

Solvent-dependent moulding of porphyrin-based nanostructures: solid state, solution and on surface self-assembly

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1. Materials and Methods

Chemicals were purchased in high purity from Sigma Aldrich, Fluorochem, Acros Organics and TCI Europe and were used as received, unless otherwise noted. Deuterated solvents were purchased from Cambridge Isotopes Laboratory and VWR International. Thin layer chromatography (TLC) was conducted on pre-coated aluminum sheets with 0.20 mm Macherey-Nagel Alugram SIL G/UV254 with fluorescent indicator UV254. Column chromatography was carried out using Merck Gerduran silica gel 60 (particle size 40-63 μm). All spectroscopic measurements in solution were carried out in fluorimetric 10.0 mm path cuvettes using spectroscopic grade solvents UV-Vis spectra were recorded on a Varian Cary 5000 spectrometer. Fluorescence spectra were recorded with a Varian spectrophotometer (model Cary Eclipse).

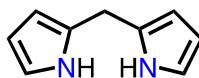
NMR data were collected on a Varian Unity Inova operating at 500 MHz or 126 MHz for ^1H and ^{13}C , respectively. NMR spectra were referenced internally to residual solvent peaks (chloroform-d $\delta = 7.26$ ppm ^1H and $\delta = 77.23$ ppm for ^{13}C ; tetrahydrofuran-d8 $\delta = 3.58$ and 1.73 ppm for ^1H and $\delta = 67.57$ and 25.37 ppm for ^{13}C).

Mass spectrometry Electrospray Ionization (EI) mass analysis was performed on a Perkin-Elmer by Analytical Services at the School of Chemistry – Cardiff University.

Melting Points (m.p.) were measured on a Büchi SMP-20 and are uncorrected.

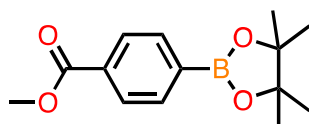
AFM samples were prepared by spin coating (3000 rpm, 30 sec) onto a freshly cleaved mica surface. AFM measurements were carried out in air at room temperature by using a Nanoscope IIIa (Digital Instruments Metrology Group, USA) instrument, model MMAFMLN. The collected images were then analyzed with WsXm 4.0 software (Nanotec Electronica S. L.), and Gwyddion 2.39.

2. Synthesis



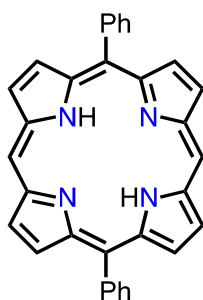
Dipyrrromethane (2). Synthesised according to a blend of literature procedure.^{1,2} A suspension of paraformaldehyde (1.9 g, 62.0 mmol) in freshly distilled pyrrole (100.0 mL, 1.4 mol) was degassed for about 10 minutes at room temperature. The mixture was heated at 70 °C until a clear solution was obtained. TFA (1.2 mL, 16.2 mmol) was then added, and the mixture was stirred at 70 °C for 2 hours. The heat source was removed and the reaction was quenched with 0.5 M NaOH. CH₂Cl₂ was added and the organic phase was washed with water, dried (Na₂SO₄) and removed under reduced pressure. The excess of pyrrole was recovered by distillation and the dark crude solid was purified by column chromatography (Pet. Et./EtOAc 85:15) to obtain the product as crystalline white solid (4.6 g, 51 % yield).

m.p. 69-70 °C. ¹H-NMR (500 MHz, Chloroform-*d*): δ 7.82 (bs, 2H), 6.72 – 6.57 (m, 2H), 6.19 – 6.12 (m, 2H), 6.04 (s, 2H), 3.97 (s, 2H). ¹³C-NMR (126 MHz, Chloroform-*d*): δ 129.19, 117.41, 108.51, 106.53, 26.52. IR (KBr): cm⁻¹ 3336, 3086, 2960, 2897, 1715, 1656, 1583, 1561, 1471, 1439, 1421, 1397, 1328, 1267, 1245, 1227, 1182, 1120, 1109, 1096, 1026, 962, 886, 857, 798, 749, 734, 724, 684, 665, 587. MS (ES +): found 146.08 (M⁺), C₉H₁₀N₂ requires 146.08.



Methyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (3). Synthesised according to a slightly modified literature procedure.³ A mixture of methyl 4-bromobenzoate (2.0 g, 9.30 mmol), bis(pinacolato)diboron (2.8 g, 11.16 mmol) and KOAc (2.7 g, 27.9 mmol) in toluene (30 mL) was degassed for about 20 minutes under Ar. Pd(dppf)Cl₂ (0.34 g, 0.46 mmol, 5 % mmol) was added, the flask was sealed and the mixture was heated at 90 °C for 2 hours. The mixture was quenched with 1 M aq. NH₄Cl, extracted with CH₂Cl₂, the organic phase washed with water, dried (Na₂SO₄) and removed under reduced pressure. The crude was purified by column chromatography (Pet. Et./ EtOAc 95:5) to obtain the product as white solid (1.8 g, 91 % yield).

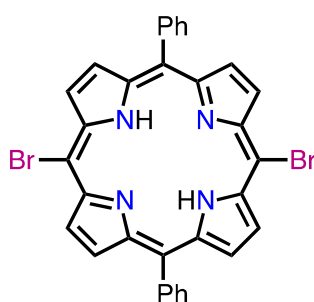
m.p. 78-79 °C. ¹H-NMR (500 MHz, Chloroform-*d*): δ 8.02 (d, *J* = 8.2 Hz, 2H), 7.87 (d, *J* = 8.1 Hz, 2H), 3.92 (s, 3H), 1.35 (s, 12H). ¹³C-NMR (126 MHz, Chloroform-*d*): δ 167.28, 134.80, 132.45, 128.74, 84.33, 52.29, 25.03. IR (KBr): cm⁻¹ 2986, 1724, 1509, 1435, 1398, 1372, 1361, 1327, 1278, 1141, 1110, 1018, 962, 857, 773, 710, 652. MS (ES +): found 263.12 (M + H⁺), C₁₄H₁₉BO₄ requires 262.14.



5,15-Diphenylporphyrin (4). Synthesised according to a modified literature

procedure.² A solution of dipyrromethane (1.10 g, 7.52 mmol) and benzaldehyde (0.80 mL, 7.90 mmol) in dry CH₂Cl₂ (1.50 L) was deoxygenated by bubbling Ar for 60 minutes. TFA (0.13 mL, 1.67 mmol) was added dropwise and the mixture was stirred overnight at room temperature, under dark. DDQ (5.18 g, 22.83 mmol) was added and the mixture was refluxed for 2 hours. Et₃N (0.5 mL) was added and the mixture was concentrated under reduced pressure. The solution was passed through a silica plug (CH₂Cl₂) and the crude was purified by column chromatography (Pet. Et./CH₂Cl₂ 4:1) to obtain product as purple crystals (0.85 g, 49 % yield).

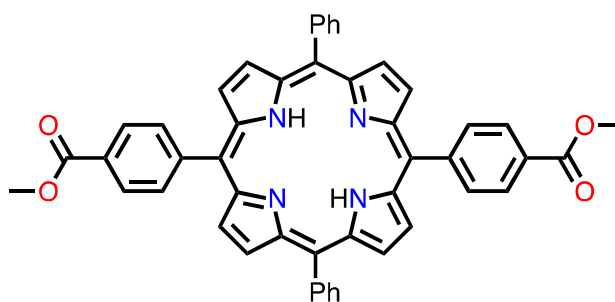
m.p. > 250 °C. ¹H-NMR (500 MHz, Chloroform-*d*): δ 10.32 (s, 2H), 9.40 (d, *J* = 4.5 Hz, 4H), 9.09 (d, *J* = 4.5 Hz, 4H), 8.34 – 8.24 (m, 4H), 7.82 (dd, *J* = 4.9, 1.8 Hz, 6H). ¹³C-NMR (126 MHz, Chloroform-*d*) δ 147.33, 145.36, 141.54, 135.00, 131.76, 131.20, 127.87, 127.12, 119.25, 105.41. IR (KBr): cm⁻¹ 1594, 1580, 1532, 1483, 1438, 1416, 1238, 1197, 1178, 1147, 1066, 1052, 1002, 987, 973, 957, 860, 850, 796, 787, 749, 719, 690. MS (ES +): found 463.15 (M + H⁺), C₃₂H₂₂N₄ requires 462.18.



