Electronic Supplementary Material (ESI) for ChemComm.

SUPPORTING INFORMATION

Conformational Control of Nonplanar Free Base Porphyrins: Towards Bifunctional Catalysts of Tunable Basicity

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Contents

1. General methods

Catalyst screening: All reactions were carried out in screw-cap 1 mL vials under a protective argon atmosphere. All solvents used were degassed and dried over Al_2O_3. Screening in diluted conditions was set up in 5 mL round-bottomed flasks. The nucleophile (1.1 equiv.), catalyst (3 mol%) and Michael acceptor (1 equiv.) were dissolved in the appropriate solvent and the mixture was stirred in the dark at rt for 24 h. For each reaction a blank sample without catalyst was set up, too. At the end of each reaction, the internal standard (CH_2Br_2, 0.5 equiv.) was added into the reaction mixture and a ^{1}HNMR spectrum was recorded.

The conversion was determined *via* quantitative ^{1}H NMR using an internal standard by comparison of the product integrals with the integrals of the internal standard.**Kinetics measurements:** Porphyrin **8** and compound **3** were mixed in the corresponding ratio and dissolved in CD_2Cl_2. The NMR spectra were recorded at a frequency of 600.13 MHz.

Instrumentation and chemicals: All reagents were used as received unless otherwise noted. Tetrahydrofuran (THF), diethylether (Et_2O), toluene and dichloromethane (DCM) were obtained by passing the degassed solvents through an activated alumina column. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous material, unless otherwise noted. Reactions were monitored by thin layer chromatography (TLC) carried out on silica gel plates using UV light as a visualizing agent. Silica gel 60 *Merck, 230–400 mesh or aluminium oxide (neutral, activated with 6.5% water, Brockmann Grade III) were used for flash column chromatography. Melting points are uncorrected and were measured with a Stuart SMP-50 melting point apparatus. NMR spectra were recorded using Bruker DPX400 (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR), Bruker AV 600 (600 MHz for ^{1}H NMR, 151 MHz for ^{13}CNMR), Bruker AV 400 (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR) instruments. Chemical shifts are given in ppm and referenced either to the deuterium peak in the NMR solvent or to TMS used as an internal standard. The assignment of the signals was confirmed by 2D spectra (COSY, HMBC, HSQC). ESI mass spectra were acquired in positive or negative modes as required, using a Micromass time-of-flight mass spectrometer (TOF), interfaced to a Waters 2690 HPLC or a Bruker mircoOTOF-Q II spectrometer interfaced to a Dionex UltiMate 3000 LC. APCI experiments were carried out on a Bruker micrOTOF-Q III spectrometer interfaced to a Dionex Ultimate 3000 C or direct insertion probe in positive or negative modes. IR spectra were recorded on a PerkinElmer Spectrum 100 FT-IR spectrometer.

2. Kinetic studies

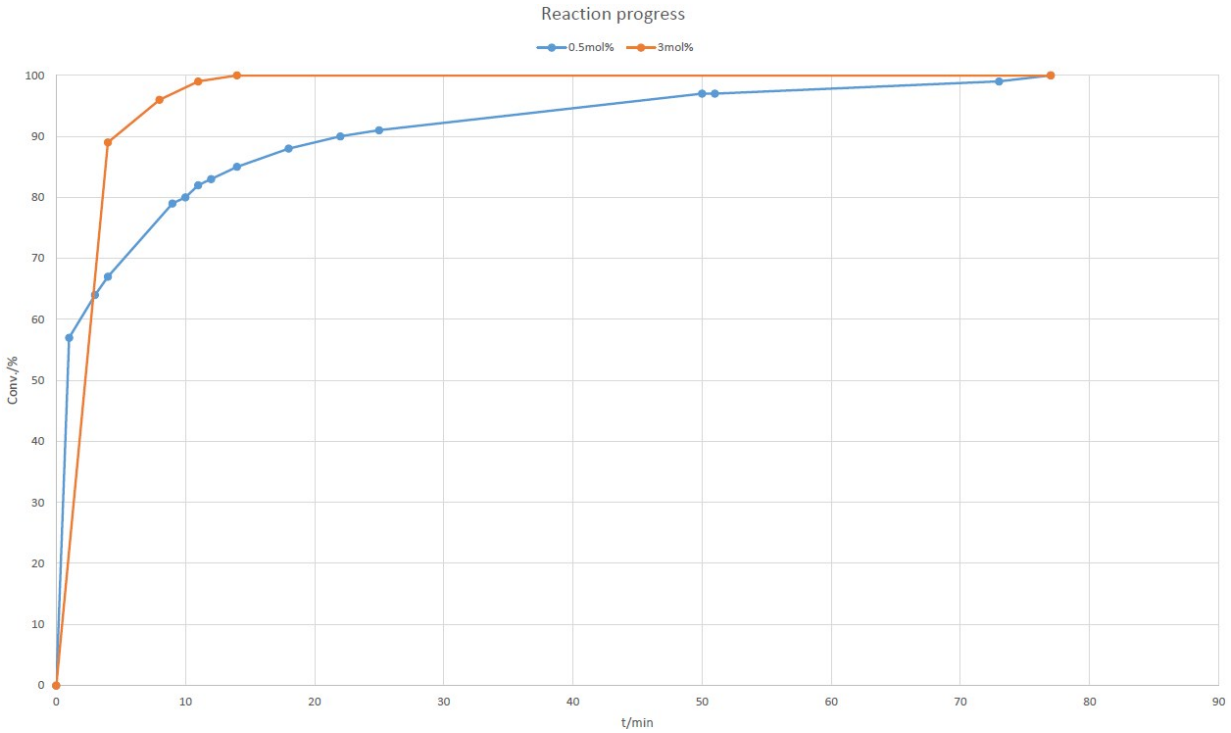
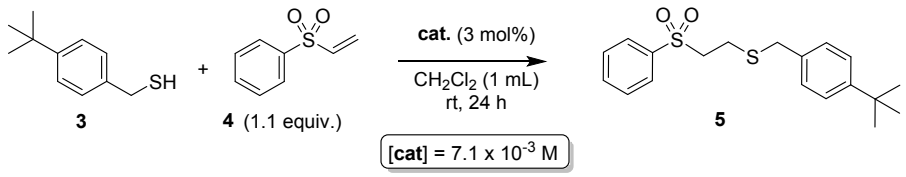


Figure S1: Kinetic plots for a mixture of compound 8 and 3; ratio 1:200 (blue) and ratio 1:33 (red).

3. Comparative screening of 8 and amine bases under diluted conditions

Table S1. A comparison of the activity of **8** with amine bases under dilute conditions.



entry	catalyst	$pK_{AH}(H_2O, 25\ °C)^a$	yield (%)[b]
1	**aniline**	4.6	0
2	**pyridine**	5.2	0
3	**DMAP**	9.7	43
4	**NEt_3**	10.9	76
5[c]	**8**	n/d	80
6	**DBU**[d]	*ca*. 13	>98

[a] Refers to the conjugate acid of the base listed. [b] Determined by ^1H NMR spectroscopy using an internal standard. [c] Data from Table 1. [d] Strong amidine base could accelerate the process to completion in the same reaction time.

