Remote template effect in the synthesis of bipyridine-strapped porphyrins

Mathilde Berthe, Yoshiyuki Kagawa, Axel Riquet, Takashi Hayashi, Jean Weiss and Jennifer A. Wytko

Content

Experimental Methods

General. 4'-Bromo-[1,1'-biphenyl]-2-carbaldehyde (**4**)[S1] and dipyrrylmethane[S2] were prepared according to literature procedures. 6,6'-Dibromo-2,2'-bipyridine (95%) was purchased from ABCR (Karlsruhe, Germany). Dichloromethane stabilized with ~0.2% EtOH was purchased from Carlo Erba (Val de Reuil, France) and used as received. All other reagents were purchased from Sigma Aldrich or Fischer Scientific and were used as received. Column chromatography was performed with silica gel from Merck (Kieselgel 60; 63-200 µm or 40-63 µm) or alumina (Merck aluminum oxide 60 standardized). ^{1}H NMR spectra were recorded on Bruker Advance 300 (300 MHz), 400 (400 MHz) or 500 (500 MHz) spectrometers. Chemical shifts are given in ppm and were determined by taking the solvent as a reference. All coupling constants are in Hz. Mass spectrometry was performed on a Bruker Daltonics microTOF spectrometer (Bruker Daltonik GmbH, Bremen, Germany) by the Service de Spectrométrie de Masse de la Fédération de Chimie "Le Bel" (FR 2010).

X-ray crystallography. The crystals were placed in oil, and a single crystal was selected, mounted on a glass fibre and placed in a low-temperature N_2 stream.

For compounds [**2Zn**] and **3**, X-Ray diffraction data collection was carried out on a Bruker PHOTON-III DUO CPAD diffractometer equipped with an Oxford Cryosystem liquid N_2 device, using Mo-Kα radiation ($\lambda = 0.71073$ Å). The crystal-detector distance was 37 mm. The cell parameters were determined (APEX3 software)[S3] from reflections taken from one set of 180 frames, each at 1s exposure. The structures were solved using the program SHELXT-2014.[S4] The refinement and all further calculations were carried out using SHELXL-2014.[S5] The H-atoms were included in calculated positions and treated as riding atoms using SHELXL default parameters. The non-H atoms were refined anisotropically, using weighted full-matrix least-squares on F^2. A semi-empirical absorption correction was applied using SADABS in APEX3;[S3] transmission factors: $T_{min}/T_{max} = 0.7215/0.7458$; $T_{min}/T_{max} = 0.6692/0.7456$; respectively for [**2Zn**] and **3**. For **3**, the structure was refined as a two-component twin with the twin law -1 0 0 0 -1 0 0.99 0 1 and a BASF of 0.04485.

For compounds **2** and **5**, X-ray diffraction data collection was carried out on a Bruker PHOTON-III DUO CPAD diffractometer equipped with an Oxford Cryosystem liquid N_2 device, using Cu-Kα radiation ($\lambda = 1.54178$ Å). The crystal-detector distance was 40 mm. The cell parameters were determined (APEX3 software[S3] for **1** and APEX4 software[S6] for **5**) from reflections taken from one set of 180 frames, each at 1s exposure. The structure was solved using the program SHELXT-2014.[S4] The refinement and all further calculations were carried out using SHELXL-2014.[S5] The hydrogen atoms of the NH group were located from Fourier difference. The other H-atoms were included in calculated positions and treated as riding atoms using SHELXL default parameters. The non-H atoms were refined anisotropically, using weighted full-matrix least-squares on F^2. A semi-empirical absorption correction was applied using SADABS in APEX3[S3] for **2** and APEX4[S6] for **5**; transmission factors: $T_{min}/T_{max} = 0.6227/0.7528$; $T_{min}/T_{max} = 0.4011/0.7528$; respectively for **2** and **5**. For **2**, the methylenes C56, C57, C59 and C60 of the cyclohexane solvent are disordered over two positions with an occupancy ratio of 0.80/0.20 For **5**, the SQUEEZE instruction in PLATON[S7] was applied. The residual electron density was assigned to one molecule of the dichloromethane solvent.

[S1] L. A. Fontana, M. P. Almeida, A. F. P. Alcântara, V. H. Rigolin, M. A. Ribeiro, W. P. Barros, J. Megiatto. *ChemRxiv* **2020**. DOI: 10.26434/chemrxiv.12625772.v1

[S2] a) P. S. Clezy, G. A. Smythe, *Aust. J. Chem.* 1969, **22**, 239-249; b) R. Chong, P. S. Clezy, A. J. Liepa, A. W. Nichol, *Aust. J. Chem.* 1969, **22**, 229-238.

[S3] "M86-EXX229V1 APEX3 User Manual", Bruker AXS Inc., Madison, USA, 2016.

[S4] G. M. Sheldrick, *Acta Cryst.* 2015*,* A71, 3-8.

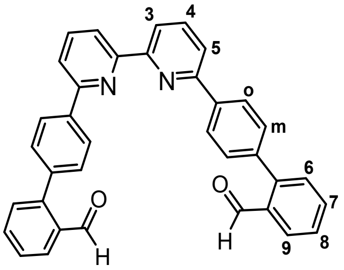
[S5] G. M. Sheldrick, *Acta Cryst.* 2015, C71, 3-8.

[S6] "M86-EXX278V1 APEX4 User Manual," Bruker Corporation, 2021.

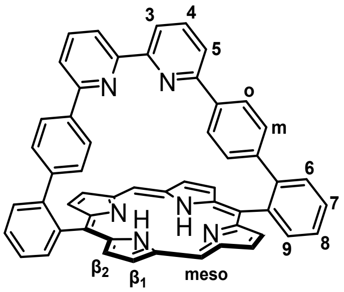
[S7] A. L Spek, *J.Appl.Cryst.* 2003, **36**, 7-13

Experimental procedures

4',4'''-([2,2'-Bipyridine]-6,6'-diyl)bis(([1,1'-biphenyl]-2-carbaldehyde)) (3). To a degassed mixture of compound **4** (1.13 g, 3.36 mmol) and 6,6'-dibromo-2,2'-bipyridine (550 mg, 1.75 mmol) in 2 M Na_2CO_3 aq. (1 mL) and 1,4-dioxane (5 mL), Pd(dppf)Cl_2 (26 mg, 0.035 mmol) was added. The mixture was stirred at 90 °C for 20 h. After cooling to room temperature, the mixture was extracted with CH_2Cl_2 and the organic layer was dried over $MgSO_4$. After removal of solvent under reduced pressure, the residue was filtered through a SiO_2 column (CH_2Cl_2) and recrystallized from CH_2Cl_2/Et_2O to yield compound **3** (832 mg, 1.61 mmol, 92%) as a white powder. mp (from CH_2Cl_2/Et_2O). ^1H NMR δH(300 MHz; $CDCl_3$) 10.10 (2 H, d, J = 0.7, H_{CHO}), 8.67 (2 H, dd, J = 7.8, 0.8, H_3), 8.30 (4 H, dt, J = 8.4, 1.8, H_o), 8.08 (2 H, dd, J = 8.3, 1.6, H_9), 7.99 (2 H, t, J = 7.8, H_4), 7.88 (2 H, dd, J = 7.8, 0.8, H_5), 7.72–7.67 (2 H, m, H_7), 7.58–7.52 (8 H, m, $H_{m,6,8}$).^{13}C NMR δH(100 MHz, $CDCl_3$) 192.4, 156.0, 155.6, 145.5, 139.3, 138.4, 137.9, 133.9, 133.7, 130.8, 130.6, 128.0, 127.8, 127.1, 120.5, 119.9. ESI HRMS: *m/z* = 517.1909 ($[M+H]^+$, 100%)



Zinc(II)-templated synthesis of the bipyridine-strapped porphyrin 2. To a degassed solution of compound **3** (100 mg, 0.194 mmol) and $Zn(OAc)_2·2H_2O$ (36 mg, 0.19 mmol) in CH_2Cl_2 (stabilized with 0.2% EtOH; 700 mL), dipyrrylmethane (57 mg, 0.39 mmol) and then TFA (0.4 mL, 5 mmol) were added under argon atmosphere. The reaction mixture was stirred for 20 h at room temperature, then DDQ (365 mg, 1.61 mmol) was added and the solution was stirred for 4 h. NEt_3 (12 mL) was added and the solution was stirred for 20 min. The organic layer was washed with H_2O (3 x 500 mL) and dried over Na_2SO_4. After removal of the solvent, the product was purified by SiO_2 column chromatography (CH_2Cl_2) and the collected red fraction were recrystallized from CH_2Cl_2/Et_2O to yield porphyrin **2** (61 mg, 0.079 mmol, 41%). mp >300 °C (from CH_2Cl_2/Et_2O). UV-visible (solvent) λ (nm (ε ($M^{-1}cm^{-1}$)): 284 (23000), sh 396 (2900), 413 (150000), sh 479 (2100), 506 (7500), 539 (2400), 579 (3000), sh 586 (3000), 635 (1300). ^1H NMR δH(400 MHz; $CDCl_3$) 10.14 (2 H, s, H_{meso}), 9.25 (4 H, d, *J* = 4.5, $H_β$), 8.93 (4 H, d, *J* = 4.5, $H_β$), 8.67 (2 H, dd, *J* = 7.2, 1.2 H_9), 7.94-7.83 (6 H, m, $H_{6,7,8}$), 7.48 (2 H, t, *J* = 7.8, H_4), 7.31 (2 H, dd, *J* = 7.8, 0.9, H_5), 7.12 (2 H, dd, *J* = 7.8, 0.9, H_3), 6.78 (4 H, m, H_o), 6.67 (4 H, m, H_m), -3.15 (2 H, s, H_{N-H}). ^{13}C NMR δC(126 MHz, $CDCl_3$) 157.5, 157.3, 147.2, 145.3, 144.8, 141.6, 139.9, 136.8, 136.7, 134.6, 131.7, 130.5, 129.2, 128.8, 128.7, 126.3, 125.6, 120.6, 119.6, 117.2, 105.4. MALDI-TOF MS: *m/z* = 767.320 ($[M+H]^+$, 100%).

