A Chan–Evans–Lam Approach to Trisubstituted Vinyl Ethers

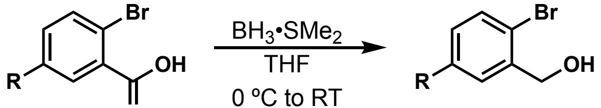
Supplementary Information

Index

General Methods

Unless otherwise stated, reactions were performed in flame- or oven-dried glassware equipped with rubber septa under a positive pressure of argon. Anhydrous dichloromethane (DCM) was dried by passage through activated alumina or obtained from a Sigma Sure/Seal™ bottle (≥ 99.8 % with 40–150 ppm amylene as stabilizer). Anhydrous toluene (PhMe) was dried by passage through activated alumina or obtained from a Sigma Sure/Seal™ bottle (99.8 %). Anhydrous *N,N*-dimethylformamide (DMF) was obtained from a Sigma Sure/Seal™ bottle. Tetrahydrofuran (THF) was distilled over sodium and benzophenone under a nitrogen atmosphere. Solvents and air-sensitive solutions were transferred via stainless steel cannula or via plastic syringe equipped with a stainless-steel needle. Analytical thin layer chromatography (TLC) was performed on MACHEREY-NAGEL pre-coated ALUGRAM® SILG/UV$_{254}$ TLC plates (0.20 mm silica gel 60 with 254 nm fluorescent indicator). TLC plates were visualized under UV light (254 nm) and developed by staining and heating with $KMnO_4$. Flash column chromatography was performed on silica gel (60 Å, 40-63 µm, Silicycle SiliaFlash® F60). NMR spectra were recorded at ambient temperature (298-300 K) on a Bruker AVANCE NEO 500 spectrometer equipped with a BBF probe or a Bruker AVANCE 300 spectrometer equipped with a 5mm PABBO BB-1H/D Z-GRD probe. ^{2}H{^{1}H} NMR spectra were recorded on a Bruker 360 BZH/52 spectrometer equipped with a 5mm Multinuclear Z3061/ 012 probe. ^{1}H chemical shifts (δ) are reported in parts-per-million (ppm) relative to tetramethylsilane and referenced to the solvent peak ($CDCl_3$, δ 7.26; $(CD_3)_2CO$, δ 2.05; $(CD_3)_2SO$, δ 2.50). NMR data is presented as follows: chemical shift, multiplicity (s = singlet, br = broad, d = doublet, dd = doublet of doublets, dq = doublet of quartets, ddd = doublet of doublet of doublets, ddt = doublet of doublet of triplets, dt = doublet of triplets, td = triplet of doublets, tt = triplet of triplets, tq = triplet of quartets, m = multiplet, app = apparent, qd = quartet of doublets, qq = quartet of quartets), coupling constants (*J*, reported in Hz), integration. All ^{13}C NMR spectra are proton-decoupled (^{13}C{^{1}H}). ^{13}C chemical shifts (δ) are reported in parts-per-million (ppm) relative to tetramethylsilane and referenced to the solvent peak ($CDCl_3$, δ 77.16; $(CD_3)_2CO$, δ 29.84; $(CD_3)_2SO$, δ 39.52). All ^{19}F NMR spectra are proton-decoupled (^{19}F{^{1}H}) and chemical shifts are reported as obtained. All ^{11}B NMR spectra are proton-decoupled (^{11}B{^{1}H}) and chemical shifts are reported as obtained. Infrared spectra were obtained using a Perkin-Elmer Spectrum Two ATR spectrometer. Wavenumbers are reported in cm^{-1}. Accurate masses were obtained by electrospray ionization high resolution mass spectrometry (HRMS) using a Thermo Scientific™ Exactive™ Plus Orbitrap Ultimate 3000 LC-MS system. Melting points were measured using a Gallenkamp melting point apparatus and are uncorrected.

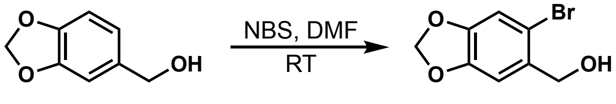
Synthesis of Benzyl Alcohol Substrates



SI-1 R = Me Quant. Yield (> 95 %)
SI-2 R = NO_2 Quant. Yield (> 95 %)

Synthesis of **SI-1**: To a stirred and chilled (0 °C) solution of 2-bromo-5-methylbenzoic acid (1.51 g, 7 mmol) in anhydrous THF (20 mL) was added 2.8 mL of BH_3•SMe_2 solution (5.0 M in Et_2O, 14 mmol, 2 equiv.) dropwise via syringe over 3 minutes. The reaction foamed for approximately 10 minutes. The reaction was left to gradually warm to room temperature over the course of 45 hours. The clear, pale yellow reaction mixture was cooled to 0 °C then slowly quenched with methanol (5 mL), which caused the reaction to foam. Once the foaming subsided, the reaction was opened to air, diluted with water (20 mL) and acidified to pH ≈ 0 with 1M HCl (~ 4 mL). The mixture was extracted with Et_2O (~ 50 mL). The aqueous phase was then back extracted with Et_2O (3 x ~ 12 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$ (1 x 40 mL), washed with brine (1 x 40 mL), dried over anhydrous Na_2SO_4, then concentrated to afford a clear, pale yellow oil that solidified under high vacuum to afford a white solid in high purity (1.41 g, Quantitative Yield). The product was used without further purification. **^{1}H NMR** (300.27 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.1 Hz, 1H), 7.28 (d, *J* = 1.7 Hz, 1H), 6.97 (dd, *J* = 8.1, 1.7 Hz, 1H), 4.70 (s, 2H), 2.32 (s, 3H), 2.09 (br s, 1H). **^{13}C NMR** (75.51 MHz, $CDCl_3$) δ 139.38, 137.77, 132.44, 130.02, 129.90, 119.31, 65.22, 21.08.

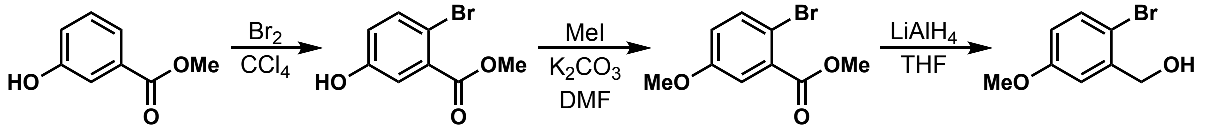
Synthesis of **SI-2**: **SI-2** was prepared using the same general procedure as **SI-1** using 1.72 g of 2-bromo-5-nitrobenzoic acid (7 mmol) and 2.7 mL of BH_3•SMe_2 solution (5.0 M in Et_2O, 13.5 mmol, 1.9 equiv.) to afford the title compound as a pale-yellow solid (1.66 g, Quantitative Yield). The product was used without further purification. **^{1}H NMR** (300.27 MHz, $CDCl_3$) δ 8.41 (d, *J* = 2.1 Hz, 1H), 8.00 (dd, *J* = 8.7, 2.4 Hz, 1H), 7.70 (d, *J* = 8.7 Hz, 1H), 4.82 (s, 2H), 2.33 (br s, 1H). **^{13}C NMR** (75.51 MHz, $CDCl_3$) δ 147.61, 142.12, 133.48, 128.89, 123.47, 122.98, 64.12.



SI-3, 54 % Yield

Synthesis of **SI-3**: Piperonyl alcohol (1.52 g, 10.0 mmol, 1 equiv.) was dissolved in anhydrous DMF (4 mL) and stirred to afford a clear, yellow solution. In a separate flask under argon, *N*-bromosuccinimide (1.78 g, 10.0 mmol, 1 equiv.) was dissolved in anhydrous DMF (4 mL) to afford a clear, yellow solution. The NBS solution was subsequently transferred via syringe to the piperonyl alcohol solution dropwise over 11.5 minutes. The reaction mixture turned clear, dark orange. The reaction was left to stir for 42.5 hours at room temperature. The reaction mixture was transferred to a separatory funnel and then aqueous LiCl solution (5 % w/v, 60 mL) and Et_2O (30 mL) were added. The phases were separated, and then the aqueous phase was back extracted with Et_2O (3 x 30 mL). The combined Et_2O phases were washed with brine (1 x 50 mL), dried over anhydrous Na_2SO_4, then concentrated to afford a crude brown solid. The product was purified by recrystallization from a mixture of hot EtOAc and hexanes. During the recrystallization, some insoluble particulate was removed via hot filtration through cotton into a clean Erlenmeyer flask.

Upon cooling to room temperature, and after sitting for approximately one hour, needles began to form. After sitting at room temperature overnight, the flask was briefly chilled at 0 °C. The product was isolated by vacuum filtration on a M glass frit and rinsed with cold hexanes. The title compound was obtained as beige needles (1.24 g, 54 % Yield) in excellent purity as determined by NMR analysis. **^{1}H NMR** (300.27 MHz, $CDCl_3$) δ 7.00 (s, 1H), 6.97 (s, 1H), 5.98 (s, 2H), 4.64 (s, 2H), 1.99 (br s, 1H). **^{13}C NMR** (75.51 MHz, $CDCl_3$) δ 147.91, 147.66, 133.20, 113.14, 112.81, 109.26, 101.91, 65.10.



SI-4, 58 % Yield **SI-5**, 98 % Yield **SI-6**, 94 % Yield

Synthesis of **SI-4**: **SI-4** was prepared using a procedure modified from Hertweck and co-workers.[1] In a 1000-mL round-bottom flask open to air, methyl 3-hydroxybenzoate (20.08 g, 132 mmol) was suspended in reagent grade CCl_4 (200 mL). Bromine (7 mL, 137 mmol, 1.04 equiv.) was then added in a single portion. The flask was equipped with a reflux condenser, which was fitted with a rubber septum. The septum was pierced with a needle connected to a long piece of rubber tubing to direct HBr fumes away from the apparatus and towards the back of the fume hood. The reaction was heated to 60 °C to give a clear, dark reddish solution. HBr evolution persisted for one hour. The reaction was then left to stir at 60 °C for an additional 16.5 hours. The reaction was removed from heating, and then concentrated to afford a crude pale orange solid. Recrystallization from hot hexanes and minimal EtOAc afforded **SI-4** as white crystals (12.5 g). Upon recovery of the mother liquor, an additional crop of product was obtained (5.15 g) to afford a total of 17.65 g (58 % Yield). **^{1}H NMR** (300.27 MHz, $CDCl_3$) δ 7.50 (d, J = 8.7 Hz, 1H), 7.30 (d, J = 3.1 Hz, 1H), 6.85 (dd, J = 8.7, 3.1 Hz, 1H), 5.39 (br s, 1H), 3.93 (s, 3H). **^{13}C NMR** (75.51 MHz, $CDCl_3$) δ 166.77, 154.91, 135.50, 132.83, 120.38, 118.45, 112.07, 52.80.

Synthesis of **SI-5**: A dry 250-mL round-bottom flask was charged with **SI-4** (4.98 g, 21.6 mmol), powdered K_2CO_3 (4.51 g, 32.6 mmol, 1.5 equiv.), and a magnetic stir bead. Under argon, anhydrous DMF (50 mL) was added by syringe to afford a yellow suspension, which was cooled to 0 °C and stirred vigorously. Iodomethane (1.5 mL, 24.1 mmol, 1.1 equiv.) was then added dropwise at 0 °C. The reaction was left to gradually warm to room temperature over 18 hours to afford an off-white creamy mixture. The reaction was quenched at room temperature by the addition of aqueous LiCl solution (5 % w/v; 140 mL) followed by the addition of Et_2O (200 mL). The two phases were separated, and the aqueous phase was subsequently extracted with Et_2O (2 x 70 mL). The combined organic phases were washed with brine (2 x 150 mL), dried over anhydrous Na_2SO_4, and concentrated to afford a clear, yellow oil (5.18 g, 98 % Yield) that was obtained in high purity and used directly in the next step. **^{1}H NMR** (300.27 MHz, $CDCl_3$) δ 7.53 (d, J = 8.8 Hz, 1H), 7.31 (d, J = 3.1 Hz, 1H), 6.89 (dd, J = 8.8, 3.1 Hz, 1H), 3.93 (s, 3H), 3.82 (s, 3H). **^{13}C NMR** (75.51 MHz, $CDCl_3$) δ 166.64, 158.69, 135.19, 132.87, 119.21, 116.37, 112.10, 55.81, 52.66.

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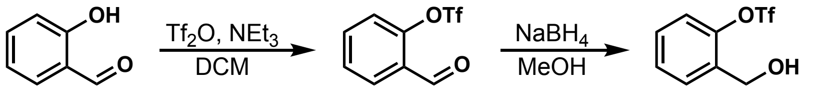
[1] Ueberschaar, N.; Xu, Z.; Scherlach, K.; Metsä-Ketelä, M.; Bretschneider, T.; Dahse, H.-M.; Görls, H.; Hertweck, C. Synthetic Remodeling of the Chartreusin Pathway to Tune Antiproliferative and Antibacterial Activities. *J. Am. Chem. Soc.* **2013**, *135*, 17408–17416.

Synthesis of **SI-6**: In a 250-mL round-bottom flask, **SI-5** (5.18 g, 21.1 mmol) was dissolved in anhydrous THF (25 mL) at room temperature under argon. In a separate 500-mL round-bottom flask, $LiAlH_4$ (1.26 g, 33.2 mmol, 1.6 equiv.) was suspended in THF (50 mL) and cooled to 0 °C. The solution of **SI-5** was transferred via cannula to the $LiAlH_4$ suspension over 5 minutes. To ensure quantitative transfer of **SI-5**, the cannula was rinsed with additional THF (25 mL). The reaction was left to gradually warm to room temperature over 47.5 hours, at which point unreacted **SI-5** was observed by TLC analysis. The reaction was re-cooled to 0 °C and additional $LiAlH_4$ (1.10 g, 29.0 mmol, 1.4 equiv.) was added as a solid in a single portion. After stirring for 30 minutes, TLC analysis indicated complete consumption of **SI-5**. The reaction was quenched at 0 °C by the addition of EtOAc (60 mL). The quenched reaction was transferred to a 1 L Erlenmeyer flask containing EtOAc (150 mL) and an aqueous solution of 0.5 M Rochelle's salt (300 mL). The resulting mixture was stirred vigorously at room temperature overnight. The phases were separated, and the aqueous phase was subsequently extracted with EtOAc (2 x 150 mL). The combined organic phases were washed with brine (2 x 200 mL), dried over anhydrous Na_2SO_4, and concentrated to afford a clear, pale yellow oil. Under high vacuum, the oil crystallized to afford **SI-6** as an off-white solid in high purity (4.32 g, 94 % Yield). **SI-6** was used without further purification. **^{1}H NMR** (300.27 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.7 Hz, 1H), 7.06 (d, *J* = 3.1 Hz, 1H), 6.72 (dd, *J* = 8.7, 3.1 Hz, 1H), 4.71 (br s, 2H), 3.81 (s, 3H), 2.02 (br s, 1H). **^{13}C NMR** (75.51 MHz, $CDCl_3$) δ 159.40, 140.86, 133.29, 114.93, 114.39, 112.66, 65.21, 55.66.

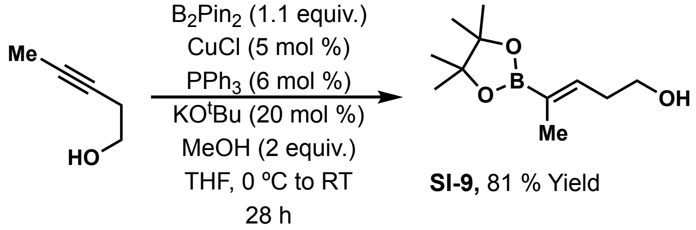


SI-7, 95 % Yield **SI-8**, 95 % Yield

Synthesis of **SI-7**: An oven-dried 3-neck 250-mL round-bottom flask was equipped with a large magnetic stir bead and an oven-dried 100-mL addition funnel. The side-necks were capped with rubber septa. The apparatus was flushed with argon, and then each septum was fitted with an argon-filled balloon. Reagent grade salicylaldehyde (2.2 mL, 20.6 mmol), anhydrous DCM (30 mL), and NEt_3 (4 mL, 28.7 mmol, 1.4 equiv.) were successively added via syringe to afford a clear yellow solution. The solution was then stirred at 0 °C. An entire freshly opened bottle of trifluoromethanesulfonic anhydride (1 M in DCM, 25 mL, 25 mmol, 1.2 equiv.) was quickly poured into the addition funnel. The opening of the addition funnel was quickly sealed with a rubber septum. The Tf_2O solution was added dropwise (~ 1 drop per second) to the reaction mixture over 55 minutes to afford a clear, dark brown solution. The reaction was left to gradually warm to room temperature over 18.5 hours. The reaction mixture was directly concentrated to give a dark reddish-brown oil, which was then suspended in Et_2O (50 mL). The supernatant, which was clear, pale yellow, was filtered through a plug of SiO_2. The plug was thoroughly rinsed with Et_2O (3 x 50 mL). The filtrate was concentrated to afford **SI-7** (4.99 g, 95 % yield) as a dark reddish-purple oil in good purity as judged by ^{1}H and ^{19}F NMR analysis. **SI-7** was used without further purification. **^{1}H NMR** (300.27 MHz, $CDCl_3$) δ 10.29 (s, 1H), 8.01 (dd, *J* = 7.7, 1.9 Hz, 1H), 7.73 (ddd, *J* = 8.3, 7.5, 1.9 Hz, 1H), 7.57 (app tt, *J* = 7.5, 0.9 Hz, 1H), 7.42 (dd, *J* = 8.3, 0.6 Hz, 1H). **^{19}F NMR** (282.51 MHz, $CDCl_3$) δ –72.87.

Synthesis of **SI-8**: In a 250-mL round-bottom flask open to air, **SI-7** (4.99 g, 19.6 mmol) was dissolved in HPLC grade MeOH (60 mL) to afford a clear, orange-yellow solution. The flask was sealed with a rubber septum, and the headspace was briefly sparged with argon and equipped with an argon-filled balloon. The solution was cooled to 0 °C and stirred vigorously. The reaction was briefly opened to air, and $NaBH_4$ (1.21 g, 32 mmol, 1.6 equiv.) was carefully added in a portion-wise manner resulting in vigorous, but controlled gas evolution. After stirring for 5 minutes, TLC analysis indicated complete consumption of the aldehyde. The reaction was removed from cooling and stirred at room temperature for 15 minutes. The crude reaction mixture was poured onto ~ 200 mL of crushed ice. The mixture was acidified to pH ≈ 3 by the addition of 1 M HCl solution (~ 40 mL). The product was extracted with Et_2O (1 x 200 mL then 2 x 100 mL). The combined organic phases were divided into two approximately equal portions and washed with brine (1 x 100 mL), then recombined and dried over anhydrous Na_2SO_4 and concentrated to afford a crude yellow oil (4.88 g). The crude oil was adsorbed onto Celite® 545 (10 g) and purified by column chromatography on SiO_2 (4:1 Hexanes / EtOAc). **SI-8** was obtained as a clear yellow oil (4.75 g, 95 % yield). **^{1}H NMR** (300.27 MHz, $CDCl_3$) δ 7.66-7.59 (m, 1H), 7.46-7.35 (m, 2H), 7.31-7.25 (m, 1H), 4.81 (d, *J* = 6.0 Hz, 2H), 1.97 (t, *J* = 6.1 Hz, 1H). **^{19}F NMR** (282.51 MHz, $CDCl_3$) δ –73.61.

Synthesis of Vinyl Boronates



SI-9, 81 % Yield

The use of fresh B_2Pin_2 and KO^tBu (both handled and stored in a nitrogen-filled glovebox) was critical to the success of this reaction!

<u>Synthesis of known vinyl boronate **SI-9**:</u> This is a modified procedure from Aggarwal and co-workers.[2] In a nitrogen-filled glovebox, a large oven-dried Schlenk tube was charged with CuCl (198.1 mg, 2.00 mmol, 5 mol%), PPh_3 (629.8 mg, 2.40 mmol, 6 mol%), and KO^tBu (899.0 mg, 8.00 mmol, 20 mol %). The tube was equipped with a magnetic stir bead and a rubber septum. Also in the glovebox, an oven-dried 100-mL round-bottom flask was charged with B_2Pin_2 (11.475 g, 45.19 mmol, 1.13 equiv.) and sealed with a rubber septum. Both vessels were removed from the glovebox. The Schlenk tube was connected to a Schlenk line, and the nitrogen atmosphere was exchanged for argon. Anhydrous THF (20 mL) was added to the Schlenk tube via syringe at room temperature to initially give a yellowish-brown mixture. The reaction was stirred for 40 minutes to afford a dark grey mixture.[3] The flask containing B_2Pin_2 was equipped with an argon balloon, and then anhydrous THF (25 mL) was added via syringe to afford a clear, colourless solution. The B_2Pin_2 solution was added to the Schlenk tube dropwise by syringe over 30 minutes at room temperature to afford a dark brownish-black solution. After stirring at room temperature for 30 minutes, the reaction was cooled to 0 °C. 3-pentyn-1-ol (3.37 g, 40.06 mmol, 1 equiv.), anhydrous MeOH (3.2 mL, 79.0 mmol, 1.97 equiv.),[4] and THF (10 mL) were combined in a flame-dried 25-mL round-bottom flask under argon. This solution was subsequently added to the Schlenk tube dropwise by syringe over 40 minutes at 0 °C. The reaction was left to stir and gradually warm to room temperature over 28 hours. At this point, the black reaction mixture was exposed to air, and filtered through a SiO_2 plug pre-equilibrated with Et_2O. The plug was thoroughly rinsed with Et_2O (~ 400 mL) to give a clear, colourless filtrate. The filtrate was washed with 0.01 M HCl (3 x 200 mL),[5] washed with brine (1 x 200 mL), dried over anhydrous Na_2SO_4, and then concentrated to afford a cloudy white oily residue (7.82 g). The crude residue was adsorbed onto Celite® 545 (15.69 g) and purified by column chromatography on SiO_2 (isocratic elution with 6.5:3.5 hexanes / EtOAc) to afford **SI-9** as a clear, slightly pale-yellow oil in good yield and purity (6.81 g, 81 % Yield). **^{1}H NMR** (300.27 MHz, $CDCl_3$) δ 6.30 (tq, *J* = 7.0, 1.7 Hz, 1H), 3.71 (q, *J* = 6.1 Hz, 2H), 2.43 (app qq, *J* = 6.7, 1.0 Hz, 2H), 1.72 (dt, *J* = 1.9, 1.0 Hz, 3H), 1.49-1.40 (m, 1H), 1.26 (s, 12H). **^{13}C NMR** (75.51 MHz, $CDCl_3$) δ 141.51, 83.39, 61.95, 32.33, 24.92, 14.23. **^{11}B NMR** (96.34 MHz, $CDCl_3$) δ 29.99. **R_f** = 0.38 (6.5:3.5 Hexanes / EtOAc).

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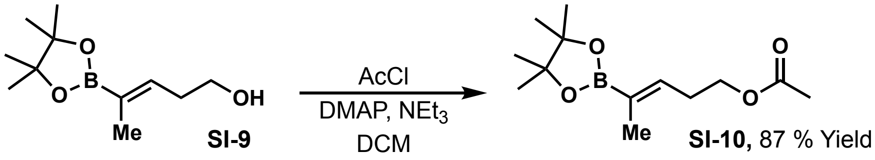
[2] Hesse, M. J.; Butts, C. P.; Willis, C. L.; Aggarwal, V. K. Diastereodivergent Synthesis of Trisubstituted Alkenes through Protodeboronation of Allylic Boronic Esters: Application to the Synthesis of the Californian Red Scale Beetle Pheromone. *Angew. Chem., Int. Ed.* **2012**, *51*, 12444–12448.

[3] Empirically, the dark grey appearance is a good indicator of a successful reaction setup. When setup on the benchtop or when poorer quality KO^tBu was used, the reaction turned orange at this stage.

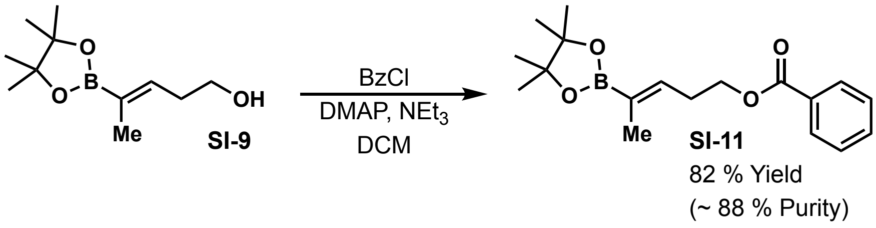
[4] HPLC grade MeOH was dried over activated 4 Å MS prior to use.

[5] Washing with 0.01 M HCl prior to column chromatography enabled a more efficient chromatographic separation, and routinely afforded the desired product in higher purity.



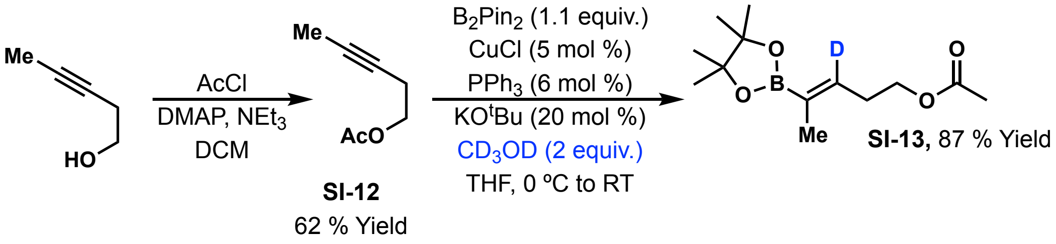
Synthesis of **SI-10**: To a 500-mL round-bottom flask containing **SI-9** (6.8 g, 32.1 mmol) was added DMAP (397.6 mg, 3.25 mmol, 10 mol %) and a large magnetic stir bead. The flask was sealed with a rubber septum, sparged with argon, and fitted with an argon-filled balloon. Anhydrous DCM (160 mL) and NEt_3 (6.5 mL, 46.6 mmol, 1.45 equiv.) were successively added by syringe at room temperature. The reaction was cooled to 0 °C and acetyl chloride (2.9 mL, 40.8 mmol, 1.27 equiv.) was added dropwise over 7 minutes to give a yellow suspension. The reaction was left to stir and gradually warm to room temperature over 12.5 hours. The reaction mixture was directly concentrated to give a bright orange oily residue. The crude residue was suspended in Et_2O (100 mL) and filtered through a plug of Celite® 545. The plug was rinsed with a copious amount of Et_2O (~ 500 mL total) to afford a clear yellow filtrate, which was concentrated to give a clear, dark amber oil (8.83 g). The crude oil was adsorbed onto Celite® 545 (17.9 g) and purified by column chromatography on SiO_2 (isocratic elution with 9:1 hexanes / EtOAc). **SI-10** was obtained as a clear, colourless oil in excellent yield and purity (7.06 g, 87 % Yield).

^{1}H NMR (500.27 MHz, $CDCl_3$) δ 6.27 (tq, *J* = 6.8, 1.7 Hz, 1H), 4.10 (t, *J* = 7.0 Hz, 2H), 2.46 (qq, *J* = 6.9, 1.0 Hz, 2H), 2.04 (s, 3H), 1.70 (dt, *J* = 1.9, 1.0 Hz, 3H), 1.26 (s, 12H).
^{13}C NMR (125.81 MHz, $CDCl_3$) δ 171.28, 140.48, 83.43, 63.53, 28.24, 24.94, 21.18, 14.20.
^{11}B NMR (160.51 MHz, $CDCl_3$) δ 30.13.
R_f = 0.50 (4:1 Hexanes / EtOAc); 0.31 (9:1 Hexanes / EtOAc)
IR: 2979, 2933, 1740, 1634, 1370, 1305, 1236, 1135, 1034, 859, 669 cm^{-1}.
HRMS (ESI+) *m/z* [M + H] calcd for $C_{13}H_{24}BO_4$+ 255.17624, found: 255.17655.



<u>Synthesis of **SI-11**:</u> **SI-11** was prepared analogously to **SI-10**, using benzoyl chloride as the electrophile, and starting from 5.27 g (24.9 mmol) of **SI-9**. The crude product was purified by column chromatography on SiO$_2$ (95:5 Hexanes / EtOAc) to yield **SI-11** (6.44 g, 82% yield) as oily white solid in moderate purity (~ 88 % purity; estimated by ^{1}H NMR). The product was contaminated with traces of excess benzoyl chloride. This bulk material was used directly purification in the next step, at which point the excess benzoyl chloride was easily removed. For analytical purposes, a 600 mg sample was re-purified by column chromatography on SiO$_2$ (97:3 PhMe / DCM) to afford **SI-11** as a white solid in high purity.

^{1}H NMR (500.27 MHz, CDCl$_3$) δ 8.04 (app dd, *J* = 8.3, 1.4 Hz, 2H), 7.55 (app tt, *J* = 7.4, 1.4 Hz, 1H), 7.43 (app t, *J* = 7.8 Hz, 2H), 6.36 (app qq, *J* = 7.0, 1.8 Hz, 1H), 4.36 (t, *J* = 7.0 Hz, 2H), 2.62 (app q, *J* = 7.0 Hz, 2H), 1.75 (br s, 3H), 1.26 (s, 12H).
^{13}C NMR (125.81 MHz, CDCl$_3$) δ 166.77, 140.43, 132.97, 130.54, 129.74, 128.44, 83.44, 64.02, 28.37, 24.93, 14.24.
^{11}B NMR (96.34 MHz, CDCl$_3$) δ 29.76.
IR (solid): 2978, 2937, 1720, 1634, 1370, 1307, 1272, 1136, 1111, 1070, 860, 712, 668 cm^{-1}.
R$_f$ = 0.18 (40:1 Hexanes / EtOAc); 0.34 (97:3 PhMe / DCM)
m.p. 40-42 °C
HRMS (ESI+) *m/z*: [M + Na] calcd for $C_{18}H_{25}BO_4Na^+$: 339.17381, found: 339.17387.



SI-12
62 % Yield

SI-13, 87 % Yield

Synthesis of **SI-12**: A flame-dried 100-mL round-bottom flask equipped with a magnetic stir bead was charged with 3-pentyn-1-ol (1.40 g, 16.6 mmol) and DMAP (223.1 mg, 1.83 mmol, 11 mol %). The flask was sealed with a rubber septum, sparged with argon, and fitted with an argon-filled balloon. Anhydrous DCM (50 mL) and NEt_3 (3.5 mL, 25.1 mmol, 1.5 equiv.) were successively added by syringe at room temperature. The reaction was cooled to 0 °C and acetyl chloride (1.4 mL, 19.7 mmol, 1.2 equiv.) was added dropwise. The reaction was left to gradually warm to room temperature over 12 hours. The cloudy pale yellow reaction mixture was directly concentrated, and the crude residue was suspended in Et_2O (~ 20 mL). The supernatant was filtered through a plug of Celite® 545. The plug was thoroughly rinsed with additional Et_2O (~ 150 mL) to afford a clear yellow filtrate, which was concentrated to give a clear, yellow oil. Purification of the crude oil by column chromatography on SiO_2 (20:1 Hexanes / EtOAc) afforded **SI-12** as a clear, colourless oil (1.30 g, 62 % Yield). **^{1}H NMR** (300.27 MHz, $CDCl_3$) δ 4.12 (t, *J* = 6.9 Hz, 2H), 2.53-2.38 (m, 2H), 2.07 (s, 3H), 1.78 (app tt, *J* = 1.6, 0.8 Hz, 3H). **^{13}C NMR** (125.81 MHz, $CDCl_3$) δ 171.01, 77.40, 74.84, 62.99, 21.05, 19.33, 3.59.

Synthesis of **SI-13**: In a nitrogen-filled glovebox, a flame-dried Schlenk tube was charged with CuCl (39.6 mg, 0.40 mmol, 5 mol %), PPh_3 (125.8 mg, 0.48 mmol, 6 mol%), and KO^tBu (178.2 mg, 1.59 mmol, 20 mol %). The tube was equipped with a magnetic stir bead and a rubber septum. Also in the glovebox, an oven-dried 100-mL round-bottom flask was charged with B_2Pin_2 (2.285 g, 9.00 mmol, 1.13 equiv.) and sealed with a rubber septum. Both vessels were removed from the glovebox. The Schlenk tube was connected to a Schlenk line, and the nitrogen atmosphere was exchanged for argon. Anhydrous THF (2 mL) was added to the Schlenk tube via syringe at room temperature. The mixture was stirred for 40 minutes to afford a dark grey mixture. The round-bottom flask containing B_2Pin_2 was equipped with an argon balloon, and then anhydrous THF (6 mL) was added via syringe to afford a clear, colourless solution. The B_2Pin_2 solution was added to the Schlenk tube dropwise over 6 minutes at room temperature to afford a dark brownish-black solution. After stirring at room temperature for 20 minutes, the reaction was cooled to 0 °C. **SI-12** (1.00 g, 7.93 mmol, 1 equiv.), CD_3OD (0.65 mL, 16.0 mmol, 2.02 equiv.),[6] and THF (3 mL) were combined in a dry 10-mL round-bottom flask under argon. This solution was then added to the Schlenk tube dropwise via syringe over 12 minutes at 0 °C. The reaction was left to stir and gradually warm to room temperature over 19 hours. At this point, the black reaction mixture was exposed to air and filtered through a plug of Celite® 545. The plug was thoroughly rinsed with Et_2O (~ 200 mL). The filtrate was concentrated to afford a crude yellow oil (3.37 g). The crude oil was adsorbed onto Celite® 545 (6.76 g) and loaded onto a SiO_2 column pre-equilibrated with hexanes. Gradient elution (100:0 → 20:1 → 10:1 Hexanes / EtOAc) afforded **SI-13** as a clear, colourless oil (1.30 g, 87 % Yield; ~12.3 : 1 r.r.; ~ 65 % D incorporation).

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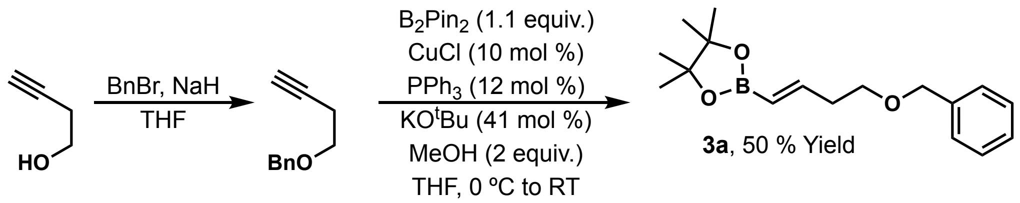
[6] CD_3OD was pre-dried by storage over activated 4 Å MS in a desiccator.

^{1}H NMR (500.27 MHz, $CDCl_3$) δ 4.10 (t, *J* = 7.0 Hz, 2H), 4.05 (t, *J* = 7.2 Hz, 2H, minor regioisomer), 2.49-2.43 (m, 2H), 2.04 (s, 3H), 2.01 (s, 3H, minor regioisomer), 1.69 (s, 3H), 1.25 (s, 12H), 1.24 (s, 12H, minor regioisomer).
^{13}C NMR (125.81 MHz, $CDCl_3$) δ 171.25, 140.47 (vinylic C–H), 140.12 (t, *J* = 23.6 Hz, vinylic C–D), 83.41, 83.35 (minor), 64.19 (minor), 63.50, 28.23 (minor), 28.12, 24.93, 21.16, 14.19 (minor), 14.14.
^{11}B NMR (160.51 MHz, $CDCl_3$) δ 30.10.
^{2}H{^{1}H} NMR (55.31 MHz, acetone-*h*6) δ 5.54.
R_f = 0.15 (20:1 Hexanes / EtOAc)
IR: 2978, 2930, 2899, 2866, 1740, 1634, 1621, 1410, 1367, 1305, 1235, 1142, 1034, 857, 669 cm^{-1}
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{13}H_{22}DBO_4Na+$ 278.16444, found: 278.16432.



SI-14, 98 % Yield

3a, 50 % Yield

<u>Synthesis of **SI-14**:</u> Sodium hydride (2.55 g of 60 % w/w mineral oil dispersion, 63.8 mmol, 2.3 equiv.) was suspended in anhydrous THF (25 mL) and cooled to 0 °C. In a separate flask, 3-butyn-1-ol (1.97 g, 28.1 mmol) was dissolved in THF (15 mL). This solution was transferred to the sodium hydride suspension via cannula to afford an orange slurry. The cannula was rinsed with additional THF (5 mL). A solution of benzyl bromide (5.77 g, 33.7 mmol, 1.2 equiv.) in THF (10 mL) was then added to the slurry dropwise via syringe over 5 minutes. The reaction was left to warm to room temperature over 23.5 hours. The reaction was quenched with saturated aqueous NH_4Cl (20 mL) and diluted with water (40 mL). Et_2O (150 mL) was added, and the phases were separated. The aqueous phase was extracted with Et_2O (3 x 30 mL). The combined organic phases were washed with brine (1 x 120 mL), dried over anhydrous Na_2SO_4, and concentrated to give a crude orange oil (5.74 g). The crude oil was loaded onto a SiO_2 plug and rinsed thoroughly with hexanes to remove mineral oil. Subsequent elution with 1:1 hexanes / EtOAc and concentration of the filtrate afforded **SI-16** as a clear yellow oil (4.4 g, 98 % Yield) in good purity as determined by ^1H NMR. **SI-16** was used in the next step without further purification. **^{1}H NMR** (300. 27 MHz, $CDCl_3$) δ 7.40-7.32 (m, 5H), 4.57 (s, 2H), 3.61 (t, *J* = 6.9 Hz, 2H), 2.51 (dt, *J* = 7.0, 2.7 Hz, 2H), 2.00 (t, *J* = 2.7 Hz, 1H).

<u>Synthesis of known[7] vinyl boronate **3a**[8]:</u> A flame-dried 50-mL Schlenk tube equipped with a magnetic stir bar was charged with CuCl (98.9 mg, 0.99 mmol, 10 mol %), PPh_3 (315.2 mg, 1.20 mmol, 12 mol %), and KO^tBu (453.0 mg, 4.04 mmol, 41 mol %). The Schlenk tube was evacuated and back-filled with argon, then anhydrous THF (5 mL) was added by syringe. The reaction was stirred vigorously at room temperature for 40 minutes. A solution of B_2Pin_2 (2.92 g, 11.5 mmol, 1.16 equiv. in 6 mL THF) was added to the reaction by syringe at room temperature. To ensure quantitative transfer, the syringe was rinsed with additional THF (2 mL). The cloudy yellowish-brown reaction mixture was stirred at room temperature for 20 minutes then cooled to 0 °C in an ice-water bath. Alkyne **SI-14** (1.59 g, 9.92 mmol, 1 equiv.), anhydrous MeOH (0.82 mL, 20.24 mmol, 2.0 equiv.), and THF (3 mL) were combined in a flame-dried 50-mL round-bottom flask under argon. This solution was subsequently added to the Schlenk tube dropwise by syringe over 5 minutes at 0 °C. To ensure quantitative transfer, the 50-mL flask and syringe were rinsed with additional THF (2 mL). The reaction was removed from the ice-water bath and stirred at room temperature for 23 hours. At this point, the reaction mixture was exposed to air and filtered through a plug of Celite® 545. The plug was thoroughly rinsed with Et_2O. The filtrate was concentrated to afford a crude yellow oil (4.61 g). The crude oil was adsorbed onto Celite® 545 (10.8 g) and purified by column chromatography on SiO_2. Gradient elution (20:1 → 10:1 Hexanes / EtOAc) afforded **3a** as a clear, colourless oil that crystallized to a white solid upon storage at –20 °C (1.428 g, 50 % Yield). The NMR data for **3a** were in excellent agreement with the literature.[7] **^{1}H**

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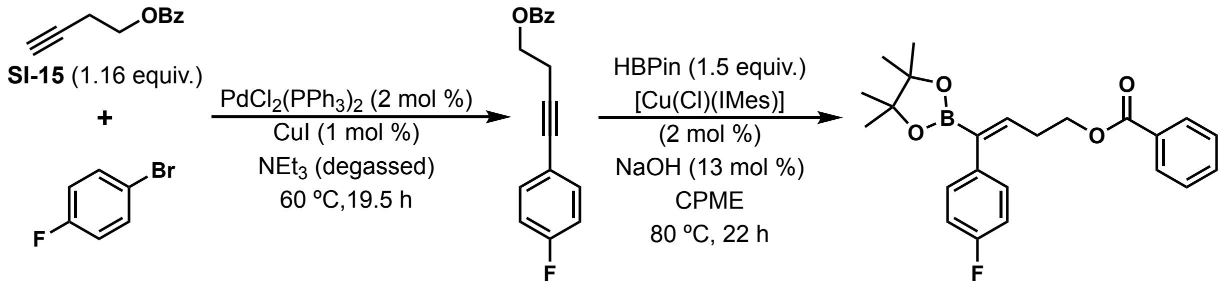
[7] Shade, R. E.; Hyde, A. M.; Olsen, J.-C.; Merlic, C. A. Copper-Promoted Coupling of Vinyl Boronates and Alcohols: A Mild Synthesis of Allyl Vinyl Ethers. *J. Am. Chem. Soc.* **2010**, *132*, 1202–1203.

[8] It should be noted that the protocol below for the synthesis of compound **3a** is unoptimized. This reaction was setup without the use of a glovebox, and with older batches of B_2Pin_2 and KO^tBu that were ***not*** stored under a rigorously inert atmosphere. For better, highly optimized reaction conditions, refer to the synthesis of **SI-9**.

NMR (300.27 MHz, $CDCl_3$) δ 7.35-7.24 (m, 5H), 6.63 (dt, *J* = 18.0, 6.4 Hz, 1H), 5.53 (dt, *J* = 18.0, 1.6 Hz, 1H), 4.51 (s, 2H), 3.56 (t, *J* = 6.9 Hz, 2H), 2.49 (app qd, *J* = 6.8, 1.6 Hz, 2H), 1.26 (s, 12H). **^{13}C NMR** (75.51 MHz, $CDCl_3$) δ 150.56, 138.52, 128.49, 127.82, 127.68, 83.22, 73.05, 69.05, 36.25, 24.92. **^{11}B NMR** (96.34 MHz, $CDCl_3$) δ 29.29.



SI-15 (1.16 equiv.)

SI-16, 80 % Yield

SI-17, 33 % Yield
(r.r. ≈ 20 : 1)*
*after purification

<u>Synthesis of **SI-16**:</u> A flame-dried and stir bead-equipped 100-mL round-bottom flask was charged with triethylamine[9] (~ 40 mL), and the flask was sealed with a rubber septum. The septum was pierced with a vent needle and a needle connected to a Schlenk line. While stirring vigorously at room temperature for 45 minutes, the NEt_3 was degassed with bubbling argon. A separate flame-dried 100-mL round-bottom flask was charged with $PdCl_2(PPh_3)_2$ (140.8 mg, 0.20 mmol, 2 mol %), CuI (19.5 mg, 0.10 mmol, 1 mol %), and a magnetic stir bead. The flask was sealed with a rubber septum. Using a needle connected to the Schlenk line, the flask was evacuated and back-filled with argon (x 4). The flask was equipped with a large argon-filled balloon, and degassed NEt_3 (30 mL) was added by syringe to afford a bright yellow suspension. 1-bromo-4-fluorobenzene (1.1 mL, 10.0 mmol, 1 equiv.) was then added by syringe. Alkyne **SI-15**[10] (2.01 g, 11.56 mmol, 1.16 equiv.) was added by syringe over 4 minutes. Upon addition of **SI-15**, the reaction initially turned orange before turning brown. The reaction was stirred at room temperature for 3 minutes, then placed in a pre-heated (60 °C) oil bath. After stirring vigorously at 60 °C for 16 minutes, the reaction had a very dark brown appearance, and a precipitate was observed. The reaction was left to continue stirring at 60 °C overnight (19 h), which gave a black reaction mixture. Upon cooling to room temperature, the crude reaction mixture was filtered through a SiO_2 plug, which was thoroughly rinsed with EtOAc (80 mL). The filtrate was concentrated to afford the crude product as a dark brown oil (3.45 g). The crude oil was directly loaded onto a SiO_2 column (equilibrated with hexanes) as a neat oil. Residual material was transferred by rinsing with hexanes. Isocratic elution (20:1 Hexanes / EtOAc) then afforded **SI-16** (2.15 g, 80 % Yield) as a clear yellow oil in high yield and purity. Upon storage at –20 °C the product solidified to give a pale yellow solid.

^{1}H NMR (500.27 MHz, $CDCl_3$) δ 8.08 (app dd, *J* = 8.4, 1.3 Hz, 2H), 7.57 (app tt, *J* = 7.4, 1.3 Hz, 1H), 7.45 (app t, *J* = 7.8 Hz, 2H), 7.37 (app dd, *J* = 8.6, 5.5 Hz, 2H), 6.98 (app t, *J* = 8.7 Hz, 2H), 4.50 (t, *J* = 6.9 Hz, 2H), 2.88 (t, *J* = 6.9 Hz, 2H).

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[9] A freshly opened bottle of peptide synthesis grade triethylamine was used directly without additional drying or distillation.

[10] **SI-15** exists as a viscous oil at room temperature. It was prepared in a single step from 3-butyn-1-ol.

^{13}C NMR (125.81 MHz, $CDCl_3$) δ 166.51, 162.42 (d, J = 248.7 Hz), 133.61 (d, J = 8.4 Hz), 133.23, 130.17, 129.82, 128.54, 119.56 (d, J = 3.5 Hz), 115.61 (d, J = 22.0 Hz), 85.25, 81.22, 62.92, 20.16.
^{19}F NMR (470.68 MHz, $CDCl_3$) δ –111.61.
R_f = 0.37 (9:1 Hexanes / EtOAc)
m.p. 49-52 °C
IR (film): 3064, 2962, 2906, 1718, 1601, 1506, 1452, 1268, 1230, 1221, 1110, 835, 709 cm^{-1}.
HRMS (ESI+) *m/z* [M + H] calcd for $C_{17}H_{14}FO_2$+ 269.09724, found: 269.09721.

Synthesis of **SI-17**: This is a modified procedure from Cazin and co-workers.[11] The [Cu(Cl)(IMes)] catalyst was readily prepared using a known procedure.[12] An oven-dried 10–20 mL size Biotage microwave vial was charged with **SI-16** (1.9976 g, 7.446 mmol, 1 equiv.), [Cu(Cl)(IMes)] (61.5 mg, 0.152 mmol, 2 mol %), NaOH beads (~ 39.3 mg, 0.9825 mmol, 13 mol %), and a magnetic stir bead. While open to air, 10 mL of CPME (Sigma ReagentPlus®) was added. The mixture was stirred at room temperature for 5 minutes to afford a mostly clear yellow solution (a small amount of solid didn't dissolve). The solution was subsequently cooled to –30 °C. With the reaction still open to air, HBPin (1.6 mL, 11.027 mmol, 1.48 equiv.)[13] was added dropwise by syringe over 3.5 minutes to afford a pale yellow suspension. At this stage, the vial was capped (crimp-sealed) and removed from the –30 °C bath. The reaction was stirred at room temperature for 5 minutes to give a mostly clear yellow solution. The reaction was placed in a pre-heated (80 °C) oil bath and stirred vigorously. After 2 minutes, the reaction was very dark brown in appearance (nearly black). The reaction was left to stir at 80 °C[14] for 22 hours to afford a dark reddish-brown mixture. Upon cooling to room temperature, the crude reaction mixture was filtered through an EtOAc-equilibrated plug of Celite® 545 (~ 2 cm diameter, ~ 4.5 cm length). The plug was rinsed with EtOAc (~ 70 mL total) and the filtrate was concentrated to give a dark reddish-brown oil (3.73 g). The crude oil was directly loaded (neat) onto a SiO_2 column (equilibrated with 20:1 hexanes / EtOAc). Residual material was transferred by rinsing with 20:1 hexanes / EtOAc. Isocratic elution (20:1 hexanes / EtOAc) afforded **SI-17** (977.1 mg, 33 % Yield) as an off-white pale yellowish solid. **SI-17** was isolated as a single regioisomer (~ 20:1 r.r.). It is worth noting, that slightly higher yields could be obtained on a smaller scale. For 2.0 mmol and 4.3 mmol scale batches, **SI-17** was obtained in 41 % and 39 % yield, respectively.

^{1}H NMR (500.27 MHz, $CDCl_3$) δ 8.01 (app dd, J = 8.4, 1.3 Hz, 2H), 7.55 (app tt, J = 7.4, 1.4 Hz, 1H), 7.43 (t, J = 7.8 Hz, 2H), 7.12 (app dd, J = 8.6, 5.6 Hz, 2H), 7.00 (t, J = 8.7 Hz, 2H) , 6.63 (t, J = 7.2 Hz, 1H), 4.35 (t, J = 6.8 Hz, 2H), 2.62 (q, J = 6.9 Hz, 2H), 1.27 (s, 12H).
^{13}C NMR (125.81 MHz, $CDCl_3$) δ 166.65, 161.64 (d, J = 244.4 Hz), 142.77, 135.54 (d, J = 3.4 Hz), 133.05, 130.42 (d, J = 8.0 Hz), 130.41, 129.74, 128.46, 114.97 (d, J = 21.2 Hz), 83.89, 64.04, 29.55, 24.88.
^{11}B NMR (160.51 MHz, $CDCl_3$) δ 30.30.
^{19}F NMR (470.68 MHz, $CDCl_3$) δ –116.90.
R_f = 0.24 (20:1 Hexanes / EtOAc)

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[11] Bidal, Y. D.; Larzeg, F.; Cazin, C. S. J. Copper-Catalyzed Regioselective Formation of Tri- and Tetrasubstituted Vinylboronates in Air. *ACS Catal.*, **2014**, *4*, 1564–1569.

[12] Santoro, O.; Collado, A.; Slawin, A. M. Z.; Nolan, S. P.; Cazin, C. S. J. A general synthetic route to [Cu(X)(NHC)] (NHC = N-heterocyclic carbene, X = Cl, Br, I) complexes. *Chem. Commun.,* **2013**, *49*, 10483–10485.

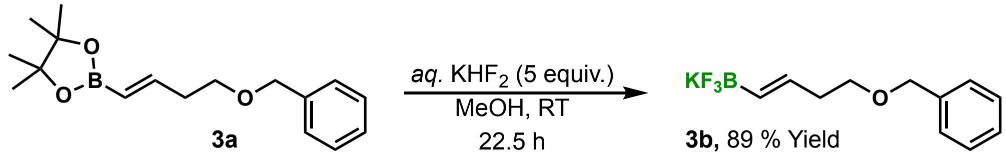
[13] Neat pinacolborane was purchased from Oakwood and transferred to a Schlenk tube in a nitrogen-filled glovebox. It was then stored outside of the glovebox in a –20 °C freezer and handled using standard Schlenk techniques.

[14] As a precautionary measure for this relatively large-scale (7.4 mmol) setup, the sealed reaction vessel was heated behind a blast shield.

m.p. 78-81 °C
IR (film): 2978, 1720, 1619, 1602, 1508, 1379, 1372, 1345, 1314, 1271, 1219, 1144, 855, 712 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{23}H_{26}BFO_4Na+$ 419.18004, found: 419.18016.

Synthesis of Vinyl Trifluoroborates

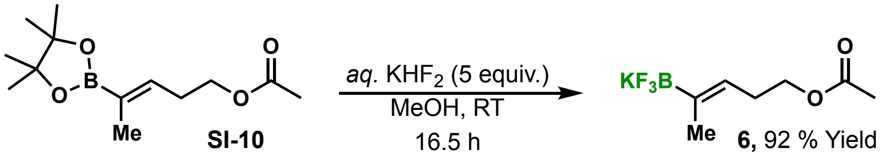
In general, all trifluoroborates were obtained without the need for further purification. As a general practice, all trifluoroborates were stored in plastic scintillation vials at room temperature in a desiccator. Under this regime, these materials demonstrated excellent stability towards air and moisture for months at a time.



Representative procedure using the synthesis of **3b** as an example:

In a 20-mL scintillation vial open to air, vinyl boronate **3a** (509.8 mg, 1.77 mmol) was dissolved in HPLC grade MeOH (2 mL) to afford a clear, colourless solution. While stirring at room temperature, saturated aqueous KHF$_2$ (4.5 M, 2 mL, 5 equiv.) was added dropwise by syringe to give a thick white suspension. Additional MeOH (1 mL) was added to facilitate efficient stirring. The reaction was left to stir at room temperature for 22.5 hours. The reaction mixture was subsequently transferred to a 100-mL round-bottom flask, using acetone to thoroughly rinse the reaction vial. The crude reaction mixture was directly concentrated by rotary evaporation to remove the organic solvents. The remaining water was removed as an azeotrope with toluene (4 x 3 mL) to afford a white solid. The trifluoroborate was extracted with warm acetone as follows. To the 100-mL flask containing the crude white solid, was added acetone (10 mL). The mixture was swirled and gently heated with a heat gun, and subsequently filtered through cotton into a separate 100-mL round-bottom flask. This extraction process was repeated twice more, using 10 mL of acetone each time. The combined acetone extracts (clear and colourless) were concentrated to afford **3b** as a white solid, which was subsequently suspended in Et$_2$O (~ 15 mL). **3b** was isolated by vacuum filtration on a M glass frit and rinsed thoroughly with Et$_2$O (~ 50 mL). After air-drying for ~ 35 minutes, **3b** was obtained as a fluffy white solid (421.1 mg, 89 % Yield).

^{1}H NMR (500.27 MHz, DMSO-*d*6) δ 7.35-7.27 (m, 5H), 5.46 (dt, *J* = 17.3, 6.7 Hz, 1H), 5.30 (d, *J* = 17.3 Hz, 1H), 4.44 (br s, 2H), 3.39 (t, *J* = 7.2 Hz, 2H), 2.16 (app q, *J* = 7.0 Hz, 2H).
^{13}C NMR (125.81 MHz, DMSO-*d*6) δ 138.76, 129.49 (app q, *J* = 4.4 Hz), 128.17, 127.45, 127.24, 71.71, 70.23, 35.87.
^{11}B NMR (160.51 MHz, DMSO-*d*6) δ 2.22.
^{19}F NMR (470.68 MHz, DMSO-*d*6) δ –137.57.
IR: 3066, 2998, 2953, 2901, 2865, 2844, 2784, 1646, 1454, 1304, 1096, 996, 948, 916, 745, 731, 697 cm^{-1}.
m.p. decomp. above 195 °C
HRMS (ESI–) *m/z* [M – K] calcd for $C_{11}H_{13}BF_3O$– 229.10170, found: 229.10178.



Synthesis of compound **6**: While open to air, four 20-mL scintillation vials were charged with **SI-10** (in total, 3.01 g, 11.85 mmol). Vials 1–3 were charged with 860.3 mg, 894.9 mg, and 880.7 mg, respectively. Vial 4 was charged with 375.4 mg **SI-10**. Each vial was charged with HPLC grade MeOH (4 mL to vials 1–3; 2 mL to vial 4), to afford a clear, colourless solution. While stirring at room temperature, saturated aqueous KHF$_2$ (4.5 M, 5 equiv.) was added dropwise by syringe to each vial (4 mL to vials 1–3; 2 mL to vial 4), affording a white suspension. The individual reactions were left to stir vigorously for 16.5 hours. The four reactions were subsequently combined in a single 100-mL round-bottom flask. Each reaction vial was thoroughly rinsed with acetone. The combined reaction mixtures were directly concentrated by rotary evaporation to remove the organic solvents. The remaining water was removed as an azeotrope with toluene (4 x 4 mL) to afford a white solid, which was further dried under high vacuum for 5 hours. The trifluoroborate was extracted with acetone as follows. To the 100-mL flask containing the crude solid, was added acetone (20 mL). The mixture was swirled at room temperature, and subsequently filtered through cotton into a separate 100-mL round-bottom flask. This extraction process was repeated three more times, using 20 mL of acetone each time. The combined extracts were concentrated to afford a cloudy white oil, which was precipitated with Et$_2$O to give a white solid. This was achieved by the iterative addition and concentration of Et$_2$O (3 x 20 mL).[15] Once the oil had completely precipitated, the product was suspended in Et$_2$O (~ 20 mL), poured onto a M glass frit, and isolated by vacuum filtration. The product was thoroughly rinsed with chilled Et$_2$O and air-dried. Compound **6** was obtained as a white solid (2.54 g, 92 % Yield).

^{1}H NMR (500.27 MHz, acetone-*d*6) δ 5.43 (t, *J* = 6.2 Hz, 1H), 3.95 (t, *J* = 7.5 Hz, 2H), 2.26 (app q, *J* = 7.3 Hz, 2H), 1.96 (s, 3H), 1.54 (br s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 171.15, 122.13 (app q, *J* = 3.2 Hz), 65.04, 28.13, 20.92, 14.75.
^{11}B NMR (160.51 MHz, acetone-*d*6) δ 3.22.
^{19}F NMR (470.68 MHz, acetone-*d*6) δ –146.37.
m.p. 95-99 °C
IR: 2960, 2909, 2855, 1731, 1645, 1250, 1203, 966, 936, 408 cm^{-1}.
HRMS (ESI–) *m/z* [M – K] calcd for $C_7H_{11}BF_3O_2$– 195.08097, found: 195.08093.

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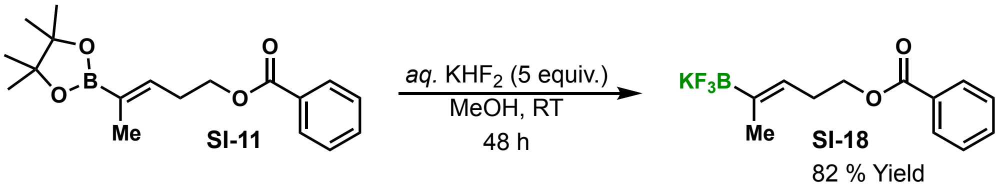
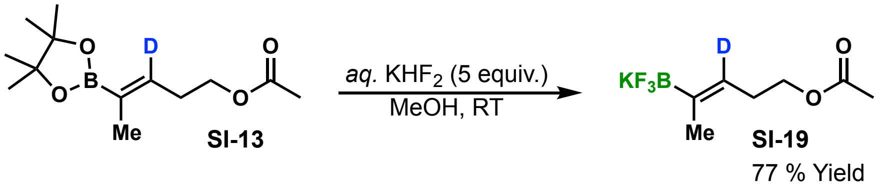
[15] Due to its high solubility in acetone, compound **6** exists in an oily state when traces of acetone are present. The iterative addition and removal of Et$_2$O by rotary evaporation reliably converted **6** to a crystalline solid. Precipitation was also promoted by agitating the oily material with a spatula.



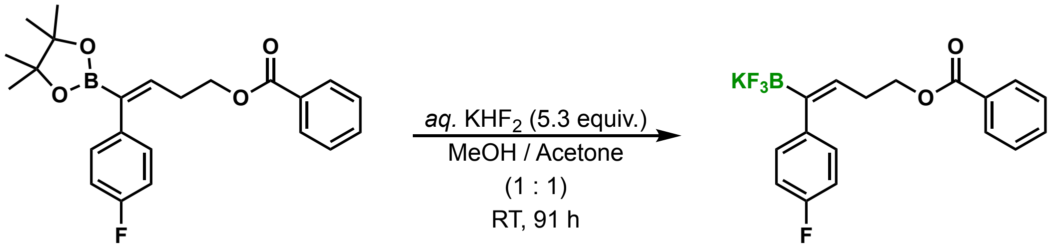
Synthesis of **SI-18**: In a 20-mL scintillation vial open to air, vinyl boronate **SI-11** (1.007 g, 3.18 mmol) was dissolved in HPLC grade MeOH (3.5 mL) to afford a clear, colourless solution. While stirring at room temperature, saturated aqueous KHF_2 (4.5 M, 3.5 mL, 5 equiv.) was added dropwise by syringe to give a white suspension. The reaction was left to stir at room temperature for 48 hours. The reaction mixture was subsequently transferred to a 100-mL round-bottom flask, using acetone to thoroughly rinse the reaction vial. The crude reaction mixture was directly concentrated by rotary evaporation to remove the organic solvents. The remaining water was removed as an azeotrope with toluene (4 x 3 mL) to afford a white solid. The trifluoroborate was extracted with warm acetone as follows. To the 100-mL flask containing the crude white solid, was added acetone (~20 mL). The mixture was swirled and gently heated with a heat gun, and subsequently filtered through cotton into a separate 100-mL round-bottom flask. This extraction process was repeated once more, using (~20 mL of acetone each time. The combined acetone extracts (clear and colourless) were concentrated to afford **SI-18** as a white solid, which was isolated by vacuum filtration on a M glass frit and rinsed with Et_2O (~ 30 mL). **SI-18** was obtained as a fluffy white solid (775.8 mg, 82 % Yield).

^{1}H NMR (500.27 MHz, acetone-*d*6) δ 8.02 (app dd, *J* = 8.3, 1.4 Hz, 2H), 7.61 (app tt, *J* = 7.4, 1.3 Hz, 1H), 7.50 (app t, *J* = 7.8 Hz, 2H), 5.52 (t, *J* = 6.6 Hz, 1H), 4.23 (t, *J* = 7.4 Hz, 2H), 2.43 (q, *J* = 7.3 Hz, 2H), 1.59 (br s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 166.91, 133.64, 131.73, 130.15, 129.31, 121.65 (q, *J* = 3.4 Hz), 65.89, 28.18, 14.91.
^{11}B NMR (96.34 MHz, acetone-*d*6) δ 3.16.
^{19}F NMR (282.51 MHz, acetone-*d*6) δ –146.38.
IR (solid): 3005, 2904, 2853, 1708, 1642, 1452, 1274, 1089, 934, 847, 712, 687 cm^{-1}.
m.p. 210-212 °C
HRMS (ESI–) *m/z*: [M – K] calcd for $C_{12}H_{13}BF_3O_2^-$: 257.09662, found: 257.09639.



Synthesis of **SI-19**: **SI-19** was prepared analogously to compound **6**, starting from **SI-13** (1.60 g, 6.28 mmol). **SI-19** was obtained as a white solid (1.14 g, 77 % Yield).

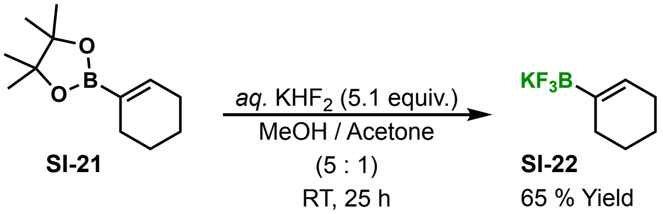
^{1}H NMR (500.27 MHz, acetone-*d*6) δ 3.95 (t, *J* = 7.5 Hz, 2H), 2.30-2.22 (m, 2H), 1.96 (s, 3H), 1.53 (br s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 171.16, 122.08, 65.04, 28.11, 28.01, 20.92, 14.75, 14.72.
^{11}B NMR (160.51 MHz, acetone-*d*6) δ 3.29.
^{19}F NMR (470.68 MHz, acetone-*d*6) δ –144.56 (minor), –146.29.
^{2}H{^{1}H} NMR (55.31 MHz, acetone-*h*6) δ 4.71.
IR (solid): 2969, 2911, 2857, 1731, 1646, 1631, 1249, 1220, 1206, 1017, 968, 933, 873, 844 cm^{-1}.
m.p. 84-91 °C
HRMS (ESI–) *m/z* [M – K] calcd for $C_7H_{10}DBF_3O_2^-$ 196.08724, found: 196.08702.



SI-17 **SI-20**, 66 % Yield

Synthesis of **SI-20**: To a 100-mL round-bottom flask open to air, **SI-17** (870.6 mg, 2.20 mmol) was combined with acetone (4 mL) and MeOH (4 mL) to afford a clear, pale yellow solution. While stirring at room temperature, saturated aqueous KHF_2 (4.5 M, 2.6 mL, 5.3 equiv.) was added dropwise by syringe, causing the reaction to turn slightly cloudy. The reaction was left to stir at room temperature for 91 hours. The reaction mixture was directly concentrated by rotary evaporation to remove the organic solvents. The remaining water was removed as an azeotrope with toluene (4 x 3 mL) to afford an off-white flaky solid, which was further dried under high vacuum for 2.75 hours. The trifluoroborate was extracted with acetone as follows. To the 100-mL flask containing the crude solid, was added acetone (10 mL). The mixture was swirled at room temperature, and subsequently filtered through cotton into a separate 100-mL round-bottom flask. This extraction process was repeated three more times, using 10 mL of acetone each time. The combined acetone extracts (clear, pale yellow) were concentrated to afford a yellow oil interspersed with a small amount of a white solid. Et_2O (5 mL) was added to this residue, and it was then re-concentrated. More Et_2O (5 mL) was added, and the contents of the flask were gently swirled. A white solid precipitated to afford a cloudy white suspension, which quickly turned to a white gel. This was suspended in additional Et_2O (50 mL). The suspension was poured onto a M glass frit, and **SI-20** was isolated by vacuum filtration. The product was rinsed with a copious amount of Et_2O (~ 100 mL total). After air-drying for ~ 40 minutes, **SI-20** was obtained as a white solid (546.6 mg, 66 % Yield).

^{1}H NMR (500.27 MHz, acetone-*d*6) δ. 8.00 (app dd, *J* = 8.3, 1.4 Hz, 2H), 7.63-7.59 (m, 1H), 7.49 (app t, *J* = 7.8 Hz, 2H), 7.18-7.13 (m, 2H), 6.90 (app t, *J* = 9.0 Hz, 2H), 5.82 (t, *J* = 7.2 Hz, 1H), 4.24 (t, *J* = 7.1 Hz, 2H), 2.36 (app q, *J* = 7.1 Hz, 2H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 166.79, 161.28 (d, *J* = 238.8 Hz), 143.01 (d, *J* = 3.2 Hz), 133.67, 131.62, 130.63 (d, *J* = 7.2 Hz), 130.17, 129.31, 124.95 (q, *J* = 3.0 Hz), 114.20 (d, *J* = 20.5 Hz), 65.97. *Allylic CH_2 signal overlaps with acetone solvent peak. **^{13}C NMR** (125.81 MHz, DMSO-*d*6) δ 165.70, 159.72 (d, *J* = 239.1 Hz), 141.71 (d, *J* = 3.0 Hz), 133.18, 129.93, 129.41 (d, *J* = 7.3 Hz), 129.05, 128.69, 123.76, 113.49 (d, *J* = 20.4 Hz), 73.50 (impurity), 64.94, 28.32 (allylic CH_2), 24.95 (impurity).
^{11}B NMR (160.51 MHz, acetone-*d*6) δ 2.66.
^{19}F NMR (470.68 MHz, acetone-*d*6) δ –122.14, –143.52.
m.p. 119-125 °C
IR (solid): 2952 (w), 1697, 1683, 1504, 1453, 1317, 1290, 1279, 1218, 1118, 979, 711 cm^{-1}.
HRMS (ESI–) *m/z* [M – K] calcd for $C_{17}H_{14}BF_4O_2$– 337.10285, found: 337.10276.



Synthesis of **SI-22**: In a 20-mL scintillation vial open to air, **SI-21**[16] (917.3 mg, 4.41 mmol) was dissolved in HPLC grade MeOH (5 mL) to afford a clear, colourless solution. While stirring at room temperature, saturated aqueous KHF_2 (4.5 M, 5 mL, 5.1 equiv.) was added dropwise by syringe to give a thick white suspension. Acetone (1 mL) was added to facilitate efficient stirring. The reaction was left to stir at room temperature for 25 hours. The reaction mixture was subsequently transferred to a 100-mL round-bottom flask, using acetone (3 x 5 mL) to thoroughly rinse the reaction vial. The crude reaction mixture was directly concentrated by rotary evaporation to remove the organic solvents. The remaining water was removed as an azeotrope with toluene (3 x 5 mL) to afford a crude white solid, which was further dried under high vacuum for 2 hours. The trifluoroborate was extracted with warm acetone as follows. To the 100-mL flask containing the crude white solid, was added acetone (20 mL). The mixture was swirled and gently heated with a heat gun, and subsequently filtered through cotton into a separate 100-mL round-bottom flask. This extraction process was repeated twice more, using 20 mL of acetone each time. The combined acetone extracts were concentrated to afford **SI-22** as a slightly oily white solid. Et_2O (20 mL) was added to give a suspension, and then it was re-concentrated to afford a drier solid. The solid was subsequently suspended in Et_2O (20 mL). **SI-22** was isolated by vacuum filtration on a M glass frit and rinsed with chilled Et_2O. After air-drying for ~ 20 minutes, **SI-22** was obtained as a white powder (538.5 mg, 65 % Yield).

^{1}H NMR (500.27 MHz, DMSO-*d6*) δ 5.45 (br s, 1H), 1.90-1.77 (m, 4H), 1.50-1.36 (m, 4H).
^{13}C NMR (125.81 MHz, DMSO-*d6*) δ 122.12, 26.48, 25.55, 23.22, 23.07.
^{11}B NMR (160.51 MHz, DMSO-*d6*) δ 2.56 (br).
^{19}F NMR (470.68 MHz, DMSO-*d6*) δ –142.58.
m.p. > 260 °C; the solid gradually decomposes without melting (turns from white to orange-brown) above 205 °C
IR (solid): 3030, 2929, 2838, 1640, 1447, 1340, 1271, 1201, 1176, 1132, 976, 921, 897, 830, 801, 726, 631, 513 cm^{-1}.
HRMS (ESI–) *m/z* [M – K] calcd for $C_6H_9BF_3^-$ 149.07549, found: 149.07547.

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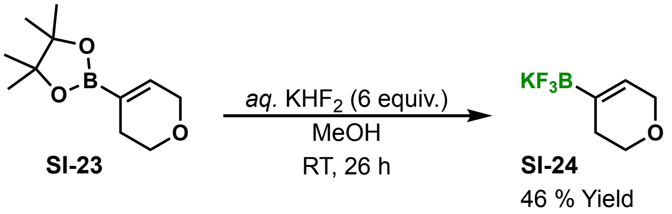
[16] **SI-21** was purchased from AK Scientific and used as received.



<u>Synthesis of **SI-24**:</u> In a 20-mL scintillation vial open to air, **SI-23**[17] (1.06 g, 5.04 mmol) was dissolved in HPLC grade MeOH (5 mL). While stirring at room temperature, saturated aqueous KHF_2 (4.5 M, 5.5 mL, 4.9 equiv.) was added dropwise by syringe. The reaction was only slightly cloudy. The reaction was left to stir at room temperature overnight (18 h). At this stage, TLC analysis indicated the presence of unreacted starting material. Solid KHF_2 (433 mg, 5.5 mmol, 1.1 equiv.) was added, and the reaction was stirred vigorously for another 8 hours at room temperature. The reaction mixture was subsequently transferred to a 100-mL round-bottom flask, using acetone to thoroughly rinse the reaction vial. The crude reaction mixture was directly concentrated by rotary evaporation to remove the organic solvents. The remaining water was removed as an azeotrope with toluene (5 x 5 mL) to afford a crude pale orange solid, which was further dried under high vacuum for 3 hours. The trifluoroborate was extracted with warm acetone as follows. To the 100-mL flask containing the crude white solid, was added acetone (20 mL). The mixture was swirled and gently heated with a heat gun, and subsequently filtered through cotton into a separate 100-mL round-bottom flask. This extraction process was repeated three more times, using 20 mL of acetone each time. The combined acetone extracts were concentrated to afford a static yellow-orange solid (~ 280 mg). A large amount of orange solid was left behind in the 100-mL flask. This remaining material was suspended in acetone, transferred to a 125-mL Erlenmeyer flask, and then vigorously boiled for ~ 5 min. The supernatant was filtered hot through cotton into a separate 100-mL flask and concentrated to give a pale yellow powder (~ 160 mg). For the remaining crude material, this hot extraction process was repeated once more to give more yellow powder (~ 82 mg). The solid extracts were combined on a M glass frit, isolated by vacuum filtration, and rinsed with Et_2O. **SI-24** was obtained as a pale orange solid (436.7 mg, 46 % Yield).

^{1}H NMR (500.27 MHz, DMSO-*d*6) δ 5.43 (br s, 1H), 3.89 (br s, 2H), 3.53 (t, *J* = 5.5 Hz, 2H), 1.95-1.87 (m, 2H).
^{13}C NMR (125.81 MHz, DMSO-*d*6) δ 122.00 (q, *J* = 3.1 Hz), 65.39, 64.06, 26.88.
^{11}B NMR (160.51 MHz, DMSO-*d*6) δ 2.25 (br).
^{19}F NMR (470.68 MHz, DMSO-*d*6) δ –143.33, –148.35 (minor impurity)
m.p. decomposes above 45 °C
IR (film): 2952, 2920, 2851, 2819, 1649, 1238, 1210, 1172, 1113, 1033, 989, 964, 915, 840, 812, 759, 651, 534, 499 cm^{-1}.
HRMS (ESI–) *m/z* [M – K] calcd for $C_5H_7BF_3O^-$ 151.05475, found: 151.05473.

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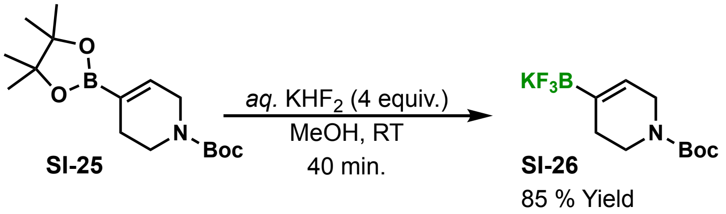
[17] **SI-23** was purchased from AK Scientific and used as received.



Synthesis of known[18] trifluoroborate **SI-26** using Molander's procedure:

While open to air, a 100-mL round-bottom flask was equipped with a magnetic stir bead and charged with **SI-25**[19] (1.55 g, 5.01 mmol) and HPLC grade MeOH (25 mL). The mixture was stirred vigorously. Additional MeOH (5 mL) was added to help **SI-25** dissolve. A solution of saturated aqueous (4.5 M) KHF_2 (4.5 mL, 20.25 mmol, 4 equiv.) was added dropwise via syringe at room temperature, causing the reaction to turn slightly cloudy. The reaction was stirred for ~ 40 minutes. TLC analysis indicated complete consumption of **SI-25**. The reaction was removed from stirring and concentrated to remove the MeOH. The remaining water was removed as an azeotrope with toluene (5 x 5 mL). The crude material was subsequently dried under hi-vacuum for 40 minutes to afford a sticky crude solid. The crude solid was suspended in Et_2O (~ 20 mL) and concentrated. This was repeated twice to afford a less-sticky solid that was easier to handle. To a 250-mL round-bottom flask was added acetone (165 mL). The crude solid was transferred to a Soxhlet extraction thimble. Soxhlet extraction was performed at 75 °C (bath temperature) for 19.5 hours. The extract was cooled to room temperature then concentrated to afford a clear, brownish oil. Et_2O (60 mL) was added to precipitate the product, but the material remained oily. The Et_2O was removed *in vacuo*. This process was repeated once more with the addition and concentration of more Et_2O (40 mL). The crude material was suspended in Et_2O (50 mL) and cooled to 0 °C for 5 minutes. A solid mixture looked slightly inhomogeneous (white solid + gummy orange solid). The product was isolated by pouring onto a M glass frit. The product was rinsed with copious amounts of Et_2O (300 mL) then air-dried for ~ 30 minutes. **SI-25** was obtained as an amorphous tan powder (1.23 g, 85 % Yield), whose ^{1}H NMR, ^{11}B NMR, ^{19}F NMR, and HRMS data were in good agreement with the literature.[18] **^{1}H NMR** (500.27 MHz, acetone-*d*6) δ 5.56 (br s, 1H), 3.72 (br s, 2H), 3.32 (t, *J* = 5.7 Hz, 2H), 2.09-2.03 (m, 2H, overlaps with acetone solvent peak), 1.42 (s, 9H). **^{11}B NMR** (160.51 MHz, acetone-*d*6) δ 2.89. **^{19}F NMR** (470.68 MHz, acetone-*d*6) δ –146.81, –152.13 (minor impurity). **HRMS (ESI–)** *m/z* [M – K] calcd for $C_{10}H_{16}BF_3NO_2$– 250.12317, found: 250.12308.

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[18] Presset, M.; Oehlrich, D.; Rombouts, F.; Molander, G. A. Copper-Mediated Radical Trifluoromethylation of Unsaturated Potassium Organotrifluoroborates. *J. Org. Chem.* **2013**, *78*, 12837–12843.

[19] **SI-25** was purchased from Oakwood and used as received.

Chan–Evans–Lam Coupling: Preliminary Optimization Experiments

General workflow for Chan–Evans–Lam screening experiments:

On the benchtop, an oven-dried 2–5 mL size Biotage microwave vial was charged with a magnetic stir flea, powdered 4 Å MS, DMAP, any additive(s), and the appropriate copper salt. 2-bromobenzyl alcohol was then added as a stock solution in DCM. When other solvents were used, the alcohol was first added as a solid followed by the solvent. The reaction vial was capped with a Teflon-lined silicone septum and sealed with a crimper. The septum was pierced with a vent needle and the vial headspace was sparged with oxygen using a needle connected to an oxygen supply. After sparging, the reaction mixture was allowed to stir vigorously at room temperature for 24 hours. The crude reaction mixture was filtered through a short Pasteur pipet plug of Celite® 545 and basic alumina that had been pre-equilibrated with EtOAc. The plug was rinsed with EtOAc (8 mL).[20] The filtrate was collected and concentrated in a 20-mL scintillation vial, and the mass of the crude residue was recorded. A stock solution of 4-bromoanisole was prepared in acetone-*d*6, and 0.3 mL of this stock solution was transferred via syringe to an NMR tube. Acetone-*d*6 (~ 0.3 mL) was added to the crude residue, and the resultant solution was transferred to the NMR tube via Pasteur pipet. The mass of the crude residue that was *not* transferred to the NMR tube was determined, and the mass of material in the NMR tube was determined by difference. The ^1H NMR was measured with a relaxation delay of 30 s. The NMR yield was determined by integration of the product relative to the internal standard.

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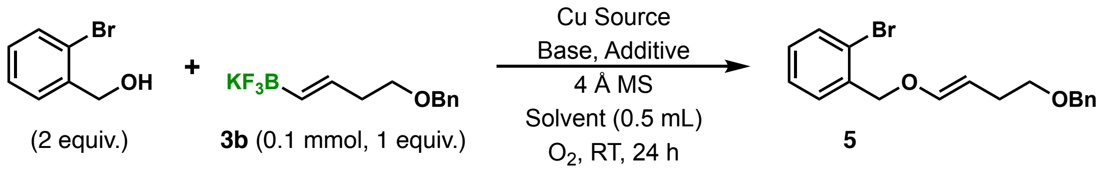
[20] When DMSO was used as the solvent, the crude filtrate was subsequently washed with water and brine, then extracted with Et_2O.

Table S1. Preliminary screening of copper sources for the Chan–Evans–Lam coupling.

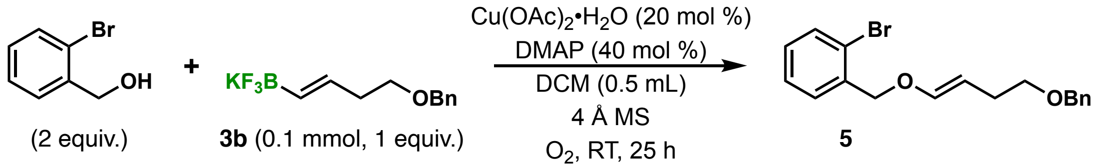


(2 equiv.) **3b** (0.1 mmol, 1 equiv.) **5**

Entry	Cu Source	Base	Additive	Solvent	NMR Yield[a]
1[b]	$Cu(OAc)_2{\cdot}H_2O$ (20 mol %)	DMAP (40 mol %)	/	DCM	48 %
2[c]	$Cu(OAc)_2$ (20 mol %)	DMAP (40 mol %)	/	DCM	83 %
3	$Cu(OAc)_2$ (20 mol %)	DMAP (40 mol %)	/	DCM	32 %
4[d]	$Cu(OAc)_2$ (20 mol %)	DMAP (40 mol %)	/	DCM	60 %
5	$Cu(OTf)_2$ (20 mol %)	DMAP (40 mol %)	/	DCM	49 %
6	$Cu(OTf)_2$ (20 mol %)	DMAP (40 mol %)	K_2CO_3 (200 mol %)	DCM	32 %
7	$Cu(OTf)_2$ (20 mol %)	DMAP (40 mol %)	/	MeCN	< 5 %
8	$Cu(acac)_2$ (20 mol %)	DMAP (40 mol %)	/	DCM	< 5 %
9	$CuSO_4{\cdot}5H_2O$ (20 mol %)	DMAP (40 mol %)	/	DCM	11 %
10	$CuCl_2$ (20 mol %)	DMAP (40 mol %)	/	DCM	29 %
11	CuI (20 mol %)	DMAP (40 mol %)	/	DCM	30 %
12	CuCl (20 mol %)	DMAP (40 mol %)	/	DCM	19 %
13	$CuBr{\cdot}SMe_2$ (20 mol %)	DMAP (40 mol %)	/	DCM	24 %
14	CuCl (40 mol %)	NEt_3 (300 mol %)	KPF_6 (120 mol %)	MeCN	7 %
15	CuCl (40 mol %)	DMAP (80 mol %)	KPF_6 (120 mol %)	MeCN	< 5 %
16	CuCl (40 mol %)	NEt_3 (300 mol %)	AgOTf (120 mol %)	MeCN	< 5 %
17	CuCl (40 mol %)	DMAP (80 mol %)	AgOTf (120 mol %)	MeCN	5 %

[a] Determined using 4-bromoanisole as internal standard.
[b] Reported yield is an average of three separate runs.
[c] Anomolously high & irreproducible yield.
[d] Using 3 equivalents of the alcohol coupling partner.

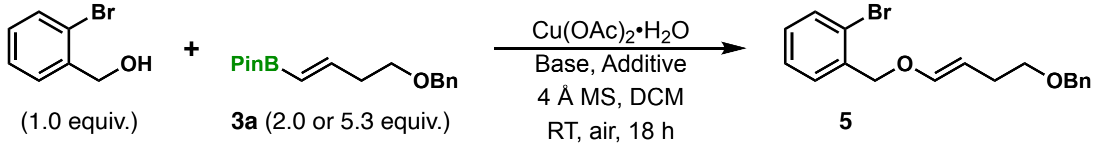
Table S2. Preliminary solvent and additive screening.



Entry	Deviation from Above Conditions	NMR Yield[a]
1	None	39 %
2	Exclusion of 4 Å MS	9 %
3	NEt_3 (3 equiv.) additive	22 %
4	MeCN instead of DCM	30 %
5	PhMe instead of DCM	7 %
6	DMSO instead of DCM[b]	< 5 %
7	DCM / Acetone (1 : 1) co-solvent[c]	< 5 %

[a] Determined using 4-bromoanisole as internal standard.
[b] Reaction was run for 24 h.
[c] Reaction was performed on 0.5 mmol scale.

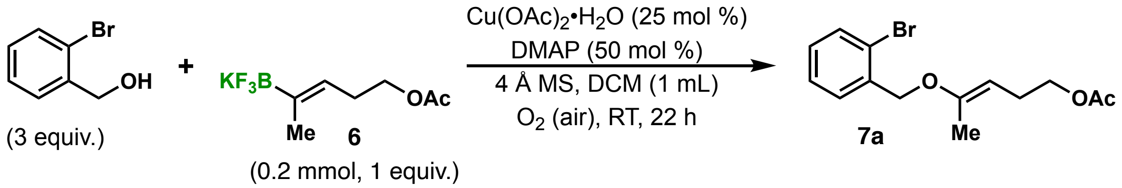
Table S3. Unsuccessful attempts for the Chan–Evans–Lam coupling using vinyl boronate **3a**.



Entry	Equiv. 3a	[Cu] (mol %)	Base	Additive	NMR Yield[a]
1	2.0	20	DMAP (40 mol %)	/	< 5 %
2	2.0	20	Pyridine (300 mol %)	/	< 5 %
3	2.0	100	Pyridine (300 mol %)	/	< 5 %
4	2.0	100	Pyridine (300 mol %)	3-hexyne (400 mol %)	< 5 %
5	5.3	200	Pyridine (300 mol %)	/	< 5 %

[a] Determined using 4-bromoanisole as internal standard.

Table S4. Ligand screening experiment for the synthesis of vinyl ether **7a**.



Entry	Deviation from Above Conditions	NMR Yield[a]
1	None	18 %
2	*N*-Methylimidazole (50 mol %) instead of DMAP	8 %
3	DABCO (50 mol %) instead of DMAP	< 5 %
4	2,2'-Bpy (27.5 mol %) instead of DMAP	< 5 %
5	Tetramethylguanidine (50 mol %) instead of DMAP	6 %
6	HMTA (50 mol %) instead of DMAP	< 5 %
7	Adamantyl-BippyPhos (27.5 mol %) instead of DMAP	< 5 %
8	2,6-Lutidine (50 mol %) instead of DMAP	< 5 %
9	Pyridine (50 mol %) instead of DMAP	< 5 %
10	$NaHCO_3$ (100 mol %) additive	20 %

[a]Determined using 4-bromoanisole as internal standard.

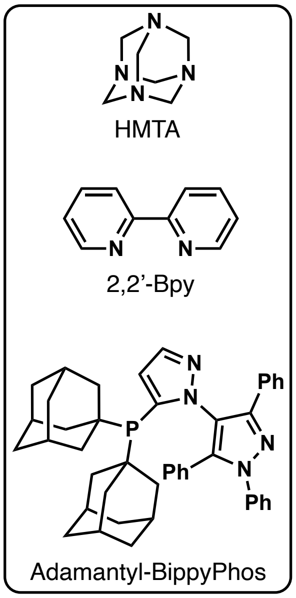
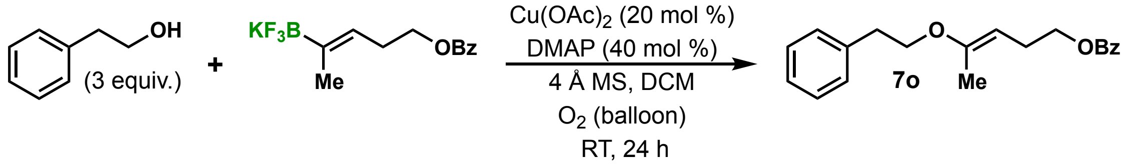


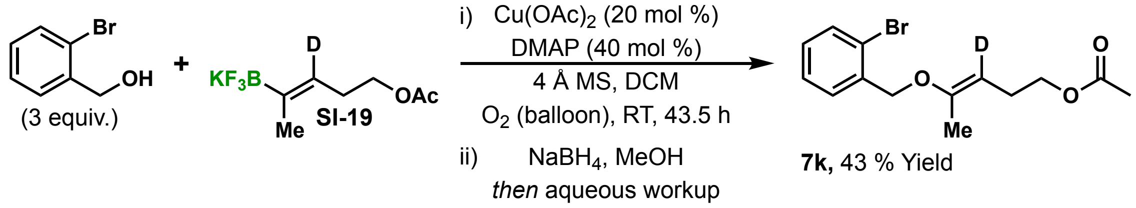
Table S5. Further reaction parameters tested for the synthesis of vinyl ether **7o**.



Entry	Deviation from Above Conditions	NMR Yield[a]
1	None	58 %
2	air atmosphere instead of O_2	14 %
3	$CHCl_3$ instead of DCM; 45 °C under air atmosphere	36 %
4	3-hexyne (80 mol %) additive[b]	11 %
5	$Mn(OAc)_3•2H_2O$ (3 equiv.) additive[b]	< 5 %

[a]Determined by ^1H NMR using 1,3,5-trimethoxybenzene as internal standard. Unless otherwise stated, reactions were performed on 0.2 mmol scale. [b]Performed on 0.5 mmol scale.

General Procedure for the Chan–Evans–Lam Coupling



7k, 43 % Yield

Representative procedure using the synthesis of **7k** as an example:

On the benchtop, a flame-dried 50-mL round-bottom flask was charged with a magnetic stir bead, trifluoroborate **SI-19** (235.8 mg, 1.0 mmol, 1 equiv.), powdered 4 Å MS[21] (400.3 mg, 400 mg•mmol^{-1}), anhydrous $Cu(OAc)_2$ (36.1 mg, 0.199 mmol, 20 mol %), DMAP (48.6 mg, 0.398 mmol, 40 mol %), and 2-bromobenzyl alcohol (565.3 mg, 3.02 mmol, 3 equiv.). The flask was equipped with a rubber septum and a large oxygen-filled balloon. While stirring the solids, the headspace was briefly (~ 2 min.) sparged. At room temperature, anhydrous DCM (3 mL) was then added by syringe to afford a turquoise suspension. The reaction was vigorously stirred at room temperature for 43.5 hours to afford a thick blue-green suspension. The crude reaction mixture was filtered through a layered[22] plug of basic alumina and Celite® 545 that had been equilibrated with EtOAc. The plug was thoroughly rinsed with EtOAc (40 mL), and the filtrate was concentrated.

