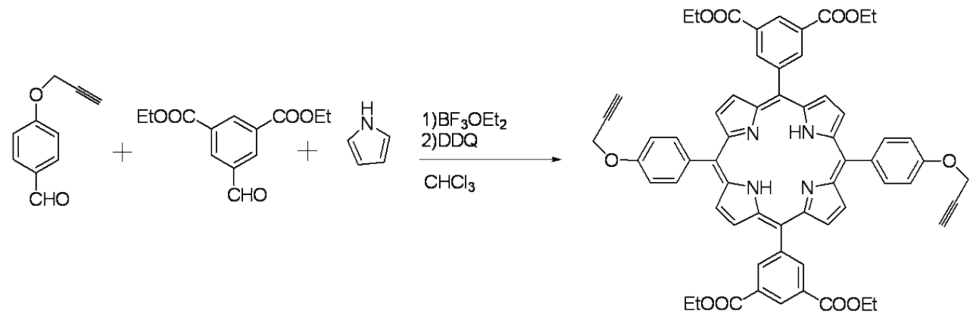
Supporting Information

1. General Experimental.

Unless specifically mentioned, all chemicals were obtained from Sigma-Aldrich or Acros Organics and the solvents were purchased from Fischer Scientific. Poly (propylene glycol) bis(2-aminopropyl ether) (CAS Registry # 9046-10-0) was obtained from Sigma-Aldrich Company. 0.45µm ultracleaning syringe filter units (mixed esters of cellulose membrane) were obtained from Fisher Scientific. NMR spectra were recorded on either a Varian 300MHz or 400 MHz spectrometer in $CDCl_3$ solvent (unless otherwise specified) and chemical shifts are reported in ppm and referenced to the residual solvent peaks at 7.26 ppm for ^{1}H NMR or at 77.23 ppm for ^{13}C NMR. High-resolution mass spectra was performed at the Department of Chemistry, Indiana University. MALDI-TOF spectra were recorded on a Bruker Autoflex3 Matrix Assisted Laser Desorption Ionization-Time of Flight Mass Spectrometer (MALDITOF MS), using α-cyano-4-hydroxycinnamic acid or 2, 5-dihydroxybenzoic acid (DHB) matrices. UV-vis spectra were obtained using a Hewlett Packard 8452A Diode Array Spectrophotometer. Fluorescence spectra were recorded on a Varian Cary Eclipse Fluorescence Spectrophotometer. TEM experiments were performed on a Joel 2011

Transmission Electron Microscope Instrument (accelerating voltage=120 kV). SEM measurements were recorded on Hitachi 4800 Scanning Electron Microscope (accelerating voltage=3.0 kV). The SEM samples were prepared by placing a drop of aqueous solution containing porphyrin NSs onto gold coated glass slides (1cm×1cm, Platypus Technologies), followed by evaporation of aqueous solution in air. Dynamic light scattering (DLS) was measured using a Brookhaven 90-Plus detector (l=670 nm) operating at a scattering angle of 90^{o}, at room temperature. Particle hydrodynamic diameter, D_h (the intensity-weighted average diameter) was determined based on the Stokes-Einstein relation for hydrodynamic radius derived from the intensity autocorrelation function, expanded in terms of cumulants. Singlet oxygen emission experiments were performed using a PTI quanta master fluorimeter equipped with a 75 W Xe lamp, and an InGaAs detector, which is thermo electrically cooled, equipped with a lock-in amplifier. A 1000 nm long-pass filter was placed before the detector.

2. Synthesis

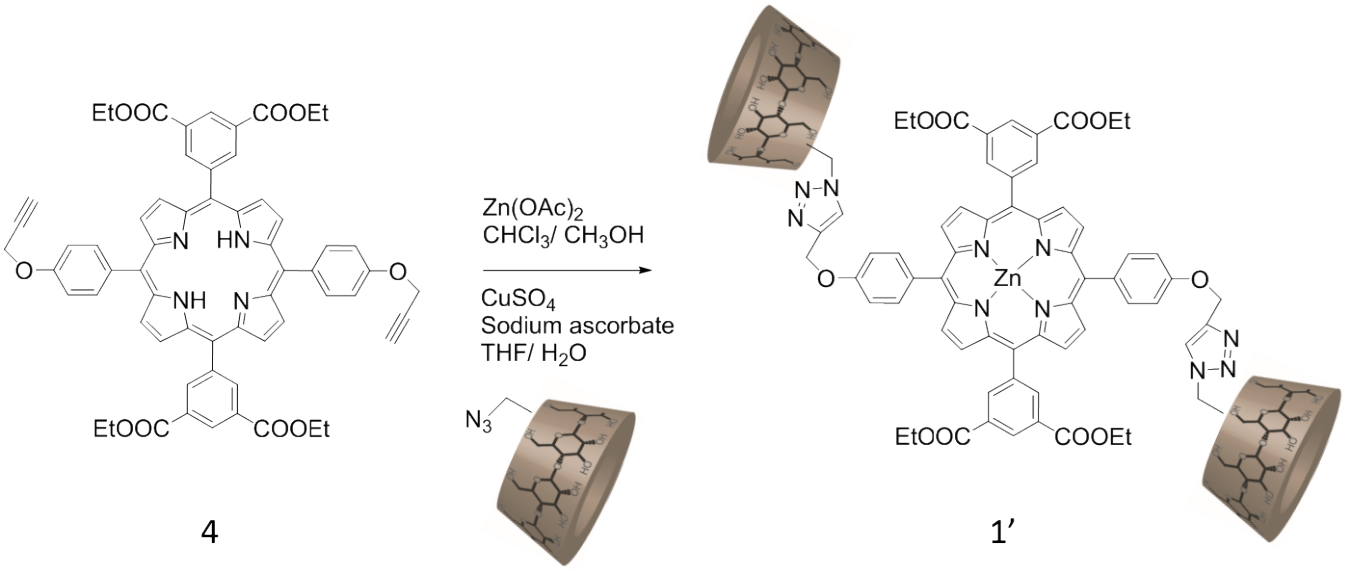


4

Synthesis of 5,15-Bis(3,5-diethoxycarbonylphenyl)-10,20-bis(4-propargyloxyphenyl)porphyrin (4)

$BF_3.O(Et)_2$ (132 µl of 2.5 M stock solution in $CHCl_3$, 0.33mmol) was added to a solution of 5-formyl-isophthalic acid diethyl ester (125 mg, 0.5 mmol), 4-propargyloxybenzaldehyde (80 mg, 0.5 mmol), and pyrrole (67 mg, 1 mmol) in $CHCl_3$ (100 mL) under argon. The reaction mixture was stirred for 1h, followed by the addition of 2, 3-dichloro-5, 6-dicyano-1, 4-benzoquinone (DDQ) (700 mg, 3.08 mmol). After the mixture was stirred for another 1h, the solvents were evaporated under *vacuo* and the residue was purified by column chromatography using dichloromethane/hexanes (1:2) as the eluent. The second