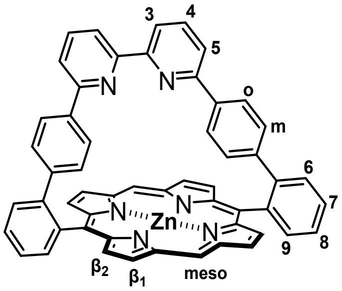


Lithium-templated synthesis of the bipyridine-strapped porphyrin 2.

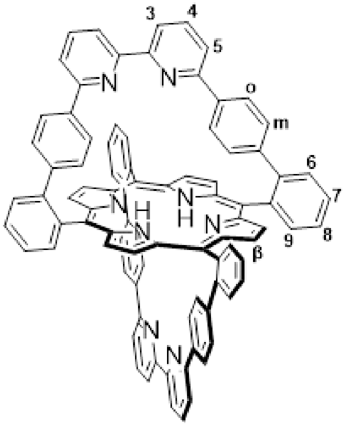
To a degassed solution of compound **3** (100 mg, 0.194 mmol) and lithium trifluoromethanesulfonate (151 mg, 0.970 mmol) in CH_2Cl_2 (stabilized with 0.2% EtOH; 700 mL), dipyrrylmethane (57 mg, 0.39 mmol) and TFA (0.4 mL, 5 mmol) were added under Ar. The solution was stirred for 20 h at room temperature, then DDQ (365 mg, 1.61 mmol) was added and the solution was stirred for 4 h. NEt_3 (12 mL) was added and the solution was stirred for 20 min. The organic layer was washed with H_2O until the aqueous layer was pale yellow and dried over Na_2SO_4. After removal of the solvent, the product was purified by SiO_2 column chromatography (CH_2Cl_2) and the collected red fraction were recrystallized from CH_2Cl_2/Et_2O to yield the porphyrin **2** (13 mg, 0.017 mmol, 9%).

Attempted copper(I)-templated synthesis of the bipyridine-strapped porphyrin 2.

To a degassed solution of **3** (100 mg, 0.194 mmol) and $Cu(MeCN)_4BF_4$ (31 mg, 0.097 mmol) in CH_2Cl_2 (stabilized with 0.2% EtOH; 700 mL) dipyrrylmethane (57 mg, 0.39 mmol) and TFA (0.4 mL, 5 mmol) were added under Ar. The reaction mixture was stirred for 20 h at room temperature, then DDQ (365 mg, 1.61 mmol) was added and the solution was stirred for 4 h. NEt_3 (12 mL) was added and the solution was stirred for 20 min. The organic layer was washed with H_2O until the aqueous layer was pale yellow. The organic layer was then washed with a saturated aqueous solution of EDTA and an aqueous solution of KCN, and dried over Na_2SO_4. Purification by column chromatography over alumina (CH_2Cl_2) then over SiO_2 (CH_2Cl_2) gave a main red fraction that still contained numerous porphyrins (see Figure S17).



Bipyridine-strapped Zn(II) porphyrin [**2Zn**]. A solution of strapped porphyrin **2** (61 mg, 0.080 mmol) and $Zn(OAc)_2 \cdot 2H_2O$ (175 mg, 0.795 mmol) in $CHCl_3$ (9 mL) and MeOH (1 mL) was refluxed for 14 h. The solution was cooled, then washed with water. The organic layer was dried over Na_2SO_4 and solvent was removed under vacuum. The crude residue was purified by column chromatography (alumina, CH_2Cl_2) to yield a purple solid (54 mg, 0.065 mmol, 82%). The porphyrin could be recrystallized from CH_2Cl_2/pentane if necessary. Crystals of [**2Zn**] suitable for X-ray crystallography were grown from acetone/CH_2Cl_2. mp >300 °C (from CH_2Cl_2/pentane). UV-visible λmax (CH_2Cl_2)/nm (ε/dm^3 mol^{-1} cm^{-1}): 290 (39000), sh 398 (26000), 419 (260000), 512 (1800), 547 (13000), 583 (1600). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 10.06 (s, 2H$_{meso}$), 9.22 (d, *J* = 4.5 Hz, 4H, H$_β$), 8.97 (d, *J* = 4.5 Hz, 4H, H$_β$), 8.62 (dd, *J* = 7.4, 1.1 Hz, 2H, H$_9$), 7.94-7.82 (m, 4H, H$_{7,8}$), 7.78 (dd, *J* = 7.5, 1.5 Hz, 2H, H$_6$), 7.45 (t, *J* = 7.8 Hz, 2H, H$_4$), 7.23 (dd, *J* = 7.8 Hz, 0.9 Hz, 2H, H$_3$), 7.10 (dd, *J* = 7.8 Hz, 0.9 Hz 2H, H$_5$), 6.75 (d, *J* = 8.5 Hz, 4H, H$_o$), 6.62 (d, *J* = 8.5 Hz, 4H, H$_m$). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 157.4, 157.0, 150.3, 149.4, 145.3, 142.8, 141.8, 137.0, 136.7, 134.0, 131.8, 129.4, 128.5, 128.4, 125.8, 125.6, 120.6, 120.1, 117.8, 106.1. MALDI-TOF MS: *m/z* = 829.331 ([M+H]$^+$, 100%).



Double bipyridine-strapped porphyrin 5. To a degassed solution of compound **3** (250 mg, 0.484 mmol) and $Zn(OAc)_{2.}2H_2O$ (106 mg, 0.484 mmol) in degassed CH_2Cl_2 (1.75 L), freshly distilled pyrrole (67 µL, 0.97 mmol) and then 1 mL of TFA were added under argon atmosphere. The reaction mixture was stirred for 20 h at room temperature, then DDQ (1.1 g, 4.8 mmol) was added and the solution was stirred for 4 h. NEt_3 (30 mL) was added and the solution was stirred for 20 min. The organic layer was washed with H_2O (3 x 1.5 L) and dried over Na_2SO_4. After removal of the solvent, the product was purified by SiO_2 column chromatography (gradient of CH_2Cl_2 to CH_2Cl_2/MeOH: 9/1). The first red fraction was recrystallized from CH_2Cl_2/MeOH to yield compound **5** (20 mg, 0.016 mmol, 7%). mp (from CH_2Cl_2/MeOH). UV-visible λmax (CH_2Cl_2)/nm (ε/dm^3 mol^{-1} cm^{-1}): 287 (92000), sh 412 (56000), 430 (305000), 491 (3600), 524 (16000), 559 (6200), 599 (5400), 656 (2800). ^{1}H NMR δH(500 MHz; $CDCl_3$) 8.72 (4 H, d, *J* = 7.3, H$_9$), 8.57 (8 H, s, H$_β$), 7.81 (4 H, dt, *J* = 7.4, 1.4, H$_7$), 7.73 (8 H, m, H$_{6,8}$), 7.52 (4 H, t, *J* = 7.8, H$_4$), 7.36 (4 H, d, *J* = 7.8, H$_5$), 7.21 (4 H, d, *J* = 7.8, H$_3$), 6.92 (8 H, d, *J* = 8.5, H$_o$), 6.73 (8 H, d, *J* = 8.5, H$_m$), -2.65 (2 H, s, H$_{N-H}$).^{13}C NMR δC(126 MHz, $CDCl_3$) 157.9, 157.5, 144.4, 142.0, 140.8, 140.7, 136.9, 135.3, 129.2, 129.0, 128.4, 126.7, 125.4, 120.6, 119.8, 118.1. ESI-HR MS: *m/z* 1223.4525 ([M+H]$^+$, 100%), 612.2315 ([M+2H]$^{2+}$, 20%).

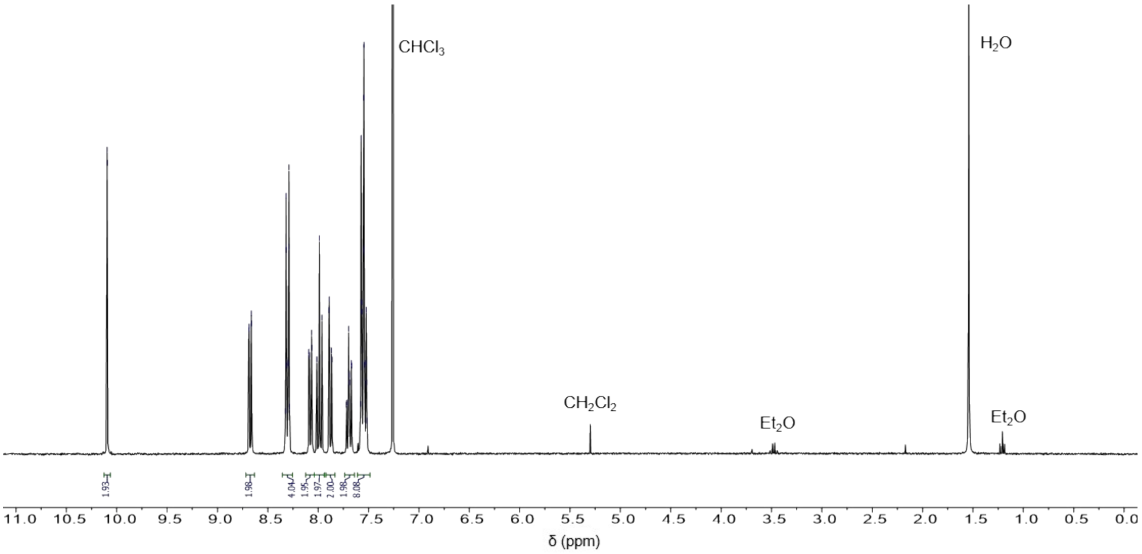


Figure S1. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound **3** (recrystallized from CH_2Cl_2/Et_2O and dried under vacuum for 5 days).

