4H), 7.32 (t, *J* = 7.2 Hz, 4H), 6.62 (d, *J* = 9.1 Hz), 6.27 – 6.16 (m, 4H), 5.47 (s, 8H), 3.97 (s, 12H), -2.91 (s, 2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.85, 162.67, 142.78, 139.87, 137.71, 137.36, 135.69, 134.62, 129.58, 129.21, 128.45, 121.60, 106.74, 52.54, 52.18, 1.04 ppm; UV/Vis (DMSO): λ_{max} (log ε) = 421 (5.78), 515 (4.32), 552 (3.92), 591 (3.82), 643 nm (3.54); HRMS (MALDI): *m/z* calcd. for $C_{76}H_{58}N_8O_{12}$ [M]: 1274.4174, 1274.4174 found.

5,10,15,20-((3-Methoxycarbonyl-5-(methylpyridin-2(1H)-one)phenyl)porphyrin, 9



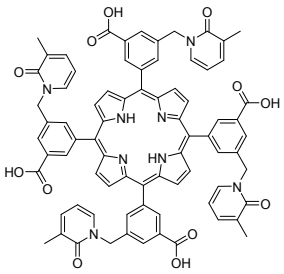
Compound **9** was synthesized in accordance with general procedure B using compound **7** (250 mg, 0.206 mmol), 3-methyl-1,2-dihydropyridin-2-one (337 mg, 3.09 mmol) THF (100 mL) and NaH (123 mg, 60 % in mineral oil, 3.09 mmol). The product was purified by recrystallization from MeOH and DCM to yield purple crystals (149 mg, 57 %). M.p. = >300 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δH = 8.79 (s, 4H), 8.74 (d, J = 5.6 Hz, 8H), 8.38 (s, 4H), 8.30 (s, 4H), 7.38 (d, J = 5.4 Hz, 4H), 7.19 (d, J = 6.8 Hz, 4H), 6.21 – 6.06 (m, 4H), 5.57 – 5.40 (m, 8H), 3.97 (d, J = 3.4 Hz, 12H), 2.14 (s, 12H), -2.91 (s, 2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.95, 166.81, 163.06, 143.06, 137.73, 137.03, 135.24, 134.40, 133.77, 130.58, 129.55, 128.50, 106.35, 84.24, 81.73, 52.56, 47.42, 17.42, 14.61 ppm; UV/Vis (DMSO): λ_{max} (log ε) = 421 (5.72), 517 (4.34), 551 (3.96), 591 (3.85), 646 nm (3.64); HRMS (MALDI): *m/z* calcd. for $C_{81}H_{66}N_8O_{12}$ [M+H]: 1331.4878, 1331.4871 found.

5,10,15,20-((3-Carboxy-5-((2-oxopyridin-1(2H)-yl)methyl)phenyl)porphyrin, P5



Compound **P5** was synthesized in accordance with general procedure C using compound **8** (100 mg, 0.08 mmol), THF (110 mL), KOH (1 g, 0.02 mol), methanol (20 mL) and water (7 mL) to yield a green solid (69 mg, 72 %). M.p = >300 °C; ^{1}H NMR (400 MHz, d6-DMSO) δ 8.81 (s, 8H), 8.57 (s, 4H), 8.19 (s, 8H), 8.01 (d, *J* = 5.1 Hz, 4H), 7.45 (t, *J* = 7.8 Hz, 4H), 6.47 (d, *J* = 8.8 Hz, 4H), 6.30 (s, 4H), 5.43 (s, 8H), -2.93 (s, 2H); UV/Vis (DMSO): λ_{max} (log ε) = 422 (5.48), 517 (4.65), 551 (3.39), 593 (3.30), 646 nm (3.23); HRMS (MALDI): *m/z* calcd. for $C_{73}H_{50}N_8O_{12}$ [M+H]: 1219.3626, 1219.3621 found.

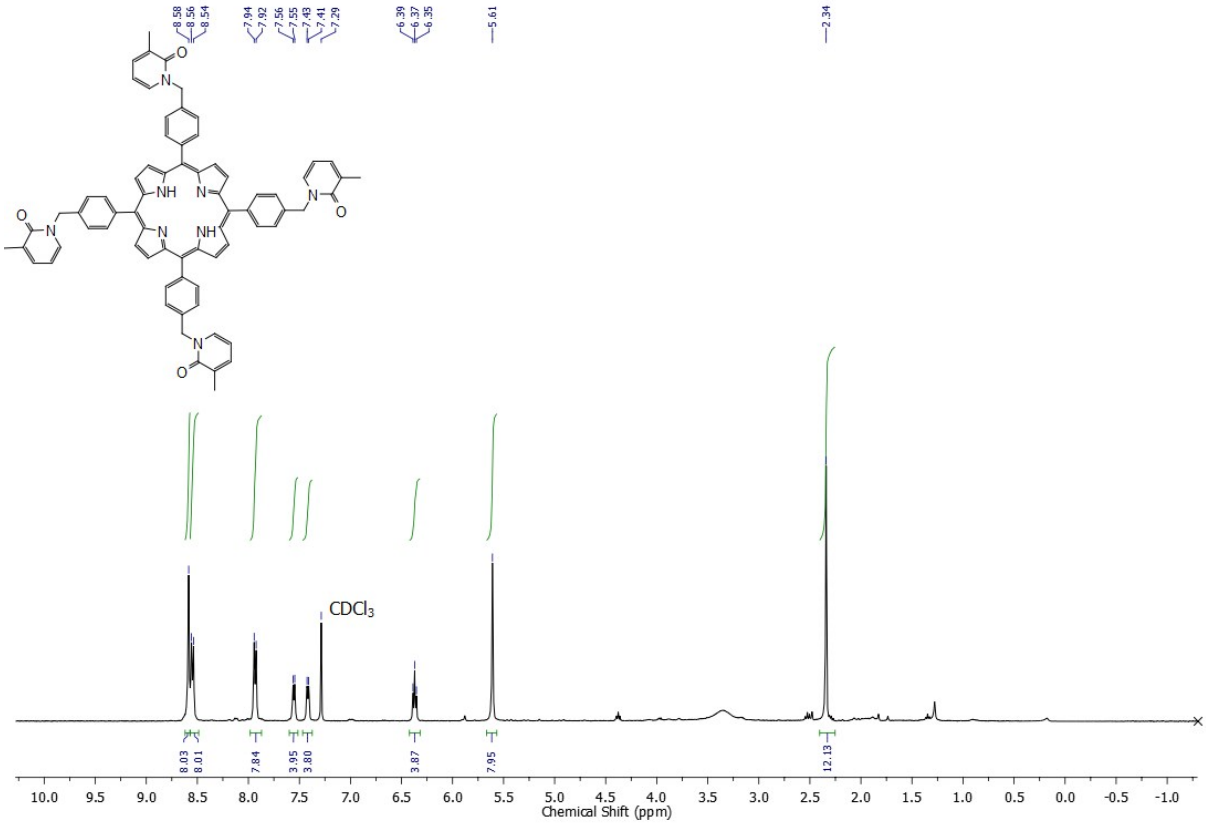
5,10,15,20-((3-Carboxy-5-((2-oxomethylpyridin-2(1H)-yl)methyl)phenyl)porphyrin, P6

