Electronic supplementary information

Unique Prototropy of *meso*-Alkylidenyl Carbaporphyrinoid Possessing one *meso*-Exocyclic Double Bond

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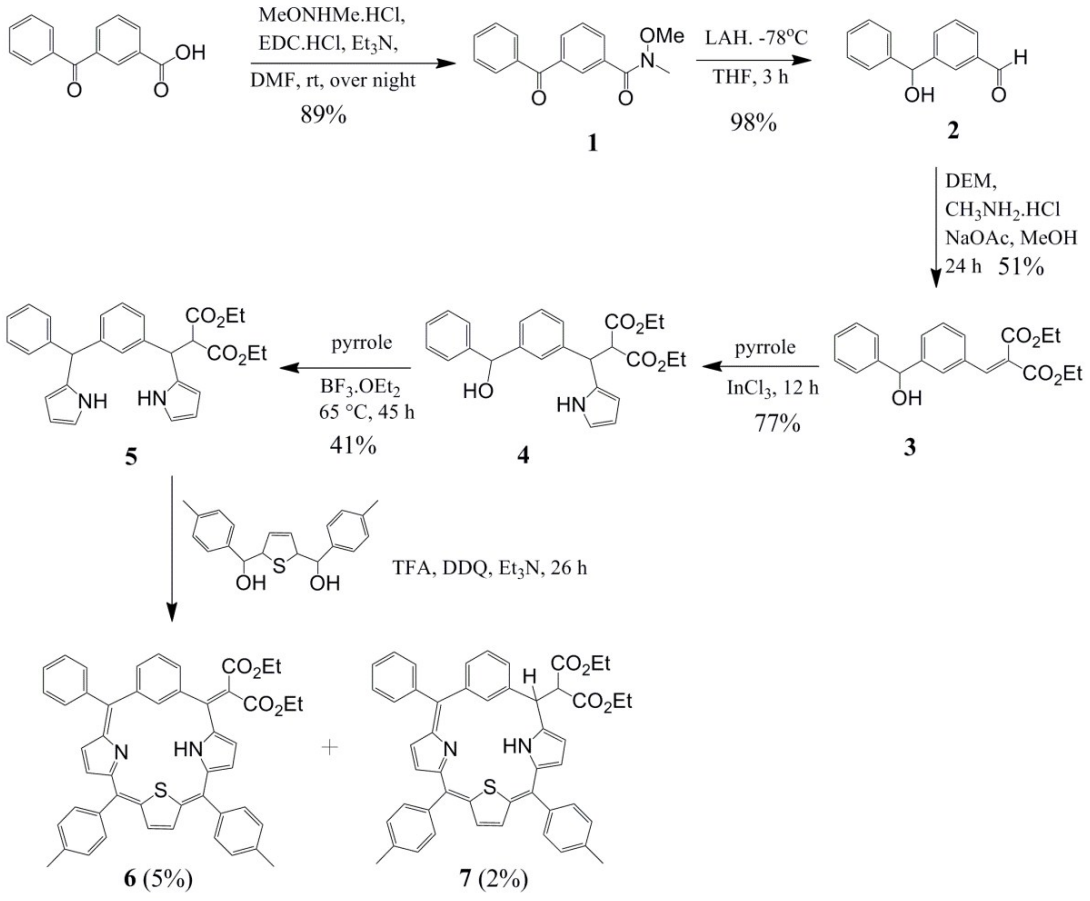
Experimental Section

General information and instrumentations

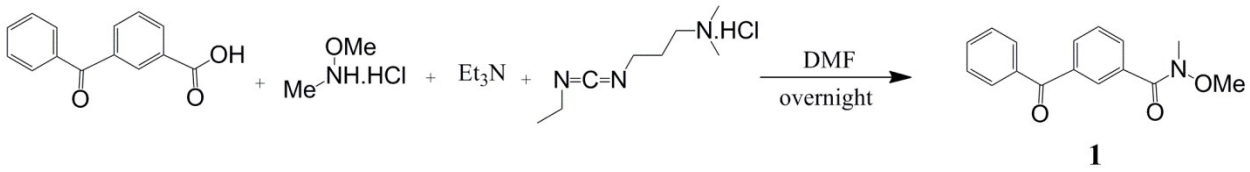
^{1}H NMR spectra were recorded on 600, 400 and 300 MHz Bruker NMR spectrometer using TMS as the internal standard. Chemical shifts are reported in parts per million (ppm). When peak multiplicities are given, the following abbreviations are used: s, singlet; br s, broad singlet; d, doublet; t, triplet; m, multiplet. ^{13}C NMR spectra were proton decoupled and recorded on a 100 or 150 MHz Bruker spectrometer using TMS as the internal standard. Pyrrole was distilled at atmospheric pressure from CaH_2. Absorption spectra were recorded on SCINCO S-3100 UV-vis spectrophotometer. All titrations were performed using HPLC grade CH_3CN purchased from Aldrich. All other chemicals and solvents were purchased from commercial sources and were used as such, unless otherwise mentioned.

Synthetic Scheme



Synthetic procedure

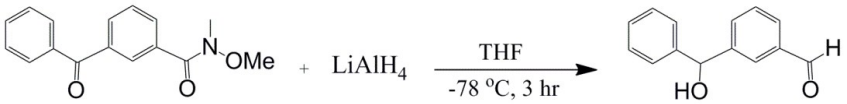
3-benzoyl-N-methoxy-N-methylbenzamide (1).[1]



1

To a stirred suspension of 3-benzoylbenzoic acid (4.5 g, 19.89 mmol) in DMF (100 mL) were added N,O-dimethyl hydroxylamine hydrochloride (2.33 g, 23.87 mmol), Et_3N (3.33 mL, 23.87mmol), and EDC.HCl (4.58g, 23.87mmol). After being stirred for overnight at room temperature, solvent was removed under reduced pressure. Water (100 mL) was added to the residue and extracted with EtOAc (3 x 50 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed in vacuo. The crude oily residue was chromatographed on silica-gel using 25% EtOAc in hexane as eluent to afford the Weinreb amide **1** as colorless oily compound (4.8 g, 89%). All spectroscopic data for this compound proved consistent with those reported in literature.[1]

3-(hydroxy(phenyl)methyl)benzaldehyde (2).[1]



1 **2**

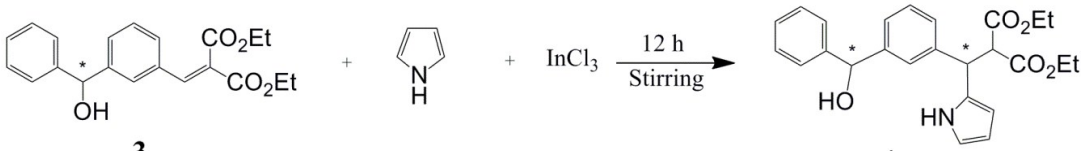
A solution of Weinreb amide **1** (4.8 g, 17.82 mmol) in anhydrous THF (70 mL) was cooled to -78°C under a nitrogen atmosphere. To the resulting solution was added $LiAlH_4$ (21.39 mL of 1.0 M solution in THF, 21.39 mmol) via syringe. The reaction mixture was stirred for 3 h at the same temperature. At this point, H_2O (10 mL) was slowly added to the reaction mixture at -78°C to quench the reaction.The reaction mixture was then diluted with 50 mL of EtOAc and the resulting precipitate was removed by Celite filtration. The filtrate was washed with brine and the combined organic layer was dried over Na_2SO_4. Removal of solvent under reduced pressure yielded oily residue which was purified by silica-gel column chromatography using 20% EtOAc in hexane as eluent to afford an oil of compound **2** (3.69 g, 98%).All spectroscopic data for this compound proved consistent with those reported in literature.[1]

Diethyl 2-(3-(hydroxy(phenyl)methyl)benzylidene)malonate (3).

2 **3**

A solution of NaOAc (1.55 g, 18.85mmol), methylamine hydrochloride (1.27 g, 18.85mmol) and diethyl malonate (3.02 g, 18.85mmol) in methanol (20 mL) was stirred for 30 minute at room temperature. To the resulting solution 3-(hydroxy(phenyl)methyl)benzaldehyde **2** (2.0 g, 9.42mmol) in methanol (20 mL) was added. After being stirred for 24 h at room temperature, solvent was removed in vacuo. Water was poured to the reaction mixture and the aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL) and dried over anhydrous Na_2SO_4. Solvent was removed under reduced pressure and the residue was purified by column chromatography on neutral alumina using 20% EtOAc in hexane to afford the oil of compound **3** (1.70 g, 51%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.71 (s, 1H), 7.49 (br s, 1H), 7.43-7.41 (m, 1H) 7.36-7.35 (m, 6H), 7.33-7.27 (m, 1H), 5.849, (d, *J* = 3 Hz, 1H), 4.29 (q, *J* = 7 Hz), 4.24-4.22 (m, 2H), 2.25 (d, *J* = 3 Hz, 1H), 1.32 (t, *J* = 7 Hz, 3H), 1.24 (t, *J* = 7 Hz, 3H). **MALDI-TOF** m/z 354.1467 M^+ and 379.1521(M + Na + 2H)$^+$ calcd for $C_{21}H_{22}O_5$ (M) found m/z 354.5773 and 379.4725, respectively.

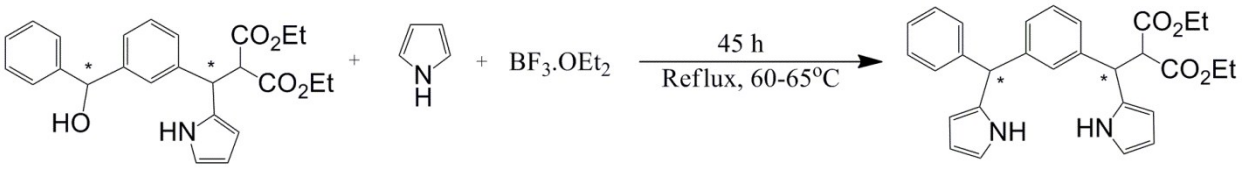
Diethyl 2-((3-(hydroxy(phenyl)methyl)phenyl)(1H-pyrrol-2-yl)methyl)malonate (4).[2]



3 **4**

To a stirred solution **3** (1.2 g, 3.39 mmol) in pyrrole (23.5 mL, 338.6 mmol) was added $InCl_3$ (0.375 g, 1.69 mmol). After stirring for 12 h at 25 °C under nitrogen atmosphere, water (50 mL) were added to the reaction mixture. The aqueous layer was extracted with CH_2Cl_2 (30 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4 and solvent was removed under reduced pressure. The crude residue was purified by column chromatography on silica using 20% EtOAc in hexane as eluent to yield **4** (1.10 g, 77%) as thick liquid which becomes solid on keeping in refrigerator. **^{1}H NMR ($CDCl_3$, 400 MHz, mixture of stereoisomers**) δ 8.47 (brs, 1 H, N*H*), 7.36-7.30 (m, 5H), 7.27-7.23 (m, 3H), 7.17-7.15(m 1H), 6.63 (br s, 1H), 6.07-6.05 (m, 1H), 5.91-5.90 (m, 1H), 5.79(s, 1H), 4.77 (d, J = 10.5 Hz), 4.15-4.09 (m, 3H), 3.88-3.79 (m, 2H), 2.25 (brs, 1H, O*H*), 1.18-1.14 (m, 3H), 0.90-0.85 (m, 3H). **^{13}C NMR ($CDCl_3$, 100 MHz, mixture of stereoisomers)** δ 168.6, 167.4, 144.1, 143.7, 140.0, 130.8, 128.7, 128.5, 127.5,127.4 126.5, 126.4, 126.3, 126.2 125.3,125.2, 117.5,108.0,106.6,106.5, 76.1, 61.8, 61.4, 58.01, 44.3, 13.9,13.6.
MALDI-TOF m/z 422.1967 (M +H)$^+$ and 444.1781 (M + Na)$^+$ calcd for $C_{25}H_{27}NO_5$ (M), found m/z 421.5738 and 444.5635, respectively.

Diethyl 2-((3-(phenyl(1H-pyrrol-2-yl)methyl)phenyl)(1H-pyrrol-2-yl)methyl)malonate (5).



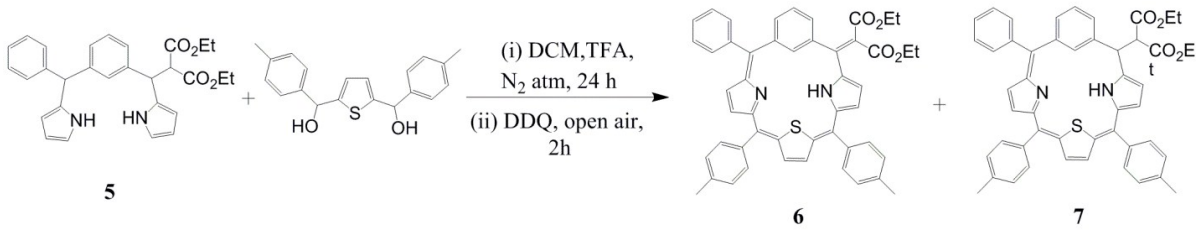
4 **5**

A solution of compound **4** (0.400 g, 0.95 mmol) and pyrrole (6.6 mL, 95.0mmol) was purged with nitrogen gas for 20 minutes. Subsequently, $BF_3.OEt_2$ (0.118 mL, 0.95 mmol) was added and the reaction mixture was refluxed at 65 °C for 45 h under nitrogen atmosphere. On cooling to the room temperature, the reaction mixture was quenched by adding Et_3N (0.264mL, 1.89 mmol). The crude reaction mixture was directly chromatographed on silica gel using 25% EtOAc in hexane to afford pure **5** (0.185 mg, 41%) as semi-solid. **^{1}H NMR ($CDCl_3$, 400 MHz, mixture of stereoisomers)** δ 8.45 (br d, *J* = 17 Hz, 1H, N*H*), 7.89 (br d, *J* = 19 Hz, 1H, N*H*), 7.30-7.25 (m, 2H), 7.23- 7.19 (m, 2H), 7.15-7.11 (m, 4H), 7.08-7.03 (m, 1H), 6.70-6.68(m, 1H), 6.63- 6.60 (m, 1H), 6.14(q, *J* = 3 Hz, 1H), 6.07-6.01 (m, 1H), 5.86(d, *J* = 36Hz, 1H), 5.80-5.79 (m, 1H), 5.41(d, *J* = 2.4 Hz, 1H), 4.72 (d, *J* = 10.6 Hz, 1H), 4.16-4.03(m, 3H), 3.86 (q, *J* = 6.2 Hz, 2H), 1.16 (t, *J* = 7.1 Hz, 3H), 0.92 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz, mixture of stereoisomers) δ 169.85, 169.78, 168.80, 144.87, 144.82, 144.57, 144.48, 141.59, 141.48, 141.59, 141.48, 134.43, 134.38, 132.24, 132.19, 129.90, 129.87, 129.85, 129.70, 129.63, 129.61, 128.87, 128.75, 127.82, 127.80, 127.78, 127.6, 118.45, 118.43, 118.30, 118.25, 109.16, 109.13, 109.09, 108.74, 108.73, 107.17, 107.15,62.57, 62.29, 58.76, 58.68, 51.14, 44.93, 44.88, 14.18, 14.04,

MALDI-TOF m/z 471.2206 $(M+H)^+$, 453.1940 $(M+Na)^+$ and 509.1940 $(M+ K)^+$calcd for $C_{29}H_{30}N_2O_4$(M), found m/z 471.5547, 453.5263 and 509.4926, respectively.