$NaBH_4$ Treatment Step (Optional for Benzyl Vinyl Ethers):

While open to air, the crude residue was dissolved in HPLC grade MeOH (4 mL) and stirred at room temperature. $NaBH_4$ (18.6 mg, 0.49 mmol, 49 mol %) was added in a single portion, which caused the reaction to immediately effervesce and turn dark brownish orange. The reaction was stirred for 5 minutes, quenched with saturated aqueous NH_4Cl (1 mL), and subsequently diluted with water (10 mL) and EtOAc (10 mL).[23] The phases were separated, and then the aqueous phase was back extracted with EtOAc (3 x 5 mL). The combined organic extracts were washed with brine (1 x 15 mL), dried over anhydrous $MgSO_4$, and concentrated to afford the crude product (0.78 g) as an oily semi-solid. The crude product was adsorbed onto Celite® 545 (1.39 g) and loaded onto a SiO_2 column (equilibrated with hexanes). Gradient elution (100:0 → 40:1 hexanes / EtOAc with ~1 % v/v NEt_3) afforded **7k** as a clear, very pale yellow oil (137.1 mg, 43 % Yield).

^{1}H NMR (500.27 MHz, acetone-*d*6) δ 7.61 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.54-7.51 (m, 1H), 7.40 (td, *J* = 7.5, 1.3 Hz, 1H), 7.26 (td, *J* = 7.8, 1.8 Hz, 1H), 4.79 (s, 2H), 4.00 (t, *J* = 7.0 Hz, 2H), 2.33 (app q, *J* = 6.7 Hz, 2H), 1.98 (s, 3H), 1.87 (br s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 170.96, 154.96, 154.90 (minor), 137.66, 133.38, 130.28, 130.26, 128.54, 123.18, 94.21, 68.84, 64.86, 27.33 (minor), 27.23, 20.83, 16.35, 16.33 (minor).

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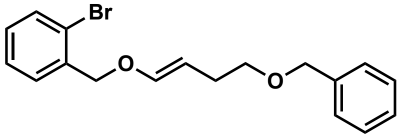
[21] 4 Å MS (–325 mesh) were purchased from Sigma-Aldrich. Prior to use, they were activated by flame-drying under vacuum and stored in an oven (~ 110 ºC).
[22] Using a 2 cm diameter plug; basic alumina (~ 1 cm) was layered on top of Celite® 545 (~ 2 cm).
[23] In general, the aqueous workup following the $NaBH_4$ treatment was essential for obtaining the desired products in high purity. Direct concentration of the reaction mixture followed by immediate chromatographic purification led to the isolation of the vinyl ether products contaminated with intractable benzyl acetate impurities.

^{2}H{^{1}H} NMR (55.31 MHz, acetone-*h*6) δ 3.82.
R$_f$ = 0.36 (9:1 Hexanes / EtOAc)
IR (film): 2954, 2926, 2895, 1738, 1668, 1655, 1244, 1029, 751 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{14}H_{16}DBrO_3Na+$ 336.03160, found: 336.03164.

Characterization of Chan–Evans–Lam Products

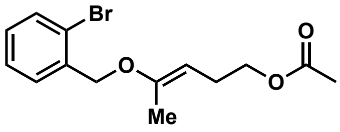


5, 60 % NMR Yield

Compound **5**:

*Crude reaction mixture was not treated with $NaBH_4$

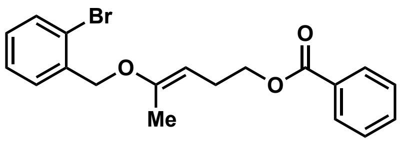
Physical State: Clear, slightly pale-yellow oil
^{1}H NMR (500.27 MHz, acetone-*d*6) δ 7.61 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.51 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.40 (td, *J* = 7.5, 1.2 Hz, 1H), 7.35-7.32 (m, 4H), 7.28-7.25 (m, 2H), 6.49 (d, *J* = 12.6 Hz, 1H), 4.96 (dt, *J* = 12.6, 7.4 Hz, 1H), 4.81 (s, 2H), 4.50 (br s, 2H), 3.46 (t, *J* = 6.7 Hz, 2H), 2.24 (dt, *J* = 7.4, 6.7 Hz, 2H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 148.04, 140.02, 137.65, 133.40, 130.37, 130.25, 129.03, 128.55, 128.27, 128.09, 123.08, 102.23, 73.12, 71.60, 70.99, 29.07.
R$_f$ = 0.44 (9:1 Hexanes / EtOAc)
IR: 3062, 3030, 2930, 2907, 2854, 2790, 1673, 1653, 1570, 1496, 1471, 1453, 1442, 1362, 1214, 1156, 1097, 1027, 929, 748, 736, 697 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{18}H_{19}BrO_2Na+$ 369.04606, found: 369.04612.



7a, up to 55 % Yield

Compound **7a**: up to 55 % Yield (0.7 mmol scale)

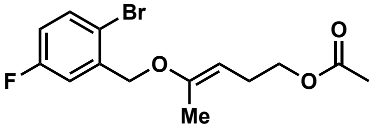
Physical State: Clear, colourless oil
^{1}H NMR (500.27 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.53 (app ddd, *J* = 7.7, 1.5, 0.6 Hz, 1H), 7.40 (td, *J* = 7.5, 1.2 Hz, 1H), 7.26 (app tdd, *J* = 7.7, 1.7, 0.5 Hz, 1H), 4.78 (s, 2H), 4.55 (t, *J* = 7.5 Hz, 1H), 4.00 (t, *J* = 7.1 Hz, 2H), 2.33 (dt, *J* = 7.6, 7.1 Hz, 2H), 1.98 (s, 3H), 1.87 (q, *J* = 0.7 Hz, 3H).
^{13}C NMR (125.81 MHz, $CDCl_3$) δ 170.94, 154.92, 137.60, 133.34, 130.24, 130.21, 128.51, 123.15, 94.16, 68.80, 64.84, 27.30, 20.83, 16.35.
R$_f$ = 0.21 (20:1 Hexanes / EtOAc)
IR: 3073, 2958, 2923, 2897, 1736, 1668, 1570, 1229, 1188, 1027, 748 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{14}H_{17}BrO_3Na+$ 335.02532, found: 335.02563.



7b, 41 % Yield

Compound **7b**: 41 % Yield (0.5 mmol scale)

Physical State: Clear, colourless oil
^{1}H NMR (500 MHz, acetone-*d6*) δ 8.02 (app dd, *J* = 8.4, 1.4 Hz, 2H), 7.63 (app tt, *J* = 7.4, 1.3 Hz, 1H), 7.60 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.54-7.49 (m, 3H), 7.37 (td, *J* = 7.5, 1.3 Hz, 1H), 7.24 (td, *J* = 7.7, 1.8 Hz, 1H), 4.82 (s, 2H), 4.65 (t, *J* = 7.7 Hz, 1H), 4.29 (t, *J* = 6.8 Hz, 2H), 2.51 (q, *J* = 7.1 Hz, 2H), 1.91 (br s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d6*) δ 166.77, 155.02, 137.64, 133.81, 133.37, 131.50, 130.27, 130.24, 130.17, 129.39, 128.52, 123.18, 94.39, 68.89, 65.60, 27.44, 16.42.
R$_f$ = 0.31 (20:1 Hexanes / EtOAc)
ATR-IR (neat oil): 3060, 2955, 2892, 1718, 1669, 1451, 1272, 1110, 1021, 750, 711 cm^{-1}.
HRMS (ESI+) *m/z*: [M + Na] calcd for $C_{19}H_{19}BrO_3Na+$: 397.04098, found: 397.04131.

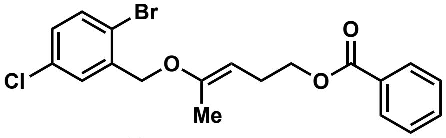


7c, 43 % Yield

Compound **7c**: 43 % Yield (1.0 mmol scale)

*Crude reaction mixture was not treated with $NaBH_4$

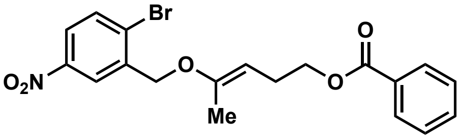
Physical State: Clear, slightly pale yellow oil
^{1}H NMR (500.27 MHz, acetone-*d6*) δ 7.64 (dd, *J* = 8.8, 5.2 Hz, 1H), 7.30 (ddt, *J* = 9.6, 3.2, 0.8 Hz, 1H), 7.08 (app td, *J* = 8.5, 3.2 Hz, 1H), 4.78 (s, 2H), 4.54 (t, *J* = 7.5 Hz, 1H), 4.00 (t, *J* = 7.0 Hz, 2H), 2.34 (app q, *J* = 7.1 Hz, 2H), 1.98 (s, 3H), 1.90 (br s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d6*) δ 170.94, 163.06 (d, *J* = 244.9 Hz), 154.68, 140.23 (d, *J* = 7.9 Hz), 134.89 (d, *J* = 8.1 Hz), 117.00 (d, *J* = 22.9 Hz), 116.79 (d, *J* = 3.3 Hz), 116.61 (d, *J* = 24.3 Hz), 94.66, 68.26, 64.79, 27.29, 20.81, 16.29.
^{19}F NMR (282.51 MHz, acetone-*d6*) δ –114.41 (minor impurity), –115.91.
R$_f$ = 0.52 (4:1 Hexanes / EtOAc)
IR: 3077, 2955, 2927, 2898, 1738, 1670, 1581, 1470, 1366, 1267, 1239, 1194, 1031, 874, 809, 597 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{14}H_{16}BrFO_3Na+$ 353.01591, found: 353.01573.



7d, 53 % Yield

Compound **7d**: 53 % Yield (1.0 mmol scale)

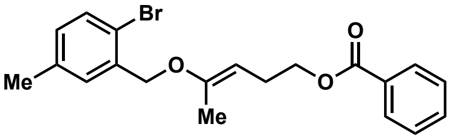
Physical State: Clear, colourless oil that solidified upon storage at –20 °C to give a white solid
^{1}H NMR (500.27 MHz, acetone-*d*6) δ 8.02 (app dd, *J* = 8.4, 1.3 Hz, 2H), 7.66-7.59 (m, 2H), 7.54-7.48 (m, 3H), 7.29 (dd, *J* = 8.5, 2.6 Hz, 1H), 4.81 (s, 2H), 4.66 (t, *J* = 7.5 Hz, 1H), 4.30 (t, *J* = 6.8 Hz, 2H), 2.51 (q, *J* = 7.1 Hz, 2H), 1.93 (br s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 166.77, 154.83, 139.84, 134.83, 134.16, 133.81, 131.47, 130.16, 130.05, 129.61, 129.39, 120.90, 94.85, 68.32, 65.56, 27.41, 16.38.
R$_f$ = 0.39 (9:1 Hexanes / EtOAc)
m.p. 40-43 °C
IR (film): 3067, 2955, 2926, 2895, 1718, 1670, 1452, 1272, 1108, 1098, 1027, 810, 711 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{19}H_{18}BrClO_3Na+$ 431.00200, found: 431.00218.



7e, 40 % Yield

Compound **7e**: 40 % Yield (1.0 mmol scale)

Physical State: Pale yellow solid
^{1}H NMR (500.27 MHz, acetone-*d*6) δ 8.31 (d, *J* = 2.8 Hz, 1H), 8.09 (dd, *J* = 8.7, 2.8 Hz, 1H), 8.00 (app dd, *J* = 8.3, 1.4 Hz, 2H), 7.90 (d, *J* = 8.7 Hz, 1H), 7.63 (app tt, *J* = 7.4, 1.3 Hz, 1H), 7.50 (app t, *J* = 7.8 Hz, 2H), 4.92 (s, 2H), 4.70 (t, *J* = 7.5 Hz, 1H), 4.30 (t, *J* = 6.8 Hz, 2H), 2.52 (q, *J* = 7.0 Hz, 2H), 1.97 (br s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 166.74, 154.63, 148.47, 139.95, 134.73, 133.82, 131.42, 130.13, 129.71, 129.38, 124.60, 124.08, 95.37, 68.12, 65.51, 27.40, 16.38.
R$_f$ = 0.46 (4:1 Hexanes / EtOAc)
m.p. 63-68 °C
IR (film): 3109, 2953, 2897, 2859, 1713, 1665, 1523, 1341, 1291, 1272, 1102, 709 cm^{-1}.



7f, 36 % Yield

Compound **7f**: 36 % Yield (1.0 mmol scale)

Physical State: Low-melting yellow solid

^{1}H NMR (500.27 MHz, acetone-*d*6) δ 8.02 (app dd, *J* = 8.3, 1.4 Hz, 2H), 7.63 (app tt, *J* = 7.4, 1.3 Hz, 1H), 7.53-7.49 (m, 2H), 7.45 (d, *J* = 8.1 Hz, 1H), 7.33 (d, *J* = 2.2 Hz, 1H), 7.06 (dd, *J* = 8.1, 2.3 Hz, 1H), 4.77 (s, 2H), 4.65 (t, *J* = 7.5 Hz, 1H), 4.29 (t, *J* = 6.8 Hz, 2H), 2.51 (q, *J* = 7.1 Hz, 2H), 2.29 (s, 3H), 1.90 (br s, 3H).

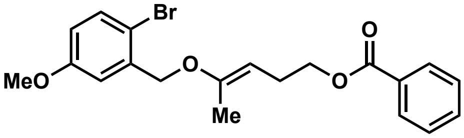
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 166.78, 155.10, 138.46, 137.21, 133.80, 133.10, 131.50, 131.01, 130.97, 130.16, 129.39, 119.91, 94.30, 68.93, 65.64, 27.45, 20.89, 16.44.

R_f = 0.56 (4:1 Hexanes / EtOAc)

m.p. Melts at slightly above room temperature (~ 26 °C on a warm day); solidifies upon storage at –20 °C.

IR (film): 3062, 2953, 2923, 2895, 1717, 1668, 1271, 1108, 710 cm^{-1}.

HRMS (ESI+) *m/z* [M + Na] calcd for $C_{20}H_{21}BrO_3Na+$ 411.05663, found: 411.05673.



7g, 25 % Yield

Compound **7g**: 25 % Yield (0.7 mmol scale)

Physical State: Low-melting off white solid

^{1}H NMR (500.27 MHz, acetone-*d*6) δ 8.03-8.00 (m, 2H), 7.65-7.61 (m, 1H), 7.53-7.49 (m, 2H), 7.47 (d, *J* = 8.8 Hz, 1H), 7.09 (d, *J* = 3.1 Hz, 1H), 6.83 (dd, *J* = 8.7, 3.1 Hz, 1H), 4.77 (s, 2H), 4.64 (t, *J* = 7.5 Hz, 1H), 4.29 (t, *J* = 6.8 Hz, 2H), 3.79 (s, 3H), 2.50 (app q, *J* = 7.0 Hz, 2H), 1.91 (br s, 3H).

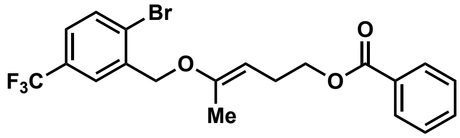
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 166.78, 160.31, 154.98, 138.60, 133.99, 133.80, 131.49, 130.17, 129.39, 115.89, 115.63, 113.10, 94.47, 68.84, 65.63, 55.85, 27.43, 16.42.

R_f = 0.32 (9:1 Hexanes / EtOAc)

m.p. Melts at slightly above room temperature (~26 °C on a warm day); solidifies upon storage at –20 °C.

IR (film): 3066, 2954, 2838, 1718, 1670, 1273, 1110, 712 cm^{-1}.

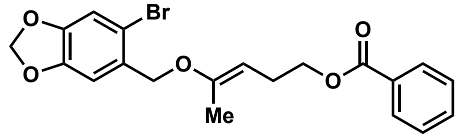
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{20}H_{21}BrO_4Na+$ 427.05154, found: 427.05166.



7h, 61 % Yield

Compound **7h**: 61 % Yield (1.0 mmol scale)

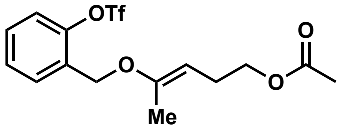
Physical State: Clear, colourless oil that solidified upon storage at –20 °C to give a white solid
^{1}H NMR (500.27 MHz, acetone-*d*6) δ 8.03-7.99 (m, 2H), 7.85 (d, *J* = 8.3 Hz, 1H), 7.82 (d, *J* = 2.3 Hz, 1H), 7.66-7.61 (m, 1H), 7.59 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.51 (app t, *J* = 7.8 Hz, 2H), 4.89 (s, 2H), 4.70 (t, *J* = 7.5 Hz, 1H), 4.30 (t, *J* = 6.8 Hz, 2H), 2.52 (q, *J* = 7.1 Hz, 2H), 1.94 (s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 166.77, 154.83, 139.29, 134.45, 133.81, 131.47, 130.36 (q, *J* = 32.9 Hz), 130.15, 129.39, 127.22, 126.78 (q, *J* = 3.6 Hz), 126.43 (q, *J* = 3.9 Hz), 124.99 (q, *J* = 271.3 Hz), 95.00, 68.35, 65.56, 27.41, 16.36.
^{19}F NMR (470.68 MHz, acetone-*d*6) δ –63.24.
R_f = 0.43 (9:1 Hexanes / EtOAc)
m.p. 49-54 °C
IR (film): 3070, 2956, 2926, 2895, 1718, 1671, 1327, 1272, 1169, 1125, 1081, 711 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{20}H_{18}BrF_3O_3Na+$ 465.02836, found: 465.02878.



7i, 39 % Yield

Compound **7i**: 39 % Yield (0.65 mmol scale)

Physical State: Clear, colourless oil that solidified upon storage at –20 °C to give a white solid
^{1}H NMR (500.27 MHz, acetone-*d*6) δ 8.03-8.00 (m, 2H), 7.63 (app tt, *J* = 7.4, 1.3 Hz, 1H), 7.53-7.49 (m, 2H), 7.06 (s, 1H), 7.00 (s, 1H), 6.04 (s, 2H), 4.71 (s, 2H), 4.62 (t, *J* = 7.5 Hz, 1H), 4.29 (t, *J* = 6.8 Hz, 2H), 2.50 (q, *J* = 7.0 Hz, 2H), 1.89 (br s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 166.77, 154.99, 149.05, 148.64, 133.80, 131.49, 130.87, 130.16, 129.38, 113.64, 113.11, 110.01, 103.04, 94.34, 68.84, 65.63, 27.43, 16.42.
R_f = 0.36 (9:1 Hexanes / EtOAc)
m.p. 57-60 °C
IR (solid): 3093, 3064, 3034, 2993, 2956, 2924, 2897, 1720, 1659, 1489, 1451, 1381, 1286, 1269, 1256, 1249, 1120, 1105, 1096, 705, 681 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{20}H_{19}BrO_5Na+$ 441.03081, found: 441.03142.

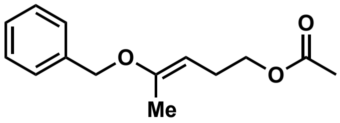


7j, 51 % Yield

Compound **7j**: 51 % Yield (Two parallel reactions were performed on 1.3 and 1.2 mmol scale, and then combined for purification)

*Crude reaction mixture was not treated with $NaBH_4$

Physical State: Clear, colourless oil
^{1}H NMR (500.27 MHz, acetone-*d*6) δ 7.67 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.61-7.50 (m, 2H), 7.45 (dd, *J* = 8.1, 1.3 Hz, 1H), 4.86 (s, 2H), 4.57 (t, *J* = 7.5 Hz, 1H), 3.99 (t, *J* = 7.0 Hz, 2H), 2.33 (q, *J* = 7.1 Hz, 2H), 1.98 (s, 3H), 1.85 (br s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 170.96, 154.98, 148.61, 131.85, 131.37, 131.10, 129.72, 122.32, 119.49 (q, *J* = 319.3 Hz), 94.23, 64.83, 64.16, 27.26, 20.78, 16.29.
^{19}F NMR (470.68 MHz, acetone-*d*6) δ –75.22.
R_f = 0.24 (9:1 Hexanes / EtOAc)
IR: 2957, 2933, 1738, 1671, 1491, 1421, 1247, 1206, 1138, 1093, 1070, 1034, 893, 767 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{15}H_{17}F_3O_6SNa+$ 405.05901, found: 405.05909.

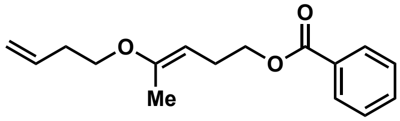


7l, 26 % Yield

Compound **7l**: 26 % Yield (0.6 mmol scale)

*Crude reaction mixture was not treated with $NaBH_4$

Physical State: Clear, colourless oil
^{1}H NMR (500.27 MHz, acetone-*d*6) δ 7.40-7.27 (m, 5H), 4.73 (s, 2H), 4.54 (t, *J* = 7.5 Hz, 1H), 3.99 (t, *J* = 7.1 Hz, 2H), 2.32 (q, *J* = 7.2 Hz, 2H), 1.98 (s, 3H), 1.84 (br s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 170.97, 155.19, 138.72, 129.12, 128.33, 128.25, 93.72, 69.26, 64.95, 27.36, 20.83, 16.48.
R_f = 0.29 (9:1 Hexanes / EtOAc)
IR (film): 3068, 3033, 2954, 2928, 2897, 2871, 1737, 1667, 1455, 1384, 1365, 1232, 1190, 1030, 738, 697 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{14}H_{18}O_3Na+$ 257.11481, found: 257.11466.

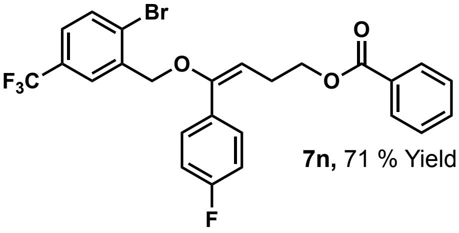


7m, 24 % Yield

Compound **7m**: 24 % Yield (0.5 mmol scale)

*Crude reaction mixture was not treated with $NaBH_4$

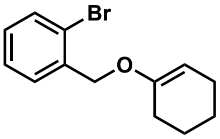
Physical State: Clear, colourless oil
^{1}H NMR (300.27 MHz, acetone-*d6*) δ 8.06-7.99 (m, 2H), 7.67-7.59 (m, 1H), 7.55-7.47 (m, 2H), 5.85 (ddt, *J* = 17.1, 10.2, 6.7 Hz, 1H), 5.09 (app dq, *J* = 17.3, 1.8 Hz, 1H), 5.01 (app ddt, 10.3, 2.4, 1.2 Hz, 1H), 4.49 (t, *J* = 7.5 Hz, 1H), 4.26 (t, *J* = 7.0 Hz, 2H), 3.68 (t, *J* = 6.7 Hz, 2H), 2.46 (q, *J* = 7.2 Hz, 2H), 2.38 (app q, *J* = 6.7 Hz, 2H), 1.80 (br s, 3H).
^{13}C NMR (75.51 MHz, acetone-*d6*) δ 166.76, 155.36, 136.08, 133.78, 131.47, 130.12, 129.36, 116.74, 92.85, 66.47, 65.73, 34.22, 27.43, 16.49.
R_f = 0.30 (98.5:1.5 Hexanes / EtOAc)
IR (neat): 3073, 2952, 2922, 2869, 1717, 1667, 1451, 1382, 1269, 1194, 1107, 1070, 1026, 916, 798, 709 cm^{-1}.
HRMS (ESI+) *m/z*: [M + H] calcd for $C_{16}H_{21}O_3$+: 261.14852, found: 261.14868.



7n, 71 % Yield

Compound **7n**: 71 % Yield (0.3 mmol scale)

Physical State: Clear, colourless oil that solidified upon storage at –20 °C to give a white solid
^{1}H NMR (500.27 MHz, acetone-*d6*) δ 8.00-7.97 (m, 2H), 7.89-7.85 (m, 2H), 7.66-7.59 (m, 2H), 7.56 (app dd, *J* = 8.6, 5.6 Hz, 2H), 7.51 (app t, *J* = 7.8 Hz, 2H), 7.18 (t, *J* = 8.8 Hz, 2H), 5.12 (t, *J* = 7.5 Hz, 1H), 5.06 (s, 2H), 4.35 (t, *J* = 6.6 Hz, 2H), 2.59 (q, *J* = 6.9 Hz, 2H).
^{13}C NMR (125.81 MHz, acetone-*d6*) δ 166.70, 163.53 (d, *J* = 246.0 Hz), 155.85, 139.03, 134.59, 133.86, 132.88 (d, *J* = 3.4 Hz), 131.83 (d, *J* = 8.4 Hz), 131.35, 130.40 (q, *J* = 32.2 Hz), 130.19, 129.39, 127.79, 127.09 (app pentet, *J* = 3.4 Hz; two overlapping quartets), 124.94 (q, *J* = 271.5 Hz), 115.87 (d, *J* = 21.6 Hz), 99.13, 69.59, 65.50, 28.11.
^{19}F NMR (470.68 MHz, acetone-*d6*) δ –63.24, –114.34.
R_f = 0.38 (9:1 Hexanes / EtOAc)
m.p. 45-49 °C
IR (film): 3064, 2957, 2898, 1717, 1655, 1604, 1510, 1328, 1272, 1231, 1170, 1124, 1097, 1081, 1027, 842, 826, 711 cm^{-1}.
HRMS (ESI+) *m/z* [M + H] calcd for $C_{25}H_{20}BrF_4O_3$+ 523.05265, found: 523.05292.

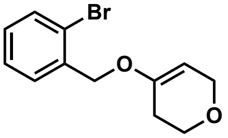


7p, 38 % Yield

Compound **7p**: 38 % Yield (0.6 mmol scale)

*Crude reaction mixture was not treated with $NaBH_4$

Physical State: Clear, colourless oil
^{1}H NMR (500.27 MHz, acetone-*d6*) δ 7.59 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.51 (app dd, *J* = 7.7, 1.7 Hz, 1H), 7.38 (td, *J* = 7.5, 1.2 Hz, 1H), 7.24 (td, *J* = 7.7, 1.8 Hz, 1H), 4.80 (s, 2H), 4.78 (t, *J* = 3.9 Hz, 1H), 2.13-2.11 (m, 2H), 2.11-2.00 (m, 2H, overlaps with acetone solvent peak), 1.72-1.63 (m, 2H), 1.59-1.49 (m, 2H).
^{13}C NMR (125.81 MHz, acetone-*d6*) δ 155.04, 137.92, 133.33, 130.17, 130.16, 128.51, 123.09, 95.44, 68.47, 28.38, 24.15, 23.60, 23.42.
R_f = 0.31 (Hexanes)
m.p. melts upon sitting at room temperature (23 °C); Freezes to a white solid at –20 °C.
IR (film): 3067, 2928, 2858, 2841, 1667, 1442, 1366, 1209, 1182, 1169, 1026, 783, 747 cm^{-1}.
HRMS (ESI+) *m/z* [M + H] calcd for $C_{13}H_{16}BrO+$ 267.03791, found: 267.03809.

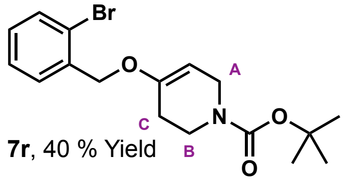


7q, 40 % Yield

Compound **7q**: 40 % Yield (0.6 mmol scale)

*Crude reaction mixture was not treated with $NaBH_4$

Physical State: Clear, colourless oil that solidified upon storage at –20 °C to give a white solid
^{1}H NMR (500.27 MHz, acetone-*d6*) δ 7.62 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.54 (ddd, *J* = 7.7, 1.8, 0.9 Hz, 1H), 7.41 (td, *J* = 7.5, 1.2 Hz, 1H), 7.27 (ddd, *J* = 8.0, 7.4, 1.7 Hz, 1H), 4.85 (s, 2H), 4.81 (app dq, *J* = 2.8, 1.4 Hz, 1H), 4.13 (dt, *J* = 2.8, 2.3 Hz, 2H), 3.78 (t, *J* = 5.6 Hz, 2H), 2.21 (ttd, *J* = 5.6, 2.2, 1.1 Hz, 2H).
^{13}C NMR (125.81 MHz, acetone-*d6*) δ 152.50, 137.43, 133.42, 130.40, 130.37, 128.58, 123.28, 95.02, 68.70, 64.99, 64.86, 28.91.
R_f = 0.29 (9:1 Hexanes / EtOAc)
m.p. 32-37 °C
IR (film): 3059, 2964, 2932, 2852, 2819, 2757, 1672, 1358, 1233, 1216, 1180, 1130, 1023, 852, 771, 749, 738 cm^{-1}.
HRMS (ESI+) *m/z* [M + H] calcd for $C_{12}H_{14}BrO_2+$ 269.01717, found: 269.01724.

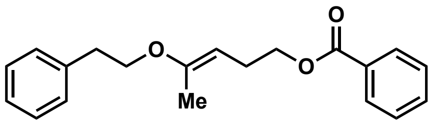


7r, 40 % Yield

Compound **7r**: 40 % Yield (0.6 mmol scale)

*Crude reaction mixture was not treated with $NaBH_4$

Physical State: Clear, colourless oil that solidified upon storage at –20 °C to give a white solid. *Isolated as a solvate with Et_2O despite drying under high vacuum.
^{1}H NMR (500.27 MHz, acetone-*d*6) δ 7.62 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.54 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.41 (td, *J* = 7.6, 1.2 Hz, 1H), 7.27 (td, *J* = 7.7, 1.8 Hz, 1H), 4.84 (s, 2H), 4.80 (br s, 1H), 3.92 (br s, 2H), 3.56 (t, *J* = 5.9 Hz, 2H), 2.25-2.19 (m, 2H), 1.45 (s, 9H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 155.00, 153.64, 137.37, 133.43, 130.44, 130.42, 128.59, 123.32, 93.56, 79.57, 69.01, 42.69 (C_A), 40.53 (C_B), 32.31 (tentatively assigned as C_C), 28.57.
R_f = 0.31 (9:1 Hexanes / EtOAc)
m.p. 54-59 °C
IR (film): 3073, 2975, 2930, 2865, 2840, 1693, 1679, 1418, 1364, 1160, 1113, 1024, 772, 751 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{17}H_{22}BrNO_3Na+$ 390.06753, found: 390.06782.

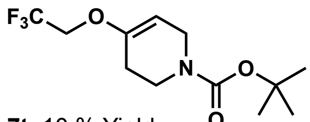


7s, 31 % Yield

Compound **7s**: 31 % Yield (0.4 mmol scale)

*Crude reaction mixture was not treated with $NaBH_4$

Physical State: Clear, colourless oil
^{1}H NMR (500.27 MHz, acetone-*d*6) δ 8.03-8.00 (m, 2H), 7.65-7.60 (m, 1H), 7.53-7.48 (m, 2H), 7.32-7.16 (m, 5H), 4.51 (t, *J* = 7.5 Hz, 1H), 4.26 (t, *J* = 6.9 Hz, 2H), 3.85 (t, *J* = 6.9 Hz, 2H), 2.94 (t, *J* = 6.9 Hz, 2H), 2.46 (app q, *J* = 7.2 Hz, 2H), 1.80 (br s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 166.78, 155.26, 139.88, 133.79, 131.51, 130.14, 129.81, 129.38, 129.12, 127.02, 93.05, 68.04, 65.74, 36.16, 27.45, 16.53.
R_f = 0.20 (40:1 Hexanes / EtOAc spiked with ~1 % v/v NEt_3)
IR (film): 3063, 3029, 2952, 2924, 2869, 1717, 1667, 1452, 1271, 1108, 711, 700 cm^{-1}
HRMS (ESI+) *m/z* [M + H] calcd for $C_{20}H_{23}O_3+$: 311.16417, found: 311.16435.

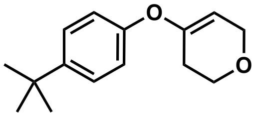


7t, 10 % Yield

Compound **7t**: 10 % Yield (0.6 mmol scale)

*Crude reaction mixture was not treated with $NaBH_4$

Physical State: White solid film
^{1}H NMR (500.27 MHz, acetone-*d6*) δ 4.86 (br s, 1H), 4.31 (q, *J* = 8.6 Hz, 2H), 3.91 (br s, 2H), 3.55 (t, *J* = 5.9 Hz, 2H), 2.21-2.17 (m, 2H), 1.44 (s, 9H).
^{13}C NMR (125.81 MHz, acetone-*d6*) δ 154.93, 152.87, 124.87 (q, *J* = 276.3 Hz), 94.88, 79.72, 64.83 (q, *J* = 35.0 Hz), 42.09 (assigned by HSQC), 40.93 (assigned by HSQC), 28.54, 28.12.
^{19}F NMR (470.68 MHz, acetone-*d6*) δ –74.62.
R_f = 0.22 (9:1 Hexanes / EtOAc)
IR (film): 2978, 2937, 2873, 2845, 1694, 1422, 1285, 1159, 1116, 976, 863, 772, 666 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{12}H_{18}F_3NO_3Na^+$ 304.11310, found: 304.11334.

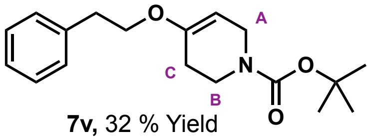


7u, 31 % Yield

Compound **7u**: 31 % Yield (0.6 mmol scale)

*Crude reaction mixture was not treated with $NaBH_4$

Physical State: Yellow oil that solidified upon storage at –20 °C to give a yellow solid
^{1}H NMR (500.27 MHz, acetone-*d6*) δ 7.40 (d, *J* = 8.7 Hz, 2H), 6.96 (d, *J* = 8.7 Hz, 2H), 4.79 (tt, *J* = 2.8, 1.2 Hz, 1H), 4.09 (q, *J* = 2.6 Hz, 2H), 3.82 (t, *J* = 5.5 Hz, 2H), 2.30-2.25 (m, 2H), 1.31 (s, 9H).
^{13}C NMR (125.81 MHz, acetone-*d6*) δ 153.75, 152.39, 147.16, 127.23, 120.27, 103.07, 64.84, 64.82, 34.85, 31.80 (minor), 31.77, 28.33.
R_f = 0.32 (9:1 Hexanes / EtOAc)
m.p. 37-43 °C
IR (film): 3038, 2961, 2905, 2865, 2823, 1678, 1506, 1464, 1364, 1222, 1176, 1129, 863, 850, 830, 578 cm^{-1}.
HRMS (ESI+) *m/z* [M + H] calcd for $C_{15}H_{21}O_2^+$ 233.15361, found: 233.15374.



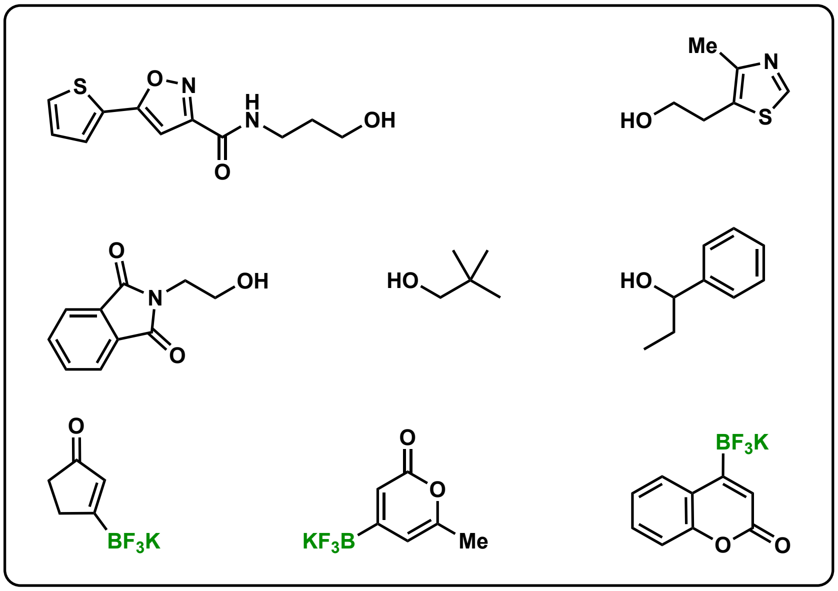
7v, 32 % Yield

Compound **7v**: 32 % Yield (0.6 mmol scale)

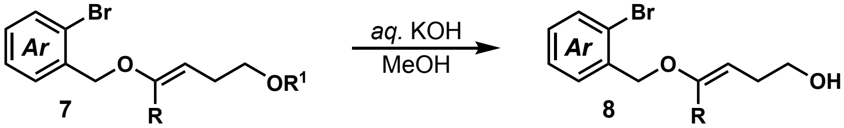
*Crude reaction mixture was not treated with NaBH$_4$

Physical State: Colourless oil
^{1}H NMR (500.27 MHz, acetone-*d*6) δ 7.31-7.26 (m, 4H), 7.23-7.18 (m, 1H), 4.65 (br s, 1H), 3.88 (t, *J* = 6.9 Hz, 2H), 3.88 (m, 2H), 3.50 (t, *J* = 5.9 Hz, 2H), 2.96 (t, *J* = 6.9 Hz, 2H), 2.12-2.08 (m, 2H), 1.44 (s, 9H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 154.95, 153.73, 139.68, 129.77, 129.12, 127.05, 92.42, 79.47, 68.12, 42.66 (C$_A$ conformer), 42.11 (C$_A$ conformer), 41.68 (C$_B$ conformer), 40.48 (C$_B$ conformer), 36.08, 28.72 (C$_C$), 28.57.
R$_f$ = 0.40 (9:1 Hexanes / EtOAc)
IR (film): 3063, 3028, 2975, 2932, 2870, 2840, 1733, 1694, 1676, 1417, 1364, 1159, 1113, 1029, 769, 750, 699 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{18}H_{25}NO_3Na+$ 326.17266, found: 326.17263.

Incompatible Substrates for the Chan–Evans–Lam Coupling



Procedures for Acetate and Benzoate Cleavage Reactions

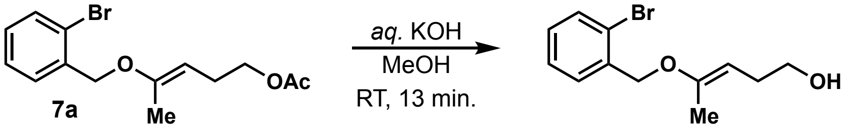


R = Me or 4-F-Ph
R^1 = Ac or Bz

N.B. In contrast to the acetate substrates, benzoate substrates generally had poor solubility in methanol. Consequently, benzoate substrates typically required longer reaction times (several hours) and/or higher temperature (40 °C).

Representative procedure using the synthesis of **8a** as an example:

In a 50-mL round-bottom flask open to air, acetate **7a** (0.79 mmol) was dissolved in HPLC grade MeOH (3.5 mL) at room temperature. Aqueous KOH solution (~ 9 % w/v; 1 mL) was added dropwise via syringe, causing the reaction to turn pale yellow and slightly cloudy. The reaction was stirred for 13 minutes, at which point TLC analysis indicated complete consumption of the starting material. The reaction was directly concentrated to remove the MeOH. The crude residue was partitioned between EtOAc (5 mL) and H_2O (5 mL). This mixture was quantitatively transferred to a separatory funnel,[24] using additional EtOAc (10 mL) and H_2O (5 mL) to thoroughly rinse the reaction flask. The phases were separated, and then the aqueous phase was back extracted with EtOAc (3 x 5 mL). The combined EtOAc extracts were washed with brine (1 x 15 mL), dried over anhydrous Na_2SO_4, then concentrated to provide the crude product, which was adsorbed onto Celite® 545 and directly purified by column chromatography on SiO_2 (4:1 Hexanes / EtOAc with ~1 % v/v NEt_3). Compound **8a** was obtained as a clear, slightly pale yellow oil in high yield and purity (191.6 mg, 90 % Yield).



8a, 90 % Yield

^{1}H NMR (500.27 MHz, acetone-*d*6) δ 7.60 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.53 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.39 (td, *J* = 7.5, 1.2 Hz, 1H), 7.24 (td, *J* = 7.7, 1.8 Hz, 1H), 4.77 (br s, 2H), 4.60 (t, *J* = 7.4 Hz, 1H), 3.58 (br s, 1H), 3.53 (t, *J* = 6.7 Hz, 2H), 2.24 (app q, *J* = 7.1 Hz, 2H), 1.86 (q, *J* = 0.8 Hz, 3H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 154.04, 137.73, 133.25, 130.10, 130.07, 128.43, 123.02, 95.35, 68.62, 63.06, 31.61, 16.42.
R_f = 0.49 (1:1 Hexanes / EtOAc)
IR: 3334 (br), 2923, 2873, 1667, 1570, 1223, 1172, 1044, 1027, 746 (strong) cm^{-1}
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{12}H_{15}BrO_2Na+$ 293.01475, found: 293.01497.

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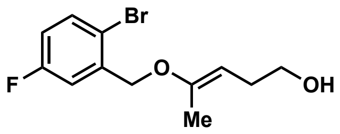
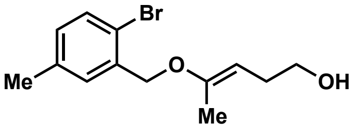
[24] For most smaller scale reactions, a modified workup procedure was adopted. Instead of using a separatory funnel, a 15-mL Falcon tube was used, and the phases were separated by pipet or syringe. Additionally, the brine wash was avoided, and the organic extracts were directly dried over anhydrous $MgSO_4$.



8b, 95 % Yield

Compound **8b**: 95 % Yield (0.3 mmol scale; from acetate)

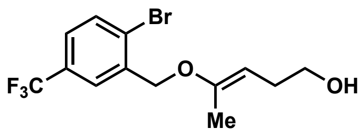
Physical State: White, waxy solid
^{1}H NMR (500.27 MHz, acetone-*d6*) δ 7.64 (dd, *J* = 8.8, 5.2 Hz, 1H), 7.31 (dd, *J* = 9.7, 3.2 Hz, 1H), 7.07 (td, *J* = 8.5, 3.1 Hz, 1H), 4.76 (s, 2H), 4.60 (t, *J* = 7.4 Hz, 1H), 3.52 (t, *J* = 6.9 Hz, 2H), 3.52 (br s, 1H), 2.23 (app q, *J* = 6.9 Hz, 2H), 1.88 (s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d6*) δ 163.09 (d, *J* = 244.9 Hz), 153.86, 140.44 (d, *J* = 7.6 Hz), 134.87 (d, *J* = 8.1 Hz), 116.93 (d, *J* = 22.9 Hz), 116.72 (d, *J* = 3.1 Hz), 116.56 (d, *J* = 24.5 Hz), 95.90, 68.15, 63.02, 31.61, 16.36.
^{19}F NMR (470.68 MHz, acetone-*d6*) δ –115.97.
R$_f$ = 0.18 (4:1 Hexanes / EtOAc)
m.p. 34-37 °C
IR (film): 3334, 3076, 2925, 2874, 1668, 1610, 1581, 1470, 1456, 1267, 1031, 962, 873, 807, 596 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{12}H_{14}BrFO_2Na+$ 311.00534, found: 311.00537.



8c, 87 % Yield

Compound **8c**: 87 % Yield (0.3 mmol scale; from benzoate)

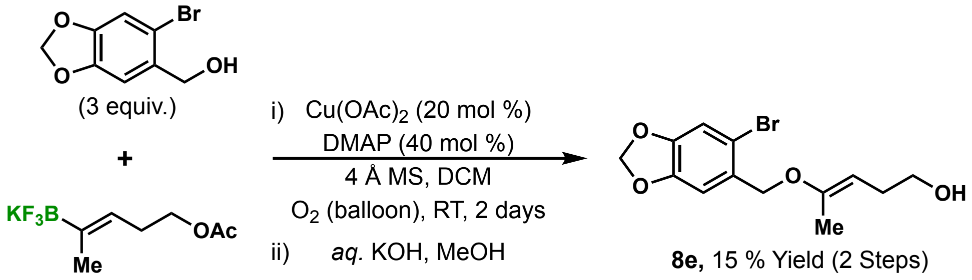
Physical State: White, waxy solid
^{1}H NMR (500.27 MHz, acetone-*d6*) δ 7.46 (d, *J* = 8.1 Hz, 1H), 7.35 (d, *J* = 2.3 Hz, 1H), 7.07 (dd, *J* = 8.1, 2.3 Hz, 1H), 4.72 (s, 2H), 4.59 (t, *J* = 7.4 Hz, 1H), 3.52 (t, *J* = 6.9 Hz, 2H), 3.52 (br s, 1H), 2.31 (s, 3H), 2.23 (app q, *J* = 6.9 Hz, 2H), 1.85 (br s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d6*) δ 154.16, 138.42, 137.38, 133.05, 130.93, 130.87, 119.82, 95.34, 68.71, 63.11, 31.67, 20.92, 16.44.
R$_f$ = 0.19 (4:1 Hexanes / EtOAc)
m.p. 27-30 °C
IR (film): 3333, 2923, 2871, 1667, 1473, 1392, 1222, 1173, 1045, 1026, 807 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{13}H_{17}BrO_2Na+$ 307.03041, found: 307.03054.



8d, 90 % Yield

Compound **8d**: 90 % Yield (0.5 mmol scale; from benzoate)

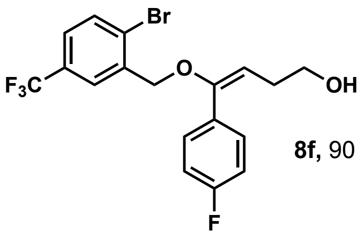
Physical State: White solid
^{1}H NMR (500.27 MHz, acetone-*d*6) δ 7.87 (d, *J* = 8.3 Hz, 1H), 7.84 (d, *J* = 2.3 Hz, 1H), 7.61 (dd, *J* = 8.2, 2.3 Hz, 1H), 4.86 (s, 2H), 4.64 (t, *J* = 7.4 Hz, 1H), 3.54-3.48 (m, 3H), 2.24 (app q, *J* = 6.9 Hz, 2H), 1.89 (s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 153.87, 139.48, 134.41, 130.36 (q, *J* = 32.7 Hz), 127.09, 126.71 (q, *J* = 3.9 Hz), 126.33 (q, *J* = 3.9 Hz), 125.02 (q, *J* = 271.6 Hz, CF_3), 96.11, 68.14, 63.01, 31.61, 16.35.
^{19}F NMR (470.68 MHz, acetone-*d*6) δ –63.26.
R_f = 0.15 (4:1 Hexanes / EtOAc)
m.p. 51-54 °C
IR (film): 3334, 2927, 2877, 1670, 1605, 1327, 1260, 1169, 1127, 1081, 1029, 901, 825 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{13}H_{14}BrF_3O_2Na^+$ 361.00215, found: 361.00224.



8e, 15 % Yield (2 Steps)

Compound **8e**: 15 % Yield over 2 steps

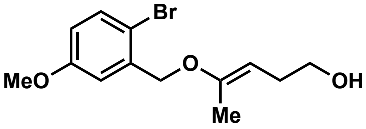
Physical State: White solid
^{1}H NMR (500.27 MHz, acetone-*d*6) δ 7.08 (s, 1H), 7.02 (s, 1H), 6.06 (s, 2H), 4.67 (s, 2H), 4.56 (t, *J* = 7.4 Hz, 1H), 3.51 (t, *J* = 6.9 Hz, 1H), 3.51 (br s, 1H), 2.22 (q, *J* = 7.0 Hz, 2H), 1.84 (br s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 154.10, 149.01, 148.64, 131.06, 113.52, 113.09, 109.99, 103.04, 95.38, 68.65, 63.09, 31.66, 16.42.
R_f = 0.29 (3:2 Hexanes / EtOAc)
m.p. 61-65 °C
IR (film): 3334, 2889, 1667, 1502, 1479, 1245, 1233, 1111, 1038, 933, 865, 830 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{13}H_{15}BrO_4Na^+$ 337.00459, found: 337.00463.



8f, 90 % Yield

Compound **8f**: 90 % Yield (0.16 mmol scale; from benzoate)

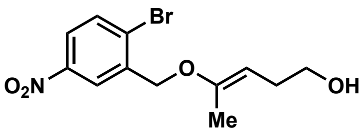
Physical State: White solid
^{1}H NMR (500.27 MHz, acetone-*d*6) δ 7.90 (d, *J* = 8.3 Hz, 1H), 7.88 (d, *J* = 2.4 Hz, 1H), 7.63 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.57 (app dd, *J* = 8.6, 5.6 Hz, 2H), 7.18 (app t, *J* = 8.8 Hz, 2H), 5.08 (t, *J* = 7.5 Hz, 1H), 5.02 (s, 2H), 3.63 (br s, 1H), 3.59 (t, *J* = 6.7 Hz, 2H), 2.31 (q, *J* = 6.8 Hz, 2H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 163.41 (d, *J* = 245.6 Hz), 154.91, 139.23, 134.56, 133.19 (d, *J* = 3.5 Hz), 131.81 (d, *J* = 8.3 Hz), 130.39 (q, *J* = 32.7 Hz), 127.62, 127.00 (q, *J* = 3.9 Hz), 126.93 (q, *J* = 3.9 Hz), 124.97 (q, *J* = 271.5 Hz), 115.70 (d, *J* = 21.8 Hz), 100.59, 69.40, 62.96, 32.12.
^{19}F NMR (470.68 MHz, acetone-*d*6) δ –63.25, –114.78.
R$_f$ = 0.53 (1:1 Hexanes / EtOAc)
m.p. 66-69 °C
IR (film): 3334, 2927, 2879, 1653, 1604, 1509, 1326, 1225, 1168, 1121, 1080, 1026, 899, 841, 825 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{18}H_{15}BrF_4O_2Na+$ 441.00838, found: 441.00841.



8g, 80 % Yield

Compound **8g**: 80 % Yield (0.15 mmol scale; from benzoate)

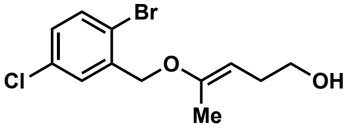
Physical State: Clear, colourless oil
^{1}H NMR (500.27 MHz, acetone-*d*6) δ 7.48 (d, *J* = 8.8 Hz, 1H), 7.11 (d, *J* = 3.2 Hz, 1H), 6.84 (dd, *J* = 8.7, 3.1 Hz, 1H), 4.72 (s, 2H), 4.59 (t, *J* = 7.4 Hz, 1H), 3.81 (s, 3H), 3.52 (t, *J* = 6.9 Hz, 2H), 3.52 (br s, 1H), 2.23 (app q, *J* = 6.9 Hz, 2H), 1.86 (s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 160.31, 154.05, 138.79, 133.95, 115.84, 115.53, 113.00, 95.54, 68.62, 63.10, 55.85, 31.67, 16.42.
R$_f$ = 0.41 (1:1 Hexanes / EtOAc)
IR (film): 3346, 3074, 3002, 2937, 2874, 1668, 1596, 1575, 1474, 1464, 1393, 1297, 1274, 1231, 1163, 1054, 1024, 873, 806, 602 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{13}H_{17}BrO_3Na+$ 323.02533, found: 323.02514.



8h, 90 % Yield

Compound **8h**: 90 % Yield (0.3 mmol scale; from benzoate)

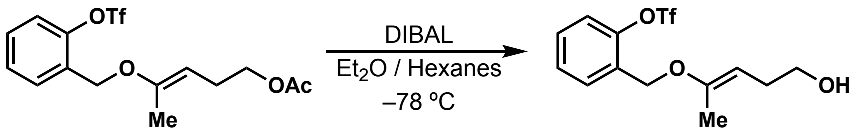
Physical State: Pale yellow solid
^{1}H NMR (500.27 MHz, acetone-*d*6) δ 8.34 (d, *J* = 2.8 Hz, 1H), 8.12 (dd, *J* = 8.7, 2.8 Hz, 1H), 7.94 (d, *J* = 8.7 Hz, 1H), 4.88 (s, 2H), 4.65 (t, *J* = 7.4 Hz, 1H), 3.55-3.50 (m, 3H), 2.24 (q, *J* = 6.4 Hz, 2H), 1.92 (s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 153.74, 148.51, 140.15, 134.72, 129.63, 124.56, 124.03, 96.41, 67.94, 62.98, 31.59, 16.37.
R$_f$ = 0.38 (1:1 Hexanes / EtOAc)
m.p. 63-66 °C
IR (film): 3346, 3104, 2924, 2872, 1669, 1574, 1524, 1342, 1223, 1031, 903, 812, 741 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{12}H_{14}BrNO_4Na+$ 337.99984, found: 337.99997.



8i, 82 % Yield

Compound **8i**: 82 % Yield (0.5 mmol scale; from benzoate)

Physical State: White solid
^{1}H NMR (500.27 MHz, acetone-*d*6) δ 7.63 (d, *J* = 8.5 Hz, 1H), 7.54 (d, *J* = 2.6 Hz, 1H), 7.30 (dd, *J* = 8.5, 2.7 Hz, 1H), 4.76 (s, 2H), 4.60 (t, *J* = 7.4 Hz, 1H), 3.54-3.49 (m, 3H), 2.23 (app q, *J* = 6.8 Hz, 2H), 1.88 (br s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 153.89, 140.02, 134.80, 134.15, 129.97, 129.53, 120.79, 95.92, 68.11, 63.03, 31.62, 16.37.
R$_f$ = 0.23 (4:1 Hexanes / EtOAc)
m.p. 50-53 °C
IR (film): 3333, 3072, 3003, 2924, 2871, 1668, 1454, 1393, 1370, 1224, 1096, 1027, 879, 809 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] $C_{12}H_{14}BrClO_2Na+$ 326.97579, found: 326.97640.



7j

8j, 82 % Yield

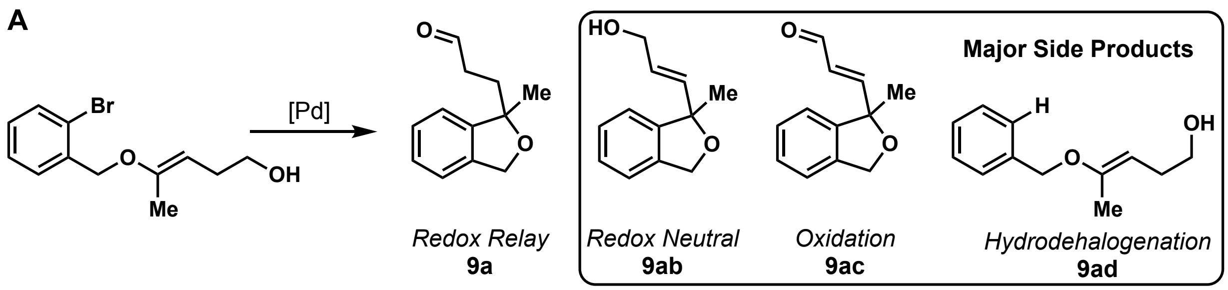
<u>Synthesis of compound **8j**:</u> Compound **7j** (439.9, 1.15 mmol) was dissolved in reagent grade Et_2O (7.5 mL) under argon atmosphere and then cooled to –78 °C. DIBAL solution (1 M in Hexanes; 3.5 mL, 3.5 mmol, 3 equiv.) was added dropwise by syringe over 8 minutes. After stirring for approximately 5 minutes at –78 °C, TLC analysis indicated complete consumption of **7j.** The reaction was removed from cooling and warmed to room temperature. The reaction was poured into an Erlenmeyer flask containing a vigorously stirred mixture of 0.5 M aqueous Rochelle's salt (50 mL), Et_2O (50 mL), and glycerol (~ 0.7 mL). Upon quenching, the reaction turned cloudy white. After stirring vigorously for 25 minutes, the mixture was clear and colourless. At this point, the phases were easily separated. The aqueous phase was back extracted with Et_2O (2 x 25 mL). The combined organic phases were washed with brine (1 x 50 mL), dried over anhydrous Na_2SO_4 then concentrated to afford a crude pale yellow oil. Purification by column chromatography on SiO_2 (7:3 Hexanes / EtOAc with ~1 % v/v NEt_3) afforded the title compound (320.1 mg, 82 % yield) as a clear very pale yellow oil.

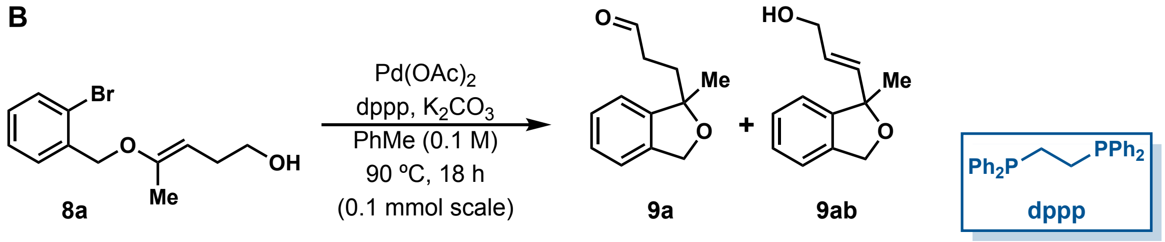
^{1}H NMR (500.27 MHz, acetone-*d*6) δ 7.68 (dd, *J* = 7.4, 2.0 Hz, 1H), 7.59-7.50 (m, 2H), 7.45 (dd, *J* = 8.0, 1.4 Hz, 1H), 4.84 (s, 2H), 4.61 (t, *J* = 7.4 Hz, 1H), 3.55-3.46 (m, 3H), 2.23 (q, *J* = 6.9 Hz, 2H), 1.83 (app d, *J* = 0.8 Hz, 3H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 154.17, 148.58, 131.80, 131.55, 131.01, 129.70, 122.27, 119.49 (q, *J* = 319.2 Hz), 95.40, 64.01, 63.07, 31.62, 16.35.
^{19}F NMR (470.68 MHz, acetone-*d*6) δ –75.22.
R_f = 0.23 (7:3 Hexanes / EtOAc)
IR: 3347 (broad) 2929, 2876, 1669, 1617 (weak), 1583 (weak), 1420, 1206, 1136, 892, 765, 594 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{13}H_{15}F_3O_5SNa+$ 363.04845, found: 363.04854.

Optimization of the Redox-Relay Heck Reaction

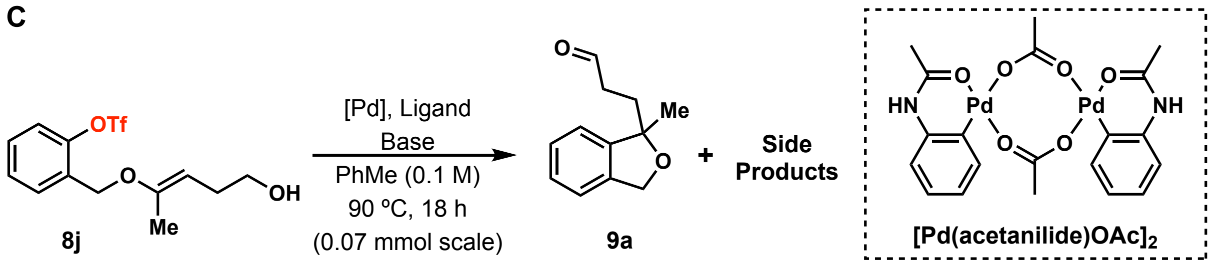
General workflow for redox-relay screening experiments:

All reactions were run using toluene as solvent. Anhydrous toluene was obtained by passage through activated alumina, subsequently degassed by four freeze-pump-thaw cycles and taken into a nitrogen-filled glovebox. In the glovebox, an oven-dried 1-dram vial was charged with the palladium pre-catalyst, ligand, base, and a magnetic stir flea. In a separate vial, the aryl bromide (**8a**) or aryl triflate (**8j**) substrate was dissolved in dry, degassed toluene to afford a stock solution. The 1-dram reaction vial was dosed with an appropriate volume of the substrate stock solution. The vial was sealed with a Teflon-lined screw cap and secured with Parafilm. The vial was removed from the glovebox and placed in a pre-heated (90 °C) aluminum heating block. The reaction was left to vigorously stir (1000 RPM) at this temperature overnight, then allowed to cool to room temperature. The crude reaction mixture was filtered through a short Pasteur pipet plug of Celite® 545 and basic alumina that had been pre-equilibrated with EtOAc. The plug was rinsed with EtOAc (6 mL). The filtrate was collected and concentrated in a 20-mL scintillation vial, and the mass of the crude residue was recorded. A stock solution of trimethyl 1,3,5-benzenetricarboxylate was prepared in acetone-*d*6, and 0.3 mL of this stock solution was transferred via syringe to an NMR tube. Acetone-*d*6 (~ 0.3 mL) was added to the crude residue, and the resultant solution was transferred to the NMR tube via Pasteur pipet. The mass of the crude residue that was *not* transferred to the NMR tube was determined, and the mass of material in the NMR tube was determined by difference. The ^{1}H NMR was measured with a relaxation delay of 30 s. The NMR yield was determined by integration of the product relative to the internal standard.





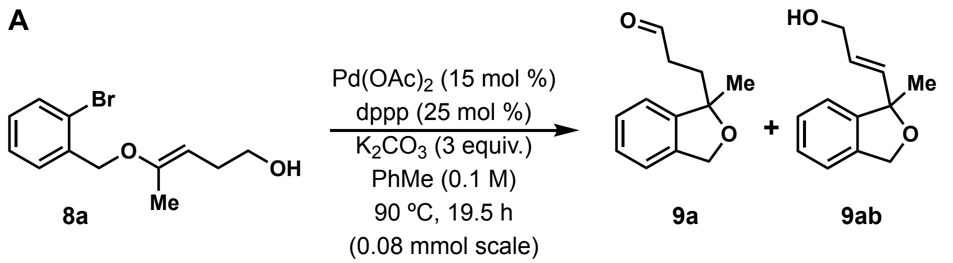
Entry	$Pd(OAc)_2$	dppp	K_2CO_3	Yield **9a**	Yield **9ab**	Comments
1	10 mol %	21 mol %	2.7 equiv.	15 %	40 %	< 5 % **9ac** & **9ad**
2	12 mol %	30 mol %	2.7 equiv.	11 %	36 %	< 5 % **9ac** & **9ad**
3	18 mol %	38 mol %	3.3 equiv.	2 %	12 %	< 80 % Conversion



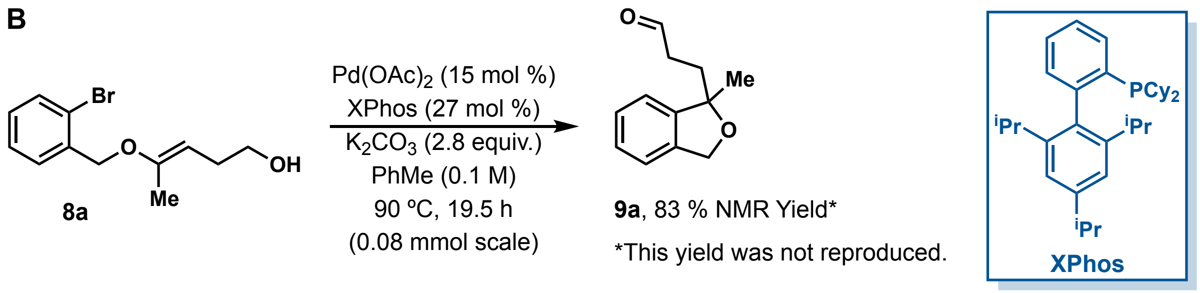
Entry	Pre-Catalyst	Equiv.	Ligand	Equiv.	Base	Equiv.	Yield **9a**
1	$Pd(OAc)_2$	10 mol %	dppp	26 mol %	$NaHCO_3$	3.7	< 5 %
2	$Pd(OAc)_2$	11 mol %	dppp	30 mol %	K_2CO_3	3.2	< 5 %
3	$Pd(OAc)_2$	10 mol %	SPhos	31 mol %	K_2CO_3	3.0	7 %
4	$Pd(OAc)_2$	16 mol %	XPhos	28 mol %	K_2CO_3	3.2	11 %
5	$Pd_2(dba)_3$	5 mol %	XPhos	26 mol %	K_2CO_3	3.0	< 5 %
6	$Pd_2(dba)_3$	5 mol %	BINAP	14 mol %	K_2CO_3	3.2	7 %
7	$[Pd(allyl)Cl]_2$	7 mol %	dppp	29 mol %	K_2CO_3	3.2	14 %
8	$[Pd(acetanilide)OAc]_2$	6 mol %	dppp	27 mol %	K_2CO_3	3.2	< 5 %

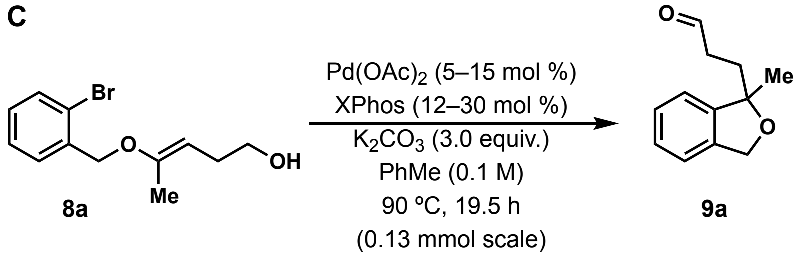
Only trace of **9ac** observed

Scheme S1. Preliminary screening experiments for the synthesis of **9a** via redox-relay Heck cyclization. All yields were determined by ^{1}H NMR using trimethyl 1,3,5-benzenetricarboxylate as the internal standard. A) Overview of the redox-relay transformation along with major observed side products. B) Preliminary screening with dppp as ligand. C) Screening with aryl triflate substrate, **8j**.



Entry	Deviation from Above	Result	NMR Yield
1	none	Mixture of **9a** + **9ab**	17 % (49 % **9ab**)
2	Cs_2CO_3 instead of K_2CO_3	Hydrodehalogenation	< 5 %
3	$[Pd(allyl)Cl]_2$ (4 mol %) instead of $Pd(OAc)_2$	Recovered SM	< 5 %

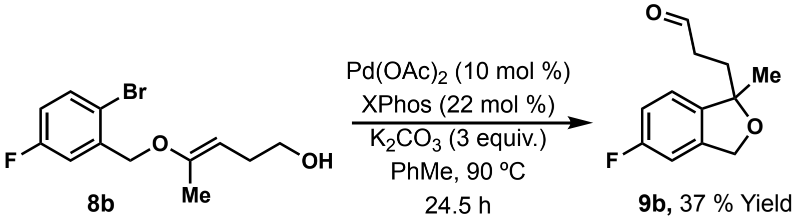




Entry	$Pd(OAc)_2$	XPhos	NMR Yield
1	5 mol %	12 mol %	59 %
2	10 mol %	22 mol %	64 %
3	15 mol %	30 mol %	67 %

Scheme S2. A) Further examination of redox-relay conditions for the aryl bromide substrate, **8a**. B) Identification of successful conditions for the redox-relay Heck reaction, using XPhos as ligand. C) Follow-up screening focused on the loadings of $Pd(OAc)_2$ and XPhos. All yields were determined by ^1H NMR using trimethyl 1,3,5-benzenetricarboxylate as the internal standard.

General Procedure for the Redox-Relay Heck Reaction

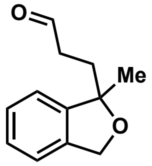


Representative procedure using the synthesis of **9b** as an example:

A 2-dram vial containing **8b** (69.2 mg) was fitted with a rubber septum and firmly secured with electrical tape. Using a 1 ½” 22G needle connected to a Schlenk line, the vial was evacuated and back-filled with argon (x 4). The vial was equipped with an argon-filled balloon. Anhydrous toluene (1.2 mL; Sigma Sure/Seal™) was added by syringe to afford a clear, colourless solution (*c* = 57.7 mg•mL^{-1}). On the benchtop, an oven-dried 2–5 mL size Biotage microwave vial was equipped with a magnetic stir flea, $Pd(OAc)_2$ (4.6 mg, 0.02 mmol, 10 mol %), XPhos (20.9 mg, 0.044 mmol, 22 mol %), and powdered K_2CO_3 (82.0 mg, 0.59 mmol, 3 equiv.). The vial was capped with a Teflon-lined silicone septum and sealed with a crimper. Using a 1 ½” 22G needle connected to a Schlenk line, the vial was evacuated and back-filled with argon (x 4). The solution of **8b** (1.0 mL; 57.7 mg, 0.20 mmol) was subsequently added by syringe under positive argon pressure to give an orange mixture. While still maintaining a positive pressure, the argon supply needle was disconnected from the vial. The reaction was stirred at room temperature for approximately 5 minutes, at which point the reaction was very dark reddish-brown. The reaction was placed in a pre-heated (90 °C) oil bath and stirred vigorously. Within 1 minute, the solution became clear, dark green then turned yellow. After 30 minutes, the reaction had a brownish-yellow appearance. The reaction was left to stir at 90 °C for 24 h to afford a black reaction mixture. Upon cooling to room temperature, the crude reaction was filtered through a short (3 cm) Pasteur pipet plug of EtOAc-equilibrated basic alumina. The plug was rinsed with EtOAc (6 mL), and the filtrate was concentrated to afford a clear, yellow-orange oil (76.3 mg). The crude oil was adsorbed onto Celite® 545 (0.15 g) and loaded onto a SiO_2 column (equilibrated with petroleum ether). Gradient elution (100:0 → 9:1 → 4:1 petroleum ether / Et_2O) afforded **9b** as a pale yellow oil (15.3 mg, 37 % Yield).

^{1}H NMR (500.27 MHz, acetone-*d*6) δ 9.62 (m, 1H), 7.29-7.20 (m, 1H), 7.09-6.98 (m, 2H), 4.98 (d, *J* = 13.0 Hz, 1H), 4.91 (d, *J* = 13.0 Hz, 1H), 2.30-2.09 (m, 4H), 1.45 (s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 202.12, 163.59 (d, *J* = 242.4 Hz), 142.89 (d, *J* = 8.8 Hz), 141.48 (d, *J* = 2.2 Hz), 123.31 (d, *J* = 8.9 Hz), 115.27 (d, *J* = 23.1 Hz), 109.07 (d, *J* = 23.8 Hz), 88.02, 71.37 (d, *J* = 3.0 Hz), 39.71, 34.77, 27.80.
^{19}F NMR (470.68 MHz, acetone-*d*6) δ –117.54.
R_f = 0.40 (1:1 Petroleum ether / Et_2O)
IR (film): 2970, 2926, 2855, 2726, 1722, 1693, 1617, 1604, 1489, 1438, 1264, 1032, 941, 861, 820 cm^{-1}.
HRMS (ESI+) *m/z* [M + H] calcd for $C_{12}H_{14}FO_2$+ 209.09724, found: 209.09731.

Characterization of 1,3-Dihydroisobenzofuran Products

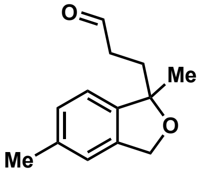


9a, 57 % Yield
(64 % NMR Yield)

<u>Compound **9a**</u>: 57 % Isolated Yield (0.16 mmol scale)

*Reaction was setup in the glovebox and heated for 22 hours

Physical State: Yellow oil
^{1}**H NMR** (500.27 MHz, acetone-*d*6): δ 9.61 (m, 1H), 7.42-7.18 (m, 4H), 5.00 (d, *J* = 12.5 Hz, 1H), 4.92 (d, *J* = 12.5 Hz, 1H), 2.25-2.11 (m, 4H), 1.44 (s, 3H).
^{13}**C NMR** (125.81 MHz, acetone-*d*6): δ 202.22, 145.59, 140.27, 128.39, 128.32, 121.94, 121.70, 88.24, 71.78, 39.75, 34.82, 27.79.
R$_f$ = 0.26 (9:1 Hexanes / EtOAc)
IR (film): 2968, 2925, 2851, 2725, 1721, 1456, 1360, 1258, 1249, 1028, 763, 724 cm^{-1}.
HRMS (ESI–) *m/z* [M – H] calcd for $C_{12}H_{13}O_2$– 189.09210, found: 189.09217.

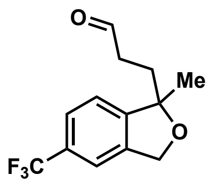


9c, 28 % Yield

<u>Compound **9c**</u>: 28 % Isolated Yield (0.4 mmol scale)

*Reaction was heated for 24 hours

Physical State: Clear, slightly pale yellow oil
^{1}**H NMR** (500.27 MHz, acetone-*d*6) δ 9.61 (m, 1H), 7.13-7.02 (m, 3H), 4.95 (d, *J* = 12.5 Hz, 1H), 4.86 (d, *J* = 12.5 Hz, 1H), 2.33 (s, 3H), 2.22-2.07 (m, 4H), 1.42 (s, 3H).
^{13}**C NMR** (125.81 MHz, acetone-*d*6) δ 202.23, 142.80, 140.59, 138.04, 129.12, 122.35, 121.44, 88.09, 71.65, 39.79, 34.89, 27.91, 21.23.
R$_f$ = 0.39 (4:1 Hexanes / EtOAc)
IR (film): 3016, 2969, 2924, 2859, 2725, 1722, 1494, 1448, 1372, 1347, 1031, 819 cm^{-1}.
HRMS (ESI+) *m/z* [M + Na] calcd for $C_{13}H_{16}O_2Na$+ 227.10425, found: 227.10434.



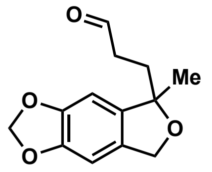
9d, 11 % Yield
(32 % NMR Yield)

Compound **9d**: 32 % NMR Yield (0.4 mmol scale, 19 hours); 11 % Isolated Yield (0.4 mmol scale, 24 hours)

Physical State: Pale yellow oil
^{1}H NMR (500.27 MHz, acetone-*d*6) δ 9.63 (m, 1H), 7.68-7.62 (m, 2H), 7.48 (d, *J* = 7.8 Hz, 1H), 5.09 (d, *J* = 12.9 Hz, 1H), 5.01 (d, *J* = 13.1 Hz, 1H), 2.28-2.19 (m, 4H), 1.49 (s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 202.00, 150.19, 141.71, 125.70 (q, *J* = 3.9 Hz),122.71, 119.38 (q, *J* = 4.0 Hz), 88.36, 71.52, 39.63, 34.42, 27.42.

The ^{13}C NMR signals for the CF_3 carbon and ipso-CF_3 carbon on the aromatic ring were not clearly observed due to a low signal-to-noise ratio.

^{19}F NMR (470.68 MHz, acetone-*d*6) δ –62.45 (minor impurity), –62.50.
R_f = 0.25 (4:1 Hexanes / EtOAc)
IR (film): 2972, 2929, 2861, 2728, 1724, 1435, 1326, 1260, 1164, 1122, 1088, 1060, 1033, 892, 835 cm^{-1}.
HRMS (ESI–) *m/z* [M – H] calcd for $C_{13}H_{12}F_3O_2$– 257.07948, found: 257.07944.



9e, (30 % NMR Yield)

Compound **9e**: 30 % NMR Yield (0.1 mmol scale)

*Reaction was heated for 18.5 hours

^{1}H NMR (500.27 MHz, acetone-*d*6) δ 9.61 (m, 1H), 8.76 (s, 3H, int. std.), 6.72 (br s, 1H), 6.71 (br s, 1H), 6.01-5.99 (m, 2H), 4.89 (d, *J* = 12.0 Hz, 1H), 4.80 (d, *J* = 11.9 Hz, 1H), 3.98 (s, 9H, int. std.), 2.23-2.08 (m, 4H), 1.41 (s, 3H).
^{13}C NMR (125.81 MHz, acetone-*d*6) δ 202.24, 165.70 (int. std.), 148.73, 148.68, 138.43, 134.64 (int. std.), 132.86, 132.36 (int. std.), 102.41, 102.31, 102.27, 88.28, 71.87, 53.03 (int. std.), 39.74, 34.84, 27.91.

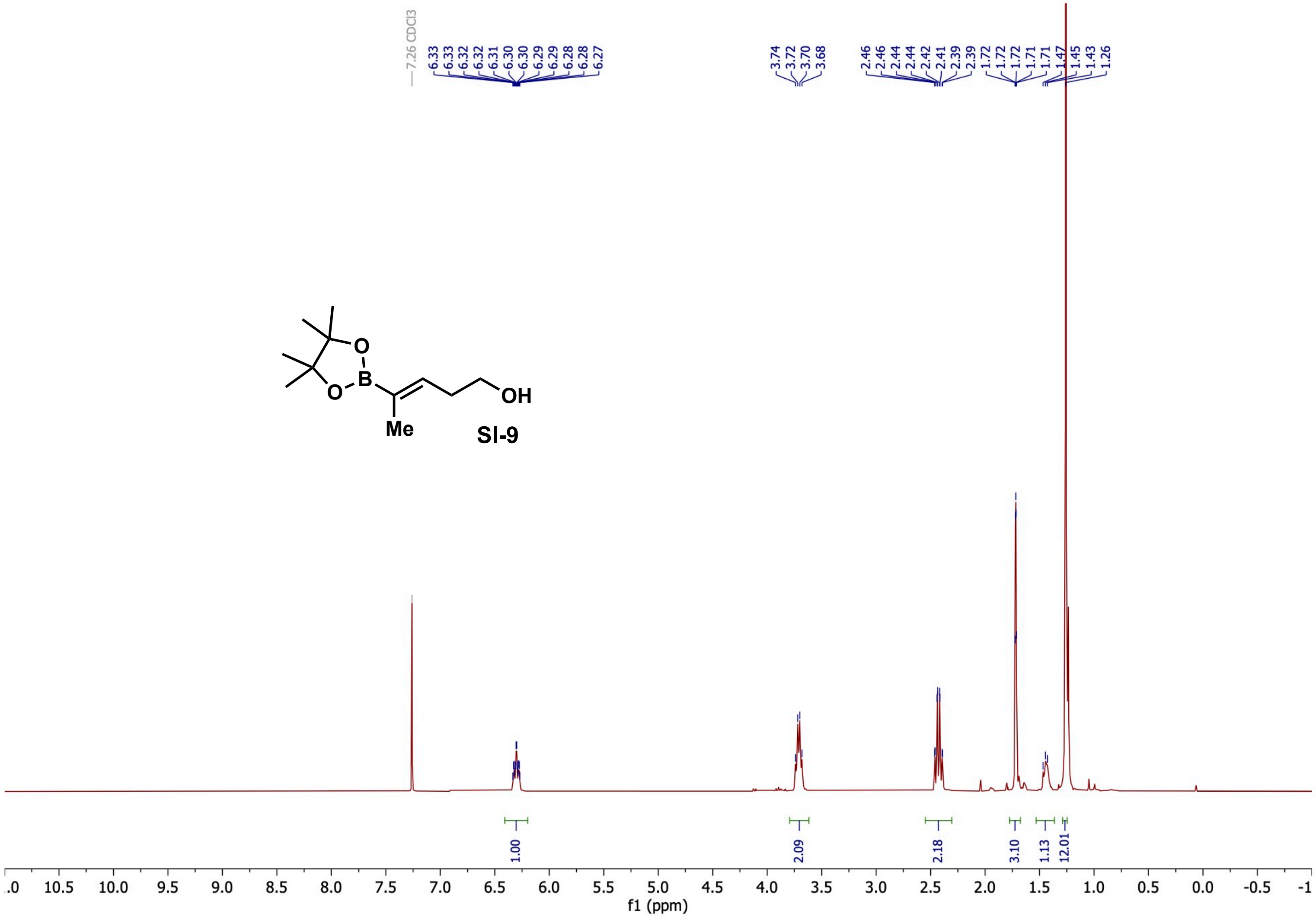


Figure S1. ^{1}H NMR of **SI-9** (300.27 MHz, $CDCl_3$).

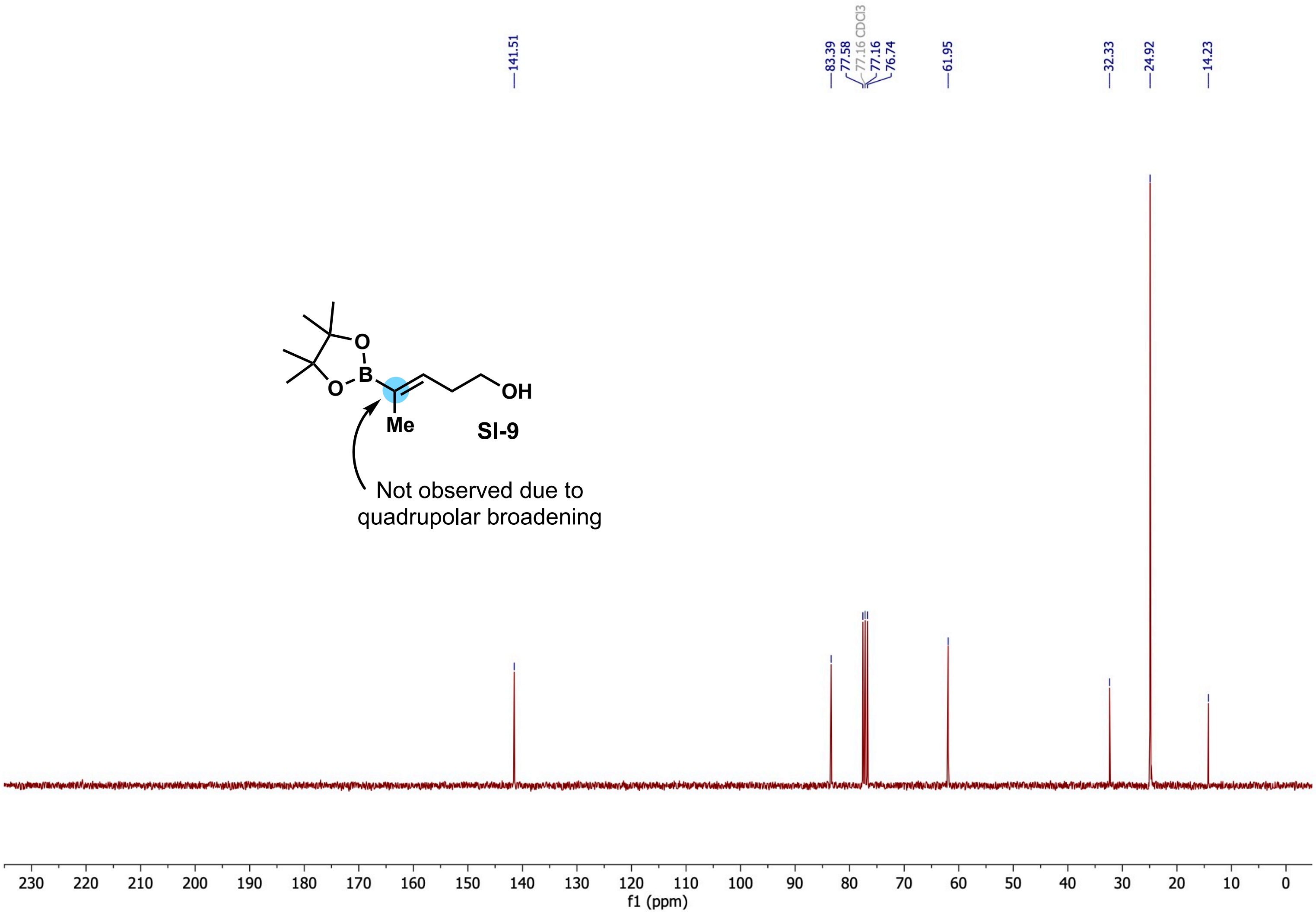


Figure S2. ^{13}C NMR of **SI-9** (75.51 MHz, CDCl$_3$).

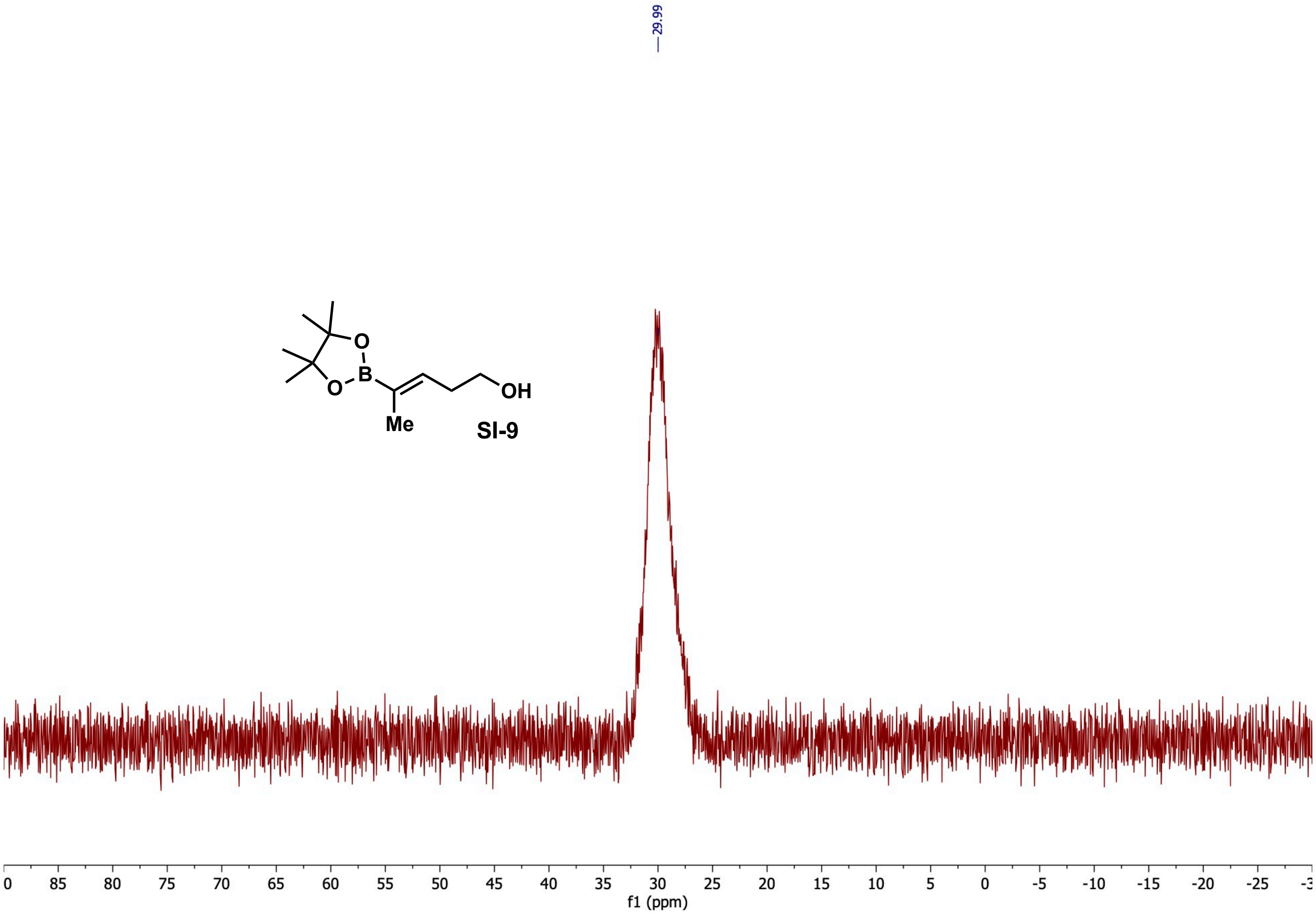


Figure S3. ^{11}B NMR of **SI-9** (96.34 MHz, $CDCl_3$).