4. Studies on the protonation of 8

4.1. Deprotonation of amine bases by 8

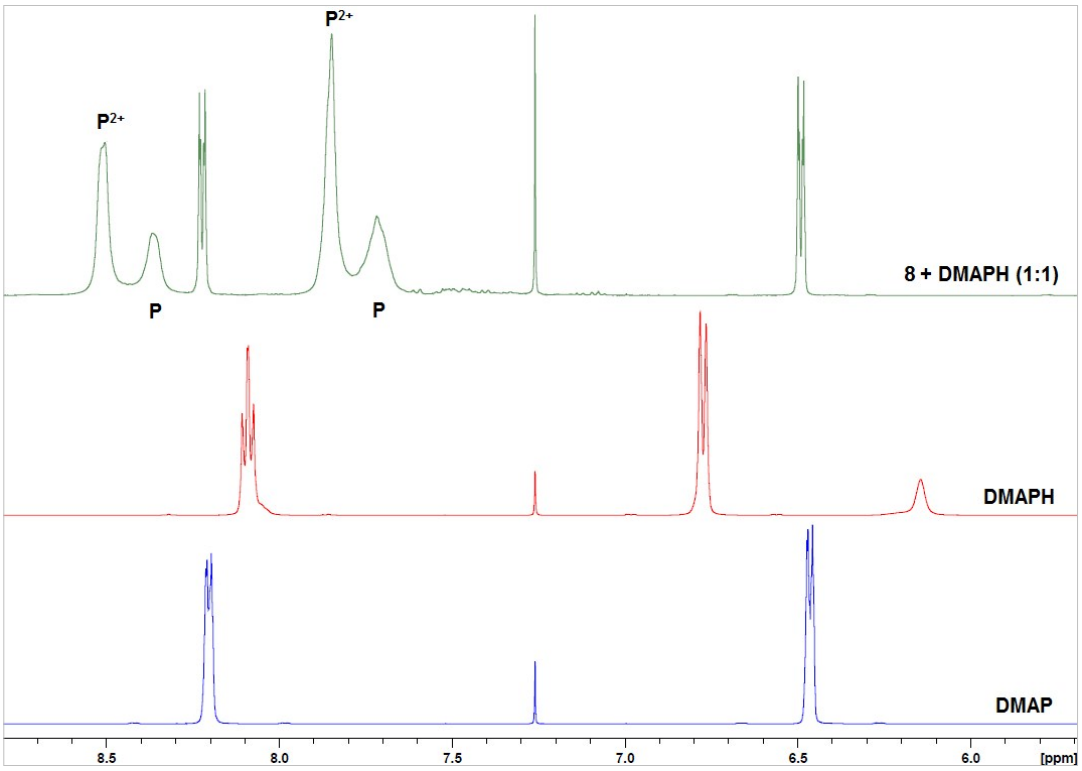


Figure S2: NMR studies on the protonation of 8 by DMAP•HCl.

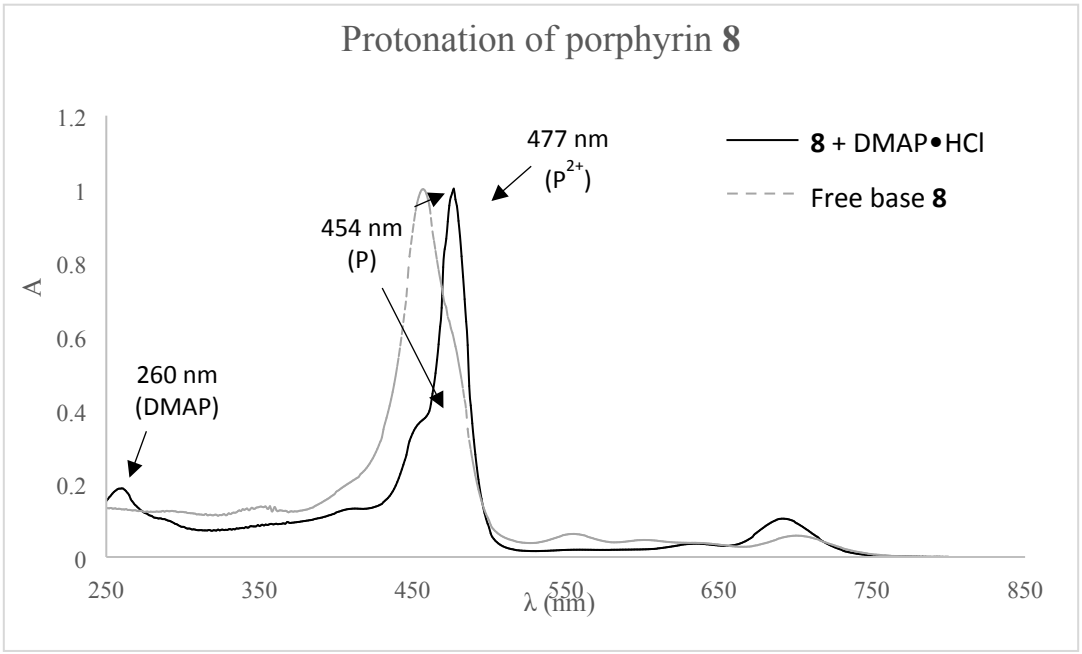


Figure S3: UV-vis studies on the protonation of 8 by DMAP•HCl.

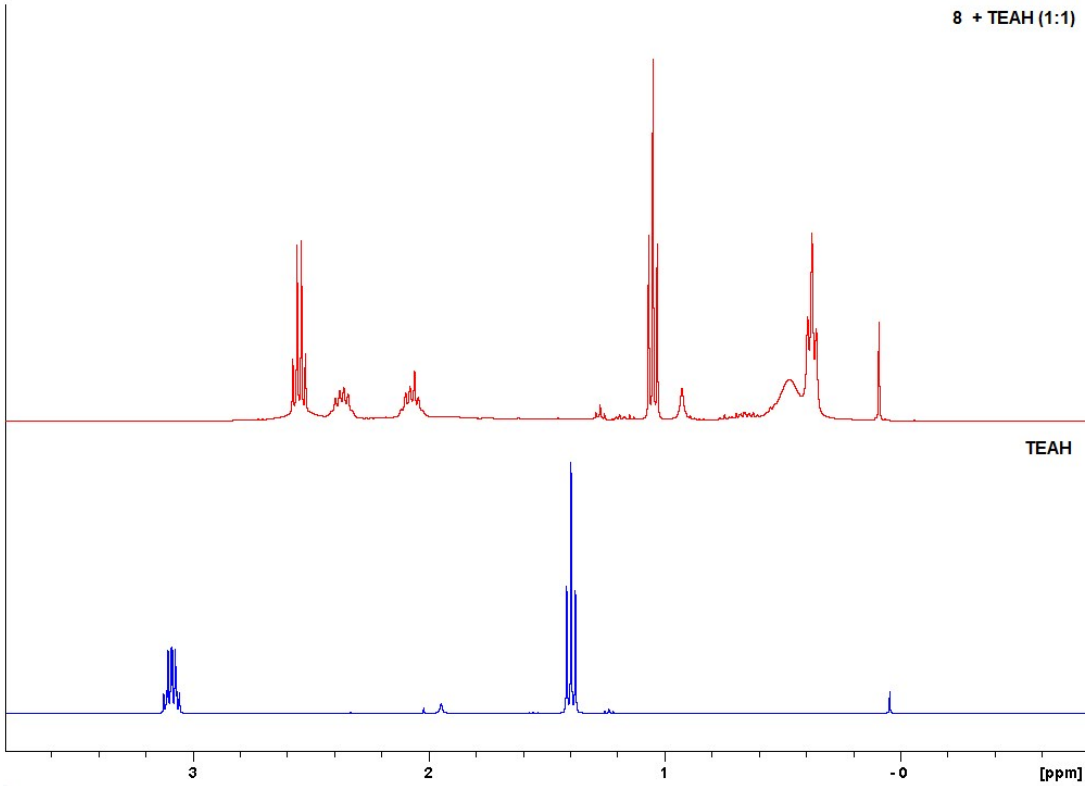


Figure S4: Deprotonation of NEt_3•HCl by 8.