5,15-Dibromo-10,20-diphenylporphyrin (5). Synthesised according to literature procedure.⁴ To a solution of 5,15-Diphenylporphyrin **4** (200 mg, 0.43 mmol) in CHCl₃ (100 mL) at 0 °C was added pyridine (1.0 mL) and N-bromosuccinimide (154 mg, 0.85 mmol). The reaction was followed by TLC (Pet. Et./CH₂Cl₂ 1:1) and was quenched with acetone (10 mL) after 15 minutes. The solvent was removed under reduced

pressure, the crude was passed through a silica plug (Pet. Et./CH₂Cl₂ 1:1) and finally washed with MeOH to obtain product as reddish purple crystals (223 mg, 84 % yield).

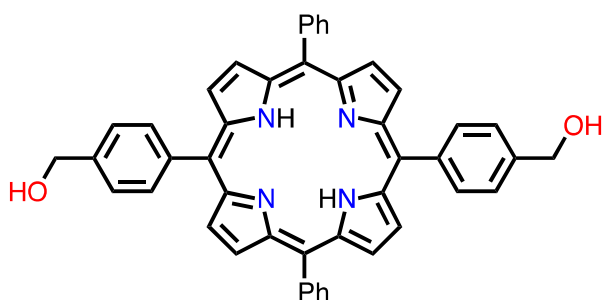
m.p. > 250 °C. **¹H-NMR** (500 MHz, Chloroform-*d*): δ 9.86 (d, *J* = 4.8 Hz, 3H), 9.08 (s, 3H), 8.48 – 8.34 (m, 4H), 8.03 (s, 6H). **¹³C-NMR** (126 MHz, Chloroform-*d*): δ 141.61, 134.73, 128.28, 127.05, 121.64, 103.9; 4 signals missing due to low solubility. **IR** (KBr): cm⁻¹ 1597, 1558, 1464, 1440, 1350, 1334, 1269, 1243, 1192, 1174, 1072, 1056, 997, 979, 961, 844, 794, 784, 737, 730, 706, 695. **MS** (ES +): found 619.01 (M + H⁺), C₃₂H₂₀Br₂N₄ requires 618.01.



5,15-Bis(4-methoxycarbonylphenyl)-10,20-diphenylporphyrin (6). Synthesised according to a modified literature procedure.⁵ To a solution of porphyrin **5** (0.10 g, 0.16 mmol) in anhydrous THF (35 mL) was added boronate ester **3** (0.85 g, 3.22 mmol) and K₃PO₄ (1.36 g, 6.40 mmol). The mixture was degassed with a ‘freeze-pump-thaw’ cycle. Pd(PPh₃)₄ (36 mg, 0.03 mmol, 20 % mmol) was added and the mixture was degassed once again. The mixture was refluxed at 85 °C overnight, under dark. The reaction mixture was cooled down and filtered over celite (with aid of CH₂Cl₂). The solvents were removed under reduced pressure and the crude was purified by column chromatography (Pet. Et./EtOAc 95:5) to obtain the pure product as purple solid (80 mg, 91 % yield).

m.p. > 250 °C. **¹H-NMR** (500 MHz, Chloroform-*d*): δ 8.87 (d, *J* = 4.8 Hz, 4H), 8.80 (d, *J* = 4.8 Hz, 4H), 8.45 (d, *J* = 8.2 Hz, 4H), 8.31 (d, *J* = 8.2 Hz, 4H), 8.24 – 8.20 (m, 4H),

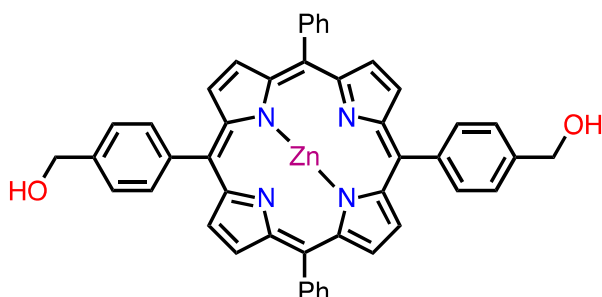
7.82 – 7.69 (m, 6H), 4.12 (s, 6H). $^{13}\text{C-NMR}$ (126 MHz, Chloroform-*d*): δ 167.53, 147.15, 142.12, 134.88, 134.77, 134.74, 129.85, 128.81, 128.14, 128.08, 126.97, 120.82, 119.16, 52.66. **IR** (KBr): cm^{-1} 1720, 1606, 1558, 1474, 1435, 1400, 1350, 1311, 1276, 1213, 1178, 1110, 1099, 1019, 1001, 981, 964, 878, 866, 800, 754, 731, 702. **MS** (ES +): found 731.22 ($\text{M} + \text{H}^+$) and 753.20 ($\text{M} + \text{Na}^+$), $\text{C}_{48}\text{H}_{34}\text{N}_4\text{O}_4$ requires 730.26.



5,15-Bis(4-hydroxymethylphenyl)-10,20-diphenylporphyrin (1). To a solution of porphyrin **6** (70.0 mg, 0.10 mmol) in dry THF (10.0 mL) was added dropwise a suspension of LiAlH_4 (4.6 mg, 0.12 mmol) in dry THF (5.0 mL) at 0 °C. The mixture was left to warm up to room temperature and was left stirring for 60 minutes. The mixture was cooled back to 0 °C and the reaction was quenched with MeOH. The mixture was concentrated under reduced pressure, diluted with CHCl_3 , the organic phase was washed with H_2O , dried (Na_2SO_4) and eliminated under reduced pressure. The crude was purified by column chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH}$ 98:2) to obtain pure product was purple solid (59 mg, 88 % yield).

m.p. > 240 °C. $^1\text{H-NMR}$ (500 MHz, THF-*d*₈): δ 8.88 – 8.69 (m, 8H), 8.21 (dd, $J = 7.3$, 2.0 Hz, 4H), 8.16 (d, $J = 8.0$ Hz, 4H), 7.84 – 7.65 (m, 10H), 4.94 (d, $J = 5.6$ Hz, 4H), 4.51 (t, $J = 5.8$ Hz, 2H), -2.68 (bs, 2H). $^{13}\text{C-NMR}$ (126 MHz, THF-*d*₈): δ 143.68, 143.36, 141.59, 135.33, 135.18, 128.62, 127.60, 125.64, 121.11, 120.93, 64.89. **IR** (KBr): cm^{-1} 3435, 3308, 1597, 1474, 1442, 1401, 1349, 1215, 1185, 1014, 1002, 981,

966, 878, 853, 797, 755, 733, 700. **MS** (ES +): found 675.27 (M + H⁺) and 697.26 (M + Na⁺), C₄₆H₃₄N₄O₂ requires 674.27.



{5,15-Bis(4-hydroxymethylphenyl)-10,20-diphenylporphyrinato(2-)-κN²¹, ηηN²²,κ

N²³, ηηN²⁴}-zinc(II) (1·Zn). To a vigorously stirred solution of free base porphyrin **1**

(50.0 mg, 0.07 mmol) in CHCl₃ (10.0 mL) was added dropwise a solution of Zn(OAc)₂·H₂O (162.7 mg, 0.74 mmol) in MeOH (3.0 mL) and the mixture was stirred at room temperature, in the dark. After 2 hours, the organic phase was diluted with CHCl₃ and was washed with H₂O, dried (Na₂SO₄) and removed under reduced pressure. Finally, the porphyrin was crystallised from THF/hexane to obtain the desired product as purple crystals (53 mg, quant.).

m.p. > 250 °C. **¹H-NMR** (500 MHz, THF-*d*₈): δ 8.86 (d, *J* = 4.6 Hz, 4H), 8.83 (d, *J* = 4.6 Hz, 4H), 8.20 (dd, *J* = 7.3, 2.0 Hz, 4H), 8.15 (d, *J* = 7.9 Hz, 4H), 7.79 – 7.69 (m, 10H), 4.94 (d, *J* = 5.7 Hz, 4H), 4.48 (t, *J* = 5.9 Hz, 2H). **¹³C-NMR** (126 MHz, THF-*d*₈): δ 151.15, 150.99, 144.66, 143.11, 142.94, 135.37, 135.18, 132.24, 132.14, 128.11, 127.20, 125.30, 121.58, 121.43, 65.00. **IR** (KBr): cm⁻¹ 3435, 1595, 1522, 1485, 1440, 1204, 1120, 1067, 995, 904, 797, 719, 703. **MS** (ES +): found 736.18 (M⁺), C₄₆H₃₂N₄O₂Zn requires 736.18.