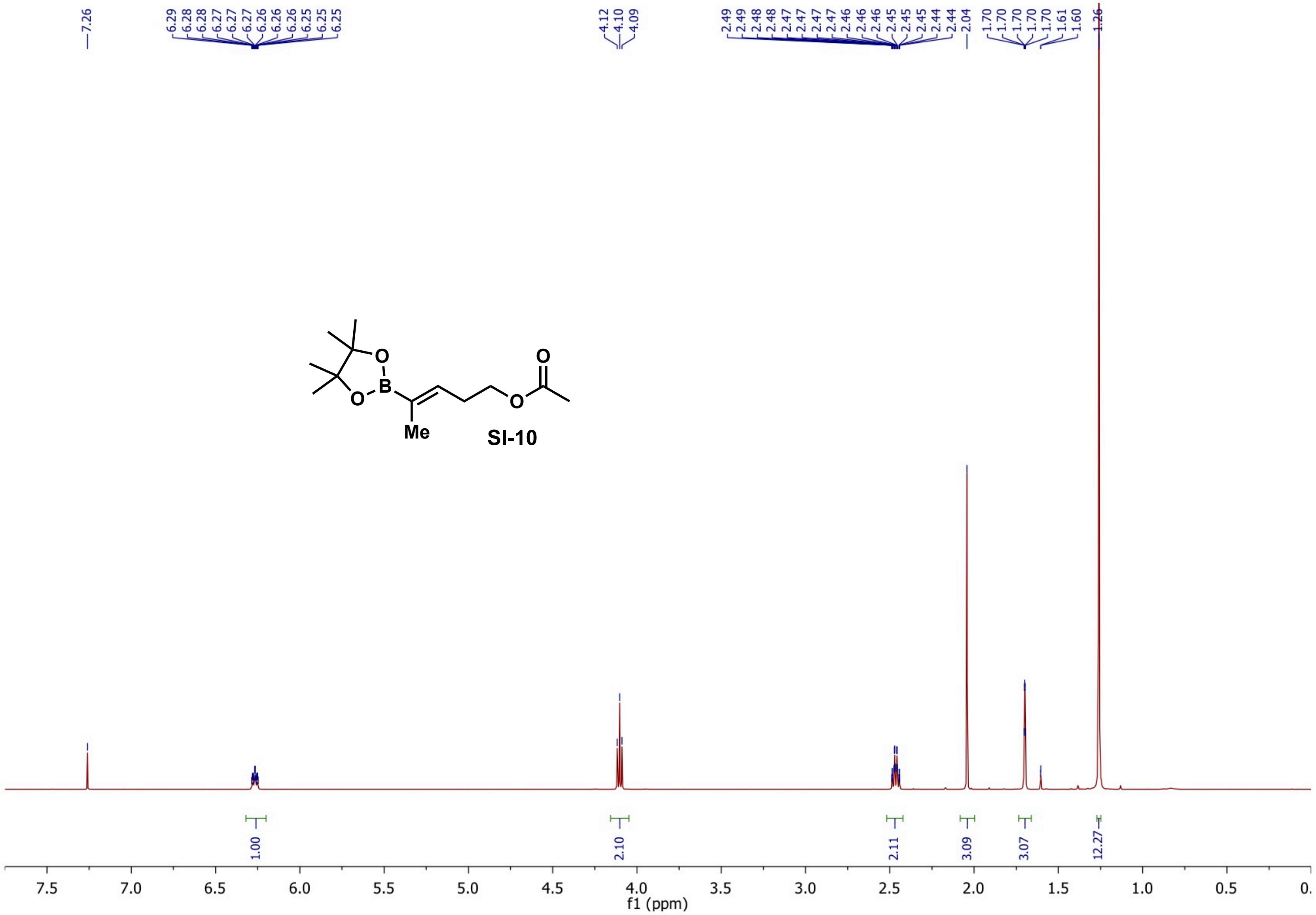
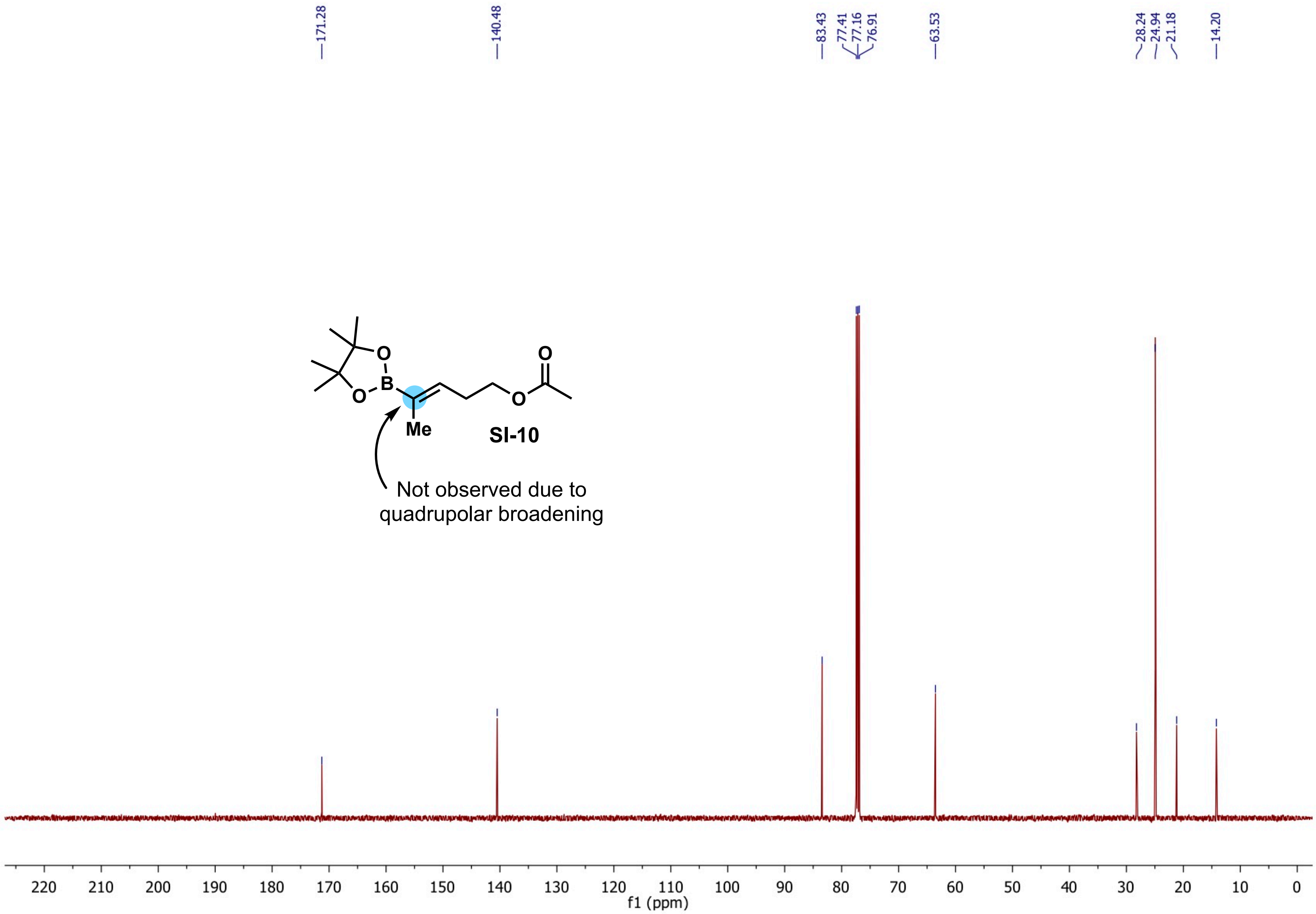


Figure S4. ^{1}H NMR of **SI-10** (500.27 MHz, CDCl$_3$).



Not observed due to quadrupolar broadening

Figure S5. ^{13}C NMR of **SI-10** (125.81 MHz, $CDCl_3$).

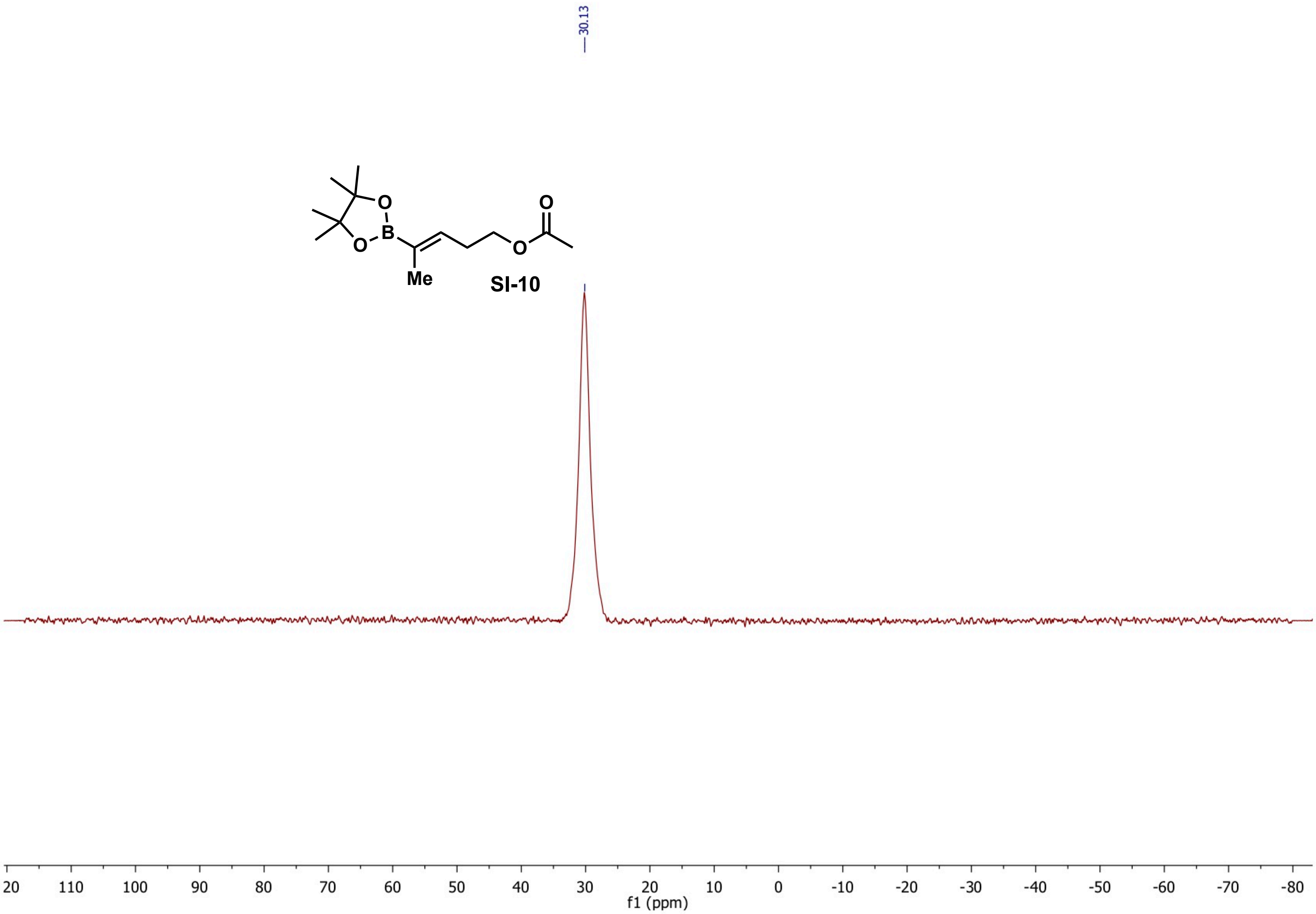


Figure S6. ^{11}B NMR of **SI-10** (160.51 MHz, $CDCl_3$).

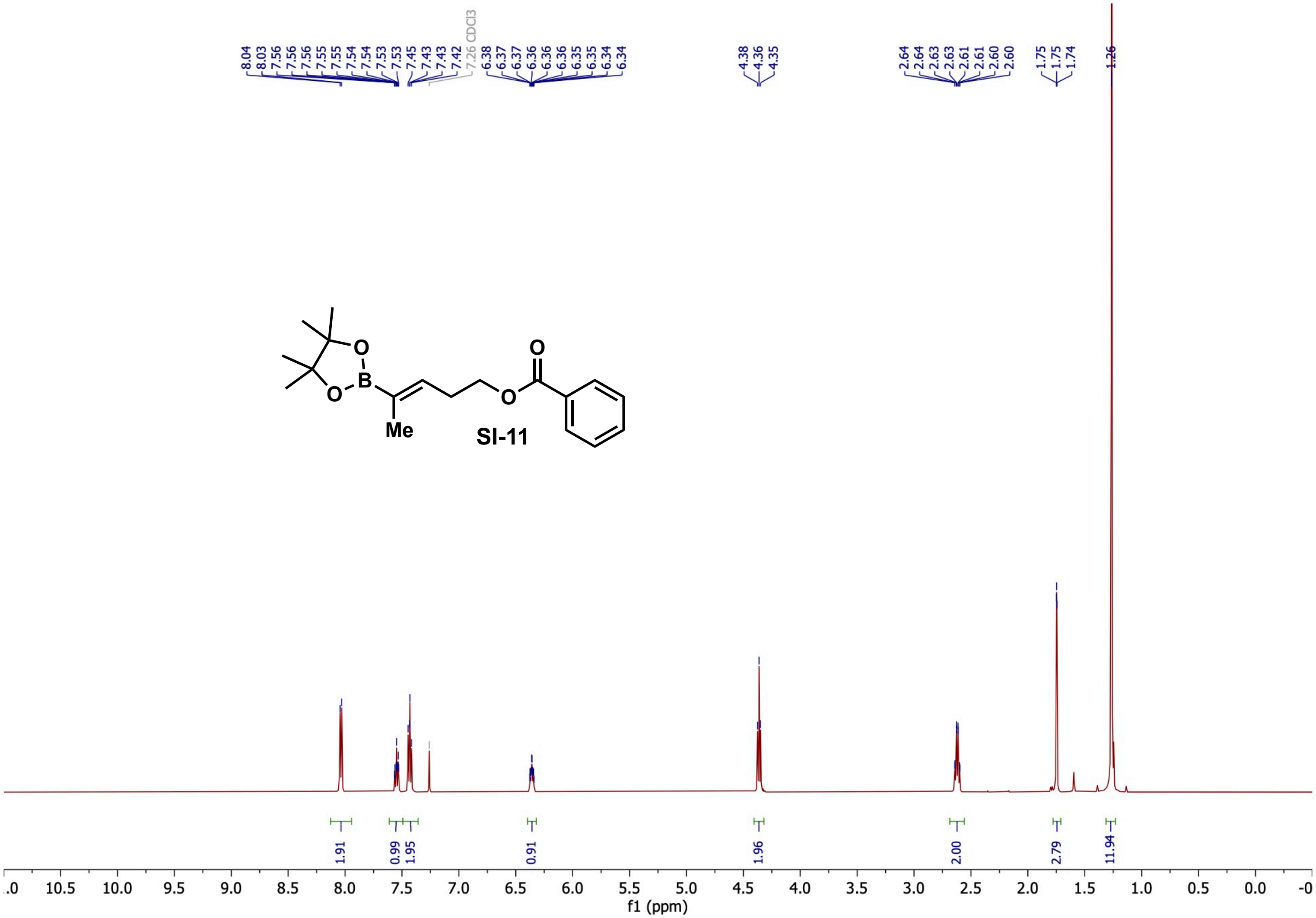


Figure S7. ^{1}H NMR of **SI-11** (500.27 MHz, $CDCl_3$).

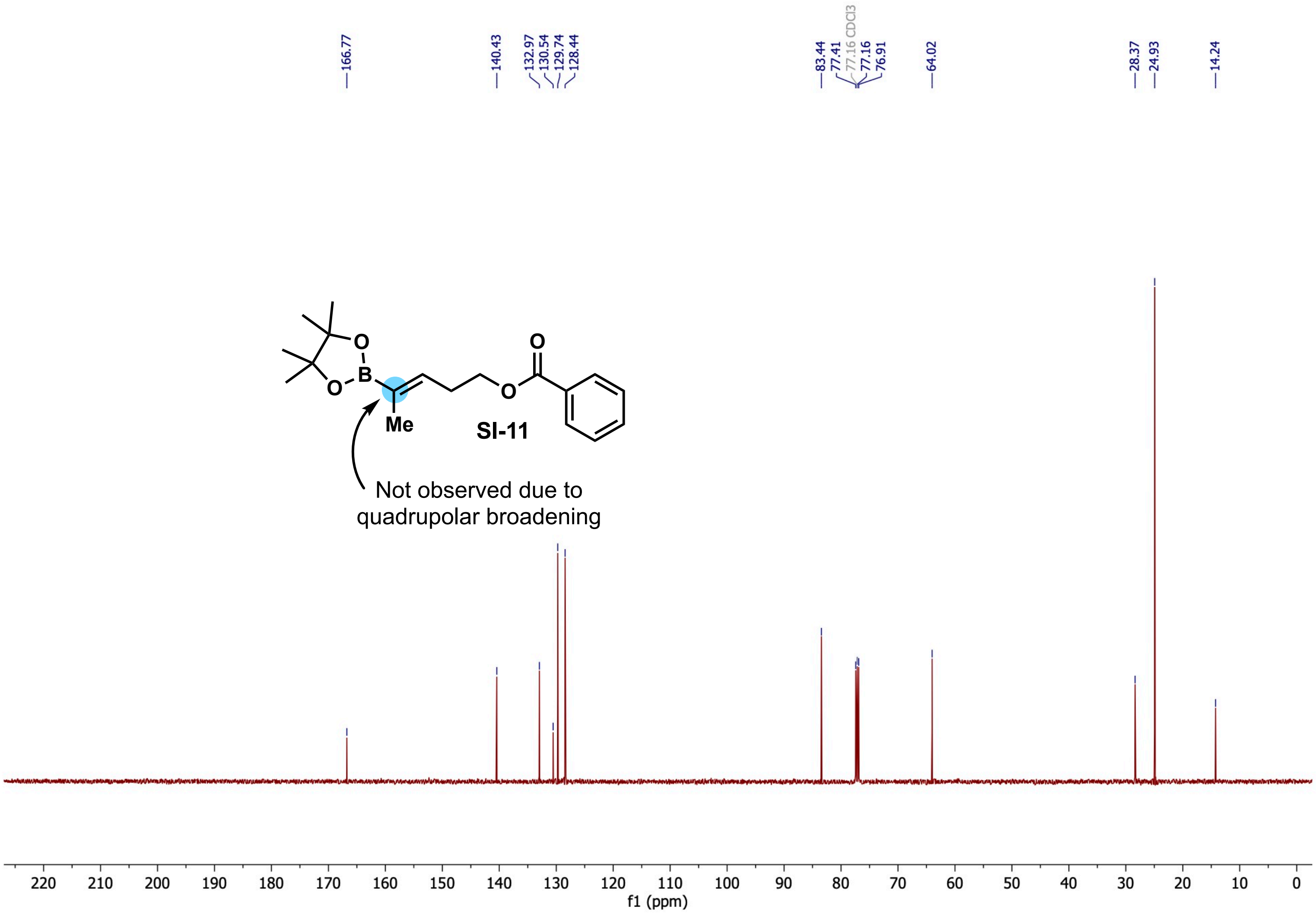


Figure S8. ^{13}C NMR of **SI-11** (125.81 MHz, CDCl$_3$).

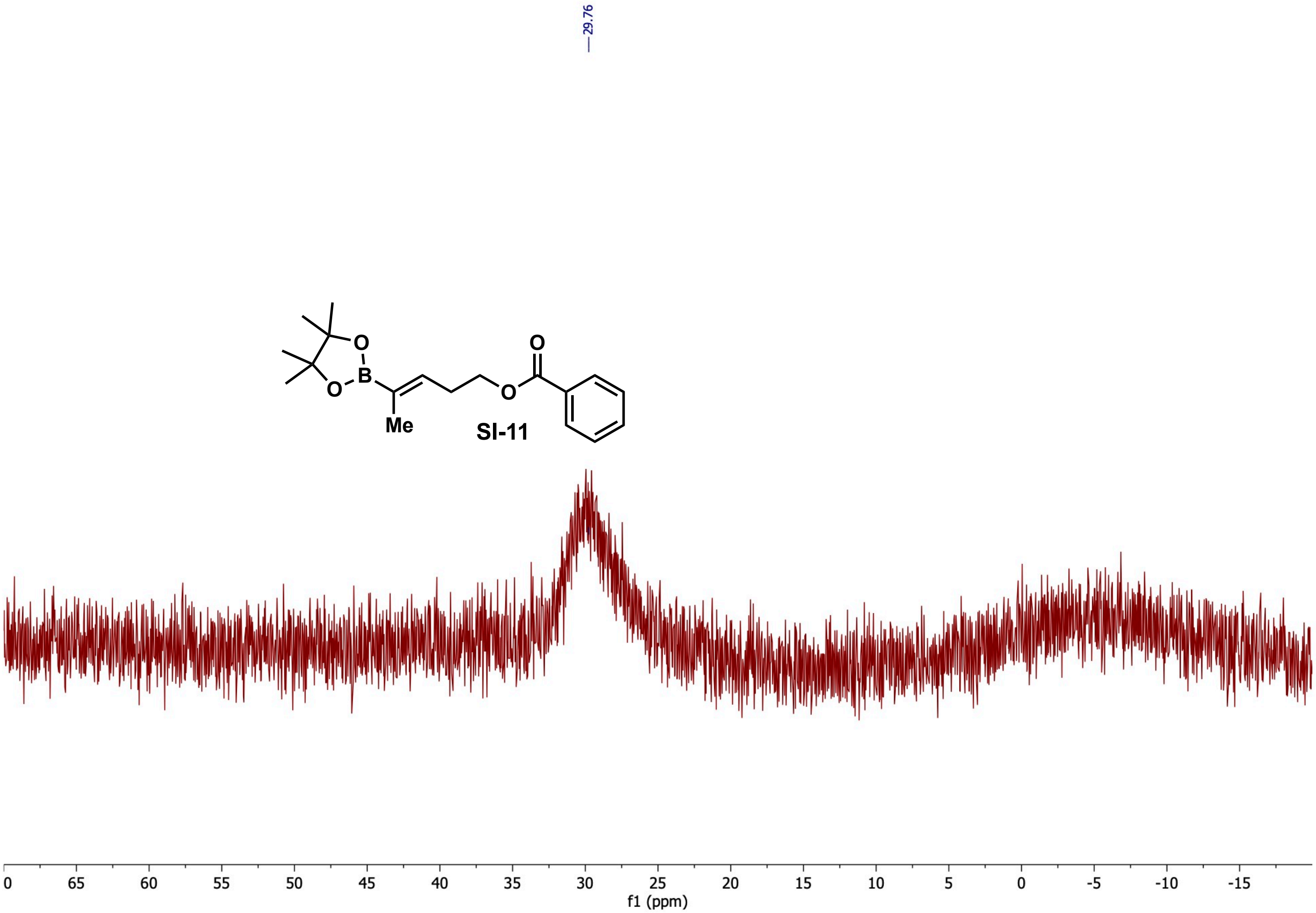


Figure S9. ^{11}B NMR of **SI-11** (96.34 MHz, $CDCl_3$).

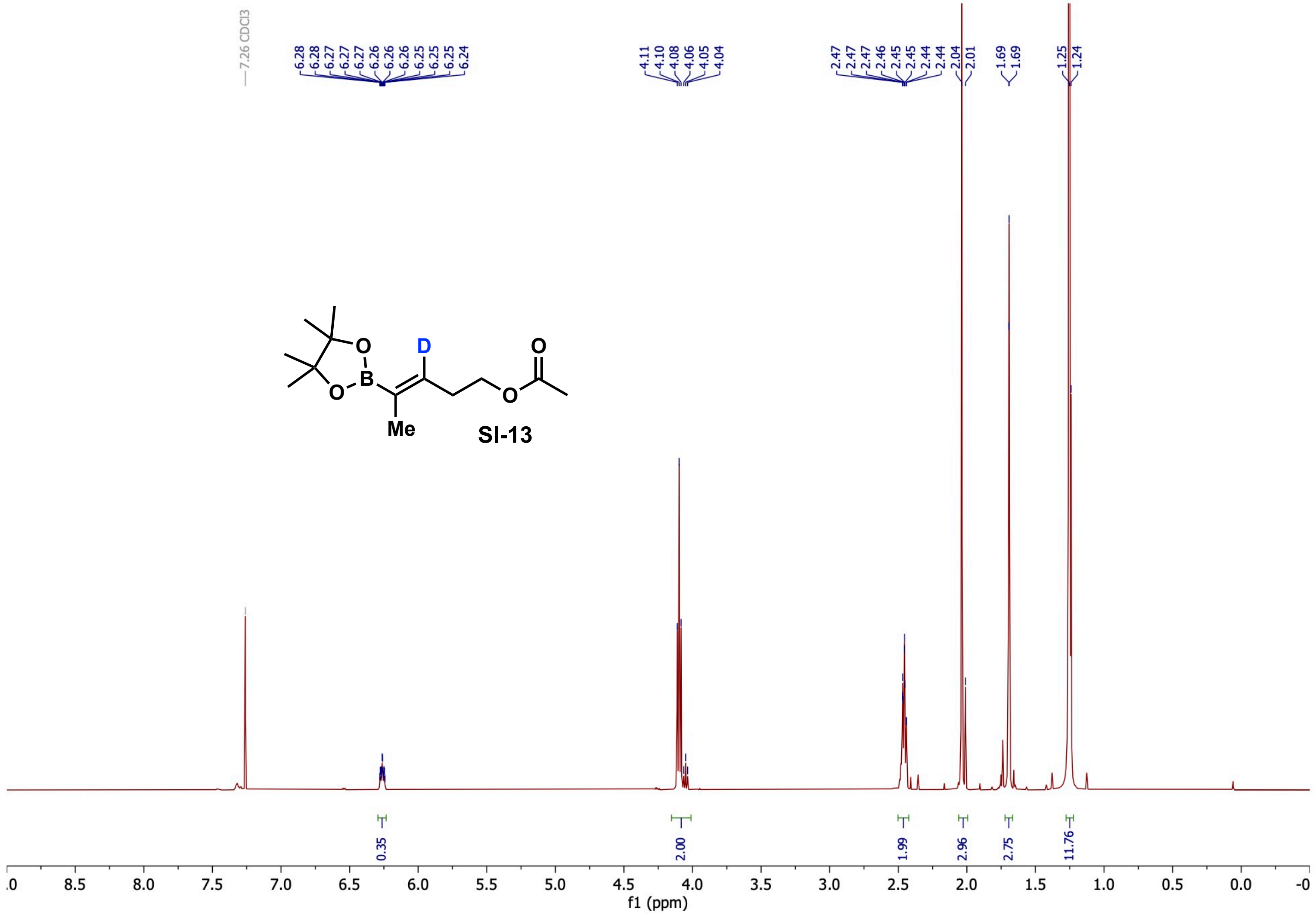


Figure S10. ^{1}H NMR of **SI-13** (500.27 MHz, $CDCl_3$).

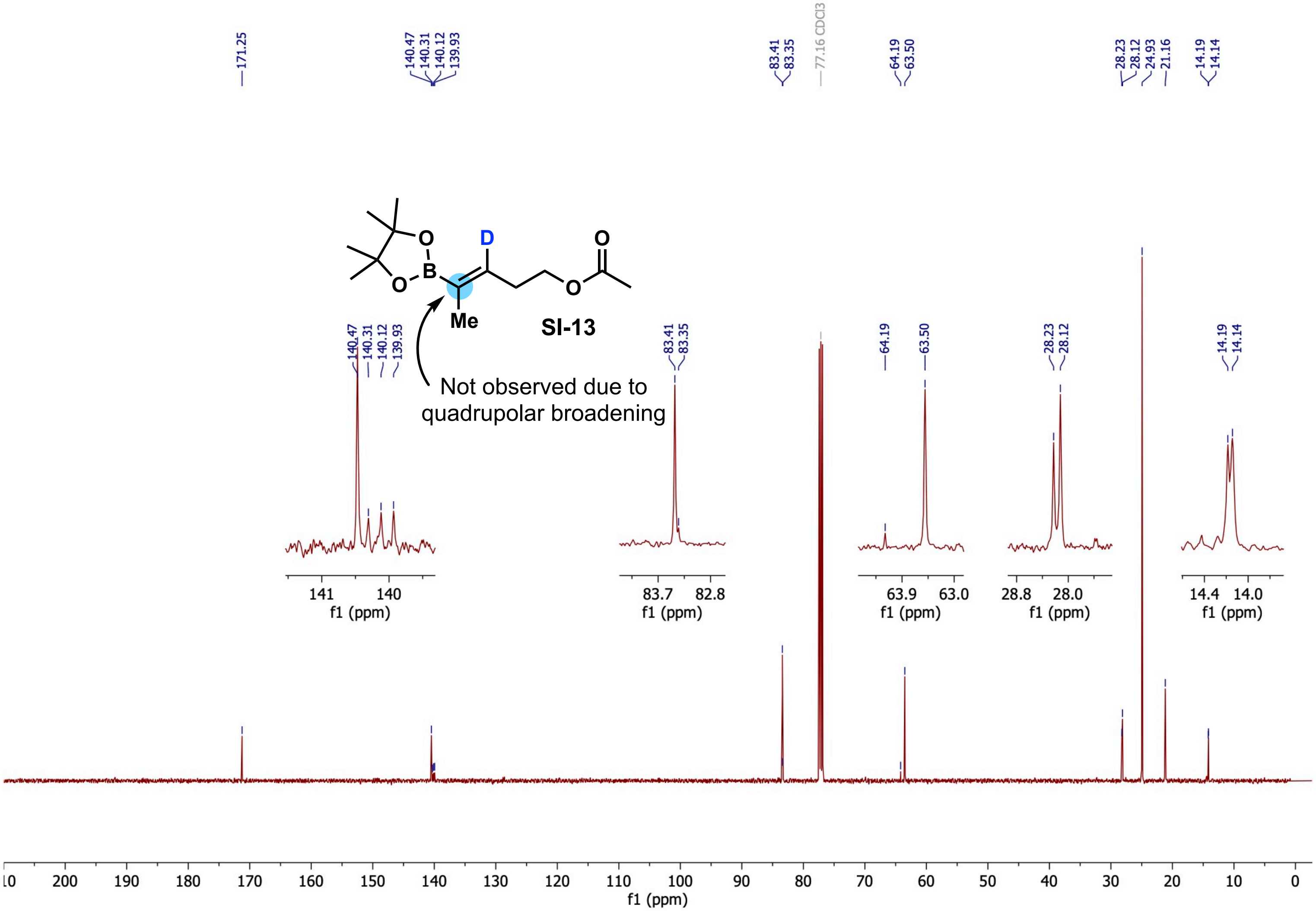
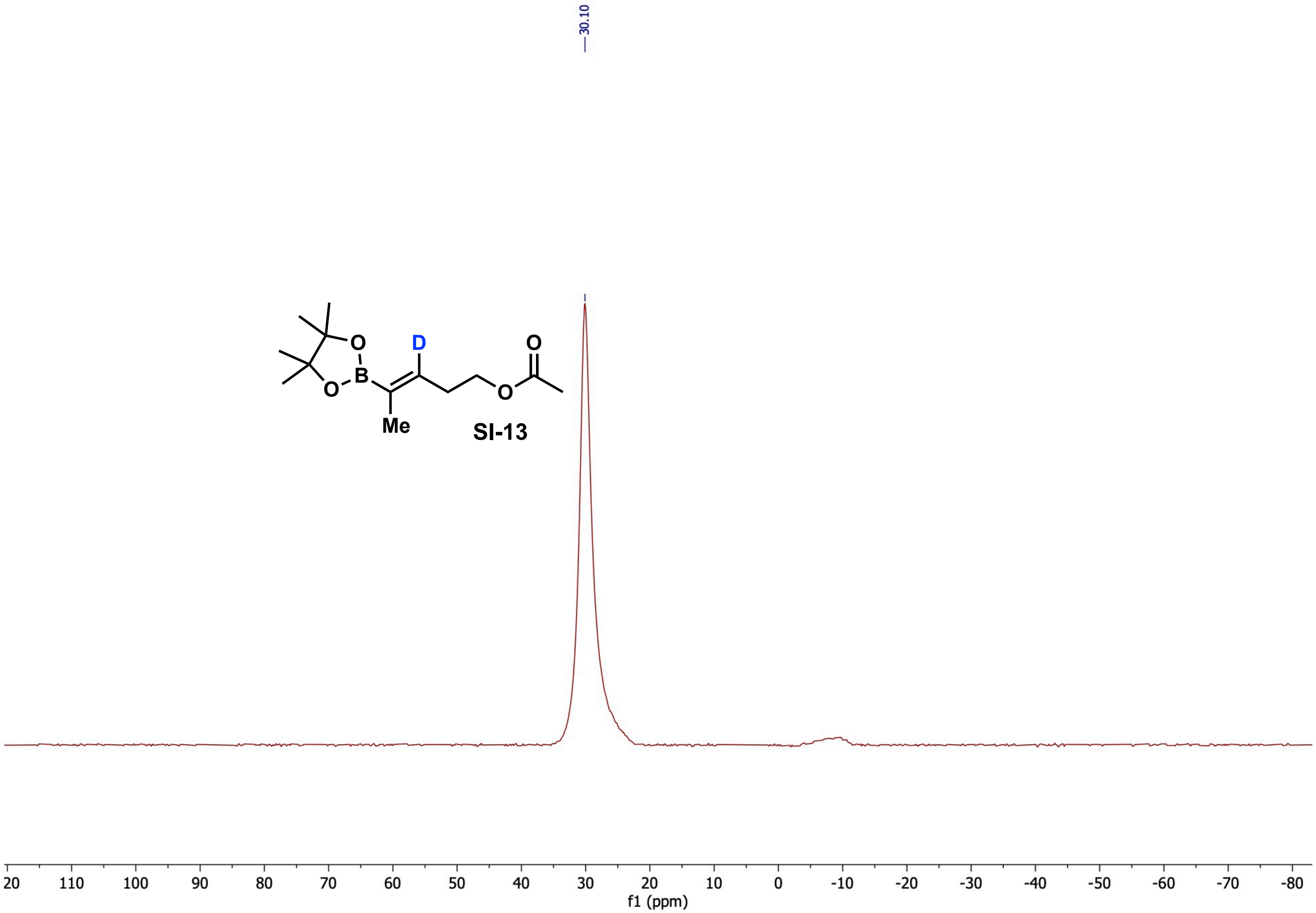


Figure S11. ^{13}C NMR of **SI-13** (125.81 MHz, $CDCl_3$).



SI-13

Figure S12. ^{11}B NMR of **SI-13** (160.51 MHz, $CDCl_3$).

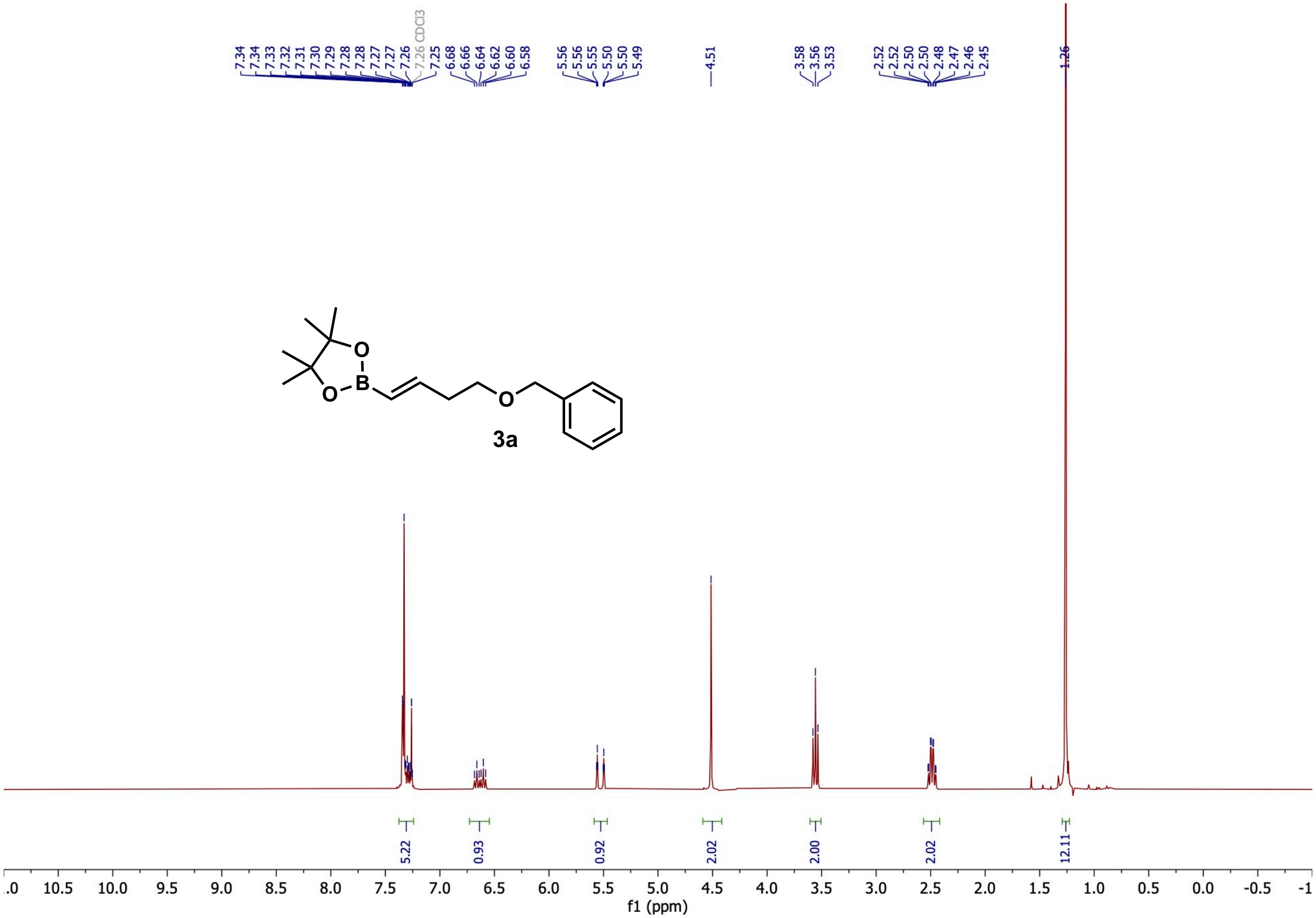


Figure S13. ^{1}H NMR of compound **3a** (300.27 MHz, $CDCl_3$).

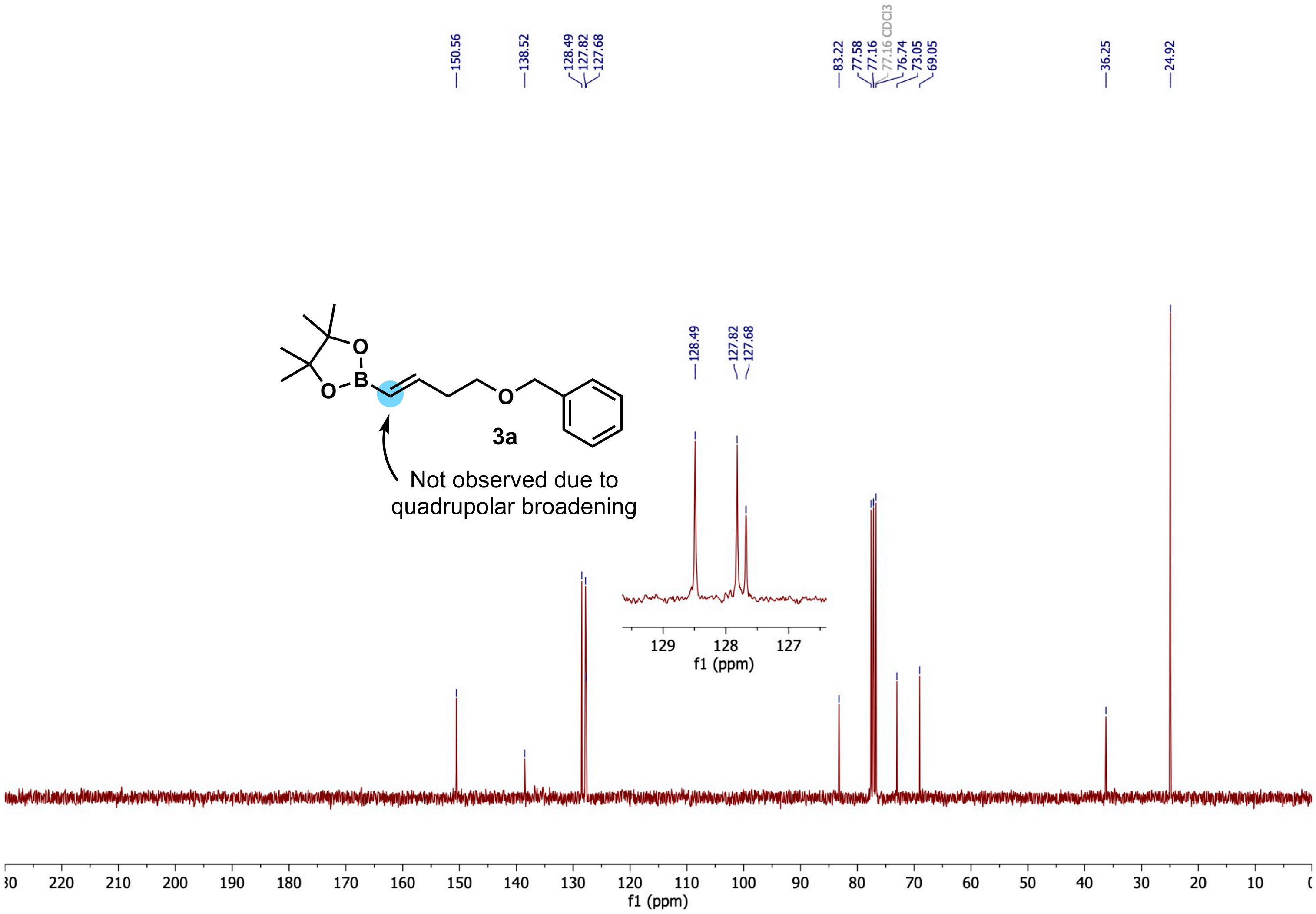


Figure S14. ^{13}C NMR of compound **3a** (75.51 MHz, CDCl$_3$).

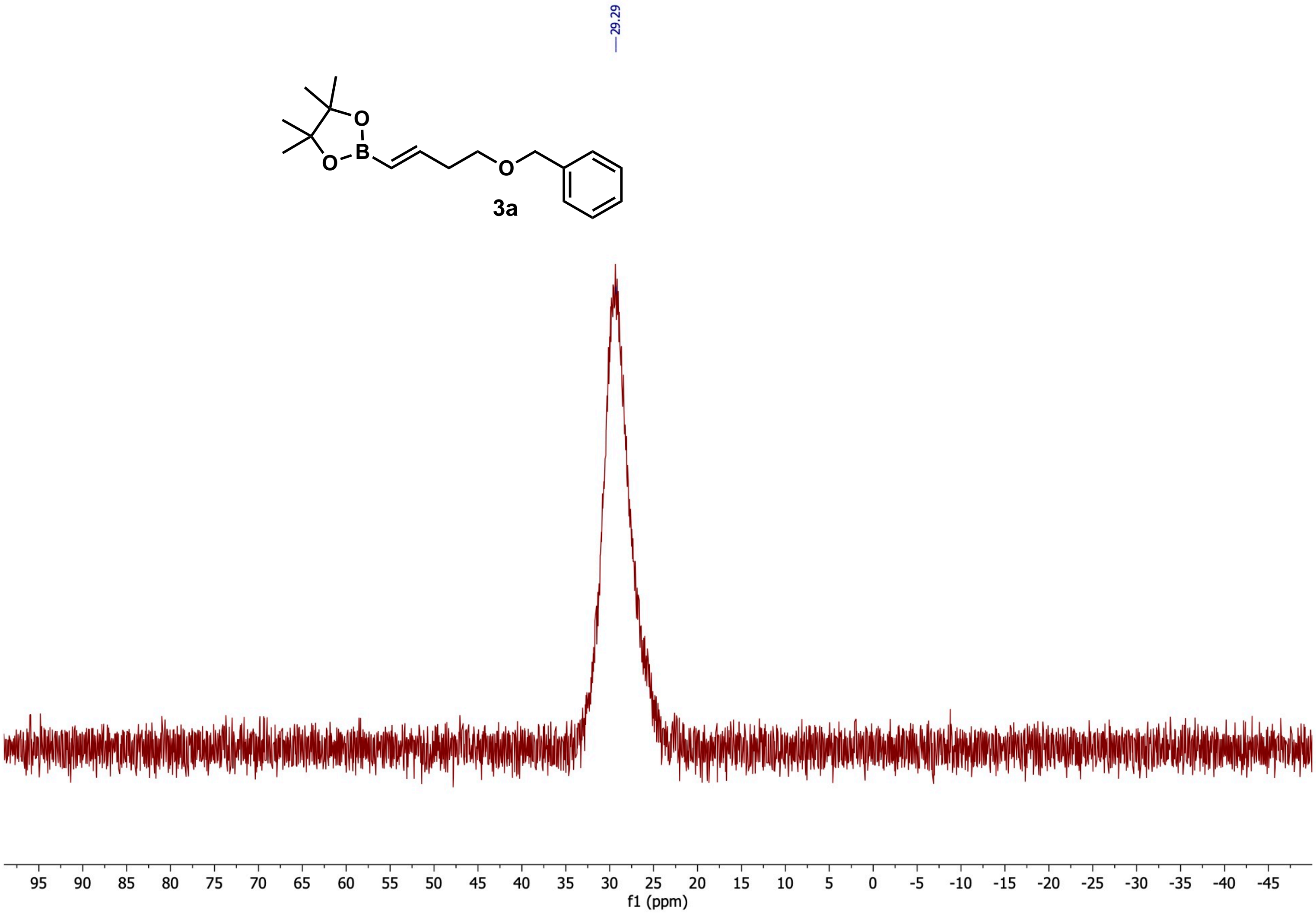

3a

Figure S15. ^{11}B NMR of compound **3a** (96.34 MHz, $CDCl_3$).

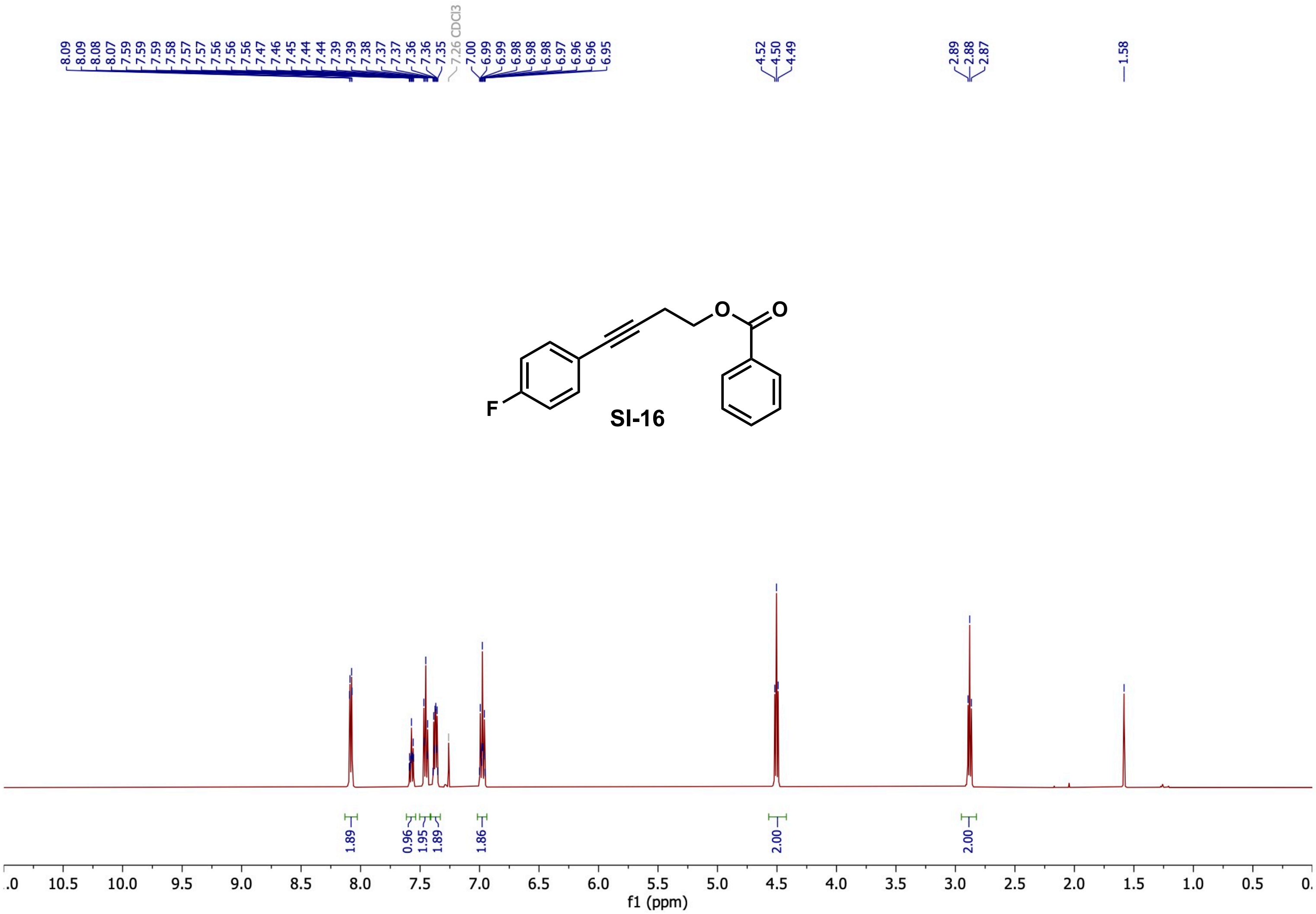


Figure S16. ^{1}H NMR of **SI-16** (500.27 MHz, $CDCl_3$).

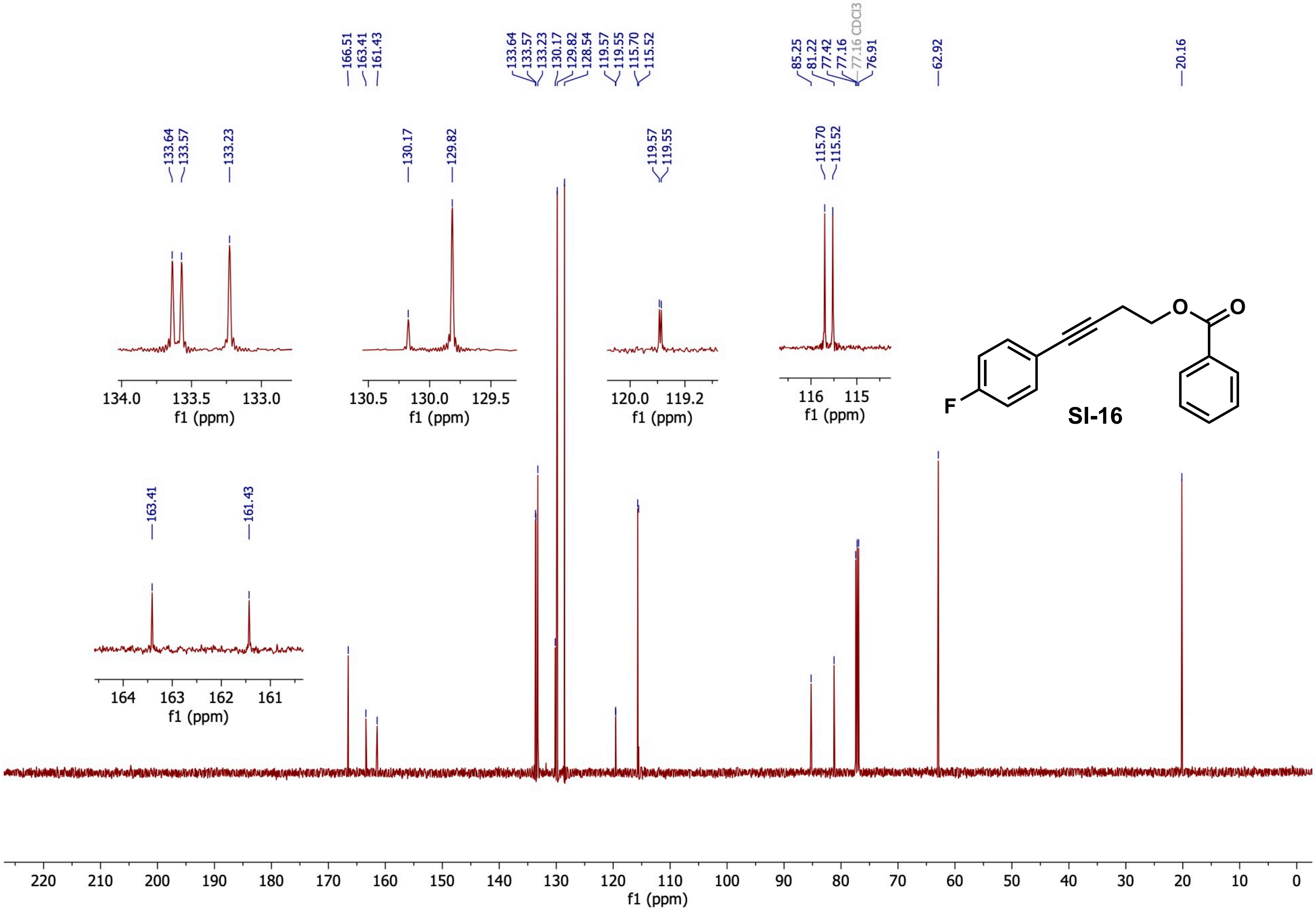


Figure S17. ^{13}C NMR of **SI-16** (125.81 MHz, $CDCl_3$).

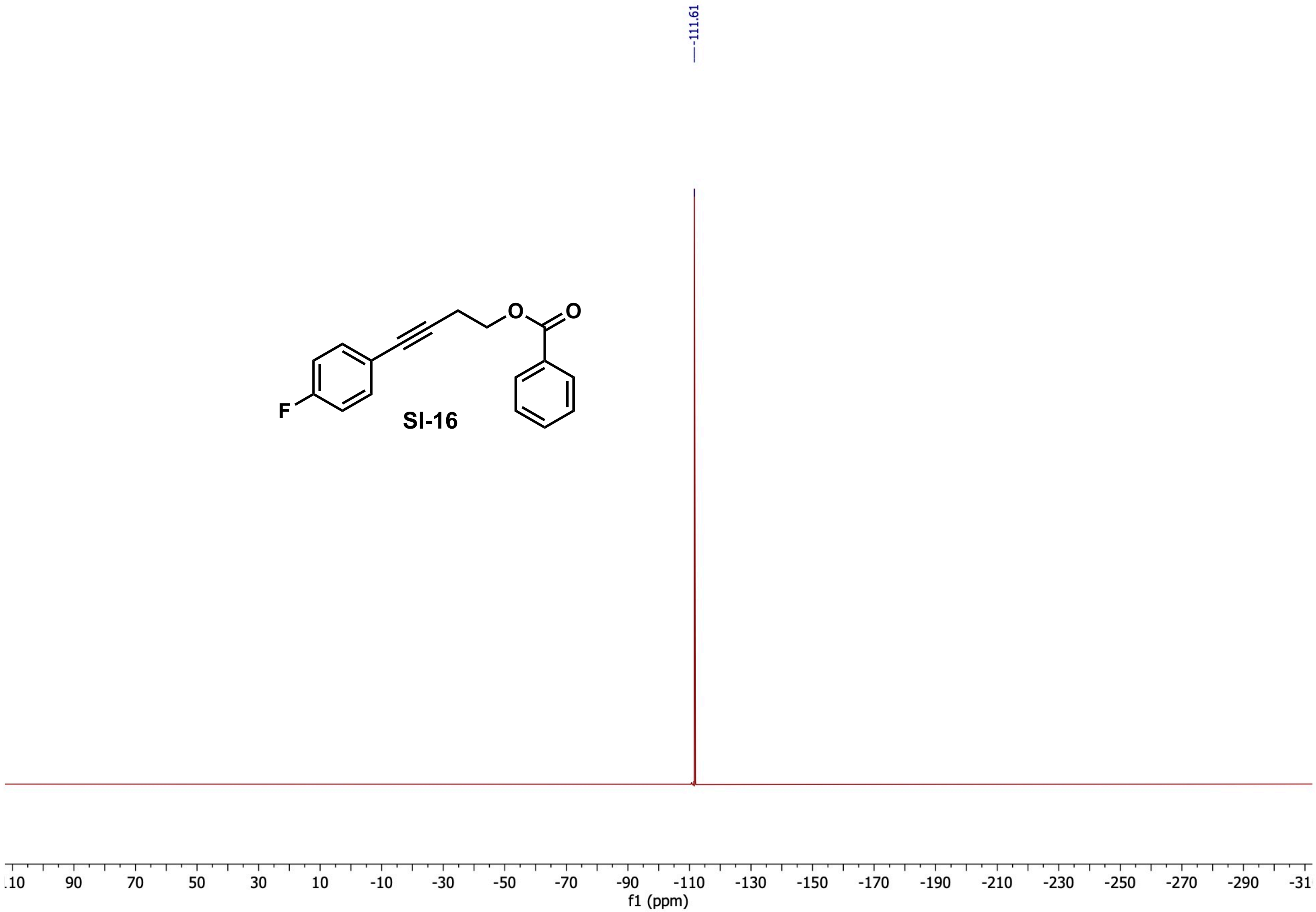


Figure S18. ^{19}F NMR of **SI-16** (470.68 MHz, CDCl$_3$).

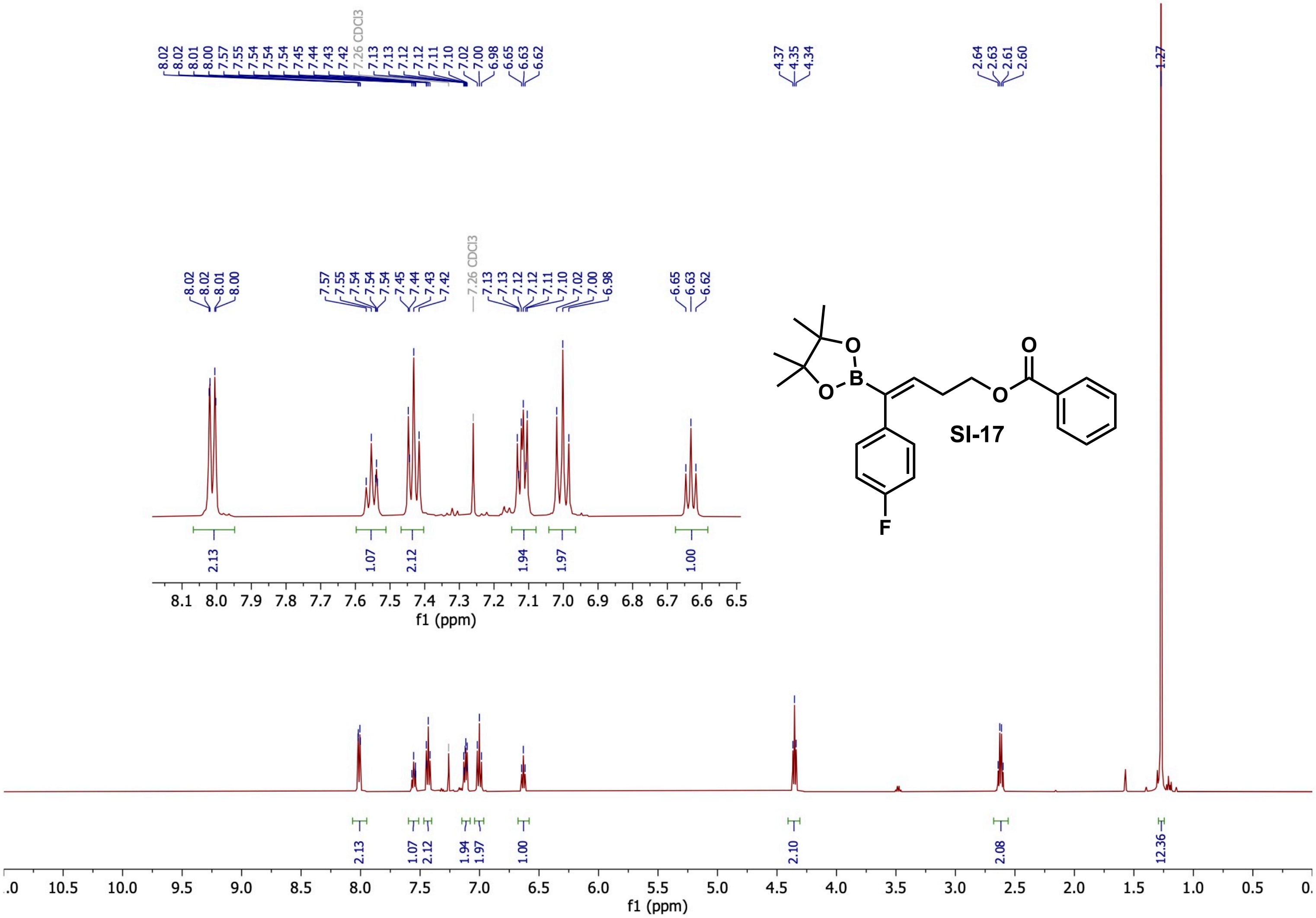


Figure S19. ^{1}H NMR of **SI-17** (500.27 MHz, $CDCl_3$).

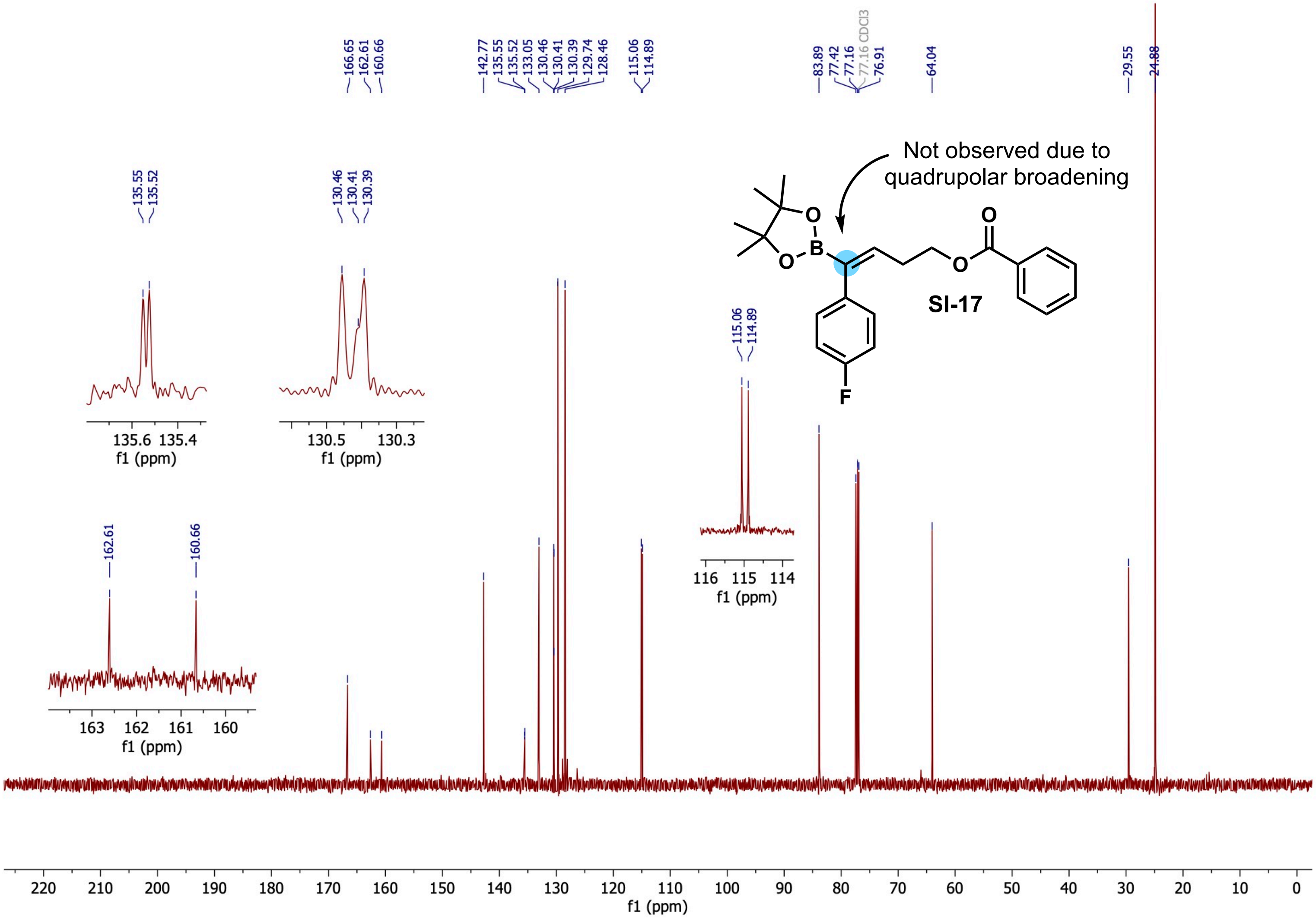


Figure S20. ^{13}C NMR of **SI-17** (125.81 MHz, $CDCl_3$).

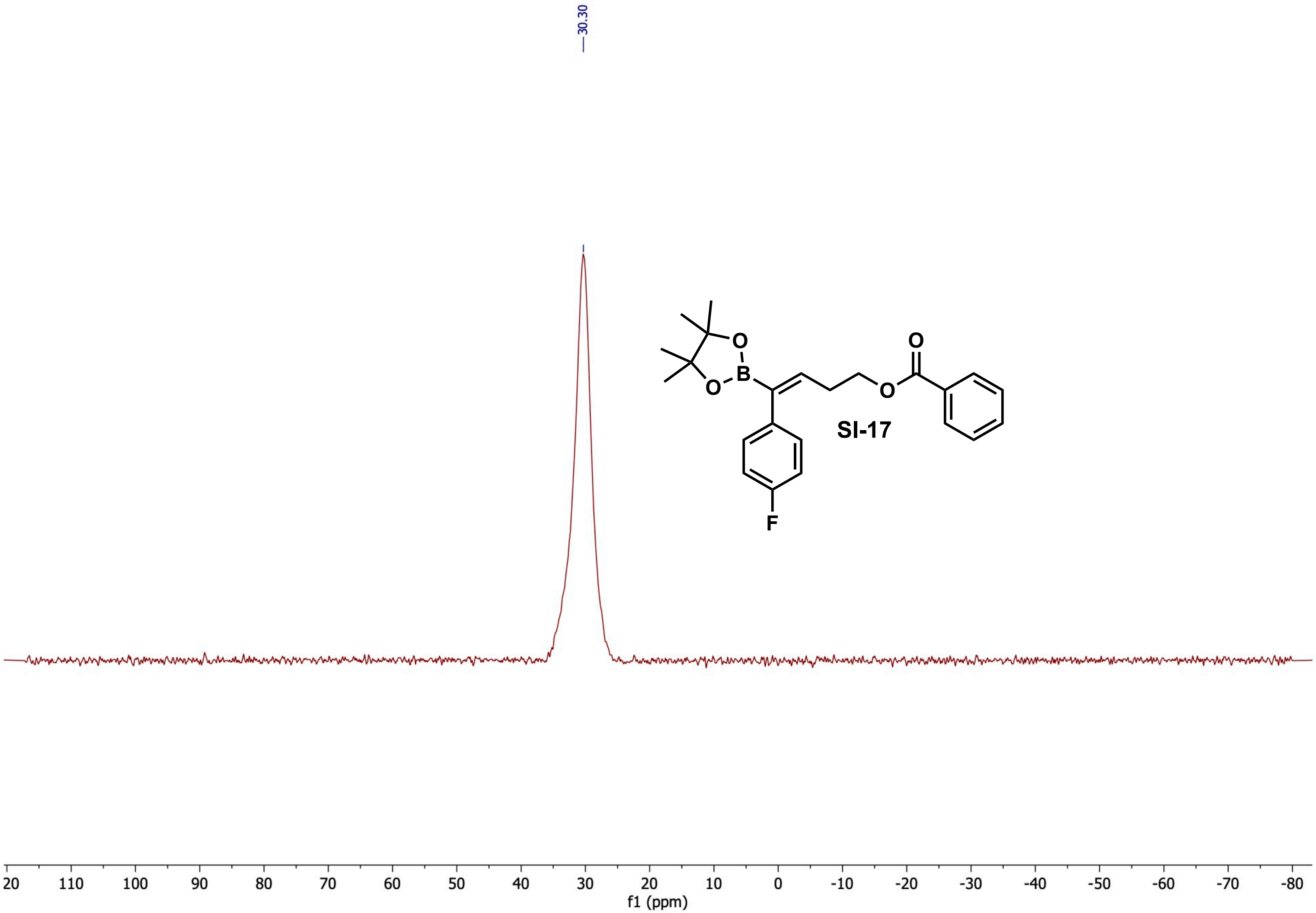


Figure S21. ^{11}B NMR of **SI-17** (160.51 MHz, $CDCl_3$).

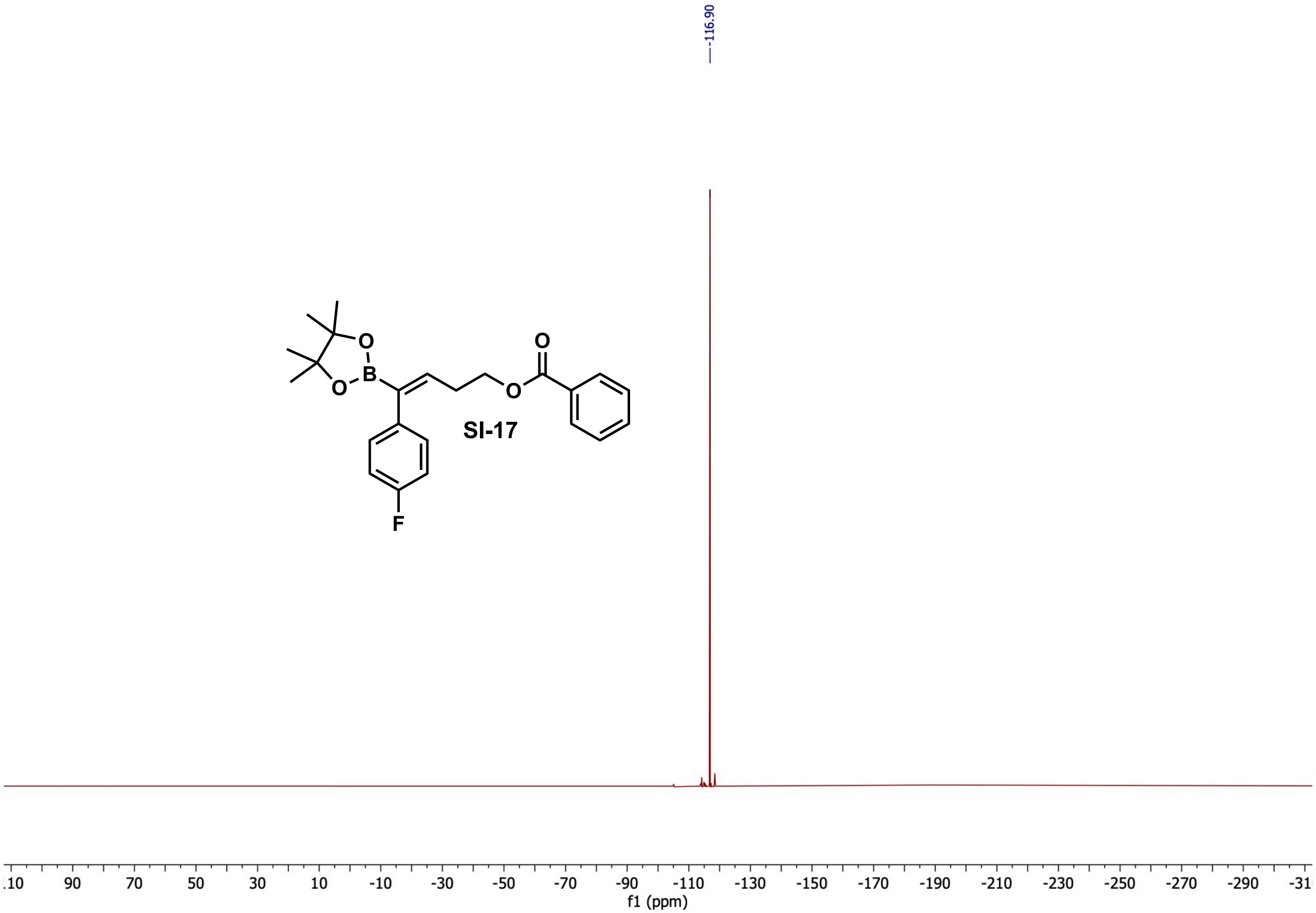


Figure S22. ^{19}F NMR of **SI-17** (470.68 MHz, $CDCl_3$).

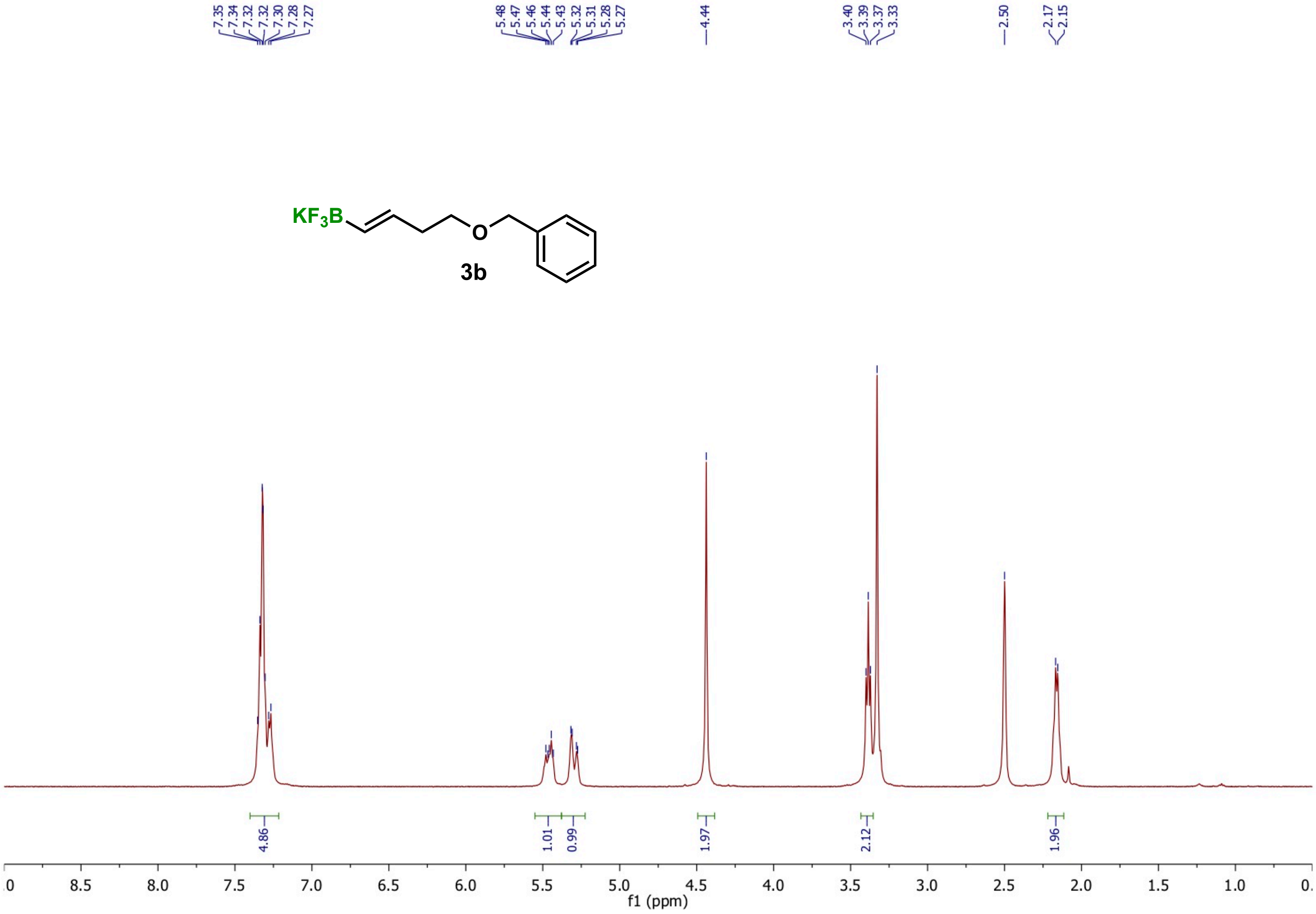


Figure S23. ^{1}H NMR of compound **3b** (500.27 MHz, DMSO-*d*6).

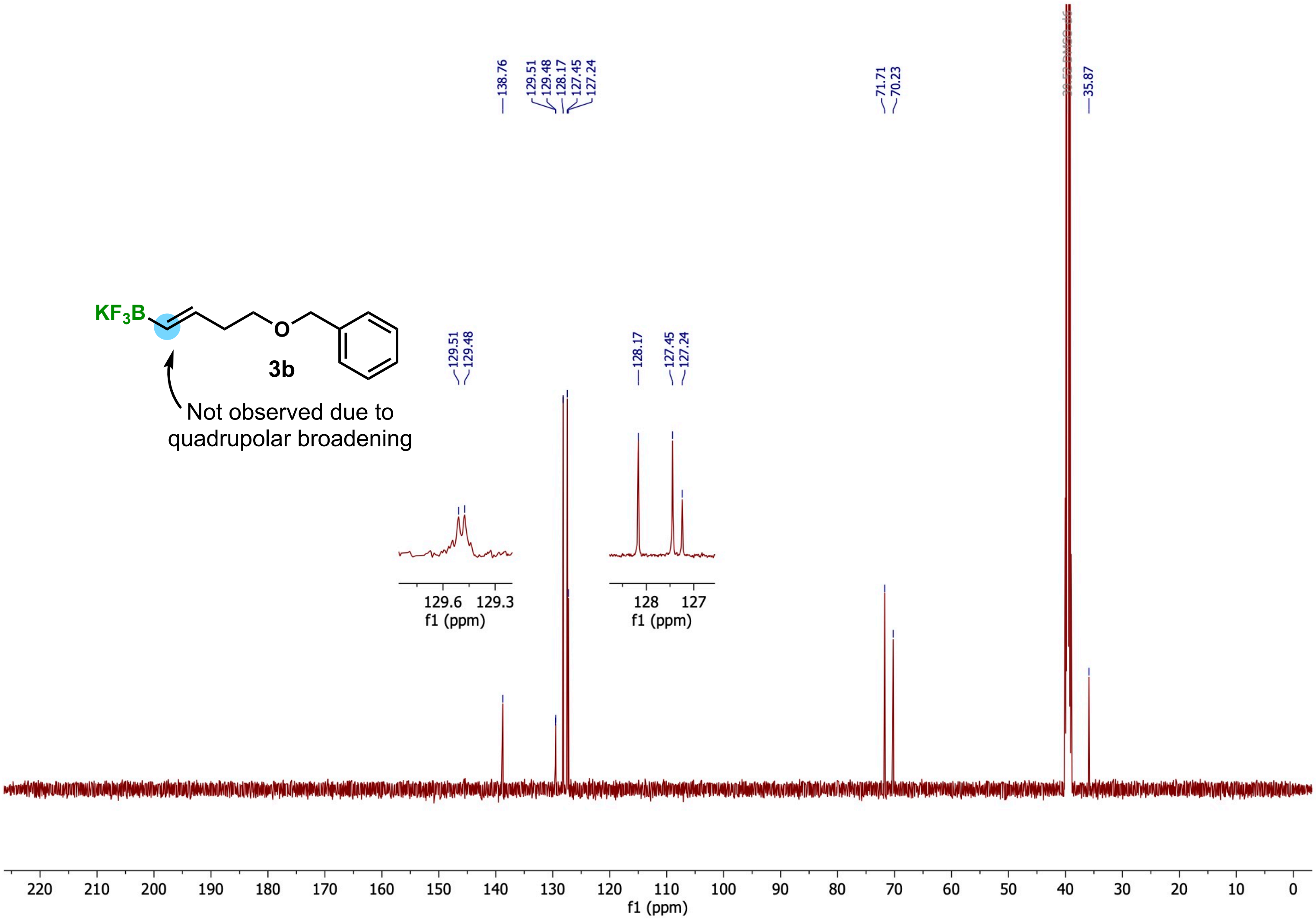


Figure S24. ^{13}C NMR of compound **3b** (125.81 MHz, DMSO-*d*6).

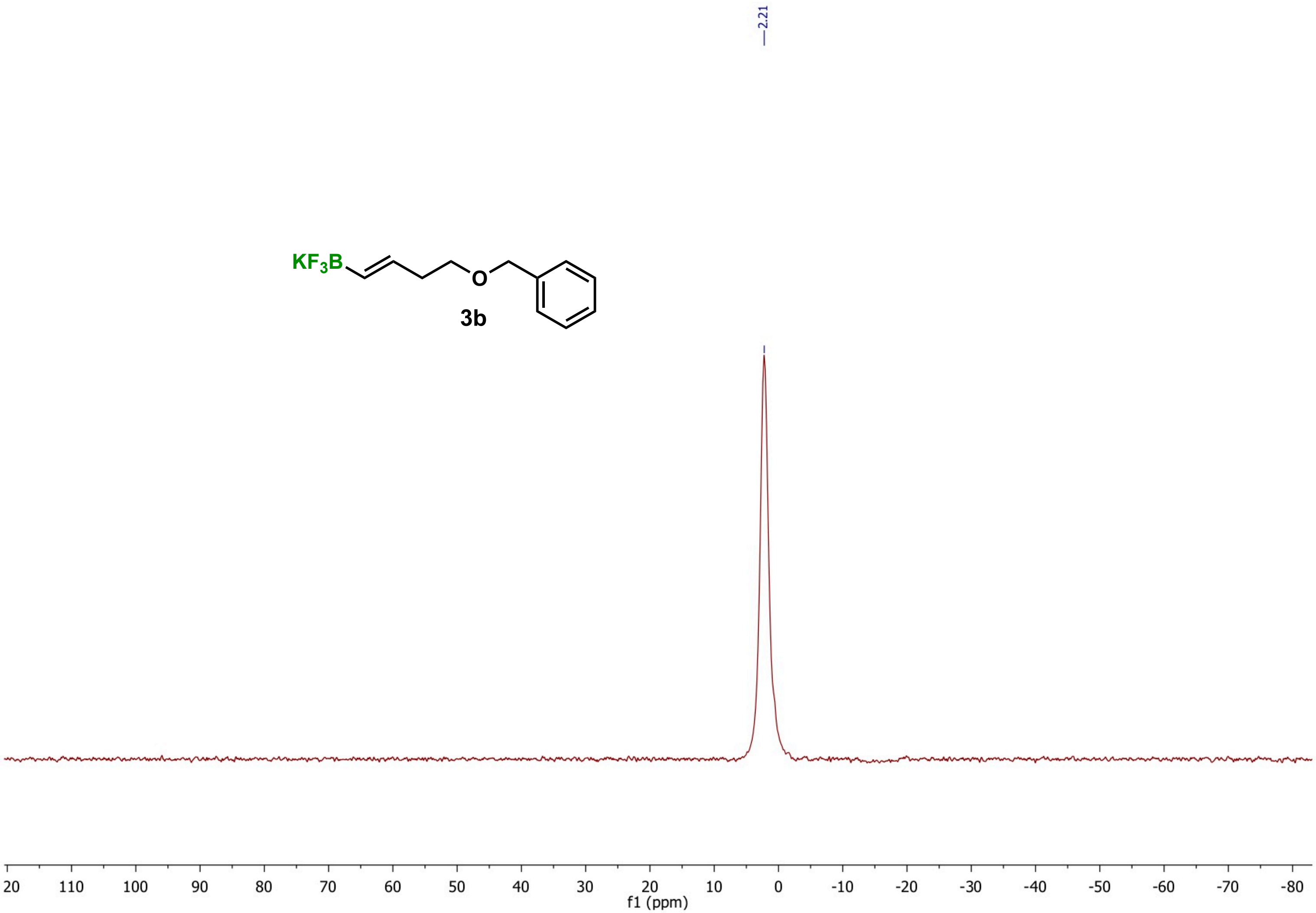


Figure S25. ^{11}B NMR of compound **3b** (160.51 MHz, DMSO-*d*6).

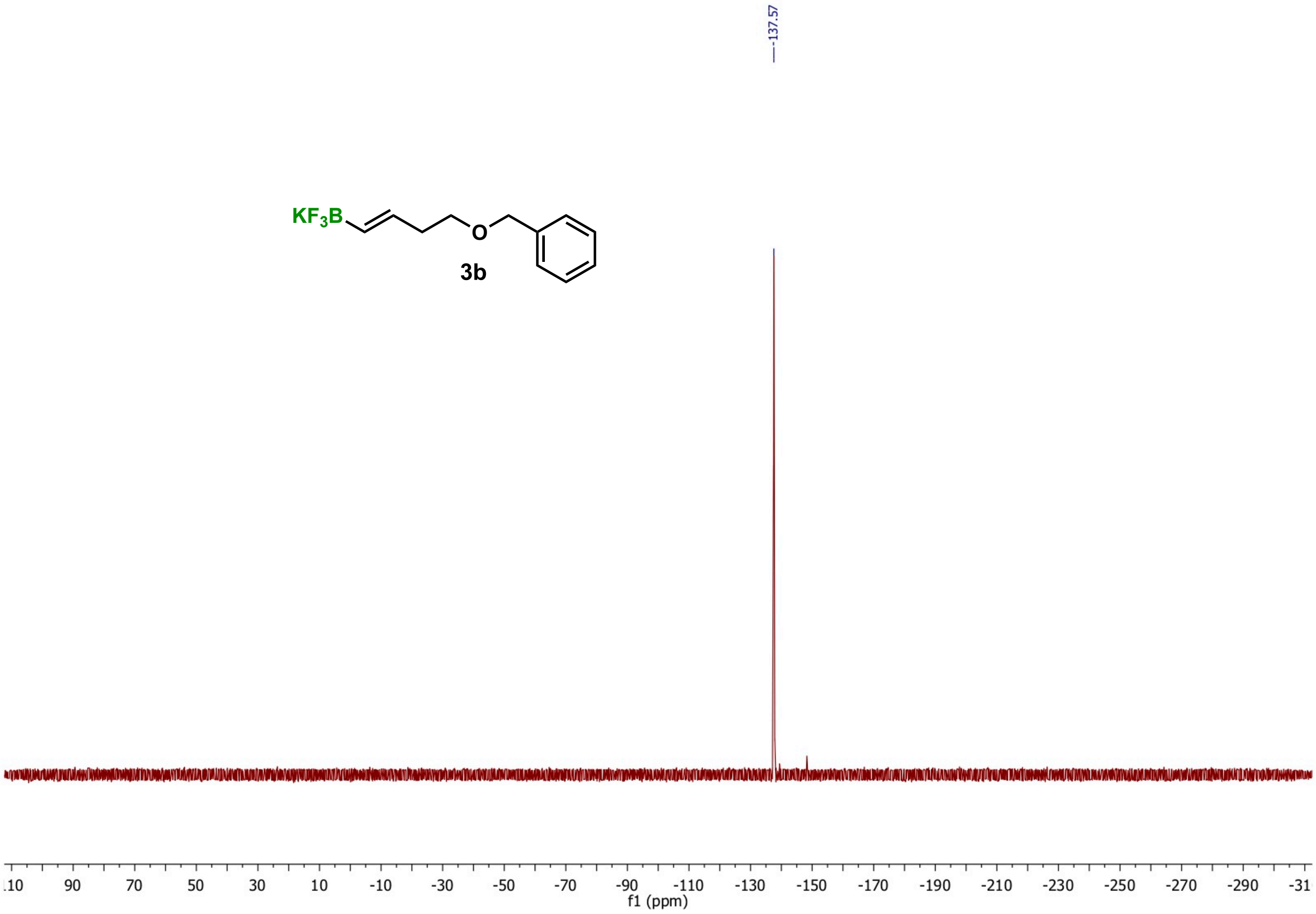


Figure S26. ^{19}F NMR of compound **3b** (470.68 MHz, DMSO-*d*6).