4.2. Deprotonation of amine bases by 9

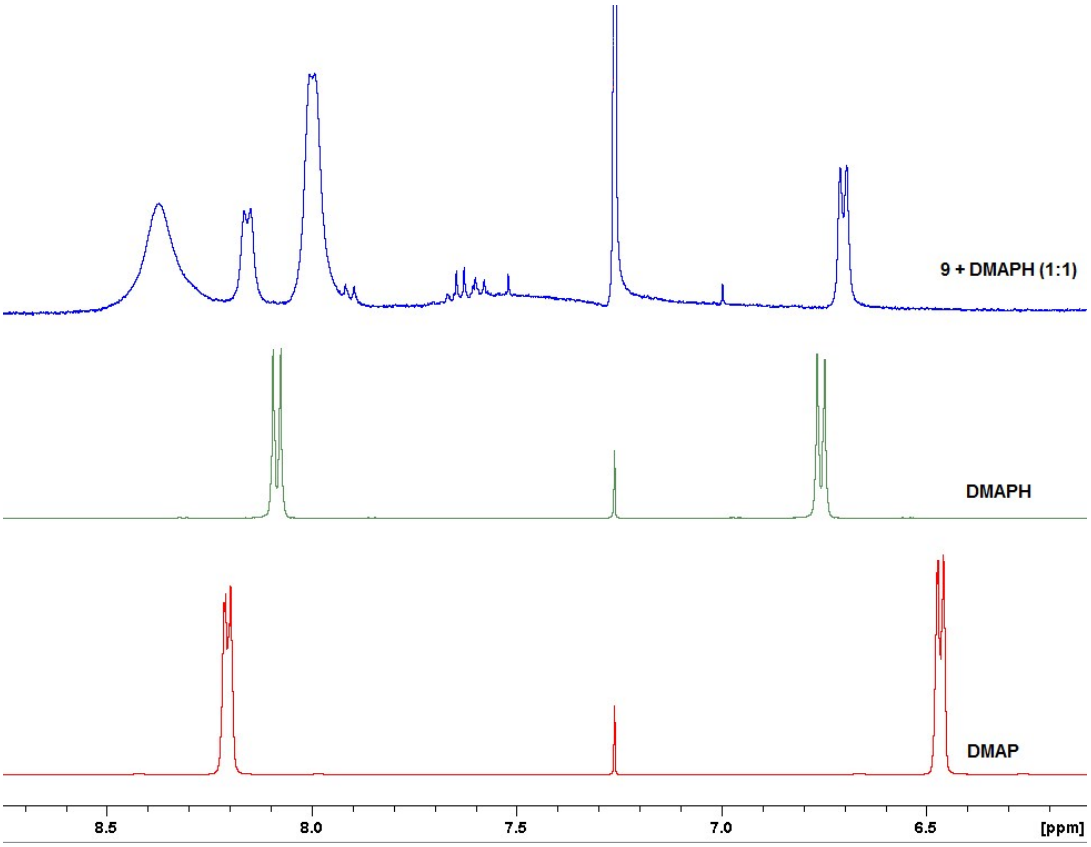


Figure S5: NMR studies on the protonation of 9 by DMAP•HCl.

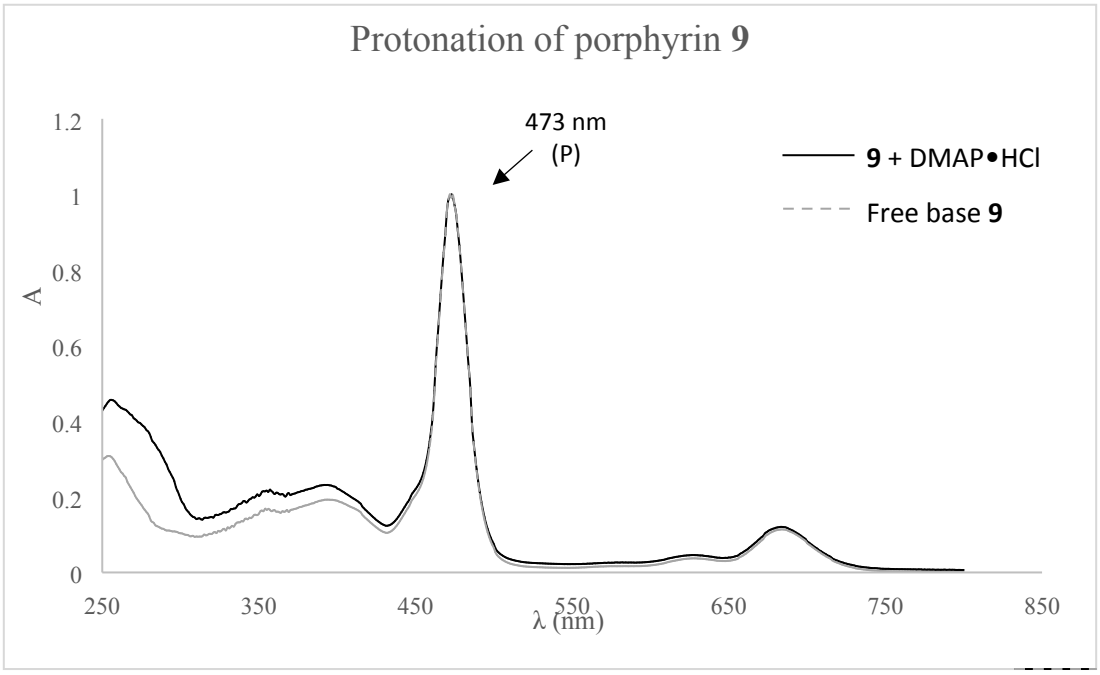


Figure S6: UV-vis studies on the protonation of 9 by DMAP•HCl.

The basicity of porphyrin **9** is not high enough to deprotonate DMAP•HCl. However, we can see an offset in the NMR spectra, which probably is due to electrostatic interaction between the free base porphyrin **9** and DMAP•HCl.