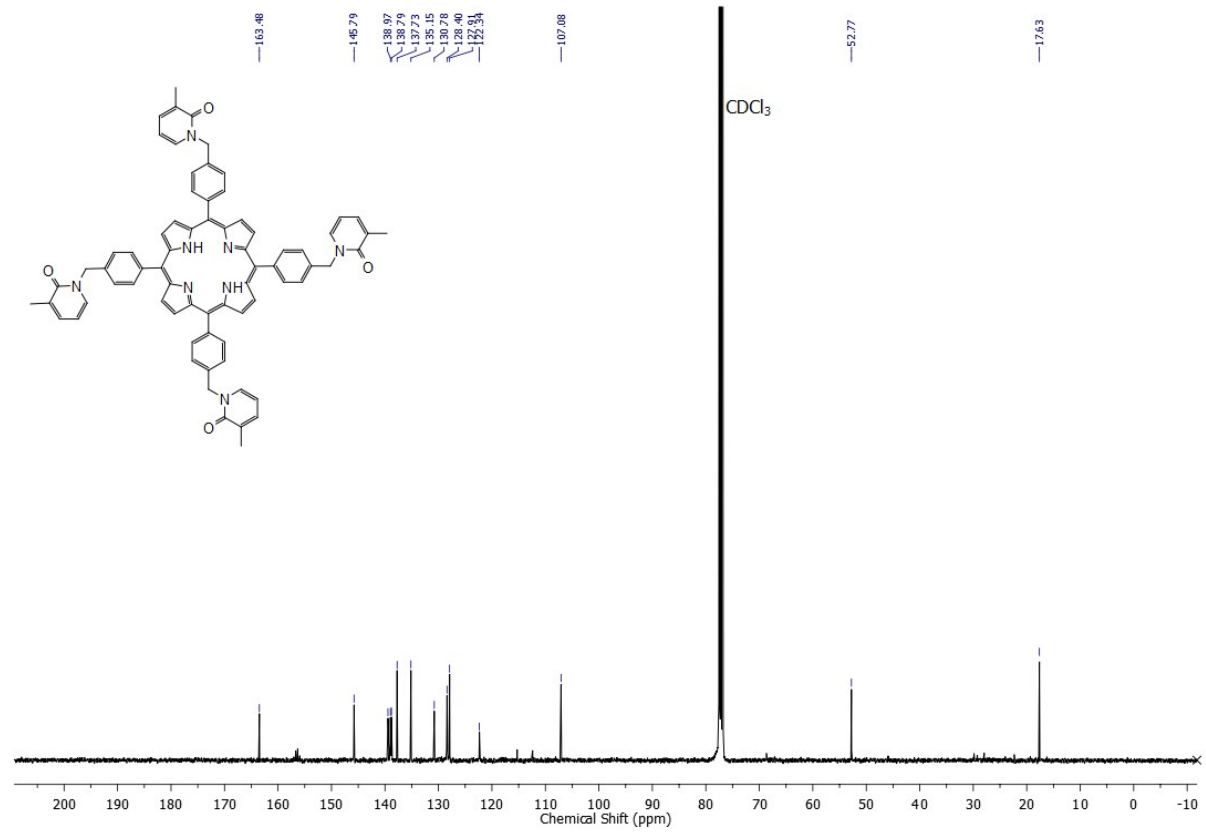


Compound **P6** was syntheized in accordance with general procedure C using compound **9** (100 mg, 7.52×10^{-5} mol), THF (80 mL), KOH (1 g, 0.02 mol), MeOH (20 mL) and water (7 mL) to yield a green solid (83 mg, 87 %). ^{1}H NMR (400 MHz, d^{6}-DMSO) δ 13.42 (s, br, 4H), 8.84 (s, 8H), 8.69-8.57 (m, 4H), 8.48-8.32 (m, 8H), 7.92 (d, J = 4.7 Hz, 4H), 7.42-7.27 (m, 4H), 6.29-6.15 (m, 4H), 5.51 (s, 8H), 2.03 (s, 12H), -2.97 (s, 2H) ppm; ^{13}C NMR (101 MHz, d^{6}-DMSO) δ 175.50, 167.27, 162.17, 141.42, 137.39, 136.66, 130.04, 128.62, 119.41, 119.07, 105.53, 68.78, 51.46, 48.64, 46.26, 42.16, 29.11, 27.35, 17.06 ppm; UV/Vis (DMSO): λ_{max} (log ε) = 422 (5.68), 518 (4.27), 553 (3.94), 592 (3.76), 647 nm (3.65); HRMS (MALDI): *m/z* calcd. for $C_{76}H_{58}N_8O_{12}$ [M]: 1274.4174, 1274.4205 found.

5. NMR and UV/Vis Spectra:

5.1 Characterization Spectra for Compound **P2**





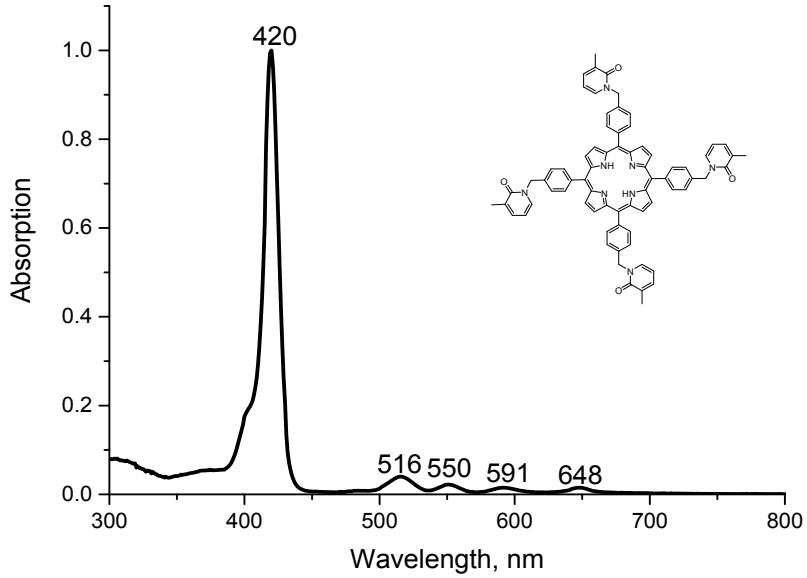
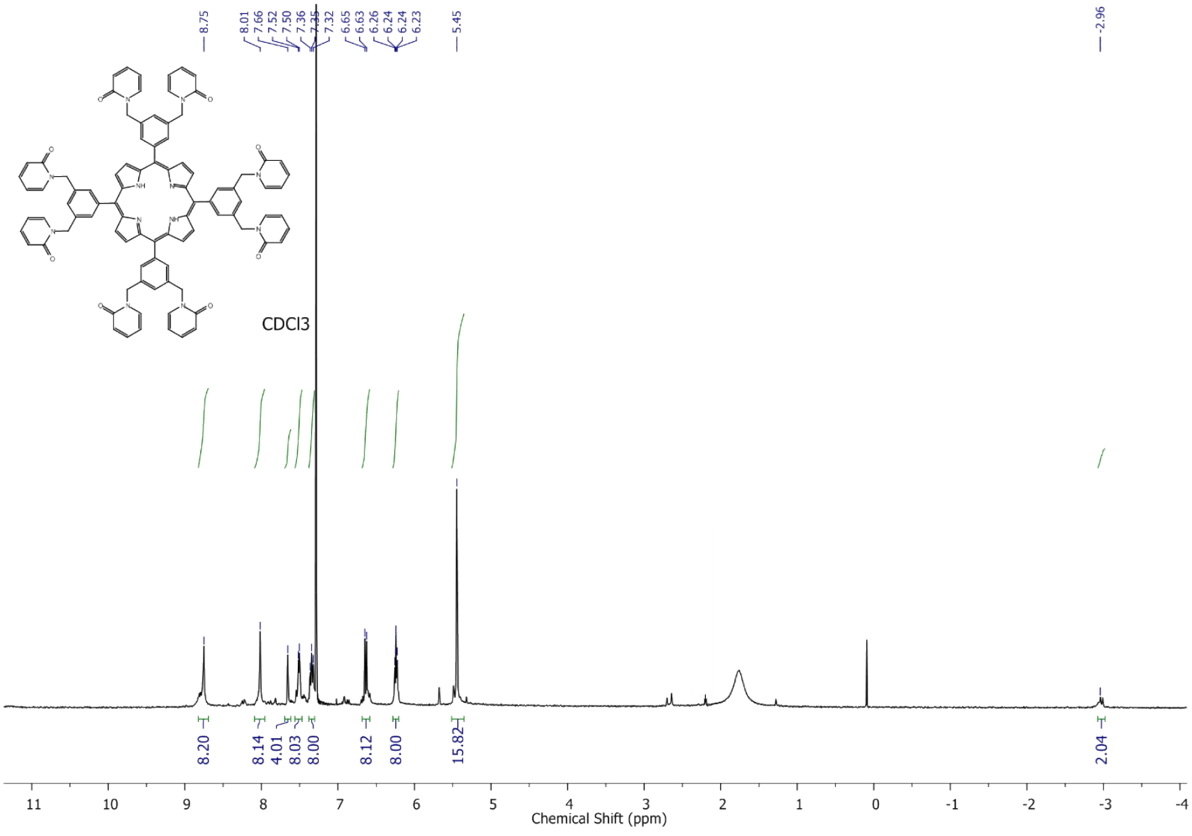


Figure S6: ^{1}H, ^{13}C NMR ($CDCl_3$) and UV/Vis spectra (DMSO) of compound **P2**.