3. Characterisations

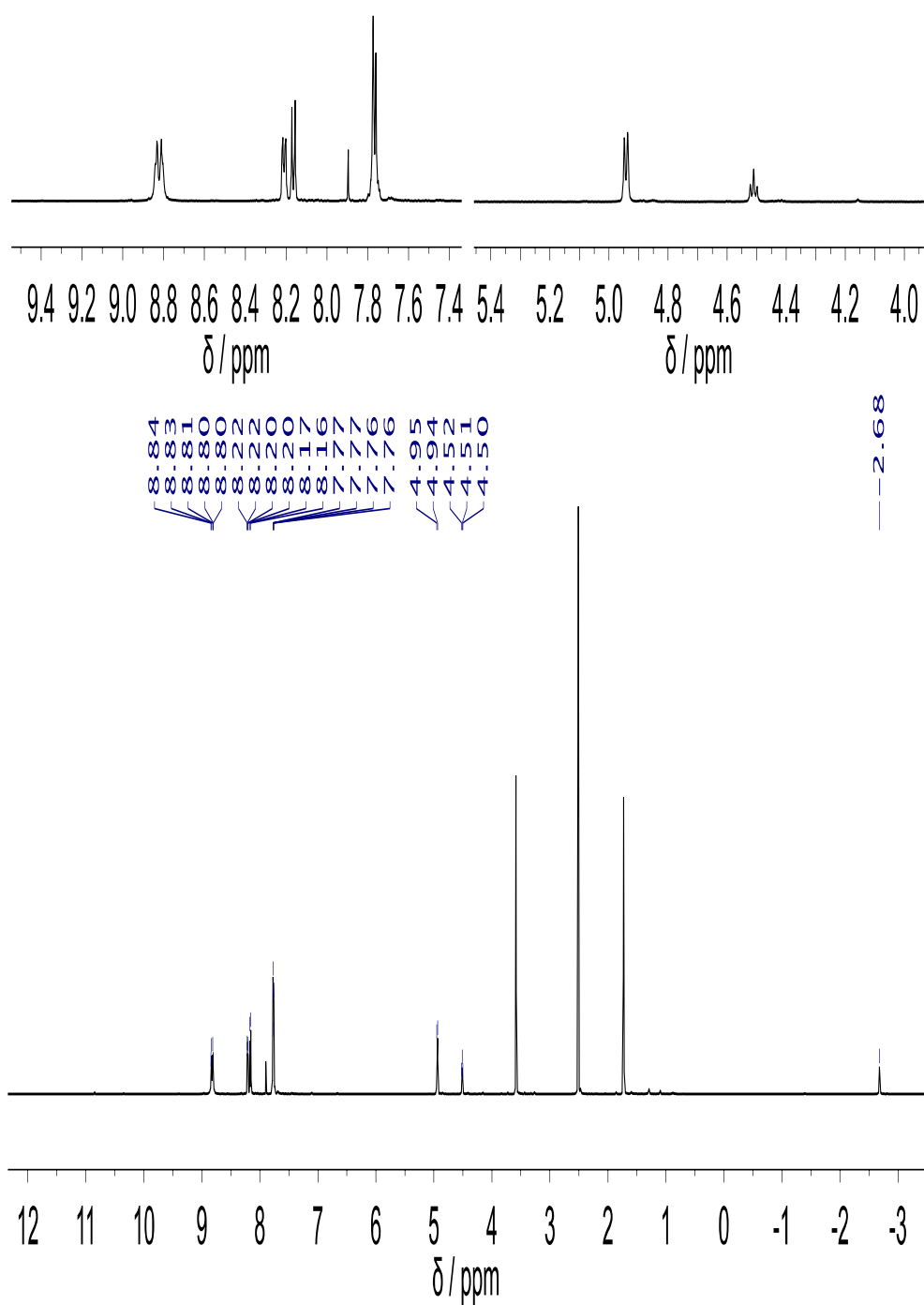


Figure S1. ¹H-NMR (500 MHz, THF-d₈) of porphyrin **1**.

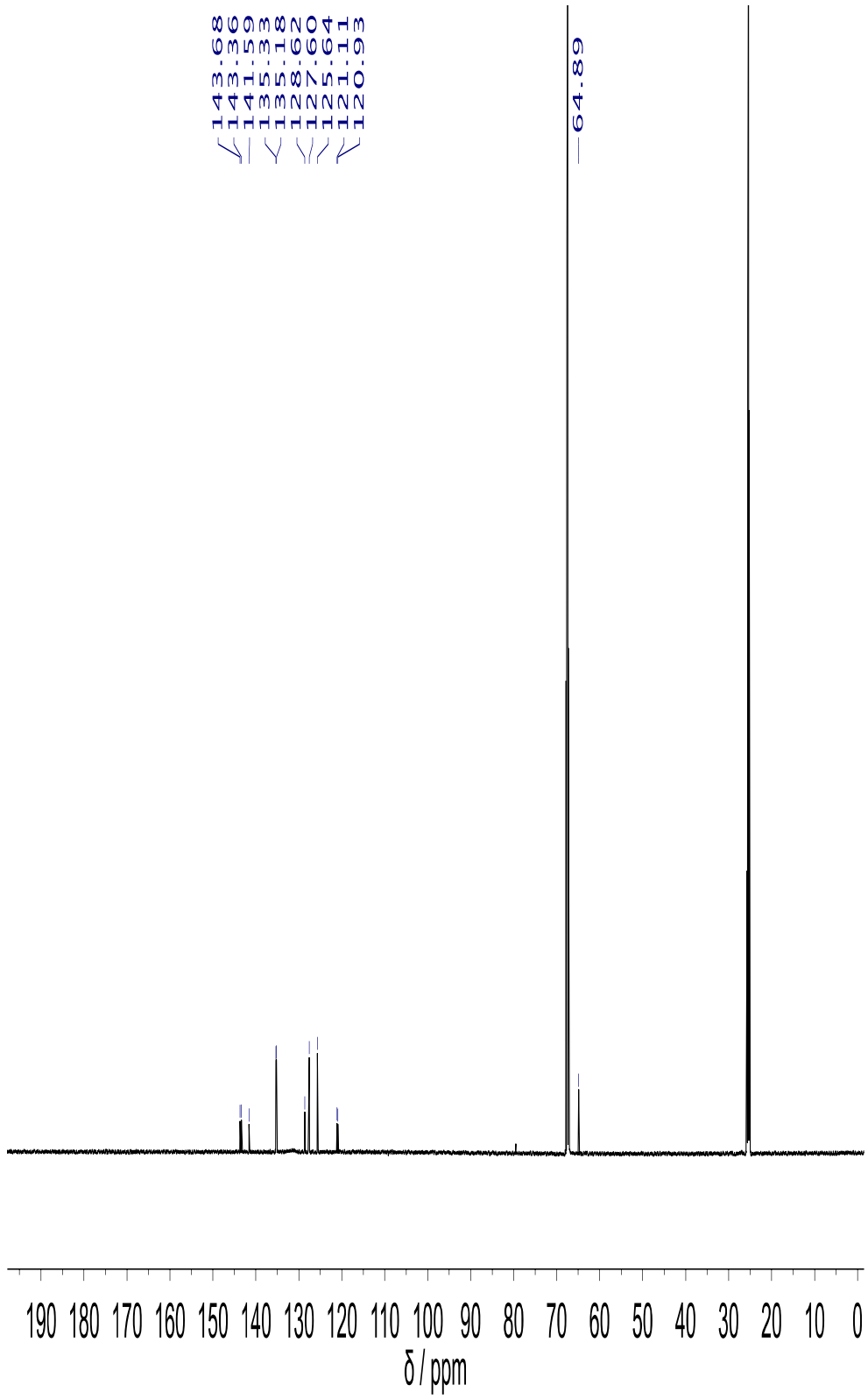


Figure S2. ^{13}C -NMR (126 MHz, THF-d_8) of porphyrin **1**.