4.3. Deprotonation of amine bases by 10

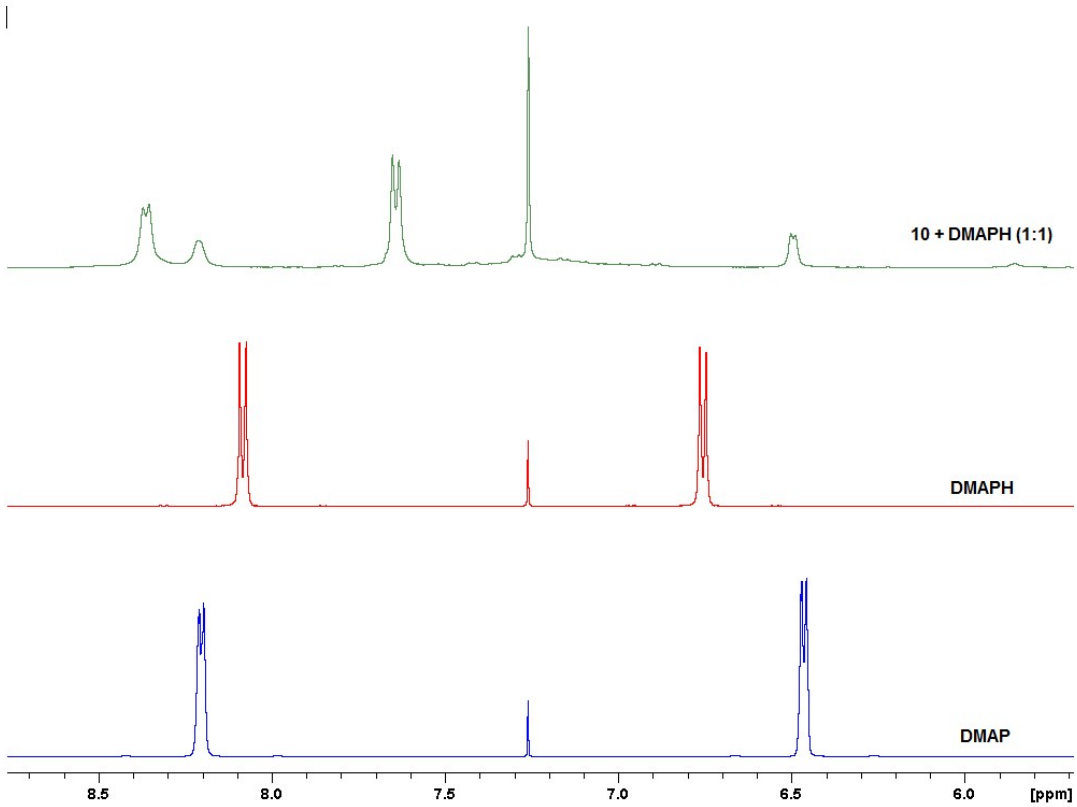


Figure S7: NMR studies on the protonation of 10 by DMAP•HCl.

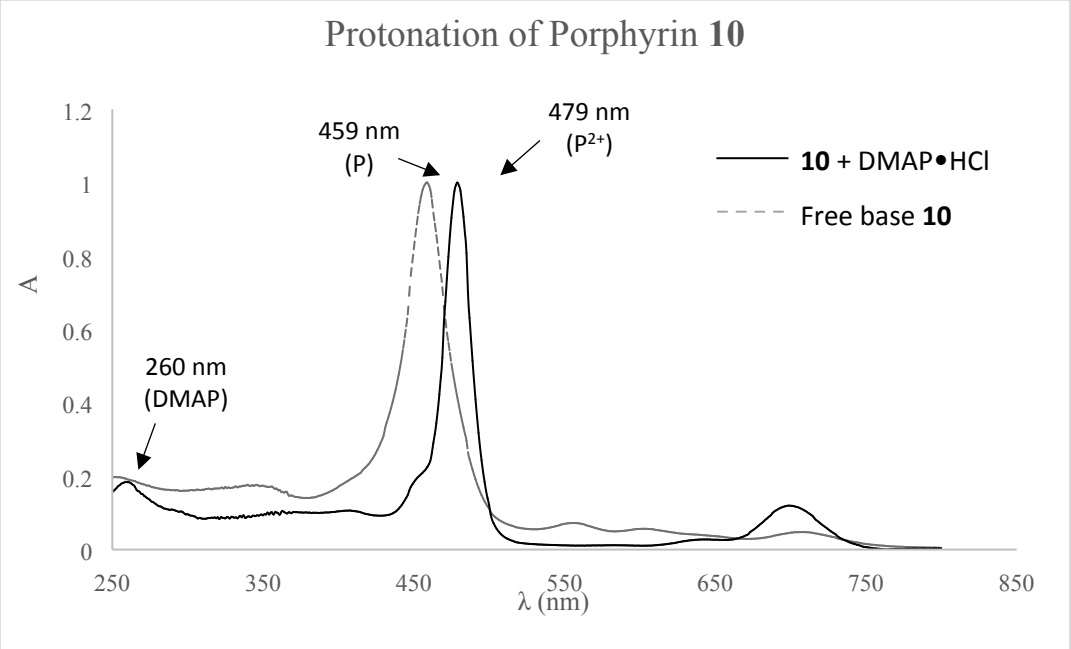


Figure S8: UV-vis studies on the protonation of 10 by DMAP•HCl.

4.4. Protonation of 8 by 3

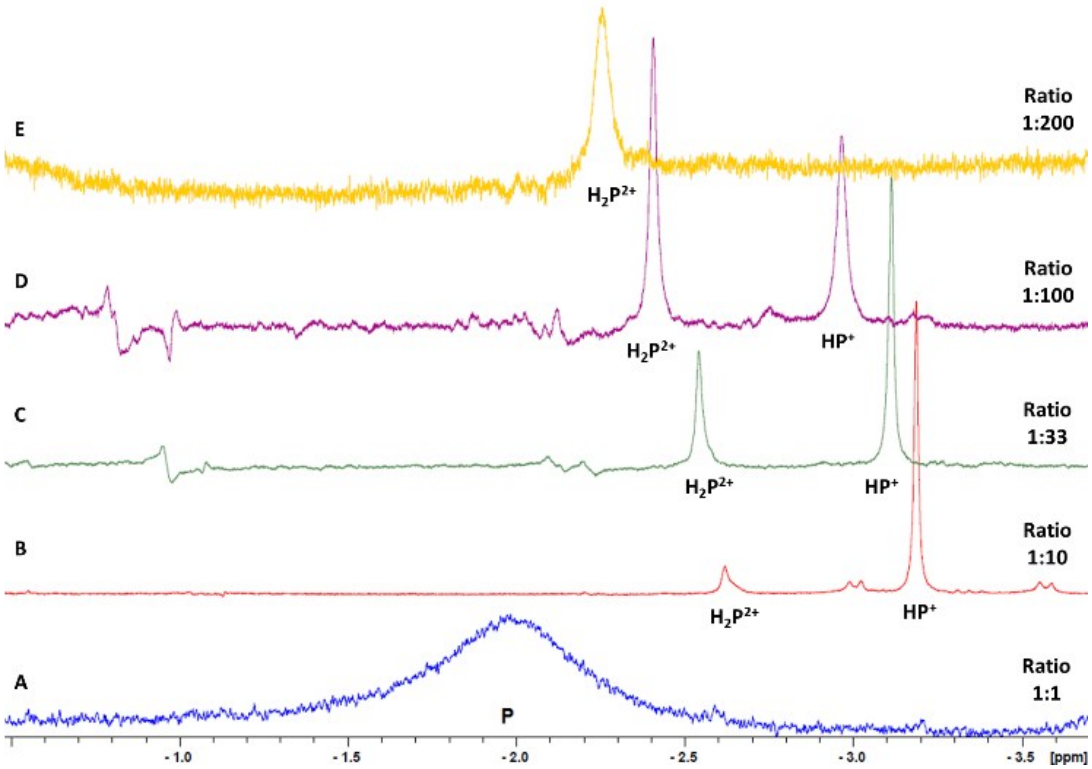


Figure S9: Protonation of 8 by 3 at increasing substrate/catalyst ratios.