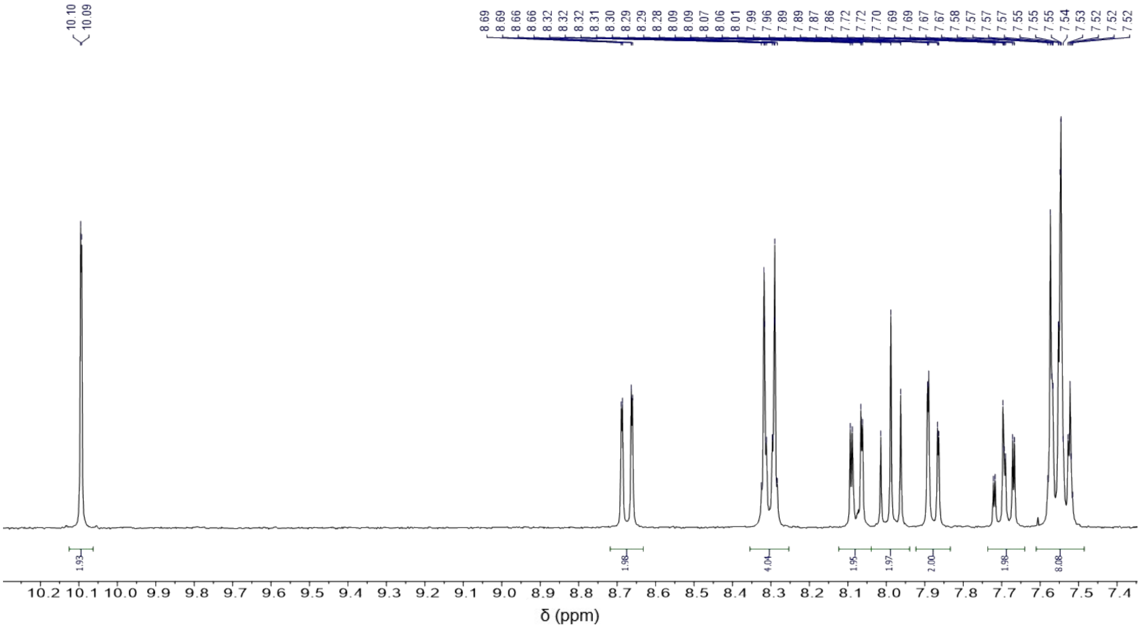


Figure S2. Aromatic region of the ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound **3** (recrystallized from CH_2Cl_2/Et_2O and dried under vacuum for 5 days).

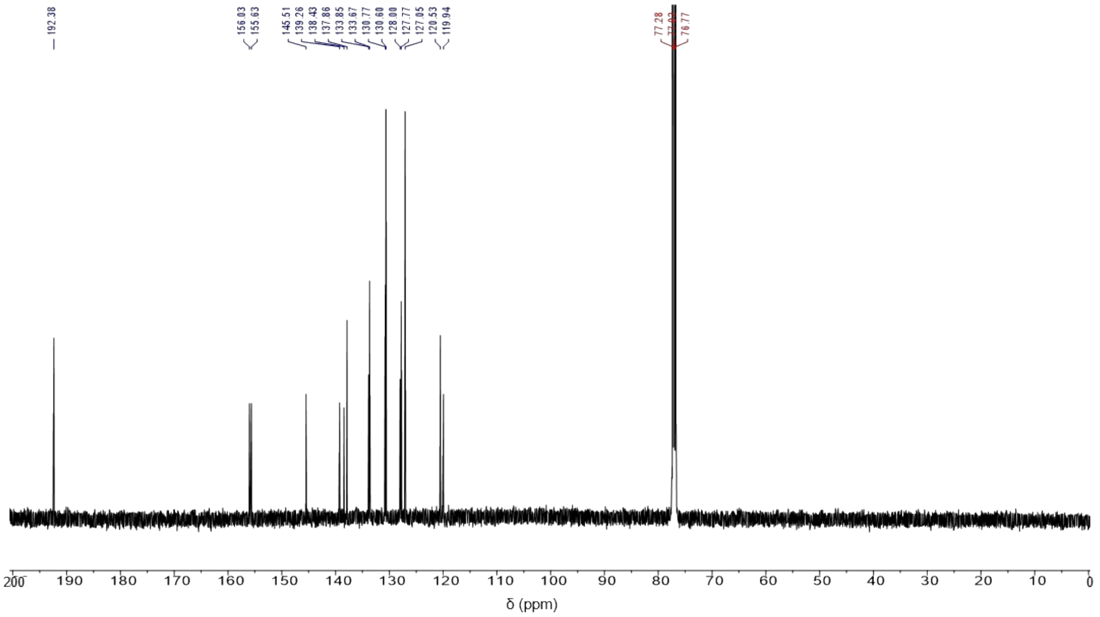


Figure S3. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of compound **3.**

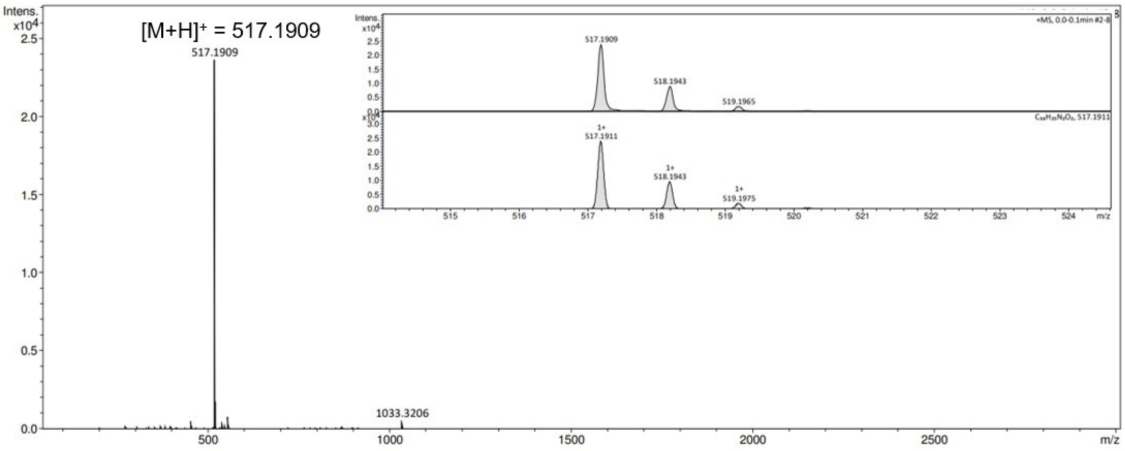


Figure S4. ESI HRMS spectrum of compound **3.**

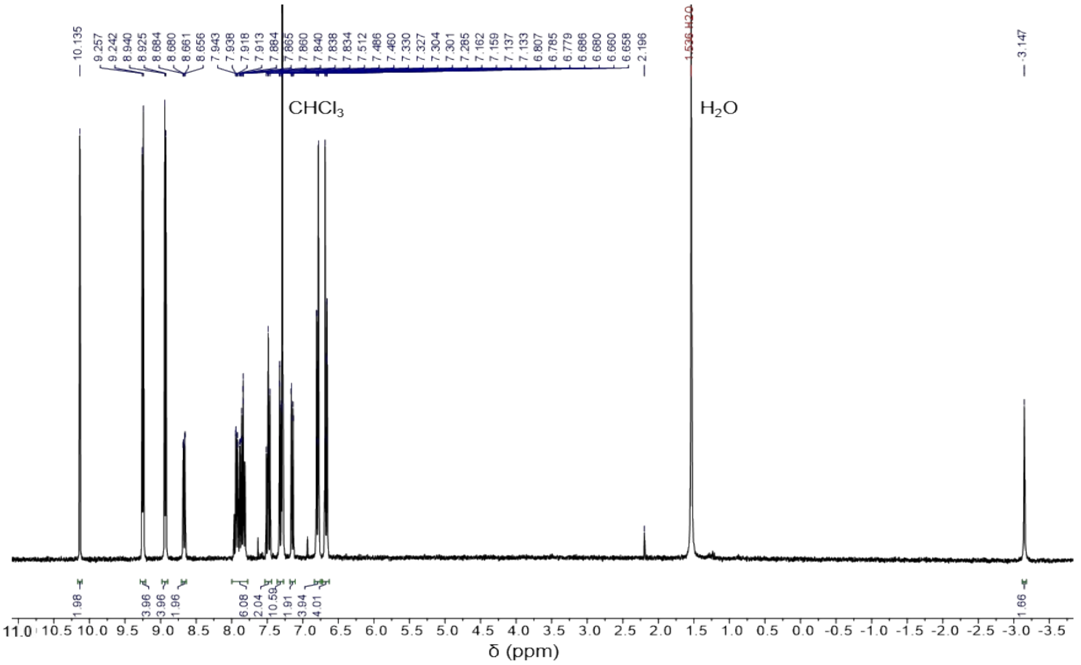


Figure S5. ^{1}H NMR spectrum (300 MHz, CDCl$_3$) of compound **2**.

