Intramolecular Hydrogen Bonding as a Synthetic Tool to Induce Chemical Selectivity in Acid Catalyzed Porphyrin Synthesis†

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SUPPORTING INFORMATION

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1 – Materials

All chemicals were purchased from Aldrich, Alfa Aesar, and Acros and were used without further purification. Solvents were obtained from EM Science and were used as received unless otherwise noted. Thin layer chromatography (TLC) was performed with silica gel coated glass plates from Analtech. Column chromatography was carried out using Silicycle silica gel 60 with 230-400 mesh.

2 – Spectroscopic Measurements

The ^{1}H-NMR spectra were recorded on a Varian spectrometer at 400 MHz or 500 MHz. NMR samples were prepared in deuterated solvents with tetramethylsilane as an internal reference using a Wilmad 528-PP 5 mm NMR tube. Deuterated chloroform was distilled from CaH_2. Mass spectra were obtained with a matrix-assisted laser desorption/ionization time-of-flight spectrometer (MALDI-TOF), using (1E, 3E)-1,4-diphenylbuta-1,3-diene (DPB), cyano-4-hydroxycinnamic acid (CCA) or terthiophene as a matrix. The reported mass is of the most abundant isotopic ratio observed. To facilitate comparison, calculated values for the most abundant isotopic ratio expected are listed after the experimental result.

3 – Electrochemical Measurements

Cyclic voltammetry was performed with a CHI 650C potentiostat (CH Instruments) using a glassy carbon (3 mm diameter) or platinum (1.6 mm diameter) disc working electrode, a platinum gauze counter electrode, and a Ag^{+}/Ag quasireference electrode in a conventional three-electrode cell. Benzonitrile, distilled from phosphorus pentoxide, was used as the solvent for electrochemical measurements. The supporting electrolyte was 0.1 M tetrabutylammonium hexafluorophosphate. The solution was deoxygenated by bubbling with argon. The potential of

the quasireference was determined using the ferrocenium/ferrocene (Fc^+/Fc) redox couple as an internal standard ($E_{Fc+/Fc}$ = 0.45 V vs. SCE in benzonitrile). The voltammograms were recorded at 100 mV s^{-1}.

4 - Synthesis

5-Formyl-3-*tert*-butyl-2-hydroxybenzaldehyde **2**:[1]

A solution of commercially available 2-*tert*-butylphenol (6.00 g, 40 mmol, 1 equiv.), hexamethylenetetramine (14.00 g, 100 mmol, 2.5 equiv.) and trifluoroacetic acid (40 mL) was heated at reflux for 12 h. The reaction was quenched while hot with a 33% (v/v) aqueous H_2SO_4 solution (20 mL) and the resulting mixture was allowed to cool to room temperature with stirring. The crude product was extracted with diethyl ether (3 × 50 mL), and the extract was neutralized with a saturated aqueous solution of sodium bicarbonate (2 × 100 mL) and finally washed with water (3 × 100 mL). The organic phase was dried over sodium sulfate, filtered through paper, and concentrated under reduced pressure. The final purification was achieved by column chromatography (SiO_2), using hexanes/EtOAc (9:1, v/v) as eluent to afford the title compound **2** as a light yellow solid in 55% yield (4.53 g). ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 12.37 (s, 1H, O<u>H</u>); 9.96 (s, 1H, C<u>H</u>O); 9.89 (s, 1H, C<u>H</u>O); 8.03 (d, *J* = 2.0 Hz, 1H, Ar<u>H</u>$_6$); 7.96 (d, *J* = 2.0 Hz, 1H, Ar<u>H</u>$_4$); 1.42 (s, 9H, C(C<u>H</u>$_3$)$_3$).