5. Synthesis and characterization of new compounds

5.1. Experimental procedures

21-Methyl-5,10,15,20-tetrakis(*p*-chlorophenyl)porphyrin 18: This compound has already been described in the literature but full characterization was not reported.[1] In a 250 mL three-necked round-bottomed flask, 5,10,15,20-tetrakis(*p*-chlorophenyl)porphyrin (200 mg, 0.27 mmol) was dissolved in 70 mL of CH_2Cl_2, and acetic acid, 5% v:v, was then added to the solution. The solution was heated to reflux and methyl trifluoromethanesulfonate (45 µL, 0.37 mmol) in 1 mL of CH_2Cl_2 was added. After heating to reflux for 16 h, the mixture was cooled, alkalized with 1 M aqueous ammonia (10 mL) and washed with water. The organic phase was dried over $MgSO_4$, filtered, the solvent was evaporated, and the product was purified by column chromatography (SiO_2, CH_2Cl_2:EtOAc = 10:0–0:10, v:v) yielding, after evaporation of the solvent, a purple solid, compound **18** (142 mg, 0.186 mmol, 69%). M.p. > 300 °C; R_f = 0.82 (SiO_2, CH_2Cl_2:EtOAc = 1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = −4.88 (s, 1H, NH), −4.13 (s, 3H, N-CH_3), 7.45 (s, 2H, $CH_{\beta\text{-pyrrole}}$), 7.74 (br s, 4H, CH_{aryl}), 7.81 (d, *J* = 8.0 Hz, 4H, CH_{aryl}), 8.08 (d, *J* = 7.0 Hz, 2H, $CH_{\beta\text{-pyrrole}}$), 8.16 (d, *J* = 7.1 Hz, 2H, $CH_{\beta\text{-pyrrole}}$), 8.27 (br s, 4H, CH_{aryl}), 8.43 (d, *J* = 4.5 Hz, 2H, $CH_{\beta\text{-pyrrole}}$), 8.60 (d, *J* = 4.5 Hz, 2H, $CH_{\beta\text{-pyrrole}}$), 8.80 ppm (s, 2H, $CH_{\beta\text{-pyrrole}}$); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 157.0, 155.2, 153.7, 152.4, 140.9, 140.6, 139.3, 138.5, 135.1, 134.4, 134.0, 132.8, 128.4, 127.6, 127.2, 124.7, 118.6, 118.5, 44.1 ppm; UV-vis ($CHCl_3$): λ_{max} (log ε) = 436 (5.46), 578 (4.23), 617 (3.57), 678 nm (3.41); HRMS (MALDI) m/z calcd. for $C_{45}H_{28}N_4Cl_4$ $[M+H]^+$: 765.1146, found 765.1138.

21,22-Dimethyl-5,10,15,20-tetrakis(*p*-chlorophenyl)porphyrin trifluoromethanesulfonate (21 $CF_3SO_3^-$): In a 100 mL three necked round-bottomed flask, 5,10,15,20-tetrakis(*p*-chlorophenyl)porphyrin (50 mg, 0.07 mmol) was dissolved in 18 mL of CH_2Cl_2. The solution was heated to reflux, and a solution of methyl trifluoromethanesulfonate (9 µL, 0.08 mmol) in 1 mL of CH_2Cl_2 was added. After refluxing for 16 h, the mixture was cooled, alkalized with 1 M aqueous ammonia (10 mL) and washed with H_2O. The organic phase was dried over $MgSO_4$, filtered, the solvent was evaporated, and the product was purified by column chromatography (SiO_2, hexane:EtOAc:MeOH:TEA = 70:20:5:5, v:v) yielding, after evaporation of the solvent, compound **18** (20 mg, 0.026 mmol, 40%) and a green solid, compound **21** (25 mg, 0.032 mmol, 50%). M.p. = 227–233 °C; R_f = 0.26 (SiO_2, EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = −4.91 (s, 6H, N_{21} and N_{22}-CH_3), 7.69 (d, *J* = 4.8 Hz, 2H, CH_{aryl}), 7.78 (d, *J* = 2.5 Hz, 2H, $CH_{\beta\text{-pyrrole}}$), 7.80 (d, *J* = 6.4 Hz, 2H, CH_{aryl}), 7.86 (d, *J* = 1.3 Hz, 2H, CH_{aryl}), 7.88 (d, *J* = 2.2 Hz 2H, $CH_{\beta\text{-pyrrole}}$), 7.91 (d, *J* = 8.4 Hz, 2H, $CH_{\beta\text{-pyrrole}}$), 8.14 (d, *J* = 1.6 Hz, 4H, CH_{aryl}), 8.26 (br s, 2H, CH_{aryl}); 8.30

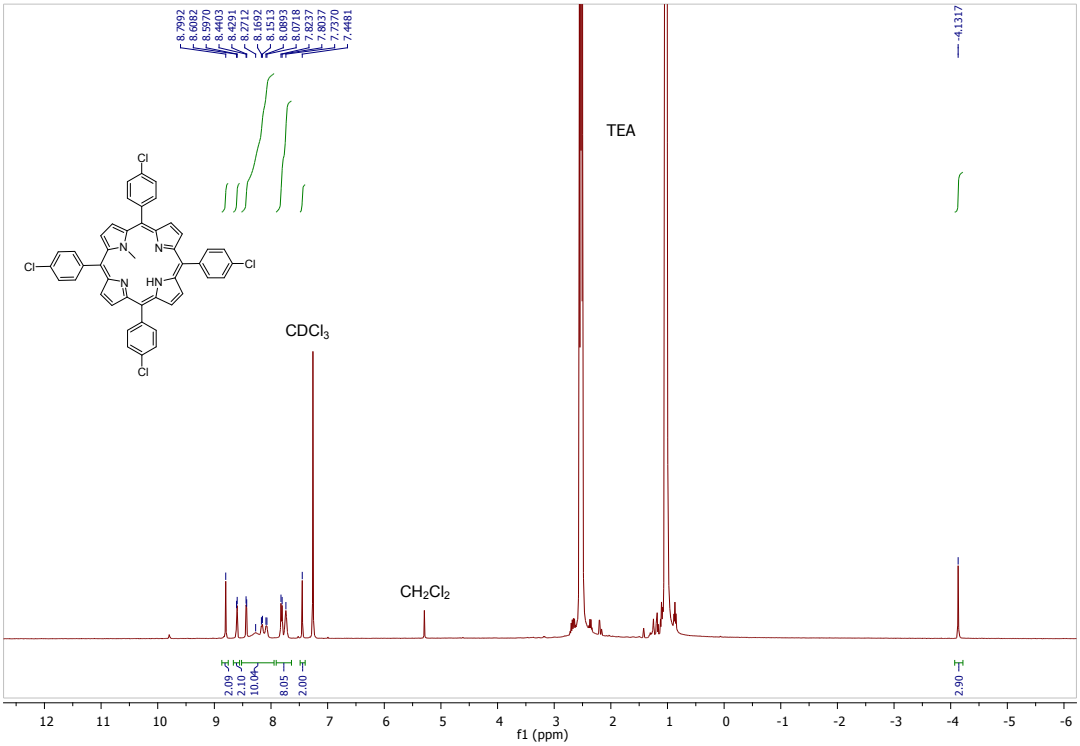
(d, *J* = 8.3 Hz, 2H, $CH_{\beta\text{-pyrrole}}$), 8.51 ppm (d, *J* = 8.2 Hz, 4H, CH_{aryl}); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 158.2, 155.9, 155.8, 148, 140.4, 138.6, 138.3, 135.3, 132.6, 130.4, 128.9, 127.0, 124.4, 121.1, 118.1, 59.5 ppm; UV-vis ($CHCl_3$): λ_{max} (log ε) = 346 (4.30), 463 (5.04), 653 (4.05), 712 nm (3.58); HRMS (MALDI) m/z calcd. for $C_{46}H_{31}N_4Cl_4$ $[M]^+$: 779.1303, found 779.1306.