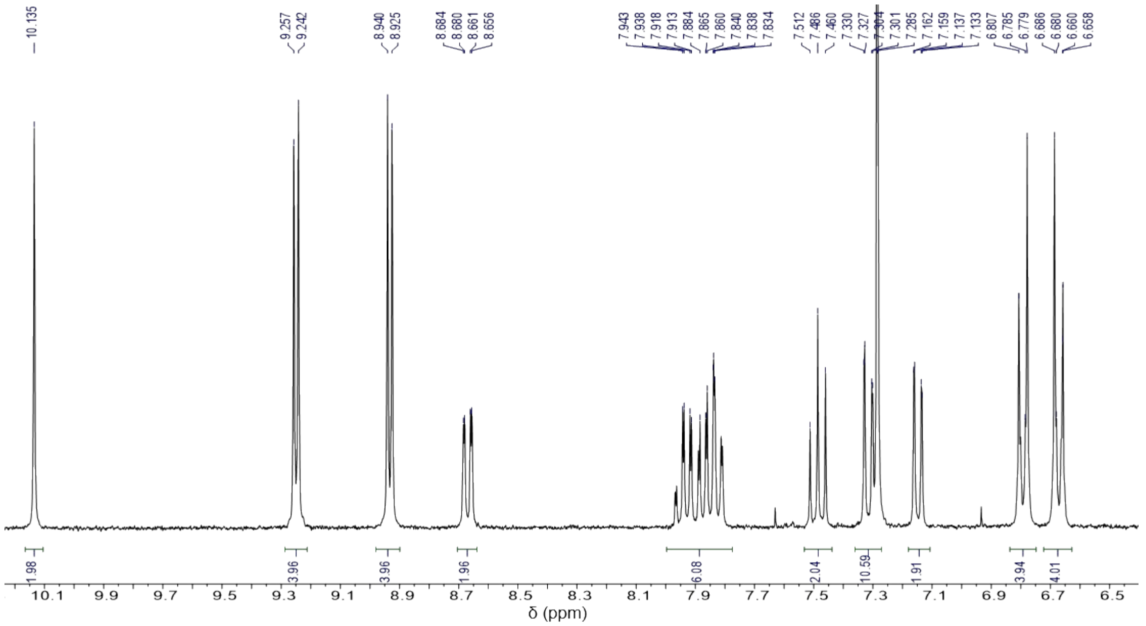


Figure S6. Aromatic region of the ^{1}H NMR spectrum (300 MHz, CDCl$_3$) of compound **2.**

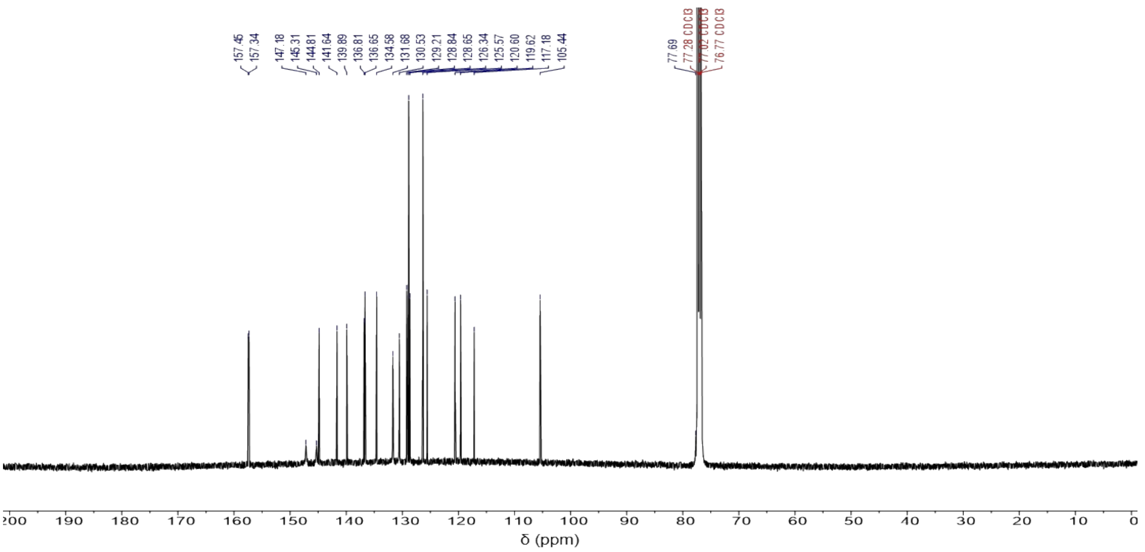


Figure S7. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of compound **2**.

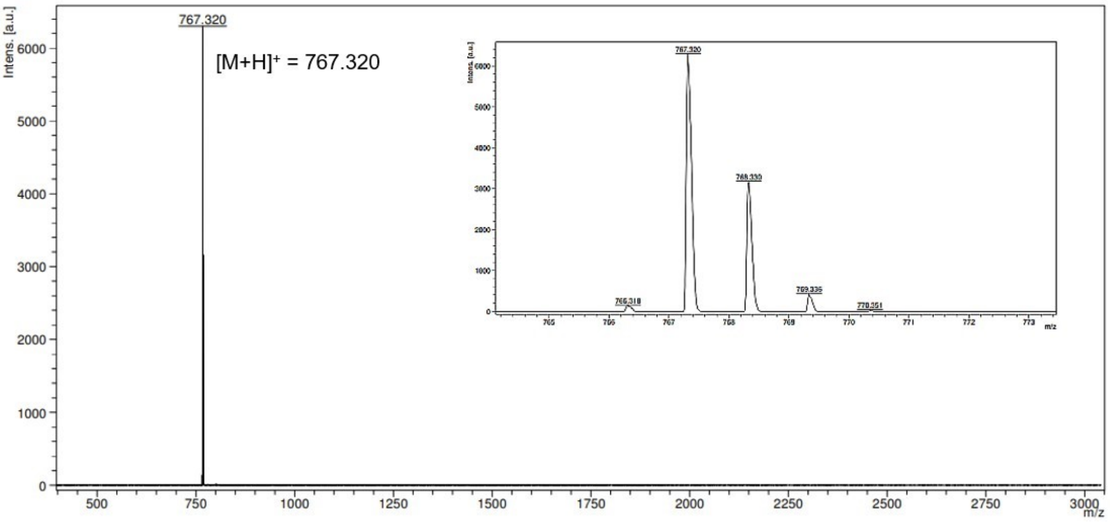


Figure S8. MALDI-TOF MS spectrum of compound **2**.

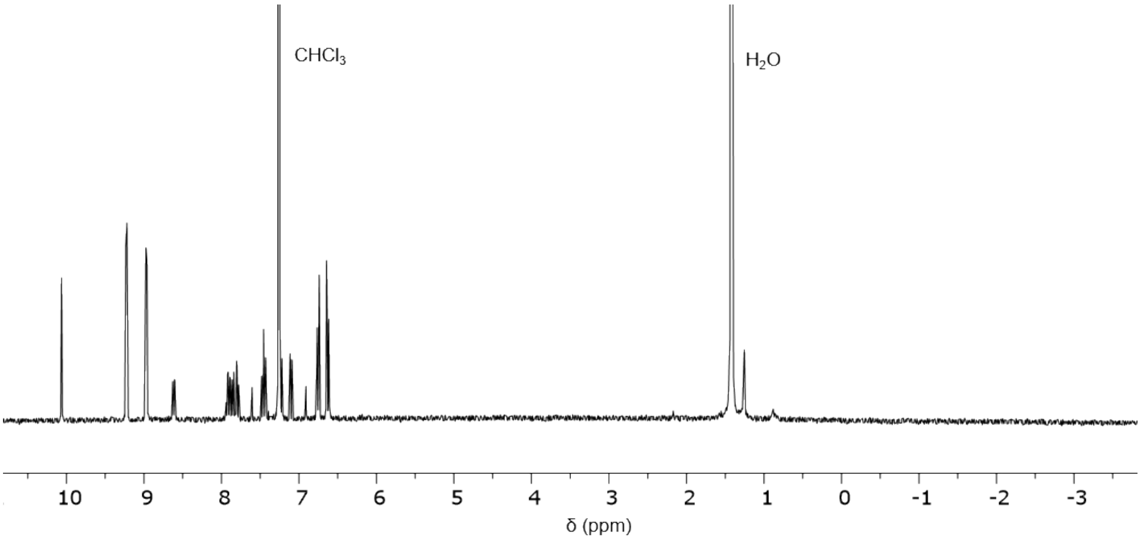


Figure S9. ^{1}H NMR spectrum (300 MHz, CDCl$_3$) of compound [**2Zn**].