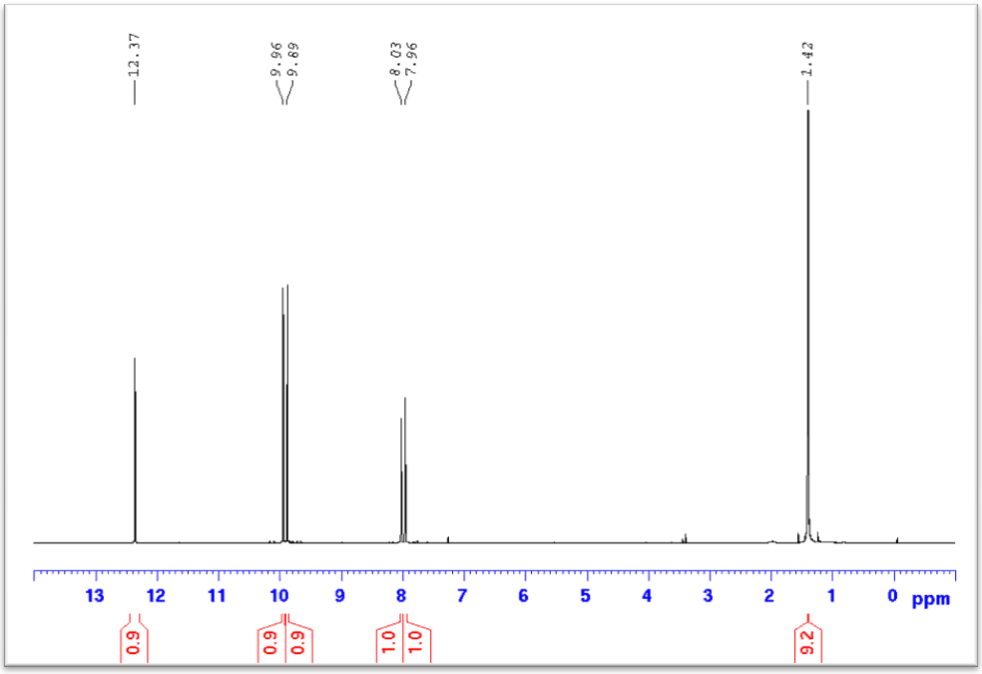

Figure S1. ^{1}H NMR spectrum of compound **2**, 400 MHz, $CDCl_3$, 25 ^{o}C.

5-(Pentafluorophenyl)dipyrromethane **3**:[2,3]

A solution of pentafluorobenzaldehyde (2.0 mL, 16.2 mmol) in freshly distilled pyrrole (50 mL, 720 mmol) was degassed with a stream of argon for 10 min before adding trifluoroacetic acid (120 μL, 1.62 mmol). The mixture was stirred for 30 min at room temperature, diluted with CH_2Cl_2 (400 mL), and then washed with 0.1 M NaOH (400 mL). The organic phase was washed with water (400 mL) and dried over Na_2SO_4. Evaporation of the solvent at reduced pressure gave

a brown oil. Unreacted pyrrole was removed under high vacuum at room temp, yielding a tacky solid that was purified by flash chromatography on a column of silica using a mixture of hexanes:ethyl acetate:triethylamine (80:20:1) as the eluent. The product was recrystallized from dichloromethane/hexanes to yield 3.29 g of 5-(pentafluorophenyl)dipyrromethane **3** as a white powder in 65% yield (3.28 g). ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 8.11 (2H, brs, N<u>H</u>), 6.73 (2H, m, C<u>H</u>$_1$ and C<u>H</u>$_9$), 6.16 (2H, m, C<u>H</u>$_2$ and C<u>H</u>$_8$), 6.02 (2H, brs, C<u>H</u>$_3$ and C<u>H</u>$_7$), 5.89 (1H, brs, C<u>H</u>$_5$), 5.29 (residual solvent C<u>H</u>$_2$Cl$_2$), 1.56 (residual water in the deuterated solvent).

