Electronic Supplementary Material (ESI) for Chemical Science

Electronic Supplementary Information

Proof of Principle for a Molecular 1:2 Demultiplexer to Function as an Autonomously Switching Theranostic Device

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Contents

1. General

All chemicals and solvents purchased from Sigma-Aldrich were used without further purification. Spectra of ^{1}H NMR and ^{13}C NMR were recorded using a Bruker DPX-400 in $CDCl_3$ with TMS as internal reference. Splitting in the spectra are shown as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), and br (broad).

Absorption spectrometry was performed using a Varian spectrophotometer. Steady state fluorescence measurements were conducted using a Varian Eclipse spectrofluorometer. Column chromatography of all products was performed using Merck Silica Gel 60 (particle size: 0.040–0.063 mm, 230–400 mesh ASTM). Reactions were monitored by thin layer chromatography using fluorescent coated aluminum sheets. Solvents used for spectroscopy experiments were spectrophotometric grade. Flourescence life time measurements were determined on a HORIBA Jobin Yvon fluorolog, FL-1057. HORIBA Scientific NanoLEDs at 650 and 667 nm (pulse width < 250 ps) was used. The instrument response function was measured with an aqueous Ludox solution. The decays were analyzed with a multi-exponential fitting function by iterative reconvolution and chi-square minimization. Mass spectra were recorded on Agilent Technologies 6530 Accurate-Mass Q-TOF LC/MS.

FRET efficiency was determined using time-resolved approach with the formula below:

$$\mathbf{E = 1 - \tau_{DA}/\tau_{D}}$$

where τ_D and τ_{DA} refer to excited state decay time (lifetime) of protonated donor (protonated compound **2**) alone and donor as a part of theragnostic agent (protonated compound **3**) respectively. Both measurements were done in acidic conditions and absorbance values are all below 0.1 to avoid inner filter effect.

2. Singlet Oxygen Generation Experiment

Singlet oxygen generation capability of theragnostic compound was detected using the bleaching of singlet oxygen trap molecule 1,3-diphenylisobenzofuran (DPBF). For light source 625 nm emitting LED source was used. A solution containing DPBF (50 μM), theragnostic compound (20 nM) and trifluoroacetic acid (20μl/3ml) was prepared in chloroform. Two negative control solutions were prepared with DPBF alone (50 μM) (with TFA and without TFA) and DPBF (50 μM) with compound **3** (20 nM) (without TFA). As positive control, a solution with DPBF (50 μM) and photosensitizer (**PS, 1)** (20 nM) was prepared. Solutions were aerated for 5 minutes. Then, absorbance spectrum of each sample was taken in 5 minutes intervals while the solutions were kept in dark. Then 625 nm light was exposed from 10 cm cell distance for 45 minutes and absorbance was taken in 5 minutes intervals for each solution. No decrease in absorbance was observed in negative controls and in dark while there is a substantial decrease in both positive controls and in solution containing compound **3**.

Relative singlet oxygen generation efficiencies were calculated by using the decrease in absorbance of DPBF at 411 nm. Absorbance of DPBF at 411 nm during 625 nm light irradiation was plotted with respect to time and slope was calculated for compound **1** and protonated compound **3**. For each compounds singlet oxygen generation efficiencies were taken as 1 and others species of each compound were normalized accordingly (by dividing each slope to the calculated slope of **PS** or protonated compound **3**). The decrease in the efficiency of **PS** in the presence of acid is probably due to decrease in spectral match of lamp after the bathochromic shift in **PS**. For TFA containing samples, the background irradiation-independent decrease in trap absorbance due to decomposition of DPBF was eliminated from the data by subtracting the slope of this control graph.

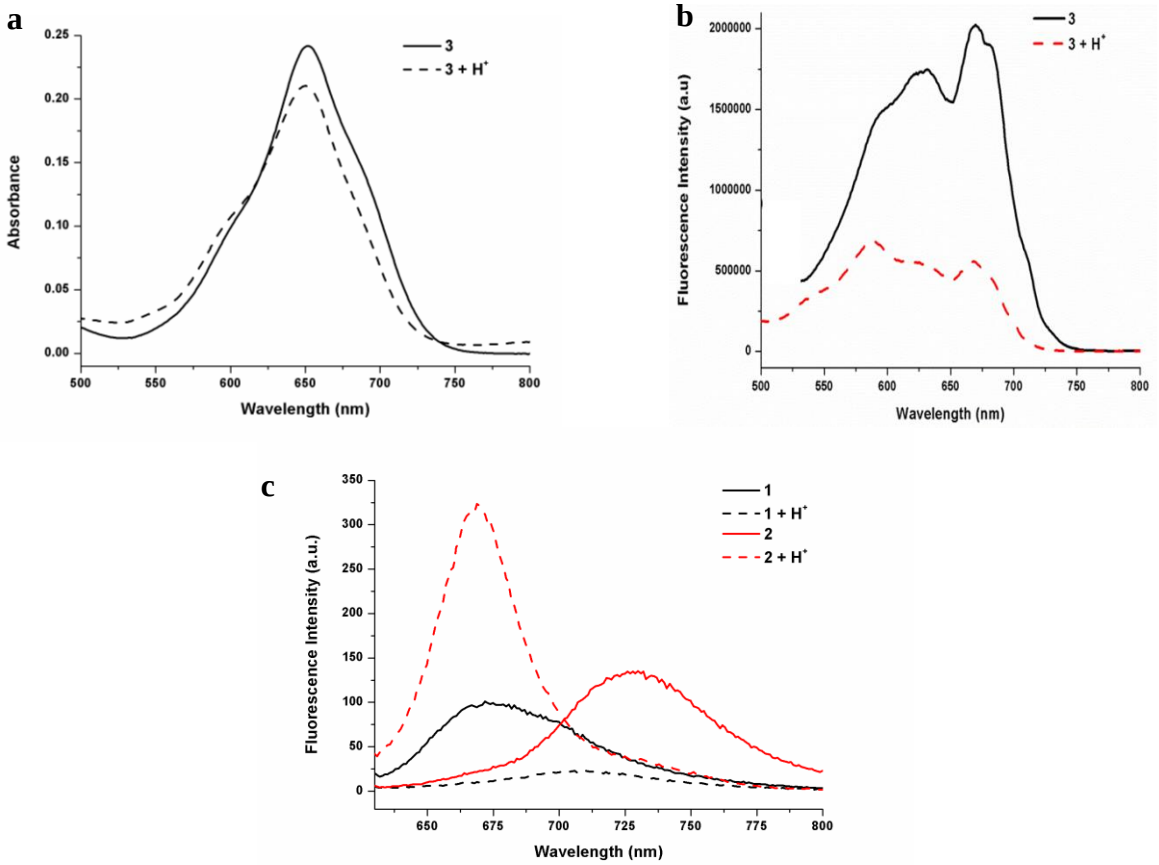


Figure S1. Absorbance (a) and excitation spectra (b) of 2 μM of molecular demultiplexer (compound **3**) in the absence and presence of acid in chloroform. Overlapping peaks result in the observed broad absorption peak. Emission was collected at 715 nm and at 700 nm for compound **3** and acid-added compound **3** respectively. Emission spectra of module compounds **1** and **2** (2 μM) in acidic and neutral media in chloroform (c).

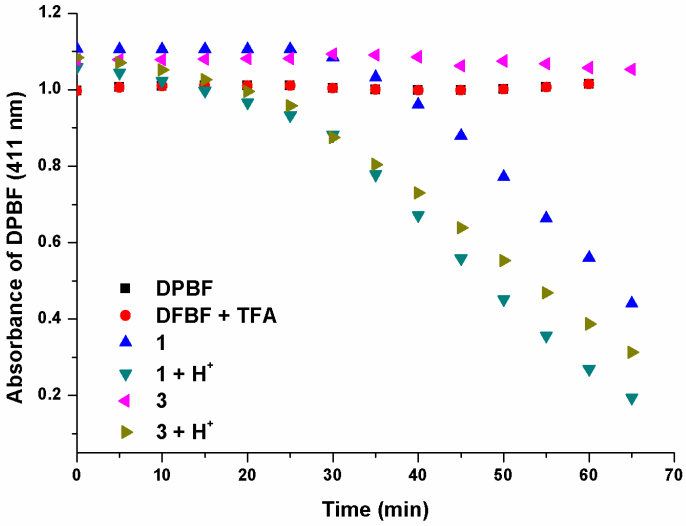


Figure S2. Singlet oxygen mediated photobleaching of DPBF with molecular demultiplexer, (a.k.a, DEMUX device, compound **3**, purple), compound **3** in acidic media (light green), PS (blue), PS in acidic media (green), DPBF alone (black), DPBF alone in acidic media (red), followed by decrease in its absorbance at 411 nm. The compounds in each solutions were 20 nM and the trap was 50 μM. Measurements were done in the dark for the first 25 min. Samples were then irradiated with 625 nm LED starting at t=25 minutes, and measurements were repeated in 5 minute intervals.

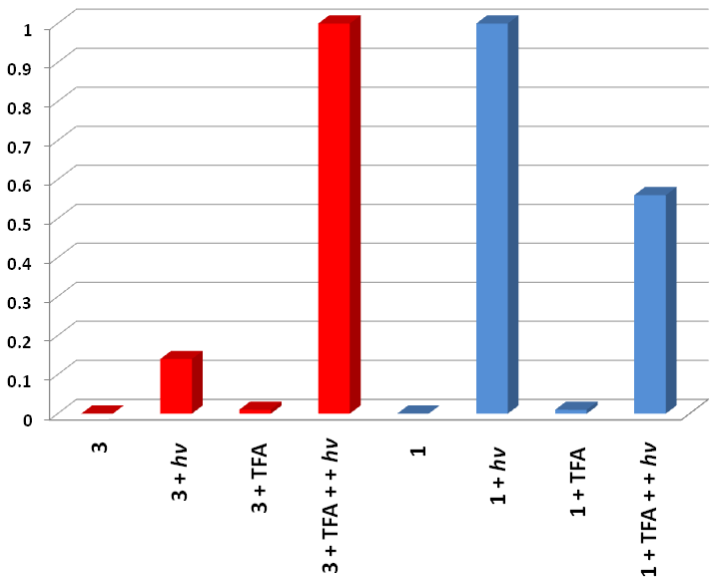


Figure S3. Relative singlet oxygen generation efficiency of photosensitizer (compound **1**, blue) alone or molecular demultiplexer (compound **3**, red) in the presence or absence of light and/or TFA.

Table S1. Results of singlet oxygen generation in positive and negative control experiments.

Type of Control Experiment		DEMUX (Figure 4)	Positive-1 (Figure S1)	Positive-2 (Figure S2)	Negative-1 (Figure S3)	Negative-2 (Figure S4)	Negative-3 (Figure S5)	Negative-4 (Figure 4)
Contents	DPBF[a]	50 μM	50 μM	50 μM	50 μM	50 μM	50 μM	50 μM
	TFA[b]	20μl/3ml	-	20μl/3ml	-	-	20μl/3ml	20μl/3ml
	1[c]	-	20 nM	20 nM	-	-	-	-
	3[d]	20 nM	-	-	20 nM	-	-	20 nM
Irradiation (625 nm)		Light	Light	Light	Dark / Light	Dark / Light	Dark/Light	Dark
Relative Rate of $^1O_2$ Generation		1	1	0.56	~0/0	~0	~0	0.14

[a] DPBF: 1,3-diphenylisobenzofuran, [b] TFA: Trifluoroacetic acid, [c] PS: photosensitizer, compound **1**, [d] Molecular Demultiplexer

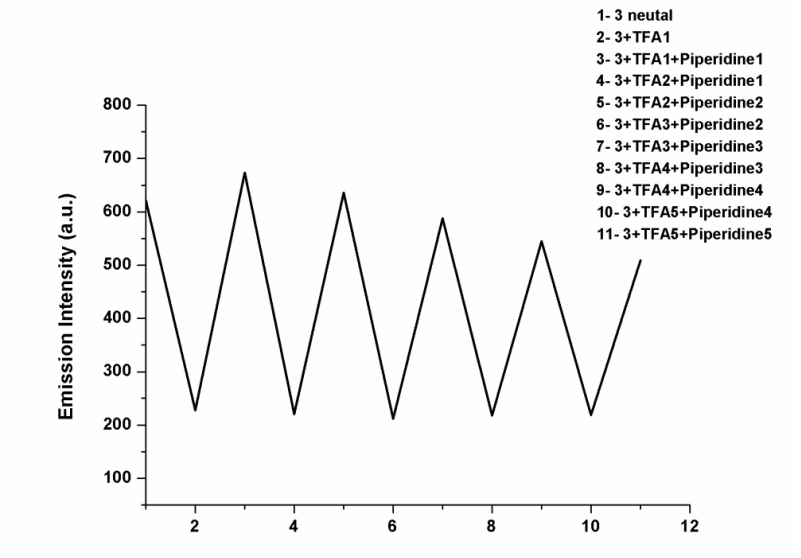
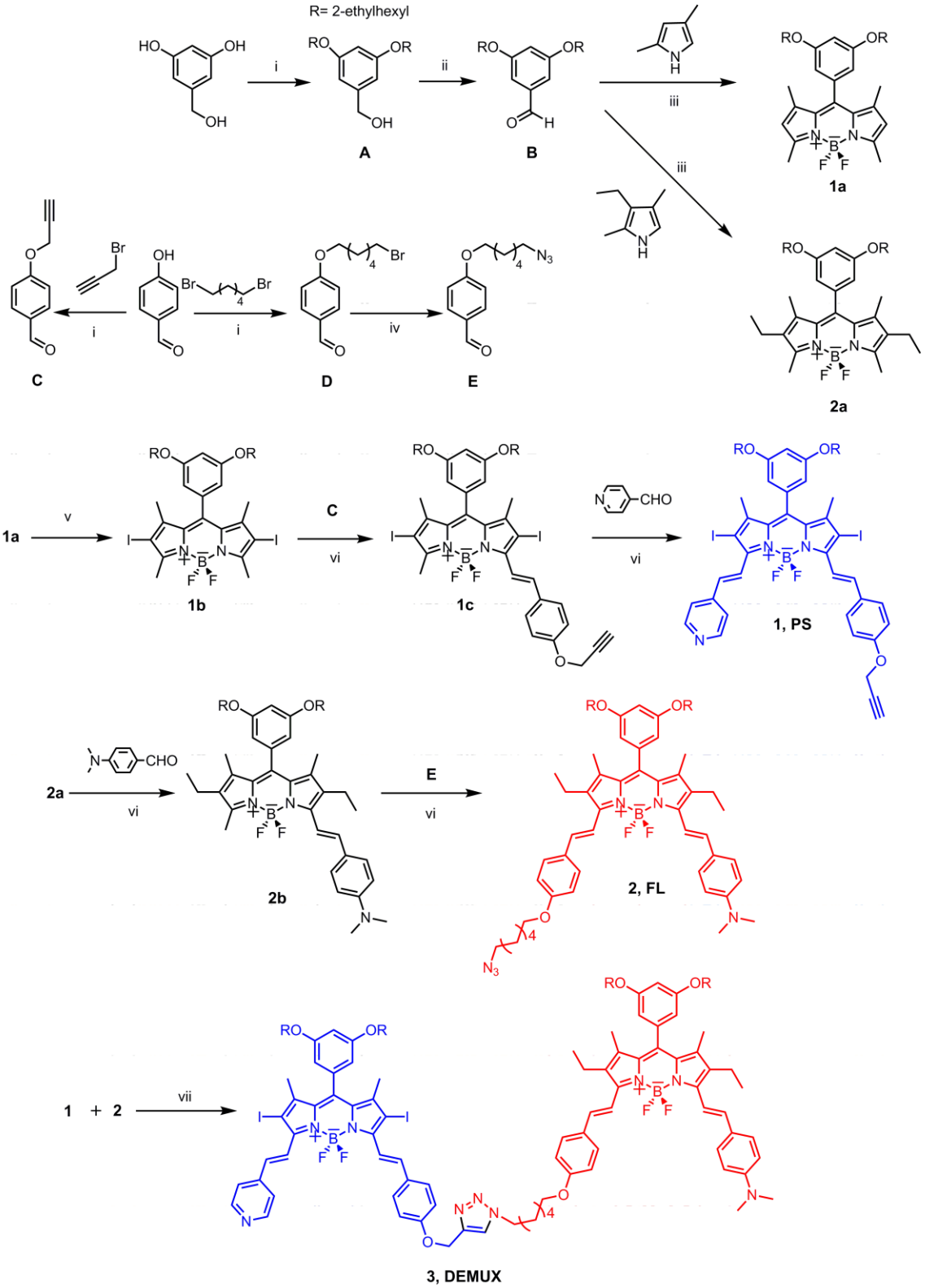


Figure S4. Reversibility of fluorescence of compound **3** in the presence of acid and base in chloroform followed at 715 nm. The first measurement was done in neutral conditions, for each following measurements TFA and piperidine were added in 50 □l portions, times of addition were given as numbers following the name of reagents.

3. Synthesis



i= 2-Ethylhexyl Bromide, K_2CO_3, Acetonitrile, reflux, overnight, ii= PCC, CH_2Cl_2, 30 min, iii= TFA, p-Chloranil, NEt_3, $BF_3.OEt_2$, iv= NaN_3, DMSO, 60°C, 2,5h, v= I_2, HIO_3, EtOH, 60°C, 20 min, vi= Piperidine, AcOH, Benzene, Dean-Stark apparatus, reflux, vii= $CuSO_4.5H_2O$, Sodium Ascorbate, Cu(0), Et_3N, $CHCl_3$:Acetonitrile:H_2O

Scheme S1. Synthesis scheme of molecular demultiplexer (DEMUX device, **3**)

3.1 Synthesis of Compound A

3,5-dihydroxybenzylalcohol (2 g, 14.3 mmol) and 2-ethylhexyl bromide (5.8 ml, 28.56 mmol) were dissolved in 50 ml acetone. K_2CO_3 (16 g, 112 mmol) and catalytic amount of 18-crown-6 were added. The reaction mixture was refluxed for 12h. Then, acetone was evaporated in vacuum evaporator; the crude product was extracted with water and chloroform. Organic layer was collected, dried with Na_2SO_4 and evaporated in vacuo**.** The product was obtained as viscous yellow liquid (13.73 mmol, 4.98 g, 96%).

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm) 6.54 (d, 2H, *J* = 2.2 Hz; ArH), 6.41 (t, 1H, *J* = 2.2 Hz; ArH), 4.64 (s, 2H, CH_2O) 3.85 (dd, 4H, *J* = 3.64 Hz; OCH_2), 3.50 (1H, CH_2OH), 1.76 (m, 2H; OCH_2CH), 1.3-1.6 (m, 16H; CH_2), 0.9-1.0 (m, 12H; CH_3)

3.2 Synthesis of Compound B

3,5-di(2-ethylhexyl)benzylalcohol, compound **A** (4.2 g, 11.6 mmol) and pyridinium chlorochromate (5 g, 20 mmol) were dissolved in 50 ml dichloromethane. The reaction mixture was stirred at room temperature for 30 minutes. Then, the crude product was filtered from celite, filtrate was collected, vacuum evaporated. The product was purified by silica gel column chromatography using $CHCl_3$ as mobile phase. Fraction containing compound **B** was collected then the solvent was removed under reduced pressure (3.91 g, 10.8 mmol, 93%).