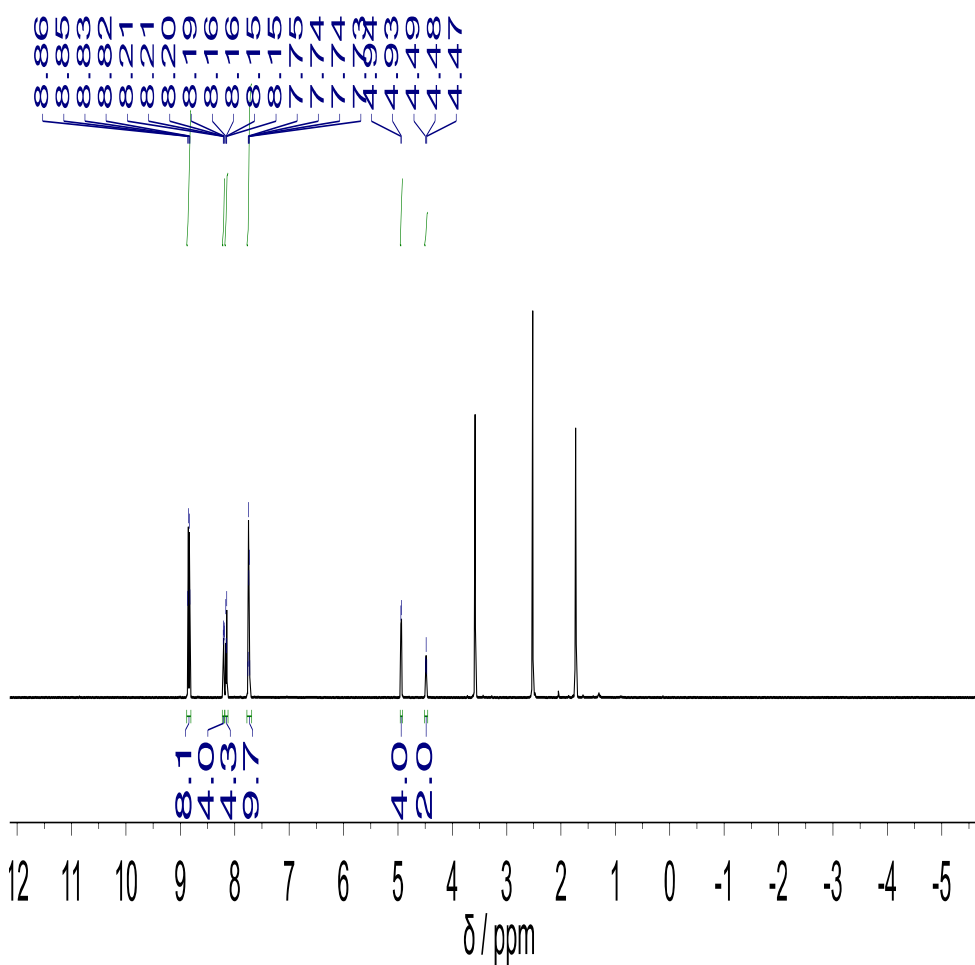
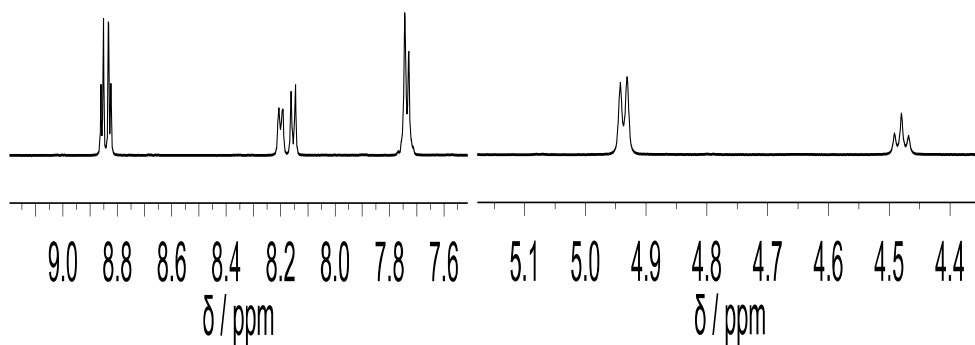


Figure S3. ^1H -NMR (500 MHz, THF-d_8) of porphyrin **1**·**Zn**.

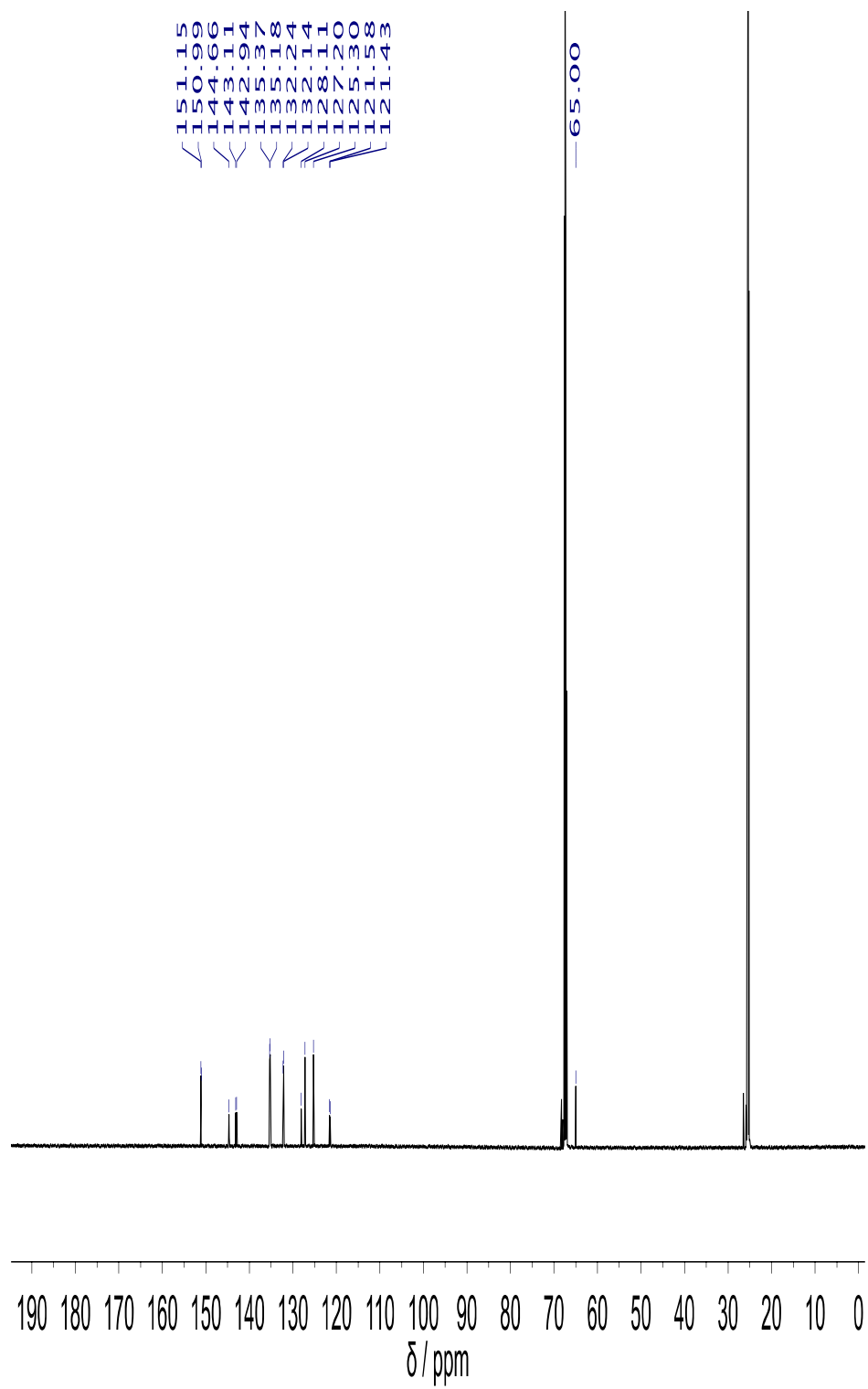


Figure S4. ^{13}C -NMR (126 MHz, THF- d_8) of porphyrin **1**·Zn.