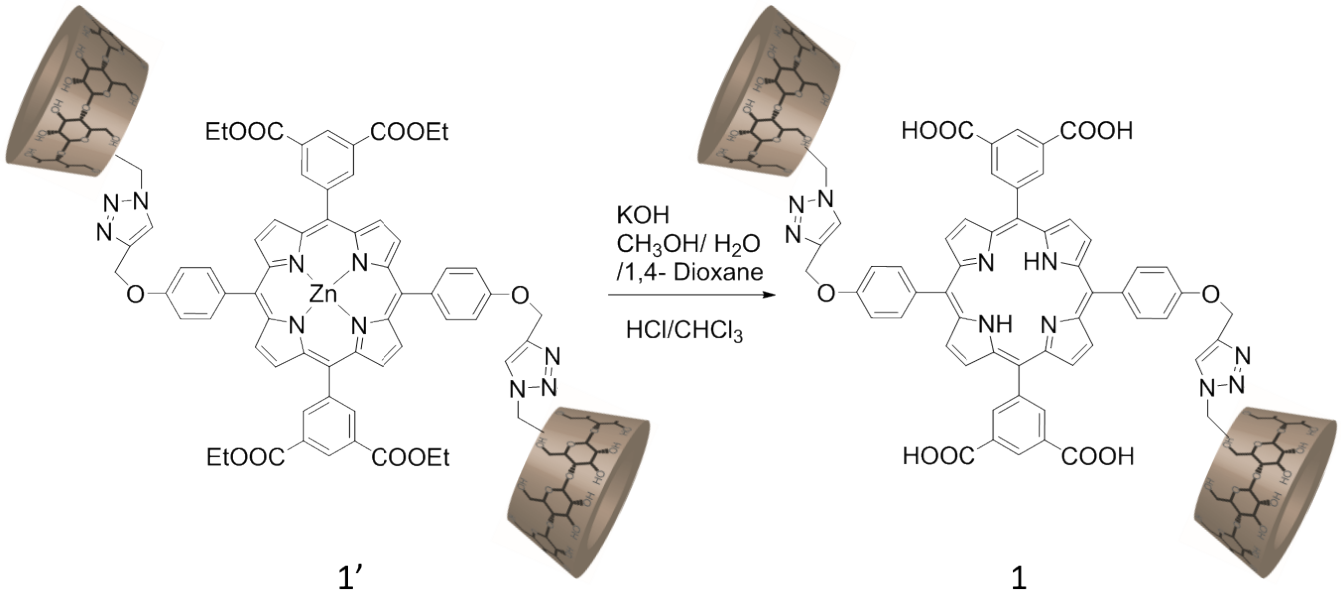
fraction was collected to give porphyrin **4** as a purple solid (10 mg, 4 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ= -2.75(s, 2H, NH), 1.44 (t, 12H, *J* = 7.1 Hz, $CO_2CH_2C\mathbf{H_3}$), 2.70 (s, 2H), 4.50 (q, 8H, $CO_2C\mathbf{H_2}CH_3$, *J* = 7.1 Hz), 4.99 (s, 4H), 7.38 (d, 4H, phenyl *J* = 8.4 Hz), 8.15 (d, 4H, phenyl *J* = 8.4 Hz), 8.75 (d, 4H, pyrrole *J* = 4.8 Hz), 8.93 (d, 4H, pyrrole *J* = 4.8 Hz), 9.08 (s, 4H, phenyl), 9.16 (s, 2H, phenyl). ^{13}C NMR (75 MHz, $CDCl_3$): δ= 14.5, 56.4, 61.8, 76.0, 78.8, 113.4, 117.9, 120.5, 129.5, 129.8, 129.9, 130.3, 135.2, 135.7, 138.4, 143.1, 157.8, 166.2. MALDI-TOF MS: m/z = 1011.4 $[M+H]^+$, Calcd for $C_{62}H_{51}N_4O_{10}$ (1011.4). HR: ESI-TOF MS: m/z = 1011.3580 $[M+H]^+$, Calcd for $C_{62}H_{51}N_4O_{10}$ (1011.3605). UV-vis (CH_2Cl_2): 422 (ε 511 500 dm^3 mol^{-1} cm^{-1}), 516 (13 500), 550 (20 500), 590 (14 100), 647 (9900).



Synthesis of porphyrin 1'.

To a solution of porphyrin **4** (100 mg, 0.099 mmol) in chloroform (30 mL), was added a solution of zinc acetate (0.216 g, 0.99 mmol) in methanol (3 mL). The mixture was stirred at room temperature for 3 h and then was washed with water three times and dried over anhydrous $MgSO_4$. The solvent was then removed under reduced pressure and the resultant compound was dissolved in THF (20 ml). To this solution was added 6'-azido-6'-deoxy-permethyl-β-cyclodextrin[1] (427 mg, 0.3 mmol; i.e., 1.5 eq. per each alkyne group) and sodium ascorbate (19.8 mg, 0.1 mmol). $CuSO_4$ (5 mg, 0.02 mmol) was dissolved in water (1mL) and was added to the reaction. The reaction vessel was then charged with argon, sealed, and left to stir at 40 ºC for

48h. Subsequently, the solvents were removed *in vacuo* and the crude product was dissolved in $CHCl_3$ and washed with water three times (3×20ml) and dried over anhydrous $MgSO_4$. The solvent was them removed under reduced pressure, and resultant compound was purified via flash chromatography using chloroform: methanol (30:1) eluent to afford porphyrin **1'** as a purple solid. (257 mg, *65%).* Further chromatography via Bio-beads SEC (size exclusion chromatography) in THF gave the purified product (120 mg, 32%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.41 (t, 12H, $CO_2CH_2C\mathbf{H_3}$, *J* = 7.1 Hz), 3.19-4.03 (per-*O*Me-β-CD), 4.48 (q, 8H, $CO_2C\mathbf{H_2}CH_3$, *J* = 7.1 Hz), 5.13-5.31(per-*O*Me-β-CD), 5.43(s, 4H), 7.36 (d, 4H, phenyl, *J* = 8.4 Hz), 7.93 (s, 2H, triazole), 8.13 (d, 4H, phenyl, *J* = 8.4 Hz), 8.81 (d, 4H, pyrrole, *J* = 4.8 Hz), 8.98(d, 4H, pyrrole, *J* = 4.8 Hz), 9.04(s, 4H, phenyl), 9.13 (s, 2H, phenyl). MALDI-TOF MS: m/z = 3951.6 $[M]^+$, Calcd for $C_{186}H_{266}N_{10}O_{78}Zn$ (3951.6). UV-vis (CH_2Cl_2): 422 (ε 559 000 dm^3 mol^{-1} cm^{-1}), 550 (23 800), 590 (9000).

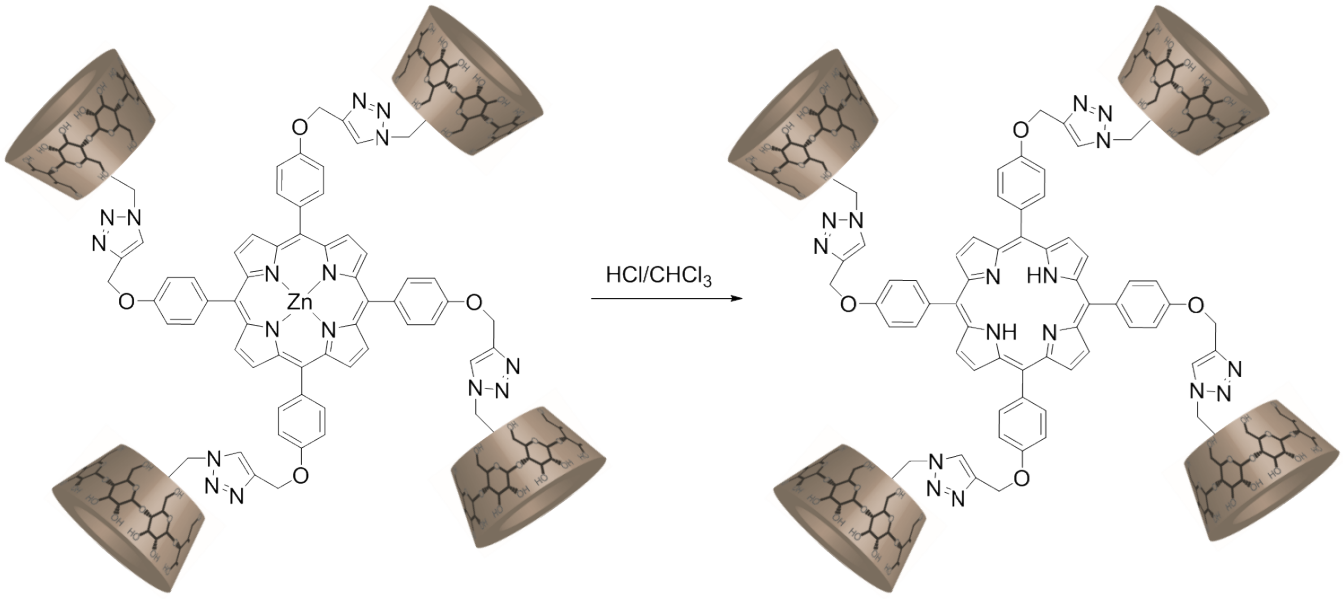


1′ 1

Synthesis of porphyrin 1.

