Chemoselective Reaction of Methoxyaminomethyl BODIPYs with Unprotected Carbohydrates: A Powerful Tool for Accessing BODIPY Neoglycosides

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1. Materials and methods

General information and materials

Most chemicals and solvents were used as received from commercial suppliers. Before use traces of water present in the commercially available methoxyamine hydrochloride were removed by co-evaporation with dry toluene. All synthetic transformations were performed under inert argon in dry flasks with stoppers or septa. Air and/or moisture-sensitive liquids were transferred using syringes or cannulas. Microwave-Assisted reactions were performed in an Anton Paar Monowave 300 instrument at 600 W with full air cooling and stirring on. Thin-layer chromatography (TLC) on Kieselgel 60 F254 plates was used for analysis. TLC spots were visualized by UV light (254 nm) and then by charring after spraying with 20% sulfuric acid in ethanol. Organic solutions were dried with anhydrous $MgSO_4$ or Na_2SO_4. Solvents were evaporated under reduced pressure using a rotary evaporator. Purification by flash column chromatography was performed on silica gel (230-400 mesh, Merck). High-resolution mass spectra were obtained using electrospray ionization (ESI) on a Q-TOF LC/MS instrument. Specific rotations (in deg cm^2 g^{-1}) were measured in a 10 cm thermostated quartz cell on a JASCO P2000 polarimeter. The ^{1}H- and ^{13}C{1H}-NMR spectra were measured on a 300, 400 or 500 MHz and 75, 101, 126 MHz, respectively. Chemical shifts were expressed in parts per million (δ scale) and referenced to the residual H signal of the deuterated solvent ($CHCl_3$: δ 7.26 ppm; CH_3OH: δ 4.84 ppm). Coupling constants (*J*) are given in Hz. All ^{13}C-NMR spectra presented are decoupled from protons. Formyl-BODIPYs **8a**,[1] **8b**[2] and **8c**[3] were prepared according to the previously described methods.

X-ray diffraction. X-ray data for compound **6d** was collected using a microsource CuKα radiation in a Bruker APEX II diffractometer and a Photon 100 CCD detector at 120K. Data were processed with APEX3,[4] the structure was solved by direct methods using SHELXS program[5] and refined by -matrix least-squared using SHELXL software incorporated in Olex2-1.5.[6] CCDC 2351271 contains the supplementary crystallographic data for compound **6d**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via **www.ccdc.cam.ac.uk/structures**

[1] L. Jiao, C. Yu, J. Li, Z. Wang, M. Wu and E. Hao "β-Formyl-BODIPYs from the Vilsmeier-Haack Reaction", *J. Org. Chem.* 2009, **74**, 7525–7528.

[2] A. Ramos-Torres, E. Avellanal-Zaballa, A. Prieto-Castañeda, F. García-Garrido, J. Bañuelos, A. R. Agarrabeitia and M. J. Ortiz, FormylBODIPYs by PCC-Promoted Selective Oxidation of α-methylBODIPYs. Synthetic Versatility and Applications, *Org. Lett.*, 2019, **21**, 4563–4566.

[3] M. del Río, F. Lobo, J. C. López, A. Oliden, J. Bañuelos, I. López-Arbeloa, I. García-Moreno and A. M. Gómez, One-Pot Synthesis of Rotationally Restricted, Conjugatable, BODIPY Derivatives from Phthalides. *J. Org. Chem*. 2017, **82**, 1240-1247.

[4] APEX3 Software; Bruker AXS Inc.: Madison, Wisconsin, USA, 2016.

[5] G. M. Sheldrick, *Acta Crystallogr. C Struct. Chem*. 2015, **71**, 3–8.

[6] O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, OLEX2: A complete structure solution, refinement and analysis program 2009.

Photophysical measurements. The dye solutions at different concentrations were prepared by diluting a concentrated stock solution in water (Milli-Q grade). The photophysical properties at different concentrations in aqueous solutions were recorded using quartz cuvettes with the required optical pathlength (l) to match the optical densities and minimize the reabsorption/reemission phenomena at each concentration (10^{-6} M – l = 1 cm, 10^{-5} M – l = 0.1 cm, 10^{-4} M – l = 0.01 cm and 10^{-6} M – l = 0.001 cm). Visible absorption and fluorescence spectra were recorded on an Agilent spectrophotometer (model CARY 7000) and an Edinburgh Instruments spectrofluorometer (model FLSP 920), respectively. The fluorescence spectra were recorded in right-angle for the diluted solutions (10^{-6} M), whereas for the rest of concentrated solution a front-face configuration to further decrease the reabsorption/reemission phenomena. The relative fluorescence quantum yields (ϕ) of the diluted solutions (10^{-6} M) were obtained using Fluorescein (laser grade from Exciton, ϕ^{ρ} = 0.79 in aqueous 0.1 M NaOH) as reference. For the more concentrated solutions the absolute fluorescence quantum yield was measured using an integrating sphere coupled to the said spectrofluorometer and a cuvette with an optical pathlength of 0.1 cm. In both cases, the fluorescence spectra were corrected to take into account the detector sensibility to the wavelength. Radiative decay curves were registered with the time correlated single-photon counting technique as implemented in the aforementioned spectrofluorometer. Fluorescence emission was monitored at the maximum emission wavelength after excitation by means of a Fianium pulsed laser (time resolution of picoseconds) with tunable wavelength. The fluorescence lifetime (τ) was obtained after the deconvolution of the instrumental response signal from the recorded decay curves by means of an iterative method. The goodness of the exponential fit was controlled by statistical parameters (chi-square and the analysis of the residuals).

Biological studies

Cell culture

Biological studies were conducted on healthy human breast epithelial cells (HMEpiC, Innoprot), human breast adenocarcinoma epithelial cells (MCF-7, ECACC) and human fibroblast (FBH, ATCC). HMEpiC cells were cultured in mammary epithelial cell medium (Innoprot) supplemented with 5 wt% fetal bovine serum (FBS, Sigma), 1 wt% penicillin/streptomycin (Invitrogen), and 1 wt% Mammary Epithelial Cell Growth Supplement (MEpiCGS , Innoprot). MCF-7 and FBH were cultured in Dulbecco modified eagle medium (DMEM, Sigma) supplemented with 10 wt% of fetal bovine serum (FBS, Sigma), 1 wt% penicillin/streptomycin (Invitrogen) and 2 wt% l-glutamine (Invitrogen).

Cells were maintained at 37 °C and 5 % CO_2 in a humidified chamber until reaching confluence prior to experimentation. Cells within passages 4 to 8 were employed in all experiments.

Toxicity test

HMEpiC and MCF-7 cells were seeded separately in 96-well plates at a density of 100,000 cells/mL and incubated at 37 °C and 5 % CO_2. After 24 hours, the culture medium was replaced with sequential dilutions of the different BODIPYs in fresh culture medium starting from the maximum concentration at which no aggregates were formed. The cells were subsequently incubated at 37 °C and 5 % CO_2 for an additional 24 hours. Following this incubation period, the culture medium was substituted with phenol red-free culture medium (Sigma Aldrich).

Cell viability was assessed by the addition of Alamar Blue (AB, Invitrogen) at a concentration of 10% (v/v), following ISO 10993-5:2009 guidelines. The cells were then incubated at 37 ºC for 4 hours. Subsequently, cell viability was quantified using a plate reader (Biotek Synergy HT spectrophotometer) with laser excitation at 590 nm, and the emitted fluorescence was measured at 530 nm. The percentage of cell viability was determined using the following equation (eqn (1)):

$$\boldsymbol{Cell\ viability}\ (\mathbf{5}) = \mathbf{100} \times \frac{\boldsymbol{OD_S - OD_B}}{\boldsymbol{OD_C - OD_B}}$$

where ODS, ODB, and ODC represent the emitted fluorescence at 530 nm for the sample (S), blank (B, culture medium without cells), and control (C, culture medium without BODIPY), respectively. All experiments were performed with an n=7, and the resulting data were presented as mean values ± standard deviation (SD).

BODIPYs accumulation inside the cell was visualized using epifluorescence microscopy. The cell stain was performed using DAPI (Invitrogen) to stain the nucleus and Alexa Fluor Plus 647 Phalloidin to stain the actin. Epifluorescence images were taken using a Nikon ECLIPSE TE2000-S microscope with a LED light source and using the software NIS ELEMENTS BR (Nikon). BODIPYs were visualized using a green filter (Ex. 465/30; Em. 515/30), actin in red (Ex. 628/40; Em. 692/40) and nucleus in blue (Ex. 387/11; Em. 447/60).

Acarbose-BODIPY cell internalization

To visualize the internalizations of acarbose-BODIPY a lightning confocal microscopy (LEICA TCS SP8) technique was applied. This technique provides optical sectioning, allowing imaging into thick samples. By using lighting confocal microscopy it is possible to obtain high-quality images and study the spatiotemporal dynamics of biological systems.[7] 200 µL of FBH (100,000 cell/mL) were added to a µ-Slide 8 well IbiTreat (Ibidi) culture slide and incubated for 24 hours at 37 ºC and 5% CO2. After the incubation

[7] W. M. Reilly and C. J. Obara, Advances in confocal microscopy and selected applications. *Methods Mol. Biol*. 2021, **2304**, 1–35.

period, the culture medium was replaced by a non-toxic solution of 100 µM of acarbose-BODIPY in a fresh medium and incubated again for 24 hours. Cells were fixed by replacing the culture media with a 4% paraformaldehyde solution and culture for 1 hour. The stain of the cell was performed by using MitoTracker Red CMXRox (Molecular Probes) and LysoTracker Red DND-99 (Invitrogen) to stain the mitochondria and the lysosomes respectively, DAPI (Invitrogen) to stain the nucleus and Alexa Fluor Plus 647 Phalloidin to stain the actin. Analysis of the images was performed using LAS X software (Leica)

Enzyme Kinetic Studies

Kinetic studies were performed at 25 ^{o}C in an appropriate buffer (specific conditions depicted below). In a typical assay, the enzyme was incubated with different inhibitor concentrations for up to 5 min before initiating the reaction by the addition of substrate. The initial reaction rate was measured by monitoring the increase in absorbance at 400 nm for five minutes using a JASCO V-730 UV-vis spectrophotometer. IC50 determinations were performed using 2-chloro-4-nitrophenyl α-D-maltotrioside as chromogenic substrate (1 mM). For each inhibitor, a range of four to seven concentrations bracketing the IC50 value ultimately determined was used. Dose-response plots (% activity vs. log[I]) were constructed to validate the use of a competitive inhibition model. The data were then fit using non-linear regression based on the Hill equation with Quest Graph™ IC50 Calculator (AAT Bioquest, Inc).

Specific assay conditions for each enzyme:

- *oryzae* α-amylase (AOA): 20 mM sodium acetate, 1 mM calcium chloride (pH 5.6).
- Human salivary α-amylase (HSA): 50 mM sodium phosphate, 100 mM sodium chloride (pH 7).

2. General Synthetic Procedures

Procedure I. *General method for methyloxime formation*. To a mixture of the appropriate aldehyde **8a–c** (1 equiv.) and methoxyamine hydrochloride (3 equiv.) in anhydrous methanol (5 mL/mmol) and under an argon atmosphere, dry pyridine (4.5 equiv.) was added. The reaction mixture was stirred at room temperature until complete consumption of the starting material was observed by TLC (30 min). The solution was concentrated and the crude material was purified through silica column chromatography (hexane−ethyl acetate 95:5).

Procedure II. *General method for methoxyamine formation.* $NaCNBH_3$ (6 equiv.), was added to a cooled solution (15 ^{o}C, water bath) of the corresponding methyloxime **9a–c** (1 equiv.) dissolved in glacial AcOH (10 mL/mmol) under an argon atmosphere. The

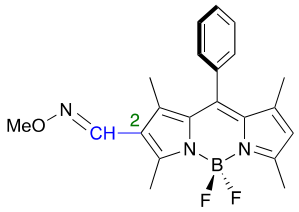
mixture was stirred until complete consumption of the starting material was observed by TLC (1 h). Then, it was diluted with ethyl acetate and successively washed with water, saturated solution of $NaHCO_3$ and brine. The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated at reduced pressure. The residue was purified by chromatography on silica gel (hexane−ethyl acetate 9:1 to 8:2).

Procedure III. *General method for neoglycosylation reaction.* A mixture of the corresponding methoxyaminomethyl BODIPY **6a–c** or N-cyanoboronated-N-alkoxyamine derivative **6d** (1 equiv.) and D-glucose (3 equiv.) dissolved in DMF/glacial acetic acid (1:1, 10 mL/mmol) was stirred for 20 h at room temperature. After removal of the solvent, the residue was purified by flash chromatography on silica gel (Dichloromethane−methanol 95:5 to 9:1).

Procedure IV. *General method for neoglycosylation reaction under microwave irradiation.* To a mixture of the corresponding methoxyaminomethyl BODIPY **6a–c** or N-cyanoboronated-N-alkoxyamine derivative **6d** (1 equiv.) dissolved in methanol/glacial acetic acid (1:1, 10 mL/mmol) in a microwave tube was added the appropriate free sugar (D-glucose, D-cellobiose, D-lactose, D-maltose, D-maltotriose or acarbose, 3 equiv., respectively) and 2-amine-5-methoxy benzoic acid (10% w/w). The tube was then exposed to microwave irradiation at 60 ºC until completion of the reaction (1-8 h). The solvents were then evaporated in vacuo and chromatography of the residue on silica gel gave glyco-BODIPYs **10a**–**c**, **12**–**16**.

Procedure V. *General method for acetylation reaction.* Glyco-BODIPYs **10a** and **10b** (1.0 equiv.) was dissolved in Ac_2O/pyridine (0.5:2, 5 mL) and a catalytic amount of *N*,*N*-dimethylaminopyridine was added. The mixture was stirred 4 h and then diluted with methanol to destroy the excess of Ac_2O. Solvents were evaporated in vacuo and chromatography of the residue on silica gel afforded the corresponding acetylated derivatives. These compounds were used to unambiguously establish the stereochemistry in the neoglycosylation reaction.

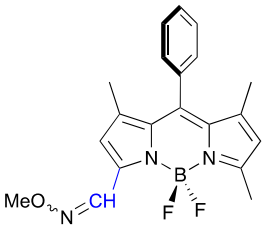
3. Synthetic procedures and compound characterization



9a

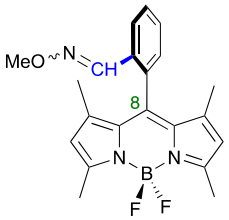
Compound 9a. This compound was prepared according to general procedure I from formyl BODIPY **8a** (1,5 g, 4.26 mmol) and methoxyamine hydrochloride (1.06 g, 12.78 mmol). The residue was purified by flash chromatography (hexane:ethyl acetate 95:5) to give **9a** as an orange non crystalline solid (1.47g, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ

7.80 (s, 1H), 7.32 – 7.18 (m, 3H), 7.10 – 6.98 (m, 2H), 5.81 (s, 1H), 3.67 (s, 3H), 2.49 (s, 3H), 2.35 (s, 3H), 1.23 (s, 3H), 1.15 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.9, 154.6, 144.9, 143.0, 142.5, 140.2, 134.9, 132.5, 130.7, 129.4, 129.3, 128.1, 128.0, 122.5, 121.8, 62.0, 14.9, 14.7, 14.2, 12.5. $[M+H]^+$ calcd for $C_{21}H_{23}BF_2N_3O$: 382.1900; found 382.1906.



9b

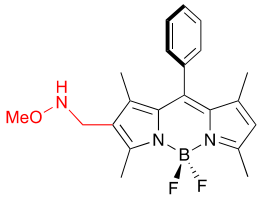
Compound 9b. This compound was prepared according to general procedure I from formyl BODIPY **8b** (500 mg, 1.48 mmol) and methoxyamine hydrochloride (370 mg, 4.44 mmol). The residue was purified by flash chromatography (hexane:ethyl acetate 95:5) to give **9b** as an orange non crystalline solid (461 mg, 84%). For the major compound: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (s, 1H), 7.58 – 7.42 (m, 3H), 7.39 – 7.20 (m, 2H), 6.65 (s, 1H), 6.06 (s, 1H), 4.00 (s, 3H), 2.57 (s, 3H), 1.40 (s, 6H) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.32 – 7.18 (m, 3H), 7.10 – 6.98 (m, 2H), 5.81 (s, 1H), 3.67 (s, 3H), 2.49 (s, 3H), 2.35 (s, 3H), 1.23 (s, 3H), 1.15 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 145.9, 144.5, 142.3, 142.3, 141.4, 134.7, 133.1, 132.5, 129.5, 129.5, 129.4, 129.4, 128.0, 127.9, 122.8, 122.8, 117.9, 62.7, 15.1, 14.7, 14.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -141.11 (q, 33.1 Hz, minor isomer), -141.53 (q, 33.0 Hz, major isomer). HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ calcd for $C_{20}H_{21}BF_2N_3O$: 368.17439; found 368.1751; $[M+Na]^+$ calcd for $C_{20}H_{20}BF_2N_3NaO$: 390.1563; found 390.1557.



9c

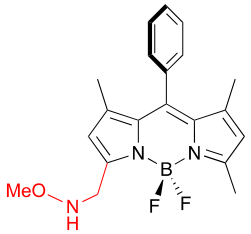
Compound 9c. This compound was prepared according to general procedure I from formyl BODIPY **8c** (500 mg, 1.42 mmol) and methoxyamine hydrochloride (355 mg, 4.26 mmol). The residue was purified by flash chromatography (hexane:ethyl acetate 95:5) to give **9c** as an orange non crystalline solid (390 mg, 74%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 – 7.94 (m, 2H), 7.57 – 7.42 (m, 2H), 7.24 (ddd, *J* = 5.5, 3.4, 2.3 Hz, 1H), 5.98 (s, 2H), 3.91 (s, 3H), 2.56 (s, 6H), 1.36 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.0, 145.2, 142.9, 138.4, 134.1, 131.3, 130.7, 130.5, 129.5, 128.7, 125.9, 121.5, 62.1, 14.6, 13.9. HRMS

(ESI/Q-TOF) m/z: $[M+H]^+$ calcd for $C_{21}H_{23}BF_2N_3O$: 382.1900; found 382.1911; $[M+Na]^+$ calcd for $C_{21}H_{22}BF_2N_3NaO$: 404.1720; found 404,1732.



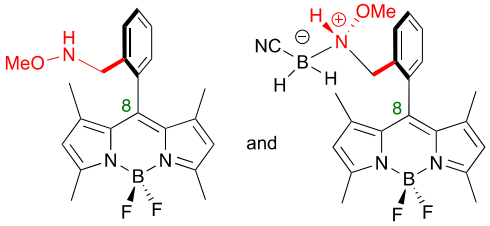
6a

Compound 6a. This compound was prepared according to general procedure II from BODIPY-O-methyl oxime **9a** (1,25 g, 3.28 mmol) and $NaCNBH_3$ (1.23 g, 19.7 mmol). The residue was purified by flash chromatography (hexane:ethyl acetate 9:1 to 8:2) to give **9a** as an dark red non crystalline solid (829 mg, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (m, 3H), 7.32 – 7.24 (m, 2H), 5.99 (s, 1H), 3.81 (s, 2H), 3.51 (s, 3H), 2.60 (s, 3H), 2.55 (s, 3H), 1.38 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.2, 155.5, 143.8, 142.1, 141.7, 135.4, 131.9, 131.1, 129.5, 129.3, 128.3, 125.4, 121.8, 62.1, 45.1, 14.9, 14.7, 12.9, 12.2. ^{11}B NMR (128 MHz, $CDCl_3$) δ 0.71 (t, *J* = 33.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -146.86 (q, *J* = 32.8 Hz). HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ calcd for $C_{21}H_{25}BF_2N_3O$: 384.2057; found 384.2061; $[M+Na]^+$ calcd for $C_{21}H_{24}BF_2N_3NaO$: 406.1876; found 406,1888.



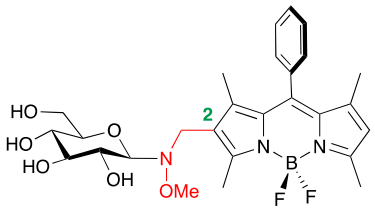
6b

Compound 6b. This compound was prepared according to general procedure II from BODIPY-O-methyl oxime **9b** (400 mg, 1.05 mmol) and $NaCNBH_3$ (395 mg, 6.3 mmol). The residue was purified by flash chromatography (hexane:ethyl acetate 9:1 to 8:2) to give **9a** as an dark red non crystalline solid (281 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.48 (m, 3H), 7.35 – 7.26 (m, 2H), 6.22 (s, 1H), 6.03 (s, 1H), 4.34 (s, 2H), 3.60 (s, 3H), 2.56 (s, 3H), 1.39 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1, 152.9, 145.3, 143.2, 142.5, 135.0, 132.5, 131.7, 129.5, 129.4, 129.4, 128.2, 128.1, 122.4, 121.1, 61.8, 48.7, 15.1, 14.8, 14.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -146.86 (q, *J* = 32.8 Hz). HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ calcd for $C_{20}H_{23}BF_2N_3O$: 370.1900; found 370.1916; $[M+Na]^+$ calcd for $C_{20}H_{22}BF_2N_3NaO$: 392.1720; found 392.1733.



6c **6d**

Compounds 6c and 6d. These compounds were prepared according to general procedure II from BODIPY-O-methyl oxime **9c** (370 mg, 0.97 mmol) and $NaCNBH_3$ (366 mg, 5.8 mmol). The residue was purified by flash chromatography (hexane:ethyl acetate 9:1 to 8:2) to give **6c** (141 mg, 38%) as a dark red non crystalline compound followed by **6d** (131 mg, 32%) as an dark red solid. For **6c**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (ddd, *J* = 7.7, 1.4, 0.7 Hz, 1H), 7.47 (td, *J* = 7.5, 1.5 Hz, 1H), 7.39 (td, *J* = 7.5, 1.4 Hz, 1H), 7.19 (dd, *J* = 7.5, 1.5 Hz, 1H), 5.97 (s, 2H), 3.95 (s, 2H), 3.42 (s, 3H), 2.55 (s, 6H), 1.37 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.1, 143.4, 140.5, 136.2, 134.5, 131.5, 129.8, 129.6, 128.6, 128.5, 121.7, 121.7, 61.8, 53.1, 15.0, 14.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -145.46 – -146.54 (m, 2F); ^{11}B NMR (128 MHz, $CDCl_3$) δ -0.19 (t, *J* = 33.7 Hz). HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ calcd for $C_{21}H_{25}BF_2N_3O$: 384.2057; found 384.2037; $[M+Na]^+$ calcd for $C_{21}H_{24}BF_2N_3NaO$: 406.1876; found 406.1859. For **6d**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (dd, *J* = 5.6, 3.4 Hz, 1H), 7.57 (dd, *J* = 5.6, 3.3 Hz, 2H), 7.35 (dd, *J* = 5.6, 3.4 Hz, 1H), 6.53 (bs, 1H), 6.10 (s, 1H), 6.07 (s, 1H), 4.28 (dd, *J* = 13.5, 5.4 Hz, 1H), 4.18 (dd, *J* = 13.5, 6.6 Hz, 1H), 3.43 (s, 3H), 2.58 (s, 3H), 2.56 (s, 3H), 1.39 (s, 3H), 1.33 (s, 3H). HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ calcd for $C_{21}H_{25}BF_2N_3O$: 384.2057; found 384.2048; $[M+Na]^+$ calcd for $C_{21}H_{24}BF_2N_3NaO$: 406.1876; found 406.1862.

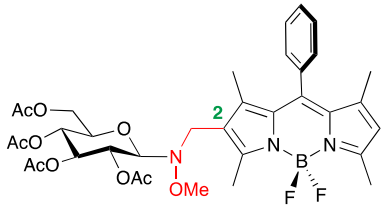


10a

Compound 10a. This compound was prepared according to general procedure III from methoxyamine **6a** (50 mg, 0.13 mmol) and D-glucose (70 mg, 0.39 mmol). The residue was purified by flash chromatography (ethyl acetate: methanol 95:5) to give **10a** as a red solid (26 mg, 37%). $[\alpha]_D^{25}$ +2270 (c 0.2, CH_3OH); Mp 134 – 136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.36 (m, 3H), 7.25 (m, 2H), 5.98 (s, 1H), 3.84 – 3.62 (m, 5H), 3.64 – 3.55 (m, 2H), 3.47–3.42 (m, 1H), 3.45 (s, 3H), 3.14 (d, *J* = 9.3 Hz, 1H), 2.55 (s, 3H), 2.52 (s, 3H), 1.35 (s, , 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.2, 155.4, 143.9, 142.1, 141.8, 135.0, 131.8, 130.8, 129.4, 129.2, 128.1, 124.6, 121.7, 90.5, 69.9, 69.5, 62.3, 61.6, 45.3, 14.8, 14.6,

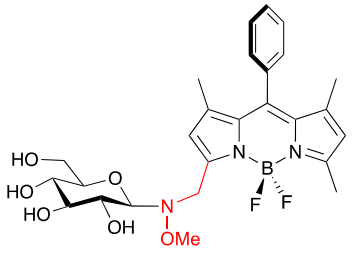
12.6, 11.8. HRMS (ESI/Q-TOF) m/z: $[M+Na]^+$ calcd for $C_{27}H_{34}BF_2N_3NaO_6$: 568.2406; found 568.2376.

This compound was also prepared, in a preferred manner, following general procedure IV from methoxyamine **6a** (50 mg, 0.13 mmol), D-glucose (70 mg, 0.39 mmol) and 5-methoxyanthranilic acid (2.2 mg, 0.013 mmol) under microwave irradiation for 1 h. The residue was purified by flash chromatography (ethyl acetate: methanol 95:5) to give **10a** as a red solid (62 mg, 87%).



10a-OAc

Due to the overlap of signals in the ^{1}H NMR spectrum, in **10a** and in order to unequivocally assign the stereochemistry with which the neoglycosylation reaction took place, an acetylation reaction according to general procedure V was carried out **10a-OAc:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 – 7.42 (m, 3H), 7.39 – 7.26 (m, 2H), 6.02 (s, 1H), 5.28 (t, *J* = 9.2 Hz, 1H), 5.14 (t, *J* = 9.2, 1H), 5.02 (t, *J* = 9.2 Hz, 1H), 4.21 – 4.09 (m, 2H), 4.01 (d, *J* = 12.7 Hz, 1H), 3.96 (d, *J* = 9.2 Hz, 1H, $H_{anomeric}$), 3.86 (d, *J* = 12.3 Hz, 1H), 3.57 – 3.35 (m, 1H), 3.47 (s, 3H), 2.59 (s, 3H), 2.58 (s, 3H), 2.01 (s, 3H), 1.99 (s, 3H), 1.98 (s, 3H), 1.97 (s, 3H), 1.39 (s, 3H), 1.36 (s, 3H).

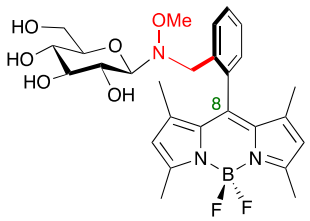


10b

Compound 10b. This compound was prepared according to general procedure III from methoxyamine **6b** (50 mg, 0.135 mmol) and D-glucose (73 mg, 0.40 mmol). The residue was purified by flash chromatography (ethyl acetate: methanol 95:5) to give **10b** as a red solid (18 mg, 25%). $[\alpha]_D^{25}$ +845.5 (c 0.18, CH_3OH); Mp 126 – 128 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.59 – 7.55 (m, 3H), 7.46 – 7.25 (m, 2H), 6.44 (s, 1H), 6.14 (s, 1H), 4.43 (d, *J* = 16 Hz, 1H), 4.33 (d, *J* = 16 Hz, 1H), 4.16 (d, *J* = 9.0 Hz, 1H, $H_{anomeric}$), 3.88 (dd, *J* = 12.0, 2.3 Hz, 1H), 3.73 (dd, J = 12.1, 5.2 Hz, 1H), 3.58 (s, 3H), 3.52 (t, *J* = 9.0 Hz, 1H), 3.41 (t, J = 8.7 Hz, 1H), 3.25 (ddd, *J* = 9.4, 5.2, 2.3 Hz, 1H), 2.52 (s, 3H), 1.44 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (101 MHz, CD_3OD) δ 158.8, 154.7, 146.2, 144.6, 143.4, 136.1, 132.3, 130.5, 130.4, 129.1, 123.1, 122.4, 94.2, 79.7, 79.2, 71.7, 71.1, 62.8, 62.2, 50.0, 49.5,14.5, 14.3;

^{19}F NMR (376 MHz, CD_3OD) δ -143.81 (ddd, *J* = 101.0, 65.2, 32.5 Hz), -146.08 (ddd, *J* = 103.0, 65.0, 32.0 Hz).HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ calcd for $C_{26}H_{33}BF_2N_3O_6$: 532.2430; found 532.2453; $[M+Na]^+$ calcd for $C_{26}H_{32}BF_2N_3NaO_6$: 554.2249; found 554.2258.

This compound was also prepared, in a preferred manner, following general procedure IV from methoxyamine **6b** (50 mg, 0.135 mmol), D-glucose (73 mg, 0.40 mmol) and 5-methoxyanthranilic acid (2.2 mg, 0.013 mmol) under microwave irradiation for 1 h. The residue was purified by flash chromatography (ethyl acetate: methanol 95:5) to give **10a** as a red solid (55 mg, 76%).

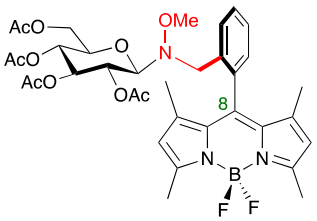


10c

Compound 10c. This compound was prepared according to general procedure III from methoxyamine **6c** (50 mg, 0.13 mmol) and D-glucose (70 mg, 0.39 mmol). The residue was purified by flash chromatography (ethyl acetate: methanol 95:5) to give **10c** as a red solid (28 mg, 40%). $[\alpha]_D^{25}$ +824 (c 0.2, CH_3OH); Mp 128 – 130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 6.6 Hz, 1H), 7.50 – 7.43 (m, 2H), 7.30 – 7.27 (m, 1H), 6.02 (s, 1H), 6.00 (s, 1H), 4.07 (d, *J* = 13.3 Hz, 1H), 3.93 (d, *J* = 13.3 Hz, 1H), 3.87 – 3.76 (m, 3H), 3.56 – 3.34 (m, 2H), 3.31 (s, 3H), 3.16 – 3.08 (m, 1H), 2.55 (s, 3H), 2.54 (s, 3H), 1.38 (s, 3H), 1.34 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.3, 156.1, 143.0, 142.8, 139.9, 135.2, 133.8, 131.8, 131.6, 131.0, 129.8, 129.2, 128.9, 128.9, 128.4, 125.4, 121.8, 121.6, 91.3, 70.5, 70.1, 62.4, 61.5, 52.5, 29.8, 14.9, 14.8, 14.8, 14.3; ^{11}B NMR (128 MHz, $CDCl_3$) δ 0.68 (t, *J* = 32.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -145.5 – -145.9 (m, 1F), -147.7– -148.1 (m, 1F). HRMS (ESI/Q-TOF) m/z: $[M+Na]^+$ calcd for $C_{27}H_{34}BF_2N_3NaO_6$: 568.2406; found 568.2393.

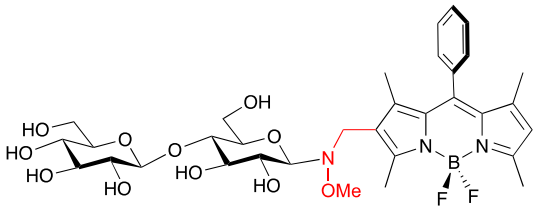
In an alternative experiment this compound was prepared according to general procedure III from N-cyanoboronated-N-methoxyamine **6d** (50 mg, 0.12 mmol) and D-glucose (65 mg, 0.36 mmol). The residue was purified by flash chromatography (ethyl acetate: methanol 95:5) to give **10c** (16 mg, 25%).

This compound was also prepared, in a preferred manner, following general procedure IV from methoxyamine **6c** (50 mg, 0.13 mmol), D-glucose (70 mg, 0.39 mmol) and 5-methoxyanthranilic acid (2.2 mg, 0.013 mmol) under microwave irradiation for 1 h. The residue was purified by flash chromatography (ethyl acetate: methanol 95:5) to give **10a** as a red solid (59 mg, 87%).



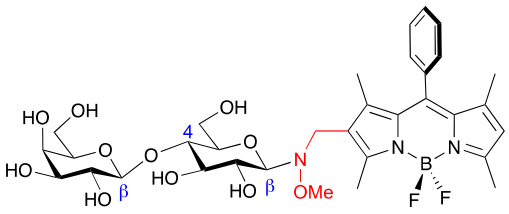
10c-OAc

Due to the overlap of signals in the ^{1}H NMR spectrum of compound **10c** and to unequivocally assign the stereochemistry with which the neoglycosylation reaction took place, an acetylation reaction according to general procedure V was carried out to yield compound **10c-OAc:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 7.4, 1.6 Hz, 1H), 7.46 (dtd, *J* = 16.2, 7.4, 1.6 Hz, 2H), 7.20 – 7.12 (m, 4H), 6.01 (s, 1H), 5.97 (s, 1H), 5.37 – 5.21 (m, 1H), 5.14 – 4.93 (m, 2H), 4.32 – 4.16 (m, 2H), 4.09 (d, *J* = 9.2 Hz, 1H, $H_{anomeric}$), 4.03 (dd, *J* = 12.4, 2.4 Hz, 1H), 3.96 (d, *J* = 13.7 Hz, 1H), 3.40 (ddd, *J* = 10.0, 5.0, 2.6 Hz, 1H), 3.30 (s, 3H), 2.55 (s, 3H), 2.54 (s, 3H), 2.04 (s, 3H), 2.00 (s, 3H), 1.98 (s, 3H), 1.97 (s, 3H), 1.39 (s, 3H), 1.36 (s, 3H).; ^{19}F NMR (376 MHz, $CDCl_3$) δ -147.15 (ddd, *J* = 66.2, 40.5, 32.7 Hz); ^{11}B NMR (128 MHz, $CDCl_3$) δ 0.65 (t, *J* = 32.8 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 170.5, 169.5, 169.4, 156.3, 155.6, 143.4, 142.3, 139.8, 138.0, 135.1, 134.2, 131.8, 130.8, 130.5, 129.5, 129.2, 128.9, 128.7, 128.4, 125.4, 121.5, 89.6, 77.5, 77.4, 77.2, 76.8, 74.4, 73.7, 68.4, 68.3, 62.1, 61.1, 52.3, 32.1, 20.8, 20.8, 20.8, 20.7, 14.8, 14.7, 14.3, 14.2.



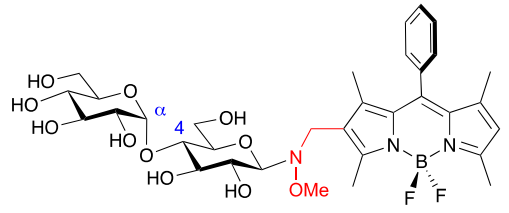
12

Compound 12. This compound was also prepared following general procedure IV from methoxyamine **6a** (50 mg, 0.13 mmol), D-cellobiose (133 mg, 0.39 mmol) and 5-methoxyanthranilic acid (2.2 mg, 0.013 mmol) under microwave irradiation for 4 h. The residue was purified by flash chromatography (dichloromethane: methanol 9:1 to 8:2) to give **12** as a red solid (63 mg, 69%). $[\alpha]_D^{25}$ -188.5 (c 0.2, CH_3OH); Mp 159 – 160 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.56 –7.53 (m, 3H), 7.32 – 7.29 (m, 2H), 6.06 (s, 1H), 4.41 (d, *J* = 7.8 Hz, 1H), 3.96 (d, *J* = 12.0 Hz, 1H), 3.92 (d, *J* =12.0 Hz, 1H), 3.90 – 3.75 (m, 3H), 3.65 (dd, *J* = 12, 8.0 Hz, 1H), 3.60 – 3.45 (m, 5H), 3,34 (s, 3H), 3.31 – 3.12 (m, 1H), 2.59 (s, 3H), 2.48 (s, 3H), 1.45 (s, 3H), 1.33 (s, 3H). ^{13}C NMR (101 MHz, CD_3OD) δ 156.6, 156.1, 144.1, 142.9, 142.7, 135.7, 132.0, 131.3, 129.8, 129.7, 128.7, 126.2, 121.7, 103.9, 91.6, 79.4, 77.5, 77.4, 77.3, 77.2, 76.9, 74.3, 70.7, 70.5, 61.8, 61.2, 45.5, 14.0, 12.3, 11.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -144.2 – -152.2 (m, 2F). HRMS (ESI/Q-TOF) m/z: $[M+Na]^+$ calcd for $C_{33}H_{44}BF_2N_3NaO_{11}$: 730.2935; found 730.2941.



13

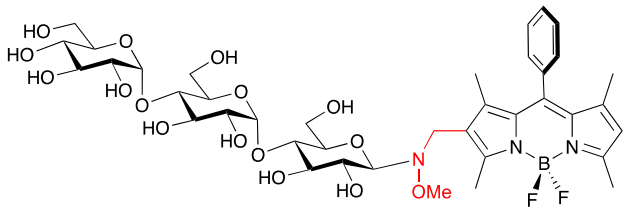
Compound 13. This compound was also prepared following general procedure IV from methoxyamine **6a** (50 mg, 0.13 mmol), D-lactose (133 mg, 0.39 mmol) and 5-methoxyanthranilic acid (2.2 mg, 0.013 mmol) under microwave irradiation for 6 h. The residue was purified by flash chromatography (dichloromethane: methanol 9:1 to 8:2) to give **13** as a red solid (68 mg, 74%). $[\alpha]_D^{25}$ +617.5 (c 0.8, CH_3OH); Mp 140 – 142 °C; ^1H NMR (400 MHz, CD_3OD) δ 7.56 –7.53 (m, 3H), 7.32 – 7.29 (m, 2H), 6.08 (s, 1H), 4.39 (d, *J* = 7.3 Hz, 1H), 4.05 – 3.91 (m, 2H), 3.90 – 3.86 (m, 3H), 3.85 – 3.77 (m, 2H), 3.72 (dd, *J* = 11.5, 4.6 Hz, 1H), 3.63 – 3.55 (m, 2H), 3.54 (s, 3H), 3.51 (ddd, *J* = 12.4, 5.6, 3.0 Hz, 2H), 3.28 (dt, *J* = 9.6, 3.1 Hz, 1H), 2.61 (s, 3H), 2.51 (s, 3H), 1.46 (s, 3H), 1.40 (s, 3H).δ 6.06 (s, 1H), 4.41 (d, *J* = 7.8 Hz, 1H), 3.96 (d, *J* = 12.0 Hz, 1H), 3.92 (d, *J* =12.0 Hz, 1H), 3.90 – 3.75 (m, 3H), 3.65 (dd, *J* = 12, 8.0 Hz, 1H), 3.60 – 3.45 (m, 5H), 3,34 (s, 3H), 3.31 – 3.12 (m, 1H), 2.59 (s, 3H), 2.48 (s, 3H), 1.45 (s, 3H), 1.33 (s, 3H). ^{13}C NMR (101 MHz, CD_3OD) δ 156.6, 156.1, 144.1, 142.9, 142.7, 135.7, 132.0, 131.3, 129.8, 129.7, 128.7, 126.2, 121.7, 103.9, 91.6, 79.4, 77.5, 77.4, 77.3, 77.2, 76.9, 74.3, 70.7, 70.5, 61.8, 61.2, 45.5, 14.0, 12.3, 11.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -144.2 – -152.2 (m, 2F). HRMS (ESI/Q-TOF) m/z: $[M+Na]^+$ calcd for $C_{33}H_{44}BF_2N_3NaO_{11}$: 730.2935; found 730.2952.



14

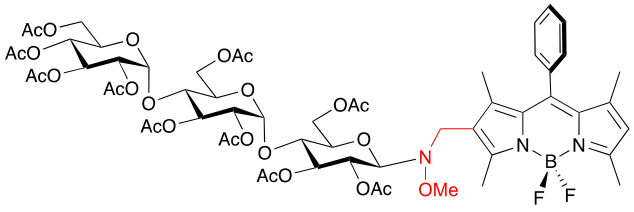
Compound 14. This compound was prepared following general procedure IV from methoxyamine **6a** (50 mg, 0.13 mmol), D-maltose (133 mg, 0.39 mmol) and 5-methoxyanthranilic acid (2.2 mg, 0.013 mmol) under microwave irradiation for 6 h. The residue was purified by flash chromatography (dichloromethane: methanol 9:1 to 8:2) to give **13** as a red solid (71 mg, 77%). $[\alpha]_D^{25}$ +560.4 (c 0.9, CH_3OH); Mp 170 – 172 °C; ^1H NMR (400 MHz, CD_3OD) δ 7.57 (m, 3H), 7.34 (m, 2H), 6.08 (s, 1H), 5.17 (d, *J* = 3.7 Hz, 1H), 3.97 – 3.23 (m, 18H), 2.61 (s, 3H), 2.51 (s, 3H), 1.46 (s, 3H), 1.40 (s, 3H). ^{13}C NMR (101 MHz, CD_3OD) δ 157.3, 156.7, 144.7, 143.5, 143.4, 136.4, 132.7, 131.9, 130.5, 130.4,

130.3, 129.3, 126.9, 122.3, 102.9, 92.3, 80.9, 79.0, 78.3, 75.1, 74.8, 74.2, 71.5, 71.1, 62.7, 62.4, 62.2, 46.1, 14.6, 12.9, 12.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ - 145.9 – -146.8 (m, 2F). HRMS (ESI/Q-TOF) m/z: $[M+Na]^+$ calcd for $C_{33}H_{44}BF_2N_3NaO_{11}$: 730.2935; found 730.2958.