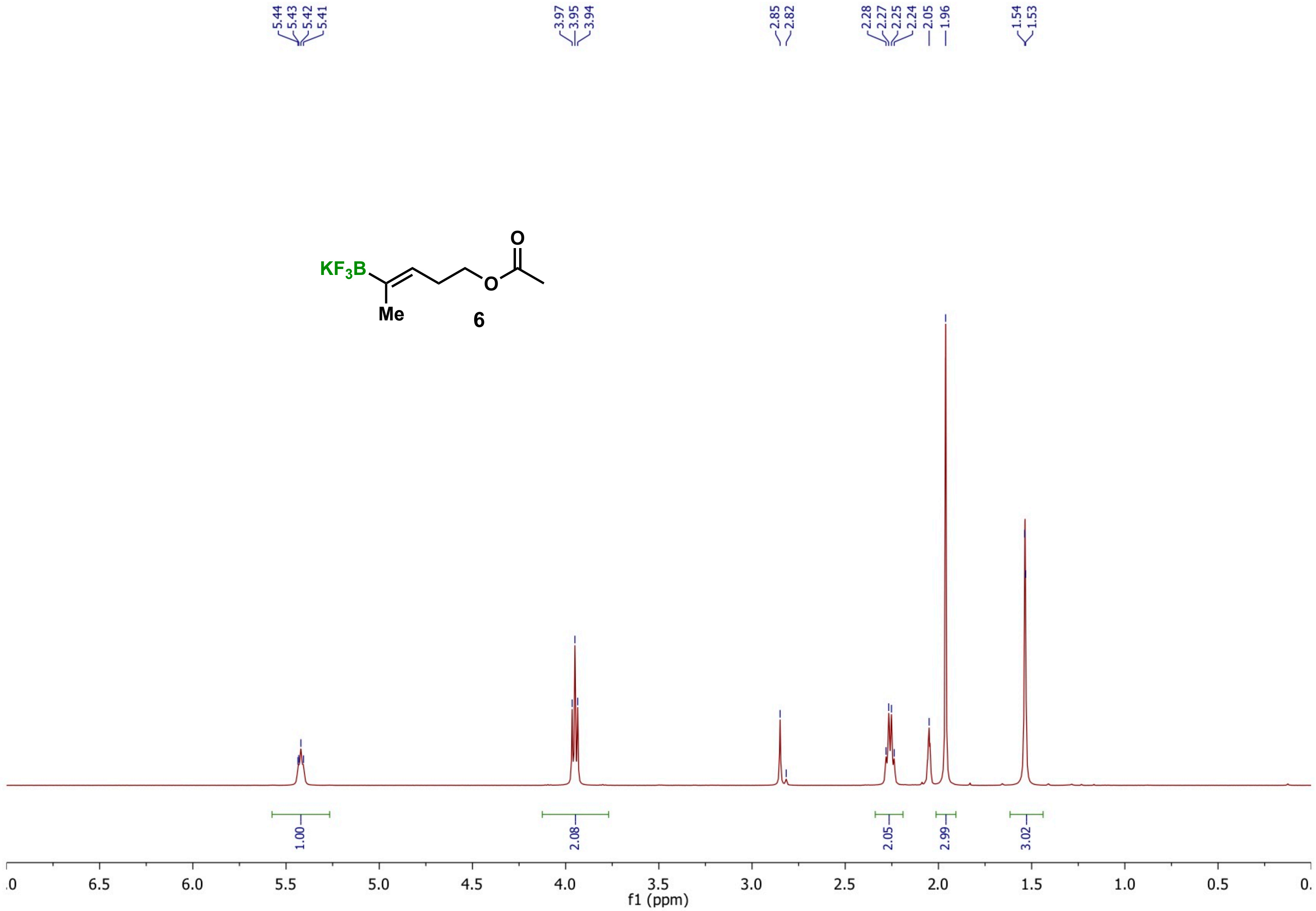
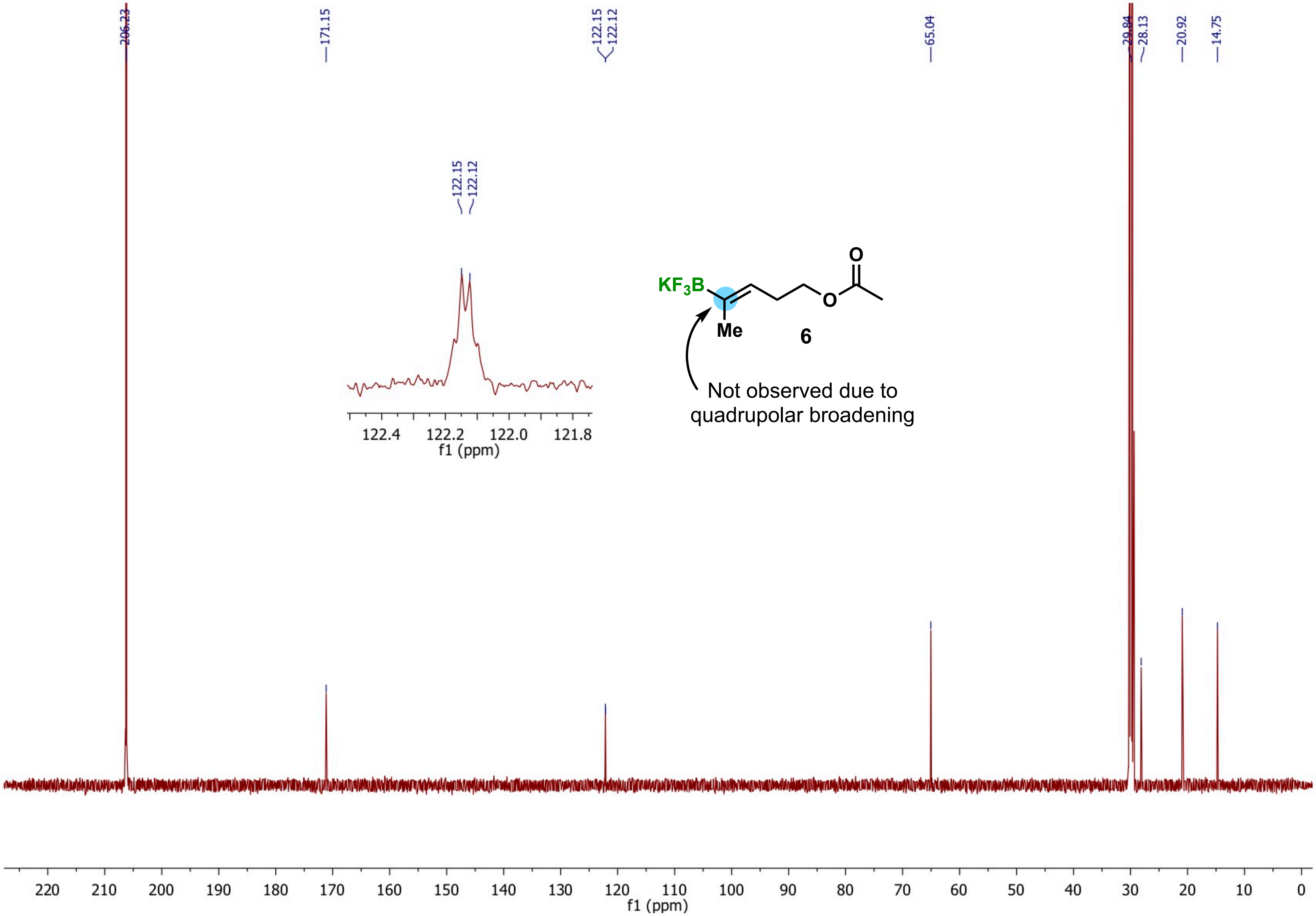


Figure S27. ^{1}H NMR of compound **6** (500.27 MHz, acetone-*d*6).



6

Not observed due to quadrupolar broadening

Figure S28. ^{13}C NMR of compound **6** (125.81 MHz, acetone-*d*6).

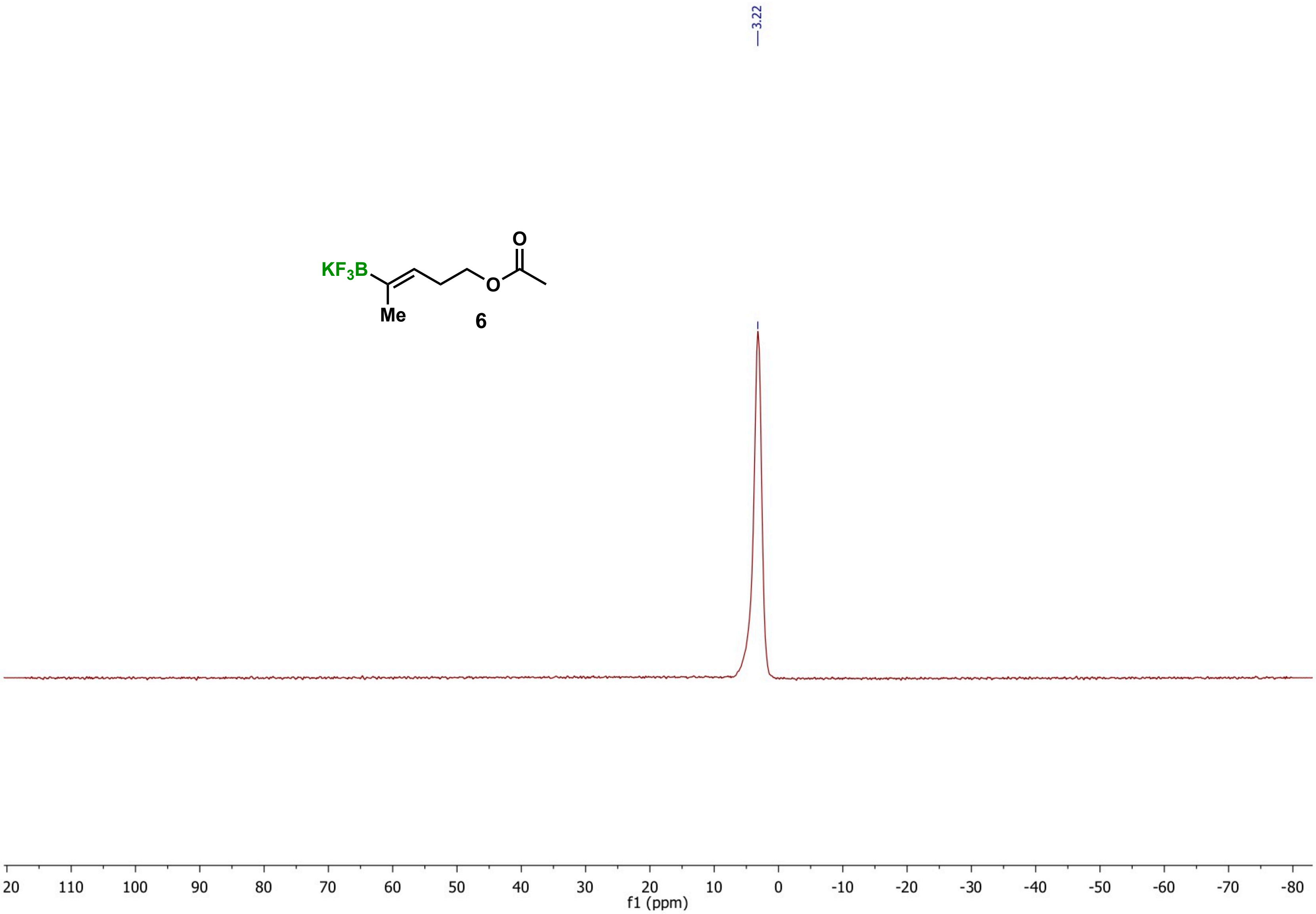


Figure S29. ^{11}B NMR of compound **6** (160.51 MHz, acetone-*d*6).

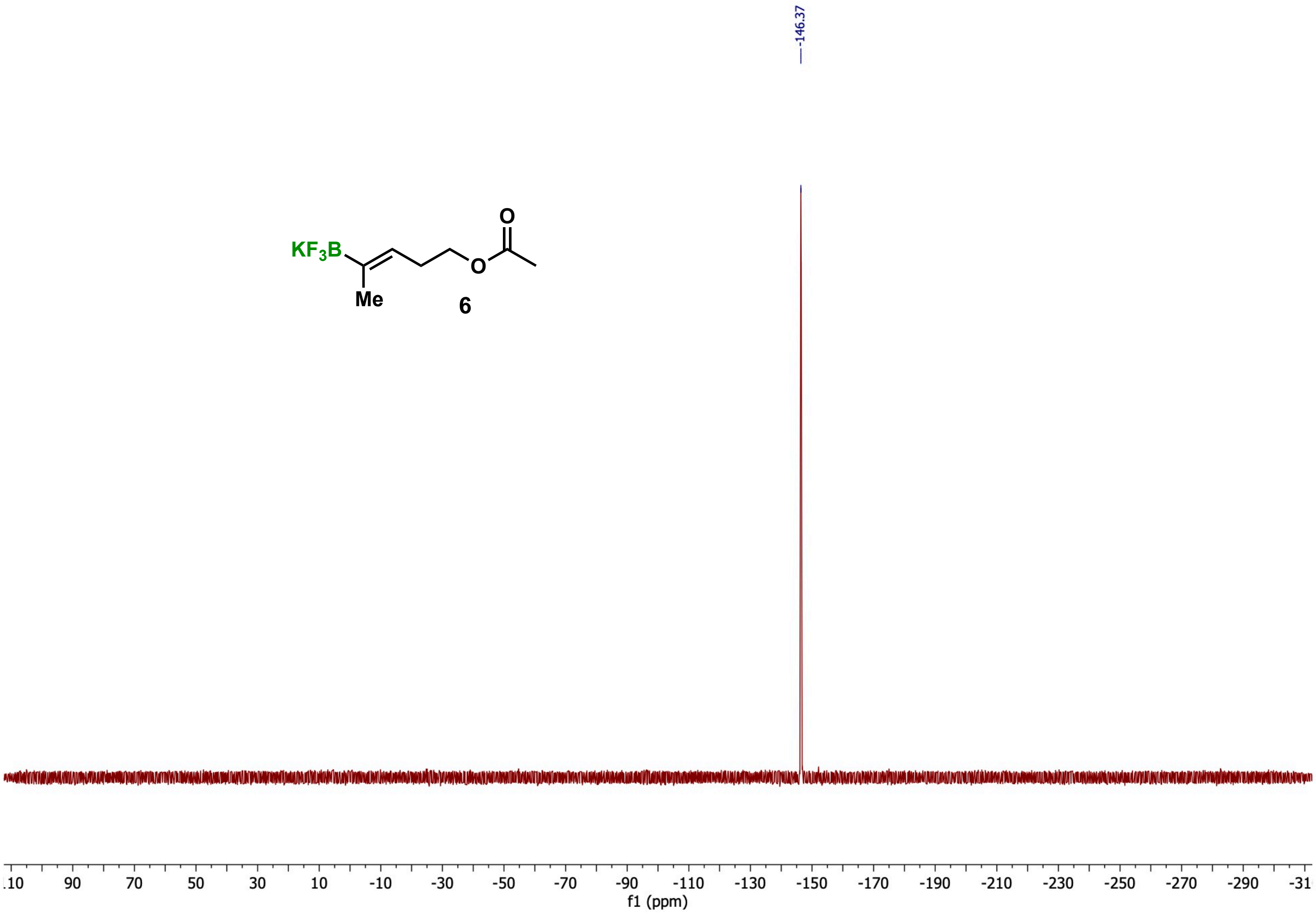


Figure S30. ^{19}F NMR of compound **6** (470.68 MHz, acetone-*d*6).

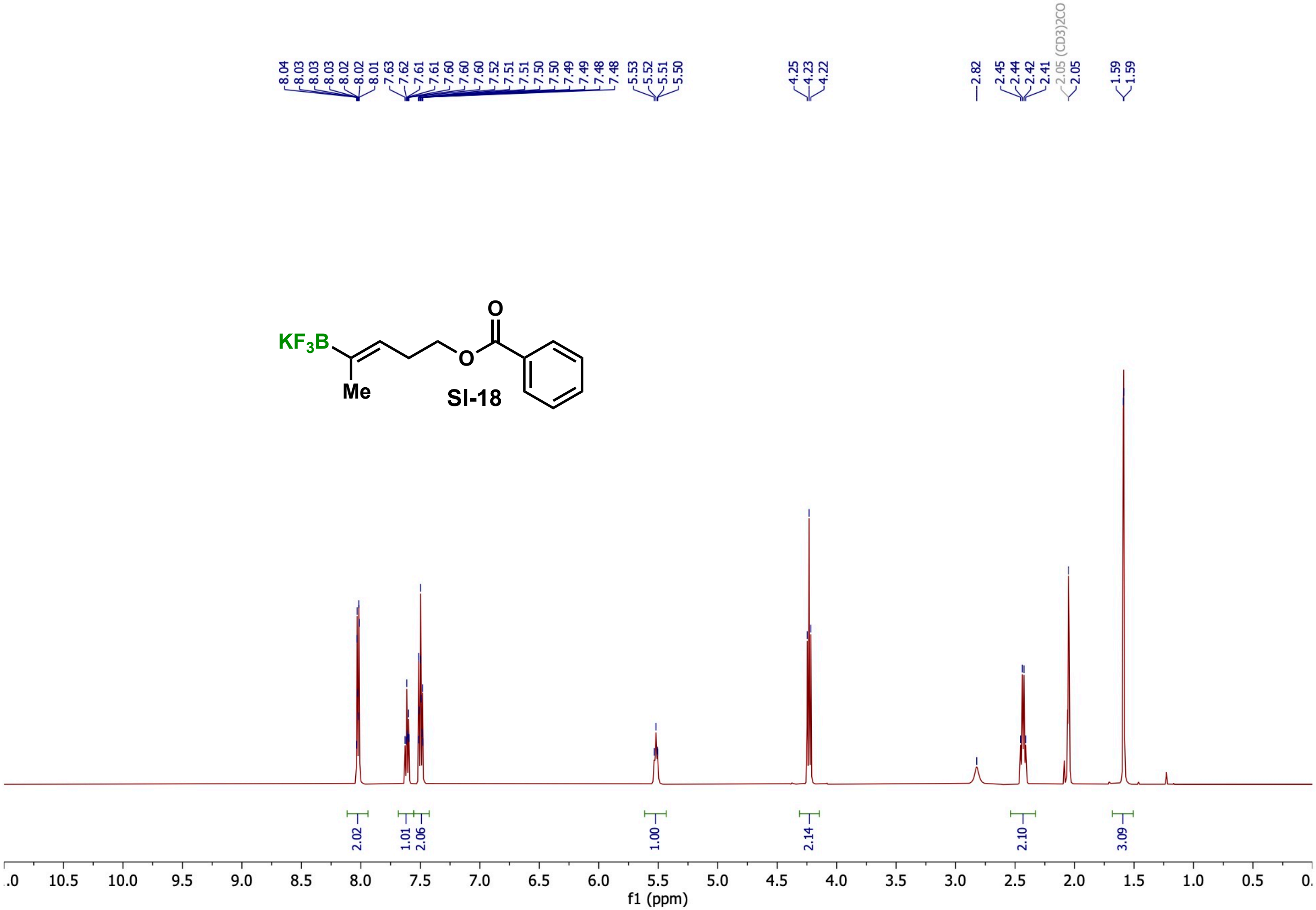
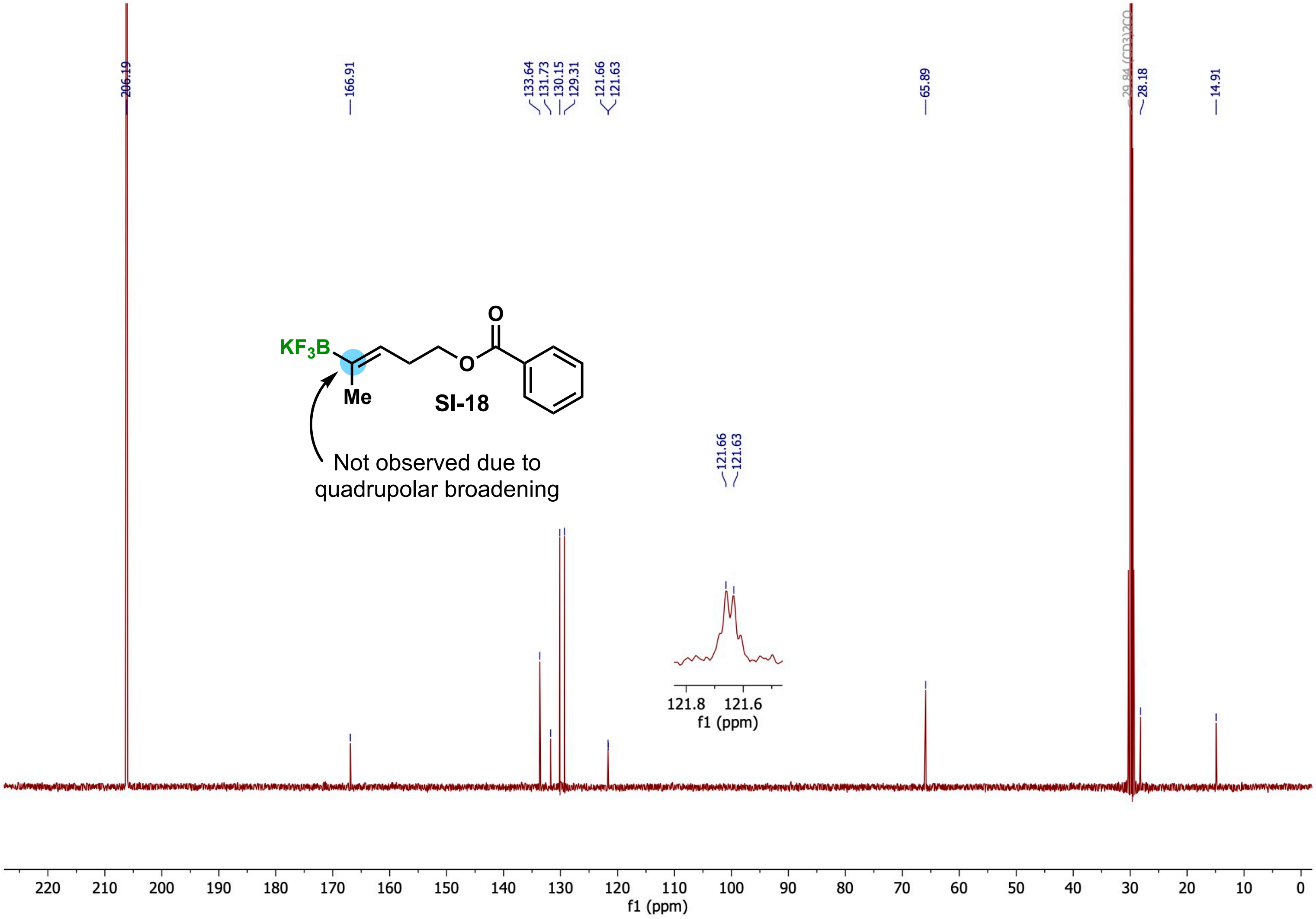


Figure S31. ^{1}H NMR of **SI-18** (500.27 MHz, acetone-*d*6).



Not observed due to quadrupolar broadening

Figure S32. ^{13}C NMR of **SI-18** (125.81 MHz, acetone-*d*6).

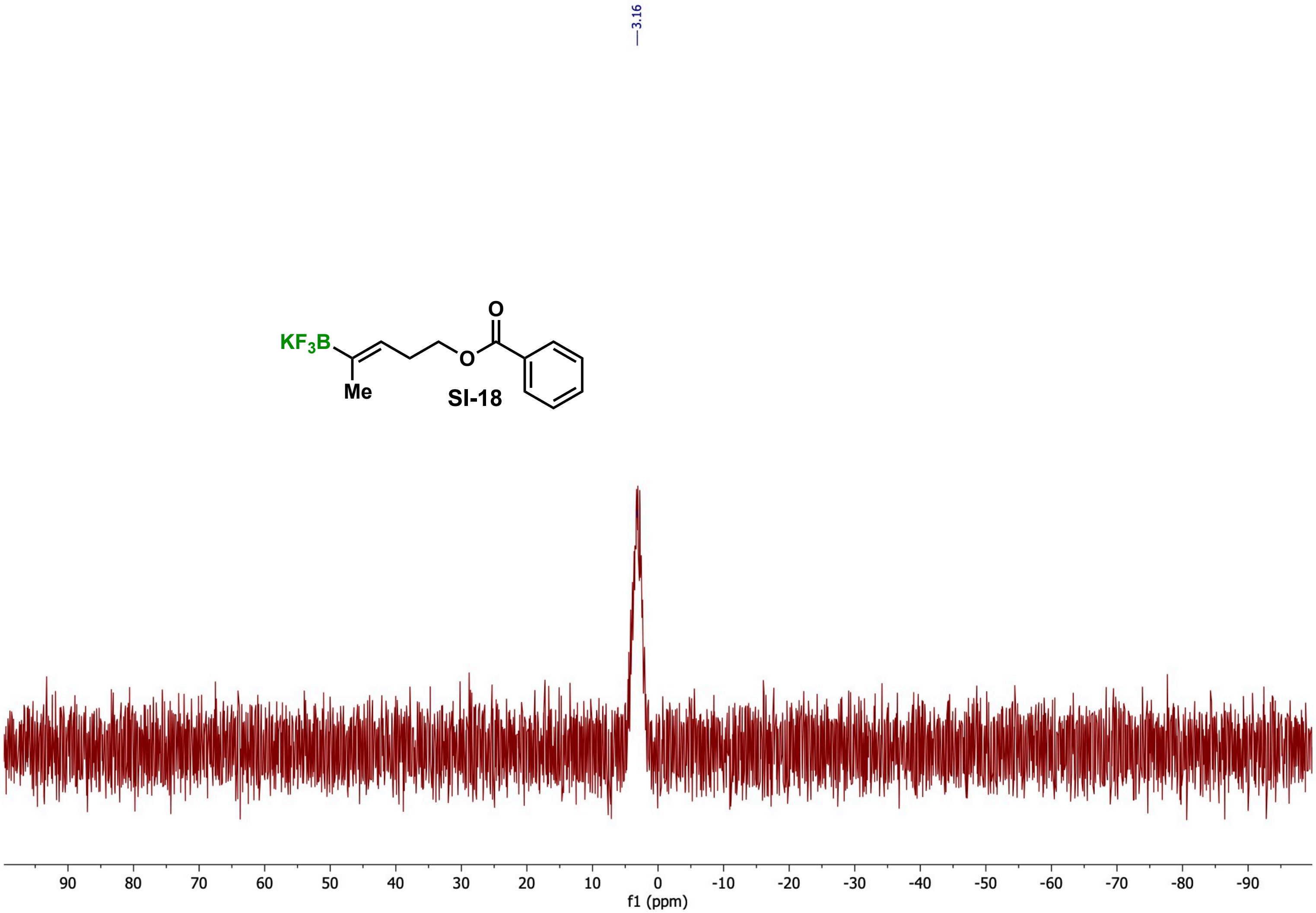


Figure S33. ^{11}B NMR of **SI-18** (96.34 MHz, acetone-*d*6).

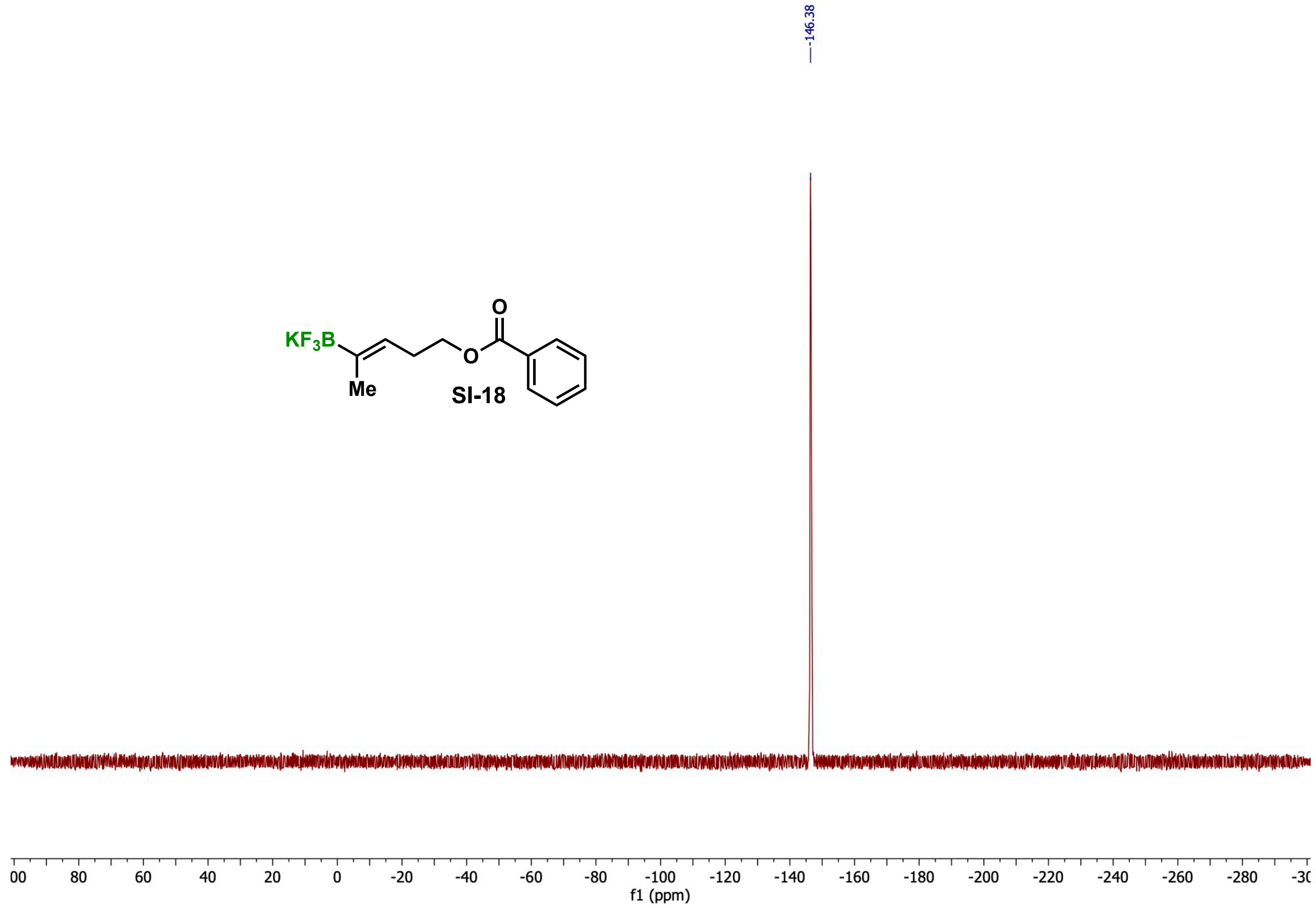


Figure S34. ^{19}F NMR of **SI-18** (282.51 MHz, acetone-*d*6).

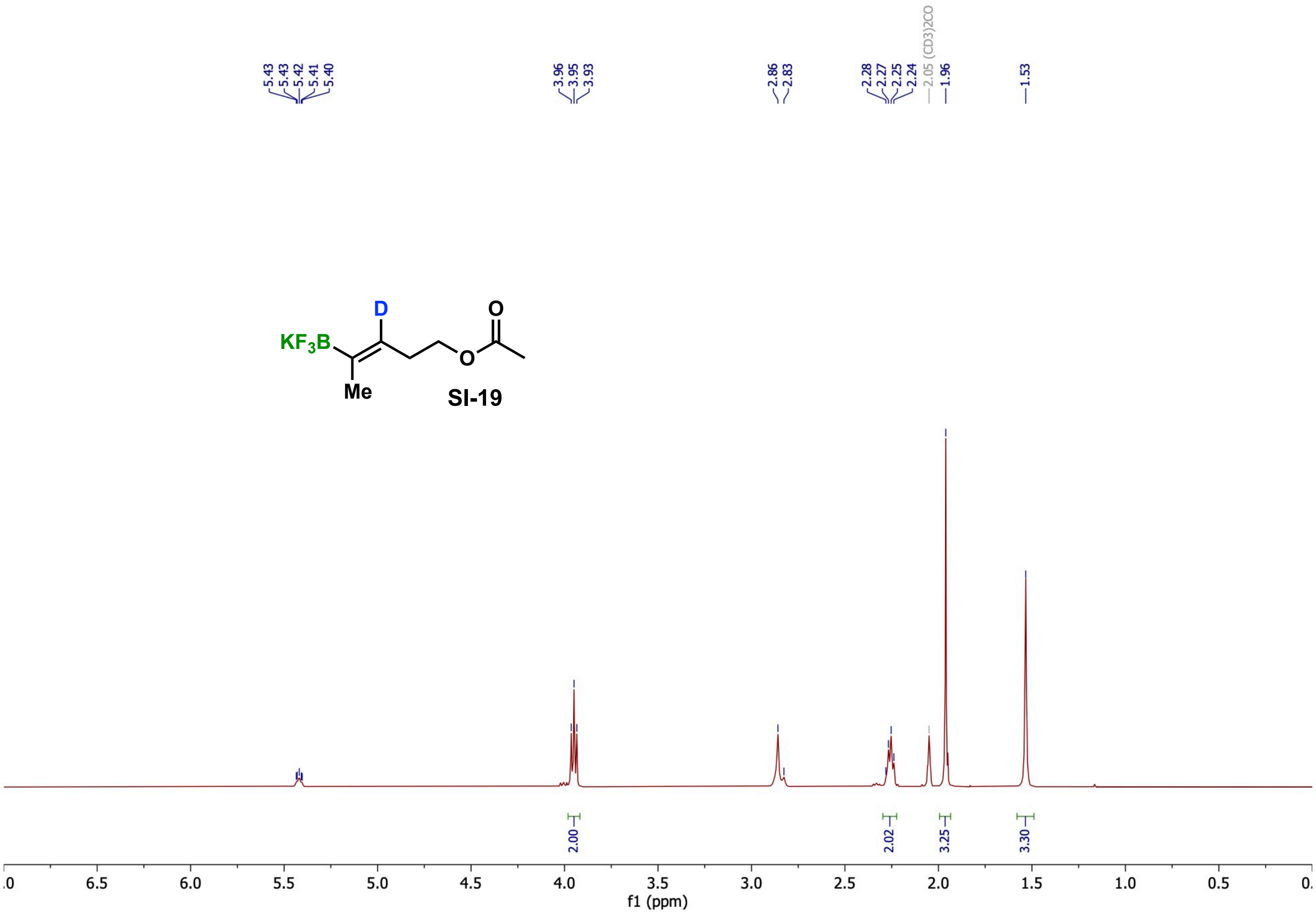


Figure S35. ^{1}H NMR of **SI-19** (500.27 MHz, acetone-*d*6).

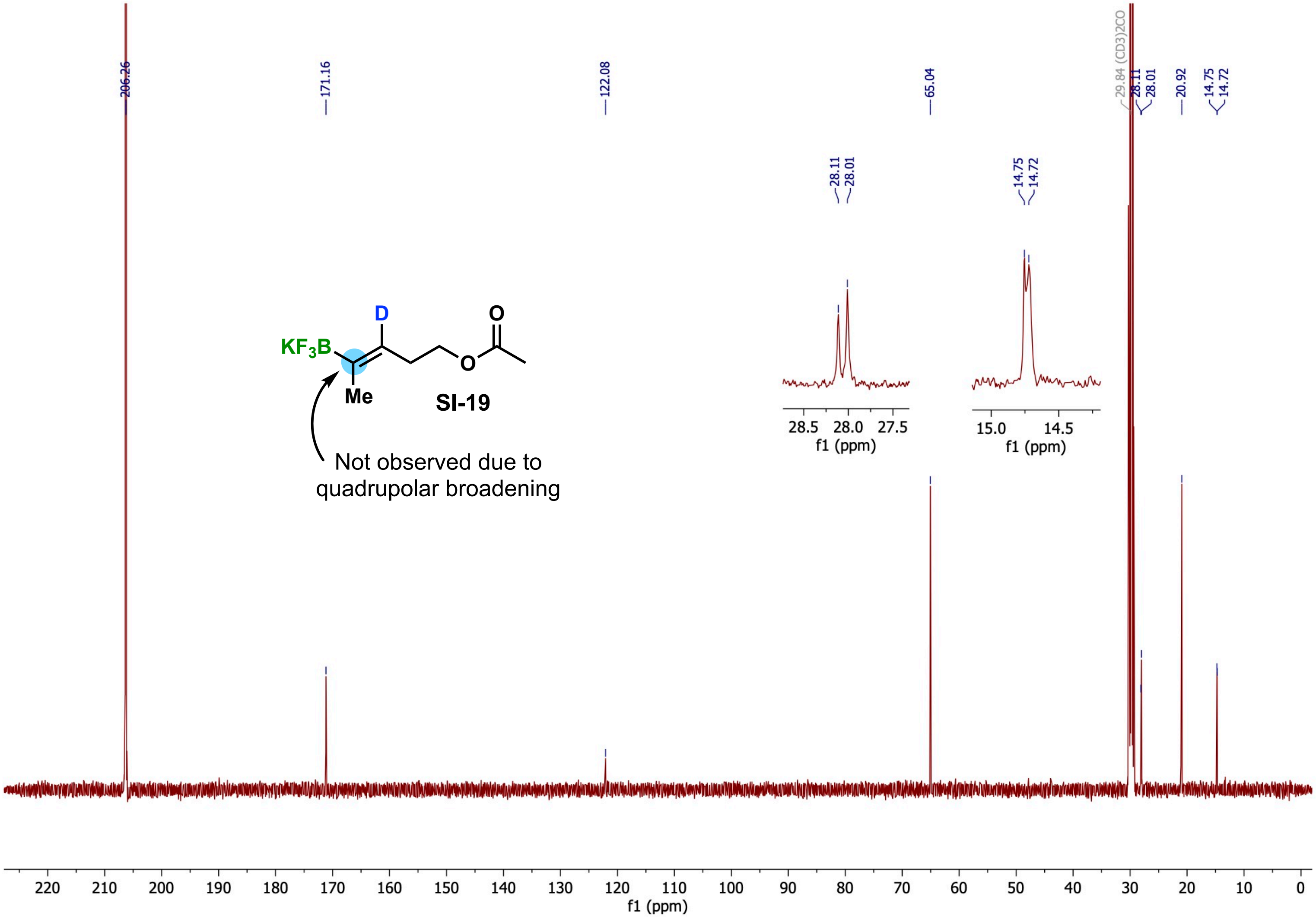


Figure S36. ^{13}C NMR of **SI-19** (125.81 MHz, acetone-*d*6).

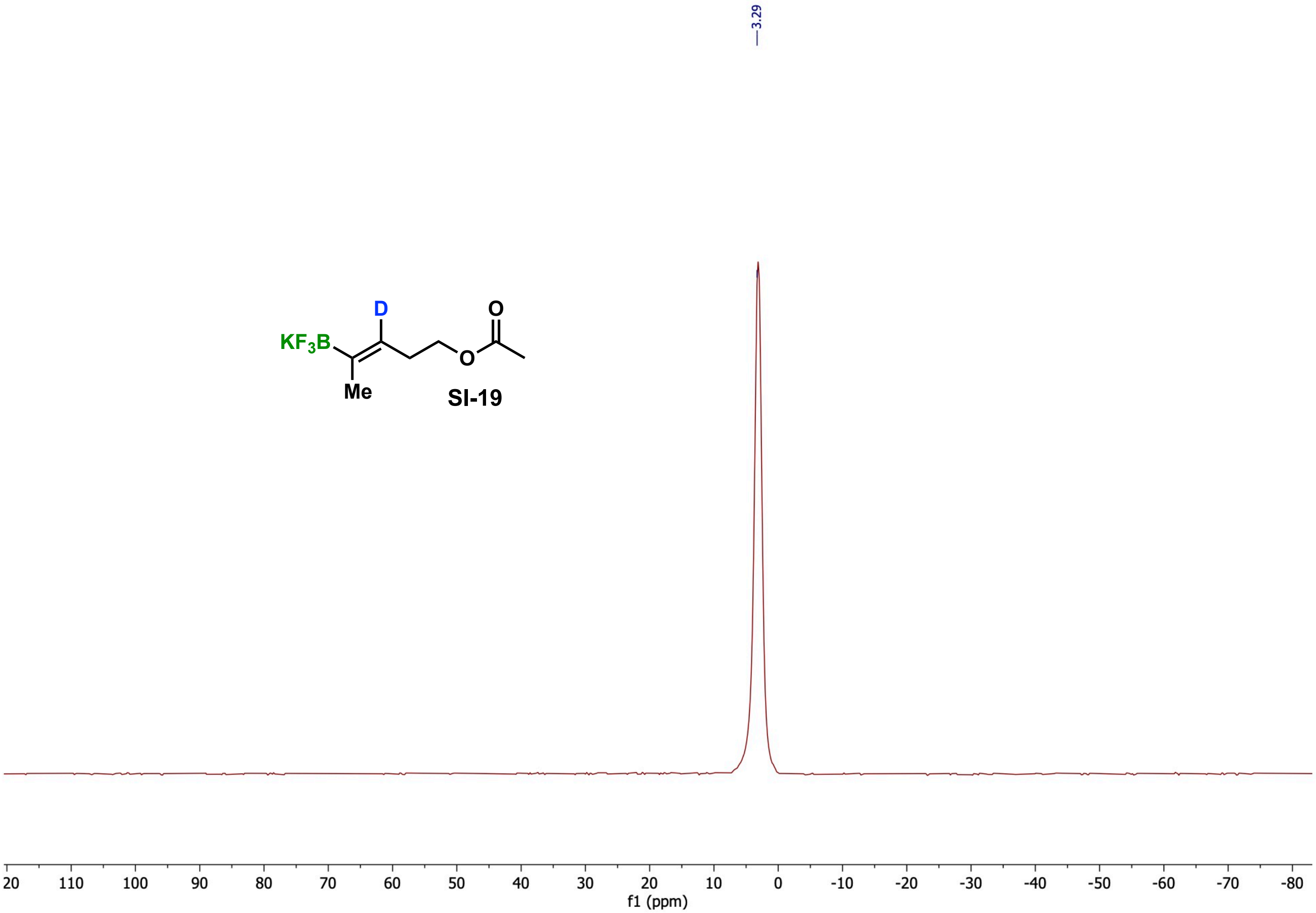


Figure S37. ^{11}B NMR of **SI-19** (160.51 MHz, acetone-*d*6).

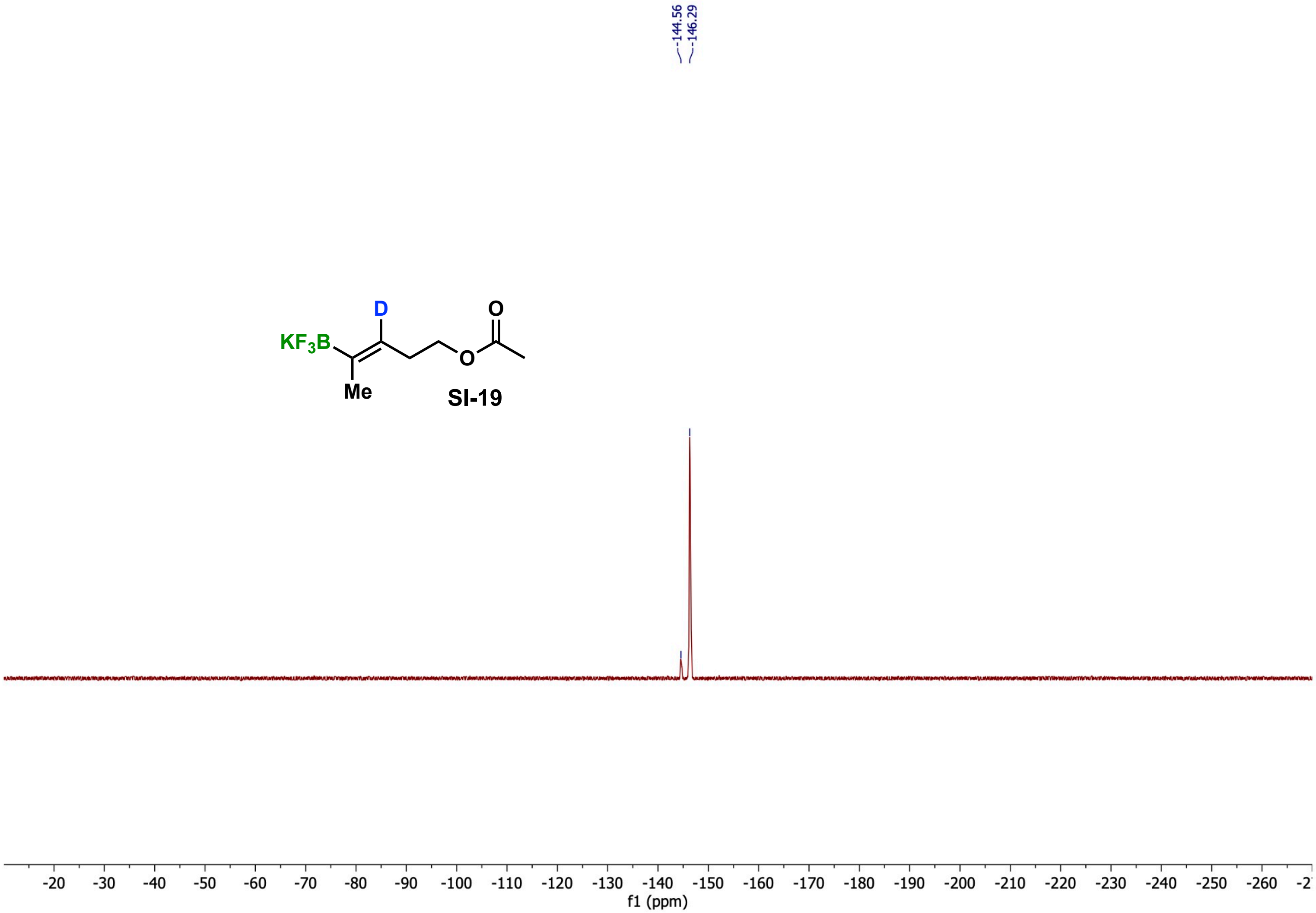


Figure S38. ^{19}F NMR of **SI-19** (470.68 MHz, acetone-*d*6).

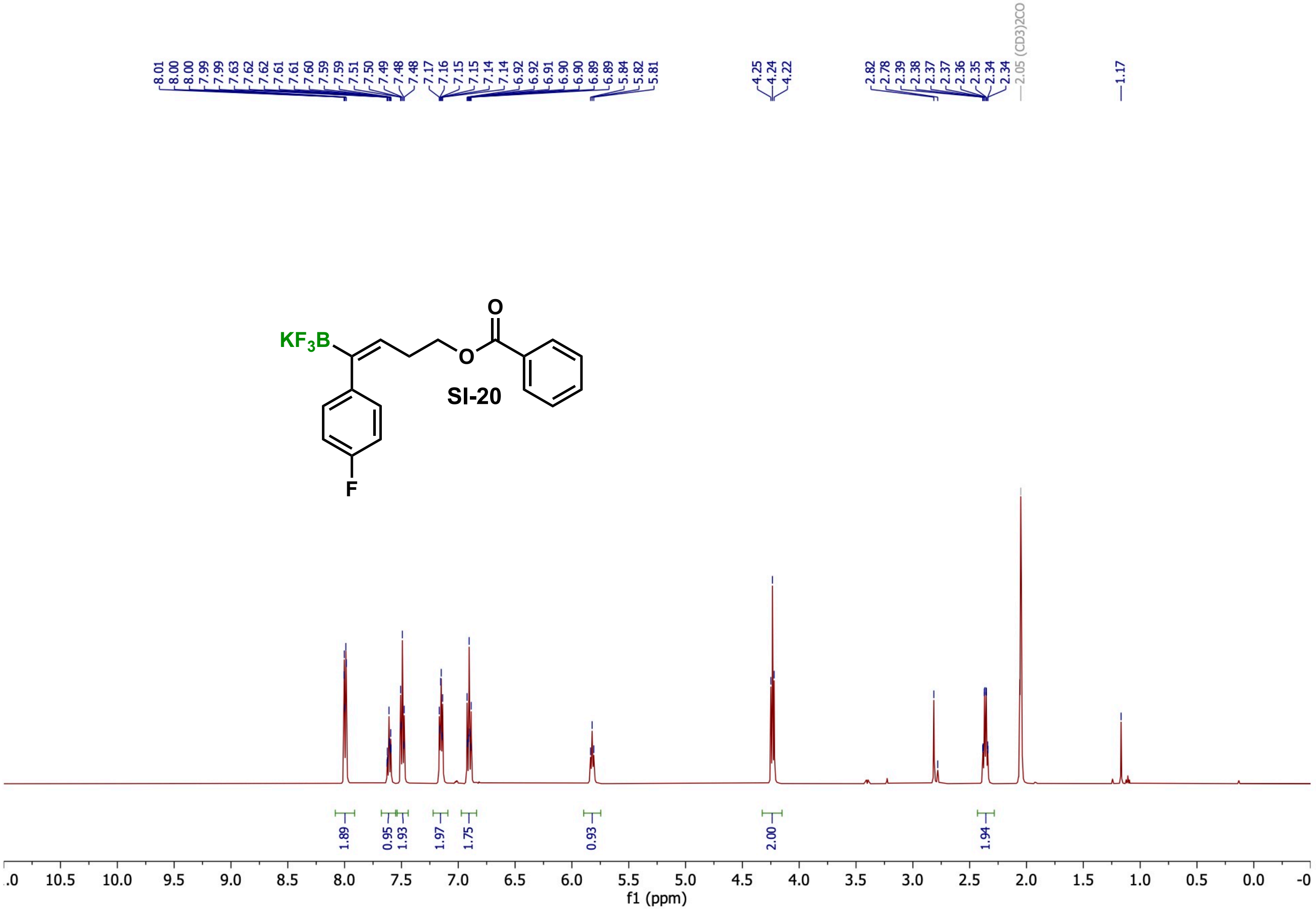
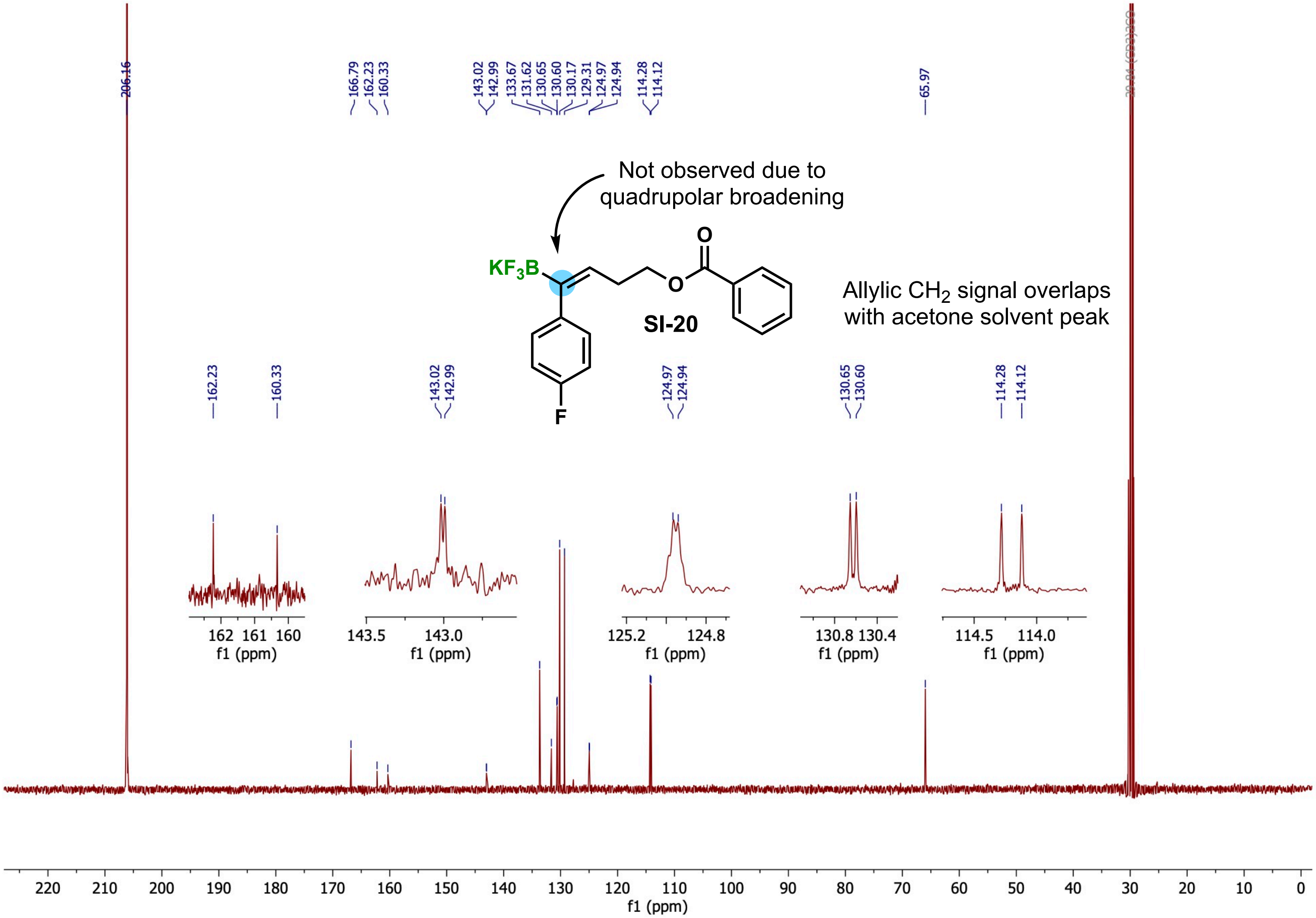


Figure S39. ^{1}H NMR of **SI-20** (500.27 MHz, acetone-*d*6).



Not observed due to quadrupolar broadening

Allylic CH_2 signal overlaps with acetone solvent peak

Figure S40. ^{13}C NMR of **SI-20** (125.81 MHz, acetone-*d*6).

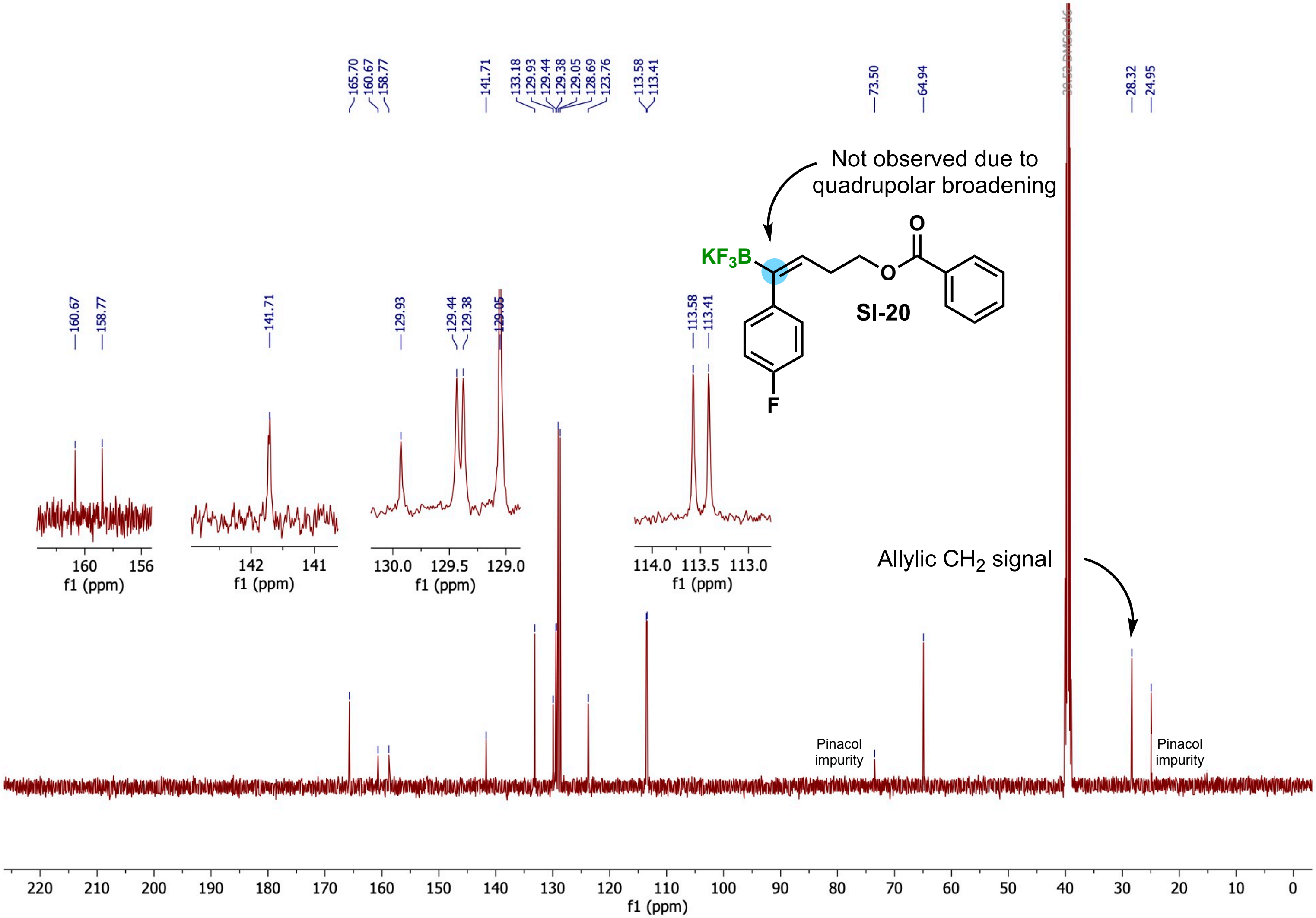


Figure S41. ^{13}C NMR of **SI-20** (125.81 MHz, DMSO-*d*6).

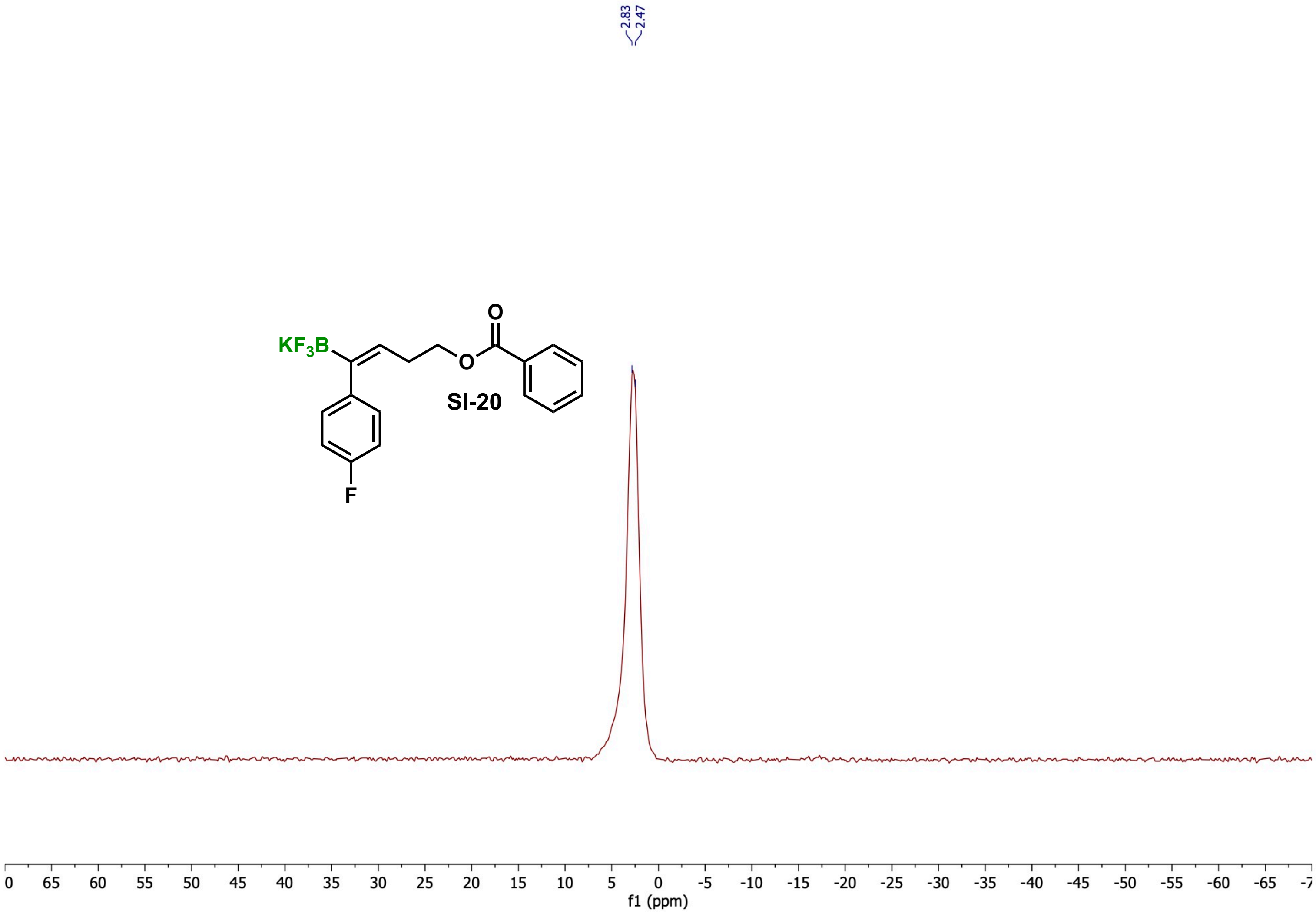


Figure S42. ^{11}B NMR of **SI-20** (160.51 MHz, acetone-*d*6).

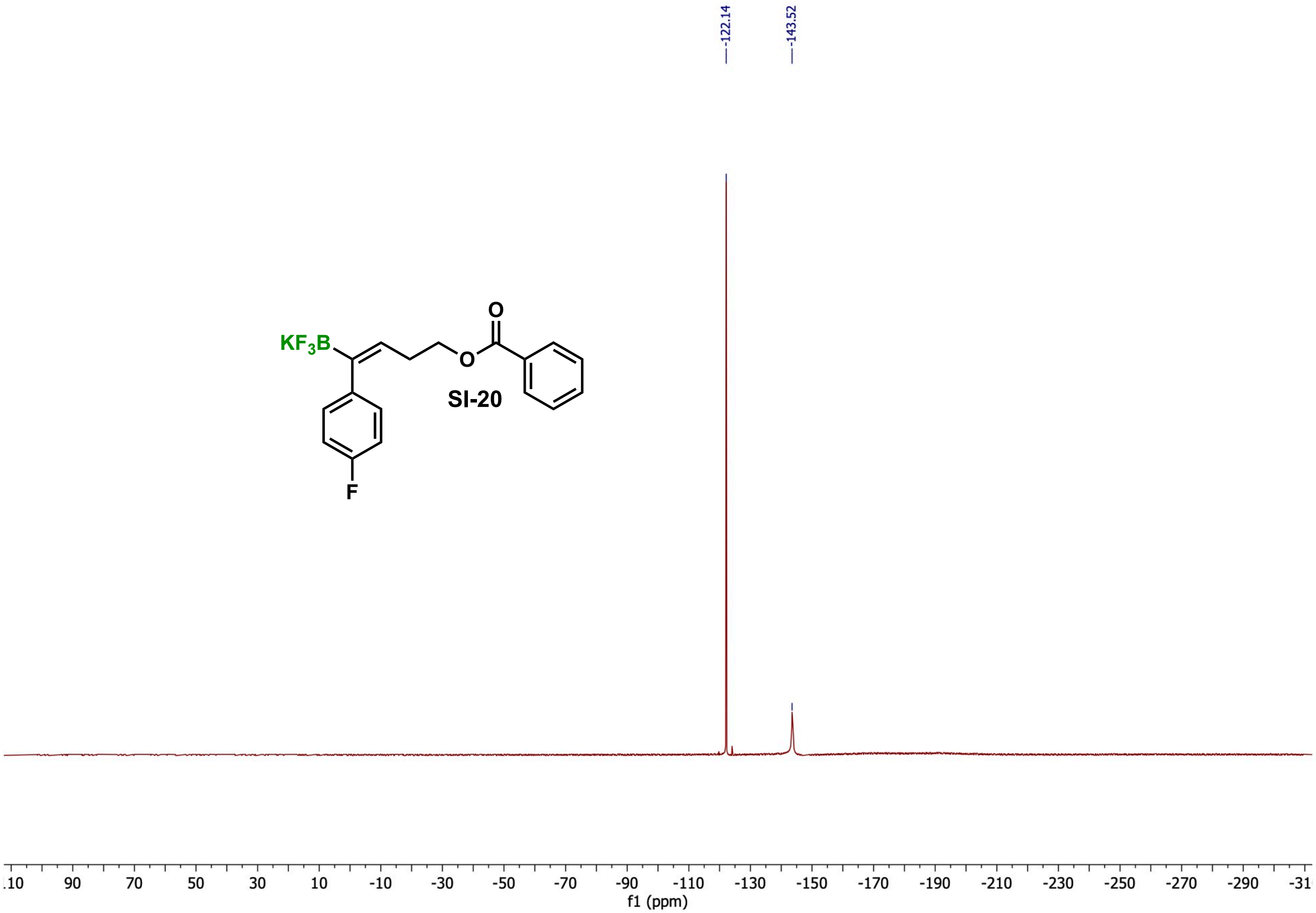


Figure S43. ^{19}F NMR of **SI-20** (470.68 MHz, acetone-*d*6).

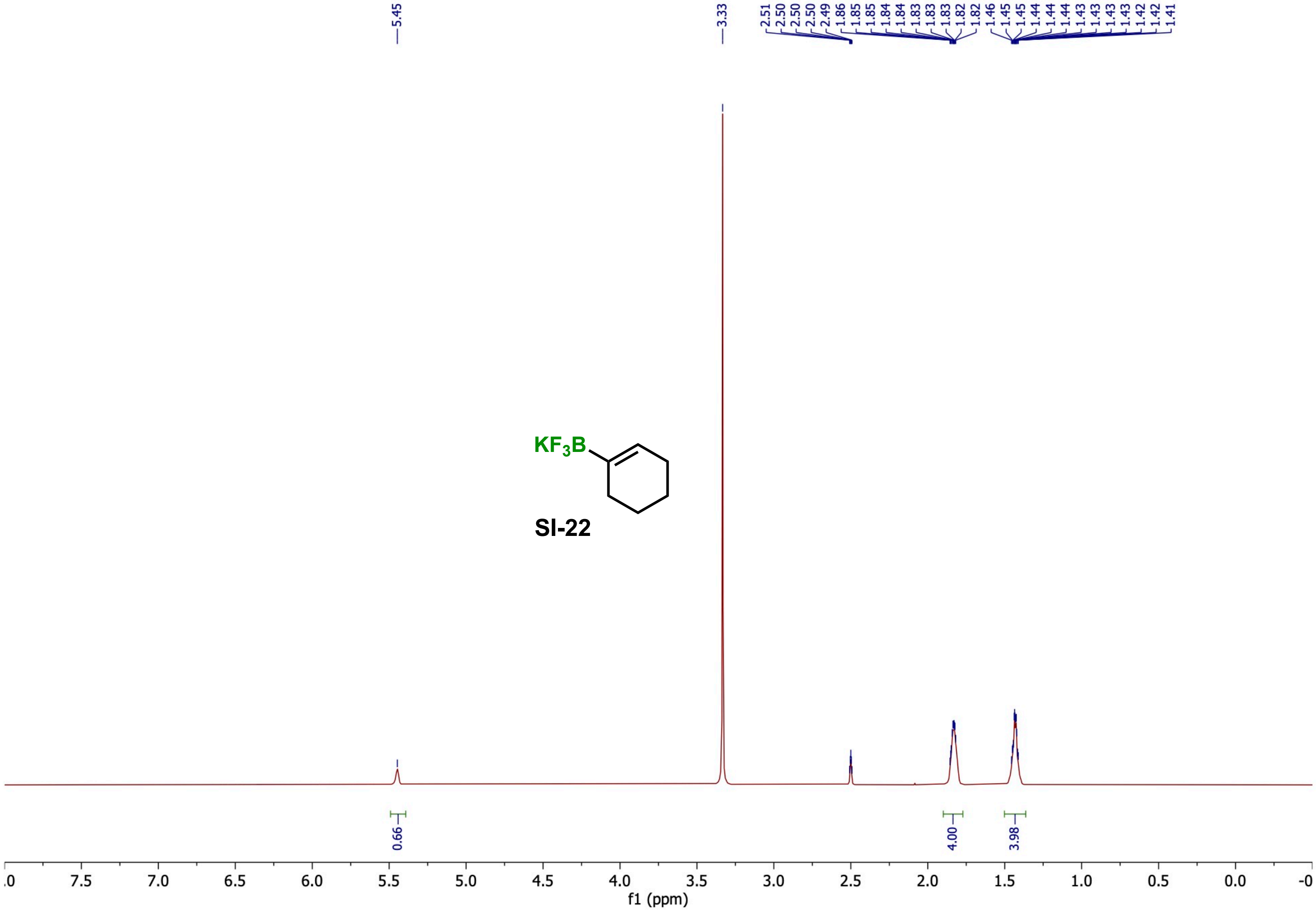


Figure S44. ^{1}H NMR of **SI-22** (500.27 MHz, DMSO-*d*6).

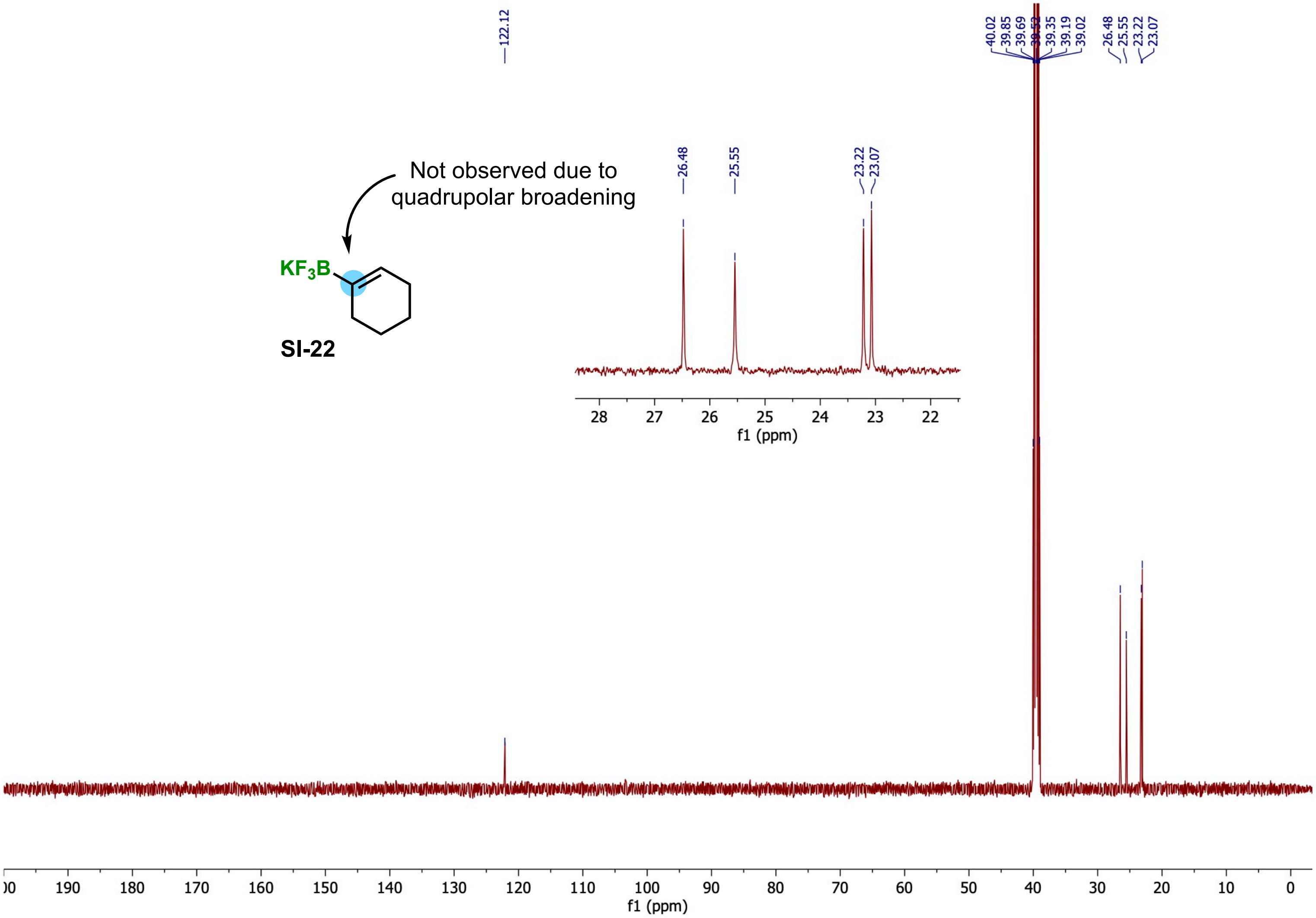


Figure S45. ^{13}C NMR of **SI-22** (125.81 MHz, DMSO-*d*6).

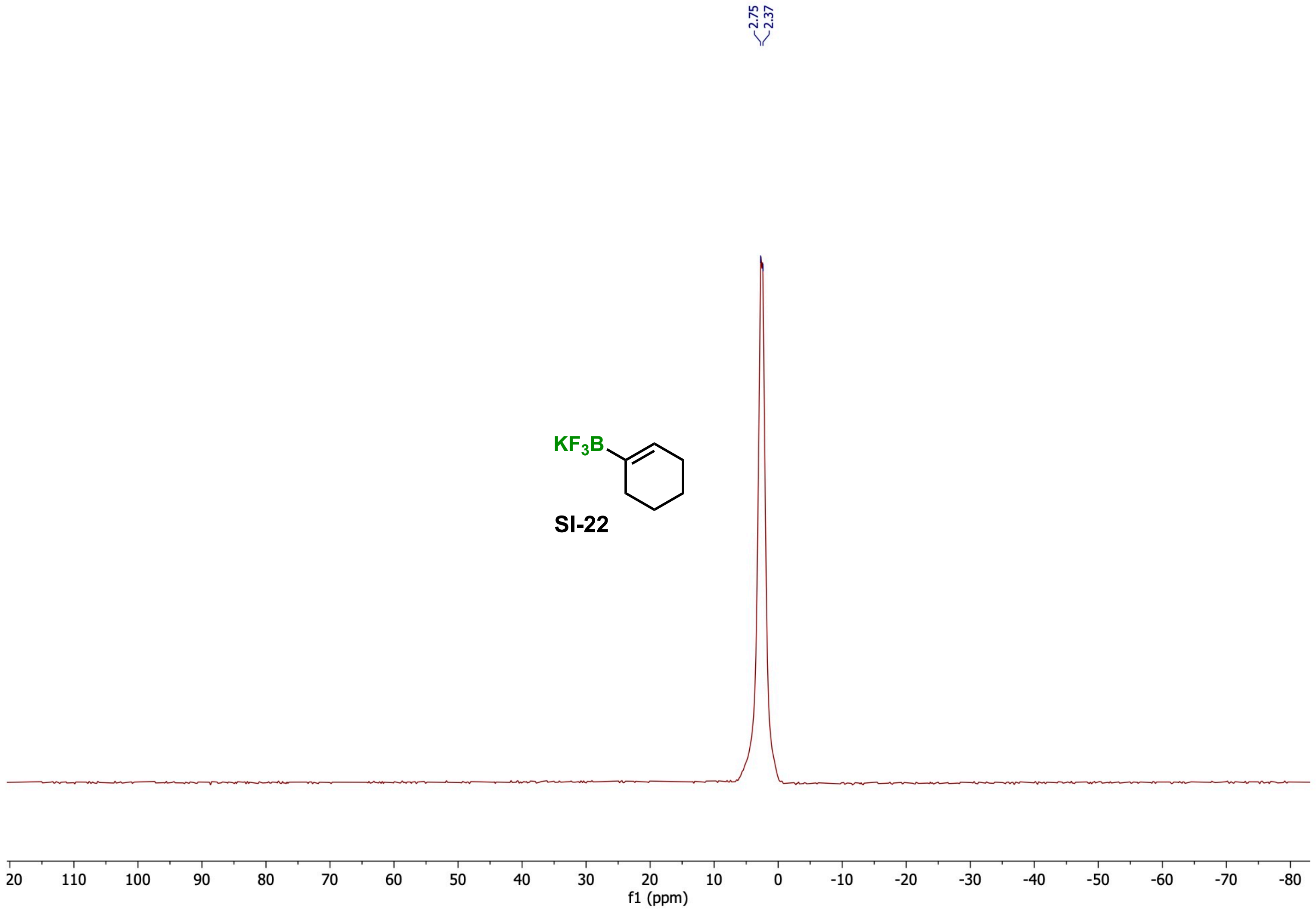


Figure S46. ^{11}B NMR of **SI-22** (160.51 MHz, DMSO-*d*6).

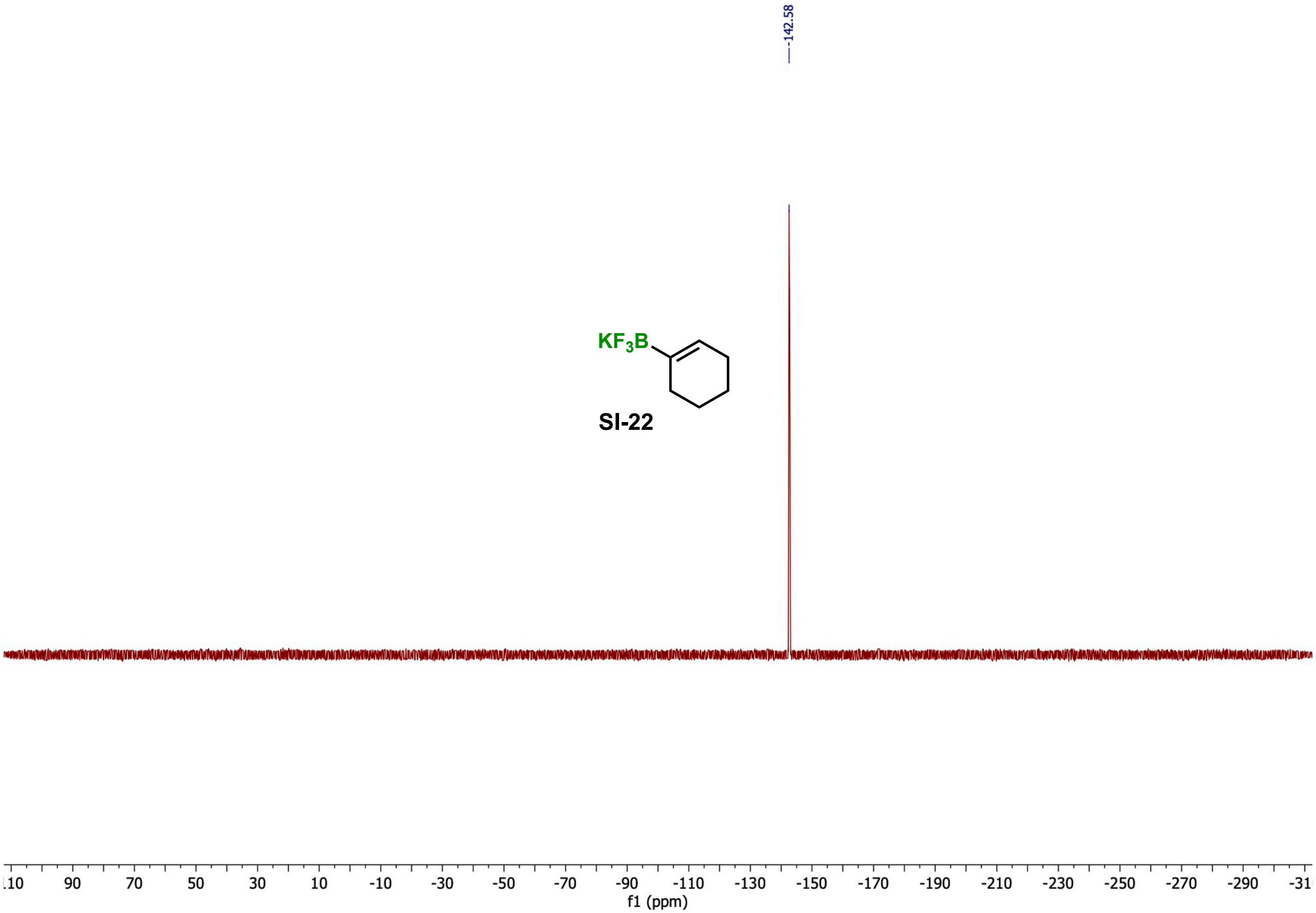


Figure S47. ^{19}F NMR of **SI-22** (470.68 MHz, DMSO-*d*6).

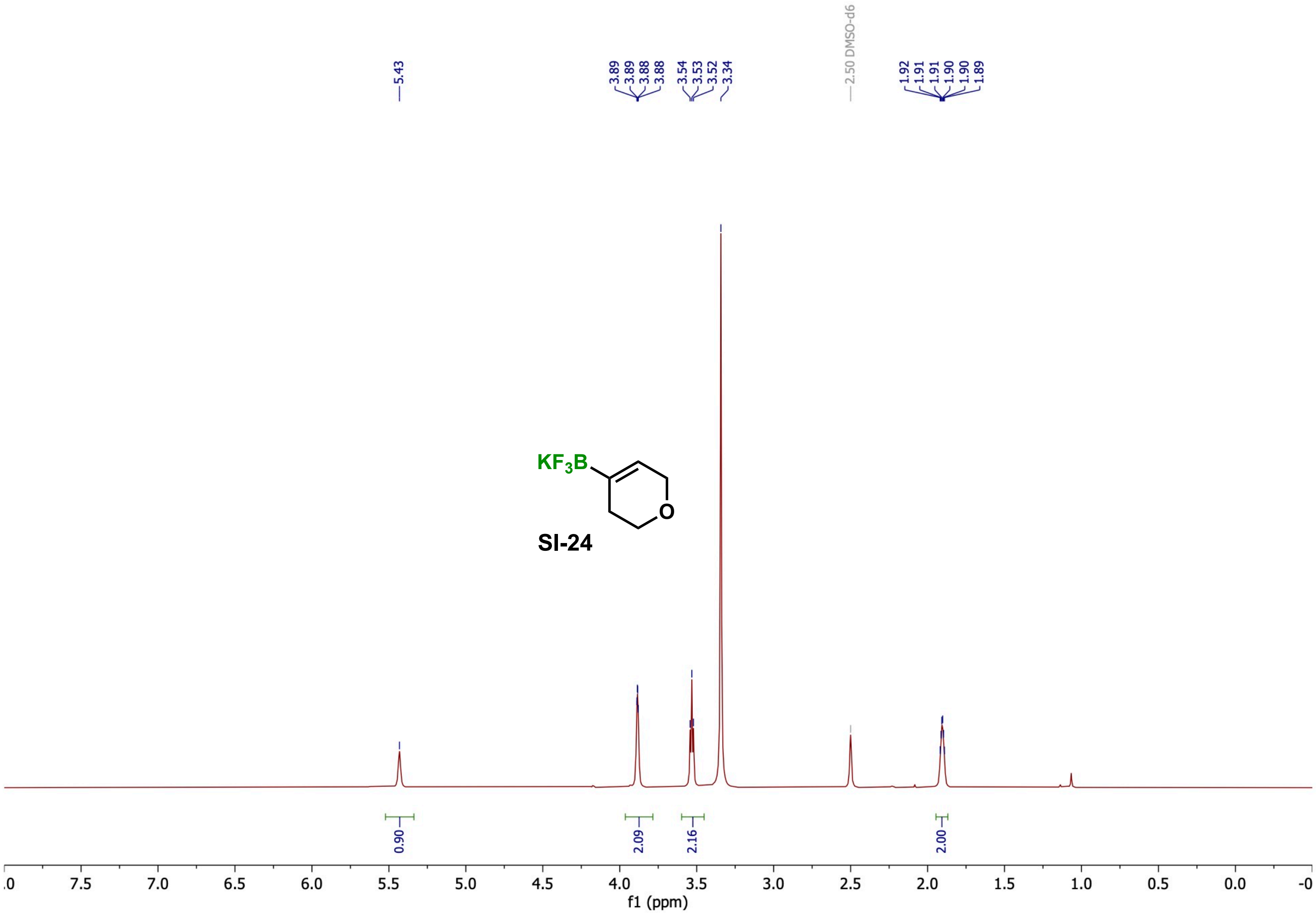
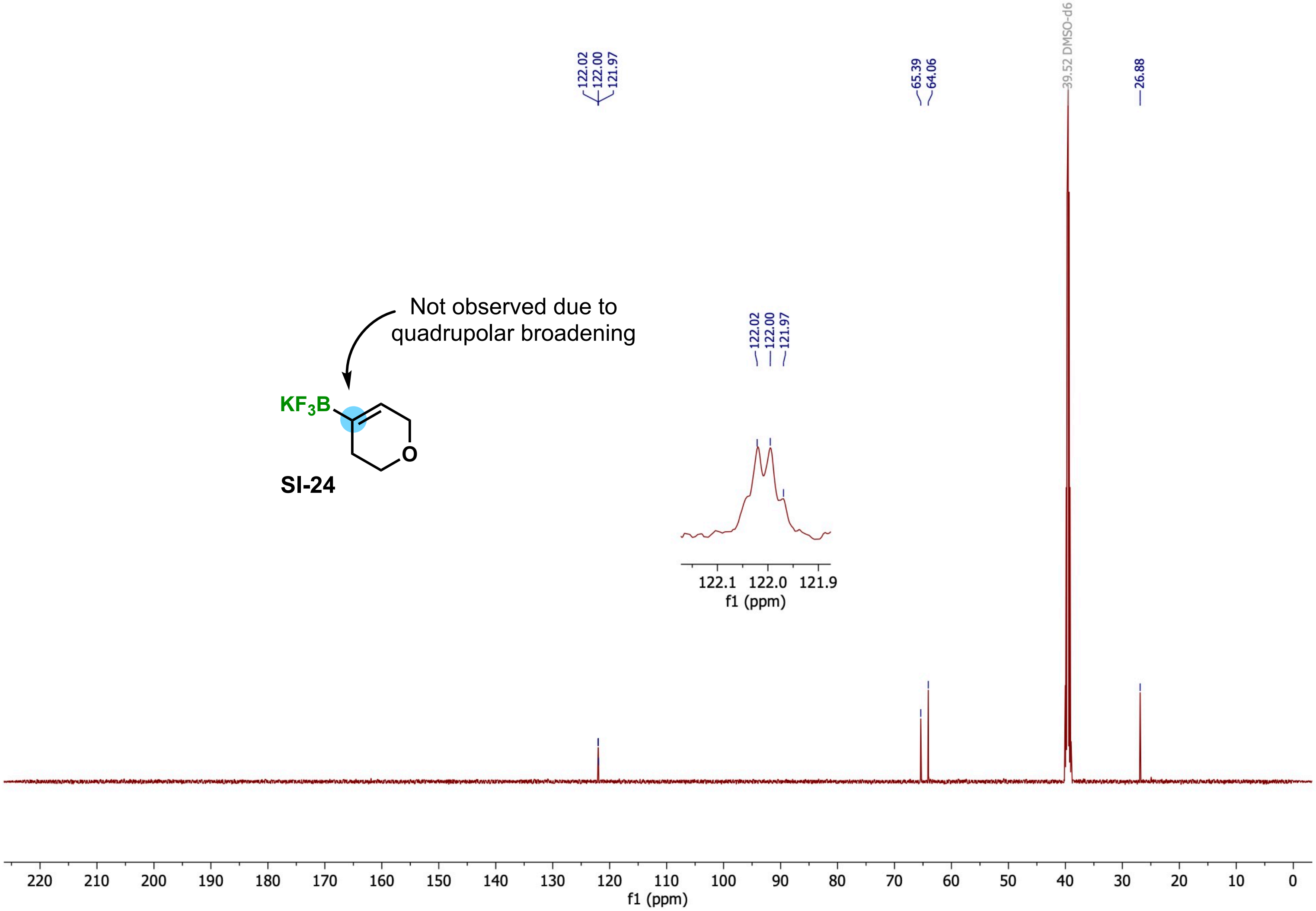


Figure S48. ^{1}H NMR of **SI-24** (500.27 MHz, DMSO-*d*6).


Not observed due to quadrupolar broadening

SI-24

Figure S49. ^{13}C NMR of **SI-24** (125.81 MHz, DMSO-*d*6).

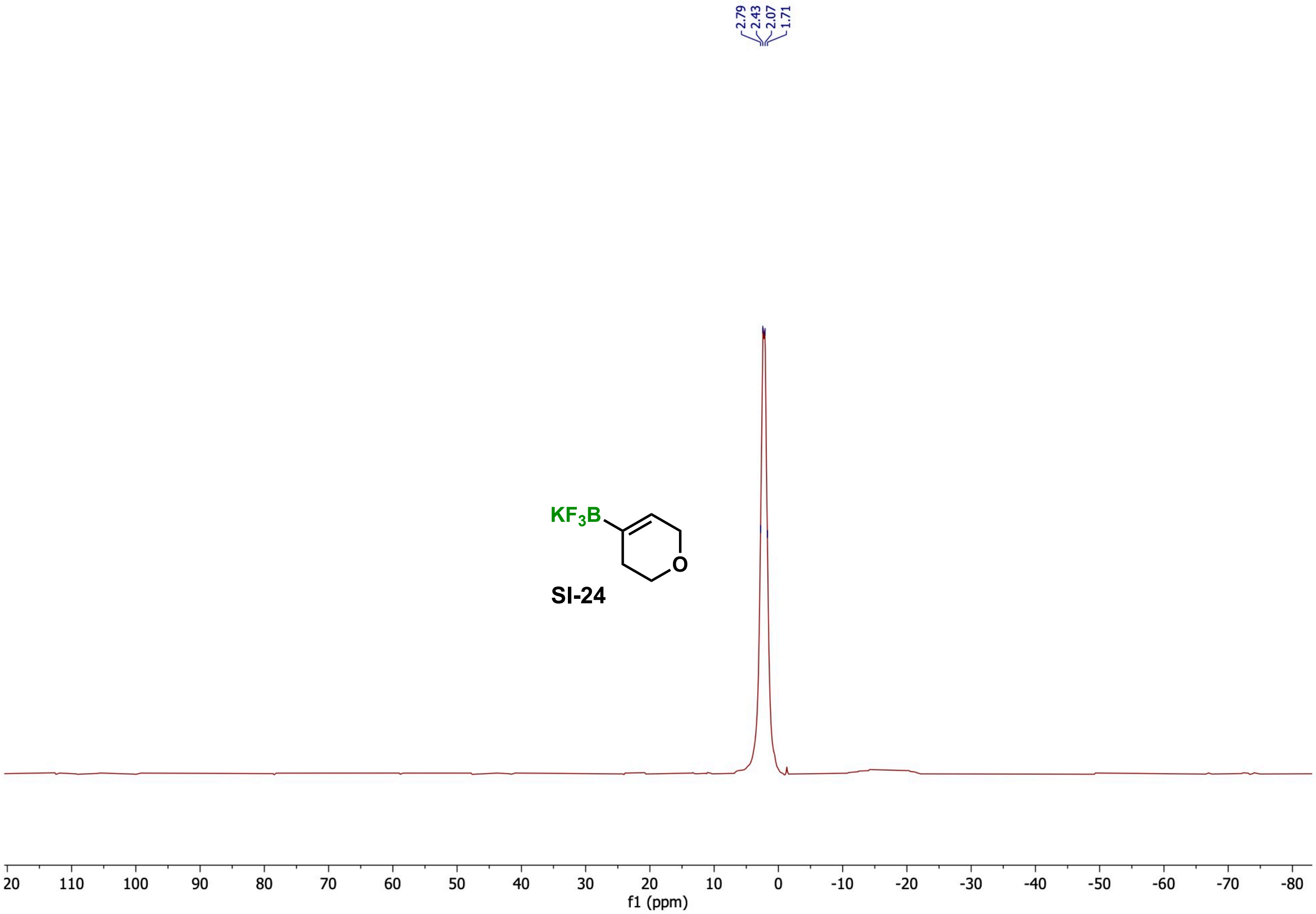


Figure S50. ^{11}B NMR of **SI-24** (160.51 MHz, DMSO-*d*6).

