Supporting Information

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I. General. All commercial materials (Sigma-Aldrich, Ambeed, and ThermoFisher) were used without further purification. All solvents were reagent or HPLC (Fisher) grade. Conversions refer to chromatographically pure compounds; percent conversions were obtained by comparison of HPLC peak areas of products and starting materials. Reaction progress was monitored by TLC plates (TLC Silica gel 60 F_{254}) and visualized with UV lamps. Probes were mixed with 1 equivalence of TCEP prior to usage.

II. Materials. 3-bromo-4-nitrobenzaldehyde, 4-bromo-3-nitrobenzaldehyde, ethyl 2,4-dimethyl-1H-pyrrole-3-carboxylate, and ethyl 2-methyl-1H-pyrrole-3-carboxylate were purchased from Ambeed, Inc. Daidzin (DDZ) was purchased from phytolab (89182). Alda-1 was purchased from Sigma Aldrich (SML0462-5MG). Cell Mask dye and Hoechst 3342 was purchased from ThermoFisher. AV/PI stains (FITC and PacificBlue) were purchased from Biolegend. Cell lines were obtained from the Spangle Lab at Winship Cancer Institute of Emory University School of Medicine.

III. **Purification.** All compounds were purified with column chromatography using silica gel, 230-400 mesh, SiliaFlash P60 (Silicycle).

IV. Analytical Methods.

NMR: NMR spectra were recorded on a 400 MHz or 600 MHz Bruker NMR spectrometer. Proton chemical shifts were referenced to residual $CDCl_3$ at 7.26 ppm and carbon chemical shifts were referenced to $CDCl_3$ at 77.16 ppm. Spectra were processed using Mnova ver. 12.0.4 and TOPSPIN software. The following abbreviations (or combinations thereof) are used to refer to multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, p = quintet, and m = multiplet. Coupling constants (*J*), are reported in Hertz units (Hz).

HPLC: Chemoselectivity reactions were analyzed using high performance liquid chromatography (HPLC) on an Agilent 1100 series HPLC equipped with a 5 μm particle size, C-18 reversed-phase column. All separations involved a mobile phase of water with 0.1% formic acid (solvent A) and acetonitrile with 0.1% formic acid (solvent B). The HPLC method employed a linear gradient of 30-100% solvent B over 30 minutes at ambient temperature with a flow rate of 1 mL/min. The eluent was monitored by absorbance at 220 nm and 280 nm.

LC-MS: Reactions were checked on an Agilent 1100 Series HPLC with MSD VL mass spectrometer using positive polarity electrospray ionization (+ESI).

HRMS. High resolution MS data were acquired on a Thermo Exactive Plus using positive-ion electrospray ionization (ESI+). Data were processed with Thermo Scientific Freestyle software ver. 1.8.63.0.

Fluorimeter: Fluorescence spectroscopy was performed with an Agilent Cary Eclipse. Probe **1a** had an excitation of 485 nm and an emission of 520 nm. Probe **1c** had an excitation of 725 nm and an emission of 780 nm. Probe **1d** had an excitation of 650 nm

and an emission of 710 nm. Excitation and emission slits were set to five for each experiment.

Microwell Plate Reader: Fluorescence intensity was measured by a Synergy H1 by BioTek. An excitation of 485 nm and an emission of 520 nm was used with Probe **1a**.

V. Cell Culture Technique: Cells were maintained at 37 °C and 5% CO_2. T-47D cells were cultured in RPMI supplemented with 10% (V/V) fetal bovine serum (FBS), 1% (V/V) penicillin/streptomycin (100 μg/mL), and 1% (V/V) L-glutamate (100 μg/mL). MCF10A cells were cultured in DMEM/F12 supplemented with 10% (V/V) FBS, 1% (V/V) penicillin/streptomycin (100 μg/mL), EGF (20 ng/mL), hydrocortisone (0.5 mg/mL), cholera toxin (100 ng/mL), and insulin (10 μg/mL).

VI. Organoid Culture:
Mouse intrahepatic biliary organoid culture. BECs were dissociated as previously described.[31,32] Mouse intrahepatic cholangiocyte organoid (mICO) lines were banked in Freezing Media [Advanced DMEM/F12 (Thermo Fisher; 12634028), 20% fetal bovine serum (Genesee Scientific; 25-525H), and 10% DMSO (Sigma Aldrich; D2650)] followed by a gradual reduction in temperature down to −80 °C and transfer to liquid nitrogen storage. Before culture, mICOs were thawed quickly in a 37 °C water bath, resuspended in 5 mL Advanced DMEM/F12, and pelleted at 4 °C and 600g for 5 min. Supernatant was discarded, and cells were washed a second time with 5 mL Advanced DMEM/F12 and pelleted at 4 °C and 600g for 5 min. Pellet was visualized by eye, supernatant was discarded, and cells were resuspended in 1 part Advanced DMEM/F12 and 2 parts Cultrex Reduced Growth Factor Basement Membrane Extract (R&D Systems; 3533-010-02) for a final solution of 66% Cultrex. 48 well plates were prewarmed to 37 °C and cell suspensions were plated as 30 μL droplets and allowed to polymerize at 37 °C for 30min. After polymerization, droplets were overlayed with Biliary Single Cell Media [50% Advanced DMEM/F12, 40% WNT3A-conditioned media, 10% RSPO1-conditioned media, B27 supplement without vitamin A (Thermo Fisher; 12587010), N2 supplement (Thermo Fisher; 17502048), 2mM GlutaMAX (Fisher Scientific; 35050061), 10 mM HEPES (Thermo Fisher; 15630080), 100 U/mL Pen/Strip (Fisher Scientific; 15140122), 50 ng/mL recombinant murine EGF (Thermo Fisher; PMG8041), 100 ng/mL recombinant human Noggin (VWR International; 120-10C), 100 ng/mL recombinant human FGF10 (Peprotech; 100-26), 10 nM recombinant human gastrin (Sigma; G9145), 50 ng/mL recombinant human HGF (PeproTech; 100-39H), 10 mM nicotinamide (Sigma Aldrich; N0636-100G), 10 μM forskolin (Selleck Chemicals; S2449), and 10 μM Y-27632 (Selleck Chemicals; S1049)]. Biliary Single Cell Media was used for the first 2 days in culture following biliary isolation, thawing, or passaging. After 2 days, the media was changed to Biliary Expansion Media [90% Advanced DMEM/F12, 10% RSPO1-conditioned media, B27 supplement without vitamin A, N_2 supplement, 2 mM Glutamax, 10 mM HEPES, 100 U/mL Pen/Strip, 50 ng/mL recombinant murine EGF, 100 ng/mL recombinant human FGF10, 10 nM recombinant human gastrin, 50 ng/mL recombinant human HGF, 10 mM nicotinamide, and 10 μM forskolin]. Organoids were passaged every 3-5 days.

Biliary organoid retrieval. Organoids were retrieved from Cultrex by removing culture media and adding 500uL Cultrex Organoid Harvesting Solution (R&D Systems; 3700-100-01) to the wells of a 48 well plate. The plate was incubated on a nutating platform for 45-60min at 4 °C. After incubation, organoids were retrieved by resuspending well contents 5-10x with a P1000 pipettor, allowing organoids to sediment, and then supernatant was removed with a P1000 pipettor until only 200 uL remained in the well. 200 uL of solution was kept in the well at all times to avoid discarding organoids. Organoids were overlayed with 200 uL Biliary Expansion Media until treatment.

VII. Animal Studies:

C57Bl/6 mice were used for this study. All animal studies were reviewed and approved by the Institutional Animal Care and Use Committee of Emory University. Male Balb/cJ mice 9 weeks of age (Jackson Labs) were maintained in a regulated humidity and temperature environment under pathogen-free conditions and provided food and water *ad libitum* under a controlled light and dark cycle. Organs derived from CO_2 euthanized mice were perfused by administering 10 mL of sterile PBS through the heart. Following perfusion, the heart, kidney, brain, liver, lungs, and spleen were collected, washed with ice cold PBS, and residual PBS removed with blotting paper. Organs were cut into pieces and snap frozen for long-term storage at -80 ^{o}C. All mouse experiments were conducted in accordance with protocols approved by the Institutional Animal Care and Use Committee of Emory University School of Medicine.

VIII. Experimental Section.

Chemoselectivity studies of probe 1a with biological compounds. Probe **1a** (1 mM, 1 equiv.) was incubated in DMSO for 2 h at 37 °C with 50 mM (50 equiv.) of the following biological compounds: Formaldehyde, acetaldehyde, propanal, valeraldehyde, octantal, 4-nitrobenzaldehyde, glutathione (GSH), H_2O_2, di-*tert*-butyl peroxide (DTBP), SNAP (NO donor), and methylglyoxal. Each reaction was frozen in liquid nitrogen and thawed individually for HPLC analysis and MS verification to determine the percent conversion of probe **1a** into any modified reactant.

Rate of benzothiazole formation in solution. The rate of benzothiazole formation was determined upon the reaction of probe **1a** (10 μM, 1 equiv.) with propanal (1 μM, 0.1 equiv.) in DMSO. The reaction was monitored over 30 min with fluorescence intensity measurements collected every 1 min by fluorimeter. Increases in fluorescence were plotted against time and a one-phase association curve was used to determine the rate constant. The reaction was performed in triplicate.

Flow cytometry analysis of cell death by probe 1a. T-47D and MCF10A cells were incubated with 10 μM of probe **1a** for 2 h or 24 h with equal amounts of DMSO as control. Cells were then detached with trypsin and stained using Annexin V/PI following manufacturer's protocol. To avoid fluorescent crosstalk, Annexin V (AV) conjugated to PacificBlue or FITC was used to determined apoptosis. Propidium Iodide (PI) was used to determine necrosis within the cellular populations. Cells were analyzed via flow cytometry within 1 h to quantify cell death. FlowJo software was used to analyze the

cytometry data. PI and AV controls were used to determine quadrant placement. All the experiments were performed in triplicate.

Probe 1a limit of detection of exogenous aldehyde in live cells. Live T-47D cells were plated on a 24 well IBIDI plate in supplemented RPMI media and incubated for 24 h at 37^{o}C and 5% CO_2. Cells were then treated with 10 μM of probe **1a** and incubated for an additional 1 h. Cells were washed with PBS and incubated with increasing levels of propanal (1 μM, 10 μM, 25 μM, and 100 μM) for 1 h. Cells were immediately monitored for fluorescence increase with a microwell plate reader (kinetic run, ex. 485, em. 520).

Live cell monitoring of acetaldehyde levels through the addition of ethanol and ALDH2 inhibitor. Live T-47D cells were plated on glass bottomed 35 mm dishes in supplemented RPMI and incubated for 24 h. Cells were then incubated with 10 μM concentration of probe **1a** with or without ALDH2 inhibitor, DDZ (5 μM). After 1 h, the cells were washed once with PBS, then incubated with 10 mM ethanol for 1h. Prior to imaging, cells were stained with Cell Mask and incubated for 10 min. Cells were subsequently washed 3 times in cold PBS (5 min) and stained with 1 μg/mL Hoechst for 5 min. Cells were imaged on Leica SP8 confocal microscope and images were processed and analyzed using ImageJ software.

Live cell monitoring of endogenous aldehyde levels in the presence of ALDH2 activator and inhibitor. Live T-47D cells were plated on glass bottomed 8-well plates in supplemented RPMI media and incubated for 24 h. Cells were then treated DDZ (20 μM) or Alda-1 (50 μM). After 1 h, cells were cotreated with 10 μM of probe **1a** with or without DDZ (20 μM) or Alda-1 (50 μM). Cells were then stained with Cell Mask and incubated for 10 min. Cells were subsequently washed 3 times with PBS (5 min) and stained with 1 μg/mL Hoechst for 5 min. Cells were then placed in fresh supplemented RPMI media and imaged on Leica SP8 confocal microscope. The images were processed and analyzed using ImageJ software to determine pixel intensity per cell. Data was normalized to probe **1a** only wells to show increases and decreases in intensity signal from DDZ and Alda-1, respectively.

Flow cytometry analysis of cell death by probe 1c. T-47D cells were incubated with 15 μM of probe **1c** for 2 h with equal amounts of DMSO as control. Cells were then detached with trypsin and stained using Annexin V/PI following manufacturer's protocol. To avoid fluorescent crosstalk, Annexin V (AV) conjugated to FITC was used to determined apoptosis. Propidium Iodide (PI) was used to determine necrosis within the cellular populations. Cells were analyzed via flow cytometry within 1 h to quantify cell death. FlowJo software was used to analyze the cytometry data. PI and AV controls were used to determine quadrant placement. All the experiments were performed in triplicate.

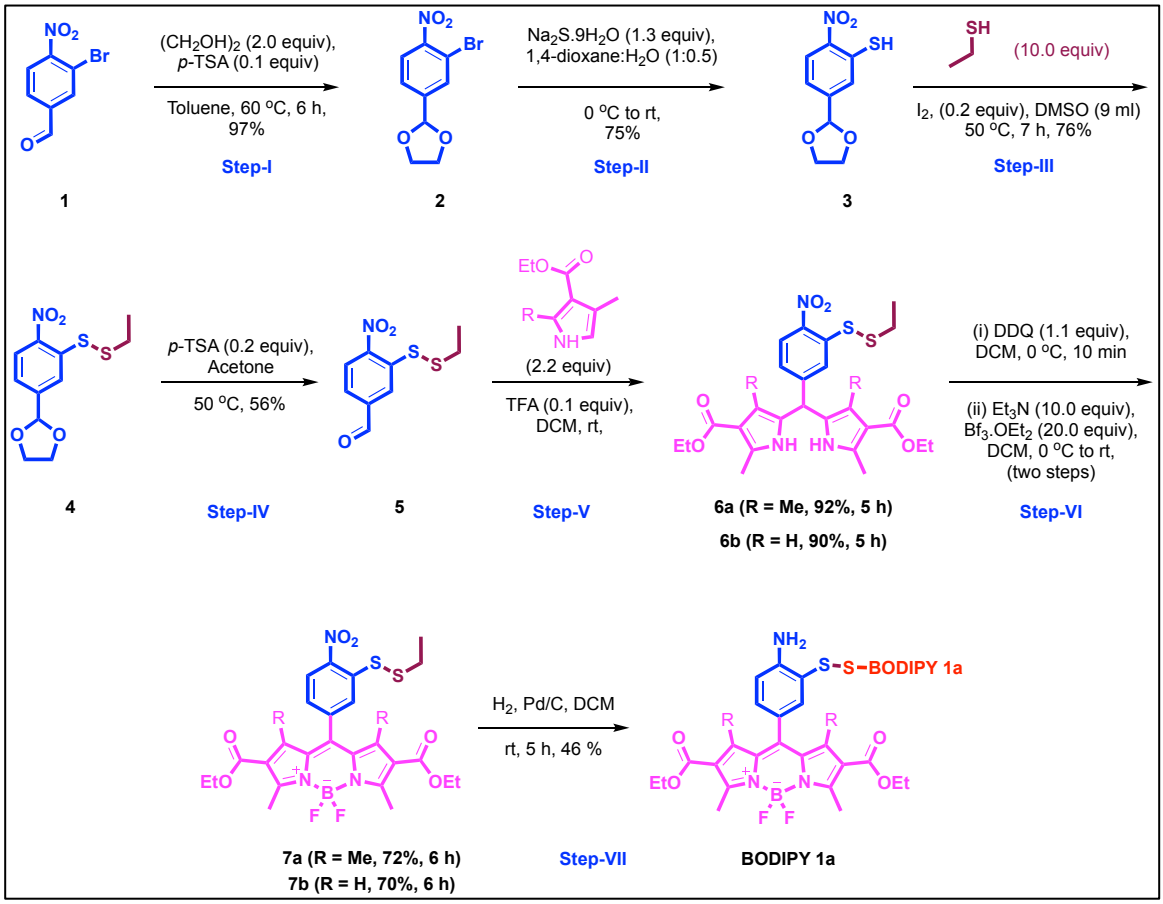
Cellular monitoring of exogenous aldehydes with probe 1c. T-47D cells were plated in 6 cm culture dishes and incubated for 24 h. Cells were treated with 20 μM or 100 μM propanal for 1 h before being washed with PBS. 15 μM of probe **1c** in media was added to cells and incubated for an additional 1 h. Cells were then fixed with methanol and

mounted with fluoroshield mounting media with DAPI. Cells were then imaged on the Leica Stellaris 8 confocal microscope.

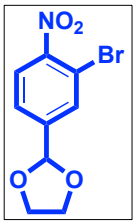
Live organoid monitoring of endogenous aldehyde levels in the presence of ALDH2 activator and inhibitor. Live murine biliary organoids were retrieved from extracellular matrix through above protocol. Organoids were pretreated with 20 µM DDZ and 10 mM of ethanol or 50 µM Alda-1 for 1 h. Organoids were then cotreat with 15 µM probe **1c** with or without 20 µM DDZ and 10 mM of ethanol or 50 µM Alda-1 for 4 h. Subsequently, organoids were treated with Cell Mask 488 and incubated for 10 mins followed by 3 PBS washes before Hoechst staining for 5 min. Organoids were placed in fresh media and imaged on Lecia Stellaris confocal microscope. Average pixel intensity of z stacks was determined and plotted for 20 organoids of each trial.

Probe 1c efficiency inside mouse lung tissue. Freshly excised mouse lungs were obtained and placed into 15 µM of probe **1c** in PBS. Tissues were gently rocked at 4 ^{o}C in the dark for 6 h or 24 h. Tissues were removed from treatment and snap frozen. Frozen samples were submitted to Emory Cancer Tissue and Pathology core for sectioning. Sectioned samples were imaged on the Leica Stellaris confocal microscope.

IX. Supplementary Figure 1. a) Synthesis of Probe 1a and product with aldehyde 2a.



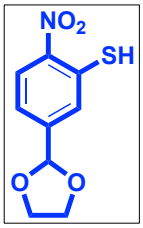
Representative procedure for the synthesis of 2-(3-Bromo-4-nitrophenyl)-1,3-dioxolane (Figure S1a, step I):



An oven-dried 100 mL RB flask was charged with 2-bromo-4-nitro benzaldehyde (1.0 equiv), ethylene glycol 2 mL, *p*-TSA (0.1 equiv) in 10 mL dry toluene at rt. The reaction mixture kept stirring at 60 ^{o}C for 6 h. The reaction progress was monitored by the TLC. Upon completion, the reaction mixture was quenched with water and extracted with ethyl acetate. The organic extracts were combined, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (5:1) as eluent to afford protected aldehyde. This compound was isolated as colorless thick oil with 97% yield.

R_f = 0.5 (1/1 = EtOAc /Hexane).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (m, 1H), 7.84 (d, *J* = 1.6 Hz, 1H), 5.85 (m, 1H), 4.09 (m, 4H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 149.9, 144.0, 133.0, 126.3, 125.6, 114.4, 101.4, 65.4.
HRMS (ESI): $[M]^+$ Calcd for $[C_9H_8BrNO_4]$ 272.9636, found 272.9630.

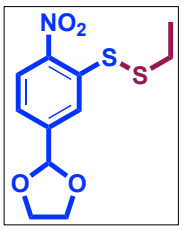
Representative procedure for the synthesis of 5-(1,3-Dioxolan-2-yl)-2-nitrobenzenethiol (Figure S1a, step II):



An oven-dried 100 mL RB flask was charged with protected aldehyde (1.0 equiv) in 10 mL1,4-dioxane and 5 ml H_2O placed at 0 °C. Then, sodium sulfide nonahydrate (1.3 equiv) was added portion wise at the same temperature and stirred for 20 h at rt. The reaction progress was monitored by the TLC. Upon completion, the reaction mixture was quenched with dil. HCl slowly and extracted with ethyl acetate. The organic extracts were combined, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (5:2) as eluent to afford thiol adduct. This compound was isolated as colorless thick oil with 75% yield.

R_f = 0.4 (1/1 = EtOAc /Hexane).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (m, 1H), 7.72 (m, 1H), 7.5 (m, 1H), 5.81 (m, 1H), 4.08 (m, 4H).
^{13}C NMR (100 MHz, $CDCl_3$): δ149.6, 139.6, 135.0, 131.2, 123.7, 114.7, 101.5, 4.08.
HRMS (ESI): $[M+H]^+$ Calcd for $[C_9H_{10}NO_4S]$ 227.0252, found 228.02555.

Representative procedure for the synthesis of 2-(3-(Ethyldisulfaneyl)-4-nitrophenyl)-1,3-dioxolane (Figure S1a, step III):

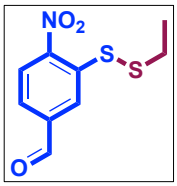


The compound thiol adduct was dissolved in DMSO and added ethanethiol (10.0 equiv), I_2 (0.1 equiv), and stirred at 50 °C for 7 h. The reaction progress was monitored by the TLC. Upon completion, the reaction mixture was quenched with ice cold water and extracted with ethyl acetate. The organic extracts were combined, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was

purified by silica gel column chromatography using hexane/ethyl acetate (5:2) as eluent to afford ethanethiol disulfide adduct. This compound was isolated as colorless thick oil with 76% yield.

R_f = 0.6 (1/1 = EtOAc /Hexane).
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.40 (s, 1H), 8.25 (d, *J* = 8.4 Hz, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 5.9 (s, 1H), 4.11 (d, *J* = 4.8 Hz, 4H), 2.77 (q, *J* = 7.6 Hz, 2H), 1.32 (t, *J* = 7.2 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 145.6, 144.4, 138.2, 126.3, 125.4, 124.0, 102.2, 65.5, 32.3, 14.3.

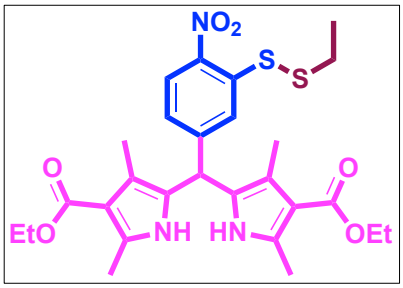
Representative procedure for the synthesis of 3-(Ethyldisulfaneyl)-4-nitrobenzaldehyde (Figure S1a, Step IV):



The ethanethiol disulfide adduct was dissolved in acetone, and *p*-TSA (1.0 equiv) was introduced at rt. Then, the reaction mixture stirred for 8 h at 50 °C. The reaction progress was monitored by the TLC. Upon completion, the crude reaction mixture concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (5:3) as eluent to afford aldehyde. This compound was isolated as colorless thick oil with 56% yield.

R_f = 0.6 (1/1 = EtOAc/Hexane).
^{1}H NMR (400 MHz, $CDCl_3$): δ 10.1 (d, *J* = 1.2 Hz, 1H), 8.8 (t, *J* = 2.0 Hz, 1H), 8.38 (dd, *J* = 1.6, 8.4 Hz, 1H), 7.82 (m, 1H), 2.79 (m, 2H), 1.34 (m, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 190.6, 148.2, 139.0, 128.8, 126.8, 126.1, 116.7, 32.3, 14.0.
HRMS (ESI): $[M+H]^+$ Calcd for $[C_9H_{10}NO_4S]$ 243.0021, found 243.0022.

Representative procedure for the synthesis of diethyl 5,5'-((3-(ethyldisulfaneyl)-4-nitrophenyl)methylene) bis(2,4-dimethyl-1H-pyrrole-3-carboxylate) (Figure S1a, step V):



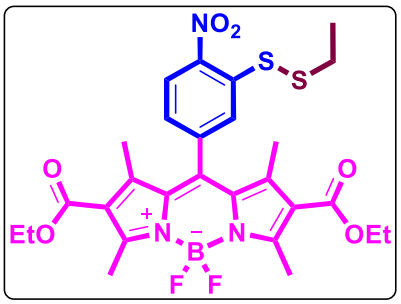
An oven-dried 100 mL RB flask was charged with aldehyde (1.0 equiv), methyl pyrrole (2.2 equiv), TFA (0.1 equiv) in 15 mL dry DCM at rt. The reaction mixture kept stirring at rt for 5 h. The reaction progress was monitored by the TLC. Upon completion, the reaction mixture was quenched with water and extracted with ethyl acetate. The organic extracts were combined, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (5:1) as eluent to afford conjugated adduct. This compound was isolated as yellow solid with 92% yield.