Synthesis of compound 6 and 7



5 **6** **7**

A solution of compound **5** (0.770 g, 1.64 mmol) and 2,5-bis-thiophene-dimethanol[3] (0.530 g, 1.64 mmol) in dry CH_2Cl_2 (250mL) was purged with nitrogen for 20 minutes. To the resulting solution TFA (62µl, 0.82 mmol) was added and the reaction mixture was stirred for 24 h at room temperature under nitrogen atmosphere. At this point, DDQ (1.11 g, 4.95 mmol) was added and the reaction was stirred for a further 2.0 hour in air. Triethylamine (342µl, 2.45 mmol) was added to the reaction flask and the solvent was removed under reduced pressure. The residue thus obtained was purified by repeated column chromatography. Column chromatography on silica-gel using 15% EtOAc in hexane gave the mixture of compound **6** and **7** as a green band which was further chromatographed on silica using 2% EtOAc in CH_2Cl_2 as eluent to afford pure **6** (62 mg, 5%) and **7** (25 mg, 2%).

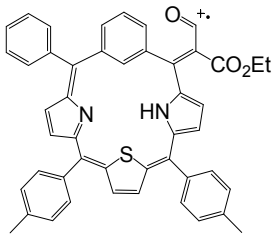
Compound 6

^{1}H NMR (CD_2Cl_2, 400 MHz) δ 8.49 (br s, 1H), 7.53-7.51 (m, 2 H), 7.47-7.41 (m, 5H), 7.30-7.23 (m, 10 H), 7.19 (s, 1H), 6.81 (s, 2H), 6.79 (d, *J* = 4.16 Hz), 6.66 (d, *J* = 4.8, 1H), 6.13 (br s, 1H), 4.30 (br s, 2H), 3.98 (br s, 2H), 2.42 (s, 3H), 2.41 (s, 3H), 1.29 (t, *J* = 7.12 Hz, 3 H), 1.02 (t, *J* = 7.12 Hz, 3H).

^{1}H NMR (DMSO-*d_6*, 400 MHz) δ 9.94 (s, 1H), 7.52-7.46 (m, 3H), 7.44-7.40 (m, 3H), 7.35 (d, *J* = 4.8 Hz, 1H), 7.32-7.16 (m, 11H), 6.91 (d, *J* = 5.9Hz, 1H), 6.83 (d, *J* = 5.9 Hz, 1H), 6.65 (d, *J* = 3.5 Hz, 1H), 6.55 (d, *J* = 4.8 Hz, 1H), 5.95 (d, *J* = 3.5Hz, 1H) 4.22 (q, *J* = 7.1 Hz, 2H), 3.88 (q, *J* = 7.1 Hz, 2H), 2.38 (s, 3H), 2.37 (s, 3H), 1.21 (t, *J* = 7.1 Hz, 3H), 0.88 (t, *J* = 7.1 Hz, 3H)

^{13}C NMR (CD_2Cl_2, 150 MHz) δ 169.9,167.4, 164.5, 156.0, 148.2, 147.5, 147.2, 142.2, 140.4, 138.5, 138.0, 137.7, 137.0, 136.1, 135.7, 135.4, 135.1, 133.2, 132.9, 131.7, 131.5, 131.4, 130.5, 130.3, 129.9, 129.0, 128.9, 127.7, 127.1, 125.5, 122.1, 118.3, 114.6, 62.0, 61.1, 21.3, 14.1, 14.0.

MALDI-TOF m/z 753.2787 $(M+H)^+$ and 752.2709 (M^+) calcd for $C_{49}H_{40}N_2O_4S$(M), found m/z 753.5890 and 752.5767, respectively. A characteristic fragment peak at m/z 708.5539 was observed which corresponds to the loss of one –OEt group from **6**. This peak is absent in the MALDI-TOF spectrum of **7**.



$C_{47}H_{36}N_2O_3S$
Exact Mass: 708.2447

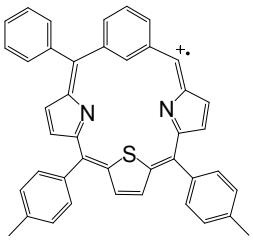
Compound 7

^{1}H NMR (CD_2Cl_2, 400 MHz) δ 7.75 (d, *J* = 7.6 Hz, 1H), 7.44-7.30 (m, 9H), 7.29-7.23 (m, 5H), 7.19 (t, *J* = 7.7 Hz, 1H), 7.15 (d, *J* = 5.2 Hz, 1H), 6.97 (d, *J* = 7.9 Hz, 1H), 6.91 (d, *J* = 5.2Hz, 1H), 6.79 (d, *J* = 5.0 Hz, 1H), 7.76 (s, 1H), 6.64 (br s, 1H), 6.49 (br s, 1H), 4.86 (br s, 1H) 4.26 (d, *J* = 12.1 Hz, 1H), 4.12-4.04 (m, 2H), 4.04-3.97 (m, 2H), 2.43 (s, 3H), 2.42 (s, 3H), 1.16 (t, *J* = 7.1 Hz, 3H) 1.03 (t, *J* = 7.1 Hz, 3H).(NH was not observed may be due peak broadening).

^{1}H NMR (DMSO-*d_6*, 400 MHz) δ 10.27 (s, 1H), 7.90 (d, *J* = 7.4 Hz, 1H), 7.49-7.47 (m, 3H), 7.38-7.25(m, 10H), 7.22 (d, *J* = 5.7 Hz, 1H), 7.19 (d, *J* = 4.7 Hz, 1H), 7.16 (t, *J* = 7.7 HSAz, 1H), 6.98 (d, *J* = 5.7 Hz, 1H), 6.88 (s, 1H), 6.75 (d, *J* = 7.7 Hz, 1H), 6.65 (d, *J* = 4.7 Hz, 1H), 6.53 (t, *J* = 3.2/2.3 Hz, 1H), 5.98 (t, *J* = 3.2/2.7 Hz, 1H), 5.05 (d, *J* = 12.6 Hz, 1H), 4.66 (br s, 1H), 4.12-4.03 (m, 2H), 4.02-3.93 (m, 2H), 2.41 (s, 3H), 2.38 (s, 3H), 1.11 (t, *J* = 7.1 Hz, 3H), 0.94 (t, *J* = 7.1 Hz, 3H),

^{13}C NMR (DMSO-*d_6*, 150 MHz) δ 169.2, 167.8, 167.7, 155.0, 150.0, 147.1, 142.6, 141.1, 138.6, 137.1, 136.4, 136.3, 135.4, 133.3, 132.4, 131.9, 131.5, 131.2, 131.0, 130.8, 130.0, 129.5,129.4, 129.0, 128.4, 128.3, 126.7, 121.7, 120.1, 115.9, 61.4, 61.3, 53.8, 44.6, 21.3, 14.2, 14.1.(one carbon in aromatic region is not resolved).

MALDI-TOF m/z 755.2944 $(M+3H)^+$, 754.2865$(M+2H)^+$, 753.2787 $(M+H)^+$) and 752.2709 (M^+) calcd for $C_{49}H_{40}N_2O_4S$(M), found m/z 755.5912, 754.5866, 753.6102 and 752.5901, respectively. A characteristic fragment peak at 596.5811 was observed which corresponds to the loss of *meso*-malonyl group from **7**. This peak is absent in the MALDI-TOF spectrum of **6**.



$C_{42}H_{30}N_2S$
Exact Mass: 594.2130
$(M + 2H)^+$ =596.2286

References

1. Y. Yamazaki, Y. Kido, K. Hidaka, H. Yasui, Y. Kiso, F. Yakushiji, Y. Hayashi, *Bioorg. Med. Chem.***2011,** *19*, 595–602.
2. S.-J. Hong, M.-H.Lee, C.-H. Lee, *Bull. Korean Chem. Soc.* **2004**, 25, 1545-1550.
3. A. Ulman, J. Manassen, *J. Am.Chem. Soc*.**1975**, *97,* 6540.

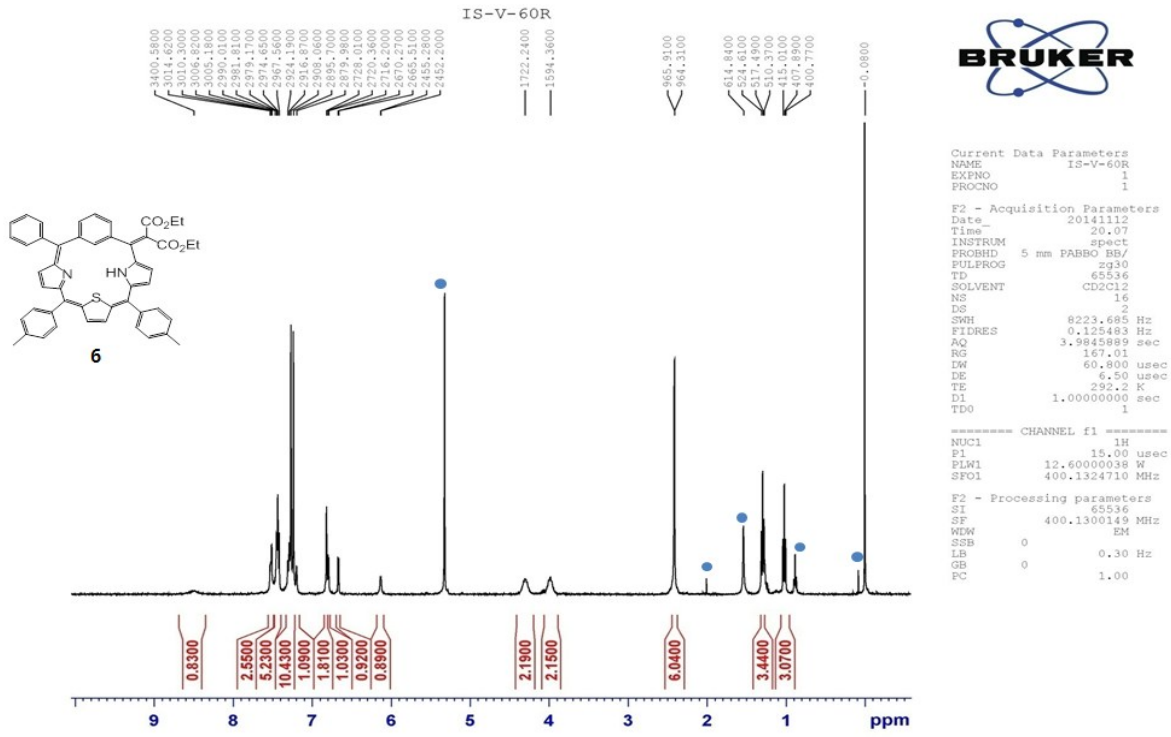


Figure S1. ^{1}H NMR spectrum of **6** in CD_2Cl_2. Dot indicates peak from residual solvents/ impurities.

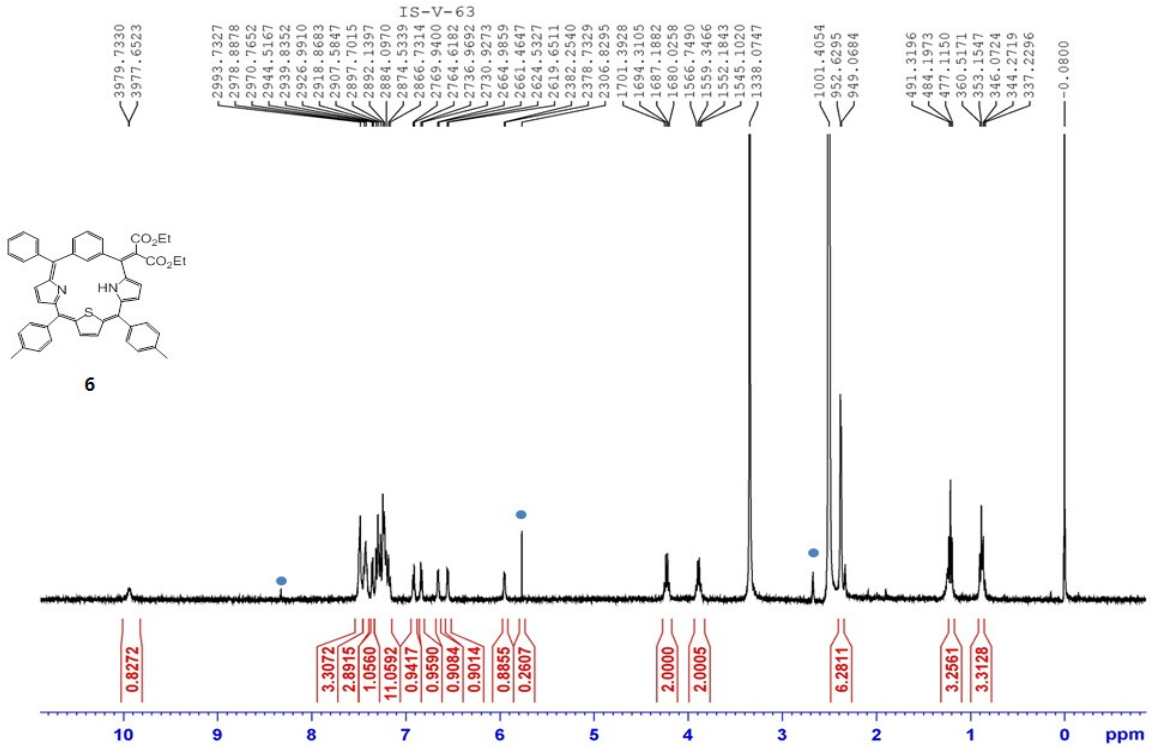


Figure S2. ^{1}H NMR spectrum of **6** in DMSO-d_6. Dots indicate peaks from residual solvents/ impurities.

