Electronic Supplementary Information

meso-Alkylidenyl dibenzihexaphyrins: Synthesis and protonation studies

Seong-Jin Hong, Ranjan Dutta, Ravi Kumar, Qing He, Vincent M. Lynch, Jonathan L. Sessler and Chang-Hee Lee

Table of Contents

Synthetic Experimental	S2 – S4
Spectroscopic data for compound **3-7**	S5 - S13
^{1}H NMR titration data for compound **5**, **6**, and **7** with TFA	S13-S18
UV-vis titration data for compound **5** and **6** with TFA and TBAF	S18-S22
Possible tautomeric forms of compound **5** and **6**	S23
Crystallographic data	S24-S28
References	S28

General Procedure: ^{1}H and ^{13}C NMR spectra (JNM-ECZ400S/L1 400 MHz and Bruker Avance II 600 MHz) were recorded using TMS as the internal standard. High resolution mass spectra were obtained on a Voyager-DE STR MALDI-TOF mass spectrometer and a JEOL JMS-700 GC mass spectrometer. UV-visible spectral studies were performed using Varian Cary 100 Conc spectrophotometer. Column chromatography was performed over silica gel (Merck, 230-400 mesh). Pyrrole was distilled at atmospheric pressure from CaH_2. All other reagents were obtained from Aldrich and used as received unless noted otherwise.

Synthetic Experimental

Synthesis of compound (3): To the solution of compound **1**[1] (0.20 g, 0.51 mmol) and pyrrole (5 mL, 72.1 mmol) was added $InCl_3$ (0.036 g, 0.16 mmol). The mixture was stirred for 1 h at 40 ^{o}C. Then aqueous NaOH solution (0.1 *N*, 5 mL) and brine (30 mL) were added in order to quench the reaction before the mixture was extracted with CH_2Cl_2 (20 mL × 3). The organic layer was dried (Na_2SO_4) and the volatiles were removed in *vacuo*. The crude product was recrystallized from MeOH and hexanes to give a brownish solid. Yield: 0.182 g (68%); ^{1}H NMR (400 MHz, $CDCl_3$, diastereomers) δ 3.59 – 3.61 (m, 2H), 4.95 – 4.97 (m, 2H), 5.86 – 5.90 (m, 2H), 6.05 – 6.09 (m, , 2H), 6.73 – 6.76 (m, 2H), 6.76 – 6.86 (m, 3H), 6.95 – 6.96 (m, 1H), 7.70 – 7.73 (m, 3H), 7.73 – 7.86 (m, 4H), 7.91 – 7.93 (m, 1H), 9.71 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 42.4, 42.6, 59.0, 59.0, 106.8, 106.8, 107.9, 117.9, 123.3, 123.4, 123.4, 123.5, 126.6, 126.8, 127.5, 127.6, 128.5, 128.6, 130.9, 131.0, 135.5, 135.9, 136.0, 140.0, 140.0, 142.3, 142.4, 142.5, 198.5, 198.6, 200.9, 200.9; EI MS calcd for $C_{34}H_{24}N_2O_4$ 524.1736, found 524.1735.

Synthesis of *m*-dibenzihexaphyrin (5): Compound **3** (1.01 g, 1.93 mmol) and pentafluorobenzaldehyde (290 μL, 2.35 mmol) were dissolved in CH_2Cl_2 (200 mL) with stirring and then TFA (80 μL, 1.04 mmol) was added. The resulting mixture was stirred for 12 h at room temperature. DDQ (1.32 g, 5.81 mmol) and TEA (140 μL, 1.00 mmol) were added and the stirring continued for 1 h. After quenching with brine (100 mL), an organic layer was obtained by extracting with CH_2Cl_2 (50 mL x 4). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product obtained in this way was purified by column chromatography over silica (from CH_2Cl_2 to CH_2Cl_2/EtOAc = 95/5) to give a yellowish

solid. Yield: 79 mg (6%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.38 (s, 2H), 6.74 – 6.75 (d, J = 4.8 Hz, 2H), 6.95 – 6.97 (d, J = 4.7 Hz, 2H), 7.31 (s, 2H), 7.36 – 7.38 (d, J = 7.6 Hz, 2H), 7.50 – 7.53 (m, 4H), 7.62 – 7.64 (m, 2H), 7.66 – 7.72 (m, 4H), 7.73 – 7.77 (s, 4H), 7.80 – 7.83 (m, 4H), 7.97 – 8.01 (m, 4H), 14.27 (s, 2H); ^{13}C NMR (150 MHz, TFA-*d*) δ 110.2, 126.0, 126.5, 129.6, 130.5, 131.1, 132.3, 133.0, 133.6, 135.9, 137.0, 137.5, 138.5, 138.9, 139.2, 139.6, 140.1, 140.3, 140.4, 140.4, 142.2, 142.8, 143.3, 143.6, 144.2, 146.9, 148.6, 151.9, 159.2, 191.6, 193.2, 194.9; MALDI-TOF MS calcd for $C_{82}H_{34}F_{10}N_4O_8$ 1392.222, found 1393.227.

Synthesis of compound (4): To a solution of compound **2**[1-2] (1.51 g, 3.86 mmol) and pyrrole (20 mL, 288.3 mmol) was added $InCl_3$ (0.255 g, 1.15 mmol). The resulting mixture was stirred for 1 h at 40 ^{o}C. An aqueous solution of NaOH (0.1 *N*, 5 mL) and brine (50 mL) was then added in order to quench the reaction before the mixture was extracted with CH_2Cl_2 (40 mL × 3). The organic layer was dried (Na_2SO_4) and the volatiles removed in *vacuo*. The crude product obtained in this way was recrystallized from MeOH and hexanes to give a brownish solid. Yield: 1.43 g (71%); ^{1}H NMR (400 MHz, $CDCl_3$, diastereomers) δ 3.62 – 3.63 (m, 2H), 4.98 – 4.99 (m, 2H), 5.92 – 5.94 (m, 2H), 6.04 – 6.07 (m, 2H), 6.73 – 6.75 (m, 2H), 6.78 (s, 4H), 7.71 – 7.82 (m, 6H), 7.85 – 7.89 (m, 2H), 9.72 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 41.8, 41.9, 59.1, 59.2, 106.8, 107.9, 108.2, 117.9, 123.3, 123.4, 123.4, 128.1, 131.2, 131.2, 135.7, 136.0, 138.4, 142.3, 142.3, 142.4, 142.4, 198.5, 198.6, 200.8, 200.9; EI MS calcd for $C_{34}H_{24}N_2O_4$ 524.1736, found 524.1737.

Synthesis of *p*-dibenzihexaphyrin (6): Compound **4** (1.01 g, 1.93 mmol) and pentafluorobenzaldehyde (285 μL, 2.31 mmol) were dissolved in CH_2Cl_2 (200 mL) with stirring. Then, TFA (130 μL, 1.69 mmol) was added. The resulting mixture was stirred for 12 h at room temperature. DDQ (1.30 g, 5.74 mmol) and TEA (240 μL, 1.72 mmol) were added and the stirring continued for an additional 1 h. After quenching with brine (100 mL) an organic phase was obtained by extracting with CH_2Cl_2 (50 mL x 4). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product generated in this manner was purified by column chromatography over silica (from CH_2Cl_2 to CH_2Cl_2/EtOAc = 95/5) to give a yellowish solid. Yield: 195 mg (15%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.38 – 6.40 (m, 2H), 6.88 (d, J = 4.7 Hz, 2H), 7.27 (s, 2H), 7.31 – 7.33 (m, 4H), 7.49 – 7.51 (m, 6H), 7.73 – 7.77 (m, 4H), 7.81 – 7.86 (m, 8H), 8.01 – 8.04 (m, 4H), 14.45 (s, 2H); ^{1}H NMR (600 MHz, TFA-*d*) δ 6.72 (d, J = 4.2 Hz, 2H), 7.17 (s, 2H), 7.51 (s, 2H), 7.53 (d, J = 7.80 Hz, 4H),

7.71 (d, J = 8.4 Hz, 4H), 7.73-7.74 (m, 2H), 7.90 - 7.94 (m, 6H), 7.98 - 8.02 (m, 6H), 8.05 - 8.07 (m, 2H), 8.13 - 8.14 (m, 2H); ^{13}C NMR (150 MHz, TFA-*d*) δ 110.1, 126.3, 126.7, 126.8, 126.8, 130.3, 130.8, 131.9, 132.1, 133.6, 134.6, 136.0, 136.2, 137.1, 138.0, 139.0, 140.0, 140.2, 140.6, 140.7, 140.8, 140.8, 142.1, 142.5, 143.1, 143.2, 143.4, 143.9, 147.2, 148.4, 149.0, 151.4, 160.7, 192.2, 193.1, 193.8, 195.2; MALDI-TOF MS calcd for $C_{82}H_{34}F_{10}N_4O_8$ 1392.222, found 1393.259.

Synthesis of *p*-benzithiaporphyrin (7): Compound **4** (0.2 g, 0.38 mmol) and 2,5-bis-thiophene-dimethanol (0.14 g, 0.47 mmol) were dissolved in CH_2Cl_2 (40 mL) with stirring. Then, TFA (15 μL, 0.19 mmol) was added. The resulting mixture was stirred for 24 h at room temperature. At this point, DDQ (0.26 g, 1.15 mmol) and TEA (27 μL, 0.19 mmol) were added and the stirring continued for an additional 1 h. After quenching with brine (100 mL) and extracting with CH_2Cl_2 (50 mL x 3), the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product obtained in this way was purified by column chromatography over silica gel (eluent gradient from CH_2Cl_2 to CH_2Cl_2/EtOAc = 95/5) to give a black solid. Yield: 17 mg (6%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.24 – 6.25 (m, 2H), 6.48 (s, 2H), 7.30 – 7.32 (m, 4H), 7.43 – 7.45 (m, 6H), 7.58 (s, 4H), 7.68 – 7.73 (m, 4H), 7.88- 7.89 (m, 2H), 7.93 – 7.95 (m, 2H), 8.50 (br s, 2H), 8.52 – 8.53 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 119.7, 121.9, 122.2, 123.0, 124.0, 125.9, 128.5, 128.6, 129.2, 130.7, 133.8, 134.1, 134.3, 134.6, 138.0, 139.2, 139.9, 140.4, 140.9, 141.3, 145.9, 189.8, 189.8; MALDI-TOF MS calcd for $C_{52}H_{30}N_2O_4S$ 778.193, found 778.269.

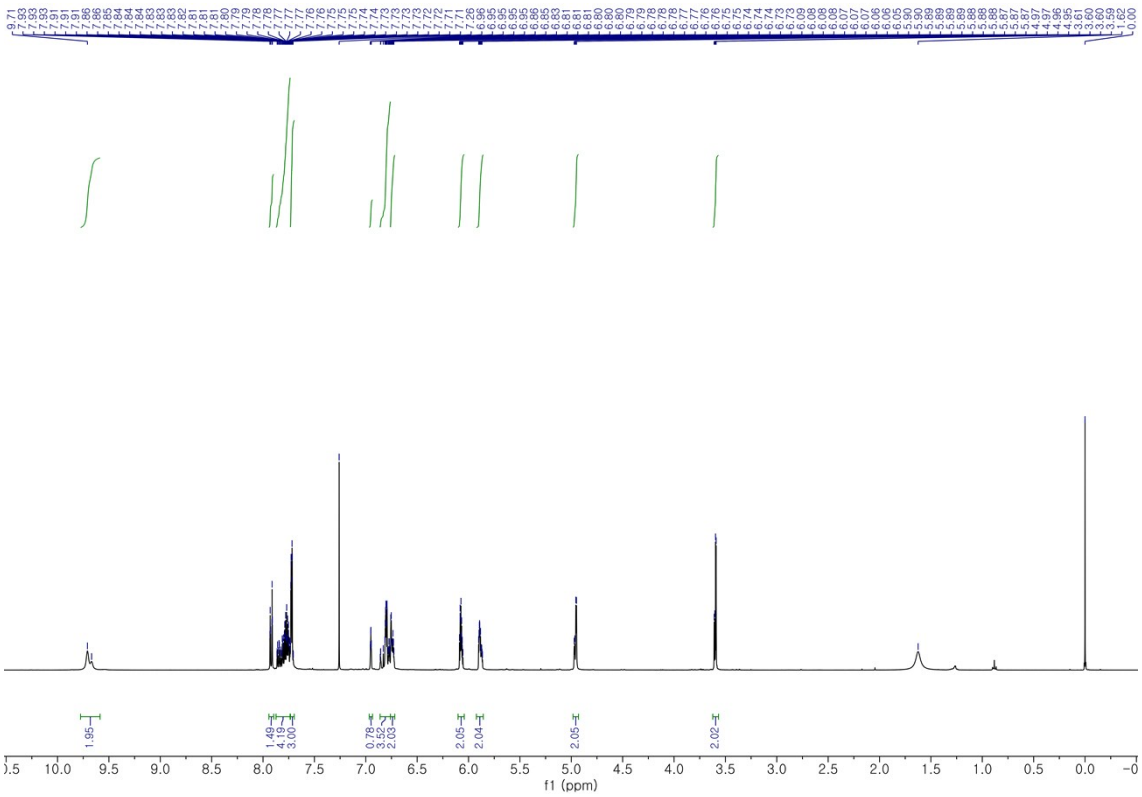


Figure S1. ^{1}H NMR spectrum of compound **3** in $CDCl_3$.