R_f = 0.5 (1:1 = EtOAc/Hexane).
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (s, 1H), 8.12 (s, 2H), 7.89 (S, 1H), 7.09 (d, *J* = 8.4 Hz, 1H), 5.63 (s, 1H), 4.23 (q, *J* = 7.2 Hz, 2H), 2.43 (s, 6H), 2.09 (s, 6H), 1.34 (t, *J* = 7.2 Hz, 6H), 2.53 (q, *J* = 7.2 Hz, 2H), 1.15 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 166.1, 148.3, 143.8, 138.9, 135.9, 135.3, 126.7, 126.6, 126.1, 124.0, 118.2, 111.7, 59.2, 39.2, 14.4, 13.9, 13.8, 11.1.
HRMS (ESI): $[M]^+$ Calcd for $[C_{27}H_{33}N_3O_6S_2]$ 559.1811, found 559.1810.

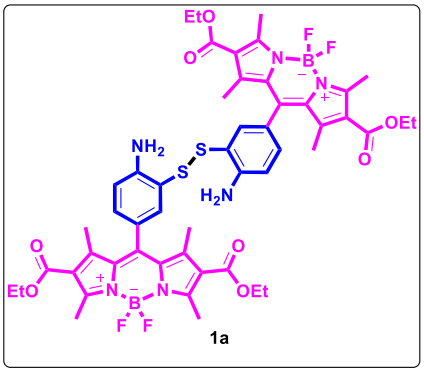
Representative procedure for the synthesis of diethyl 10-(3-(ethyldisulfaneyl)-4-nitrophenyl)-5,5-difluoro-1,3,7,9-tetramethyl-5H-4l4,5l4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinine-2,8-dicarboxylate (Figure S1a, Step VI):

An oven-dried 100 mL RB flask was charged with conjugated adduct (1.0 equiv) in 30



mL dry DCM at 0 °C. Then, DDQ (1.1 equiv) was added portion wise at the same temperature and stirred for 10 min. The reaction progress was monitored by the TLC. Upon completion, Et_3N (10 equiv) was added into the same reaction mixture. The reaction mixture was stirred at 0 °C for 1 hour, followed by the addition of $BF_3.OEt_2$ (20 equiv) and stirring for additional 5 h. The reaction progress was monitored by TLC. Upon completion, the reaction mixture was quenched with dil. $NaHCO_3$ and extracted with DCM. The organic extracts were combined, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (5:2) as eluent to afford BODIPY adduct. This compound was isolated as yellow solid with 72% yield.
$\mathbf{R_f}$ = 0.5 (5:3 = EtOAc/Hexane).
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.47 (d, J = 8.4 Hz, 1H), 8.27 (d, J = 2.0 Hz, 1H), 7.32 (dq, J = 8.4, 1.6 Hz, 1H), 4.30 (q, J = 7.2 Hz, 4H), 2.86 (s, 6H), 2.72 (q, J = 7.2 Hz, 2 H), 1.70 (s, 6H), 1.37 (t, J = 2.8 Hz, 3H), 1.32 (t, J = 2.8 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 163.9, 160.6, 146.8, 146.0, 142.1, 140.5, 130.6, 127.3, 127.2, 125.7, 123.1, 60.5, 46.7, 32.6, 15.1 14.2, 14.0, 8.6.
^{11}B NMR (128 MHz, $CDCl_3$): δ 0.62 (t, J = 32.0 Hz).
^{19}F NMR (376 MHz, $CDCl_3$) δ -142.7 (dq, J = 33.8 Hz).
HRMS (ESI): $[M+H]^+$ Calcd for $[C_{27}H_{31}BF_2N_3O_6S_2]$ 605.1637, found 606.1639.

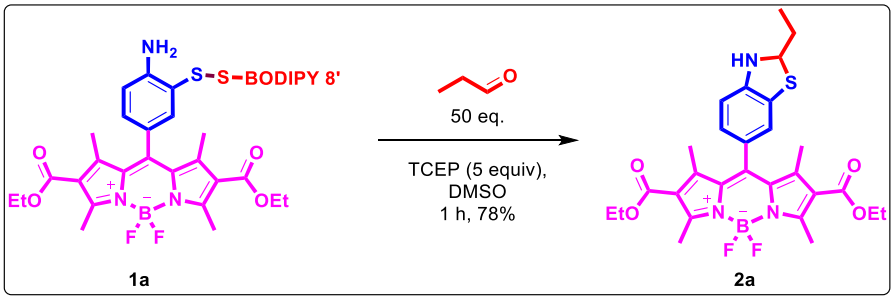
Representative procedure for the synthesis of Tetraethyl 10,10'-(disulfanediylbis(4-amino-3,1-phenylene))bis(5,5-difluoro-1,3,7,9-tetramethyl-5H-4l4,5l4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinine-2,8-dicarboxylate) 1a (Figure S1a, Step VII):



BODIPY adduct was taken in DCM (2 mL) followed by the addition of 10% Pd/C (0.01 mol%) under the argon atmosphere. The reaction mixture was stirred under hydrogen atmosphere for 5 h. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was filtered through celite pad and washed with DCM, concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using ethyl acetate/hexane (1:1) as an eluent to afford **1a.** This compound was isolated as dark red solid with 46 % yield.

R_f = 0.3 (1:1 = EtOAc/Hexane).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (s, 1H), 6.95 (d, *J* = 5.6 Hz, 1H), 6.81 (d, *J* = 5.6 Hz, 1H), 4.61 (s, 2H), 4.24 (q, *J* = 1.2 Hz, 4H), 2.78 (s, 6H), 1.28 (t, *J* = 4.8 Hz, 6H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 172.4, 164.1, 159.3, 149.4, 147.2, 144.7, 134.9, 131.7, 131.1, 127.7, 123.7, 122.4, 119.8, 116.09, 60.21, 14.9, 14.34, 14.24, 10.97.
^{11}B NMR (128 MHz, $CDCl_3$): δ 0.69 (t, *J* = 32.0 Hz).
^{19}F NMR (376 MHz, $CDCl_3$) δ -142.6 (dq, *J* = 63.6, 31.9, 13.9 Hz).
HRMS (ESI): [M-H] Calcd for [$C_{50}H_{53}B_2F_4N_6O_8S_2$] 1027.3489, found 1027.3423.

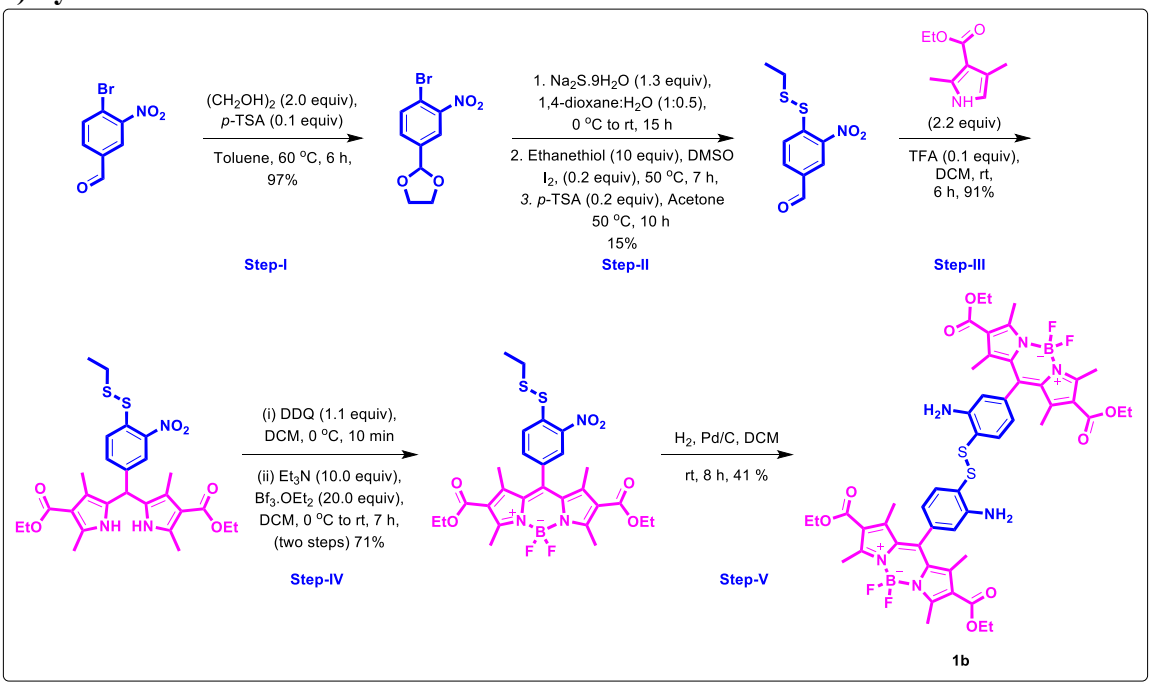
General procedure for the reaction of probe 1a with aldehydes.



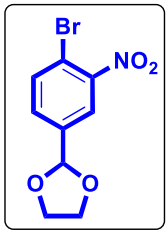
Representative procedure for the synthesis of 2a.
Compound **1a** was taken in THF (2 mL) followed by the addition of TCEP (5.0 equiv) and propionaldehyde (50 equiv). The reaction mixture was stirred for 1 h. The progress of the reaction was monitored by TLC. Upon completion, the reaction mixture was quenched with water and extracted with ethyl acetate. The organic extracts were combined, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (5:1) as eluent to afford **2a** 78% yield.

R_f = 0.4 (1/1 = EtOAc /Hexane).
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.90 (d, *J* = 1.6 Hz, 1H), 7 (d, *J* = 1.6 Hz, 1H), 6.73 (d, *J* = 1.6 Hz, 1H), 4.38 (t, *J* = 6.0 Hz, 1H), 4.4 (s, 1H), 4.32 (q, *J* = 7.2 Hz, 4H), 2.84 (s, 6H), 1.94 (q, *J* = 6.8 Hz, 2H), 1.89 (s, 3H), 1.87 (s, 3H), 1.35 (t, *J* = 7.2 Hz, 6H), 1.05 (t, *J* = 7.2 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 164.4, 159.1, 159.0, 148.0, 147.6, 146.4, 131.9, 128.3, 125.5, 124.8, 122.3, 121.1, 109.7, 70.2, 60.2, 32.0, 14.9, 14.3, 14.1, 9.8.
^{11}B NMR (128 MHz, $CDCl_3$): δ 0.73 (t, *J* = 31.9 Hz).
^{19}F NMR (376 MHz, $CDCl_3$) δ -142.7 (dq, *J* = 63.9, 33.8, 11.2 Hz).
HRMS (ESI): $[M+H]^+$ Calcd for [$C_{28}H_{32}BF_2N_3O_4S$] 556.2253, found 556.2255.

b) Synthesis of Probe 1b.



Representative procedure for the synthesis of 2-(4-bromo-3-nitrophenyl)-1,3-dioxolane (Figure S1b, step I):



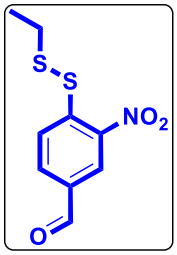
An oven-dried 100 mL RB flask was charged with 4-bromo-3-nitro benzaldehyde (1.0 equiv), ethylene glycol 2 mL, *p*-TSA (0.1 equiv) in 10 mL dry toluene at rt. The reaction mixture kept stirring at 60 °C for 6 h. The reaction progress was monitored by the TLC. Upon completion, the reaction mixture was quenched with water and extracted with ethyl acetate. The organic extracts were combined, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (5:1) as eluent to afford protected aldehyde. This compound was isolated as colorless thick oil with 97% yield.

$\mathbf{R}_f$ = 0.5 (1/1 = EtOAc /Hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (dt, *J* = 6.2, 2.5 Hz, 1H), 7.78 – 7.69 (m, 1H), 7.53 (td, *J* = 5.3, 2.5 Hz, 1H), 5.81 (dt, *J* = 5.8, 2.9 Hz, 1H), 4.15 – 3.96 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 149.6, 139.6, 135.0, 131.2, 123.7, 114.7, 101.5, 65.5.

HRMS (ESI): $[M]^+$ Calcd for $[C_9H_8BrNO_4]$ 272.9637, found 272.9630.



Representative procedure for the synthesis of 4-(ethyldisulfaneyl)-3-nitrobenzaldehyde (Figure S1b, Step II):

(I) An oven-dried 100 mL RB flask was charged with protected aldehyde (1.0 equiv) in 10 mL 1,4-dioxane and 5 ml H_2O placed at 0 °C. Then, sodium sulfide nonahydrate (1.3 equiv) was added portion wise at the same temperature and stirred for 15 h at rt. The reaction progress was monitored by the TLC. Upon completion, the reaction mixture was quenched with dil. HCl slowly and extracted with ethyl acetate. The

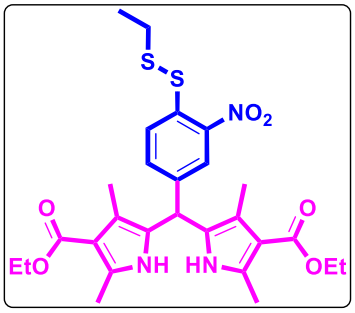
organic extracts were combined, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure, and then proceeded directly to the next step.

(II) The crude thiol adduct was dissolved in DMSO and added ethanethiol (10.0 equiv), I_2 (0.1 equiv), and stirred at 50 °C for 7 h. The reaction progress was monitored by the TLC. Upon completion, the reaction mixture was quenched with ice cold water and extracted with ethyl acetate. The organic extracts were combined, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure, and then proceeded directly to the next step.

(III) The ethanethiol disulfide crude adduct was dissolved in acetone, and *p*-TSA (0.2 equiv) was introduced at rt. Then, the reaction mixture stirred for 10 h at 50 °C. The reaction progress was monitored by the TLC. Upon completion, the crude reaction mixture concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (5:3) as eluent to afford aldehyde. This compound was isolated as pale-yellow thick oil with 15% yield.

R_f = 0.6 (1/1 = EtOAc/Hexane).
^{1}H NMR (400 MHz, $CDCl_3$): δ 10.08 (s, 1H), 8.74 (d, *J* = 1.8 Hz, 1H), 8.52 (d, *J* = 8.5 Hz, 1H), 8.17 (dd, *J* = 8.4, 1.8 Hz, 1H), 2.83 (q, *J* = 7.4 Hz, 2H), 1.37 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 189.0, 145.8, 134.2, 132.4, 128.3, 127.8, 32.4, 14.3.
HRMS (ESI): $[M+H]^+$ Calcd for $[C_9H_{10}NO_3S_2]$ 244.0024, found 244.0048.

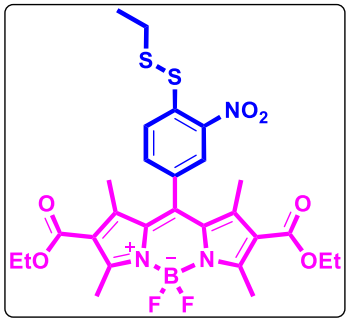
Representative procedure for the synthesis of diethyl 5,5'-((4-(ethyldisulfaneyl)-3-nitrophenyl)methylene)bis(2,4-dimethyl-1H-pyrrole-3-carboxylate) (Figure S1b, step III):



An oven-dried 100 mL RB flask was charged with aldehyde (1.0 equiv), dimethyl pyrrole (2.2 equiv), TFA (0.1 equiv) in 15 mL dry DCM at rt. The reaction mixture kept stirring at rt for 6 h. The reaction progress was monitored by the TLC. Upon completion, the reaction mixture was quenched with water and extracted with ethyl acetate. The organic extracts were combined, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (5:1) as eluent to afford conjugated adduct. This compound was isolated as yellow solid with 91% yield.

R_f = 0.5 (1:1 = EtOAc/Hexane).
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 – 8.16 (m, 3H), 7.93 (dd, *J* = 2.0, 0.8 Hz, 1H), 7.44 (dd, *J* = 8.5, 2.0 Hz, 1H), 5.59 (s, 1H), 4.20 (q, *J* = 7.1 Hz, 4H), 2.75 (q, *J* = 7.3 Hz, 2H), 2.40 (s, 6H), 2.07 (s, 6H), 1.35 – 1.32 (m, 6H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 166.3, 145.4, 140.1, 136.7, 135.3, 134.0, 127.6, 125.3, 124.1, 118.0, 111.6, 59.2, 38.2, 32.3, 14.4, 14.3, 14.0, 11.1.
HRMS (ESI): $[M]^+$ Calcd for $[C_{27}H_{33}N_3O_6S_2]$ 559.1811, found 559.1810.

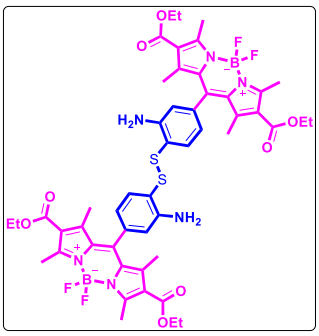
Representative procedure for the synthesis of diethyl 10-(4-(ethyldisulfaneyl)-3-nitrophenyl)-5,5-difluoro-1,3,7,9-tetramethyl-5H-4l4,5l4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinine-2,8-dicarboxylate (Figure S1b, Step IV):



An oven-dried 100 mL RB flask was charged with conjugated adduct (1.0 equiv) in 30 mL dry DCM at 0 °C. Then, DDQ (1.1 equiv) was added portion wise at the same temperature and stirred for 10 min. The reaction progress was monitored by the TLC. Upon completion, Et_3N (10 equiv) was added into the same reaction mixture. The reaction mixture was stirred at 0 °C for 1 h, followed by the addition of $BF_3.OEt_2$ (20 equiv) and stirring for additional 5 h. The reaction progress was monitored by TLC. Upon completion, the reaction mixture was quenched with dil. $NaHCO_3$ and extracted with DCM. The organic extracts were combined, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (5:2) as eluent to afford BODIPY adduct. This compound was isolated as yellow solid with 71% yield.

R_f = 0.5 (5:3 = EtOAc/Hexane).
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (d, *J* = 8.4 Hz, 1H), 8.27 (d, *J* = 2.0 Hz, 1H), 7.62 (dd, *J* = 8.4, 1.9 Hz, 1H), 4.31 (q, *J* = 7.1 Hz, 4H), 2.86 (s, 6H), 1.72 (s, 6H), 1.36 (d, *J* = 7.5 Hz, 6H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 163.9, 160.6, 146.8, 146.1, 141.3, 140.6, 133.3, 132.4, 131.2, 128.9, 125.8, 123.1, 60.4, 32.7, 15.1, 14.4, 14.4, 14.2.
^{11}B NMR (128 MHz, $CDCl_3$): δ 0.66 (t, *J* = 32.0 Hz).
^{19}F NMR (376 MHz, $CDCl_3$) δ -142.7 (dq, *J* = 11.2, 33.8, 63.9 Hz).
HRMS (ESI): $[M]^+$ Calcd for $[C_{27}H_{30}BF_2N_3O_6S_2]$ 605.1637, found 605.1640.

Representative procedure for the synthesis of diethyl 10-(3-amino-4-((2-amino-4-(2,8-bis(ethoxycarbonyl)-5,5-difluoro-1,3,7,9-tetramethyl-5H-4l4,5l4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl)phenyl)disulfaneyl)phenyl)-5,5-difluoro-1,3,7,9-tetramethyl-5H-4l4,5l4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinine-2,8-dicarboxylate1b (Figure S1b, Step V):



BODIPY adduct was taken in DCM (2 mL) followed by the addition of 10% Pd/C (0.01 mol%) under argon atmosphere. The reaction mixture was stirred under hydrogen atmosphere for 8 h. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was filtered through celite pad and washed with DCM, concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using ethyl acetate/hexane (1:1) as an eluent to afford **1a.** This compound was isolated as dark red with 41 % yield.

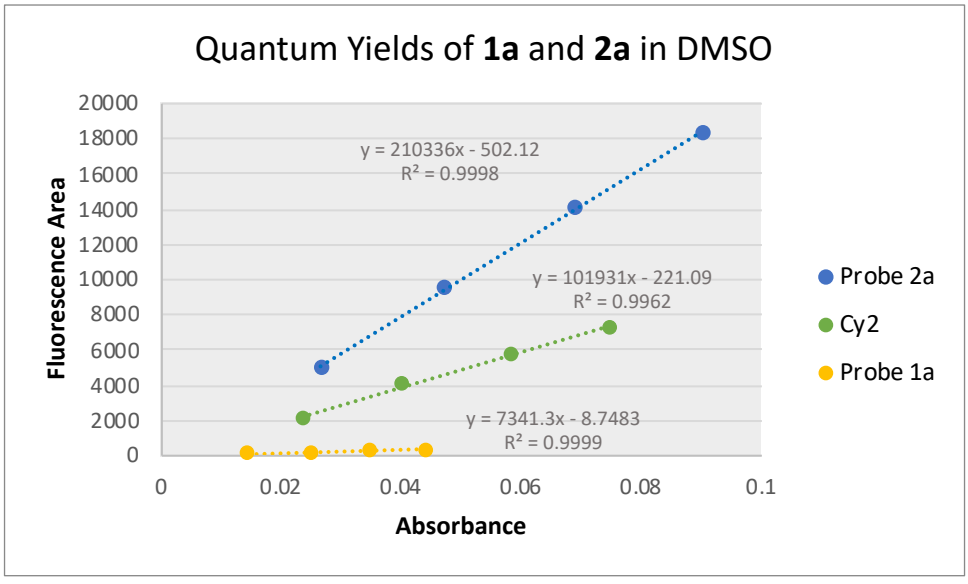
R_f = 0.3 (1:1 s= EtOAc/Hexane).

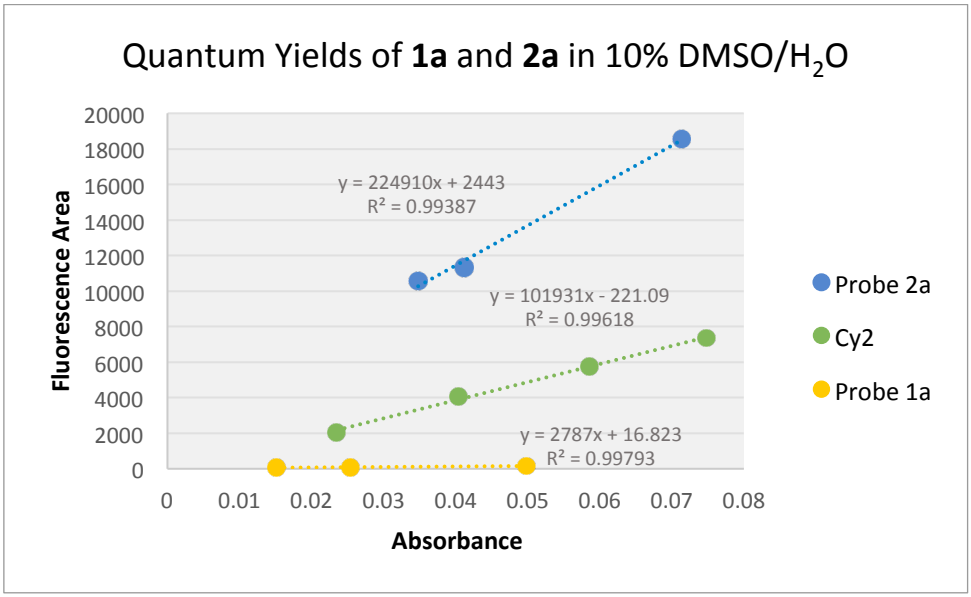
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (d, *J* = 1.9 Hz, 1H), 6.97 – 6.92 (m, 1H), 6.81 (dd, *J* = 8.3, 1.4 Hz, 1H), 4.61 (s, 2H), 4.29 – 4.20 (m, 4H), 2.79 (s, 6H), 1.73 (s, 6H), 1.29 (t, *J* = 7.1 Hz, 6H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 172.49, 164.17, 159.35, 149.45, 147.21, 144.77, 134.99, 131.78, 131.16, 123.70, 122.40, 119.82, 116.10, 60.21, 14.98, 14.34, 14.24, 10.98.
^{11}B NMR (128 MHz, $CDCl_3$): δ 0.69 (t, *J* = 32.0 Hz)
^{19}F NMR (376 MHz, $CDCl_3$): δ -142.67 (dq, *J* = 63.6, 31.8, 13.9 Hz).
HRMS (ESI): [M-H] Calcd for $[C_{50}H_{54}B_2F_4N_6O_8S_2]$ 1027.3489, found 1027.3480.