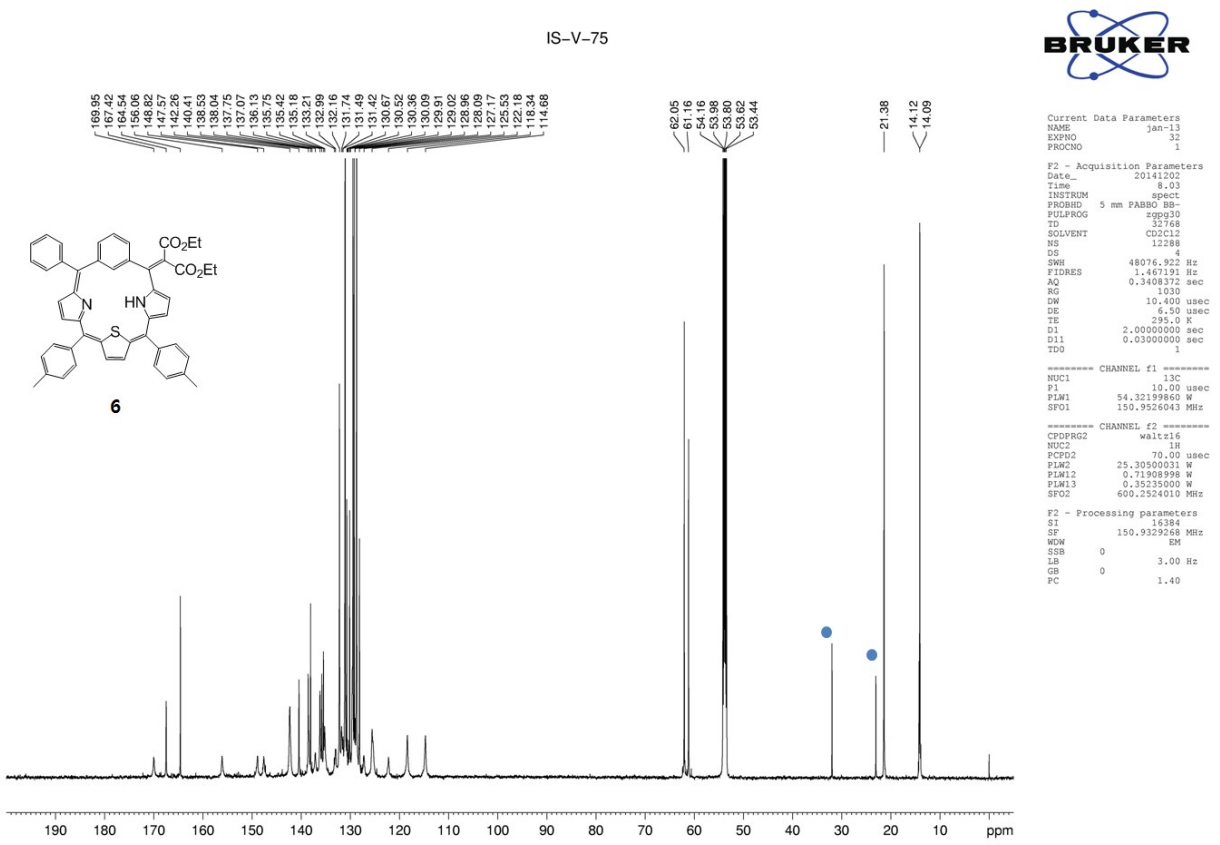


Figure S3. ^{13}C NMR spectrum of **6** in CD_2Cl_2. Dot indicates peak from residual solvents/ impurities.

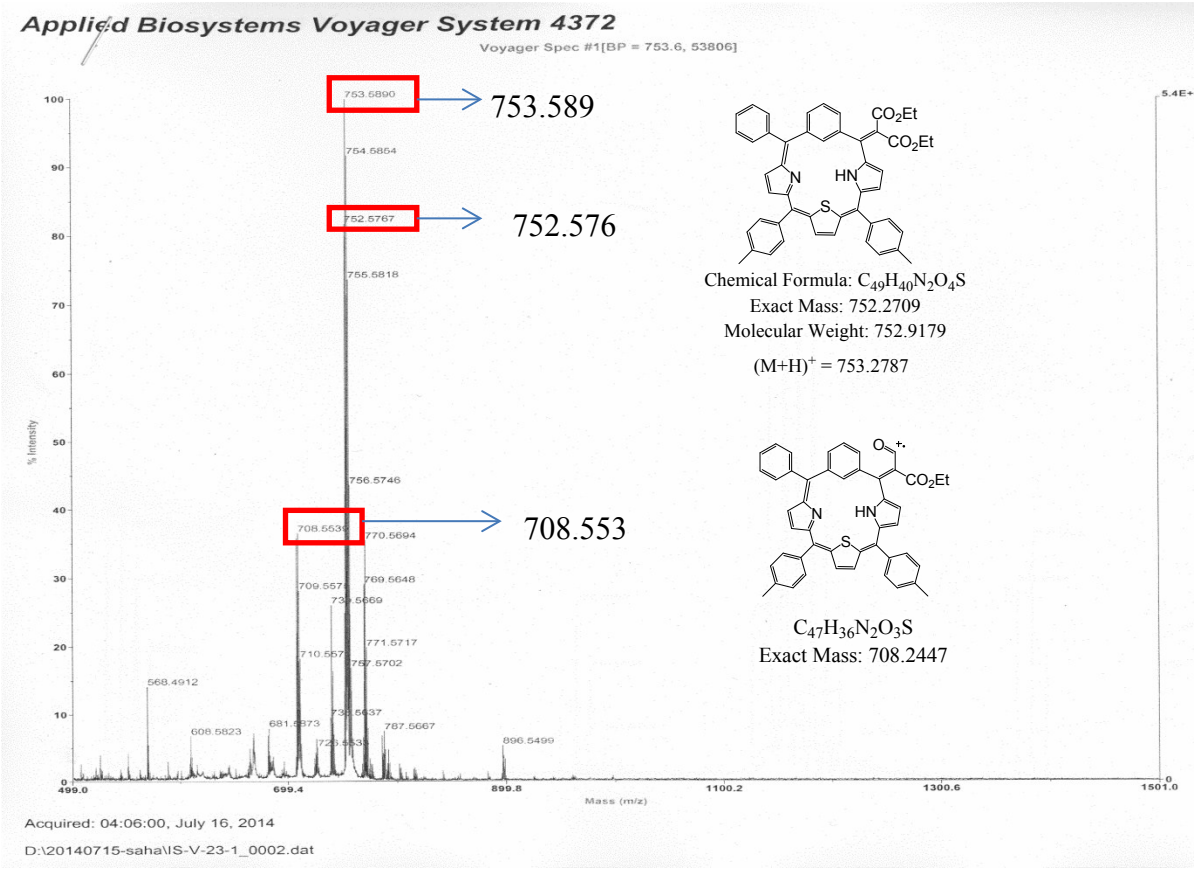
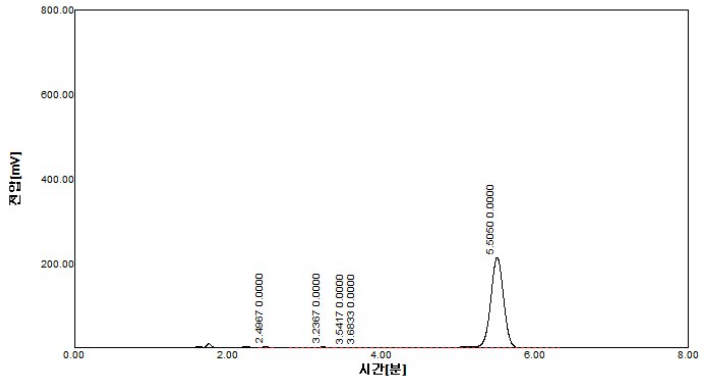


Figure S4. MALDI-TOF mass spectrum of **6**.



No	RT[분]	Area [mV*s]	Area ratio[%]
1	2.4967	9.3409	0.36
2	3.2367	18.9517	0.73
3	3.5417	17.2238	0.66
4	3.6833	22.3931	0.86
5	5.5050	2532.3936	97.39

Figure S4-1. HPLC trace of the compound **6** (in acetonitrile)

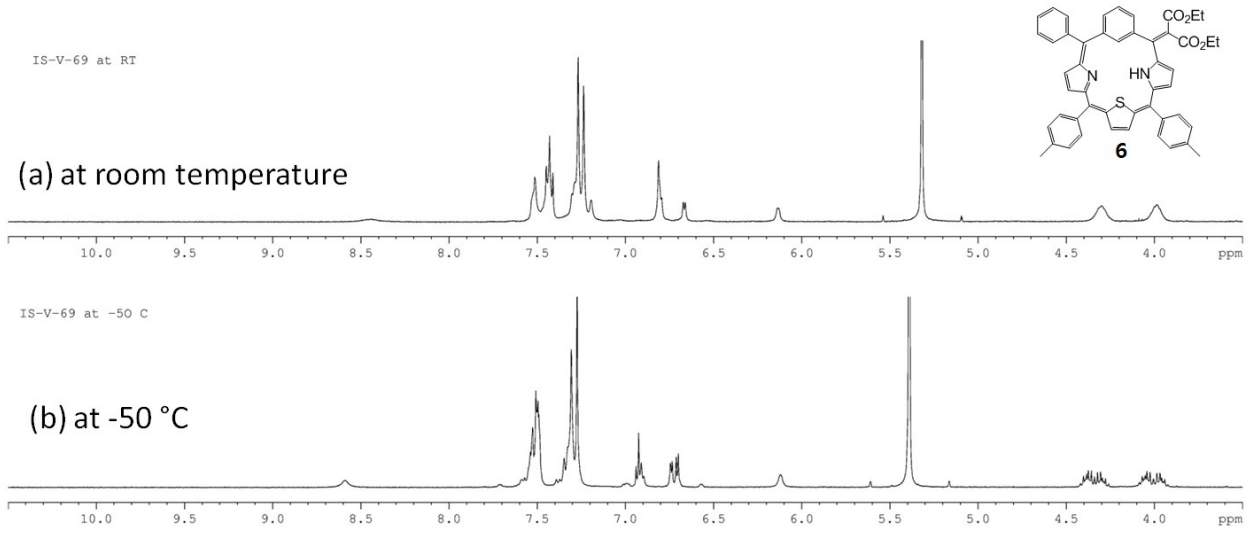


Figure S5. Low temperature ^{1}H NMR spectrum of **6** in CD_2Cl_2.

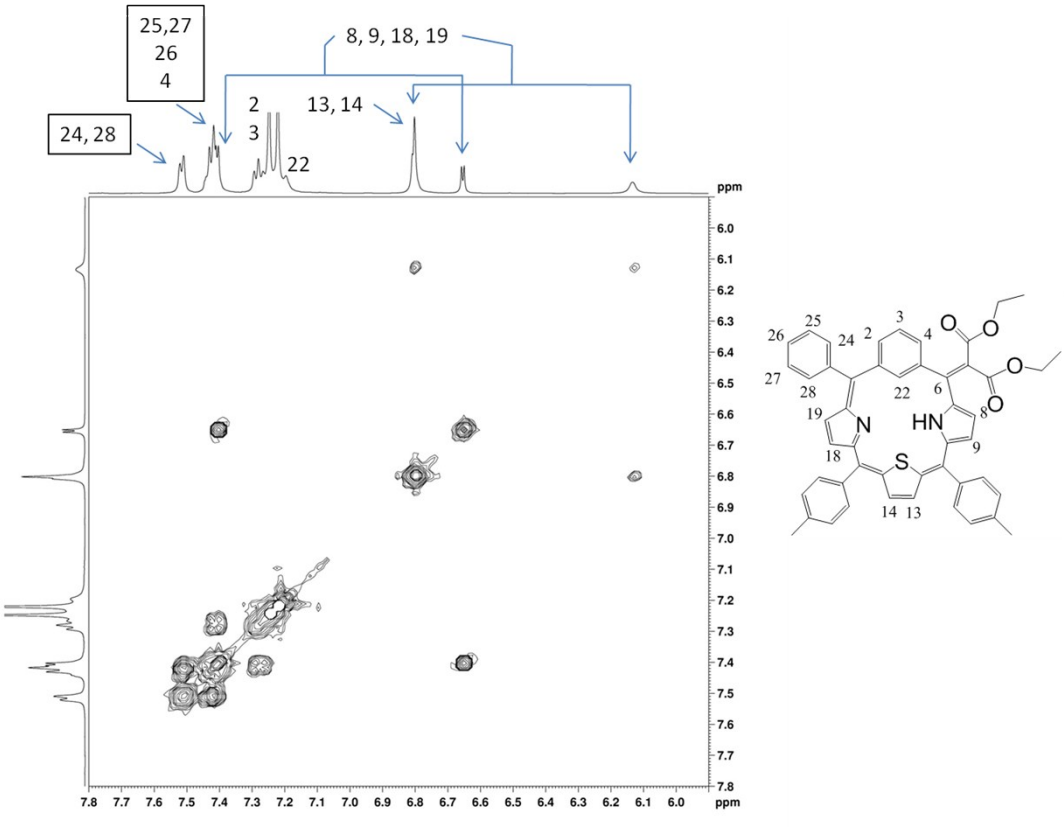


Figure S6. Selected region of ^{1}H -^{1}H COSY spectrum of **6** in CD_2Cl_2 (downfield region).