A solution of porphyrin **1'** (50 mg, 0.0126 mmol) and KOH (0.4 g, 7.14 mmol) in a mixed solvent of water (10 mL), methanol (30 mL), and dioxane (10 mL) was refluxed for 12 h. The organic solvent were evaporated and the aqueous residue was acidified to pH 1 with hydrochloric acid. The green clouds aqueous solution was extracted using $CHCl_3$ (100 mL) and the organic layer was washed with water (3 × 100 mL).

The solvent was then removed under reduced pressure and afforded a purple solid. ^{1}H NMR (300 MHz, water suppression, 0.1 M phosphate buffer (D_2O) pH = 7.0): δ = 0.6-5.58 (per-*O*Me-β-CD), 6.97 (d, phenyl), 7.16 (s, triazole), 7.77 (d, phenyl), 7.95-8.4 (m, pyrrole), 8.58 (s, phenyl), 8.79 (s, phenyl). MALDI-TOF MS: m/z = 3778.6 $[M+H]^+$, Calcd for $C_{178}H_{253}N_{10}O_{78}$ (3778.6). UV-vis (H_2O): 418 (ε 190 600 dm^3 mol^{-1} cm^{-1}), 515 (17 400), 546 (11 600), 588 (9500), 645 (8000).



5 2

Synthesis of porphyrin 2.

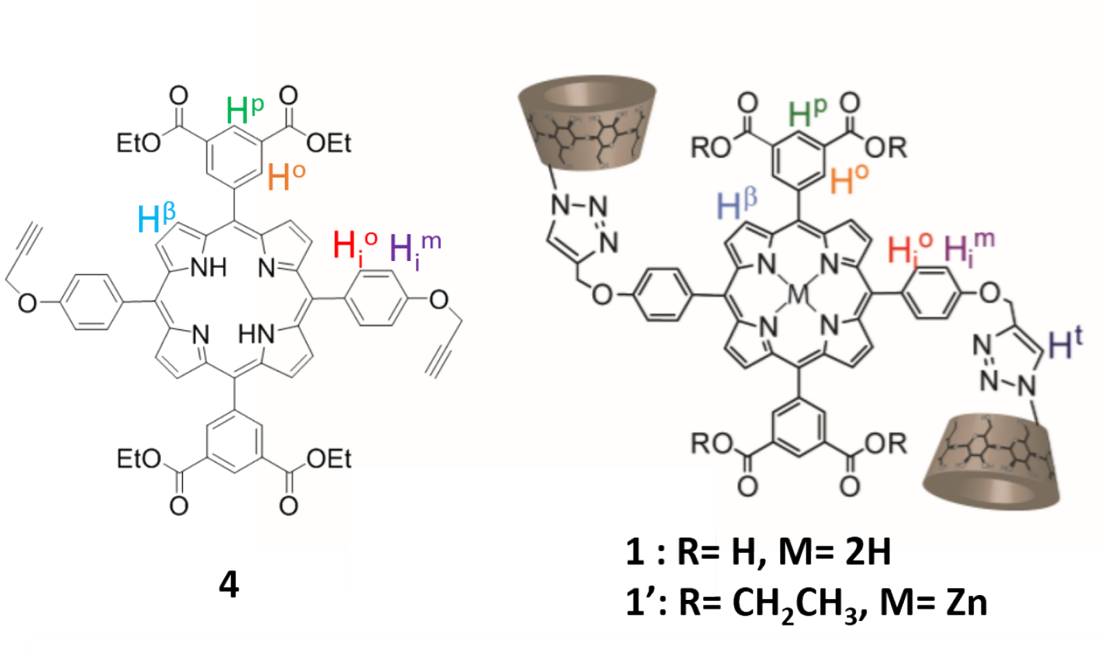
Four drops of concentrated HCl was added into a solution of **5**[2] (66 mg, 0.01 mmol) in 100 mL chloroform. The reaction mixture was stirred for 10 min and then was neutralized with triethylamine. After washing with saturated sodium bicarbonate, the organic layer was dried over anhydrous Na_2SO_4. The solvent was removed under *vacuo* to give porphyrin **2** as a purple solid (63 mg, 96%). ^{1}H NMR (400 MHz, $CDCl_3$) -2.78 (s, 2H), 3.09-3.95 (per-*O*Me-β-CD), 5.07-5.35 (per-*O*Me-β-CD), 5.46 (s, 8H), 7.37 (d, phenyl, *J* = 8.4 Hz, 8H), 7.95 (s, triazole, 4H), 8.13 (d, phenyl, *J* = 8.4 Hz, 8H), 8.84 (s, pyrrole, 8H). MALDI-TOF MS: m/z = 6590.3 $[M+H]^+$, Calcd for $C_{304}H_{475}N_{16}O_{140}$ (6590.1). UV-vis (CH_2Cl_2): 421 (ε 583 600 dm^3 mol^{-1} cm^{-1}), 518 (23 000), 555 (15 800), 595 (8400), 648 (7800).

Porphyrin 3 was used as obtained from TCI America Chemicals.

Preparation of nanospheres composed of Porphyrins 1, 2, and 3.

A 3 mM porphyrin (**1** or **2** or **3**) solution in 50 μL THF was injected into 2 mL of deionized water containing one equivalent of poly(propylene glycol) bis(2-aminopropyl ether), while stirring vigorously. The resulting solution was stirred for an additional 4 h. The THF was then removed under *vacuo*, and the remaining aqueous solution was filtered through a 0.45 μm filter. This filtered solution was then kept as a porphyrin NS stock solution for further characterization. Note: The concentration of porphyrin NSs are given in terms of the estimated concentration of the individual porphyrin units in solution, based on the molar absorption coefficients of monomeric porphyrin (**1** and **2** in water and **3** in THF).

3. ^{1}H NMR of porphyrins **4**, **1'** and **1**.