X. Supplementary Figure 2: Quantum yield determination of probe 1a. Quantum yield was calculated using the area under the curve of fluorescence versus absorption. Absorption was measured with a Cary 3500 UV-Vis utilizing the samples at using four separate concentrations with values being divided by ten for accurate analysis. Fluorescence area was measured with a Cary Eclipse fluorimeter using the same samples above with a 10X dilution. All measurements were run in triplicate. Quantum yields of probe **1a** and the corresponding propanal product (probe **2a**) were determined using Cy2 as a reference compound. The following equation was used to calculate quantum yield:

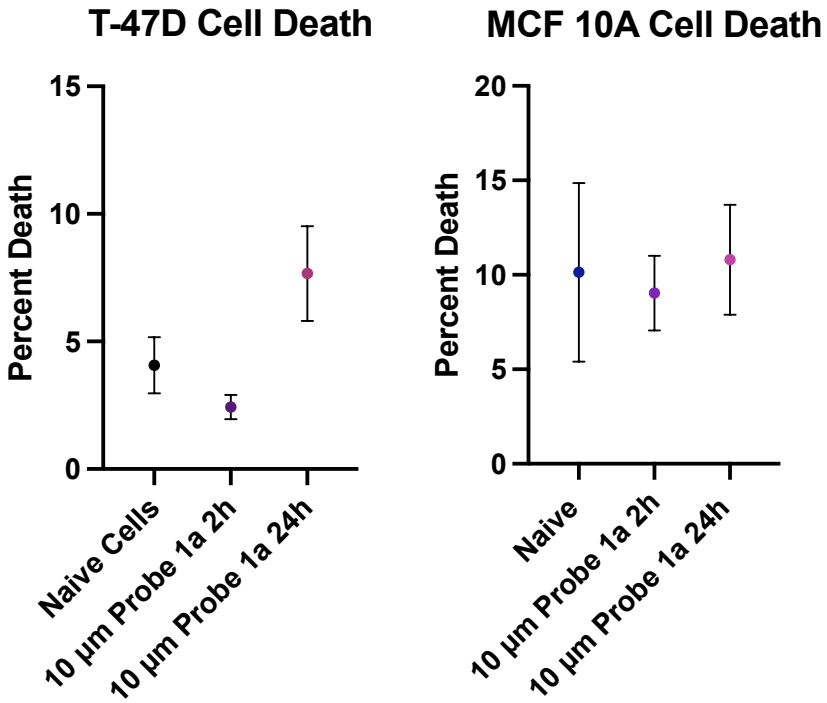
$$Q = Q_r \times \frac{m}{m_r} \times (\frac{n}{n_r})^2$$

Q is the quantum yield; m is the slope of the line described above; n is the refractive index of the solvent. Subscript r denotes the appropriate values for the reference (Cy2).

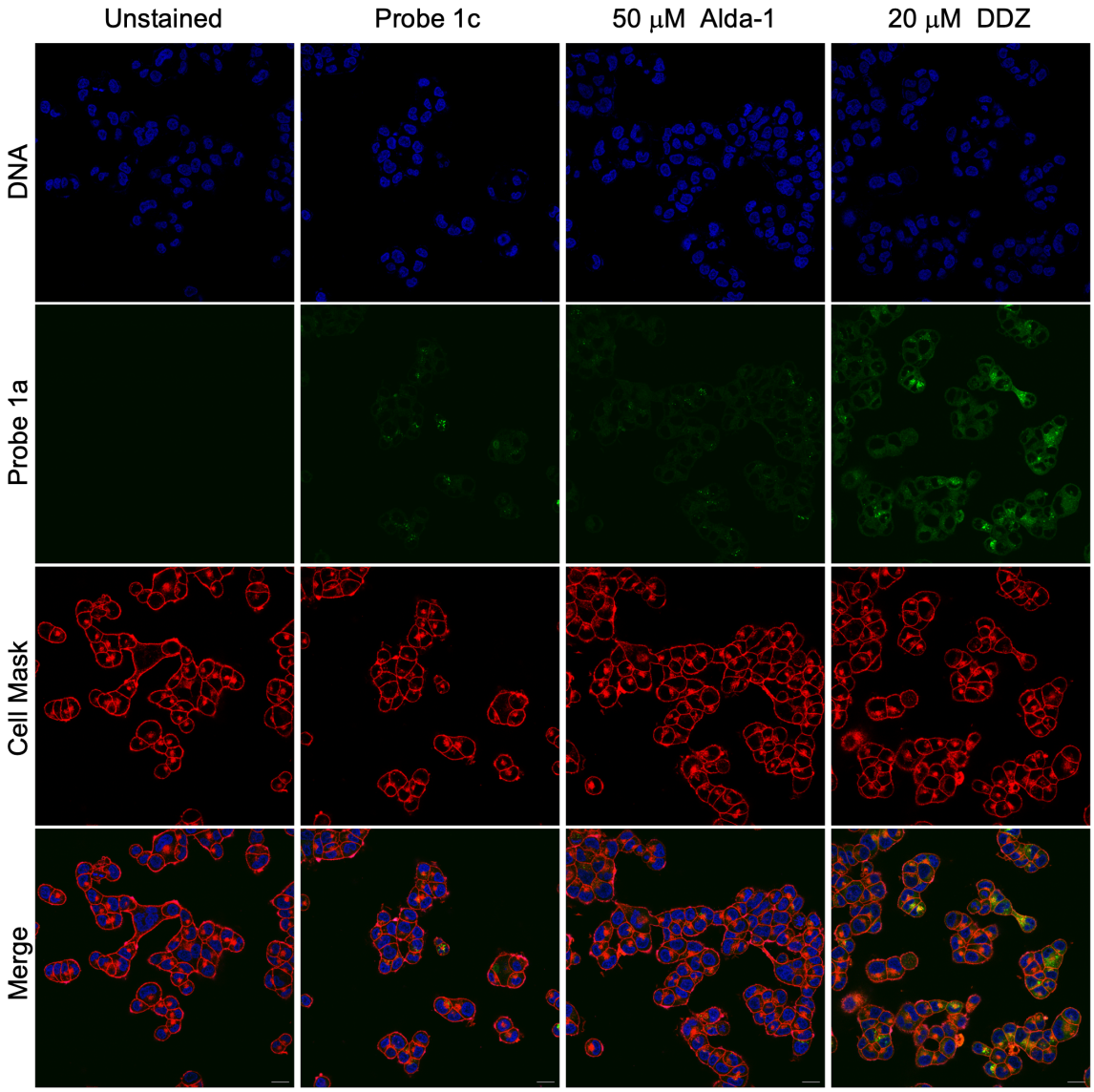




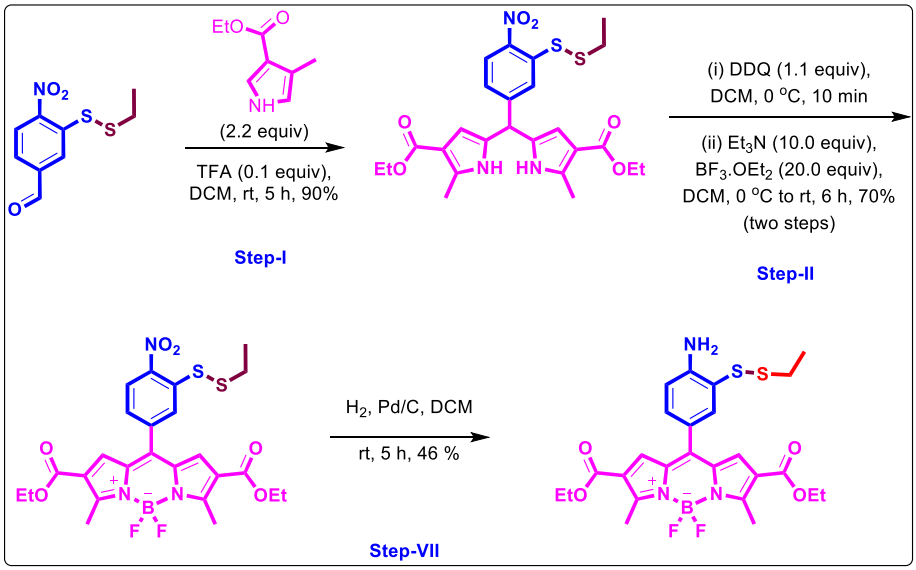
XI. Supplementary Figure 3: Flow cytometry analysis of cell death by probe 1a. Cell death of T-47D cells treated with probe **1a** (10 µM) for 2 h and 24 h. Cell death of MCF 10A cells treated with probe **1a** (10 µM) for 2h and 24 h. All the experiments showed no increase in cell death as compared to naïve cells.



XII. Supplementary Figure 4: Live cell monitoring of endogenous aldehyde levels in the presence of ALDH2 activator and inhibitor. Cells were treated with 10 μM of probe **1a** with or without DDZ (20 μM) or Alda-1 (50 μM). Average pixel intensity per area shows that the addition of DDZ increases pixel intensity, while the addition of Alda-1 decreases signal. These results are as expected in relation to the concentration of available aldehydes in the cells.

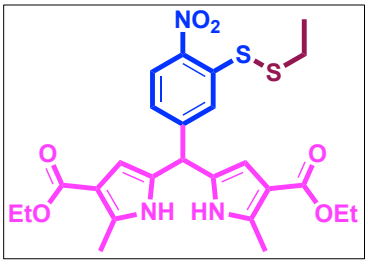


XIII. Supplementary Figure 5: Synthesis of Probe 1c.



Representative procedures for the synthesis of 3-(Ethyldisulfaneyl)-4-nitrobenzaldehyde (Step I-IV) is same as in Figure 1.

Representative procedure for the synthesis of diethyl 5,5'-((3-(ethyldisulfaneyl)-4-nitrophenyl)methylene)bis(2-methyl-1H-pyrrole-3-carboxylate) (Figure S6, step V):



An oven-dried 100 mL RB flask was charged with aldehyde (1.0 equiv), pyrrole (2.2 equiv), TFA (0.1 equiv) in 15 mL dry DCM at rt. The reaction mixture kept stirring at rt for 5 h. The reaction progress was monitored by the TLC. Upon completion, the reaction mixture was quenched with water and extracted with ethyl acetate. The organic extracts were combined, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (5:1) as eluent to afford conjugated adduct. This compound was isolated as yellow solid with 90% yield.

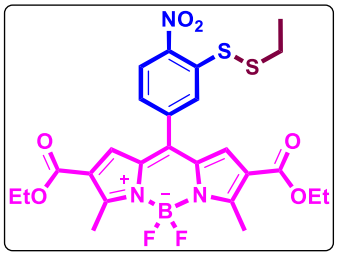
R_f = 0.5 (1:1 = EtOAc/Hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.67 (s, 2H), 8.13 (d, *J* = 8.4 Hz, 1H), 8.04 (d, *J* = 2.0 Hz, 1H), 7.14 (dd, *J* = 8.8, 2.0 Hz, 1H), 6.15 (d, *J* = 2.8 Hz, 2H), 5.42 (s, 1H), 4.23 (q, *J* = 6.8 Hz, 4H), 2.58 (q, *J* = 7.2 Hz, 2H), 2.46 (s, 6H), 1.31 (t, *J* = 7.2 Hz, 6H), 1.18 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 147.9, 144.1, 138.5, 136.1, 128.3, 127.0, 126.4, 126.1, 111.9, 109.7, 59.5, 43.2, 32.1, 14.4, 13.9, 13.2.

HRMS (ESI): $[M]^+$ Calcd for $[C_{25}H_{29}N_3O_6S_2]$ 531.1498, found 531.1493.

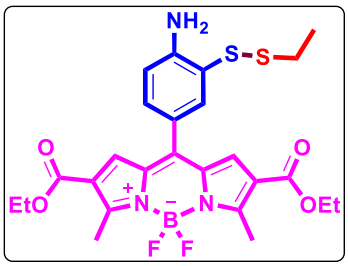
Representative procedure for the synthesis of diethyl 10-(3-(ethyldisulfaneyl)-4-nitrophenyl)-5,5-difluoro-3,7-dimethyl-5H-4l4,5l4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinine-2,8-dicarboxylate (Figure S6, Step VI):



An oven-dried 100 mL RB flask was charged with conjugated adduct (1.0 equiv) in 30 mL dry DCM at 0 °C. Then, DDQ (1.1 equiv) was added portion wise at the same temperature and stirred for 10 min. The reaction progress was monitored by the TLC. Upon completion, Et_3N (10 equiv) was added into the same reaction mixture. The reaction mixture was stirred at 0 °C for 1 hour, followed by the addition of $BF_3.OEt_2$ (20 equiv) and stirring for additional 5 h. The reaction progress was monitored by TLC. Upon completion, the reaction mixture was quenched with dil. $NaHCO_3$ and extracted with DCM. The organic extracts were combined, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (5:2) as eluent to afford BODIPY adduct. This compound was isolated as yellow solid with 70% yield.

R_f = 0.5 (5:3 = EtOAc/Hexane).
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.46 (d, *J* = 8.4 Hz, 1H), 8.42 (d, *J* = 1.6 Hz, 1H), 7.50 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.24 (s, 2H) 4.30 (q, *J* = 6.8 Hz, 4H), 2.97 (s, 6H), 2.79 (q, *J* = 7.2 Hz, 2 H), 1.35 (m, 6H), 1.33 (m, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 162.8, 162.5, 146.6, 142.9, 139.3, 138.3, 138.3, 133.0, 132.6, 127.5, 126.4, 124.3, 124.3, 60.6, 32.5, 14.7, 14.3.
^{11}B NMR (128 MHz, $CDCl_3$): δ 0.78 (t, *J* = 32 Hz).
^{19}F NMR (376 MHz, $CDCl_3$) δ -144.7 (dq, *J* = 62.2, 31.1, 16.3 Hz).
HRMS (ESI): $[M+H]^+$ Calcd for $[C_{25}H_{27}BF_2N_3O_6S_2]$ 578.1402, found 578.1401.

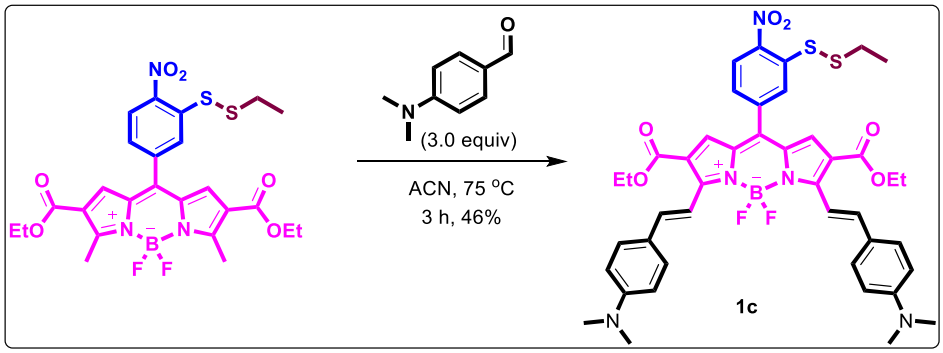
Representative procedure for the synthesis of diethyl 10-(4-amino-3-(ethyldisulfaneyl)phenyl)-5,5-difluoro-3,7-dimethyl-5H-4l4,5l4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinine-2,8-dicarboxylate (Figure S6, Step VII):



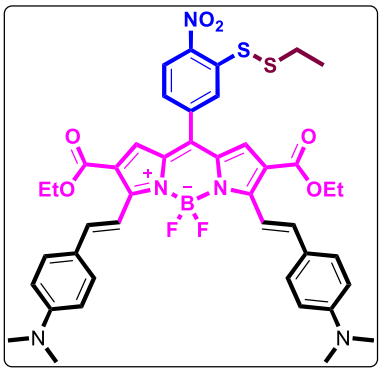
BODIPY adduct was taken in DCM (2 mL) followed by the addition of 10% Pd/C (0.01 mol%) under the argon atmosphere. The reaction mixture was stirred under hydrogen atmosphere for 5 h. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was filtered through celite pad and washed with DCM, concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using ethyl acetate/hexane (1:1) as an eluent**.** This compound was isolated as dark red with 46 % yield.

R_f = 0.3 (5:3 = EtOAc/Hexane).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (s, 1H), 6.95 (d, *J* = 5.6 Hz, 1H), 6.81 (d, *J* = 5.6 Hz, 1H), 4.61 (s, 2H), 4.24 (q, *J* = 1.2 Hz, 4H), 2.78 (s, 6H), 1.28 (t, *J* = 4.8 Hz, 6H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 172.4, 164.1, 159.3, 149.4, 147.2, 144.7, 134.9, 131.7, 131.1, 127.7, 12.4, 119.8, 116.09, 60.21, 14.9, 14.34, 14.24, 10.97.

^{11}B NMR (128 MHz, $CDCl_3$): δ 0.79 (t, *J* = 30.7 Hz).
^{19}F NMR (376 MHz, $CDCl_3$) δ -144.8 (q, *J* = 31.7 Hz).
HRMS (ESI): $[M+H]^+$ Calcd for $[C_{25}H_{28}BF_2N_3O_4S_2]$ 548.1660, found 548.1661.



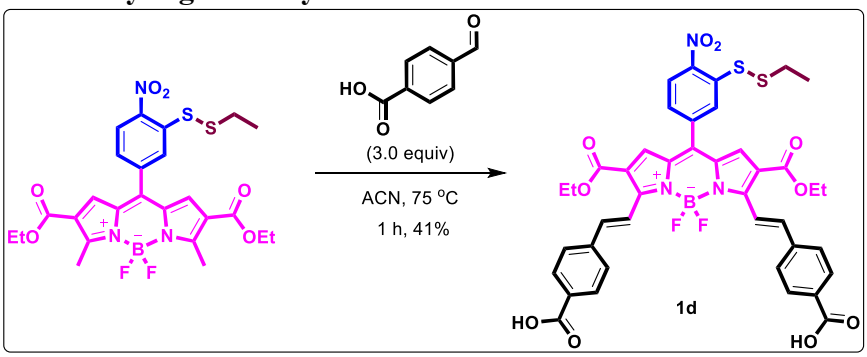
Representative procedure for the synthesis of Diethyl 10-(4-amino-3-(ethyldisulfaneyl)phenyl)-3,7-bis((E)-4-(dimethylamino)styryl)-5,5-difluoro-5H-4l4,5l4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinine-2,8-dicarboxylate (1c).



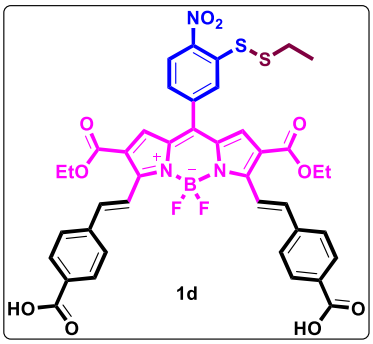
The dark red disulfide compound obtained from above synthesis was taken in ACN (2 mL) followed by the addition of aldehyde (5.0 equiv). The reaction mixture was stirred at 75 °C for 3 h. The progress of the reaction was monitored by TLC. Upon completion, the reaction mixture was quenched with water and extracted with ethyl acetate. The organic extracts were combined, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (1:1) as eluent**.** This compound **1c** was isolated as dark blue viscous compound with 46% yield.

R_f = 0.3 (5:3 = EtOAc/Hexane).
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (d, *J* = 16.8 Hz, 2H), 8.03 (m, 1H), 7.80 (d, *J* = 16.8 Hz, 2H), 7.65 (m, 4H), 7.40 (s, 2H), 7.36 (s, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 6.78 (m, 4H), 4.79 (s, 2H), 4.33 (q, *J* = 7.2 Hz, 4H), 3.07 (s, 2H), 2.84 (q, *J* = 7.2 Hz, 2H), 1.42 (t, *J* = 7.2 Hz, 3H), 1.36 (m, 6H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 163.8, 163.6, 157.8, 156.4, 151.6, 150.0, 144.11, 144.1, 142.5, 137.4, 135.8, 134.2, 133.4, 132.6, 130.3, 130.0, 126.0, 125.1, 124.1, 123.5, 122.1, 119.2, 115.1, 112.5, 112.0, 60.7, 60.1, 40.2, 32.3, 14.4, 14.4, 14.0.
^{11}B NMR (128 MHz, $CDCl_3$): δ 1.24 (t, *J* = 32.5 Hz).
^{19}F NMR (376 MHz, $CDCl_3$): δ -144.8 (dq, *J* = 62.2, 31.1, 16.3 Hz).
HRMS (ESI): $[M]^+$ Calcd for $[C_{43}H_{46}BF_2N_5O_4S_2]$ 809.3052, found 809.3052.

XIV. Supplementary Figure 6: Synthesis of Probe 1d.



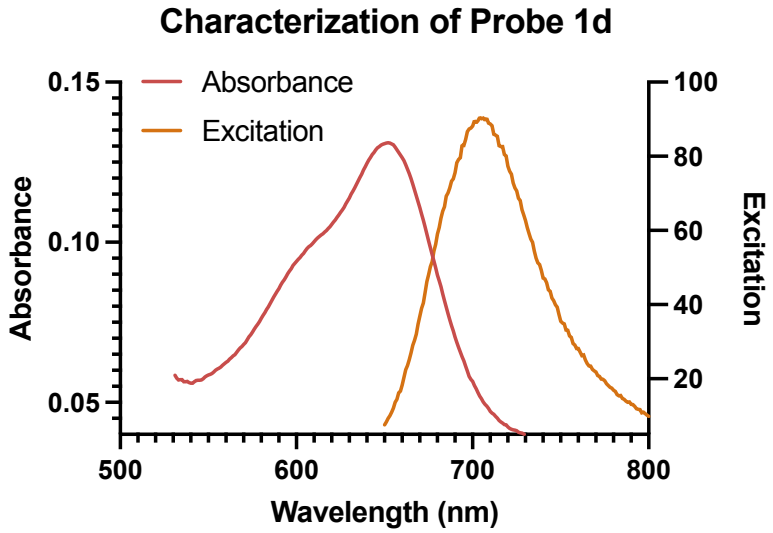
Representative procedure for the synthesis of 4,4'-((1E,1'E)-(10-(4-amino-3-(ethyldisulfaneyl)phenyl)-2,8-bis(ethoxycarbonyl)-5,5-difluoro-5H-4l4,5l4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinine-3,7-diyl)bis(ethene-2,1-diyl))dibenzoic acid (1d).



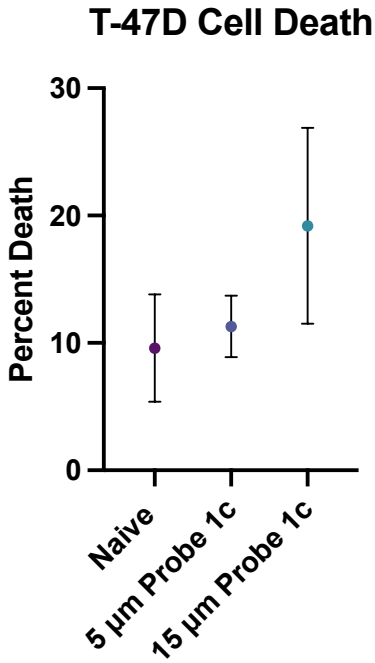
The dark red disulfide compound obtained from above synthesis was taken in ACN (2 mL) followed by the addition of aldehyde (5.0 equiv). The reaction mixture was stirred at 75 °C for 1 h. The progress of the reaction was monitored by TLC. Upon completion, the reaction mixture was quenched with water and extracted with DCM. The organic extracts were combined, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using DCM/MeOH**.** The compound **1d** was isolated as dark blue solid with 41% yield.