15

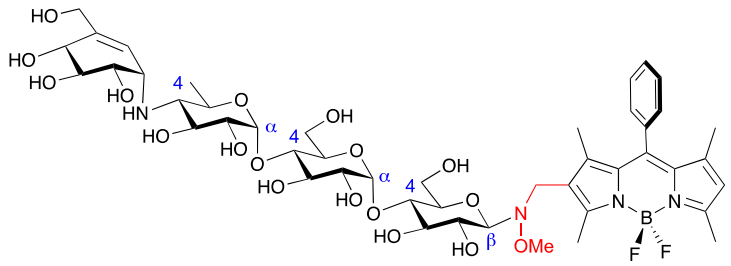
Compound 15. This compound was prepared following general procedure IV from methoxyamine **6a** (50 mg, 0.13 mmol), D-maltotriose (205 mg, 0.39 mmol) and 5-methoxyanthranilic acid (2.2 mg, 0.013 mmol) under microwave irradiation for 8 h. The residue was purified by flash chromatography (Ethyl acetate: methanol: water 17:2:1) to give **13** as a red solid (77 mg, 68%). $[\alpha]_D^{25}$ -44.0 (c 0.88, CH_3OH); Mp 185 – 187 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.57 – 7.56 (m, , 3H), 7.43 – 7.26 (m, 2H), 6.08 (s, 1H), 5.18 (dd, *J* = 4.0, 2.0 Hz, 2H), 4.05 – 3.93 (m, 2H), 3.93 – 3.75 (m, 7H), 3.75 – 3.44 (m, 12H), 3.35 – 3.24 (m, 2H), 2.61 (s, 3H), 2.51 (s, 3H), 1.46 (s, 3H), 1.40 (s, 3H).^{13}C NMR (101 MHz, CD_3OD) δ ^{13}C NMR (101 MHz, CDCl3) δ 157.3, 156.7, 144.6, 143.5, 143.3, 136.3, 132.7, 131.9, 130.5, 130.3, 129.9, 129.3, 129.3, 129.2, 126.9, 126.3, 122.4, 102.8, 102.7, 92.3, 81.3, 80.8, 79.0, 78.3, 75.1, 74.9, 74.7, 74.2, 73.8, 73.3, 71.5, 71.0, 62.7, 62.4, 62.2, 62.1, 46.1, 14.6, 13.0, 12.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ - 143.3 (bs, 2F). HRMS (ESI/Q-TOF) m/z: $[M+Na]^+$ calcd for $C_{39}H_{54}BF_2N_3NaO_{16}$: 892.3604; found 892.3463.



15-OAc

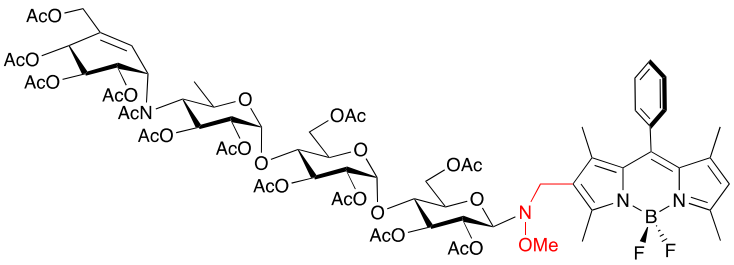
Due to the overlap of signals in the ^{1}H NMR spectrum, in **15** and in order to unequivocally assign the stereochemistry with which the neoglycosylation reaction took place, an acetylation reaction according to general procedure V was carried out **15-OAc:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 – 7.44 (m, 3H), 7.42 – 7.34 (m, 2H), 6.01 (s, 1H), 5.41 – 5.31 (m, 4H), 5.26 (d, *J* = 4.2 Hz, 1H), 5.22 (t, *J* = 9.0 Hz, 1H), 5.11 (t, *J* = 9.2 Hz, 1H), 5.06 (t, *J* = 9.9 Hz, 1H), 4.86 (dd, *J* = 10.4, 4.0 Hz, 1H), 4.74 (dd, *J* = 10.4, 4.2 Hz, 1H), 4.45 (dd, *J* = 12.4, 2.5 Hz, 1H), 4.40 (dd, *J* = 12.0, 3.0 Hz, 1H), 4.27 – 4.22 (m, 3H), 4.19 (dd, *J* = 12.3, 4.0 Hz, 1H), 4.05 (dd, *J* = 12.5, 2.3 Hz, 1H), 4.02 – 3.93 (m, 4H), 4.01 (d, *J* = 8.9 Hz, 1H, $H_{anomeric}$) 3.92 – 3.81 (m, 4H), 3.52 (ddd, *J* = 8.8, 5.5, 3.0 Hz, 1H), 3.41 (s, 3H), 2.58 (s, 3H), 2.56 (s,

3H), 2.14 (s, 3H), 2.10 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H), 2.03 (s, 3H), 2.00 (s, 6H), 1.99 (s, 3H), 1.96 (s, 3H), 1.94 (s, 3H), 1.39 (s, 3H), 1.38 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.5, 170.3, 170.1, 169.8, 169.7, 169.6, 169.4, 156.3, 141.8, 141.1, 134.9, 130.6, 129.3, 129.1, 129.0, 128.0, 127.8, 121.6, 95.7, 87.2, 77.2, 77.1, 76.9, 76.7, 74.0, 73.6, 72.7, 71.6, 70.2, 70.0, 69.3, 69.0, 68.8, 68.4, 67.8, 63.5, 62.3, 61.3, 61.0, 45.2, 44.3, 29.6, 27.6, 21.4, 20.8, 20.8, 20.7, 20.6, 20.5, 20.4, 14.6, 14.4, 12.3, 11.3.



16

Compound 16. This compound was prepared following general procedure IV from methoxyamine **6a** (50 mg, 0.13 mmol), acarbose (168 mg, 0.13 mmol) and 5-methoxyanthranilic acid (2.2 mg, 0.013 mmol) under microwave irradiation for 8 h. The residue was purified by flash chromatography (Ethyl acetate: methanol: water 12:2:1) to give **16** as a red solid (71 mg, 52%). $[\alpha]_D^{25}$ -28.1 (c 0.4, CH_3OH); Mp 174 – 176 °C; ^{1}H NMR (500 MHz, CD_3OD) δ 7.57 – 7.36 (m, 3H), 7.41 – 7.22 (m, 2H), 6.08 (s, 1H), 5.94 – 5.79 (m, 1H), 5.17 (d, *J* = 3.8 Hz, 1H), 5.04 (d, *J* = 3.7 Hz, 1H), 4.24 – 4.08 (m, 2H), 4.02 – 3.90 (m, 3H), 3.88 – 3.65 (m, 9H), 3.62 – 3.39 (m, 13H), 3.36 (s, 3H), 3.23 (ddd, *J* = 9.4, 4.2, 2.1 Hz, 1H), 2.60 (s, 3H), 2.50 (s, 3H), 2.34 (t, *J* = 9.8 Hz, 1H), 1.46 (s, 3H), 1.39 (s, 3H), 1.32 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (126 MHz, CD_3OD) δ 157.3, 156.7, 144.7, 143.5, 143.4, 141.5, 136.4, 132.7, 131.9, 130.5, 130.3, 129.3, 129.3, 126.9, 123.8, 122.3, 103.3, 102.7, 92.3, 81.8, 80.8, 79.0, 78.3, 75.5, 75.0, 74.9, 74.5, 73.8, 73.5, 73.0, 72.8, 71.2, 71.0, 66.9, 63.3, 62.4, 62.3, 62.2, 57.8, 46.1, 18.7, 14.6, 12.9, 12.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -146.73– -147.27(m, 2F). HRMS (ESI/Q-TOF) m/z: $[M+Na]^+$ calcd for $C_{48}H_{68}BF_2N_4O_{16}$: 1053.4541; found 1053.4576



16-OAc

Due to the overlap of signals in the ^{1}H NMR spectrum, in **16** and in order to unequivocally assign the stereochemistry with which the neoglycosylation reaction took place, an acetylation reaction according to general procedure V was carried out to yield **16-OAc**. ^{1}H NMR (500 MHz, CD_3OD) δ 7.57 – 7.36 (m, 3H), 7.41 – 7.22 (m, 2H), 6.02 (s, 1H), 5.94 (d, J = 4.0 Hz, 1H), 5.61 – 5.49 (m, 3H), 5.34 (dd, *J* = 10.3, 8.7 Hz, 1H), 5.26 (d, *J* = 4.2 Hz, 1H), 5.18 – 5.16 (m, 2H), 5.12 – 5.06 (m, 2H), 4.92 (dd, *J* = 10.1, 4.1 Hz, 1H), 4.78 – 4.70 (m, 2H), 4.65 (d, *J* = 13.1 Hz, 1H), 4.50 – 4.32 (m, 3H), 4.24 (dd, *J* = 12.0, 5.3 Hz, 1H), 4.18 (dd, *J* = 12.3, 3.8 Hz, 1H), 4.00 – 3.81 (m, 5H), 3.71 (t, *J* = 4.8 Hz, 1H), 3.59 – 3.45 (m, 2H), 3.40 (s, 3H), 2.58 (s, 3H), 2.56 (s, 3H), 2.38 (t, *J* = 10.0 Hz, 1H), 2.13 (s, 3H), 2.10 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H), 2.03 (s, 9H), 2.00 (s, 6H), 1.98 (s, 3H), 1.96 (s, 3H), 1.95 (s, 3H), 1.93 (s, 3H), 1.38 (s, 3H), 1.36 (s, 3H), 1.20 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 170.9, 170.8, 170.8, 170.7, 170.5, 170.4, 170.4, 170.3, 170.2, 169.9, 169.6, 156.4, 155.0, 143.9, 141.9, 141.3, 135.0, 133.9, 131.8, 130.7, 129.4, 129.2, 129.1, 128.1, 128.0, 127.9, 123.8, 121.6, 96.0, 95.9, 95.7, 87.3, 73.7, 72.6, 72.3, 72.2, 71.9, 71.1, 71.0, 70.9, 70.7, 70.5, 70.4, 70.1, 69.8, 69.1, 69.1, 63.5, 63.1, 62.4, 61.3, 61.1, 52.2, 44.4, 21.0, 20.9, 20.9, 20.8, 20.8, 20.8, 20.8, 20.7, 20.7, 20.6, 20.6, 20.6, 18.1, 14.7, 14.5, 12.4, 11.4.