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm) 9.92 (s, 1H), 7.02 (d, 2H, *J* = 2.16 Hz; ArH), 6.73 (t, 1H, *J* = 2.00 Hz; ArH), 3.90 (dd, 4H, *J* = 3.64 Hz; OCH_2), 1.76 (m, 2H; OCH_2CH), 1.3-1.6 (m, 16H; CH_2), 0.9-1.0 (m, 12H; CH_3)

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm) 191.5, 160.9, 138.4, 107.8, 107.3, 70.6, 39.3, 30.5, 29.0, 23.8, 23.0, 14.0, 11.0.

3.3 Synthesis of Compound 1a

CH_2Cl_2 (300 ml) was purged with Ar for 30 min. 3,5-di(2-ethylhexyl)benzaldehyde, compound **B** (1.76 g, 4.85 mmol) and 2,4-dimethyl pyrrole (1 ml, 9.71 mmol) were added. The color of the solution turned into red after the addition of 3 drops of trifluoroacetic acid. The reaction mixture was stirred at room temperature for 12h. Then, tetrachloro-1,4-benzoquinone (1.192 g, 9.7 mmol) was added and the reaction mixture was stirred at room temperature for 45 min. Then triethyl amine (6 ml) and boron trifluoride diethyl etherate (6 ml) were added sequentially. After stirring at room temperature for 30 min, it was extracted with water. Organic layer was dried with Na_2SO_4 and evaporated under reduced pressure. The product was purified by silica gel column chromatography using $CHCl_3$/Hexane (50:50/v:v) as mobile phase. Fraction containing compound **3** was collected then the solvent was removed under reduced pressure (673.5 mg, 1.16 mmol, 24%).

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm) 6.58 (t, 1H, *J* = 2.2 Hz; ArH), 6.45 (d, 2H, *J* = 2.2 Hz; ArH), 6.01 (s, 2H; ArH), 3.85 (dd, 4H, *J* = 3.64 Hz; OCH_2), 2.60 (s, 6H; ArCH_3), 1.75 (m, 2H; OCH_2CH), 1.60 (s, 6H; ArCH_3), 1.3-1.6 (m, 16H; CH_2), 0.9-1.0 (m, 12H; CH_3)

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm) 161.4, 155.4, 143.2, 136.4, 121.0, 113.2, 110.0, 106.3, 102.3, 71.0, 39.3, 30.5, 29.1, 23.8, 23.0, 14.6, 14.2, 14.1, 11.1.

HRMS (TOF-ESI): m/z calcd for $C_{35}H_{51}BF_2N_2O_2$: 579.3933 $[M-H]^-$; found: 579.4002 $[M-H]^-$, Δ = 11.8 ppm.

3.4 Synthesis of Compound 2a

CH_2Cl_2 (300 ml) was purged with Ar for 30 min. 3, 5-di(2-ethylhexyl)benzaldehyde, compound **B** (1.3 g, 3.57 mmol) and 2,4-dimethyl-5-ethyl pyrrole (0.96 ml, 7.14 mmol) were added. The color of the solution turned into red after the addition of 3 drops of trifluoroacetic acid. The reaction mixture was stirred at room temperature for 12h. Then, tetrachloro-1,4-benzoquinone (878 mg, 3.57 mmol) was added and the reaction mixture was stirred at room temperature for 45 min. Then triethyl amine (7 ml) and boron trifluoride diethyl etherate (7 ml) were added sequentially. After stirring at room temperature for 30

min, it was extracted with water. Organic layer was dried with Na_2SO_4 and evaporated under reduced pressure. The product was purified by silica gel column chromatography using $CHCl_3$ as mobile phase. Fraction containing compound **2a** was collected then the solvent was removed under reduced pressure (394 mg, 0.62 mmol, 17%).

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm) 6.58 (t, 1H, *J* =2.3 Hz; ArH), 6.45 (d, 2H, *J* =2.3 Hz; ArH), 3.82 (dd, 4H, *J* = 3.7 Hz; OC*H*$_2$), 2.55 (s, 6H; ArC*H*$_3$), 2.33 (q, 4H, *J* =11.3 Hz; ArC*H*$_2$CH$_3$), 1.73(m, 2H; OCH$_2$C*H*), 1.49 (s, 6H; ArC*H*$_3$), 1.2-1.6(m, 16H; C*H*$_2$), 1.02(t, 6H, J=16.0 Hz; ArCH$_2$C*H*$_3$), 0.8-1.0 (m, 12H; C*H*$_3$).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm) 161.4, 153.6, 140.3, 138.4, 137.2, 132.6, 130.5, 106.6, 102.2, 71.0, 39.3, 30.5, 29.1, 23.9, 23.1, 17.1, 14.6, 14.1, 12.5, 11.5, 11.1.

HRMS (TOF-ESI): m/z calcd for $C_{39}H_{59}BF_2N_2O_2$: 635.4559 $[M-H]^-$; found: 635.4643 $[M-H]^-$, Δ = 13.0 ppm.

3.5 Synthesis of Compound C

4-hydroxybenzaldehyde (2.45 g, 20 mmol) and propargyl bromide (2.5 g, 30 mmol) were dissolved in 100 ml acetonitrile. K_2CO_3 (5.5 g, mmol) and a few crystals of benzo-18-crown-6 were added. The reaction was refluxed until all 4-hydroxybenzaldehyde was consumed. The solvent was evaporated in vacuo, extracted with water and $CHCl_3$. Organic layer was dried with Na_2SO_4 and evaporated under reduced pressure. The product was purified by silica gel column chromatography using $CHCl_3$/Hexane (50:50, v/v). Fraction containing compound **C** was collected then the solvent was removed under reduced pressure (2.85 g, 17.8 mmol, 89%).

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm) 9.92 (s, 1H), 7.87 (d, *J*=8.92 Hz, 2H, ArH), 7.11 (d, *J*=8.72 Hz, 2H, ArH), 4.80 (d, *J*=2.44 Hz, O*CH*$_2$), 2.58 (t, *J*=2.48 Hz, 1H, OCH$_2$C*CH*).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm) 190.8, 162.4, 131.9, 130.0, 115,2, 77.5, 76.4, 55.9.

HRMS-ESI: calculated for M+Na 183.0422, found 183.0422, Δ= 0 ppm

3.6 Synthesis of Compound D

4-hydroxybenzaldehyde (5 g, 41 mmol) and 1,6 dibromohexane (2 g, 82 mmol) were dissolved in acetonitrile (150 ml). K_2CO_3 (17.2 g, 123 mmol) and catalytic amount of benzo-18-crown-6 were added. The reaction mixture was refluxed for 12h. Then, acetonitrile was evaporated in vacuo and extracted with water and chloroform. Organic layer was dried with Na_2SO_4 and evaporated in vacuo**.** The product was purified by silica gel column chromatography using $CHCl_3$/Hexane (75:25, v/v). Fraction containing compound **D** was collected then the solvent was removed under reduced pressure (13.4 mmol, 3.82 g, 32%).

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm) 9.7 (s, 1H), 7.68 (d, *J*= 8.64 Hz, 2H, ArH), 6. 82 (d, *J*= 8.76 Hz, 2H, ArH), 3.88 (t, *J*= 6.4 Hz, 2H, O*CH*$_2$), 3.4 (t, *J*= 6.68 Hz, 2H, *CH*$_2$Br), 1.65 (m, 4H, *CH*$_2$CH$_2$Br), 1.35 (m, 4H, OCH$_2$*CH*$_2$).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm) 190.6, 164.1, 131.9, 129.7, 114.7, 68.1, 44.9, 32.4, 28.8, 26.5, 25.2.

HRMS (TOF-ESI): m/z calcd for $C_{13}H_{17}BrO_2$: 285.04902 $[M+H]^+$; found: 285.05413 $[M+H]^+$, Δ = 17.9 ppm.

3.7 Synthesis of Compound E

4-(6-bromohexoxy)benzaldehyde, compound **D** (1.5 g, 5.3 mmol) was dissolved in 25 ml DMSO. Sodium azide (1.37 g, 21.2 mmol) was added and the reaction mixture was stirred at 60^{o}C for 2.5 hours. Then, it was extracted with water and $CHCl_3$ a few times and organic layer was collected, dried with Na_2SO_4 and evaporated under reduced pressure. No further purification was required.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm) 9.86 (s, 1H), 7.82 (d, J= 8.80 Hz, 2H, ArH), 7.00 (d, J=8.76 Hz, 2H, ArH), 4.05 (t, J=6.40 Hz, 2H, OCH_2), 3.28 (t, J=6.80 Hz, 2H, N_3CH_2), 1.75-1.85 (m, 2H, $N_3CH_2CH_2$), 1.55-1.65 (m, 2H, OCH_2CH_2), 1.4-1.55 (m, 4H, CH_2).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm) 190.8, 164.1, 132.0, 129.8, 114.7, 68.1, 51.3, 28.9, 28.7, 26.4, 25.6.

HRMS (TOF-ESI): m/z calcd for $C_{13}H_{17}N_3O_2$: 248.13990 $[M+H]^+$; found: 248.14573 $[M+H]^+$, Δ = 23.5 ppm.

3.8 Synthesis of Compound 1b

Compound **1a** (300 mg, 0.516 mmol) and I_2 (328 mg, 1.29 mmol) were dissolved in ethanol (150 ml). Iodic acid, HIO_3 (181.6 mg, 1.32 mmol) was dissolved in a few drops of water and adde into previous solution. The reaction mixture was stirred at 60^{o}C for a few hours untill all reeactant was consumed. After the reaction was completed, saturated sodium thiosulfate solution was added (50 ml) and it was stirred at room temparature for additional 30 min. Following that, it was extracted with $CHCl_3$ and water. Organic layer was dried with Na_2SO_4 and evaporated under reduced pressure. The product was purified by silica gel column chromatography using $CHCl_3$/Hexane (50:50, v/v). Fraction containing compound **1b** was collected, the solvent was removed under reduced pressure (280 mg, 0.34 mmol, 66%).

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm) 6.60 (t, 1H, *J* = 2.2 Hz; ArH), 6.40 (d, 2H, *J* = 2.2 Hz; ArH), 3.81 (dd, 4H, *J* = 3.94 Hz ;OCH_2), 2.68 (s, 6H; ArCH_3), 1.73 (m, 2H; OCH_2CH), 1.60 (s, 6H; ArCH_3), 1.2-1.5 (m, 16H; CH_2), 0.91 (m, 12H; CH_3)

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm) 55161.7, 156.7, 145.4, 141.5, 136.0, 131.0, 106.0, 102.6, 85.5, 71.1, 39.3, 30.5, 29.1, 23.9, 23.0, 16.9, 16.0, 14.1, 11.1.

HRMS (TOF-ESI): m/z calcd for $C_{35}H_{49}BF_2I_2N_2O_2$: 831.1866 $[M-H]^-$; found: 831.1951 $[M-H]^-$, Δ = 10.0 ppm.

3.9 Synthesis of Compound 1c

Compound **1b** (200 mg, 0.24 mmol) and compound **C** (31 mg, 0.19 mmol) were dissolved in benzene (40 ml). Piperidine (0.3 ml) and acetic acid (0.3 ml) were added. The reaction mixture was refluxed using Dean Stark apparatus until all aldehyde was consumed. After the reaction was completed, it was extracted with $CHCl_3$ and water. Organic layer was collected and dried with Na_2SO_4, evaporated under reduced pressure. The product was purified by silica gel column chromatography using $CHCl_3$/Hexane (50:50, v/v). Fraction containing compound **1c** was collected then the solvent was removed under reduced pressure (73 mg, 0.074 mmol, 39%).

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm) 8.11 (d, 1H, *J* = 16.6 Hz; C*H*), 7.61 (d, 2H, *J* = 8.8 Hz; ArC*H*$_3$), 7.55 (d, 1H, *J* = 16.8 Hz ; C*H*), 7.02 (d, 2H, *J* = 8.8 Hz; ArH), 6.60 (t, 1H, *J* =2.2 Hz ; ArH), 6.41 (d, 2H, *J* = 2.2 Hz; ArH), 4.71 (d, 2H, *J* =2.4 Hz; OC*H*$_2$), 3.85 (dd, 4H, *J* = 3.8 Hz; OC*H*$_2$), 2.70 (s, 3H; ArC*H*$_3$), 2.55 (t, 1H, *J* = 2.4 Hz ; C*H*), 1.75 (m, 2H; OCH$_2$C*H*), 1.65(s, 3H; ArC*H*$_3$), 1.60(s, 3H; ArC*H*$_3$), 1.2-1.5 (m, 16H; C*H*$_2$), 0.8-1.0 (m, 12H; C*H*$_3$).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm) 161.7, 158.5, 156.9, 150.4, 146.1, 145.1, 140.2, 138.6, 136.3, 132.0, 131.7, 130.4, 129.1, 117.1, 115.3, 106.3, 102.6, 106.3, 102.6, 86.1, 82.1, 78.3, 75.8, 71.1, 55.9, 39.3, 30.5, 29.1, 23.8, 23.0, 17.3, 16.9, 16.2, 14.1, 11.1.

HRMS (TOF-ESI): m/z calcd for $C_{45}H_{49}BF_2I_2N_2O_2$: 973.2285 $[M-H]^-$; found: 973.2347 $[M-H]^-$, Δ = 6.4 ppm.

3.10 Synthesis of 1 (PS)

Compound **1c** (75 mg, 0.075 mmol) and 4-pyridinecarboxaldehyde (17 mg, 0.15 mmol) were dissolved in benzene (40 ml). Piperidine (0.3 ml) and acetic acid (0.3 ml) were added. The reaction mixture was refluxed using Dean Stark apparatus until all aldehyde was consumed. After the reaction was completed, it was extracted with $CHCl_3$ and water. Organic layer was collected and dried with Na_2SO_4, evaporated under reduced pressure. The product was purified by silica gel column chromatography using $CHCl_3$/MetOH (95:5, v/v). Fraction

containing **1 (PS)** was collected then the solvent was removed under reduced pressure (35 mg, 0.033 mmol, 44%).

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm) 8.67(d, 2H, *J* = 5.8 Hz; ArH), 8.23(d, 1H, *J* = 16.8 Hz; C*H*), 8.01(d, 1H, *J* = 16.8 Hz; C*H*), 7.86(d, 1H, *J* = 16.7 Hz; C*H*), 7.65(d, 2H, *J* = 8.8 Hz; ArH), 7.62(d, 1H, *J* = 16.9 Hz; C*H*), 7.52(d, 2H, *J* = 6.0 Hz; ArH), 7.06(d, 2H, *J* = 8.8 Hz; ArH), 6.61(t, 1H, *J* = 2.2 Hz; ArH), 6.42(d, 2H, *J* = 2.2 Hz; ArH), 4.79(d, 2H, *J* = 2.4 Hz; CH_2), 3.75(dd, 4H, *J* = 3.8 Hz; CH_2), 2.48(t, 1H, *J* = 2.3 Hz; C*H*), 1.65(m, 2H; OCH2C*H*), 1.58(s, 3H; ArCH_3), 1.53(s, 3H; ArCH_3), 1.2-1.5(m, 16H; CH_2), 0.7-0.9(m, 12H; CH_3)

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm) 161.8, 158.9, 152.7, 150.3, 148.1, 147.5, 144.9, 144.3, 140.7, 139.9, 136.3, 134.8, 130.1, 129.5, 123.3, 121.5, 116.9, 115.4, 106.4, 102.7, 78.2, 75.9, 71.1, 55.9, 39.3, 30.5, 29.7, 29.1, 23.9, 23.0, 17.7, 17.1, 14.1,11.1.

HRMS (TOF-ESI): m/z calcd for $C_{51}H_{58}BF_2I_2N_3O_3$: 1062.2550 $[M-H]^-$; found: 1062.2625 $[M-H]^-$, Δ = 7.1 ppm.

3.11 Synthesis of Compound 2b

Compound **2a** (200 mg, 0.314 mmol) and 4-dimethylaminobenzaldehyde (37.5 mg, 0.25 mmol) were dissolved in benzene (40 ml). Piperidine (0.3 ml) and acetic acid (0.3 ml) were added. The reaction mixture was refluxed using Dean Stark apparatus until all aldehyde was consumed. After the reaction was completed, it was extracted with $CHCl_3$ and water. Organic layer was collected and dried with Na_2SO_4, evaporated under reduced pressure. The product was purified by silica gel column chromatography using $CHCl_3$/Hexane (75:25, v/v). Fraction containing compound **2b** was collected then the solvent was removed under reduced pressure (0.039 mmol, 30 mg, 16%).

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm) 7.60(d, 1H, J = 16.6 Hz; *CH*), 7.54(d, 2H, J = 8.8 Hz; ArH), 7.22(d, 1H, J = 16.7 Hz; *CH*), 6.73(d, 2H, J = 8.6 Hz; ArH), 6.57(t, 1H, J = 2.2 Hz; ArH), 6.48(d, 2H, J = 2.2 Hz; ArH), 3.85(dd, 4H, J = 3.6 Hz; OCH_2), 3.03(s, 6H; N(CH_3)$_2$), 2.64(q, 2H, J = 11.1 Hz; ArCH_2), 2.59(s, 3H; ArCH_3), 2.36(q, 2H, J = 11.3 Hz; ArCH_2), 1.74(m, 2H; OCH$_2$*CH*), 1.52(s,

3H; Ar*CH*$_3$), 1.49(s, 3H; Ar*CH*$_3$), 1.2-1.5(m, 16H; *CH*$_2$), 1.19(t, 3H, J = 6.0 Hz; ArCH$_2$*CH*$_3$), 1.03(t, 3H, J = 6.0 Hz; ArCH$_2$*CH*$_3$), 0.9-1.0(m, 12H; *CH*$_3$)

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm) 161.5, 150.9, 150.8, 139.0, 138.5, 137.5, 136.2, 133.0, 132.7, 131.8, 131.1, 131.0, 128.7, 115.8, 115.7, 112.2, 107.0, 102.2, 71.0, 40.4, 39.3, 30.5, 29.1, 23.8, 23.0, 18.5, 17.2, 14.7, 14.1, 14.0, 12.6, 11.5, 11.3, 11.1

HRMS (TOF-ESI): m/z calcd for $C_{61}H_{83}BF_2N_6O_3$: 767.5373 [M]; found: 767.5446 [M+H], Δ = 9.5 ppm.

3.12 Synthesis of 2 (FL)

Compound **2b** (30 mg, 0.039 mmol) and compound **E** (11.6 mg, 0.047 mmol) were dissolved in benzene (40 ml). Piperidine (0.2 ml) and acetic acid (0.2 ml) were added. The reaction mixture was refluxed using Dean Stark apparatus until all aldehyde was consumed. After the reaction was completed, it was extracted with $CHCl_3$ and water. Organic layer was collected and dried with Na_2SO_4, evaporated under reduced pressure. The product was purified by silica gel column chromatography using $CHCl_3$/Hexane (75:25, v/v). Fraction containing compound **2** (**FL)** was collected then the solvent was removed under reduced pressure (0.022 mmol, 21.5 mg, 56 %).