R_f = 0.3 (5:3 = MeOH/DCM).
^{1}H NMR (400 MHz, DMSO-d_6): δ 8.08 (s, 1H), 8.04 (d, *J* = 8.0 Hz, 4H), 7.80 (d, *J* = 16.4 Hz, 2H), 7.71 (d, *J* = 6.8 Hz, 4H), 7.50 (m, 3H), 6.98 (d, *J* = 8.0 Hz, 1H), 6.74 (s, 2H), 4.27 (q, *J* = 6.8 Hz, 4H), 2.84 (q, *J* = 7.2 Hz, 2H), 1.31 (t, *J* = 7.2 Hz, 3H), 1.26 (t, *J* = 6.8 Hz, 6H).
^{13}C NMR (100 MHz, DMSO-d_6): δ 167.6, 167.4, 165.3, 163.2, 153.6, 152.3, 148.2, 145.7, 143.6, 140.6, 140.2, 138.4, 137.3, 136.1, 134.1, 133.7, 132.6, 132.0, 130.4, 129.0, 127.8, 126.1, 123.7, 123.0, 121.1, 119.2, 118.2, 115.5, 61.1, 59.2, 32.0, 14.6, 14.5.
^{11}B NMR (128 MHz, $CDCl_3$): δ 1.15 (t, *J* = 32.7 Hz).
^{19}F NMR (376 MHz, $CDCl_3$) δ -144.8 (q, *J* = 32.6 Hz).
HRMS (ESI): $[M]^+$ Calcd for $[C_{41}H_{36}BF_2N_3O_8S_2]$ 811.2005, found 811.2007.

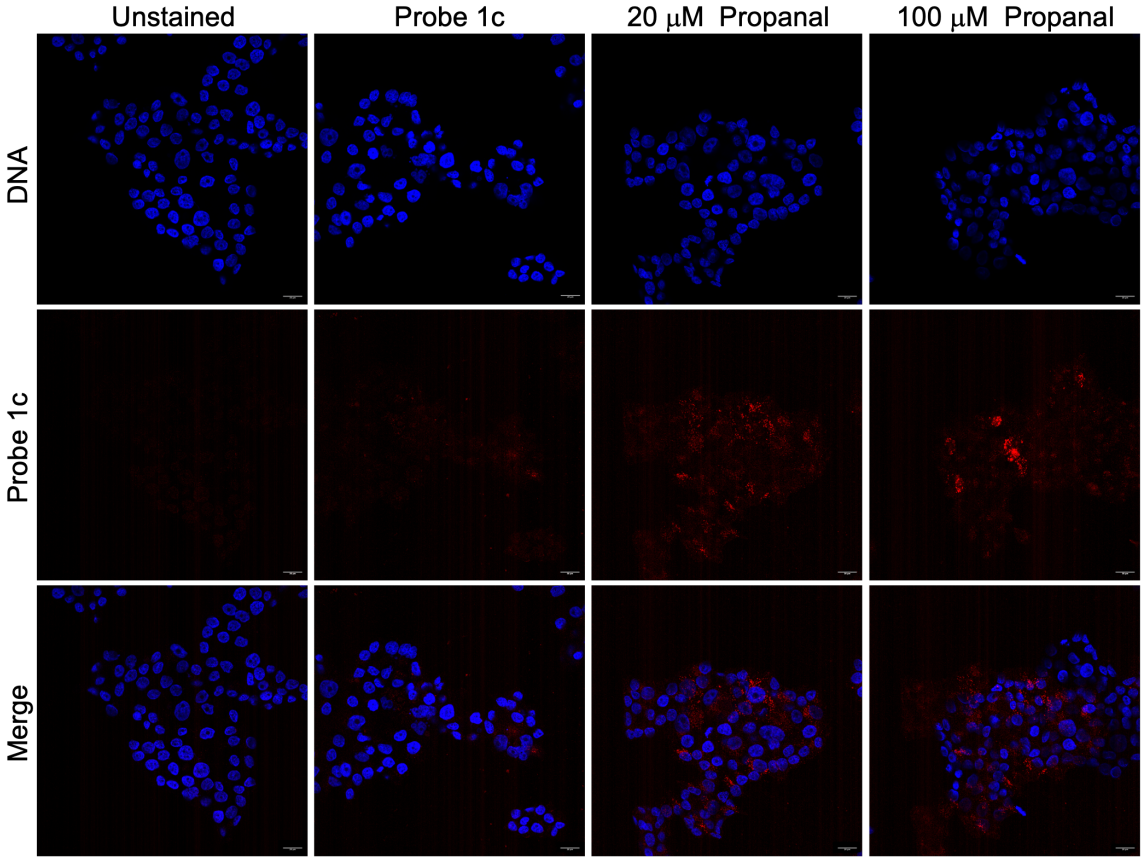
XV. Figure 7: Fluorescence Characterization of Probe 1d. Probe **1d** was mixed with propanal to create benzothiazole product **2d**. The product was then tested for absorbance with an UV-Vis and excitation with a fluorimeter.



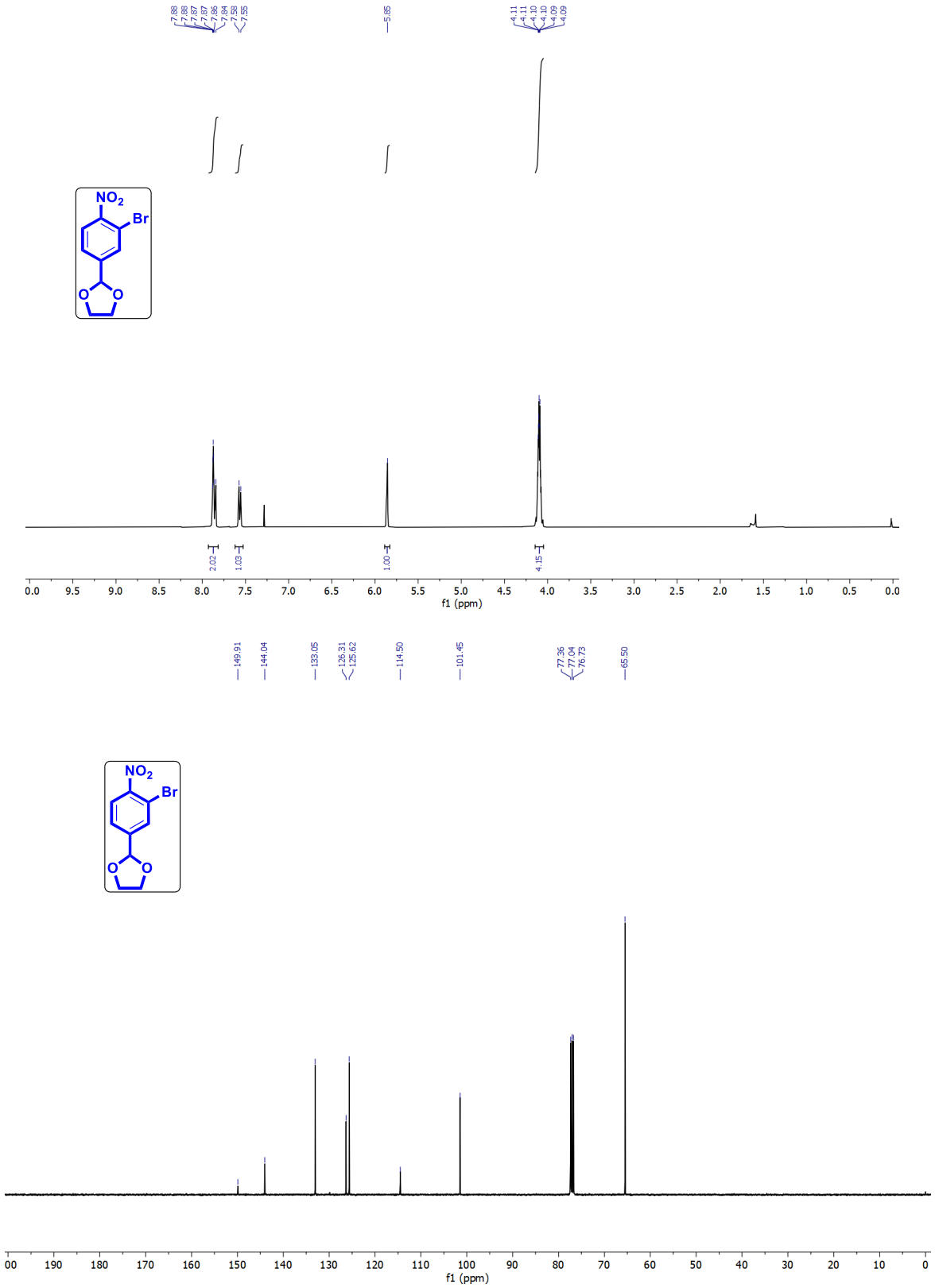
XVI. Figure 8: Flow cytometry analysis of cell death by probe 1c. T-47D cell line was treated with probe **1c** (5 μM or 15 μM) for two hours. A slight increase in cell death was observed upon addition of 15 μM of probe **1c**, but the probe remains non-cytotoxic per regulations.

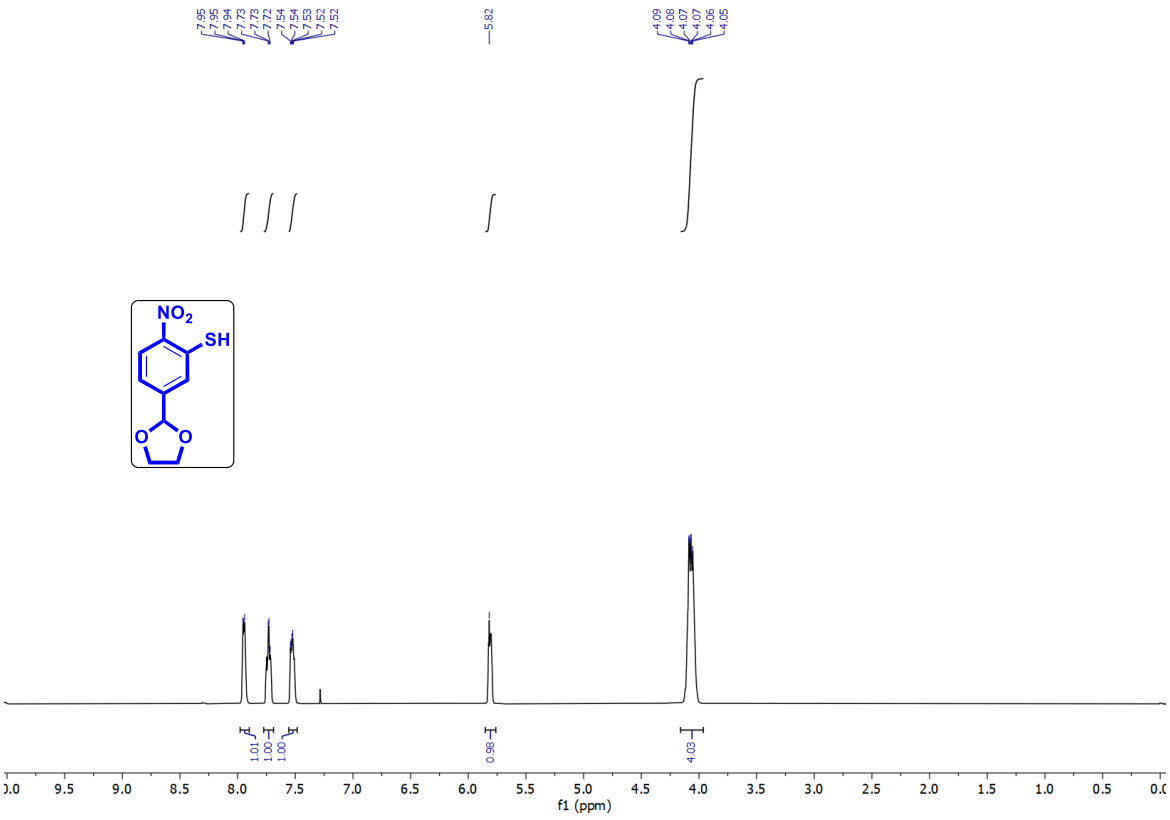


XVII. Figure 9: Confocal analysis of probe 1c in T-47D cells. T-47D cells were treated for 1 h with exogenous propanal at varying concentrations. Cells were washed with PBS and Probe **1c** was subsequently added and incubated for 1 h. Confocal imaging should an increase in fluorescent intensity upon increase in exogenous aldehyde concentration.