3. Copies of 1 H, 13C {1 H}, 19F, 11B NMR Spectra

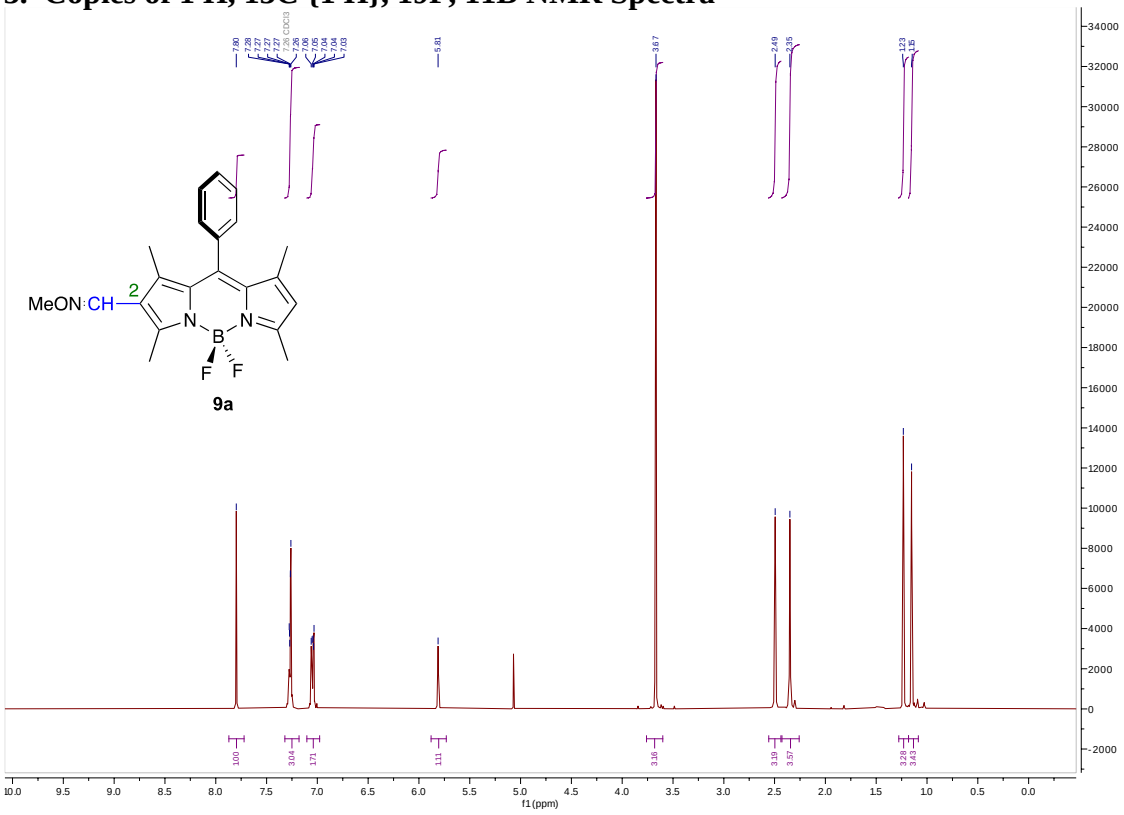


Fig S1. ^{1}H-NMR (400 MHz, $CDCl_3$) for **9a**

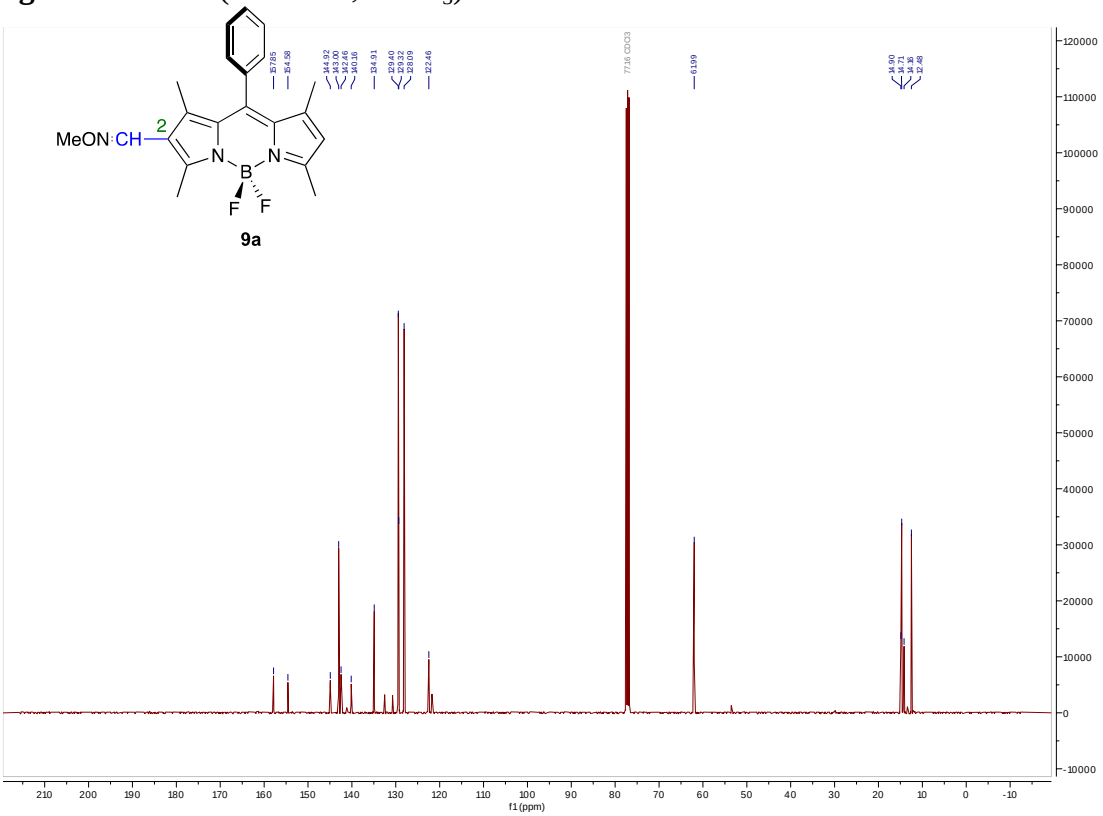


Fig S2. ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) of **9a**

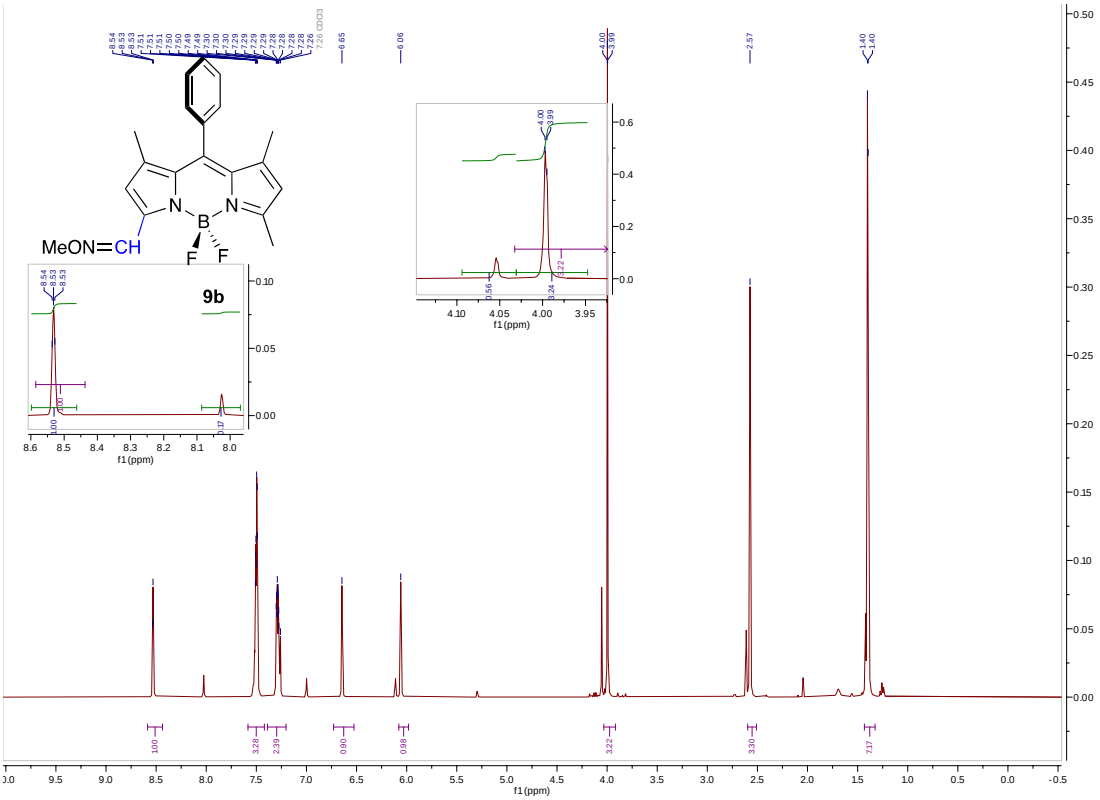


Fig S3. ^{1}H-NMR (400 MHz, $CDCl_3$) for **9b**

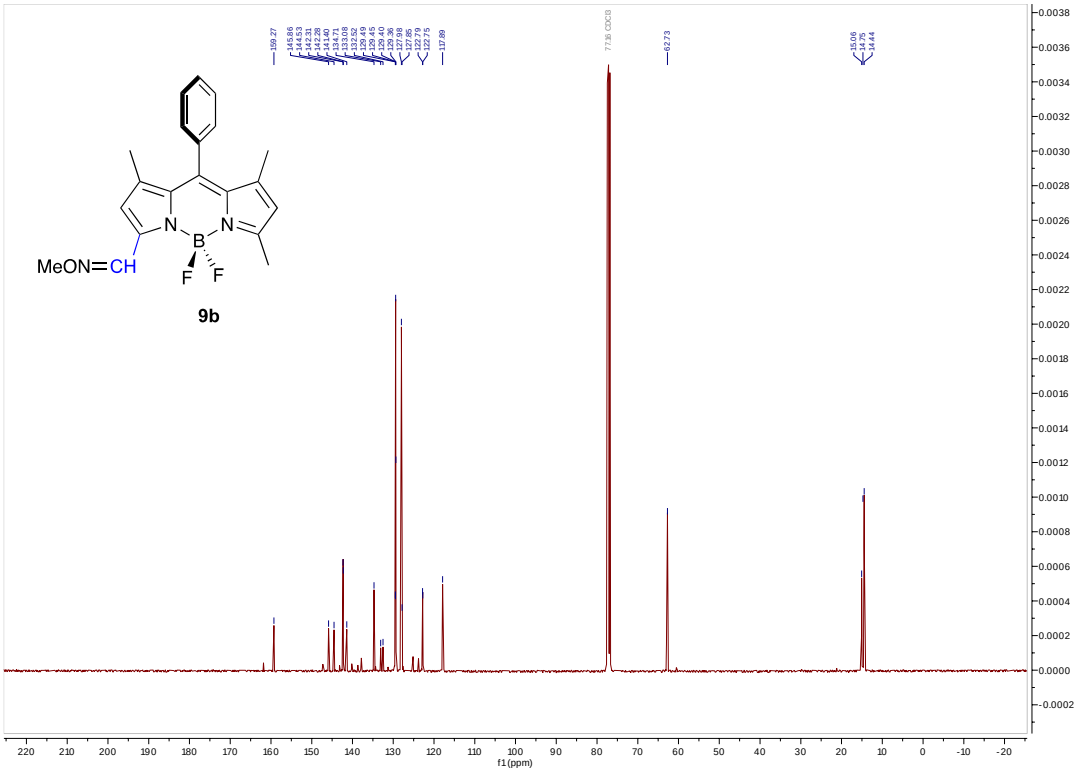


Fig S4. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **9b**

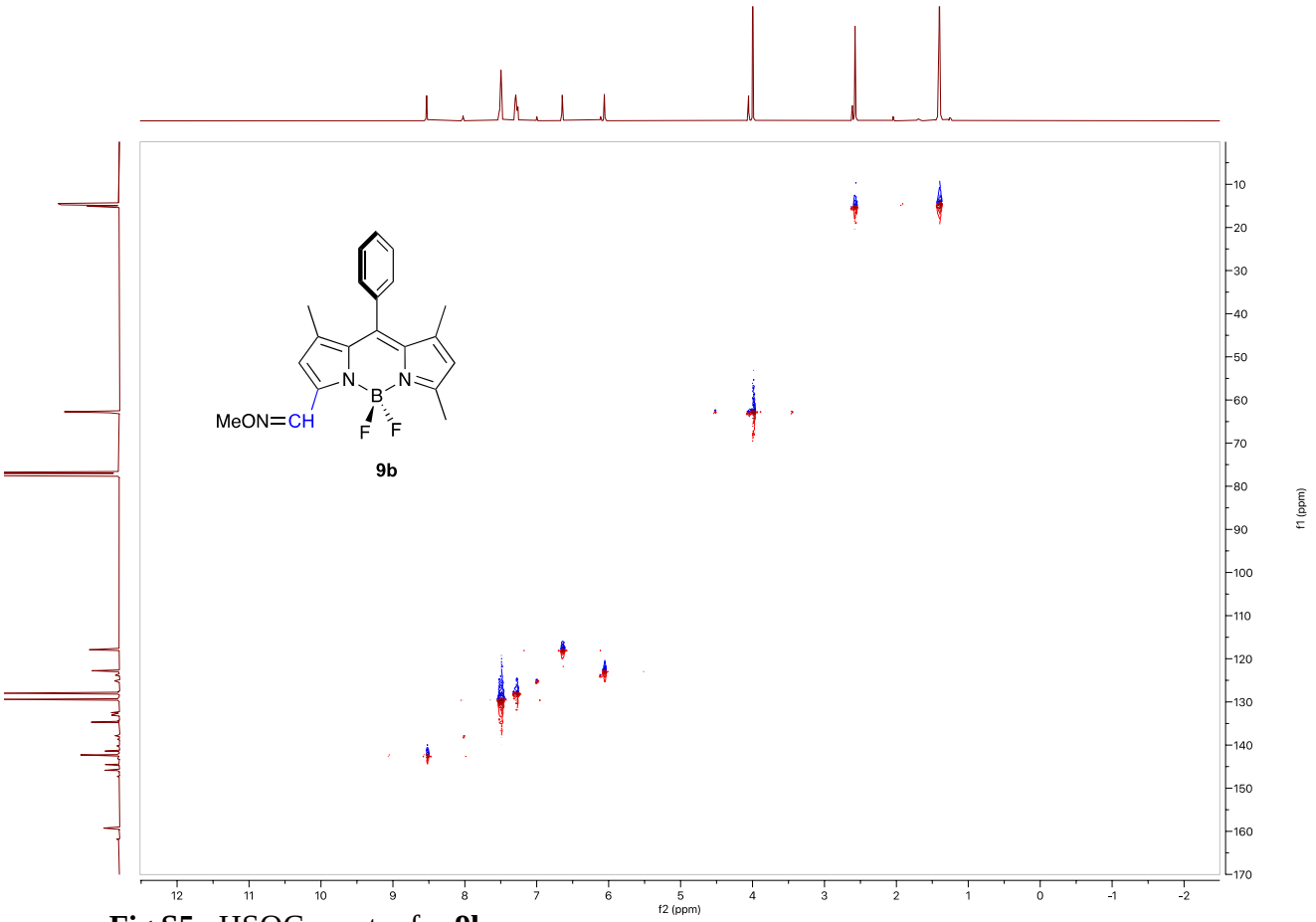


Fig S5. HSQC spectra for **9b**

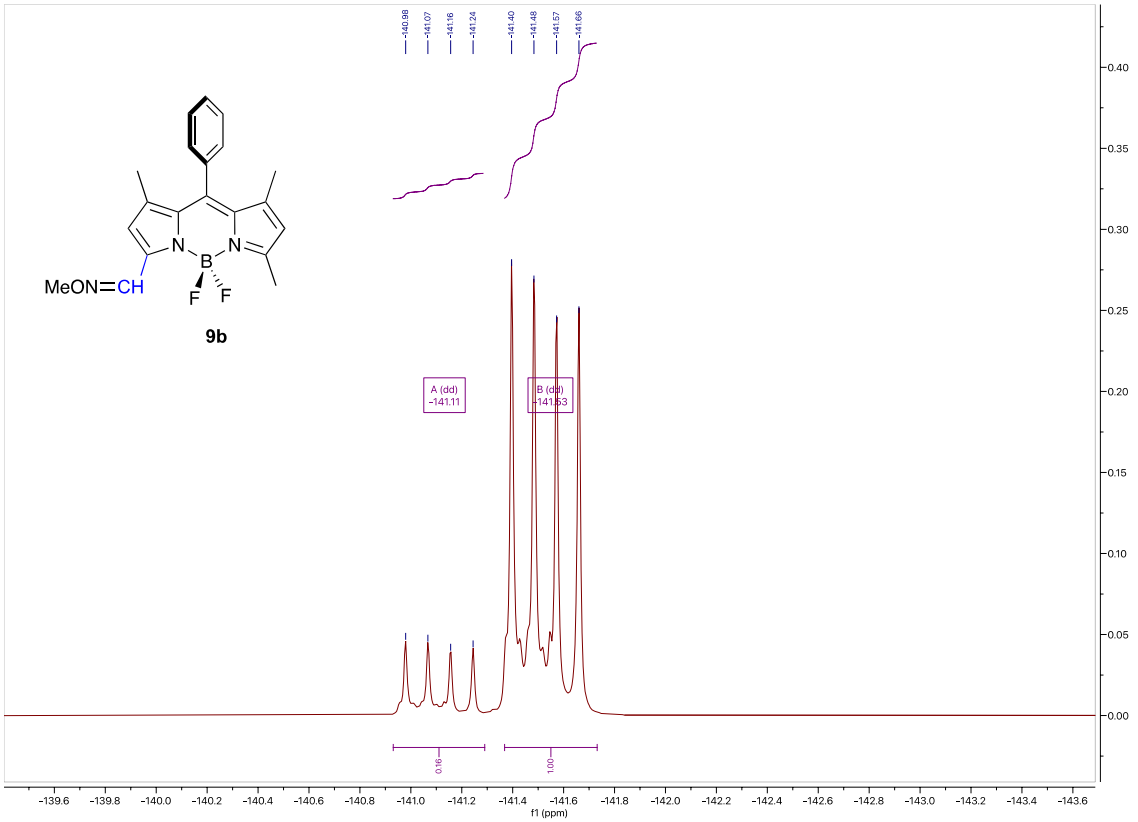


Fig S6. ^{19}F NMR (376 MHz, $CDCl_3$) of **9b**

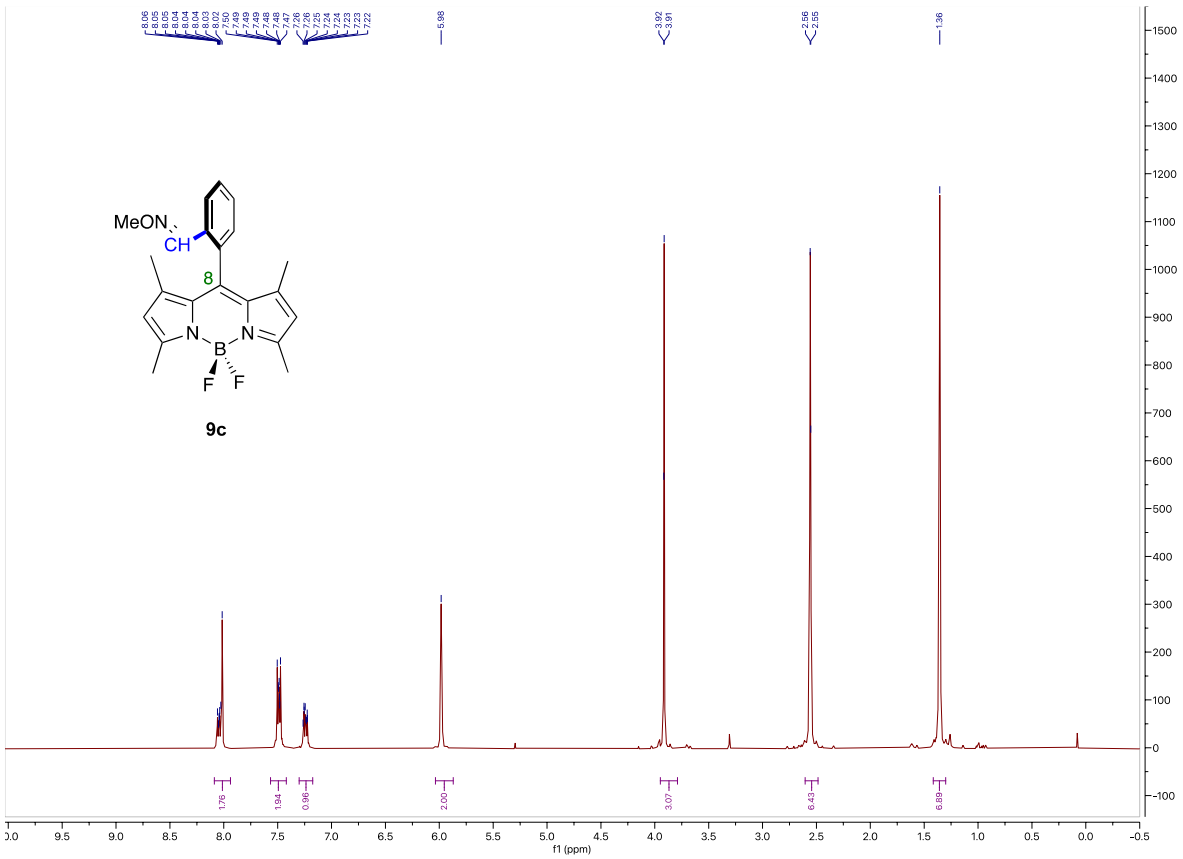


Fig S7. ^{1}H-NMR (400 MHz, $CDCl_3$) for **9c**

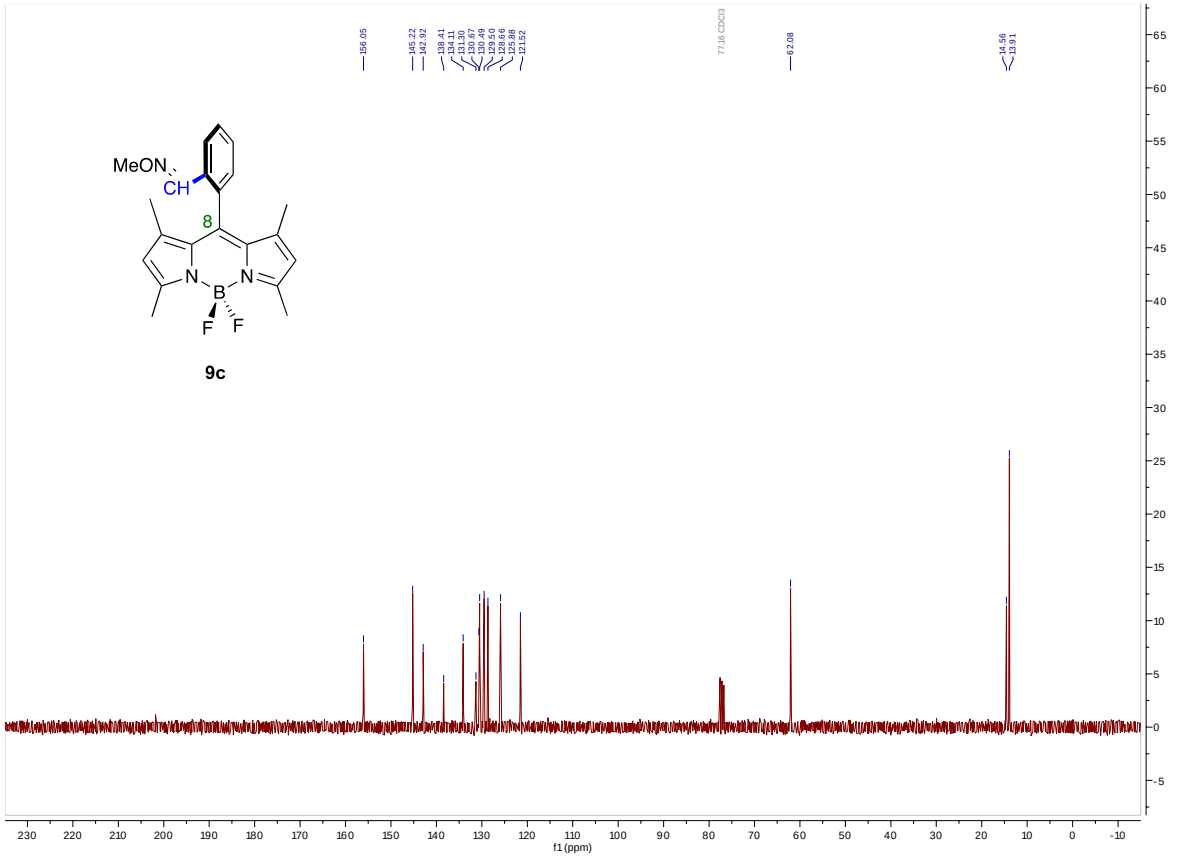


Fig S8. ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) of **9c**

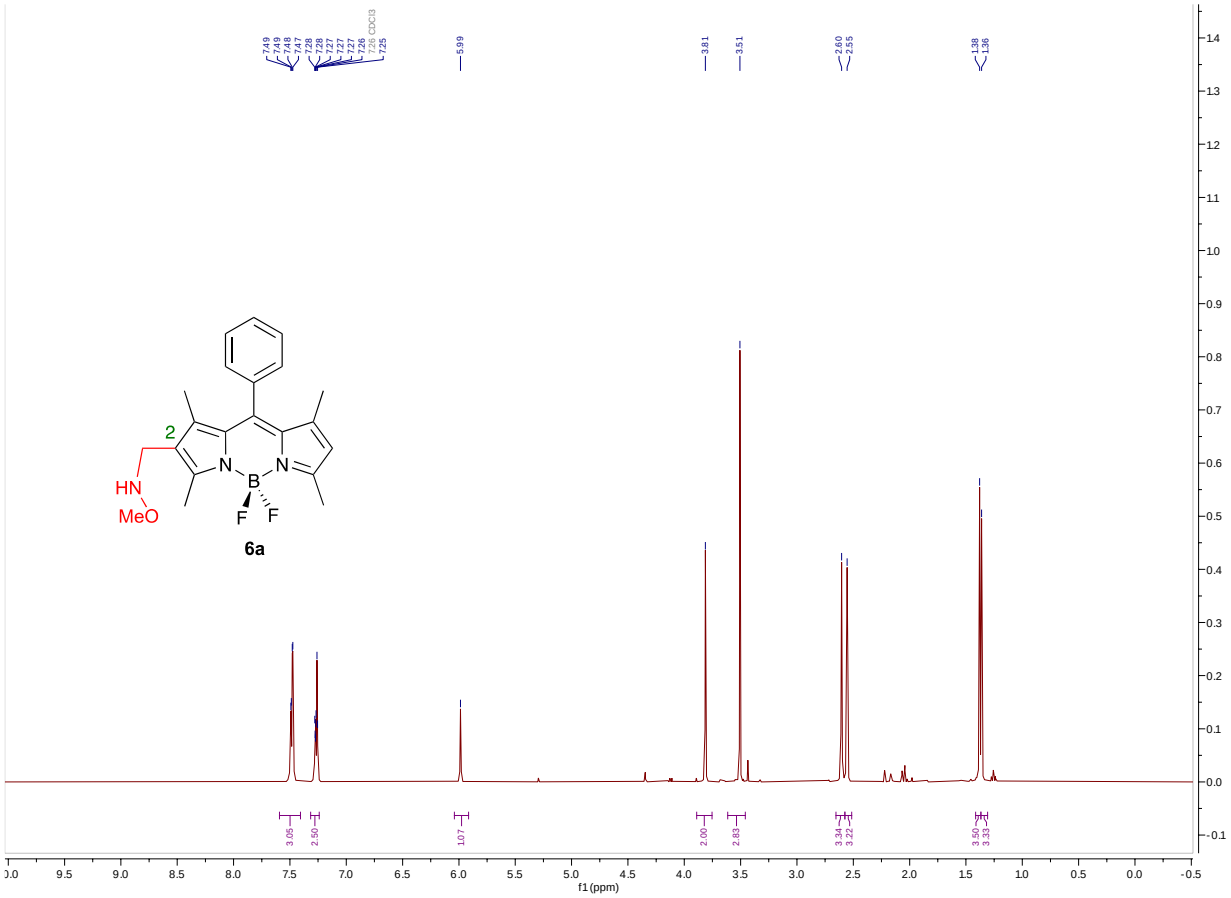


Fig S9. ^{1}H-NMR (400 MHz, $CDCl_3$) for **6a**

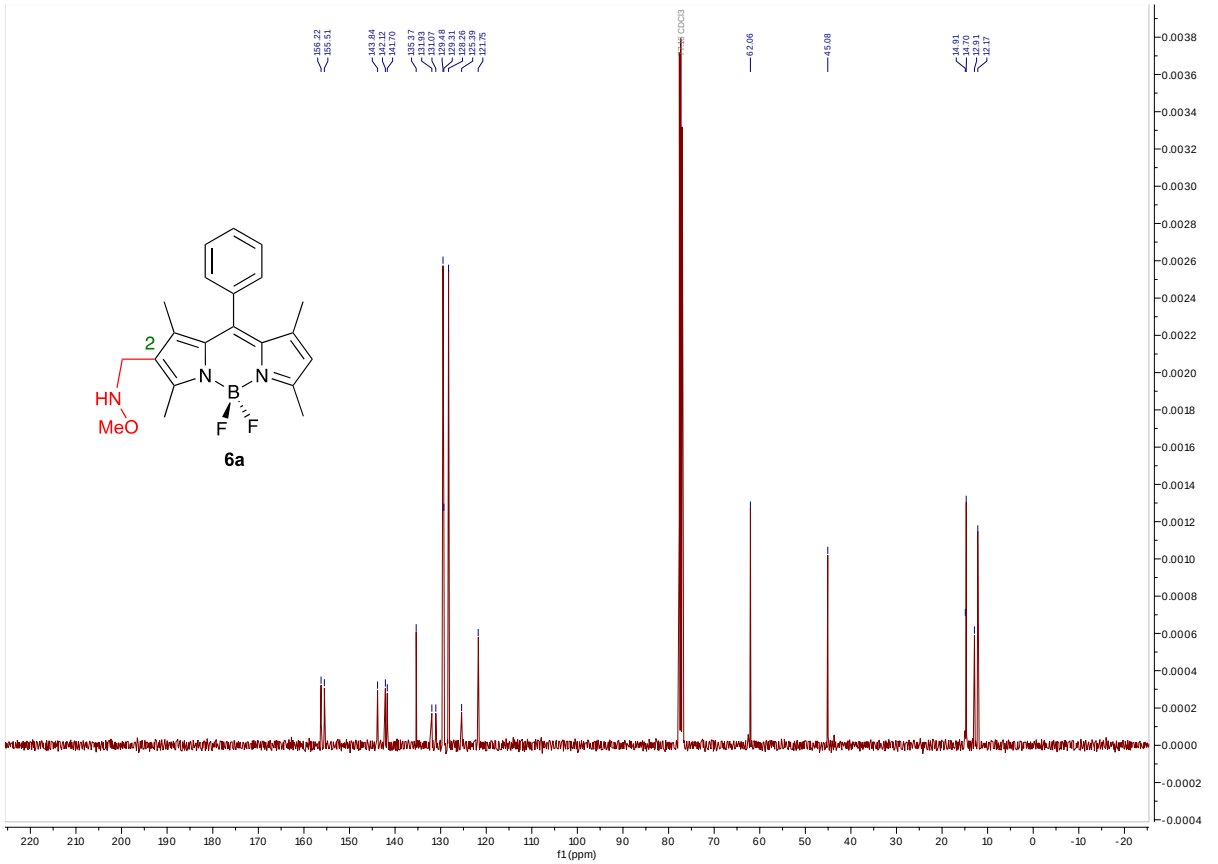


Fig S10. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **6a**

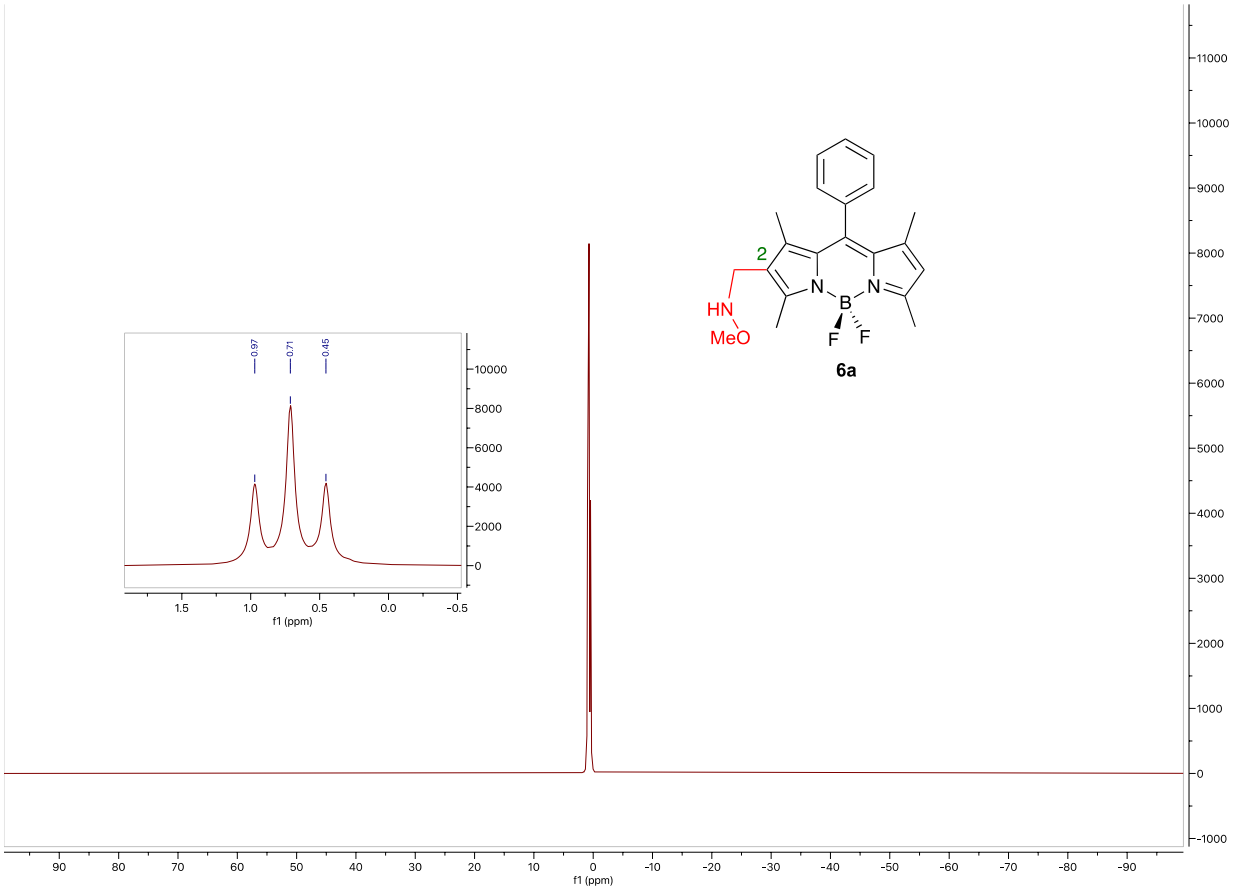


Fig S11. ^{11}B-NMR (128 MHz, $CDCl_3$) for **6a**

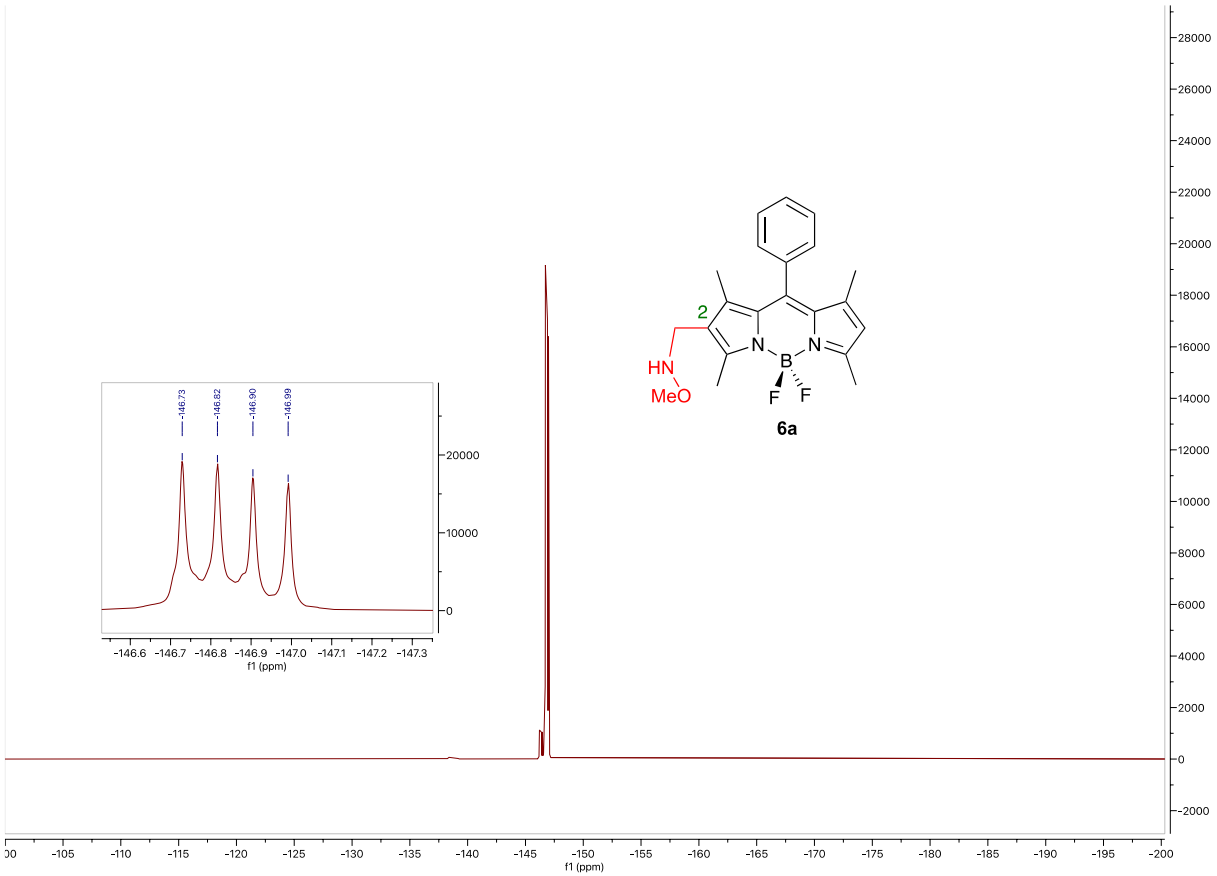


Fig S12. ^{19}F-NMR (376 MHz, $CDCl_3$) for **6a**

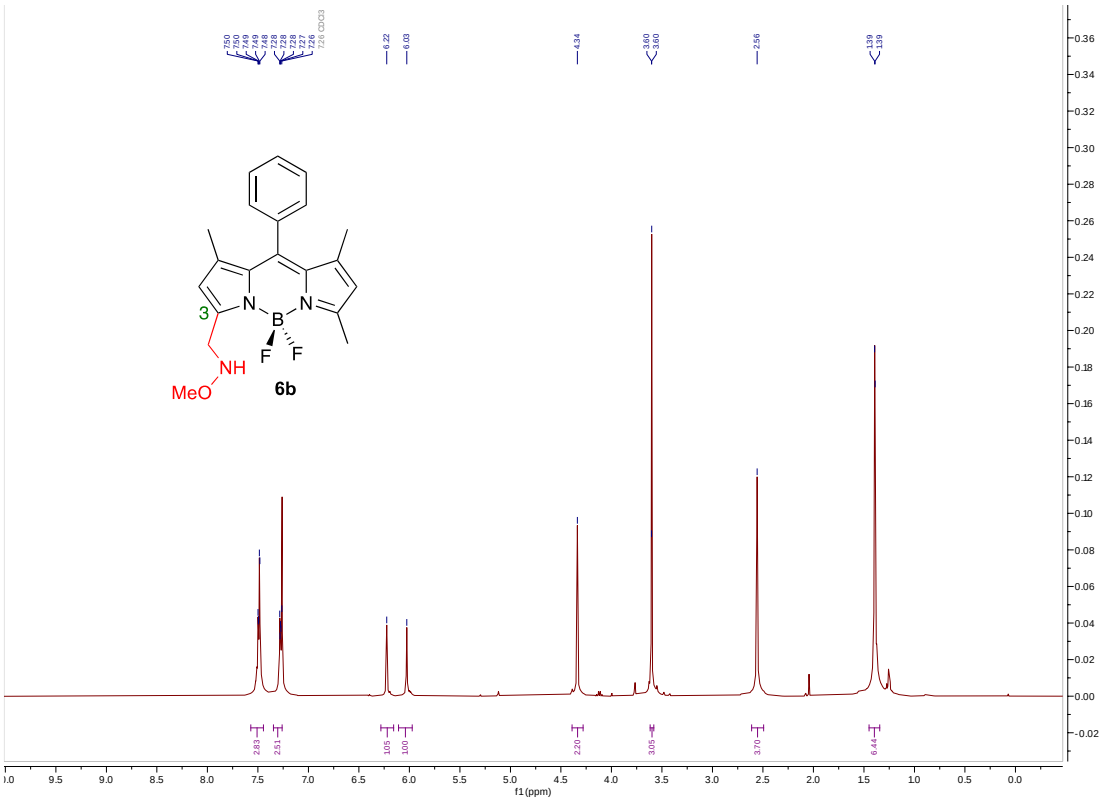


Fig S13. ^{1}H-NMR (400 MHz, $CDCl_3$) for **6b**

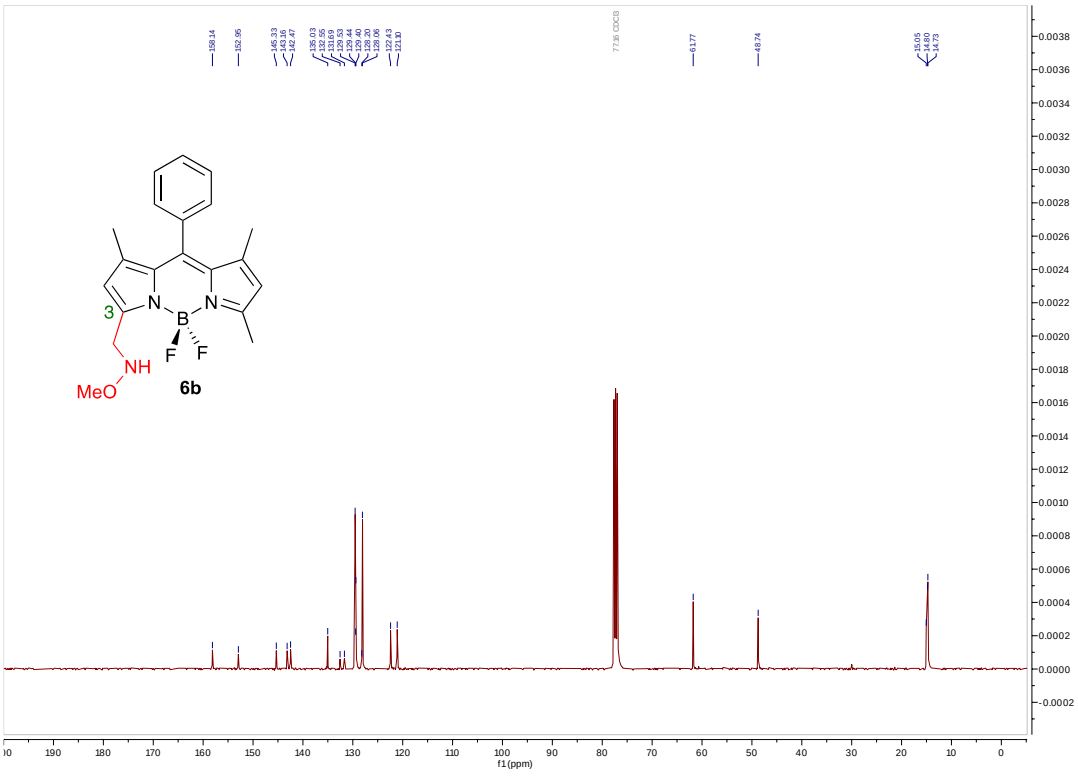


Fig S14. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **6b**

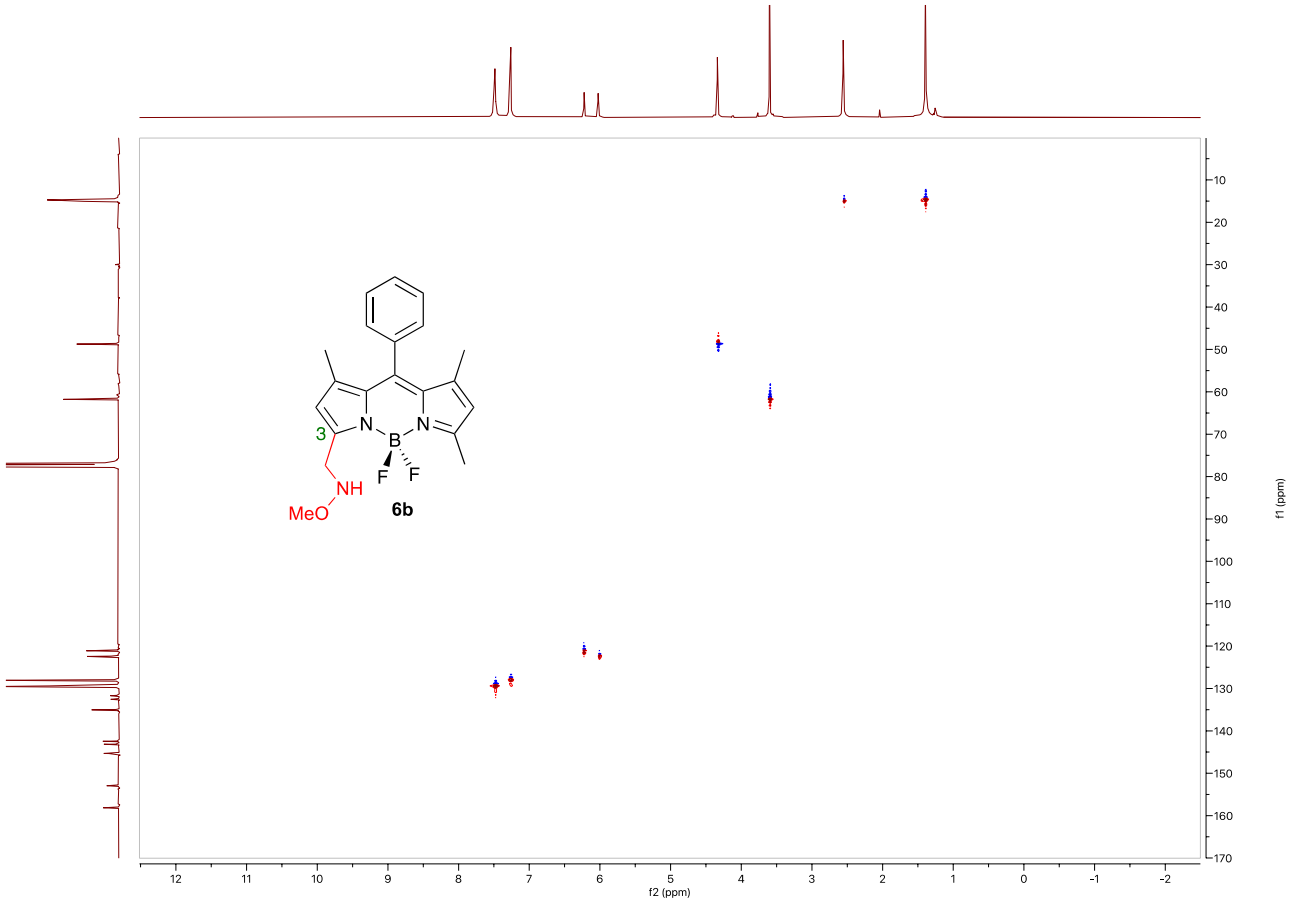


Fig S15. HSQC spectra for **9b**

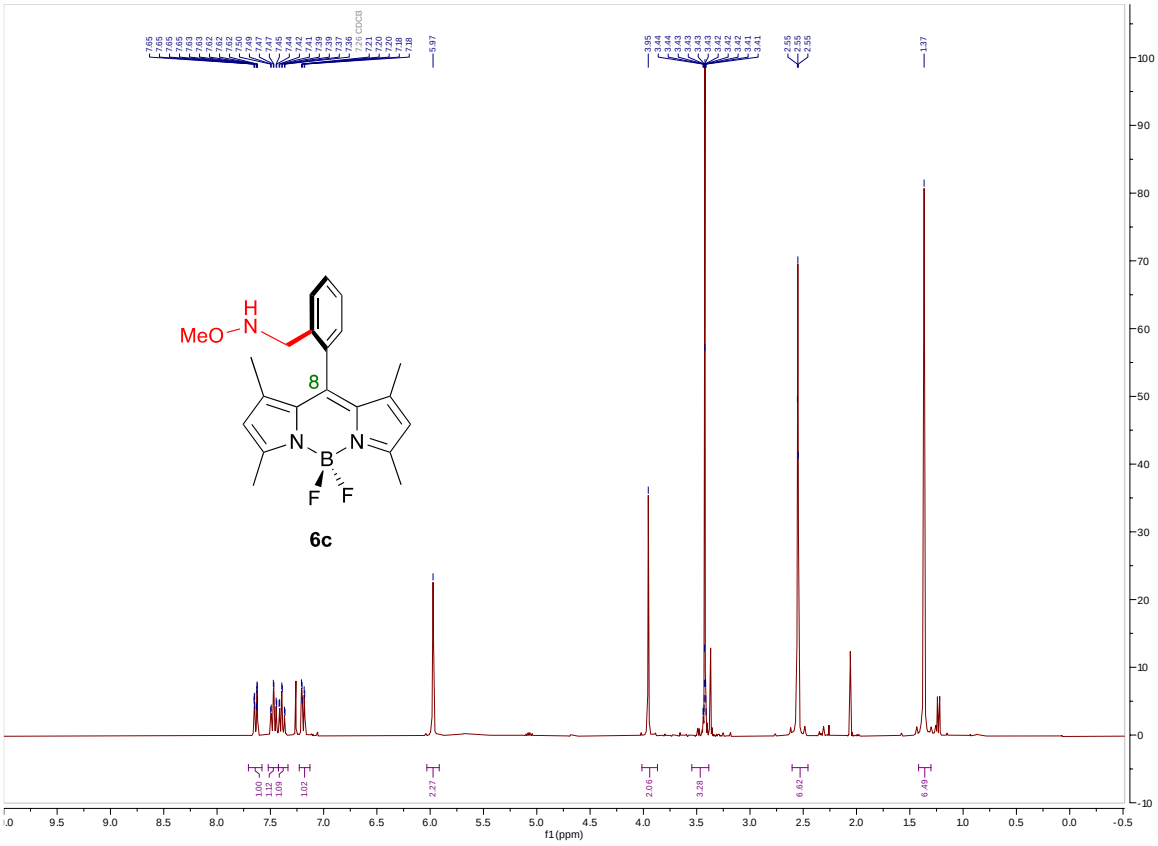


Fig S16. ^{1}H-NMR (400 MHz, $CDCl_3$) for **6c**

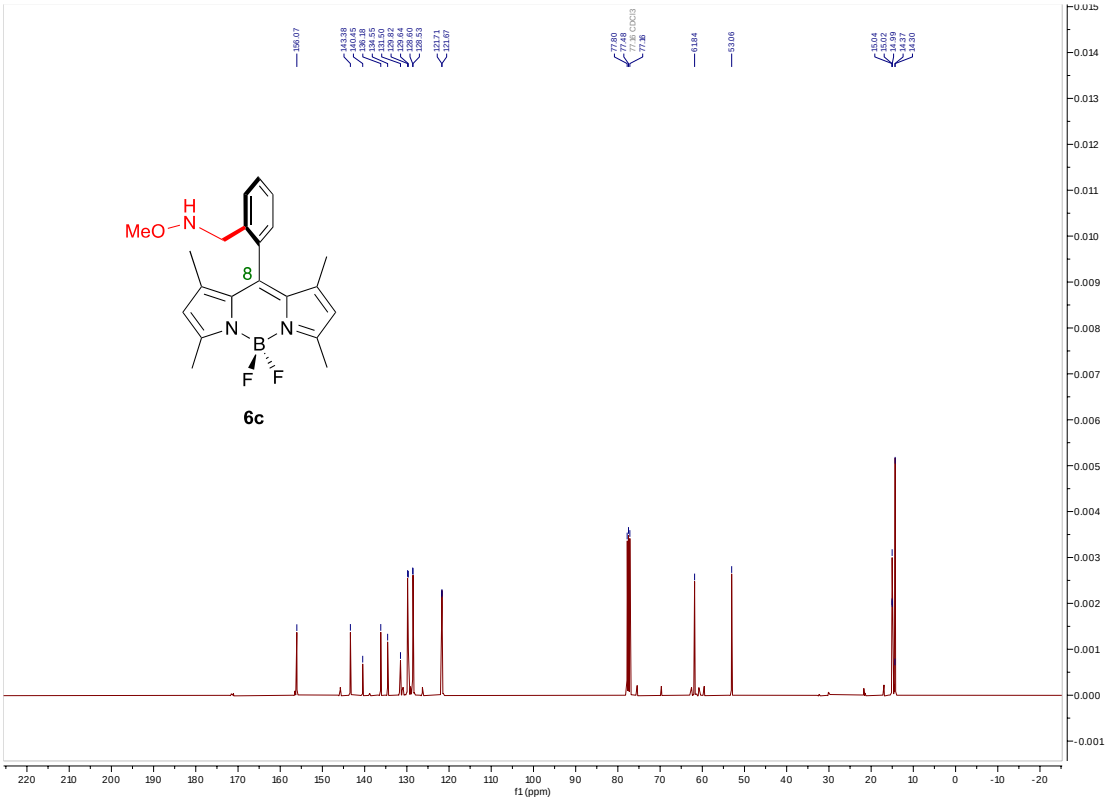


Fig S17. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **6c**

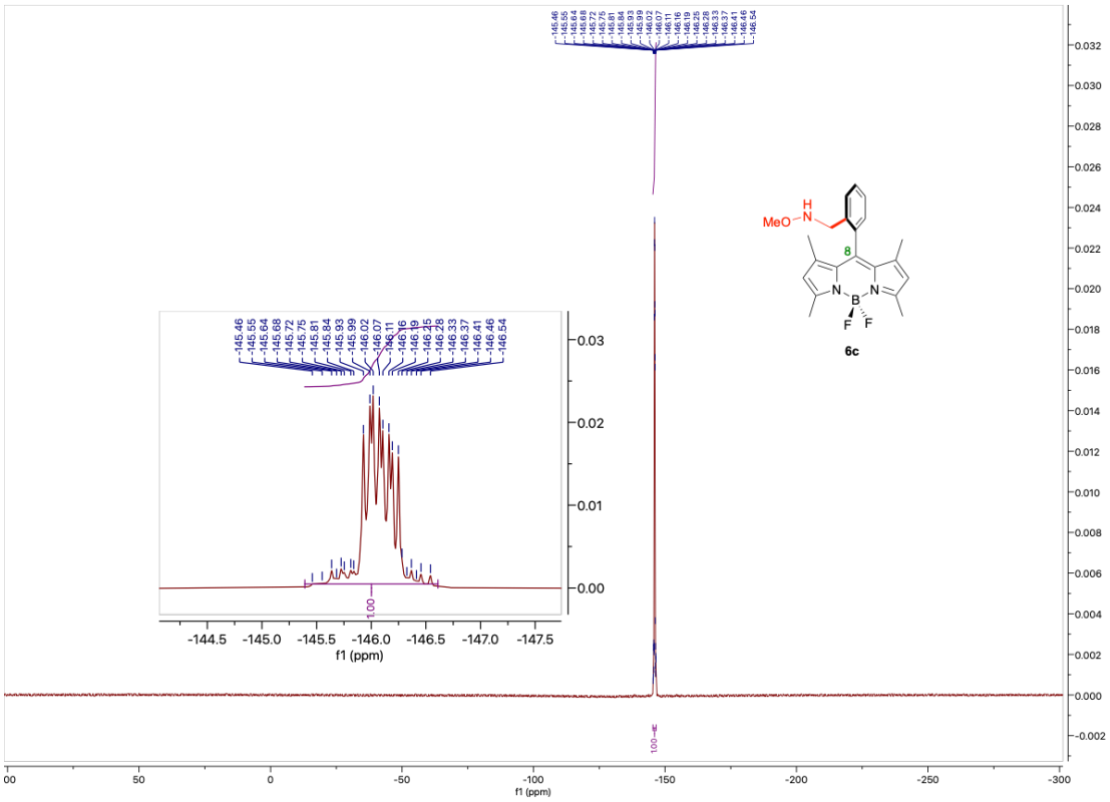


Fig S18. ^{19}F-NMR (376 MHz, $CDCl_3$) for **6c**

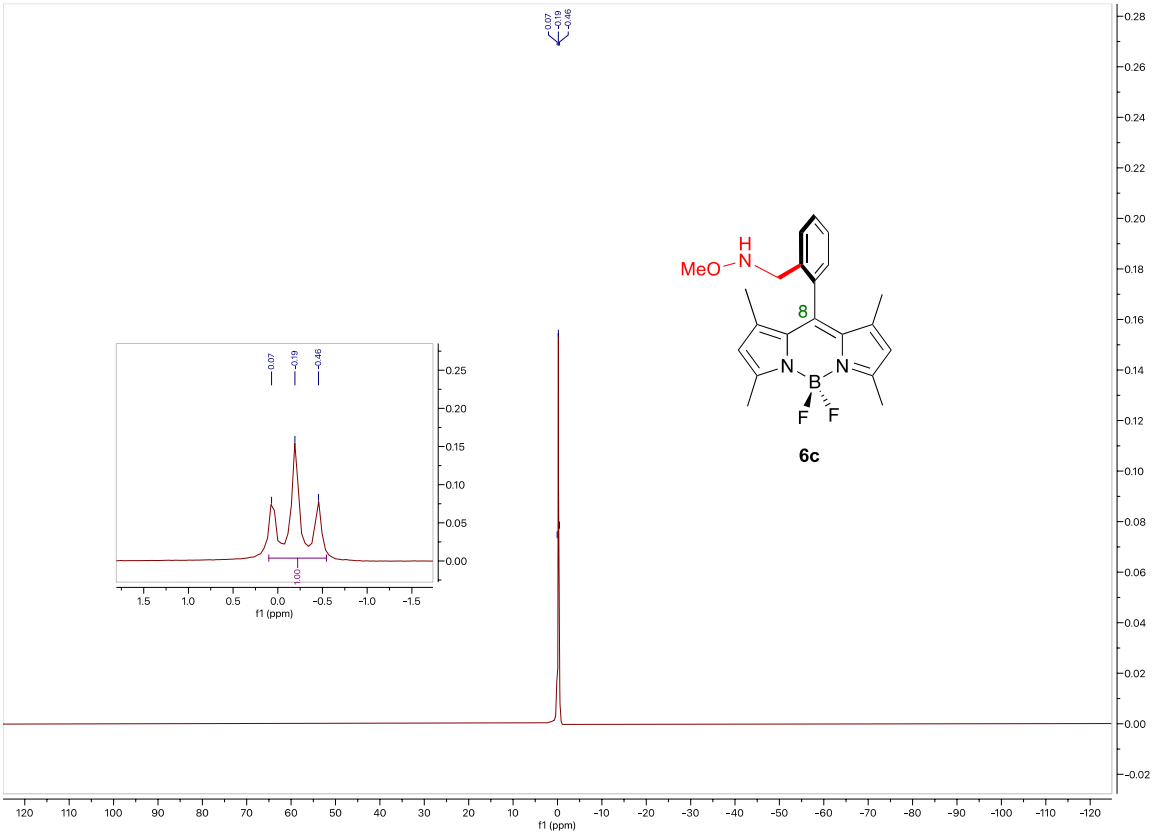


Fig S19. ^{11}B-NMR (128 MHz, $CDCl_3$) for **6c**

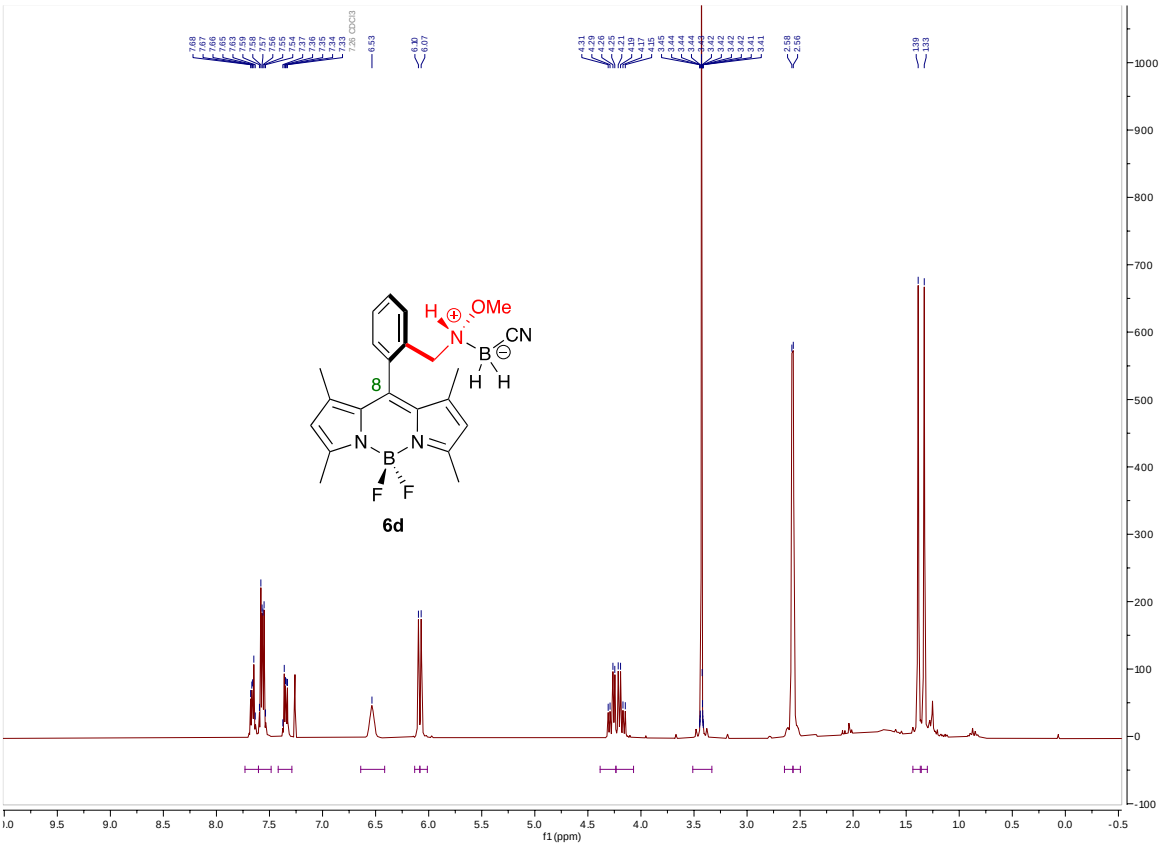


Fig S20. ^{1}H-NMR (300 MHz, $CDCl_3$) for **6d**

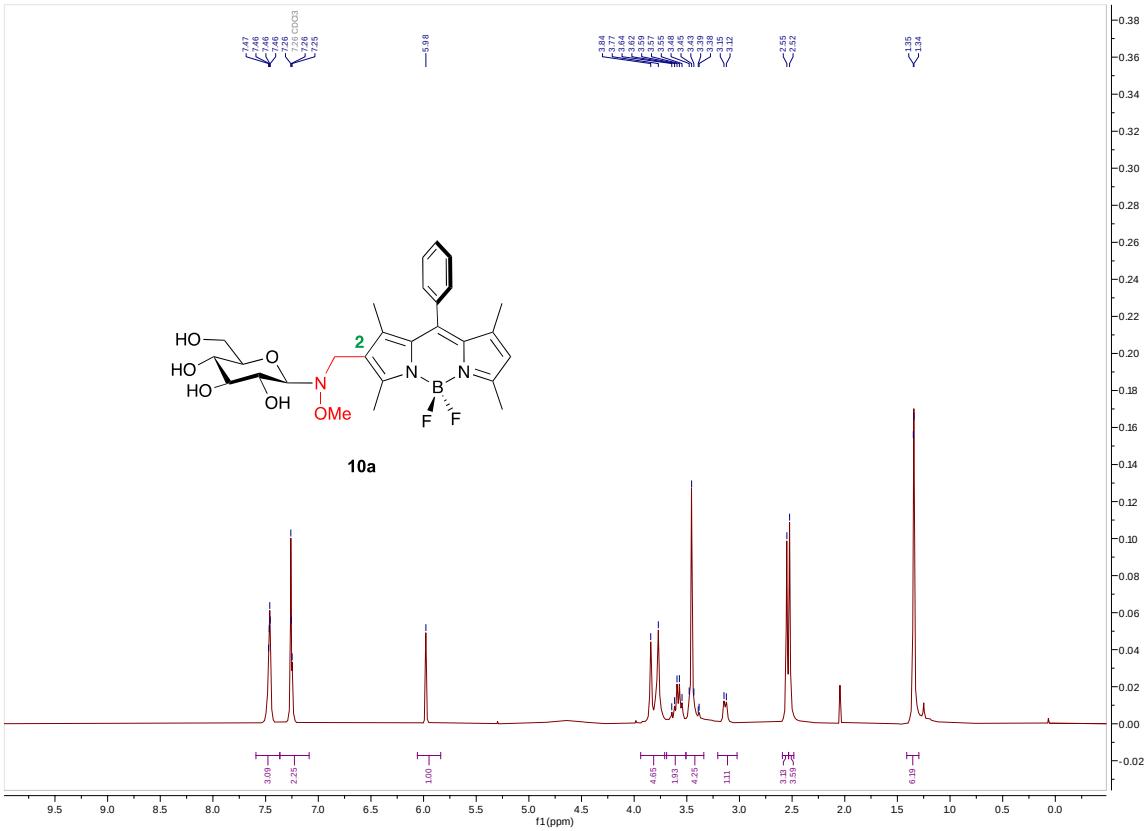


Fig S21. ^{1}H-NMR (400 MHz, $CDCl_3$) for **10a**

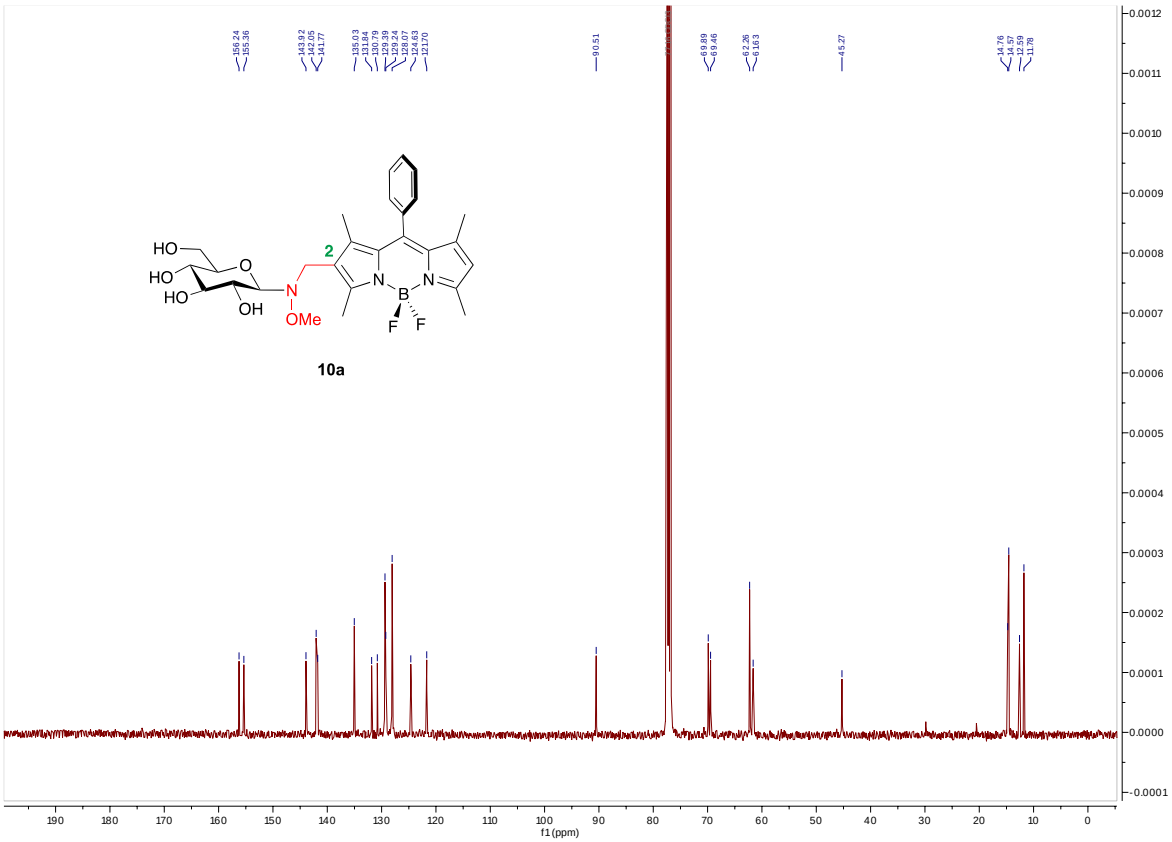


Fig S22. ^{13}C{^{1}H} NMR (101 MHz, CDCl3) of **10a**

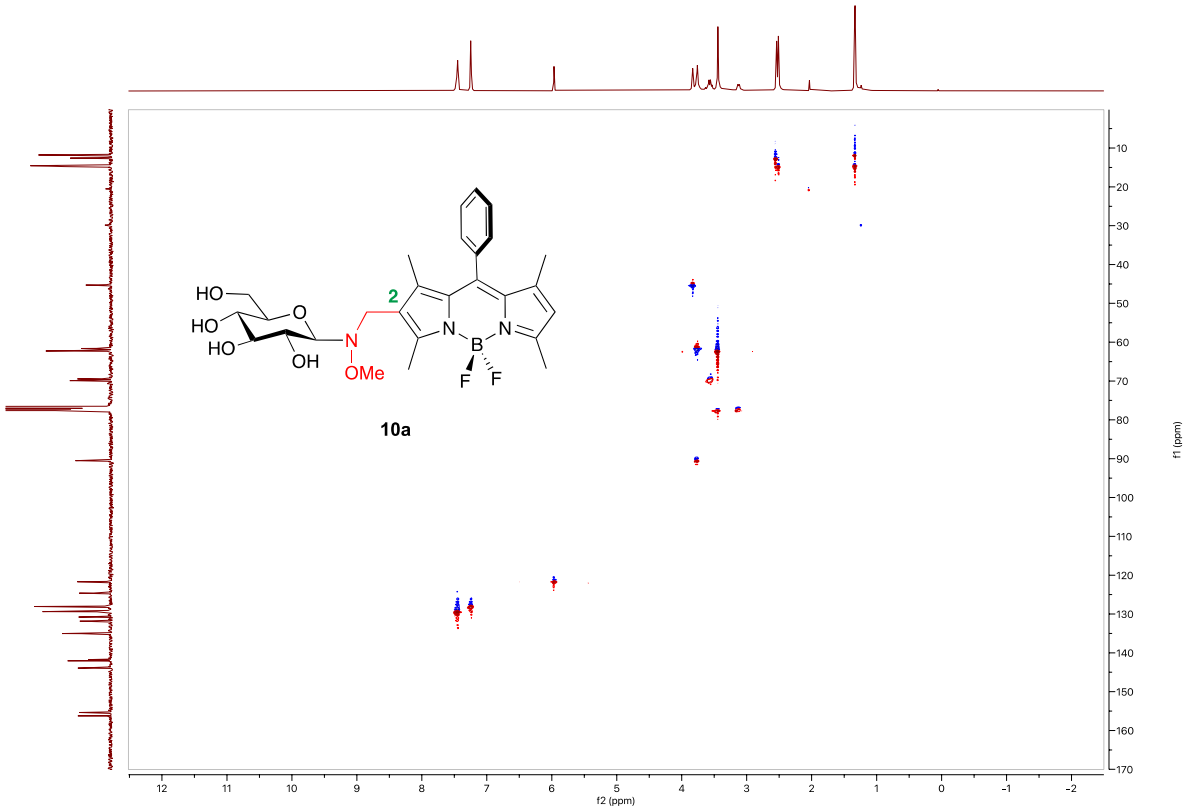


Fig S23. HSQC spectra for **9b**

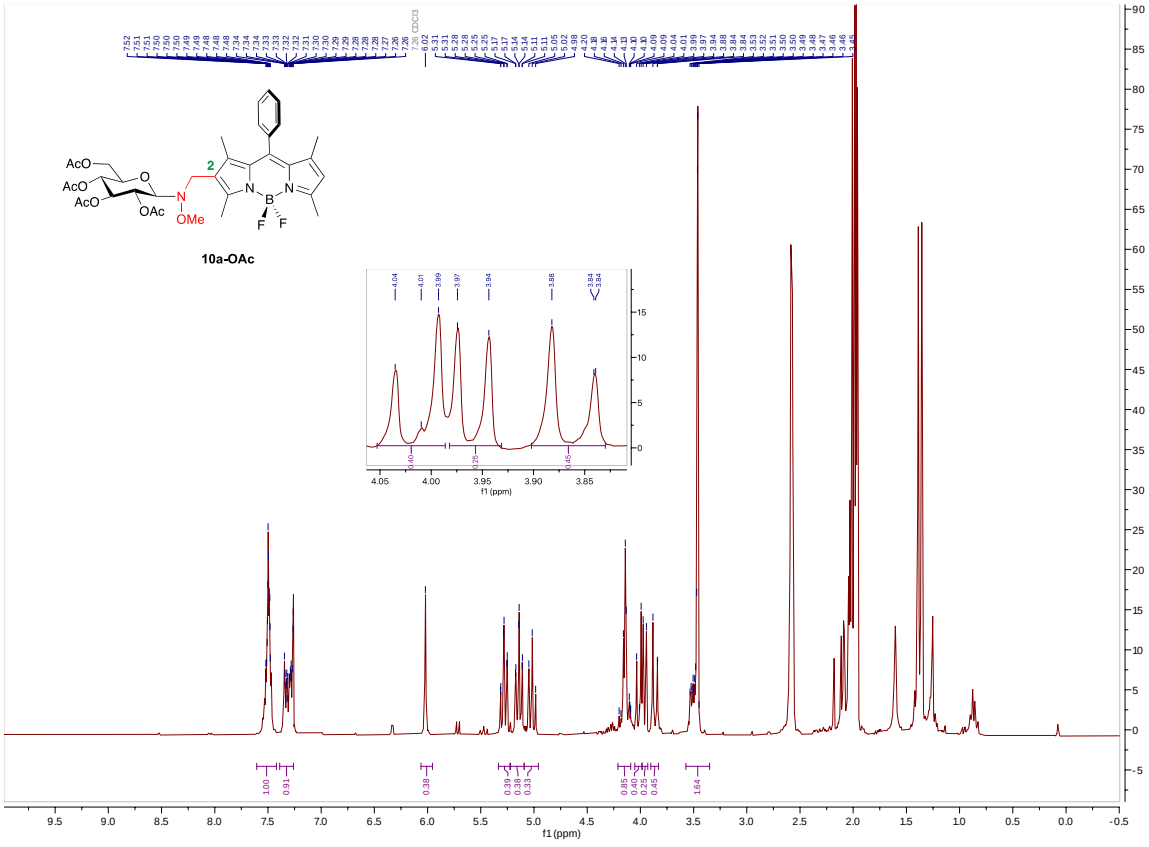


Fig S24. ^{1}H-NMR (400 MHz, $CDCl_3$) for **10a-OAc**

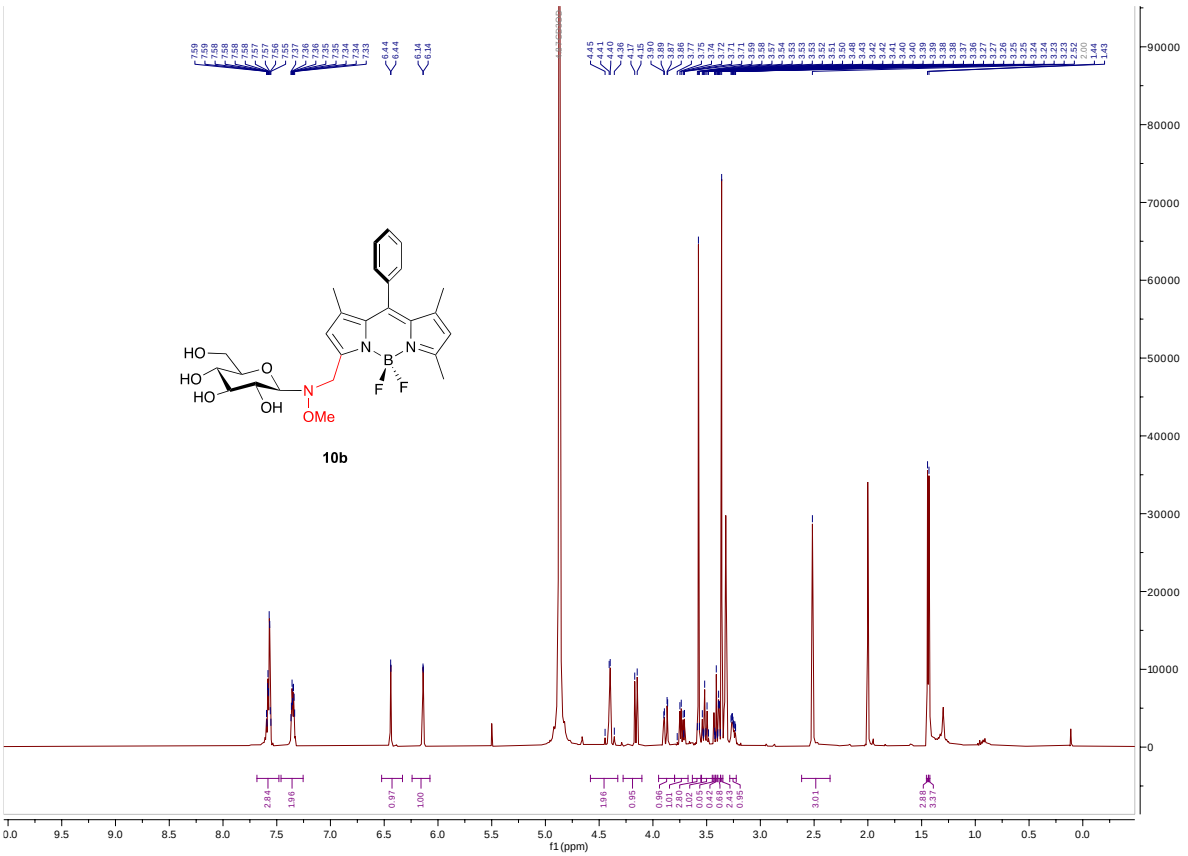


Fig S25. ^{1}H-NMR (400 MHz, $CDCl_3$) for **10b**

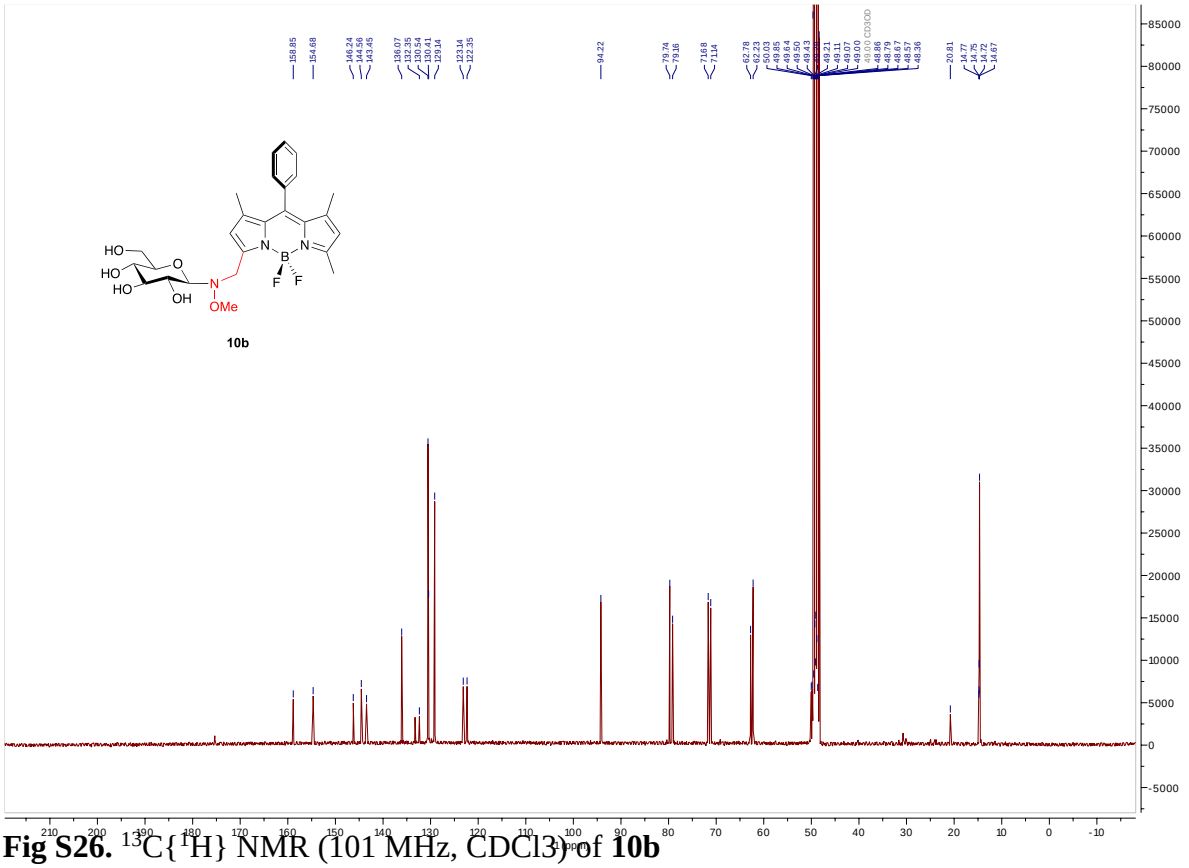


Fig S26. ^{13}C{^{1}H} NMR (101 MHz, CDCl3) of **10b**

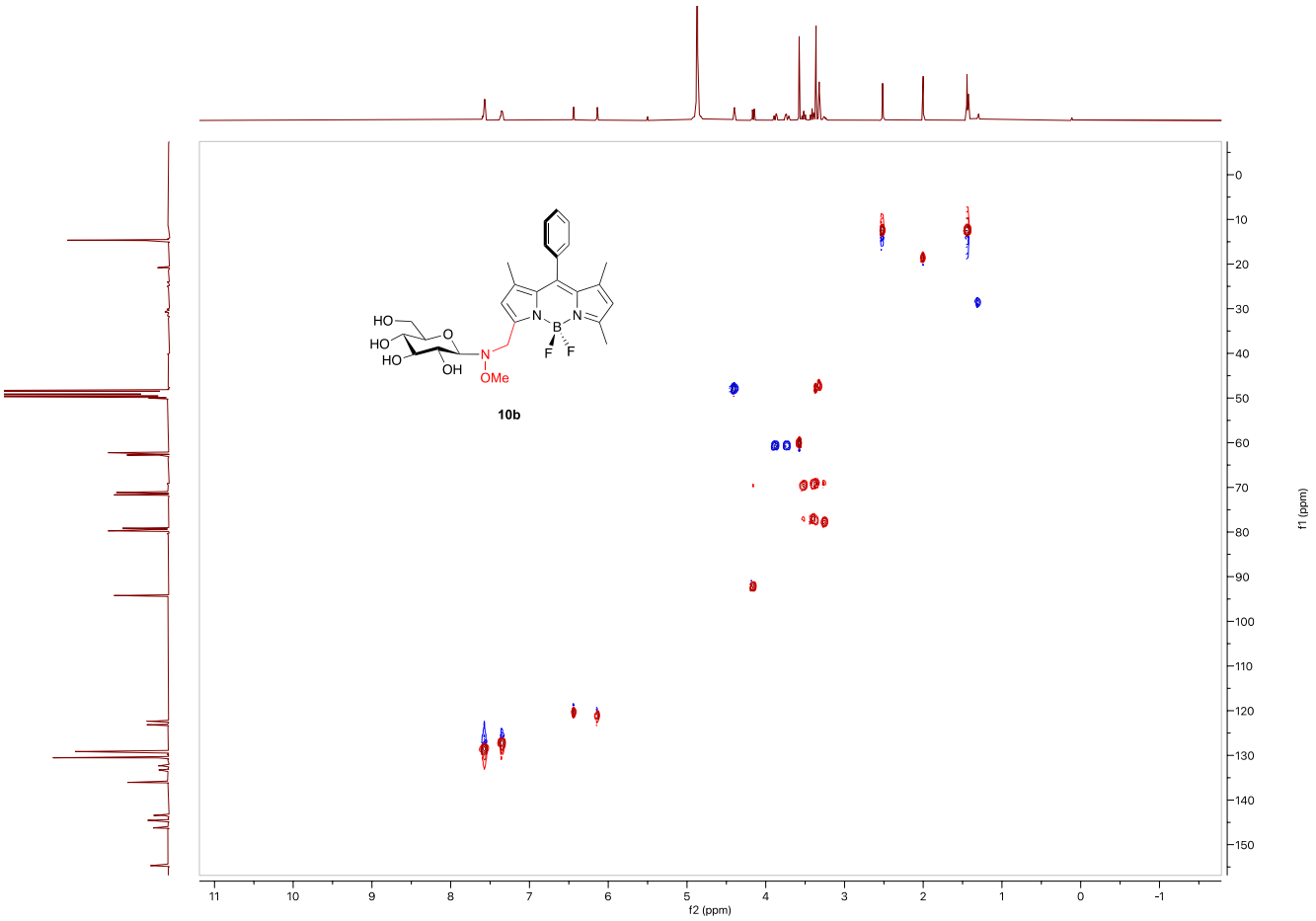


Fig S27. HSQC spectra for **10b**

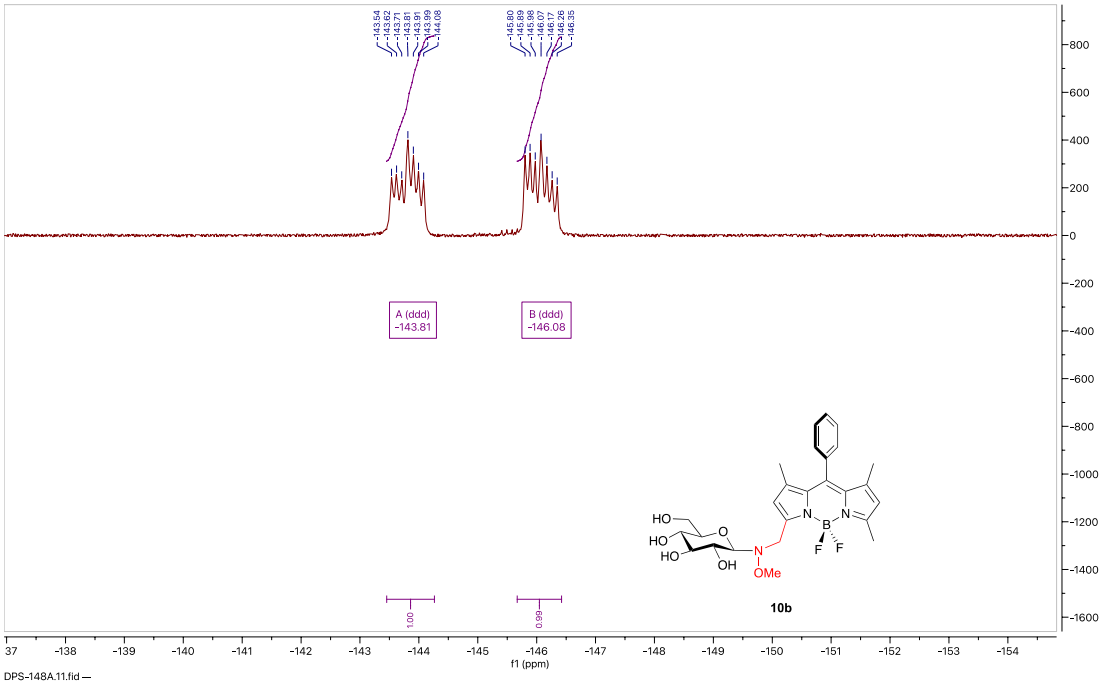


Fig S28. ^{19}F-NMR (376 MHz, $CDCl_3$) for **10b**

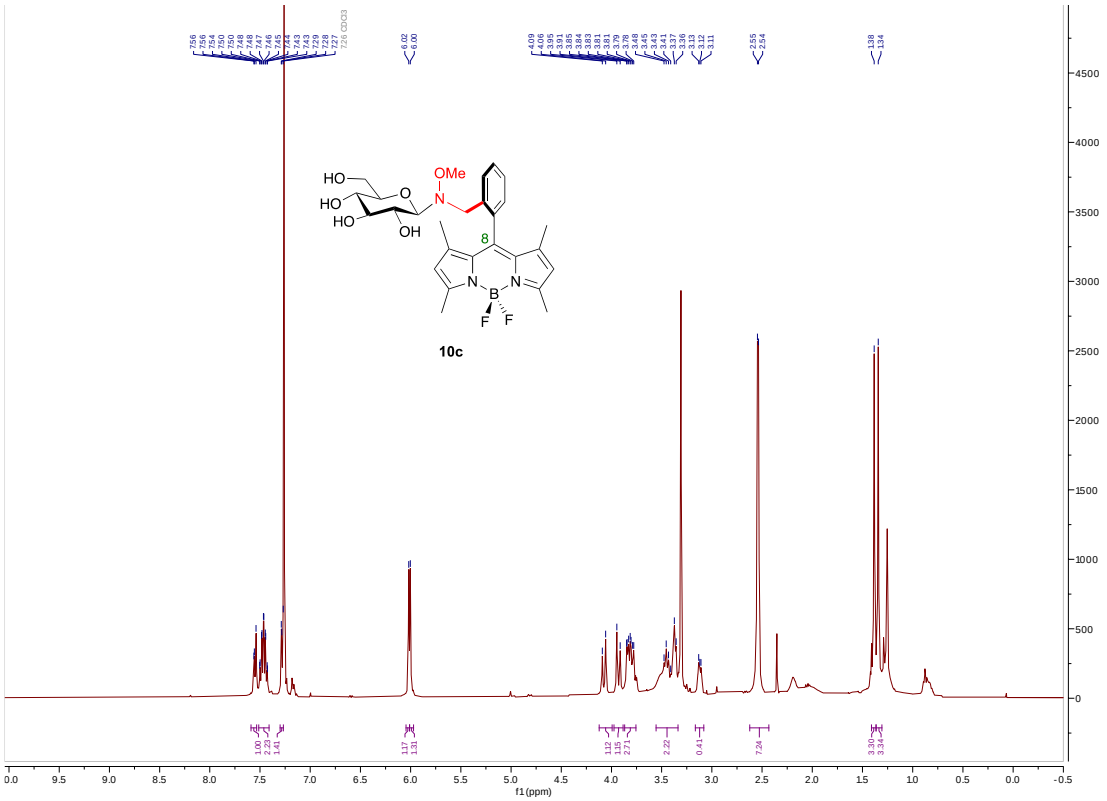


Fig S29. ^{1}H-NMR (400 MHz, $CDCl_3$) for **10c**

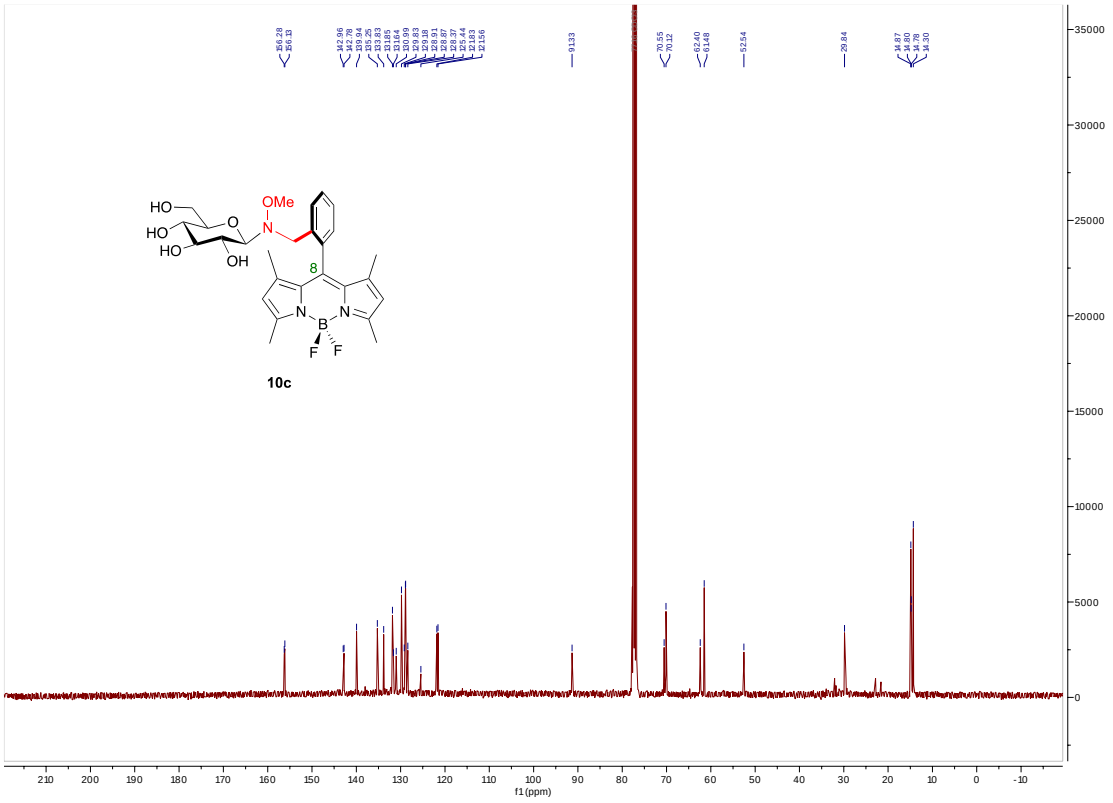