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm) 7.70 (d, 1H, J = 16.6 Hz; *CH*), 7.65(d, 1H, J = 17.0 Hz; *CH*). 7.56(m, 4H; ArH), 7.27(d, 1H, J = 18.0 Hz; *CH*), 7.18(d, 1H, J = 16.6 Hz; *CH*), 6.94(d, 2H, J = 8.4 Hz; ArH), 6.75(d, 2H, J = 8.2 Hz; ArH), 6.58(s, 1H; ArH), 6.49(s, 2H; ArH), 4.03(t, 2H, J = 6.4 Hz; O*CH*$_2$CH$_2$), 3.85(d, 4H, J = 5.8 Hz; O*CH*$_2$CH), 3.31(t, 2H, J = 6.8 Hz; *CH*$_2$N$_3$), 3.07(s, 6H; N(*CH*$_3$)$_2$), 2.65(m, 4H; Ar*CH*$_2$CH$_3$), 1.85(m, 2H; OCH$_2$*CH*$_2$), 1.2-1.9(m, 24H; *CH*$_2$), 1.51(s, 6H; Ar*CH*$_3$), 1.20(t, 6H, J = 6.5 Hz; ArCH$_2$*CH*$_3$), 0.95(m, 12H; *CH*$_3$)

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm) 161.4, 159.4, 151.8, 150.9, 149.1, 139.0, 137.7, 137.1, 136.7, 134.4, 133.7, 133.0, 132.3, 131.7, 130.6, 128.9, 128.7, 125.9, 124.6, 118.4, 115.8, 114.7, 112.2, 107.2, 102.2, 71.1, 67.9, 51.4, 40.4, 39.4, 30.5, 29.2, 29.1, 28.8, 26.5, 25.7, 23.8, 23.0, 18.5, 14.1, 14.1.

HRMS (TOF-ESI): m/z calcd for $C_{61}H_{83}BF_2N_6O_3$: 996.65878 [M]; found: 996.67410 [M], Δ = 15.4 ppm.

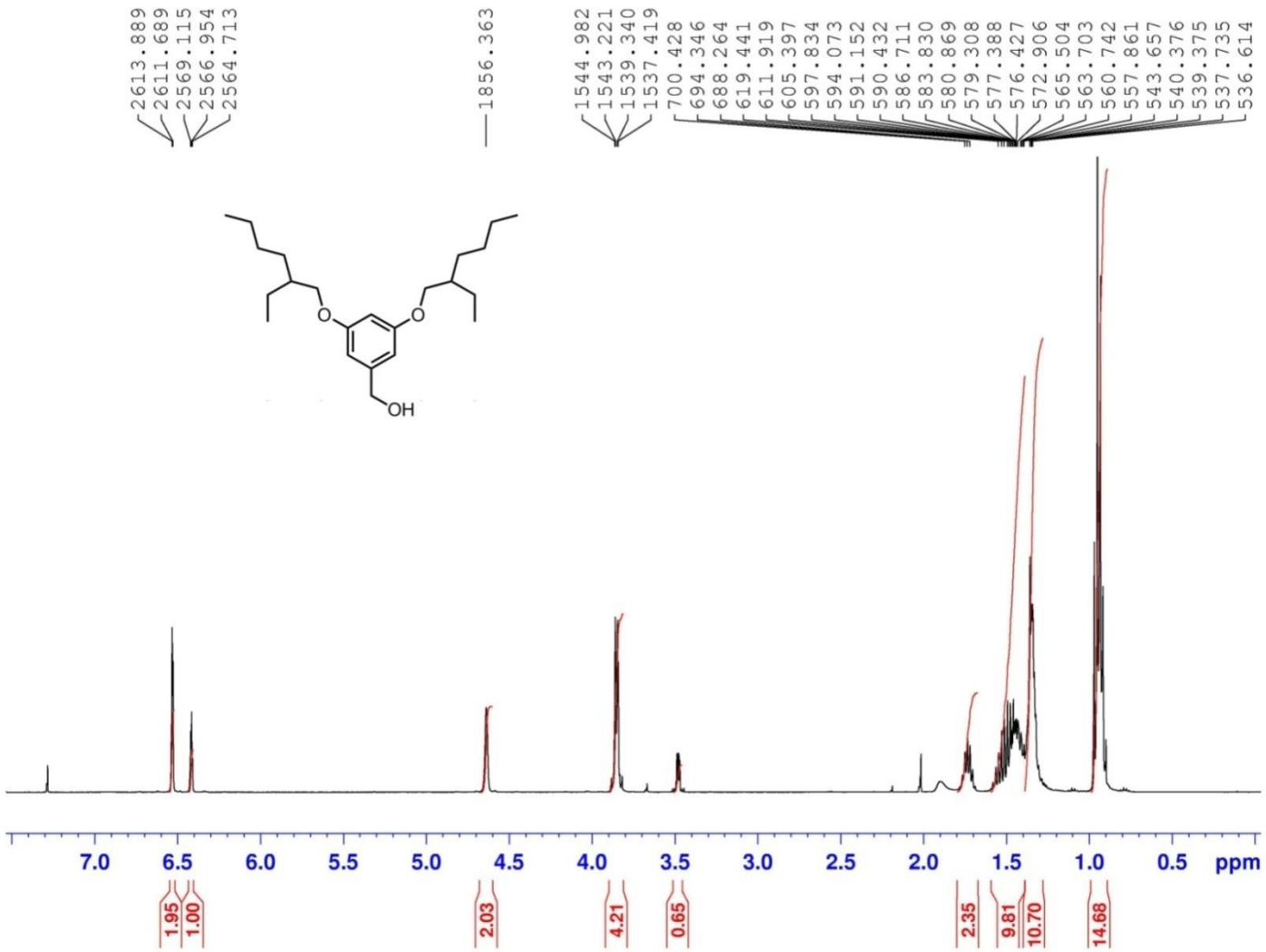
2.13 Synthesis of Molecular Demultiplexer 3

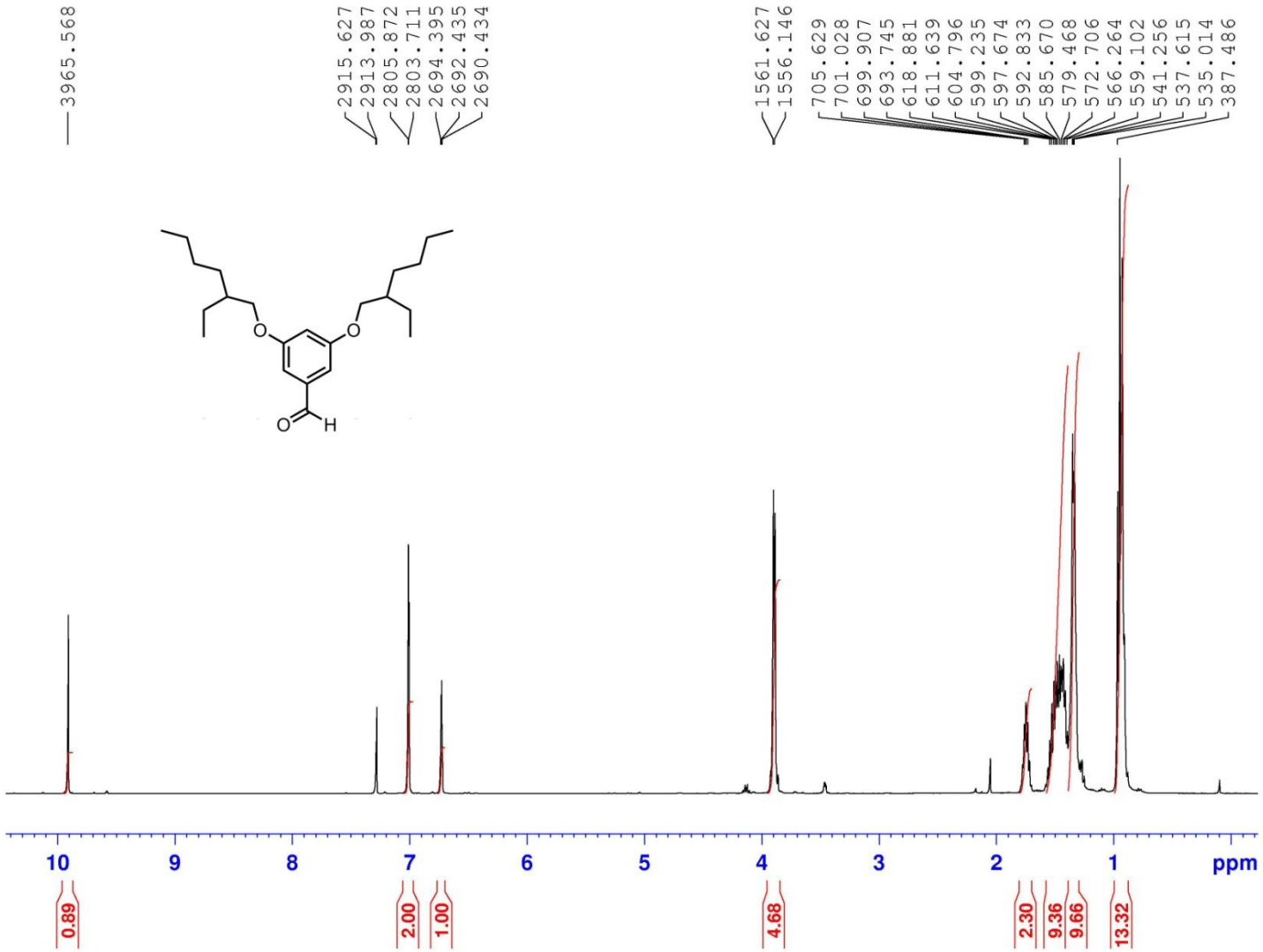
1 (**PS)** (22 mg, 21 μmol) and **2** (**FL)** (16 mg, 16 μmol) were dissolved in $CHCl_3$/acetonitrile mixture (10 ml: 10 ml). Triethylamine (20 μl) was added. Saturated aqueous solutions of $CuSO_4.5H_2O$ (1 ml) and Sodium ascorbate (1 ml) were prepared in separate viels. Then, 0.15 ml of each solution were added to reaction mixture. A small piece of Cu (0) wire was added. The mixture was stirred overnight at room temperature. Then, it was extracted using $CHCl_3$ and water. Organic layer was collected and dried with Na_2SO_4, evaporated under reduced pressure. The product was purified by silica gel column chromatography using $CHCl_3$/MetOH (96:4, v/v). Fraction containing **3** was collected then the solvent was removed under reduced pressure (10 μmol, 21 mg, 63%).

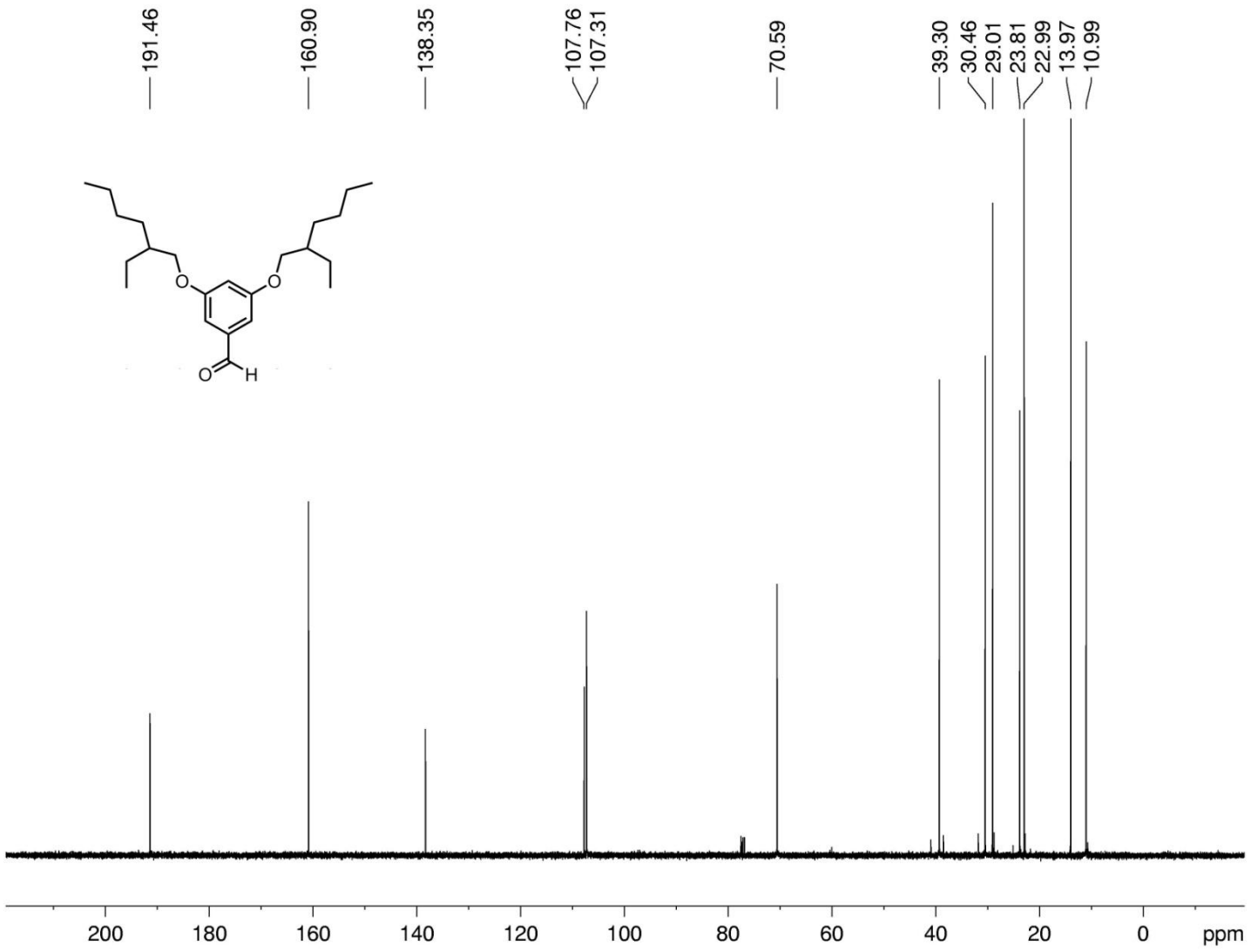
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm) 8.67(d, 2H, J = 6.1 Hz; ArH), 8.23(d, 1H, J = 16.4 Hz; *CH*), 8.00(d, 1H, J = 16.8 Hz; *CH*), 7.85(d, 1H, J = 16.8 Hz; *CH*), 7.69(d, 1H, J = 17.2 Hz; *CH*) 7.8-7.4(m, 11H; *CH*, ArH), 7.25(d, 1H, J = 16.6 Hz; *CH*), 7.17(d, 1H, J = 17.1 Hz; *CH)*, 7.08(d, 2H, J = 8.8 Hz; ArH), 6.92(d, 2H, J = 8.8 Hz; ArH), 6.73(d, 2H, J = 8.9 Hz; ArH), 6.61(d, 2H, J = 2.2 Hz; ArH), 6.57(d, 2H, J = 2.2 Hz; ArH), 6.47(d, 2H, J = 2.2 Hz; ArH), 6.42(d, 2H, J = 2.2 Hz; ArH), 5.30(s, 2H; O*CH*$_2$), 4.42(t, 2H, J = 7.2 Hz; N*CH*$_2$), 4.02(t, 2H, J = 6.3Hz; O*CH*$_2$CH$_2$), 3.85(m, 8H; O*CH*$_2$CH), 3.03(s, 6H; N(*CH*$_3$)$_2$), 2.63(m, 4H; Ar*CH*$_2$CH$_2$), 2.00(m, 2H; NCH$_2$*CH*$_2$), 1.82(m, 2H; OCH$_2$*CH*$_2$), 1.8-1.7(m, 4H; *CH*$_2$), 1.70(s, 3H; Ar*CH*$_3$), 1.68(s, 3H; Ar*CH*$_3$), 1.52(s, 6H; Ar*CH*$_3$), 1.5-1.2(m, 32H; *CH*$_2$), 1.16(m, 6H; ArCH$_2$*CH*$_3$), 1.0-0.8 (m, 24H; *CH*$_3$)

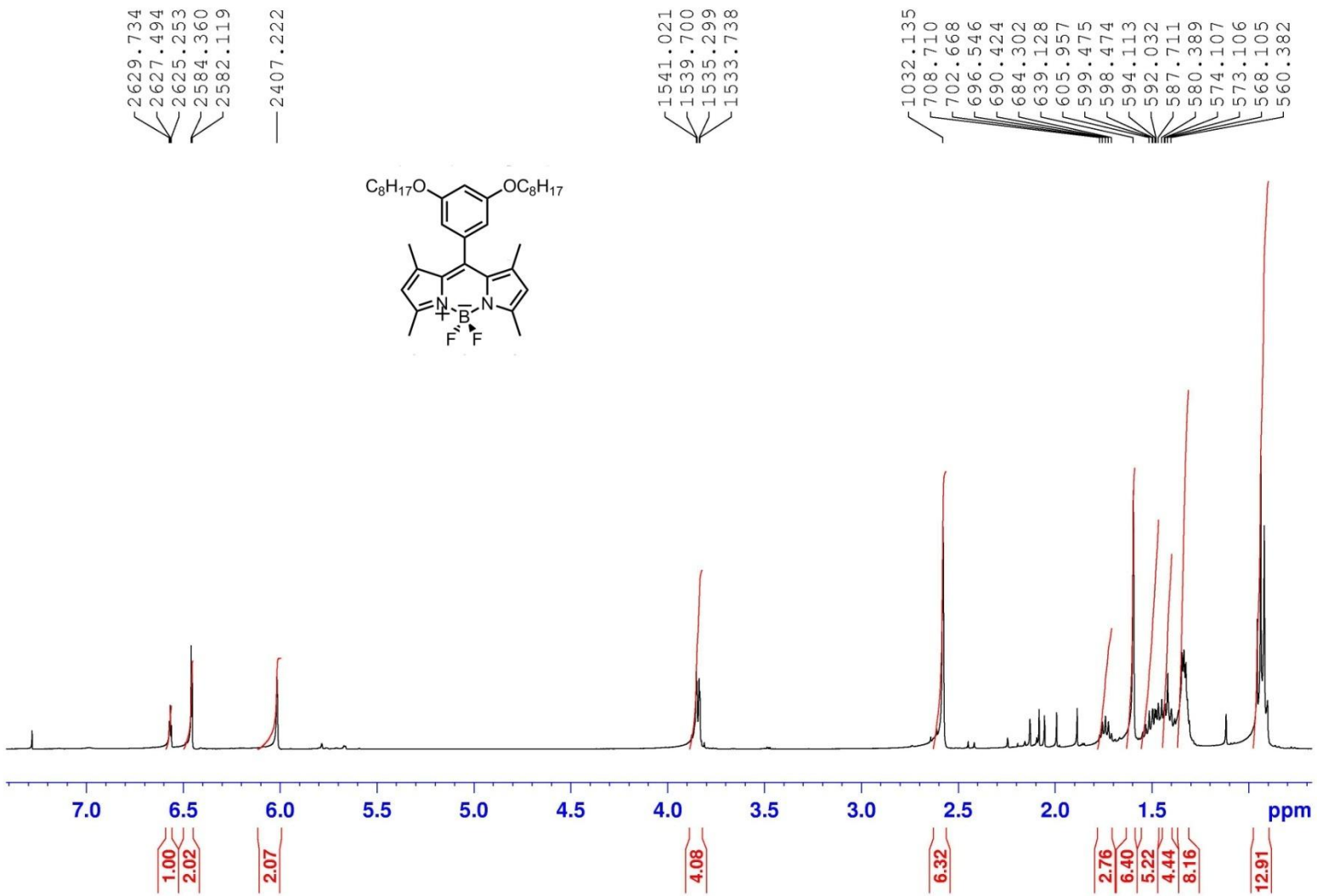
^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm) 161.8, 161.3, 159.7, 159.4, 150.9, 150.2, 143.8, 140.8, 137.7, 136.8, 136.2, 134.8, 134.3, 133.7, 133.0, 130.6, 129.8, 128.9, 128.7, 125.8, 122.6, 121.5, 118.4, 116.7, 115.8, 115.2, 114.8, 112.1, 107.2, 106.3, 102.7, 102.2, 71.1, 67.7, 62.2, 50.4, 40.3, 39.4, 30.5, 30.2, 29.7, 29.1, 26.3, 25.6, 23.8, 23.0, 18.5, 17.6, 17.2, 14.1, 11.3, 11.1, 8.6.