XVIII. Figure 10: ^{1}H and ^{13}C spectra of synthesized compounds.

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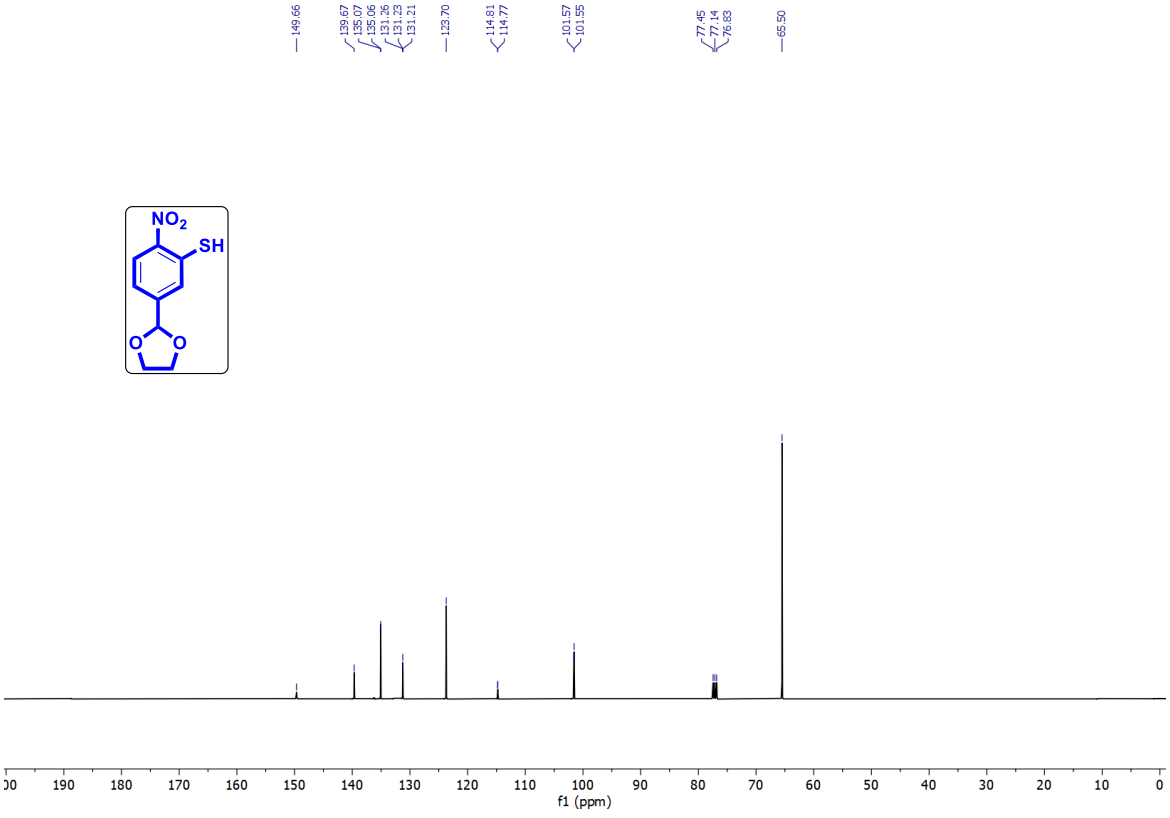
7.95
7.94
7.73
7.73
7.72
7.54
7.54
7.53
7.52
7.52
5.82
4.09
4.08
4.07
4.07
4.06
4.05
NO2
SH
O
O
1.01
1.00
1.00
0.98
4.03
f1 (ppm)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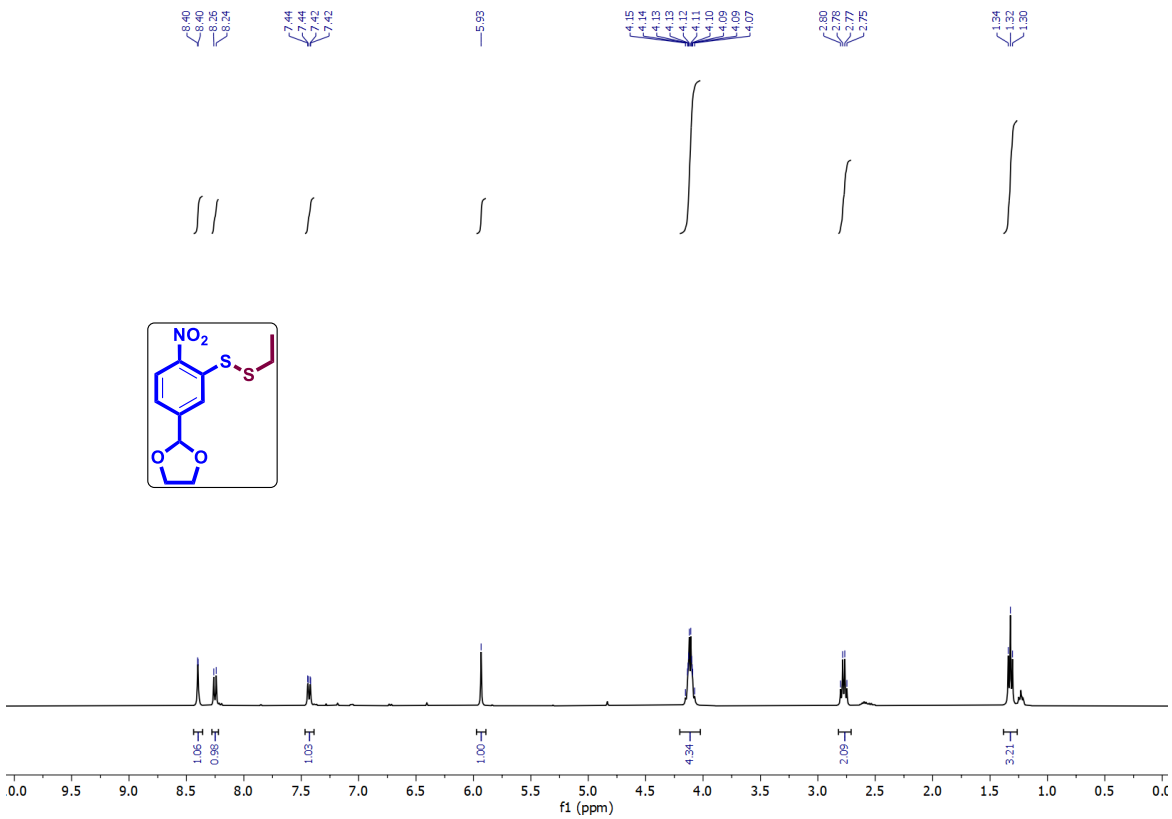
139.67
135.07
135.06
131.26
131.23
131.21
123.70
114.81
114.77
101.57
101.55
77.45
77.14
76.83
65.50
NO2
SH
O
O
f1 (ppm)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8.26
8.24
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7.44
7.42
7.42
5.93
4.15
4.14
4.13
4.12
4.11
4.10
4.09
4.09
4.07
2.80
2.78
2.77
2.75
1.34
1.32
1.30
NO2
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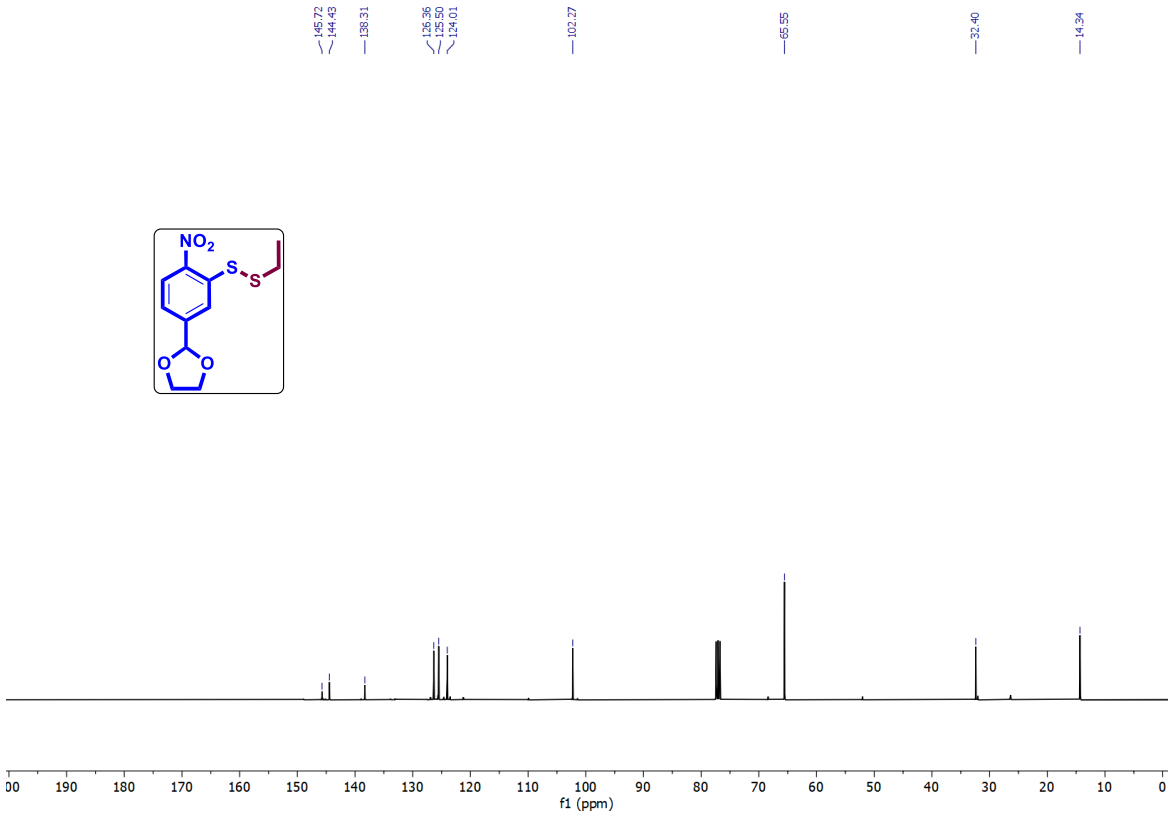
S
O
O
1.06
0.98
1.03
1.00
4.34
2.09
3.21
f1 (ppm)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NO2
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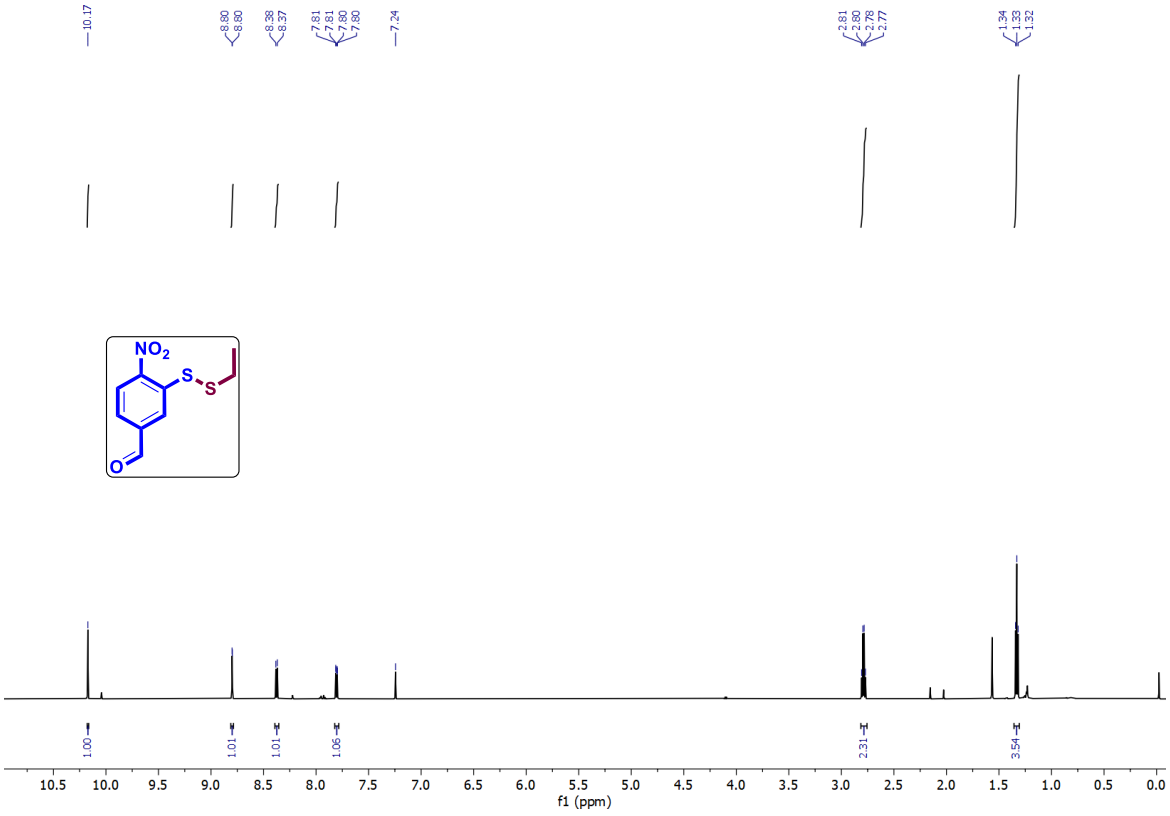
S
O
O
f1 (ppm)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8.80
8.38
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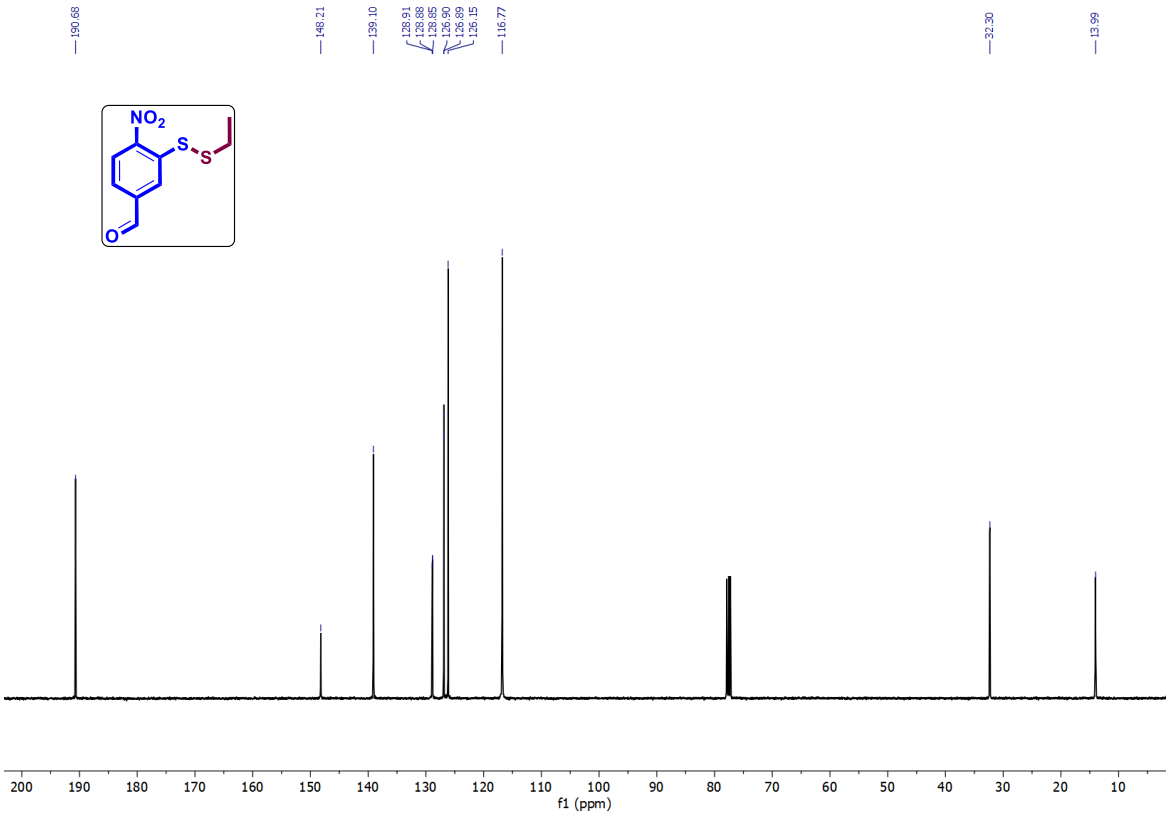
7.81
7.80
7.80
7.24
2.81
2.80
2.78
2.77
1.34
1.33
1.32
NO2
S
S
O
1.00
1.01
1.01
1.06
2.31
3.54
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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128.85
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125.89
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32.30
13.99
NO2
S
S
O
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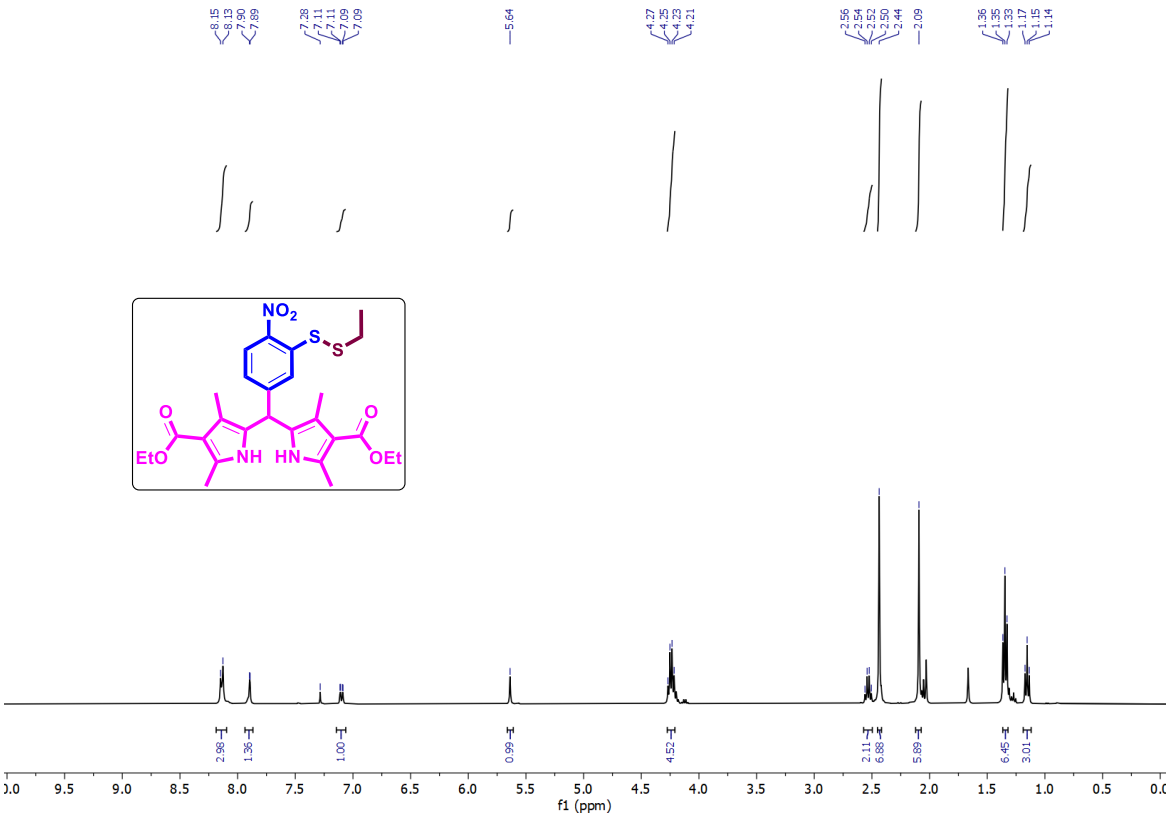
f1 (ppm)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7.89
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7.11
7.11
7.09
7.09
5.64
4.27
4.25
4.23
4.21
2.56
2.54
2.52
2.50
2.44
2.09
1.36
1.35
1.33
1.17
1.15
1.14
NO2
S
S
O
EtO
NH
HN
O
OEt
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1.00
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4.52
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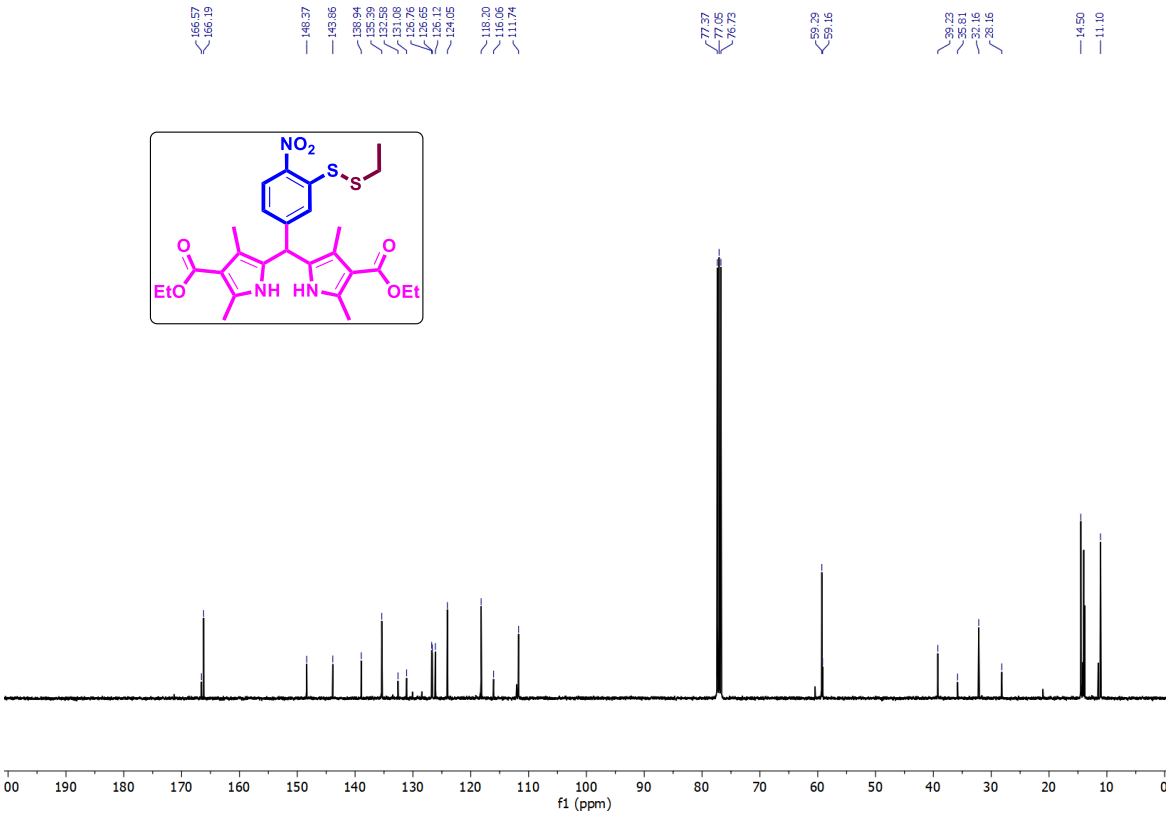
6.88
5.89
6.45
3.01
f1 (ppm)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131.08
126.76
126.65
126.12
124.05
118.20
116.06
111.74
77.37
77.05
76.73
59.29
59.16
39.23
35.81
32.16
28.16
14.50
11.10
NO2
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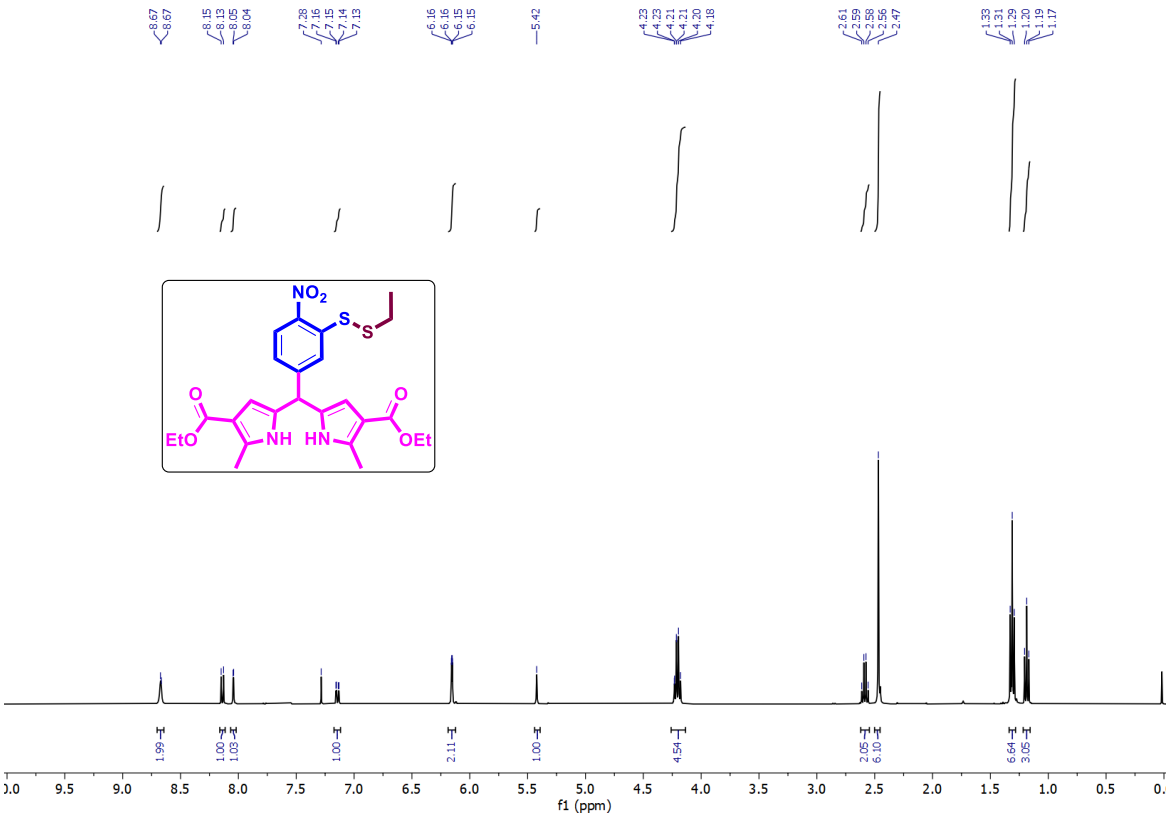
S
O
EtO
NH
HN
O
OEt
f1 (ppm)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6.15
6.15
5.42
4.23
4.23
4.21
4.21
4.20
4.18
2.61
2.59
2.58
2.56
2.47
1.33
1.31
1.29
1.20
1.19
1.17
NO2
S
S
O
EtO
NH
HN
O
OEt
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1.00
2.11
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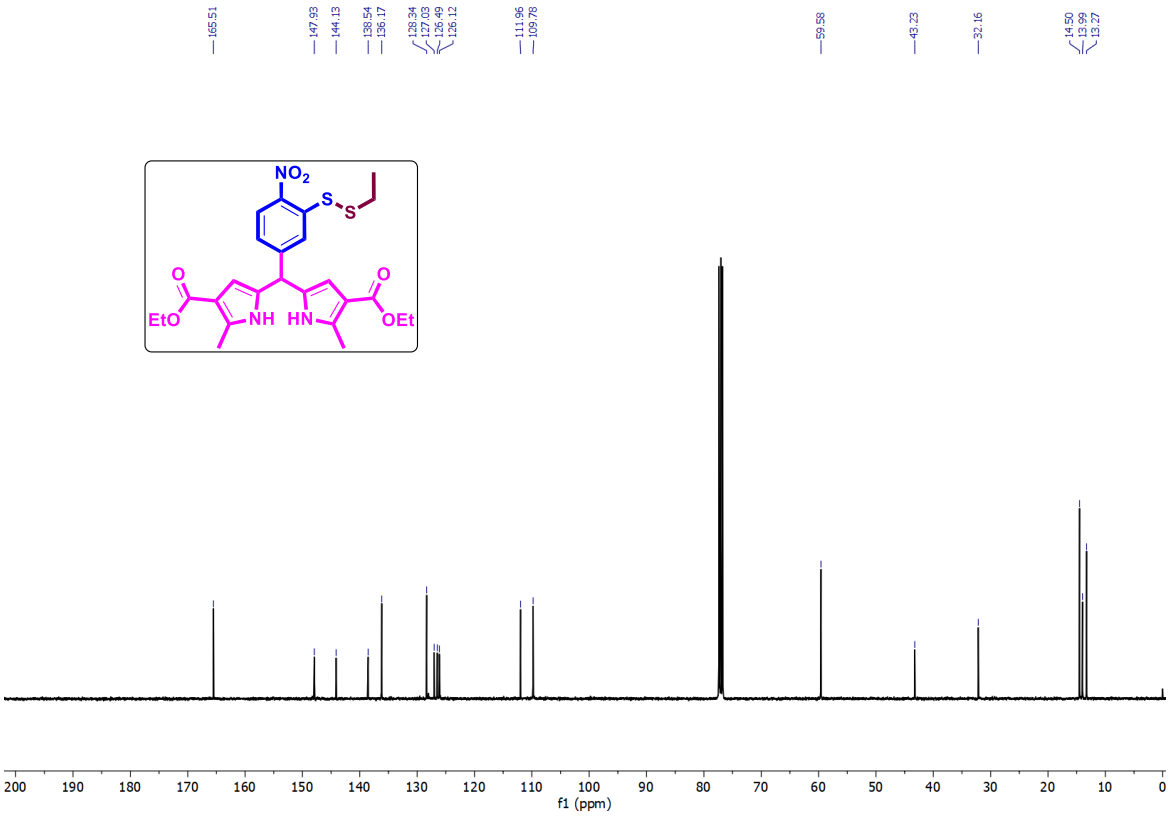
3.05
f1 (ppm)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128.34