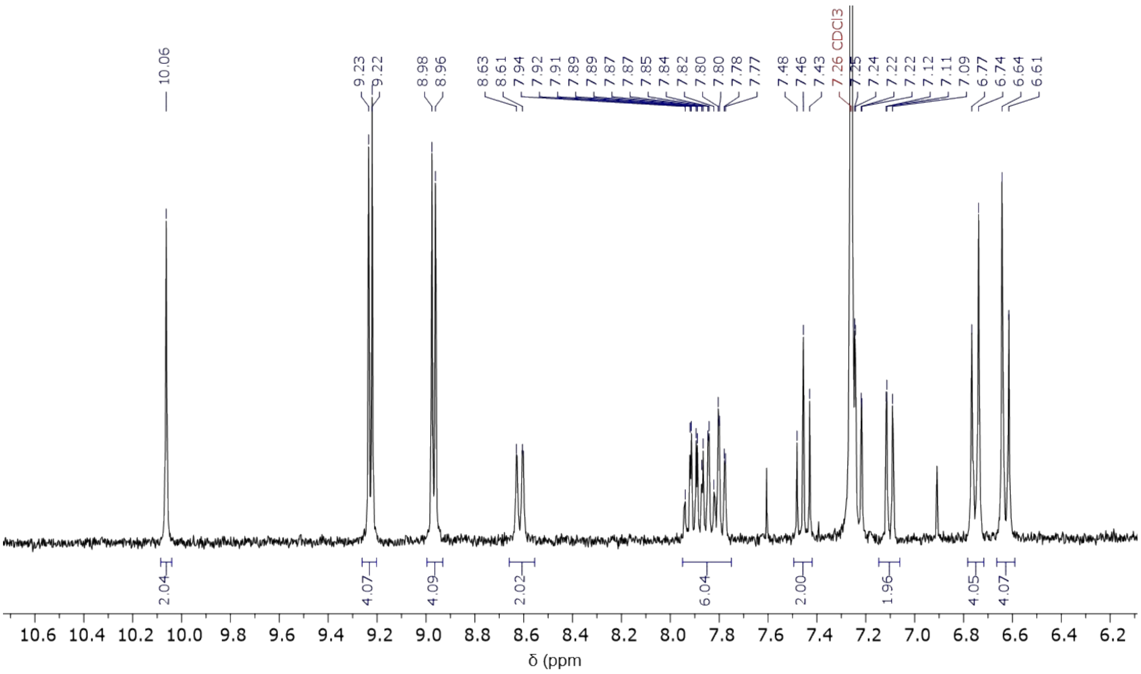


Figure S10. ^{1}H NMR spectrum (300 MHz, CDCl$_3$) of compound [**2Zn**] (aromatic region).

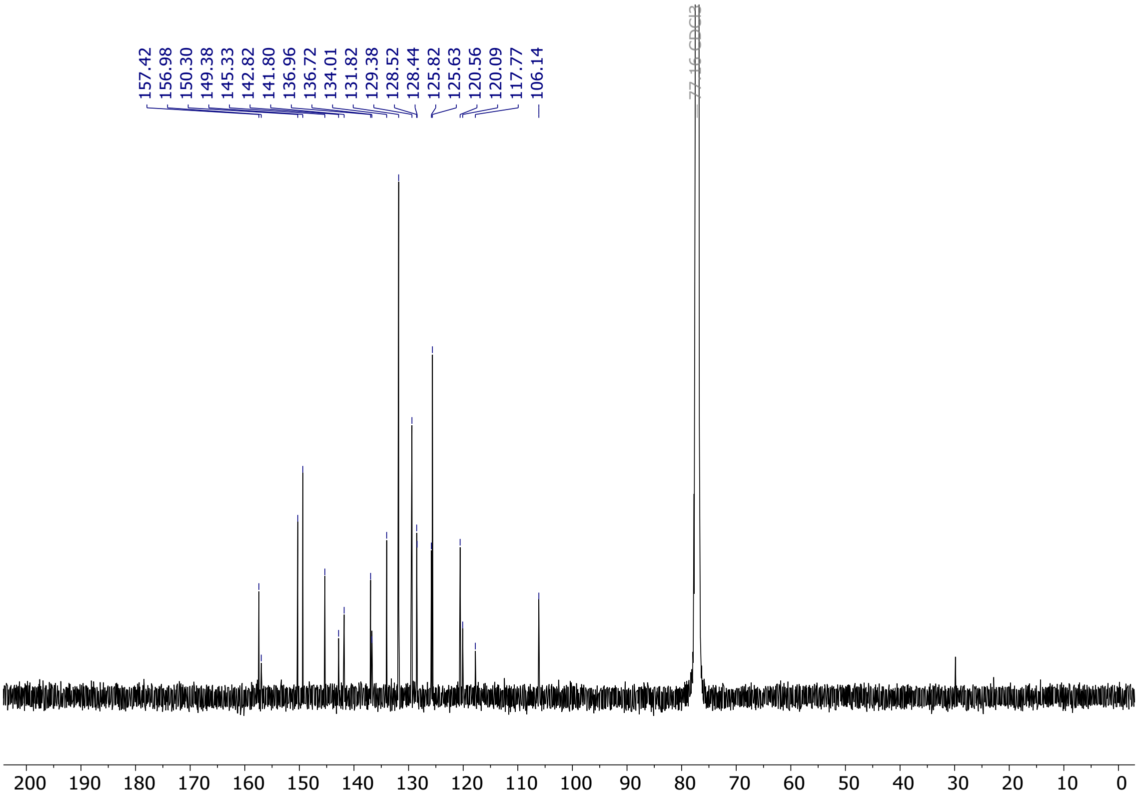


Figure S11. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of compound [**2Zn**]

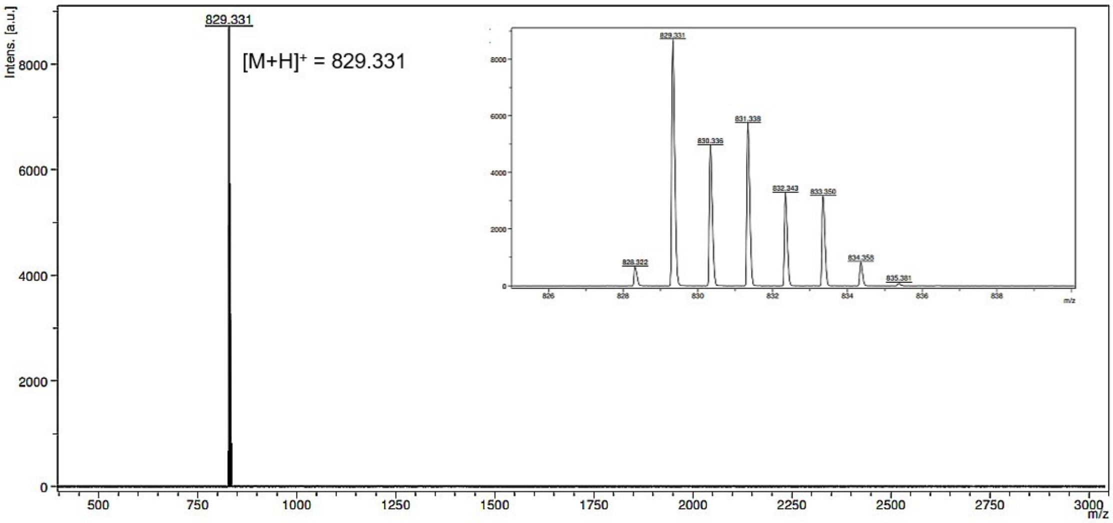


Figure S12. MALDI-TOF MS spectrum of compound [**2Zn**].

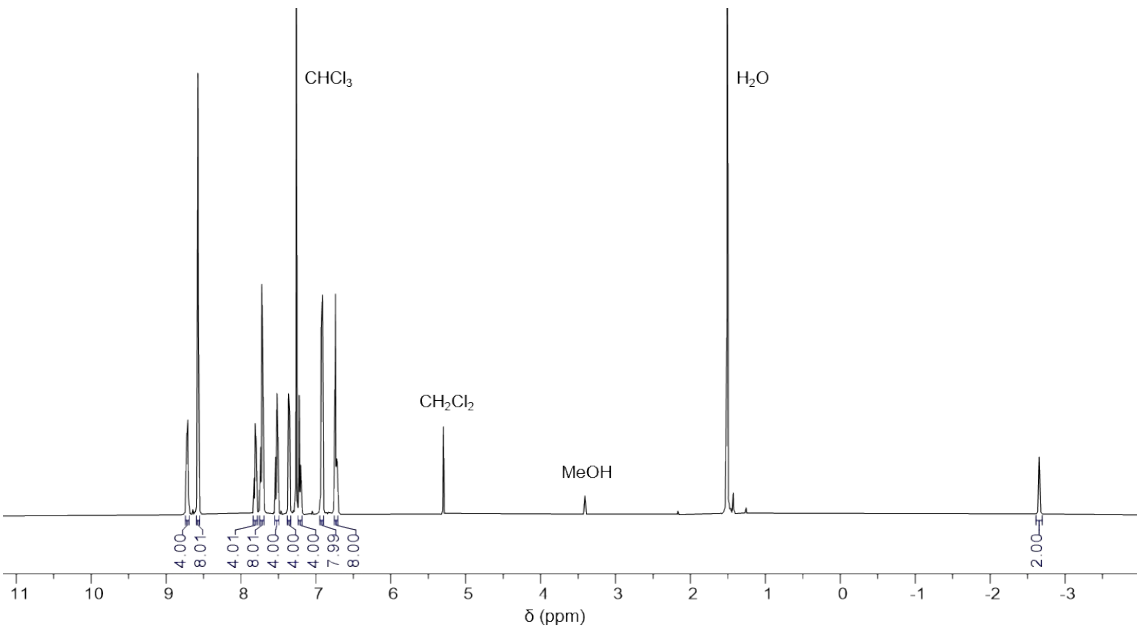


Figure S13. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **5**.