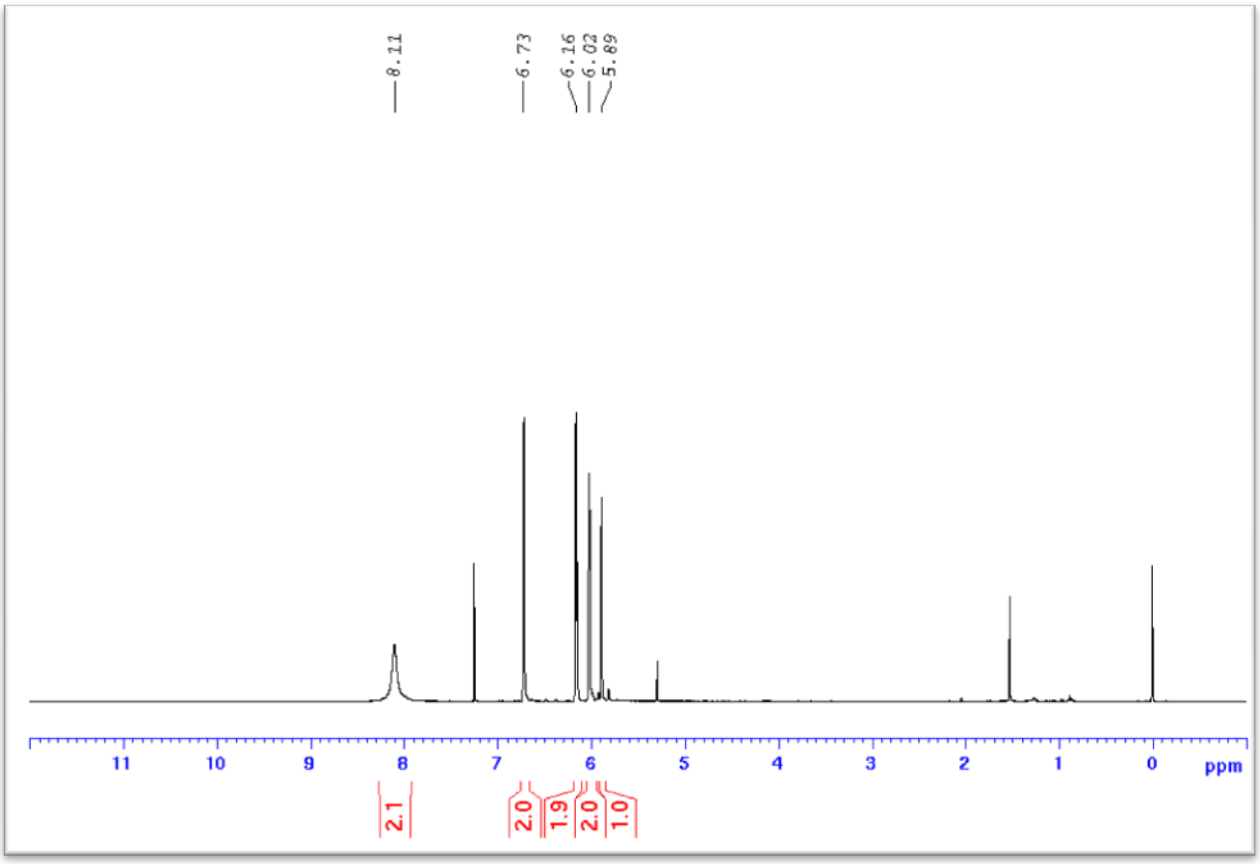

Figure S2. ^{1}H NMR spectrum of compound **3**, 400 MHz, $CDCl_3$, 25 ^{o}C.

5,15-*Bis*(pentafluorophenyl)-10-(4-methoxycarbonylphenyl)-20-(3-formyl-4-hydroxy-5-*tert*-butylpheynyl)porphyrin **5**:[2]

Compound **2** (0.265 g, 1.28 mmol), 5-(pentafluorophenyl)dipyrromethane **3** (0.800 g, 2.56 mmol), and methyl-4-formylbenzoate **4** (0.211 g, 1.56 mmol) were dissolved in 325 mL of chloroform containing 2.45 mL (0.75%, v/v) of ethanol under a nitrogen atmosphere, boron-trifluoride etherate (BF_3OEt_2) was added (0.142 g, 0.125 mL, 1.00 mmol), and the reaction mixture was stirred for 1 h at room temperature. The resulting dark red porphyrogenic mixture was oxidized with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (0.732 g, 3.25 mmol) for 12 h at room temperature, yielding a black crude mixture. Filtration through a silica pad to remove tar and polymeric byproducts, followed by concentration under reduced pressure, afforded a deep purple reddish solid. Purification through column chromatography (SiO_2, hexanes/dichloromethane as eluent) yielded three porphyrin fractions (23% total porphyrin yield). The first porphyrin fraction corresponded to compound **6** (0.178 g, 7% yield) followed by target porphyrin **5** (0.268 g, 11% yield), and compound **7** (0.116 g, 5% yield). A small amount of the target porphyrin **5** was recrystallized from slow diffusion of acetonitrile into a methanol solution of **5** in order to afford an analytical sample for spectroscopic characterization.

^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 12.20 (1H, s, OH), 10.12 (1H, s, CHO), 8.93 (2H, d, J = 5.0 Hz, H_8 and H_{12}), 8.87 (2H, d, J = 5.0 Hz, H_2 and H_{18}), 8.80 (4H, t, H_3, H_7, H_{13} and H_{17}), 8.45

(2H, d, J = 8.3 Hz, $H_{3''}$ and $H_{5''}$), 8.39 (1H, d, J = 2.0 Hz, $H_{2'}$), 8.28 (2H, brt, $H_{2''}$ and $H_{6''}$), 8.20 (1H, d, J = 2.0 Hz, $H_{6'}$), 4.12 (3H, s, $COOCH_3$), 1.58 (9H, s, $C(CH_3)_3$), - 2.75 (2H, s, NH). MALDI-TOF: (positive mode, 1,4-diphenylbutadiene as matrix) 952.46 $(M)^+$, calculated 952.21 for $C_{51}H_{30}F_{10}N_4O_4$.