Fig S30. ^{13}C{^{1}H} NMR (101 MHz, CDCl3) of **10c**

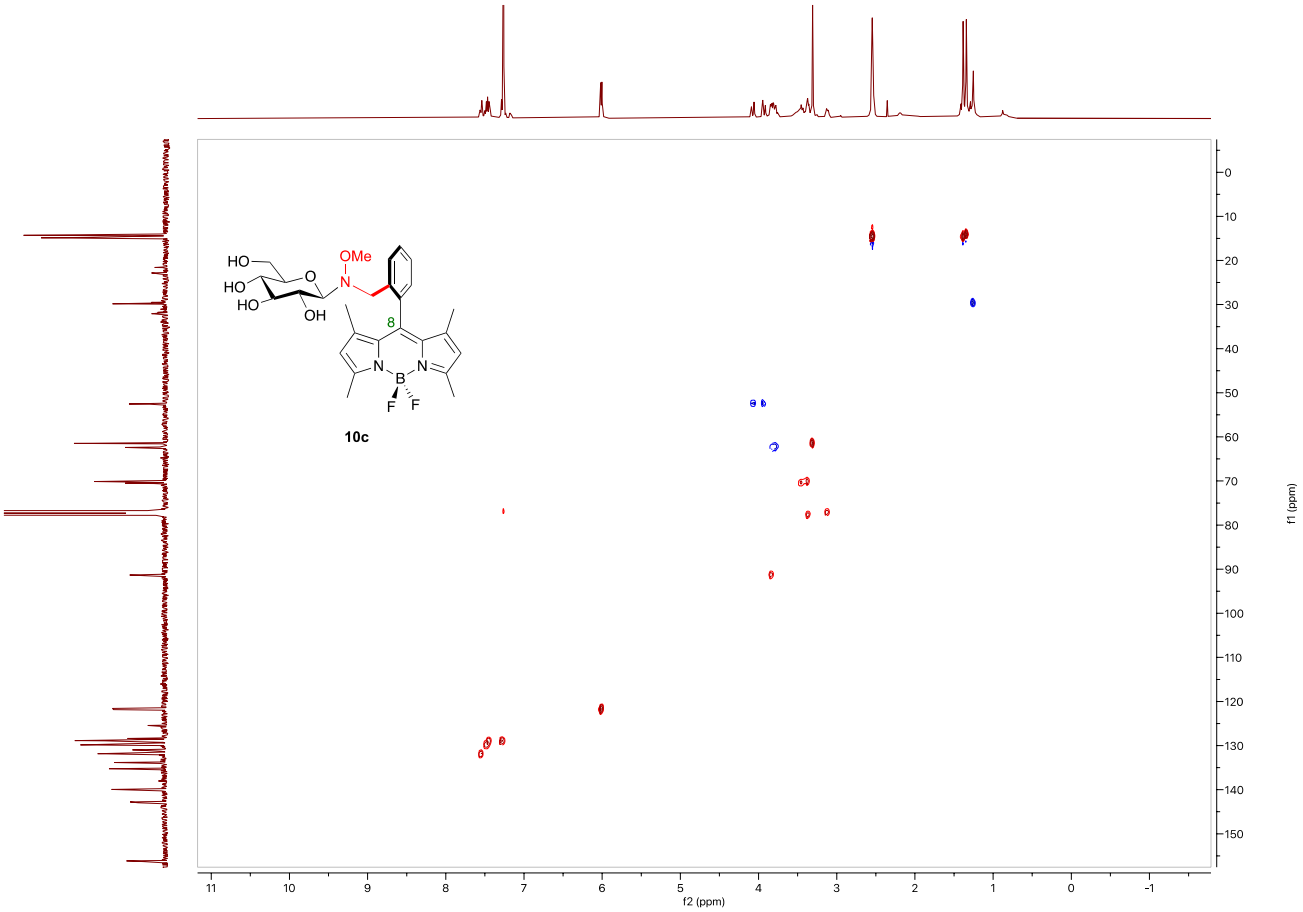


Fig S31. HSQC spectra for **10c**

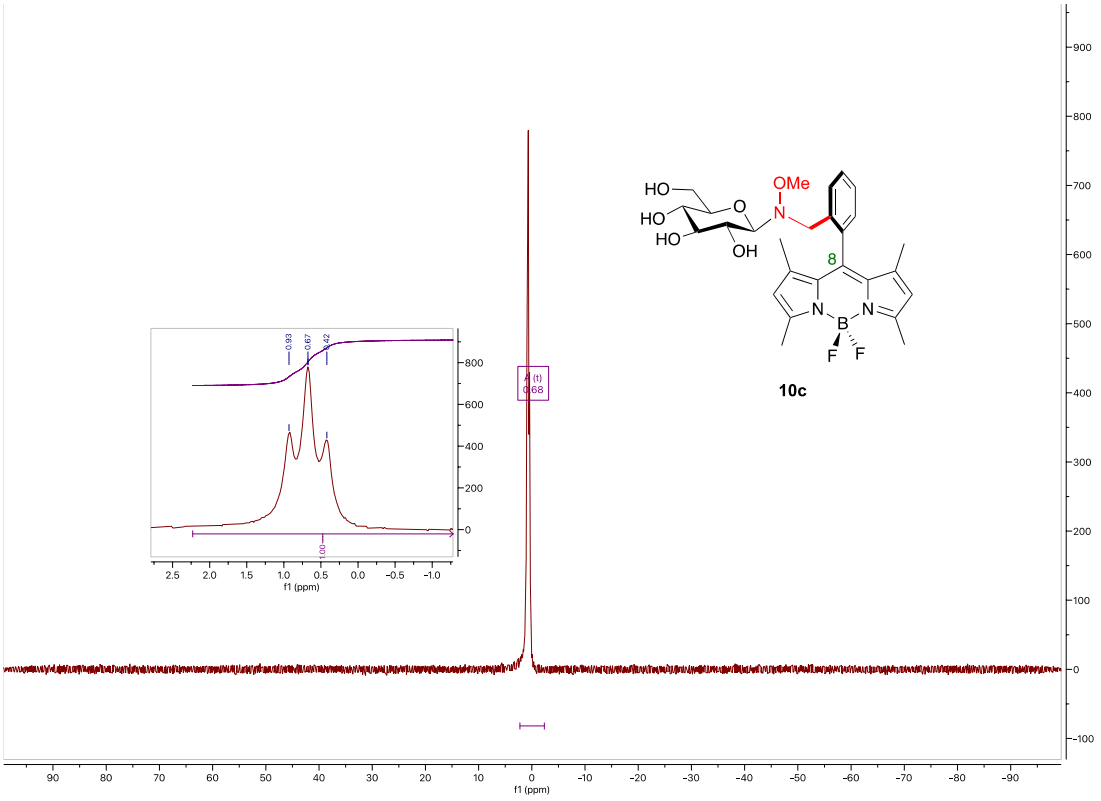


Fig S32. ^{11}B-NMR (128 MHz, $CDCl_3$) for **10c**

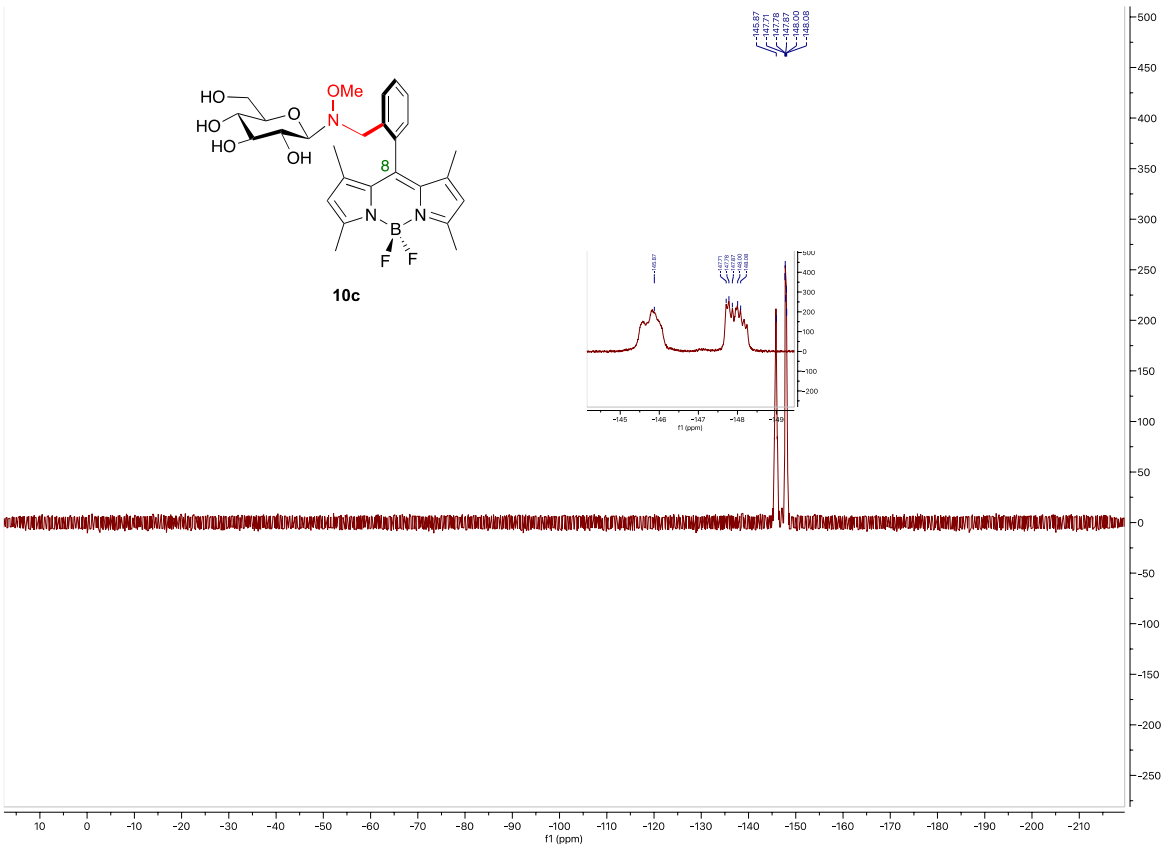


Fig S33. ^{19}F-NMR (376 MHz, $CDCl_3$) for **10c**

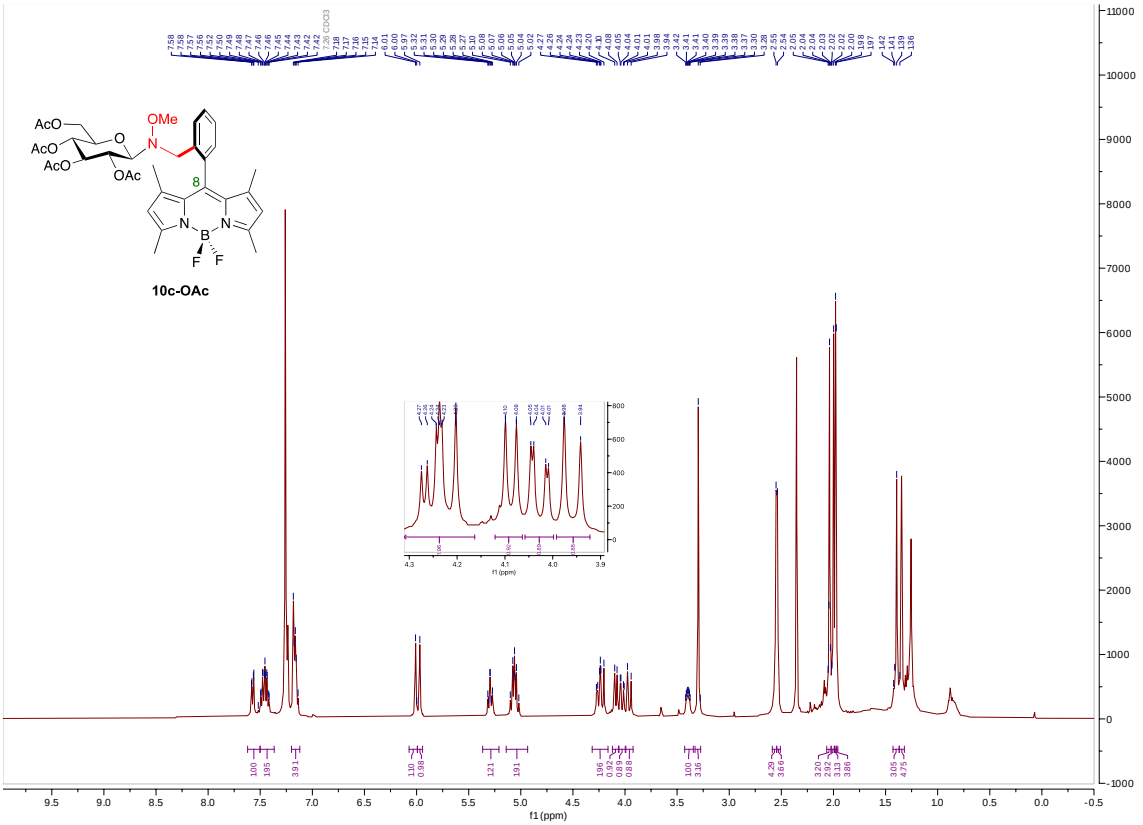


Fig S34. ^{1}H-NMR (400 MHz, $CDCl_3$) for **10c-OAc**

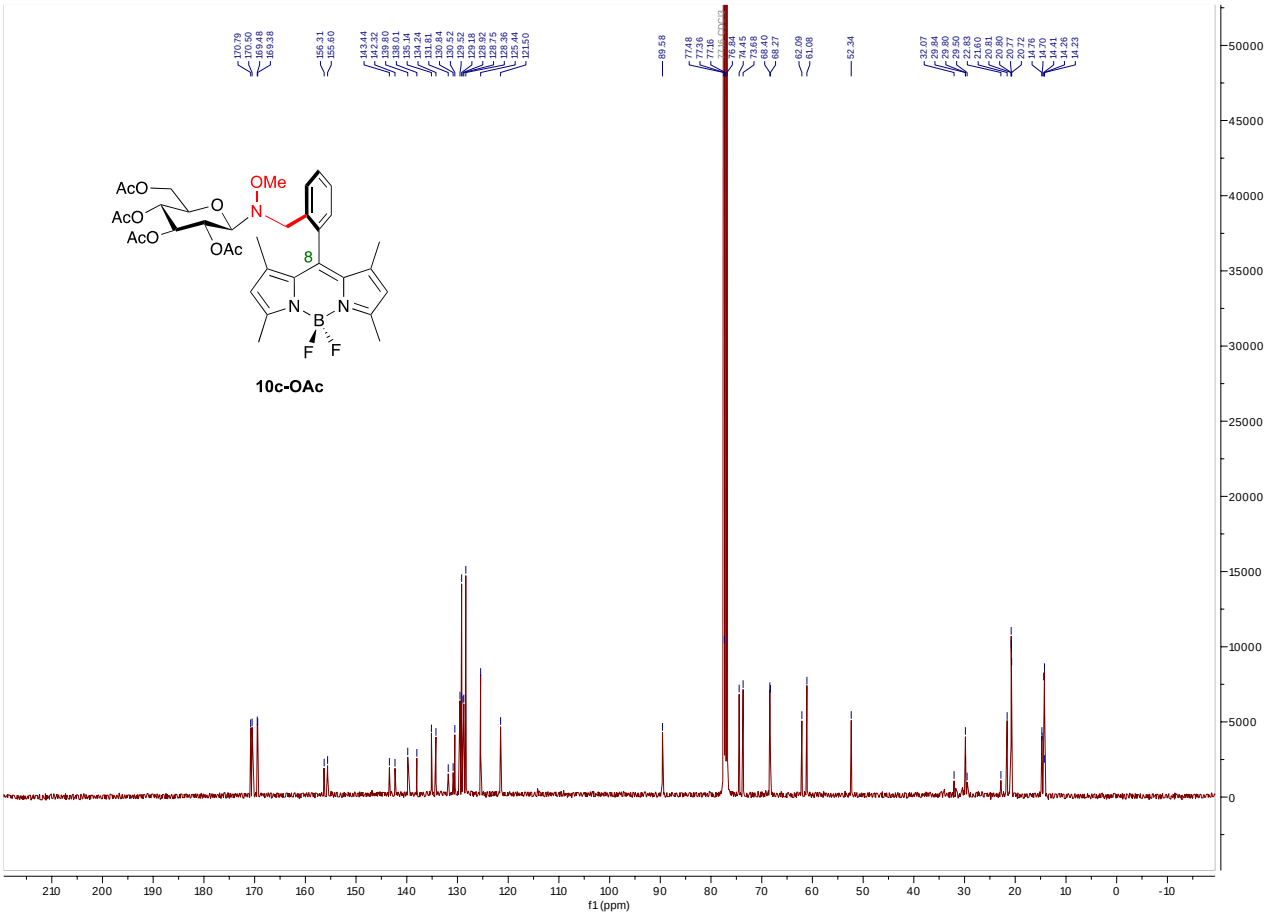


Fig S35. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **10c-OAc**

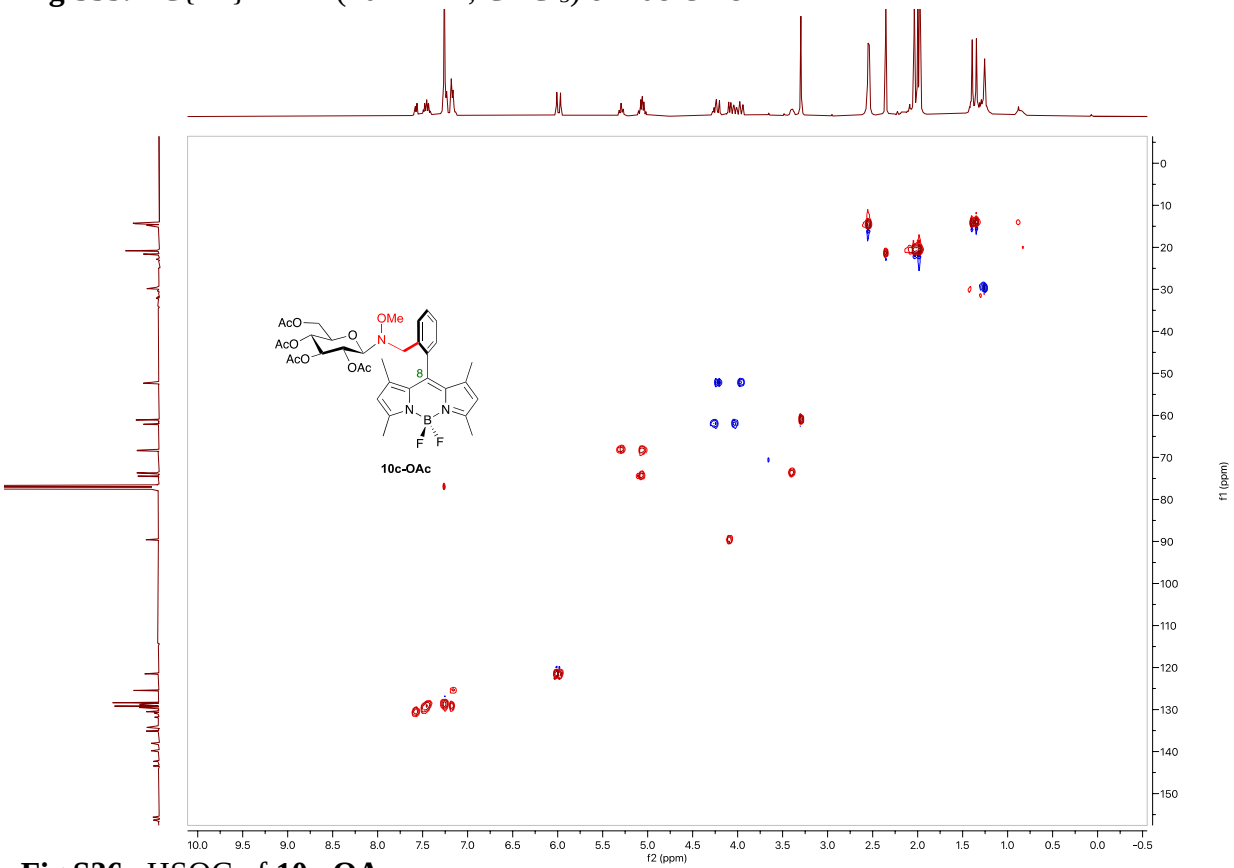


Fig S36. HSQC of **10c-OAc**

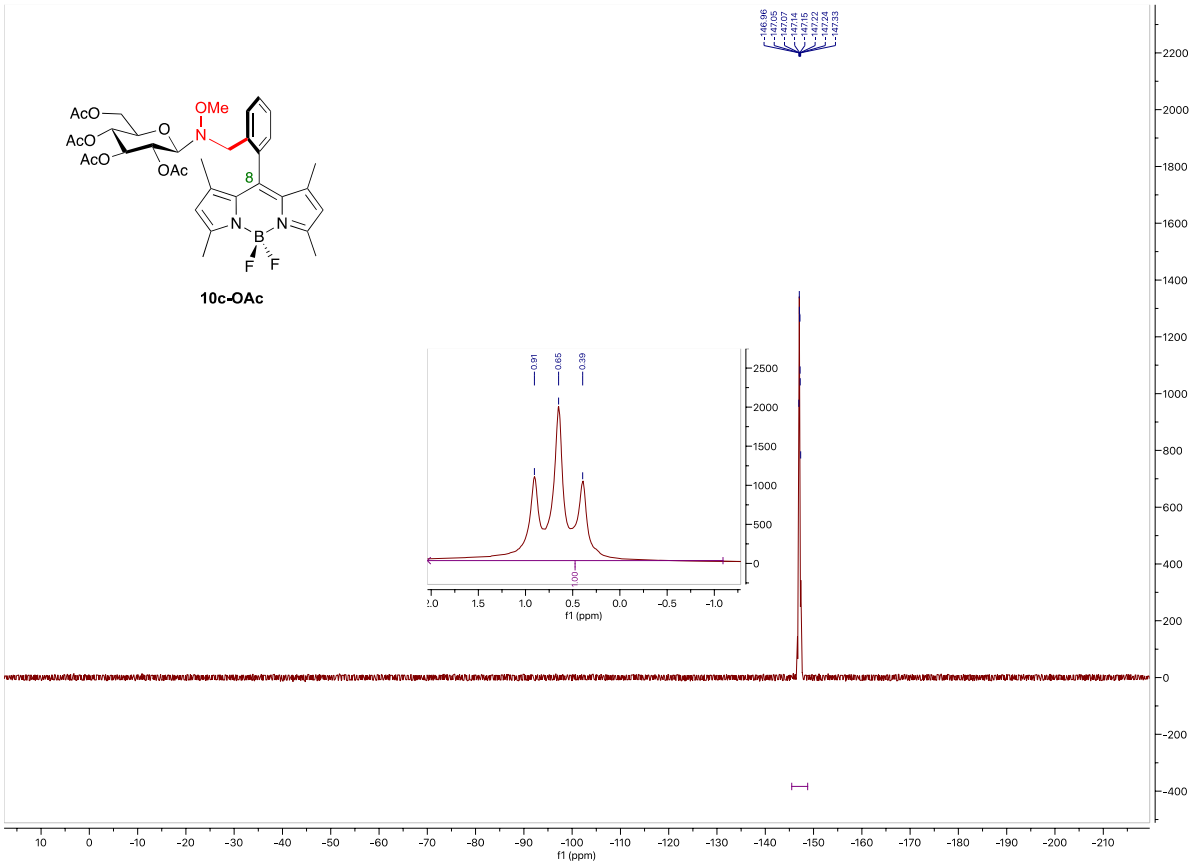


Fig S37. ^{19}F-NMR (376 MHz, $CDCl_3$) for **10c-OAc**

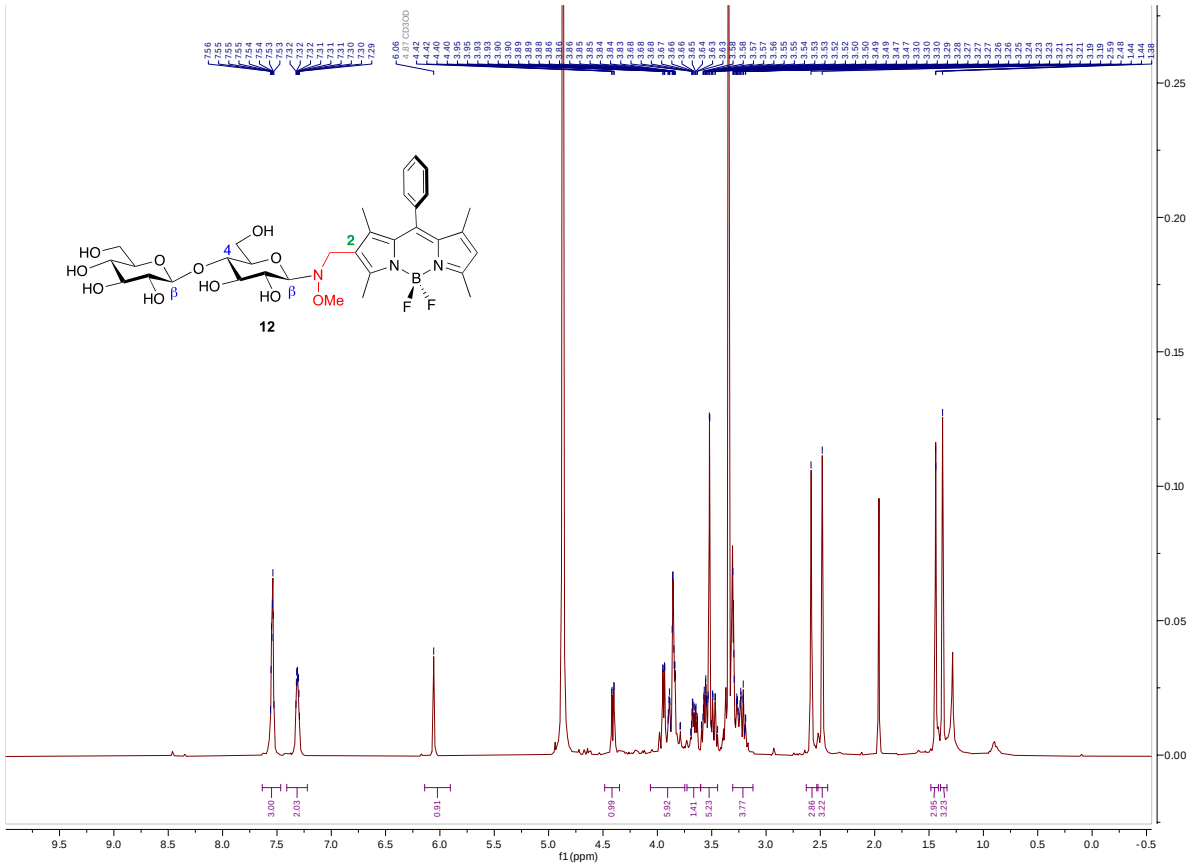


Fig S38. ^{1}H-NMR (400 MHz, CD_3OD_3) for **12**

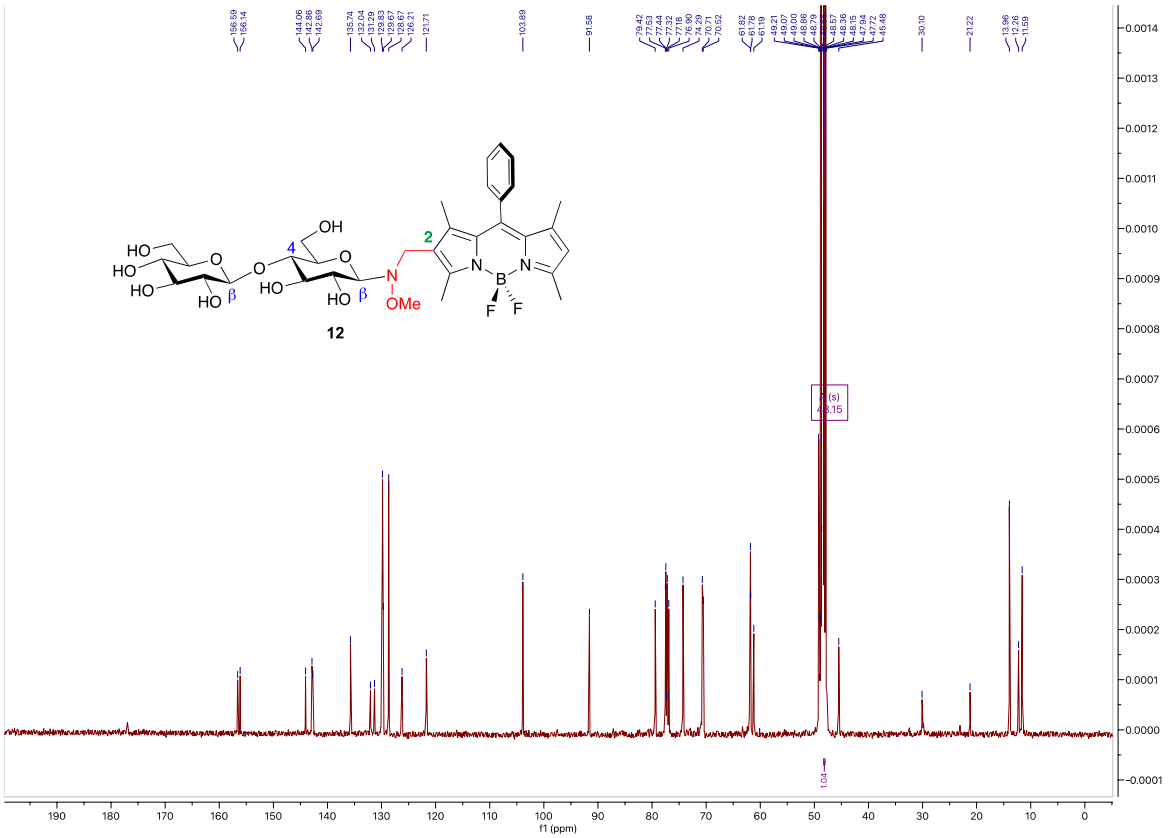


Fig S39 $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3OD) of **12**

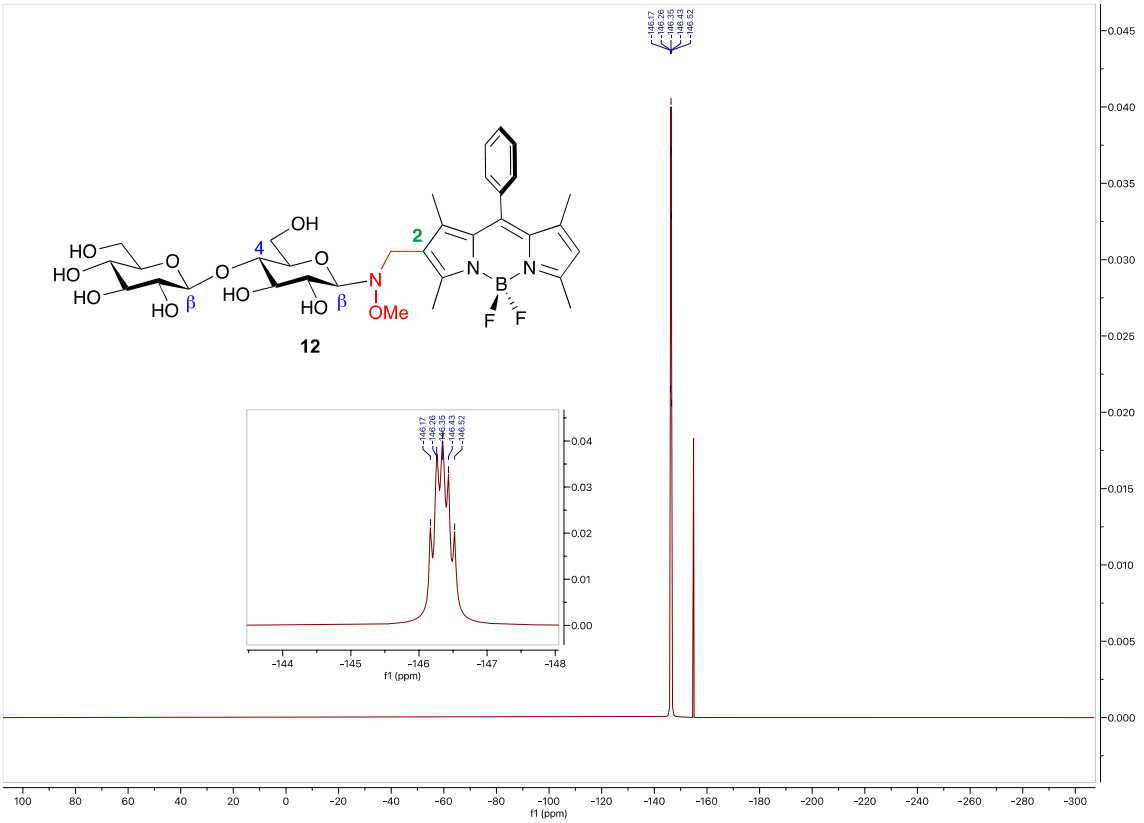


Fig S40 ^{19}F-NMR (376 MHz, CD_3OD) of **12**

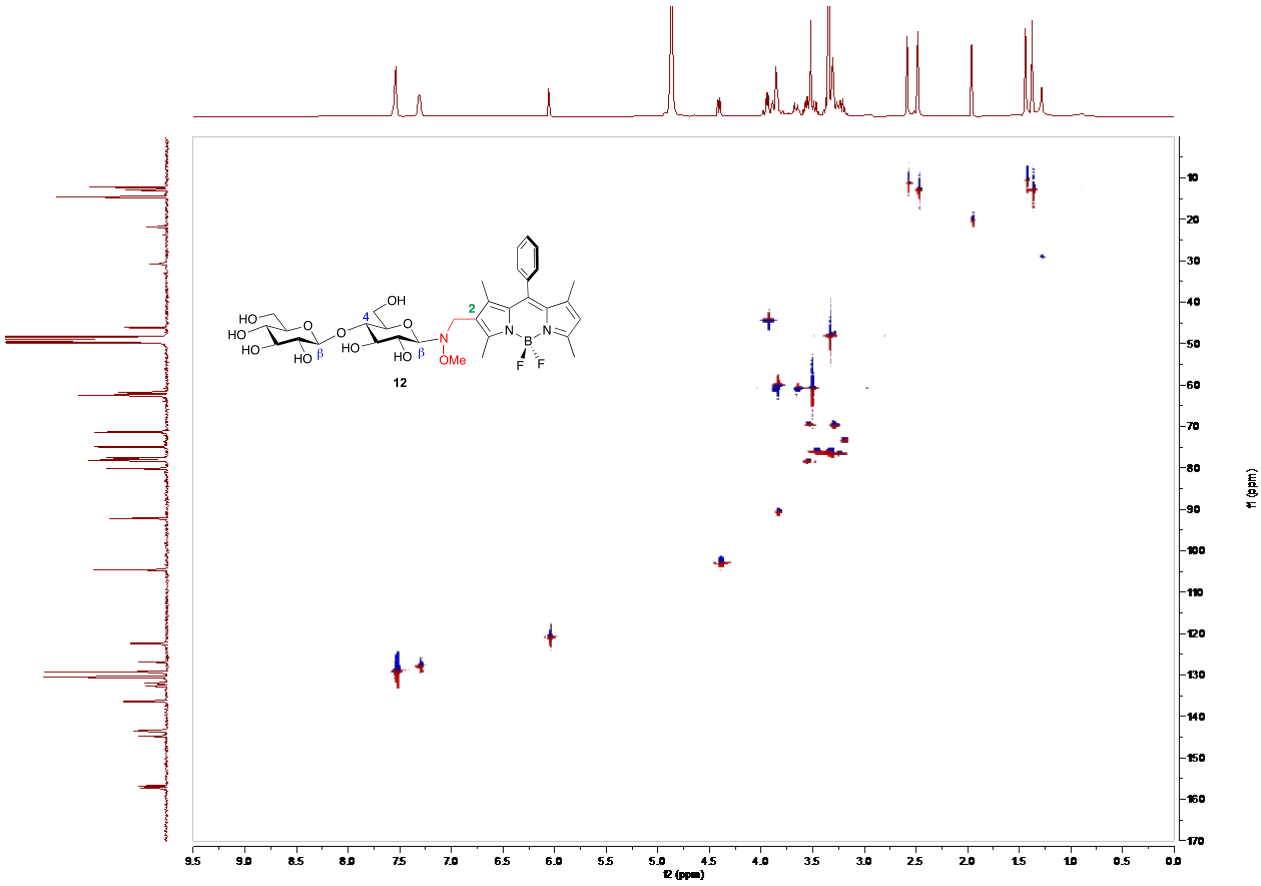


Fig S41. HSQC of **12**

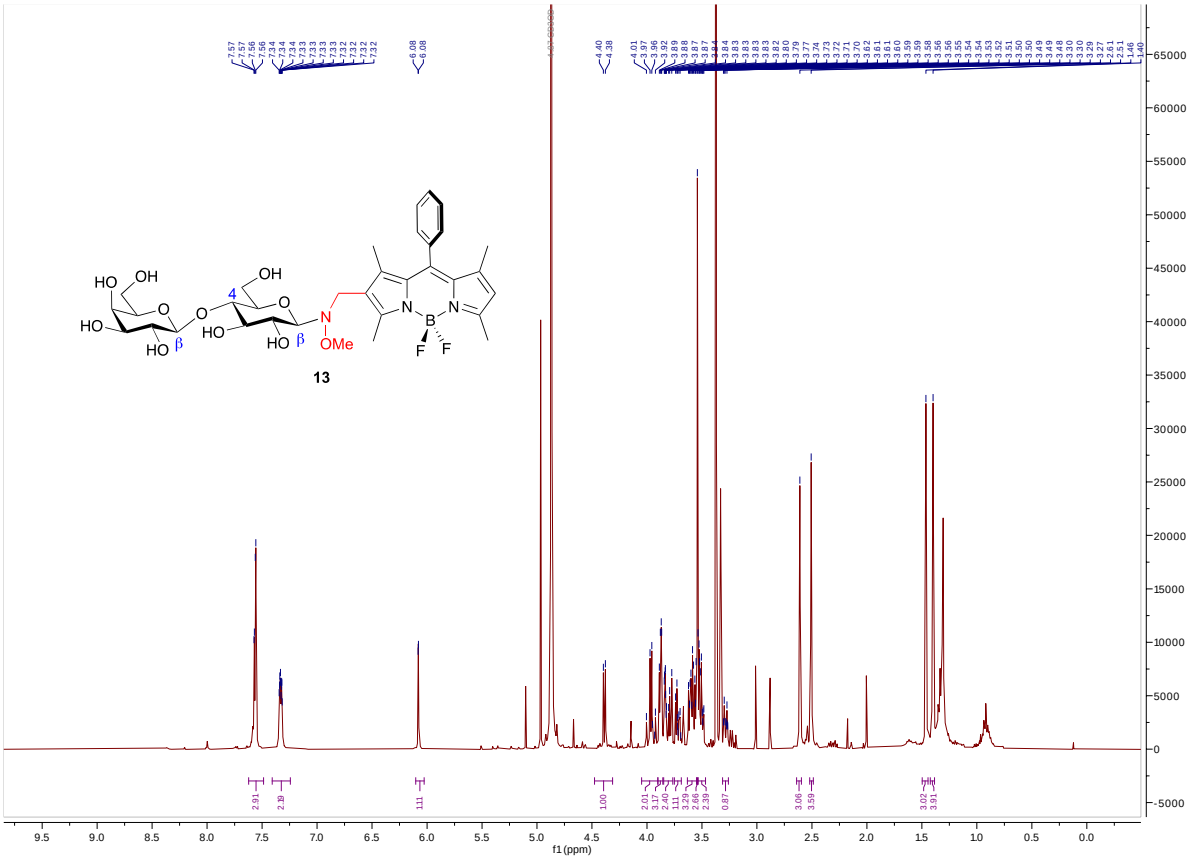


Fig S42. ^{1}H-NMR (400 MHz, CD_3OD_3) for **13**

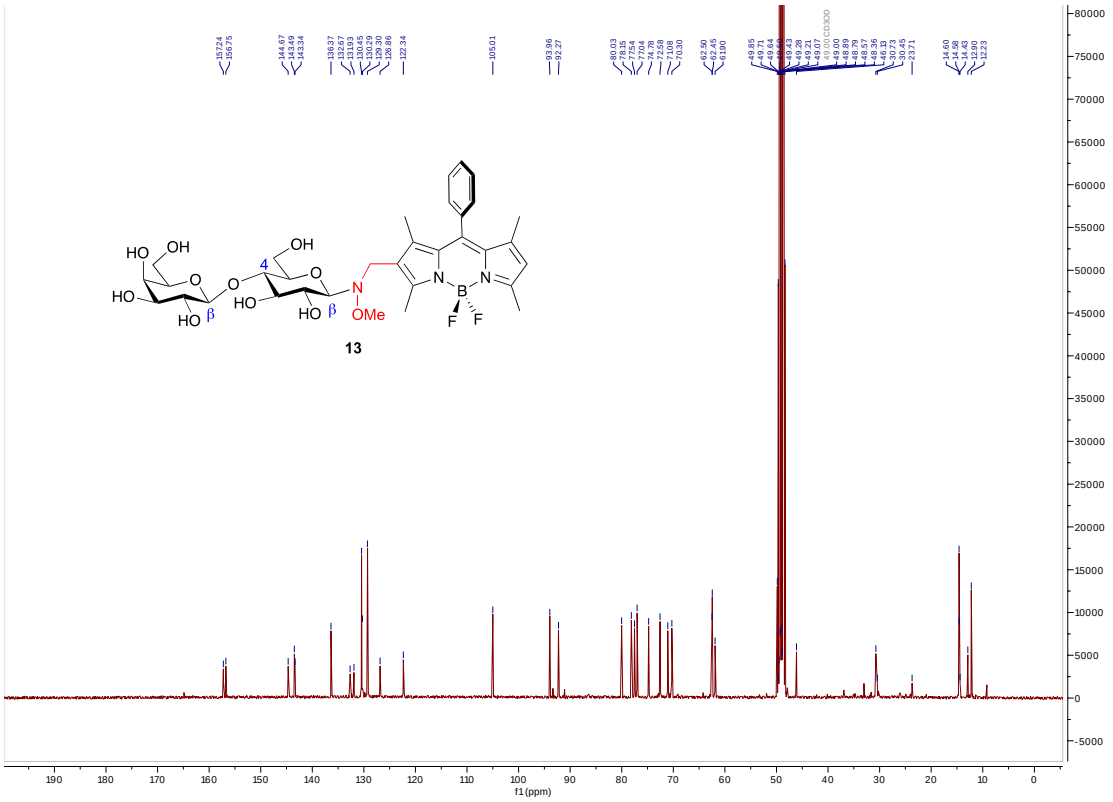


Fig S43 $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3OD) of **13**

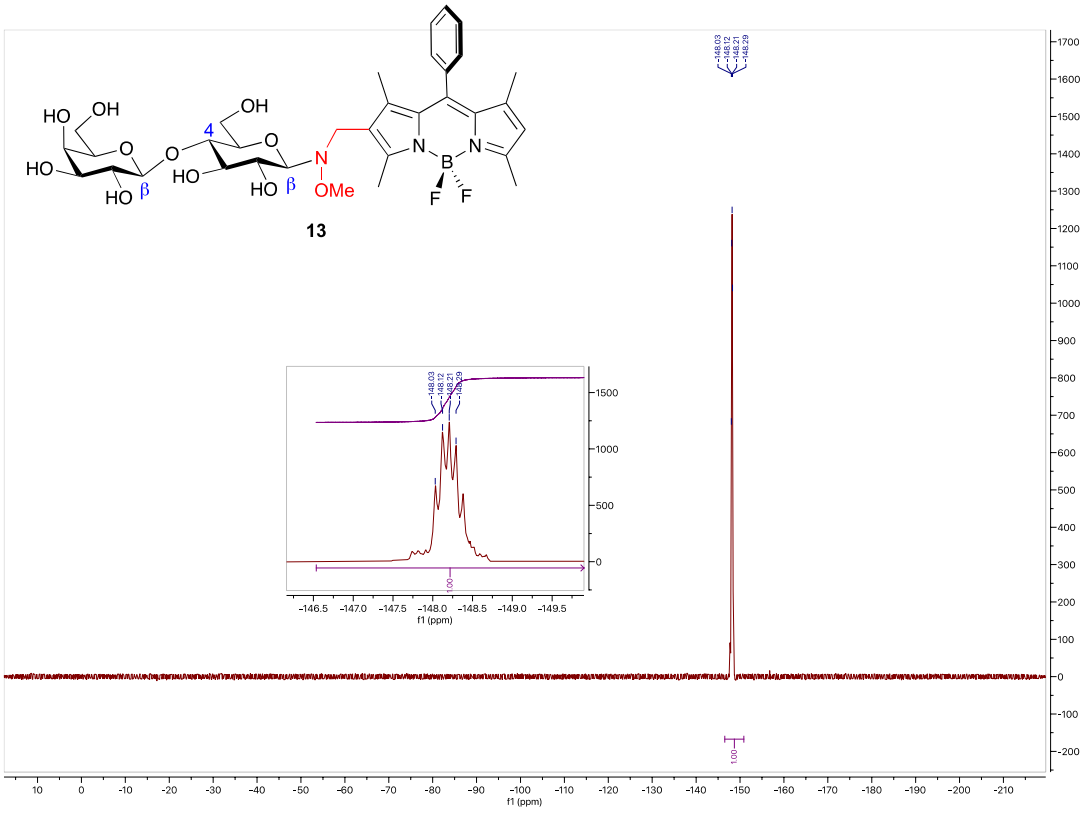


Fig S44 ^{19}F-NMR (376 MHz, CD_3OD) of **12**

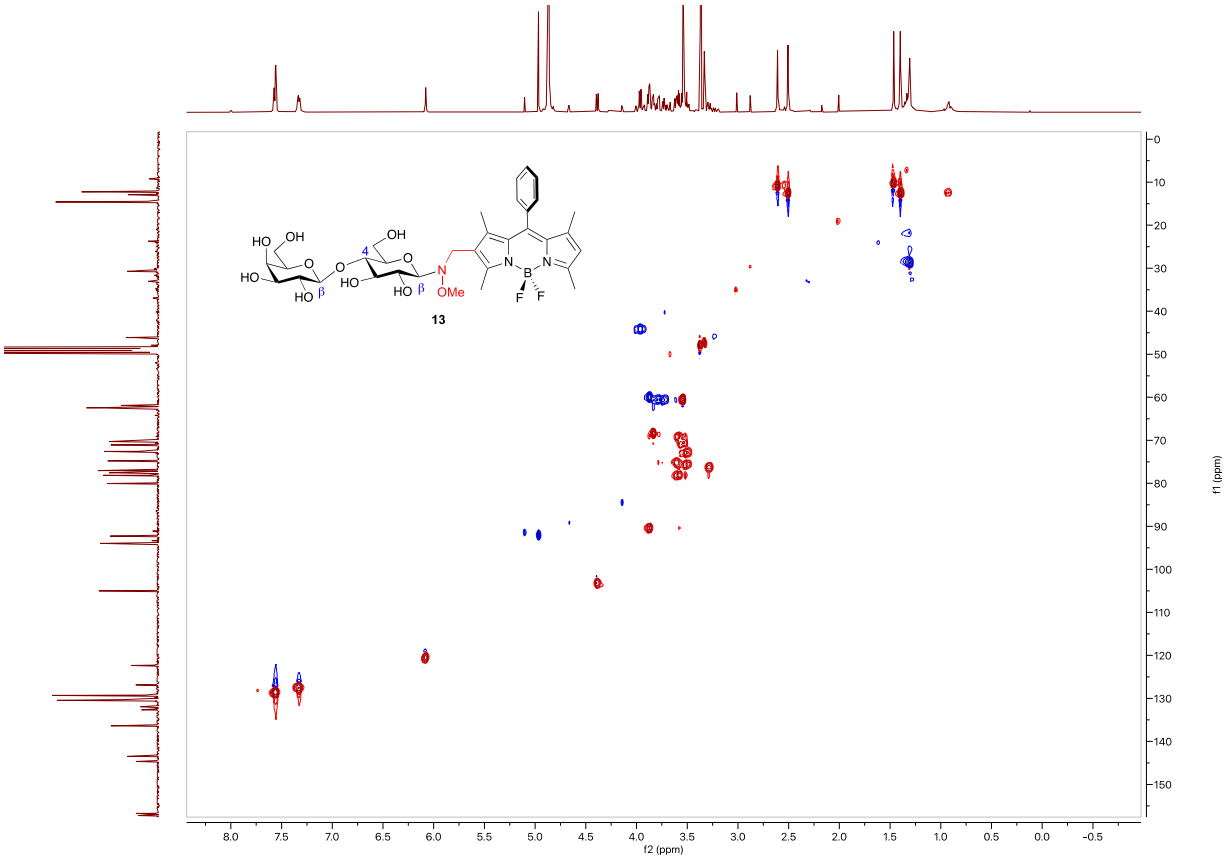


Fig S45. HSQC of **12**

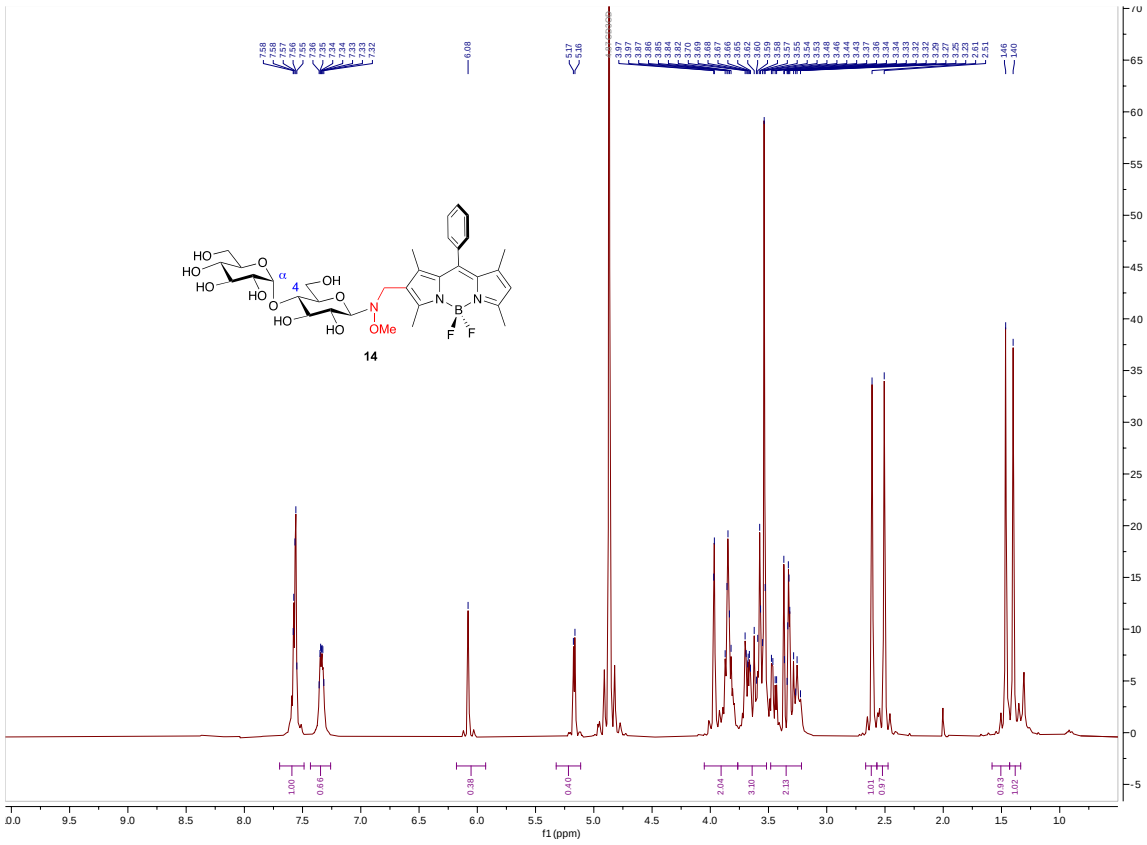


Fig S46. ^{1}H-NMR (400 MHz, CD_3OD_3) for **14**

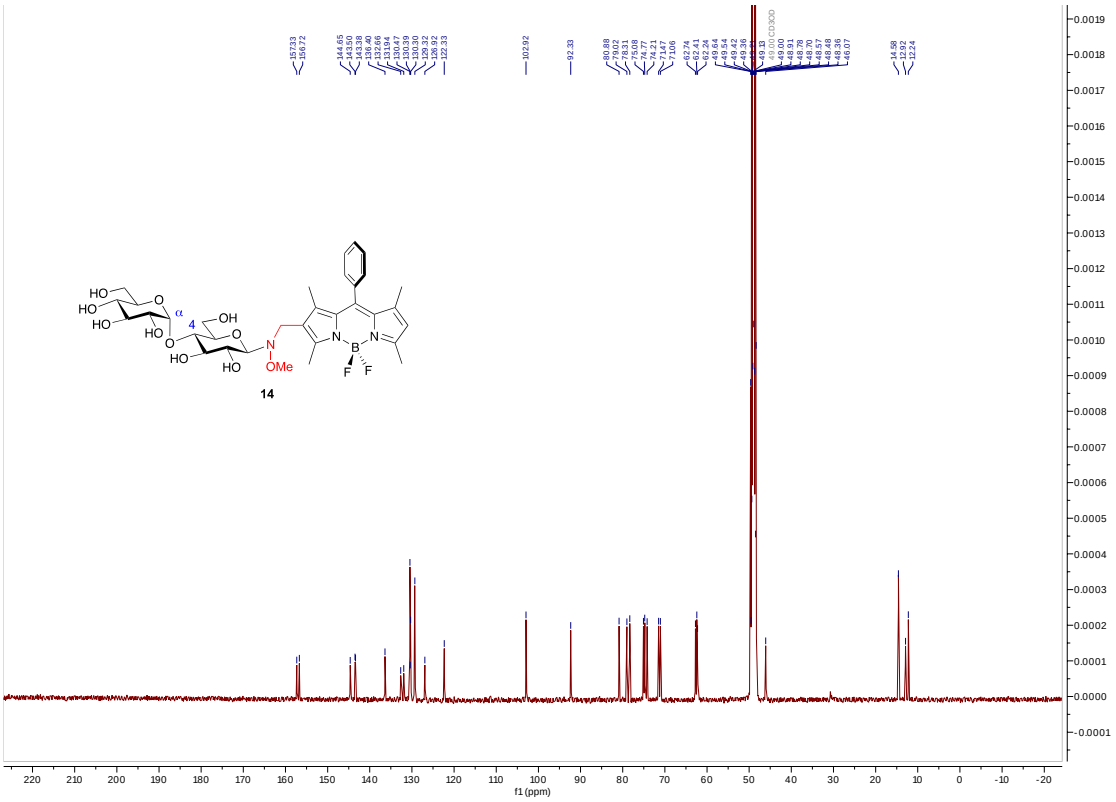


Fig S47$^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3OD) of **14**

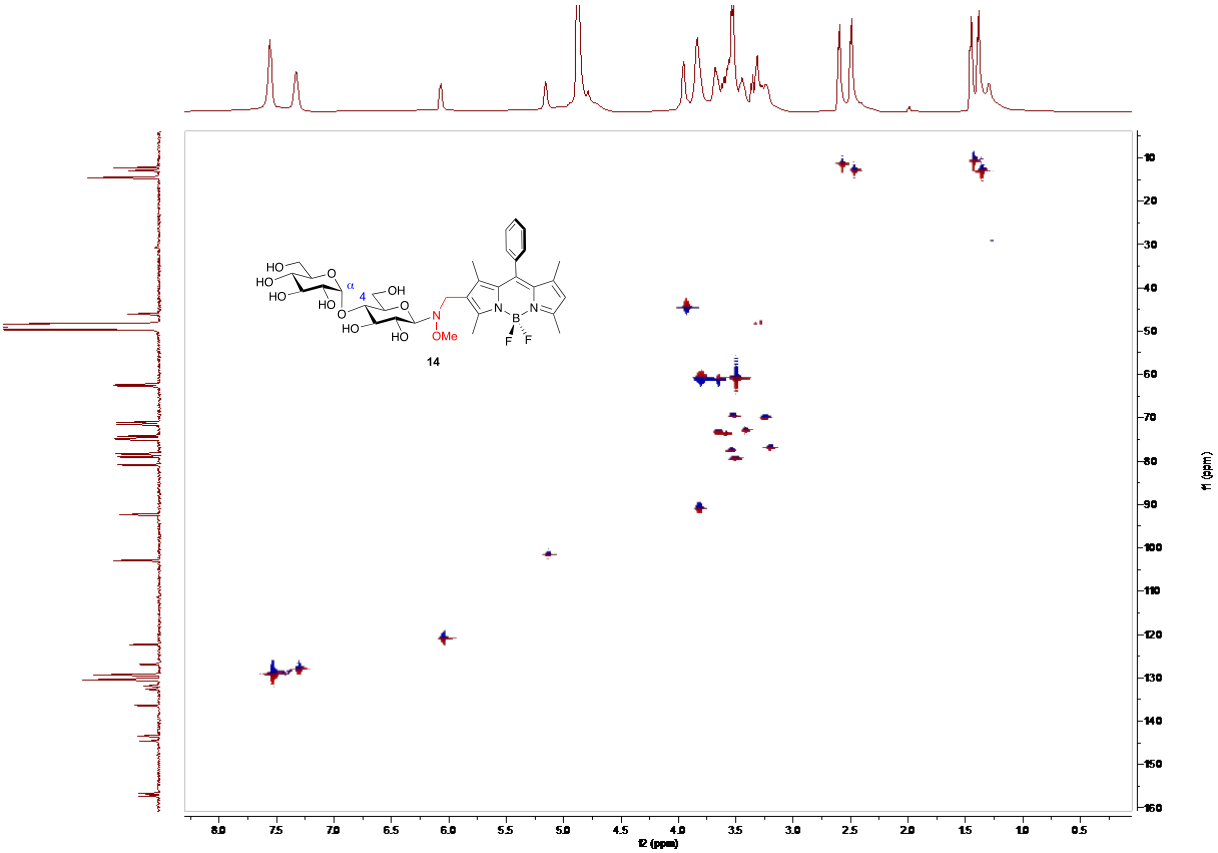


Fig S48. HSQC of **12**

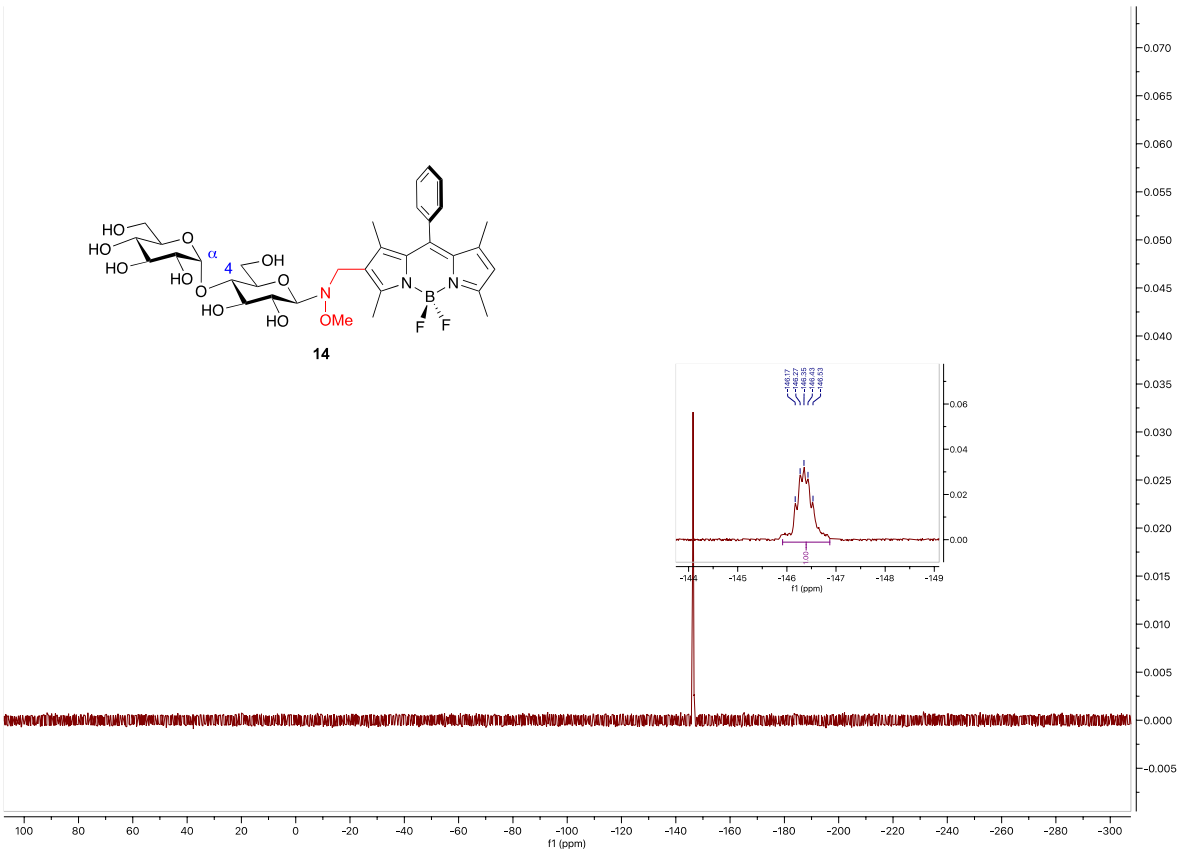


Fig S49 ^{19}F-NMR (376 MHz, CD_3OD) of **14**

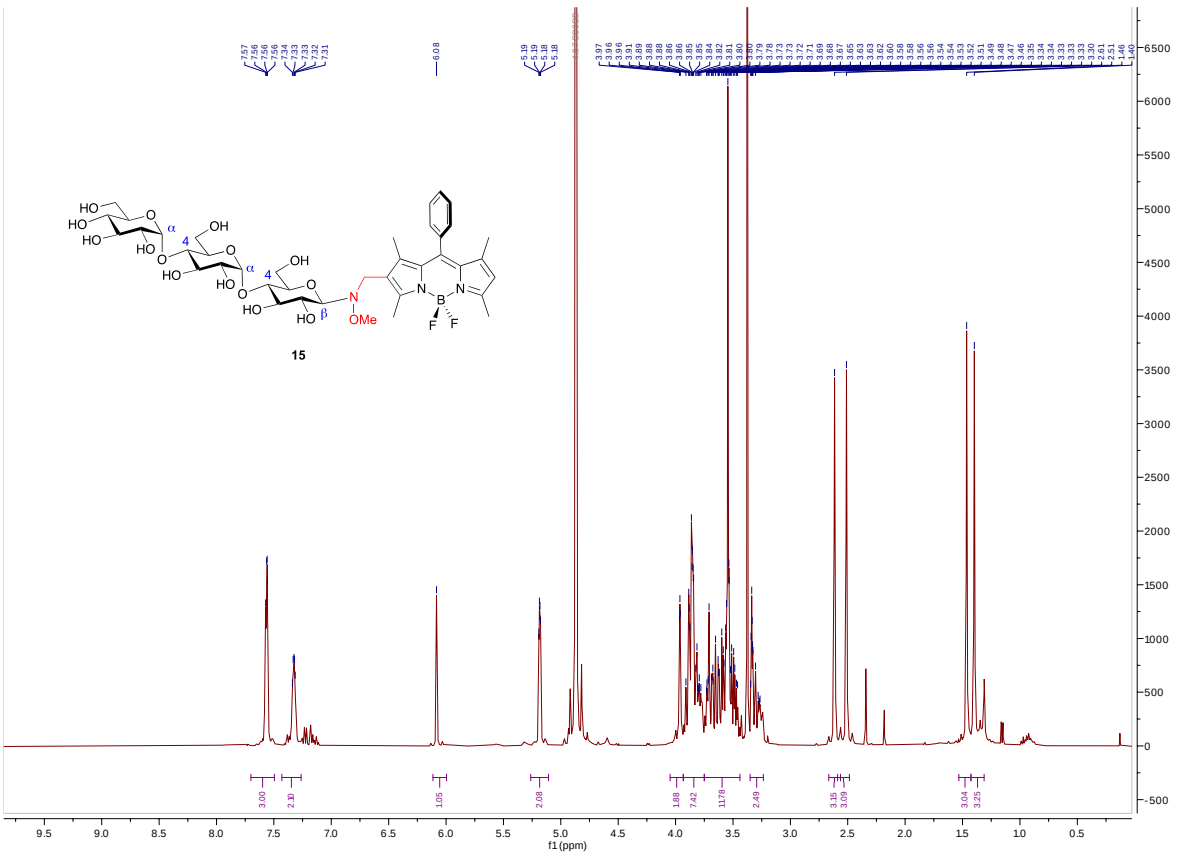


Fig S50. ^{1}H-NMR (400 MHz, CD_3OD_3) for **15**

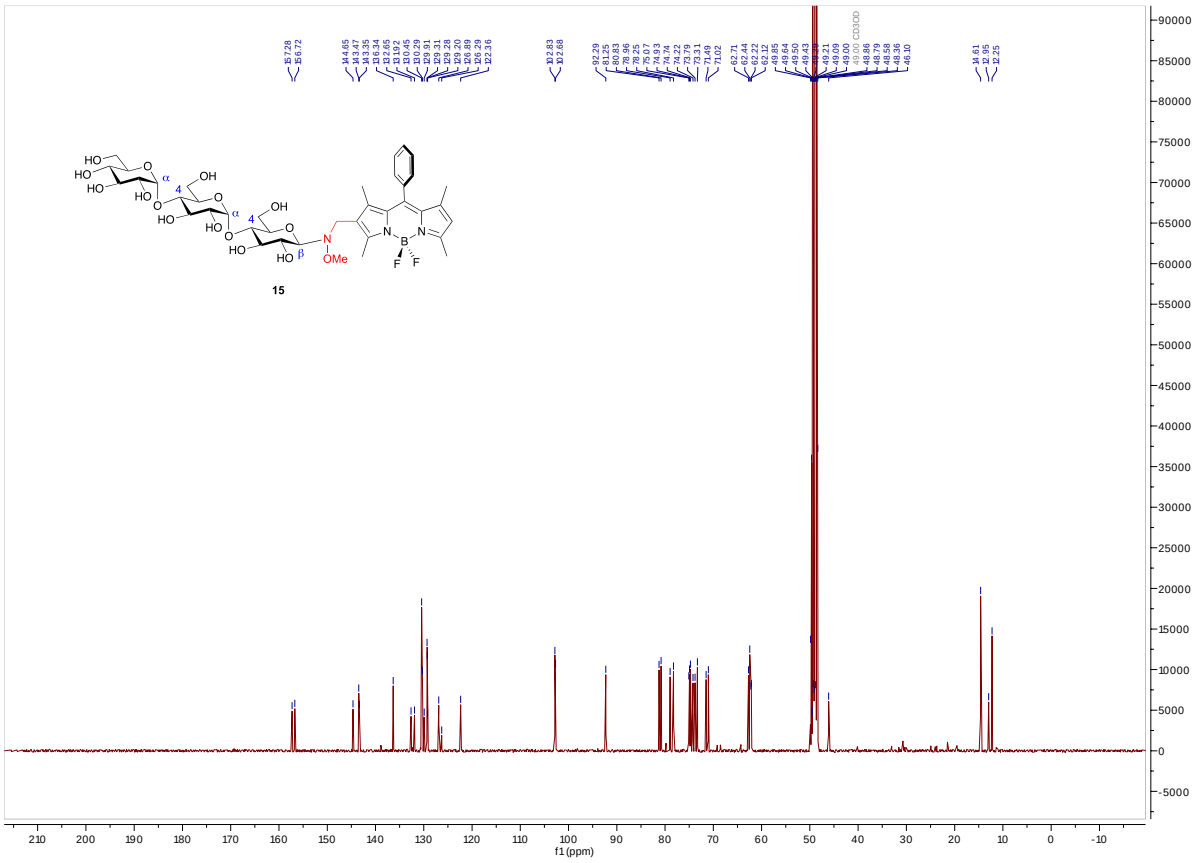


Fig S51$^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3OD) of **15**

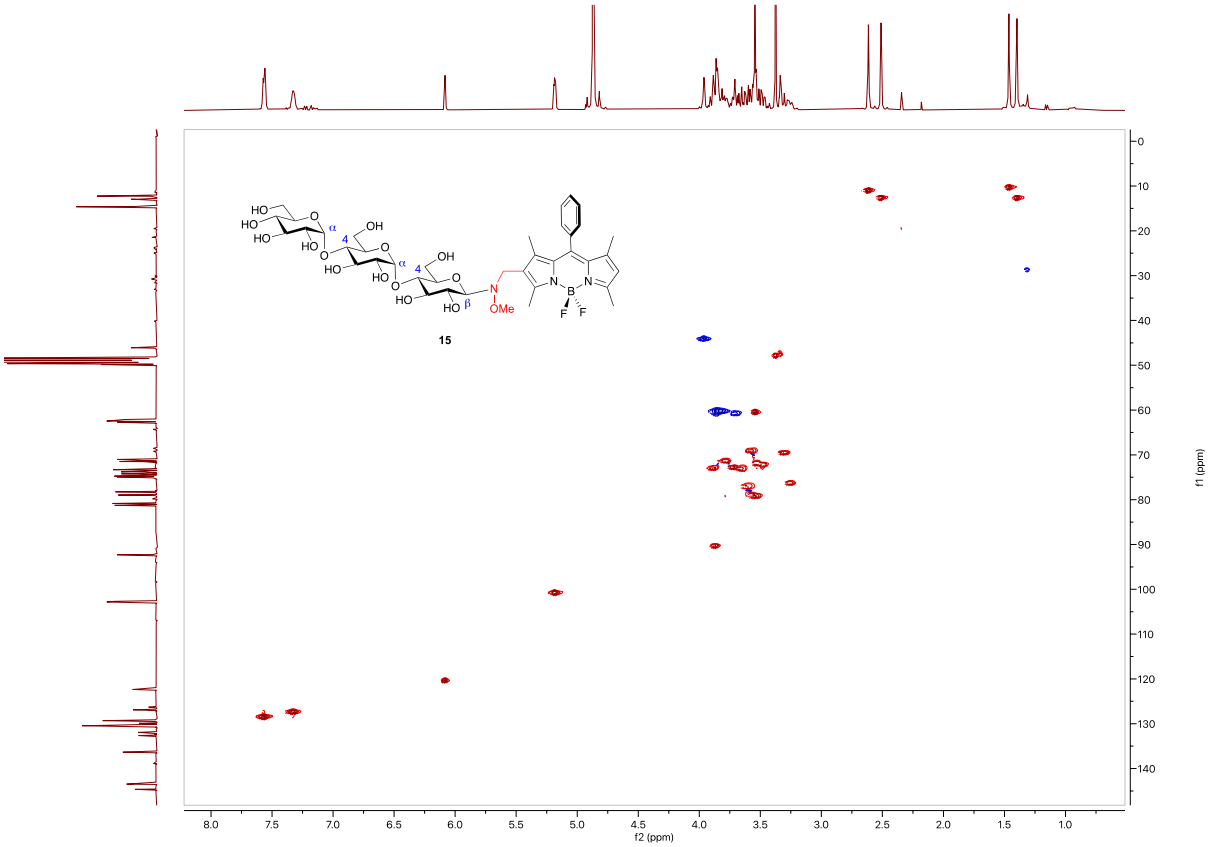


Fig S52. HSQC of **15**

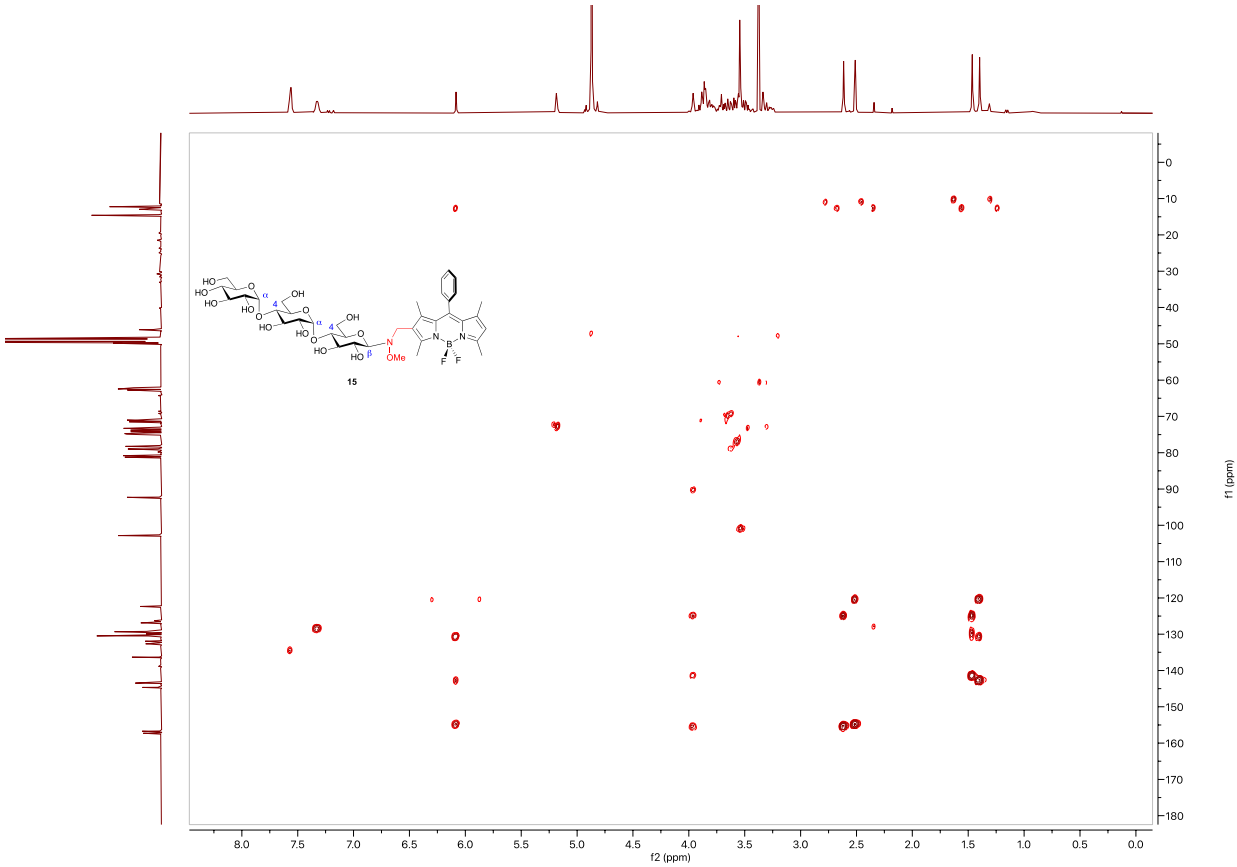


Fig S53. HMBC of **15**

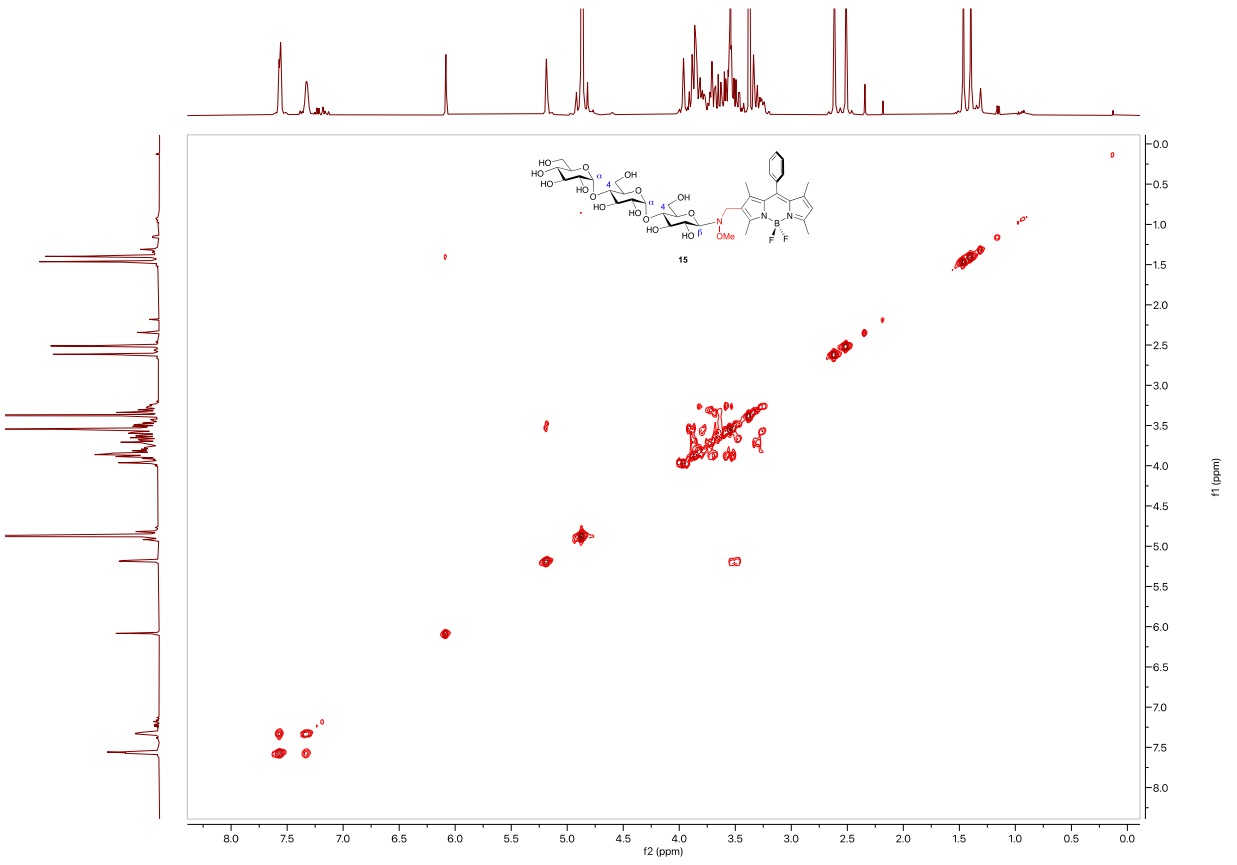


Fig S54. COSY of **15**

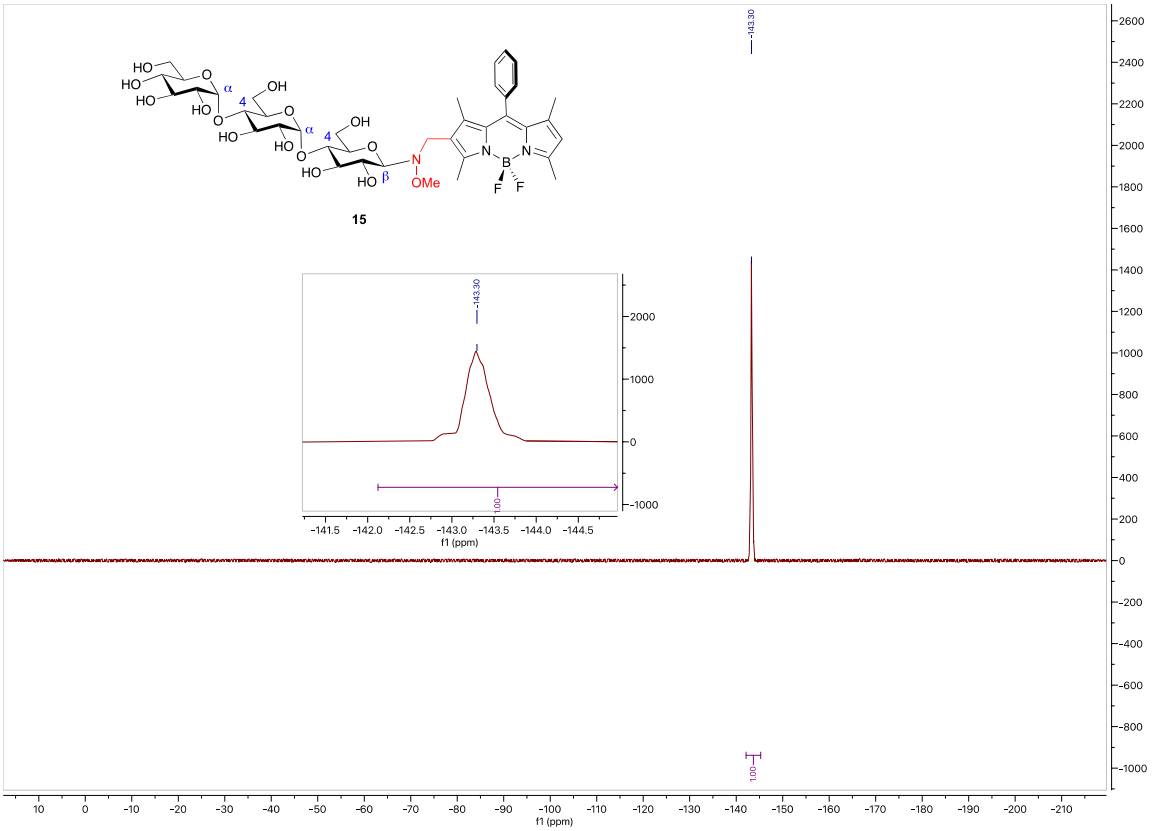


Fig S55 ^{19}F-NMR (376 MHz, CD_3OD) of **15**

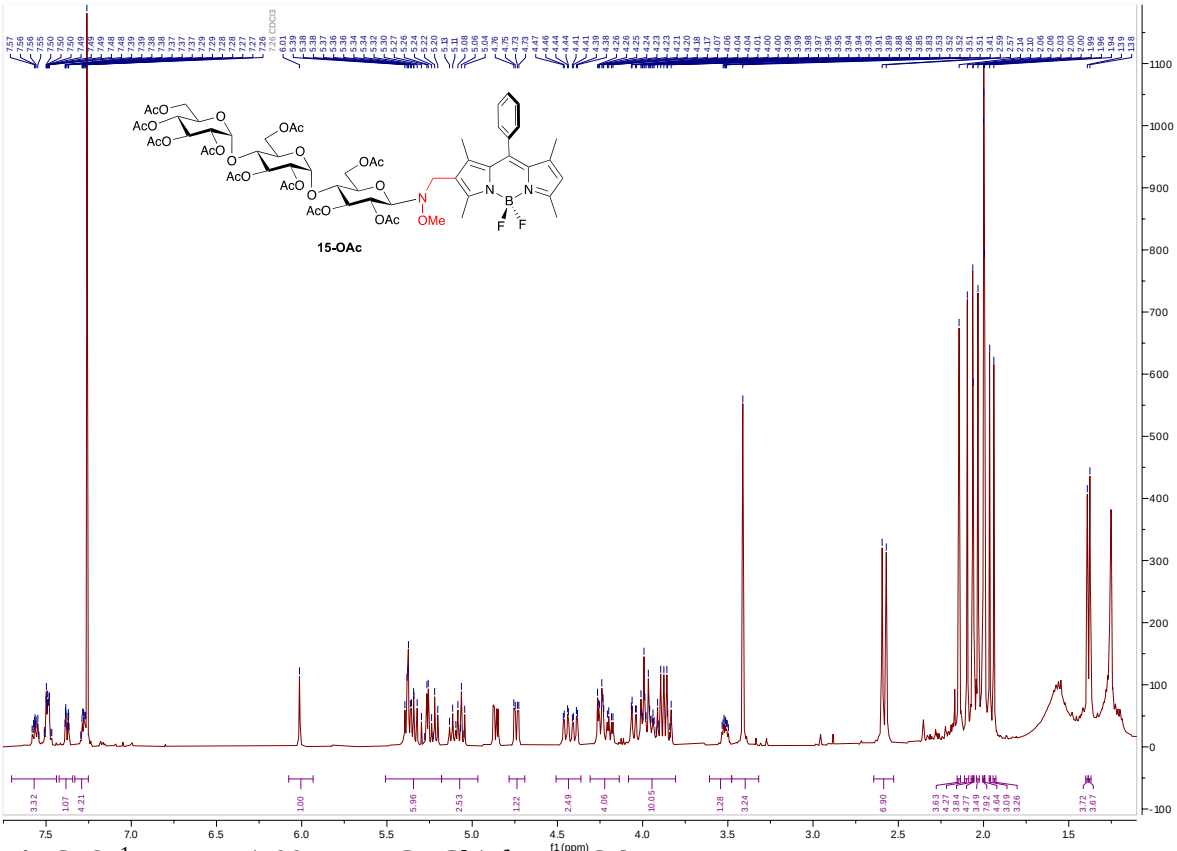


Fig S56. ^{1}H-NMR (400 MHz, $CDCl_3$) for **15-OAc**

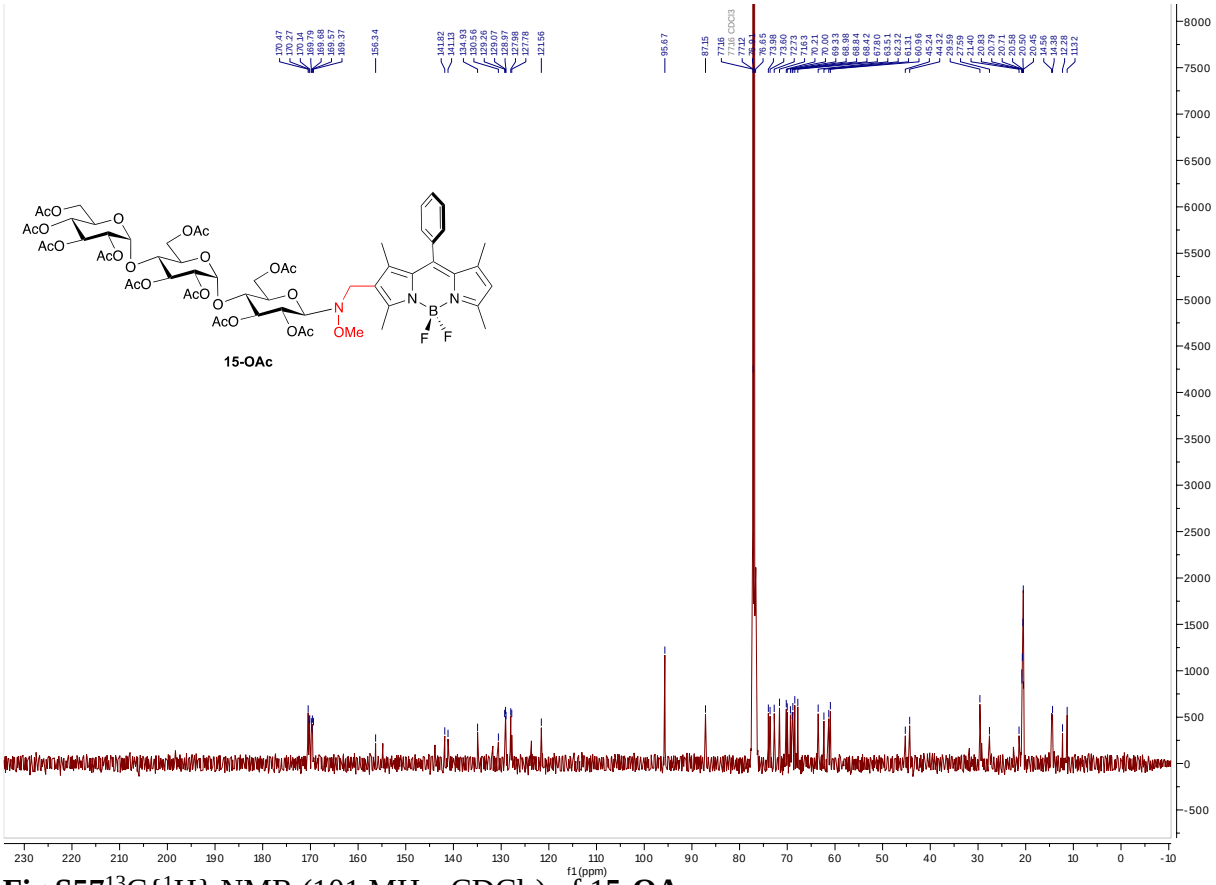


Fig S57 $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **15-OAc**

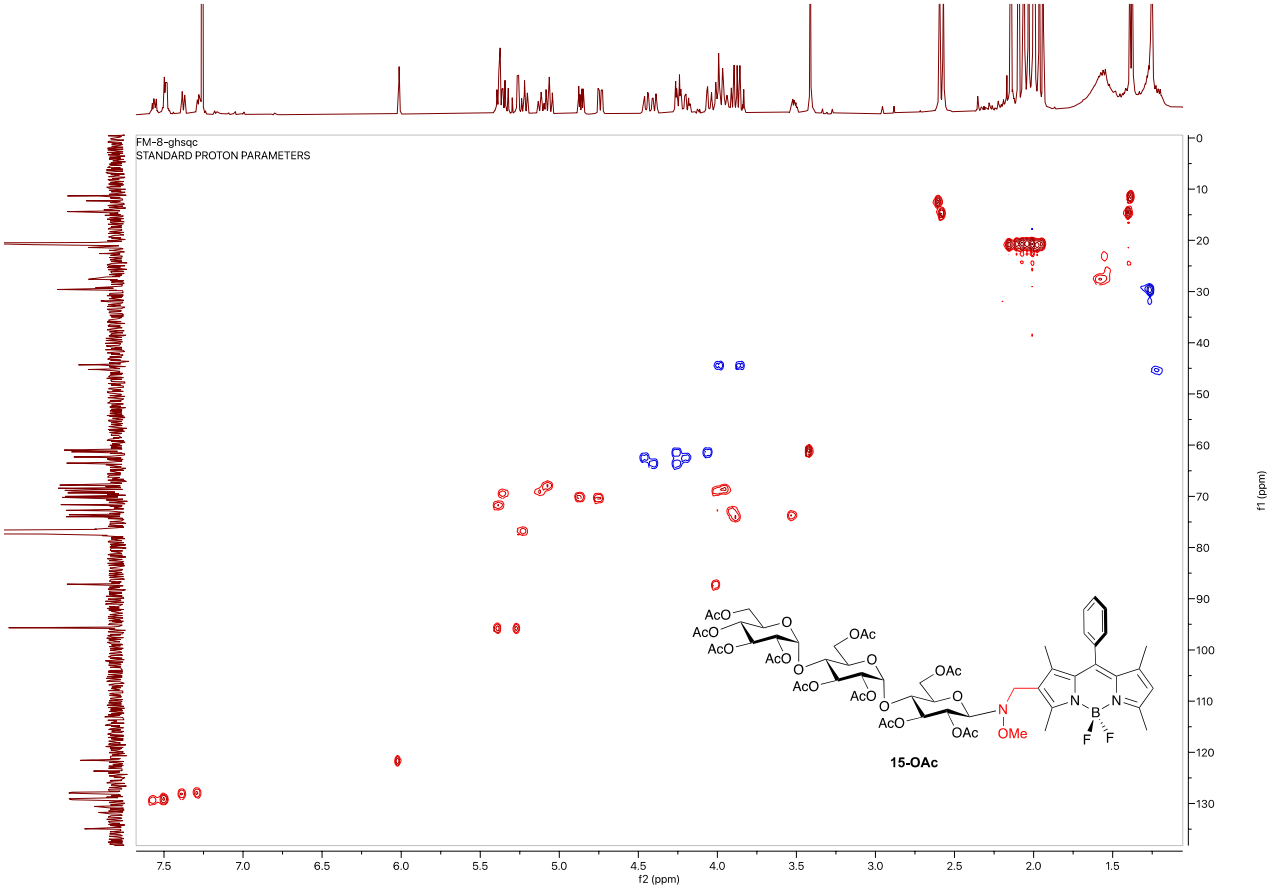


Fig S58. HSQC of **15-OAc**

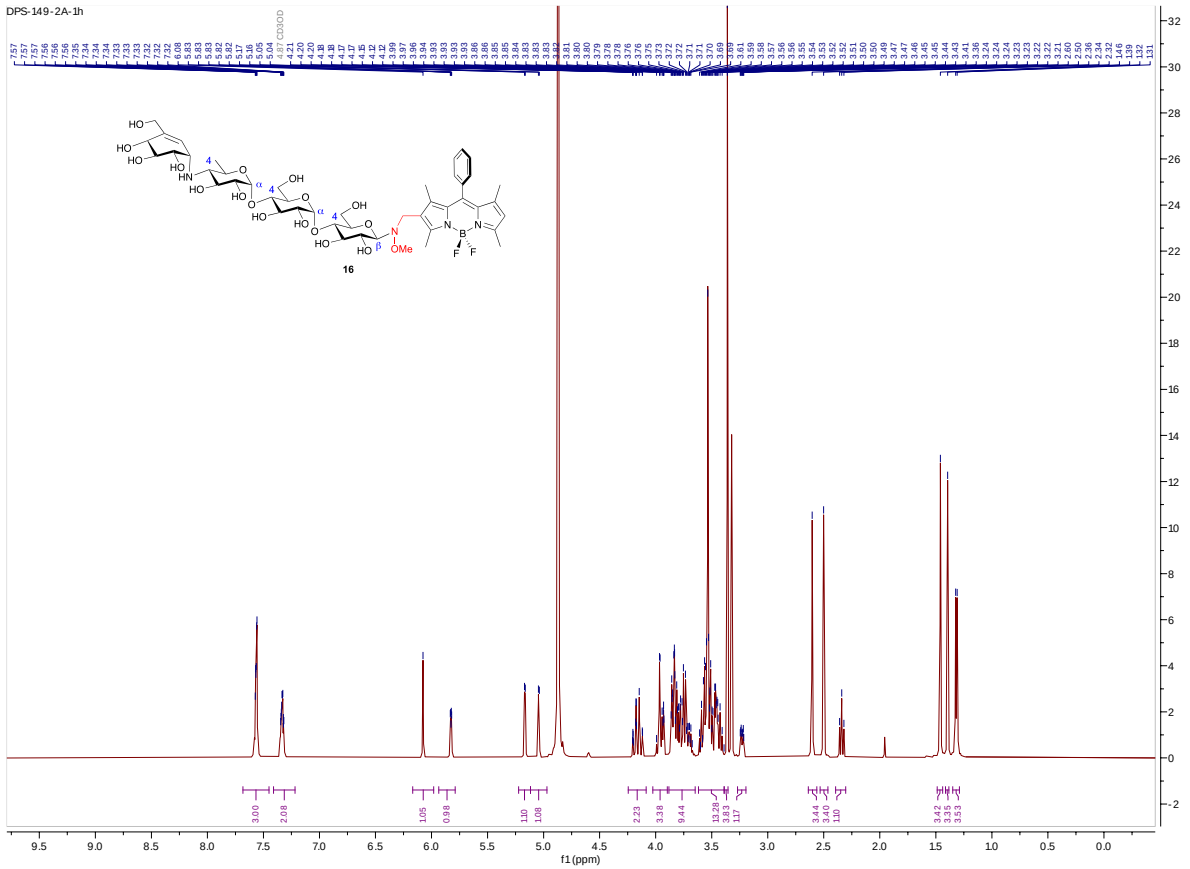


Fig S59. ^{1}H-NMR (500 MHz, CD_3OD) for **16**

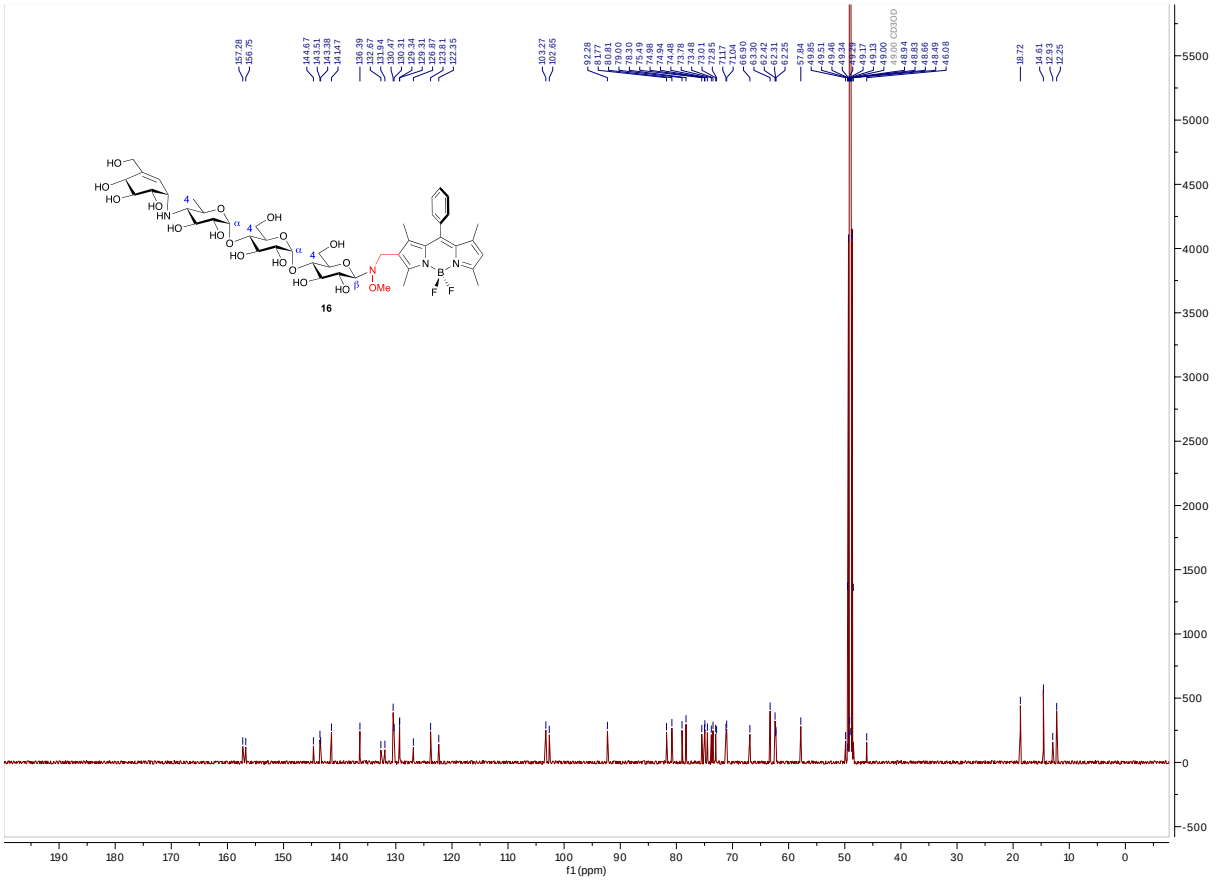


Fig S60. $^{13}C\{^{1}H\}$ NMR (126 MHz, CD_3OD) of **16**

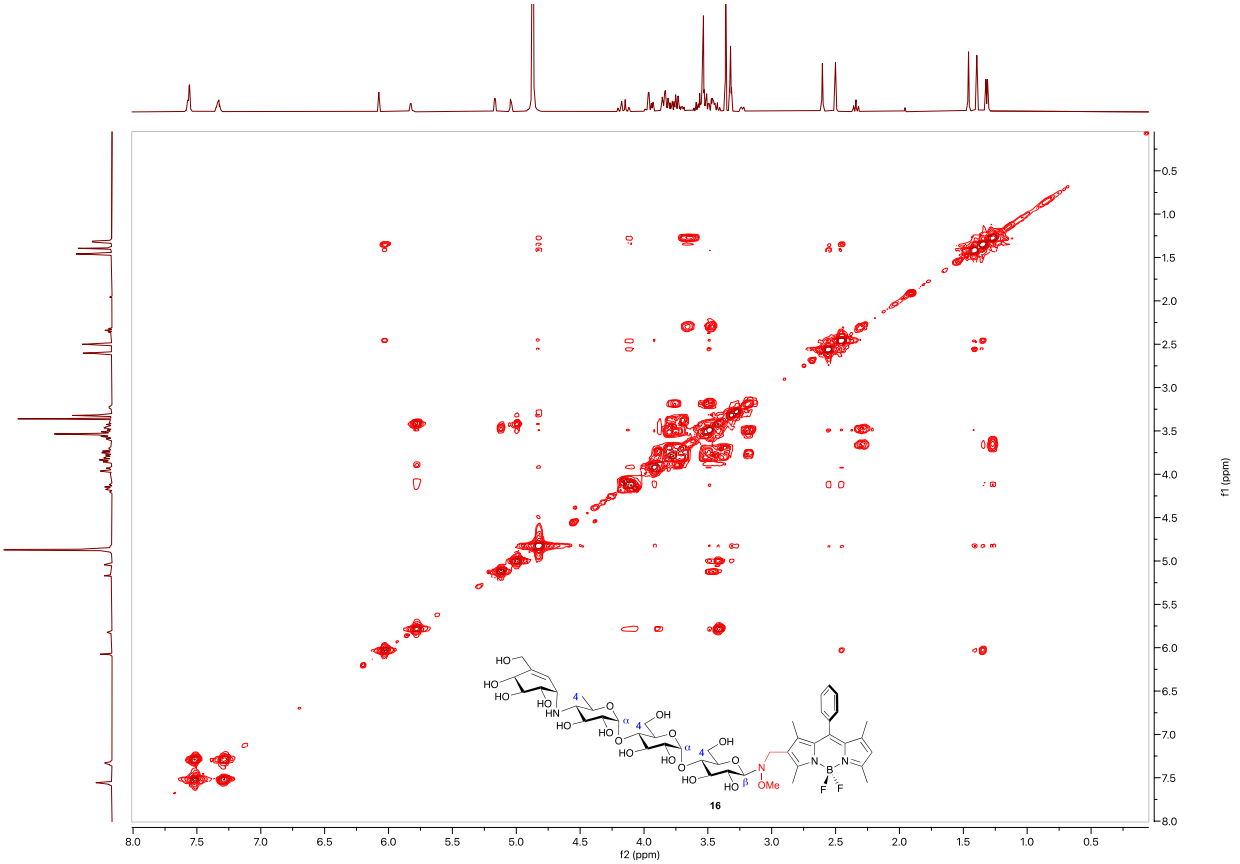