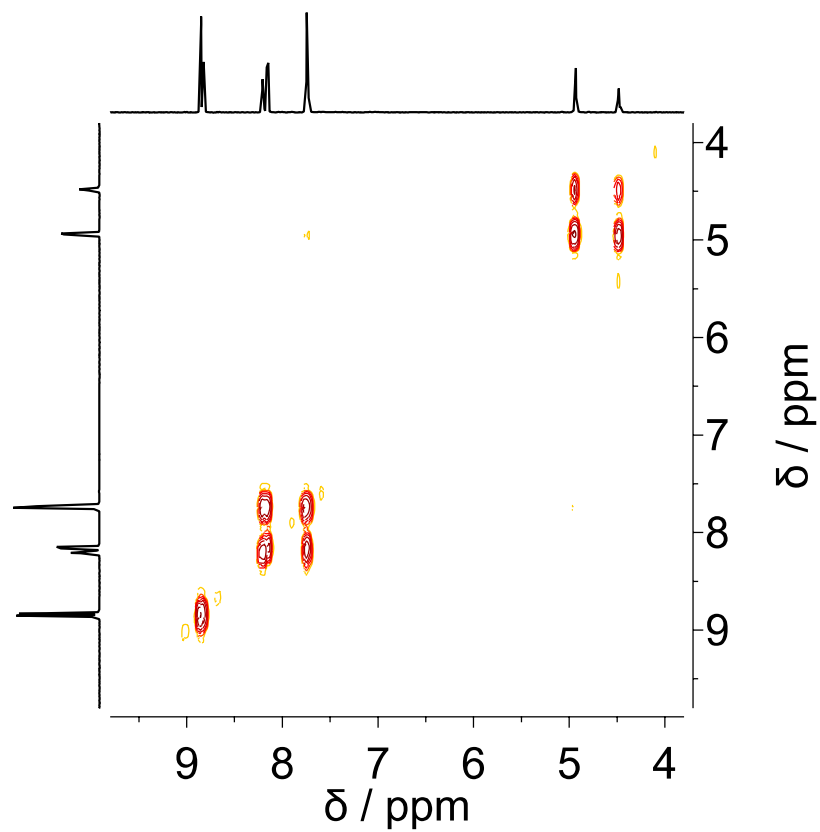


Figure S5. HH-NMR (gCOSY, 500 MHz, THF-d₈) of porphyrin **1·Zn**.

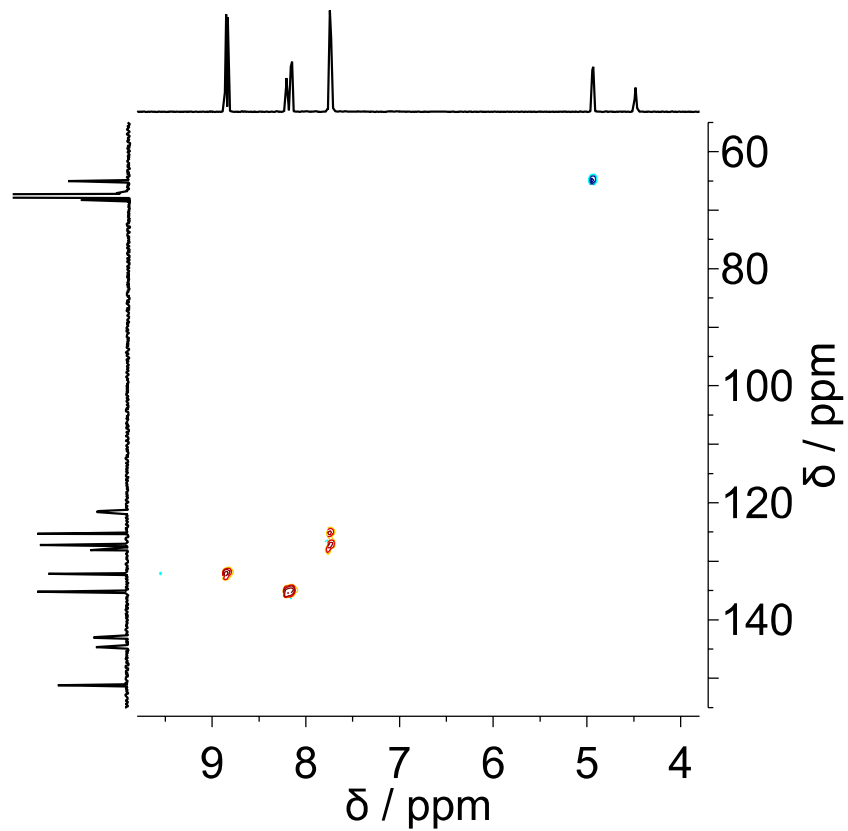


Figure S6. ¹H-¹³C single quantum correlation (HSQC) spectra of porphyrin **1·Zn**.

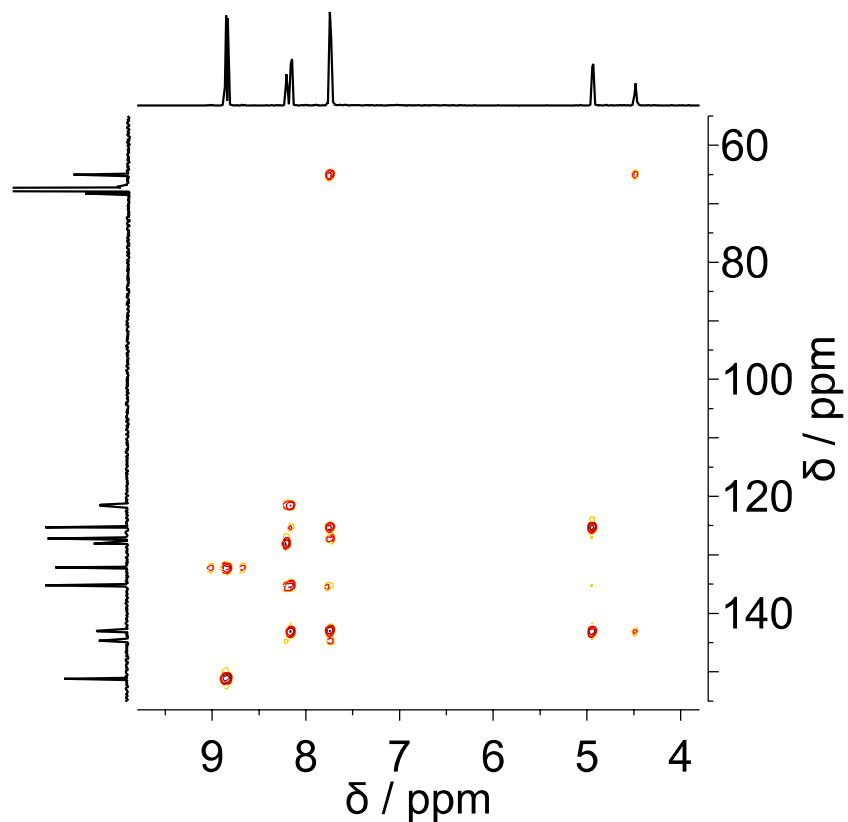


Figure S7. ^1H - ^{13}C multiple bond correlations (gHMBCAD) spectra of porphyrin **1**·**Zn**.