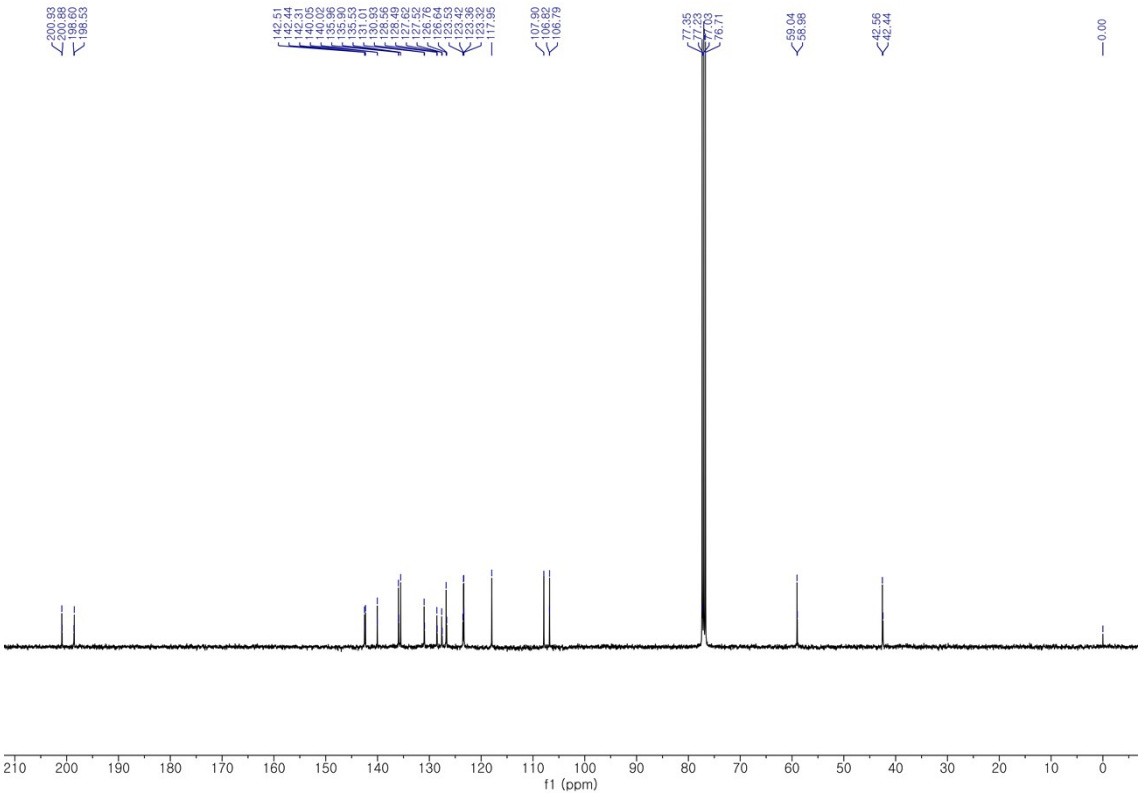


Figure S2. ^{13}C NMR spectrum of compound **3** in $CDCl_3$.

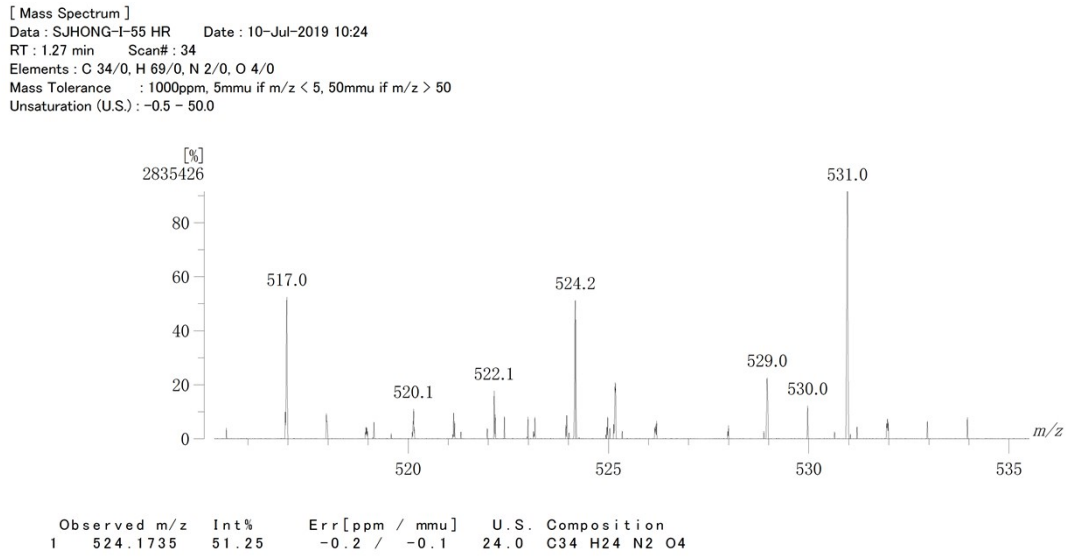


Figure S3. EI MS spectrum of compound **3.**

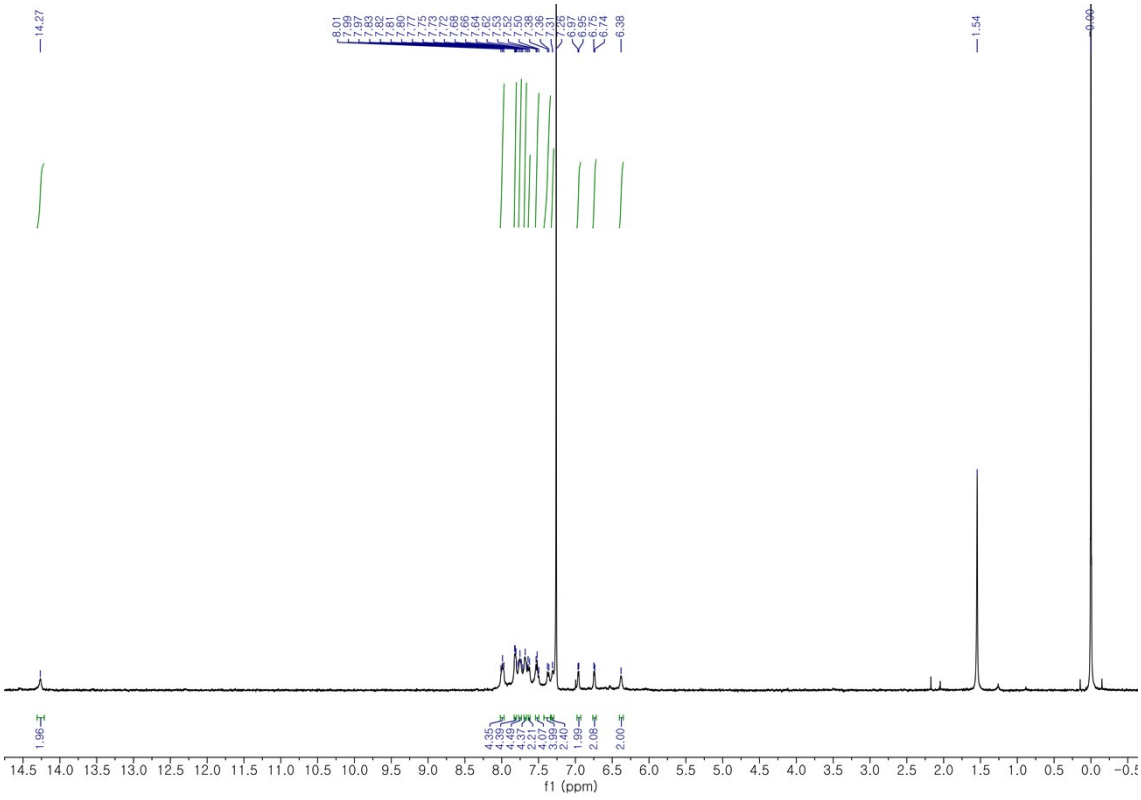


Figure S4. ^{1}H NMR spectrum of compound **5** in $CDCl_3$.

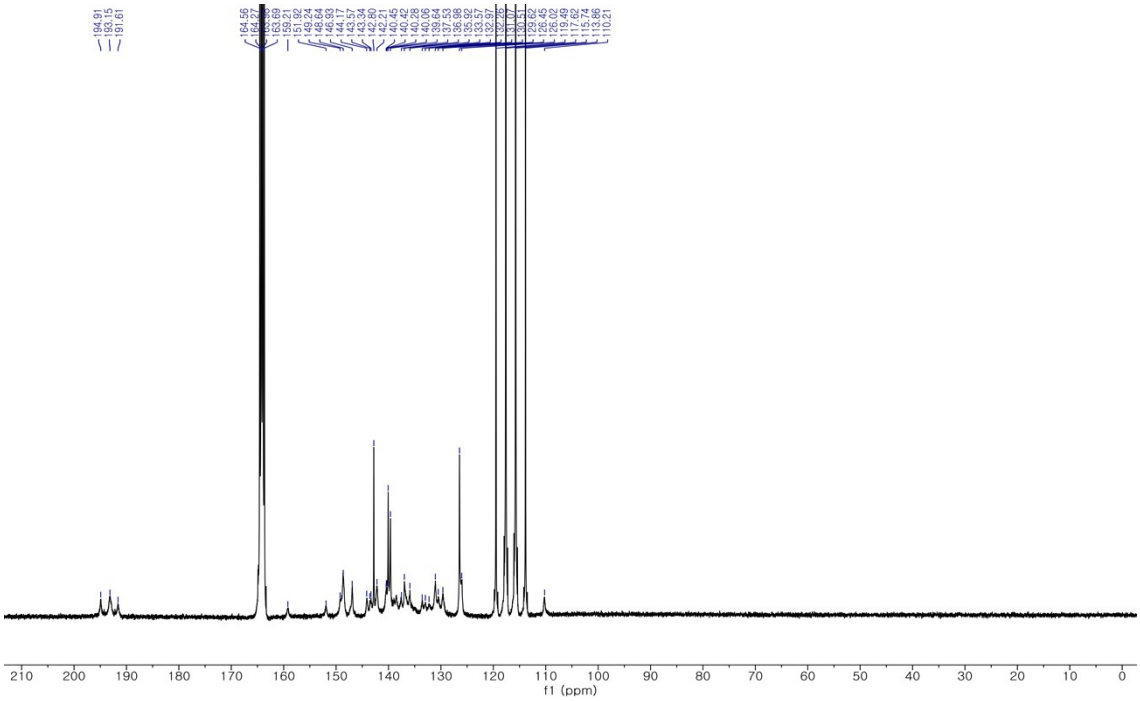


Figure S5. ^{13}C NMR spectrum of compound **5** in TFA-*d*.

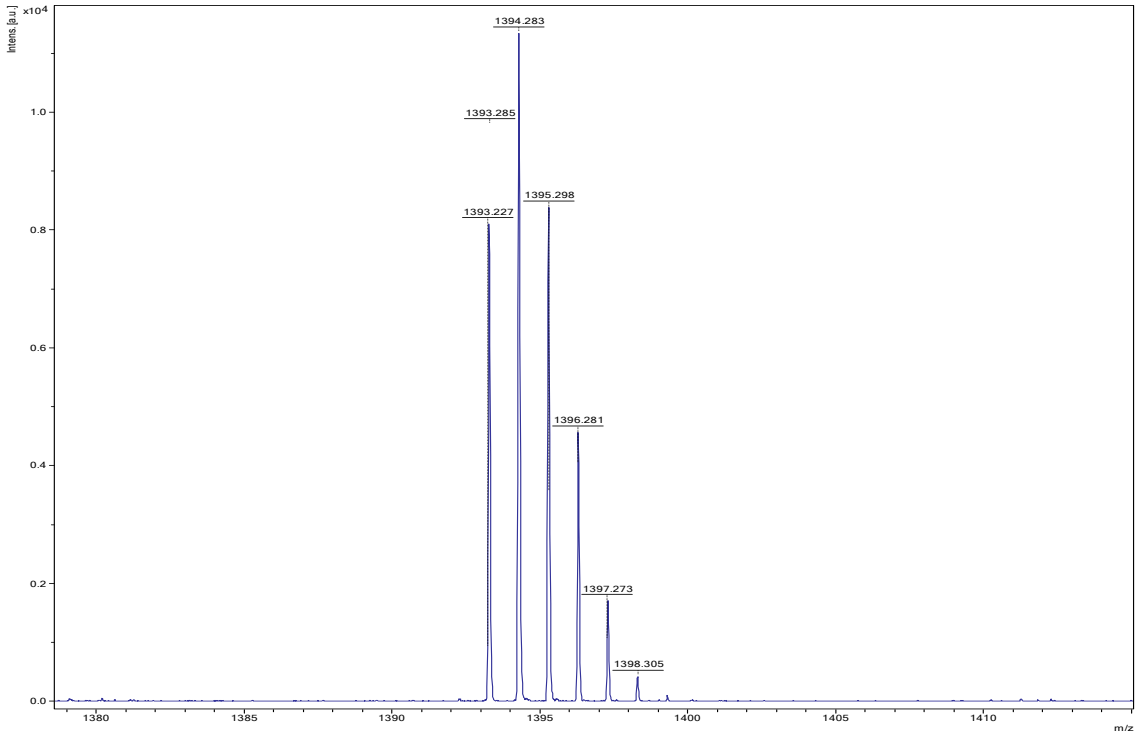


Figure S6. MALDI-TOF MS spectrum of compound **5**.