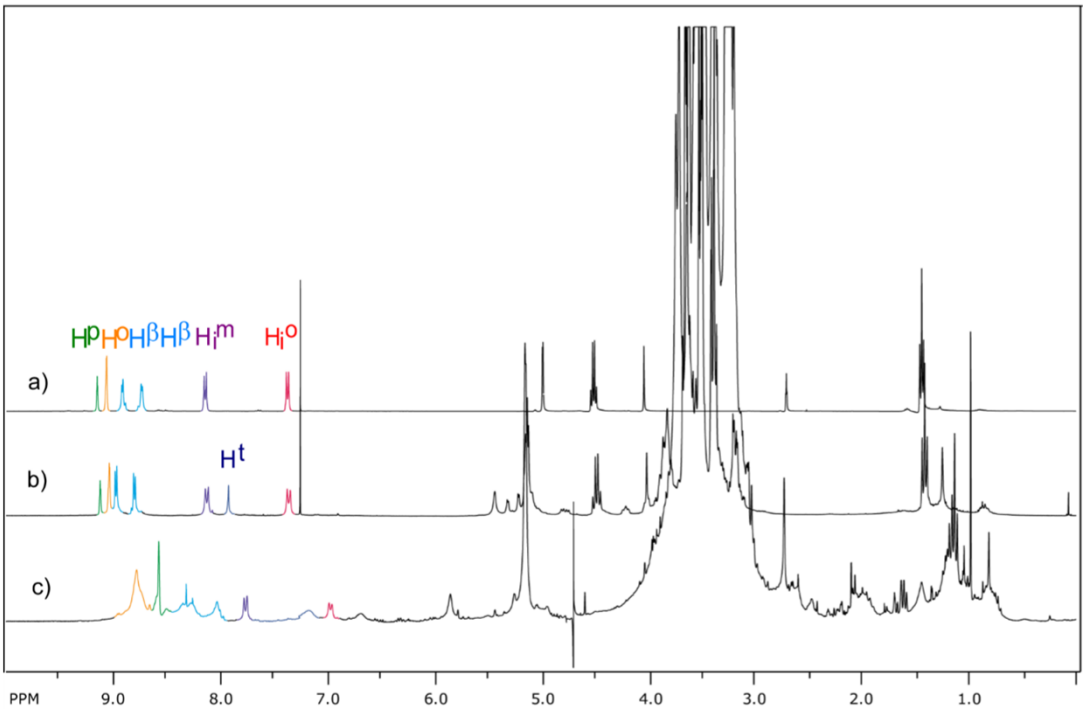


Figure S1. ^{1}H NMR of (a) porphyrin **4** in $CDCl_3$, (b) Zinc containing ethyl ester of porphyrin **1** (i.e., porphyrin **1'**) in $CDCl_3$, and (c) porphyrin **1** in D_2O (water suppression, 0.1 M phosphate buffer at pH = 7.0).

From the results shown in Figure S1, we observe that the low field proton peaks of the porphyrin does

not show significant changes after the click reaction with mono azido-PMβCD. After hydrolysis of the ethyl ester group of porphyrin **1'**, however, the phenyl and pyrrole protons of porphyrin **1** exhibit significant up-field shifts. Further, new peaks in the 2.0 - 3.0 ppm region (corresponding to CD protons) emerge.

4. 2D COSY and ROESY of porphyrins **1** and **1'**.

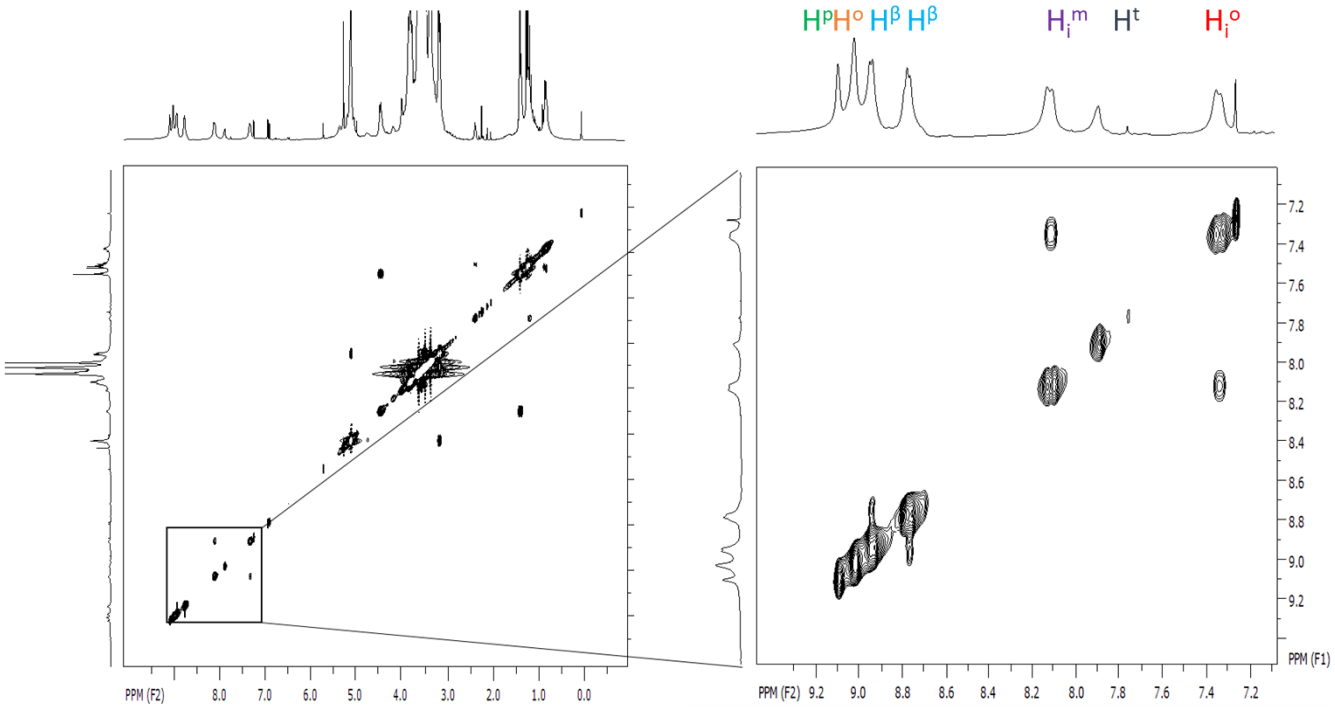


Figure S2. ^{1}H COSY of porphyrin **1'** in $CDCl_3$ (300 MHz). From this spectra, it is possible to confirm the *ortho* (H_i^o) and *meta* (H_i^m) protons of the phenyl group as well as the pyrrole protons (H^β) of the porphyrin core due to through bond correlations.