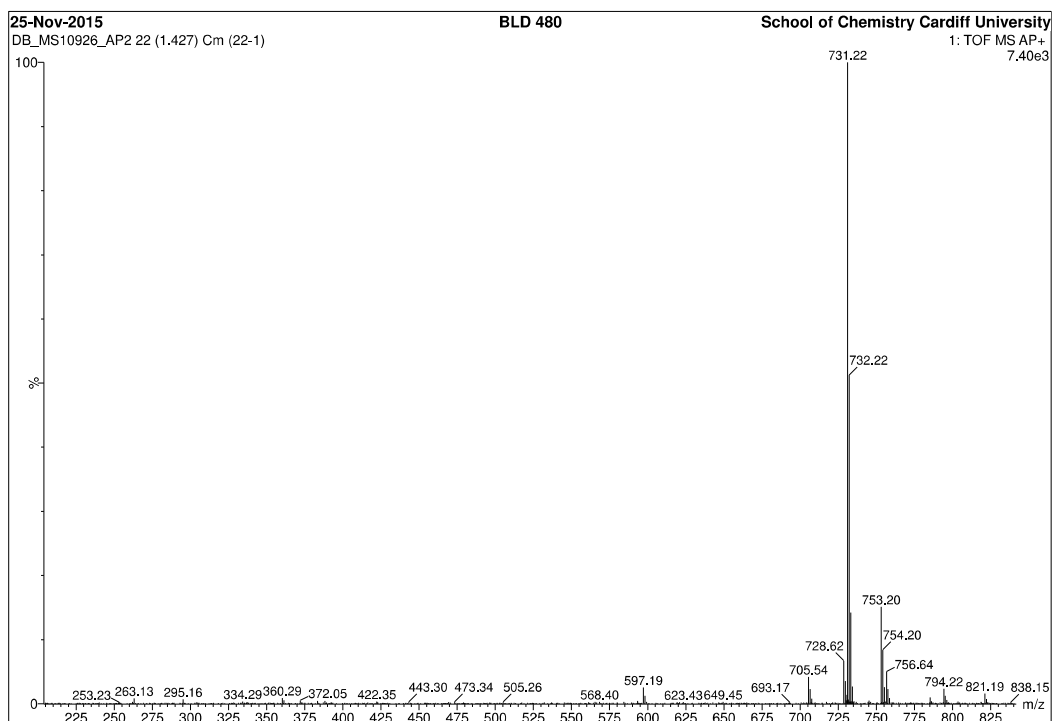


Figure S8. ES-MS of porphyrin **1**.

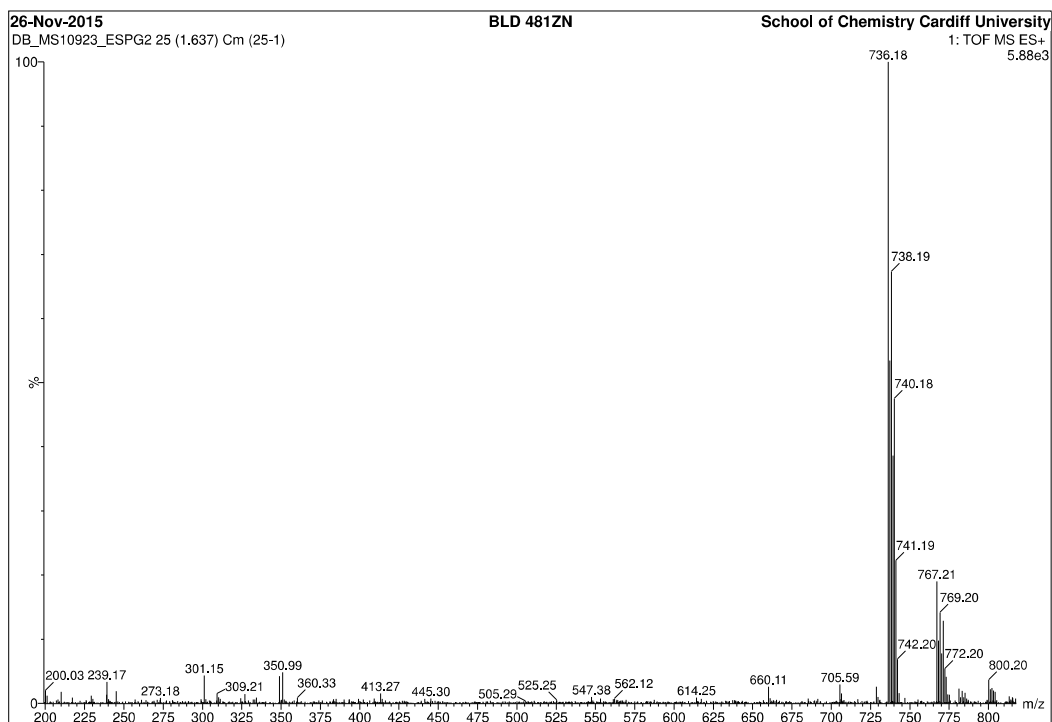


Figure S9. ES-MS of porphyrin 1·Zn.

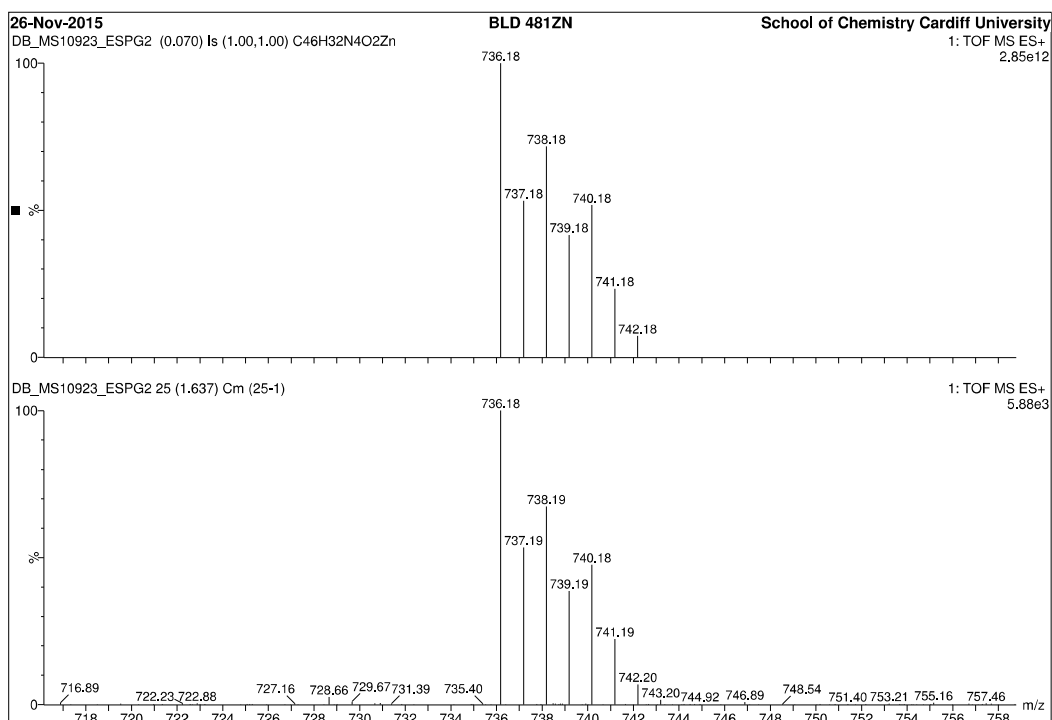


Figure S10. ES-MS of porphyrin 1·Zn (zoom).

