Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Boosting the singlet oxygen photosensitization abilities of Zn(II) phthalocyanines through functionalization with bulky fluorinated substituents

Miguel A. Revuelta-Maza,[a] Santi Nonell,[b] Gema de la Torre,*[a,c] and Tomás Torres*[a,c,d]

STRUCTURAL CHARACTERIZATION

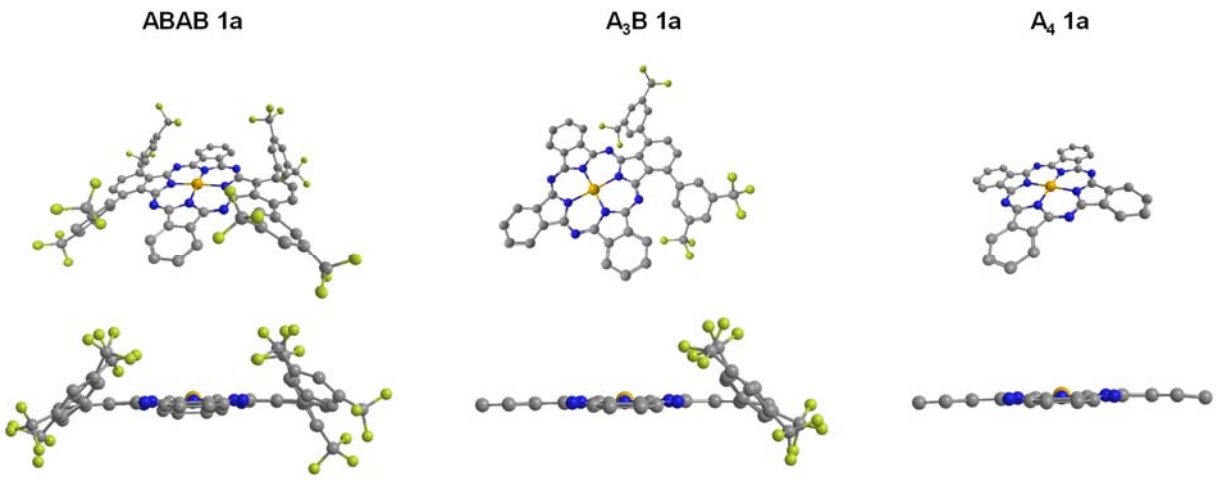

Figure S1. Geometry optimization of Zn(II)Pcs **1a** with SCIGRESS (FJ 2.8.1 EU 3.3.1) MM2 geometry optimization.

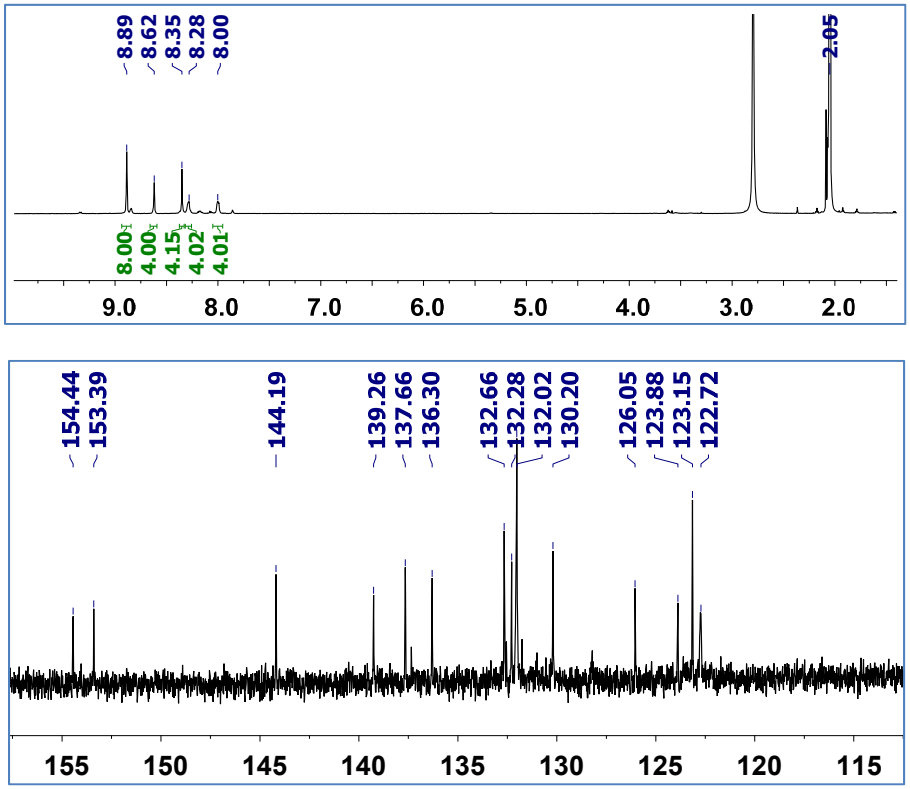

Figure S2. ^{1}H-NMR (500 MHz, acetone-d_6) and ^{13}C-NMR (125 MHz, acetone-d_6) of **ABAB 1a**.

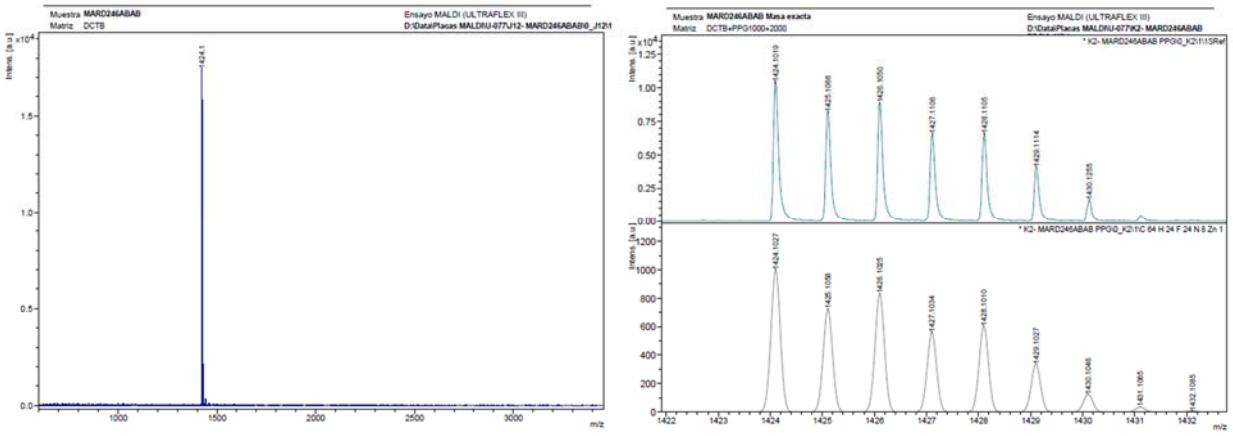

Figure S3. HR-MS (MALDI) of **ABAB 1a**.

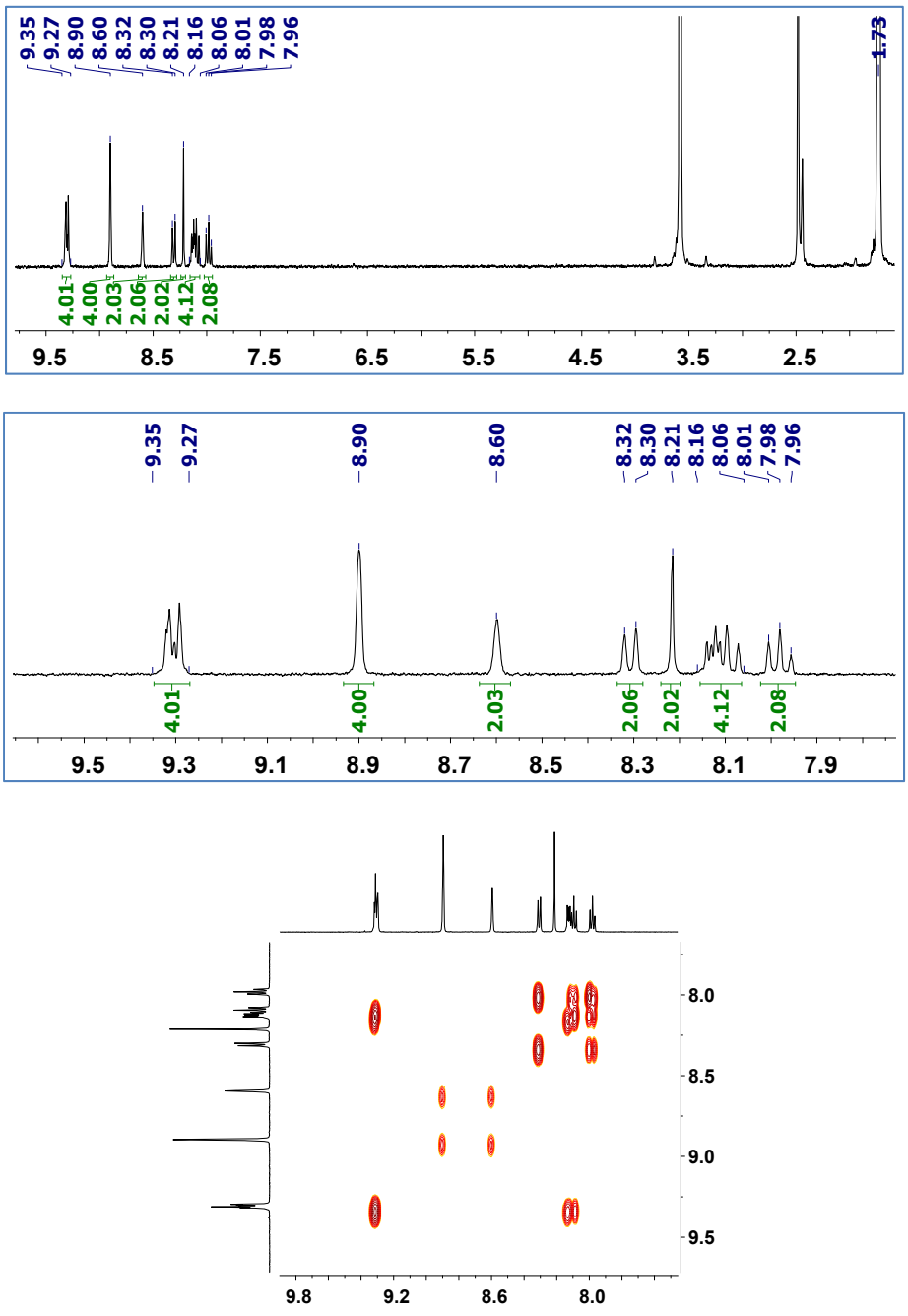

Figure S4. ^{1}H-NMR and COSY (500 MHz, THF-d_8) of **A_3B 1a**.

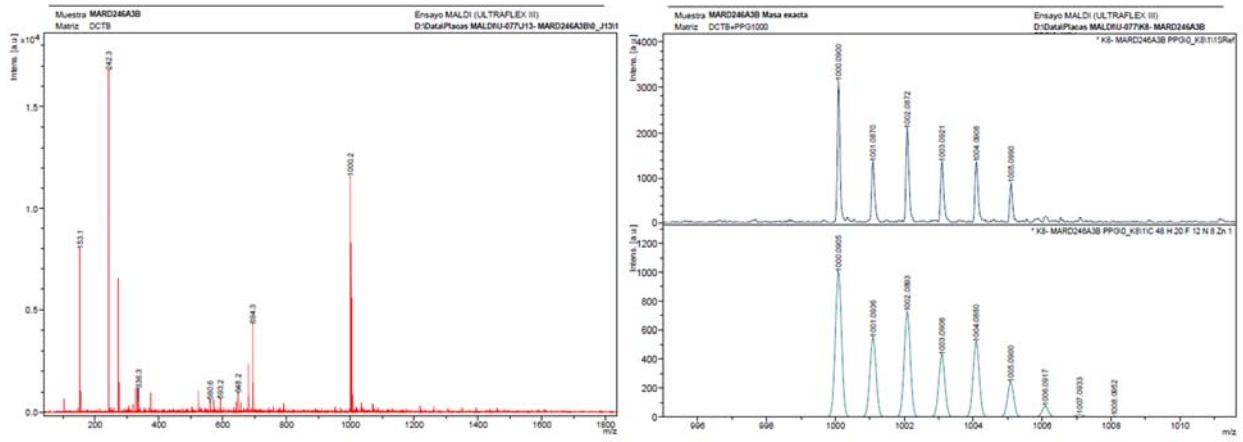

Figure S5. HR-MS (MALDI) of **A_3B-ZnPc 1a**.