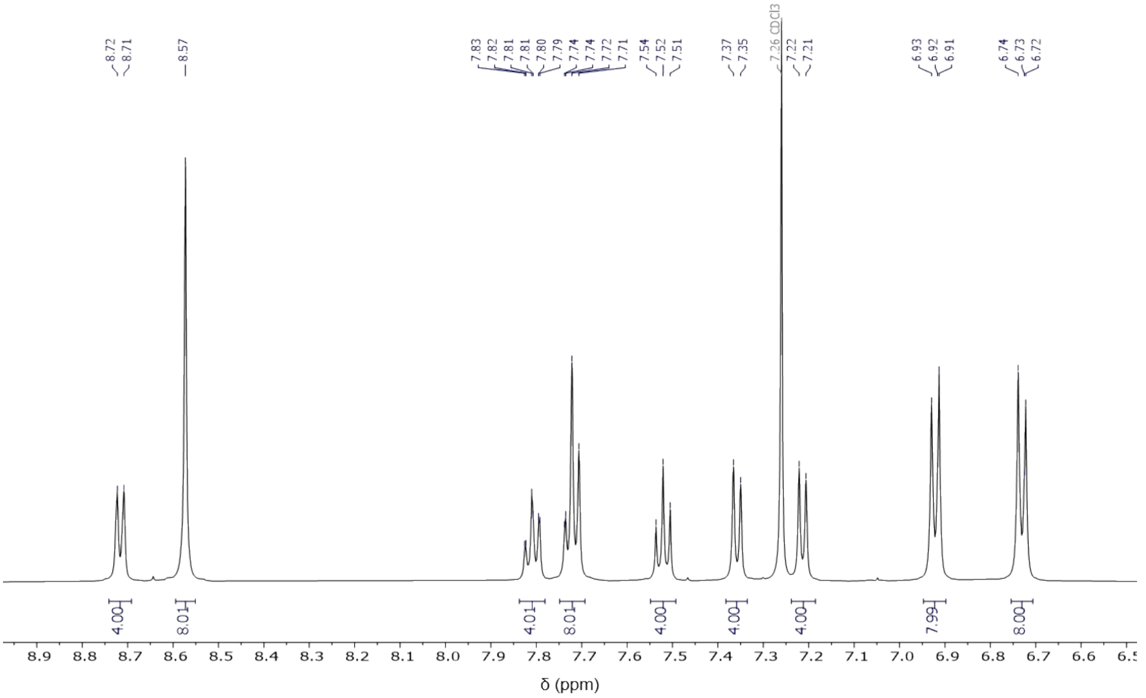


Figure S14. Aromatic region ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **5**.

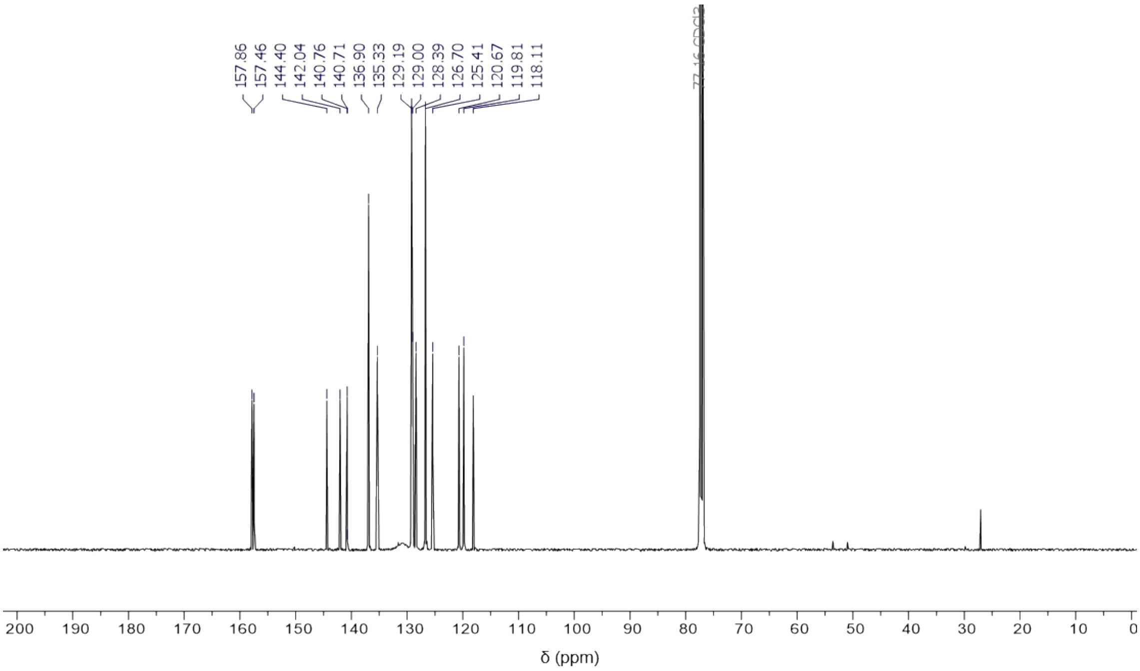
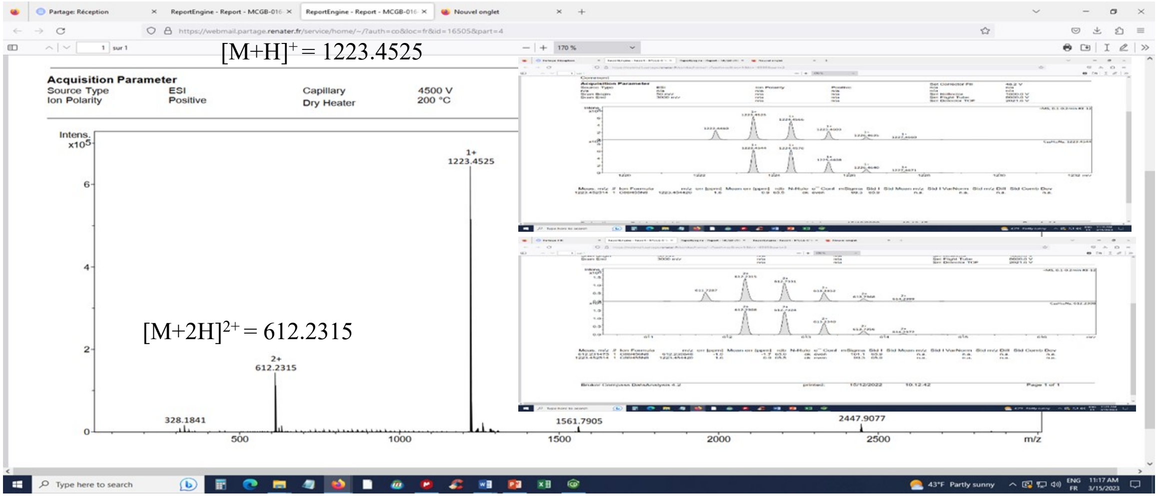


Figure S15. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of compound **5**.


$[M+H]^+ = 1223.4525$

Acquisition Parameter

Source Type	ESI	Capillary	4500 V
Ion Polarity	Positive	Dry Heater	200 °C

$[M+2H]^{2+} = 612.2315$

Figure S16. ESI HRMS spectrum of compound **5**.

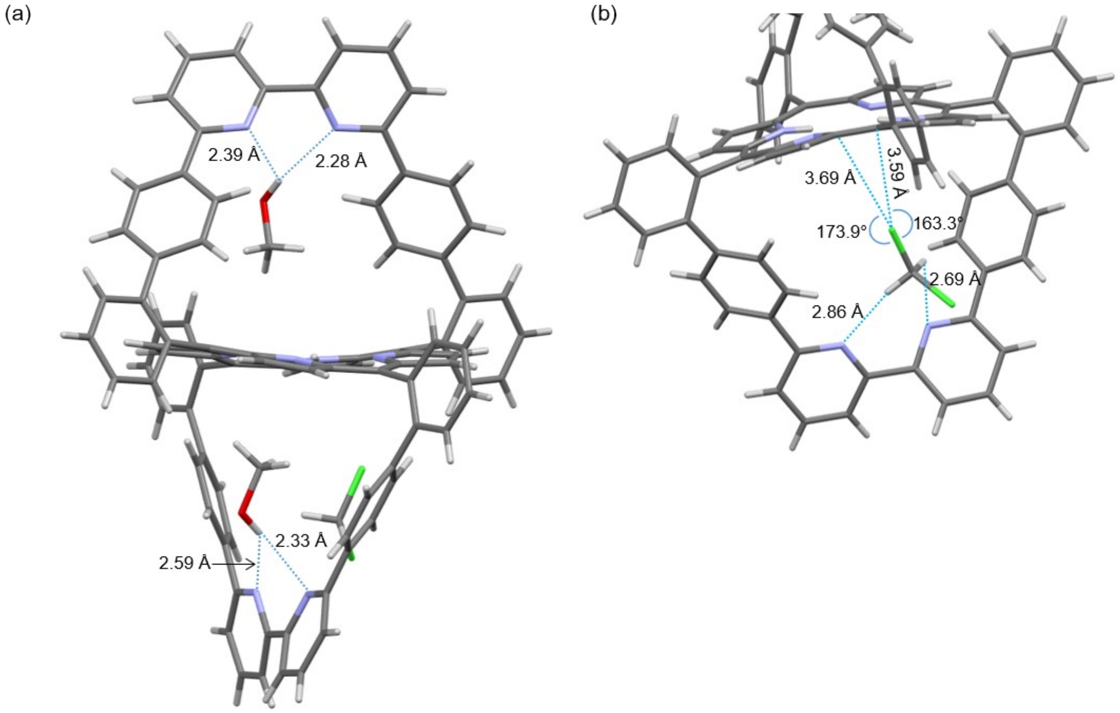


Figure S17. Relevant distances and angles of solvent molecules observed within the strap of **5** in its crystal structure. (a) Distances between the hydroxyl protons of methanol and the nitrogen atoms of the bipyridine strap of **5**. (b) Distances and angles between the CH_2Cl_2 molecule and porphyrin **5**. The MeOH molecule was omitted for sake of clarity.