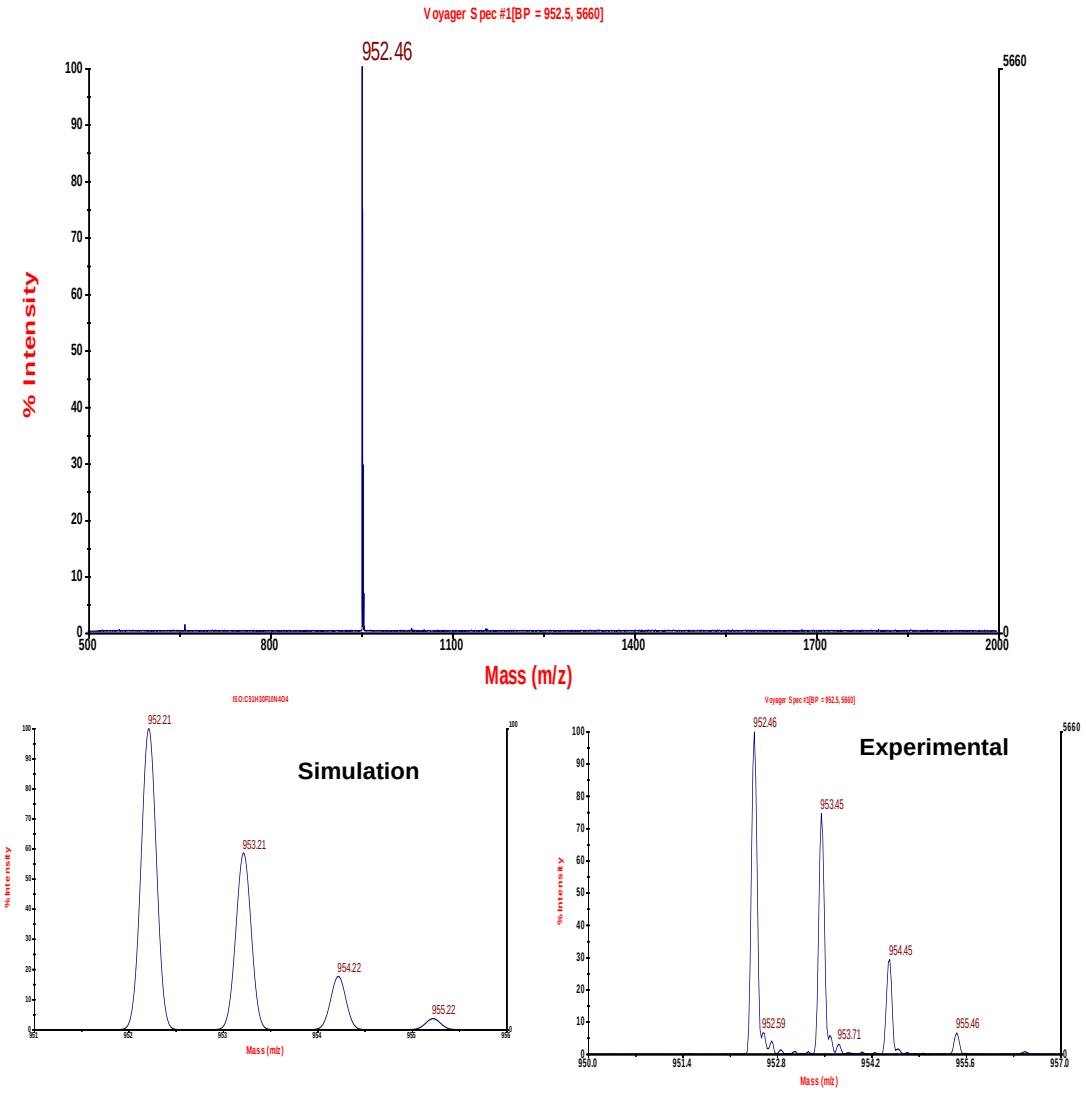

Figure S4. MALDI-TOF spectrum (positive mode, 1,4-diphenylbutadiene as matrix) of compound **5** (top and bottom right) and the corresponding isotope simulation (bottom left) expected for $C_{51}H_{30}F_{10}N_4O_4$.

5,15-*Bis*(pentafluorophenyl)-10,20-bis(3-formyl-4-hydroxy-5-*tert*-butylpheynyl)porphyrin **6**:

^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 12.25 (2H, s, OH), 10.16 (2H, s, CHO), 8.97 (4H, d, *J* = 5.0 Hz, H_2, H_8, H_{12} and H_{18}), 8.86 (4H, d, *J* = 5.0 Hz, H_3, H_7, H_{13} and H_{17}), 8.45 (1H, d, *J* = 2.0 Hz, $H_{2'}$), 8.41 (1H, d, *J* = 2.0 Hz, $H_{2'}$), 8.24 (1H, d, *J* = 2.0 Hz, $H_{6'}$), 8.22 (1H, d, *J* = 2.0 Hz, $H_{6'}$), 1.65 (18H, s, $C(CH_3)_3$), - 2.79 (2H, s, NH). MALDI-TOF: (positive mode, 1,4-diphenylbutadiene as matrix) 994.46 $(M)^+$, calculated 994.26 for $C_{54}H_{36}F_{10}N_4O_4$.