Fig S61. COSY for **16**

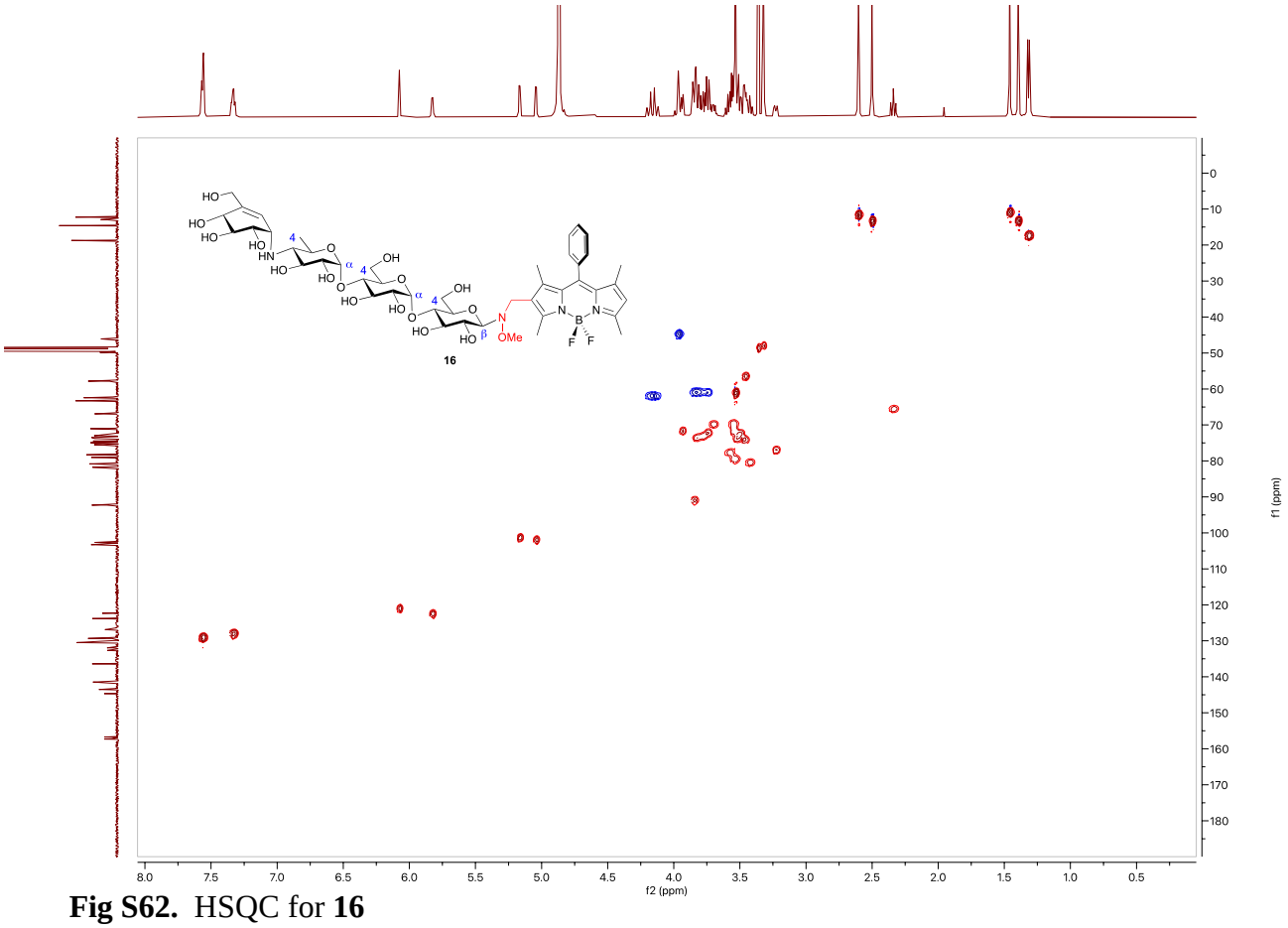


Fig S62. HSQC for **16**

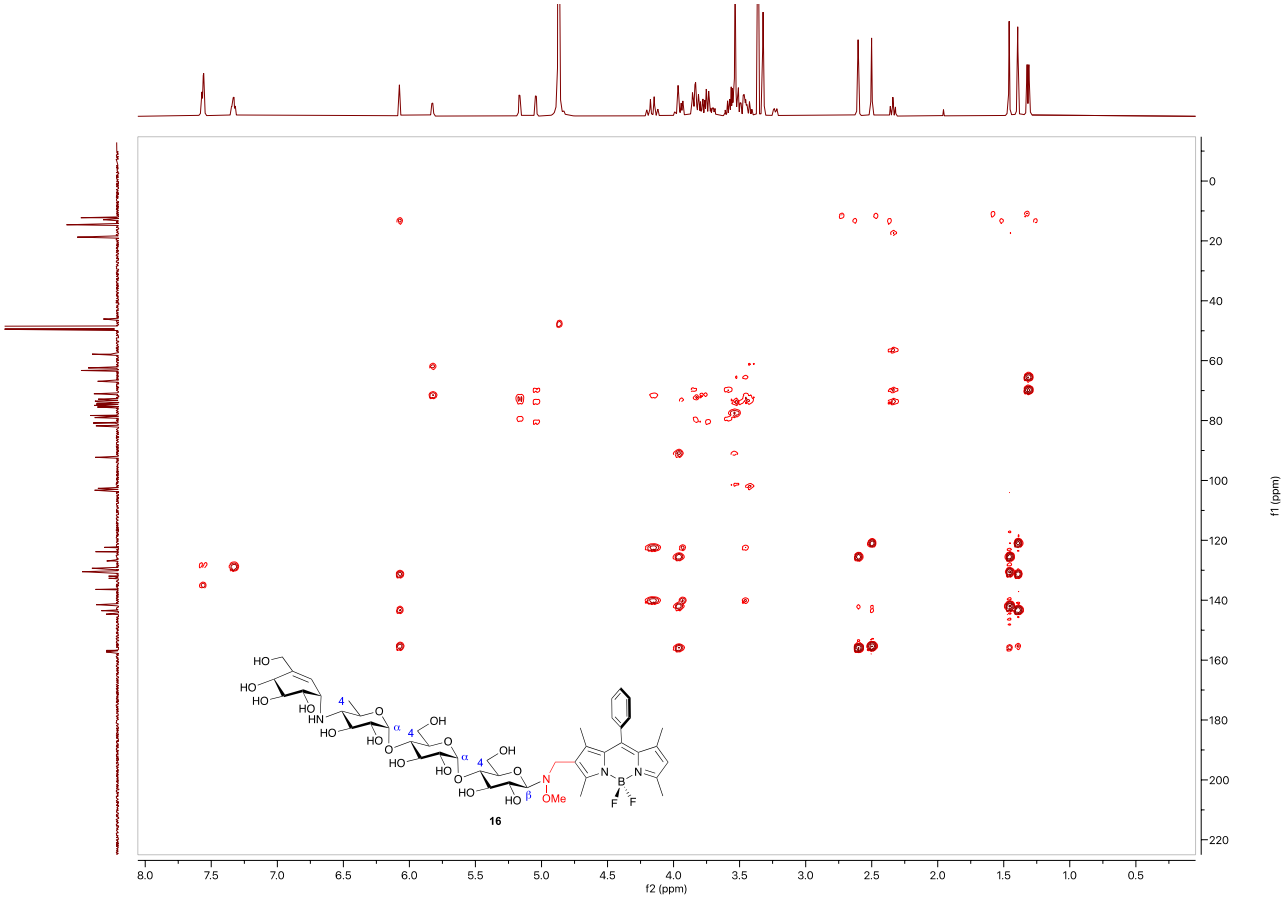


Fig S63. HMBC for **16**

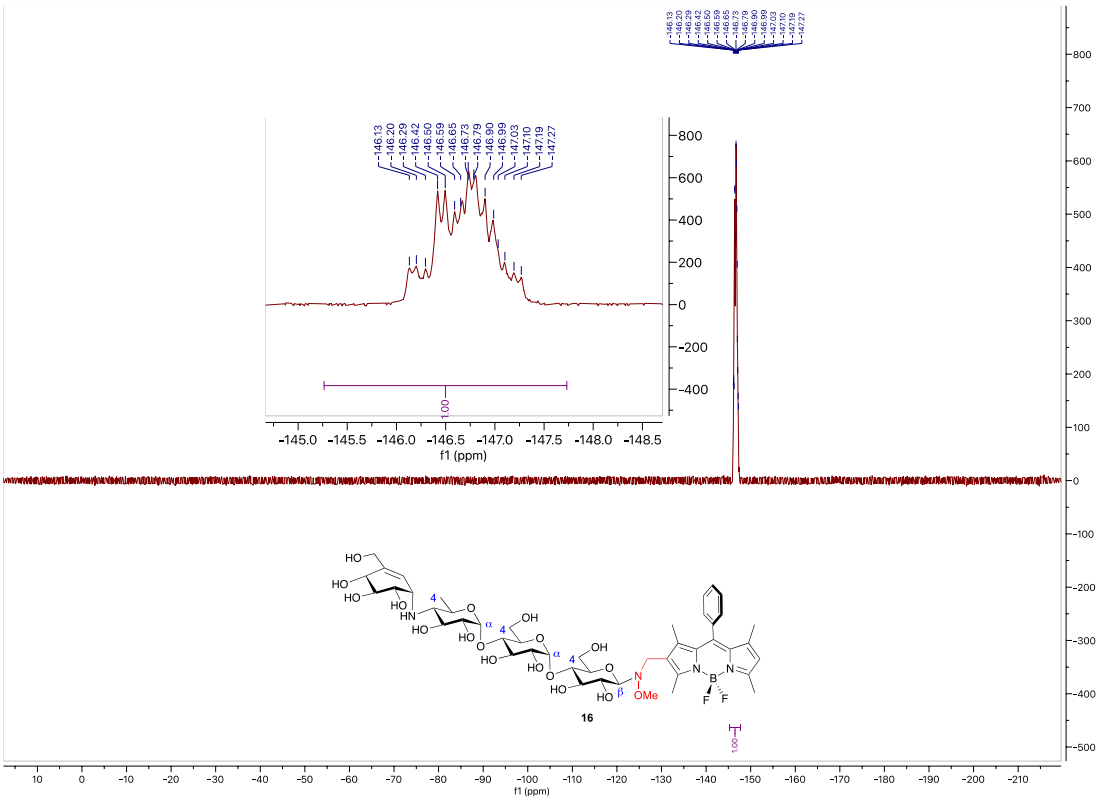


Fig S64 ^{19}F-NMR (376 MHz, CD_3OD) of **16**

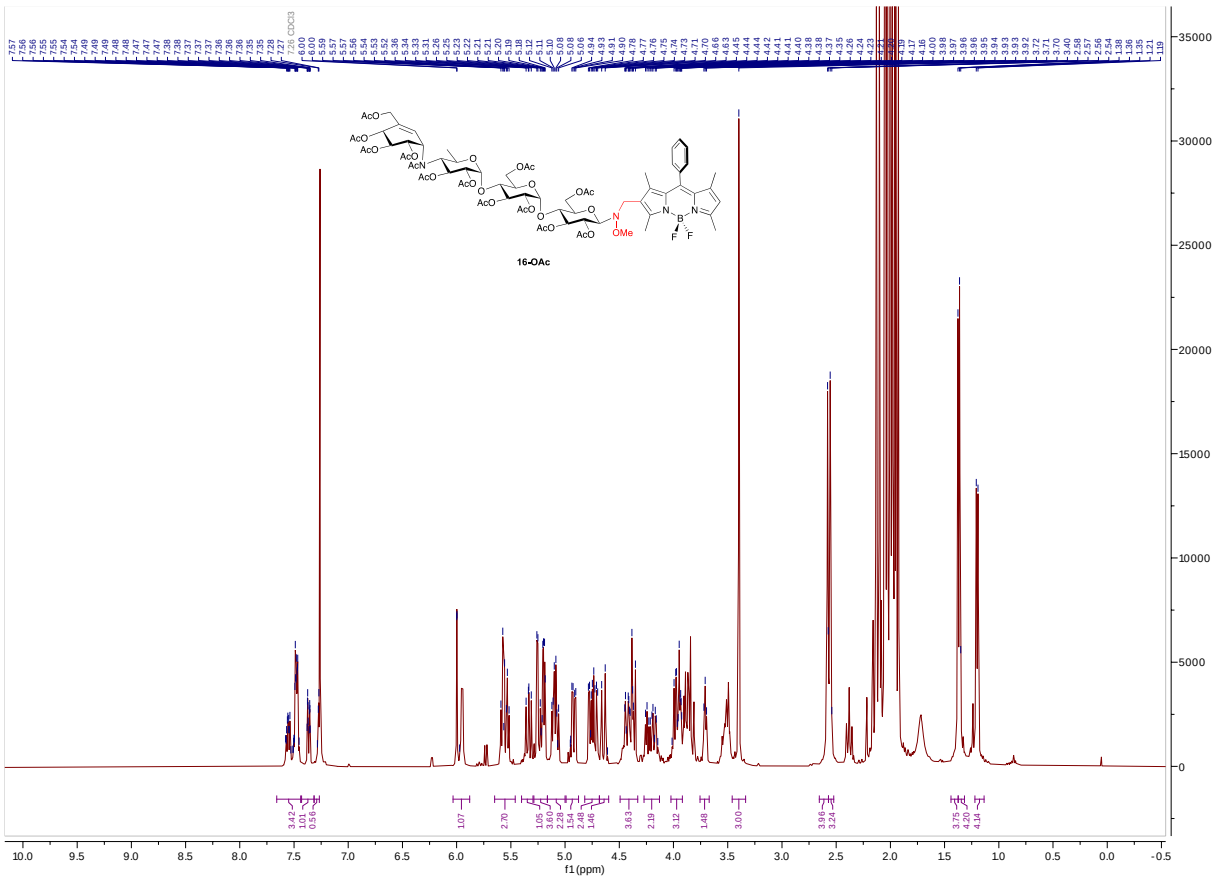


Fig S65. ^{1}H-NMR (500 MHz, $CDCl_3$) for **16-OAc**

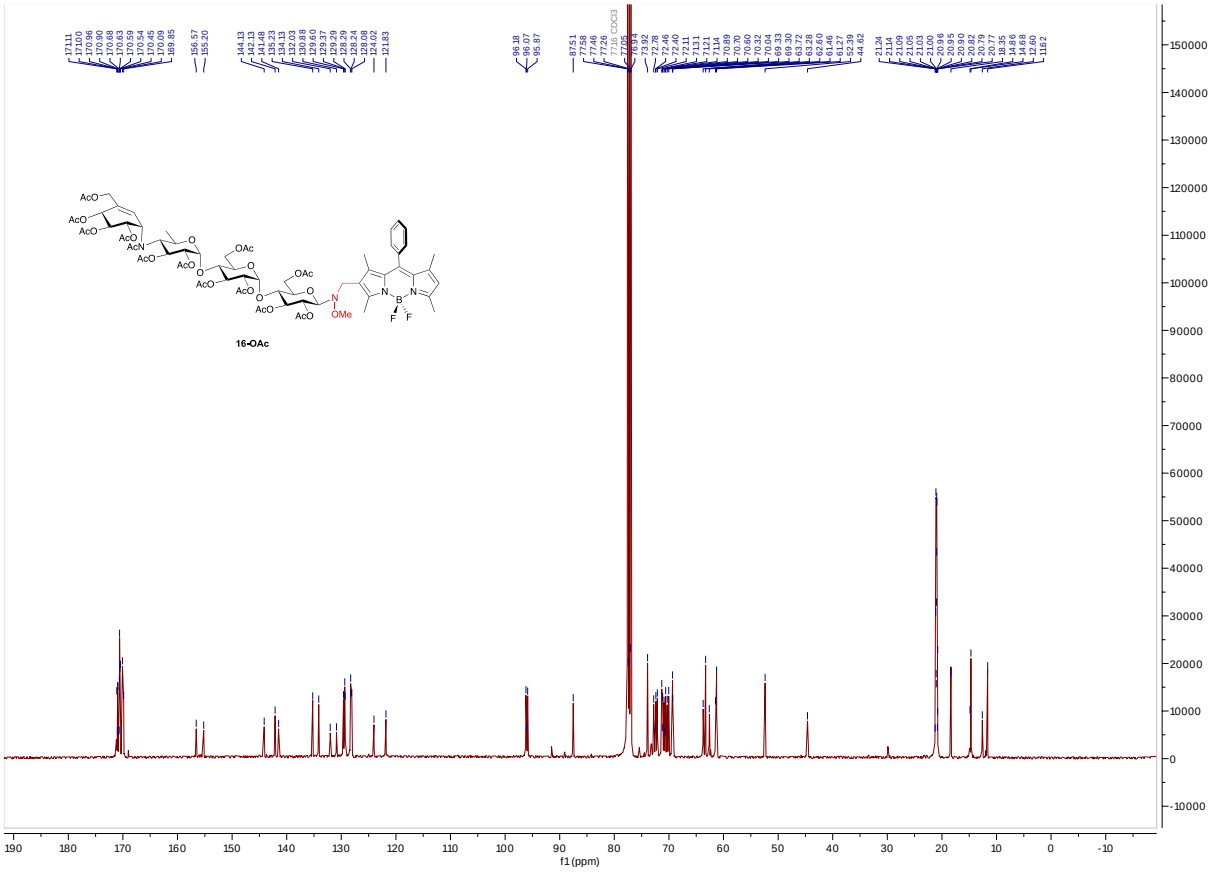


Fig S66. $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of **16-OAc**

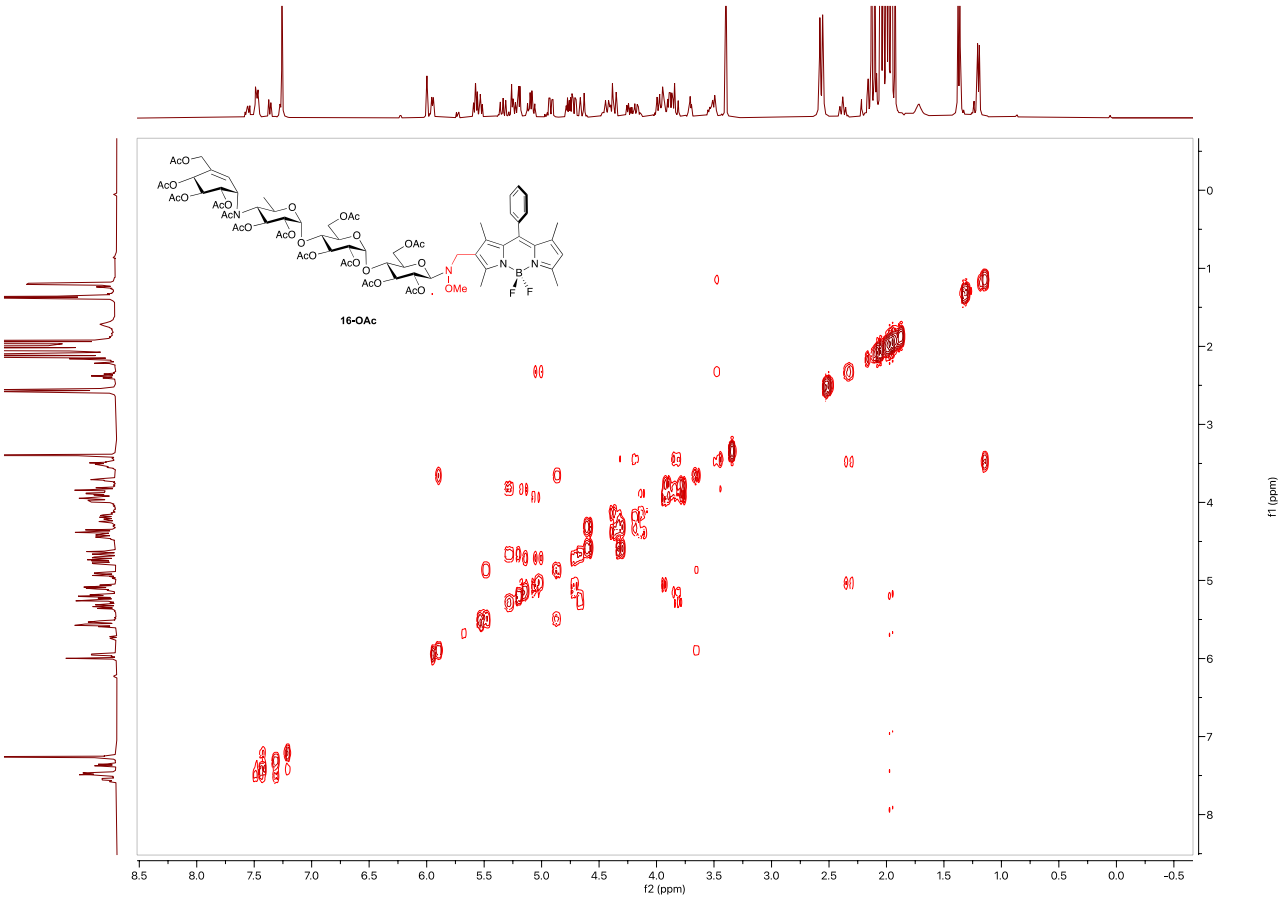


Fig S67. COSYof **16-OAc**

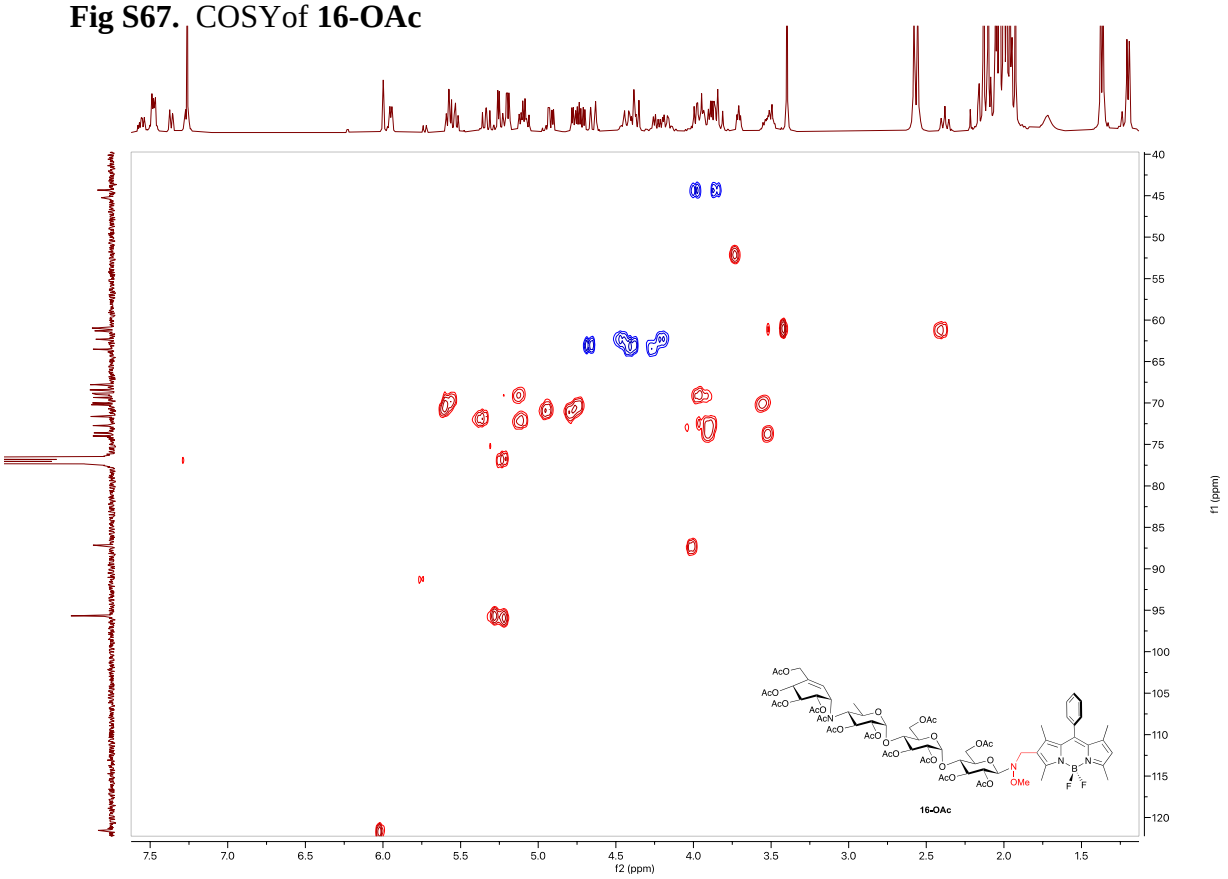


Fig S68. HSQC of **16-OAc**

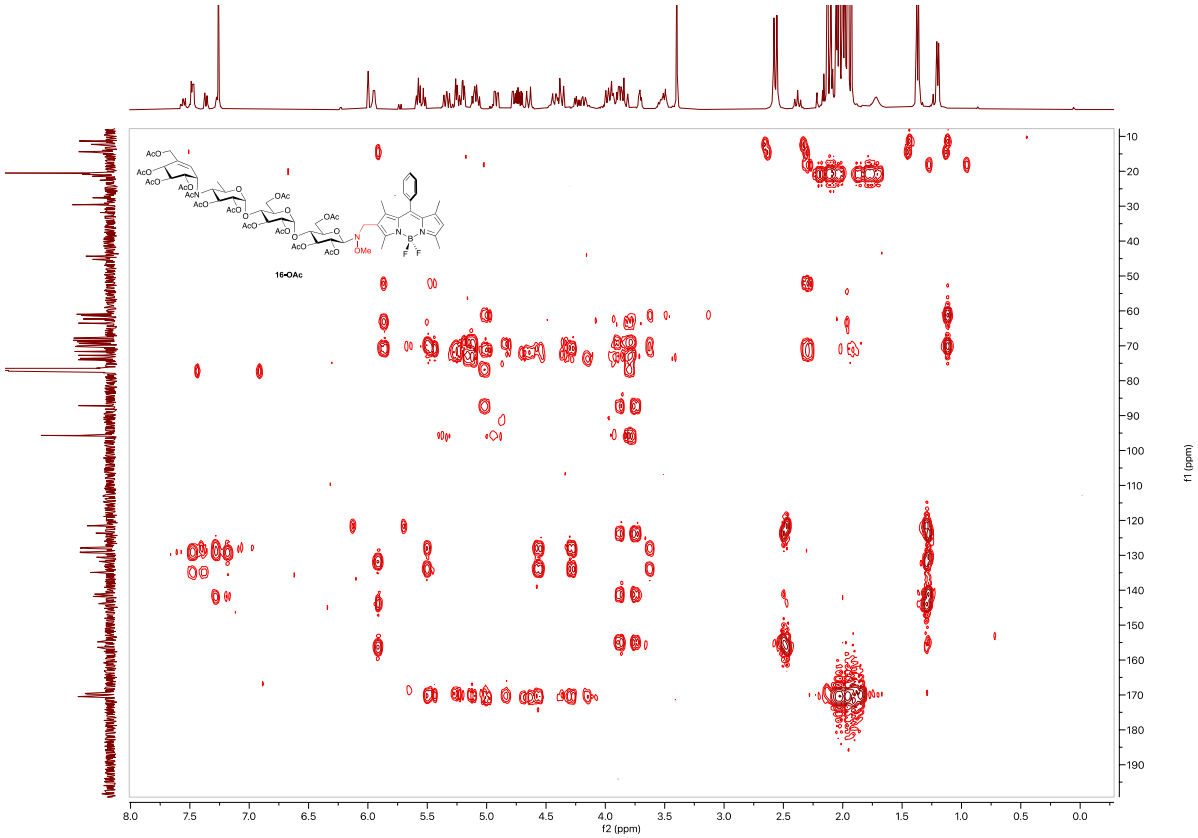
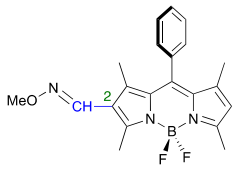


Fig S69. HMBC of **16-OAc**

5. Copies of HRMS spectra



9a

Qualitative Compound Report

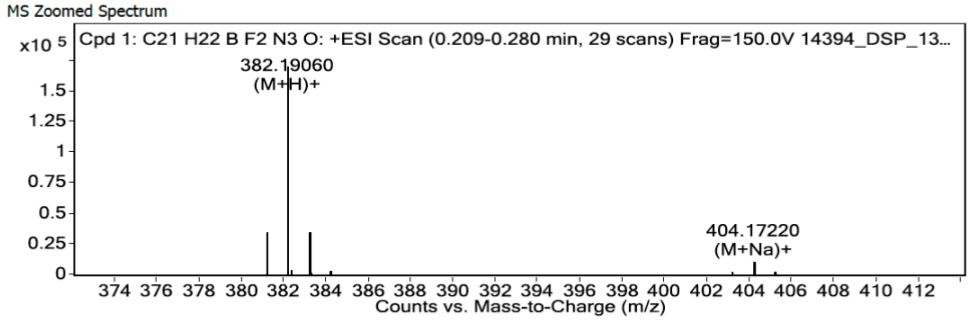
Data File	14394_DSP_130_A_01.d	**Sample Name**	DSP_130_A
Sample Type	Sample	**Position**	Vial 3
Instrument Name	Instrument 1	**User Name**	
Acq Method	ESI_ACN_75_pos.m	**IRM Calibration Status**	Some Ions Missed
DA Method	Defecto_modificado_CS.m	**Comment**	

Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C21 H22 B F2 N3 O	0.252	380.18657	169953	C21 H22 B F2 N3 O	380.18603	1.42

Compound Label	RT	Algorithm	Mass
Cpd 1: C21 H22 B F2 N3 O	0.252	Find By Formula	380.18657

MS Zoomed Spectrum

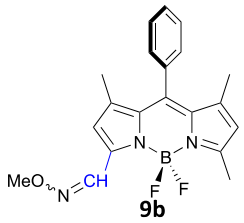


MS Spectrum Peak List

m/z	*Calc m/z*	Diff(ppm)	z	Abund	Formula	Ion
381.1934				35130		
381.25504				1367		
382.1906	382.19006	1.41		169953	C21 H23 B F2 N3 O	(M+H)+
382.34204				4733		
382.36793				1693		
383.19324	383.19297	0.7		35024	C21 H23 B F2 N3 O	(M+H)+
383.25711				1762		
384.19615	384.19586	0.74		4015	C21 H23 B F2 N3 O	(M+H)+
404.1722	404.172	0.49	1	10625	C21 H22 B F2 N3 Na O	(M+Na)+
405.17685	405.17492	4.76	1	2707	C21 H22 B F2 N3 Na O	(M+Na)+

--- End Of Report ---

Fig S70. HRMS of compound **9a**



9b

Qualitative Compound Report

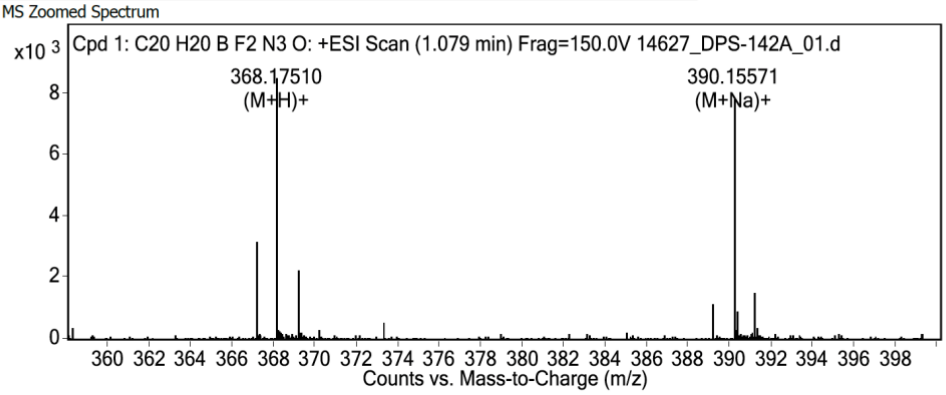
Data File	14627_DPS-142A_01.d	**Sample Name**	DPS-142A
Sample Type	Sample	**Position**	Vial 1
Instrument Name	Instrument 1	**User Name**	
Acq Method	ESI_ACN_75_pos.m	**IRM Calibration Status**	Success
DA Method	Defecto_modificado_CS.m	**Comment**	

Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C20 H20 B F2 N3 O	1.079	366.17048	8473	C20 H20 B F2 N3 O	366.17038	0.28

Compound Label	RT	Algorithm	Mass
Cpd 1: C20 H20 B F2 N3 O	1.079	Find By Formula	366.17048

MS Zoomed Spectrum

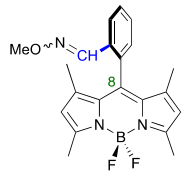


MS Spectrum Peak List

m/z	*Calc m/z*	Diff(ppm)	z	Abund	Formula	Ion
347.17113				2111		
348.16744				9404		
348.2197				473		
348.25948				347		
348.33841				316		
349.16935				2345		
368.1751	368.17439	1.92	1	8473	C20 H21 B F2 N3 O	(M+H)+
369.1752	369.1773	-5.67	1	2262	C20 H21 B F2 N3 O	(M+H)+
390.15571	390.15633	-1.61	1	7788	C20 H20 B F2 N3 Na O	(M+Na)+