5.2 Characterization Spectra for Compound **P3**



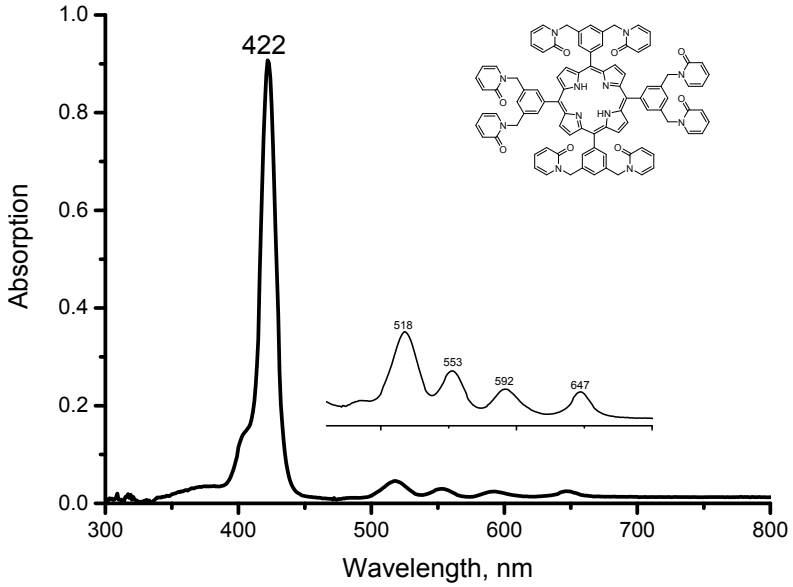
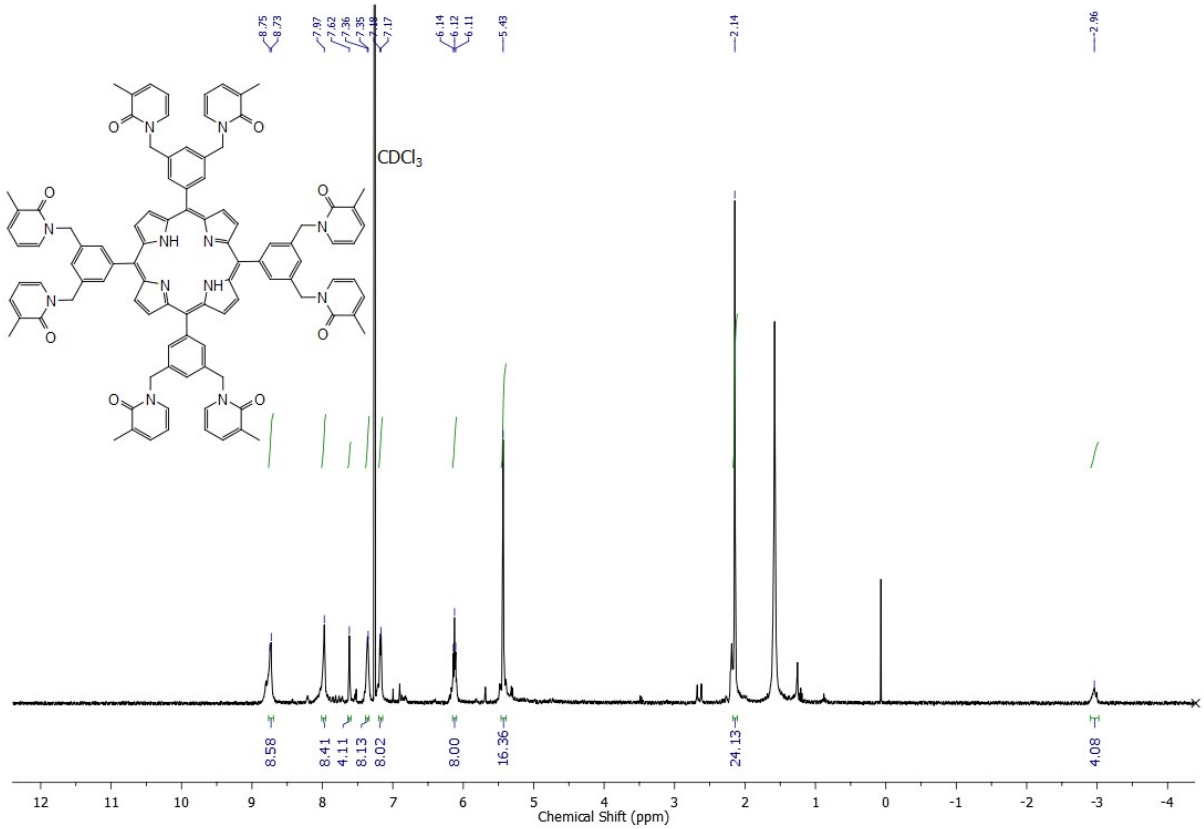
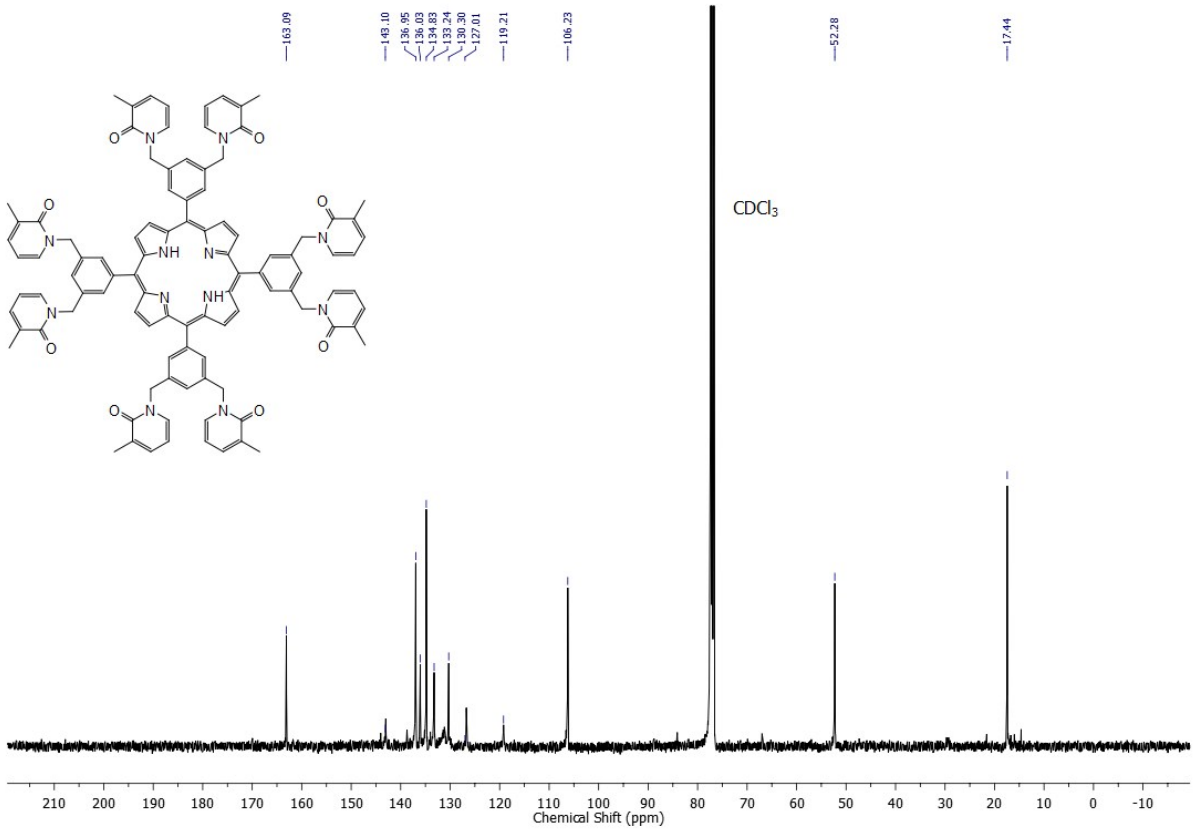


Figure S7: ^{1}H NMR ($CDCl_3$) and UV/Vis spectra (DMSO) of compound **P3**.