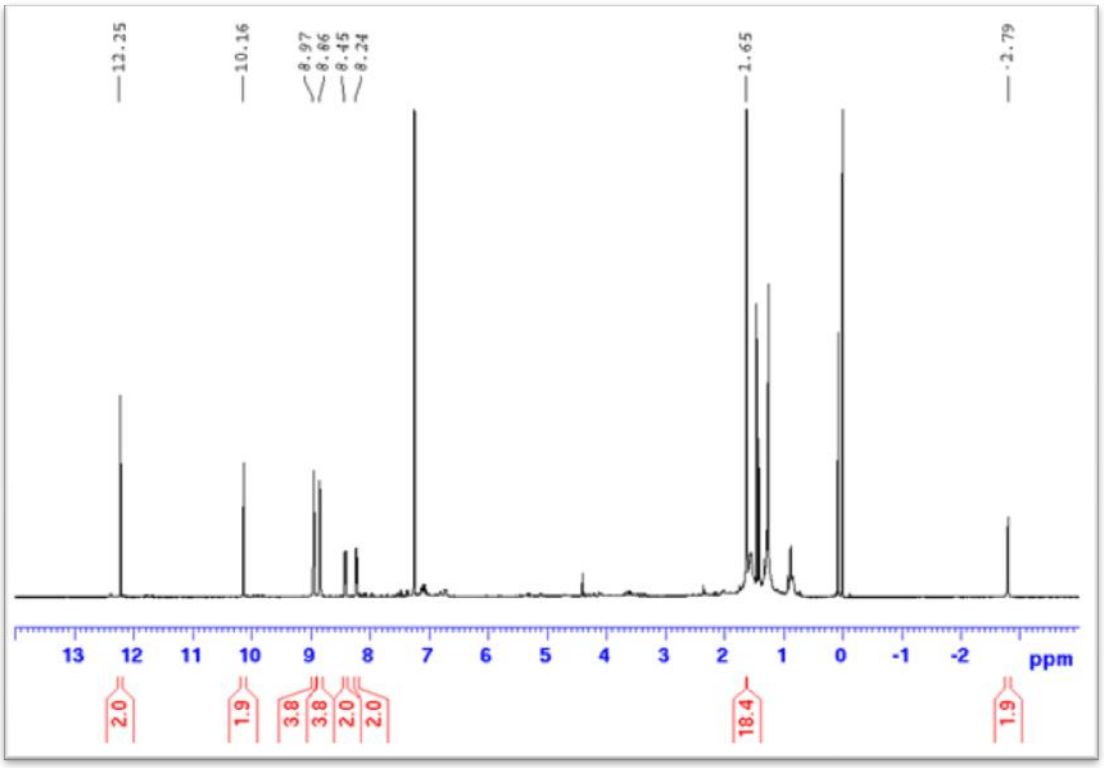

Figure S5. ^{1}H NMR spectrum of porphyrin **6**, 400 MHz, $CDCl_3$, 25 ^{o}C.

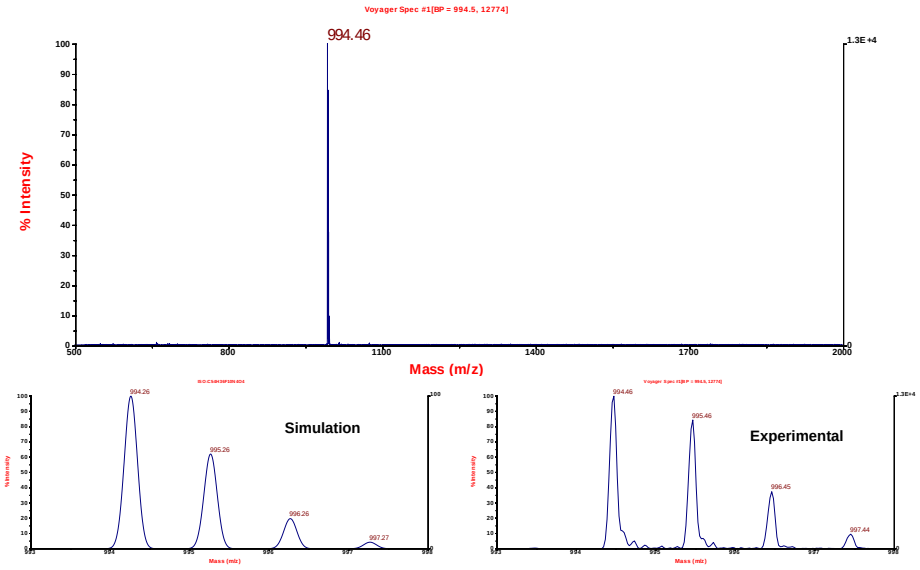

Figure S6. MALDI-TOF spectrum (positive mode, 1,4-diphenylbutadiene as matrix) of porphyrin **6** (top and bottom right) and corresponding isotope simulation (bottom left) expected for $C_{54}H_{36}F_{10}N_4O_4$.

5,15-*Bis*(pentafluorophenyl)-10,20-*bis*(4-methoxycarbonylphenyl)porphyrin **7**:

^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 8.93 (4H, d, J = 5.0 Hz, H_2, H_8, H_{12} and H_{18}), 8.83 (4H, d, J = 5.0 Hz, H_3, H_7, H_{13} and H_{17}), 8.46 (4H, d, J = 8.3 Hz, $H_{3'}$ and $H_{5'}$), 8.31 (4H, d, J = 8.3 Hz, $H_{2'}$ and $H_{6'}$), 4.13 (6H, s, COOCH_3), -2.86 (2H, s, NH). MALDI-TOF: (positive mode, 1,4-diphenylbutadiene as matrix) 911.51 $(M + H)^+$, calculated 910.16 for $C_{48}H_{24}F_{10}N_4O_4$.