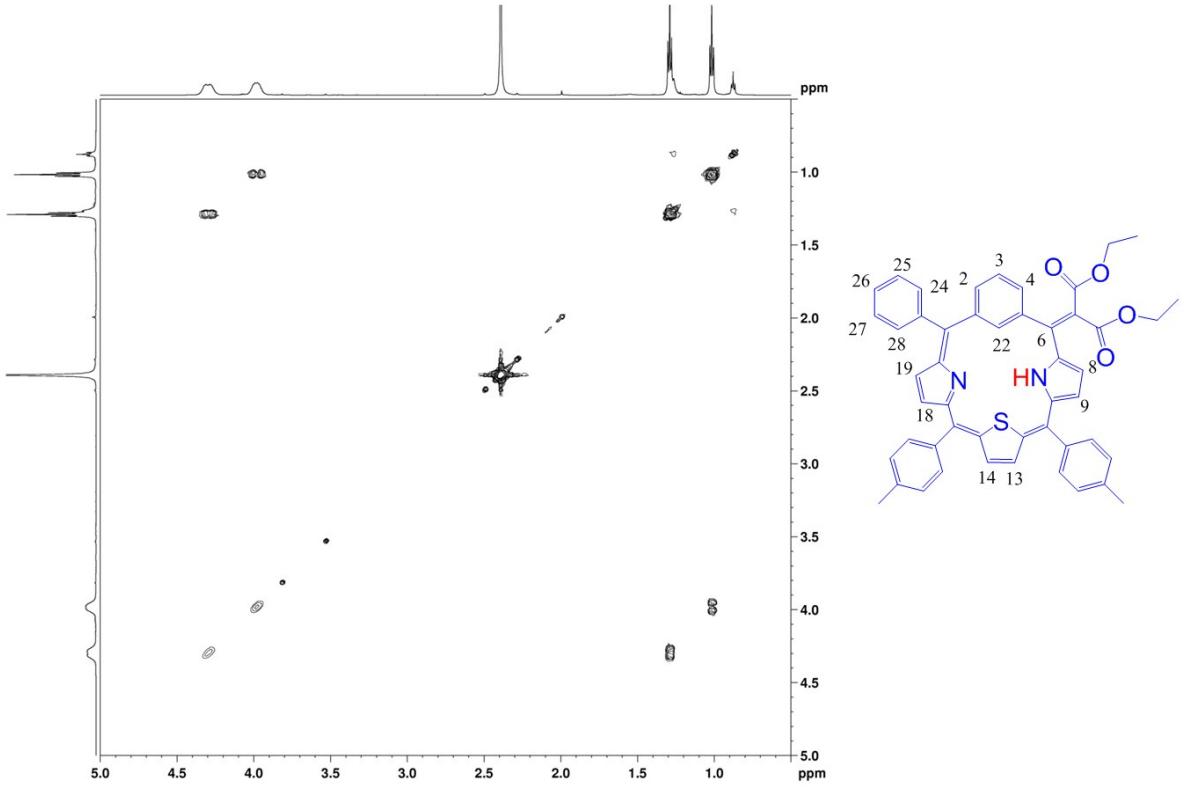


Figure S7. Selected region of ^{1}H -^{1}H COSY spectrum of **6** in CD_2Cl_2 (up field region).

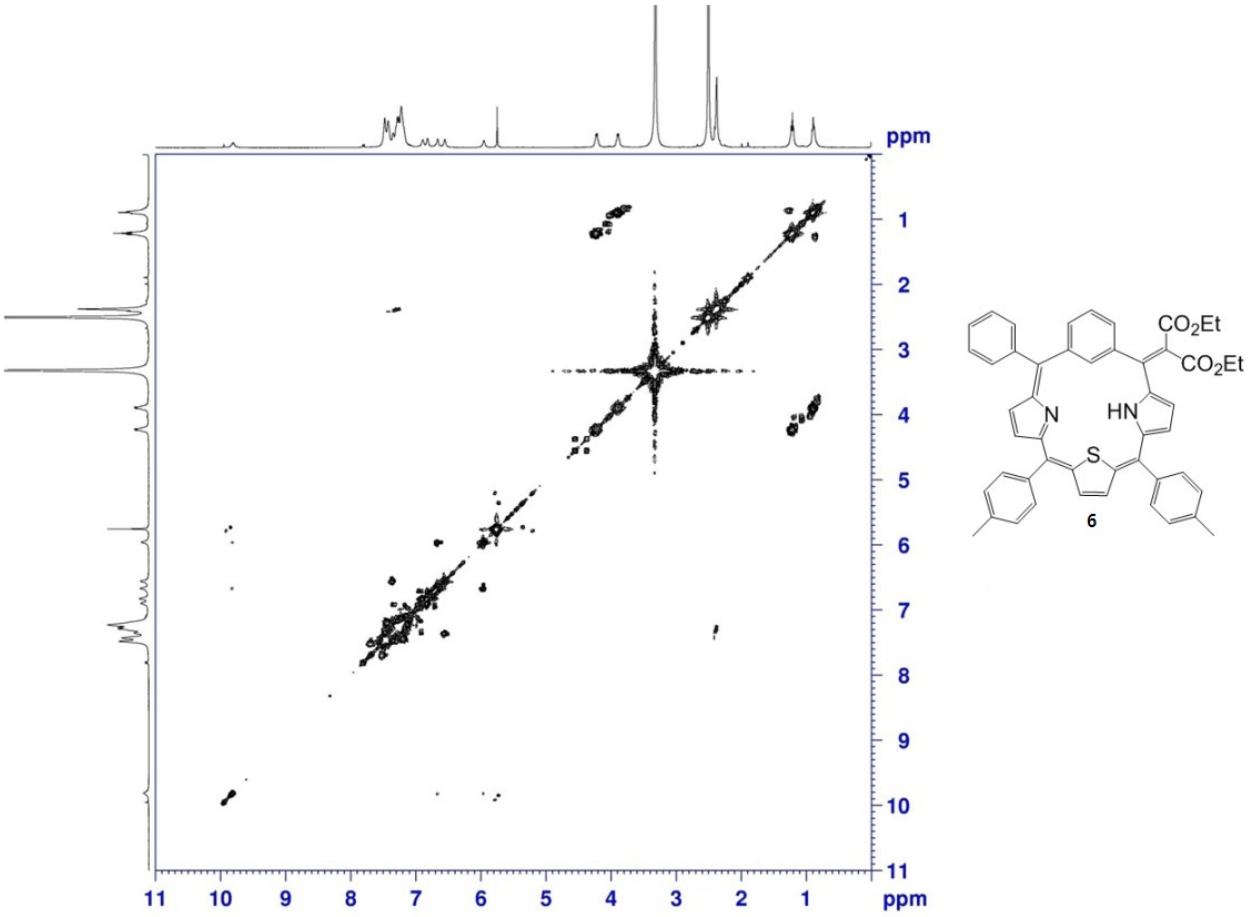


Figure S8. ^{1}H -^{1}H COSY spectrum of **6** in DMSO-d_6.

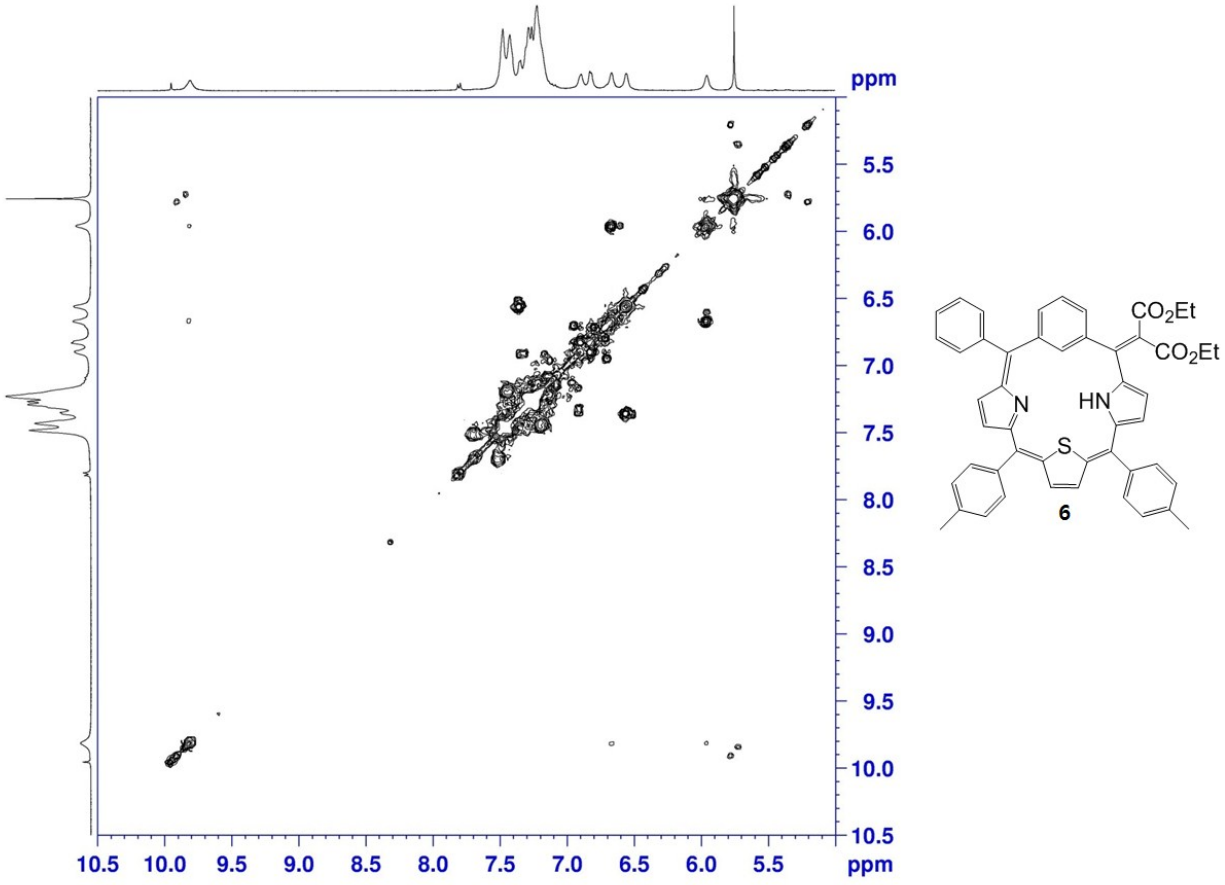
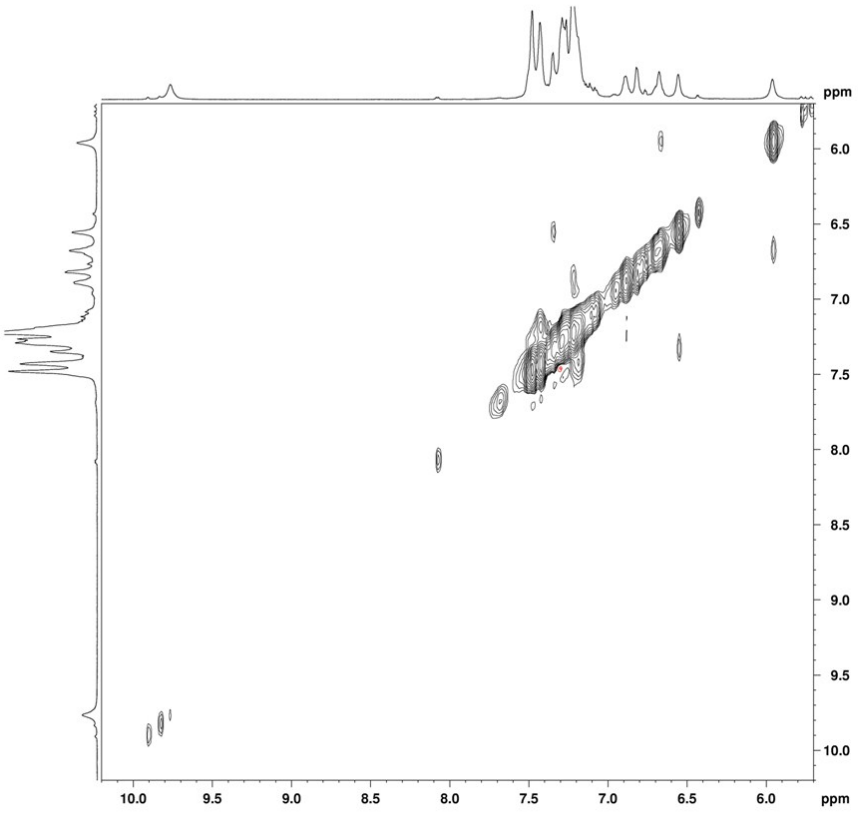
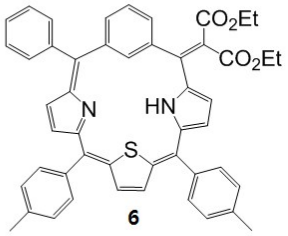


Figure S9. Selected region of ^{1}H -^{1}H COSY spectrum of **6** in DMSO-d_6.





6

Figure S10. Selected region of NOESY spectrum of **6** in DMSO-d_6.

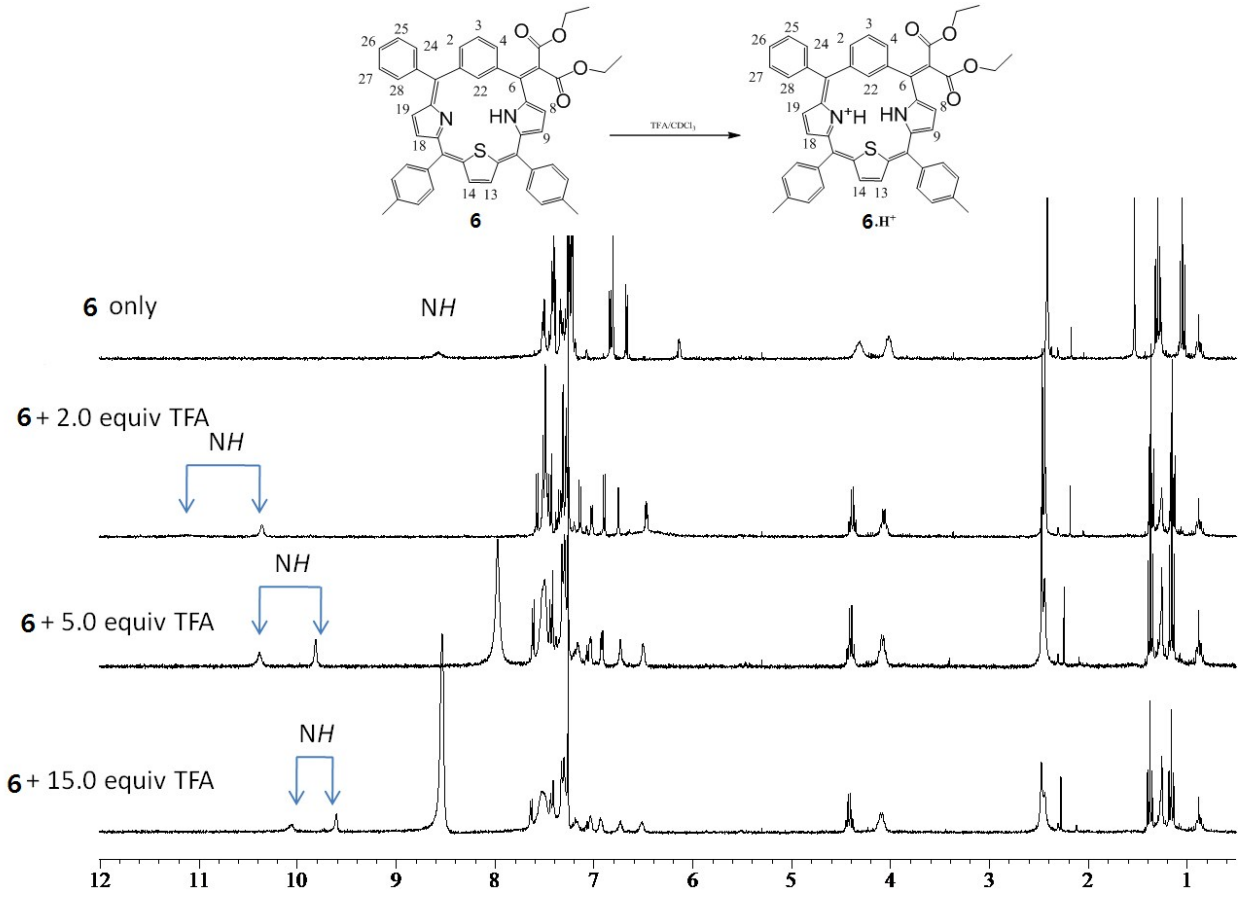


Figure S11. ^{1}H NMR spectra recorded during the titration of **6** with TFA in $CDCl_3$.