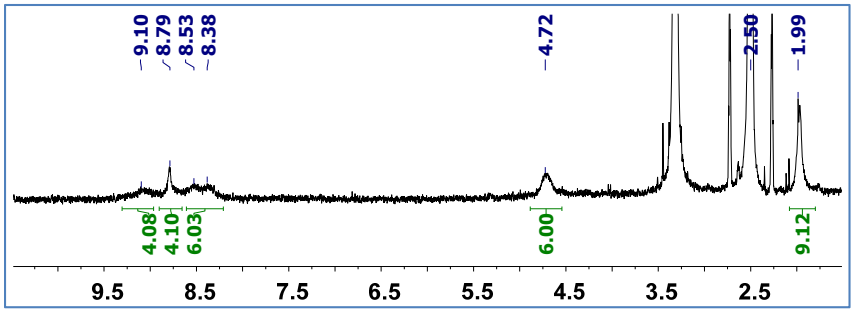

Figure S6. ^{1}H-NMR (300 MHz, DMSO-d_6) of **A_3B 1b**.

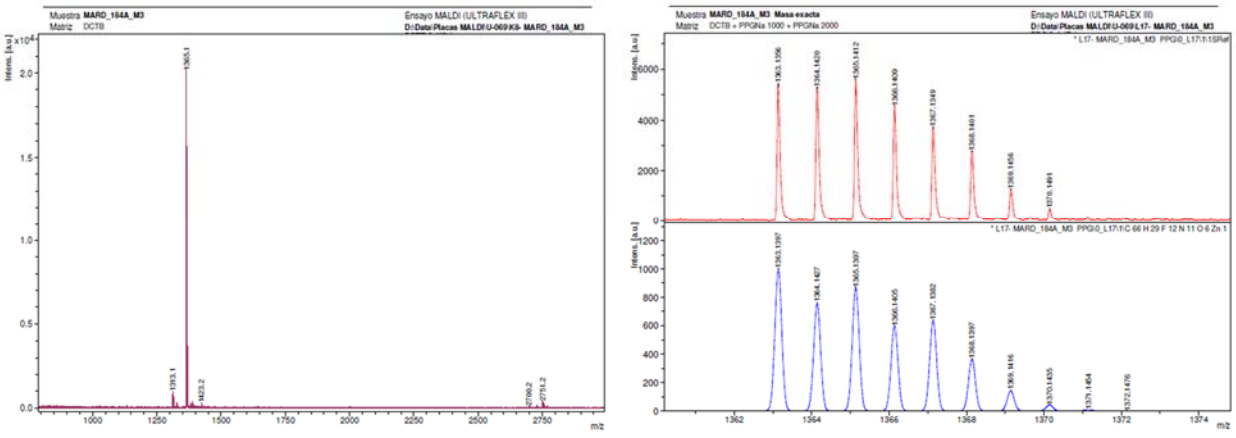

Figure S7. HR-MS (MALDI) of **A_3B 1b**.

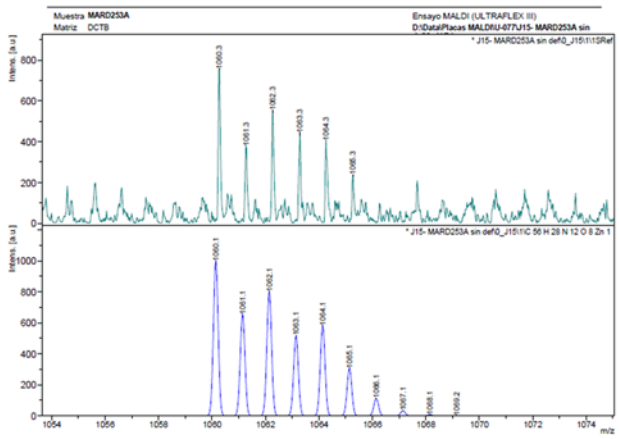

Figure S8. MS (MALDI) of **A_4 1b**.

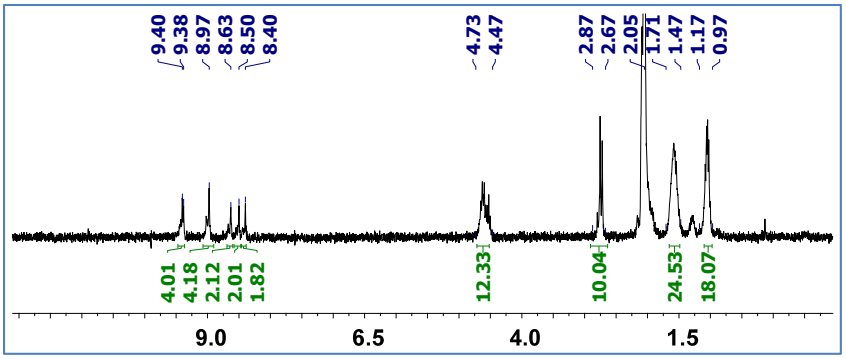

Figure S9. ^{1}H-NMR (300 MHz, acetone-d_6) of **A_3B 1c**.

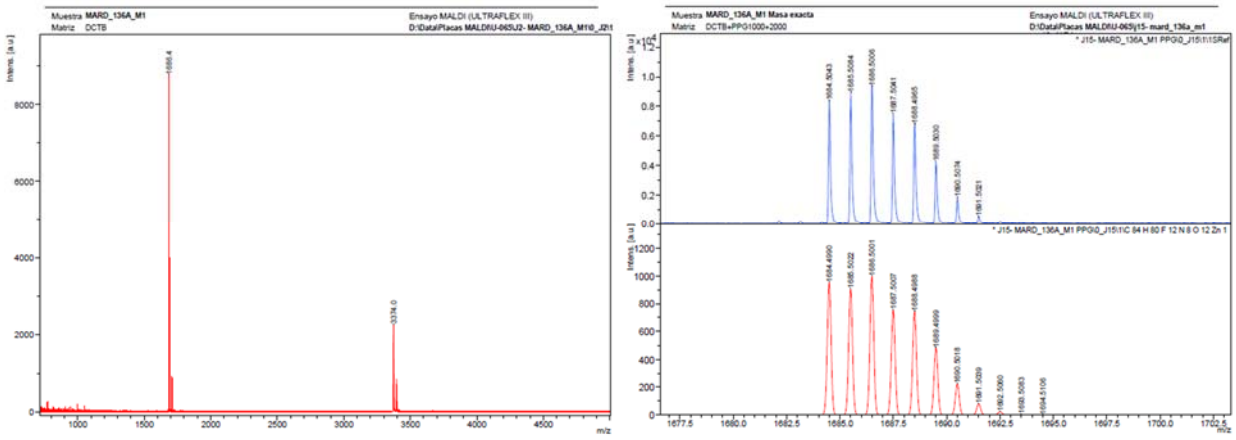

Figure S10. HR-MS (MALDI) of **A_3B 1c**.

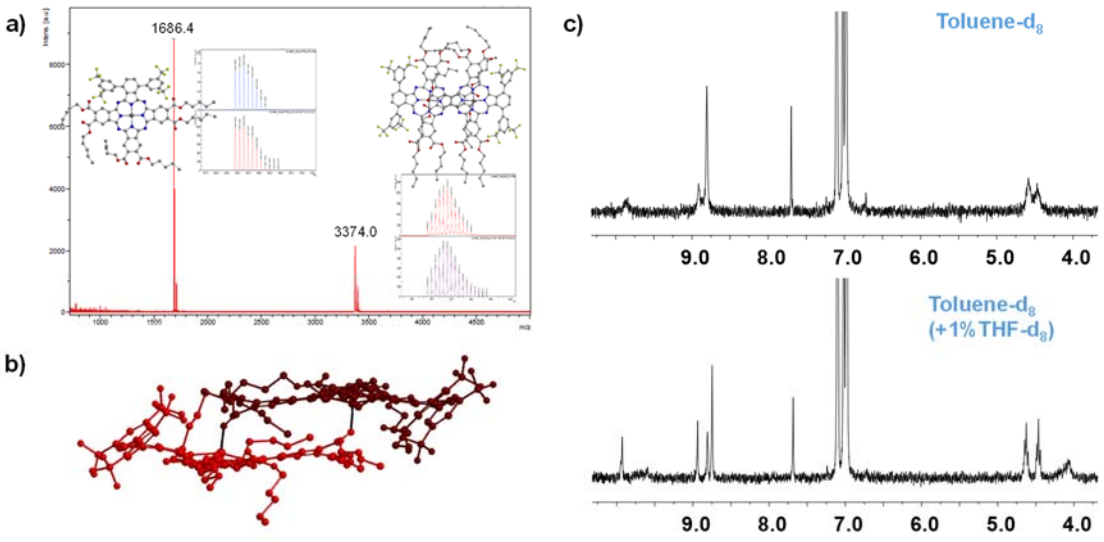

Figure S11. a) MS (MALDI) of **A_3B 1c** with identified peaks for monomer and dimer; b) Model structure of a plausible dimeric aggregate of **A_3B 1c** with SCIGRESS (FJ 2.8.1 EU 3.3.1) MM2 geometry optimization; c) ^{1}H-NMR (300 MHz, toluene-d_8) of **A_3B 1c**, before and after 1%THF-d_8 addition for disaggregation.

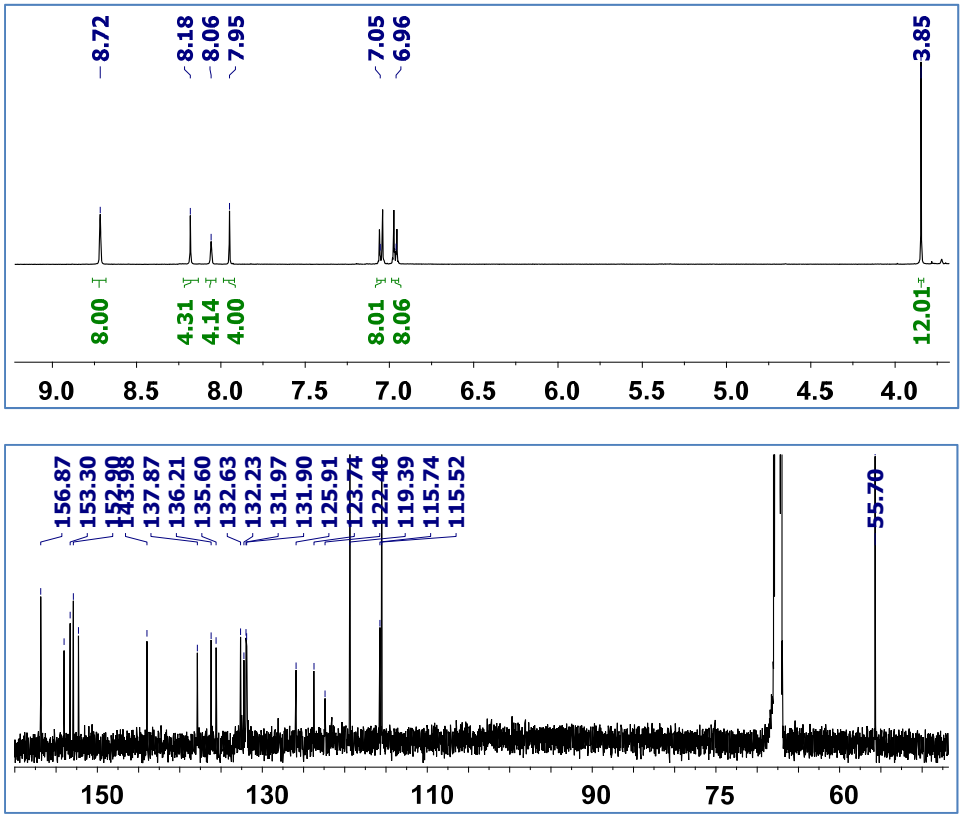

Figure S12. ^{1}H-NMR (500 MHz, THF-d_8) and ^{13}C-NMR (125 MHz, THF-d_8) of **ABAB 1d**.

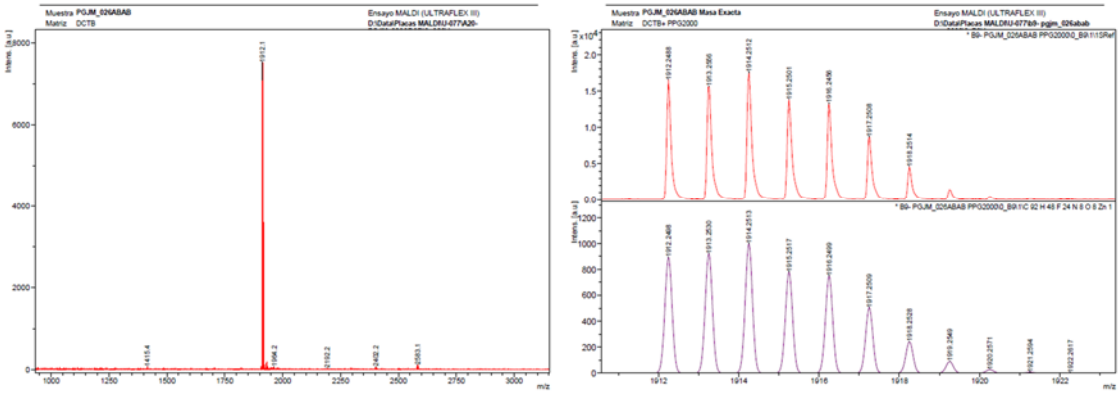

Figure S13. HR-MS (MALDI) of **ABAB 1d**.