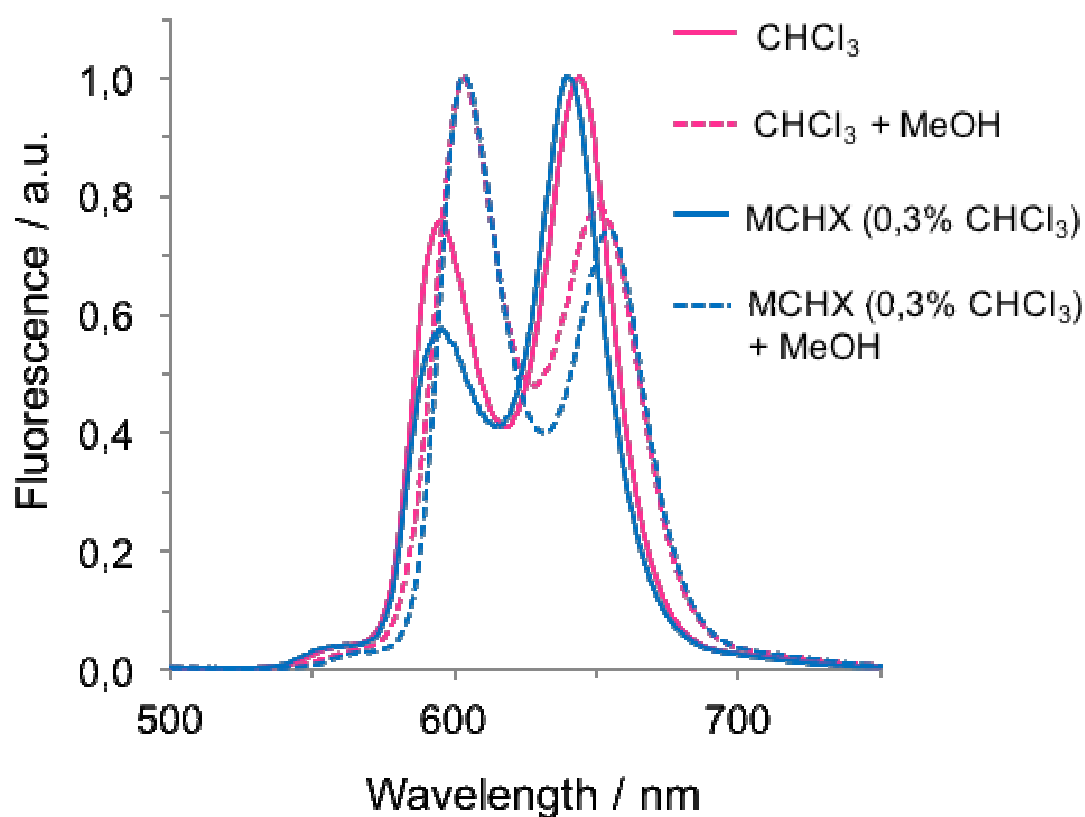


Figure S11. Fluorescence profiles of **1·Zn** before and after the addition of MeOH, a polar protic solvent.

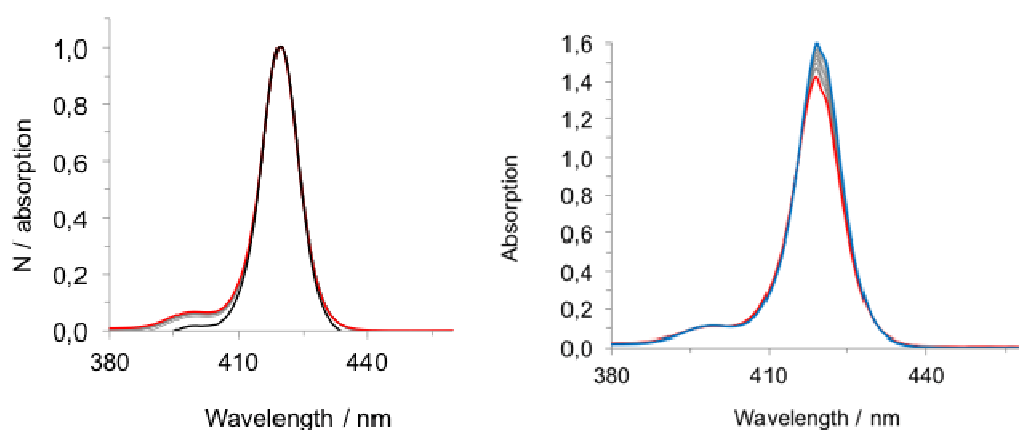


Figure S12. Concentration- (left) and temperature- dependent UV-Vis profiles of **1·Zn** in CHCl₃.

MCHX (<1% CHCl₃)

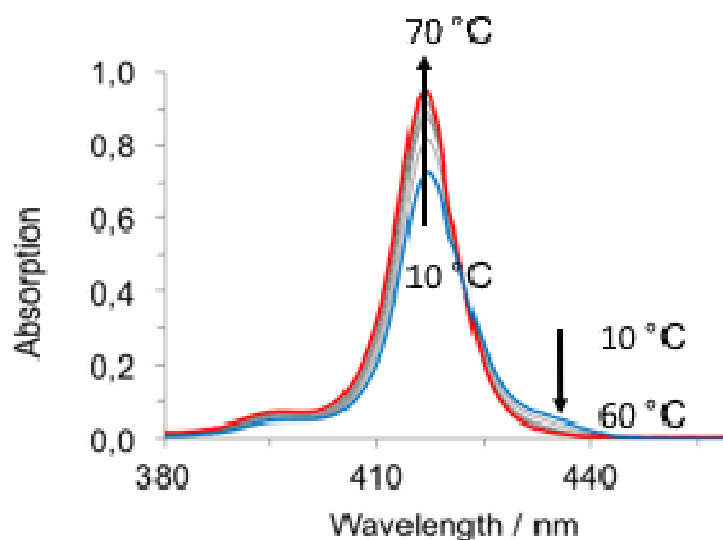


Figure S13. Temperature- depended UV-Vis profiles of **1·Zn** in MCH (0.3% CHCl₃).

4. Crystallographic data

Data collections were performed at the X-ray diffraction beamline (XRD1) of the Elettra Synchrotron, Trieste (Italy), with a Pilatus 2M image plate detector. Complete datasets were collected at 100 K (nitrogen stream supplied through an Oxford Cryostream 700) with a monochromatic wavelength of 0.700 Å through the rotating crystal method. The crystals of **1** and **1·Zn** were dipped in N-paratone and mounted on the goniometer head with a nylon loop. The diffraction data were indexed, integrated and scaled using XDS.⁶ For each sample, complete datasets have been obtained merging two data collections obtained from different orientations of the same crystal. The structures were solved by direct methods using SIR2014,⁷ Fourier analysed and refined by the full-matrix least-squares based on F^2 implemented in SHELXL-2014.⁸ The Coot program was used for modeling.⁹ Anisotropic thermal motion was then applied to all atoms excluding disordered THF solvent molecules, in **1** model. Hydrogen atoms were included at calculated positions with isotropic $U_{\text{factors}} = 1.2 U_{\text{eq}}$ or $U_{\text{factors}} = 1.5 U_{\text{eq}}$ for methyl

and hydroxyl groups. Restrain on bond lengths, angles and thermal motion (DFIX, DANG, SIMU and/or DELU) have been applied for poorly defined THF solvent molecules.

Both **1** and **1·Zn** crystal forms obtained showed twinning: 2-component inversion twin for **1** and 4-component inversion twin for **1·Zn**. Enantiomorphic domains in **1** model show a ‘not perfect’ 70%:30% population.

Pseudo-merohedral twin law has been identified in **1·Zn** data, using COSET program,¹⁰ as a 90° roto-inversion about (010) direct lattice direction. This relation is consistent with a monoclinic unit cell with tetragonal supergroup's symmetry metrically available ($a \approx c$ and $\beta \approx 90^\circ$). Population of the four domains has been refined, using Shelxl BASF command, and appear to be evenly distributed (~20-30%).

One full and two half porphyrin molecules have been found in crystal **1** asymmetric unit (ASU) (Figure 1S): crystallographic inversion centres lying in the middle of the partial moieties generate the complete molecules. A chiral helicoidal arrangement of hydrogen bonds connects 32 neighbour porphyrins ($d_{O-O} = 2.749(8)$ Å). Two THF molecules with partial occupancies (50%) lies on 2-fold crystallographic axis, occupying crystal channels parallel to unit cell *a* axis.

1·Zn model shows two crystallographically independent porphyrin molecules with different coordinated ligand: one bound to a THF, while the other is bound to a water molecule (Figure 2S). As previously seen for molecule **1** packing, neighbour porphyrins show intermolecular hydrogen bonds connections (average $d_{O-O} = 3.126(7)$ Å). Interstitial voids are filled by three additional THF molecules tightly connected to exposed hydroxyl groups (from porphyrins and water).

Essential crystal and refinement data (**Table S1**) are reported below.

Table S1. Crystallographic data and refinement details for compound **1** and **1·Zn**.