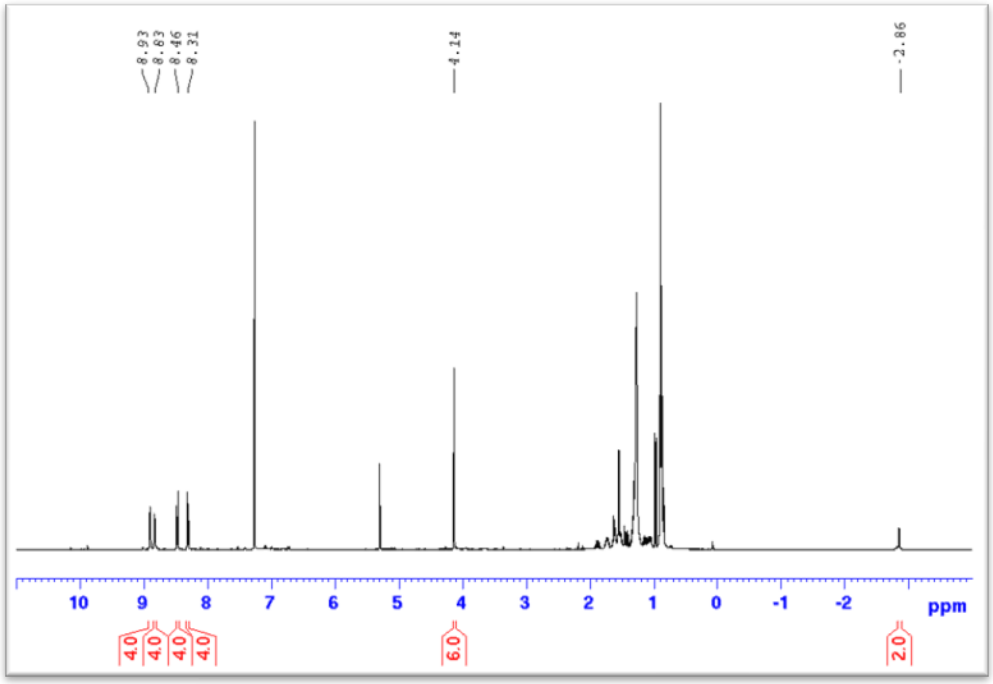

Figure S7. ^{1}H NMR spectrum of porphyrin **7**, 500 MHz, $CDCl_3$, 25 ^{o}C.

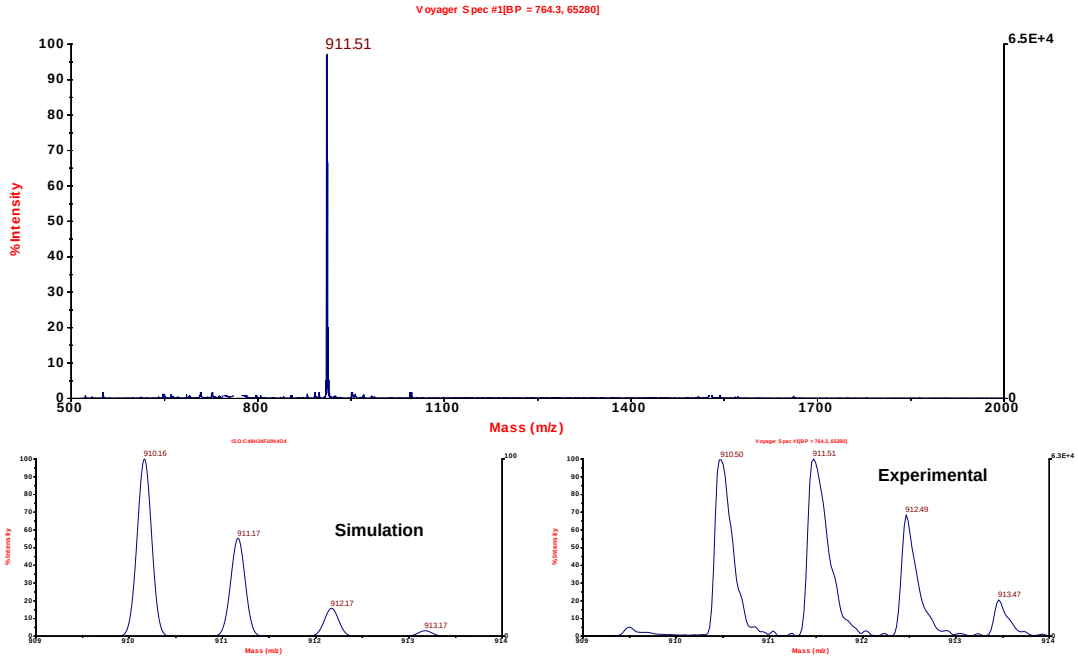

Figure S7. MALDI-TOF spectrum (positive mode, 1,4-diphenylbutadiene as matrix) of porphyrin **7** (top and bottom right) and corresponding isotope simulation (bottom left) expected for $C_{48}H_{24}F_{10}N_4O_4$.