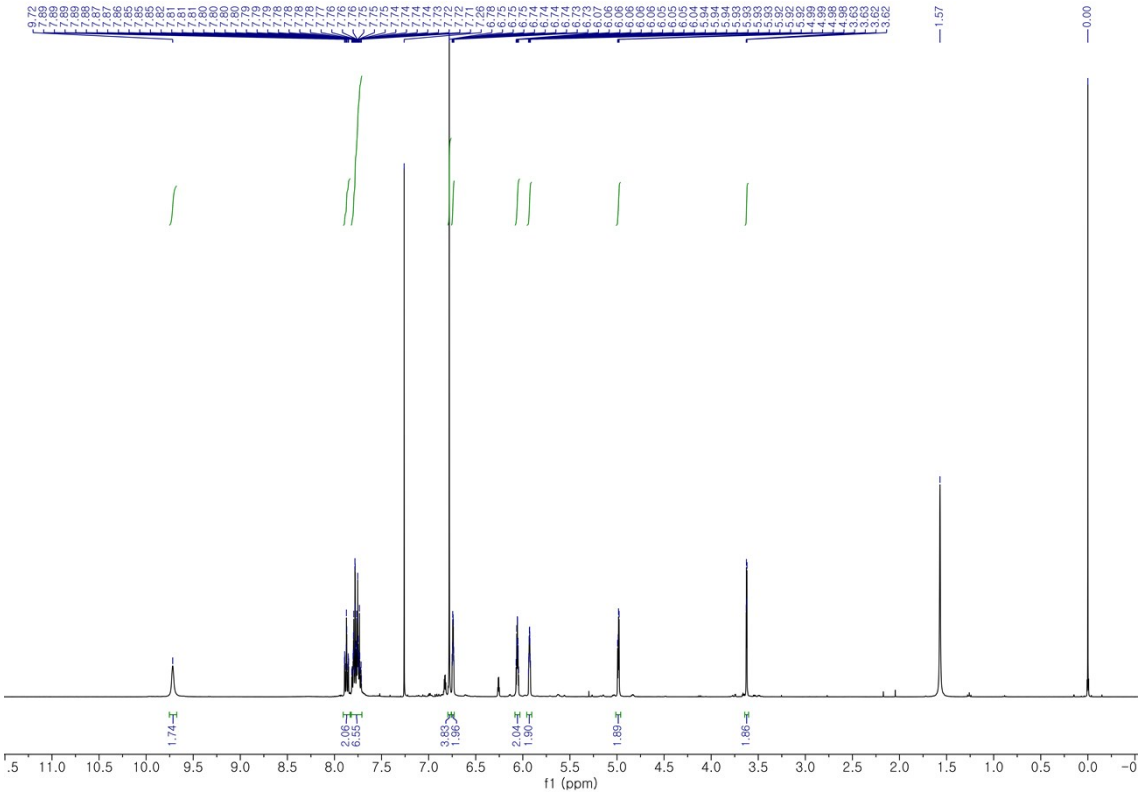


Figure S7. ^{1}H NMR spectrum of compound **4** in $CDCl_3$.

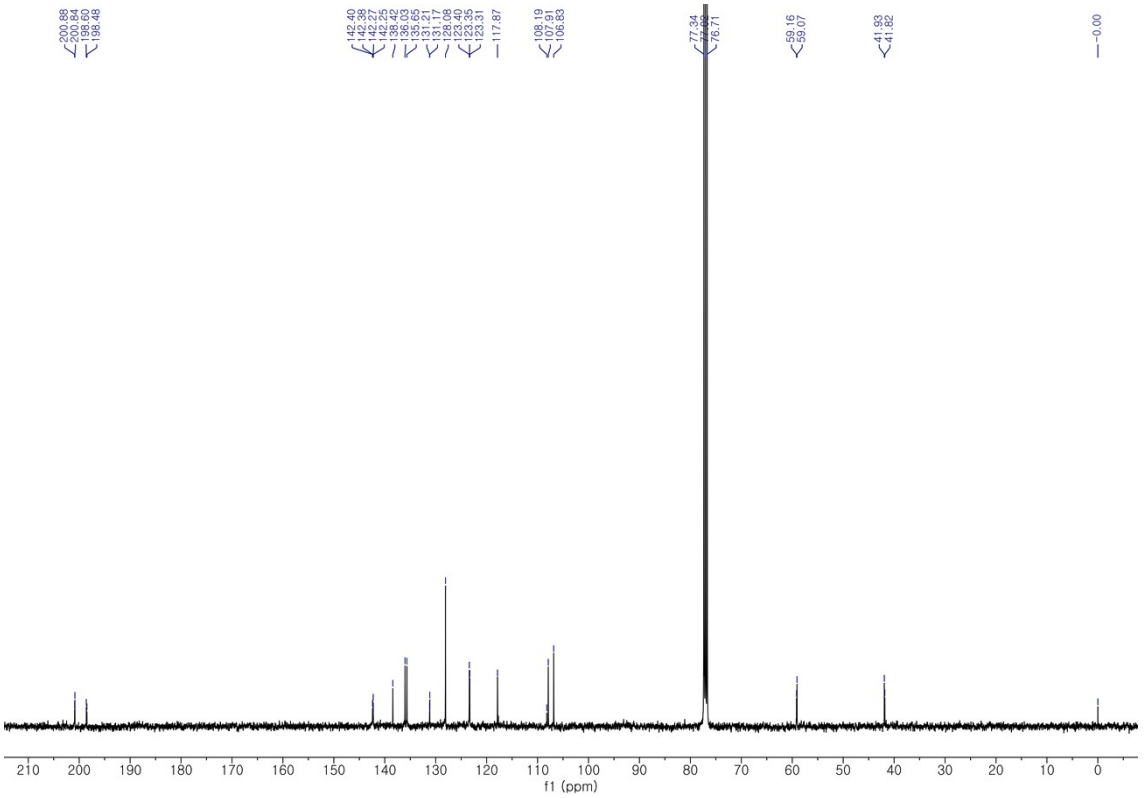


Figure S8. ^{13}C NMR spectrum of compound **4** in $CDCl_3$.

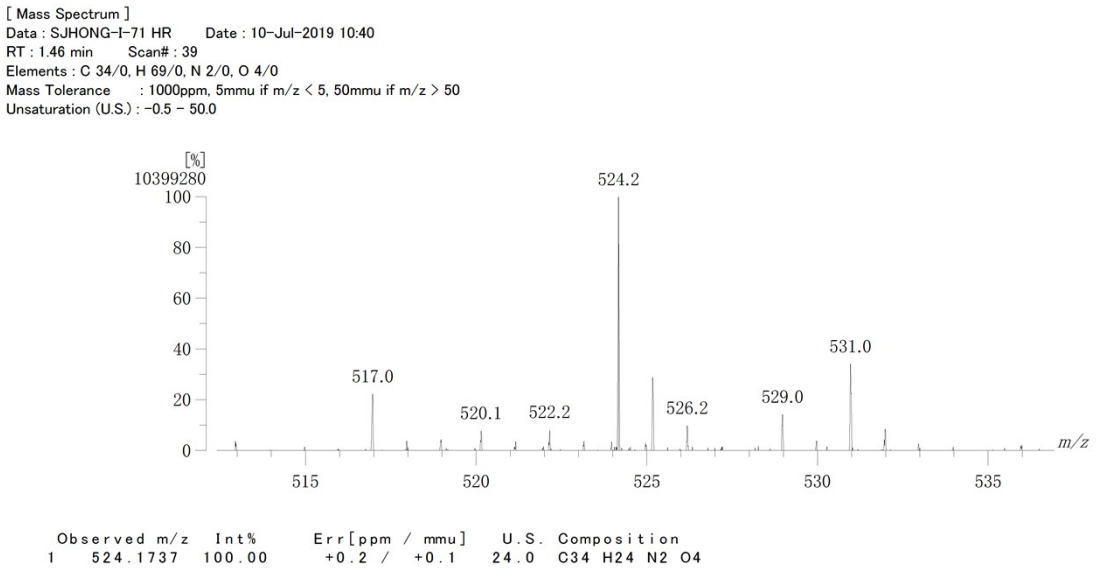


Figure S9. EI MS spectrum of compound **4.**

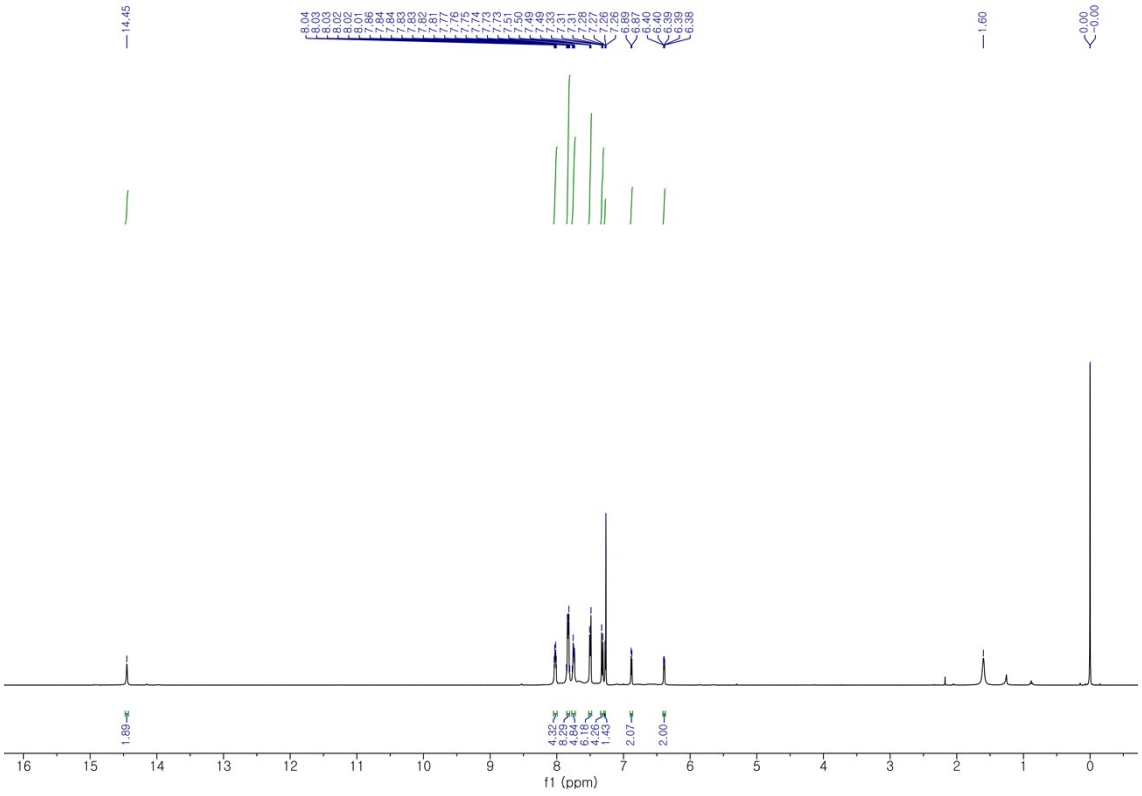


Figure S10. ^{1}H NMR spectrum of compound **6** in $CDCl_3$.

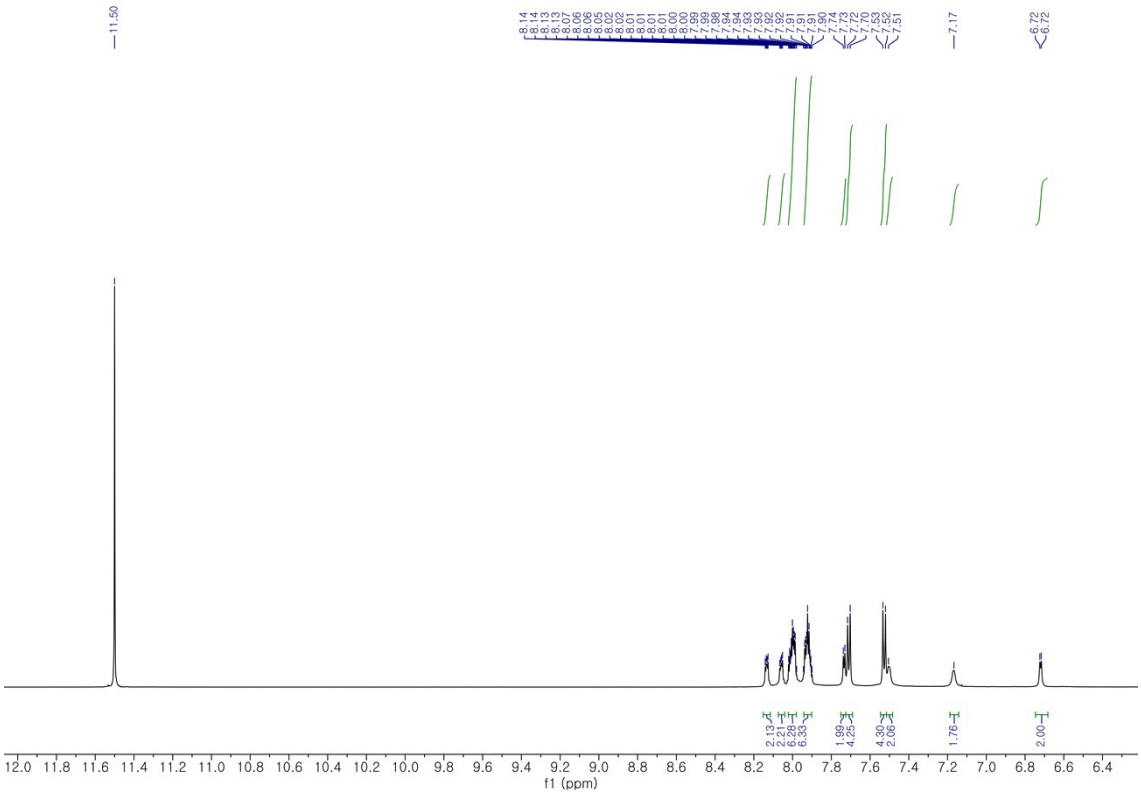


Figure S11. ^{1}H NMR spectrum of compound **6** in TFA-*d*.