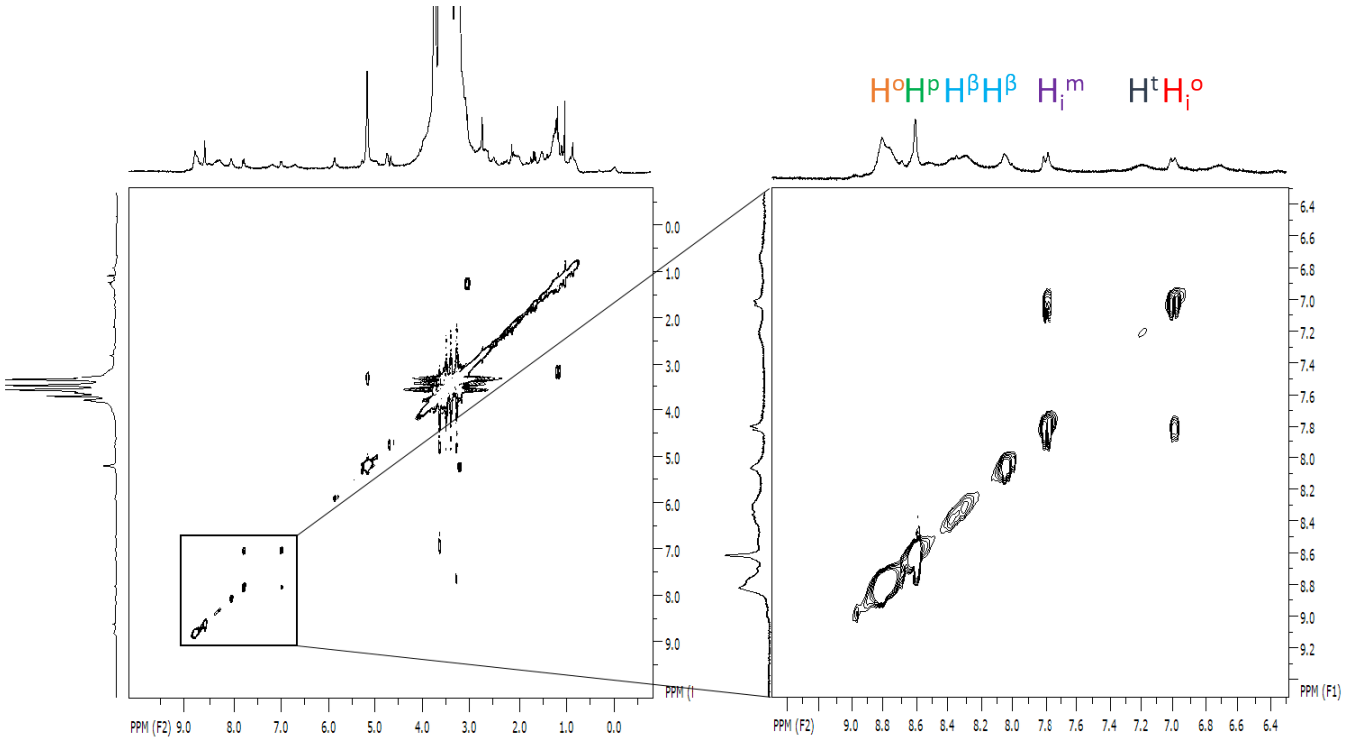


Figure S3.[1]H COSY of porphryin **1** in D_2O (300 MHz, water suppression, 0.1 M phosphate buffer at pH = 7.0). From this spectra, it is possible to confirm the *ortho* (H_i^o) and *meta* (H_i^m) protons of the phenyl group due to through bond correlations.

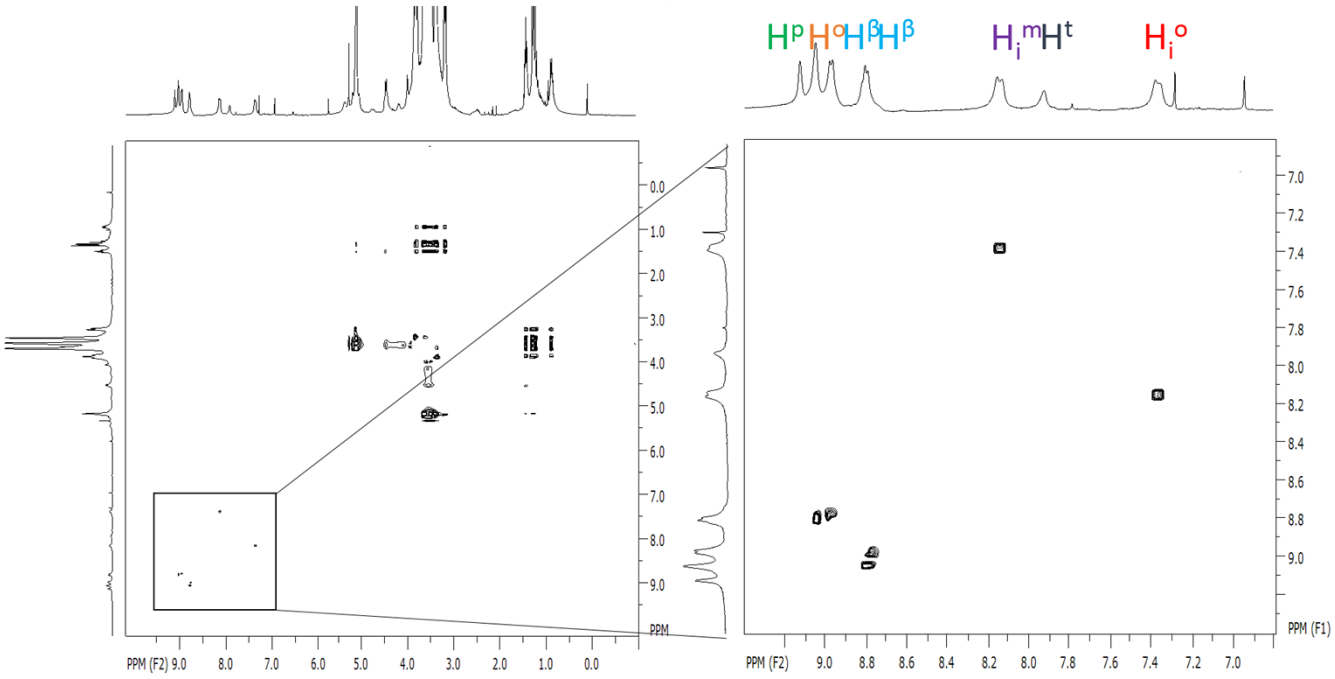


Figure S4. 2D ROESY NMR of porphyrin **1'** in $CDCl_3$ (300 MHz). From this spectra, it is possible to

confirm the *ortho* (H_i^o) and *meta* (H_i^m) protons of the phenyl group, originally assigned via J-coupling constant. Further, the *ortho* proton (H^o) of the carboxylic acid phenyl group can be assigned as it couples with the pyrrole proton (H^β) of the porphyrin due to the Nuclear Overhauser Effect. Importantly, there are no cross peaks observed between the downfield protons of the porphyrin phenyl/pyrrole units and the methyl protons on the cyclodextrins (3.0-4.0 ppm), indicating that porphyrin **1'** is not in a self-included state in $CDCl_3$.

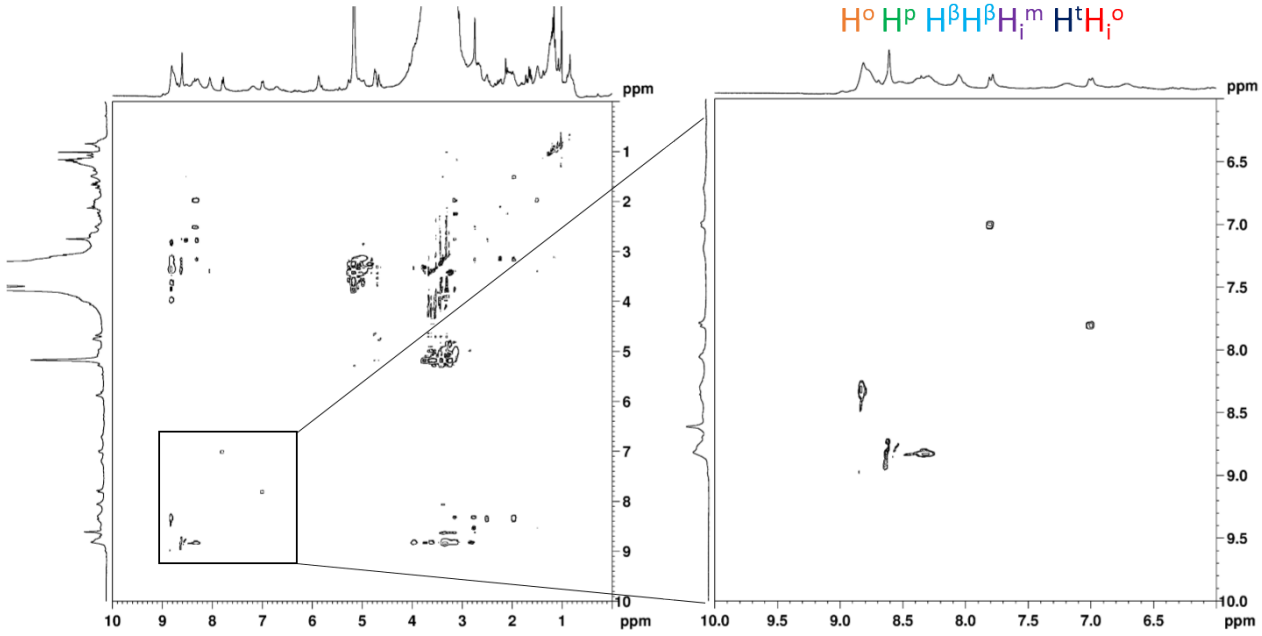


Figure S5. 2D ROESY of porphyrin **1** in D_2O (300 MHz, water suppression, 0.1 M phosphate buffer at pH = 7.0). From this spectra, it is possible to assign the *ortho* (H_i^o) and *meta* (H_i^m) protons of the phenyl group, and the *ortho* (H^o) proton of carboxylic acid phenyl group and the pyrrole (H^β) proton of porphyrin **1** due to the Nuclear Overhauser Effect.