5.3 Characterization Spectra for Compound **P4**





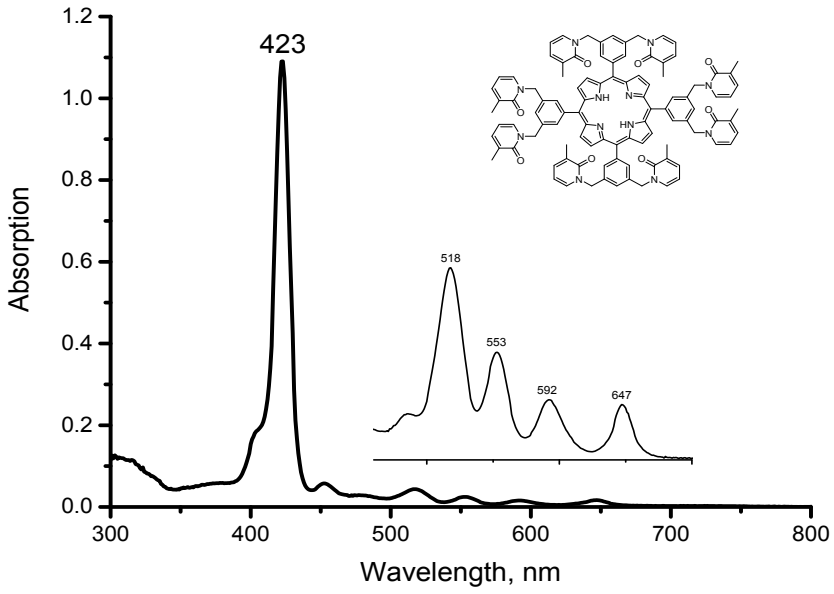
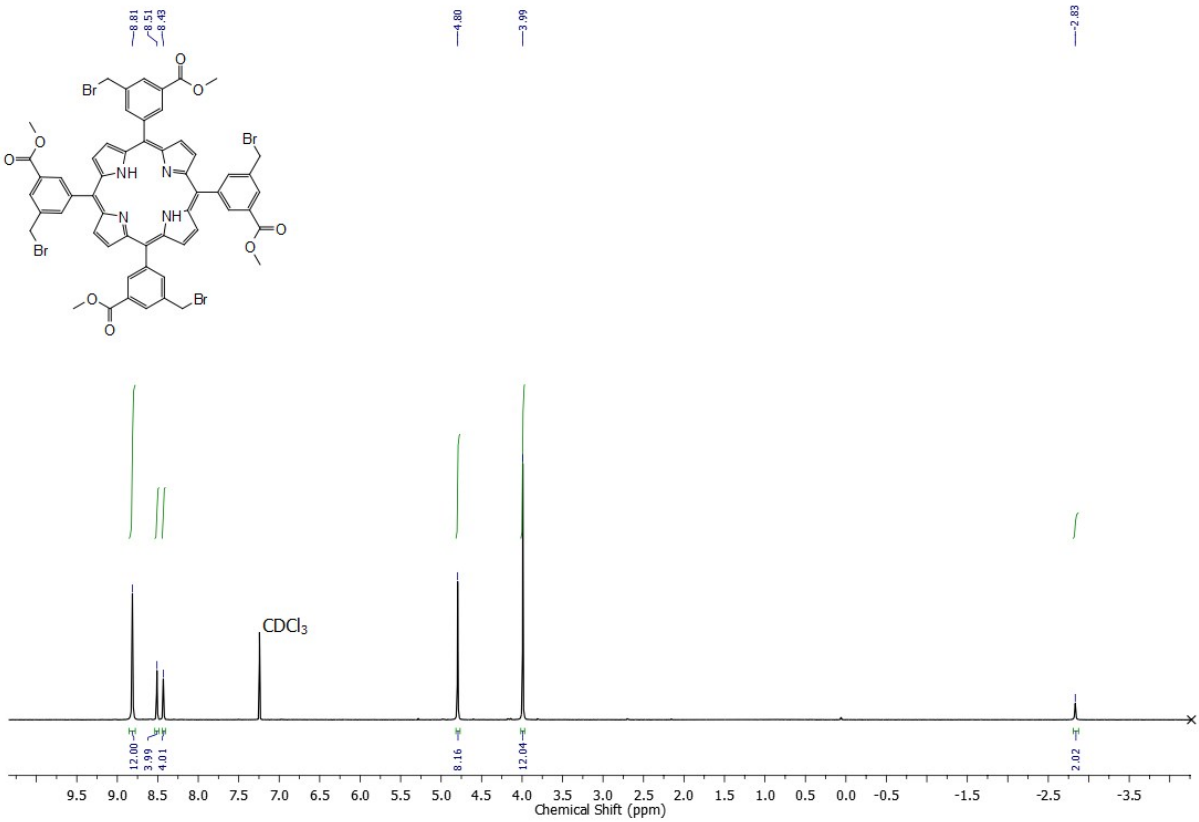
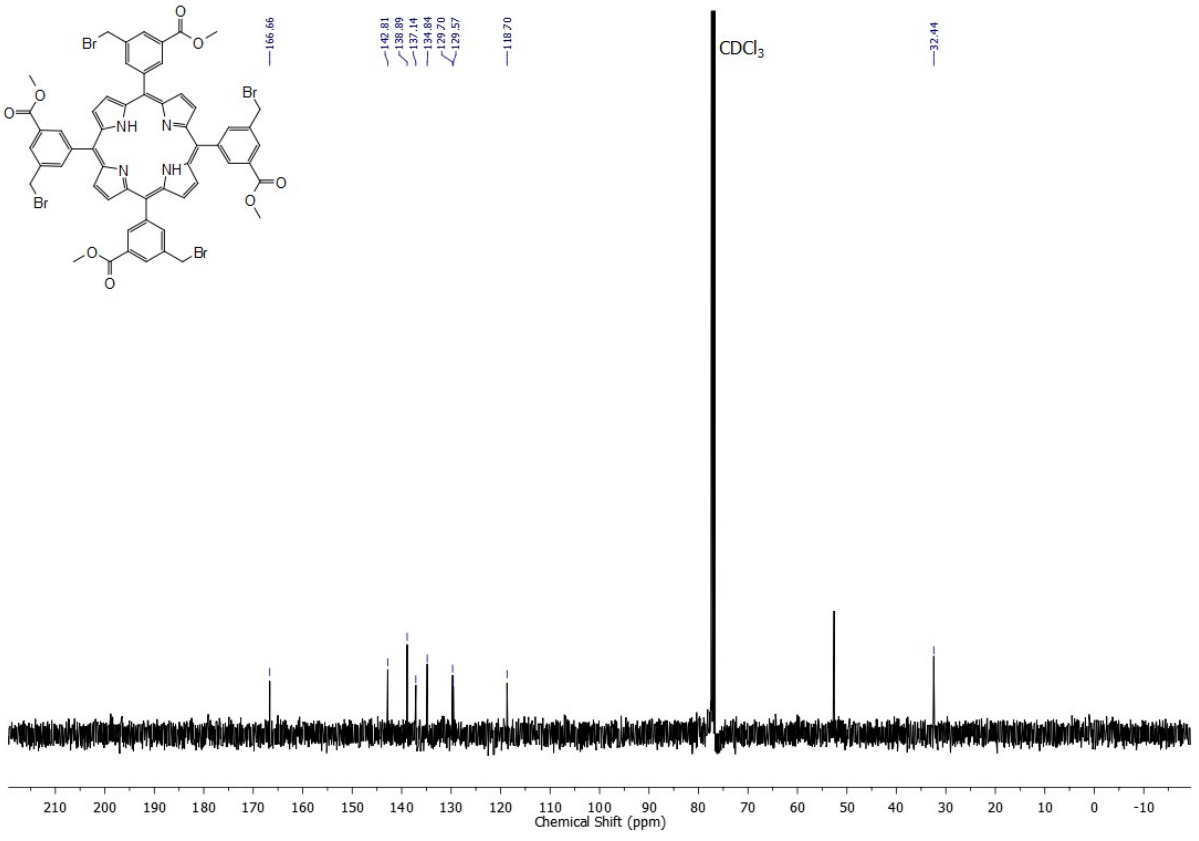


Figure S8: ^{1}H, ^{13}C NMR ($CDCl_3$) and UV/Vis spectra (DMSO) of compound **P4**.