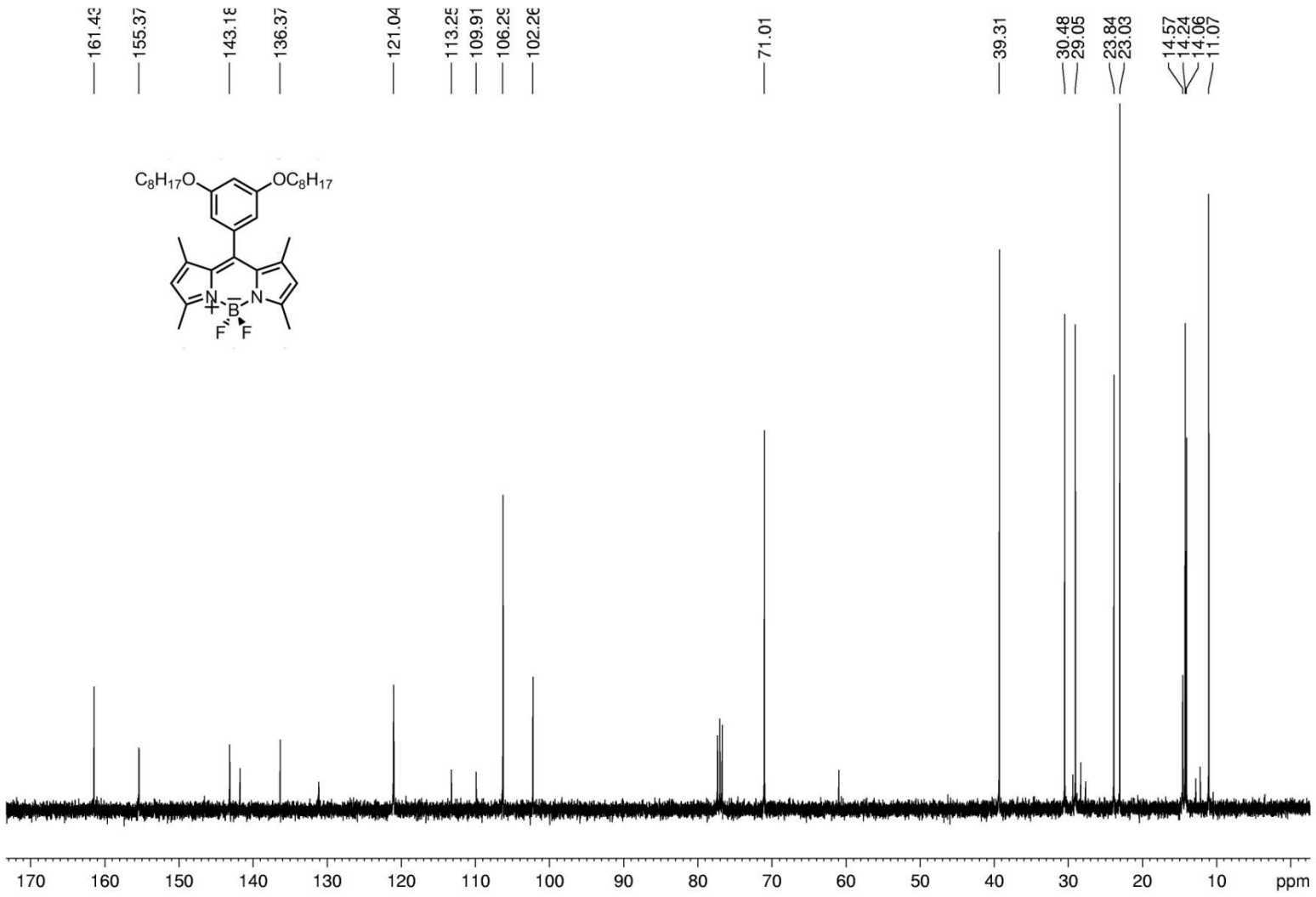
4. NMR Spectra

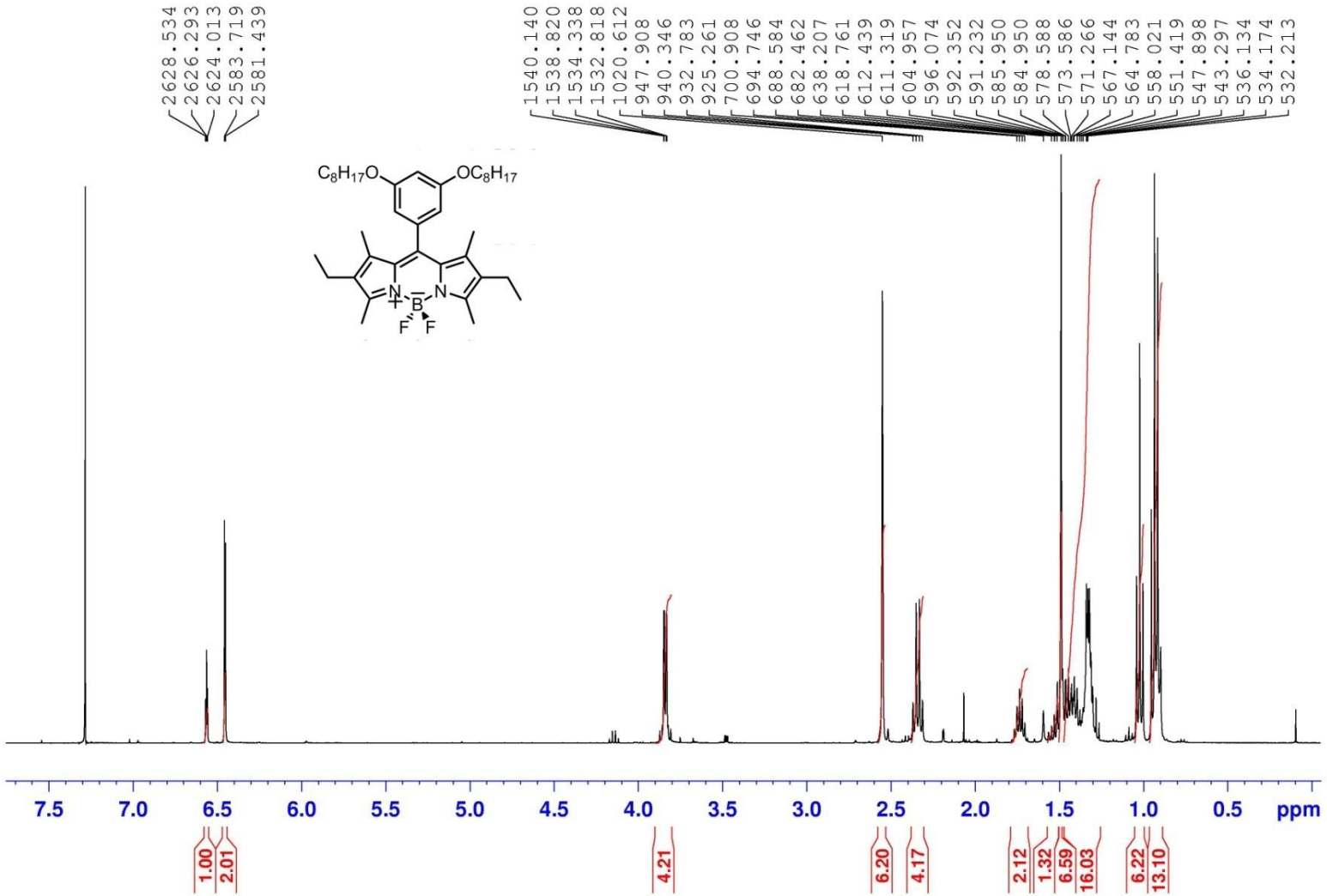


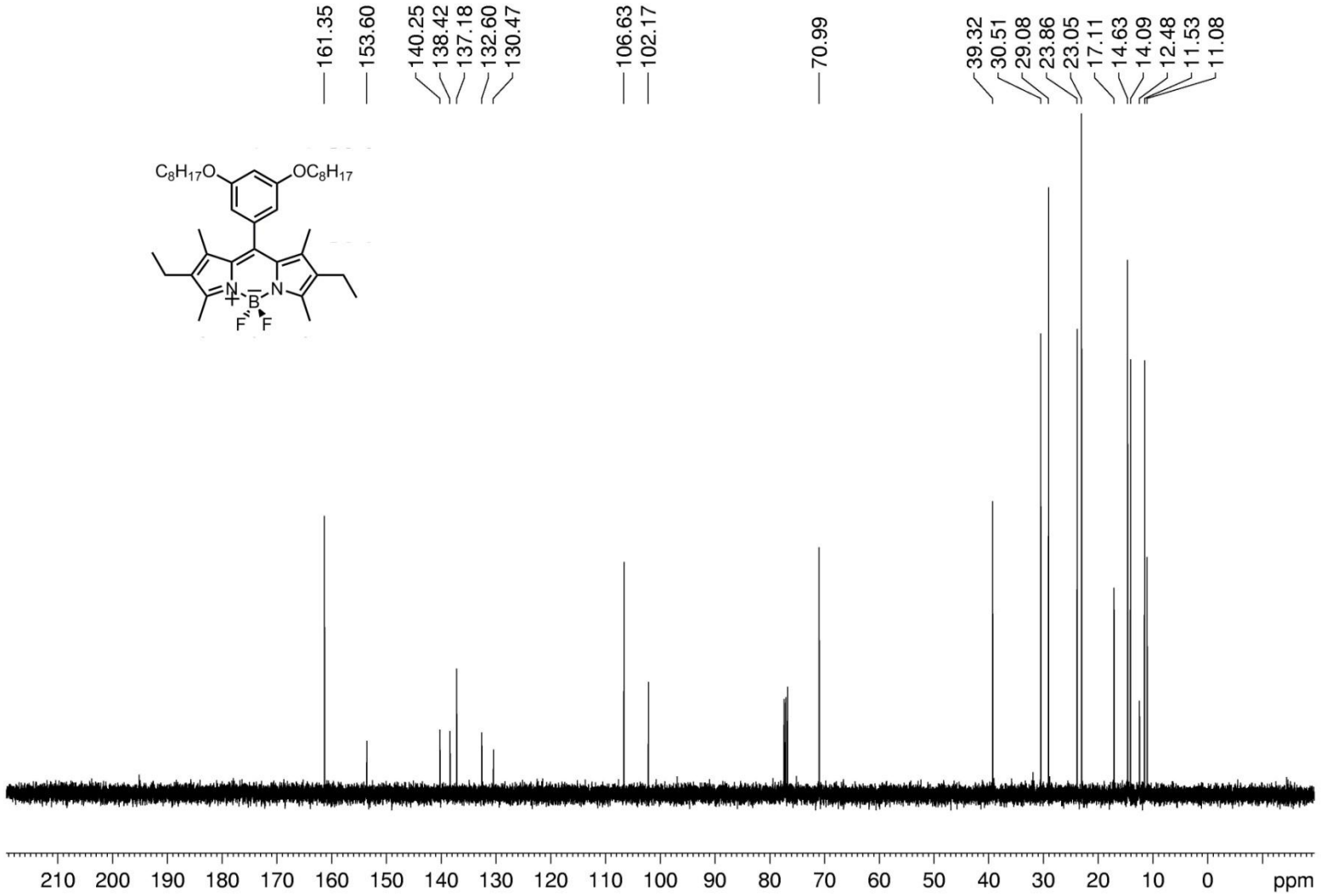


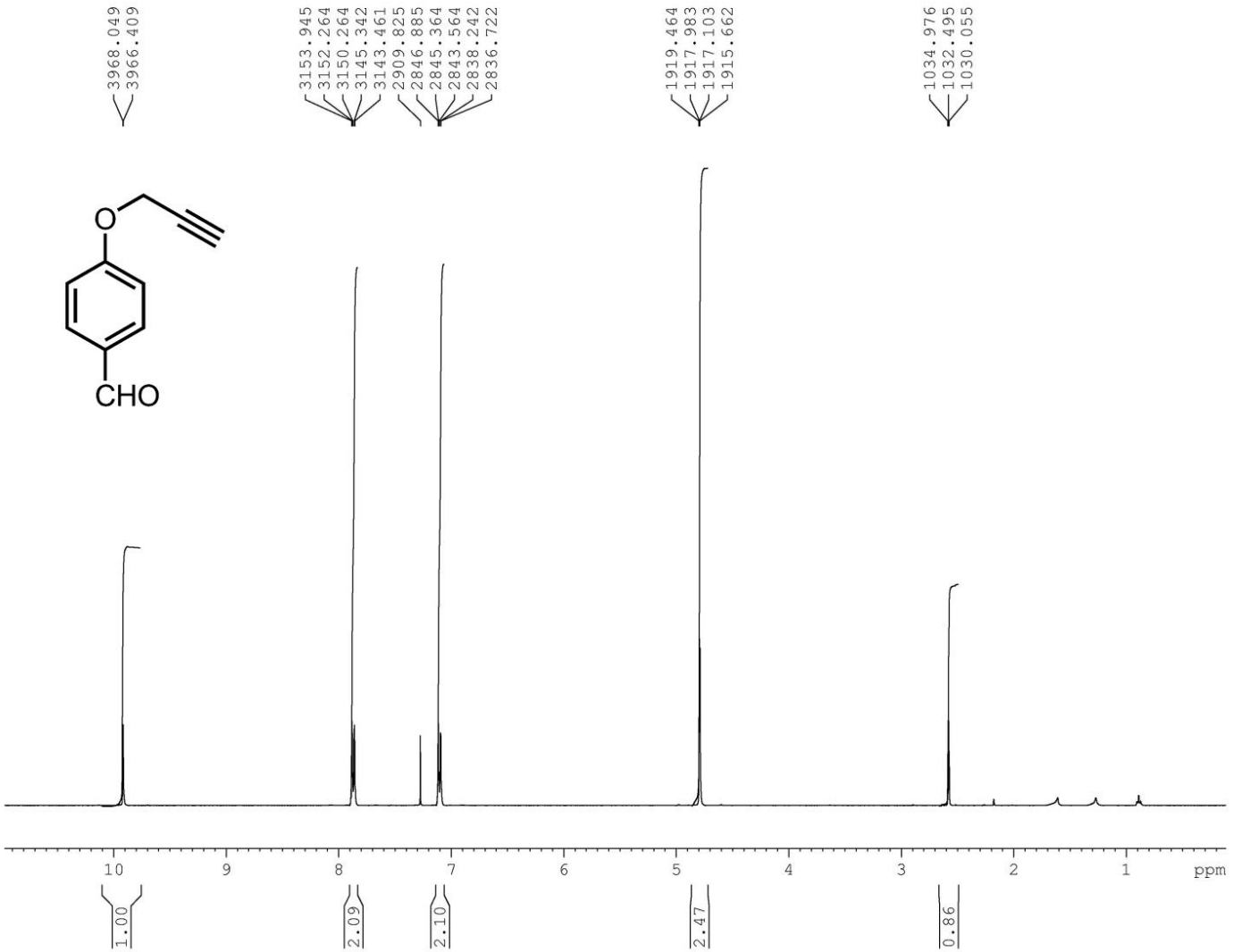


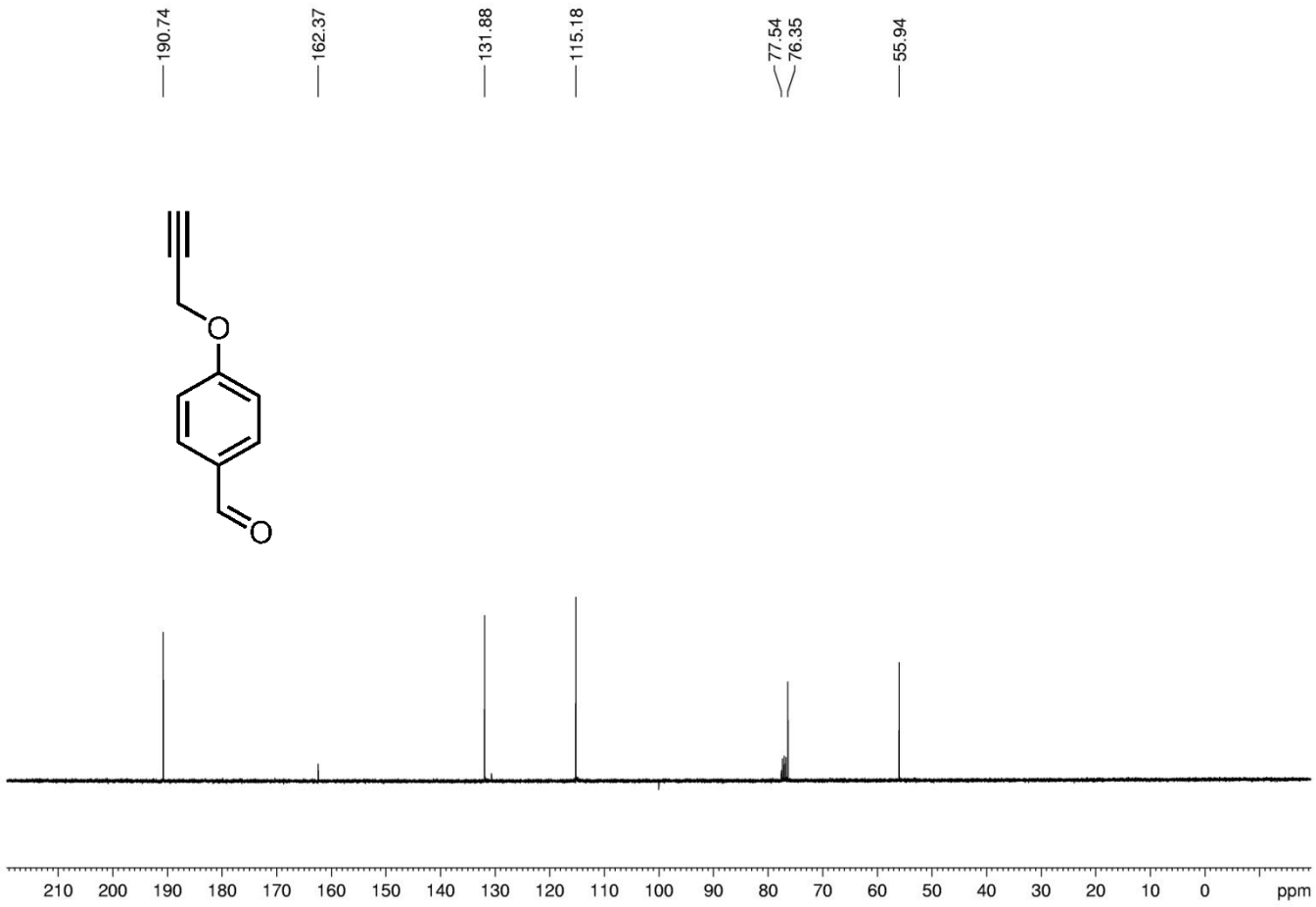