127.03
126.49
126.12
111.96
109.78
59.58
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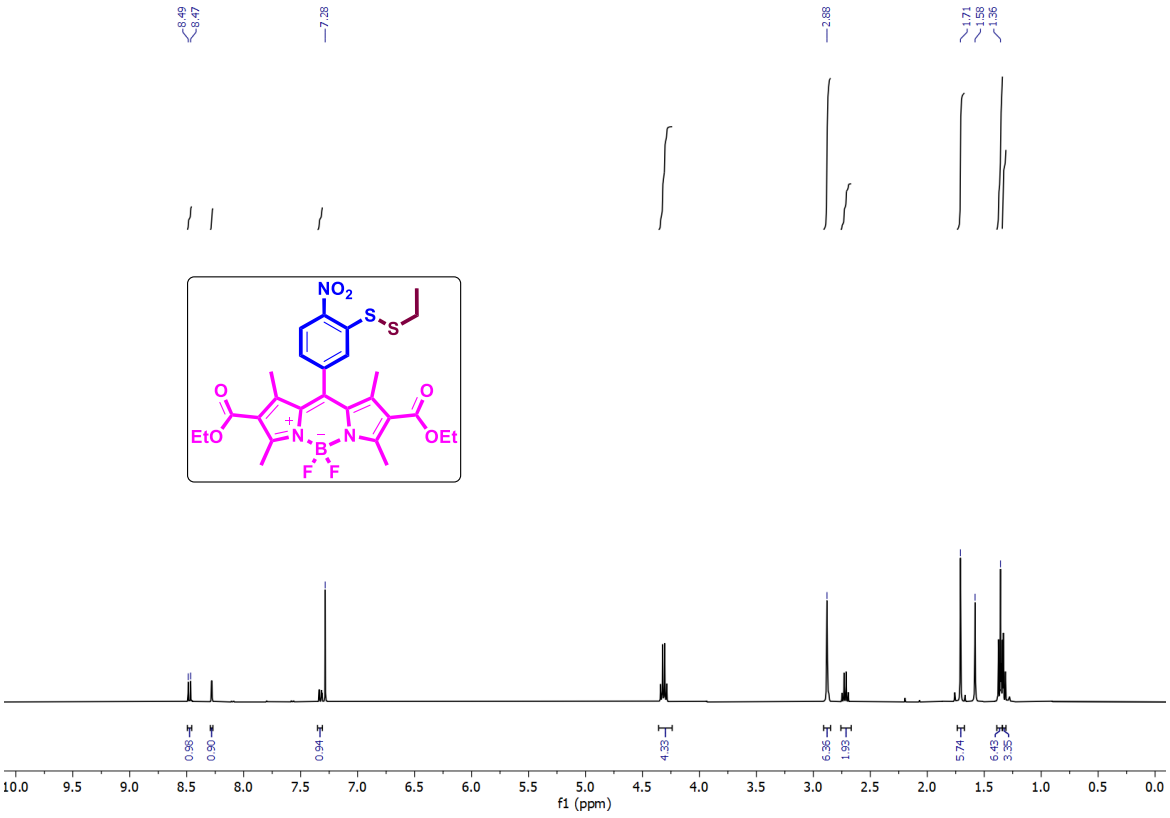
32.16
14.50
13.99
13.27
NO2
S
S
O
EtO
NH
HN
O
OEt
f1 (ppm)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O
EtO
O
OEt
N
B
F
F
0.98
0.90
0.94
4.33
6.36
1.93
5.74
6.43
3.35
10.0
9.5
9.0
8.5
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6.0
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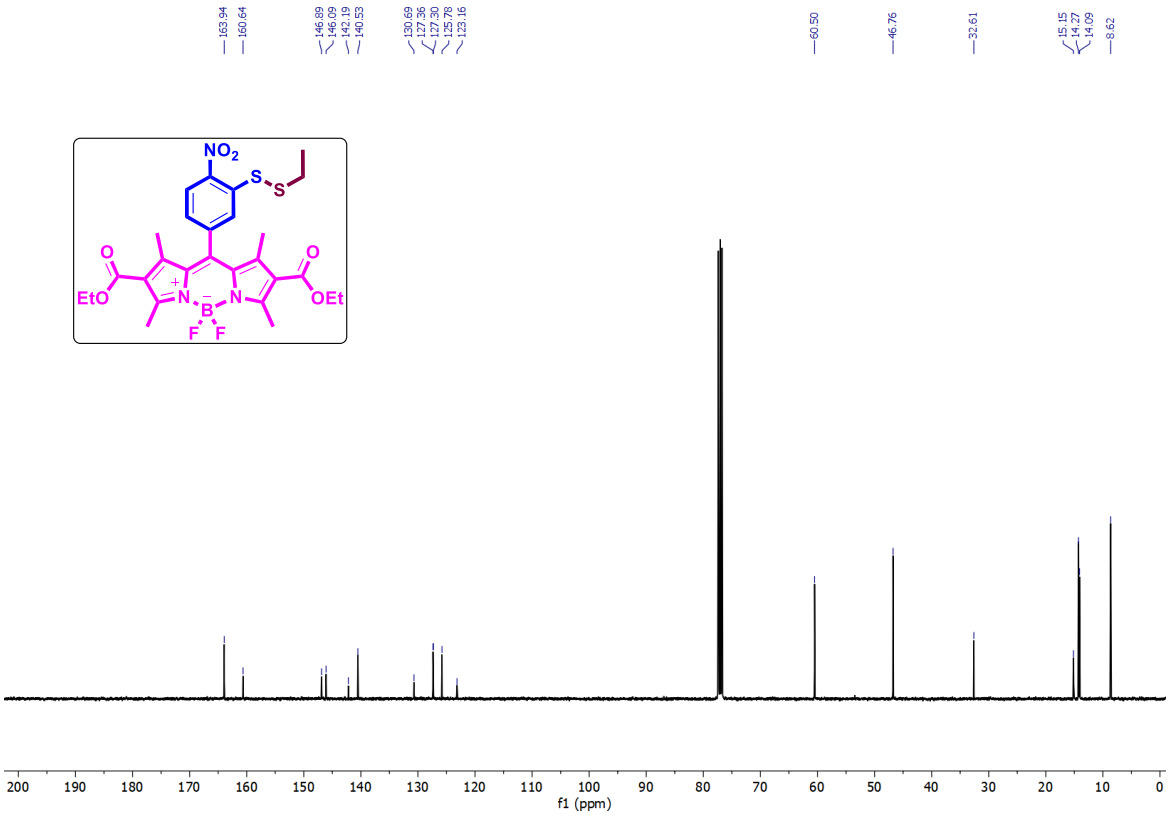
f1 (ppm)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32.61
15.15
14.27
14.09
8.62
NO2
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O
EtO
O
OEt
N
B
F
F
200
190
180
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130
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110
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90
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50
40
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10
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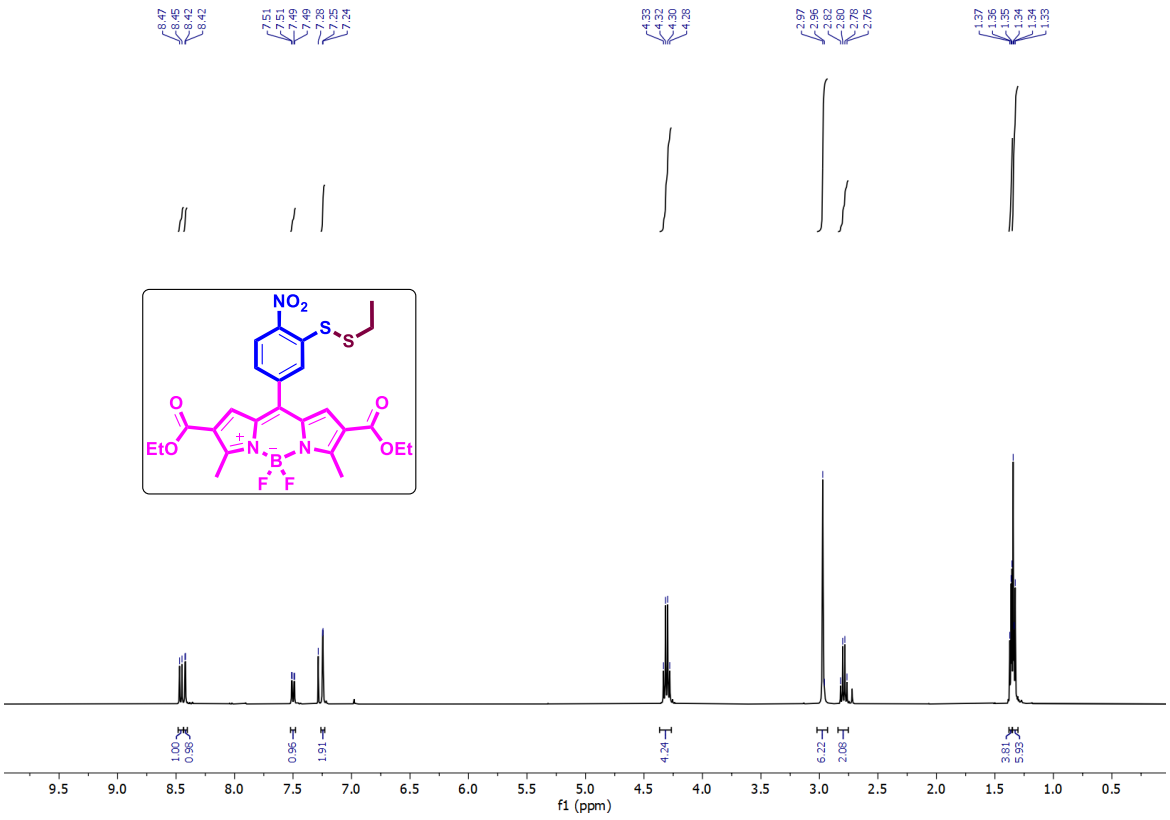
f1 (ppm)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4.30
4.28
2.97
2.96
2.62
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2.78
2.76
1.37
1.36
1.35
1.34
1.34
1.33
NO2
S
S
O
EtO
N
B
F
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1.91
4.24
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2.08
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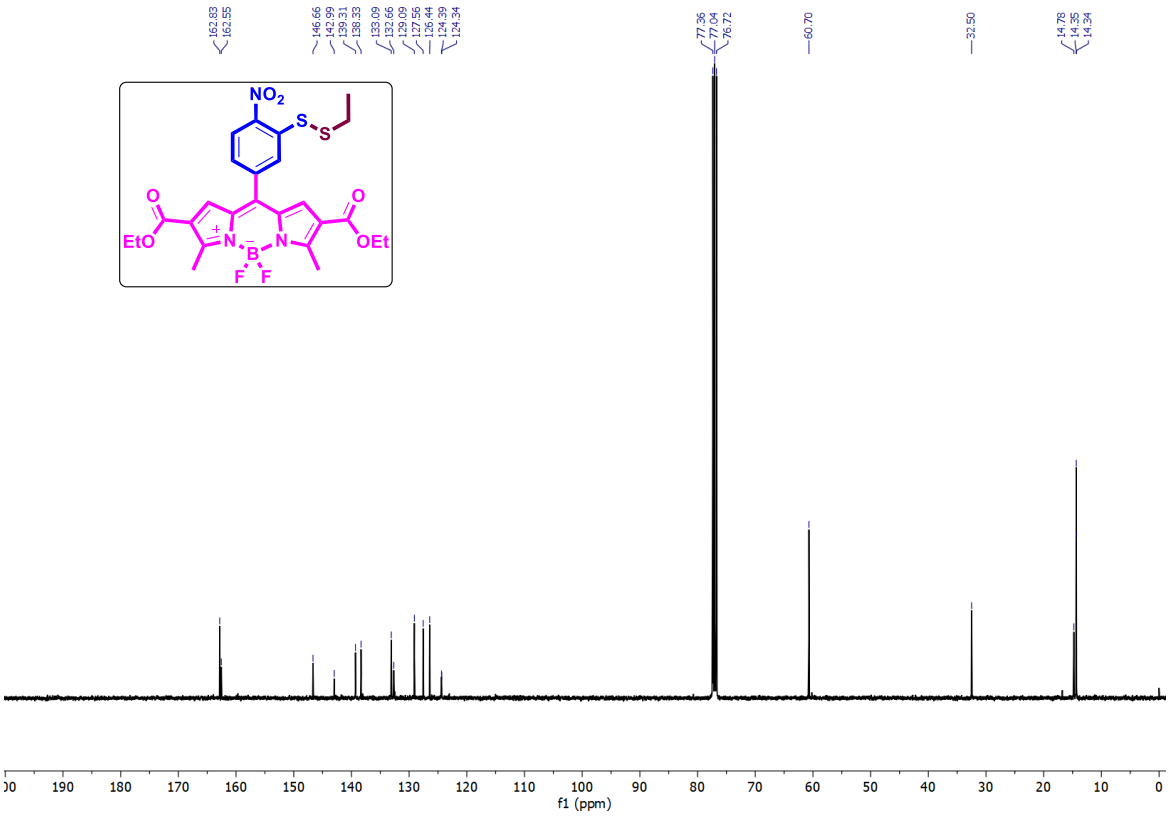
5.93
f1 (ppm)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124.34
77.36
77.04
76.72
60.70
32.50
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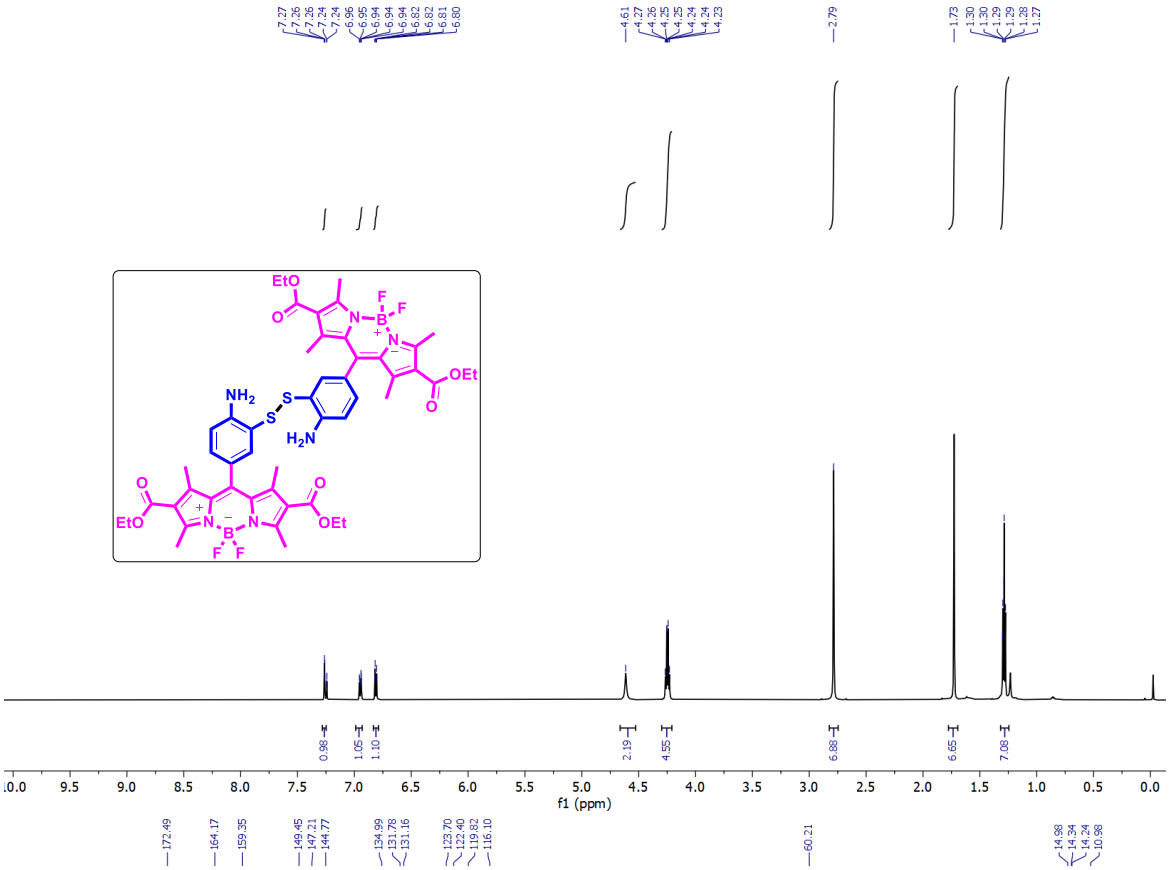
14.34
NO2
S
S
O
EtO
N
B
F
F
O
OEt
f1 (ppm)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1.30
1.30
1.29
1.29
1.29
1.28
1.27
EtO
O
F
F
N
B
N
OEt
O
NH2
S
S
H2N
O
EtO
O
N
B
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F
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1.10
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4.55
6.88
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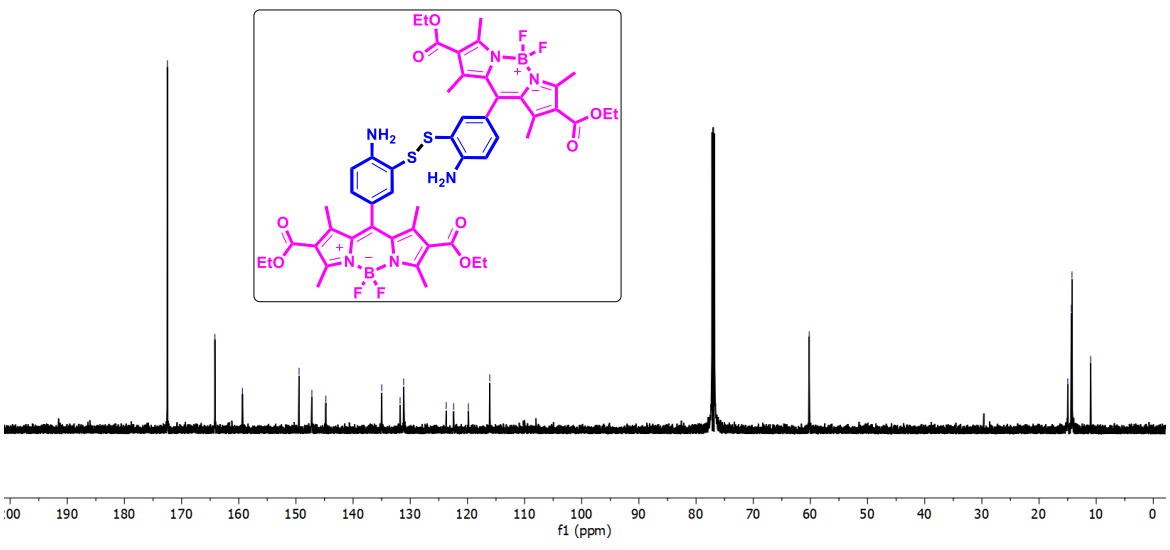
7.08
f1 (ppm)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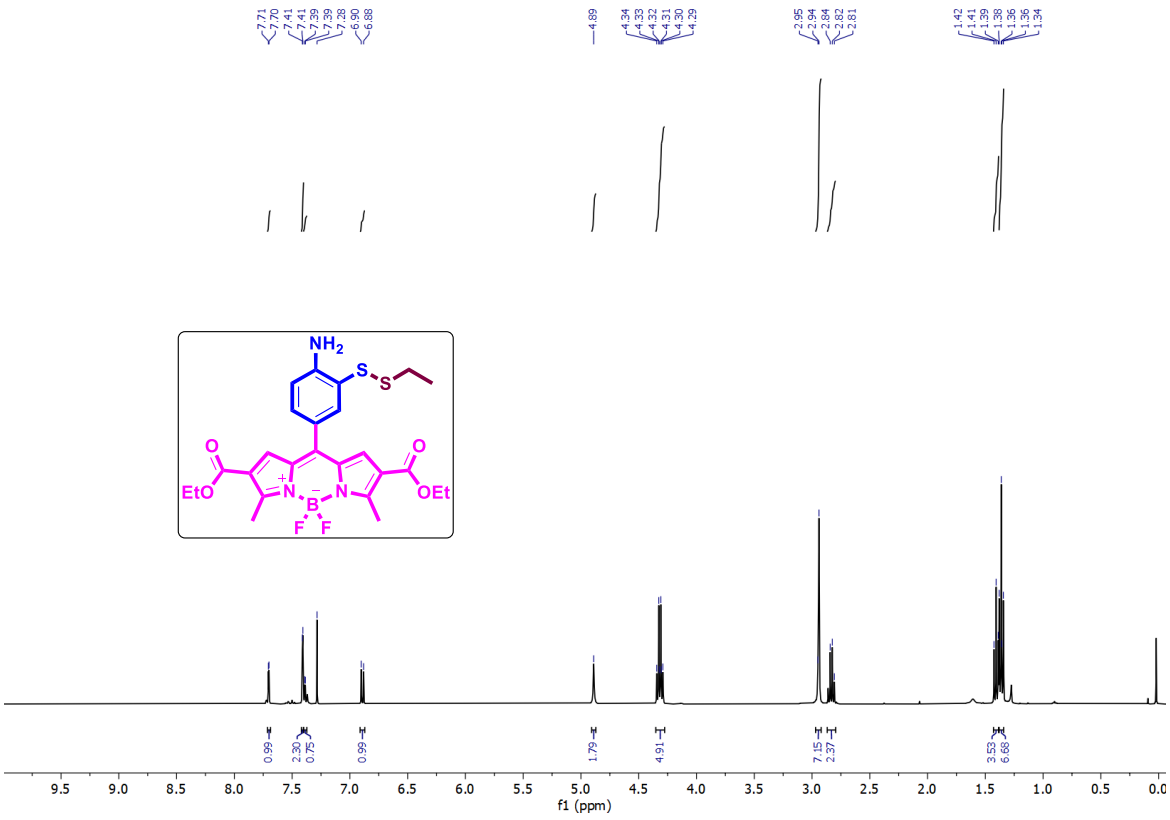
116.10
60.21
14.98
14.34
14.24
10.98
EtO
O
F
F
N
B
N
OEt
O
NH2
S
S
H2N
O
EtO
O
N
B
N
O
OEt
F
F
f1 (ppm)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6.88
4.89
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1.36
1.34
NH2
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S
O
O
EtO
OEt
N
B
F
F
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2.30
0.75
0.99
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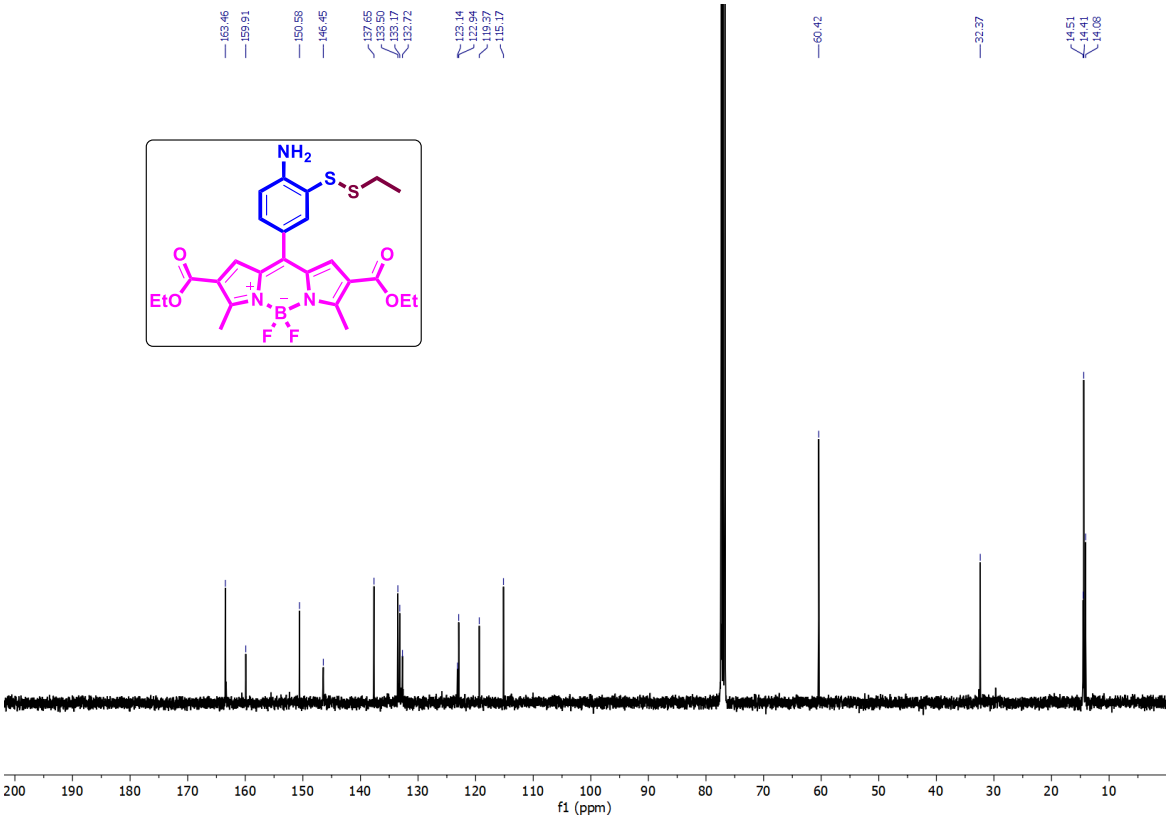
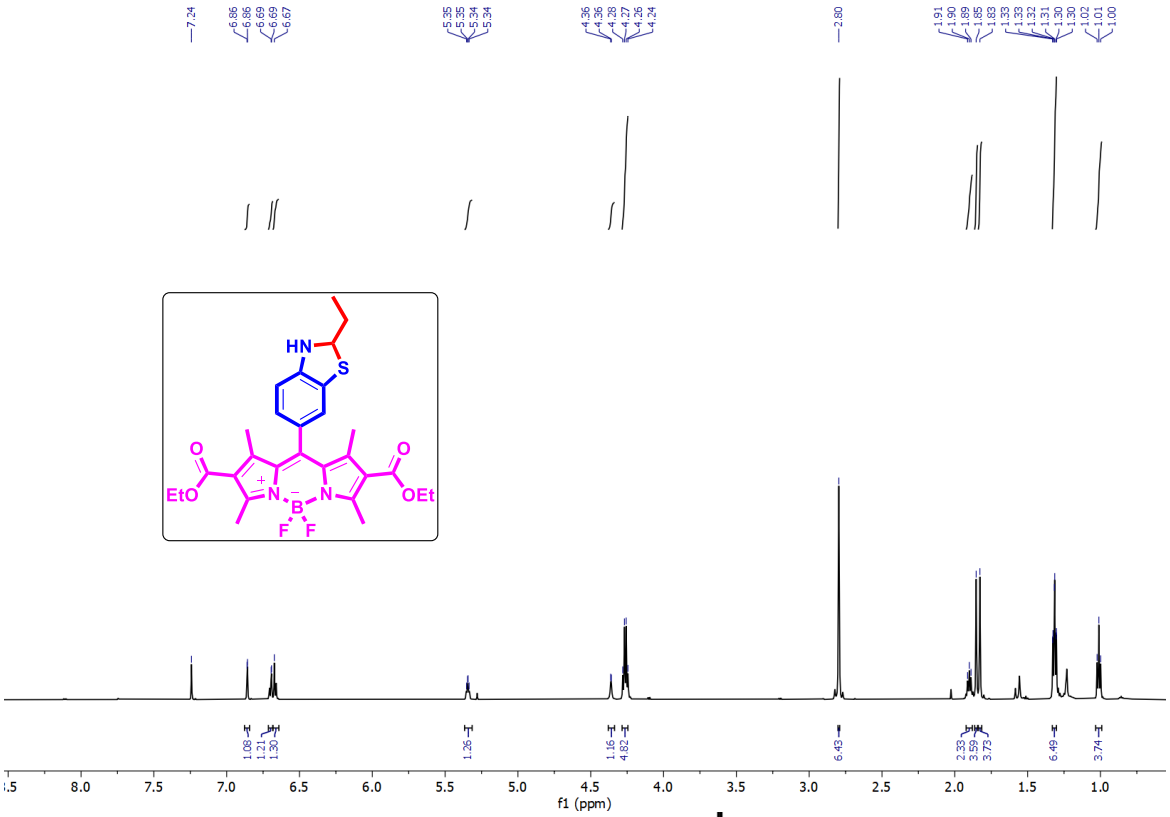
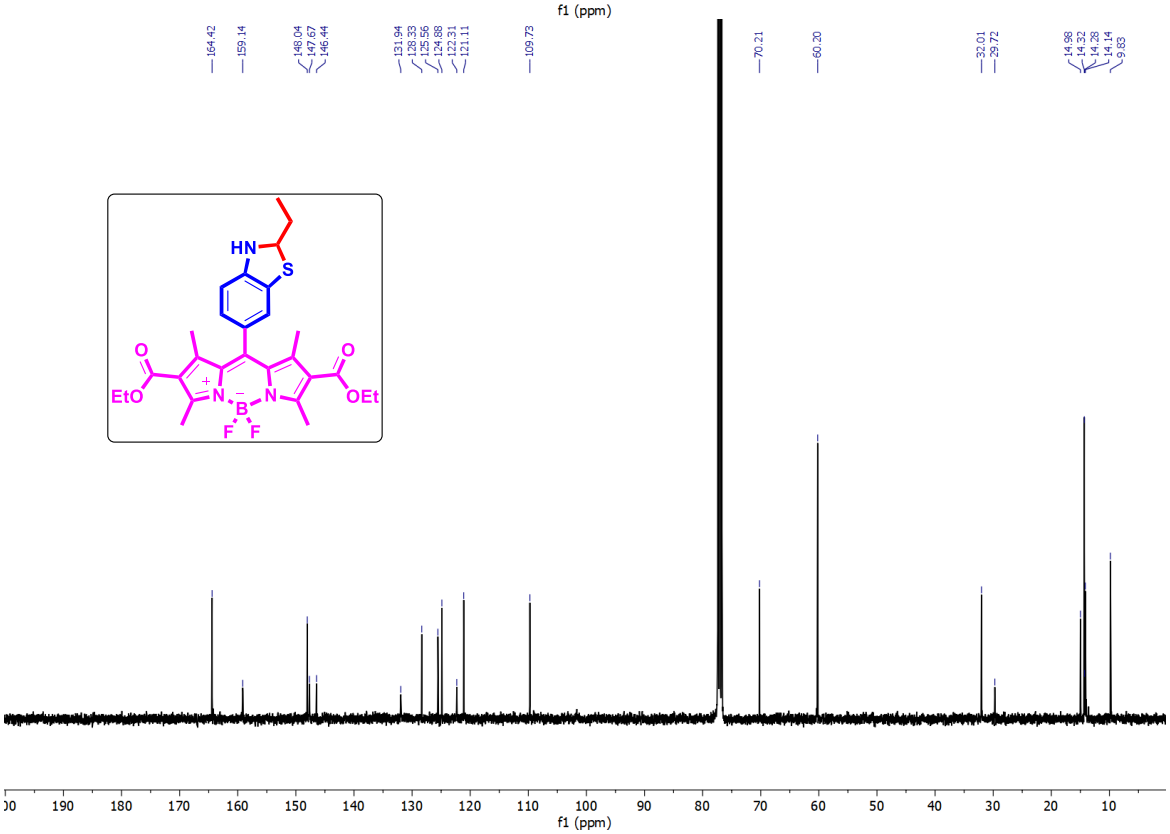
4.91
7.15
2.37
3.53
6.68
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