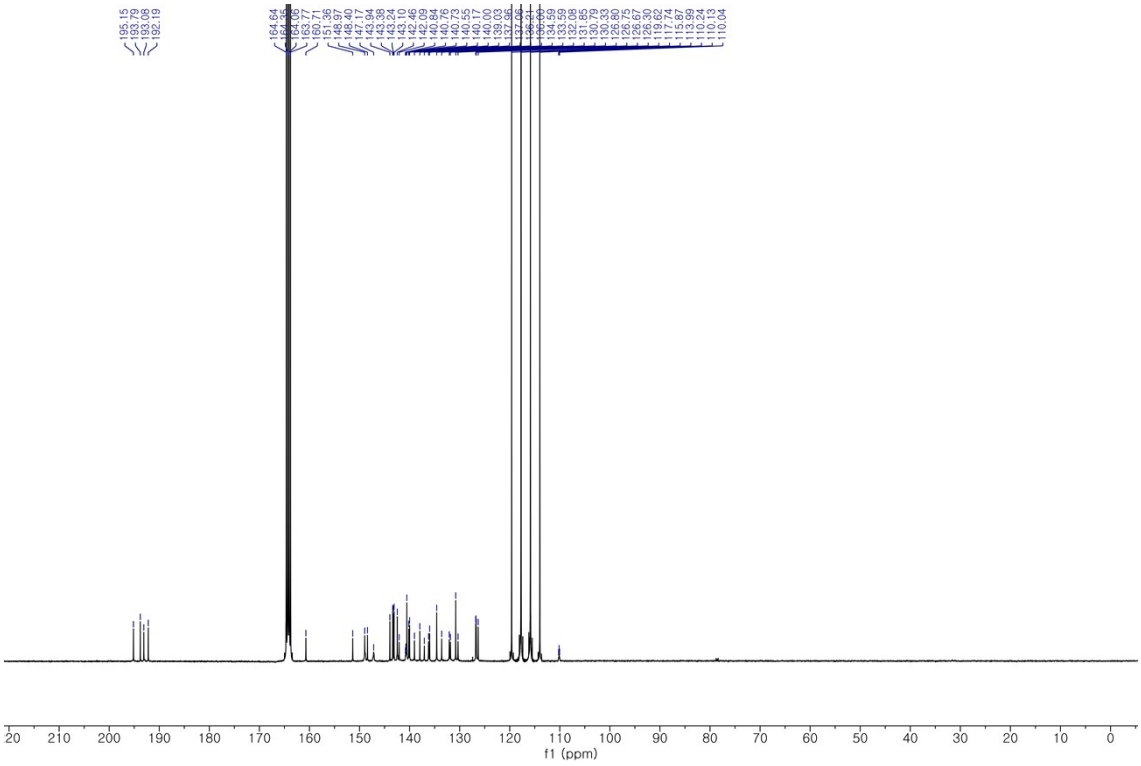


Figure S12. ^{13}C NMR spectrum of compound **6** in TFA-*d*.

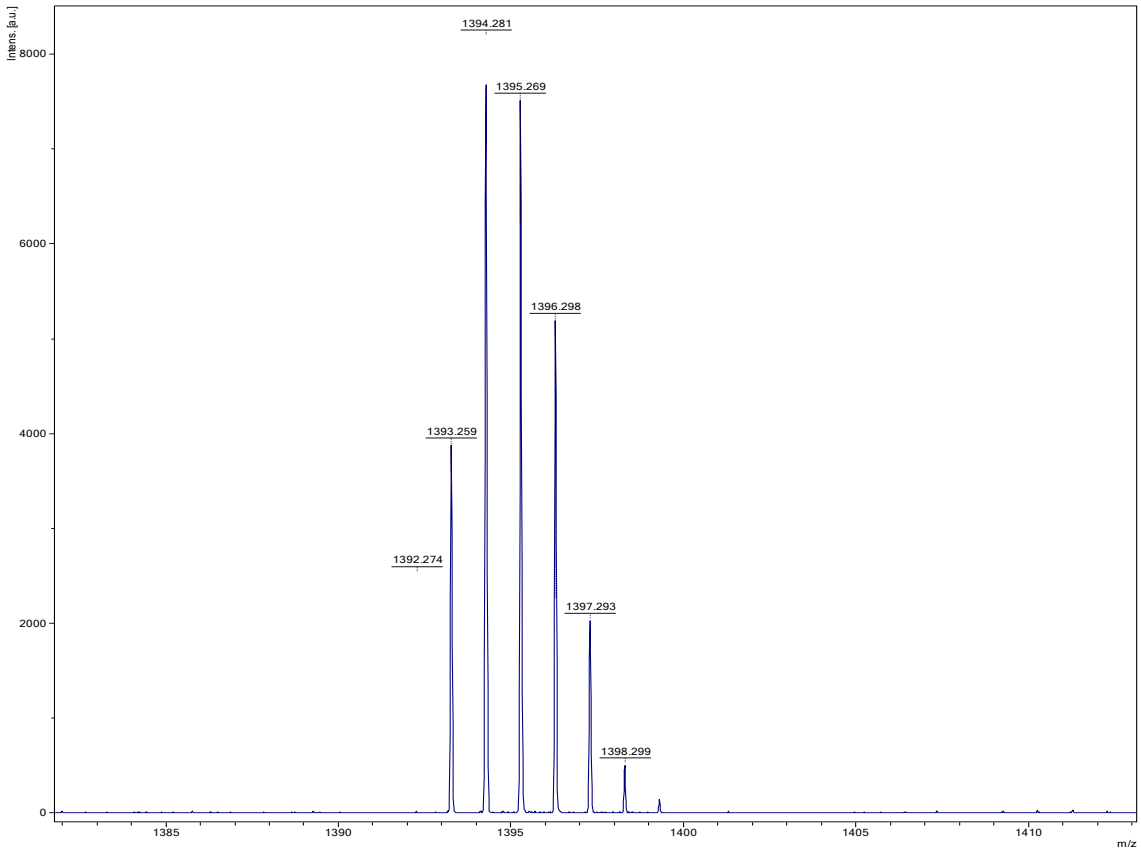


Figure S13. MALDI-TOF MS spectrum of compound **6**.

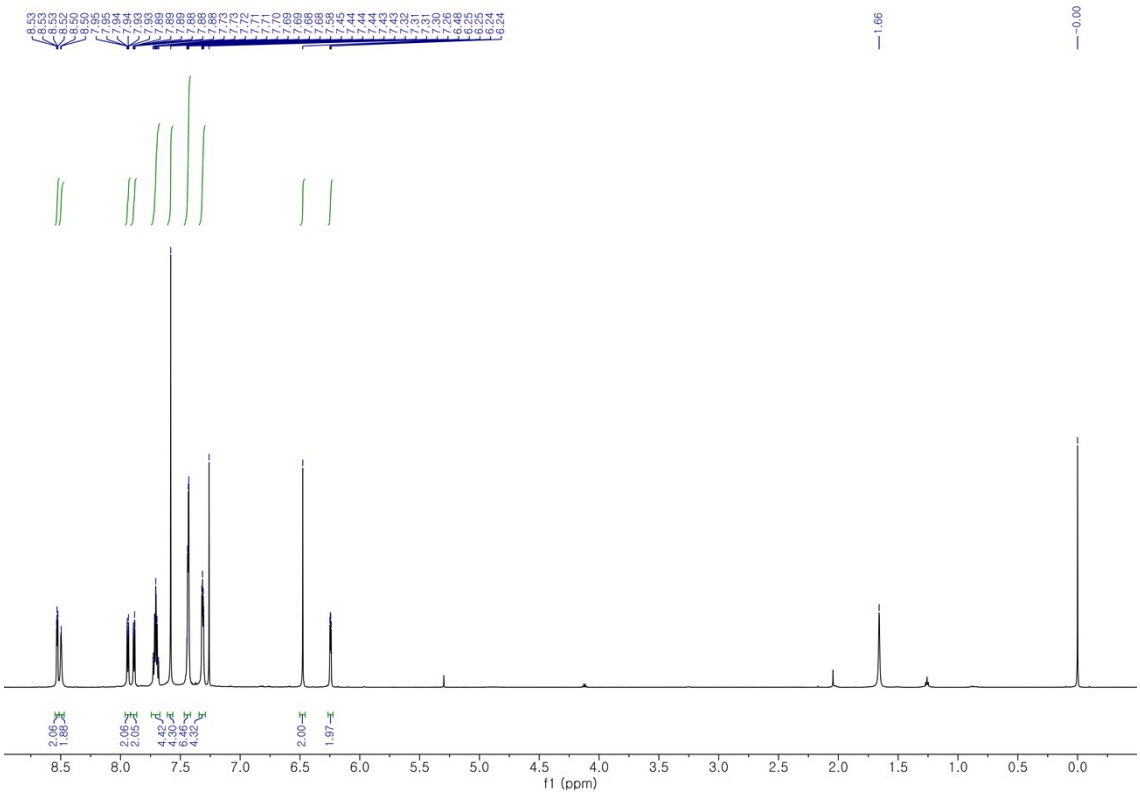


Figure S14. ^{1}H NMR spectrum of compound **7** in $CDCl_3$.

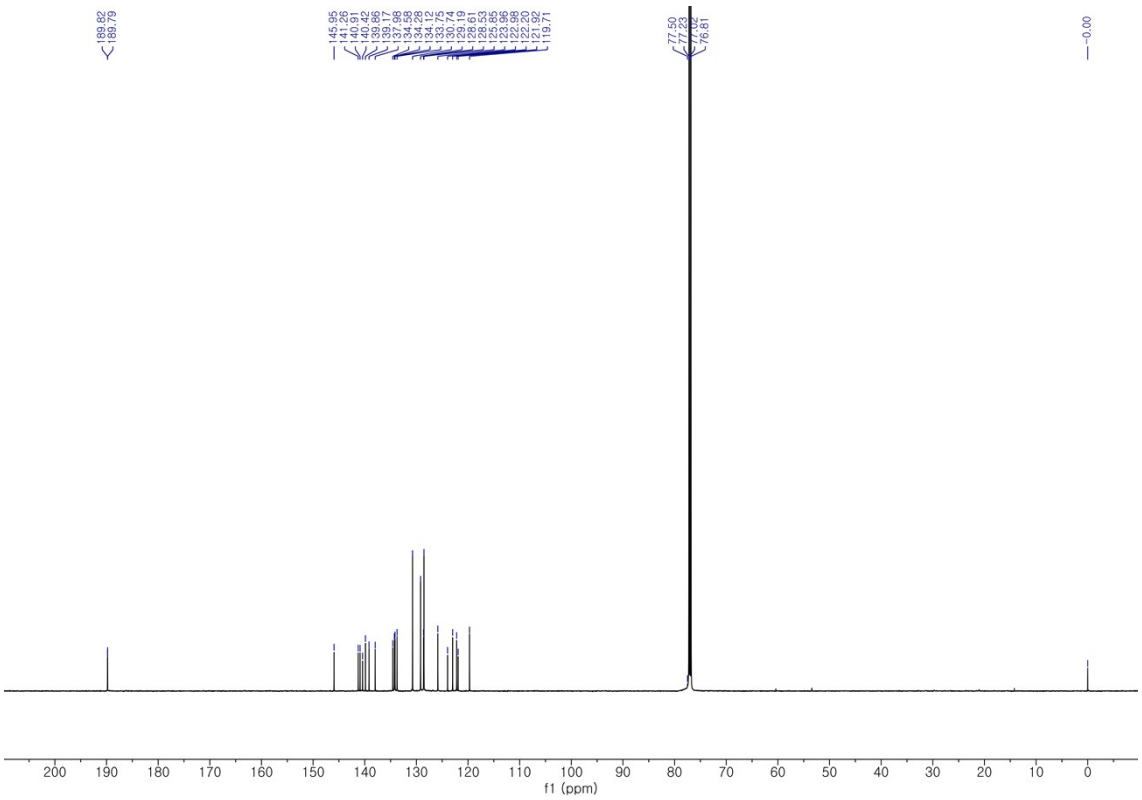


Figure S15. ^{13}C NMR spectrum of compound **7** in $CDCl_3$.