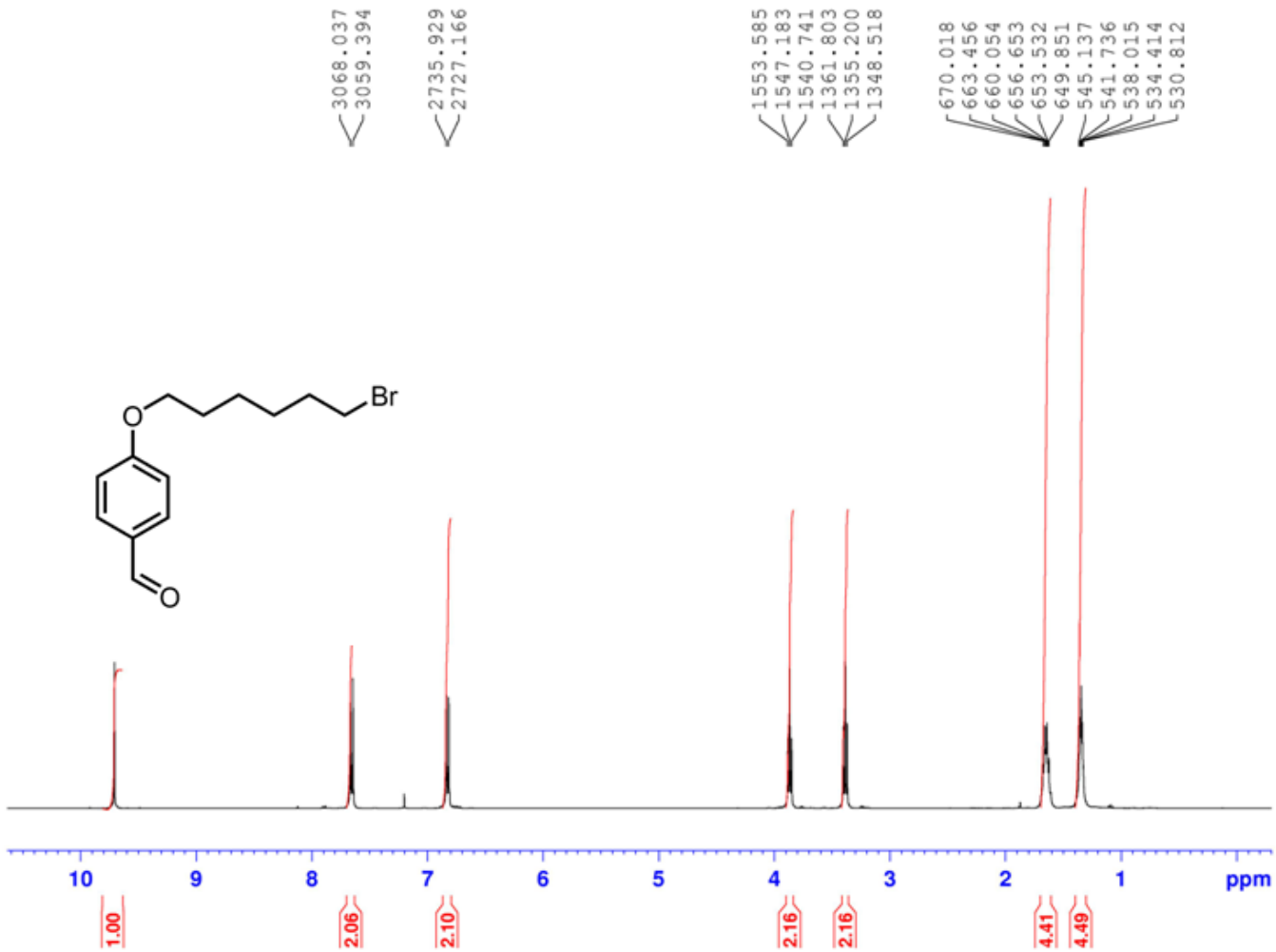


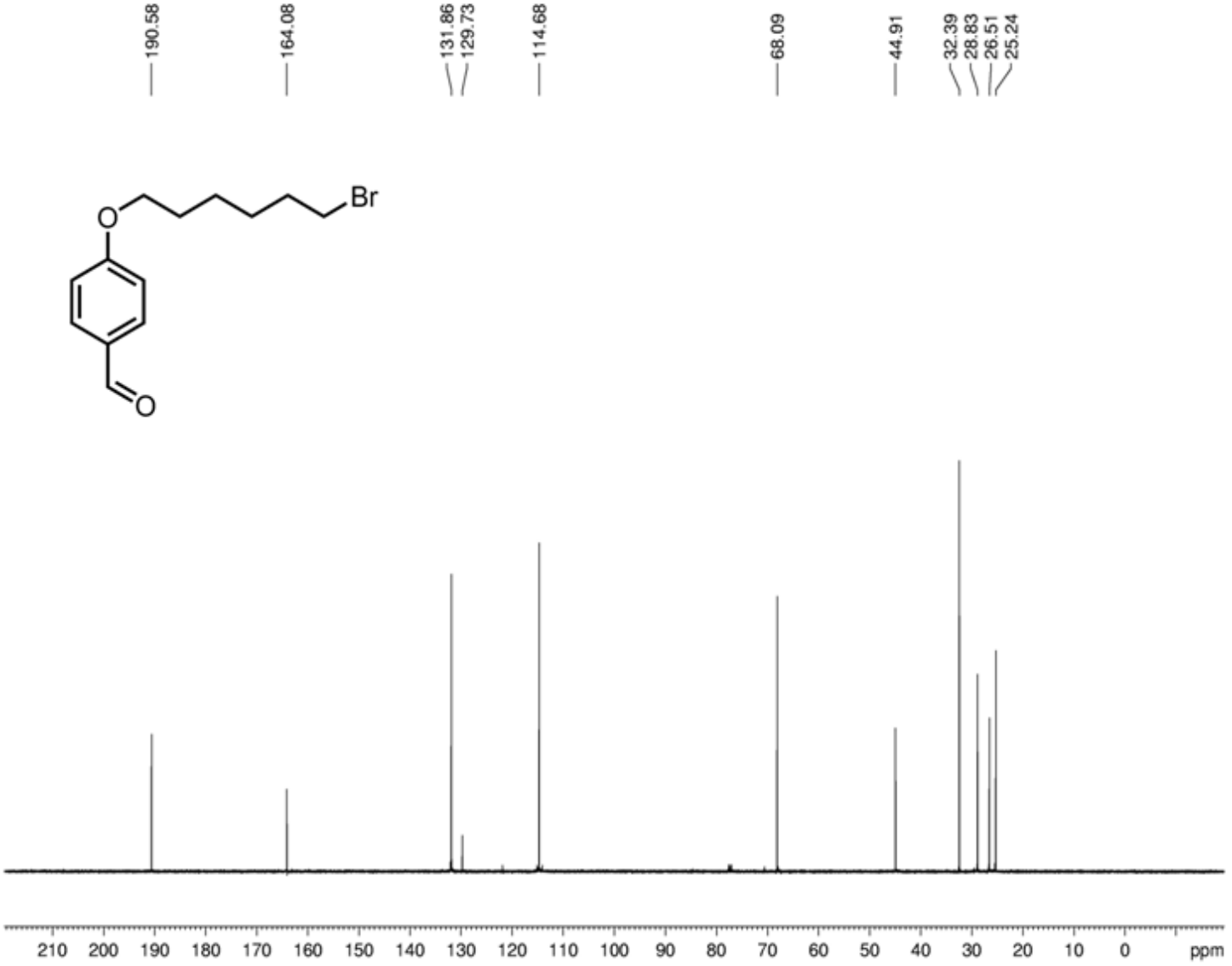


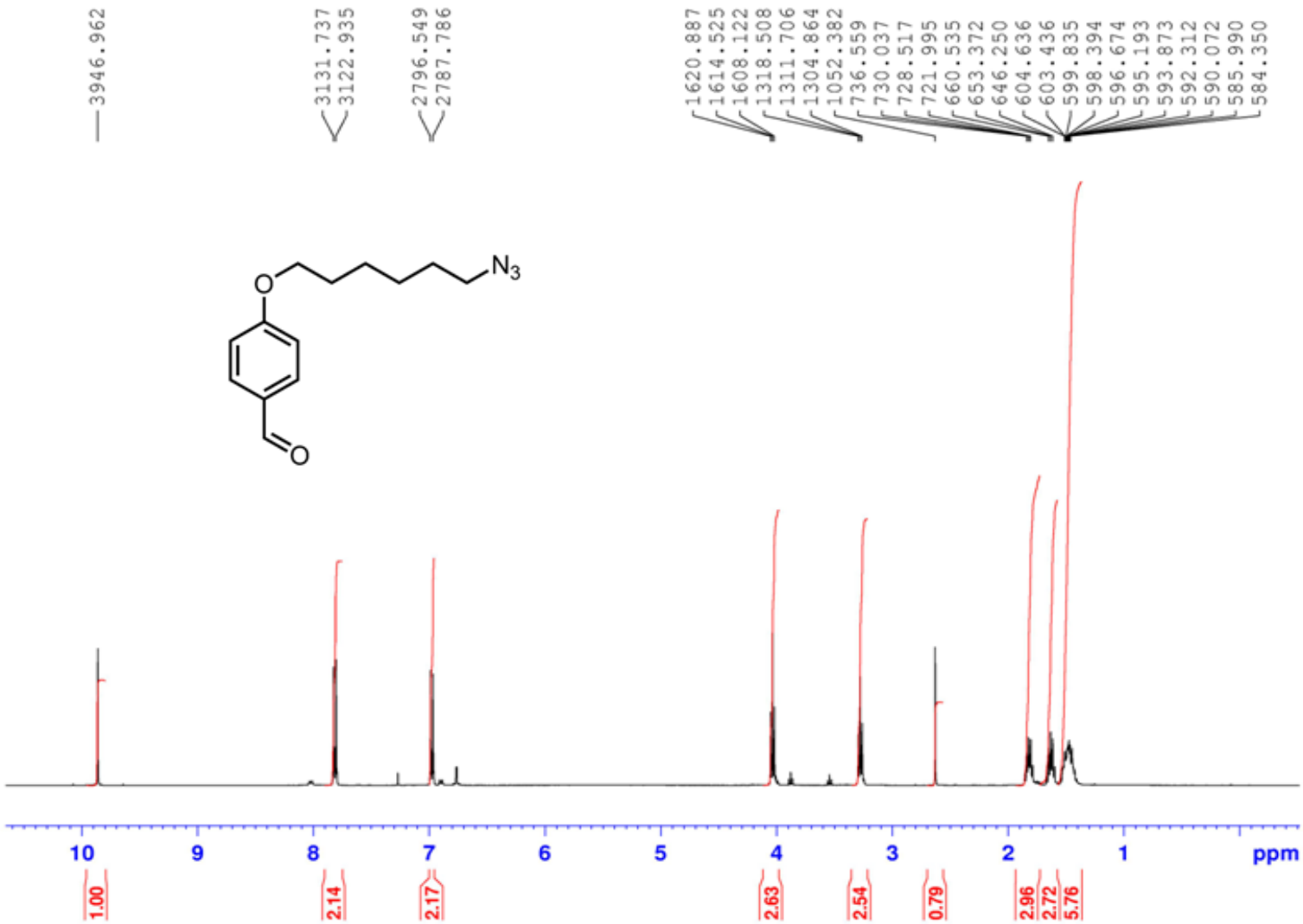








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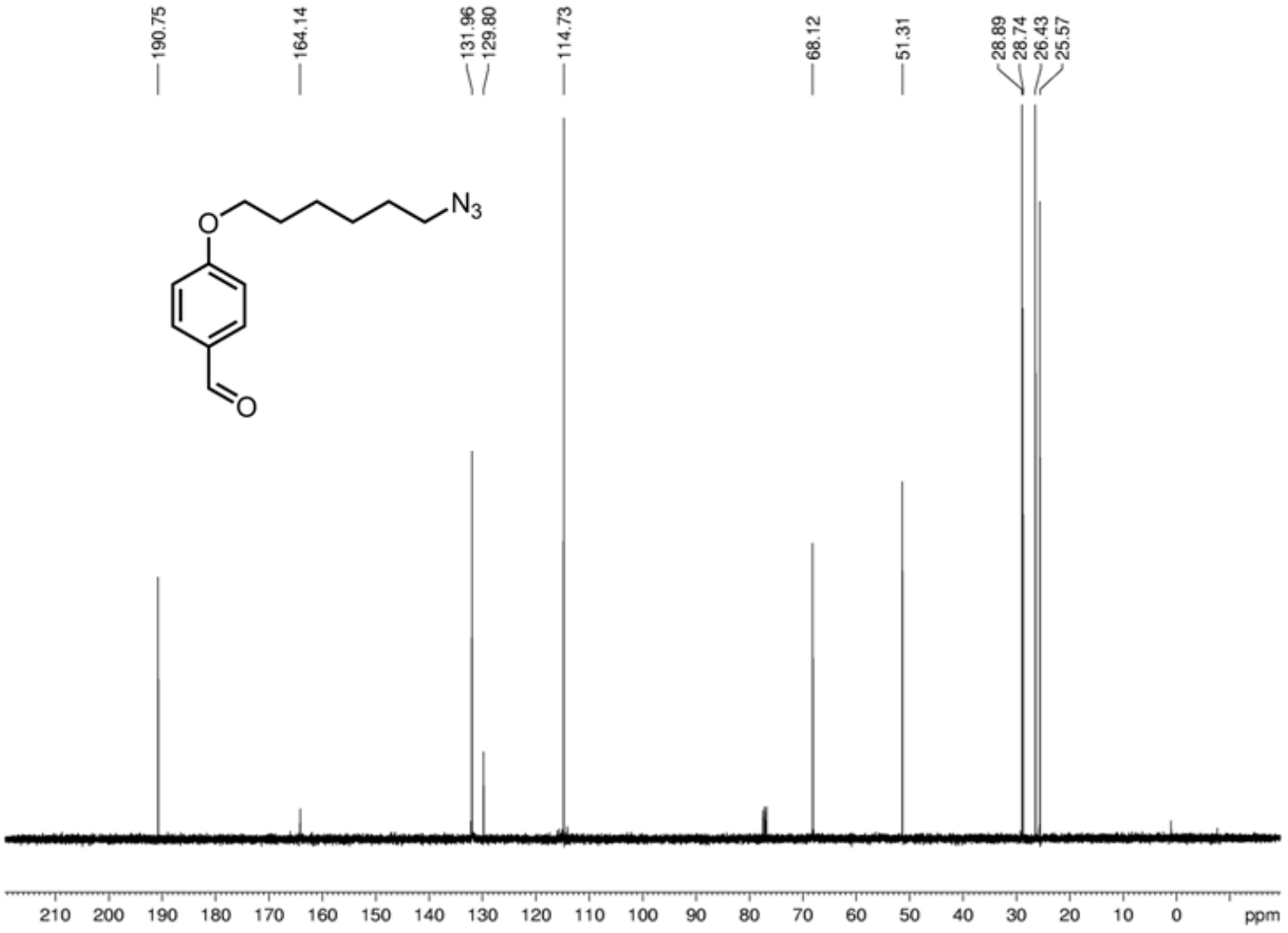