391.16018	391.15924	2.4	1	1498	C20 H20 B F2 N3 Na O	(M+Na)+

--- End Of Report ---

Fig S71. HRMS of compound **9b**



9c

Qualitative Compound Report

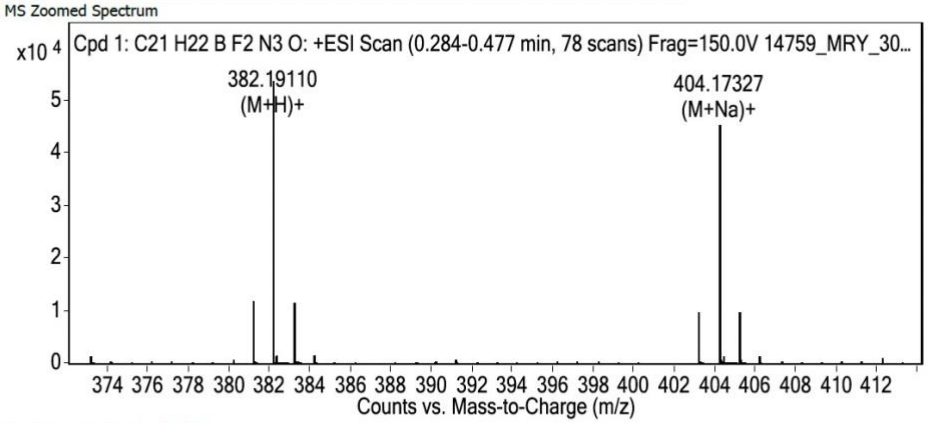
Data File	14759_MRY_306_01.d	**Sample Name**	MRY_306
Sample Type	Sample	**Position**	Vial 16
Instrument Name	Instrument 1	**User Name**	
Acq Method	ESI_ACN_75_pos.m	**IRM Calibration Status**	Success
DA Method	Defecto_modificado_CS.m	**Comment**	

Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C21 H22 B F2 N3 O	0.355	380.18716	53727	C21 H22 B F2 N3 O	380.18603	2.96

Compound Label	RT	Algorithm	Mass
Cpd 1: C21 H22 B F2 N3 O	0.355	Find By Formula	380.18716

MS Zoomed Spectrum

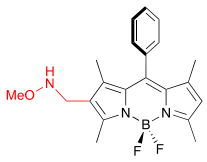


MS Spectrum Peak List

m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
361.18796				14521		
362.18496				66915		
362.35951				2112		
363.18754				14636		
364.19015				2195		
382.1911	382.19006	2.73	1	53727	C21 H23 B F2 N3 O	(M+H)+
383.1938	383.19297	2.15	1	11737	C21 H23 B F2 N3 O	(M+H)+
384.19647	384.19586	1.57	1	1605	C21 H23 B F2 N3 O	(M+H)+
404.17327	404.172	3.14	1	45310	C21 H22 B F2 N3 Na O	(M+Na)+
405.17579	405.17492	2.16	1	9929	C21 H22 B F2 N3 Na O	(M+Na)+

--- End Of Report ---

Fig S72. HRMS of compound **9c**



6a

Qualitative Compound Report

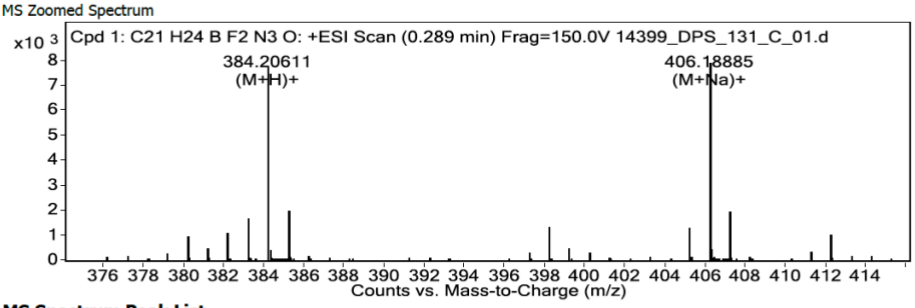
Data File	14399_DPS_131_C_01.d	**Sample Name**	DPS_131_C
Sample Type	Sample	**Position**	Vial 4
Instrument Name	Instrument 1	**User Name**	
Acq Method	ESI_ACN_75_pos.m	**IRM Calibration Status**	Some Ions Missed
DA Method	Defecto_modificado_CS.m	**Comment**	

Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C21 H24 B F2 N3 O	0.289	382.20247	7760	C21 H24 B F2 N3 O	382.20168	2.07

Compound Label	RT	Algorithm	Mass
Cpd 1: C21 H24 B F2 N3 O	0.289	Find By Formula	382.20247

MS Zoomed Spectrum

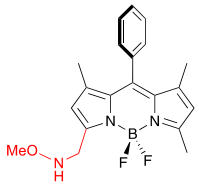


MS Spectrum Peak List

m/z	*Calc m/z*	Diff(ppm)	z	Abund	Formula	Ion
336.17203				32975		
337.16896				161740		
337.25446				3395		
337.33631				5758		
338.17122				29651		
339.17634				3417		
384.20611	384.20571	1.04	1	7760	C21 H25 B F2 N3 O	(M+H)+
385.20842	385.20863	-0.53	1	2007	C21 H25 B F2 N3 O	(M+H)+
406.18885	406.18765	2.94	1	7888	C21 H24 B F2 N3 Na O	(M+Na)+
407.19074	407.19057	0.42	1	1971	C21 H24 B F2 N3 Na O	(M+Na)+

--- End Of Report ---

Fig S73. HRMS of compound **6a**



6b

Qualitative Compound Report

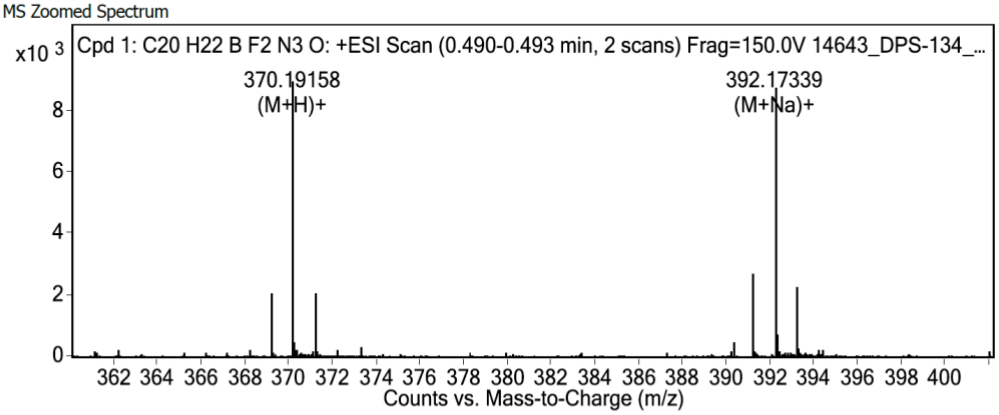
Data File	14643_DPS-134_A_01.d	**Sample Name**	DPS-134_A
Sample Type	Sample	**Position**	Vial 17
Instrument Name	Instrument 1	**User Name**	
Acq Method	ESI_ACN_75_pos.m	**IRM Calibration Status**	Success
DA Method	Defecto_modificado_CS.m	**Comment**	

Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C20 H22 B F2 N3 O	0.49	368.18749	8776	C20 H22 B F2 N3 O	368.18603	3.97

Compound Label	RT	Algorithm	Mass
Cpd 1: C20 H22 B F2 N3 O	0.49	Find By Formula	368.18749