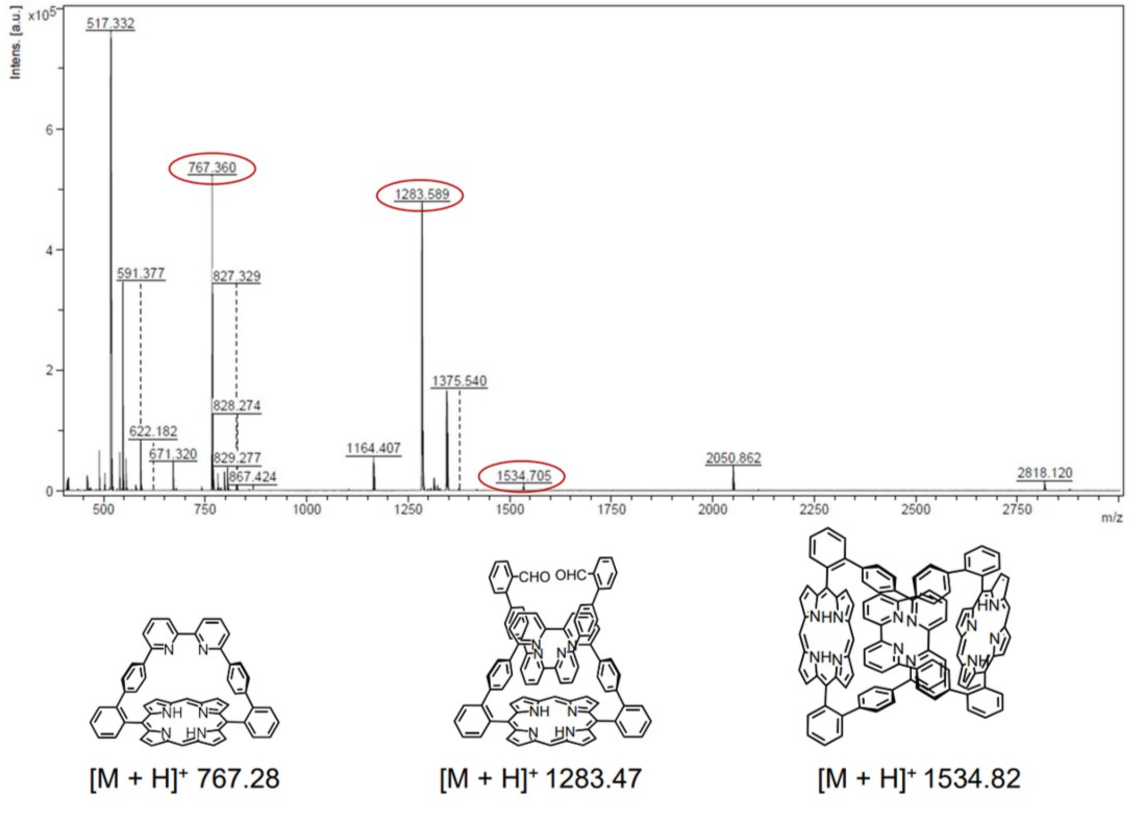


Figure S18. MALDI-TOF mass spectrum of the crude product of the attempted copper-templated synthesis of **2**.

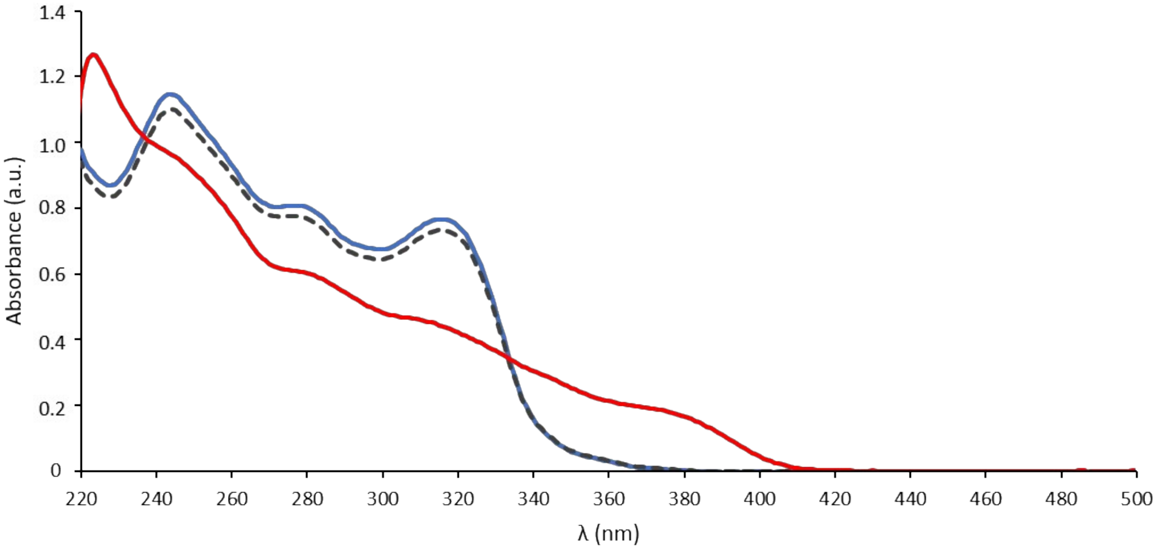


Figure S19. UV-vis spectra of **3** (blue line, 0.1 mM, CH_2Cl_2) after addition of 1 eq of $Zn(OAc)_2$•$2H_2O$ (dotted black line) and after addition of 1 eq of $Zn(OAc)_2$•$2H_2O$ and an excess of TFA (red line).

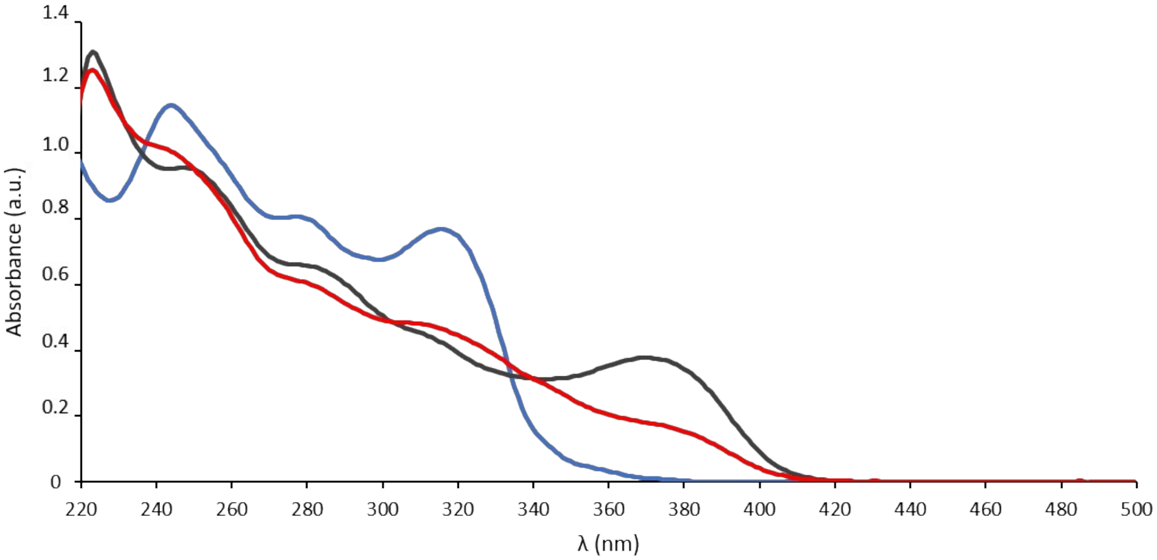


Figure S20. UV-vis spectra of **3** (blue line, 0.1 mM, CH_2Cl_2) after addition of excess TFA (black line) and after the addition of 1 eq of $Zn(OAc)_2$•$2H_2O$ and an excess of TFA (red line).

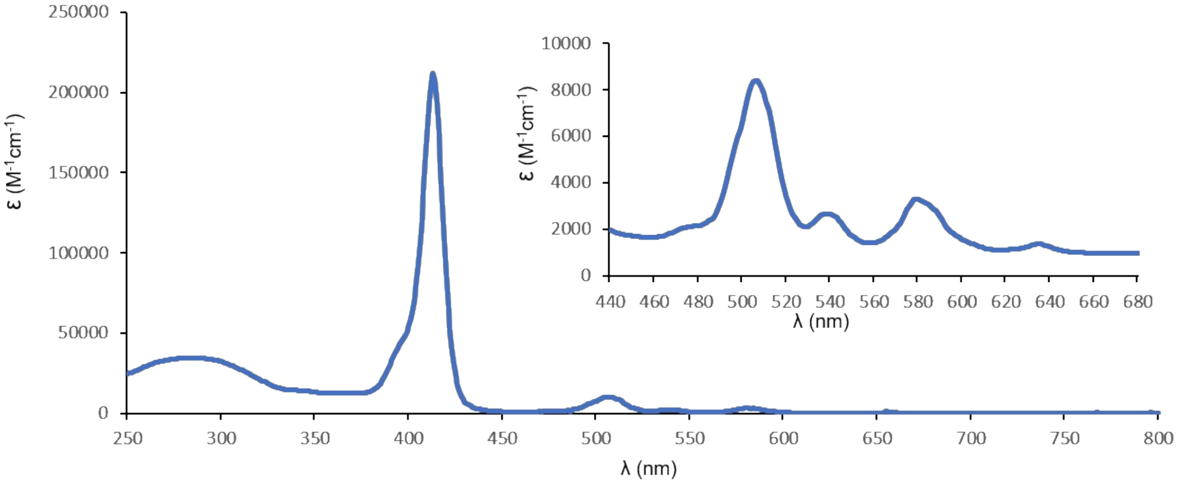


Figure S21. UV-visible spectrum of **2** in CH_2Cl_2.