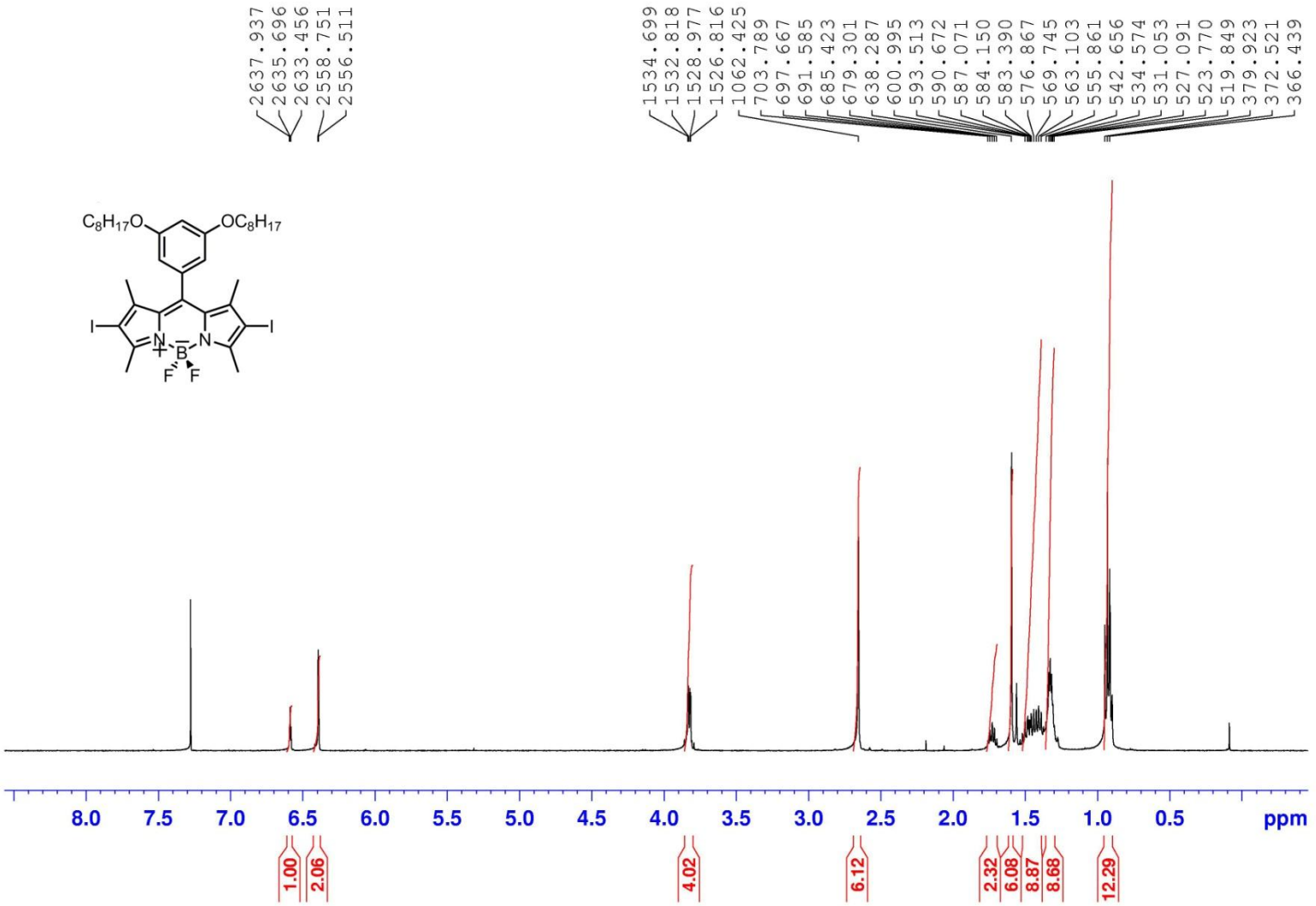

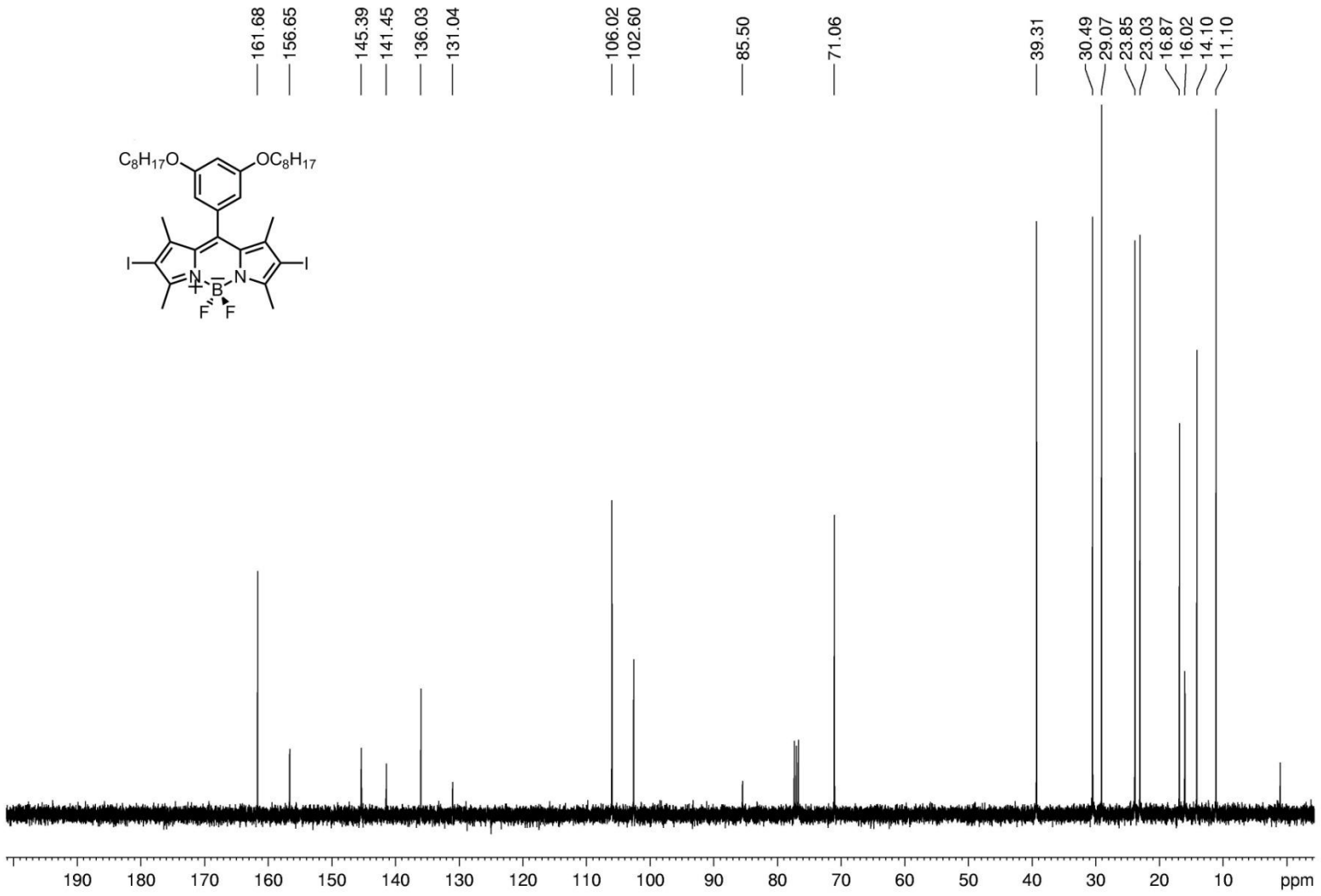

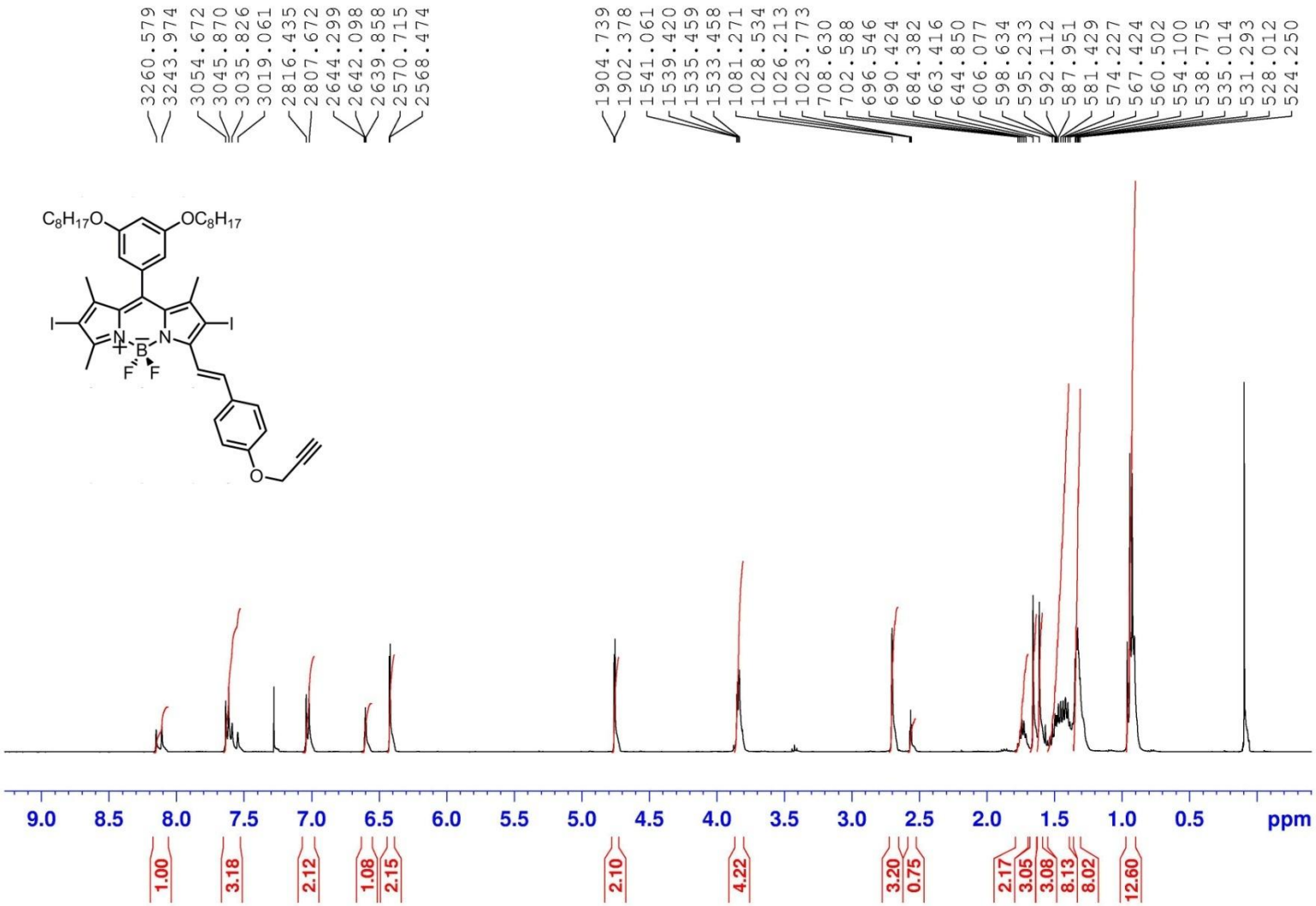

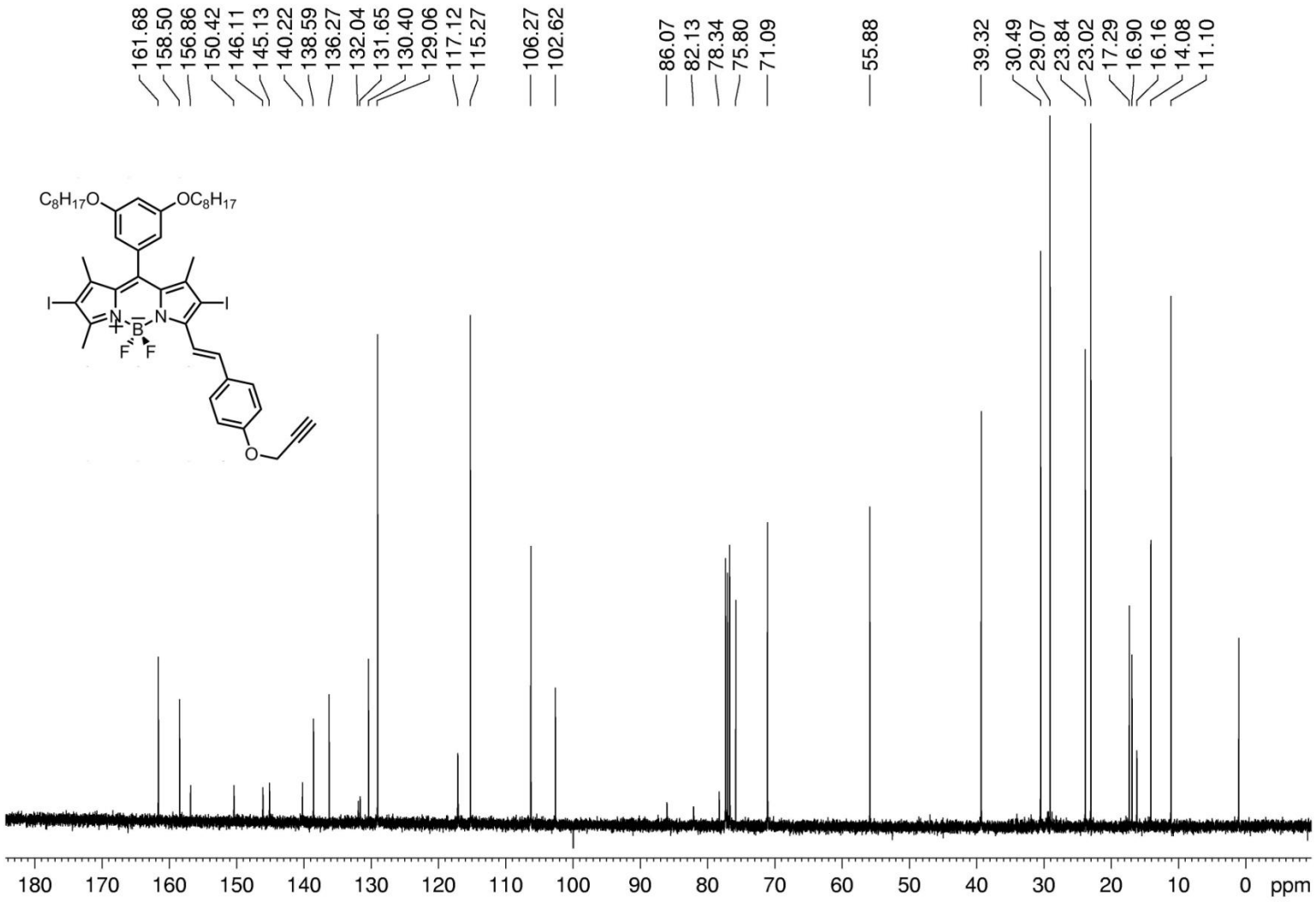

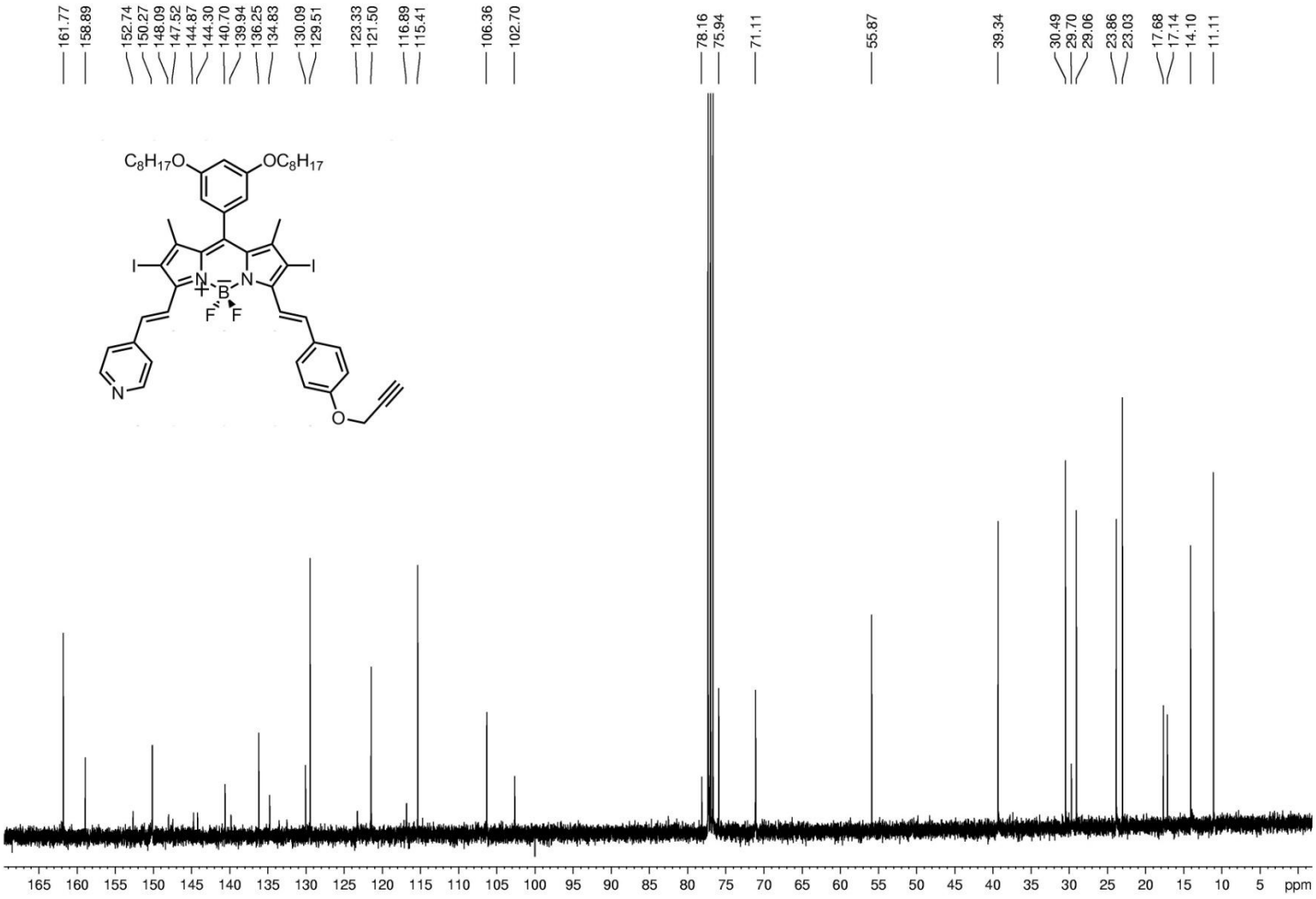

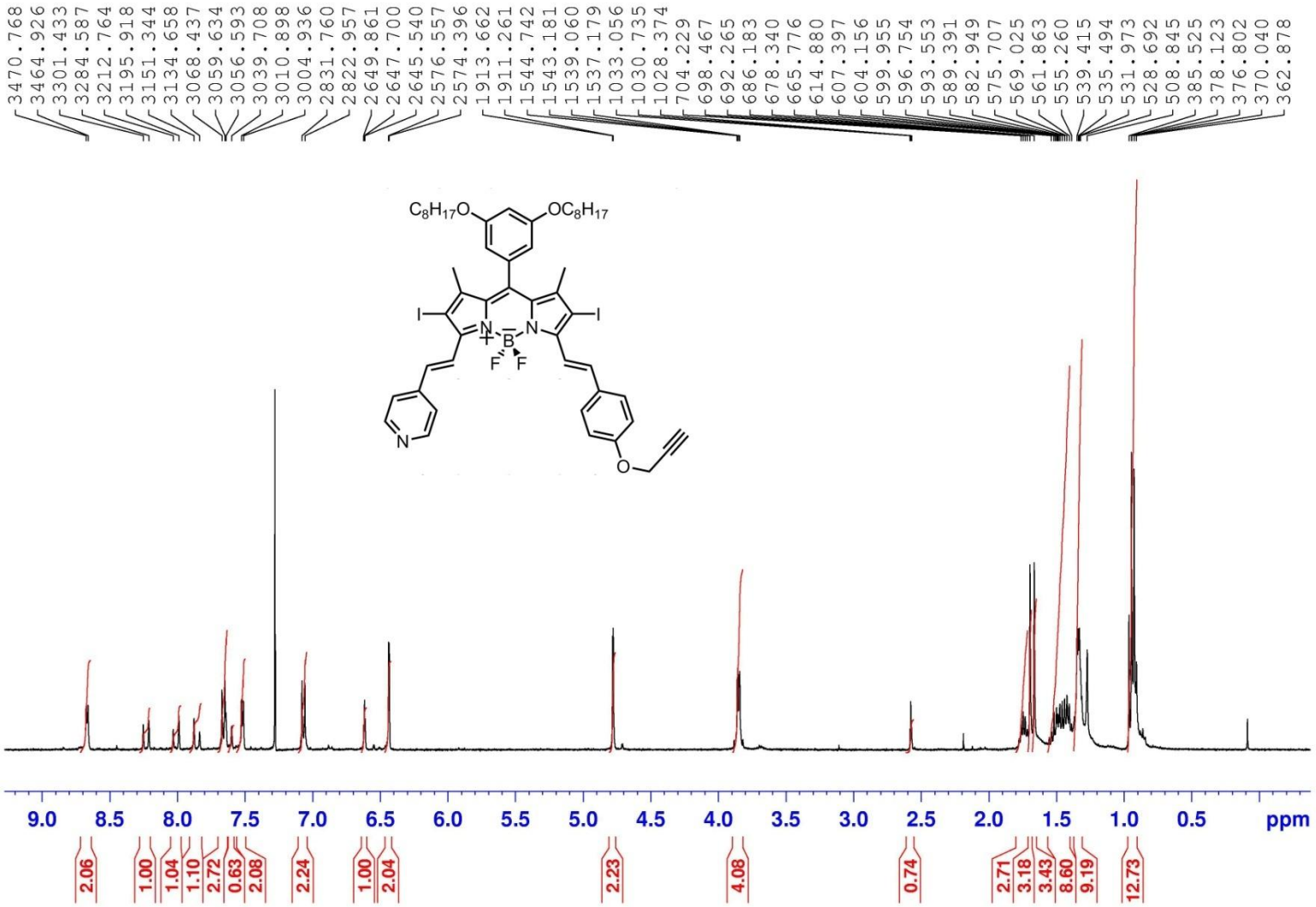

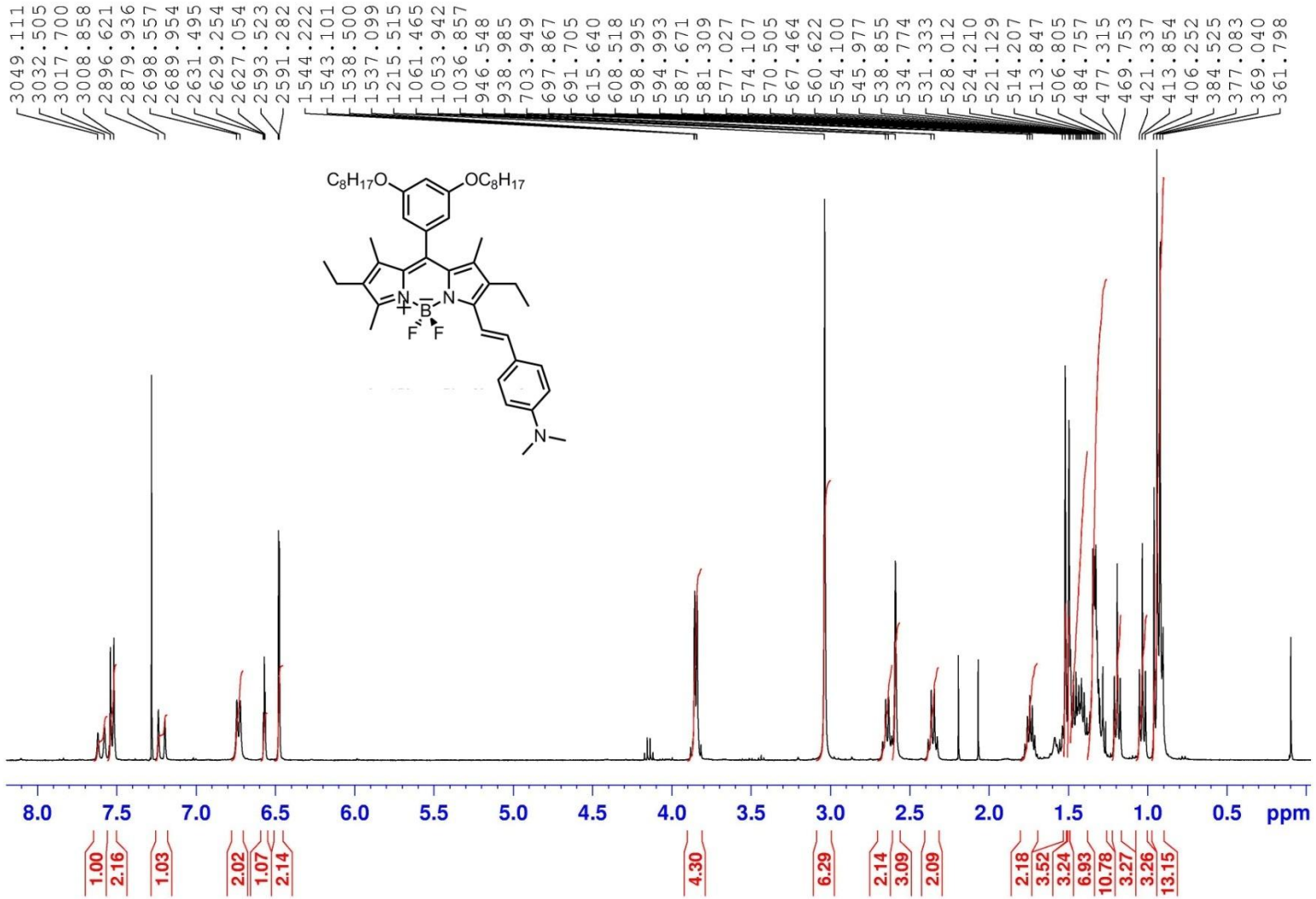