163.46
159.91
150.58
146.45
137.65
133.50
133.17
132.72
123.14
122.94
119.37
115.17
60.42
32.37
14.51
14.41
14.08
NH2
S
S
O
O
EtO
OEt
N
B
F
F
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


7.24
6.86
6.86
6.69
6.69
6.67
5.35
5.35
5.34
5.34
4.36
4.36
4.28
4.27
4.26
4.24
2.80
1.91
1.90
1.88
1.85
1.83
1.33
1.33
1.32
1.31
1.30
1.30
1.02
1.01
1.00
HN
S
O
EtO
O
OEt
N
B
F
F
1.08
1.21
1.30
1.26
1.16
4.82
6.43
2.33
3.59
3.73
6.49
3.74
f1 (ppm)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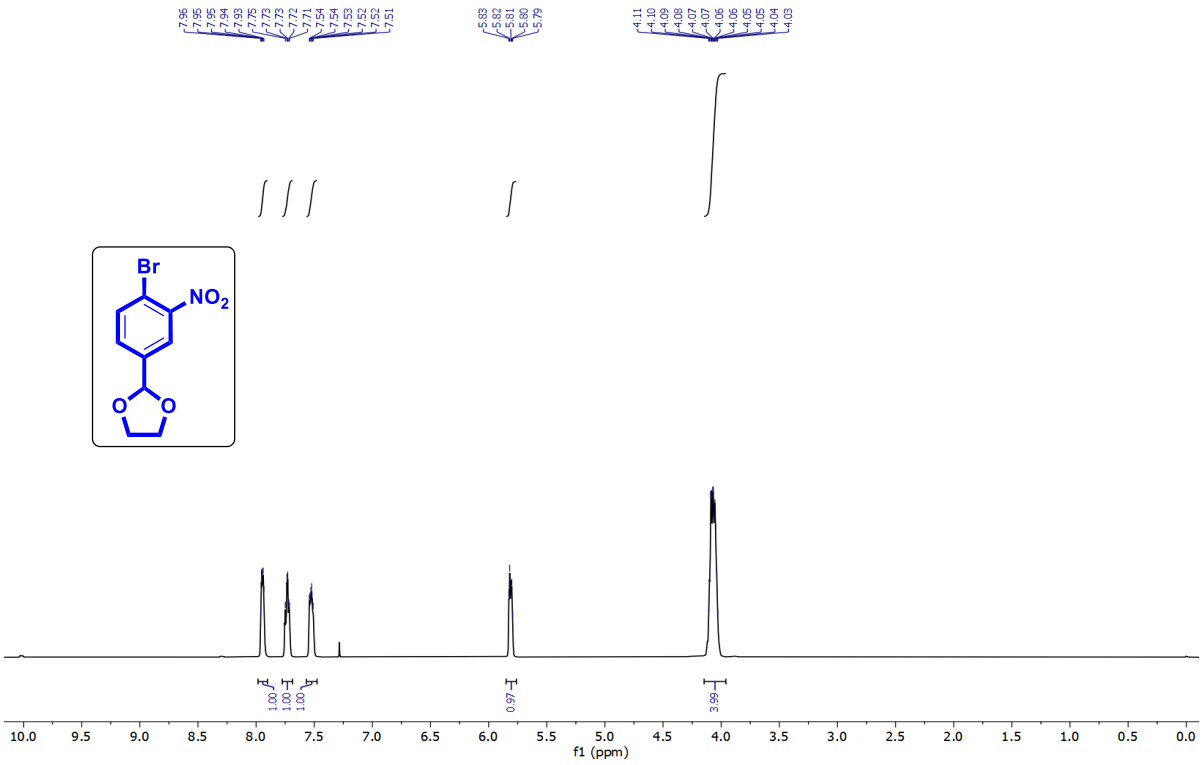
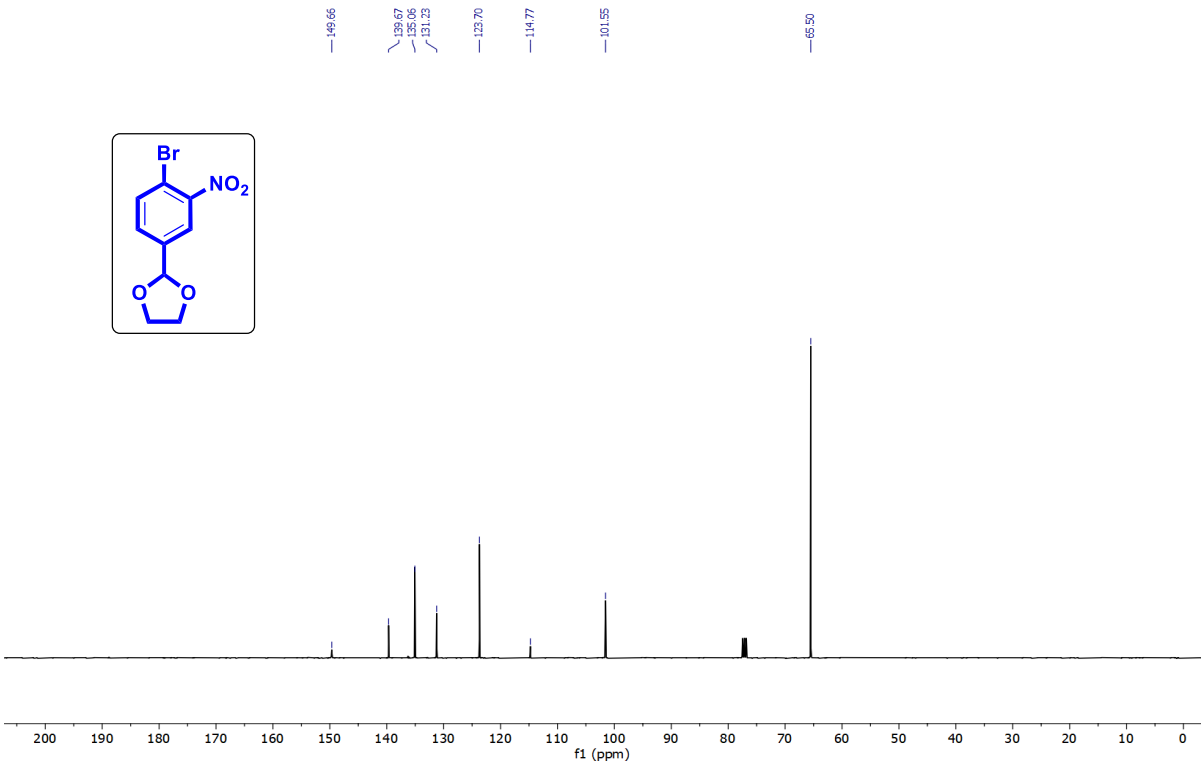
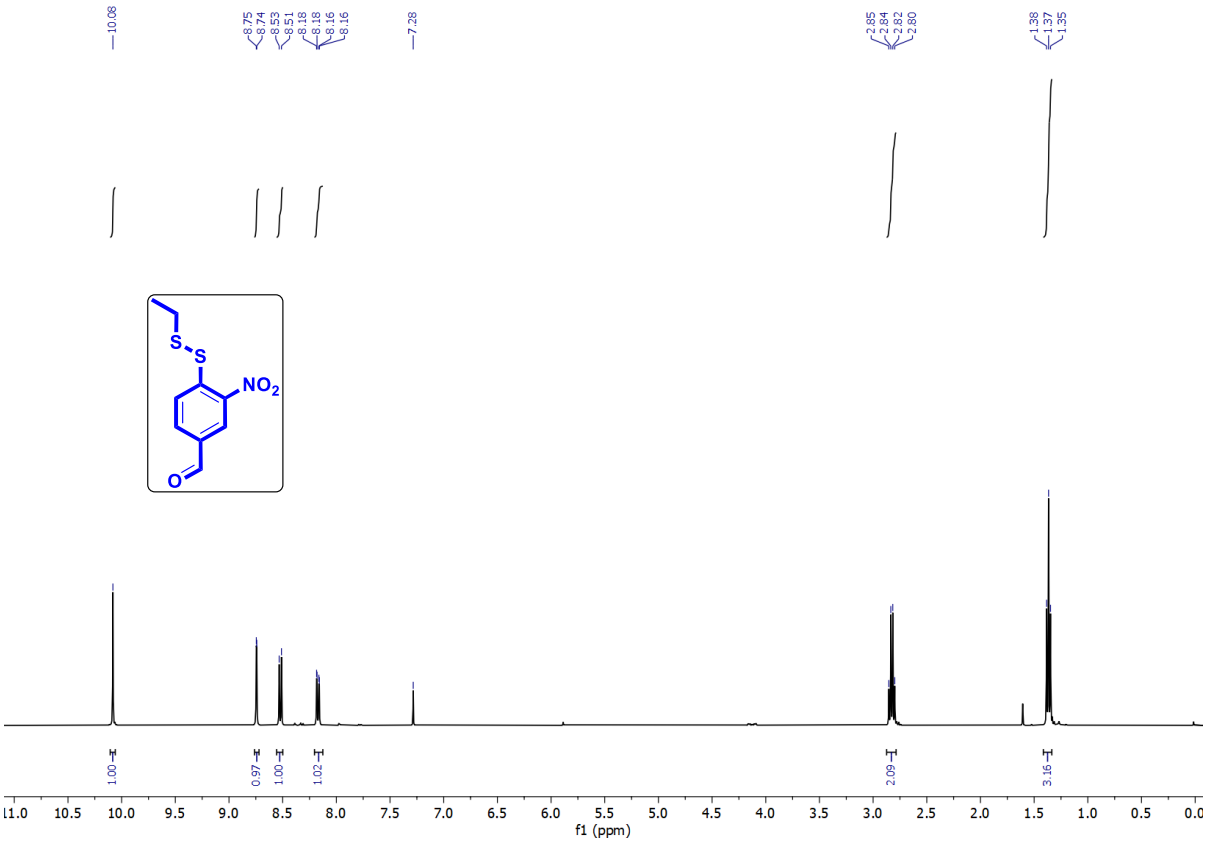
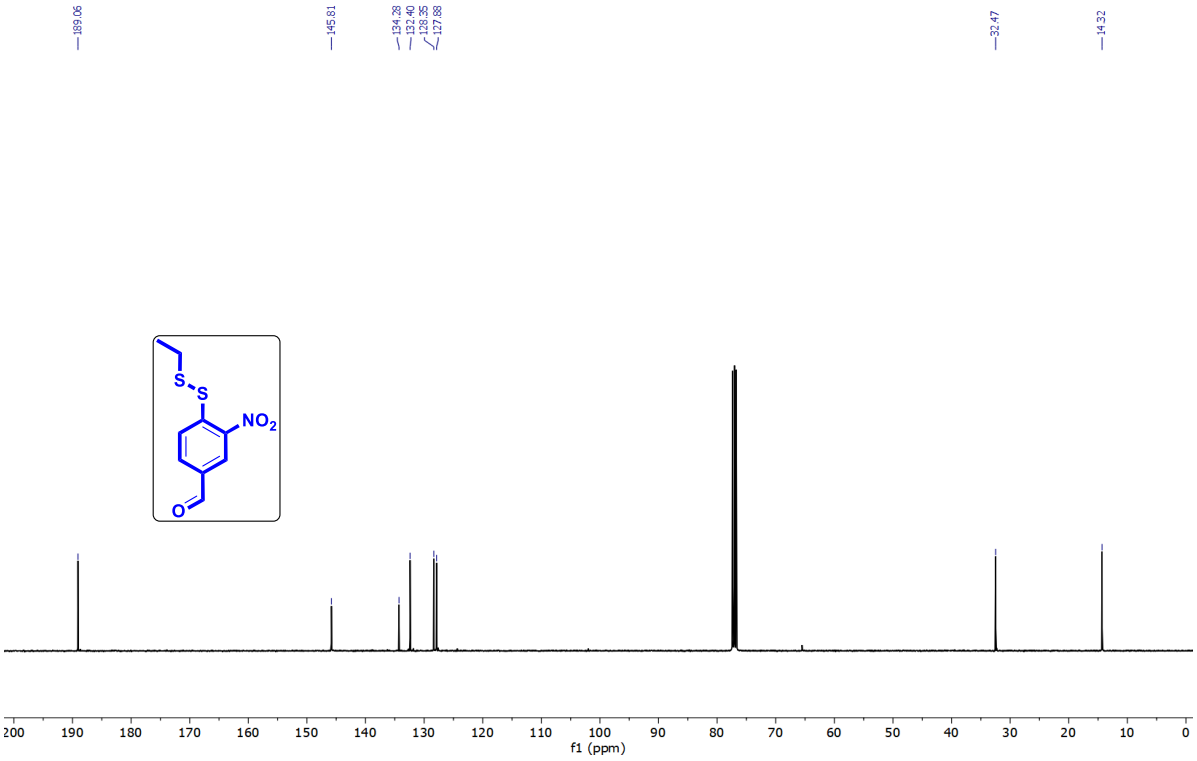
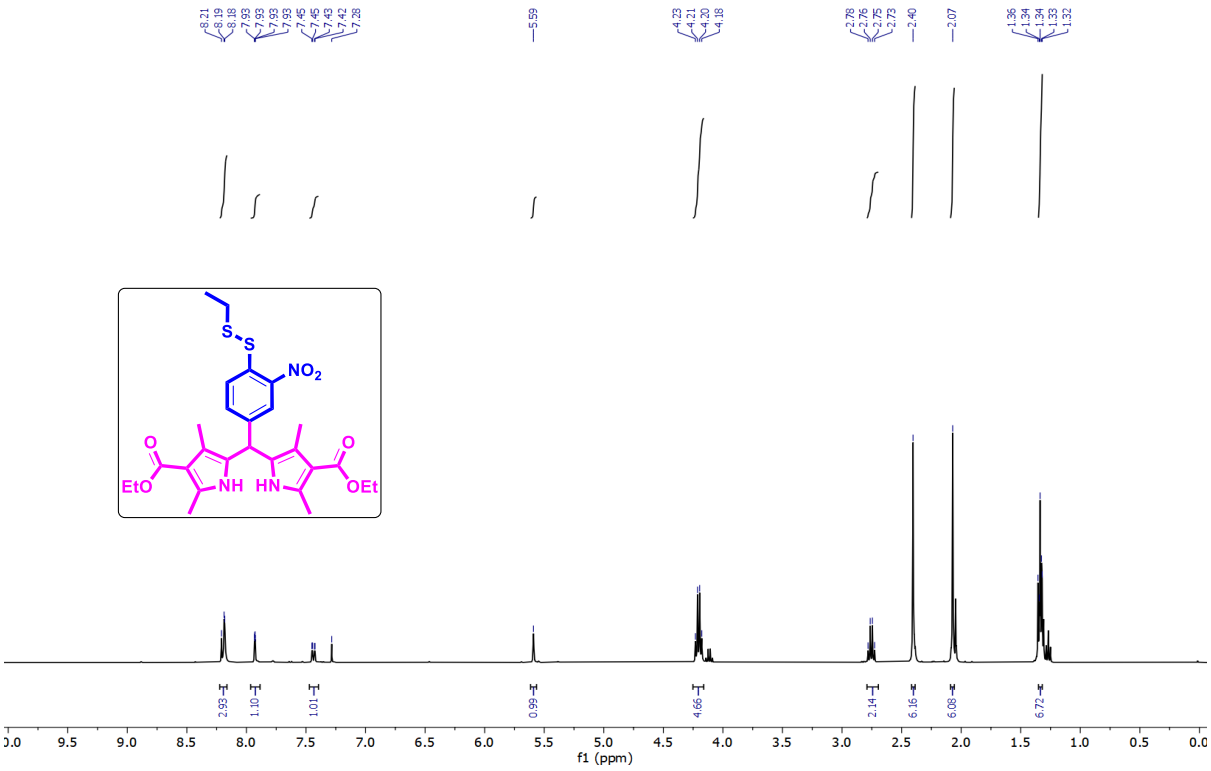
159.14
148.04
147.67
146.44
131.94
128.33
125.56
124.88
122.31
121.11
109.73
70.21
60.20
32.01
29.72
14.98
14.32
14.28
14.14
9.83
HN
S
O
EtO
O
OEt
N
B
F
F
f1 (ppm)

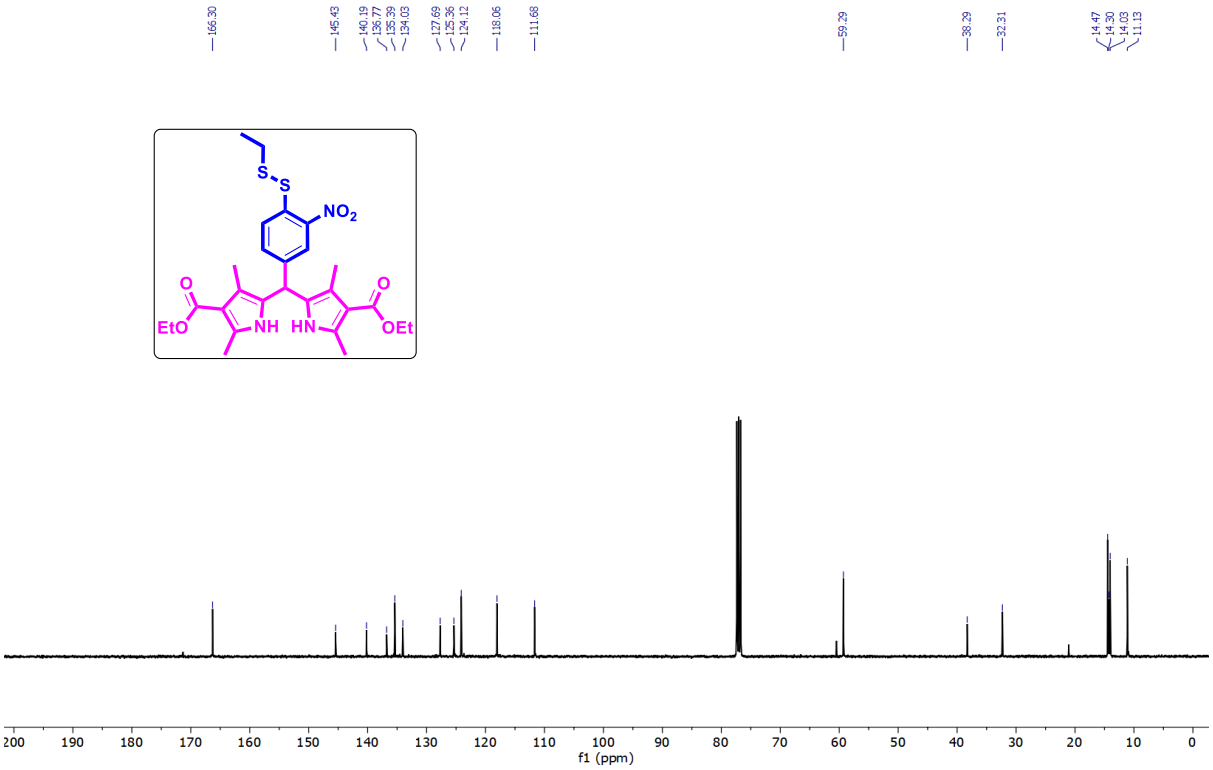

7.96
7.95
7.95
7.94
7.93
7.75
7.73
7.73
7.72
7.71
7.54
7.54
7.53
7.52
7.52
7.51
5.83
5.82
5.81
5.80
5.79
4.11
4.10
4.09
4.08
4.07
4.07
4.06
4.06
4.05
4.05
4.04
4.03
Br
NO2
O
O
1.00
1.00
1.00
0.97
3.99
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

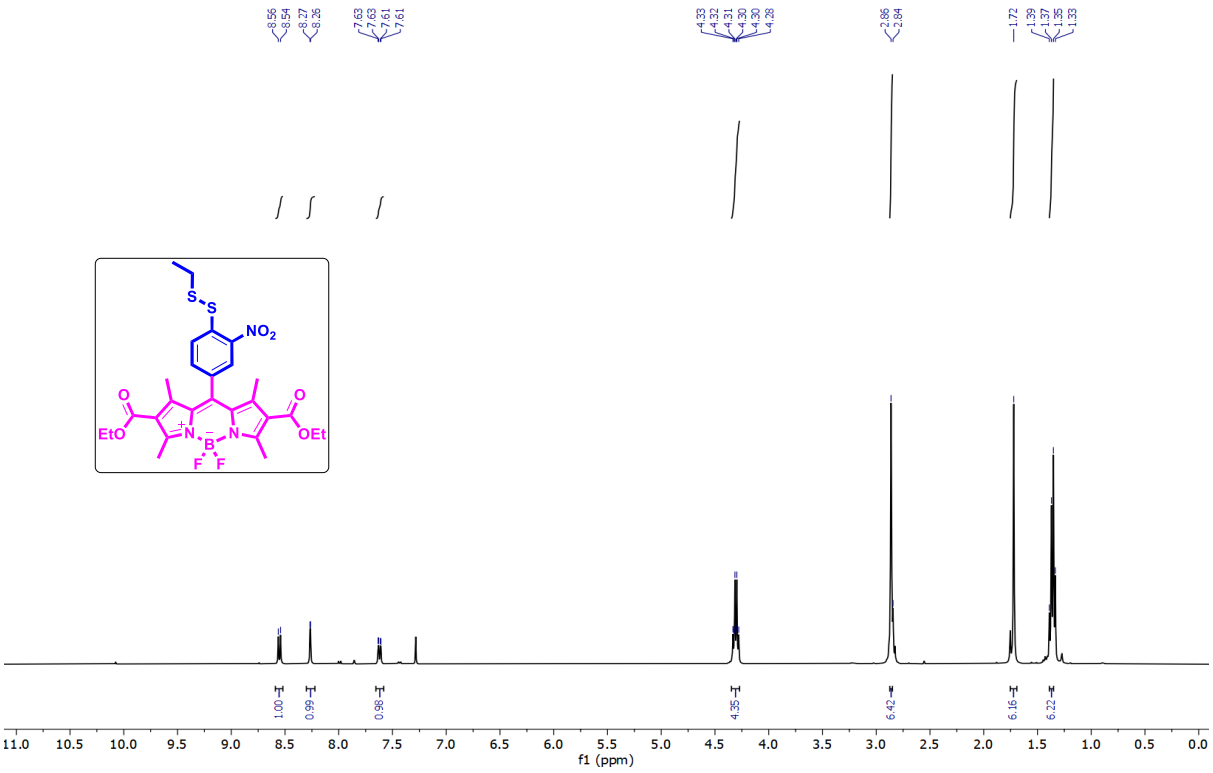

149.66
139.67
135.06
131.23
123.70
114.77
101.55
65.50
Br
NO2
O
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