5,15-*Bis*(pentafluorophenyl)-10-(4-methoxycarbonylphenyl)-20-[2'-(3''-*tert*-butyl-2''-hydroxyphenyl)benzimidazole]porphyrin **8**:

Commercially available 1,2-phenylenediamine (0.0045 g, 0.042 mmol) in nitrobenzene (3 mL) was added drop-wise to a solution of porphyrin **5** (0.040 g, 0.042 mmol) in nitrobenzene (7 mL), and the purple solution was heated at reflux (210 ^{o}C) in a sand bath for 12 h. After cooling and without any workup, the crude mixture was transferred to a chromatography column (SiO_2 in hexanes) and nitrobenzene was eluted with a mixture of hexanes/dichloromethane (90:10, v/v). The target compound was then eluted with a hexanes/dichloromethane (50:50, v/v), and was washed with hexanes (20 mL) to afford **8** as a purple solid in 70% yield (0.031 g).

^{1}H NMR (500 MHz, $(CD_3)_2CO$, δ ppm): 14.57 (s, 1H, OH); 12.42 (s, 1H, NH); 9.25 (m, 6H, pyrrolic protons); 9.10 (d, 2H, J = 4.8 Hz, pyrrolic protons); 8.82 (d, 1H, J = 2.0 Hz, $H_{2'}$); 8.48 (m, 4H, H_2, H_3, H_5 and H_6); 8.38 (d, 1H, J = 2.0 Hz, $H_{6'}$); 7.84 (d, 1H, J = 7.6 Hz, $H_{7''}$); 7.50 (d, 1H, J = 7.6 Hz, $H_{4''}$); 7.30 (m, 2H, $H_{5''}$ and $H_{6''}$); 4.10 (s, 3H, $COOCH_3$); 1.70 (s, 9H, Bu_t); -2.79 (s, 2H, NH). MALDI-TOF (positive mode, 1,4-diphenylbutadiene as matrix) 1041.41 $(M + H)^+$, calculated 1040.25 for $C_{57}H_{34}F_{10}N_6O_3$.