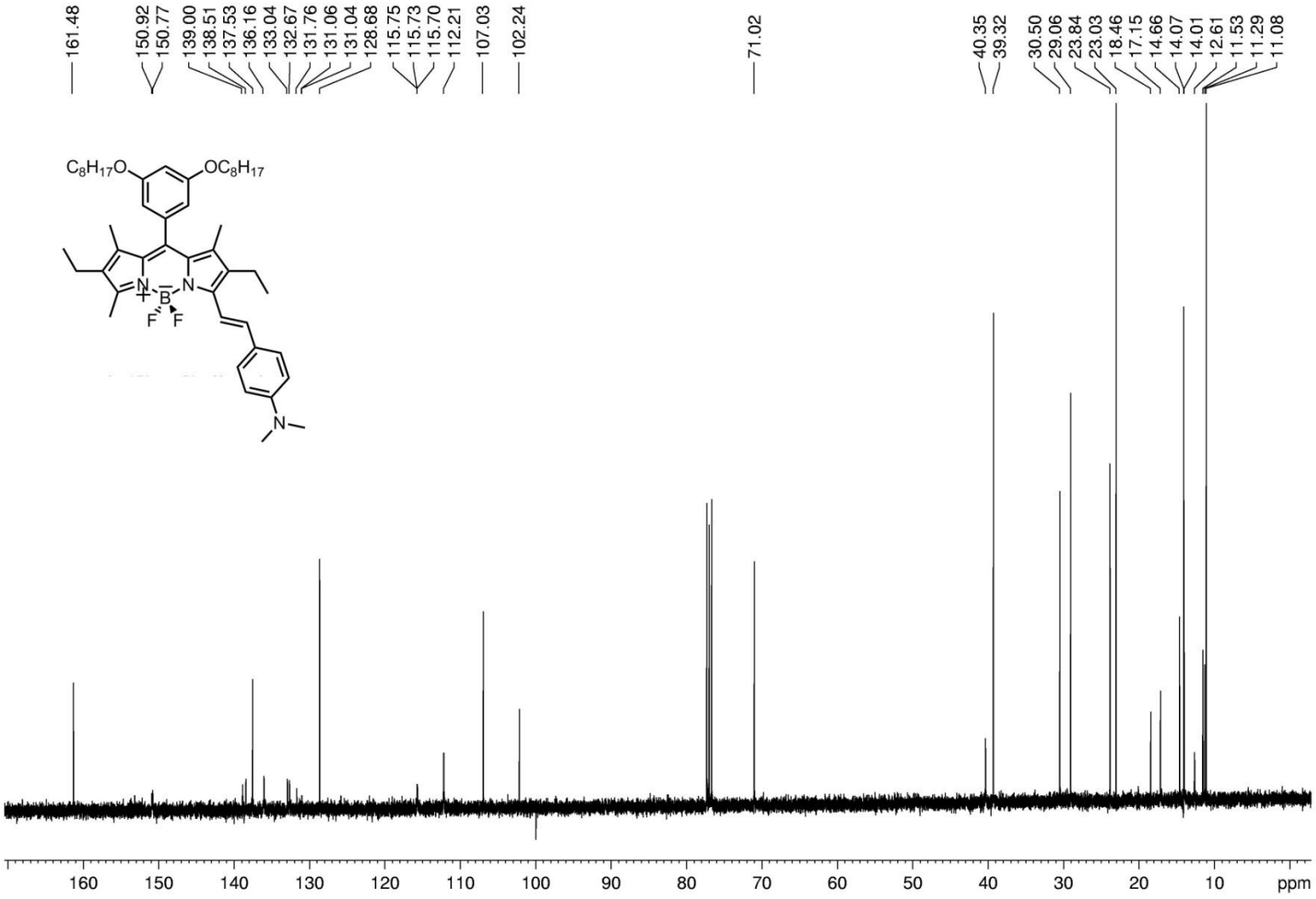
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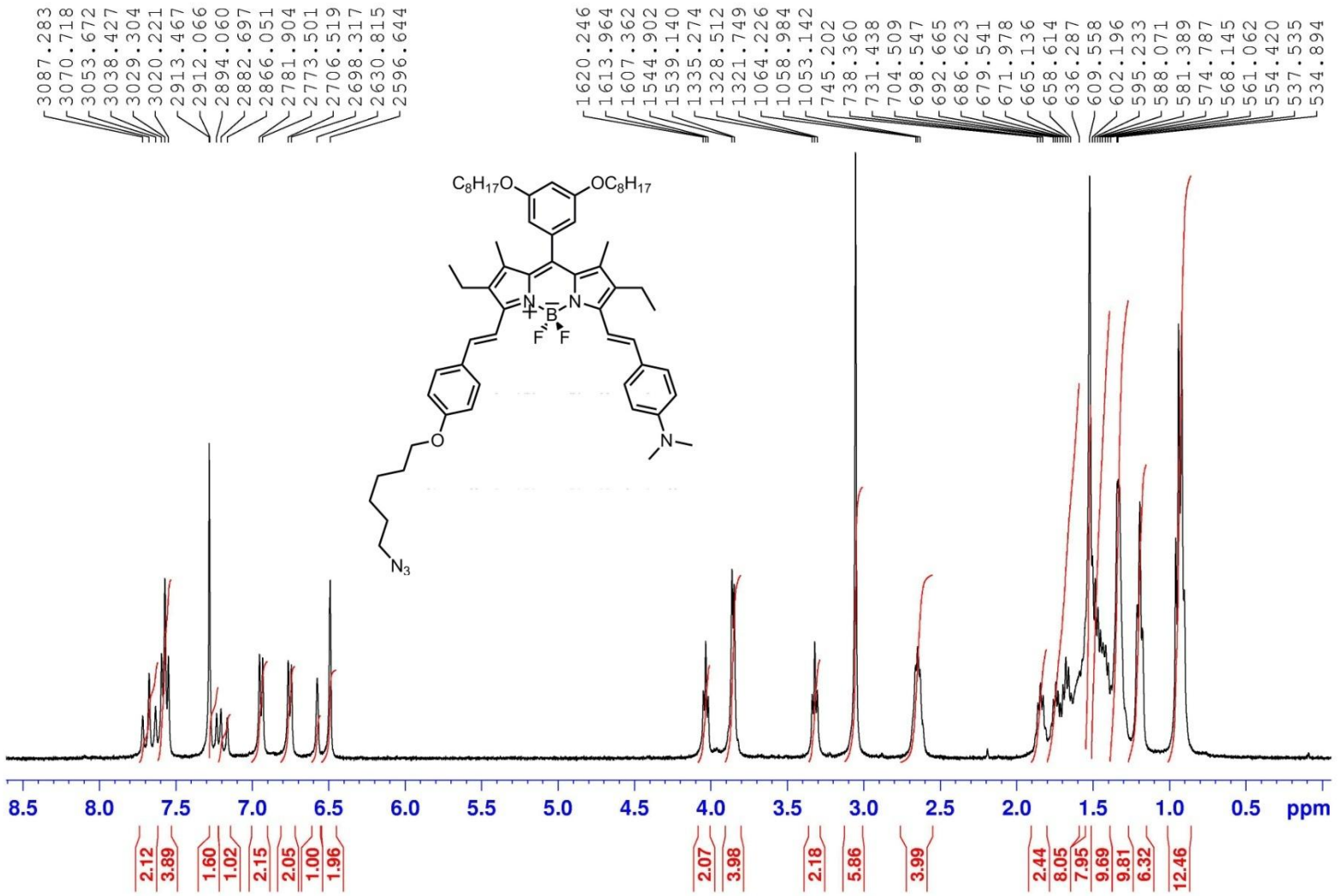
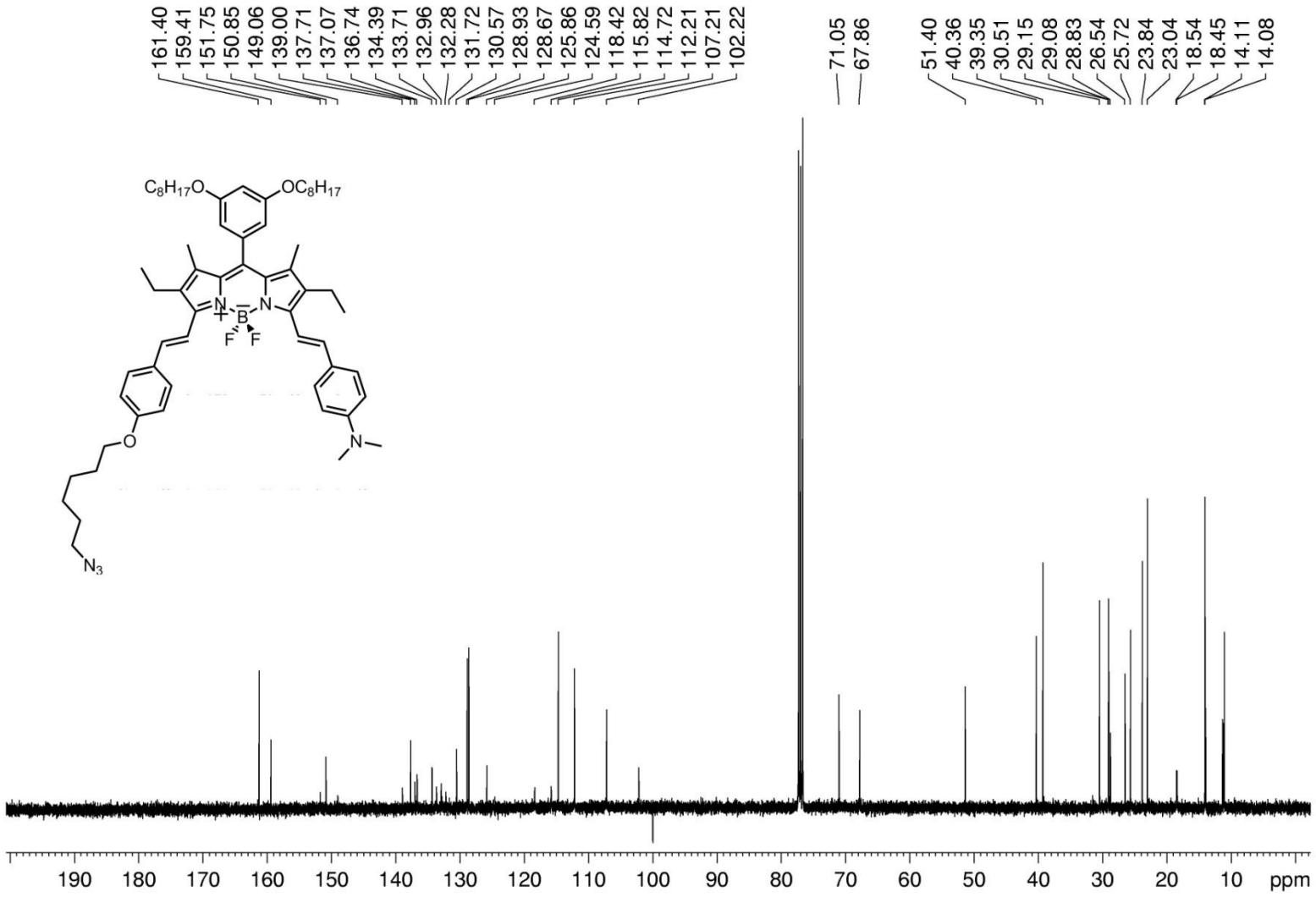
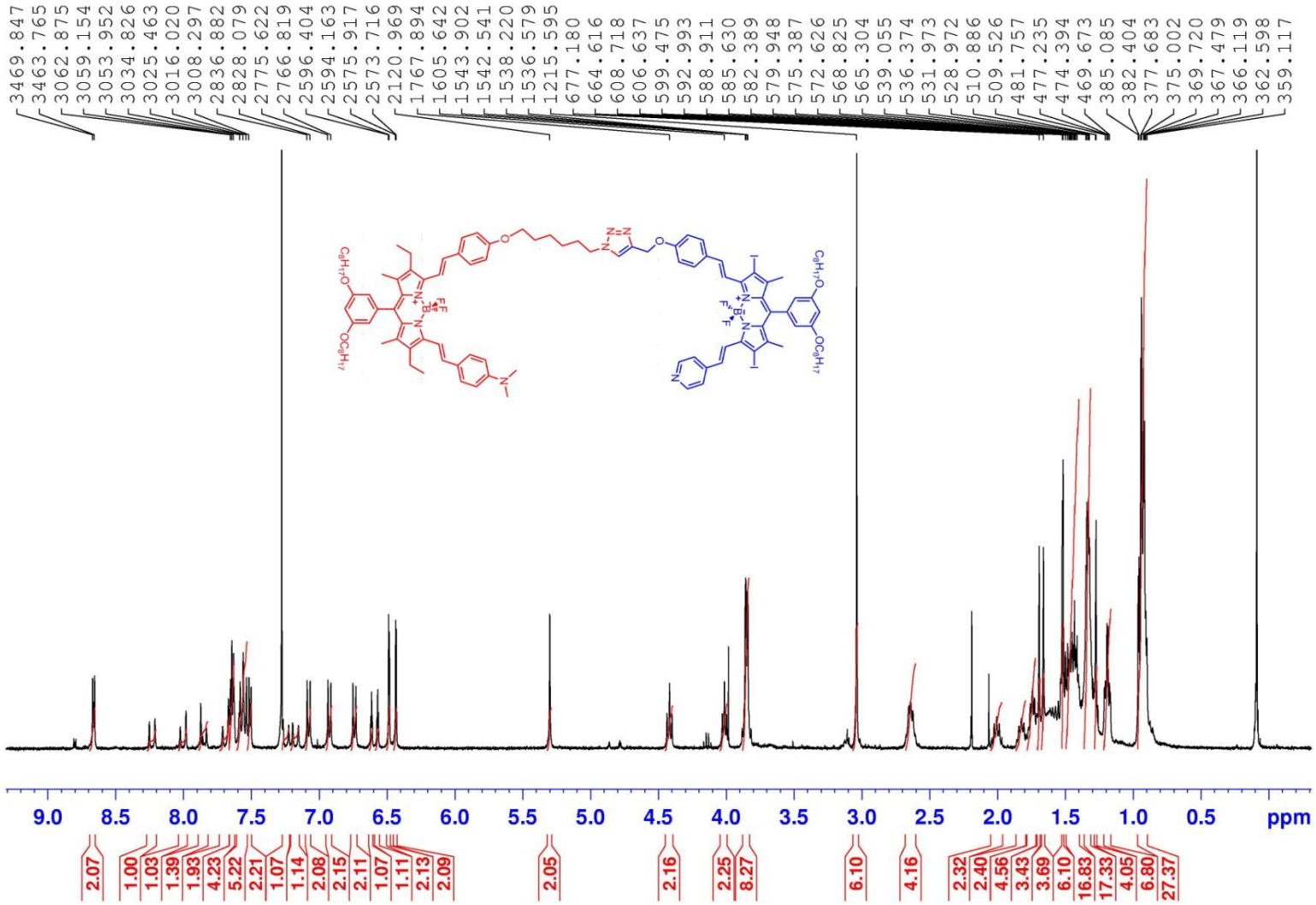
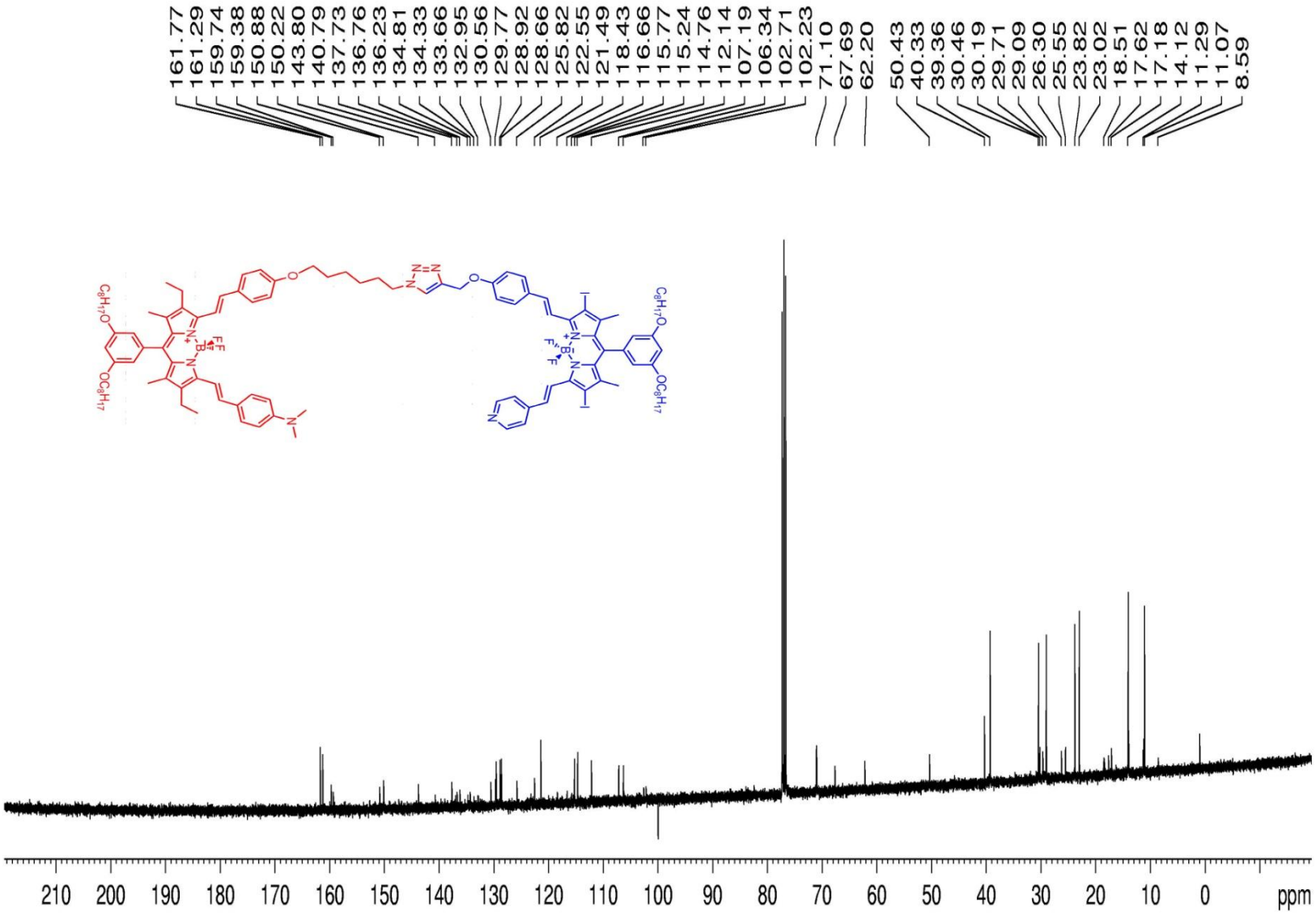
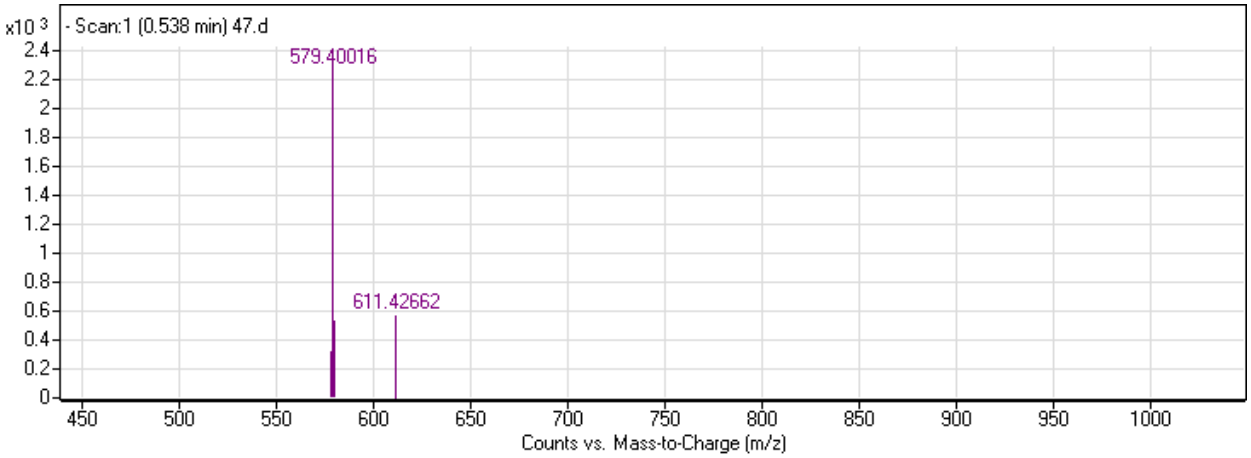