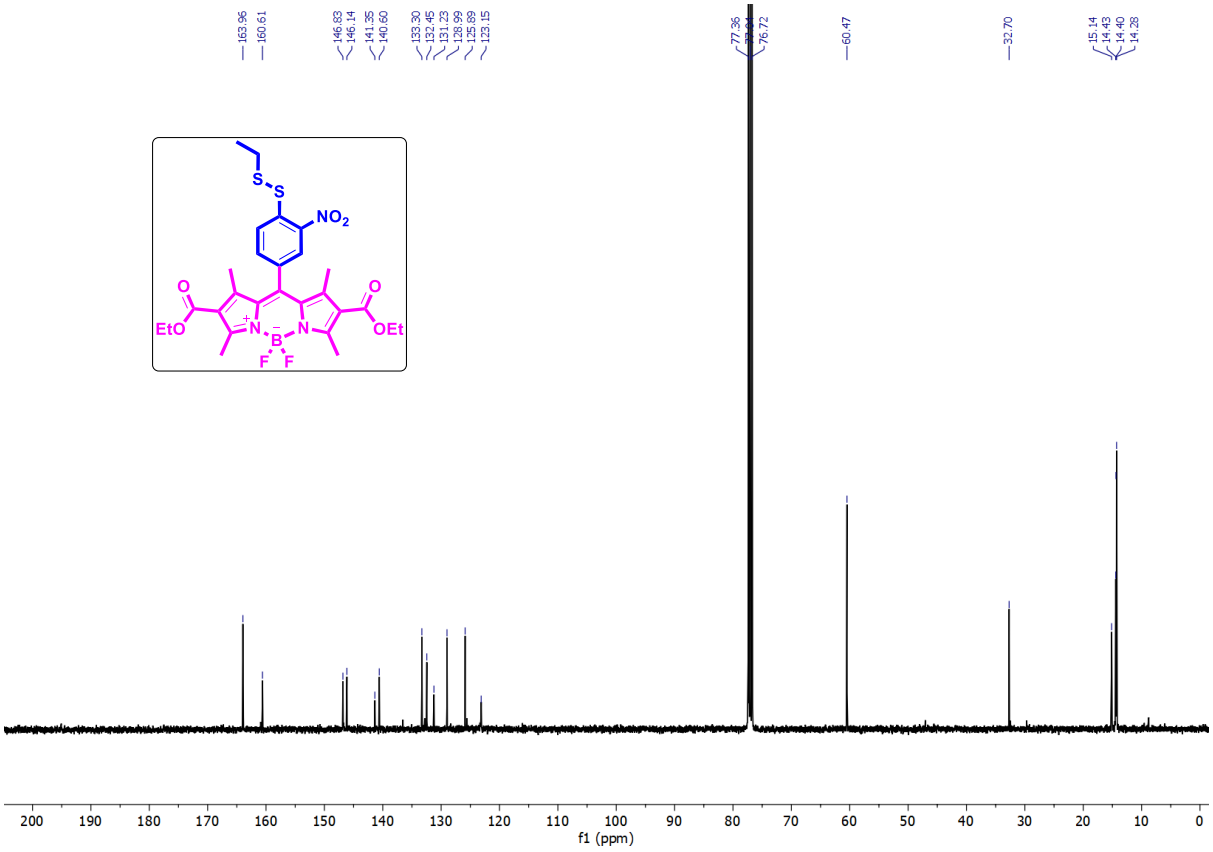

10.08
8.75
8.74
8.53
8.51
8.18
8.18
8.16
8.16
7.28
2.85
2.84
2.82
2.80
1.38
1.37
1.35
S
S
NO2
O
1.00
0.97
1.00
1.02
2.09
3.16
f1 (ppm)

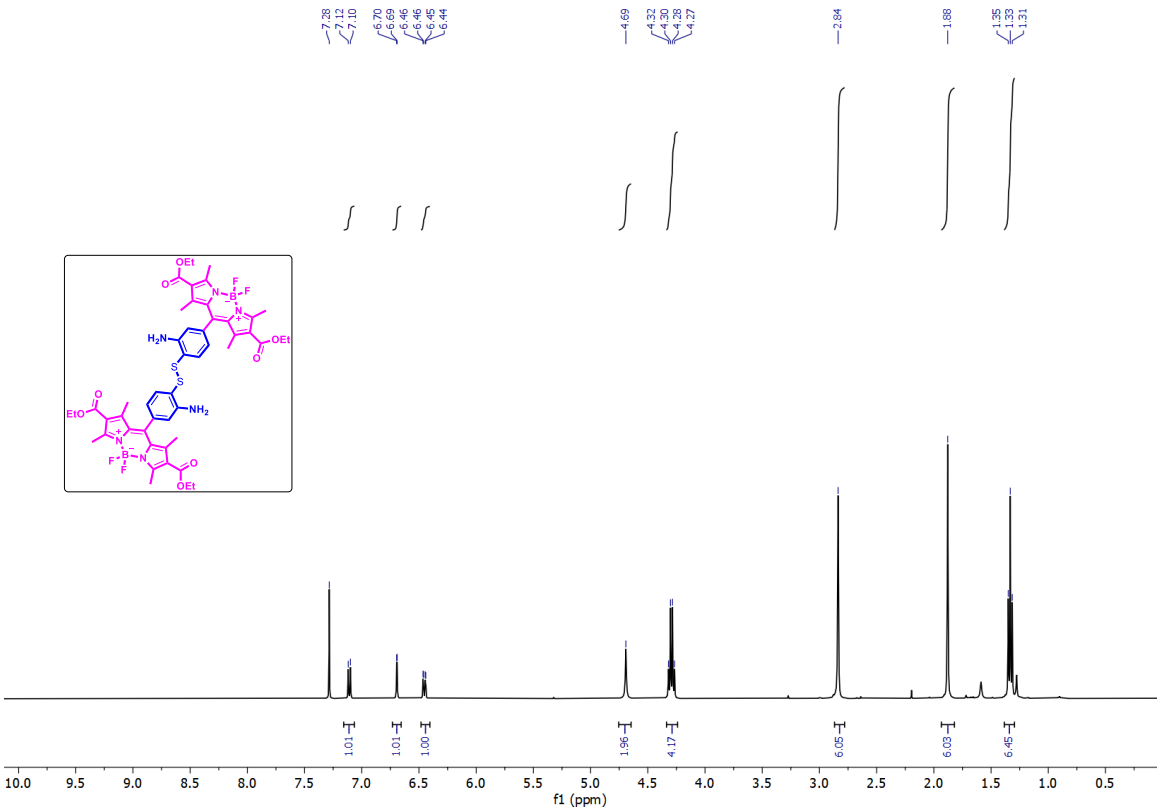

189.06
145.81
134.28
132.40
128.35
127.88
32.47
14.32
S
S
NO2
O
f1 (ppm)

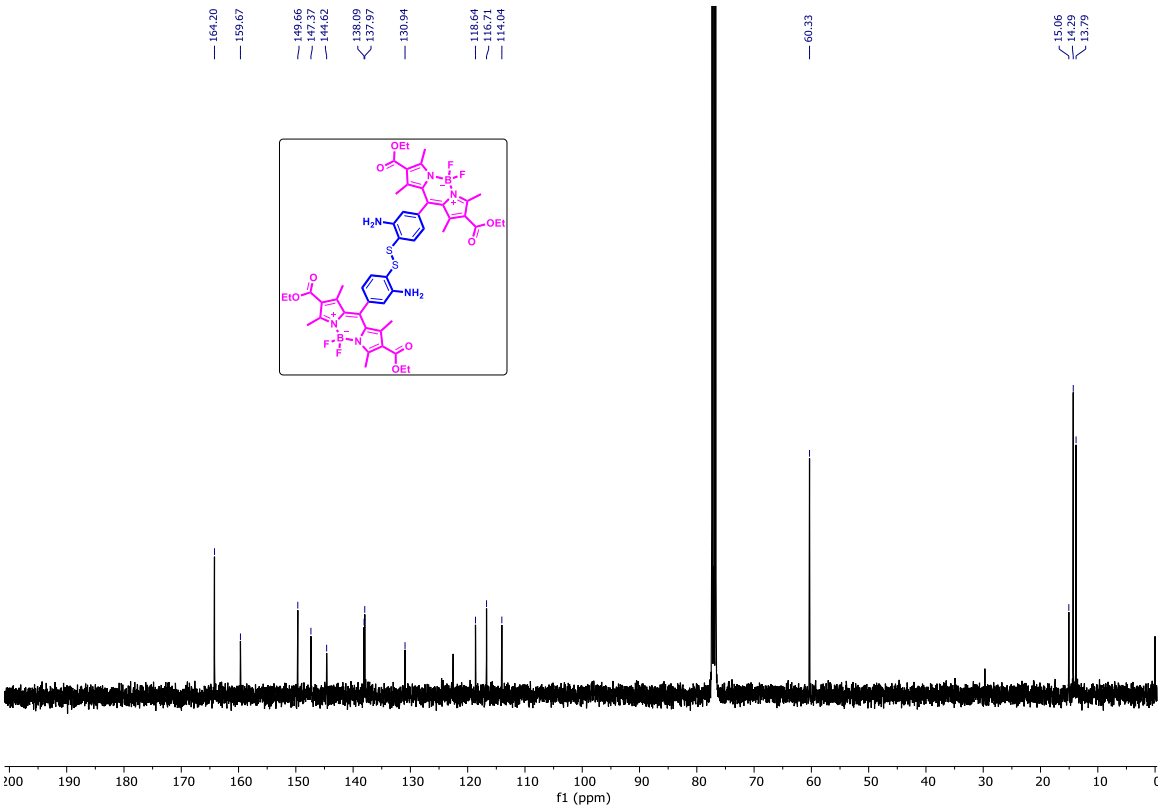

8.21
8.19
8.18
7.93
7.93
7.93
7.93
7.45
7.45
7.43
7.42
7.28
5.59
4.23
4.21
4.20
4.18
2.78
2.76
2.75
2.73
2.40
2.07
1.36
1.34
1.34
1.33
1.32
NO2
EtO
NH
HN
OEt
2.93
1.10
1.01
0.99
4.66
2.14
6.16
6.08
6.72
f1 (ppm)

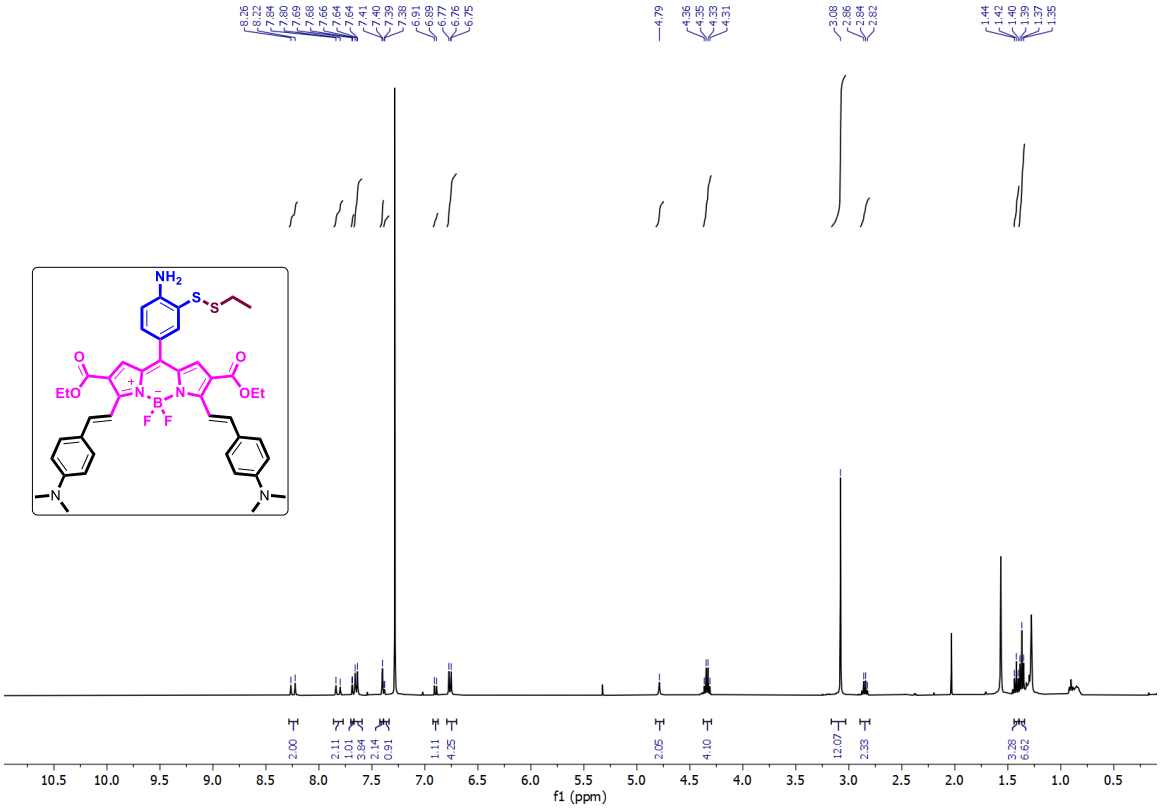

166.30
145.43
140.19
136.77
135.39
134.03
127.69
125.36
124.12
118.06
111.68
59.29
38.29
32.31
14.47
14.30
14.03
11.13
NO2
EtO
NH
HN
OEt
f1 (ppm)

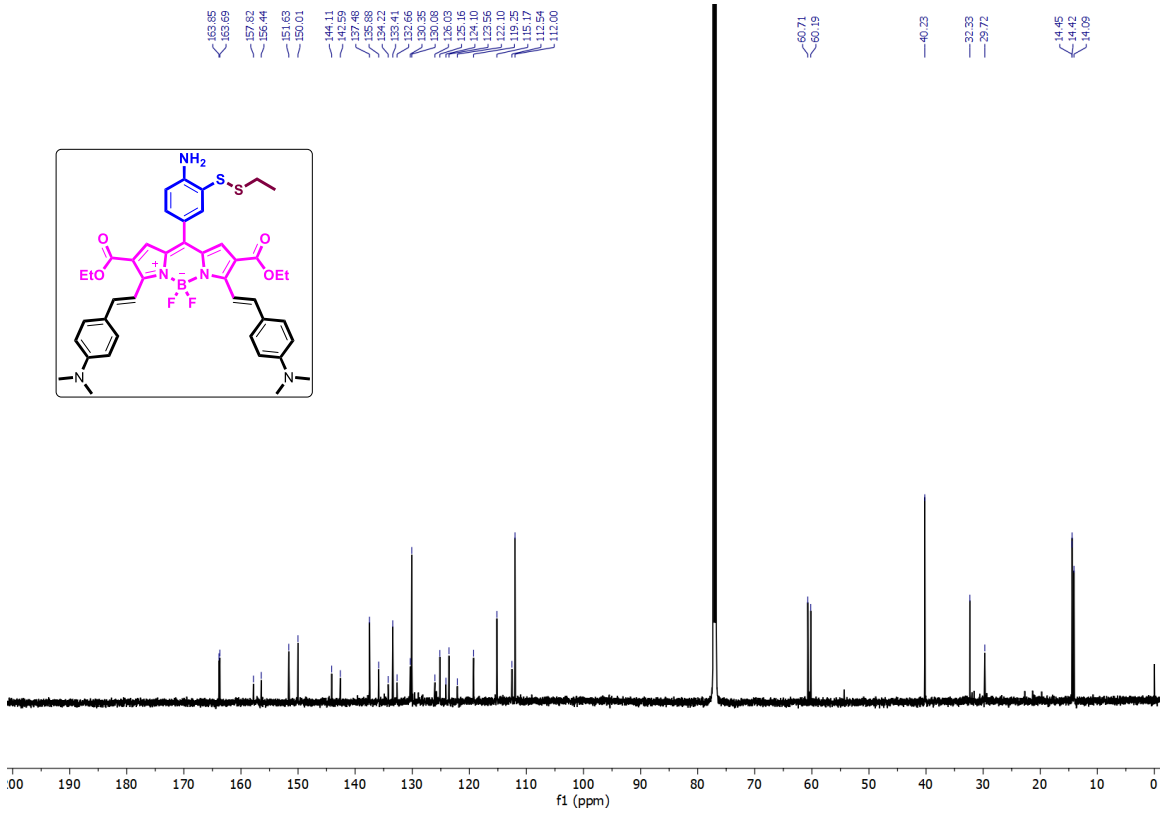

8.56
8.54
8.27
8.26
7.63
7.63
7.61
7.61
7.61
4.33
4.32
4.31
4.30
4.30
4.28
2.86
2.84
1.72
1.39
1.37
1.35
1.33
NO2
EtO
OEt
F F
1.00
0.99
0.98
4.35
6.42
6.16
6.22
f1 (ppm)


163.96
160.61
146.83
146.14
141.35
140.60
133.30
132.45
131.23
128.99
125.89
123.15
77.36
77.04
76.72
60.47
32.70
15.14
14.43
14.40
14.28
NO2
EtO
OEt
F F
f1 (ppm)


7.28
7.12
7.10
6.70
6.69
6.46
6.46
6.45
6.44
4.69
4.32
4.30
4.28
4.27
2.84
1.88
1.35
1.33
1.31
1.01
1.01
1.00
1.96
4.17
6.05
6.03
6.45
f1 (ppm)


164.20
159.67
149.66
147.37
144.62
138.09
137.97
130.94
118.64
116.71
114.04
60.33
15.06
14.29
13.79
f1 (ppm)


8.26
8.22
7.84
7.80
7.69
7.68
7.66
7.64
7.64
7.41
7.40
7.39
7.38
6.91
6.89
6.77
6.76
6.75
4.79
4.36
4.35
4.33
4.31
3.08
2.86
2.84
2.82
1.44
1.42
1.40
1.39
1.37
1.35
NH2
S
S
EtO
OEt
O
O
N
B
F
F
2.00
2.11
1.01
3.84
2.14
0.91
1.11
4.25
2.05
4.10
12.07
2.33
3.28
6.62
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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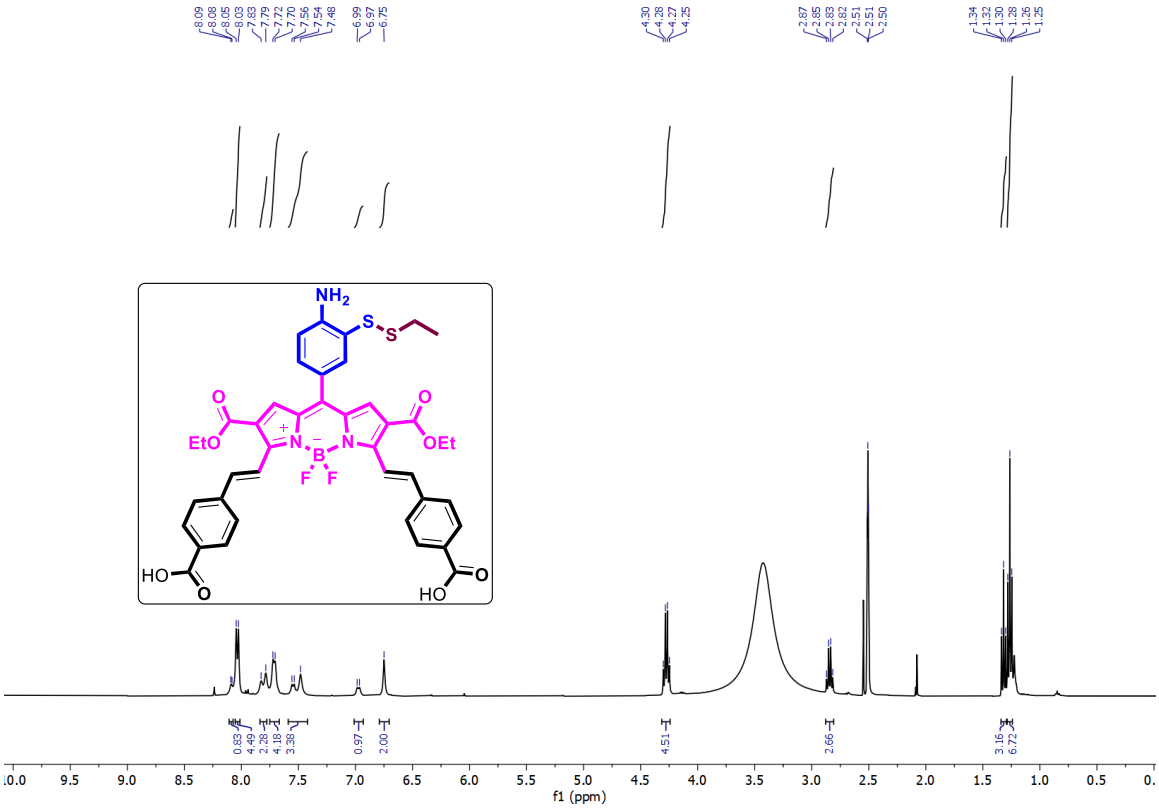
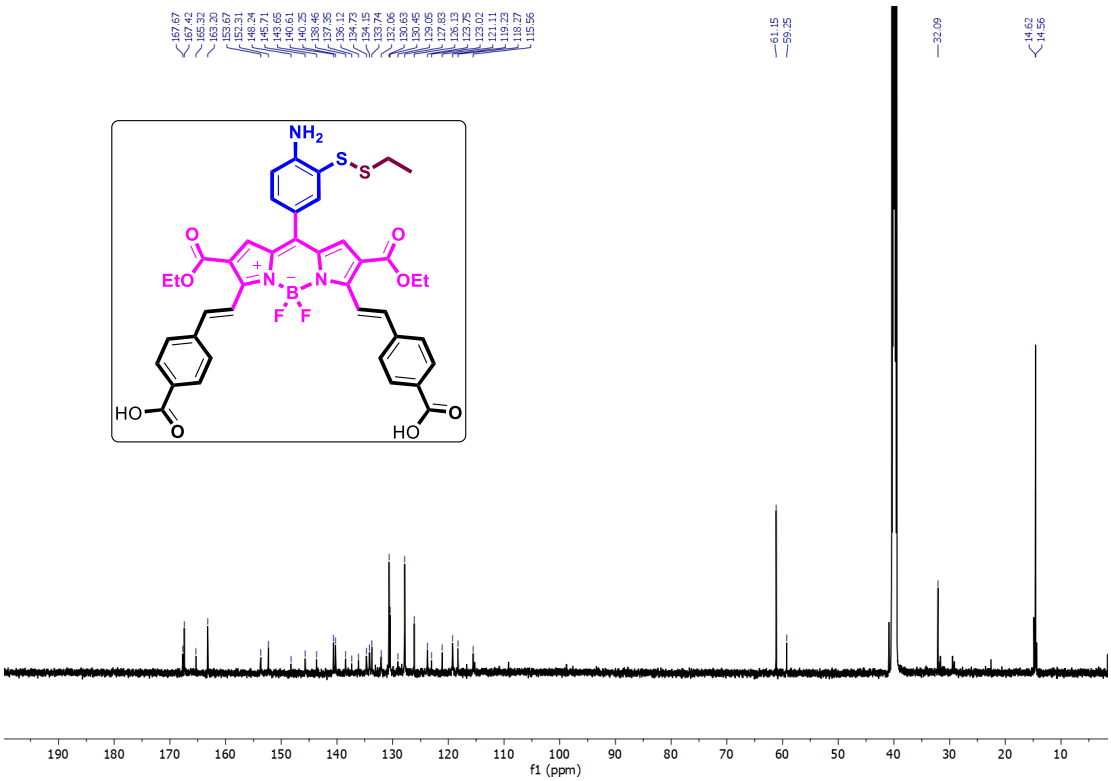
163.69
157.82
156.44
151.63
150.01
144.11
142.59
137.48
135.88
134.22
133.41
132.66
130.35
130.08
126.63
125.15
124.10
123.56
122.10
119.25
115.17
112.54
112.00
60.71
60.19
40.23
32.33
29.72
14.45
14.42
14.09
NH2
S
S
EtO
OEt
O
O
N
B
F
F
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


NH2
S
S
EtO
OEt
O
N
B
F F
HO
HO
f1 (ppm)


NH2
S
S
EtO
OEt
O
N
B
F F
HO
HO
f1 (ppm)