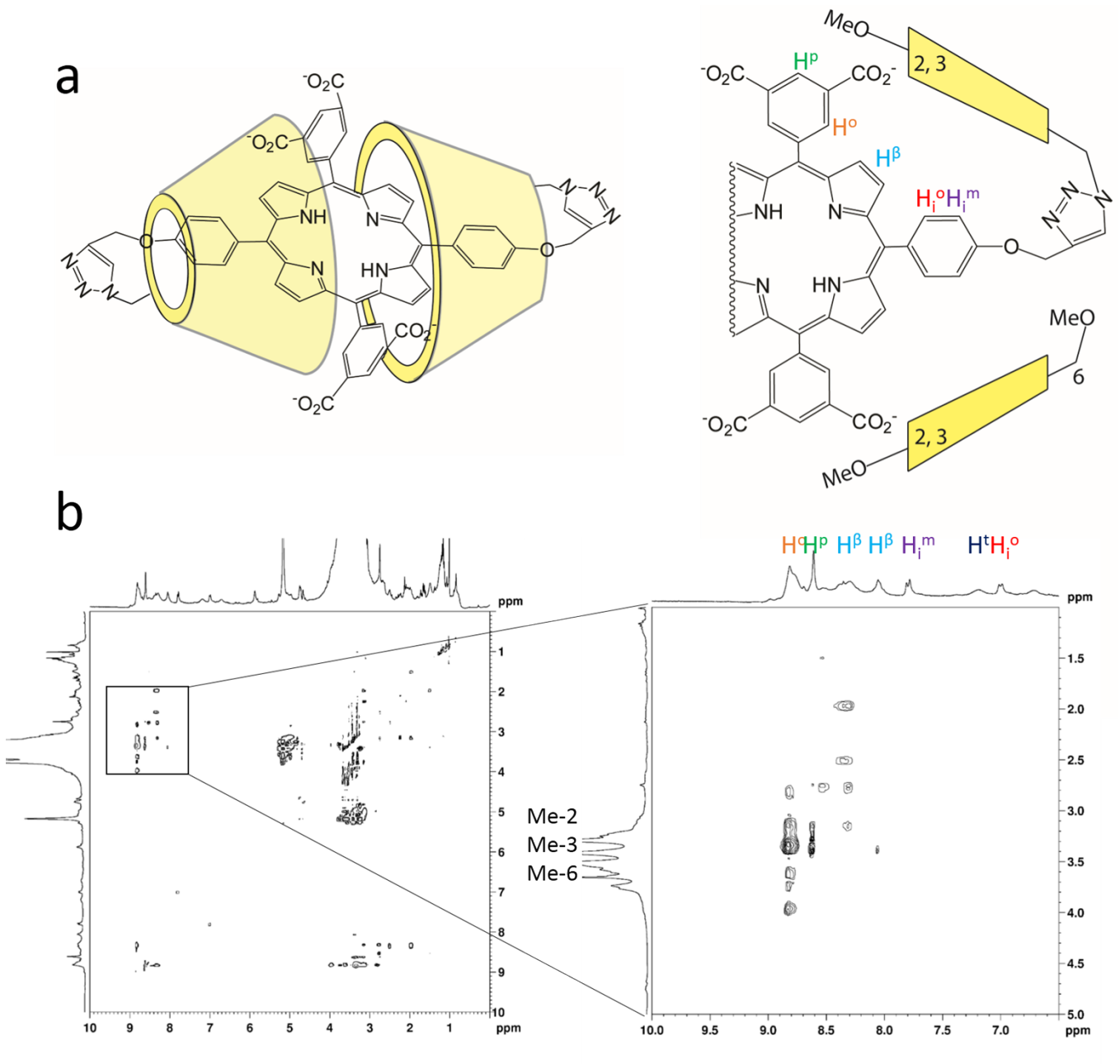


Figure S6. (a) Self-inclusion complex of porphyrin **1**. (b) 2D ROESY NMR of porphyrin **1** in D_2O (300 MHz, water suppression, 0.1 M phosphate buffer at pH = 7.0). From this spectrum, it is observed that the OCH_3 groups of the CD have cross peaks with the *ortho* (H^o) and *para* (H^p) protons of the phenyl groups and the (H^β) pyrrole protons of the porphyrin backbone. In addition, there are cross peaks between the CD protons in the 2 -3 ppm region with protons on the porphyrin/benzene rings[3].

5. ^{1}H NMR of porphyrin **2**

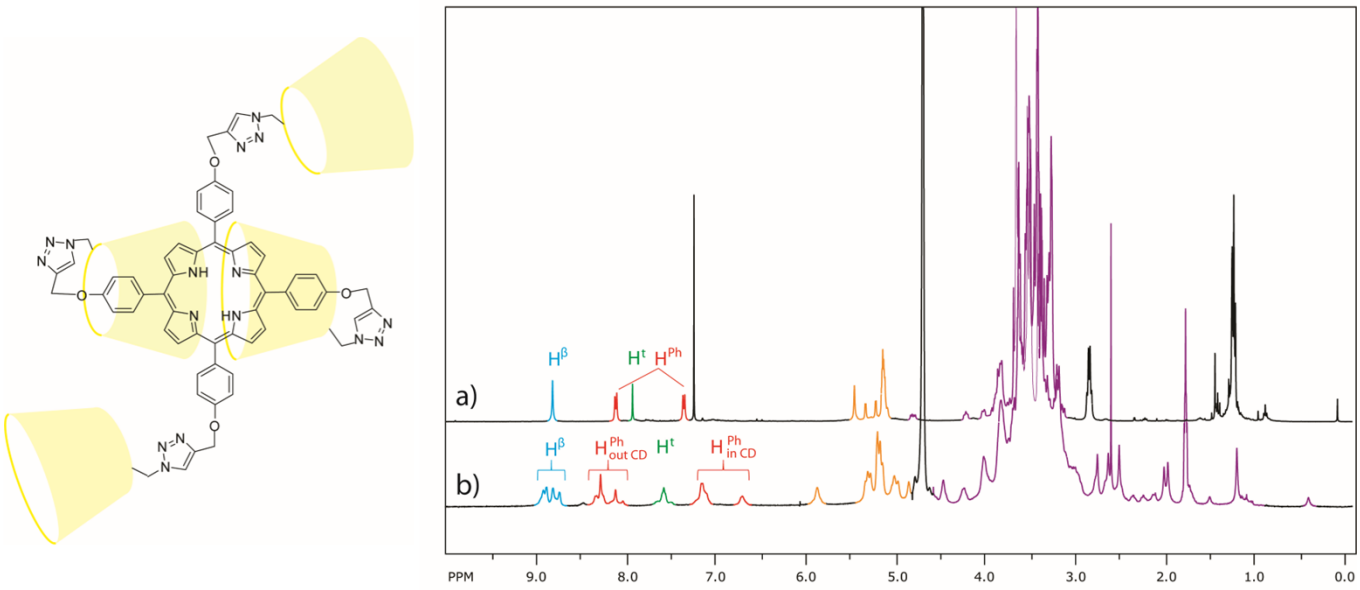


Figure S7. ^{1}H NMR of porphyrin **2** in $CDCl_3$ (top) and D_2O (bottom). From these results, it is observed that the downfield protons of the phenyl groups and the pyrrole protons show splitting and chemical shifts after changing the solvent from $CDCl_3$ to D_2O. Also new cyclodextrin peaks emerge in the upfield region (2.0-3.0 ppm) due to the deshielding effects from the ring currents of the porphyrin and /or benzene rings. These results are similar to the observations by Liu and co-workers[2] who investigated the zinc version of porphyrin **2** and are consistent with self-inclusion via host-guest interactions. Furthermore, based on the size of the CD molecules and extensive work by Kano[4] it is reasonable that only two CDs can encapsulate the porphyrin core and they should come from opposite meso-phenyl positions.