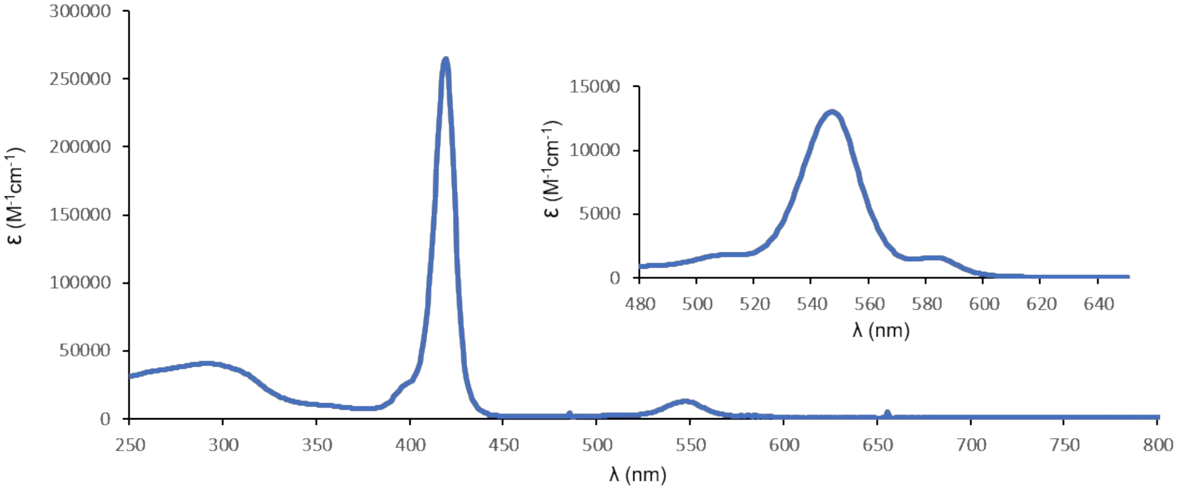


Figure S22. UV-visible spectrum of [**2Zn]** in CH_2Cl_2.

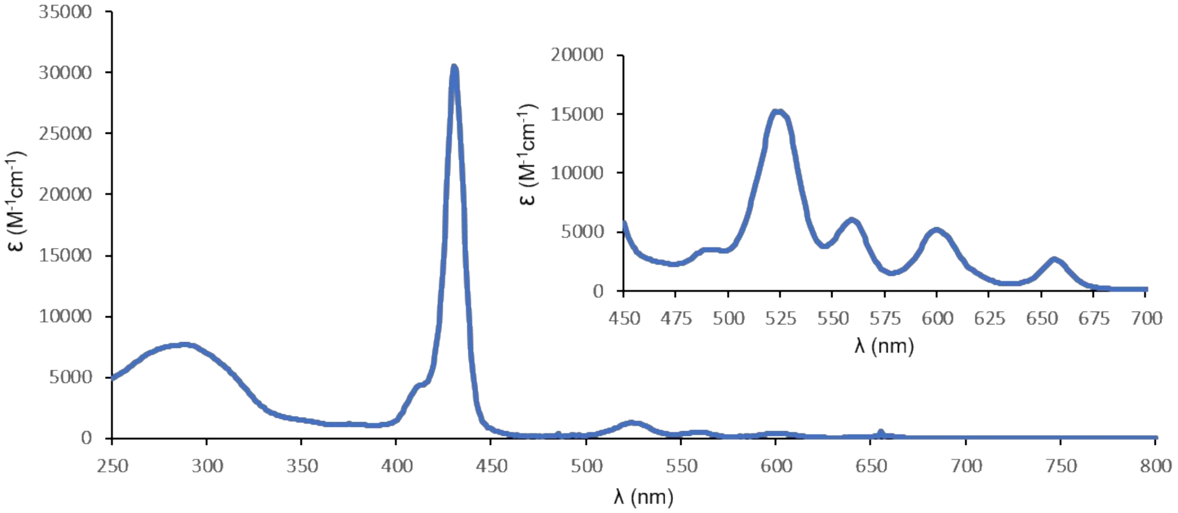


Figure S23. UV-visible spectrum of **5** in CH_2Cl_2.

Table S1. Comparision of UV-visible data of bipyridine-strapped porphyrins **2**, **5** and [**2Zn]** with those of the phenanthroline-strapped porphyrins **1** and [**1Zn**]. All spectra recorded in CH_2Cl_2.

compound	λ (nm)									reference
1	284		412	sh 479[a]	506	540	580	sh 586[a]	635	S8
2	284	sh 396	413	sh 479	506	539	579	sh 586	635	
5	287	sh 412	430	491	524	559	599		656	
[**1Zn**]	284, 308		418		546	578				S9
[**2Zn**]	290	sh 298	419	512	547	583				

[a] Not reported in the literature reference but observed in the spectrum.

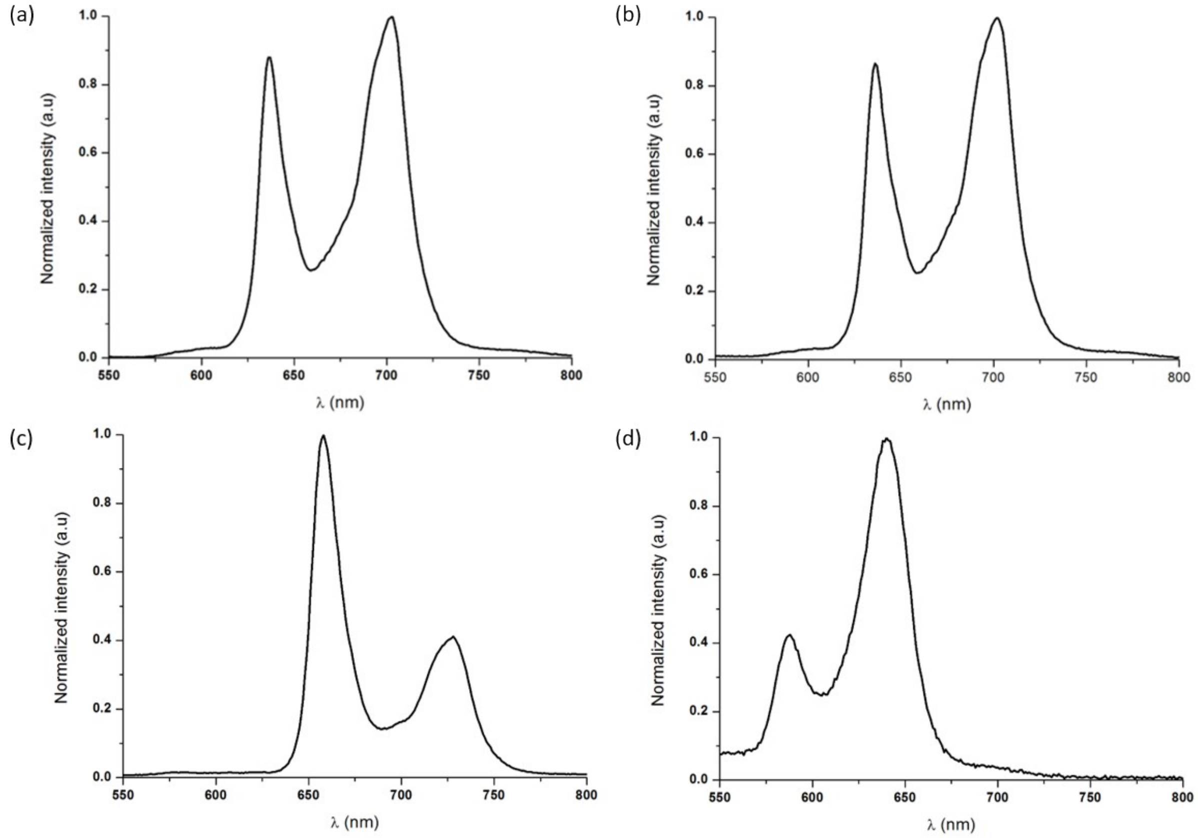


Figure S24. Emission spectra in CH_2Cl_2 + 0.01% of 2,6-lutidine (to prevent photoprotonation[S10]). (a) **1** (λ_{ex}= 506 nm), (b) **2** (λ_{ex}= 506 nm), (c) **5** (λ_{ex}= 524 nm) and (d) [**2Zn**] (λ_{ex}= 512 nm).

Table S2. Comparison of emission wavelengths of **1**, **2**, **5**, [**1Zn]** and [**2Zn]** in CH_2Cl_2+ 0.01% 2,6-lutidine.

compound	λ_{em} (nm)		λ_{ex} (nm)	reference
1	636	703	506	
2	636	702	506	
5	658	728	524	
[**1Zn**]	595	646	556	S10
[**2Zn**]	588	640	512	

[S8] J. A. Wytko, E. Graf and J. Weiss, *J. Org. Chem.* 1992, **57**, 1015.

[S9] P. Ochsenbein, M. Bonin, K. Schenk, J. Froidevaux, J. Wytko, E. Graf and J. Weiss *Eur. J. Inorg. Chem.* 1999, **7**, 1175.

[S10] D. Paul, J. A. Wytko, M. Koepf, J. Weiss, *Inorg. Chem.* 2002, **41**, 3699.