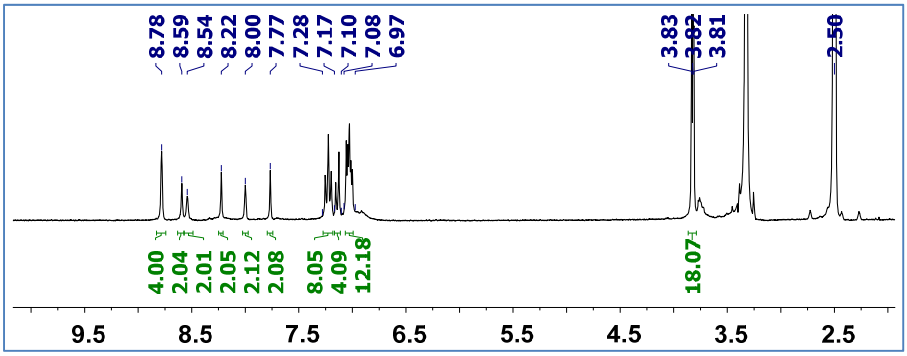

Figure S14. ^{1}H-NMR (300 MHz, DMSO-d_6) of **A_3B 1d**.

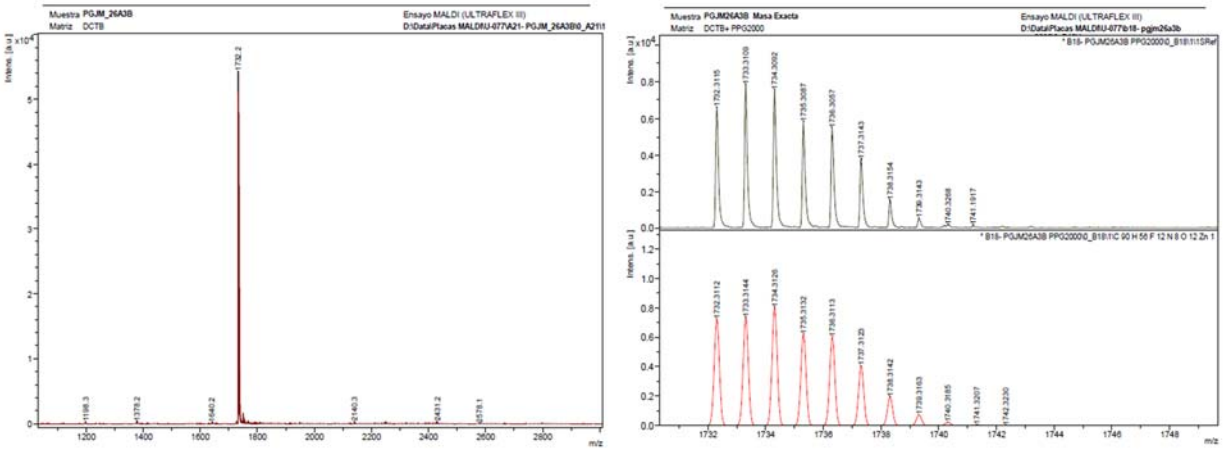

Figure S15. HR-MS (MALDI) of **A_3B 1d**.

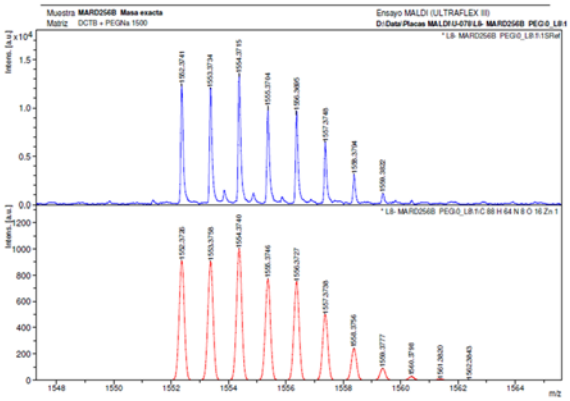

Figure S16. HR-MS (MALDI) of **A_4 1d**.

SPECTROPHOTOMETRY

Spectroscopic techniques employed in the determination of the photophysical properties of ZnPcs **1a-d**. All spectroscopic measurements were carried out in 1 cm quartz cuvettes (Hellma, Germany) in air-saturated solutions, at room temperature using spectroscopic grade solvents.

Table S1. Photophysical properties in toluene. [a] in air-saturated solutions; [b] Q-band maximum.

ZnPc	Solvent	logε (λ.)	λ_f / nm	ϕ_f	τ_S / ns	τ_T / μs[a]	ϕ_Δ
ABAB 1a	toluene	4.54 (350), 4.75 (664), 5.00 (705)[b]	709	0.13	1.8	0.12	0.76
A_3B 1a	toluene	4.86 (349), 5.22 (664), 5.30 (687)[b]	690	0.23	2.1	0.27	0.69
A_4 1a[c]	toluene	4.53 (340), 5.22 (669)[b]	673	0.53	2.4	0.21	0.66
ABAB 1b	toluene	4.81 (359), 5.11 (682), 5.28 (707)[b]	711	0.24	2.3	0.22	0.65
A_3B 1b	toluene	4.71 (365), 5.29 (698)[b]	706	0.23	2.6	0.30	0.65
ABAB 1c	toluene	4.84 (351), 5.49 (689)[b]	695	0.16	3.0	0.22	0.69
A_3B 1c	toluene	aggregation	693	0.29	3.2	0.20	0.62
A_4 1c	toluene	aggregation	691	0.20	3.2	0.20	0.49
ABAB 1d	toluene	4.99 (349), 5.37 (673), 5.39 (712)[b]	716	0.11	1.7	0.30	0.62
A_3B 1d	toluene	4.89 (349), 5.28 (676)[b], 5.28 (695)	699	0.20	2.0	0.20	0.57

[a] In air-saturated solutions. [b] Q-band maximum. [c] Prepared from a stock solution of the ZnPc in DMSO (Final content: 1% DMSO).

UV-Vis spectra

Absorption spectra were recorded using a double beam UV-Vis-NIR Varian Cary 6000i spectrophotometer (Varian, Palo Alto, CA, USA). Absorption coefficients were derived from the slopes of Lambert-Beer plots.

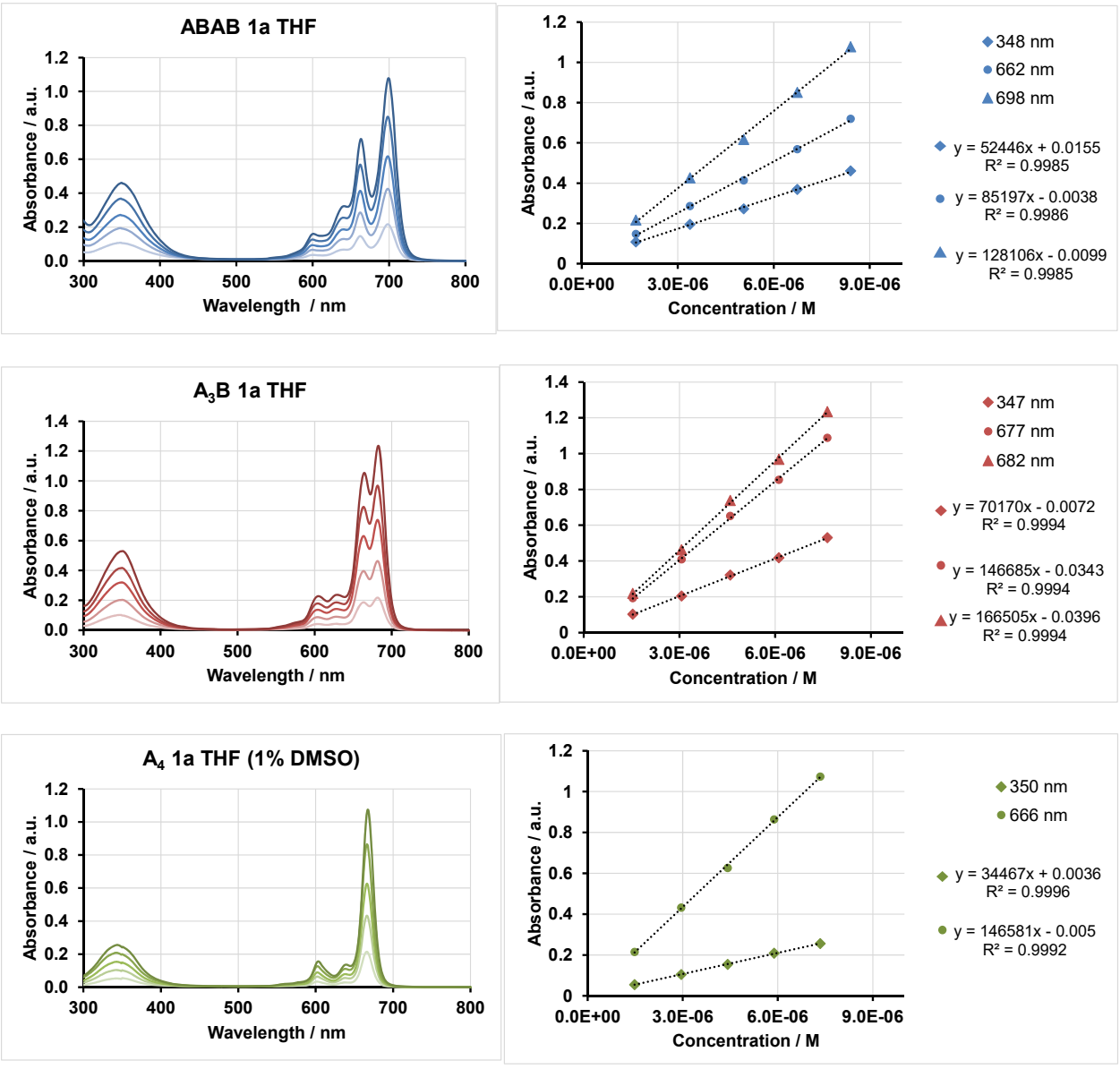

Figure S17. Concentration-dependent studies for ZnPcs **1a** in THF.