	1	1·Zn
CCDC Number	1442721	1442722
Moiety Formula	C ₄₆ H ₃₄ N ₄ O ₂ •0.5C ₄ H ₈ O	2C ₄₆ H ₃₄ N ₄ O ₂ Zn•4C ₄ H ₈ O•H ₂ O
Sum Formula	C ₄₈ H ₃₈ N ₄ O _{2.5}	C ₁₀₈ H ₉₈ N ₈ O ₉ Zn ₂
Formula weight (Da)	710.82	1782.68
Temperature (K)	100(2)	100(2)
Wavelength (Å)	0.700	0.700
Crystal system	Monoclinic	Triclinic
Space Group	<i>P</i> 2/ <i>c</i>	<i>P</i> 1
<i>a</i> (Å)	32.628(7)	11.311(2)
<i>b</i> (Å)	6.9070(14)	14.100(3)
<i>c</i> (Å)	32.568(7)	14.556(3)
α (°)	90	102.09(3)
β (°)	90.64(3)	98.80(3)
γ (°)	90	99.49(3)
<i>V</i> (Å ³)	7339(3)	2196.2(8)
<i>Z</i>	8	1
ρ (g·cm ⁻³)	1.287	1.348
F(000)	2992	934
μ (mm ⁻¹)	0.077	0.588
θ min,max (°)	0.6, 24.6	1.4, 29.1
Resolution (Å)	0.84	0.72
Total refl. collectd	25205	74269
Independent refl.	13431 [R(int) = 0.0275]	23000 [R(int) = 0.0158]
Obs. Refl. [F _o >4 σ (F _o)]	12616	22806
<i>I</i> / σ (<i>I</i>) (all data)	31.57	75.57
<i>I</i> / σ (<i>I</i>) (max resltn)	13.42	38.39
Completeness (all data)	0.99	0.98
Completeness (max resltn)	0.99	0.96
Rmerge (all data)	0.0200	0.0267
Rmerge (max resltn,)	0.0421	0.0528
Multiplicity (all data)	1.8	6.0
Multiplicity (max resltn)	1.8	5.1
Data/restraint/parameters	13431/245/1155	23000/26/1128
Goof	1.063	1.017
<i>R</i> ₁ ^a [<i>I</i> >2.0 σ (<i>I</i>)], <i>wR</i> ₂ ^a [<i>I</i> >2.0 σ (<i>I</i>)]	0.1274, 0.3324	0.0486, 0.1319
<i>R</i> ₁ ^a (all data), <i>wR</i> ₂ ^a (all data)	0.1374, 0.3453	0.0489, 0.1323

$$^a R_1 = \sum |F_o| - |F_c| / \sum |F_o|, wR_2 = [\sum w (F_o^2 - F_c^2)^2 / \sum w (F_o^2)^2]^{1/2}.$$

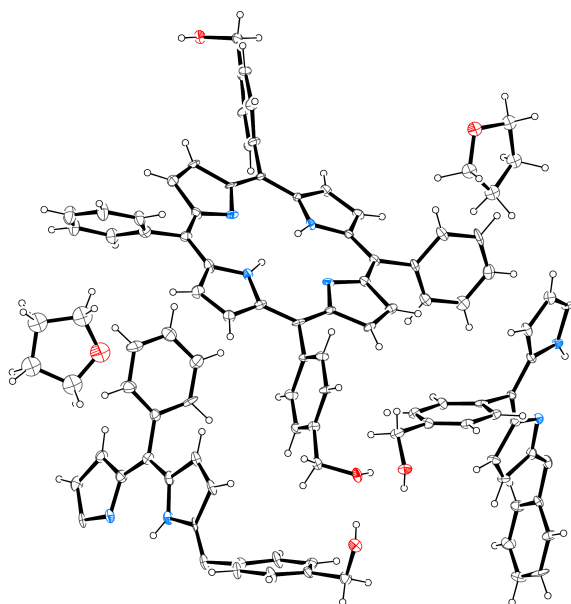


Figure S11. Asymmetric unit content for **1** ($2C_{46}H_{34}N_4O_2 \cdot C_4H_8O$; 50% probability ellipsoids). THF molecules have been modelled with alternative conformations (hidden for clarity).

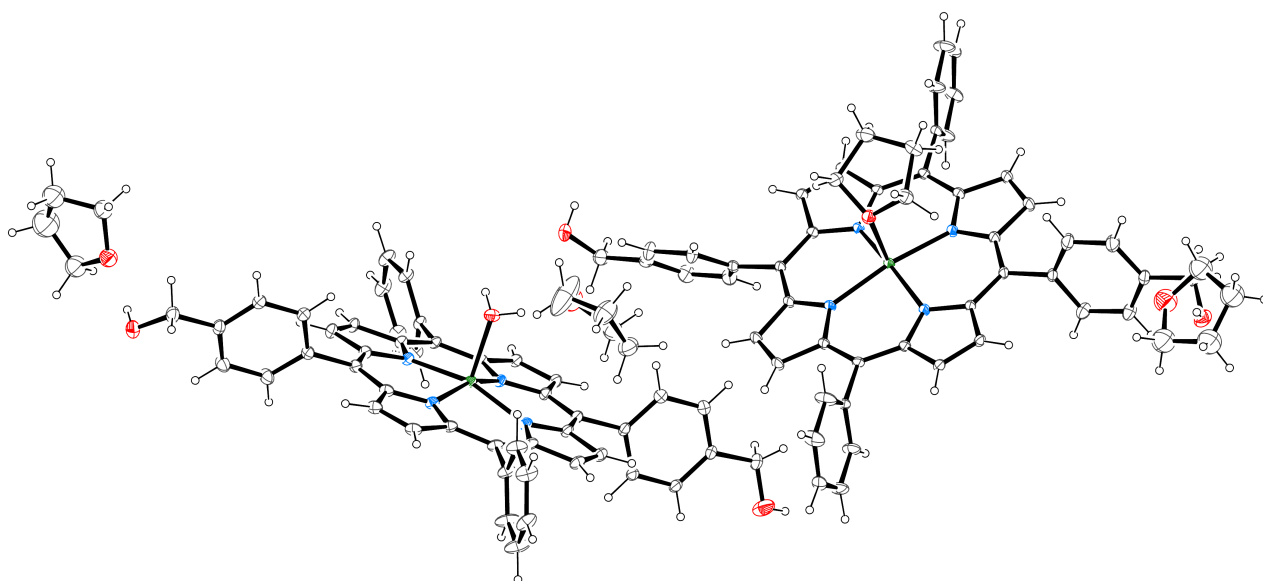


Figure S12. Ellipsoid representation of **1·Zn** ASU content ($2C_{46}H_{34}N_4O_2Zn \cdot 4C_4H_8O \cdot H_2O$; 50% probability). Two different zinc coordination environments have been found for the two crystallographically independent porphyrins.

5. References

- (1) Laha, J. K.; Dhanalekshmi, S.; Taniguchi, M.; Ambroise, A.; Lindsey, J. S. *Org. Process Res. Dev.* **2003**, *7*, 799–812.
- (2) Gou, F.; Jiang, X.; Fang, R.; Jing, H.; Zhu, Z. *ACS Appl. Mater. Interfaces* **2014**, *6*, 6697–6703.
- (3) Ye, Q.; Chen, S.; Zhu, D.; Lu, X.; Lu, Q. *J. Mater. Chem. B* **2015**, *3*, 3091–3097.
- (4) Dimagno, S. G.; Lin, V. S. Y.; Therien, M. J. *J. Org. Chem.* **1993**, *58*, 5983–5993.
- (5) Bakar, M. B.; Oelgemöller, M.; Senge, M. O. *Tetrahedron* **2009**, *65*, 7064–7078.
- (6) Kabsch, W. *Acta Cryst. D* **2010**, *66*, 125–132.
- (7) Burla, M. C.; Caliendo, R.; Carrozzini, B.; Cascarano, G. L.; Cuocci, C.; Giacovazzo, C.; Mallamo, M.; Mazzone, A.; Polidori, G. *J. Appl. Cryst.* **2015**, *48*, 306–309.
- (8) Sheldrick, G. M. *Acta Cryst. A* **2008**, *64*, 112–122.
- (9) Emsley, P.; Cowtan, K. *Acta Cryst. D* **2004**, *60*, 2126–2132.
- (10) Boyle, P. D. *J. Appl. Crystallogr.* **2014**, *47*, 467–470.