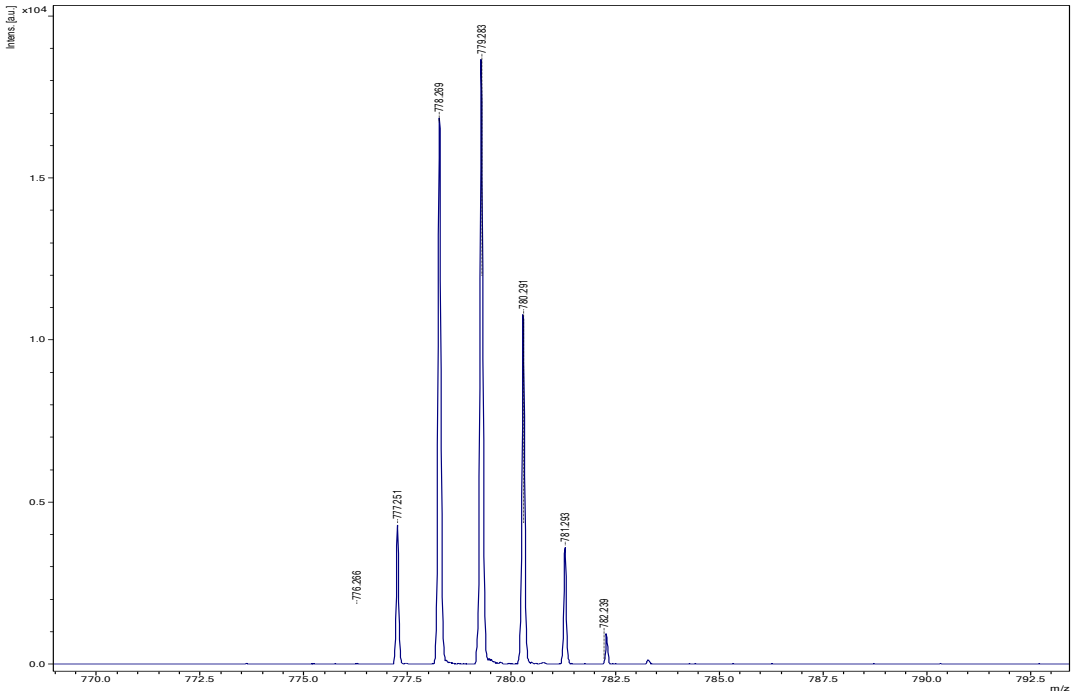


Figure S16. MALDI-TOF MS spectrum of compound **7**.

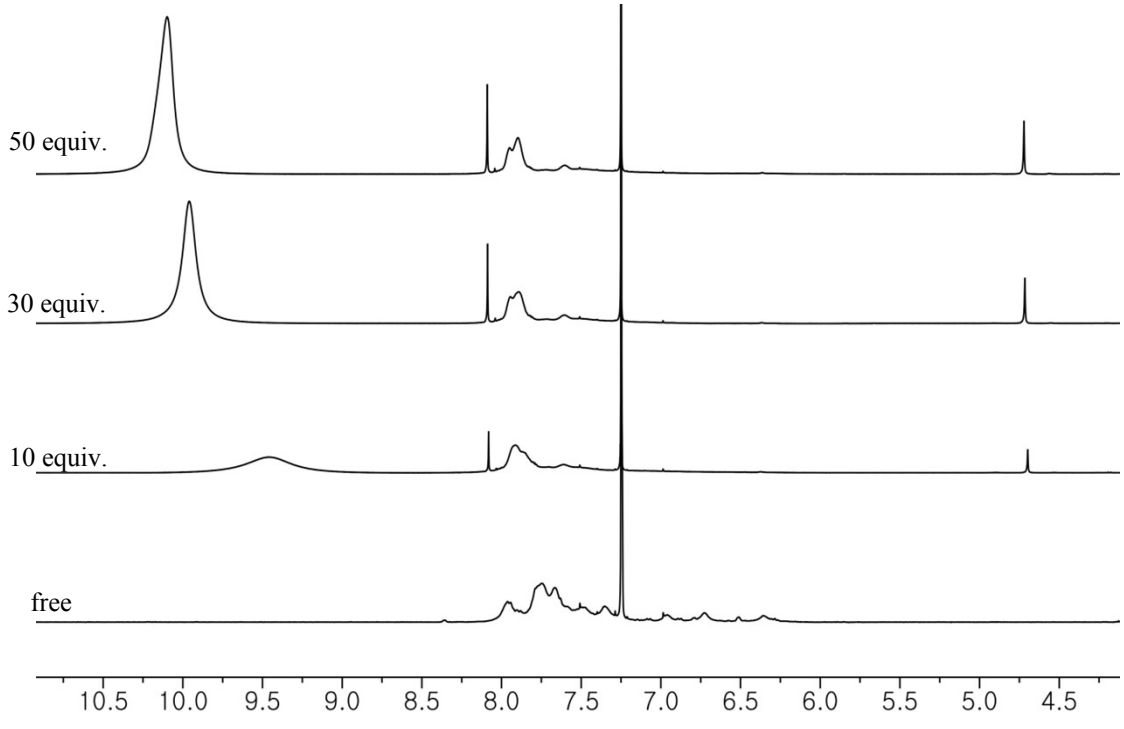


Figure S17. Partial ^{1}H NMR spectral changes observed when compound **5** is subject to treatment with TFA in $CDCl_3$ (8.37 X 10^{-3} M) at 50 ^{o}C. The new resonance at 4.72 ppm is ascribed to protonation at the *meso*-α-position.

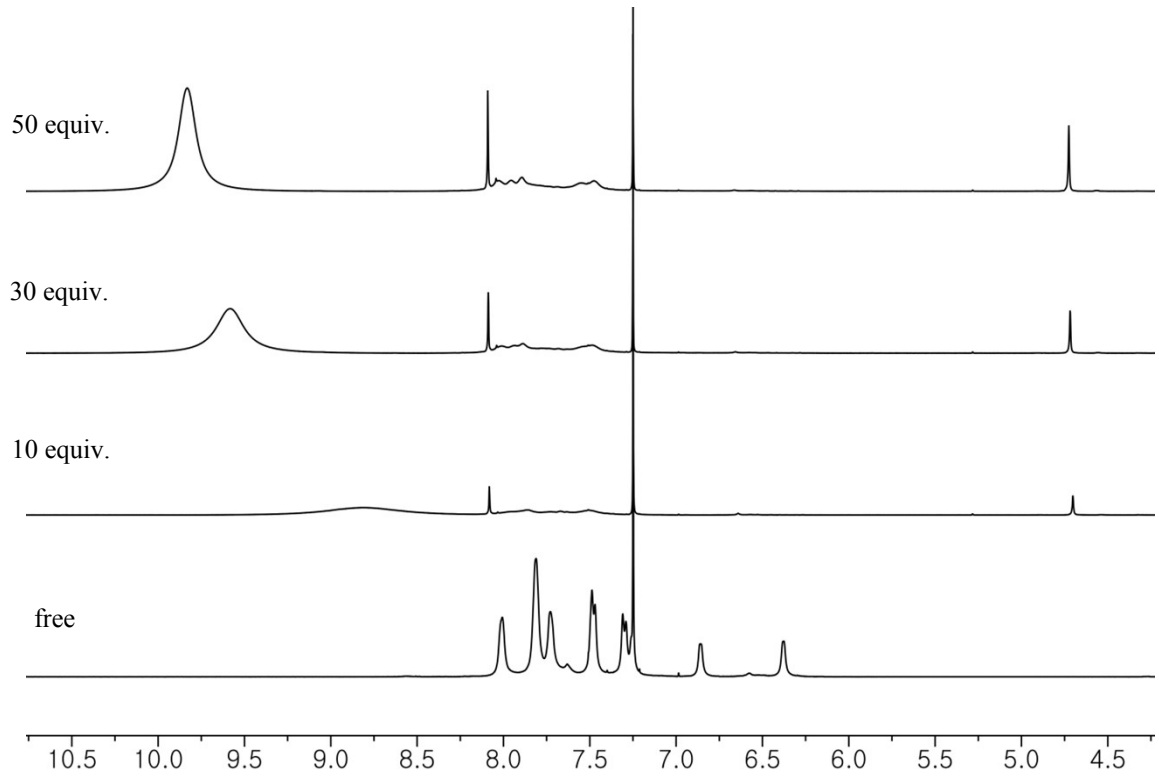


Figure S18. Partial ^{1}H NMR spectral changes observed when compound **6** is treated with TFA in $CDCl_3$ (8.37×10^{-3} M) at 50 ^{o}C. The new resonance at 4.72 ppm is ascribed to protonation at the *meso*-α-position.

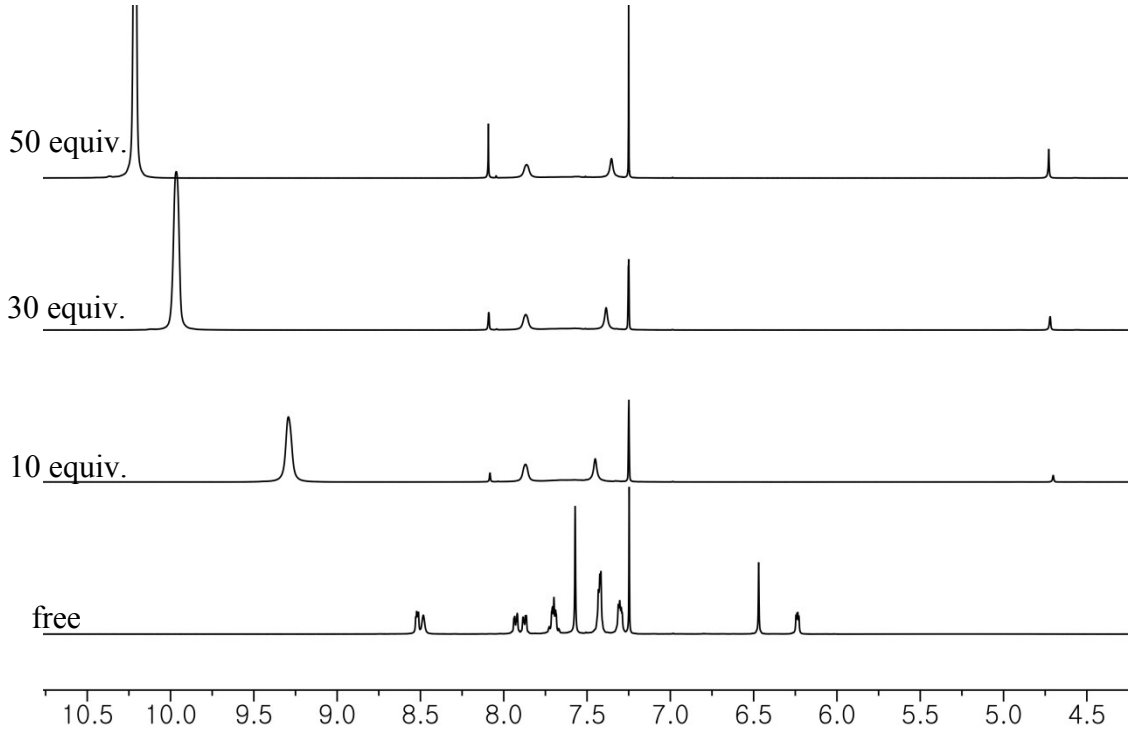


Figure S19. Partial ^{1}H NMR spectral changes observed when compound **7** is treated with TFA in $CDCl_3$ (1.07 X 10^{-2} M) at 50 ^{o}C. The new resonance at 4.72 ppm results from protonation at the *meso*-α-position.

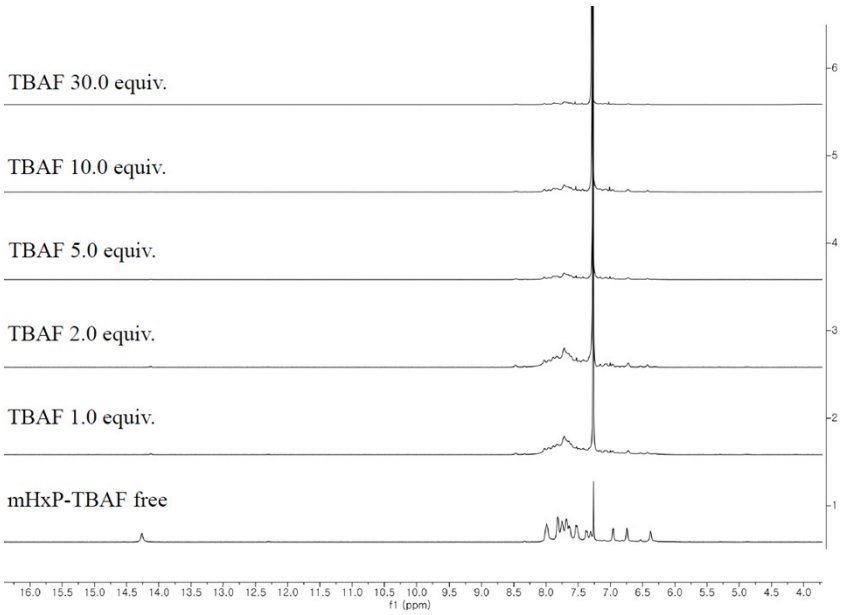


Figure S20. Partial ^{1}H NMR spectral changes observed when compound **5** (8.37 X 10^{-3} M) is subject to treatment with TBAF in $CDCl_3$ at room temperature.