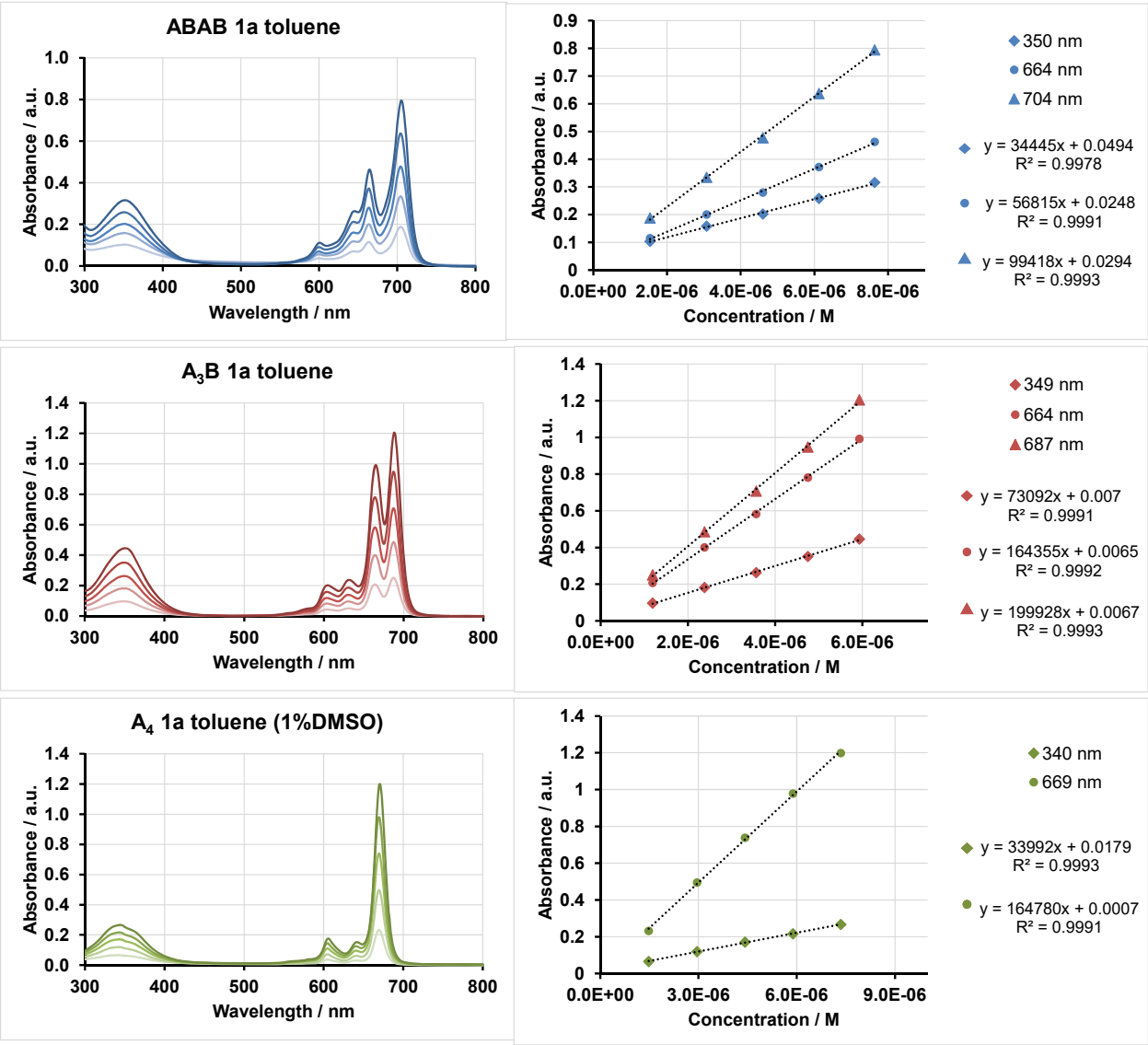

Figure S18. Concentration-dependent studies for ZnPcs **1a** in toluene.

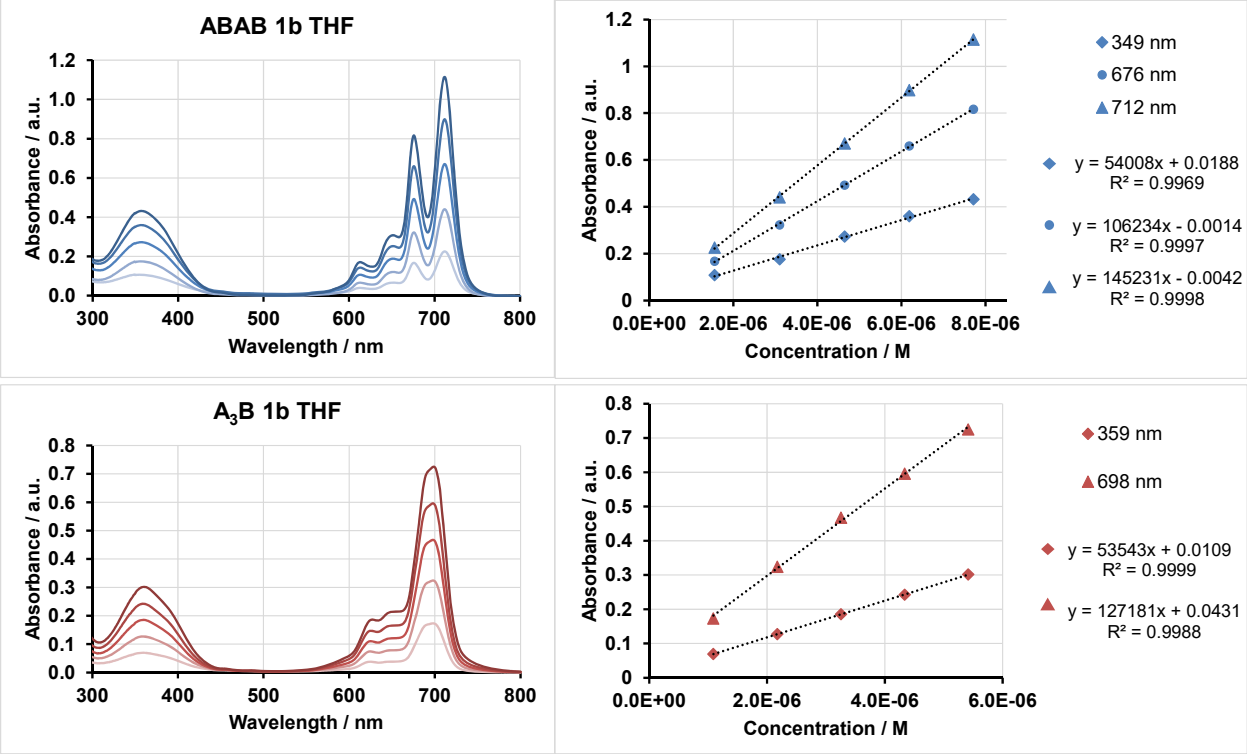

Figure S19. Concentration-dependent studies for ZnPcs **1b** in THF.

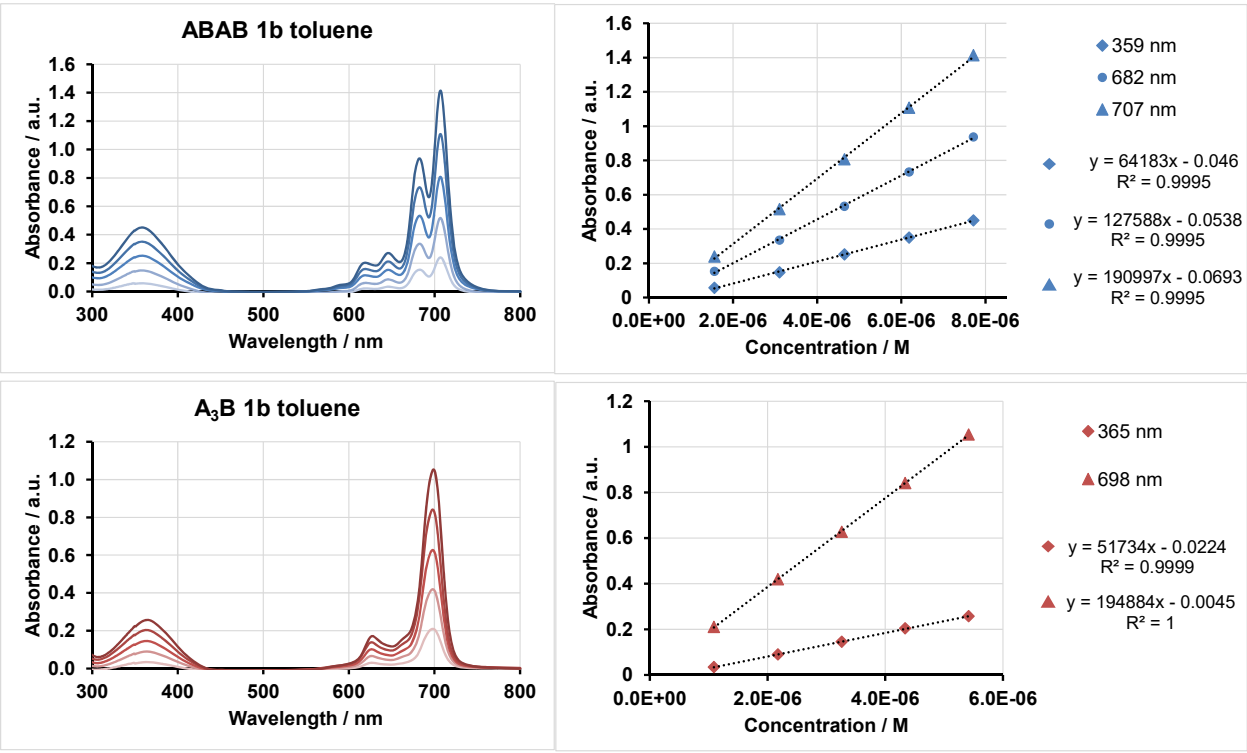

Figure S20. Concentration-dependent studies for ZnPcs **1b** in toluene.

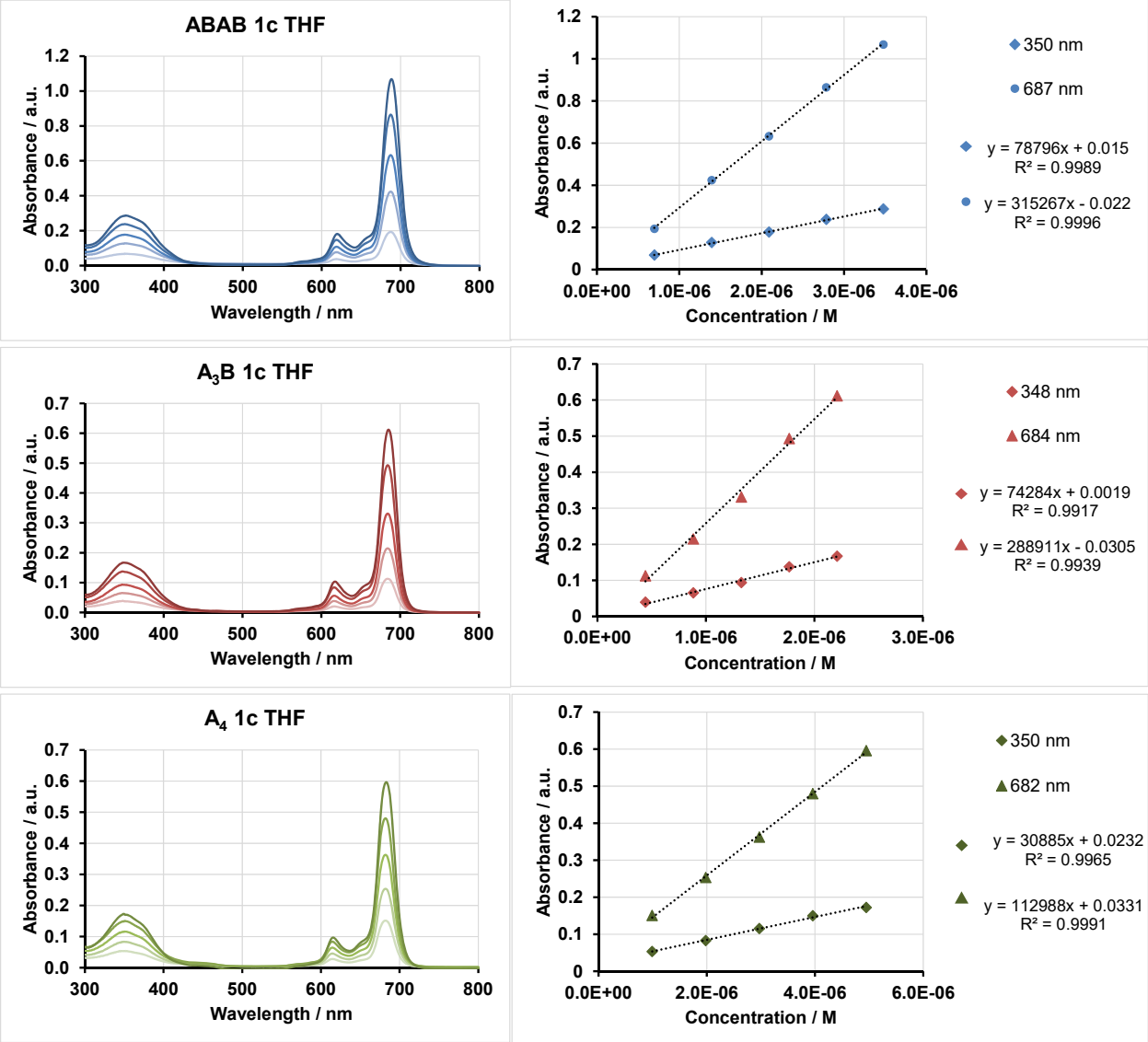

Figure S21. Concentration-dependent studies for ZnPcs **1c** in THF.