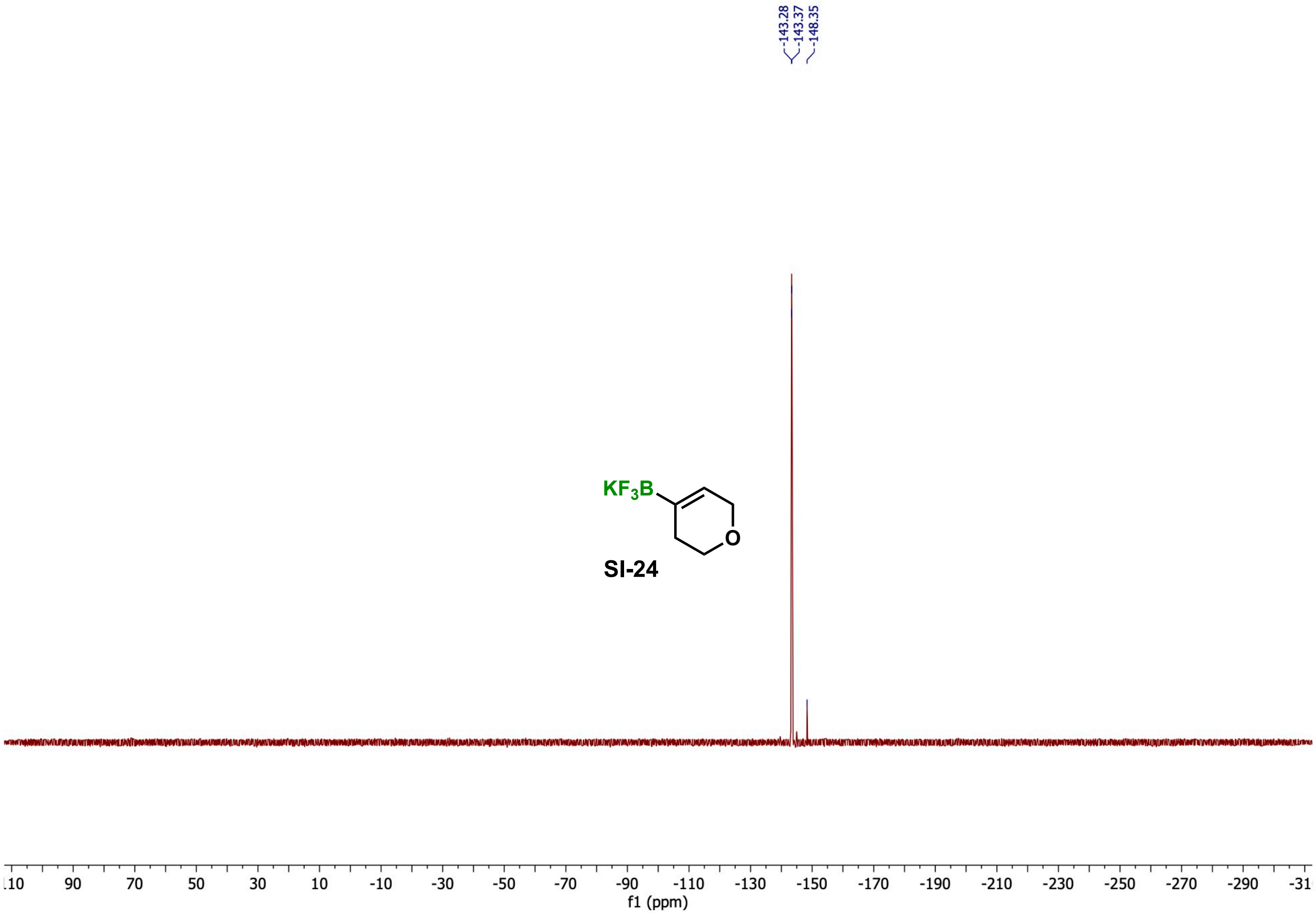
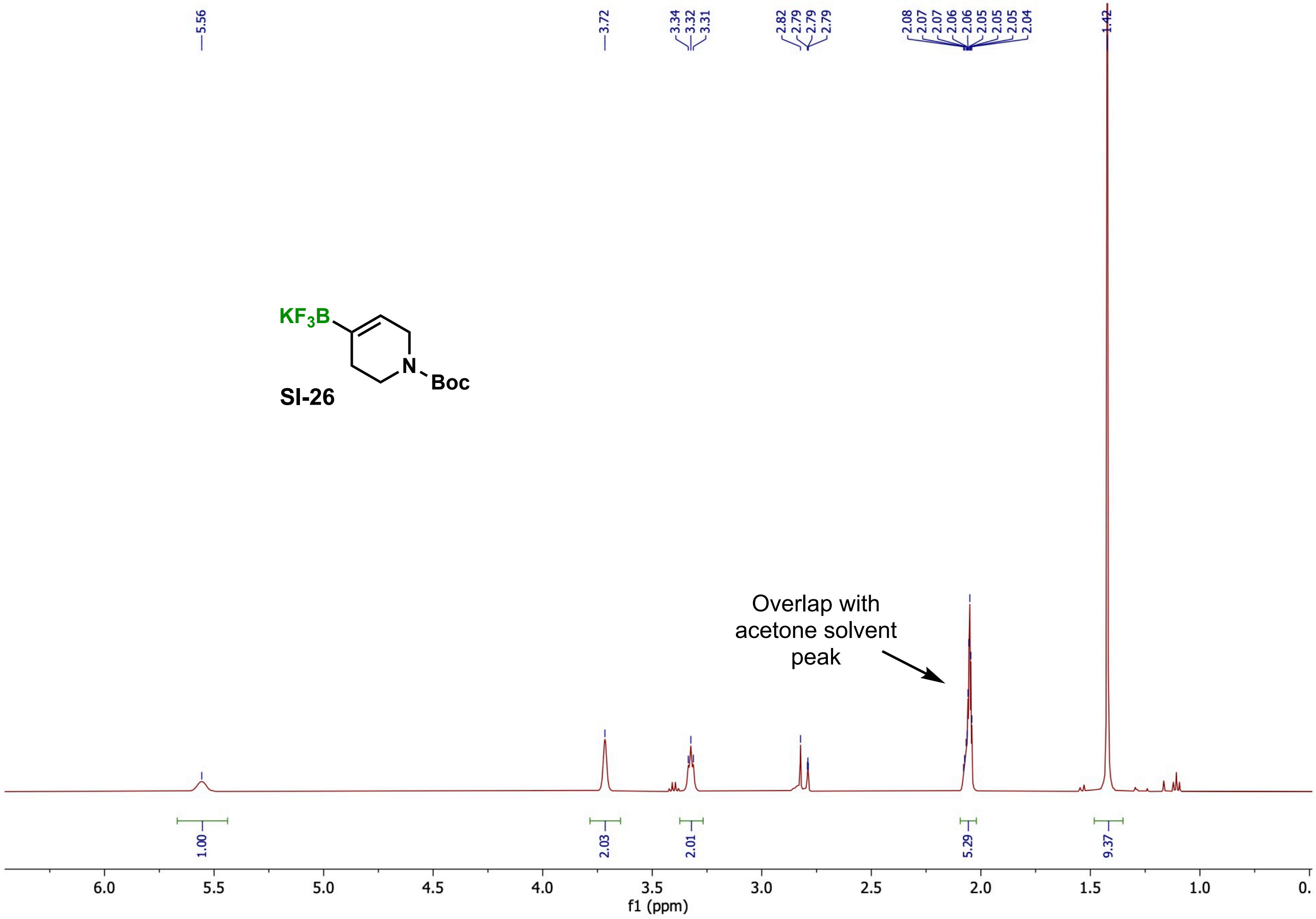


Figure S51. ^{19}F NMR of **SI-24** (470.68 MHz, DMSO-*d*6).



SI-26

Overlap with acetone solvent peak

Figure S52. ^{1}H NMR of **SI-26** (500.27 MHz, acetone-*d*6).

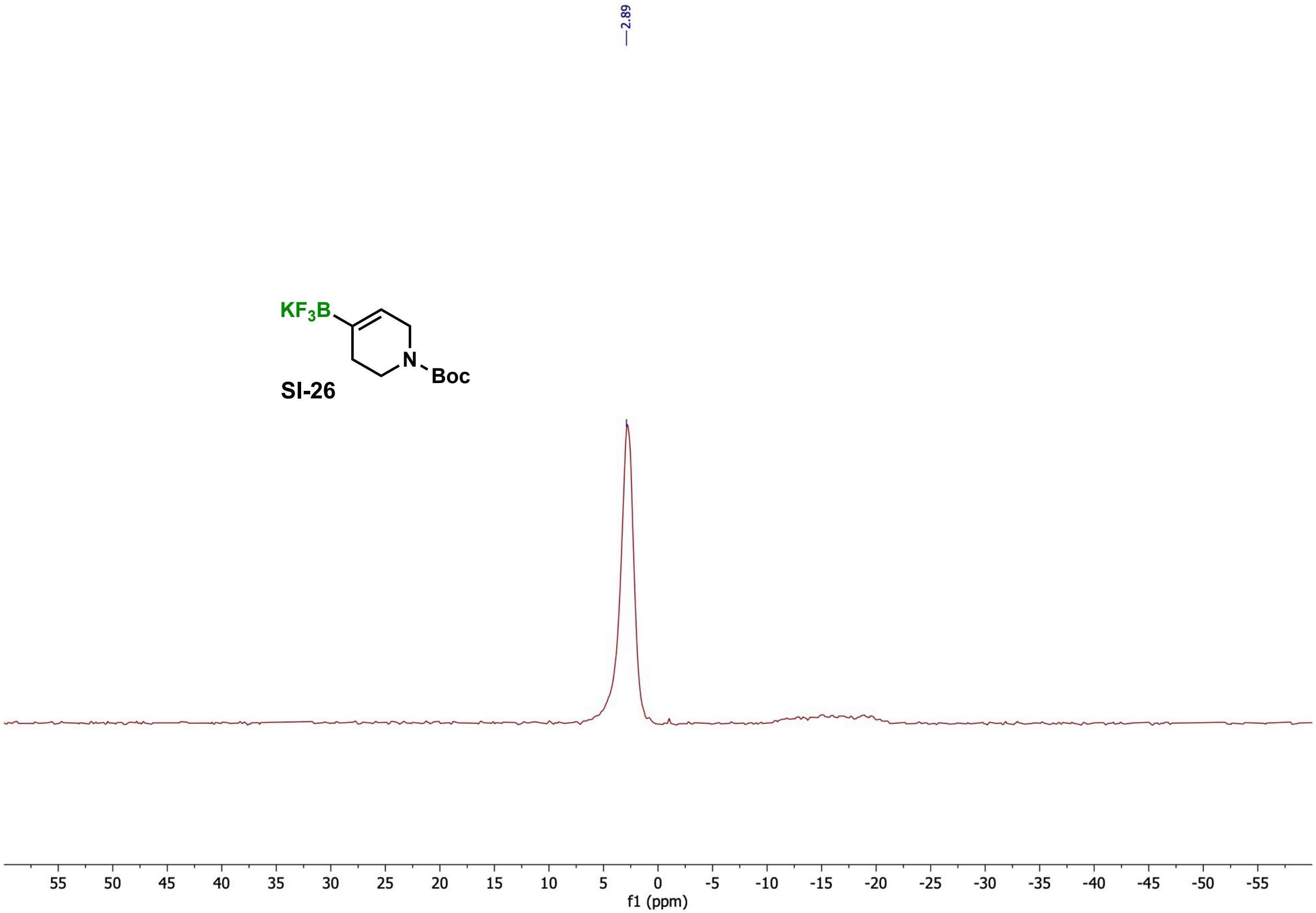


Figure S53. ^{11}B NMR of **SI-26** (160.51 MHz, acetone-*d6*).

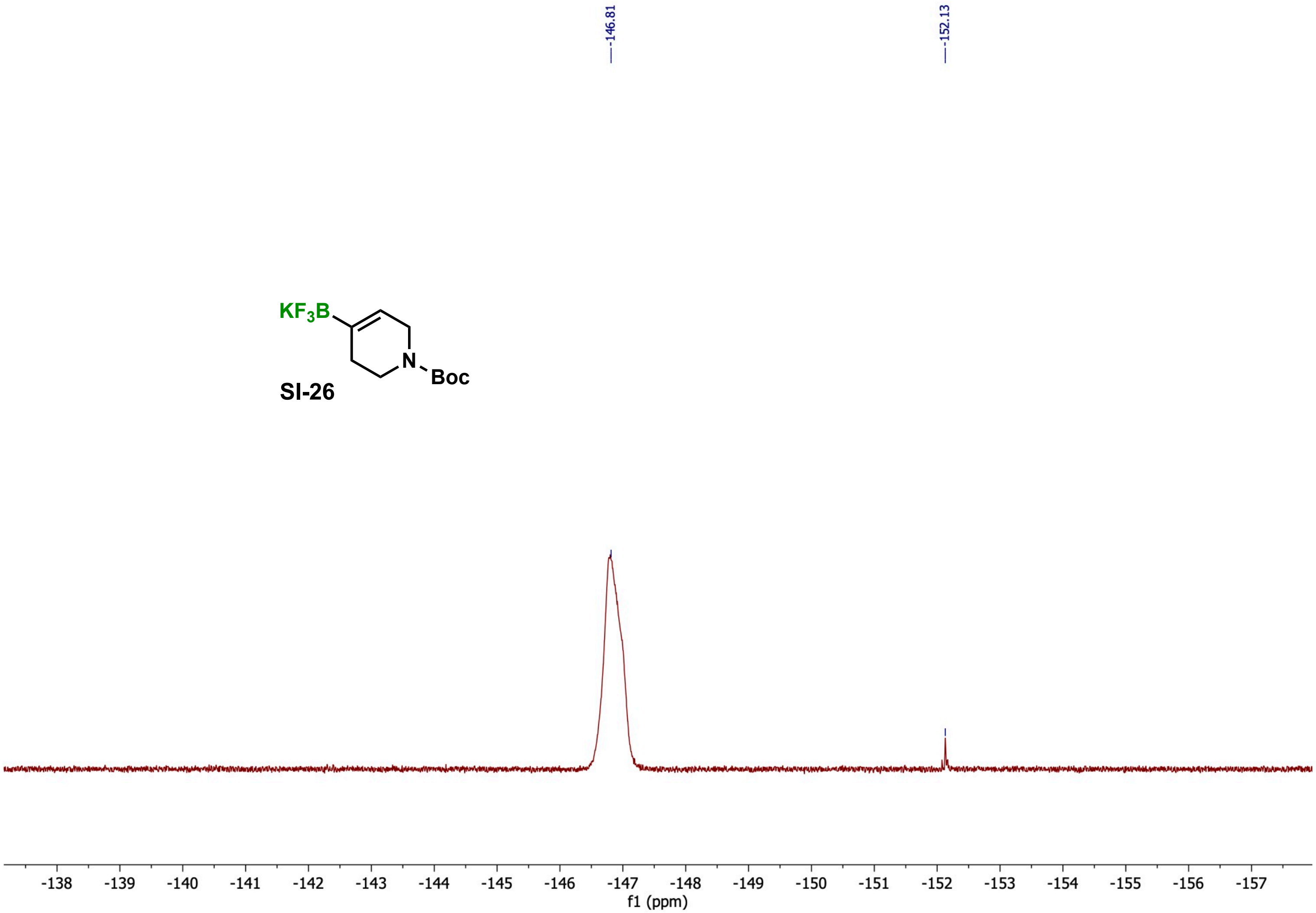


Figure S54. ^{19}F NMR of **SI-26** (470.68 MHz, acetone-*d*6).

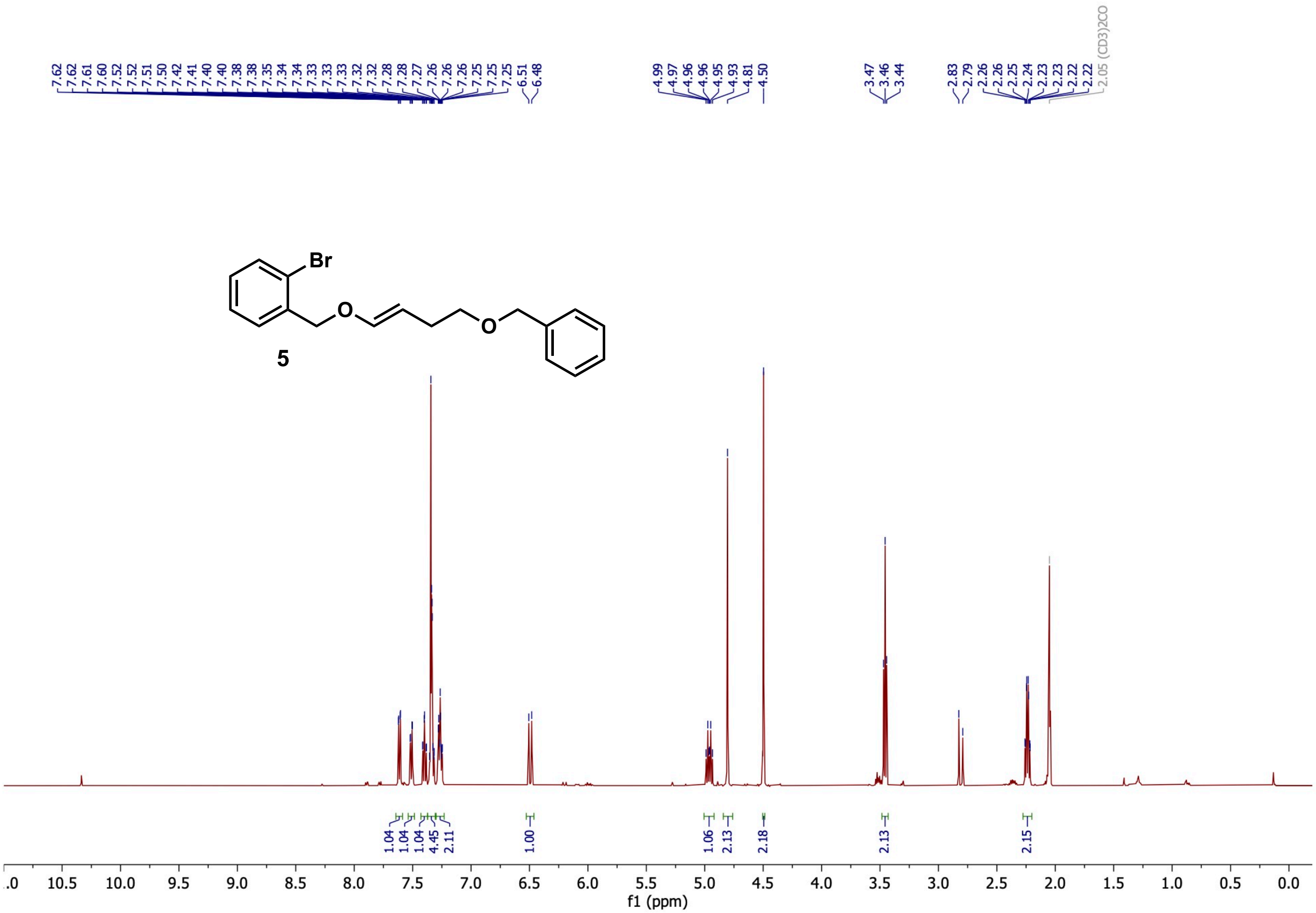


Figure S55. ^{1}H NMR of compound **5** (500.27 MHz, acetone-*d*6).

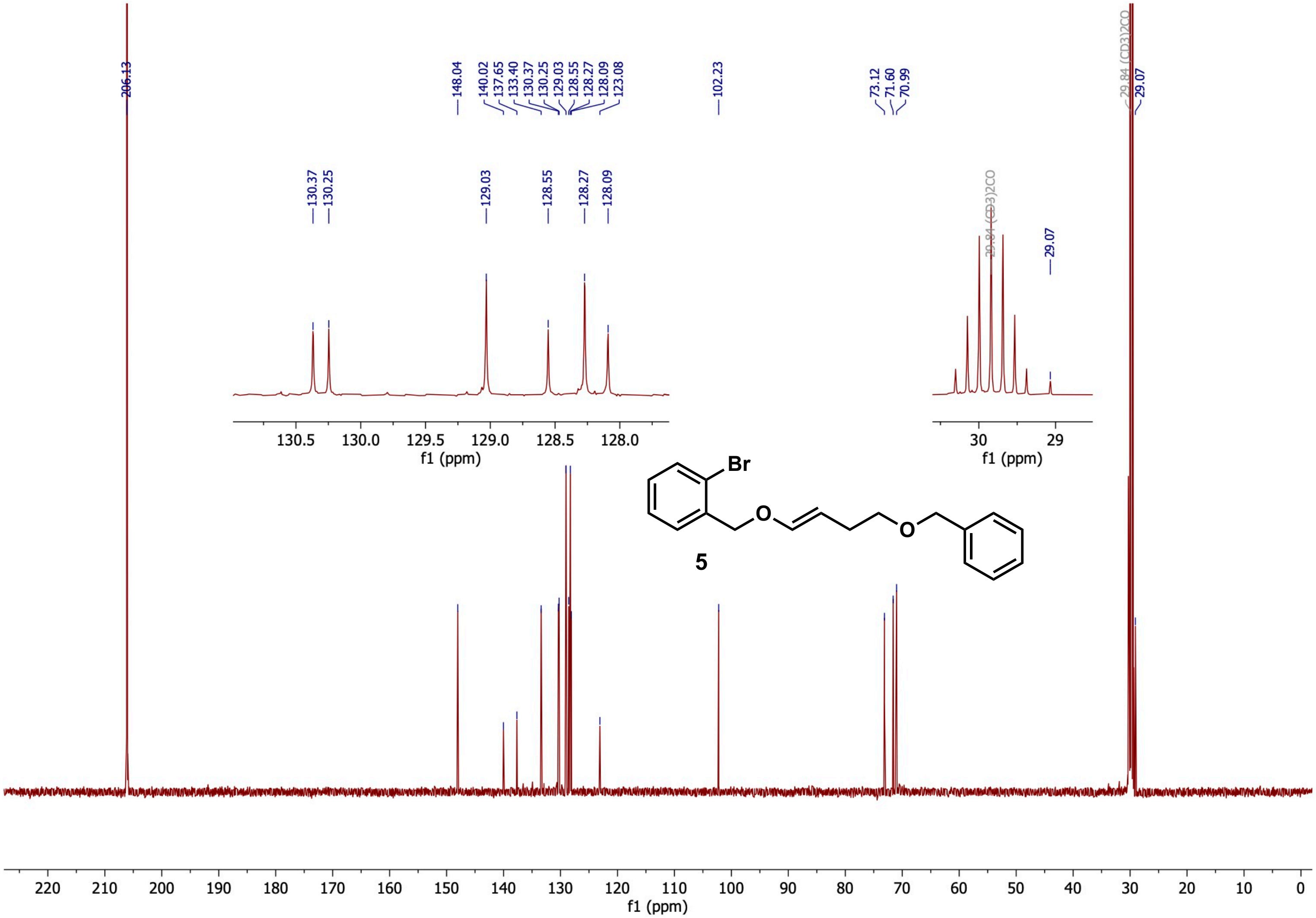


Figure S56. ^{13}C NMR of compound **5** (125.81 MHz, acetone-*d*6).

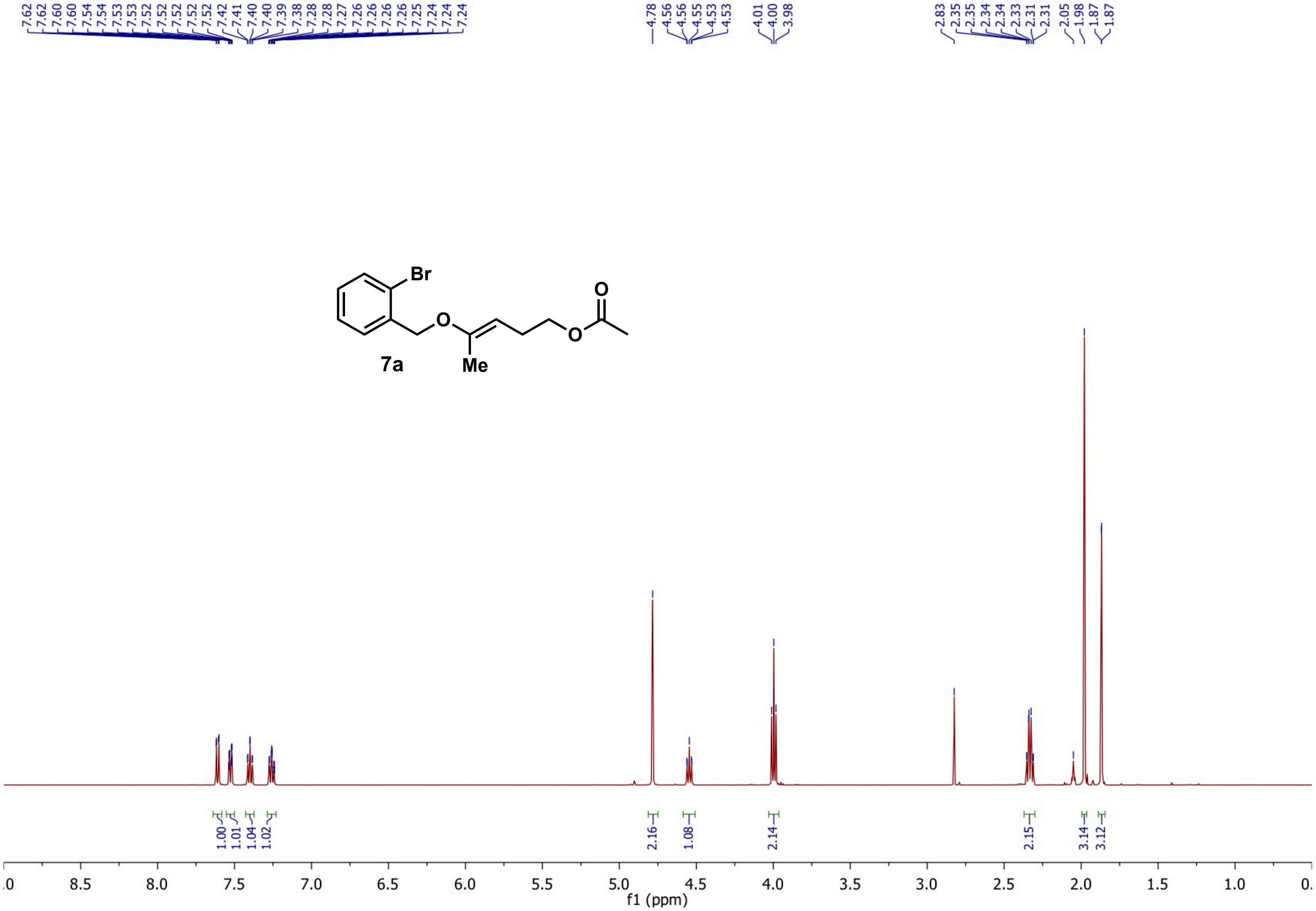


Figure S57. ^{1}H NMR of compound **7a** (500.27 MHz, acetone-*d*6).

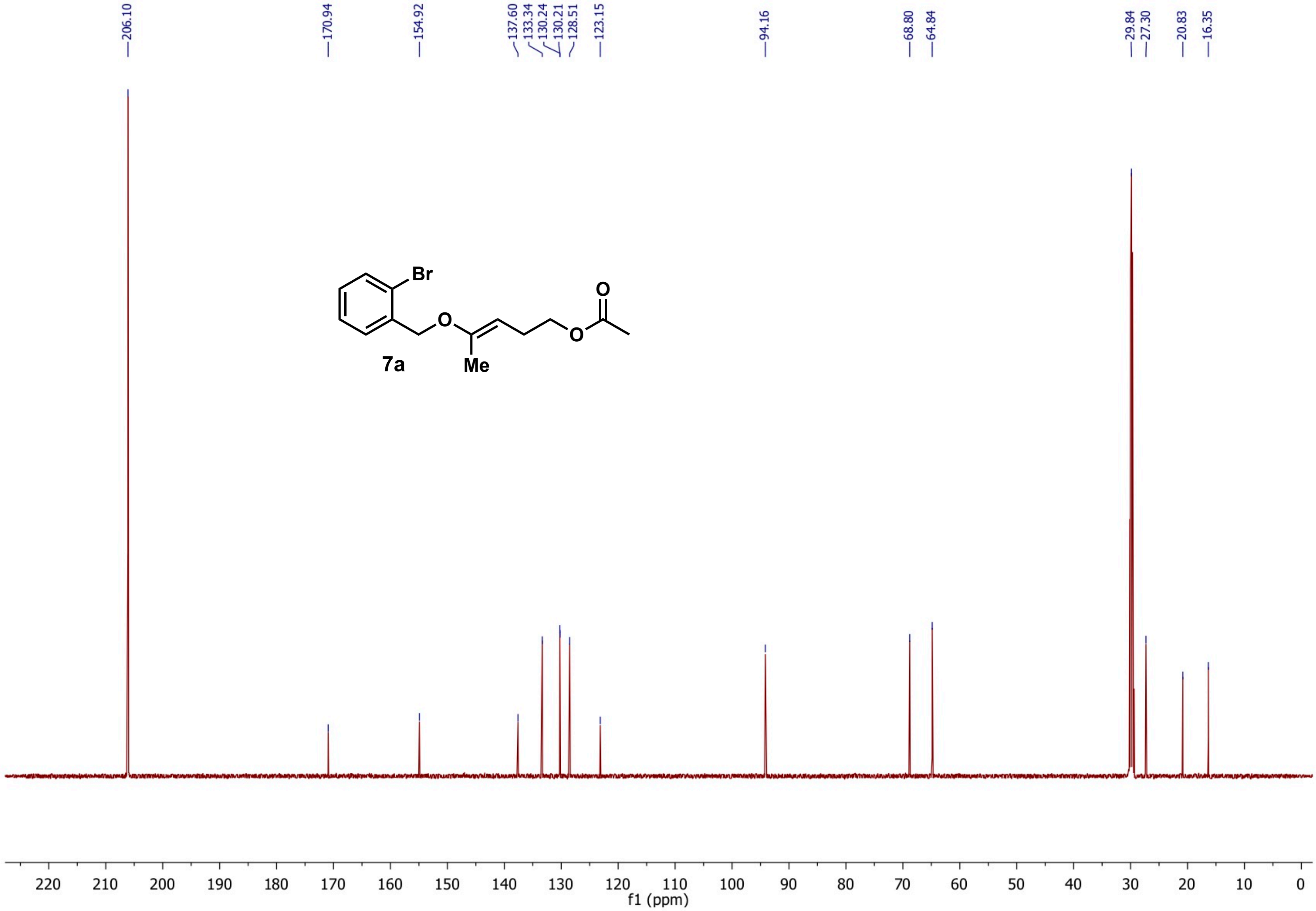


Figure S58. ^{13}C NMR of compound **7a** (125.81 MHz, acetone-*d*6).

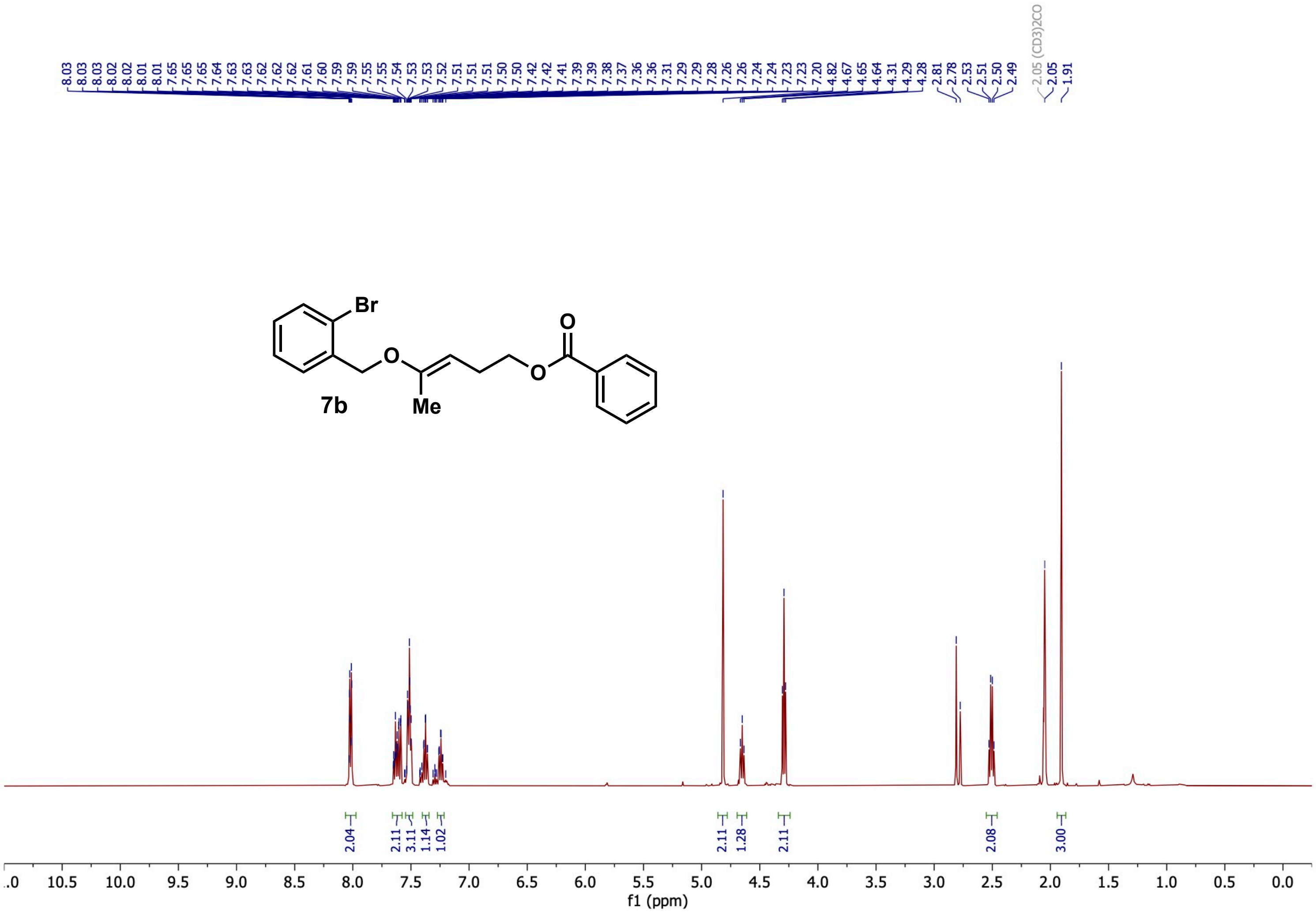


Figure S59. ^{1}H NMR of compound **7b** (500.27 MHz, acetone-*d*6).

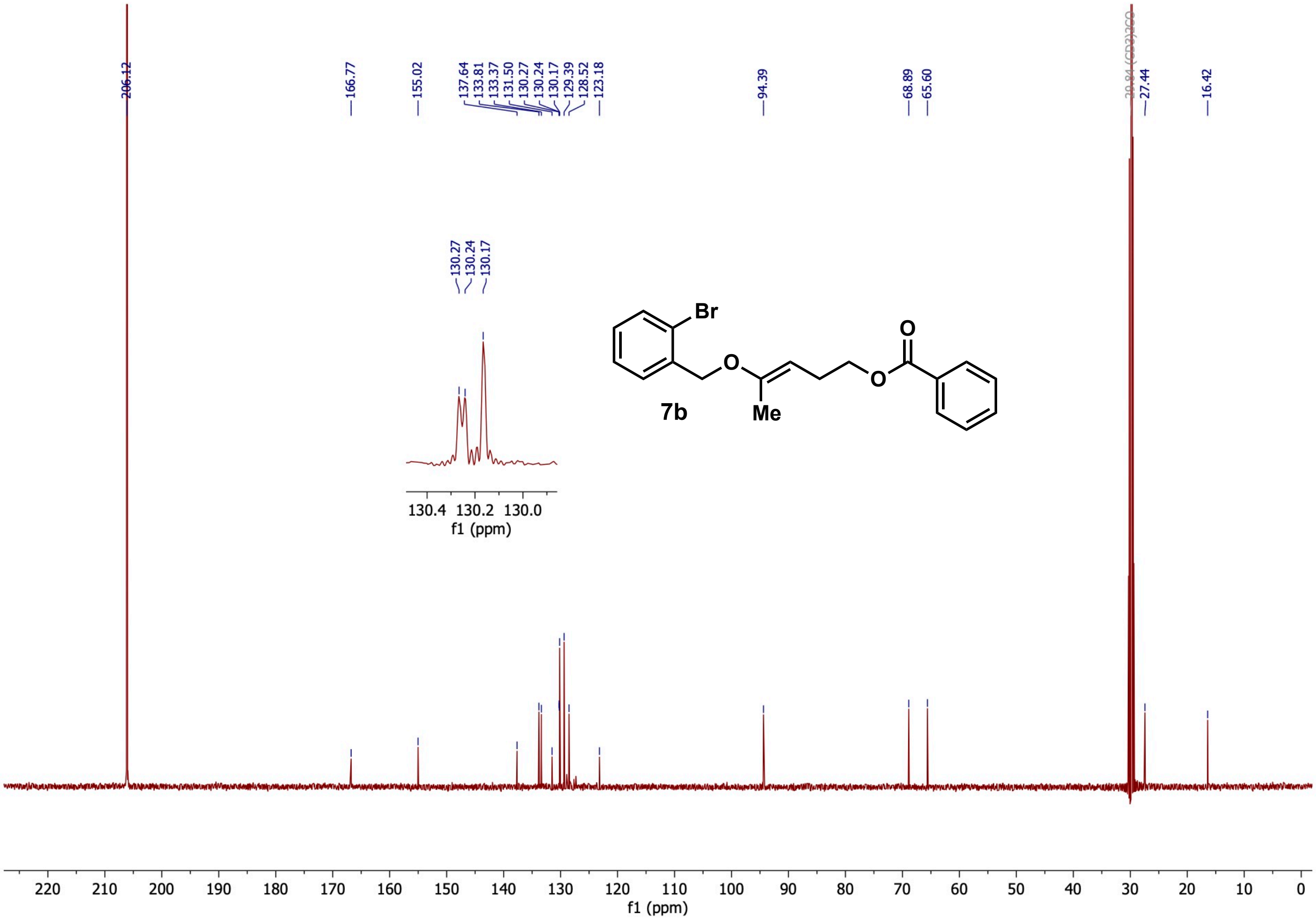


Figure S60. ^{13}C NMR of compound **7b** (125.81 MHz, acetone-*d*6).

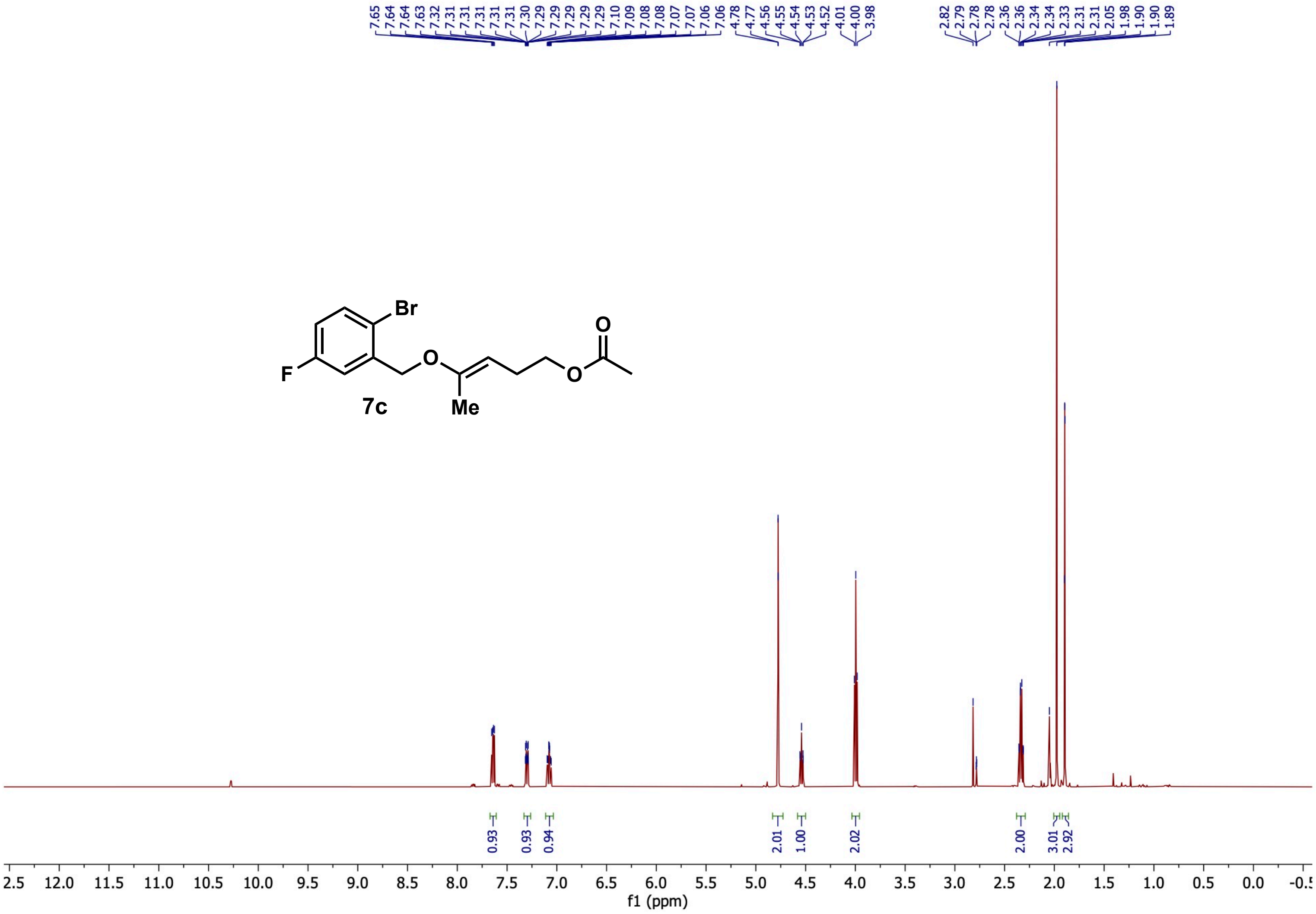


Figure S61. ^{1}H NMR of compound **7c** (500.27 MHz, acetone-*d*6).

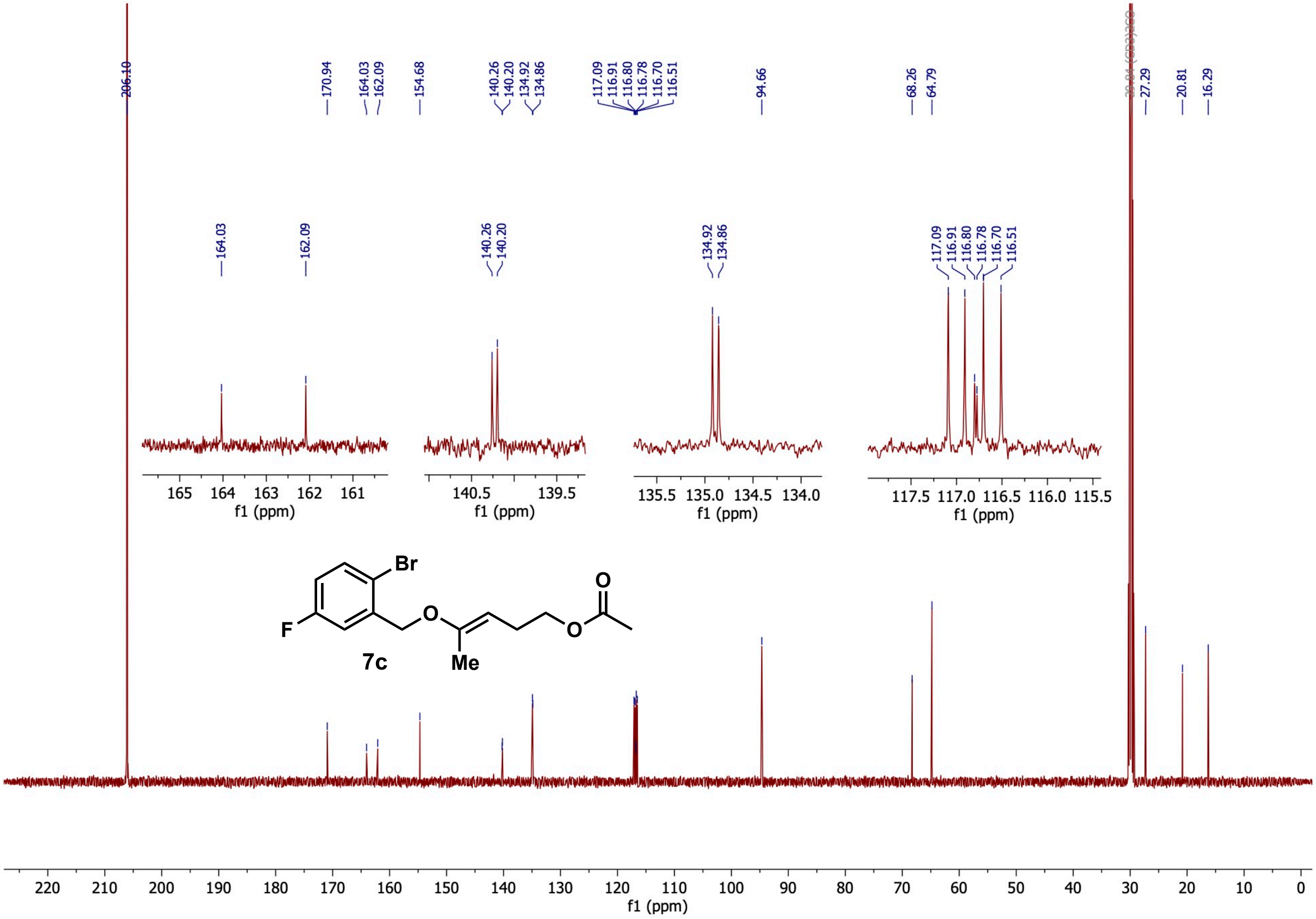
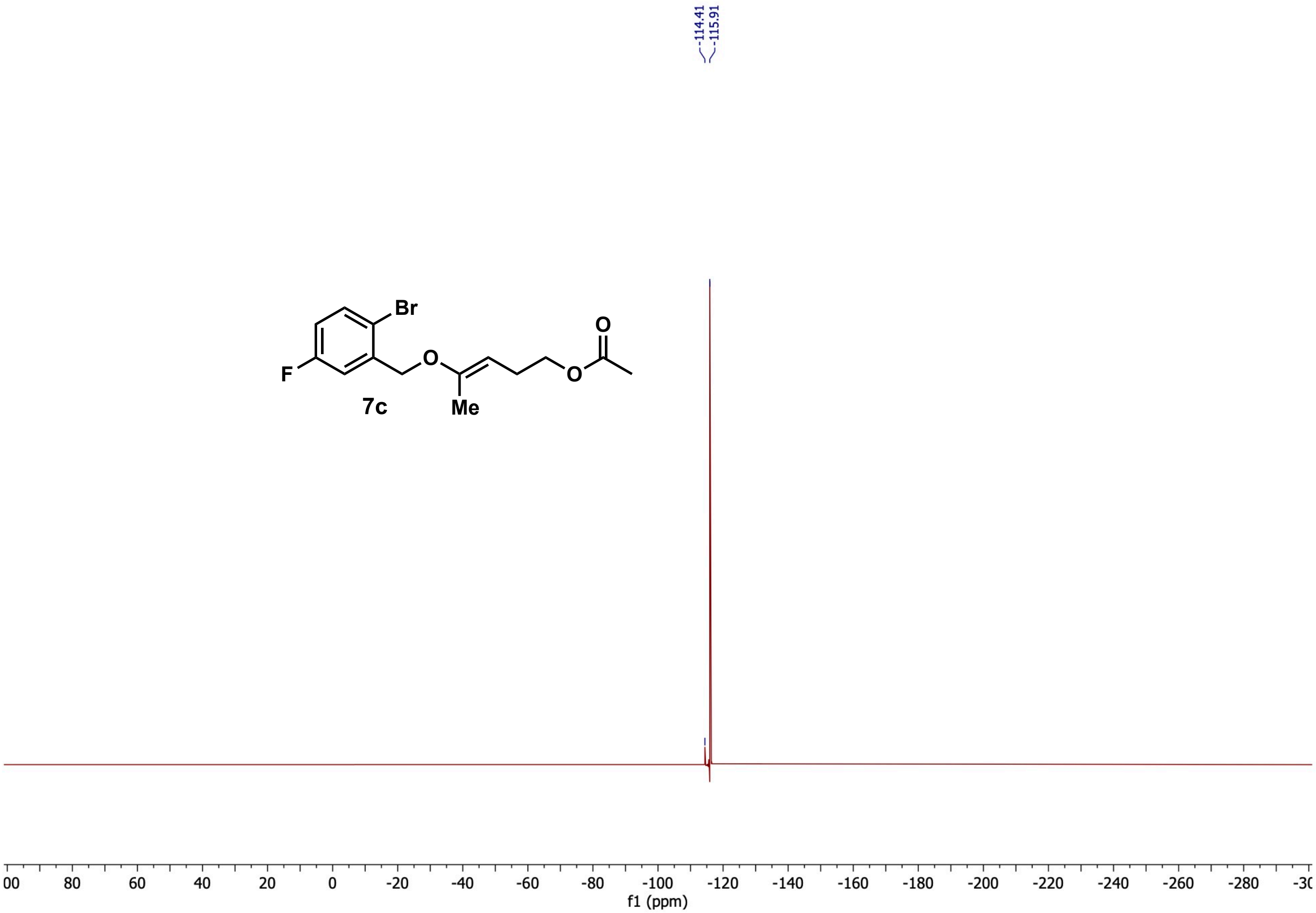


Figure S62. ^{13}C NMR of compound **7c** (125.81 MHz, acetone-*d*6).



7c

Figure S63. ^{19}F NMR of compound **7c** (470.68 MHz, acetone-*d*6).

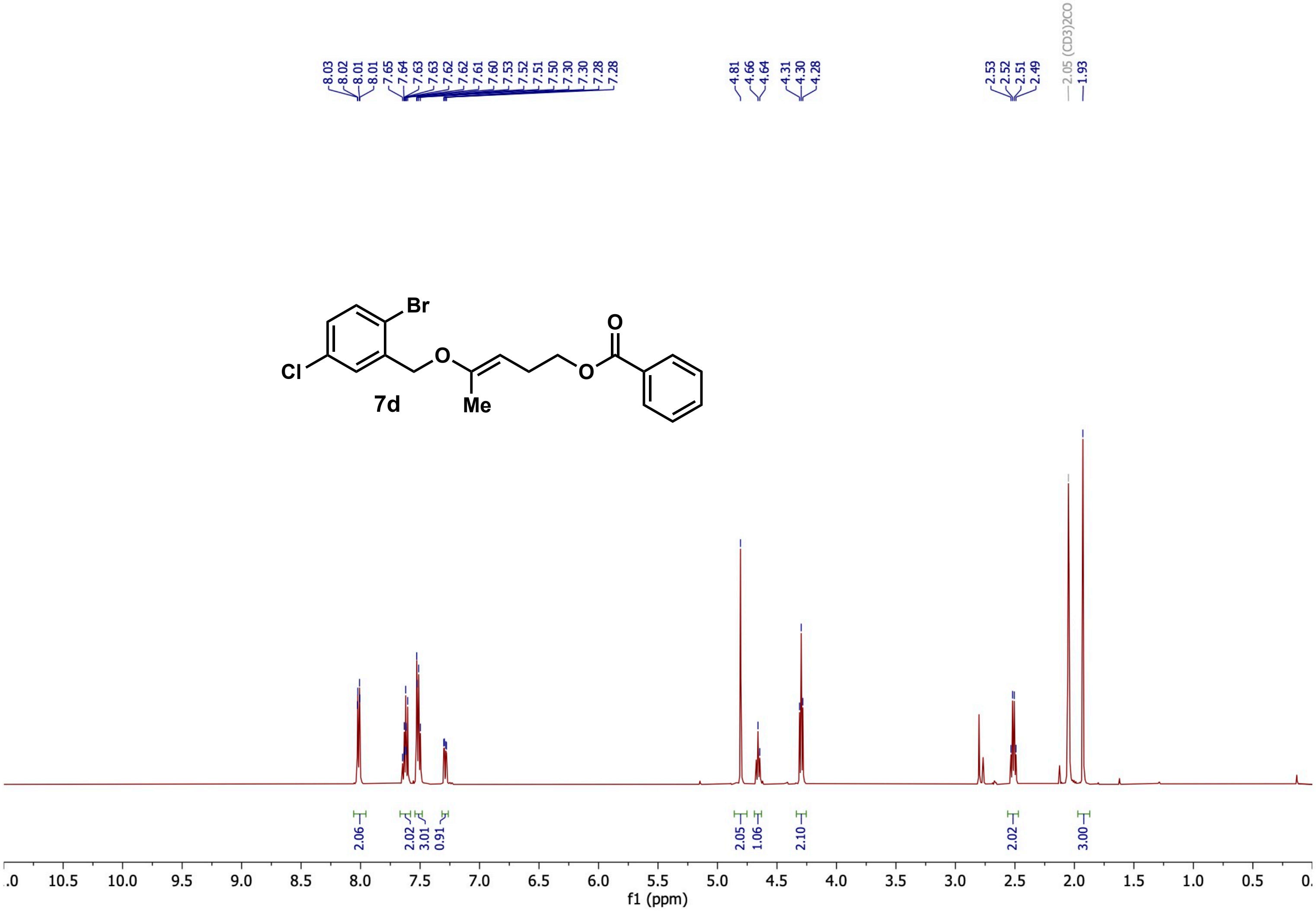


Figure S64. ^{1}H NMR of compound **7d** (500.27 MHz, acetone-*d*6).

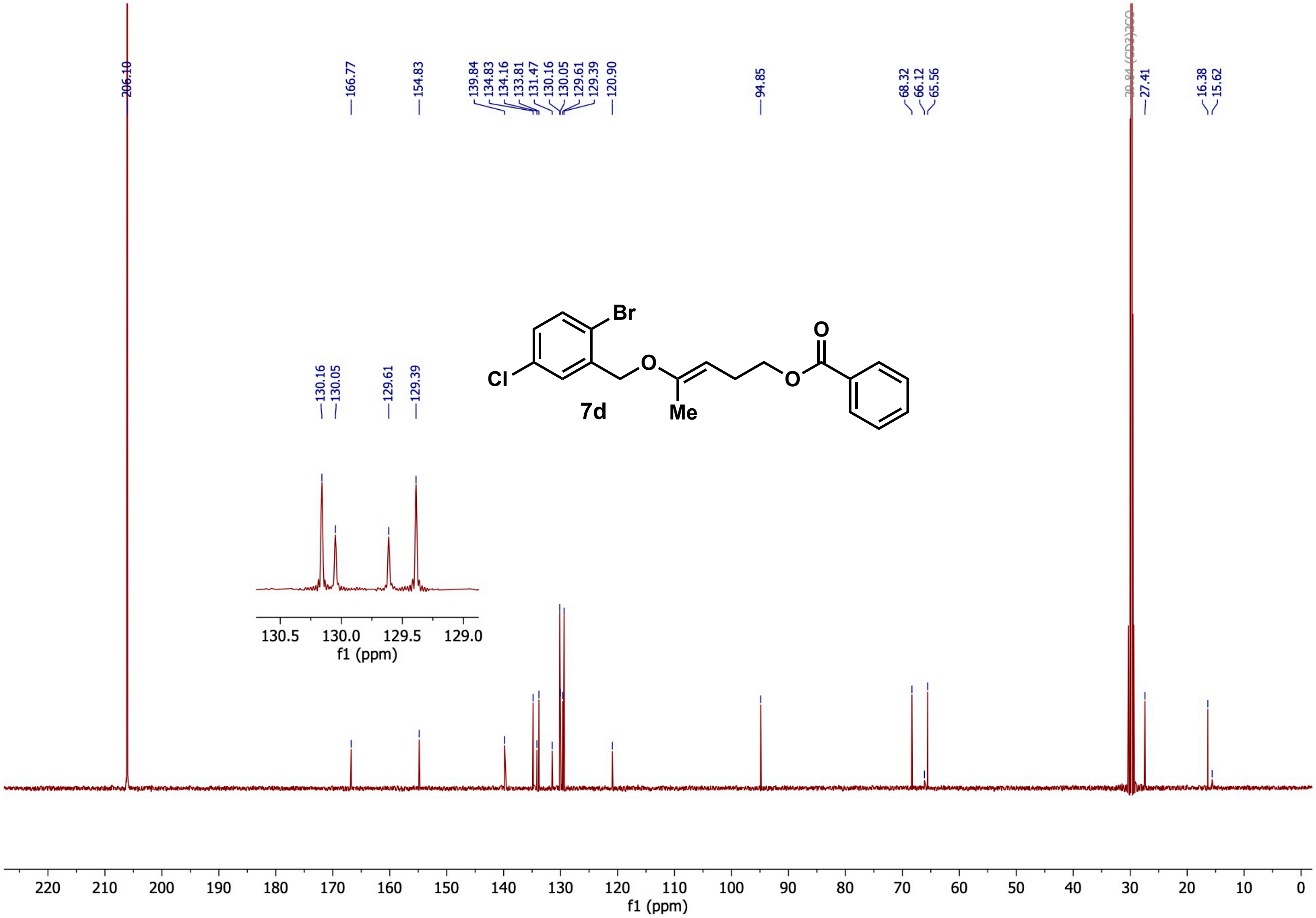


Figure S65. ^{13}C NMR of compound **7d** (125.81 MHz, acetone-*d*6).

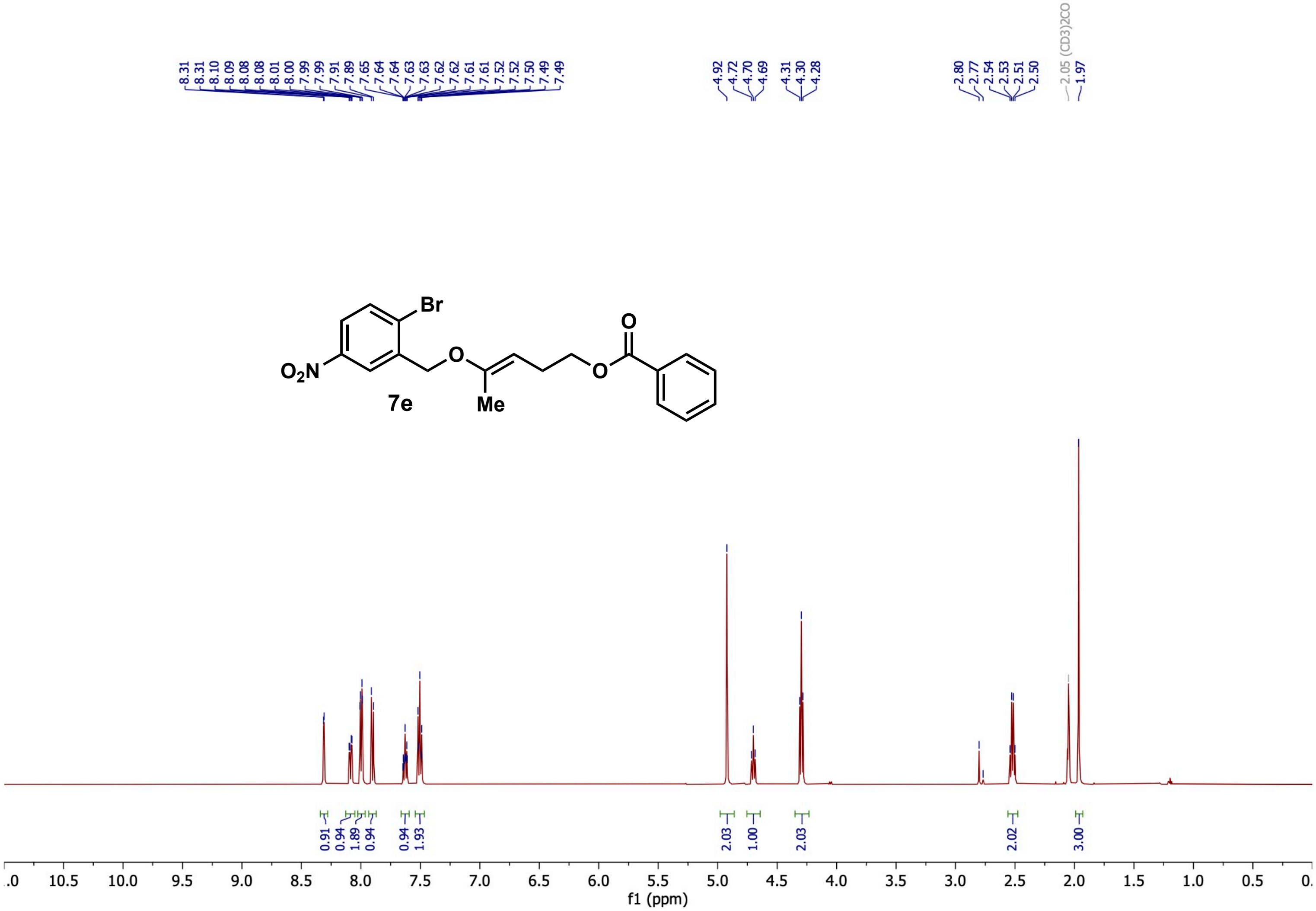


Figure S66. ^{1}H NMR of compound **7e** (500.27 MHz, acetone-*d*6).

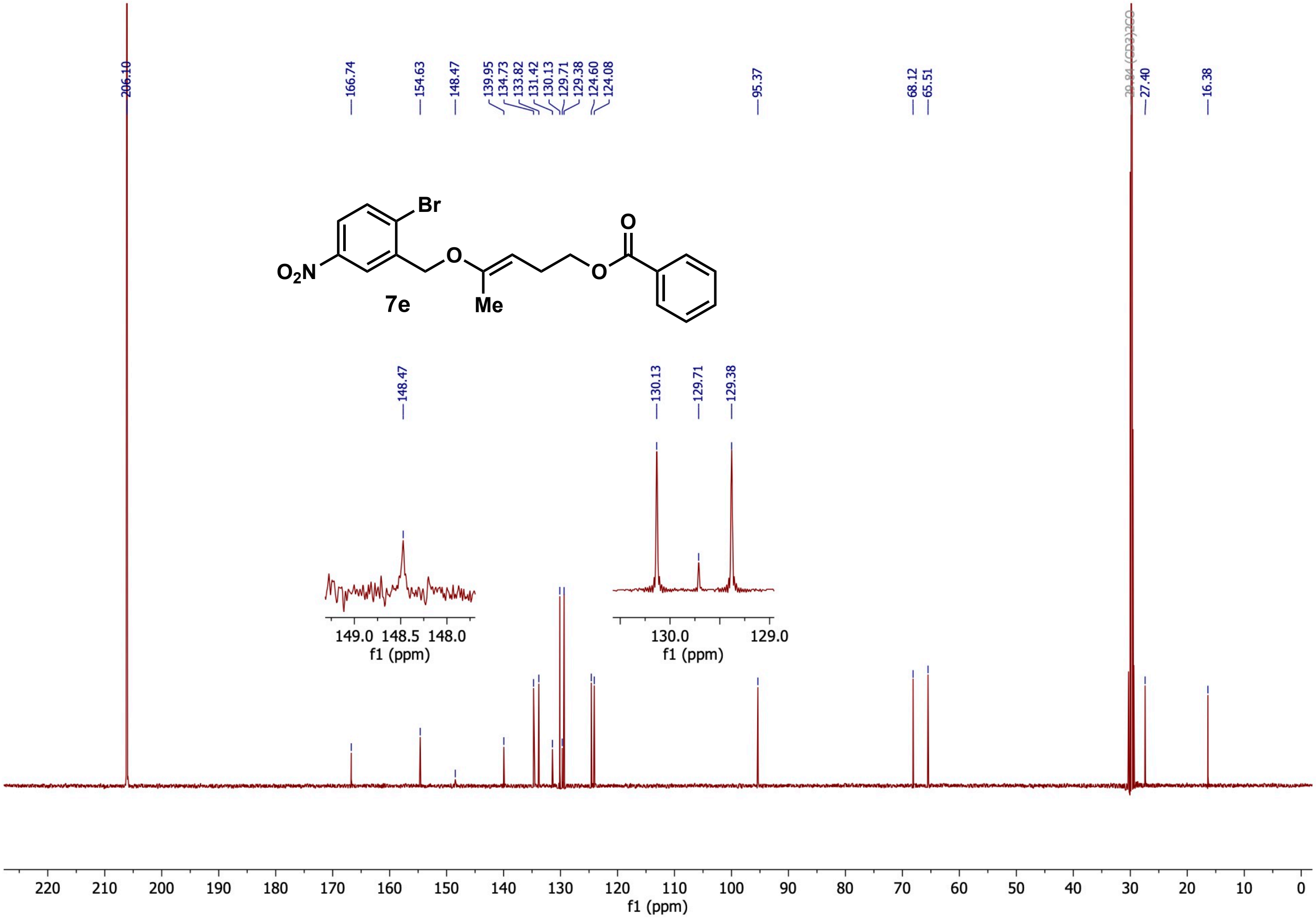


Figure S67. ^{13}C NMR of compound **7e** (125.81 MHz, acetone-*d*6).

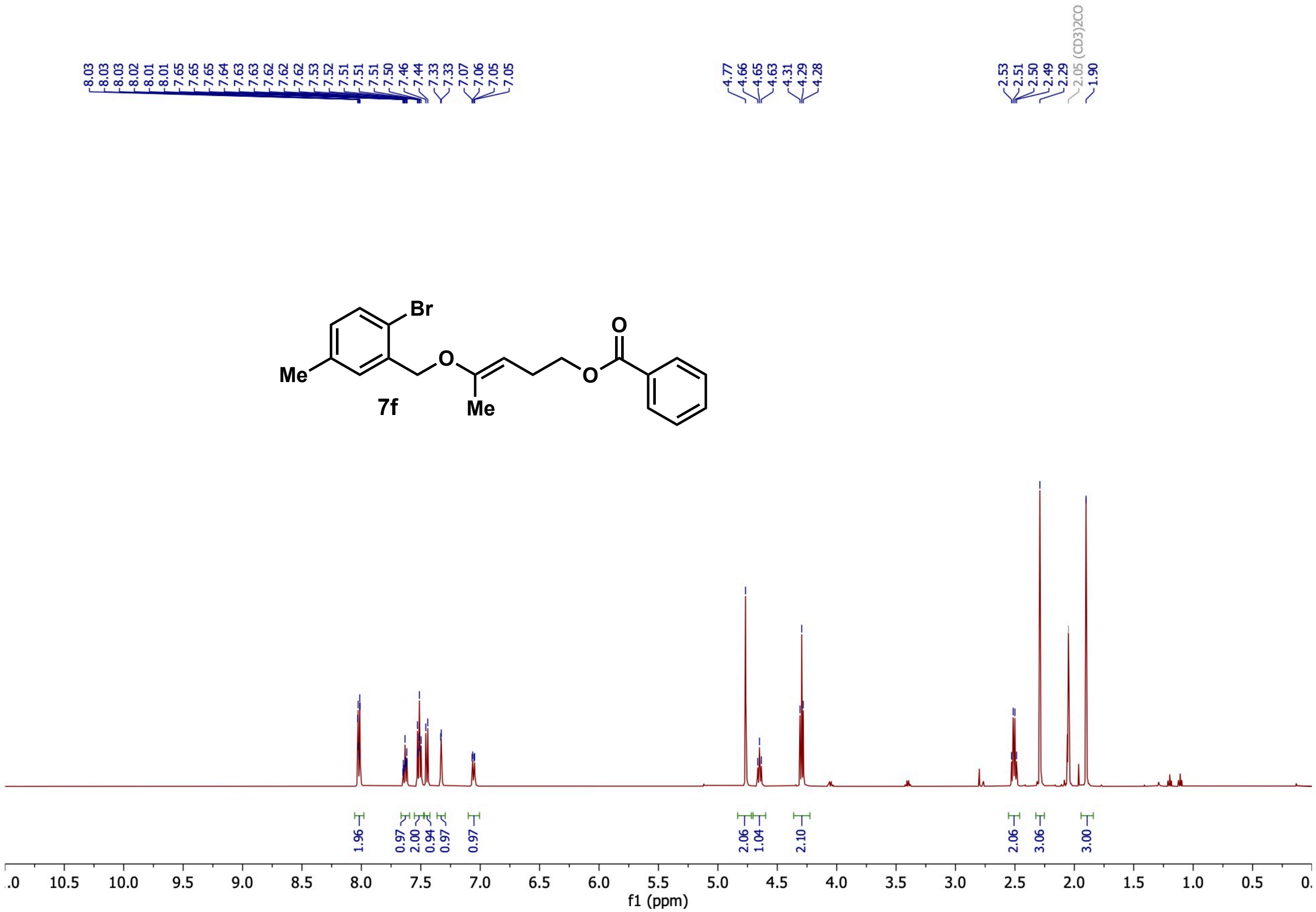


Figure S68. ^{1}H NMR of compound **7f** (500.27 MHz, acetone-*d*6).

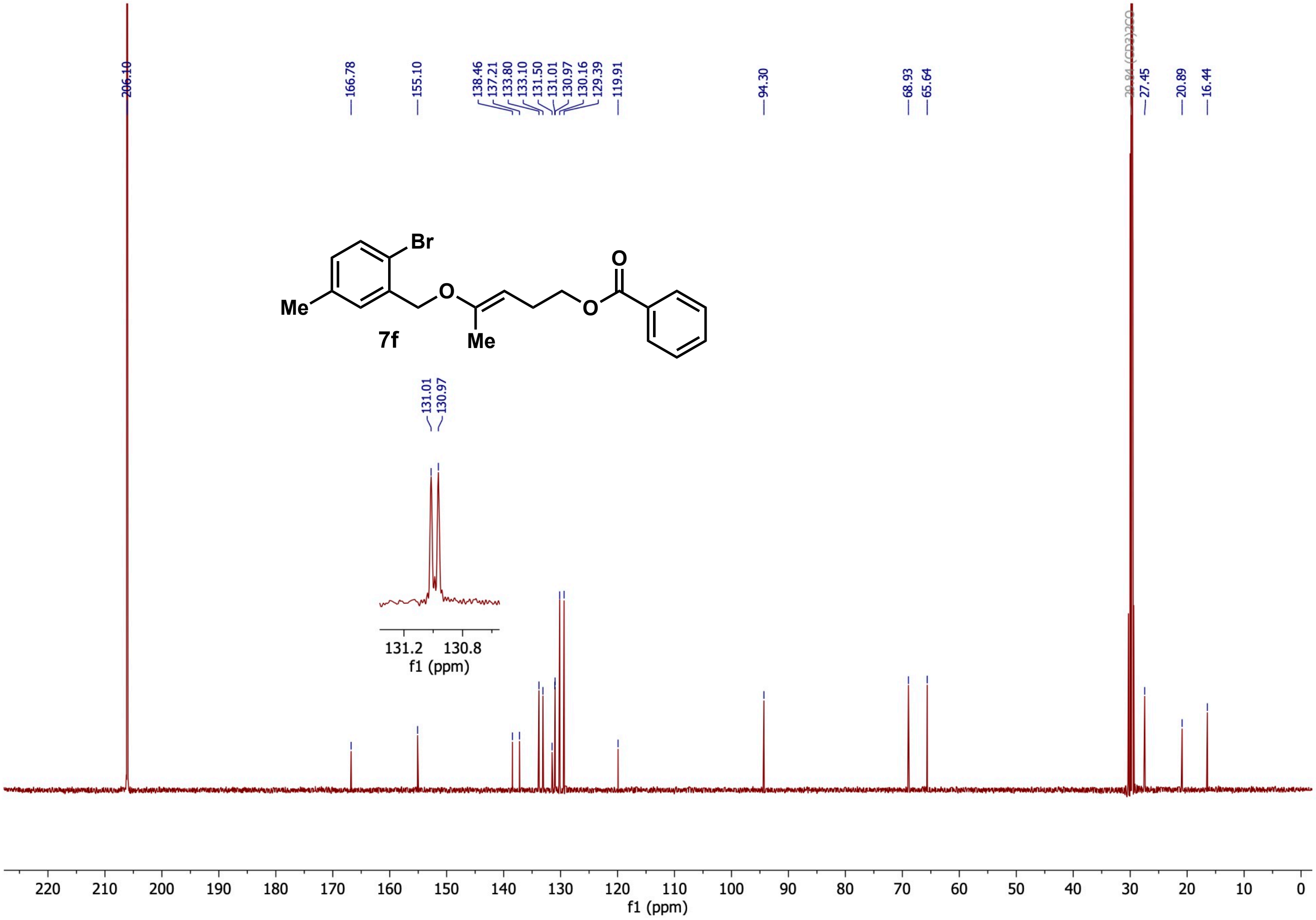


Figure S69. ^{13}C NMR of compound **7f** (125.81 MHz, acetone-*d*6).

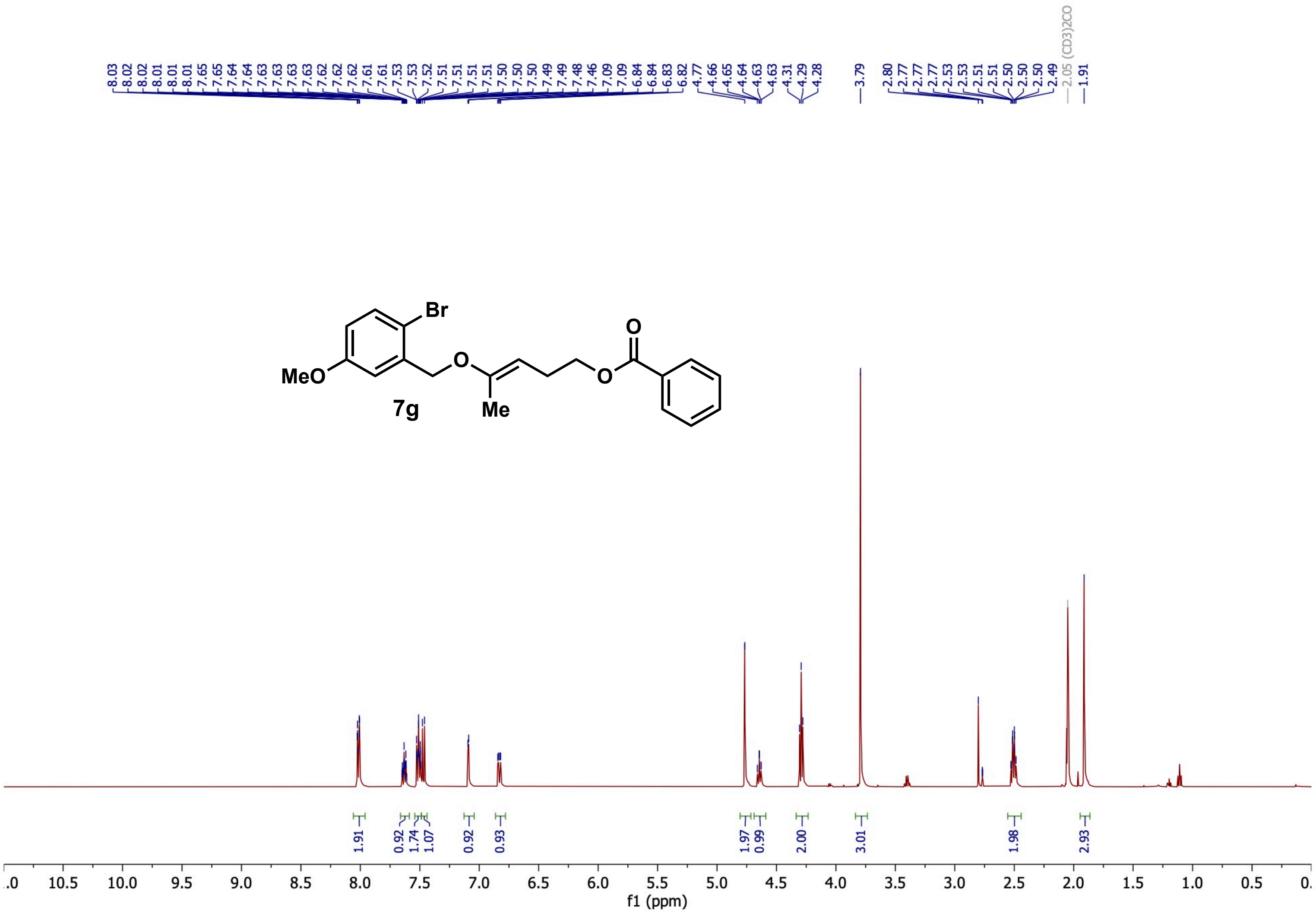


Figure S70. ^{1}H NMR of compound **7g** (500.27 MHz, acetone-*d*6).

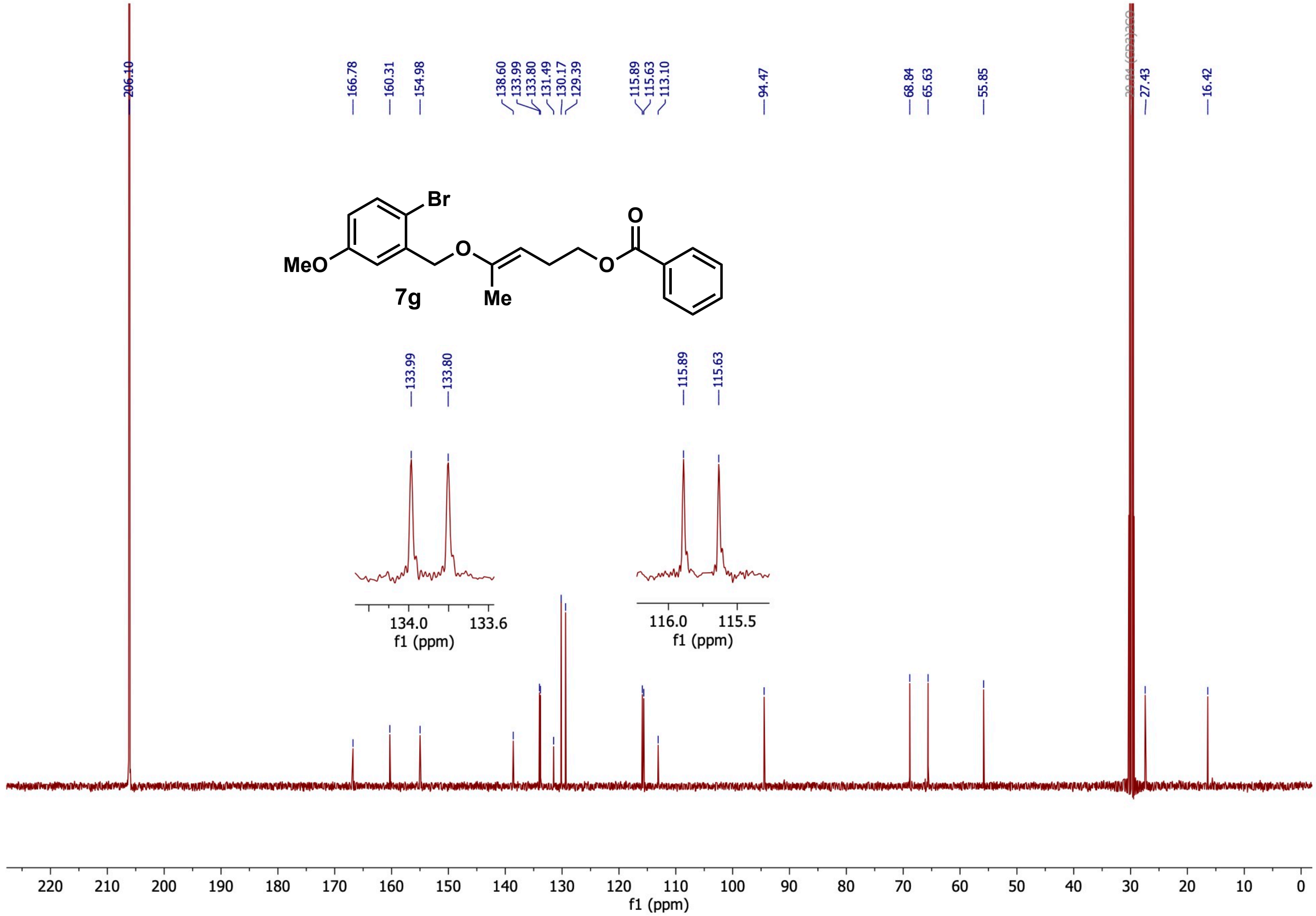


Figure S71. ^{13}C NMR of compound **7g** (125.81 MHz, acetone-*d*6).

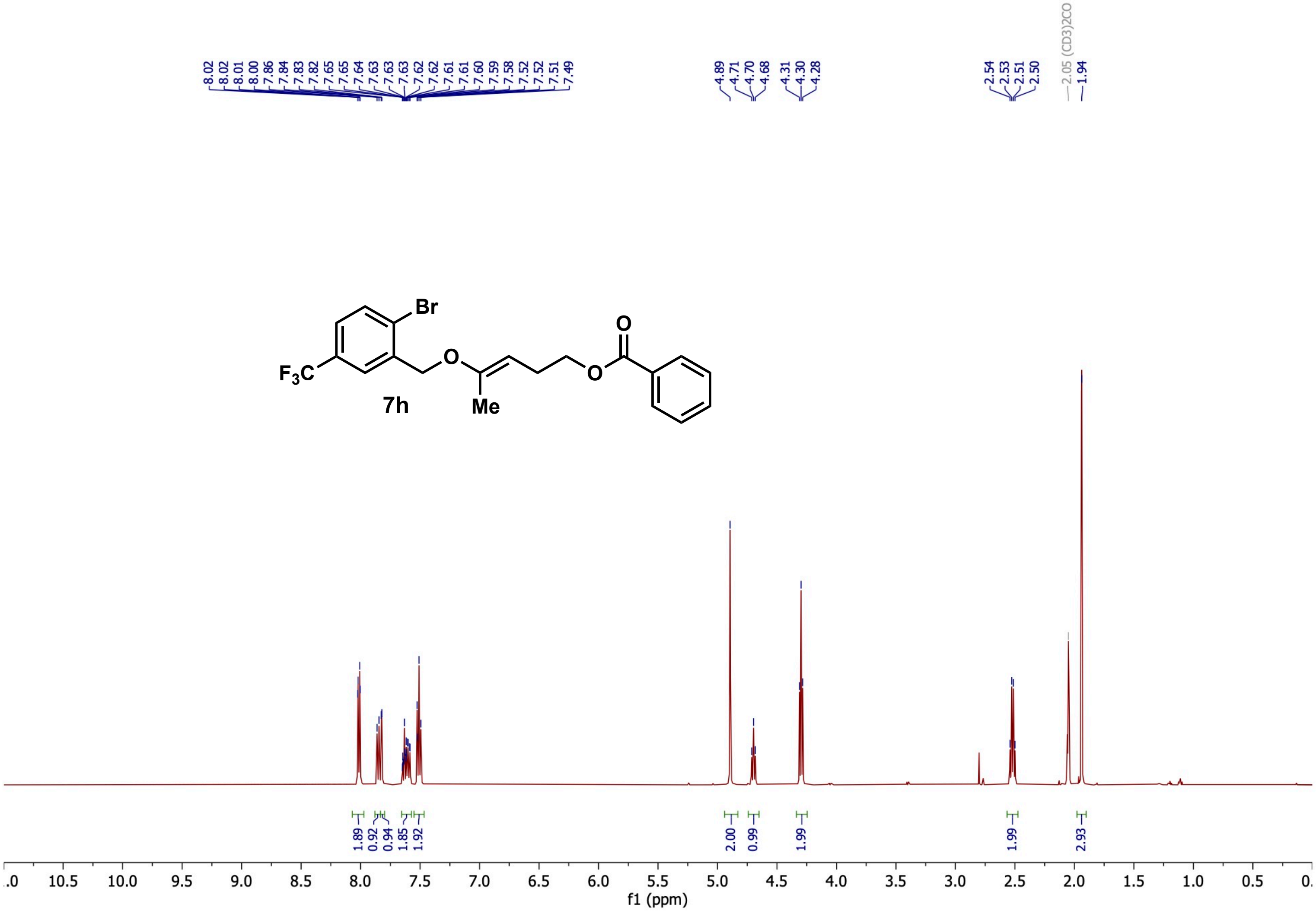


Figure S72. ¹H NMR of compound **7h** (500.27 MHz, acetone-*d*6).

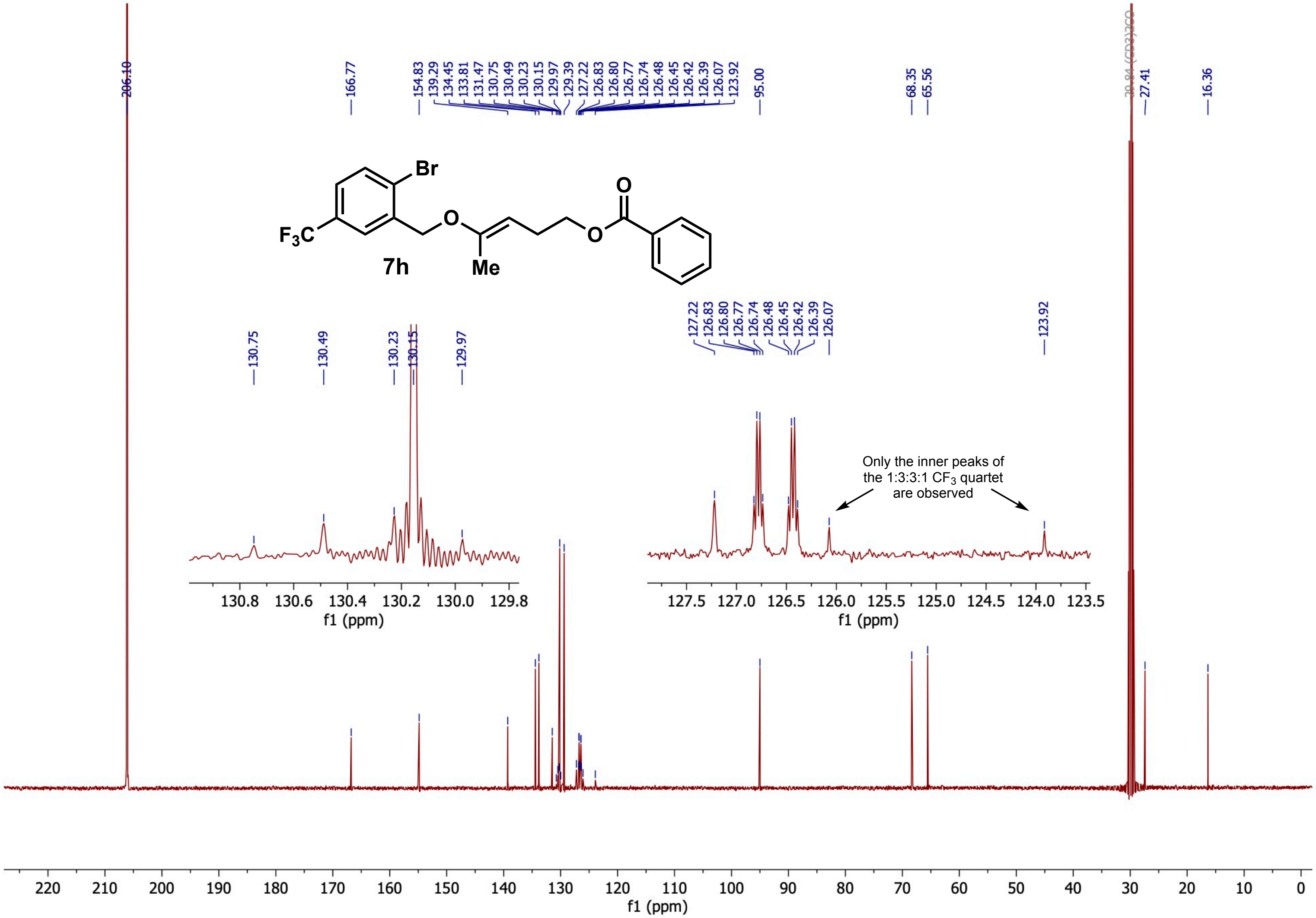


Figure S73. ^{13}C NMR of compound **7h** (125.81 MHz, acetone-*d*6).