5.4 Characterization Spectra for Compound **7**


8.81
8.51
8.49
4.80
3.99
2.83
Br
O
O
NH
N
N
NH
Br
Br
Br
CDCl3
12.00
3.99
4.01
8.16
12.04
2.02
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.5 -2.5 -3.5
Chemical Shift (ppm)


166.66
142.81
138.89
137.14
134.84
129.70
129.57
118.70
CDCl3
32.44
Br
O
O
NH
N
N
NH
Br
Br
Br
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
Chemical Shift (ppm)

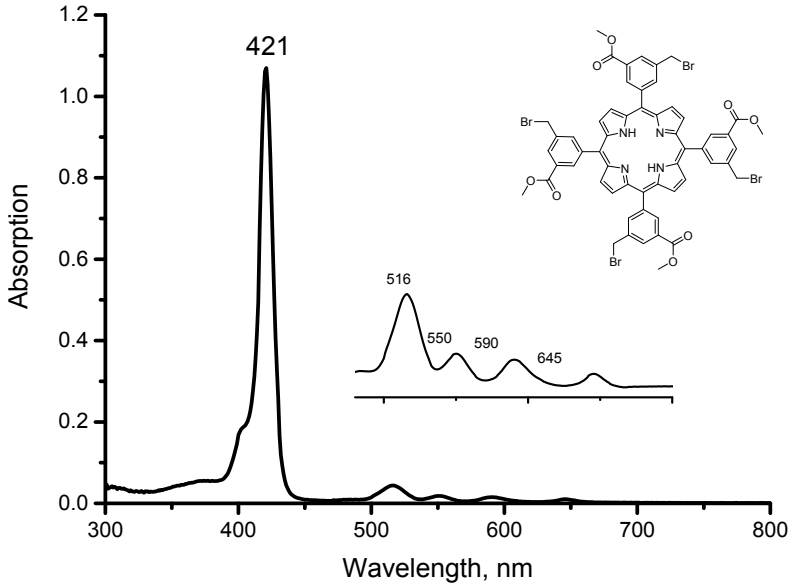
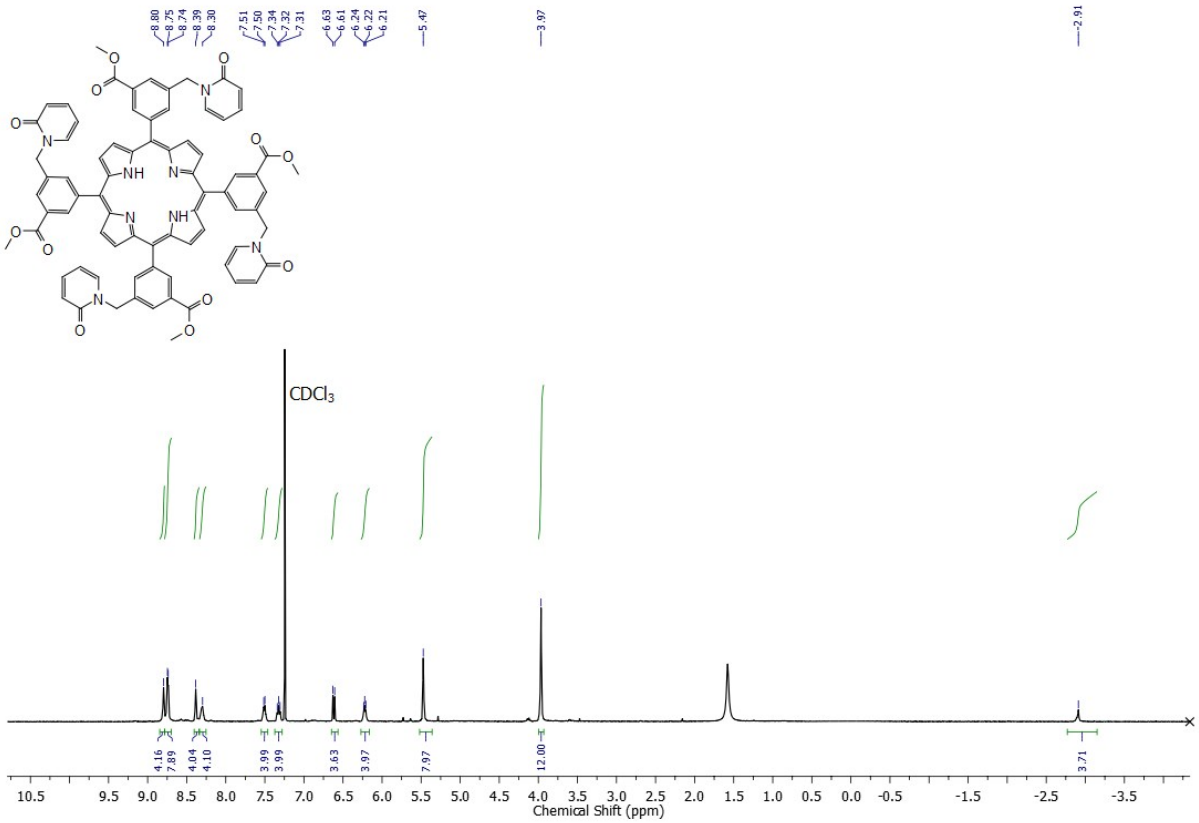
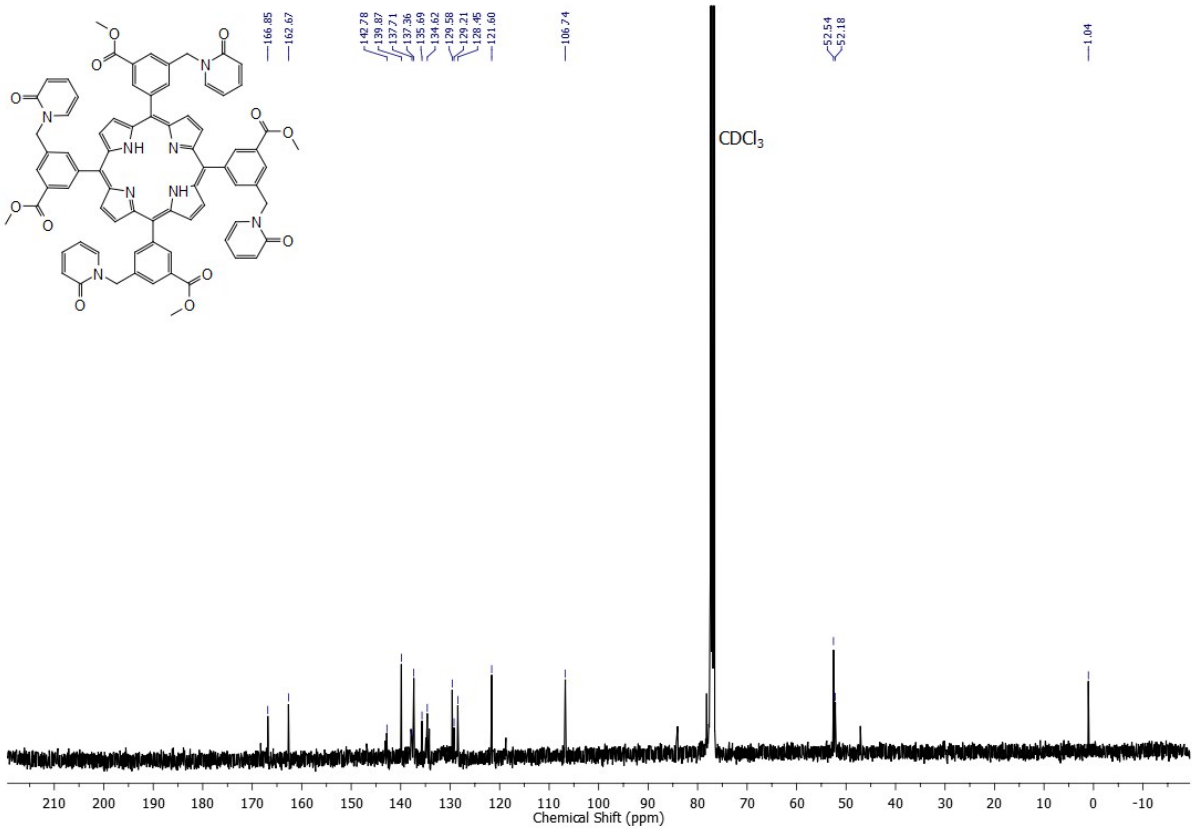


Figure S9: ^{1}H, ^{13}C NMR ($CDCl_3$) and UV/Vis spectra (DMSO) of compound **7**.