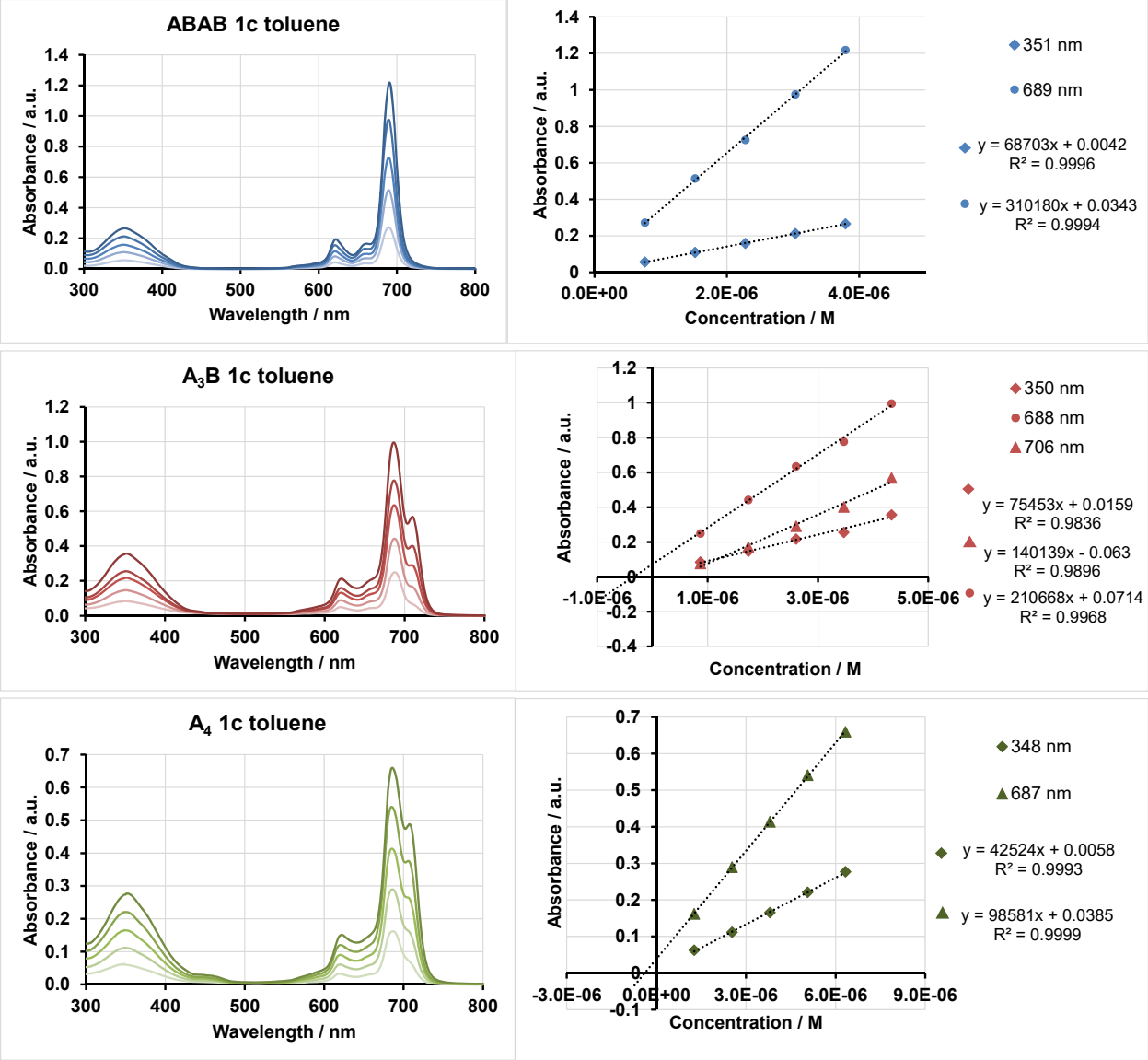

Figure S22. Concentration-dependent studies for ZnPcs **1c** in toluene.

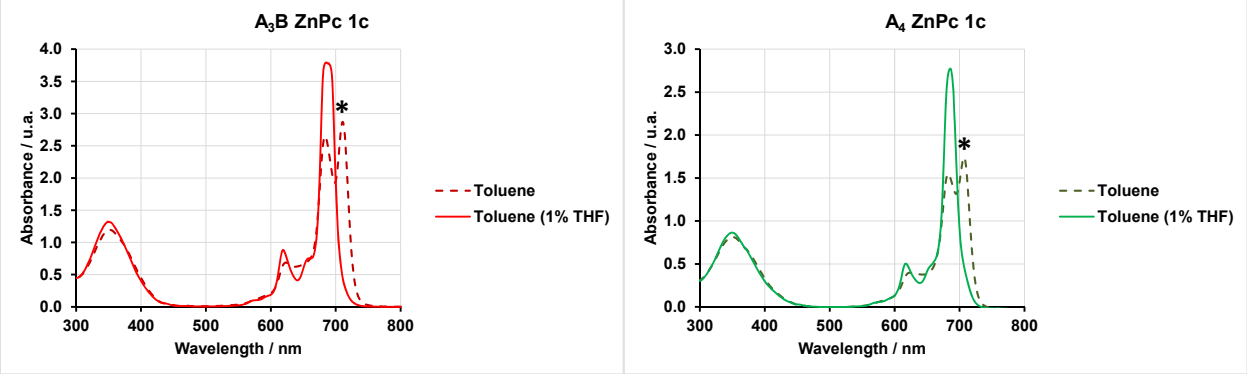

Figure S23. Qualitative UV-Vis spectra of **A_3B 1c** and **A_4 1c** in toluene, before and after addition of 1% of THF. More concentrated solution of the compounds were prepared (~$2 \cdot 10^{-5}$M) in comparison with previous concentration dependent studies (~$1\text{-}6 \cdot 10^{-6}$M), with the aim of reaching a situation of high aggregation. Please, notice the disappearance of aggregation bands (*) and Q-bands recovery.

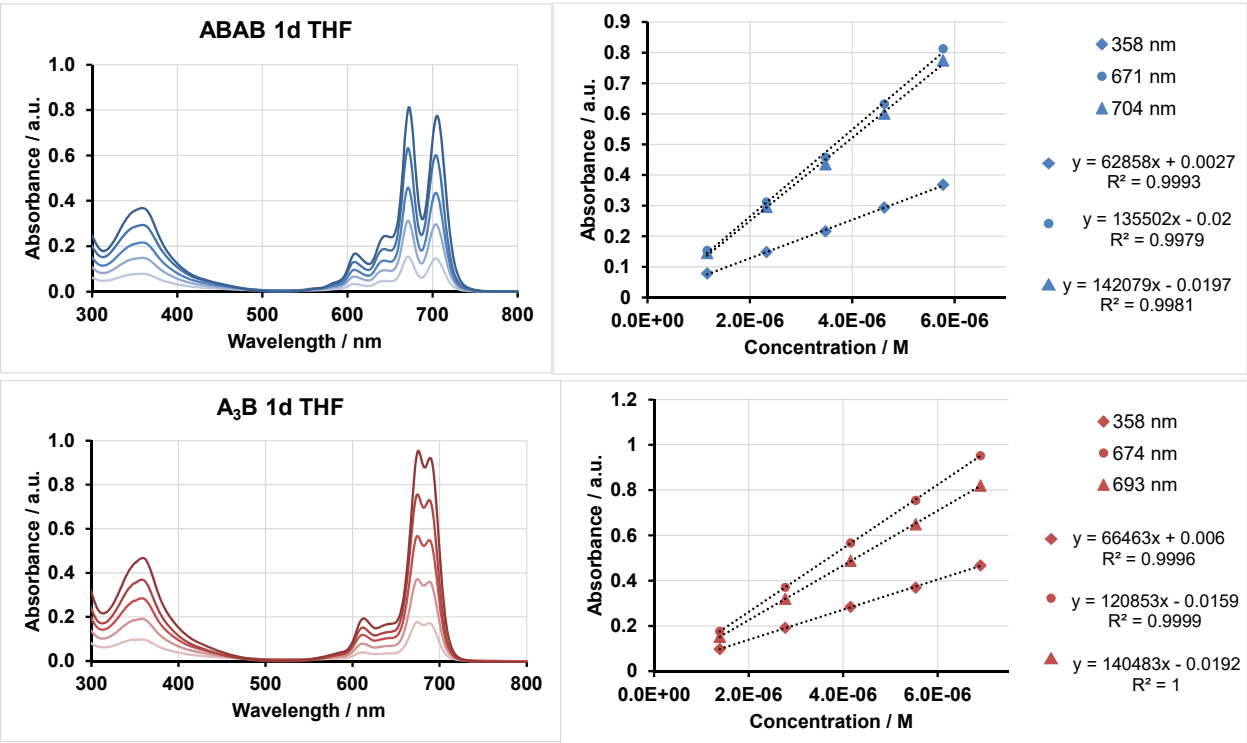

Figure S24. Concentration-dependent studies for ZnPcs **1d** in THF.

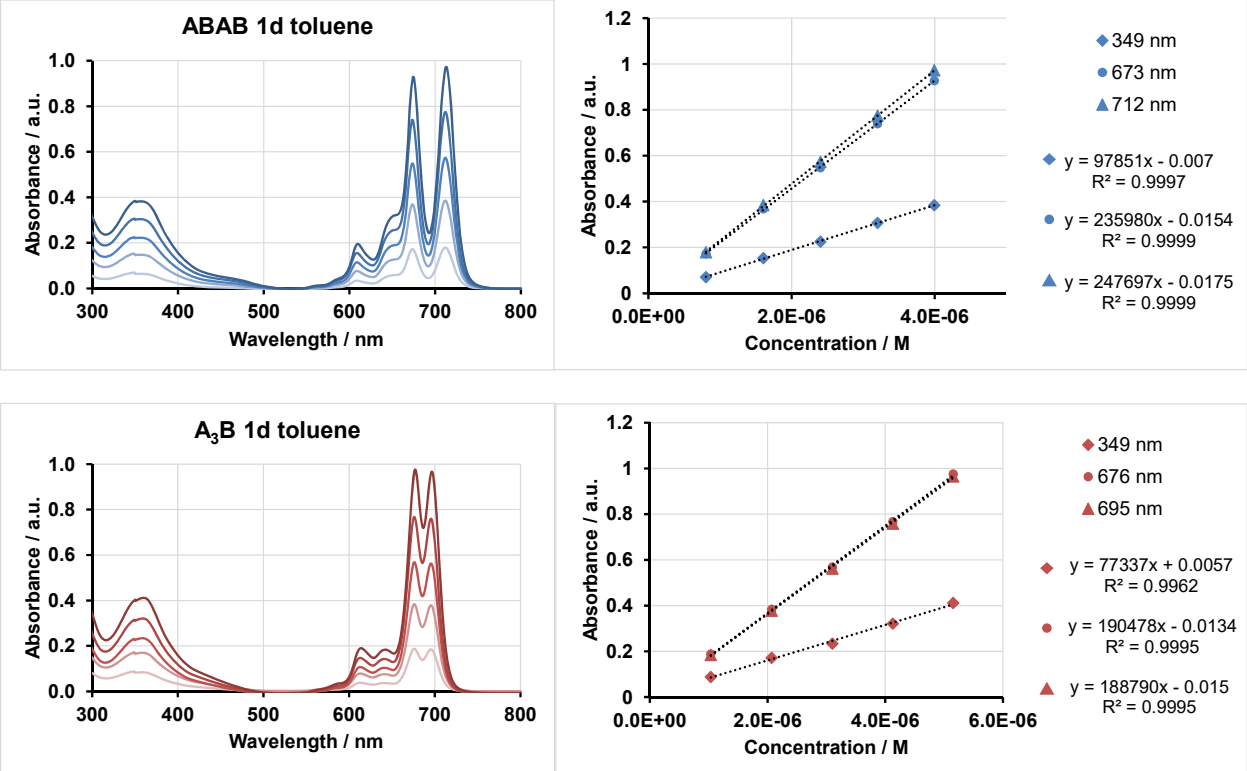

Figure S25. Concentration-dependent studies for ZnPcs **1d** in toluene.

Fluorescence spectra

Emission spectra were recorded using a Spex Fluoromax-4 spectrofluorometer (Horiba Jobin-Yvon, Edison, NJ, USA). The samples were excited at: **ABAB** (THF), 690 (**1a**), 692 (**1b**), 677 (**1c**) and 694 nm (**1d**); **ABAB** (toluene), 690 (**1a**), 678 (**1b**), 679 (**1c**) and 700 nm (**1d**); **A_3B** (THF), 662 (**1a**), 678 (**1b**), 674 (**1c**) and 685 nm (**1d**); **A_3B** (toluene), 667 (**1a**), 678 (**1b**), 674 (**1c**) and 687 nm (**1d**); **A_4** (THF), 672 nm (**1c**); **A_4** (toluene), 677 nm (**1c**).