MS Zoomed Spectrum

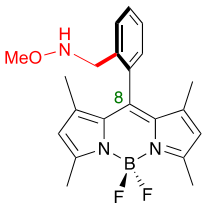


MS Spectrum Peak List

m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
318.15631				1640		
322.15673				16062		
323.15414				74107		
323.31912				2467		
324.15633				15032		
325.15972				1526		
370.19158	370.19004	4.16	1	8953	C20 H23 B F2 N3 O	(M+H)+
371.19404	371.19295	2.93	1	2067	C20 H23 B F2 N3 O	(M+H)+
392.17339	392.17198	3.59	1	8776	C20 H22 B F2 N3 Na O	(M+Na)+
393.17478	393.1749	-0.29	1	2292	C20 H22 B F2 N3 Na O	(M+Na)+

--- End Of Report ---

Fig S74. HRMS of compound **6b**



6c

Qualitative Compound Report

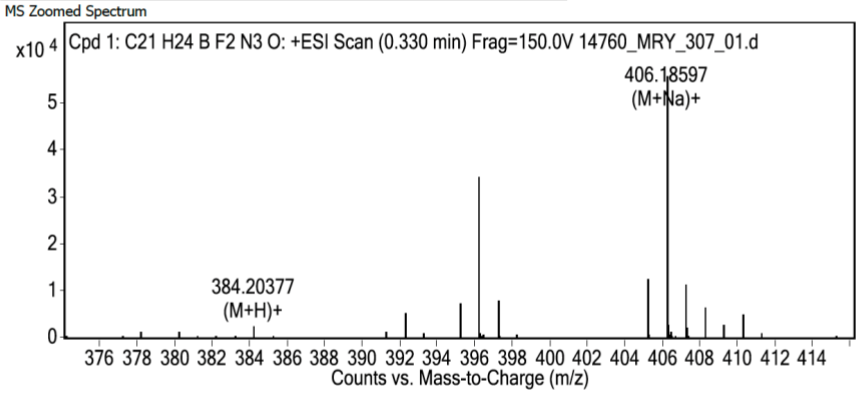
Data File	14760_MRY_307_01.d	**Sample Name**	MRY_307
Sample Type	Sample	**Position**	Vial 17
Instrument Name	Instrument 1	**User Name**	
Acq Method	ESI_ACN_75_pos.m	**IRM Calibration Status**	Some Ions Missed
DA Method	Defecto_modificado_CS.m	**Comment**	

Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C21 H24 B F2 N3 O	0.33	382.2	55772	C21 H24 B F2 N3 O	382.20168	-4.4

Compound Label	RT	Algorithm	Mass
Cpd 1: C21 H24 B F2 N3 O	0.33	Find By Formula	382.2

MS Zoomed Spectrum

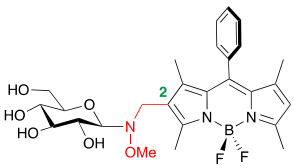


MS Spectrum Peak List

m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
363.20082				71566		
364.19804				338839		
364.30695				7228		
364.3725				16234		
364.44972				4827		
365.20034				79705		
366.20302				8451		
384.20377	384.20571	-5.05	1	2667	C21 H25 B F2 N3 O	(M+H)+
406.18597	406.18765	-4.14	1	55772	C21 H24 B F2 N3 Na O	(M+Na)+
407.18877	407.19057	-4.41	1	11614	C21 H24 B F2 N3 Na O	(M+Na)+

--- End Of Report ---

Fig S75. HRMS of compound **6c**



10a

Qualitative Compound Report

Data File	338_DPS-188A_01.d	**Sample Name**	DPS-188A
Sample Type	Sample	**Position**	Vial 16
Instrument Name	Instrument 1	**User Name**	
Acq Method	ESI_ACN_75_pos_new.m	**Acquired Time**	3/12/2021 12:34:10 PM (UTC+01:00)
IRM Calibration Status	Success	**DA Method**	Defecto_modificado.m
Comment			

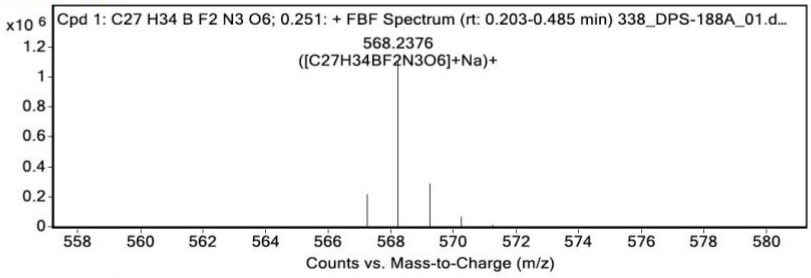
Sample Group		**Info.**	
User	DIEGO POZAS	**Stream Name**	LC 1
Acquisition Time (Local)	3/12/2021 12:34:10 PM (UTC+01:00)	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.08.00 (B8058.3 SP1)
QTOF Driver Version	8.00.00	**QTOF Firmware Version**	2.712
Tune Mass Range Max.	3200		

Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)	Hits (DB)
Cpd 1: C27 H34 B F2 N3 O6; 0.251	0.251	544.2524	1104030	C27 H34 B F2 N3 O6	544.2545	-3.83	1

Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C27 H34 B F2 N3 O6; 0.251	568.2376	0.251	Find by Formula	544.2524

MS Zoomed Spectrum

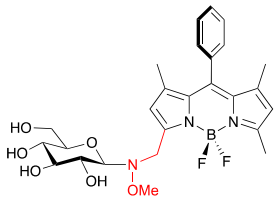


MS Spectrum Peak List

m/z	z	Abund	Formula	Ion
567.2423	1	212627.56	C27H34BF2N3O6	(M+Na)+
568.2376	1	1104029.5	C27H34BF2N3O6	(M+Na)+
569.2437	1	285883.94	C27H34BF2N3O6	(M+Na)+
570.2472	1	63614.71	C27H34BF2N3O6	(M+Na)+
571.2524	1	10027.86	C27H34BF2N3O6	(M+Na)+