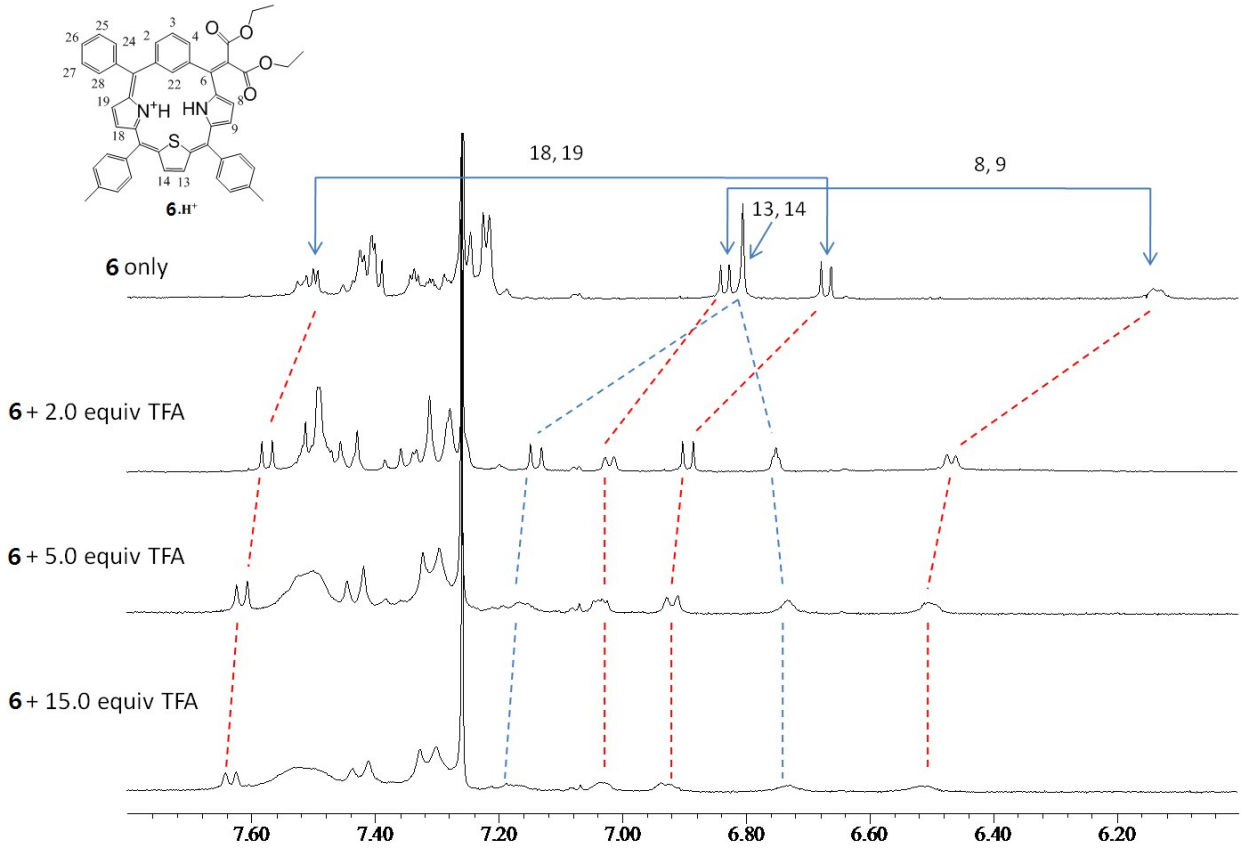


Figure S12. Partial ^{1}H NMR spectra during the titration of **6** with TFA in $CDCl_3$ (downfield region).

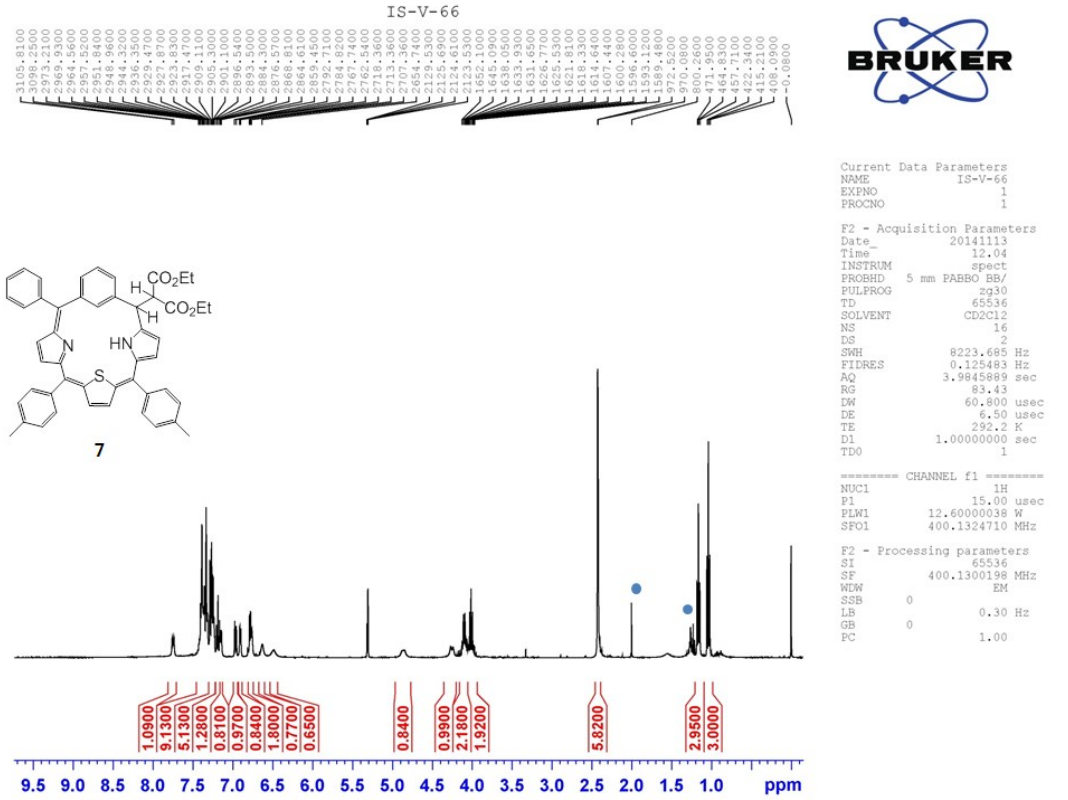


Figure S13. ^{1}H NMR spectrum of **7** in CD_2Cl_2. Dot indicates peak from residual solvents/ impurities.

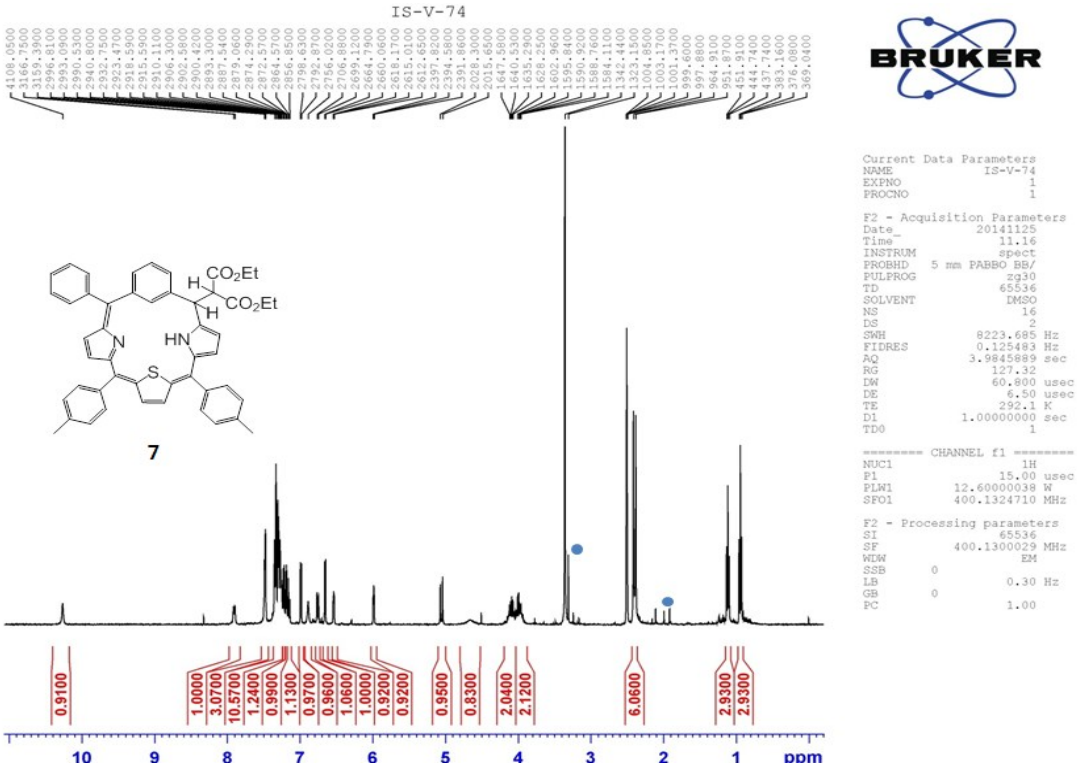


Figure S14. ^{1}H NMR spectrum of **7** in DMSO-d_6. Dot indicates peak from residual solvents/ impurities.

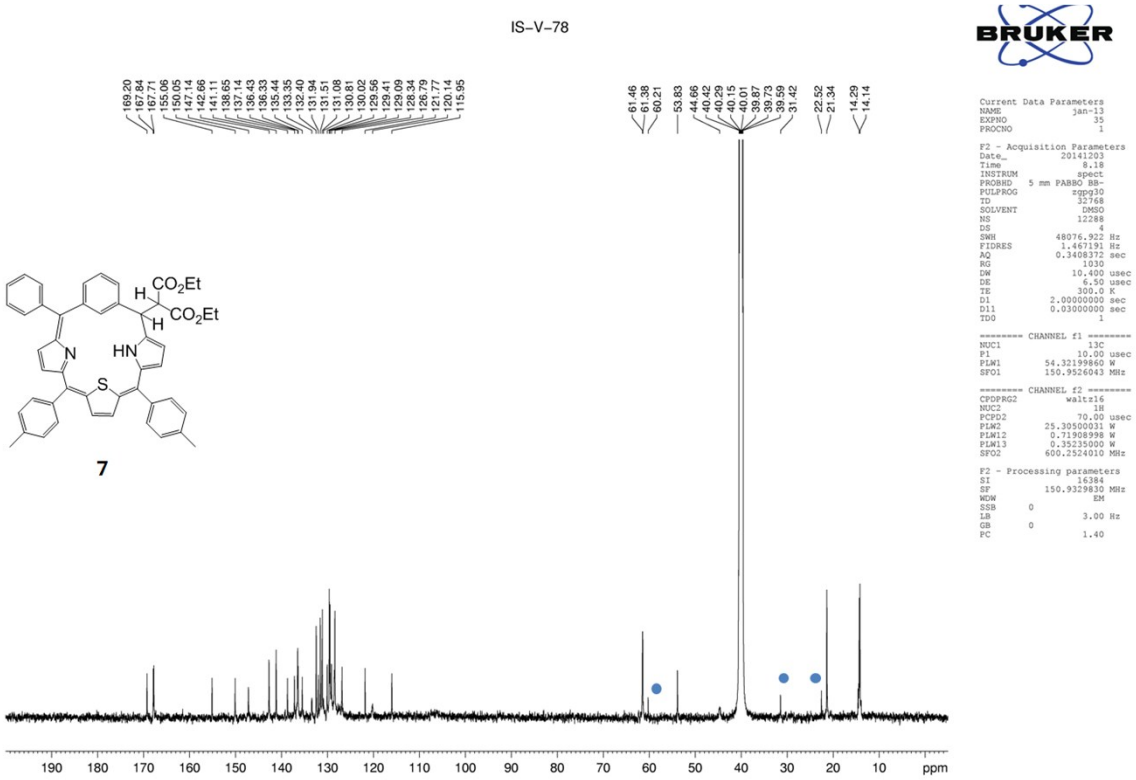


Figure S15. ^{13}C NMR spectrum of **7** in DMSO-d_6. Dot indicates peak from residual solvents/ impurities.