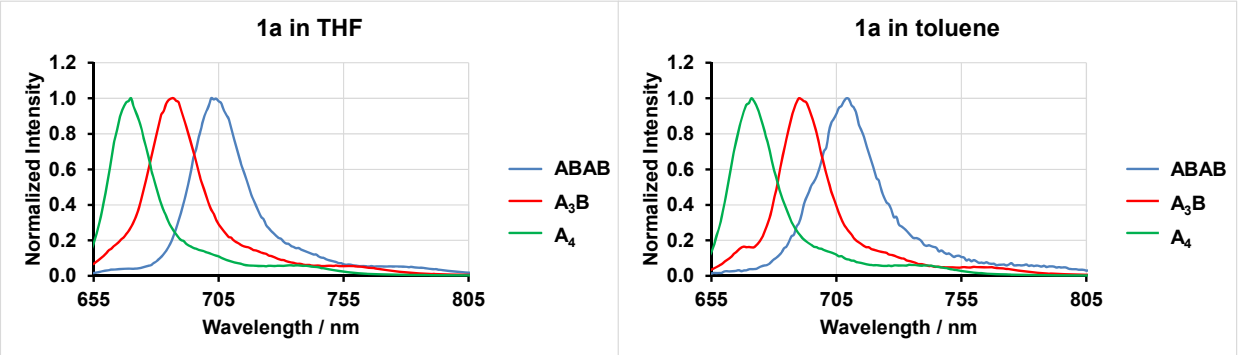

Figure S26. Emission spectra for ZnPcs **1a** in THF and toluene.

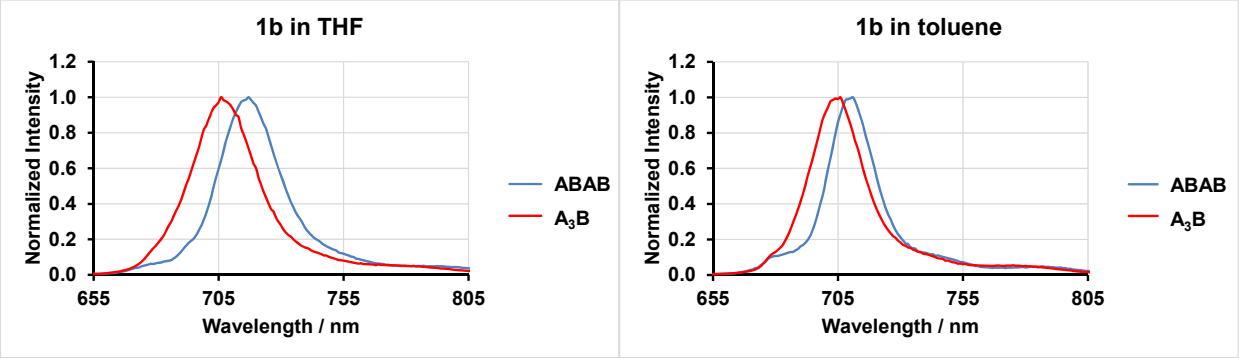

Figure S27. Emission spectra for ZnPcs **1b** in THF and toluene.

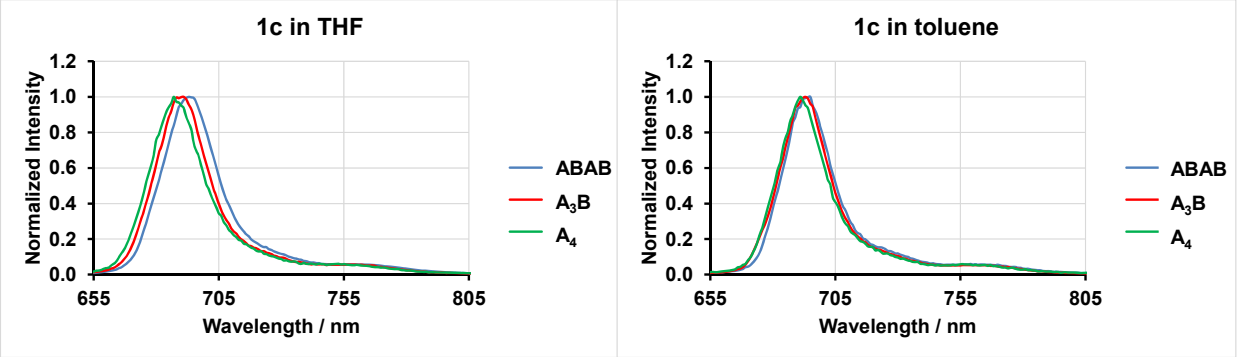

Figure S28. Emission spectra for ZnPcs **1c** in THF and toluene.

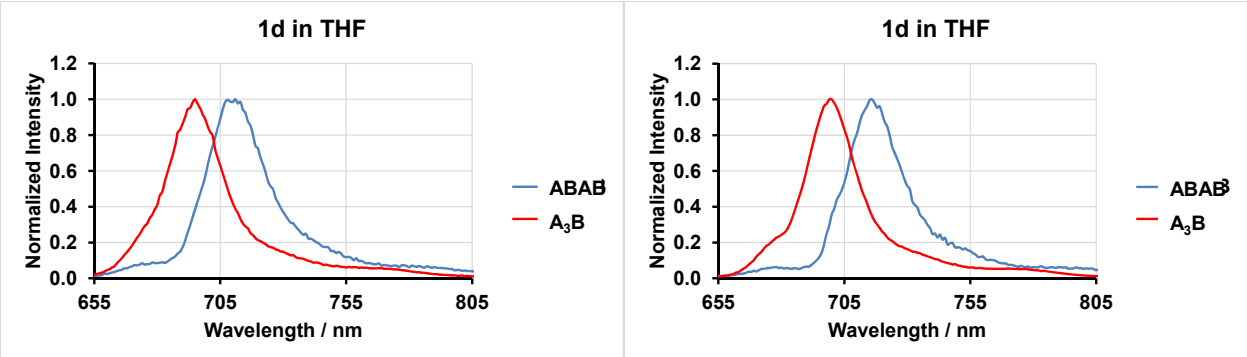

Figure S29. Emission spectra for ZnPcs **1d** in THF and toluene.

Fluorescence Quantum Yields

Fluorescent quantum yields (Φ_F) were determined by comparing the integrated fluorescent intensity of optically matched solutions between **1a-d** and ZnPc in 1-propanol (Φ_F = 0.20 ± 0.03). The original literature value for this solvent (Φ_F = 0.45) [1] was reassessed as it resulted in the sum of fluorescence and singlet oxygen quantum yields exceeding 1. To this end, ZnPc in DMSO (Φ_F = 0.20)[2] and ZnPc in toluene (Φ_F = 0.35)[3] were used as references. The samples were excited at: **ABAB** (THF), 638 (**1a**), 636 (**1b**), 630 (**1c**) and 632 nm (**1d**); **ABAB** (toluene), 644 (**1a**), 611 (**1b**), 632.5 (**1c**) and 634 nm (**1d**); **A_3B** (THF), 632 (**1a**), 635 (**1b**), 630.5 (**1c**) and 636 nm (**1d**); **A_3B** (toluene), 636 (**1a**), 634.5 (**1b**), 627.5 (**1c**) and 632 nm (**1d**); **A_4** (THF), 631.5 nm (**1c**); **A_4** (toluene), 629.5 nm (**1c**).

and fluorescence intensity was corrected using the refractive index of the solvents used (eq. 1).

$$\Phi_F = \frac{Area_{Sample} \cdot n^2{}_{Sample}}{Area_{Reference} \cdot n^2{}_{Reference}} \qquad (1)$$

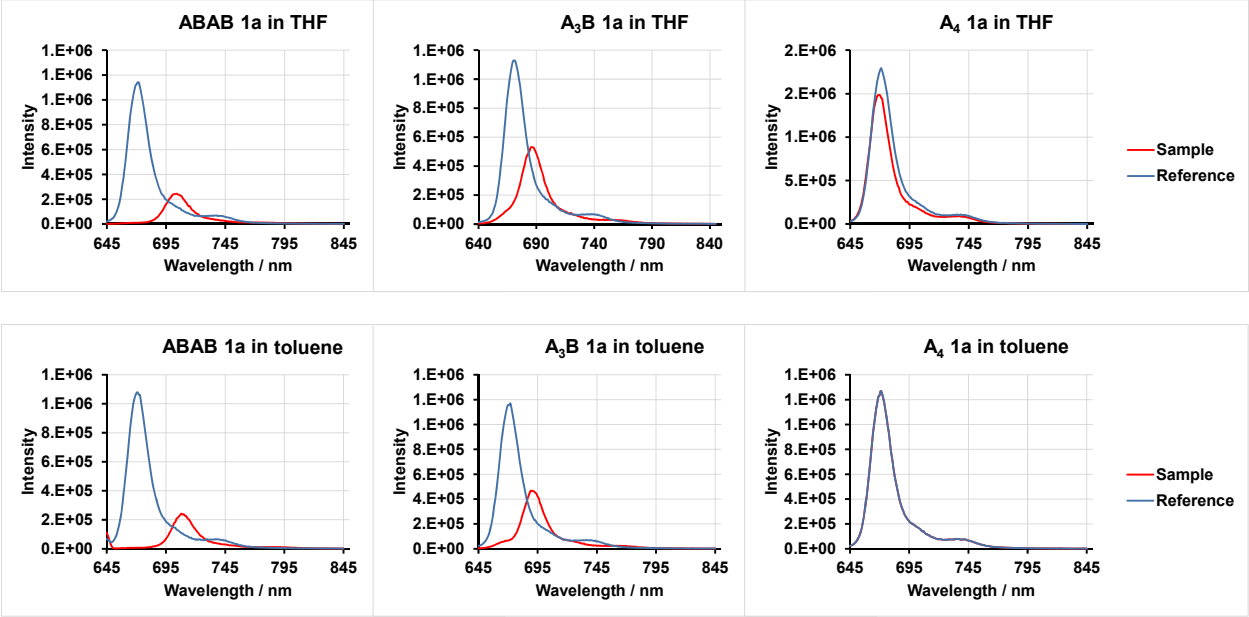

Figure S30. Compared fluorescence intensity for ZnPcs **1a** and the unsubstituted ZnPc reference in THF and toluene.

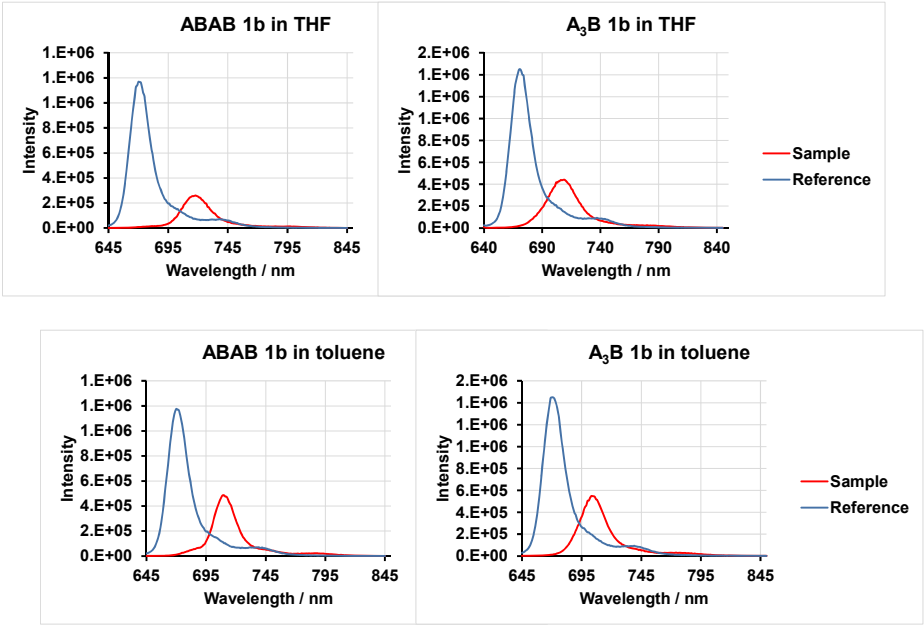

Figure S31. Compared fluorescence intensity for ZnPcs **1b** and the unsubstituted ZnPc reference in THF and toluene.