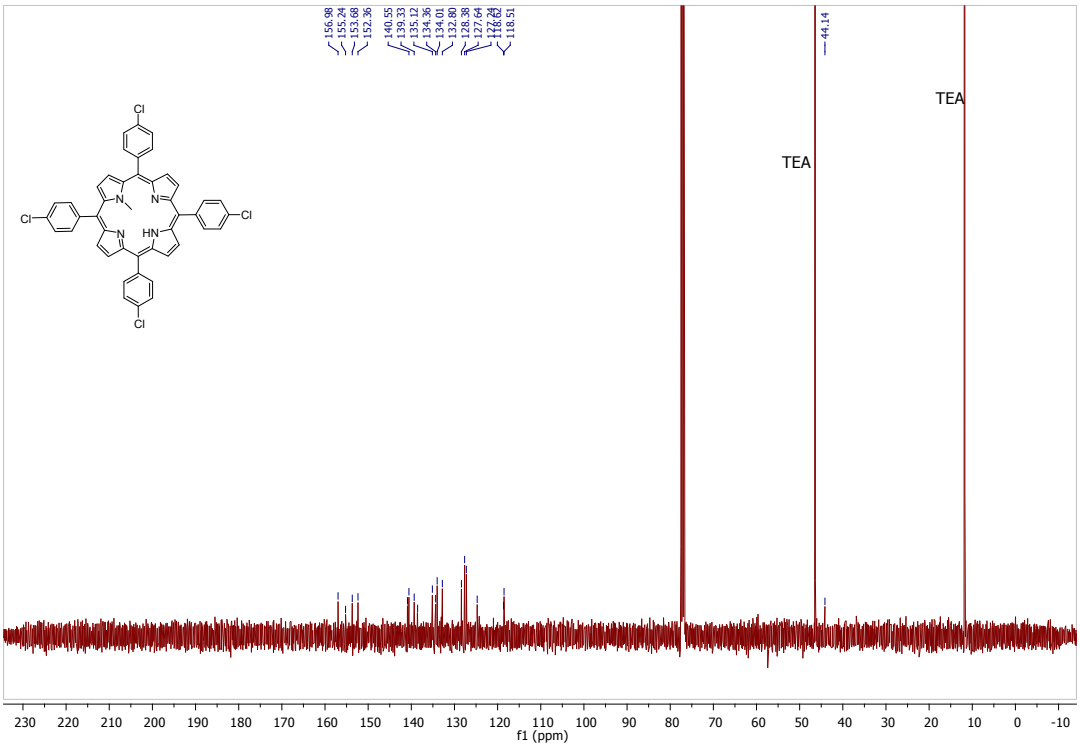
21-Methyl-5,10,15,20-tetrakis(*p*-methoxyphenyl)porphyrin 19: This compound has already been described in the literature but full characterization was not reported.[1] In a 250 mL three necked round-bottomed flask, 5,10,15,20-tetrakis(*p*-methoxyphenyl)porphyrin (200 mg, 0.27 mmol) was dissolved in 70 mL of CH_2Cl_2. Acetic acid, 5% v:v, was then added to the solution. The solution was heated to reflux, and methyl trifluoromethanesulfonate (9 µL, 0.37 mmol) in 1 mL of CH_2Cl_2 was added. After heating to reflux for 16 h, the mixture was cooled, alkalised with 1 M aqueous ammonia (10 mL) and washed with H_2O. The organic phase was dried over $MgSO_4$, filtered, the solvent was evaporated, and the product was purified by column chromatography (SiO_2, CH_2Cl_2:EtOAc = 10:0–0:10, v:v) yielding, after evaporation of the solvent, a purple solid, compound **19** (102 mg, 0.14 mmol, 50%). M.p. > 300 °C; R_f = 0.79 (SiO_2, EtOAc); ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = −4.77 (s, 1H, NH), −4.06 (s, 3H, N-CH3), 4.10 (s, 12H, O-CH3), 7.30 (*d*, J = 8.6 Hz, 4H, CH_{aryl}), 7.38 (*d*, 4H, CH_{aryl}), 7.40 (s, *J* = 8.8 Hz, 2H, $CH_{\beta\text{-pyrrole}}$), 8.10 (d, *J* = 6.6 Hz, 2H, $CH_{\beta\text{-pyrrole}}$), 8.17 (dd, *J* = 5.9 Hz, 2H, $CH_{\beta\text{-pyrrole}}$), 8.30 (dd, 2H, $CH_{\beta\text{-pyrrole}}$), 8.43 (d, *J* = 4.5, 4H, CH_{aryl}), 8.63 (d, *J* = 4.5, 4H, CH_{aryl}), 8.82 ppm (s, 2H, $CH_{\beta\text{-pyrrole}}$); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 160.0, 159.4, 157.3, 153.7, 153, 139.7, 139.1, 135.9, 135, 133.6, 132.3, 128.2, 125.4, 119.1, 118.1, 112.9, 112.4, 55.8, 55.7 ppm; UV-vis ($CHCl_3$): λ_{max} (log ε) = 439 (5.44), 586 (4.28), 685 nm (3.96); HRMS (MALDI) m/z calcd. for $C_{49}H_{40}N_4O_4$ $[M+H]^+$: 749.3128, found 749.3130.

(4-(*tert*-Butyl)benzyl)(2-(phenylsulfonyl)ethyl)sulfane 5: Vinyl phenyl sulfone **4** (370 mg, 1.61 mmol) and 4-*tert*-butylbenzyl mercaptan **3** (300 µL, 1.61 mmol) were dissolved in dry and degassed CH_2Cl_2. DBU (24.5 µL, 0.161 mmol, 10 mol%) was then added and the reaction was stirred at rt for 24 h. The solvent was evaporated and the product was purified with a 2M sodium hydroxide solution followed by recrystallization from hot hexane, yielding a white solid of compound **5** (200 mg, 0.539 mmol, 34%). M.p. = 63.9–66.5°C; R_f = 0.4 (SiO_2, CH_2Cl_2:EtOAc = 8:2, v/v); ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.33 (s, 9H, *tert*-butyl), 2.73 (m, 2H, S-$CH_2$$CH_2$), 3.23-3.13 (m, 2H, S-$CH_2$$CH_2$), 3.66 (s, 2H, Ar-$CH_2$-S), 7.12 (d, *J* = 8.3 Hz, 2H, CH_{aryl}), 7.29–7.26 (m, 2H, CH_{aryl}), 7.59 (t, *J* = 7.7 Hz, 2H, CH_{aryl}), 7.70 (t, *J* = 7.5 Hz, 1H, CH_{aryl}), 7.87 ppm (dd, *J* = 8.4Hz, 2H, CH_{aryl}); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 150.4, 138.8, 134.8, 134.3, 133.9, 129.4, 128.5, 128.2, 125.7, 55.9, 36.1, 34.5, 31.3, 23.8 ppm; IR: ν_{max} (neat): 2958, 1447, 1316, 1304, 1286, 1206, 1148, 1120, 1083, 848, 834, 793, 751, 741, 720, 686, 657, 552 cm^{-1}; HRMS (ESI) m/z calcd. for $C_{19}H_{25}O_2S_2$ $[M+H]^+$: 349.1290, found 349.1286.