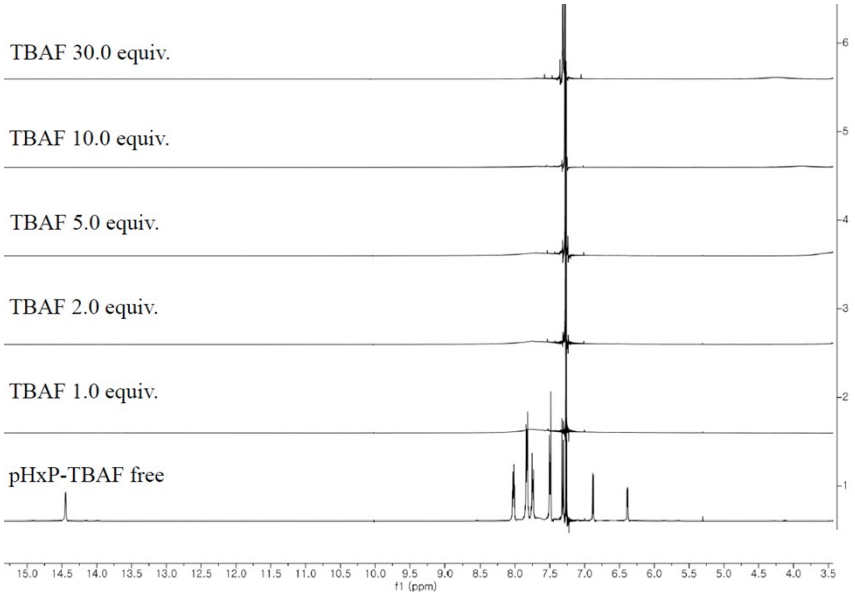


Figure S21. Partial ^{1}H NMR spectral changes observed when compound **6** (8.37 X 10^{-3} M) is subject to treatment with TBAF in $CDCl_3$ at room temperature.

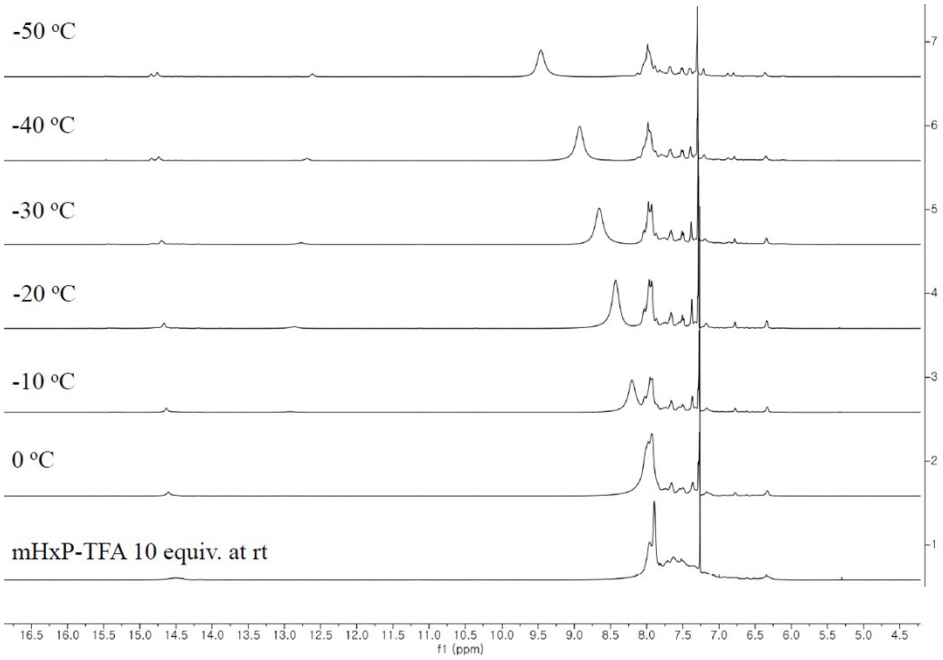


Figure S22. Partial ^{1}H NMR spectral changes of compound **5** (8.37 X 10^{-3} M) in the presence of 10 equiv. of TFA in $CDCl_3$ at low temperatures.

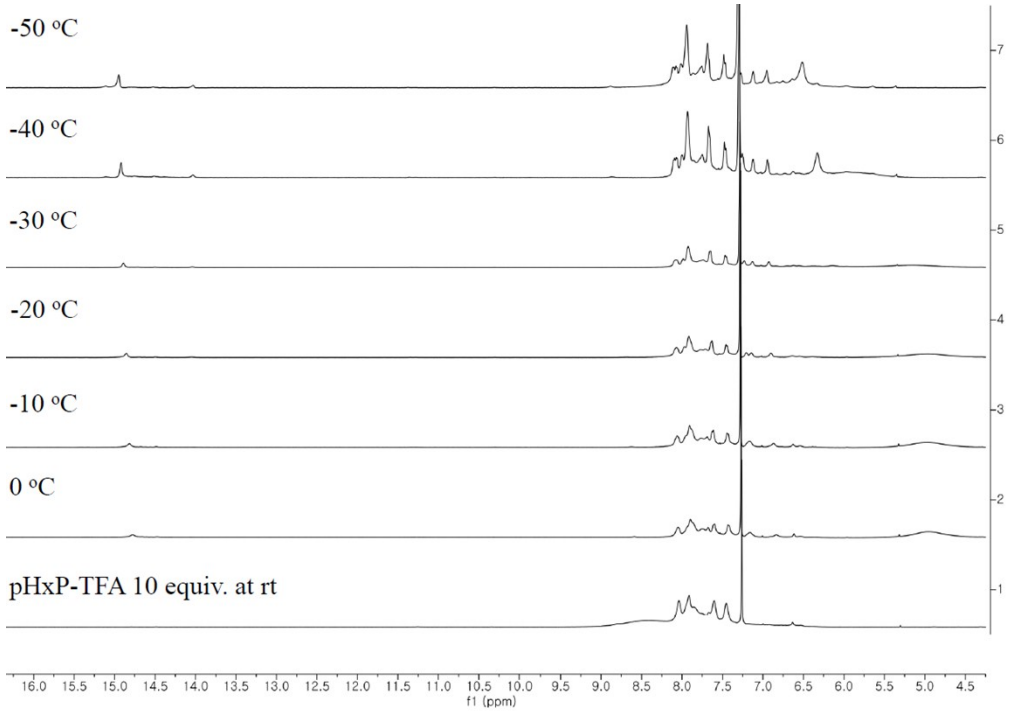


Figure S23. Partial ^{1}H NMR spectral changes of compound **6** (8.37 X 10^{-3} M) in the presence of 10 equiv. of TFA in $CDCl_3$ at low temperatures.

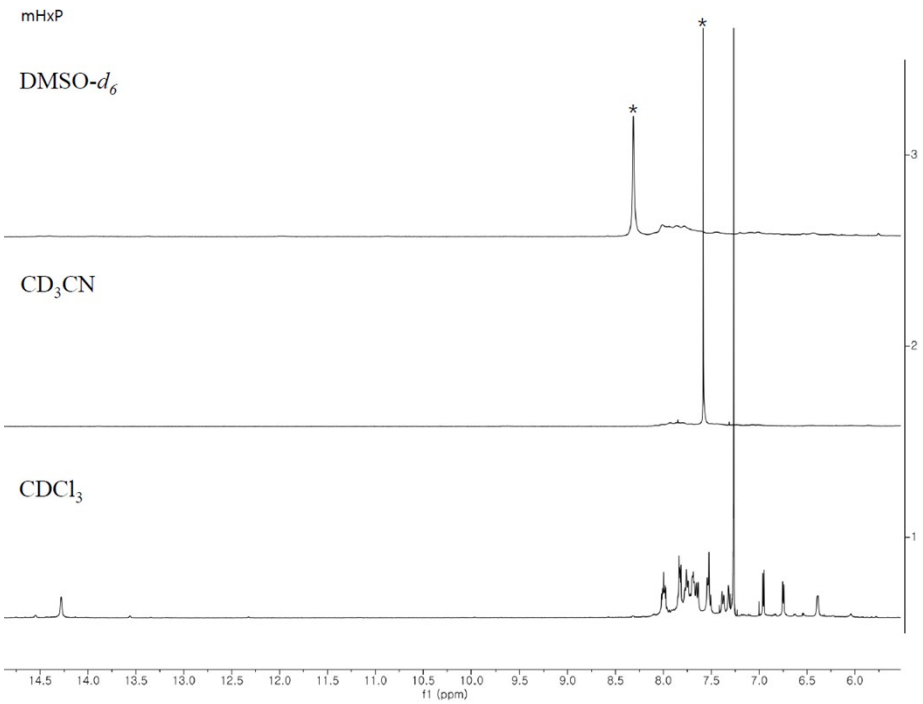


Figure S24. Partial ^{1}H NMR spectra of compound **5** (8.37 X 10^{-3} M) in different solvents. Signals marked with (*) denote residual $CHCl_3$ solvent signals.

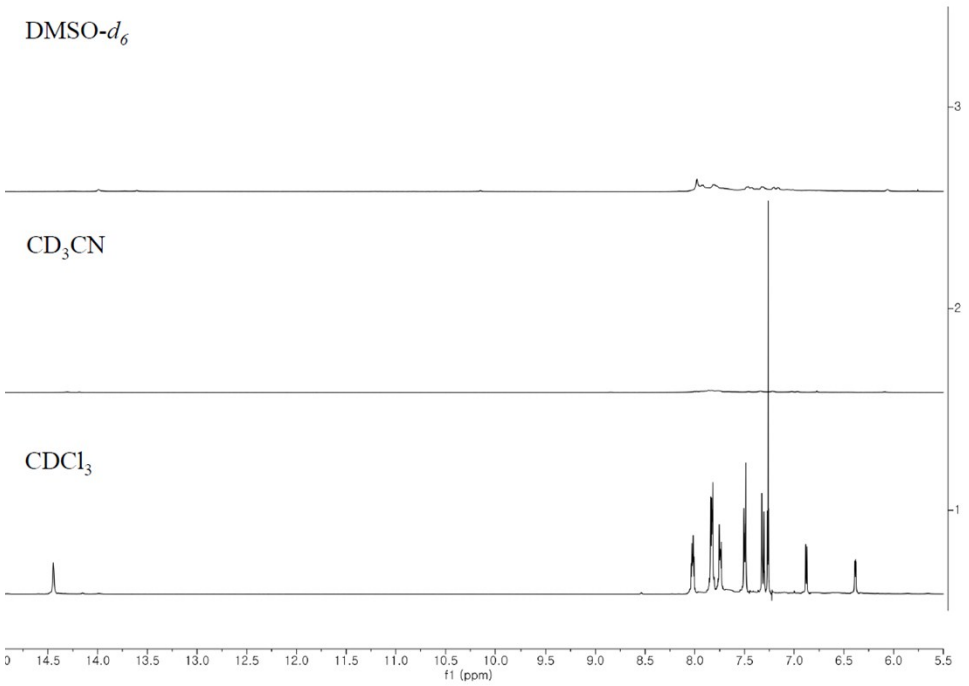


Figure S25. Partial ^{1}H NMR spectra of compound **6** (8.37 X 10^{-3} M) in different solvents.

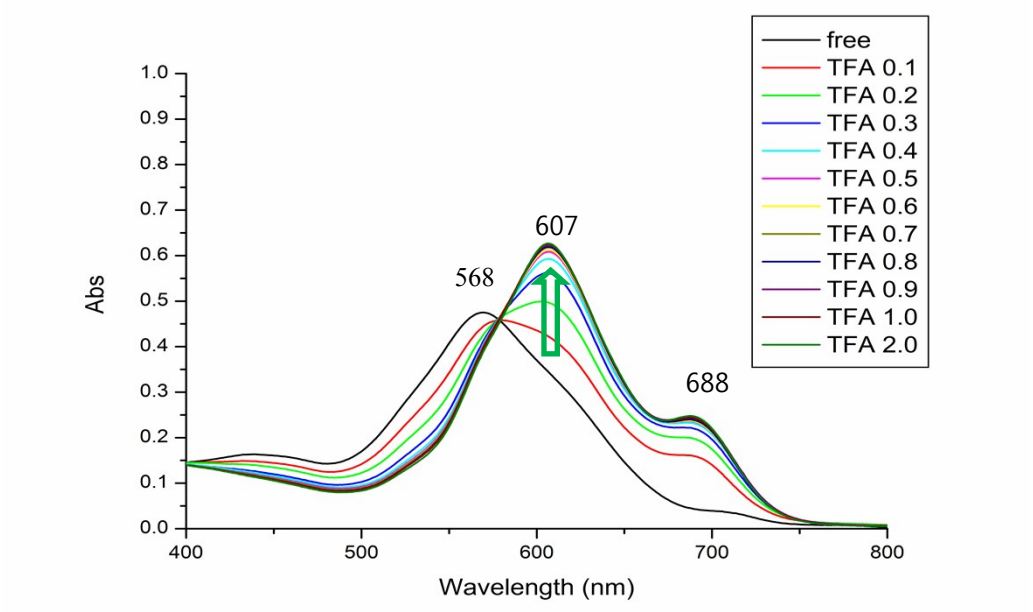


Figure S26. UV-vis spectral changes seen when **5** (4.31 x 10^{-6} M) is treated with TFA in CH_2Cl_2.