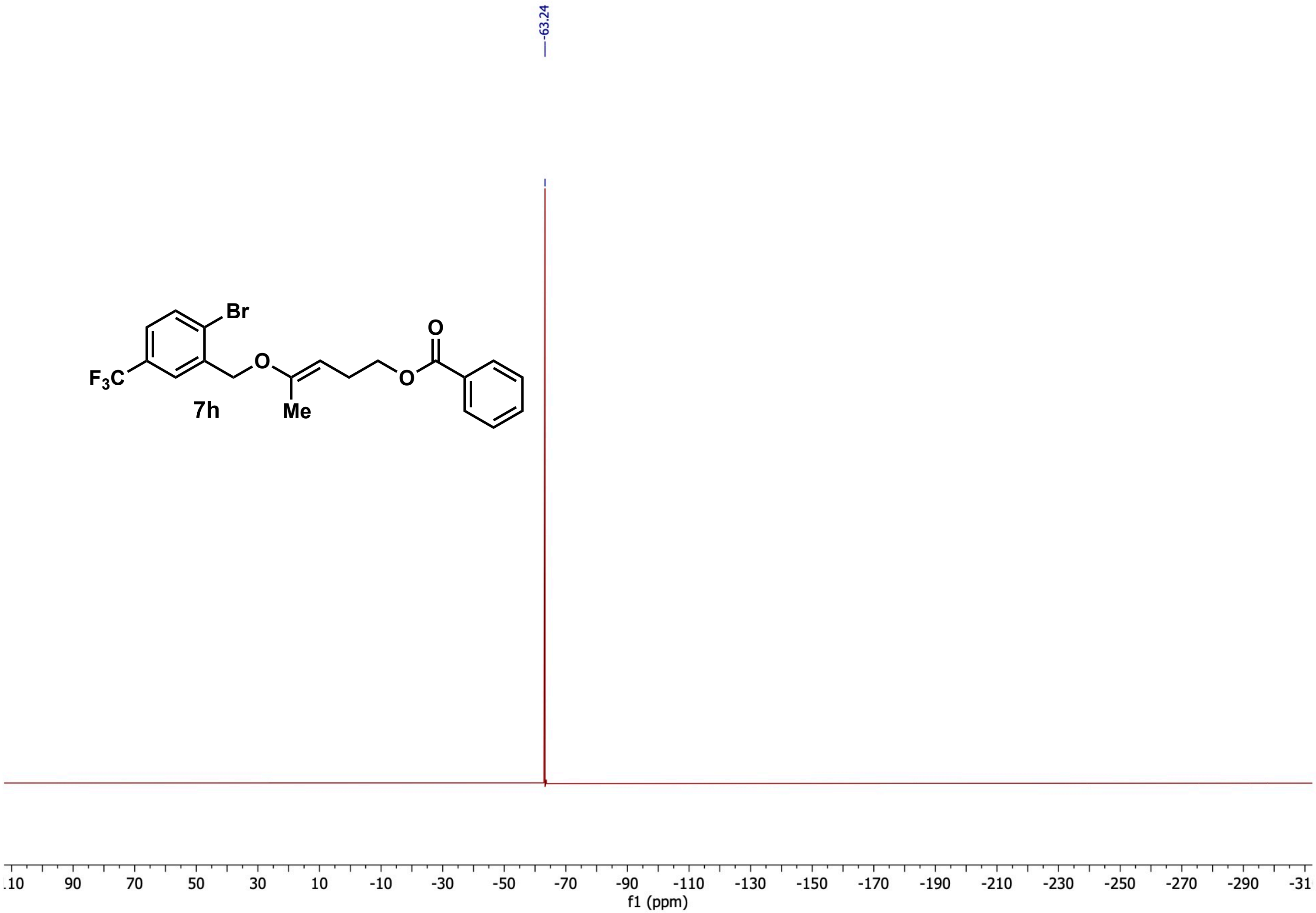


Figure S74. ^{19}F NMR of compound **7h** (470.68 MHz, acetone-*d*6).

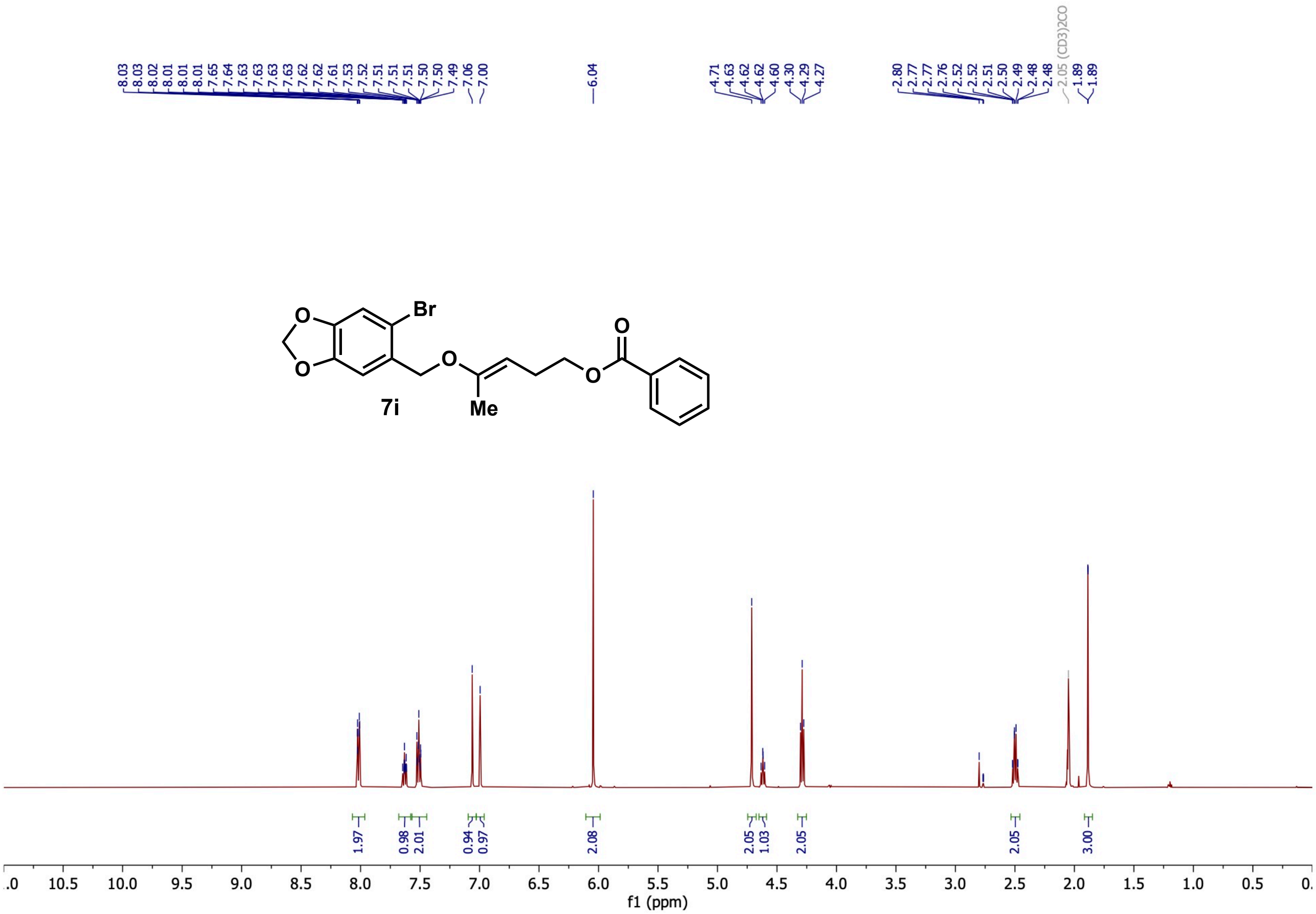

7i

Figure S75. ^{1}H NMR of compound **7i** (500.27 MHz, acetone-*d*6).

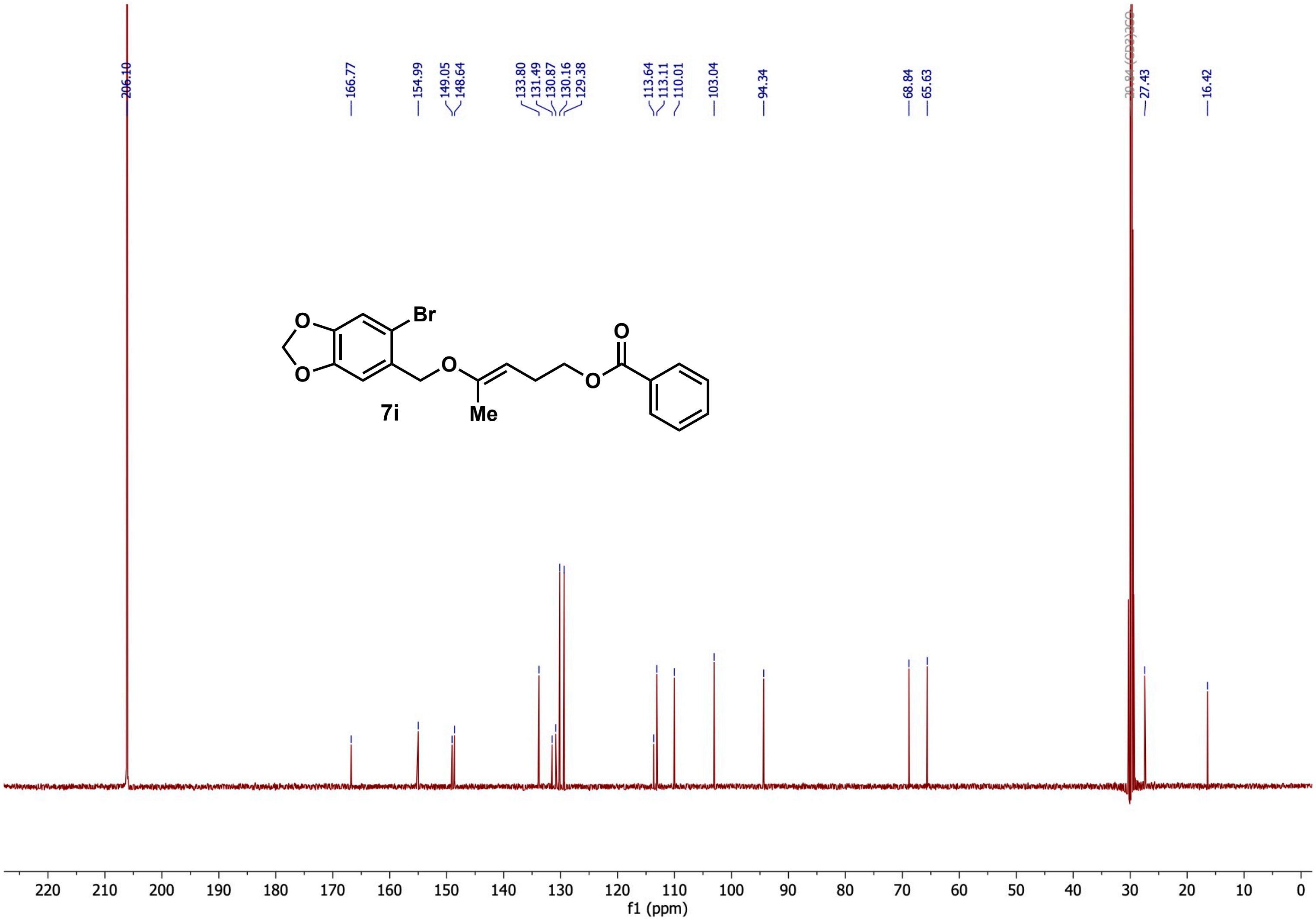


Figure S76. ^{13}C NMR of compound **7i** (125.81 MHz, acetone-*d*6).

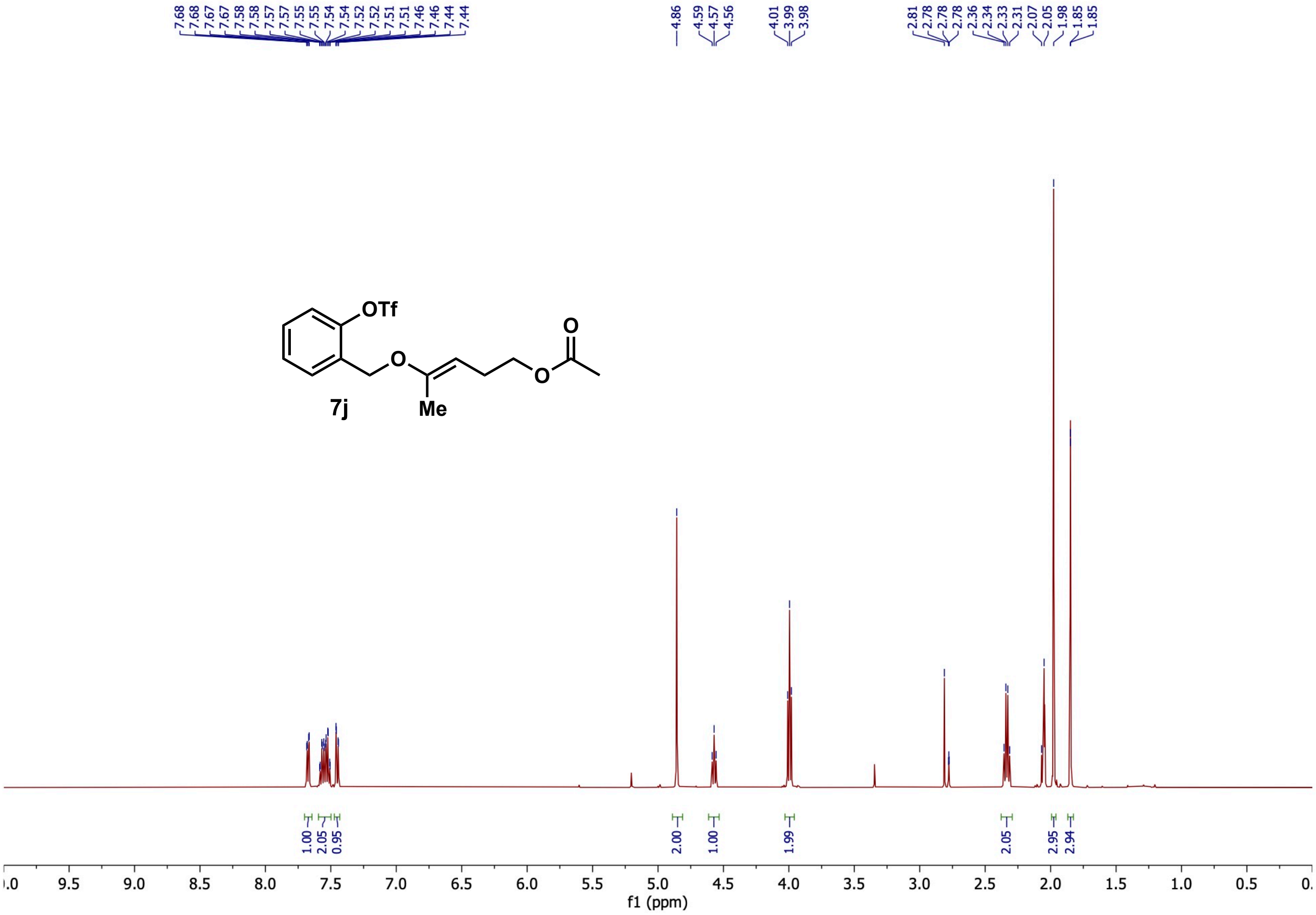


Figure S77. ^{1}H NMR of compound **7j** (500.27 MHz, acetone-*d*6).

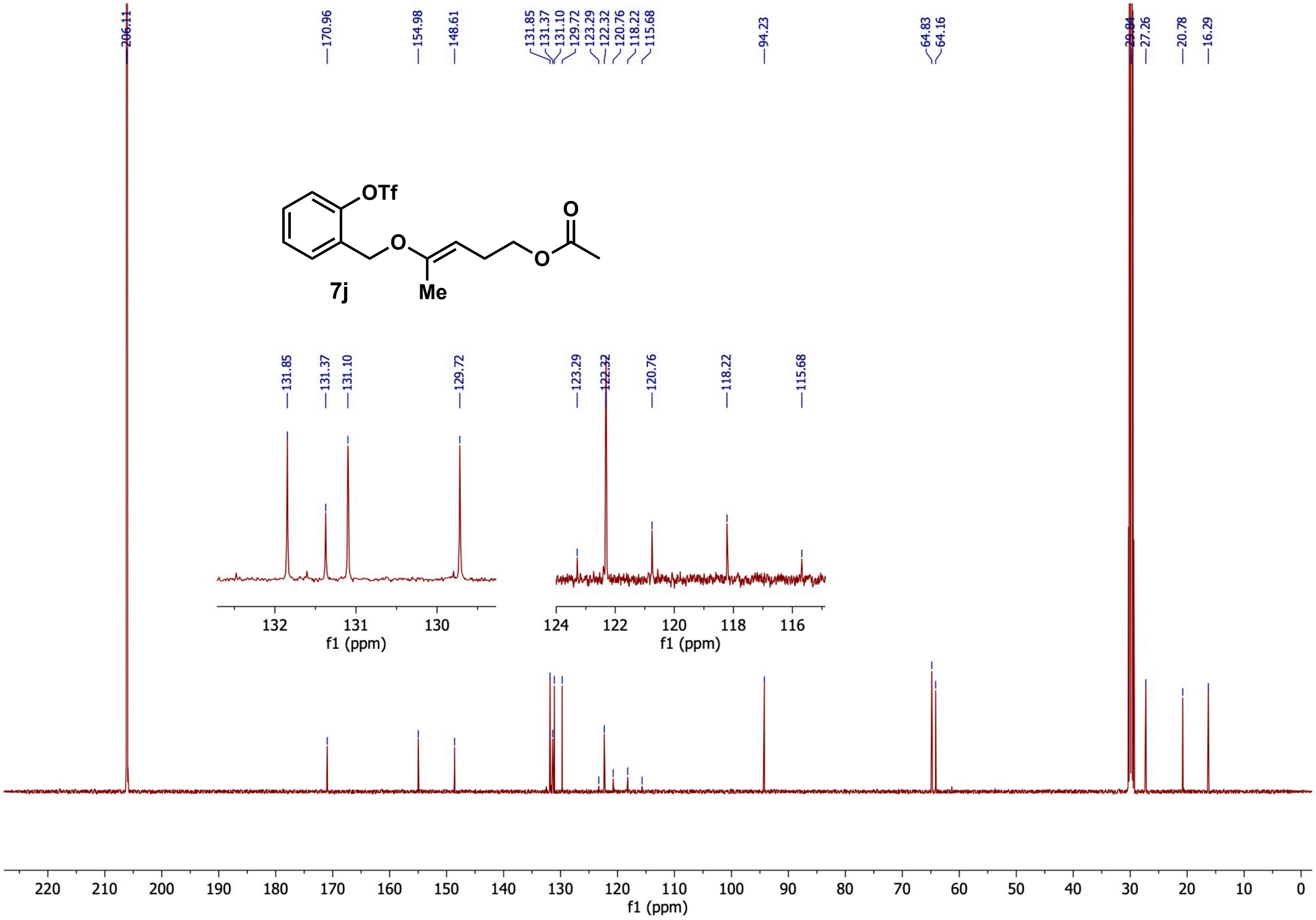


Figure S78. ^{13}C NMR of compound **7j** (125.81 MHz, acetone-*d*6).

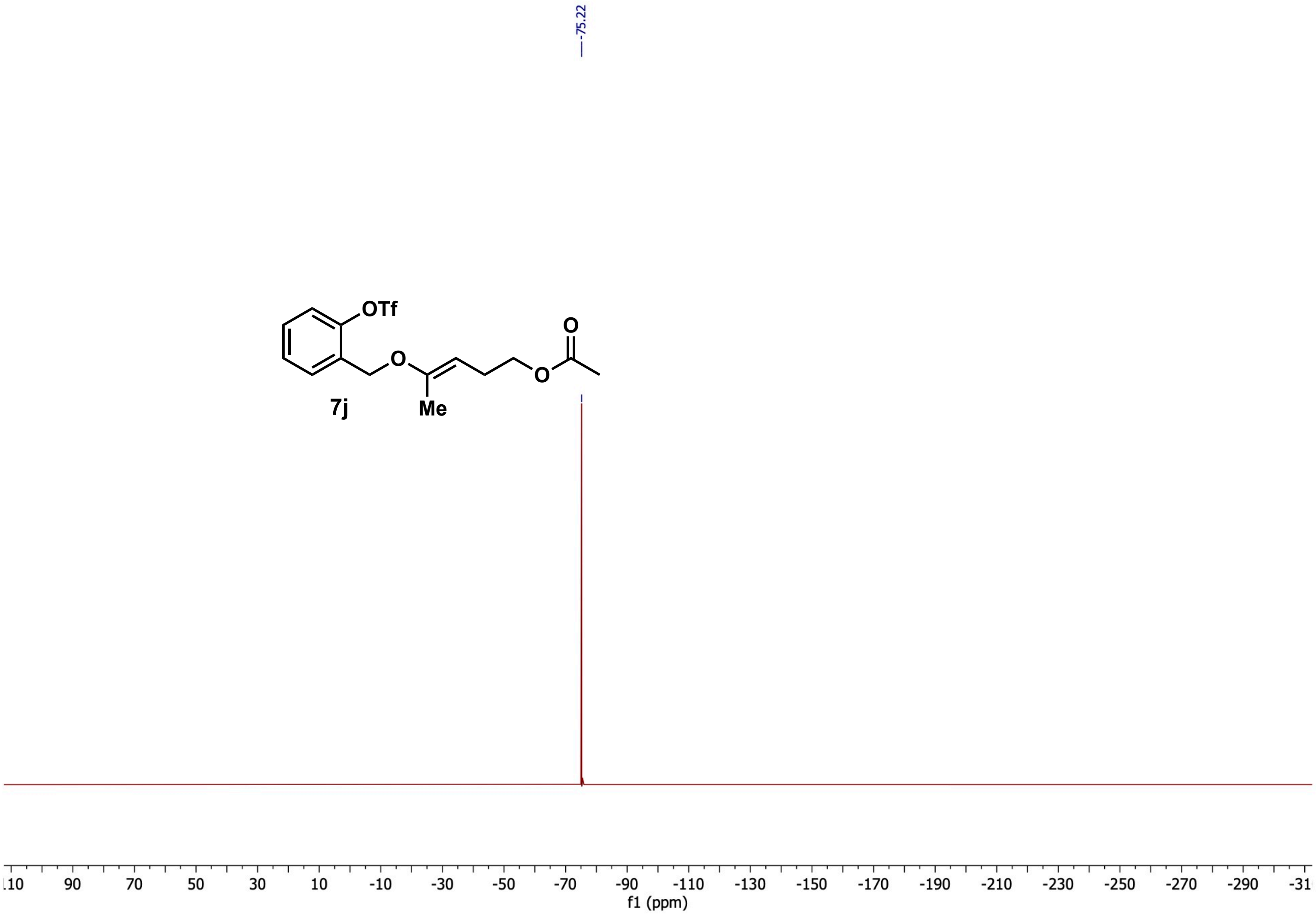


Figure S79. ^{19}F NMR of compound **7j** (470.68 MHz, acetone-*d*6).

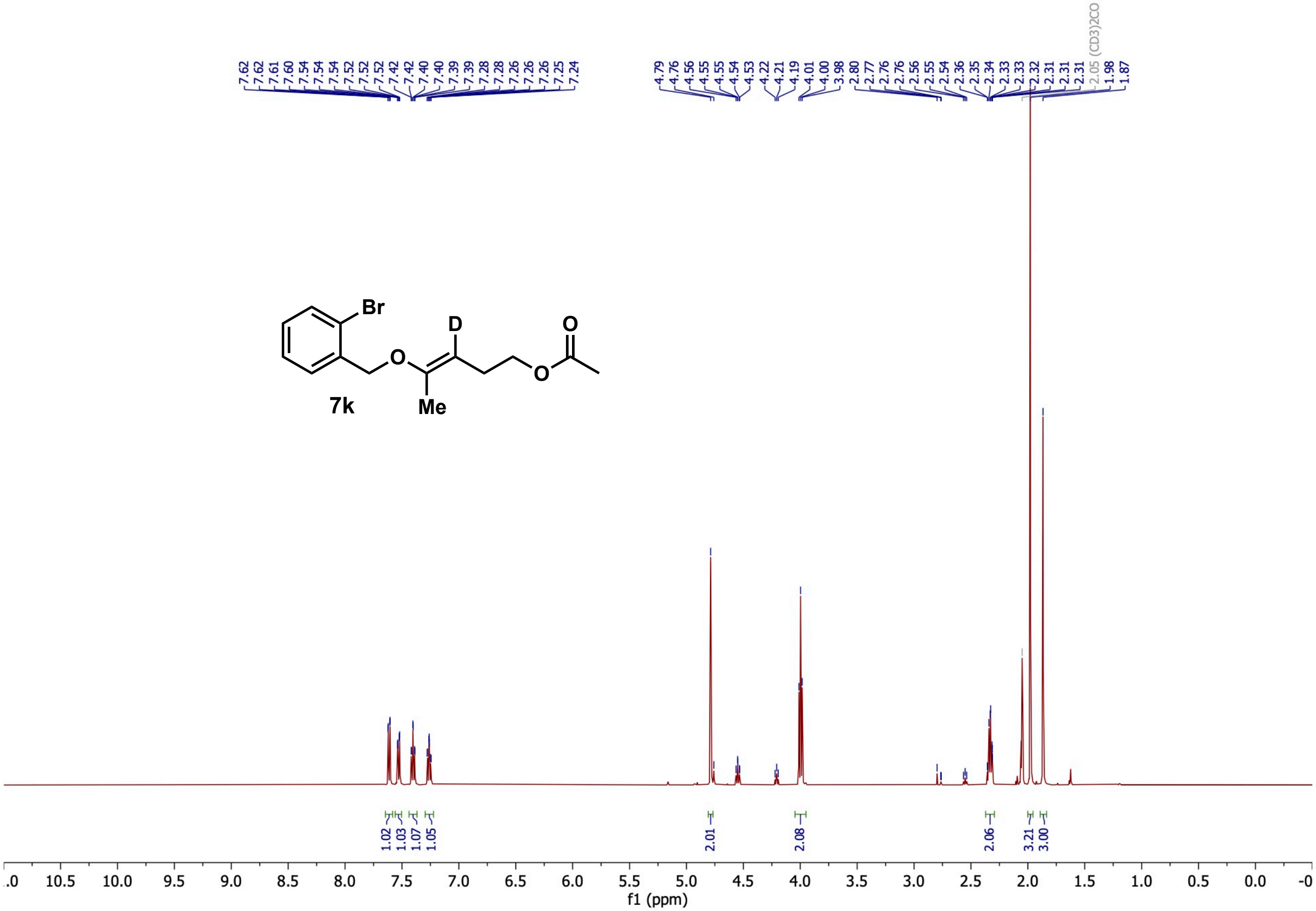


Figure S80. ^{1}H NMR of compound **7k** (500.27 MHz, acetone-*d*6).

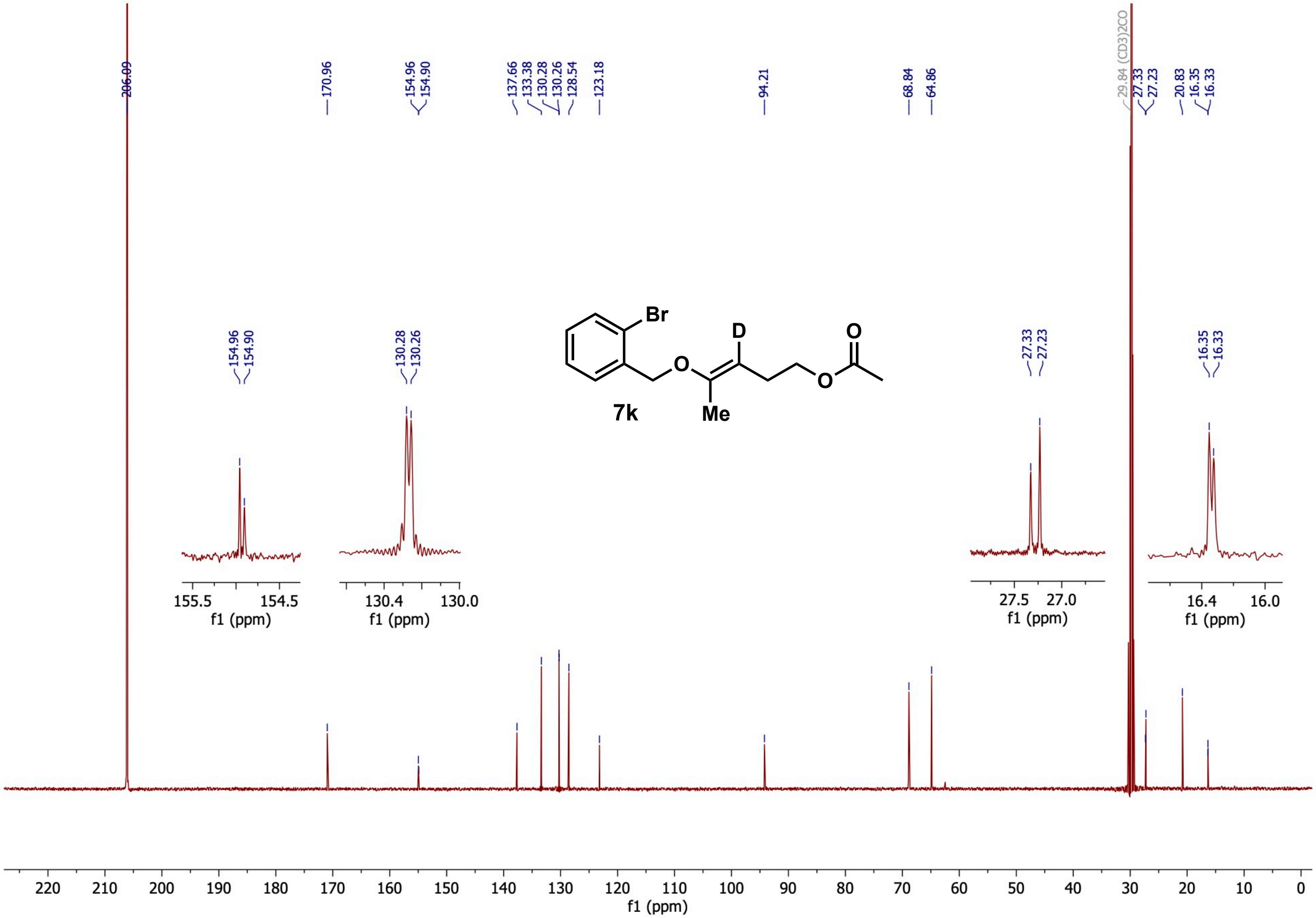


Figure S81. ^{13}C NMR of compound **7k** (125.81 MHz, acetone-*d*6).

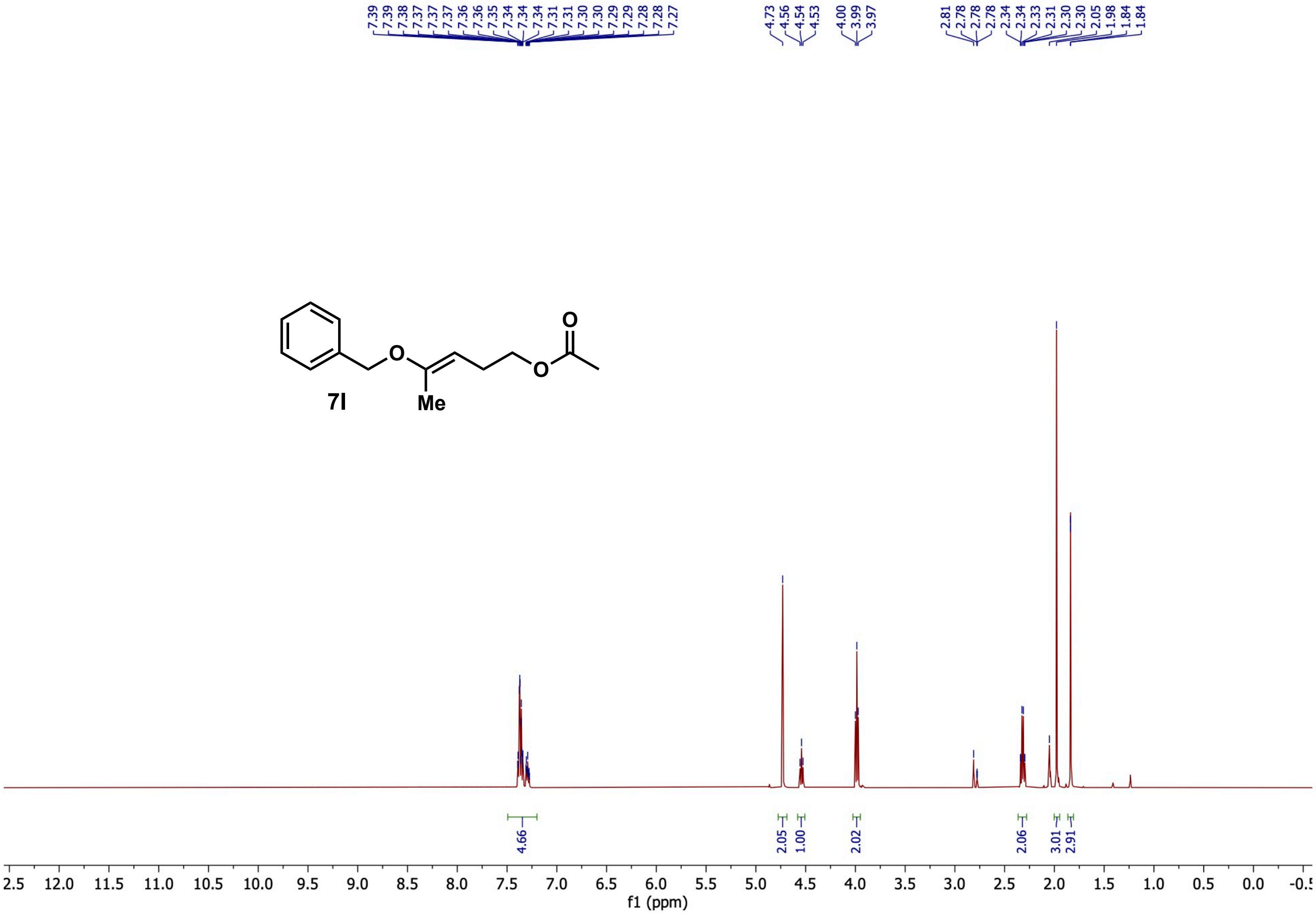


Figure S82. ^{1}H NMR of compound **7l** (500.27 MHz, acetone-*d*6).

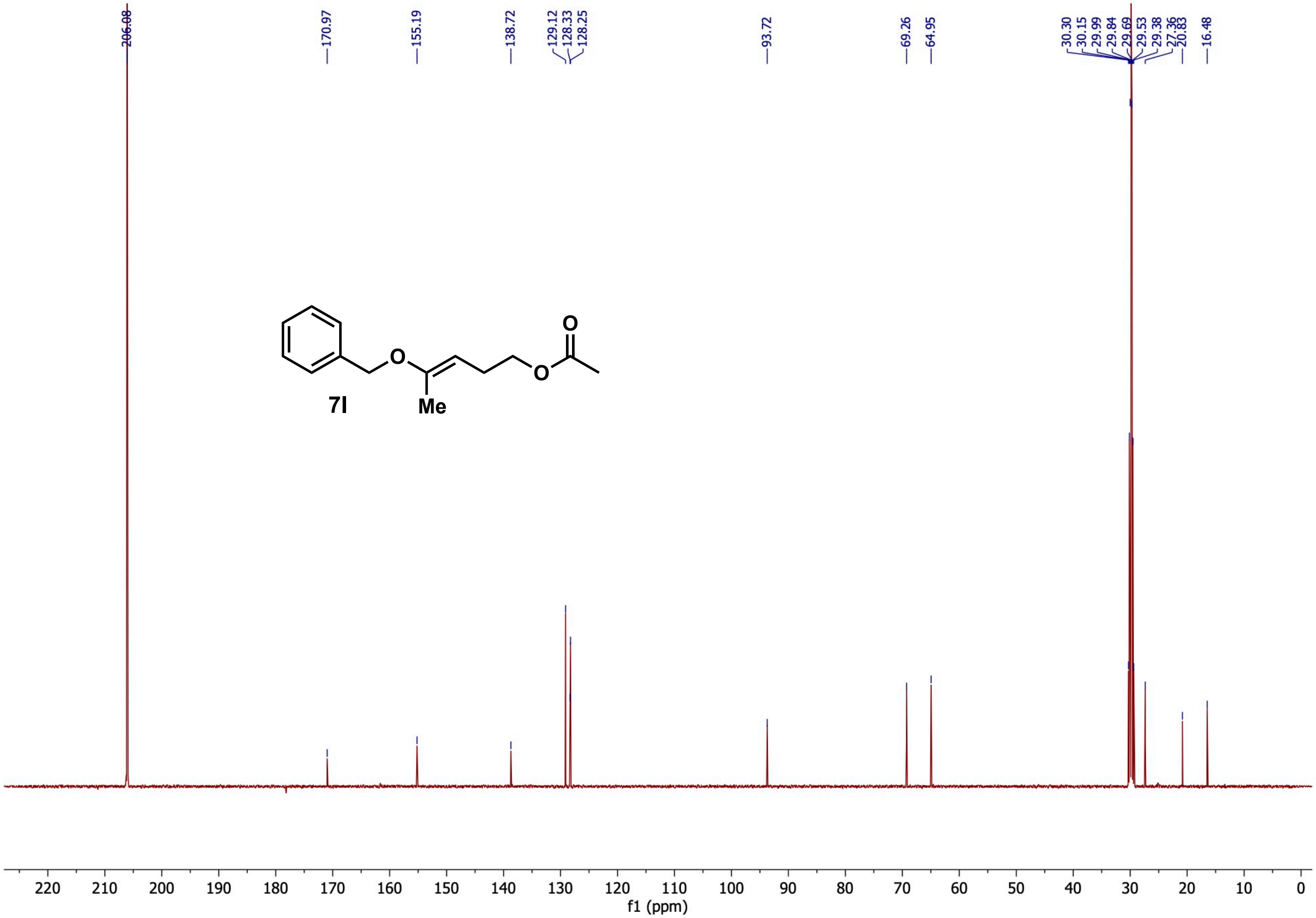


Figure S83. ^{13}C NMR of compound **7l** (125.81 MHz, acetone-*d*6).

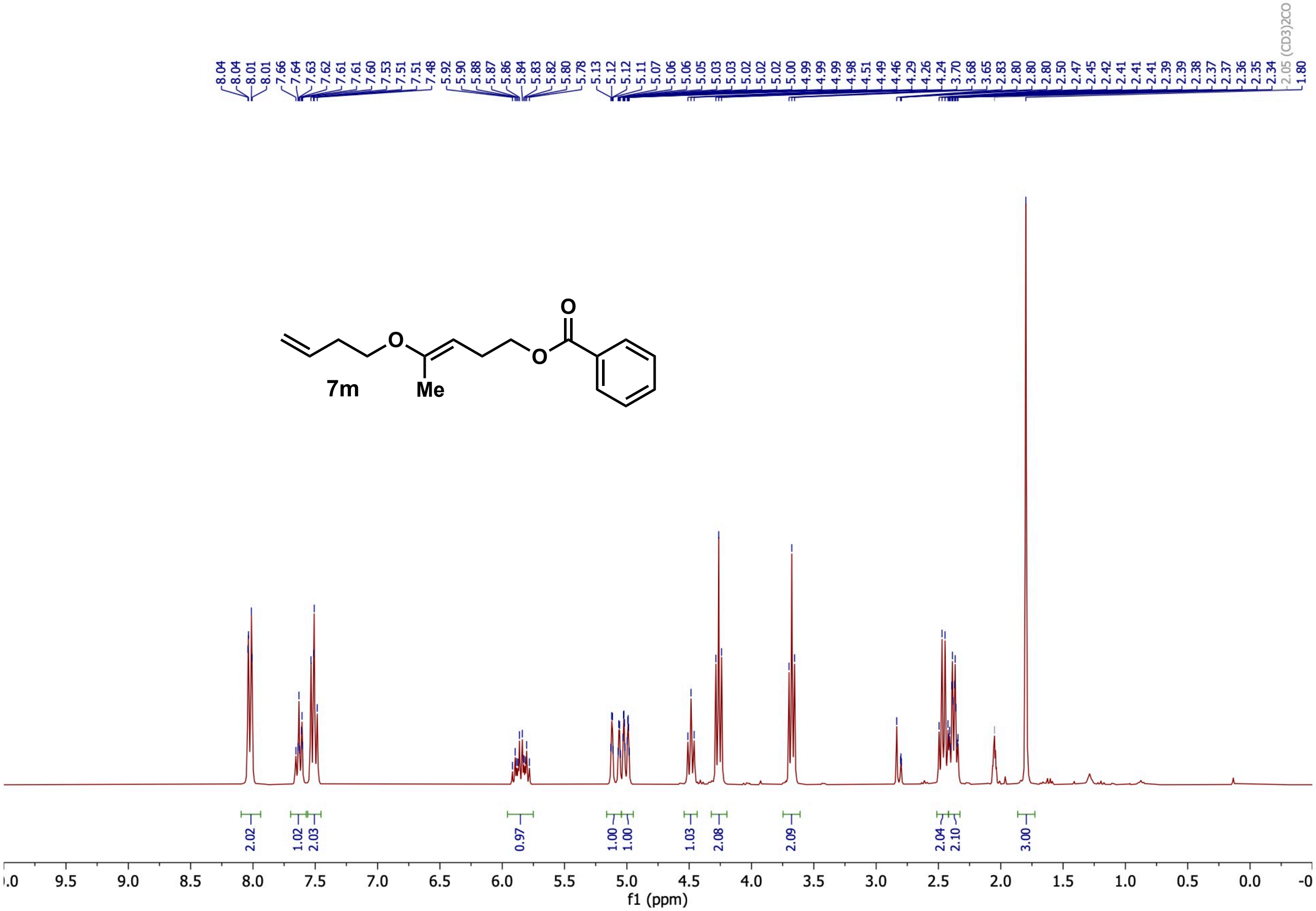


Figure S84. ^{1}H NMR of compound **7m** (300.27 MHz, acetone-*d*6).

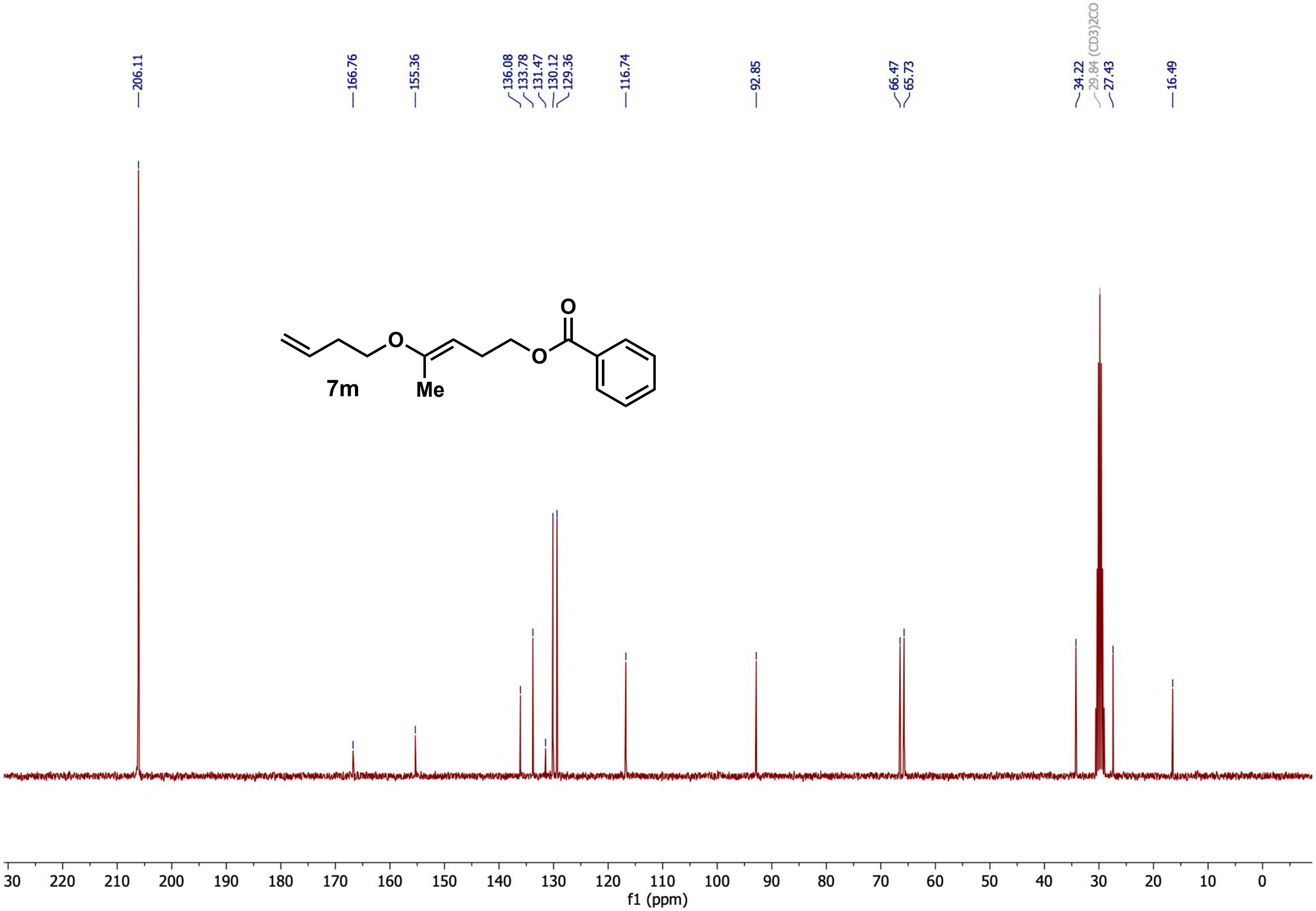


Figure S85. ^{13}C NMR of compound **7m** (75.51 MHz, acetone-*d*6).

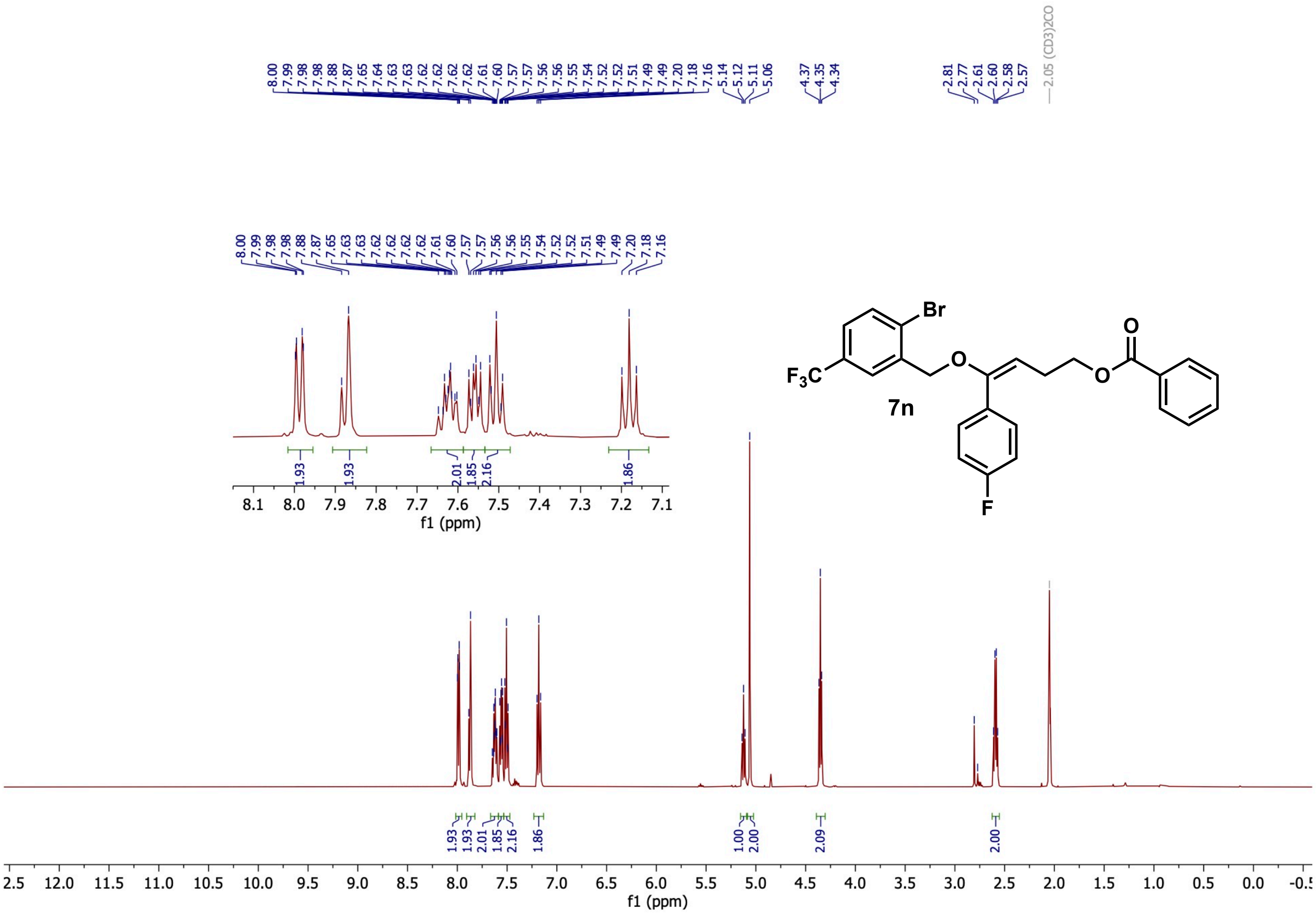


Figure S86. ^{1}H NMR of compound **7n** (500.27 MHz, acetone-*d*6).

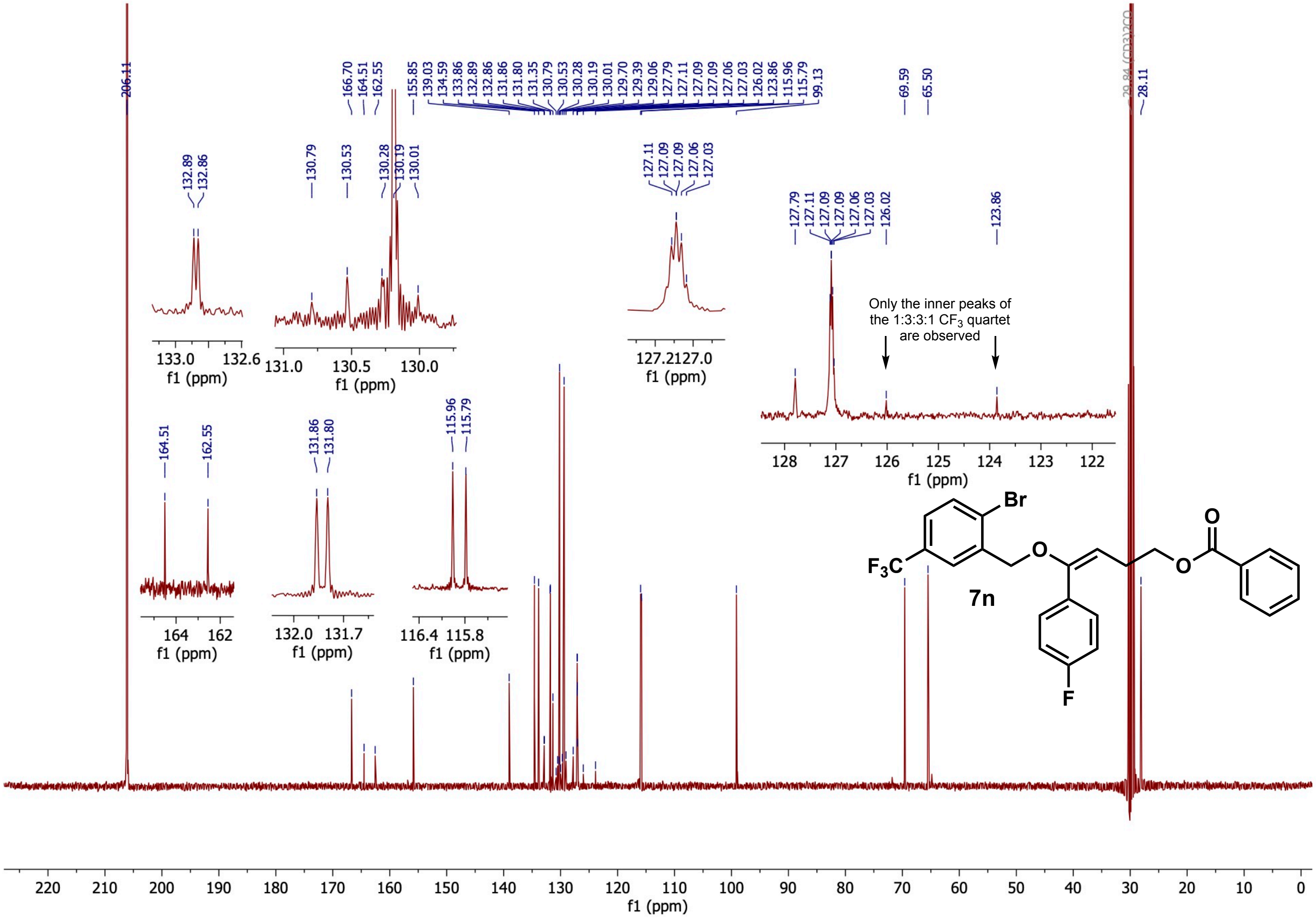


Figure S87. ^{13}C NMR of compound **7n** (125.81 MHz, acetone-*d*6).

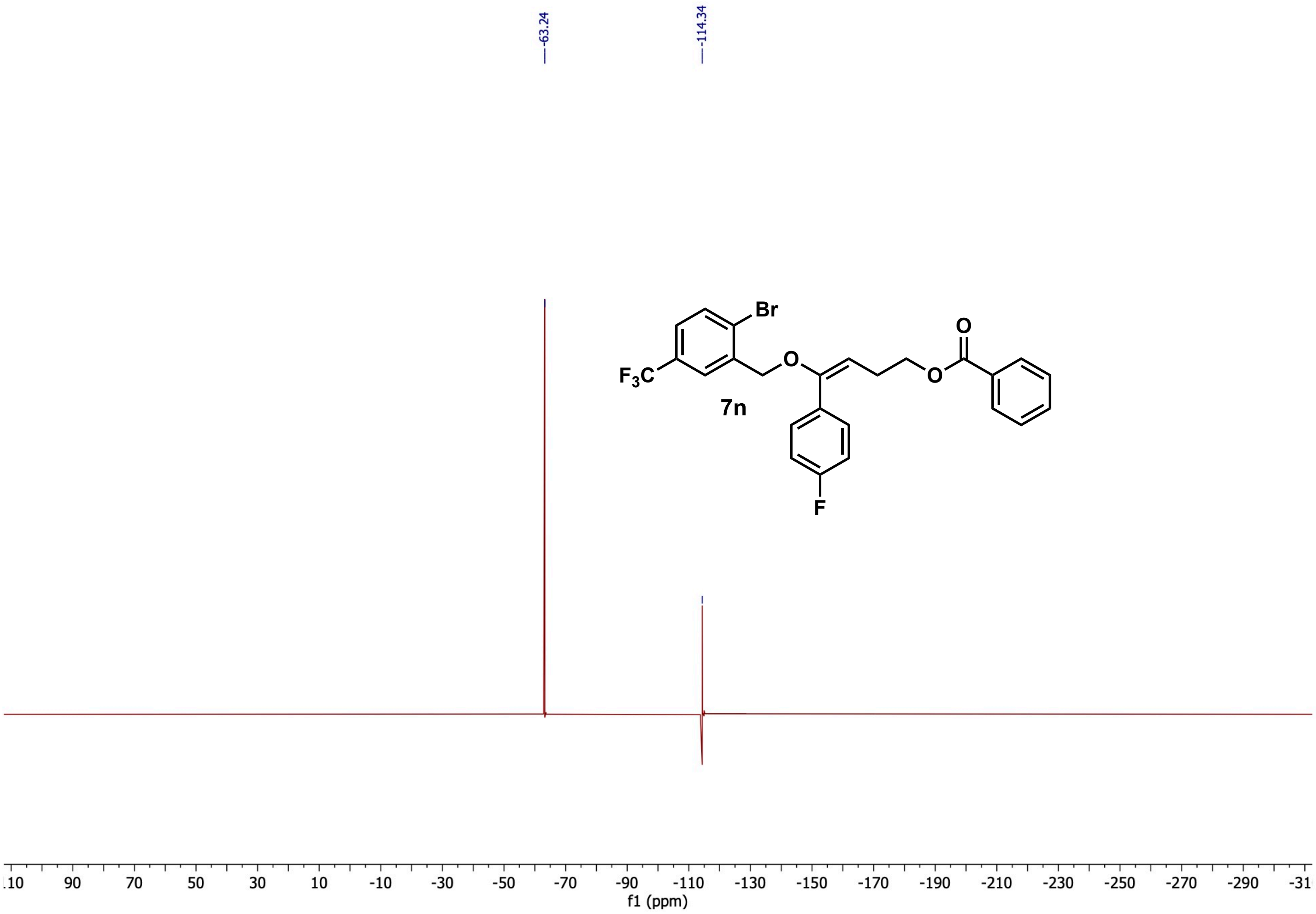


Figure S88. ^{19}F NMR of compound **7n** (470.68 MHz, acetone-*d*6).

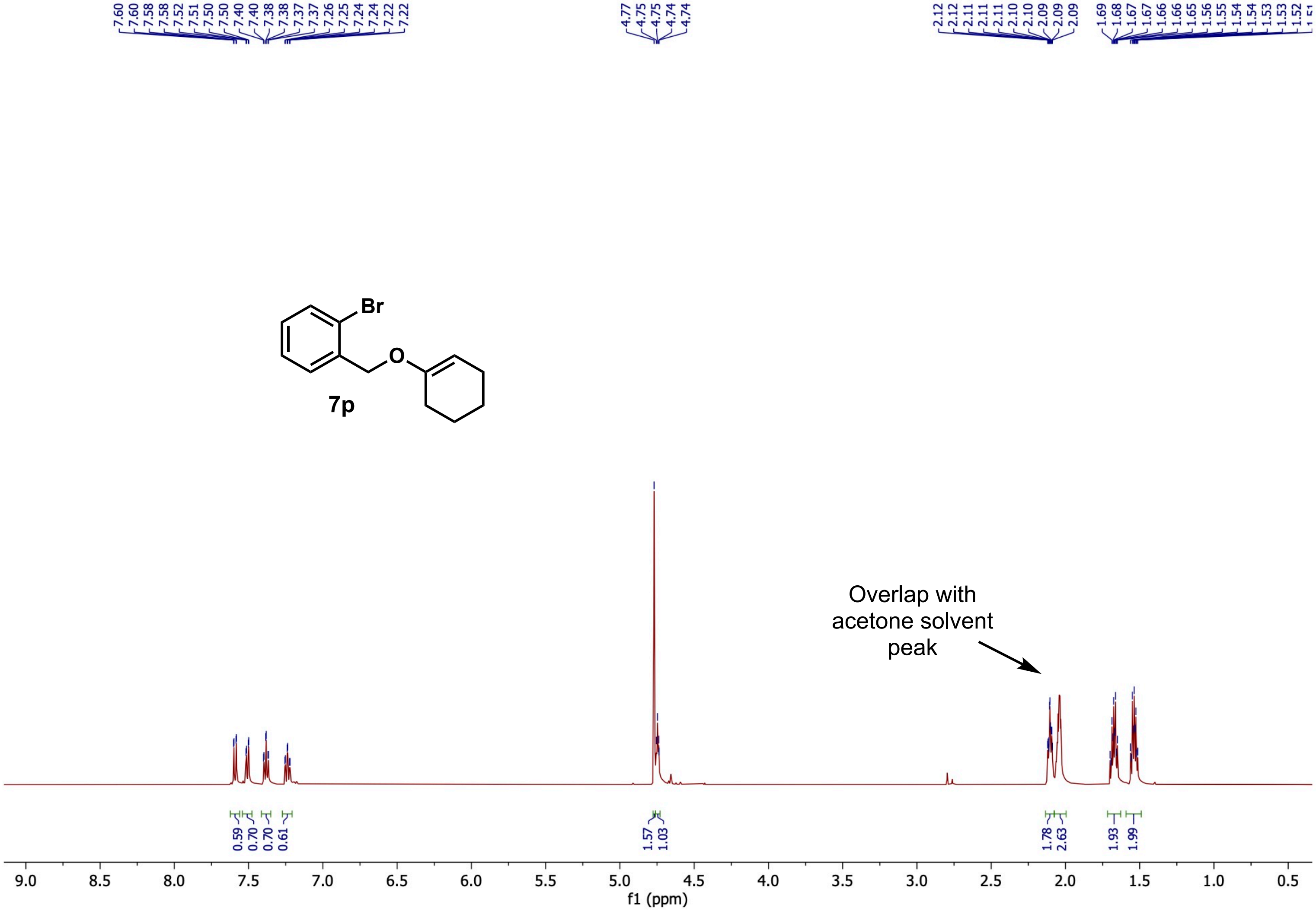


Figure S89. ^{1}H NMR of compound **7p** (500.27 MHz, acetone-*d*6).

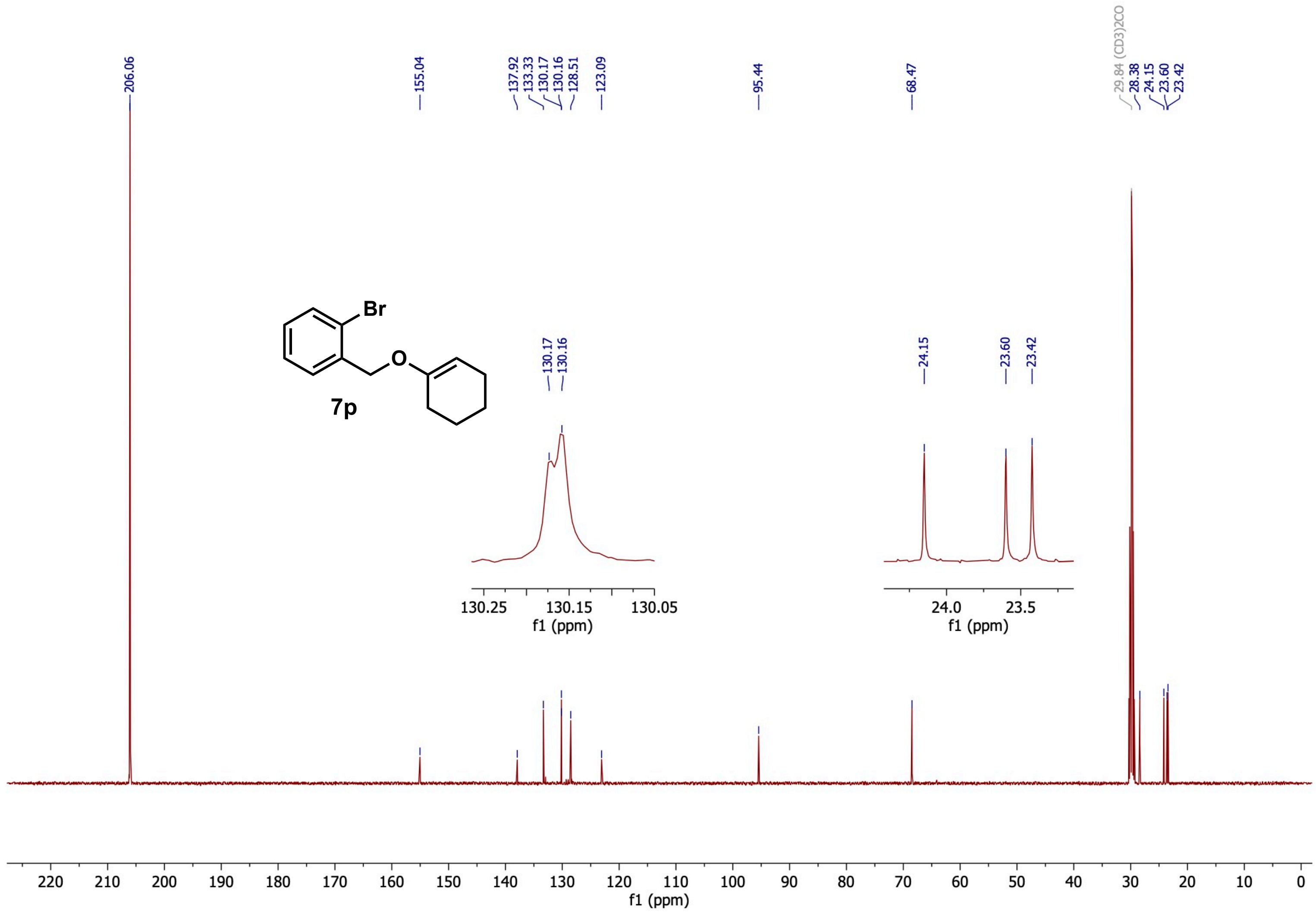


Figure S90. ^{13}C NMR of compound **7p** (125.81 MHz, acetone-*d*6).

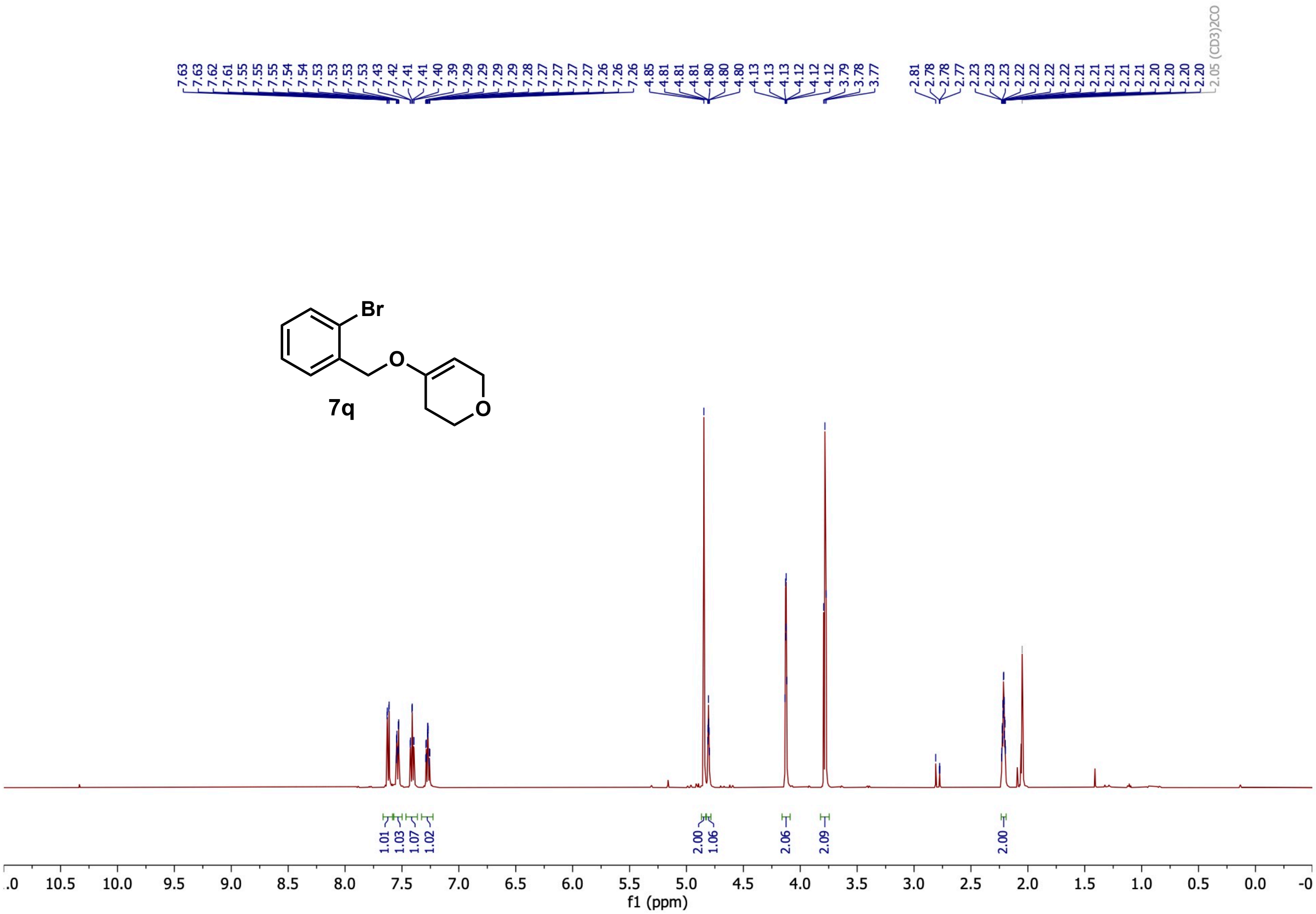


Figure S91. ¹H NMR of compound **7q** (500.27 MHz, acetone-*d*6).

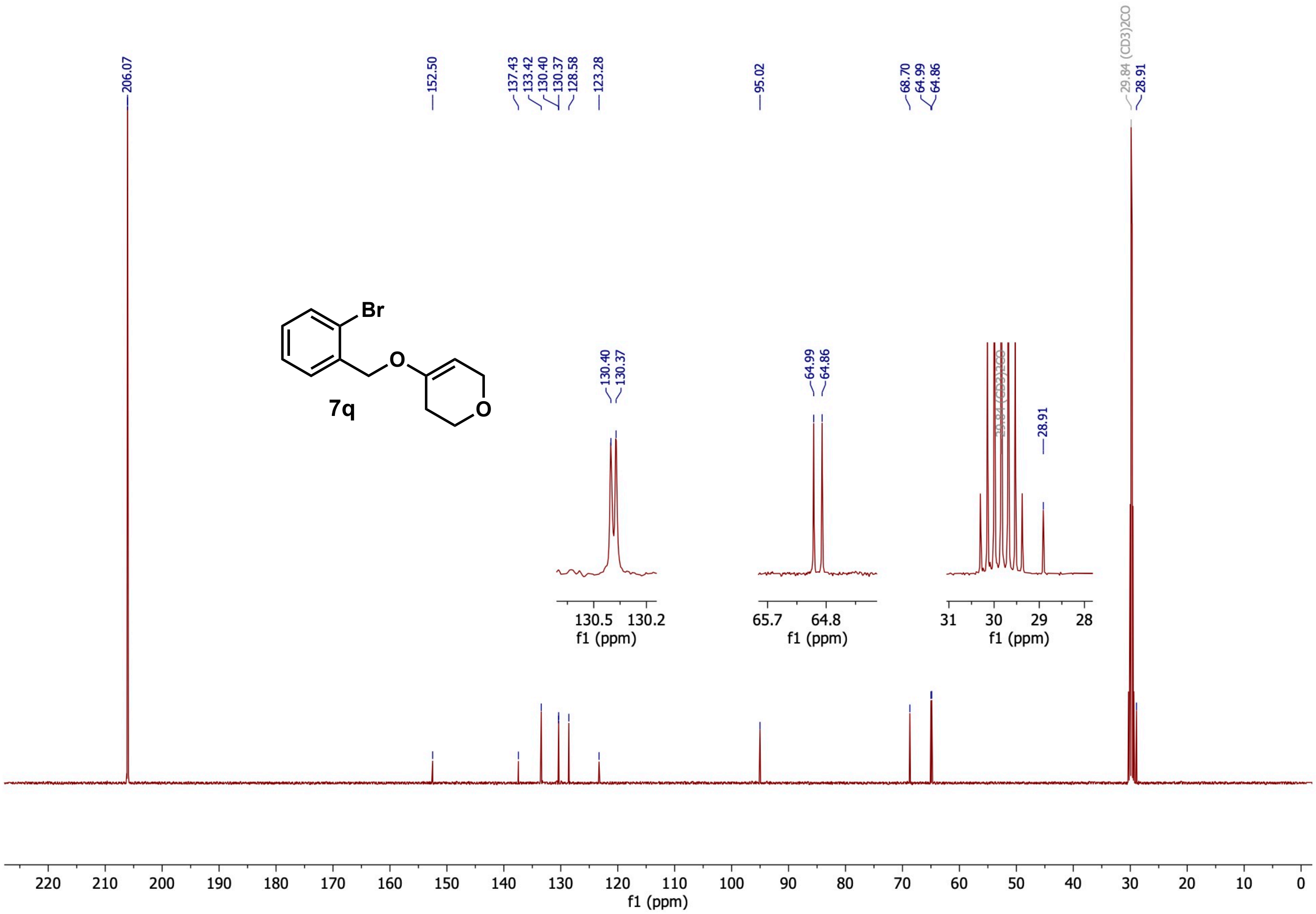


Figure S92. ^{13}C NMR of compound **7q** (125.81 MHz, acetone-*d*6).

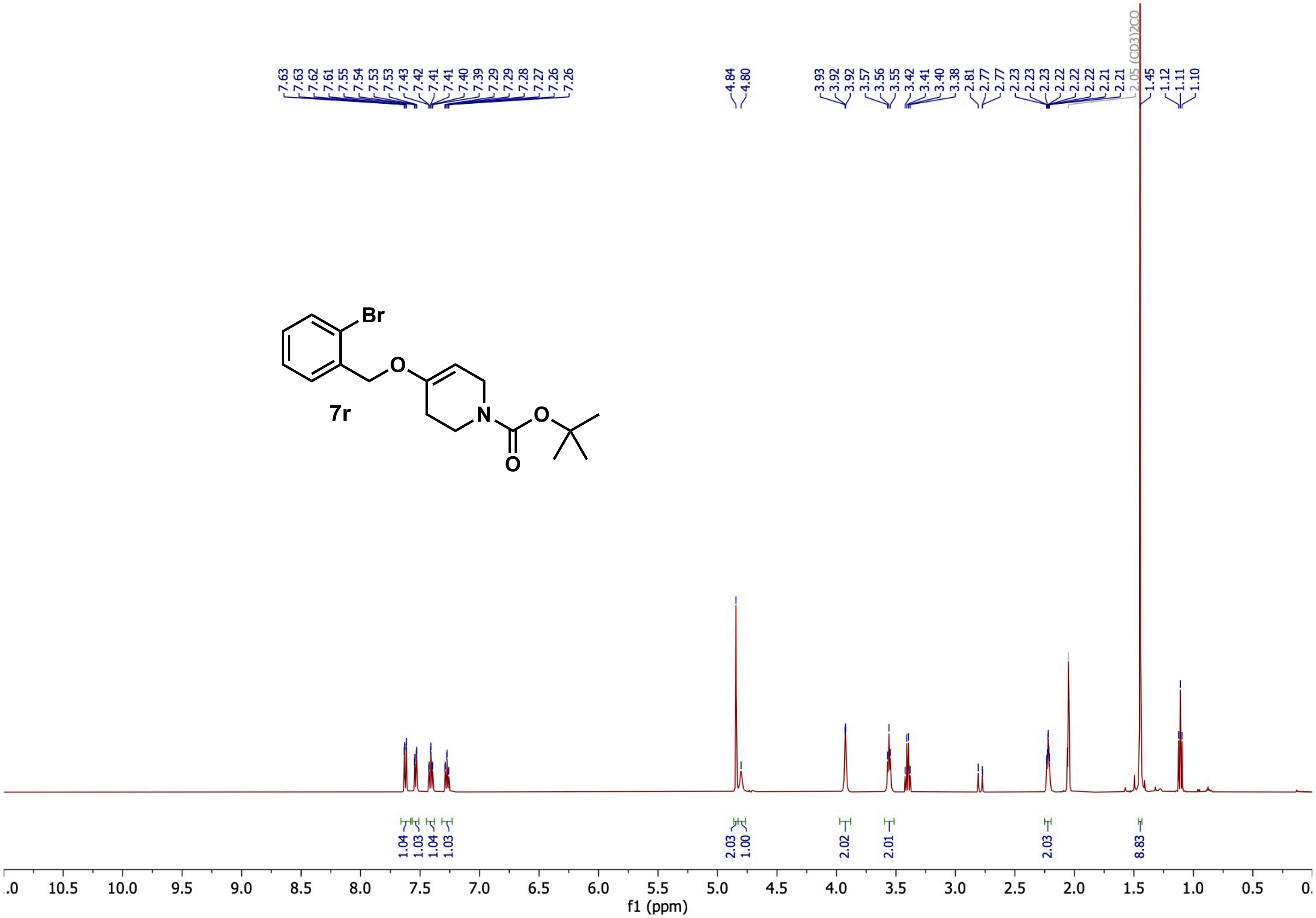


Figure S93. ^{1}H NMR of compound **7r** (500.27 MHz, acetone-*d*6).

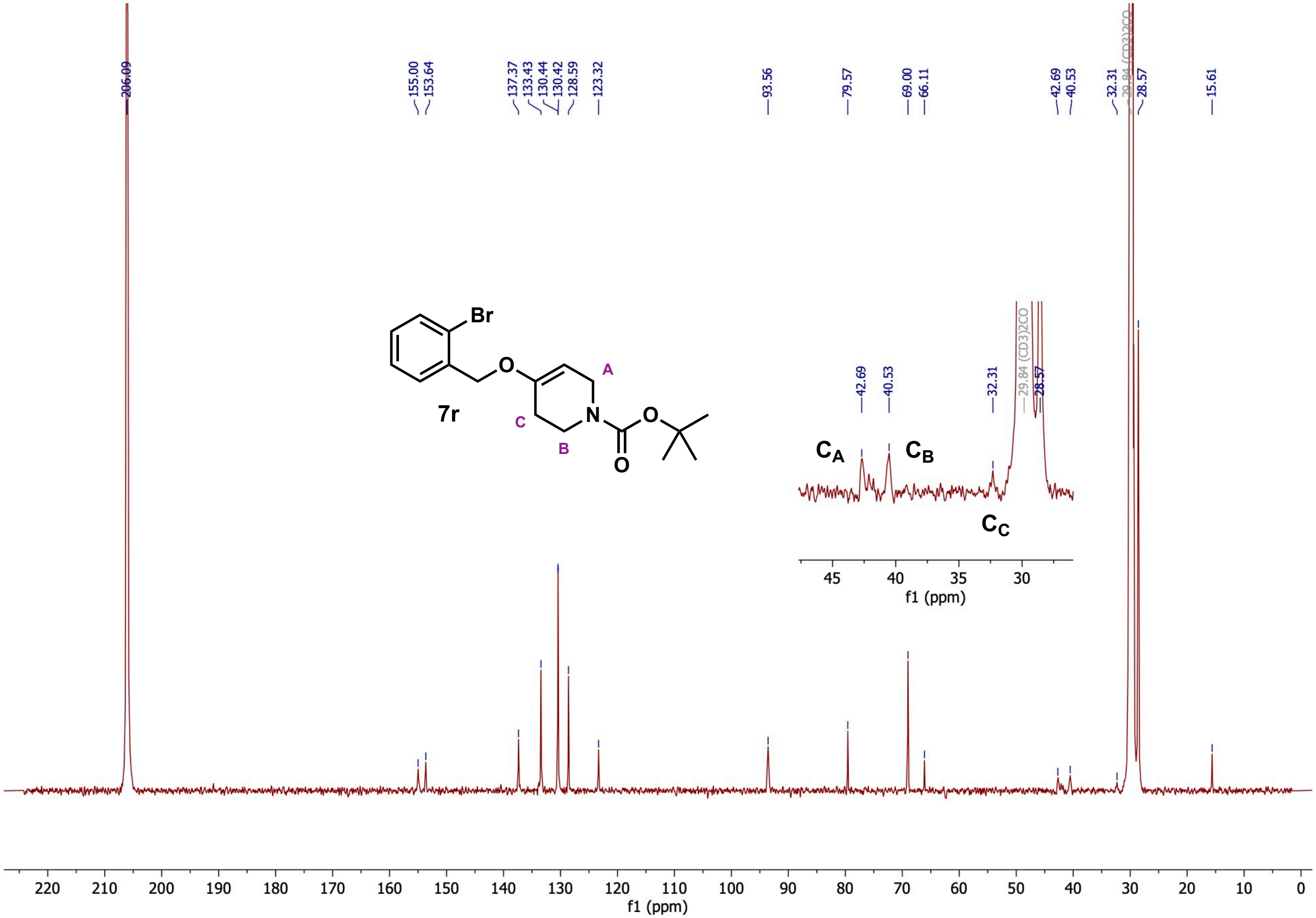


Figure S94. ^{13}C NMR of compound **7r** (125.81 MHz, acetone-*d*6).

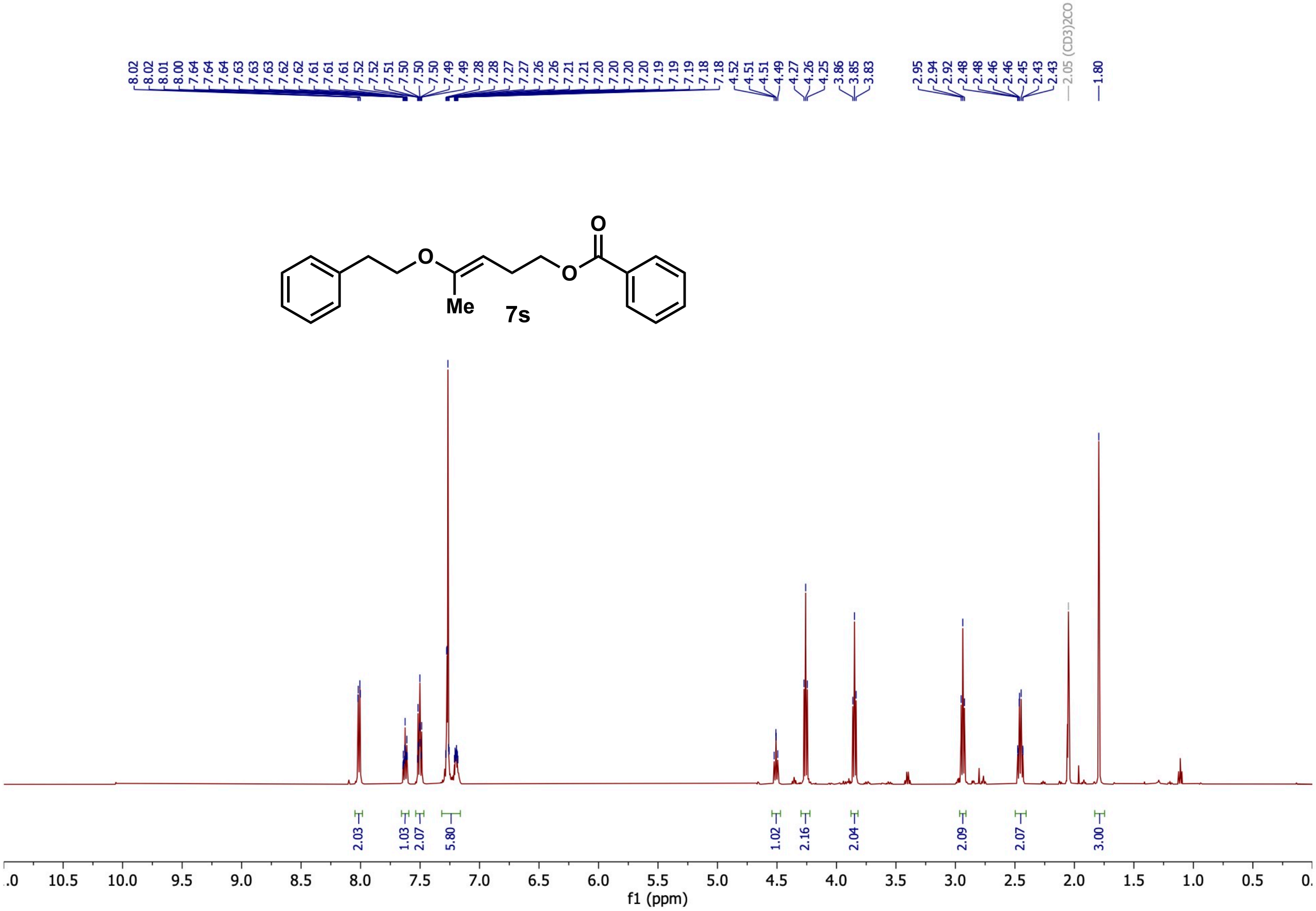


Figure S95. ^{1}H NMR of compound **7s** (500.27 MHz, acetone-*d*6).

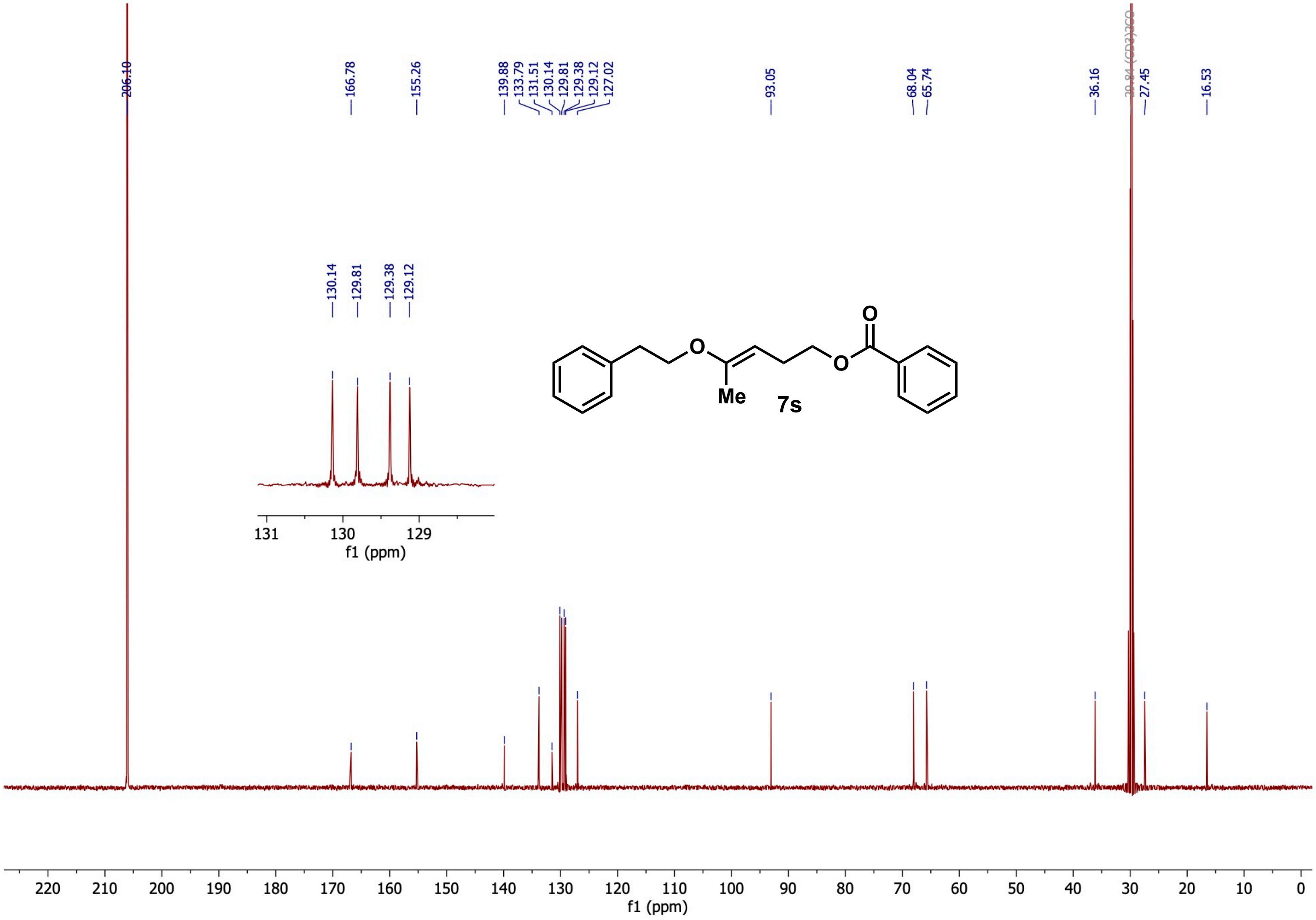


Figure S96. ^{13}C NMR of compound **7s** (125.81 MHz, acetone-*d*6).

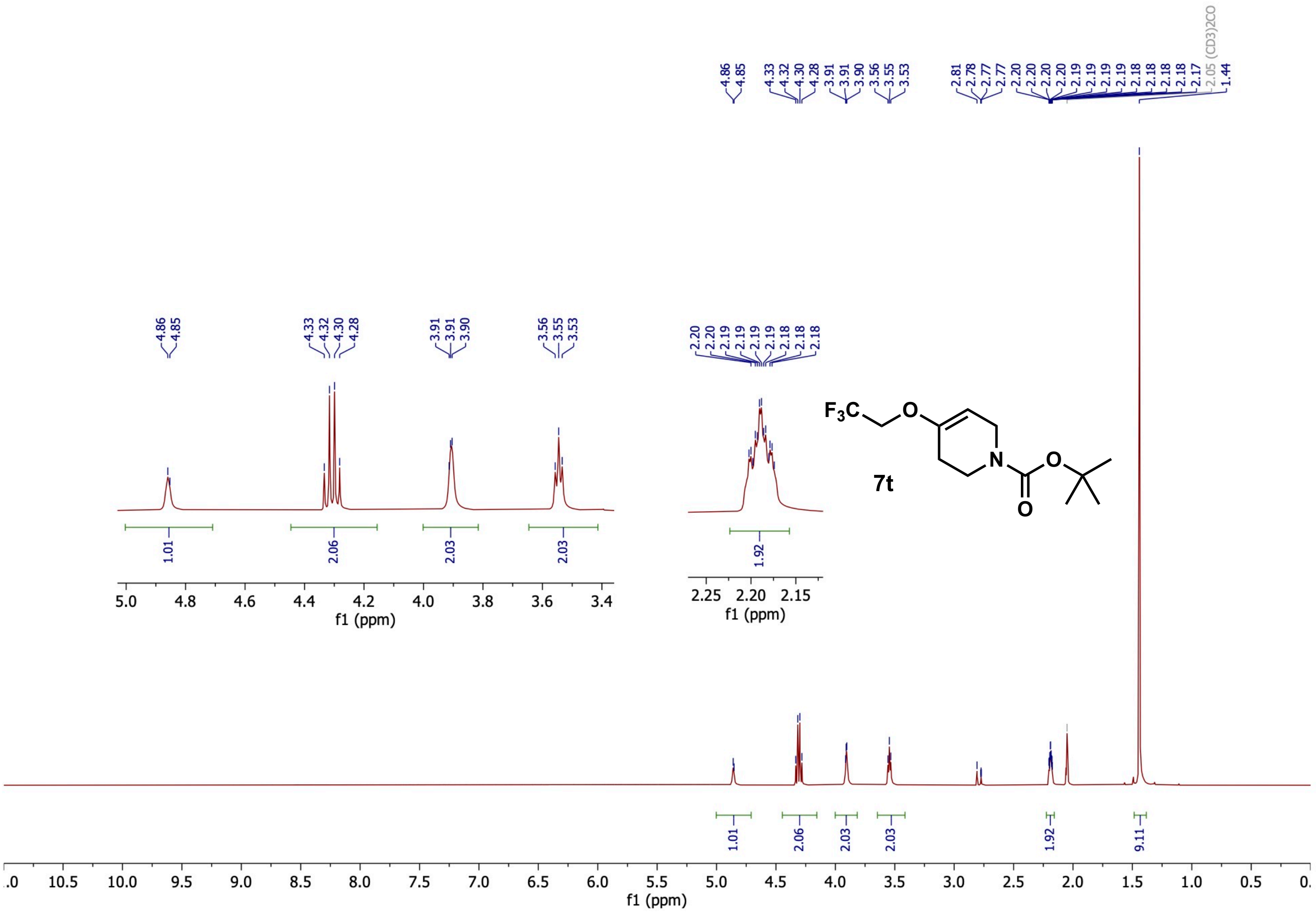


Figure S97. ^{1}H NMR of compound **7t** (500.27 MHz, acetone-*d*6).