6. UV-vis spectra of porphyrins **1**, **2** and **3**

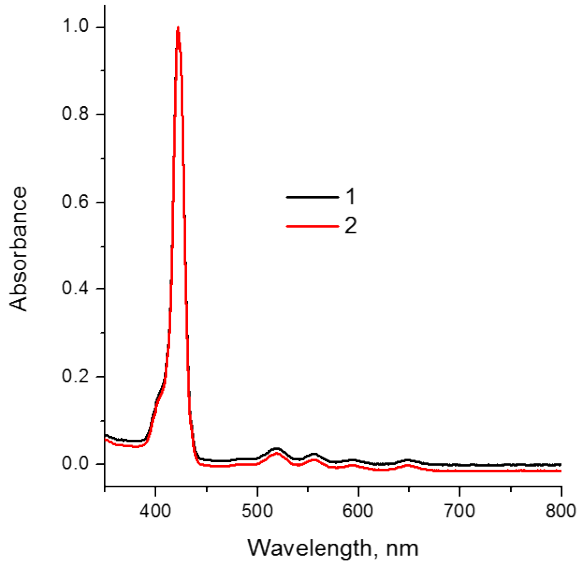


Figure S8. Normalized UV- vis spectrum of porphyrin **1** and **2** in $CHCl_3$ (λ_{max} = 422 nm).

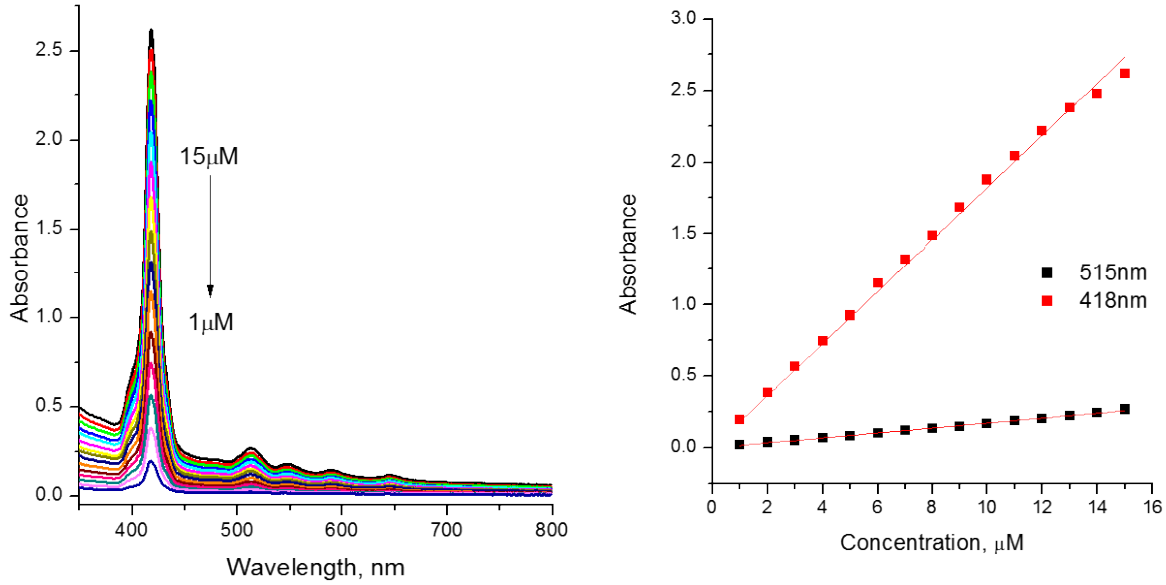


Figure S9. (Left) UV-vis spectrum of porphyrin **1** at varying concentrations in H_2O. (Right) Graph of absorbance λ_{max} (418 nm) and (515 nm) versus concentration of porphyrin **1** in H_2O.

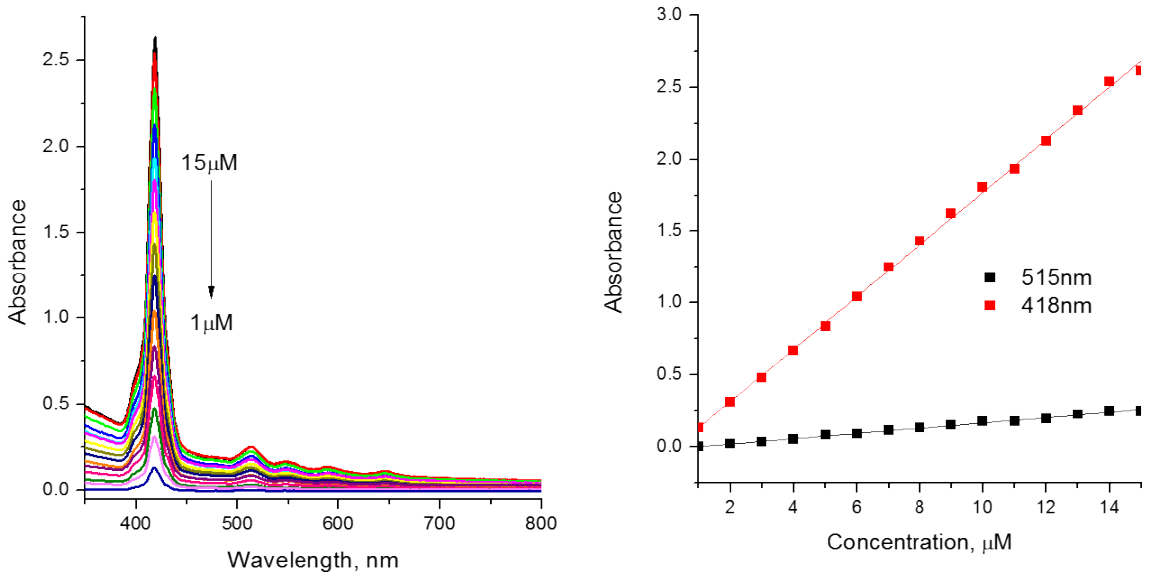


Figure S10. (Left) UV-vis spectrum of porphyrin **2** at varying concentrations in H_2O. (Right) Graph of absorbance λ_{max} (418 nm) versus concentration of porphyrin **2** in H_2O.