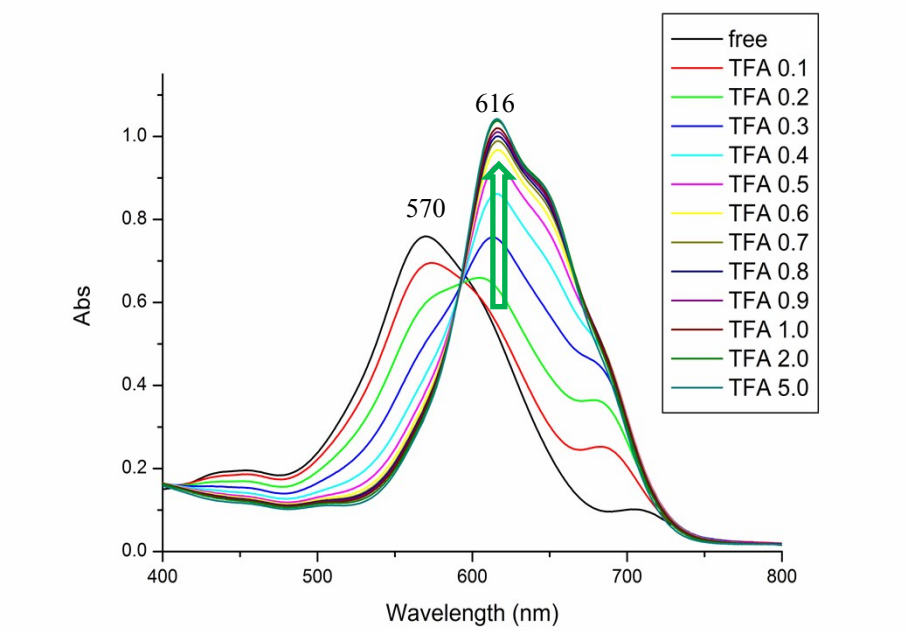
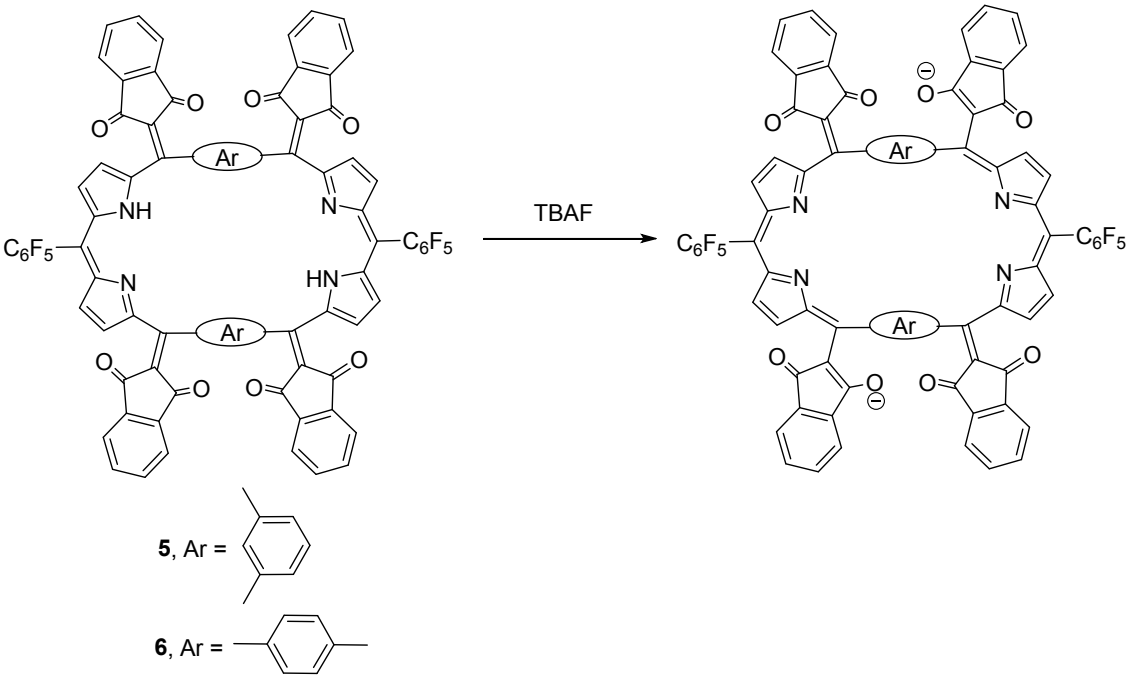


Figure S27. UV-vis spectral changes observed when **6** (4.31 x 10^{-6} M) is subject to treatment with TFA in CH_2Cl_2.



Scheme S1. Possible chemical structures generated from **5** and **6** upon treatment with TBAF.

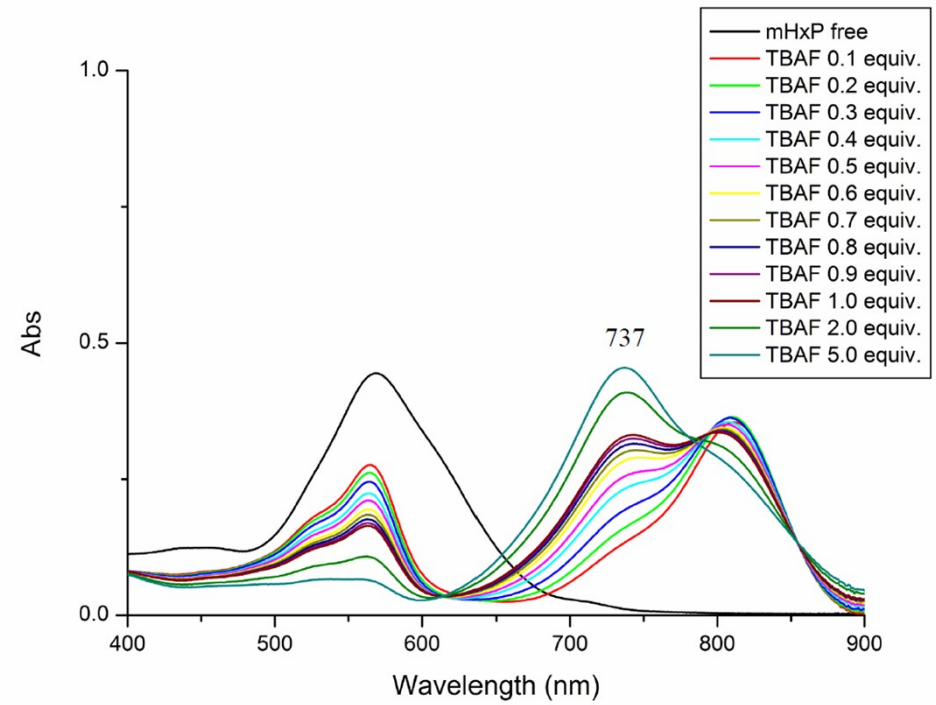


Figure S28. UV-vis spectral changes observed when **5** (4.31 x 10^{-6} M) is subject to treatment with TBAF in CH_2Cl_2.

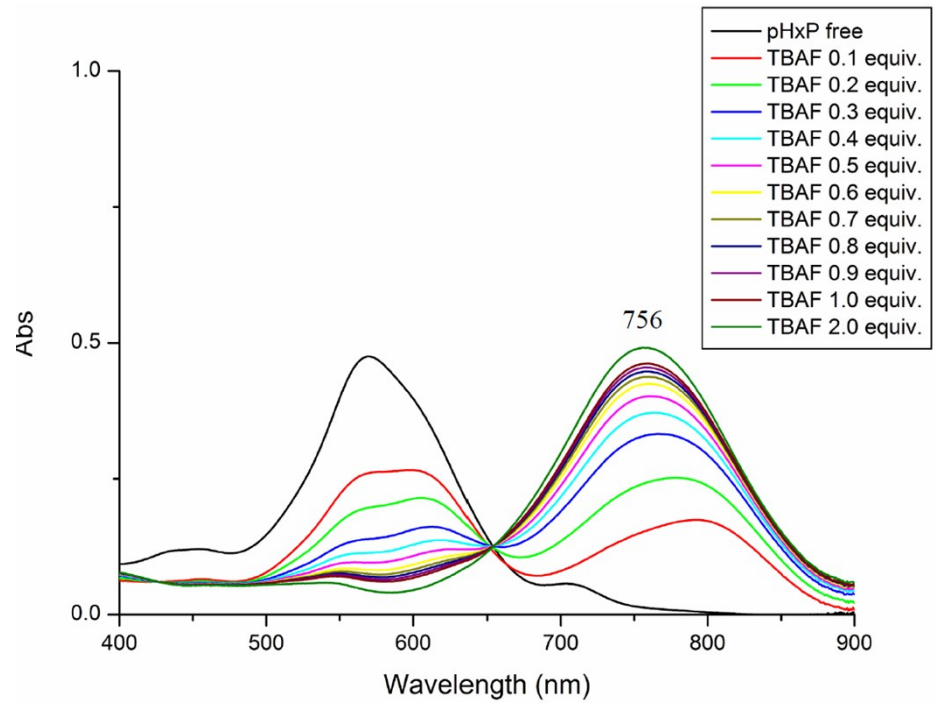


Figure S29. UV-vis spectral changes observed when **6** (2.87 x 10^{-6} M) is subject to treatment with TBAF in CH_2Cl_2.

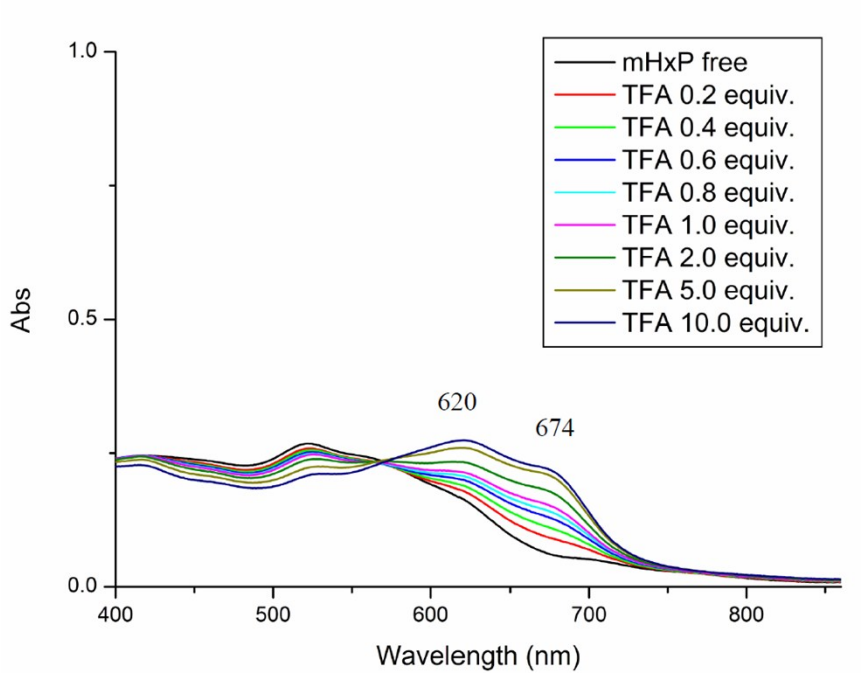


Figure S30. UV-vis spectral changes observed when **5** (4.31 x 10^{-6} M) is subject to treatment with TFA in CH_3CN.

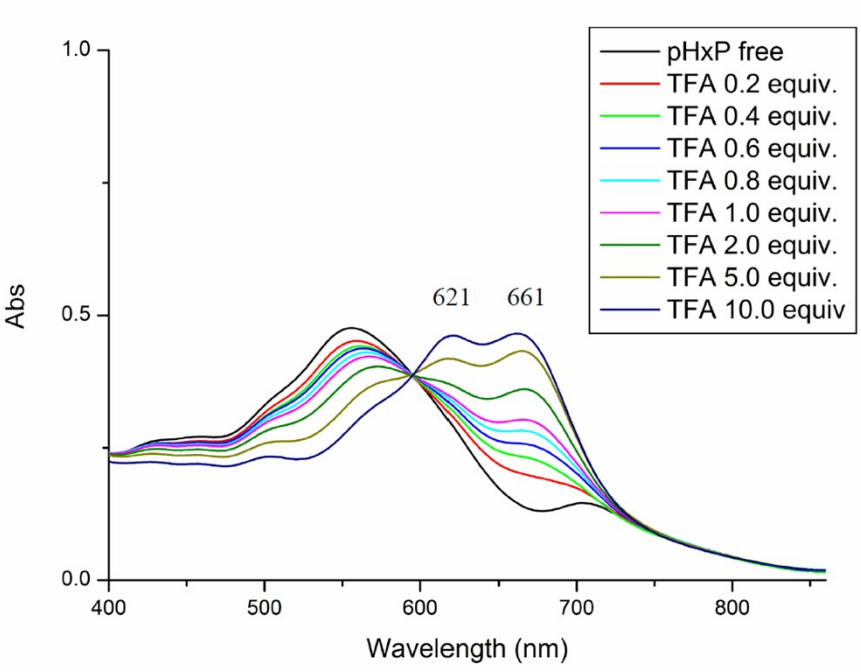


Figure S31. UV-vis spectral changes observed when **6** (2.87 x 10^{-6} M) is subject to treatment with TFA in CH_3CN.