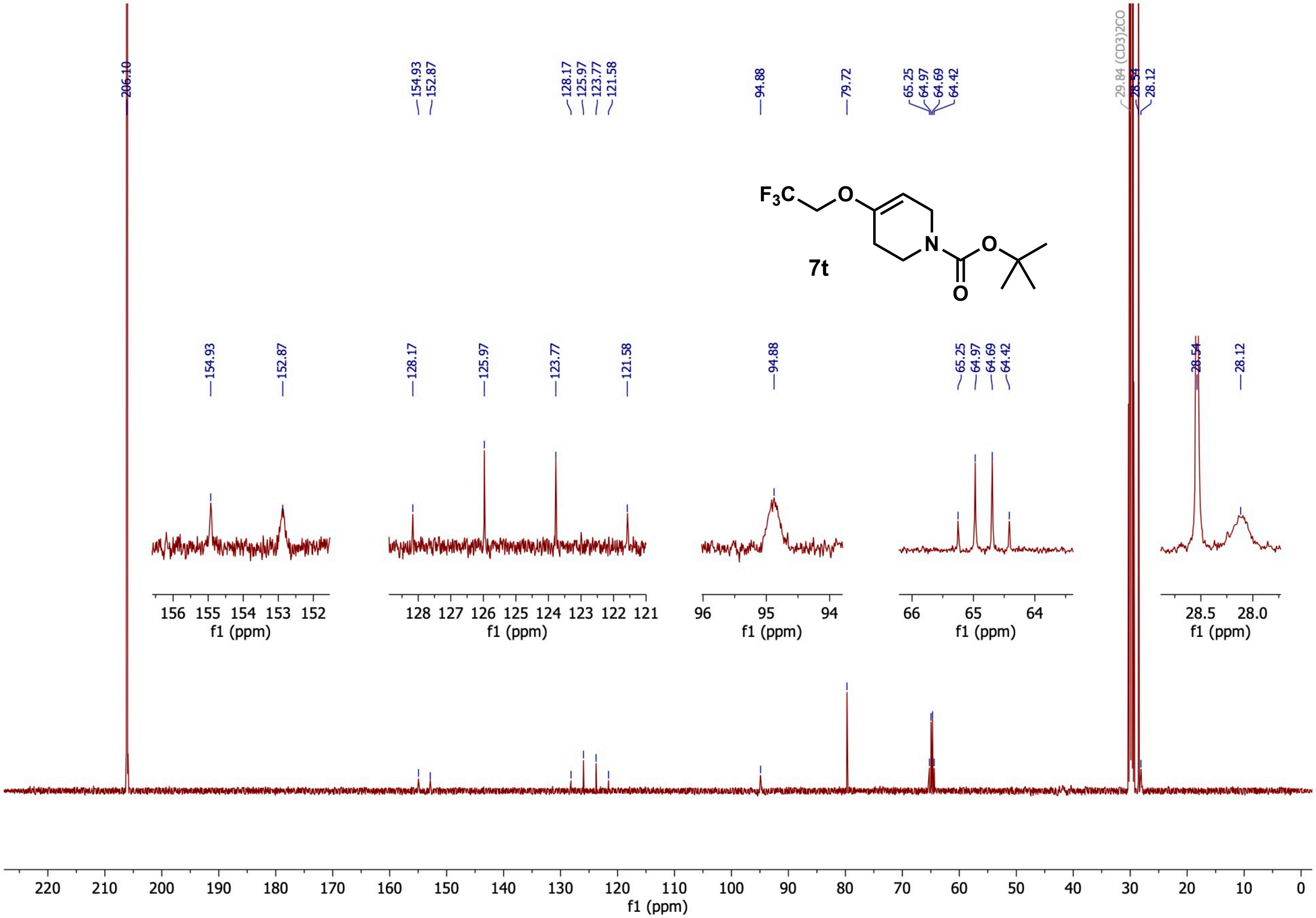


Figure S98. ^{13}C NMR of compound **7t** (125.81 MHz, acetone-*d*6).

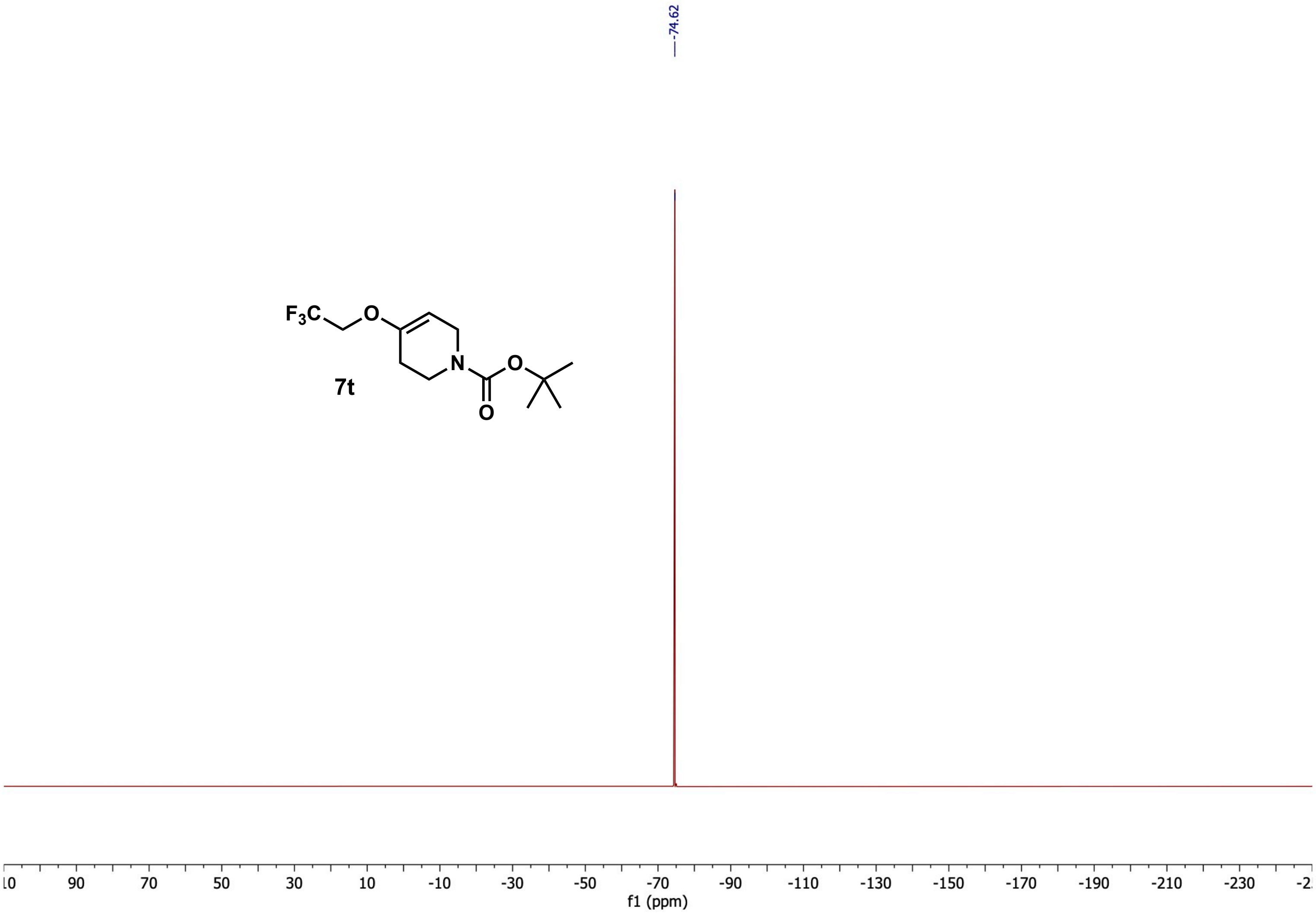


Figure S99. ^{19}F NMR of compound **7t** (470.68 MHz, acetone-*d*6).

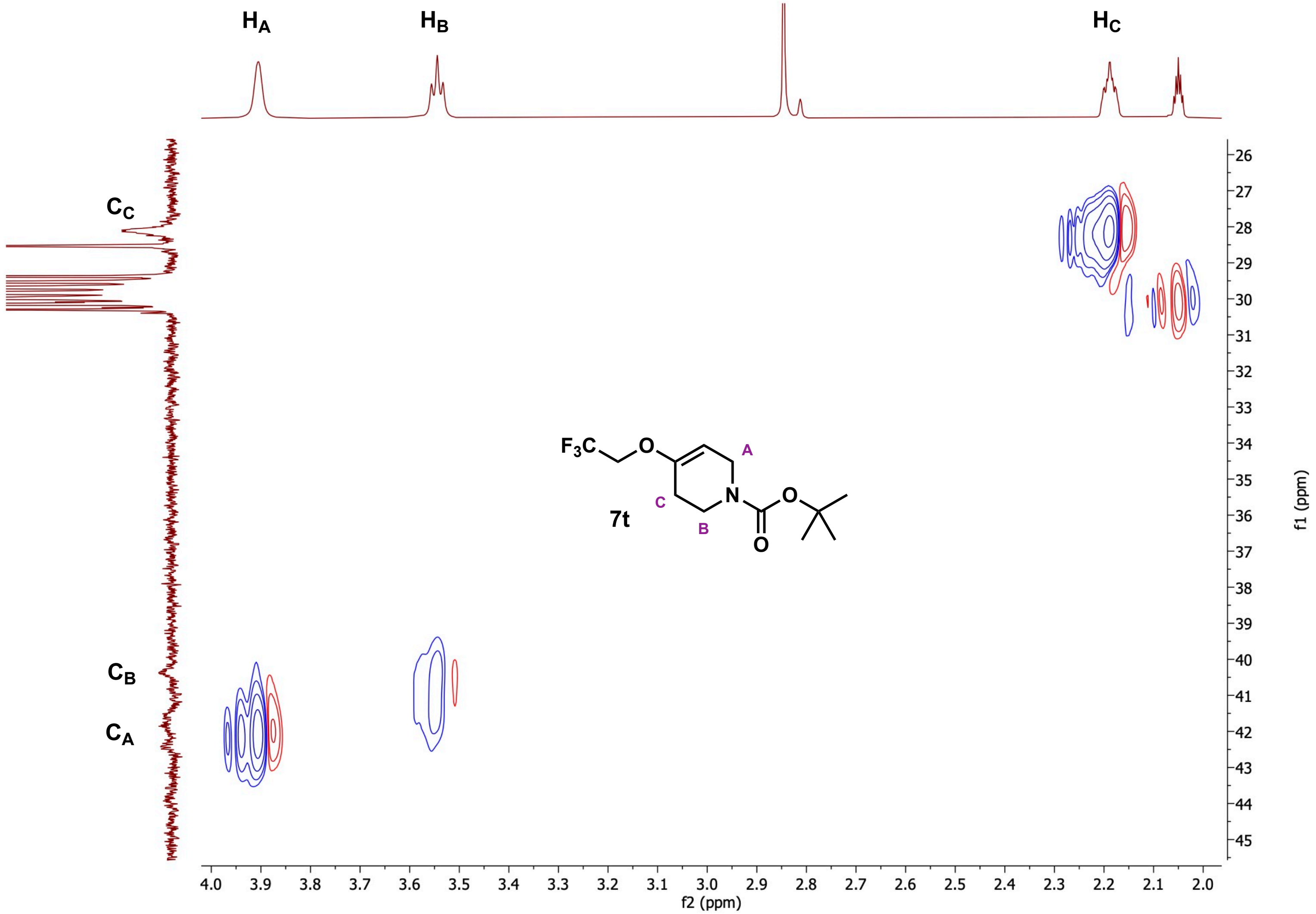


Figure S100. Gradient HSQC spectrum of compound **7t** (500.27, 125.81 MHz, acetone-*d*6) zoomed-in to show key ^{13}C assignments.

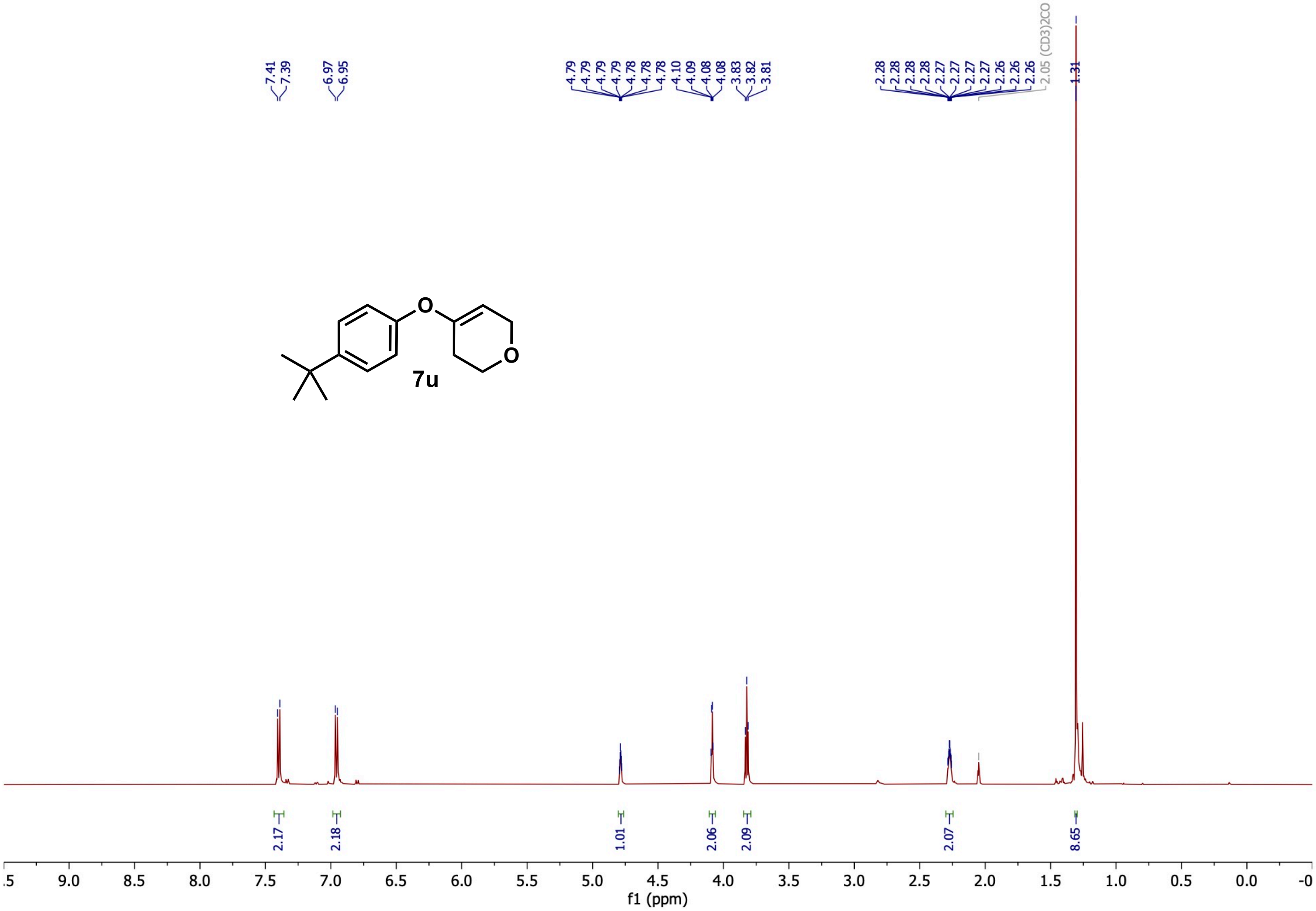


Figure S101. ^{1}H NMR of compound **7u** (500.27 MHz, acetone-*d*6).

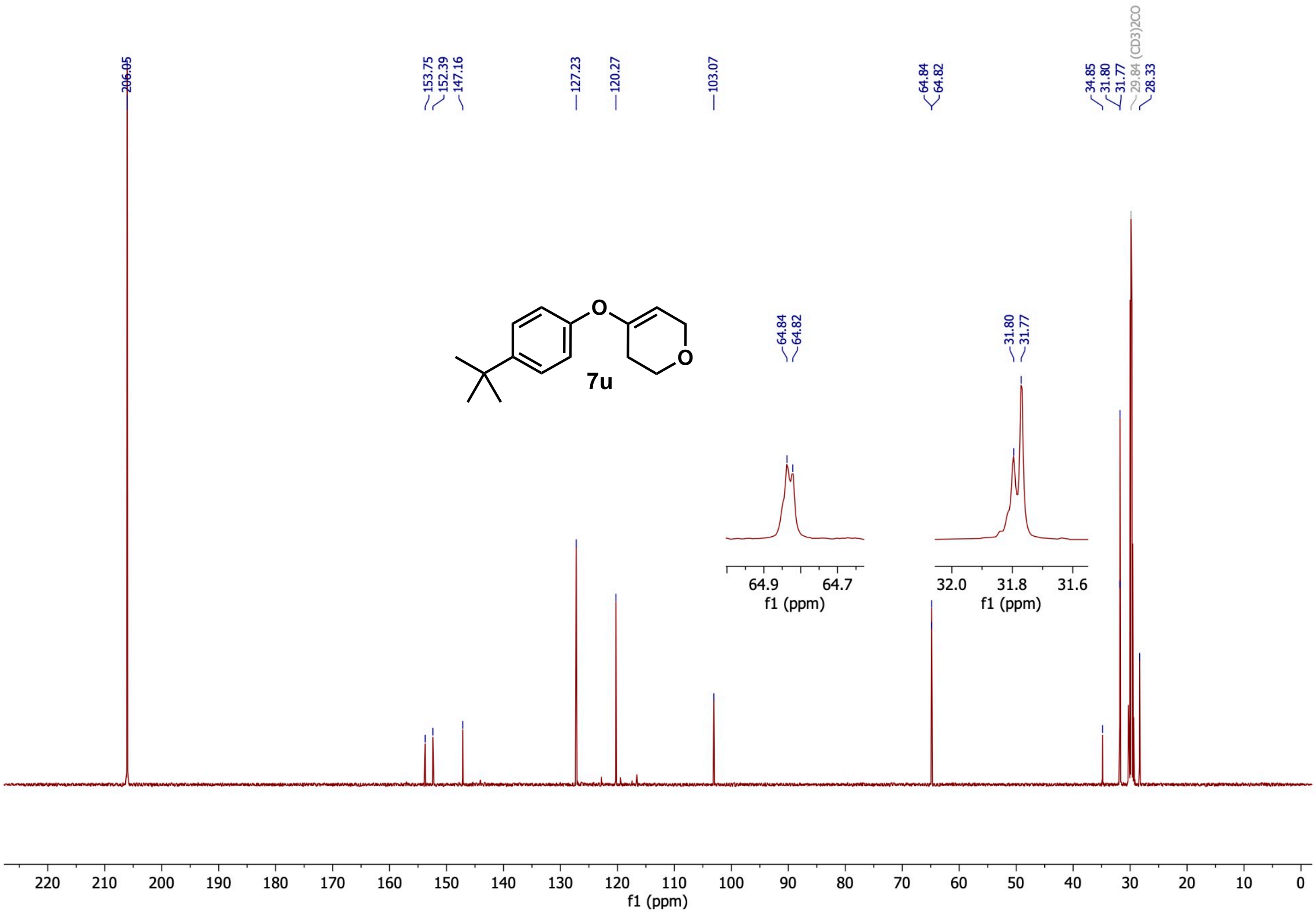


Figure S102. ^{13}C NMR of compound **7u** (125.81 MHz, acetone-*d*6).

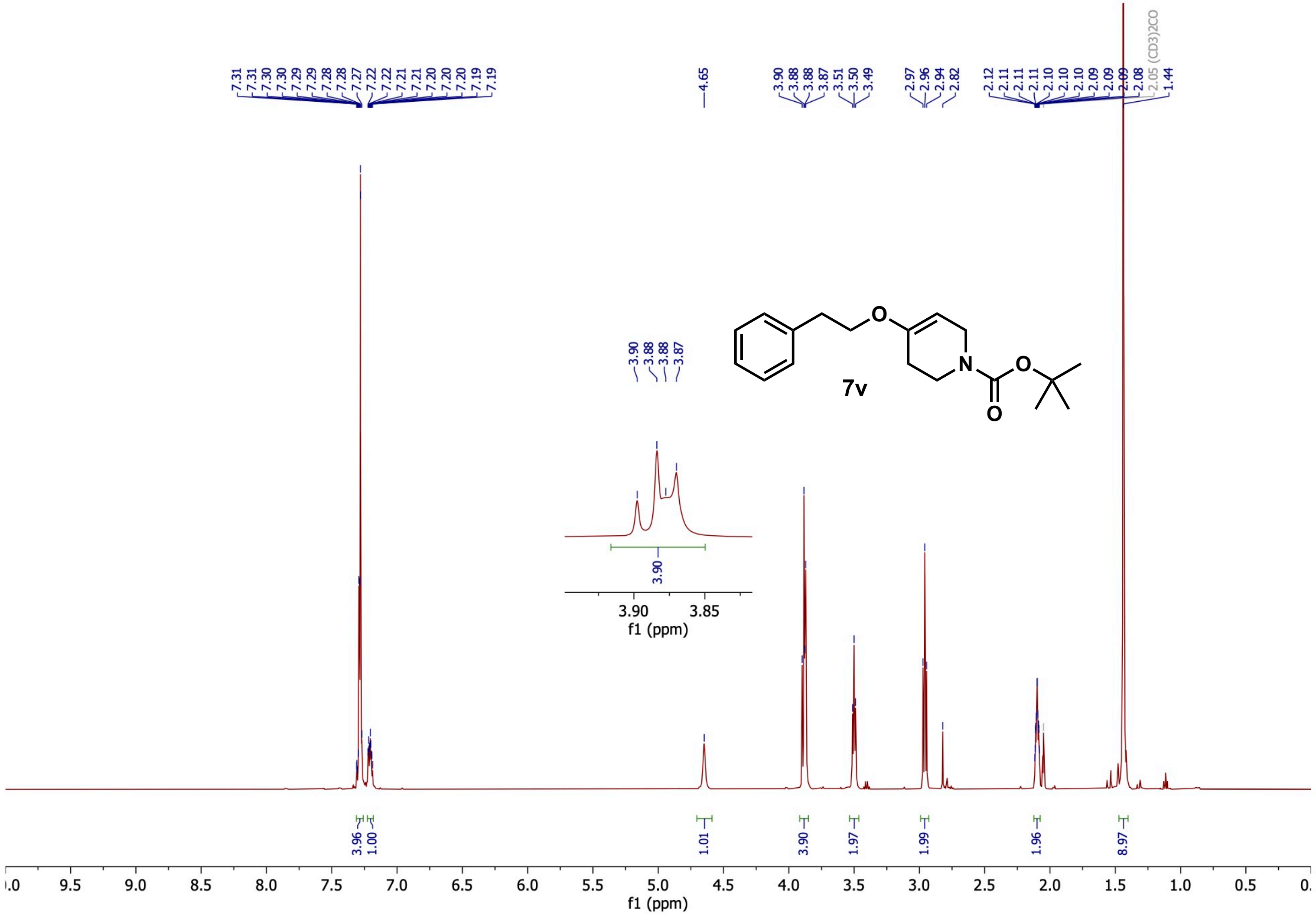


Figure S103. ^{1}H NMR of compound **7v** (500.27 MHz, acetone-*d*6).

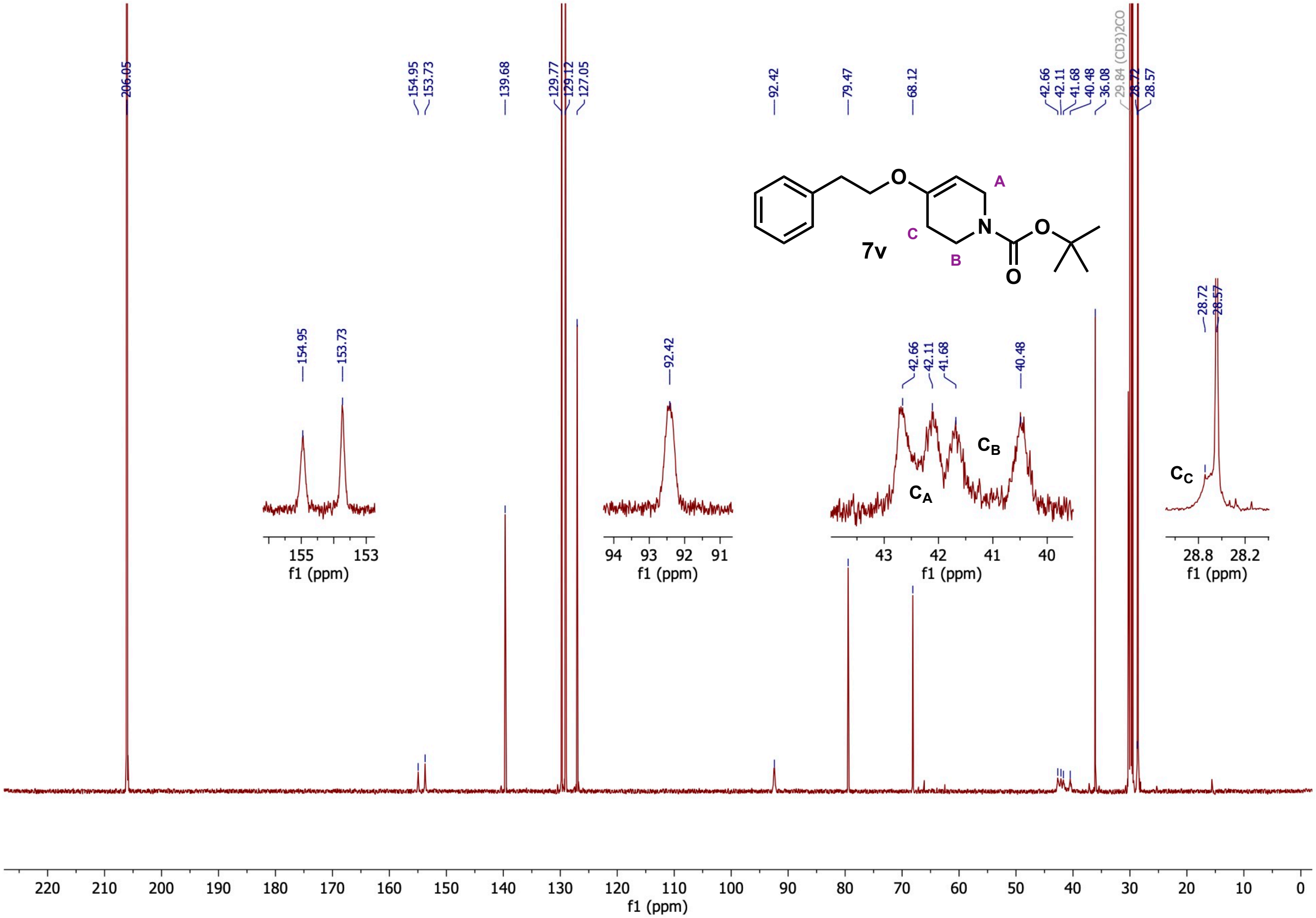


Figure S104. ^{13}C NMR of compound **7v** (125.81 MHz, acetone-*d*6).

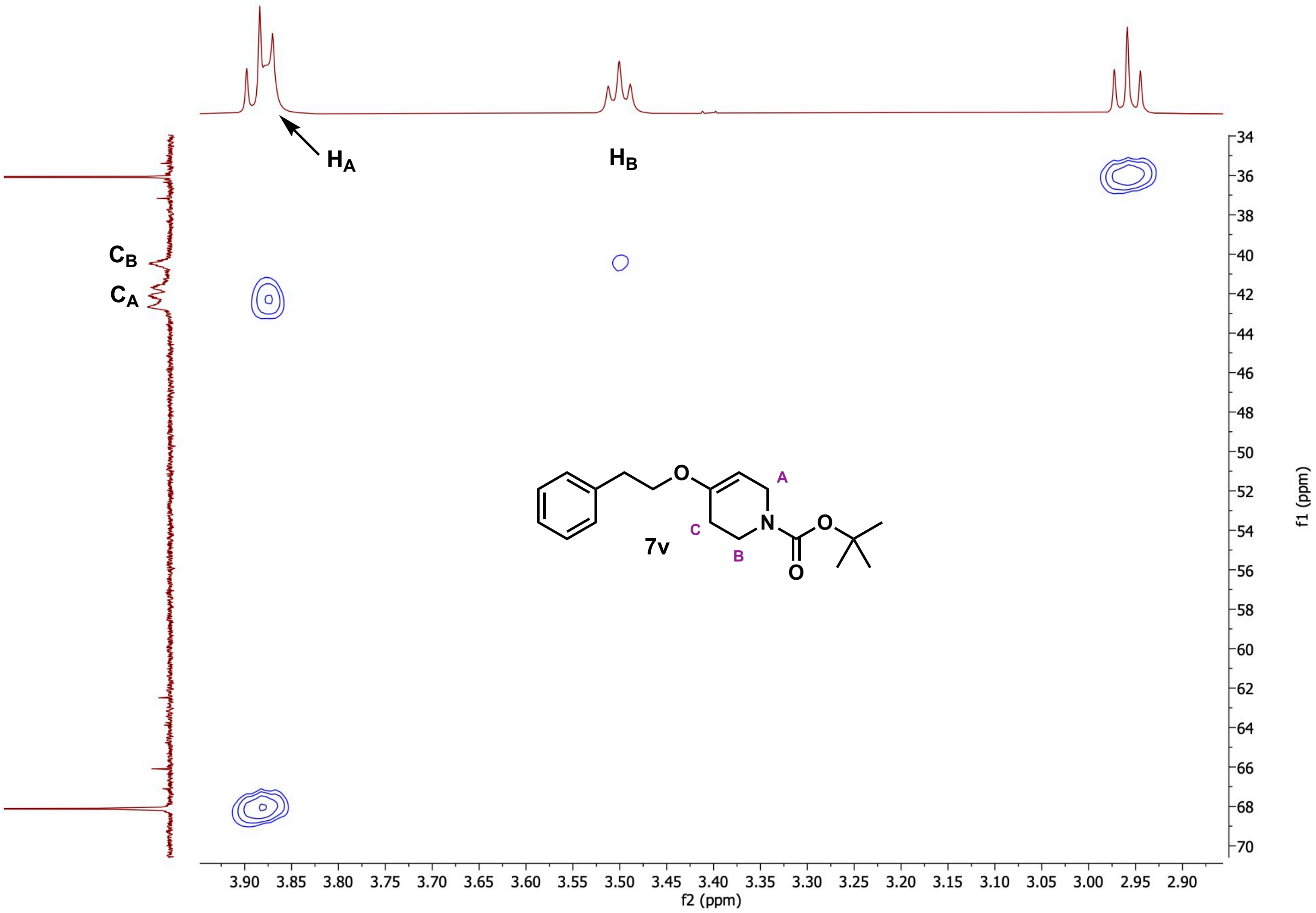


Figure S105. Gradient HSQC spectrum of compound **7v** (500.27, 125.81 MHz, acetone-*d*6) zoomed-in to show key correlations.

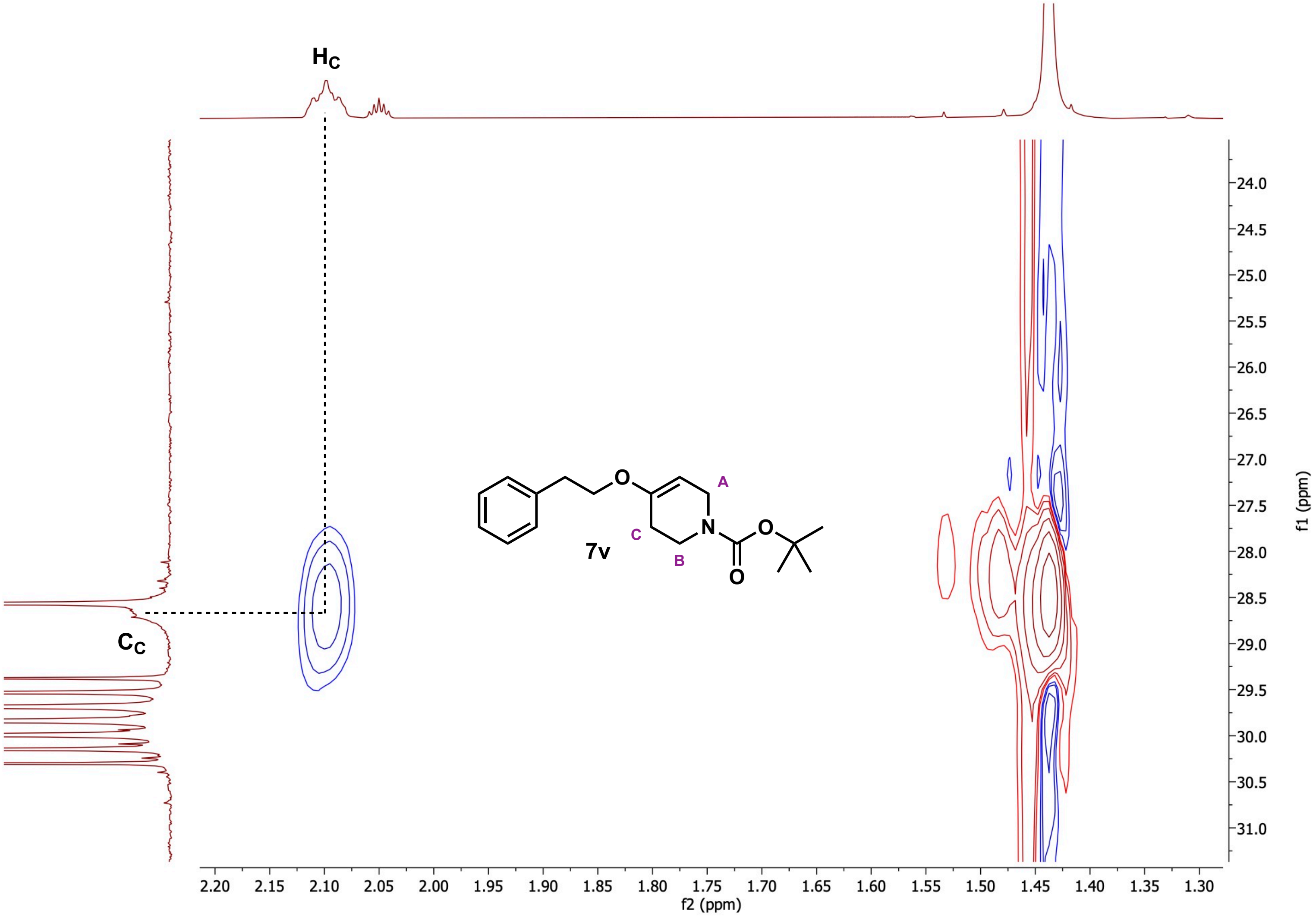


Figure S106. Gradient HSQC spectrum of compound **7v** (500.27, 125.81 MHz, acetone-*d*6) showing an upfield allylic correlation.

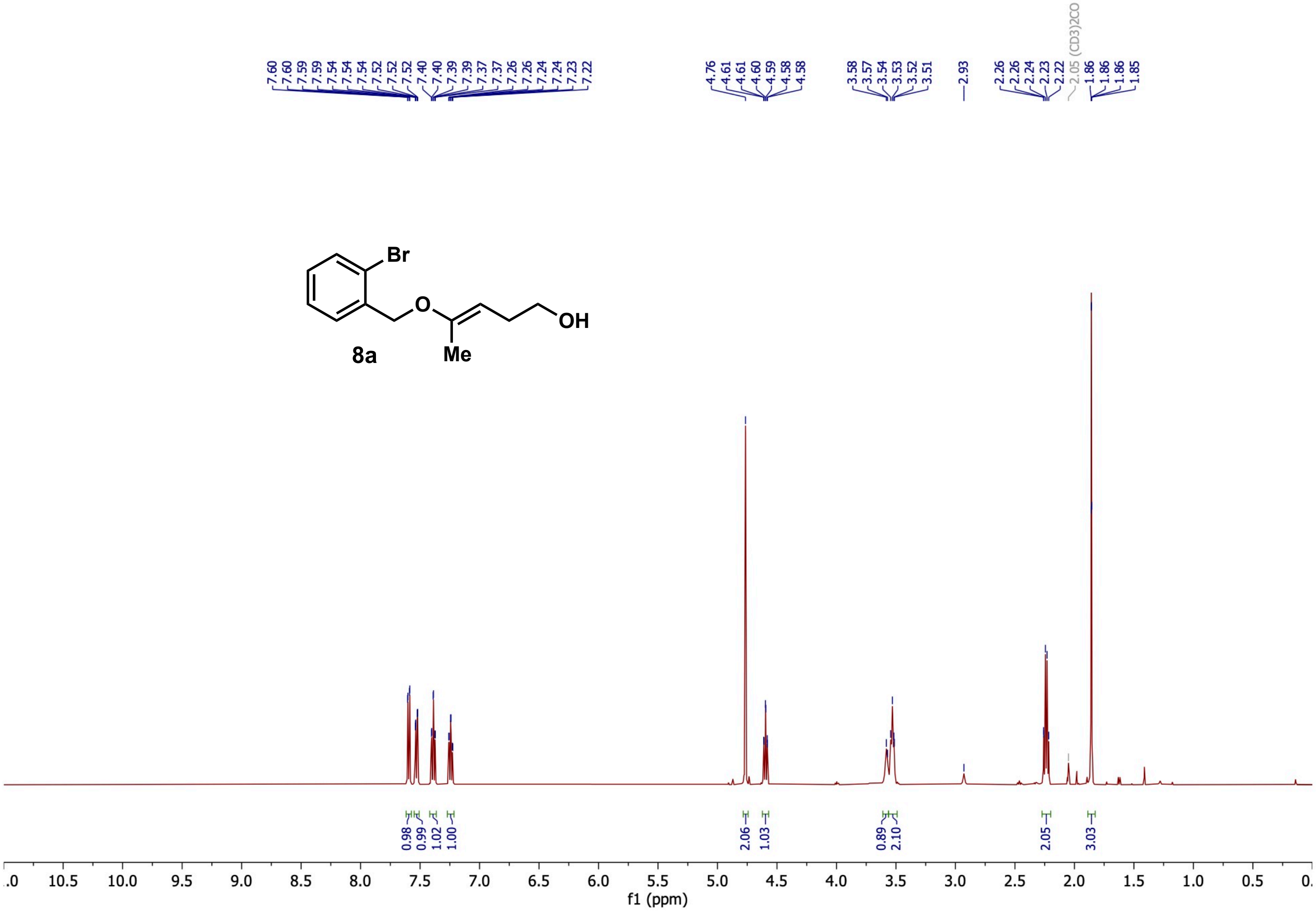


Figure S107. ^{1}H NMR of compound **8a** (500.27 MHz, acetone-*d*6).

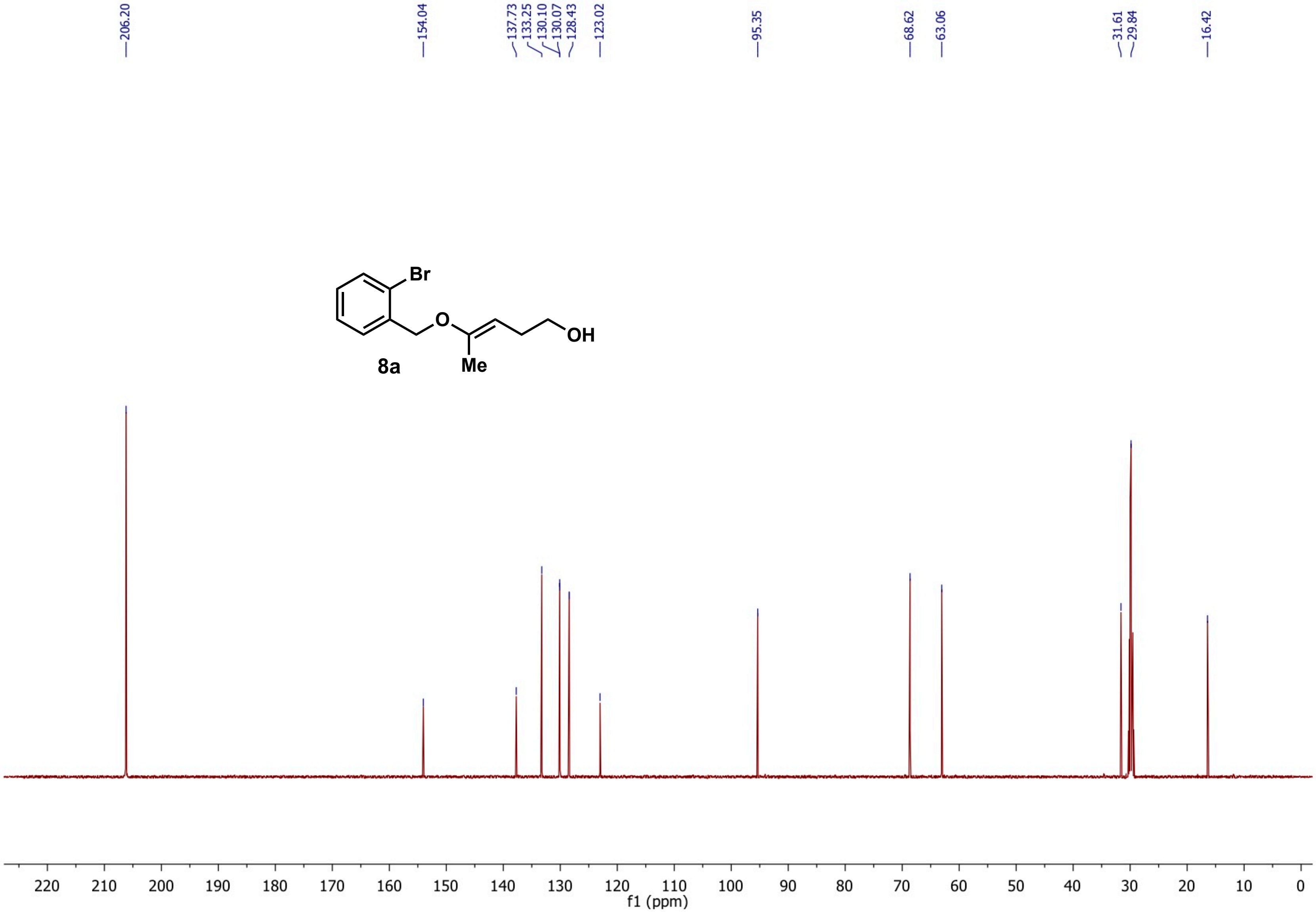


Figure S108. ^{13}C NMR of compound **8a** (125.81 MHz, acetone-*d*6).

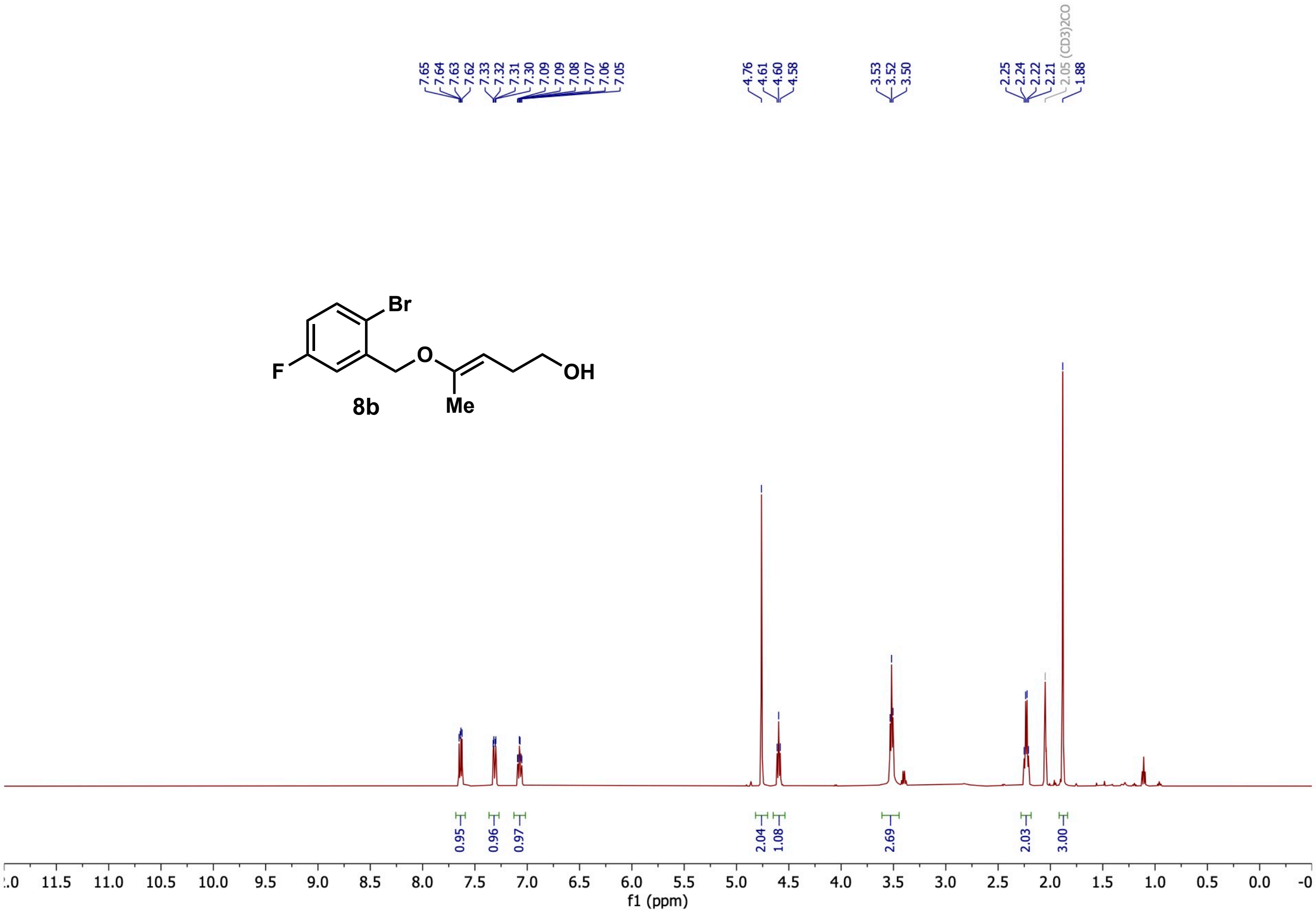


Figure S109. ^{1}H NMR of compound **8b** (500.27 MHz, acetone-*d*6).

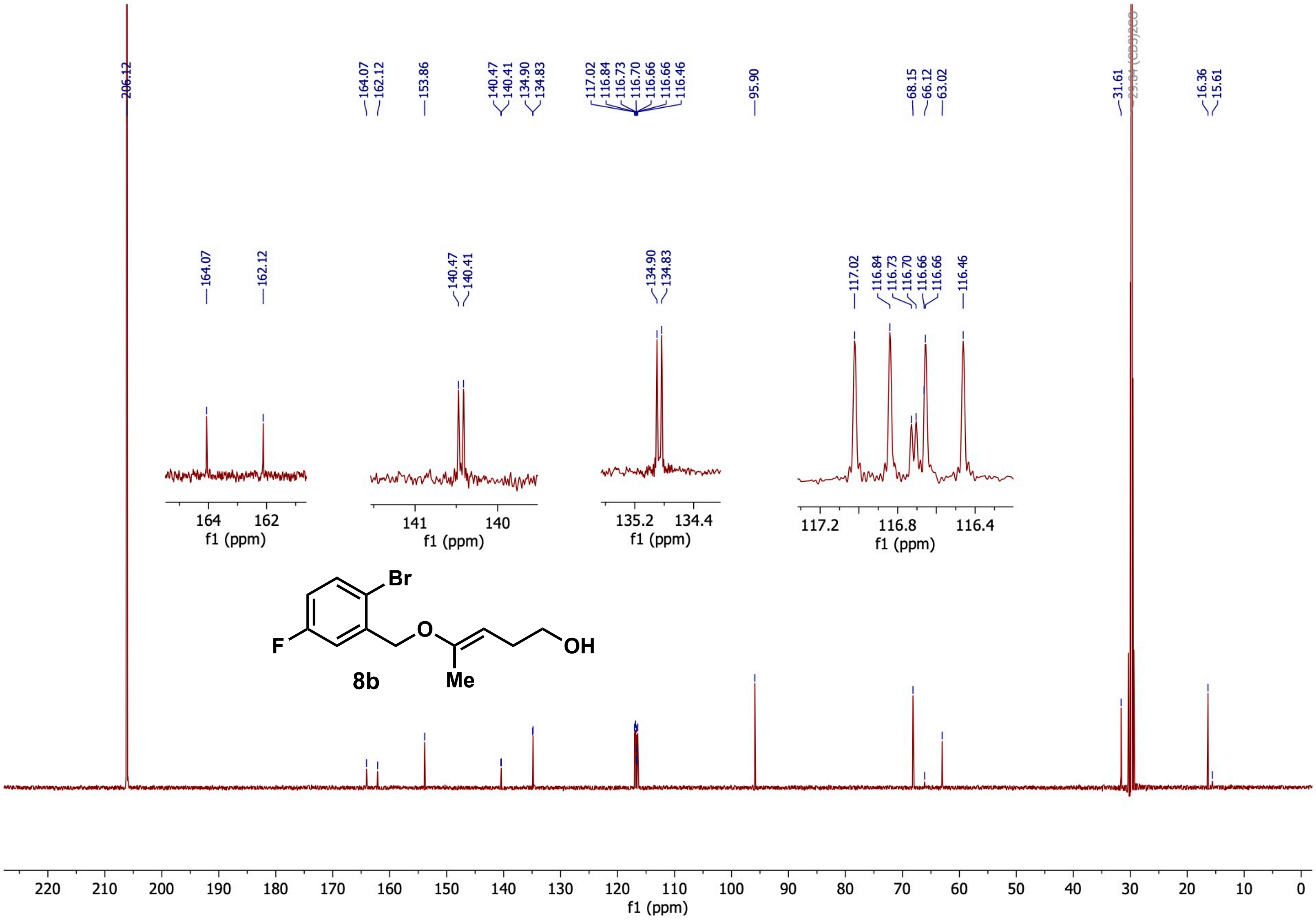


Figure S110. ^{13}C NMR of compound **8b** (125.81 MHz, acetone-*d*6).

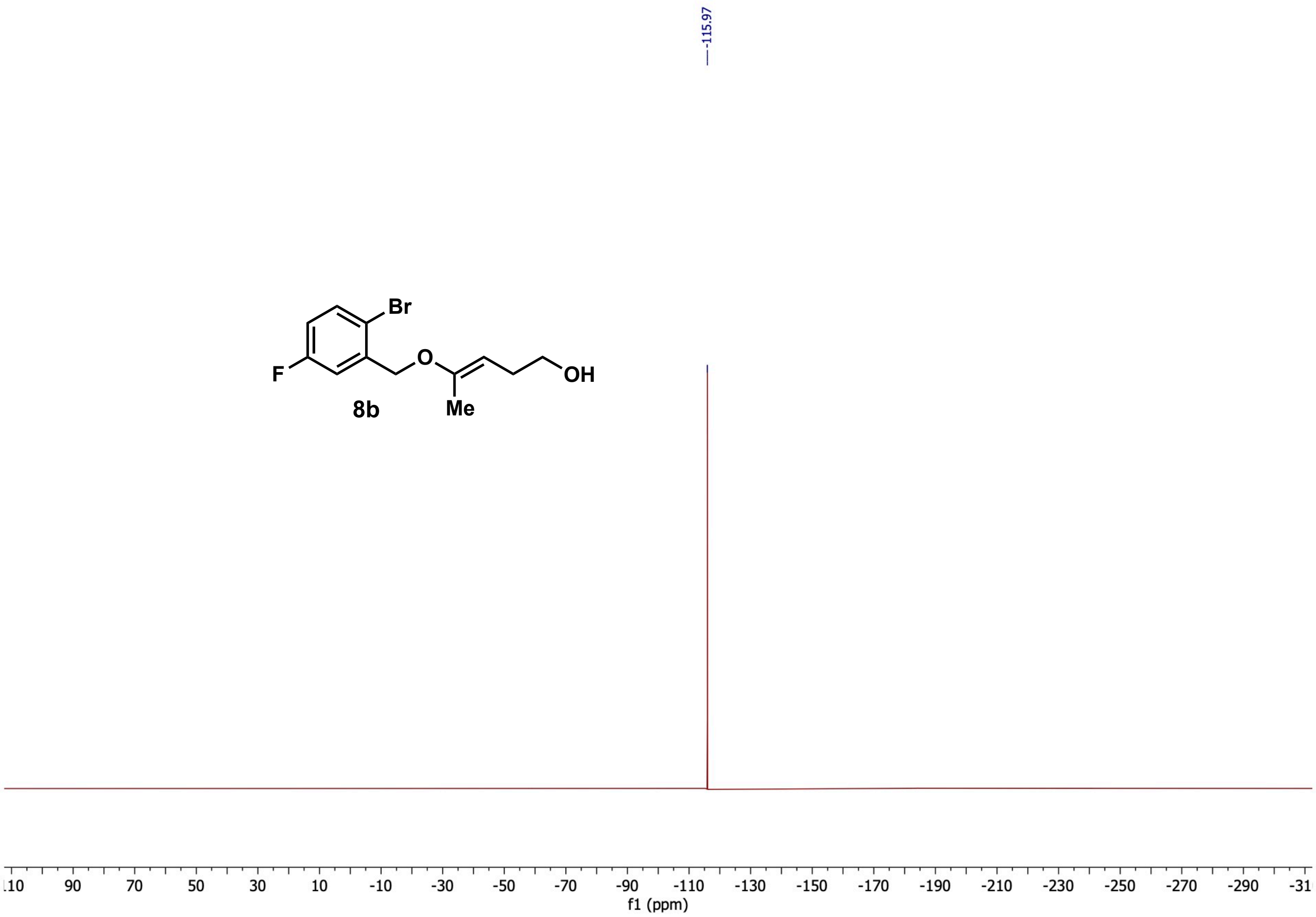


Figure S111. ^{19}F NMR of compound **8b** (470.68 MHz, acetone-*d*6).

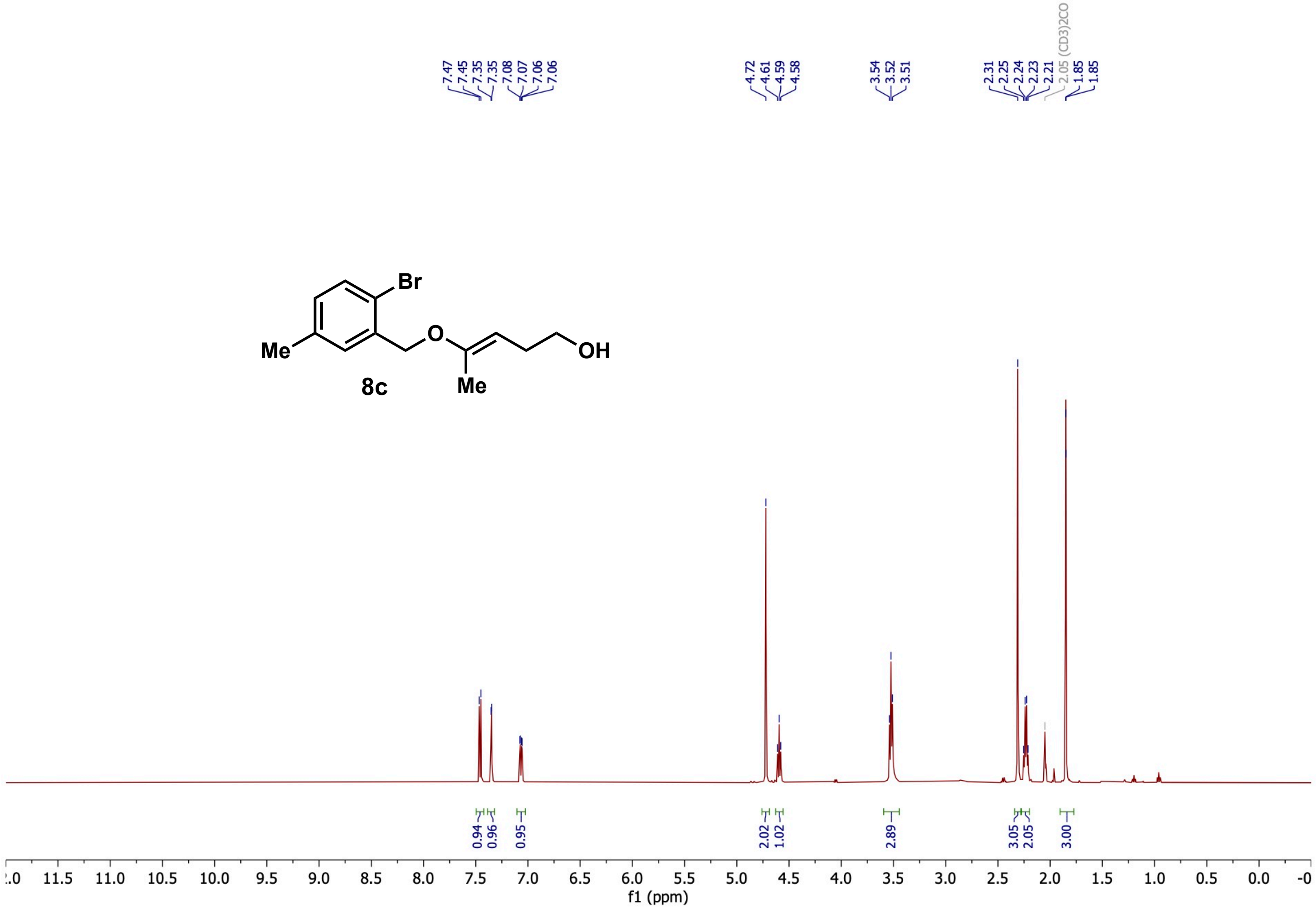


Figure S112. ^{1}H NMR of compound **8c** (500.27 MHz, acetone-*d*6).

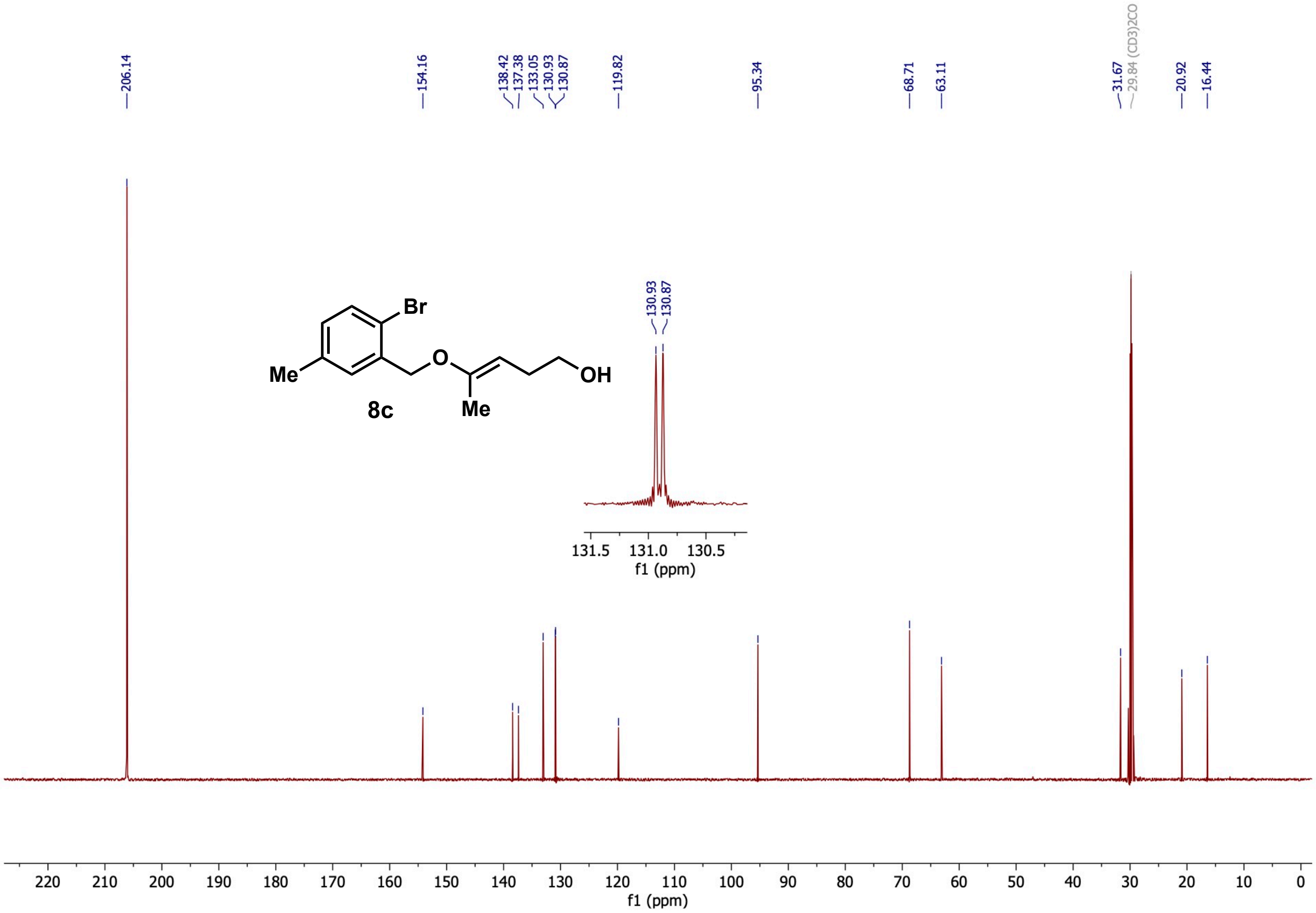


Figure S113. ^{13}C NMR of compound **8c** (125.81 MHz, acetone-*d*6).

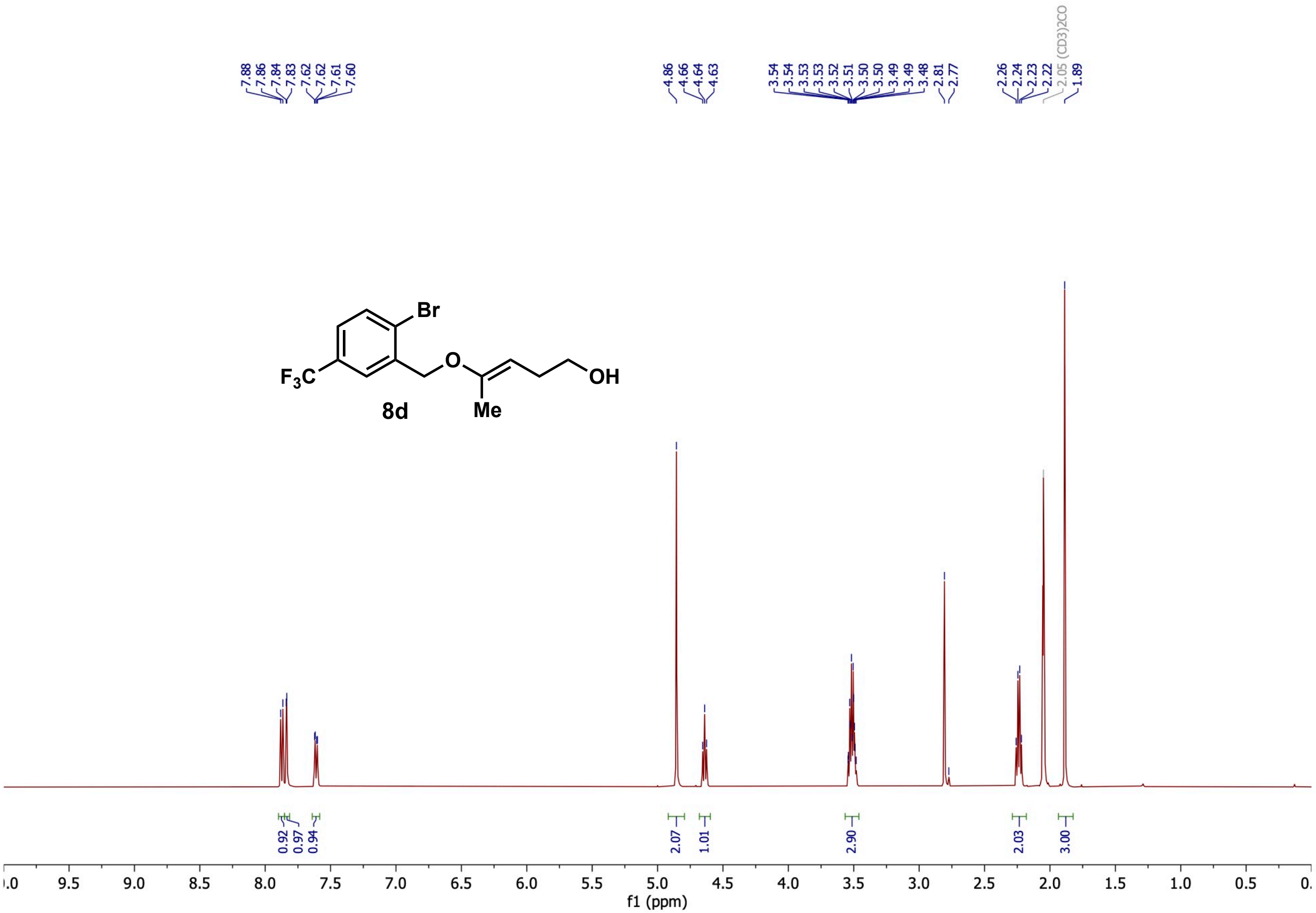


Figure S114. ¹H NMR of compound **8d** (500.27 MHz, acetone-*d*6).

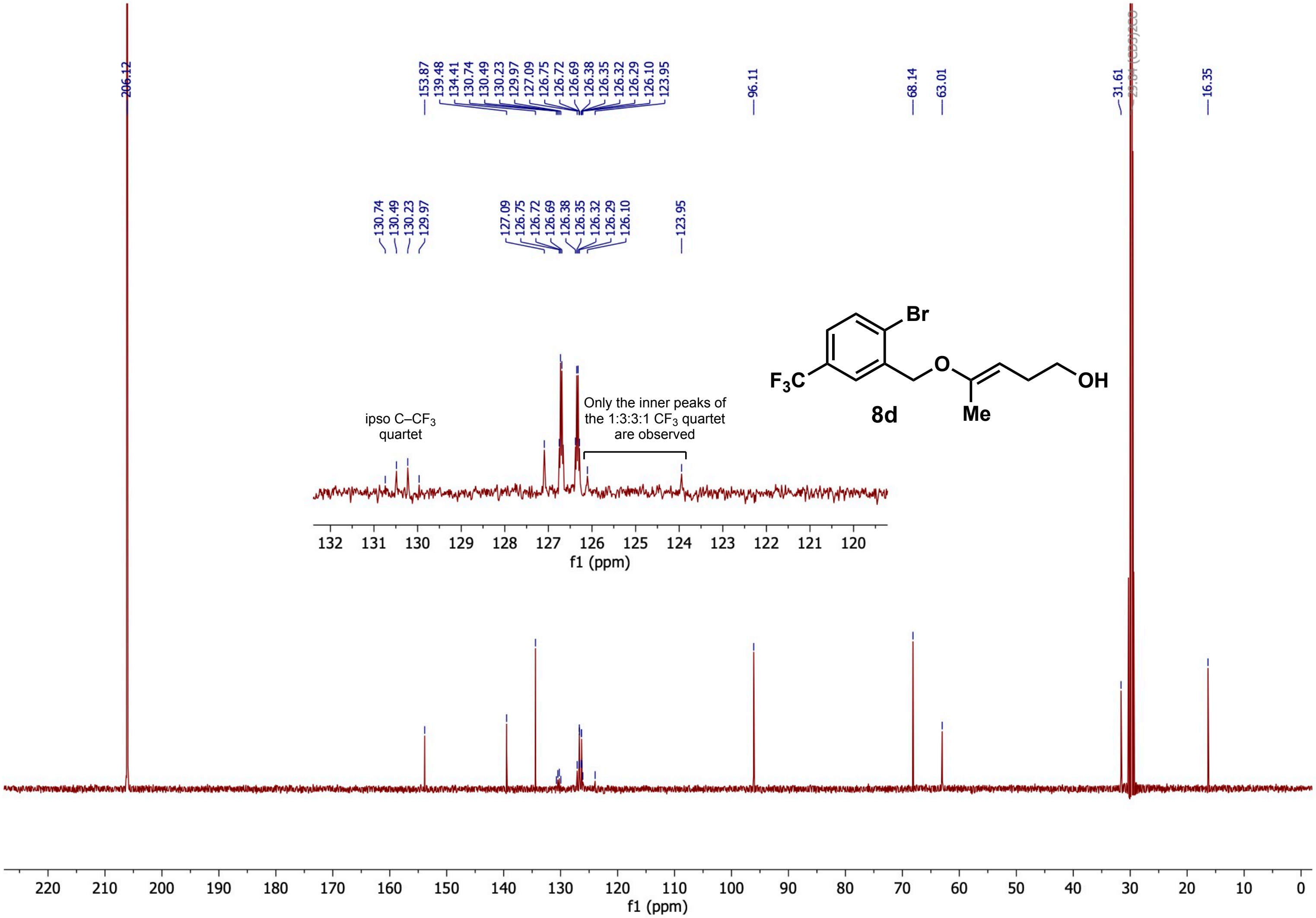


Figure S115. ^{13}C NMR of compound **8d** (125.81 MHz, acetone-*d*6).

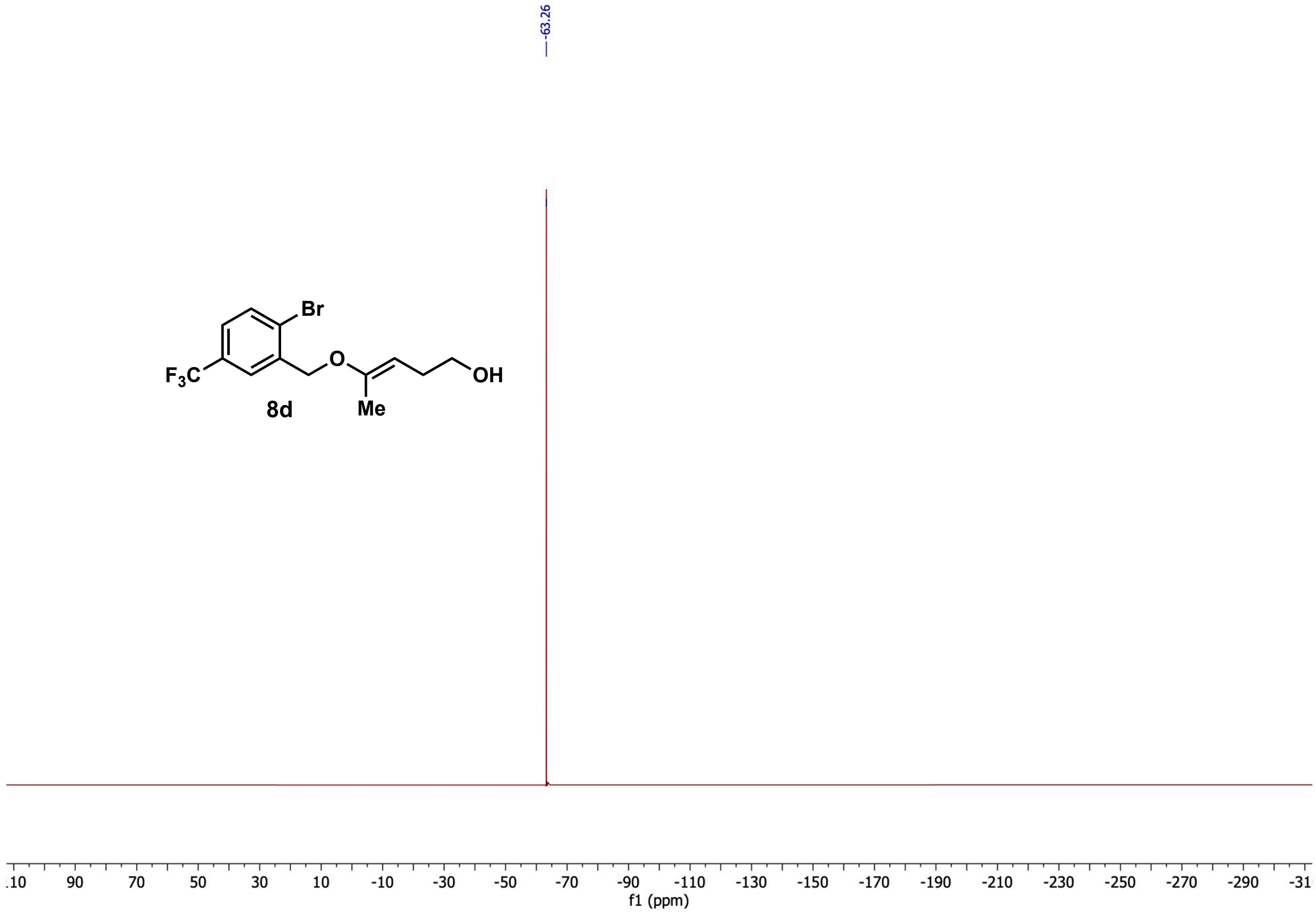


Figure S116. ^{19}F NMR of compound **8d** (470.68 MHz, acetone-*d*6).

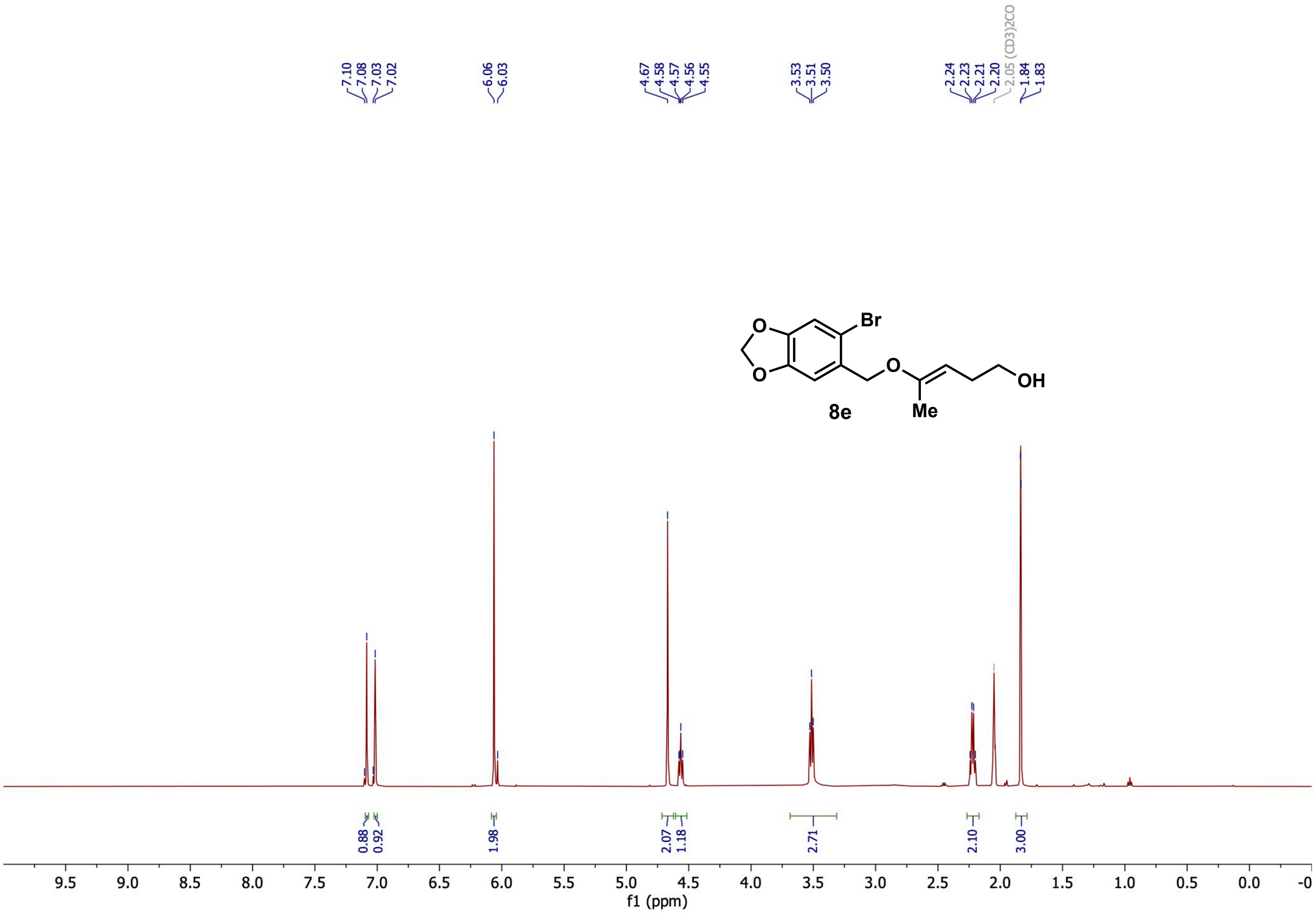


Figure S117. ^{1}H NMR of compound **8e** (500.27 MHz, acetone-*d*6).

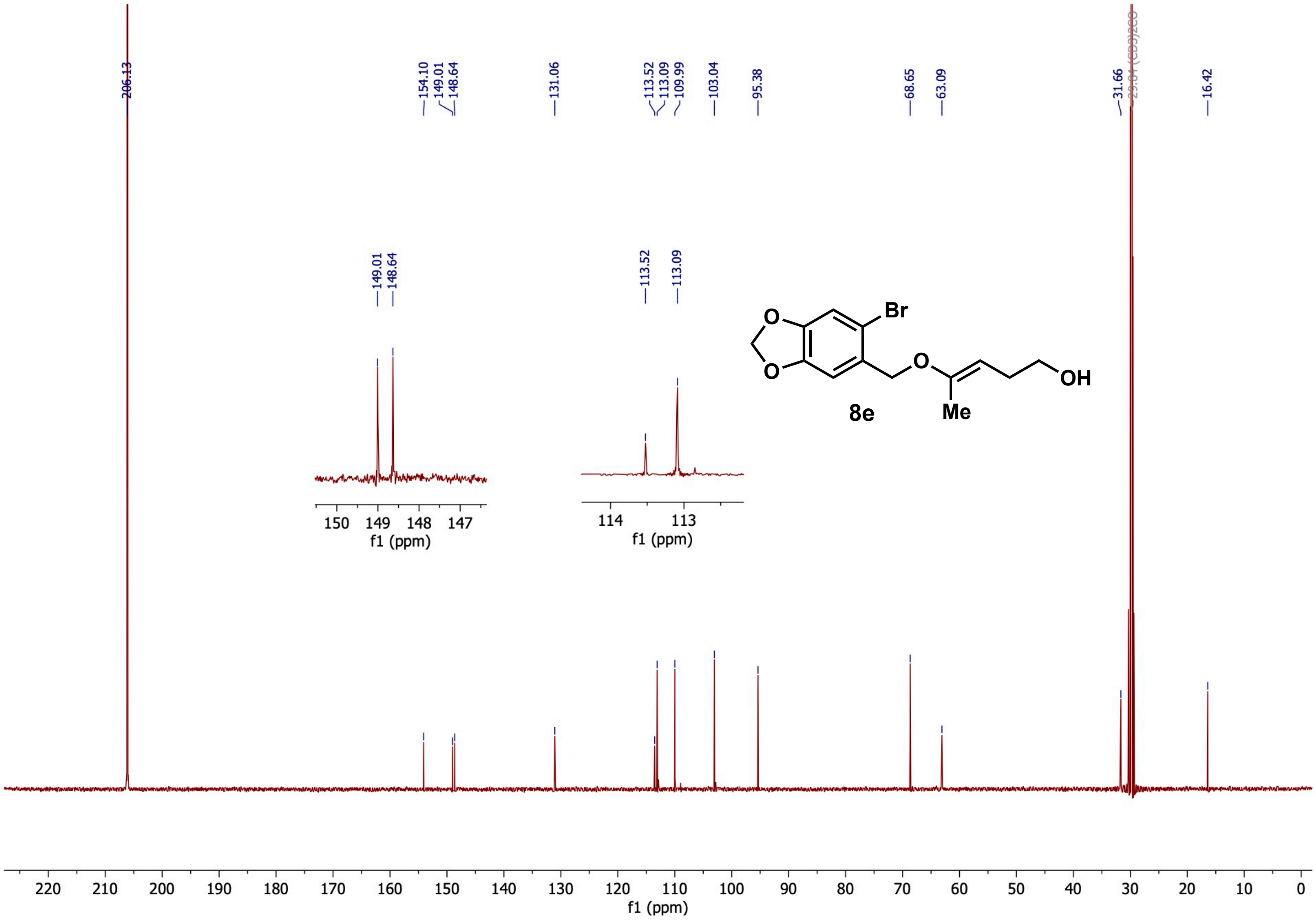


Figure S118. ^{13}C NMR of compound **8e** (125.81 MHz, acetone-*d*6).

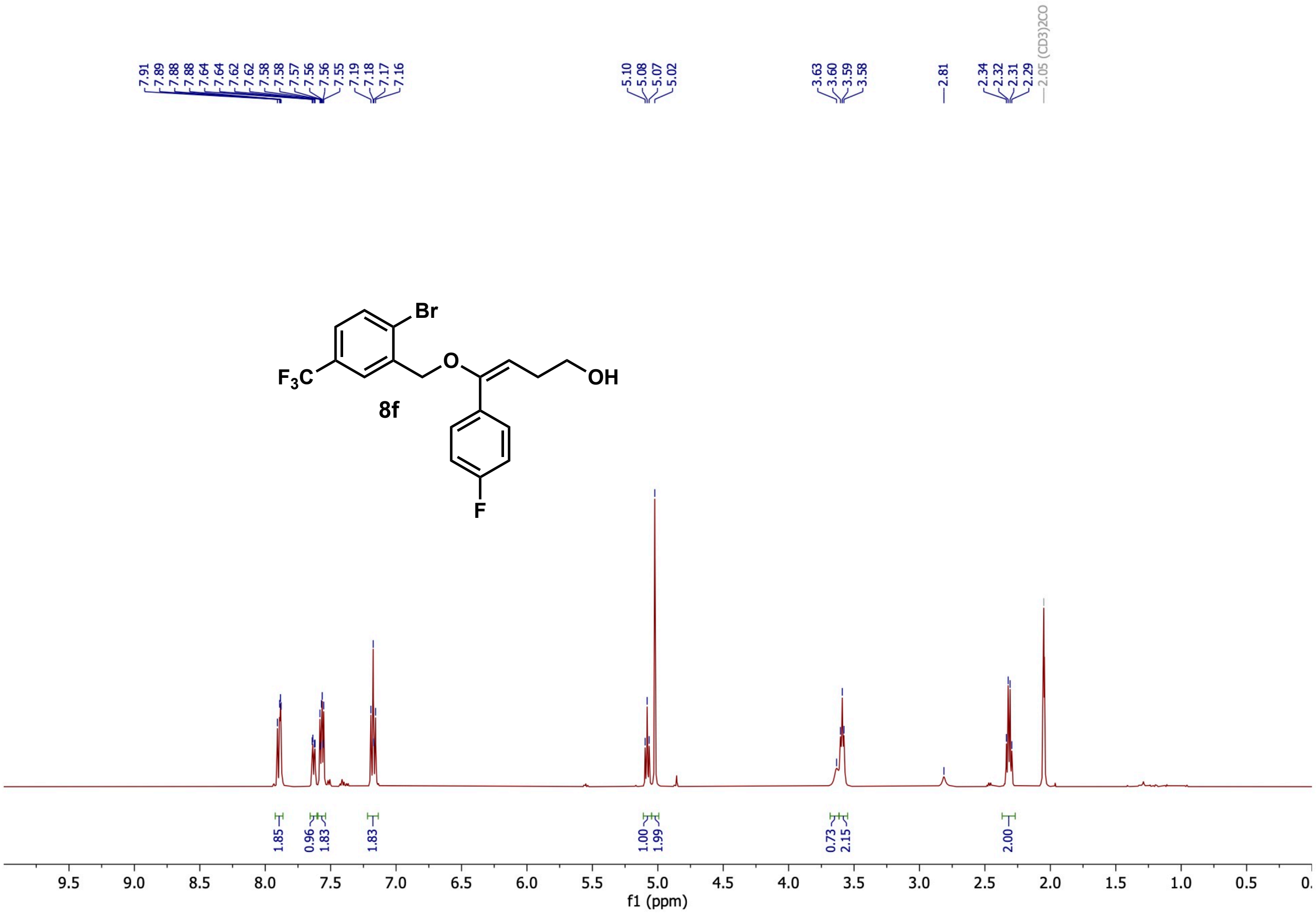


Figure S119. ^{1}H NMR of compound **8f** (500.27 MHz, acetone-*d*6).

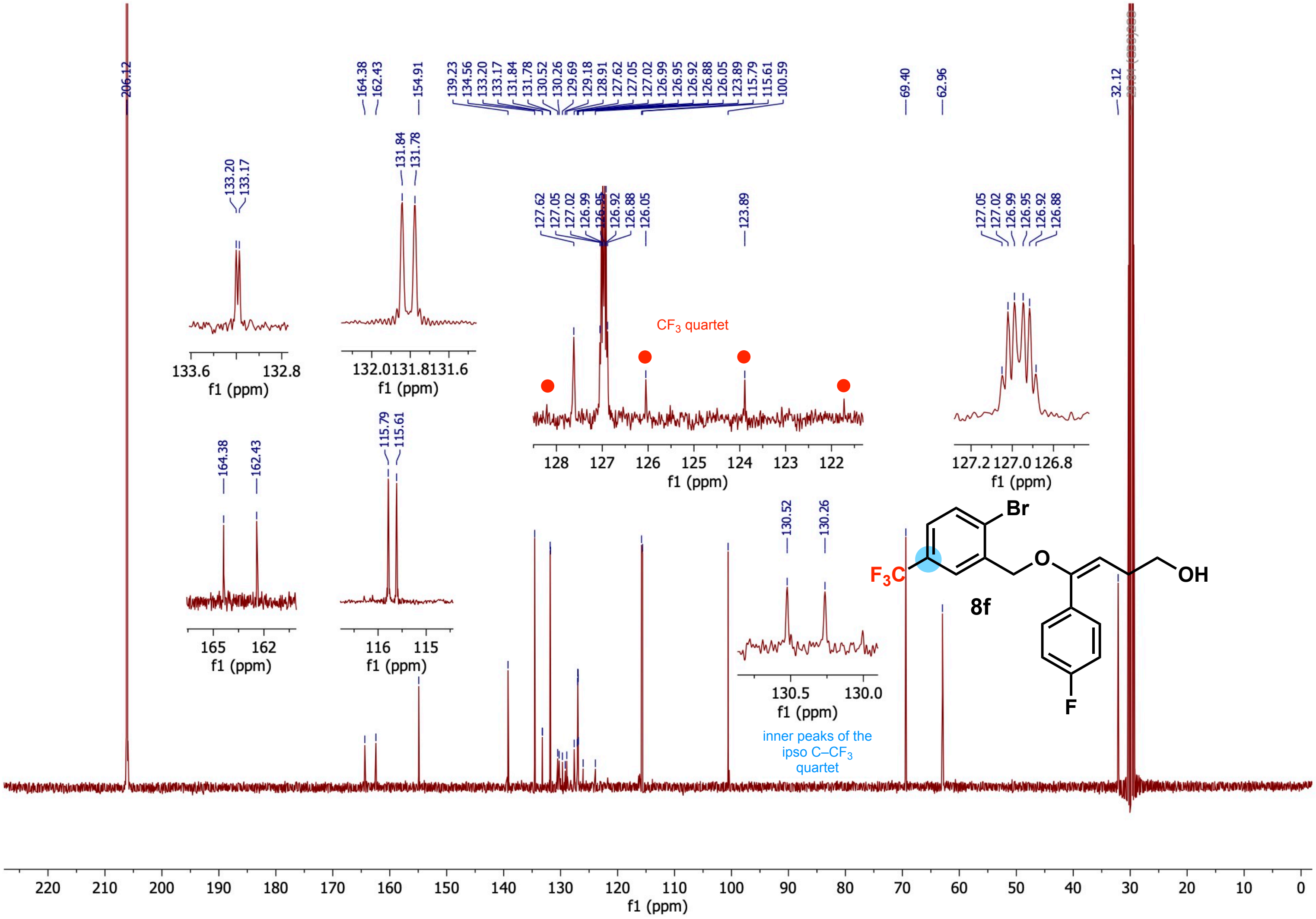


Figure S120. ^{13}C NMR of compound **8f** (125.81 MHz, acetone-*d*6).