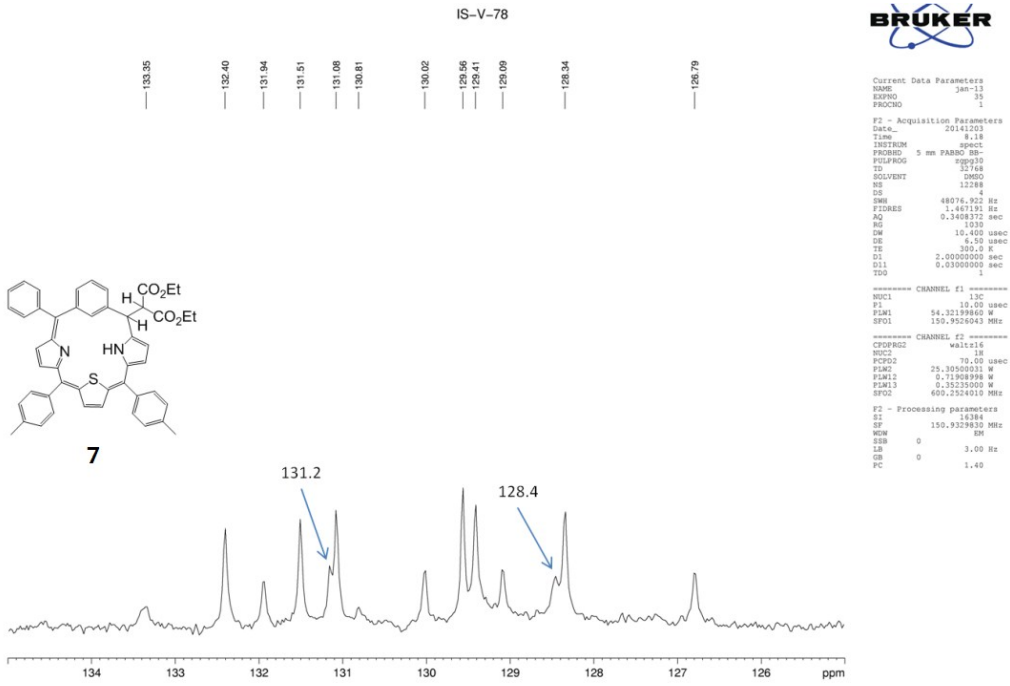


Figure S16. Selected ^{13}C NMR spectrum of **7** in DMSO-d_6.

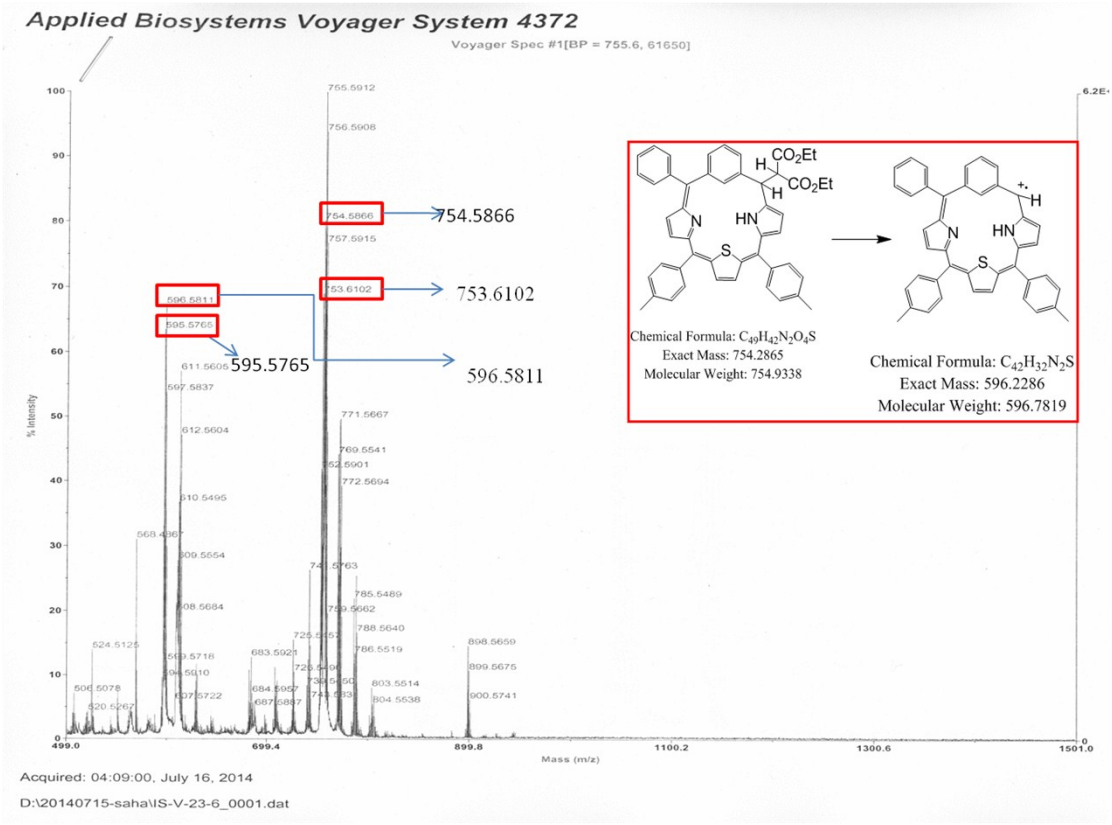
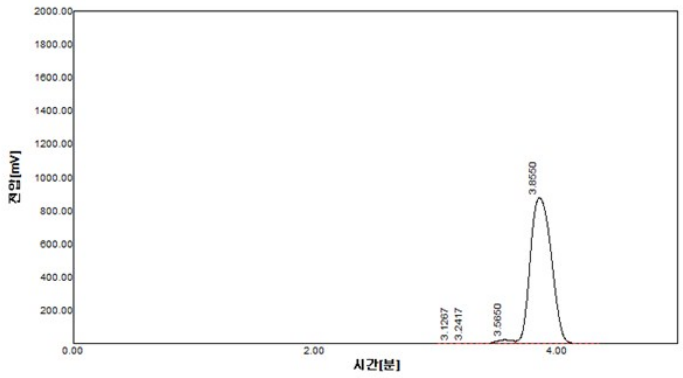


Figure S17. MALDI-TOF mass spectrum of **7**.



No	RT[min]	Area[mV*s]	Area ratio[%]
1	3.1267	8.6006	0.08
2	3.2417	10.2119	0.09
3	3.5650	214.1200	1.98
4	3.8550	10572.2898	97.84
		10805.2227	

Figure S17-1. HPLC trace of the compound **7** (in acetonitrile)

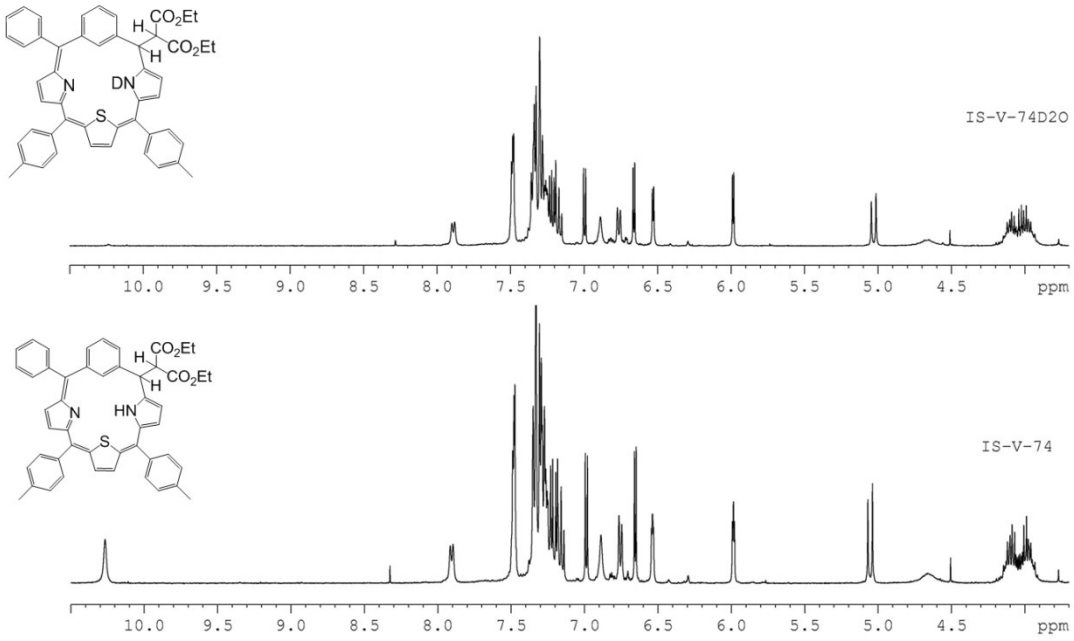


Figure S18. Partial ^{1}HNMR spectra of **7** recorded in absence and presence of D_2O in DMSO-d_6.

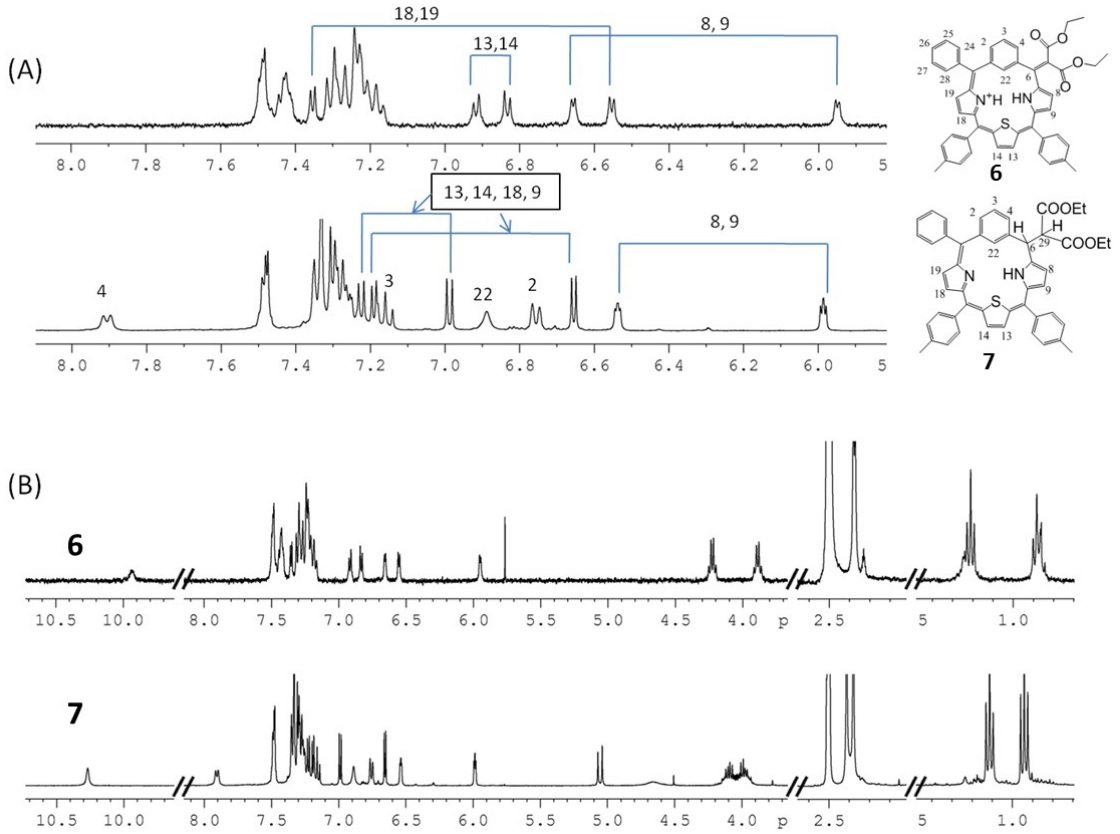


Figure S19. Comparison of ^{1}H NMR spectra of **6** and **7** in DMSO-d_6 (A) aromatic regions (B) full spectra.

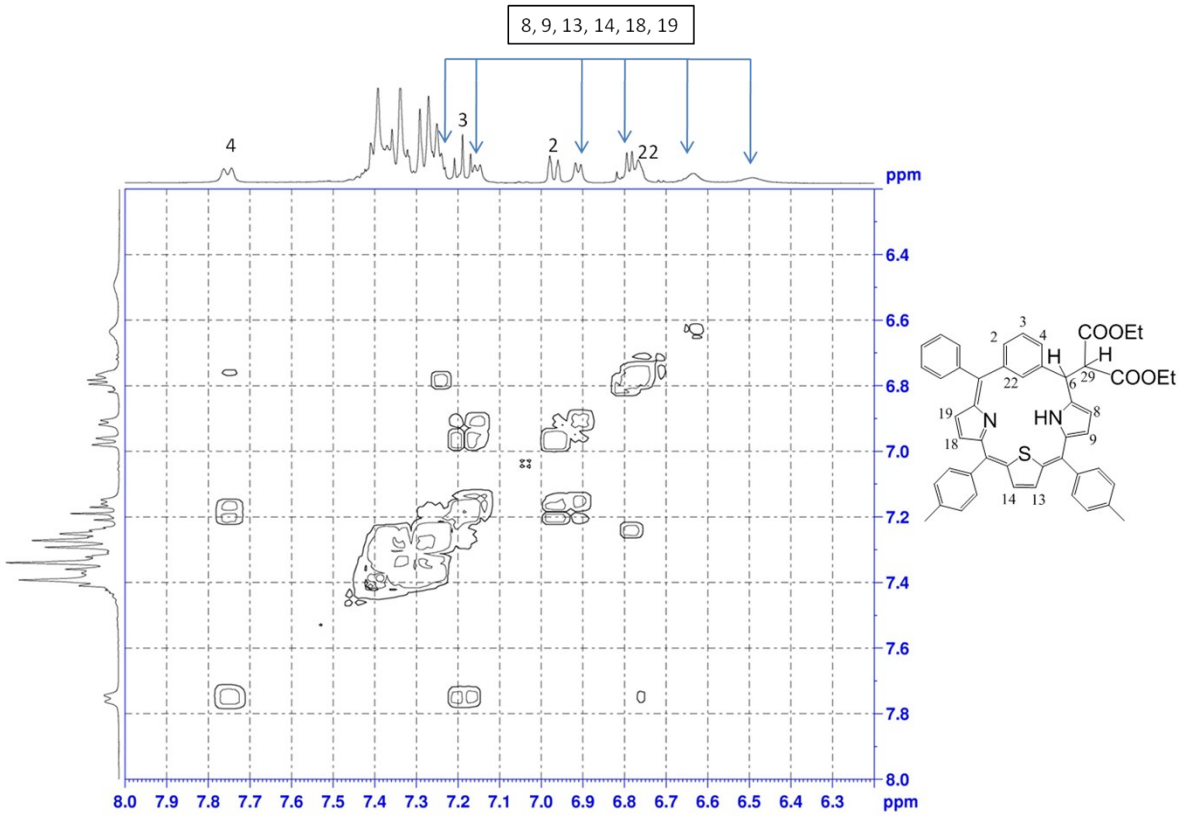


Figure S20. ^{1}H -^{1}H COSY spectrum of **7** in CD_2Cl_2 (downfield region).