5.2. NMR data

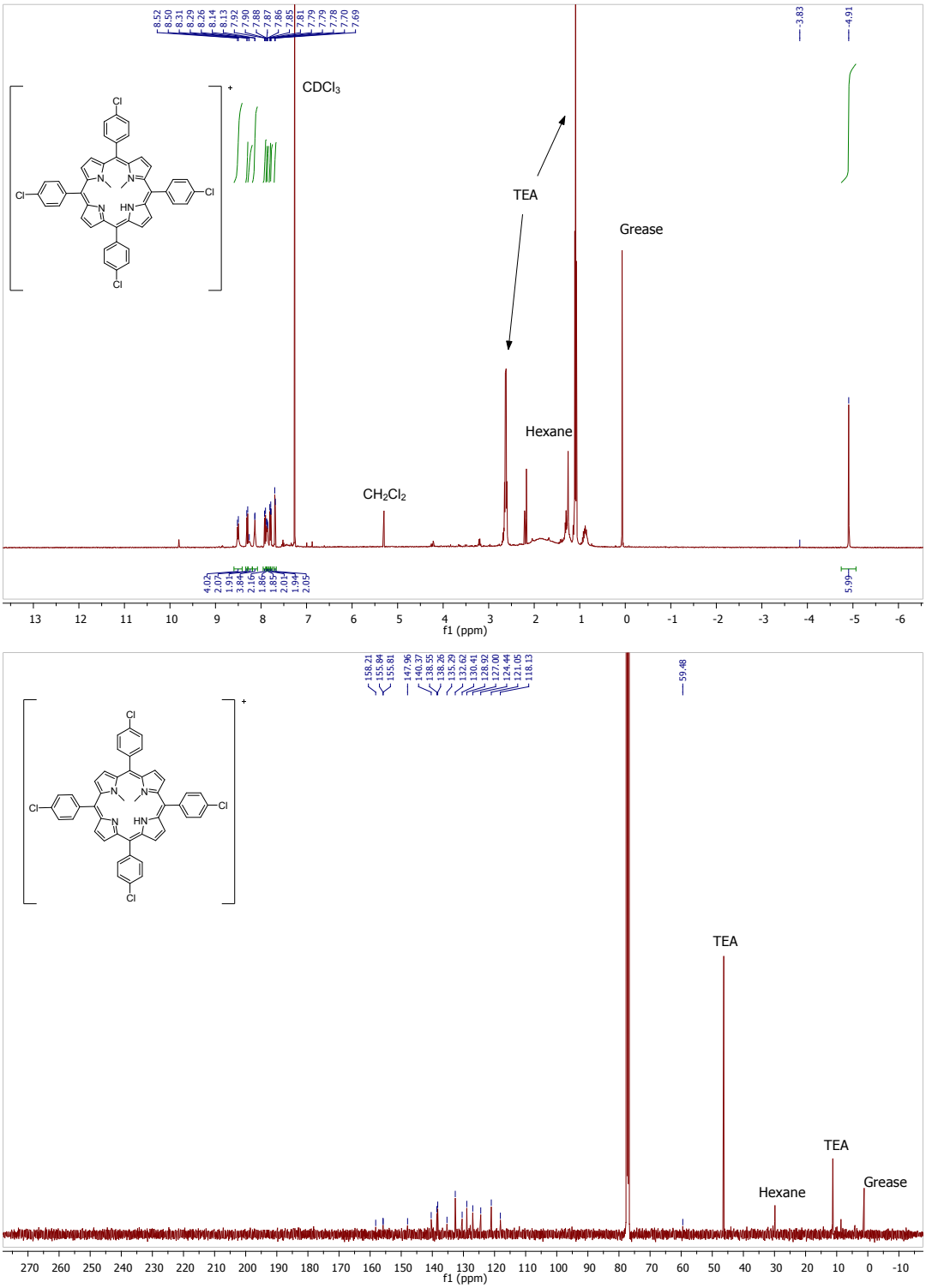
21-Methyl-5,10,15,20-tetrakis(*p*-chlorophenyl)porphyrin 18





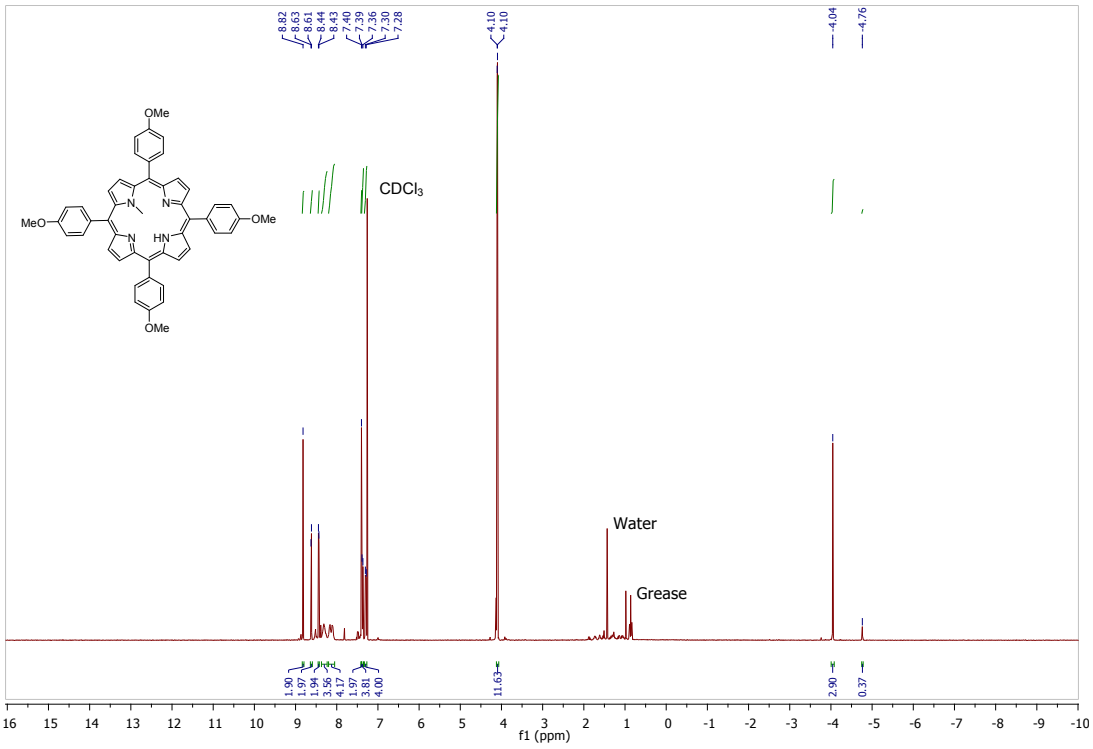
(1 mol% of TEA was added to increase solubility and to prevent protonation by acidic impurites of $CDCl_3$)