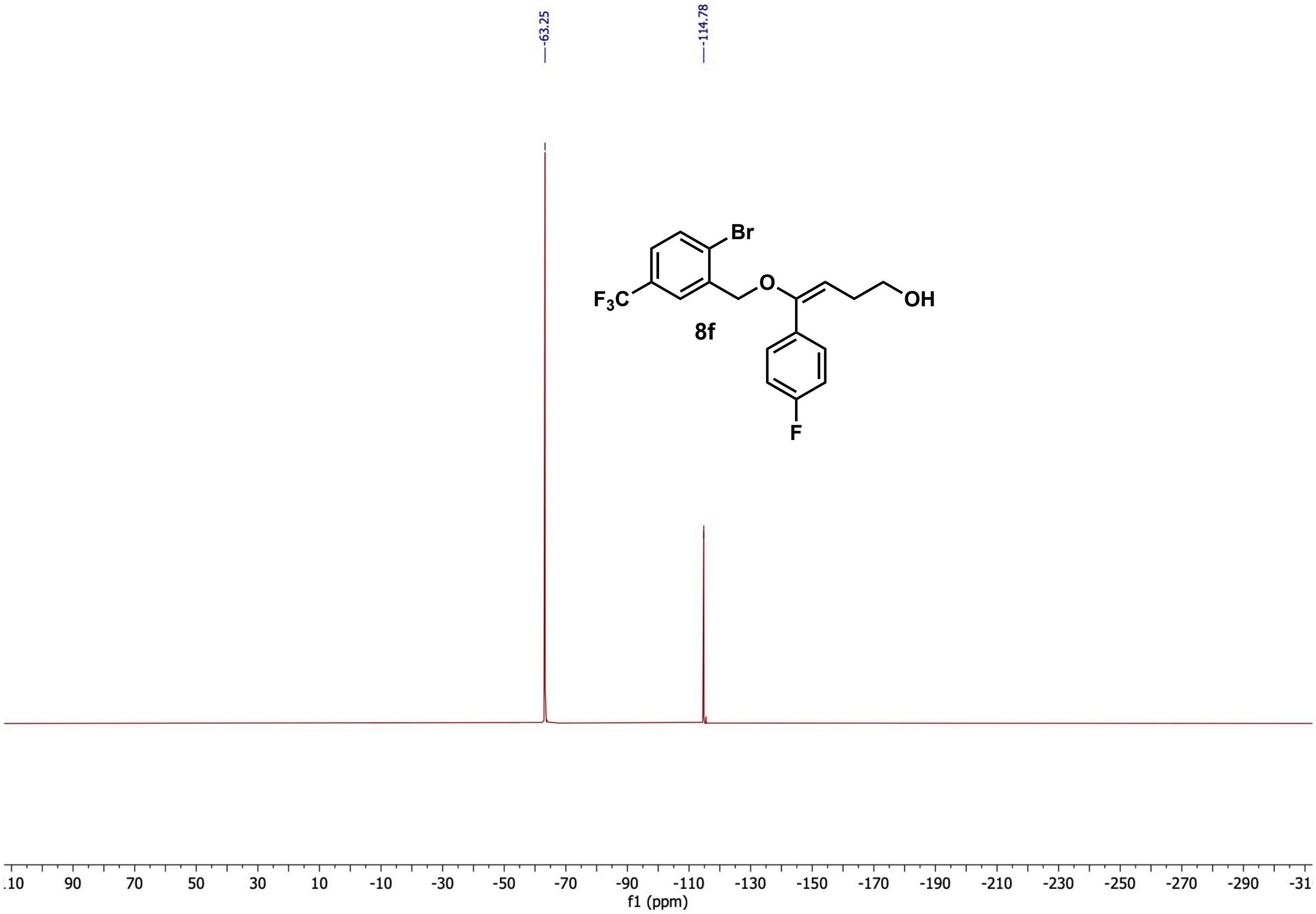


Figure S121. ^{19}F NMR of compound **8f** (470.68 MHz, acetone-*d*6).

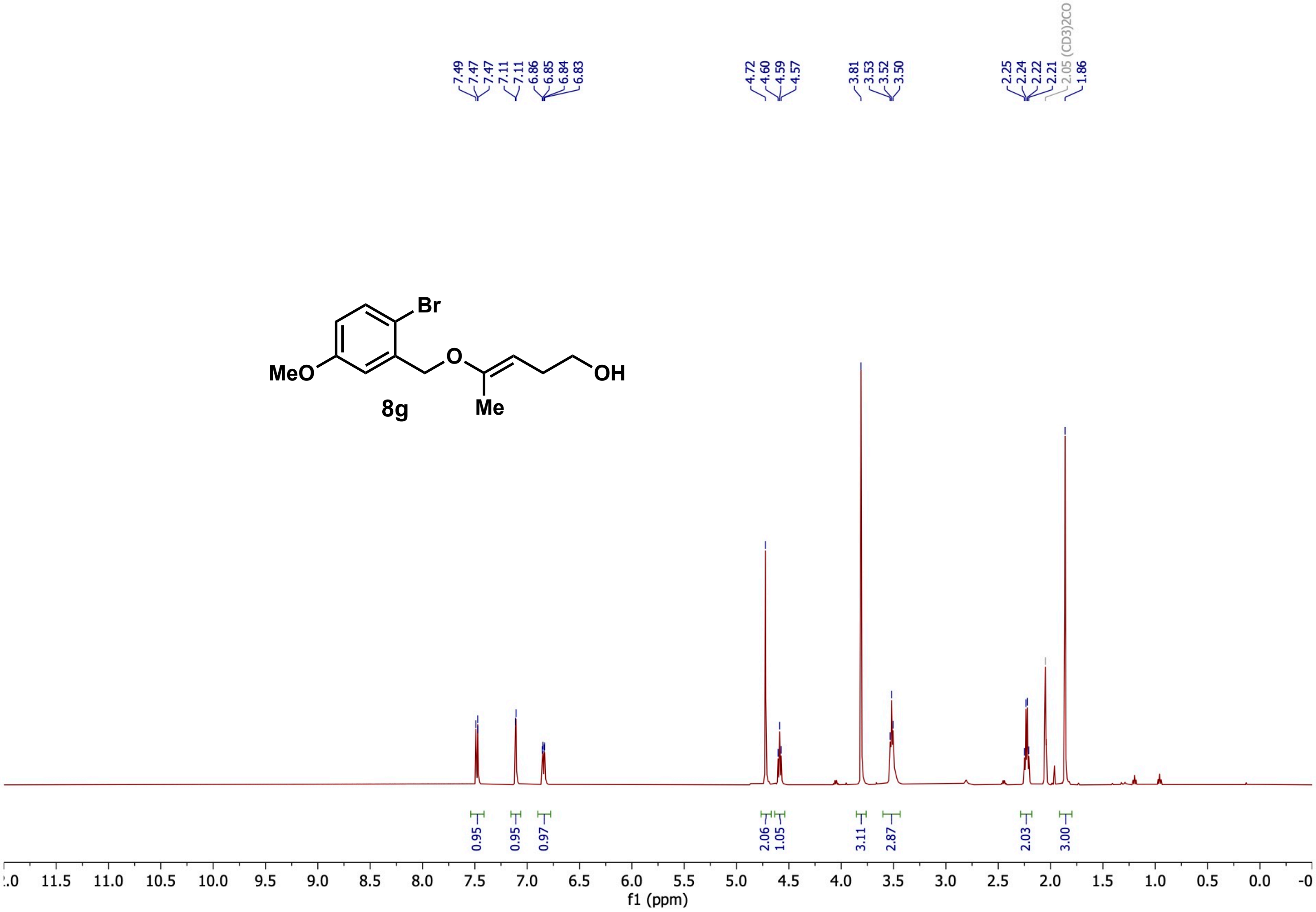


Figure S122. ^{1}H NMR of compound **8g** (500.27 MHz, acetone-*d*6).

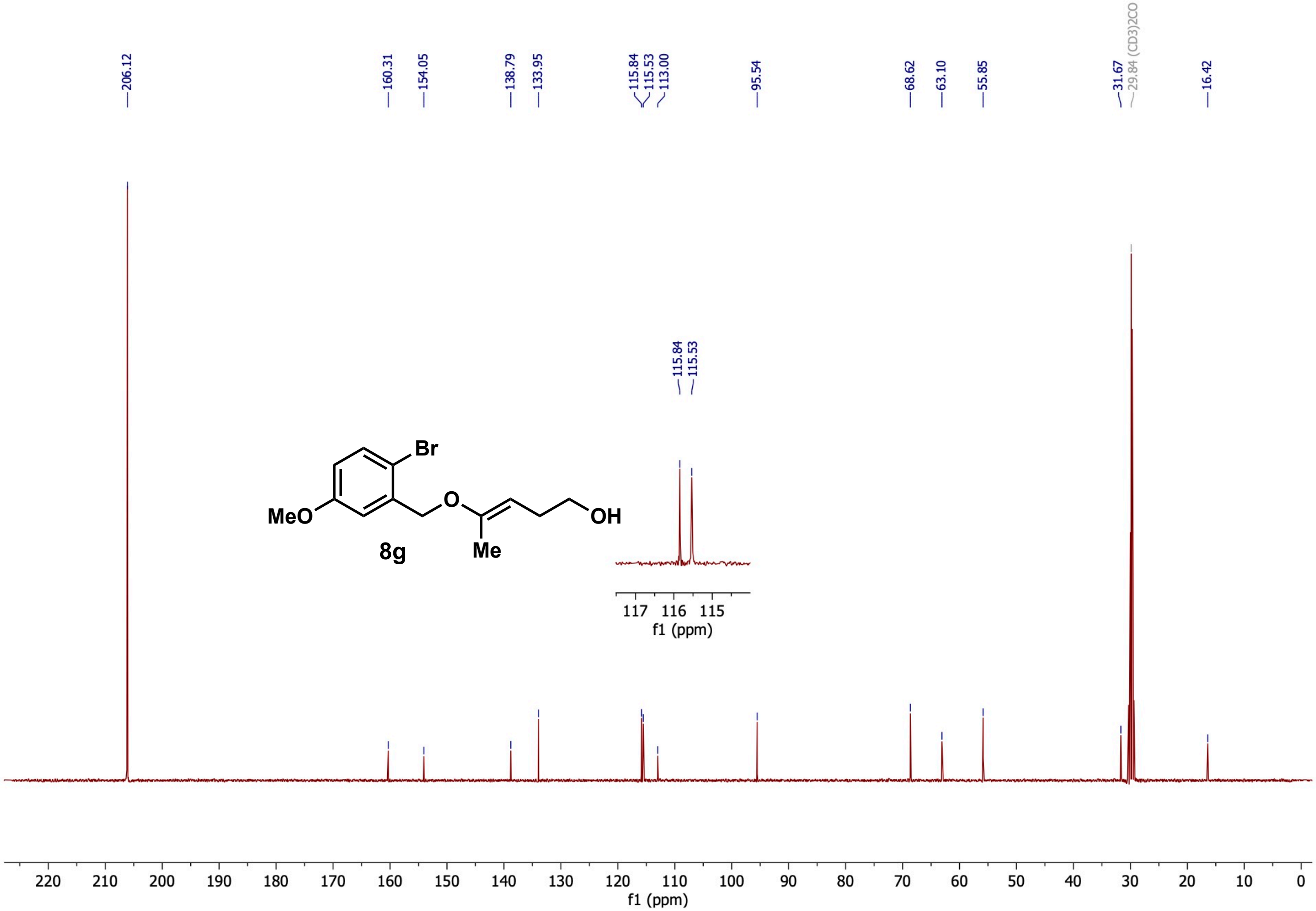


Figure S123. ^{13}C NMR of compound **8g** (125.81 MHz, acetone-*d*6).

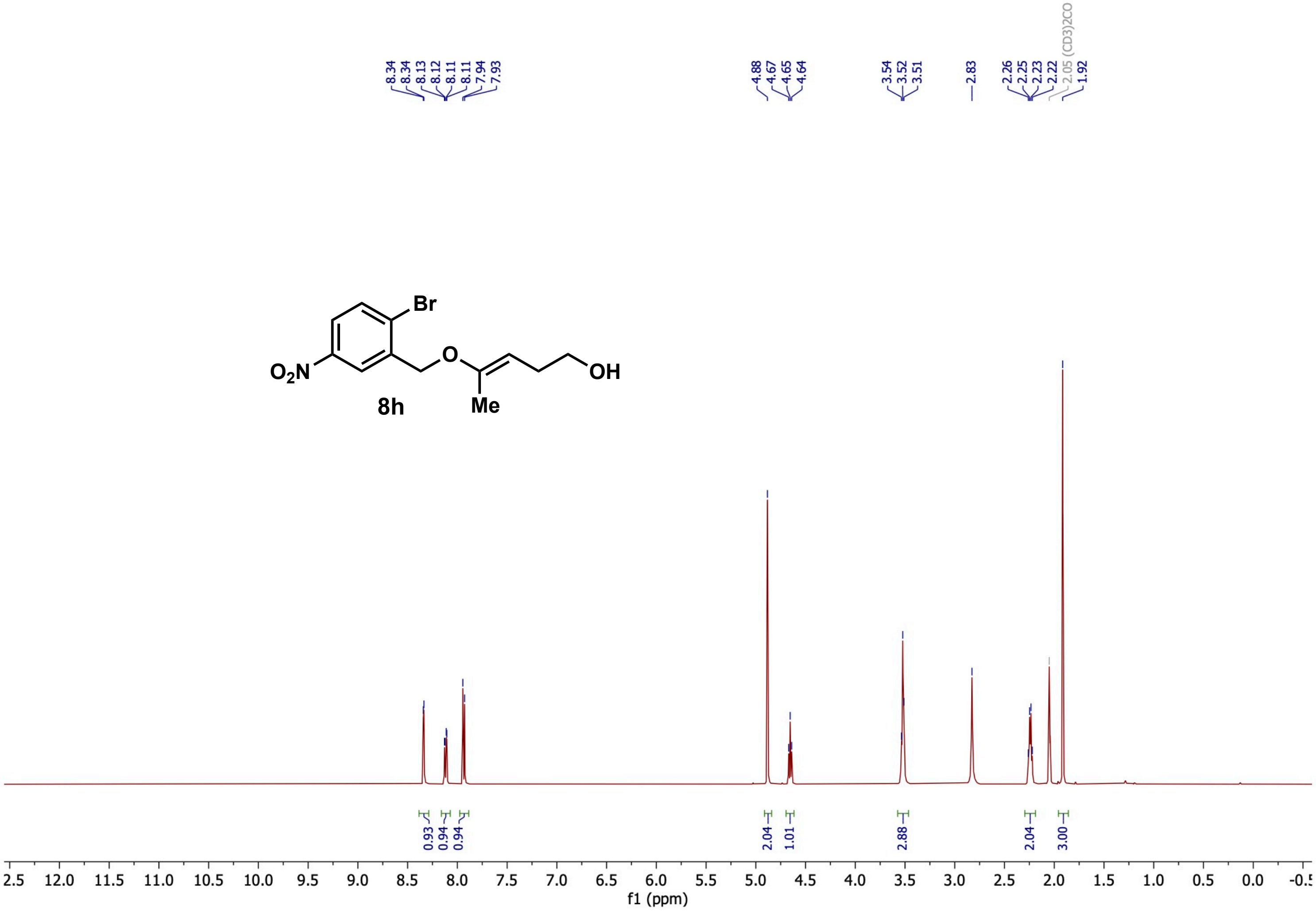


Figure S124. ^{1}H NMR of compound **8h** (500.27 MHz, acetone-*d*6).

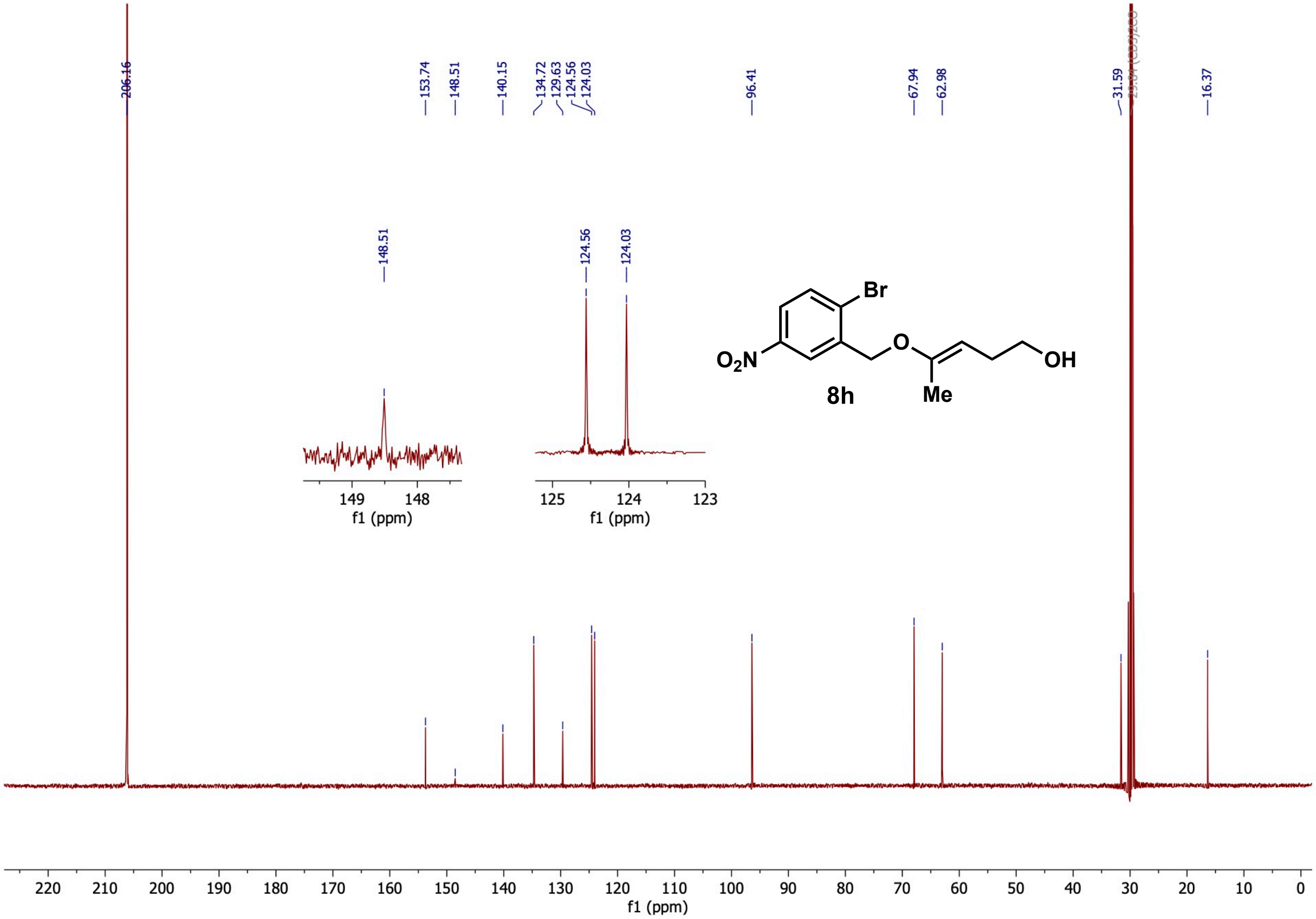


Figure S125. ^{13}C NMR of compound **8h** (125.81 MHz, acetone-*d*6).

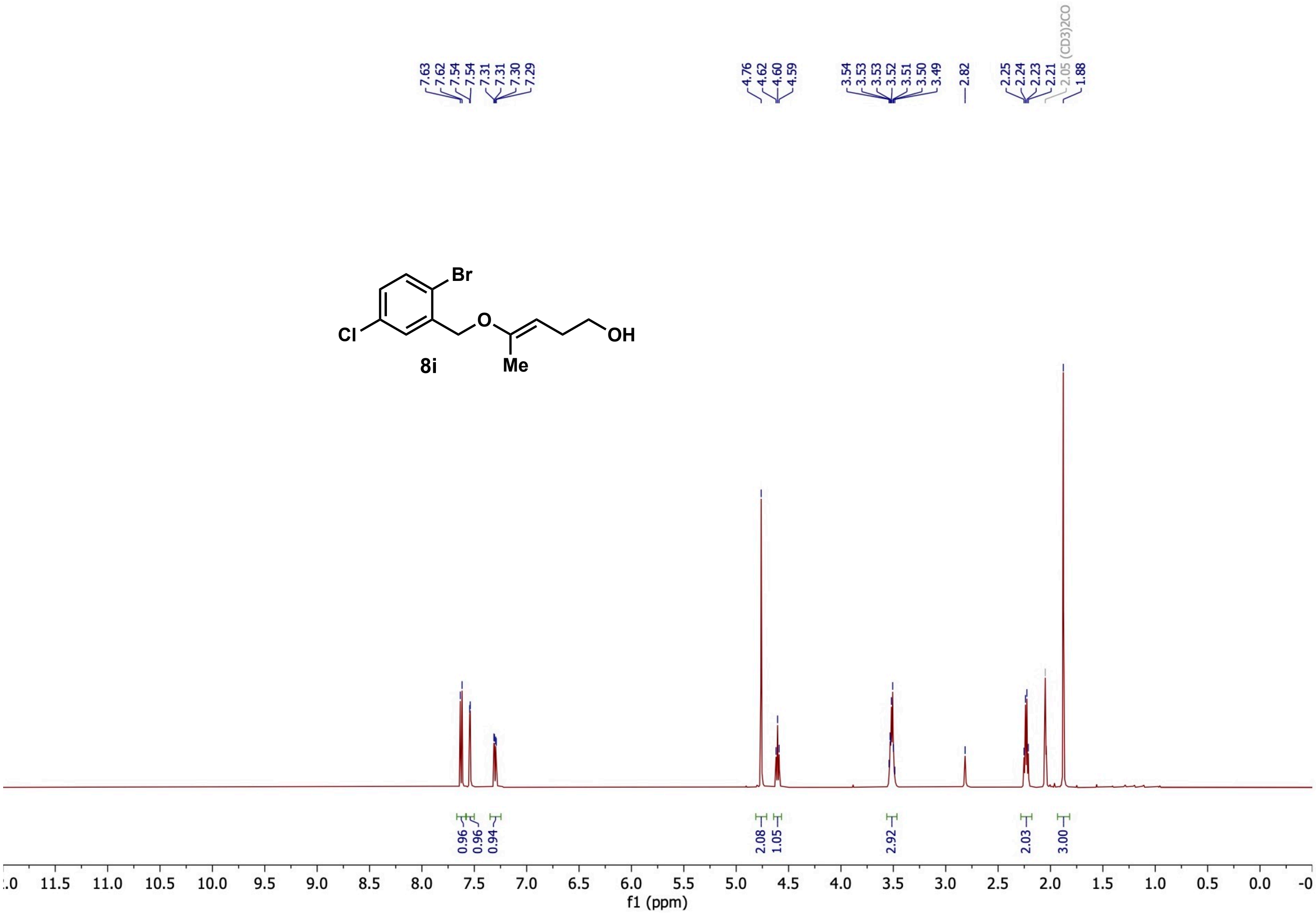


Figure S126. ^{1}H NMR of compound **8i** (500.27 MHz, acetone-*d*6).

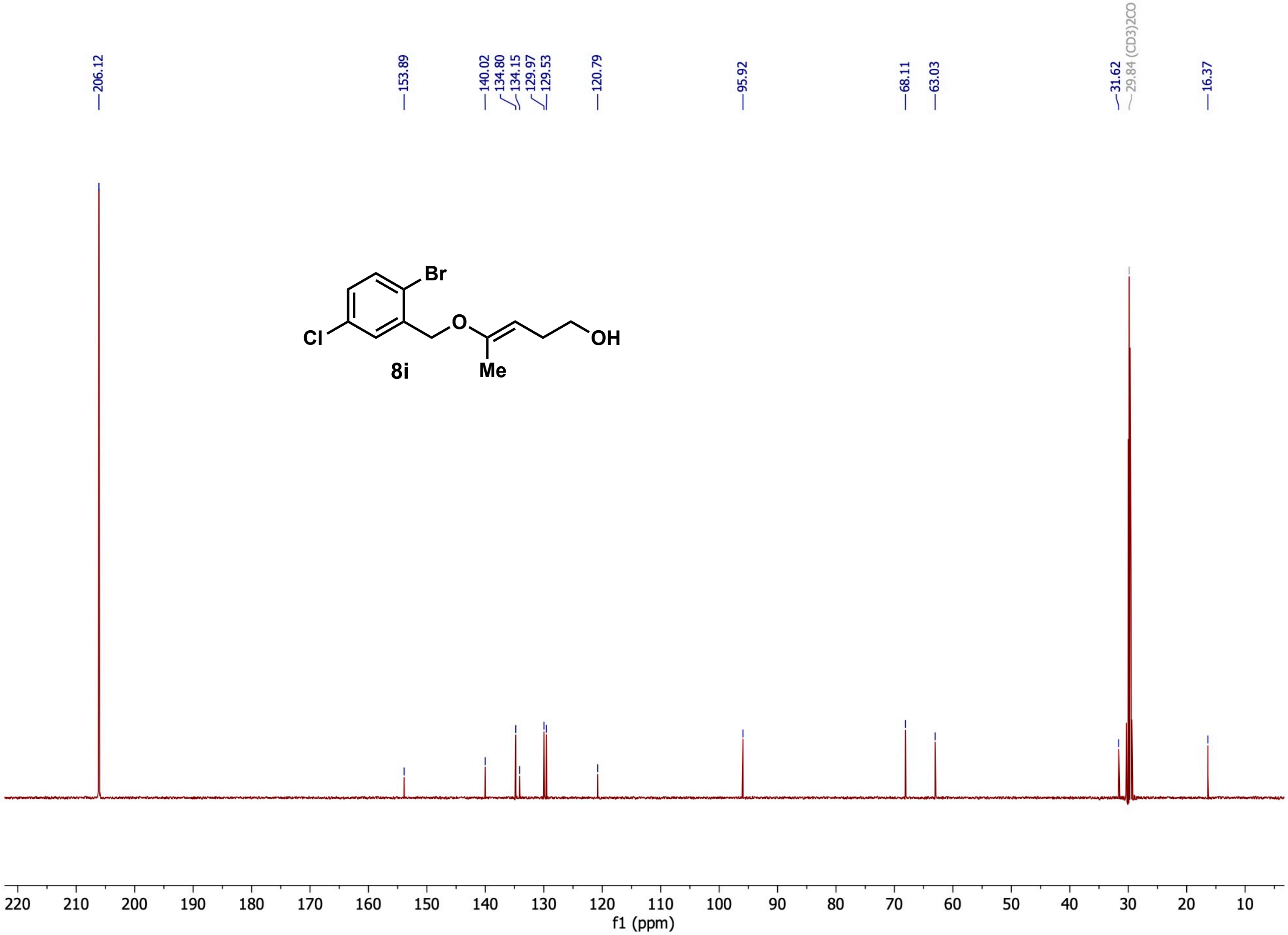


Figure S127. ^{13}C NMR of compound **8i** (125.81 MHz, acetone-*d*6).

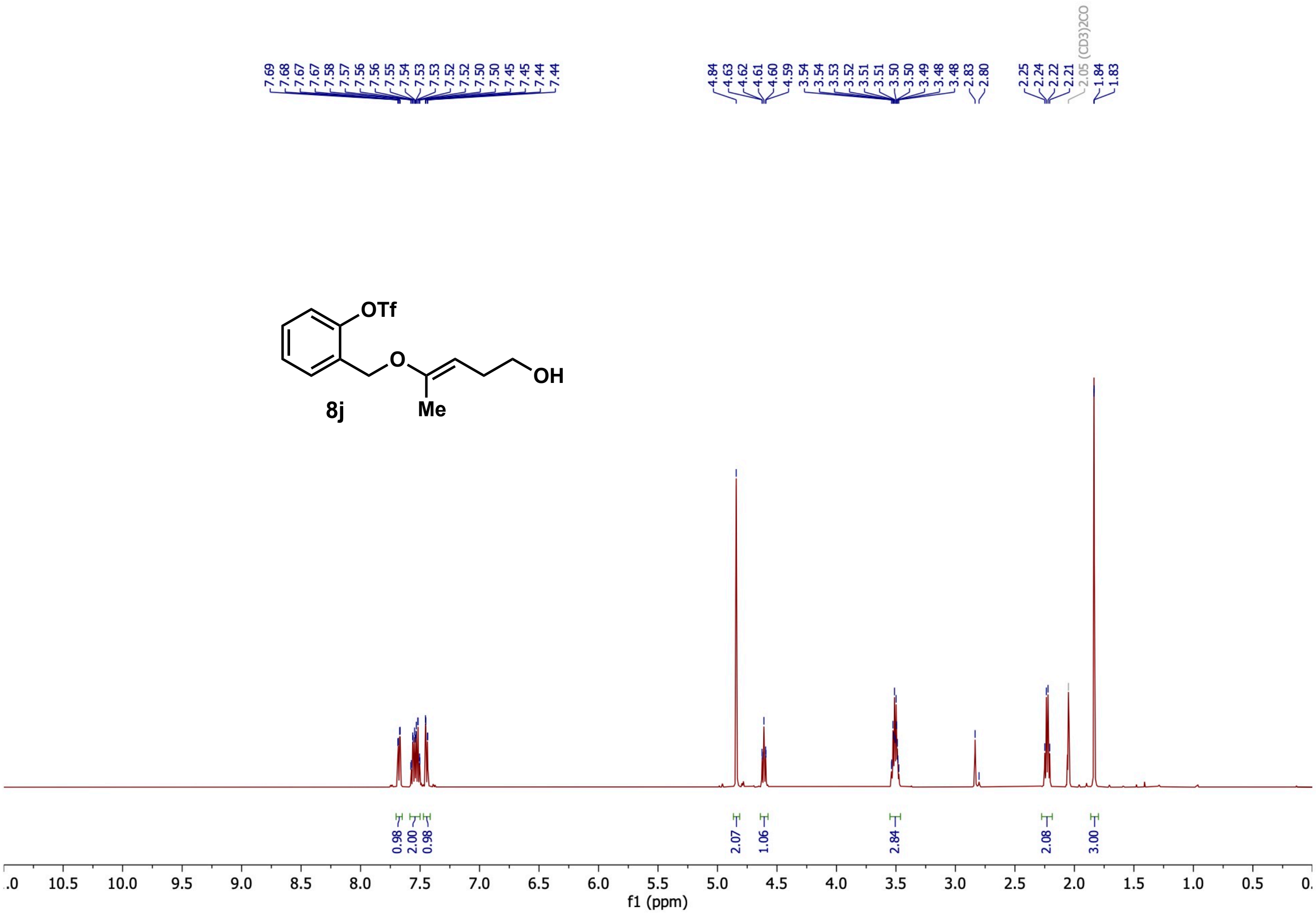


Figure S128. ^{1}H NMR of compound **8j** (500.27 MHz, acetone-*d*6).

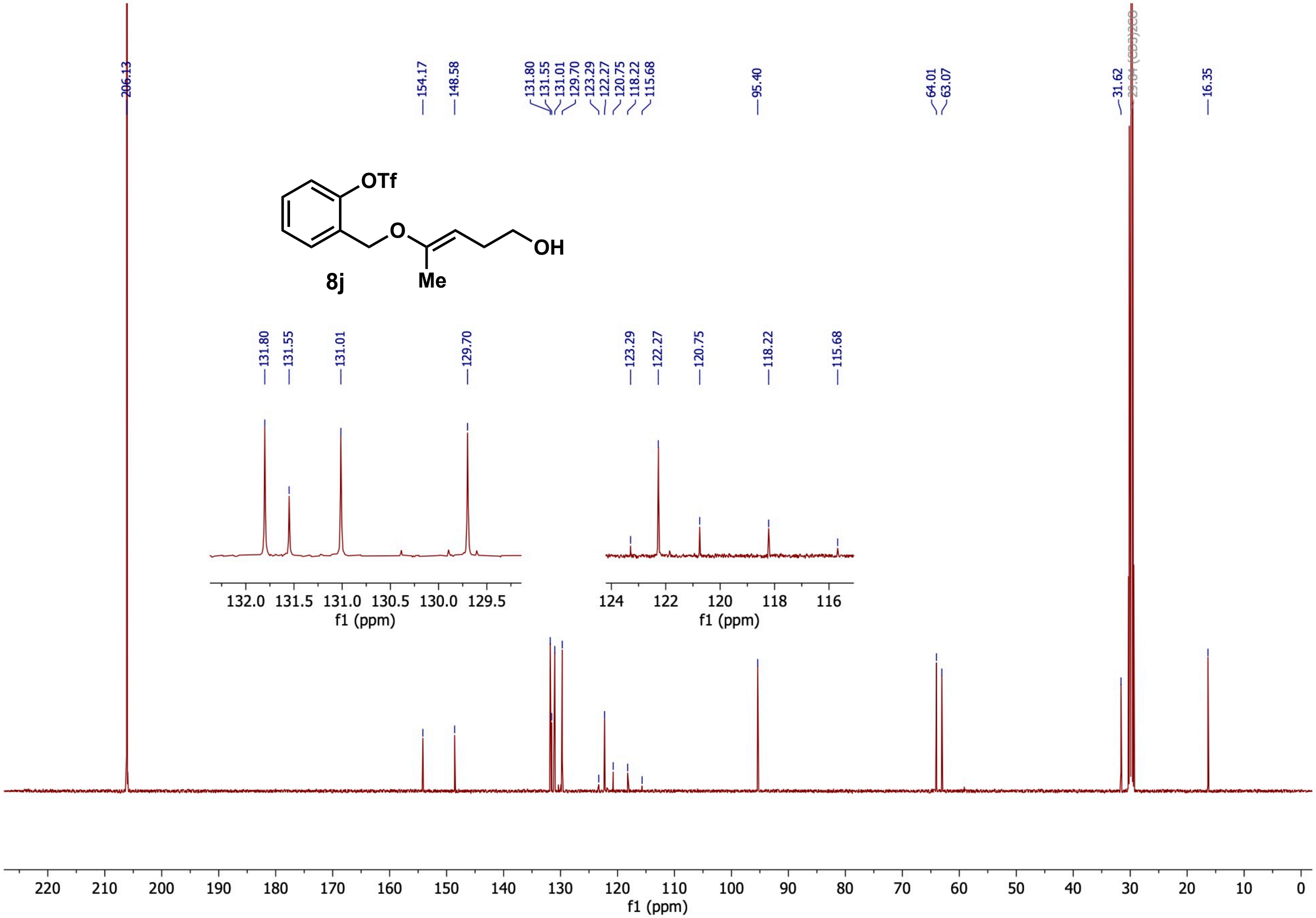


Figure S129. ^{13}C NMR of compound **8j** (125.81 MHz, acetone-*d*6).

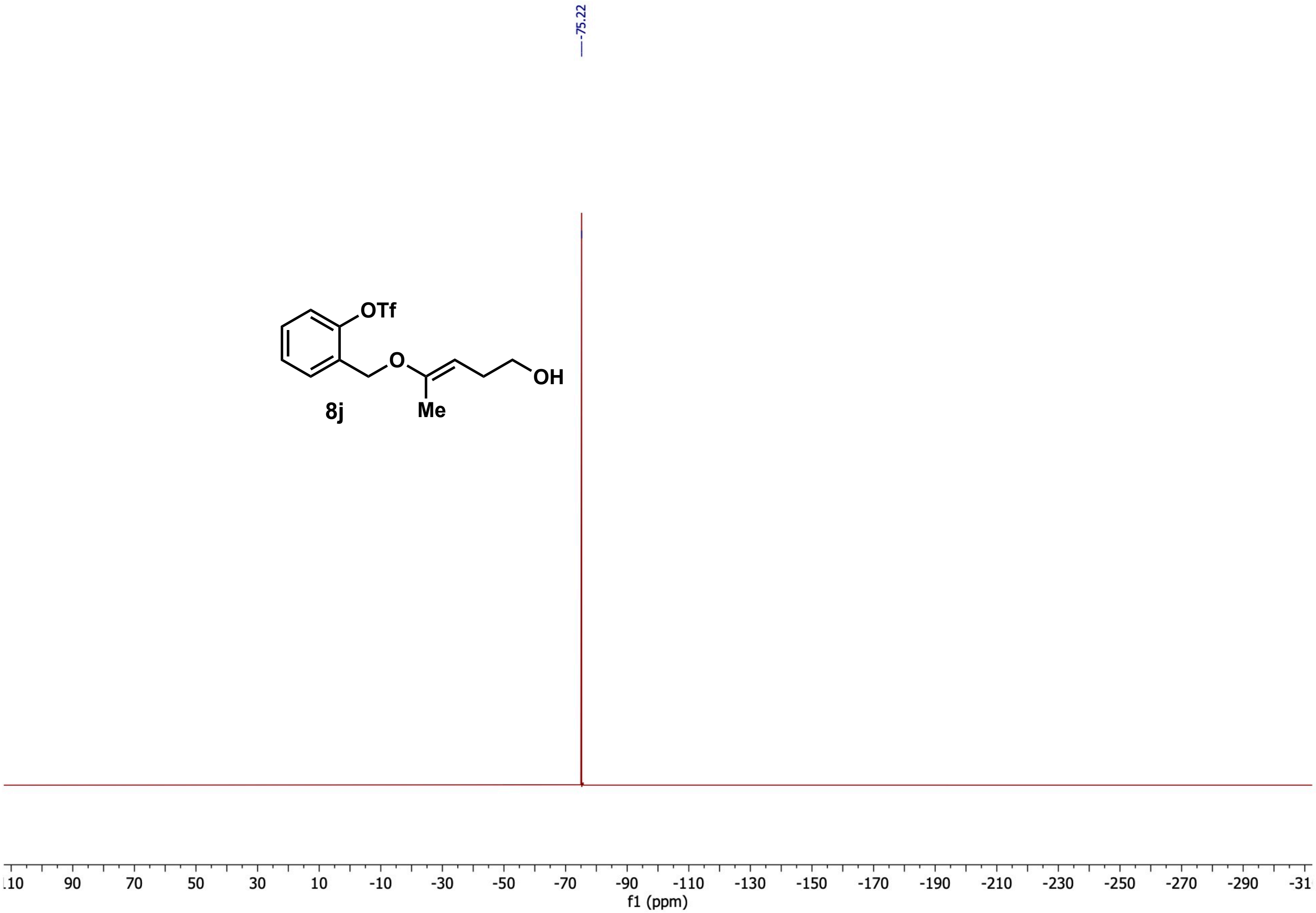


Figure S130. ^{19}F NMR of compound **8j** (470.68 MHz, acetone-*d*6).

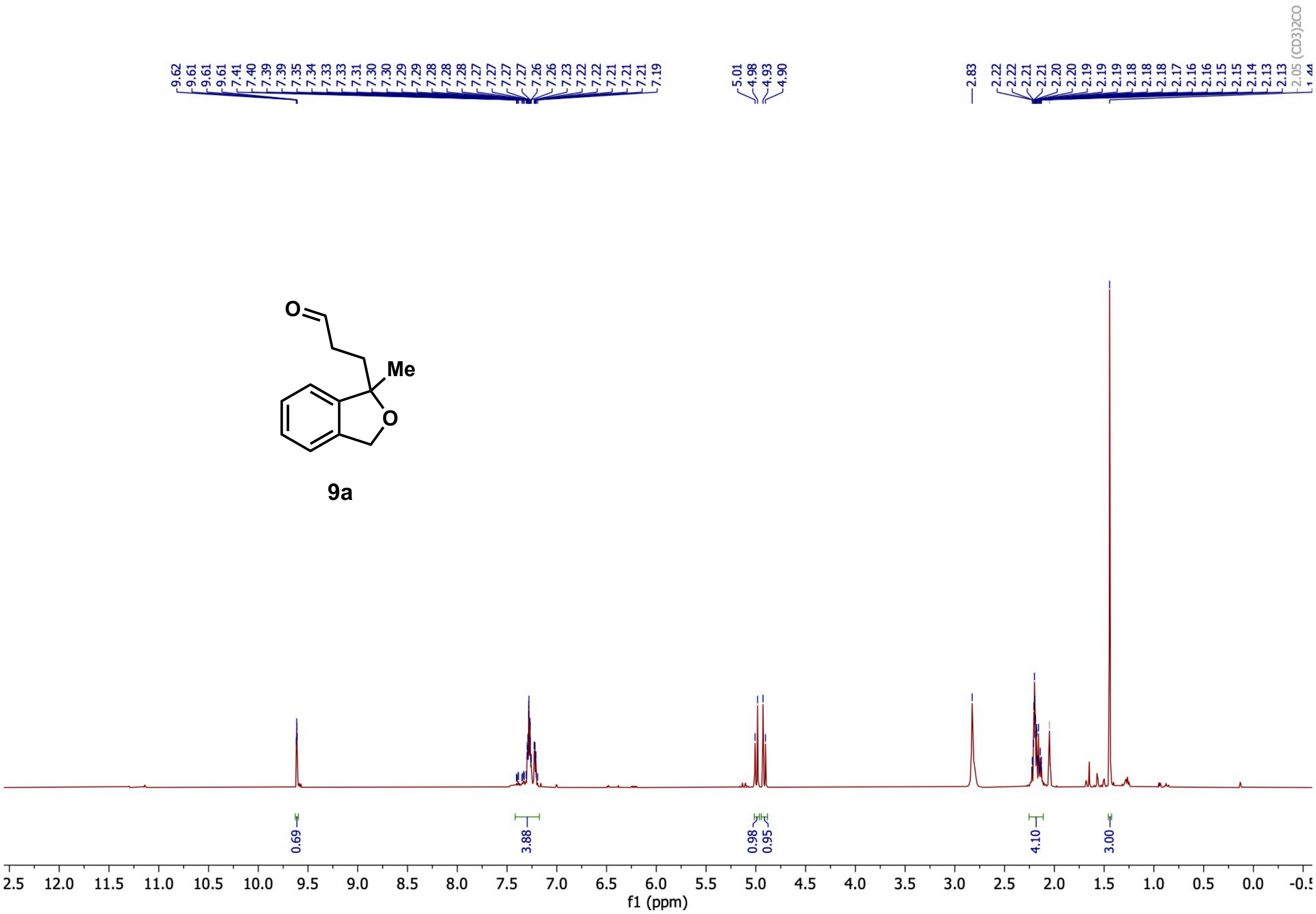


Figure S131. ^{1}H NMR of compound **9a** (500.27 MHz, acetone-*d*6).

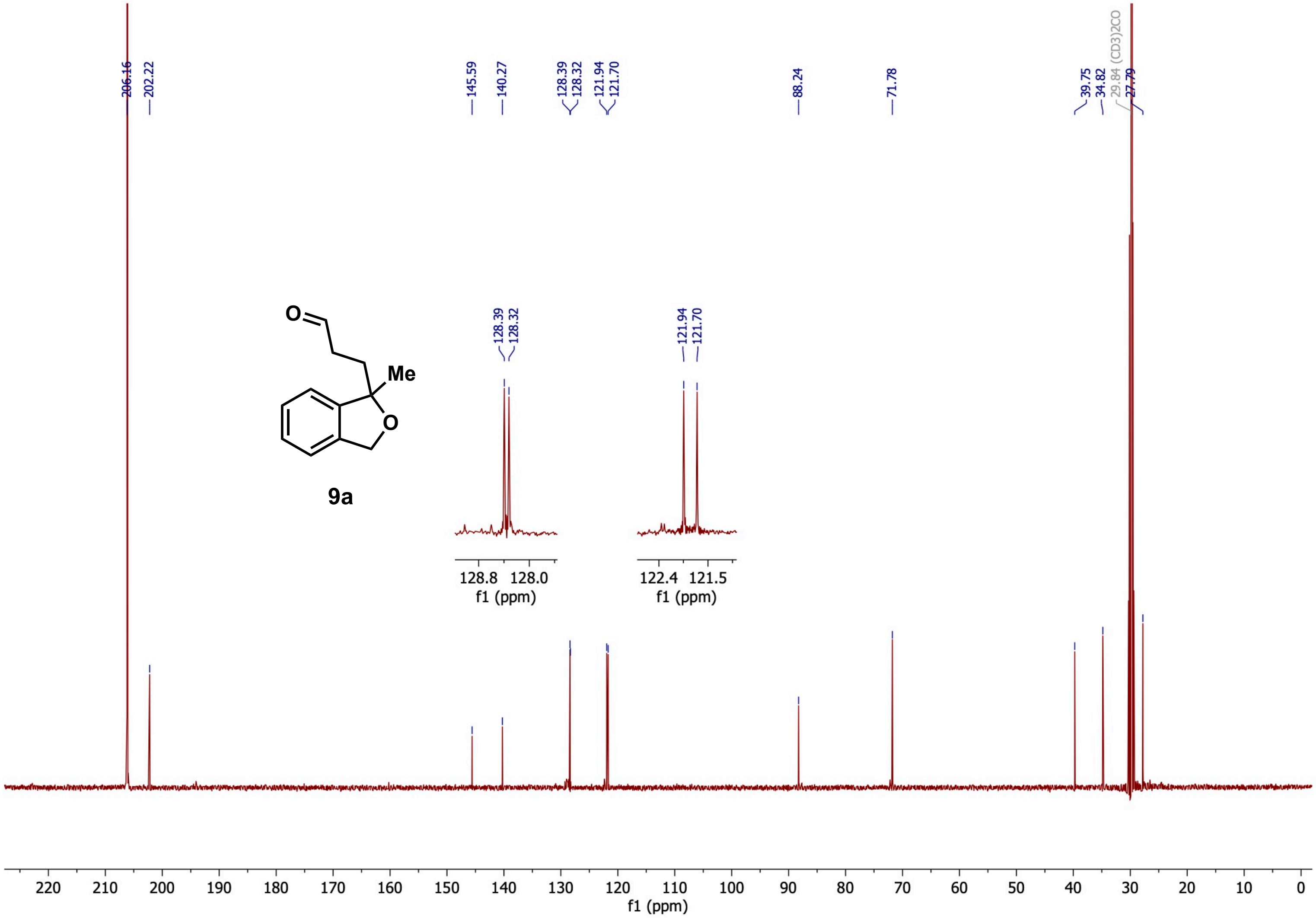


Figure S132. ^{13}C NMR of compound **9a** (125.81 MHz, acetone-*d*6).

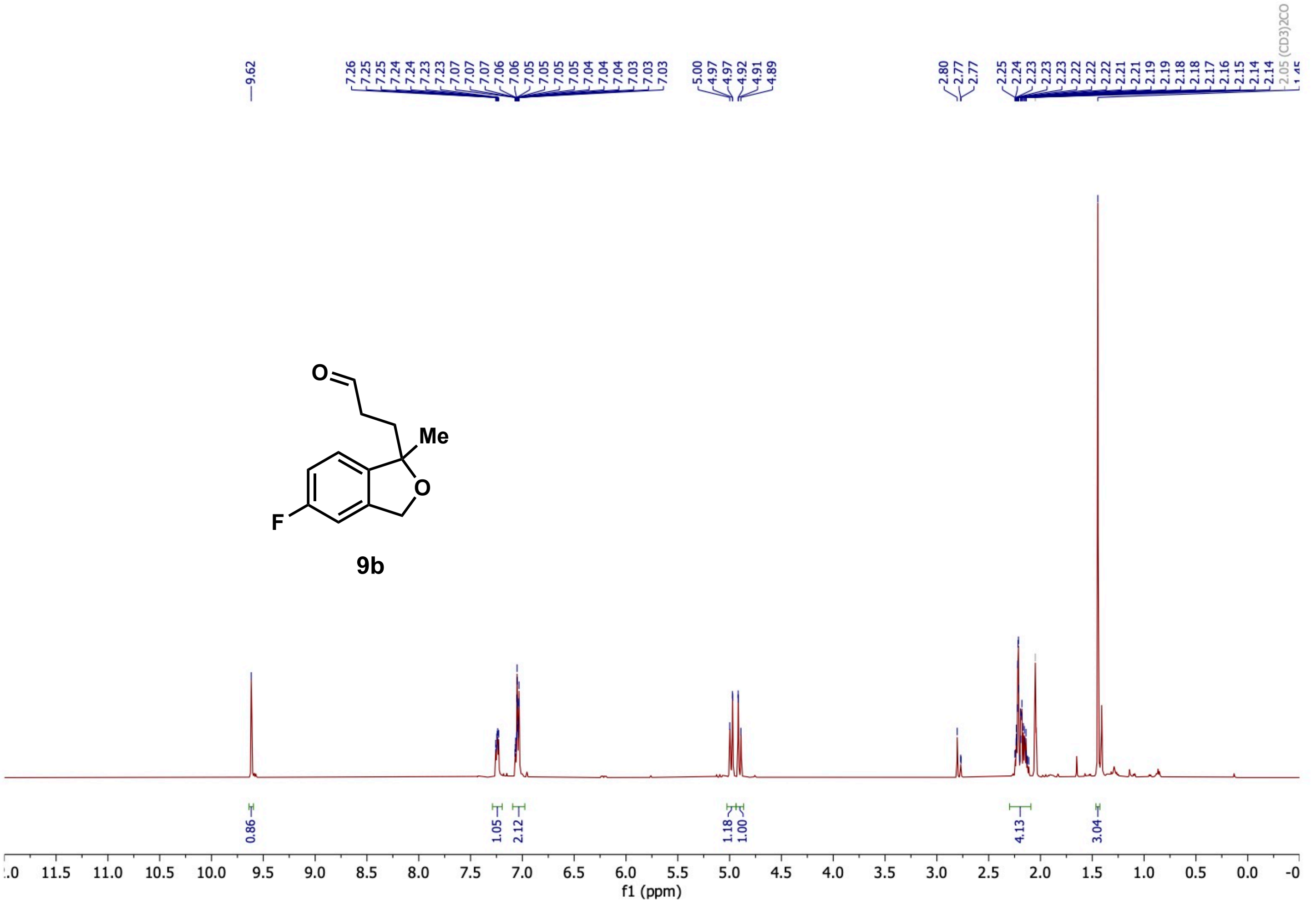


Figure S133. ^{1}H NMR of compound **9b** (500.27 MHz, acetone-*d*6).

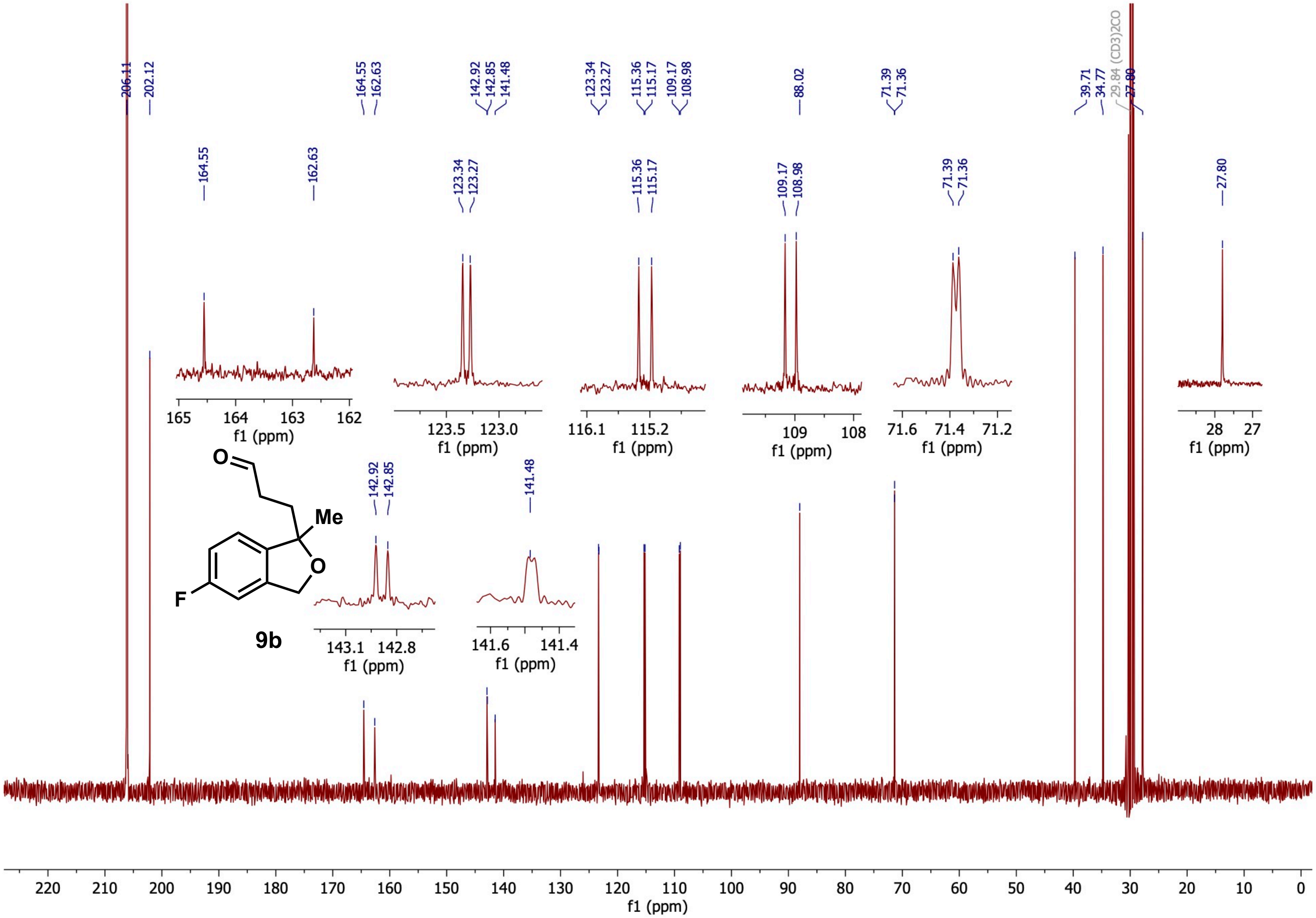


Figure S134. ^{13}C NMR of compound **9b** (125.81 MHz, acetone-*d*6).

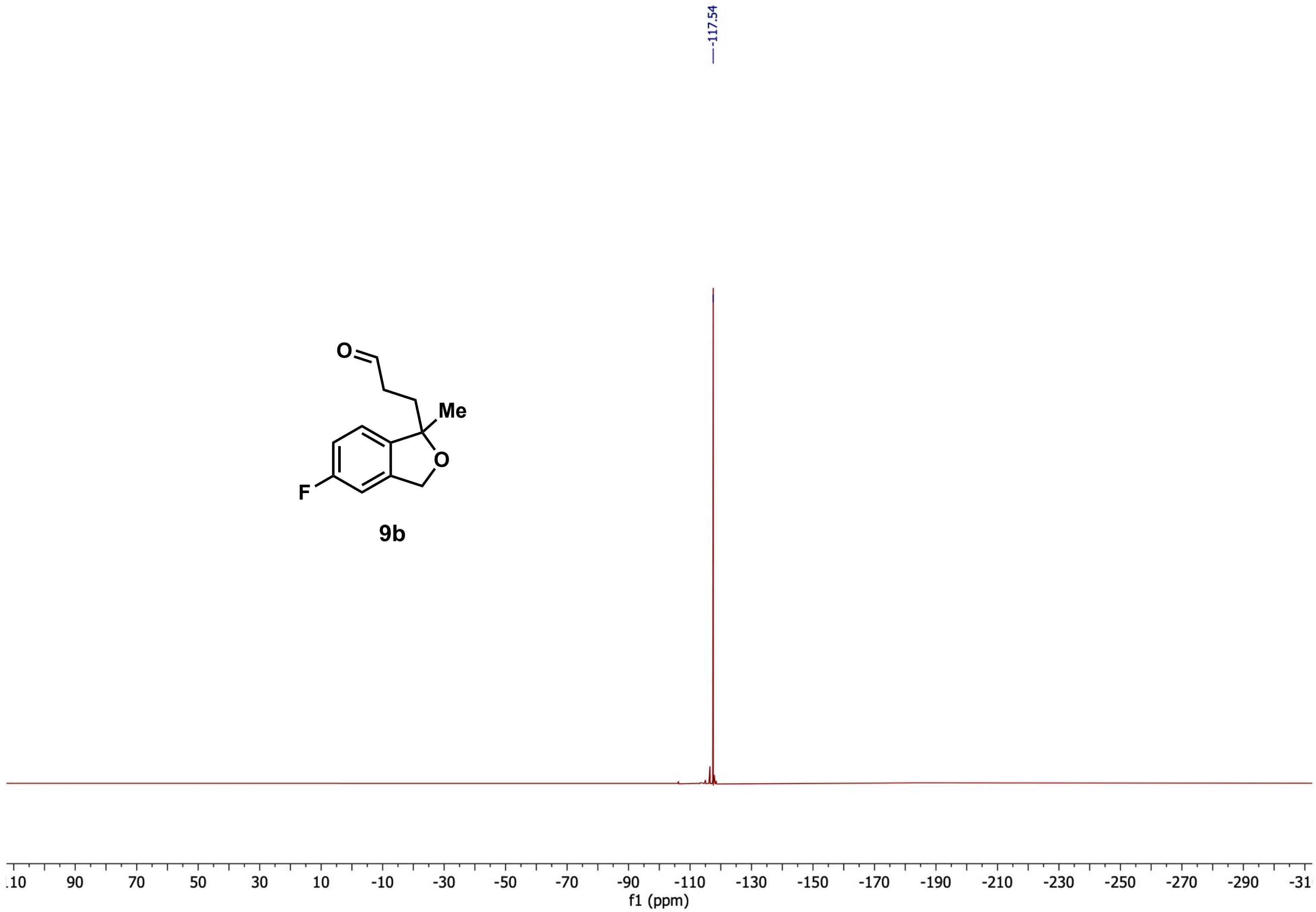


Figure S135. ^{19}F NMR of compound **9b** (470.68 MHz, acetone-*d*6).

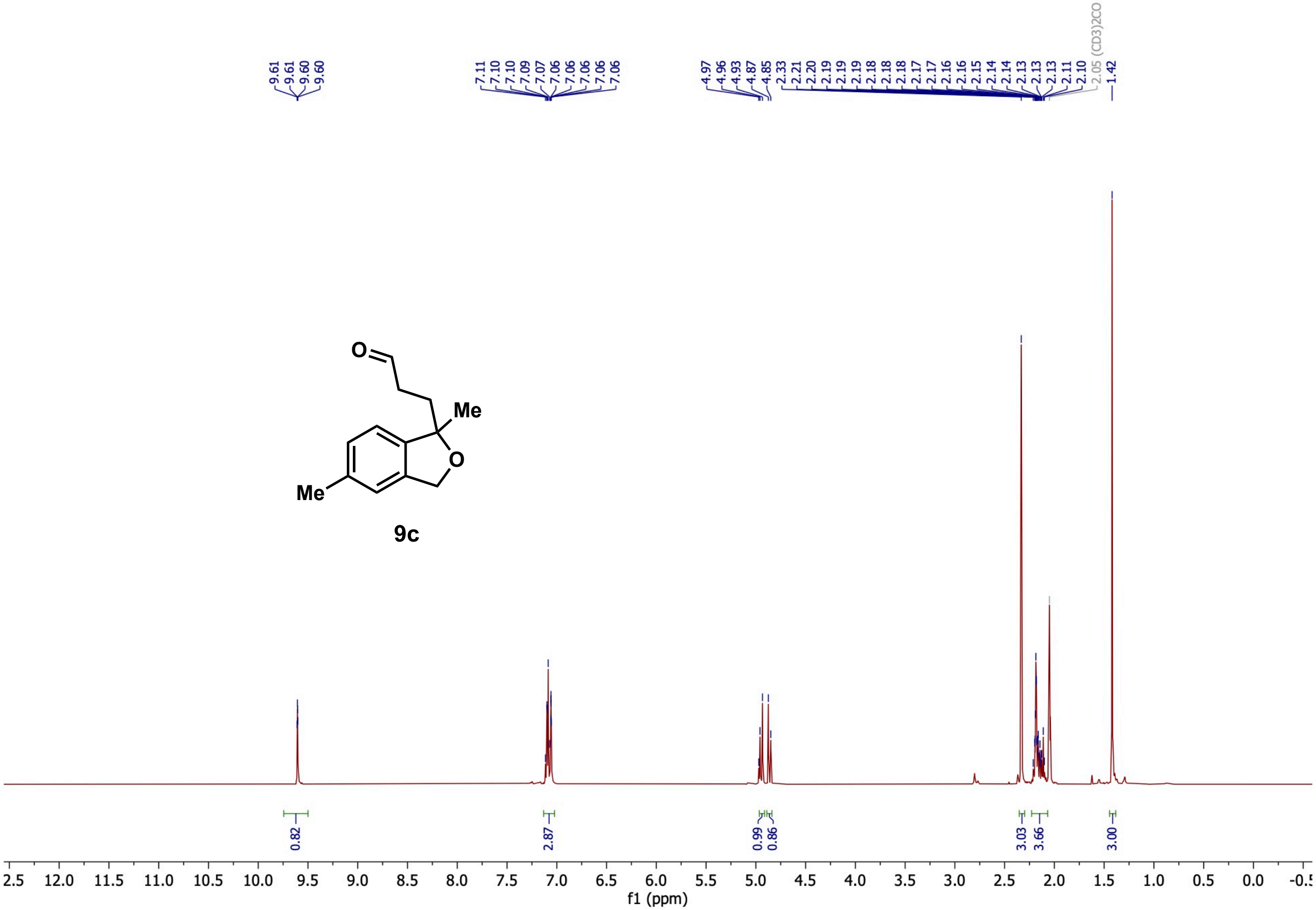


Figure S136. ^{1}H NMR of compound **9c** (500.27 MHz, acetone-*d*6).

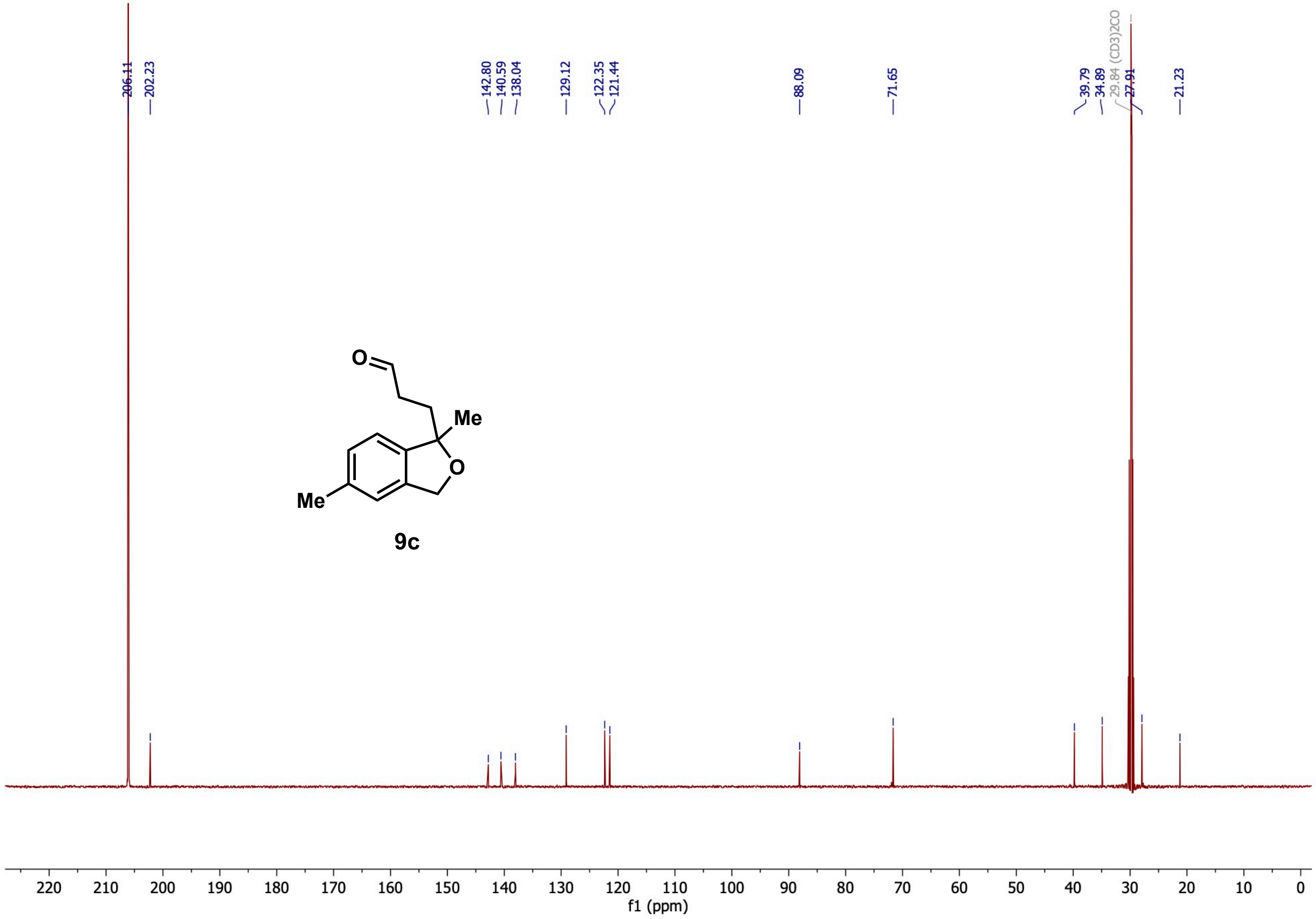


Figure S137. ^{13}C NMR of compound **9c** (125.81 MHz, acetone-*d*6).

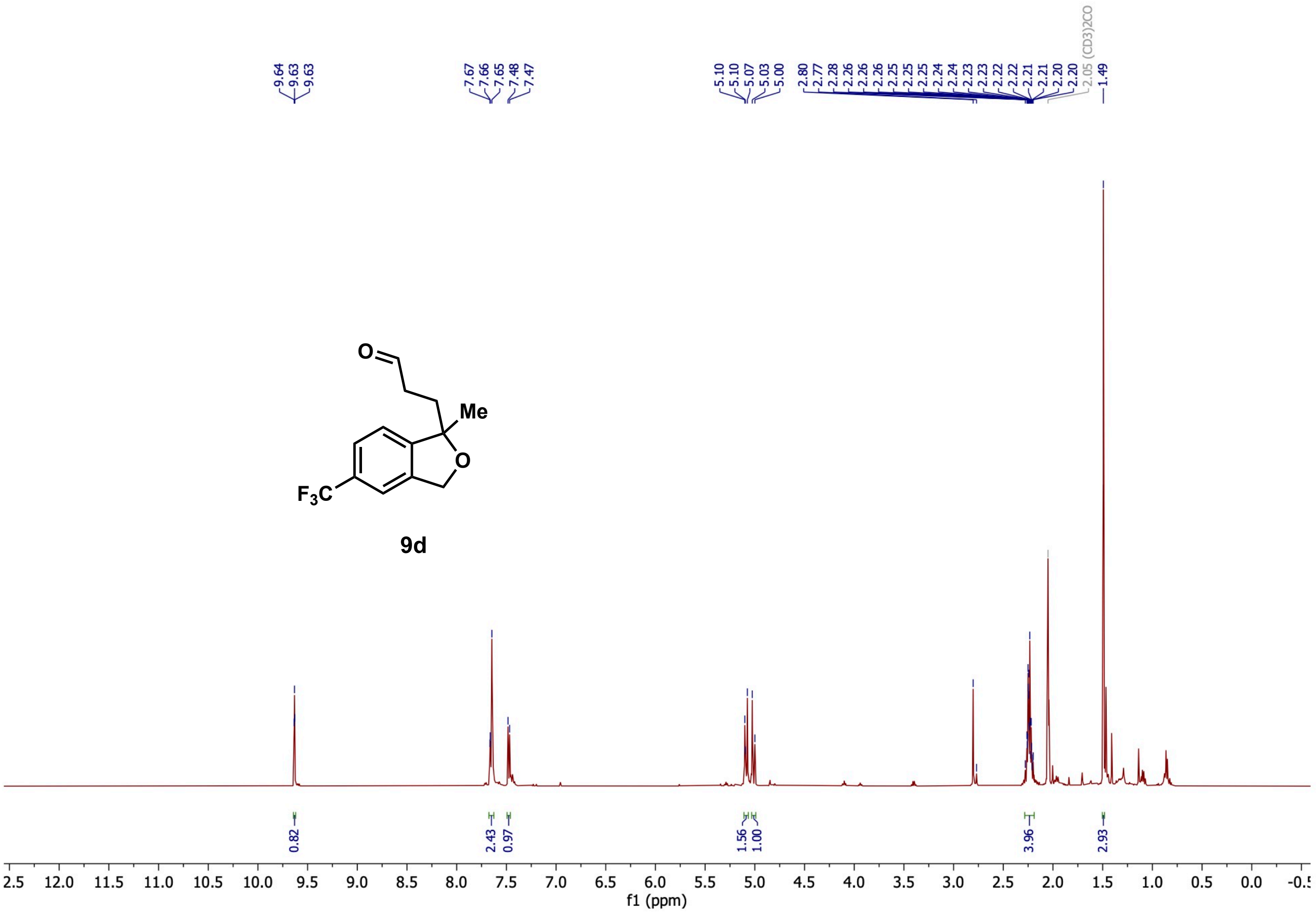


Figure S138. ^{1}H NMR of compound **9d** (500.27 MHz, acetone-*d*6).

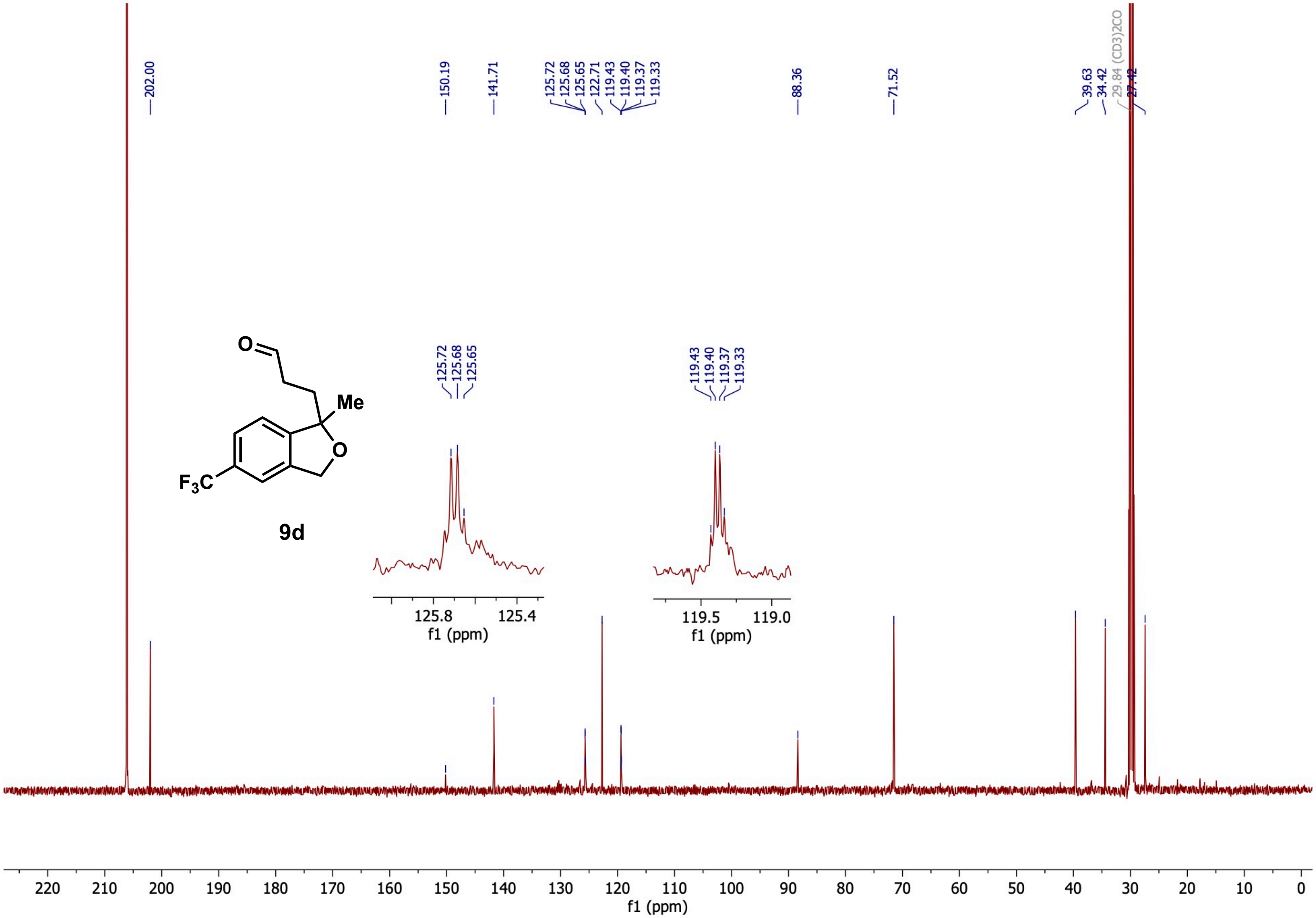


Figure S139. ^{13}C NMR of compound **9d** (125.81 MHz, acetone-*d*6). The expected quartets for the CF_3 carbon and ipso-CF_3 carbon on the aromatic ring were not observed due to a low signal-to-noise ratio.

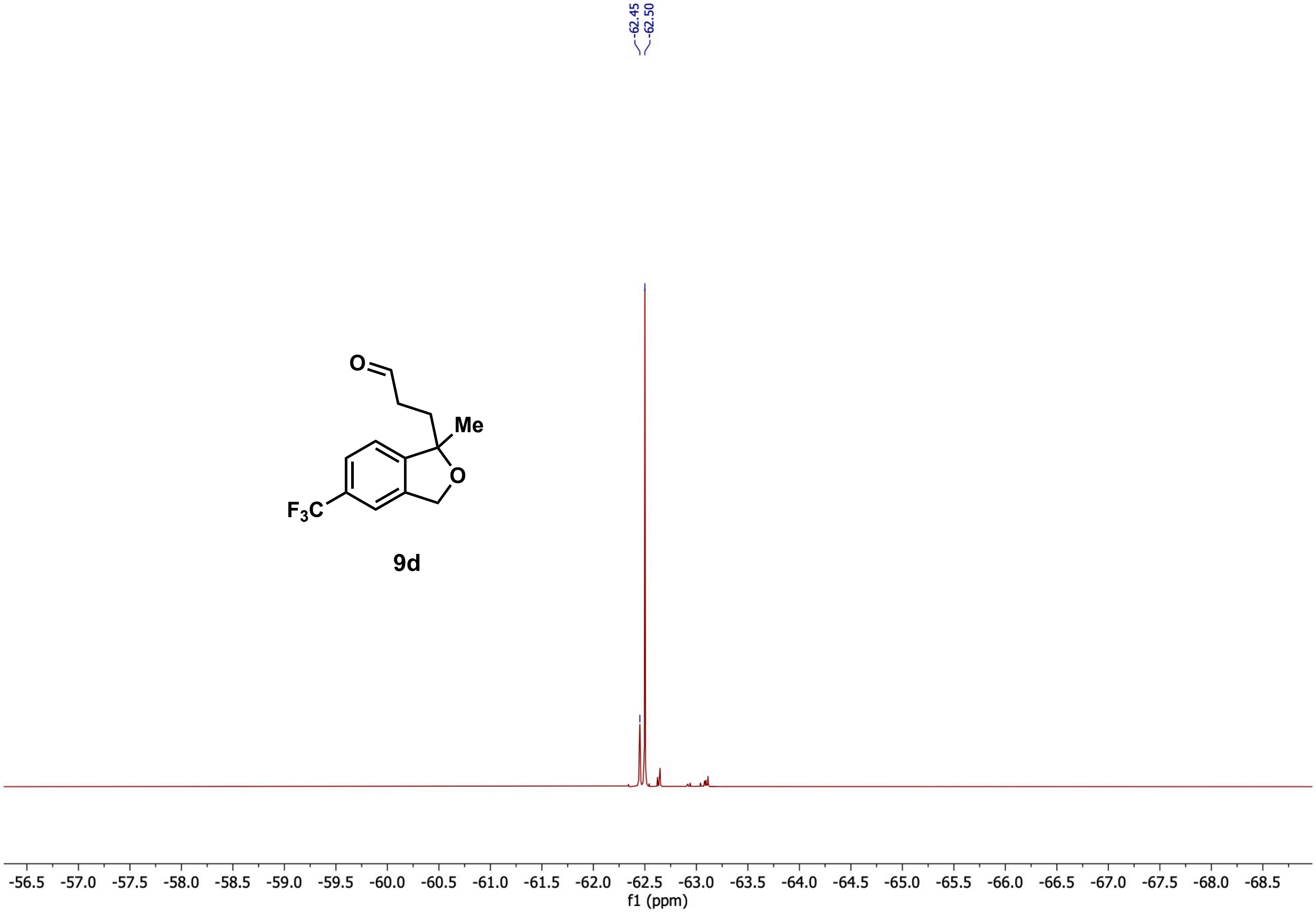


Figure S140. ^{19}F NMR of compound **9d** (470.68 MHz, acetone-*d*6).

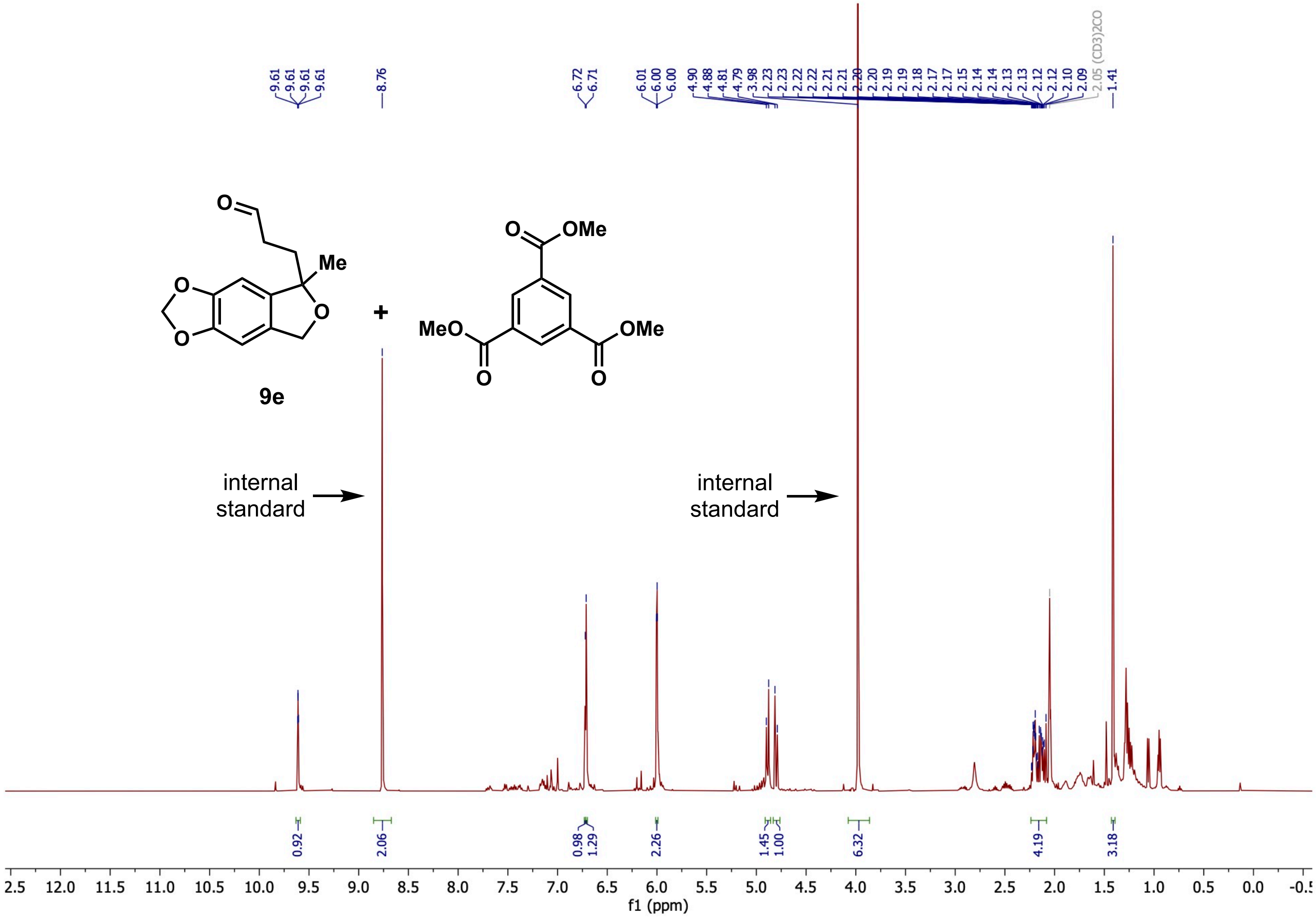


Figure S141. Crude ¹H NMR of **9e** with trimethyl 1,3,5-benzenetricarboxylate internal standard (500.27 MHz, acetone-*d*6).

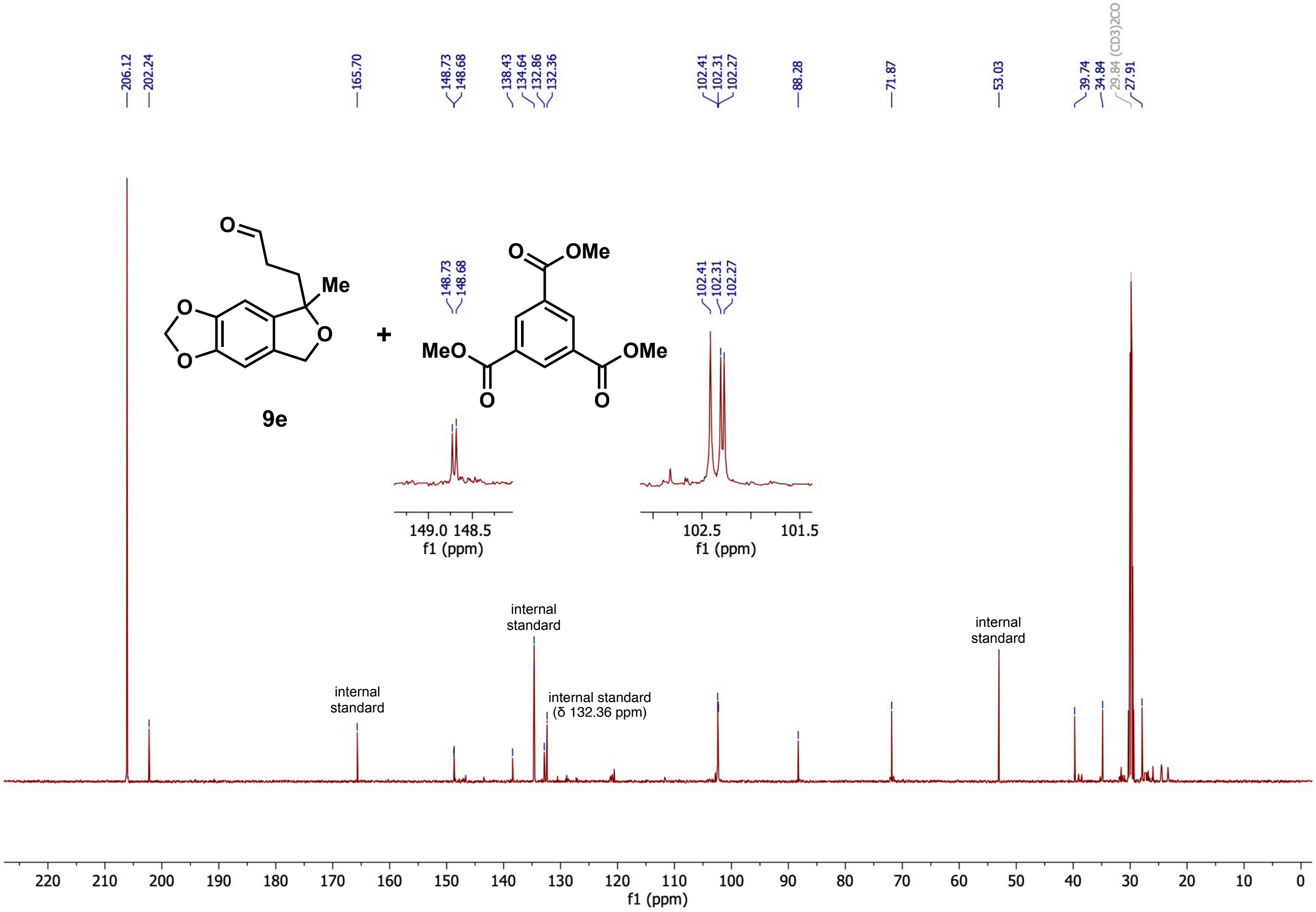


Figure S142. Crude ^{13}C NMR of **9e** with trimethyl 1,3,5-benzenetricarboxylate internal standard (125.81 MHz, acetone-*d*6).

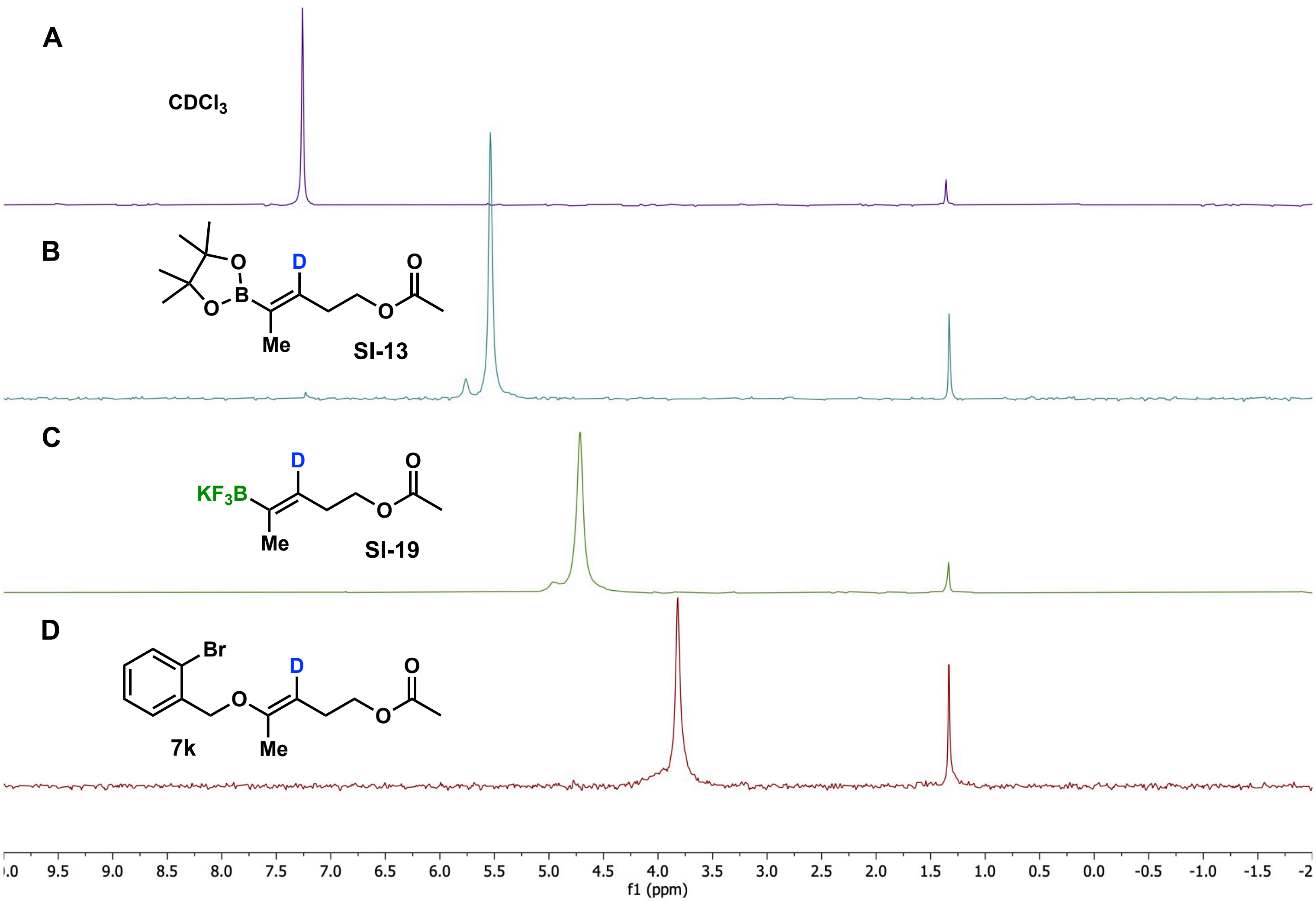


Figure S143. Overlaid $^2H\{^1H\}$ NMR (55.31 MHz, acetone-*h*6) of A) $CDCl_3$, B) **SI-13**, C) **SI-19**, D) compound **7k.**