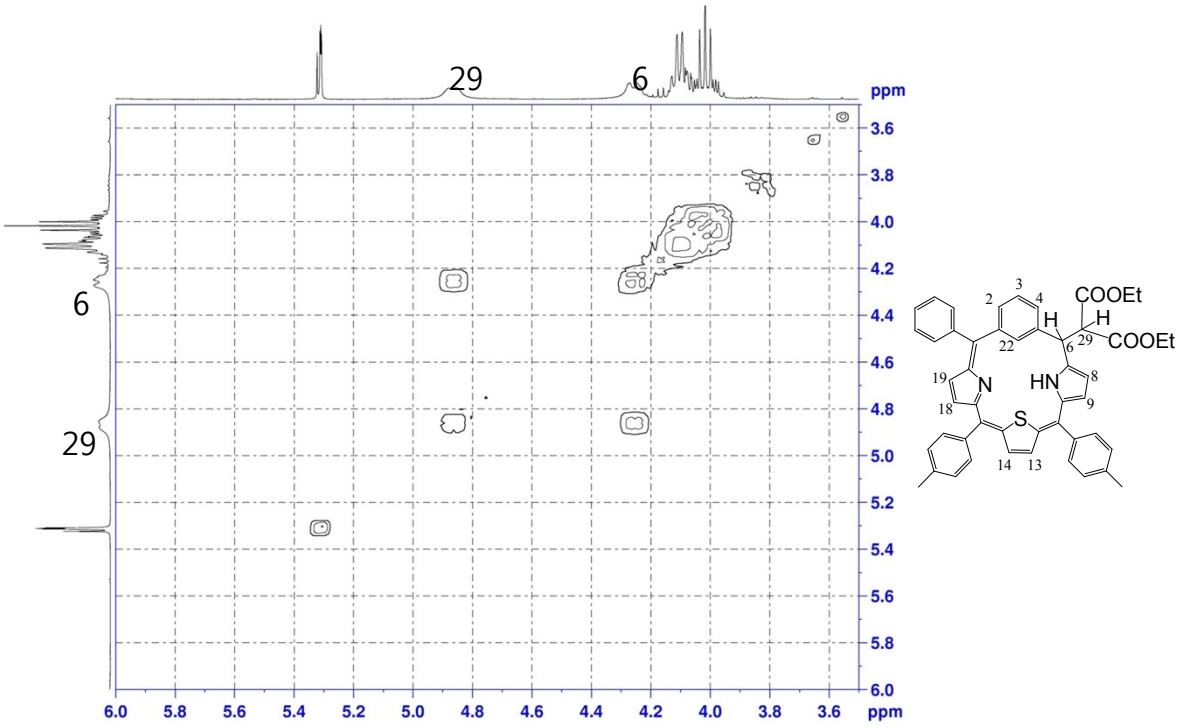


Figure S21. Selected region of ^{1}H -^{1}H COSY spectrum of **7** in CD_2Cl_2.

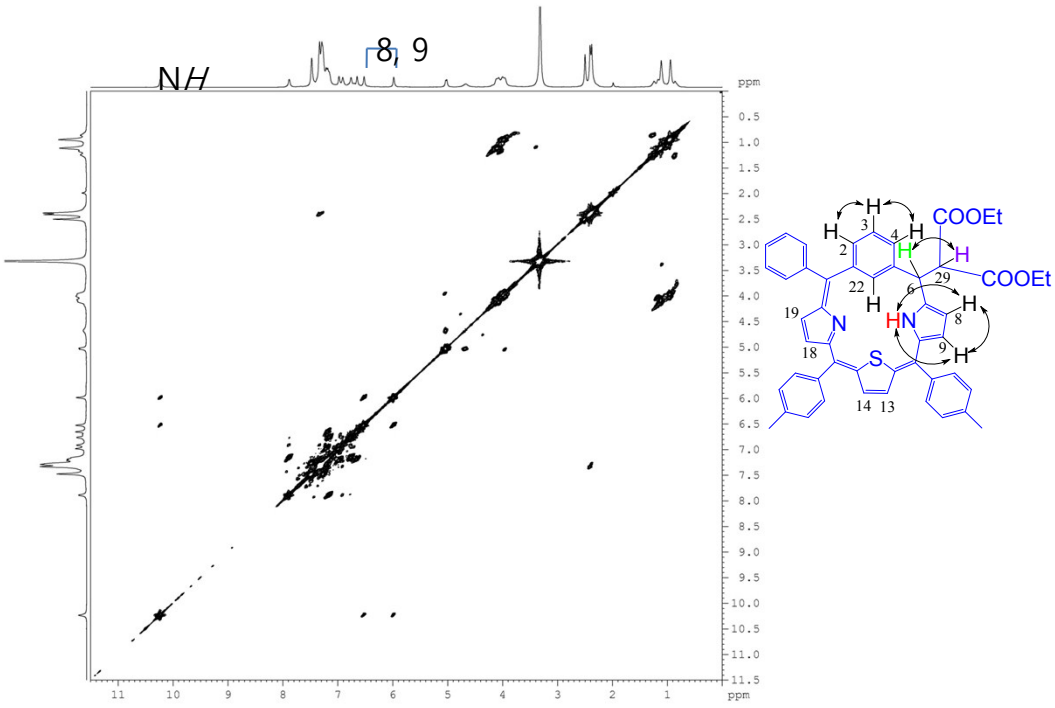


Figure S22. ^{1}H -^{1}H COSY spectrum of **7** in DMSO-d_6.

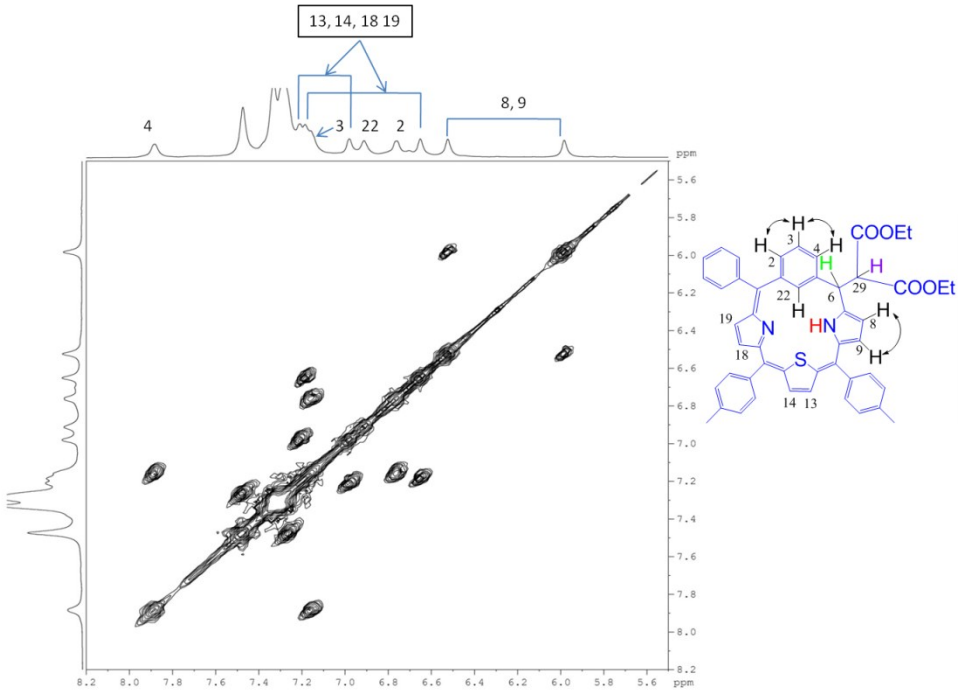


Figure S23. Selected region of ^{1}H -^{1}H COSY spectrum of **7** in DMSO-d_6.

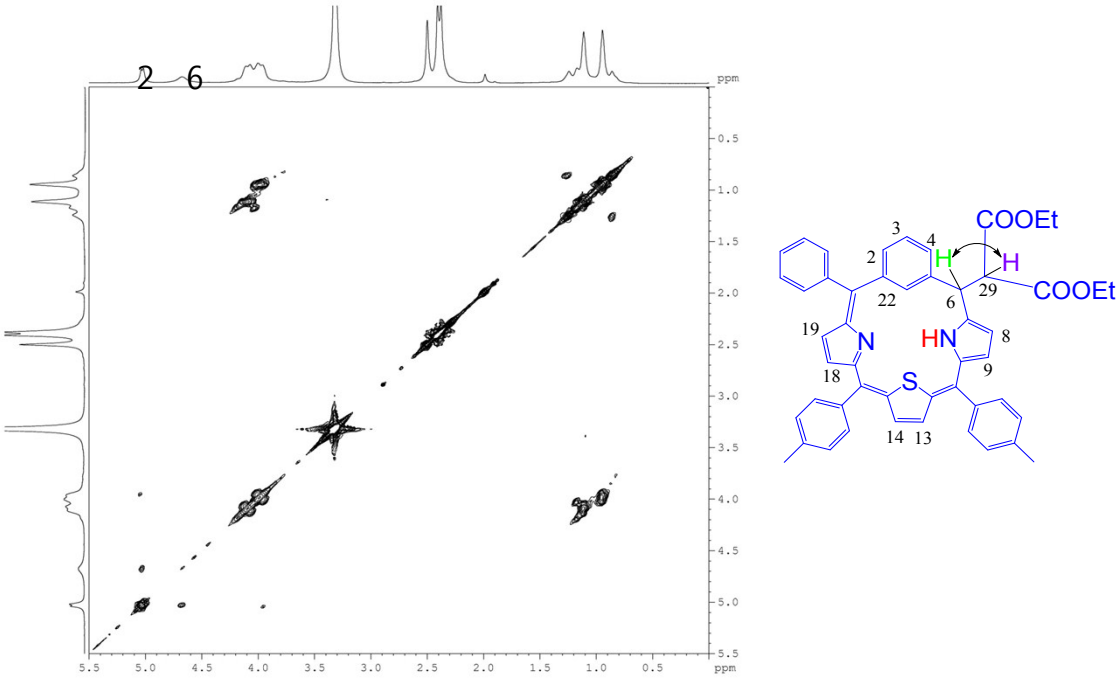


Figure S24. Selected region of ^{1}H -^{1}H COSY spectrum of **7** in DMSO-d_6.

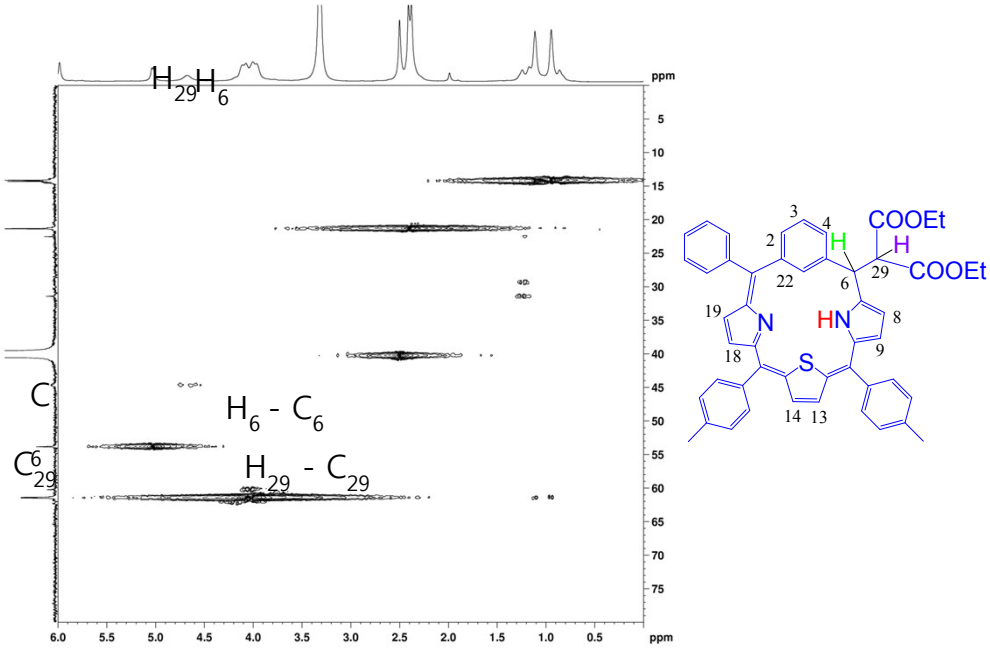


Figure S25. Selected region of ^{1}H - ^{13}C HSQC NMR of **7** in DMSO-d_6.

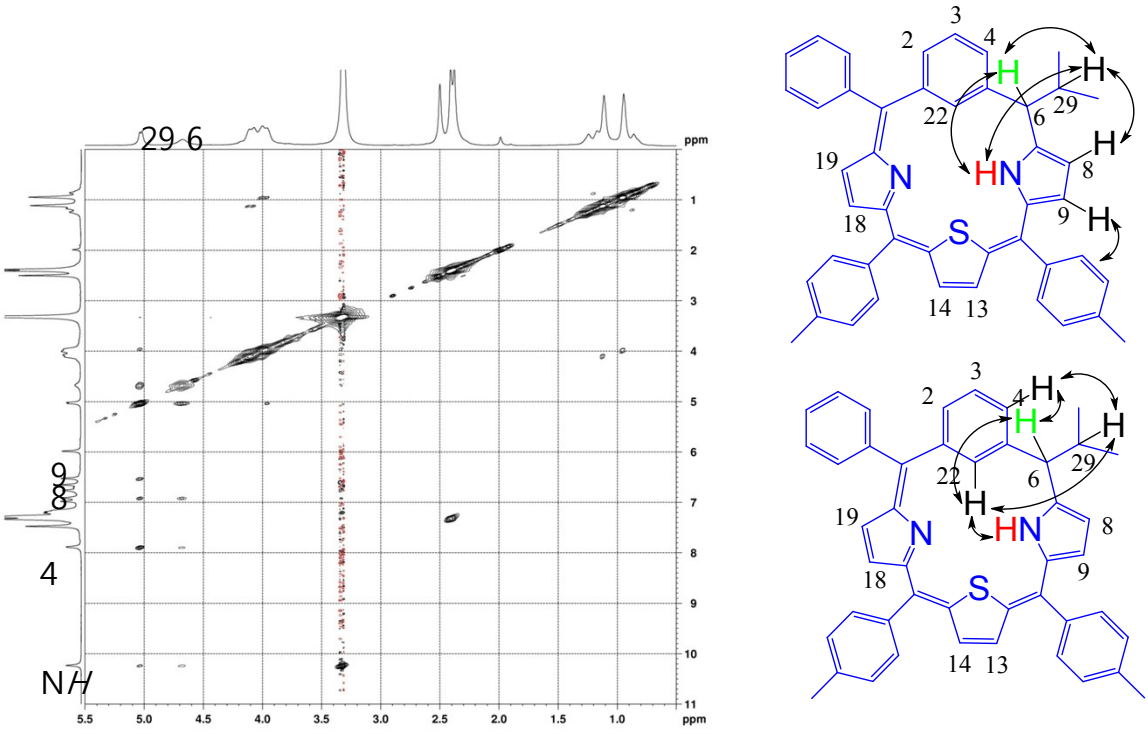


Figure S26. Selected region of NOESY spectrum of **7** in DMSO-d_6.