5.5 Characterization Spectra for Compound **8**





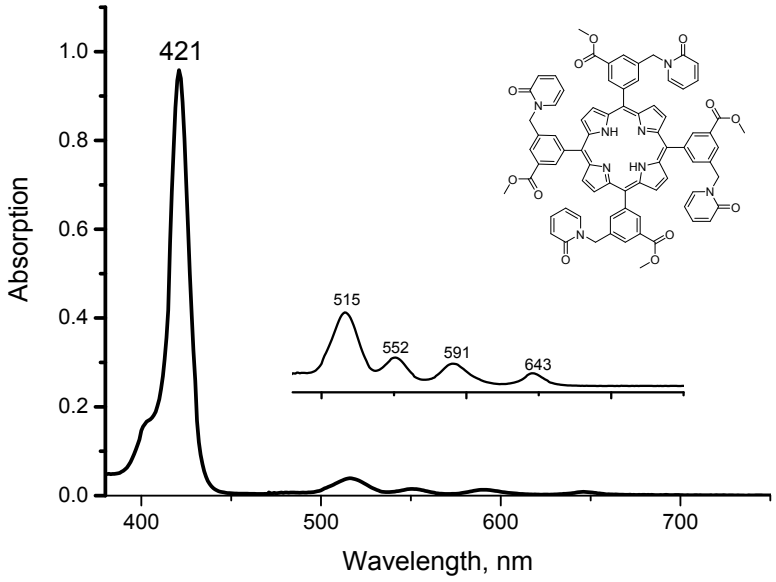
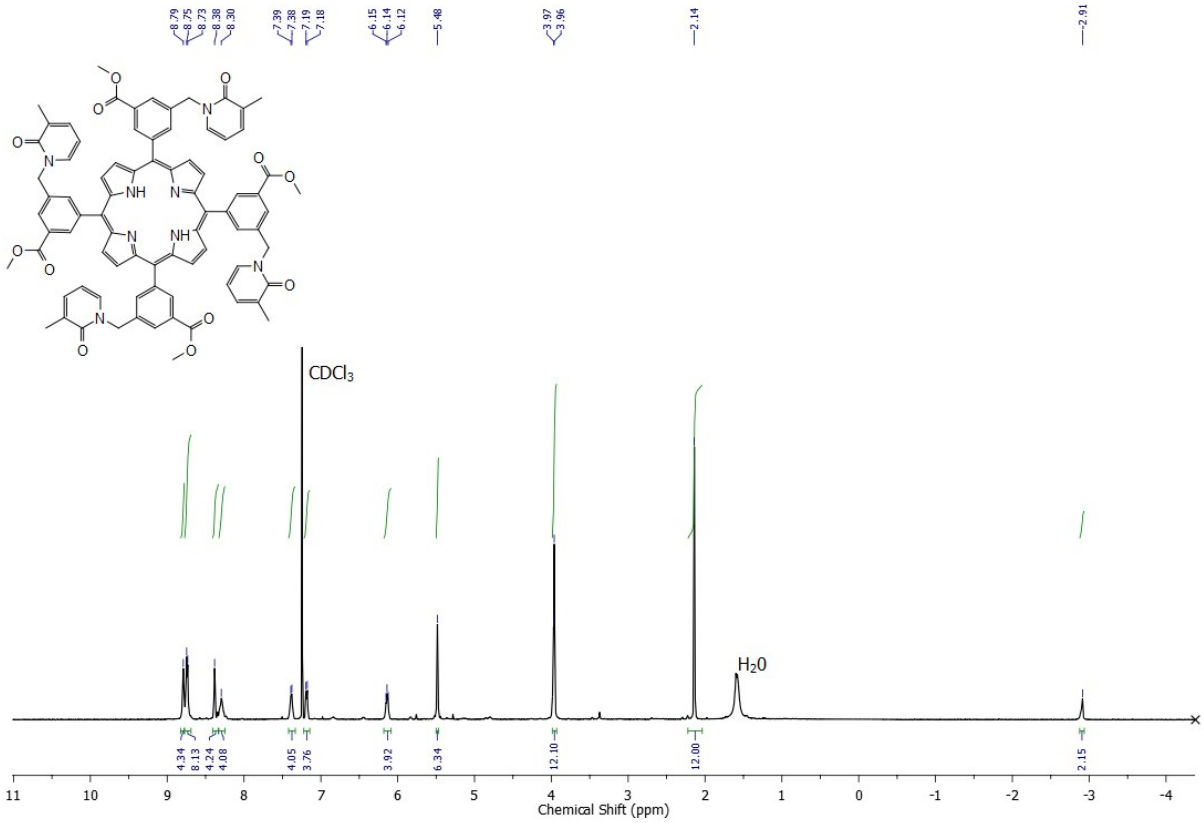
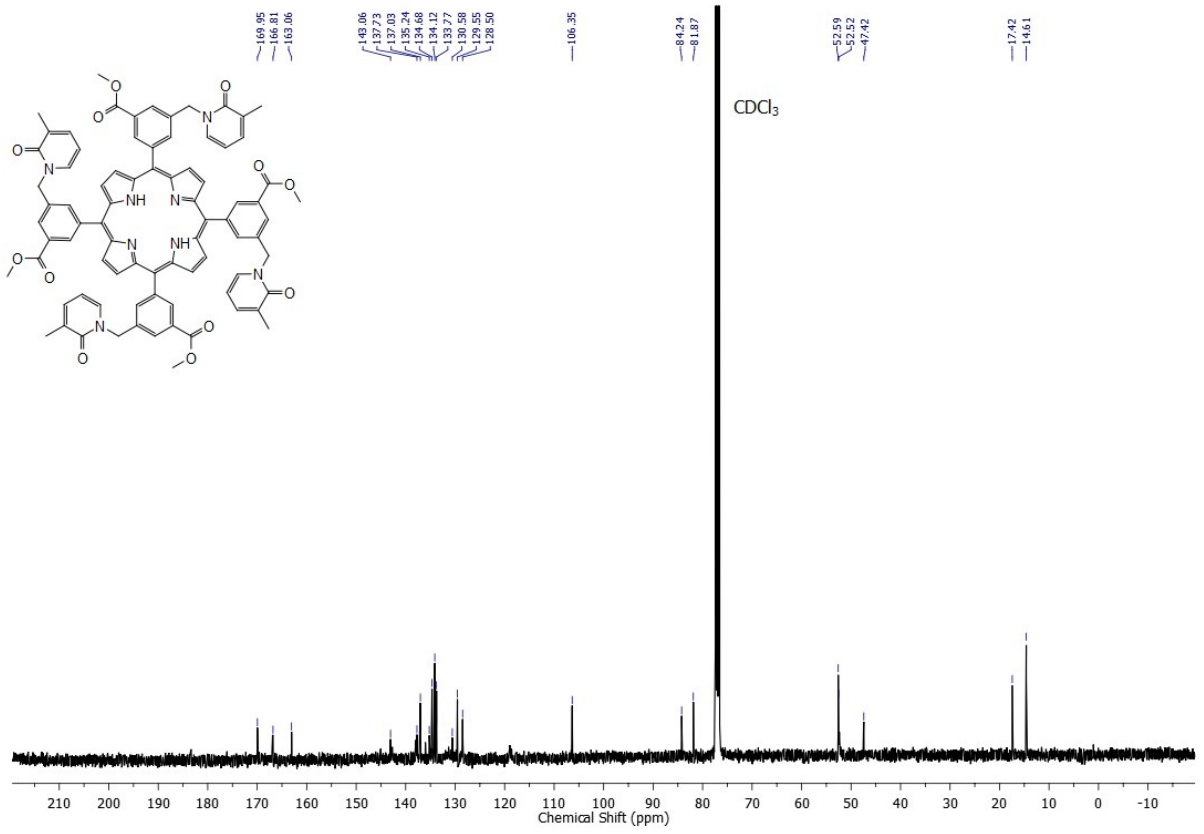


Figure S10: ^{1}H, ^{13}C NMR ($CDCl_3$) and UV/Vis spectra (DMSO) of compound **8**.