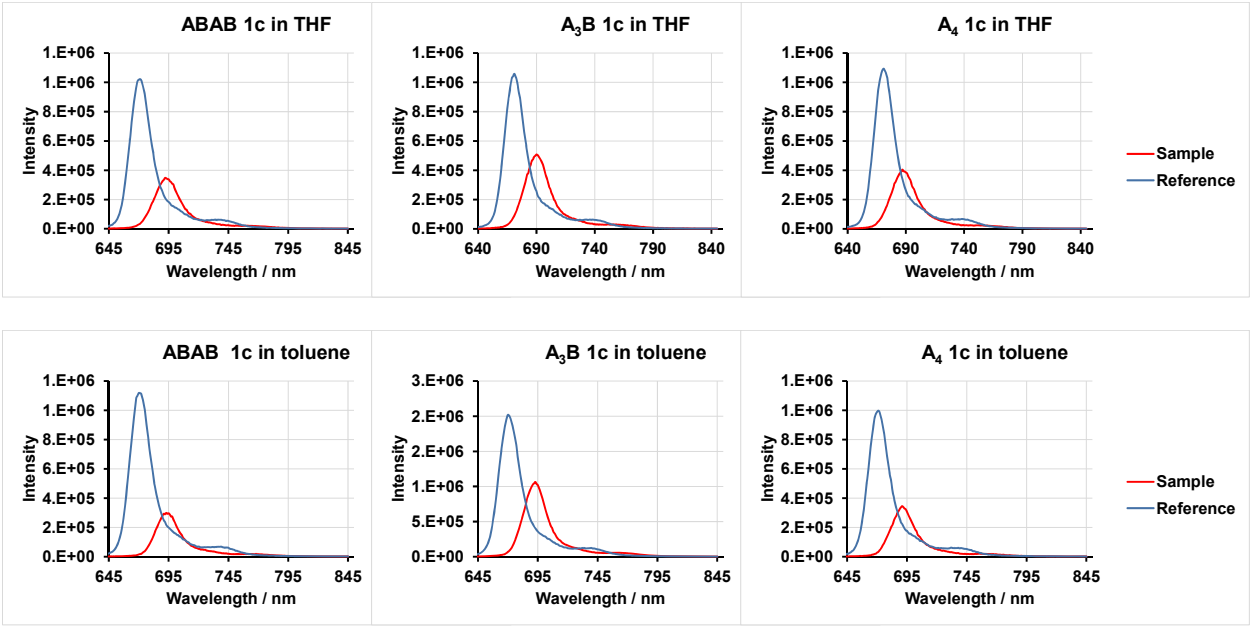

Figure S32. Compared fluorescence intensity for ZnPcs **1c** and the unsubstituted ZnPc reference in THF and toluene.

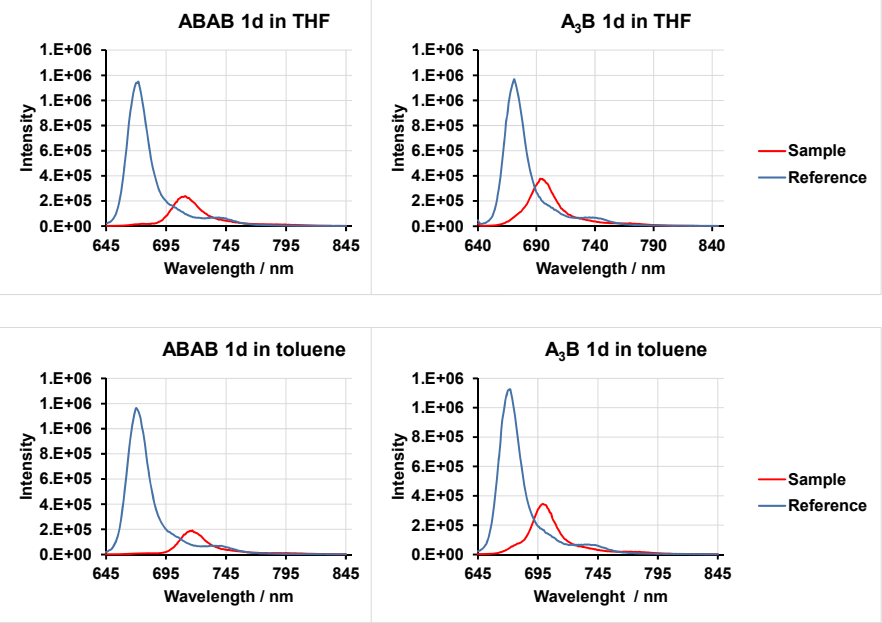

Figure S33. Compared fluorescence intensity for ZnPcs **1d** and the unsubstituted ZnPc reference in THF and toluene.

Singlet Oxygen Quantum Yields

Singlet oxygen generation was studied by time-resolved near-infrared phosphorescence by means of a customised setup.[4] Briefly, a pulsed Nd:YAG laser (FTSS355-Q, Crystal Laser, Berlin, Germany) working at 1 kHz repetition rate (for THF and toluene) or 10 kHz (DMSO) at 355 nm (third harmonic, 0.5 µJ per pulse) was used to excite the sample. A 1064-nm rugate notch filter (Edmund Optics) and an uncoated SKG-5 filter (CVI Laser Corporation) were placed in the laser path to remove any residual NIR emission. The light emitted by the sample was filtered with a 1100-nm long-pass filter (Edmund Optics) and later by a narrow bandpass filter at 1275 nm (BK-1270-70-B, bk Interferenzoptik). A thermoelectric-cooled NIR-sensitive photomultiplier tube assembly (H9170-45, Hamamatsu Photonics, Hamamatsu, Japan) was used as detector. Photon counting was achieved with a multichannel scaler (NanoHarp 250, PicoQuant, Berlin, Germany). The time dependence of the $^1O_2$ phosphorescence with the signal intensity $S(t)$ is described by Equation 2, in which τ_T and τ_Δ are the lifetimes of the photosensitizer triplet state and of $^1O_2$ respectively, and $S(0)$ is a pre-exponential parameter proportional to Φ_Δ.

$$S(t) = S(0) \times \frac{\tau_\Delta}{\tau_\Delta - \tau_T} \times \left(e^{-t/\tau_\Delta} - e^{-t/\tau_T} \right) \qquad (2)$$

Curve fitting was performed with the Graphpad Prism version 7.00 for Windows,(GraphPad Software, La Jolla California USA, www.graphpad.com). Φ_Δ was determined by comparing the $S(0)$ values of optically matched solutions of the drug and the reference (phenalenone (PN), in toluene and THF Φ_Δ = 0.99 and 0.96 respectively;[5] as described by Equation 3.

$$\Phi_{\Delta,\text{sample}} = \Phi_{\Delta,\text{ref}} \times \frac{S(0)_{Sample}}{S(0)_{ref}} \qquad (3)$$

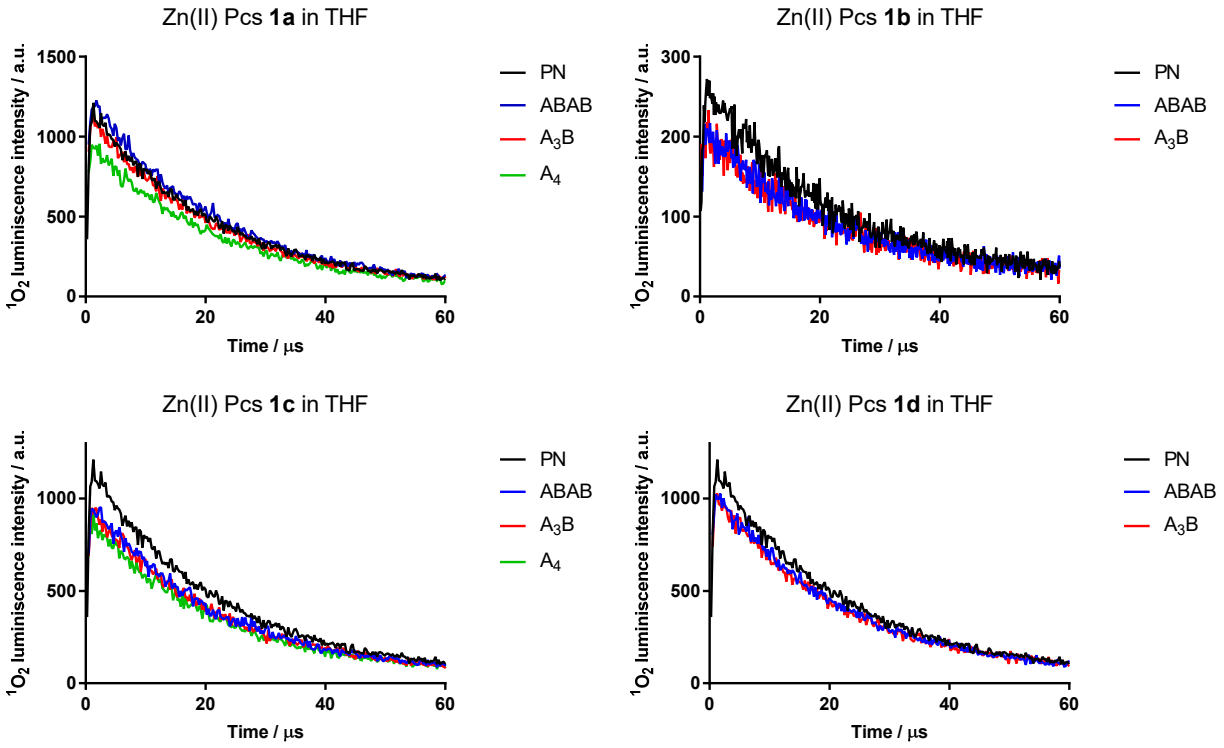

Figure S34. $^1O_2$ production of ZnPcs **1a-d** against phenalenone (PN) as reference in THF.

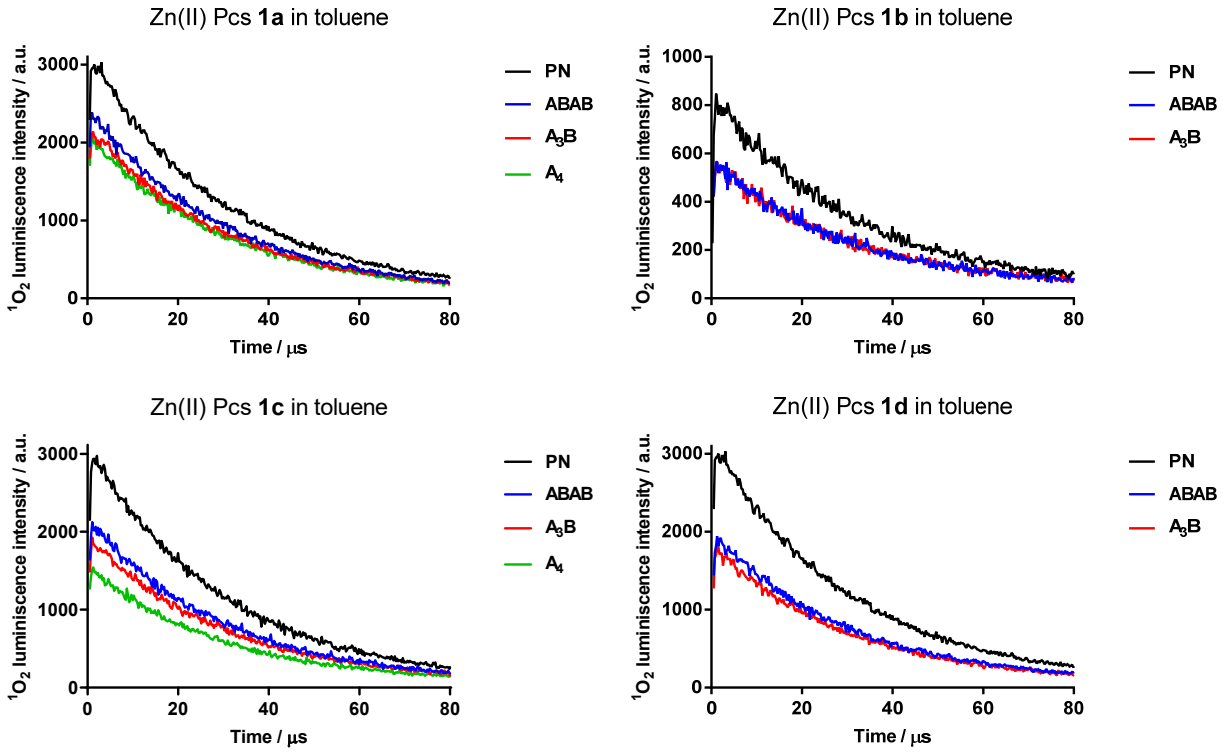

Figure S35. $^1O_2$ production of ZnPcs **1a-d** against phenalenone (PN) as reference in toluene.

Time-resolved fluorescence

Time-resolved fluorescence decays were measured using a Fluotime 200 time-correlated fluorescence lifetime spectrophotometer (PicoQuant, Berlin, Germany), equipped with a red sensitive photomultiplier. Excitation was achieved by means of a 654 nm picosecond laser working at 10 MHz repetition rate. The counting frequency was always below 1%. Fluorescence lifetimes were analyzed using PicoQuant FluoFit 4.0 data analysis software.