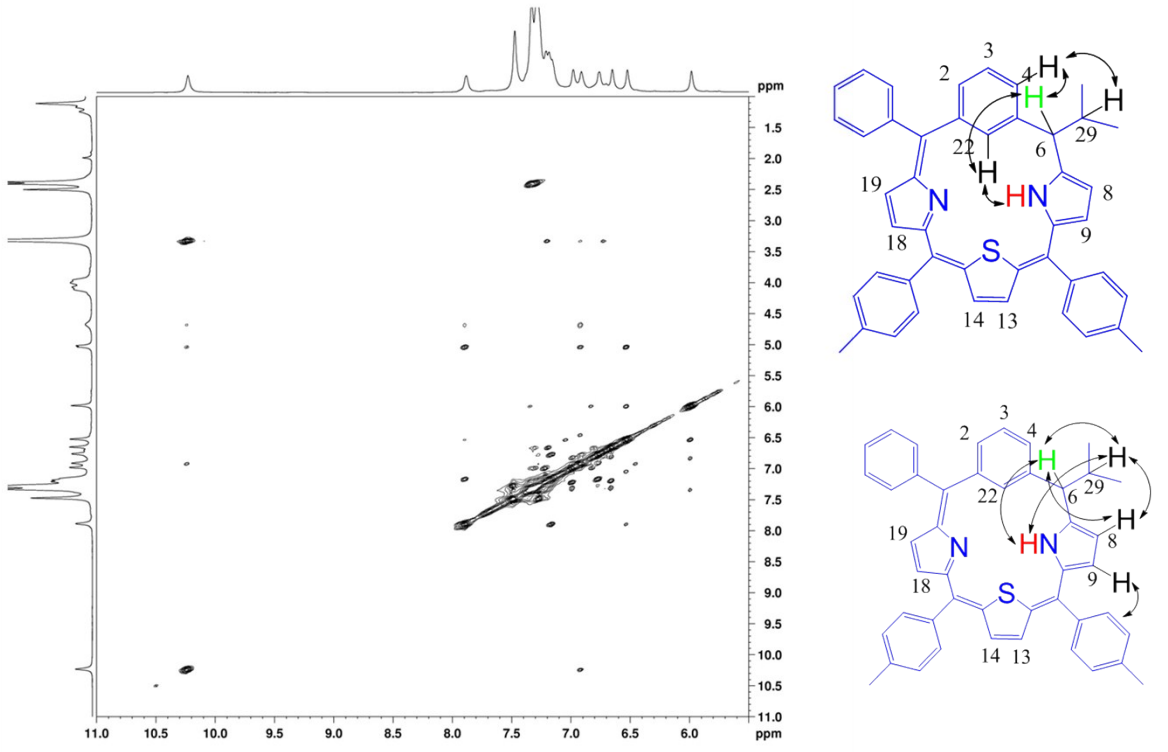


Figure S27. Selected region of NOESY spectrum of **7** in DMSO-d_6.

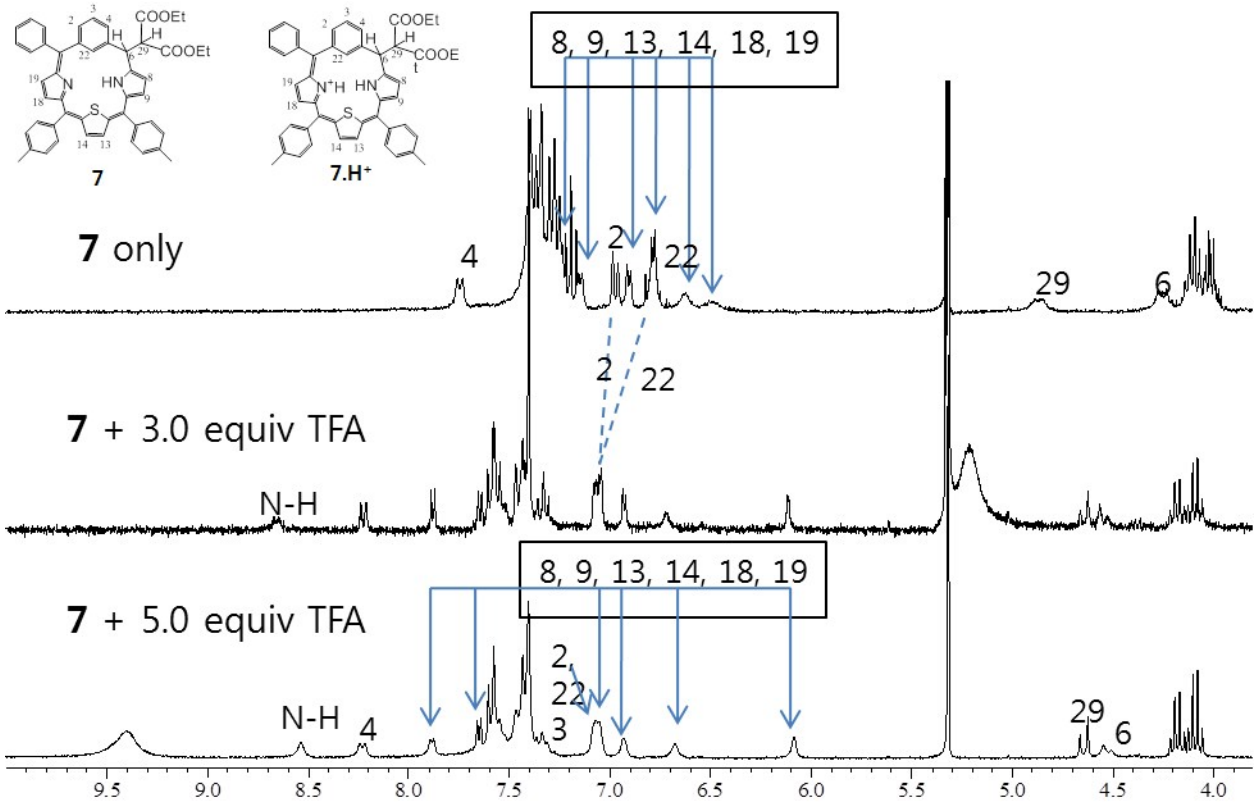
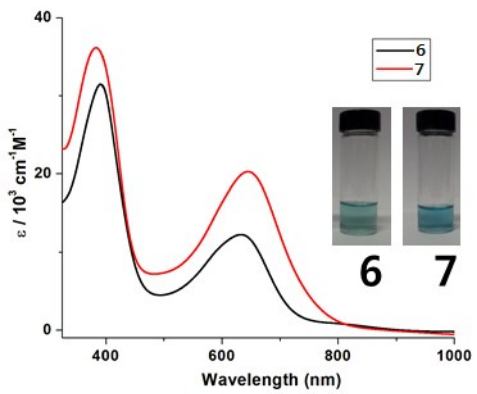


Figure S28. Partial ^{1}H NNMR spectra recorded during the titration of **7** (*c* = 10.60 x 10^{-3} M) with TFA in CD_2Cl_2.



For **6**
Soret-like band at 392 (ε = 3.2 x 10^4 $M^{-1}cm^{-1}$)
Q-band at 636 nm (ε = 1.2 x 10^4 $M^{-1}cm^{-1}$)

For **7**
Soret-like band at 385 (ε = 3.7 x 10^4 $M^{-1}cm^{-1}$)
Q-band at 645 (ε = 2.0 x 10^4 $M^{-1}cm^{-1}$)

Figure S29. Uv-vis spectra of **6** (c = 2.39 x 10^{-5} M) and **7** (c = 2.65 x 10^{-5} M) in CH_3CN.

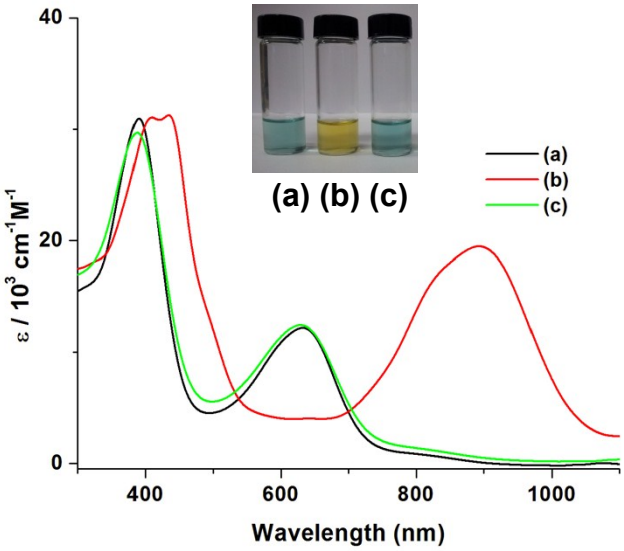


Figure S30. Uv-vis spectra of (a) **6** (b) **6**+ CF_3COOH (10.0 equiv.) and (c) **6** + CF_3COOH (10.0 quiv) + Et_3N (10.0 equiv) in CH_3CN ([**6**] = 2.39 x 10^{-5} M).

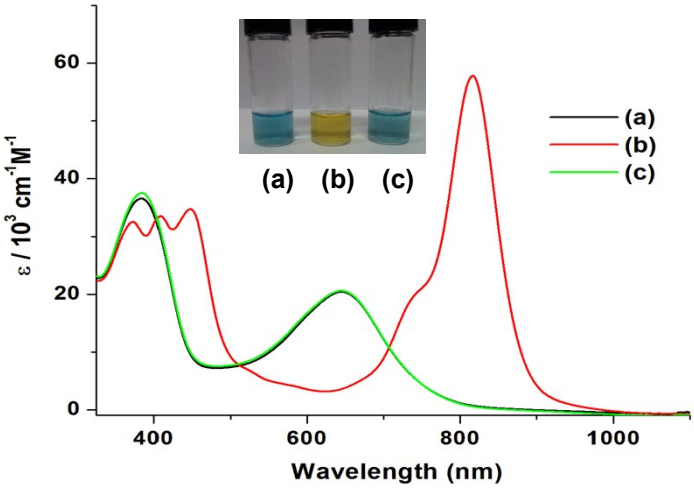
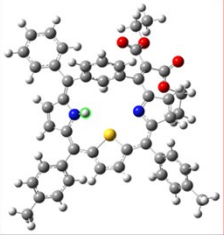
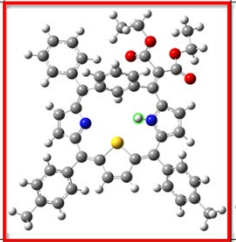
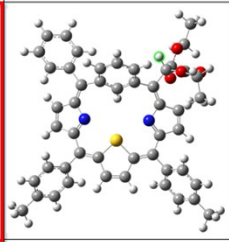
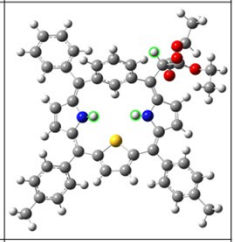


Figure S31. Uv-vis spectra of (a) **7** (b) **7**+ CF_3COOH (10.0 equiv.) and (c) **7** + CF_3COOH (10.0 quiv) + Et_3N (10.0 equiv) in CH_3CN ([**7**] = 2.65 x 10^{-5} M).

M062X/6-31G(d,p)	compound-A	compound-B	compound-C	22-pi (compound-mid)
optimized structure				
relative energy (kcal/mol)	**2.83**	**0**	**13.5**	**-763.6**

Bond length and dihedral angles

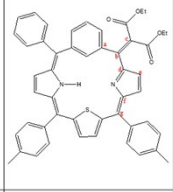
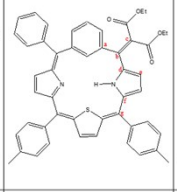
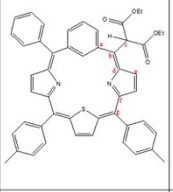
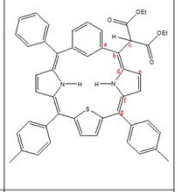
	compound-A	compound-B	compound-C	22-pi (compound-mid)
structure				
r(b-d), Å	1.47	1.45	1.36	1.36
r(f-g), Å	1.39	1.46	1.46	1.37
r(N-H), Å	1.011	1.011		1.008
∠(a-b-d-e), °	-145.7	-171.7	-177.1	-174.9
∠(c-b-d-e), °	34.9	8.4	-0.3	-1.9

Figure S32. Optimized geometry, energy and bond length and dihedral angle

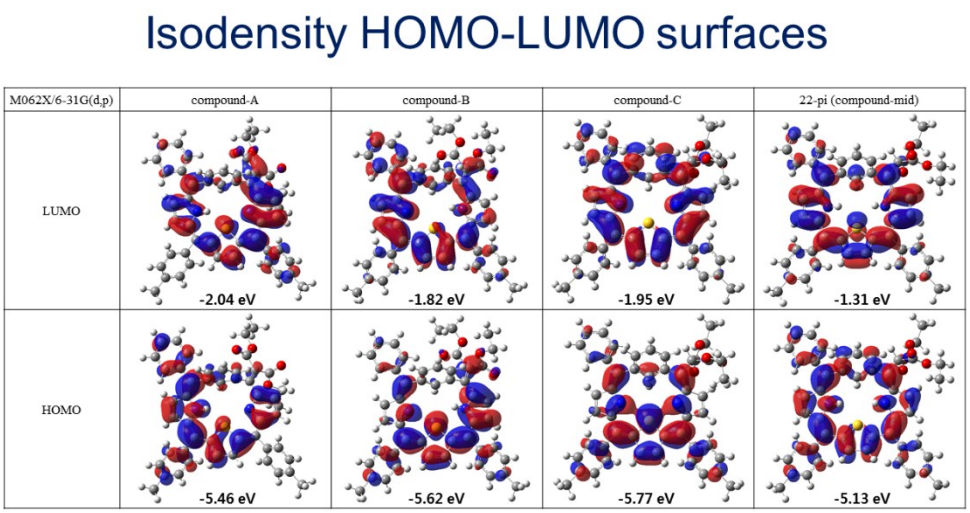


Figure S33. Isodensity HOMO-LUMO surface