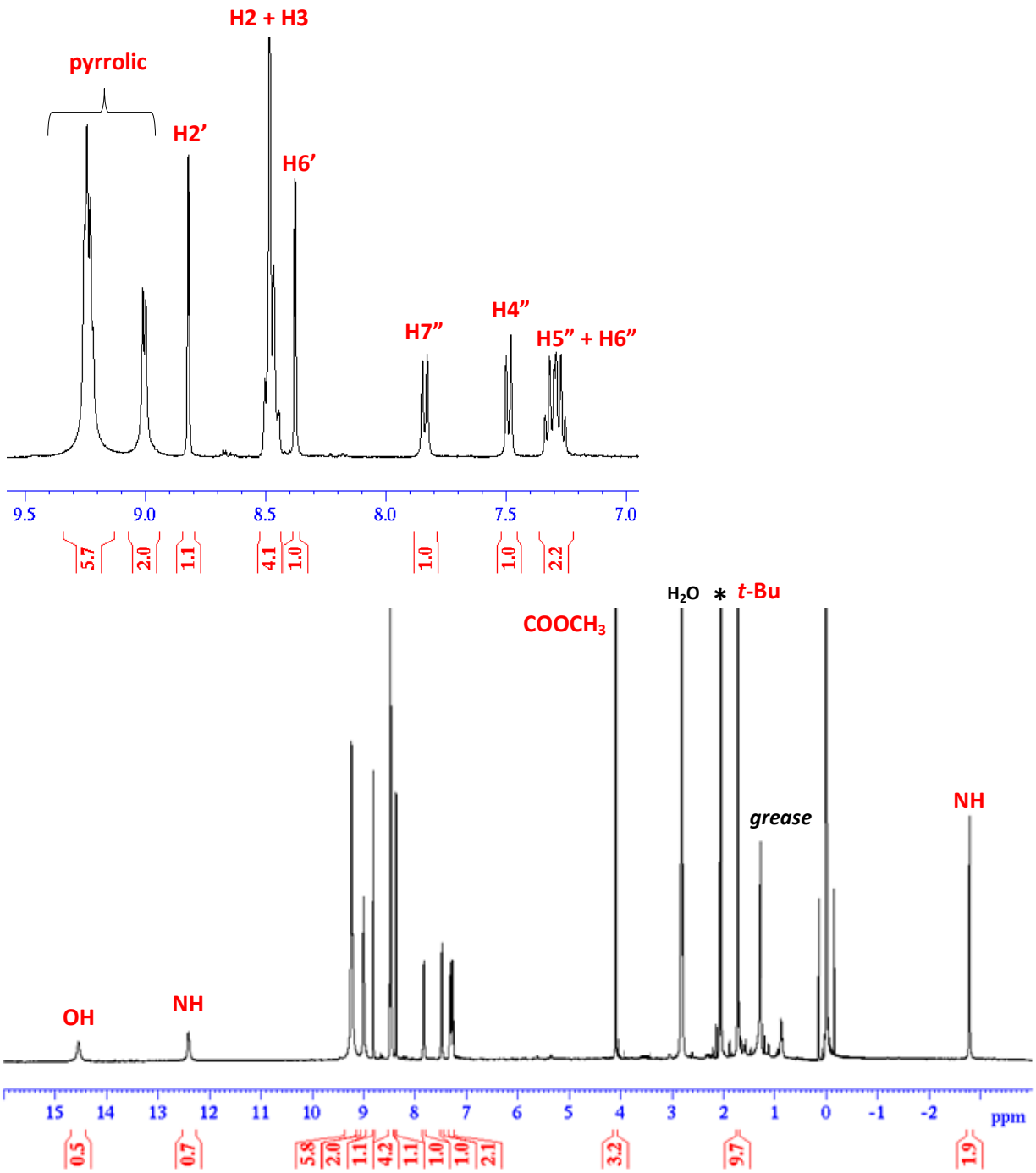

Figure S8. ^{1}H NMR spectrum of porphyrin **8**, 500 MHz, $(CD_3)_2CO$, 25 ^{o}C.

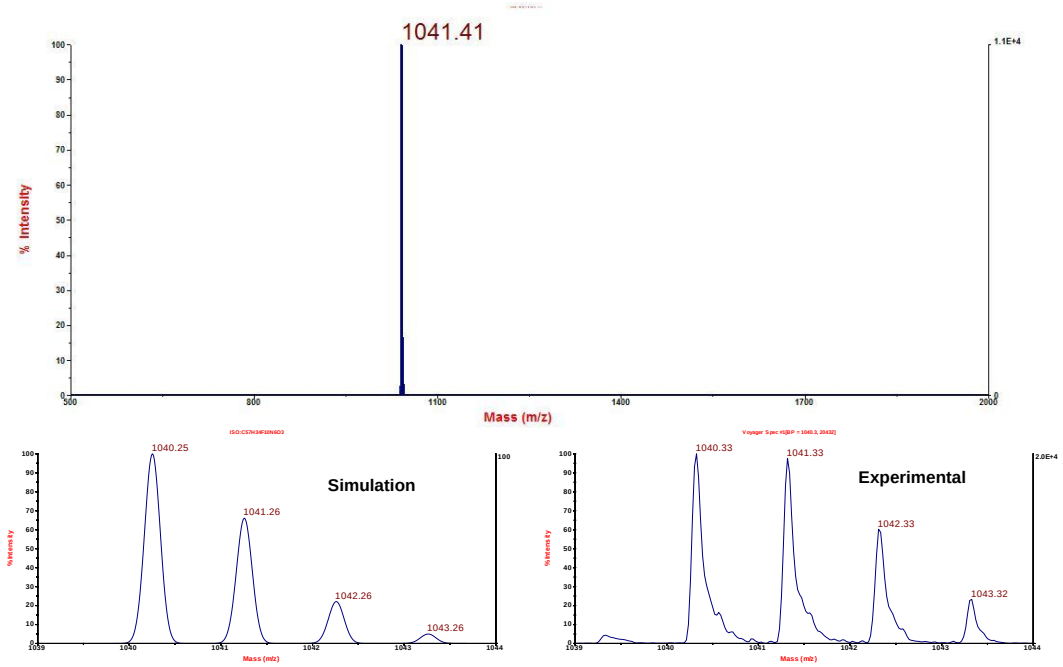

Figure S9. MALDI-TOF spectrum (positive mode, 1,4-diphenylbutadiene as matrix) of porphyrin **8** (top and bottom right) and corresponding isotope simulation (bottom left) expected for $C_{57}H_{34}F_{10}N_6O_3$.

5,15-*Bis*(pentafluorophenyl)-10-(4-carboxyphenyl)-20-[2'-(3"-*tert*-butyl-2"-hydroxyphenyl)benzimidazole]porphyrin **9**:

Porphyrin **8** (0.042 g, 0.04 mmol) was dissolved in trifluoroacetic acid (10 mL), and 20 mL of concentrated HCl was added. The green mixture was stirred at 90°C for 24 h. After cooling, the

mixture was taken up in dichloromethane (50 mL), washed with water (50 mL) and then neutralized with a saturated aqueous sodium carbonate solution. The organic phase was dried over sodium sulfate, filtered through paper, and concentrated under reduced pressure. The crude product was purified by flash chromatography (SiO_2) using a mixture of dichloromethane/methanol (9:1, v/v) as eluent to afford 0.041 g (98% yield) of the target porphyrin **9** as a purple solid. MALDI-TOF (positive mode, 1,4-diphenylbutadiene as matrix) 1026.41 $(M)^+$, calculated 1026.20 for $C_{56}H_{32}F_{10}N_6O_3$.

References:

1 – J. F. Larrow and E. N. Jacobsen, *J. Org. Chem.*, 1994, **59**, 1939-1942.

2 – J. S. Lindsey, *Acc. Chem. Res.*, 2010, **43**, 300–311.

3 – G. F. Moore, M. Hambourger, M. Gervaldo, O. G. Poluektov, T. Rajh, D. Gust, T. A. Moore and A. L. Moore, *J. Am. Chem. Soc.*, 2008, **130**, 10466–10467.