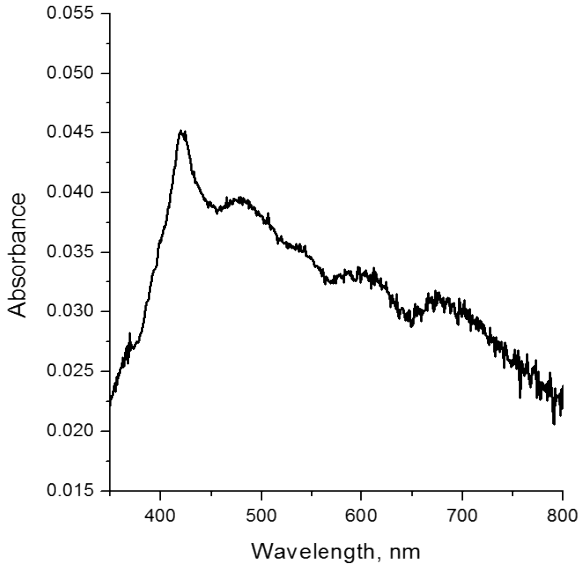


Figure S11. UV-vis spectrum of some soluble porphyrin **3** after filtration of black precipitate in H_2O. The concentration prior to filtration was 5 μM. It is well known that porphyrin **3** is hardly soluble and extensively aggregated in aqueous environment.[5]

7. SEM of NSs composed of porphyrins **1**,**2** and **3**

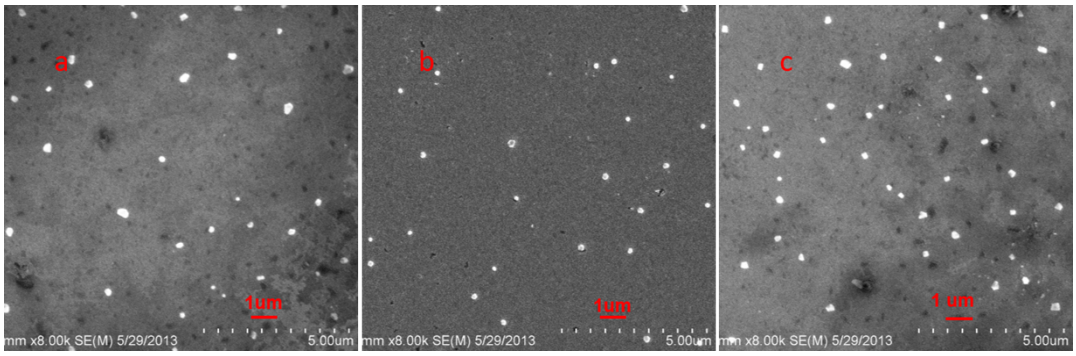


Figure S12. SEM of nanospheres formed by (a)porphyrin **1**, (b)porphyrin **2**, and (c)porphyrin **3**.

8. TEM of porphyrins **1** ,**2** and **3** assembly without PPGN.

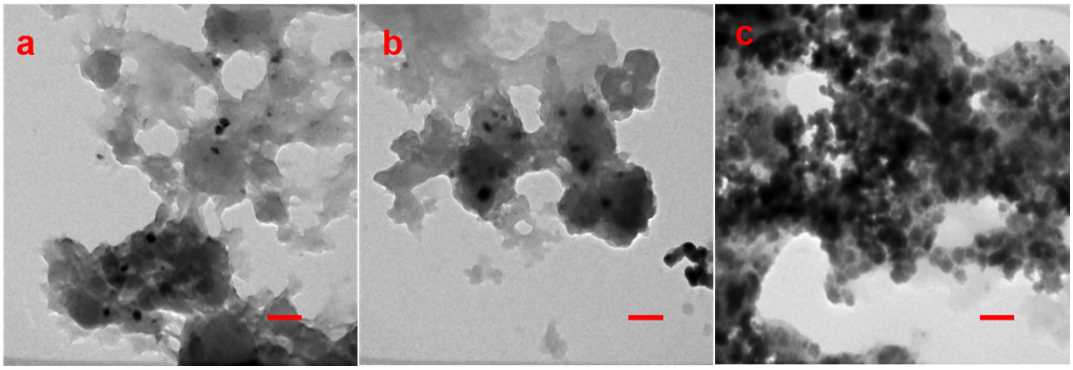


Figure S13. TEM micrographs of (a) assembly of porphyrin **1** without PPGN in water; (b) assembly of porphyrin **2** without PPGN in water; and (c) assembly of porphyrin **3** without PPGN in water. The scale bar is 200 nm. From these images, it is observed that without the agglomeration inhibiting polymer, porphyrins **1**, **2** and **3** form large irregular clusters.

9. UV-vis spectra of NSs composed of porphyrins **1**, **2** and **3**.

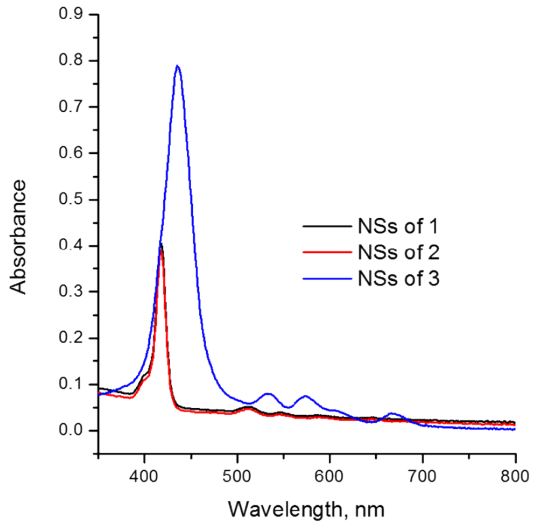


Figure S14. UV-vis spectrum of NSs composed of porphyrin **1**, porphyrin **2** and porphyrin **3** in D_2O. These solutions were used for singlet oxygen generation measurements (absorbance matches at $\lambda = 419$ nm).

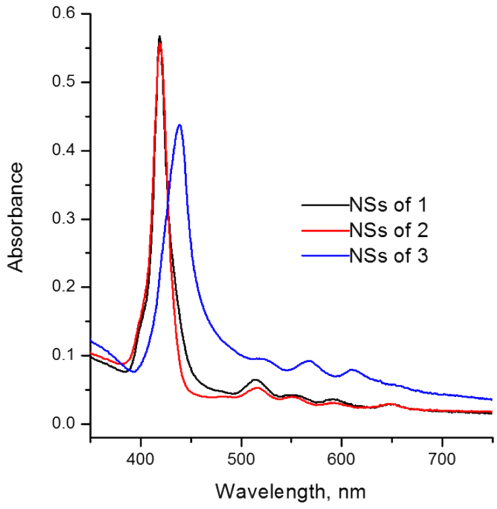


Figure S15. UV-vis spectrum of NSs formed by porphyrin **1**, **2** and **3** in water. These solutions were used for steady state fluorescence measurements (absorbance matches at $\lambda = 427$ nm).

10. Quantum yields of NSs composed of porphyrin **1**, **2** and **3**.

Fluorescence quantum yields were calculated using the comparative method from the following equation:

$\Phi_f(U) = \Phi_f(St)\ S(U) / S\ (St)$

Where U and St denote unknown and standard, respectively, and S represents the slope. Φ_f represents fluorescence quantum yield. Slope is obtained from the plot of integrated fluorescence intensity (i.e. the integrated fluorescence (550-800 nm)) *vs* absorbance (425 nm). Tetraphenylporphine sulfonate (H_2TPPS) was used as the standard, because its emission bands (see table S1) are close to the emission bands of NSs composed of porphyrin **1**, **2** and **3**. All these measurements were done in water.

Samples	First emission band (λ /nm)	Second emission band (λ /nm)	Φ_f
H_2TPPS	645	700	0.080[6]
NSs of **1**	650	715	0.029
NSs of **2**	646	713	0.024
NSs of **3**	655	720	0.002

Table S1. Fluorescence properties of NSs composed of Porphyrin **1**, **2** and **3** in water.

1. C. Hocquelet, J. Blu, C. K. Jankowski, S. Arseneau, D. Buisson, and L. Mauclaire, *Tetrahedron*, 2006, **62**, 11963–11971.
2. Y. Liu, C.-F. Ke, H.-Y. Zhang, J. Cui, and F. Ding, *J. Am. Chem. Soc.*, 2008, **130**, 600–605.
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