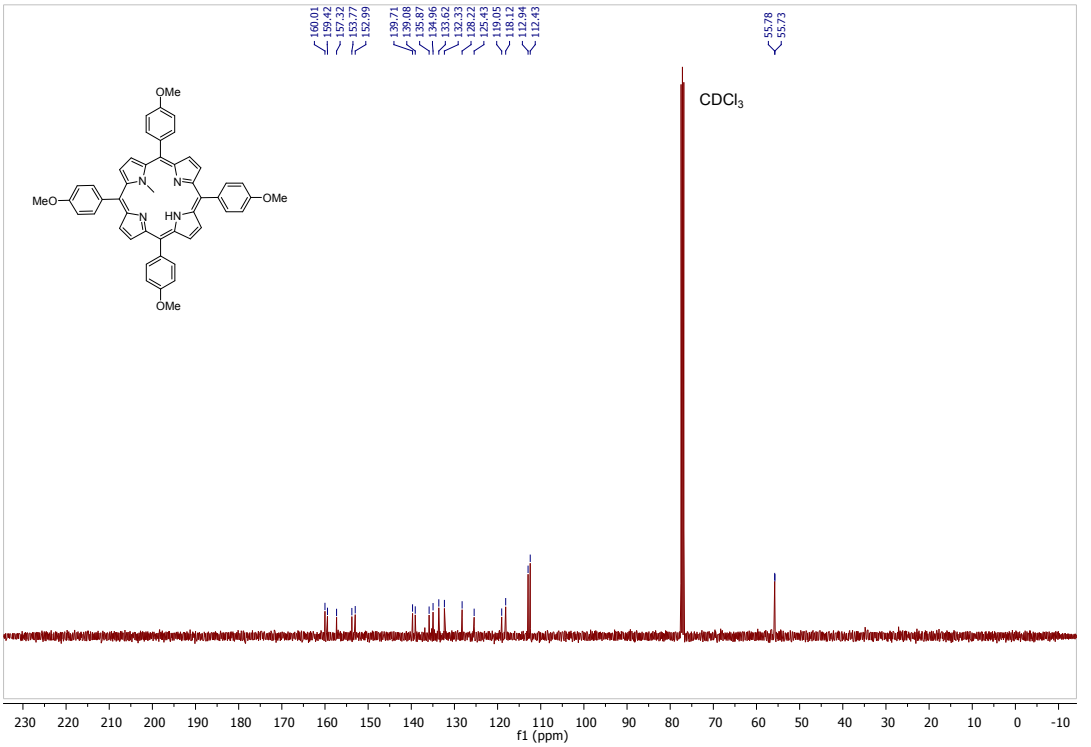
21,22-Dimethyl-5,10,15,20-tetrakis(*p*-chlorophenyl)porphyrin trifluoromethanesulfonate (21 $CF_3SO_3^-$)



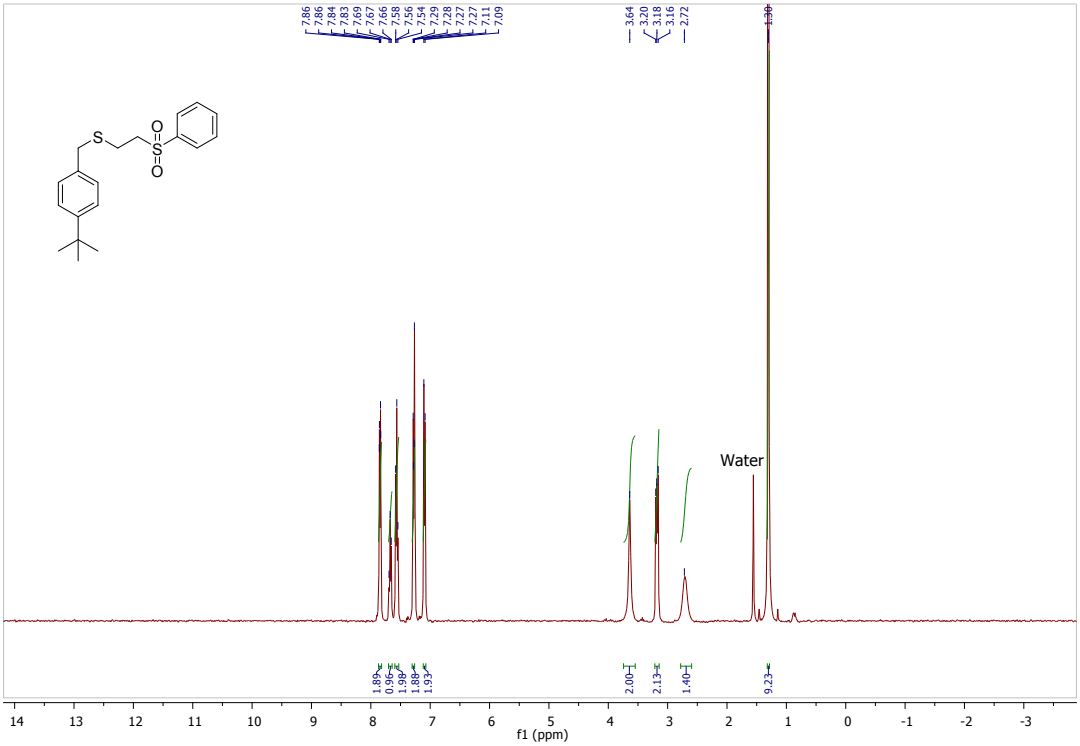
(1 mol% of TEA was added to increase solubility and to prevent protonation by acidic impurites of $CDCl_3$)

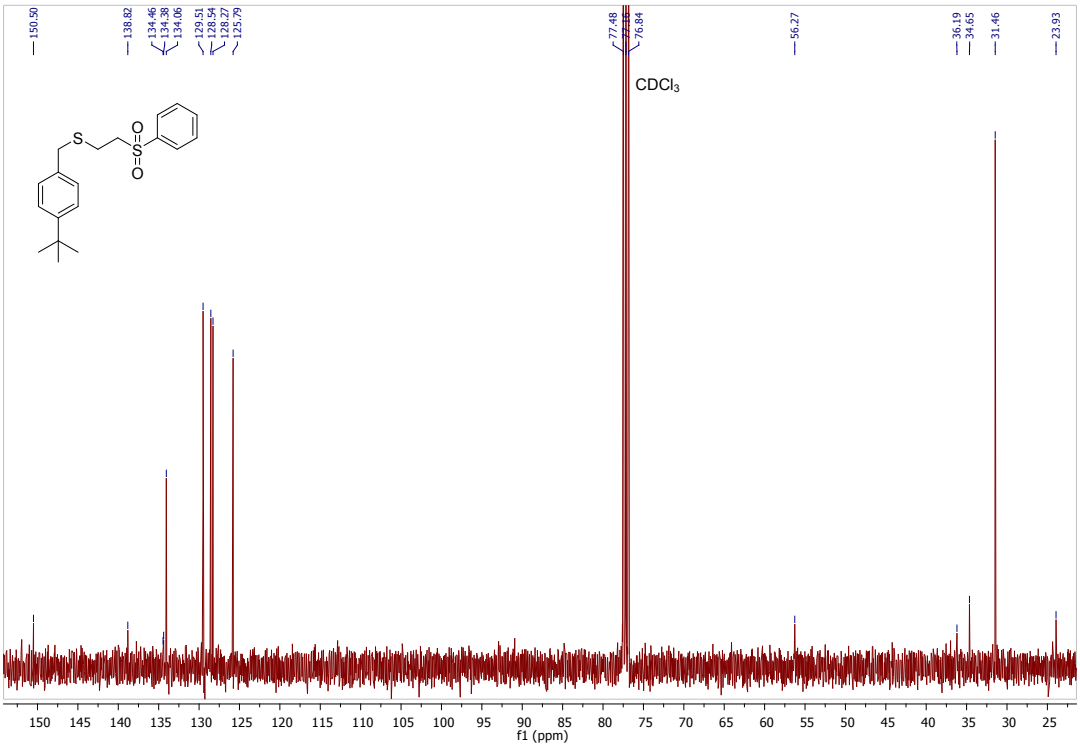
21-Methyl-5,10,15,20-tetrakis(*p*-methoxyphenyl)porphyrin 19





(4-(*tert*-Butyl)benzyl)(2-(phenylsulfonyl)ethyl)sulfane 5





6. References

[1] D. K. Lavallee, *The Chemistry and Biochemistry of N-Substituted Porphyrins*, VCH Publishers, Inc., New York, **1987**.