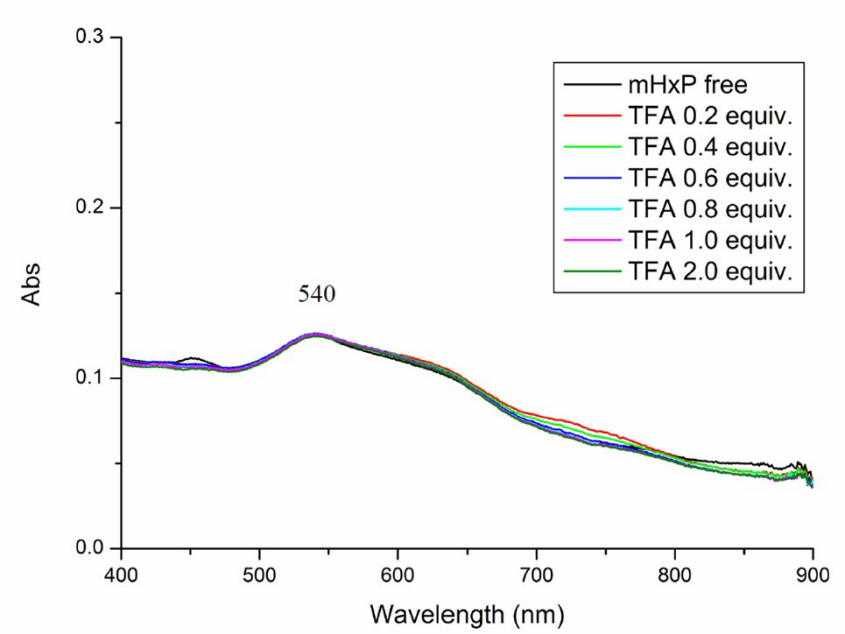


Figure S32. UV-vis spectral changes observed when **5** (4.31 x 10^{-6} M) is subject to treatment with TFA in DMSO.

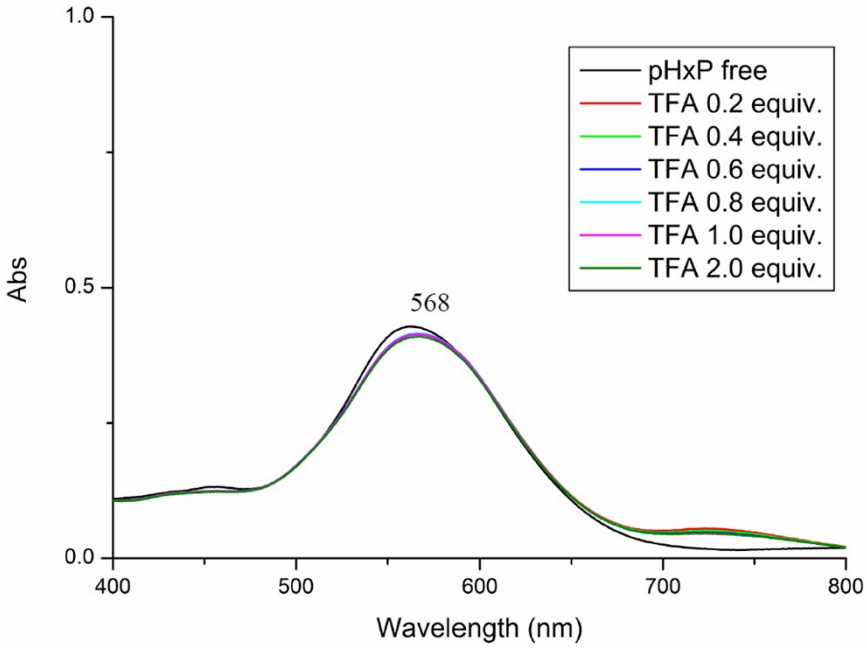
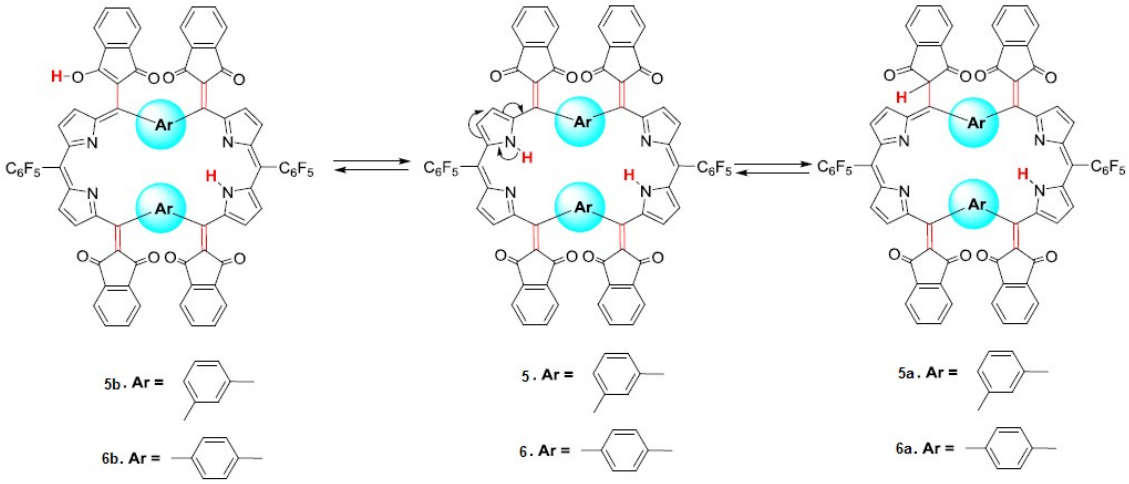


Figure S33. UV-vis spectral changes observed when **6** (2.87 x 10^{-6} M) is subject to treatment with TFA in DMSO.



Scheme S2. Possible tautomeric forms of compounds **5** and **6**.

Crystallographic data

Table S1 Crystal data and structure refinement for compound 6.

Identification code	Compound **6**
Empirical formula	$C_{168}H_{72}Cl_{12}F_{20}N_8O_{16}$
Formula weight	3263.73
Temperature/K	99.95(18)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	19.5016(3)
b/Å	35.2797(7)
c/Å	23.3317(6)
α/°	90
β/°	90.269(2)
γ/°	90
Volume/Å^3	16052.3(6)
Z	4
ρ_{calc}g/cm^3	1.350
μ/mm^{-1}	2.647
F(000)	6592.0
Crystal size/mm^3	0.152 × 0.091 × 0.069
Radiation	CuKα (λ = 1.54184 Å)
2Θ range for data collection/°	4.532 to 148.312
Index ranges	$-23 \leq h \leq 22$, $-37 \leq k \leq 42$, $-28 \leq l \leq 27$
Reflections collected	91104
Independent reflections	31428 [R_{int} = 0.0941, R_{sigma} = 0.1222]
Data/restraints/parameters	31428/0/2017
Goodness-of-fit on F^2	1.008
Final R indexes [I>=2σ (I)]	R_1 = 0.0943, wR_2 = 0.2450
Final R indexes [all data]	R_1 = 0.1770, wR_2 = 0.3053
Largest diff. peak/hole / e Å^{-3}	0.91/-0.93
CCDC number	1921511

Table S2 Crystal data and structure refinement for compound 6•2TFA.

Identification code	Compound **6**•2TFA
Empirical formula	$C_{18}H_{15}ClFN_4O$
Formula weight	303.34
Temperature/K	100.15
Crystal system	triclinic
Space group	P-1
a/Å	12.9539(16)
b/Å	14.4757(18)
c/Å	14.7250(18)
α/°	70.698(3)
β/°	66.001(3)
γ/°	67.022(3)
Volume/Å^3	2273.4(5)
Z	2
ρ_{calc}g/cm^3	0.443
μ/mm^{-1}	0.029
F(000)	318.0
Crystal size/mm^3	0.54 × 0.46 × 0.33
Radiation	MoKα (λ = 0.71073 Å)
2Θ range for data collection/°	5.986 to 50.7
Index ranges	$-15 \leq h \leq 15$, $-16 \leq k \leq 17$, $-17 \leq l \leq 17$
Reflections collected	32004
Independent reflections	8323 [R_{int} = 0.0324, R_{sigma} = 0.0278]
Data/restraints/parameters	8323/88/663
Goodness-of-fit on F^2	1.058
Final R indexes [I>=2σ (I)]	R_1 = 0.0478, wR_2 = 0.1351
Final R indexes [all data]	R_1 = 0.0531, wR_2 = 0.1395
Largest diff. peak/hole / e Å^{-3}	0.54/-0.65
CCDC number	1921509

Table S3 Crystal data and structure refinement for compound 7.

Identification code	Compound **7**
Empirical formula	$C_{53}H_{31}Cl_3N_2O_4S$
Formula weight	898.21
Temperature/K	100.00(10)
Crystal system	triclinic
Space group	P-1
a/Å	11.9568(7)
b/Å	12.3682(8)
c/Å	14.6936(10)
α/°	109.732(6)
β/°	92.669(5)
γ/°	92.147(5)
Volume/Å^3	2039.9(2)
Z	2
ρ_{calc}g/cm^3	1.462
μ/mm^{-1}	2.945
F(000)	924.0
Crystal size/mm^3	0.54 × 0.32 × 0.31
Radiation	CuKα (λ = 1.54184 Å)
2Θ range for data collection/°	6.404 to 151.78
Index ranges	$-14 \leq h \leq 14$, $-15 \leq k \leq 15$, $-18 \leq l \leq 17$
Reflections collected	18981
Independent reflections	8001 [R_{int} = 0.0835, R_{sigma} = 0.1040]
Data/restraints/parameters	8001/0/568
Goodness-of-fit on F^2	1.085
Final R indexes [I>=2σ (I)]	R_1 = 0.0885, wR_2 = 0.2358
Final R indexes [all data]	R_1 = 0.1232, wR_2 = 0.2528
Largest diff. peak/hole / e Å^{-3}	0.62/-1.11
CCDC number	1921508

Table S4 Crystal data and structure refinement for Compound 8.

Identification code	Compound **8**
Empirical formula	$C_{72.89}H_{33.78}ClF_{8.89}N_{3.56}O_{10.67}$
Formula weight	1298.81
Temperature/K	99.97(16)
Crystal system	tetragonal
Space group	$I4_1/a$
a/Å	20.1536(4)
b/Å	20.1536(4)
c/Å	55.493(2)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	22539.3(12)
Z	9
ρ_{calc}g/cm^3	0.861
μ/mm^{-1}	0.593
F(000)	5952.0
Crystal size/mm^3	0.48 × 0.39 × 0.33
Radiation	CuKα (λ = 1.54184 Å)
2Θ range for data collection/°	6.974 to 152.256
Index ranges	$-25 \leq h \leq 24$, $-25 \leq k \leq 14$, $-61 \leq l \leq 69$
Reflections collected	47049
Independent reflections	11321 [R_{int} = 0.0605, R_{sigma} = 0.0535]
Data/restraints/parameters	11321/0/488
Goodness-of-fit on F^2	1.180
Final R indexes [I>=2σ (I)]	R_1 = 0.1311, wR_2 = 0.3318
Final R indexes [all data]	R_1 = 0.1782, wR_2 = 0.3889
Largest diff. peak/hole / e Å^{-3}	1.47/-0.30
CCDC number	1921510

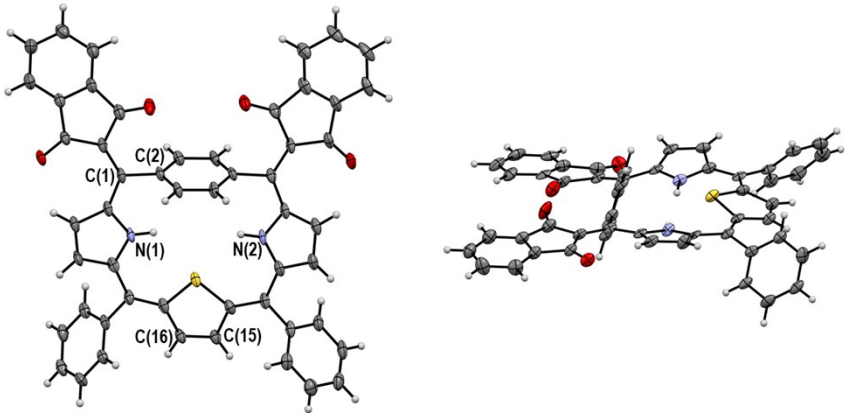


Figure S34. The single crystal X-ray structure of compound **7**. Top and side views. The indanedionyl groups are almost in the same plane as the cross-conjugated part of the macrocycle. Thermal ellipsoids are scaled to the 50% probability level.

References:

1. Siddiqui, Z. N.; Khan, T. *Tetrahedron Lett.* **2013,** *54,* 3759-3764.

2. Xiao, P.; Dumur, F.; Graff, B.; Morlet-Savary, F.; Vidal, L. Gigmes, D.; Fouassier, J. P.; Lalevee, J. *Macromolecules* **2014,** *47,* 23-34.