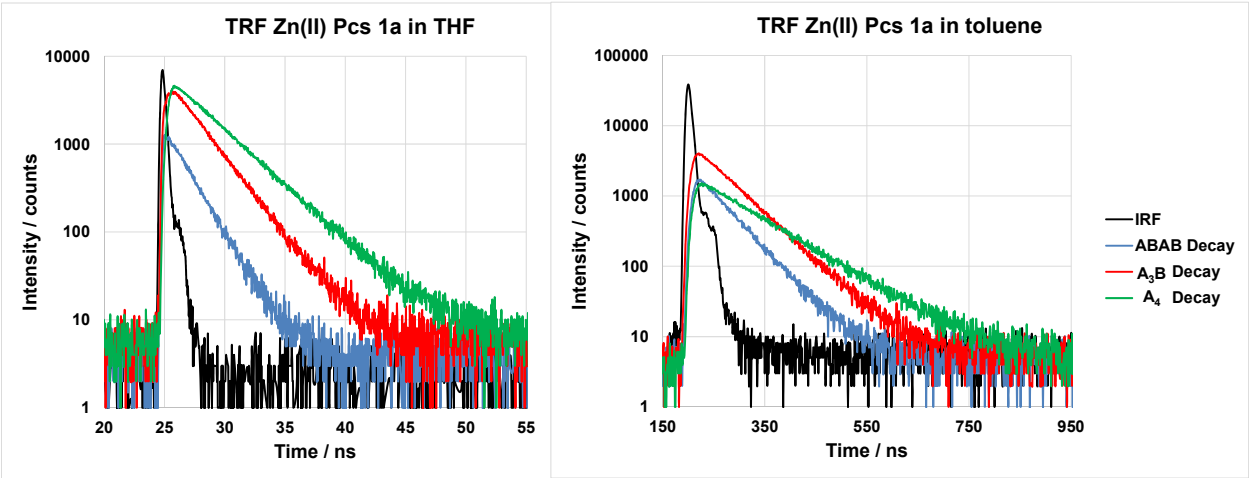

Figure S36. Time resolved fluorescence in THF and toluene for ZnPcs **1a**. IRF: Instrument response fluorescence (LUDOX®).

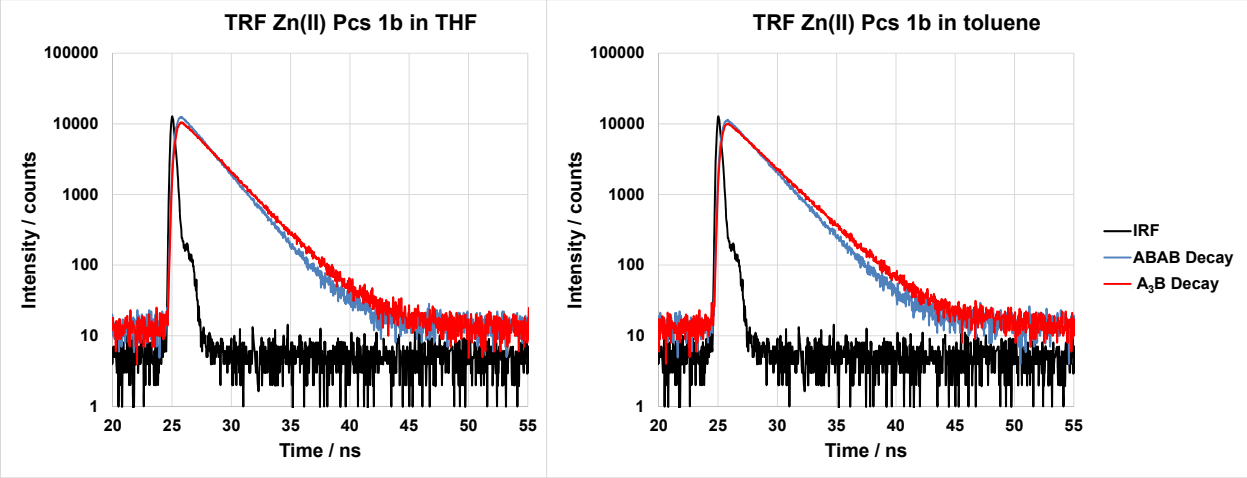

Figure S37. Time resolved fluorescence in THF and toluene for ZnPcs **1b**. IRF: Instrument response fluorescence (LUDOX®).

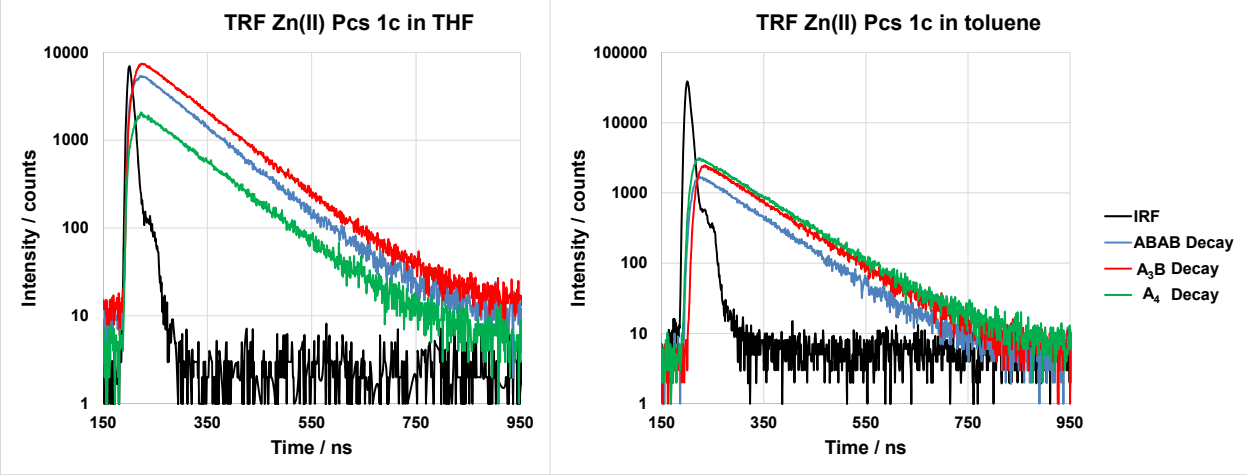

Figure S38. Time resolved fluorescence in THF and toluene for ZnPcs **1c**. IRF: Instrument response fluorescence (LUDOX®).

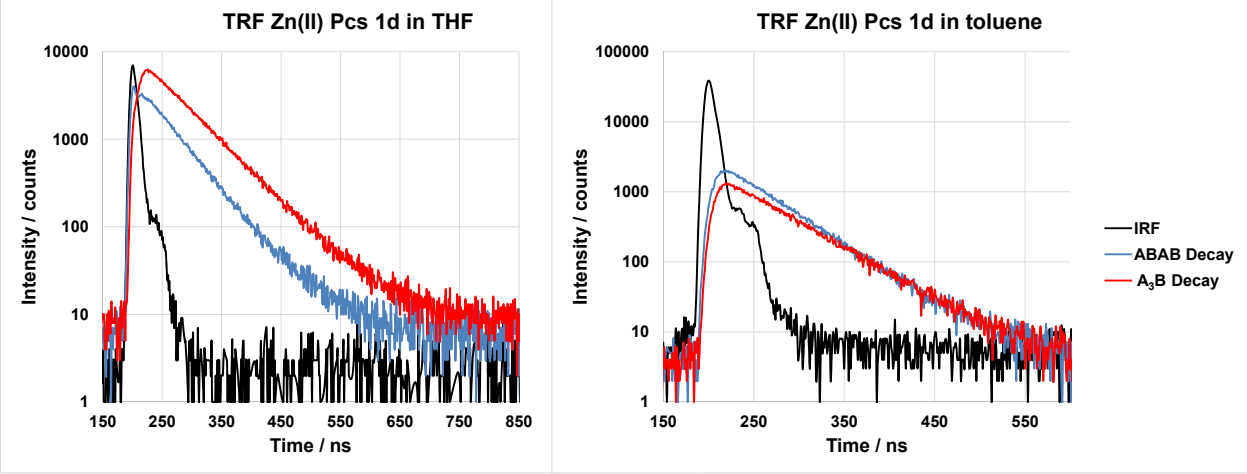

Figure S39. Time resolved fluorescence in THF and toluene for ZnPcs **1d**. IRF: Instrument response fluorescence (LUDOX®).

Octanol/water partition studies

Initially, equal volume of 1-octanol and water were mixed vigorously for 3 days at 25 °C to promote solvent saturation in both phases. Each ZnPc from family **1c** was then added to the mixture (for a range of concentration between 5.5 to 7.5·10^{-6}M) and stirred for 5min; next, after 30 minutes of incubation at room temperature, the UV–Vis spectra of both phases were recorded but only in the octanol (water saturated) phase the compounds were detected. The spectrum in dry 1-octanol was also registered for each ZnPc at the same concentrations for comparison with the spectra at the water-saturated phase.

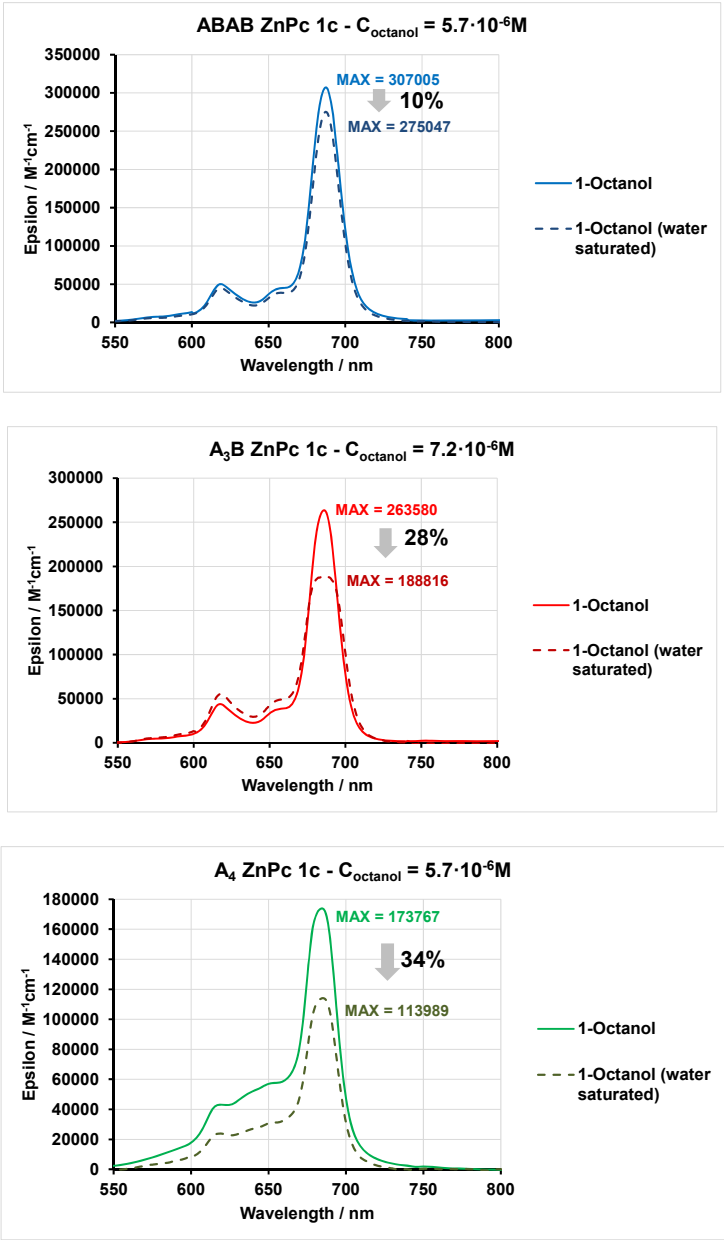

Figure S40. Absorption of **ABAB-1c**, **A_3B-1c** and **A_4-1c** in 1-octanol and in 1-octanol water-saturated.

References

[1] Gradyushko, A. T.; Sevchenko, A. N.; Solovyov, K. N.; Tsvirko, M. P. *Photochem. Photobiol.* **1970**, *11*, 387–400.

[2] Ogunsipe, A.; Maree, D.; Nyokong, T.. *J. Mol. Struct*. **2003**, *650*, 131-149

[3] Bishop, S.M.; Beeby, A.; Parker, A.W.; Foley, M.S.C.; Phillips, D. *J. Photochem. Photobiol. A: Chemistry* **1995**, *90*, 39-44

[4] a) Nonell, S.; Braslavsky, S. E. *Methods Enzymol.* **2000**, *319*, 37–49. b) Jiménez-Banzo, A.; Ragàs, X.; Kapusta, P.; Nonell, S. *Photochem. Photobiol. Sci.* **2008**, *7*, 1003–1010.

[5] a) Martí, C.; Jürgens, O.; Cuenca, O.; Casals, M.; Nonell, S. *J. Photochem. Photobiol. A Chem.* **1996**, *97*, 11–18. b) Schmidt, R.; Tanielian, C.; Dunsbach, R.; Wolff, C.; Womb, C. *J. Photochem. Photobiol. A Chem.* **1994**, *79*, 11–17.