5.6 Characterization Spectra for Compound **9**





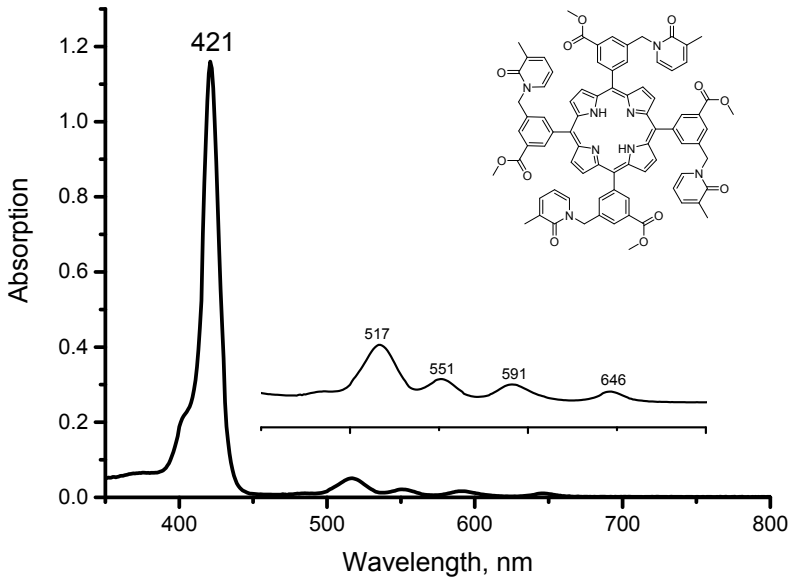
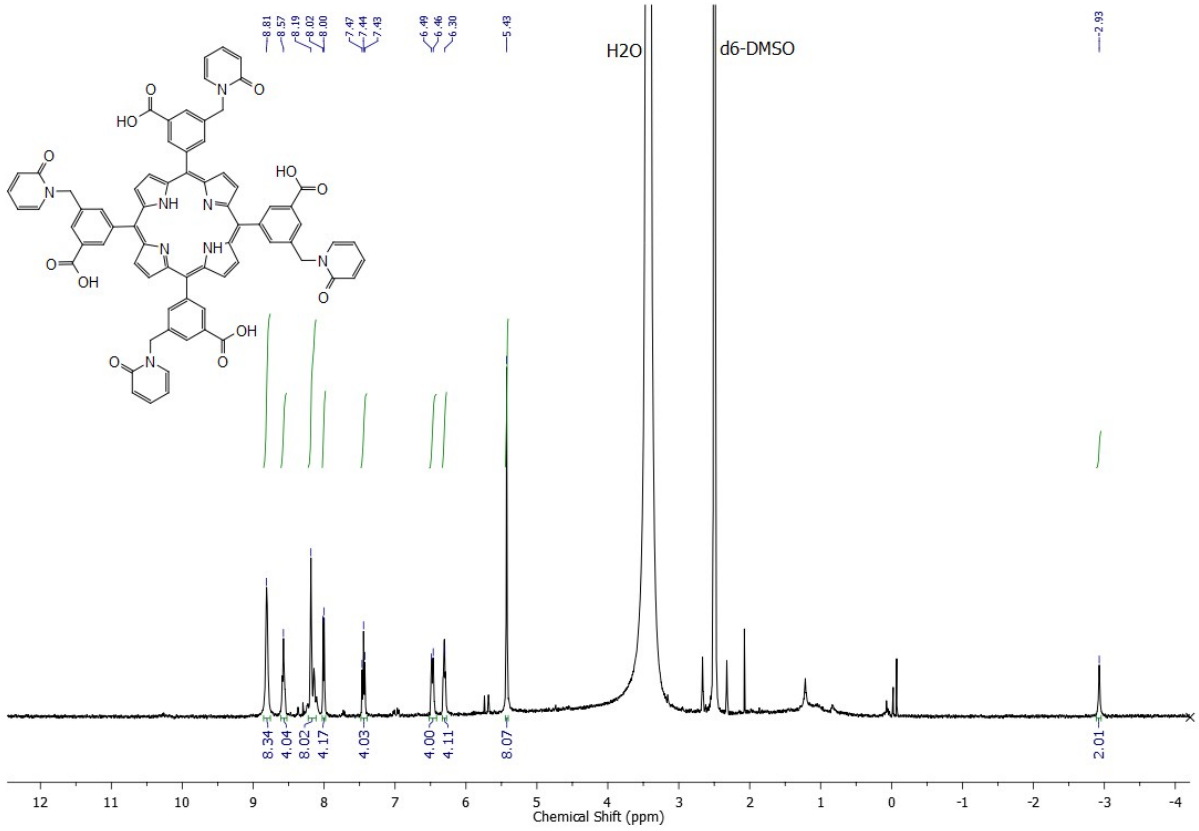
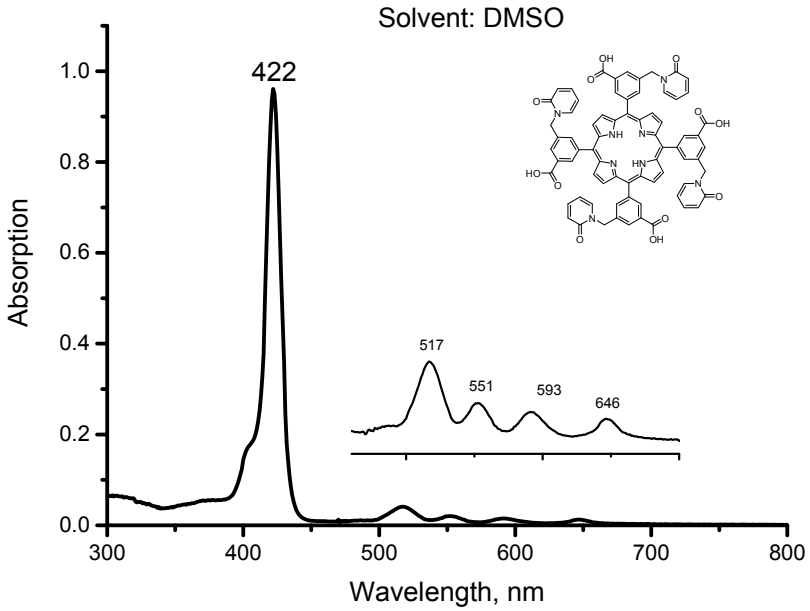


Figure S11: ^{1}H, ^{13}C NMR ($CDCl_3$) and UV/Vis spectra (DMSO) of compound **9**.