MS Zoomed Spectrum

Fig S76. HRMS of compound **10a**



10b

Qualitative Compound Report

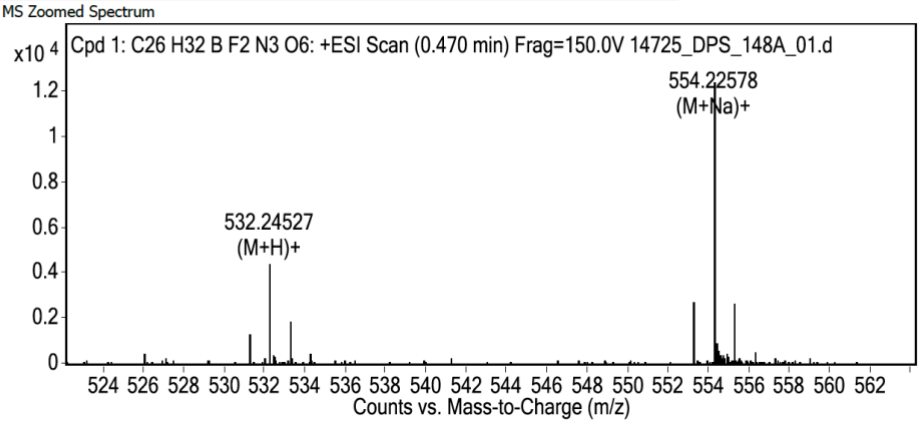
Data File	14725_DPS_148A_01.d	**Sample Name**	DPS_148A
Sample Type	Sample	**Position**	Vial 6
Instrument Name	Instrument 1	**User Name**	
Acq Method	ESI_ACN_75_pos.m	**IRM Calibration Status**	Success
DA Method	Defecto_modificado_CS.m	**Comment**	

Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C26 H32 B F2 N3 O6	0.47	530.2398	4442	C26 H32 B F2 N3 O6	530.23885	1.79

Compound Label	RT	Algorithm	Mass
Cpd 1: C26 H32 B F2 N3 O6	0.47	Find By Formula	530.2398

MS Zoomed Spectrum

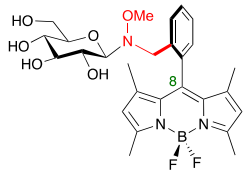


MS Spectrum Peak List

m/z	*Calc m/z*	Diff(ppm)	z	Abund	Formula	Ion
118.08463				646		
119.0834				573		
121.05103				16499		
121.11125				1125		
121.15353				886		
122.05109				1109		
532.24527	532.24297	4.33	1	4442	C26 H33 B F2 N3 O6	(M+H)+
533.2471	533.24594	2.17	1	1857	C26 H33 B F2 N3 O6	(M+H)+
554.22578	554.22491	1.57	1	12402	C26 H32 B F2 N3 Na O6	(M+Na)+
555.23024	555.22789	4.24	1	2680	C26 H32 B F2 N3 Na O6	(M+Na)+

--- End Of Report ---

Fig S77. HRMS of compound **10b**



10c

Custom Workflow Report

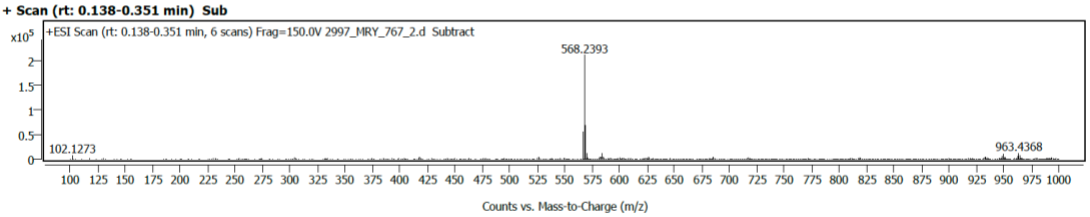
Agilent | Trusted Answers

Sample Information

Name	MRY_767_2	**Data File Path**	D:\Projects\MASAS EXACTAS_2024\Data\2024\Mar\2997_MRY_767_2.d
Sample ID		**Acq. Time (Local)**	3/14/2024 1:29:22 PM (UTC+01:00)
Instrument	UPLC-QTOF	**Method Path (Acq)**	D:\Projects\MASAS EXACTAS_2024\Methods\FIA_masa exacta_MSMS.m
MS Type	QTOF	**Version (Acq SW)**	6200 series TOF/6500 series Q-TOF (11.0.221.1)
Inj. Vol. (ul)	0.2	**IRM Status**	All ions missed
Position	P1-D1	**Method Path (DA)**	D:\Projects\MASAS EXACTAS_2023\Methods\DA_MSMS_MPS_jun.m
Plate Pos.		**Target Source Path**	
Operator	SYSTEM (SYSTEM)	**Result Summary**	1 qualified (1 targets)

Sample Spectra

+ Scan (rt: 0.138-0.351 min) Sub



Spectrum Peaks

m/z	Z	Abund	Abund %
102.1273		7734	3.65
567.2425		55595	26.22
568.2393	1	212033	100.00
569.2420	1	68943	32.52
570.2450	1	12260	5.78
584.2126		12010	5.66
948.4238		5803	2.74
949.4200		9549	4.50
963.4368	1	11472	5.41
964.4386	1	6687	3.15

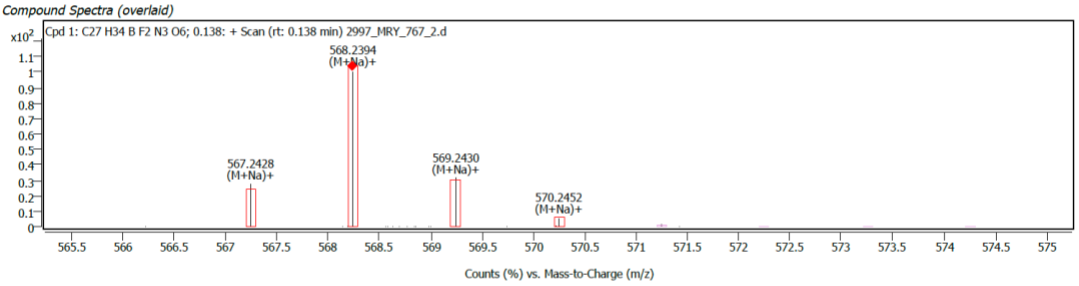
Compound Details

Cpd. 1: C27 H34 B F2 N3 O6

Compound ID Table

Name	Formula	Species	RT	RT Diff	Mass	Mass (Tgt)	ID Source	Score	Diff (ppm)	Score (MFG)
	C27 H34 B F2 N3 O6	(M+Na)+	0.138		544.2535	544.2545	FBF	95.13	-1.87	

Compound Spectra (overlaid)

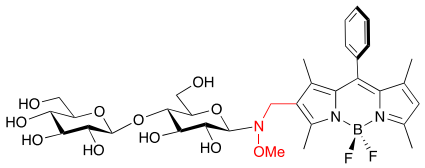


Spectrum Peaks

m/z	Z	m/z (Calc)	Diff (ppm)	Height %	Height % (Calc)	Ion Species	Formula
567.2428	1	567.2437	-1.65	27.72	23.07	(M+Na)+	C27H34BF2N3O6
568.2394	1	568.2406	-2.08	100.00	100.00	(M+Na)+	C27H34BF2N3O6
569.2430	1	569.2436	-1.01	31.62	30.06	(M+Na)+	C27H34BF2N3O6
570.2452	1	570.2462	-1.80	5.21	5.63	(M+Na)+	C27H34BF2N3O6

MassHunter Qual 10.0
(End of Report)

Fig S78. HRMS of compound **10c**



12

Qualitative Compound Report

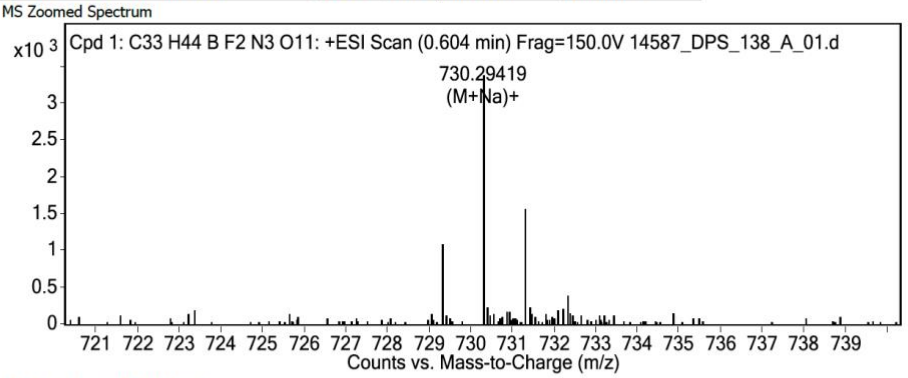
Data File	14587_DPS_138_A_01.d	**Sample Name**	DPS_138_A
Sample Type	Sample	**Position**	Vial 14
Instrument Name	Instrument 1	**User Name**	
Acq Method	ESI_ACN_75_pos.m	**IRM Calibration Status**	Success
DA Method	Defecto_modificado_CS.m	**Comment**	

Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C33 H44 B F2 N3 O11	0.604	706.30784	3383	C33 H44 B F2 N3 O11	706.30733	0.73

Compound Label	RT	Algorithm	Mass
Cpd 1: C33 H44 B F2 N3 O11	0.604	Find By Formula	706.30784

MS Zoomed Spectrum

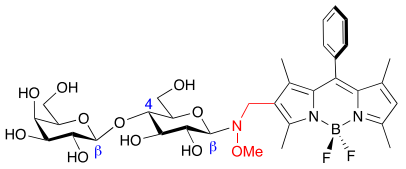


MS Spectrum Peak List

m/z	*Calc m/z*	Diff(ppm)	z	Abund	Formula	Ion
158.9631				10668		
159.01657				393		
159.07943				386		
159.1902				161		
159.96781				243		
162.90782				222		
163.13597				171		
730.29419	730.2935	0.93	1	3383	C33 H44 B F2 N3 Na O11	(M+Na)+
731.2954	731.2965	-1.5	1	1574	C33 H44 B F2 N3 Na O11	(M+Na)+
732.29765	732.29909	-1.96	1	404	C33 H44 B F2 N3 Na O11	(M+Na)+

--- End Of Report ---

Fig S79. HRMS of compound **12**



13

Qualitative Compound Report

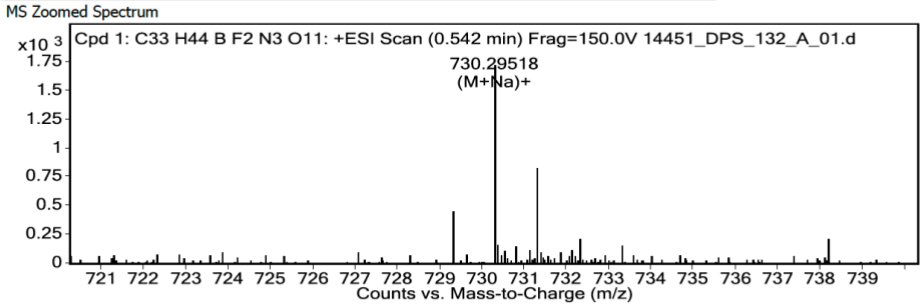
Data File	14451_DPS_132_A_01.d	**Sample Name**	DPS_132_A
Sample Type	Sample	**Position**	Vial 2
Instrument Name	Instrument 1	**User Name**	
Acq Method	ESI_ACN_75_pos.m	**IRM Calibration Status**	Success
DA Method	Defecto_modificado_CS.m	**Comment**	

Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C33 H44 B F2 N3 O11	0.542	706.30868	1720	C33 H44 B F2 N3 O11	706.30733	1.92

Compound Label	RT	Algorithm	Mass
Cpd 1: C33 H44 B F2 N3 O11	0.542	Find By Formula	706.30868

MS Zoomed Spectrum

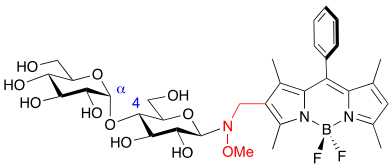


MS Spectrum Peak List

m/z	*Calc m/z*	Diff(ppm)	z	Abund	Formula	Ion
100.07583				2406		
100.1131				236		
101.07046				1643		
102.12783				9477		
102.17523				287		
102.21944				268		
102.24769				166		
103.13382				634		
103.95695				163		
730.29518	730.2935	2.29	1	1720	C33 H44 B F2 N3 Na O11	(M+Na)+
731.29504	731.2965	-1.99	1	830	C33 H44 B F2 N3 Na O11	(M+Na)+
732.29827	732.29909	-1.12	1	215	C33 H44 B F2 N3 Na O11	(M+Na)+

--- End Of Report ---

Fig S80. HRMS of compound **13**



14

Qualitative Compound Report

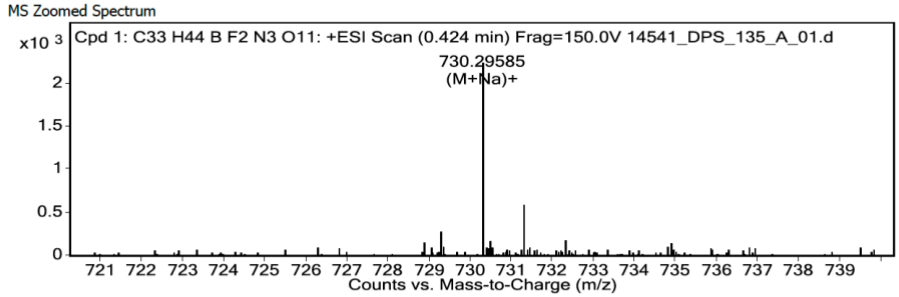
Data File	14541_DPS_135_A_01.d	**Sample Name**	DPS_135_A
Sample Type	Sample	**Position**	Vial 12
Instrument Name	Instrument 1	**User Name**	
Acq Method	ESI_ACN_75_pos.m	**IRM Calibration Status**	Success
DA Method	Defecto_modificado_CS.m	**Comment**	

Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C33 H44 B F2 N3 O11	0.424	706.30966	2238	C33 H44 B F2 N3 O11	706.30733	3.31

Compound Label	RT	Algorithm	Mass
Cpd 1: C33 H44 B F2 N3 O11	0.424	Find By Formula	706.30966

MS Zoomed Spectrum

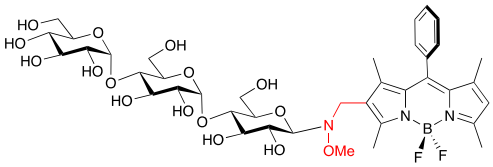


MS Spectrum Peak List

m/z	*Calc m/z*	Diff(ppm)	z	Abund	Formula	Ion
98.09916				204		
100.07629				1890		
101.07103				1064		
102.12784				15080		
102.17205				516		
102.22228				539		
103.1331				1090		
104.10845				202		
730.29585	730.2935	3.22	1	2238	C33 H44 B F2 N3 Na O11	(M+Na)+
731.29835	731.2965	2.53	1	596	C33 H44 B F2 N3 Na O11	(M+Na)+

--- End Of Report ---

Fig S81. HRMS of compound **14**



15

Qualitative Compound Report

Data File	74_DPS-166A_01.d	**Sample Name**	DPS-166A
Sample Type	Sample	**Position**	Vial 10
Instrument Name	Instrument 1	**User Name**	
Acq Method	ESI_ACN_75_pos_new.m	**Acquired Time**	12/17/2020 11:37:15 AM (UTC+01:00)
IRM Calibration Status	Success	**DA Method**	Defecto_modificado.m
Comment			

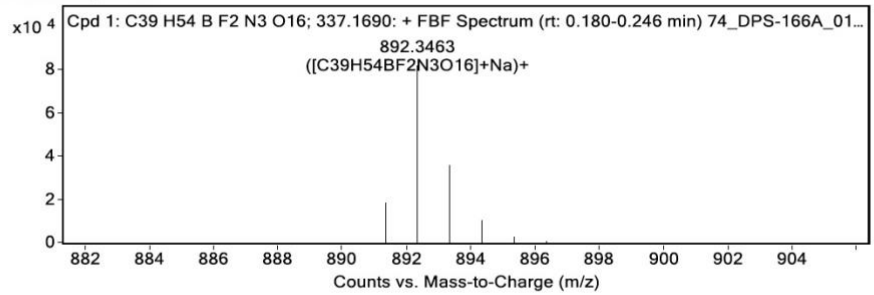
Sample Group		**Info.**	
User	DIEGO POZAS	**Stream Name**	LC 1
Acquisition Time (Local)	12/17/2020 11:37:15 AM (UTC+01:00)	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.08.00 (B8058.3 SP1)
QTOF Driver Version	8.00.00	**QTOF Firmware Version**	2.712
Tune Mass Range Max.	1700		

Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)	Hits (DB)
Cpd 1: C39 H54 B F2 N3 O16; 337.1690	0.204	868.3604	81890	C39 H54 B F2 N3 O16	868.3602	0.33	1

Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C39 H54 B F2 N3 O16; 337.1690	892.3463	0.204	Find by Formula	868.3604

MS Zoomed Spectrum

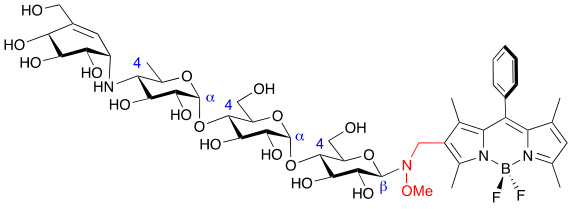


MS Spectrum Peak List

m/z	z	Abund	Formula	Ion
891.3499	1	18393.52	C39H54BF2N3O16	(M+Na)+
892.3463	1	81890.46	C39H54BF2N3O16	(M+Na)+
893.3494	1	35717.1	C39H54BF2N3O16	(M+Na)+
894.3533	1	10226.35	C39H54BF2N3O16	(M+Na)+
895.3635	1	2691.77	C39H54BF2N3O16	(M+Na)+
896.3622	1	546.8	C39H54BF2N3O16	(M+Na)+

MS Zoomed Spectrum

Fig S82. HRMS of compound **15**



16

Qualitative Compound Report

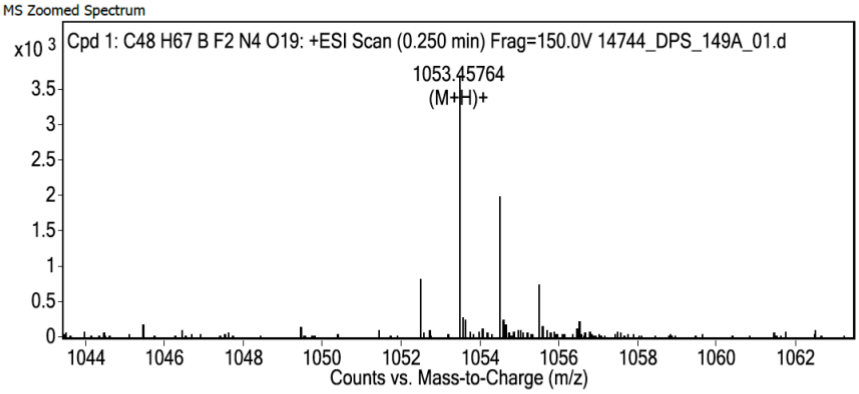
Data File	14744_DPS_149A_01.d	**Sample Name**	DPS_149A
Sample Type	Sample	**Position**	Vial 1
Instrument Name	Instrument 1	**User Name**	
Acq Method	ESI_ACN_75_pos.m	**IRM Calibration Status**	Success
DA Method	Defecto_modificado_CS.m	**Comment**	

Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C48 H67 B F2 N4 O19	0.25	1051.45356	3691	C48 H67 B F2 N4 O19	1051.44969	3.67

Compound Label	RT	Algorithm	Mass
Cpd 1: C48 H67 B F2 N4 O19	0.25	Find By Formula	1051.45356

MS Zoomed Spectrum



MS Spectrum Peak List

m/z	*Calc m/z*	Diff(ppm)	z	Abund	Formula	Ion
1010.44915				10192		
1011.4473				50705		
1011.54057				2682		
1011.60956				1735		
1012.45106				26105		
1012.53788				2176		
1013.4542				6838		
1014.45274				2435		
1053.45764	1053.45416	3.3	1	3691	C48 H68 B F2 N4 O19	(M+H)+
1054.46352	1054.45708	6.11	1	1999	C48 H68 B F2 N4 O19	(M+H)+

--- End Of Report ---

Fig S83. HRMS of compound **16**

6. X-Ray diffraction

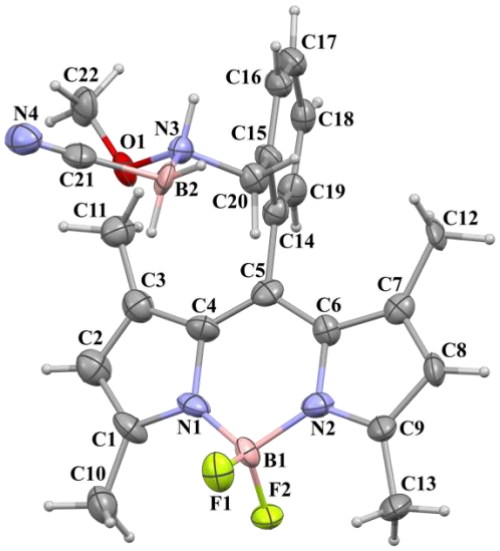


Figure S84. The molecular structure of compound **6d** showing the atom-labelling scheme and displacement ellipsoids at the 50% probability level for non-H atoms and fixed-size spheres of radius 0.1angstrom for hydrogen atoms.

7. Photophysical data

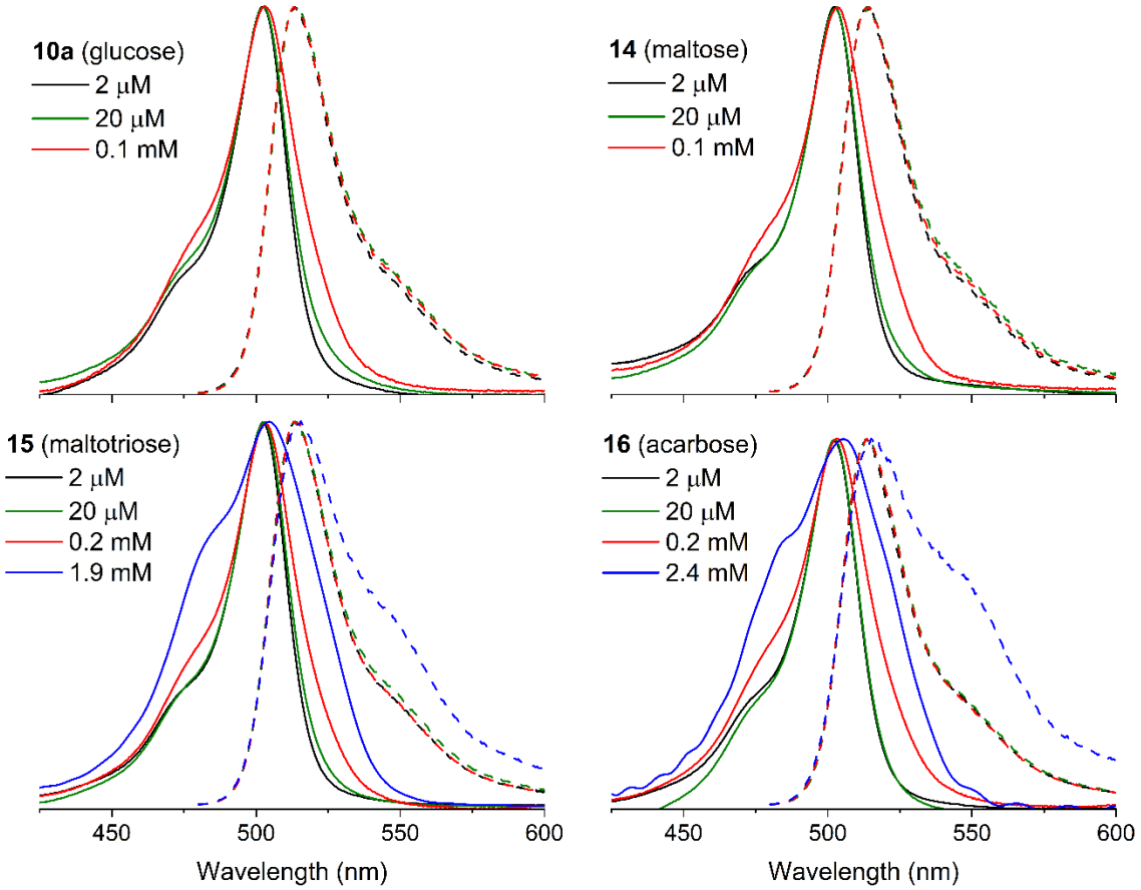


Figure S85. Normalized absorption (solid line) and fluorescence (dashed line) spectra of BODIPY glycoconjugates with different number of carbohydrate units respectively, as a function of the dye concentration in water using optically matched solutions.

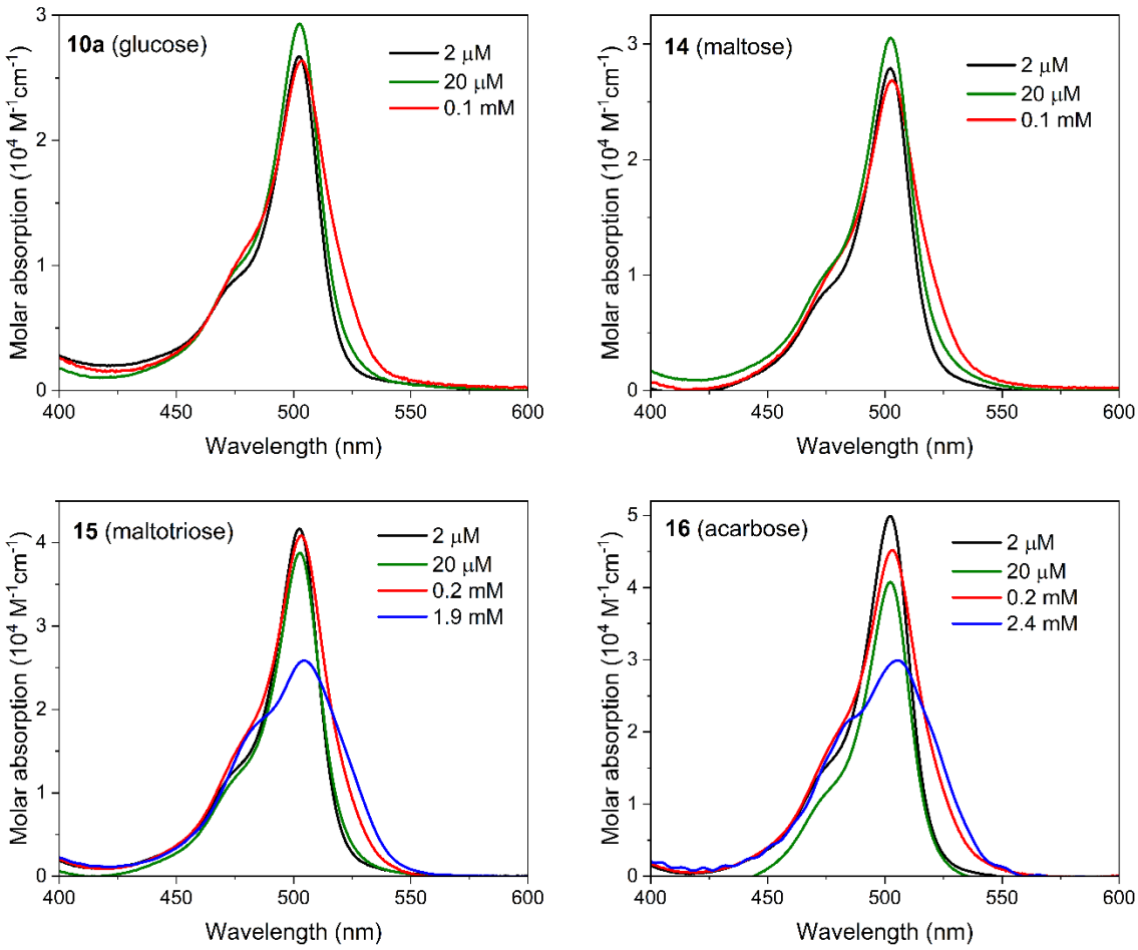


Figure S86. Absorption spectra (scaled by their respective molar absorption coefficients) of the BODIPY glycoconjugates at different dye concentrations in pure water.

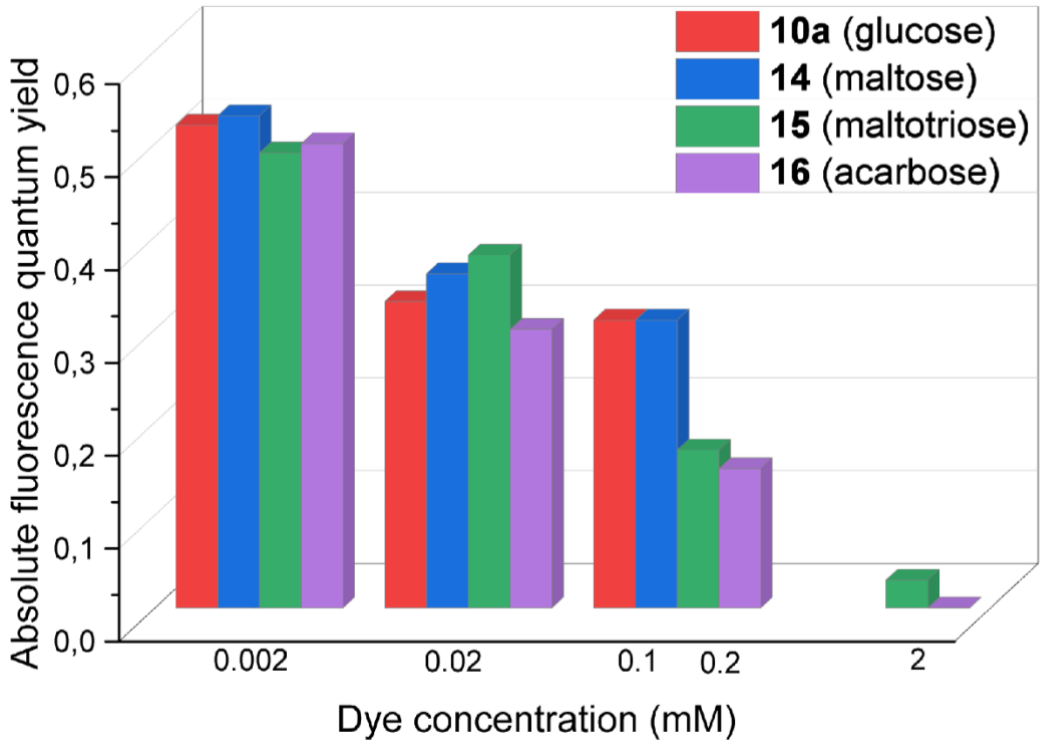


Figure S87. Evolution of the absolute fluorescence quantum yield with the dye concentration in pure water.

8. Full-size versions of confocal images

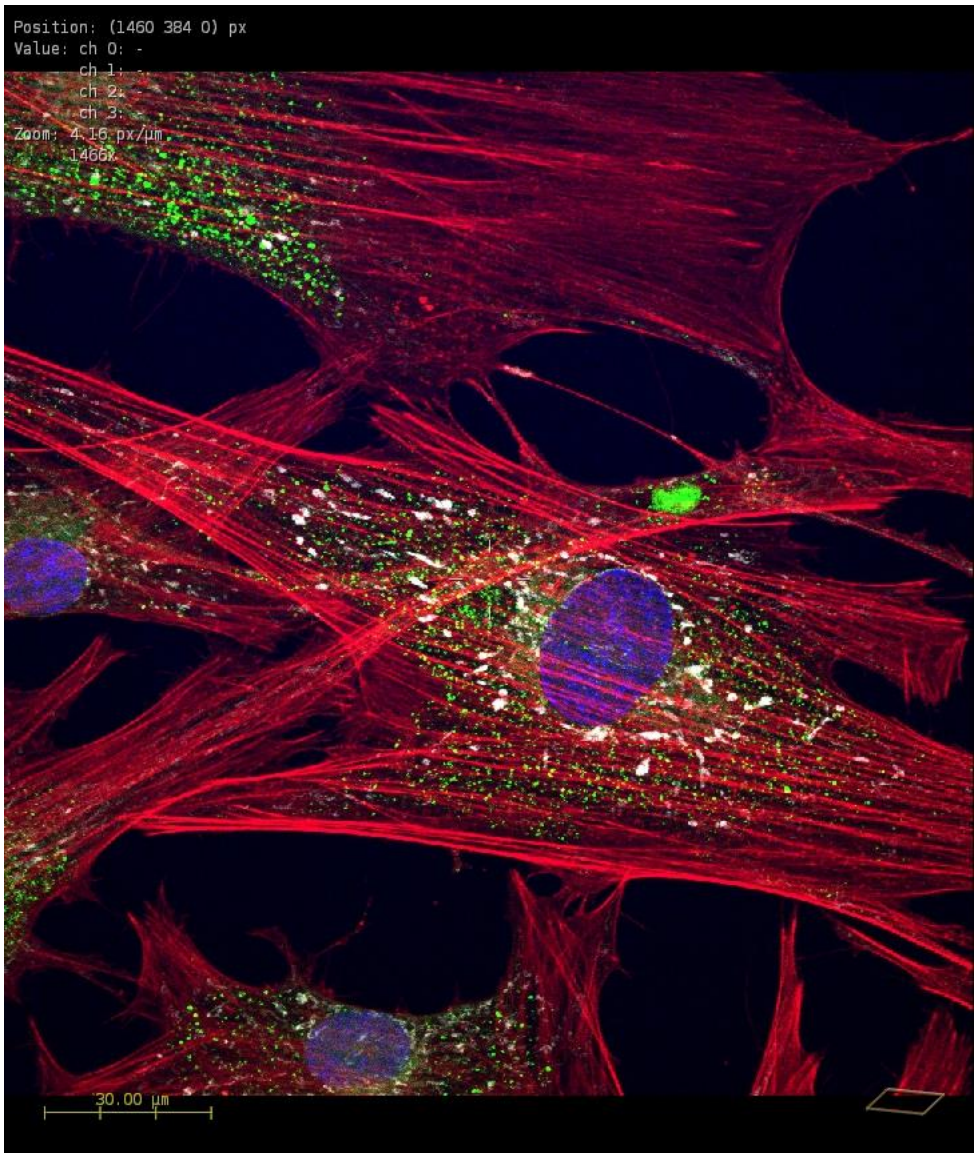


Figure S88. Confocal imaging of mitochondria (light blue), nucleus (blue), actin (red) stain and BODIPY internalization (green). Scale bar: 30 µm

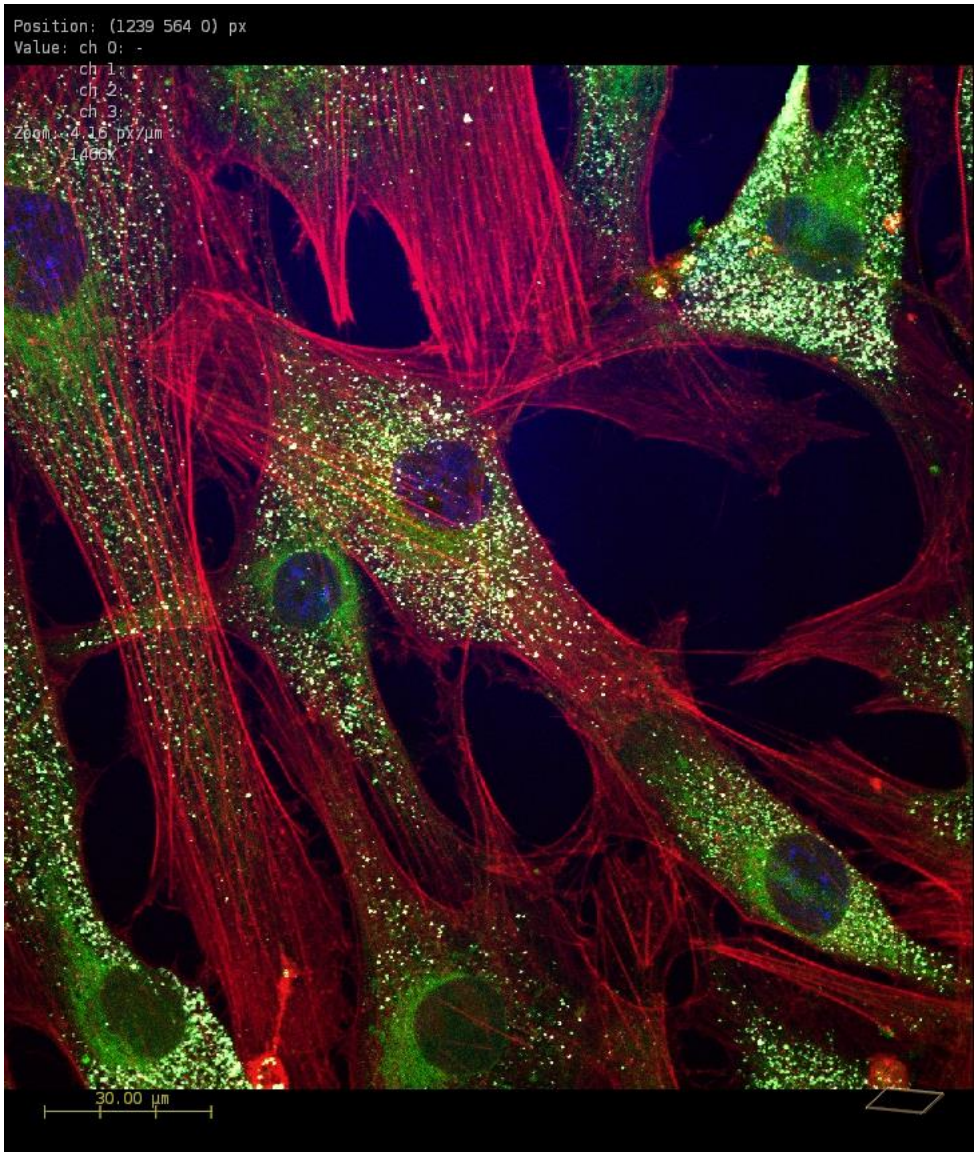


Figure S89. Confocal imaging of lysosomes (light blue), nucleus (blue), actin (red) stain and BODIPY internalization (green). Scale bar: 30 µm

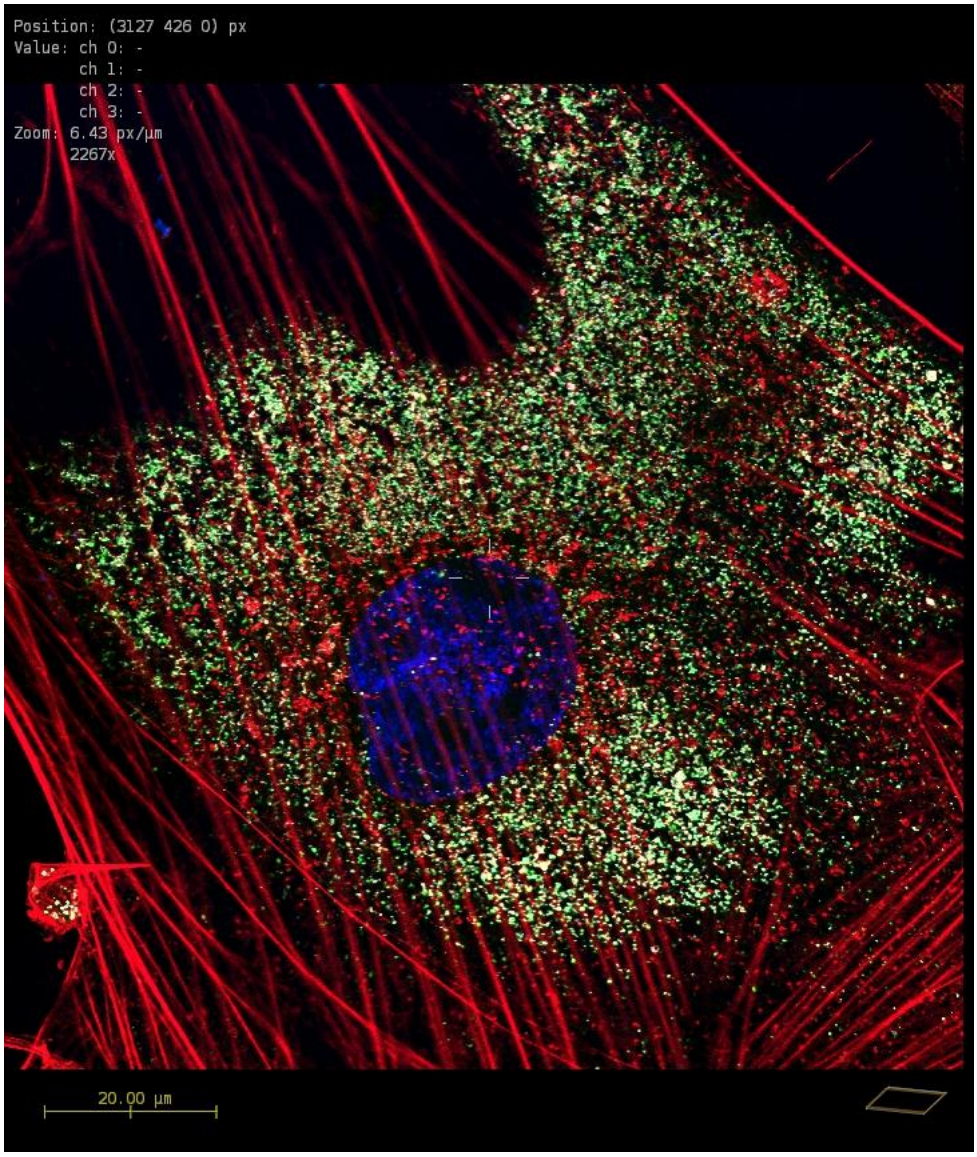


Figure S90. Lightning image of the lysosomes (red) and BODIPY (green). Scale bar: 20 µm