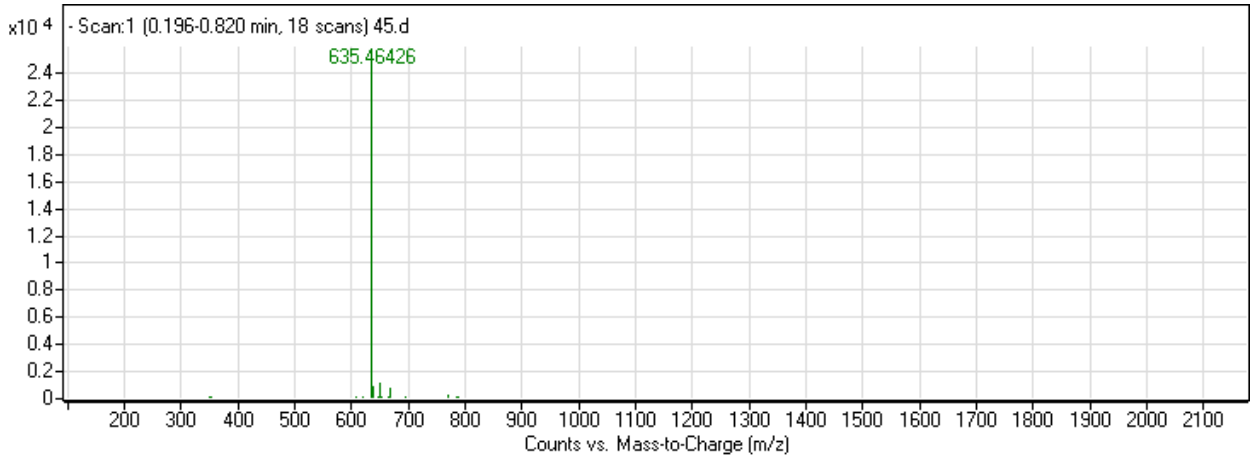




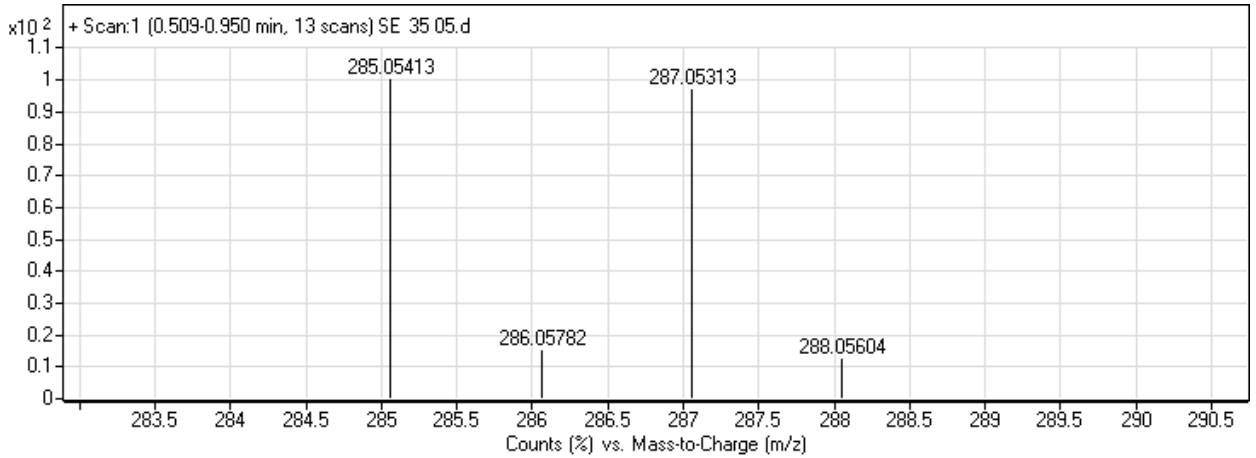
5. MASS Spectra



Multimode MASS spectrum of compound **1a**



Multimode MASS spectrum of compound **2a**



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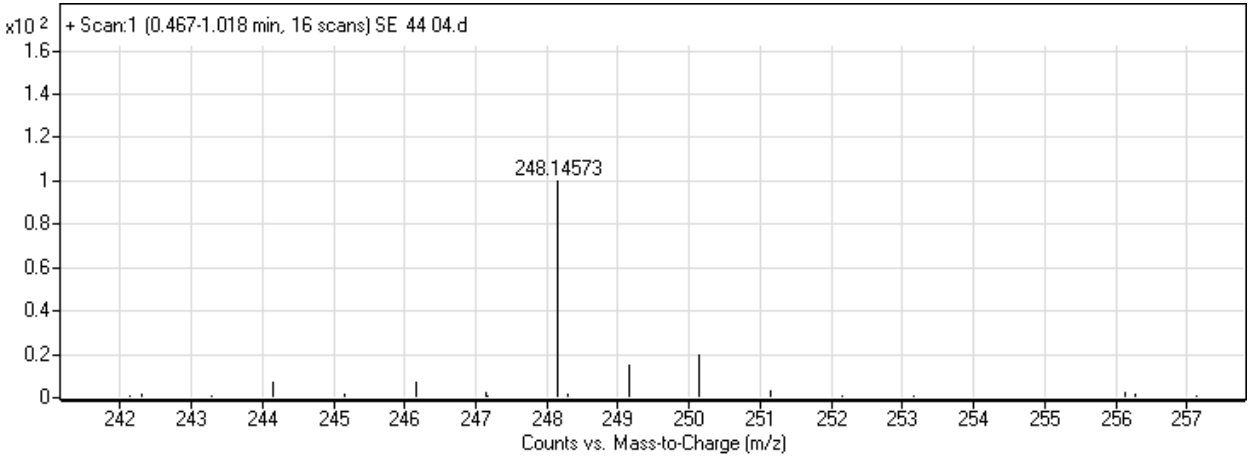

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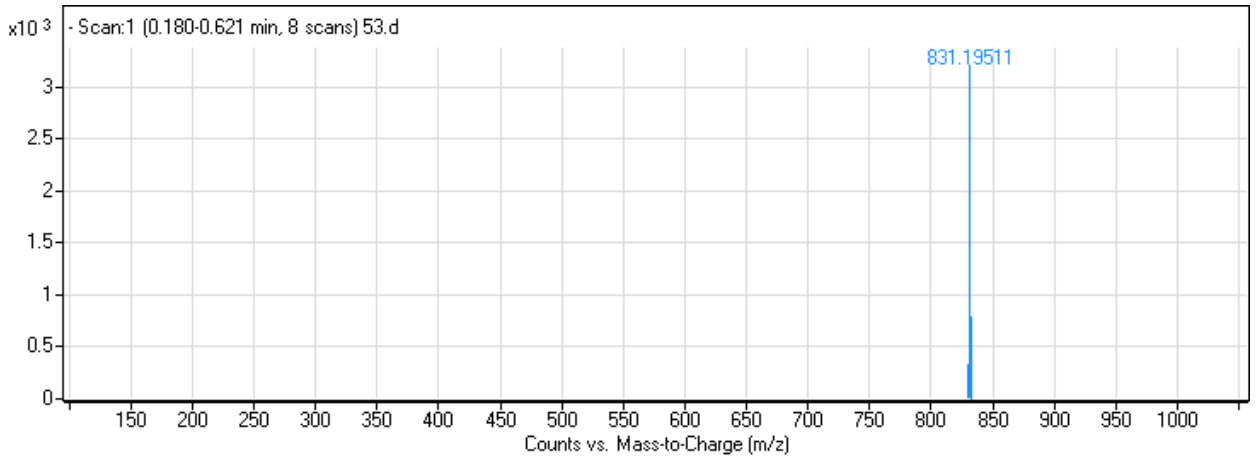

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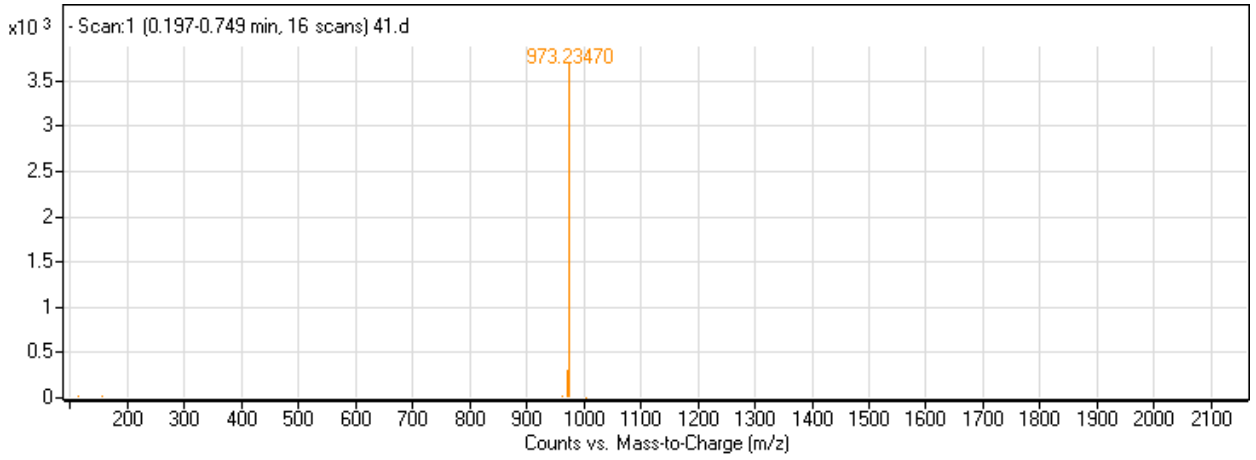

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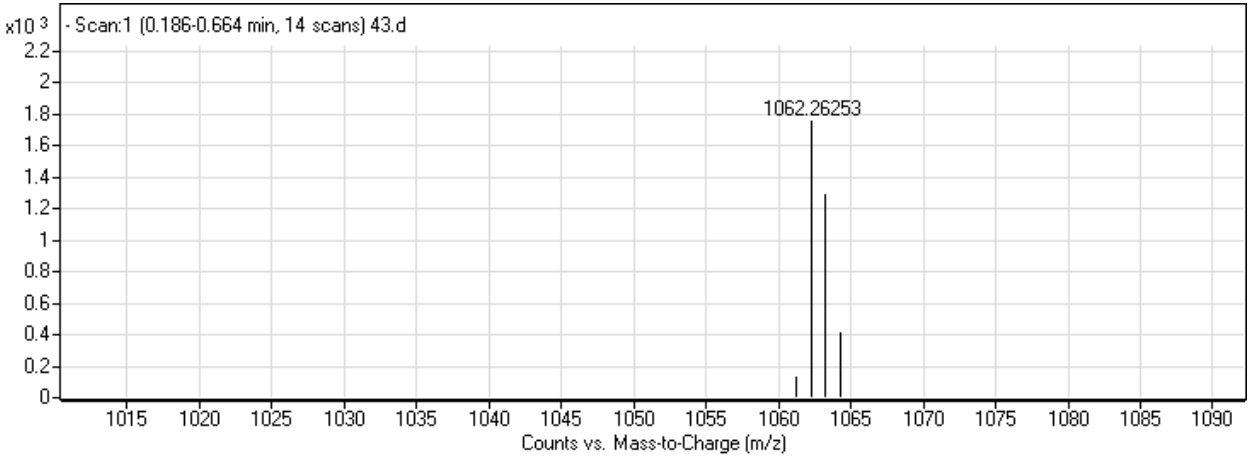

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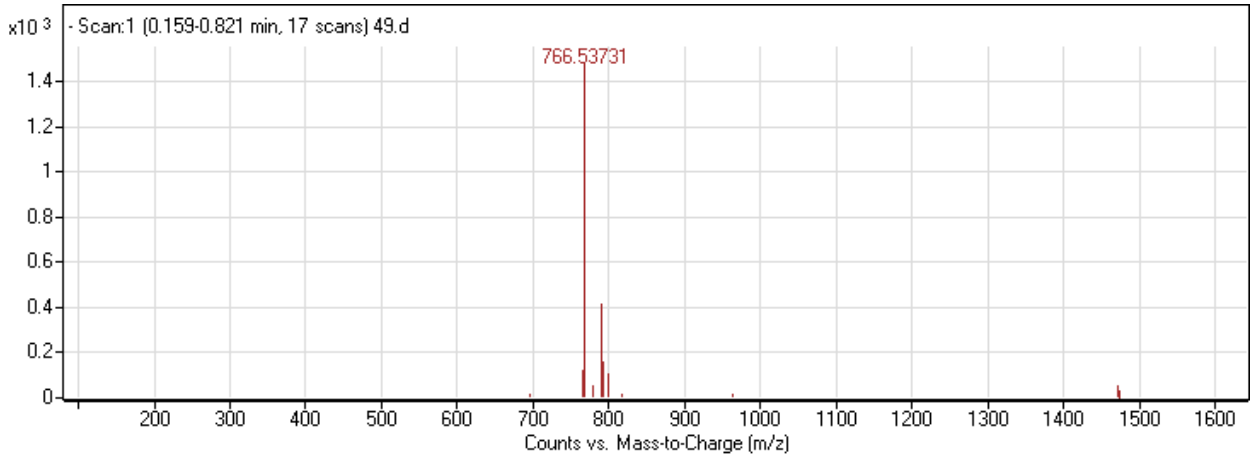

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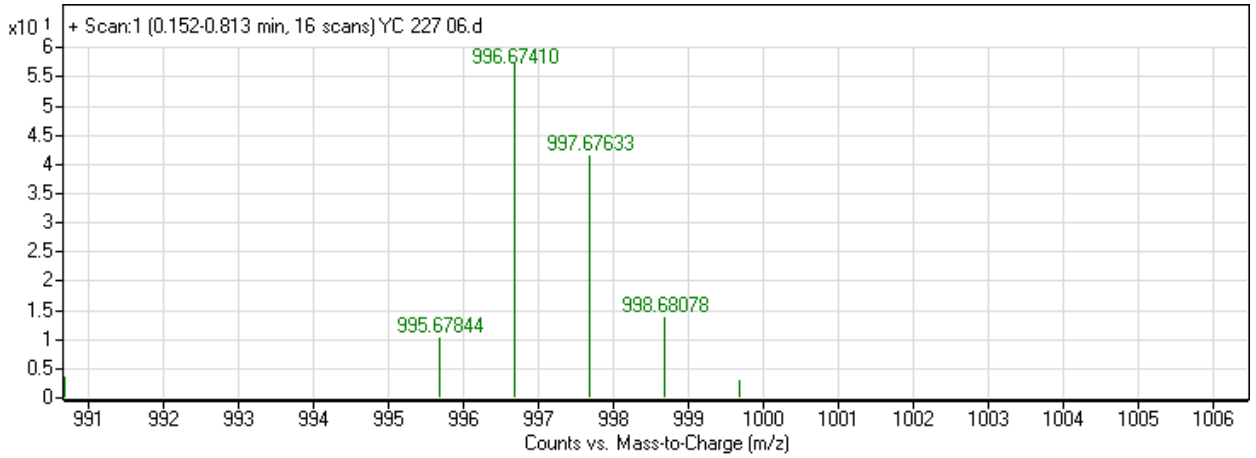

Multimode MASS spectrum of **2 (FL)** module