5.7 Characterization Spectra for Compound **P5**





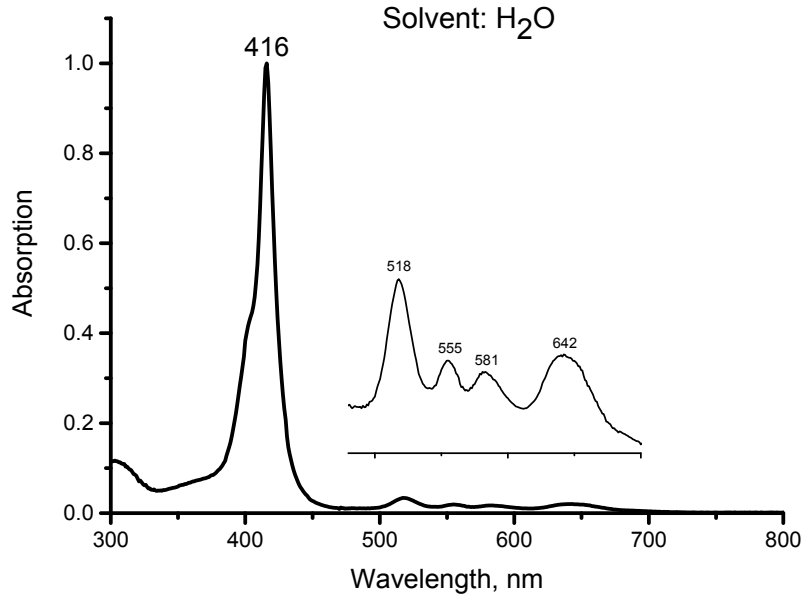
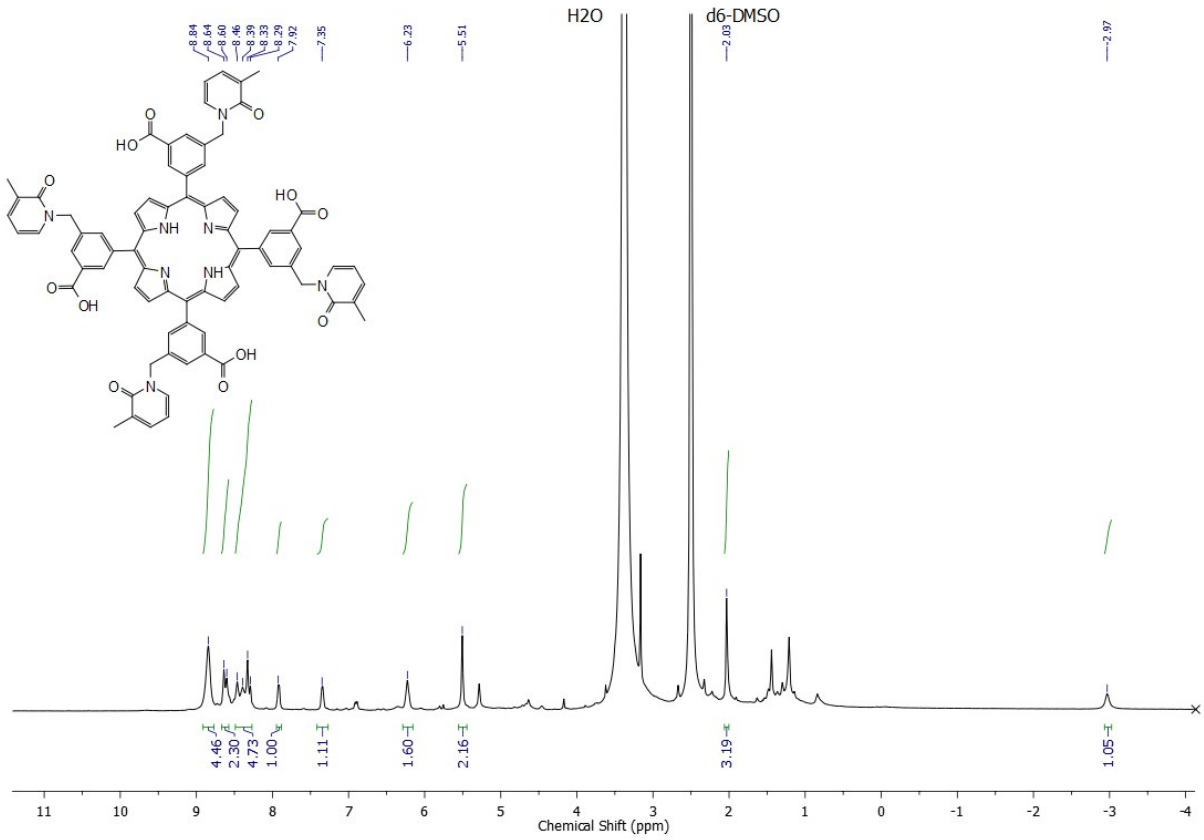
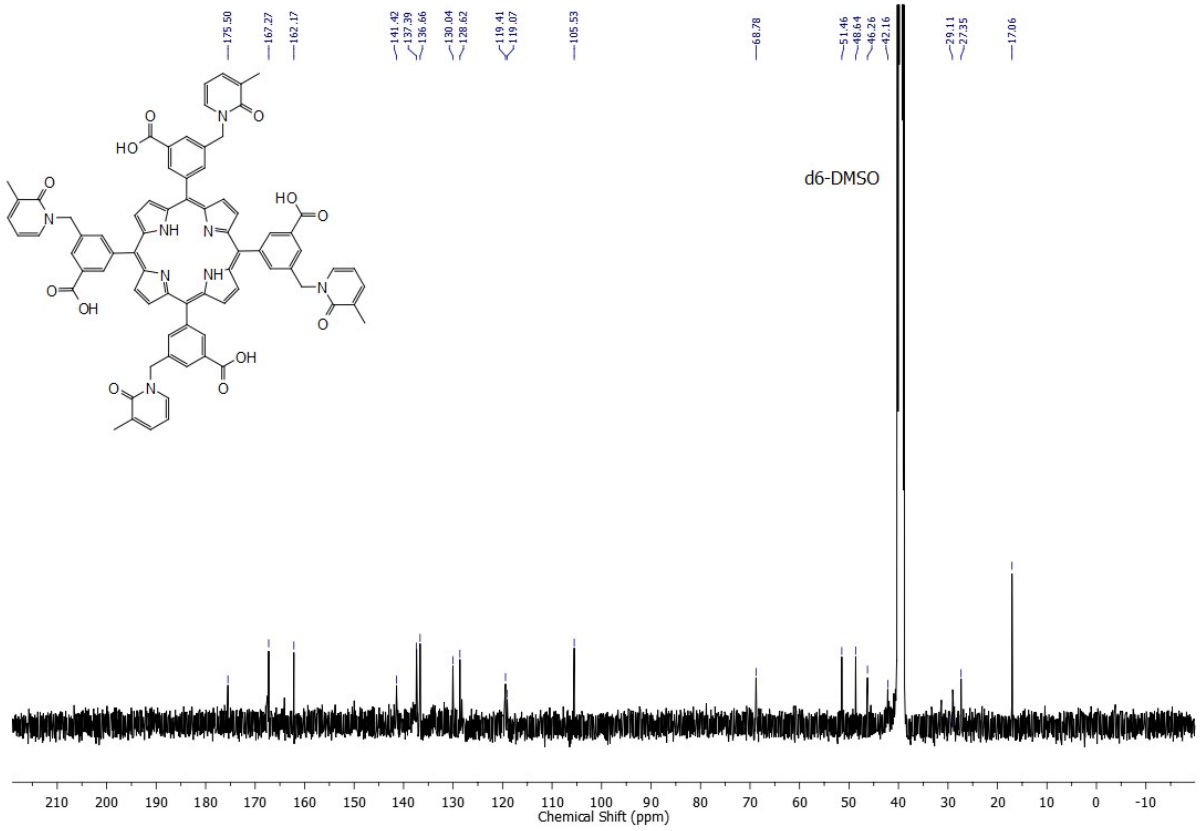


Figure S12: ^{1}H NMR ($CDCl_3$) and UV/Vis spectra in (DMSO and water) of compound **P5**.

5.8 Characterization Spectra for Compound **P6**





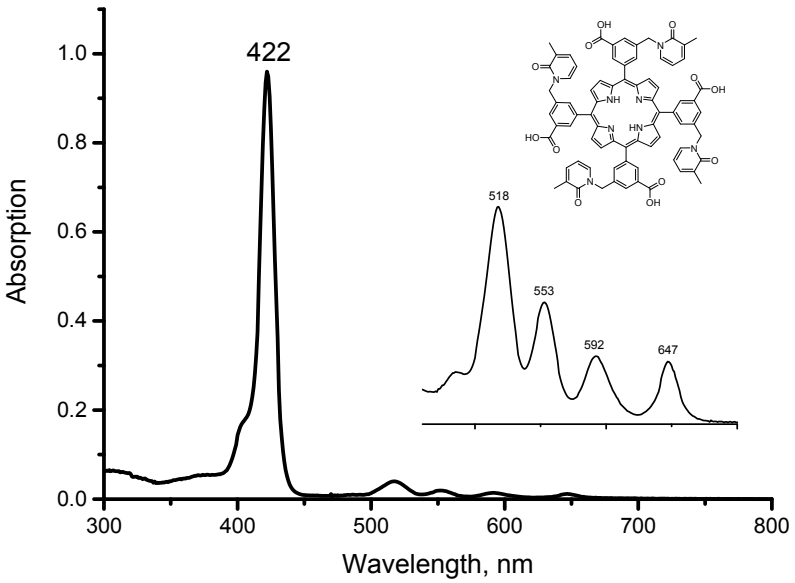


Figure S13: ^{1}H, ^{13}C NMR ($CDCl_3$) and UV/Vis spectra (DMSO) of compound **P6**.

6. References:

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